ESCOLA DE DOUTORAMENTO
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Tese de doutoramento

POLYCYCLIC AROMATIC HYDROCARBONS (PAHs) CONTAINING BIPHENYLENE AND CYCLOOCTATETRAENE UNITS

Santiago de Compostela, 2024

Programa de Doutoramento en Ciencia e Tecnoloxía Química

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PROGRAMA DE DOUTORAMENTO EN CIENCIA E TECNOLOXÍA QUÍMICA

SANTIAGO DE COMPOSTELA

2024

Table of contents

1. Abbreviations and acronyms

Ac	Acetyl	DMF	N,N-Dimethylformamide
AcOH	Acetic acid	DME	1,2-Dimethoxyethane
Ad	Adamantyl	DMSO	Dimethyl sulfoxide
AIBN	Azobisisobutyronitrile	DPEPhos	Bis[(2-Diphenylphosphino)phenyl] ether
Ar	Aryl	dppf	1,1′-Ferrocenediyl-bis(diphenylphosphine), dppf
BINAP	(2,2′-bis(diphenylphosphino)-1,1′-binaphthyl)	Et_3N	Triethylamine
BQ	1,4-Benzoquinone	EtOAc	Ethyl acetate
CI	Chemical ionization	GC	Gas Chromatography
Cp	Pentamethyl cyclopentadienyl	GPC	Gel Permeation Chromatography
Cp*	1,2,3,4,5-pentamethyl cyclopentadienyl	HPLC	High-Performance Liquid Chromatography
cod	1,5-cyclooctadiene	HMBC	Heteronuclear Multiple Bond Correlation
COSY	Homonuclear Correlation Spectroscopy	HMO	Hückel Molecular Orbital
COT	Cyclooctatetraene	HRMS	High-Resolution Mass Spectrometry
DavePhos	2-Dicyclohexylphosphino-2′-(N,N-dimethylamino)bipheny	HSQC	Heteronuclear Single Quantum Coherence
dba	Dibenzylideneacetone	JohnPhos	(2-Biphenyl)di-tert-butylphosphine
DCE	1,2-dichloroethane	L	Ligand
DCM	dichloromethane	LUMO	Lowest Unoccupied Molecular Orbital
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone	[M]	Metal
DFT	Density Functional Theory	MS	Molecular sieves
DHB	Dihydrobiphenylene	MS	Mass Spectrometry
DHTP	4,4′′-dibromo-2,2′,2′′,5,5′,5′′-hexafluoro-1,1′:4′,1′′-terphenyl	MW	Microwave
DIB	1,3-diphenylisobenzofurane	nbd	Norbornadiene
DIPEA	N,N-Diisopropylethylamine	NBS	*N*-Bromosuccinimide
DMAP	4-Dimethylaminopyridine	NCS	*N*-Chlorosuccinimide
DMAD	Dimethyl acetylenedicarboxylate	NIS	*N*-Iodosuccinimide

NICS	Nucleus Independent Chemical Shift
NMR	Nuclear Magnetic Resonance
o/n	Overnight
PAH	Polycyclic Aromatic Hydrocarbon
PCC	Pyridinium chlorochromate
Ph	Phenyl
PPTS	Pyridinium p-toluenesulfonate
Phox	[2-(Diphenylphosphino)phenyl]-2-oxazoline
Ref.	Reference
rt	Room temperature
TBAB	Tetra-n-butylammonium bromide
TBAF	Tetra-n-butylammonium fluoride
TBAI	Tetra-n-butylammonium iodide
^{t}Bu	tert-butyl
TCE	1,1,2,2-Tetrachloroethane
TEMPO	(2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
Tf	Trifuoromethanesulfonyl
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMC	Transition metal catalysed
TMS	Trimethylsilyl
TMSA	Trimethylsilylacetylene
Ts	Tosyl
Trityl	Triphenylmethyl
TS	Transition state
SPhos	2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl
Xantphos	4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene
Xphos	[2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl]

Units/Symbols

Å	Angstrom
^{o}C	Degree Celsius
Hz	Hertz
Cal	Calorie
g	Gram
L	Liter
M	Molar
mol	mole
ppm	Parts per million
Δ	Heat
hν	Light
m/z	mass/charge relationship

2. Resumo

O desenvolvemento de novas metodoloxías sostibles para a preparación de compostos e materiais orgánicos segue sendo de grande interese para a sociedade, onde a posta en marcha de métodos sintéticos "limpos" é unha esixencia das sociedades modernas.

A preparación de estruturas moleculares complexas cunha xeración mínima de residuos requiren de metodoloxías sintéticas eficientes que empreguen como materiais de partida substratos sinxelos e de fontes renovables. As reaccións catalíticas permiten activar este tipo de substratos dunha forma selectiva para transformalos en moléculas máis complexas cun alto valor engadido. Entre as metodoloxías catalíticas coñecidas, aquelas baseadas na catálise organometálica destacan pola súa eficiencia.

Desde comezos do século XX, o incremento da calidade de vida das persoas acentuouse grazas ao avance no deseño de fármacos e de novos materiais motivado en gran parte pola investigación en catálise organometálica. Co fin de avanzar cara a sostibilidade nos diferentes métodos de produción, as ferramentas sintéticas empregadas baséanse na catálise (organometálica, organocatálise e procesos foto-redox), que en contraste ás sínteses clásicas, non xeran grandes cantidades de residuos contaminantes e prexudiciais para o medio ambiente. A sociedad actual continúa enfrontándose a retos biomédicos e tecnolóxicos como o cancro, enfermedades neurodexenerativas ou desordes metabólicos que, sen duda, conleva novas investigación en catálise.

No contexto dos novos materias a aparición de diferentes alótropos do carbono, como o grafeno, os fullerenos ou os nanotubos de carbono revolucionaron o campo de traballo. Ditas estruturas poden ser obtidas de forma descendente (aproximación "top-down"), sen un control sobre a periferia, ou de forma ascendente (aproximación "bottom-up"), que si permite controlar diferentes características do material (*band gap*, anchura...). Neste último, a introdución de aneis cun tamaño diferenciado permite modificar ou incluso mellorar as propiedades dos sistemas aromáticos. Deste xeito foi posible a incorporación de subunidades antiaromáticas de tipo bifenileno e ciclooctatetraeno no deseño de novos alótropos de grafeno con propiedades diferenciadas. Mentres os ciclooctatetraenos (COTs) foron preparados por primeira vez en 1911 polo grupo de Willstater, as estruturas bifenilénicas foron obtidas inicialmente trinta anos despois polo grupo de Lathrop, e dende entón varias son as rutas de acceso aos mesmos, aínda que a maioría delas precisan condicións bastante drásticas (Tª elevadas, irradiación, etc).

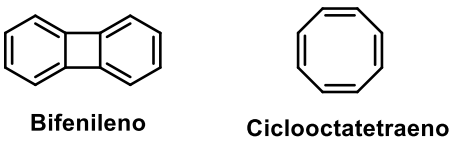


Figura 1. Núcleos de estudo propostos

Neste eido, o noso grupo de investigación desenvolveu no ano 2014 unha metodoloxía sintética de acceso a estruturas de tipo dihidrobifenileno **3** a partir de *o*-etinilestirenos **1** e alquinos terminais **2** catalizada por complexos de Ru (II). Se ben é certo que os núcleos de tipo 1,3-ciclohexadieno foron empregados de forma eficiente en reaccións de oxidación e en

cicloadicións Diels-Alder, estes compostos poderían ser considerados como potencias precursores de bifenilenos altamente funcionalizados mediante procesos de oxidación.

Tendo en conta a metodoloxía descrita polo grupo, no primeiro capítulo da presente tese doutoral recóllese un estudo máis amplo da reactividade de novos *o*-etinilestirenos (eninos), **1**, así como de alquinos internos e/ou con heteroátomos, **2**. Dos resultados obtidos pódese concluír que se ben os alquinos terminais ricos en electróns participaron nas cicloadicións [2+2+2] catalizadas por complexos de Ru (II), aqueles non terminais ou con heteroátomos deron lugar á dimerización dos eninos de partida ou a formación de produtos secundarios orixinados pola presencia do catalizador de Ru. De forma similar estudouse a reactividade dunha serie de eninos substituídos. Os *o*-etinilestirenos que presentan un grupo rico en electróns en posición relativa *para* á olefina ou un segundo grupo etinil en posición *para* relativa ao alquino do enino non participaron na ciclación promovida por Ru. Este feito podería ser explicado atendendo á reactividade non esperada do grupo vinilo e grupo etinilo causada pola presenza dun sistema dador (OMe) ou pola posibilidade de polimerización do substrato inicial. Este feito foi comprobado experimentalmente ca incorporación dun segundo grupo vinilo reactivo, o que modificou dramaticamente a reactividade facilitando unha segunda cociclación e evitando o posible proceso de polimerización para dar lugar de xeito eficiente ao correspondente bis-enino. A maiores estudouse a posibilidade de introducir átomos de nitróxeno tanto nos *o*-etinilestirenos como nos alquino de partida empregados co fin de ter acceso a sistemas de tipo aza-dihidrobifenileno, o que podería modificar as súas propiedades e/ou reactividade motivado pola presenza de heteroátomos. Desafortunadamente todos os intentos de xerar estes núcleos foron infrutuosos.

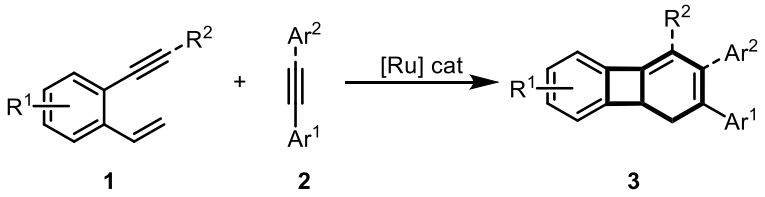


Figura 2. Cicloadición [2+2+2] catalizada por Ru entre o-etinilestirenos e alquinos para a síntese de dihidrobifenilenos.

Durante o segundo capítulo da tese levouse a cabo o estudo da reactividade dos núcleos 1,3-ciclohexadieno presentes nos dihidrobifenilenos **3** co obxectivo de acceder a sistemas bifenilénicos mediante procesos de oxidación. En primeiro lugar analizouse a ruta deshidroxenativa empregando oxidantes tales como MnO_2, DDQ ou SeO_2 entre outros. Sen embargo todos os intentos de obtención de bifenilenos deron lugar á recuperación da sustancia de partida ou a formación de mesturas complexas. Como segunda alternativa pensamos na funcionalización da posición alílica do 1,3-ciclohexadieno para posteriormente formar o bifenileno obxectivo mediante unha reacción de eliminación. No ano 2004, a Prof. Christina White reportou a síntese rexioselectiva de acetatos alílicos mediante a oxidación do enlace C-H en presenza de BQ, AcOH e cantidades catalíticas de Pd(II). Para a nosa sorpresa, o emprego das condicións de funcionalización C-H sobre os nosos dihidrobifenilenos non deron lugar ao produto de oxidación alílica esperado, se non que se obtivo un ciclooctatetraeno benzofusionado **11** caracterizado pola combinación dun núcleo aromático e un non-aromático. A formación do sistema ciclooctatetraénico pode explicarse pola presenza do Pd no medio de

reacción. A coordinación da BQ e do sistema diénico do dihidrobifenileno de partida ao centro metálico permiten o ataque nucleófilo do grupo acetato para dar lugar a un 1,3-ciclohexadieno intermedio que orixina o produto observado a través dunha apertura electrocíclica de seis electróns. Este composto foi obtivo en baixo rendemento e pese á multitude de variación levadas a cabo nas condicións de reacción non foi posible incrementar a eficiencia da transformación cara a formación do novo sistema. Alternativamente, explorouse a funcionalización alílica mediante a haloxenación radicalaria empregando NBS e AIBN. No canto de illar o produto de funcionalización alílica obtívose de novo un ciclooctatetraeno benzofusionado **16**, pero esta vez en moi bo rendemento e ca incorporación dun átomo de Br, o que lle outorga valor de cara a futuras manipulacións.

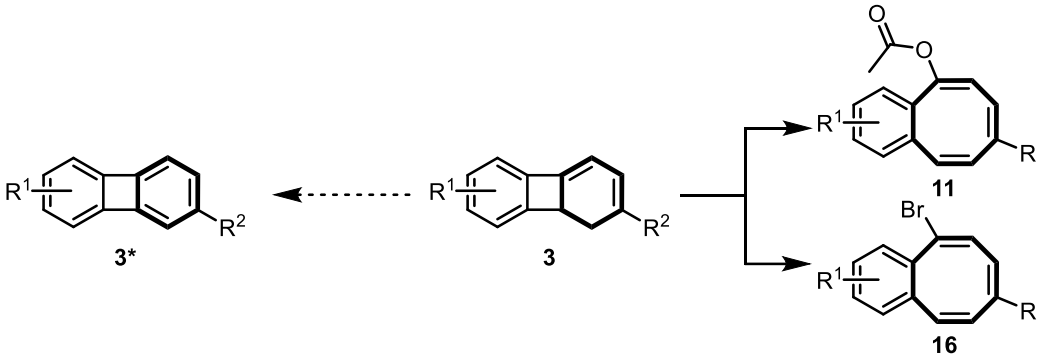


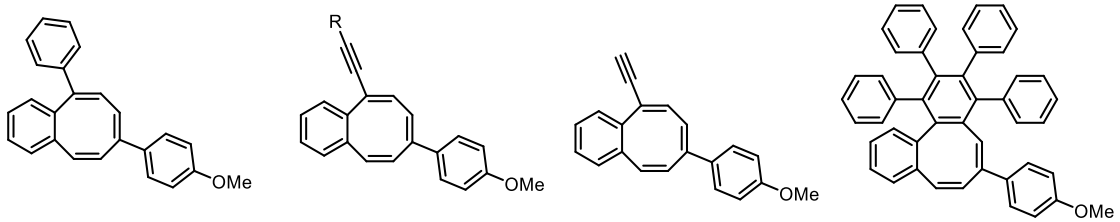
Figura 3. Estudos de oxidación dos núcleos 1,3-ciclohexadieno presentes nos dihidrobifenilenos.

Con estes últimos resultados decidiuse explorar dita transformación dende un punto de vista experimental e tamén computacional. O Prof. Jesús Varela levou a cabo cálculos DFT para unha mellor comprensión do mecanismo de reacción presente. En primeiro lugar elucidouse a formación selectiva do radical inicial mediante o cálculo da enerxía de disociación de enlace (BDE) dos dous tipos de H alifáticos presentes no núcleo central do dihidrobifenileno (terciario e secundario). De forma xeral, a formación dun radical terciario require menor enerxía que un secundario, máis a presenza do sistema ciclobuteno xera un cambio dramático na formación selectiva do radical, facendo que o radical secundario e alílico sexa 4.3 Kcal/mol máis estable que o terciario, alílico e bencílico. A continuación, o radical secundario pode evolucionar seguindo tres diferentes rutas: a) apertura electrocíclica de seis electróns π (rotura enlace $C_{sp3\text{-}sp2}$, barreira de enerxía elevada, $\Delta G‡$ = 39.2 kcal/mol) seguido do atrapado radicalario polo bromo molecular xerado na reacción; b) apertura radicalaria do ciclobuteno seguido polo atrapado radicalario do Br_2 para dar lugar a un terfenilo (produto non observado); c) bromación radicalaria do radical secundario inicial que pode dar lugar a tres estruturas bromadas resultado do atrapado radicalario do bromo molecular (entre as tres posibles estruturas aquela que presenta o bromo en posición cabeza de ponte resulta ser a máis estable). Finalmente, unha apertura electrocíclica de seis electróns π da lugar ao ciclooctatetraeno benzofusionado **16** observado.

Paralelamente levouse a cabo a optimización das condicións de reacción cas que estudamos o alcance da formación de sistemas de oito membros. Dita transformación deu lugar a rendementos dende bos a moi bos empregando outros dihidrobifenilenos con grupos electrón dadores, aromáticos e en presenza de alquinos e olefinas. Tamén foi posible a obtención dos ciclooctatetraenos benzofusionados con diferentes halóxenos (eficiencia da reacción reducida)

empregando as correspondentes halo-succinimidas. Desafortunadamente, dihidrobifenilenos con grupos electrón atraentes deron lugar á mesturas complexas de reacción. Finalmente foi posible levar a cabo un proceso tándem (cicloadición [2+2+2]/apertura radicalaria) dende o enino inicial sen necesidade de illar o dihidrobifenileno intermedio. Para rematar o alcance da reacción levouse a cabo de forma exitosa a síntese dun novidoso benzodiciclooctatetraeno (benzodiCOT) cun núcleo que combina sistemas benzenoides (aromáticos) e non benzenoides (non-aromáticos) nunha fusión 8:6:8.

Co fin de demostrar a utilidade sintética dos novos sistemas obtidos leváronse a cabo unha serie de derivatizacións posteriores baseadas en reaccións organometálicas (Suzuki e Sonogashira) obtendo os produtos de acoplamento esperados en moi bos rendementos. Tamén se levaron a cabo reacción de cicloadición Diels-Alder empregando o ciclooctatetraeno benzofusionado empregado para a optimización así como o novidoso benzodiCOT, obtendo de novo moi bos resultados. Se ben as reaccións de acoplamento cruzado levadas a cabo se serven da presenza do halóxeno para ter lugar, as cicloadicións Diels-Alder orixínanse pola combinación dun 1,4-dieno co alquino xerado no anel de oito membros grazas a presenza dunha base externa. A presenza deste alquino no ciclooctatetraeno (COTino) da paso ao comezo do capítulo 3 onde se estudará a reactividade destes sistemas.



20 **22** R = *p*-$C_6H_4N(CH_3)_2$, **21** R = TMS **23** **26**

Figura 4.Unidades de HAPs contendo unidades de oito membros.

Os COTinos poden ser considerados como os análogos non aromáticos dos bencinos. A historia dos segundos é amplamente coñecida pola súa repercusión en eidos como a catálise ou ciencia de materias, eido no que destacan pola súa capacidade de xerar Hidrocarburos Aromáticos Policíclicos (HAPs) dunha infinidade de formas e tamaños. Estas especies reactivas reaccionan con multitude de dienos en reaccións de Diels-Alder, con acidas en reaccións 1,3-dipolares e incluso consigo mesmos en cicloadicións [2+2] mediante mecanismos radicalarios para dar lugar a bifenilenos. Dado que a alta reactividade dos bencinos pode ser "atenuada" ca súa complexación a centros metálicos, a finais do século XX desenvolvéronse as cicloadicións e cociclacións [2+2+2] catalizadas por complexos de Pd (0), o que permitiu estender o seu alcance e utilidade.

Pola contra, a química dos COTinos é moito máis discreta debido, en parte, á falta de metodoloxías sintéticas que permitan acceder a eles. Neste eido debemos ter en conta que os estudos existentes derivan dos desexos de comprender as súas propiedades electrónicas como a non-aromaticidade. Dende o COTino máis sinxelo ata o máis estable con tres bencenos fusionados están constituídos por tres dobres enlaces conxugados e un triple enlace tensionado. A presenza do sistema acetilénico proporciona baixa estabilidade e alta reactividade, característica que pode ser modificada ca fusión de bencenos e a subsecuente protección do triple enlace fronte a ataques nucleófilos, facéndoo máis estable e plano. Ao

igual que os bencinos, os COTinos poden ter tres formas resonantes nas que os dous electróns constituíntes do triple enlace poden existir como especie diradicalaria, triple enlace ou especie cumulénica.

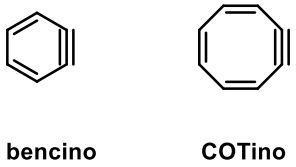


Figura 5. Alquino bencenoide e non bencenoide a estudar

Poucos son os autores que mostran o comportamento destes núcleos. Comezando polo COTino máis sinxelo (sen ningún benceno fusionado), Krebs tratou de illar esta especie esquiva (xerada a partir do ciclooctatetraeno bromado e por tratamento en medio básico) mediante experimentos de captura en presencia de acidas, ciclopentadionas, benzofuranos ou dienos obtendo os correspondentes aductos, o que indica que o COTino formado se atopa como alquino e non como radical ou especie cumulénica. Sondheimer estudou a formación e reactividade do benzoCOTino. Neste caso e dependendo da posición inicial do átomo a eliminar (posición bencílica ou homo bencílica) ten lugar a formación da especie acetilénica ou da especia cumulénica, respectivamente. De igual xeito que no COTino máis sinxelo, a formación do intermedio alquínico puido ser atrapada con diferentes dienos. Sondheimer e Wong adicaron parte do seu traballo ao estudo do dibenzoCOTino, obtible principalmente a partir do dibenzoCOT mediante bromación e subsecuente eliminación. Dada a simetría do sistema, non hai duda algunha da formación do sistema acetilénico, feito confirmado con experimentos de atrapado así como co seu illamento e estrutura de raios X. Finalmente, o sistema *a priori* máis estable, o tribenzoCOTino, foi estudado independentemente por Meier e os propios Sondheimer e Wong. Curiosamente, a presenza dos tres aneis de benceno causa unha desestabilización da planaridade provocada polas repulsións dos hidróxenos en posición *peri*, o que impide o seu illamento e estudo. A preparación deste alquino soe requirir o uso de precursores como o tribenzoCOT e posterior haloxenación e eliminación (semellante ao caso do dibenzoCOTino) ou o tribenzocicloalcano, o cal ten que ser funcionalizado mediante deshidrohaloxenación, fragmentación de aneis de selenazois ou por oxidación de dihidrazonas. De xeito similar ao resto de COTinos, a especie con tres bencenos pode ser atrapada con furanos ou outras especies.

Sen embargo, é de destacar a ausencia da reactividade destes sistemas en presenza de metais, é dicir, se ben os bencinos foron estudados en cicloadicións [2+2+2] catalizadas por metais de transición (Pd principalmente), a reactividade dos benzoCOTinos neste eido é descoñecida.

Motivados pola posibilidade de acceder a sistemas extremadamente interesantes nos que se combinarían núcleos aromáticos e non aromáticos, no Capítulo 3 desta tese de doutoramento propuxémonos o estudo da reactividade dos ciclooctatetraenos benzofusionados **16** obtidos durante o desenvolvemento do Capítulo 2 e que poden ser considerados precursores de benzoCOTinos mediante unha eliminación formal de "HX" en medio básico. En concreto estudouse a reactividade en presenza e en ausencia de cantidades catalíticas de metais.

O emprego das condicións habituais de trimerización de arinos planos (Pd(0)) deu lugar a formación do produto esperado **52** (benzotri[8]anuleno) composto por un anel central de benceno rodeado por tres aneis de oito membros nun rendemento moderado. Debido á asimetría e a xeometría en forma de bote do benzoCOT inicial, o produto obtido resultou ser a combinación de tres anulenos (confórmeros/rexioisómeros) diferentes onde a posición e/ou orientación dos aneis de oito eslavóns cambia entre si. A maiores deste produto, o atrapado nucleófilo do alquino por parte da base foi obtido como produto secundario e en baixo rendemento. A optimización das condicións de reaccións permitiunos aumentar a eficiencia catalítica cara a formación do anuleno obxectivo ao mesmo tempo que a formación do produto secundario se veu diminuída. Curiosamente, a fonte de Pd (0) empregado provocou unha diferenza no número e confórmeros/rexioisómeros formados, mentres que o uso de Pd_2dba_3 deu lugar a tres anulenos, o uso de $Pd(PPh_3)_4$ orixinou un anuleno máis. A natureza de tres dos catro confórmeros/rexioisómeros foi confirmada por difracción de raios X observando dous anulenos asimétricos e un simétrico. A selectividade da cicloadición [2+2+2] foi avaliada co uso dun amplo abanico de ligandos tipo fosfina (monodentados, bidentados e alquílicos). Lamentablemente non foi posible obter a formación selectiva de ningún dos anulenos, se ben o uso de ligandos como ^{t}BuDavePhos melloraron lixeiramente a formación dun dos anuleno asimétricos mantendo o mesmo rendemento xeral. O baixo control da selectividade e o alto número de anulenos formados pode ser explicada polo mecanismo de trimerización mediado polo Pd. O alquino cíclico formado actúa como ligando e coordínase a esfera do Pd para dar lugar a un paladaciclo plano cuadrado inicial de 5 membros, no que os dous COT poden situar os aneis de benceno cara a mesma cara ou en sentidos opostos. A continuación, a entrada da terceira unidade de alquino marca a formación de un ou outro anuleno. De igual xeito á asimetría, a xeometría tipo bote xera dous paladaciclos inicias diferentes nos que os COT s están dobrados cara a mesma cara ou cara caras opostas. O moderado impedimento estérico dos benzoCOTs non permite a interconversión de ambos complexos, polo que a entrada da terceira unidade de alquino non é trivial. Porén, tendo en conta os dous aspectos, asimetría e xeometría tipo bote, poderíanse formar ata un máximo de seis anulenos (existen outros posibles confórmeros/rexioisómeros, sen embargo moitos deles poden ser interconvertidos entre eles mediante operación de simetría (principalmente rotacións)).

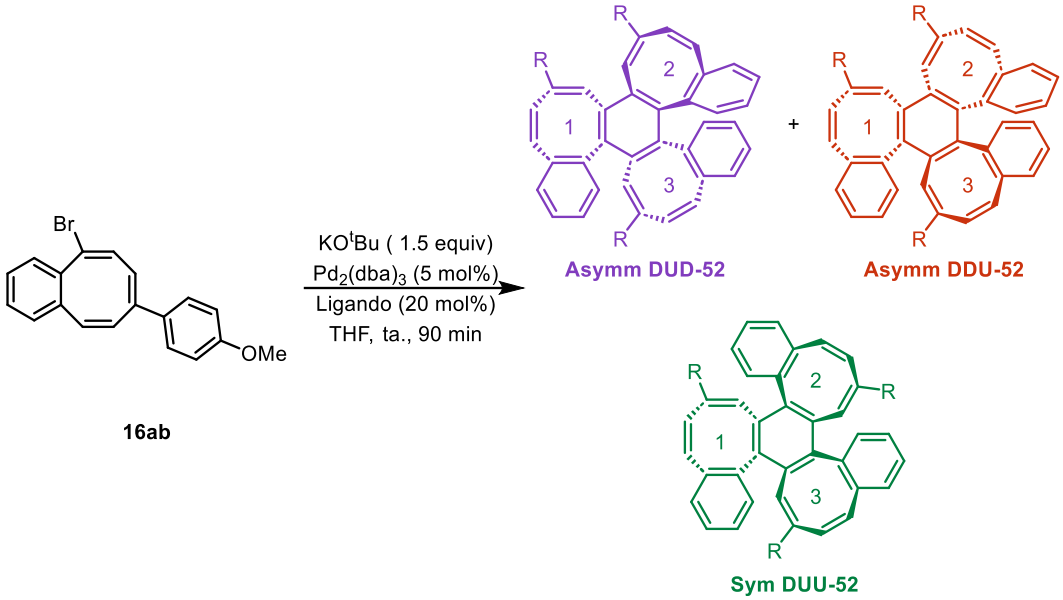


*Figura 6.Formación do benzotri[8]anuleno **52** a partir do ciclooctatetraeno bromado **16ab***

Durante o proceso de optimización da cicloadición [2+2+2] catalizada por Pd dos ciclooctatetraenos bromados benzofusionados 16 atopámonos ca formación dun novo produto cando se prescinde do uso do metal de transición. Este novo produto presenta a mesma masa molecular que o anuleno illado pero un espectro de RMN totalmente diferente e onde se poden apreciar tres isómeros en proporción 1/0.3/0.1. Todos os intentos de desenmascarar o novo trímero foron infrutuosos, polo que se levaron a cabo derivatizacións sobre o trímero final e sobre o benzoCOT inicial. Desafortunadamente ningún dos intentos de solventar a nova estrutura foi exitosos.

Debido aos problemas observados na reactividade do COTino asimétrico, encaramos o Capítulo 4 da tese doutoral co obxectivo de estudar o comportamento das variantes simétricas nos mesmos medios de reacción co fin de minimizar/evitar problemas de rexioisomería. Ao longo dos anos soamente foron descritos tres exemplos onde os sistemas diben-, tribenzo- e COTino se estudaron en condicións similares as propostas polo noso grupo. En primeiro lugar, a reactividade térmica do COTino máis sinxelo foi descrita foi Stevenson. Neste traballo achégase que o tratamento do COTino xerado *in situ* a partir do Br-COT correspondente da lugar á trimerización do anel de oito membros rendendo o tri[8]anuleno máis sinxelo no que un dos aneis de 8 eslavóns se atopa na cara oposta aos outros dous ($\alpha\alpha\beta$). Pola súa banda, Nuckolls reporta como o dibenzoCOTino illado en presenza de cantidades catalíticas de Ru (II) evoluciona cara a formación dunha mestura de dous compostos formada polo dibenzotri[8]anuleno con un dos aneis de COT dobrado cara a cara oposta dos outros dous ($\alpha\alpha\beta$) e o Dewar Benceno. Finalmente, Müllen revela a reactividade do naftodibenzoCOTino, xerado *in situ* por dobre eliminación de HBr, cara a formación do correspondente naftodibenzotri[8]anulene. O máis destacable deste traballo é a dependencia metálica do sistema cara a formación do anuleno $\alpha\alpha\beta$ (catálise de Pd) ou $\alpha\alpha\alpha$ (catálise de Ru).

Con estes precedentes, comezamos a exploración dos sistemas simétricos. En primeiro lugar o tratamento do BrCOT 60 en presenza de fontes de Pd (0) deu lugar ao tri[8]anuleno $\alpha\alpha\beta$ 61 en moderado rendemento, mentres que a variante térmica deu lugar en baixo

rendemento ao naftoCOT **72** derivado da dimerización do COTino inicial. Pola súa banda, o dibenzoCOT funcionalizado **67** orixinou o anuleno αaβ **62** en moderado rendemento en presenza de base e independentemente da fonte de Pd (0) engadida, mentres que o uso de diferentes fontes de Ru (II) deron lugar ao Dewar benceno **63**. Seguindo o traballo de Nuckolls plantexouse o emprego do dibenzoCOTino previo illamento **30**. Así, a reacción entre o alquino illado **30** e a fonte de Pd (0) orixinou en mellor rendemento o anuleno αaβ **62**, a ausencia do metal orixinou o Dewar benceno **63** en baixo rendemento e en presenza de Ru deu lugar á mestura de ambos produtos. A formación do Dewar benceno **63** pode racionalizarse atendendo á formación inicial dun ciclobutadieno central mediante unha cicloadición radicalaria [2+2] entre dúas unidades de alquino para, a continuación, evolucionar mediante unha nova cicloadición radicalaria [2+2] con outra molécula de alquino (cando o material de partida é o propio dibenzoCOTino **30**) ou mediante unha cicloadición [4+2] entre a forma isomérica do ciclobutadieno central (ambas especies presentan enerxías similares) e unha molécula de dibenzoCOTino **30** (cando a especie inicial é o dibenzoCOT funcionalizado).

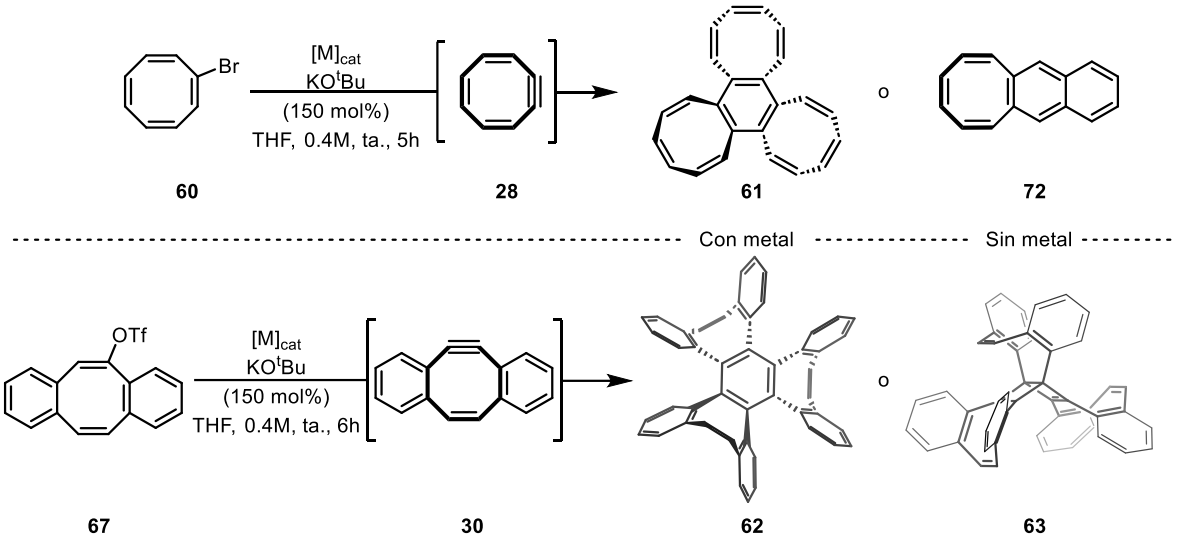


*Figura 7. Reactivade térmica e metálica do BrCOT **60** e dibenzoCOT **67***

Finalmente estudamos a reactividade do tribenzoCOTino **31** en condicións similares as anteriormente mencionadas. O emprego do tribenzoCOT **68** en presenza de base e metais (Pd ou Ru) deu lugar a unha mestura dos anulenos ααα e αaβ **73** en relación 5/1. Durante o proceso de optimización descubrimos que a reacción en ausencia de metais orixinaba a mesma mestura de produtos e na mesma relación, o que claramente indica que os metais non son necesarios para a formación do produto. Curiosamente, cando a reacción se levou en presenza de $Pd(PPh_3)_4$ a elevadas temperaturas, foi posible a inversión das proporcións de anulenos cara a formación maioritaria do confórmero αaβ-**73b**.

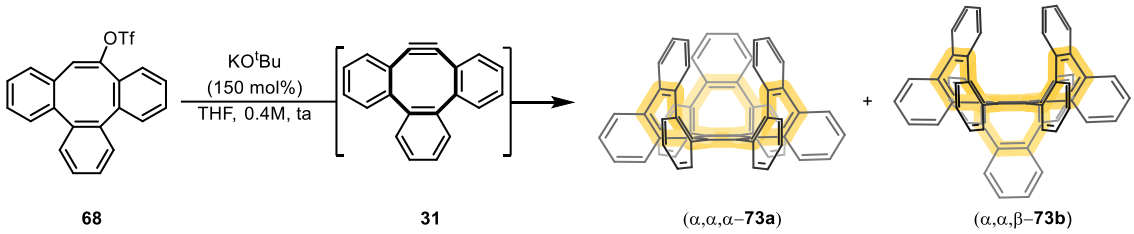


*Figura 8. Formación térmica dos isómero $\alpha\alpha\alpha$ e $\alpha\alpha\beta$ do tribenzo[8]anuleno **73***

A natureza de ambos confórmeros foi identificada por difracción de raios X, e os mecanismos de formación dos mesmos analizados por cálculos DFT. Resultados preliminares parecen indicar o acoplamento radicalario inicial de tres unidades de tribenzoCOTino 31 para dar lugar a un dieno radicalario lineal. A continuación a formación dun ciclopentadieno intermedio seguido da formación dun bisciclopropano e apertura dun dos aneis de tres membros daría lugar ao benceno hexasubstituído observado 73a.

En conclusión, na presente tese doutoral levouse a cabo a exploración da síntese e reactividade de sistemas tipo dihidrobifenileno que deu lugar á formación de ciclooctatetraenos benzofusionados. A continuación, estudouse o comportamento dos benzoCOTs asimétricos, precursores de benzoCOTinos, en medios térmicos e metálicos ca conseguinte formación de benzotri[8]anulenos. Co fin dunha mellor comprensión desta reactividade tamén se exploraron as variantes simétricas dos COTinos, obtendo produtos de dimerización e trimerización de diferente natureza. Estes novidosos materias de partida poderían ser empregados na preparación de hidrocarburos aromáticos policíclicos caracterizados pola combinación de núcleos aromáticos e non aromáticos.

3. Summary

Polycyclic aromatic hydrocarbons (PAHs) are a family of organic compounds presents around us from tar or oil to interstellar space. They can be considered as well-defined graphene fragments that usually present interesting optical and chemical properties which make them very interesting motifs for development of new materials. Defective PAHs containing non hexagonal rings have emerge as improved scaffolds due to their ability to modify supramolecular and electronic properties of their planar analogous. The synthesis of both systems generally requires regioselective fusions of many rings, where metal-catalysed annulations have become one of the most attractive synthetic strategies to construct aromatic and non-aromatic rings.

In 2014, our research group reported a straightforward access to dihydrobiphenylene cores through a Ru(II)-catalysed [2+2+2] cycloaddition of *o*- alkenylarylacetylenes and alkynes. These structures are very interesting building blocks that combine aromatic and anti aromatic alternat rings that can be used as starting materials for chemical synthesis and as spacers for functionalized organic materials. Throughout this thesis, we started analysing a variety of different *o*- alkenylarylacetylenes (enynes) and alkynes to evaluate the scope and limitations of the Ru(II)-catalysed [2+2+2] cycloaddition. From the results obtained, it can be concluded that while terminal electron-rich alkynes participate in Ru(II)-catalysed [2+2+2] cycloadditions, non-terminal ones or those with heteroatoms gave rise to the dimerization of the starting enynes or the formation of side products originating from the presence of the Ru catalyst. In addition, the reactivity of a series of substituted enynes was analysed. The o-ethynylstyrenes containing an electron-rich group in the *para* position relative to the olefin or a second ethynyl group in the *para* position relative to the enyne alkyne did not participate in the Ru-promoted cyclization. This fact could be explained by attending to the unexpected reactivity of the vinyl and ethynyl group caused by the presence of a donor system (OMe) or by the possibility of polymerization of the initial substrate. This fact was experimentally confirmed by the incorporation of a second reactive vinyl group, which dramatically modified the reactivity facilitating a second cocyclization and avoiding the possible polymerization process to efficiently render the corresponding bis-enyne. Moreover, the possibility to introduce nitrogen atoms both in the o-ethynylstyrenes and in the starting alkynes used in order to have access to aza-dihydrobiphenylene type systems, which could modify their properties and/or reactivity motivated by the presence of heteroatoms, was also studied. Unfortunately, all attempts to generate these cores have been unsuccessful.

Next, the study of the reactivity of the 1,3-cyclohexadiene nuclei present in dihydrobiphenylenes was carried out with the aim to access to biphenylene systems through oxidation processes. First, the dehydrogenative route was analyzed using oxidants such as MnO_2, DDQ or SeO_2 among others. However, all attempts to obtain biphenylenes resulted in the recovery of the starting material or in the formation of complex mixtures. As a second alternative, we thought of functionalizing the allylic position of 1,3-cyclohexadiene to subsequently form the target biphenylene through an elimination process.

In 2004, Prof. Christina White reported the regioselective synthesis of allylic acetates by C-H bond oxidation in the presence of BQ, AcOH and catalytic amounts of Pd(II). To our surprise, the use of C-H functionalization conditions over our systems did not give rise to the expected allylic oxidation product, instead a benzofused cyclooctatetraene was obtained characterized by the combination of an aromatic and a non-aromatic core. The formation of the cyclooctatetraene system can be explained by the presence of Pd in the reaction medium. Coordination of the BQ and the initial 1,3-cyclohexadiene to the metal center allows the nucleophilic attack of the acetate group to generate an 1,3-cyclohexadiene intermediate that gives rise to the observed product through a six-electron electrocyclic opening. This compound was obtained in low yield and despite the different reactions conditions carried out, it was not possible to increase the efficiency of the transformation towards the formation of the new system. Alternatively, allylic functionalization via radical halogenation was explored using NBS and AIBN. Again, instead of the allylic functionalization product, a benzofused cyclooctatetraene was obtained, but this time in very good yield and with the incorporation of a Br atom, which gives it value for future manipulations.

With these latest results, we decided to explore this observation from an experimental and computational point of view. Prof. Jesús Varela carried out DFT calculations for a better understanding of the present reaction mechanism. First, the selective formation of the initial radical was elucidated by calculating the bond dissociation energy (BDE) of the two types of aliphatic H present in the central core of dihydrobiphenylene (tertiary and secondary), founding the formation of secondary radical lower in energy. Then, the three possible routes were analysed. Radical bromination of secondary radical species to form a brominated system in the bridgehead position and subsequent electrocyclic ring opening to the isolated benzocyclooctatetraene product was found as the more favourable route.

At the same time, optimization of the reaction conditions as well as scope and limitations of the radical ring opening of dihydrobiphenylenes to brominated benzofusedcyclooctatetraenes systems were carried. Other dihydrobiphenylenes with electron-donating aromatic groups and with alkynes or olefins yielded the target compound from good to very good yields. Moreover, benzofused cyclooctatetraenes with different halogens were achieve using the corresponding halo-succinimides, albeit in lower yield. Unfortunately, dihydrobiphenylenes with electron-withdrawing groups gave rise to complex reaction mixtures. Finally, it was possible to carry out a tandem process (cycloaddition [2+2+2]/radical opening) from the initial enyne without the need to isolate the intermediate dihydrobiphenylene. To complete the scope of the reaction, a novel benzodicyclooctatetraene (benzodiCOT) combining benzenoid (aromatic) and non-benzenoid (non-aromatic) systems in an 8:6:8 fusion, was successfully synthesized.

To demonstrate the synthetic utility of the new obtained systems, a series of subsequent derivatizations based on organometallic reactions (Suzuki and Sonogashira cross couplings) were carried out, obtaining the expected coupling products in very good yields. Diels-Alder cycloaddition reactions were also performed using the standard cyclooctatetraene as well as the novel benzodiCOT, again obtaining very good results. While the cross-coupling reactions

carried out use the presence of the halogen to take place, Diels-Alder cycloadditions takes place between an external 1,4-diene and the generated alkyne in the eight-membered ring (by treatment with an external base). The presence of this alkyne in cyclooctatetraene (COTyne) leads to start section 6.3 where the reactivity of these systems will be studied.

COTynes can be considered as the non-aromatic analogues of benzynes. The history of the latter is widely known for its repercussion in fields such as catalysis or materials science, a field in which they stand out for their ability to generate polycyclic aromatic hydrocarbons (PAHs) of an infinity of shapes and sizes. These reactive species react with a multitude of dienes in Diels-Alder reactions, with acids in 1,3-dipolar reactions and even with themselves in [2+2] cycloadditions through radical mechanisms to give rise to biphenylenes. Given that the high reactivity of benzynes can be "attenuated" by their complexation to metal centers, at the end of the 20th century [2+2+2] cycloadditions and cocyclizations catalyzed by Pd (0) complexes were developed, which made it possible to extend its scope and applications.

In contrast, the chemistry of COTynes is much more discrete due, in part, to the lack of synthetic methodologies that allow access to them. In this area it is important to consider that the existing studies derive from the desire to understand their electronic properties such as non-aromaticity. From the simplest COTyne to the most substituted with three fused benzenes, COTynes consist of three conjugated double bonds and a strained triple bond. The presence of the acetylenic system provides low stability and high reactivity, a characteristic that can be modified by the fusion of benzenes and the subsequent protection of the triple bond against nucleophilic attacks, making it more stable and flatter. Like benzynes, COTynes can have three resonant forms in which the two constituent electrons of the triple bond can exist as a diradical species, a triple bond, or a cumulenic species.

There are few authors who show the behavior of these cores. Starting with the simplest COTyne (without any fused benzene), Krebs tried to isolate this elusive species (generated from brominated cyclooctatetraene and by treatment in basic medium) by trapping experiments in the presence of acids, cyclopentadienones, benzofurans or dienes obtaining the corresponding adducts, which indicates that the formed COTyne is found as an alkyne and not as a diradical or cumulenic species.

Sondheimer studied the formation and reactivity of benzoCOTyne. In this case and depending on the initial position of the atom to be eliminated (benzylic or homo benzylic position), the formation of the acetylenic species or the cumulenic species takes place, respectively. As in the simpler COTyne, the formation of the alkyne intermediate could be trapped with different dienes. Sondheimer and Wong devoted part of their work to the study of dibenzoCOTyne, obtainable mainly from dibenzoCOT by bromination and subsequent elimination. Given the symmetry of the system, there is no doubt about the formation of the acetylenic system, fact confirmed by trapping experiments as well as by its isolation and X-ray structure. Finally, the a *priori* most stable system, tribenzoCOTyne, was independently studied by Meier and Sondheimer and Wong themselves. Interestingly, the presence of the three benzene rings causes a destabilization of the planarity due to the repulsions of the hydrogens in the *peri* position, which prevents their isolation and study. The preparation of this alkyne

usually requires the use of precursors such as tribenzoCOT and subsequent halogenation and elimination (like the case of dibenzoCOTyne) or tribenzocycloalkane, which has to be functionalized through dehydrohalogenation, fragmentation of selenazole rings or by oxidation of dihydrazones. Like the rest of COTynes, the species with three benzenes can be trapped with furans or other species. However, it is worth to highlight the absence of reactivity of these systems in the presence of metals, and although benzenes have been studied in [2+2+2] cycloadditions catalyzed by transition metals (mainly Pd), the reactivity of benzoCOTinos in this area is unknown.

Motivated by the possibility to access to extremely interesting systems combining aromatic and non-aromatic nuclei, in next section we set out to study the reactivity of benzofused cyclooctatetraenes obtained during the development of previous section and which can be considered precursors of benzoCOTynes by a formal elimination of "HX" in basic conditions. Specifically, reactivity was studied in the presence and absence of catalytic amounts of metals.

Under typical trimerization conditions of planar arenes, Pd (0), benzofused cyclooctatetraene renders target benzotri[8]annulene consisting of a central benzene ring surrounded by three eight-membered rings in moderate yield. Due to the asymmetry and boat-shaped geometry of the starting benzoCOT, the obtained product turned out to be the combination of three different annulenes (conformers/regioisomers) where the position and/or orientation of the eight-membered rings changes with each other. Moreover, the nucleophilic trapping of the alkyne (alcoxyCOT product) by the base was obtained as a secondary product and in low yield. Optimization of the reaction conditions allowed us to increase the catalytic efficiency towards the formation of the target annulene while the formation of the secondary product was suppressed. Interestingly, the source of Pd(0) used led to a difference in the number and conformers/regioisomers formed, while the use of Pd_2dba_3 gave rise to three annulenes, the use of $Pd(PPh_3)_4$ gave rise to one more annulene.

The nature of three of the four conformers/regioisomers was confirmed by X-ray diffraction observing two asymmetric and one symmetric annulenes. The selectivity of the [2+2+2] cycloaddition was evaluated using a wide range of phosphine-type ligands (monodentate, bidentate and alkyl). Unfortunately, it was not possible to obtain the selective formation of any of the annulenes, although the use of ligands such as ^{t}BuDavePhos slightly improved the formation of one of the asymmetric annulenes while maintaining the same overall yield. The low selectivity control and the high number of annulenes formed can be explained by the trimerization mechanism mediated by Pd. The cyclic alkyne formed acts as a ligand and coordinates to the Pd sphere to give rise to an initial 5-membered square planar palladacycle, in which the two COTs can position the benzene rings facing the same or in opposite directions. Finally, the entry of the third alkyne unit controls the formation of one or the other annulene. Similarly to the asymmetry, the boat-like geometry generates two different initial palladacycles in which the COTs are bent to the same face or to opposite faces. The moderate steric hindrance of benzoCOTs does not allow the interconversion of both complexes (flapping process), so the entry of the third alkyne unit is not trivial. However, considering the two aspects, asymmetry and boat-like geometry, up to a maximum of six annulenes could be

formed although many of them can be interconverted between them by symmetry operation (mainly rotations).

During the optimization process of the Pd-catalyzed [2+2+2] cycloaddition of benzofused brominated cyclooctatetraenes, the formation of a new product was found when the use of the transition metal is avoided. This new product has the same molecular mass as isolated annulene but a completely different NMR spectrum, where three isomers can be observed in a 1/0.3/0.1 ratio. All attempts to unmask the new trimer were unsuccessful, so derivatizations were carried out on the final trimer and on the starting benzoCOT. Unfortunately, none of the attempts to solve the new structure were successful.

Due to the problems observed in the reactivity of the asymmetric COTyne, in section 6.4 of the doctoral thesis we propose the study of the behavior of the symmetric variants in the same reaction media to minimize/avoid regioisomers problems.

Over the years, only three examples have been described where the diben-, tribenzo- and COTyne systems were studied under conditions like those proposed by our group. First, the thermal reactivity of the simplest COTyne was described by Stevenson. In this work it is reported that the treatment of COTyne generated in situ from the corresponding Br-COT leads to the trimerization of the eight-membered ring yielding the simpler tri[8]annulene in which one of the 8-membered rings is on the opposite face to two others (ααβ). On the other hand, Nuckolls reports how isolated dibenzoCOTyne reacts in presence of catalytic amounts of Ru(II) towards the formation of a mixture of two compounds, dibenzotri[8]annulene with one of the COT rings bent towards the opposite face of the other two (ααβ) and the Dewar Benzene. Finally, Müllen reported the reactivity of naphthodibenzoCOTyne, generated *in situ* by double elimination of HBr, towards the formation of the corresponding naphthodibenzotri[8]anulene. The most remarkable thing about this work is the metal-temperature dependence of the system to the formation of the annulene ααβ (Pd catalysis) or ααα (Ru catalysis).

With these precedents, we begin the exploration of symmetric systems. First, the treatment of BrCOT **60** in the presence of Pd(0) sources gave rise to tri[8]annulene ααβ **61** in moderate yield, while the thermal-metal free variant gave rise to naphthoCOT **72** derived from the dimerization of Initial COTyne. On the other hand, the vinyl triflate dibenzoCOT **67** gave rise to the ααβ annulene **62** in moderate yield in the presence of base and regardless of the added Pd(0) source, while the use of different Ru(II) sources gave rise to the Dewar benzene **63**. Following the Nuckolls´s work, the use of dibenzoCOTyne **30**, previously isolated, was considered. Thus, while the reaction between the isolated alkyne **30** and Pd (0) gave rise to the annulene ααβ **62** in better yield, the absence of the metal gave rise to the Dewar benzene **63** in low yield; by contrast, the use of Ru (II) catalyst gave rise to the mixture of both products. The formation of Dewar benzene **63** can be rationalized by the initial formation of a central cyclobutadiene via a [2+2] radical cycloaddition between two alkyne units, subsequent [2+2] radical cycloaddition with another alkyne molecule (when the starting material is dibenzoCOTino 30 itself) or [4+2] cycloaddition between the isomeric form of the central cyclobutadiene (both species have similar energies) and a molecule of dibenzoCOTyne **30** (when the starting species is the functionalized dibenzoCOT) affords the observed adduct.

Finally, we studied the reactivity of tribenzoCOTyne **31** under similar conditions. The use of tribenzoCOT **68** in the presence of base and metals (Pd or Ru) gave rise to a mixture of annulenes ααα and ααβ-**73** in a 5/1 ratio. During the optimization process we found that the absence of metals resulted in the same mixture and ratio of products, clearly indicating that metals are not required for product formation. Interestingly, when the reaction was carried out in the presence of $Pd(PPh_3)_4$ at high temperatures, the inversion of the annulene proportions towards the formation of the conformer ααβ-**73b** as major product was feasible.

The nature of both conformers was identified by X-ray diffraction, and formation of ααα conformer was analyzed by DFT calculations. Preliminary results indicate an initial radical coupling of three units of tribenzoCOTyne **31** to give a linear diradical diene. Next, formation of a cyclopentadiene intermediate followed by the formation of a biscyclopropane and subsequent opening of one of the three-membered rings would give rise to the observed hexasubstituted benzene **73a**.

In conclusion, we have evaluated the synthesis and reactivity of dihydrobiphenylene cores towards the formation of benzofused cyclooctatetraenes. Moreover, the behavior of the asymmetric benzoCOTs, precursors of benzoCOTynes, was explored under metal-catalysed and thermal metal-free conditions to the formation of benzotri[8]annulenes. Symmetrical variants of COTynes were also explored obtaining dimerization and trimerization products of different nature. These novel starting materials could be used in the preparation of polycyclic aromatic hydrocarbons characterized by the combination of aromatic and non-aromatic nuclei.

4. Introduction

Note: The numbering of the compounds in the introduction follows the sequence established in the results and discussion section. This arrangement has been adopted to maintain coherence and facilitate the reading of the later section.

Polycyclic aromatic hydrocarbons (PAHs) are a group of organic compounds naturally presents in oil, coal and tar, or are produced in combustion process.[1] The mutagenic and carcinogenic properties of some PAHs make them of great concern as contaminants being related to different health problems. [2] PAHs are also present in the interstellar medium, in meteorites and are an important candidate molecule to act as a basis for the first forms of life.[3] On the contrary, for material science they are of great importance.

PAHs can be considered well-defined graphene fragments and are formed six-membered rings of sp^2-hybrizided carbons and a few hydrogens that present the combination of at least two fused conjugated cyclic planar systems, with benzene being the smallest PAH and naphthalene the next largest. PAHs can be classified, according to the presence or absence of geometric defects, in the hexagonal sp^2 structural layer, in non-planar or planar, respectively. Furthemore, PAHs can also be classified in light PAHs (containing up to four rings) and heavy PAHs (containing more than four rings). The synthesis of both planar and curved PAHs could follow a *top-down* approach where "destruction" of the material is necessary or, alternatively, the *bottom-up* approach would be relied upon as a powerful methodology for the construction of PAHs from smaller building blocks by gradual organic process. The synthesis allows controlling properties such as structure, composition, and/or size of the generated nuclei, which clearly affects their optical and chemical properties [4] For example, triphenylene is highly reactive against oxidation while isomer tetracene is easily oxidized.[5]

The outstanding properties of planar PAHs are linked to its regular structure, such that it has been observed that the presence of defects in the hexagonal network significantly modify their properties. Thus, non-planar PAHs have received much attention over the past several decades due to the unique supramolecular and electronic properties originated from their twisted structures.[6] Over the past few years, the synthesis of PAHs with non-hexagonal rings like four-, five-, seven- and eight membered rings has undergone limited success.

Biphenylene, which is the results of combine two aromatic benzene rings through a four-membered ring, is a highly interesting compound both in terms of structure and properties due,

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[1] Marinov, N. M.; Pitz, W. J.; Westbrook, C. K.; Castaldi, M. J.; Senkan, S. M.; *Combust. Sci. Technol*. **1996**, *116*, 211.
[2] Luch, A. *The Carcinogenic Effects of Polycyclic Aromatic Hydrocar-bons*, Imperial College Pr, London **2005.**
[3] Cook, D. J.; Schlemmer, S.; Balucani, N.; Wagner, D. R.; Steiner, B.; Saykally, R. J. *Nature* **1996**, *380*, 227-229.
[4] Bacon, M.; Bradley, S. J.; Nann, T. *Part. Part. Syst. Charact*. **2014**, *31*, 415–428.
[5] Rieger, R.; Müllen, K. *J. Phys. Org. Chem*. **2010**, *23*, 315–325.
[6] a) Li, X.; Kang, F.; Inagaki, M. *Small* **2016**, *12*,3206–3223; b) Sumy, D. P.; Dodge, N. J.; Harrison, C. M.; Finke, A. D.; Whalley, A. C. *Chem. Eur. J*. **2016**, *22*, 4709–4712.

most likely, to its antiaromatic nature. On the other hand, cyclooctatetraene is a polyene that adopts a tub-shaped geometry due angular deformation and antiaromatic behaviour.

The synthesis of PAHs with biphenylene and/or cyclooctatetraene nuclei could represent a new entry into interesting PAH with intriguingly properties for the preparation of new optical or electrical devices.

4.1. Cycloadditions

The continuous advance of scientific areas such as materials science and health has driven a continued effort in recent years on the development of new environmentally sustainable synthetic methodologies. [7] The challenge of these synthetic methodologies is to be able to transform simple substrates into complex molecular structures with chemo-, regio-, diastereo- and enantiocontrol, as well as with minimal waste generation. [8]

One of the methodologies that meet these requirements is the cycloaddition reaction. According to the IUPAC definition, cycloaddition is "*a reaction in which two or more unsaturated molecules (or parts of the same molecule) combine to form a cyclic adduct with a net reduction in bond multiplicity*".[9] The reaction can be promoted with different external agents like Lewis acids, high temperatures, light or metals, that allow to form at least two new bonds in a single step. [10]

Transition metal catalysed (TMC) cycloadditions (either using "noble" metals like Au, Ag, Rh, Ir, Pt and Pd, [11] or more abundant metals like Fe, Co, Ru and Ni)[12] stand out for proceeding under mild reaction conditions and for minimizing the generation of waste while maintaining the principle of atom economy.[13] The coordination of metallic species with different coupling partners makes possible to modify the reactivity of these groups, and even activate initially non-reactive species. Most of these transformations lead to carbocycles by combination of different types of unsaturated coupling partners (e.g., alkenes, alkynes, allenes, 1,3-dienes).[14]

[7] Wender, P. A.; Miller, B. L. *Nature*, **2009**, *460*, 197–201

[8] a) Trost, B. M. *Science* **1991**, *254*, 1471; b) Trost, B. M. *Angew. Chem*. **1995**, *107*, 285. c) Trost, B. M. *Angew. Chem. Int. Ed.* **1995**, *34*, 259; d) Trost, B. *M. Acc. Chem. Res*. **2002**, *35*, 695.

[9] Muller, P. Glossary of Terms Used in Physical Organic Chemistry (IUPAC Recommendations 1994). *Pure Appl. Chem*. **1994**, *66*, 1077−1184.

[10] Kobayashi, S.; Jørgensen, K. A. *Cycloaddition Reactions in Organic Synthesis*; Wiley-VCH, 2001 Bolm, C. (Eds); Wiley-VCH: Weinheim, **2004**.

[11] a) *Comprehensive Organometallic Chemistry II,* Vol 12. Abel. E. W.; Stone, F. G. A.; Wilkinson, G. (Eds); Elsevier: Oxford, 1995. b) *Comprehensive Organometallic Chemistry III*, Vol 10, Vol 11. Mingos, D. M. P.; Crabtree, R. H. (Eds); Elsevier: Oxford, 2007. c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev*. **1996**, *96*, 49.

[12] a) Gebbink, R. J. M. K.; Moret, M.-E. *Non-Noble Metal Catalysis: Molecular Approaches and Reactions*, Wiley-VCH, 2019. b) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl*. **1984**, *23*, 539−556.

[13] Lautens, M.; Klute, W.; Tam, W. *Chem. Rev*. **1996**, 96, 49.

[14] a) García-Rubí, S.; Varela, J. Á.; Castedo, L.; Saá, C. *Chem. Eur. J*. **2008**, *14*, 9772 – 9778; b) Gulías, M.; López, F.; Mascareñas, J. L. *Pure Appl. Chem.,* **2011**, *83*, 495–506; c) Lam, H.; Lautens, M. *Synthesis* **2020**, *52*, 2427−2449; d) Schultz, J. E.; Zuo, Z.; Trost, B.M. *Chem. Eur. J*. **2020**, *26*, 15354–15377.

4.1.1. Transition metal-catalysed [2+2+2] cycloadditions

TM catalysed [2+2+2] cycloadditions make a superb methodology to the construction of six-membered ring systems with high complexity from readily available starting materials. From the first one reported by Reppe and Schweckendiek in 1948,[15] many others have been developed overcoming some drawbacks like low yields or harsh conditions. Metal catalysed [2+2+2] cyclotrimerization of three alkynes to polysubstituted benzenes and metal catalysed [2+2+2] cycloaddition of two alkynes and another unsaturated coupling partner such as alkenes,[16] nitriles,[17] aldehydes[18], carbon dioxide,[19] allenes, [20] and imines[21] to a wide range of six-membered carbo or heterocyclic systems have already been developed.[22]

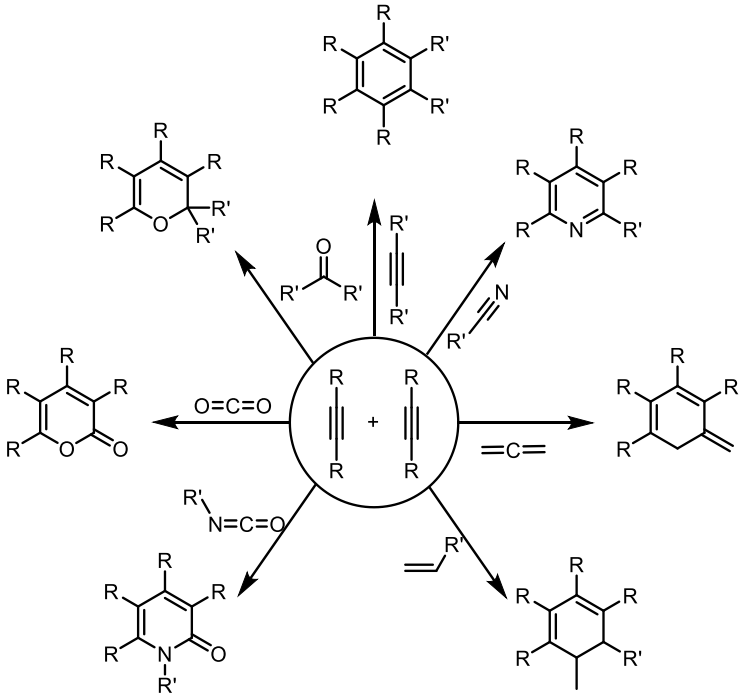

Figure 1. Metal catalysed [2+2+2] cycloadditions of two alkynes and another unsaturated coupling partner

Intermolecular, partially intramolecular or fully intramolecular [2+2+2] cyclotrimerization of alkynes gives access to a variety of (poly)cyclic skeletons (Figure 2).

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[15] Reppe, W; Schweckendiek, W.J. Justus Liebigs *Ann. Chem.* **1948**, 560,104-116.

[16] Domínguez, G.; Perez-Castells, J. *Chem. Eur. J*. **2016**, *22*, 6720−6739.

[17] a) Varela, J.A.; Saá. C *Synlett*, **2008**, *17*, 2571-2578 b) Varela, J. A.; Saá, C. *Chem. Rev.* **2003**, *103*, 3787− 3801; c) You,X.; Xie, X.; Wang, G.; Xiong, M.; Sun, R.; Chen, H.; Liu, Y. *Chem. Eur. J.* **2016**, *22*, 16765 – 16769

[18] a) Yamamoto, Y.; Okude, Y.; Mori, S.; Shibuya, M. *J. Org. Chem*. **2017**, *82*, 7964−7973 b) Yamamoto, Y.; Takagishi, H.; Itoh, K. *J. Am. Chem. Soc*. **2002**, *124*, 6844−6845.

[19] Louie, J.; Gibby, E.; Farnworth, M.V; Tekavec, T. M. *J. Am. Chem. Soc.* **2002**, *124*, 15188-15189.

[20] Lledo, A.; Pla-Quintana, A.; Roglans, A. *Chem. Soc. Rev.* **2016**, *45*, 2010−2023.

[21] Ogoshi, S.; Ikeda, H.; Kurosawa, H. *Pure Appl. Chem.* **2008**, *80*, 1115-1125.

[22] For mechanistic studies of metal catalysed [2+2+2] cycloadditions, see: Roglans, A.; Pla-Quintana, A.; Solà, M. *Chem. Rev.* **2021**, *121*, 1894−1979. For a recent review of metal catalysed [2+2+2] cycloadditions see: a) Kotha, S.; Brahmachary, E.; Lahiri, K. *Eur. J. Org. Chem*. **2005**, 4741–4767; b) Matton, P.; Huvelle, S.; Haddad, M.; Phansavath, P.; Ratovelomanana-Vidal, V. *Synthesis*, **2022**, *54*, 4-32.

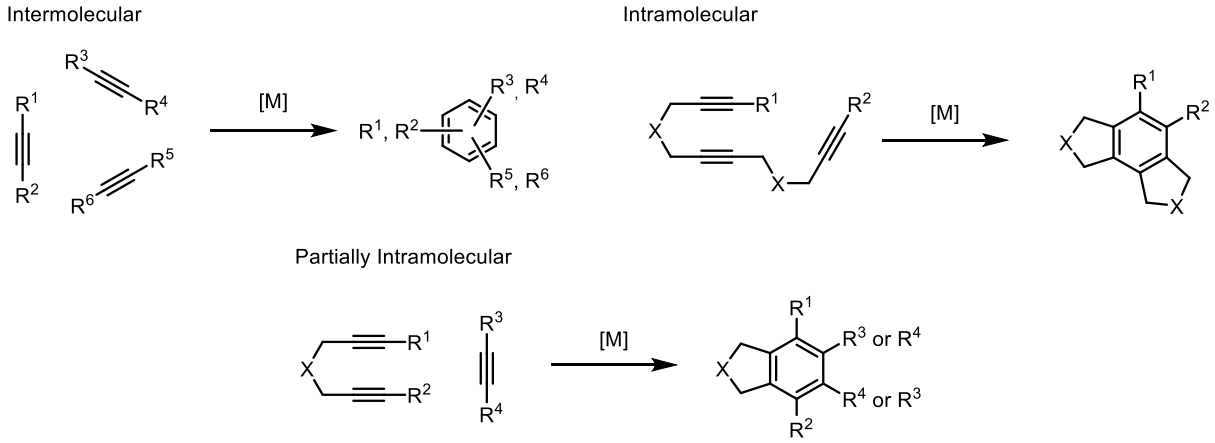


Figure 2. TMC [2+2+2] cycloadditions of alkynes

The general accepted mechanism for the TMC alkyne cyclotrimerization involves the initial formation of a metallacyclopentadiene **A** or a metallacyclopentatriene **A'** complex after coordination of two alkyne ligands and oxidative coupling.

Coordination of a third alkyne unit followed by insertion can produce either a metallacycloheptatriene **C** or metallacycloheptatetraene **C'**, a 7-metallanorbornadiene complex **D** through a Diels-Alder cycloaddition or a metallabicyclo[3,2,0]-heptatriene **E** formed through a [2+2] cycloaddition. Subsequent reductive elimination releases the benzene product **F** while the metal catalyst is regenerated (Figure 3).

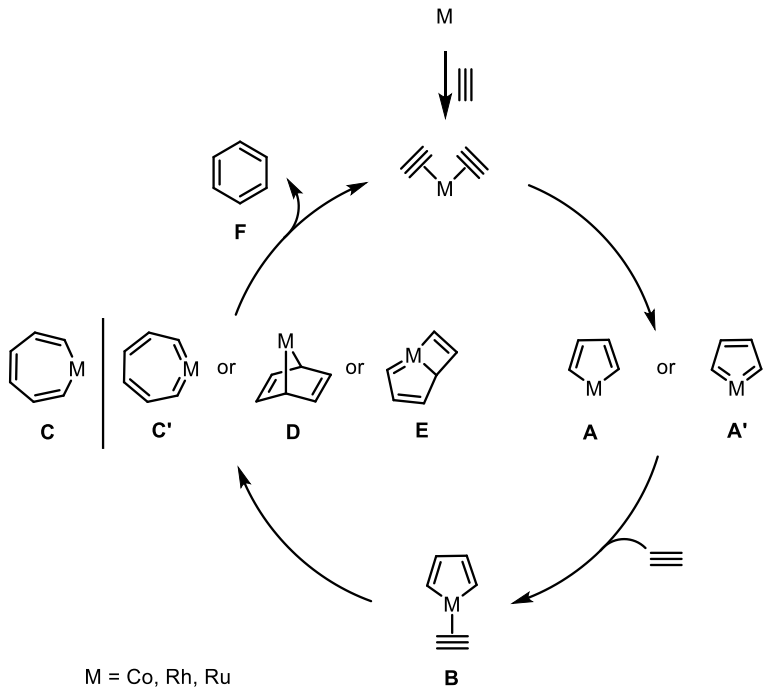


Figure 3. General accepted mechanism for TMC [2+2+2] alkyne cyclotrimerization

4.1.2. Transition metal-catalysed [2+2+2] cycloaddition of alkynes and alkenes

Cycloaddition reactions of alkynes and alkenes are one of the most efficient methodologies for the synthesis of 1,3-cyclohexadienes. These cyclic unsaturated cores are key building blocks for the preparation of a wide range of organic frameworks and are also ideal partners on [4+2] Diels-Alder reactions for the construction of interesting polycyclic structures.[23]

As in alkyne cyclotrimerizations, intermolecular and intramolecular processes are known. While in the first case, the final 1,3-cyclohexadiene will present only one isomer (in terms of the position of double bonds), the fully intramolecular process can generate two isomers depending on the position of the initial alkene (Figure 4).[24]

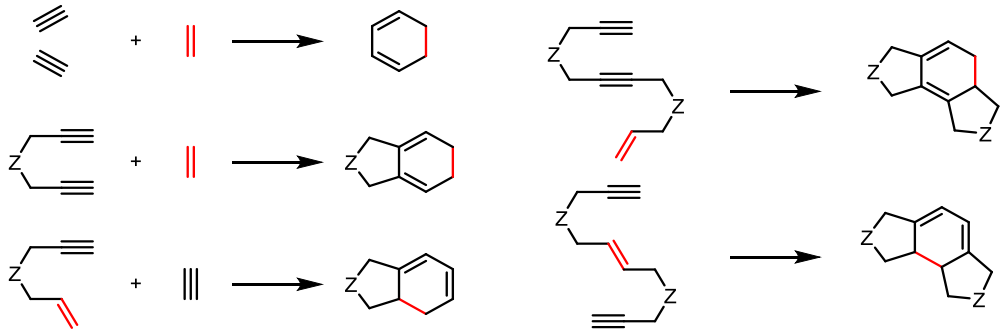
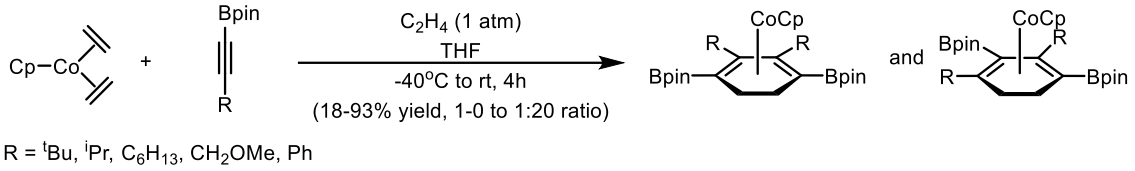


Figure 4. Different isomers of bicyclic and tricyclic 1,3-cyclohexadienes

4.1.2.1. Intermolecular

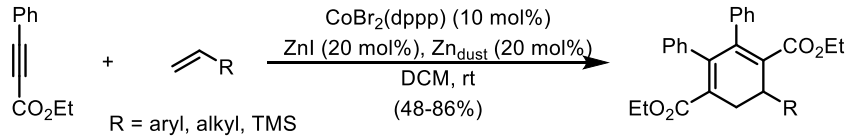
The synthesis of a single 1,3-cyclohexadiene with simultaneous control of regio-, diastereo-, chemo-, and enantioselectivity remains as a difficult challenge in an intermolecular process.[25] Aubert and coworkers reported in 2006 the chemo-, regio-, and stereoselective Co-mediated [2+2+2] cycloaddition between alkynyl boronates and ethylene to diboryl-cyclohexadienes (Scheme 1).[26]Later on, in 2016, Obora reported the use of a Nb catalyst for a selective [2+2+2] cycloaddition of terminal alkynes and alkenes. [27]

[23] a) Jones, A. L.; Snyder, J. K. *Org. Lett*. **2010**, *12*, 1592−1595; b) Shibuya, M.; Sudoh, T.; Kawamura, T.; Yamamoto, Y. *Org. Biomol. Chem*. **2015**, *13*, 5862−5866.
[24] a) Shibata, T.; Kurokawa, H.; Kanda, K. *J. Org. Chem*. **2007**, *72*, 6521–6525; b) Amatore, M.; Aubert, C. *Eur. J. Org. Chem*.**2015**, 265–286
[25] For Ni-catalysed [2+2+2] of alkynes and enones, see: a) Mori, N.; Ikeda S-I.; Sato, Y. *J. Am. Chem. Soc*. **1999**, *121*, 2722–2727; b) Ikeda, S-I.; Kondo, H.; Arii, T.; Odashima K. *Chem. Commun*. **2002**, 2422–2423; c) Kumar, R.; Tokura, H.; Nishimura, A.; Mori, T.; Hoshimoto, Y.; Ohashi, M.; Ogoshi, S. *Org. Lett*. **2015**, *17*, 6018–6021.
[26] Gandon, V.; Leboeuf, D.; Amslinger, S.; Vollhardt, K. P. C.; Malacria, M.; Aubert, C. *Angew. Chem. Int. Ed.* **2005**, *44*, 7114 –7118.
[27] a) Kamei, M.; Watanabe, K.; Fuji, M.; Obora, Y. *Chem. Lett.* **2016**, *45*, 943–945.



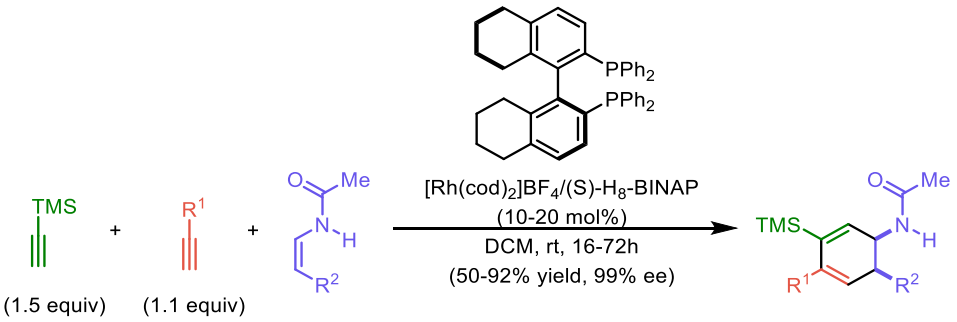
Scheme 1. CpCo-mediated cycloaddition of alkynylboronic esters to ethene

In 2008 Hilt and coworkers reported the use of a terminal alkene in combination with an electron poor alkyne, ethyl propionate, under cobalt catalysis to form the six membered adduct (Scheme 2).[28]



Scheme 2. Cobalt-catalysed [2 + 2 + 2] cycloaddition of alkynes and alkenes to 1,3-cyclohexadienes

More recently, Tanaka and coworkers reported in 2022 a successful chiral cationic Rh(I)-catalysed [2+2+2] cycloaddition of a terminal alkyne, a symmetric electron poor internal alkyne and an alkene. In 2003, the same group provided an upgraded reaction using two different terminal alkynes yielding synthetically valuable protected chiral cyclohexadienylamines. In both cases, excellent chemo-, regio-, diastereo-, and enantiocontrol were obtained (Scheme 3).[29]



Scheme 3. Rh(I)-catalyzed chemo-,regio-,diastereo-,and enantioselective [2+2+2]cycloadditions of alkynes and alkenes

4.1.2.2. Partially intramolecular

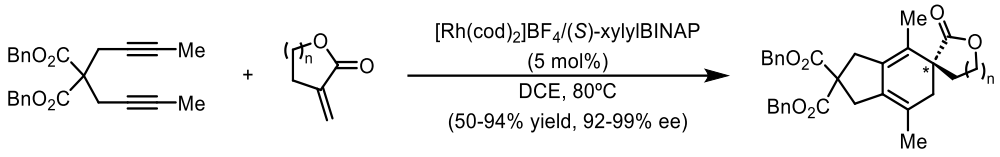
Abundant metals like Co, Ni or Ti have been employed to develop new transformations combining diynes and alkenes.[30] In 2006, Shibata and coworkers described the construction of

[28] Harms, K.; Paul, A.; Hilt, G. *J. Org. Chem*. **2008**, *73*, 5187–5190

[29] a) Fujii, K.; Nagashima, Y.; Shimokawa, T.; Kanazawa, J.; Sugiyama, H.; Masutomi, K.; Uekusa, H.; Uchiyama, M.; Tanaka, K. *Nature Synthesis* **2022**, *1*, 365–375; b) Shimotsukue, R.; Fujii, K.; Sato, Y.; Nagashima, Y.; Tanaka, K. *Angew. Chem. Int. Ed*. **2023**, *62*, e202301346. For a review on rhodium-catalyzed [2+2+2] cycloadditions, see: Pla-Quintana, A.; Roglans, A. *Molecules* **2022**, *27*, 1332.

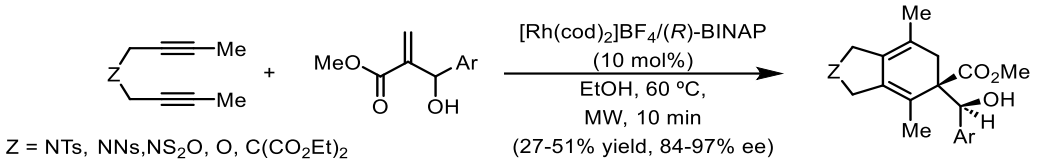
[30] a) Ikeda, S.; Watanabe, H.; Sato, Y. *J. Org. Chem*. **1998**, *63*, 7026; b) Son, S. U.; Choi, D. S.; Chung, Y. K. *Org. Lett.* **2000**, *2*, 2097-2100.

spirocyclic structures in moderate yields and high enantioselectivities by Rh-catalysed [2+2+2] cycloaddition of diynes and *exo*-methylene cyclic compounds (Scheme 4).[31]



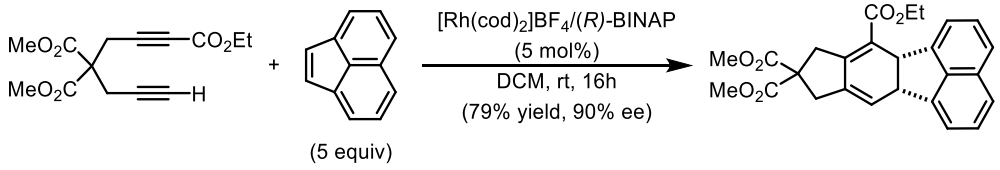
Scheme 4. Rh(I)-catalysed [2+2+2] cycloaddition of diynes and exo-methylene cyclic compounds to spirocyclohexadienes

Later on, in 2016, Roglans and coworkers reported the use of Morita-Baylis-Hillman adducts as electron-poor alkenes in a Rh(I)-catalysed [2+2+2] cycloaddition with 1,6-diynes to the enantioselective synthesis of functionalized 1,3-cyclohexadienes. The presence of the hydroxyl group close to the alkene moiety would enhance stereodiscrimination through substrate chelation or anchimeric assistance (Scheme 5).[32]



Scheme 5. Rh(I)-catalysed [2+2+2] cycloaddition of 1,6-diynes and Morita-Baylis-Hillman adducts

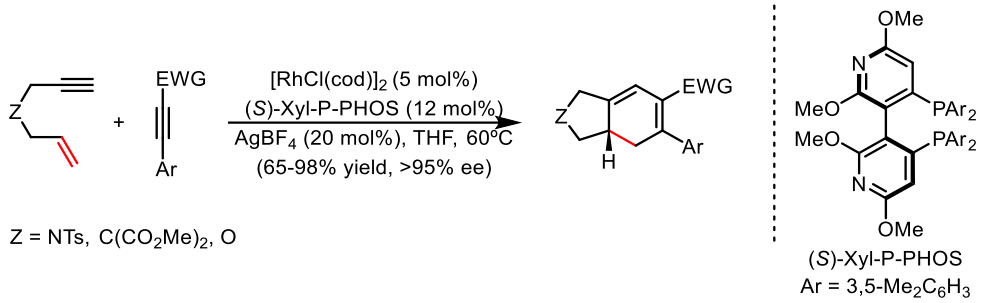
More recently, in 2018, Tanaka and coworkers developed a Rh(I)-BINAP complex that efficiently catalysed the reaction of unsymmetrical 1,6-diynes in the presence of an excess of -acenaphthylene to the expected adduct with good to excellent enantiomeric excesses (Scheme 6).[33]



Scheme 6. Rh(I)-catalysed [2+2+2] cycloaddition of 1,6-diynes and acenaphthylene

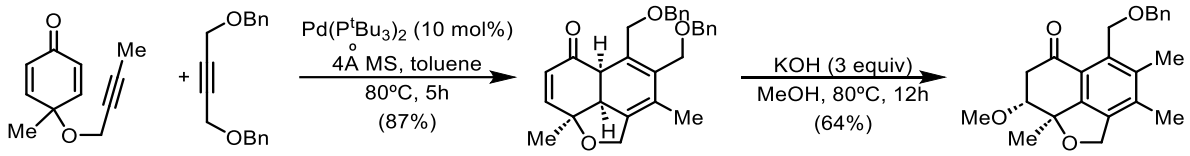
1,6-enynes also participate in metal catalysed [2+2+2] cycloadditions with alkynes. In 2005, Takeuchi reported the Ir-catalysed cyclization of 1,6-enynes in the presence of alkynes to give rise to of bicyclic cyclohexa-1,3-dienes.[34] Shortly after, Evans disclosed the synthesis of chiral bicyclic cyclohexa-1,3-dienes through Rh(I)-catalysed regio- and enantioselective intermolecular [2+2+2] cycloaddition of terminal 1,6-enyne with methyl arylpropiolates (Scheme 7).[35]

[31] Tsuchikama, K.; Kuwata, Y.; Shibata, T. *J. Am. Chem. Soc*. **2006**, *128*, 13686-13687.
[32] Fernández, M.; Parera, M.; Parella, T.; Lledó, A.; Bras, J. L.; Muzart, J.; Pla-Quintana, A.; Roglans, A. *Adv. Synth. Catal*. **2016**, *358*, 1848–1853.
[33] Aida, Y.; Shibata, Y.; Tanaka, K. *J. Org. Chem*. **2018**, *83*, 2617−2626.
[34] Kezuka, S.; Okado, T.; Niou, E.; Takeuchi, R. *Org. Lett*. **2005**, *7*, 1711-1714
[35] Evans, P. A.; Sawyer, J. R.; Inglesby, P. A. *Angew. Chem., Int. Ed*. **2010**, *49*, 5746-5749



Scheme 7. Regio- and enantioselective Rh(I)-catalysed [2+2+2] cycloaddition of enynes and alkynes

More recently, in 2021 He and coworkers reported the use of cyclohexadienone and internal alkynes in the presence of Pd catalyst to form the expected 1,3-cyclohexadiene core, which could be aromatized in basic conditions through a Michael addition and subsequent 1,3-*H*-shift (Scheme 8).[36]



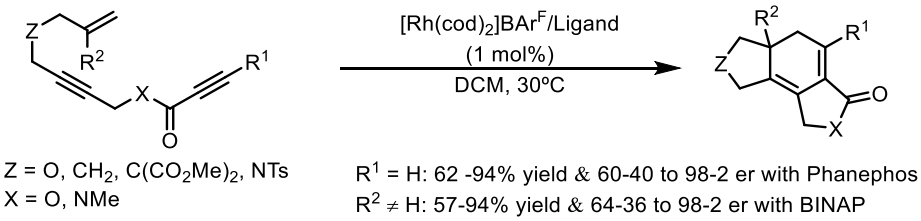
Scheme 8. Palladium-catalysed [2+2+2] cycloaddition of 1,6-enyne and alkyne

4.1.2.3. Intramolecular

Tricyclic cyclohexadienes are very interesting and versatile scaffolds for the synthesis of complex sp^3-rich molecules. In fact, metal-catalysed [2+2+2] cycloaddition of enediynes can provide these moieties that can be further transformed via functionalization of the diene unit.[37] Although one of the most employed metals is cobalt, some drawbacks such as the use of stoichiometric amount of Co complex are present because of the tendency of the cobalt complex to form a very stable η4 -(1,3-cyclohexadiene) complex with the cyclohexadiene final product. [38] For these reasons, alternative catalytic systems based on rhodium, iridium or ruthenium are becoming more popular for enediyene cycloadditions.[39]

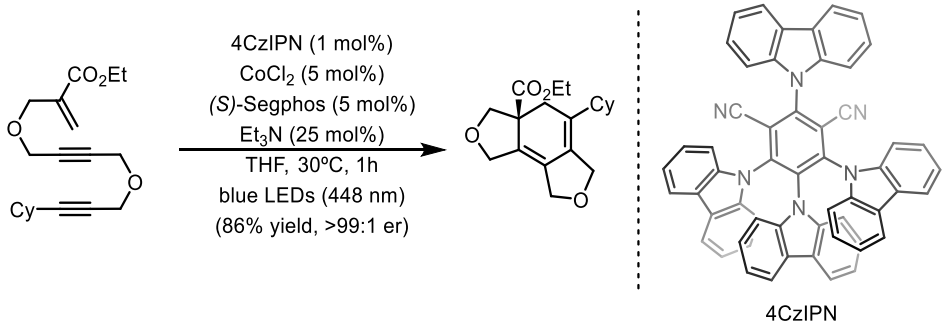
In 2021, Yamamoto and coworkers described the asymmetric Rh-catalysed [2+2+2] cycloaddition of enediynes to a 5,6,5-tricyclic lactone framework containing a quaternary bridgehead carbon (Scheme 9).[40]

[36] Zhao, W-C.; Wang, X.; Feng, J.; Tian, P.; He, Z-T. *Tetrahedron*, **2021**, *79*,131862
[37] Kawamura, T.; Moriya, H.; Shibuya, M.; Yamamoto, Y. *J. Org. Chem*. **2019**, *84*, 12508−12519
[38] Vollhardt, K. P. C. *Angew. Chem., Int. Ed.* **1984**, *23*, 539−556.
[39] a) Shibata, T.; Kurokawa, H.; Kanda, K. *J. Org. Chem*. **2007**, *72*, 6521–6525; b) Ventre, S.; Simon, C.; Rekhroukh, F.; Malacria, M.; Amatore, M.; Aubert, C.; Petit, M. *Chem. Eur. J.* **2013**, *19*, 5830 – 5835; c) Shibuya, M.; Sudoh, T.; Kawamura, T.; Yamamoto, Y. *Org. Biomol. Chem*. **2015**, *13*, 5862–5866; d) Kawamura, T.; Moriya, H.; Shibuya, M.; Yamamoto, Y. *J. Org. Chem*. **2019**, *84*, 12508-12519.
[40] Yasui, T.; Nakazato, Y.; Kurisaki, K.; Yamamoto, Y. *Adv. Synth.Catal*. **2021**, *363*, 4182–4189



Scheme 9. Rh(II)-catalysed asymmetric [2+2+2] cycloaddition of enediynes

At the same time, Yamamoto and coworkers also reported a tandem process using cobalt(II)/organophotoredox cooperative catalysis to highly enantio-enriched 1,3-cyclohexadienes. During the study on the TMC of enediynes they found that the typical known catalytic systems, like Co(II)/Zn, Rh(I) or Ir(I), were not effective for the evolution of the reaction, which proves that the presence of the photoredox component is essential to achieve the tricyclic compound (Scheme 10).[41]



Scheme 10. Co(II)/organophotoredox cooperative [2+2+2] cycloaddition of enediynes

4.2. Ruthenium-catalysed cycloadditions

Ruthenium,[42] with a $4d^7 5s^1$ electronic configuration, presents several features like the low cost, wide range of oxidation states (from -2 to +8), many coordination geometries, low redox potential, high coordination affinity and different modes of reactivity (e.g., C-C/C-X bond activation, carbene or vinylidene complexes, allenylidene or ruthenacycles intermediates),[43] to

[41] Yasui,T.; Tatsumi, R.; Yamamoto, Y. *ACS Catal*. **2021**, *11*, 9479–9484

[42] a) Varela, J. A.; Saá, C. *Chem. Rev*. **2003**, *103*, 3787−3802. b) Kuila, B.; Kaur, M.; Singh, P.; Bhargava, G. *Eur. J. Org. Chem*. **2018**, *2018*, 853−868.

[43] a) *Comprehensive Organometallic Chemistry II*, Vol 7, Vol 12. Abel. E. W.; Stone, F. G. A.; Wilkinson, G. (Eds); Elsevier: Oxford, **1995**; b) *Ruthenium in Organic Synthesis*, Murahashi, S.-I. (Ed); Wiley-VCH: Weinheim, **2004**. b) *Ruthenium Catalysts and Fine Chemistry*, Bruneau, C.; Dixneuf, P. H. (Eds); Springer: Berlin, **2004**. c) d) *Topics in Organometallic Chemistry*, Bruneau, C.; Dixneauf, P. H., Ed.; Springer: Berlin, **2004**; Vol. 11. e) Trost, B. M.; Frederiksen, M. U.; Rudd, M. T. *Angew. Chem. Int. Ed*. **2005**, *44*, 6630 – 6666.

perform cycloadditions under mild catalytic conditions[44] as well as new cycloaddition processes that are unknown for other metals.[45]

4.2.1. Ruthenium catalysed [2+2+2] cycloaddition of alkynes

As described above, Ru complexes can efficiently catalyse [2+2+2] cycloadditions of three unsaturated partners, particularly cyclotrimerization of alkynes to benzenes is a well-known process. The more accepted mechanism for this transformation involves the formation of a ruthenacyclopentadiene/ruthenacyclopentatriene (biscarbene) intermediate.

Based on computational calculations,[46] the alkyne trimerization would start by coordination of two alkynes to the metal center to form the complex **II**. Then, oxidative coupling takes place to form the ruthenium biscarbene **III**, followed by the coordination of a third unit of alkyne to generate the ruthenacyclopentadiene complex **IV**.

From complex **IV**, two different pathways can ben proposed: i) a $6e^{-}\pi$ electrocyclic ring closure to the bicyclic species **V** followed by an electrocyclic ring opening to the biscarbene **VI**. Subsequent reductive elimination releases the η^2-benzene species **VII**, which in the presence of two new alkynes liberate the trimerization product with recovery of the active catalytic species **II**; ii) an intramolecular [4+2] cycloaddition over complex **IV** to form a bicyclic complex **VI'** that isomerizes to intermediate **VII**. However, the Diels-Alder pathway has been discarded because of the low activation energy required to the formation of **V** (0.1 Kcal/mol) compared to that required for the formation of the Diels Alder adduct **VI'** (14.5 Kcal/mol).[47]

[44] a) Padín, D.; Varela, J. A.; Saá, C. *Org. Lett*. **2020**, *22*, 7, 2621–2625. b) Padín, D.; Varela, J. A.; Saá, C. *Chem. Eur.J*. **2020**, *26*, 7470 –7478. c) Padín, D.; Cambeiro, F.; Fañanás-Mastral, M.; Varela, J. A.; Saá, C. *ACS Catal*. **2017**, *7*, 992–996.

[45] a) Sato, H.; Turnbull, B. W. H.; Fukaya, K.; Krische, M. J. *Angew. Chem., Int. Ed.* **2018**, *57*, 3012−3021. For a recent review of Ruthenium to form five-, six- and seven- membered rings see: Doerksen, R. S.; Hodík, T.; Hu, G.; Huynh, N. O.; Shuler, W. G.; Krische, M. J. *Chem. Rev.* **2021**, *121*, 4045−4083.

[46] a) Yamamoto, Y.; Ogawa, R.; Itoh, K. *Chem. Commun*., **2000**, 549–550; b) Kirchner, K.; Calhorda, M. J.; Schmid, R.; Veiros, L. F. *J. Am. Chem. Soc.* **2003**, *125*, 11721–11729; c) Ruba, E.; Schimid, R.; Kirchner, K.; Calhorda, M. J. *J. Organomet. Chem*. **2003**, *682*, 204; d) Varela, J. A.; Saá, C. *Journal of Organometallic Chemistry*, **2009**, *694*, 143–149; e) Dutta, B.; Curchod, b. F. E.; Campomanes, P.; Solari, E.; Scopelliti, R.; Rothlisberger, U.; Severin, K. *Chem. Eur. J*. **2010**, *16*, 8400 – 8409; f) Casiano-González, R.; Barquera-Lozada, J. E. *Chemistry* **2021**, *3*, 1302–1313; g) Findlay, M. T.; Domingo-Legarda, P.; McArthur, G.; Yen, A.; Larrosa, I. *Chem. Sci.,* **2022**, *13*, 3335-3362.

[47] a) Le Paih, J.; Monnier, F.; Dérien, S.; Dixneuf P. H.; Clot, E.; Eisenstein, O. *J. Am. Chem. Soc.* **2003**, *125*, 11964-11975; b) M. Paneque, M.L. Poveda, N. Rendón, K. Mereiter, *J. Am. Chem. Soc.* **2004**, *126*, 1610–1611.

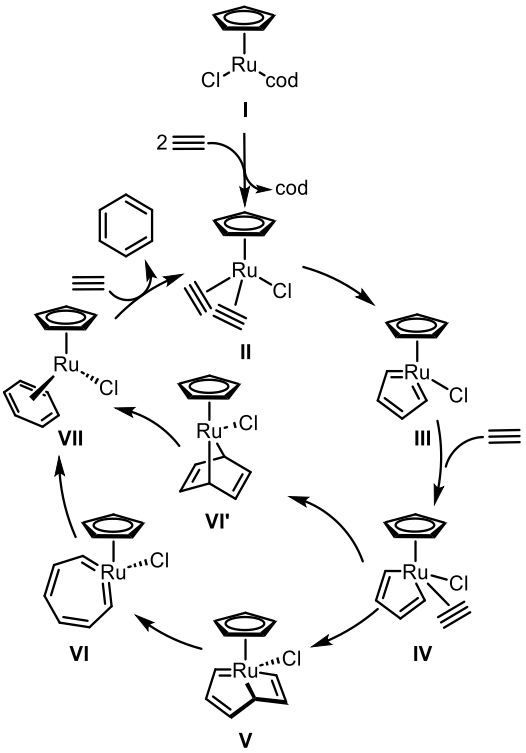
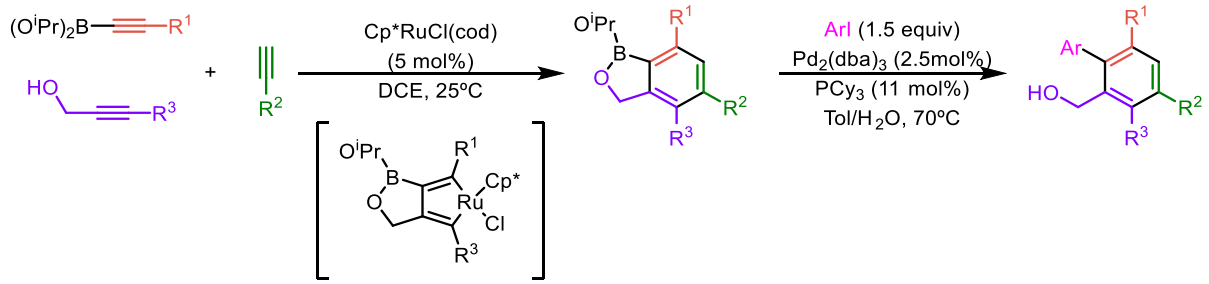


Figure 5. Catalytic cycle for the Ru-catalysed cyclotrimerization of alkynes

Yamamoto reported in 2004 a one-pot four-component coupling where Cp*RuCl(cod) catalyses the chemo- and regio-selective [2+2+2] cycloaddition of three different non-symmetric alkynes. In this reaction, the combination of propargyl alcohol with an alkynylboronate gives rise to the formation *in situ* of a 1,6-diyne bearing a boronate ester, that after oxidative coupling affords a ruthenacyclopentadiene in which the terminal alkyne is inserted.[48] A subsequent Pd(0)-catalysed Suzuki-Miyaura cross-coupling with aryl iodides led to the final diaryl products (Scheme 11).[49]

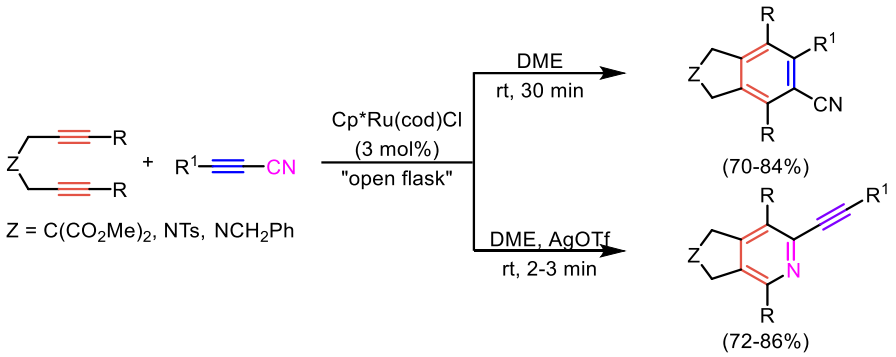


Scheme 11. One-pot four-component coupling via Ru(II)-cyclotrimerization/Suzuki–Miyaura coupling

[48]For mechanistic studies of proposed oxidative coupling-alkyne insertion pathway of the parent CpRu(II) cycloaddition, see: a) Kirchner, K.; Calhorda, M. J.; Schmid, R.; Veiros, L. F. J. *Am. Chem. Soc.* **2003**, *125*, 11721−11729; b) Kirchner, K. *Monatsh. Chem.* **2008**, *139*, 337−348; c) Varela, J. A.; Saá, C. *J. Organomet. Chem*. **2009**, *694*, 143−149.

[49]Yamamoto, Y.; Ishii, J.; Nishiyama, H.; Itoh, K. *J. Am. Chem. Soc*. **2004**, *126*, 3712−3713.

On other hand, many authors have described the synthesis of bicyclic compounds through Ru(I)-catalysed [2+2+2] cycloadditions of diynes and external alkynes. [50] In 2018, Goswami reported a Ru(II)-catalysed cycloaddition of 1,6-diynes with acetylenic nitriles. Cp*RuCl(cod) chemoselectively catalysed the reaction between the diyne and the alkynyl unit of the alkynylnitrile to deliver fused cyanoarenes. Interestingly, the chemoselectivity can be altered by adding a catalytic amount of AgOTf, resulting in the formation of 2-alkynylpyridines instead. The authors suggests that the electron deficient cationic ruthenium complex formed after addition of AgOTf prefers to coordinate with the electron-rich nitrile, giving 2-alkynylpyridines as the sole cycloadduct (Scheme 12).[51]



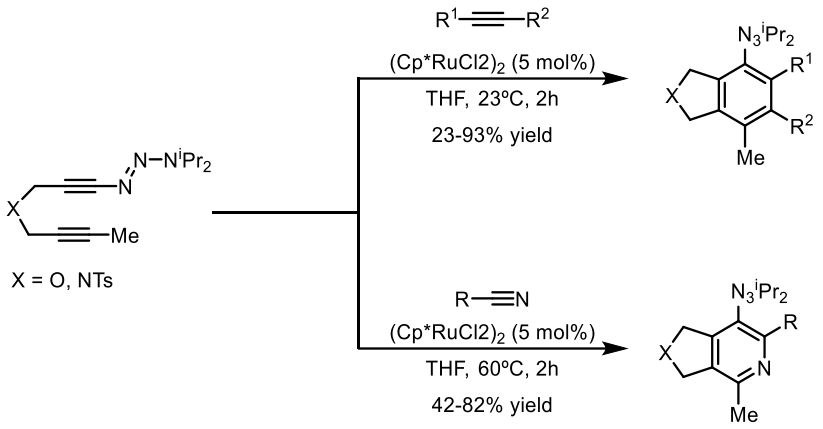
Scheme 12. Additive-controlled switchable Ru(II)-catalysed [2+2+2] cycloadditions of diynes and alkynylnitriles

In 2019, Cramer and coworkers described the synthesis of fused aromatic triazenes by Ru-catalysed [2+2+2] cyclotrimerization of alkynyl triazenes (Scheme 13).[52] High regioselectivity to the formation of the more sterically hindered product is observed. The methodology can be extended to the formation of pyridines by replacing an alkyne with a nitrile.

[50] a) Yamamoto, Y.; Hashimoto, T.; Hattori, K.; Kikuchi, M.; Nishiyama, H. *Org. Lett*. **2006**, *8*, 3565−3568; b) Teske, J. A.; Deiters, A. *Org. Lett.* **2008**, *10*, 2195−2198; c) Shchetnikov, G. T.; Osipov, S. N.; Bruneau, C.; Dixneuf, P. H. *Synlett* **2008**, *2008*, 578−582; d) Foster, R. W.; Tame, C. J.; Hailes, H. C.; Sheppard, T. D. *Adv. Synth. Catal.* **2013**, *355*, 2353−2360; e) Matousova, E.; Gyepes, R.; Císarová, I.; Kotora, M. *Adv. Synth. Catal*. **2016**, *358*, 254−257; f) Huvelle, S.; Matton, P.; Tran, C.; Rager, M-N.; Haddad, M.; Ratovelomanana-Vidal, V. *Org. Lett.* **2022**, *24*, 5126−5131. For Ru(II)-catalysed [2+2+2] cycloadditions of siladiynes and alkynes see: Amakasu, T.; Sato, K.; Ohta, Y.; Kitazawa, G.; Sato, H.; Oumiya, K.; Kawakami, Y.; Takeuchi, T.; Kabe, Y. *J. Organomet. Chem.* **2020**, *905*, 121006

[51] a) Chowdhury, H.; Goswami, A. *Adv. Synth. Catal*. **2017**, *359*, 314−322. b) Bhatt, D.; Patel, N.; Chowdhury, H.; Bharatam, P. V.; Goswami, A. *Adv. Synth. Catal*. **2018**, *360*, 1876−1882.

[52] Tan, J.-F.; Bormann, C. T.; Perrin, F. G.; Chadwick, F. M.; Severin, K. M.; Cramer, N. *J. Am. Chem. Soc.* **2019**, *141*, 10372-10383.

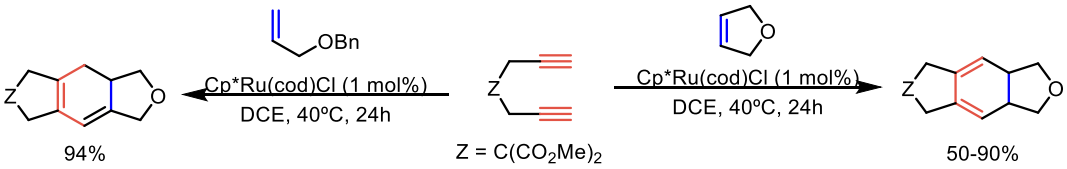


Scheme 13. Ru(II)-catalysed [2+2+2] cyclotrimerizations of 1-diynyl triazenes to benzenes or pyridynes

Later on, in 2020 Mascareñas and coworkers reported the first intracellular Ru(II)-catalysed intra- and intermolecular [2+2+2] cycloaddition of diynes with alkynes.[53] The authors showed the feasibility of multicomponent alkyne cycloaromatizations inside living mammalian cells with Ru catalysts.

4.2.2. Ruthenium catalysed [2+2+2] cycloaddition of alkynes and alkenes

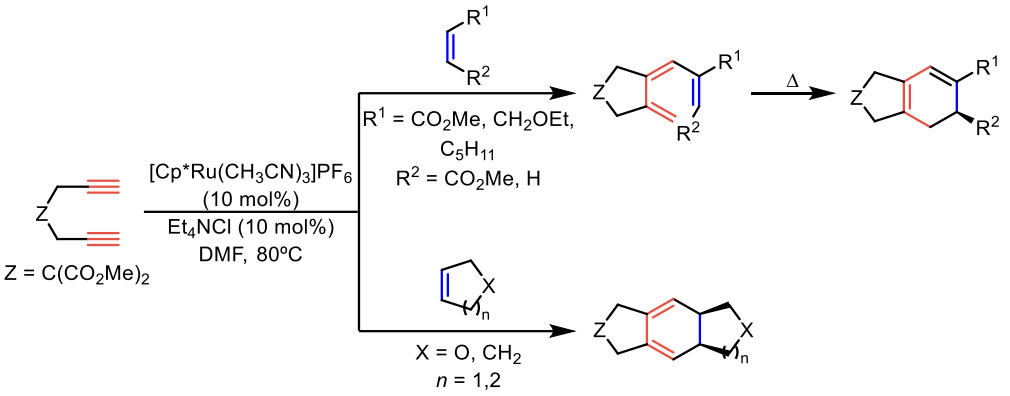
In 1998, Yamamoto and Itoh reported the novel Cp*RuCl(cod)-catalysed cycloaddition of 1,6-heptadiynes with cyclic allylic ethers to functionalized bicyclic cyclohexadienes (Scheme 14).[54] With the allyl/benzyl ether the non-expected isomerized cyclohexadiene was obtained in excellent yield. The authors suppose a concomitant 1,5-*H* shift to explain the isomerization process.



Scheme 14. Formation of unexpected cyclohexadiene isomer reported by Yamamoto/Itoh

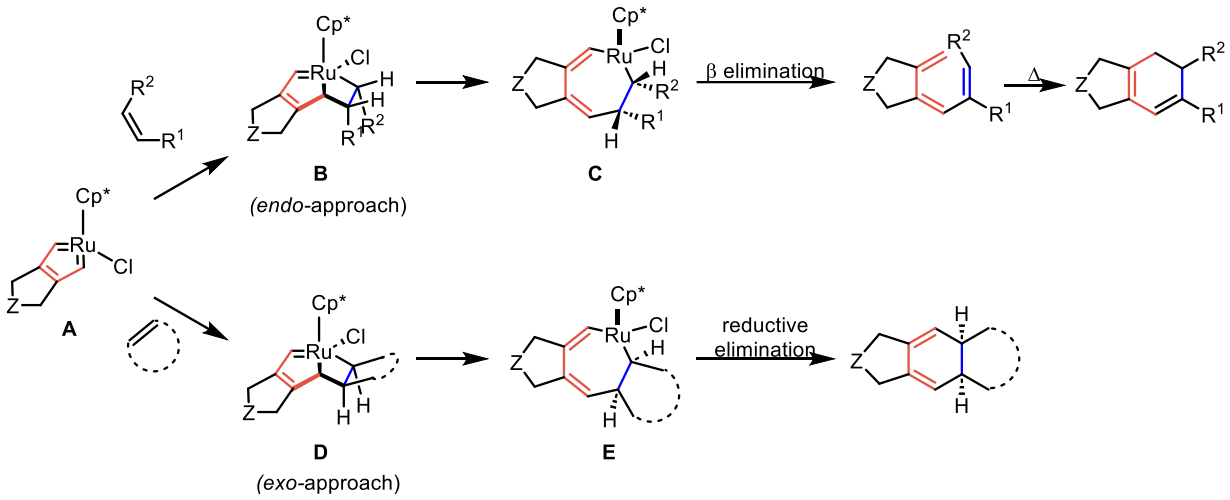
In 2008, our research group carried out a broad study of the cycloaddition of terminal 1,6-diynes with allyl-type alkenes (electron rich and electron poor, linear and cyclic) in the presence of catalytic species generated *in situ* from cationic Cp/Cp*Ru(II) complexes and Et_4NCl. Depending on the nature of the alkyne (cyclic or linear), standard or isomerized cyclohexadienes were obtained ("formal" process) (Scheme 15). [55]

[53] Miguel-Ávila, J.; Tomás-Gamasa, M.; Mascareñas, J. L. *Angew. Chem. Int. Ed*. **2020**, *59*, 17628-17633
[54] a) Yamamoto, Y.; Kitahara, H.; Hattori, R.; Itoh, K. *Organometallics* **1998**, *17*, 1910–1912; b) Yamamoto, Y.; Kitahara, H.; Ogawa, R.; Itoh, K. *J. Org. Chem*. **1998**, *63*, 9610–9611
[55] Varela, J. A.; García-Rubín, S.; Castedo, L.; Saa, C. *J. Org. Chem*. **2008**, *73*, 1320–1332.



Scheme 15. "Formal" and standard Ru(II)-catalysed [2+2+2] cycloadditions of 1,6-diynes and alkenes

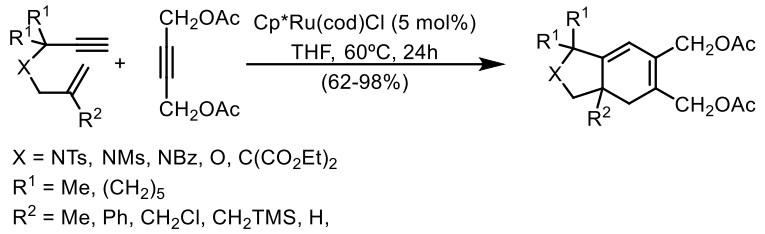
According to computational calculations, the formation of one or other isomer is dependant of the nature of the alkene and the approximation to the metal centre. The acyclic alkene *endo*-approaches to biscarbene species **A** to form a 1,3,5-hexatriene through a β-*H* elimination of intermediate **C**. Subsequent thermal $6e^{-}\pi$ electrocyclization gives rise to the final 1,3-cyclohexadiene (the so called "formal" process). In the case of cyclic alkenes, an *exo-approach* to biscarbene **A** is favoured to give the bicyclic Ru complex **D**. Electrocyclic opening to the ruthenacycloheptadiene **E** followed by a reductive elimination would afford the standard 1,3-cyclohexadiene (Scheme 16).



Scheme 16. Proposed mechanism for the Ru(II)-catalysed [2+2+2] cycloaddition between diynes and linear/cyclic alkenes.

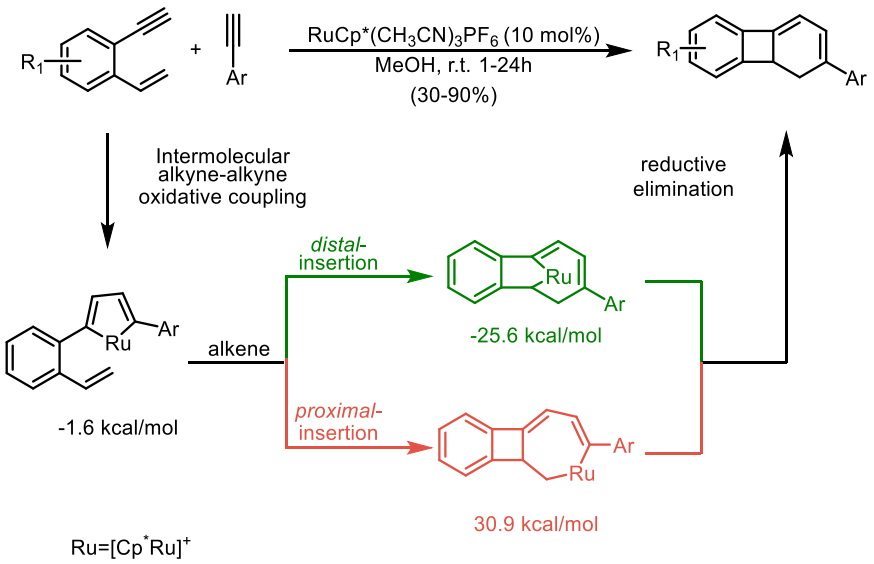
Tenaglia and coworkers disclosed the crossed intermolecular Cp*RuCl(cod) catalysed [2+2+2] cycloaddition of 1,6-enynes with non-activated alkynes to prepare bicylohexa-1,3-dienes containing a quaternary centre at the ring junction (Scheme 17).[56] The regioselectivity of the reaction was controlled by the steric bulk at the propargylic carbon atom(s) of the reactants.

[56] a) Liu, R.; Giordano, L.; Tenaglia, A. *Chem. Asian J.* **2017**, *12*, 2245–2257; b) Liu, R.; Tie, Y.; Zhao, X.; Zhu, J.; Zou, J.; Liu, T. *J. Organomet. Chem*. **2018**, *875*, 46–51.



Scheme 17. Cyclohexa-1,3-dienes through Ru(II)-catalysed [2+2+2] cycloaddition of 1,6-enynes and non-activated alkynes

Ru(II)-catalysed cycloadditions of *ortho*-alkenyl arylacetylenes (1,5-enynes) have been examined by our research group. Either dimerization of 1,5-enynes (no external alkyne added) or crossed intermolecular Ru(II)-catalysed [2+2+2] cycloadditions (in the presence of excess of alkynes) to dihydrobiphenylenes were developed. Computational calculations performed by the group of Wang proposed a possible mechanism for this transformation. The initially formed ruthenacyclopentadiene intermediate from the oxidative coupling of the two alkynes would undergo a *distal*-insertion of the alkene partner followed by reductive elimination to give rise to the four-membered ring in the last step (Scheme 18).[57]



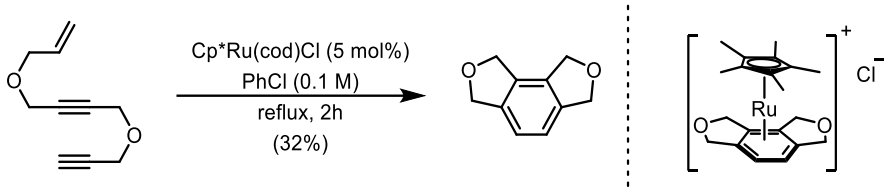
Scheme 18. Dihydrobiphenylenes through a cationic Ru(II)-catalysed [2+2+2] cycloaddition of ortho-*alkenylarylacetylenes and external alkynes*

Fully intramolecular [2+2+2] cycloadditions of alkynes and alkenes are also feasible. In 2003, Yamamoto and coworkers developed a fully intramolecular [2+2+2] cycloaddition of 1,6,11-enediynes.[58] Instead of the expected cyclohexadiene, they found the formation of the corresponding benzene product albeit in low yield. The authors suggest that the isolated cationic ruthenium η^6 -arene complex could contribute to decrease and inhibit the conversion.

[57] a) García-Rubín, S.; González-Rodríguez, C.; García-Yebra, C.; Varela, J. A.; Esteruelas, M. A.; Saá, C. *Angew. Chem. Int. Ed.* **2014**, *53*, 1841– 1844; b) Dang, Y.; Qu, S.; Tao, Y.; Song, C.; Wang, Z-X. *J. Org. Chem*. **2014**, *79*, 9046–9064.

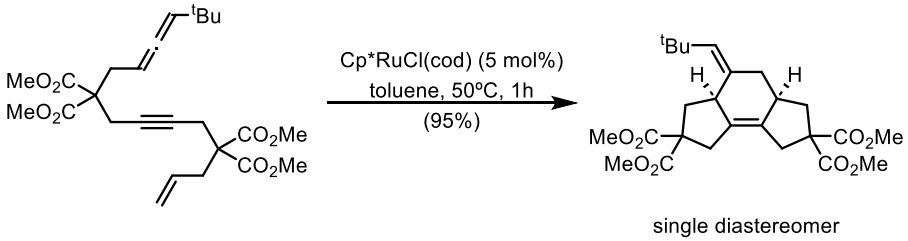
[58] Yamamoto, Y.; Arakawa, T.; Ogawa, R.; Itoh, K. *J. Am. Chem. Soc*. **2003**, *125*, 12143−12160.

In fact, the catalytic cyclization requires temperatures over 100 ºC to open a coordination site via dissociation of the arene ligand (Scheme 19).



Scheme 19. Ru(II)-catalysed [2+2+2] cycloaddition of 1,6,11-enediynes

Later on, in 2007, Sato and Mori described the use of 1,6,11-dienynes in [2+2+2] cycloadditions. The intermediate of this transformation should be the ruthenacyclopentene formed between the alkyne and one alkene. Subsequent alkene insertion followed by reductive elimination would afford the tricyclic product.[59]In 2012, Saito and Sato also reported the intramolecular [2+2+2] cycloaddition of allene-yne-enes to form fused tricyclic compounds using Cp*RuCl(cod). The reaction seems to proceed through a ruthenacyclopentene intermediate formed from the enyne or allenyne moiety to provide tricyclic compounds in a stereoselective way (Scheme 20).[60]



*Scheme 20. [Cp*RuCl(cod)]-catalysed [2+2+2] cycloaddition of allene-yne-enes*

[59] Tanaka, D.; Sato, Y.; Mori, M. *J. Am. Chem. Soc*. **2007**, *129*, 7730−7731
[60] Saito, N.; Ichimaru, T.; Sato, Y. *Chem. Asian J*. **2012**, *7*, 1521− 1523.

4.3. Polycyclic aromatic hydrocarbons (PAHs)

Polycyclic aromatic hydrocarbons (PAHs) are a family of organic compounds that contain six-membered rings of sp^2-hybridized carbons and hydrogens that present the combination of at least two fused conjugated cyclic flat systems. These structures can be divided in benzenoid, if all units are benzene rings, and non-benzenoids, when at least one ring different to benzene is present, reason why anti- and non-aromatic systems containing four-, five-, seven- or eight-membered rings are also included in this family.[61]

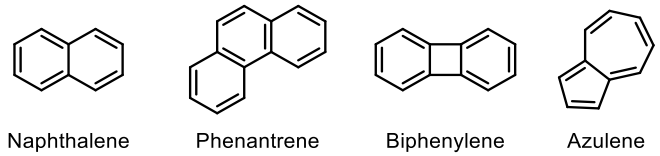


Figure 6. Benzenoids and non-benzenoid PAHs

Polycyclic conjugated π systems exhibit a direct relation between structure, stability and properties showed. Among these features, the most important one could be the correlation of their geometric structure to aromaticity, that is the stabilization of the ground state produced by electron resonance of π-bonds in the corresponding structure.[62] Aromaticity is structure and size dependent and very important to understand fundamental aspects as chemical and physical behaviour, stability and reactivity. Different authors postulated "simple" rules in order to predict if a molecule is aromatic or not. In 1931, Hückel proposed the first theorical model to predict stability and reactivity of an aromatic compound based on molecular orbital theory. Following this rule, a fully conjugated planar ring molecule will have aromatic properties if it presents 4n +2 π electrons, while having 4n π electrons it will be considered anti-aromatic.[63] Later on, E. Clar developed a simple model to determine PAH´s stability, known as Clar´s rule "the structure with the largest number of aromatics π-sextet, represents the most important resonance structure to characterize its properties" meaning that the most stable structure is the one with higher number of Clar´s sextet.[64] Therefore, those bonds not included in a Clar´s sextet are localized and therefore are the most reactive positions of the polycyclic system.

The conclusion derived from the application of these rules generally exhibits good agreement with experimental data regarding the aromatic or non-aromatic behaviour of a system by structural measurement[65] or with parameters calculated by computational methods such as NICS values (nucleus independent chemical shifts).[66] Another alternative technique to identify aromaticity is nuclear magnetic resonance spectroscopy (NMR). In presence of an

[61] a) Clar, E. *Polycyclic Hydrocarbons*, vol. I/II, Academic Press, London, **1964**; b) Harvey, R. G. *Polycyclic Aromatic Hydrocarbons*, John Wiley & Sons, New York, **1997**; c) Fetzer, J. C. *Large (c ≥ 24) Polycyclic Aromatic Hydrocarbons*, John Wiley & Sons, **2000**; d) Hopf, H. *Classics in Hydrocarbon Chemistry*, Wiley- VCH Verlag, **2000**.
[62] a) Gleiter, R.; Haberhauer, G. *Aromaticity and other conjugation effects*, Wiley-VCH, **2012**; b) Rieger, R.; Müllen, K. *J. Phys. Org. Chem*. **2010**, *23*, 315-325
[63] Hückel, E. Z. *Physik* **1931**, *70*, 204.
[64] a) Clar, E. *The aromatic sextet*, Wiley, London, **1972**; b) Armit, J. W.; Robinson, R. *J. Chem. Soc. Trans*. **1925**, 127, 1604.
[65] Krygowsky, T. M.; Szatylowicz, H.; Stasyuk, O. A.; Dominikowska, J.; Palusiak, M. *Chem. Rev.* **2014**, *114*, 6383-6422.
[66] Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; von Ragué Schleyer, P. *Chem. Rev.* **2005**, *105*, 3842-3888.

external magnetic field, diamagnetic currents present in aromatic rings suffer chemical deshielding producing a downfield shift of the nucleus signal. Typically, ^{1}H-NMR signals are present from 6.5 to 8.5 ppm, while ^{13}C-NMR signals move from 90 to 165 ppm.[67]

4.3.1. Biphenylenes

Biphenylene (dibenzocyclobutadiene, BPN) is a non-benzenoid PAH of two benzene rings joined by a strained cyclobutadiene in a 6-4-6 arene system. Due to the 4π electrons in a planar geometry, cyclobutadiene is considered antiaromatic, although its stability is higher in comparison to other antiaromatic skeletons. The biphenylene structure was well established by X-ray and electron diffraction. Those studies show an important alternation of bond lengths, where the cyclobutadiene core present a more Csp^3-Csp^3 character with a 1.514 Å bond length.[68] Moreover, this bond present a low bond dissociation energy (BDE) of 65.4 Kcal/mol.[69] Because of these features, during the last decades biphenylenes have been used as building blocks in functionalized organic materials, while the chemical behaviour of that non benzenoid compounds have attracted much attention in the field of aromatic hydrocarbons.[70]

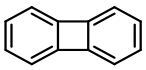


Figure 7. Biphenylene

4.3.1.1. Properties and applications

The aromatic and antiaromatic combination in biphenylene core play a very important role in its applications and properties. NICS calculations show a positive value for cyclobutadiene core (19.25) that corresponds to an anti-aromatic ring, while the adjacent benzene rings show a negative value (-2.45), related with aromatic systems (as lower is the value, higher is the aromatic character). Moreover, the aromaticity of both benzene rings is lower than the normal values because of the presence of the four-membered cycle.[71]

[67]Hesse, M.; Meier, H.; Zeeh, B. *Métodos espectroscópicos en Química Orgánica*, 2ª edition.

[68]a) Fawcett, J. K.; Trotter, J. *Acta Cryst*., **1966**, *20*, 87-93; b) Yokozeki, A.; Wilcox Jr., C. F.; Bauer, S. H. *J. Am. Chem. Soc*. **1974**, *96*, 1026–1032.

[69] Jones, W. D. in *C-C Bond Activation* (Ed.: G. Dong), Springer, Berlin Heidelberg, **2013**, pp. 1 – 31

[70]a) Shepherd, M. K. in *Cyclobutadienes: The Chemistry of Benzocyclobutene, Biphenylene and Related Compounds,* Elsevier, Amsterdam, **1991**; b) Sadana, A. K.; Saini, R. K.; Billups, W.E. *Chem. Rev*. **2003**, *103*, 1539-1602; c) Chaumontet, M.; Retailleau, P.; Baudoin, O. *J. Org. Chem*. **2009**, *74*, 1774 – 1776; d) Miljanic, O. S.; Vollhardt, K. P. C. in *Carbon-Rich Compounds: From Molecules to Materials* Eds: M. M. Haley, R. R. Tykwinski, Wiley-VCH, Weinheim, **2006**, pp. 140 – 197; e) Jones, W. D. *Top. Curr. Chem.* **2014**, *346*, 1–32.

[71] a) Inostroza, D.; García, V.; Yáñez, O.; Torres-Vega, J. J.; Vásquez-Espinal, A.; Pino-Rios, R.; Báez-Grez, R.; Tiznado, W. *New J. Chem.* **2021**, *45*, 8345-8351; b) Stanger, A. *Eur. J. Org. Chem.* **2020**, 3120.

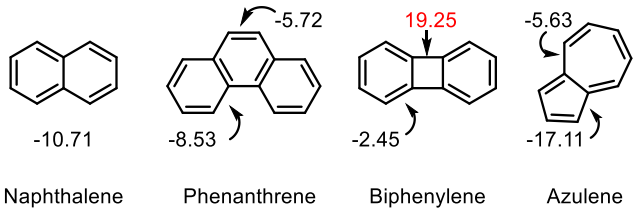


*Figure 8. NICS (0) values calculated at theory level RB3LYP/6-311+G** to naphthalene, phenanthrene, biphenylene and azulene*[72,77]

As consequence of its features, many authors have been investigating the reactivity of biphenylenes as a source of molecular fragment of biphenylene-type graphene's nets, which results in the introduction of eight- and four- membered rings into a two-dimensional carbon framework. Due to the introduction of different size rings, properties are strongly affected (e.g., band gap). For example, scanning tunnelling spectroscopy measurements show how the band gap was increased becoming a truly metallic 2D organic material.[73] Moreover, theorical simulations predicted BPN to behave as a semiconductor (band gap = 2eV),[74] although latter studies suggest BPN to be metallic.[75] In addition, biphenylene seems to present a radical character in the four membered ring, displaying a spin-polarized multiradical ground state. [76]

The first attempt to obtain a BPN framework was disclosed by Rajca in 1996 where the isolation and characterization of a dimer showed the presence of eight-, six- and four-membered rings.[77] Later on, Müllen and coworkers reported octafunctionalized biphenylenes and its application in isomeric graphene nanostructures. In this work they present the first approach to "North-South" extended graphene nanoribbons composed by eight-, six- and four-membered rings and "East-West" isomeric [n]phenylenes starting from well-defined starting materials (Figure 9).[78]

[72] a) von Ragué-Schleyer, P.; Maerker, C.; Dransfeld, A.; Jiao, H.; van Eikema-Hommes, N. J. R. *J. Am. Chem. Soc*. **1996**, *118*, 6317–6318.
[73] Fan, Q.; Yan, L.; Tripp, M. W.; Krejčí, O.; Dimosthenous, S.; Kachel, S. R.; Chen, M.; Foster, A. S.; Koert, U.; Liljeroth, P.; Gottfried, J. M. *Science* **2021**, *372*, 852−856.
[74] Tyutyulkov, N.; Dietz, F.; Müllen, K.; Baumgarten, M. *Chem. Phys. Lett*. **1997**, *272*, 111−114.
[75] a) Hudspeth, M. A.; Whitman, B. W.; Barone, V.; Peralta, J. E. *ACS Nano* **2010**, *4*, 4565−4570; b) Karaush, N. N.; Baryshnikov, G. V.; Minaev, B. F. *Chem. Phys. Lett*. **2014**, *612*, 229−233.
[76] Alcón, I.; Calogero, G.; Papior, N.; Antidormi, A.; Song, K.; Cummings, A. W.; Brandbyge, M.; Roche, S. *J. Am. Chem. Soc*. **2022**, *144*, 8278−8285
[77] Rajca, A.; Safronov, A.; Rajca, S.; Ross, C.R.; Stezowski, J. J. *J. Am. Chem. Soc*. **1996**, *118*, 7272-7279
[78] Schlütter, F.; Nishiuchi, T.; Enkelmann, V.; Müllen, K. *Angew. Chem. Int. Ed*. **2014**, *53*, 1538-1542

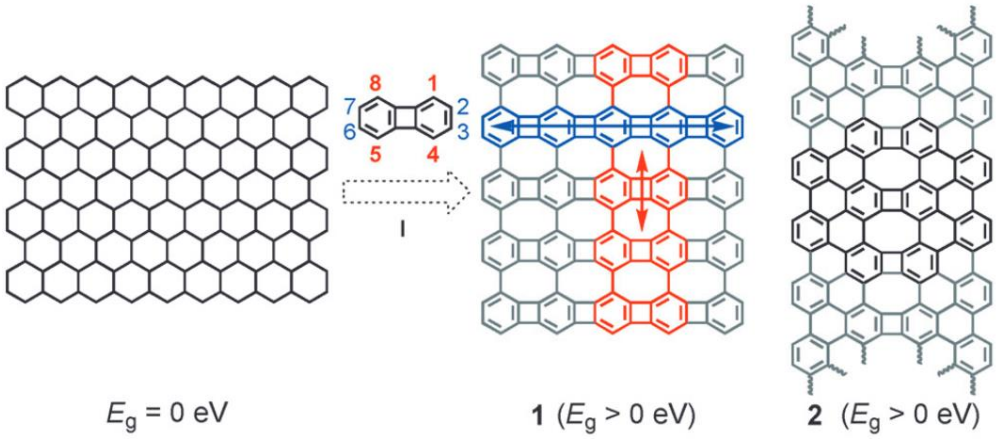


Figure 9. Graphene and isomeric graphene containing biphenylenes. The arrows indicate the direction of expansion: along the 1, 4, 5, 8 positions (North–South, red), and the 2, 3, 6, 7 positions (East–West, blue) (reproduced image from ref 78)

Recently, Gottfried and coworkers reported and alternative protocol to the preparation of a non-benzenoid biphenylene framework.[79] This new approach combines synthesis in solution to prepare the starting monomer DHTP, and further surface chemistry allow a vapor-deposition in ultrahigh-vacuum over a clean Au (111) surface held at 300K. In a first step, an Ullmann-type coupling between C-Br bonds of starting DHTP give rise to a linear polymerization, next interchain HF-zipping afford the formation of the objective framework. Using this alternative, the non-benzenoid biphenylenes are installed during a dehydrofluorination fusion of benzenoid chains. It is important to highlight that the HF-zipping coupling takes place exclusively between C-F and C-H bonds, not observing any product derived from homocoupling process (Figure 10).

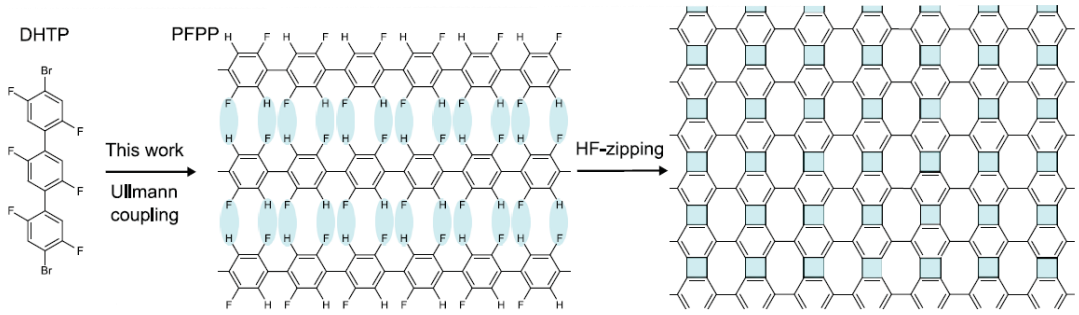


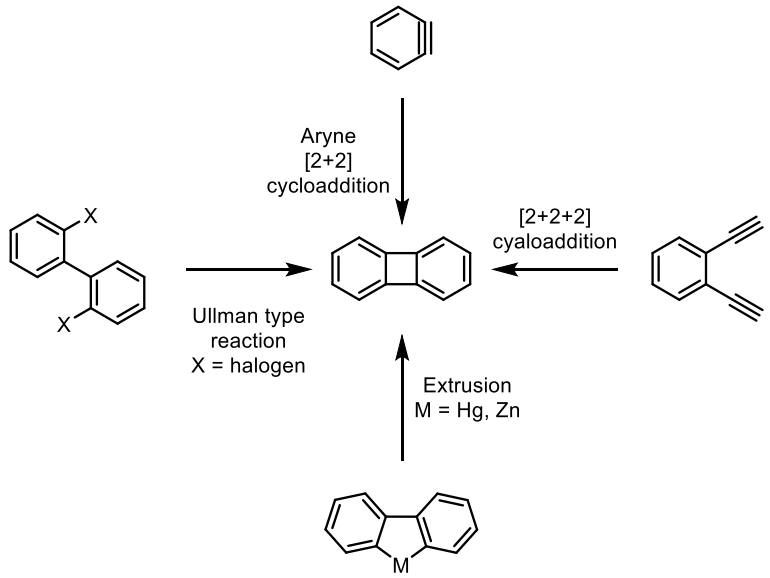
Figure 10. Synthesis of biphenylene 2D-framework combining through a two-step sequence (reproduced image from ref 79)

[79] Fan, Q.; Yan, L.; Trip, M. R.; Krejci, O.; Dimosthenous, S.; Kachel, S. R.; Chen, M.; Foster, A.; Liljeroth, P.; Gottfriend, J. M. *Science* **2021**, *372*, 852-856.

4.3.1.2. Synthesis of biphenylenes

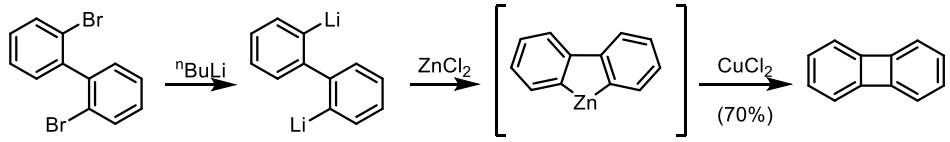
4.3.1.2.1. Traditional approach to dibenzocyclobutadienices cores

In 1941, Lothrop reported the first synthesis of biphenylene core by intramolecular Ullman coupling of 2,2'-diaminobiphenyl via biphenyl iodonium iodide.[80] From this first synthesis, many other based on Ullmann coupling, aryne [2+2] cycloaddition, [2+2+2] cycloaddition of diyne with alkyne or extrusion of tricyclic compounds allowed the synthesis of these skeletons (Scheme 21). [81]



Scheme 21. Different approaches to the biphenylene core

Iyoda and coworkers describe in 1998 a convenient synthesis of biphenylene from *in situ* formed zincacylopentadienes adduct. Basic treatment of 2,2'-dibromobiphenyl with ^{n}BuLi followed by addition of $ZnCl_2$ render the zincacyclopentadiene system, which undergoes an intramolecular coupling reaction in presence of copper salts to give rise to the biphenylene. (Scheme 22).[82]



Scheme 22. Synthesis of biphenylene through zincacyclopentadiene

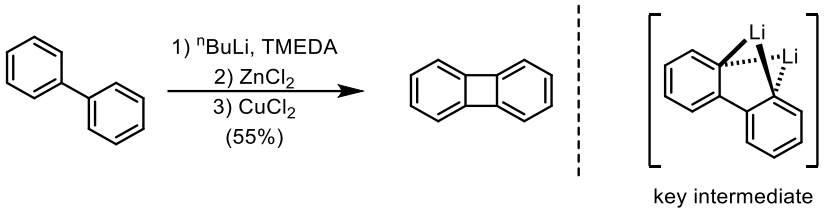
Later on, in 2005, the group of Schaub and Radius demonstrated the synthesis of biphenylene from biphenyl itself by using the same protocol as mentioned above. First lithiation

[80] Lothrop, W. C.; *J. Am. Chem. Soc.* **1941**, *63*, 1187–1191.

[81] a) Wittig, G.; Herwig, W.; Reiss, W. *Chem. Ber*. **1954**, *87*, 1511–1512; b) Logullo, F. M.; Seitz, A. H.; Friedman, L. *Org. Synth.* **1968**, *48*, 12–17; c) Campbell, C.-D., Rees, C. W. *J. Chem. Soc. C* **1969**, *742-747*.d) Berris, B. C.; Lai, Y.-H.; Vollhardt, K. P. C. *J. Chem. Soc., Chem. Commun.* **1982**, 953–954; e) Toyota, S. in *Science of Synthesis* **2008**, *45*, 858.

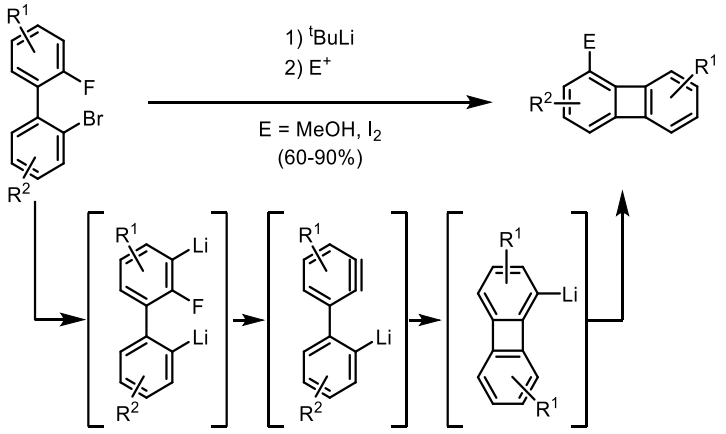
[82] Iyoda, M.; Kabir, S. M. H.; Vorasingha, A.; Kuwatani, Y.; Yoshida, M. *Tetrahedron Lett*. **1998**, *39*, 5393-5396.

process mainly takes place at the *ortho* position due to inductive effects of the phenyl rings, which stabilizes it respect to the *meta*- and *para*-lithiated isomers. The second lithiation process afford selectively the *ortho*-isomer due to interactions between lithium atoms, which enhance the stabilization of the system. After that, corresponding transmetallation and oxidation afforded biphenylene in a one-pot protocol (Scheme 23).[83]



Scheme 23. Synthesis of biphenylene from biphenyl

More recently, in 2017 Wu and coworkers published the synthesis of biphenylenes by intramolecular nucleophilic attack of *in situ* generated arynes from corresponding multihalogenated biphenyls. The use of ^{t}BuLi afford the dilithiated product by halogen-lithium extraction and abstraction of the vicinal acidic H. Once the aryne is formed after lithium-halide elimination, an intramolecular cyclization affords lithiated biphenylene. The use of different electrophiles like MeOH or I_2 render the substituted biphenylene (Scheme 24).[84]



Scheme 24. In situ aryne formation to the synthesis of biphenylenes

It is also possible to access to hetero-biphenylenes by using similar protocols, although the main advances in this field were developed under metal catalysis (see below). The first synthesis of *N*-containing biphenylenes came from 1963 in a work reported by the group of Cava;[85] after that other examples have been established (mainly to incorporate nitrogen or sulfur).[86]

[83] a) Neugebauer, W.; Kos, A. J.; von Rague Schleyer, P. J. *Organomet. Chem*. **1982**, *228*, 107-118; b) Schaub, T.; Radius, U. *Tetrahedron Lett*. **2005**, *46*, 8195–8197.

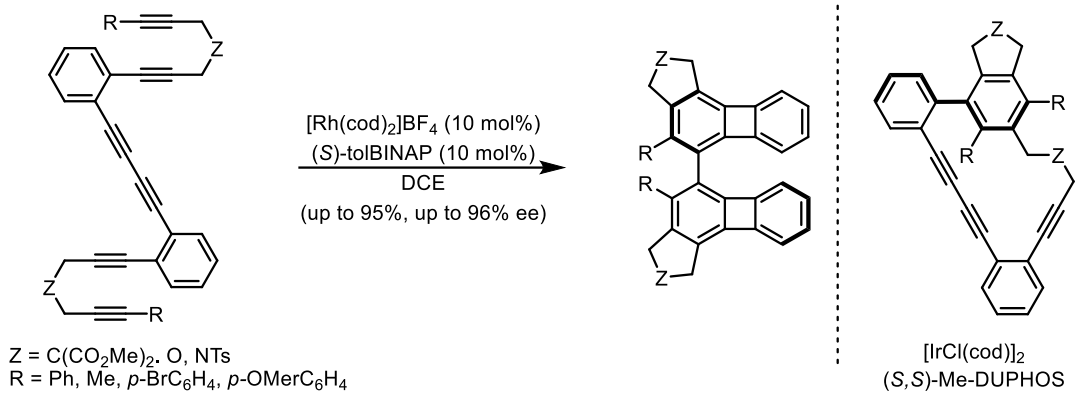
[84] a) Sheng-Li, W.; Ming-Lu, P.; Wei-Siang, S.; Yao-Ting, W. *Angew. Chem. Int. Ed*. **2017**, *56*, 14694-14697; b) Ming-Lun Pan, M.-L.; Wu, Y.-T. *Synlett*, **2020**, *31*, 97-101.

[85] Cava, M. P.; Napier, D. R.; Pohl, R. J. *J. Am. Chem. Soc.* **1963**, *85*, 2076‑2080

[86] a) Barton, J. W.; Walker, R. B. *Tetrahedron Lett.* **1975**, *16*, 569‑572; b) Barton, J. W.; Lapham, D. J. *Tetrahedron Lett.* **1979**, *20*, 3571‑3572.

4.3.1.2.2. Methodologies based on metal catalysis

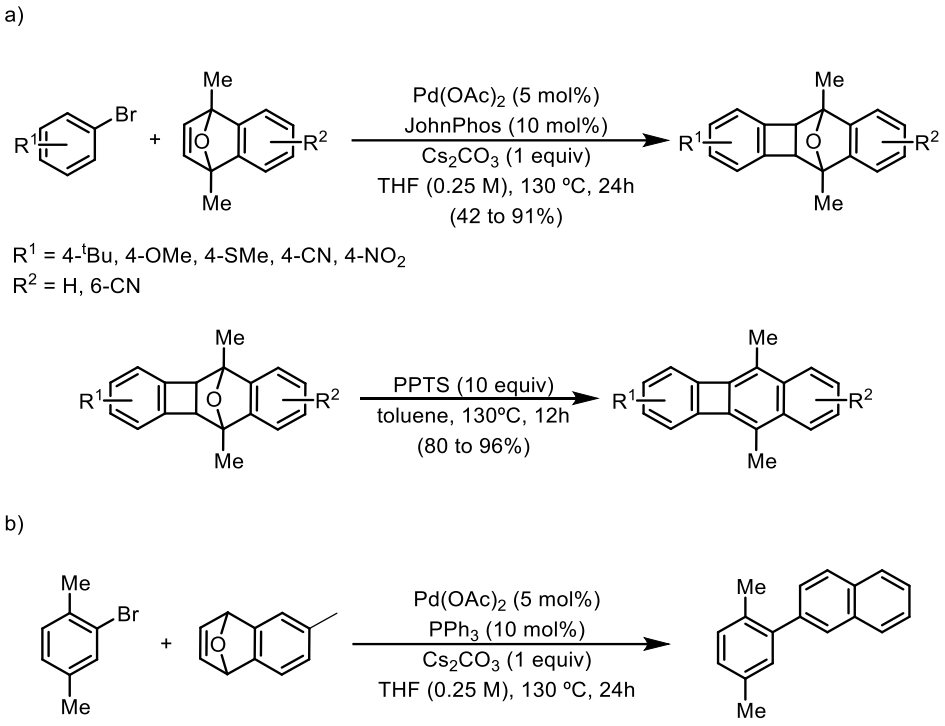
As mentioned in Section 4.1, metal catalysis allows to activate initially non-reactive species to form complex structures from simple starting materials. This approach has been widely used to develop new protocols to achieve biphenylenes cores from unsaturated systems. In 2011, Shibata and coworkers reported the synthesis of axially chiral biphenylenes by a fully intramolecular Rh (I)/(S)-tolBINAP [2+2+2] cycloaddition of hexaynes. In the first step, cationic rhodium complex renders an achiral scaffold, and subsequent cycloaddition affords the observed axially chiral skeleton. Interestingly, the use of chiral Ir (I) catalys to the same starting hexayne promote single [2+2+2] cycloaddition to form chiral macrocycles in both moderate to excellent yields and enantioselectivity (Scheme 25). [87]



Scheme 25. Chiral skeletons by Rh (I) or Ir (I) cycloaddition of hexaynes

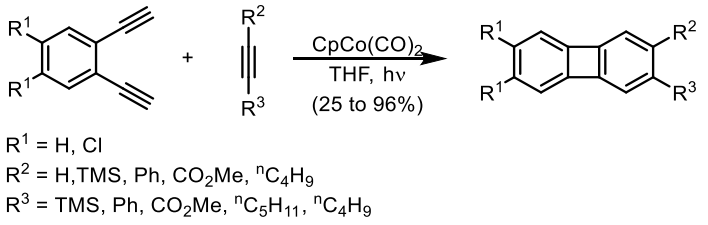
Years later, Xia's group synthesized polycyclic hydrocarbons containing biphenylene scaffolds through C-H activated annulation and aromatization of 1,4-dimethyl-benzooxanorbornadiene.[88] After oxidative addition of Pd (0) species to the C-Br bond of aryl compound and 1,2-alkene insertion of oxabenzonorbornene, C-H activation process of *ortho*-aryl position takes place to form the corresponding palladacycle intermediate, which evolves by reductive elimination to the expected product. Acidic treatment of isolated compound using pyridinium *p*-toluenesulfonate (PPTS) affords aromatized biphenylene product. Curiously, the presence of the methyl groups at the bridge-head position is crucial to the formation of annulated product, indeed the use of oxanorbornene was not successful because of a rapid aromatization caused by a β-oxygen elimination (Scheme 26).

[87] Shibata, T.; Chiba, T.;Hirashima, H.; Ueno, Y.; Endo, K. *Hetero. Chem*. **2011**, *22*, 363–370.
[88] Jin, Z.; Teo, Y. C.; Zulaybar, N. G.; Smith, M. D.; Xia, Y. *J. Am. Chem. Soc.* **2017**, *139*, 1806-1809



Scheme 26. Annulation between oxabenzonorbornene and aryl bromide

On the other hand, one of the most valuable protocols for the construction of biphenylenes was developed in 1985 by Vollhardt´s group. This protocol involves a light promoted Co(I)-catalysed [2+2+2] cycloaddition of *ortho*-diethynylarenes and external alkynes (Scheme 27).[89]



Scheme 27. Biphenylene formation by Co(I)-catalyzed [2+2+2] cycloaddition of diyne and external alkyne

The proposed mechanism starts with the CO displacement by light irradiation, leaving coordination vacancies to diyne coordination. Following oxidant coupling renders the formation of cobaltacycle **B** as the same time that cyclobutadiene ring is formed. Alkyne coordination followed by 1,2-insertion afford intermediate species **D**, subsequent reductive elimination liberates biphenylene core and the catalytic Co(I) active species **A**.

[89] a*)* Berris, B. C.; Lai, Y.-H.; Vollhardt, K. P. C. *J. Chem. Soc., Chem. Commun*., **1982**, 953-954 b) Berris, B. C.; Hovakeemian, G. H.; Lai, Y.-H.; Mestdagh, H.; Vollhardt, K. P. C. *J. Am. Chem. Soc*. **1985**, *107*, 5670-5687.

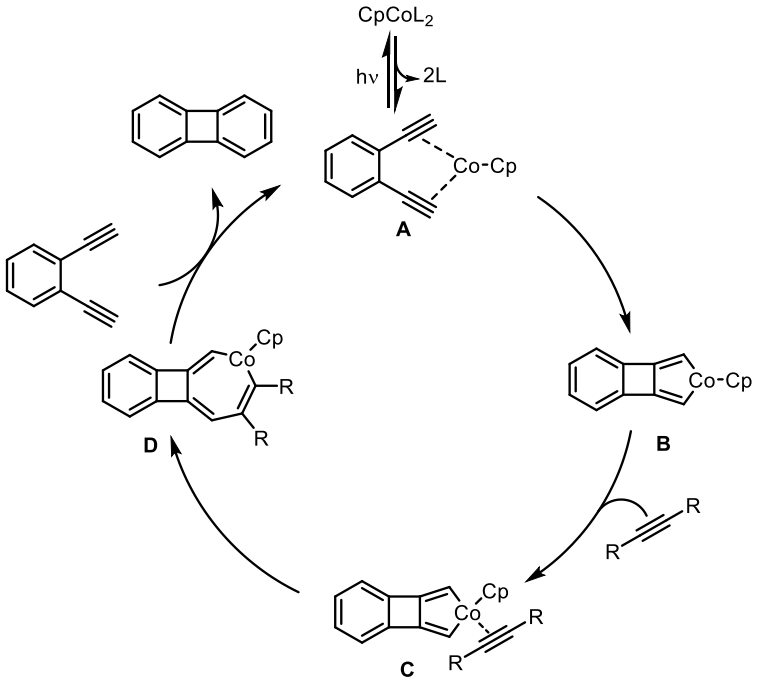
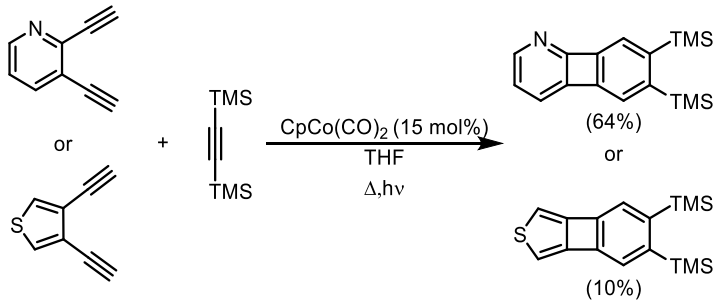


Figure 11. Synthesis of biphenylenes by Co-catalysed [2+2+2] cycloaddition of diynes

Vollhardt's synthesis have been also applied to the preparation of heterobiphenylenes, demonstrating the potential utility of the cobalt catalysed [2+2+2] cycloaddition. Thus, in 2011, Vollhardt and co-workers described the use of *o*-diethynylpyridines or thiophenes in combination with bis(trimethylsilyl)acetylene. Unfortunately, thiophene diynes gave rise to low yields in comparison to pyridines, probably due to the wider enediyne bond length and angle (Scheme 28).[90]



Scheme 28. Synthesis of heterobiphenylenes

[90] Engelhardt, V.; Garcia, J. G.; Hubaud, A. A.; Lyssenko, K. A.; Spyroudis, S.; Timofeeva, T. V.; Tongwa, P.; Vollhardt, K. P. C. *Synlett* **2011**, 280–284.

4.4. Cyclooctatetraenes

Cyclooctatetraene (COT) is a polyene that adopts a ground state nonplanar boat conformation of D_{2d} symmetry due to the angle strain and antiaromatic destabilization of the planar geometry. [91] COT with the formula C_8H_8 is an unsaturated derivative of cyclooctane with 8 π electrons. That π bond electrons are localized into four double bonds in a tub-shaped non-planar form where the p orbitals are nonparallel due to overlapping (dihedral angle between vicinal double bonds is 56° based on single-crystal X-ray structure analysis), and it is predicted to have a triplet ground state by HMO theory. [92]

Two different dynamic processes, ring inversion and π-bond shift, are present in COT (Figure 12).[91a,93] The first one, the "tub-flipping", takes place along the Z reaction coordinate (orange arrow) and is related with ring inversion between two identical D_{2d} tub forms with and activation energy of 10-11 Kcal/mol as determined by experiment and calculation.[94] Planar COT is accepted to be the transition state for this process, more concretely is a D_{4h} transition state, which itself is the local minimum for the π-bond shift process (blue arrow), which is transformed into the other planar system through delocalized D_{8h} intermediate, requiring 3-4 kcal/mol more energy than the ring inversion. As mentioned, D_{4h} conformation is accepted to be the transition state of the ring inversion, however, it is still not clear if the D_{8h} conformation is the transition state for π-bond shift, having other alternatives such as nonplanar crown and saddle-like COT conformations. [95] In fact, it was found that substituents in COT derivatives reduce the difference between the measured Gibbs enthalpy ($\Delta\Delta G^{\ddagger}$) of activation of the π-bond shift and of the ring inversion, suggesting a nonplanar geometry of the transition state of the π-bond shift process.[96]

[91] a) Klärner, F. G. *Angew. Chem. Int. Ed*. **2001**, *40*, 3977-3981; b) Kummli, D. S.; Lobsiger, S.; Frey, H.-M.; Leutwyler, S.; Stanton, J. F. *J. Phys. Chem. A* **2008**, *112*, 9134-9143.

[92] a) Karle, I. L. *J. Chem. Phys*. **1952**, *20*, 65-70; b) Bastiansen, O.; Hedberg, L.; Hedberg, K. *J. Chem. Phys*. **1957**, *27*, 1311-1317; c) Bordner, J.; Parker, R. G.; Stanford, R. H. *Acta Crystallogr. Sect. B* **1972**, *28*, 1069-1075.

[93] Nishinaga, T.; Ohmae, T.; Iyoda, M. *Symmetry* **2010**, *2*, 76-97; c) Li, L.; Lei, M.; Xie, Y.; Schaefer III, H. F.; Chen, B.; Hoffmann, R. *Proc. Natl Acad. Sci. USA*, **2017**, *114*, 9803-9808.

[94] Wenthold, P.; Hrovat, D.; Borden, W.; Lineberger, W. *Science* **1996**, *272*, 1456-1459.

[95] a) Dewar, M. J. S.; Harget, A.; Haselbach, E. *J. Am. Chem. Soc.***1969**, *91*, 7521-7523; b) Ermer, O.; Klärner, F.-G.; Wette, M.; *J. Am. Chem. Soc*.**1986**, *108*, 4908 -4911; c) Paquette, L. A.; Trova, M. P.; Luo, J.; Clough, A. E.; Anderson, L. B. *J. Am. Chem. Soc*. **1990**, *112*, 228–239; d) Paquette, L.A.; Wang, T.-Z.; Luo, J.; Cottrell, C.E.; Clough, A.E.; Anderson, L.B. *J. Am. Chem. Soc.* **1990**, *112*, 239–253.

[96] a) Müllen, K.; Heinz, W.; Klärner, F.-G.; Roth, W. R.; Kindermann, I.; Adamczek, O.; Wette, M.; Lex, J. *Chem. Ber.***1990**, *123*, 2349 – 2371; b) Paquette, L. A.; *Acc. Chem. Res.* **1992**, *25*, 57 – 62

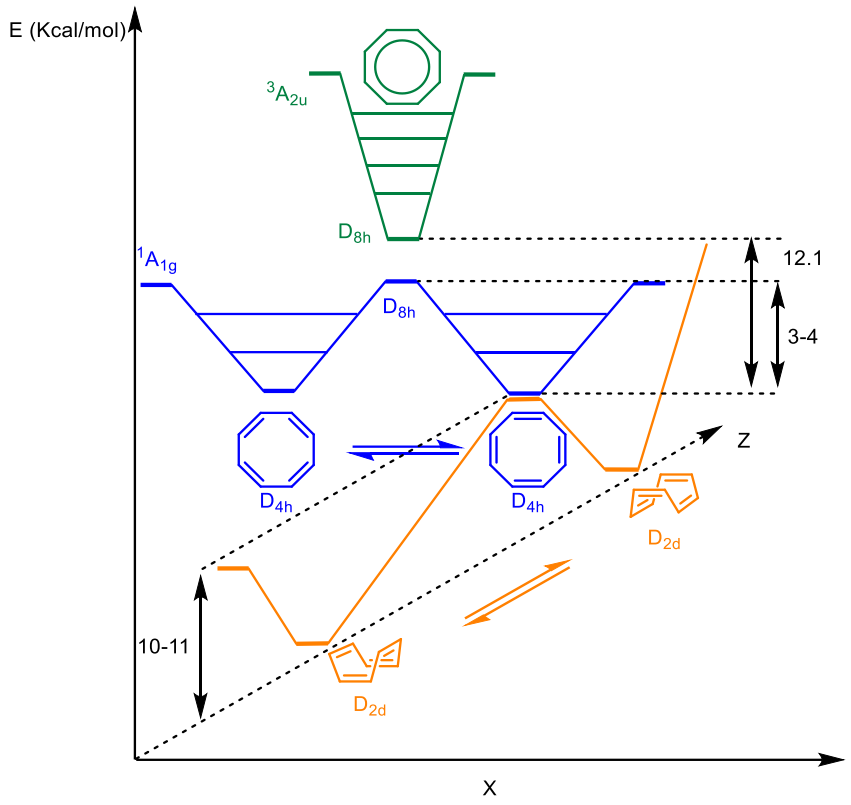


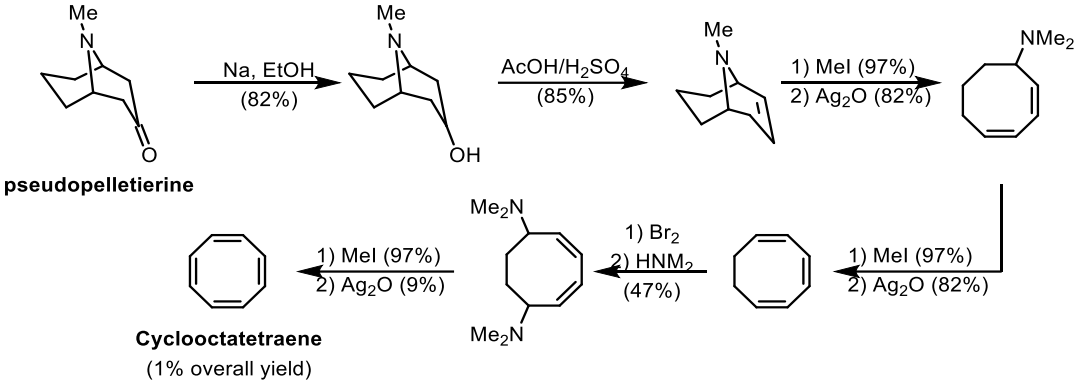
Figure 12. Schematic representation of the potential energy for singlet and triplet COT. (reproduced image from ref 91a)

Finally, it is important to highlight that dianion of COT is postulated to be a planar aromatic system, [97] which means that the geometry of COT can be modulated by oxidation/reduction protocols to produce an ideal "molecular switch".

4.4.1. Synthesis of COT

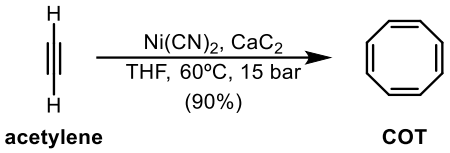
Cyclooctatetraene is still a very interesting molecule from both theoretical and synthetic point of view. It was first synthesized by Willstatter[98] in 1911 in a 10 steps synthetic route, starting from pseudopelletierine and based in multiple Hofmann eliminations, where the overall yield was near to 1% (Scheme 29). In that moment, many authors didn't believe that Willstatter synthetised COT due to the product didn't display the properties of benzene, in fact many of those authors assured that Willstatter had been synthetised styrene by accident.

[97] Katz, T. J. *J. Am. Chem. Soc.* **1960**, *82*, 3784-3785
[98] Willstatter, R.; Waser, E. *Chem. Ber.* **1911**, *44*, 3423-3445



Scheme 29. Original synthesis of cyclooctatetraene (COT) reported by Willstatter

It was not until 1948 when Reppe[99] reported the synthesis of COT by a Ni (0) catalysed [2+2+2+2] tetramerization of acetylene (Scheme 30). Thanks to this work, it was confirmed that it was possible to synthetise a COT molecule, and also that Willstatter had indeed prepared it.



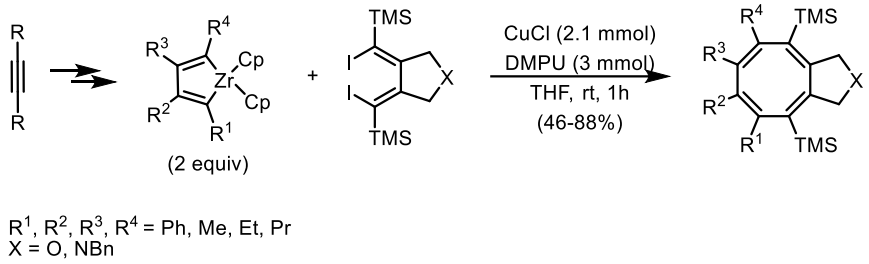
Scheme 30. Cyclooctatetraene by Reppe´s tetramerization of acetylene

Although this approach has been widely used in industry, it presents the handicap of explosion risk associated to acetylene, reason why alternative procedures need to be developed.

From that two first synthesis, many others have been developed and could be classified in three different approaches. As a first option, *the metal-mediated coupling of diene*, where the use of metals like Cu, Ni and Co is well established. [100]

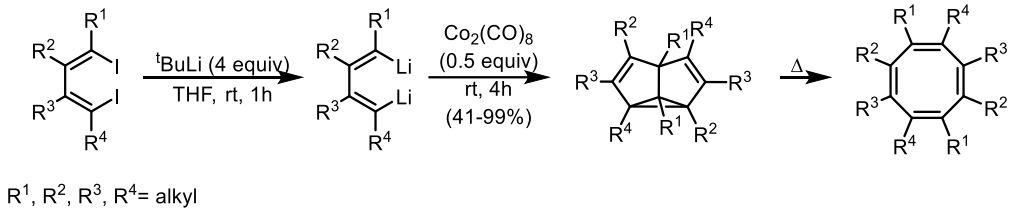
For example, in 2002 Yamamoto and coworkers developed how two different dienes could be transformed into fused COTs by [4+4] coupling.[101] The idea behind was to combine zirconacyclopentadiene scaffolds, generated using Takahashi methodology, [102] with a cyclic diiodide to afford symmetrical COTs. In this case, it is mandatory the use of an excess of Zr reagent to ensure complete consumption of the diiodide (Scheme 31).

[99] Reppe, W.; Schlichting, O.; Klager, K.; Toepel, T. *Liebigs Ann. Chem*. **1948**, *560*, 1-92.
[100] For a review based on metal-mediated synthesis, see: Wang, C.; Xi, Z. *Chem. Commun*. **2007**, 5119 – 5133.
[101] Yamamoto, Y.; Ohno, T.; Itoh, K. *Chem. Eur. J.* **2002**, *8*, 4734 – 4741.
[102] Takahashi, T.; Kotora, M.; Hara, R.; Xi, Z. *Bull. Chem. Soc. Jpn*. **1999**,*72*, 2591 – 260.



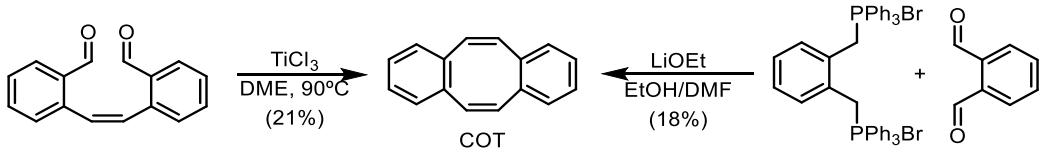
Scheme 31. Synthesis of COTs by coupling of activated dienes

Later on, in 2013, Xi and coworkers developed the synthesis of semibullvalene by dimerization of 1,3-butadienes.[103] In this work, dilithio butadienes, generated *in situ* by treatment of corresponding diiodinated dienes, react with stoichiometric amounts of $Co_2(CO)_8$ to form semibullvalenes, which can undergo a thermo-rearrangement to the corresponding cyclooctatetraene (Scheme 32).[104]



Scheme 32. Synthesis of semibullvalenes, an isomer of COT

Other alternative could be the use of Wittig or McMurry reaction.[105] Unfortunately, these approaches failed in applicability because they only are useful to the construction of mainly aryl-substituted cyclooctatetraenes (Scheme 33).

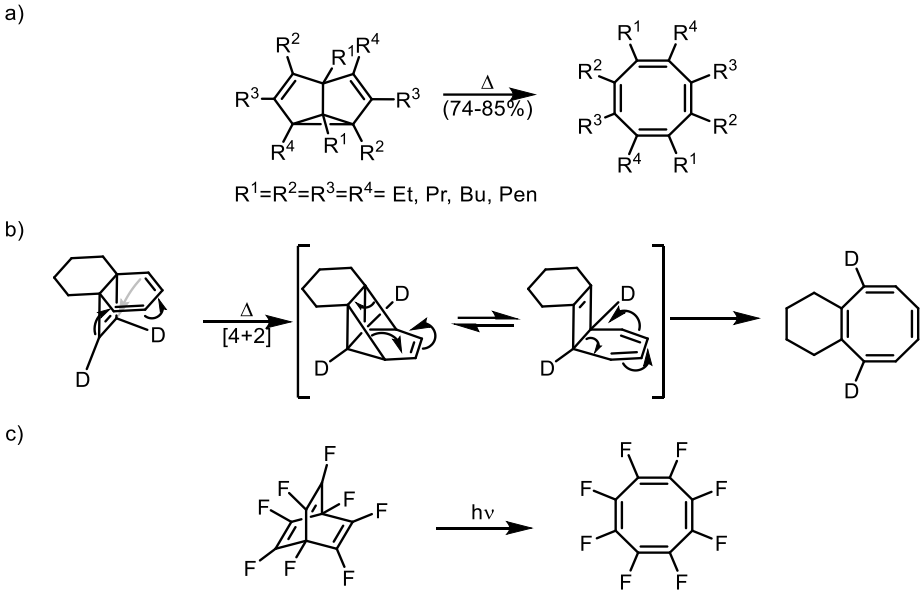


Scheme 33. Wittig and McMurry approaches to COT

The second option to prepare COTs is the use of *valence isomers* which can isomerize under thermal or light conditions (Scheme 34).[106] Xi and coworkers described the evolution of symmetrical semibulvallenes, obtained under copper reagents, to octasubstituted cyclooctatetraenes by thermal isomerization at 140 – 160 ^{o}C (eq. a). [107] Paquete and coworkers demonstrated how bicyclo[4.2.0]-type systems, that can be prepared through a Diels Alder

[103] Zhang, S.; Zhan, M.; Wang, Q.; Wang, C.; Zhang, W-X.; Xi, Z. *Org. Chem. Front*. **2014**, *1*, 130-134.
[104] Quast, H.; Heubes, M.; Dietz, T.; Witzel, A.; M. Boenke, M.; Roth, W. R. *Eur. J. Org. Chem.* **1999**, 813–822.
[105] a) Esser, B.; Bandyopadhyay, Rominger, F.; Gleiter, R. *Chem. Eur. J*. **2009**, *15*, 3368 – 3379; c) Griffin, C. E.; Peters, J. A. *J. Org. Chem*. **1963**, *28*, 1715–1716; d) Brown, C.; Sargent, M. V. *J. Chem. Soc. C*, **1969**, 1818-1820.
[106] a) Zimmerman, H. E.; Grunewald, G. L. *J. Am. Chem. Soc*. **1966**, *88*, 183-184; b) Paquette, L. A. *Tetrahedron* **1975**, *31*, 2855-2883; c) De Meijere, A.; Redlich, S.; Frank, D.; Magull, J.; Hofmeister, A.; Menzel, H.; Konig, B.; Svoboda, J. *Angew. Chem. Int. Ed*. **2007**, *46*, 4574-4576.
[107] Wang, C.; Yuan, J.; Li, G.; Wang, Z.; Zhang, S.; Xi, Z. *J. Am. Chem. Soc*. **2006**, *128*, 4564-4565

reaction, are also good precursors to for COTs (eq. b).[108] Barrelene type scaffolds afforded polysubstituted cyclooctatetraenes under light isomerization (eq. c).[109]



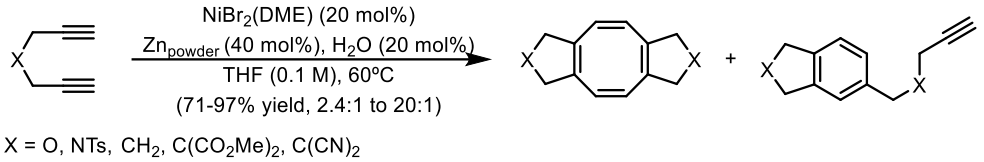
Scheme 34. Isomerization of a) semibulvallenes, b) bicyclo[4.2.0]-type systems and c) barrelenes to COT

The third option to prepare symmetrical and non-symmetrical COTs is based on *metal-mediated methodologies*. In 1993, Streitwieser showed that propargyl alcohols in presence of Ni are able to be converted into tetrasubstituted COTs. Even though the yield of the reaction is almost quantitative, the main problem is the formation of a mixture of four regiosiomers, not separable by chromatography.[110]

In 2007 Wender and coworkers described the preparation of highly functionalized COTs through a Nickel (0)-catalysed [2+2+2+2] cycloaddition of really available starting diynes.[111]

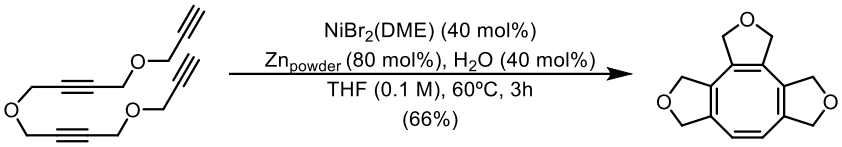
Interestingly, the use of tethered alkynes guarantees the formation of only one regioisomer by mixing inter- and intramolecular reactivity. Wender´s work demonstrated how the ligand over the Ni centre plays an important role on the reaction selectivity (COT vs arene). While the use of Ni (II) species with phosphine ligands (e.g., $NiCl_2(PPh_3)_2$) affords preferably the arene product, the use of ligands such as DME render opposite reactivity. After this change and others less determining reaction parameters (e.g., catalyst loading, molarity, reductants) they were able to achieve good selectivity and reactions yields. Additionally, cross reaction of two different diynes are possible, and although the reaction yields remain high, the selectivity drops observing the formation of the expected product as well as the homodimerization of both starting diynes (Scheme 35).

[108] Paquette, L.; Wingard, R.; Photis, J. *J. Am. Chem. Soc*. **1974**, *96*, 5801-5806.
[109] Ralli, P.; Zhang, Y.; Lemal, D. M. *Tetrahedron Lett*. **2008**, *49*, 7349-7351.
[110] Boussie, T. R.; Streitwieser, A. *J. Org. Chem*. **1993**, *58*, 2377-2380.
[111] Wender, P. A.; Christy, J. P. *J. Am. Chem. Soc*. **2007**, *129*, 13402-13403.



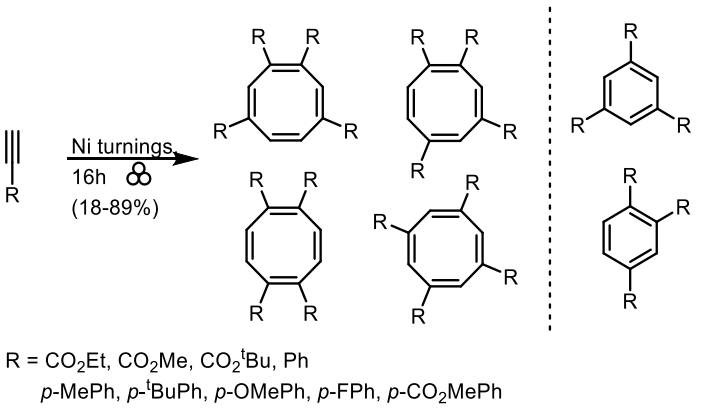
Scheme 35. Ni (0)-catalysed [2+2+2+2] cycloadditions of terminal alkynes

Later on, in 2009, the same group developed an update of the Ni (0) cycloaddition that overcome the lack of reactivity of internal alkyne, by the use of a mixed diyne bearing an internal and a terminal alkyne promoting the formation of hexa- and octasubstituted COTs. Interestingly, they also show a fully intramolecular [2+2+2+2] cycloaddition of a tetrayne (Scheme 36).[112]



Scheme 36. Fully intramolecular Ni (0) promoted [2+2+2+2] cycloaddition to hexasubstitutedCOT

Mack´s group published a mechanochemical method to the production of substituted cyclooctatetraenes compounds by Ni (0) catalysis in a high-speed ball mill.[113] In this work, although the selectivity among different COT isomers is not controlled, it is possible to use a moderate number of terminal alkynes to promote nickel [2+2+2+2] cycloaddition, observing in most of the cases high selectivity to COTs instead of benzene derivative. The use of electron-rich systems changes the selectivity to arene product (15:85), while phenylacetylenes with electron-withdrawing substituents are less effective to COT products (68:32) than phenylacetylene (94:6). Furthermore, mechanochemical systems allow to use a recyclable ligand free Ni(0) sources (Scheme 37).

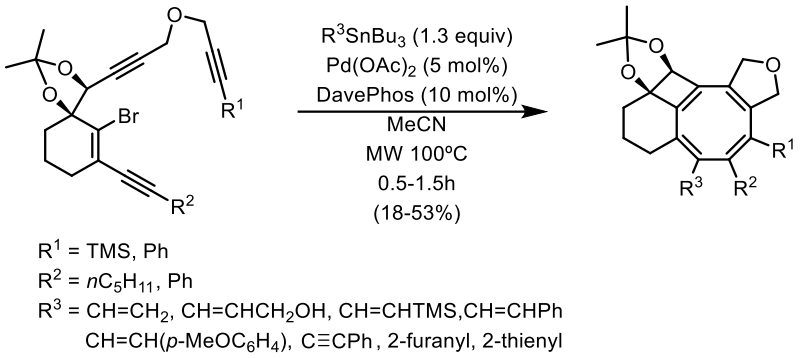


Scheme 37. Mechanochemical approach to COTs.

Suffert and coworkers described a Pd-catalysed cascade reaction of trialkynyl vinyl bromides to substituted COTs. The cascade would involve an 8π electrocyclization reaction of

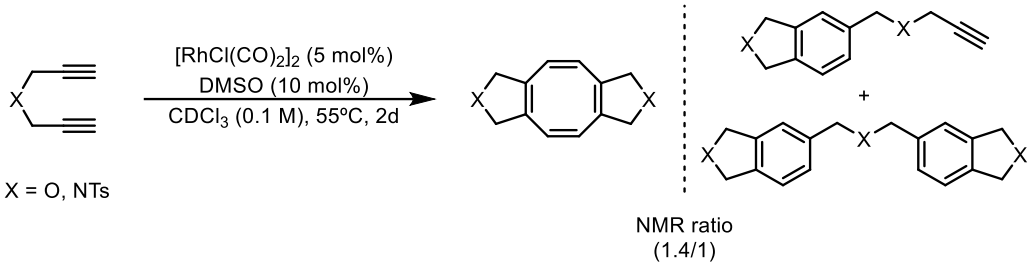
[112] Wender, P. A.; Christy, J. P.; Lesser, A. B.; Gieseler, M. T. *Angew. Chem. Int. Ed.* **2009**, *48*, 7687 –7690.
[113] Haley, R. A.; Zellner, A. R.; Krause, J. A.; Guan, H.; Mack, J. *ACS Sustainable Chem. Eng*. **2016**, *4*, 2464−2469.

a brominated ene triyne system and a subsequent 1,3 π-allyl palladium shift on a cyclooctadienal (Scheme 38).[114]



Scheme 38. COT´s synthesis through a palladium-catalysed cascade reaction

In 2014, Croatt and coworkers reported the use of tethered diynes as starting materials in the synthesis of COTs by Rh(I) catalysed [2+2+2] cycloadditions.[115] This methodology represents the first metal catalysed synthesis of COTs without the use of Ni (0). The key step is the use of DMSO to facilitate the second alkyne insertion at the same time that reductive elimination to afford the benzene product is almost suppressed due to the increase of the activation barrier. The use of terminal alkynes is mandatory to success of transformation and, indeed the scope of cyclooctatetraenes is quite poor (Scheme 39).



Scheme 39. Rh(I)-catalysed [2+2+2+2] of tethered diynes to form COTs

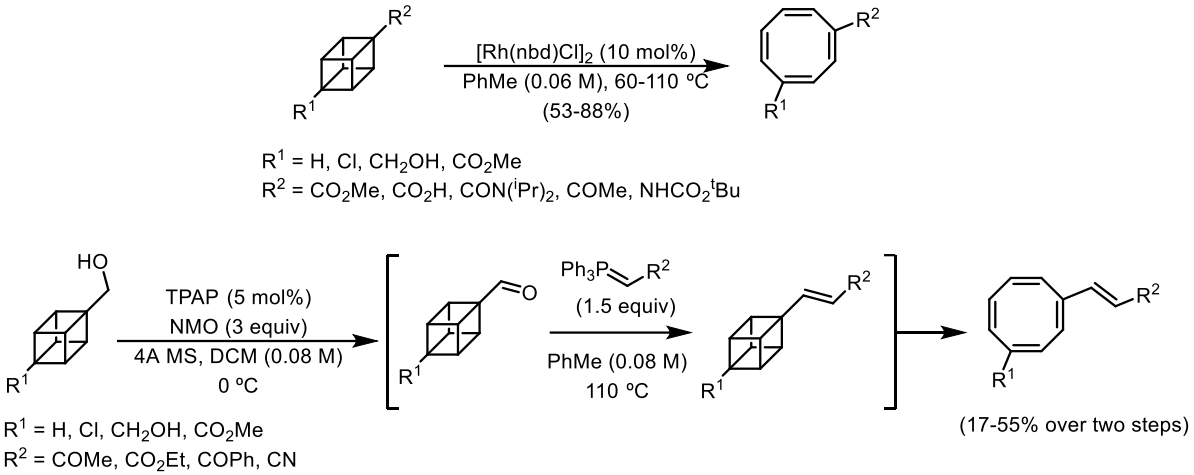
Finally, the use of Rh catalyst was also applied to transform cubanes into the corresponding disubstituted COTs. Craig applied the Eaton´s valence isomerization of cubanes[116] in presence of Rh (I) norbornadiene chloride to mono and di-substituted COT derivatives. In the same work, they also propose the synthesis of COTs by a one-pot tandem Ley-Griffith Wittig reactions without the presence of metal catalyst (Scheme 40). [117]

[114] Blouin, S.; Gandon, V.; Blond, G.; Suffert, J. *Angew. Chem. Int. Ed*. **2016**, *55*, 7208 –7211. To see similar reactivity to the formation of indolocyclooctatetraenes see: De, S.; Jash, M.; Chowdhury, C. *Chem. Commun*., **2020**, *56*, 15659-15662.

[115] Nasrallah, D. J.; Croatt, M. P. *Eur. J. Org. Chem*. **2014**, 3767–3772.

[116] Cassar, L.; Eaton, P. E.; Halpern, J. *J. Am. Chem. Soc*. **1970**, *92*, 3515–3518.

[117] Houston, S. D.; Xing, H.; Bernhardt, P. V.; Vanden Berg, T. J.; Tsanaktsidis, J.; Savage, G. P.; Williams, C. M. *Chem. Eur. J.* **2019**, *25*, 2735 – 2739.



Scheme 40. a) Rh(II)-catalysed cubane isomerization to COT and b) thermal one pot tandem cubane isomerization to COT.

4.4.2. Applications of COTs

Despite the fact that COT is a small annulene, its chemistry and applications are well received due to their characteristic tub-shaped geometry. In addition to its presence in basic science, cyclooctatetraenes are being studied from synthetic,[118] applied materials[119] and catalytic point of view. Several applications of COTs will be described next such as its presence in PAHs or its role as ligands to metal complexes.[120]

4.4.2.1. COT-embedded PAHs

PAHs can be catalogued as nonplanar or planar, depending on the presence or absence of geometric defects in the hexagonal sp^2 framework layer. The PAH´s properties, originated by the extended conjugation, allow to endow them with wide applications in molecular electronics such as organic field effect transistor (OFETs),[121] organic light emitting diodes (OLEDs)[122] or photovoltaic cells.[123] By contrast, distorted PAHs have emerged as intriguing units due to their ability to modify and improve the electronic and optical properties of their planar analogous.[124] The non planarity is typically originated by the presence of non-hexagonal rings into an

[118] a) Ernest, I. *Angew. Chem. Int. Ed.* **1976**, *15*, 207-214; b) Chaudhury, S.; Lindeman, S.; Donaldson, W. A. *Tetrahedron Lett*. **2007**, *48*, 7849-7852; c) Grange, R. L.; Gallen, M. J.; Schill, H.; Johns, J. P.; Dong, L.; Parsons, P. G.; Reddell, P. W.; Gordon, V. A.; Bernhardt, P. V.; Williams, C. M. *Chem. Eur. J*. **2010**, *16*, 8894-8903.

[119] a) Kornmayer, S. C.; Hellbach, B.; Rominger, F.; Gleiter, R. *Chem. Eur. J*. **2009**, *15*, 3380-3389. b) Gleiter, R.; Esser, B.; Kornmayer, S. C. *Acc. Chem. Res.* **2009**, *42*, 1108-1116. For its application as molecular detention devices, see: a) Lu, P., Hong, H., Cai, G., Djurovich, P., Weber, W. P., Thompson, M. E. *J. Am. Chem. Soc.* **2000**, *122*, 7480-7486; b) Andrew, T. L.; Swager, T. M. *Macromolecules* **2008**, *41*, 8306-8308.

[120] a) Roesky, P. W. Eur. *J. Inorg. Chem*. **2001**, *2001*, 1653−1660; b) Defieber, C., Grtzmacher, H., Carreira E. M. *Angew. Chem. Int. Ed*. **2008**, *47*, 4482 – 4502.

[121] Dong, H.; Fu, X.; Liu, J.; Wang, Z.; Hu, W. *Adv. Mater*. **2013**, *25*, 6158–6183.

[122] Hong, G.; Gan, X.; Leonhardt, C.; Zhang, Z.; Seibert, J.; Busch, J. M.; Brase, S. *Adv. Mater*. **2021**, *33*, e2005630

[123] Zhang, Z. G.; Li, Y. *Angew. Chem., Int. Ed.* **2021**, *60*, 4422–4433.

[124] a) Hashimoto, A.; Suenaga, K.; Gloter, A.; Urita, K.; Lijima, S. *Nature* **2004**, *430*, 870–873; b) Segawa, Y.; Ito, H.; Itami, K. *Nat. Rev. Mater*. **2016**, *1*, 1–14; c) Stepien, M.; Gonka, E.; Zyla, M.; Sprutta, N. *Chem. Rev.* **2017**, *117*, 3479–3716.

otherwise hexagonal framework. This fact is best illustrated by the [n]circulene family of compounds where a central n-membered ring is surrounded by n fused benzenoid rings giving rise a planar compound when the central ring is a six membered, and a negatively curved like a saddle-shaped[125] or positively curved like bowl-shaped[126] structures when the ring is larger (n = 7-16) or smaller (n = 3-5), respectively. While planar systems show zero Gaussian curvature, bowl shaped framework and saddle shaped carbon scaffolds present positive and negative Gaussian curvature, respectively.[127]

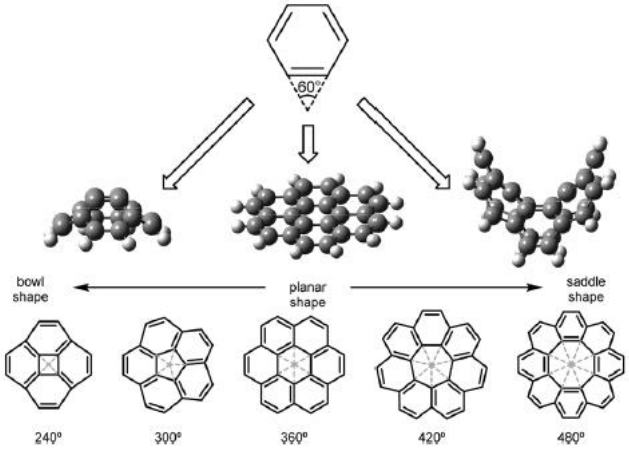


Figure 13. Wedge angles and nanographenes with positive, zero and negative Gaussian curvature (reproduced image from ref 127)

The introduction of eight-membered carbon rings into the PAH framework is a well established strategy to induce a deep curvature into the aromatic lattice. Based on these improved properties, one promising application of COTs is the incorporation of that scaffolds in the development of novel materials.

The first attempt to prepare a saddle-shaped molecule [8]circulene was reported by Wennerstöm and Thulin in 1976; however, the last step of the synthetic route failed presumably due to its instability.[128] Later on, many groups have been involved in the preparation and characterization of different scaffolds containing eight membered systems. Wu´s group published the first study of *peri*-substituted [8]circulenes showing its synthesis, properties and structural analysis. To achieve that goal, the synthetic protocol relied on the use of functionalised tetraphenylene and the subsequent generation of peripheral benzenes

[125]a) Marquez, I. R.; Castro-Fernández, S.; Millán, A.; Campaña, A. G. *Chem. Commun*. **2018**, *54*, 6705–6718; b) Pun, S. H.; Miao, Q. *Acc. Chem. Res.* **2018**, *51*, 1630–1642; c) Chaolumen, I. A. S.; Yamada, K.; Ito, H.; Itami, K. *Angew. Chem. Int. Ed*. **2021**, *60*, 23508-23532; d) Urieta-Mora, J.; Krug, M.; Alex, W.; Perles, J.; Fernández, I.; Molina-Ontoria, A.; Guldi, D. M.; Martín, N. *J. Am. Chem. Soc*. **2020**, *142*, 4162−4172.

[126] a) Bharat, A.; Bhola, R.; Bally, T.; Valente, A.; Cyranski, M. K.; Dobrzycki, Ł; Spain, S. M.; Rempała, P.; Chin, M. R.; King, B. T. *Angew. Chem. Int. Ed*. **2010**, *49*, 399–402; b) Kawasumi, K.; Zhang, Q.; Segawa, Y.; Scott, L. T.; Itami, K. *Nature Chem*. **2013**, *5*, 739–744; c) Evans, P. J.; Ouyang, J.; Favereau, L.; Crassous, J.; Fernández, I.; Perles, J.; Martín, N. *Angew. Chem. Int. Ed*. **2018**, *57*, 6774–6779.

[127] Gonzalez-Miera, G.; Matsubara, S.; Kono, H.; Murakami, K.; Itami, K. *Chem. Sci.,* **2022**, *13*, 1848-1868.

[128] Thulin, B.; Wennerström, O. *Acta Chem. Scand., Ser. B*. **1976**, *30*, 369–371.

through palladium-catalysed annulation. [129] Other authors described the construction of the same type of systems via generation of COT in the last step of the synthetic route by Scholl dehydrogenation. [130] Interestingly, Miao´s group disclosed the synthesis of a short-twisted ribbon curved nanographene constituted by 96 sp^2 carbon atoms. As in the previous case, the curvature arises from an embedded COT moiety originated by a cyclodehydrogenation reaction under acidic conditions (Figure 14). [131]

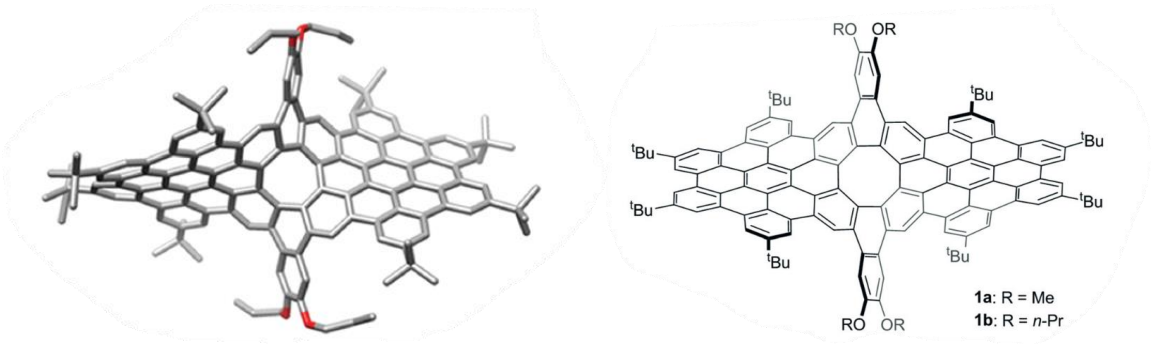


Figure 14. X-ray image of short-twisted ribbon curved nanographene published by Miao´s group (reproduced imaged from ref 131)

At the beginning of this decade, N. Martín and coworkers proposed the synthesis of two new homo and hetero molecular 3D nanographenes containing cyclooctatetraene motifs. The important point of this work is the incorporation of a horse saddle-shaped geometry which is expected to afford nonclassical applications.[132] Simultaneously, Mastalerz and coworkers reported a monkey saddle PAH consisting on six-, three-, five- and eight-membered rings starting from a truxene precursor.[133]

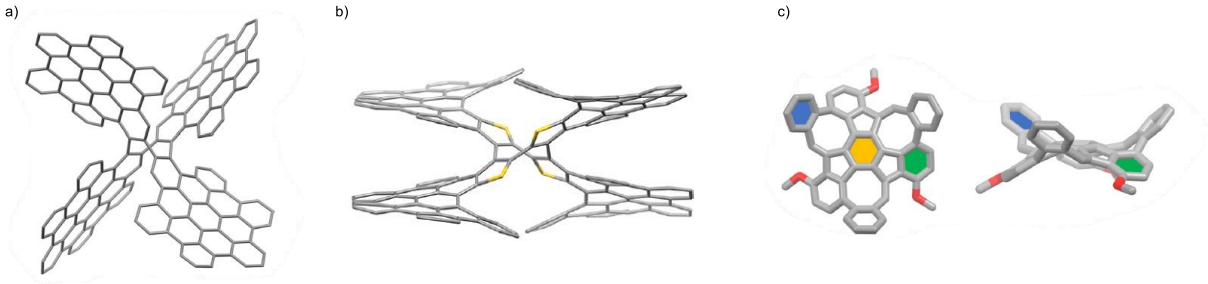


Figure 15. X ray structure of a) cyclooctatetraene-Ph based system, b) cyclooctatetrathiophene based system and c) monkey-saddle PAH (reproduced image from ref 132 a) and133)

[129] a) Feng, C-N.; Kuo, M-Y.; Wu, Y-T. *Angew. Chem. Int. Ed*. **2013**, *52*, 7791 –7794. Another examples where the COT core is introduced in the first step of synthesis: a) Miller, R. W.; Duncan, A. K.; Schneebeli, S. T.; Gray, D. L.; Whalley, A. C. *Chem. Eur. J*. **2014**, *20*, 3705–3711; b) Miller, R. W.; Averill, S. E.; Van Wyck, S. J.; Whalley, A. C. *J. Org. Chem*. **2016**, *81*, 12001–12005.

[130] Sakamoto, Y.; Suzuki, T. *J. Am. Chem. Soc*. **2013**, *135*, 14074‑14077.

[131] Cheung, K. Y.; Chan, C. K.; Liu, Z.; Miao, Q. *Angew. Chem. Int. Ed.* **2017**, *56*, 9003–9007.

[132] a) Urieta-Mora, J.; Krug, M.; Alex, W.; Perles, J.; Fernández, I.; Molina-Ontoria, A.; Guldi, D. M.; Martín, N. *J. Am. Chem. Soc.* **2020**, *142*, 4162–4172; b) Urieta-Mora, J.; García-Benito, I.; Zimmermann, I.; Aragó, J.; Calbo, J.; Grancini, G.; Molina-Ontoria, A.; Ortí, E.; Martín, N.; Nazeeruddin, M. K. *J. Mater. Chem. C* **2019**, *7*, 6656−6663; c) Marsella, M. J. *Acc. Chem. Res*. **2002**, *35*, 944–951.

[133] Kirschbaum, T.; Rominger, F.; Mastalerz, M. *Angew. Chem. Int. Ed*. **2020**, *59*, 270 –274.

More recently, Campaña´s group reported a new family of chiral nanographenes consisting on a highly distorted carbohelicene containing 8 and 7 membered rings. This saddle-helix hybrid nanographene represents the known carbohelicene with the largest torsion angle. In addition, these twisted PAHs present interesting chiroptical properties such as circularly polarized luminescence (CPL) emission.[134]

4.4.2.2. Other applications of COTs

OLEDs have received a great deal of attention recently. Thompson described the synthesis of octasubstituted cyclooctatetraenes using diaryldiynes with $RuH_2(CO)(PPh_3)_3$ as catalyst and its use as hole transporting layer (HTL) or electron transporting layer (ETL).[135] Esser reported that dibenzoCOT-functionalized polymers act as a potential battery electrode material. To achieve this goal, it is necessary the use of a redox-active group to obtain more sustainable rechargeable batteries. COTs, (dibenzo COTs in this work), perfectly match in this task because of it can be reversibly reduced in a two-electron process, where it changes from tub-shaped to planar conformation (non-aromatic and aromatic behaviour) (Figure 16).[136]

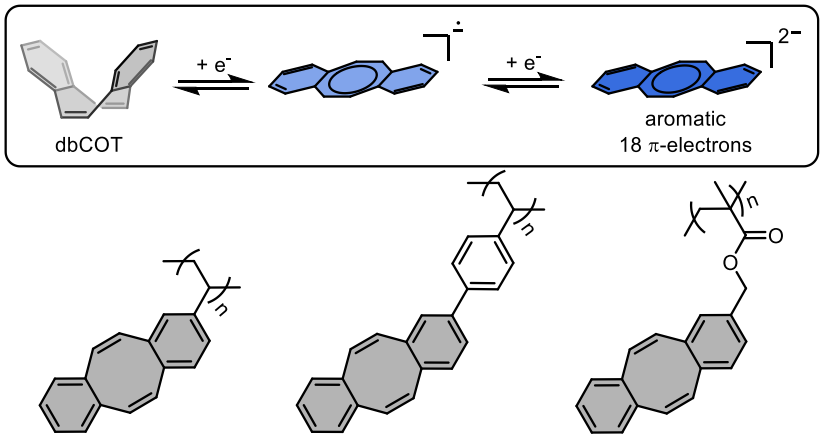


Figure 16. Stepwise reduction of dbCOT and functionalized polyhexacontaining dbCOT derivatives

The use of hydrocarbons with conjugation and shape properties, such as COTs, appear as an ideal model of new responsive material and single molecule electronics that can be switched by external stimuli. Recently, Strand and coworkers reported the preparation of alkyne-linked oligomeric [8]annulene-based materials that meet the desired characteristics (Figure 17).[137]

[134] Medel, M. A.; Tapia, R.; Blanco, V.; Miguel, D.; Morcillo, S. P.; Campaña, A. G. *Angew. Chem. Int. Ed*. **2021**, *60*, 6094–6100. For other helicene see: Xu, Q.; Wang, C.; Liu, X.; Wang, Y.; Chen, X.; Shen, Z.; Jiang, H. *Tetrahedron Lett.* **2023**, *115*, 154310. For a buckybowl example see: Duan, Y.; Chen, M.; Hayashi, H.; Yamada, H.; Liu, X.; Zhang, L. *Chem. Sci.,* **2023**, Advance Article

[135] Lu, P.; Hong, H.; Cai, G.; Djurovich, P.; Weber, W. P.; Thompson, M. E. *J. Am Chem. Soc*. **2000**, *122*, 7480-7486.

[136] Desmaizieres, G.; Speer, M. E.; Thiede, I.; Gaiser, P.; Perner, V.; Kolek, M.; Bieker, P.; Winter, M.; Esser, B. *Macromol. Rapid Commun*. **2021**, *42*, 2000725.

[137] Tasić, M.; Ivković, J.; Carlström, G.; Melcher, M.; Bollella, P.; Bendix, J.; Gorton, L.; Persson, P.; Uhlig, J.; Strand, D. *Nat. Commun*, **2022**, *13*, 860.

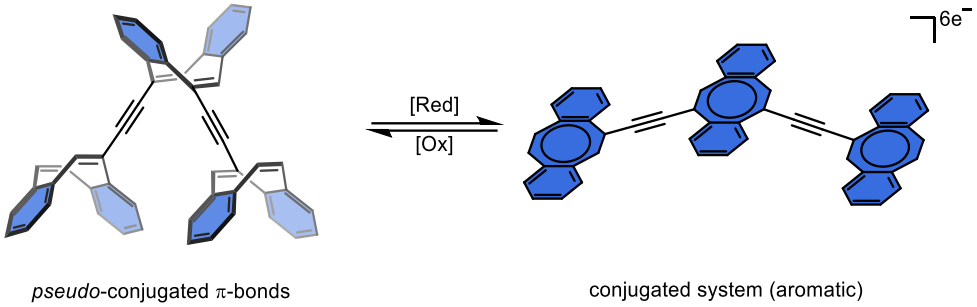


Figure 17. Alkynyl connected [6-8-6]-annulenes

Another applications are the flapping molecules (FLAPs), which are characterized to merge a rigid aromatic scaffold with a flexible 8π ring, such as COT, phenothiazine or dibenzo-oxepin. That combination allows to apply FLAPs in a variety of functions like photoresponsive liquid crystals, flexible mechanophore or environment-sensitive fluorophores. Usually, FLAPs adopt a bent conformation in equilibrium between "V" and "A" shaped form in singlet ground state (S_0) and, after photoexcitation, a fully π-conjugated planar system in the lowest singlet excited state (S_1). Saito and coworkers reported a flapping peryleneimide and a *N*-flapping anthracene which show strong visible absorption and fluorogenic properties and that act as a fluorescent viscosity probe, respectively (Figure 18). [138]

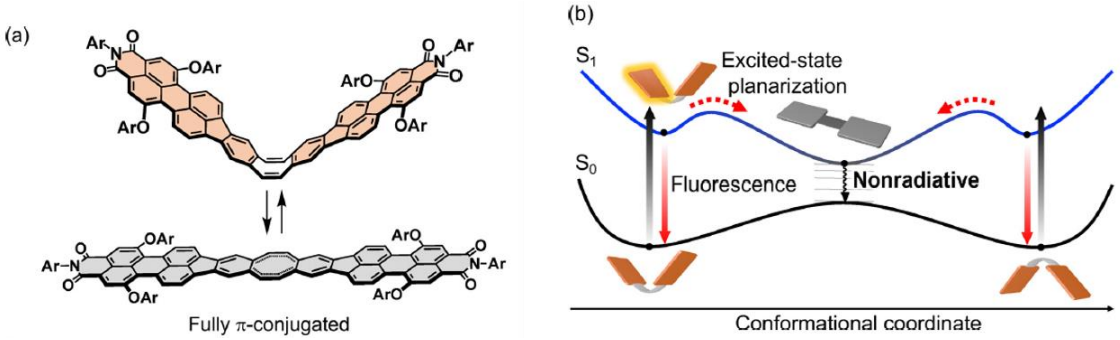


Figure 18. a) Conformational isomers of a flapping peryleneimide and b) energy profiles in S_0 and S_1 (reproduced images from ref 138 a))

Other applications of COTs include its use as ambipolar semiconductors for field effect transistors, [139] functionalized porphyrins with improved properties[140] or in inorganic chemistry as ligand to metal complexes due to its variable hapticity, [141] encompassing from simple alkene

[138] a) Kimura, R.; Kuramochi, H.; Liu, P.; Yamakado, T.; Osuka, A.; Tahara, T.; Saito, S. *Angew. Chem. Int. Ed*. **2020**, *59*, 16430 –16435; b) Goto, Y.; Omagari, S.; Sato, R.; Yamakado, T.; Achiwa, R.; Dey, N.; Suga, K.; Vacha, M.; Saito, S. *J. Am. Chem. Soc*. **2021**, *143*, 14306-14313.
[139] Nishinaga, T.; Ohmae, T.; Aita, K.; Takase, M.; Iyoda, M.; Arai, T.; Kunugi, Y. *Chem. Commun*., **2013**, *49*, 5354-5356.
[140] Ostapko, J.; Gorski, A.; Buczyńska, J.; Golec, B.; Nawara, K.; Kharchenko, A.; Listkowski, A.; Ceborska, M.; Pietrzak, M.; Waluk, J. *Chem. Eur. J*. **2020**, *26*, 16666 – 16675.
[141] Hill, A. F.; Smith, M. K. *Organometallics* **2007**, *26*, 3900-3903.

binding to η^8 binding mode. Although is mainly presence in f-block metals,[142] other works reported the use of COTs derivates in d-block complex.[143]

[142] a) Roesky, P. *Eur. J. Inorg. Chem*. **2001**, 1653- 1660; b) Summerscales, O. T. *Science* **2006**, *311*, 829-831; c) Panda, T.; Zulys, A.; Gainer, M.; Roesky, P. *Organometallics* **2005**, *24*, 2197-2202.

[143] a) Wender, P. A.; Lesser, A. B.; Sirois, L. E. *Angew. Chem. Int. Ed*. **2012**, *51*, 2736 –2740; b) Murahashi, T.; Kato, N.; Ogoshi, S.; Kurosawa, H. *J. Organomet. Chem*. **2008**, *693*, 894-898. For the use of tetraphenylenes as ligands see: c) Wang, X.; Cui, Y.; Mak, T.; Wong, H. *J. Chem. Soc., Chem. Commun*. **1990**, 167-169; d) Huang, H.; Hau, C.-K.; Law, C. C. M.; Wong, H. N. C. *Org. Biomol. Chem*. **2009**, *7*, 1249-1257.

4.5. Benzynes

Reactivity can be described as a measure of the impulse for which a substance undergoes a chemical reaction, either by itself or with other materials to form a more complex system, generally accompanied by an overall release of energy. Reactivity is dependant of parameters such as temperature, functional groups, thermal or kinetic stability, stereochemistry, molecular strain… among other. [144] In this section we will address the reactivity of certain molecules associated to bond strain in a non-planar scaffold.

During the last century, many authors had wanted to find a better understanding of electronic properties of cyclooctatetraene (e.g., non-aromaticity), reason why they explore the introduction of one (or two) alkynes moieties into the COT core, which could result in strained sp-sp hybrid bonds, contributing to the planarity of a fully conjugated system.

Throughout this section, we will be focused on the reactivity shown by the family of COTynes (cycloocta-1,3,5-trien-7-yne) and their similarities and differences with their six-membered analogues, benzynes. Before the discussion a brief introduction of benzynes followed by a more detailed description of COTynes comprises the introduction of this section.

Arynes are neutral reaction intermediates derived from the abstraction of two hydrogen atoms from arene precursors, reason why they are also denominated didehydroarenes.[145] As a result, two new electrons are positioned in two sp^2 orbitals. Although the first reference to an aryne as a reaction intermediate was published by Stoermer and Kahlert in 1902,[146] it was not until 25 years later, when Clarke and Bachmann described the ortho-benzyne as a diradical species.[147] Later on, Roberts and coworkers demonstrated in 1953 the existence of benzyne employing ^{14}C labelling experiments.[148] From this time, many authors contributed to a better understanding of the aryne nature, mainly *o*-benzyne, with the use of different spectroscopic characterizations.[149]

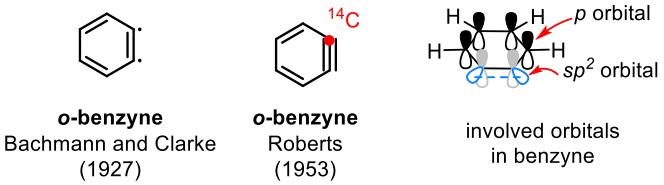


Figure 19. Postulated o-benzynestructures and its orbitals

[144] Hopf, H.; Grunenberg, J. Angle-Strained Cycloalkynes. *In Strained Hydrocarbons*; Wiley: Weinheim, **2009**; pp 375–397.

[145] a) Hoffman, R. W. *Dehydrobenzene and Cycloalkynes*, Academic Press, New York, **1967**; b) Pellissier, H.; Santelli, M. *Tetrahedron* **2003**, *59*, 701-730; c) García, F.; Peña, D.; Pérez, D.; Guitián, E. *Aryne Cycloadditions for the Synthesis of Functional Polyarenes in Modern Aryne Chemistry.* Ed. Biju, A. Wiley-VCH, **2021**

[146] Stoermer, R.; Kahlert, B. *Ber. Dtsch. Chem. Ges*. **1902**, *35*, 1633-1640.

[147] Bachmann, W. E.; Clarke, H. T. *J. Am. Chem. Soc*. **1927**, *49*, 2089-2098.

[148] Roberts, J. D.; Simmons, H. E.; Carlsmith, L. A.; Vaughan, C. W. *J. Am. Chem. Soc.* **1953**, *75*, 3290-3291.

[149] a) Radziszewski, J. G.; Hess, B. A.; Zahradnik, R. J. *Am. Chem. Soc*. **1992**, *114*, 52-57; b) Berry, R. S.; Spokes, G. N.; Stiles, M. *J. Am. Chem. Soc*. **1962**, *84*, 3570–3577; c) Fisher, I. P.; Lossing, F. P. *J. Am. Chem. Soc*. **1963**, *85*, 1018–1019; d) Warmuth, R. *Angew. Chem. Int. Ed.* **1997**, *36*, 1347-1350.

4.5.1. Structure and generation

The most studied aryne is the 1,2-didehydrobenzene, known as *o*-benzyne or simply benzyne. Its structure can be represented by three different resonant forms as shown in Figure 20.

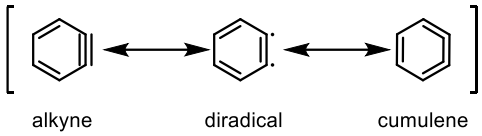


Figure 20. Resonant structures of 1,2-didehydrobenzene

It is widely accepted the major contribution of the strained alkyne between two adjacent carbon atoms, although cumulenic contribution has been demonstrated through its generation on the surface and its analysis by atomic force microscopy.[150] Due to their structure, benzynes present a short life time that make them a very interesting species to perform several synthetic applications. In fact, it is known that the six π electrons are not-involucrate in its reactivity, and moreover, computational calculations show a low LUMO energy value, which makes benzyne a very interesting electrophile and dienophile in cycloaddition reactions.[151]

Regarding its preparation, due to the short live of these species, arynes cannot be stored, and its application in synthesis requires their formation *in situ*.[152] A variety of methodologies for the formation of arynes have been developed, where most of them require the use of aromatic precursors. One of the most employed classic methodologies is based on the elimination of a leaving group located in an *ortho* position to a benzenic anion (Figure 21, a and b).[153] To form that anion two different procedures can be applied; the first one requires the use of halogenated compounds (triflates are also compatibles) and strong bases to remove the hydrogen located at the *ortho* position. However, the main handicap rely on the use of strong bases, which have to be compatibles with the functional groups present at the substrates. As second option, the use of *ortho*-dihalogenated benzenes in presence of organometallic reactants to carry out, through a metal-halogen exchange, the corresponding metal salts (mainly lithium or magnesium) that evolve to benzyne by *ortho*-elimination.

On other hand, it is possible to generate benzynes by fragmentation of cyclic substrates. For example, although in this process stable molecules (CO or CO_2) are formed, the use of phthalic anhydride (isobenzofuranes) requires the use of harsh conditions as high temperatures or photochemical process (Figure 21, c).[154] Another common employed benzyne precursor is the benzenediazonium 2-carboxylate, which evolves into benzyne at moderate temperatures releasing N_2 and CO_2 (Figure 21, d).[155]

[150] Pavliček, N.; Schuler, B.; Collazos, S.; Moll, N.; Pérez, D.; Guitián, E.; Meyer, G.; Peña, D.; Gross, L. *Nature Chem.* **2015**, *7*, 623-628.
[151] Rauk, A. *Orbital Interaction Theory of Organic Chemistry*, Second Edition, Willey, **2001**.
[152] Wenk, H. H.; Winkler, M.; Sander, W. *Angew. Chem. Int. Ed*. **2003**, *42*, 502–528.
[153] a) Wotiz, J. H.; Huba, F. *J. Org. Chem*. **1959**, *24*, 595; b) Bachelet, J. P.; Caubère, P. *J. Org. Chem*. **1982**, *47*, 234-238; c) Matsumoto, T.; Hosoya, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett*. **1991**, *32*, 6735.
[154] Campbell, C. D.; Rees, C. W. *J. Chem. Soc. C.* **1969**, *5*, 742-747.
[155] Friedman, L.; Logullo, F. M. *J. Am. Chem. Soc.* **1963**, *85*, 1549.

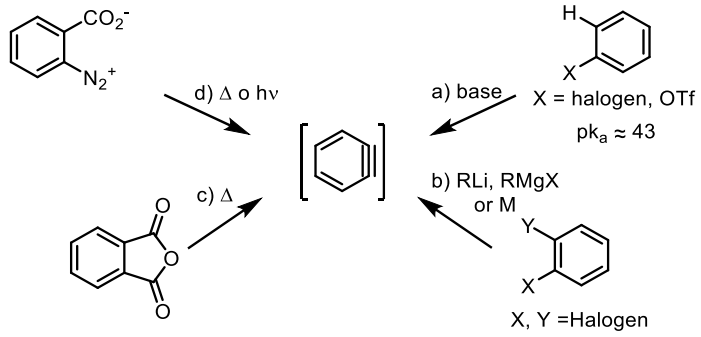


Figure 21. Classical methods for benzyne´s generation

In 1983, Kobayashi reported an important breakthrough for the generation of benzyne.[156] The treatment of *ortho*-(trimethylsilyl)aryl triflates with a fluoride source (TBAF, CsF, etc) gives rise to the formation of benzyne specie in mild conditions and without the necessity of strong bases, which makes this methodology highly selective in the presence of different functional groups. The first step involves the formation of a pentavalent silyl species, which undergoes elimination of Si-F bond leading an anion in *ortho* position to the triflate group. Subsequent elimination of OTf group renders the benzyne species. Alternatively, formation of benzynes through a concerted process cannot be ruled out. Years later, Kitamura developed a similar procedure of benzyne´s generation using a different leaving group (Figure 22). [157]

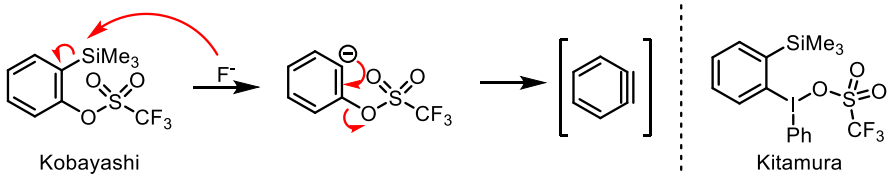


Figure 22. Proposed mechanism for benzyne generation

Kobayashi´s method presents several advantages like the high compatibility with different functional groups and the good solubility of fluoride sources based on good election of solvent, temperature and additive, that allow to control how fast the benzyne is generated.

Due to the great opportunity that *ortho*-(trimethylsilyl)aryl triflates offer for the preparation of benzynes, many authors have described synthetic routes that give access to these systems. From the original one reported by Kobayashi with 2-chlorophenol and subsequent treatment with triflic anhydride the target triflate was obtained in very good yield (Figure 23). Later on, in 2002, Guitián and coworkers developed a one-pot three steps procedure starting from substituted 2-bromophenols based on sequential o-silylation, metal-halogen exchange and triflation. [158] Thereafter, Brimble and coworkers reported a modification of Kobayashi´s original procedure that avoid the use of ^{n}BuLi. [159]

[156] Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett*. **1983**, *12*, 1211-1214. For a recent review of Kobayashi approach and its history see: Shi, J.; Li, L.; Li, Y. *Chem. Rev*. **2021**, *121*, 3892–4044.
[157] Kitamura, T.; Yamane, M. *J. Chem. Soc., Chem. Commun.* **1995**, 983-984.
[158] Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454–1458. For a flow version of this protocol see: Michel, B.; Greaney, M. F. *Org. Lett*. **2014**, *16*, 2684–2687.
[159] Atkinson, D. J.; Sperry, J.; Brimble, M. A. *Synthesis* **2010**, *2010*, 911–913.

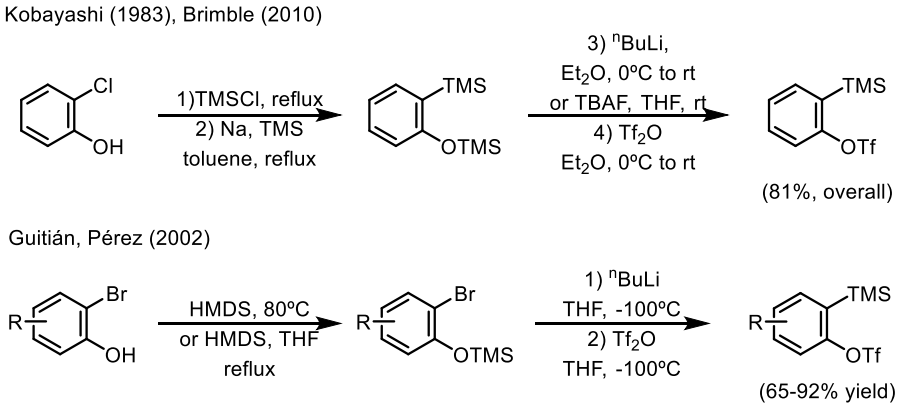


Figure 23. Formation of ortho*-(trimethylsilyl)aryl triflates by metal-halogen strategies*

The mentioned strategies probably are the most used, however many others have been developed using alternatives such as *ortho*-lithiation, arene ring formation or transition-metal-catalysed *ortho*-C–H bond functionalization.[160]

4.5.2. Reactivity

Arynes present a markedly electrophilic character and, therefore, undergo attacks by a wide range of nucleophiles. The corresponding contiguous formed anion can undergo intra- or inter-molecular evolutions to form a wide variety of products. [161]

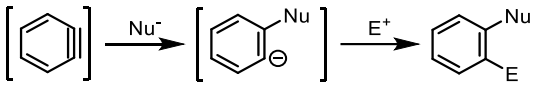


Figure 24. Nu/E addition to an aryne

Arynes are also able to participate as dienophiles in cycloaddition reactions. Examples of [4+2] cycloadditions of benzyne with benzofuranes, isoindoles, 1,3-cyclohexadienes, etc, have been well studied. [162] Interestingly, one of the most used methodologies to synthetize PAHs makes use of benzynes in combination with dienes containing a group that could be released after the cycloadditions such as cyclopentadienones (CO), pyrones (CO_2) or tetrazines (N_2) (Figure 25).[163]

[160] a) García-López, J. A.; Greaney, M. F. *Org. Lett*. **2014**, *16*, 2338−2341; b) Shi, J.; Li, L.; Li, Y. *Chem. Rev*. **2021**, *121*, 3892–4044.

[161] Yoshida, H.; Shirakawa, E.; Honda, Y.; Hiyama, T. *Angew. Chem. Int. Ed.* **2002**, *41*, 3247-3249; b) Okuma, K.; Nojima, A.; Matsunaga, N.; Shioji, K. *Org. Lett*. **2009**, *11*, 169-171; c) Yoshida, H.; Morishita, T.; Ohshita, J. *Org. Lett.* **2008**, *10*, 3845-3847.

[162] Wittig, G.; Pohmer, L. *Angew. Chem.* **1955**, *67*, 348-348. For a review see: Bhojgude, S. S.; Bhunia, A.; Biju, A. T. *Acc. Chem. Res*. **2016**, *49*,1658–1670.

[163] a) Krompiec, S.; Kurpanik-Wójcik, A.; Matussek, M.; Angelika Mieszczanin, B.; Fijołek, A. *Materials* **2022**, *15*, 172; b) Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Tetrahedron Lett*. **1997**, *38*, 5375-5378; c) Sauer, J.; Heinrichs, G. *Tetrahedron Lett*. **1966**, *7*, 4979; d) Suh, S-E.; Barrosa, S. A.; Chenoweth, D. M. *Chem. Sci*., **2015**, *6*, 5128-5132.

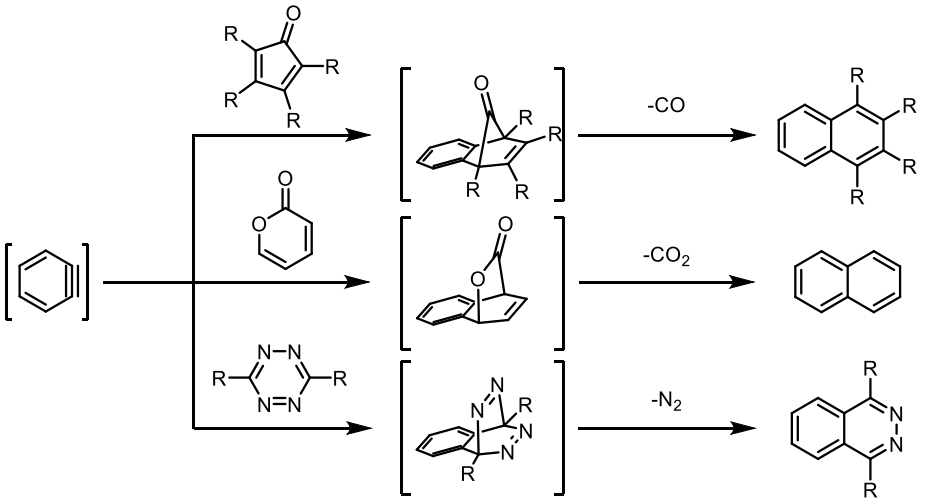


Figure 25. Diels-Alder reaction of benzyne with cyclopentadienones (up), pyrones (middle) and tetrazines (down)

Benzynes are able to participate in [2+2] cycloadditions (dimerizations under thermal conditions) to afford biphenylenes probably through a radical mechanism.[164] Recently, Tokiwa and Akai reported a synthesis of biphenylene by a formal [2+2] cycloaddition in which the driving force for the regioselective cyclodimerization is the presence of London dispersion forces between *ortho*-substituents. A plausible mechanism could include a stepwise transformation involving singlet diradical intermediates. [165] This approach has been applied to the synthesis of helical molecules using fused tetracyclic benzynes in a high selective form (Figure 26).

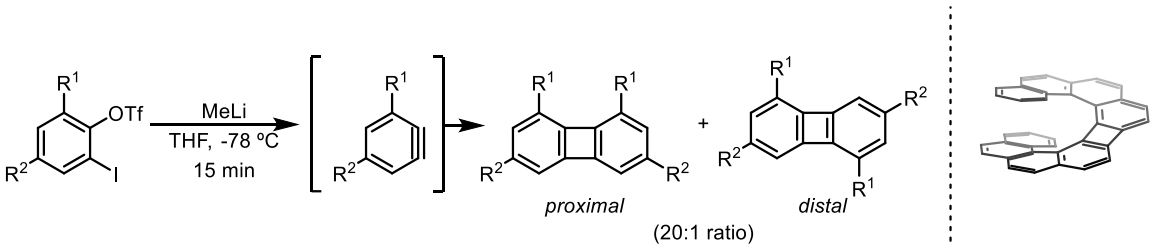


Figure 26. [2+2] cycloaddition of arynes to helical molecules

On the other hand, arynes and metals feedback on each other. While alkynes release part of their tension by coordination to a metal atom, metals gain electrons from arynes to complete the 18-electron rule. In fact, the first complex of monomeric niobium- and tantalum-benzyne complex was unambiguously characterised by X-ray diffraction.[166] Interestingly, Buchwald and Broene reported how some of these complexes show the insertion of unsaturated partners such as alkynes, nitriles, alcohols or ketones; however, stoichiometric amounts of metals were required. [167]

[164] a) Feltenberger, J. B.; Hayashi, R.; Tang, Y.; Babiash, E. S. C.; Hsung, R. P. *Org. Lett*. **2009**, *11*, 3666–3669; b) Hosoya, T.; Hasegawa, T.; Kuriyama, Y.; Suzuki, K. *Tetrahedron Lett.* **1995**, *36*, 3377-3380.
[165] Ikawa, T.; Yamamoto, Y.; Heguri, A.; Fukumoto, Y.; Mukarami, T.; Tagaki, A.; Masuda, Y.; Yahata, K.; Aoyama, H.; Shigeta, Y.; Tokiwa, H.; Akai, S. *J. Am. Chem. Soc.* **2021**, *143*, 10853-10859.
[166] McLain, S. J.; Schrock, R. R.; Sharp, P. R.; Churchill, M. R.; Youngs, W. J. *J. Am. Chem. Soc.* **1979**, *101*, 263-265.
[167] Broene, R. D.; Buchwald, S. L. *Science* **1993**, *261*, 1696-1701.

At the end of the 20th century, this fact was taken advantage of Pérez-Guitián´s group to develop a powerful strategy to the synthesis of a wide variety of PAHs based on the first Pd-catalysed [2+2+2] cyclotrimerization of arynes.[168] The combination of benzynes with electron poor alkynes, like dimethyl acetylenedicarboxylate (DMAD), afford phenanthrenes or naphthalenes by insertion of one or two molecules of benzyne depending of which ligand is present in the Pd (0) source. While the use of $Pd(PPh_3)_4$ render the insertion of one molecule of alkyne, the use of $Pd_2(dba)_3$ gives rise to the introduction of two molecules of alkyne. This observation can be rationalized taking into account which ligand is present in the catalyst. In one hand, PPh_3 can be considered as a strong ligand that is not easy to displace from the coordination sphere of metal, what prevents the entry of a second alkyne molecule. On the contrary, dibenzylideneacetone (dba) acts as a weaker ligand that may be moving in and out of the coordination sphere, allowing DMAD to coordinate and insert (Figure 27).[169]

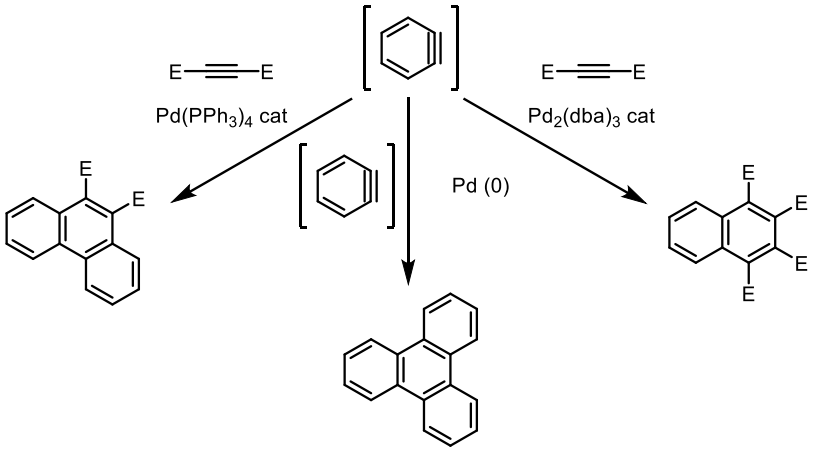


Figure 27. Pd(0)-catalysed [2+2+2] cycloaddition of benzynes and alkynes

Since this pioneering work, many other have been published. Examples of that can be the one reported by Mastalerz on the synthesis of pyrenylenes or the synthesis of tris(benzocyclobutadieno)triphenylene reported by Pérez and Vollhardt.[170]

[168] Peña, D.; Escudero, S.; Pérez, D.; Guitián, E.; Castedo, L. *Angew. Chem. Int. Ed.* **1998**, *37*, 2659-2661.
[169] Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Am. Chem. Soc.* **1999**, *121*, 5827-5828.
[170] a) Popp, D.; Elbert, S. M.; Barwig, C.; Petry, J.; Rominger, F.; Mastalerz, M. *Angew. Chem. Int. Ed*. **2023**, *62*, e202219277; b) Iglesias, B.; Cobas, A.; Pérez, D.; Guitián, E.; Vollhardt, K. P. C. *Org. Lett*. **2004**, *6*, 3557–3560.

4.6. COTynes´s family

COTyne (cycloocta-1,3,5-trien-7-yne) can be considered as the non-aromatic eight-membered analogous of benzyne, presenting three conjugated doubled bonds and one strained triple bond (acetylenic-type bond).[171] The acetylenic moiety presents a deviation from linearity affording to COTynes low stability and high reactivity. There are many examples in the literature where unstable systems can be stabilized by the introduction of fused benzene rings.[172] Stability of COTynes is closely related to planarity of the molecule that depends on the number of benzene rings around the central eight-membered ring, the higher number the greatest stability, except for the case of three benzene rings in which the steric hindrance of *peri* hydrogens must be avoided. This behaviour can be rationalized taking into account that compounds with an acetylenic moiety protected from nucleophilic attacks will be more stable. Thus, dibenzoCOTyne will be the less reactive among the simple COTynes.[173]

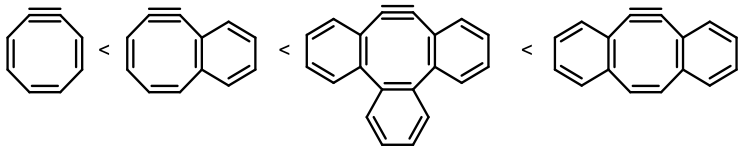


Figure 28. Stability comparison of COTynes

There are few examples in literature that show the behaviour of these species under different conditions owing to, most likely, the lack of available synthetic methodologies to prepare symmetrical and unsymmetrical COTynes. Besides the COTs and benzoCOTs already discussed in section 4.4, the family of COTyne will be discussed next, including the synthesis of precursors, the preparation of alkynes themselves and their applications.

4.6.1. COTynes

The first example of formation of COTyne **28** was described by Krebs in 1967. [174]The treatment of bromocyclooctatetraene with potassium t-butoxide (KO^tBu) affords an intermediate COTyne which could be trapped with several reagents such as azides, cyclopentadienones, benzofuranes or dienes, indicating that the nature of that intermediate could be the acetylenic one instead of its cumulenic form. In addition, the isolation in low yield of naphtho-2,3-cyclooctatetraene as dimerization product also supports the alkyne formation.[175] Nevertheless, it was not possible to isolate the elusive COTyne **28** because of its intrinsic instability (Figure 29).

[171] Krebs, A., Wilke, J. (1983). *Angle strained cycloalkynes*. In: Wittig Chemistry. Topics in Current Chemistry, vol 109. Springer, Berlin, Heidelberg.
[172] Shi, X.; Chi, C. *Chem. Rec*. **2016**, *16*, 1690–1700.
[173] a) Huang, N. Z.; Mak, T. C. W.; Li, W.-K. *Tetrahedron Lett.* **1981**, *22*, 3765-3768; b) Huang, N. Z. *Acc. Chem. Res.* **1982**, *15*, 96-102
[174] Krebs, A.; Byrd, D. *Liebigs Ann. Chem*. **1967**, *707***,** 66-74.
[175] Krebs, A. *Angew. Chem. Int. Ed. Engl*. **1965**, *11*, 953-954.

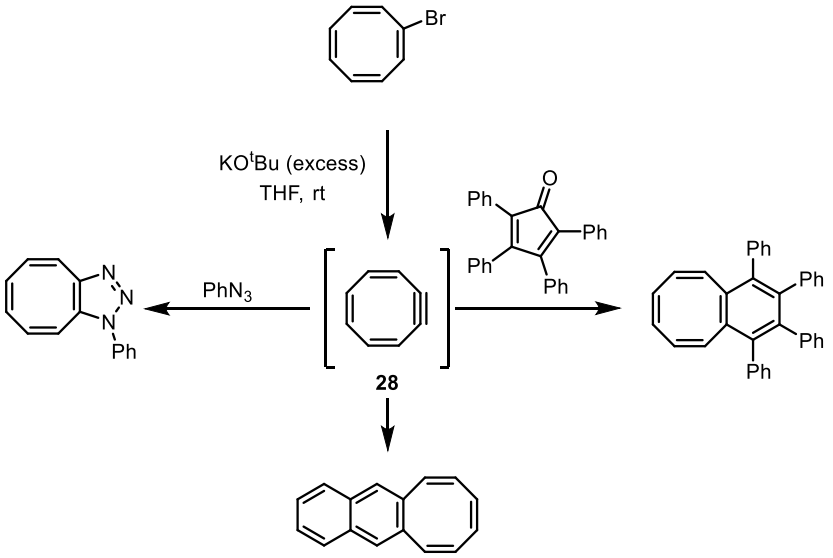
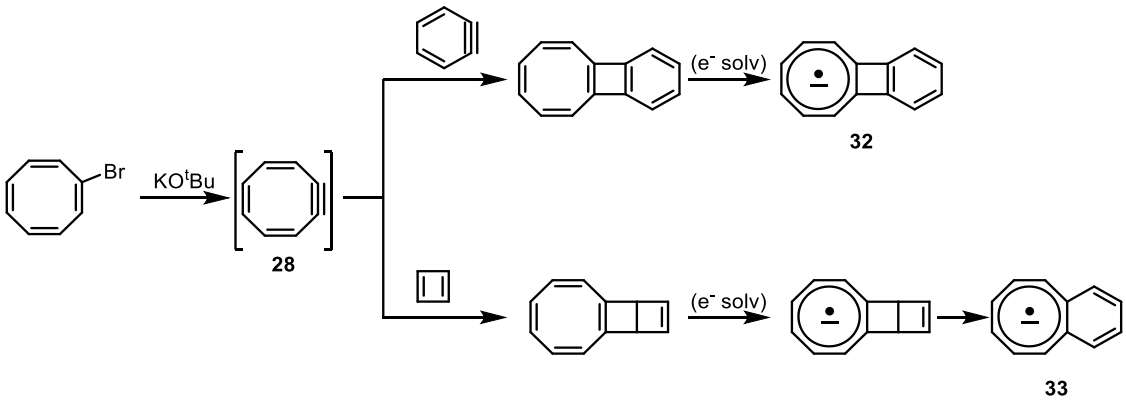


Figure 29. Evidences of formation of COTyne

Years later, Stevenson ad coworkers tried to rescue COTyne chemistry. Keeping the idea of planarize COTyne, they focused their attention in a previous work of Wenthold and Lineberger[176]where the combination of KO^{t}Bu in a liquid nitrogen-cooled flowing afterglow apparatus renders the [8]annulyne anion radical. With this idea in mind, Stevenson propose the observation (kinetically stable for hours) and reactivity of [8]annulyne radical anion in presence of solvated electrons with species such as cyclobutadiene or benzyne to give rise to the corresponding radical planar adducts **32** and **33** through a formal [2+2] cycloaddition (Scheme 41).[177]

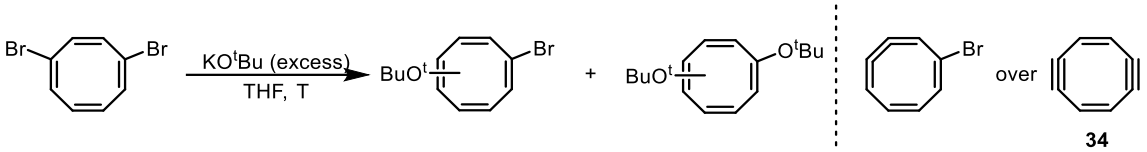


Scheme 41. Formal [2+2] cycloaddition of COTyne with benzyne and cyclobutadiene

As an alternative to isolation of COTyne **28** some authors thought about the dienediyne **34** (COTdiyne). Sondheimer and Huang describe in 1982 their attempts to isolate it from dibenzoCOT.[173] Their initial experiments were based on the method described by Krebs, assuming that the treatment of 1,4-dibromocyclooctatetraene with KO^{t}Bu would lead to the desired COTdiyne **34**. Unfortunately, a mixture of two products, the partial and fully

[176] Wenthold, P. G.; Lineberger, W. C. *J. Am. Chem. Soc*. **1997**, *119*, 7772-7777.
[177] a) Peters, S. J.; Turk, M. R.; Kiesewether, M. K.; Stevenson, C. D.; *J. Am. Chem. Soc*. **2003**, *125*, 11264-11268; b) Kiesewetter, M. K.; Reiter, R. C.; Stevenson, C. D. *Org. Lett*. **2005**, *7*, 2623–2626.

functionalized COT, were obtained confirming that the formed intermediate might be the cumulene type species instead of the COTdiyne **34** (Scheme 42)



*Scheme 42. Attempt to form COTdiyne **34***

Stevenson and coworkers also contribute to this field describing a similar work to simple COTyne **28**. Treatment of 1,4-dibromocyclooctatetraene with KO^{t}Bu, 18-crown-6 ether in THF at 173K renders the [2+2] polymerization of presumably formed dienediyne **34**.[178] To verify the formation of **34** they tried to trap it as a radical anion, however the formation of polymer seems to be very fast making it very difficult to detect.

4.6.2. BenzoCOTynes

Due to the lack of stability shown by the parent cycloocta-1,3,5-trien-7-yne **28**, Sondheimer and coworkers described different approaches to prepare benzofused derivatives.[179] The treatment of 6-bromobenzocyclooctene **35** under basic conditions led to the formation of 7-t-butoxybenzocyclooctene **36** as a single product that might suggest a trapping of a cumulenic unstable species (Figure 30, a). In order to solve this drawback, Sondheimer hypothesized that the use of 5-bromo-10-methylbenzocyclooctene **37** should afford the aryne intermediate instead of the cumulenic species. Following this idea, the treatment of the monobrominated COT **37** with an excess of KO^{t}Bu affords the benzoCOT **39** derived from the nucleophilic attack over the alkyne intermediate **38**, which confirms the formation of an acetylenic species. In addition, trapping experiments with 1,3-diphenylisobenzofurane (DIB) led to adduct **40**, that again suggest the formation of an acetylenic intermediate **38** (Figure 30, b).

[178] Kiesewetter, M. K.; Reiter, R. C.; Stevenson, C. D. *Org. Lett*. **2005**, *7*, 2623-2626.
[179] a) Wong, H.N.C.; Chan, T.L.; Sondheimer, F. *Tetrahedron Lett*. **1978**, *7*, 667-670; b) Chan, T. L.; Huang, N. Z.; Sondheimer, F. *Tetrahedron*, **1983**, *39*, 427-432.

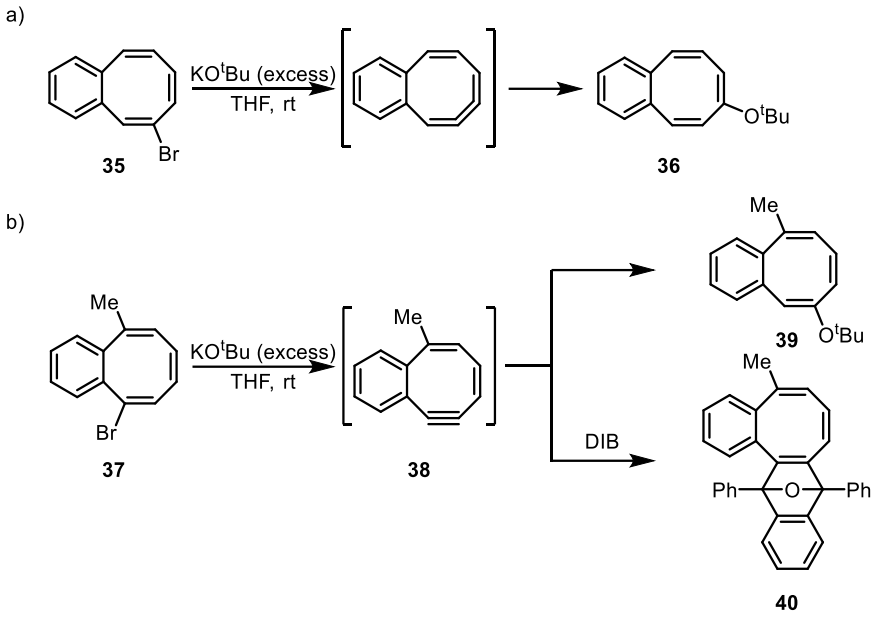


Figure 30. Attempts to isolate benzoCOTyne from a) 6-bromobenzoCOT and b) 5-bromo-10-methylbenzoCOT

Although the isolation of benzoCOTyne **29** remains unsolved and all the attempts were based on trapping experiments, some other efforts to isolate the parent benzoCOTdiyne **42** show the low stability of this interesting diacetylenic intermediate. Following the same procedure, treatment of 5-10-dibromobenzoCOT **41** with an excess of KO^{t}Bu in THF for just 30 seconds at rt followed by isolation using chromatography afford the benzoCOTdiyene **42**, which rapidly decomposes even at 0 ^oC. IR analysis shows a weak triple bond band at 2100 cm^{-1} and its NMR analysis performed at -20 ^oC exhibit a sharp olefinic signal at 5.07 ppm. As in the monoacetylene case, this species can also be trapped by dienes. (Figure 31).

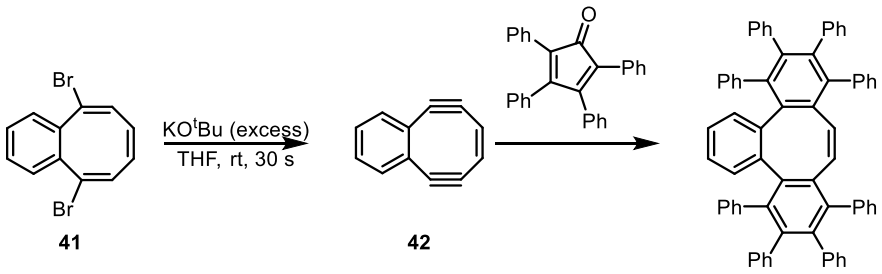


*Figure 31. Isolation of benzoCOTdiyne **42** under basic conditions and its trapping using TPCPDN as diene*

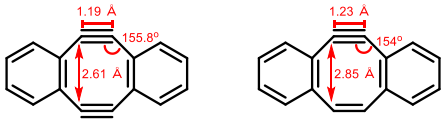
From the results found, we can conclude that the presence of a second unit of alkyne over the benzofused cyclooctatetraene scaffold affords stability enough to allow its isolation although in certain limited conditions.

4.6.3. DibenzoCOTynes

As mentioned previously, as higher is the number of acetylenic systems over the COT unit, greater is the stability. In fact, Sondheimer was the first to report the isolation of *sym* -dibenzo-1,5-cyclooctadiene-3,7-diyne **43** (dibenzoCOTdiyne) from bromination of *sym*-

dibenzocyclooctatetraene and subsequent basic treatment with KO^{t}Bu. [180] DibenzoCOTdiyne **43** seems to be very stable, observing just some traces of decomposition after two days when the solid is allowed to stand at room temperature without protection from light or air. This stability allowed Simonetta to describe its X-ray structure, observing how both acetylenic units exhibit an angle distortion of 155.8º, an alkyne-alkyne distance of 2.61 Å and an alkyne length distance of 1.19 Å, making the dibenzoCOTdiyne essentially planar.[181]

By contrast, dibenzo-1,3,5-cyclooctatrien-7-yne (dibenzoCOTyne **30**) presents a low stability in comparison with dibenzoCOTdiyne **43** as observed by experimental procedures. Despite the fact that fast decomposition of **30** is observed, it was also possible to achieve an X-ray image. In this case, the angle distortion falls to 154º, the distance alkyne-alkene increase to 2.85 Å and the alkyne length distance grows up to 1.23 Å, supporting the expected less planar behaviour of dibenzoCOTyne (Figure 32).[182]



43 **30**

*Figure 32. Acetylenic measurements of dibenzoCOTdiyne **43** and dibenzoCOTyne **30**.*

The majority of synthetic methodologies to dibenzo[8]annulene **44** were long and inefficient that hampered further applications. [183]

A summary of known synthetic protocols is depicted in Figure 33. The dimerization of dibromobenzocyclobutane proceeds with catalytic amounts of low valent nickel species rendering a mixture of linear dimerization, trimerization and cyclooctene. [184] Following the Cope´s approach, *o*-xylylene dibromide affords dibenzocyclooctatetraene **44** after treatment with metal lithium and subsequent bromination and elimination.[185] A straightforward manner to achieve the target molecule would involve the McMurry reaction, although it is necessary the previous preparation of the starting diketone; a similar procedure is based on a double Wittig reaction.[186] Finally, the efficient ring expansion of dibenzosuberenone reported by Wudl significantly shortened the synthetic route to dibenzo[8]annulene **44** (Figure 33).[187]

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[180] Wong, H. N. C.; Garratt, P. J.; Sondheimer, F. *J. Amer. Chem. Soc*.; **1974**, *96*, 5604-5605

[181] Destro, R.; Pilati, T.; Simonetta, M. *J. Am. Chem. Soc*. **1975**, *97*, 658-659.

[182] de Graaff, R. A. G.; Gorter, S.; Romers, C.; Wong, H. N. C.; Sondheimer, F. *J. Chem. Soc. Perkin Trans. 2*, **1981**, 478-480.

[183] a) Wawzonek, S. *J. Am. Chem. Soc.* **1940**, *62*, 745-749; b) Bachman, G. B.; Hoaglin, R. I. *J. Org. Chem.* **1943**, *8*, 300-315; c) Wittig, G. *Angew. Chem.* **1951**, *63*, 15-17; d) Dürr, H.; Klank, G.; Peters, K.; von Schnering, H. G. *Angew. Chem.* **1983**, *95*, 321; e) Chan, T-. L.; Mak, T. C. W.; Poon, C.-D.; Wong, H. N. C.; Jia, J. H.; Wang, L. L. *Tetrahedron*, **1986**, *42*, 655-661; f) To on-surface synthesis of Sondheimer-diyne see: Kawai, S.; Sang, H.; Kantorovich, L.; Takahashi, K.; Nozaki, K.; Ito, S. *Angew. Chem. Int. Ed*. **2020**, *59*, 10842–10847.

[184] a) Avram, M.; Dinu, D.; Mateescu, G.; Nenitzescu, C. D. *Chem. Ber*., **1960**, *93*, 1789-1794; b) Iyoda, M.; Kuwatani, Y.; Yamauchi, T.; Oda, M. *J. Chem. Soc., Chem. Commun*., **1988**, 65-66; c) Kuwatani, Y.; Yoshida, T.; Kusaka, A.; Oda, M.; Hara, K.; Yoshida, M.; Matsuyama, H.; Iyoda, M. *Tetrahedron*, **2001**, *57*, 3567-3576.

[185] a) Cope, A. C.; Fenton, S. W. *J. Am. Chem. Soc.* **1951**, *73*,1668-1673; b) Gärtner, D.; Stein, A. L.; Grupe, S.; Arp, J.; von Wangelin, A. J. *Angew. Chem. Int. Ed*. **2015**, *54*, 10545–10549.

[186] See section 4.4.1.

[187] Chaffins, S.; Brettreich, M.; Wudl, F. *Synthesis* **2002**, *9*, 1191-1194.

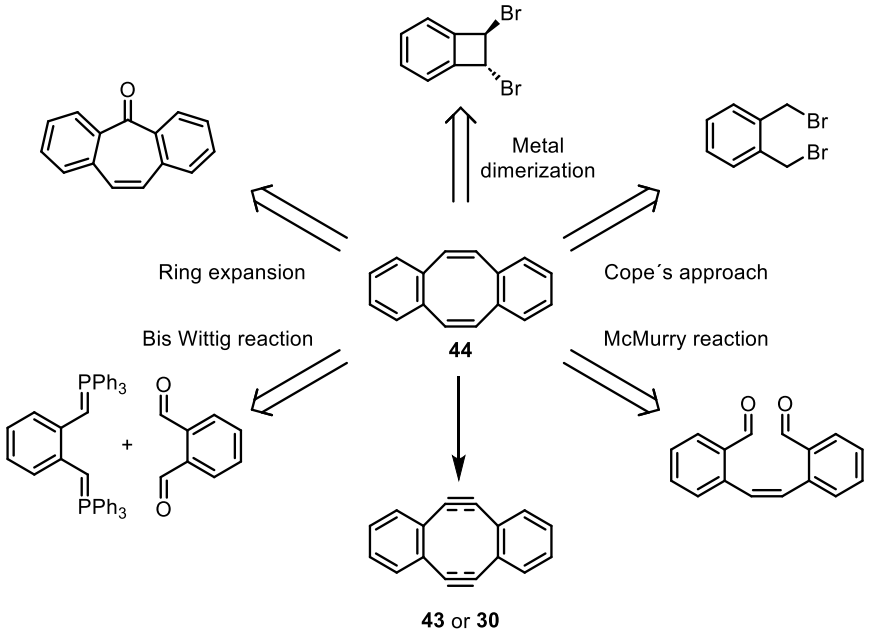


*Figure 33. Synthetic approaches to dibenzo[8]annulene **44***

Regarding the reactivity of dibenzoCOTyne 30 and dibenzoCOTdiyne 43 present a similar behaviour than COTynes on the strained acetylenic moiety(ies). A variety of cycloadditions in presence of DIB, furane, azides or ketenes were reported to afford PAHs containing 8-membered carbocycles.[188] Although the main applications are devoted to material science[189] or understanding electronic properties, there are some examples where Sondheimer alkyne is used as fluorescent probe using click chemistry. [190]

4.6.4. TribenzoCOTynes

In principle, COTyne with the highest number of fused benzene rings, the 13,14-didehydrotribenzo[a,c,e]cyclooctene 31 (tribenzoCOTyne) could be kinetically stabilized by benzene-annelation. Nevertheless, Meier, Sondheimer[179] and Wong [191]independently describe the difficulties presented with the isolation of 31; in fact, they found a half-life of barely 30 min when 31 is dissolved in DCM at -60 °C. From these results it is possible to rationalize that the presence of that benzenes provokes a destabilization due to the repulsion of hydrogens at peri position (Figure 34). In order to avoid that behaviour, one solution arises from removing peri hydrogens via fusion of benzene rings, which slightly increases the stability enough to allow its isolation. X-ray analysis confirmed the planar structure of tribenzoCOTyne 45 observing how

[188] a) Hisaki, I.; Sonoda, M.; Tobe, Y. *Eur. J. Org. Chem.* **2006**, 833–847; b) Pun, S. H.; Wang, Y.; Chu, M.; Chan, C. K.; Li, Y.; Liu, Z.; Miao, Q. *J. Am. Chem. Soc*. **2019**, 141, 9680−9686.

[189] Chen, H.; Miao, Q.; *ChemPlusChem* **2019**, *84*, 627–62.

[190] a) Kii, I.; Shiraishi, A.; Hiramatsu, T.; Matsushita, T.; Uekusa, H.; Yoshida, S.; Yamamoto, M.; Kudo, A.; Hagiwara, M.; Hosoya, T. *Org. Biomol. Chem*., **2010**, *8*, 4051-4055; b) Sutton, D. A.; Yu, S.-H.; Steet, R.; Popik, V. V. *Chem. Commun.*, **2016**, *52*, 553-556; c) Wu, D.; Durán-Sampedro, G.; Fitzgerald, S.; Garre, M.; O'Shea, D. F. *Chem. Commun.,* **2023**, *59*, 1951-1954.

[191] Felder, P.; Gerson, F.; Gescheidt, G.; Heckendom, R.; Tong, T.- H.; Wang, X.-M.; Wong, H. N. C.; Hou, X.-L. *Helv. Chim. Acta* **1991**,*74*, 644-653.

the acetylenic moiety changes from the dibenzoCOTyne, showing an angle distortion of 146.5º and an alkyne length of 1.23 Å. NMR analysis also supports the symmetry of the molecule observing a doublet with a chemical shift of 6.7 ppm attributable to the closer H to the alkyne moiety; in ^{13}C-NMR, acetylenic carbon presents a downfield shift signal in comparison with a linear sp-hybridized standard alkyne (108.4 ppm), probably due to the hybridization change caused by angle strain. [192]

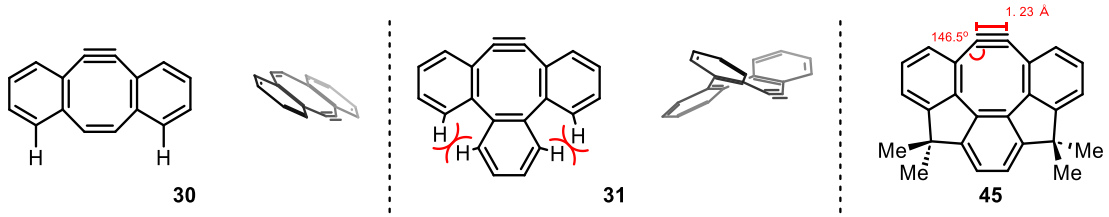
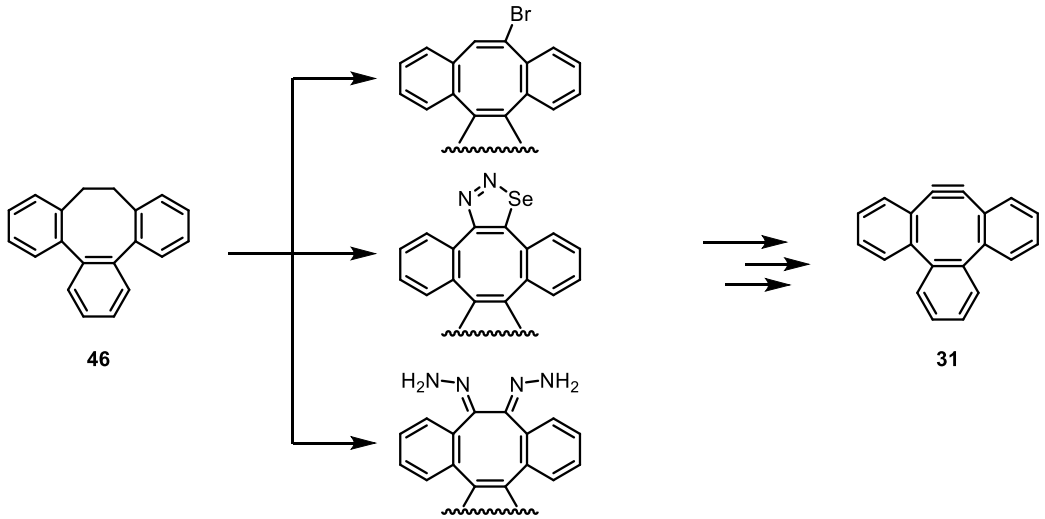


*Figure 34. Comparison of COTynes **30** and **31** regarding their theoretically planarity. Acetylenic measurements of isolated tribenzoCOTyne **45***

Despite of its isolation remains as a challenge, the reactivity of tribenzoCOTyne **31** was eagerly studied from middle 20th century. Two different approaches have been used to form that elusive species. The first one is based on the use of tribenzocyclooctane **46**, a product of tetraphenylene degradation. Meier[193] described three different routes to introduce the triple bond via (a) dehydrohalogenation, (b) through fragmentation of selenazole rings, and (c) by oxidation of 1,2-dihydrazone. However, all methodologies need long reaction routes and gave inefficient low yields of **31** (Scheme 43).

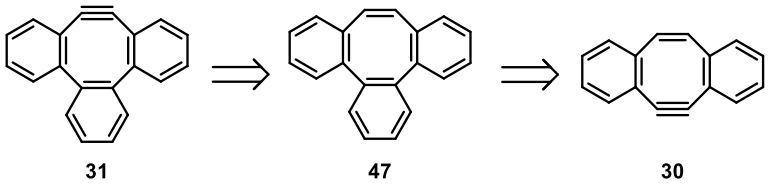


*Scheme 43. Meier´s synthetic methodologies to tribenzoCOTyne **31***

Probably the main route to achieve the strained alkyne, is based on the bromination of tribenzo[a,c,e]cyclooctene **47** (Scheme 44). This later compound was first described almost 80 years ago by Stewart[194] via oxidation and subsequent decarboxylation of tetraphenylene. Wong also reported another way to access to benzoannulated cyclooctatetraenes starting from

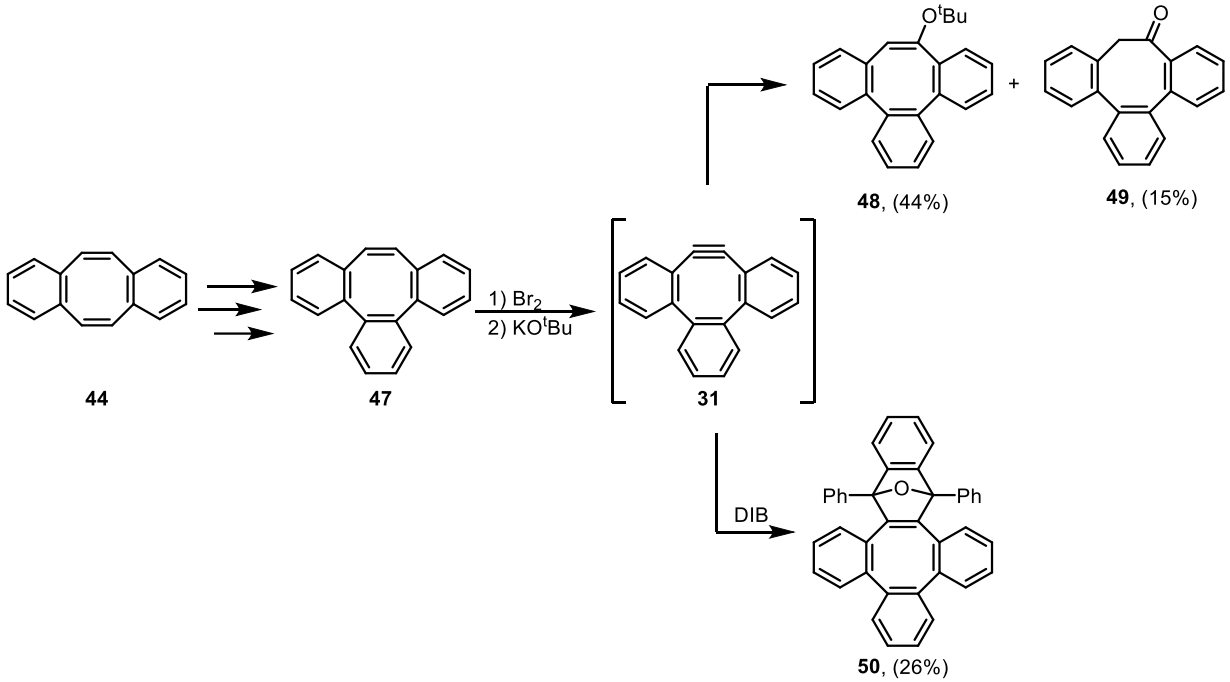
[192] Wang, X.-M.; Wang, R.-J.; Mak, T. C. W.; Wong, H. N. C. *J. Am. Chem. Soc*. **1990**, *112*, 7791-7793.
[193] Gugel, H.; Meier, H. *Chem. Ber.* **1980**, *113*, 1431-1443.
[194] Shuttleworth, R. G.; Rapson, W. S.; Stewart, E. T. *J. Chem. Soc*. **1944**, 71-73.

anthracene and employing harsh reaction conditions.[195] Other superior and simpler methods were proposed based on oxygen-bridged extrusion from six-membered carbocycles adducts derived from Diels-Alder cycloaddition of previously discussed dibenzoCOTyne **30**. [196]



*Scheme 44. Standard approach to tribenzoCOTyne **31***

In an attempt to isolate tribenzoCOTyne **31**, Sondheimer and Huang describe how bromination of tribenzoCOT **47** followed by treatment with KO^{t}Bu affords a mixture **48** and **49**, products derived from a putative alkyne intermediate (Scheme 45).[179b] They hypothesize that tribenzoCOTyne **31** seems to be highly reactive and undergoes nucleophilic addition of tert-butoxide anion to form compound **48**; as in previous cases, the presence of that elusive species could be reconfirmed adding DIB to the reaction mixture, to give the corresponding endoxide adduct **50**. [197,]



*Scheme 45. Attempts to isolate tribenzoCOTyne intermediate **31***

[195] Wang, X.-M.; Hou, X.-L.; Zhou, Z.-Y.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem*. **1993**, *58*, 7498-7506.
[196] a) Wong, H. N. C.; Hou, X. L. *Synthesis* **1985**, *12*, 1111-1115; b) Hou, X. L.; Wong, H. N. C. *J. Am. Chem. Soc*. **1987**, *109*, 1868-1869; c) Man, Y.-M.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem.* **1990**, *55*, 3214-3221.
[197] a) Tochtermann, W.; Oppenlaender, K.; Walter, U. *Chem. Ber*. **1964**, *97*, 1329-1336; b) Xing, Y. D.; Huang, N. Z. *J. Org. Chem*. **1982**, *47*, 140-142.

In 2005, Wong and coworkers summarize the known chemistry of tribenzoCOTyne adducts, showing all the possibilities through the formation of planar dehydro[8]annulenes.[198]

After this account, the initial hypothesis regarding the stability of COTyne´s family had to be corrected. It is true that as higher is the number of fused benzenes over the eight membered core, greater is the stability; however, planarity is also an important feature that dictates either reactivity and stability. Therefore, reactivity of COTynes could be rationalized as follows:

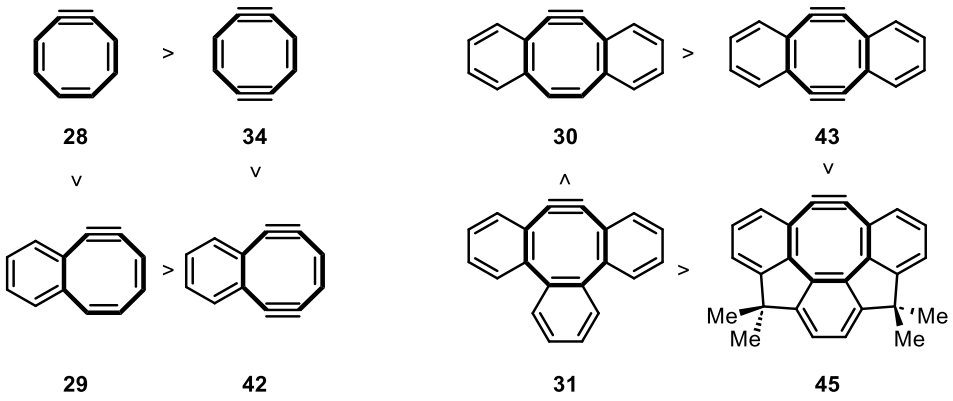


Figure 35. Reactivity order of COTyne´s family

[198] Hou, X.-L.; Huang, H.; Wong, H. N. C. *Synlett* **2005**, *7*, 1073-1089.

4.7. Trimerization of symmetric COTynes

The immense interest in planar carbon nanostructures (graphenes, PAHs) is driven by the extraordinary properties displayed by molecular nanocarbons themselves.[199] The synthesis of planar PAHs usually requires regioselective fusions of many rings. Recently, much progress has been made to address this challenge,[200] and metal-catalysed annulations have proven particularly valuable due to their efficacy in the formation of aromatic rings.[201] In particular, metal-catalysed [2+2+2] cycloadditions and thermal [2+2] cycloadditions involving arynes/alkynes became one of the most engaging synthetic strategies for constructing triphenylene[202] and biphenylene cores,[203]and also helicenes[204] and helicene-like molecules.[205]

More recently, distorted polycyclic aromatic hydrocarbons (PAHs) have emerged as intriguing units due to their ability to modify and improve the electronic and optical properties of their planar analogous.[206] The non-planarity is typically originated by the installation of non-hexagonal rings into the framework to induce negatively (saddle-shaped structure) or positively curvature (bowl-shaped structure).[207]

While the metal-catalysed trimerization ([2+2+2] cycloadditions) of planar arynes is well established (see section 4.5) the trimerization of symmetric tub-shaped cyclooctatrienynes (COTynes or dehydro[8]annulenes) under TM catalysis has been scarcely studied. Puzzling results have been found on the three examples reported in the literature.

Regarding the parent COTyne **28**, Stevenson and coworkers reported, in a series of spectroscopic measurements, the formation of a tri[8]annulenylene **61**, the "second triannulenylene" as they name it.[208]

Under high-vacuum conditions, when BrCOT **60** is treated with KO^{t}Bu in hexamethylphosphoramide (HMPA), and the solution is immediately exposed to a potassium metal mirror, formation of the bi[8]annulenylene radical is observed by EPR analysis. By contrast, if the solution is treated with the metal mirror after a few seconds, the tri[8]annulenylene radical can be identified by EPR techniques. Addition of molecular iodine to quench the radical solution and subsequent purification allowed the isolation of pure

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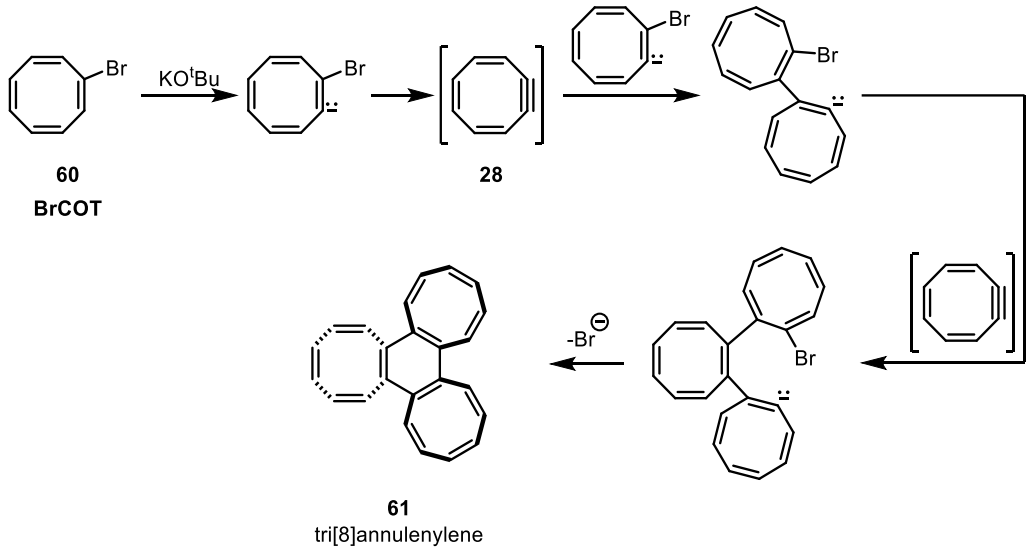
[199] Q. Miao. Polycyclic Arenes and Heteroarenes: Synthesis, Properties, and Applications. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 2015.
[200] Ito, H.; Segawa, Y.; Murakami, K.; Itami, K. *J. Am. Chem. Soc*. **2019**, *141*, 3−10.
[201] Jin, T.; Zhao, J.; Asao, N.; Yamamoto, Y. *Chem. Eur. J.* **2014**, *20*, 3554–3576.
[202] Kawai, Y.; Nogami, J.; Nagashima, Y.; Tanaka, K. *Chem. Sci.* **2023**, *14*, 3963-3972.
[203] See section 4.3.1 for synthetic approach based on metal [2+2+2] cycloaddition.
[204] Han, S.; Bond, A. D.; Disch, R. L.; Holmes, D.; Schulman, J. M.; Teat, S. J.; Vollhardt, K. P. C.; Whitner, G. D. *Angew. Chem. Int. Ed*. **2002**, *41*, 3223–3227.
[205] Tanaka, K.; Kamisawa, A.; Suda, T.; Noguchi, K.; Hirano, M. *J. Am. Chem. Soc*. **2007**, *129*, 12078–12079.
[206] a) Baldridge, K. K.; Siegel, J. S. *Angew. Chem. Int. Ed.* **2013**, *52*, 5436–5438; b) Segawa, Y.; Ito, H.; Itami, K. *Nat. Rev. Mater*. **2016**, *1*, 1–14; c) Stepien, M.; Gonka, E.; Zyla, M.; Sprutta, N. *Chem. Rev*. **2017**, *117*, 3479–3716; d) S. H. Pun, Q. Miao, *Acc. Chem. Res.* **2018**, *51*, 1630–1642.
[207] a) Márquez, I. R.; Castro-Fernández, S.; Millán, A.; Campaña, A. G. *Chem. Commun.* **2018**, *54*, 6705 - 6718. b) Evans, P. J.; Ouyang, J.; Favereau, L.; Crassous, J.; Fernández, I.; Perles, J.; Martín, N. *Angew. Chem. Int. Ed.* **2018**, *57*, 6774–6779.
[208] a) Kiesewetter, M. K.; Reiter, R. C.; Stevenson, C.D. *J. Am. Chem. Soc*. **2004**, *126*, 8884–8885; b) Stevenson, C.D. *Acc. Chem. Res*. **2007**, *40*, 703–711.

annulenylene $(C_8H_6)_3$ **61**. Nor synthetic procedure nor full spectroscopic data of **61** have been provided in the literature for this compound (Scheme 46).

Due to the tub shaped geometry of COT, two different αααα- and ααβ- conformers of **61** can be formed. One of them, the higher in energy as judged by DFT calculations, presents all three COT rings displaced above the plane of the benzene ring (αααα), while the other one presents one COT bent below the plane of aromatic ring (ααβ). ^{1}H-NMR analysis suggests that the formed conformer is the ααβ- due to the number of observed peaks (if the other annulenylene αααα-conformer was formed, the spectrum should be simpler because of the resulting symmetry of the molecule).

The proposed mechanism involves the formation of a COTyne intermediate **28** which is trapped by the BrCOT anion as nucleophile to form a bromo diCOT species, that in presence of another COTyne intermediate and subsequent quenching render the observed tri[8]annulenylene **61** (Scheme 46).

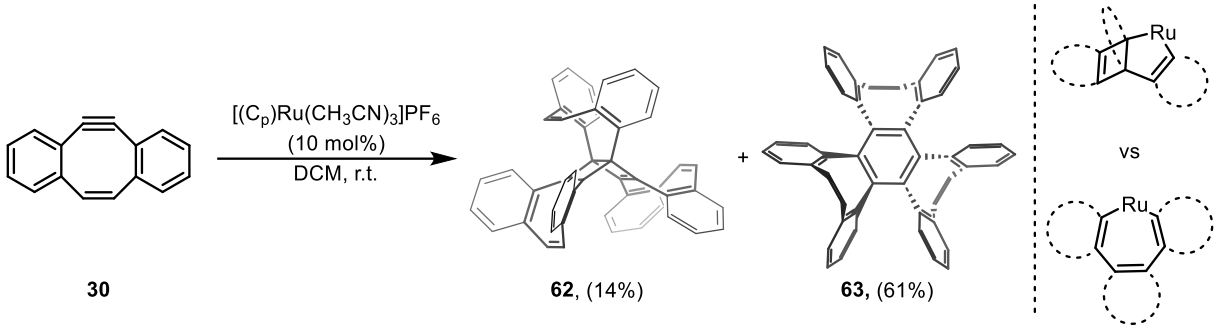


*Scheme 46. Proposed trimerization pathway for the formation of tri[8]annulenylene **61** from BrCOT **60***

The second example deals with the study of Nuckolls on the reactivity of dibenzoCOTyne **30** in presence of a metal complex.[209] The interest of Nuckolls´s group is related to the ring-opening metathesis of **30** to determine how and where alkyne/alkene metathesis polymerization takes place. In one hand, using the Schrock alkyne metathesis W(VI) catalyst and subsequent hydrogenation affords polymerization of starting cyclic alkyne. By contrast, treatment of the dibenzoCOTyne **30** with Grubbs catalyst gives rise to the unusual Dewar benzene **62**, where each of the eight-membered rings fold in a common direction forming a paddle-wheel-type structure. Interestingly, the same product was observed, although in a low 14% yield, as side product when dibenzoCOTyne **30** is allowed to react with cationic $[CpRu(CH_3CN)_3]PF_6$. In this case, the main product is the triannulenylene **63**, which seems to be

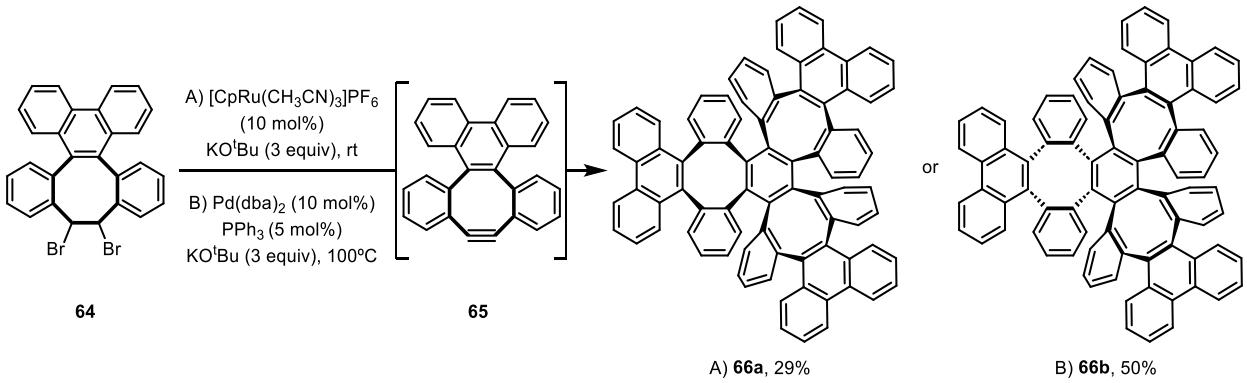
[209] a) Carnes, M.; Bucella, D.; Decatur, J.; Steigerwald, M. L.; Nuckolls, C. *Angew. Chem. Int. Ed*. **2008**, *47*, 2982 – 2985; b) Carnes, M.; Buccella, D.; Siegrist, T.; Steigerwald, M. L.; Nuckolls, C. *J. Am. Chem. Soc*. **2008**, *130*, 14078– 14079.

more stable than the non-benzannulated Dewar benzene **62**. This new tri[8]annulene **63** presents two of the three COTs moieties bent to the same face, probably in order to properly accommodate them. Importantly, all the attempts to isomerize the Dewar benzene **62** to benzene isomer **63** with either light or heat failed. Regarding the formation of both products, the initial proposal is based on a Ru(II) catalysed [2+2+2] trimerization of dibenzoCOTyne **30**. In one hand, reductive elimination of ruthenacyclopentene would render the isolated Dewar benzene **62**, while reductive elimination of the seven-membered ruthenacycle would afford the observed tri[8]annulene **63**. However, detailed mechanistic rationale is still lacking (Scheme 47).



*Scheme 47. Reactivity of dibenzoCOTyne **30** under cationic Ru (II) catalyst and proposed key intermediates*

The third example deals with the study of Müllen and coworkers about trimerization of tribenzoCOTyne directed to the challenging access to new non-planar allotropes of graphene such as the "cubic graphite". [210] They examined the reactivity of tribenzoCOT derivative **64** (a benzene moiety is replaced by a phenanthrene unit), in metal-catalysed [2+2+2] cycloadditions. They found a metal dependant change of reactivity when the *in situ* COTyne **65** reacts with Pd(0) (planar geometry) and Ru(II) catalyst (tetrahedral geometry) (Scheme 48).



*Scheme 48. Metal-dependant reactivity of COTyne **65** reported by Müllen*

Two different tribenzotri[8]annulenes (three COT rings connected by a central benzene ring) were formed depending on the catalyst/temperature employed. While the use of Ru catalyst at rt affords the α,α,α-form **66a**, where all of three COT units are bended to the same face forming a "molecular cup", the Pd complex at 100 ºC gives rise to the thermodynamically

[210] Ejlli, B.; Nuβbaum, P.; Rominger, F.; Freudenberg, J.; Bunz, U. H. F.; Müllen, K. *Angew. Chem. Int. Ed*. **2021**, *60*, 20220-20224.

more stable α,α,β-isomer **66b** in which one of the COTs moieties is flipped over to the opposite face of central benzene ring.

The authors analysed the selectivity of the reaction depending on the catalyst/temperature. When the reaction takes place in presence of Ru catalyst at 100 °C, inversion to the more stable α,α,β-isomer **66b** is observed (68 Kcal/mol more stable as judged by DFT calculations), albeit just in traces. However, with Pd (0) catalyst at rt yields a debrominated precursor of starting annulene **64**. Different attempts to interconvert both conformers one into the other such as temperature-dependant ^{1}H-NMR analysis or thermal or light-induced isomerization were unsuccessful.

Identification of both products **66a** and **66b** was possible by NMR analysis. α,α,α-conformer **66a**, presents a simple spectrum due to the C3-symmetry axis, in which only appear 6 and 14 signals in ^{1}H and ^{13}C-NMR, respectively. On the other hand, ^{1}H-NMR of α,α,β-isomer **66b** shows three proton resonances characteristic of the phenanthrenylene bay, that indicates the non-symmetry nature of the system (α,α,α-conformer of **66a** exhibits only one signal). Finally, both products were unambiguously confirmed by X-ray diffraction; α,α,α-isomer **66a** shows a cavity that might be able to host cations as suggested by theorical calculations.

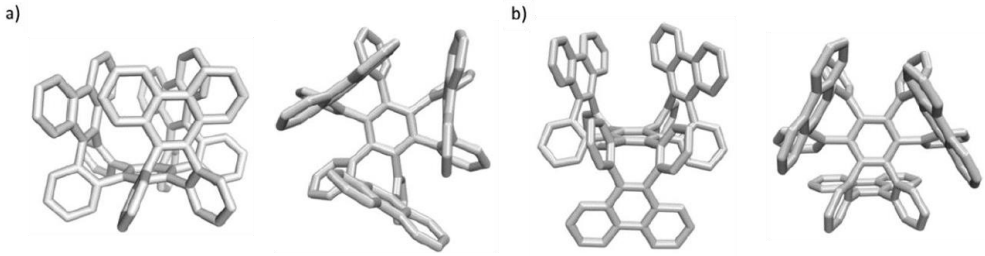


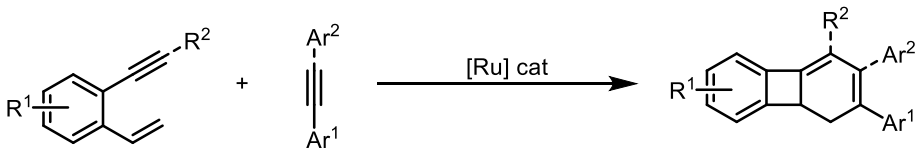
*Figure 36. Top and side view of single crystal X-ray image of a) α,α,α-conformer **66a** and b) α,α,β-conformer **66b** (reproduced images from ref 210)*

5. Objectives

Throughout this PhD thesis, 1,3-cyclohexadiene nuclei, presents in dihydrobiphenylenes systems, will be explored towards annulated systems containing biphenylenes units through oxidative process. In addition, synthesis and reactivity of strained alkynes species (COTynes) for the formation of PAHs with cyclooctatetraene units will also be addressed. The sub-objectives covered in each of the four sections that make up this PhD thesis are listed below:

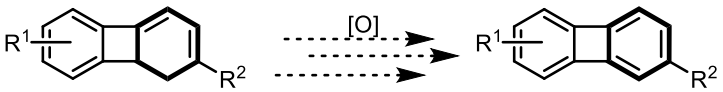
Exploring Ru catalysed [2+2+2] cycloadditions of ortho-alkenylarylacetylenes with alkynes

Dihydrobiphenylenes are interesting building blocks combining aromatic and anti aromatic alternant rings that can be used as starting materials for chemical synthesis and as spacers for functionalized organic material. The main challenge of this section would be the evaluation of the scope and limitations of the Ru(II) catalysed [2+2+2] cycloaddition of *o*-alkenylarylacetylenes and alkynes. Application to the synthesis of aza-dihydrobiphenylene will also be explored.



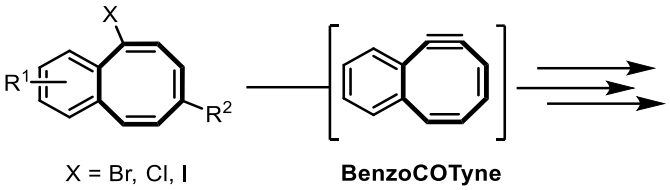
Reactivity of dihydrobiphenylenes

Biphenylene is an interesting building block that contains anti aromatic cyclobutadiene and aromatic benzene rings in a 6-4-6 fusion. In this section the reactivity of dihydrobiphenylenes under oxidative conditions to generate biphenylenes will be discussed under different conditions.



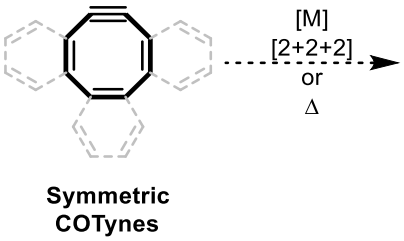
Reactivity of non-aromatic COTynes

BenzoCOTynes (eight membered cyclic alkynes) could be considered as the non-aromatic analogues of benzynes, but while the evolution of the six-membered benzenoid was widely studied, the eight-membered counterpart is poorly known. From the results obtained in *reactivity of dihydrobiphenylenes* regarding the synthesis of highly functionalized benzofused cyclooctatetraenes (benzoCOTynes precursors), we envision the reactivity of these reactive species in a metal-catalysed and thermal scenario.



Metal-catalysed vs thermal trimerizations of symmetric COTynes

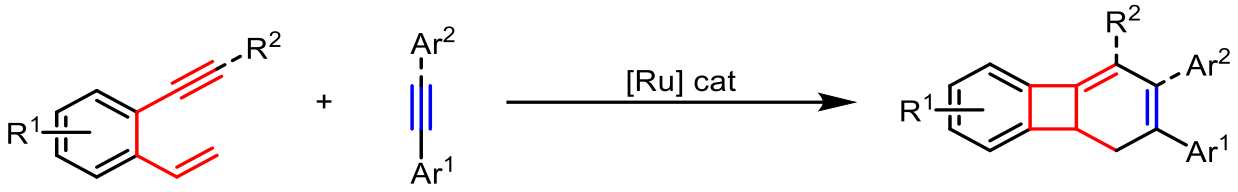
COTyne´s trimerization turns out to be a powerful tool to access new carbon allotropes incorporating antiaromatic eight membered rings. From the results obtained in *reactivity of non-aromatic COTynes* previously mentioned, related symmetric tribenzo-, dibenzo-, and parent COTynes will be analysed either under metal-catalysed [2+2+2] cycloadditions and thermal conditions along this section.



6. Results and Discussion

Our contribution to PAHs field developed during this PhD thesis is present below. A subdivision has been made into four different sections to facilitate the reading of the obtained results.

Exploring Ru catalysed [2+2+2] cycloadditions of *ortho*-alkenylarylacetylenes with alkynes

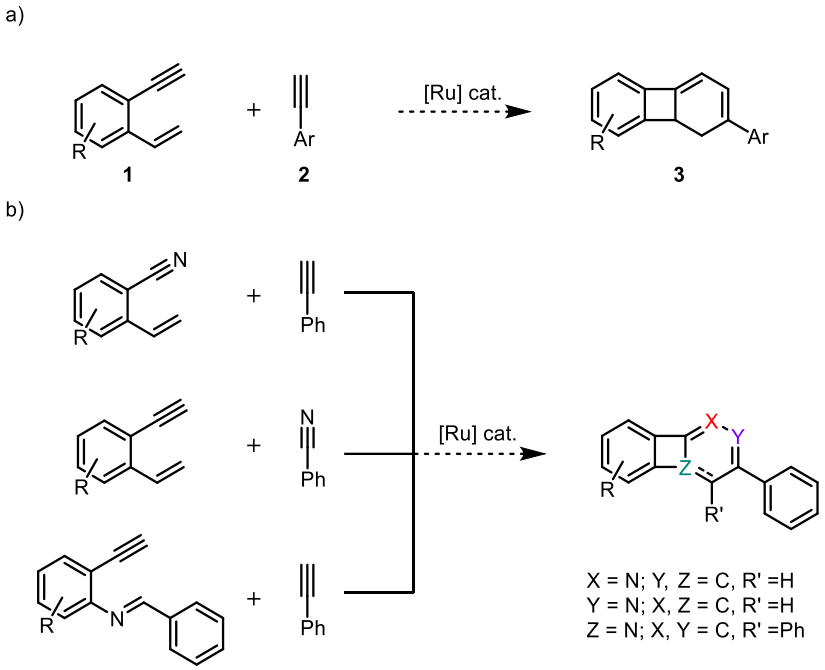


Structural units containing cyclobutene and benzannulated cyclobut(adi)ene cores are often used as spacers and building blocks of functionalized organic materials. Ru(II) catalysed dimerization of *ortho*-alkenylarylacetylenes and Ru(II) catalysed [2+2+2] cycloaddition of *ortho*-alkenylarylacetylenes with alkynes are recognized powerful methods to access to dihydrobiphenylene cores. Scope of Ru(II) cycloadditions to more complex dihydrobiphenylenes will be discussed in this section.

6.1. Exploring Ru catalysed [2+2+2] cycloadditions of *ortho*-alkenylarylacetylenes with alkynes

6.1.1. Specific objectives

Having in mind the relevance of combining aromatic and anti-aromatic alternant rings in the design of new graphenic materials and the relative lack of robust synthetic methodologies to access to benzofused four-membered rings, the main challenge of this section entails the evaluation of the scope and limitations of the Ru(II)-catalysed [2+2+2] cycloaddition of *ortho*-alkenyl arylacetylenes and alkynes to dihydrobiphenylenes. Application to the synthesis of aza-dihydrobiphenylenes will also be explored (Scheme 49).

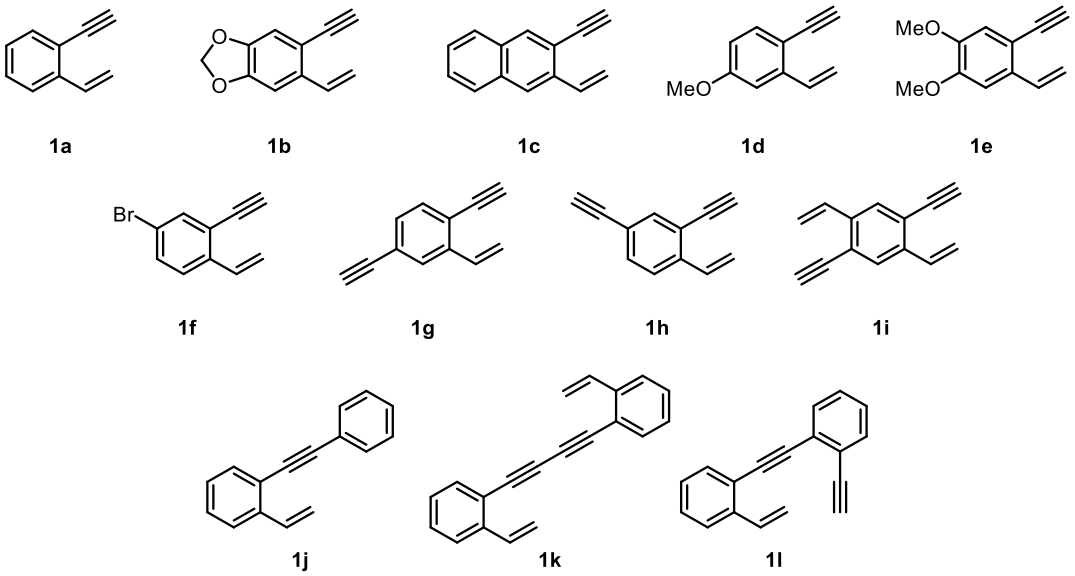


Scheme 49. Ru(II)-catalysed [2+2+2] cycloaddition of ortho*-alkenyl arylacetylenes and alkynes to dihydrobiphenylenes. Approaches to aza-dihydrobiphenylenes*

6.1.2. Ru(II)-catalysed [2+2+2] cycloadditions between *o*-alkenyl arylacetylenes and alkynes

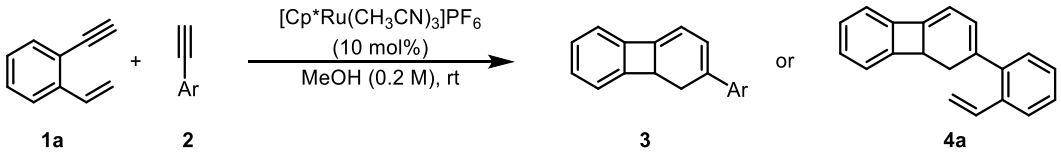
6.1.2.1 Synthesis of *o*-alkenyl arylacetylenes 1a-1l

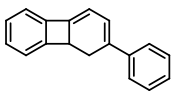
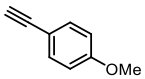
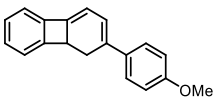
The *o*-vinyl (*o*-alkenyl) arylacetylenes **1a-1l** were prepared following published (or adapted) synthetic procedures.[211]



6.1.2.2 Use of 1-ethynyl-2-vinylbenzene 1a as enyne

The optimized conditions used were enyne **1a** (0.3 mmol) alkyne **2** (5 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (10 mol%), MeOH (1.5 mL, 0.2 M),rt, 1-2h. The results found are collected in Table 1.



Entry	Ar	Product (yield)[b]
1	 **2a**	 **3aa** (60%)
2	 **2b**	 **3ab** (72%)

[211] See section 7.1.2. in Methodology

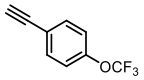
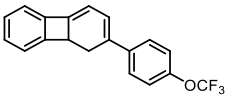
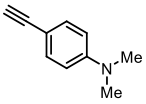
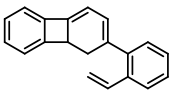
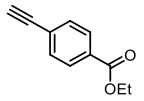
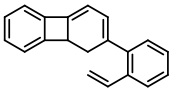
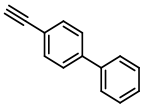
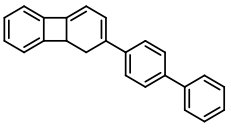
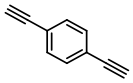
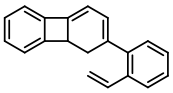
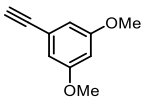
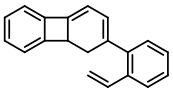
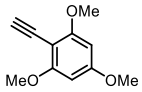
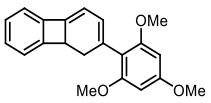
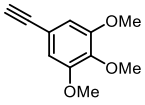
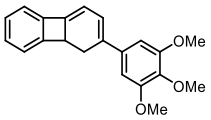
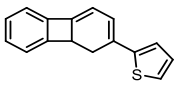
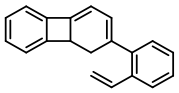
3	 **2c**		**3ac** (34%)
4	 **2d**		**4a** (nd)
5	 **2e**		**4a** (nd)
6	 **2f**		**3af** (52%)
7	 **2g**		**4a** (nd)
8	 **2h**		**4a** (nd)
9	 **2i**		**3ai**[d]
10	 **2j**		**3aj** (80%)
11	 **2k**		**3ak** (45%)
12	 **2l**		**4a** (nd)

Table 1. *Conditions:* ***1a*** *(0.2 mmol), alkyne (5 equiv), [Ru] (10 mol%) in MeOH (0.2 M) b) Isolated yield. nd = not determined c) 60 °C d) Product detected by GC-MS*

Pleasingly, enyne 1a and phenylacetylene 2a cocyclized uneventfully to dihydrobiphenylene 3aa in a fairly good yield (60%, entry 1). *Para*-substituted alkynes were then examined. Electron-rich *p*-OMe-phenylacetylene 2b smoothly undergo the cocyclization to give dihydrobiphenylene 3ab in a quite good 72% yield (entry 2). By contrast, the more electron

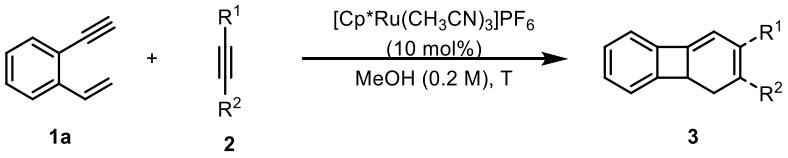
deficient -OCF_3 substituted **2c** afforded **3ac** in a moderate 34% yield (entry 3). Dimethyl amine group as well as the electron poor ester group were not well tolerated, rendering the dimerization product **4a** from enyne **1a** (entries 4 and 5).[57]

Not unexpectedly, an extended conjugated alkyne, biphenyl **2f**, gave rise to dihydrobiphenylene **3af** in a reasonable 52% yield (entry 6). Unfortunately, the alkyne bearing a conjugated alkynyl group **2g** (to perform an eventual-double [2+2+2] cycloaddition) failed to cocyclize being the known dimer **4a** of enyne **1a** the only adduct detected (entry 7).

Electron-rich alkoxy arylacetylenes **2h-j** were then analysed. While dihydrobiphenylene adduct **3ai** from trialkoxy alkyne derivative **2i** was detected by GC-MS when the reaction was heated at 60°C, *meta*-disubstituted alkyne **2h** was not tolerated (entries 8 and 9). The low or even lack of reactivity of alkynes to cocyclize could be attributed to the formation of a benzene-type Ru complex, which can catch the alkynes and form a non-active η^6-benzene species or, alternatively, to the steric hindrance caused by the *ortho*-OMe groups around the metal centre. By contrast, electron-rich arylacetylene **2j** with *meta* and *para* alkoxy substituents afforded the dihydrobiphenylene **3aj** in an excellent 80% yield (entry 10).

Finally, heteroaromatic alkynes were analysed. Whereas 2-ethynylthiophene **2k** afforded the expected dihydrobiphenylene **3ak** in a moderate 45% yield (entry 11), the 3-ethynylpyridine **2l** failed to cocyclize giving rise to the dimer **4a** in very low yield.

The use of non-terminal functionalized alkynes **2m-p** were also evaluated in spite of the putative formation of regioisomers (Table 2).



1a **2** **3**

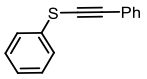
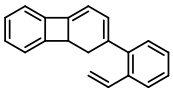
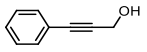
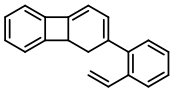
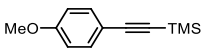
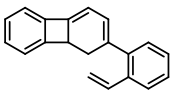
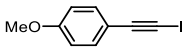
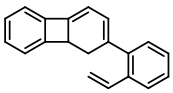
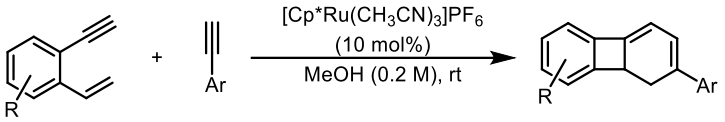
Entry	Alkyne	Product (yield)[b]
1	 **2m**	 **4a** (nd)
2	 **2n**	 **4a** (nd)
3[c]	 **2o**	 **4a** (nd)
4[c]	 **2p**	 **4a** (nd)

Table 2. *Conditions: **1a** (0.2 mmol), alkyne **2** (5 equiv), [Ru] (10 mol%) in MeOH (0.2 M) b) Isolated yield. nd = not determined c) 60 °C*

Unfortunately, all attempts failed to give the expected 1,3-cyclohexadienes being the dimerization product **4a** the major product obtained. Neither the thiophenyl, propargyl alcohol, silyl or iodide groups were tolerated in the cocyclization reaction.

6.1.2.3 Use of dioxolane 1b and 2-ethynyl-3-vinylnaphthalene 1c



1 **2** **3**

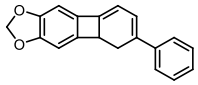
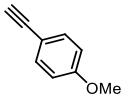
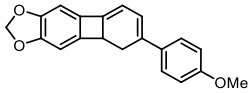
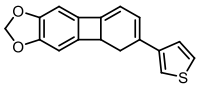
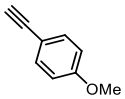
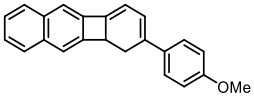
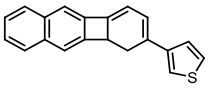
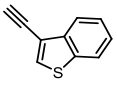
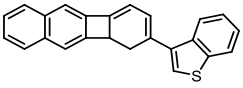
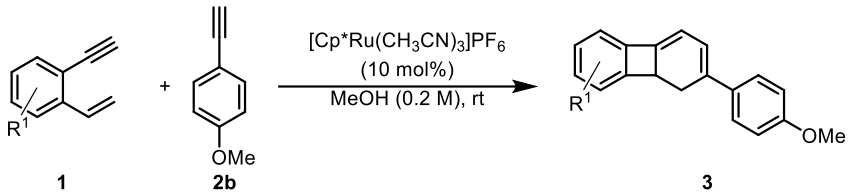
Entry	Enyne	Alkyne	Product (yield)[b]
1	**1b**	 **2a**	 **3ba**, (62%)
2	**1b**	 **2b**	 **3bb**, (80%)
3	**1b**	 **2q**	 **3bq**, (55%)
4	**1c**	 **2b**	 **3cb**, (63%)
5	**1c**	 **2q**	 **3cq**, (58%)
6	**1c**	 **2r**	 **3cr** (60%)

Table 3. *Conditions:* ***SM*** *(0.2 mmol), alkyne (5 equiv), [Ru] (10 mol%) in MeOH (0.2 M) b) Isolated yield.*

Dioxolane and naphthalenic enynes **1b-c** were tested as cocyclization partners with three electronically different alkynes (Table 3). While the behaviour of dioxolane **1b** probed similar to the simple vinylbenzene **1a** with yields ranging from 55-80% (entries 1-3), naphthalene enyne **1c** behaved slightly less reactive than **1a** in all cases (58-63% yields, entries 4-6). Coordination of the naphthalene unit to the Ru catalyst could affect its catalytic efficacy.

6.1.2.4 Use of *meta*- and *para* substituted enynes

The behaviour of the more functionalized enynes **1d-1i** were then tested in cycloadditions with the very reactive alkyne 4-methoxyphenylacetylene **2b** (Table 4).



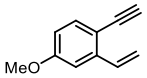
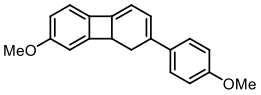
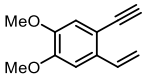
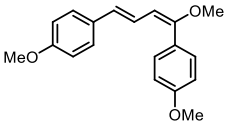
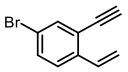
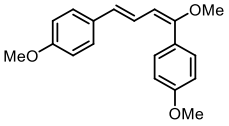
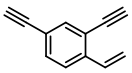
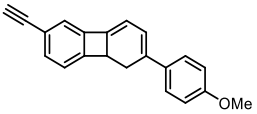
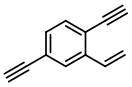
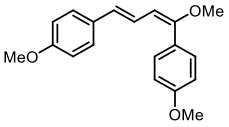
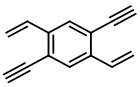
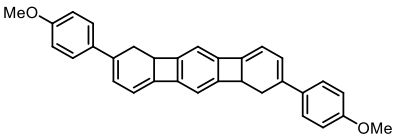
Entry	Enyne	Product (yield)[b]
1	 **1d**	 **3db** (59%)
2	 **1e**	 **5b** (nd)
3	 **1f**	 **5b** (nd)
4	 **1g**	 **3gb** (47%)
5	 **1h**	 **5b** (nd)
6	 **1i**	 **3ib** (80%)

Table 4. *Conditions:* ***SM*** *(0.2 mmol), alkyne* ***2b*** *(5 equiv), [Ru] (10 mol%) in MeOH (0.2 M) b) Isolated yield. nd = not determined*

To our initial surprise, while the 4-methoxyphenyl enyne **1d** smoothly reacts with the alkyne **2b** to give the biphenylene **3db** (59%, entry 1), the 4,5-dimethoxyphenyl enyne **1e** did not cocyclize with the alkyne **2b** being Dixneuf´s diene **5b** the major compound formed (entry 2).[212] A possible explanation would be that the presence of a methoxy group in *para* position to the vinyl group might activate this olefin to undesired side reactions instead the desired cocyclization (Figure 37).

[212] a) Zhang, M.; Jiang, H.-F.; Neumann, H.; Beller, M.; Dixneuf, P.-H. *Angew. Chem. Int. Ed*. **2009,** *48*, 1681-1684; b) Le Paih, J.; Monnier, F.; Dèrien, S.; Dixneuf, P. H.; Clot, E.; Eisenstein, O. *J. Am. Chem. Soc.* **2003,** *125*, 11964-11975

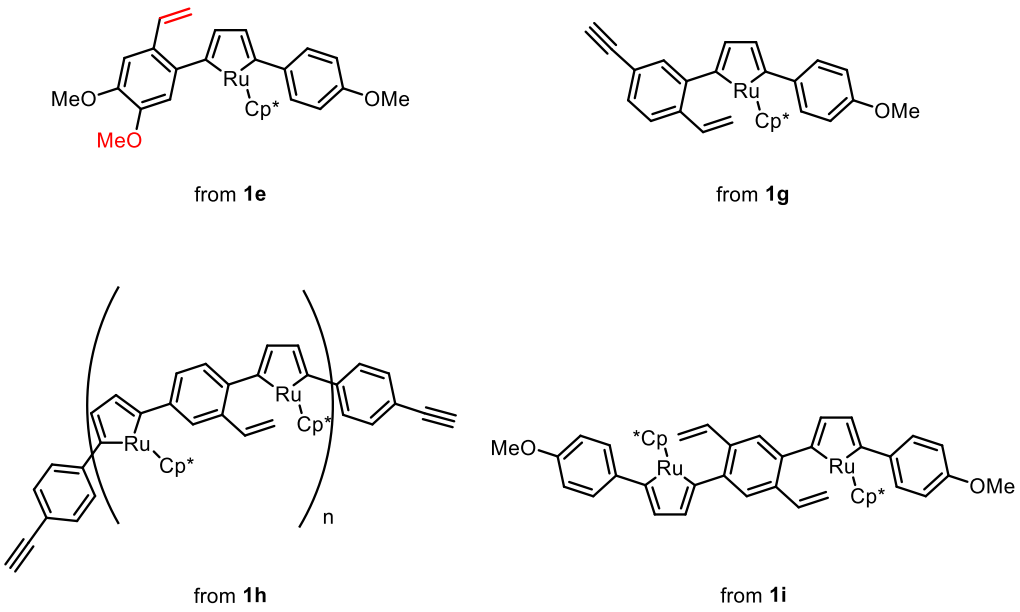
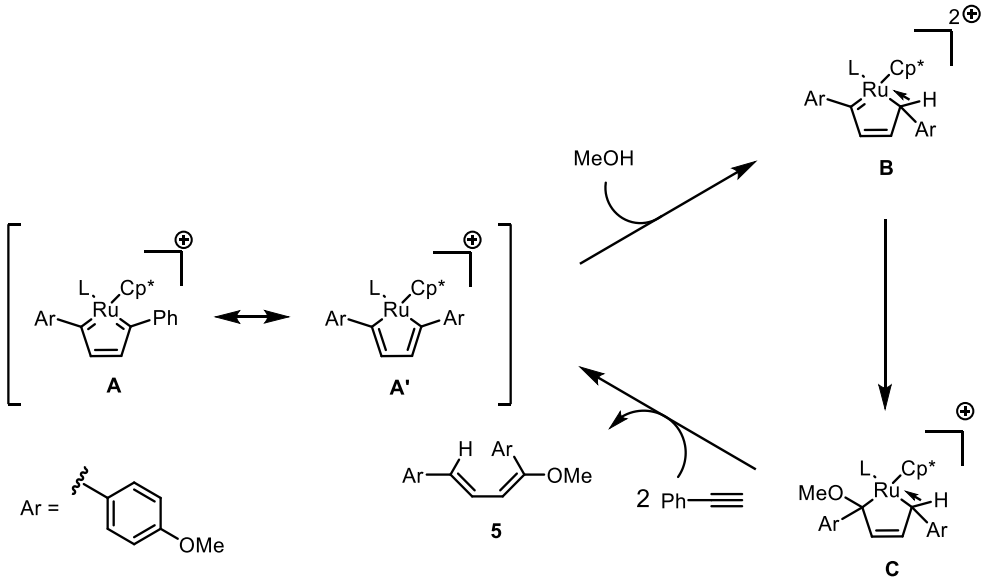


Figure 37. Possible ruthenacycle intermediates

The bromo enyne **1f** resulted almost unreactive (traces of dimerization product **3f** were detected by GC-MS) affording the same Dixneuf´s diene **5b** as major compound formed (entry 2). A plausible mechanism for the formation of Dixneuf´s diene **5b** is shown in Scheme 50. Diene **5b** could be formed by a Ru (II) mediated dimerization of 4-methoxyphenylacetylene **2b** and subsequent nucleophilic trapping with MeOH.

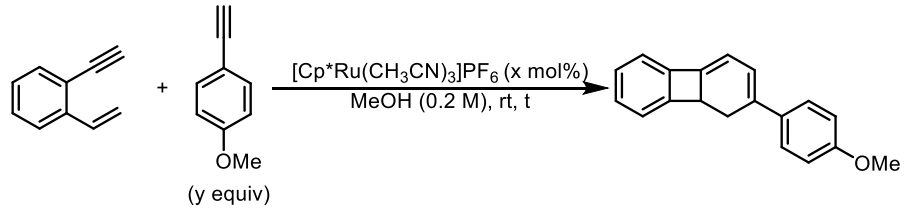


*Scheme 50. Formation of Dixenuf´s diene **5b** promoted by Ru (II)*

Alkynyl derivatives were then analysed. The 2,4-diethyl-1-vinylbenzene **1g** smoothly cocyclized with alkyne **2b** to give the dihydrobiphenylene **3gb** in a moderate 47% yield (entry 4). Unexpectedly, the isomeric 1,4-diethynyl-2-vinylbenzene **1h** did not undergo cocylization with **2b** being Dixneuf´s diene **5b** the major compound present (entry 5). A possible explanation of these conflicting results would be that the formation/reactivity of the ruthenacycle

intermediate would be affected for the position of an "extra" alkynyl group. When this group is located in *meta* respect to the Ru carbene bond the cocylization is feasible, but when is located in *para, the* formation of a Ru-polymer is favoured consuming the starting enyne (Figure 37). In fact, the situation was dramatically reversed when a second reacting vinyl group (enyne **1i**) was installed in the substrate facilitating a second cocyclization process avoiding polymerization (Figure 37). To our delight, the bis-enyne **1i** smoothly cocyclized with alkyne **2b** at rt to afford the fused bis-dihydrobiphenylene **3ib** in an excellent 80% yield using only 2.5 equivalent of external alkyne (entry 6).

Based on the above results we carried out an actualization of the optimized conditions with the enyne 1-ethynyl-2-vinylbenzene **1a** and the alkyne 4-methoxyphenylacetylene **2b** as cocyclization partners (Table 5).



1a **2b** **3ab**

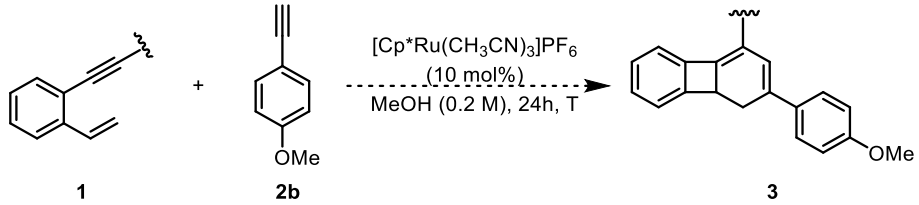
Entry	[Cp*Ru(CH$_3$CN)$_3$]PF$_6$ (x mol %)	**2b** (y equiv)	t	Yield **3ab**[b]
1	10	5	24 h	72
2	10	2.5	24 h	85
3	10	2	24 h	86
4	4	2	24	65
5[c]	4	2	5 min	81
6[c]	4	1.2	5 min	85
7[c]	3	1,2	5 min	83

***Table 5**. Conditions: **1a** (0.2 mmol), [Ru] (x mol%), **2b** (x equiv) in MeOH (0.2 M) rt, t b) isolated yield c) Homemade catalyst*

Standard reaction conditions afforded the expected dihydrobiphenylene **3ab** in an excellent 72% yield (entry 1). With a reduced amount of alkyne (2 or 2.5 equiv) excellent yields of **3ab** were obtained (entries 2 and 3). Reducing both the amount of alkyne and catalyst significatively affected the yield of **3ab** (entry 4). Interestingly, using "home-made" catalyst rendered the product **3ab** in an excellent 81% yield in only 5 min of reaction (entry 5). Finally, the amount of catalyst and alkyne could even be further reduced to only 3 mol% and 1.2 equiv, without the yield of **3ab** being affected (entries 6 and 7).

6.1.2.5 Intramolecular Ru(II)-catalysed [2+2+2] cycloaddition of enynes 1j-1k and enediyne 1l

To expand the scope of Ru(II)-catalysed [2+2+2] cycloaddition, we envisioned the possibility to achieve interesting building blocks for organic materials (by combination of aromatic and antiaromatic rings) with the use of internal enediynes/dienediynes as cocyclization partners (Table 6).



1 **2b** **3**

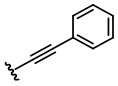
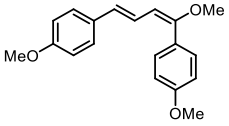
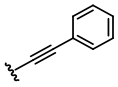
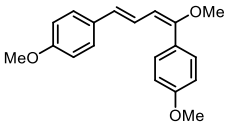
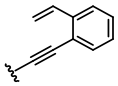
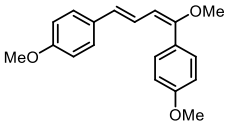
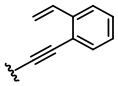
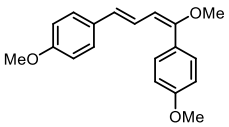
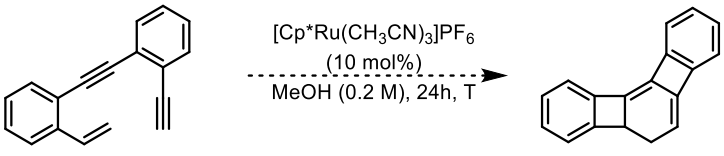
Entry	Substrate	T[a] (°C)	Product (yield)
1	 **1j**	rt	 **5b** (nd)
2	 **1j**	60	 **5b** (nd)
3	 **1k**	rt	 **5b** (nd)
4	 **1k**	60	 **5b** (nd)

Table 6*. Conditions:* ***SM*** *(0.3 mmol), alkyne* ***2b*** *(5 equiv), [Ru] (10 mol%) in MeOH (0.2 M) during 24h. b) Isolated yield n.d. = not determined*

The 4-methoxyphenylacetylene **2b** was used as alkyne partner due to its good behaviour in the above cycloadditions When using 1-(phenylethynyl)-2-vinylbenzene **1j** as substrate, starting material was recovered unaltered with observation of Dixneuf´s product **5b** as major compound (entries 1 and 2). Same behaviour occurred when di-endiyne **1k** was employed at rt or 60 °C being again Dixneuf´s product **5b** the major compound observed (entries 3 and 4).

Unfortunately, all attempts of intramolecular cycloaddition of enediyne **1l** gave complex mixtures that were not further analysed (Table 7).



1l **3l**

Entry	Solvent	T (°C)	Product
1	MeOH	rt	-
2	MeOH	60	-
3	THF	rt	-
4	THF	60	-

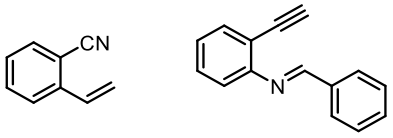
Table 7. Conditions: ***SM*** *(0.2 mmol), [Ru] (10 mol%) in MeOH (0.2 M) during 24h*

Unfortunately, all attempts of intramolecular cycloaddition of enediyne 1l gave complex mixtures that were not further analysed (Table 7).

6.1.3. Study of Ru(II)-catalysed [2+2+2] cycloaddition of nitrogenated substrates

6.1.3.1. Synthesis of starting materials

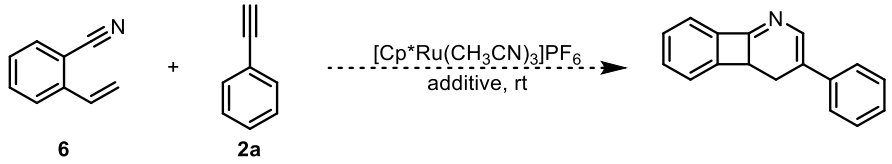
The *o*-vinyl benzonitrile **6** and benzaldimine **7** were prepared following published (or adapted) synthetic procedures.[213]



6 **7**

6.1.3.2. *O*-vinylbenzonitrile 6 as partner

Attempts performed using alkyne **2a** as cocyclization partner are collected in Table 8.



6 **2a**

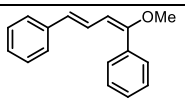
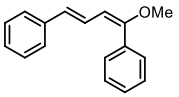
Entry	Solvent	Additive	Product
1	MeOH	-	 **5a** (nd)
2	MeOH	$ZnCl_2$	 **5a** (nd)
3	1,4-dioxane	$ZnCl_2$	**SM**

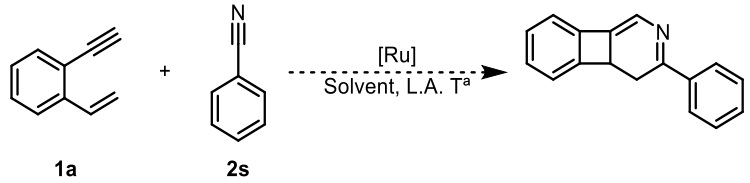
***Table 8**. Conditions: **6** (0.3 mmol), alkyne **2a** (5 equiv), [Ru] (10 mol%) in solvent (0.2 M) during 24h at rt. n.d. = not determined.*

Typical conditions used previously in [2+2+2] cycloadditions gave rise to Dixneuf´s diene **5a** (entry 1). Activation with $ZnCl_2$ as a Lewis acid to facilitate the formation of an azaruthenacyclopentadiene by the activation of nitrile renders the formation of the same product (entry 2). By contrast, reaction in the aprotic solvent 1,4-dioxane showed no conversion of starting material (entry 3).

[213] See section 7.1.2 in Methodology.

6.1.3.3. Benzonitrile as alkyne-type partner

Attempts performed using benzonitrile **2s** as alkyne-type partner are collected in Table 9.



1a **2s**

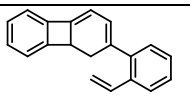
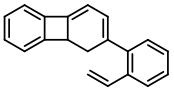
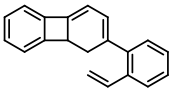
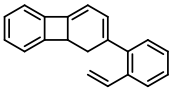
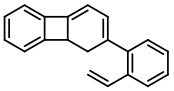
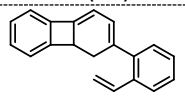
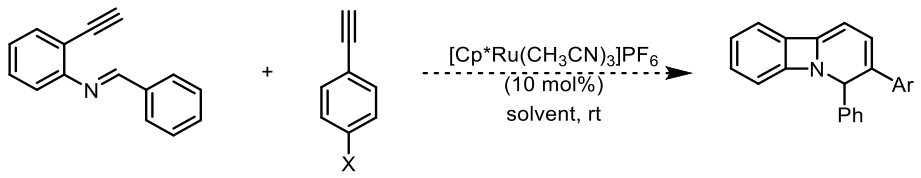
Entry	Catalyst (10 mol%)	Solvent	Lewis acid	T[a] (°C)	Product
1	$[(Cp^*Ru(CH_3CN)_3]PF_6$	MeOH	-	rt	 **4a** (nd)
2	$[(Cp^*Ru(CH_3CN)_3]PF_6$	MeOH	-	60	 **4a** (nd)
3	$[(Cp^*Ru(CH_3CN)_3]PF_6$	THF	-	rt	 **4a** (nd)
4	$[(Cp^*Ru(CH_3CN)_3]PF_6$	THF	$ZnCl_2$	rt	 **4a** (nd)
5	$[(Cp^*Ru(CH_3CN)_3]PF_6$	THF	$ZnCl_2$	60	-
6[b]	$[(Cp^*Ru(CH_3CN)_3]PF_6$	MeOH	-	rt	 **4a** (nd)
7	[(Cp*RuCl(cod)]	MeOH	-	rt	 **4a** (nd)
8	[(Cp*RuCl(cod)]	THF	$ZnCl_2$	rt	-
9	[(Cp*RuCl(cod)]	EtOH	AgOTf	rt	-

Table 9*. Conditions:* ***1a*** *(0.3 mmol), benzonitrile* ***2s*** *(5 equiv), [Ru] (10 mol%) in solvent (0.2 M) during 24h at T. b) pyruvonitrile instead of benzonitrile*

In any of the conditions tried varying temperature, nature of solvent, presence of $ZnCl_2$ as additive, or using neutral Ru (II) complexes alone or in the presence of Lewis acids gave cyclized products with no incorporation of the benzonitrile (entries 1-9). The major product observed was the dihydrobiphenylene **4a** from dimerization of enyne **1a**.

6.1.3.4. Benzaldimine 7 as partner

All attempts performed with benzaldimine **7** gave hydrolysis of the starting material irrespective of the nature of the solvent used (Table 10).



7

2a, X = H
2b, X = OMe

Entry	Alkyne	Solvent	Product
1	-	MeOH	-
2	**2a**	MeOH	-
3	**2b**	MeOH	-
4[a]	**2a**	MeOH	-
5	**2a**	THF	-
6	**2a**	DCE	-

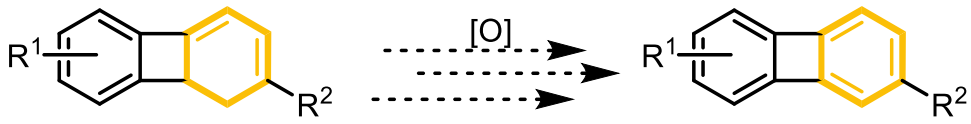
***Table 10**. Conditions: **7** (0.3 mmol), alkyne (5 equiv), [Ru] (10 mol%) in solvent (0.2 M) during 24h at rt. a) 60 °C*

6.1.4. Conclusion

From the results, the following conclusions may be drawn:

- Scope of Ru (II)-catalysed [2+2+2] cycloaddition was expanded to the electron poor *p*-OFC_3 **2c**, the neutral biphenyl **2f** and the electron rich alkynes **2j-k,** and the obtaining the corresponding dihydrobiphenylenes **3ac**, **3af** and **3aj-ak** (1,3-cyclohexadiene cores) from moderate to good yields.
- Dioxolane and naphthalene-type enynes **1b-c** participate in Ru (II)-catalysed cycloadditions with three different electron rich alkynes **2b**, **2q** and **2r** yielding the corresponding dihydrobiphenylene from moderate to excellent yields.
- *Meta* and *para* substituted enynes **1d**, **1g** and **1i** reacts in the presence of 4-ethynylanisole **2b** to form the target dihydrobiphenylenes in moderate to excellent yields. The presence of substituents in *para* position to vinyl group (OMe, Br) activate side reactions as major reaction pathways instead the desire cocyclizations.
- Reoptimization of reported conditions was achieved using 1.2 equivalents of alkyne **2b**, 3 mol% of cationic Ru (II) catalyst and 5 min of reaction time.

Reactivity of dihydrobiphenylenes



Biphenylene is an interesting building block that contains an anti-aromatic cyclobutadiene and aromatic benzene rings. The alternating fusion benzene and cyclobutadiene rings (6-4-6) causes unusual activation of the π and σ frameworks. The combination of these electronic properties makes these structural units very attractive for the preparation of new organic materials. The reactivity of dihydrobiphenylenes under oxidative conditions to generate biphenylenes will be discussed in this section.

6.2. Reactivity of dihydrobiphenylenes

Part of the obtained results shared in this section were published in *Organic Letters* under the following authors contribution and copyright permissions:

Jesús Bello-García, Damián Padín, Jesús A. Varela and Carlos Saá. Nonplanar Tub-Shaped Benzocyclooctatetraenes via Halogen-Radical Ring Opening of Dihydrobiphenylenes. *Org. Lett*. 2021, *23*, 5539–5544. DOI: 10.1021/acs.orglett.1c01881.

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Personal contribution of Jesús Bello-García:

Experimental procedures, preliminary DFT calculations, results discussion and preliminary manuscript.

Journal information:

Print Edition ISSN:1523-7060.

Web Edition ISSN: 1523-7052

Impact factor: 5.2

6.2.1. Specific objectives

As we have shown in section 6.1, dihydrobiphenylenes can be easily accessed from Ru(II)-catalysed [2+2+2] cycloaddition of *o*-alkenylenynes and alkynes. Transformation of these systems into biphenylenes would be well received as an alternative synthetic protocol. In this section we will discuss our results in this topic. (Figure 38).

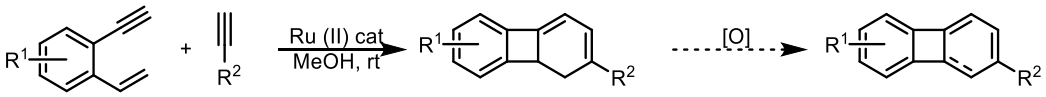
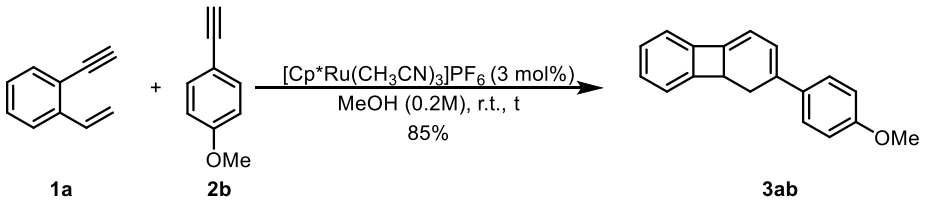


Figure 38. Proposed route to access to biphenylenes

6.2.2. Oxidation methods

6.2.2.1 Synthesis of dihydrobiphenylene 3ab

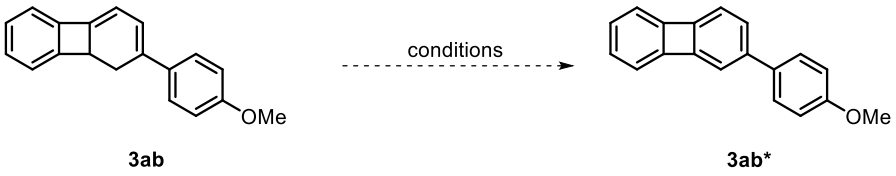
Dihydrobiphenylene 3ab was prepared in 85% yield following our procedure and used as model compound to study the oxidation process.



Scheme 51. Ru(II)-catalysed [2+2+2] cycloaddition of enyne ***1a*** *and 4-ethynyl anisole* ***2b*** *to dihydrobiphenylene* ***3ab***

6.2.2.2 Dehydrogenative methods

All attempts involved typical dehydrogenation conditions summarized on the Table 11.



Entry	Conditions	Solvent	T (°C)	Product
1	Pd/C (20%)	toluene	100	dec
2	Pd/C (20%)	mesitylene	200	dec
3	DDQ	benzene	100	dec
4	TEMPO	toluene	80	SM
5	SeO_2	dioxane	80	CM
6	MnO_2	EtOAc	rt	SM

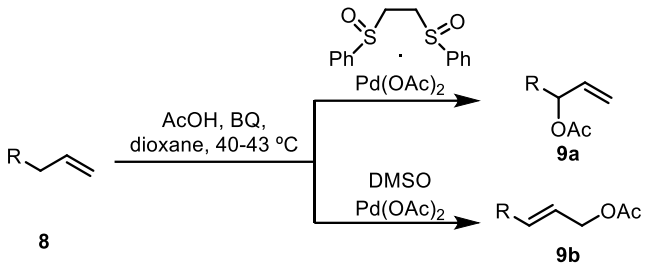
Table 11*. Conditions:* ***3ab*** *(0.2 mmol), solvent at corresponding T (°C), dec = decomposition*

Unfortunately, all efforts to achieve the desired oxidation to biphenylene failed, giving instead complex mixtures, decomposition of starting dihydrobiphenylene or the recovery of unaltered starting material.

6.2.2.3 Oxidation via allylic functionalization

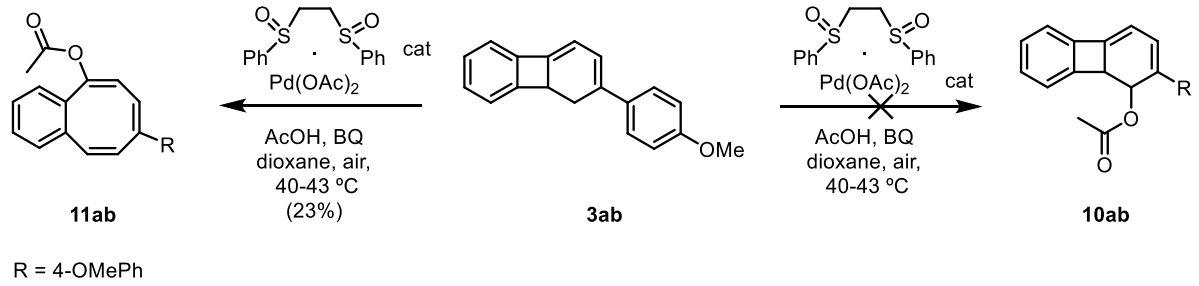
An alternative oxidation process for aromatization would involve the functionalization of 1,3-cyclohexadiene core in the allylic position followed by elimination of the incorporated functional group.

White and coworkers reported the use of Pd (II) species to promote allylic functionalization (avoiding Wacker oxidation) by the introduction of an acetoxy group via C-H oxidation. In that work, the combination of $Pd(OAc)_2$/BQ/AcOH under DMSO or bis-sulfoxide ligand afforded allylic lineal and branched acetates, **9b** and **9a** respectively (Scheme 52).[214]



Scheme 52. Synthesis of allylic acetates from monosubstituted olefins via C-H oxidation

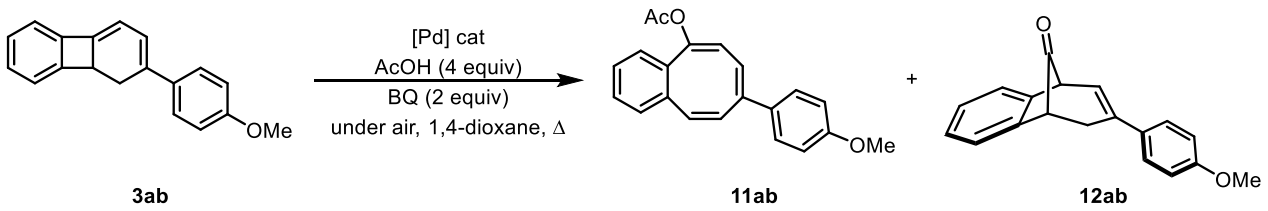
To our surprise, when dihydrobiphenylene **3ab** was subjected to White´s conditions, instead of the expected allylic oxidation product **10ab**, benzofused cyclooctatetraene **11ab** was obtained albeit in a low yield (Scheme 53, Table 12).



*Scheme 53. Allylic functionalization of dihydrobiphenylene **3ab***

Identification of the nature of cyclooctatetraene **11ab** was based on the analysis of its NMR spectra. The appearance in ^{1}H-NMR of a singlet at 2.16 ppm as well as the presence in ^{13}C-NMR of a carbonyl signal at 169 ppm suggests the presence of an acetate group. In addition, four new signals appeared at the olefinic region. These signals, 6.94 ppm (d, *J* = 11.6 Hz), 6.38 ppm (d, *J* = 11.6 Hz), 6.11 ppm (d, *J* = 4.3 Hz) and 6.04 ppm (d, *J* = 3.8 Hz), suggest the formation of a cyclooctatetraene unit with its typical coupling constants and chemical shift.

Encouraged by these interesting results, we decide to explore the allylic functionalization of **3ab** under different reaction conditions (Table 12).



[214] a) Chen M. S.; White M. C. *J Am. Chem. Soc*. **2004**, *126*, 1346-1347. b) Chen M. S.; Prabagaran N.; Labenz N. A.; White M. C. *J. Am. Chem. Soc*. **2005**, *127*, 6970-6971.

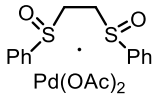
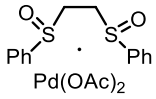
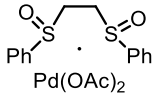
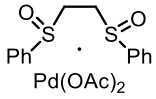
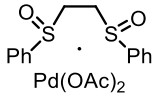
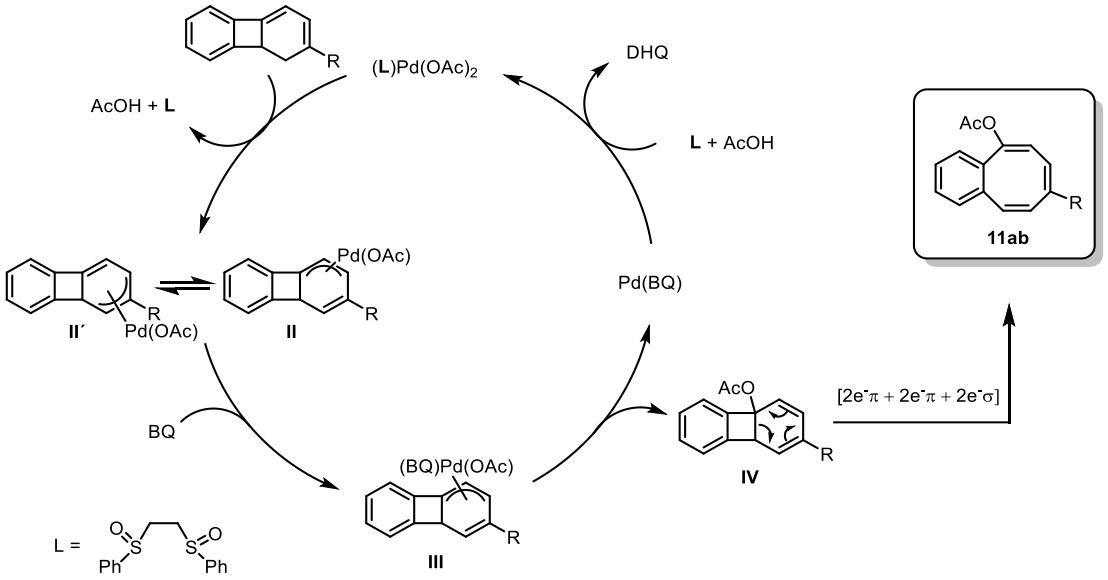
Entry	[Pd]	T (°C)	T (h)	**11ab** (%)[a]	**12ab** (%)[a]
1		43	24	23	
2	-	43	24	-	traces
3[b]		43	72	traces	-
4[b]		80	72	traces	-
5[c]		43	2	-	traces
6	-	rt	1	-	6
7[d]		43	24	-	-
8	$Pd(OAc)_2$	43	24	28	-
9	$Pd(OAc)_2$	80	24	19	-
10[e]	$Pd(OAc)_2$	43	24	28	-

Table 12 Conditions: **3ab** (0.1-0.2 mmol) in solvent (0.22M), a) isolated yield, b) under Ar, c) under O_2, d) 1 equiv of AcOH, e) 15 mol% $Pd(OAc)_2$

The metal catalyst is mandatory since in its absence **11ab** is not observed with the bicyclic ketone**12ab** present albeit in traces (entry 2). The presence of oxygen in the reaction is also necessary since the reaction run under Ar at 43°C or 80°C gave only rise to traces of **11ab** (entries 3 and 4). Pure O_2 atmosphere is not beneficial for the reaction (entry 5), only a low 6% yield of **12ab** could be isolated when the reaction was stirred at rt for 1h (entry 6). The amount of AcOH seems to be key to perform this transformation. With only 1 equiv of acetic acid instead of 4 equiv (entry 7) the reaction evolves to the formation of an unknown product (detected by GC-MS, not shown). The presence of bis-sulfoxide ligand was not necessary for the formation of **11ab**. On using $Pd(OAc)_2$ in the presence of AcOH and BQ in air, expected cyclooctatetraene **11ab** was obtained in slightly better yield (entries 8 and 10). Reaction temperature also affects to the reaction since at 80°C gave a lower yield of **11ab** (entry 9).

The formation of **11ab** could be rationalized as follows: in a first step, Pd catalyst is coordinated to the diene to form the η^3 π -allyl complex (**II**). Subsequent coordination of BQ to

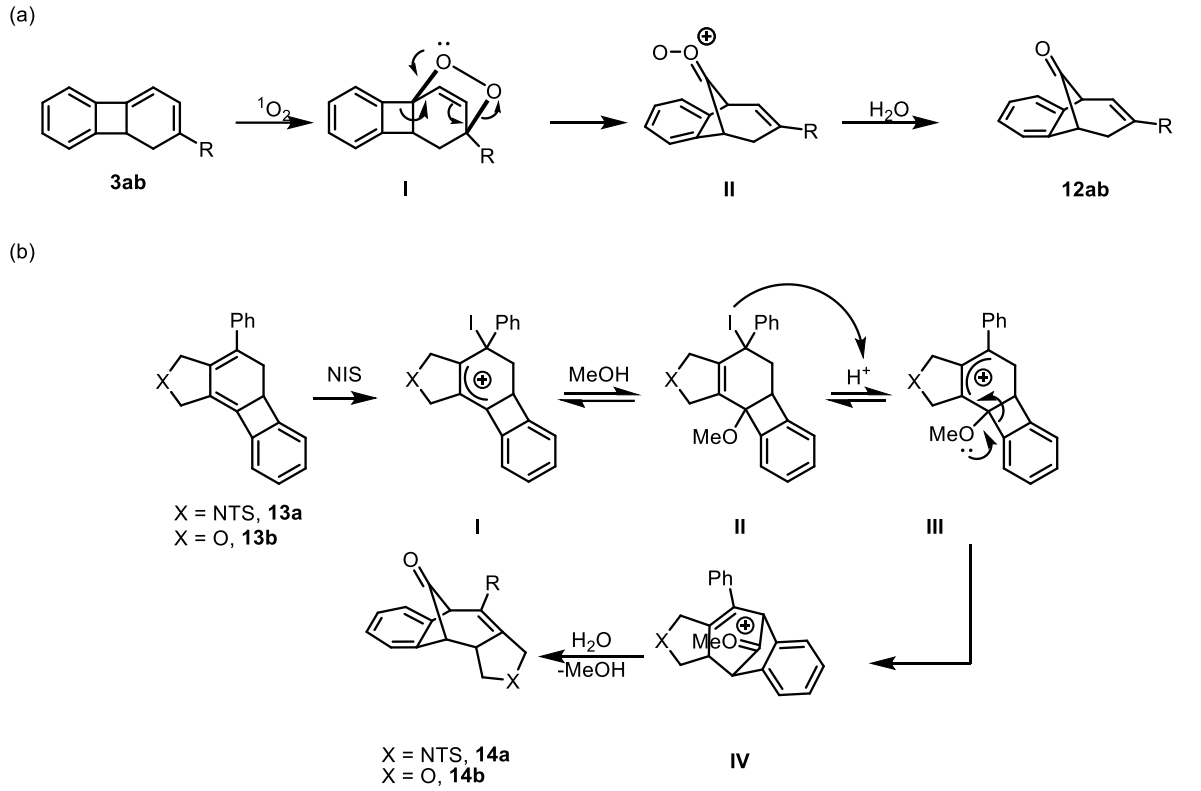
form Pd complex **III** allows the nucleophilic attack of acetate from the inner sphere to give the acetylated 1,3-cyclohexadiene species **IV**, which evolves to the observed benzofused cyclooctatetraene **11ab** through an electrocyclic ring opening of 6 π electrons (Scheme 54).



*Scheme 54. Proposed mechanism for the formation of benzofused cyclooctatetraene **11ab***

To explain the formation of **12ab** an initial endoperoxide intermediate **I** could be generated through a Diels-Alder reaction between $^1O_2$ and dihydrobiphenylene. Subsequent pinacol-type rearrangement would afford species **II**. Final hydrolysis would afford the observed ketone **12ab** (Scheme 55, eq. a). A similar rearrangement had been already proposed by Yamamoto and coworkers for the formation of bicyclic ketones. [215] Iodination of starting cyclohexadiene generates an allylic cation intermediate **I**, that is trapped by MeOH affording **II**. Subsequent loss of HI in acidic media would afford allylic species **III**. Finally, pinacol-type rearrangement renders oxocarbenium intermediate **IV**, which is hydrolysed to form the observed bicyclic ketone **14** (Scheme 55, eq. b).

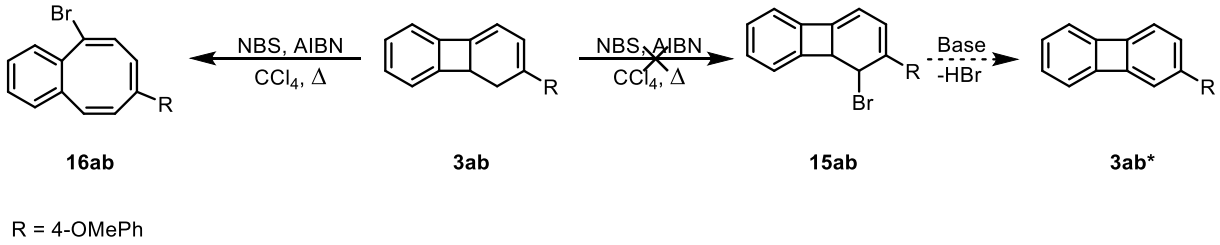
[215] Yamamoto, Y., Nishimura, K, Mori, S., Shibuya, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 5494–5497.



*Scheme 55. Proposed mechanism for the formation of benzofused bridged ketone **12ab** and **14** using a) O_2 and b) NIS/MeOH*

6.2.2.4 Oxidation via free-radical halogenation

Alternatively, radical halogenation (bromination) might be another way of functionalization of the allylic position, that eventually could also evolve to the target biphenylene **3ab*** by HBr elimination. Unexpectedly bromination with NBS and AIBN of dihydrobiphenylene **3ab** gave rise to the new benzofused cyclooctatetraene **16ab** in very good yield instead of the expected brominated dihydrobiphenylene **15ab**. BenzoCOT **16ab** showed similar spectroscopic data than benzoCOT **11ab** previously described (Scheme 53).

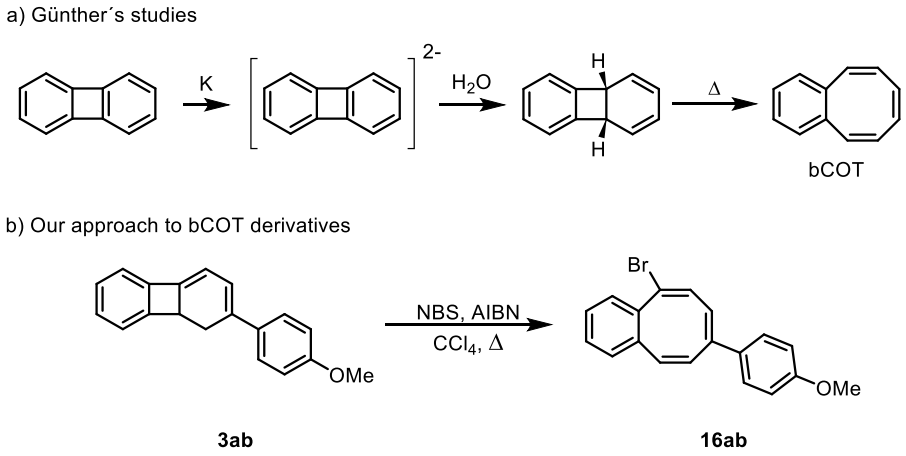


*Scheme 56. Bromination of dihydrobiphenylene **3ab***

6.2.3. COTs through radical ring opening of DHBs

As previously explained in this section, COTs are very interesting structural units that can be found in a large number of PAHs with a wide variety of useful applications. Many efforts have been made to obtain straightforward ways to prepare them. In fact, (poly)benzofused COTs have been broadly studied, finding many research works to obtain dibenzoCOTs (dbCOTs)[216], tribenzoCOTs (tribCOTs)[217] and tetraphenylenes.[218] In sharp contrast, benzocyclooctatetraenes (bCOTs) have received significantly less synthetic attention due to the difficulty to control its formation.[219]

Interestingly, the parent benzocyclooctatetraene had already been observed in pioneer Günther´s studies of Birch reduction of biphenylene in which the double protonation of the formed dianion took place at the bridgehead position to generate the 4a,8b-dihydrobiphenylene (1,3-cyclohexadiene isomer). This intermediate very rapidly evolves to the more stable bCOT via a thermal electrocyclic ring opening of six electrons (Scheme 57, a)).[220] As earlier mentioned, we have developed a new route to brominated benzofused cyclooctatetraene **16ab** (bCOT derivative) when dihydrobiphenylene **3ab** was treated with NBS and AIBN in hot CCl_4 (Scheme 57, b)).



Scheme 57. a) Birch reduction of biphenylene to bCOT, and b) bCOT by halogenradical ring opening of DHB

6.2.3.1. Mechanism proposal and DFT calculations

[216] a) Man, Y. M.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem.* **1990**, *55*, 3214−3221; b) Nishiuchi, T.; Kuwatani, Y.; Nishinaga, T.; Iyoda, M. *Chem. Eur. J.* **2009**, *15*, 6838−6847.
[217] Wong, H. N. C. *Acc. Chem. Res.* **1989**, *22*, 145−152.
[218] For a review, see: Han, J.-W.; Peng, X.-S.; Wong, H. N. C. *Natl. Sci. Rev*. **2017**, *4*, 892−916.
[219] For early studies of bromination of biphenylenes to bromo derivatives of bCOT, see: a) Barton, J. W.; Henn, D. E.; McLaughlan, K. A.; McOmie, J. F. W. *J. Chem. Soc*. **1964**, 1622−1625; b) Barton, J. W.; Whitaker, K. E. *J. Chem. Soc. C*. **1968**, 28−30; c) Elix, J. A.; Sargent, M. V. *J. Am. Chem. Soc*. **1969**, *91*, 4734−4739; d) Wong, H. N. C.; Sondheimer, F. *Angew. Chem. Int. Ed. Engl*. **1976**, *15*, 117−118; e) Kidokoro, H.; Sato, M.; Ebine, S. *Chem. Lett*. **1981**, *10*, 1269−1270. For a general review, see: Han, J.- W.; Li, X.; Wong, H. N. C. *Chem. Rec*. **2015**, *15*, 107−131.
[220] Günther, M. E.; Aydin, R.; Buchmeier, W.; Engelen, B.; Günther, H. *Chem. Ber*. **1984**, *117*, 1069−1076.

In order to gain further insights into the reaction mechanism, DFT calculations were performed to analyse all possible radical pathways. The radical selectivity was elucidated between the two different radical species formed depending on the abstraction of the tertiary hydrogen H_1 of the cyclobutene or a secondary hydrogens H_2 on the 1,3-cyclohexadiene moiety. Although the abstraction of a radical in a tertiary C-H bond require less energy than in a secondary one, the presence of the cyclobutene moiety dramatically changes the selectivity on the dihydrobiphenylene core, making the formation of the secondary bis-allylic radical **I** easier (4.3 Kcal/mol lower in energy) than the allylic benzylic tertiary radical (Figure 39).

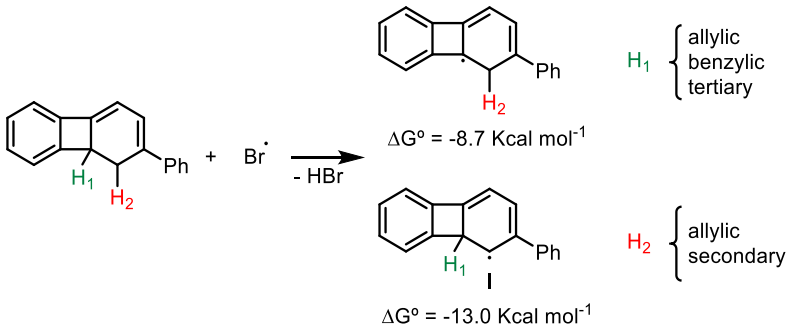


Figure 39. Bond Dissociation Energies (BDE's) of H_1 and H_2

The three possible evolution pathways for the most favourable radical **I** were then evaluated: (1) six-π-electron electrocyclic ring opening followed by trapping of the resulting radical with molecular bromine Br_2 to afford the observed benzofused cyclooctatetraene; however, a high energy barrier for the first C_{sp3}-C_{sp2} bond cleavage is predicted (ΔG‡ = 39.2 kcal/mol, red pathway); (2) radical opening of the cyclobutene ring (C_{sp3}-C_{sp2} bond cleavage) followed by trapping with Br_2 to afford the terphenyl **II** (ΔG‡ = 19.4 kcal/mol, blue pathway);[221] (3) the most favourable one involves first a direct bromination of the allylic radical **I**. Three different brominated structures could be formed depending on whether the radical is trapped in the tertiary, allylic and benzylic position (**III**, -16.2 Kcal/mol), in the tertiary, bisallylic and benzylic position (**IIIb**, -7.7 Kcal/mol) or in the secondary and allylic position (**IIIa**, -8.1 Kcal/mol) position. Once **III** was formed as the most favourable product of radical bromination of starting dihydrobiphenylene, the isolated benzofused cyclooctatetraene **16aa** would be formed by a six-π-electrocyclic ring opening process. The electronic richness of the phenyl (aryl) substituent could affect to the efficiency of this last opening (Figure 40).

[221] In this possible pathway, although the energy barrier is lower than in the previous route and the final product is the most stable, the product is not observed.

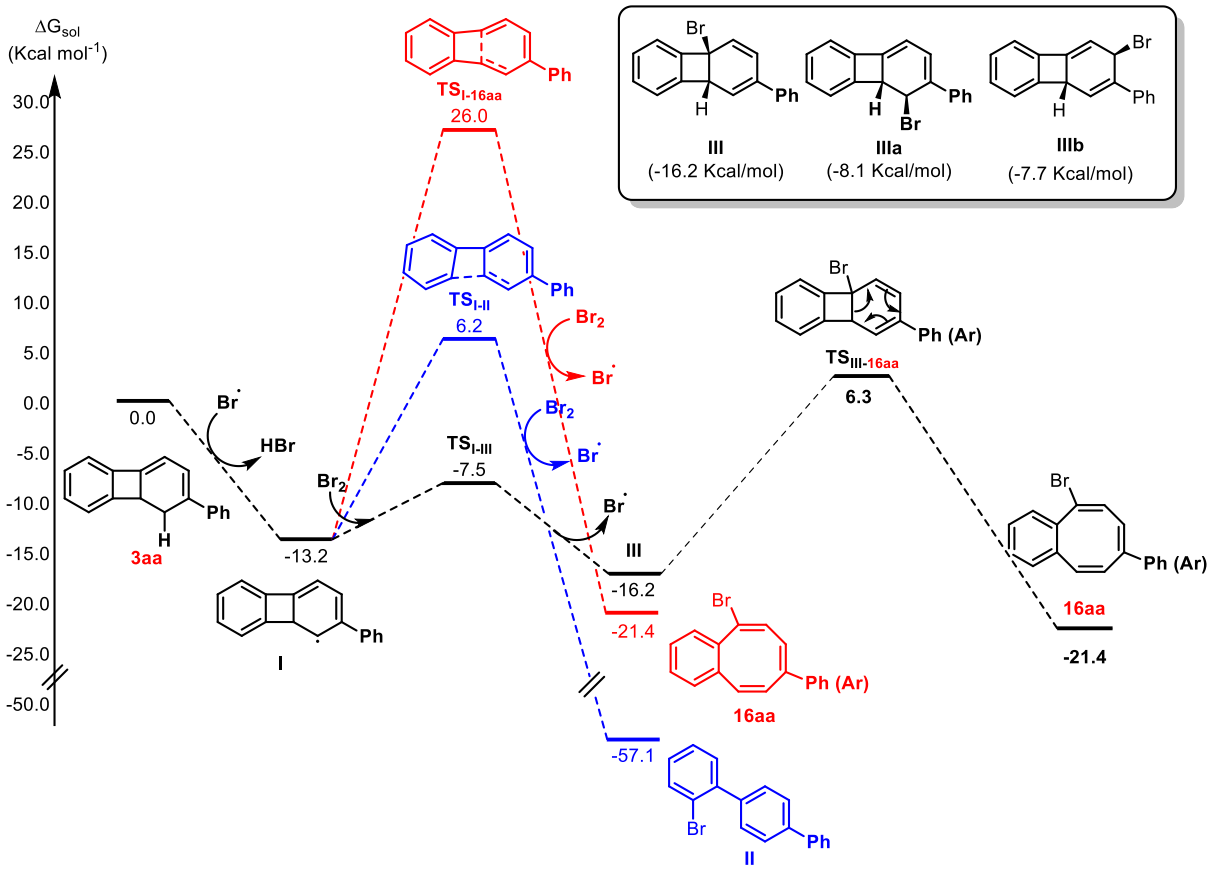
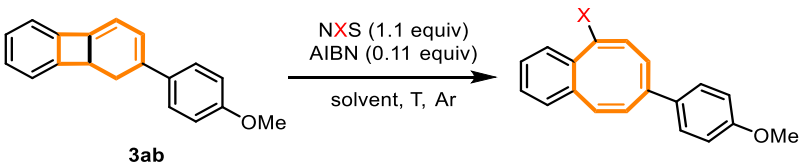


*Figure 40. Free energy profiles for the three possible radical bromination pathways of **3aa** and electrocyclic ring opening to the observed brominated bCOT **16aa***

6.2.3.2. Optimization of reaction conditions

We began our investigation by examining the well-known Wohl-Ziegler bromination of dihydrobiphenylene **3ab**.[222] Thus, as a proof of concept, the use of NBS and AIBN as radical initiator in CCl_4 at rt promoted the formation of the target bromo-benzocyclooctatetraene **16ab** in a low 30% of yield (entry 1).



3ab

X= Br, **16ab**
X= I, **16ab'**
X= Cl, **16ab''**

Entry	Solvent	T (ºC)	**16ab** (yield) [a]
1	CCl_4	rt	30
2	CCl_4	Reflux	89
3	DCM	Reflux	32

[222] Saikia, I.; Borah, A. J.; Phukan, P. *Chem. Rev*. **2016**, *116*, 6837-7042.

4	$CHCl_3$	Reflux	38
5	Heptane	Reflux	44
6	CH_3CN	Reflux	40
7	1,4-dioxane	Reflux	61
8	DCE	Reflux	66
9	Benzene	Reflux	65
10	CCl_4 (darkness)	Reflux	53
11	CCl_4 (no AIBN)	Reflux	30
12	CCl_4 (no NBS)	Reflux	SM (50)
13[b]	CCl_4	Reflux	77, **16ab'**
14[c]	CCl_4	Reflux	36, **16ab''**

Table 13. Reaction conditions: **3ab** (0.2-0.3 mmol) in solvent (0.036 M), NBS (1.1 equiv), AIBN (0.11 equiv), 1–1.5h; a) Isolated yield; b) NIS; c) NCS

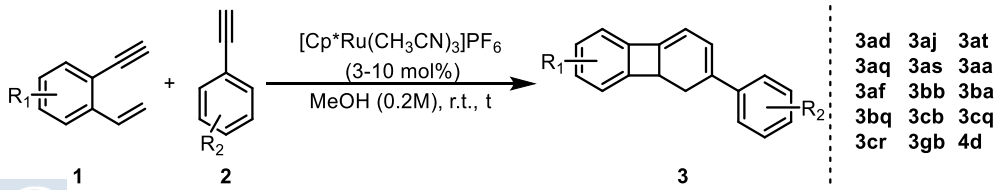
Satisfactorily, when the reaction was performed at reflux temperature, the isolated yield of cyclooctatetraene increased up to 89% (entry 2). Others solvents were then tested. Reactions in chlorinated solvents like $CHCl_3$ or DCM, as well as non-polar heptane or polar CH_3CN afforded lower yields of 16ab (entries 3-6). In contrast, polar ethereal or aprotic solvents like 1,4-dioxane or DCE, or non-polar solvents like benzene rendered 16ab in fairly good yields (entries 7-9). Re-examination of experimental reaction conditions using CCl_4 as solvent was next. When the reaction is performed in the absence of light (entry 10) or in the absence of AIBN (entry 11), a lower yield of 16ab is obtained. The presence of NBS probed mandatory for the consumption of starting dihydrobiphenylene 3ab (entry 12). The reaction also tolerates the use of other halogens. NIS and NCS as halogen source are also feasible to render the corresponding iodinated (16ab') and chlorinated (16ab'') bCOTs although in lower yields (entries 13 and 14).

From these results, experimental conditions of entries 2 and 8 were selected as optimal conditions.

6.2.3.3. Scope and limitations

6.2.3.3.1. Synthesis of starting materials

A variety of electronically different dihydrobiphenylenes were prepared following the described Ru(II) catalysed [2+2+2] cycloaddition of enynes and alkynes (Scheme 58).



Scheme 58. Synthesis of dihydrobiphenylenes by Ru(II)-catalysed [2+2+2] cycloaddition of substituted ortho-*ethynylbenzenes and external alkynes.*

6.2.3.3.2. Radical ring opening of dihydrobiphenylenes

With the optimized conditions in hand, scope and limitations were then examined: dihydrobiphenylene **3** (0.2-0.3 mmol), NBS (1.1 equiv), AIBN (0.11 equiv) in CCl_4 or DCE (0.036 M) at reflux temperature under Ar atmosphere during 1-1.5h in a two-neck round-bottomed flask.

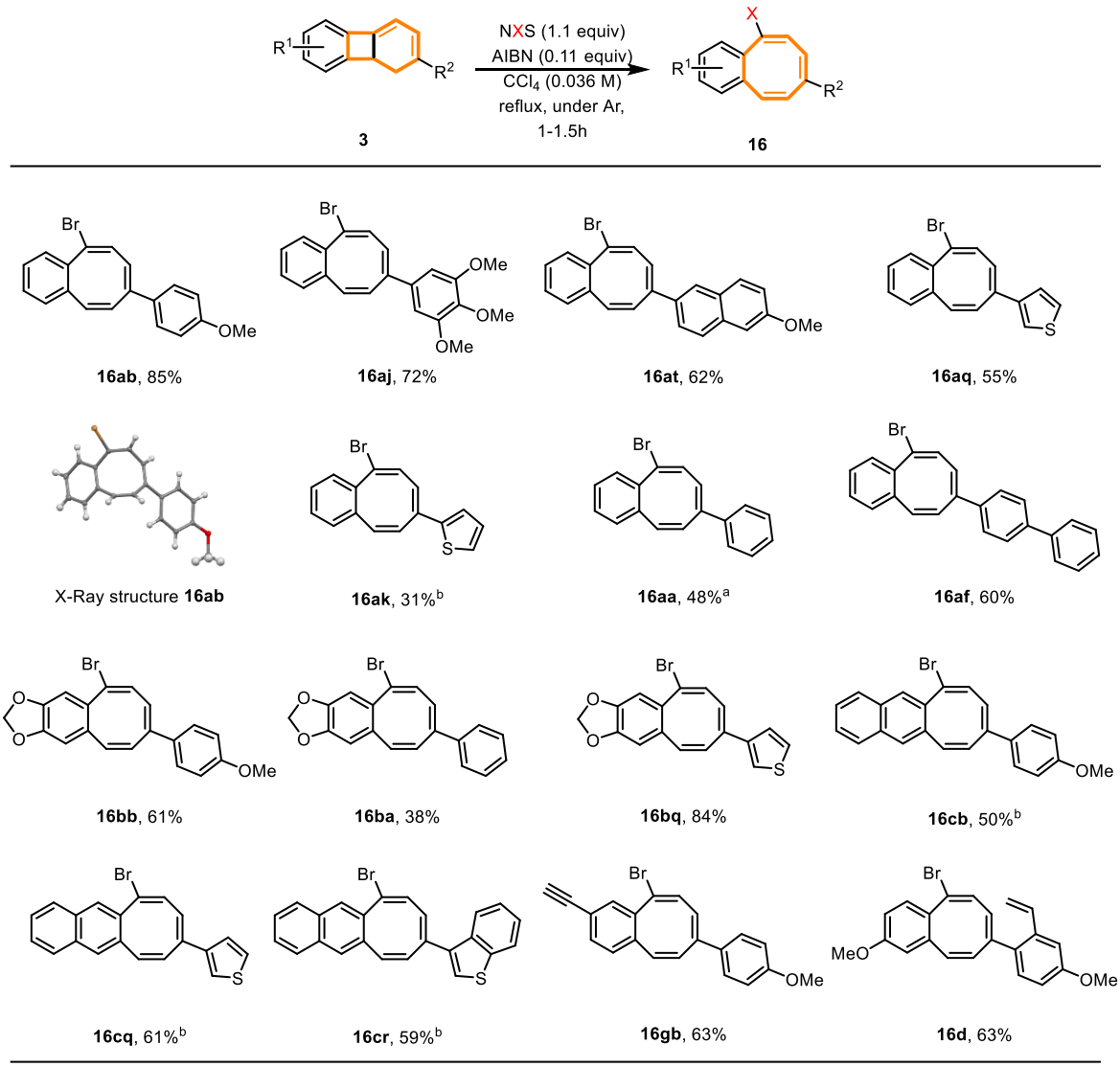
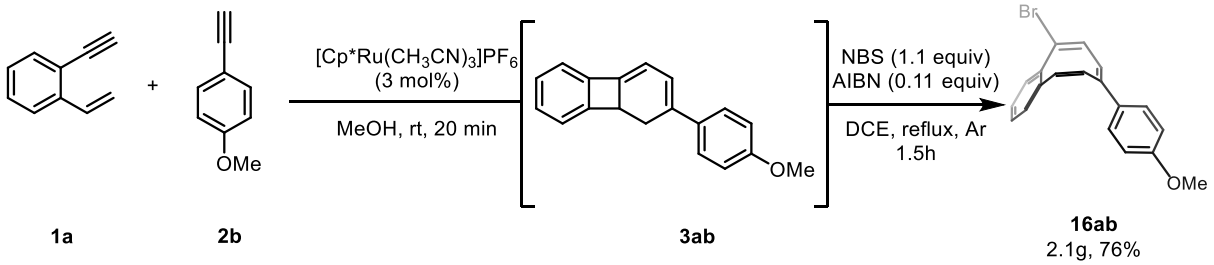


*Figure 41. Reaction conditions: **9** (0.2-0.3 mmol) in CCl_4 (0.036 M), NBS (1.1 equiv), AIBN (0.11 equiv), 1–1.5h. Isolated yield; a) Reaction time was 4h; b) DCE as solvent. AIBN = Azobisisobutyronitrile*

Reactions with dihydrobiphenylenes **3** arising from arylenyne **1a** (R_1 = H) and electron-rich alkynes **2**, (*p*-anisole **3ab**, trialkoxyphenyl **3aj**, 6-methoxynaphthyl **3at** and heteroaryl 3-thiophene **3aq**) gave rise to fairly good yields of corresponding bCOT´s (55-85%). Curiously, the position of the heteroatom affected the efficiency of the reaction since dihydrobiphenylene bearing a 2-thiophenyl group yielded bCOT **16ak** in moderate yield using DCE as solvent. Not unexpectedly, the parent phenyl substituted dihydrobiphenylene **3aa** gave rise to the expected bCOT **16aa** although in lower yield (48%), probably due to the lower electronic richness of the

influential aryl ring involved in the electrocyclic opening. However, the use of an extended conjugated π-system as substituent, dihydrobiphenylene **3af**, was beneficial for the ring opening giving rise to the biphenyl benzocyclooctetraene **16af** in a good yield (60%). On the other hand, dihydrobiphenylenes **3** bearing the electron-rich dialkoxy arylenyne **1b** (R_1/R_1 = OCH_2O) and parent electron-rich alkynes **2** afforded the corresponding brominated benzofused cyclooctatetraenes **16ba-bq** in moderate to good yields (38-84%), showing the versatility of combining one or two electron-rich partners. Dihydrobiphenylenes derived from the benzofused 2-ethynyl-3-vinylnaphthalene **1c** gave moderate yields (50—61%) of the corresponding bCOT´s (**16cb**, **16cq**, **16cr**).[223] Finally, π-unsaturated substituents on the starting aryl enyne were well tolerated. The ethynyl and vinyl substituents of dihydrobiphenylene **3gb** and **4e** remained intact under the radical conditions giving the corresponding acetylenic bCOT **16gb** and styrenic COTs **16d** in fairly good yields that might be capable of further manipulations.

In addition, scaling up was also feasible as shown by performing a tandem process from initial enyne **1a** and alkyne **2b** without the isolation of dihydrobiphenylene **3ab** (Scheme 59).The reaction of **1a** (8.1 mmol) and **2b** (9.7 mmol) in MeOH under catalytic conditions (as little as 3% of Ru) followed by a rapid replacement of the solvent with the apolar DCE to perform the radical reaction allowed us to obtain bCOT **16ab** (2.1 g) in an excellent 76% overall yield.



*Scheme 59. Scale-up synthesis of bCOT **16ab***

Unfortunately, the following dihydrobiphenylenes were not tolerated under radical conditions (Figure 42).

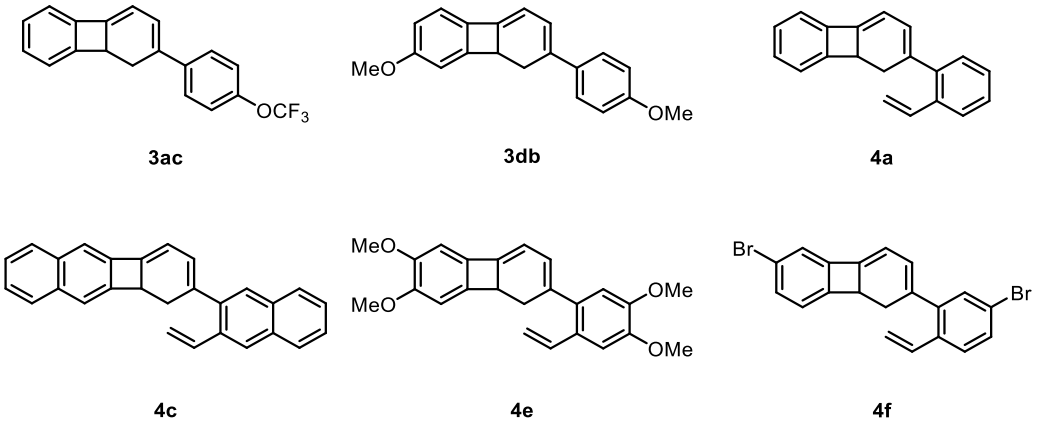
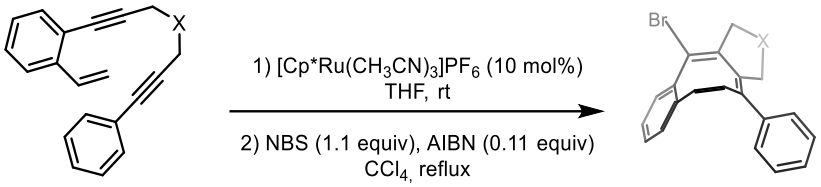


Figure 42. Unsuccessful dihydrobiphenylenes to the formation of brominated bCOT´s.

[223] The use of CCl_4 probably would afford better results, however we decided to move to DCE due to solvent availability and environmentally issues.

Decomposition of dihydrobiphenylene **3ac** was observed under the reaction conditions. In sharp contrast with the vinyl substituted dihydrobiphenylene **4d**, π-electron-rich conjugated vinyl dihydrobiphenylenes **4a**, naphthyl derivative **4c** or dimethoxyl enyne **4e** afforded complex mixtures due, most likely, to the competition between electrophilic and radical brominations. Similar behaviour was observed when dihydrobiphenylene **4f**, bearing a bromine substituent, or electron rich dihydrobiphenylene **3db**, were subjected to radical conditions.[224]

6.2.3.3.3. One-pot tandem fully intramolecular Ru(II)-catalysed [2+2+2] cycloaddition of heteroannulated enediynes / radical opening to tricyclic COTs



17a, X = O
17b, X = NTs

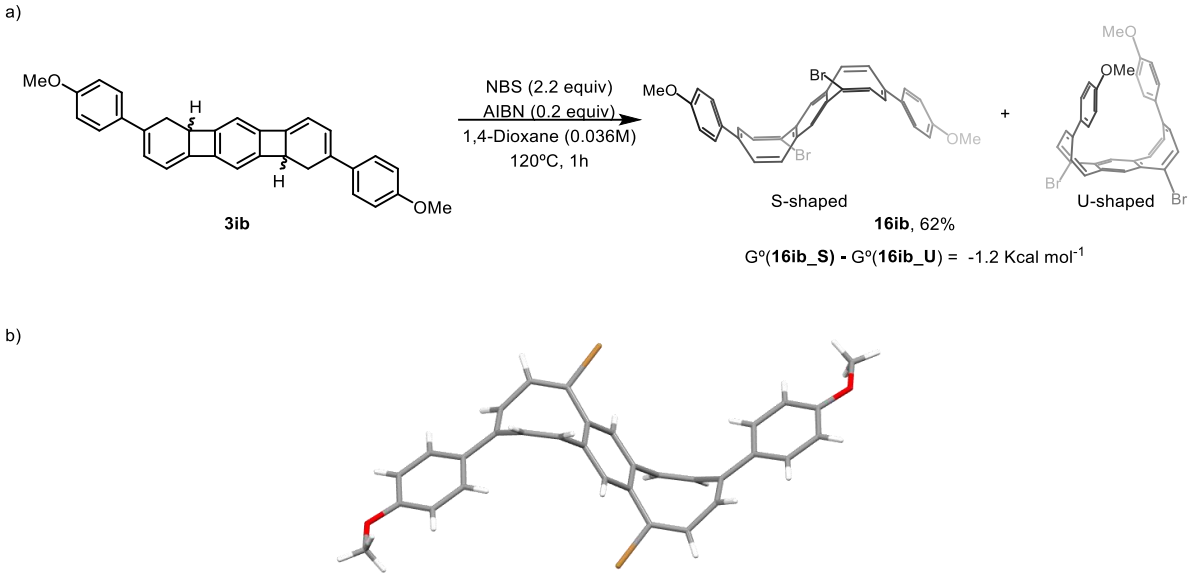
18a, X = O, 30%
18b, X = NTs, 40%

Based on Yamamoto´s results,[114] we also decided to explore the one-pot tandem process from fully intramolecular reaction of *N*- and *O*-tethered enediynes. Interestingly, it was possible to assemble tricyclic heteroannulated benzocyclooctatetraenes **18a** and **18b** in moderate yields via one-pot two steps process from the corresponding starting arylenynes.

6.2.3.3.4. Synthesis of linear benzodiCOT 16ib

We also envisioned the possibility to access to a very interesting scaffold combining benzenoids (aromatic) and non-benzenoids (non-aromatic) rings in a 8-6-8 fusion from dihydrobiphenylene **3ib** (section 6.1.2, Table 4). This compound had been obtained by double Ru(II) catalysed [2+2+2] cycloaddition of symmetric enyne **1i** with 4-ethynylanisole **2b** in an excellent 80% yield. The halogen radical ring opening of **3ib** with NBS in DCE afforded an excellent 62% yield of a mixture of U- and S-shaped conformers of linear benzodiCOT **16ib**, a novel non-benzenoid PAH scaffold with intriguing electronic and aromatic properties (Scheme 60a).

[224] GC-MS analysis show the presence of several products, among which are biphenylene (oxidation product) and the brominated in the allylic position. The same products were also observed when the reaction was performed in the presence of molecular bromine (Br_2).



*Scheme 60. a) Synthesis of linear benzodiCOT **16ib** from dihydrobiphenylene **3ib**; b) X-ray image of **16ib***

DFT calculations revealed that the S-shaped conformer is more stable than the U-shaped by 1.2 Kcal/mol,[225] while ^{1}H-NMR analysis showed that the initially formed 1:2.5 ratio of U- and S-shaped conformers could be thermally equilibrated to 1:1.5 ratio by heating at 100 ºC in deuterated tetrachloroethane. Suitable crystals of 16ib for X-ray analysis were grown from a solution in a hot $CHCl_3$/hexane mixture by slow evaporation of the solvents showing an S-shaped geometry with the bromine atoms on opposite faces with respect to the central benzene plane (Scheme 60b). Furthermore, the two eight-membered rings are considerably bent up and down from the plane of the central benzene unit with a large dihedral angle of ~ 138º. As simple bCOT, the two eight-membered rings of benzodiCOT 16ib adopt a tub-shaped conformation, with large bond length alternation. Central six membered ring presents the typical range of 1.39-1.40 Å for bond length, disclosing an aromatic benzenoid behaviour.

[225] See section 7.1.3.10 in Methodology.

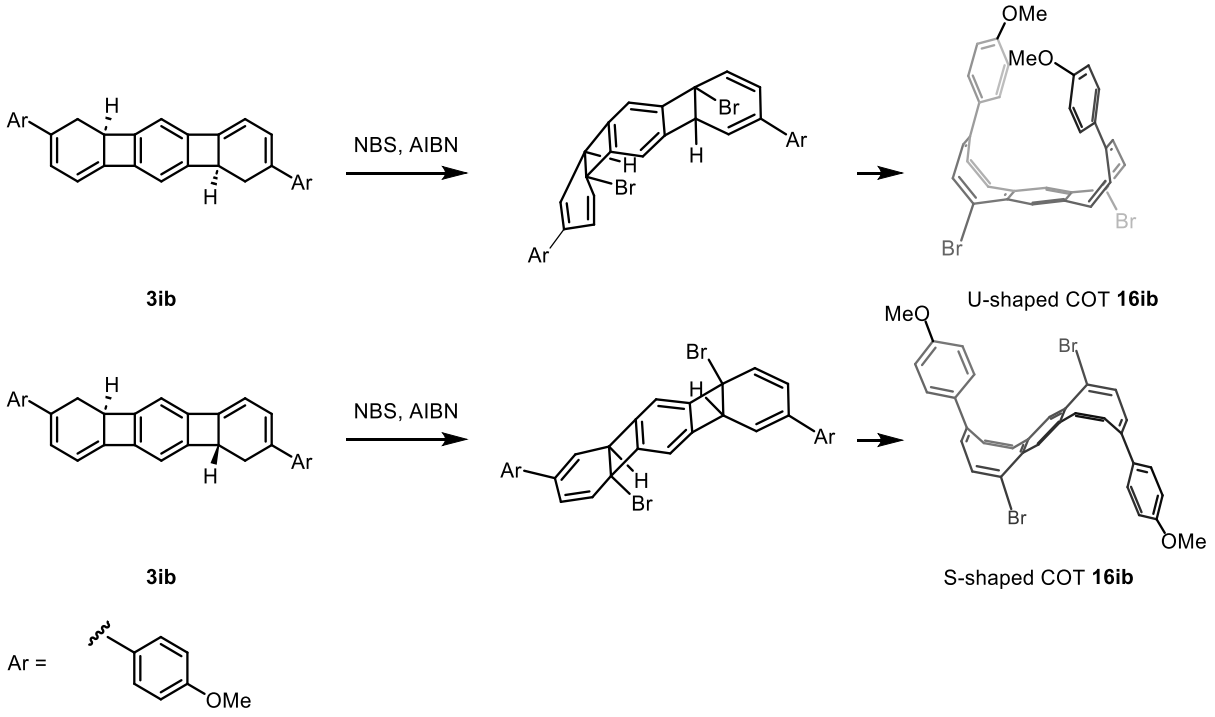


Figure 43. Suitable explanation for the formation of U- and S- shaped COTs

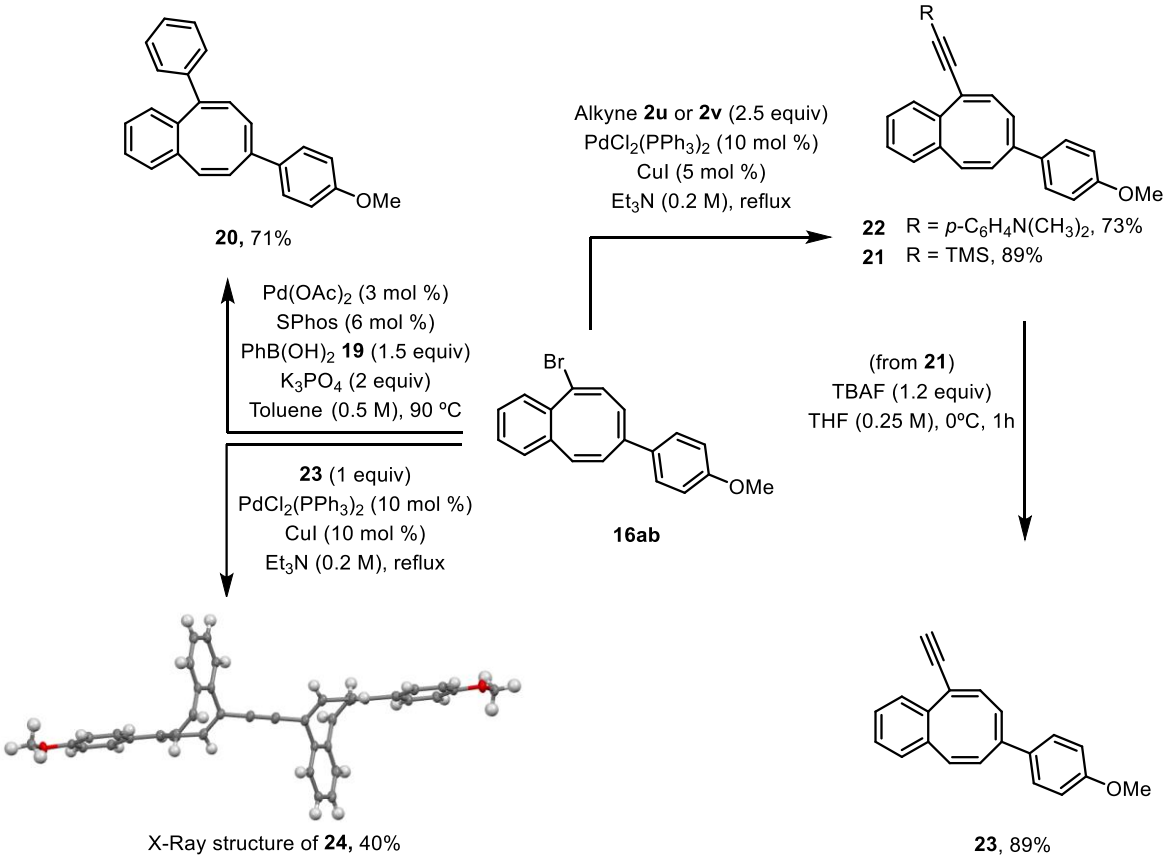
Formation of the two shaped U- and S- benzodiCOTs **16ib** can be rationalized assuming the initial formation of dihydrobiphenylene **3ib** as a mixture of two diastereoisomers (Figure 43). The initial position of bromine atoms in the four membered ring after radical bromination dictates the final shape of the COT after the disrotatory $6e^-$ πelectrocyclic ring opening.

6.2.3.4. Derivatization

As a proof of concept to demonstrate the synthetic utility of brominated bCOTs, a variety of functionalizations were carried out to obtain valuable COT-embedded PAH´s.

6.2.3.4.1. Cross-couplings of brominated bCOT 16ab

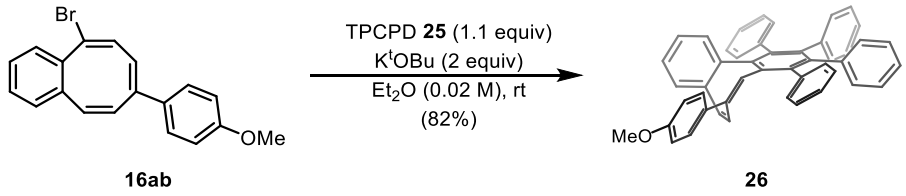
Suzuki-Miyaura cross coupling between bCOT **16ab** and phenylboronic acid **19** smoothly evolved to the expected phenyl-substituted bCOT **20** in a quite good 70% yield. Sonogashira couplings were also feasible under typical reaction conditions. Thus, alkynyl COT derivatives **21** and **22** were successfully obtained in good to excellent yields using trimethylsilylacetylene **2u** and alkynylaniline **2v**, respectively. To our delight, an efficient Sonogashira coupling between **16ab** and alkynylCOT **23** (from protodesilylation of **21**) afforded uneventfully the interesting bis-COT derivative **24**, as confirmed by X-ray analysis (Scheme 61).



*Scheme 61. Cross-couplings of bCOT **16ab***

6.2.3.4.2. Diels-Alder reaction of benzo- and benzodiCOTynes from brominated benzoCOT 16ab and benzodiCOT 16ib

Treatment of **16ab** with KO^{t}Bu generates a strained cyclic alkyne (benzoCOTyne), under very mild reaction conditions,[226] that could be subsequently trapped as a dienophile with tetraphenylcyclopentadienone (TPCPD) **25** in a Diels-Alder reaction giving rise to the formation of the π-extended dibenzoCOT **26** in an excellent 82% yield (Scheme 62).



*Scheme 62. Diels-Alder reaction of bCOT **16ab** to cycloadduct **26***

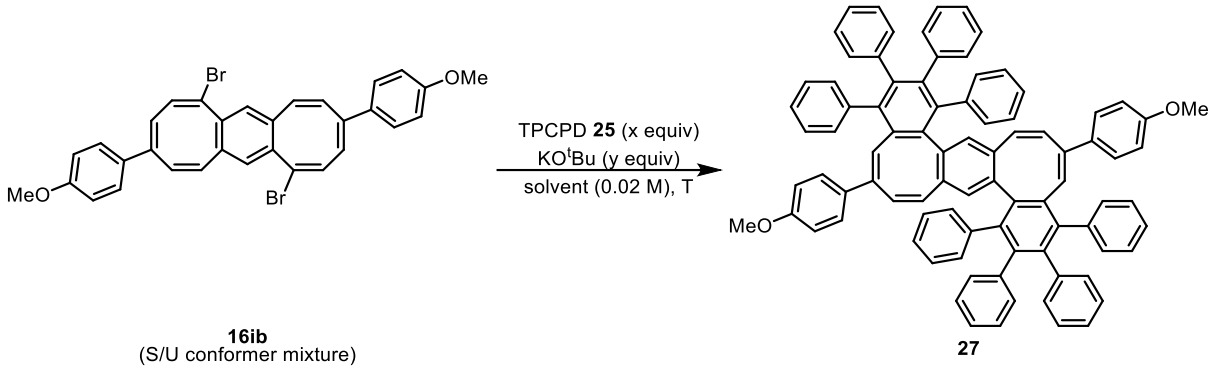
Based on the excellent performance of the Diels-Alder reaction leading to adduct **26**, we envisioned to go one step further and perform a double Diels Alder reaction between the

[226] It is very remarkable to highlight the higher reactivity of the planarized triple bond in a benzofused COT (rt, 25 °C) in comparison with the typical dibenzo-fused systems (Ph_2O reflux, > 250 °C). Huang, N. Z.; Sondheimer, F. *Acc. Chem. Res*. **1982**, *15*, 96−102.

COTyne derived from benzodiCOT **16ib** and TPCPD **25** in order to assemble a benzodi[8]annulene derivative **27** capable of further dehydrogenations.

As a first attempt under typical standard conditions, adjusting the amounts of reagents, a mixture of starting material **16ib** and the expected Diels-Alder adduct **27** in a 3:1 ratio was obtained (Table 14, entry 1). Again, incomplete reactions at rt of non benzenoid **16ib** under various ethereal solvents were also observed. Reaction temperature was then modified. In THF at 50 ^{o}C full conversion of starting benzodiCOT occurred although the isolated yield of **27** was very low (entry 2). By contrast, reaction in 1,4-dioxane at reflux gave decomposition of starting material (entry 3).

Heating the reaction mixture in THF with an extra 2 equiv of TPCPD **25** gave the cycloadduct **27** in a remarkable 64% yield, meaning 80% yield for each cycloaddition reaction (entry 4). Similar result was obtained when the amount of dienone was increased up to 6 equiv (entry 5). By contrast, on increasing the amount of base to 5 equiv led to a lower yield (entry 6). Finally, concentration of the reaction was examined observing that both higher concentration and dilution render lower yields (entries 7 and 8). With the best conditions in hand (entry 4), scale-up synthesis was accomplished using 1 mmol of starting benzodiCOT **16ib** obtaining again **27** in an excellent 67% yield (entry 9).



16ib
(S/U conformer mixture)

27

Entry	KO^{t}Bu (y equiv)	TPCPD **25** (x equiv)	Solvent	T (^{o}C)	Product (%)[a]
1	4	2.2	Et_2O	rt	**16ib** + **27** (3/1)
2	4	2.2	THF	50	**27** (17)
3	4	2.2	1,4-dioxane	100	Decomposition
4	4	4	THF	50	**27** (64)
5	4	6	THF	50	**27** (65)
6	5	4	THF	50	**27** (53)
7[b]	4	4	THF	50	**27** (52)
8[c]	4	4	THF	50	**27** (48)
9[d]	4	4	THF	50	**27** (67)

***Table 14**. Conditions: **16ib** (0.2 mmol), KO^{t}Bu (y equiv), TPCPD **25** (x equiv) in solvent (0.02 M); a) isolated yields; b)0.04 M; c) 0.01 M; d) 1 mmol scale.*

Encouraged by these results, current studies are being performed in our lab in order to planarize/dehydrogenate the adduct **27** by using Scholl´s conditions.[227] Initial results suggest the cyclization of at least 12 C-C bonds as well as the introduction of a chlorine atom under radical-cation conditions ($FeCl_3/NO_2Me$). The alternative use of arenium-cation conditions (DDQ/TfOH) led to a product with a mass 14 or 16 units less than starting cycloadduct **27** (7 or 8 formed C-C bonds).

Unfortunately, none of these PAH structures derived from Scholl´s conditions could be definitively confirmed (Figure 44)

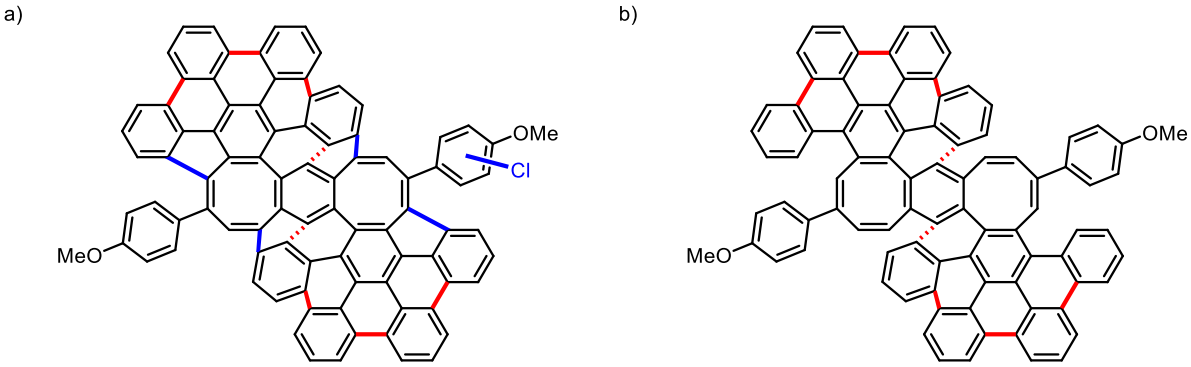


*Figure 44. Plausible dehydrogenative adducts from annulene **27** under a) $FeCl_3/NO_2Me$ and b) DDQ/TfOH Scholl´s conditions.*

[227] Zhang, Y.; Pun, S. H.; Miao, Q. *Chem. Rev*. **2022**, *122*, 14554−14593.

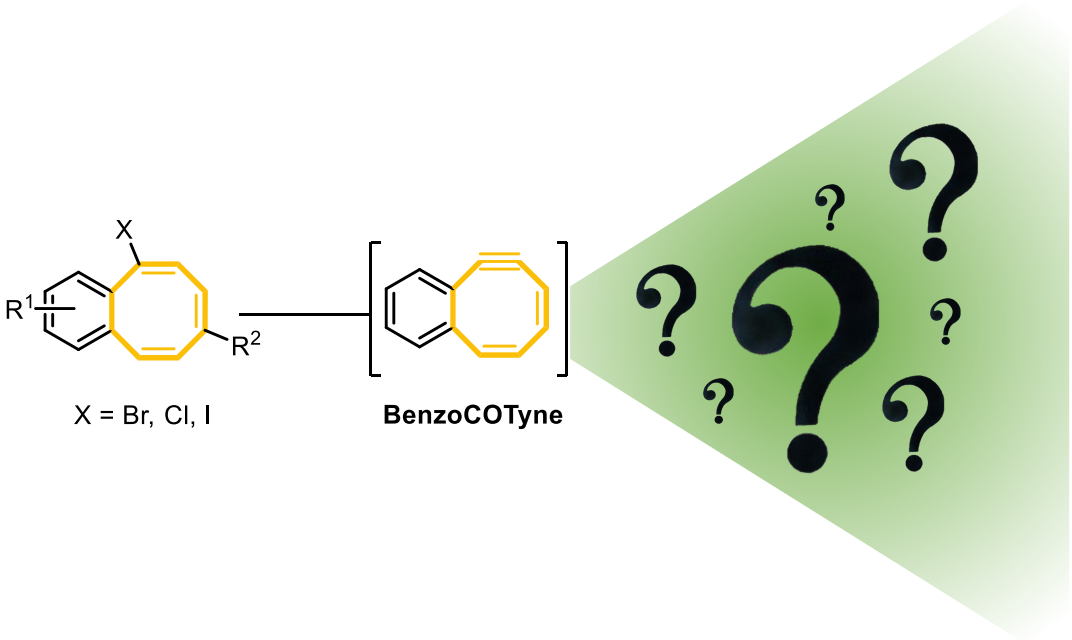
6.2.4. Conclusions

From the results, the following conclusions may be drawn: [228]

- Allylic functionalization of **3ab** under Pd(II)/bis-sulfoxide catalysis (White´s conditions) gave rise to acetylated COT **12ab**.
- Halogenated (mainly brominated) benzofusedCOTs **16** were obtained from moderate to excellent yields when dihydrobiphenylenes **3** were subjected to halogen radical conditions in presence of *N*-bromosuccinimide and AIBN as radical initiator.
- Scope and limitations of radical ring opening of dihydrobiphenylenes were explored. As a rule of thumb, the higher electronic richness of the alkyne partner, the grater is the yield of bCOT. By contrast, electron poor systems lead to decomposition of SM as well as formation of complex mixtures.
- A one-pot tandem fully intramolecular Ru(II)-catalysed [2+2+2] cycloaddition of heteroanulated enediynes **17a-b** and radical ring opening to COTs **18a-b** was achieved in moderate yield.
- BenzodiCOT **16ib**, PAH that combine benzenoid and non-benzenoid rings, was obtained in high yield under standard radical conditions from dihydrobiphenylene **3ib**.
- DFT calculations suggest a selective abstraction of a secondary allylic hydrogen against the tertiary one in the 1,3-cyclohexadiene core of dihydrobiphenylenes **3**. The lower energy pathway to the formation of bromoCOTs involves an allylic bromination followed by a $6e^{-}\pi$-electrocyclic ring opening process.
- BromoCOT **16ab** reacted smoothly under Suzuki-Miyaura and Sonogashira cross-coupling conditions to give the corresponding benzoCOT derivative, **20**, **22** and the linked alkyne bis-COT **24** in moderate to excellent yields.
- Diels Alder reaction of TPCPD with benzo- and benzodiCOTynes as dienophiles (from **16ab** and **16ib)** afforded the expected cycloadducts, **26** and **27**, in excellent yields.

[228] Bello-García, J.; Padín, D.; Varela, J. A.; Saá. C. *Org. Lett*. **2021**, 23, 5539–5544.

Reactivity of non-aromatic COTynes



BenzoCOTynes (eight membered cyclic alkynes) could be considered as the non-aromatic analogues of benzynes. While the reactivity of the six-membered benzenoid was widely studied, the eight-membered counterpart is poorly known, in part because of the lack of available synthetic methodologies to prepare them. Formation of benzoCOTynes and reactivity of the generated species in a metal and thermal scenario will be discussed in this section.

6.3. Reactivity of non-aromatic COTynes

6.3.1. Specific objectives

COTynes have been relatively poorly studied although its use in synthesis could provide a versatile and straightforward entry to intriguing systems bearing aromatic and non-aromatic nuclei. In section 6.2.3 we have described a straightforward methodology to achieve highly functionalized (and halogenated) benzofused cyclooctatetraenes, which can be considered as COTynes precursors via "HX" elimination in the presence of an external base. The reactivity of these elusive species under metal-catalysed and thermal conditions will be disclosed in this section.

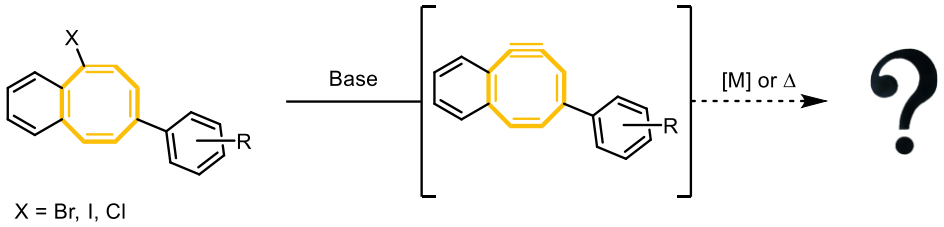
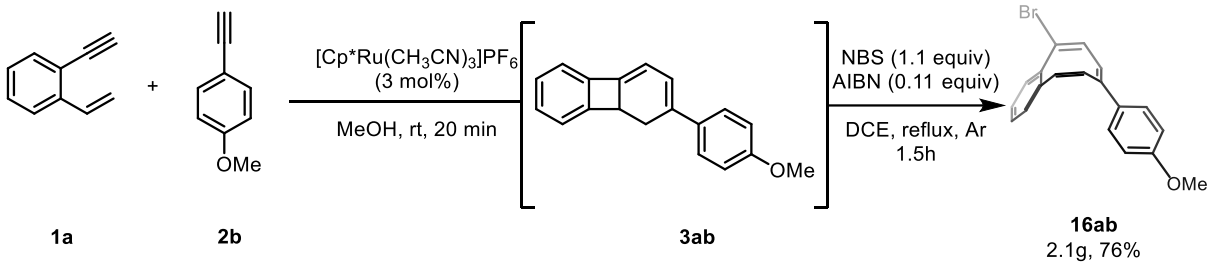


Figure 45. Unknown reactivity of benzoCOTynes

6.3.2. Studies of reactivity of benzoCOT 16ab

6.3.2.1 Synthesis of starting materials

Brominated benzofused cyclooctatetraene **16ab** was prepared by halogen radical ring opening of dihydrobiphenylene **3ab** following our developed methodology (see 6.2.3). As previously mentioned, a one-pot two-steps synthesis allowed us to obtain the target benzoCOT **16ab** in gram scale with high yield.

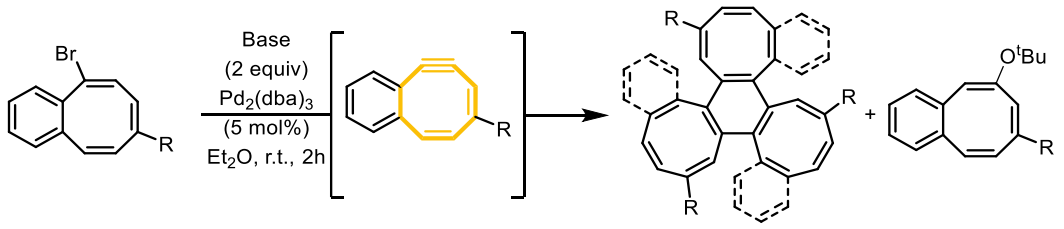


*Scheme 63. Synthesis of benzoCOT **16ab***

6.3.2.2 Studies of reactivity of benzoCOT 16ab

6.3.2.2.1. Metal catalysed cycloadditions

Based on the well-known metal-catalysed trimerization of planar arynes (benzynes)[168], we first investigated the conditions for the formation of benzoCOTyne **51**. This reactive species was prepared *in situ* from benzoCOT **16ab** using KO^{t}Bu as base and Et_2O as solvent. The formation of COTyne **51** was supported by the isolation of a mixture of tri[8]annulene **52** in a moderate 44% yield and the alkoxy derivative **53ab** (15%) as byproduct (Table 15, entry 1).



Entry	Variation	Product (yield)[a]
1	none	**52** (44%) +**53ab** (15%)
2	NaO^{t}Bu, LiO^{t}Bu, CsF, K_2CO_3 or BuLi[b]	**16ab** (90 - 95%)
3	THF	**52** (74%) + **53ab** (10%)
4	DCM or toluene	**16ab** (47%) + **52** (38%)
5	DMF	decomposition

6	1.5 equiv of KO^{t}Bu	**52** (66%) + **53ab** (<5%)
7[c]	0.33 M and 1.5h	**52** (78%)
8	without KO^{t}Bu	**16ab** (99%)
9	without $Pd_2(dba)_3$	**56ab** (66%)
10	$Pd(PPh_3)_4$ instead of $Pd_2(dba)_3$	**52** (65%) [d]

Table 15. Conditions: **16ab** (0.2 mmol) in solvent (0.1 M), 2h at rt. a) Isolated yields. b) Products **54** and **55**, derivatives of **16ab**, were obtained. c) Longer reactions times didn´t affect to the yield. d) Different number and ratio of products as compared with $Pd_2(dba)_3$ as judged by NMR.

Other alkoxides were also tested (NaO^{t}Bu, LiO^{t}Bu) but the reaction did not show evolution of starting material, probably due to the less ionic character (entry 2). The same behaviour was observed using weaker bases like CsF or K_2CO_3. The use of a strong base, BuLi, rendered a mixture of two products, 54 and 55, by trapping of the reactive alkyne (Figure 46a).

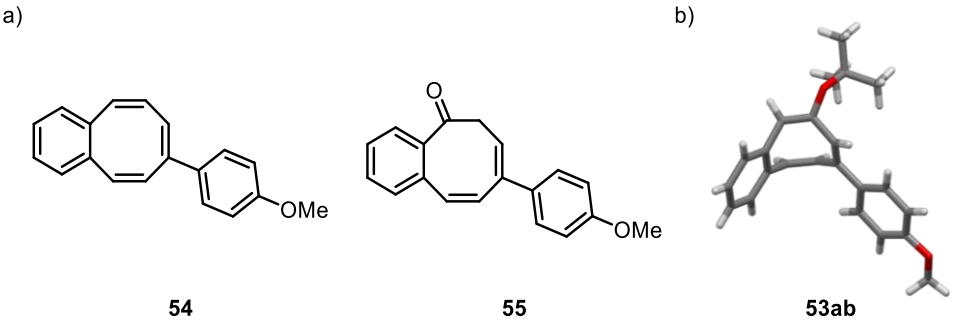


*Figure 46. a) Side product obtained by treatment of brCOT **16ab** with BuLi; b) X-Ray image of alkoxy derivative **53ab***

On changing to the more polar THF, the starting material was fully consumed allowing the isolation of the desired tri[8]annulene 52 in a fairly good 74% yield. The alkoxy derivative 53ab was also isolated in a low 10% yield derived from the nucleophilic trapping of the COTyne intermediate 51 (entry 3). The nature of the last compound was confirmed by X-ray diffraction (Figure 46b). Other non-coordinating solvents like DCM or toluene gave lower conversion and the reaction needed longer reactions times (entry 4). A coordinating aprotic polar solvent as DMF gave decomposition (entry 5). Further optimization using THF as solvent was then examined. With only 1.5 equiv of KO^{t}Bu full conversion of benzofusedCOT was achieved while the side product 53ab was almost supressed (entry 6). To our delight, using a more concentrated solution (0.33M) in only 90 min at the same temperature gave rise to the best isolated yield of 52 (78%) as the only reaction product (entry 7).[229] Finally, different control experiments were evaluated. The presence of the base is mandatory to consume starting material (entry 8), while the absence of Pd source gave to the intriguing new trimer 56ab (entry 9). Interestingly, the use of other metals like Ru, Ni, Rh or Co rendered the same new trimer 56ab, that will be discussed later in another section. Interestingly, the use of catalytic $Pd(PPh_3)_4$ as Pd (0) source furnished the expected mixture of tri[8]annulenes 52, but now containing different regioisomers/conformers in a slightly lower yield (entry 10).

[229] Reactions at higher temperatures gave rise to the formation of important amounts of side product **53**.

The non-symmetric and non-planar nature of starting cyclooctatetraene dictates the formation of a mixture of tri[8]annulenes **52**. From analysis of the possible regioisomers/conformers arise the formation of six possible products. ^{1}H-NMR analysis of two different mixtures from $Pd_2(dba)_3$ and $Pd(PPh_3)_4$ showed the formation of three and four regioisomers/conformers, respectively (Figure 47).

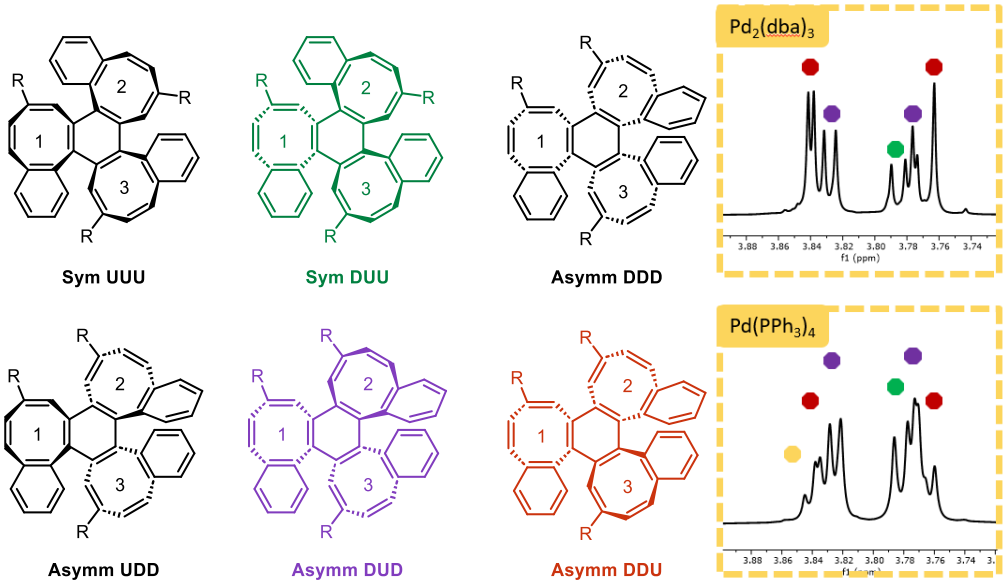


*Figure 47. a) Possible six regioisomers/conformers of benzotri[8]annulene **52** from Pd(0)-catalyzed [2+2+2] cycloaddition of benzoCOT **16ab**. Substituents were omitted for clarity, R = p-OMePh. b) ^{1}H-NMR analysis ($CDCl_3$) of -OMe region of the different regioisomers/conformers of **52** obtained using the two Pd(0) catalysts.*

In order to identify the nature of the isolated regioisomers/conformers of 52, crystallization by slow diffusion of hexane into a solution of **52** (from the reaction of $Pd(PPh_3)_4$) in DCM was performed. Two different crystalline structures were separated and analysed by X-Ray diffraction, corresponding to two regioisomers, the symmetric **DUU** and the asymmetric **DUD**, that show two COT rings placed in different α and β faces (1 and 3), while the second ring is orientated in both left and right sides. Luckily, crystallization in Et_2O of a mixture of **52** from reaction with $Pd_2(dba)_3$ allow us to isolate another asymmetric conformer **DDU,** also confirmed by single-crystal X-Ray diffraction analysis. Pleasingly, conformer **DDU** could be obtained as pure compound after washing the reaction mixture with Et_2O, allowing us to obtain the pure NMR spectra. Unfortunately, all attempts to determine the structure of the lats isolated conformer were unsuccessful.

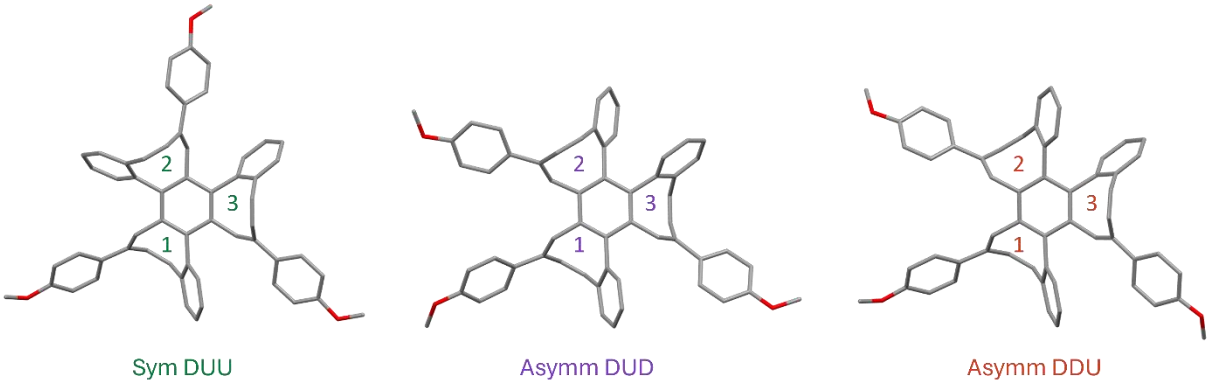


Figure 48. X-Ray structures of tri[8]annulenes ***52.*** *Sym DUU, asymm DUD and asymm DDU conformers* (hydrogen atoms were omitted for clarity).

After identification of three of the four regioisomers/conformers obtained, we decided to explore the selectivity of the Pd(0)-catalysed [2+2+2] cycloaddition. First, NMR analysis of the obtained mixture with $Pd_2(dba)_3$ revealed the presence of two conformers asymm **DUD**, asymm **DDU** and one regioisomer sym **DUU** in a 1/2.6/0.1 ratio (entry 1). With $Pd(PPh_3)_4$ as catalyst, a mixture of 1/2.3/1.3/0.3 ratio was obtained, being the fourth non-isolated conformer the minor one. Trying to modify selectivity different phosphine ligands were evaluated (Table 16).

Entry	Ligand (mol%)	Overall yield (%)	Regioisomers/Conformers α/β/γ/δ
1	-	**52** (78)	1/2.6/0.1
2[b]	$Pd(PPh_3)_4$ instead of $Pd_2(dba)_3$	**52** (77)	1/2.3/1.3/0.3
3	Monodentated type (20)	listed below	-
4	Bidentated type (10)	listed below	-
5	Hemilabile type (20)	listed below	-
6	Alkyl type (20)	listed below	-

Monodentated ligand effect

L1: JohnPhos	80%	1/1.9/0.2
L2: (Cy)JohnPhos	80%	1/1.7/0.3
L3: Xphos	80%	1/2.0/0.3
L4: (^{t}Bu)Xphos	80%	1/1.9/0.3

Bidentated ligand effect

L5: rac-BINAP	-	-
L6: dppf	-	-
L7: Xantphos	-	-
L8: DPEPphos	-	-

Hemilabile ligand effect

L9: DavePhos	71%	1/1.5/0.3
L10: ^{t}BuDavePhos	75%	1/6.1/0.3
L11: Sphos	75%	1/1.1/0.05
L12: (S)-^{t}Bu-Phox	62%	1/2.1/0.65

Alkyl ligand effect

L13: $P(Bu)_3$	60%	1/1.8/0.1
L14: PBu_3	-	-
L15: PMe_3	-	-
L16: PAd_3	83%	1/2.1/0.3

Monodentated ligand effect

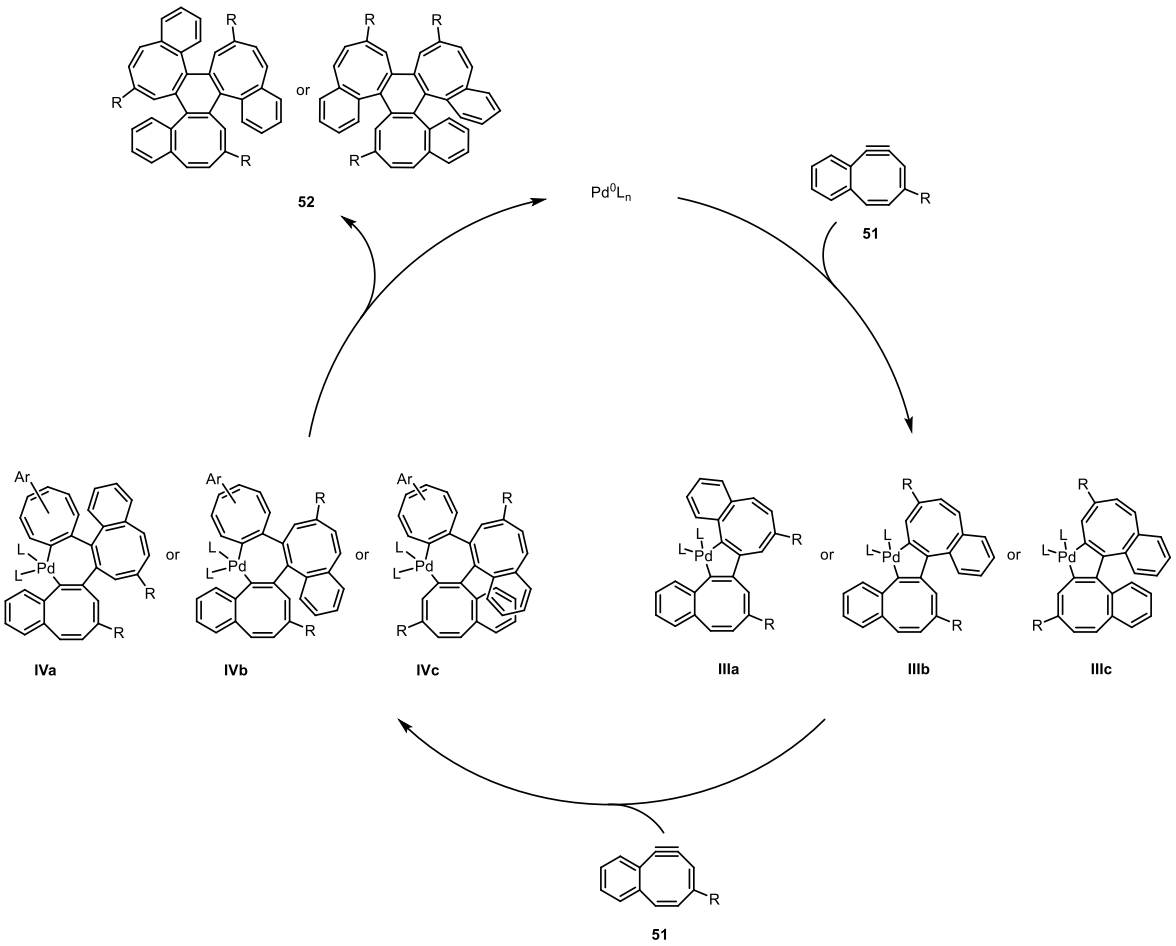
L17: PPh_3	81%	1/2.2/1.2/0.2
L18: $P(4\text{-}OMePh)_3$	70%	1/2.1/0.65/-
L19: $P(4\text{-}FPh)_3$	81%	1/2.3/1.1/0.4
$Pd(PPh_3)_4$	77%	1/2.3/1.3/0.4

Table 16. *Conditions:* ***16ab*** *(0.1 mmol), $Pd_2(dba)_3$ (5 mol%), ligand (x mol%) and KO^{t}Bu (1.5 equiv, previously sublimated) in THF (0.33 M), 90 min at rt. ^{1}H-NMR ratio of conformers b) $Pd(PPh_3)_4$ (10 mol%) c) Metal-free product are also observed, the ratio of the conformers may not be exact due to overlapping of the signals.*

The use of monodentated phosphine ligands (**L1-L4**, entry 3) rendered the formation of the known mixture in excellent yields keeping the same ratio of conformers (1/2/0.3). By contrast, bidentated ligands (**L5**-**L8**) were not effective due, most likely, to the formation of a non-active palladium species (entry 4). A variety of hemilabile phosphine ligands bearing O and N atoms

as potential anchor points were then examined (entry 5). Interestingly, biaryl SPhos **L11** renders quite good yield of a 1:1 mixture of unsymmetrical conformers with just traces of the symmetrical one. Satisfactorily, the use of ^{t}BuDavePhos as ligand (**L10**) favors the formation of asymm **DDU** up to 1/6/0.3 ratio while (S)-^{t}BuPhos (**L12**) favors the sym **DUU** regioisomer up to 1/2.1/0.65. On the other hand, alkyl phosphine ligands did not improve the previous results (entry 6). Linear alkyl phosphines, such as Me and Bu, failed to afford the expected tri[8]annulene **52**, whereas bulkier alkyl phosphines (^{t}Bu or Ad) gave excellent yields but lower selectivity (entry 6). Finally, aryl phosphines (**L17**-**L19**) with different electronic richness in combination with $Pd_2(dba)_3$ were analyzed. Neutral and electron-poor phosphines like PPh_3 or P(4-FPh)$_3$ present the same behavior in terms of yield and regioselectivity than preformed $Pd(PPh_3)_4$ as catalyst. By contrast, electron-rich aryl phosphine, P(4-OMePh)$_3$ slightly increases the formation of the symmetric **DUU** regioisomer as happens with (S)-^{t}BuPhos.

The formation of different conformers/regioisomers could be explained according to the proposed palladium trimerization catalytic cycle. After *in situ* formation of two COTynes (from the corresponding bromo precursors in the presence of KO^{t}Bu) they can act as ligands forming a square planar five-membered palladacycle intermediate. Subsequent insertion of a third alkyne unit and final reductive elimination from the seven-membered palladacycle would afford the observed tri[8]annulenes. Unlike aryne´s trimerization, the non-planar structure and non-symmetric nature of COT **16ab** plays a capital role in this process. All the possible intermediates are depicted in Scheme 64.



*Scheme 64. Mechanistic proposal of Pd(0)-catalysed [2+2+2] cycloaddition of benzofused COTyne **51**. Tub-shaped geometry of starting and final COTs are not considered. Note: intermediates **IVa**, **IVb** and **IVc** are drawn in terms that the third unit of alkyne (Ar) can present the benzene ring in both orientations, close to another benzene unit or close to R group.*

In addition, due to the non-planar COT´s nature six conformer/regioisomers could be formed (see above). The reason why it occurs is detailed in Figure 49. While benzoCOTyne **51** is almost planar (see introduction for more details), once oxidative coupling takes place, COT nature dictates the formation of two different palladacycle intermediates in which both COTs could be located at the same or in different faces (α,β). Due to the relative steric hindrance of monosubstituted COTs rings, a flapping process is allowed and, therefore, the entry of the third alkyne partner is not trivial (insertion on the Pd-C bond with less steric hindrance).

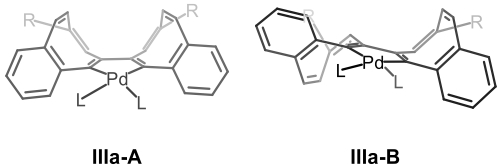


*Figure 49. Illustration of two possible palladacycles of **IIIa** regarding the location of COTs*

6.3.2.2.2. Thermal metal-free conditions

During the optimization process of Pd(0)-catalysed [2+2+2] cycloaddition of brominated benzofused cyclooctatetraenes, a control experiment shed light to the unknown metal-free reactivity of COTynes. The reaction of starting material **16ab** and KO^{t}Bu in THF gave rise to a new trimer (chemical formula $C_{57}H_{42}O_3$) in a quite good 66% yield.[230] NMR analysis showed the formation of three isomers of the new trimer in a 1/0.3/0.1 ratio. Unlike benzotri[8]annulene **52**, whose ^{1}H-NMR signals are located in the range 7.5 - 6.1 ppm, the major isomer of this new trimer **56ab** presents one signal at 4.42 ppm as a doublet with a *J* = 10Hz. In addition, ^{13}C-NMR also reveals two interesting peaks near to OMe region at 61.4 and 50.4 ppm as a quaternary and CH sp^3 carbons, respectively, as judged by ^{13}C-NMR-DEPT analysis (see 7.1.4.5).

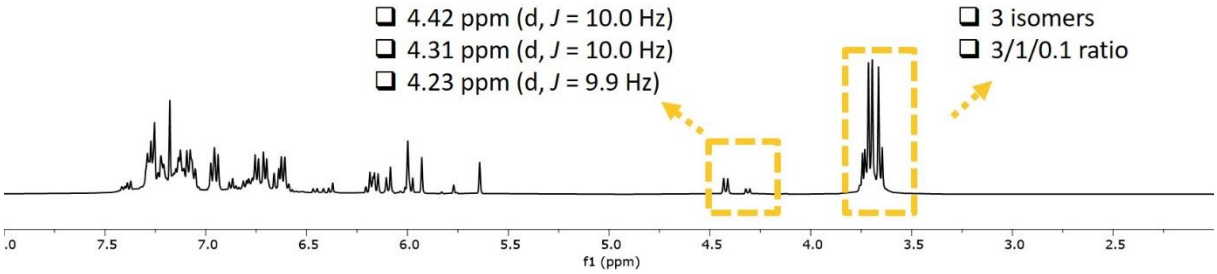
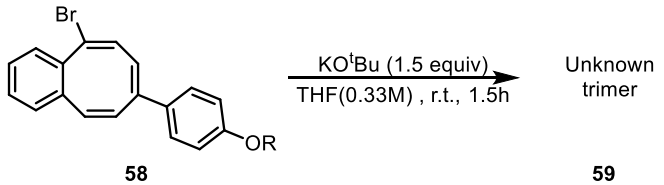


*Figure 50. ^{1}H-NMR spectrum (300 MHz) of unknown new trimer **56ab***

As NMR spectroscopy details that clarify the nature of the new trimer are missing, we proceed to its crystallization to obtain information on its structure. Unfortunately, all attempts gave amorphous solids, probably because of the presence of three isomers that do not allow proper accommodation of the target molecule. The introduction of functional groups that could enhance the crystallization process was then addressed. A variety of functional groups containing NO_2, CF_3 and sulfonyl (SO_2) groups were prepared from the corresponding alcohol **57** (demethylation reaction of **16ab** to phenol **57** occurred in a 70% yield) treated under basic conditions (Table 17). The use of tosyl protected alcohol **58a** furnished the expected trimer in fairly good yield (entry 1). However, the introduction of electron poor sulfonyl groups (entries 2 and 3) afforded starting phenol **57**, most likely due to nucleophilic attack on the sulfonyl group. Hampering this attack by introduction electron rich ^{i}Pr substituent in the aryl ring yielded the target trimer in a good 45% yield (entry 4).



[230] Thermal trimerization of the related planar cyclic alkyne (benzyne) has been suggested but has been questioned Heaney, H. *Chem. Rev*. **1962**, *62*, 81-97.

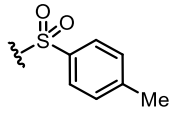
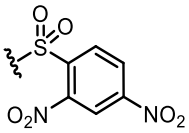
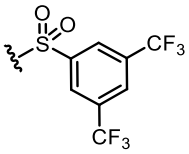
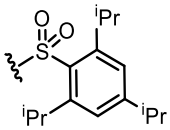
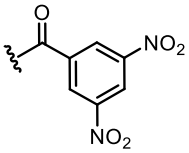
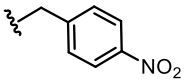
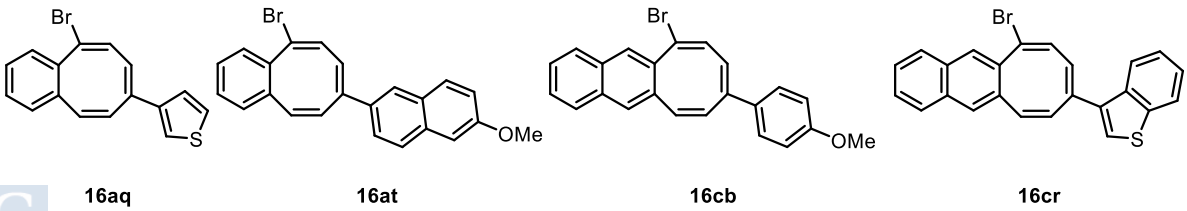
Entry		R	Product (yield)[b]
1	**58a**		**59a** (58%)
2	**58b**		**57** (31%)
3	**58c**		**57** (57%)
4	**58d**		**59d** (45%)
5	**58e**		**57** (76%)
6	**58f**		**57** (50%)
7	**58g**		**58g** (90%)

Table 17*. Conditions:* ***58*** *(0.1 mmol) and KO^{t}Bu (1.5 equiv) in THF (0.33 M), 90 min at r.t. b) Isolated yields.*

As above, other nitrobenzenes (keto and ether derivatives) presented the same behaviour yielding the starting phenol (entries 5 and 6). Finally, the trityl derivative was recovered unaltered under the reaction conditions (entry 7). Unfortunately, all attempts to crystallize the new trimers 59a and 59d failed.

Other brominated benzofused COTs were also tested for the new trimerization under thermal conditions (Figure 51).



16aq **16at** **16cb** **16cr**

Figure 51. Others BrbCOTs tested under thermal conditions

While thiophenyl COT **16aq** and naphthalenyl COT **16at** behave similarly to *p*-OMephenyl COT **16ab** in terms of yield and ratio, naphthalene-COT **16cb** afforded the corresponding trimer in lower yield keeping the same 3/1/0.1 ratio of regioisomers. Unexpectedly, benzothiophenyl COT **16cr** turned out to be unreactive, recovering more than 90% of starting COT. In all of these examples, the corresponding alkoxy derivative **53** (from trapping the alkyne intermediate) was obtained as side product ranging from 15-30% yield. Concurrently, we also tried to derivatize the unknown trimer **56ab** but, unfortunately, any clear product was obtained.

Several techniques to unmask the three regioisomers of mixture **56ab** were also attempted. First of all, various X-ray types like, micro-electron diffraction (MicroED) and X-ray powder diffraction (XRD) were tested. In all cases, good size, well defined borders and laminated appearance crystal were detected when mixture **56** was grown by slow diffusion of a concentrated DCM solution in hexane. Nevertheless, there was no ordered internal structure, observing an amorphous orange solid.

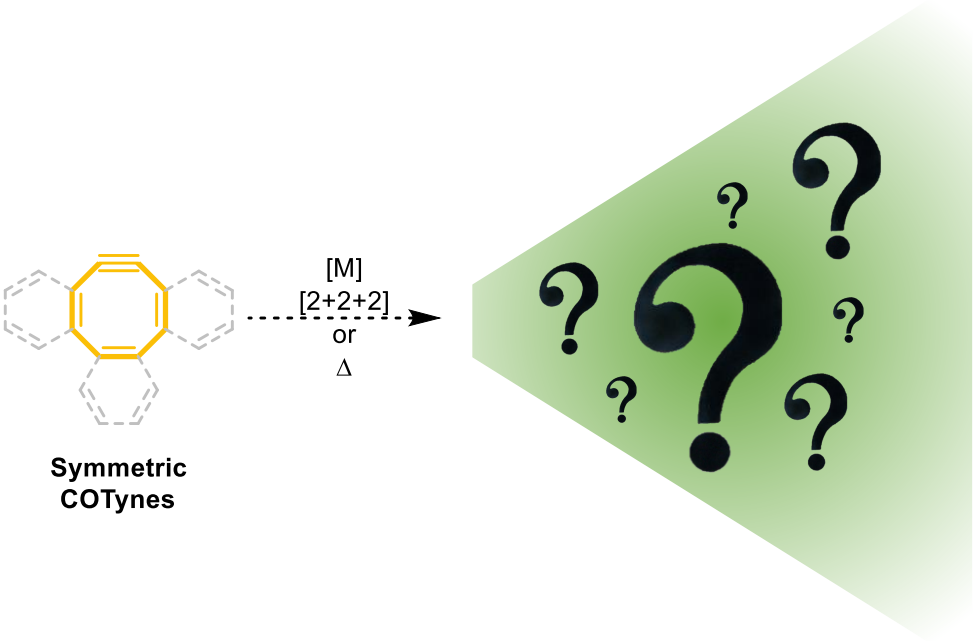
Finally, a variety of chromatography techniques were evaluated. The use of gel permeation chromatography (GPC) shows just one peak, suggesting that all regioisomers present a similar hydrodynamic volume. High-performance liquid chromatography (HPLC) did not furnish any good result among all the tested conditions.

6.3.3. Conclusions

From the results discussed above, the following conclusions may be drawn:

- Brominated benzofusedCOT **16ab** reacts in the presence of KO^tBu to form benzotri[8]annulene **52** in very good yield.
- Among the six possible regioisomers/conformers originated by the asymmetry and tub-shaped geometry of starting benzoCOT **16ab**, only three or four are obtained depending on the Pd (0) catalyst used, (Pd_2dba_3 or $Pd(PPh_3)_4$).
- Three different regioisomers/conformers of **52** were successfully crystallized.
- A variety of phosphine ligands (mono- and bidentated, alkyl or aromatic) were tested in order to increase the selectivity in Pd(0)-catalysed [2+2+2] cycloadditions. Among them, ^{t}BuDavePhos afforded the best selectivity keeping the same reaction yield.
- BenzofusedCOT **16ab** yielded a new cyclotrimer **56** in good yield when the reaction is performed under thermal metal-free conditions.
- Cyclotrimer **56** appears as a mixture of three isomers in a 3/1/0.1 ratio due to the non-symmetric and non-planar nature of starting benzoCOT **16ab**.
- BenzoCOT derivatives of **16ab** were also evaluated under thermal metal-free conditions. Tosylates **58a** and **58d** (sterically hindered sulfonyl derivative) yielded the new trimers **59a** and **59d** in moderate yields.
- Other benzofusedCOTs **16aq**, **16at** and naphthaleneCOT **16cb** gave rise to the corresponding trimers **56** as a mixture in a similar 3/1/0.1 ratio.

Metal-catalysed *vs* thermal trimerizations of symmetric COTynes

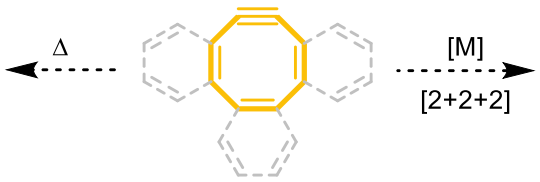


Trimerization of COTyne emerges as a powerful tool for the access to new carbon allotropes with incorporation of antiaromatic eight-membered rings that modify its properties entailing new intriguing applications. Based on the interesting results surged during the study of metal-catalysed cycloaddition of asymmetric benzofusedCOTs, reactivity of the parent COTyne and its benzofused derivatives, tribenzo- and dibenzoCOTynes, will be described along this section.

6.4. Metal-catalysed vs thermal trimerizations of symmetric COTynes

6.4.1. Specific objectives

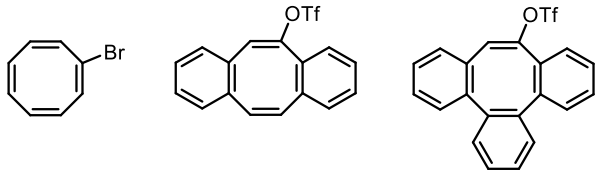
From our previous results on thermal evolution of benzoCOTyne **51** (section 6.3) and the puzzling results described on metal-catalysed trimerization of dibenzo- and tribenzoCOTynes, we decided to explore the behaviour of three symmetric COTynes (parent COTyne, dibenzo- and tribenzoCOTynes) either under metal-catalysed [2+2+2] cycloadditions and metal-free trimerizations. We anticipate that the presence of symmetry in the COTynes should facilitate the analysis of results avoiding the formation of multiple regioisomers and/or conformers.



Symmetric COTynes

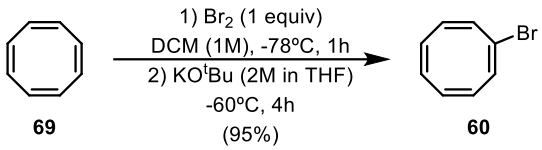
6.4.2. Synthesis of COTynes´s precursors

The bromoCOT **60** and the vinyl triflates of dibenzo- and tribenzoCOTs **67** and **68** were selected as suitable precursors of their corresponding COTynes following published (or adapted) synthetic procedures.



60 **67** **68**

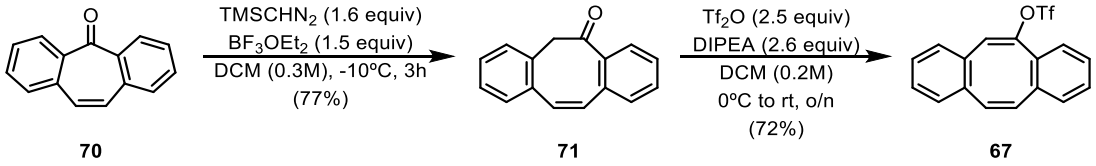
BromoCOT **60** was prepared by a bromination-debromination sequence starting from cyclooctatetraene **69** as starting material. Introduction of molecular bromine followed by treatment of dihalogenated intermediated with KO^{t}Bu rendered the expected brominated COT **60** by formal HBr elimination (Scheme 65).[231]



69 **60**

*Scheme 65. Synthesis of BrCOT **60***

Synthesis of vinyl triflate of dibenzoCOT **67** was carried out in two steps following Wudl´s methodology. First, ring expansion of dibenzosuberenone **70** with trimethylsilyldiazomethane renders the dibenzofusedcyclooctanone **71** in quite good yield, followed by subsequent treatment of **71** with DIPEA and Tf_2O to the triflate precursor **67** in a 55% overall yield (Scheme 66).[187]

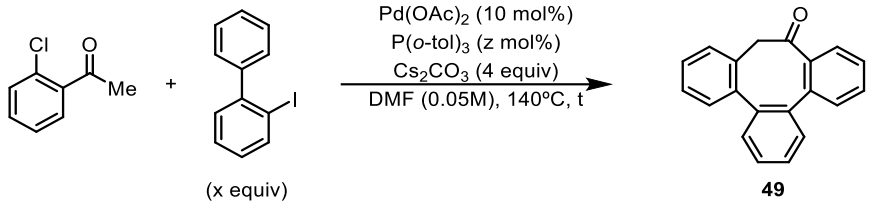


70 **71** **67**

*Scheme 66. Synthesis of vinyl triflate of dibenzoCOT **67***

For the synthesis of vinyl triflate of tribenzoCOT **68**, the straightforward Zhang´s approach to tribenzocyclooctanone **49** from Pd-catalysed cross-coupling of 2-iodobiphenyl with *o*-chloroacetophenone was selected.[232] After optimization of a gram scale process to **49** an efficient conversion to the starting vinyl triflate **68** could be carried out following Wudl´s protocol (Table 18, Scheme 67).[187] The screening carried out to obtain ketone **49** is summarized in the next Table 18.

[231] Blanchard, S. C.; Altman, R.; Warren, J. D.; Zhou, Z. Dye compositions, methods of preparation, conjugated thereof, and methods of use. WO 2013109859, 7/2013.
[232] Zuo, X.; Cheng, C.; Zhang, Y. *Org. Chem. Front*. **2022**, *9*, 4937-4942.



Entry	x equiv	z mol %	Additive (equiv)	t (h)	[M]	Product (yield)[a]
1[b]	1.2	20	-	36	0.05	Decomposition
2	1.5	20	-	36	0.05	Decomposition
3	1.5	40	-	36	0.05	**49** (5%)
4	1.5	40	-	72	0.05	**49** (5%)
5	1.5	20	TBAI (1)	36	0.05	**49** (55%)
6	1.5	20	TBAI (1)	36	0.1	**49** (67%)
7	1.5	20	TBAI (1)	18	0.1	**49** (67%)
8[c]	1.3	20	TBAI (1)	18	0.1	**49** (67%)

***Table 18**. Conditions: 0.2 mmol of* o*-chloroacetophenone; a) isolated yield; b) Zhang´s conditions using 6 cycles of freeze-pump-thaw; c) 3 mmol scale.*

To our initial surprise, Pd-catalysed cross coupling under the reported conditions failed, observing consumption of both starting materials but not affording the target product (entries 1 and 2). Addition of an excess of phosphine ligand (entries 3 and 4) yields poor results of the expected ketone **49** (5% yield) even at longer reactions times. We initially speculate that the presence of molecular oxygen could consume the active Pd(II) species by oxidation to Pd(IV) non-active species. After a careful examination of Zhang´s work, in some cases it was necessary the addition of tetrabutylammonium iodide (TBAI) to achieve the corresponding tribenzocyclooctanone in reasonable yields. Gratifyingly, cross couplings in the presence of the ammonium salt as additive gave rise to the desired ketone **49** in a reasonable 55% yield (entry 5). Further optimization by modification of concentration of the reaction as well as reaction duration raised the yield up to 67% (entries 6 and 7). To our delight, same yield of **49** could be obtained in a scale up process using 3 mmol of *o*-chloroacetophenone and only 1.3 equiv of 2-iodobiphenyl.

Formation of ketone **49** might be explained according to the following catalytic cycle (Figure 52). Initial oxidative addition of 2-iodobiphenyl to Pd(0) species would afford arylpalladium complex **A**. Subsequent ligand exchange promoted by the presence of Cs_2CO_3 furnish complex **B**, which undergoes an intramolecular C-H activation through concerted metalation-deprotonation (CMD) process to render palladacycle **D**. Second oxidative addition of *o*-chloroacetophenone to the transient Pd(II) species would generate the Pd(IV) species **E**. Then, C-C bond formation via reductive elimination and nucleophilic attack of the *in situ* formed ketone enolate takes place to generate intermediate **F**, which undergoes another reductive elimination to yield the observed ketone **49**.

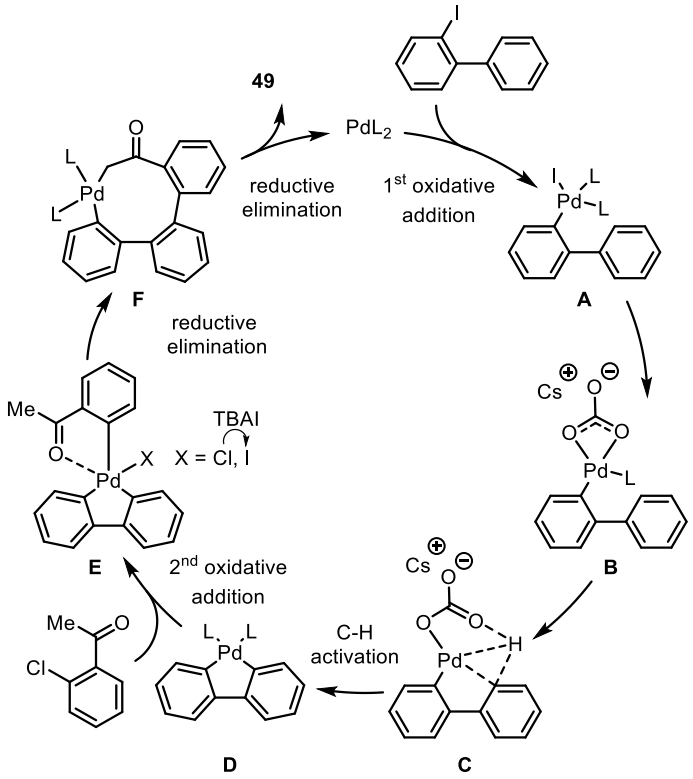
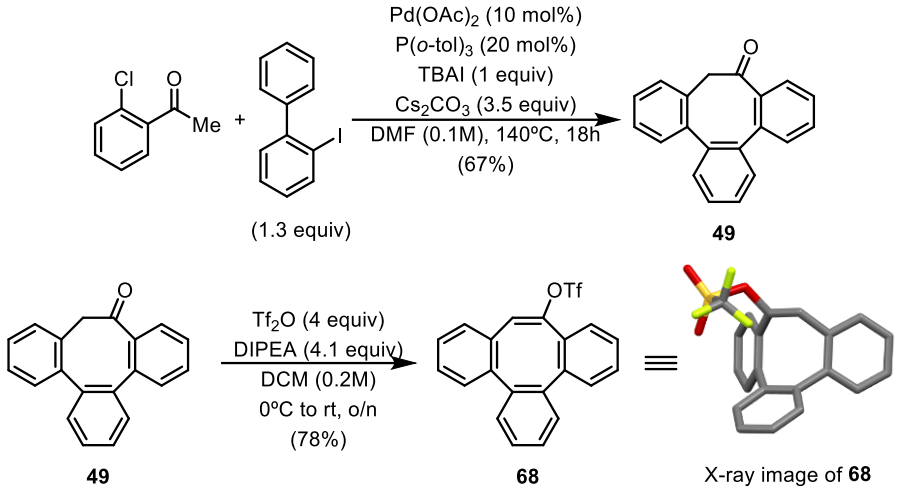


*Figure 52. Proposed mechanism for the synthesis of ketone **49** though Pd-catalysed cross coupling of 2-iodobiphenyl and o-chloroacetophenone*

The TBAI as additive might facilitate the halogen exchange in the Pd(IV) species **E** that would undergo the key enolate attack to form Pd(IV) species **F**.

Then, ketone **49** was smoothy converted into vinyl triflate **68** in 78% yield by treatment with DIPEA and Tf_2O under mild conditions with 10% recovery of starting ketone **49** (Scheme 67). Tub-shaped structure of vinyl triflate **68** could be firmly established by X-ray diffraction analysis.[233]

[233] See 7.1.5.6.1 in Methodology.



*Scheme 67. Synthesis and X-Ray image of vinyl triflate **68***

6.4.3. Metal-catalysed and thermal cycloadditions

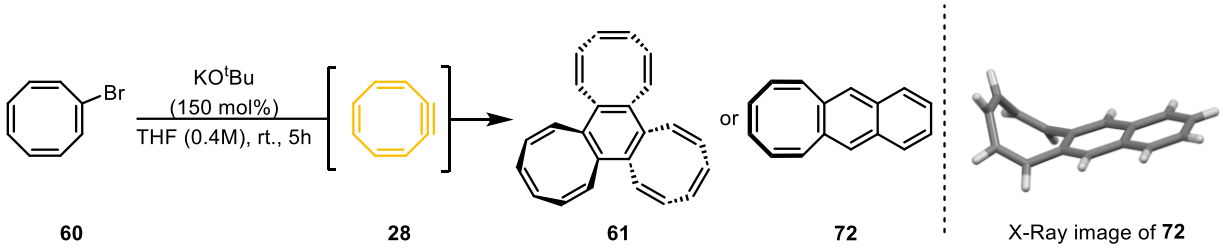
Once prepared the corresponding precursors, formation and reactivity of parent COTyne and symmetrical dibenzo- and tribenzoCOTynes under metal-catalysed and thermal metal-free conditions were explored. At the outset, changes on the geometry of cyclic alkynes (COTynes) from tub-shaped to almost planar due to the absence or presence of benzofused rings might dramatically affect to the course of the reaction.

6.4.3.1. Parent COTyne´s reactivity

Treatment of bromoCOT **60** under the optimized conditions for Pd(0)-catalyzed trimerization of benzoCOTynes **51** (Table 15, entry 7) gave rise to the parent tri[8]annulene **61** with a moderate 33-35% yield using $Pd_2(dba)_3$ or $Pd(PPh_3)_4$ as Pd(0) source (Table 19, entries 1-3). The appearance of nine signals in the ^{1}H-NMR spectrum of **61**, indicative of the presence of one plane of symmetry, led us to assign the α,α,β-conformer structure, where one of the COT cores is bended to the opposite face of the other COTs moieties.

Unluckily, although the formation of this tri[8]annulene was reported by Stevenson in a metal free trimerization of starting bromoCOT **60** in the presence of KO^{t}Bu, we could not compare its spectroscopic data.[208] In fact, we were quite surprised that similar metal free treatment under basic conditions had already been reported by Krebs to give a dimeric product of COTyne intermediate, naphthoCOT **74**, in very low yield instead of the trimeric annulene **61**.[175] To solve these puzzling results on whether dimerization or trimerization of **28** under basic conditions occurs, the bromo compound **60** was subjected to similar conditions obtaining the dimeric naphthoCOT **72** in low yield (Table 19, entry 4), without observing traces of the corresponding tri[8]annulene **61**. On increasing the reaction temperature to 50 ºC (entry 5) led to a lower reaction yield. The nature of naphthoCOT **72** was unambiguously characterized by X-ray diffraction.[234]

[234] See 7.1.5.6.2 in Methodology.



Entry	Catalyst (x mol%)	Variations	Product (yield)[b]
1	$Pd_2(dba)_3$ (5)	-	**61** (33%)
2	$Pd_2(dba)_3$ (5)	0.33M	**61** (33%)
3	$Pd(PPh_3)_4$ (10)	-	**61** (35%)
4	-	-	**72** (20%)
5	-	50 °C	**72** (12%)

***Table 19**. Conditions: **60** (0.2 mmol) and KO^{t}Bu (1.5 equiv) in THF (0.4 M), 4h at rt. b) Isolated yields.*

Formation of **72** could be rationalized by a series of consecutive pericyclic reactions of a transient diene partner with an *in situ* formed COTyne **28**. The diene partner, a bicyclo[4.2.0]tetraene, might be formed via 6e$^-$π-electrocyclic ring closure of starting bromoCOT followed by dehydrobromination. This intermediate species would then undergo a [4+2] cycloaddition with a COTyne followed by a final 4e$^-$π-electrocyclic ring opening to afford the observed naphthoCOT **72** (Figure 53).

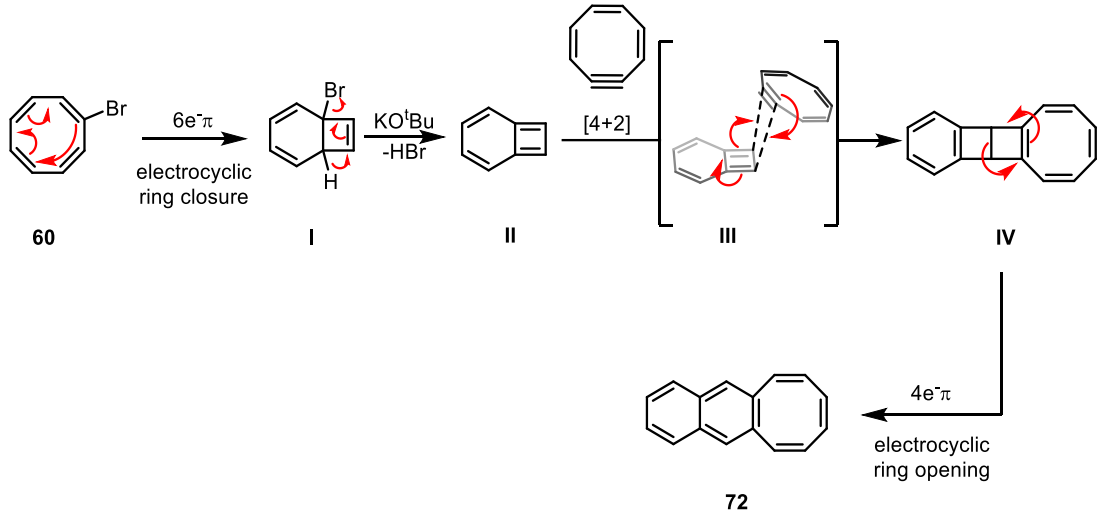


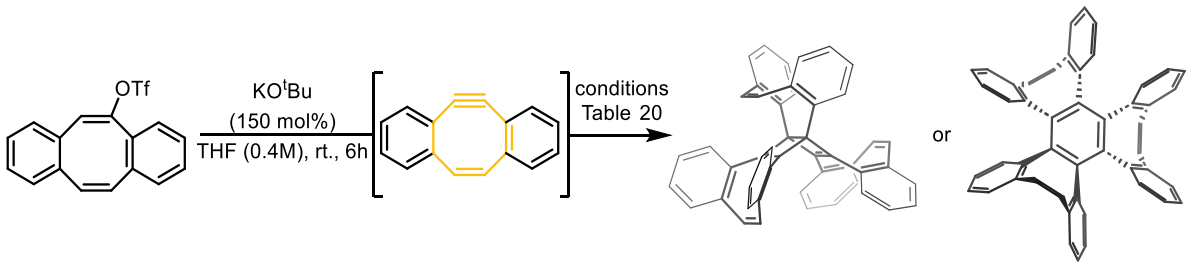
*Figure 53. Proposed mechanism for the formation of naphthoCOT **72***

6.4.3.2. DibenzoCOTyne´s reactivity

Following the same methodology, treatment of vinyl triflate **67** under similar Pd(0)-catalysed [2+2+2] conditions afforded the dibenzotri[8]annulene **63** in a low 25% yield (Table 20, entries 1 and 2), which seems to confirm that the more stabilized dibenzoCOTyne intermediate is less reactive than the benzoCOTyne (see Table 15).

The structure of **63** was confirmed by NMR analysis; in fact, X-ray structure of α,α,β-conformer of dibenzotri[8]annulene **63** had already been reported by Nuckolls in a Ru(II)-catalysed trimerization of preformed dibenzoCOTyne **30** (61% yield, DCM) but the NMR spectra were missing.[209] From our results, the appearance of 15 signals in ^{1}H-NMR and 24 in ^{13}C-NMR, 9 of them as quaternary carbons, confirm the same α,α,β disposition (one plane of symmetry is present) as the one previously reported.

Unexpectedly, on performing the reaction of vinyl triflate precursor **67** in the presence of $[CpRu(CH_3CN)_3]PF_6$ as catalyst gave moderate yields of either the Dewar benzene **62** (44%) or the ketone **71** (40%) when THF is replaced by DCM (entries 3 and 4). This last product **62** had already been observed by Nuckolls when the preformed dibenzoCOTyne **30** was reacted in the presence of 2nd generation Grubb´s or $[CpRu(CH_3CN)_3]PF_6$ catalyst (traces and 14% yield in DCM, respectively).[209] Surprisingly, in a control experiment in the absence of metal catalyst, treatment of vinyl triflate **67** under basic conditions at rt yielded the Dewar benzene **62** in 60% yield (entry 5), which opens an alternative thermal metal-free route to this product. Control-temperature experiments where then performed. On decreasing the reaction temperature to 0 °C allowed us to isolate the intermediate dibenzoCOTyne **30** in a low 20% yield (entry 6). By contrast, on heating up the reaction mixture to 50 °C rendered a 70% overall yield of a mixture of Dewar benzene **62** and ketone **71** in a 3-1 ratio (entry 7).



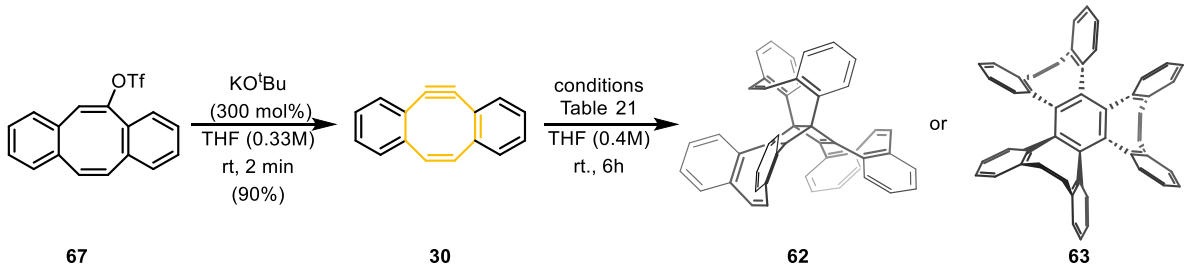
67 **30** **62** **63**

Entry	Catalyst (x mol%)	Variations	Product (yield)[b]
1	$Pd_2(dba)_3$ (5)	0.33M	**63** (24%)
2	$Pd_2(dba)_3$ (5)	-	**63** (25%)
3	$[(C_P)Ru(CH_3CN)_3]PF_6$ (10)	-	**62** (44%)
4	$[(C_P)Ru(CH_3CN)_3]PF_6$ (10)	DCM	**71** (40%)
5	-	-	**62** (60%)
6	-	0 °C	**30** (20%) + **62** (35%)
7	-	50 °C	**62** + **71** (70%)[c]

***Table 20**. Conditions: **67** (0.2 mmol) and KO^{t}Bu (1.5 equiv) in THF (0.4 M), 6h at rt. b) Isolated yields; c) **62/71** 3:1 ratio*

Aimed by these results, we proceeded to study the behaviour of preformed COTyne (Table 21). Thus, treatment of vinyl triflate **67** with an excess of KO^{t}Bu (3 equiv) in THF during 2 min followed by a fast work-up and purification yielded the expected dibenzoCOTyne **30** in an

excellent 90% yield.[235] Somewhat unexpectedly, a solution of this species in THF led to the formation of Dewar benzene **62** albeit in a rather low 17% yield (Table 21, entry 1). By contrast, a solution of **30** in DCM led to a complex mixture (entry 2). However, the Pd(0)-catalysed trimerization of **30** afforded dibenzotri[8]annulene **63** with better yield (40%) than the reported using vinyl triflate **67** as starting material (Table 21, entry 3 vs Table 20, entry 2), showing that coordination of an alkyne as ligand to Pd is essential to form an efficient trimerization. In the case of Ru(II)-catalysed [2+2+2] cycloaddition, the use of preformed alkynes is required for a successful trimerization. When dibenzoCOTyne **30** is subjected to Nuckoll´s conditions,[209] the tri[8]annulene **63** is formed in 30% yield as a major product being the Dewar benzene **62** (13% yield) a minority product (Table 21, entry 4). We also checked the influence of the electronic richness and steric bulkiness of the ligands on the Ru centre. Thus, performing the reaction with $[(Cp^*)Ru(CH_3CN)_3]PF_6$ as catalyst the ratio of products found is inverted being annulene **63** the minor product (8% yield) and Dewar benzene **62** (33% yield) the major product (Table 21, entry 5). As the overall yield of the reaction is almost maintained (entries 4 and 5), it is assumed that the steric hindrance over the Ru centre is, most likely, the main reason for this behaviour. Furthermore, the use of neutral Cp*RuCl(cod) as catalyst completely shuts down the formation of cyclotrimer **63** being only present the Dewar benzene **62** (Table 21, entry 6). Most likely, the absence of a vacant coordination of the Ru centre prevents the trimerization event to **63** making only available the thermal process.



67 **30** **62** **63**

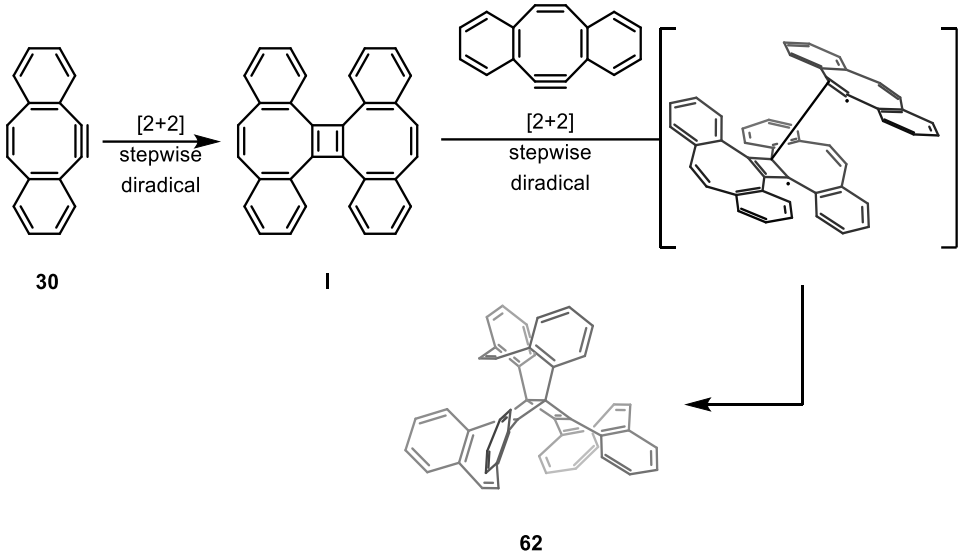
Entry	Catalyst (x mol%)	Variation	Product (yield)[b]
1	-	-	**62** (17%)
2	-	DCM	CM
3	$Pd_2(dba)_3$ (5)	-	**63** (40%)
4	$[(Cp^*)Ru(CH_3CN)_3]PF_6$ (10)	DCM	**62** (13%) + **63** (30%)
5	$[(Cp^*)Ru(CH_3CN)_3]PF_6$ (10)	DCM	**62** (33%) + **63** (8%)
6	Cp*RuCl(cod) (10)	DCM	**62** (52%)

Table 21. *Conditions:* ***30*** *(0.2 mmol) in THF (0.4 M), 6h at rt. b) Isolated yields; CM = complex mixture*

Regarding the thermal process of formation of Dewar benzene **62** from either dibenzoCOTyne **30** or from the vinyl triflate precursor **67**, comparison of our results with the known experimental and DFT calculations of dimerization[236] and thermal cyclotrimerization of substituted linear alkynes was performed.[237] On the basis of these calculations, the process

[235] See 7.1.5.1.3 in Methodology.
[236] Fabig, S.; Haberhauer, G.; Gleiter, R. *J. Am. Chem. Soc*. **2015**, *137*, 1833−1843.
[237] Yao, Z-K.; Yu, Z-X. *J. Am. Chem. Soc*. **2011**, *133*, 10864–10877.

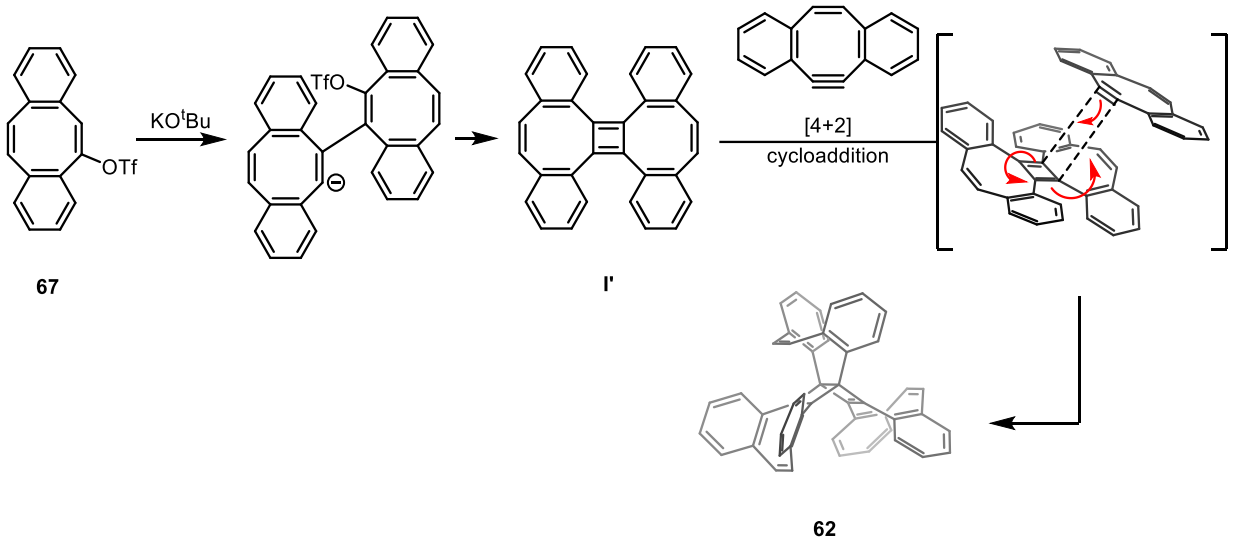
could involve an initial formation of a cyclobutadiene by a stepwise diradical [2+2] cycloaddition of two cyclic dibenzoCOTyne units. This cyclobutadiene intermediate **I** would then undergo a stepwise diradical [2+2] cycloaddition with another dibenzoCOTyne **30** to give the final Dewar benzene **62**. For sterical reasons due to the congested cyclic nature of the dibenzoCOTyne, this Dewar benzene **62** could not undergo the typical ring opening to the corresponding benzene derivative (Scheme 68).



*Scheme 68. Stepwise diradical trimerization of preformed dibenzoCOTyne **30** to Dewar benzene **62***

It really catched our attention that the formation of Dewar benzene **62** was favoured from dibenzoCOTyne **30** prepared *in situ* (Table 20, entry 5) vs the preformed one (Table 21, entry 1), that prompted us to analyse an alternative course of the trimerization process. Besides the above mechanistic rationale from the preformed dibenzoCOTyne, it would be also plausible that the cyclobutadiene isomer **I'** could arise directly from the starting vinyl triflate **67** under basic conditions. Both isomers are readily interconvertible through a relatively low energetic barrier.[238] Trapping of this isomer **I'** in a [4+2] cycloaddition with dibenzoCOTyne **30** would directly afford the observed Dewar benzene **62** (Scheme 69).

[238] Gellini, C.; Salvi, P. R. *Symmetry* **2010**, *2*, 1846-1924.



*Scheme 69. Mechanistic hypothesis for the formation of Dewar benzene **62** from vinyltriflate **67***

*From the results of thermal metal-free reaction with the symmetric dibenzoCOTyne **30**, we could assume that in the case of asymmetric benzoCOTyne **16ab** (6.3.2.2.2), formation of a mixture of three inseparable Dewar benzenes **56a**, **56b** and **56c** due to the non-symmetrical nature of the starting cyclic alkyne and the diradical nature of the cycloadditions involved. As mentioned in section 6.3.2.2.2, the M^+ in the MS spectra corresponds to a Dewar benzene, however, it could not be interpreted by ^1H and ^{13}C-NMR spectra.*

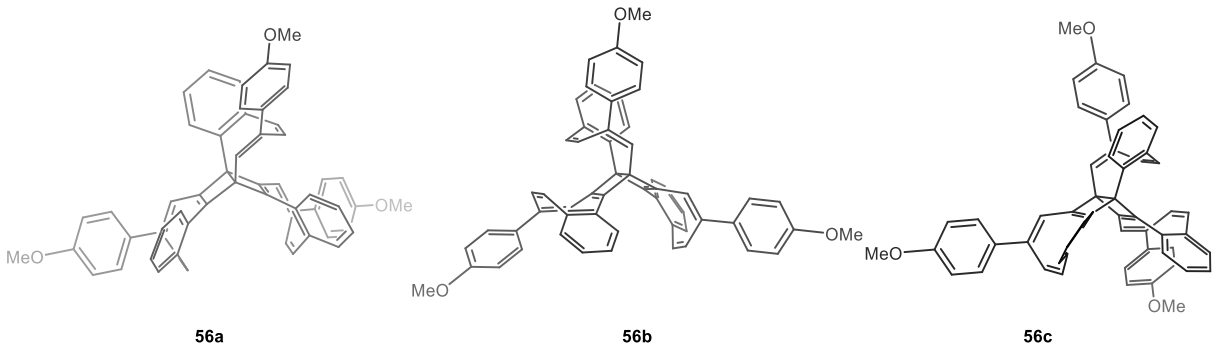


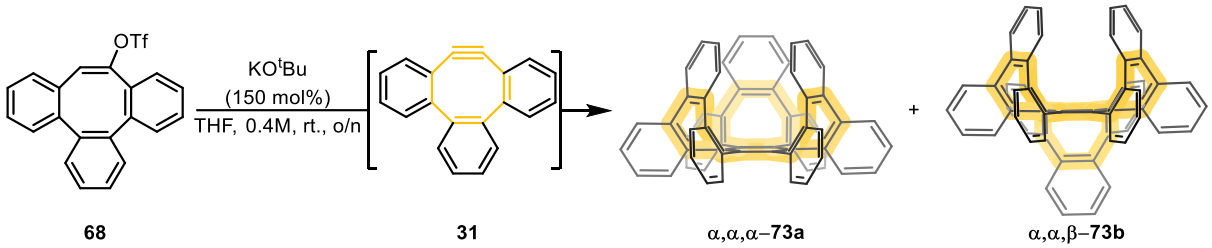
Figure 54. Expected mixture of Dewar benzenes **56** obtained from benzoCOTyne **16ab**

6.4.3.3. TribenzoCOTyne´s reactivity

To complete the study of COTynes´s family, the behaviour of tribenzoCOT triflate **68** under metal catalysis and thermal metal-free conditions was analysed. We were aware that in the case of metal-catalysed trimerizations of phenanthrene-dibenzoCOTyne reported by Müllen,[210] the use of Pd or Ru catalysts was capital to form the less crowed Cs symmetric (α,α,β)-tri[8]annulene conformer or the (α,α,α)-conformer, respectively, where the COT rings all point toward the same side of the central benzene ring (see Scheme 48).

The initial Pd(0)-catalysed trimerization of tribenzoCOTyne **31** was carried out under the conditions described for dibenzoCOTyne **30** trimerization (Table 20) giving rise to a mixture of two isomers of tribenzotri[8]annulene **73** in 33% overall yield and 5:1 ratio (Table 22, entry 1).

To our initial surprise, when the Pd(0) source was changed from $Pd_2(dba)_3$ to $Pd(PPh_3)_4$, the overall yield and ratio of isomers were both affected, obtaining a lower yield and 1:1 ratio of isomers as judged by NMR (Table 22, entry 2).



Entry	Catalyst (mol%)	Variation	Product (yield)[b]
1	$Pd_2(dba)_3$ (5)	-	**73** (33%) (5:1 mixture)
2	$Pd(PPh_3)_4$ (10)	-	**73** (20%) (1:1 mixture)
3	$[(C_P^*)Ru(CH_3CN)_3]PF_6$ (10)	-	**73** (35%) (5:1 mixture)
4	$[(C_P^*)Ru(CH_3CN)_3]PF_6$ (10)	DCM	**73** (34%) (5:1 mixture)
5	-	-	**73** (34%) (5:1 mixture)

***Table 22**. Conditions: **68** (0.4 mmol) in THF (0.4 M), sublimated KO^{t}Bu (1.5 equiv) before use, o/n at rt. b) Isolated yields.*

Even further surprise, reaction preformed with $[Cp^*Ru(CH_3CN)_3]PF_6$ as catalyst afforded similar results than $Pd_2(dba)_3$ in terms of yield and selectivity (entries 3 and 4). These identical results obtained with two different metals catalyst (Pd(0), square planar and Ru(II), tetrahedral geometry) led us to carry out a control test under thermal conditions without a catalyst, as its role in the reaction was not clear enough. Strikingly, the cyclotrimerization reaction of tribenzoCOT **68** at rt gave rise again to the same ratio of isomers (5:1) and overall yield (34%, entry 5). These latter result firmly suggest that the cyclotrimerization of tribenzoCOTyne **31** occurs thermally at room temperature and that metal catalyst doesn´t play any significative role in the course of the reaction (except under conditions of entry 2).

Single crystal X-ray analysis of the major isomer, grown from a solution of **73** in DCM by slow diffusion in hexane, unambiguously confirmed the formation of the (α,α,α)-conformer of tribenzo[8]annulene **73** consisting of three boat-shaped COT moieties bended to the same face of central benzene ring (see Figure 56).[239] ^{1}H-NMR and ^{13}C-NMR spectra of diffracted crystals showed the appearance of only six and ten signals, respectively, confirming the C3 symmetry of the conformer (Figure 55).

To our delight, it was possible to separate and purify the major isomer **73a** from the mixture of tribenzo[8]annulenes **73** by just washing the crude mixture with hexane.

[239] See 7.1.5.6.3 in Methodology.

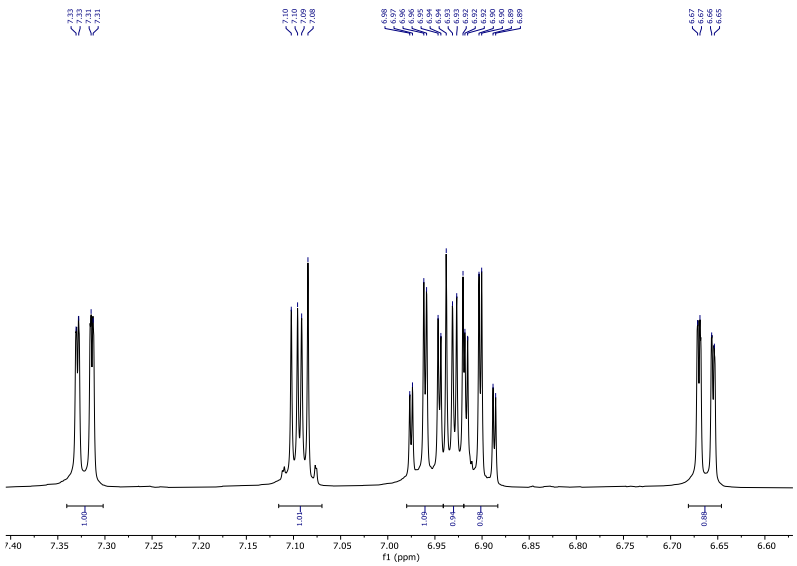


*Figure 55. Aromatic region of ^{1}H NMR spectrum (500 MHz) of ($\alpha\alpha\alpha$)-conformer **73a** in CD_2Cl_2*

In order to shine light on the above results, we proceeded to carry out a broader study of reaction conditions (Table 23), starting with the evaluation of thermal metal-free conditions.

Entry	Solvent	[M]	T (°C)	Product (yield)[b]	**73a** (yield)[c]
1	THF	0.4	rt	**73** (34%) (5:1 mixture)	(28%)
2	THF	0.04	rt	**73** (31%) (20:1 mixture)	(29%)
3	THF	0.04	80[d]	**73** (32%) (20:1 mixture)	(26%)
4	THF	0.04	4	**73** (36%) (20:1 mixture)	(32%)
5	Et_2O	0.04	4	**73** (38%) (20:1 mixture)	(28%)
6	1,2-dioxane	0.04	4	**73** (40%) (20:1 mixture)	(30%)
7[e]	THF	0.04	4	-	(15%)

***Table 23**. Conditions: **68** (0.4 mmol) in solvent (x M), o/n, sublimated KO^{t}Bu before use; b) isolated yield of chromatographic mixture; c) yield of **73a** after hexane washing the chromatographic mixture; d) The alkoxy derivative from nucleophilic attack to tribenzoCOTyne is the major compound observed; e) slow addition of base (1M solution) in THF during 30 min.*

Concentration of the reaction did not significatively affect to the overall yield, although the amount of the major (α,α,α)-conformer **73a** raised to 20:1 ratio (Table 23, entries 1 and 2). Temperature control experiments showed a slightly increase of reaction yield when is performed at 4°C in a cold room; by contrast, at higher temperatures is favoured the alkoxy derivative **48** from the nucleophilic addition to the tribenzoCOTyne intermediate (entries 3 and 4).[179b] Reaction performed in other ethereal solvents (Et_2O and 1,4-dioxane) gave slightly better reaction yields but, unfortunately, with traces of multiple products in the same fraction, that after the corresponding purification led to similar yield of pure **73a** (entries 5 and 6). Unexpectedly, slowly generation of the alkyne intermediate by adding KO^{t}Bu dropwise gave poor results (entry 7).

Following the results found in Table 22, we further evaluate the reaction course in the presence of a metal catalyst starting with Ru(II) catalysts (Table 24).

Entry	Catalyst (x mol%)	[M]	T (°C)	Product (yield)[b]	**73a** (yield)[c]
1	$[(C_P^*)Ru(CH_3CN)_3]PF_6$ (10)	0.4	rt	**73** (34%) (5:1 mixture)[d]	nd
2	$[(C_P^*)Ru(CH_3CN)_3]PF_6$ (10)	0.04	rt	**73** (42%) (5: 1 mixture)[d]	29%
3	$[(C_P)Ru(CH_3CN)_3]PF_6$ (10)	0.04	rt	**73** (39%) (5: 1 mixture)[d]	20%
4	C_P*Ru(cod)Cl (10)	0.04	rt	**73** (48%) (5: 1 mixture)[d]	28%
5	$[(C_P^*)Ru(CH_3CN)_3]PF_6$ (10)	0.04	60	-	22%
6	$[(C_P)Ru(CH_3CN)_3]PF_6$ (10)	0.04	60	**73** (40%) (5: 1 mixture)[d]	21%
7	C_P*Ru(cod)Cl (10)	0.04	60	**73** (37%) (4: 1 mixture)[d]	29%

***Table 24**. Conditions: **68** (0.4 mmol) in DCM, o/n, sublimated KO^{t}Bu before use; b) isolated yield of chromatographic mixture; c) yield of **73a** after hexane washing the chromatographic mixture; d) Minor amounts of starting ketone **49** are present as impurities; nd = not determined*

As somewhat expected, a change in concentration reaction did not affect to the yield and ratio of products (entries 1 and 2). On changing the catalyst to the less electron rich/bulkier Cp ligand lower amount of pure 73a was isolated (entry 3). When the neutral Cp*Ru(cod)Cl catalyst was used a higher reaction yield was obtained but, after washing with hexane, led to the similar amounts of pure 73a (entry 4).[240] A temperature reaction control was then undertaken with the same catalysts (entries 5 to 7) without significant variations of the reaction course. In sum, our initial hypothesis that Ru catalysts are not playing any significative role during formation of 73a/73b were confirmed.

Next, a similar evaluation using Pd(0) catalysts is reflected in Table 25.

Entry	Catalyst (x mol%)	Solvent	T (°C)	Product (yield)[b]
1[c]	$Pd_2(dba)_3$ (5)	THF	rt	**73** (35%) (5: 1 mixture)
2	$Pd_2(dba)_3$ (5)	THF	rt	**73** (37%) (5: 1 mixture)
3[d]	$Pd_2(dba)_3$ (5)	Toluene	120	**73** (37%) (1: 1 mixture)
4	$Pd_2(dba)_3$ (10) + PPh_3 (20)	Toluene	120	**73** (36%) (1: 1 mixture)
5[c]	$Pd(PPh_3)_4$ (10)	THF	rt	**73** (20%) (1:1 mixture)
6	$Pd(PPh_3)_4$ (10)	THF	rt	**73** (33%) (1:1 mixture)
7	$Pd(PPh_3)_4$ (10)	Toluene	120	**73** (25%) (1:3 mixture)
8[e]	$Pd(PPh_3)_4$ (10)	Toluene	120	**73** (28%) (1:3 mixture)

***Table 25.** Conditions: **68** (0.4 mmol) in solvent (0.04M), o/n, sublimated KO^{t}Bu before use; b) isolated yield of chromatographic mixture; c) 0.4M; d) longer reaction times led to the formation of side products; e) 1 mmol scale; nd = not determined*

As already mentioned in Table 22, reactions performed with $Pd_2(dba)_3$ or $Pd(PPh_3)_4$ as catalysts render different results. While the first one practically affords similar results to a thermal metal-free mixture in a 5:1 ratio (Table 25, entries 1 and 2), in the presence of

[240] NMR analysis of the liquor mothers showed the presence of starting ketone as well as traces of another unknown products as contaminants.

$Pd(PPh_3)_4$ as catalyst the amount of the second isomer increases up to a 1:1 ratio (entries 5 and 6). Having in mind the work reported by Müllen[210] in which the reaction with $Pd(dba)_2$ as catalyst in refluxing toluene afforded selectively the αaβ-conformer, we decided to test similar conditions with tribenzoCOTyne (entry 3). Intriguingly, total selectivity of the reaction towards the second αaβ-conformer **73b** was not observed, but 1:1 mixture was obtained (37% yield), which means that temperature affects to the evolution of the putative palladacycle intermediate (Table 22, entry 1 vs Table 25, entry 3). Addition of PPh_3 ligand to the reaction mixture seemed not affect to the yield and ratio of isomers found (entry 4). Gratifyingly, when the reaction was performed at 120 °C using $Pd(PPh_3)_4$ as catalyst, slightly lower overall yield was obtained but the amount of the desired αaβ-conformer could be increased up to 1:3 ratio (entries 7 and 8).

Gratifyingly, after elaboration and chromatographic purification of this last mixture (entry 8), crystallization of a DCM-hexane solution smoothly occurred with the appearance of two apparent shape-different nuclei of crystallization. After "Pasteur-like" differentiation and careful examination by ^{1}H-NMR of the nature of the conformer present, X-Ray crystal diffraction confirmed the isolation of the αaβ-conformer **73b** (Figure 56).

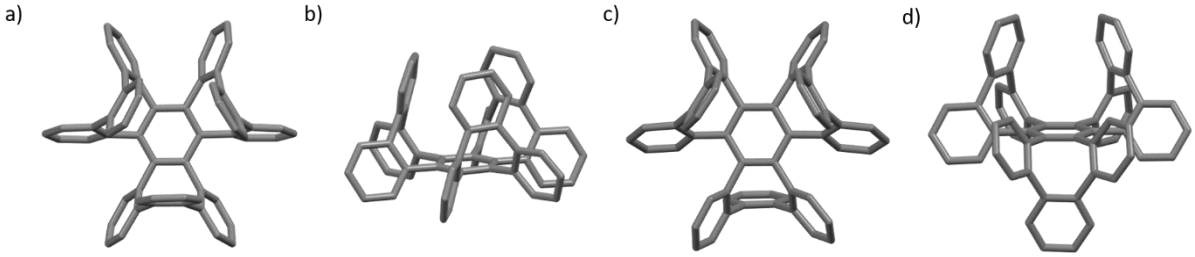


*Figure 56. Top view of the single crystal X-ray structure of **73a** (a) and **73b** (c). Top view, illustrating cavity within **73a** (b) and saddle-shaped **73b** (d). H atoms were omitted for clarity.*

The spatial arrangement of the terphenyl units of both conformers was compared by X-Ray analysis. While a nearly perpendicular arrangement is observed in the ααα-conformer of **73a** with an average dihedral angle (Φ) of 3 degrees, an alternative arrangement is observed with dihedral angles (Φ) of 0.79 for the symmetrical unit and 40.70 degrees for the asymmetric one are observed in the αaβ-conformer **73b** (Figure 57). Therefore, the ααα-conformer **73a** could be considered an ideal monomer for polymerization to cubic graphite in which the *p*-phenyl moieties are arranged in a perpendicular disposition.[241]

[241] Berresheim, A. J.; Müller, M.; Müllen, K. *Chem. Rev.* **1999**, *99*, 1747-1786.

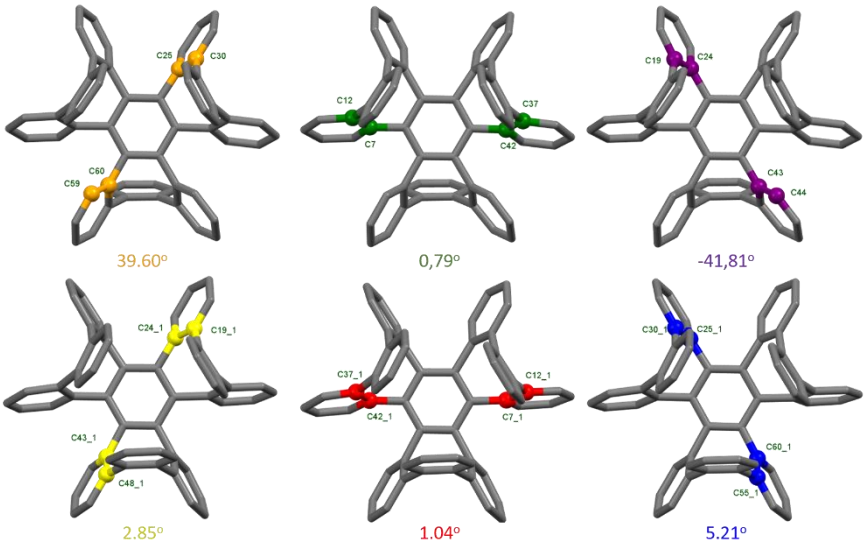


*Figure 57. Dihedral angles (Φ) of three terphenyls units presents in ααβ-conformer **73b** (top) and ααα-conformer **73a** (down)*

In solution, ^{1}H-NMR of **73b** shows the presence pf 18 protons as well as in ^{13}C-NMR 18 C-H signals and 12 quaternary centers are present (Figure 58), confirming the plane of symmetry of the molecule.

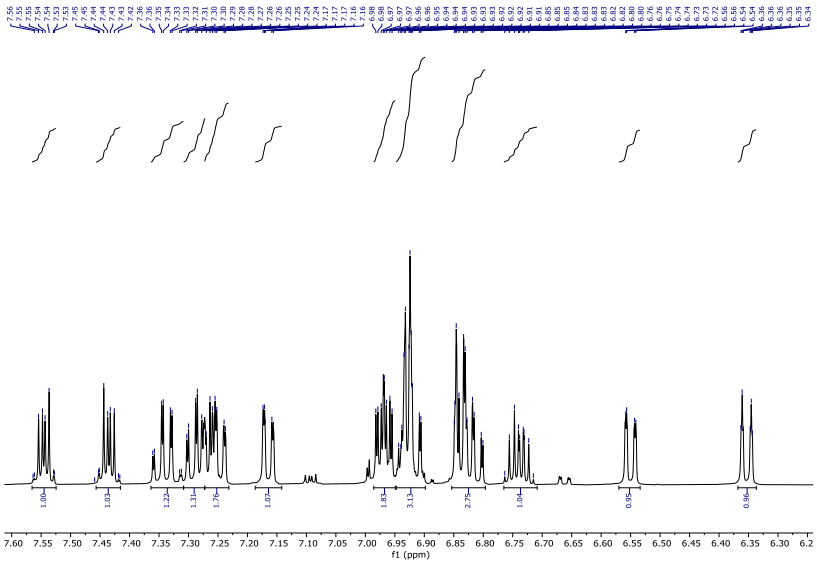


*Figure 58. Aromatic region of the ^{1}H NMR spectra of ααβ-conformer **73b** (500 MHz) in CD_2Cl_2. Traces of ααα-conformer are present at 6.65 and 7.10 ppm*

From the results in Tables 22-25 we can assume that the ααα-conformer **73a** is mainly formed by a thermal process while the ααβ-conformer **73b** is mainly produced by Pd(0)-catalysed cyclotrimerization ($Pd(PPh_3)_4$). Regarding this last process, it would seem that tribenzoCOTyne **31** act as a ligand on Pd. Depending on the nature of the source of Pd (0), Pd_2dba_3 or $Pd(PPh_3)_4$, and temperature the evolution is different (Table 22, entries 1 and 2). Thus, at rt the soft ligand dba and COTyne dissociate easily from the Pd coordination sphere and a thermal metal-free process would occur (Table 22, entry 1). In the presence of a Pd(0) complex with a strong PPh_3 ligand competition between the thermal process and metal-

catalysed occurs to give 1:1 mixture of conformers (Table 22, entry 2). Heating is also a crucial factor since even with soft dba as ligand or in the presence of added phosphine the amount of ααβ-conformer **73b** increases (Table 22 entry 1 *vs* Table 25, entries 3 and 4). The effect is even more pronounced with the preformed phosphine complex $Pd(PPh_3)_4$ since the amount of the ααβ-conformer **73b** is greater than that of the other isomer (Table 25, entries 7 and 8)).

The ααβ-conformer must probably be derived from the palladacycle intermediate **A** in which the two first units of COTyne **31** are orientated on opposite faces of the planar palladacycle, with the complex being more energetically favourable (less steric crowding). The phosphine ligand probably helps to stabilize such complex and facilitates the third coordination and insertion of COTyne into the Pd-C bond that avoids the steric clash between the ligands (Figure 59).

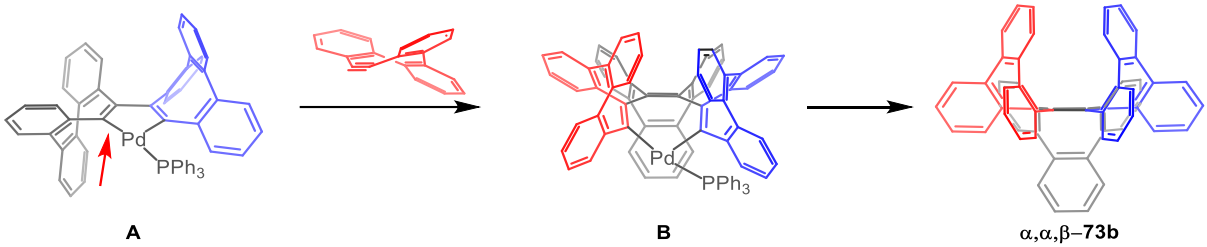


Figure 59. Illustration of two possible palladacycles on the path to ααβ-conformer ***73b***

From the results in Table 24, it would appear that the influence of the Cp*Ru or CpRu catalyst on the course of the reaction is almost negligible (entries 1-4) with the observed results being derived from a predominant thermal process.

Regarding the thermal metal-free process for the formation of ααα-conformer **73a,** preliminary DFT computational studies were carried out showing an exergonic process. Based on these calculations, the process could involve an initial formation of tribenzoCOTyne **31**, a perpendicular radical-radical bond formation could provide intermediate **I**. Subsequent trapping of another COTyne unit would give rise to linear diradical species **II**. The latter COTyne is then rotated to facilitate radical-radical scavenging to form a cyclopentadiene intermediate which, through a carbene species, yields the biscyclopropane **III** intermediate. Finally, opening of one of the cyclopropane units gives the final observed aromatic annulene **73a** (Figure 60).

Alternative formation of a cyclobutadiene ring by a stepwise diradical [2+2] cycloaddition of two cyclic alkynes units as well as a direct [4+2] cycloaddition of the formed cyclobutadiene and another tribenzoCOTyne (similar to the mechanism proposed for the formation of Dewar benzene **62**) were also evaluated but finding higher energetic pathways.

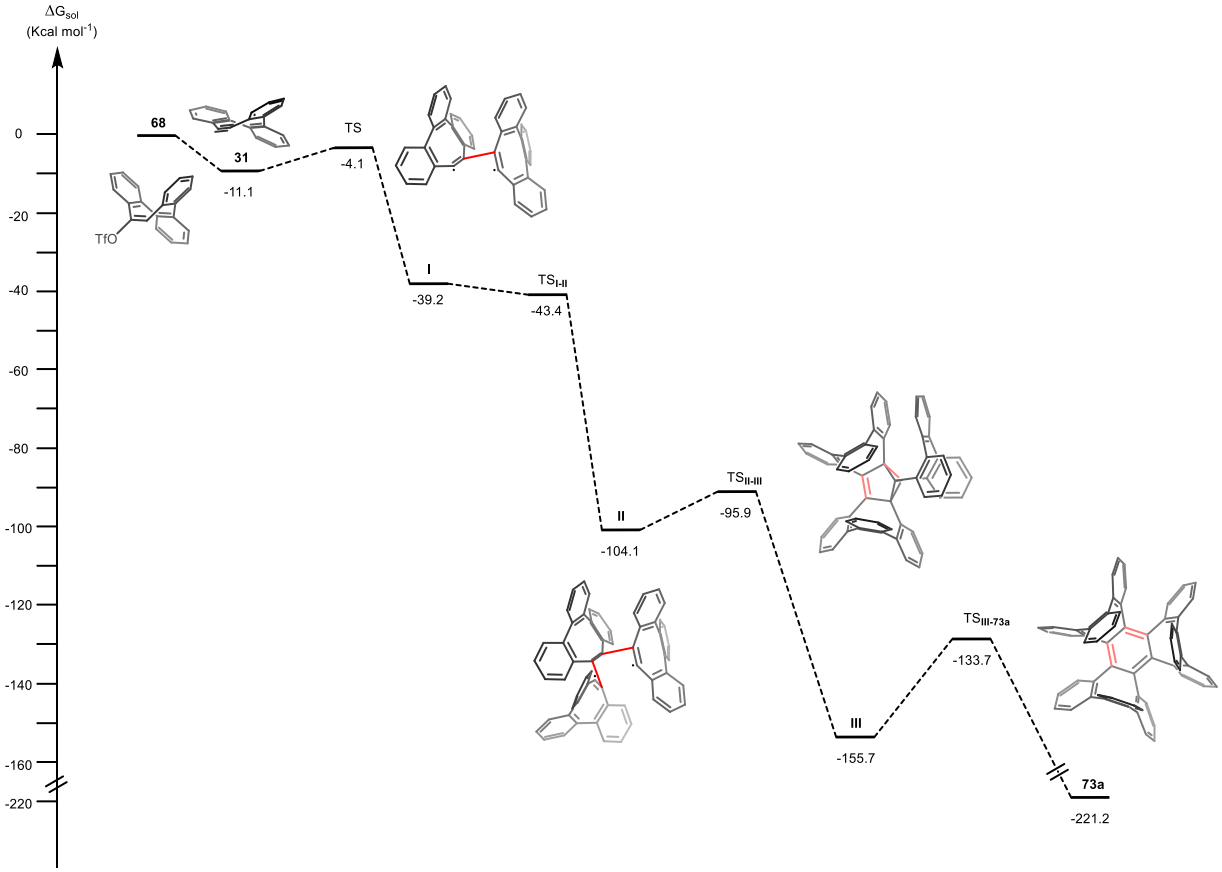


Figure 60. Free energy profiles for the thermal trimerization of tribenzoCOT ***68***

6.4.4. Conclusions

From the results discussed above, the following conclusions may be drawn:

- BrCOT **60** reacts in the presence of base (*in situ* formed COTyne) and Pd(0) sources to produce tri[8]annulene **61** in moderate yield where one of the cyclooctatetraene units is folded towards the opposite face of the other COT moieties ($\alpha\alpha\beta$-conformer).
- BrCOT **60** reacts in the absence of metals to produce naphthoCOT **72** in low yield through dimerization of *in situ* generated COTyne **28**.
- DibenzoCOTyne prepared *in situ* from vinyl triflate **67** was subjected to similar metal-catalysed [2+2+2] conditions. While Pd(0)-catalysed trimerization gave rise to dibenzotri[8]annulene **63** ($\alpha\alpha\beta$-conformer) in low yield, Ru(II)-catalysed trimerization led to Dewar benzene **62** in moderate yield. Interestingly, the same Dewar benzene **62** was obtained under thermal metal-free conditions with fairly good yield.
- The isolated dibenzoCOTyne **30** participates in Pd(0)-catalysed trimerization with better yield than the triflate precursor **67**, showing that the coordination of an alkyne as a ligand to the Pd (0) species is essential to form an efficient trimerization.
- In the case of Ru(II)-catalysed trimerization of preformed dibenzoCOTyne **30**, the steric/electronic nature of the catalyst is critical to the course of the reaction. While the cationic CpRu(II) catalyst produces dibenzotri[8]annulene **63** as major product and Dewar benzene **62** as the minor one, the cationic Cp*Ru(II) catalyst reverses the reactivity of dibenzoCOTyne **30** yielding the Dewar benzene **62** as the major product and tri[8]annulene **63** as a minor in the same overall yield.
- Strikingly, tribenzoCOTyne **31** prepared *in situ* from vinyl triflate **68** trimerizes in moderate yield to tribenzotri[8]annulene **73,** as a mixture of two isomers in a ratio 5:1, regardless of the presence of metal catalyst (Ru or Pd) or under thermal metal-free conditions.
- The major $\alpha\alpha\alpha$-conformer **73a** is formed mainly under thermal metal-free conditions. In a control test, the Ru(II) catalyst seems to play no role in the formation of this conformer.
- The amount of the minor $\alpha\alpha\beta$-conformer **73b** formed in the presence of Pd(0) catalyst is affected by the nature of the ligand on Pd and also by the temperature. The use of strong ligands such as PPh_3 provides a 1:1 mixture of conformers at rt, which can be increased to 1:3 at higher reaction temperatures.
- The analysis of the terphenyl units of the $\alpha\alpha\alpha$-conformer **73a** show an almost perpendicular arrangement of the three benzene rings, which means that unit might be considered as an ideal monomer for polymerization to cubic graphite.

7. Methodology

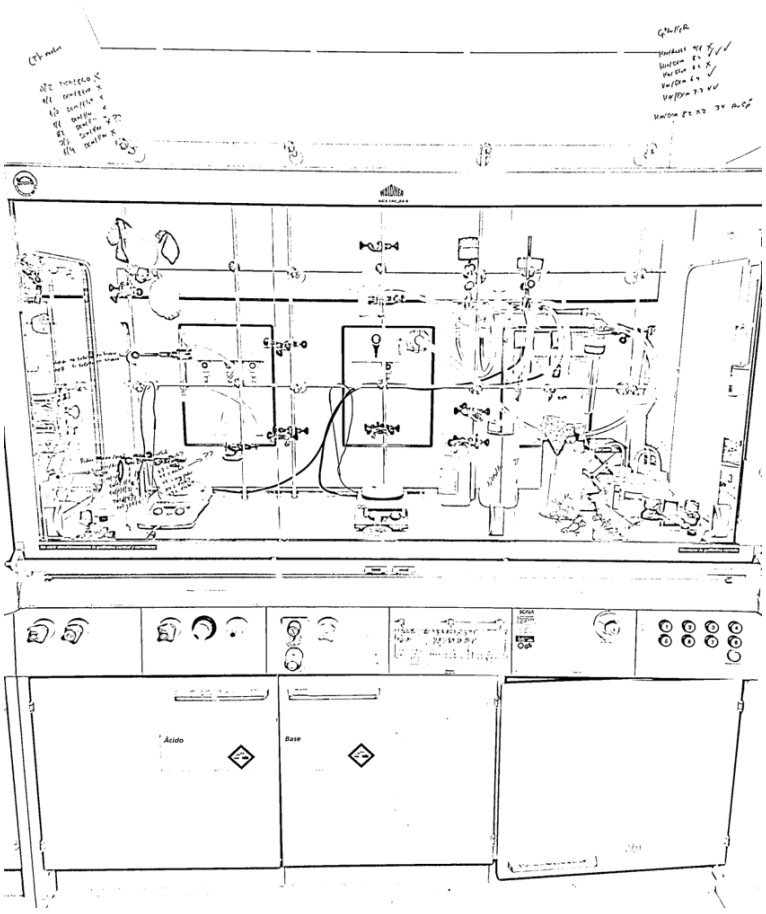
This doctoral thesis was carried out at the Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CiQUS), Universisdade de Santiago de Compostela.

For the completion of the doctoral thesis, the preparation of a set of ortho-arylalkylbenzenes (enynes) as well as organometallic ruthenium complexes (among other metals) following the procedures described in the bibliography was necessary. In order to prepare the aforementioned substrates as well as the metals catalysts, it was necessary to become familiar with the usual techniques of organic synthesis (argon atmosphere, anhydrous conditions, etc.) and organometallic synthesis (Schlenk technique).

Moreover, it was essential to acquire skills related to the different techniques for handling reagents, purification of products (chromatography, crystallization, distillation) as well as their characterization using different instrumental equipment such as nuclear magnetic resonance equipment (Varian Mercury 300 and Varian Innova 500), equipment for separation and structural determination of organic molecules (GC-MS and/or HPLC), Vis-UV/IR spectroscopy and X-ray crystallography equipment.

In addition, the use of common bibliographic search bases in science (Scifinder) and scientific software (MestreNova, ChemDraw, MBook) was necessary for writing scientific articles and the present PhD thesis.

Experimental section



General procedures for the preparation of starting materials and final products as well as late-stage manipulations are shown in this section. NMR spectra, X-ray crystallographic structures and computational details are also included.

7.1. Experimental section

7.1.1. General experimental procedures

All reactions were performed under an inert atmosphere of argon and with anhydrous solvents in glassware oven or flame dried at 80 ºC unless otherwise stated. Commercially available chemicals were purchased from Acros Organics Ltd., Aldrich Chemical Co. Ltd., Alfa Aesar, Fluorochem Ltd., Strem Chemicals Inc. or TCI Europe N.V. chemical companies and used without further purification, unless otherwise stated.

Analytical thin layer chromatography was carried out on silica-coated aluminium plates (silica gel 60 F254 Merck) or on aluminium sheets (aluminium oxide 60 F254 neutral Merck) using UV light as visualizing agent (254 nm) and $KMnO_4$ (solution of 1.5 g of potassium permanganate, 10 g of potassium bicarbonate and 1.25 mL of 10% sodium hydroxide in 200 mL of water) with heat as developing agents. Flash column chromatography was performed on silica gel 60 (Merck, 230-400 mesh) or aluminium oxide (Brockmann I neutral, 100-250 mesh) with the indicated eluent.[242]

Reactions at -78 °C were carried out with a dry ice/acetone bath. Melting points were recorded in a Buchi Melting Point B-540 apparatus and reported uncorrected. Mass spectrometry analysis was carried out using a Micromass Autospec, a TRACE MS or a HP-5988-A with chemical ionization and a Bruker Microtof ESI-TOF using chemical ionization spectrometers at CACTUS Facility (Universidade de Santiago de Compostela).

^{1}H and ^{13}C nuclear magnetic resonance experiments were carried out using a Varian Inova 500MHz, a Varian Inova 400 MHz, a Varian Mercury 300MHz or a Bruker DPX 250 or a Bruker Avance 300 NMR spectrometers. All NMR experiments were recorded at 298 K, unless otherwise stated. Chemical shifts are referenced to residual solvent peaks (1H, 13C{1H}). Coupling constants *J* are given in Hertz (Hz). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or as a combination of them. Multiplicities of 13C NMR signals were determined by DEPT experiments.

Yields refer to isolated compounds estimated to be > 95% pure as determined by $_{1}H$-NMR and capillary GC analysis.

X-ray crystallographic analysis was performed at the CACTUS facilities of the University of Santiago de Compostela.

[242] W. C. Still, M.; Kahn, A.; Mitra, *J. Org. Chem.* **1978**, *43*, 2923-2925.

7.1.2. Exploring Ru catalysed [2+2+2] cycloadditions of ortho-alkenylarylacetylenes with alkynes: Experimental procedures

7.1.2.1. Synthesis of [Ru (η5-(C_5Me_5) (CH_3CN)$_3$]PF_6[243]

A solution of $RuCl_3.H_2O$ (1.3 g, 5.0 mmol) in degassed EtOH (25 mL, 0.2 M) was deoxygenated by bubbling argon for 15 min in a Schlenk flask. Then, pentamethylcyclopentadiene, Cp*, (1.9 mL, 11.3 mmol, 2.25 eq.) was added and the resulting mixture was refluxed o/n. The resulting brown suspension was stored at -20 °C for 15 h, and then, the brown solid was filtered under argon atmosphere and washed with degassed EtOH (4 × 3 mL), diethyl ether (4 × 3 mL) and hexane (4 × 3 mL). The dark brown solid was dried under vacuum to give $[Cp^*RuCl_2]_x$ polymer as a brown/red powder in quantitative yield.

$[Cp^*RuCl_2]_x$ (1.1 g, 1.8 mmol) was placed in a dry Schlenk flask. The flask was evacuated and backfilled with argon three times and degassed THF (12 mL, 0.15 M) was added. Subsequent dropwise addition of $LiEt_3BH$ (3.6 mL, 1 M solution in THF, 2 equiv) afforded a gas release (H_2) and a color change. The resulting solution was stirred at room temperature for 2 h. The reaction mixture was concentrated under reduced pressure to half of its original volume and stored under argon atmosphere at -20 °C overnight, affording a dark red solid which was filtered under argon, washed with cold hexane (2 x 5 mL) and dried in vacuo to give $[Cp^*Ru(\mu_3\text{-}Cl]_4$ as a brown/red solid which was used directly in next step.

In a dry Schlenk flask, previous red brick solid was dissolved in dry and degassed MeCN (16 mL, 0.1 M). Then dry KPF_6 (1.3 g, 4 equiv) was added and the resulting mixture was stirred at rt o/n. After this time, a clear brown solution was obtained. This solution was heated at reflux and filtered while hot under argon atmosphere to another dry Schlenk flask. The final solution was allowed to slowly cool down to rt and then to -20ºC. After this time, the solution deposited an orange solid. The supernatant was filtered and the orange precipitated was washed with Et_2O (3 x 4 mL), hexane (3 x 4 mL) and finally dried under vacuum obtaining $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.71 g, 79%) as a yellow solid. Spectroscopic data matched with the commercially available complex.

^{1}H NMR (300 MHz, Methylene Chloride-d_2) δ 2.32 (s 9H), 1.59 (s, 15H).

7.1.2.2. Synthesis of *ortho*-alkenylarylacetylenes

7.1.2.2.1. General procedures

General procedure A for Sonogashira cross-coupling

A double-neck round bottom flask was charged with corresponding halide (1 equiv), $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (2 mol%) and Et_3N (0.2 M). The resulting mixture was bubbled with

[243] a) Fagan, P. J.; Mahoney, W. S.; Calabrese, J. C.; Williams, I. D. *Organometallics* **1990**, *9*, 1843- 1852; b) Fagan, P. J.; Ward, M. D.; Calabrese, J. C. *J. Am. Chem. Soc*. **1989**, *111*, 1698-1719; c) Mercier, A.; Yeo, W. C.; Chou, J.; Chaudhuri, P. D.; Bernardinelli, G.; Kündig, E. P. *Chem. Commun.* **2009**, 5227-5229.

Ar during 15 min and then corresponding alkyne (1.5 equiv) was added. A reflux condenser was attached and the final solution was heated at reflux using an aluminium heating block until disappearance of starting material (TLC monitoring). Upon completion, the crude reaction was filtered through a plug of silica and rinsed with EtOAc. The organic phase was washed twice with a solution of $NH_4Cl_{(sat)}$ and brine and extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated under vacuum. The resulting crude was purified by flash column chromatography through silica gel using the appropriate mobile phase as eluent to afford the cross-coupling product

General procedure B for Wittig reaction

^{n}BuLi (1.5 equiv, 2.5 M in hexane) was added dropwise to a solution of methyl(triphenyl)phosphonium bromide (2 equiv) in THF (2/3 total solvent) cooled at 0 ^{o}C. The resulting mixture was stirred during 45 min and then, a solution of corresponding aldehyde (1 equiv) in THF (1/3 of total solvent, 0.25 M) was added. The reaction mixture was stirred at room temperature until disappearance of stating material (TLC monitoring). After this time, a saturated NH4Cl solution was added to the reaction mixture and then extracted with EtOAc (4 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The residue was purified by flash column chromatography through silica gel using the appropriate mobile phase as eluent to afford olefin product.

General procedure C for protodesylilation

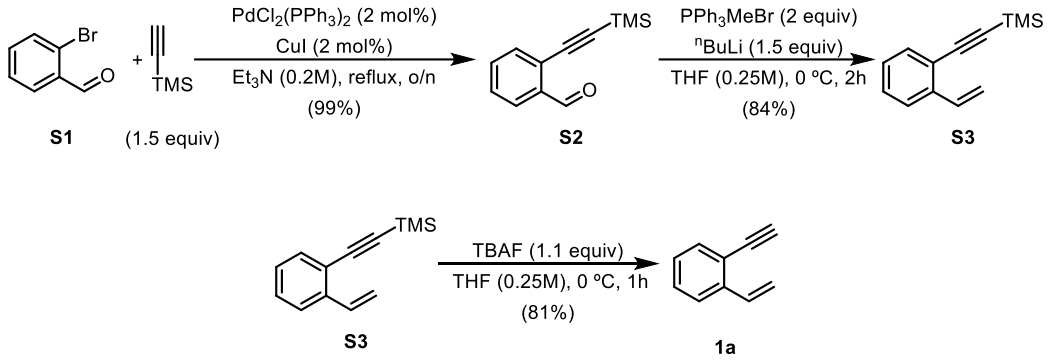
To a solution of protected alkyne (1 equiv) in THF (0.25 M) cooled at 0 ^{o}C, TBAF (1.1 equiv, 1 M in THF) was added. Then, the mixture was stirred at the same temperature until disappearance of starting material (TLC monitoring). Upon completion, a solution of NH_4Cl(sat) was added and the resulting mixture was extracted with Et_2O (3 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated under vacuum. The final crude was purified by flash column chromatography through silica gel using the appropriate mobile phase affording the protodesilylated product.

General procedure D for protodesiyilation

To a solution of protected alkyne in MeOH (0.5 M) was added solid K_2CO_3 (1 equiv). The reaction mixture was stirred at rt until disappearance of the starting material (TLC monitoring). The solvent was removed under reduced pressure and the residue was dissolved in EtOAc and washed twice with an aqueous solution of HCl 5% and once with brine. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The residue was purified by flash column chromatography through silica gel using the appropriate mobile phase affording the protodesilylated product.

7.1.2.2.2. Synthesis of *ortho*-alkenylarylacetylenes 1

Synthesis of 1-ethynyl-2-vinylbenzene ***1a***[244]



Following *general procedure A*, 2-((trimethylsilyl)ethynyl)benzaldehyde **S2** (6.0 g, 99%) was obtained as a white solid using *o*-bromobenzaldehyde **S1** (3.5 mL, 30 mmol), $Pd(PPh_3)_2Cl_2$ (421 mg, 0.6 mmol, 0.02 equiv), CuI (114 mg, 0.6 mmol, 0.02 equiv), ethynyltrimethylsilane (6.8 mL, 45 mmol, 1.5 equiv) and Et_3N (150 mL, 0.2 M) stirring at reflux temperature o/n. Purification conditions:Hex/EtOAc (98/2) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 10.58 (s, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.62 – 7.51 (m, 2H), 7.44 (dddd, *J* = 7.6, 6.8, 2.0, 0.8 Hz, 1H), 0.30 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 191.8 (CH), 136.2 (C), 133.7 (CH), 133.5 (CH), 128.8 (CH), 126.9 (CH), 126.8 (C), 102.4 (C), 100.1 (C), -0.2 (3 x CH_3).

Following *general procedure B*, trimethyl((2-vinylphenyl)ethynyl)silane **S3** (3.3 g, 84%) was obtained as a colorless oil using **S2** (4.1 g, 20 mmol), ^{n}BuLi (12 mL, 1.5 equiv, 2.5 M in hexane) and methyl(triphenyl)phosphonium bromide (14.3 g, 40 mmol, 2 equiv) in THF (81 mL) stirring at rt for 1.5h. Purification conditions: Hex/EtOAc (99/1) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.59 (d, *J* = 7.8 Hz, 1H), 7.53 – 7.44 (m, 1H), 7.35 – 7.27 (m, 1H), 7.27 – 7.17 (m, 2H), 5.86 (dd, *J* = 17.7, 1.2 Hz, 1H), 5.39 (dd, *J* = 11.1, 1.2 Hz, 1H), 0.30 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 139.3 (C), 134.8 (CH), 132.9 (CH), 128.6 (CH), 127.4 (CH), 124.5 (CH), 121.8 (C), 115.6 (CH_2), 103.3 (C), 99.1 (C), 0.0 (3 x CH_3).

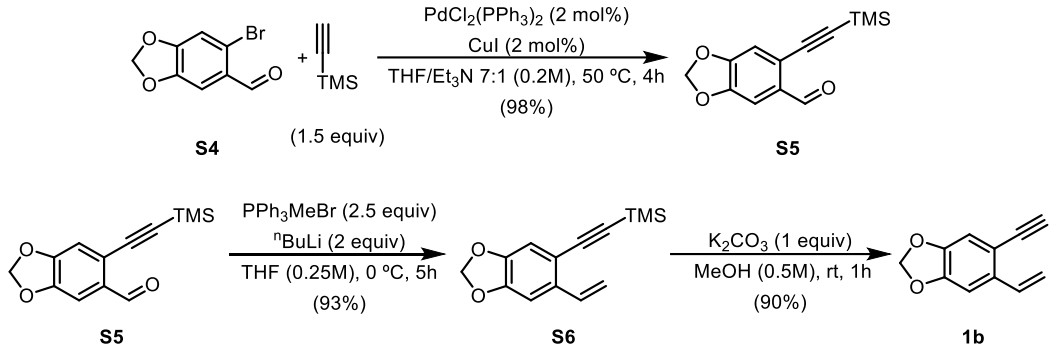
Following *general procedure B*, o-ethynyl vinylbenzene **1a** (1.75 g, 81%) was obtained as a colorless oil using **S3** (3.4 g, 16.8 mmol) and TBAF (19 mL, 1.1 equiv, 1 M in THF) in THF (64 mL, 0.25 M) stirring at 0ºC for 1h. Purification conditions: Hexane as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.62 (d, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 7.1 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.25 – 7.22 (m, 1H), 5.85 (d, *J* = 17.6 Hz, 1H), 5.40 (d, *J* = 11.0 Hz, 1H), 3.35 (s, 1H).

[244] García-Rubín, S.; González-Rodríguez, C.; García-Yebra, C.; Varela, J. A.; Esteruelas, M. A.; Saá, C. *Angew. Chem. Int. Ed.* **2014**, *53*, 1841–1844.

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 139.7 (C), 134.7 (CH), 133.1 (CH), 128.9 (CH), 127.5 (CH), 124.6 (CH), 120.8 (C), 115.9 (CH_2), 81.9 (C), 81.8 (CH).

Synthesis of 5-ethynyl-6-vinylbenzo[d][1,3]dioxole ***1b***[244]



General procedure A was followed with some modifications. Aldehyde **S5** (4.9 g, 98%) was obtained as a white solid using dioxolane **S4** (4.6 g, 20 mmol), $Pd(PPh_3)_2Cl_2$ (280 mg, 0.4 mmol, 0.02 equiv), CuI (76 mg, 0.4 mmol, 0.02 equiv) and ethynyltrimethylsilane (4.2 mL, 30 mmol, 1.5 equiv) in THF/Et_3N (7:1, 106 mL, 0.2 M) stirring at 50 ºC for 4h. Purification conditions:Hex/EtOAc (9/1) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm):10.37 (s, 1H), 7.31 (s, 1H), 6.95 (s, 1H), 6.06 (s, 2H), 0.26 (s, 9H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 190.2 (CH), 152.2 (C), 148.8 (C), 132.6 (C), 123.4 (C), 112.3 (CH), 105.9 (CH), 102.4 (CH_2), 101.1 (C), 99.9 (C), -0.2 (3 x CH_3).

General procedure B was followed with some modifications. Vinyl product **S6** (4.5 g, 93%) was obtained as a colorless oil using aldehyde **S5** (4.9 g, 20 mmol), ^{n}BuLi (16 mL, 2 equiv, 2.5 M in hexane) and methyl(triphenyl)phosphonium bromide (17.8 g, 50 mmol, 2.5 equiv) in THF (80 mL, 0.25M) stirring at rt for 5h. Purification conditions: Hex/EtOAc (99/1) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm):7.16 (dd, *J* = 17.5, 11.0 Hz, 1H), 7.02 (s, 1H), 6.87 (s, 2H), 5.96 (s, 1H), 5.64 (dd, *J* = 17.5, 0.9 Hz, 1H), 5.26 (dd, *J* = 11, 0.9 Hz, 1H), 0.26 (s, 1H).

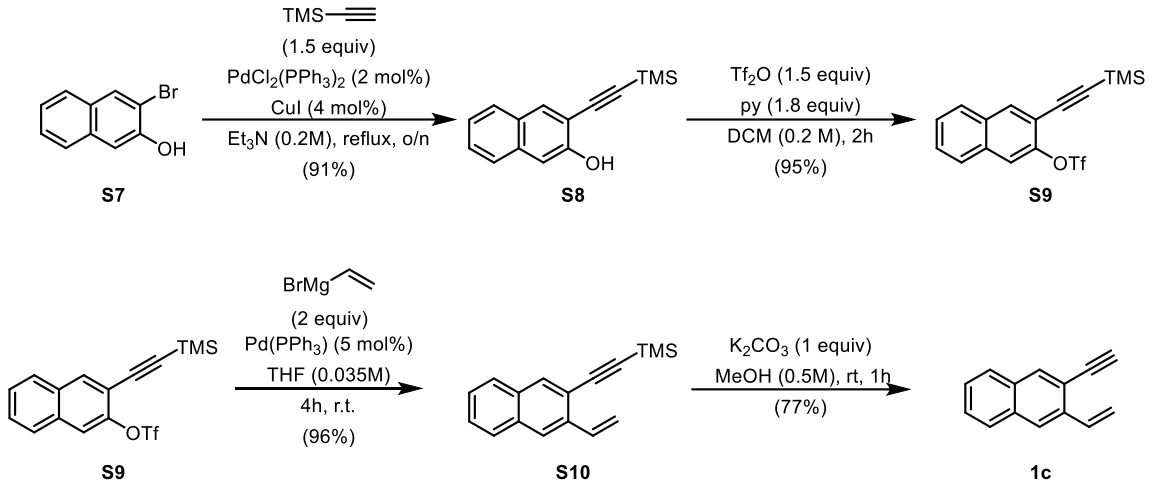
^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 148.6 (C), 146.9 (C), 135.0 (C), 134.5 (CH), 115.6 (C), 113.8 (CH_2), 111.7 (CH), 104.1 (CH), 103.2 (C), 101.5 (CH_2), 97.8 (C), 0.1 (3 x CH_3).

Following *general procedure D*, 5-ethynyl-6-vinylbenzo[d][1,3]dioxole **1b** (2.85 g, 90%) was obtained as a pale yellow solid using **S6** (4.5 g, 18.5 mmol) and K_2CO_3 (2.6 g, 18.5 mmol, 1 equiv) in dry MeOH (37 mL, 0.5 M) stirring at rt during 1h. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.20 (dd, *J* = 17.5, 11.0 Hz, 1H), 7.06 (s, 1H), 6.92 (s, 1H), 5.99 (s, 2H), 5.66 (dd, *J* = 17.5, 0.9 Hz, 2H), 5.29 (dd, *J* = 11, 0.9 Hz, 2H), 3.26 (s, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 148.8 (C), 147.0 (C), 135.3 (C), 134.3 (CH), 114.4 (C), 114.1 (CH2), 111.9 (CH), 104.2 (CH), 101.5 (CH_2), 81.9 (C), 80.6 (C).

Synthesis of 2-ethynyl-3-vinylnaphthalene ***1c***[244]



Following *general procedure A*, alcohol **S8** (1.1 g, 91%) was obtained as a white solid using bromonaphthol **S7** (1.1 g, 4.8 mmol), $Pd(PPh_3)_2Cl_2$ (68 mg, 0.1 mmol, 0.02 equiv), CuI (18 mg, 0.1 mmol, 0.02 equiv), ethynyltrimethylsilane (1 mL, 7.2 mmol, 1.5 equiv) and Et_3N (24 mL, 0.2 M) stirring at reflux temperature o/n. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.93 (s, 1H), 7.69 (t, *J* = 8.7 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.32 (d, *J* = 14.1 Hz, 2H), 5.90 (s, 1H), 0.33 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 152.9 (C), 135.1 (C), 132.5 (CH), 128.3 (C), 127.8 (CH), 127.6 (CH), 126.7 (CH), 124.2 (CH), 112.0 (C), 109.2 (CH), 103.1 (C), 99.2 (C), 0.1 (3 x CH_3).

To a solution of **S8** (3 g, 12.5 mmol) and pyridine (1.8 mL, 22.5 mmol, 1.8 equiv) in DCM (63 mL, 0.2 M) at 0 °C was slowly added trifluoromethanesulfonic anhydride (3.1 mL, 18.7 mmol, 1.5 equiv). After reaching room temperature the mixture was stirred for 2 h until disappearance of the starting material (TLC monitoring). Upon completion, the reaction was quenched by adding a 5% aqueous solution of Na_2SO_4 (20 mL) and extracted with DCM (3 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9:1) as eluent to afford triflate **S9** (4.4 g, 95 %) as a light-yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.80 (s, 1H), 7.57 – 7.48 (m, 2H), 7.44 (s, 1H), 7.31 – 7.24 (m, 2H), 0.03 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 146.8 (C), 134.8 (CH), 132.8 (C), 131.9 (C), 128.4 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 119.6 (CH), 116.8 (C), 116.0 (C), 102.3 (C), 98.0 (C), -0.3 (3 x CH_3).

Vinylmagnesium bromide (6.4 mL, 2 equiv, 1 M in THF) was added dropwise over a solution of **S9** (1.2 g, 3.2 mmol) and $Pd(PPh_3)_4$ (0.19 g, 0.16 mmol, 0.05 equiv) in dry THF (85 mL, 0.035 M) at room temperature. The resulting mixture was stirred at rt until disappearance of the starting material (4h, TLC monitoring). Then, the reaction was worked up by adding water (40 mL) followed by extraction with Et_2O (3 x 30 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95:5) as eluent to afford triflate **S10** (0.77 g, 96%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 8.02 (d, *J* = 9.9 Hz, 2H), 7.78 (ddd, *J* = 15.4, 7.6, 2.5 Hz, 2H), 7.46 (ddd, *J* = 6.1, 3.1, 1.7 Hz, 2H), 7.34 (ddd, *J* = 17.6, 11.0, 0.6 Hz, 1H), 6.00 (dt, *J* = 17.6, 1.2 Hz, 1H), 5.45 (dd, *J* = 11.0, 1.2 Hz, 1H), 0.34 (s, 9H).

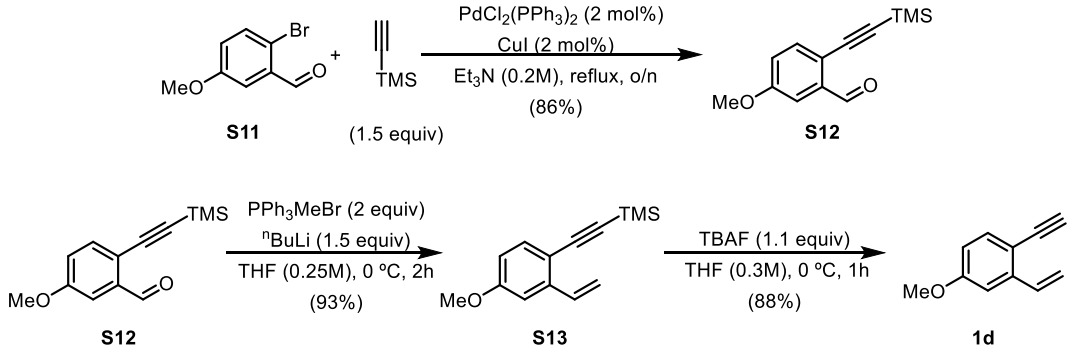
^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 136.0 (C), 135.1 (CH), 133.2 (C), 133.1 (CH), 132.4 (C), 128.0 (CH), 127.5 (CH), 127.1 (CH), 126.5 (CH), 123.9 (CH), 120.2 (C), 116.0 (CH_2), 103.8 (C), 99.0 (C), 0.2 (3 x CH_3).

Following *general procedure D*, 2-ethynyl-3-vinylnaphthalene **1c** (0.64 g, 77%) was obtained as a white solid using K_2CO_3 (0.65 g, 4.7 mmol, 1 equiv) and MeOH (9.4 mL, 0.5 M) stirring at rt for 1h. Purification conditions: Hex/EtOAc (99/1) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 8.04 (d, *J* = 11.4 Hz, 2H), 7.86 – 7.73 (m, 2H), 7.56 – 7.43 (m, 2H), 7.35 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.97 (dd, *J* = 17.5, 1.2 Hz, 1H), 5.45 (dd, *J* = 11.0, 1.2 Hz, 1H), 3.37 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 136.3 (C), 135.1 (CH), 133.5 (CH), 133.4 (C), 132.5 (C), 128.1 (CH), 127.5 (CH), 127.3 (CH), 126.6 (CH), 124.0 (CH), 119.2 (C), 116.2 (CH_2), 82.4 (C), 81.5 (CH).

Synthesis of 1-ethynyl-4-methoxy-2-vinylbenzene ***1d***[244]



Following *general procedure A*, cross-coupling product **S12** (2 g, 86%) was obtained as a light yellow oil using bromoarene **S11** (2.1 g, 10 mmol), $Pd(PPh_3)_2Cl_2$ (140 mg, 0.2 mmol, 0.02 equiv), CuI (38 mg, 0.2 mmol, 0.02 equiv), ethynyltrimethylsilane (2.1 mL, 15 mmol, 1.5 equiv) and Et_3N (50 mL, 0.2 M) stirring at 50 ^oC during 4h. Purification conditions: Hex/EtOAc (9/1) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 10.48 (s, 1H), 7.45 (d, *J* = 8.5 Hz, 1H), 7.33 (d, *J* = 2.8 Hz, 1H), 7.04 (dd, *J* = 8.6, 2.8 Hz, 1H), 3.81 (s, 3H), 0.25 (s, 9H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 191.6 (CH), 160.0 (C), 137.8 (C), 135.0 (CH), 121.5 (CH), 119.5 (C), 109.7 (CH), 100.6 (C), 100.4 (C), 55.7 (CH3), -0.0 (3 x CH_3).

Following *general procedure B*, vinyl product **S13** (1.1 g, 93%) was obtained as a white solid using aldehyde **S12** (1.2 g, 5.2 mmol), ^{n}BuLi (3.1 mL, 1.5 equiv, 2.5 M in hexane), methyl(triphenyl)phosphonium bromide (3.7 g, 10.3 mmol, 2 equiv) and THF (21 mL, 0.25 M) stirring at rt for 2h. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.40 (d, *J* = 8.6 Hz, 1H), 7.18 (dd, *J* = 17.6, 11.0 Hz, 1H), 7.06 (d, *J* = 2.6 Hz, 1H), 6.75 (dd, *J* = 8.6, 2.6 Hz, 1H), 5.81 (d, *J* = 17.6 Hz, 1H), 5.37 (d, *J* = 11.0 Hz, 1H), 3.83 (s, 3H), 0.26 (s, 9H).

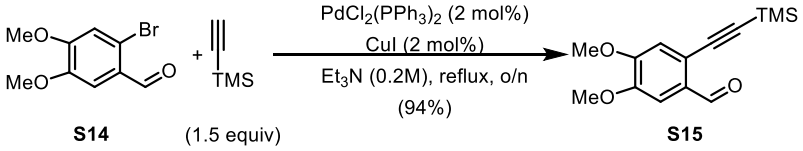
^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.8 (C), 140.9 (C), 134.9 (CH), 134.3 (CH), 115.7 (CH_2), 114.5 (C), 113.7 (CH), 109.5 (CH), 103.4 (C), 97.4 (C), 55.3 (CH_3), 0.1 (3 x CH_3).

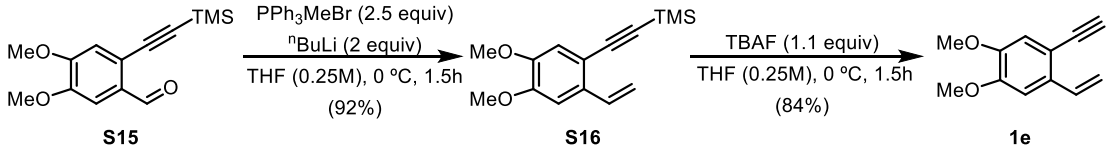
Following *general procedure C*, 1-ethynyl-4-methoxy-2-vinylbenzene **1d** (0.66 g, 88 %) was obtained as a white solid using **S13** (1.1 g, 4.8 mmol), TBAF (5.3 mL, 1.1 equiv, 1 M in THF) and THF (16 mL, 0.3 M) stirring at 0ºC for 1h. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.43 (d, *J* = 8.6 Hz, 1H), 7.21 (dd, *J* = 18.2, 11.0 Hz, 1H), 7.09 (d, *J* = 2.6 Hz, 1H), 6.78 (dd, *J* = 8.6, 2.6 Hz, 1H), 5.81 (d, *J* = 17.6 Hz, 1H), 5.38 (d, *J* = 11.0 Hz, 1H), 3.83 (s, 3H), 3.25 (s, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 160.0 (C), 141.2 (C), 134.7 (CH), 134.5 (CH), 116.0 (CH_2), 113.8 (CH), 113.4 (C), 109.6 (CH), 82.0 (C), 80.4 (C), 55.3 (CH_3).

*Synthesis of 1-ethynyl-4,5-dimethoxy-2-vinylbenzene **1e**[245]*





Following *general procedure A,* aldehyde **S15** (2.1g, 94%) was obtained as a white solid using bromoveratraldehyde **S14** (2.2 g, 8.6 mmol), $Pd(PPh_3)_2Cl_2$ (120 mg, 0.17 mmol, 0.02 equiv), CuI (32.6 mg, 0.17 mmol, 0.02 equiv), ethynyltrimethylsilane (1.9 mL, 12.8 mmol, 1.5 equiv) and Et_3N (43 mL, 0.2 M) stirring at reflux o/n. Purification conditions: Hex/EtOAc (95/5 to 85/15) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 10.38 (s, 1H), 7.36 (s, 1H), 6.97 (s, 1H), 3.95 (s, 3H), 3.92 (s, 3H), 0.26 (s, 9H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 190.7 (CH), 153.6 (C), 150.0 (C), 130.8 (C), 121.5 (C), 114.7 (CH), 108.1 (CH), 100.2 (C), 99.7 (C), 56.4 (CH_3), 56.2 (CH_3), -0.1 (3 x CH3).

General procedure B was followed with some modifications. **S16** (0.91 g, 92%) was obtained as a white solid using aldehyde **S15** (1.0 g, 3.8 mmol), ^{n}BuLi (2.3 mL, 2 equiv, 2.5 M in hexane), methyl(triphenyl)phosphonium bromide (2.7 g, 7.6 mmol, 2.5 equiv) and THF (15 mL, 0.25 M) stirring at rt for 1.5h. Purification conditions: Hex/EtOAc (9/1) as mobile phase.

[245] Hamada, N.; Yamaguchi, A.; Inuki, S.; Oishi, S.; Ohno, H. *Org. Lett*. **2018**, *20*, 4401−4405.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.15 (dd, *J* = 17.8, 11.0 Hz, 1H), 7.02 (s, 1H), 6.91 (s, 1H), 5.69 (d, *J* = 17.6 Hz, 1H), 5.27 (d, *J* = 10.9 Hz, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 0.24 (s, 9H).

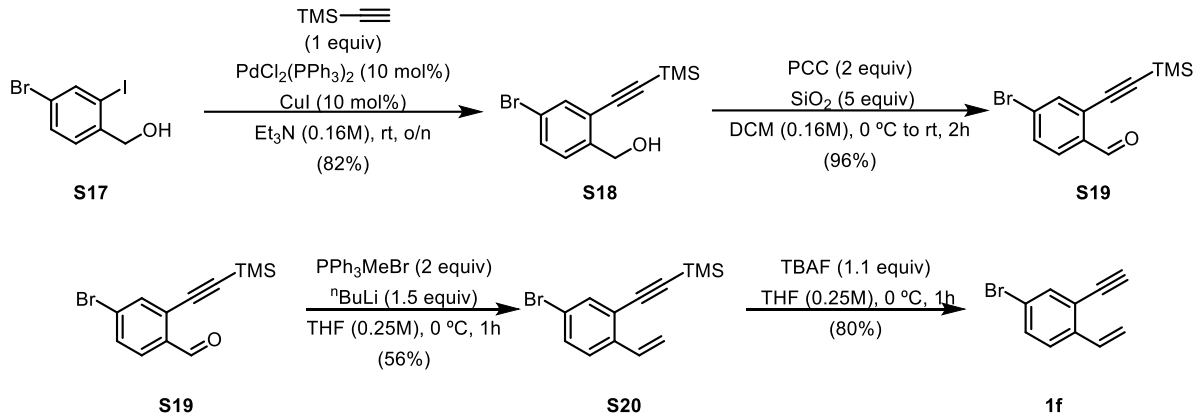
^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 150.1 (C), 148.4 (C), 134.5 (CH), 132.2 (C), 114.5 (CH), 112.7 (CH_2), 105.9 (CH), 102.9 (C), 56.0 (CH_3), 55.8 (CH_3), 0.8 (3 x CH_3).

Following *general procedure C*, enyne **1e** (0.55 g, 84 %) was obtained as a white solid using **S16** (0.91 g, 3.5 mmol), TBAF (4.4 mL, 1.1 equiv, 1 M in THF) and THF (14 mL, 0.3 M) stirring at 0 °C during 1.5h. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.21 (dd, *J* = 17.6, 11.0 Hz, 1H), 7.08 (s, 1H), 6.98 (s, 1H), 5.73 (d, *J* = 17.6 Hz, 1H), 5.33 (d, *J* = 11.1 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 3.31 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 149.9 (C), 148.5 (C), 134.4 (CH), 133.4 (C), 114.7 (CH), 113.8 (CH_2), 113.2 (C), 106.7 (CH), 82.0 (C), 80.5 (CH), 56.0 (CH_3), 55.9 (CH_3).

Synthesis of 4-bromo-2-ethynyl-1-vinylbenzene ***1f***[244]



General procedure A was followed with some modifications. Alcohol **S18** (1.1 g, 82%) was obtained as a light yellow solid using **S17** (1.4 g, 4.5 mmol), $Pd(PPh_3)_2Cl_2$ (310 mg, 0.45 mmol, 0.1 equiv), CuI (85 mg, 0.45 mmol, 0.1 equiv), TMSA (0.65 mL, 4.5 mmol, 1 equiv) and Et_3N (27 mL, 0.16 M) stirring at rt o/n. Purification conditions: Hex/EtOAc (8/2) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.60 (d, *J* = 2.1 Hz, 1H), 7.45 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 4.77 (d, *J* = 6.4 Hz, 2H), 0.26 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 142.2 (C), 135.0 (CH), 132.1 (CH), 128.7 (CH), 123.2 (C), 120.9 (C), 101.4 (C), 101.0 (C), 63.5 (CH_2), 0.0 (3 x CH_3).

PCC (1.56 g, 7.2 mmol, 2 equiv) was slowly added to the mixture of alcohol **S18** (1.1 g, 3.6 mmol) and SiO_2 (1.2 g, 19.1 mmol, 5 equiv) in CH_2Cl_2 (23 mL, 0.16 M) at 0 °C. The resulting mixture was allowed to stir at room temperature for additional 2 hours. Then the reaction mixture was filtrated and concentrated under vacuo. The crude residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9:1) as eluent to afford 0.98 g (96%) of aldehyde **S19**, as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 10.46 (d, *J* = 0.8 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 1.9 Hz, 1H), 7.55 (ddd, *J* = 8.4, 2.0, 0.8 Hz, 1H), 0.27 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 190.8 (CH), 136.3 (CH), 135.0 (C), 132.4 (CH), 128.8 (C), 128.4 (CH), 128.3 (C), 104.3 (C), 98.6 (C), -0.2 (3 x CH_3).

Following *general procedure B*, vinyl arene **S20** (0.55 g, 56%) was obtained as a colorless oil using **S19** (0.98 g, 3.5 mmol), ^{n}BuLi (2 mL, 1.5 equiv, 2.5 M in hexane), methyl(triphenyl)phosphonium bromide (2.5 g, 6.9 mmol, 2 equiv) and THF (14 mL, 0.25 M) stirring at rt for 1h. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm):7.60 (dd, *J* = 1.7, 0.9 Hz, 1H), 7.40 (t, *J* = 1.4 Hz, 2H), 7.12 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.82 (dd, *J* = 17.6, 0.9 Hz, 1H), 5.39 (dd, *J* = 11.0, 0.9 Hz, 1H), 0.28 (s, 9H).

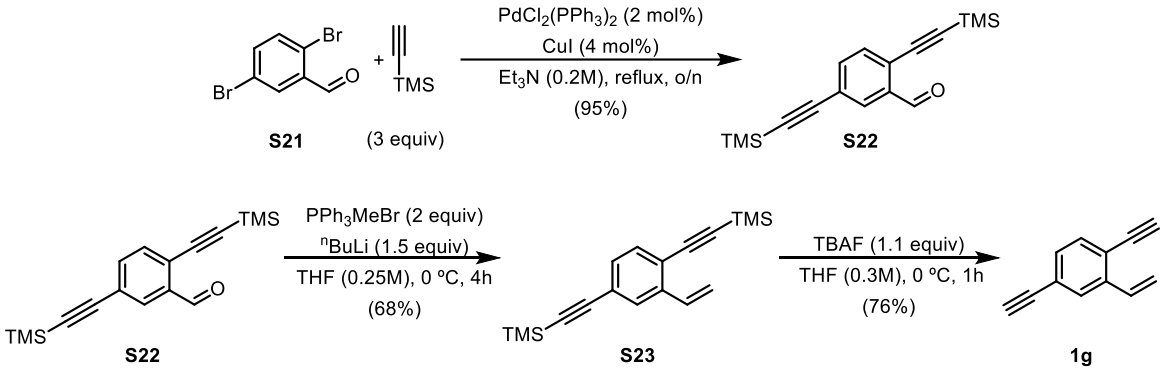
^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 138.3 (C), 135.4 (CH), 134.1 (CH), 131.9 (CH), 126.1 (CH), 123.8 (C), 120.9 (C), 116.3 (CH_2), 101.8 (C), 100.9 (C), 0.0 (3 x CH_3).

Following *general procedure B*, enyne **1f** (0.32 g, 80 %) was obtained as a colourless oil using **S20** (0.54 g, 1.9 mmol), TBAF (2.3 mL, 2.2 equiv, 1 M in THF) and THF (8 mL, 0.25 M) stirring at 0 ^{o}C during 1.5h. Purification conditions: Hex/EtOAc (98/2) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.64 (t, *J* = 1.2 Hz, 1H), 7.46 (d, *J* = 1.2 Hz, 2H), 7.16 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.83 (dd, *J* = 17.6, 1.0 Hz, 1H), 5.41 (dd, *J* = 11.1, 1.0 Hz, 1H), 3.37 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 138.7 (C), 135.6 (CH), 133.8 (CH), 132.3 (CH), 126.2 (CH), 122.7 (C), 121.0 (C), 116.7 (CH_2), 83.1 (CH), 80.6 (C).

*Synthesis of 1,4-diethynyl-2-vinylbenzene **1g***



General procedure A was followed with some modifications. Aldehyde **S22** (5.6 g, 95%) was obtained as a white solid using dibromoarene **S21** (5.2 g, 19.7 mmol), $Pd(PPh_3)_2Cl_2$ (280 mg, 0.4 mmol, 0.02 equiv), CuI (150 mg, 0.78 mmol, 0.04 equiv), ethynyltrimethylsilane (8.4 mL, 60 mmol, 3 equiv) and Et_3N (99 mL, 0.2 M) stirring at reflux o/n. Purification conditions: Hex/EtOAc (97/3) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm):10.48 (s, 1H), 7.96 (d, *J* = 2.5 Hz, 1H), 7.57 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.48 (dd, *J* = 8.0, 0.7 Hz, 1H), 0.27 (s, 9H), 0.24 (s, 9H).

^{13}C NMR, DEPT (75 MHz, CDCl3), δ (ppm):190.9 (CH), 136.3 (CH), 136.0 (C), 133.4 (CH), 130.5 (CH), 126.1 (C), 123.9 (C), 104.3 (C), 103.2 (C), 99.7 (C), 97.5 (C), -0.21 (3 x CH_3), -0.28 (3 x CH_3).

Following *general procedure B*, vinyl arene **S23** (0.85 g, 68%) was obtained as a white solid using aldehyde **S22** (1.25 g, 4.2 mmol), ^{n}BuLi (2.5 mL, 2 equiv, 2.5 M in hexane), methyl(triphenyl)phosphonium bromide (3 g, 9.2 mmol, 2.5 equiv) and THF (17 mL) stirring at rt during 4h. Purification conditions: Hex/EtOAc (99/1) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.71 (d, *J* = 1.6 Hz, 1H), 7.43 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.32 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.20 (ddd, *J* = 17.8, 11.1, 1.7 Hz, 1H), 0.32 (s, 9H), 0.32 (s, 9H).

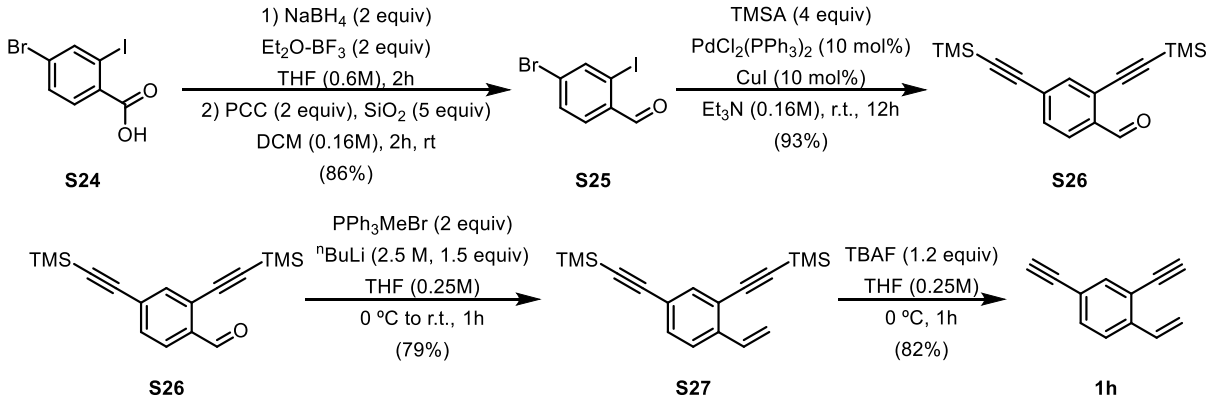
^{13}C NMR, DEPT (75 MHz, CDCl3), δ (ppm): 139.4 (C), 134.2 (CH), 132.8 (CH), 130.7 (CH), 128.2 (CH), 123.4 (C), 122.0 (C), 116.5 (2 x CH_2), 104.8 (C), 103.0 (C), 101.1 (C), 96.1 (C), 0.1 (6 x CH_3).

Following *general procedure C*, enediyne **1g** (0.27 g, 76 %) was obtained as a colourless oil using **S23** (0.7 g, 2.4 mmol), TBAF (2.6 mL, 1.1 equiv, 1 M in THF) and THF (8 mL, 0.3 M) stirring at 0 °C for 1h. Purification conditions: Hex/EtOAc (99/1) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.70 (d, *J* = 1.6 Hz, 1H), 7.44 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.32 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.17 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.83 (dd, *J* = 17.6, 0.9 Hz, 1H), 5.41 (dd, *J* = 11.0, 0.9 Hz, 1H), 3.40 (s, 1H), 3.16 (s, 1H).

^{13C} NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 139.9 (C), 134.0 (CH), 133.1 (CH), 130.9 (CH), 128.5 (CH), 122.8 (C), 121.4 (C), 117.0 (CH_2), 83.6 (CH), 83.2 (C), 81.5 (C), 79.0 (CH).

*Synthesis of 2,4-diethynyl-1-vinylbenzene **1h***



To a solution of 4-bromo-2-iodobenzoic acid **S24** (2.88 g, 8.81 mmol) and $NaBH_4$ (0.68 g, 17.6 mmol, 2 equiv) in THF (14 mL) at 0 °C, was slowly added $Et_2O{\cdot}BF_3$ (2.2 mL, 17.6 mmol, 2 equiv) over a period of 30 minutes and then, the mixture was vigorously stirred at room temperature. When the reaction was completed as determined by TLC analysis (2h), the reaction mixture was cooled to 0°C, H_2O was slowly added and then extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was evaporated in vacuum obtaining the (2-iodophenyl)methanol **S17** derivative as a white solid in quantitative yield (2.7 g). It was used without further purification.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.96 (d, *J* = 1.9 Hz, 1H), 7.50 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 4.62 (s, 2H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 141.9 (C), 141.1 (CH), 131.7 (CH), 129.5 (CH), 121.9 (C), 97.5 (C), 68.8 (CH_2).

PCC (2.01 g, 9.3 mmol, 2 equiv) was slowly added to the mixture of (4-bromo-2-iodophenyl)methanol **S17** (1.46 g, 4.6 mmol) and SiO_2 (1.4 g, 24.5 mmol, 2 equiv) in CH_2Cl_2 (0.16 M, 29 mL) at 0 °C. The resulting mixture was allowed to stir at room temperature for additional 2 hours. Then the reaction mixture was filtrated and concentrated under vacuo. The crude residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9:1) as eluent to afford 1.25 g (86%) of 4-bromo-2-iodobenzaldehyde, **S25**, [246] as a white solid.

Melting point: 82.3-83.3 °C

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 10.00 (d, *J* = 0.8 Hz, 1H), 8.14 (d, *J* = 1.8 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.62 (dd, *J* = 8.3, 2.5 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 194.7 (CH), 142.8 (CH), 134.1 (C), 132.3 (CH), 131.2 (CH), 130.2 (C), 100.9 (C).

General procedure A was followed with some modifications. Cross coupling product **S26** (1.07 g, 93%) was obtained as a white solid using 4-bromo-2-iodobenzaldehyde **S25** (1.2 g, 3.9 mmol), $Pd(PPh_3)Cl_2$ (0.27 g, 0.39 mmol, 0.1 equiv), CuI (0.074 mg, 0.39 mmol, 0.1 equiv), TMSA (2.2 mL, 15.4 mmol, 4 equiv) and Et_3N (24 mL, 0.16 M) stirring at rt o/n. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

Melting point: 131.5-132.0 °C

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 10.50 (d, *J* = 0.9 Hz, 1H), 7.83 (dd, *J* = 8.1, 0.6 Hz, 1H), 7.66 (dd, *J* = 1.6, 0.6 Hz, 1H), 7.47 (ddd, *J* = 8.1, 1.6, 0.9 Hz, 1H), 0.27 (s, 9H), 0.25 (s, 9H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 191.2 (CH), 136.9 (CH), 135.3 (C), 132.1 (CH), 129.0 (C), 126.9 (CH), 103.2 (C), 103.2 (C), 99.7 (C), 99.4 (C), -0.1 (3 x CH_3), -0.12 (3 x CH_3).

HRMS (CI) calculated for $C_{17}H_{23}OSi_2$ $[M+H]^+$: 299.1282, found 299.1285

Following *general procedure B*, ((4-vinyl-1,3-phenylene)bis(ethyne-2,1-diyl))bis(trimethylsilane), **S27** (0.78 g, 79%) was obtained as a colorless oil using 2,4-bis((trimethylsilyl)ethynyl)benzaldehyde **S26** (1.0 g, 3.3 mmol), ^{n}BuLi (1.9 mL, 1.5 equiv, 2.5 M), methyl(triphenyl)phosphonium bromide (2.39 g, 6.7 mmol, 2 equiv) and THF (14 mL, 0.25 M) stirring at rt for 1h. Purification conditions: Hex/EtOAc (98/2) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.72 – 7.66 (m, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.52 – 7.40 (m, 1H), 7.27 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.93 (d, *J* = 17.6 Hz, 1H), 5.49 (d, *J* = 11.0 Hz, 1H), 0.36 (s, 9H), 0.35 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 139.4 (C), 136.8 (CH), 134.6 (CH), 132.2 (CH), 124.8 (CH), 122.7 (C), 122.4 (C), 117.9 (CH_2), 104.5 (C), 102.7 (C), 100.7 (C), 96.6 (C), 0.34 (6 x CH_3).

HRMS (CI) calculated for $C_{18}H_{25}Si_2$ $[M+H]^+$: 297.1489, found 297.1485

[246] A. C. Jr, J. D. Tovar, *J.Org. Chem*. **2011**, *76*, 2227-223.

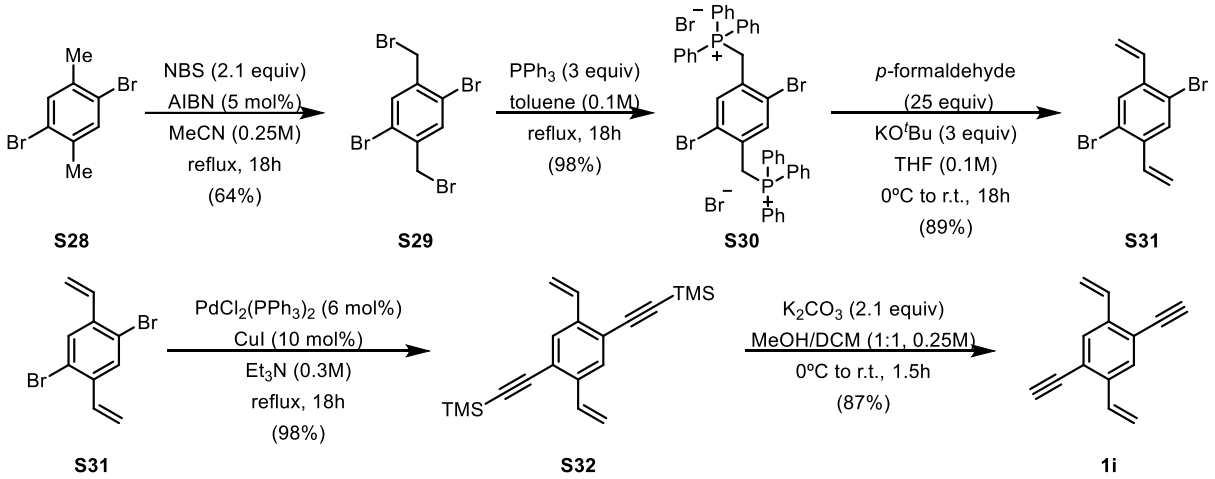
Following *general procedure C*, 2,4-diethynyl-1-vinylbenzene, **1h**, (0.31 g, 82%) was obtained as a colorless oil using ((4-vinyl-1,3-phenylene)bis(ethyne-2,1-diyl))bis(trimethylsilane) ,**S27,** (0.75 g, 2.53 mmol), TBAF (3 mL, 1.2 equi, 1M in THF) and THF (10 mL, 0.25 M) stirring at 0ºC during 1h. Purification conditions: Hex/EtOAc (98/2) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.62 (d, *J* = 1.8 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.42 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.20 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.84 (dd, *J* = 17.6, 0.9 Hz, 1H), 5.42 (dd, *J* = 11.0, 0.9 Hz, 1H), 3.32 (s, 1H), 3.11 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 140.0 (C), 136.8 (CH), 134.1 (CH), 131.9 (CH), 124.1 (CH), 121.5 (C), 120.2 (C), 117.1 (CH_2), 82.7 (C), 82.5 (CH), 81.0 (C), 78.5 (C).

HRMS (CI) calculated for $C_{12}H_9$ $[M+H]^+$:153.0699, found 153.0695

*Synthesis of 1,4-diethynyl-2,5-divinylbenzene **1i***



1,4-Dibromo-2,5-dimethylbenzene **S28** (5 g, 19 mmol), NBS (7.1 g, 40 mmol, 2.1 equiv) and AIBN (0.164 g, 1 mmol, 0.05 equiv) were dissolved in acetonitrile (75 mL) in a round-bottomed flask equipped with a stirring bar. The reaction mixture was heated at 100 ºC in an aluminium heating block during 24h. The reaction was then cooled to room temperature and the solvent evaporated under reduced pressure. The crude was washed with hot methanol to yield the tetrabrominated product **S29** (5.1 g, 64% yield) as a white solid. NMR data is in accordance with the previously reported.[247]

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.65 (d, *J* = 1.1 Hz, 2H), 4.50 (d, *J* = 1.0 Hz, 4H).

In a round-bottomed flask equipped with a stirring bar, **S29** (5 g, 11.8 mmol) and PPh_3 (9.3 g, 35.6 mmol, 3.0 equiv) were dissolved in toluene (119 mL). The solution was then heated at 120 ºC in an aluminium heating block for 19h. Upon completion the reaction was cooled to room temperature, filtered and the resulting solid was washed with hexane. The obtained white solid was dried several hours at high vacuum. 2,5-Dibromo-*p*-

[247] Auffray, M.; Charra, F.; Sosa Vargas, L.; Mathevet, F.; Attias, A.-J.; Kreher, D. *New J. Chem*., **2020**, *44*, 7665-7674.

xylenebis(triphenylphosphonium) dibromide, **S30**, was obtained as a white powder (10.9 g, 98% yield). NMR data is in accordance with the previously reported.[248]

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.86 – 7.78 (m, 6H), 7.76 – 7.62 (m, 24H), 7.39 (d, *J* = 2.0 Hz, 2H), 5.75 (d, *J* = 10.3, 4H).

S30 (10.8 g, 11.5 mmol) and *p*-formaldehyde (8.6 g) were dissolved in anhydrous THF (114 mL) in a round-bottomed flask equipped with a stirring bar under nitrogen. The solution was cooled at 0 °C in an ice/water bath and, then, anhydrous KO^{t}Bu (4 g, 34.5 mmol, 3 equiv) was added in one portion. The reaction mixture was allowed to warm to rt and stirred at the same temperature during 19 h. The solvent was removed at reduced pressure and the crude was purified by flash column chromatography using hexane as solvent to afford the styrene **S31** (2.9 g, 89% yield) as a white solid. NMR data is in accordance with the previously reported.[249]

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.71 (s, 2H), 6.95 (dd, *J* = 17.2, 10.4 Hz, 2H), 5.71 (d, *J* = 17.2 Hz, 2H), 5.40 (d, *J* = 10.4 Hz, 2H).

General procedure A was followed with some modifications. Silylated arenyne **S32** (3.2g, 98% yield) was obtained as a white solid using **S31** (2.9 g, 10.1 mmol), $PdCl_2(PPh_3)_2$ (0.428 g, 0.61 mmol, 0.06 equiv), CuI (0.194 g, 1 mmol, 0.1 equiv), TMSA (5.8 mL, 41 mmol, 4 equiv) and Et_3N (35 mL, 0.3 M) stirring at reflux o/n. Purification conditions: Hexane as mobile phase.

Melting point: 111.0-111.9 °C

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.65 (s, 2H), 7.10 (dd, *J* = 17.6, 11.0 Hz, 2H), 5.85 (dd, *J* = 17.6, 0.9 Hz, 2H), 5.36 (dd, *J* = 11.0, 0.9 Hz, 2H), 0.27 (s, 18H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 137.1 (2 x C), 132.7 (2 x CH), 127.9 (2 x CH), 120.9 (2 x C), 115.2 (2 x CH_2), 101.8 (2 x C), 99.6 (2 x C), -1.1 (6 x CH_3).

HRMS (APCI) calculated for $C_{20}H_{27}Si_2$ $[M+H]^+$: 323.1646, found 323.1643

General procedure D was followed with some modifications. 1,4-diethynyl-2,5-divinylbenzene **1i** (1.54 g, 89% yield) was obtained as a white solid using **S32** (3.1 g, 9.6 mmol), K_2CO_3 (2.8 g, 20.2 mmol, 2.1 equiv) and MeOH/DCM (1:1, 36 mL) stirring at rt for 2h. Purification conditions: Hexane as mobile phase.

Melting point: 99.3–100.0 °C

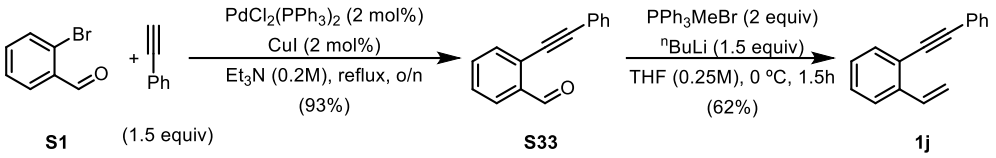
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.70 (s, 2H), 7.13 (dd, *J* = 17.6, 11.0 Hz, 2H), 5.83 (dd, *J* = 17.6, 0.8 Hz, 2H), 5.39 (dd, *J* = 11.0, 0.8 Hz, 2H), 3.38 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 137.5 (2x C), 132.5 (2 x CH), 128.3 (2 x CH), 120.4 (2 x C), 115.6 (2 x CH_2), 82.0 (2 x CH), 80.0 (2 x C).

HRMS (APCI) calculated for $C_{14}H_{11}$ $[M+H]^+$: 179.0855, found 179.0854

*Synthesis of 1-(phenylethynyl)-2-vinylbenzene **1j**[250]*

[248] Jones, D. R.; Point, B.; Levine, M. *J. Phys. Chem. B*, **2019**, *123*, 4604–4610
[249] Gagnon, C.; Godin, É.; Minozzi, C.; Sosoe, J.; Pochet, C.; Collins, S.K. *Science*, **2020**, *367*, 917-921
[250] Mondal, S.; Gold, B.; Mohamed, R. K.; Alabugin, I. V.; *Chem. Eur. J*. **2014**, *20*, 8664 – 8669.



Following *general procedure A*, cross-coupling product **S33** (3.3g, 93%) was obtained as an orange oil using **S1** (2 mL, 17.1 mmol), $Pd(PPh_3)_2Cl_2$ (241 mg, 0.34 mmol, 0.02 equiv), CuI (66 mg, 0.34 mmol, 0.02 equiv), phenylacetylene **2a** (2.8 mL, 25.7 mmol, 1.5 equiv) and Et_3N (86 mL, 0.2 M) stirring at reflux o/n. Purification conditions: Hex/EtOAc (98/2) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 10.66 (s, 1H), 7.95 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.56 (td, *J* = 6.2, 3.3 Hz, 3H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.38 (p, *J* = 3.7 Hz, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 191.6 (CH), 135.9 (C), 133.8 (CH), 133.3 (CH), 131.7 (2 x CH), 129.1 (CH), 128.7 (CH), 128.6 (2 x CH), 127.3 (CH), 126.9 (C), 122.4 (C), 96.4 (C), 85.0 (C).

HRMS (APCI) calculated for $C_{15}H_{11}O$ $[M+H]^+$: 207.0804, found 207.0804

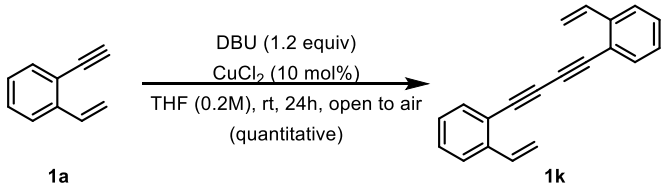
Following *general procedure B,* 1-(phenylethynyl)-2-vinylbenzene **1j** (1.6 g, 90%) was obtained as a colorless oil using **S33** (1.8 g, 8.7 mmol), ^{n}BuLi (5.2 mL, 1.5 equiv, 2.5 M in hexane), methyl(triphenyl)phosphonium bromide (6.2 g, 17.5 mmol, 2 equiv) and THF (11 mL, 0.25 M) stirring at rt for 1.5h. Purification conditions: Hex/EtOAc (98/2) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.66 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.63 – 7.59 (m, 2H), 7.58 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.38 – 7.33 (m, 2H), 7.29 (td, *J* = 7.5, 1.4 Hz, 1H), 5.91 (dd, *J* = 17.6, 1.2 Hz, 1H), 5.44 (dd, *J* = 11.1, 1.1 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 139.1 (C), 135.1 (CH), 132.6 (CH), 131.7 (2 x CH), 128.6 (CH), 128.5 (2 x CH), 128.5 (CH), 127.6 (CH), 124.8 (CH), 123.5 (C), 122.1 (C), 115.7 (CH_2), 94.1 (C), 87.9 (C).

HRMS (APCI) calculated for $C_{16}H_{13}$ $[M+H]^+$: 205.1012, found 205.1008

*Synthesis of 1,4-bis(2-vinylphenyl)buta-1,3-diyne **1k***

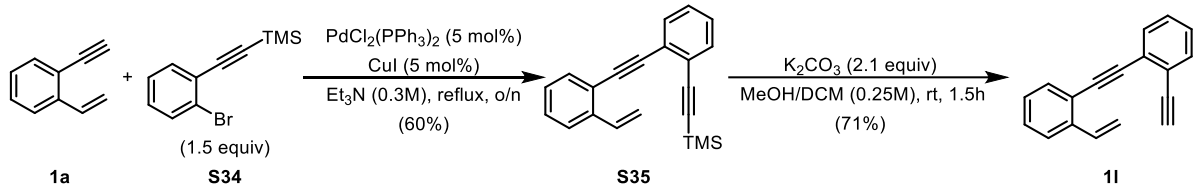


To a solution of enyne **1a** (0.13 g, 1 mmol) in THF (5.1 mL, 0.2 M) was added $CuCl_2$ (0.014 g, 0.1 mmol, 0.1 equiv) and the reaction mixture was allowed to stir at rt during 10 min. After that, DBU (0.19 g, 1.3 mmol) was added to the reaction mixture which was allowed to stir vigorously at room temperature open to the atmosphere until disappearance of the starting material (24h, TLC monitoring). The reaction was concentered to dryness and the residue was purified by flash column chromatography through silica gel using hexane as solvent to afford **1k** in quantitative yield as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm):7.60 (dd, *J* = 7.9, 1.3 Hz, 2H), 7.54 (dd, *J* = 7.7, 1.5 Hz, 2H), 7.35 (td, *J* = 7.7, 1.5 Hz, 2H), 7.30 – 7.19 (m, 4H), 5.86 (dd, *J* = 17.5, 1.1 Hz, 2H), 5.43 (dd, *J* = 11.0, 1.1 Hz, 2H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 140.7 (2 x C), 134.7 (2 x CH), 133.7 (2 x CH), 129.4 (2 x CH), 127.7 (2 x CH), 124.9 (2 x CH), 120.7 (2 x C), 116.5 (2 x CH_2), 81.0 (2 x C), 78.4 (2 x C).

Synthesis of 1-ethynyl-2-((2-vinylphenyl)ethynyl)benzene ***1l***[251]



General procedure A was followed with some modifications. Enediyne **S35** (365 mg, 60%) was obtained as an orange oil using enyne **1a** (0.26 mg, 2 mmol), $Pd(PPh_3)_2Cl_2$ (70 mg, 0.1 mmol, 0.05 equiv), CuI (19 mg, 0.1 mmol, 0.05 equiv), bromo alkyne **S34** (760 mg, 3 mmol, 1.5 equiv) and Et_3N (6.6 mL, 0.3 M) stirring at reflux o/n. Purification conditions: Hex/EtOAc (98/2) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.68 – 7.59 (m, 1H), 7.55 (ddd, *J* = 9.0, 4.7, 1.9 Hz, 2H), 7.43 (dd, *J* = 17.6, 11.0 Hz, 1 H), 7.37 – 7.16 (m, 5H), 5.89 (dd, *J* = 17.6, 1.1 Hz, 1H), 5.40 (dd, *J* = 11.0, 1.1 Hz, 1H), 0.27 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm):139.1 (C), 135.3 (CH), 133.0 (CH), 132.7 (CH), 132.0 (CH), 128.7 (CH), 128.3 (CH), 127.9 (CH), 127.6 (CH), 126.2 (C), 125.6 (C), 124.7 (CH), 122.2 (C), 115.7 (CH_2), 103.7 (C), 98.8 (C), 92.8 (C), 91.9 (C), 0.1 (3 x CH_3).

General procedure D was followed with some modifications. 1-ethynyl-2-((2-vinylphenyl)ethynyl)benzene **1l** (176 mg, 71% yield) was obtained as an orange oil using **S35** (0.32 g, 1.1 mmol), K_2CO_3 (0.31 g, 2.3 mmol, 2.1 equiv) and MeOH/DCM (1:1, 4.2 mL, 0.25 M) stirring at rt for 1.5h. Purification conditions: Hexane as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm):7.49 – 7.46 (m, 1H), 7.45 – 7.42 (m, 1H), 7.42 – 7.39 (m, 2H), 7.36 (d, *J* = 11.0 Hz, 1H), 7.17 (tt, *J* = 7.9, 1.4 Hz, 2H), 7.14 – 7.07 (m, 2H), 5.72 (dd, *J* = 17.6, 1.0 Hz, 1H), 5.23 (dd, *J* = 11.0, 1.0 Hz, 1H), 3.24 (s, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 139.2 (C), 135.3 (CH), 132.8 (CH), 132.7 (CH), 131.9 (CH), 128.8 (CH), 128.6 (CH), 128.0 (CH), 127.6 (CH), 126.5 (C), 124.6 (CH), 124.5(C), 121.9 (C), 115.5 (CH_2), 92.5 (C), 92.0 (C), 82.6 (C), 81.4 (CH).

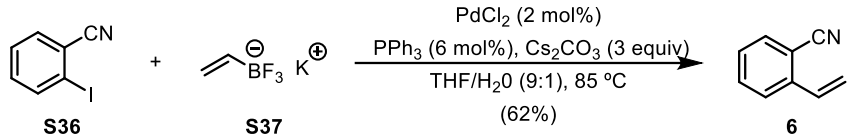
As observed in ^{13}C-NMR DEPT spectrum, a C_q alkyne signal (82.6 ppm) is present when it should not appear in a decoupled experiment. This signal is assigned to a residual ^{1}H-^{13}C NMR coupling. To confirm this, a spin-spin coupling ^{13}C-^{1}H NMR was performed. Terminal C_{sp} is coupled with the contiguous H, 81.4 ppm (d, ^2J = 252 Hz). Diphenylacetylene-type alkyne is coupled to a three bonds length with the aromatic H, 92.5 ppm (d, ^3J = 5.6 Hz) and 92.0 ppm (d,

[251] Hau, S. C. K.; Mak, T. C. W. *Chem. Eur. J.* **2013**, *19*, 5387 – 5400.

^3J = 5.7 Hz). Finally, the internal phenylacetylene-type alkyne is coupled to a three and two bonds length to aromatic and terminal alkyne H, 82.6 ppm (dd, J = 49.7, 5.6 Hz) respectively.

HRMS (APCI) calculated for $C_{18}H_{13}[M+H]^+$: 229.1012, found 229.1012

7.1.2.3. Synthesis of of 2-vinylbenzonitrile 6

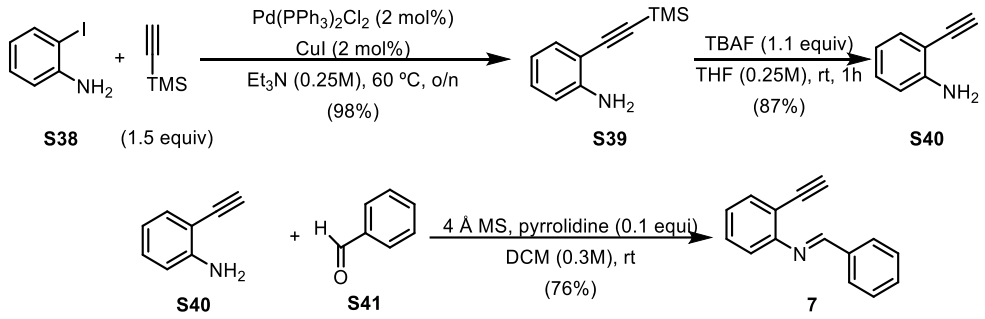


In a sealed tube, a solution of $PdCl_2$ (10.8 mg, 0.061 mmol, 0.02 equiv), PPh3 (47.1 mg, 0.18 mmol, 0.06 equiv), potassium trifluoro(vinyl)borate, **S37,** (0.45 g, 3.19 mmol, 1 equiv), Cs_2CO_3 (2.9 g, 9 mmol, 3 equiv) and 2-iodobenzonitrile, **S36,** (0.688 g, 3 mmol, 1 equiv) in a mixture of THF/H_2O (9:1, 6 mL) was stirred at 85 ^oC until disappearance of the starting material (22h, TLC monitoring). The reaction was quenched by the addition of water (3 mL) and the aqueous phase was extracted with DCM (3 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The residue was purified by flash column chromatography through silica gel using a mixture of hexane/EtOAc (95:5) as eluent to give vinyl product **6** (0.24 g, 62% yield) as a light red oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm):7.60 (m, 3H), 7.33 (m, 1H), 7.07 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.94 (d, *J* = 17.4 Hz, 1H), 5.53 (d, *J* = 11Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 140.7 (CN), 133.0 (CH), 132.9 (CH), 132.8 (CH), 128.0 (CH), 125.5 (CH), 119.0 (CH_2), 117.9 (C), 111.2 (C).

7.1.2.4. Synthesis of (E)-*N*-(2-ethynylphenyl)-1-phenylmethanimine 7[252]



Following *general procedure A*, aniline **S39** (1.89 g, 98%) was obtained as a light orange oil using 2-iodoaniline **S38** (2.20 g, 10 mmol) $Pd(PPh_3)_2Cl_2$ (0.140 g, 0.2 mmol, 0.02 equiv), CuI (0.038 g, 0.2 mmol, 0.02 equiv), TMSA (2.1 mL, 15 mmol, 1.5 equiv) and Et_3N (40 mL, 0.25 M) stirring at 60 ^oC o/n. Purification conditions: Hex/EtOAc (8/2) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.36 (d, *J* = 6.4 Hz, 1H), 7.21 – 7.10 (m, 1H), 6.76 – 6.66 (m, 2H), 4.28 (s, 2H), 0.34 (s, 9H).

[252] Kusama, H.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc*. **2002**, *124*, 11592-11593.

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 148.3 (C), 132.3 (CH), 129.9 (CH), 117.7 (CH), 114.2 (CH), 107.8 (C), 102.0 (C), 99.7 (C), 0.2 (3 x CH_3).

Following *general procedure C*, alkyne **S40** (0.790 g, 87%) was obtained as a light orange oil using **S39** (1.47 g, 7.76 mmol), TBAF (8.8 mL, 1.1 equiv, 1 M in THF) and THF (29 mL, 0.25 M) stirring at 0 ^{o}C during 1h. Purification conditions: Hex/EtOAc (9/1) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.38 – 7.29 (m, 1H), 7.15 (ddd, *J* = 9.3, 7.5, 1.5 Hz, 1H), 6.75 – 6.66 (m, 2H), 4.23 (s, 2H), 3.39 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 148.7 (C), 132.7 (CH), 130.2 (CH), 117.9 (CH), 114.4 (CH), 106.7 (C), 82.5 (CH), 80.8 (C).

In a sealed tube, 2-ethynylaniline **S40** (0.699 g, 5.96 mmol), benzaldehyde **S41** (0.64 mL, 6.26 mmol, 1.05 equiv), pyrrolidine (0.05 mL, 0.6 mmol, 0.1 equiv) and 4 Å MS (1g/mmol) were dissolved in DCM (20 mL,0.3 M). The final mixture was stirred at rt until disappearance of starting material (o/n, GC-MS monitoring). After completion, the reaction mixture was filtered over a plug of celite to render imine **7** (0.93 g, 76%) as a light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 8.46 (s, 1H), 8.00 – 7.90 (m, 2H), 7.57 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.50 (dt, *J* = 5.2, 2.5 Hz, 3H), 7.37 (td, *J* = 7.7, 1.5 Hz, 1H), 7.20 – 7.11 (m, 1H), 7.05 (dd, *J* = 7.9, 1.1 Hz, 1H), 3.21 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm):162.2 (CH), 154.6 (C), 136.1 (C), 133.7 (CH), 131.8 (CH), 129.8 (CH), 129.1 (2 x CH), 128.9 (2 x CH), 125.2 (CH), 119.6 (CH), 115.3 (C), 81.5 (CH), 81.5 (C).

7.1.2.5. Synthesis of starting alkynes 2

Alkynes **2a**, **2b**, **2c**, **2d**, **2e**, **2f**, **2l**, **2n**, **2o**, **2q**, **2s** and **2t** are commercially available. Alkynes **2h**,[253] **2i**,[254] and **2j**[255] were prepared according to the reported literature using the corresponding aldehyde or halogenated compound as starting material through a Corey-Fuchs reaction or Sonogashira reaction followed by protodesylilation reaction, respectively, and characterization data match those reported in the literature. Alkynes **2k**,[256] **2m**,[257] **2p**,[258] and **2r**,[259] were prepared according to reported literature methodology and characterization data match those reported in the literature.

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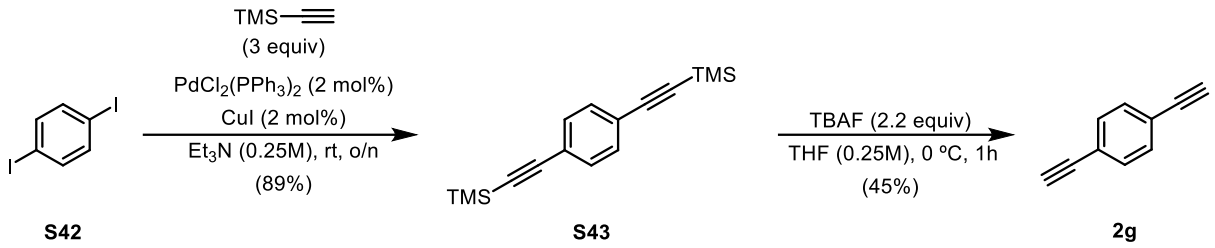
Synthesis of 1,4-diethynylbenzene **2g**



General procedure A was followed with some modifications. Protected alkyne **S43** (1.2 g, 89%) was obtained as a light yellow oil using 1,4-diidobenzene **S42** (1.7 g, 5 mmol), $Pd(PPh_3)_2Cl_2$ (0.07 g, 0.1 mmol, 0.02 equiv), CuI (0.019 g, 0.1 mmol, 0.02 equiv), TMSA (2.1 mL, 15 mmol, 3 equiv) and Et_3N (20 mL, 0.25 M) stirring at rt o/n. Purification conditions: Hex/EtOAc (99/1) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.39 (s, 4H), 0.25 (s, 18H).

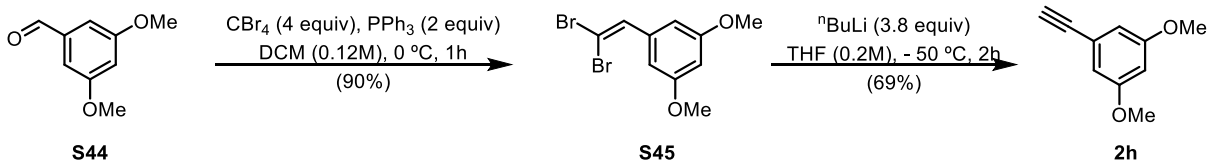
^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 131.7 (4xCH), 123.2 (2 x C), 104.6 (2 x C), 96.3 (2 x C), -0.1 (6 x CH_3).

General procedure C was followed with some modifications. 1,4-diethynylbenzene **2g** (0.31 g, 45 %) was obtained as a white solid using **S43** (1.5 g, 5.5 mmol), TBAF (12.2 mL, 2.2 equiv, 1 M in THF) and THF (22 mL, 0.25 M) stirring at 0 ºC for 1h. Purification conditions: Hex/EtOAc (99/1) as mobile phase.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.44 (s, 4H), 3.17 (s, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 132.2 (4xCH), 122.7 (2 x C), 83.2 (2 x C), 79.2 (2 x CH).

Synthesis of 1-ethynyl-3,5-dimethoxybenzene **2h**



To a solution of PPh_3 (9.6 g, 36.6 mmol, 4 equiv) in DCM (25 mL, 0.12 M) cooled at 0 ºC, was added a solution of CBr_4 (6 g, 18.3 mmol, 2 equiv) in DCM (25 mL). The mixture was stirred at 0 ºC during 30 min, and then, a solution of **S44** (1.5 g, 9.2 mmol) in DCM (25 mL) was added at the same temperature. The final mixture was stirred at room temperature during 30 min (TLC monitoring). The resultant mixture was quenched with a 1:1 mixture of DCM/H_2O, extracted with DCM (3 × 30 mL), dried over $MgSO_4$, filtered and reduced in vacuo, giving a solid yellow crude. The residue was purified by flash chromatography on silica gel (Hex/EtOAc, 8:2) to give **S45** (2.7 g, 90%) as a white solid.

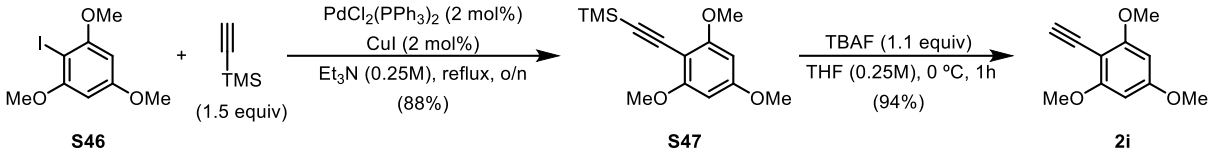
^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.42 (s, 1H), 6.68 (s, 2H), 6.45 (d, *J* = 2.5 Hz, 1H), 3.80 (s, 6H).

Dibromo derivative **S45** (2.6 g, 8.2 mmol) was dissolved in THF (45 ml, 0.2 M) and cooled to -50 °C. ^{n}BuLi (13.5 mL, 34 mmol, 2.5 M in hexane) was added dropwise for 30 min. The solution was stirred for another 2 h at the same temperature. Saturated NH_4Cl (20 mL) was added and the solution warmed to room temperature. The solution was extracted with EtOAc (3x15 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hex/EtOAc, 3:1) to give **2h** (0.92 g, 69%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 6.65 (d, *J* = 2.3 Hz, 2H), 6.47 (t, *J* = 2.3 Hz, 1H), 3.78 (s, 9H), 3.04 (s, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 160.7 (2 x C), 123.5 (C), 110.1 (2 x CH), 102.4 (CH), 83.8 (C), 76.8 (CH), 55.5 (2 x CH_3).

*Synthesis of 2-ethynyl-1,3,5-trimethoxybenzene **2i***



S46 **S47** **2i**

Following *general procedure A*, **S47** (1.1 g, 88%) was obtained as a light orange oil using iodoarene **S46** (1.4 g, 4.6 mmol) $Pd(PPh_3)_2Cl_2$ (0.065 g, 0.093 mmol, 0.02 equiv), CuI (0.018 g, 0.093 mmol, 0.02 equiv), TMSA (1 mL, 6.9 mmol, 1.5 equiv) and Et_3N (19 mL, 0.25 M) stirring at relux o/n. Purification conditions: Hex/EtOAc (8/2) as mobile phase.

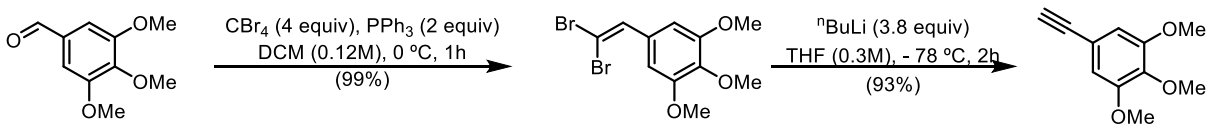
^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 6.06 (s, 2H), 3.84 (s, 3H), 3.81 (s, 3H), 0.26 (s, 9H).

Following *general procedure C*, terminal alkyne **2i** (0.68 g, 94 %) was prepared as a light-yellow oil using **S47** (1.0 g, 3.8 mmol), TBAF (4.3 mL, 1.1 equiv, 1 M in THF) and THF (15 mL, 0.25 M) stirring at 0 ºC during 1h. Purification conditions: Hex/EtOAc (8/2) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 6.09 (s, 2H), 3.86 (s, 6H), 3.81 (s, 3H), 3.47 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 163.1 (2 x C), 162.1 (C), 90.5 (2 x CH), 93.2 (C), 83.8 (CH), 76.7 (C), 56.1 (2 x CH_3), 55.5 (CH_3).

*Synthesis of 5-ethynyl-1,2,3-trimethoxybenzene **2j***



S48 **S49** **2j**

To a solution of PPh_3 (8.0 g, 30.8 mmol, 4 equiv) in DCM (21 mL, 0.12 M) cooled at 0 ºC, was added a solution of CBr_4 (5. G, 15.4 mmol, 2 equiv) in DCM (21 mL). The mixture was stirred at 0 ºC during 30 min, and then, a solution of **S48** (1.5 g, 7.7 mmol) in DCM (22 mL) was added at the same temperature. The final mixture was stirred at room temperature during 30 min (TLC monitoring). The resultant mixture was quenched with a 1:1 mixture of DCM:H_2O, extracted

with DCM (3 × 30 mL), dried over $MgSO_4$, filtered and reduced in vacuo, giving a solid yellow crude. The residue was purified by flash chromatography on silica gel (Hex/EtOAc, 8:2) to give **S49** (2.7 g, 99%) as a white solid.

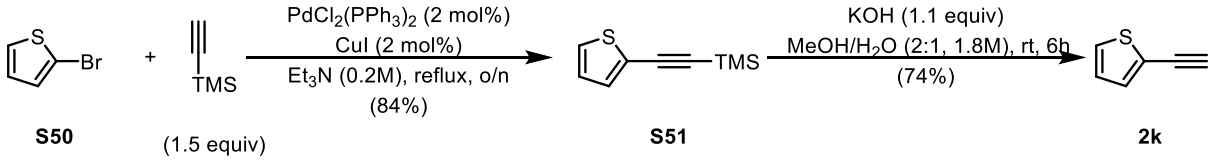
^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.41 (s, 1H), 6.80 (s, 2H), 3.86 (s, 9H).

Dibromo derivative **S49** (2.5 g, 7.1 mmol) was dissolved in THF (25 ml, 0.3 M) and cooled to -78 °C. ^{n}BuLi (11 mL, 27 mmol, 2.5 M in hexane) was added dropwise for 30 min. The solution was stirred for another 2 h at the same temperature. Saturated NH_4Cl (20 mL) was added and the solution warmed to room temperature. The solution was extracted with EtOAc (3x15 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, and then concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hex/EtOAc, 3:1) to give **2j** (1.3 g, 93%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 6.73 (s, 2H), 3.85 (s, 9H), 3.03 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 153.2 (2 x C), 139.5 (C), 117.1 (C), 109.5 (2 x CH), 83.8 (C), 76.3 (CH), 61.0 (CH_3), 56.2 (2 x CH_3).

*Synthesis of 2-ethynyltiophene **2k***



S50 (1.5 equiv) **S51** **2k**

Following *general procedure A*, thiophen **S51** (1.6g, 84%) was prepared as an orange oil using 2-bromothiophene **S50** (1 mL, 10.3 mmol), $Pd(PPh_3)_2Cl_2$ (145 mg, 0.21 mmol, 0.02 equiv), CuI (40 mg, 0.21 mmol, 0.02 equiv), TMSA (2.1 mL, 15.5 mmol, 1.5 equiv) and Et_3N (52 mL, 0.2 M) stirring at reflux o/n. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.23 (d, *J* = 4.4 Hz, 2H), 6.97 – 6.90 (t, *J* = 4.6 Hz, 1H), 0.25 (s, 9H).

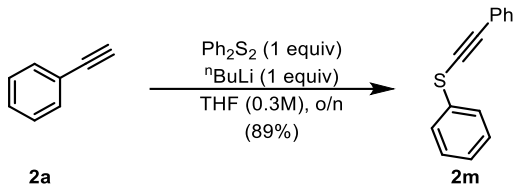
^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 132.6 (CH), 127.2 (CH), 126.8 (CH), 123.3 (C), 98.7 (C), 97.5 (C), -0.2 (3 x CH_3).

To a solution of **S51** (1.75 g, 9.7 mmol) in a mixture of MeOH/H_2O (5.4 mL, 2:1, 1.8 M) was added solid KOH (0.60 g, 10.7 mmol, 1.1 equiv). The reaction mixture was stirred at rt until disappearance of the starting material (6h, TLC monitoring). After this time, water (10 mL) was added to the reaction and then extracted with DCM (3 x 10 mL) The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (99:1) as eluent to afford alkyne **2k** (0.77 g, 74%) as a light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.41 – 7.14 (m, 2H), 6.98 (dd, *J* = 5.2, 3.7 Hz, 1H), 3.34 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 133.2 (CH), 128.5 (CH), 127.0 (CH), 122.2 (C), 81.4 (CH), 77.1 (C).

*Synthesis of phenyl(phenylethynyl)sulfane **2m***

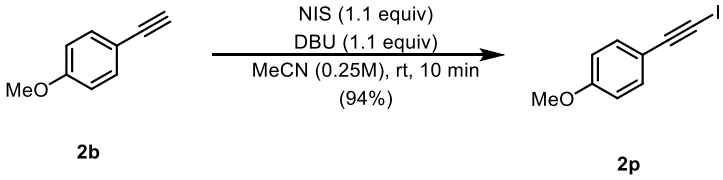


^{n}BuLi (2 mL, 5 mmol, 2.5 M in hexane) was added dropwise to a solution of phenylacetylene **2a** (0.5 mL, 4.5 mmol) in THF (18 mL, 0.25 M) cooled at -78 ^{o}C and the mixture was stirred during 1h at the same temperature. Then, phenyl disulfide (0.98 g, 4.5 mmol, 1 equiv) was added and the reaction was stirred at the same temperature during 1 h and then at room temperature until disappearance of starting material (o/n, TLC monitoring). The resulting mixture was quenched with $NH_4Cl_{(sat)}$ and extracted three times with Et_2O. The organic phase was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) to afford **2m** (0.84 g, 89%) as a light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.55 (ddd, *J* = 7.8, 5.6, 3.5 Hz, 4H), 7.45 – 7.35 (m, 5H), 7.35 – 7.16 (m, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 133.1 (C), 131.9 (CH), 129.4 (2 x CH), 128.8 (CH), 128.5 (CH), 126.7 (CH), 126.4 (2 x CH), 123.1 (C), 98.0 (C), 75.6 (C).

*Synthesis of 1-(iodoethynyl)-4-methoxybenzene **2p***

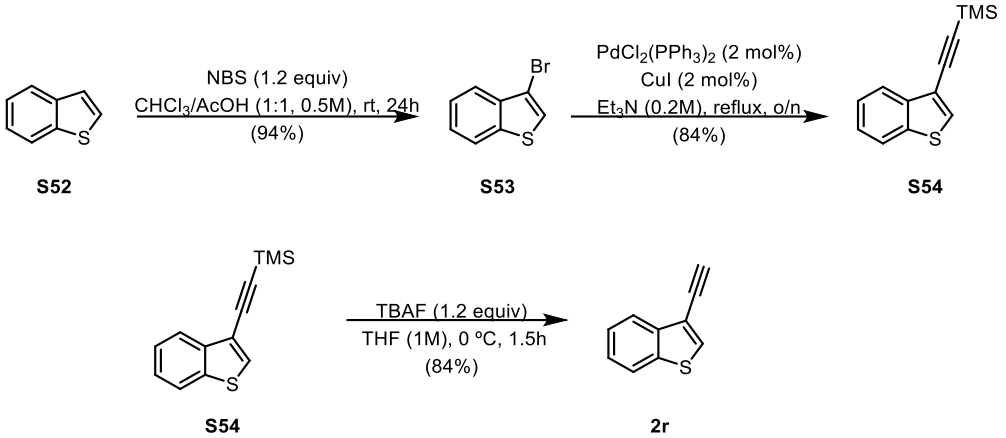


To a solution of 1-ethynyl-4-methoxybenzene **2b** (0.26 mL, 2 mmol) in MeCN (8 mL, 0.25 M) was added NIS (0.5 g, 2.2 mmol, 1.1 equiv) and DBU (0.33 mL, 2.2 mmol, 1.1 equiv). The mixture was stirred at room temperature for 10 min and then, poured into water and extracted with DCM (3 × 10 mL). The combined organic phase was washed with water (3 x 10 mL), filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography using hex as eluent to afford **2p** (0.49 g, 94%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.37 (d, *J* = 9.2 Hz, 2H), 6.83 (d, *J* = 9.1 Hz, 2H), 3.81 (s, 9H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 160.1 (C), 133.9 (2 x CH), 115.7 (C), 114.0 (2 x CH), 94.1 (C), 55.4 (CH_3).

*Synthesis of 3-ethynylbenzo[b]thiophene **2r***



To a solution of **S52** (2 g; 14.9 mmol) in a mixture of $CHCl_3$/AcOH (30 mL, 1:1, 0.5 M), was added stepwise NBS (3.2 g; 17.9 mmol, 1.2 equiv) for 4 h at 0 ^oC and then allowed to stir at room temperature for 24 h. Then $CHCl_3$ (10 mL) was added and the resulting mixture was successively washed with an aqueous solution of sodium thiosulfate (20 mL), a saturated K_2CO_3 solution (10 mL) and water (15 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The resulting red liquid was then filtered of a pad of silica and eluting with hexane to afford **S53** (3g, 94%) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.86 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.50 (d, *J* = 6.8 Hz, 1H), 7.43 (d, *J* = 8.8 Hz, 2H).

Following *general procedure A*, alkynylated thiophene **S54** (2g, 74%) was obtained as a light yellow oil using bromo arene **S53** (2.5 g, 11.8 mmol), $Pd(PPh_3)_2Cl_2$ (165 mg, 0.24 mmol, 0.02 equiv), CuI (45 mg, 0.24 mmol, 0.02 equiv), TMSA (2.4 mL, 17.7 mmol, 1.5 equiv) and Et_3N (59 mL, 0.2 M) stirring at reflux o/n. Purification conditions: Hex/EtOAc (95/5) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.94 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.64 (s, 1H), 7.46 (td, *J* = 7.5, 1.4 Hz, 1H), 7.39 (td, *J* = 7.5, 1.5 Hz, 1H), 0.33 (s, 9H).

Following *general procedure C*, alkyne **2r** (1.2 g, 84 %) was obtained as a light yellow oil using **S54** (1.99 g, 8.6 mmol), TBAF (11 mL, 1.2 equiv, 1 M in THF) and THF (8 mL, 1 M) stirring at 0 ^oC during 1h. Purification conditions: Hex/EtOAc (99/1) as mobile phase.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.99 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.71 (s, 1H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 1H), 3.31 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 139.4 (C), 138.9 (C), 131.5 (CH), 125.3 (CH), 124.9 (CH), 123.1 (CH), 122.7 (CH), 117.4 (C), 79.9 (CH), 77.6 (C).

7.1.2.6. Ru(II)-catalysed [2+2+2] cycloaddition of *ortho*-alkenylarylacetylenes and alkynes

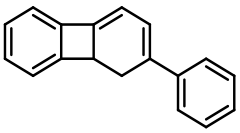
7.1.2.6.1. General procedure

General procedure E for Ru(II)-catalysed [2+2+2] cycloaddition of enynes and alkyne:

In a 10 mL round-bottomed flask, dry and under argon, enyne **1** and alkyne **2** (x equiv) were dissolved in dry MeOH (0.2 M). Then, $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.1 equiv) was added and the resulting solution was stirred at room temperature until disappearance of the starting material (TLC and GC-MS monitoring). The mixture was concentrated under vacuum and the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc as eluent to afford the corresponding dihydrobiphenylene **3**.

7.1.2.6.2. Synthesis of dihydrobiphenylenes 3

*Synthesis of 2-phenyl-1,8b-dihydrobiphenylene **3aa***



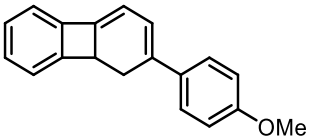
3aa

General procedure E was followed using: $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.012 mg, 0.025 mmol, 0.1 equiv), **1a**, (0.032 g, 0.25 mmol) and phenylacetylene **2a** (0.11 mL, 1 mmol, 4 equiv) in MeOH (1.2 mL). Upon completion (24h, TLC monitoring), purification by column chromatography using a mixture of Hex/EtOAc (98/2) as eluent to afford 2-phenyl-1,8b-dihydrobiphenylene, **3aa**, (35 mg, 60%) as a pale yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.58 – 7.45 (m, 2H), 7.38 (ddd, *J* = 7.8, 6.8, 1.3 Hz, 3H), 7.33 – 7.22 (m, 4H), 6.55 (dd, *J* = 5.1, 2.9 Hz, 1H), 6.25 (dt, *J* = 5.0, 1.3 Hz, 1H), 4.02 (ddd, *J* = 15.2, 7.0, 1.6 Hz, 1H), 3.18 (dd, *J* = 15.3, 7.0 Hz, 1H), 2.67 (tdd, *J* = 15.2, 3.0, 1.0 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm):147.0 (C), 142.8 (C), 141.8 (C), 139.4 (C), 137.9 (C), 128.8 (CH), 128.4 (2 x CH), 128.1 (CH), 127.0 (CH), 125.4 (2 x CH), 123.5 (CH), 122.7 (CH), 119.7 (CH), 113.1 (CH), 43.3 (CH), 31.4 (CH_2).

*Synthesis of 2-(4-methoxyphenyl)-1,8b-dihydrobiphenylene **3ab***



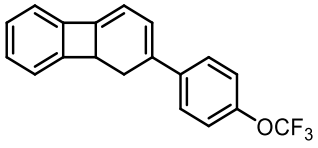
3ab

General procedure E was followed using: $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.006 mg, 0.012 mmol, 0.1 equiv), **1a**, (0.052 g, 0.4 mmol) and 4-ethynylanisole **2b** (0.065 mL, 0.5 mmol, 1.2 equiv) in MeOH (2 mL). Purification by column chromatography using a mixture of Hex/EtOAc (95/5) as eluent to afford 2-(4-methoxyphenyl)-1,8bdihydrobiphenylene, **3ab**, (92 mg, 87%) as a pale yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.49 – 7.42 (m, 2H), 7.34 – 7.24 (m, 4H), 6.97 – 6.89 (m, 2H), 6.48 (dd, *J* = 5.1, 2.9 Hz, 1H), 6.25 (ddd, *J* = 5.1, 1.6, 0.9 Hz, 1H), 4.01 (ddd, *J* = 15.2, 7.0, 1.6 Hz, 1H), 3.86 (s, 3H), 3.16 (dd, *J* = 15.2, 7.0 Hz, 1H), 2.64 (tdd, *J* = 15.2, 2.9, 0.9 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm):158.8 (C), 147.0 (C), 142.9 (C), 139.0 (C), 137.2 (C), 134.5 (C), 128.6 (CH), 128.1 (CH), 126.6 (2 x CH), 122.7 (CH), 121.8 (CH), 119.6 (CH), 113.9 (2 x CH), 113.3 (CH), 55.3 (CH_3), 43.3 (CH), 31.4 (CH_2).

*Synthesis of 2-(4-(trifluoromethoxy)phenyl)-1,8b-dihydrobiphenylene **3ac***



3ac

General procedure E was followed using: $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.025 mg, 0.05 mmol, 0.1 equiv), **1a**, (0.064 g, 0.5 mmol) and 1-ethynyl-4-(trifluoromethoxy)benzene, **2c**, (0.39 mL, 2.5 mmol, 5 equiv) in MeOH (2.5 mL). Upon completion (24h, TLC monitoring), purification by column chromatography using Hex as eluent to afford 2-(4-(trifluoromethoxy)phenyl)-1,8b-dihydrobiphenylene, **3ac**, (52 mg, 33%) as a pale yellow solid.

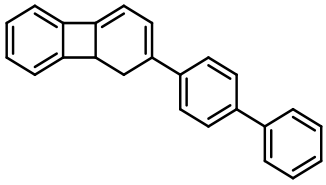
^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.48 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 3.8 Hz, 4H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.51 (d, *J* = 3.8 Hz, 1H), 6.23 (d, *J* = 5.0 Hz, 1H), 4.00 (dd, *J* = 15.2, 7.0 Hz, 1H), 3.11 (dd, *J* = 15.3, 6.9 Hz, 1H), 2.65 (td, *J* = 15.3, 3.0 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm):148.0 (C), 146.9 (C), 142.7 (C), 140.5 (C), 138.3 (C), 137.8 (C), 129.0 (CH), 128.2 (CH), 126.6 (2 x CH), 124.2 (CH), 122.7 (CH), 120.9 (2 x CH), 119.8 (CH), 112.7 (CH), 43.2 (CH_2), 31.3 (CH).

^{19}F NMR (282 MHz, $CDCl_3$), δ (ppm): -57.85.

HRMS (APCI) calculated for $C_{19}H_{12}F_3O$ [M+H]+: 313.0835, found: 313.0834.

*Synthesis of 2-([1,1'-biphenyl]-4-yl)-1,8b-dihydrobiphenylene **3af***



3af

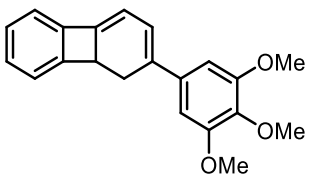
Following the *general procedure **E***, the cycloaddition was carried out using 1-ethynyl-2-vinylbenzene, **1a**, (0.026 g, 0.2 mmol), 4-ethynyl-1,1'-biphenyl, **2f**, (0.142 g, 0.8 mmol, 4 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.01 g, 0.02 mmol, 0.1 equiv) in MeOH (1 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford 2-([1,1'-biphenyl]-4-yl)-1,8b-dihydrobiphenylene, **3af**, (0.033 g, 52%) as a yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.75 – 7.53 (m, 6H), 7.53 – 7.43 (m, 2H), 7.43 – 7.35 (m, 1H), 7.35 – 7.26 (m, 4H), 6.74 – 6.52 (m, 1H), 6.27 (d, *J* = 5.0 Hz, 1H), 4.04 (dd, *J* = 15.2, 7.0 Hz, 1H), 3.23 (ddd, *J* = 15.2, 7.0, 2.2 Hz, 1H), 2.70 (dd, *J* = 17.1, 14.0 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 146.0 (C), 141.8 (C), 139.7 (C), 139.6 (C), 138.7 (C), 137.8 (C), 137.1 (C), 127.8 (CH), 127.8 (2 x CH), 127.1 (CH), 126.2 (CH), 126.1 (2 x CH), 125.9 (2 x CH), 124.7 (2 x CH), 122.4 (CH), 121.7 (CH), 118.7 (CH), 112.1 (CH), 42.3 (CH), 30.2 (CH_2).

HRMS (APCI) calculated for $C_{24}H_{19}$ $[M+H]^+$: 307.1481, found 307.1485.

*Synthesis of 2-(3,4,5-trimethoxyphenyl)-1,8b-dihydrobiphenylene **3aj***



3aj

Following the *general procedure **E***, the cycloaddition was carried out using 1-ethynyl-2-vinylbenzene, **1a**, (0.026 g, 0.2 mmol), 5-ethynyl-1,2,3-trimethoxybenzene, **2j**, (0.154 g, 0.8 mmol, 4 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.01 g, 0.02 mmol, 0.1 equiv) in MeOH (1 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column

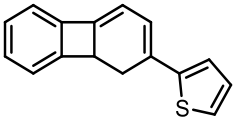
chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford 2-(3,4,5-trimethoxyphenyl)-1,8b-dihydrobiphenylene, **3aj**, (0.051 g, 80%) as a yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.35 – 7.21 (m, 4H), 6.69 (s, 2H), 6.48 (dd, *J* = 5.1, 2.9 Hz, 1H), 6.21 (ddd, *J* = 5.1, 1.7, 0.9 Hz, 1H), 3.99 (ddd, *J* = 15.2, 7.0, 1.7 Hz, 1H), 3.91 (s, 6H), 3.87 (s, 3H), 3.12 (dd, *J* = 15.2, 6.9 Hz, 1H), 2.64 (tdd, *J* = 15.2, 3.0, 0.9 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 152.7 (C), 146.9 (C), 142.9 (C), 139.8 (C), 138.1 (C), 137.9 (C), 137.6 (C), 129.0 (CH), 127.7 (CH), 123.3 (CH), 122.8 (CH), 119.8 (CH), 113.0 (CH), 109.4 (CH), 102.8 (2 x CH), 61.1 (CH_3), 56.2 (2 x CH_3), 43.4 (CH), 31.8 (CH_2).

HRMS (APCI) calculated for $C_{21}H_{21}O_3$ $[M+H]^+$: 321.1485, found 321.1487.

*Synthesis of 2-(1,8b-dihydrobiphenylen-2-yl)thiophene **3ak***



3ak

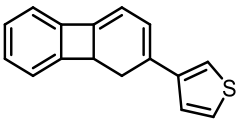
*General procedure **E*** was followed using: $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.010 mg, 0.02 mmol, 0.1 equiv), **1a**, (0.026 g, 0.2 mmol) and 2-ethynyltiophene **2k** (0.112 mg, 1 mmol, 5 equiv) in MeOH (1 mL). Upon completion (24h, TLC monitoring), purification by column chromatography using Hex as eluent to afford 2-(1,8b-dihydrobiphenylen-2-yl)thiophene, **3af**, (21 mg, 45%) as a pale yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.26 (d, *J* = 8.3 Hz, 4H), 7.17 (d, *J* = 5.1 Hz, 1H), 7.12 (d, *J* = 3.5 Hz, 1H), 7.01 (t, *J* = 4.5 Hz, 1H), 6.64 – 6.58 (m, 1H), 6.19 (d, *J* = 5.1 Hz, 1H), 4.00 (dd, *J* = 15.1, 7.0 Hz, 1H), 3.21 (dd, *J* = 15.3, 7.0 Hz, 1H), 2.59 (td, *J* = 15.3, 2.9 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm):146.8 (C), 146.2 (C), 142.9 (C), 138.2 (C), 132.9 (C), 128.9 (CH), 128.2 (CH), 127.6 (CH), 123.7 (CH), 122.7 (CH), 121.7 (CH), 119.6 (CH), 112.8 (CH), 43.3 (CH), 31.8 (CH_2).

HRMS (APCI) calculated for $C_{16}H_{13}S$ $[M+H]^+$: 237.0732, found: 237.0729.

*Synthesis of 3-(1,8b-dihydrobiphenylen-2-yl)thiophene **3aq***



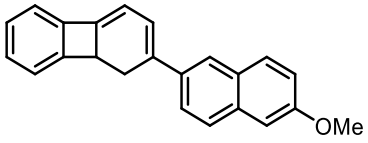
3aq

General procedure E was followed using: $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.021 mg, 0.04 mmol, 0.1 equiv), **1a**, (0.052 g, 0.4 mmol) and 3-ethynyltiophene **2q** (0.125 mL, 1.2 mmol, 3 equiv) in MeOH (2 mL). Upon completion (24h, TLC monitoring), purification by column chromatography using a mixture of Hex/EtOAc (9/1) as eluent to afford 3-(1,8b-dihydrobiphenylen-2-yl)thiophene, **3aq**, (51 mg, 53%) as a pale yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.31 (dd, *J* = 14.0, 4.3 Hz, 7H), 6.60 (dd, *J* = 5.1, 2.8 Hz, 1H), 6.23 (d, *J* = 5.1 Hz, 1H), 4.01 (dd, *J* = 15.1, 7.0 Hz, 1H), 3.19 (dd, *J* = 15.3, 7.0 Hz, 1H), 2.60 (td, *J* = 15.3, 2.9 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 147.0 (C), 143.2 (C), 143.0 (C), 137.8 (C), 134.2 (C), 128.8 (CH), 128.2 (CH), 125.9 (CH), 125.1 (CH), 122.7 (CH), 122.1 (CH), 119.7 (CH), 119.6 (CH), 113.0 (CH), 43.3 (CH), 31.1 (CH_2).

*Synthesis of 2-(6-methoxynaphthalen-2-yl)-1,8b-dihydrobiphenylene **3at***



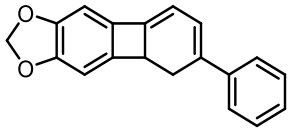
3at

Following the *general procedure* ***E***, the cycloaddition was carried out using 1-ethynyl-2-vinylbenzene, **1a**, (0.043 g, 0.34 mmol), 2-ethynyl-6-methoxynaphthalene, **2t**, (0.180 g, 1 mmol, 3 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.017 g, 0.034 mmol, 0.1 equiv) in MeOH (1.7 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford 2-(6-methoxynaphthalen-2-yl)-1,8b-dihydrobiphenylene, **3at**, (0.087 g, 84%) as a yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.85 (s, 1H), 7.79 – 7.60 (m, 4H), 7.34 – 7.28 (m, 3H), 7.16 (d, *J* = 8.9 Hz, 2H), 6.67 (dd, *J* = 5.1, 2.8 Hz, 1H), 6.33 – 6.25 (m, 1H), 4.06 (dd, *J* = 15.2, 7.0 Hz, 1H), 3.95 (s, 3H), 3.33 (dd, *J* = 15.2, 7.0 Hz, 1H), 2.74 (td, *J* = 15.2, 2.9 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm):157.7 (C), 147.1 (C), 142.9 (C), 139.3 (C), 137.8 (C), 136.8 (C), 133.7 (C), 129.6 (CH), 129.0 (C), 128.8 (CH), 128.2 (CH), 126.8 (CH), 124.5 (CH), 123.8 (CH), 123.1 (CH), 122.7 (CH), 119.7 (CH), 119.0 (CH), 113.2 (CH), 105.7 (CH), 55.3 (CH_3), 43.4 (CH), 31.3 (CH_2).

Synthesis of 6-phenyl-4b,5-dihydrobiphenyleno[2,3-d][1,3]dioxole ***3ba***



3ba

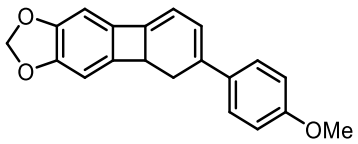
General *procedure* ***E*** was followed using: $[Cp^*Ru(CH_3CN)_3]PF6$ (0.010 mg, 0.02 mmol, 0.1 equiv), **1b**, (0.034 g, 0.2 mmol) and phenylacetylene, **2a,** (0.110 mL, 1 mmol, 5 equiv) in MeOH (1 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9/1) as eluent to afford 6-phenyl-4b,5-dihydrobiphenyleno[2,3-d][1,3]dioxole, **3ba**, (34 mg, 62%) as a pale yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.47 (d, *J* = 7.3 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 1H), 6.79 (d, *J* = 10.8 Hz, 2H), 6.53 (dd, *J* = 5.1, 23.0 Hz, 1H), 6.06 (d, *J* = 5.1 Hz, 1H), 6.04 – 5.89 (m, 2H), 3.83 (dd, *J* = 14.9, 6.6 Hz, 1H), 3.13 (dd, *J* = 14.9, 6.6 Hz, 1H), 2.55 (td, *J* = 14.9, 3.0 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 148.7 (C), 148.2 (C), 141.8 (C), 141.1 (C), 138.5 (C), 136.6 (C), 135.8 (C), 128.4 (2 x CH), 126.8 (CH), 125.3 (2 x CH), 123.6 (CH), 110.1 (CH), 105.0 (CH), 101.5 (CH), 100.7 (CH_2), 41.6 (CH), 31.7 (CH_2).

HRMS (APCI) calculated for $C_{19}H_{15}O_2$ $[M+H]^+$: 275.1067, found 275.1068

Synthesis of 6-(4-methoxyphenyl)-4b,5-dihydrobiphenyleno[2,3-d][1,3]dioxole ***3bb***



3bb

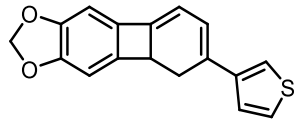
General procedure ***E*** was followed using: $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.015 mg, 0.03 mmol, 0.1 equiv), **1b**, (0.052 g, 0.3 mmol) and 1-ethynyl-4-methoxybenzene, **2b,** (0.150 mL, 1.2 mmol, 4 equiv) in MeOH (1.5 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9/1) as eluent to afford 6-(4-methoxyphenyl)-4b,5-dihydrobiphenyleno[2,3-d][1,3]dioxole, **3bb**, (74 mg, 80%) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.43 – 7.40 (m, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.81 (t, *J* = 0.8 Hz, 1H), 6.77 (t, *J* = 0.8 Hz, 1H), 6.44 (dd, *J* = 5.0, 2.9 Hz, 1H), 6.05 (ddd, *J* = 5.0, 1.5, 0.8 Hz, 1H), 5.97 (d, *J* = 1.5 Hz, 1H), 5.95 (d, *J* = 1.5 Hz, 1H), 3.85 (s, 3H), 3.83 – 3.78 (m, 1H), 3.10 (dd, *J* = 15.0, 6.6 Hz, 1H), 2.51 (tdd, *J* = 15.0, 2.9, 1.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 158.6 (C), 148.5 (C), 148.1 (C), 141.0 (C), 138.1 (C), 135.9 (C), 135.8 (C), 134.6 (C), 126.5 (2 x CH), 121.9 (CH), 113.8 (2 x CH), 110.3 (CH), 104.9 (CH), 101.5 (CH), 100.6 (CH_2), 55.3 (CH_3), 41.6 (CH), 31.7 (CH_2).

HRMS (APCI) calculated for $C_{20}H_{17}O_3$ $[M+H]^+$: 305.1172, found 305.1169.

Synthesis of 6-(thiophen-3-yl)-4b,5-dihydrobiphenyleno[2,3-d][1,3]dioxole ***3bq***



3bq

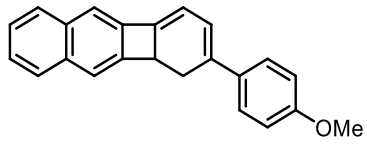
Following the *general procedure* ***E***, the cycloaddition was carried out using 5-ethynyl-6-vinylbenzo[*d*][1,3]dioxole, **1b**, (0.034 g, 0.2 mmol), 3- ethynyltiophene, **2c**, (0.098 mL, 1 mmol, 5 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.010 g, 0.02 mmol, 0.1 equiv) in MeOH (1 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford 6-(thiophen-3-yl)-4b,5-dihydrobiphenyleno[2,3-d][1,3]dioxole, **3bq**, (0.034 g, 61%) as a yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.31 (t, *J* = 1.7 Hz, 2H), 7.23 (s, 2H), 6.78 (d, *J* = 14.6 Hz, 1H), 6.56 (d, *J* = 5.5 Hz, 1H), 6.03 (d, *J* = 5.5 Hz, 1H), 5.96 (dd, *J* = 6.9, 1.7 Hz, 2H), 3.86 – 3.76 (m, 1H), 3.12 (dd, *J* = 15.0, 6.5 Hz, 1H), 2.47 (t, *J* = 15.0 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 147.6 (C), 147.1 (C), 142.3 (C), 139.9 (C), 135.4 (C), 134.9 (C), 132.4 (C), 124.7 (CH), 124.0 (CH), 121.2 (CH), 118.2 (CH), 108.9 (CH), 103.9 (CH), 100.4 (CH), 99.6 (CH_2), 40.6 (CH), 30.4 (CH_2).

HRMS (APCI) calculated for $C_{17}H_{13}O_2S$ $[M+H]^+$: 281.0631, found 281.0635.

Synthesis of 2-(4-methoxyphenyl)-1,10b-dihydrobenzo[b]biphenylene ***3cb***



3cb

Following the *general procedure* ***E***, the cycloaddition was carried out using 2-ethynyl-3-vinylnaphthalene, **1c**, (0.060 g, 0.34 mmol), 4-ethynylanisole, **2b**, (0.218 mL, 1.7 mmol, 5 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.017 g, 0.034 mmol, 0.1 equiv) in MeOH (1.7 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford 2-(4-methoxyphenyl)-1,10b-dihydrobenzo[b]biphenylene, **3cb**, (0.066 g, 63%) as a yellow solid.

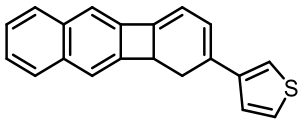
^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.74 (ddt, *J* = 12.4, 7.4, 2.8 Hz, 2H), 7.55 (s, 1H), 7.41 – 7.24 (m, 5H), 6.83 (d, *J* = 8.9 Hz, 2H), 6.41 (dd, *J* = 5.1, 2.9 Hz, 1H), 6.29 (ddd, *J* = 5.1, 2.0, 1.0 Hz, 1H), 4.08 (dd, *J* = 15.6, 7.3 Hz, 1H), 3.76 (s, 3H), 3.10 (dd, *J* = 15.5, 7.5 Hz, 1H), 2.64 (td, *J* = 16.2, 15.7, 3.5 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 157.9 (C), 143.7 (C), 139.9 (C), 138.4 (C), 135.9 (C), 133.7 (C), 133.5 (C), 133.3 (C), 127.8 (CH), 127.3 (CH), 125.5 (2 x CH), 124.5 (CH), 124.3

(CH), 120.9 (CH), 119.5 (CH), 116.5 (CH), 114.3 (CH), 112.9 (2 x CH), 54.3 (CH_3), 42.4 (CH), 30.1 (CH_2).

HRMS (APCI) calculated for $C_{23}H_{19}O$ $[M+H]^+$: 311.1430, found: 311.1421.

Synthesis of 3-(1,10b-dihydrobenzo[b]biphenylen-2-yl)thiophene ***3cq***



3cq

Following the *general procedure* ***E***, the cycloaddition was carried out using 2-ethynyl-3-vinylnaphthalene, **1c**, (0.053 g, 0.3 mmol), 3-ethynyltiophene, **2q**, (0.090 mL, 0.9 mmol, 3 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.015 g, 0.03 mmol, 0.1 equiv) in MeOH (1.5 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford 3-(1,10b-dihydrobenzo[b]biphenylen-2-yl)thiophene, **3cq**, (0.058 g, 58%) as a yellow solid.

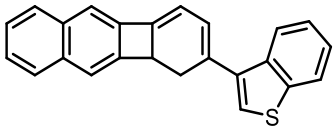
^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.85 – 7.78 (m, 2H), 7.63 (s, 2H), 7.45 – 7.40 (m, 2H), 7.35 – 7.30 (m, 2H), 7.29 (dd, *J* = 2.9, 1.4 Hz, 1H), 6.61 (dd, *J* = 5.1, 2.8 Hz, 1H), 6.35 (ddd, *J* = 5.1, 2.0, 0.9 Hz, 1H), 4.16 (ddd, *J* = 15.8, 7.5, 1.9 Hz, 1H), 3.20 (dd, *J* = 15.5, 7.6 Hz, 1H), 2.69 (tdd, *J* = 15.8, 2.9, 1.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 144.8 (C), 143.2 (C), 141.1 (C), 137.7 (C), 134.9 (C), 134.7 (C), 134.6 (C), 129.0 (CH), 128.5 (CH), 126.1 (CH), 125.7 (CH), 125.5 (CH), 125.2 (CH), 122.3 (CH), 120.7 (CH), 120.1 (CH), 117.7 (CH), 115.1 (CH), 43.5 (CH), 31.0 (CH_2).

Due to the low solubility of the product (in $CDCl_3$ and CD_2Cl_2), it was not possible to achieve a better resolution.

HRMS (APCI) calculated for $C_{20}H_{15}S$ $[M+H]^+$: 287.0889, found 287.0894.

Synthesis of 3-(1,10b-dihydrobenzo[b]biphenylen-2-yl)benzo[b]thiophene ***3cr***



3cr

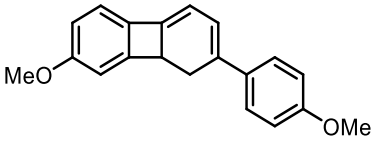
Following the *general procedure* ***E***, the cycloaddition was carried out using 2-ethynyl-3-vinylnaphthalene, **1c**, (0.089 g, 0.5 mmol), 3-ethynylbenzo[*b*]thiophene, **2r**, (0.122 mg, 0.75 mmol, 1.5 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.025 g, 0.050 mmol, 0.1 equiv) in MeOH (2.5 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (92/8) as eluent to afford 3-(1,10b-dihydrobenzo[b]biphenylen-2-yl)thiophene, **3cr**, (0.1 g, 60%) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.94 – 7.90 (m, 1H), 7.82 – 7.78 (m, 1H), 7.78 – 7.74 (m, 2H), 7.74 – 7.70 (m, 2H), 7.56 (d, *J* = 18.0 Hz, 1H), 7.36 – 7.33 (m, 1H), 7.31 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.29 (dd, *J* = 7.8, 1.4 Hz, 2H), 6.52 (dd, *J* = 5.0, 2.9 Hz, 1H), 6.31 (dd, *J* = 4.5, 1.8 Hz, 1H), 4.16 (dd, *J* = 16.0, 7.3 Hz, 1H), 3.06 (dd, *J* = 15.4, 7.3 Hz, 1H), 2.83 (td, *J* = 16.1, 15.7, 3.0 Hz, 1H)

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm):143.5 (C), 139.8 (C), 139.7 (C), 138.2 (C), 136.9 (C), 136.3 (C), 133.9 (C), 133.8 (C), 133.5 (C), 127.8 (CH), 127.4 (CH), 124.6 (CH), 124.4 (CH), 124.0 (CH), 123.4 (CH), 123.2 (CH), 122.4 (CH), 122.0 (CH), 121.3 (CH), 119.6 (CH), 116.7 (CH), 113.8 (CH), 42.3 (CH), 32.0 (CH_2).

HRMS (APCI) calculated for $C_{24}H_{17}S$ $[M+H]^+$: 335.0889, found: 335.0887.

Synthesis of 7-methoxy-2-(4-methoxyphenyl)-1,8b-dihydrobiphenylene ***3db***



3db

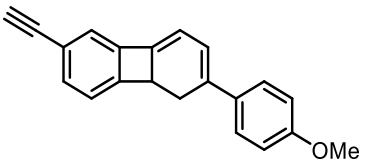
Following the *general procedure* ***E***, the cycloaddition was carried out using 1-ethynyl-4-methoxy-2-vinylbenzene, **1d**, (0.079 g, 0.5 mmol), 4-ethynylanisole, **2b**, (0.198 mg, 1.5 mmol, 3 equiv), $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.025 g, 0.050 mmol, 0.1 equiv) in MeOH (2.5 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford 7-methoxy-2-(4-methoxyphenyl)-1,8b-dihydrobiphenylene, **3cr**, (0.086 g, 59%) as a yellow solid

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.42 (d, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.88 – 6.82 (m, 2H), 6.44 (dd, *J* = 5.1, 2.9 Hz, 1H), 6.08 (dt, *J* = 5.1, 1.2 Hz, 1H), 3.92 (dd, *J* = 15.1, 6.9 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.11 (dd, *J* = 15.1, 6.9 Hz, 1H), 2.58 (td, *J* = 15.2, 3.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 161.1 (C), 158.8 (C), 148.6 (C), 138.0 (C), 136.6 (C), 135.6 (C), 134.7 (C), 126.5 (2 x CH), 122.1 (CH), 121.0 (CH), 115.1 (CH), 113.9 (2 x CH), 110.7 (CH), 108.6 (CH), 55.7 (CH_3), 55.4 (CH_3), 42.9 (CH), 31.4 (CH_2).

HRMS (APCI-probe) calculated for $C_{20}H_{18}O_2$ [M]+: 290.1301, found: 290.1292.

Synthesis of 6-ethynyl-2-(4-methoxyphenyl)-1,8b-dihydrobiphenylene ***3gb***



3gb

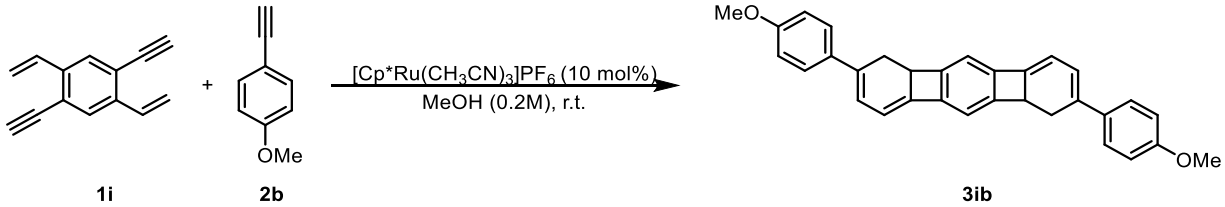
General procedure E was followed using: $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.016 mg, 0.032 mmol, 0.1 equiv), **1f**, (0.050 g, 0.32 mmol) and 4-ethynylanisole, **2b**, (0.21 mL, 1.64 mmol, 5 equiv) in MeOH (1.6 mL). Upon completion (TLC monitoring, 24h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford 6-ethynyl-2-(4-methoxyphenyl)-1,8b-dihydrobiphenylene, **3gb**, (44 mg, 47%) as a pale yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.41 (dd, *J* = 8.9, 3.0 Hz, 3H), 7.36 (s, 1H), 7.21 (d, *J* = 7.5 Hz, 1H), 6.95 – 6.84 (m, 2H), 6.44 (dd, *J* = 5.1, 2.9 Hz, 1H), 6.24 (d, *J* = 4.8 Hz, 1H), 3.96 (dd, *J* = 15.1, 6.9 Hz, 1H), 3.83 (s, 3H), 3.18 – 3.07 (m, 1H), 3.08 (s, 1H), 2.59 (td, *J* = 15.1, 2.9 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 158.9 (C), 147.7 (C), 142.8 (C), 139.3 (C), 135.9 (C), 134.2 (C), 132.7 (CH), 127.2 (2 x CH), 122.9 (CH), 122.7 (CH), 121.8 (CH), 121.6 (CH), 114.3 (CH), 113.9 (2 x CH), 84.1 (C), 76.8 (CH), 55.3 (CH), 43.3 (CH), 30.6 (CH_2).

HRMS (APCI) calculated for $C_{21}H_{17}O$ $[M+H]^+$: 285.1274, found 285.1270.

Synthesis of 2,7-bis(4-methoxyphenyl)-1,5b,6,10b-tetrahydrobenzo[3,4]cyclobuta[1,2-b]biphenylene ***3ib***



1i **2b** **3ib**

In a 10 mL round-bottomed flask, dry and under Ar, were introduced 1,4-diethynyl-2,5-divinylbenzene **1i** (55 mg, 0.31 mmol) and 4-ethynylanisole **2b** (0.12 mL, 0.93 mmol, 3 equiv) in anhydrous MeOH (1.5 mL, 0.2M). After stirring during 5 min, $[Cp^*Ru(CH_3CN)_3]PF_6$ (16 mg, 0.031 mmol, 0.1 equiv) was added and the resulting mixture was stirred at room temperature until disappearance of the starting material (TLC monitoring, 24h). Upon completion, the mixture was filtered using Et_2O as eluent to afford the tetrahydrobiphenylene **3ib** (0.110 mg, 80% yield) as a green-yellow solid.

Scale up: enyne **1i** (0. 534g, 3 mmol), alkyne **2b** (1.2 mL, 9 mmol). Product obtained: tetrahydrobiphenylene **3ib** (1.1 g, 83 % yield).

Melting point: >400 ^oC

^{1}H NMR (500 MHz, 1,1,2,2-tetrachloroethane-d_2, 50 ^oC) δ (ppm): 6.57 (d, *J* = 8.4 Hz, 2H), 6.29 (s, 1H), 6.03 (d, *J* = 8.4 Hz, 2H), 5.61 (dd, *J* = 5.1, 2.7 Hz, 1H), 5.35 (d, *J* = 5.1 Hz, 1H), 3.04 (dd, *J* = 15.2, 6.8 Hz, 1H), 2.96 (s, 3H), 2.28 (dd, *J* = 15.2, 6.8 Hz, 1H), 1.71 (m, 1H). *Due to the symmetry of the molecule, only half of the peaks are observed.*

^{13}C NMR (126 MHz, 1,1,2,2-tetrachloroethane-d_2, 50 ^oC) δ (ppm): 158.3 (C), 146.4 (C), 142.5 (C), 138.3 (C), 136.6 (C), 133.8 (C), 126.0 (2 x CH), 121.4 (CH), 113.8 (CH), 113.5 (2 x CH), 112.4 (CH), 54.9 (CH_3), 42.1 (CH), 30.8 (CH_2).

HRMS (APCI) calculated for $C_{32}H_{27}O_2$ $[M+H]^+$: 443.2006, found 443.2016.

7.1.2.7. Ru(II)-catalysed [2+2+2] dimerization of ortho-alkenylarylacetylenes

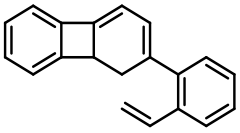
7.1.2.7.1. General procedure

General procedure F for Ru(II)-catalysed [2+2+2] dimerization of ortho-alkenylarylacetylenes:

In a 10 mL round-bottomed flask, dry and under argon, enyne **1** was dissolved in MeOH (0.2 M). Then, $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.1 equiv) was added and the resulting solution was stirred at room temperature until disappearance of the starting material (TLC and GC-MS monitoring). The mixture was concentrated under vacuum and the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc as eluent to afford the corresponding dihydrobiphenylene **4**.

7.1.2.7.2. Synthesis of dihydrobiphenylenes 4

*2-(2-vinylphenyl)-1,8b-dihydrobiphenylene **4a***



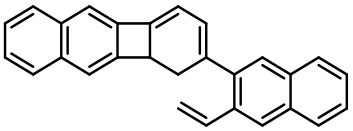
4a

General procedure ***F*** was used using 1-ethynyl-2-vinylbenzene, **1a**, (0.048 g, 0.37 mmol) and $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.019 mg, 0.037 mmol, 0.1 equiv) in MeOH (1.9 mL). Upon completion (TLC monitoring, 2h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (98/2) as eluent to afford 2-(2-vinylphenyl)-1,8b-dihydrobiphenylene, **4a,** (29 mg, 61%) as a pale yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.61 – 7.55 (m, 2H), 7.38 – 7.06 (m, 7H), 6.96 (dd, *J* = 17.5, 10.9 Hz, 1H), 6.22 (dd, *J* = 13.3, 3.8 Hz, 1H), 5.73 (d, *J* = 17.5 Hz, 1H), 5.29 (d, *J* = 11.0 Hz, 1H), 4.06 (dd, *J* = 15.2, 6.8 Hz, 1H), 2.89 (dd, *J* = 15.5, 6.8 Hz, 1H), 2.64 (t, *J* = 15.2 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 147.0 (C), 142.8 (C), 142.4 (C), 140.0 (C), 137.6 (C), 136.2 (CH), 135.4 (C), 128.8 (CH), 128.5 (CH), 128.1 (CH), 127.6 (CH), 127.1 (CH), 126.6 (CH), 126.0 (CH), 122.7 (CH), 119.7 (CH), 114.6 (CH_2), 112.8 (CH), 43.4 (CH), 34.3 (CH_2).

Synthesis of 2-(3-vinylnaphthalen-2-yl)-1,10b-dihydrobenzo[b]biphenylene ***4c***



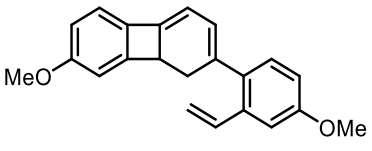
4c

General procedure ***F*** was used using 2-ethynyl-3-vinylnaphthalene, **1c**, (0.036 g, 0.2 mmol) and $[Cp^*Ru(CH_3CN)_3]PF6$ (0.010 g, 0.02 mmol, 0.1 equiv) in MeOH (1 mL). Upon completion (TLC monitoring, 2h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (98/2) as eluent to afford 2-(3-vinylnaphthalen-2-yl)-1,10b-dihydrobenzo[b]biphenylene, **4c**, (28 mg, 79%) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.91 (d, *J* = 15.0 Hz, 1H), 7.73 (dtd, *J* = 22.4, 6.4, 3.3 Hz, 4H), 7.59 (d, *J* = 6.9 Hz, 2H), 7.53 (s, 1H), 7.36 (ddt, *J* = 7.8, 6.1, 3.8 Hz, 4H), 6.95 (dd, *J* = 17.4, 10.9 Hz, 1H), 6.31 (dd, *J* = 4.9, 1.9 Hz, 1H), 6.25 (dd, *J* = 4.8, 2.9 Hz, 1H), 5.77 (dd, *J* = 17.4, 1.4 Hz, 1H), 5.27 (dd, *J* = 10.9, 1.4 Hz, 1H), 4.18 (dd, *J* = 16.0, 7.3 Hz, 1H), 2.90 (dd, *J* = 15.7, 7.3 Hz, 1H), 2.68 (td, *J* = 15.8, 3.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 143.6 (C), 139.8 (C), 139.8 (C), 139.7 (C), 136.5 (C), 135.5 (C), 133.8 (C), 133.5 (CH), 133.4 (C), 131.9 (C), 131.6 (C), 127.8 (CH), 127.4 (CH), 126.7 (CH), 126.5 (CH), 125.8 (CH), 125.5 (CH), 125.1 (CH), 125.0 (CH), 124.6 (CH), 124.3 (CH), 124.2 (CH), 119.6 (CH), 116.7 (CH), 114.4 (CH_2), 113.9 (CH), 42.5 (CH), 33.0 (CH_2).

Synthesis of 7-methoxy-2-(4-methoxy-2-vinylphenyl)-1,8b-dihydrobiphenylene ***4d***



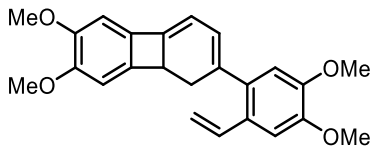
4d

General procedure ***F*** was used using 1-ethynyl-4-methoxy-2-vinylbenzene, **1d**, (0.069 g, 0.44 mmol) and $[Cp^*Ru(CH_3CN)_3]PF6$ (0.022 mg, 0.044 mmol, 0.1 equiv) in MeOH (2.2 mL). Upon completion (TLC monitoring, 2h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (98/2) as eluent to afford 7-methoxy-2-(4-methoxy-2-vinylphenyl)-1,8b-dihydrobiphenylene, **4d**, (42 mg, 61%) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.19 – 7.12 (m, 2H), 7.08 (d, *J* = 2.7 Hz, 1H), 6.92 (dd, *J* = 17.5, 10.9 Hz, 1H), 6.86 – 6.80 (m, 3H), 6.11 (dd, *J* = 4.8, 2.9 Hz, 1H), 6.06 (dt, *J* = 4.7, 1.3 Hz, 1H), 5.69 (dd, *J* = 17.5, 1.4 Hz, 1H), 5.27 (dd, *J* = 10.9, 1.3 Hz, 1H), 3.99 – 3.91 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 2.82 (dd, *J* = 15.4, 6.7 Hz, 1H), 2.56 (tdd, *J* = 15.2, 3.0, 1.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 161.0 (C), 158.6 (C), 148.5 (C), 138.5 (C), 136.6 (2 x C), 136.4 (CH), 135.6 (C), 135.4 (C), 129.6 (CH), 126.5 (CH), 121.0 (CH), 115.1 (CH), 114.6 (CH_2), 113.5 (CH), 111.0 (CH), 110.3 (CH), 108.5 (CH), 55.6 (CH_3), 55.3 (CH_3), 42.9 (CH), 34.4 (CH_2).

Synthesis of 2-(4,5-dimethoxy-2-vinylphenyl)-6,7-dimethoxy-1,8b-dihydrobiphenylene ***4e***



4e

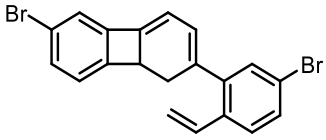
General procedure ***F*** was used using 1-ethynyl-4,5-dimethoxy-2-vinylbenzene, **1e**, (0.037 g, 0.2 mmol) and $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.010 mg, 0.02 mmol, 0.1 equiv) in MeOH (1 mL). Upon completion (TLC monitoring, 2h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (8/2) as eluent to afford 2-(4,5-dimethoxy-2-vinylphenyl)-6,7-dimethoxy-1,8b-dihydrobiphenylene, **4e**, (28 mg, 74%) as a yellow-green foam.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 6.97 (s, 1H), 6.83 – 6.78 (m, 1H), 6.77 (d, *J* = 1.9 Hz, 2H), 6.62 (s, 1H), 5.49 (dd, *J* = 17.5, 1.2 Hz, 1H), 5.08 (dd, *J* = 10.9, 1.2 Hz, 1H), 3.87 (dd, *J* = 6.6, 1.5 Hz, 1H), 3.85 (s, 3H), 3.82 – 3.81 (m, 9H), 2.75 (dd, *J* = 15.2, 6.4 Hz, 1H), 2.46 (td, *J* = 14.9, 3.1 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 151.4 (C), 150.7 (C), 148.7 (C), 148.1 (C), 139.5 (C), 138.7 (C), 136.9 (C), 136.0 (CH), 135.9 (C), 134.8 (C), 128.0 (C), 126.8 (CH), 112.5 (CH_2), 111.5 (CH), 109.7 (CH), 108.6 (CH), 106.7 (CH), 103.7 (CH), 56.4 (CH_3), 56.4 (CH_3), 56.1 (2 x CH_3), 42.8 (CH), 35.2 (CH_2).

HRMS (APCI) calculated for $C_{24}H_{25}O_4$ $[M+H]^+$: 377.1747, found 377.1750.

Synthesis of 6-bromo-2-(5-bromo-2-vinylphenyl)-1,8b-dihydrobiphenylene ***4f***



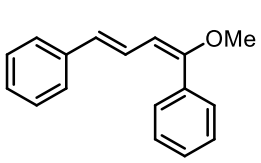
4f

General procedure ***F*** was used using 4-bromo-2-ethynyl-1-vinylbenzene, **1f**, (0.063 g, 0.3 mmol) and $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.015 mg, 0.03 mmol, 0.1 equiv) in MeOH (1.5 mL). Upon completion (TLC monitoring, 2h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (98/2) as eluent to afford 6-bromo-2-(5-bromo-2-vinylphenyl)-1,8b-dihydrobiphenylene, **4f**, (44 mg, 70%) as a green oil.

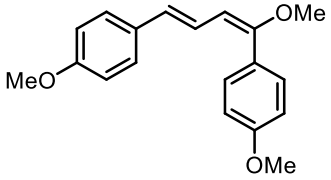
^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.41 – 7.22 (m, 6H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.72 (dd, *J* = 17.5, 11.0 Hz, 1H), 6.15 – 6.07 (m, 1H), 5.60 (dd, *J* = 17.5, 1.2 Hz, 1H), 5.21 (dd, *J* = 10.9, 1.2 Hz, 1H), 3.85 (ddd, *J* = 15.2, 6.8, 1.6 Hz, 1H), 2.73 (dd, *J* = 15.6, 6.8 Hz, 1H), 2.47 (td, *J* = 16.1, 3.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 145.4 (C), 144.1 (C), 143.9 (C), 139.2 (C), 136.6 (C), 135.2 (CH), 134.5 (C), 131.9 (CH), 131.3 (CH), 130.3 (CH), 127.8 (CH), 127.3 (CH), 124.6 (CH), 123.2 (CH), 122.4 (C), 121.5 (C), 115.5 (CH_2), 114.0 (CH), 42.8 (CH), 33.9 (CH_2).

7.1.2.8. Data of isolated 1,3-diene 5a and 5b[260]



5a



5b

5a: ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.53 – 7.48 (m, 2H), 7.48 – 7.41 (m, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.32 – 7.26 (m, 4H), 7.21 – 7.16 (m, 1H), 6.59 (d, *J* = 15.8 Hz, 1H), 6.15 (d, *J* = 10.9 Hz, 1H), 3.65 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 156.3 (C), 138.0 (C), 135.5 (C), 131.3 (CH), 128.7 (2 x CH), 128.7 (2 x CH), 128.4 (CH), 127.4 (CH), 126.5 (2 x CH), 126.2 (2 x CH), 123.6 (CH), 114.7 (CH), 59.7 (CH_3).

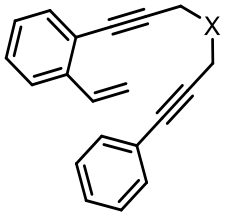
5b: ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.47 (d, *J* = 8.6 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.18 (dd, *J* = 15.8, 10.8 Hz, 1H), 6.90 (dd, *J* = 11.9, 8.5 Hz, 4H), 6.55 (d, *J* = 15.8 Hz, 1H), 6.08 (d, *J* = 10.8 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.68 (s, 3H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 159.8 (C), 159.1 (C), 155.4 (C), 131.1 (C), 130.0 (CH), 128.2 (C), 127.5 (2 x CH), 127.4 (2 x CH), 121.8 (CH), 114.2 (2 x CH), 114.1 (2 x CH), 113.4 (CH), 59.6 (2 x CH_3), 55.4 (CH_3).

[260] Characterization data match those reported in the literature: Zhang, M.; Jiang, H.-F.; Neumann, H.; Beller, M.; Dixneuf, P.-H. *Angew. Chem. Int. Ed*. **2009,** *48*, 1681-1684.

7.1.3. Reactivity of dihydrobiphenylenes: Experimental procedures

7.1.3.1. Synthesis of starting enediynes 17a-b



17a, X = O
17b, X = NTs

Enediynes **17a-b** were prepared according to the reported procedure and data analyses are in accordance with the previously reported.[215]

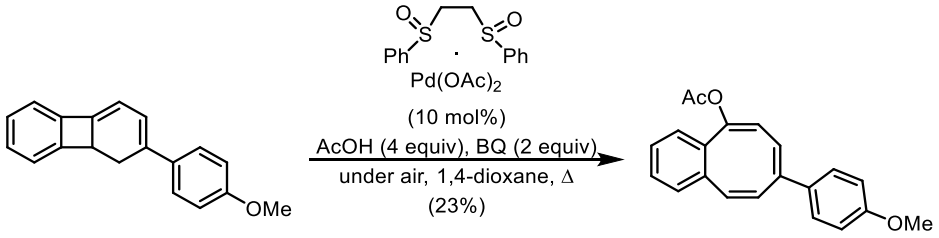
17a: ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.57 (d, *J* = 7.9 Hz, 1H), 7.46 (ddq, *J* = 7.8, 4.8, 1.8 Hz, 3H), 7.36 – 7.26 (m, 5H), 7.26 – 7.17 (m, 1H), 5.80 (dd, *J* = 17.6, 1.2 Hz, 1H), 5.35 (dd, *J* = 11.0, 1.2 Hz, 1H), 4.60 (d, *J* = 0.9 Hz, 2H), 4.56 (d, *J* = 0.9 Hz, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 139.4 (C), 134.9 (CH), 132.9 (CH), 132.0 (2 x CH), 128.8 (CH), 128.7 (CH), 128.4 (2 x CH), 127.6 (CH), 124.7 (CH), 122.6 (C), 121.3 (C), 115.9 (CH_2), 89.1 (C), 87.0 (C), 85.3 (C), 84.5 (C), 57.6 (CH_2), 57.5 (CH_2).

17b: ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.81 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.24 (tdd, *J* = 12.6, 9.5, 6.5 Hz, 10H), 7.00 (dd, *J* = 17.6, 11.1 Hz, 1H), 5.77 (d, *J* = 17.6 Hz, 1H), 5.28 (d, *J* = 11.0 Hz, 1H), 4.53 (s, 2H), 4.48 (s, 2H), 2.31 (s, 3H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 143.9 (C), 139.2 (C), 135.2 (C), 134.6 (CH), 132.7 (CH), 131.7 (2 x CH), 129.7 (2 x CH), 128.7 (CH), 128.6 (CH), 128.2 (2 x CH), 128.0 (2 x CH), 127.3 (CH), 124.5 (CH), 122.2 (C), 120.9 (C), 115.8 (CH_2), 86.2 (C), 85.9 (C), 84.3 (C), 81.6 (C), 37.6 (CH_2), 37.5 (CH_2), 21.4 (CH_3).

7.1.3.2. Synthesis of acetylated COT 11ab via allylic functionalization



3ab **11ab**

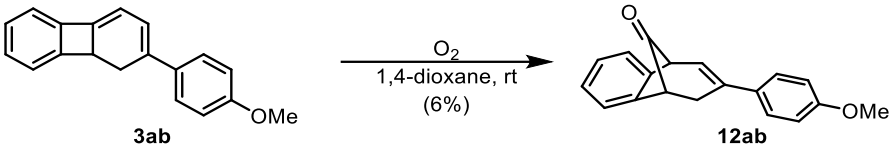
In a round-bottomed flask equipped with a stirring bar, $Pd(OAc)_2$ (0.007 g, 0.015 mmol, 0.01 equiv), BQ (0.033 g, 0.3 mmol, 2 equiv), **3ab** (0.039 g, 0.15 mmol) and AcOH (0.034 mL, 0.6 mmol, 4 equiv) in dry 1,4-dioxane (0.68 mL, 0.22 M) were added. The final solution was stirred at 43 °C until disappearance of starting material (24h, TLC monitoring). After this time, an aqueous solution of $NaHSO_3$ 10% was added and extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated under vacuum. The resulting crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9/1) as eluent to afford (5E,7E,9Z)-8-(4-methoxyphenyl)benzo[8]annulen-5-yl acetate **11ab** (0.011 mg, 23%) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.22 (d, *J* = 8.8 Hz, 2H), 7.20 – 7.16 (m, 1H), 7.15 – 7.08 (m, 2H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.86 (d, *J* = 11.6 Hz, 1H), 6.74 (d, *J* = 8.8 Hz, 2H), 6.30 (d, *J* = 11.6 Hz, 1H), 6.03 (d, *J* = 4.1 Hz, 1H), 5.97 (dd, *J* = 4.4, 1.1 Hz, 1H), 3.71 (s, 3H), 2.05 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 169.2 (C), 159.5 (C), 147.9 (C), 141.4 (C), 138.7 (C), 135.7 (C), 133.7 (CH), 132.4 (CH), 132.3 (C), 129.1 (CH), 128.6 (CH), 127.6 (3 x CH), 127.2 (CH), 121.4 (CH), 119.6 (CH), 113.8 (2 x CH), 55.4 (CH_3), 21.1 (CH_3).

HRMS (APCI) calculated for $C_{21}H_{19}O_3$ $[M+H]^+$: 319.1329, found 319.1326.

7.1.3.3. Synthesis of benzoannulen[7]one 12ab



3ab **12ab**

In a round-bottomed flask, dry and equipped with a stirring bar, **3ab** (0.14g, 0.55 mmol) was dissolved in dry 1,4-dioaxane (2.5 mL, 0.22 M). The mixture was stirred at rt until disappearance of starting dihydrobiphenylene (1h, TLC monitoring). After this time, the reaction mixture was concentrated to dryness and the resulting crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9/1) as eluent to afford product **12ab** (7 mg, 6%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.26 – 7.22 (m, 4H), 7.21 (d, *J* = 9.0 Hz, 2H), 6.79 (d, *J* = 9.0 Hz, 2H), 6.43 (dd, *J* = 7.5, 2.0 Hz, 1H), 3.77 (s, 3H), 3.67 (dd, *J* = 7.5, 1.2 Hz, 1H), 3.60 (dt, *J* = 5.4, 1.7 Hz, 1H), 3.38 (ddd, *J* = 16.8, 5.4, 2.0 Hz, 1H), 2.98 (m, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 211.4 (C), 159.5 (C), 145.9 (C), 140.5 (C), 134. (C), 131.8 (C), 127.5 (CH), 127.5 (CH), 126.7 (CH), 126.2 (2 x CH), 123.8 (CH), 121.4 (CH), 113.8 (2 x CH), 55.4 (CH), 50.5 (CH), 50.3 (CH), 39.1 (CH_2).

7.1.3.4. Radical ring expansion of dihydrobiphenylenes to halogenated benzofused cyclooctatetraenes

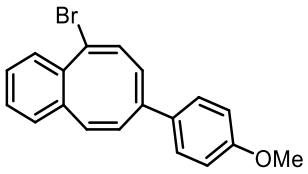
7.1.3.4.1. General procedure

General procedure G for radical ring opening of dihydrobiphenylenes:

In a double-neck round-bottomed flask, dry and under Ar, was prepared a solution of dihydrobiphenylene **3** in solvent (0.036 M) and degassed with an Ar balloon for 15 min. Then, AIBN (0.11 equiv) and NXS (1.1 equiv) were added. The resulting mixture was refluxed in an aluminium heating block until disappearance of the starting material (1h, TLC monitoring). The crude was concentrated to dryness and the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc as eluent to afford the corresponding benzofused cyclooctatetraene **16**.

7.1.3.4.2. Synthesis of benzofused cyclooctatetraenes 16

Synthesis of (5E,7E,9Z)-5-bromo-8-(4-methoxyphenyl)benzo[8]annulene ***16ab***



16ab

Amounts used: dihydrobiphenylene **3ab** (0.072 g, 0.28 mmol), AIBN (0.005 g, 0.03 mmol), NBS (0.056 g, 0.3 mmol), CCl_4 (7.8 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16ab** (80 mg, 85% yield), yellow solid.

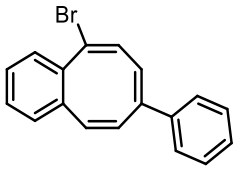
Melting point: 111.8-112.9 °C

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): δ 7.47 – 7.42 (m, 1H), 7.33 – 7.26 (m, 4H), 7.06 (ddd, *J* = 6.6, 2.3, 0.8 Hz, 1H), 6.93 (d, *J* = 11.6 Hz, 1H), 6.85 (d, *J* = 8.9 Hz, 2H), 6.76 (dd, *J* = 4.1, 1.3 Hz, 1H), 6.37 (dd, *J* = 11.6, 1.3 Hz, 1H), 6.06 (d, *J* = 4.1 Hz, 1H), 3.82 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 158.5 (C), 140.0 (C), 138.2 (C), 135.7 (C), 132.9 (CH), 132.0 (CH), 131.5 (CH), 130.6 (C), 129.2 (CH), 127.6 (CH), 127.3 (CH), 126.5 (2 x CH), 126.2 (CH), 122.9 (CH), 121.3 (C), 112.7 (2 x CH), 54.3 (CH_3).

HRMS (APCI) calculated for $C_{19}H_{16}BrO$ $[M+H]^+$: 339.0379, found 339.0380.

Synthesis of (5E,7E,9Z)-5-bromo-8-phenylbenzo[8]annulene ***16aa***



16aa

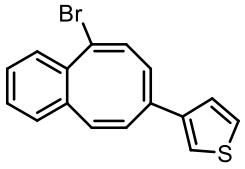
Amounts used: dihydrobiphenylene **3aa** (0.068 g, 0.29 mmol), AIBN (0.006 g, 0.034 mmol), NBS (0.058 g, 0.32 mmol), CCl_4 (8.3 mL). Solvents used: Hex/EtOAc 98/02. Product obtained: bCOT **16aa** (44 mg, 48% yield), yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.50 – 7.35 (m, 1H), 7.33 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.22 – 7.19 (m, 2H), 7.19 – 7.15 (m, 2H), 6.95 (dd, *J* = 7.0, 1.9 Hz, 1H), 6.83 (d, *J* = 11.6 Hz, 1H), 6.65 (dd, *J* = 4.1, 1.3 Hz, 1H), 6.26 (dd, *J* = 11.6, 1.3 Hz, 1H), 6.03 (d, *J* = 4.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 141.8 (C), 139.3 (C), 139.2 (C), 136.8 (C), 133.9 (CH), 133.4 (CH), 132.5 (CH), 130.4 (CH), 128.8 (CH), 128.5 (3 x CH), 128.1 (CH), 127.4 (CH), 126.5 (2 x CH), 125.7 (CH), 122.8 (C).

HRMS (APCI) calculated for $C_{18}H_{14}Br$ $[M+H]^+$: 309.0273; found: 309.0271.

Synthesis of 3-((5Z,7E,9E)-10-bromobenzo[8]annulen-7-yl)thiophene ***16aq***



16aq

Amounts used: dihydrobiphenylene **3aq** (0.072 g, 0.3 mmol), AIBN (0.006 g, 0.034 mmol), NBS (0.060 g, 0.33 mmol), CCl_4 (8.5 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16aq** (53 mg, 55% yield), yellow solid.

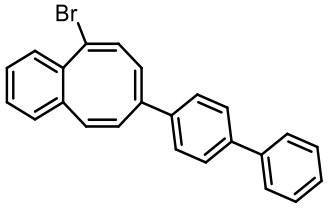
Melting point: 86.0-86.9 °C

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.51 – 7.36 (m, 1H), 7.32 – 7.24 (m, 3H), 7.19 – 7.16 (m, 2H), 7.09 – 6.99 (m, 1H), 6.91 (d, *J* = 11.6 Hz, 1H), 6.77 (dd, *J* = 4.2, 1.3 Hz, 1H), 6.44 (dd, *J* = 11.6, 1.3 Hz, 1H), 6.15 (d, *J* = 4.2 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 141.0 (C), 139.0 (C), 136.6 (C), 136.5 (C), 133.5 (CH), 133.1 (CH), 131.7 (CH), 130.3 (CH), 128.7 (CH), 128.4 (CH), 127.3 (CH), 125.9 (CH), 125.0 (CH), 124.5 (CH), 122.7 (C), 121.9 (CH).

HRMS (APCI) calculated for $C_{16}H_{12}BrS$ $[M+H]^+$: 314.9838, found 314.9835.

Synthesis of (5E,7E,9Z)-8-([1,1'-biphenyl]-4-yl)-5-bromobenzo[8]annulene ***16af***



16af

Amounts used: dihydrobiphenylene **3af** (0.031 g, 0.1 mmol), AIBN (0.002 g, 0.011 mmol), NBS (0.020 g, 0.11 mmol), CCl_4 (2.8 mL). Solvents used: Hex/EtOAc 97/03. Product obtained: bCOT **16af** (23 mg, 60% yield), yellow solid.

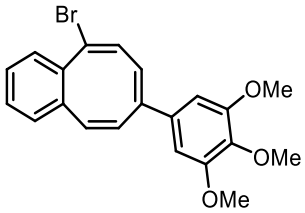
Melting point: 148.0-149.1 °C

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.57 (ddd, *J* = 11.5, 7.7, 1.8 Hz, 4H), 7.49 – 7.40 (m, 5H), 7.38 (dd, *J* = 6.7, 1.8 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.13 – 7.05 (m, 1H), 6.97 (d, *J* = 11.5 Hz, 1H), 6.79 (dd, *J* = 4.0, 1.3 Hz, 1H), 6.42 (dd, *J* = 11.6, 1.3 Hz, 1H), 6.20 (d, *J* = 4.0 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 141.2 (C), 140.8 (C), 140.6 (C), 139.2 (C), 138.0 (C), 136.6 (C), 133.8 (CH), 133.4 (CH), 132.3 (CH), 130.3 (CH), 128.8 (2 x CH), 128.6 (CH), 128.4 (CH), 127.4 (CH), 127.3 (CH), 127.1 (2 x CH), 127.0 (2 x CH), 126.7 (2 x CH), 125.6 (CH), 122.7 (C).

HRMS (APCI) calculated for $C_{24}H_{18}Br$ $[M+H]^+$: 385.0586, found 385.0583.

Synthesis of (5E,7E,9Z)-5-bromo-8-(3,4,5-trimethoxyphenyl)benzo[8]annulene ***16aj***



16aj

Amounts used: dihydrobiphenylene **3aj** (0.050 g, 0.156 mmol), AIBN (0.003 g, 0.016 mmol), NBS (0.030 g, 0.17 mmol), CCl_4 (4.5 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16aj** (45 mg, 72% yield), yellow solid.

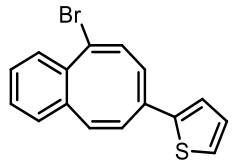
Melting point: 112.9-114.4 °C

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.49 – 7.30 (m, 1H), 7.29 – 7.18 (m, 2H), 7.07 – 6.98 (m, 1H), 6.90 (d, *J* = 11.6 Hz, 1H), 6.71 (dd, *J* = 4.0, 1.3 Hz, 1H), 6.52 (s, 2H), 6.37 – 6.27 (m, 1H), 6.05 (d, *J* = 4.0 Hz, 1H), 3.83 (s, 6H), 3.80 (s, 3H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 153.1 (2 x C), 141.5 (C), 139.1 (C), 138.3 (C), 136.5 (C), 134.8 (C), 133.6 (CH), 133.3 (CH), 132.2 (CH), 130.3 (CH), 128.5 (CH), 128.4 (CH), 127.3 (CH), 125.3 (CH), 122.7 (C), 103.8 (2 x CH), 60.9 (CH_3), 56.2 (2 x CH_3).

HRMS (APCI) calculated for $C_{21}H_{20}BrO_3$ $[M+H]^+$: 399.0590, found 399.0576.

Synthesis of 2-((5Z,7E,9E)-10-bromobenzo[8]annulen-7-yl)thiophene ***16ak***



16ak

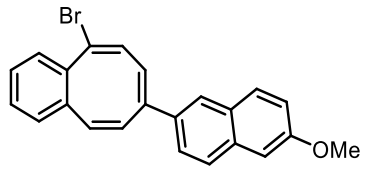
Amounts used: dihydrobiphenylene **3ak** (0.049 g, 0.21 mmol), AIBN (0.004 g, 0.02 mmol), NBS (0.042 g, 0.23 mmol), DCE (5.8 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16ak** (20 mg, 31% yield), yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.33 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.24 – 7.13 (m, 2H), 7.07 (d, *J* = 5.1 Hz, 1H), 6.94 – 6.91 (m, 1H), 6.89 (d, *J* = 3.6 Hz, 1H), 6.85 (dd, *J* = 5.1, 3.8 Hz, 1H), 6.81 (d, *J* = 11.6 Hz, 1H), 6.63 (d, *J* = 4.2 Hz, 1H), 6.33 (d, *J* = 11.4 Hz, 1H), 6.05 (d, *J* = 4.2 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 143.5 (C), 138.9 (C), 136.3 (C), 135.5 (C), 133.7 (CH), 133.1 (CH), 130.9 (CH), 130.4 (CH), 128.6 (CH), 128.4 (CH), 127.5 (CH), 127.4 (CH), 124.9 (CH), 124.7 (CH), 124.1 (CH), 123.1 (C).

HRMS (APCI) calculated for $C_{16}H_{12}BrS$ $[M+H]^+$: 314.9838, found: 314.9838.

*Synthesis of (5E,7E,9Z)-5-bromo-8-(6-methoxynaphthalen-2-yl)benzo[8]annulene **16at***



16at

Amounts used: dihydrobiphenylene **3at** (0.044 g, 0.142 mmol), AIBN (0.003 g, 0.016 mmol), NBS (0.028 g, 0.16 mmol), CCl_4 (4 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16at** (34 mg, 62% yield), yellow solid.

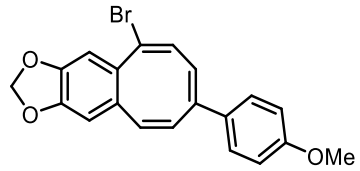
Melting point: 140.8-141.9 °C

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.73 (d, *J* = 8.9 Hz, 1H), 7.69 (d, *J* = 1.9 Hz, 1H), 7.67 (d, *J* = 8.7 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.34 – 7.25 (m, 2H), 7.18 – 7.13 (m, 1H), 7.13 – 7.09 (m, 2H), 7.00 (d, *J* = 11.6 Hz, 1H), 6.86 – 6.78 (m, 1H), 6.49 (dd, *J* = 11.6, 1.4 Hz, 1H), 6.26 (d, *J* = 4.1 Hz, 1H), 3.93 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 158.0 (C), 141.5 (C), 139.2 (C), 136.8 (C), 134.2 (C), 134.2 (C), 134.0 (CH), 133.3 (CH), 132.5 (CH), 130.3 (CH), 129.8 (CH), 128.7 (C), 128.7 (CH), 128.4 (CH), 127.3 (CH), 126.9 (CH), 125.5 (CH), 125.2 (CH), 124.5 (CH), 122.6 (C), 119.1 (CH), 105.6 (CH), 55.3 (CH_3).

HRMS (APCI) calculated for $C_{23}H_{18}BrO$ $[M+H]^+$: 389.0536, found 389.0532.

*Synthesis of (5E,7E,9Z)-5-bromo-8-(4-methoxyphenyl)cycloocta[4,5]benzo[1,2-d][1,3]dioxole **16bb***



16bb

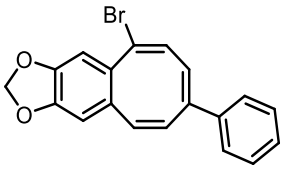
Amounts used: dihydrobiphenylene **3bb** (0.046 g, 0.15 mmol), AIBN (0.003 g, 0.017 mmol), NBS (0.029 g, 0.16 mmol), CCl_4 (4.2 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16bb** (35 mg, 61% yield), orange oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.34 – 7.19 (m, 2H), 6.86 – 6.79 (m, 3H), 6.76 (d, *J* = 11.3 Hz, 1H), 6.66 (dd, *J* = 3.9, 1.0 Hz, 1H), 6.47 (s, 1H), 6.28 (d, *J* = 10.7 Hz, 1H), 6.04 (d, *J* = 3.9 Hz, 1H), 5.93 (dd, *J* = 11.3, 1.3 Hz, 2H), 3.79 (s, 3H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 159.6 (C), 148.2 (C), 147.1 (C), 141.2 (C), 133.8 (CH), 132.8 (CH), 132.6 (C), 132.4 (CH), 131.5 (C), 130.9 (C), 127.5 (2 x CH), 124.1 (CH), 122.0 (C), 113.8 (2 x CH), 109.7 (CH), 107.8 (CH), 101.5 (CH_2), 55.3 (CH_3).

HRMS (APCI) calculated for $C_{20}H_{16}BrO_3$ $[M+H]^+$: 383.0277, found 383.0275.

*Synthesis of (5E,7E,9Z)-5-bromo-8-phenylcycloocta[4,5]benzo[1,2-d][1,3]dioxole **16ba***



16ba

Amounts used: dihydrobiphenylene **3bb** (0.058 g, 0.21 mmol), AIBN (0.004 g, 0.023 mmol), NBS (0.041 g, 0.23 mmol), CCl_4 (5.9 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16bb** (29 mg, 38% yield), yellow solid.

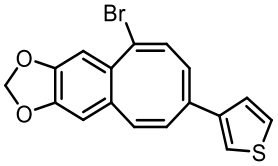
Melting point: 102.3-103.4 °C

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.36-7.27 (m, 5H), 6.87 (s, 1H), 6.80 (d, *J* = 11.5 Hz, 1H), 6.70 (dd, *J* = 3.9, 1.3 Hz, 1H), 6.50 (s, 1H), 6.33 (dd, *J* = 11.5, 1.3 Hz, 1H), 6.15 (d, *J* = 3.9 Hz, 1H), 5.96 (dd, *J* = 11.0, 1.3 Hz, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 148.2 (C), 147.2 (C), 141.8 (C), 139.0 (C), 133.6 (CH), 133.0 (CH), 132.5 (C), 132.3 (CH), 130.8 (C), 128.4 (2 x CH), 128.0 (CH), 126.3 (2 x CH), 125.7 (CH), 122.4 (C), 109.7 (CH), 107.8 (CH), 101.5 (CH_2).

HRMS (APCI) calculated for $C_{19}H_{14}BrO_2$ $[M+H]^+$: 353.0172, found 353.0174.

Synthesis of (5E,7E,9Z)-5-bromo-8-(thiophen-3-yl)cycloocta[4,5]benzo[1,2-d][1,3]dioxole 16bq



16bq

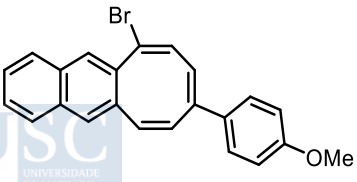
Amounts used: dihydrobiphenylene **3bq** (0.028 g, 0.1 mmol), AIBN (0.002 g, 0.011 mmol), NBS (0.020 g, 0.1 mmol), CCl_4 (2.8 mL). Solvents used: Hex/EtOAc 98/02. Product obtained: bCOT **16bq** (30 mg, 84% yield), yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.24 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.15 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.13 (dd, *J* = 2.9, 1.3 Hz, 1H), 6.84 (s, 1H), 6.74 (d, *J* = 11.3 Hz, 1H), 6.67 (dd, *J* = 4.0, 1.1 Hz, 1H), 6.44 (s, 1H), 6.37 (dd, *J* = 11.3, 1.1 Hz, 1H), 6.13 (d, *J* = 4.0 Hz, 1H), 5.95 (d, *J* = 1.4 Hz, 1H), 5.91 (d, *J* = 1.4 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm):148.2 (C), 147.2 (C), 140.9 (C), 136.7 (C), 133.3 (CH), 132.8 (CH), 132.4 (C), 131.6 (CH), 130.7 (C), 126.0 (CH), 124.9 (CH), 124.7 (CH), 122.3 (C), 121.9 (CH), 109.7 (CH), 107.8 (C), 101.5 (CH_2).

HRMS (APCI) calculated for $C_{17}H_{12}BrO_2S$ $[M+H]^+$: 358.9736, found 358.9734.

*Synthesis of (6E,8E,10Z)-6-bromo-9-(4-methoxyphenyl)cycloocta[b]naphthalene **16cb***



16cb

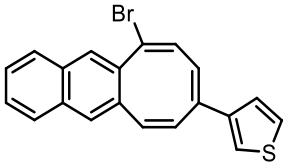
Amounts used: dihydrobiphenylene **3cb** (0.066 g, 0.21 mmol), AIBN (0.004 g, 0.021 mmol), NBS (0.043 g, 0.23 mmol), DCE (5.7 mL). Solvents used: Hex/EtOAc 98/02. Product obtained: bCOT **16cb** (40 mg, 50% yield), yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.85 (s, 1H), 7.73 – 7.61 (m, 2H), 7.43 (s, 1H), 7.33 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 11.7 Hz, 1H), 6.77 (dd, *J* = 4.1, 1.3 Hz, 1H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.32 (dd, *J* = 11.7, 1.3 Hz, 1H), 5.95 (d, *J* = 4.1 Hz, 1H), 3.67 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.7 (C), 141.0 (C), 137.6 (C), 134.4 (C), 134.3 (CH), 133.0 (C), 132.8 (CH), 132.7 (CH), 132.3 (C), 131.7 (C), 130.1 (CH), 128.1 (CH), 127.7 (CH), 127.6 (2 x CH), 127.5 (CH), 127.0 (CH), 126.3 (CH), 123.5 (CH), 122.3 (C), 113.9 (2 x CH), 55.4 (CH_3).

HRMS (APCI) calculated for $C_{23}H_{18}BrO$ $[M+H]^+$: 389.0536, found: 389.0534.

Synthesis of 3-((6Z,8E,10E)-11-bromocycloocta[b]naphthalen-8-yl)thiophene ***16cq***



16cq

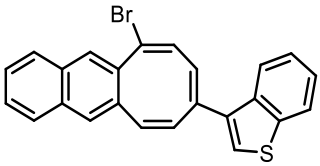
Amounts used: dihydrobiphenylene **3cq** (0.143 g, 0.5 mmol), AIBN (0.008 g, 0.05 mmol), NBS (0.100 g, 0.55 mmol), DCE (13.5 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16cq** (112 mg, 61% yield), yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 8.00 (s, 1H), 7.86 – 7.80 (m, 1H), 7.80 – 7.74 (m, 1H), 7.54 (s, 1H), 7.50 – 7.44 (m, 2H), 7.26 – 7.24 (m, 1H), 7.21 (dd, *J* = 3.1, 1.4 Hz, 1H), 7.17 (dd, *J* = 5.1, 1.4 Hz, 1H), 7.14 (d, *J* = 11.7 Hz, 1H), 6.91 (dd, *J* = 4.1, 1.3 Hz, 1H), 6.54 (dd, *J* = 11.7, 1.3 Hz, 1H), 6.17 (d, *J* = 4.1 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 141.0 (C), 137.3 (C), 136.5 (C), 134.0 (C), 133.8 (CH), 133.0 (C), 132.7 (CH), 132.3 (C), 131.9 (CH), 130.3 (CH), 128.1 (CH), 127.7 (CH), 127.5 (CH), 127.0 (CH), 126.4 (CH), 126.0 (CH), 125.0 (CH), 124.0 (CH), 122.5 (C), 122.0 (CH).

HRMS (APCI) calculated for $C_{20}H_{14}BrS$ $[M+H]^+$: 364.9994, found: 364.9996.

Synthesis of 3-((6Z,8E,10E)-11-bromocycloocta[b]naphthalen-8-yl)benzo[b]thiophene ***16cr***



16cr

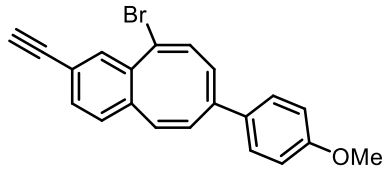
Amounts used: dihydrobiphenylene **3cr** (0.95 g, 0.28 mmol), AIBN (0.005 g, 0.028 mmol), NBS (0.057 g, 0.31 mmol), DCE (7.6 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16cr** (69 mg, 59% yield), yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 8.02 (s, 1H), 7.86 – 7.76 (m, 4H), 7.62 (s, 1H), 7.48 (ddd, *J* = 7.4, 5.2, 1.8 Hz, 2H), 7.33 – 7.29 (m, 2H), 7.10 (d, *J* = 11.7 Hz, 1H), 6.94 (d, *J* = 2.8 Hz, 1H), 6.42 (d, *J* = 11.4 Hz, 1H), 6.14 (d, *J* = 4.1 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 139.5 (C), 136.5 (C), 136.4 (C), 136.1 (C), 135.2 (C), 133.3 (C), 132.6 (CH), 132.0 (CH), 131.5 (CH), 131.3 (C), 129.4 (CH), 127.1 (CH), 126.7 (CH), 126.5 (CH), 126.5 (CH), 126.0 (CH), 125.4 (CH), 123.5 (CH), 123.4 (CH), 123.2 (CH), 122.1 (CH), 121.9 (CH), 121.8 (C).

HRMS (APCI) calculated for $C_{24}H_{16}BrS$ $[M+H]^+$: 415.0151, found: 415.0154.

Synthesis of (5Z,7E,9E)-10-bromo-2-ethynyl-7-(4-methoxyphenyl)benzo[8]annulene ***16gb***



16gb

Amounts used: dihydrobiphenylene **3gb** (0.080 g, 0.28 mmol), AIBN (0.005 g, 0.028 mmol), NBS (0.055 g, 0.31 mmol), CCl_4 (7.5 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16gb** (65 mg, 63% yield), yellow solid.

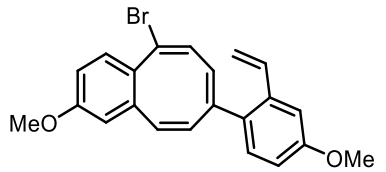
Melting point: 104.0-105.0 °C

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.54 (s, 1H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.98 (d, *J* = 6.8 Hz, 1H), 6.89 – 6.77 (m, 3H), 6.73 (d, *J* = 4.0 Hz, 1H), 6.34 (d, *J* = 11.8 Hz, 1H), 6.05 – 5.99 (m, 1H), 3.77 (s, 3H), 3.08 (s, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 159.7 (C), 141.1 (C), 139.6 (C), 137.6 (C), 134.7 (CH), 134.1 (CH), 133.3 (CH), 132.4 (CH), 131.8 (CH), 131.5 (C), 128.8 (CH), 127.6 (2 x CH), 123.5 (CH), 121.3 (C), 121.0 (C), 113.9 (2 x CH), 83.00 (C), 78.1 (CH), 55.4 (CH_3).

HRMS (APCI) calculated for $C_{21}H_{16}BrO$ $[M+H]^+$: 363.0379 , found 363.0380.

Synthesis of (5E,7E,9Z)-5-bromo-2-methoxy-8-(4-methoxy-2-vinylphenyl)benzo[8]annulene ***16d***



16d

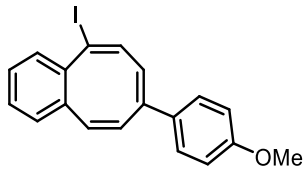
Amounts used: dihydrobiphenylene **4d** (0.038 g, 0.12 mmol), AIBN (0.003 g, 0.013 mmol), NBS (0.024 g, 0.13 mmol), CCl_4 (3.3 mL). Solvents used: Hex/EtOAc 90/10. Product obtained: bCOT **16d** (31 mg, 63% yield), amorphous orange solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.37 (d, *J* = 8.8 Hz, 1H), 7.01 – 6.96 (m, 2H), 6.88 (ddd, *J* = 8.7, 2.7, 0.5 Hz, 1H), 6.75 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.68 – 6.63 (m, 2H), 6.56 – 6.49 (m, 2H), 6.16 – 6.10 (m, 1H), 5.65 (d, *J* = 3.9 Hz, 1H), 5.56 (dd, *J* = 17.4, 1.3 Hz, 1H), 5.09 (dd, *J* = 10.9, 1.2 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm):159.6 (C), 159.2 (C), 142.2 (C), 138.5 (C), 137.3 (C), 135.7 (C), 134.3 (C), 133.0 (CH), 132.4 (C), 131.9 (CH), 131.8 (C), 131.6 (CH), 130.2 (CH), 129.7 (CH), 122.9 (C), 114.4 (CH_2), 114.0 (CH), 113.4 (CH), 112.8 (CH), 110.5 (CH), 55.4 (CH_3), 55.3 (CH_3).

HRMS (APCI) calculated for $C_{22}H_{20}BrO_2$ $[M+H]^+$: 395.0641, found 395.0642.

Synthesis of (5E,7E,9Z)-5-iodo-8-(4-methoxyphenyl)benzo[8]annulene ***16ab'***



16ab'

Amounts used: dihydrobiphenylene **3ab** (0.075 g, 0.29 mmol), AIBN (0.003 g, 0.020 mmol), NIS (0.073 g, 0.32 mmol), CCl_4 (8.5 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16ab'** (85 mg, 77% yield), yellow solid.

Melting point: 114.8-115.6 °C

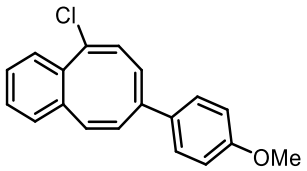
^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.43 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.32 – 7.27 (m, 3H), 7.22 (td, *J* = 7.6, 1.4 Hz, 1H), 7.04 – 6.99 (m, 2H), 6.92 (d, *J* = 11.6

Hz, 1H), 6.85 (d, *J* = 8.9 Hz, 2H), 6.34 (dd, *J* = 11.6, 1.4 Hz, 1H), 6.04 (d, *J* = 3.9 Hz, 1H), 3.81 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.6 (C), 142.6 (CH), 142.0 (C), 141.1 (C), 135.7 (C), 133.1 (CH), 132.6 (CH), 131.6 (C), 131.0 (CH), 128.5 (CH), 128.0 (CH), 127.5 (2 x CH), 127.1 (CH), 125.6 (CH), 113.8 (2 x CH), 98.0 (C), 55.3 (CH_3).

HRMS (APCI) calculated for $C_{19}H_{16}IO$ $[M+H]^+$: 387.0240, found 387.0241.

*Synthesis of (5E,7E,9Z)-5-chloro-8-(4-methoxyphenyl)benzo[8]annulene **16ab''***



16ab"

Amounts used: dihydrobiphenylene **3ab** (0.051 g, 0.20 mmol), AIBN (0.003 g, 0.020 mmol), NCS (0.028 g, 0.16 mmol), CCl_4 (5.7 mL). Solvents used: Hex/EtOAc 95/05. Product obtained: bCOT **16ab''** (21 mg, 36% yield), yellow solid.

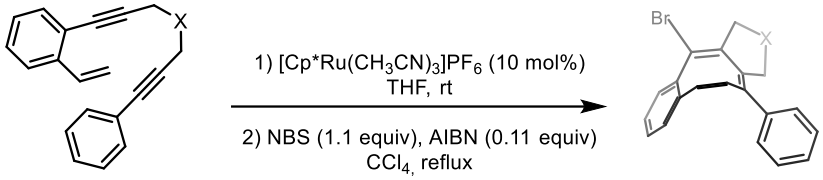
Melting point: 107.0-108.5 °C

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.42 (dd, *J* = 5.5, 3.7 Hz, 1H), 7.32 – 7.26 (m, 4H), 7.09 – 7.06 (m, 1H), 6.91 (d, *J* = 11.6 Hz, 1H), 6.86 – 6.82 (m, 2H), 6.53 (dd, *J* = 4.2, 1.4 Hz, 1H), 6.36 (dd, *J* = 11.6, 1.4 Hz, 1H), 6.10 (d, *J* = 4.2 Hz, 1H), 3.81 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.5 (C), 141.1 (C), 138.0 (C), 137.2 (C), 133.1 (CH), 132.5 (CH), 132.4 (C), 131.7 (C), 129.7 (CH), 129.5 (CH), 128.7 (CH), 128.4 (CH), 127.5 (CH), 127.5 (2 x CH), 122.9 (CH), 113.7 (2 x CH), 55.3 (CH_3).

HRMS (APCI) calculated for $C_{19}H_{16}ClO$ $[M+H]^+$: 295.0884, found 295.0884.

7.1.3.4.3. Synthesis of heteroannulated BrbCOT´s 18a,b



17a, X = O
17b, X = NTs

18a, X = O, 30%
18b, X = NTs, 40%

To a solution of **17a** (0.040 g, 0.15 mmol) in THF (0.73 mL), degassed at -196 °C using liquid N_2, was added $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.007 mg, 0.015 mmol). The reaction was stirred at room temperature until disappearance of the starting material (TLC, 25 min). The resulting mixture was filtered through a path of silica using DCM as eluent and evaporated to dryness. The final crude was used in the next step without further purification.

The *general procedure F* was followed using the previous crude, AIBN (0.0027 g, 0.016 mmol), NBS (0.029 g, 0.016 mmol) in CCl_4 (4.1 mL). Upon completion (1h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (97/3) as eluent to give **18a** (15 mg, 30% after two steps) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.46 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.32 – 7.27 (m, 4H), 7.22 (td, *J* = 7.5, 1.3 Hz, 1H), 7.16 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.68 (d, *J* =

12.0 Hz, 1H), 6.58 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 13.2 Hz, 1H), 4.42 (d, *J* = 13.2 Hz, 1H), 4.36 (dd, *J* = 11.2, 1.2 Hz, 1H), 4.13 (d, *J* = 11.2 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 142.5 (C), 140.2 (C), 139.5 (C), 138.7 (C), 137.7 (C), 136.4 (C), 134.8 (CH), 131.3 (CH), 131.2 (CH), 129.2 (CH), 128.4 (CH), 128.4 (2 x CH), 128.2 (CH), 127.4 (2 x CH), 127.3 (CH), 118.2 (C), 73.3 (CH_2), 72.1 (CH_2).

HRMS (APCI) calculated for $C_{20}H_{16}BrO$ $[M+H]^+$: 351.0379, found 351.0379.

To a solution of **17b** (0.064 g, 0.15 mmol) in THF (0.75 mL), degassed at -196 °C using liquid N_2, was added $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.008 mg, 0.015 mmol). The reaction was stirred at room temperature until disappearance of the starting material (TLC, 25 min). The resulting mixture was filtered through a path of silica using DCM as eluent and evaporated to dryness. The final crude was used in the next step without further purification.

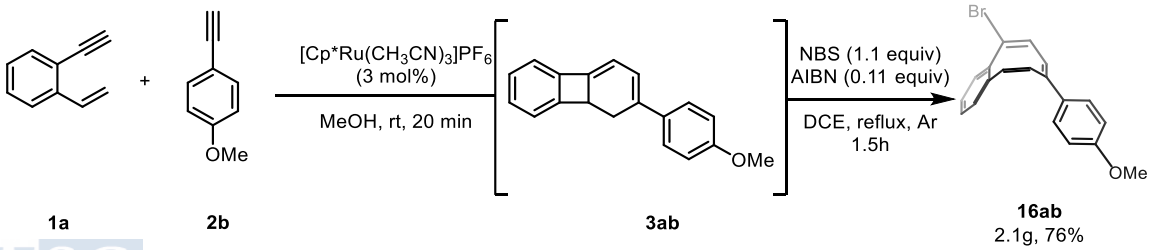
The *general procedure F* was followed using the previous crude, AIBN (0.0029 g, 0.018 mmol), NBS (0.031 g, 0.017 mmol) in CCl_4 (4.4 mL). Upon completion (1h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (97/3) as eluent to give an inseparable mixture of **18b** and 4-phenyl-2-tosyl-2,3-dihydro-1H-benzo[3,4]cyclobuta[1,2-*e*]isoindole **18b*** in a 3:1 ratio (33 mg, 40% after two steps) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.63 (d, *J* = 8.3 Hz, 2H), 7.33 (dd, *J* = 6.8, 3.0 Hz, 5H), 7.30 – 7.24 (m, 3H), 7.04 (ddd, *J* = 4.7, 2.4, 1.4 Hz, 2H), 6.89 – 6.83 (m, 1H), 6.62 (d, *J* = 11.9 Hz, 1H), 6.35 (dd, *J* = 11.9, 1.2 Hz, 1H), 4.27 (d, *J* = 14.4 Hz, 1H), 4.03 (d, *J* = 14.4 Hz, 1H), 3.86 (d, *J* = 1.2 Hz, 2H), 2.50 (s, 3H). Minor product **18b***: 7.76 (d, *J* = 8.2 Hz, 2H), 7.45 – 7.37 (m, 3H), 7.21 (ddd, *J* = 7.7, 5.1, 3.7 Hz, 4H), 6.79 (dd, *J* = 4.9, 2.9 Hz, 2H), 6.69 – 6.65 (m, 1H), 6.63 (d, *J* = 0.9 Hz, 1H), 6.56 (s, 1H), 4.44 (s, 2H), 4.41 (s, 2H), 2.44 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 143.8 (C), 139.9 (C), 139.7 (C), 139.4 (C), 139.0 (C), 136.2 (C), 134.5 (CH), 133.9 (C), 133.5 (C), 131.5 (CH), 131.1 (CH), 129.9 (2 x CH), 129.1 (CH), 128.7 (2 x CH), 128.6 (2 x CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 120.0 (C), 54.9 (CH_2), 52.9 (CH_2), 21.7 (CH_3). Minor product **18b***: 151.2 (C), 150.6 (C), 149.6 (C), 143.9 (C), 143.7 (C), 139.9 (C), 137.0 (C), 135.4 (C), 133.6 (C), 130.0 (2 x CH), 128.9 (C), 128.8 (2 x CH), 128.8 (CH), 127.8 (2 x CH), 126.6 (C), 117.9 (CH), 117.8 (CH), 117.6 (CH), 52.9 (CH_2), 51.2 (CH_2), 21.7 (CH_3).

HRMS (APCI) calculated for $C_{27}H_{23}BrNO_2S$ $[M+H]^+$: 504.0627, found 504.0635.

7.1.3.5. Sequential preparation and gram scale synthesis of bCOT 16ab



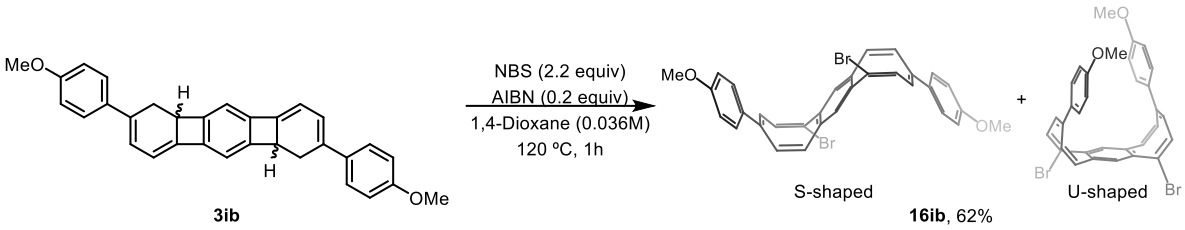
1a **2b** **3ab** **16ab** 2.1g, 76%

The *general procedure E* for the Ru(II)-catalyzed [2+2+2] cycloaddition was modified using $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.122 mg, 0.24 mmol), 1-ethynyl-2-vinylbenzene **1a** (1036 mg, 8.1 mmol)

and 4-ethynylanisole **2a** (1.3 mL, 9.7 mmol) in MeOH (40 mL). After completion (20 min) the reaction mixture was dissolved in DCM and evaporated to dryness. The final crude was used in the next step without further purification.

General procedure G was followed with some modifications. A solution of previous crude in DCE (220 mL) was degassed with Ar for 15 min. Then, AIBN (0.132 g, 0.81 mmol) and NBS (1.630 g, 8.8 mmol) were added. The resulting mixture was placed in an aluminum heating block and stirred at reflux for 1.5 h until disappearance of the starting material (TLC monitoring). The crude was concentrated to dryness and the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford **16ab** (2.10 g, 76 %) as a yellow solid.

7.1.3.6. Synthesis of linear benzodiCOT 16ib



A solution of **3ib** (0.057 g, 0.13 mmol) in 1,4-dioxane (3.6 mL) was degassed with Ar for 15 min. Then, AIBN (0.004 g, 0.026 mmol) and NBS (0.052 g, 0.28 mmol) were added. The resulting mixture was stirred at reflux in an aluminium heating block until disappearance of the starting material (TLC monitoring, 1h). The crude was concentrated to dryness and the residue was purified by filtration using hot MeOH as eluent to afford bCOT **16ib** (48 mg, 62 % yield) as a brown-green solid.

Melting point: >240 °C

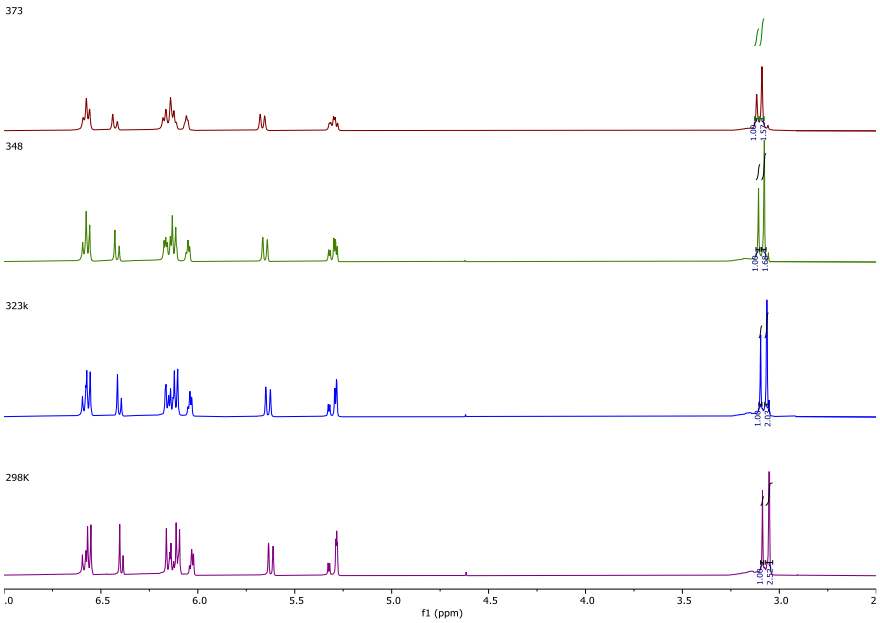
^{1}H NMR (500 MHz, 1,1,2,2-tetrachloroethane-d_2, 50ºC) δ (ppm): *major S conformer*, 6.56 (d, *J* = 8.8 Hz, 4H), 6.40 (s, 2H), 6.15 (d, *J* = 11.7 Hz, 2H), 6.10 (d, *J* = 8.8 Hz, 4H), 6.03 (dd, *J* = 4.2, 1.3 Hz, 2H), 5.62 (dd, *J* = 11.7, 1.3 Hz, 2H), 5.30 – 5.27 (m, 2H), 3.05 (s, 6H). For *minor U conformer*: 6.59 (d, *J* = 8.9 Hz, 4H), 6.39 (s, 2H), 6.15 – 6.12 (m, 2H), 6.10 (d, *J* = 8.8 Hz, 4H), 6.04 (d, *J* = 1.2 Hz, 2H), 5.62 (dd, *J* = 11.7, 1.2 Hz, 2H), 5.32 (d, *J* = 4.1 Hz, 2H), 3.09 (s, 6H). *Due to the overlapping of both conformers peaks, is not possible a clear assignment of the region from 6.0 to 6.2 ppm.*

^{13}C NMR (126 MHz, 1,1,2,2-tetrachloroethane-d_2, 50 °C) δ (ppm): *major S conformer*, 158.9 (2 x C), 140.0 (2 x C), 138.7 (2 x C), 135.3 (2 x C), 134.4 (2 x CH), 132.4 (2 x CH), 131.9 (2 x CH), 130.8 (2 x C), 130.2 (2 x CH), 127.1 (4 x CH), 123.2 (2 x CH), 120.6 (2 x C), 113.3 (4 x CH), 54.9 (2 x CH_3). *Minor U conformer*: 159.0 (2 x C), 140.5 (2 x C), 138.8 (2 x C), 135.3 (2 x C), 134.0 (2 x CH), 132.3 (2 x CH), 131.7 (2 x CH), 130.8 (2 x C), 130.1 (2 x CH), 127.1 (4 x CH), 123.2 (2 x CH), 120.7 (2 x C), 113.4 (4 x CH), 54.9 (2 x CH_3).

HRMS (APCI) calculated for $C_{32}H_{24}Br_2O_2$ $[M+]^+$: 598.0138, found 598.0136.

Scale up: tetrahydrobiphenylene **3ib** (0.885 g, 2 mmol). Product obtained: linear benzodiCOT **16ib** (0.9 g, 75% yield).

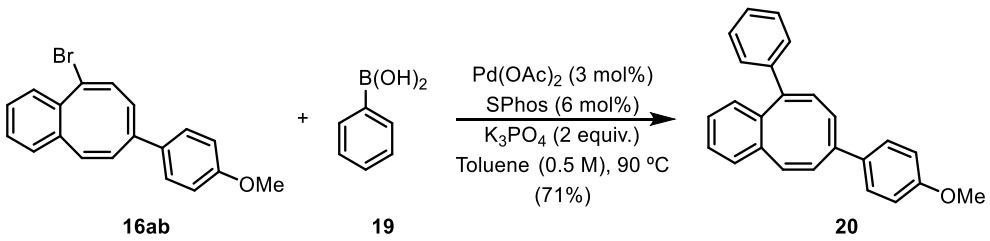
7.1.3.7. Variable temperature NMR and conformational studies of linear benzodiCOT 16ib



The ^{1}H NMR spectrum (1,1,2,2-tetrachloethane-d_2) of **16ib** at room temperature (25 °C) shows a 1:2.5 ratio, U-and S-shaped COT, as judged by the -OMe signals. This relation could be thermally equilibrated to 1:1.5 ratio at 100 °C.

7.1.3.8. Derivatization of bCOT 16ab

*(5Z,7E,9Z)-8-(4-methoxyphenyl)-5-phenylbenzo[8]annulene **20***



16ab **19** **20**

A solution of SPhos (0.008 g, 0.018 mmol), $Pd(OAc)_2$ (0.002 g, 0.009 mmol), K_3PO_4 (0.129 g, 0.59 mmol), phenyboronic acid **19** (0.054 g, 0.442 mmol) and **16ab** (0.100 g, 0.295 mmol) in toluene (0.860 mL, 0.5 M) was stirred at 90 °C in an oil bath. Upon completion (24 h), the reaction mixture was diluted in EtOAc and filtered through silica gel. The crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (98/2) as eluent to afford the phenylbenzo[8]annulene **20** (70 mg, 71% yield) as a pale yellow solid.

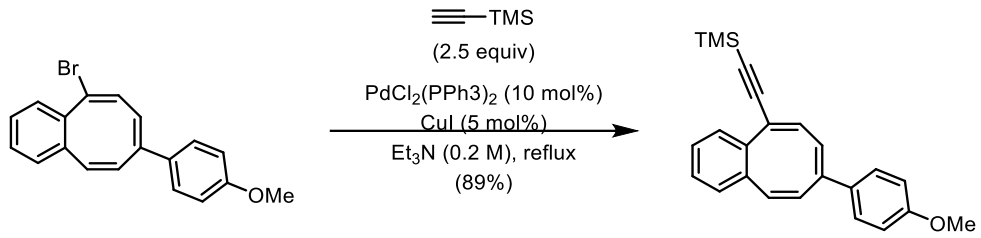
Melting point: 178.3-179.9 °C

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.38 (d, *J* = 8.6 Hz, 2H), 7.34 – 7.25 (m, 6H), 7.20 (t, *J* = 7.3 Hz, 2H), 6.98 (t, *J* = 11.1 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.69 (d, *J* = 3.5 Hz, 1H), 6.40 (dd, *J* = 7.3, 3.5 Hz, 2H), 3.83 (s, 3H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 159.3 (C), 144.6 (C), 142.9 (C), 140.6 (C), 140.6 (C), 138.9 (C), 133.3 (CH), 132.7 (CH), 132.4 (C), 130.3 (CH), 128.5 (2 x CH), 128.2 (2 x CH), 127.8 (2 x CH), 127.5 (2 x CH), 127.2 (CH), 127.0 (CH), 126.8(CH), 125.7 (CH), 113.7 (2 x CH), 55.3 (CH_3).

HRMS (APCI) calculated for $C_{25}H_{21}O$ $[M+H]^+$: 337.1587, found 337.1586.

(((5E,7E,9Z)-8-(4-methoxyphenyl)benzo[8]annulen-5-yl)ethynyl)trimethylsilane ***21***



16ab **21**

Degassed Et_3N (7 mL, 0.2M) and TMSA **2u** (0.485 mL, 3.5 mmol, 2.5 equiv) were added to a mixture of **16ab** (0.475 g, 1.4 mmol), $PdCl_2(PPh_3)_2$ (0.098 g, 0.14 mmol) and CuI (0.013 g, 0.07 mmol) in a 25 mL vial flask under argon. The resulting solution was stirred at reflux in an aluminium heating block until disappearance of the starting material (TLC monitoring, o/n). Upon completion, the mixture was filtered over a path of silica gel and evaporated to dryness. The crude was diluted in EtOAc, washed with an aqueous solution of $NH_4Cl_{(sat)}$ and with brine, dried over anhydrous $MgSO_4$, filtered and concentrated to dryness. The resulting crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (93/7) as eluent to afford the alkynyl COT **21**, (0.445 g, 89 % yield) as a yellow solid.

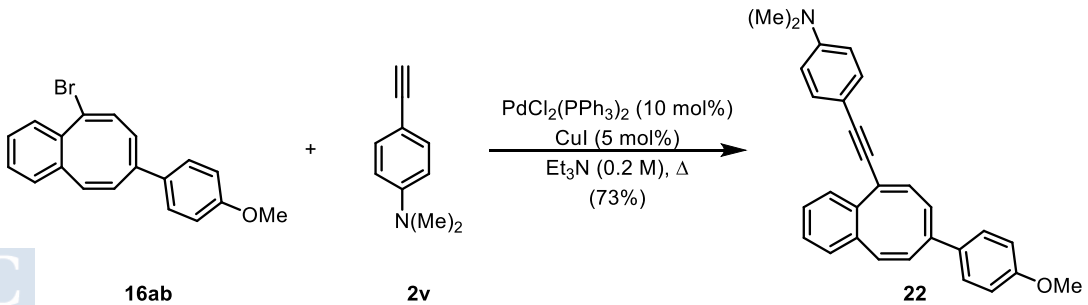
Melting point: 72.3-72.8 °C

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.37 – 7.34 (m, 1H), 7.32 – 7.28 (m, 2H), 7.26 – 7.23 (m, 2H), 7.05 – 7.02 (m, 1H), 6.85 (d, *J* = 11.6 Hz, 1H), 6.84 – 6.81 (m, 2H), 6.71 (dd, *J* = 4.5, 1.2 Hz, 1H), 6.30 (dd, *J* = 11.5, 1.2 Hz, 1H), 6.18 (d, *J* = 4.5 Hz, 1H), 3.79 (s, 3H), 0.20 (s, 9H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.5 (C), 141.5 (C), 139.3 (CH), 138.0 (C), 137.5 (C), 133.6 (CH), 132.2 (CH), 132.0 (C), 129.4 (CH), 128.8 (CH), 127.5 (CH), 127.5 (2 x CH), 127.1 (CH), 126.8 (C), 123.7 (CH), 113.7 (2 x CH), 107.3 (C), 92.6 (C), 55.3 (CH_3), 0.0 (3 x CH_3).

HRMS (APCI) calculated for $C_{24}H_{25}OSi$ $[M+H]^+$: 357.1669, found 357.1671.

4-(((5Z,7E,9Z)-8-(4-methoxyphenyl)benzo[8]annulen-5-yl)ethynyl)-N,N-dimethylaniline ***22***



16ab **2v** **22**

In a double-neck round-bottomed flask were introduced $PdCl_2(PPh_3)_2$ (0.050 g, 0.072 mmol), CuI (0.007g, 0.036 mmol), **16ab** (0.243 g, 0.716 mmol) and alkyne **2v** (0.260 g, 1.791 mmol, 2.5 equiv). Then, Et_3N (3.6 mL, 0.2 M) was added and the reaction was stirred at reflux in an aluminium heating block during 24h (TLC monitoring). The reaction mixture was filtered through silica gel and evaporated to dryness. The crude was diluted in EtOAc, washed twice with a solution of $NH_4Cl_{(sat)}$ and brine and the organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The resulting crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5 to 80/20) as eluent to afford alkynyl COT **22** (0.212 g, 73% yield) as a dark green solid.

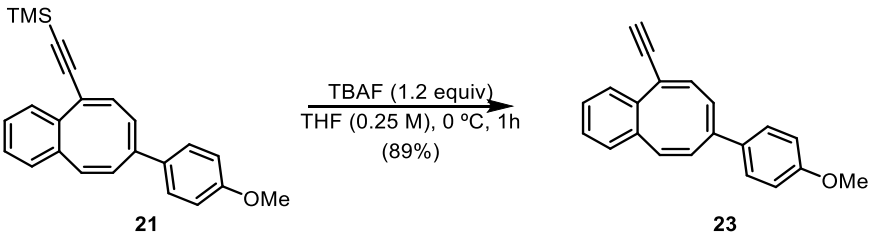
Melting point: 193.4-194.0 ^oC

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.46 (dd, *J* = 6.7, 2.4 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.37 – 7.31 (m, 3H), 7.27 (dd, *J* = 8.4, 4.4 Hz, 2H), 7.10 – 7.05 (m, 1H), 6.91 (d, *J* = 11.5 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.72 – 6.67 (m, 1H), 6.65 – 6.61 (m, 2H), 6.35 (dd, *J* = 11.5, 1.5 Hz, 1H), 6.26 (d, *J* = 4.4 Hz, 1H), 3.81 (s, 3H), 2.99 (s, 6H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.4 (C), 150.0 (C), 141.0 (C), 138.8 (C), 137.4 (C), 136.5 (CH), 133.6 (CH), 133.5 (CH), 132.7 (2 x CH), 132.2 (CH), 132.2 (CH), 129.6 (CH), 128.7 (CH), 127.4 (2 x CH), 127.3 (CH), 127.1 (CH), 124.3 (CH), 113.7 (2 x CH), 111.8 (2 x CH), 110.2 (C), 90.1 (C), 89.4 (C), 55.3 (CH_3), 40.2 (2 x CH_3).

HRMS (APCI) calculated for $C_{29}H_{26}NO$ $[M+H]^+$: 404.2009, found: 404.2002.

(5Z,7E,9Z)-5-ethynyl-8-(4-methoxyphenyl)benzo[8]annulene ***23***



21 **23**

To a solution of **21** (0.439 g, 1.231 mmol) in THF (4.9 mL) cooled at 0 ^oC was added TBAF (1M in THF, 1.2 equiv). The resulting mixture was stirred at the same temperature until disappearance of the starting material (TLC monitoring). After 1.5 h the reaction was quenched with water and extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The resulting crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford alkynyl COT **23** (0.314 g, 89% yield) as a yellow solid.

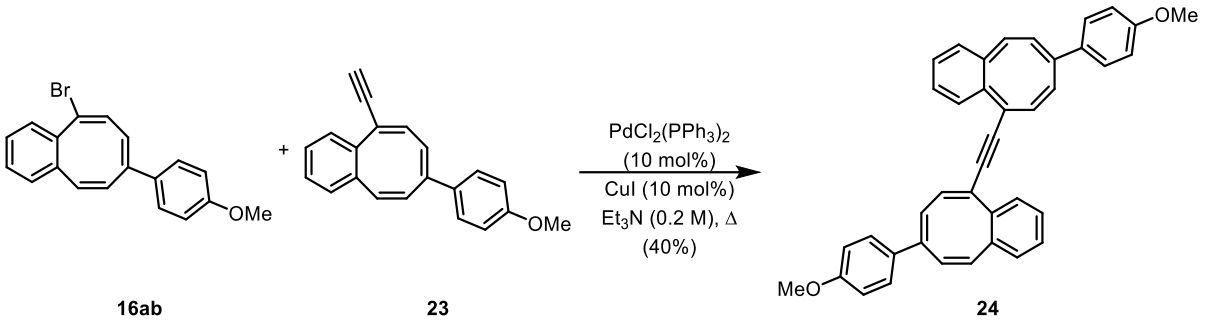
Melting point: 170.2-171.4 ^oC

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.36 – 7.33 (m, 1H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.25 – 7.23 (m, 2H), 7.06 – 7.02 (m, 1H), 6.86 (d, *J* = 11.6 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 4.4 Hz, 1H), 6.30 (dd, *J* = 11.6, 1.3 Hz, 1H), 6.18 (d, *J* = 4.4 Hz, 1H), 3.79 (s, 3H), 2.95 (s, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.7 (C), 141.8 (C), 139.9 (CH), 137.9 (C), 137.6 (C), 133.6 (CH), 132.3 (CH), 132.0 (C), 129.3 (CH), 129.0 (CH), 127.8 (CH), 127.6 (2 x CH), 127.3 (CH), 125.7 (C), 123.7 (CH), 113.9 (2 x CH), 86.0 (C), 75.9 (CH), 55.5 (CH_3).

HRMS (APCI) calculated for $C_{21}H_{17}O$ $[M+H]^+$: 285.1274; found: 285.1277.

(5Z,7E,9Z)-8-(4-methoxyphenyl)-5-(((4aE,6Z,8E,10Z)-8-(4-methoxyphenyl)benzo[8]annulen-5-yl)ethynyl)benzo[8]annulene ***24***



16ab **23** **24**

In a double-neck round-bottomed flask were introduced $PdCl_2(PPh_3)_2$ (0.035 g, 0.049 mmol), CuI (0.010 g, 0.049 mmol), **16ab** (0.200 g, 0.590 mmol) and **23** (0.140 g, 0.490 mmol). The flask was evacuated and refilled with Ar three times. Then, Et_3N (2.5 mL, 0.2 M) was added and the reaction stirred at reflux in an aluminium heating block during 4h (TLC monitoring). The reaction mixture was filtered through silica gel and evaporated to dryness. The crude was diluted in EtOAc, washed twice with a solution of NH_4Cl $_{(sat)}$ and brine. The organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness and the resulting crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5 to 90/10) as eluent to afford the alkynyl COT **24** (106 mg, 40% yield) as a yellow solid.

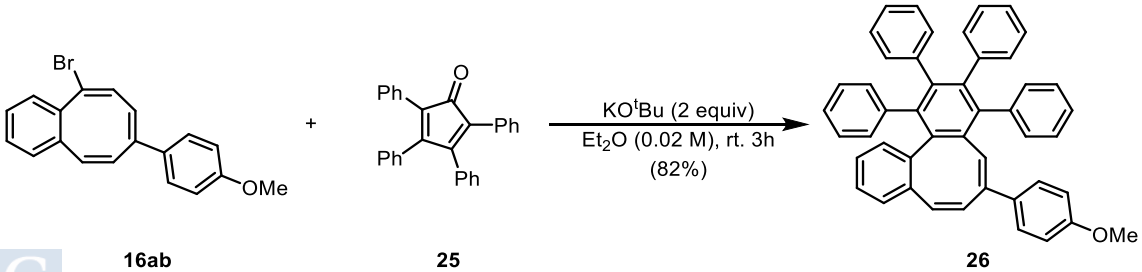
Melting point: 234.8-235.0 ^oC

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.37 – 7.31 (m, 2H), 7.31 – 7.28 (m, 4H), 7.22 (ddd, *J* = 7.3, 3.5, 1.6 Hz, 4H), 7.06 – 6.99 (m, 2H), 6.85 (dd, *J* = 11.5, 2.5 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 4H), 6.64 (ddd, *J* = 5.6, 4.5, 1.2 Hz, 2H), 6.30 (ddd, *J* = 11.5, 3.8, 1.2 Hz, 2H), 6.19 (dd, *J* = 4.4, 1.4 Hz, 2H), 3.78 (s, 6H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.5 (2 x C), 141.4 (2 x C), 138.3 (C), 138.3 (C), 138.2 (CH), 138.1 (CH), 137.4 (C), 133.5 (C), 133.5 (C), 132.2 (2 x CH), 132.0 (2 x C), 129.5 (C), 129.4 (C), 128.8 (2 x CH), 128.2 (C), 127.4 (4 x CH), 127.1 (CH), 127.0 (CH), 126.9 (2 x C), 124.0 (2 x C), 123.9 (2 x C), 113.7 (4 x CH), 90.7 (C), 90.6 (C), 55.3 (2 x CH_3).

HRMS (APCI) calculated for $C_{40}H_{31}O_2$ $[M+H]^+$: 543.2319, found: 543.2319.

(5E,7Z)-6-(4-methoxyphenyl)-1,2,3,4-tetraphenyldibenzo[a,c][8]annulene ***26***



16ab **25** **26**

To a solution of tetraphenylcyclopentadienone **25** (0.302 g, 0.77 mmol, 1.1 equiv) and KO^{t}Bu (0.157 g, 1.4 mmol, 2 equiv) in anhydrous Et_2O (35 mL) was added **16ab** (0.237 g, 0.7 mmol). The mixture was stirred at rt until disappearance of the starting material (TLC monitoring, 3h). Upon completion, the reaction was quenched with an aqueous solution of NH_4Cl $_{(sat)}$ and washed twice with brine. The organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The resulting crude was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95/5) as eluent to afford benzoCOT **26**, (0.353 g, 82% yield) as a white solid.

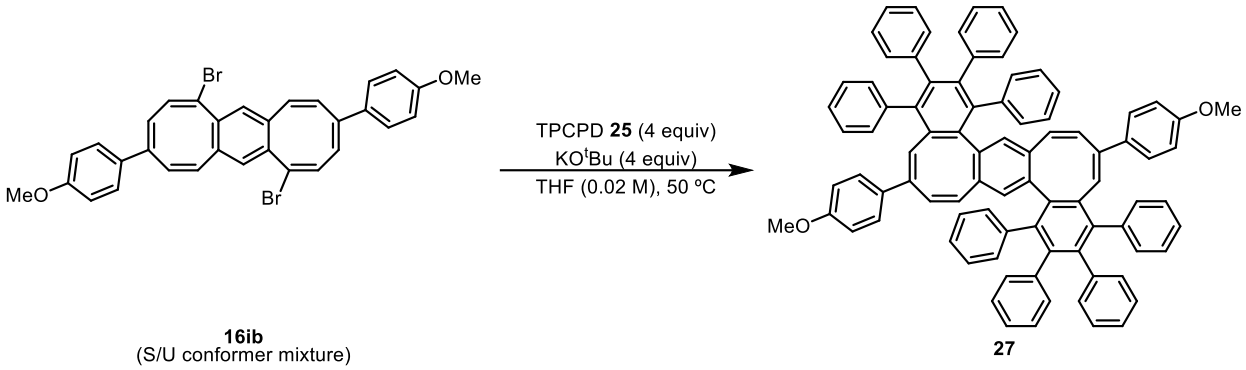
Melting point: 246.0-246.4 ^{o}C

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.39 – 7.34 (m, 1H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.23 – 7.17 (m, 2H), 7.13 (t, *J* = 6.7 Hz, 2H), 7.10 – 7.04 (m, 2H), 7.02 – 6.95 (m, 2H), 6.93 (d, *J* = 1.9 Hz, 2H), 6.88 – 6.80 (m, 5H), 6.81 – 6.75 (m, 8H), 6.70 - 6.68 (m, 4H), 6.54 (d, *J* = 5.4 Hz, 1H), 6.35 (d, *J* = 11.1 Hz, 1H), 3.73 (s, 3H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.2 (C) , 141.5 (C), 140.5 (C), 140.5 (C), 140.4 (C), 140.3 (C), 140.1 (C), 140.0 (C), 139.6 (C), 138.8 (C), 138.5 (C), 137.7 (C), 134.0 (CH), 132.8 (C), 132.3 (CH), 131.9 (CH), 131.8 (CH), 131.7 (CH), 131.5 (CH), 131.2 (CH), 131.0 (CH), 130.9 (CH), 130.7 (CH), 130.0 (CH), 129.1 (CH), 128.1 (2 x CH), 127.8 (CH), 127.3 (CH), 126.8 (2x CH), 126.8 (2 x CH), 126.7 (CH), 126.4 (2 x CH), 126.3 (2 x CH), 126.0 (CH), 125.9 (CH), 125.7 (CH), 125.4 (CH), 125.2 (CH), 125.1 (CH), 113.5 (2 x CH), 55.3 (CH_3).

HRMS (APCI) calculated for $C_{47}H_{35}O$ $[M+H]^+$: 615.2682, found 615.2683.

*Synthesis of benzodi[8]annulene **27***



16ib
(S/U conformer mixture)

27

To a solution of tetraphenylcyclopentadienone **25** (1.6 g, 4 mmol, 4 equiv) and KO^{t}Bu (0.448 g, 4 mmol, 4 equiv) in anhydrous THF (50 mL, 0.02 M) was added **16ib** (0.6 g, 1 mmol). The mixture was stirred at 50 ^{o}C until disappearance of the starting material (o/n, TLC monitoring). Upon completion, the reaction was evaporated to dryness, diluted in DCM and extracted with an aqueous solution of NH_4Cl $_{(sat)}$ and washed twice with water. The organic phase was concentrated under reduced pressure and the final solid was filtered with Et_2O, obtaining cycloadduct product **27** (775 mg, 67% yield) as a brown solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.19 (s, 4H), 7.15 (d, *J* = 9.1 Hz, 4H), 7.03 (d, *J* = 7.6 Hz, 2H), 6.97 (t, *J* = 8.0 Hz, 6H), 6.91 (d, *J* = 8.7 Hz, 4H), 6.84 (dt, *J* = 13.8, 7.7 Hz, 4H), 6.77 – 6.69 (m, 7H), 6.69 – 6.64 (m, 4H), 6.54 – 6.53 (s, 4H), 6.52 – 6.50 (m, 7H), 6.48 (d, *J* = 6.0 Hz, 2H), 6.42 (s, 2H), 6.39 (d, *J* = 11.1 Hz, 2H), 6.16 (s, 2H), 6.06 (d, *J* = 11.0 Hz, 2H), 3.61 (s, 6H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 158.0 (2 x C), 139.7 (2 x C), 139.6 (2 x C), 139.5 (2 x C), 139.4 (2 x C), 139.3 (2 x C), 139.0 (2 x C), 138.8 (2 x C), 138.5 (2 x C), 138.3 (2 x C), 137.5 (2 x C), 137.2 (2 x C), 137.1 (2 x C), 135.0 (2 x C), 132.8 (2 x CH), 131.9 (2 x C), 131.4 (2 x CH), 130.8 (2 x CH), 130.6 (2 x CH), 130.6 (2 x CH), 130.3 (2 x CH), 130.1 (2 x CH), 130.0 (2 x CH), 129.8 (2 x CH), 129.4 (2 x CH), 128.8 (2 x CH), 127.8 (2 x CH), 127.1 (4 x CH), 126.8 (2 x CH), 126.6 (2 x CH), 126.1 (2 x CH), 125.7 (2 x CH), 125.6 (2 x CH), 125.2 (4 x CH), 125.1 (2 x CH), 124.8 (2 x CH), 124.2 (2 x CH), 124.1 (2 x CH), 124.0 (2 x CH), 112.3 (4 x CH), 54.2 (2 x CH_3).

HRMS (APCI-probe): calculated for $C_{88}H_{62}O_2$: 1150.4744, found: 1150.4768.

7.1.3.9. X-ray crystallographic data

7.1.3.9.1. Crystallographic data of compound 16ab

An X-ray crystal of compound **16ab** (CCDC2085994) was grown by vapor diffusion using DCM and hexanes as mixture of solvents.

*Figure 61. ORTEP drawing of compound **16ab** (CCDC 2085994) showing thermal ellipsoids at the 50% contour probability level.*

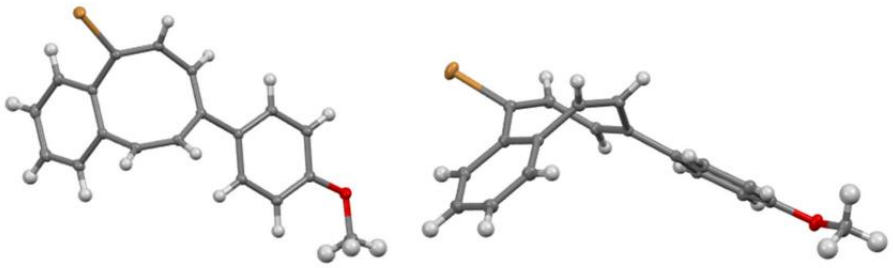


*Table 26. Crystal data and structure refinement for **16ab** (CCDC 2085994)*

Deposition Number CCDC	2085994	
Chemical formula	$C_{19}H_{15}BrO$	
Molecular weight	339.22 g/mol	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal size	0.15 × 0.08 × 0.08 mm	
Crystal habit	Colourless block	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 9.7753 (3) Å	
	b = 6.0276 (2) Å	β = 97.881 (1)º
	c = 12.8424 (5) Å	
Volume	749.55 (4) $Å^3$	
Z	2	
Density (calculated)	1.503 g/cm^3	
Absorption coefficient	2.74 mm^{-1}	
F(000)	344	

7.1.3.9.2. Crystallographic data of compound 16ib

An X-ray crystal of compound 16ib (CCDC2085993) was grown by vapor diffusion using hot $CHCl_3$ and hexane as mixture of solvents.

*Figure 62. ORTEP drawing of compound **16ib** (CCDC 2085993) showing thermal ellipsoids at the 50% contour probability level.*

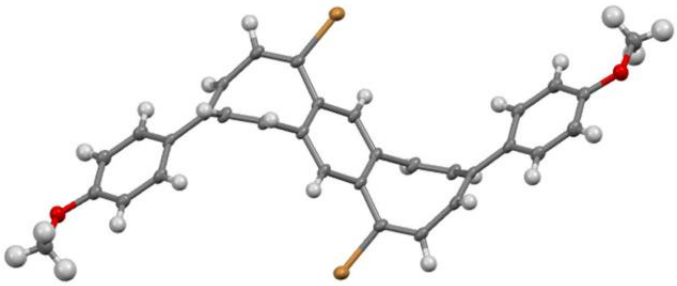


*Table 27. Crystal data and structure refinement for **16ib** (CCDC 2085993)*

Deposition Number CCDC	2085993	
Chemical formula	$C_{32}H_{24}Br_2O_2$	
Molecular weight	600.33 g/mol	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal size	0.25 × 0.12 × 0.11 mm	
Crystal habit	Block, clear yellow	
Crystal system	Monoclinic	
Space group	$P2_{1/n}$	
Unit cell dimensions	a = 10.1111 (3) Å	
	b = 5.9449 (2) Å	β = 99.697 (1)°
	c = 21.6066 (7) Å	
Volume	1280.21 (7) Å3	
Z	2	
Density (calculated)	1.557 g/cm^3	
Absorption coefficient	3.19 mm^{-1}	
F(000)	604	

7.1.3.9.3. Crystallographic data of compound 24

An X-ray crystal of compound **24** (CCDC2085992) was grown after solving in hot toluene until reach rt (o/n).

*Figure 63. ORTEP drawing of compound **24** (CCDC 2085992) showing thermal ellipsoids at the 50% contour probability level.*

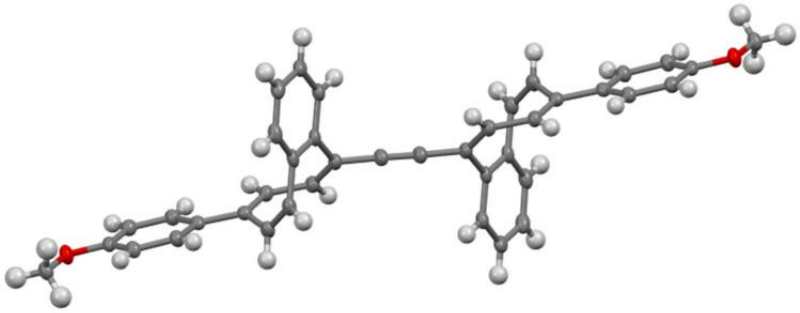


*Table 28. Crystal data and structure refinement for **24** (CCDC 2085992)*

Deposition Number CCDC	2085992	
Chemical formula	$C_{40}H_{30}O_2$	
Molecular weight	542.64 g/mol	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal size	0.23 × 0.11 × 0.01 mm	
Crystal habit	Plate, clear yellow	
Crystal system	Monoclinic	
Space group	$P2_{1/c}$	
Unit cell dimensions	a = 17.2433 (6)Å	
	b = 6.0650 (2)Å	β = 112.9148 (18)º
	c = 14.3696 (5)Å	
Volume	1384.19 (8)Å3	
Z	2	
Density (calculated)	1.302 g/cm^3	
Absorption coefficient	0.61 mm^{-1}	
F(000)	572	

7.1.3.10. DFT calculation

All electronic structure calculations were performed using the Gaussian 16 software package[261] at the CESGA facilities. The geometries of all minima and transition states involved were optimized using the ωB97XD functional[262] (which includes a version of Grimme's D2 dispersion corrections)[263] within the self-consistent reaction field (SCRF) using the SMD model (CCl_4) [264] and using the basis set aug-cc-pVTZ.[265] Frequency calculations were performed at the same level to evaluate the zero-point vibrational energy and thermal corrections at 298 K and to confirm the nature of the stationary points, yielding one imaginary frequency for the transition states and none for the minima. Each transition state was further confirmed by following the steepest descent to both sides and identifying the minima present in the reaction energy profile. The reaction profiles were built up in terms of ΔG_{sol}.

Intermediates 9_S_shaped, 9_U_Shaped and $TS_{9\_S\_shaped\text{-}9\_U\_Shaped}$ were also optimized using the ωB97XD functional[262] (which includes a version of Grimme's D2 dispersion corrections)[263] within the self-consistent reaction field (SCRF) using the SMD model (CCl_4)[264] but using the basis set 6-31G(d,p).[266] Frequency calculations were performed at the same level to evaluate the zero-point vibrational energy and thermal corrections at 298 K and to confirm the nature of the stationary points, yielding one imaginary frequency for the transition states and none for the minima. The transition state was further confirmed by following the steepest descent to both sides and identifying the minima present in the reaction energy profile. Single-point energies were calculated using ωB97XD functional[262] (which includes a version of Grimme's D2 dispersion corrections)[263] within the self- consistent reaction field (SCRF) using the SMD model (CCl_4)[264] and using the basis set aug- cc-pVTZ.[265] The resulting energies were used to correct the energies obtained from optimization calculations. The reaction profiles were built up in terms of ΔG_{sol}.

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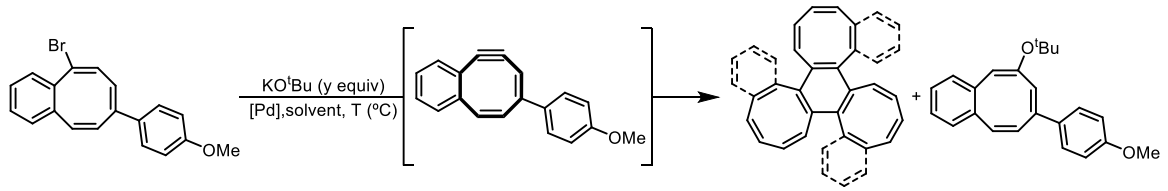
7.1.4. Reactivity of non-aromatic COTynes: Experimental procedures

Starting brominated benzofused COT **52** was prepared as described in section 7.1.3.4.2.

7.1.4.1. Pd(0)-catalysed [2+2+2] cycloaddition of bCOT 16ab



16ab **52** **53ab**

General procedure H: Corresponding solvent (x M) was added over **16ab** (0.1 mmol, 0.034 mg) and Pd(0) catalyst (5 mol%) in a round-bottomed flask under Ar. The resulting solution was stirred at rt for 10 min and then solid KO^{t}Bu (x equiv) was added. The resulting mixture was stirred at room temperature until disappearance of starting material (TLC monitoring). Upon completion, the reaction mixture was quenched with an aqueous solution of $NH_4Cl_{(sat)}$ and extracted with DCM. The organic layers were dried over anhydrous $MgSO_4$, filtered and evaporating to dryness. The resulting residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (8/2) to afford product **53ab**. (R_f = 0.5) and product **52** (R_f = 0.2) as a mixture of isomers/conformers.

Entry 1 Table 15. Following *general procedure H*, **16ab** (0.067 g, 0.2 mmol, 1 equiv), Pd_2dba_3 (0.01 g, 0.01 mmol, 0.05 equiv), KO^{t}Bu (0.045 g, 0.4 mmol, 2 equiv) and Et_2O (2 mL, 0.1 M) stirring at rt for 2h afforded alcoxyCOT **53ab** (10 mg, 15%) as a yellow solid and annulene **52** (22 mg, 44%) as a light brown solid as a mixture of three isomers/conformers (as judged by -*o*Me region in ^{1}H-NMR).

Entry 7 Table 15 (optimized conditions). Following *general procedure H*, **16ab** (0.067 g, 0.2 mmol, 1 equiv), Pd_2dba_3 (0.01 g, 0.01 mmol, 0.05 equiv), KO^{t}Bu (0.033 g, 0.3 mmol, 1.5 equiv) and THF (0.6 mL, 0.33 M) were stirring at rt for 1.5h to afford annulene **52** (40 mg, 78%) as a light brown solid as a mixture of three isomers/conformers in a 1/2.6/0.1 (Asymm DUD/Asymm DDU/Sym DDU) ratio (as judged by -*OMe* region in ^{1}H-NMR).

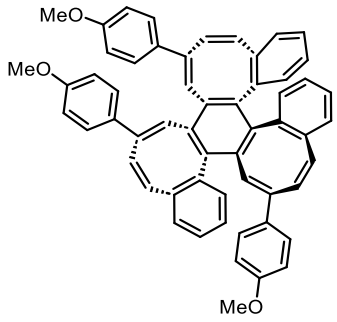
Entry 2 Table 16. Following *general procedure H*, **16ab** (0.034 g, 0.1 mmol, 1 equiv), $Pd(PPh_3)_4$ (0.012 g, 0.01 mmol, 0.01 equiv), KO^{t}Bu (0.017 g, 0.15 mmol, 1.5 equiv) and THF (0.3 mL, 0.33 M) were stirring at rt for 1.5h to afford annulene **52** (20 mg, 77%) as a light brown solid as a mixture of four isomers/conformers in a 1/2.3/1.3/0.4 (Asymm DUD/Asymm DDU/Sym DDU/unknown) ratio (as judged by - *OMe* region in ^{1}H-NMR).

When the reaction was performed in presence of ligands, the following procedure was followed. Pd_2dba_3 (0.005 g, 0.005 mmol, 0.05 equiv) and the corresponding ligand (x mol%) were stirred in THF (0.3 mL, 0.33 M) at room temperature for 1h and then, **16ab** (0.1 mmol, 0.034 g) and KO^{t}Bu (0.017 g, 0.15 mmol, 1.5 equiv) were sequentially added. Final reaction mixture was stirred at room temperature for 1.5 h. After work-up and purification following general conditions, the obtained results are summarized in Table 29.

Ligand	mol%	equiv	mg	**52** (Yield)		α/β/γ/δ[a]
L1: JohnPhos	20	0.02	5.9	20.6 mg	80%	1/1.9/0.2
L2: (Cy)JohnPhos	20	0.02	7.0	20.6 mg	80%	1/1.7/0.3
L3: Xphos	20	0.02	9.5	20.6 mg	80%	1/2.0/0.3
L4: (^{t}Bu)Xphos	20	0.02	8.5	20.6 mg	80%	1/1.9/0.3
L5: rac-BINAP	10	0.01	6.2	-	-	-
L6: dppf	10	0.01	5.6	-	-	-
L7: Xantphos	10	0.01	5.8	-	-	-
L8: DPEPhos	10	0.01	5.4	-	-	-
L9: DavePhos	20	0.02	7.9	18.3 mg	71%	1/1.5/0.3
L10: ^{t}BuDavePhos	20	0.02	6.8	19.3 mg	75%	1/6.1/0.3
L11: Sphos	20	0.02	8.2	19.3 mg	75%	1/1.1/0.05
L12: (S)-^{t}Bu-Phox	20	0.02	7.7	15.9 mg	62%	1/2.1/0.65
L13: P(^{t}Bu)$_3$	20	0.02	4.1	15.5 mg	60%	1/1.8/0.1
L14: PBu$_3$	20	0.02	4.0	-	-	-
L15: PMe$_3$	20	0.02	1.5	-	-	-
L16: PAd$_3$	20	0.02	8.7	21.4 mg	83%	1/2.1/0.3
L17: PPh$_3$	20	0.02	5.2	20.9 mg	81%	1/2.2/1.2/0.2
L18: P(4-OMePh)$_3$	20	0.02	7.1	18.1 mg	70%	1/2.1/0.65/-
L19: P(4-FPh)$_3$	20	0.02	6.3	20.9 mg	81%	1/2.3/1.1/0.4

Table 29. *Conditions:* ***16ab*** *(0.1 mmol), $Pd_2(dba)_3$ (5 mol%), ligand (x mol%) and KO^{t}Bu (1.5 equiv, previously sublimated) in THF (0.33 M), 90 min at rt a) α = Asymm DUD; β = Asymm DDU; γ = Sym DDU; δ = unknown, possible Asymm conformer.*

As mentioned in section 6.3.2.2.1, washing the reaction mixture with Et_2O causes the precipitation of pure ***Asymm*** DDU-52.



Asymm DDU-52

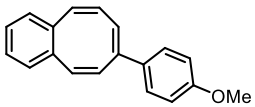
^{1}H NMR (500 MHz, CD_2Cl_2), δ (ppm): 7.40 (d, *J* = 3.2 Hz, 2H), 7.39 (d, *J* = 3.2 Hz, 2H), 7.33 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.20 (td, *J* = 7.4, 1.7 Hz, 1H), 7.14 (d, *J* = 11.1 Hz, 1H), 7.10 – 7.03 (m, 6H), 7.02 (s, 1H), 7.00 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.98 (dd, *J* = 4.4, 1.3 Hz, 1H), 6.96 (dd, *J* = 7.6, 1.3 Hz, 1H), 6.86 (d, *J* = 4.4 Hz, 2H), 6.84 (d, *J* = 4.3 Hz, 2H), 6.83 – 6.76 (m, 4H), 6.70 (d, *J* = 8.8 Hz, 2H), 6.64 (dd, *J* = 7.7, 1.2 Hz, 1H), 6.57 (dd, *J* = 7.7, 1.3 Hz, 1H), 6.39 (d, *J* = 11.2 Hz, 1H), 6.35 (d, *J* = 11.2 Hz, 1H), 6.31 (d, *J* = 11.4 Hz, 1H), 6.04 (d, *J* = 0.6 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H).

^{13}C NMR, DEPT (126 MHz, CD_2Cl_2), δ (ppm): 160.0 (2 x C), 159.8 (C), 141.8 (C), 141.6 (C), 140.9 (C), 140.6 (C), 140.0 (C), 139.8 (2 x C), 139.4 (C), 139.2 (C), 139.1 (C), 138.3 (C), 138.0 (C), 137.7 (C), 137.1 (C), 134.4 (CH), 133.9 (CH), 133.8 (CH), 132.7 (CH), 132.6 (CH), 132.5 (CH),

132.4 (CH), 132.3 (CH), 132.2 (CH), 132.1 (CH), 131.1 (CH), 130.8 (CH), 129.3 (CH), 128.2 (2 x CH), 128.1 (CH), 128.0 (2 x CH), 128.0 (2 x CH), 127.2 (2 x CH), 126.9 (CH), 126.9 (CH), 126.8 (CH), 126.7 (CH), 126.5 (CH), 126.4 (CH), 126.1 (CH), 126.0 (CH), 114.1 (2 x CH), 113.9 (CH), 55.7 (2 x CH_3), 55.6 (CH_3). *In theory there should be 21 $C_{quaternary}$ peaks but only 17 $C_{quaternary}$ peaks were observed, presumably some peaks have merged together.*

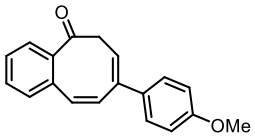
HRMS (APCI): calculated for $C_{57}H_{42}O_3$ $[M+H]^+$: 775.3207, found: 775.3217.

Following the standard procedure reported above, the use of BuLi instead of solid KO^{t}Bu gave rise to the formation of (5*Z*,7*E*,9*Z*)-7-(4-methoxyphenyl)benzo[8]annulene **54** (0.024 g, 46%) as a yellow solid. Further elution yielded (7E,9Z)-8-(4-methoxyphenyl)benzo[8]annulen-5(6H)-one **55** (0.015 g, 27%) as a green yellow solid.



54

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.33 (d, *J* = 8.6 Hz, 2H), 7.23 – 7.16 (m, 2H), 7.04 (dt, *J* = 13.0, 3.8 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 11.7 Hz, 1H), 6.63 (d, *J* = 10.2 Hz, 1H), 6.29 (d, *J* = 11.6 Hz, 1H), 6.20 (s, 1H), 3.79 (s, 3H).



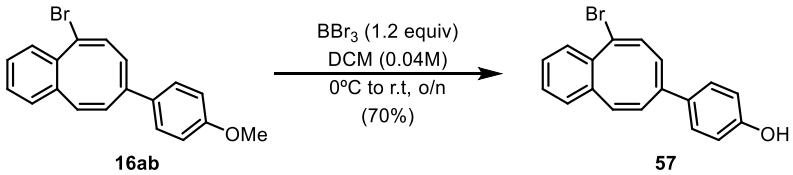
55

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 8.36 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.46 – 7.41 (m, 1H), 7.35 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 7.24 (d, *J* = 1.7 Hz, 2H), 7.08 (d, *J* = 12.6 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.60 (d, *J* = 12.5 Hz, 1H), 6.09 (t, *J* = 8.2 Hz, 1H), 3.77 (s, 3H), 3.58 (d, *J* = 8.2 Hz, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 194.5 (C), 159.5 (C), 140.7 (C), 137.2 (C), 136.2 (C), 133.3 (CH), 132.9 (CH), 132.1 (CH), 131.1 (C), 130.7 (CH), 129.3 (CH), 127.8 (2 x CH), 127.2 (CH), 122.1 (CH), 113.8 (2 x CH), 55.3 (CH_3), 45.0 (CH_2).

HRMS (APCI) calculated for $C_{19}H_{17}O_2$ $[M+H]^+$: 277.1223, found: 277.1222.

7.1.4.2. Synthesis of phenol 57



16ab **57**

In a round-bottomed flask **16ab** (1 mmol, 340 mg) was dissolved in dry DCM (20 mL, 0.05 M) and cooled to 0 ^{o}C, and then a solution of BBr_3 (1.1 equiv, 1 M in DCM) was added dropwise. The resulting mixture was stirred at rt until disappearance of starting material (o/n, TLC monitoring). Upon completion, the solution was diluted with ice-water and extracted with CH_2Cl_2 (3 x 10 mL) The organic layer was dried over $MgSO_4$, filtered and concentrated to dryness. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (8:2) to afford phenol **57** (228 mg, 70% yield) as a purple foam.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.33 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.17 (ddd, *J* = 7.4, 4.9, 1.8 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.94 (dd, *J* = 6.9, 2.0 Hz, 1H), 6.80 (d, *J* = 11.6 Hz, 1H), 6.69 – 6.56 (m, 3H), 6.23 (dd, *J* = 11.7, 1.3 Hz, 1H), 5.93 (d, *J* = 4.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 154.5 (C), 140.0 (C), 138.2 (C), 135.7 (C), 132.9 (CH), 132.1 (CH), 131.5 (CH), 130.9 (C), 129.2 (CH), 127.6 (CH), 127.3 (CH), 126.7 (2 x CH), 126.2 (CH), 123.0 (CH), 121.4 (C), 114.2 (2 x CH).

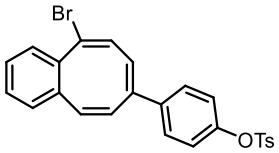
HRMS (APCI) calculated for $C_{18}H_{14}BrO$ $[M+H]^+$: 325.0209, found: 325.0222.

7.1.4.3. Synthesis of phenol derivatives 58

7.1.4.3.1. General procedure I for sulfonyl chloride reactions

Corresponding sulfonyl chloride derivative (1-1.5 equiv) was added in one portion to a solution of alcohol **57** and Et_3N (2.05 equiv) in DCM (0.4 M) cooled at 0ºC. The reaction was stirred at room temperature until disappearance of starting material (TLC monitoring). After this time the rection mixture was treated with water (10 mL), washed with NaCl $_{(sat)}$ (5 mL) and extracted with DCM (3 X 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc to afford the expected phenol derivative.

7.1.4.3.2. Synthesis of sulfonyl derivatives



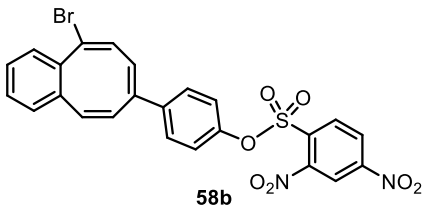
58a

Following the *general procedure I* tosylated bromoCOT **58a** was obtained as a yellow light solid (0.28 g, 87%) using starting benzoCOT **57** (0.22 g, 0.65 mmol), tosyl chloride (0.130 g, 0.67 mmol) Et_3N (0.190 mL, 2.05 equiv) and DCM (1.6 mL). Upon completion (1h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (85/15) as eluent.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.69 (d, *J* = 8.0 Hz, 2H), 7.45 – 7.37 (m, 1H), 7.33 – 7.19 (m, 6H), 7.06 – 6.98 (m, 1H), 6.94 – 6.85 (m, 3H), 6.70 (d, *J* = 4.0 Hz, 1H), 6.26 (d, *J* = 11.6 Hz, 1H), 6.06 (d, *J* = 4.0 Hz, 1H), 2.43 (s, 3H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 149.6 (C), 145.7 (C), 140.7 (C), 139.4 (C), 138.3 (C), 136.7 (C), 134.0 (CH), 133.8 (CH), 132.7 (C), 132.2 (CH), 130.6 (CH), 130.1 (2 x CH), 128.9 (CH), 128.8 (3 x CH), 127.9 (2 x CH), 127.7 (CH), 126.7 (CH), 123.3 (C), 122.6 (2 x CH), 22.0 (CH_3).

HRMS (APCI) calculated for $C_{25}H_{20}BrO_3S$ $[M+H]^+$: 479.0311, found: 479.0315.



58b

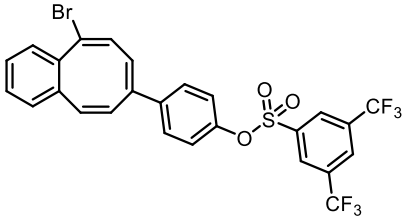
Following the *general procedure I* bromoCOT **58b** was obtained as an orange foam (0.33 g, 96%) using starting benzoCOT **57** (0.2 g, 0.62 mmol), 2,4-dinitrobenzenesulfonyl chloride (0.25 g, 0.93 mmol), Et_3N (0.180 mL, 2.05 equiv) and DCM (1.6 mL). Upon completion (1h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (7/3) to afford the target product.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 8.65 (d, *J* = 2.0 Hz, 1H), 8.47 (dd, *J* = 8.7, 2.0 Hz, 1H), 8.16 (d, *J* = 8.6 Hz, 1H), 7.43 (d, *J* = 6.9 Hz, 1H), 7.37 – 7.25 (m, 4H), 7.13 (d, *J* = 8.7 Hz, 2H), 7.05

(d, *J* = 5.5 Hz, 1H), 6.95 (d, *J* = 11.6 Hz, 1H), 6.73 (d, *J* = 4.0 Hz, 1H), 6.28 (d, *J* = 11.6 Hz, 1H), 6.10 (d, *J* = 4.0 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 151.1 (C), 149.1 (C), 148.5 (C), 140.2 (C), 139.3 (C), 139.2 (C), 136.34 (C), 134.2 (CH), 134.0 (CH), 133.8 (C), 133.4 (CH), 131.7(CH), 130.5 (CH), 128.7 (CH), 128.7 (CH), 128.2 (2 x CH), 127.6 (CH), 127.2 (CH), 126.5 (CH), 123.3 (C), 122.0 (2 x CH), 120.4 (CH).

HRMS (APCI) calculated for $C_{24}H_{16}BrN_2O_7S$ [M+H]+: 554.9856, found: 554.9866.



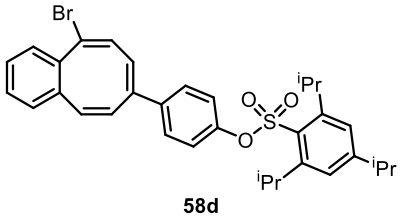
58c

Following the *general procedure I* bromoCOT **58c** was obtained as a yellow foam (0.3 g, 78%) using starting benzoCOT **57** (0.21 g, 0.65 mmol), 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (0.21 g, 0.66 mmol), Et_3N (0.185 mL, 2.05 equiv) and DCM (1.6 mL). Upon completion (1h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9/1) to afford the target product.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 8.31 (s, 2H), 8.21 (s, 1H), 7.48 – 7.39 (m, 1H), 7.31 (dd, *J* = 11.2, 8.0 Hz, 4H), 7.06 (d, *J* = 5.6 Hz, 1H), 6.96 (dd, *J* = 10.2, 4.0 Hz, 3H), 6.74 (d, *J* = 4.0 Hz, 1H), 6.29 (d, *J* = 11.7 Hz, 1H), 6.11 (d, *J* = 4.0 Hz, 1H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 148.5 (C), 140.2 (C), 139.0 (C), 138.2 (C), 136.3 (C), 134.0 (CH), 133.4 (C), 133.3 (CH), 133.0 (C), 132.5 (C), 131.6 (CH), 130.3 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 128.0 (3 x CH), 127.8 (CH), 127.4 (CH), 126.9 (CH), 124.0 (C), 123.2 (C), 122.0 (2 x CH), 120.4 (C).

HRMS (APCI) calculated for $C_{26}H_{16}BrF_6O_3S$ $[M+H]^+$: 600.9902, found: 600.9894.



58d

Following the *general procedure I* bromoCOT **58d** was obtained as a yellow foam (0.32 g, 82%) using starting benzoCOT **57** (0.22 g, 0.67 mmol), 2,4,6-triisopropylbenzenesulfonyl chloride (0.22 g, 0.65 mmol), Et_3N (0.190 mL, 2.05 equiv) and DCM (1.7 mL). Upon completion (1h) and work-up, the residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9/1) to afford the target product.

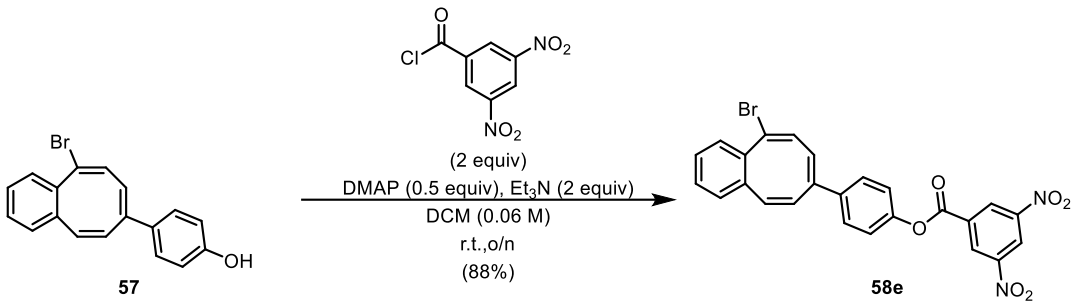
^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.46 – 7.38 (m, 1H), 7.29 – 7.23 (m, 6H), 7.00 (dd, *J* = 15.7, 8.0 Hz, 3H), 6.91 (d, *J* = 11.6 Hz, 1H), 6.72 (d, *J* = 4.0 Hz, 1H), 6.27 (d, *J* = 11.6 Hz, 1H), 6.07 (d, *J* = 4.0 Hz, 1H), 4.09 (p, *J* = 6.9 Hz, 2H), 2.96 (p, *J* = 6.9 Hz, 1H), 1.30 (d, *J* = 6.8 Hz, 6H), 1.22 (d, *J* = 6.8 Hz, 12H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 154.3 (C), 151.6 (2 x C), 149.2 (C), 140.6 (C), 139.0 (C), 138.0 (C), 136.4 (C), 133.7 (CH), 133.5 (CH), 131.9 (CH), 130.3 (CH), 129.9 (C), 128.6 (CH), 128.5 (CH), 127.6 (2 x CH), 127.4 (CH), 126.3 (C), 124.0 (2 x CH), 123.00 (C), 122.3 (2 x CH), 34.3 (CH), 29.8 (2 x CH), 24.6 (4 x CH_3), 23.6 (2 x CH_3).

HRMS (APCI) calculated for $C_{33}H_{36}BrO_3S$ $[M+H]^+$: 591.1563, found: 591.1567.

7.1.4.4. Synthesis of bCOTs 58

Synthesis of 4-((5Z,7E,9E)-10-bromobenzo[8]annulen-7-yl)phenyl 3,5-dinitrobenzoate ***58e***



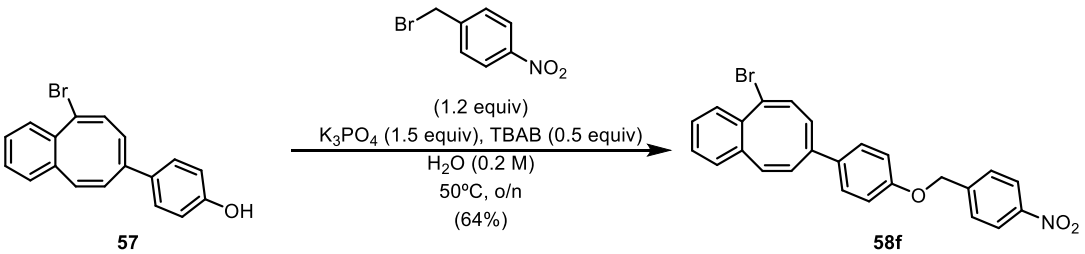
In a dried round-bottomed flask under an argon atmosphere **57** (0.13 g, 0.39 mmol), Et_3N (0.11 mL, 0.78 mmol, 2 equiv) and DMAP (0.024 mg, 0.19 mmol, 0.5 equiv) were dissolved in anhydrous DCM (6 mL, 0.06 M). The mixture was cooled to 0 °C and 3,5-dinitrobenzoyl chloride (0.181 mg, 0.78 mmol, 2 equiv) was added in one portion. The resulting mixture was stirred at room temperature until disappearance of starting material (TLC monitoring, o/n). Upon completion, the reaction was quenched with water (10 mL) and extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (8/2) to afford 10-bromobenzo[8]annulen-7-yl)phenyl 3,5-dinitrobenzoate **58e** (0.180 mg, 80%) as a yellow solid.

^{1}H NMR (300 MHz, CD_2Cl_2), δ (ppm): 9.30 (s, 3H), 7.45 (m, 3H), 7.35 – 7.28 (m, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 7.15 – 7.07 (m, 1H), 6.98 (d, *J* = 11.6 Hz, 1H), 6.78 (dd, *J* = 4.0, 1.2 Hz, 1H), 6.40 (d, *J* = 12.3 Hz, 1H), 6.20 (d, *J* = 4.0 Hz, 1H).

^{13}C NMR, DEPT (126 MHz, CD_2Cl_2), δ (ppm): 161.7 (C), 150.4 (C), 149.2 (2 x C), 140.9 (C), 139.5 (C), 138.1 (C), 137.0 (C), 134.1 (CH), 134.0 (CH), 133.6 (C), 132.4 (CH), 130.6 (CH), 130.3 (2 x CH), 129.0 (CH), 128.9 (CH), 128.0 (2 x CH), 127.8 (CH), 126.7 (CH), 123.4 (CH), 123.1 (C), 121.7 (2 x CH).

HRMS (APCI) calculated for $C_{25}H_{16}BrN_2O_6$ $[M+H]^+$: 519.0186, found: 519.0182.

Synthesis of (5E,7E,9Z)-5-bromo-8-(4-((4-nitrobenzyl)oxy)phenyl)benzo[8]annulene ***58f***



Alcohol **57** (0.17 g, 0.52mmol), 1-(bromomethyl)-4-nitrobenzene (0.134 mg, 0.62 mmol, 1.2 equiv), TBAB (0.084 g, 0.26 mmol, 0.5 equiv) and K_3PO_4 (0.165 g, 0.78 mmol, 1.5 equiv) were dissolved in water (2.5 mL, 0.2 M). The reaction mixture was stirred at 50 °C until disappearance of starting material (TLC monitoring, o/n). Upon completion, the reaction was diluted with

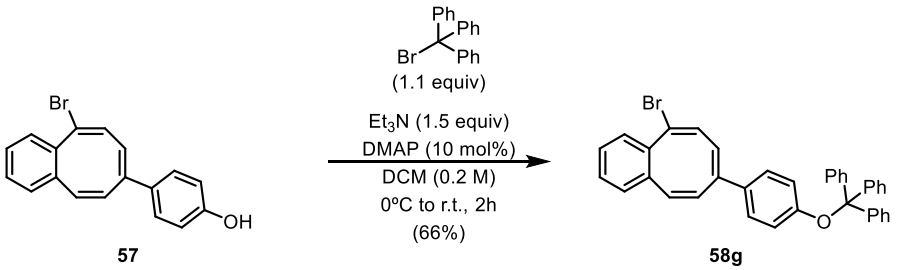
water and extracted with DCM (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (8/2) to afford 5-bromo-8-(4-((4-nitrobenzyl)oxy)phenyl)benzo[8]annulene **58f** (0.151 mg, 64%) as a green foam.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 8.24 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.43 (dd, *J* = 6.9, 2.3 Hz, 1H), 7.40 – 7.13 (m, 4H), 7.09 – 6.97 (m, 1H), 7.02 – 6.79 (m, 3H), 6.77 – 6.68 (m, 1H), 6.34 (dd, *J* = 11.6, 1.4 Hz, 1H), 6.06 (d, *J* = 4.0 Hz, 1H), 5.16 (s, 2H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 158.0 (C), 147.6 (C), 144.3 (C), 140.9 (C), 139.2 (C), 136.7 (C), 133.8 (CH), 133.2 (CH), 132.4 (CH), 130.3 (CH), 128.6 (CH), 128.4 (CH), 127.7 (2 x CH), 127.6 (2 x CH), 127.3 (CH), 124.4 (CH), 123.8 (2 x CH), 122.5 (C), 114.7 (2 x CH), 68.7 (CH_2).

HRMS (APCI) calculated for $C_{25}H_{19}BrNO_3$ $[M+H]^+$: 460.0543, found: 460.0551.

*Synthesis of (5E,7E,9Z)-5-bromo-8-(4-(trityloxy)phenyl)benzo[8]annulene **58g***

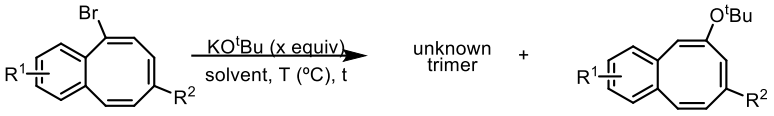


In a dried round-bottomed flask under an argon atmosphere alcohol **57** (0.10 g, 0.31 mmol), Et_3N (0.064 mL, 0.45 mmol, 1.5 equiv) and DMAP (0.004 mg, 0.031 mmol, 0.1 equiv) were dissolved in anhydrous DCM (0.8 mL, 0.2 M). The mixture was cooled to 0 ^oC and a solution of (bromomethanetriyl)tribenzene (0.112 mg, 0.34 mmol, 1.1 equiv) in DCM (0.8 mL) was added. The resulting mixture was stirred at the same temperature for 10 min and then at room temperature until disappearance of starting material (TLC monitoring, 2h). Upon completion, the reaction was quenched with water (10 mL) and extracted with DCM (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (90/10) to afford 5-bromo-8-(4-(trityloxy)phenyl)benzo[8]annulene **58g** (0.115 mg, 66%) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.50 – 7.48 (m, 8H), 7.35 – 7.27 (m, 10H), 7.01 (d, *J* = 7.8 Hz, 3H), 6.85 (d, *J* = 11.6 Hz, 1H), 6.73 – 6.62 (m, 3H), 6.26 (d, *J* = 11.6 Hz, 1H), 5.96 (d, *J* = 4.1 Hz, 1H).

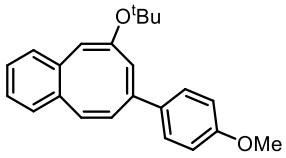
^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 155.7 (C), 144.0 (3 x C), 141.0 (C), 139.2 (C), 136.8 (C), 134.0 (2 x CH), 132.9 (2 x CH), 132.6 (2 x CH), 131.8 (C), 130.3 (CH), 128.9 (5 x CH), 128.7 (CH), 128.4 (CH), 127.8 (5 x CH), 127.3 (3 x CH), 126.5 (2 x CH), 123.9 (CH), 122.3 (C), 120.2 (2 x CH), 89.8 (C).

7.1.4.5. General procedure for thermal metal-free trimerization of bCOTs



16 **56** **53**

In a colourless vial, compound **16** (1 equiv) was dissolved in anhydrous solvent (x M) followed by the addition of solid KO^{t}Bu (x equiv). The resulting mixture was stirred at room temperature until disappearance of starting material (TLC monitoring). Upon completion, the reaction mixture was quenched with an aqueous solution of $NH_4Cl_{(sat)}$ and extracted with DCM. The organic layers were dried over anhydrous $MgSO_4$, filtered and evaporating to dryness. The resulting residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc to afford alkoxyCOT derivative **53** as a pale yellow solid and new unknown trimer **56** as a mixture of three isomers/conformers.



53ab

Reaction using bCOT **16ab** (0.068 mg, 0.02 mmol) and KO^{t}Bu (0.034 g, 0.3 mmol, 1.5 equiv) in dry THF (0.6 mL, 0.33 M) rendered (5E,7E,9Z)-6-(tert-butoxy)-8-(4-methoxyphenyl)benzo[8]annulene **53ab** (0.007 g, 10%, Rf = 0.5) as a light yellow solid by flash column chromatography through silica gel using a mixture of Hex/EtOAc (90/10) as eluent. Further elution afforded unknown trimer **56ab** (0.034 g, 66%, Rf = 0.2) as an orange-red solid as a mixture of three isomers in a 3/1/0.1 ratio.

53ab: **^{1}H NMR** (500 MHz, $CDCl_3$), δ (ppm): 7.33 (d, *J* = 8.8 Hz, 2H), 7.20 – 7.14 (m, 2H), 7.07 – 7.04 (m, 1H), 7.02 (dd, *J* = 6.4, 2.7 Hz, 1H), 6.90 (d, *J* = 11.5 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.32 (d, *J* = 11.5 Hz, 1H), 6.27 (s, 1H), 6.11 (s, 1H), 3.79 (s, 3H), 1.39 (s, 9H).

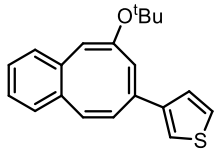
^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.5 (C), 152.0 (C), 140.1(C), 137.7 (C), 137.5 (C), 135.2 (CH), 132.3 (CH), 131.9 (C), 129.9 (CH), 128.9 (CH), 127.6 (2 x CH), 127.0 (CH), 126.4 (CH), 125.5 (CH), 120.3 (CH), 113.8 (2 x CH), 77.7 (C), 55.4 (CH_3), 29.4 (3 x CH_3).

HRMS (APCI) calculated for $C_{23}H_{25}O_2$ $[M+H]^+$: 333.1849, found: 333.1848.

Unknown trimer **56ab** (for major isomer): **^{1}H NMR** (500 MHz, $CDCl_3$), δ (ppm): 7.05 (dd, *J* = 10.4, 7.7 Hz, 4H), 6.84 (d, *J* = 8.5 Hz, 3H), 6.80 (d, *J* = 8.1 Hz, 3H), 6.74 – 6.68 (m, 4H), 6.53 (dd, *J* = 27.1, 11.4 Hz, 1H), 6.26 (dd, *J* = 12.0, 8.3 Hz, 2H), 6.18 (s, 1H), 6.09 (s, 2H), 6.02 (s, 1H), 5.74 (s, 1H), 4.52 (d, *J* = 10.1 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.76 (s, 3H). *Due to overlapping of isomers is not possible a good assignment of aromatic region from 7.15 to 7.40 ppm.*

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 159.7 (C), 159.0 (C), 158.4 (C), 158.3 (C), 152.6 (C), 145.6 (C), 144.2 (C), 142.3 (C), 140.9 (C), 140.6 (C), 140.0 (C), 139.0 (C), 138.7 (C), 137.4 (C), 136.6 (C), 135.6 (C), 134.9 (C), 134.5 (C), 133.6 (C), 133.5 (CH), 133.4 (CH), 132.5 (C), 132.3 (C), 132.1 (CH), 132.1 (CH), 131.4 (CH), 129.3 (CH), 128.5 (CH) 129.2 (CH), 128.3 (2 x CH), 128.1 (CH), 128.0 (CH), 127.6 (CH) 127.6 (CH), 127.5 (2 x CH), 127.1 (CH), 127.0 (2 x CH), 126.9 (CH), 126.4 (CH), 126.3 (CH), 124.8 (CH), 122.9 (CH), 118.0 (CH), 113.7 (2 x CH), 113.4 (2 x CH), 113.3 (2 x CH), 109.1 (CH), 61.6 (C), 55.3 (2 x CH_3), 55.2 (CH_3), 50.4 (CH).

HRMS (APCI): calculated for $C_{57}H_{42}O_3$ $[M+H]^+$: 775.3207, found: 775.3209.



53aq

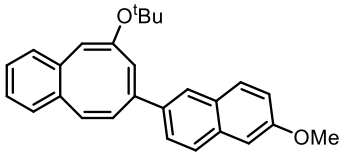
Reaction using bCOT **16aq** (0.094 mg, 0.3 mmol) and KO^{t}Bu (0.050 g, 0.45 mmol, 1.5 equiv) in dry THF (0.9 mL, 0.33 M) rendered 3-((5Z,7E,9E)-9-(tert-butoxy)benzo[8]annulen-7-yl)thiophene **53aq** (0.014 g, 15%, Rf = 0.3) as a light yellow solid by flash column chromatography through silica gel using a mixture of Hex/EtOAc (90/10) as eluent. Further elution afforded unknown trimer **56aq** (0.039 g, 56%, Rf = 0.15) as an orange solid as a mixture of three isomers in a 3/1/0.1 ratio.

53aq: ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.17 (s, 1H), 7.14 – 7.05 (m, 4H), 6.94 (dd, *J* = 6.7, 2.3 Hz, 2H), 6.79 (d, *J* = 11.6 Hz, 1H), 6.32 (d, *J* = 11.5 Hz, 1H), 6.18 (s, 1H), 6.10 (s, 1H), 1.29 (s, 9H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 150.6 (C), 140.4 (C), 136.4 (C), 136.2 (C), 134.8 (C), 134.2 (CH), 130.4 (CH), 129.0 (CH), 127.9 (CH), 126.1 (CH), 125.4 (CH), 125.2 (CH), 124.8 (CH), 124.1 (CH), 120.8 (CH), 119.3 (CH), 76.8 (C), 28.4 (3 x CH_3).

HRMS (APCI) calculated for $C_{20}H_{21}OS$ $[M+H]^+$: 309.1308, found: 309.1319.

Unknown trimer **56aq**: **HRMS (APCI)** calculated for $C_{48}H_{31}S_3$ $[M+H]^+$: 703.1582, found: 703.1597.



53at

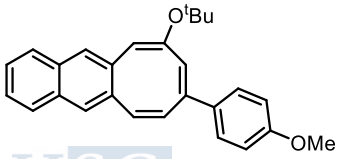
Reaction using bCOT **16at** (0.092 mg, 0.24 mmol) and KO^{t}Bu (0.040 g, 0.34 mmol, 1.5 equiv) in dry THF (0.7 mL, 0.33 M) rendered (5E,7E,9Z)-6-(tert-butoxy)-8-(6-methoxynaphthalen-2-yl)benzo[8]annulene **53at** (0.016 g, 18%, Rf = 0.4) as a light yellow solid by flash column chromatography through silica gel using a mixture of Hex/EtOAc (90/10) as eluent. Further elution afforded unknown trimer **56at** (0.041 g, 57%, Rf = 0.2) as a light orange solid as a mixture of three isomers in a 3/1/0.1 ratio.

53at: **^{1}H NMR** (500 MHz, $CDCl_3$), δ (ppm): 7.72 (dd, *J* = 5.5, 3.6 Hz, 2H), 7.66 (d, *J* = 8.6 Hz, 1H), 7.53 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.20 – 7.17 (m, 2H), 7.13 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.10 – 7.07 (m, 1H), 7.04 (ddd, *J* = 7.8, 3.1, 1.6 Hz, 1H), 6.98 (d, *J* = 11.5 Hz, 1H), 6.46 (d, *J* = 11.5 Hz, 1H), 6.31 (s, 1H), 3.91 (s, 3H), 1.42 (s, 9H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 156.9 (C), 150.9 (C), 139.4 (C), 136.6 (C), 136.3 (C), 134.4 (CH), 133.4 (C), 133.2 (C), 131.2 (CH), 128.9 (CH), 128.8 (CH), 127.9 (CH), 127.7 (C), 126.0 (CH), 125.8 (2 x CH), 125.4 (CH), 124.5 (CH), 123.5 (CH), 119.5 (CH), 118.0 (CH), 104.6 (CH), 76.8 (C), 54.3 (CH_3), 28.4 (3 x CH_3).

HRMS (APCI) calculated for $C_{27}H_{27}O_2$ $[M+H]^+$: 383.2006, found: 383.2001.

Unknown trimer **56at**: **HRMS (APCI)** calculated for $C_{69}H_{49}O_3$ $[M+H]^+$: 925.3676, found: 925.3652.



53cb

Reaction using bCOT **16cb** (0.023 mg, 0.06 mmol) and KO^{t}Bu (0.009 g, 0.08 mmol, 1.5 equiv) in dry THF (0.18 mL, 0.33 M) rendered (6E,8E,10Z)-7-(tert-butoxy)-9-(4-methoxyphenyl)cycloocta[b]naphthalene **53cb** (0.004 g, 18%, Rf = 0.5) as a light yellow solid by flash column chromatography through silica gel using a mixture of Hex/EtOAc (90/10) as eluent. Further elution afforded

unknown trimer **56cb** (0.002 g, 12%, Rf = 0.2) as an orange-red solid as a mixture of three isomers in a 3/1/0.1 ratio.

53cb: **^{1}H NMR** (500 MHz, $CDCl_3$), δ (ppm): 7.70 (dt, *J* = 5.6, 3.4 Hz, 2H), 7.54 (s, 1H), 7.49 (s, 1H), 7.38 – 7.35 (m, 1H), 7.34 (d, *J* = 8.9 Hz, 2H), 7.11 (d, *J* = 11.7 Hz, 1H), 6.97 (d, *J* = 10.8 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.49 (s, 1H), 6.42 (d, *J* = 11.7 Hz, 1H), 6.12 (s, 1H), 3.78 (s, 3H), 1.40 (s, 9H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 158.5 (C), 151.5 (C), 138.6 (C), 134.9 (C), 134.5 (C), 133.6 (CH), 131.5 (C), 131.4 (CH), 131.0 (C), 130.8 (C), 127.5 (CH), 126.8 (CH), 126.7 (CH), 126.5(2 x CH), 126.4 (CH), 124.8 (CH), 124.7 (CH), 124.0 (CH), 118.8 (CH), 112.8 (2 x CH), 76. 9 (C), 54.3 (CH_3), 28.5 (3 x CH_3).

HRMS (APCI) calculated for $C_{27}H_{27}O_2$ $[M+H]^+$: 383.2006, found: 383.2005.

Unknown trimer **56cb**: **HRMS (APCI)** calculated for $C_{69}H_{49}O_3$ $[M+H]^+$: 925.3676, found: 925.3710.

7.1.4.6. X-ray crystallographic data

7.1.4.6.1. Crystallographic data of compound 53ab

An X-ray crystal of compound **53** was grown by slow evaporation of a concentrated solution of compound **53ab** in DCM.

*Figure 64. ORTEP drawing of compound **53ab** showing thermal ellipsoids at the 50% contour probability level.*

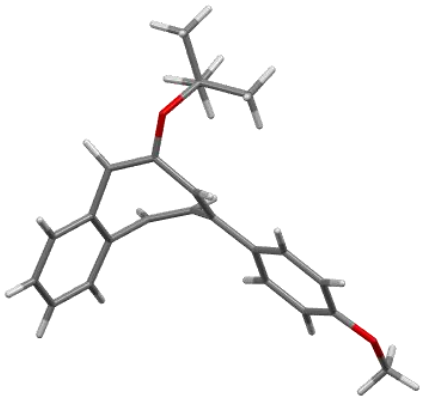


*Table 30. Crystal data and structure refinement for **53ab***

Deposition Number CCDC	-	
Chemical formula	$C_{23}H_{24}O_2$	
Molecular weight	332.42 g/mol	
Temperature	100 K	
Wavelength	0.71073Å	
Crystal size	0.12 × 0.09 × 0.04 mm	
Crystal habit	Plate, colourless	
Crystal system	Monoclinic	
Space group	$P2_{1/c}$	
Unit cell dimensions	a = 12.0835 (10) Å	
	b = 6.0075 (5) Å	β = 97.418 (3)°
	c = 25.1675 (17) Å	
Volume	1811.7 (2) $Å^3$	
Z	4	
Density (calculated)	1.219 g/cm^3	
Absorption coefficient	0.08 mm^{-1}	
F(000)	712	

7.1.4.6.2. Crystallographic data of compound Sym DUU 52

An X-ray crystal of compound Sym DUU 52 was grown by vapor diffusion using DCM and hexanes as mixture of solvents.

*Figure 65. ORTEP drawing of compound **Sym DUU 52** showing thermal ellipsoids at the 50% contour probability level. Hydrogens atoms were omitted for clarity.*

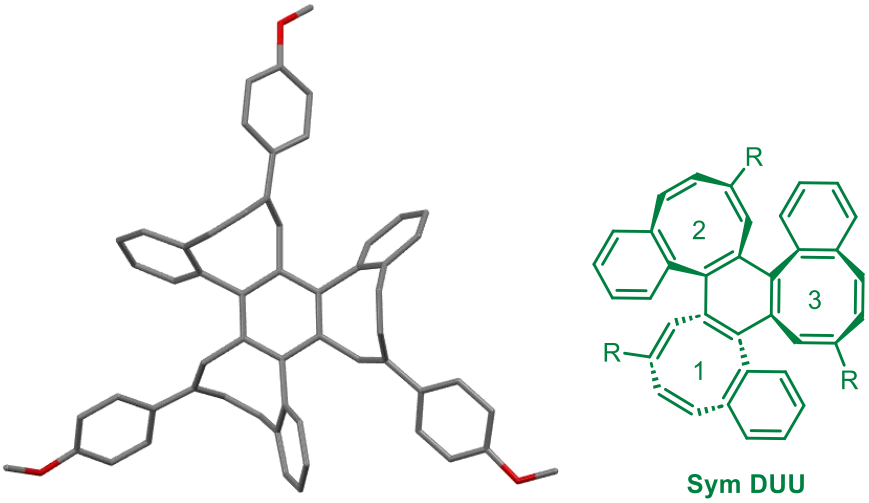


*Table 31. Crystal data and structure refinement for **Sym DUU 52***

Deposition Number CCDC	-	
Chemical formula	$C_{57}H_{42}O_3$	
Molecular weight	774.90 g/mol	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal size	0.10 × 0.09 × 0.08 mm	
Crystal habit	Block, clear colourless	
Crystal system	Monoclinic	
Space group	$P2_{1/c}$	
Unit cell dimensions	a = 24.127 (3) Å	
	b = 15.603 (2) Å	β = 93.082 (4)°
	c = 10.8431 (12) Å	
Volume	4076.0 (9) $Å^3$	
Z	4	
Density (calculated)	1.263 g/cm^3	
Absorption coefficient	0.08 mm^{-1}	
F(000)	1632	

7.1.4.6.3. Crystallographic data of compound Asymm DUD 52

An X-ray crystal of compound Asymm DUD 52 was grown by vapor diffusion using DCM and hexanes as mixture of solvents.

Figure 66. ORTEP drawing of compound **Asymm DUD 52** showing thermal ellipsoids at the 50% contour probability level. Hydrogens atoms were omitted for clarity.

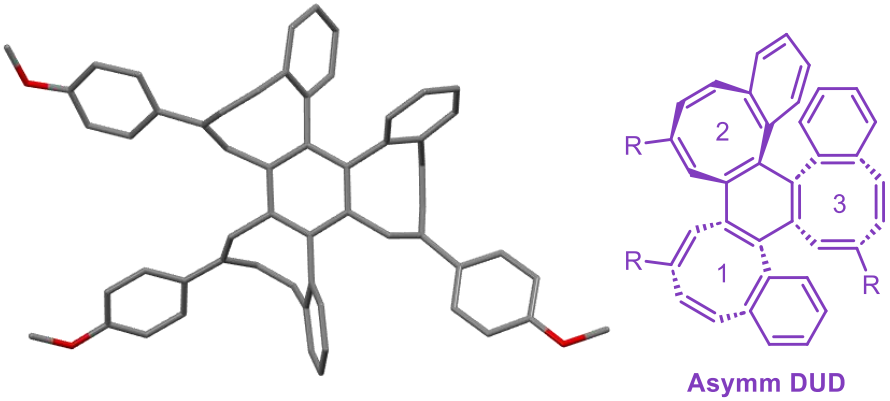


*Table 32. Crystal data and structure refinement for **Asymm DUD 52***

Deposition Number CCDC	-	
Chemical formula	$C_{57}H_{42}O_3$	
Molecular weight	774.90 g/mol	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal size	0.18 × 0.09 × 0.03 mm	
Crystal habit	Plate, clear colourless	
Crystal system	Monoclinic,	
Space group	$P2_{1/c}$	
Unit cell dimensions	a = 17.439 (3) Å	
	b = 25.330 (4) Å	β = 106.260 (4)°
	c = 10.9300 (17) Å	
Volume	4635.0 (13) $Å^3$	
Z	4	
Density (calculated)	1.110 g/cm^3	
Absorption coefficient	0.07 mm^{-1}	
F(000)	1632	

7.1.4.6.4. Crystallographic data of compound Asymm DDU 52

An X-ray crystal of compound Asymm DDU 52 was grown by vapor diffusion using DCM and hexanes as mixture of solvents.

Figure 67. ORTEP drawing of compound **Asymm DDU 52** showing thermal ellipsoids at the 50% contour probability level. Hydrogens atoms were omitted for clarity.

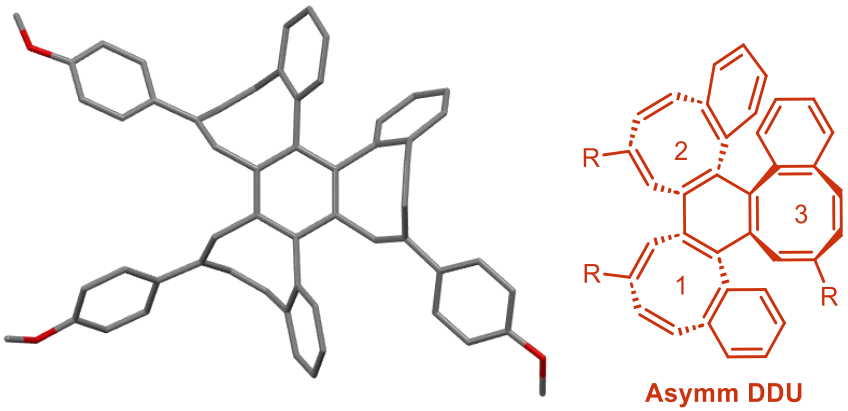


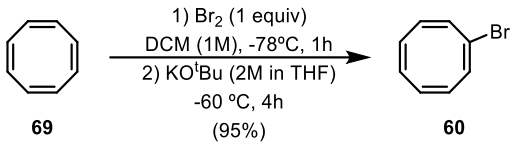
Table 33. Crystal data and structure refinement for ***Asymm DDU 52***

Deposition Number CCDC	-	
Chemical formula	$C_{57}H_{42}O_3$. CH_2Cl_2	
Molecular weight	859.83 g/mol	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal size	0.11 × 0.10 × 0.08 mm	
Crystal habit	Plate, colourless	
Crystal system	Monoclinic,	
Space group	$P2_{1/n}$	
Unit cell dimensions	a = 12.9670 (7) Å	
	b = 17.9488 (9) Å	β = 95.033 (2)°
	c = 18.6596 (10) Å	
Volume	4326.1 (4) $Å^3$	
Z	4	
Density (calculated)	1.32 g/cm^3	
Absorption coefficient	0.2 mm^{-1}	
F(000)	1800	

7.1.5. Metal-catalysed vs thermal trimerizations of symmetric COTynes: Experimental procedures

7.1.5.1. Synthesis of starting functionalized COTs

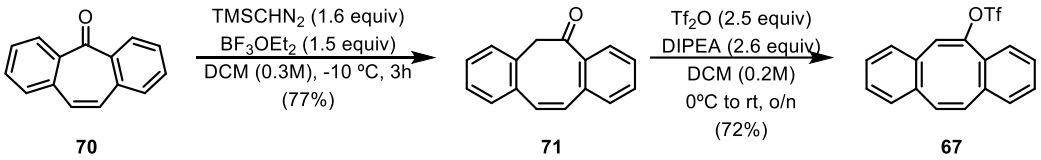
7.1.5.1.1. (1E,3Z,5Z,7Z)-1-bromocycloocta-1,3,5,7-tetraene 60[231]



A solution of Br_2 (0.1 mL, 2 mmol, 1 equiv) in DCM (0.5 mL) was slowly added to a stirred solution of COT **69** (0.23 mL, 2 mmol) in DCM (1.5 mL, 1 M) cooled at -70 ºC. The resulting solution was stirred at the same temperature for 1h and then a solution of KO^{t}Bu in THF (1.4 mL, 2 M) was added dropwise. The reaction mixture was stirred at -60 ºC for 4h, warmed to -10ºC, and poured into ice water using a small amount of solid $MgSO_4$ to break the formed emulsions. The organic layer was removed and the aqueous layer was extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford BrCOT **60** (0.35 g, 95%) as a light-yellow oil. Characterization data match those reported in the literature.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 6.22 (s, 1H), 5.97 – 5.75 (m, 5H), 5.64 (d, *J* = 10.5 Hz, 1H).

7.1.5.1.2. (5E,11Z)-dibenzo[a,e][8]annulen-5-yl trifluoromethanesulfonate 67[187]



A solution of trimethylsilyl diazomethane (5.8 mL, 2 M in hexane) in DCM (10 mL) was added dropwise to a stirred solution of dibenzosuberenone **70** (1.53 g, 7.2 mmol) and BF_3.OEt_2 (1.3 mL, 10.8 mmol, 1.5 equiv) in DCM (16 mL, 0.3 M) at -10 ºC over a period of 1h. The reaction mixture was stirred at the same temperature for 2h, and then poured into ice water. The aqueous layer was extracted with DCM (3 x 15 mL) and the combined organic layers washed with brine. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of DCM/Hex (1:2) to afford (Z)-dibenzo[*a,e*][8]annulen-5(6H)-one **71** (1.2 g, 77%) as a yellow solid. Characterization data match those reported in the literature

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 8.26 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.40 (m, 2H), 7.40 – 7.18 (m, 5H), 7.05 (d, *J* = 2.2 Hz, 2H), 4.06 (s, 2H).

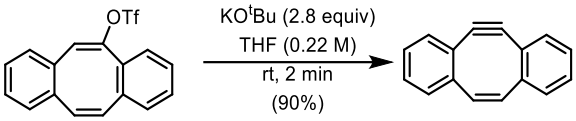
In a round-bottomed flask DIPEA (1.9 mL, 11 mmol, 2.6 equiv) and triflic anhydride (1.8 mL, 10.5 mmol, 2.5 equiv) was dissolved in dry DCM (14 mL) at 0 ^{o}C, at which point a solution of dibenzoannulenone **71** (0.92 g, 4.2 mmol) in DCM (7 mL, 0.2 M) was added dropwise. The reaction mixture was stirred at room temperature until disappearance of starting material (TLC monitoring, o/n). Upon completion, the mixture was poured into water (50 mL) and extracted with DCM (3 X 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (9:1) to afford triflate **67** (1.07g, 72%) as a light yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.35 – 7.18 (m, 5H), 7.11 – 7.06 (m, 3H), 6.92 (s, 1H), 6.82 (s, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm):146.1 (C), 137.1 (C), 135.9 (C), 132.2 (CH), 131.5 (CH), 130.9 (C), 130.4 (C), 128.9 (CH), 128.3 (CH), 128.3 (CH), 128.1 (CH), 127.6 (CH), 127.1 (CH), 126.4 (CH), 126.3 (CH), 123.8 (CH), 117.5 (CF_3, *J* =320 Hz)

HRMS (APCI-Sonda) calculated for $C_{17}H_{11}F_3O_3S$ $[M]^+$: 352.0376, found: 352.0381.

7.1.5.1.3. Sym-dibenzo-1,3,5-cyclooctatrien-7-yne 30



67 **30**

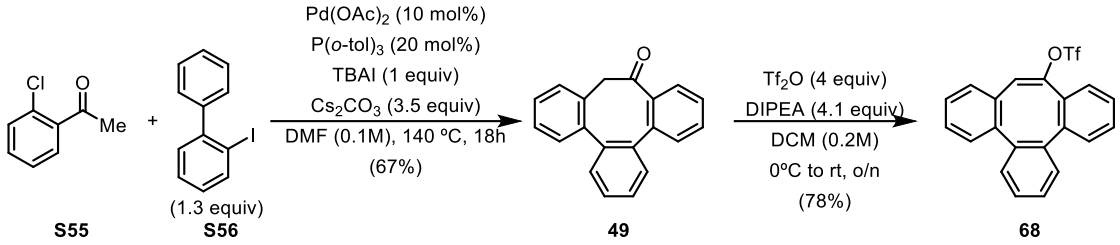
In a round-bottomed flask dried and under Ar, a solution of triflate **67** (0.2 g, 0.57 mmol) in THF (2.5 mL, 0.22 M) was added dropwise during 1 min to a stirred solution of sublimated KO^{t}Bu (0.18 mmol, 1.6 mmol, 2.8 equiv) in dry THF (20 mL, 0.08 M) at rt. The resulting mixture was stirred at the same temperature for another 1 min and then, aqueous HCl (10 mL, 2N) added followed by ether (20 mL). The ether extract was washed with water (2 x 10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through neutral alumina using a mixture of Hex/EtOAc (99:1) to afford dibenzoCOTyne **30** (0.1 g, 90%) as an orange crystal solid.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 6.95 – 6.78 (m, 4H), 6.67 (dd, *J* = 7.4, 1.7 Hz, 2H), 6.56 (dd, *J* = 7.2, 1.7 Hz, 2H), 5.49 (s, 2H).

^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 146.8 (2 x C), 134.8 (2 x CH), 132.0 (2 x CH), 129.5 (2 x CH), 129.0 (2 x CH), 126.1 (2 x CH), 123.1 (2 x C), 108.6 (2 x C).

Note: After 10 min in solution ($CDCl_3$), the product starts to form several products

7.1.5.1.4. (E)-tribenzo[a,c,e][8]annulen-9-yl trifluoromethanesulfonate 68[187,232]



A 250 mL Schlenk-type tube dry, under Ar and equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (0.07 g, 0.31 mmol, 0.1 equiv), $P(o\text{-}tol)_3$ (0.19 g, 0.62 mmol, 0.2 equiv), Cs_2CO_3 (3.5 g, 10.8 mmol, 3.5 equiv) and TBAI (1.14 g, 3.1 mmol, 1 equiv). Then DMF (31 mL, 0.1 M), 2-iodobiphenyl **S56** (0.65 mL, 3.7 mmol, 1.2 equiv) and *ortho*-chloroacetophenone **S55** (0.4 mL, 3.1 mmol, 1 equiv) were sequentially added. The reaction mixture was immediately frozen with liquid nitrogen and then the flask was evacuated and backfilled with Ar for 6 times. The mixture was stirred at 140 °C in a preheated oil bath for 18h. Upon completion the rection was cooled down to room temperature, quenched with $NH_4Cl_{(sat)}$ (20 mL) and water (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95:5) to afford tribenzo[a,c,e][8]annulen-9(10H)-one **49** (0.56 g, 67%) as a light orange solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.65 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.42 (pd, *J* = 7.4, 1.7 Hz, 2H), 7.31 (td, *J* = 7.5, 1.5 Hz, 1H), 7.30 – 7.21 (m, 4H), 7.16 (d, *J* = 2.9 Hz, 3H), 7.00 (dd, *J* = 7.7, 1.3 Hz, 1H), 3.73 (s, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 202.3 (C), 141.6 (C), 141.2 (C), 140.3 (C), 139.7 (C), 136.9 (C), 134.2 (C), 132.1 (CH), 131.7 (CH), 131.1 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.3 (2 x CH), 128.1 (CH), 127.9 (CH), 127.9 (CH), 127.6(CH), 50.0 (CH_2).

In a round-bottomed flask DIPEA (2.9 mL, 16.7 mmol, 4.1 equiv) and triflic anhydride (2.7 mL, 16.3 mmol, 4 equiv) was dissolved in dry DCM (15 mL) at 0 °C, and then a solution of tribenzoannulenone **49** (1.1 g, 4.1 mmol) in DCM (7 mL, 0.2 M) was added dropwise. The reaction mixture was stirred at room temperature until disappearance of starting material (TLC monitoring, o/n). Upon completion, the mixture was poured into water (50 mL) and extracted with DCM (3 X 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (95:5) to afford (E)-tribenzo[*a,c,e*][8]annulen-9-yl trifluoromethanesulfonate **68** (1.28g, 78%) as a light yellow solid.

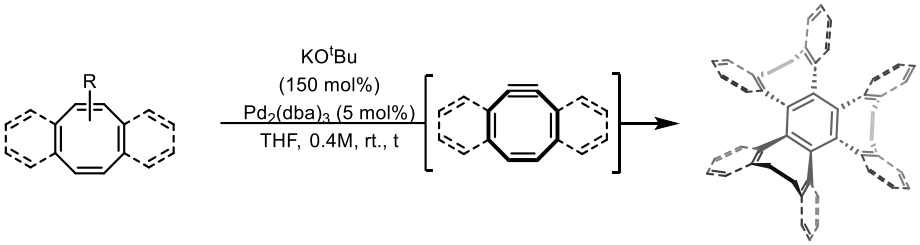
^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.47 – 7.44 (m, 2H), 7.41 (td, *J* = 7.8, 1.5 Hz, 2H), 7.37 – 7.33 (m, 1H), 7.29 (ddt, *J* = 7.7, 4.9, 2.4 Hz, 2H), 7.26 – 7.25 (m, 1H), 7.25 – 7.21 (m, 2H), 7.19 – 7.15 (m, 2H), 6.91 (s, 1H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 147.8 (C), 142.9 (C), 141.8 (C), 140.8 (C), 140.2 (C), 132.5 (C), 131.5 (C), 130.8 (CH), 130.5 (CH), 130.4 (CH), 130.3 (CH), 129.9 (CH), 128.5 (CH),

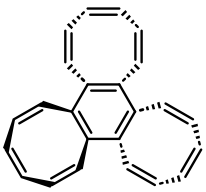
128.1 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 127.6 (CH), 127.3 (CH), 123.9 (CH), 118.5 (CF_3, d, *J* = 321.3 Hz).

HRMS (APCI) calculated for $C_{21}H_{13}F_3O_3S$ $[M]^+$: 402.0532, found: 402.0538.

7.1.5.2. Metal-catalysed [2+2+2] cycloaddition of BrCOT 60 and vinyl triflate dibenzoCOT 67



In a round-bottomed flask, dried and under argon, starting COT (1 equiv) and $Pd_2(dba)_3$ (5 mol%) were dissolved in anhydrous THF (0.4 M). The resulting mixture was stirred for 10 min and then solid KO^{t}Bu (1.5 equiv) was added. The resulting mixture was stirred at room temperature until disappearance of starting material (TLC monitoring). Upon completion, the reaction mixture was concentrated to dryness and the residue purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc to afford the corresponding tri[8]annulene.



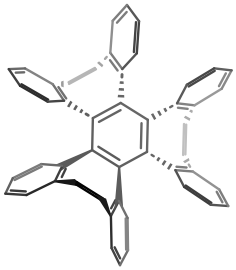
61

Tri[8]annulene **61** was obtained as a yellow-green solid (7 mg, 35%) using BrCOT **60** (0.2 mmol, 0.036 mg), $Pd_2(dba)_3$ (0.009 g, 0.01 mmol, 5 mol%), KO^{t}Bu (0.034 g, 0.3 mmol, 1.5 equiv) and THF (0.5 mL, 0.4 M) stirring at rt for 4h. Purification conditions: Hex/EtOAc (98/2).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 6.42 (d, *J* = 11.6 Hz, 2H), 6.29 (d, *J* = 11.5 Hz, 4H), 6.03 (d, *J* = 11.3 Hz, 4H), 6.00 (d, *J* = 13.3 Hz, 2H), 5.94 (s, 2H), 5.93 (s, 4H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 135.3 (2 x C), 134.8 (2 x C), 134.7 (2 x C), 131.7 (2 x CH), 131.3 (2 x CH), 131.2 (2 x CH), 130.1 (2 x CH), 130.1 (2 x CH), 130.0 (2 x CH), 129.1 (2 x CH), 129.0 (2 x CH), 129.0 (2 x CH).

HRMS (APCI) calculated for $C_{24}H_{19}$ $[M+H]^+$: 307.1481, found: 307.1481.



63

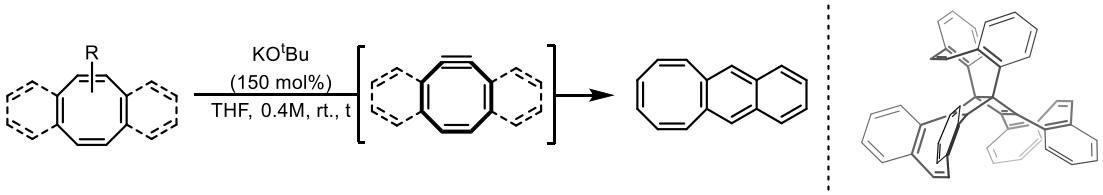
Dibenzotri[8]annulene **63** was obtained as a yellow solid (10 mg, 25%) using vinyl triflate COT **67** (0.2 mmol, 0.073 mg), $Pd_2(dba)_3$ (0.01 g, 0.01 mmol, 5 mol%), KO^{t}Bu (0.034 g, 0.3 mmol, 1.5 equiv) and THF (0.5 mL, 0.4 M) stirring at rt for 6h. Purification conditions: Hex/EtOAc (90/10)

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.20 – 7.16 (m, 2H), 7.05 (s, 2H), 6.92 (dd, *J* = 7.7, 1.3 Hz, 2H), 6.87 – 6.78 (m, 14H), 6.76 – 6.72 (m, 2H), 6.62 (td, *J* = 7.3, 1.7 Hz, 2H), 6.57 (td, *J* = 7.5, 1.4 Hz, 2H), 6.50 (dd, *J* = 7.7, 1.2 Hz, 2H), 6.38 (dd, *J* = 7.8, 1.3 Hz, 2H).

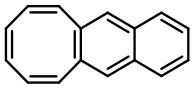
^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 141.0 (2 x C), 140.2 (2 x C), 139.5 (2 x C), 139.4 (2 x C), 139.4 (2 x C), 138.8 (2 x C), 138.5 (2 x C), 138.0 (2 x C), 137.4 (2 x C), 133.5 (2 x CH), 133.1 (2 x CH), 132.9 (2 x CH), 131.3 (2 x CH), 130.1 (2 x CH), 129.2 (2 x CH), 126.3 (2 x CH), 126.3 (2 x CH), 126.0 (2 x CH), 125.9 (2 x CH), 125.7 (2 x CH), 125.7 (2 x CH), 125.6 (2 x CH), 125.6 (2 x CH), 124.8 (2 x CH).

HRMS (APCI) calculated for $C_{48}H_{31}$ $[M+H]^+$: 607.2425, found: 607.2420.

7.1.5.3. Metal-free cycloaddition of BrCOT 60 and vinyl triflate dibenzoCOT 67



In a round-bottomed flask, dried and under argon, corresponding COT (1 equiv) was dissolved in anhydrous THF (0.4 M) followed by the addition of solid KO^{t}Bu (1.5 equiv). The resulting mixture was stirred at room temperature until disappearance of starting material (TLC monitoring). Upon completion, the reaction mixture was concentrated to dryness and the residue purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc to afford the corresponding product.



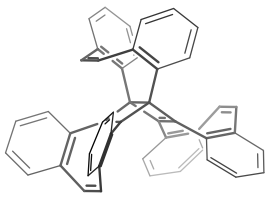
72

Dimer **72** was obtained as a yellow solid (4 mg, 20%) using BrCOT **60** (0.2 mmol, 0.036 mg), KO^{t}Bu (0.034 g, 0.3 mmol, 1.5 equiv) and THF (0.5 mL, 0.4 M) stirring at rt for 4h. Purification conditions: Hex/EtOAc (98/2).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.72 (dd, *J* = 6.2, 3.3 Hz, 2H), 7.45 (s, 2H), 7.39 (dd, *J* = 6.3, 3.2 Hz, 2H), 6.78 (d, *J* = 11.5 Hz, 2H), 6.13 (ddd, *J* = 11.5, 2.2, 1.4 Hz, 2H), 5.90 (dd, *J* = 2.2, 1.2 Hz, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 136.0 (2 x C), 133.1 (2 x CH), 132.5 (2 x C), 131.3 (2 x CH), 130.3 (2 x CH), 128.7 (2 x CH), 127.5 (2 x CH), 126.0 (2 x CH).

HRMS (APCI) calculated for $C_{16}H_{13}$ $[M+H]^+$: 205.1012, found: 205.1010.



62

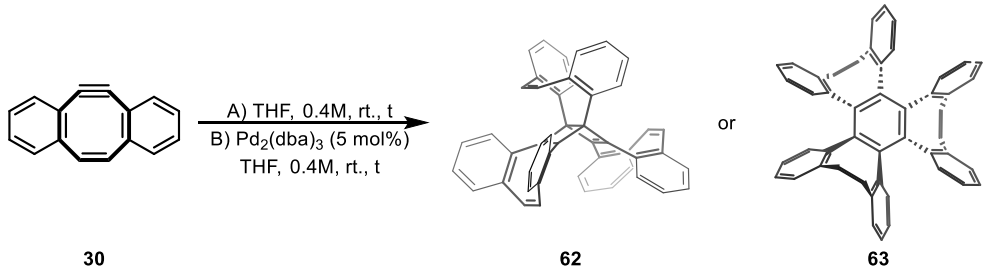
Dewar benzene **62** was obtained as a yellow solid (24 mg, 60%) using dibenzoCOT **67** (0.2 mmol, 0.071 mg), KO^{t}Bu (0.034 g, 0.3 mmol, 1.5 equiv) and THF (0.5 mL, 0.4 M) stirring at rt for 6h. Purification conditions: Hex/EtOAc (90/10).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.19 (td, *J* = 7.6, 1.3 Hz, 2H), 7.14 (q, *J* = 2.9, 2.4 Hz, 8H), 7.12 (s, 2H), 7.08 (dd, *J* = 7.8, 1.3 Hz, 2H), 7.04 (td, *J* = 7.6, 1.4 Hz, 2H), 7.00 (s, 2H), 6.95 (td, *J* = 7.5, 1.7 Hz, 2H), 6.87 – 6.75 (m, 4H), 6.72 (s, 2H), 6.59 (d, *J* = 7.8 Hz, 2H), 6.35 (s, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 153.0 (2 x C), 149.9 (2 x C), 138.2 (2 x C), 137.5 (2 x C), 137.0 (2 x C), 136.3 (2 x C), 135.6 (2 x C), 134.6 (2 x C), 133.9 (2 x CH), 133.0 (2 x CH), 132.1 (2 x CH), 131.3 (2 x CH), 130.5 (2 x CH), 130.2 (2 x CH), 129.0 (2 x CH), 127.7 (2 x CH), 127.5 (2 x CH), 127.4 (2 x CH), 127.4 (2 x CH), 127.1 (2 x CH), 127.1 (2 x CH), 126.8 (2 x CH), 126.3 (2 x CH), 69.7 (2 x C).

HRMS (APCI) calculated for $C_{48}H_{31}$ $[M+H]^+$: 607.2420, found 607.2418.

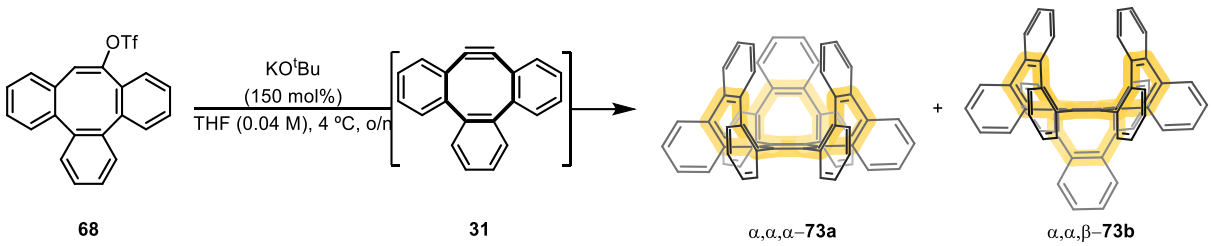
7.1.5.4. Thermal and metal-catalysed reactivity of dibenzoCOTyne 30



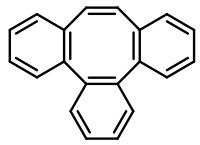
A) In a round-bottomed flask, dried and under argon, dibenzoCOTyne **30** (0.050g, 0.25 mmol) was dissolved in anhydrous THF (0.62 mL, 0.4 M). The resulting mixture was stirred at room temperature until disappearance of starting material (TLC monitoring). Upon completion, the reaction mixture was concentrated to dryness and the residue purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc (90/10) to afford Dewar benzene **62** as a yellow solid (9 mg, 17%).

B) Pd(0)-catalysed cycloaddition was carried out following a similar procedure as mentioned above using dibenzoCOTyne **30** (0.050g, 0.25 mmol) and $Pd_2(dba)_3$ (0.012 mmol, 0.011 g, 0.05 equiv) in THF (0.62 mL, 0.4 M) to afford dibenzotri[8]annulene **63** as a yellow solid (11 mg, 40%).

7.1.5.5. Synthesis of ααα- and ααβ-73a,b



In a round-bottomed flask, dried and under argon, tribenzoCOT **68** (0.161 g, 0.4 mmol, 1 equiv) was dissolved in anhydrous THF (10 mL, 0.04 M). The resulting mixture was stirred at 4 ^oC for 30 min and then fresh sublimated KO^{t}Bu (0.067 g, 0.6 mmol, 1.5 equiv) was added. The resulting mixture was stirred at room temperature until disappearance of starting material (TLC monitoring, o/n). Upon completion, the reaction mixture was quenched with $NH_4Cl_{(sat)}$ (10 mL) and extracted with DCM (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography through silica gel using a mixture of Hex/EtOAc/DCM (20:1:1) to afford tribenzoCOT **47** and a mixture of ααα- and ααβ-**73** conformers (0.035g, 36%) in a 20:1 ratio. Washing this mixture with hexane causes the precipitation of pure ααα-**73a** conformer.



47

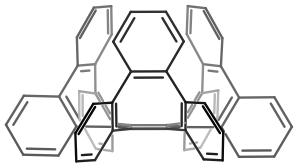
(Z)-tribenzo[a,c,e][8]annulene **47** (7 mg, 7%,R_f = 0.8) as a light yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm):7.34 – 7.26 (m, 2H), 7.15 – 7.03 (m, 8H), 6.99 (dd, *J* = 5.9, 3.0 Hz, 2H), 6.68 (s, 2H).

^{13}C NMR, DEPT (126 MHz, $CDCl_3$), δ (ppm): 142.3 (2 x C), 141.8 (2 x C), 137.2 (2 x C), 132.9 (2 x CH), 130.1 (2 x CH), 130.1 (2 x CH), 127.6 (2 x CH), 127.3 (2 x CH), 127.2 (2 x CH), 126.9 (2 x CH).

HRMS (APCI-probe) calculated for $C_{20}H_{15}$ $[M+1]^+$: 255.1168, found: 255.1166.

(ααα-conformer) tribenzo[3,4:5,6:7,8]cycloocta[1,2-a]tribenzo[3,4:5,6:7,8]cycloocta[1,2-c]tetraphenylene **73a** (31 mg, 32%) as a white solid.



α,α,α–**73a**

^{1}H NMR (500 MHz, CD_2Cl_2), δ (ppm): 7.32 (dd, *J* = 7.8, 1.3 Hz, 6H), 7.09 (dd, *J* = 5.5, 3.3 Hz, 6H), 6.96 (td, *J* = 7.5, 1.5 Hz, 6H), 6.93 (dd, *J* = 5.6, 3.3 Hz, 6H), 6.90 (td, *J* = 7.4, 1.4 Hz, 6H), 6.66 (dd, *J* = 7.5, 1.3 Hz, 6H).

^{13}C NMR, DEPT (126 MHz, CD_2Cl_2), δ (ppm): 142.0 (6 x C), 141.0 (6 x C), 139.5 (6 x C), 139.0 (6 x C), 131.7 (6 x CH), 129.1 (6 x CH), 128.7 (6 x CH), 127.3 (6 x CH), 126.5 (6 x CH), 125.2 (6 x CH).

HRMS (APCI) calculated for $C_{60}H_{37}$ $[M+H]^+$: 757.2890, found: 757.2880.

Reaction performed in presence of $Pd(PPh_3)_4$ (0.046 g, 0.04 mmol, 0.01 equiv) in toluene (10 mL, 0.04 M) at reflux temperature afforded a mixture of ααα- and ααβ-**73** conformers in a 1:3 ratio (0.025g, 25%). Analysis of different crystals grown by slow diffusion of a concentrated solution of mixture **73** in DCM in Hexane allowed the NMR characterization of ααβ-conformer **73b**.

(ααβ-conformer) tribenzo[3,4:5,6:7,8]cycloocta[1,2-a]tribenzo[3,4:5,6:7,8]cycloocta[1,2-c]tetraphenylene **73b**.

α,α,β–**73b**

^{1}H NMR (500 MHz, CD_2Cl_2), δ (ppm): 7.55 (dd, *J* = 5.6, 3.3 Hz, 2H), 7.43 (dd, *J* = 5.6, 3.4 Hz, 2H), 7.34 (qd, *J* = 7.7, 1.5 Hz, 2H), 7.31 – 7.28 (m, 2H), 7.27 – 7.23 (m, 4H), 7.16 (dd, *J* = 7.5, 1.3 Hz, 2H), 6.97 (ddd, *J* = 7.4, 4.7, 1.8 Hz, 4H), 6.95 – 6.90 (m, 6H), 6.85 – 6.79 (m, 6H), 6.77 – 6.71 (m, 2H), 6.55 (dd, *J* = 7.7, 0.9 Hz, 2H), 6.35 (dt, *J* = 7.7, 1.0 Hz, 2H).

^{13}C NMR, DEPT (126 MHz, CD_2Cl_2), δ (ppm): 141.4 (2 x C), 141.0 (2 x C), 140.6 (2 x C), 140.6 (2 x C), 140.5 (2 x C), 140.4 (2 x C), 139.5 (2 x C), 139.1 (2 x C), 138.2 (2 x C), 137.6 (2 x C), 137.5 (2 x C), 137.4 (2 x C), 130.4 (2 x CH), 127.8 (2 x CH), 127.7 (2 x CH), 127.6 (2 x CH), 127.5 (2 x CH), 127.4 (4 x CH), 127.1 (2 x CH), 126.7 (2 x CH), 126.6 (2 x CH), 126.2 (2 x CH), 126.1 (2 x CH), 125.3 (2 x CH), 125.2 (4 x CH), 125.1 (2 x CH), 124.9 (2 x CH), 123.9 (2 x CH).

HRMS (APCI) calculated for $C_{60}H_{37}$ $[M+H]^+$: 757.2890, found: 757.2880.

7.1.5.6. X-ray crystallographic data

7.1.5.6.1. Crystallographic data of compound 68

An X-ray crystal of compound **68** was grown by slow evaporation from a concentrated solution of **68** in DCM.

Figure 68. ORTEP drawing of compound **68** showing thermal ellipsoids at the 50% contour probability level.

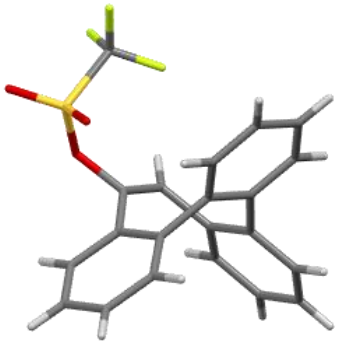


*Table 34. Crystal data and structure refinement for **68***

Deposition Number CCDC	-	
Chemical formula	$C_{21}H_{13}F3O_3S$	
Molecular weight	402.37 g/mol	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal size	0.22 × 0.15 × 0.07 mm	
Crystal habit	Plate, colourless	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 9.364 (5) Å	α = 108.16 (2)°
	b = 9.940 (5) Å	β = 97.38 (2)°
	c = 10.670 (5) Å	γ = 105.88 (2)°
Volume	882.5 (8) $Å^3$	
Z	2	
Density (calculated)	1.514 g/cm^3	
Absorption coefficient	0.23 mm^{-1}	
F(000)	412	

7.1.5.6.2. Crystallographic data of compound 72

An X-ray crystal of compound **72** was grown by vapor diffusion using DCM and hexanes as mixture of solvents.

Figure 69. ORTEP drawing of compound **72** showing thermal ellipsoids at the 50% contour probability level.

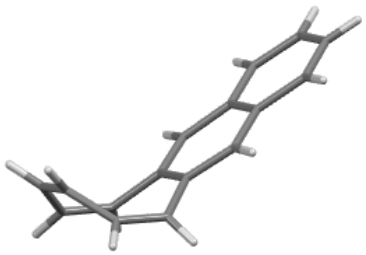


*Table 35. Crystal data and structure refinement for **72***

Deposition Number CCDC	-
Chemical formula	$C_{16}H_{12}$
Molecular weight	204.26 g/mol
Temperature	299 K
Wavelength	1.54178 Å
Crystal size	0.20 × 0.18 × 0.05 mm
Crystal habit	Plate, colourless
Crystal system	Orthorhombic,
Space group	$P2_12_12_1$
Unit cell dimensions	a = 6.4618 (2) Å
	b = 7.8144 (2) Å
	c = 22.3901 (6) Å
Volume	1130.59 (5) $Å^3$
Z	4
Density (calculated)	1.2 g/cm^3
Absorption coefficient	0.51 mm^{-1}
F(000)	432

7.1.5.6.3. Crystallographic data of compound ααα-73a

An X-ray crystal of compound ααα-73a was grown by vapor diffusion using DCM and hexanes as mixture of solvents.

Figure 70. ORTEP drawing of compound **ααα-73a** showing thermal ellipsoids at the 50% contour probability level. H atoms were removed for clarity.

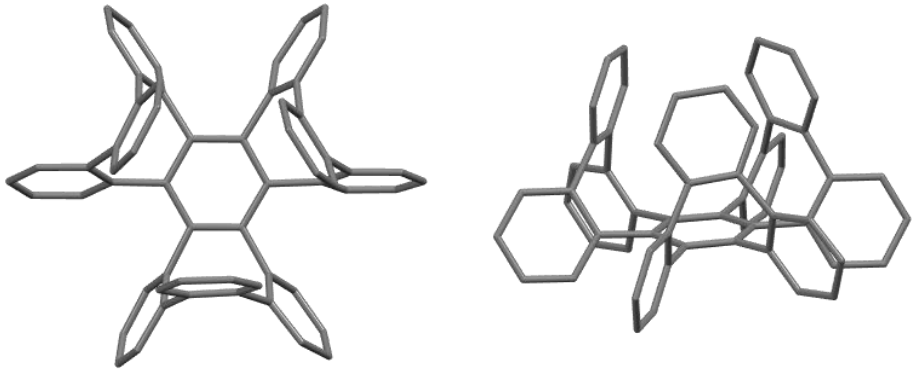


Table 36. Crystal data and structure refinement for **ααα-73a**

Deposition Number CCDC	-
Chemical formula	$2(C_{60}H_{36})\cdot C_6H_{14}\cdot 3(CH_2Cl_2)$
Molecular weight	1854.72 g/mol
Temperature	100 K
Wavelength	1.54178 Å
Crystal size	0.27 × 0.11 × 0.02 mm
Crystal habit	Plate, colourless
Crystal system	Orthorhombic,
Space group	$P2_12_12_1$
Unit cell dimensions	a = 12.1032 (3) Å
	b = 20.3609 (6) Å
	c = 38.5341 (13) Å
Volume	9496.0 (5) $Å^3$
Z	4
Density (calculated)	1.297 g/cm^3
Absorption coefficient	2.07 mm^{-1}
F(000)	3872

7.1.5.6.4. Crystallographic data of compound ααβ-73b

An X-ray crystal of compound ααβ-73b was grown by vapor diffusion using DCM and hexanes as mixture of solvents.

Figure 71. ORTEP drawing of compound ααβ-**73b** showing thermal ellipsoids at the 50% contour probability level. H atoms were removed for clarity

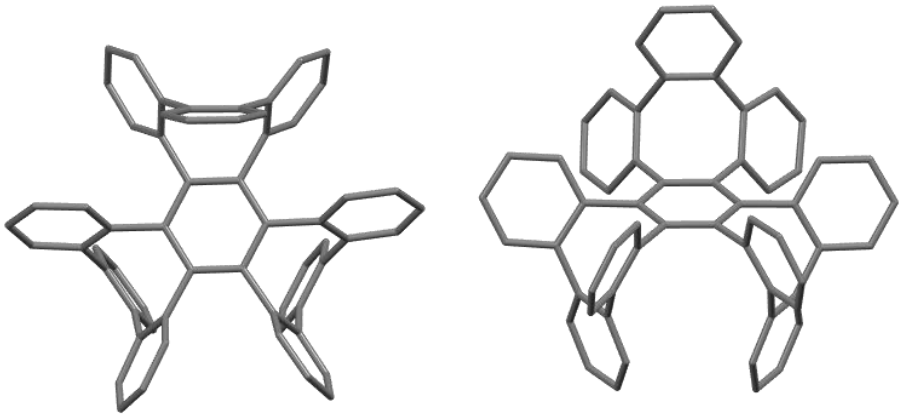


Table 37. Crystal data and structure refinement for ααβ-**73b**

Deposition Number CCDC	-	
Chemical formula	$C_{60}H_{36}·0.4(C_6H_{14})·0.2(CH_2Cl_2)$	
Molecular weight	808.34 g/mol	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal size	0.30 × 0.13 × 0.07 mm	
Crystal habit	Plate, colourless	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 12.3866 (7) Å	α = 107.485 (3)°
	b = 12.5602 (7) Å	β = 96.983 (3)°
	c = 15.1569 (8) Å	γ = 96.818 (3)°
Volume	2202.2 (2) $Å^3$	
Z	2	
Density (calculated)	1.219 g/cm^3	
Absorption coefficient	0.74 mm^{-1}	
F(000)	849	

7.1.5.7. DFT calculations

All electronic structure calculations were performed using the Gaussian 16 software package[261] at the CESGA facilities. The geometries of all minima and transition states involved were optimized using the ωB97XD functional[262] (which includes a version of Grimme's D2 dispersion corrections)[263] and using the basis set 6-31G(d,p).[266]Frequency calculations were performed at the same level to evaluate the zero-point vibrational energy and thermal corrections at 298 K and to confirm the nature of the stationary points, yielding one imaginary frequency for the transition states and none for the minima. Each transition state was further confirmed by following the steepest descent to both sides and identifying the minima present in the reaction energy profile. The reaction profiles were built up in terms of ΔG_{sol}.

8. Conclusions

During the development of this PhD thesis, an in-depth study of the synthesis and reactivity of dihydrobiphenylenes has been undertaken. The results found show the evolution of 1,3-cyclohexadiene, nuclei present in dihydrobiphenylenes, towards the formation of benzofused cyclooctatetraenes through radical mediated processes. Additional studies of these new compounds reveal their use as a precursor to benzoCOTyne; therefore, strained alkynes were subjected to thermal and metal-catalysed trimerizations to produce new intriguing compounds combining eight (non-aromatic) and six-membered rings (aromatic). An extensive analysis of parent COTyne as well as related dibenzo- and tribenzoCOTynes was performed. The results obtained allow us to a better understanding of COTyne in terms of synthesis, isolation and reactivity to the synthesis of twisted PAHs.

9. Bibliography

To facilitate an easy reading of this thesis manuscript, bibliographic references have also been included as a footnote in each section.

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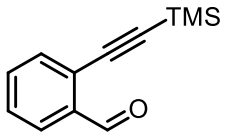
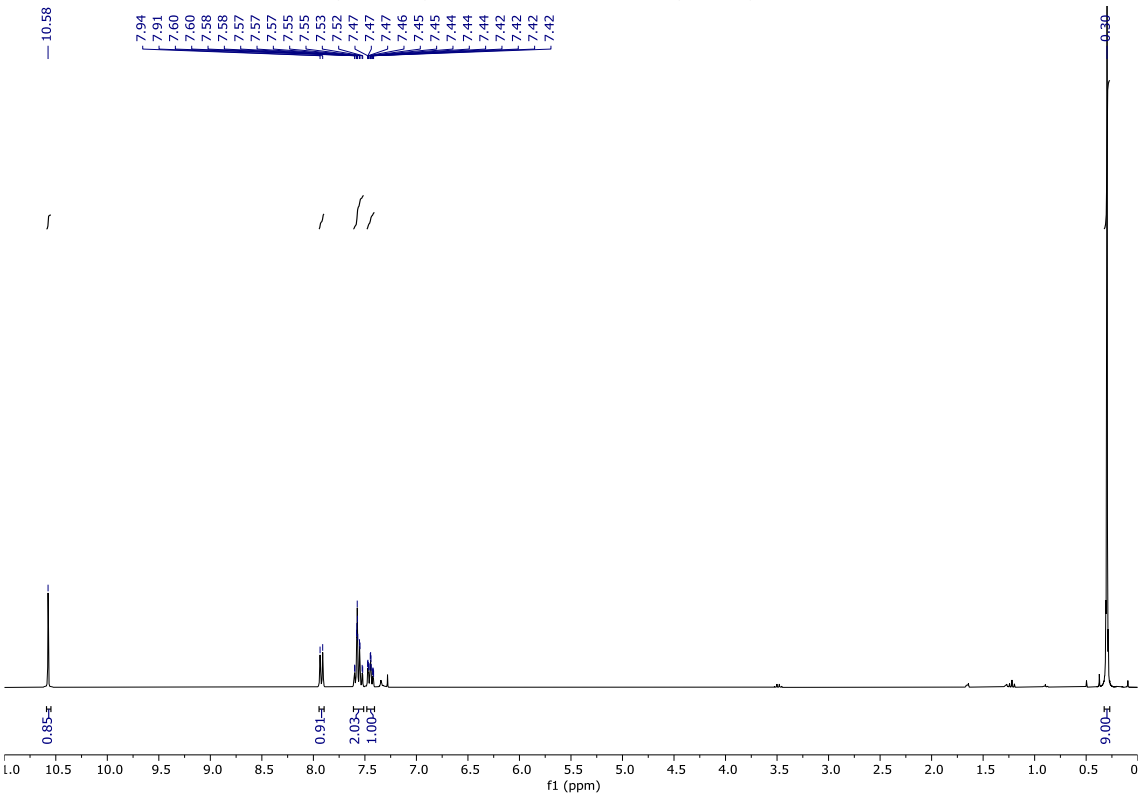
10. Annexes

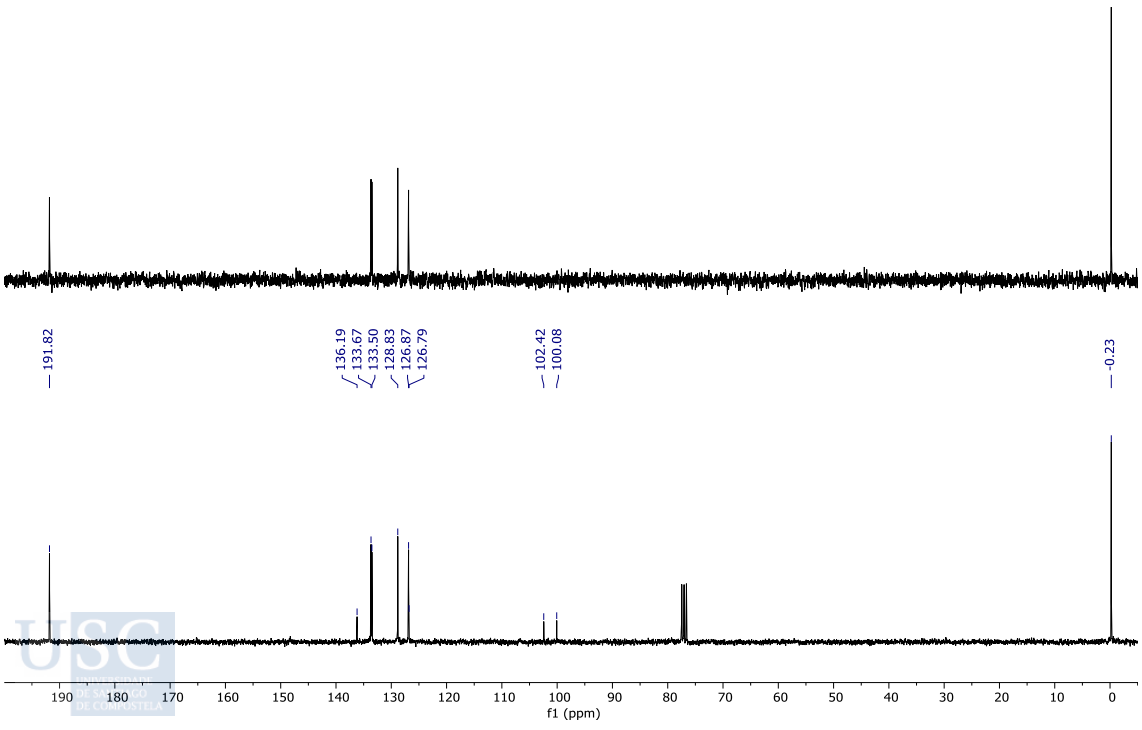
Annex I: NMR SPECTRA

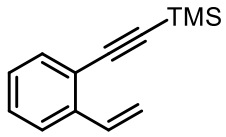


S2

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

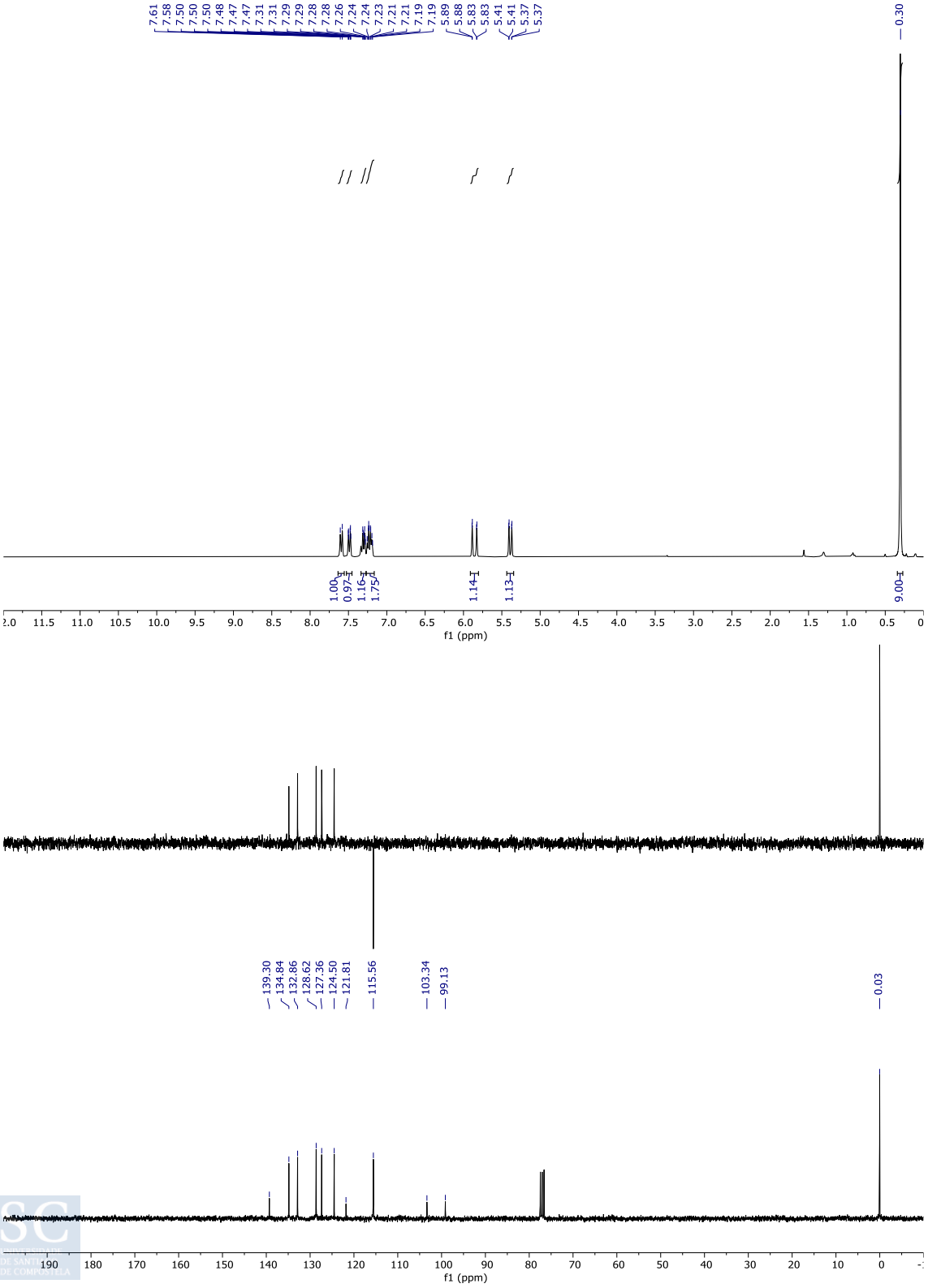


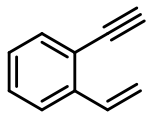




S3

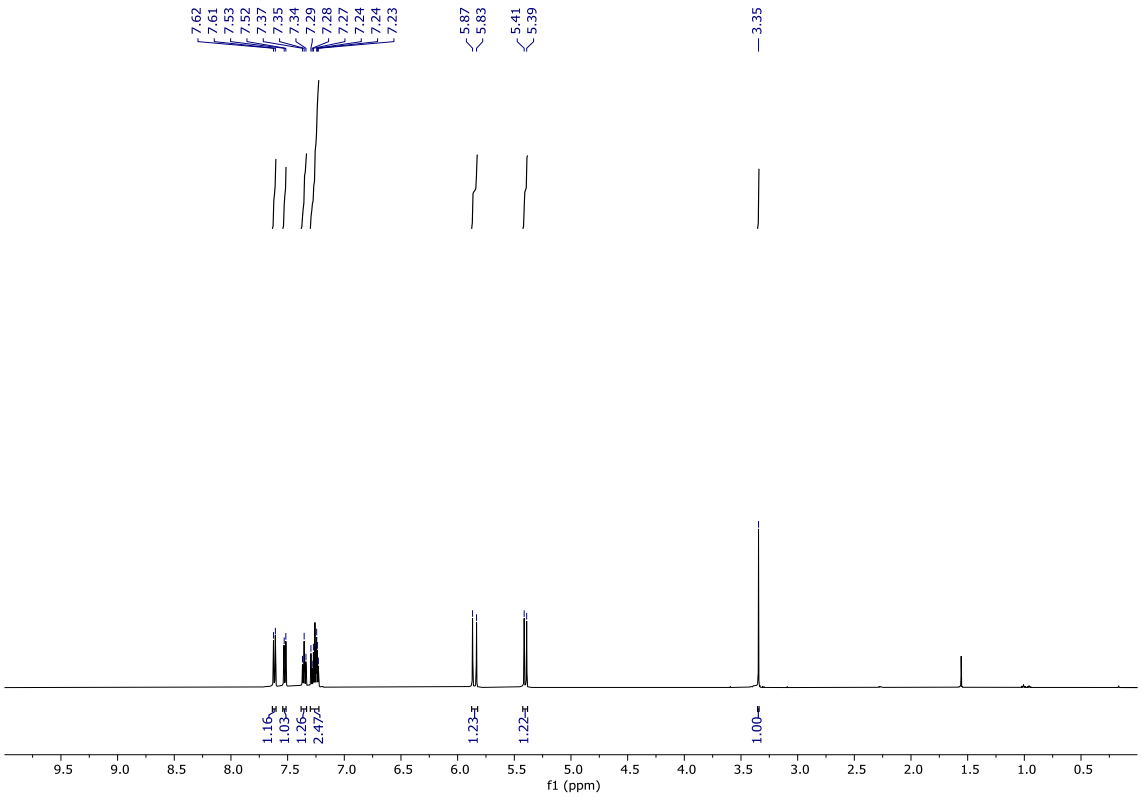
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

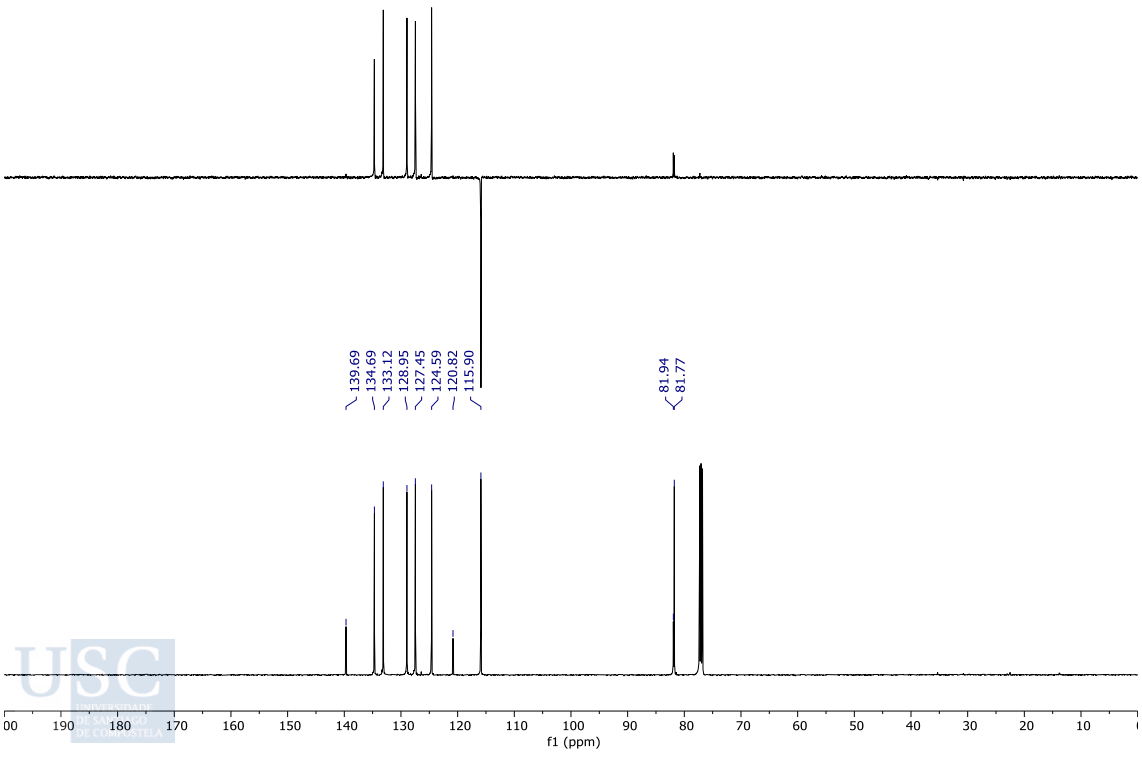


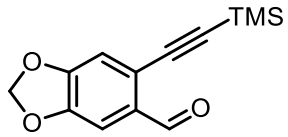


1a

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

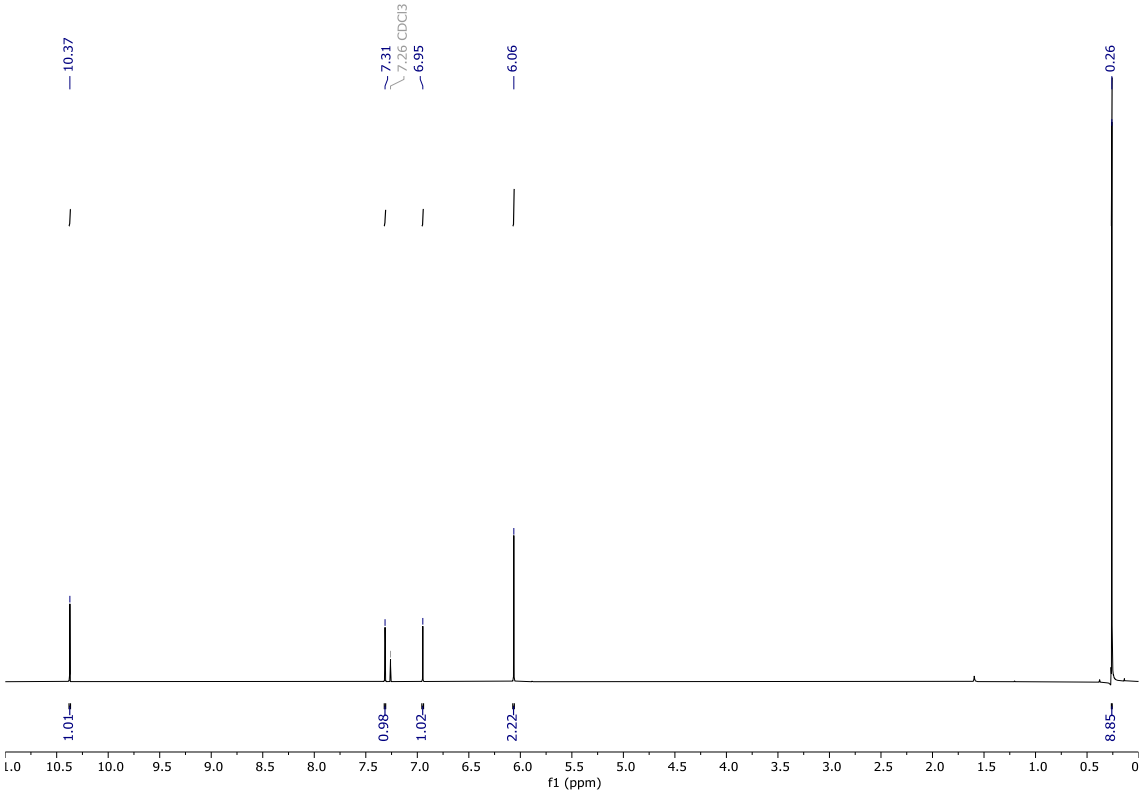


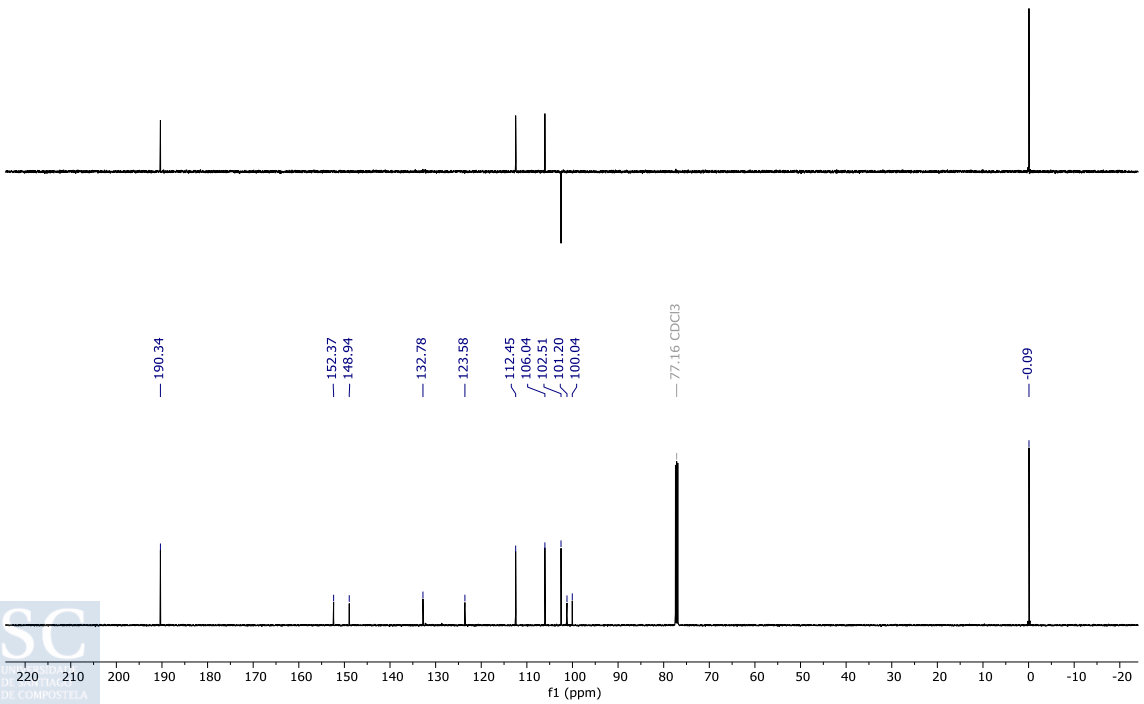


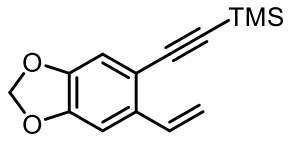


S5

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

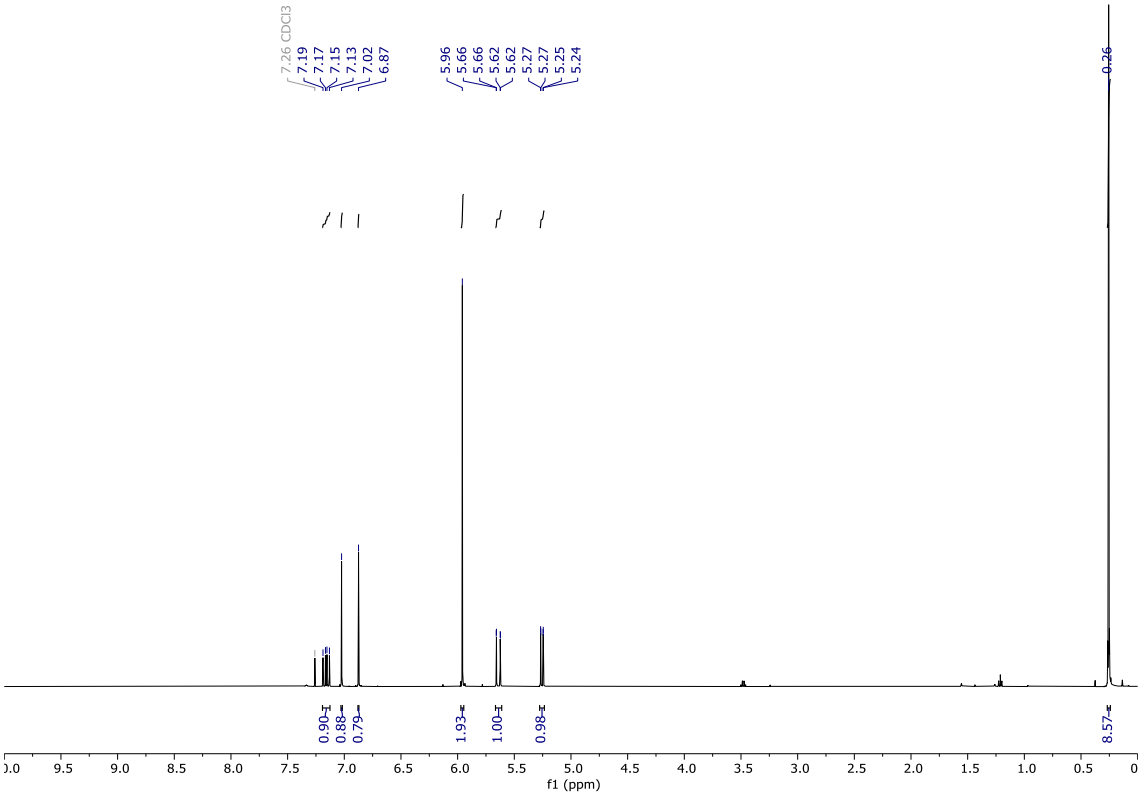


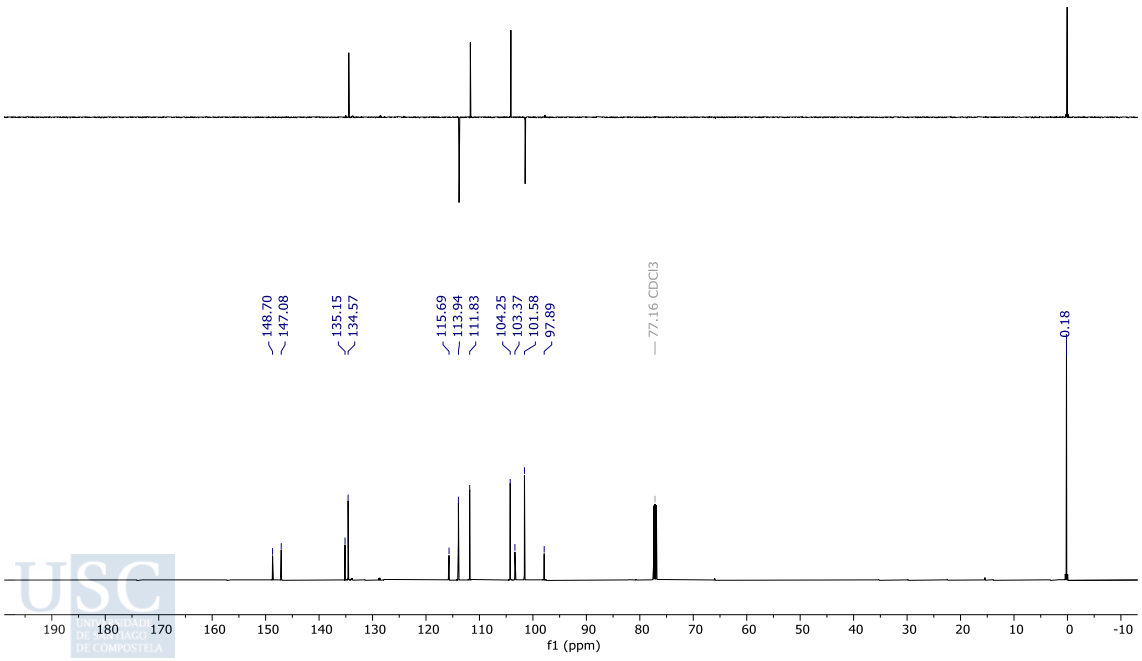


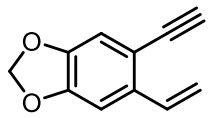


S6

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

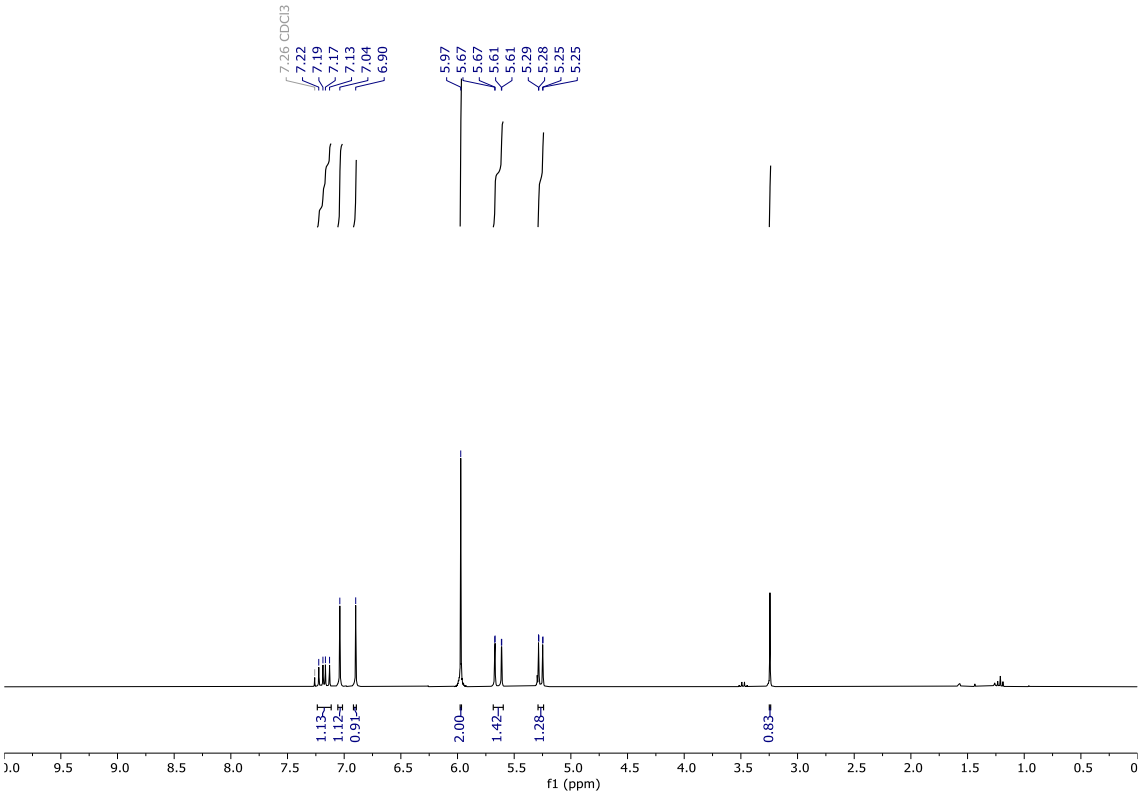


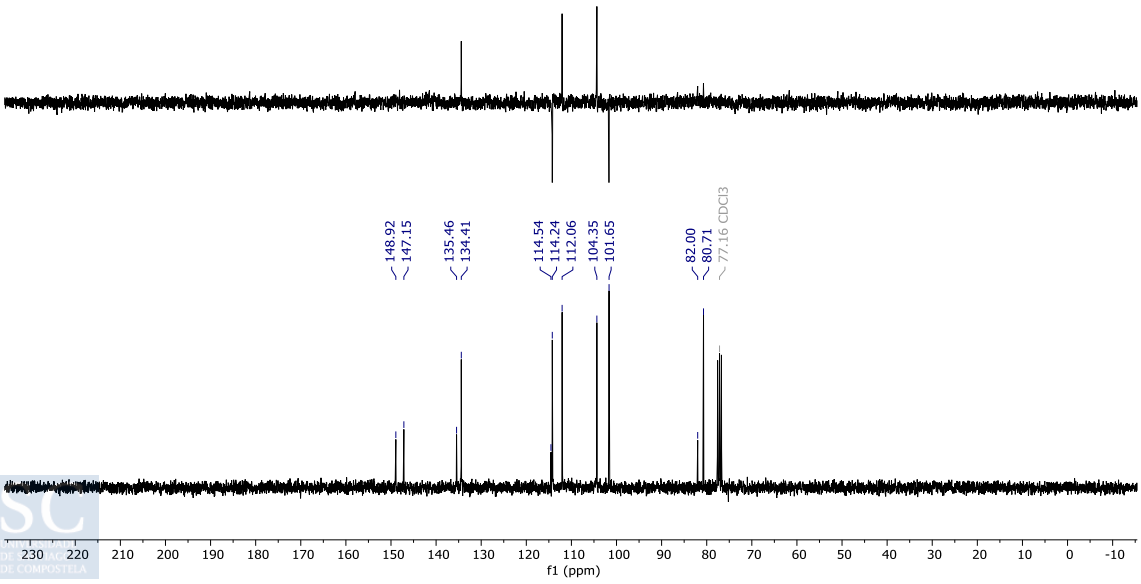


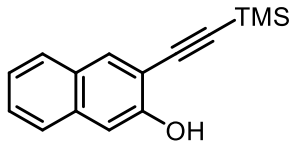


1b

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

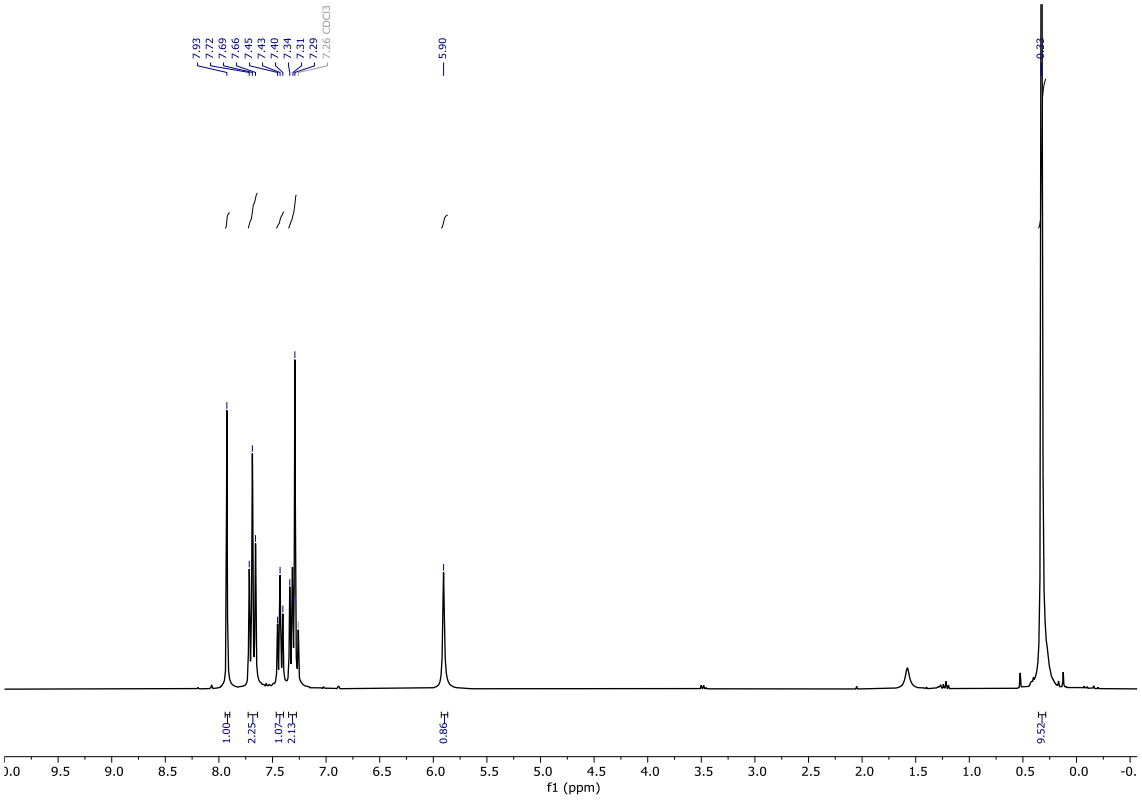


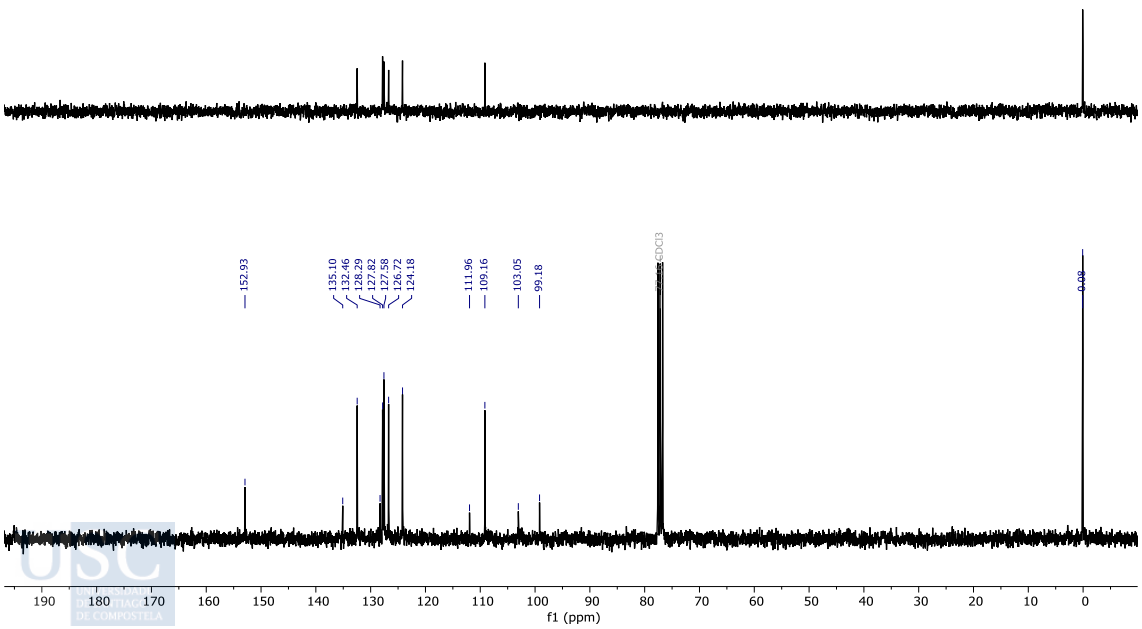


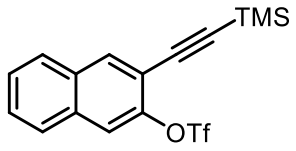


S8

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

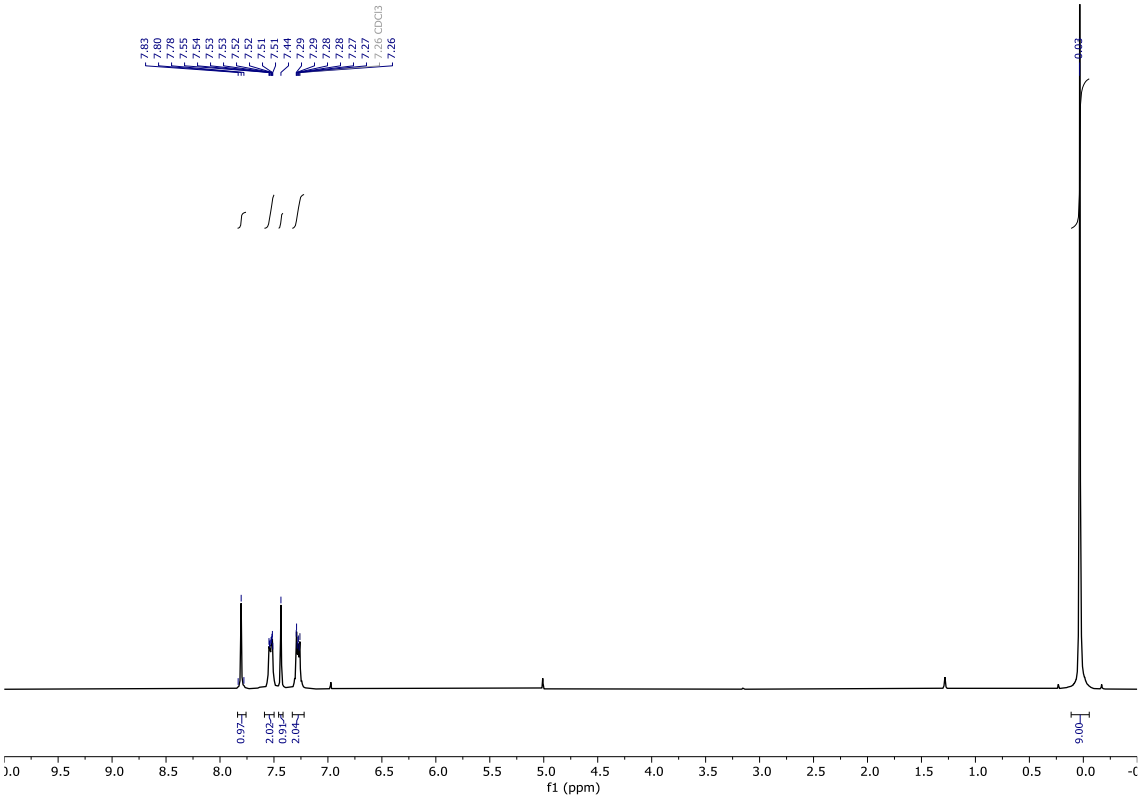


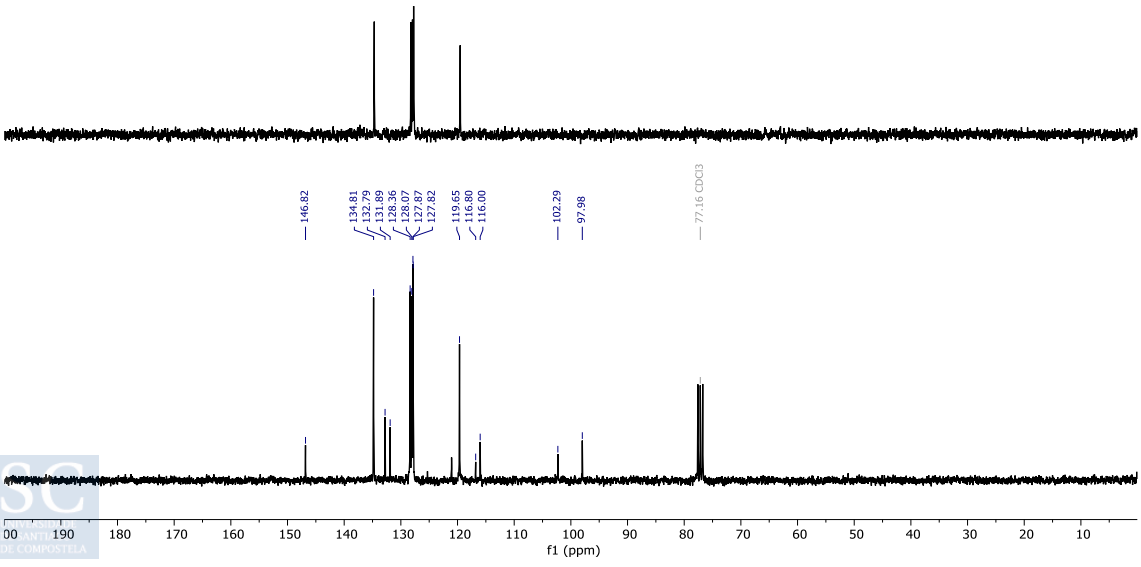


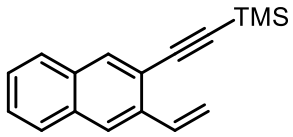


S9

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

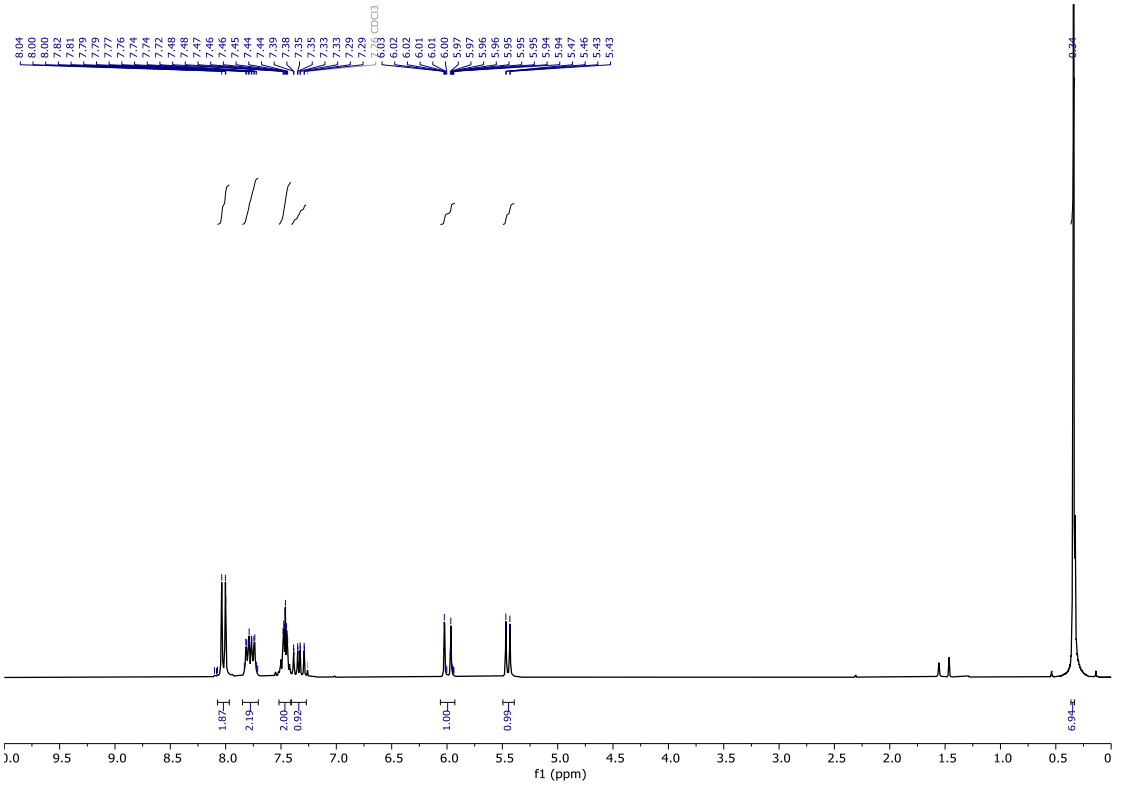


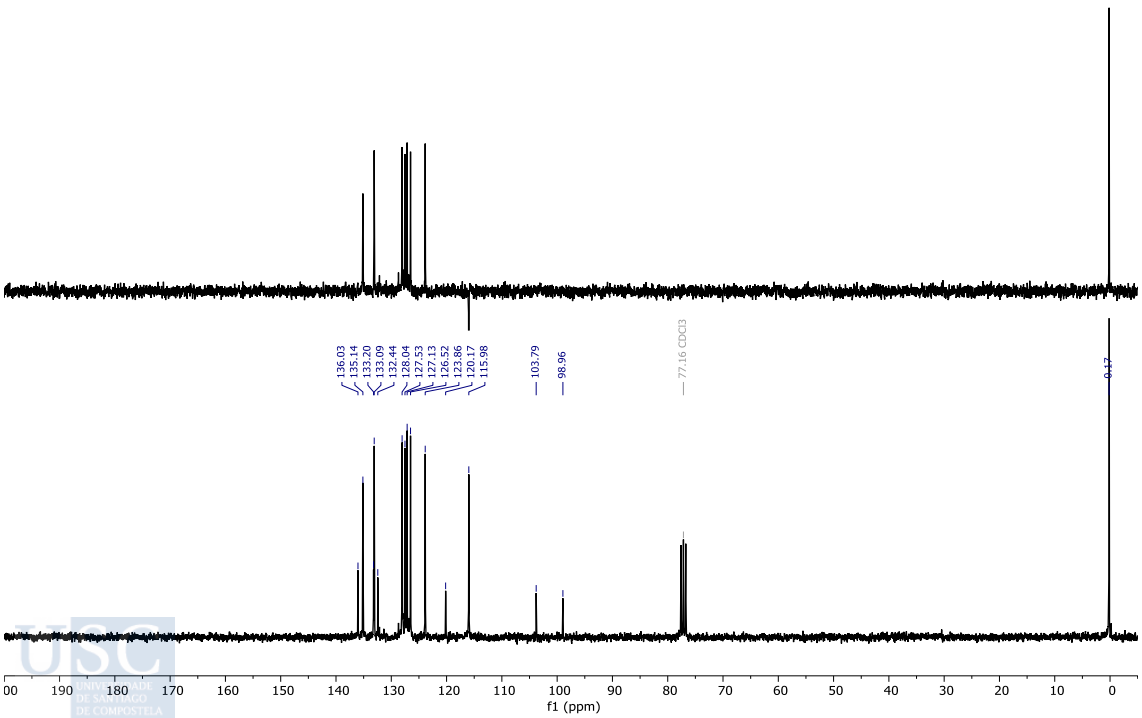


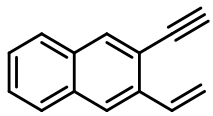


S10

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

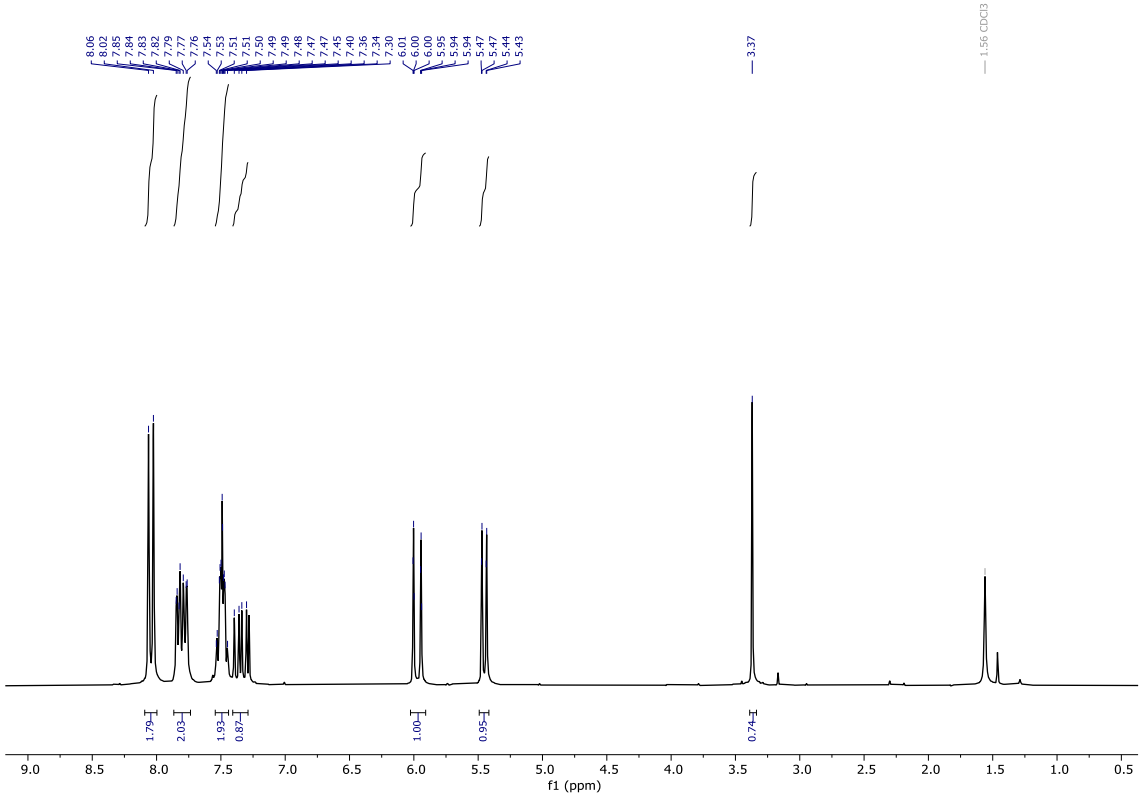


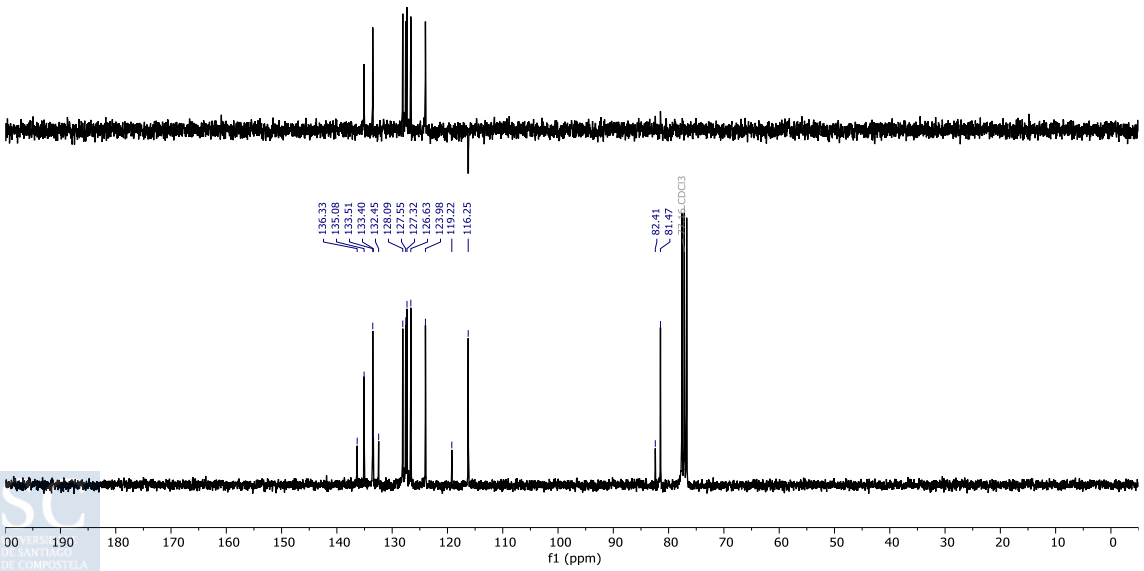


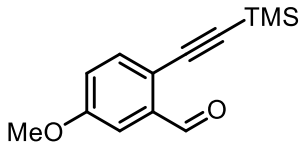


1c

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

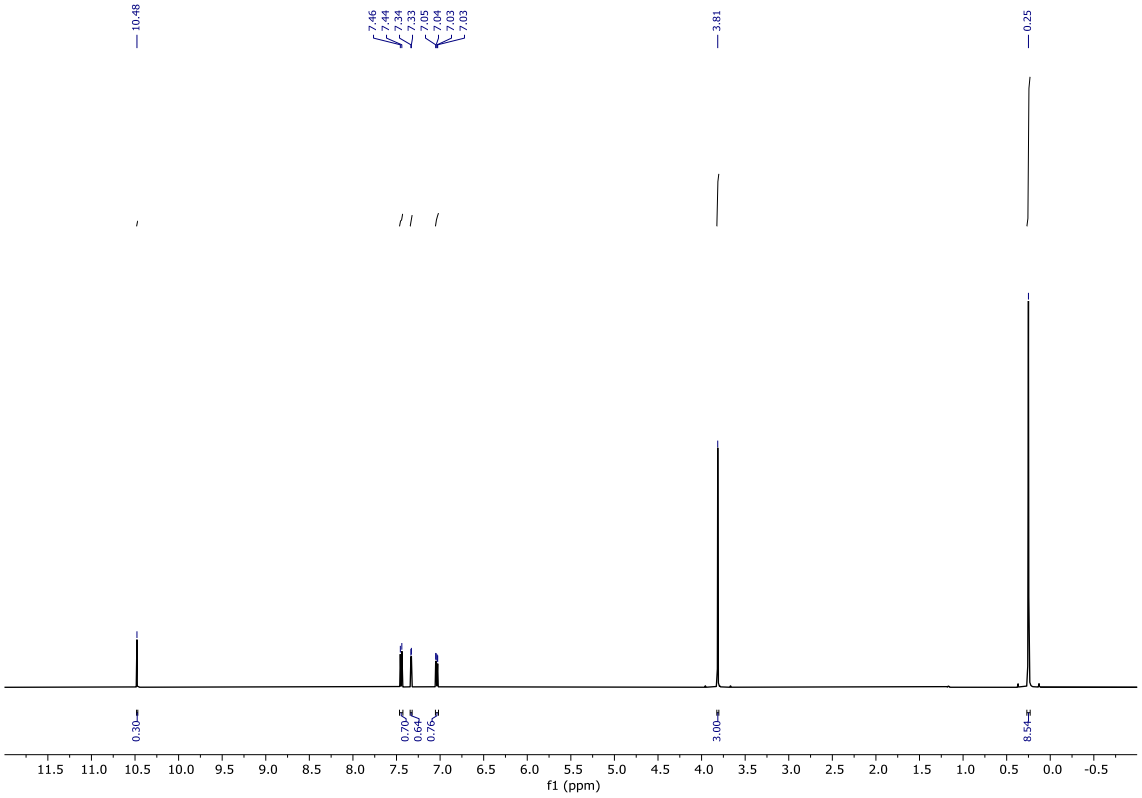


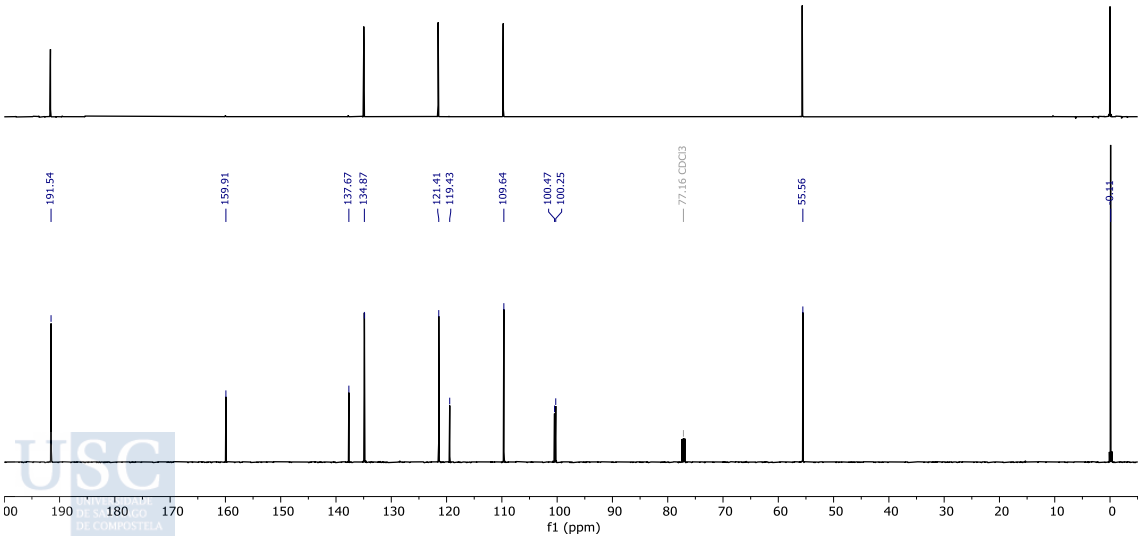


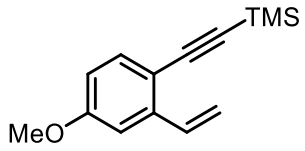


S12

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

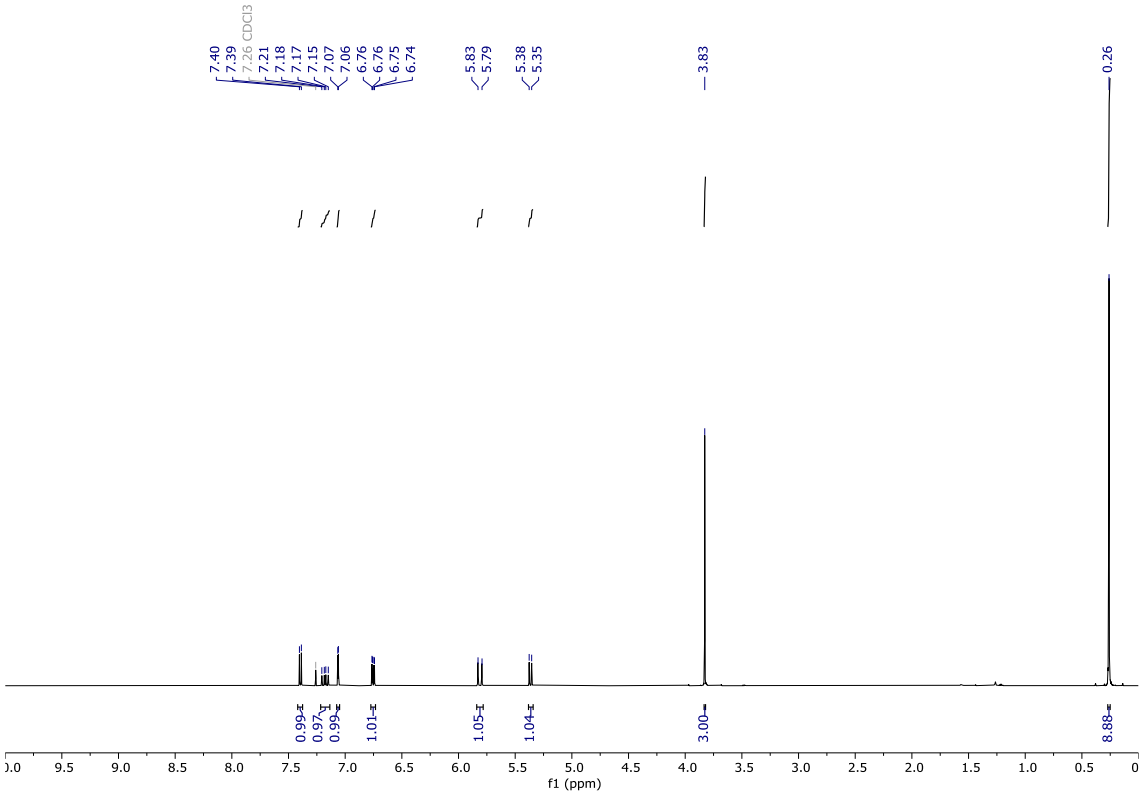


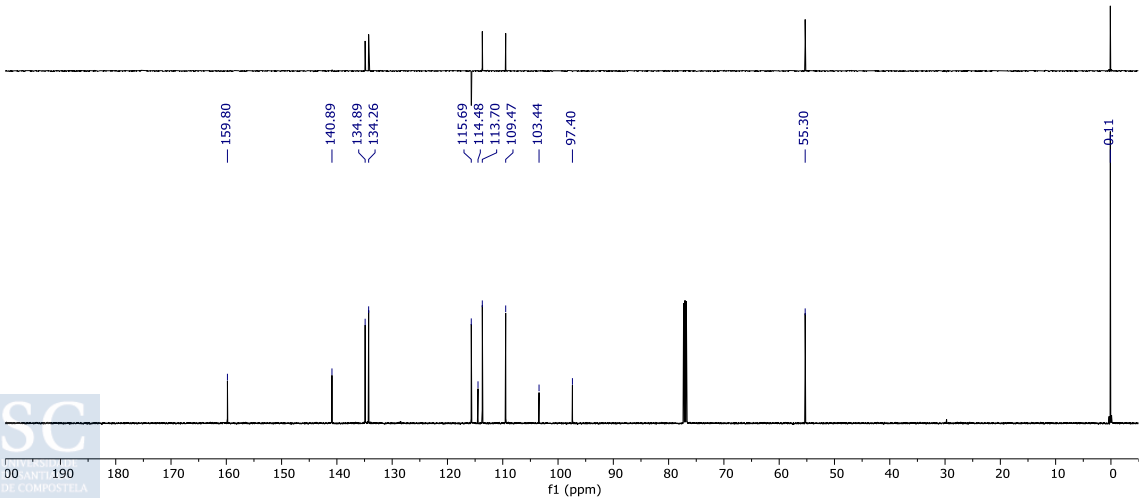


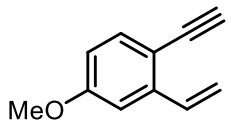


S13

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

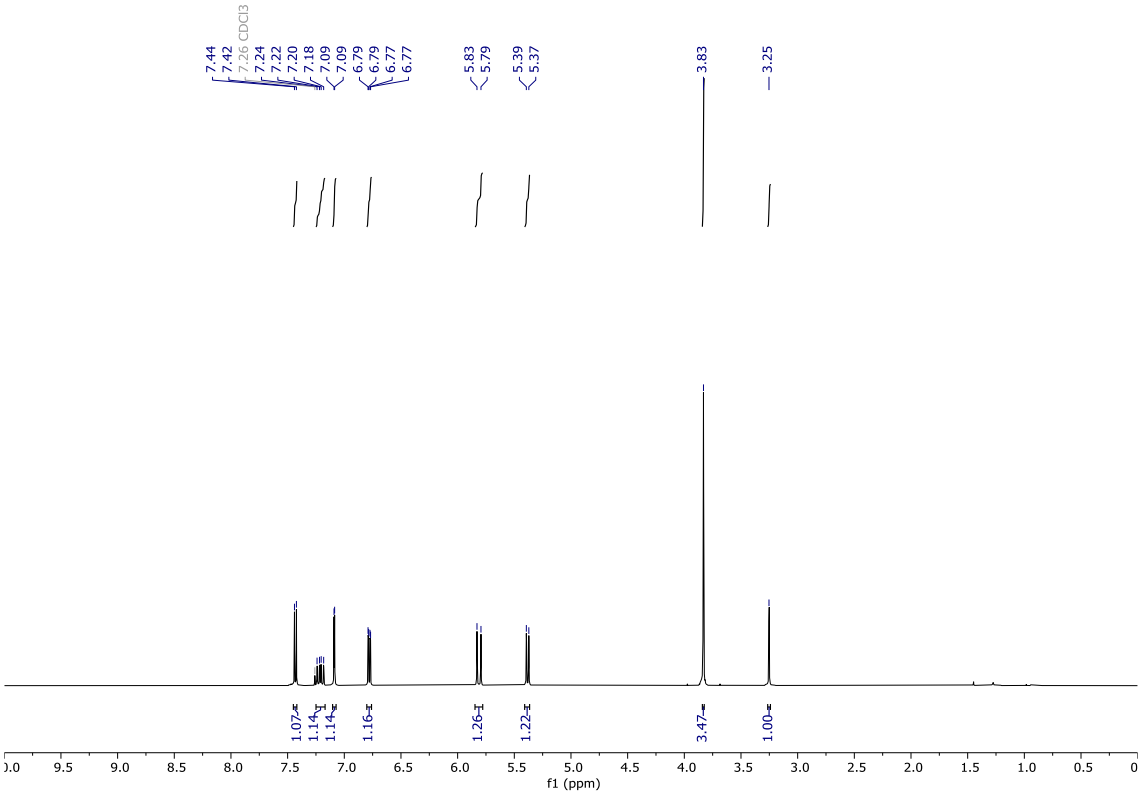


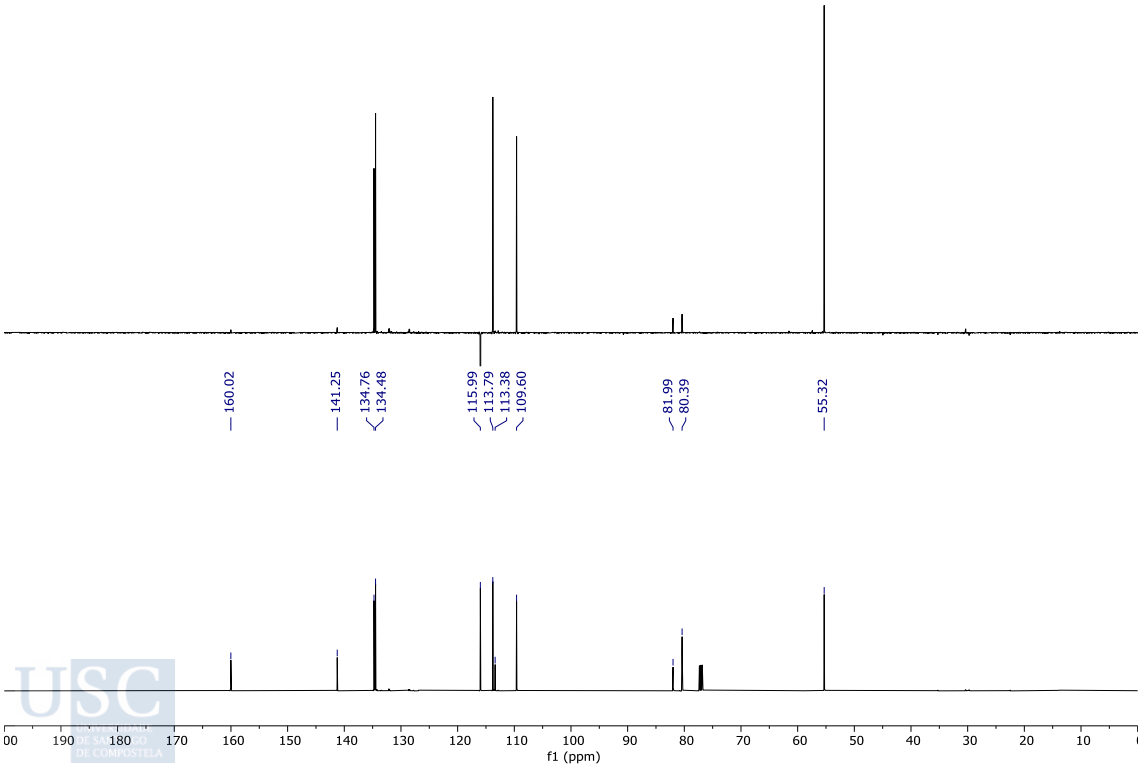


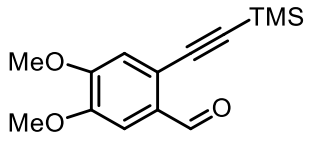


1d

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

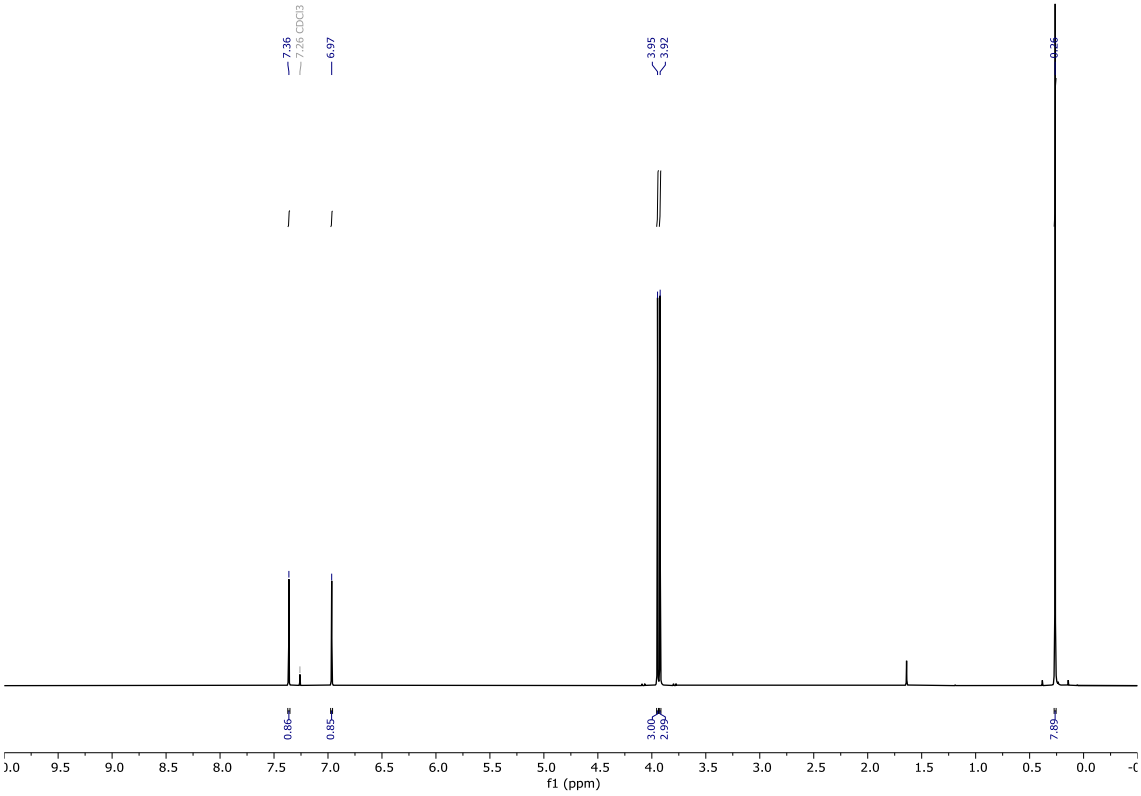


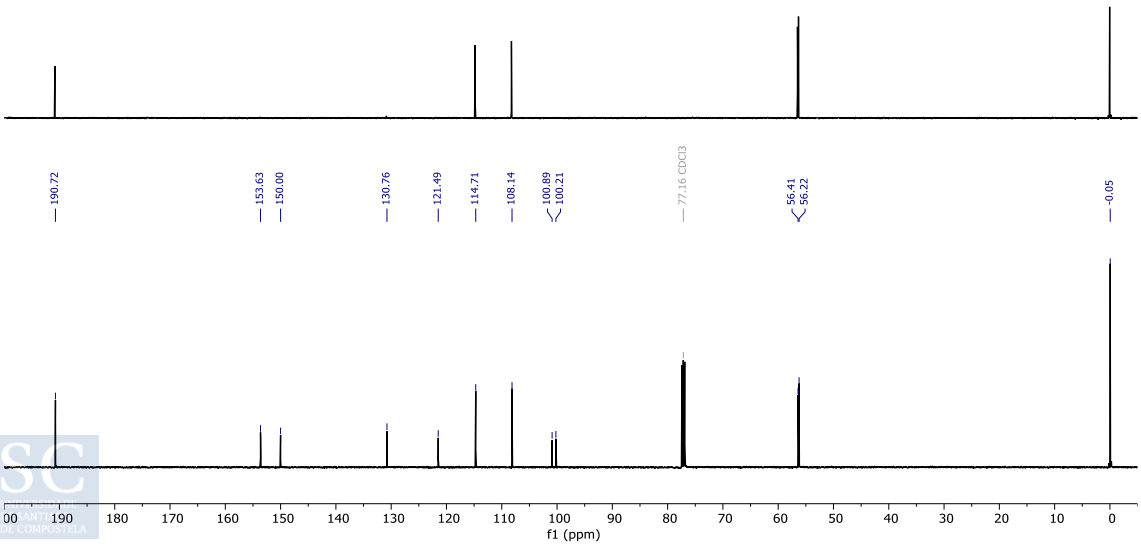


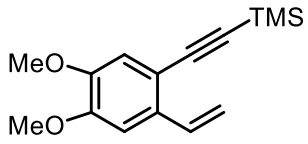


S15

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

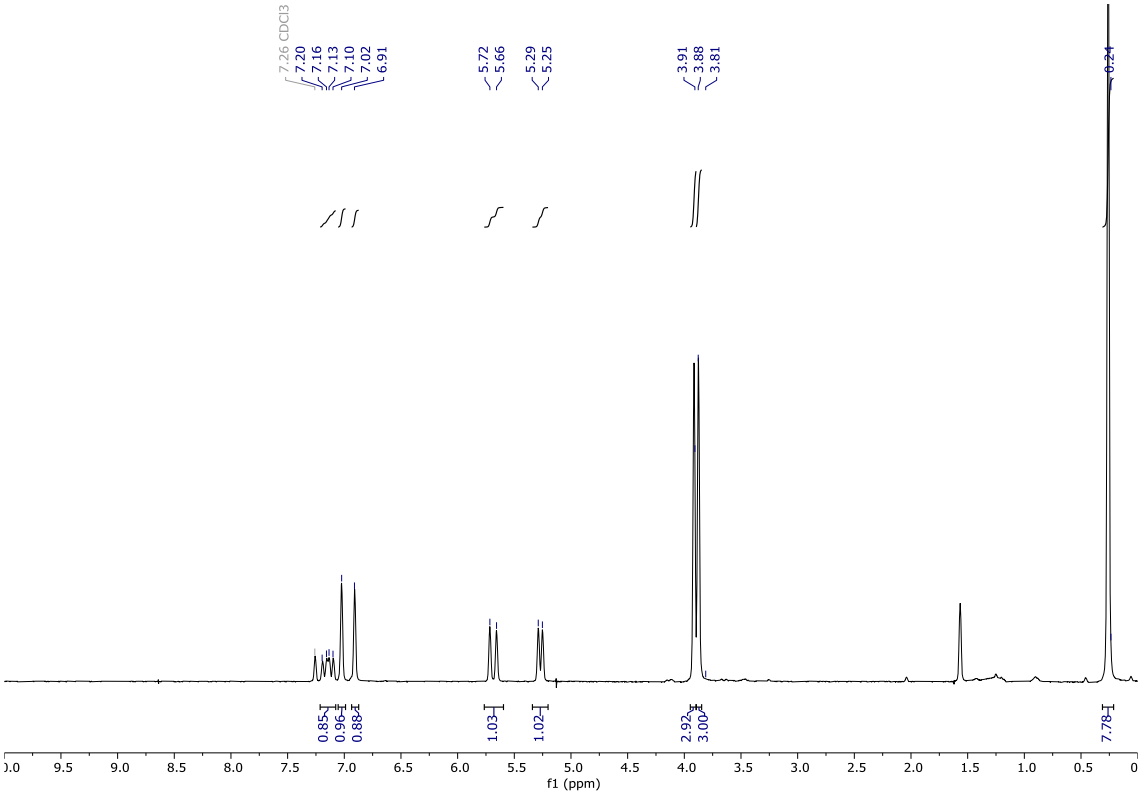


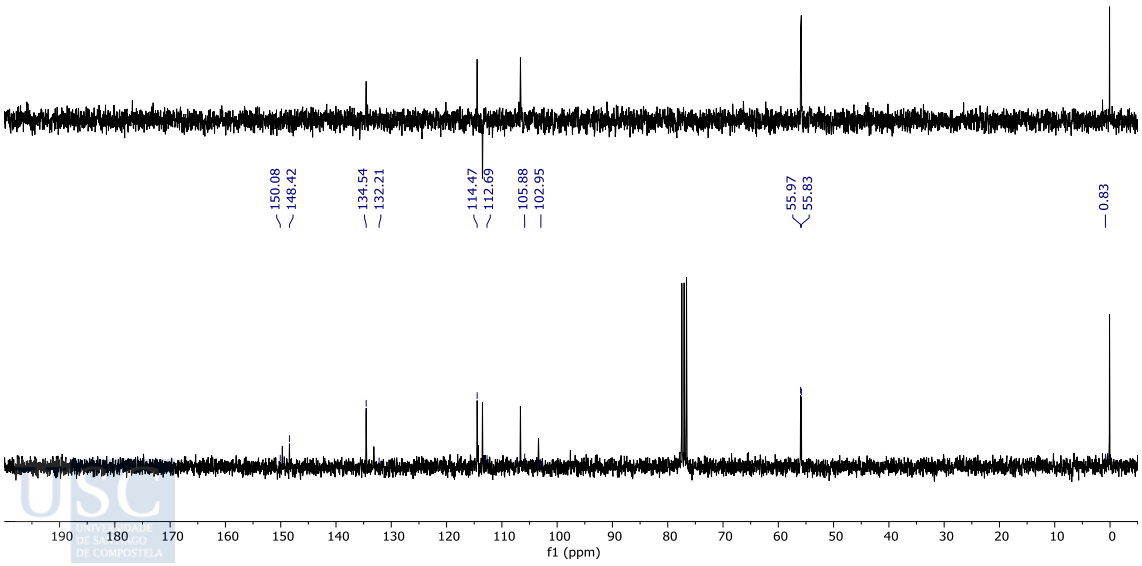


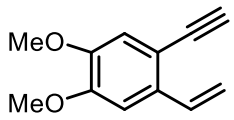


S16

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

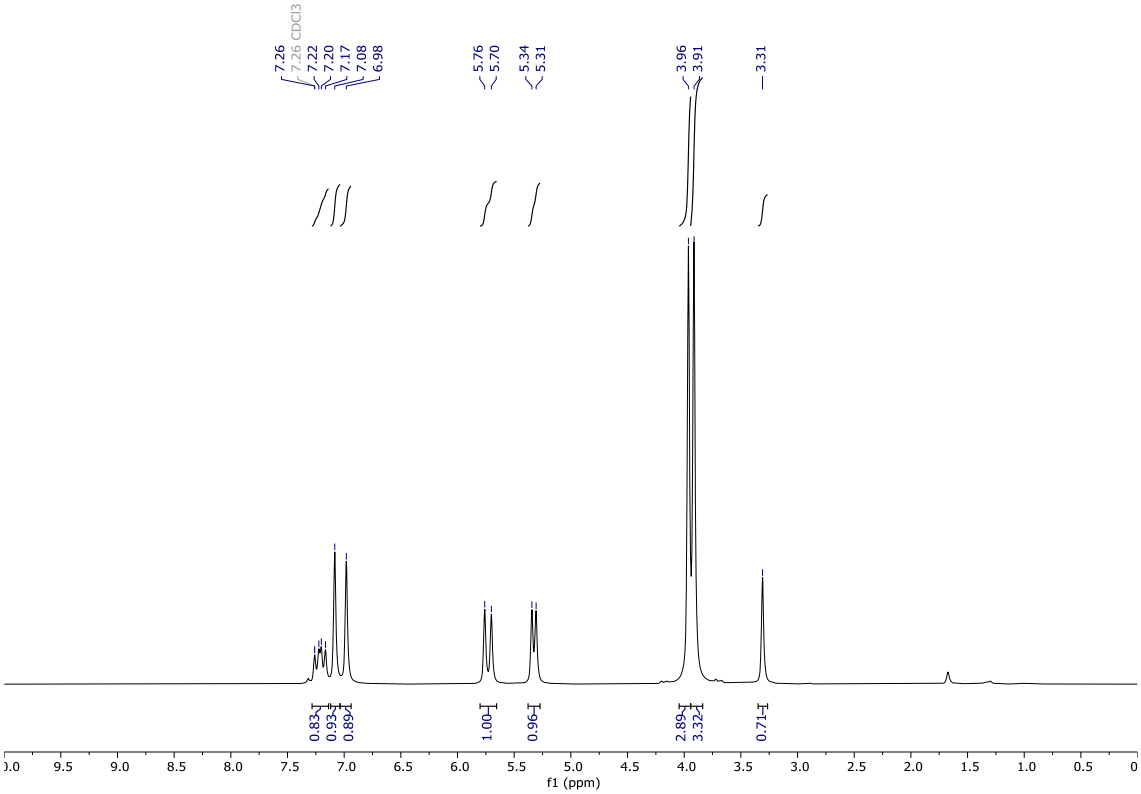


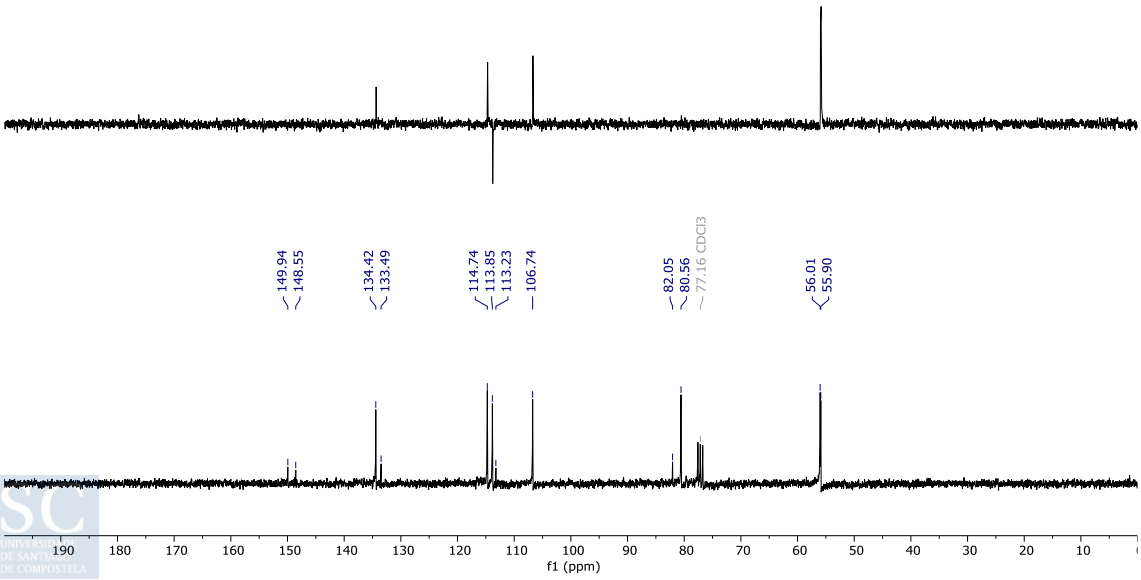


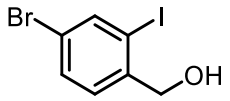


1e

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

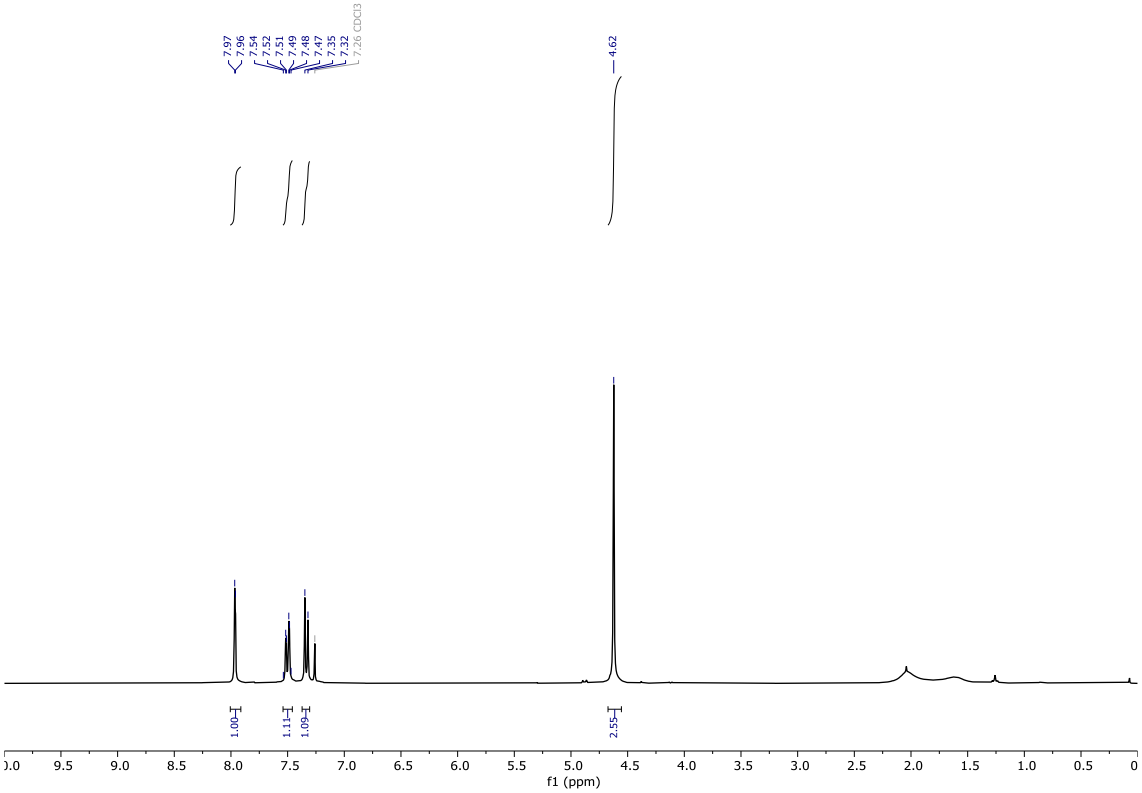


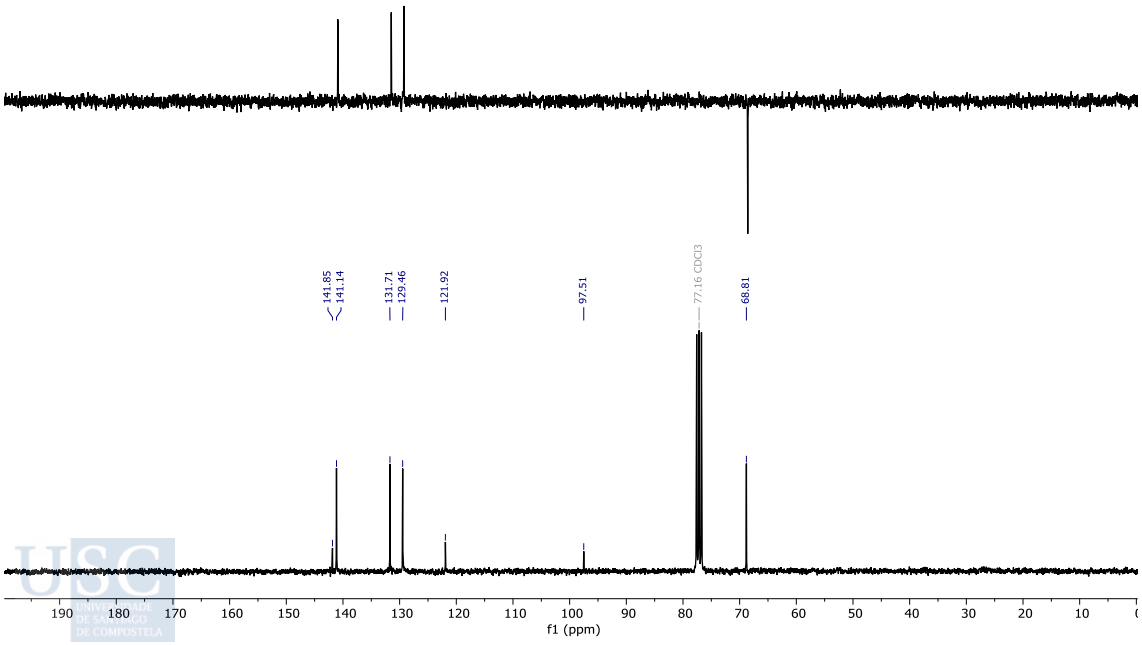


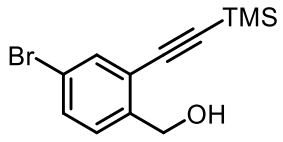


S17

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

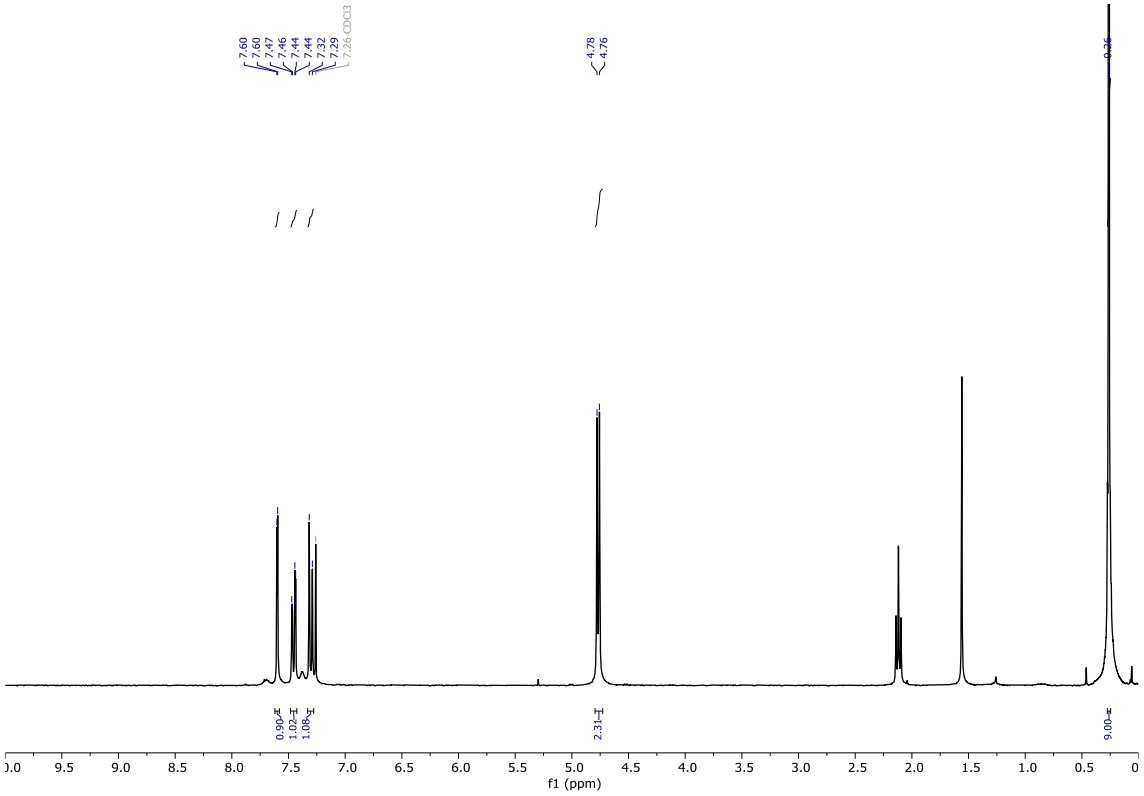


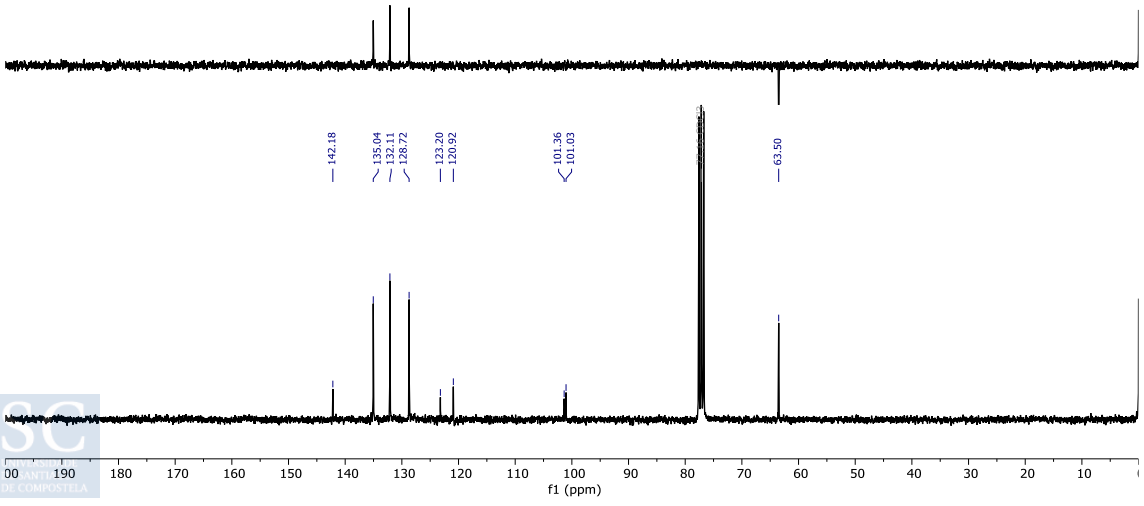


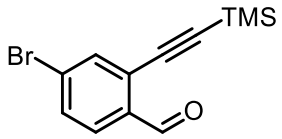


S18

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

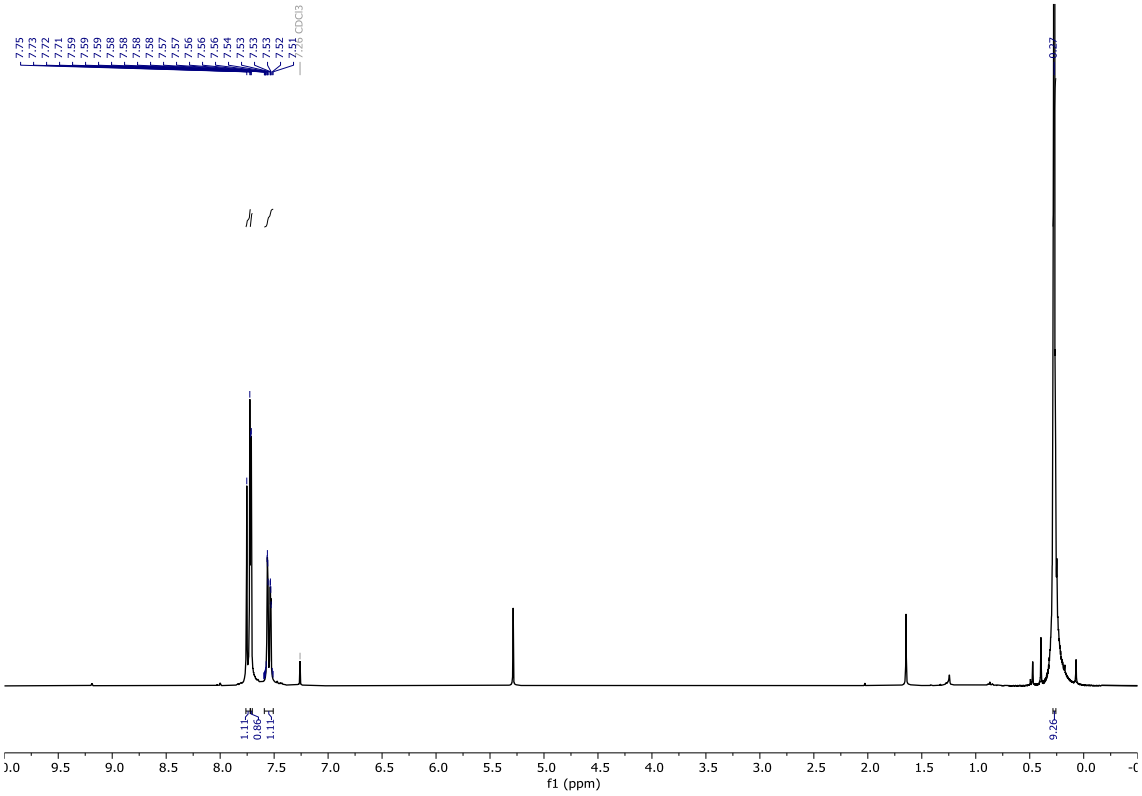


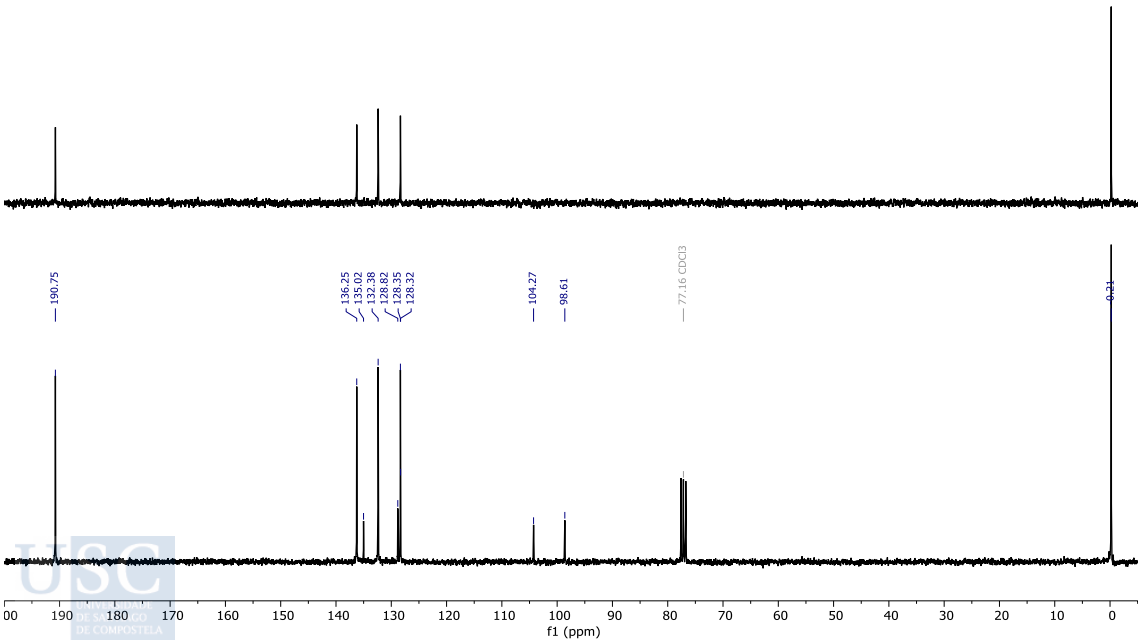


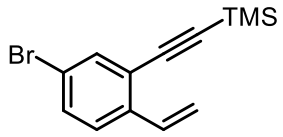


S19

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

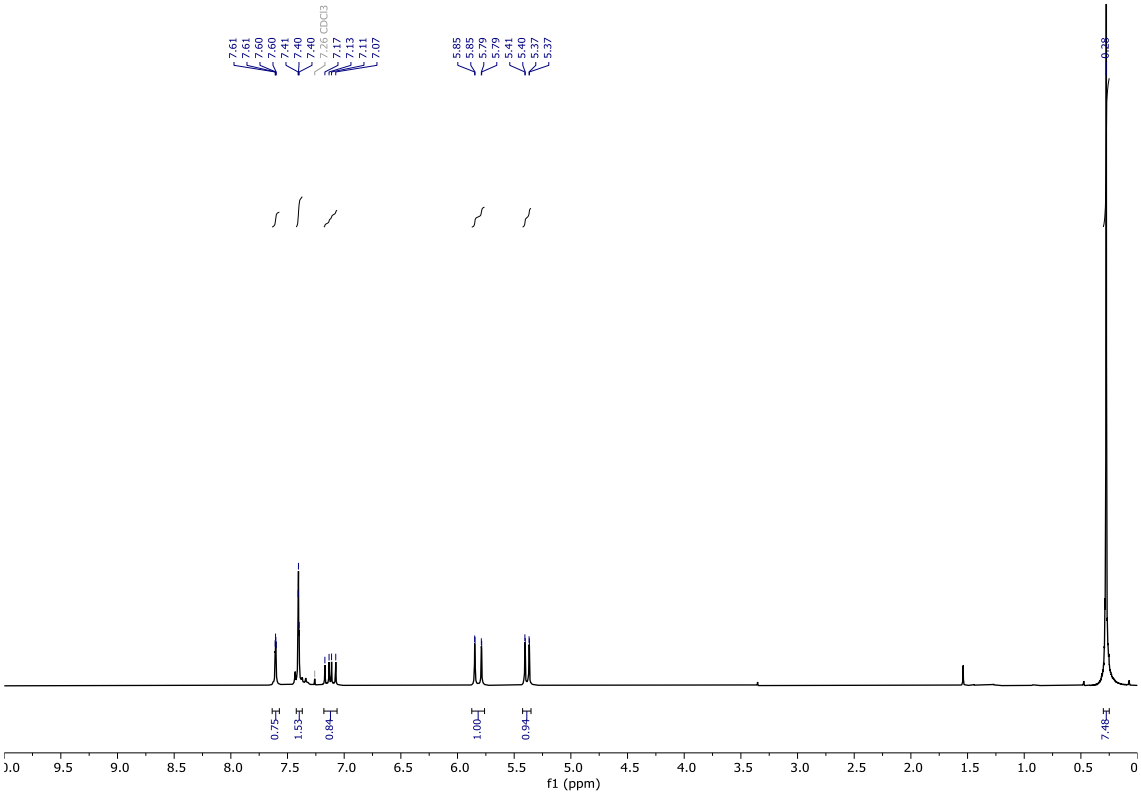


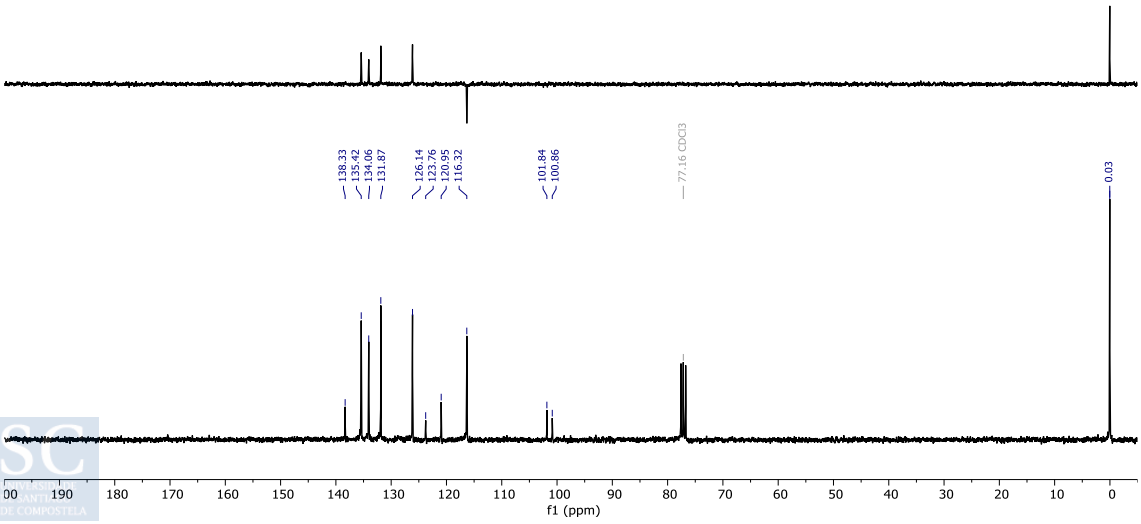


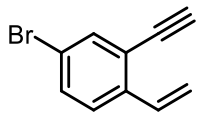


S20

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

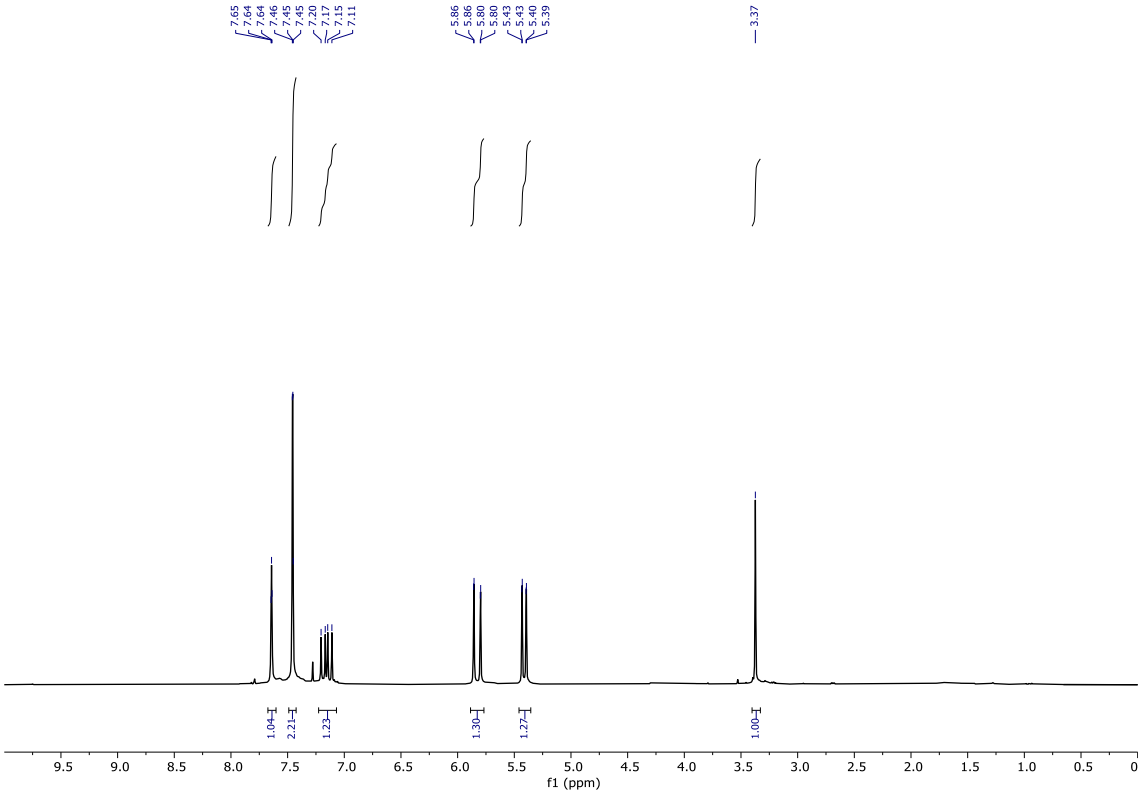


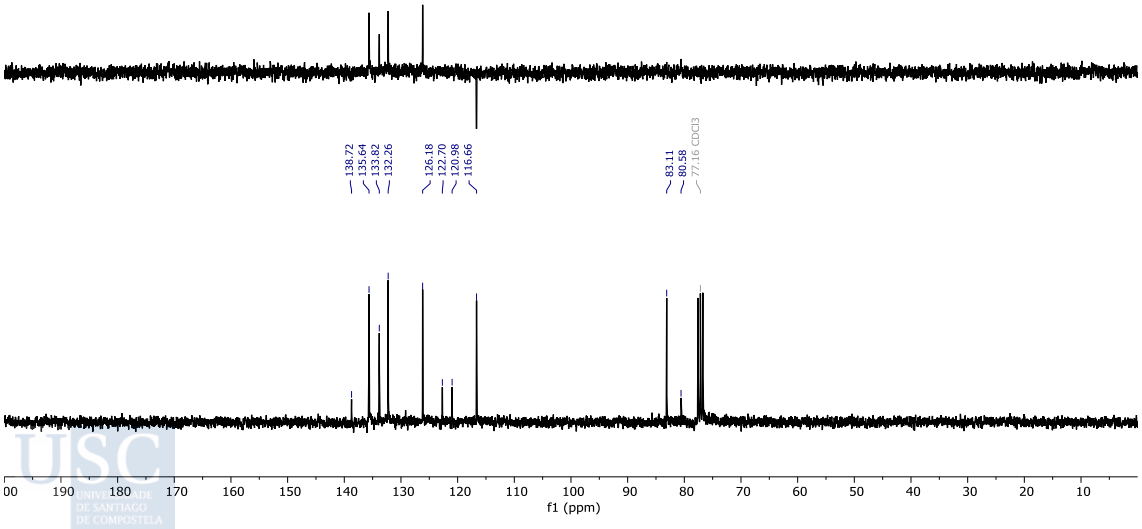


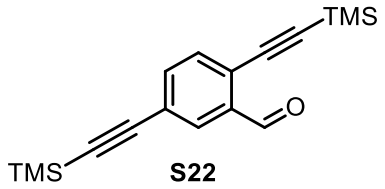


1f

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

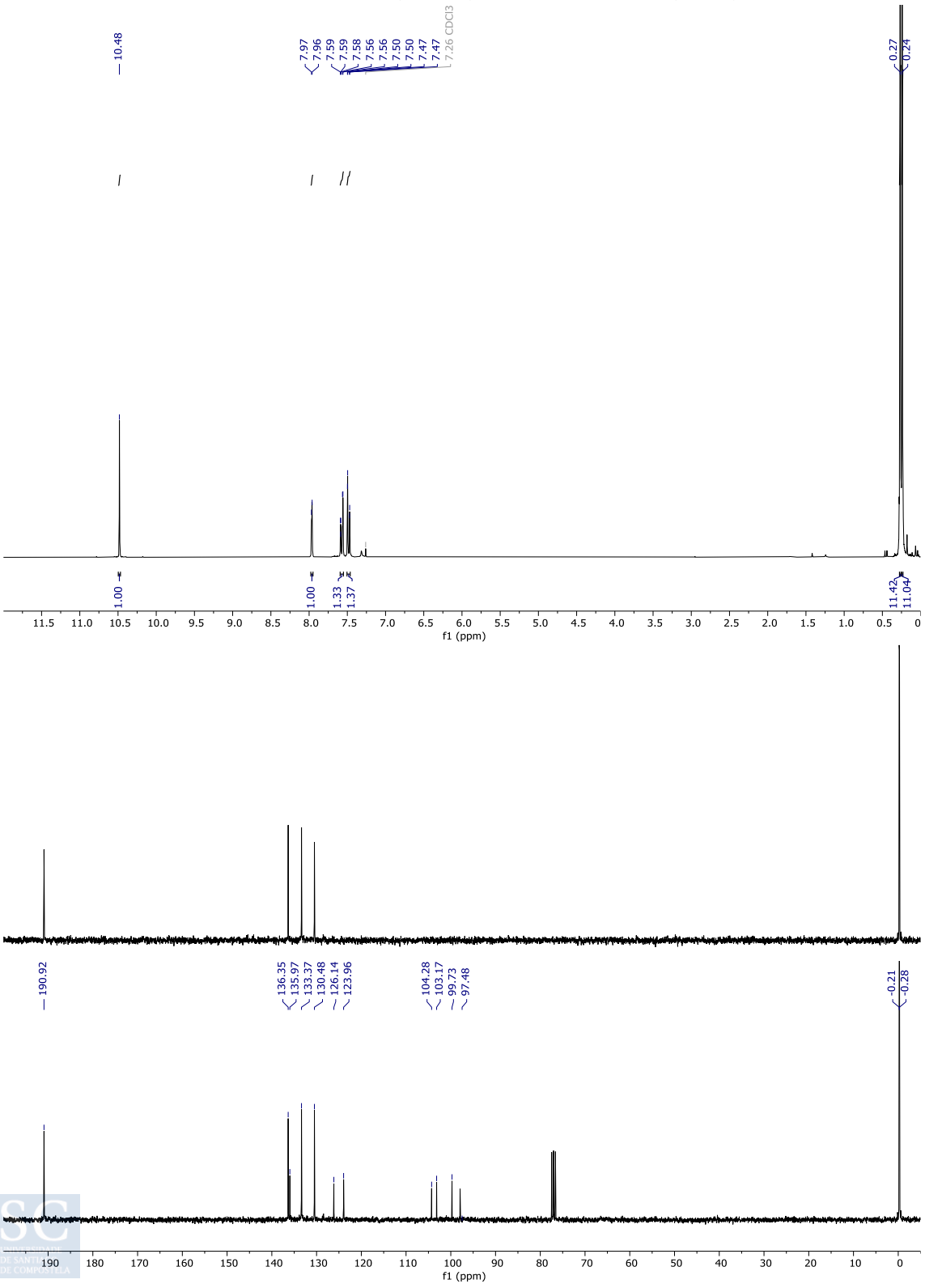


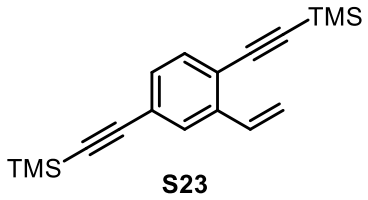




S22

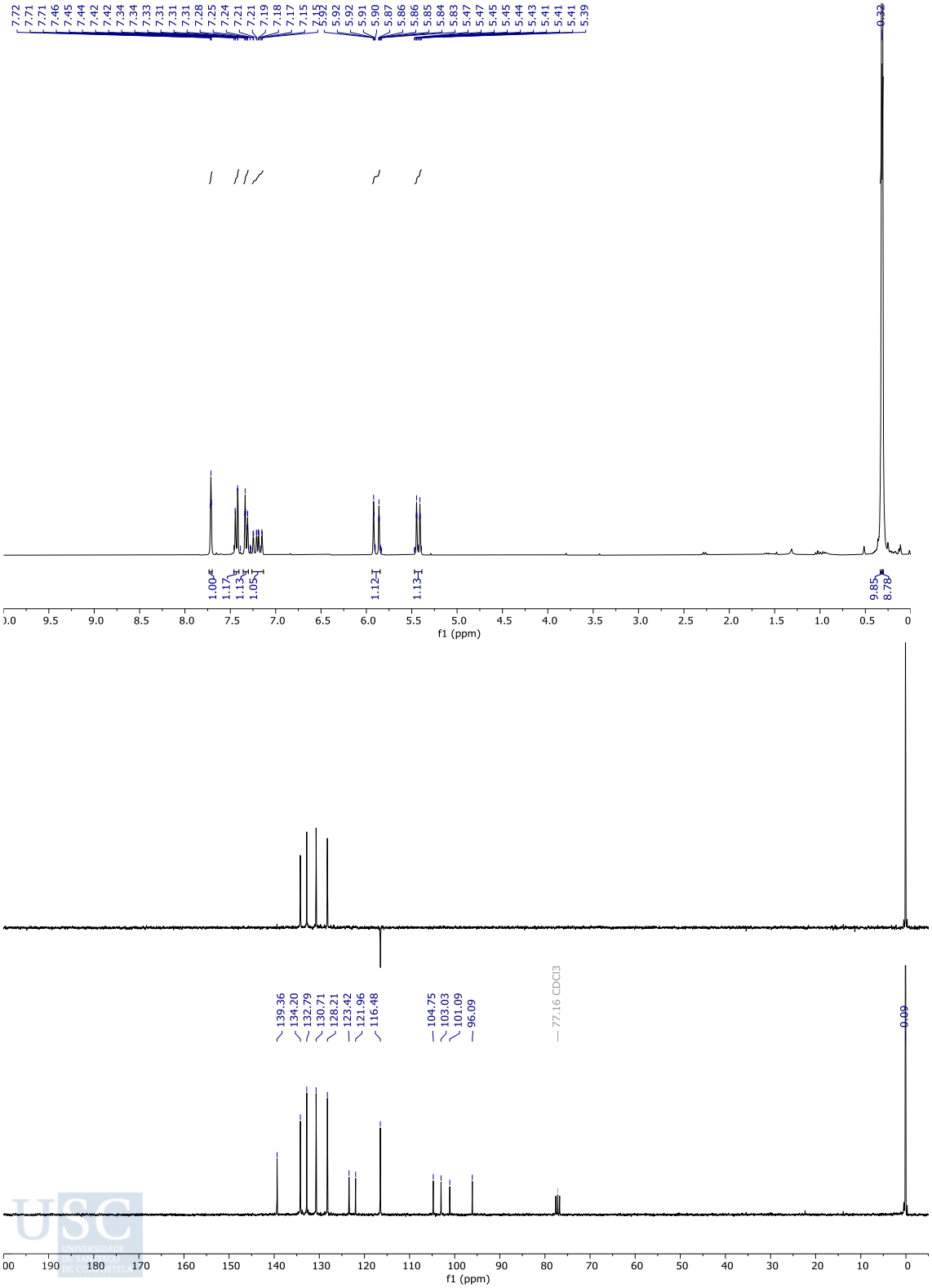
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

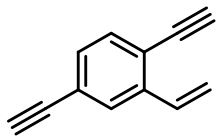




S23

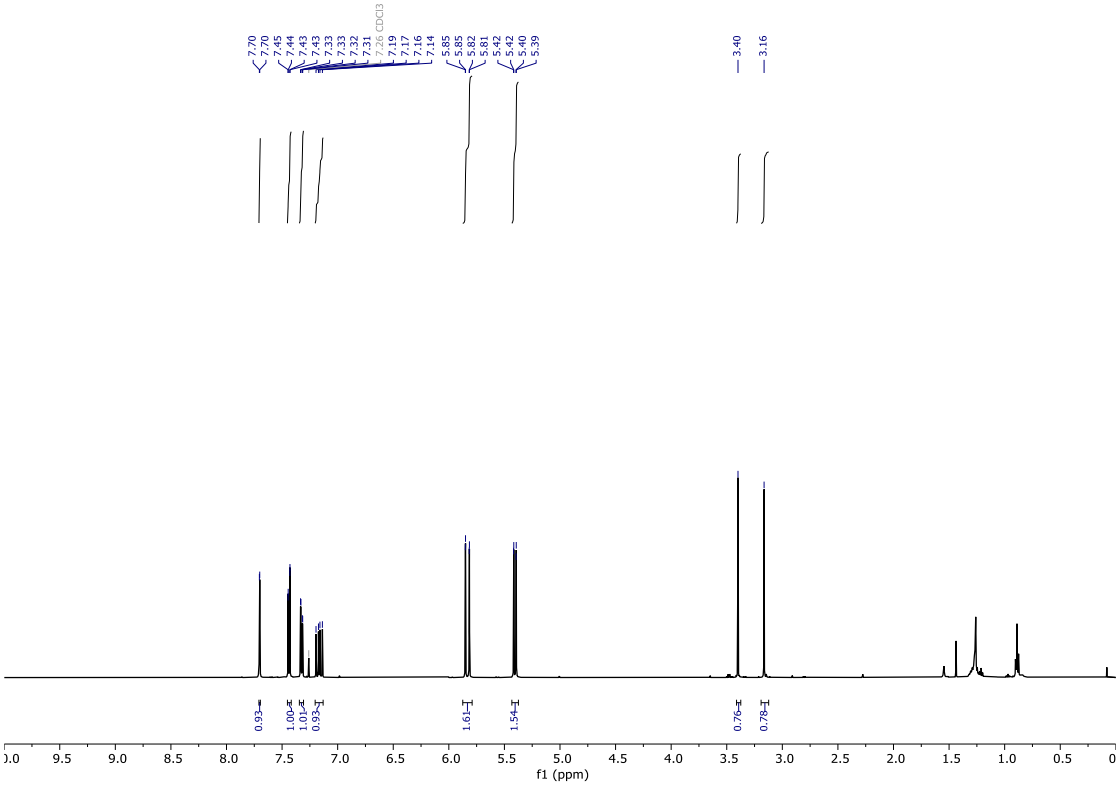
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

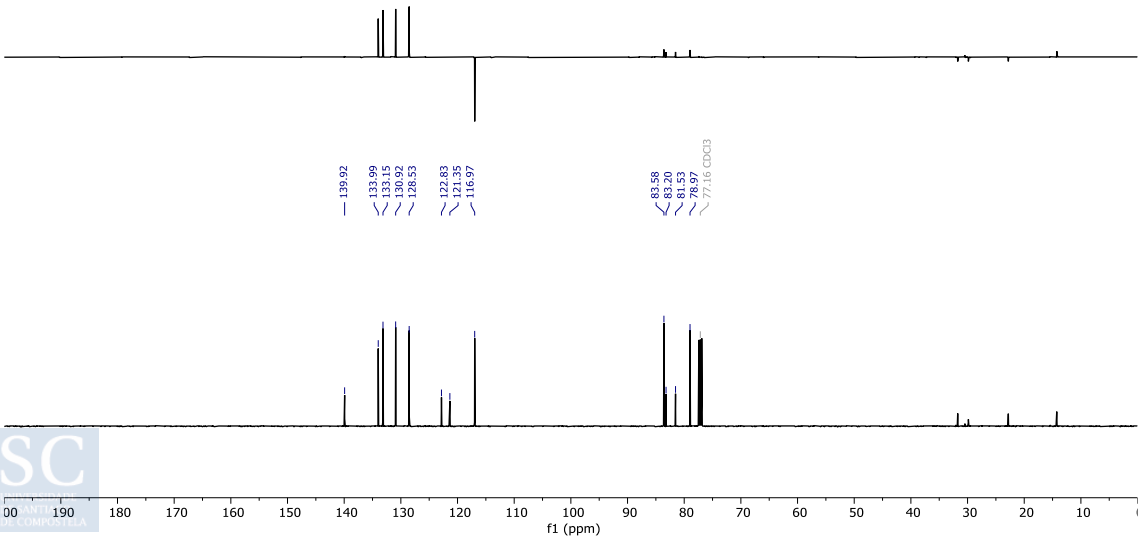


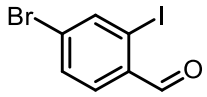


1g

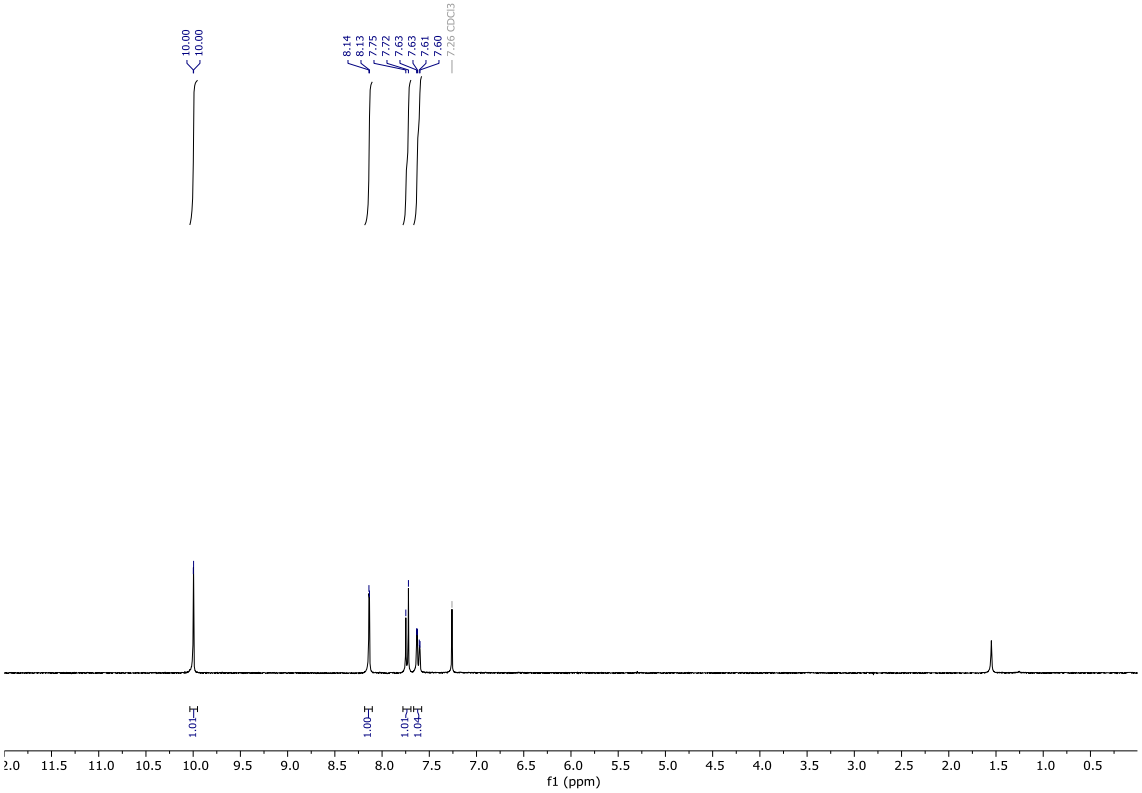
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

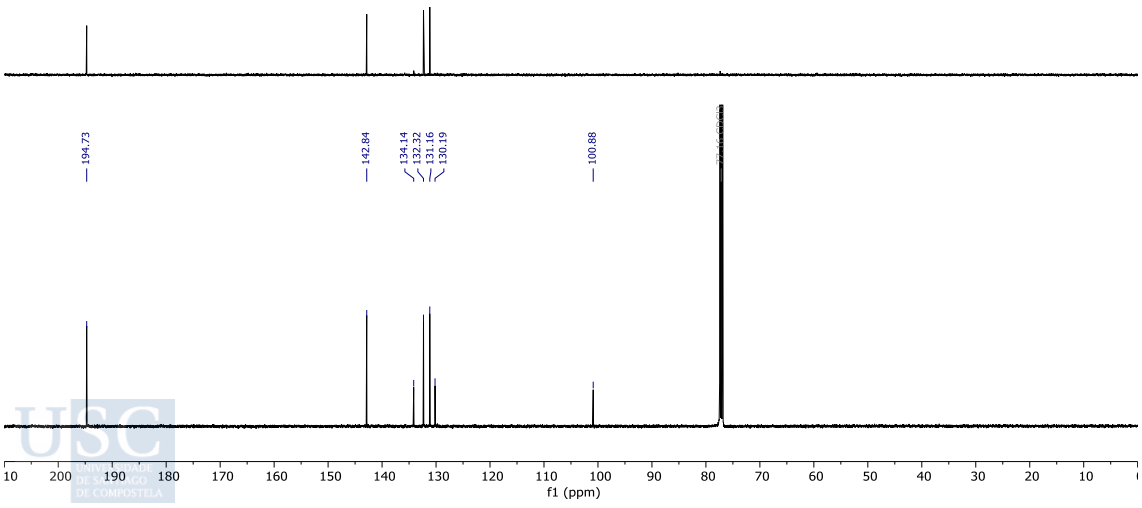


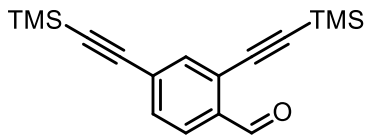




S25 ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

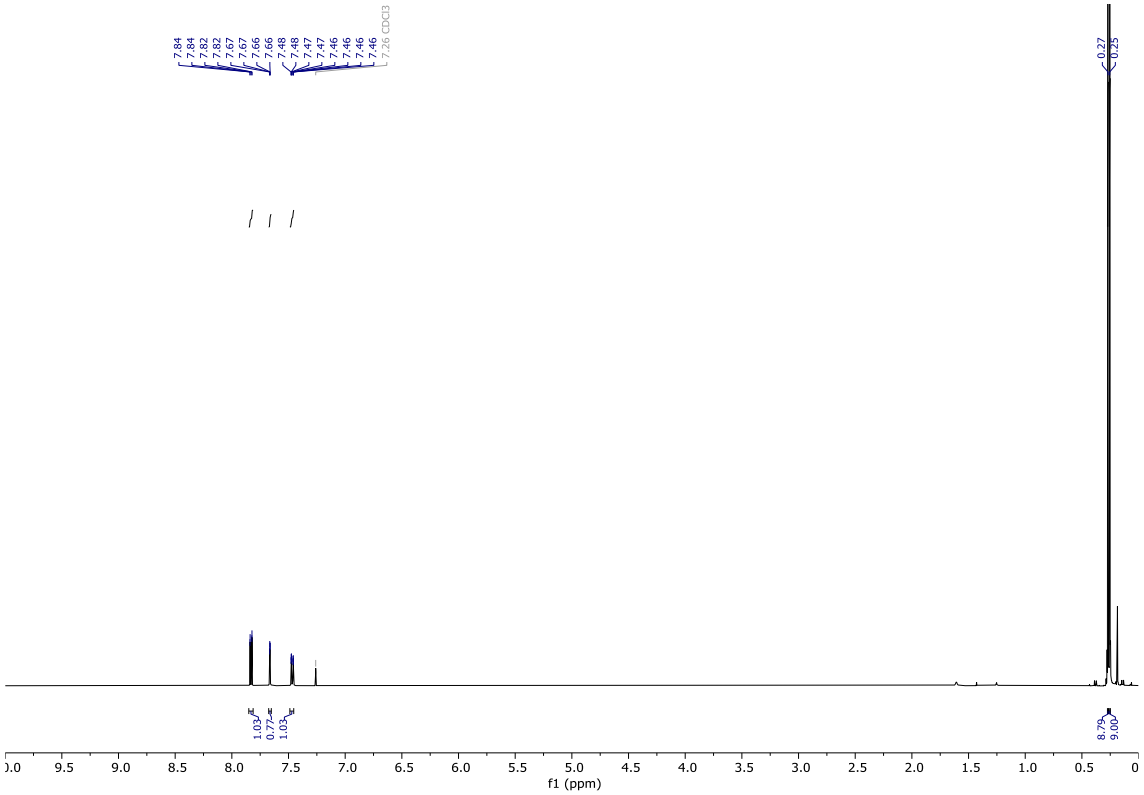


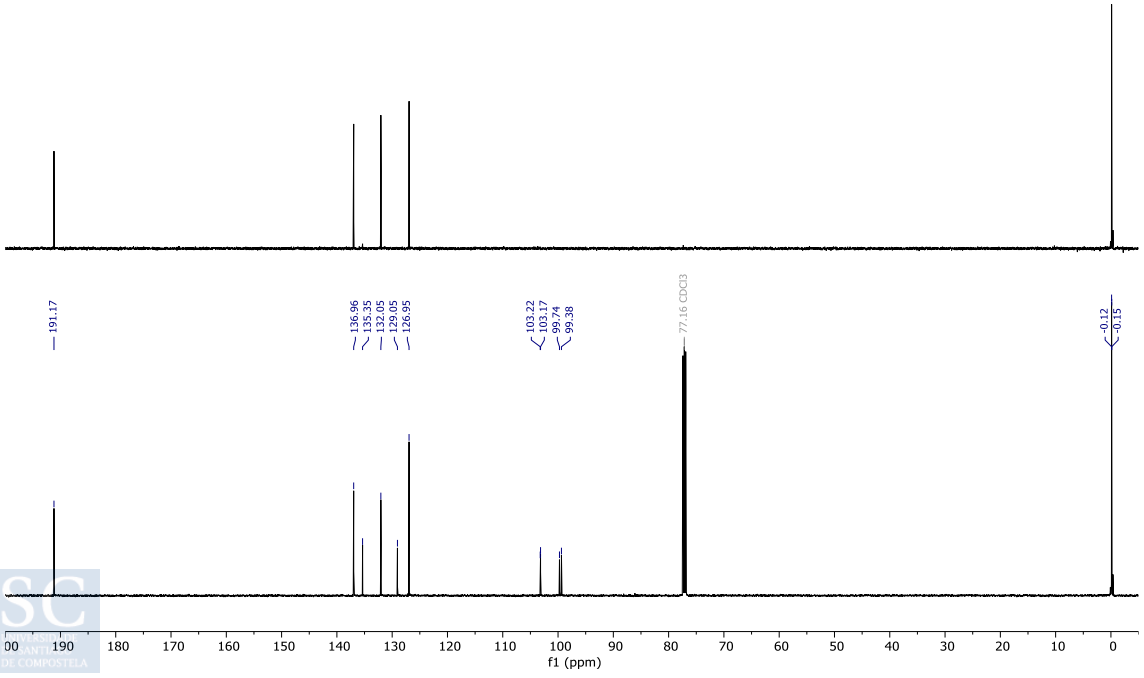


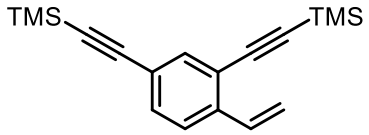


S26

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

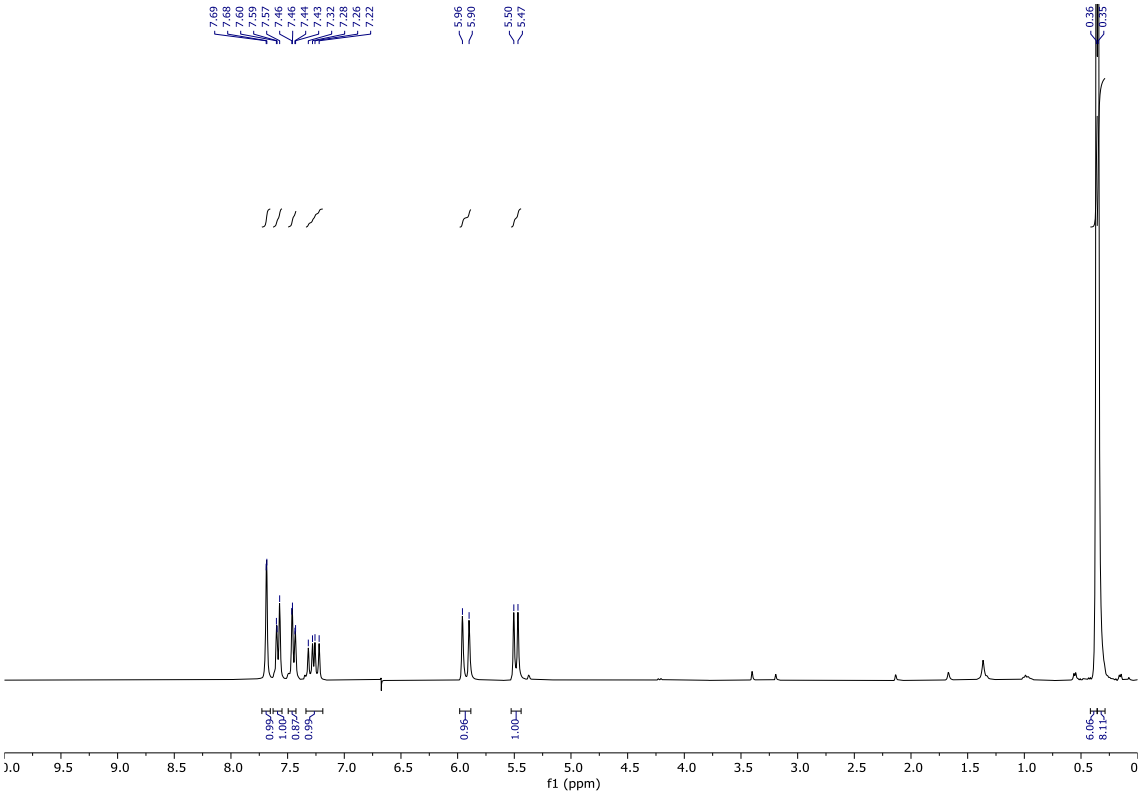


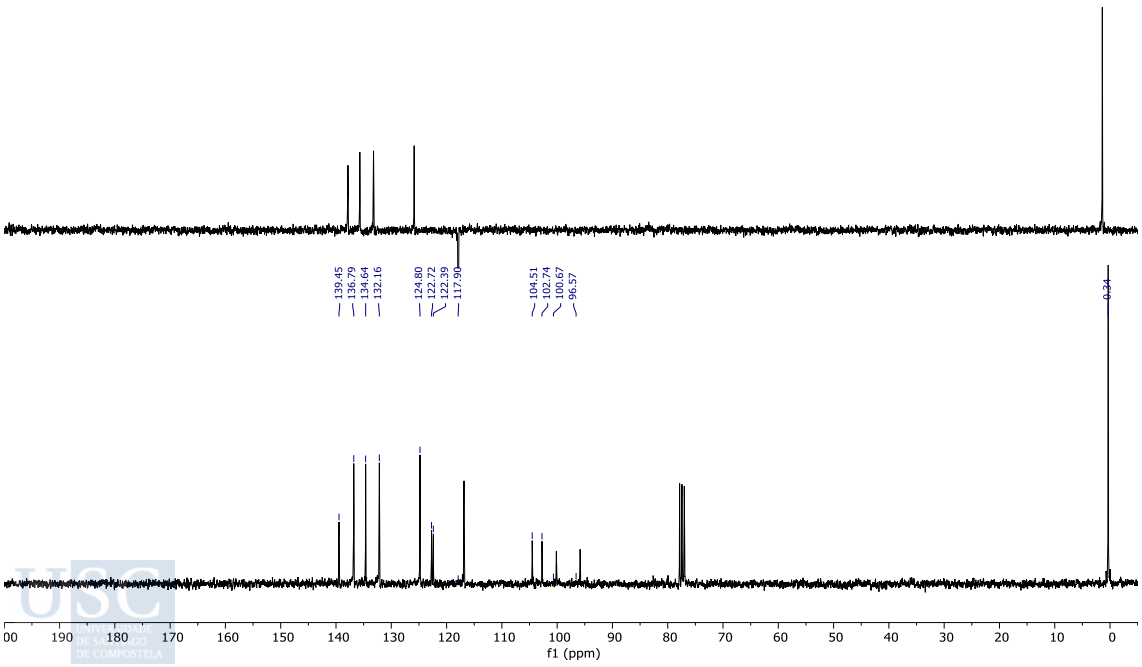


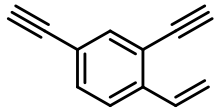


S27

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

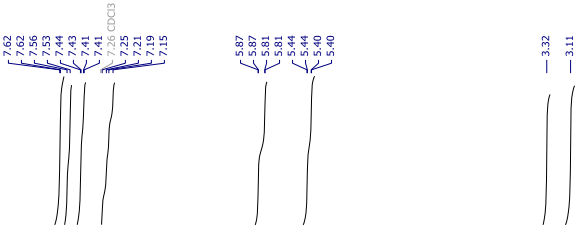


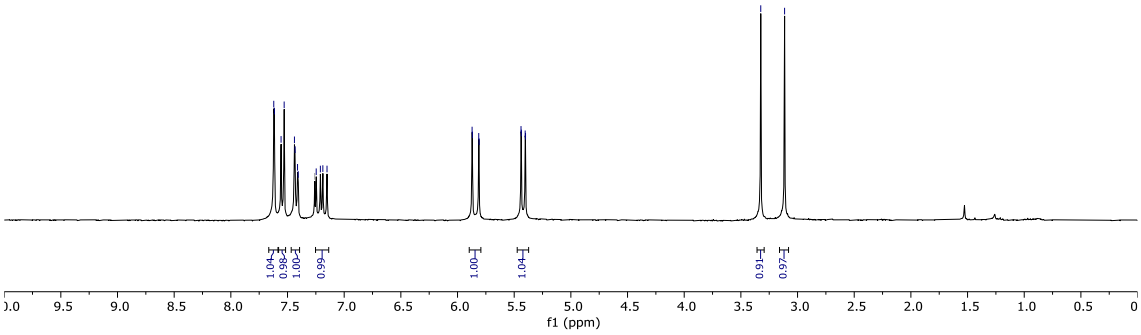


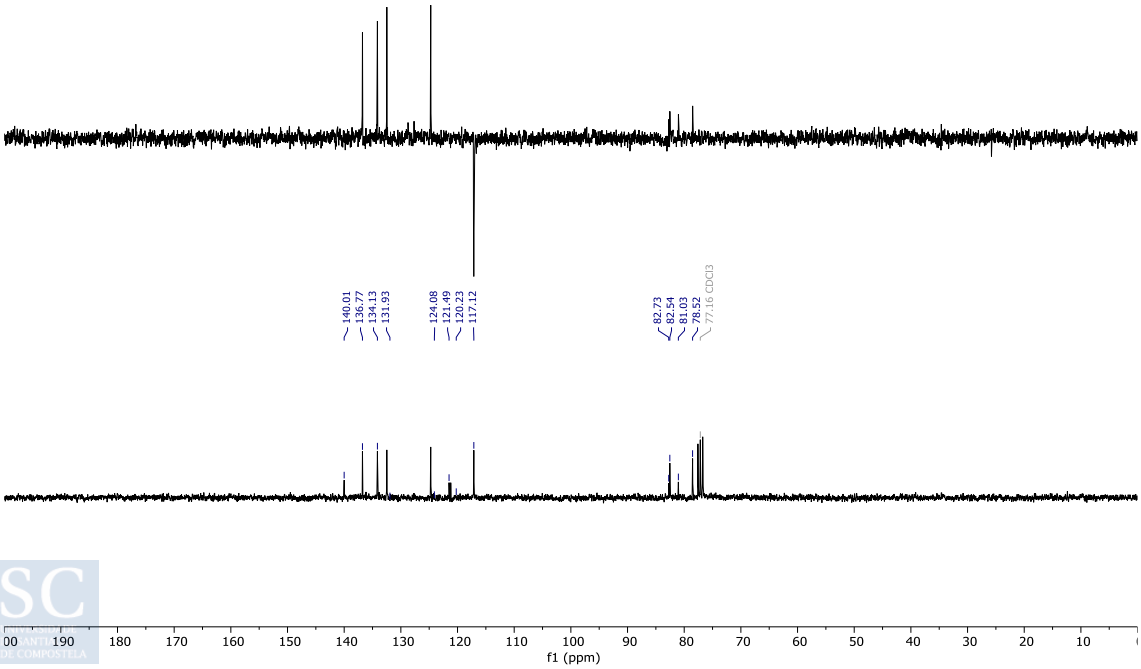


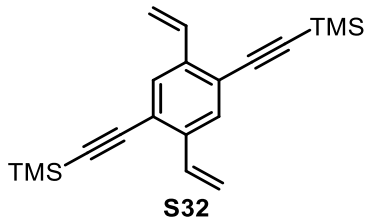
1h

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$



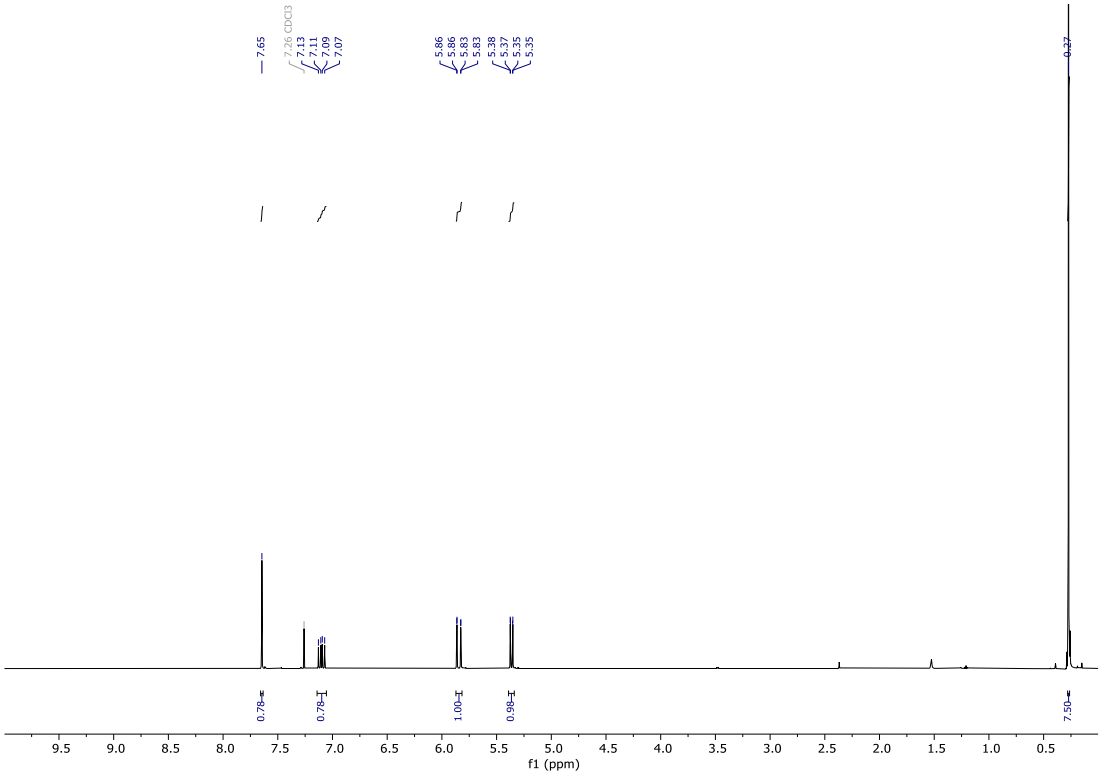


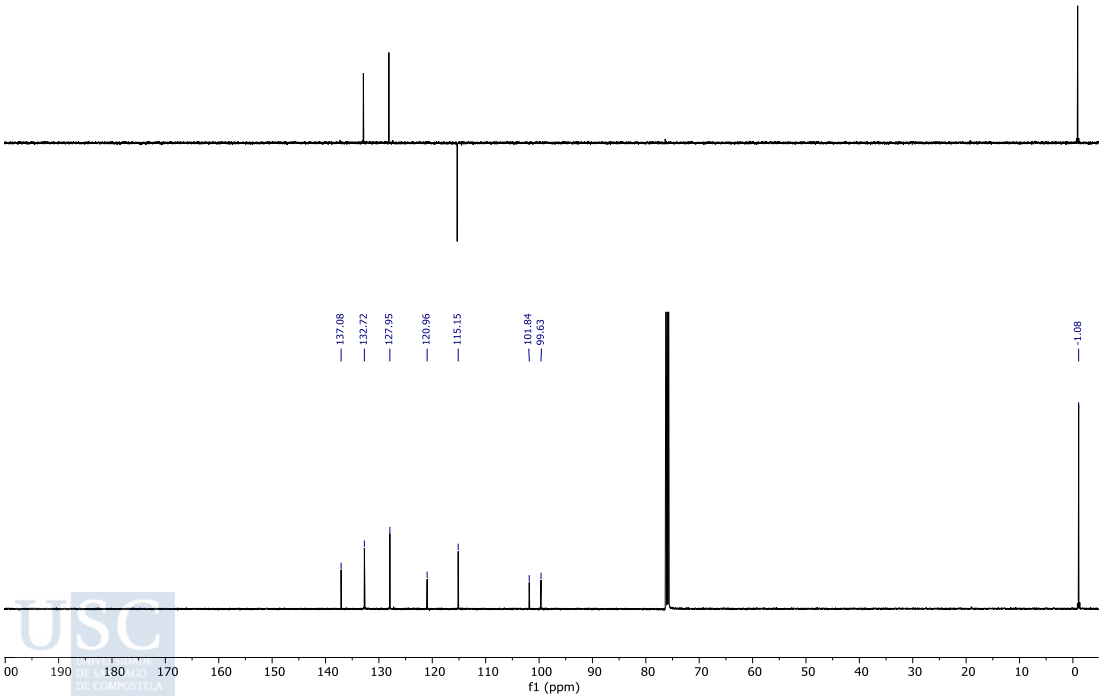


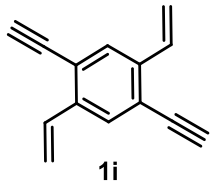


S32

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

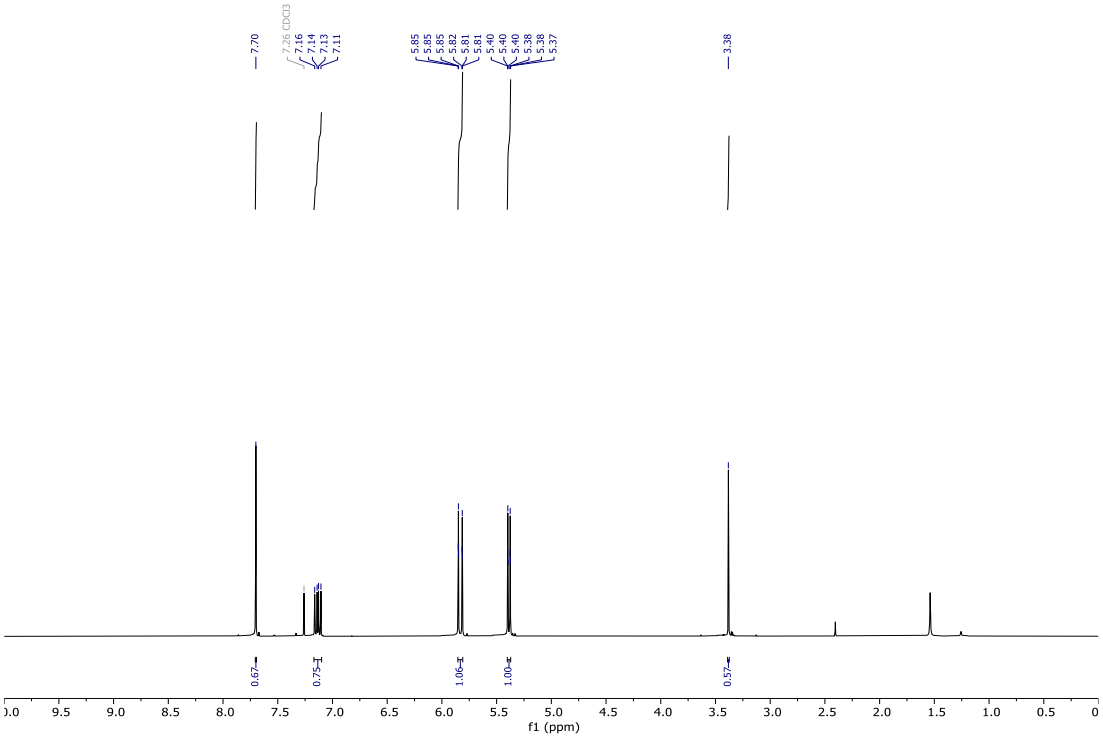


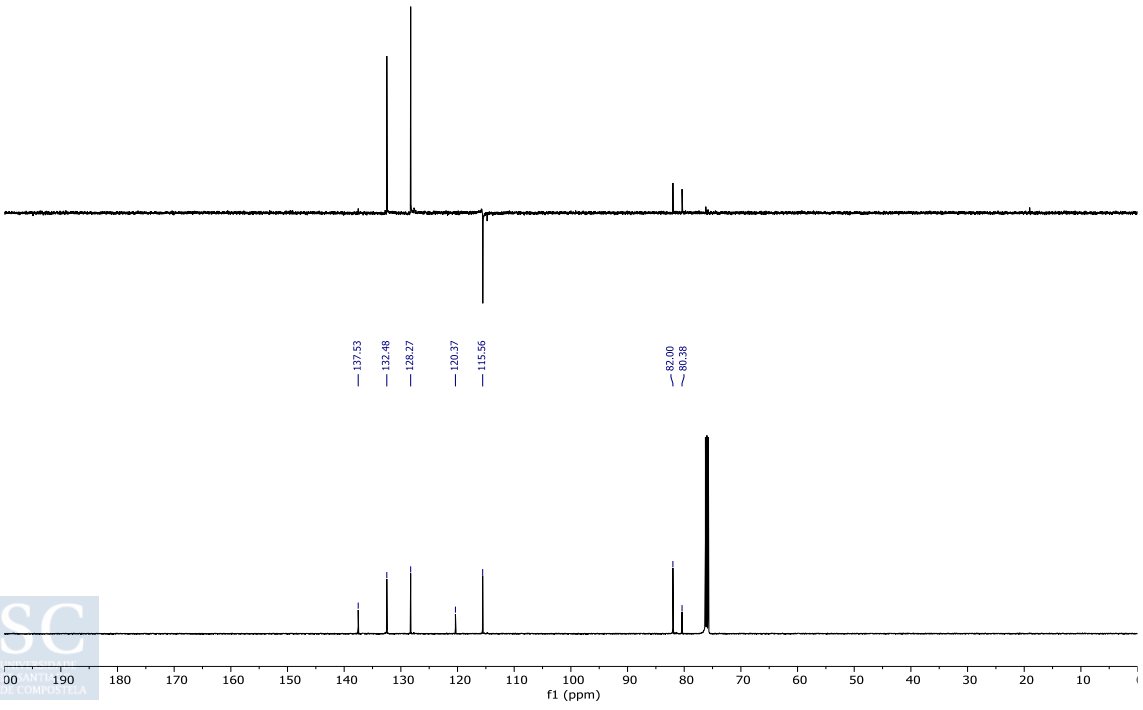


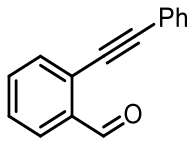


1i

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

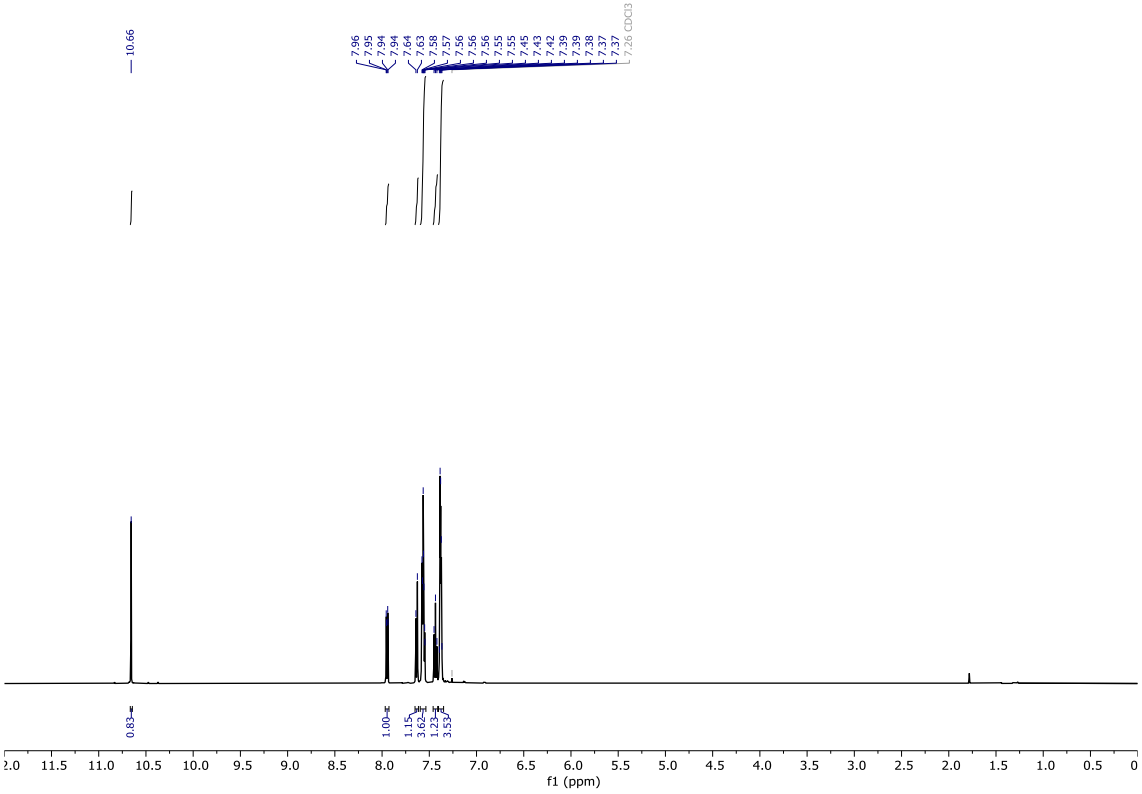


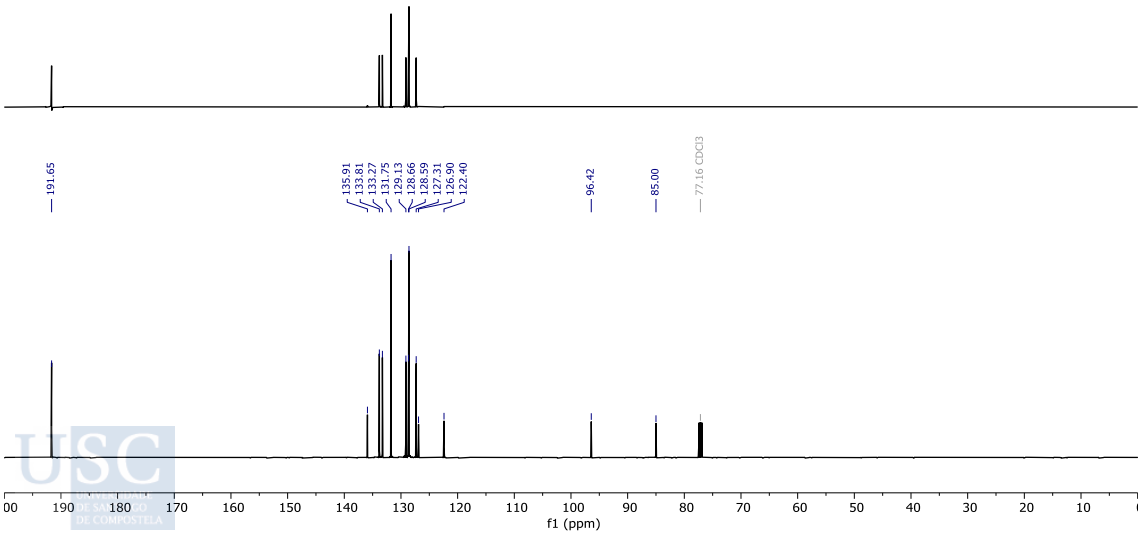


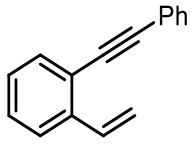


S33

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

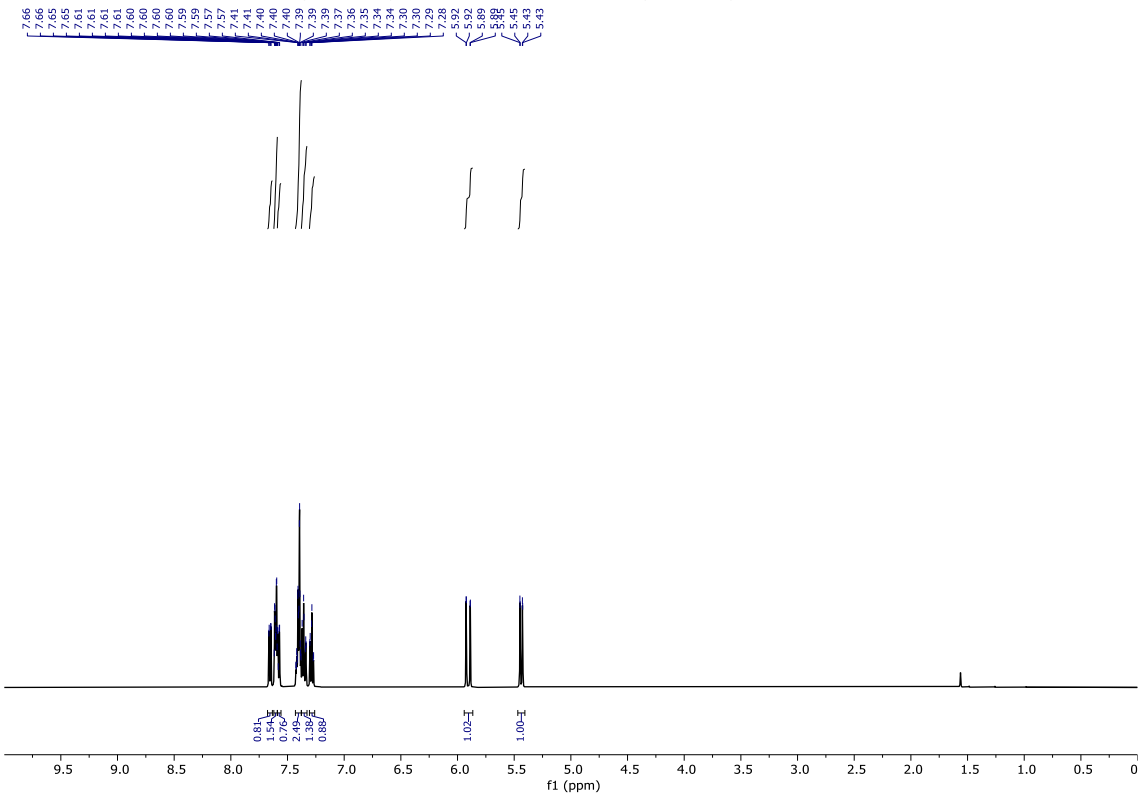


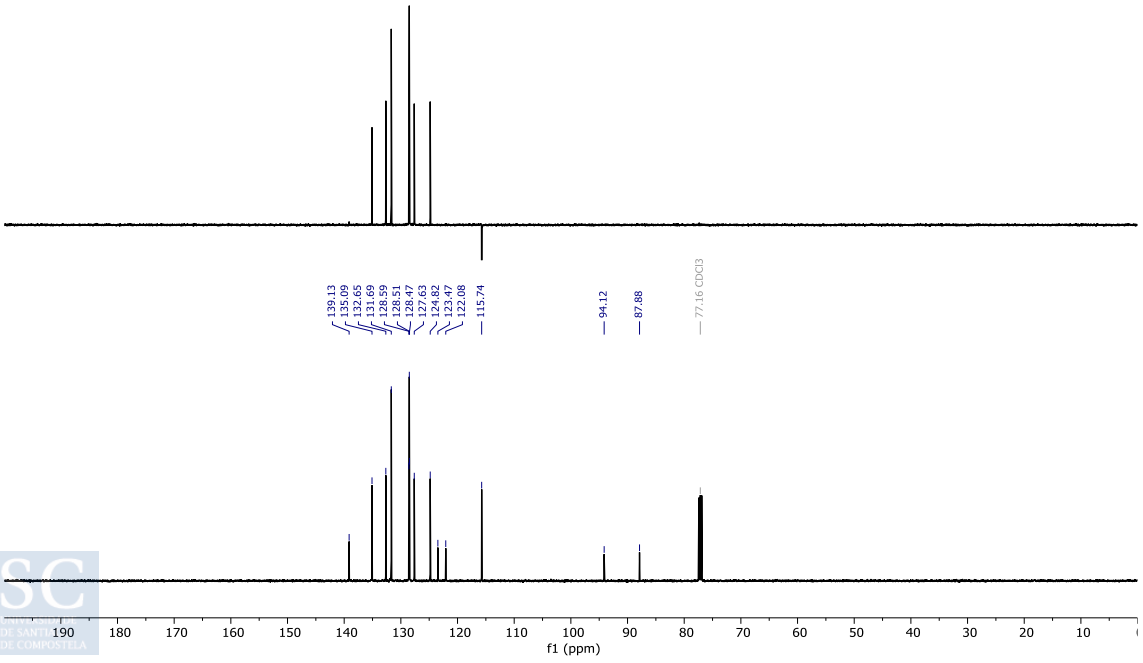


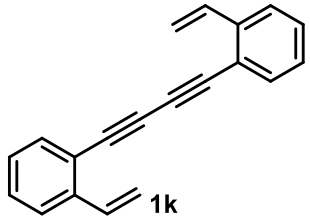


1j

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

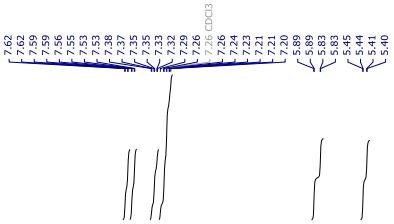


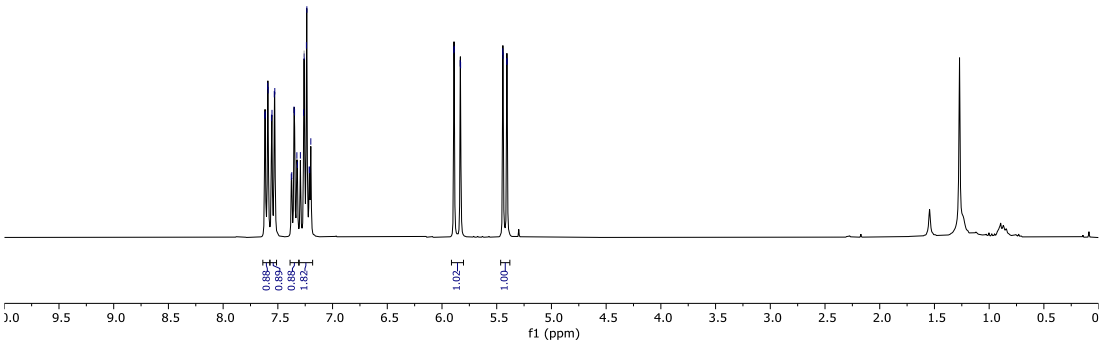


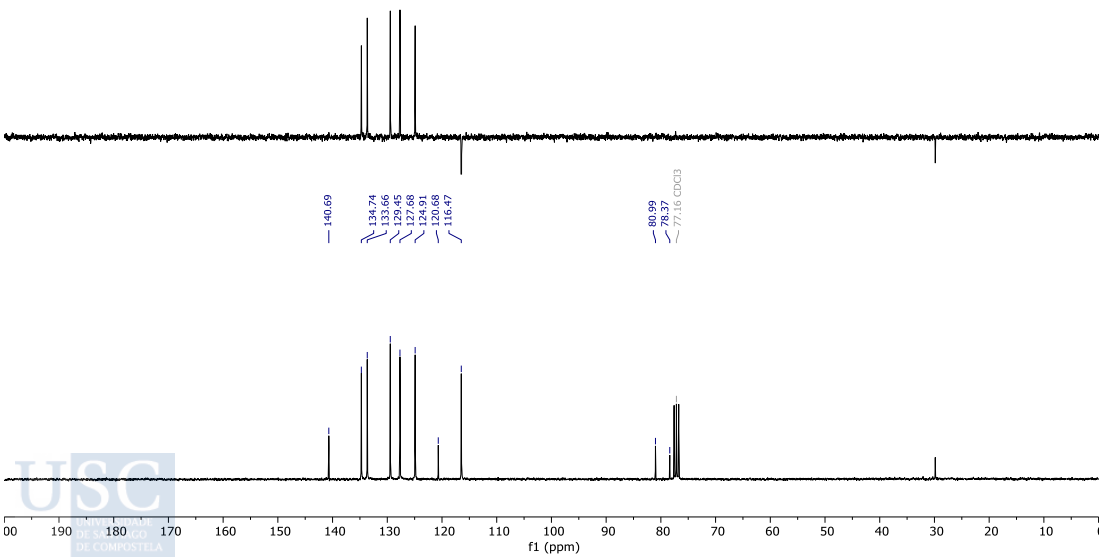


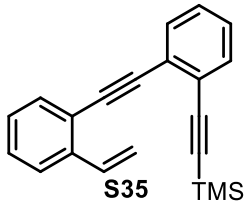
1k

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

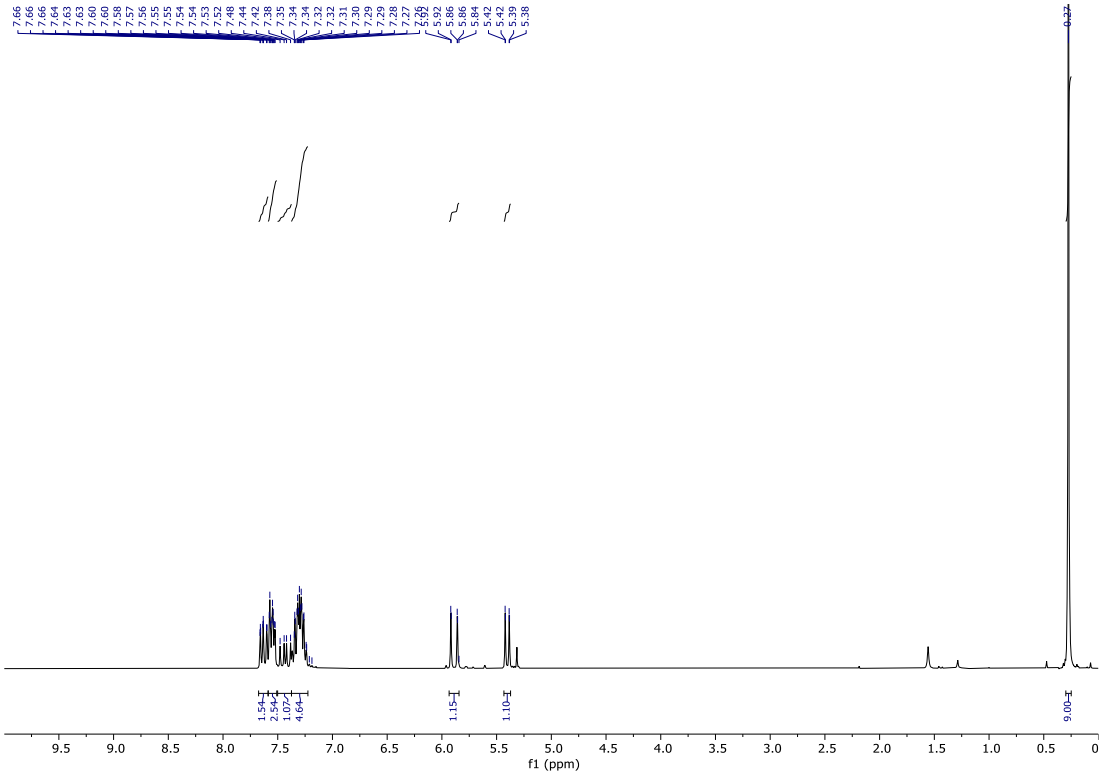


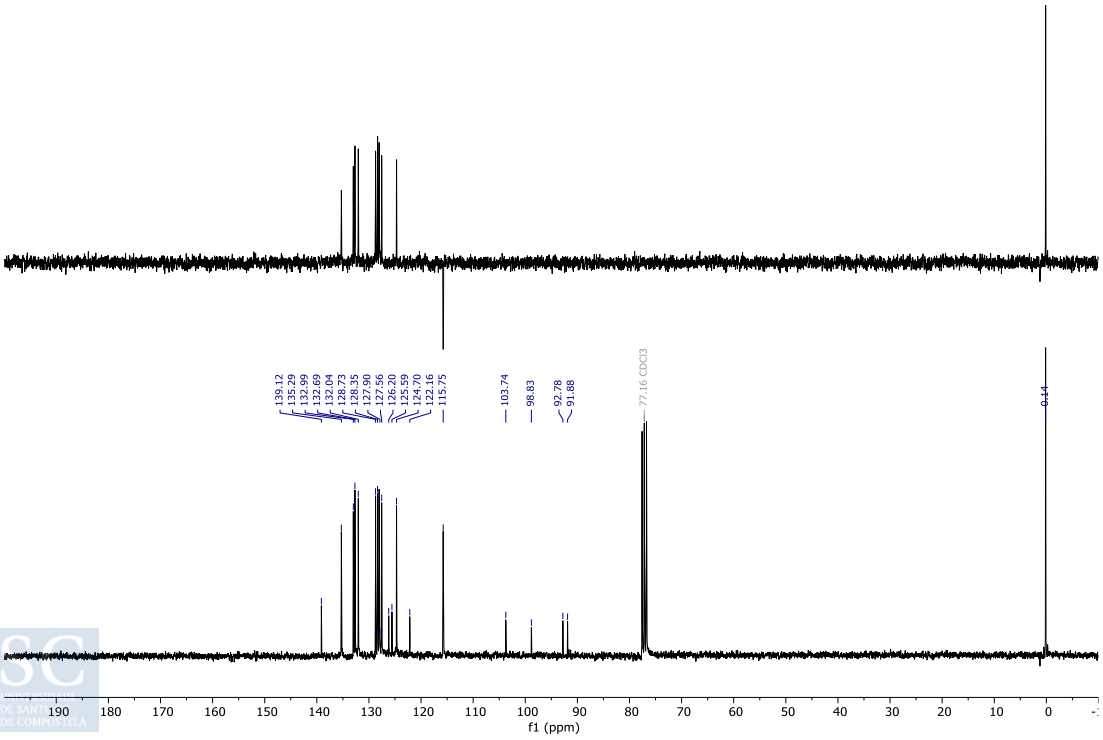


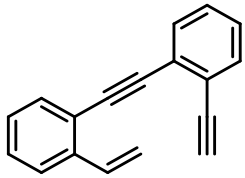




S35 TMS ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

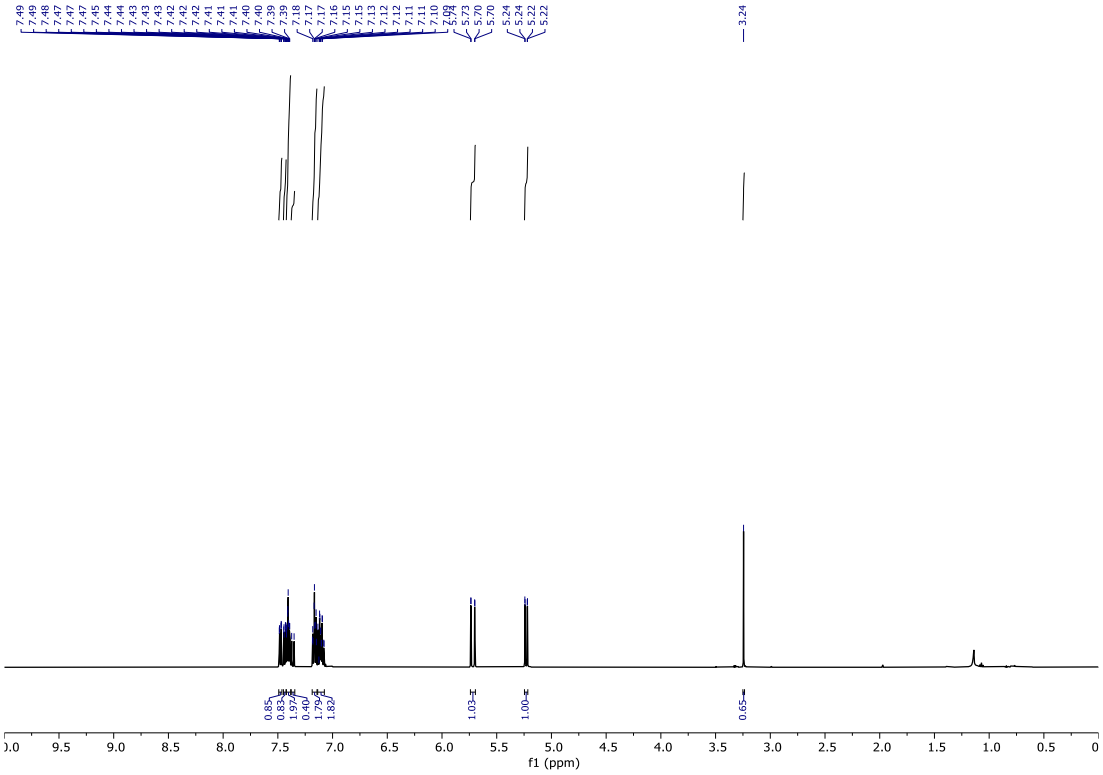


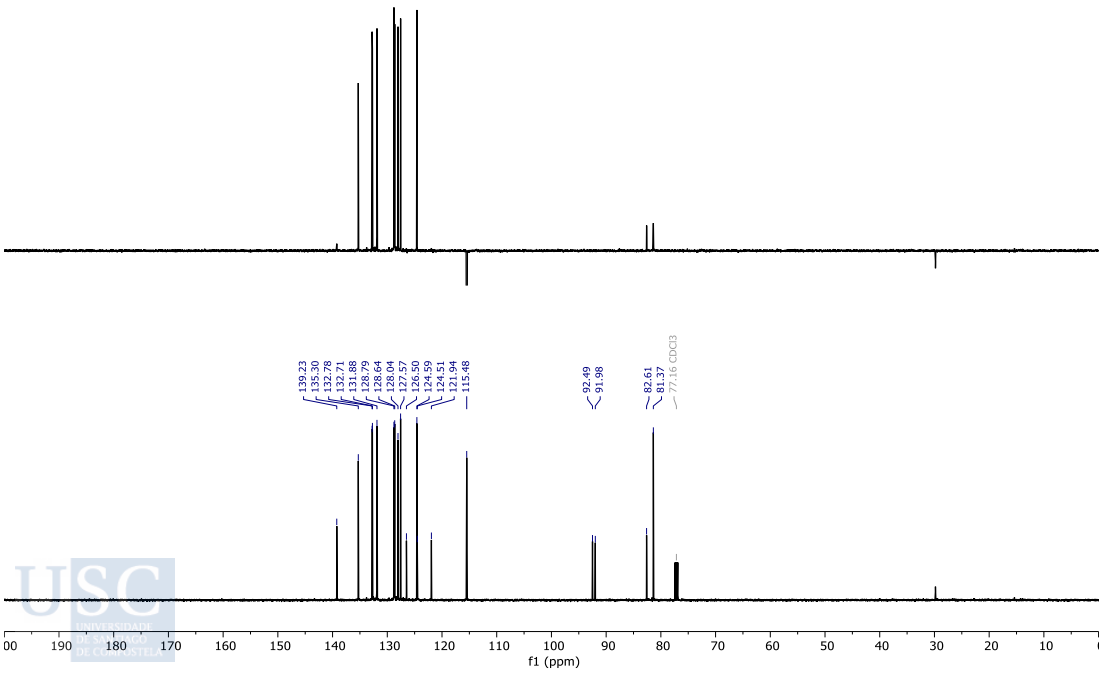


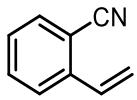


1l

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

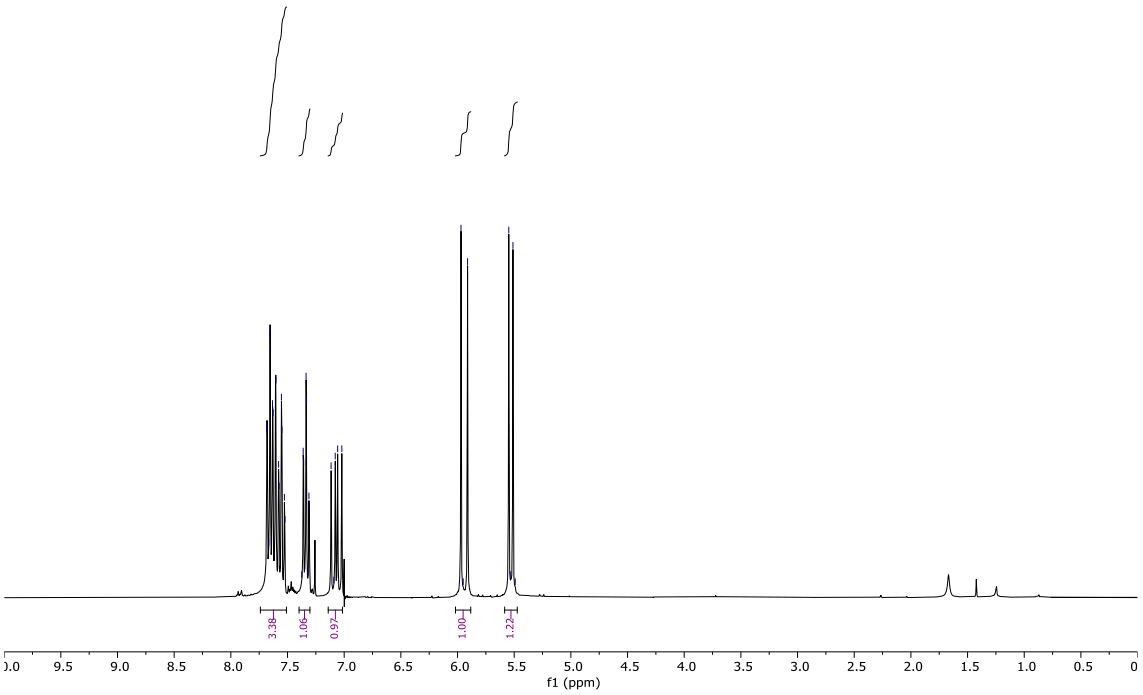


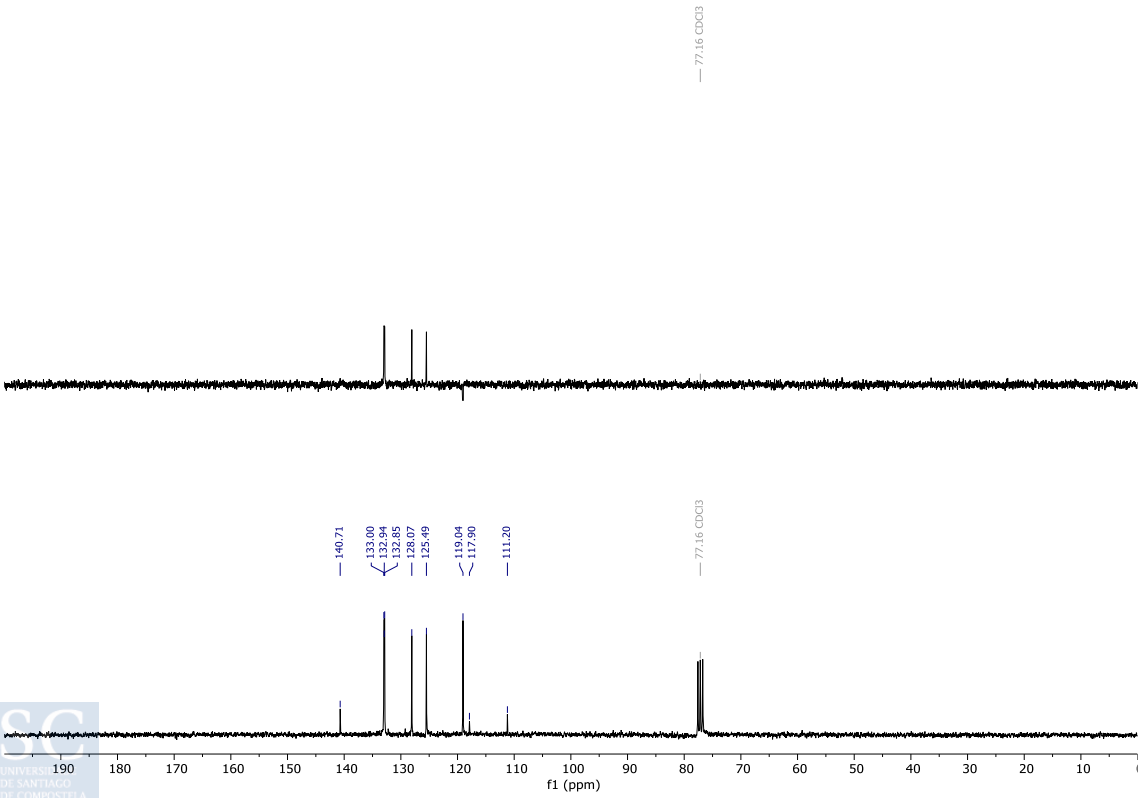


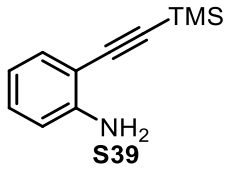


6

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

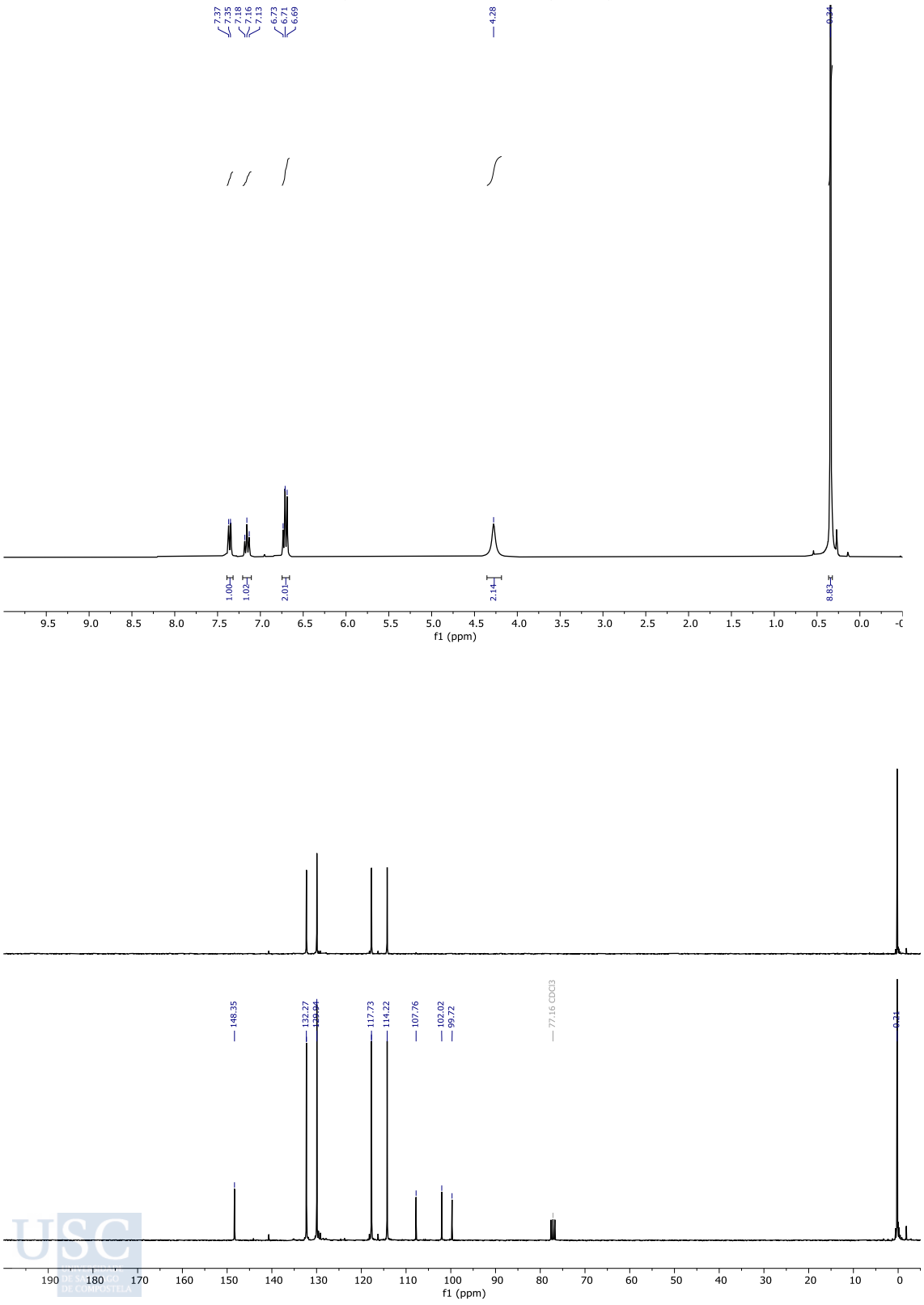


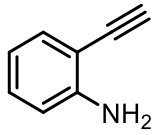




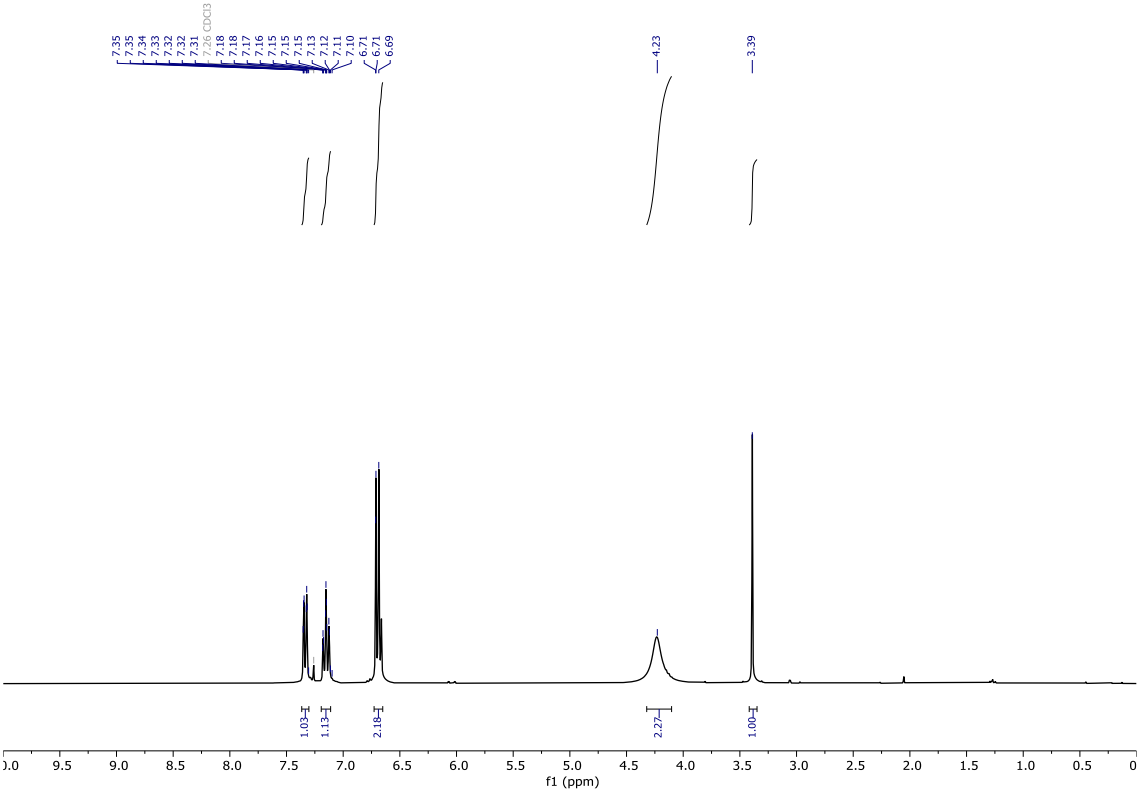
S39

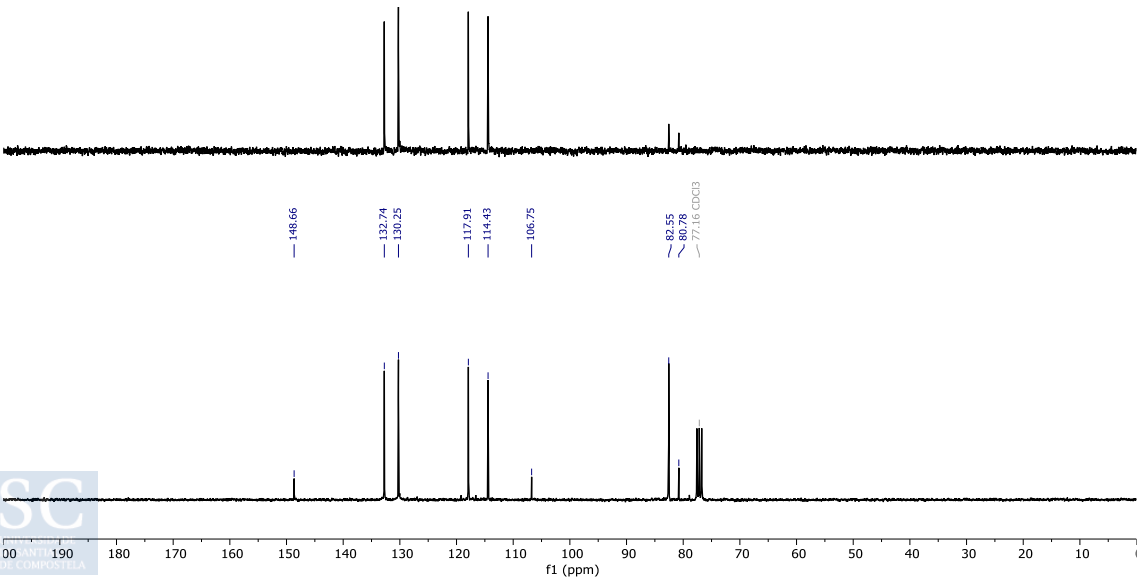
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

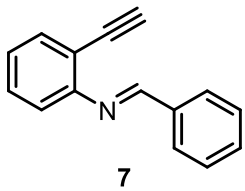




S40 ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

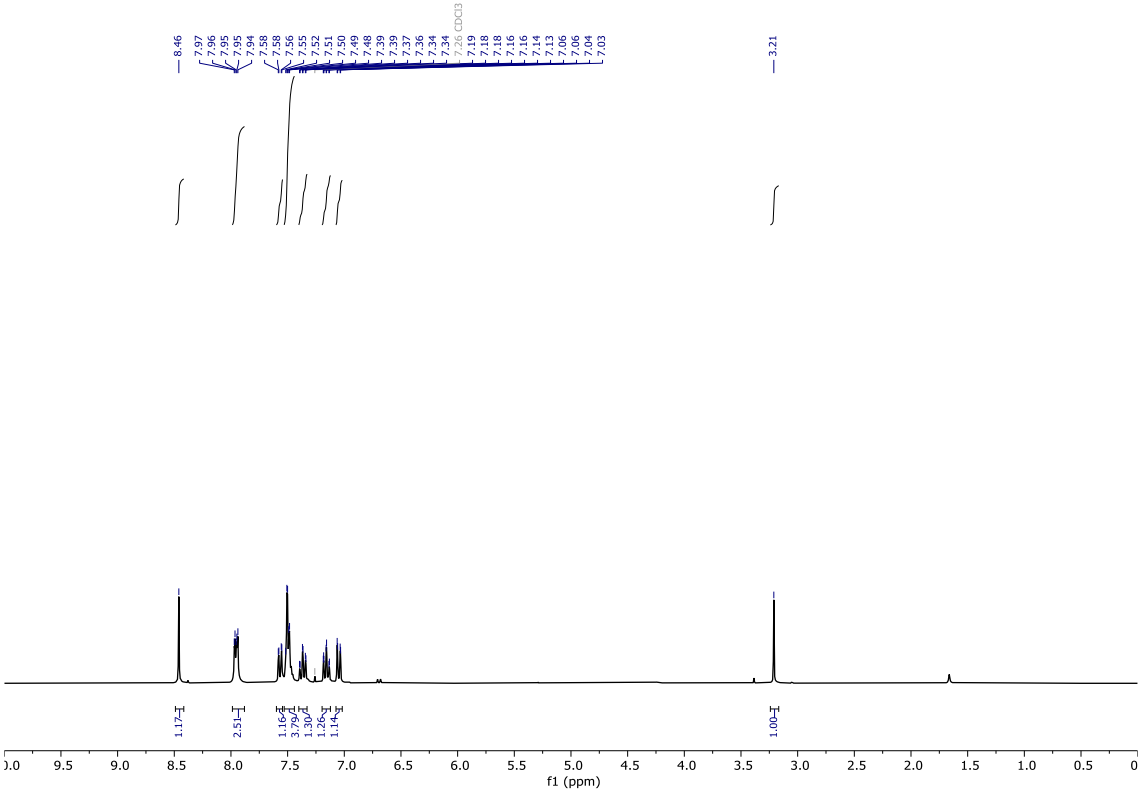


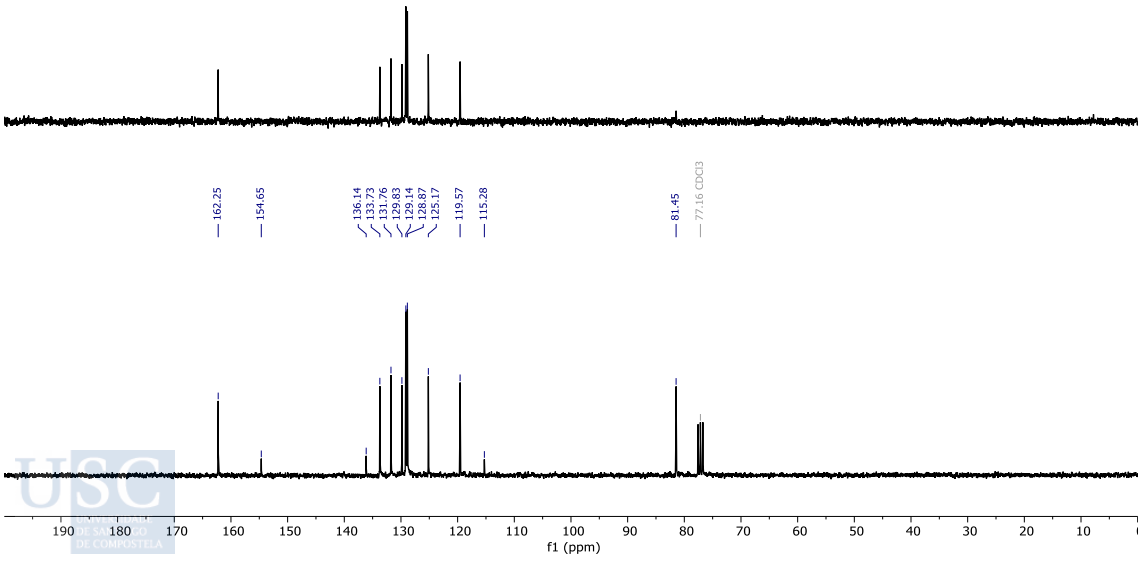


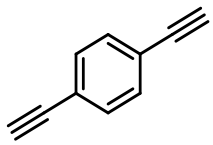


7

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

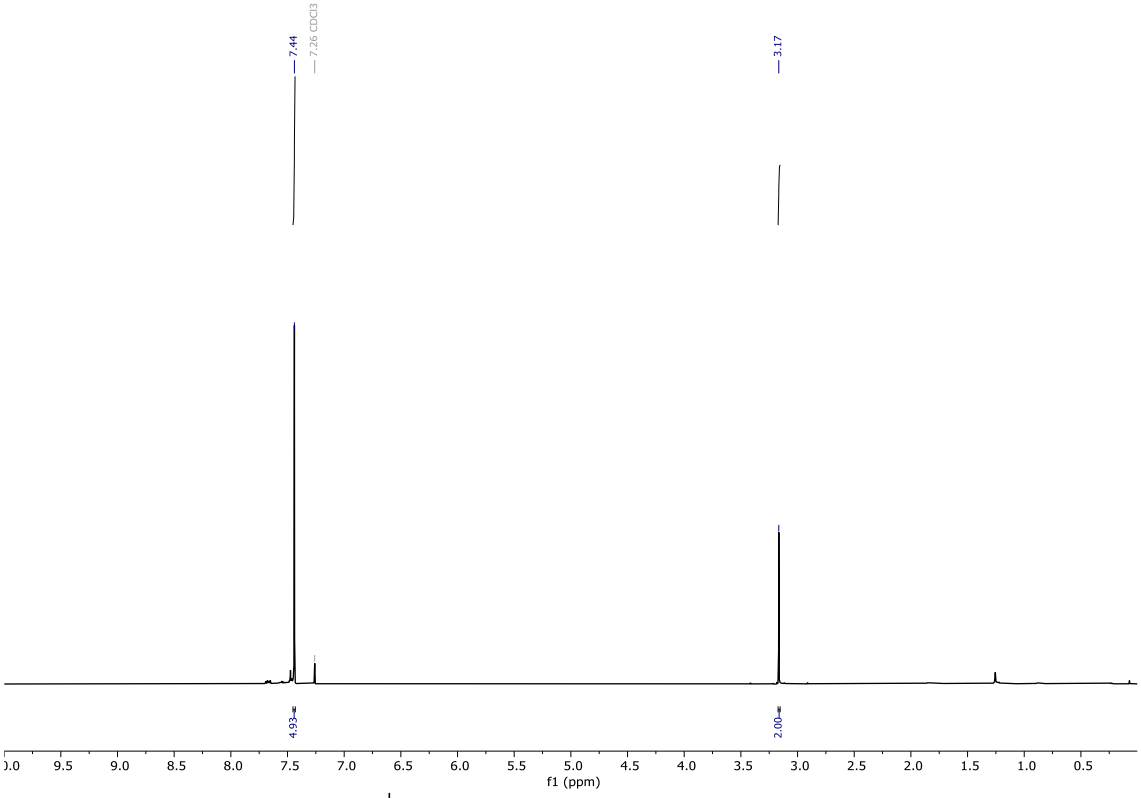


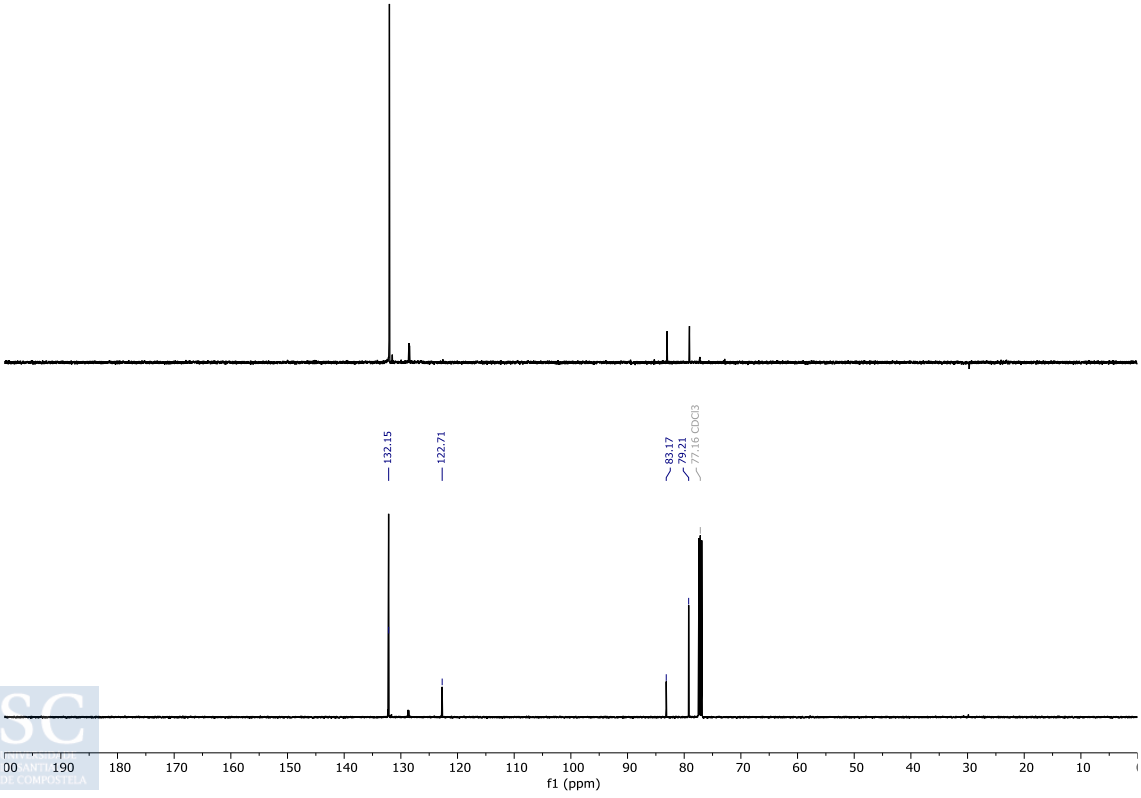


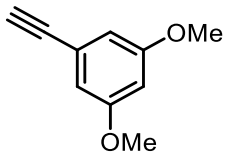


2g

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

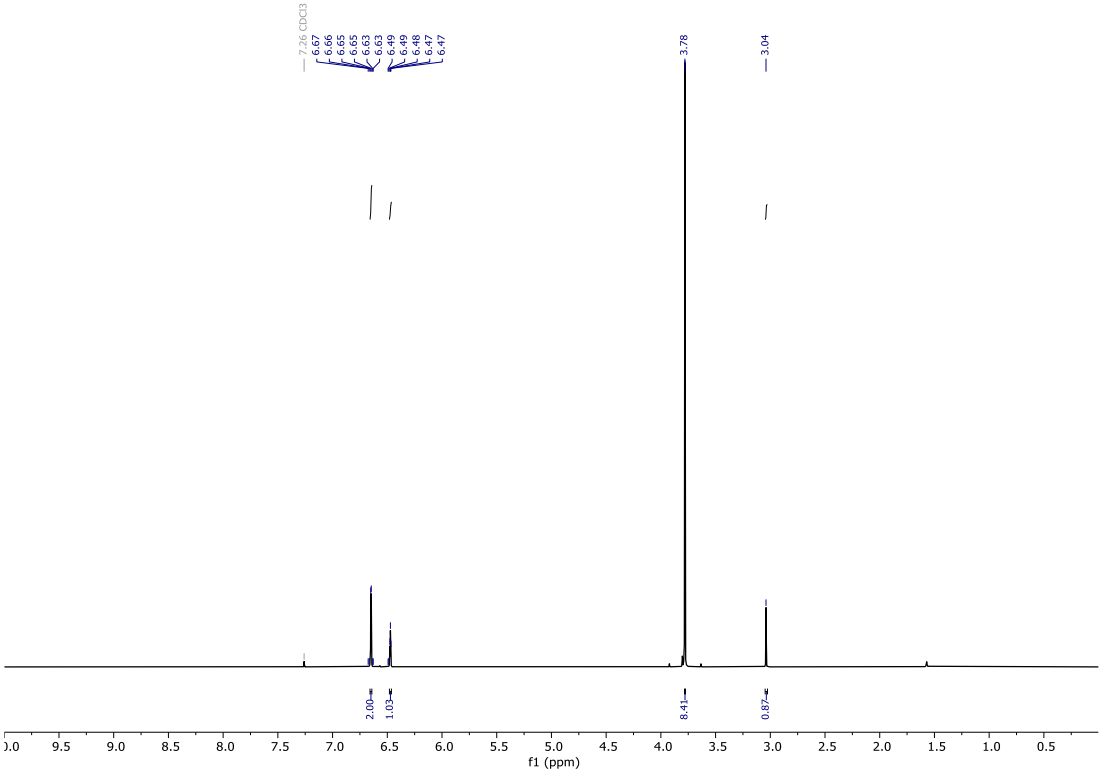


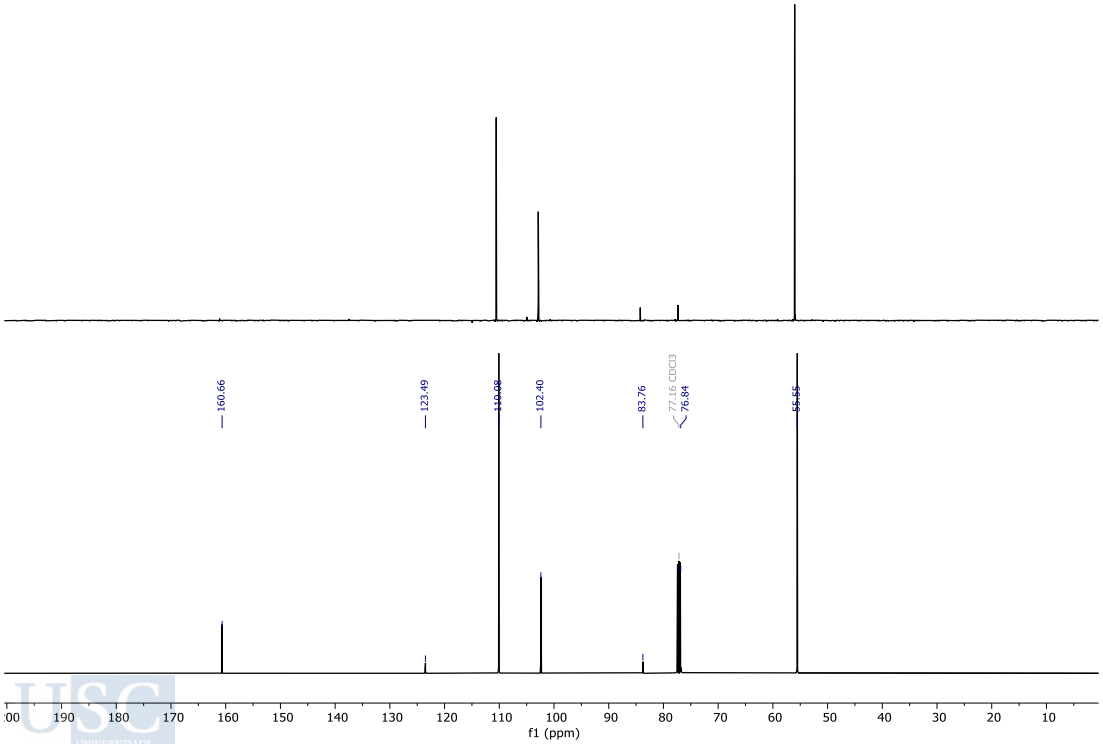


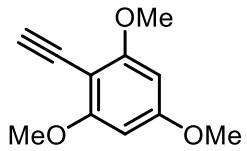


2h

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

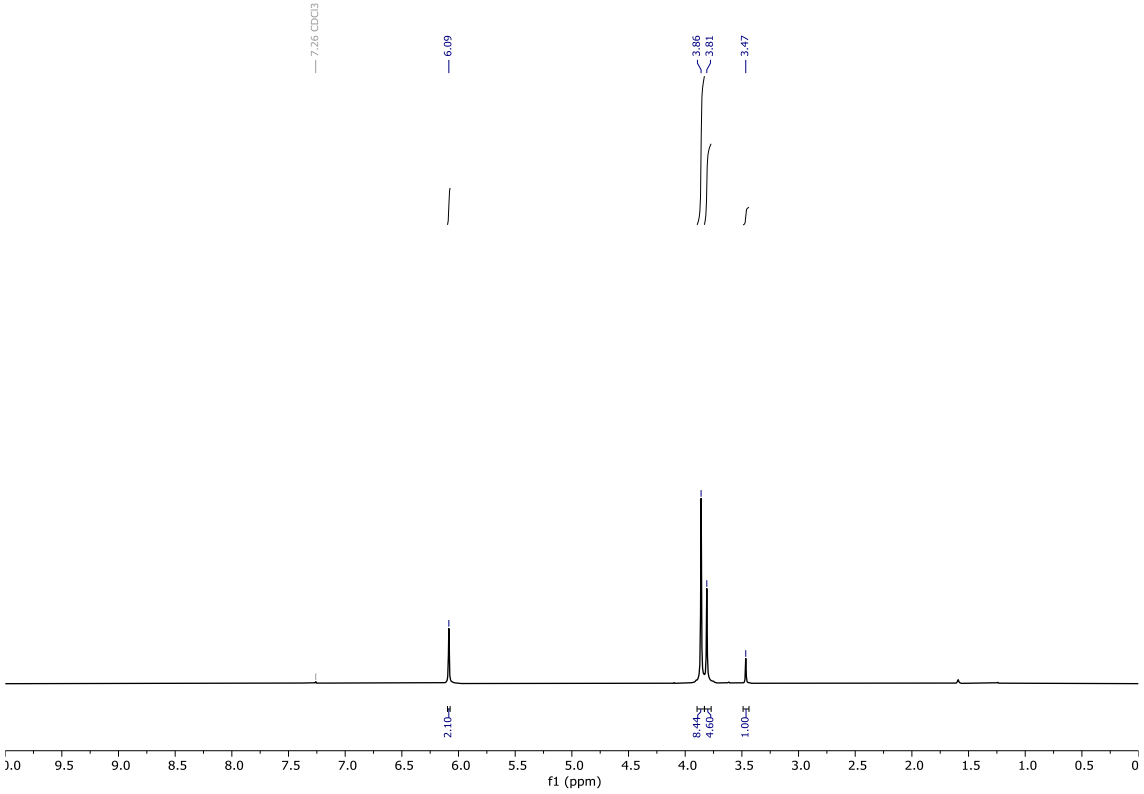


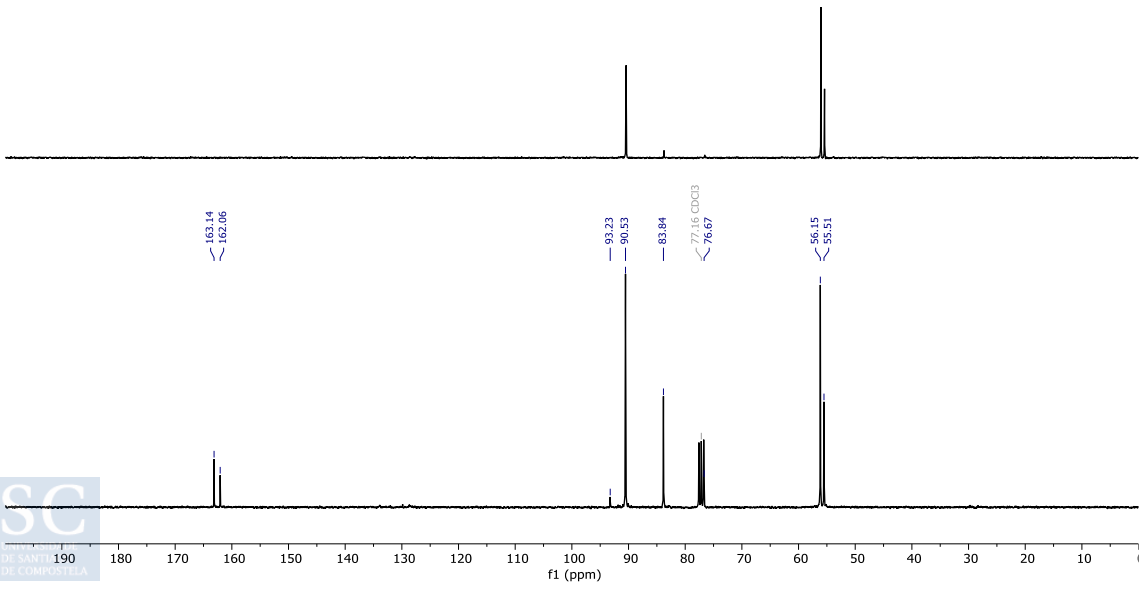


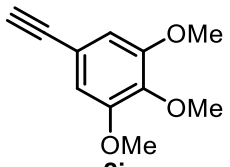


2i

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

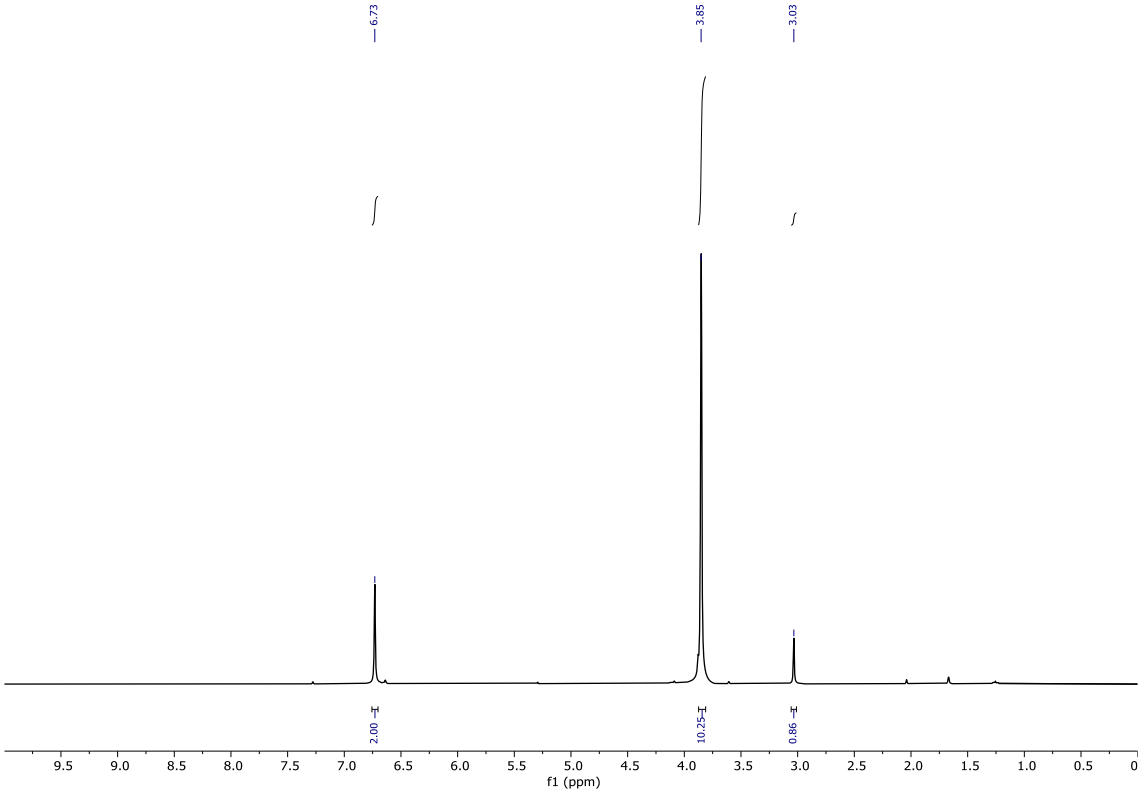


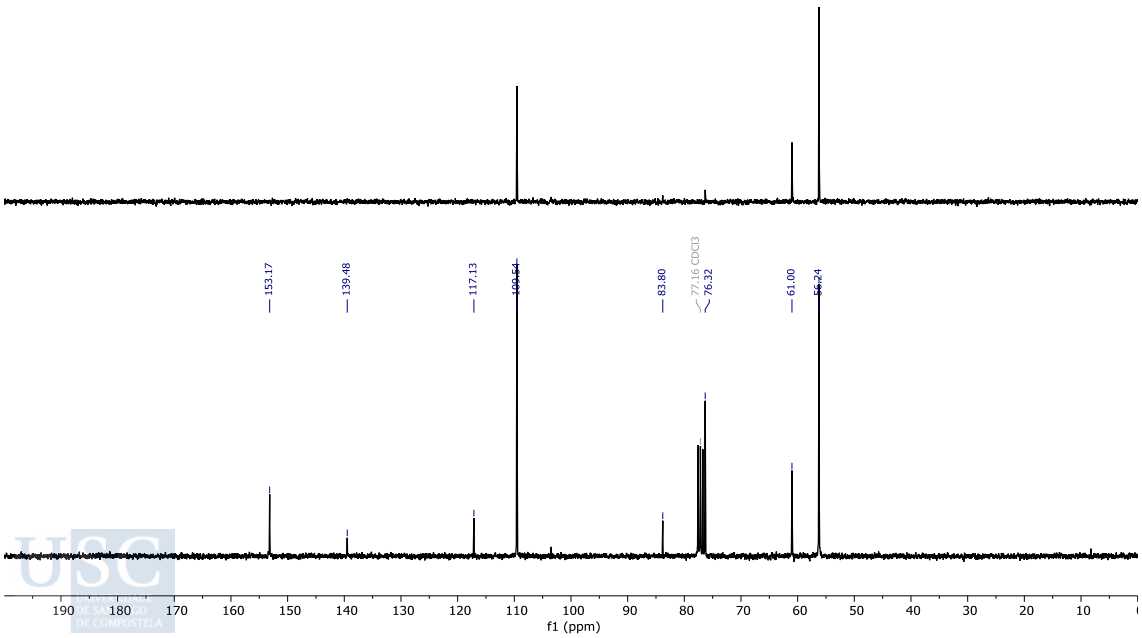


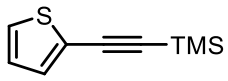


2j

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

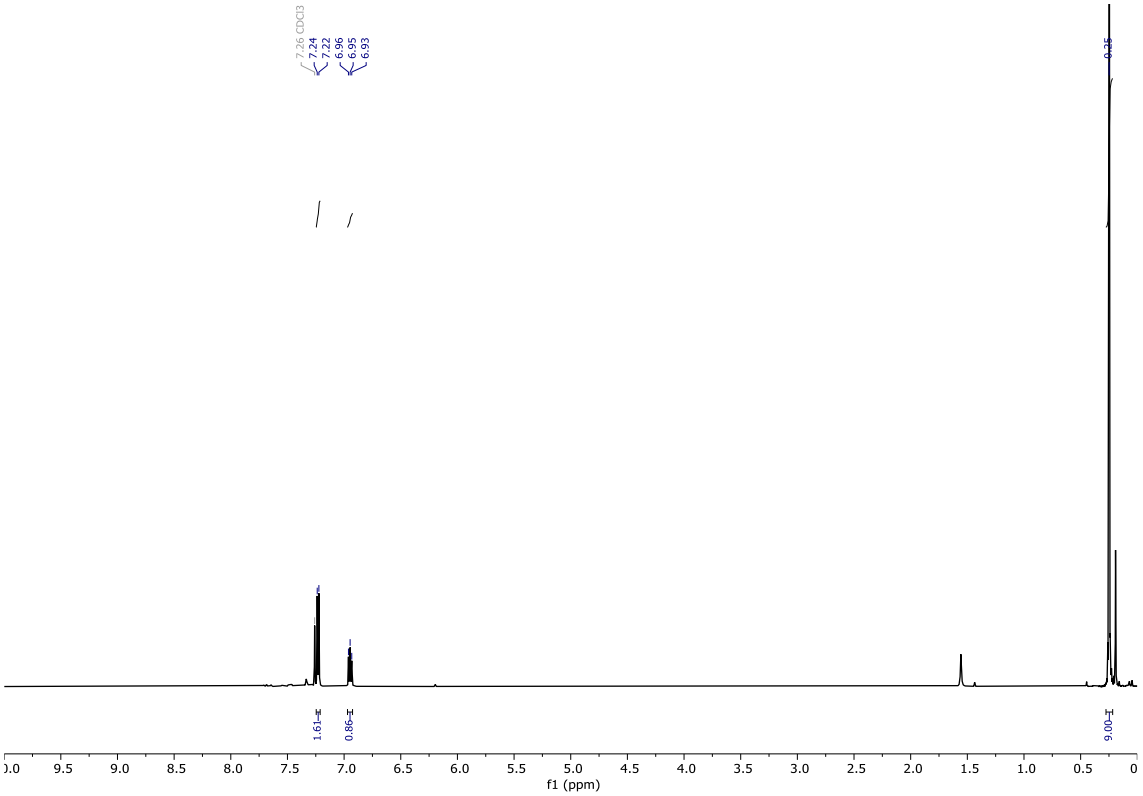


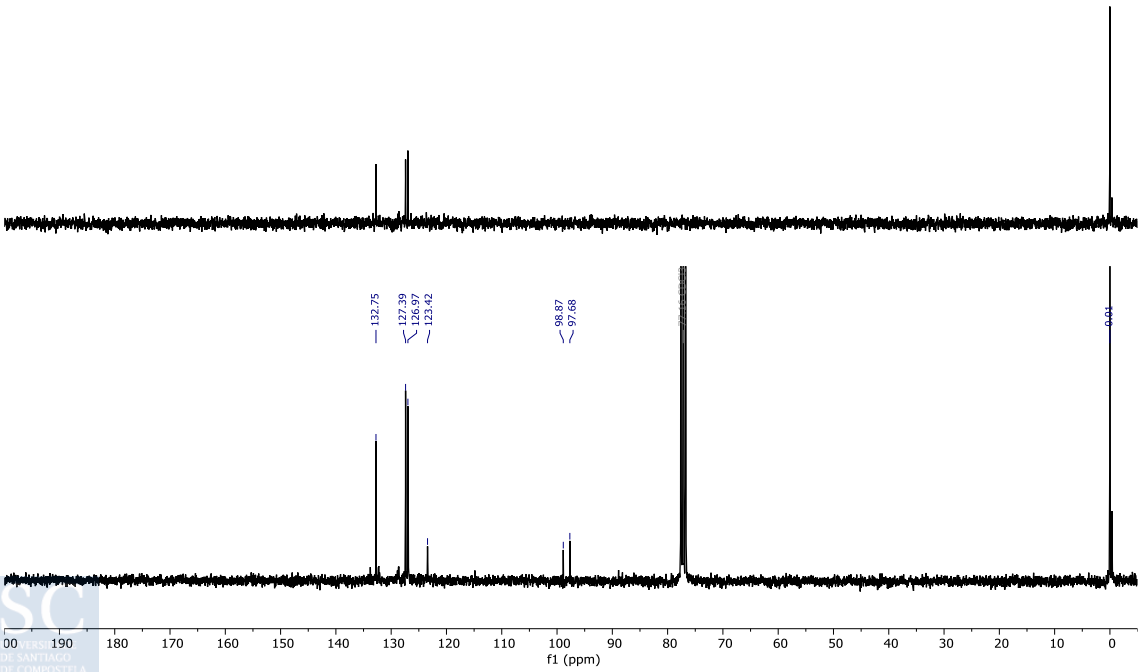


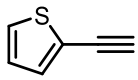


S51

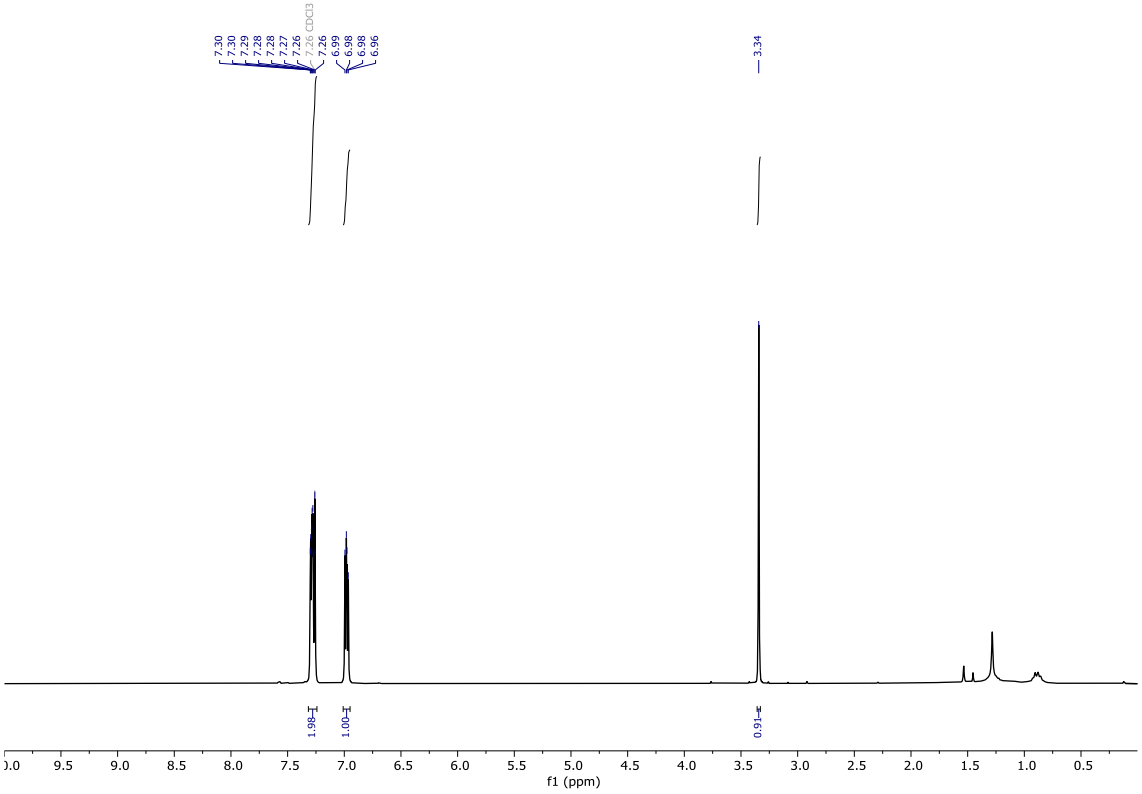
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

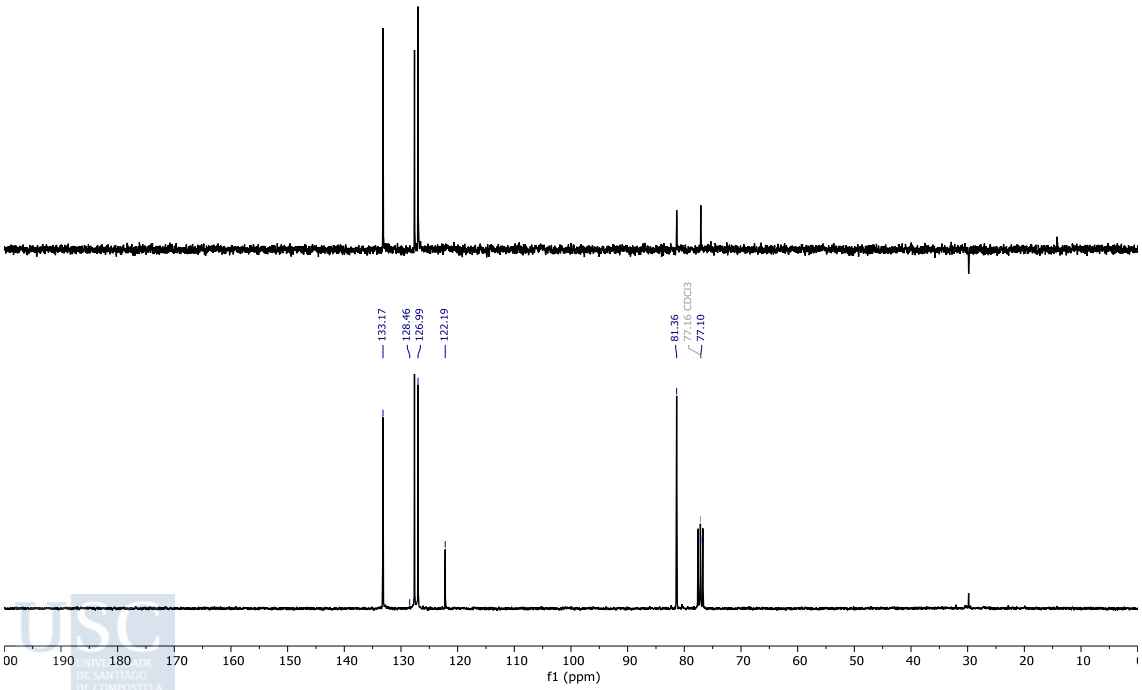


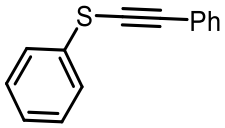




2k ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

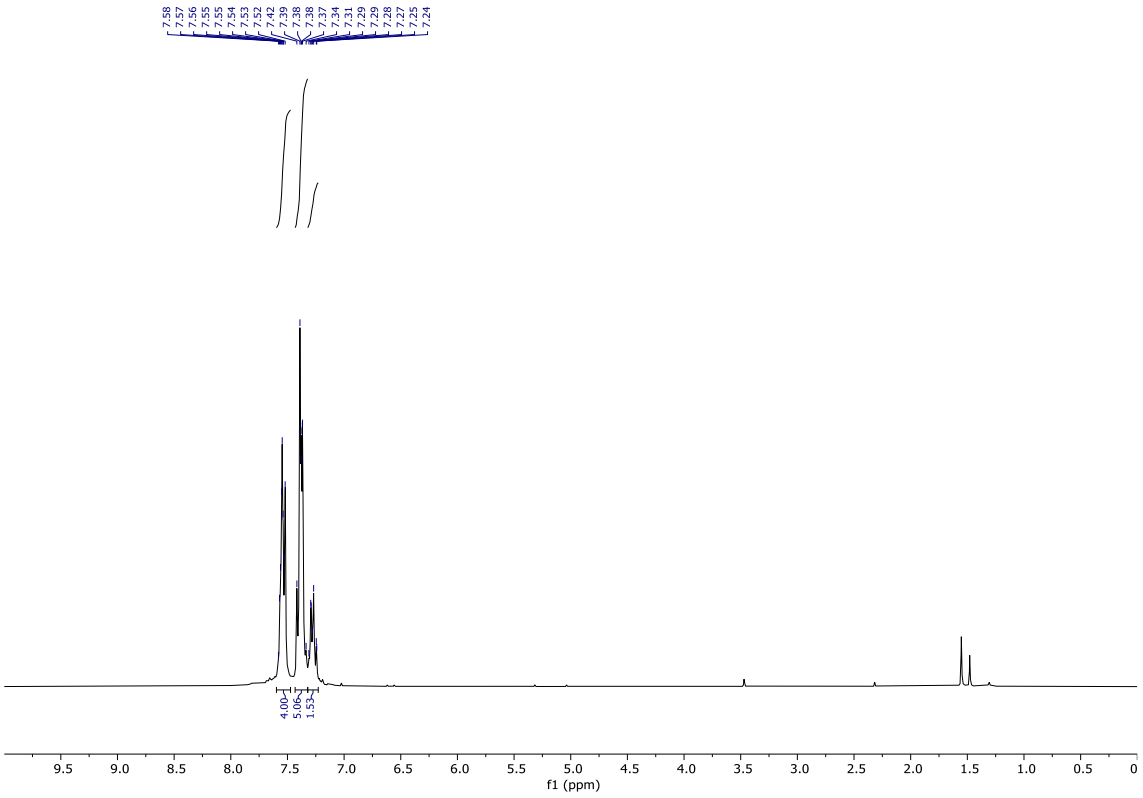


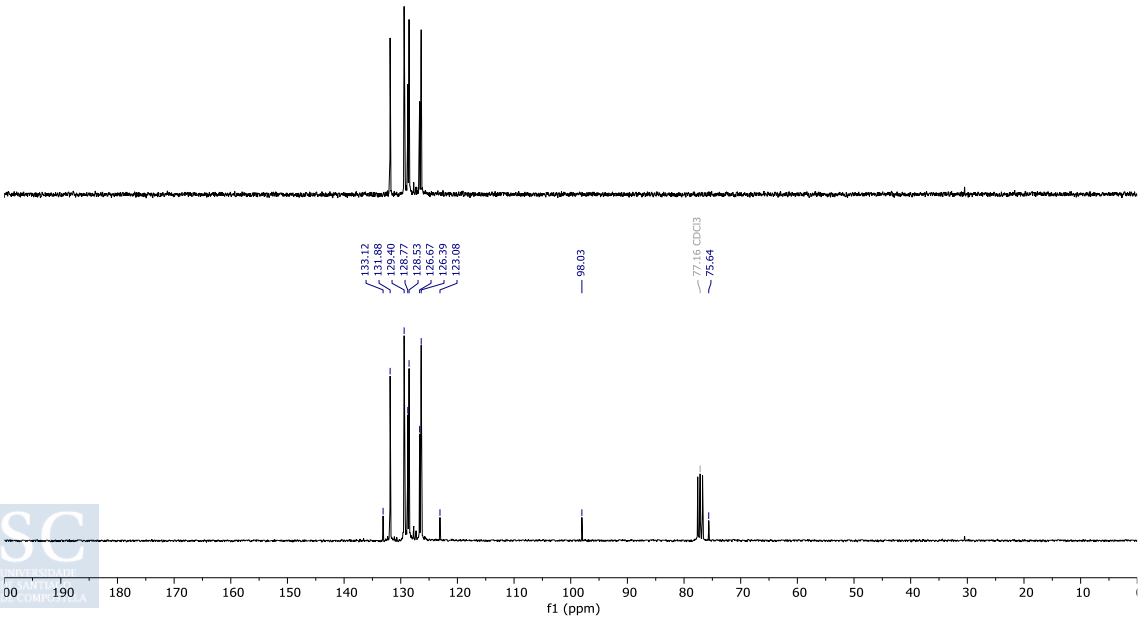


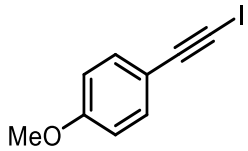


2m

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

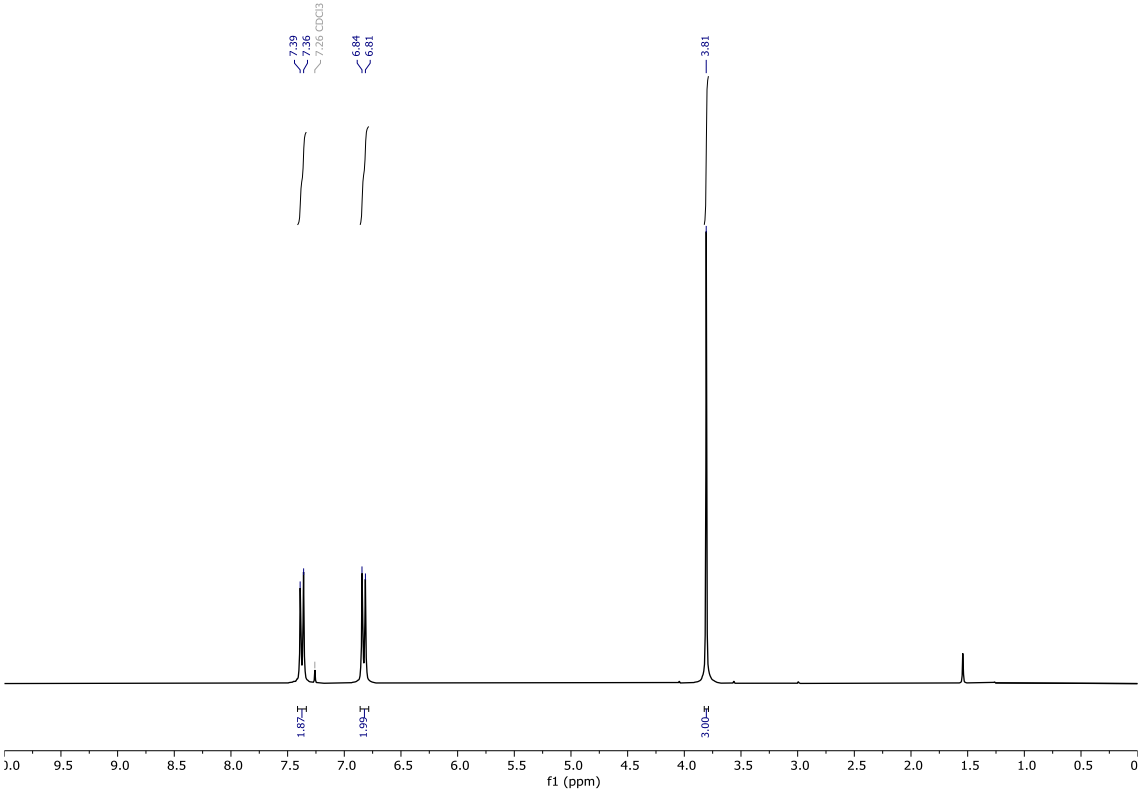


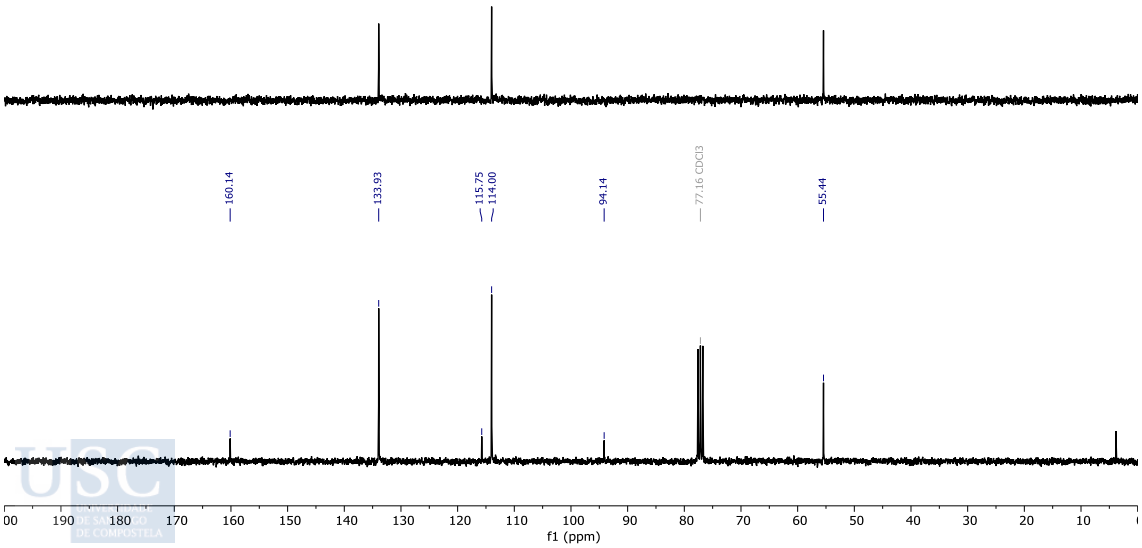


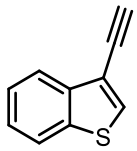


2p

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

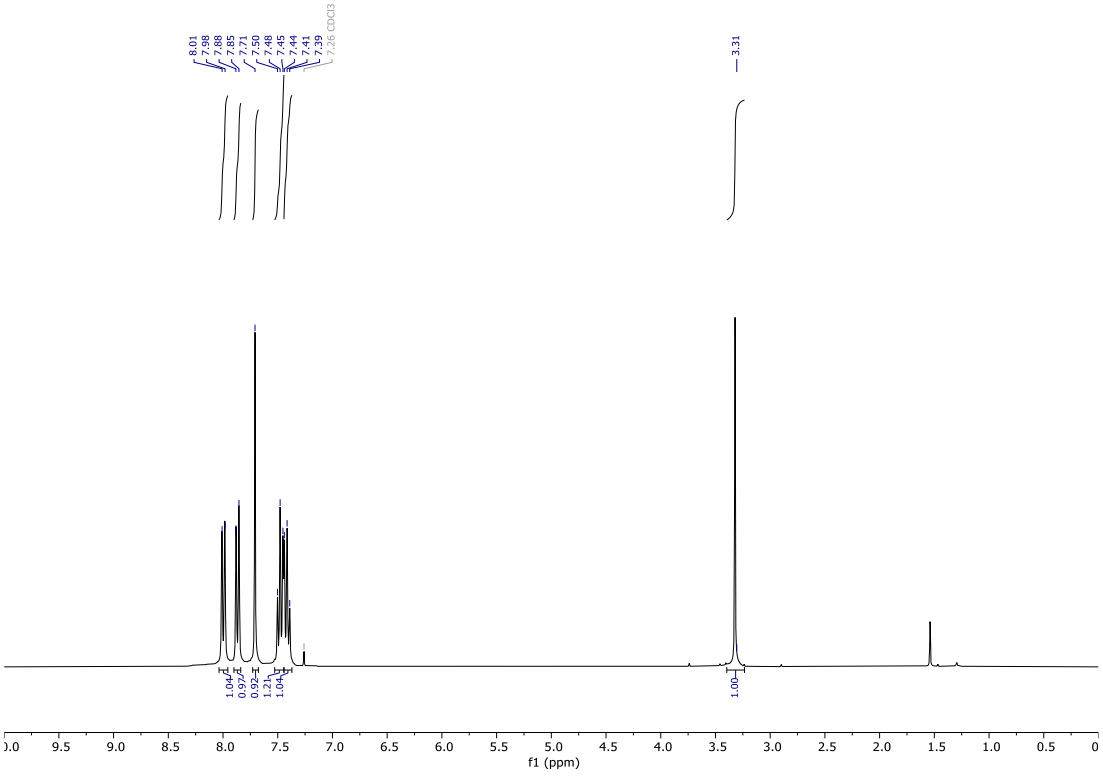


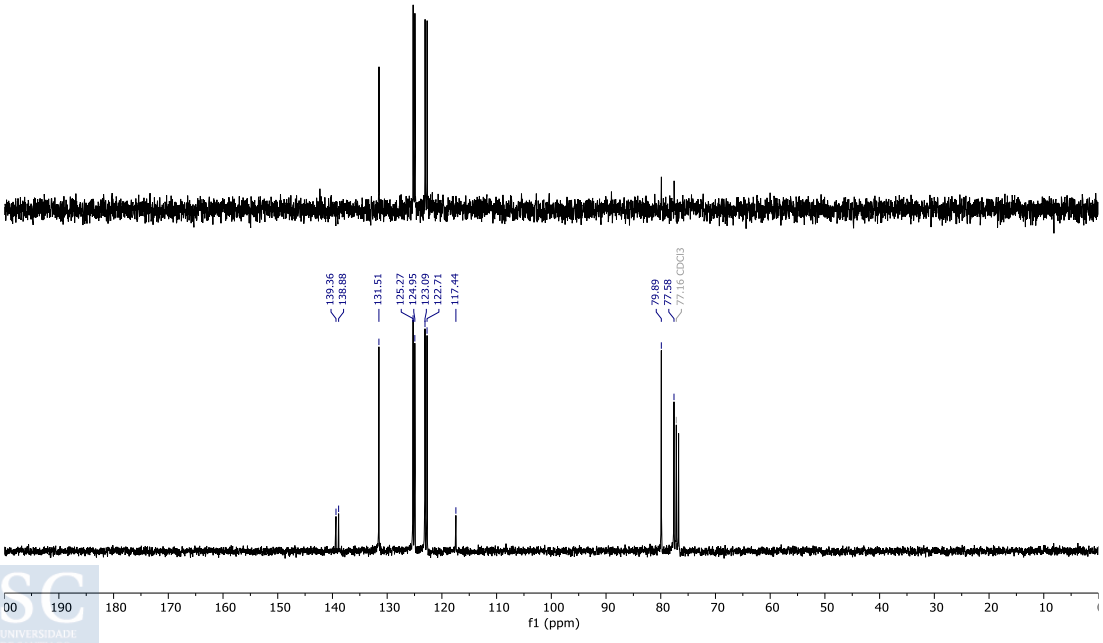


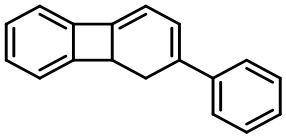


2r

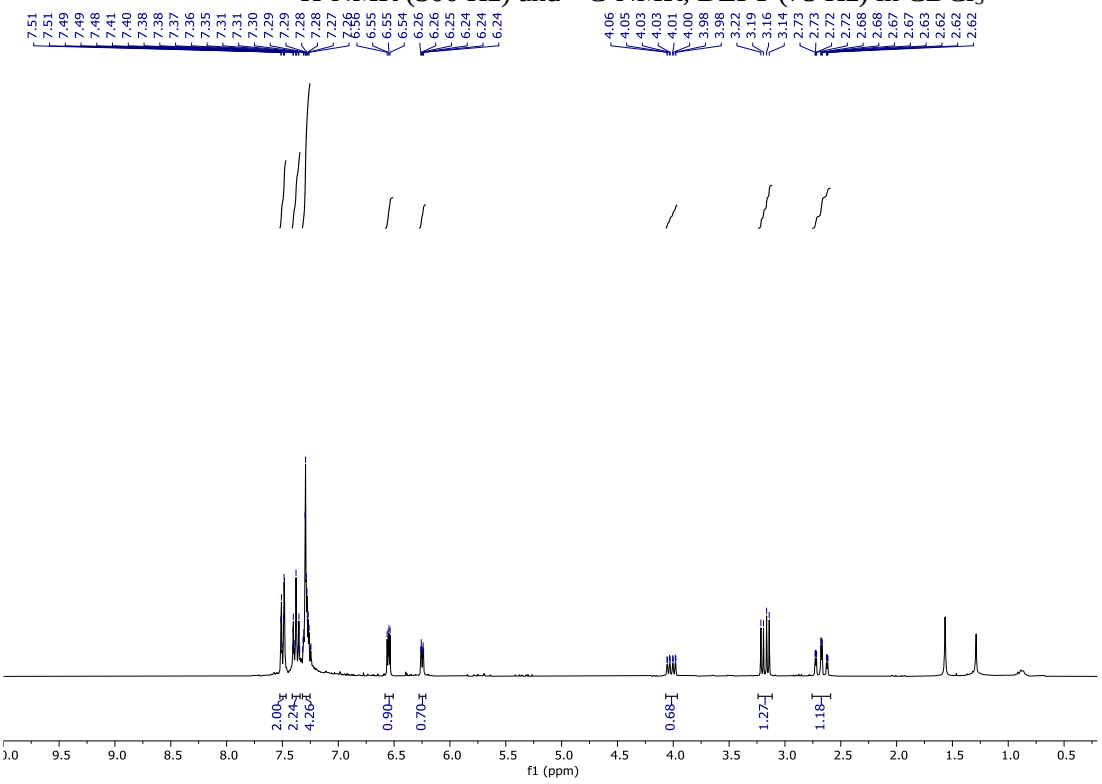
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

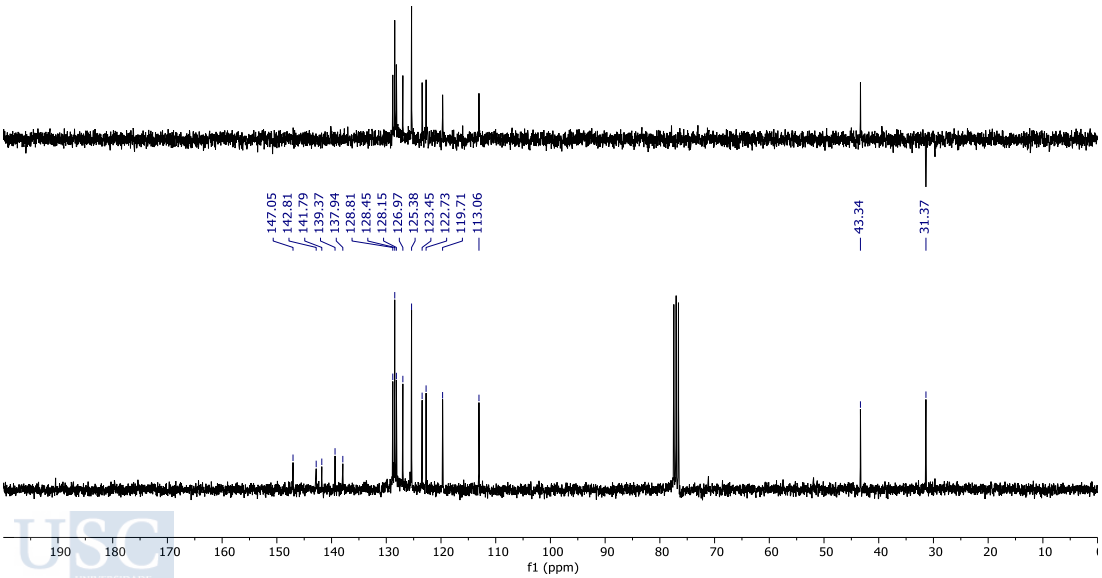


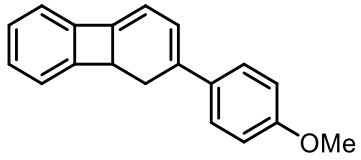




3aa ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

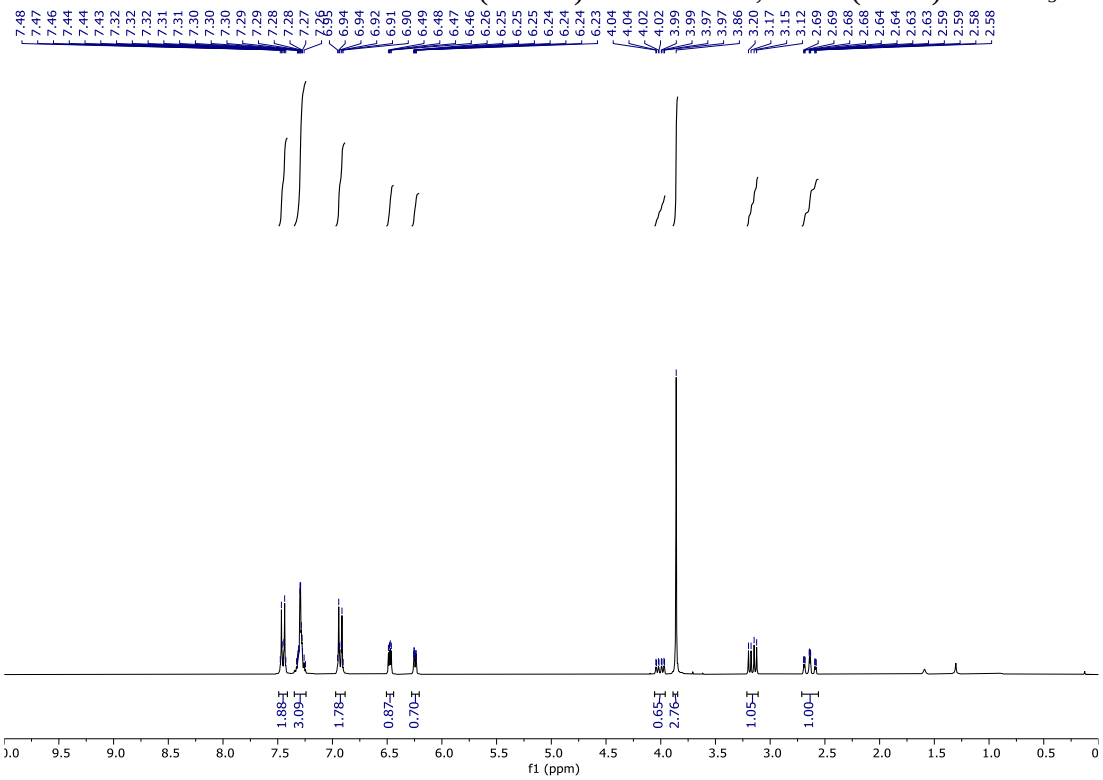


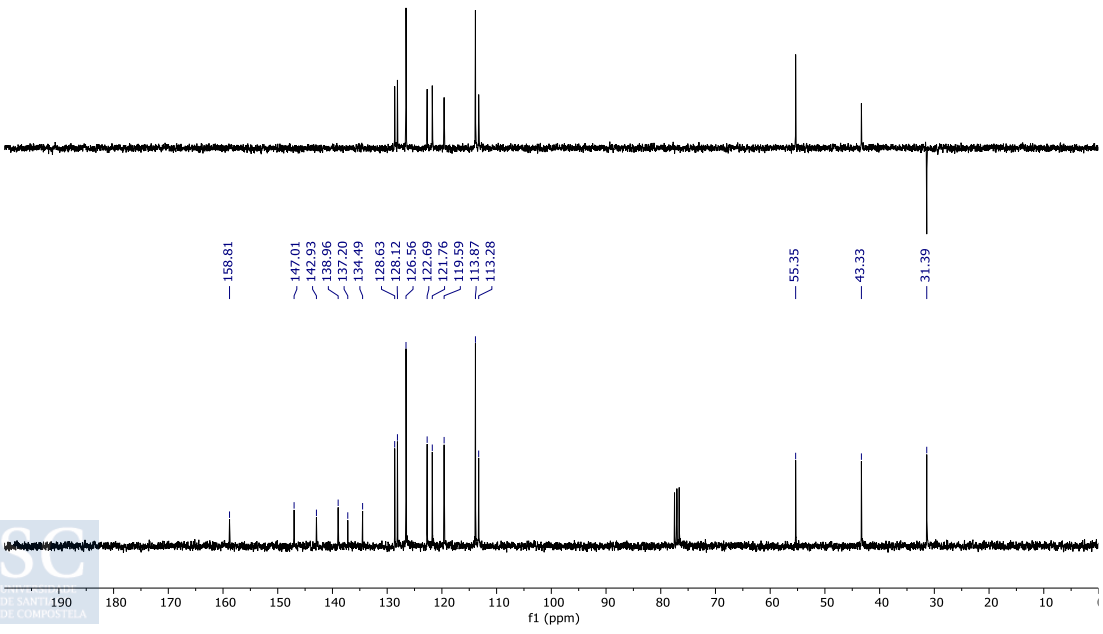


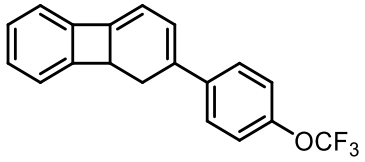


3ab

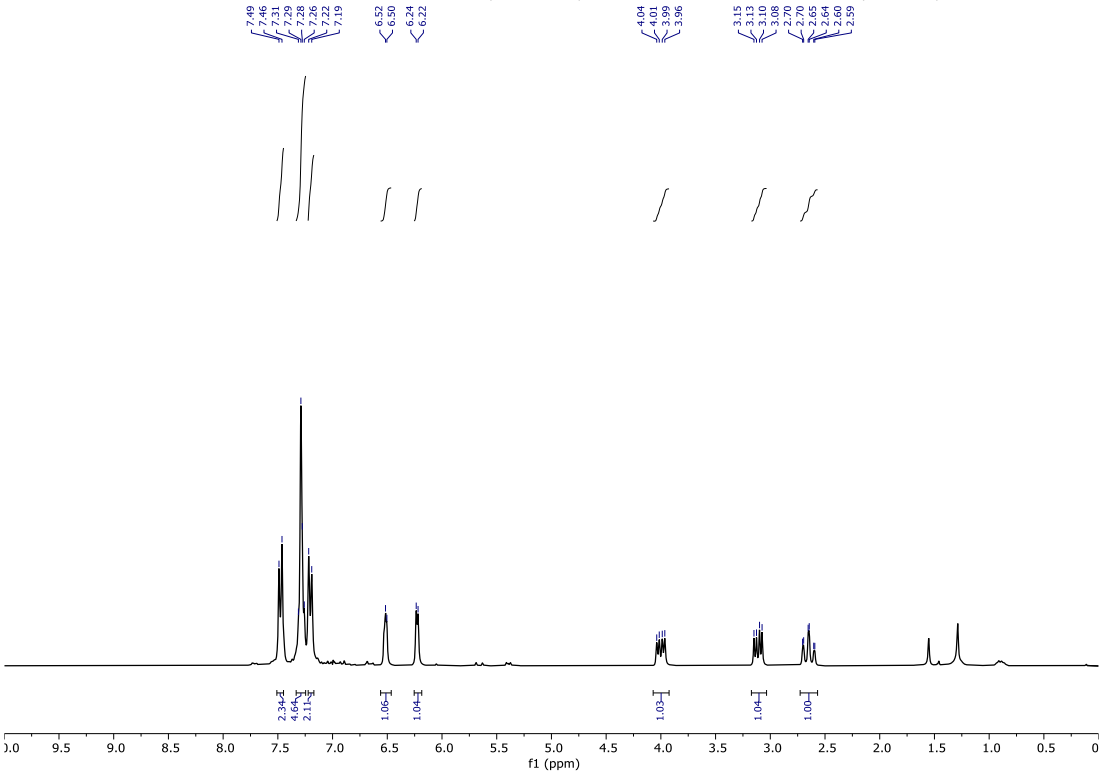
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

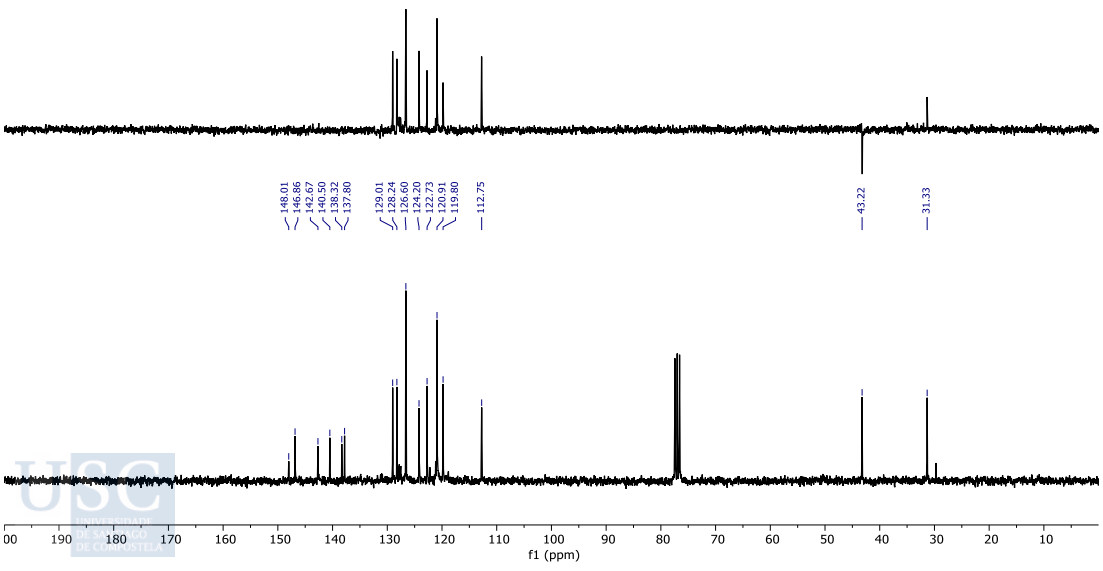


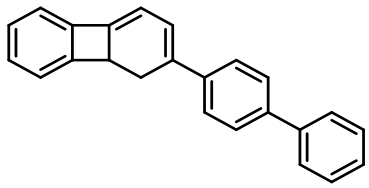




3ac ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

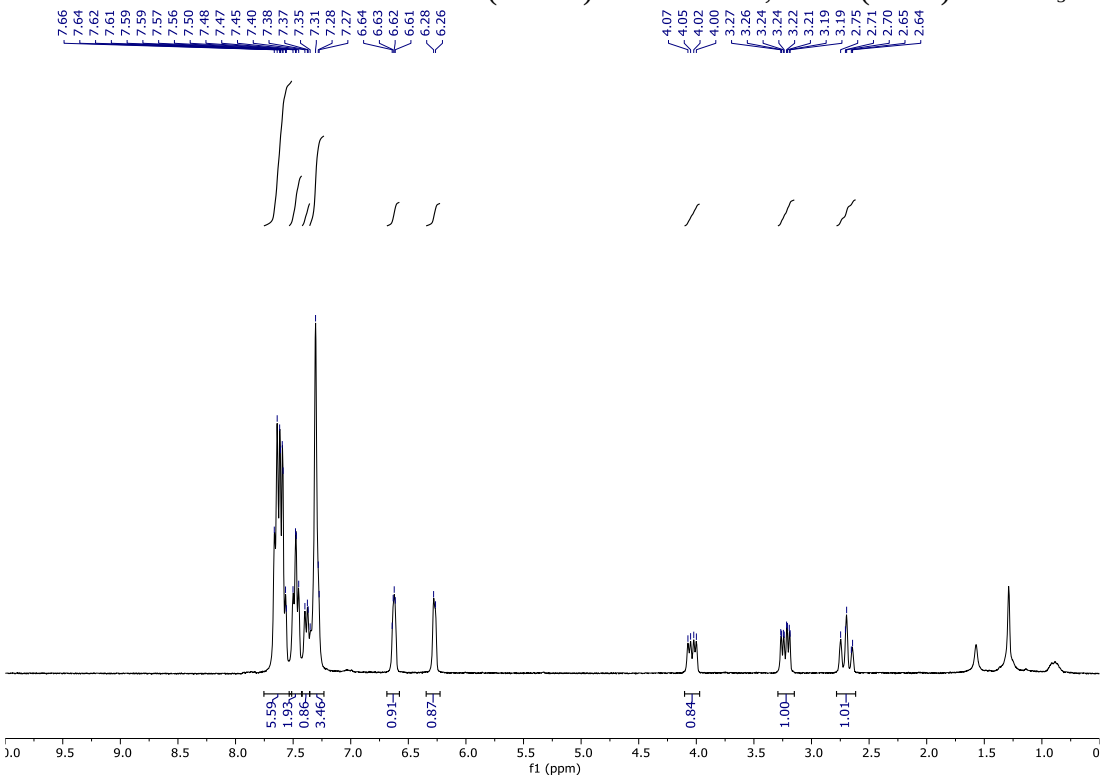


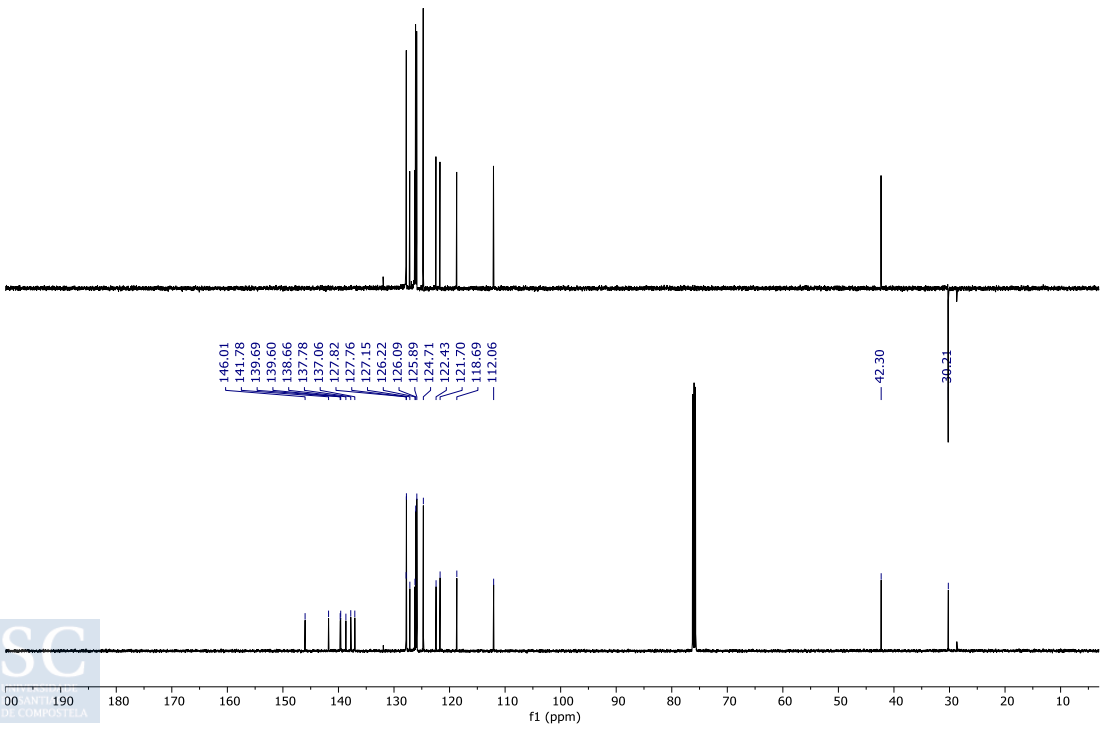


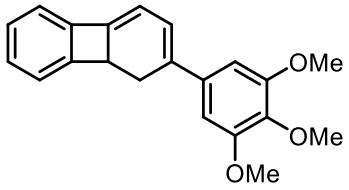


3af

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

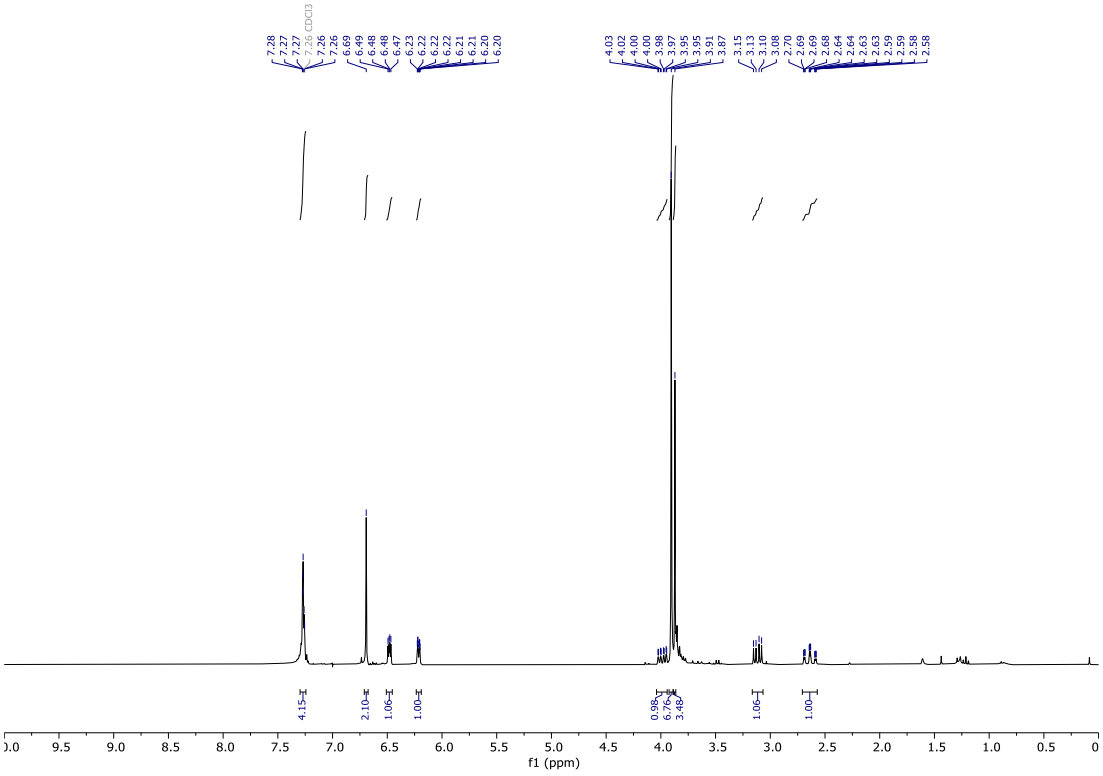


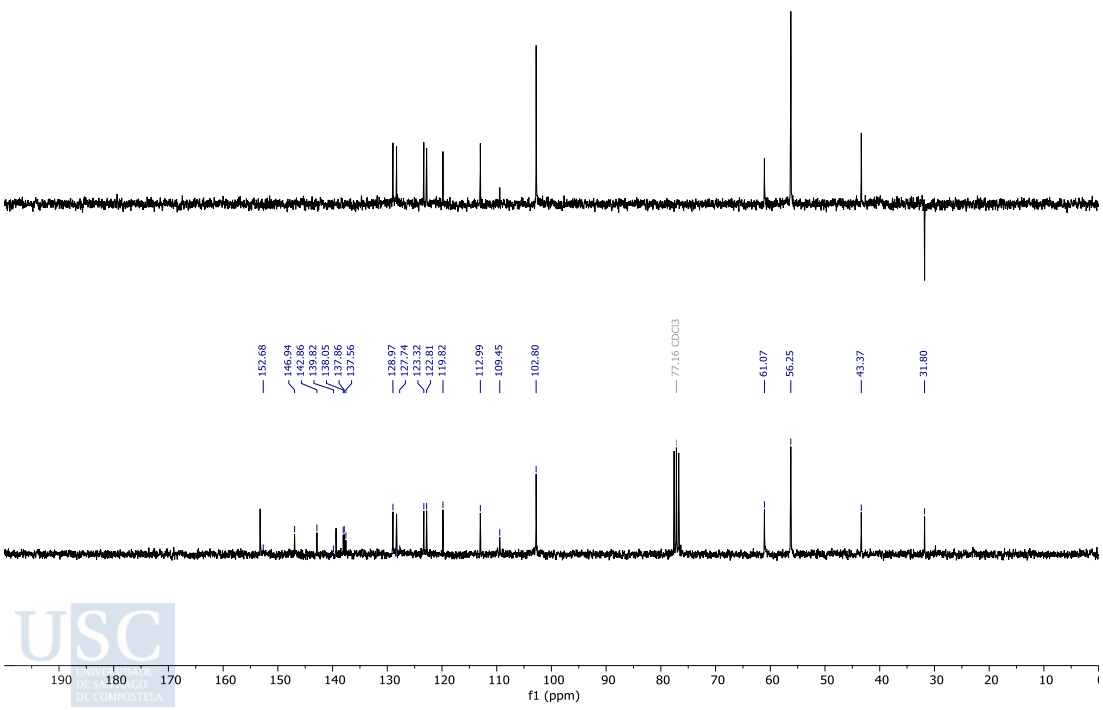


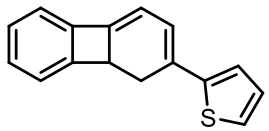


3aj

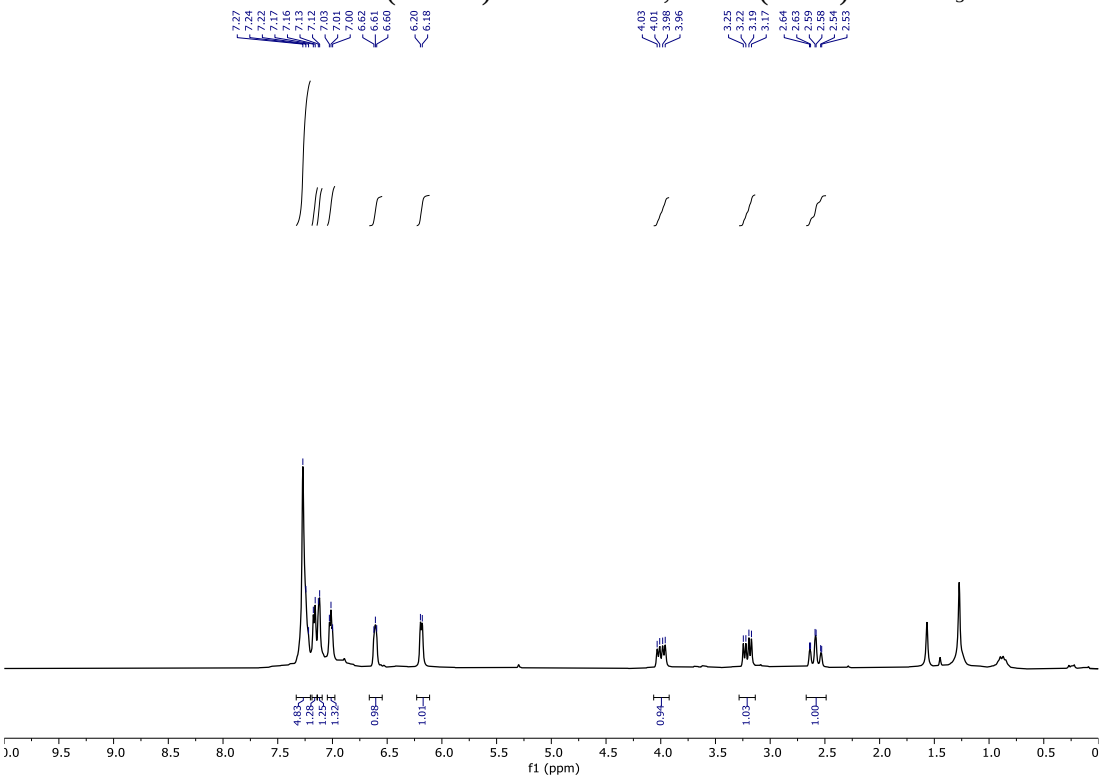
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

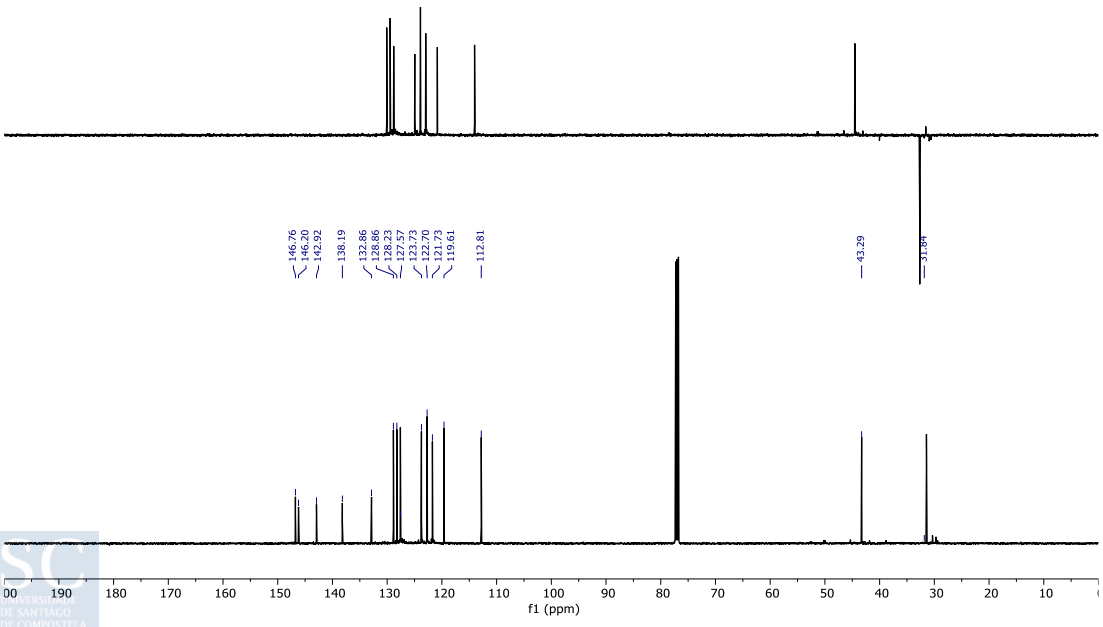


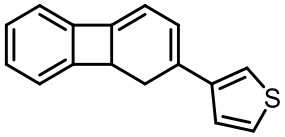




3ak ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

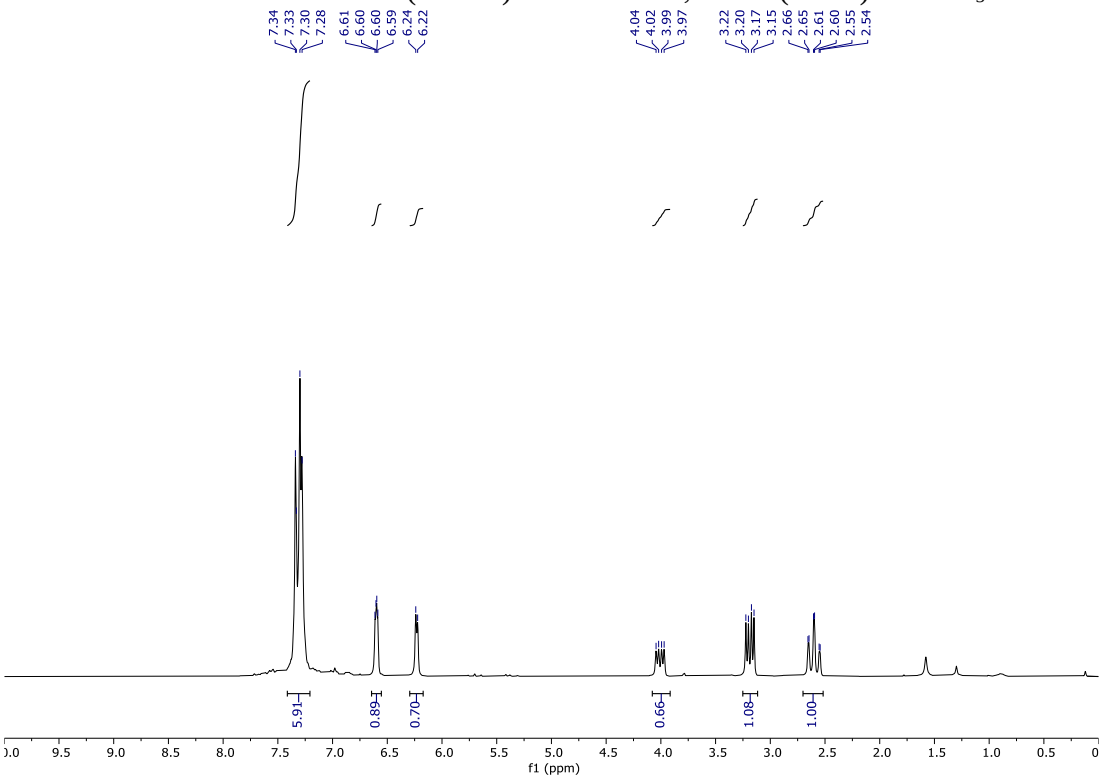


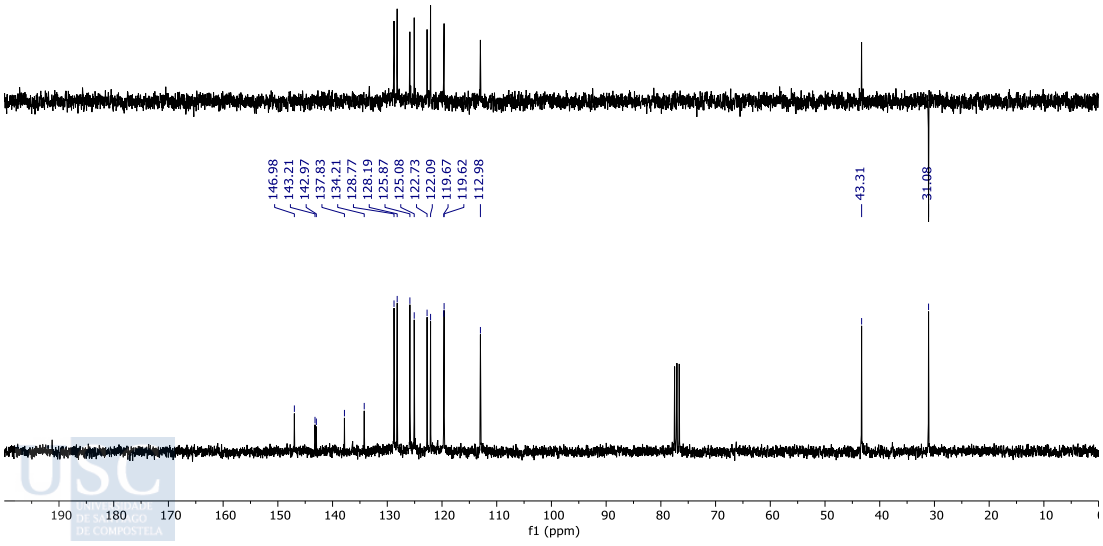


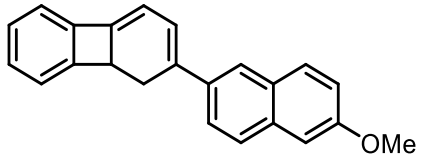


3aq

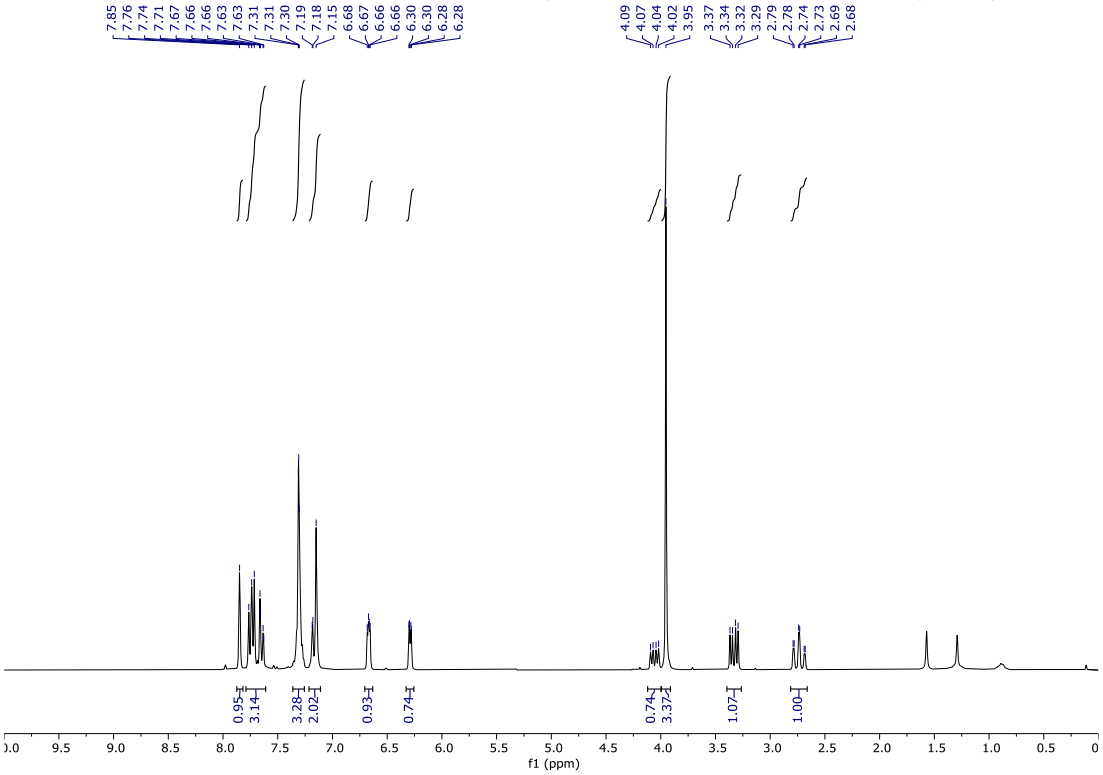
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

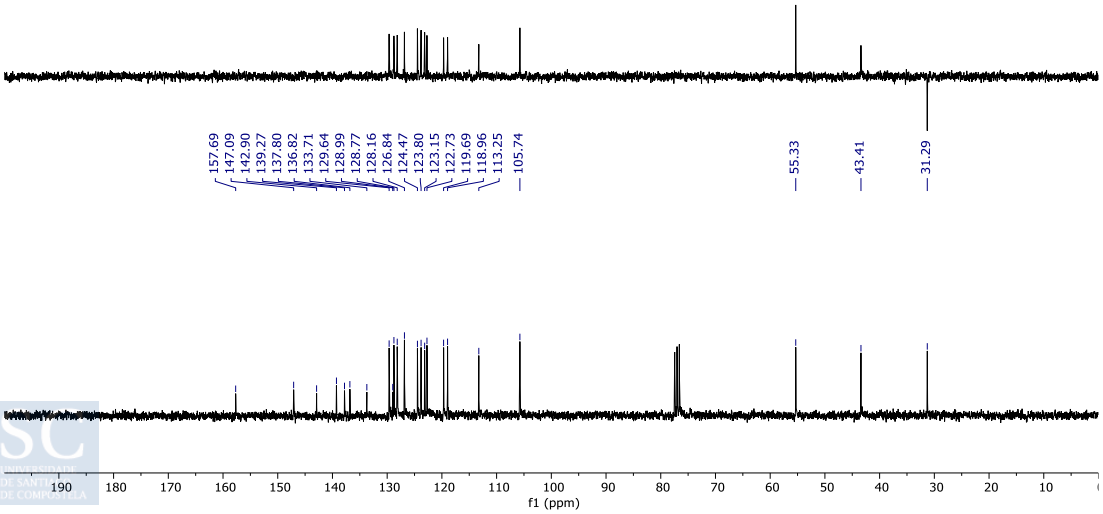


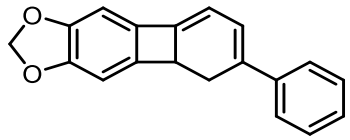




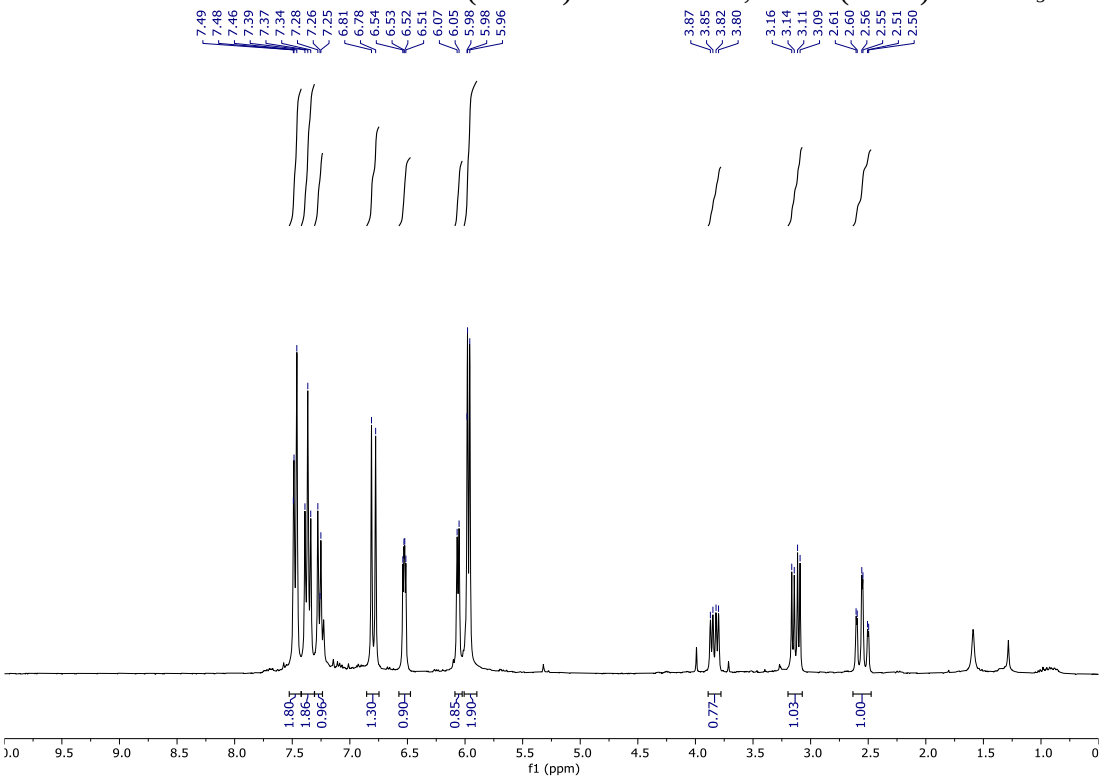
3at ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

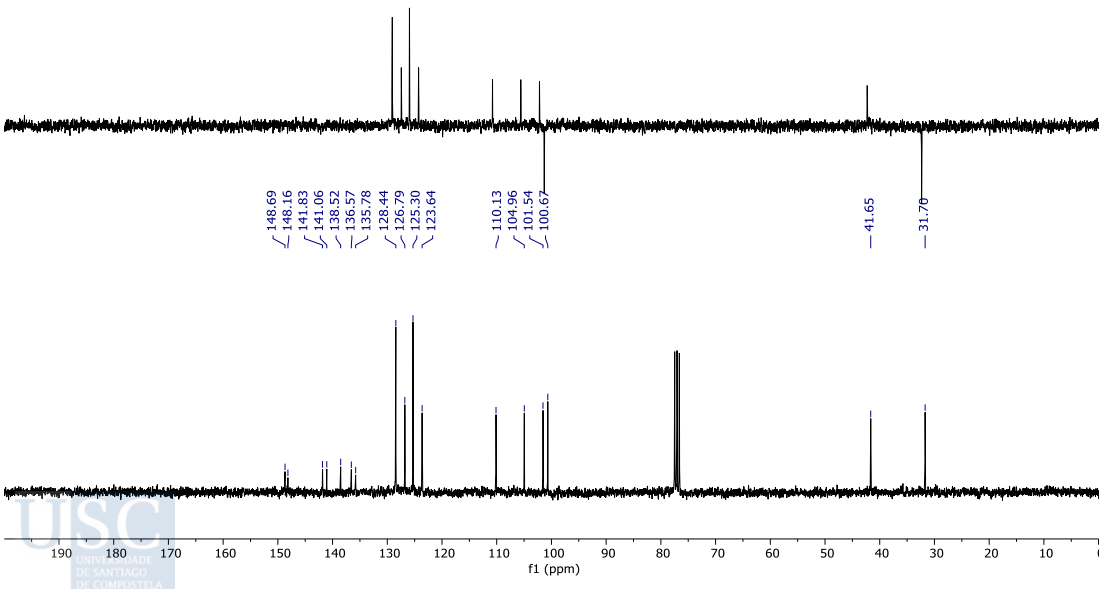


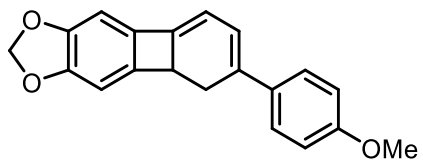




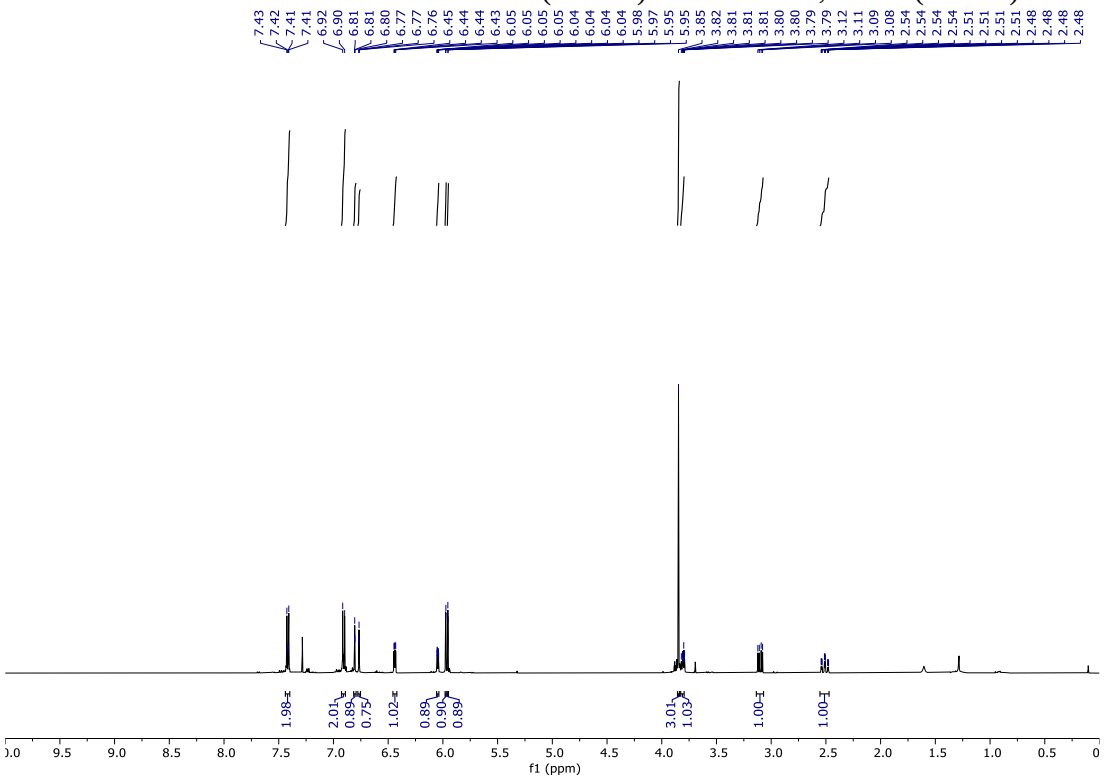
3ba ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

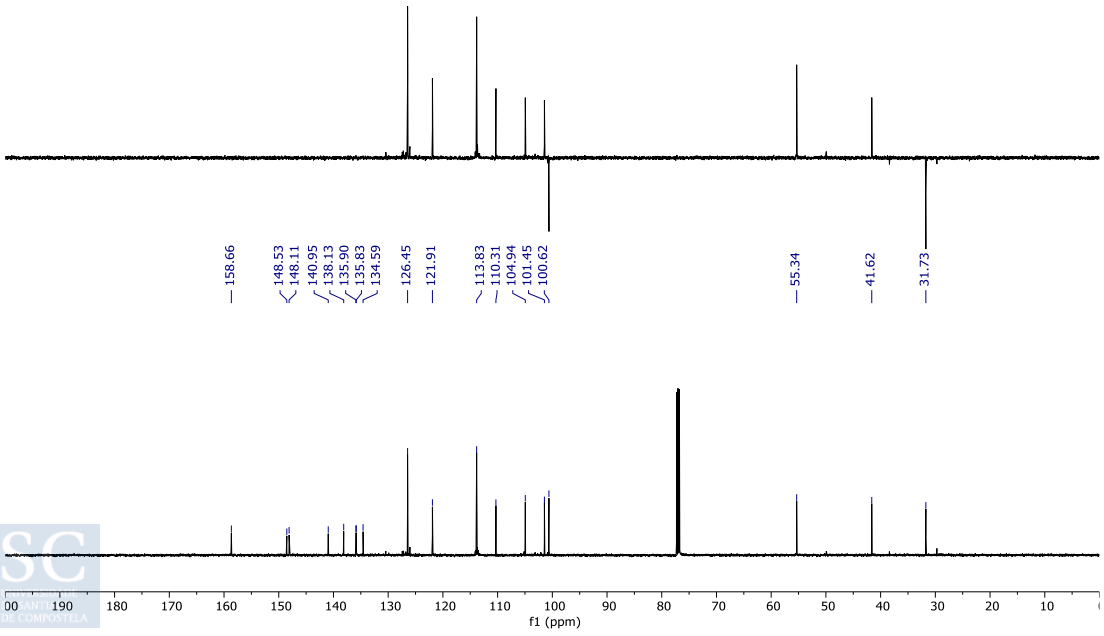


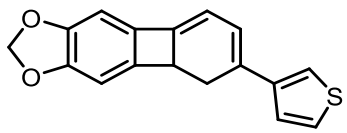




3bb ^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

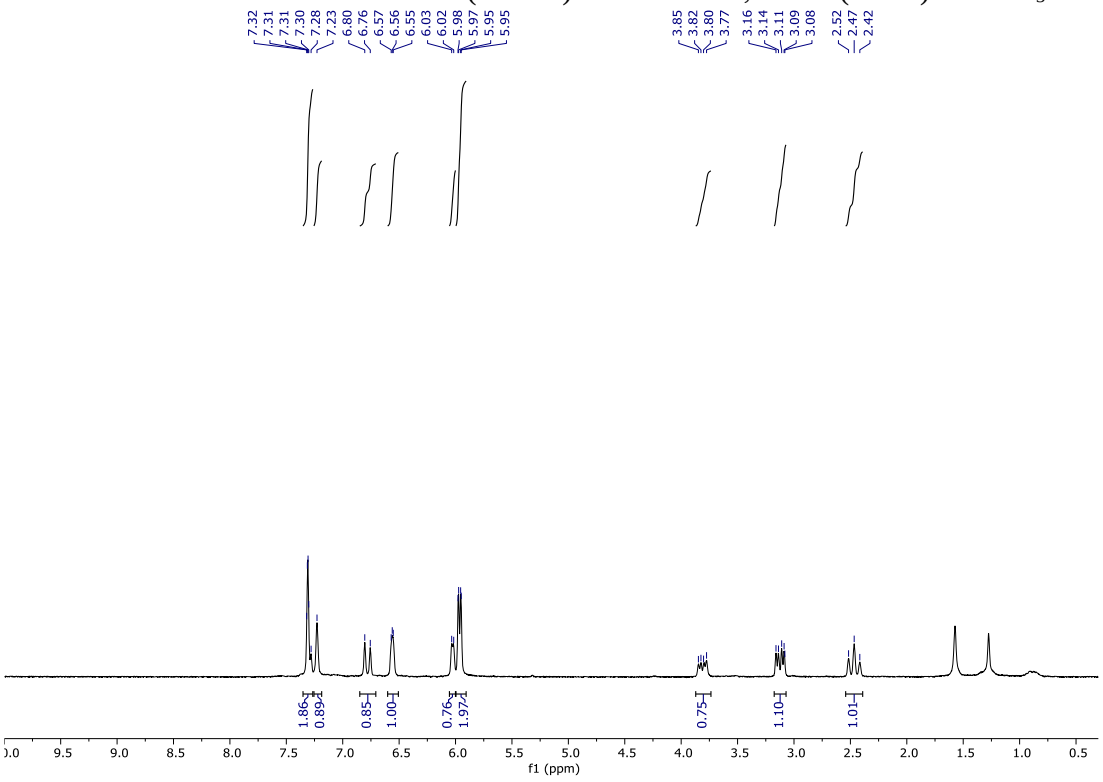


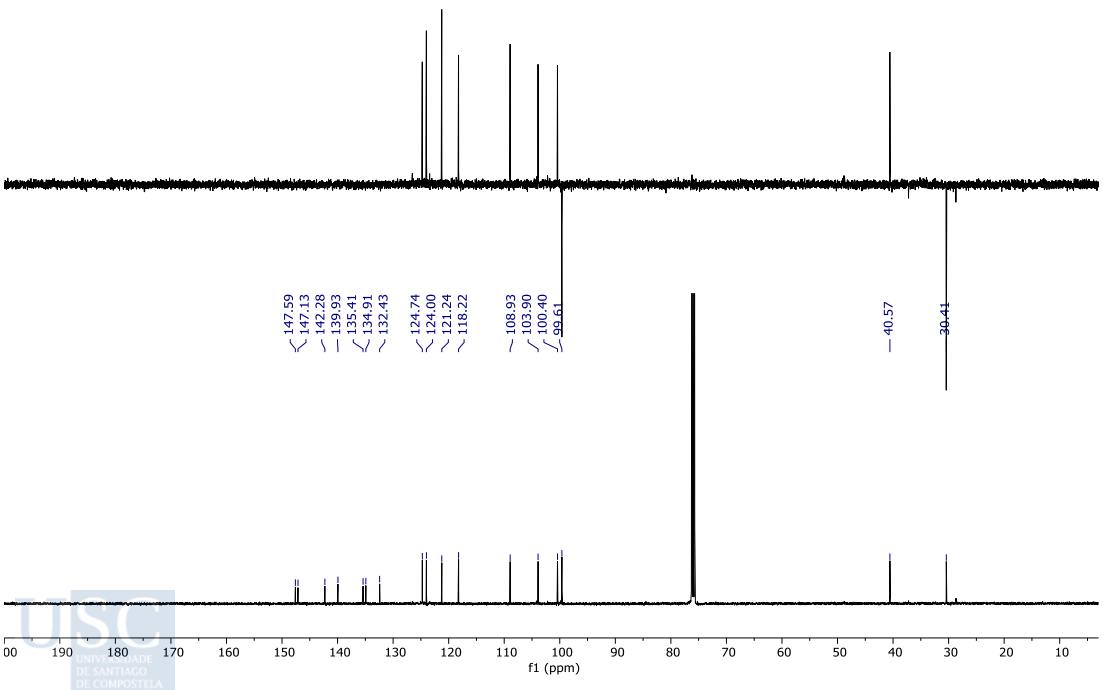


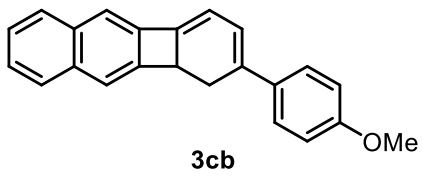


3bq

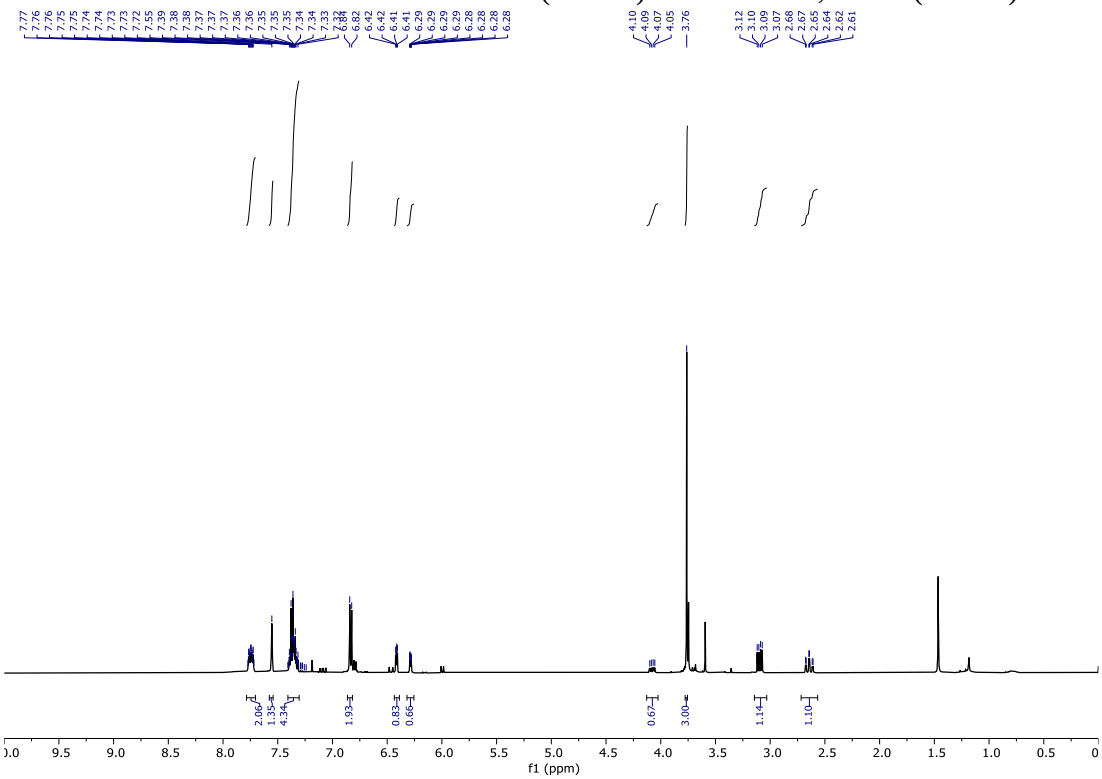
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

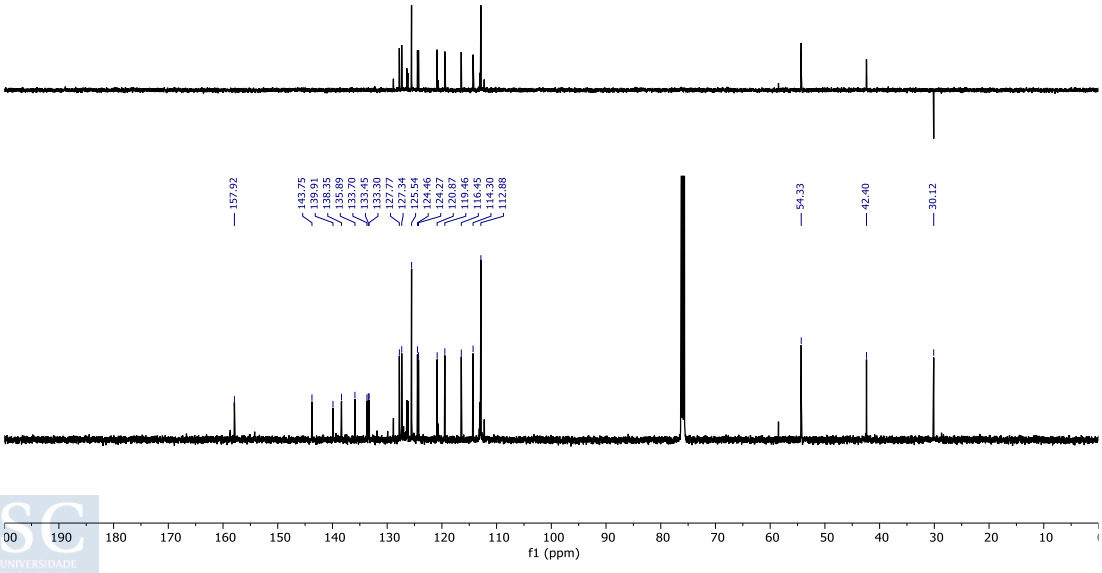


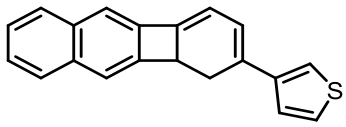




3cb ^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

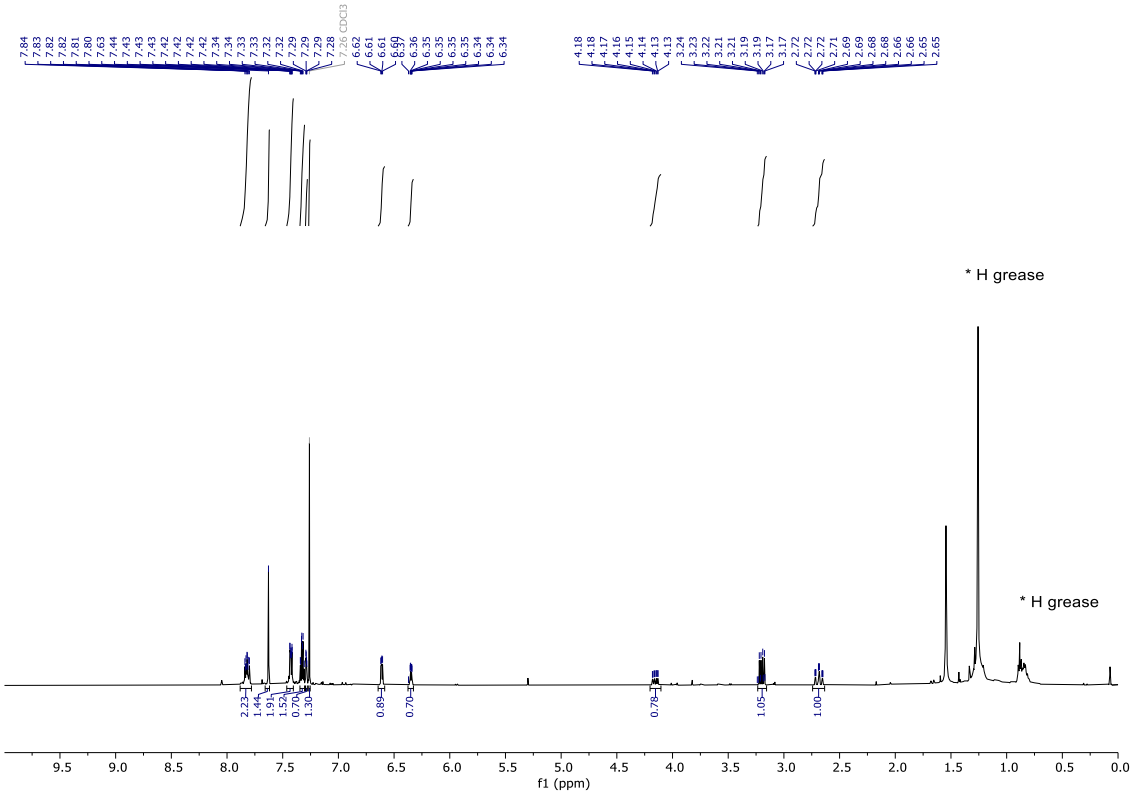


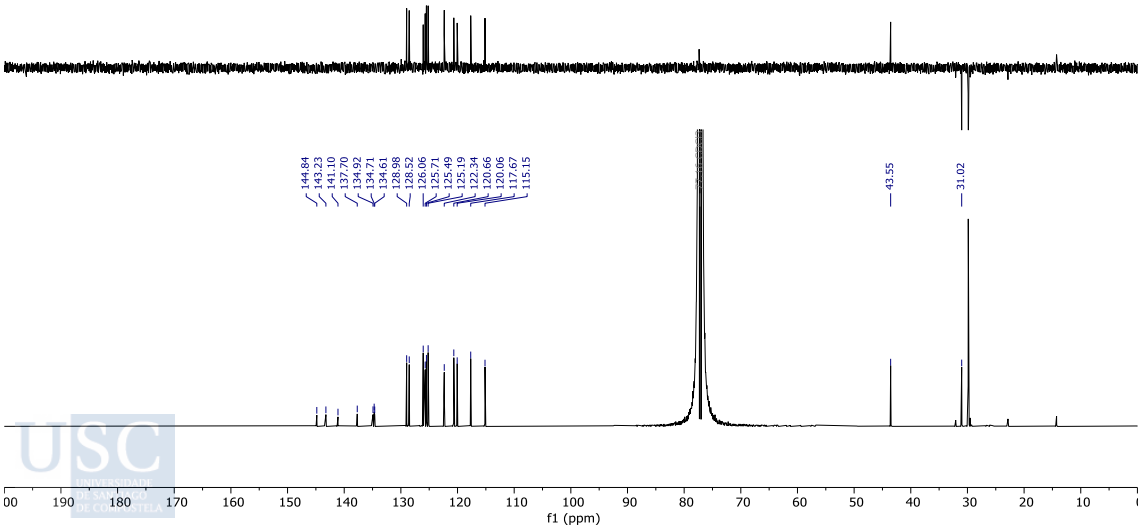


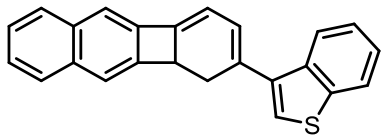


3cq

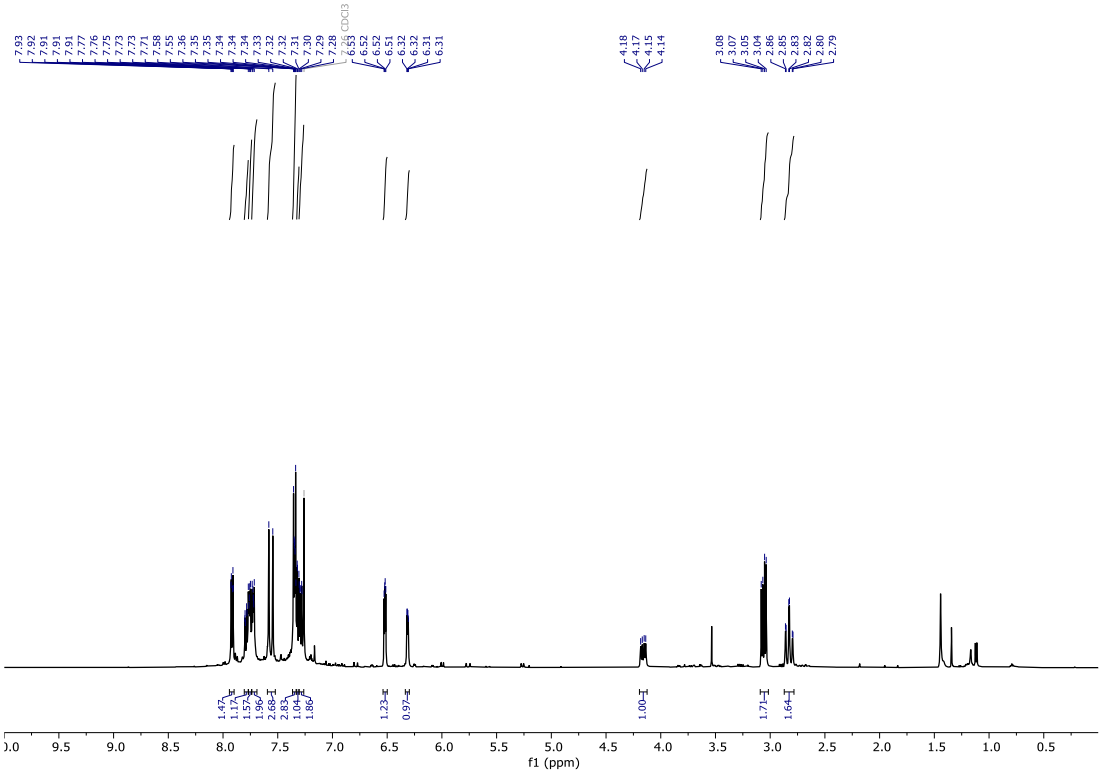
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

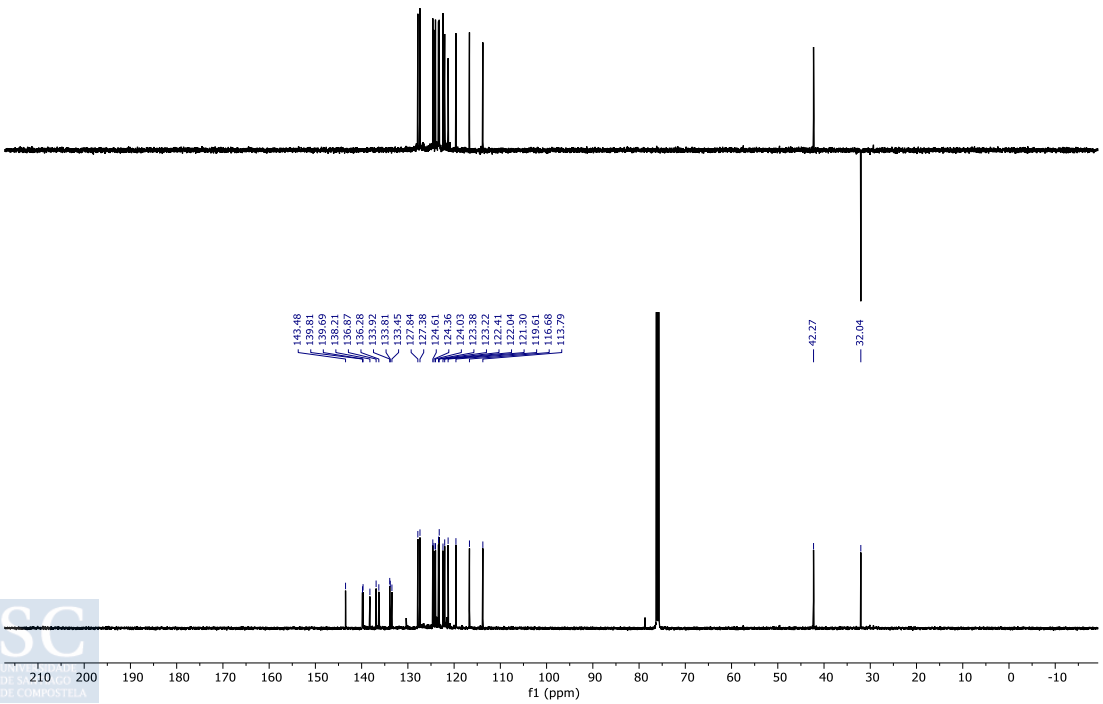


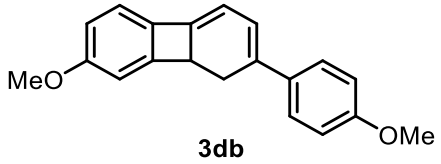




3cr ^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

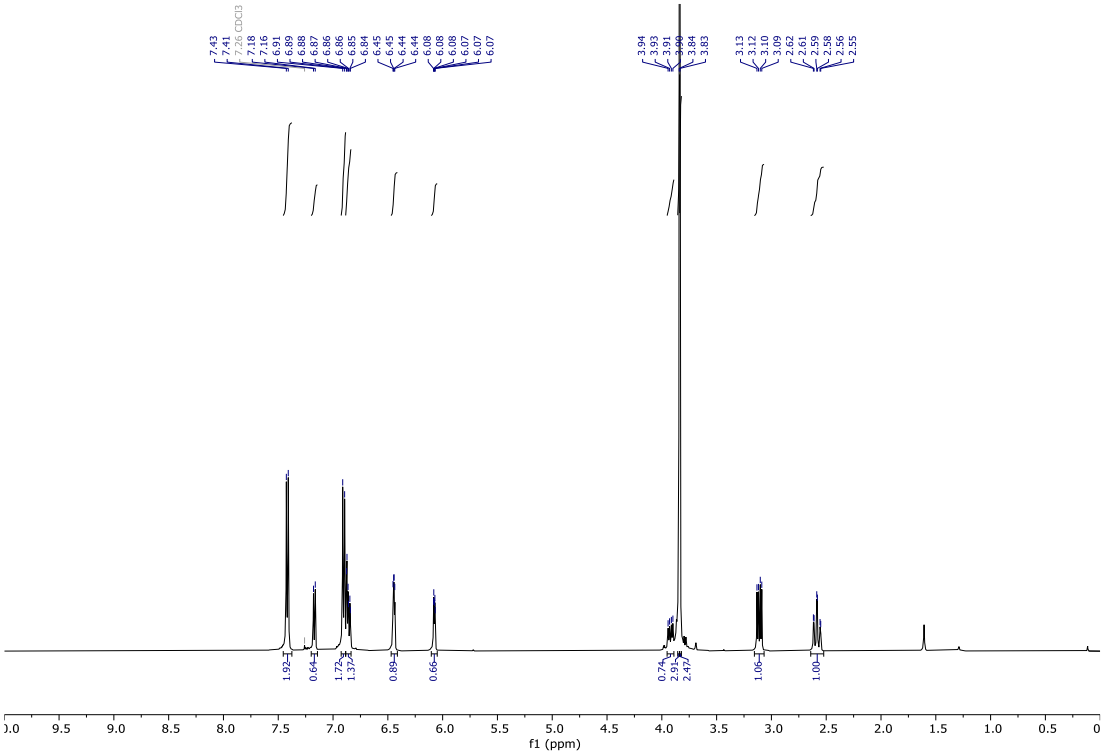


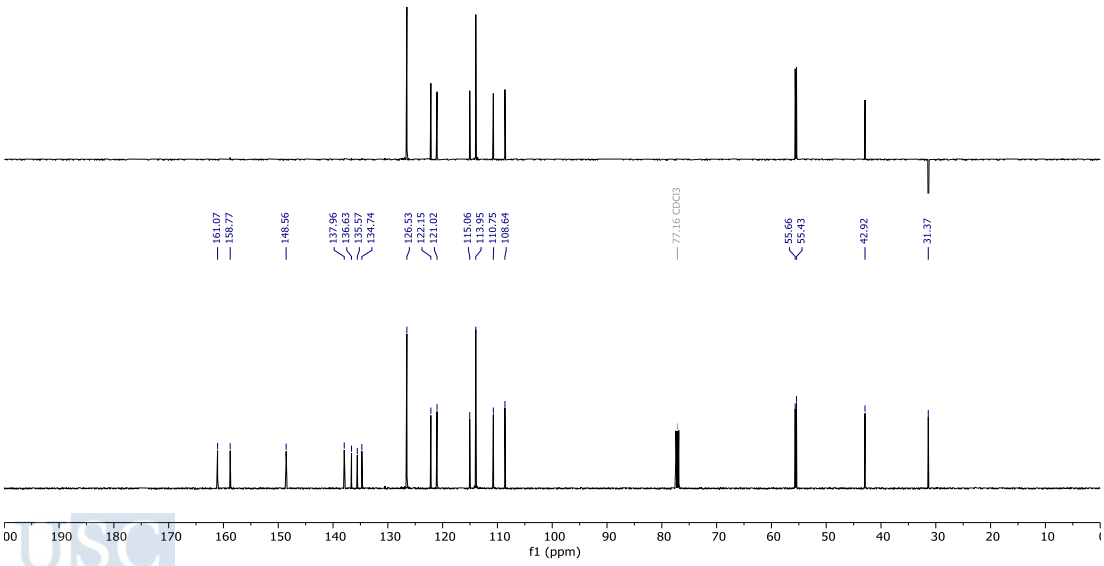


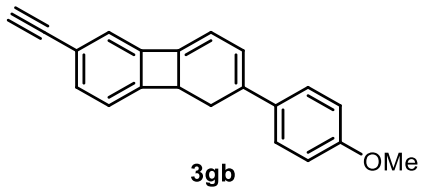


3db

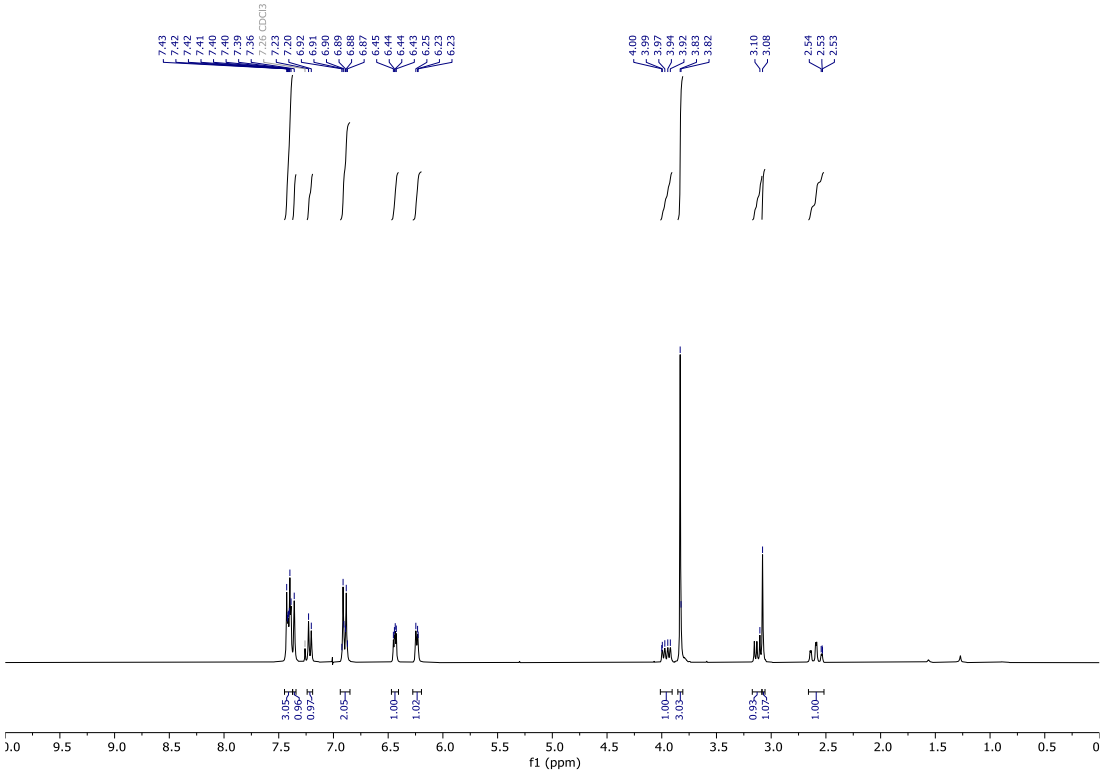
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

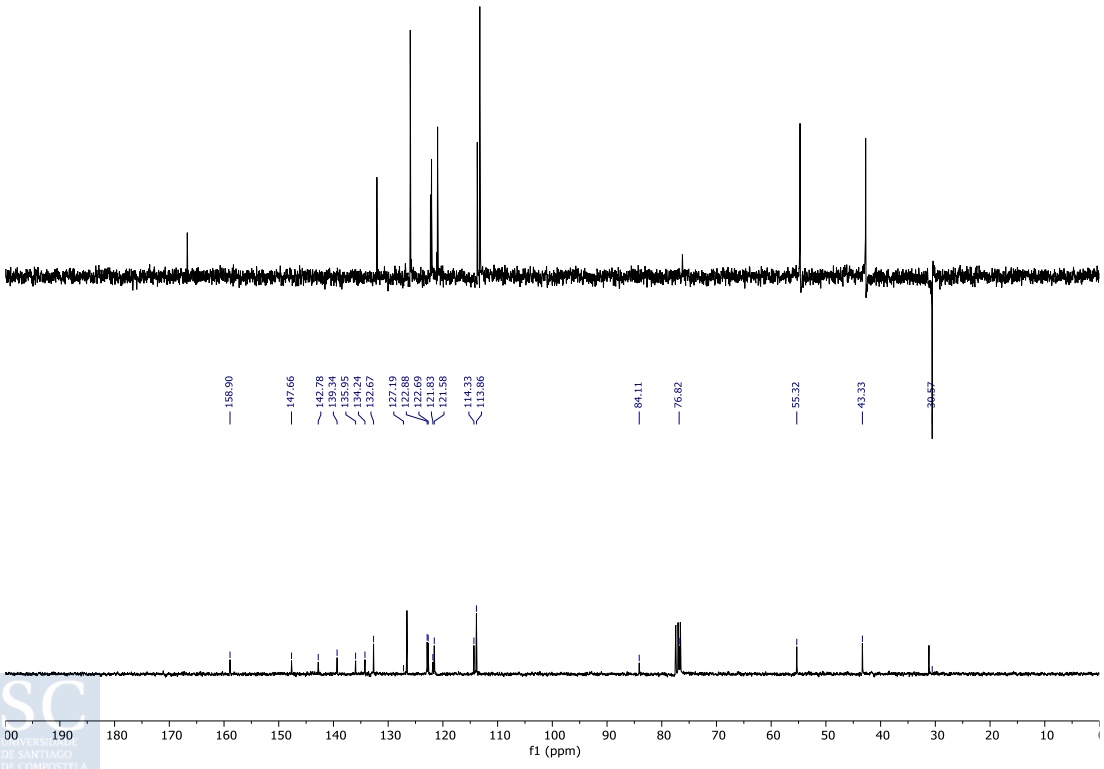


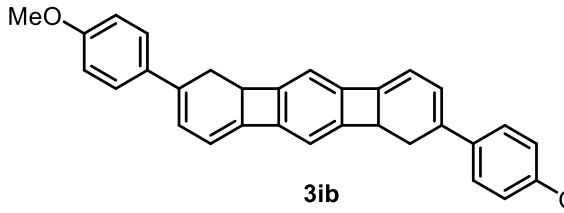




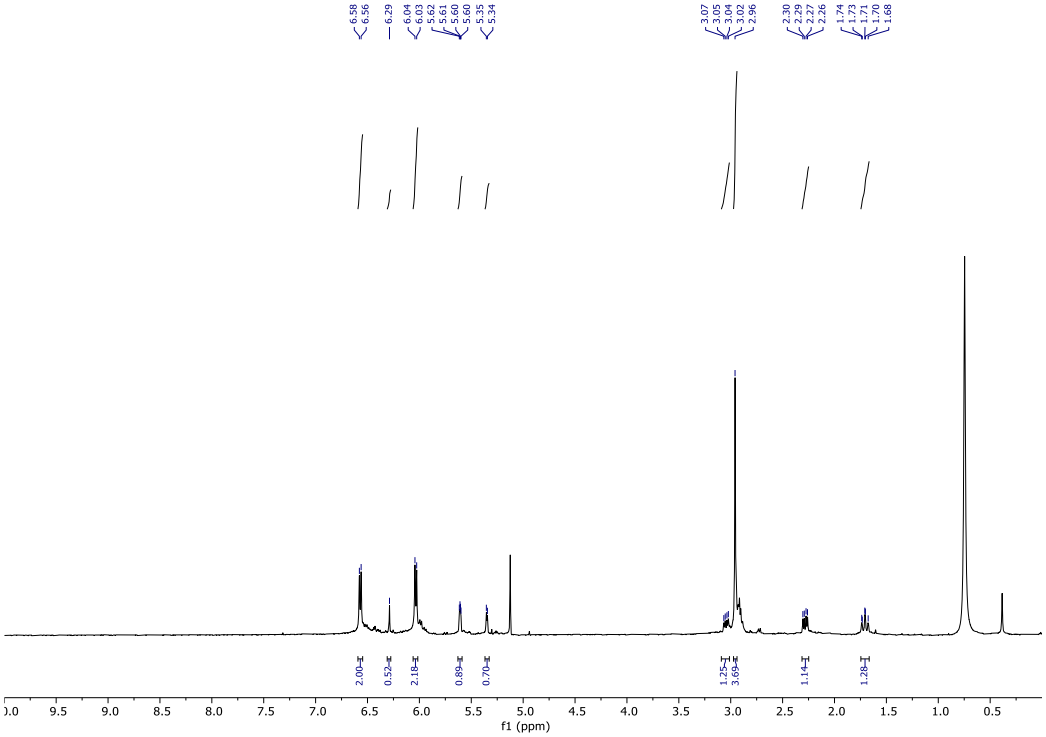
3gb ^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

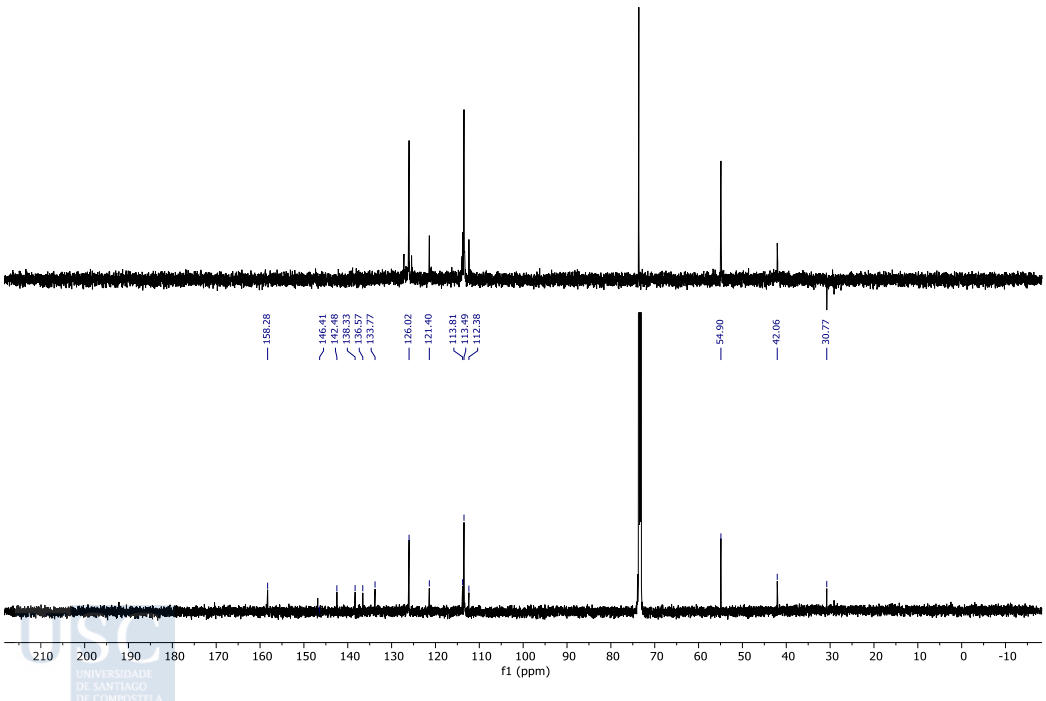


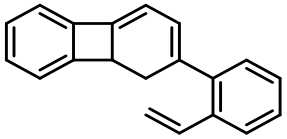




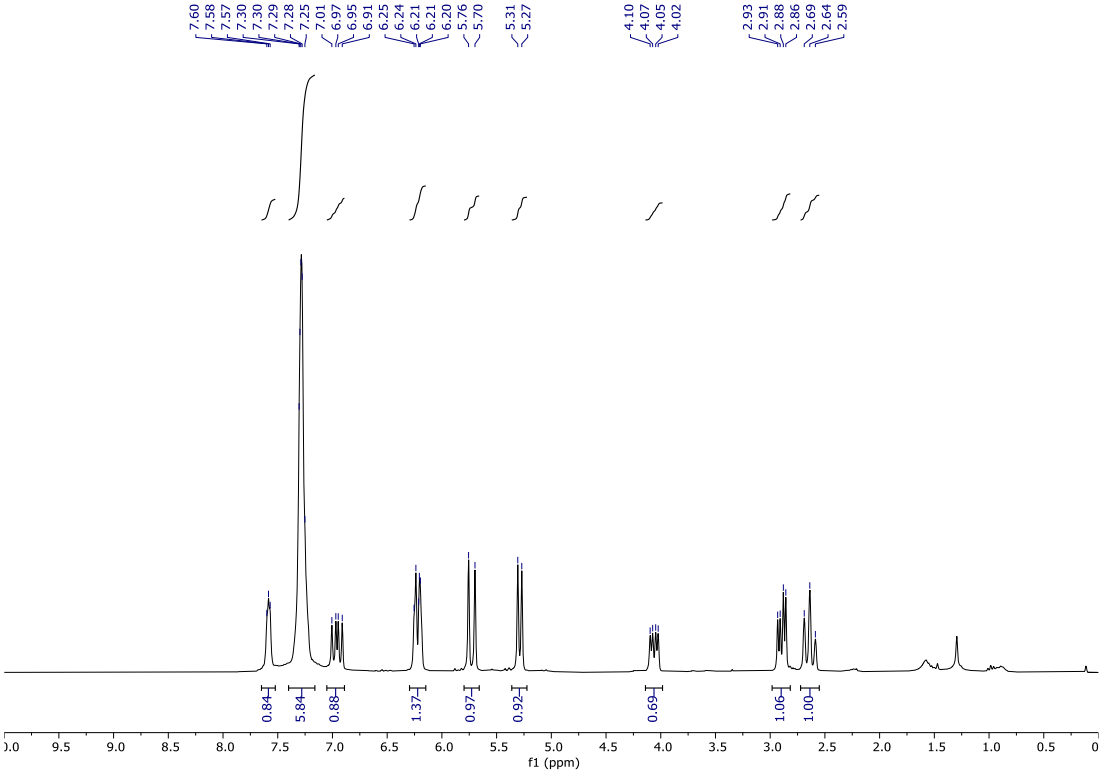
3ib ^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in 1,1,2,2-tetrachloroethane-d_2

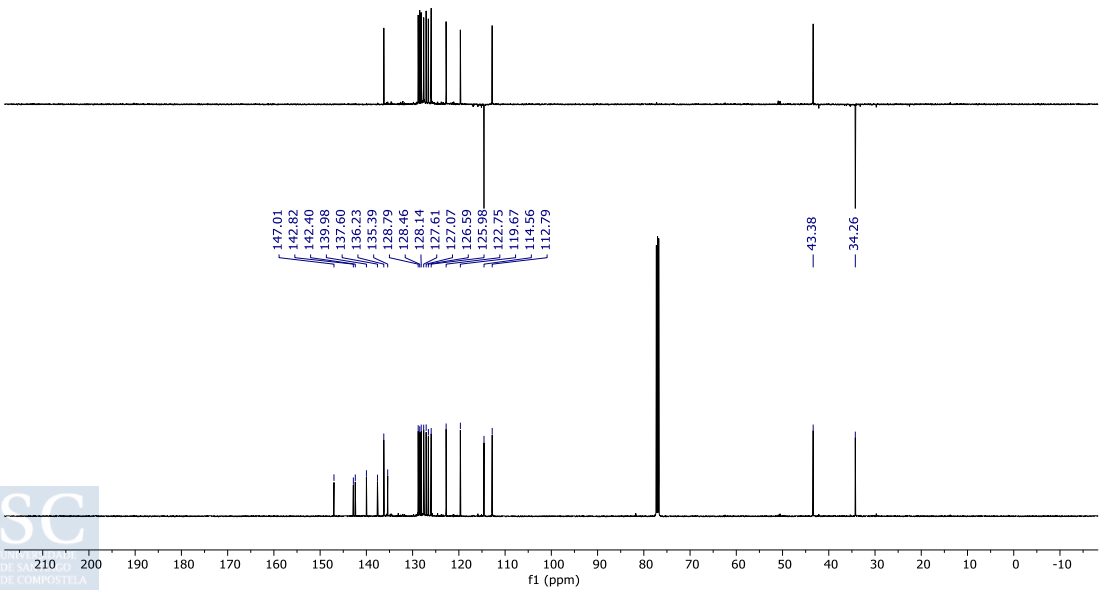


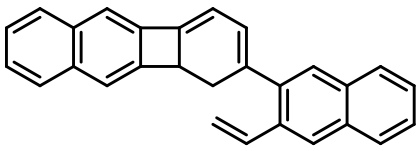




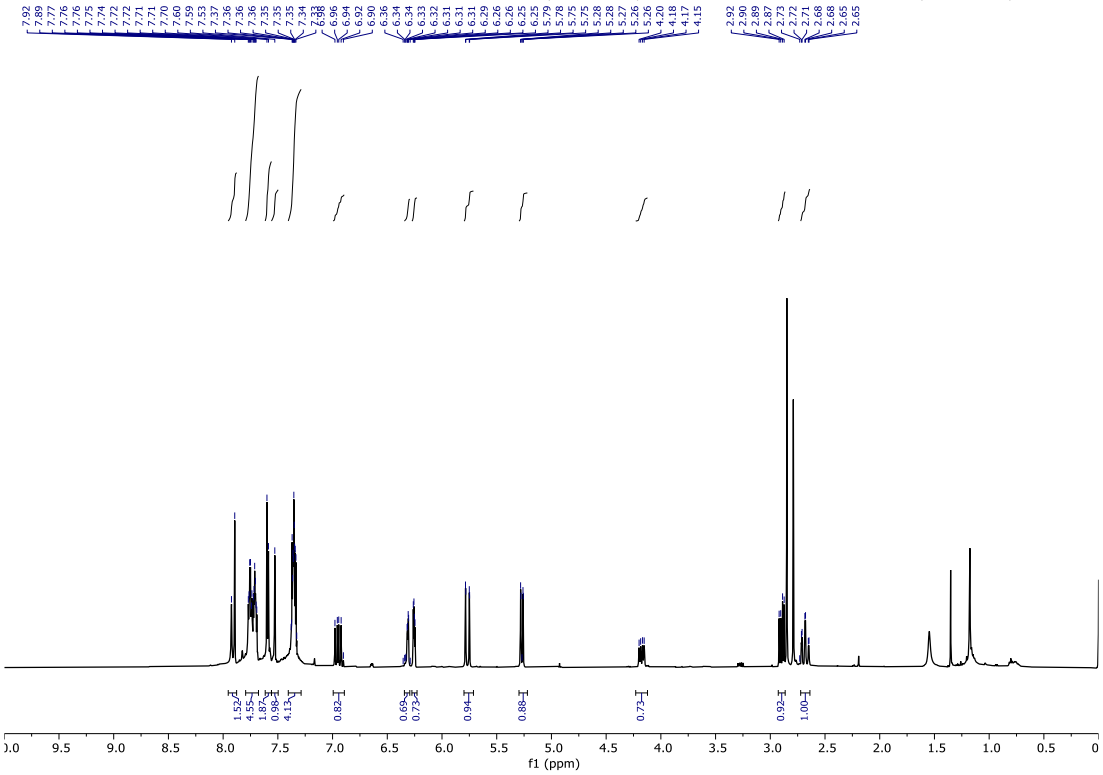
4a ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

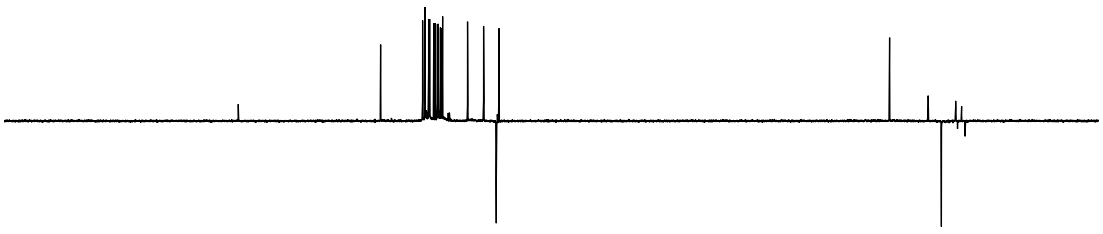


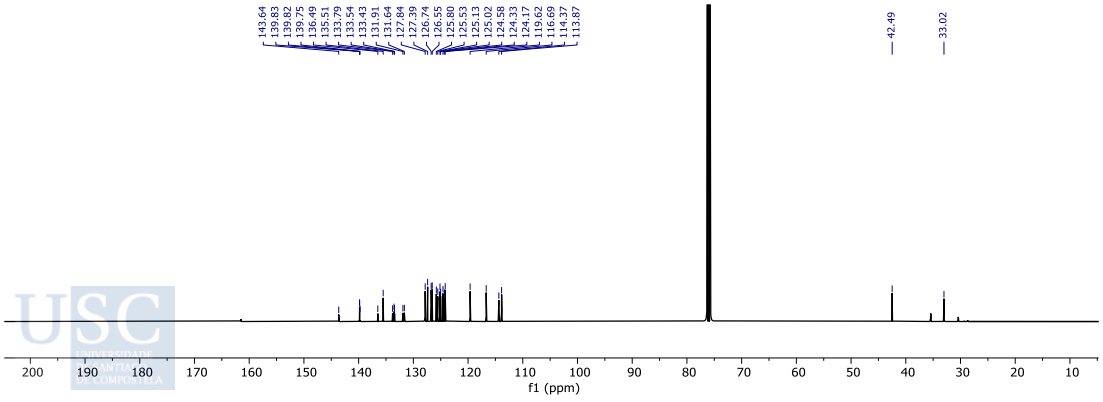


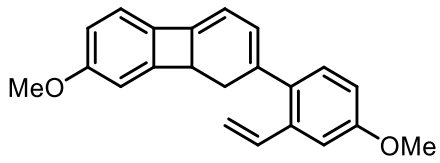


4c ^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$



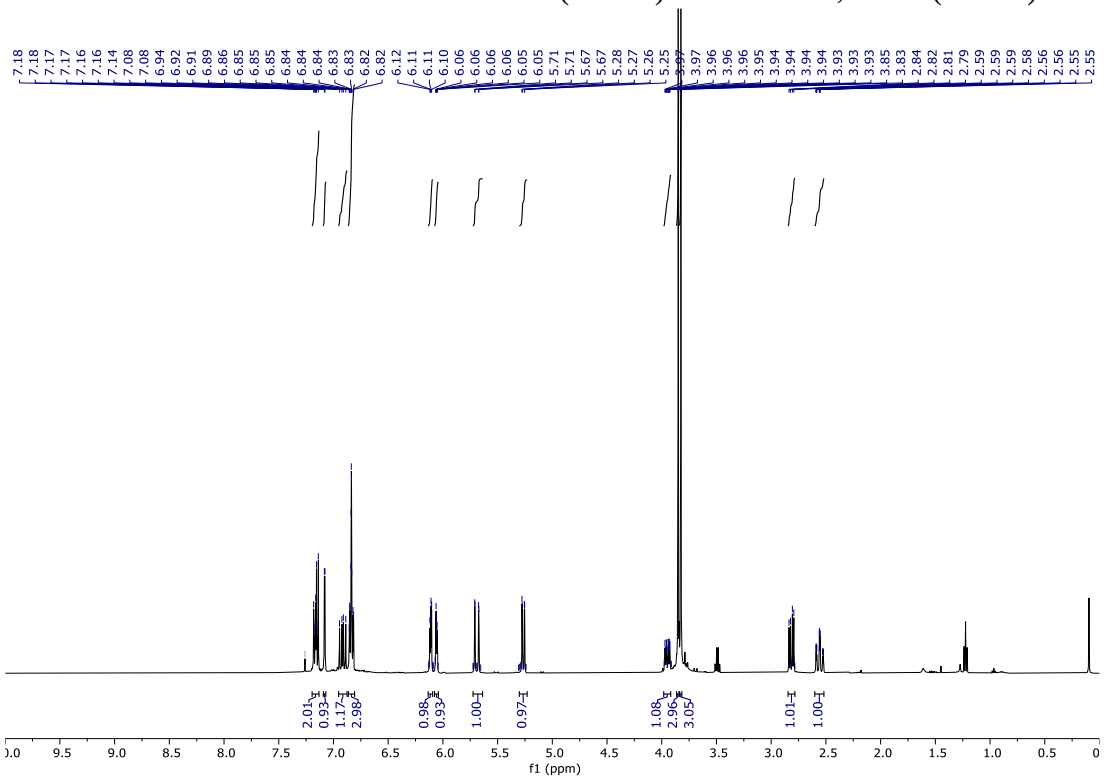


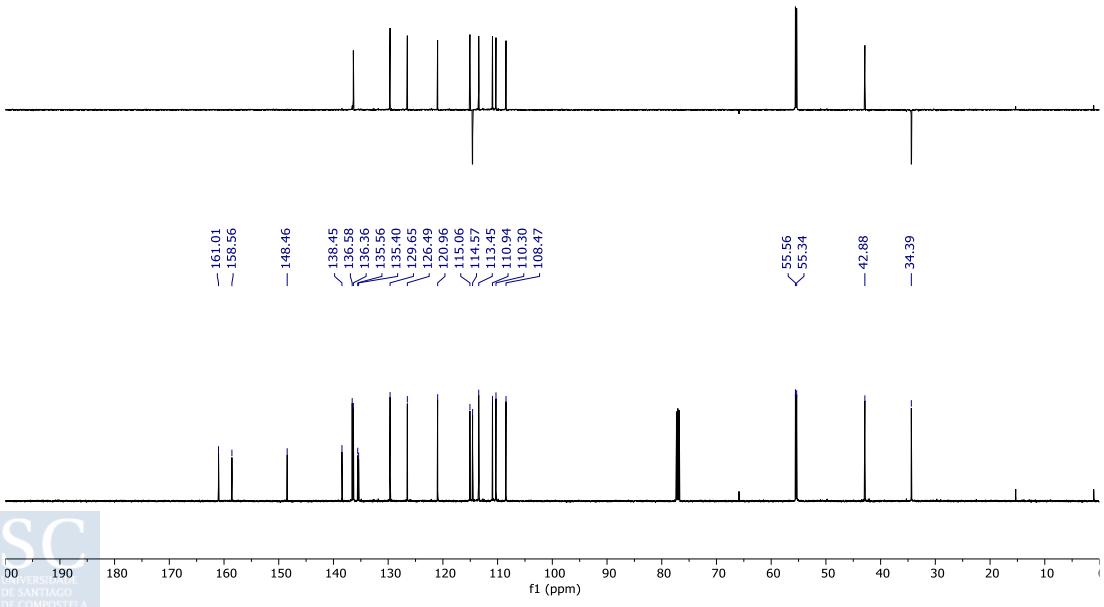


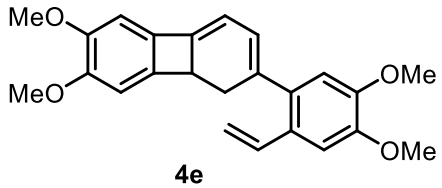


4d

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

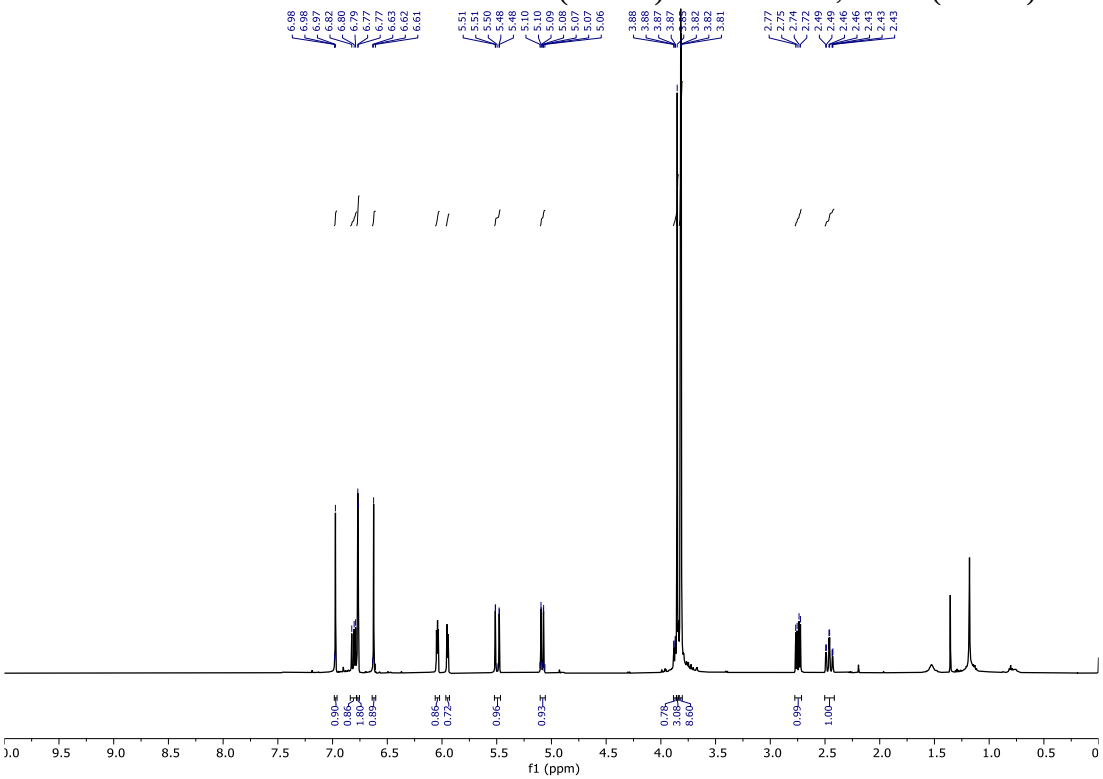


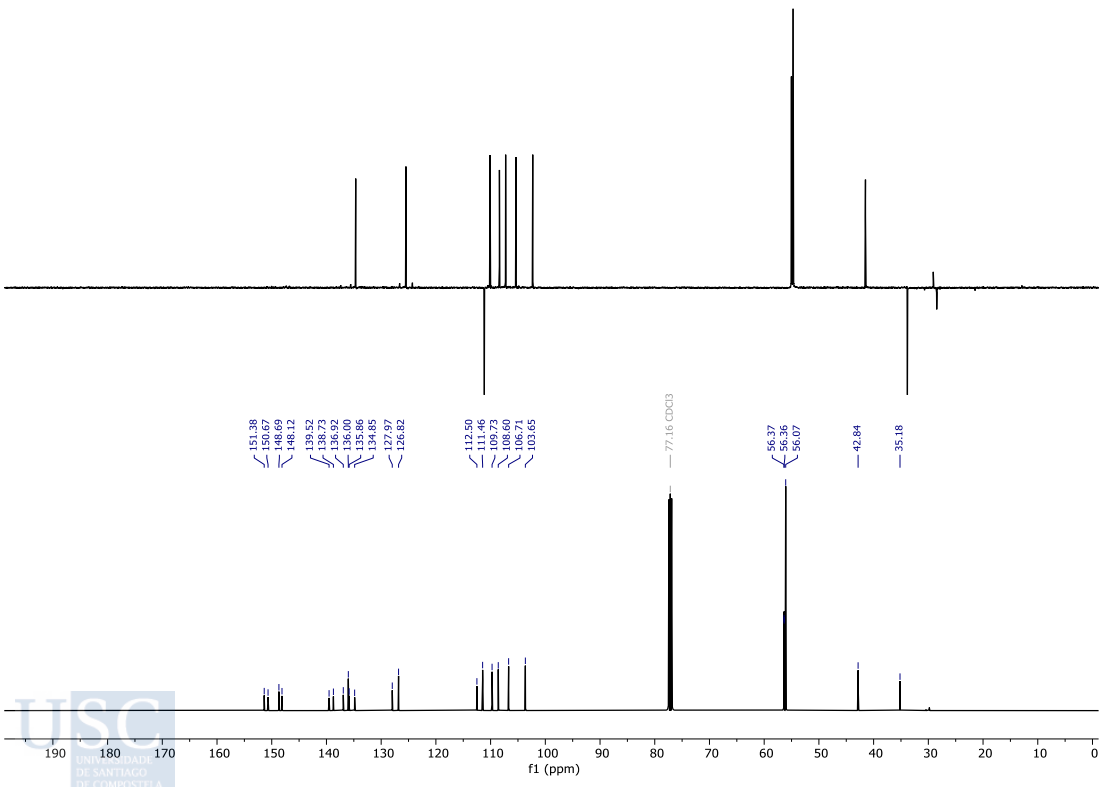


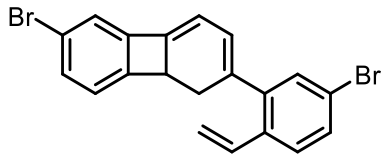


4e

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

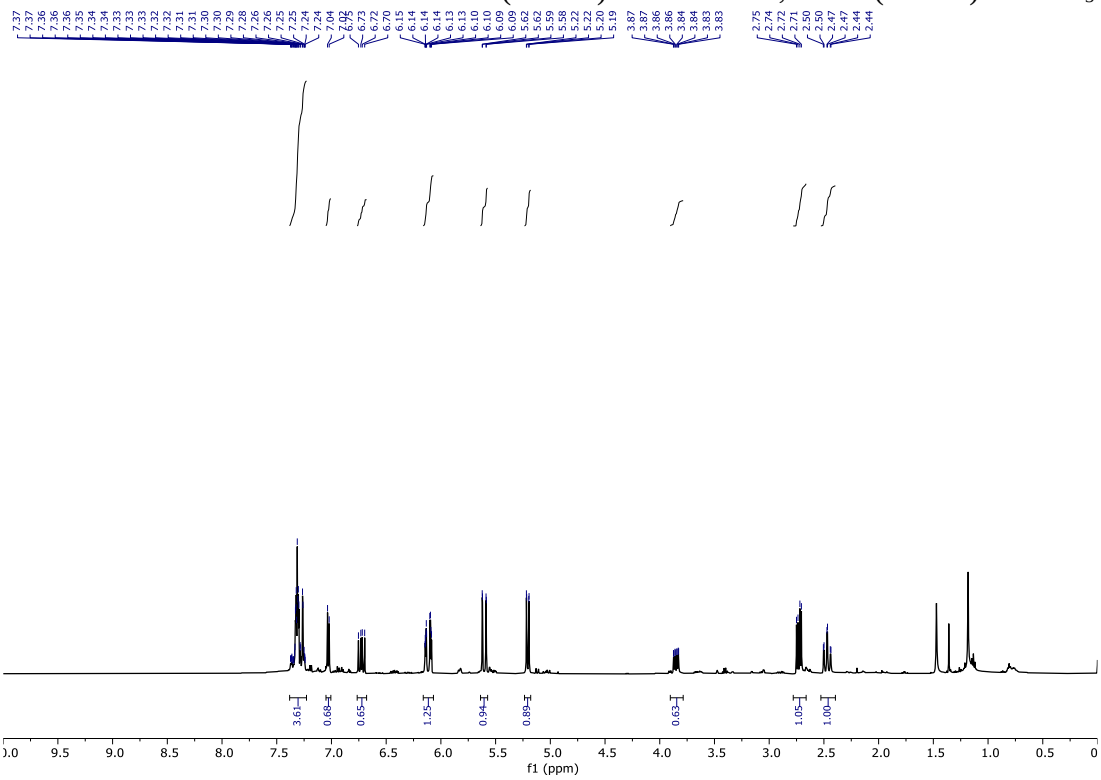


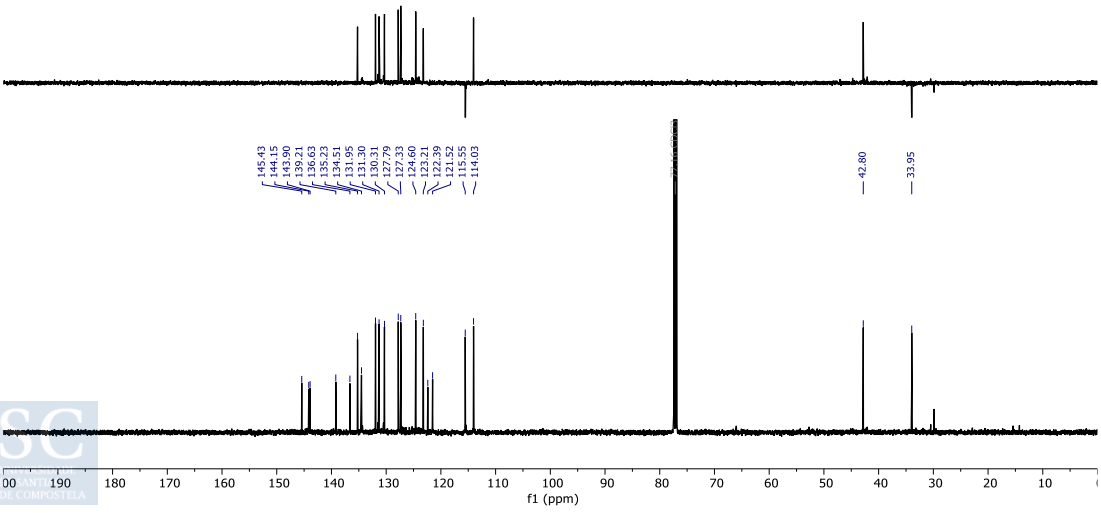


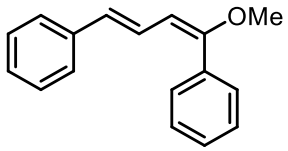


4f

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

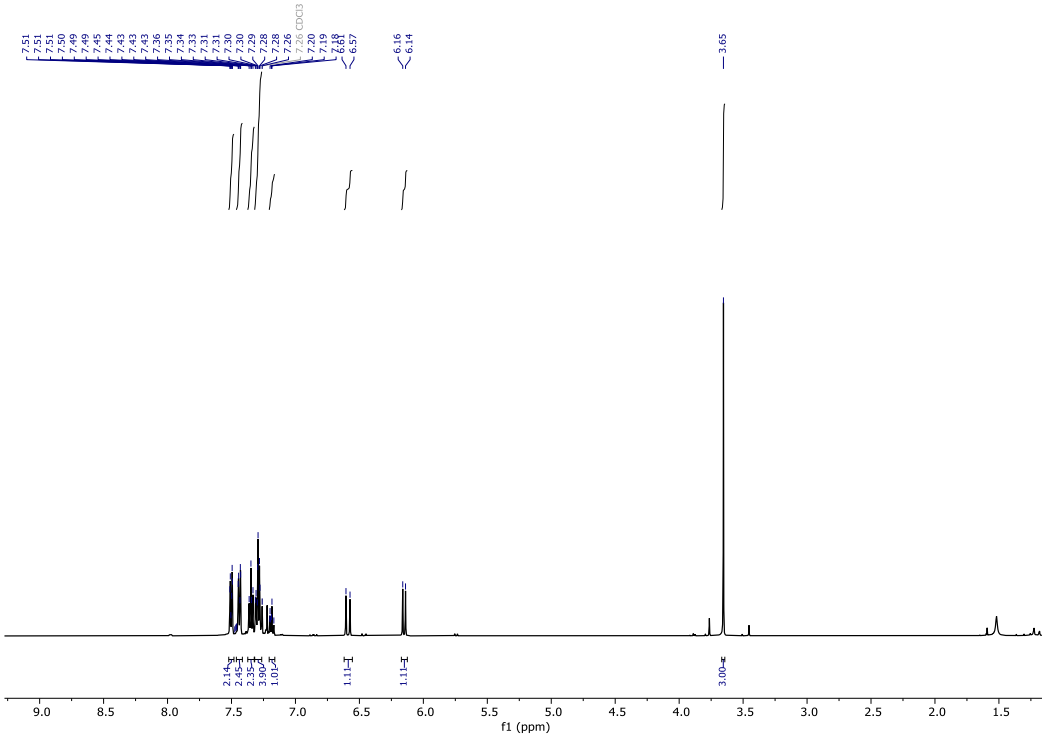


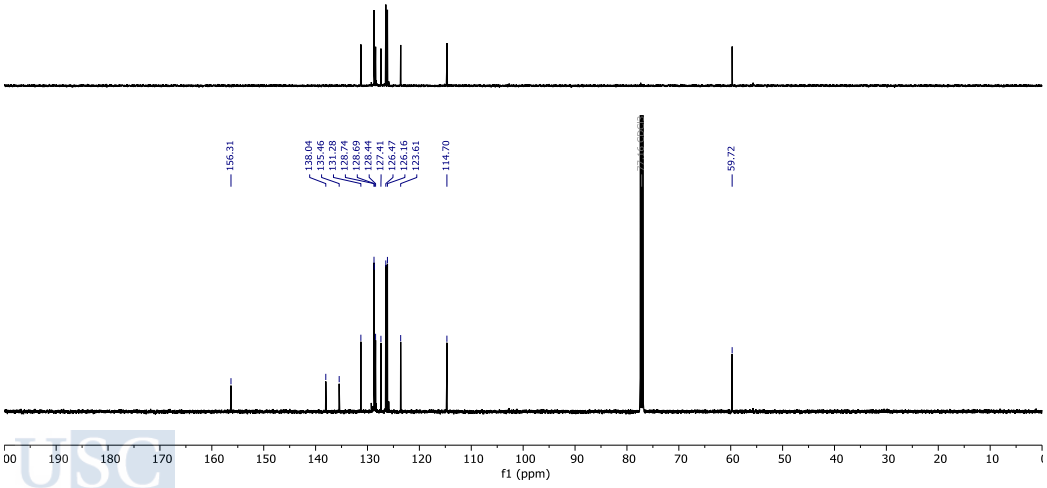


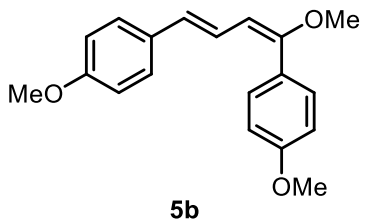


5a

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

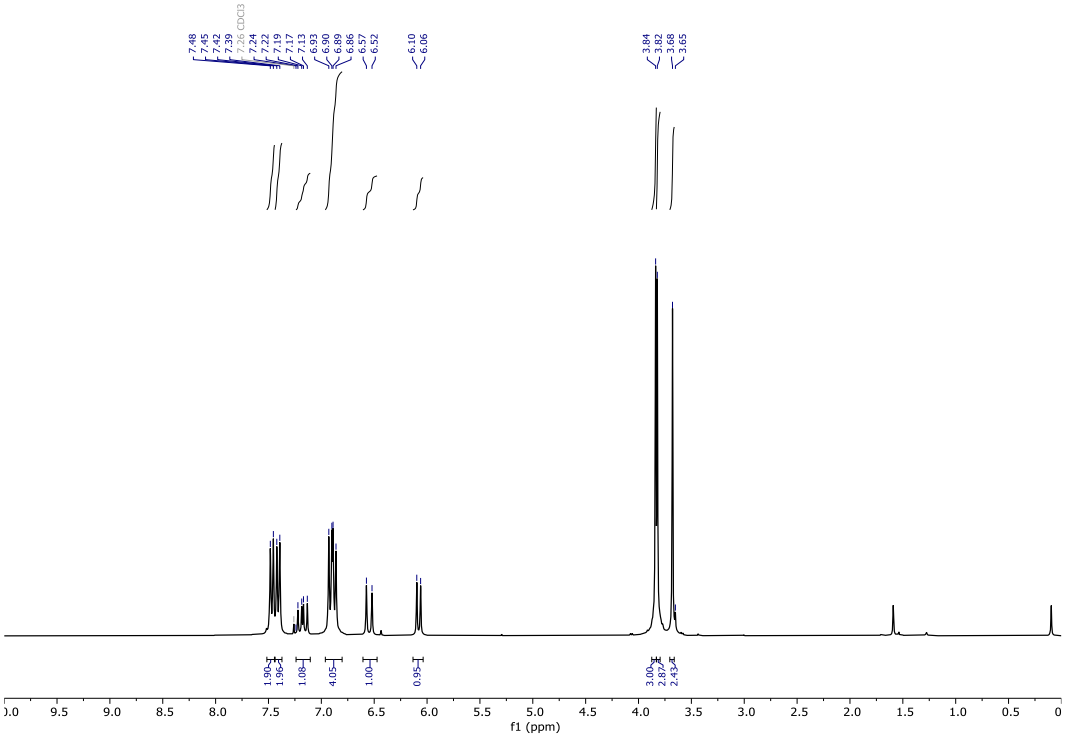


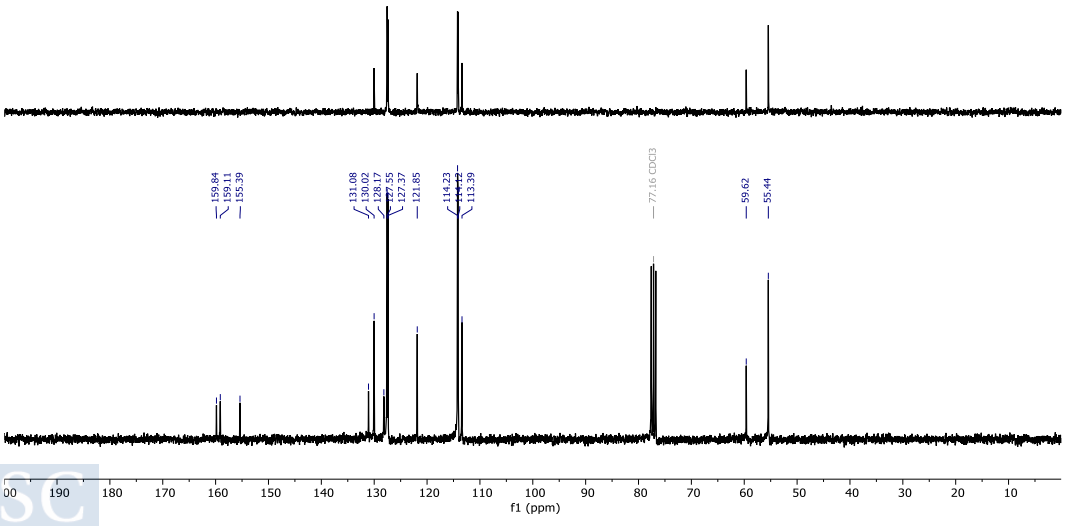


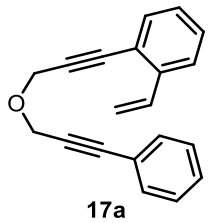


5b

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

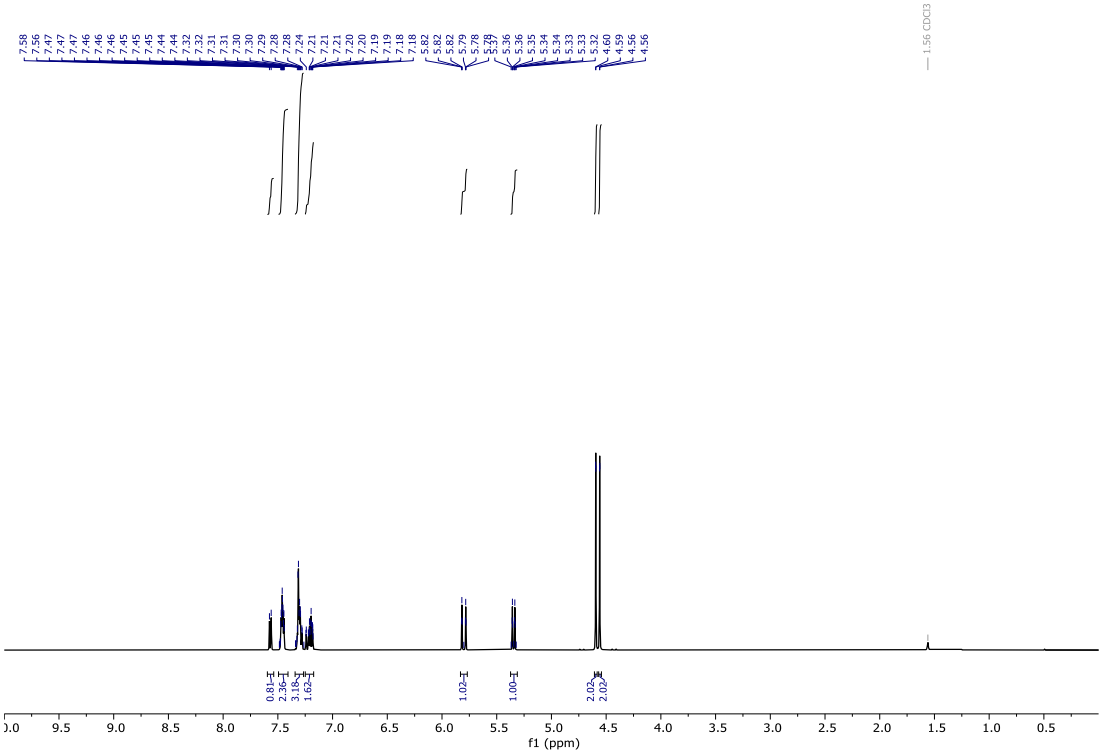


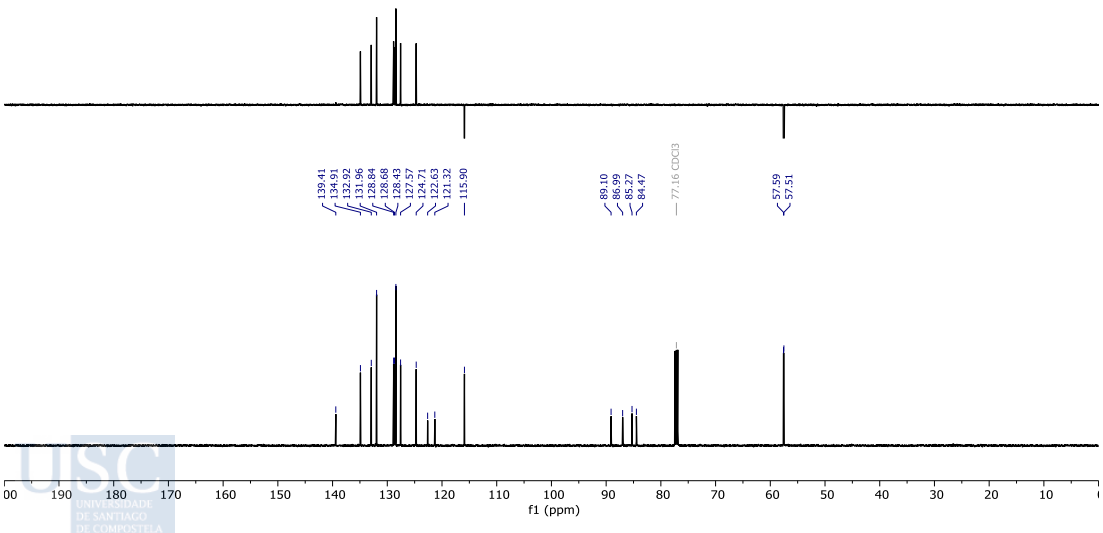


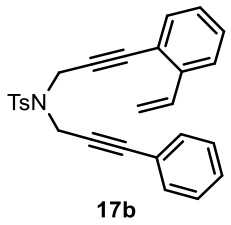


17a

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

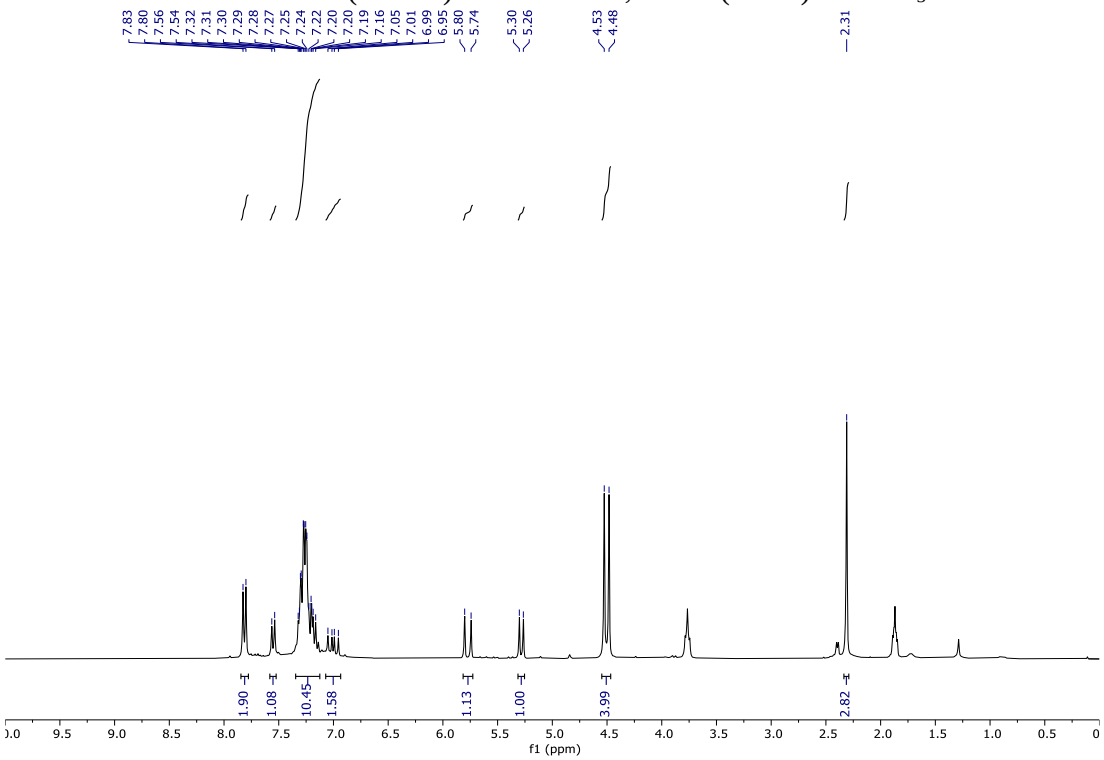


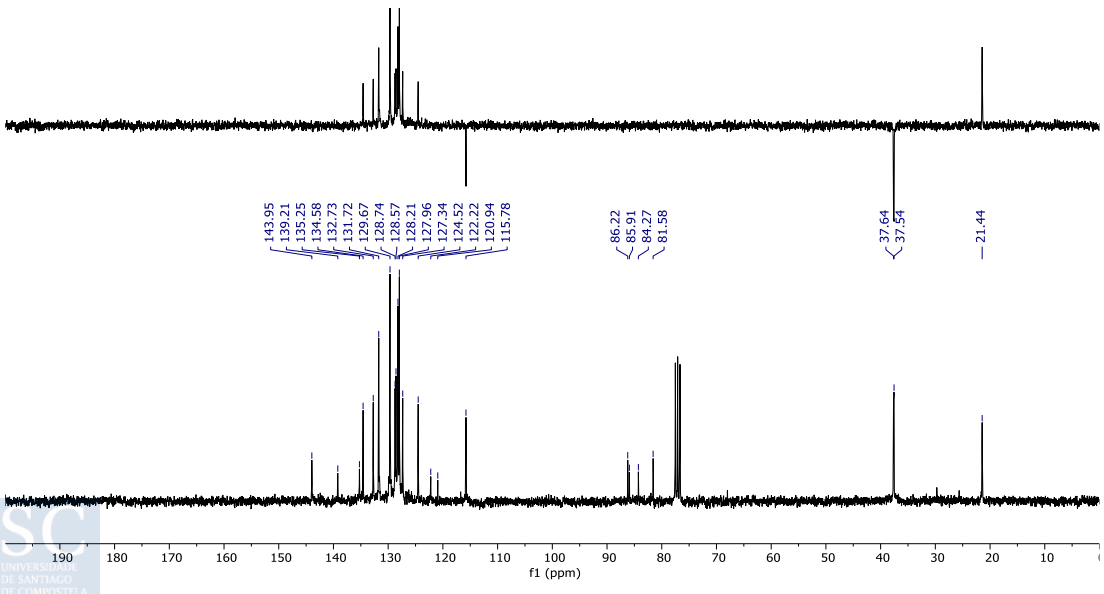


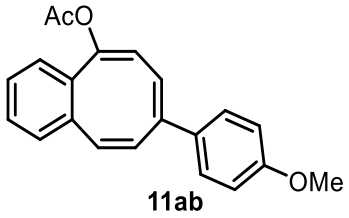


17b

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

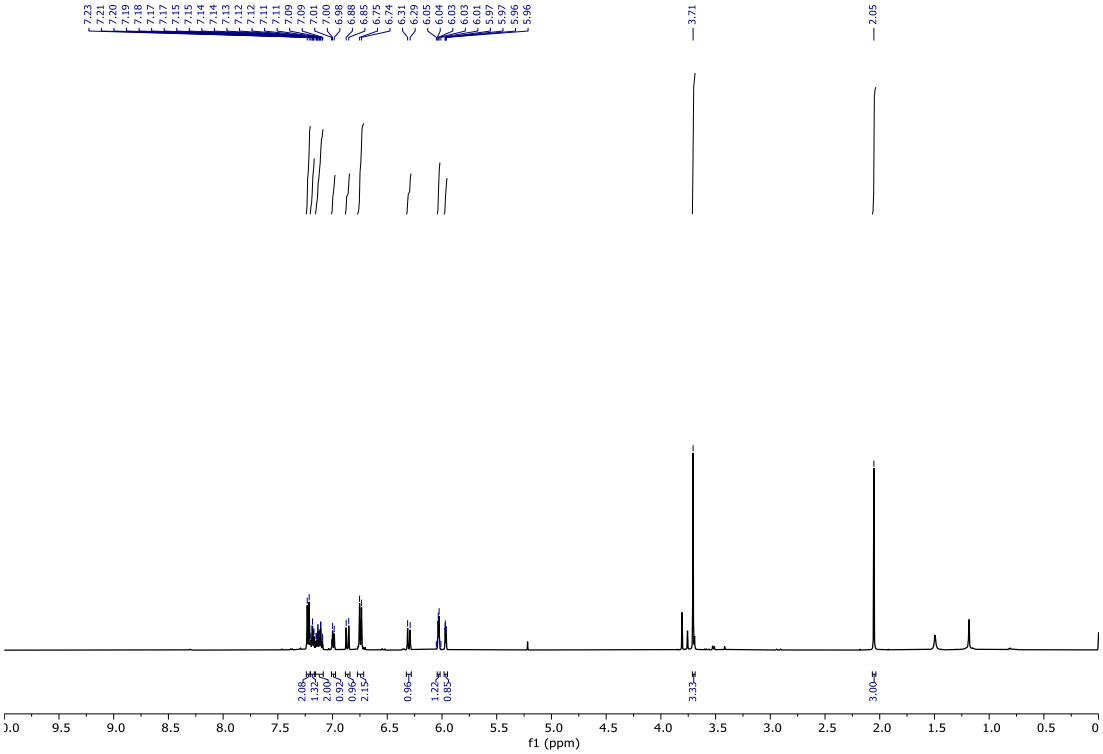


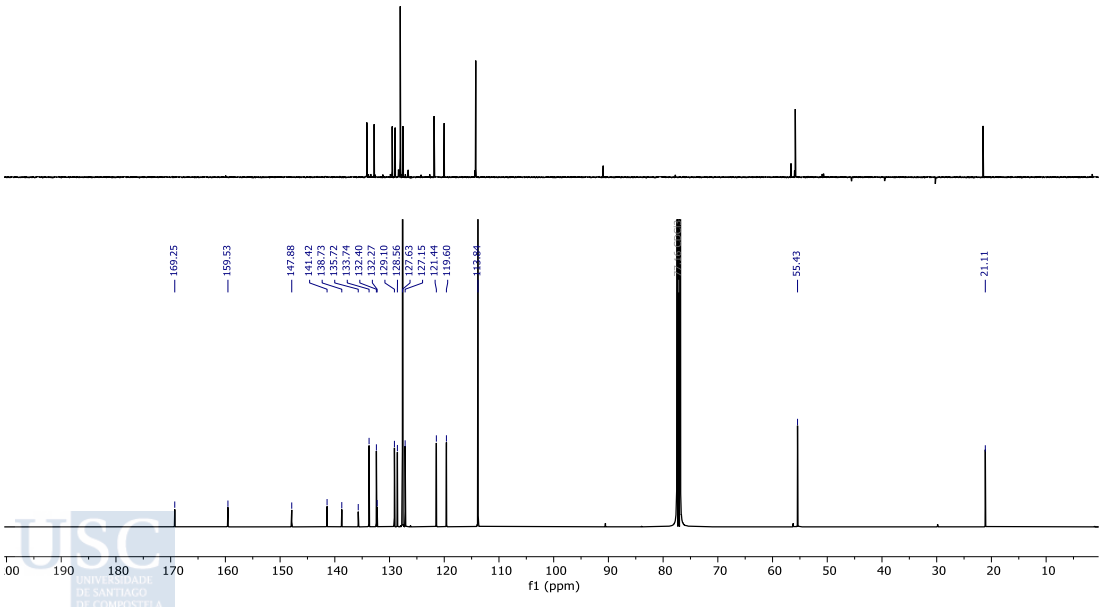


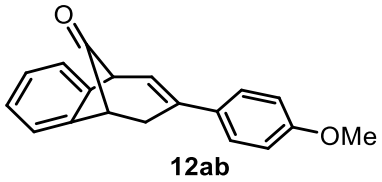


11ab

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

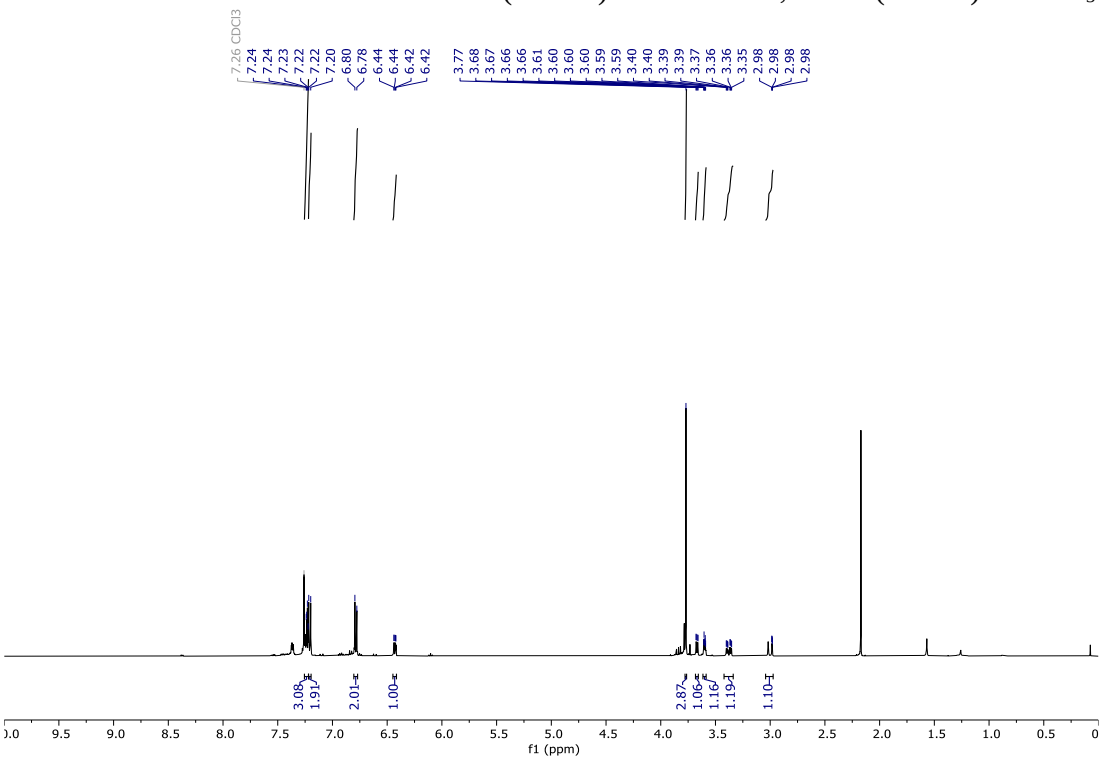


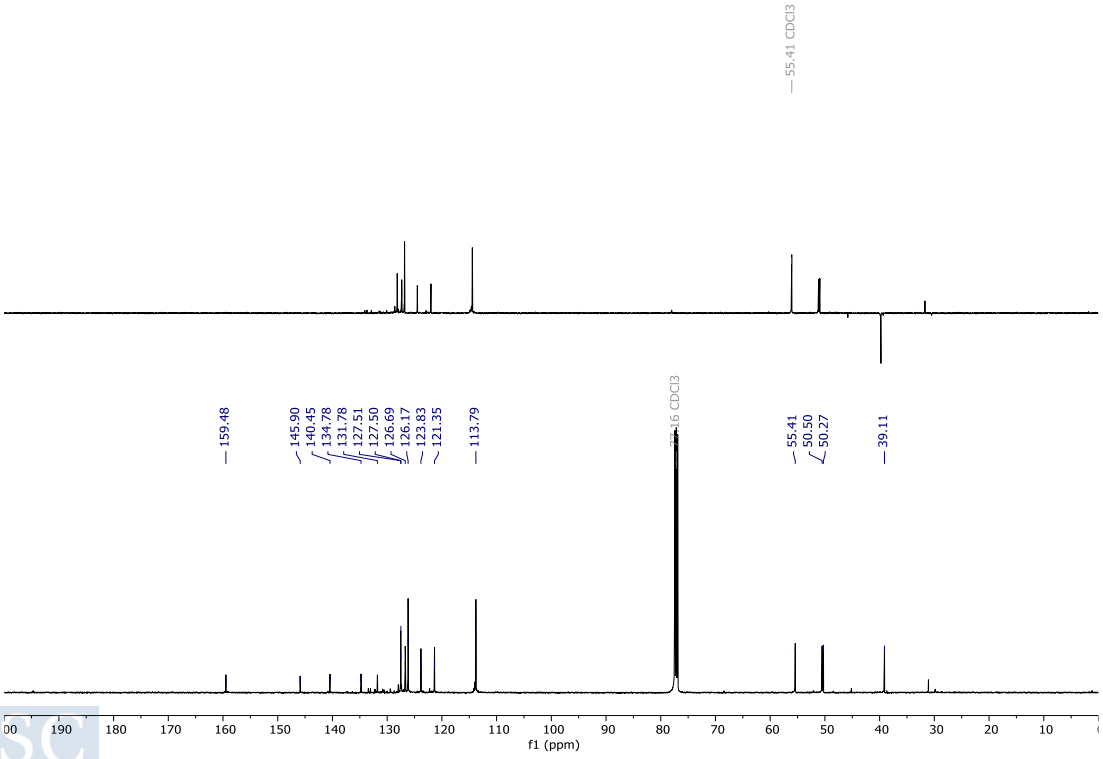


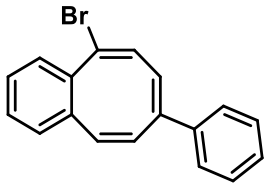


12ab

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

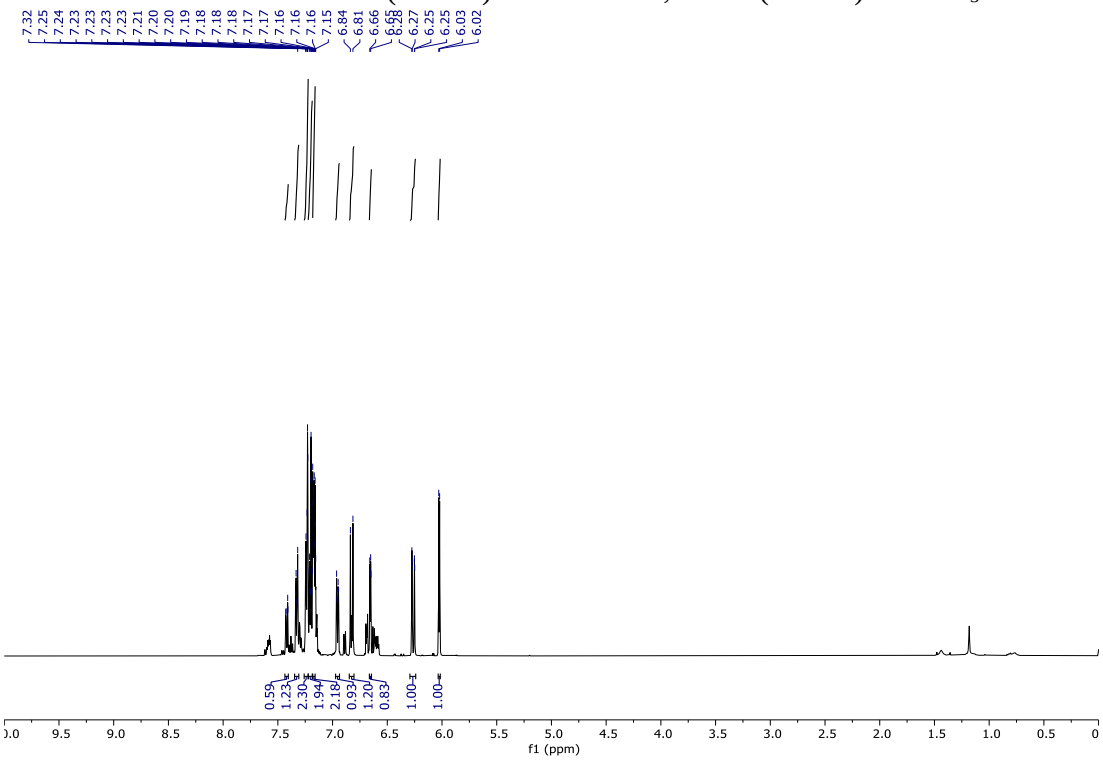


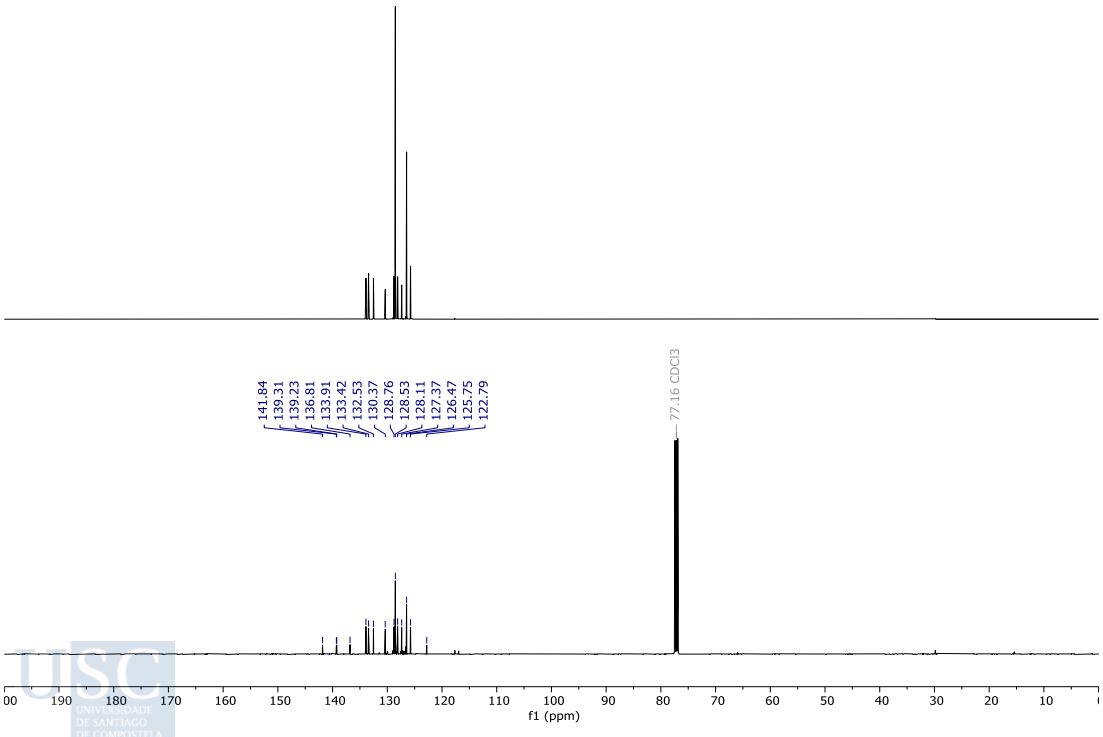


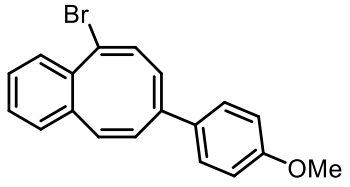


16aa

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

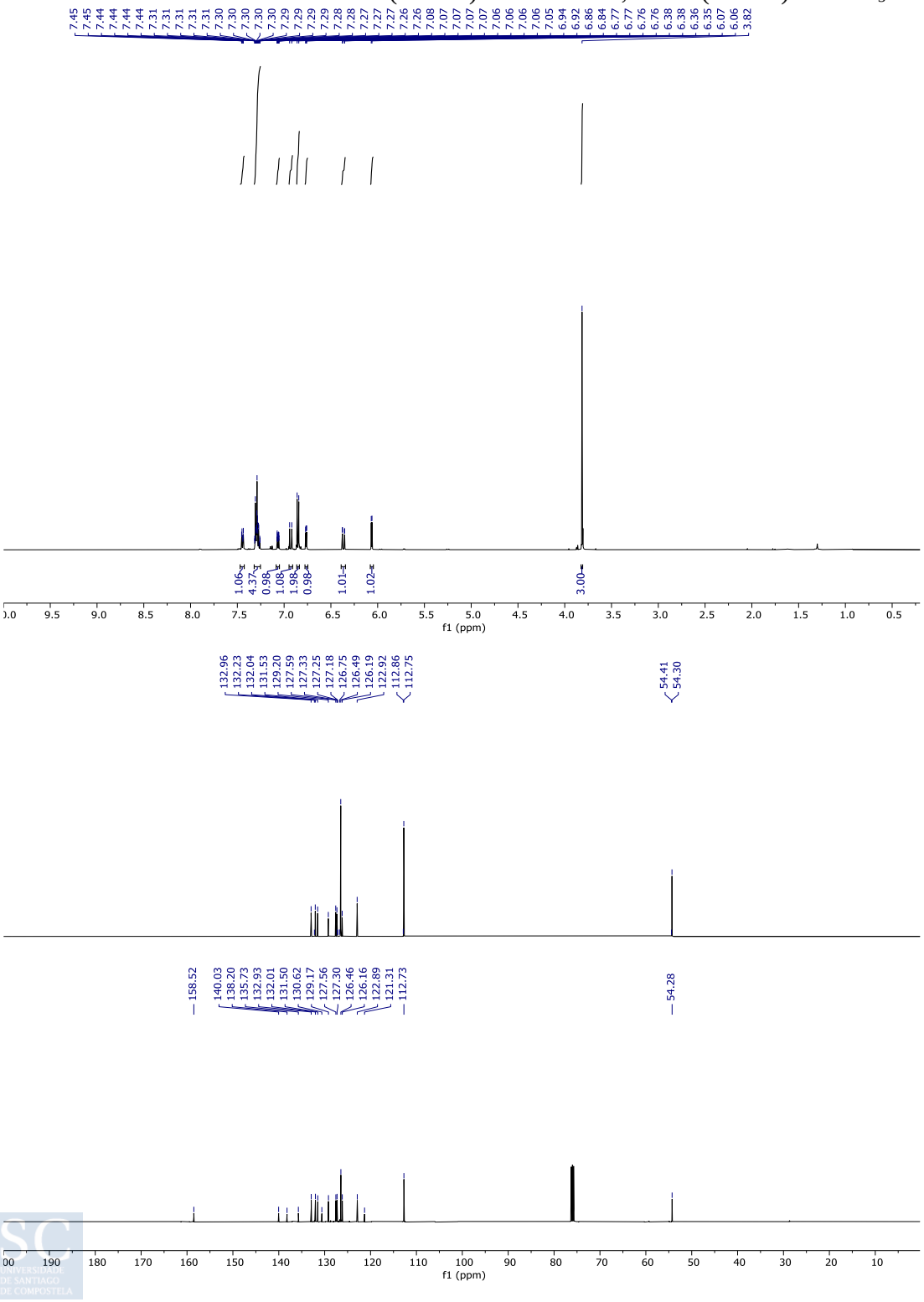




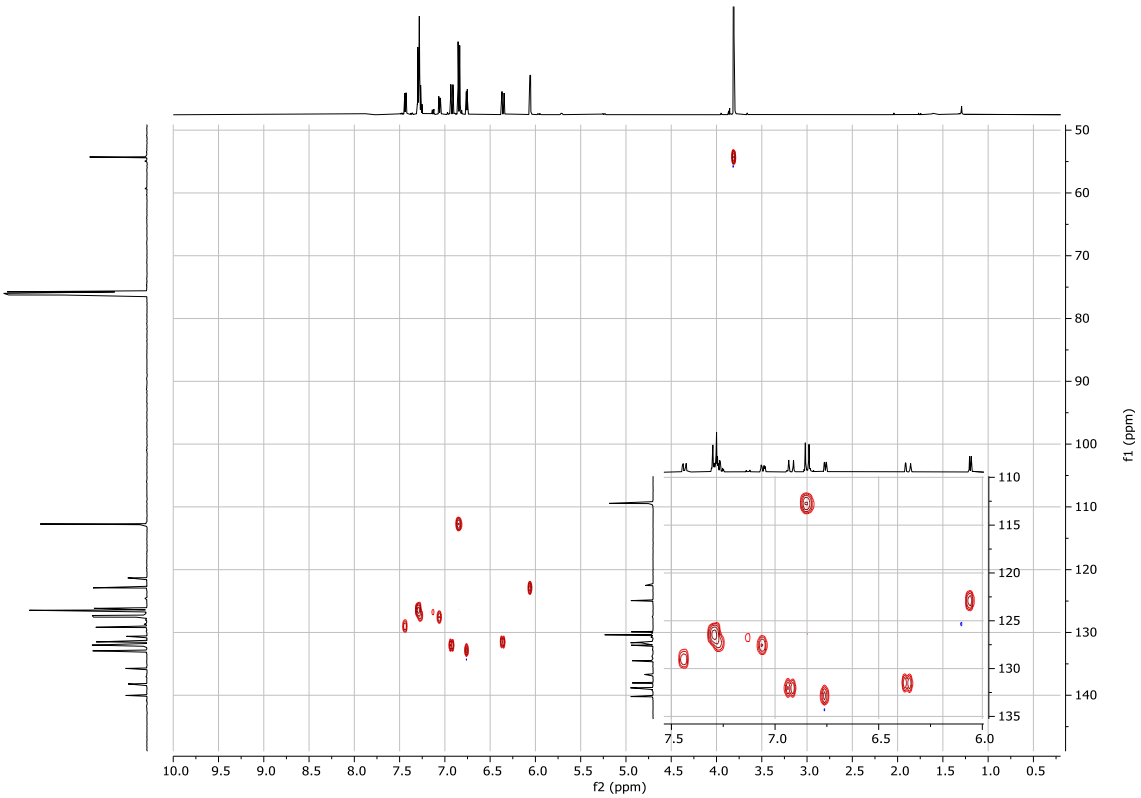


16ab

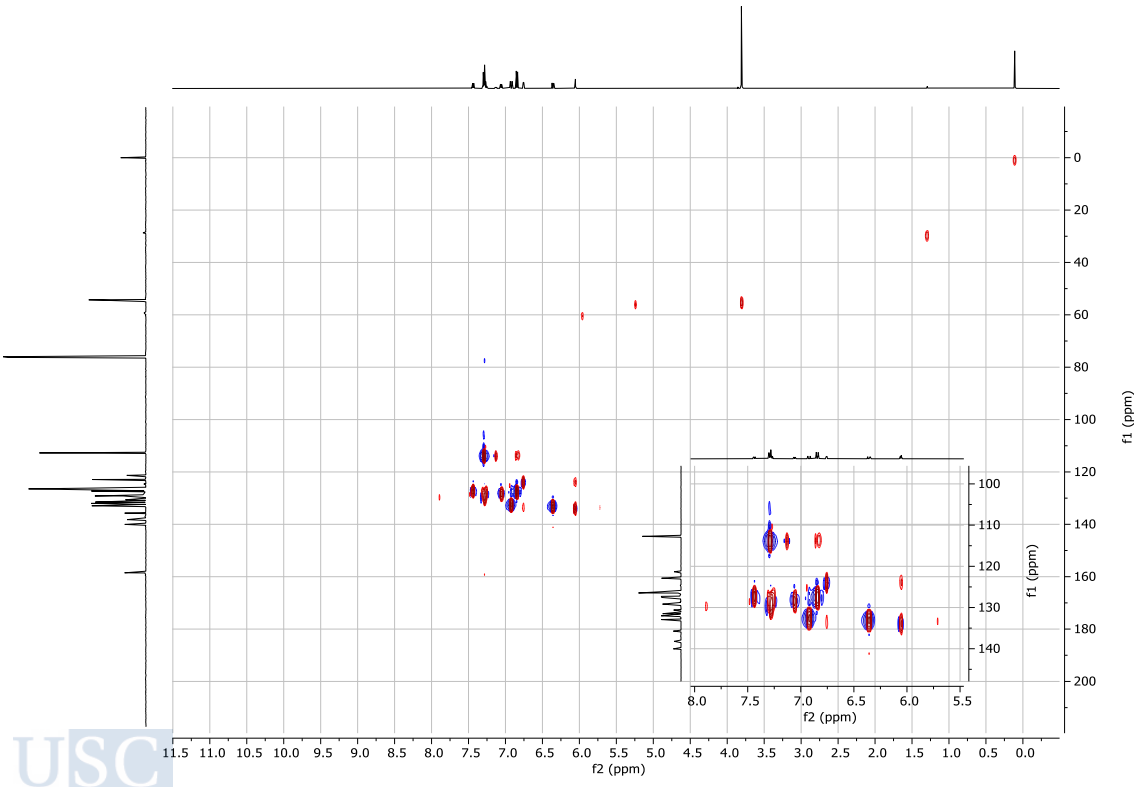
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

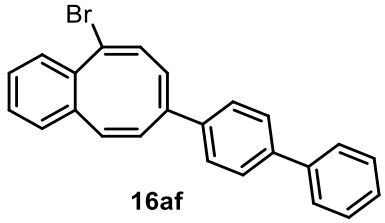


HSQC



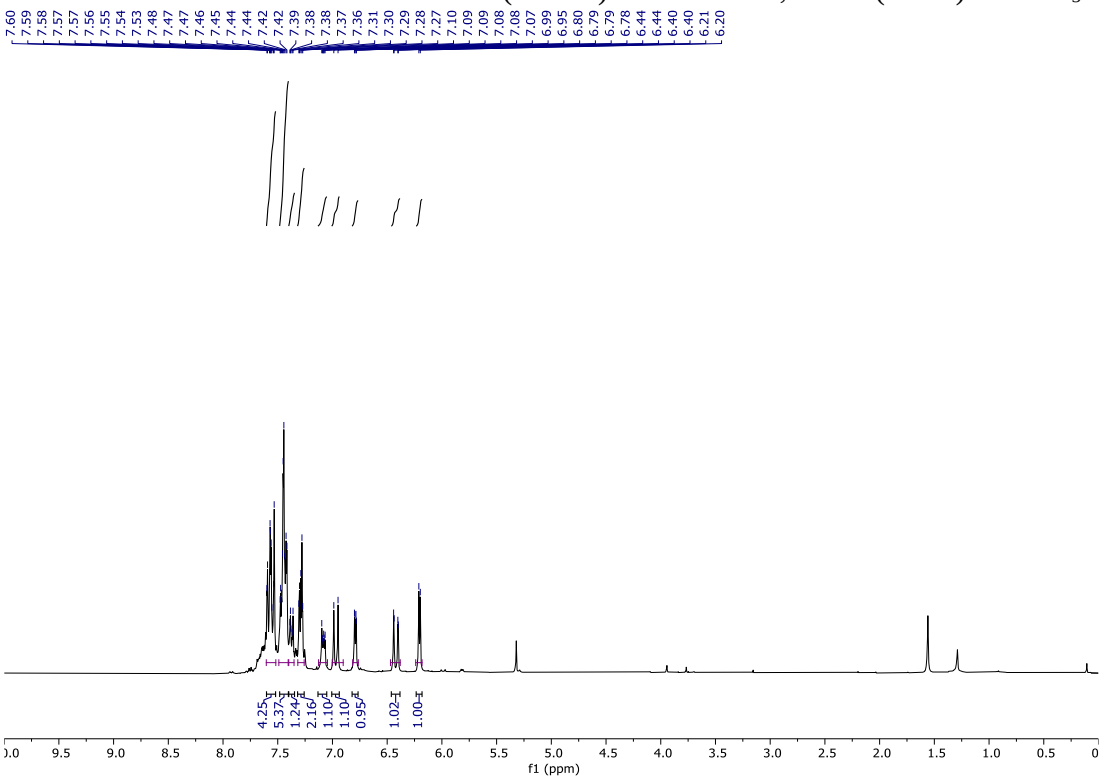
HMBC

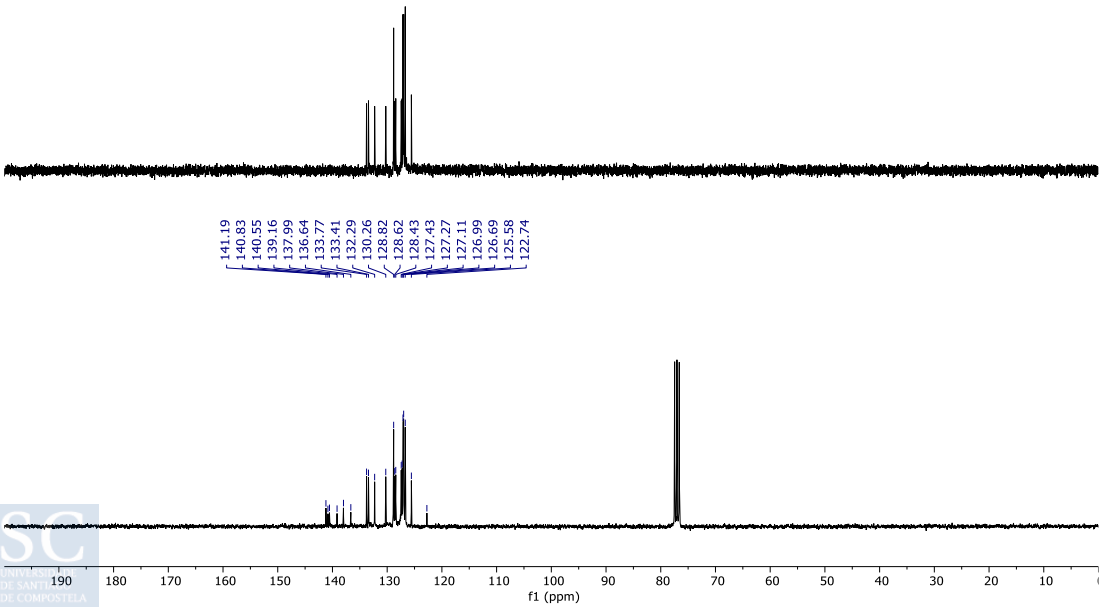


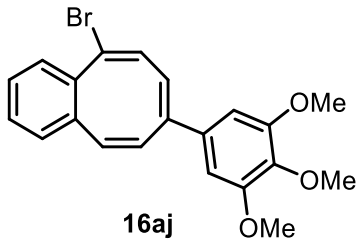


16af

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

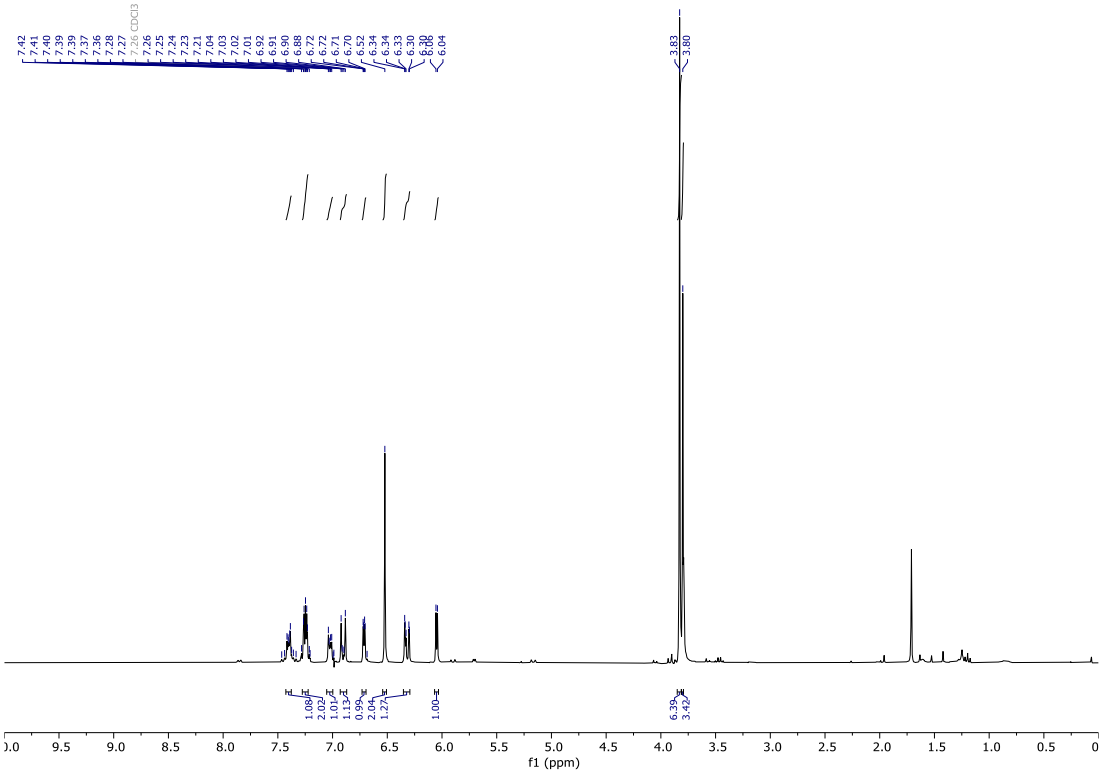


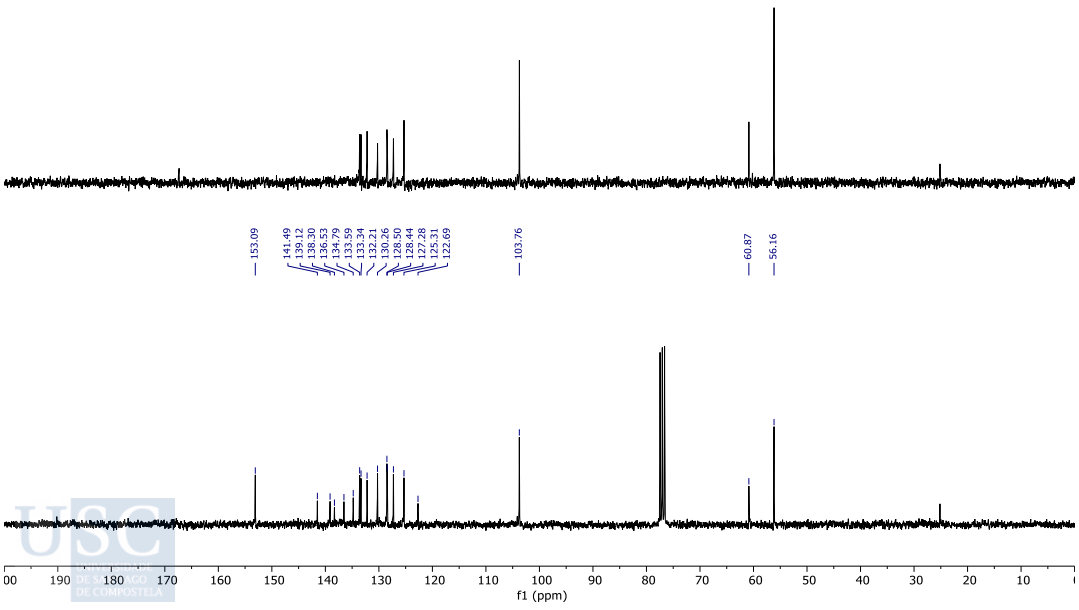


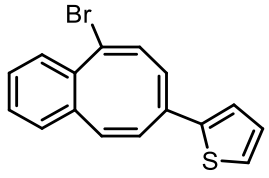


16aj

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

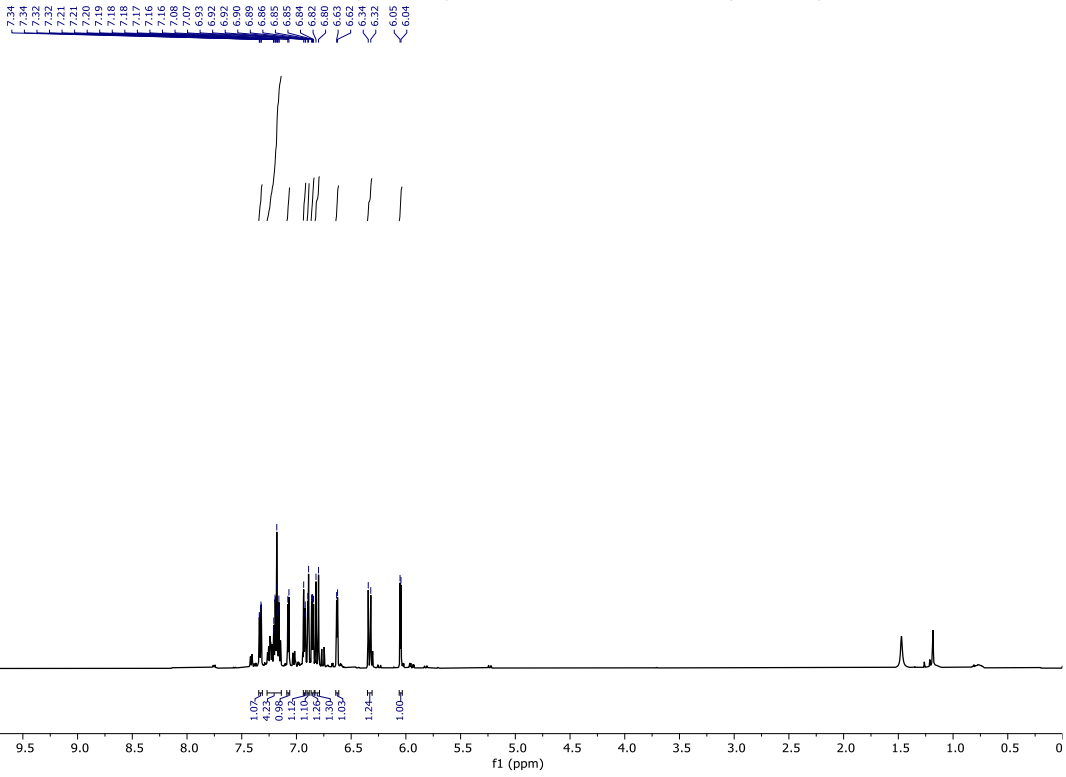


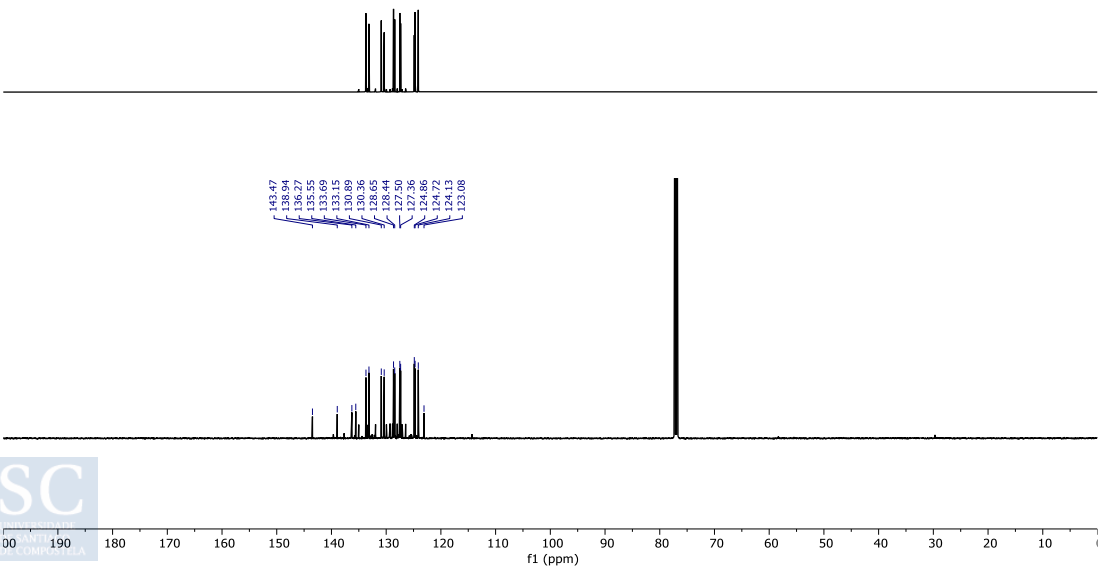


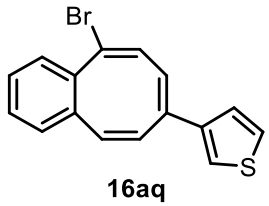


16ak

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

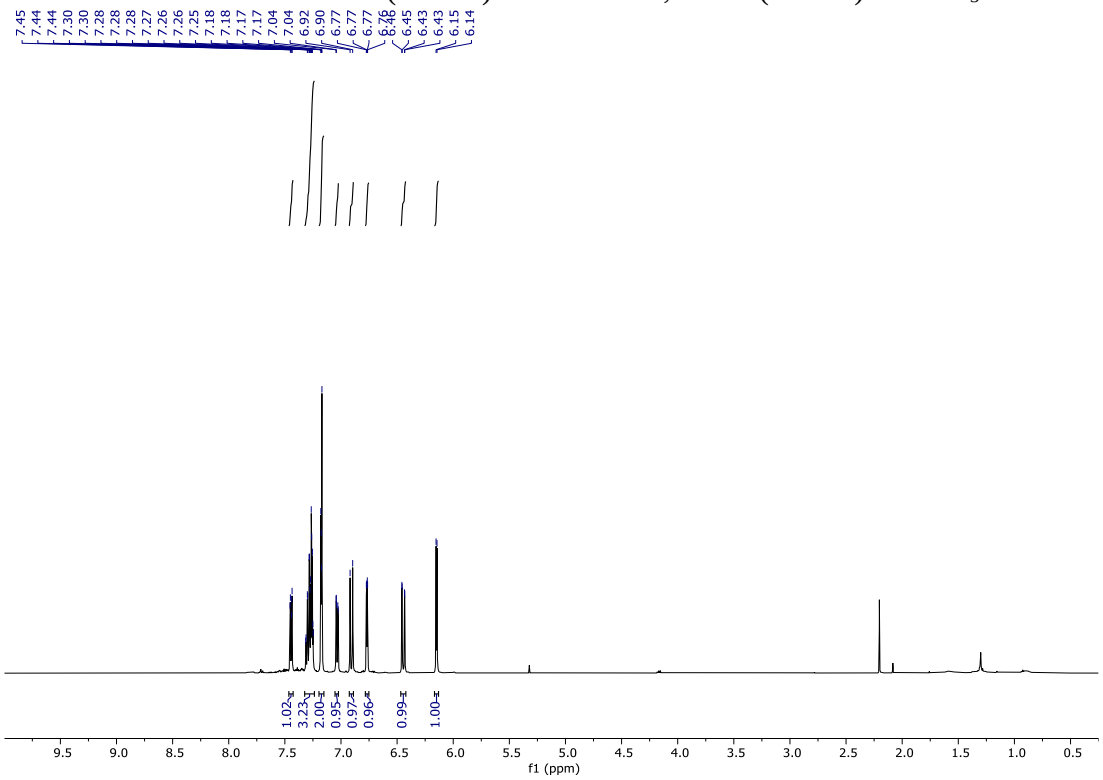


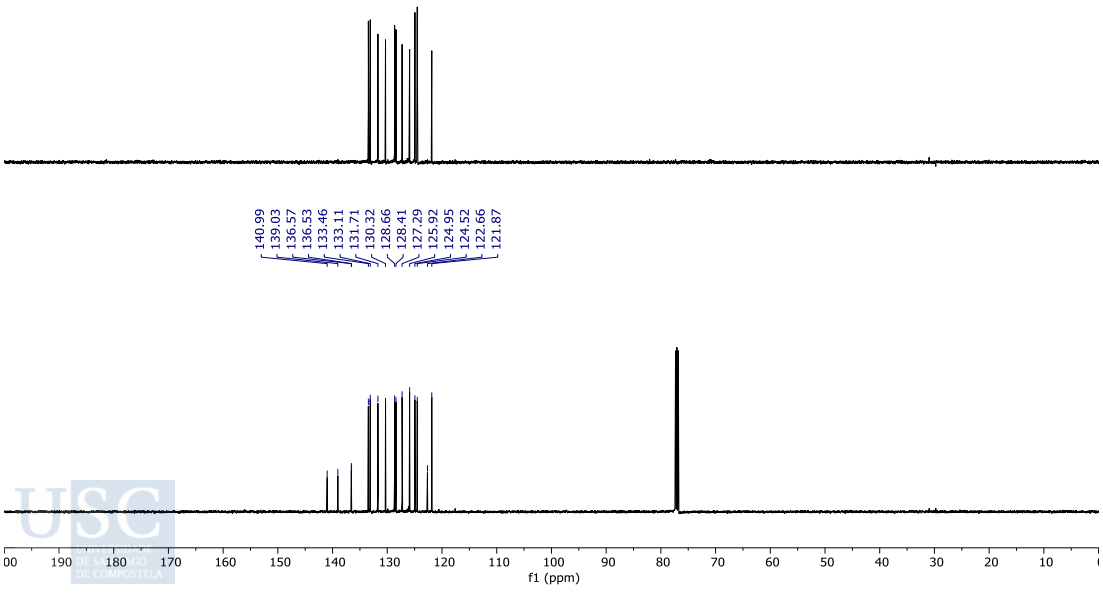


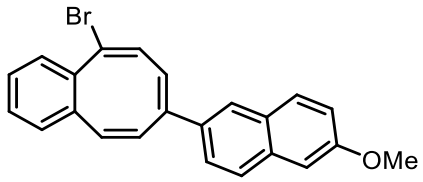


16aq

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

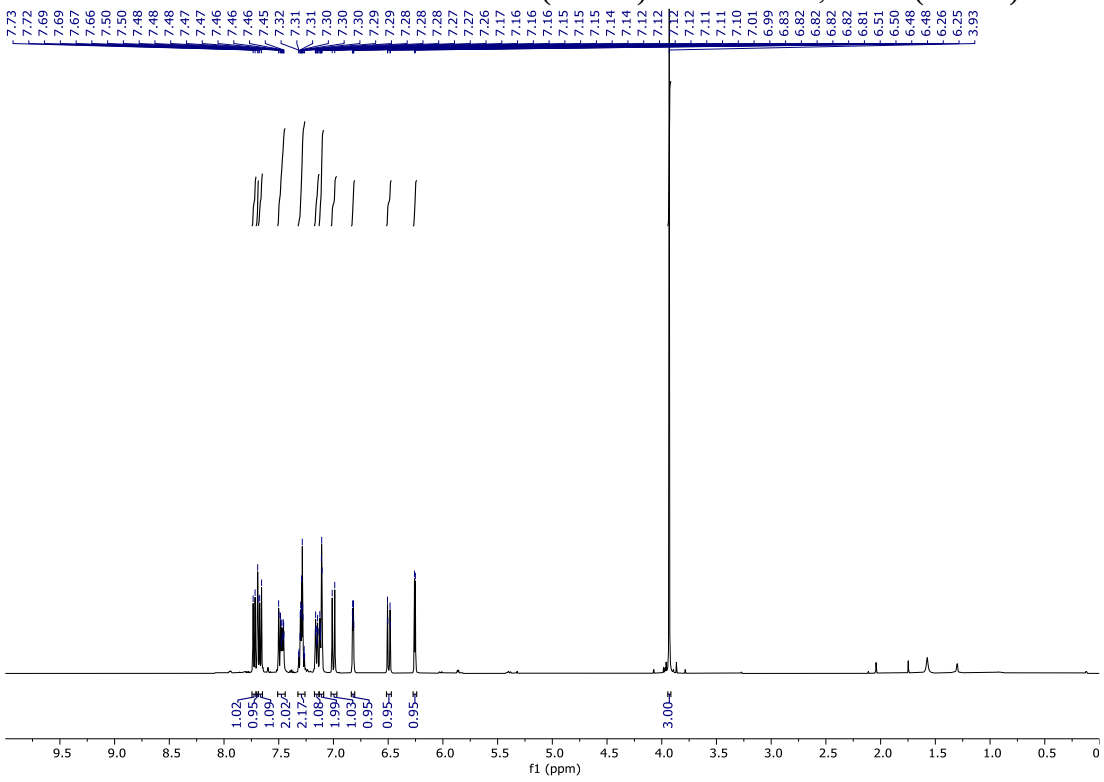


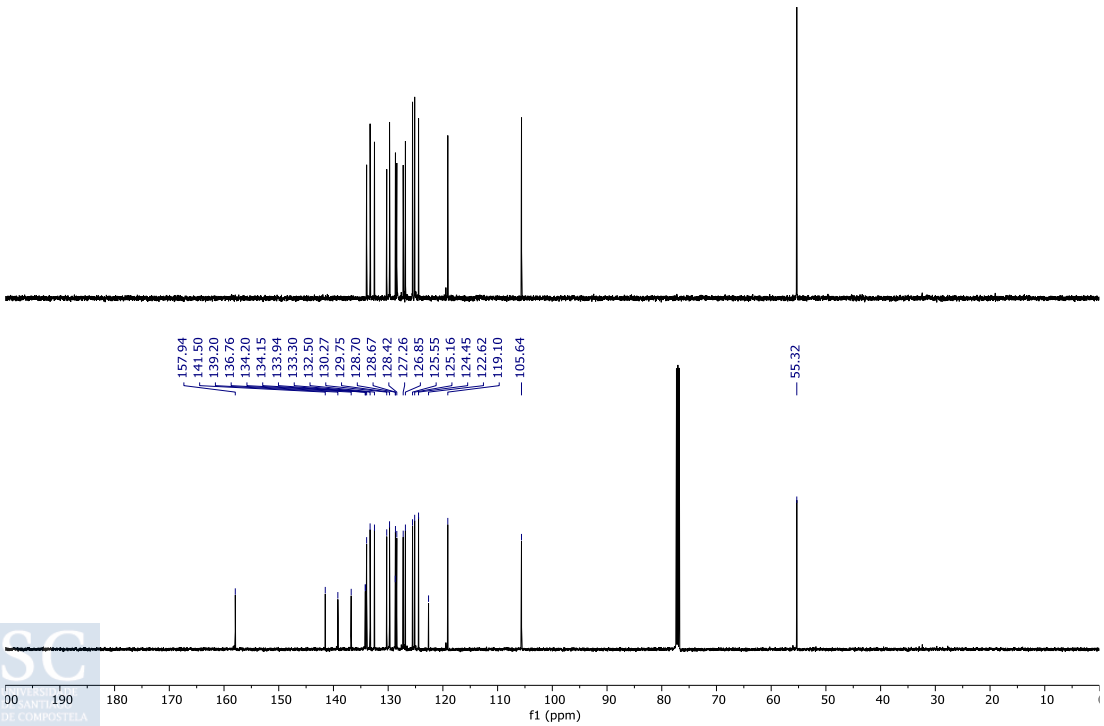


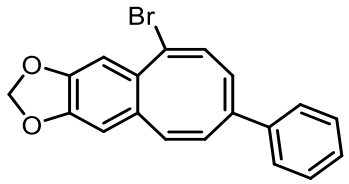


16at

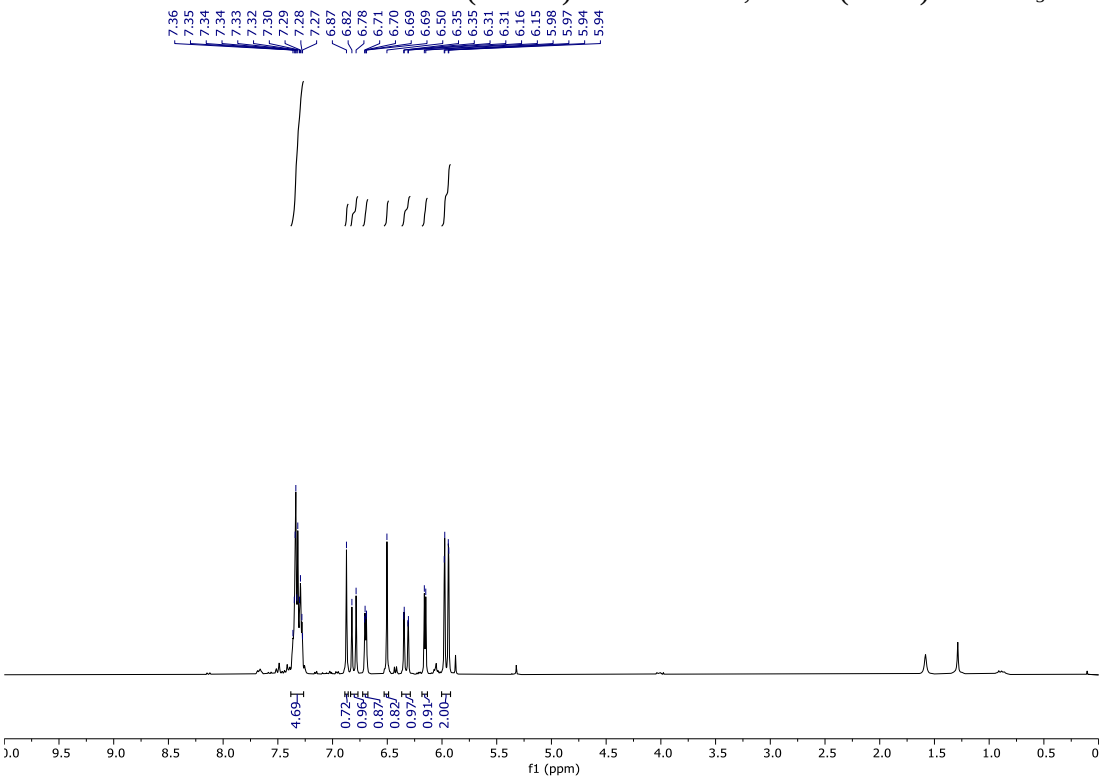
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

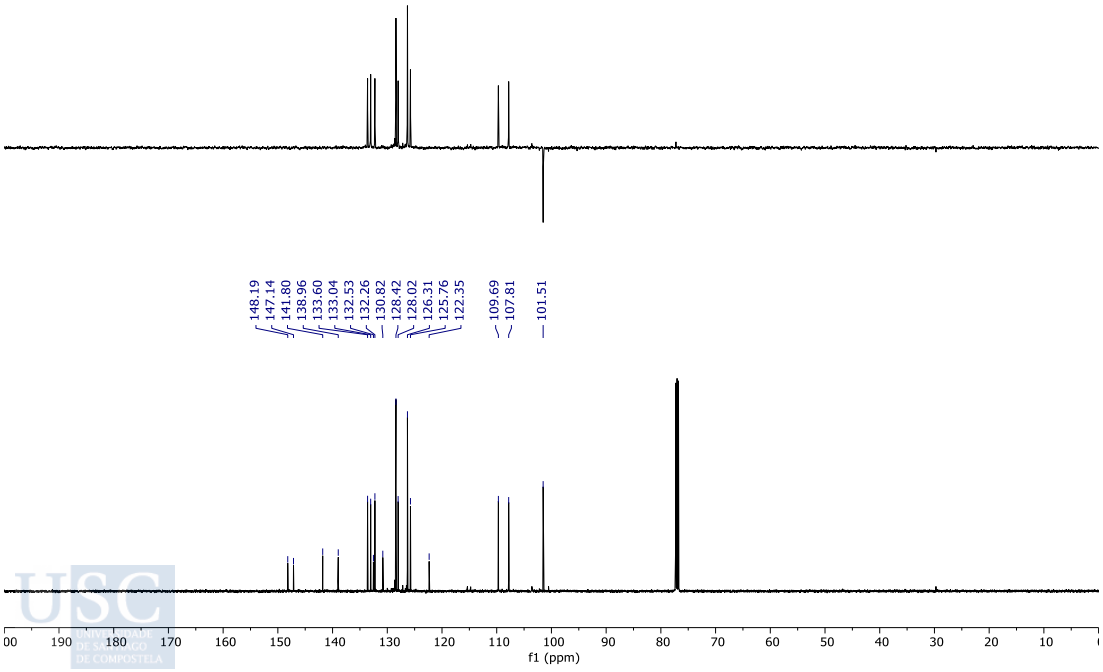


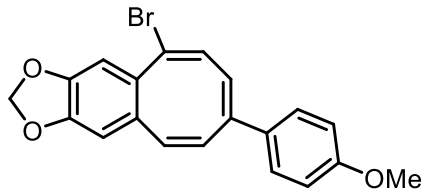




16ba ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

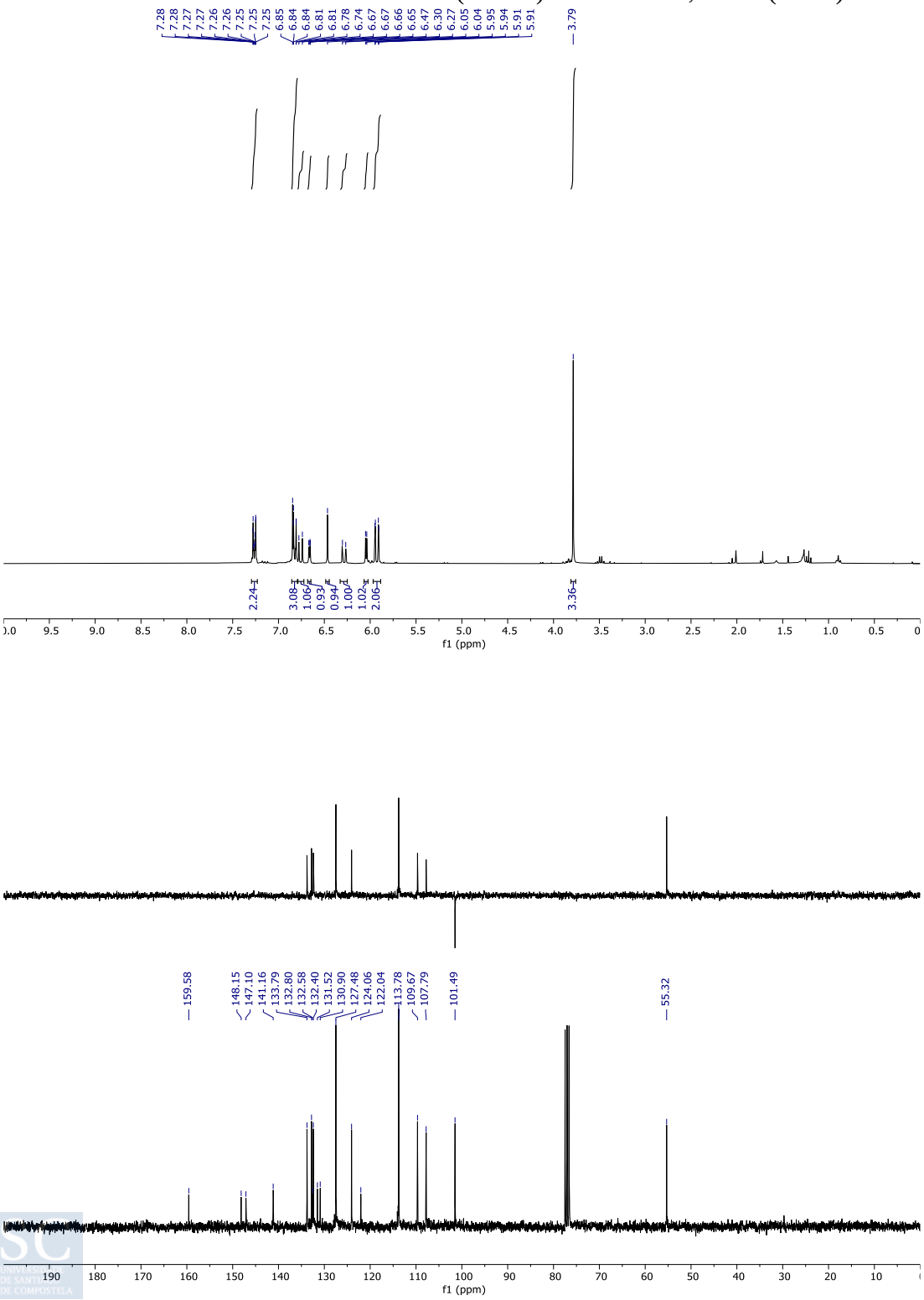


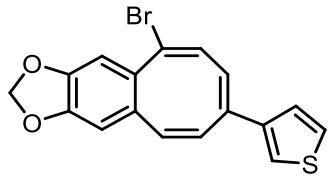




16bb

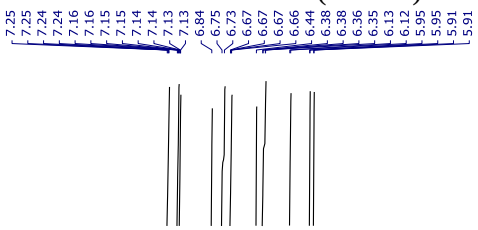
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

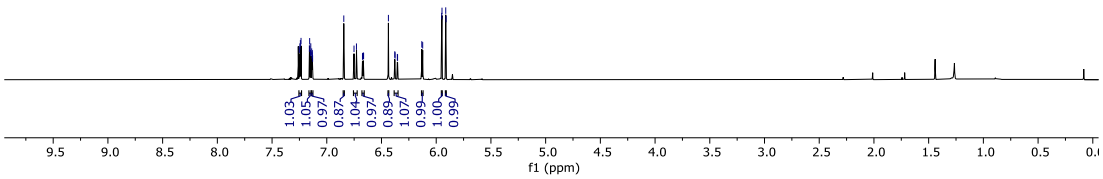


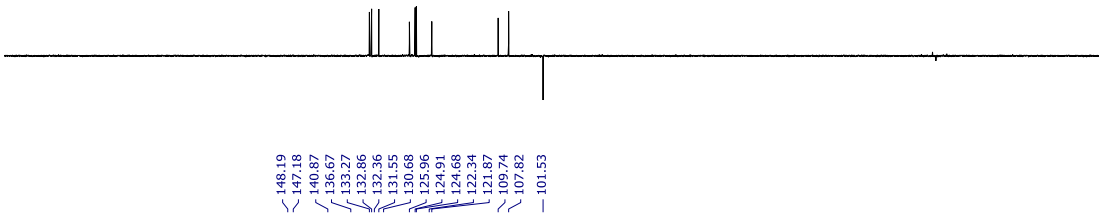


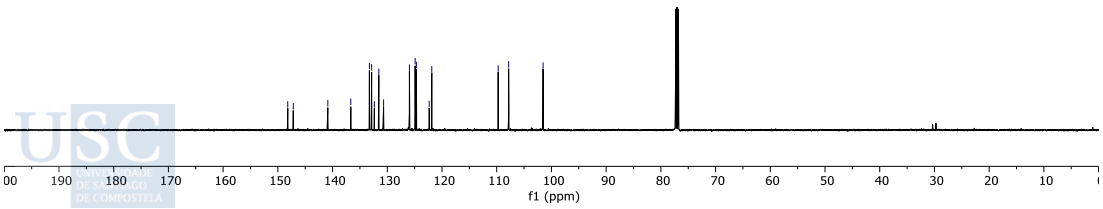
16bq

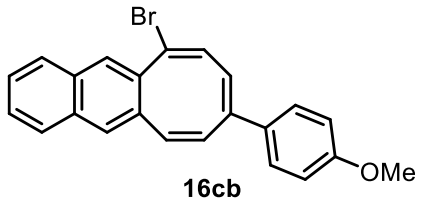
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$





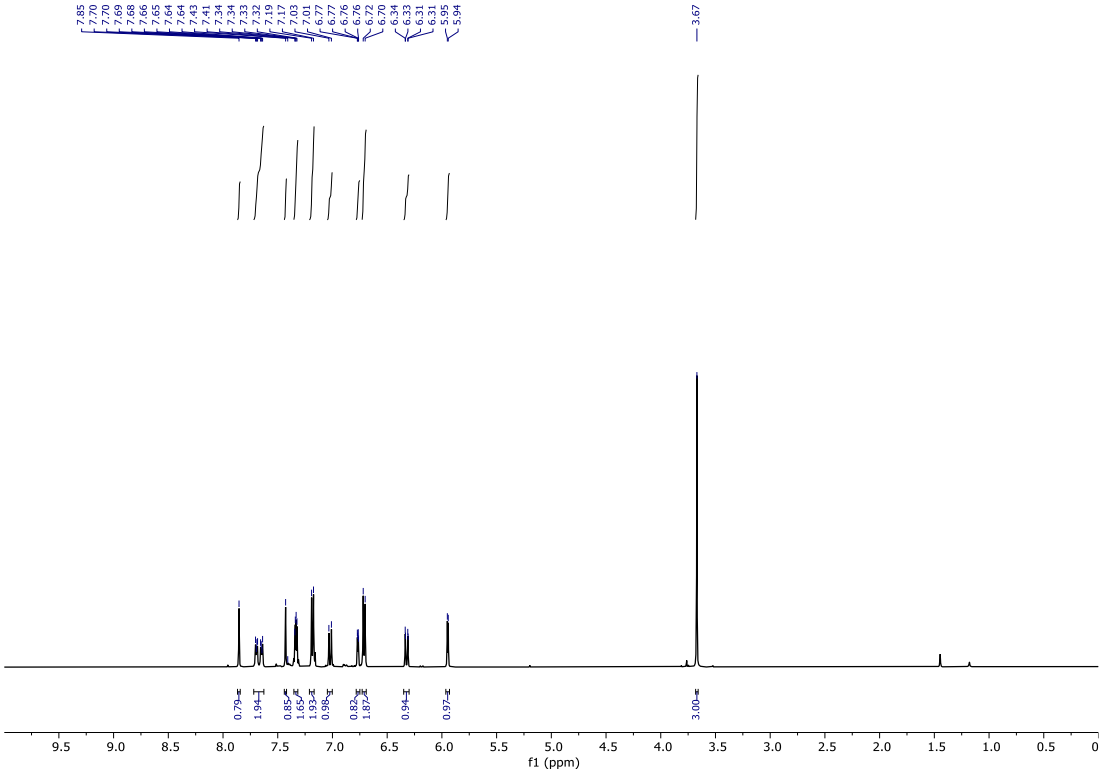


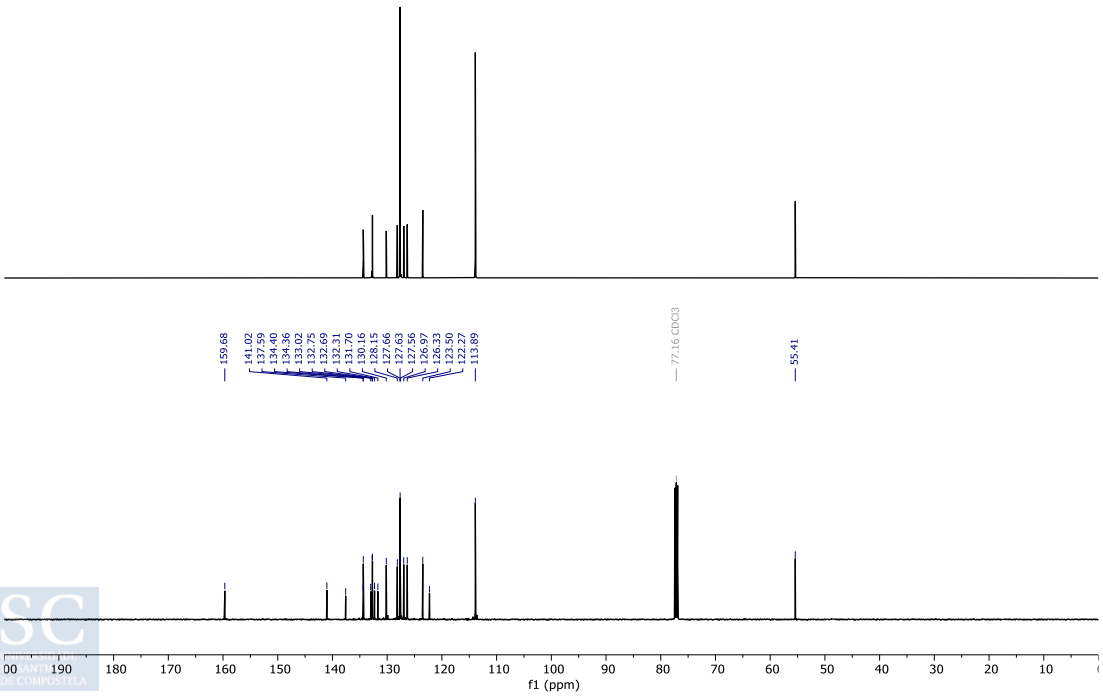


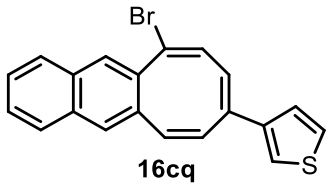


16cb

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

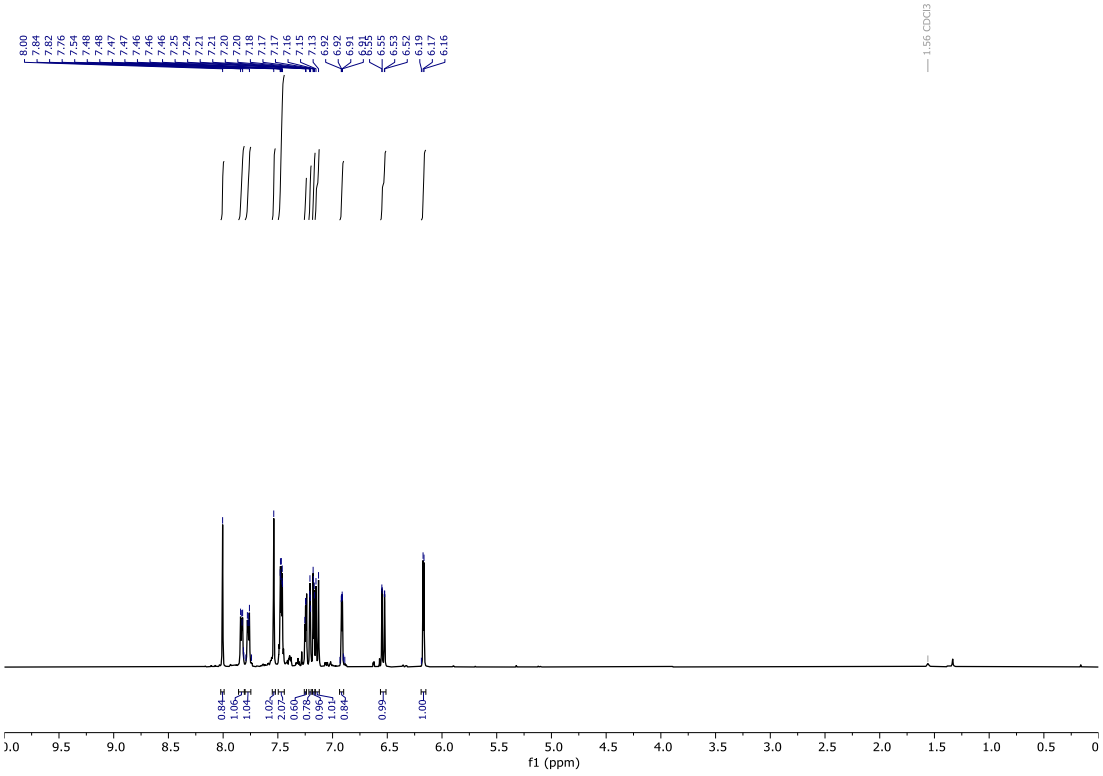


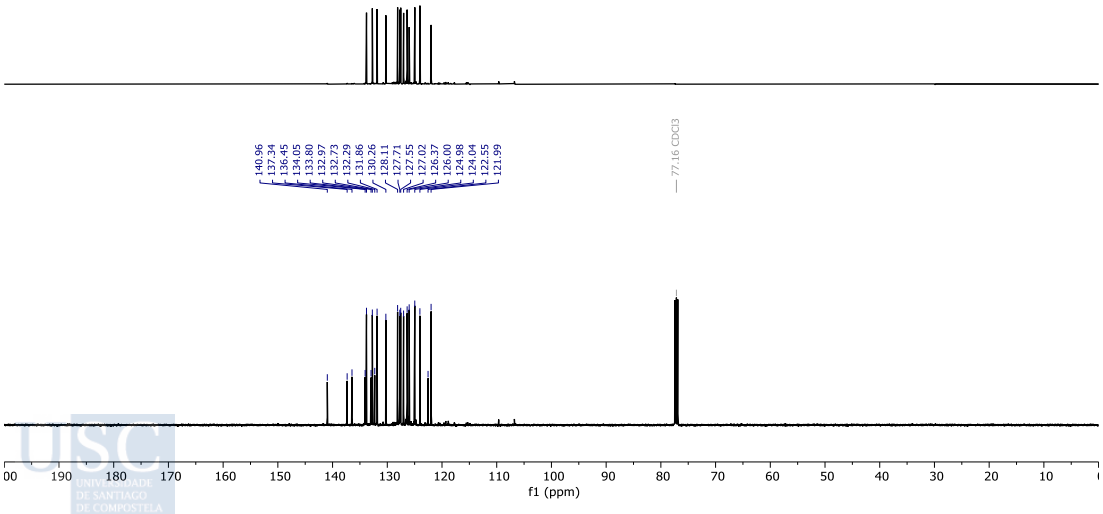


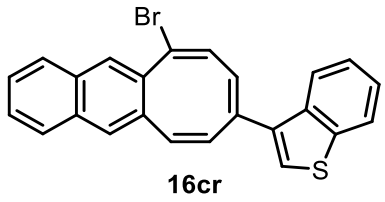


16cq

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

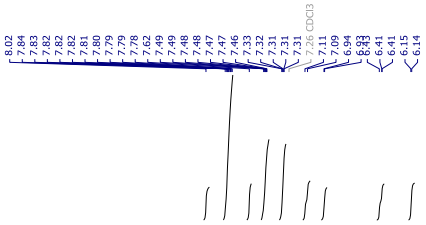


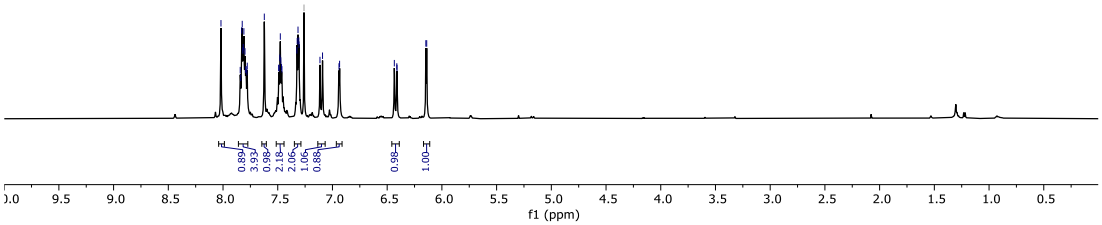


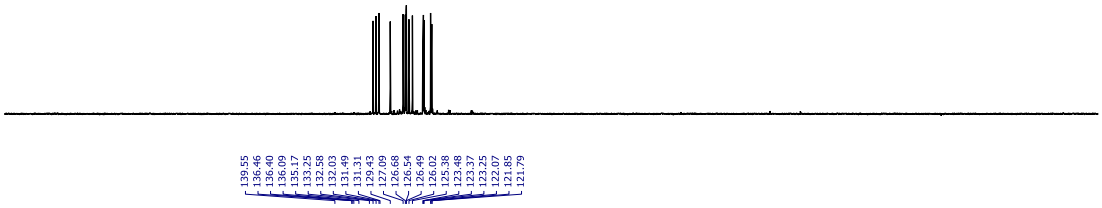


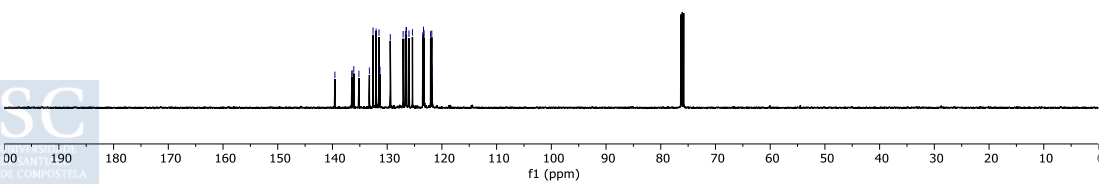
16cr

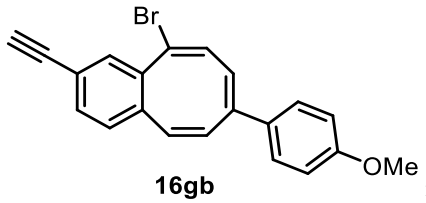
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$





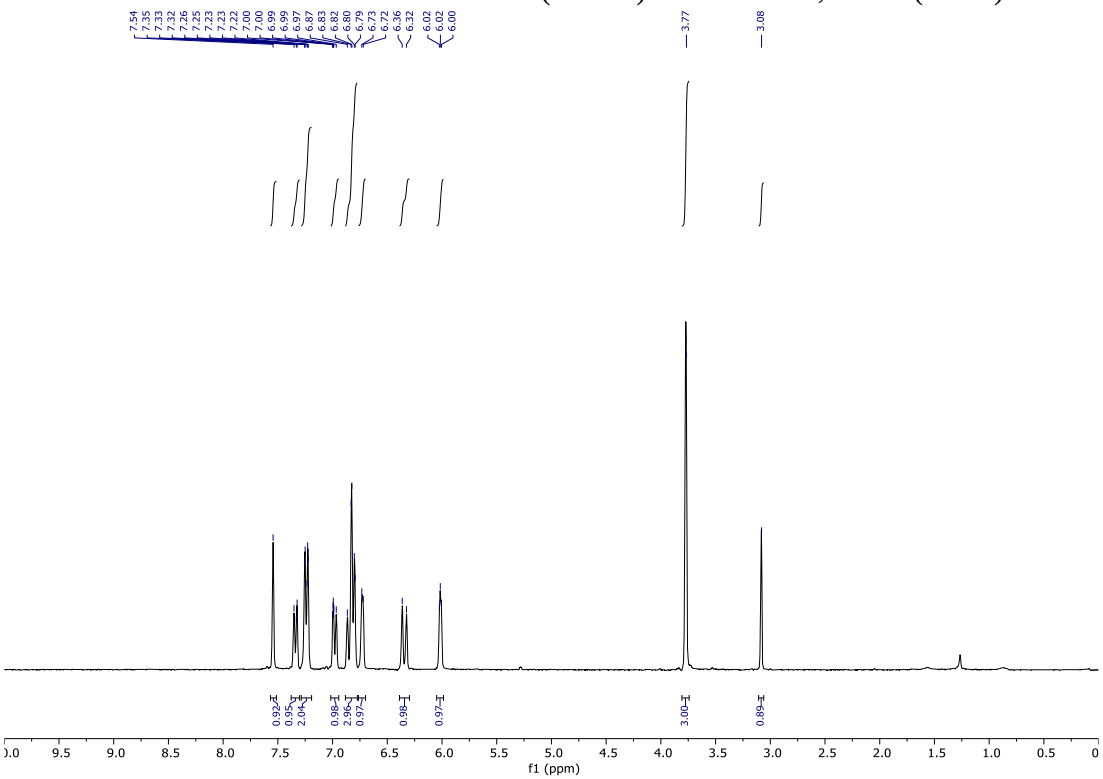


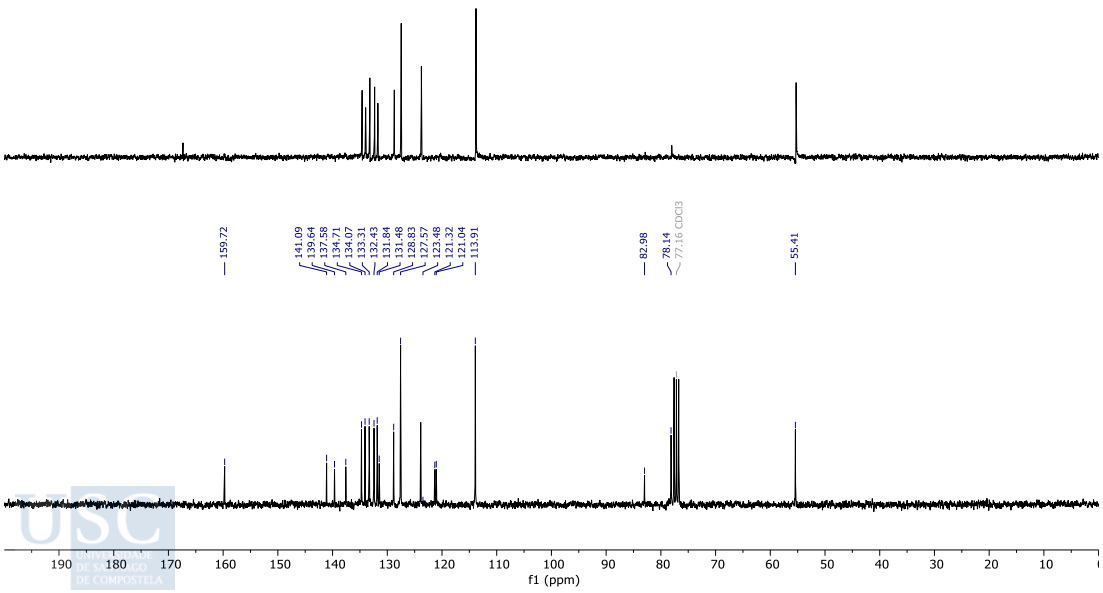


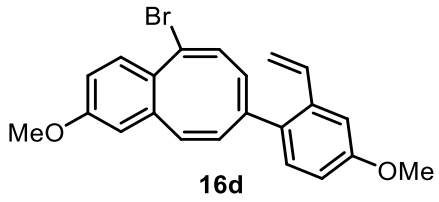


16gb

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

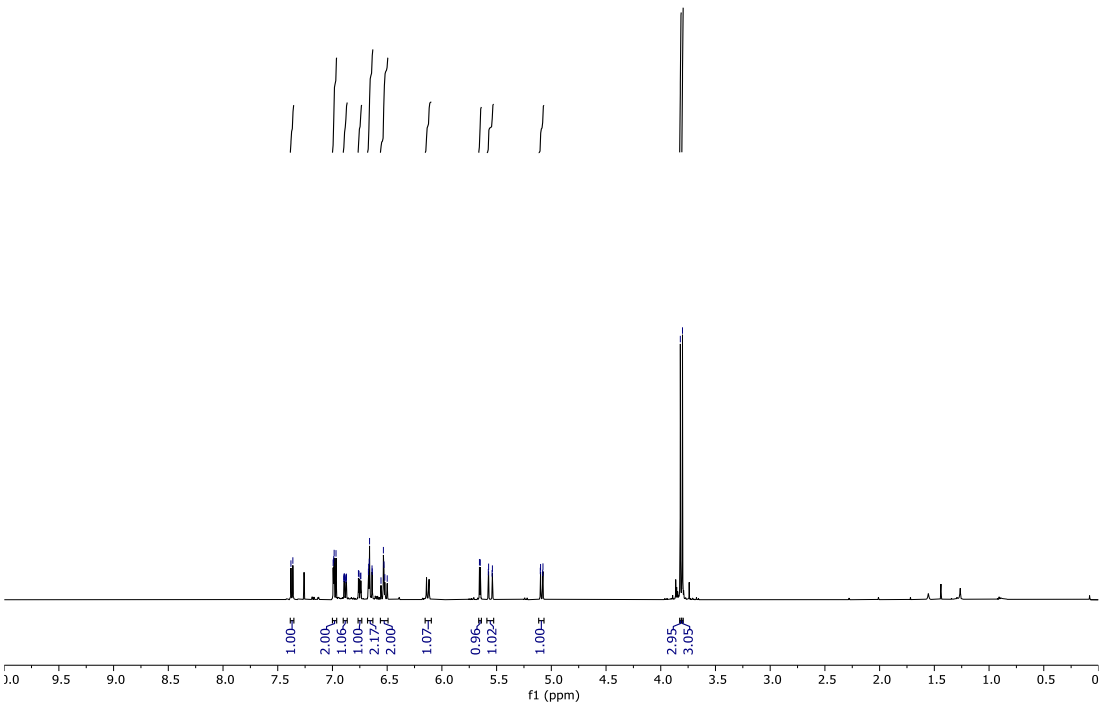


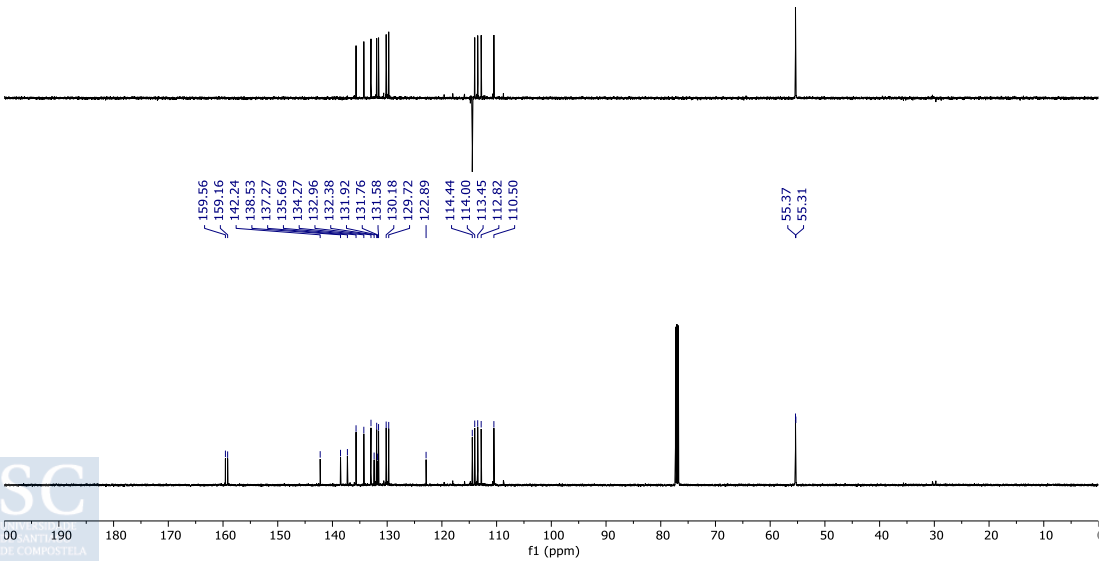


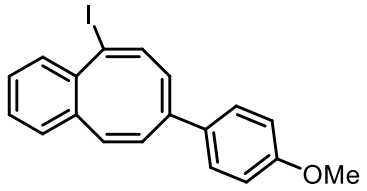


16d

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

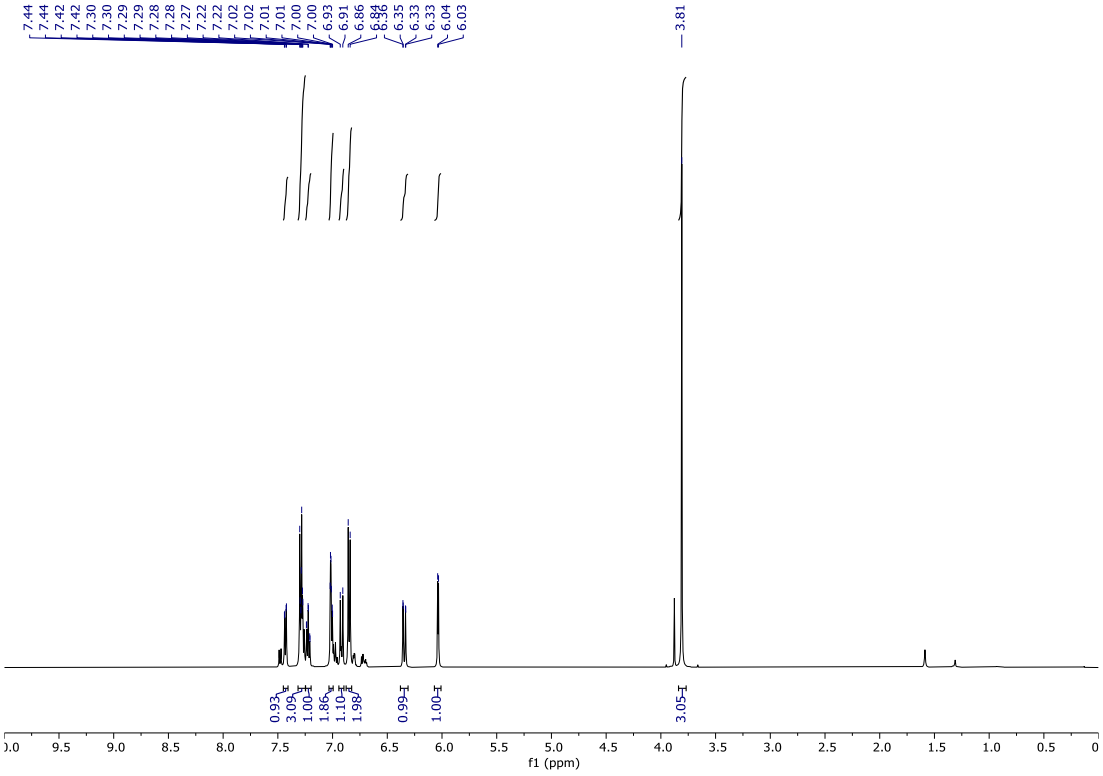


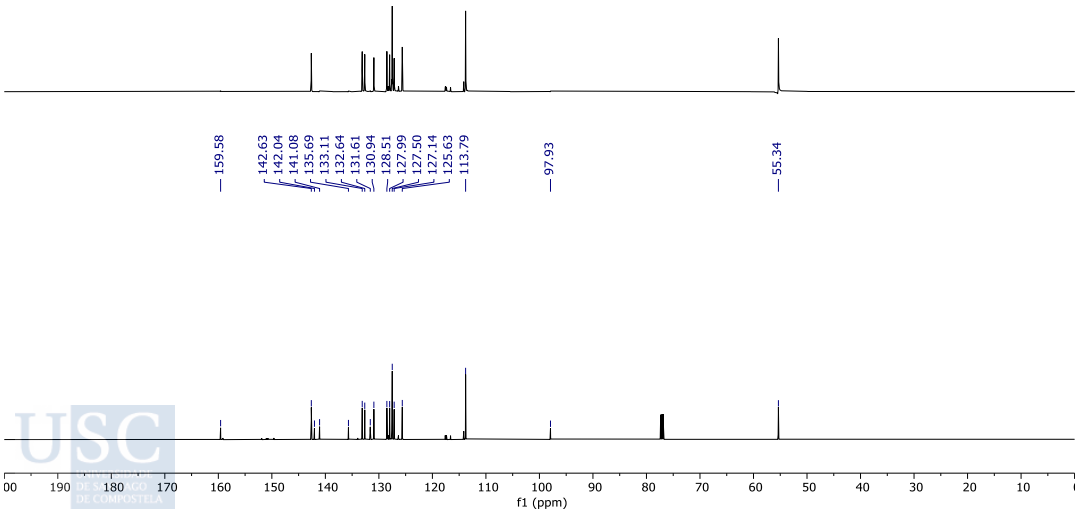


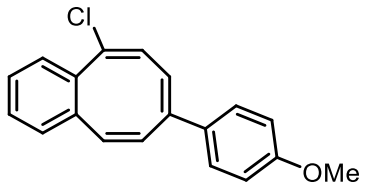


16ab'

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

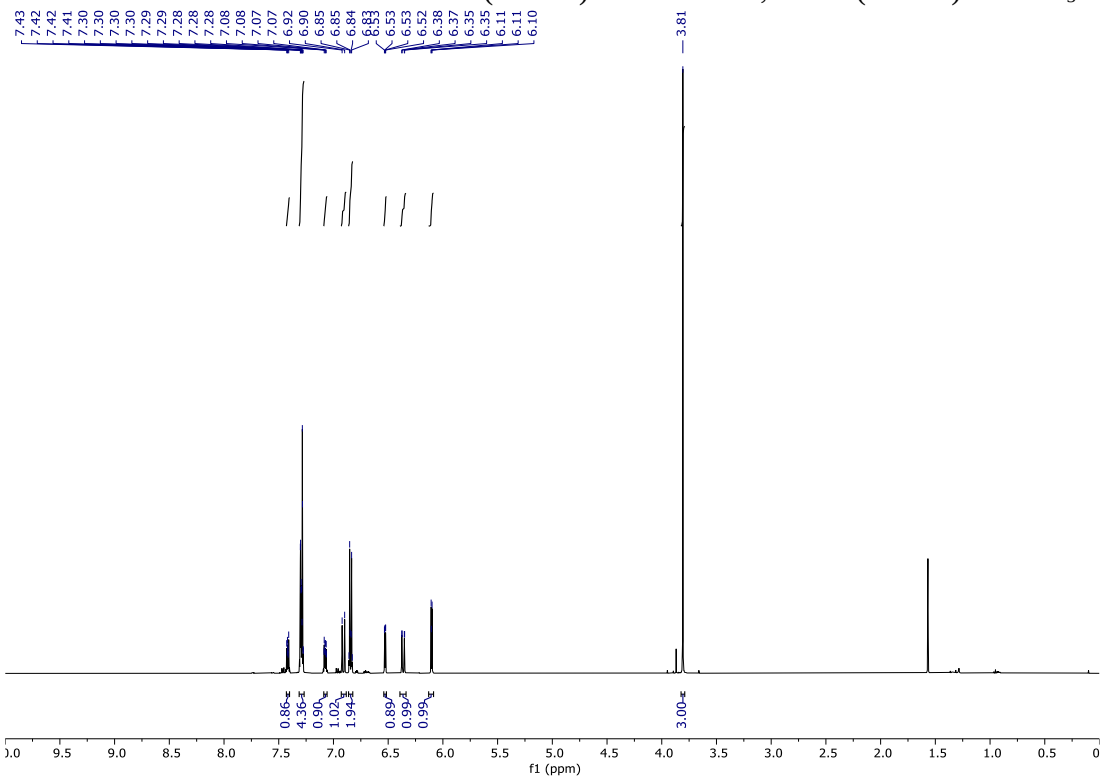


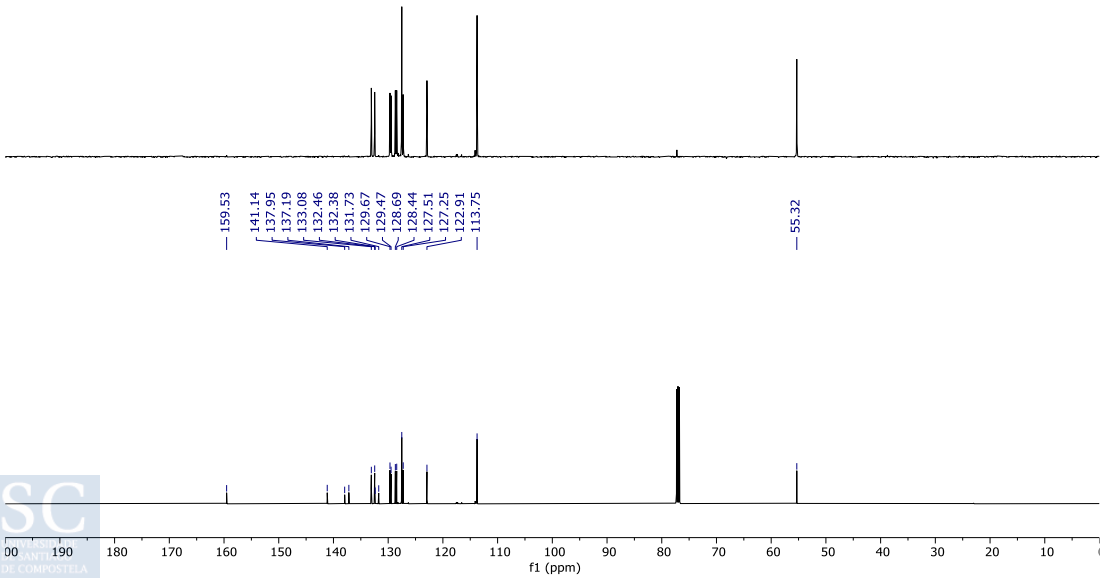


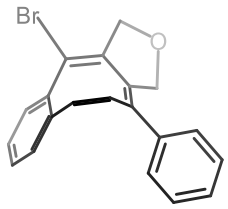


16ab"

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

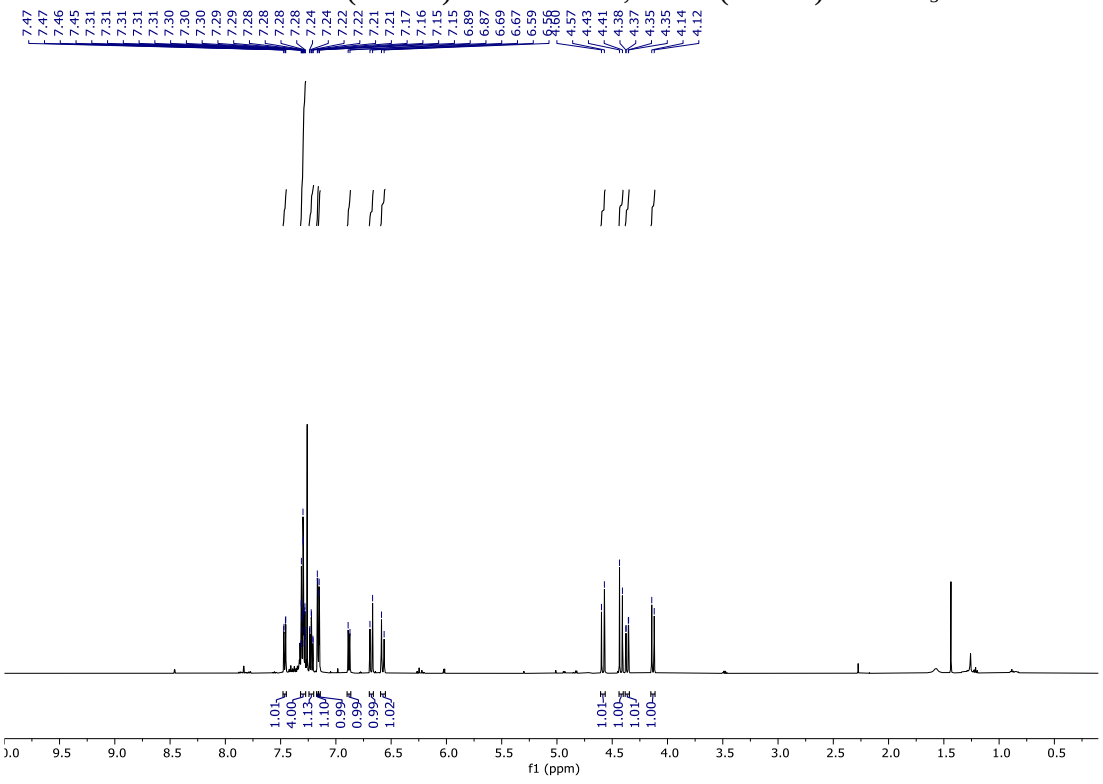


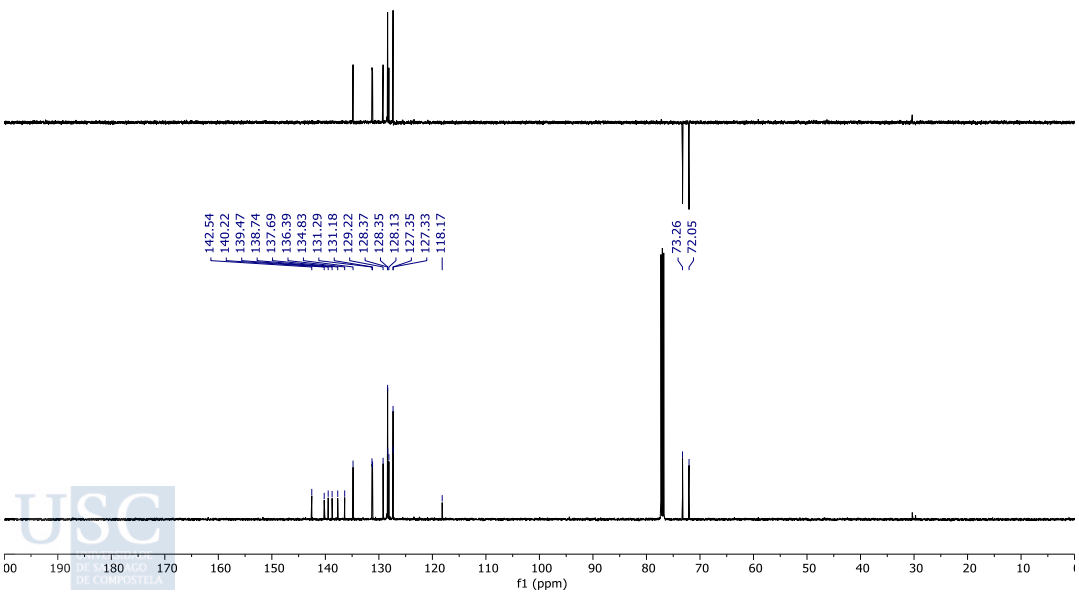


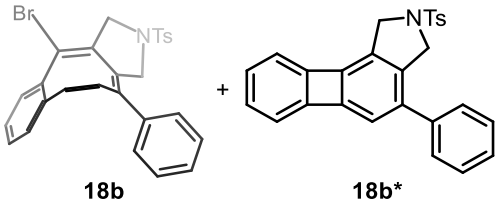


18a

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

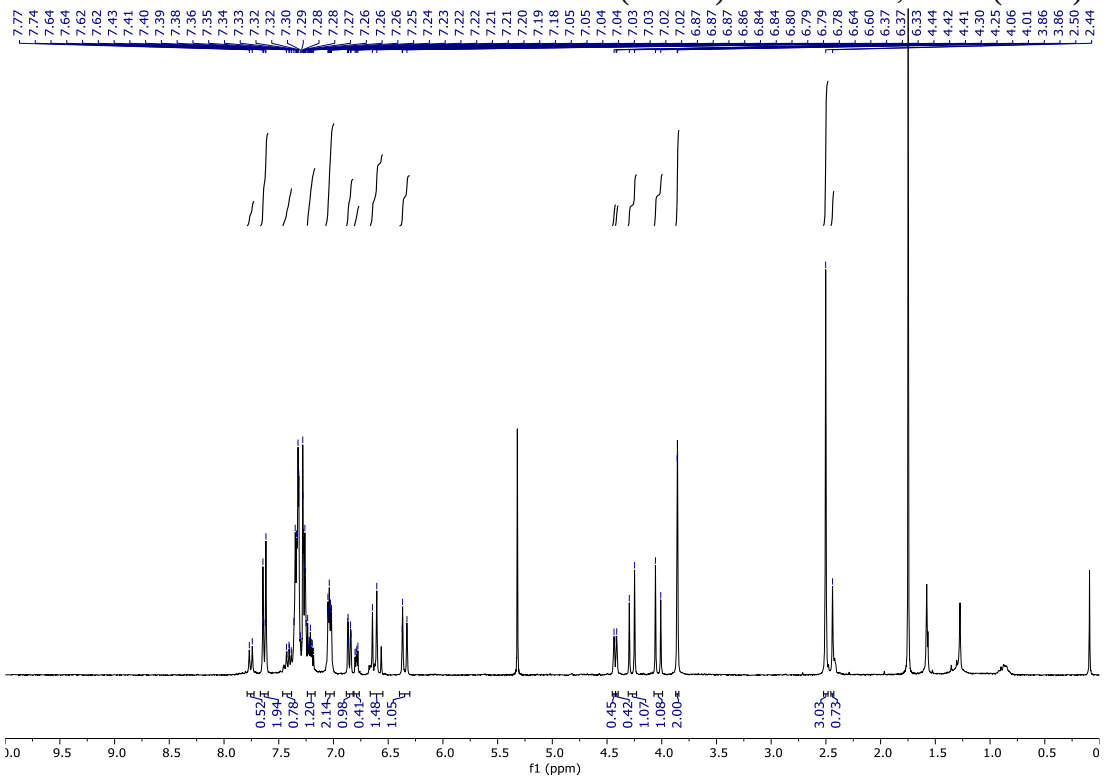


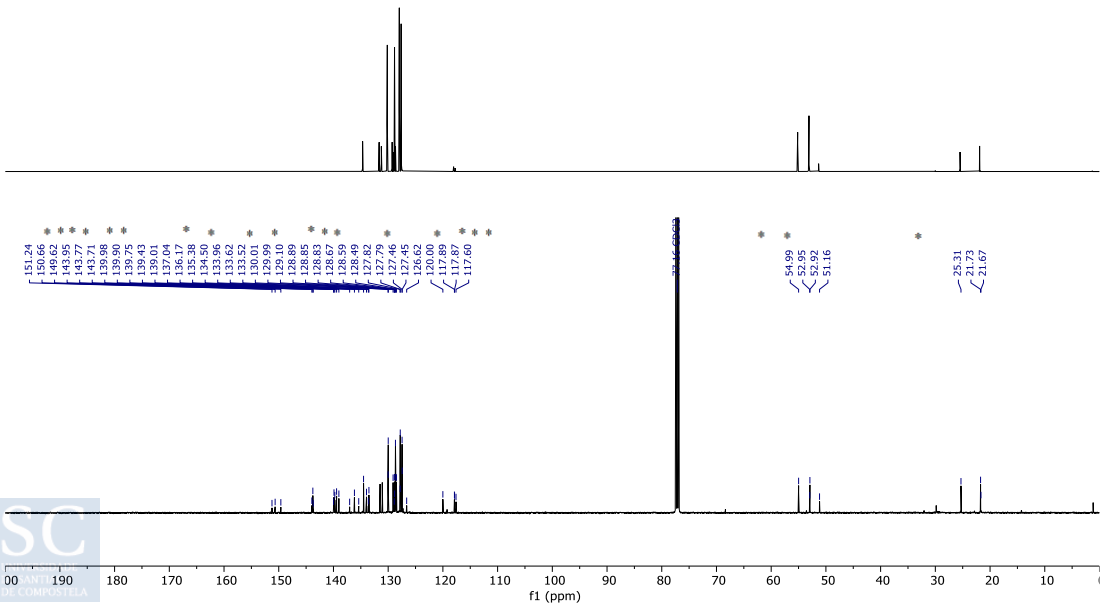




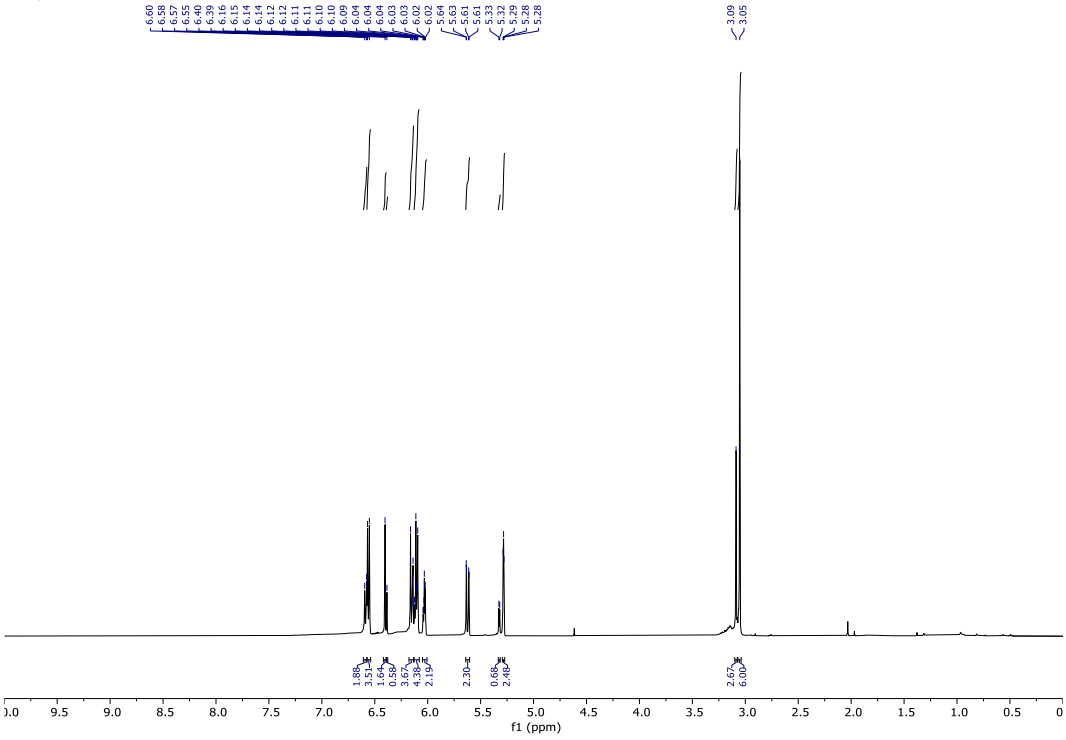
18b **18b***

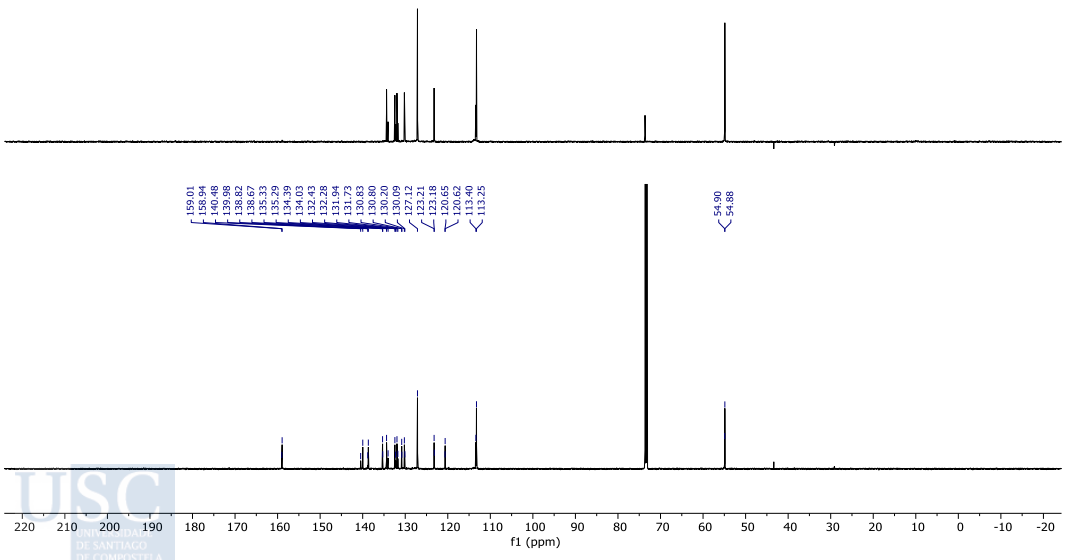
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

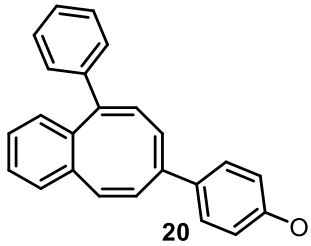




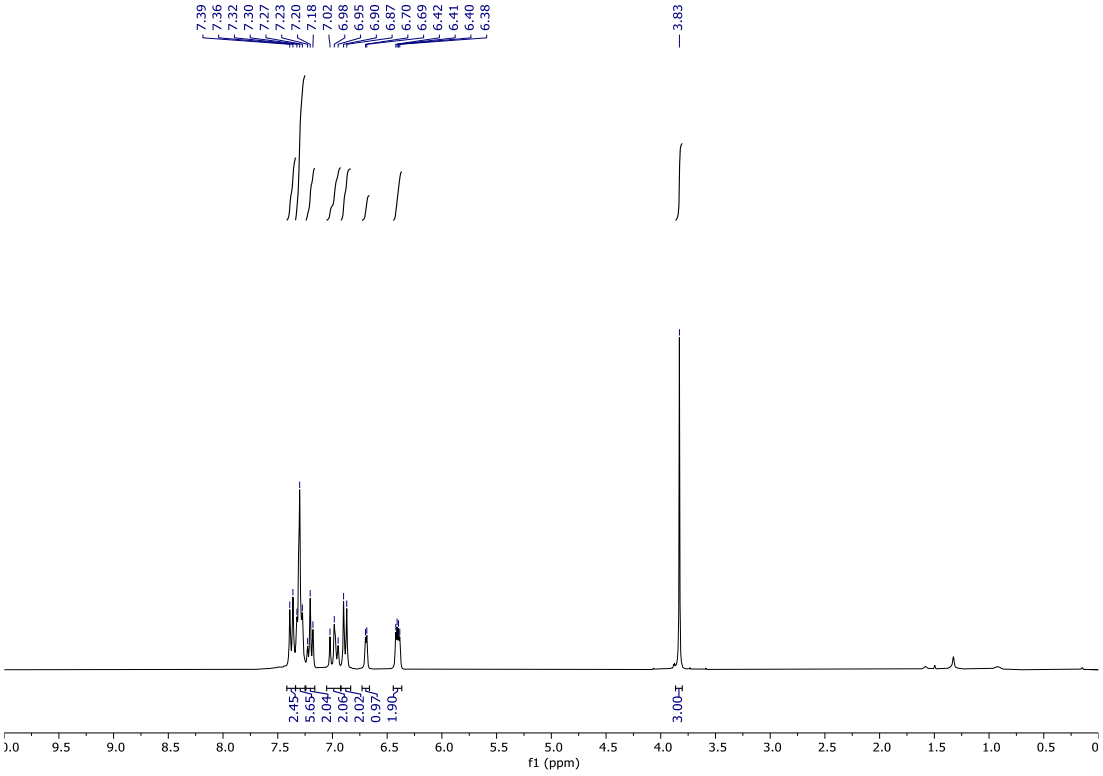
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in 1,1,2,2-tetrachloroethane-d_2

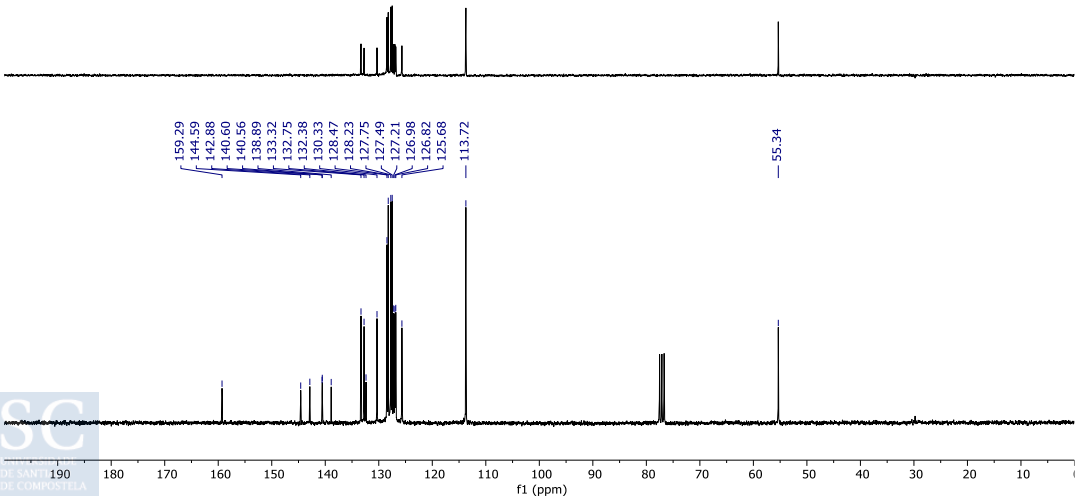


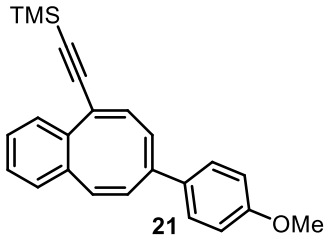




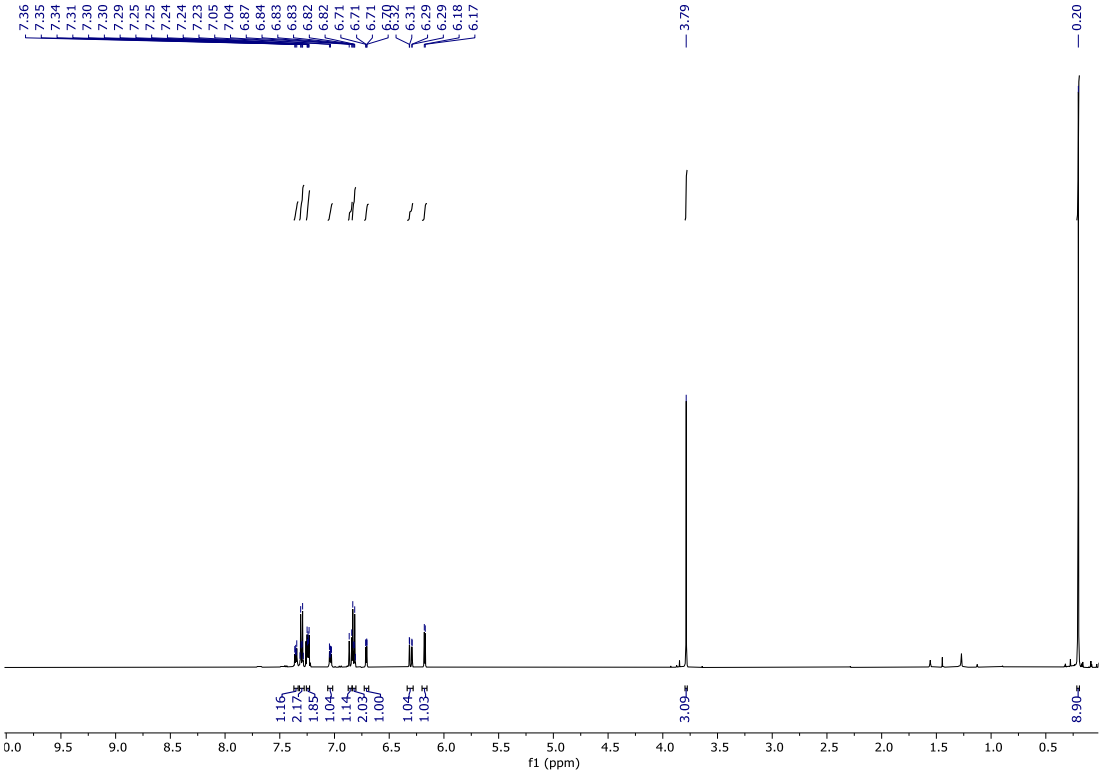
20 ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

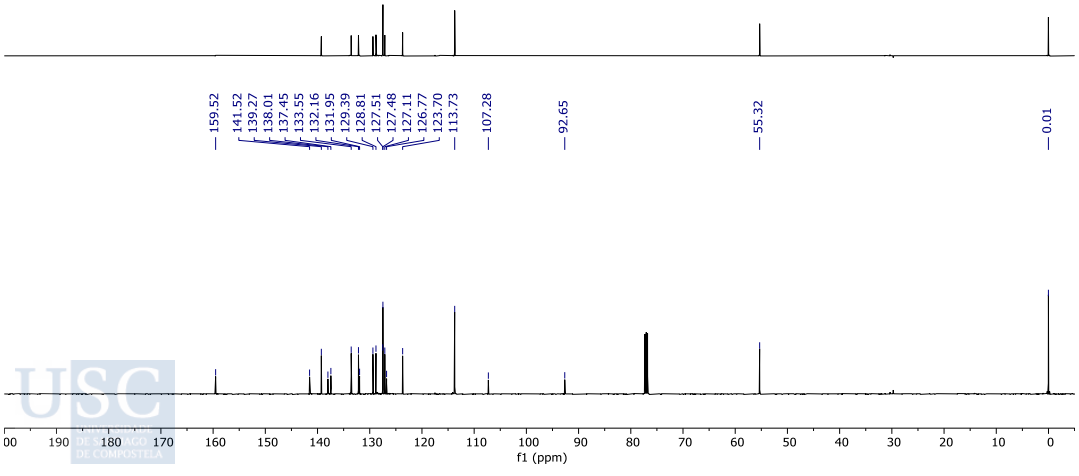


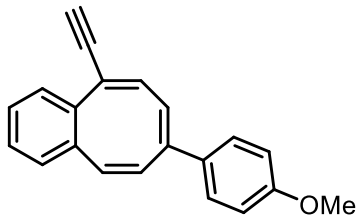




21 ^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

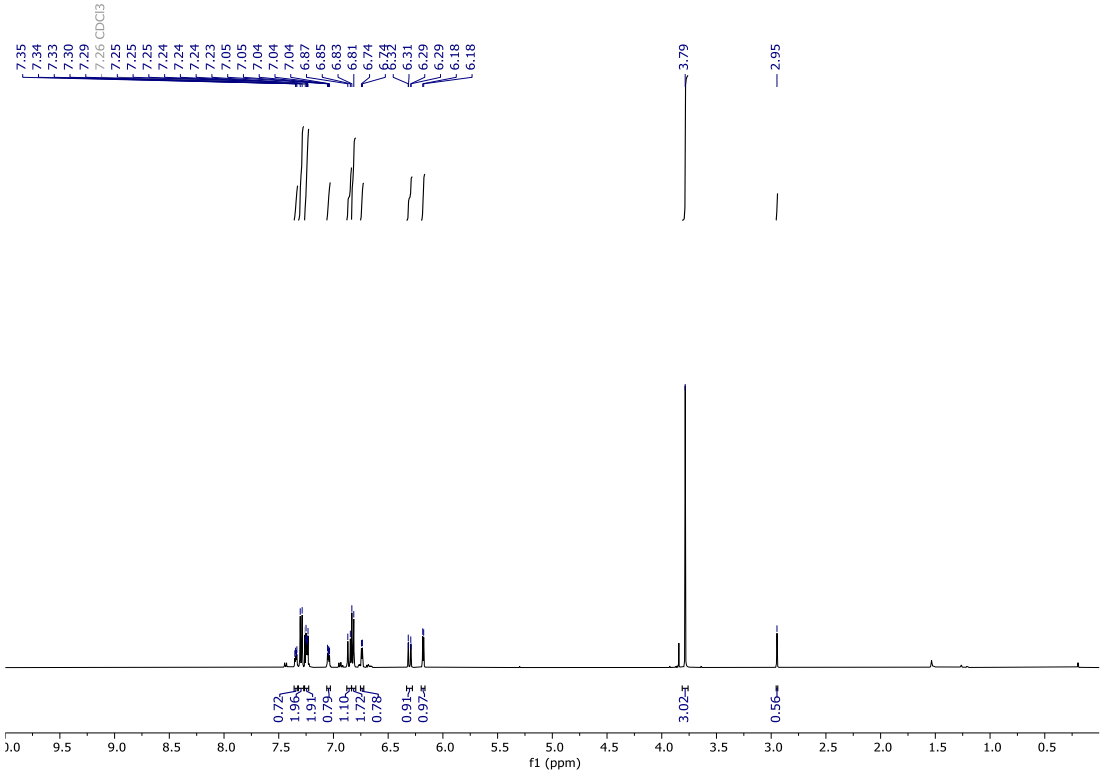


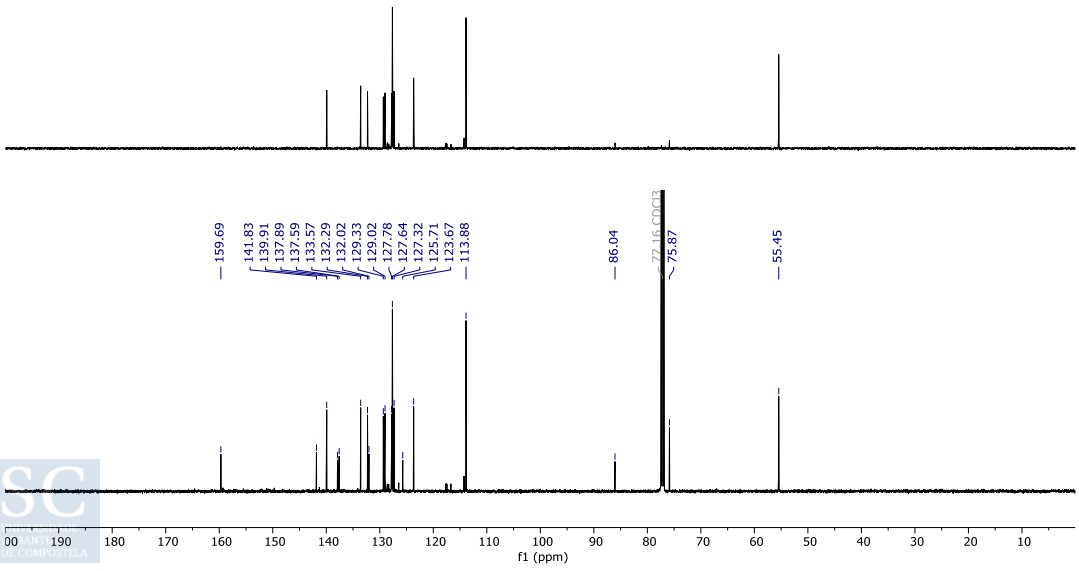


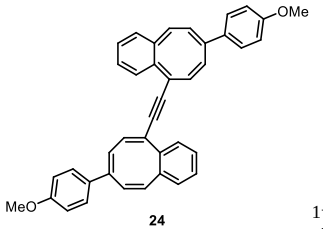


23

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

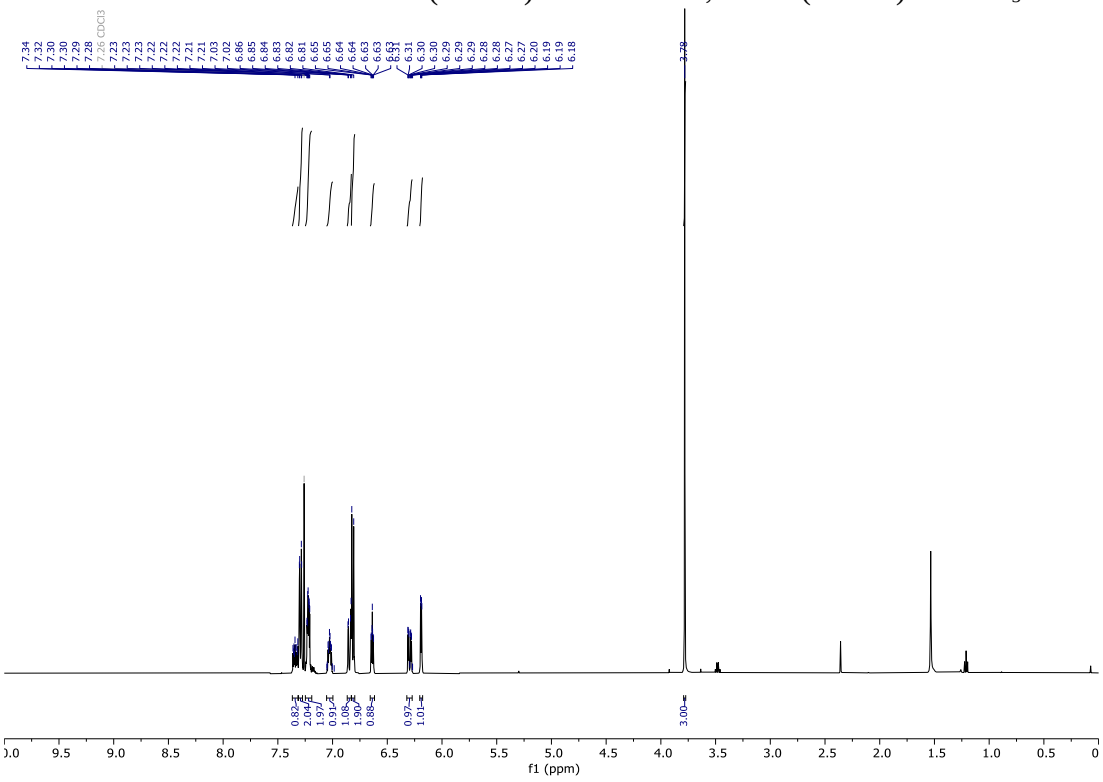


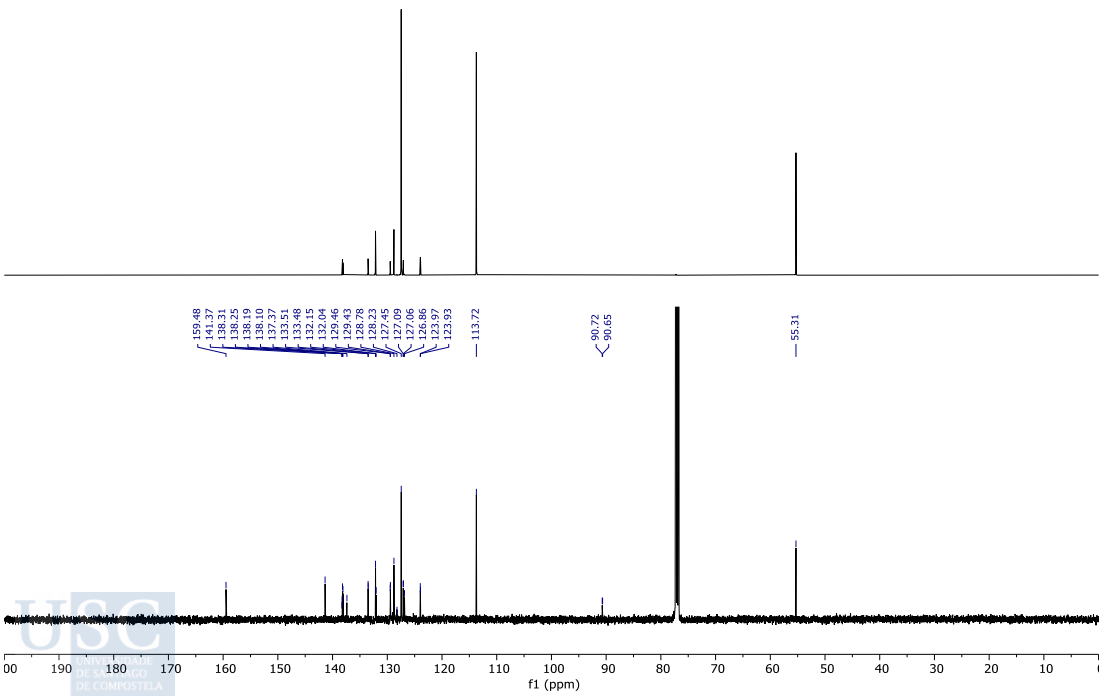


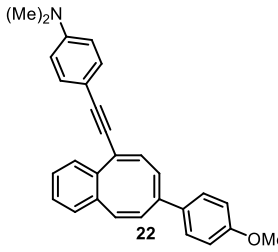


24

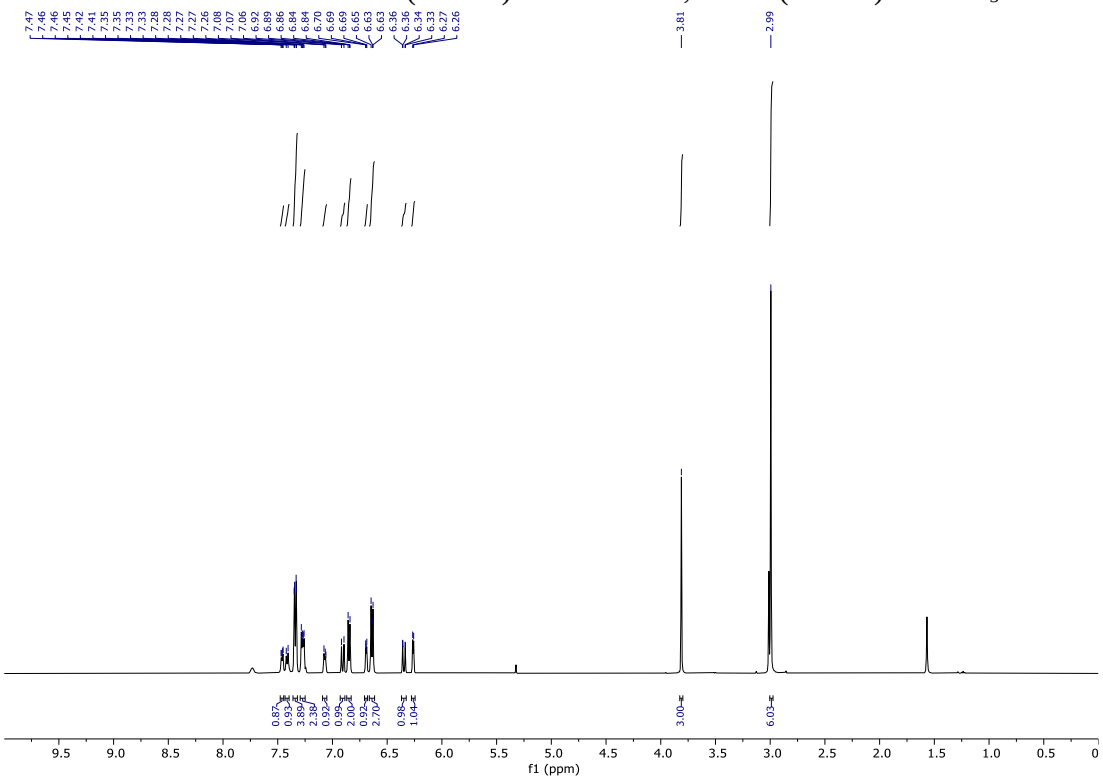
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

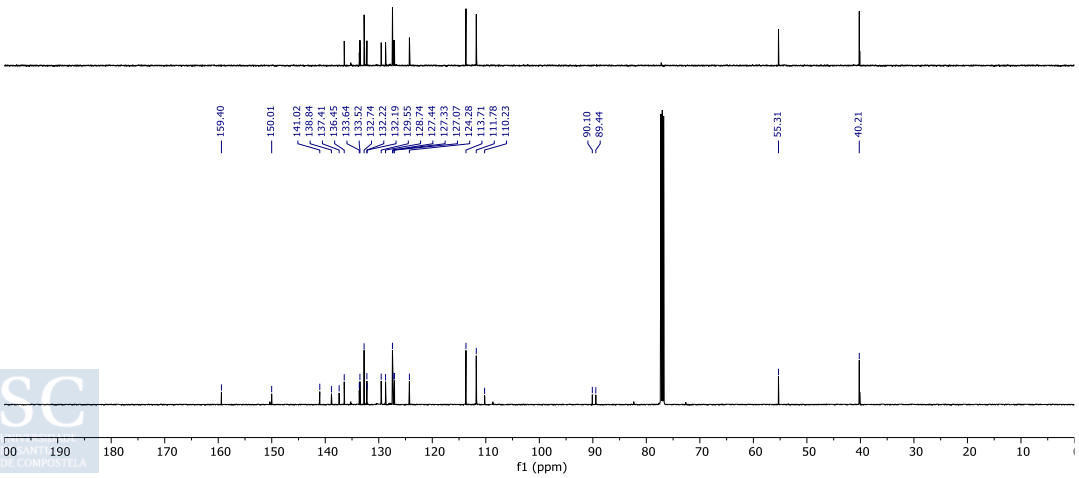


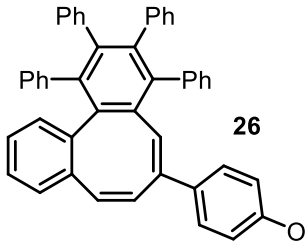




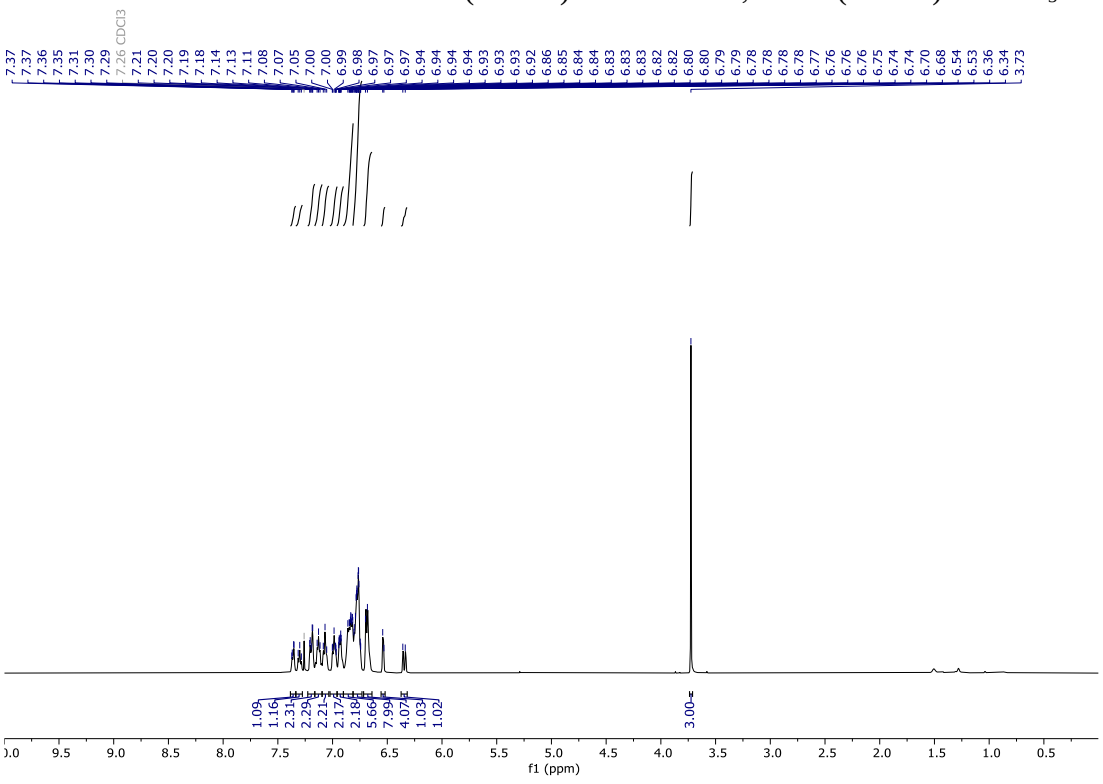
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

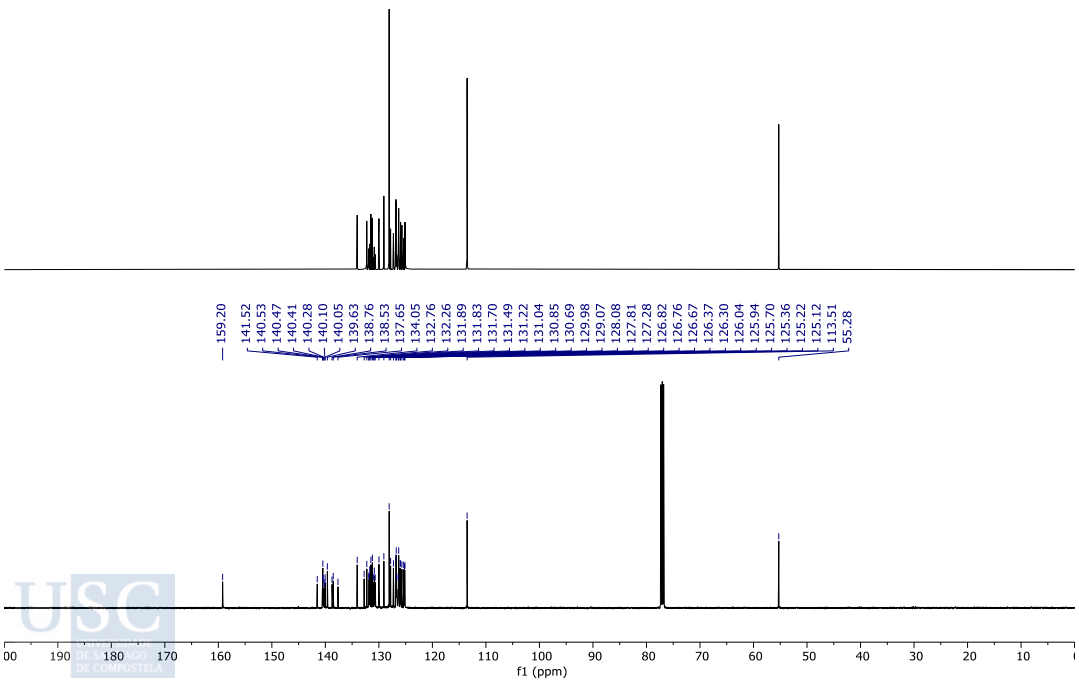


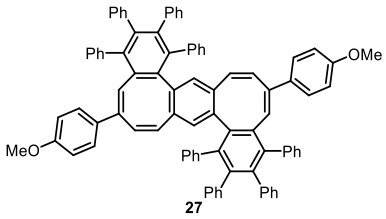




^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

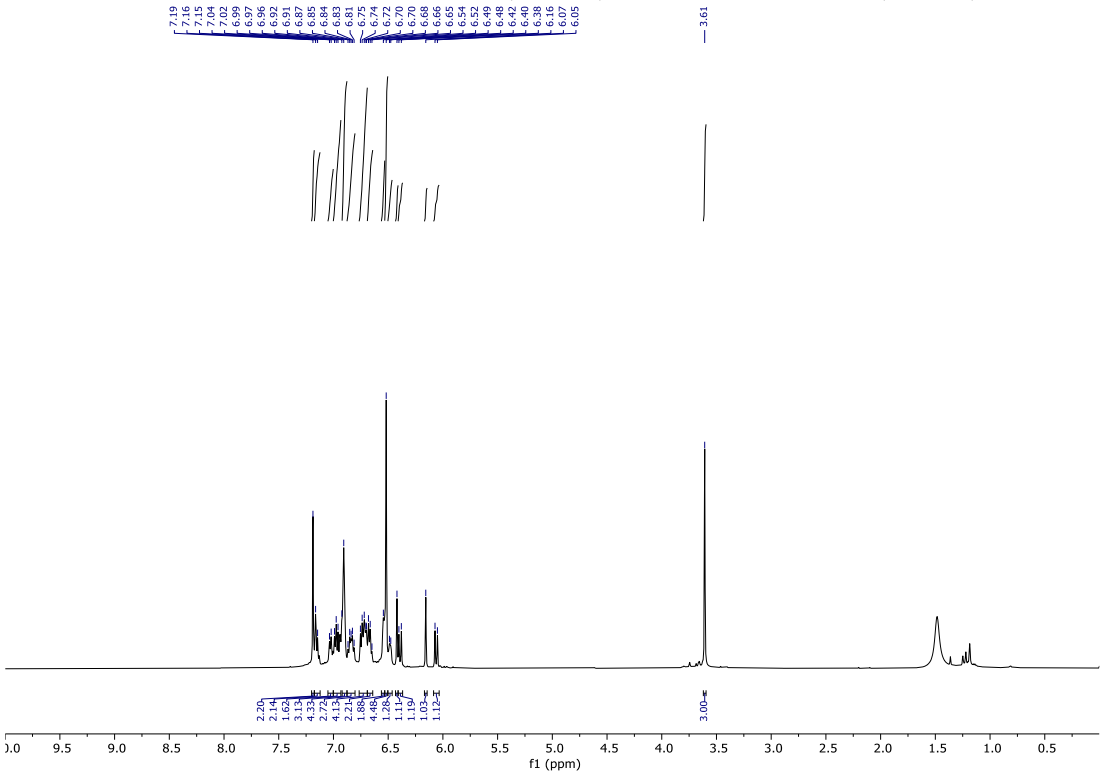


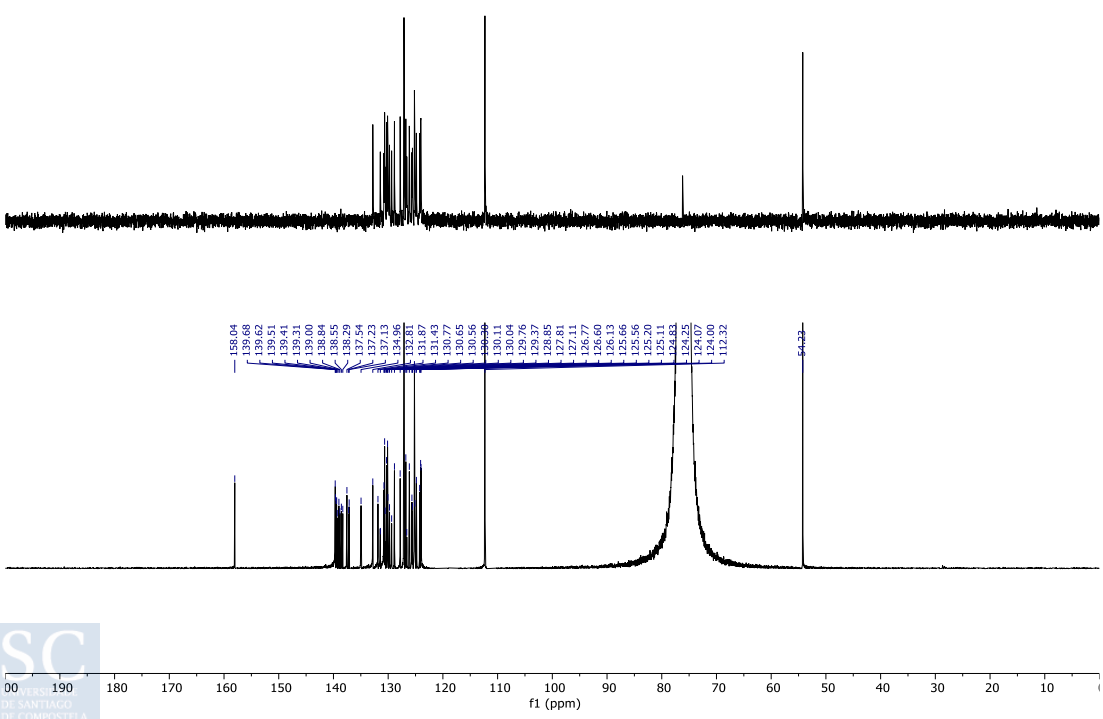


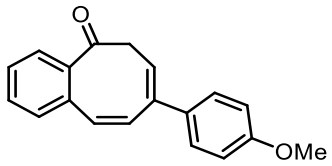


27

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

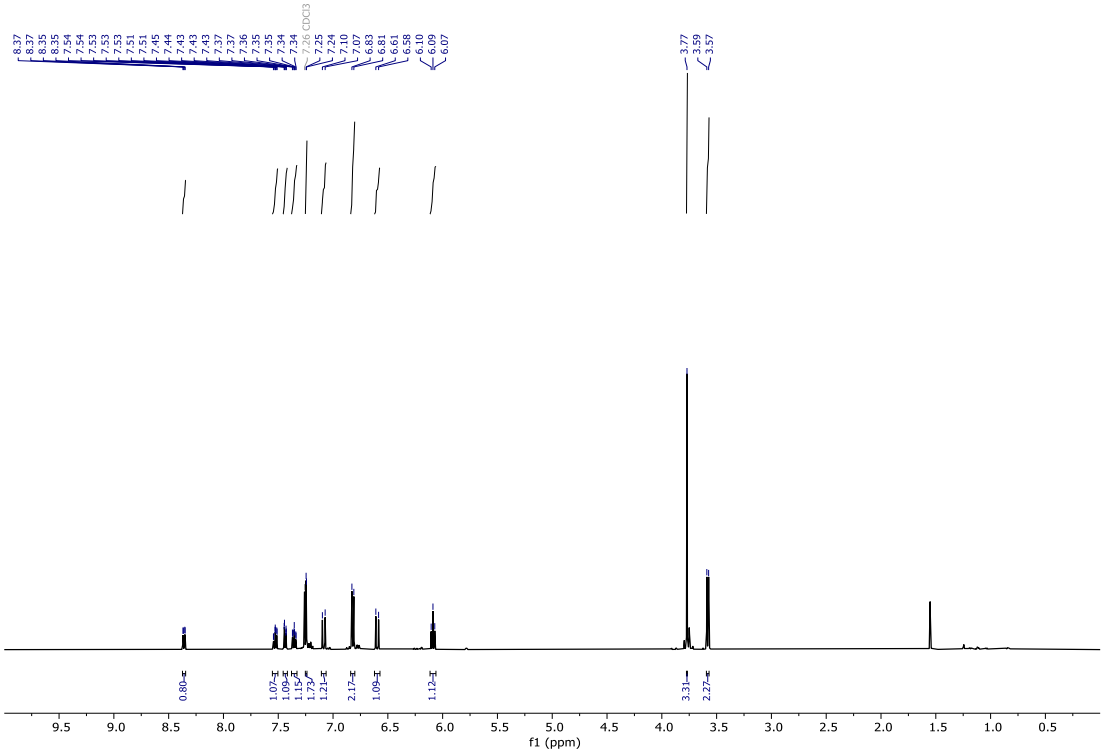


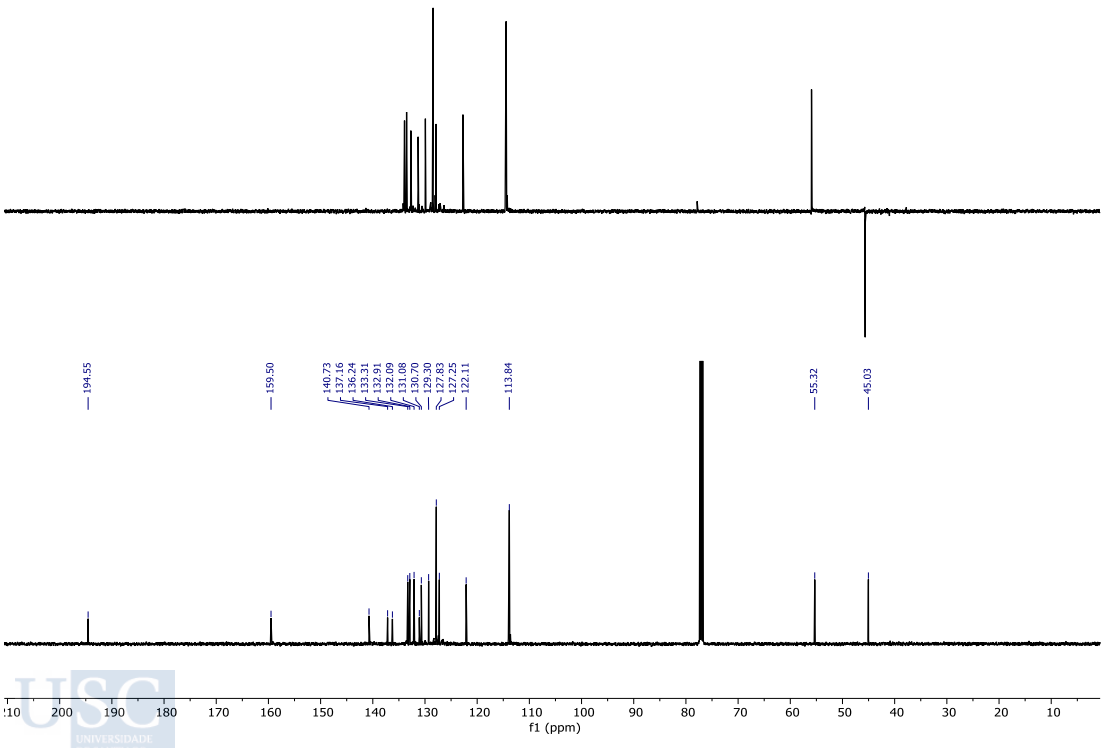


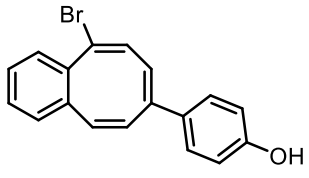


55

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

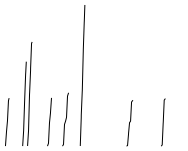


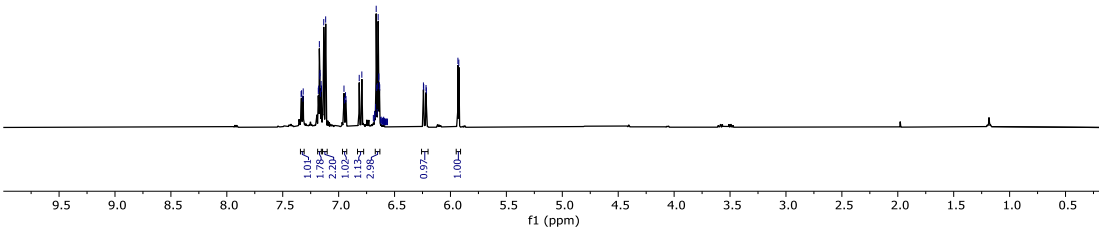


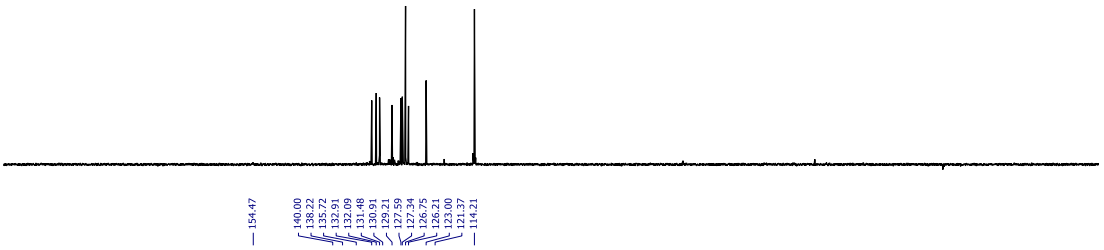


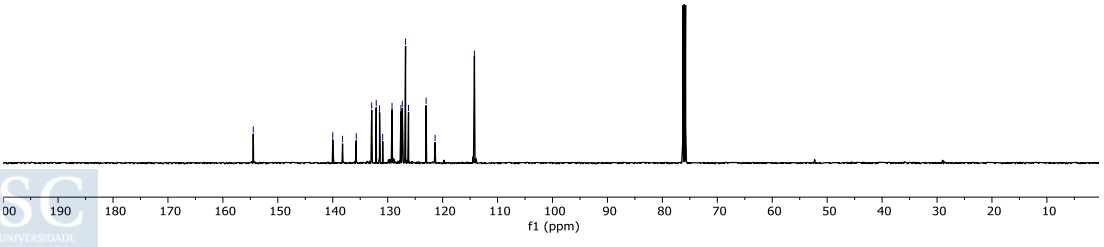
57

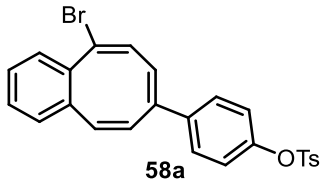
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$



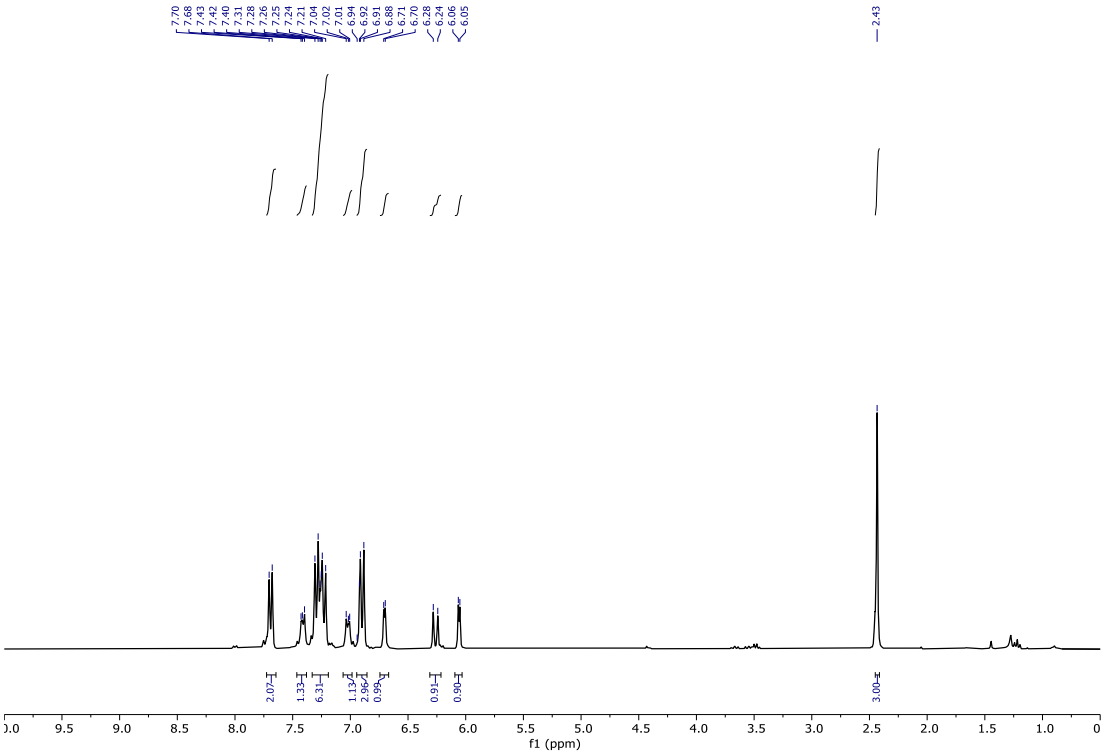


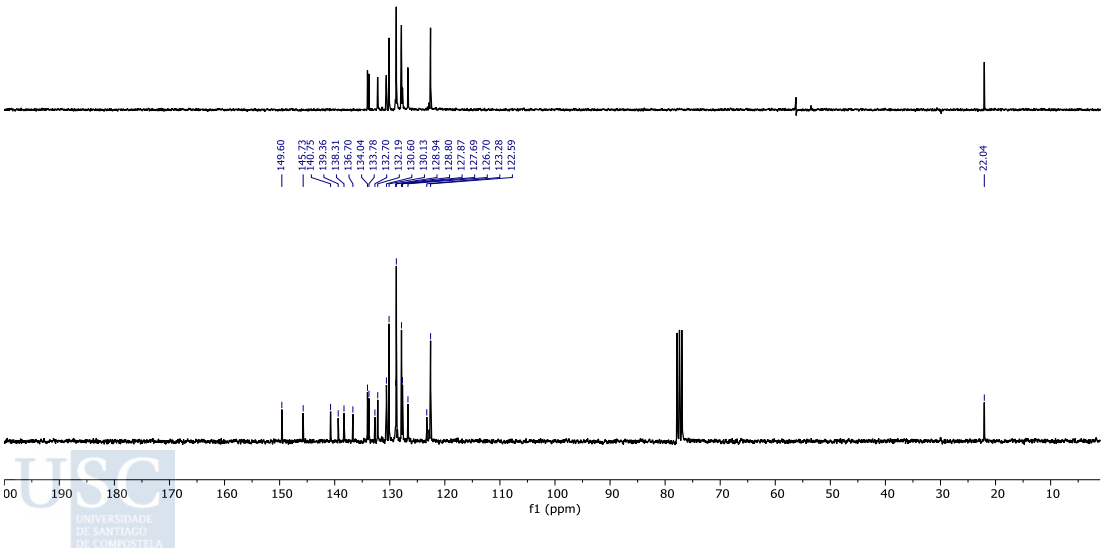


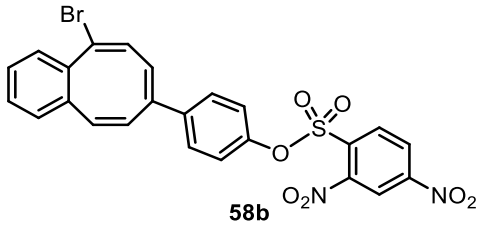




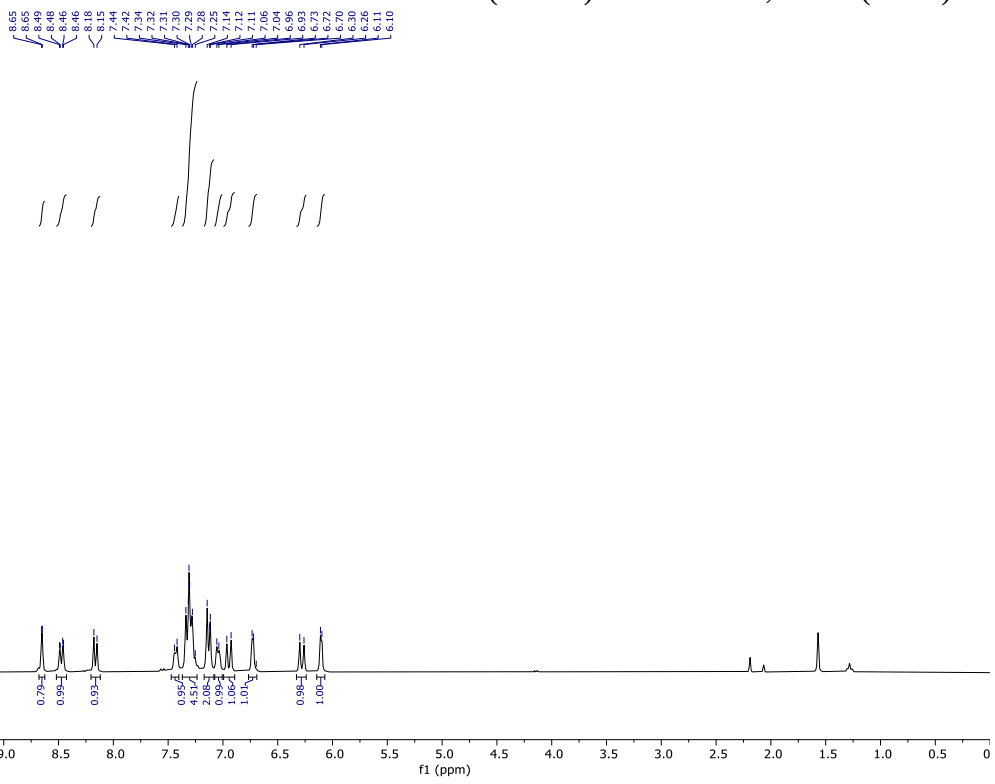
58a ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

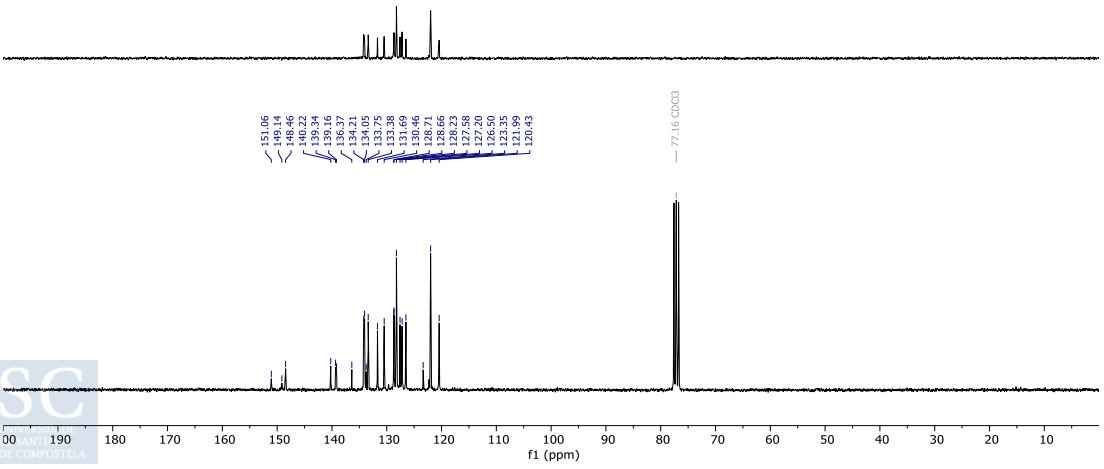


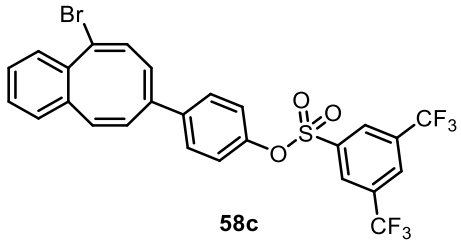




58b ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

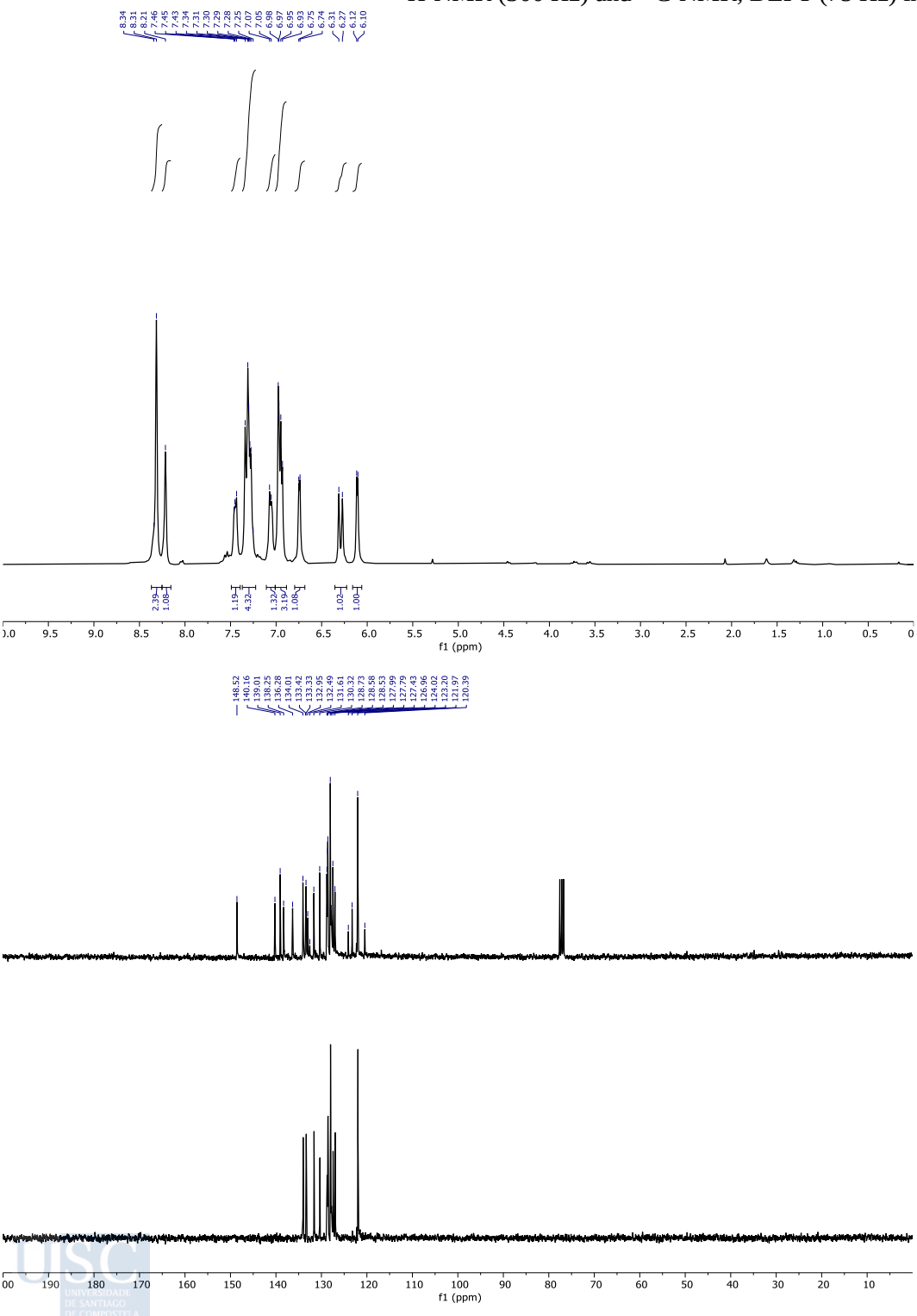


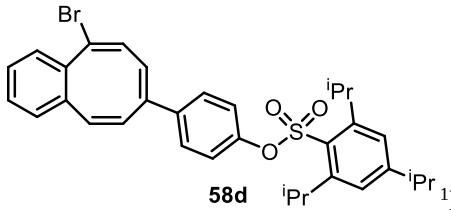




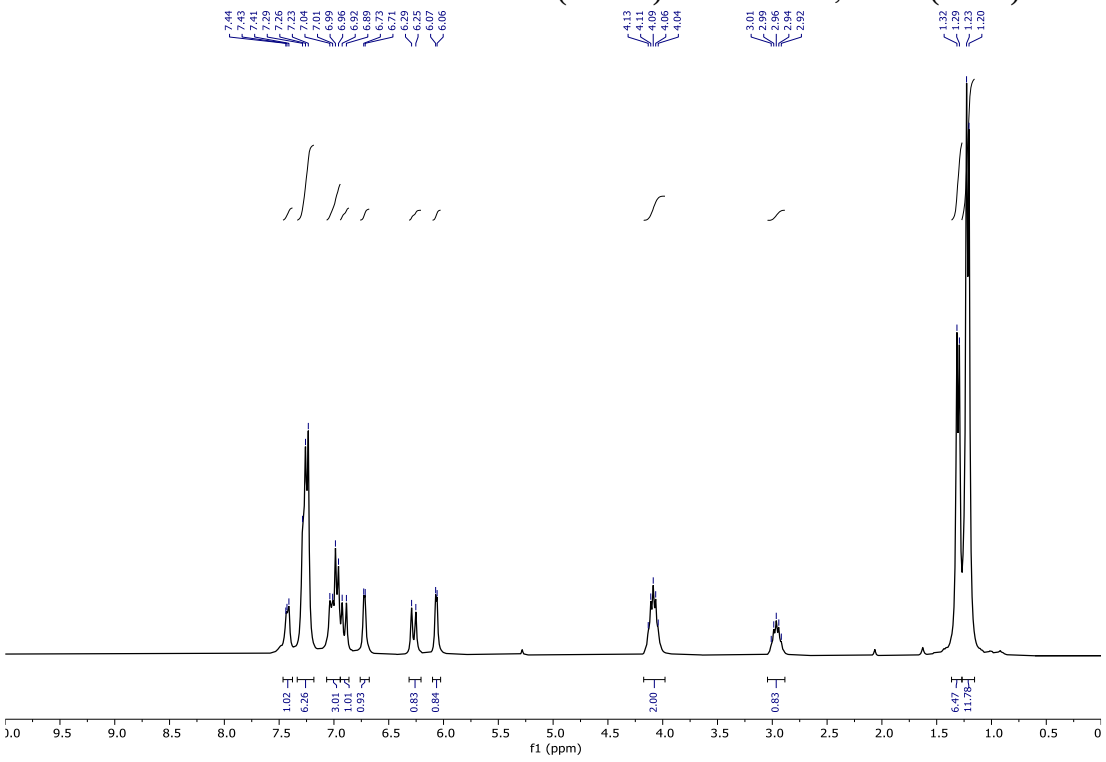
58c

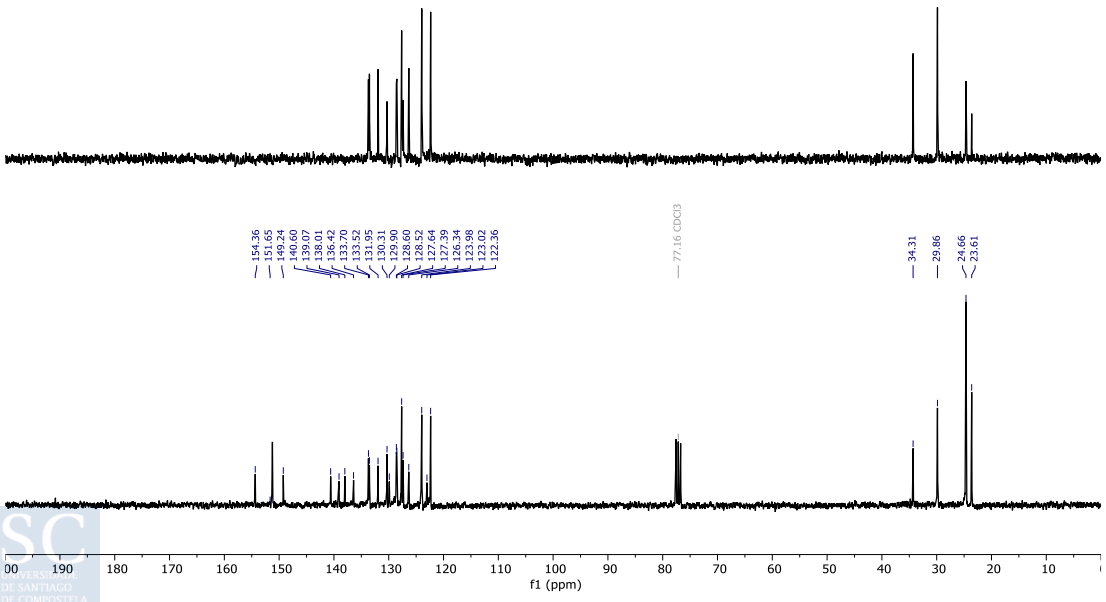
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

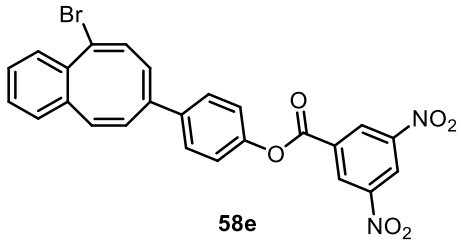




58d ^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

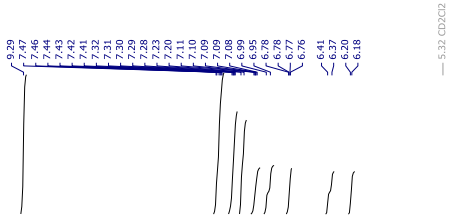


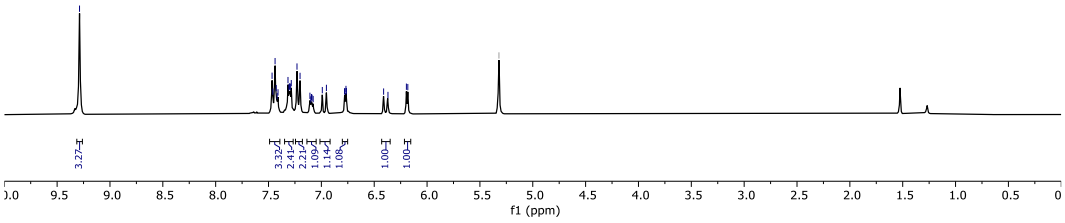


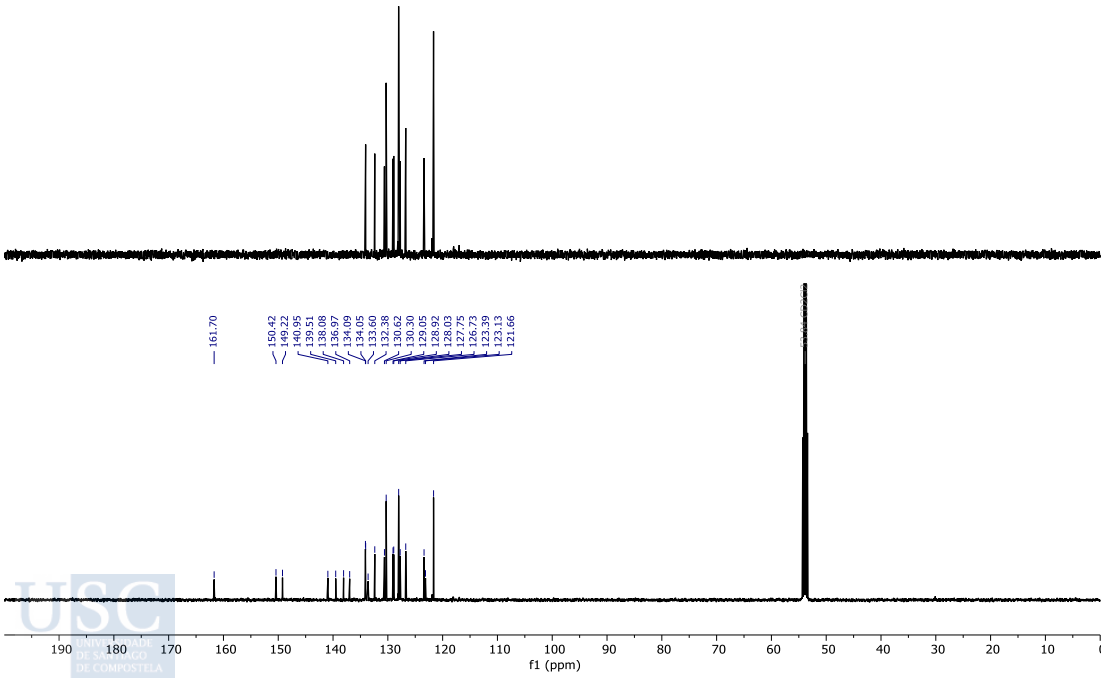


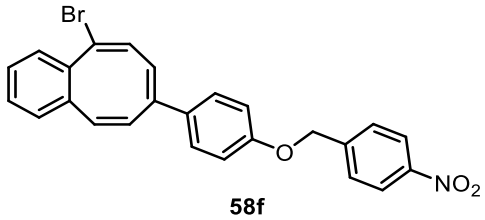
58e

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$



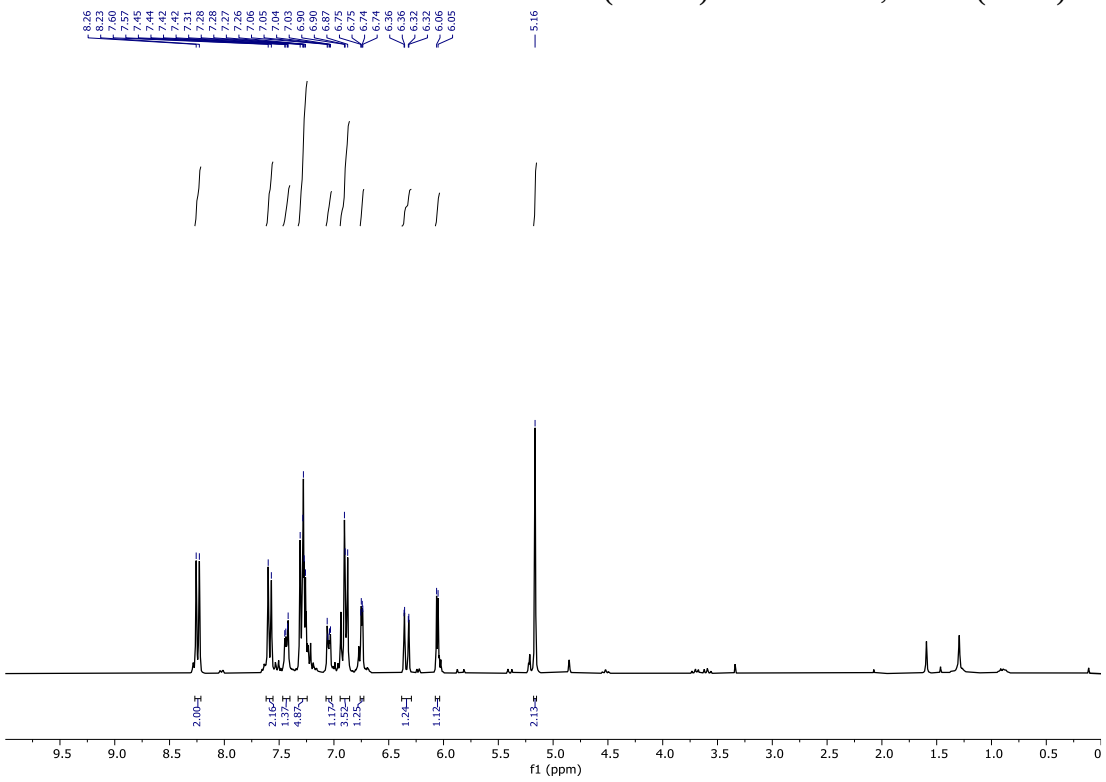


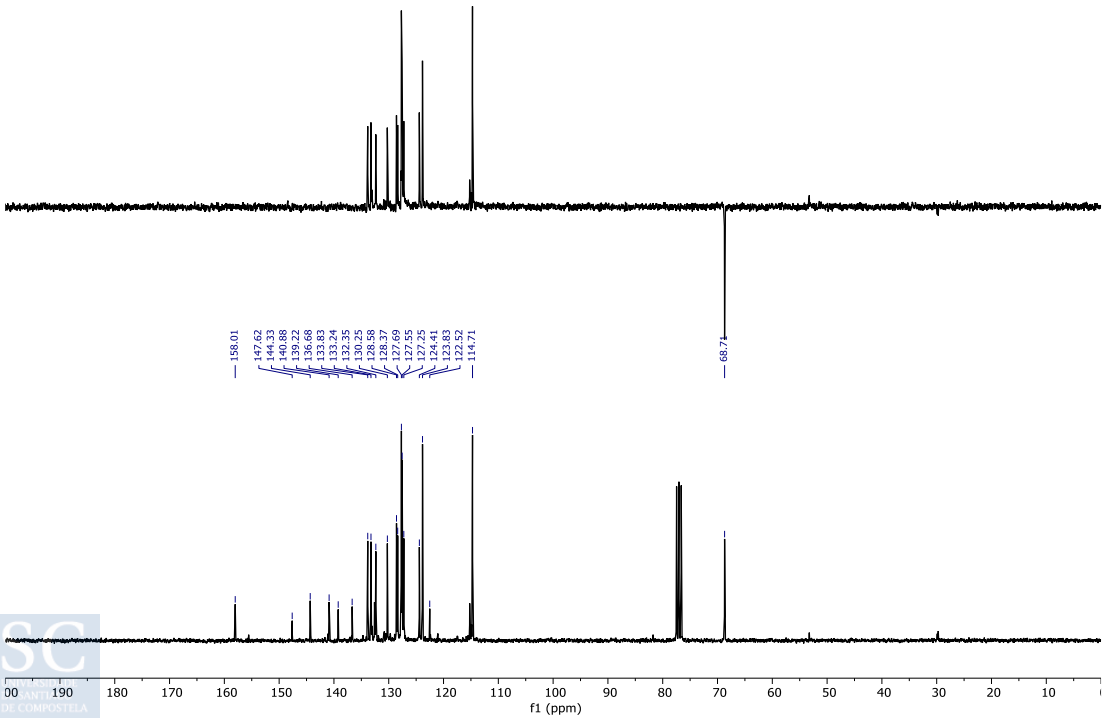


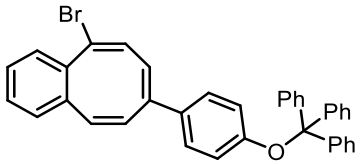


58f

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

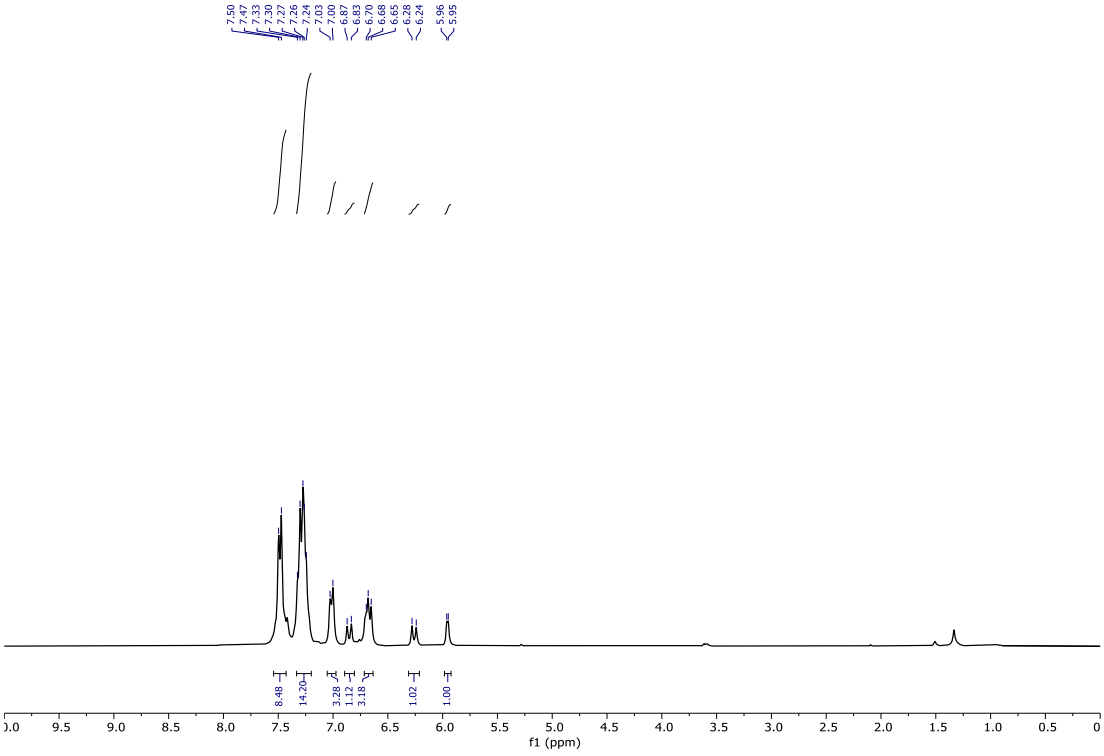


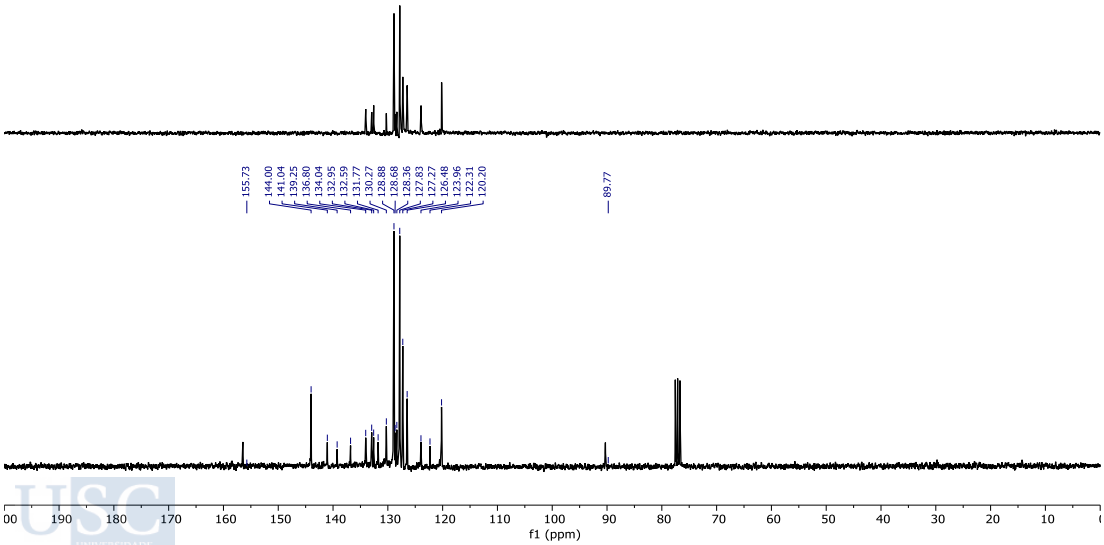


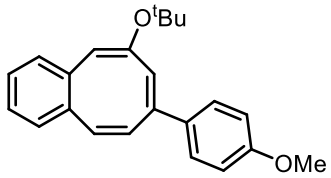


58g

^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

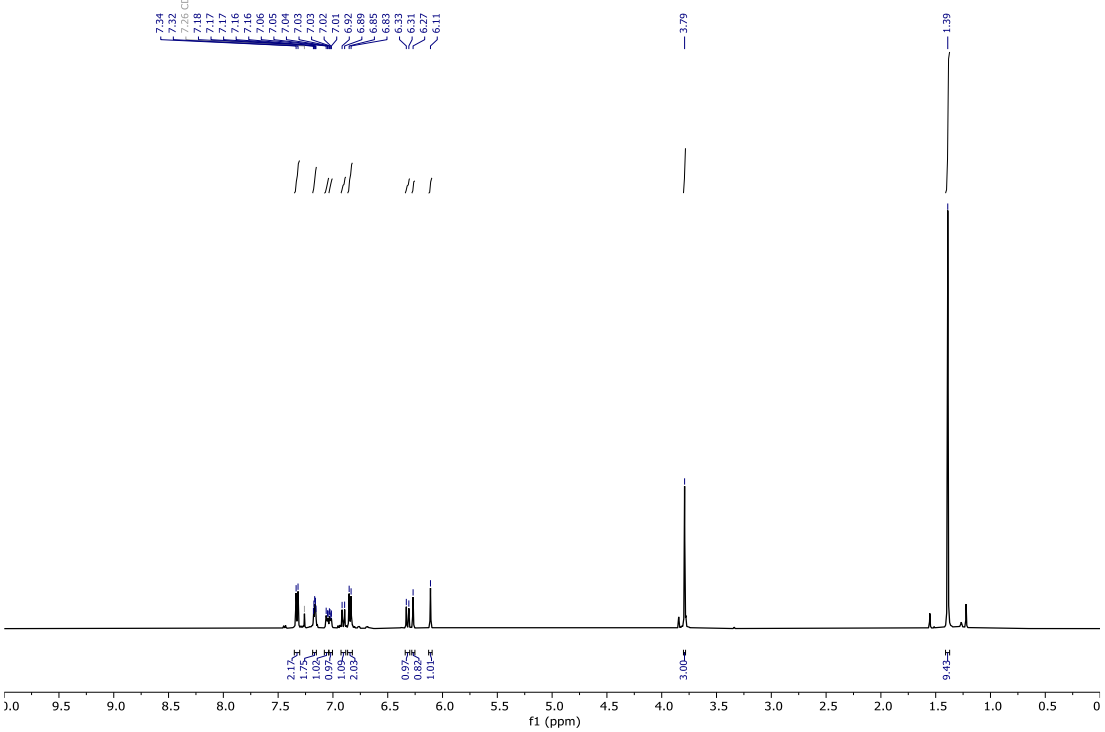


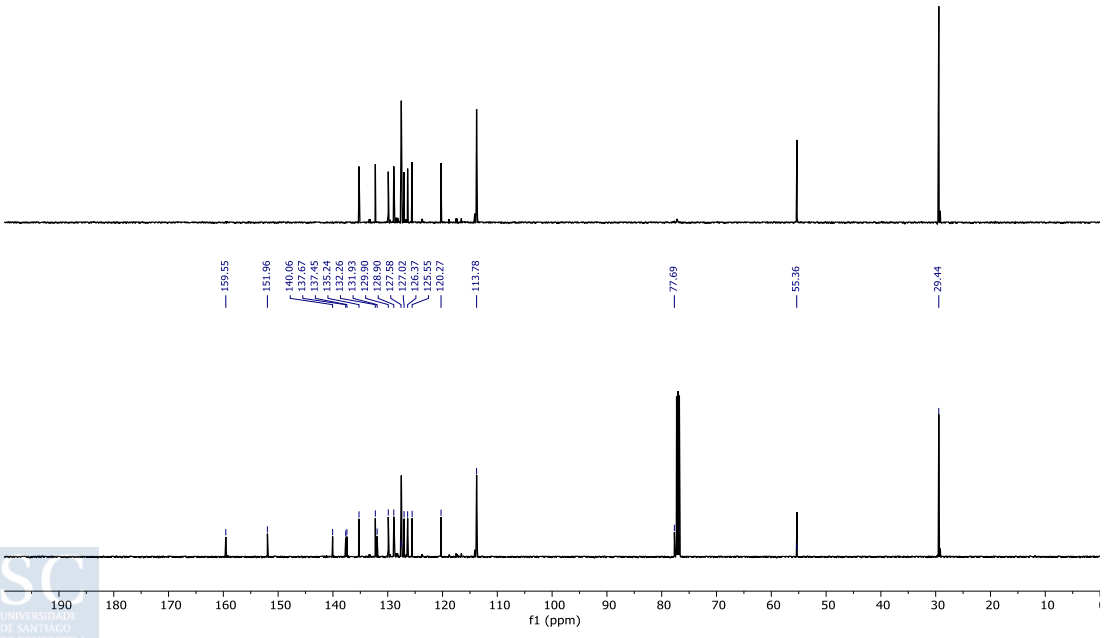


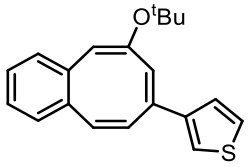


53ab

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

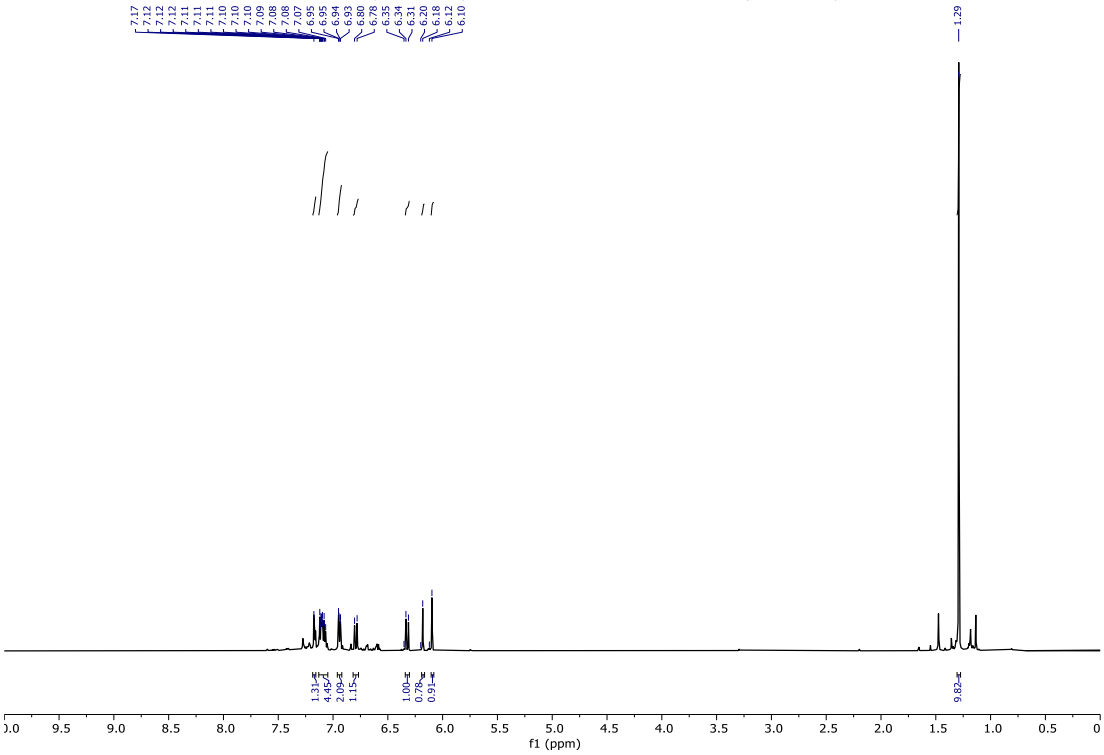


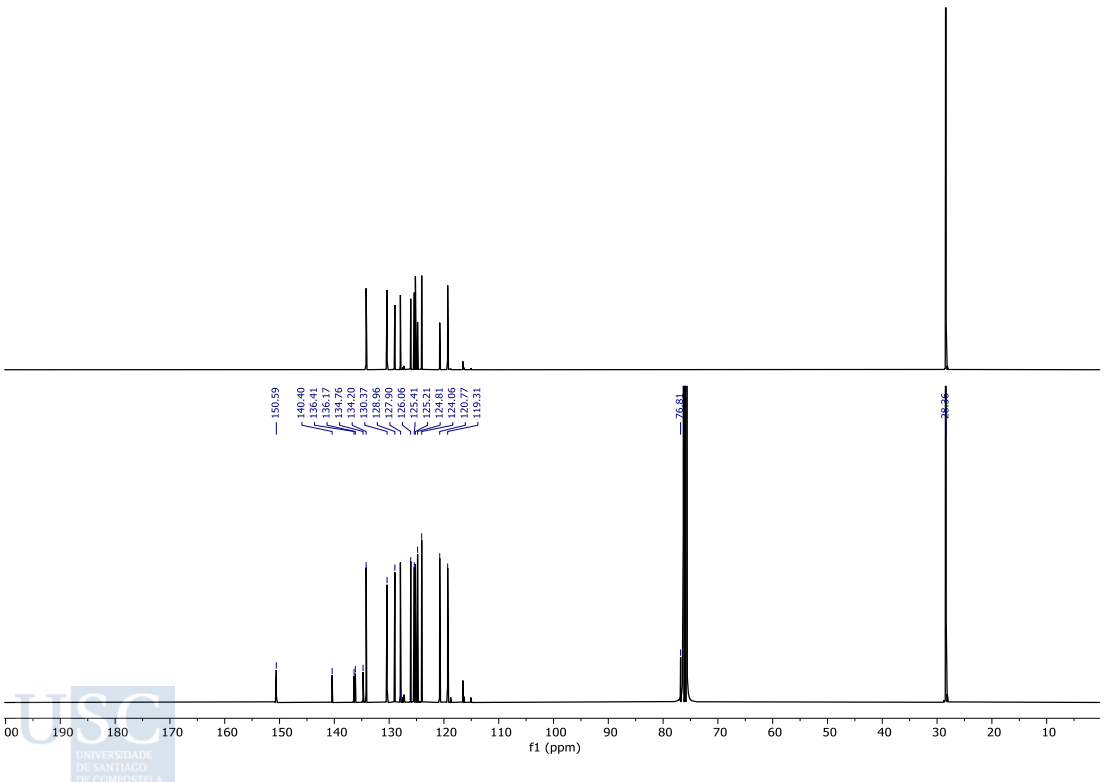


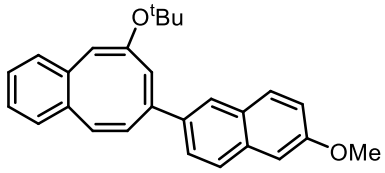


53aq

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

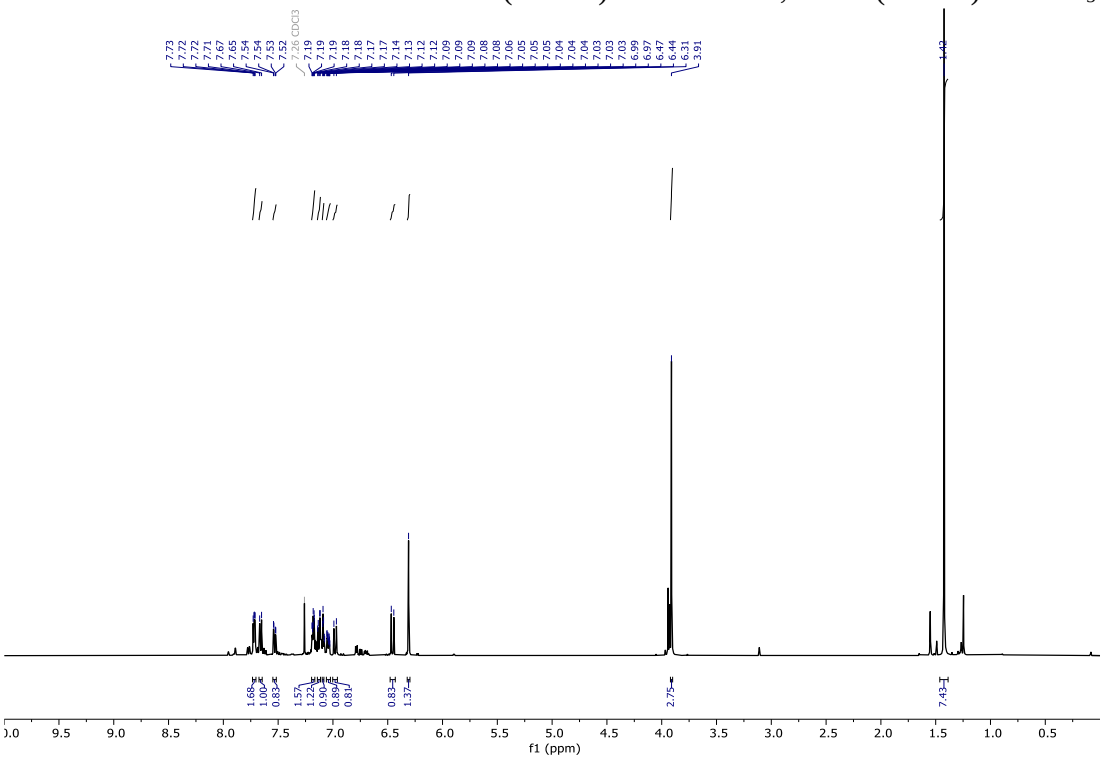


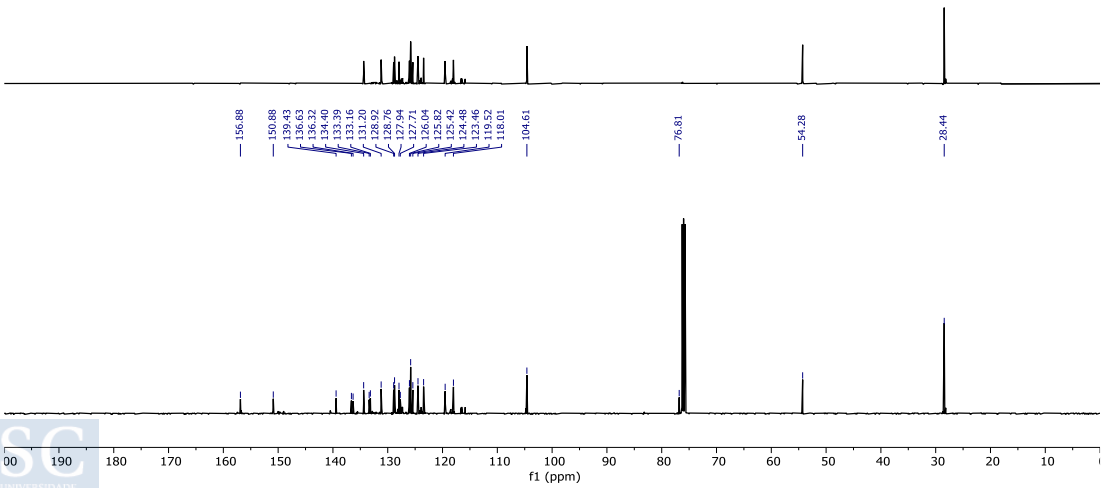


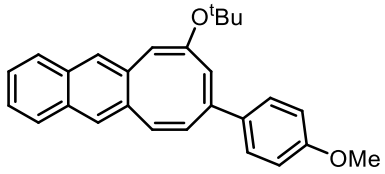


53at

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

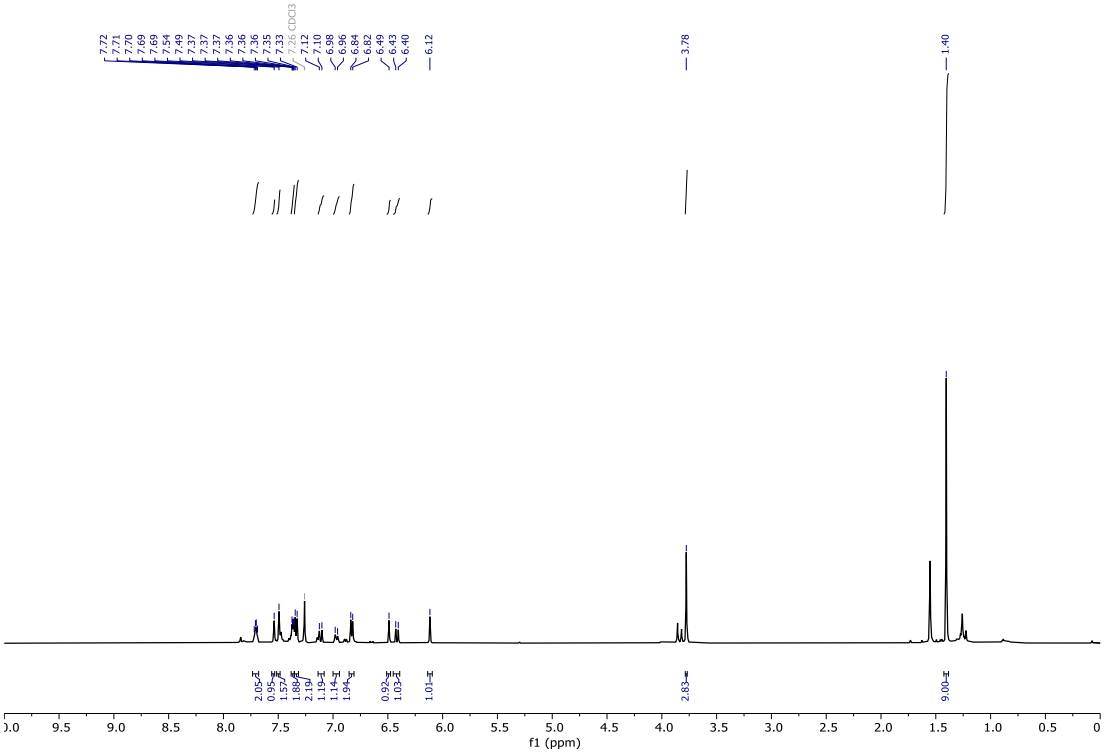


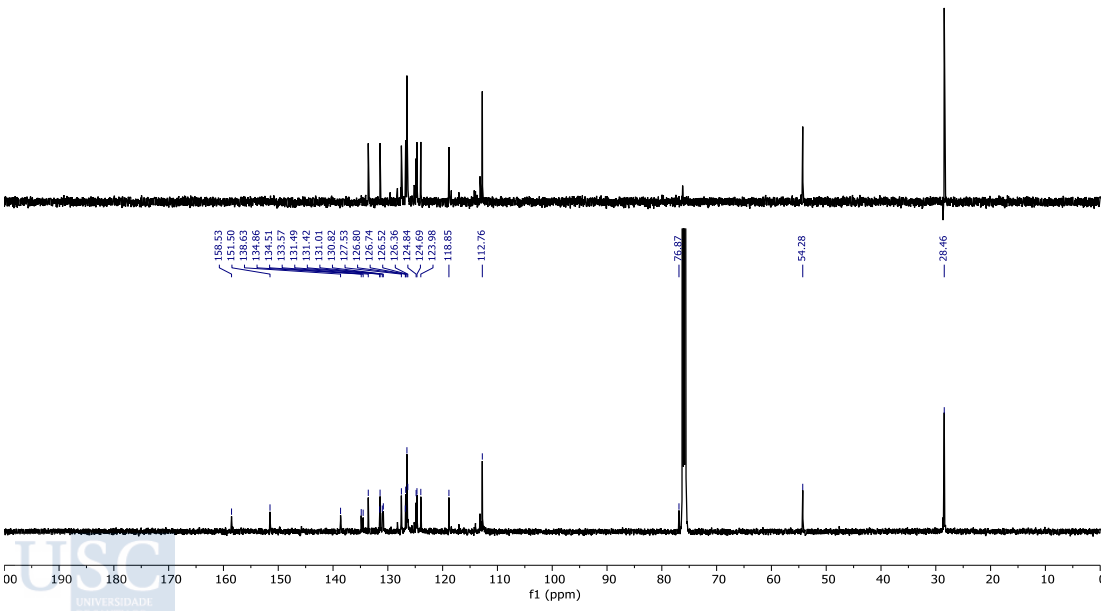


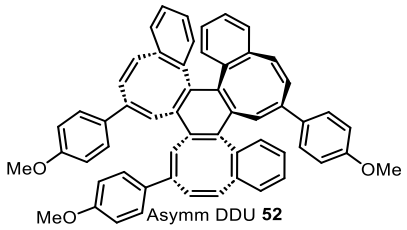


53cb

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

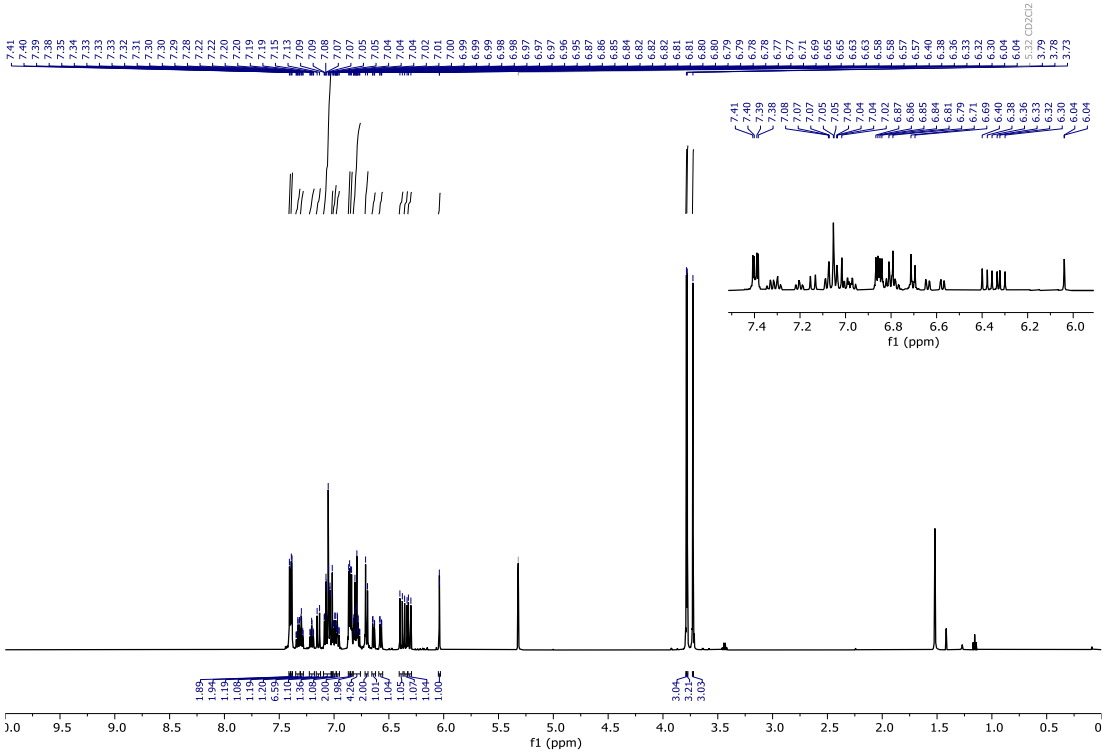


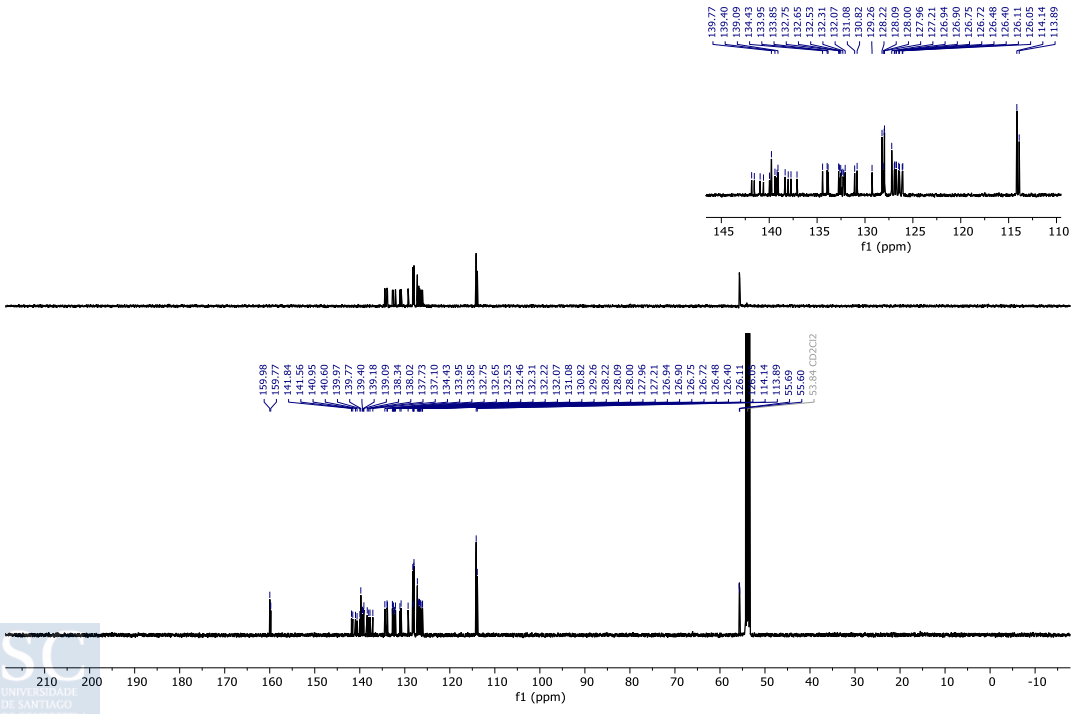




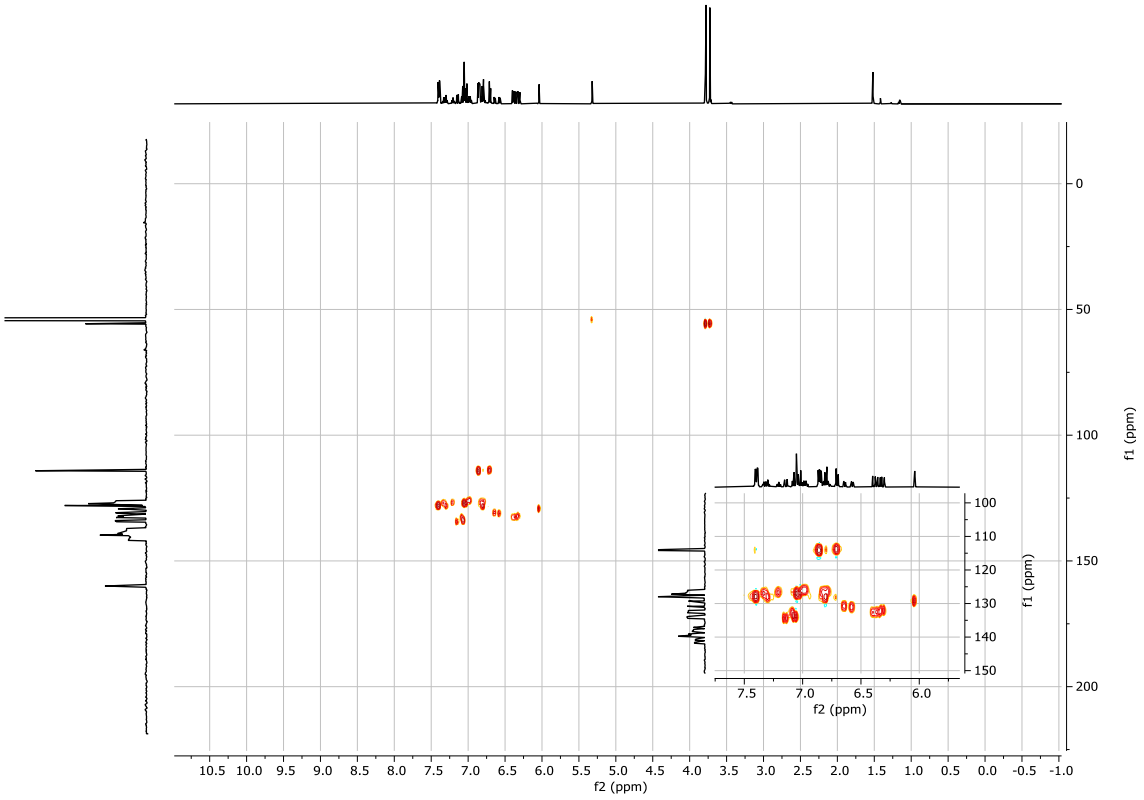
Asymm DDU **52**

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

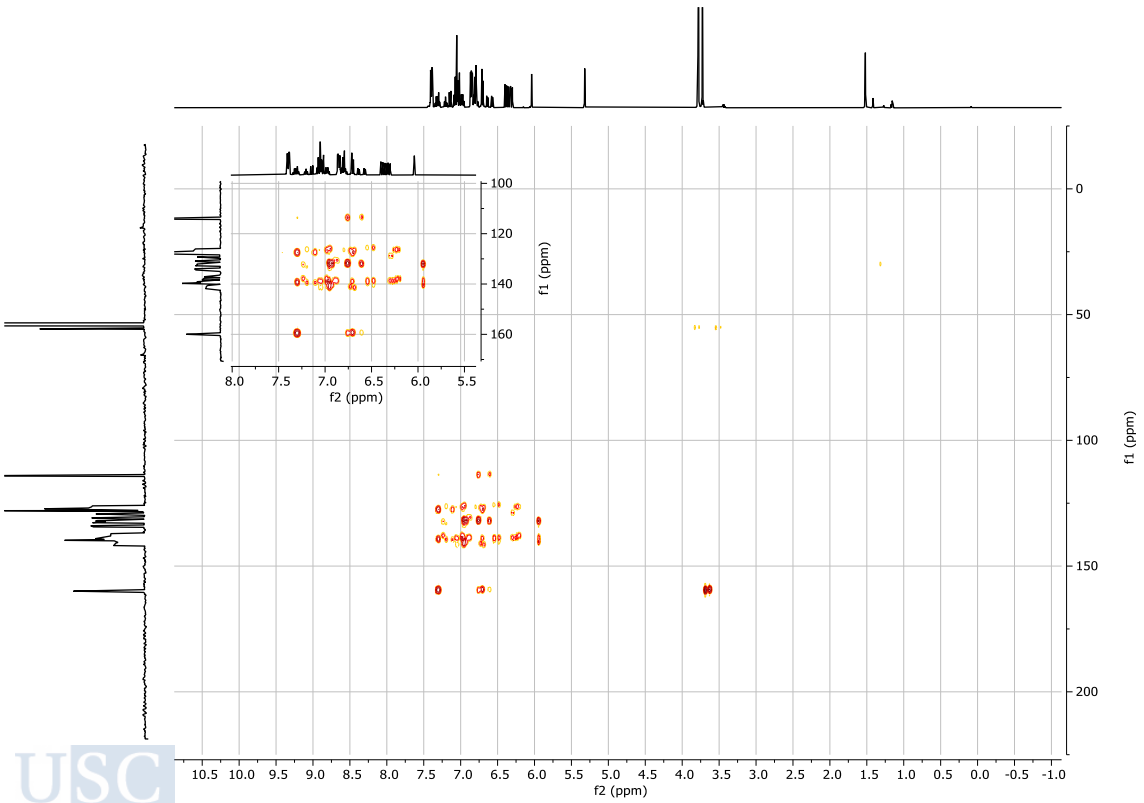


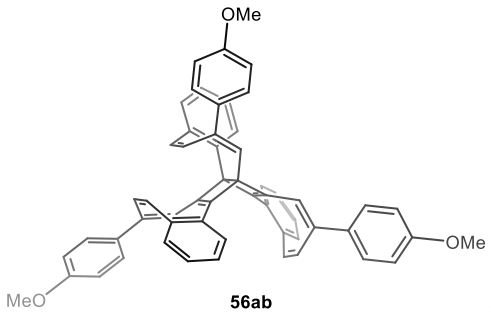


HSQC



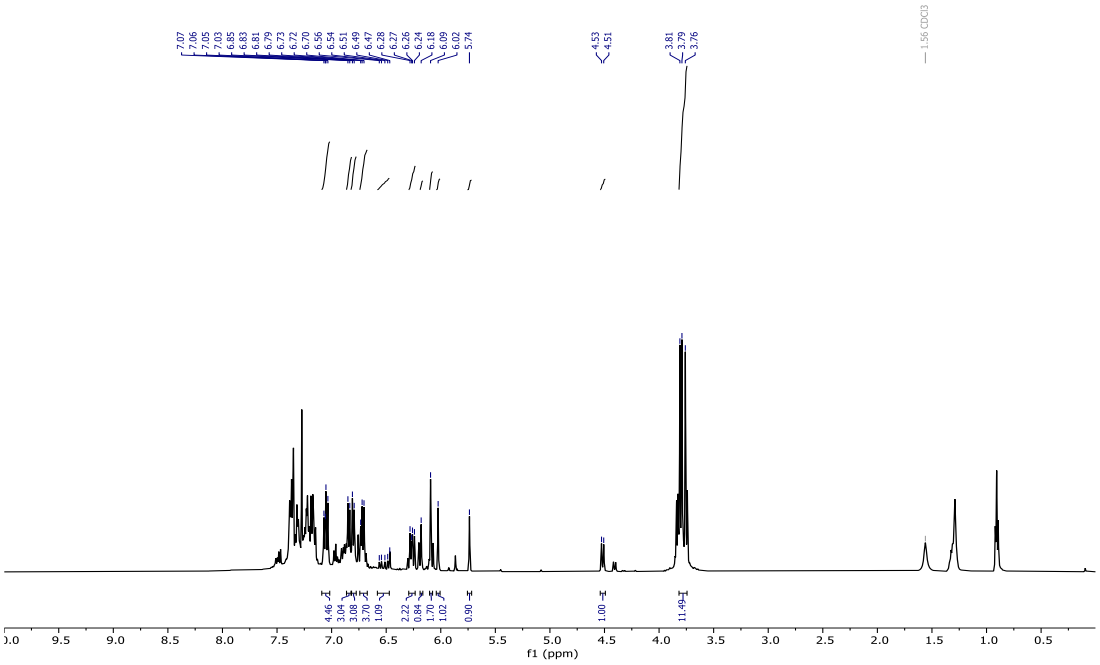
HMBC

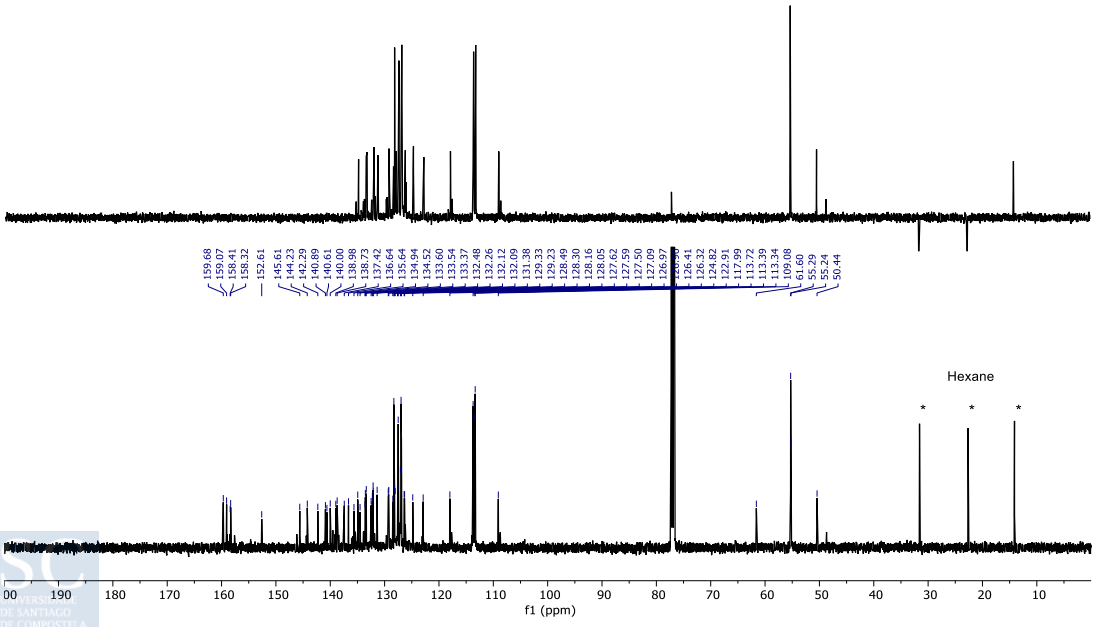




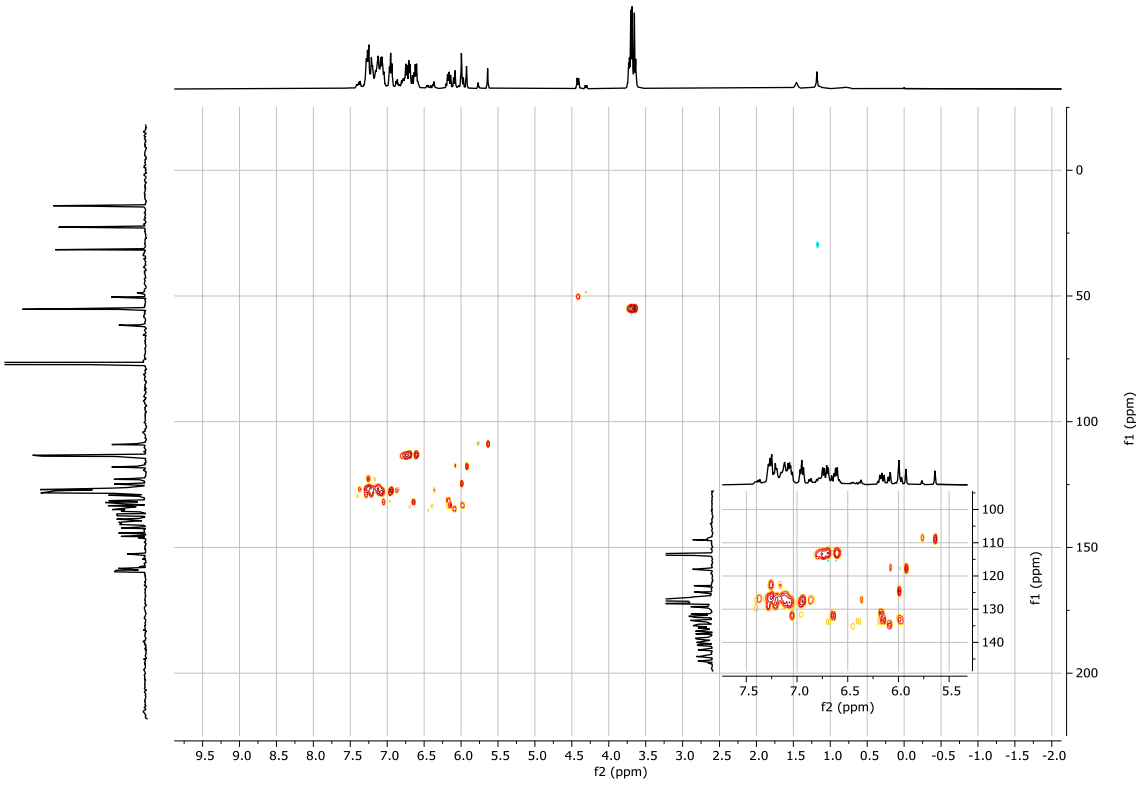
56ab

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

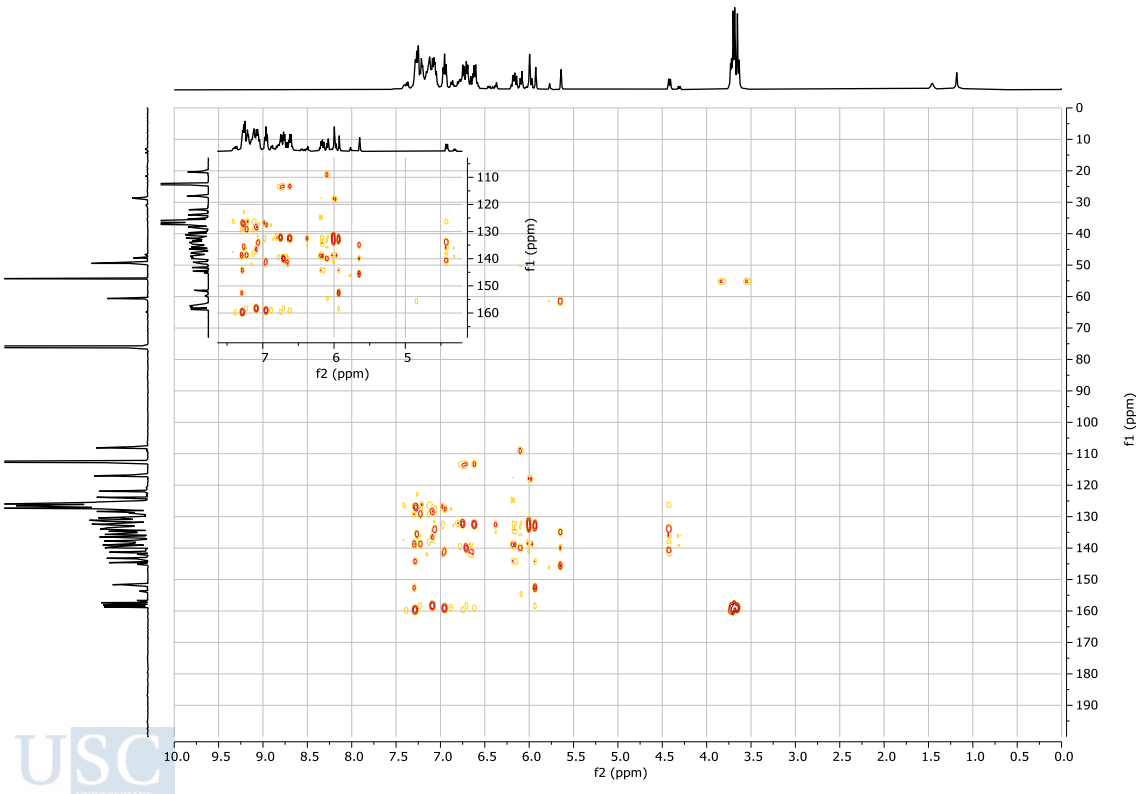


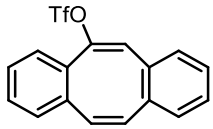


HSQC



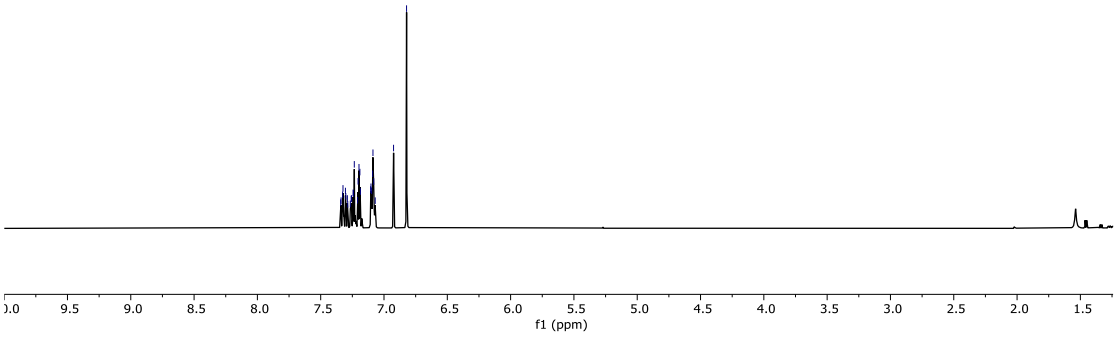
HMBC

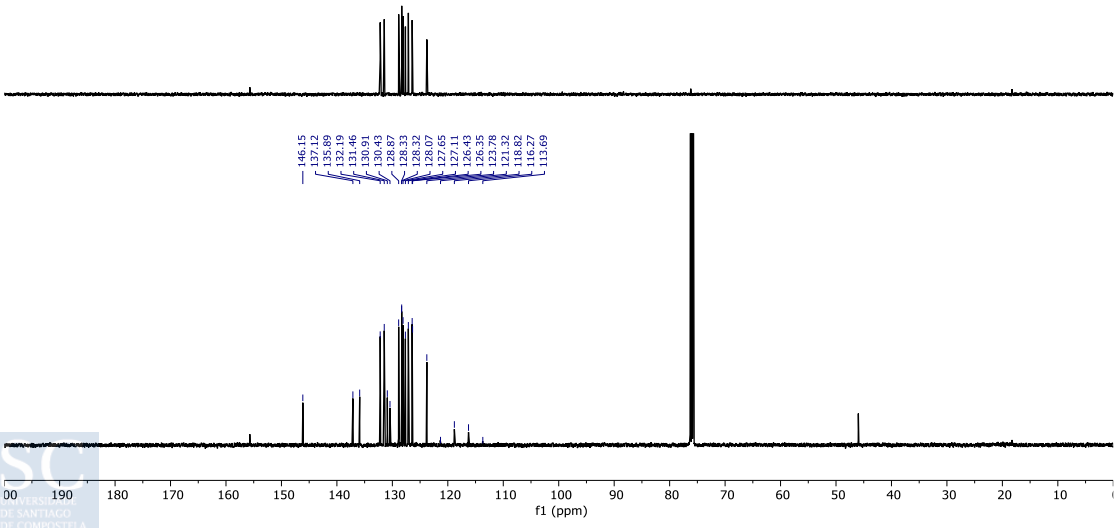


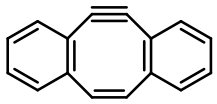


67

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

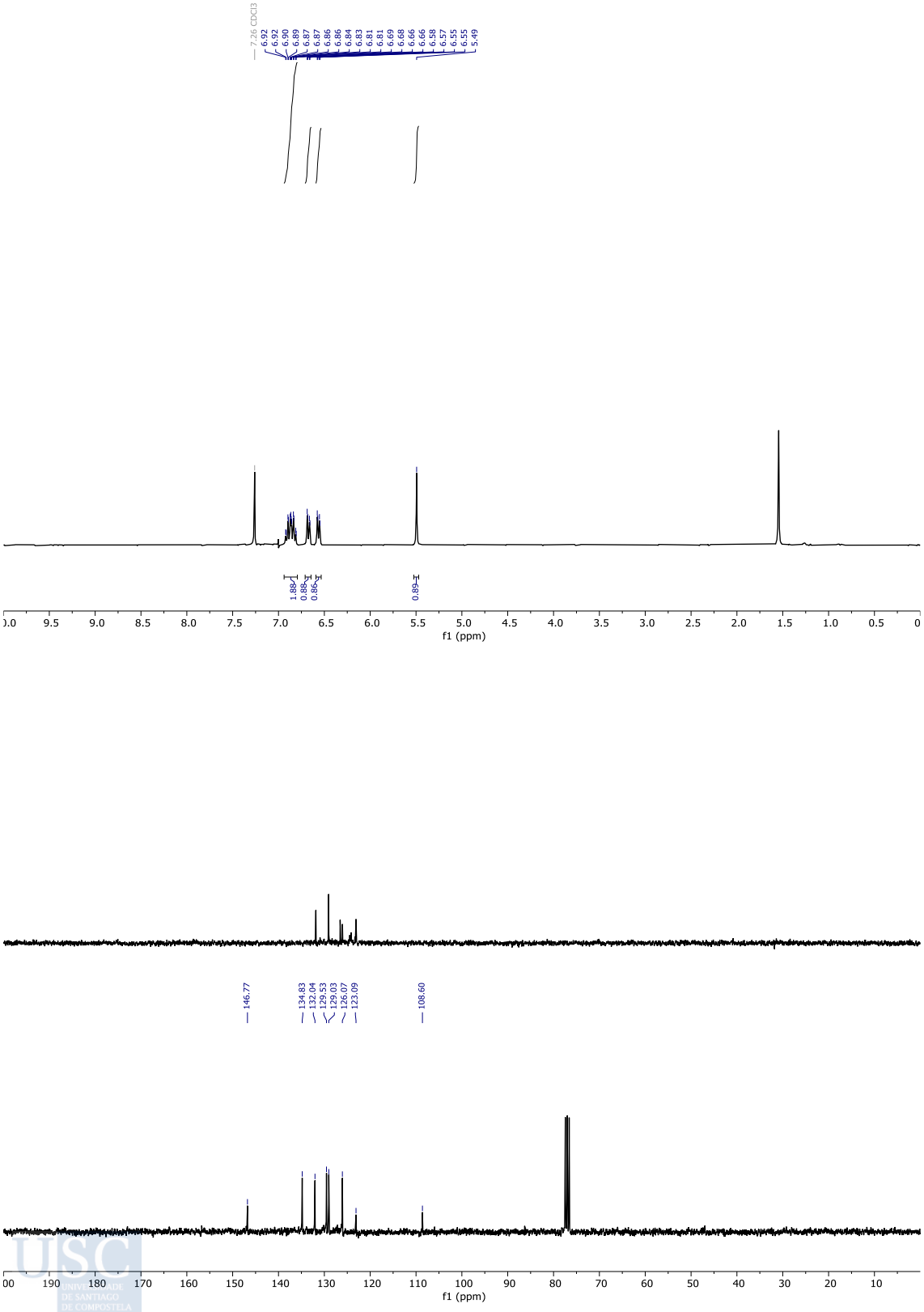


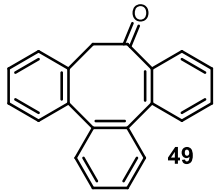




30

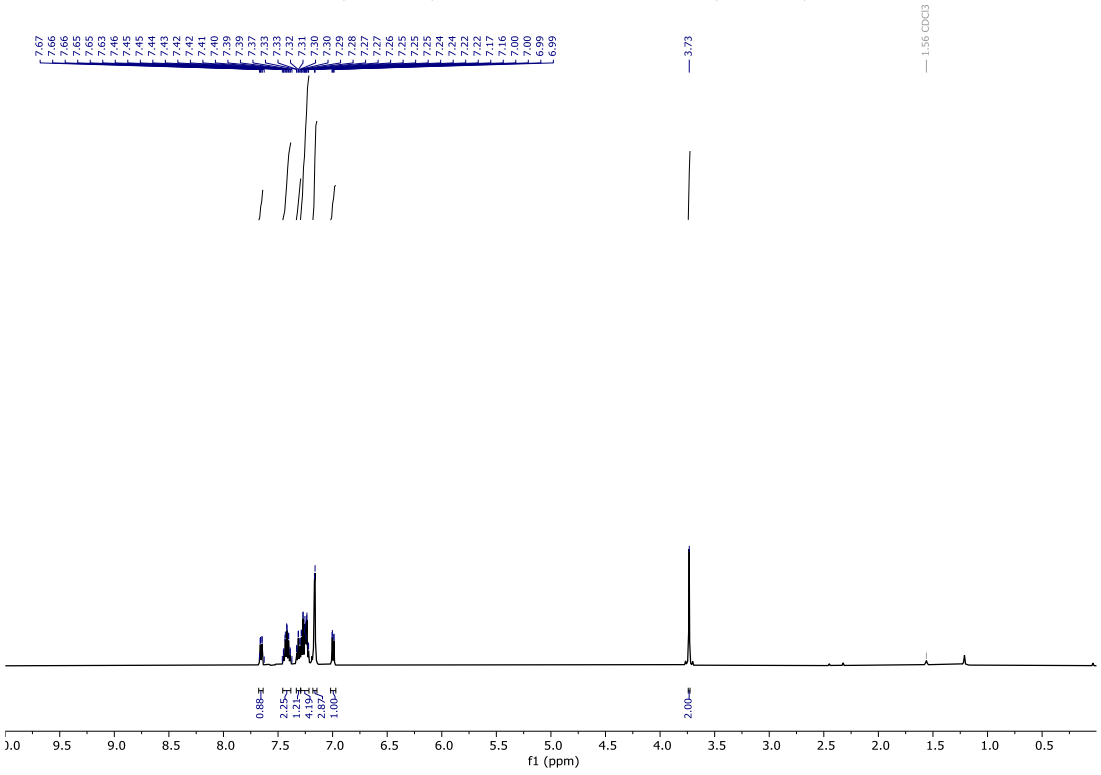
^{1}H-NMR (300 Hz) and ^{13}C-NMR, DEPT (75 Hz) in $CDCl_3$

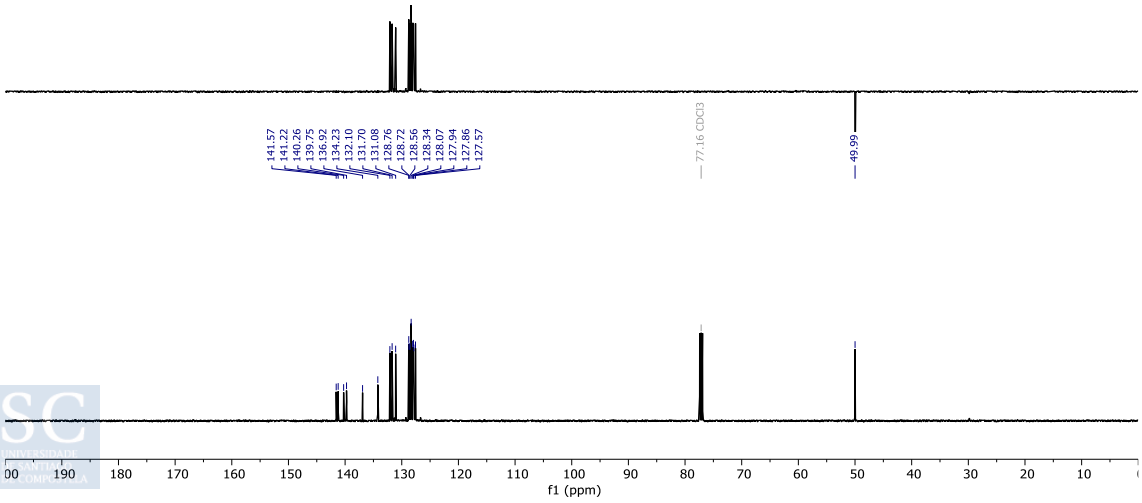


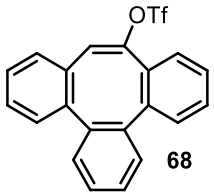


49

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

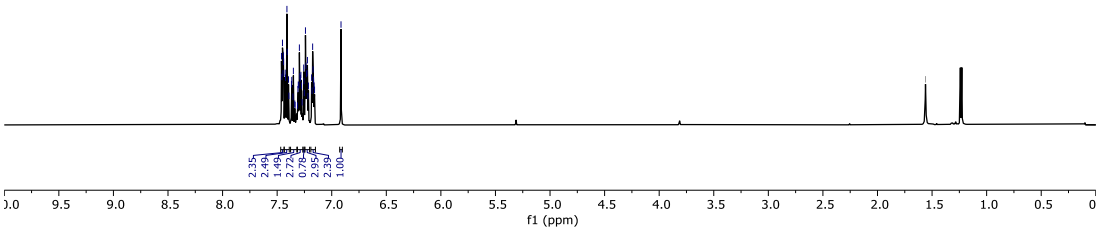


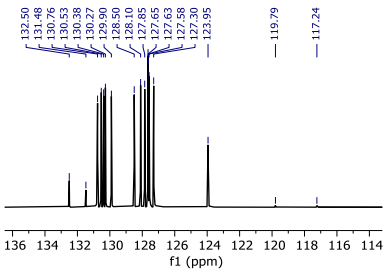


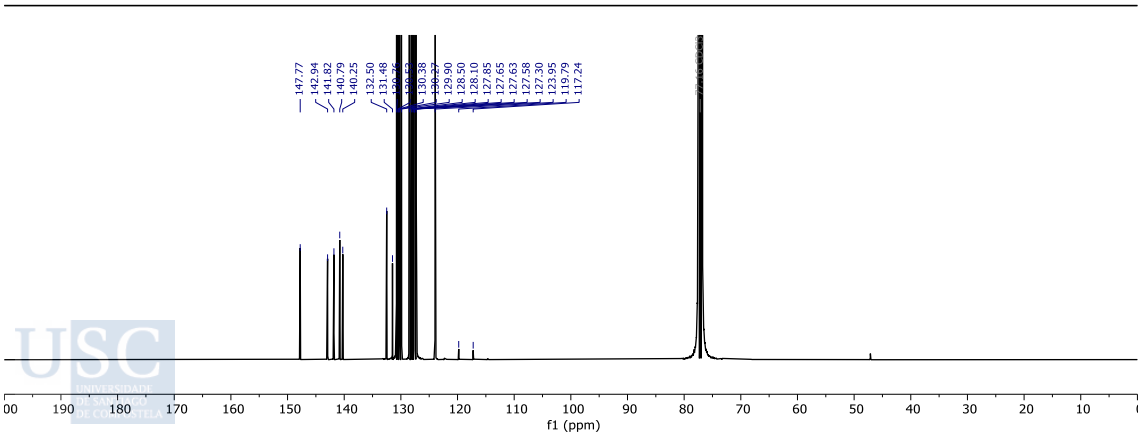


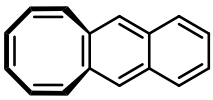
68

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$



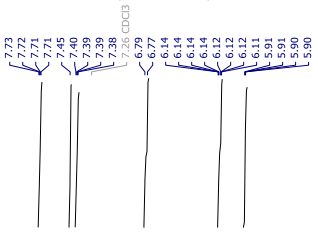


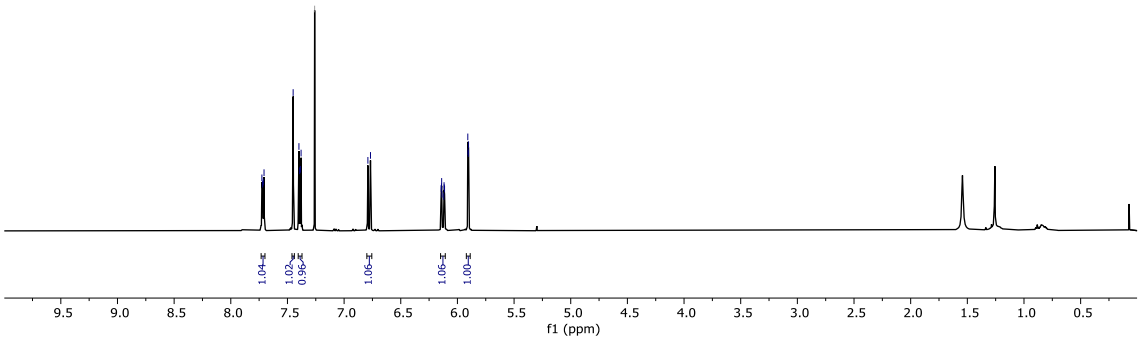


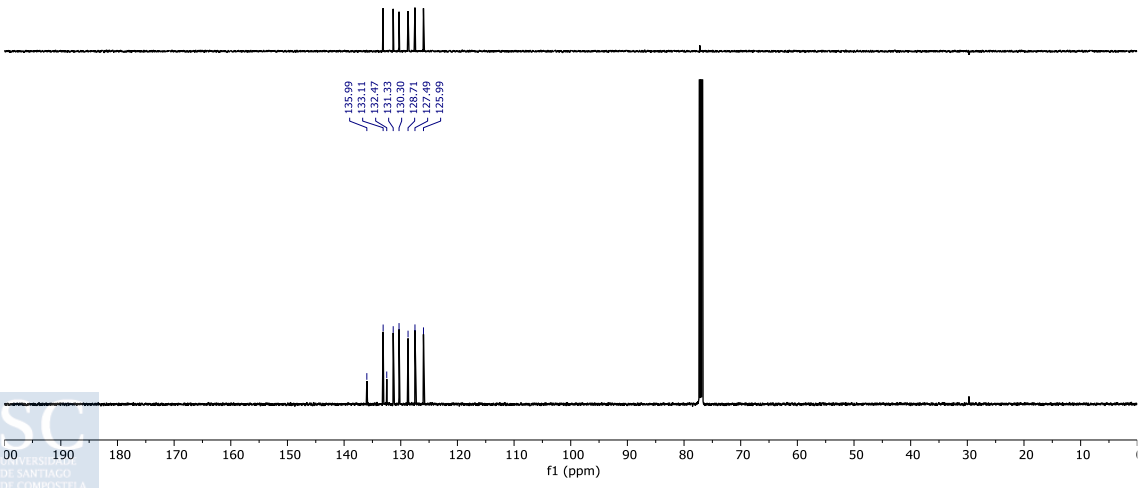


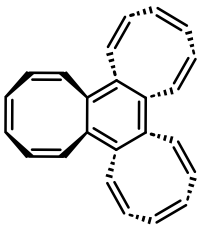
72

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$



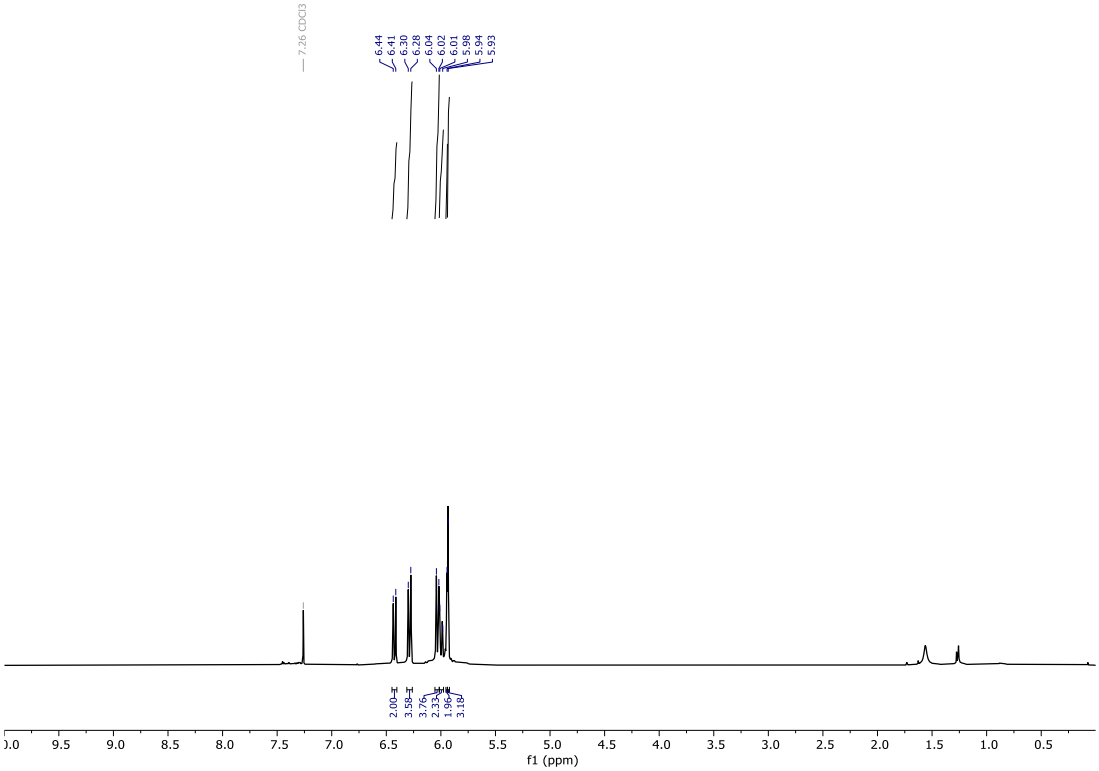


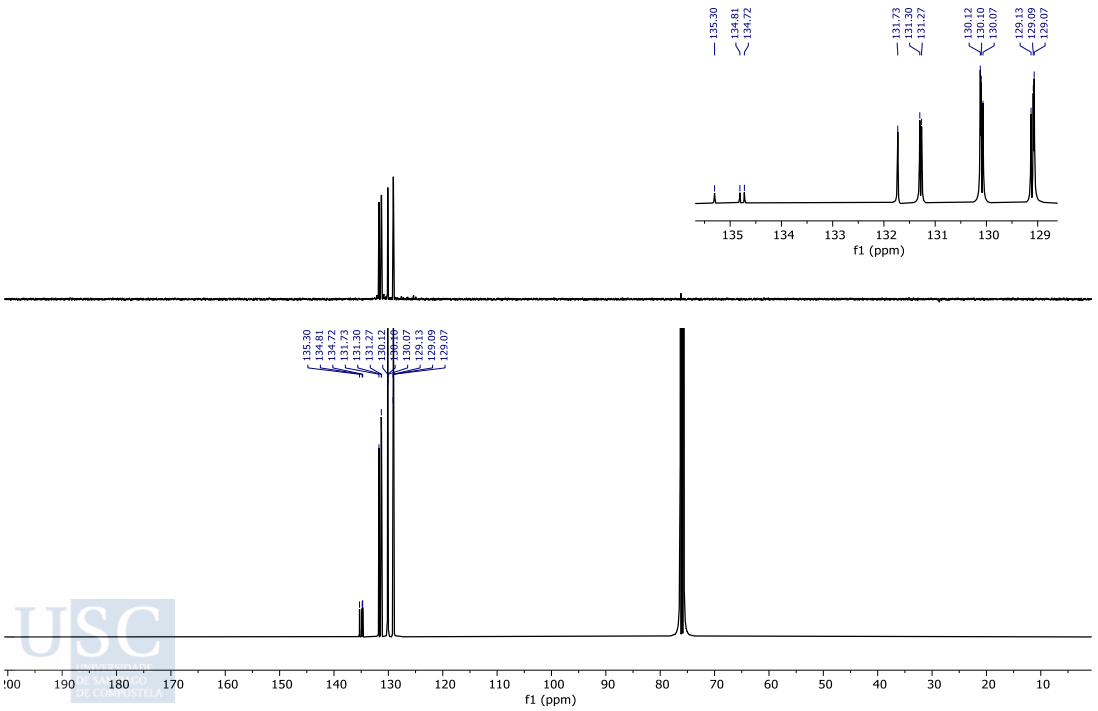


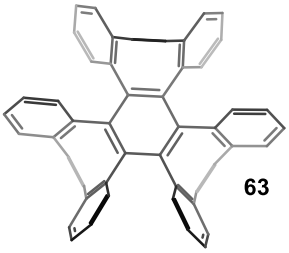


61

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

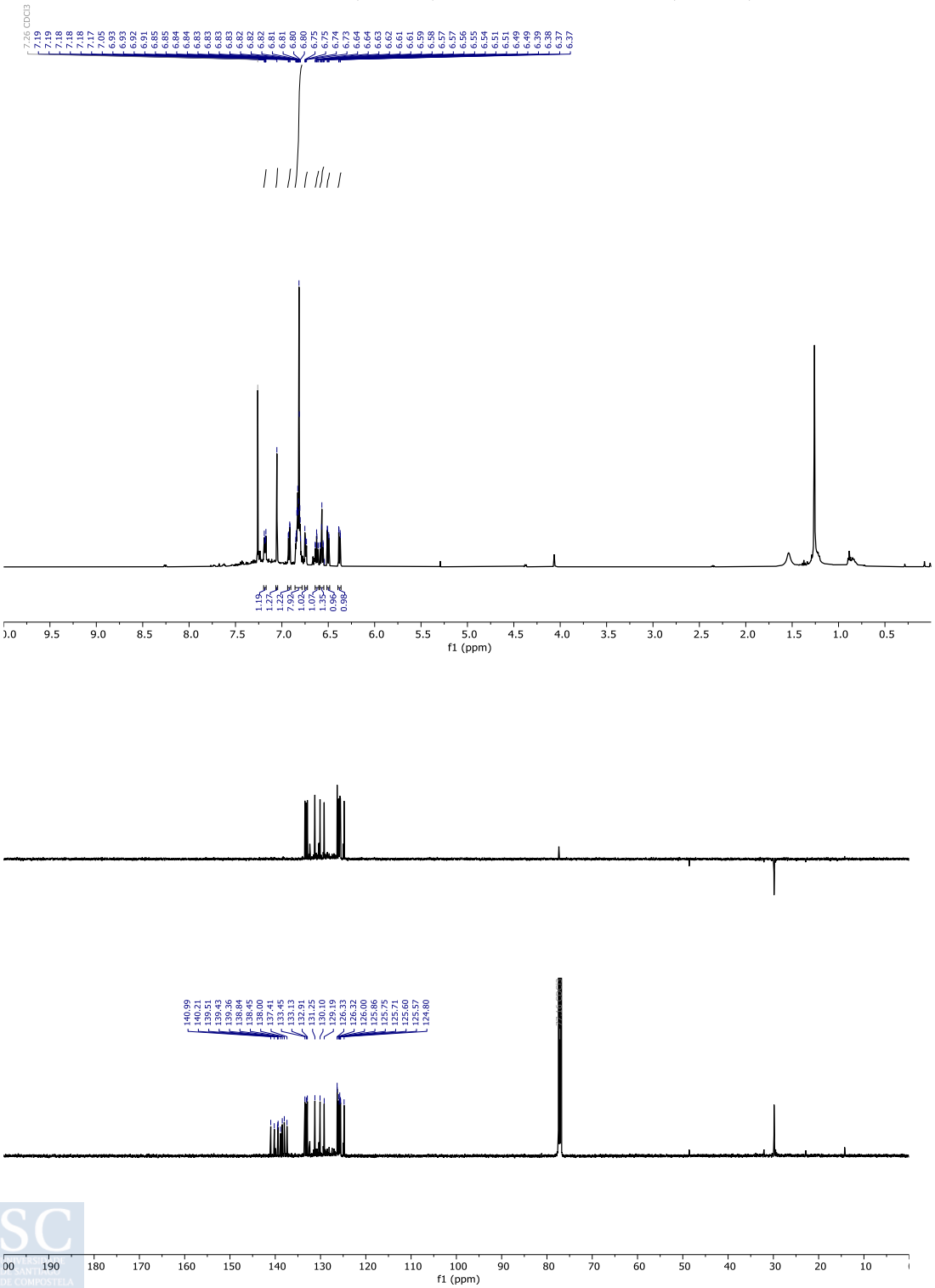


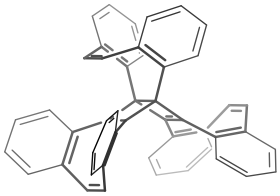




63

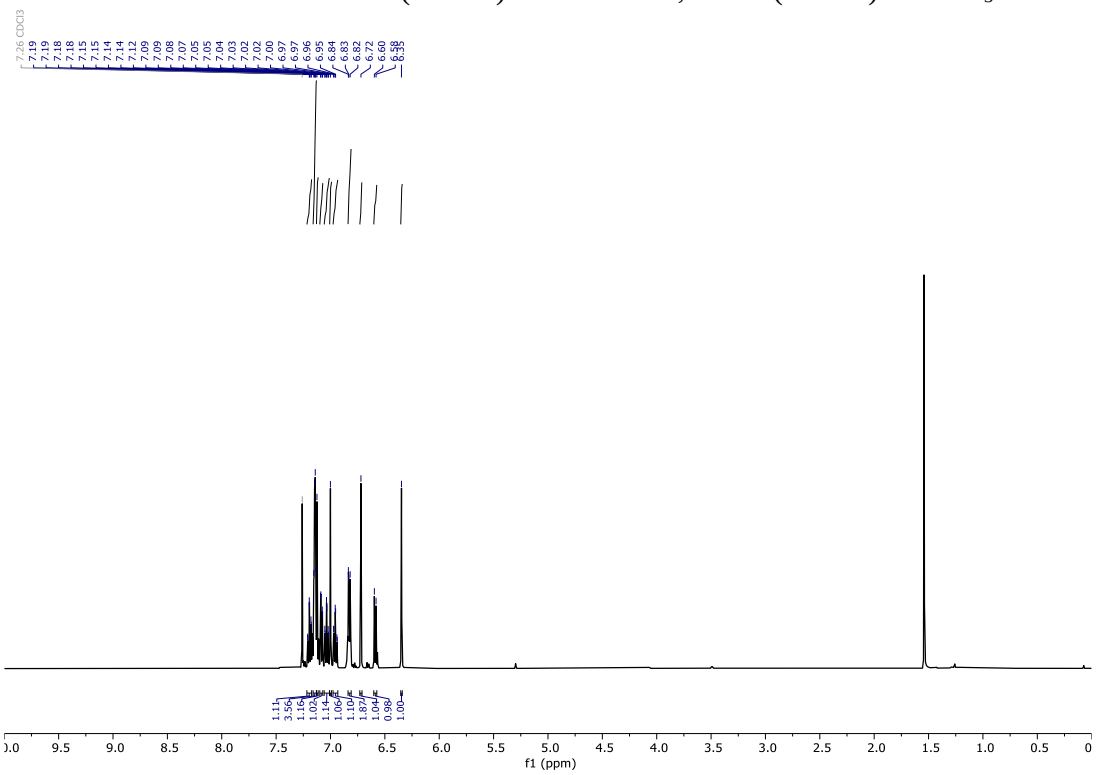
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

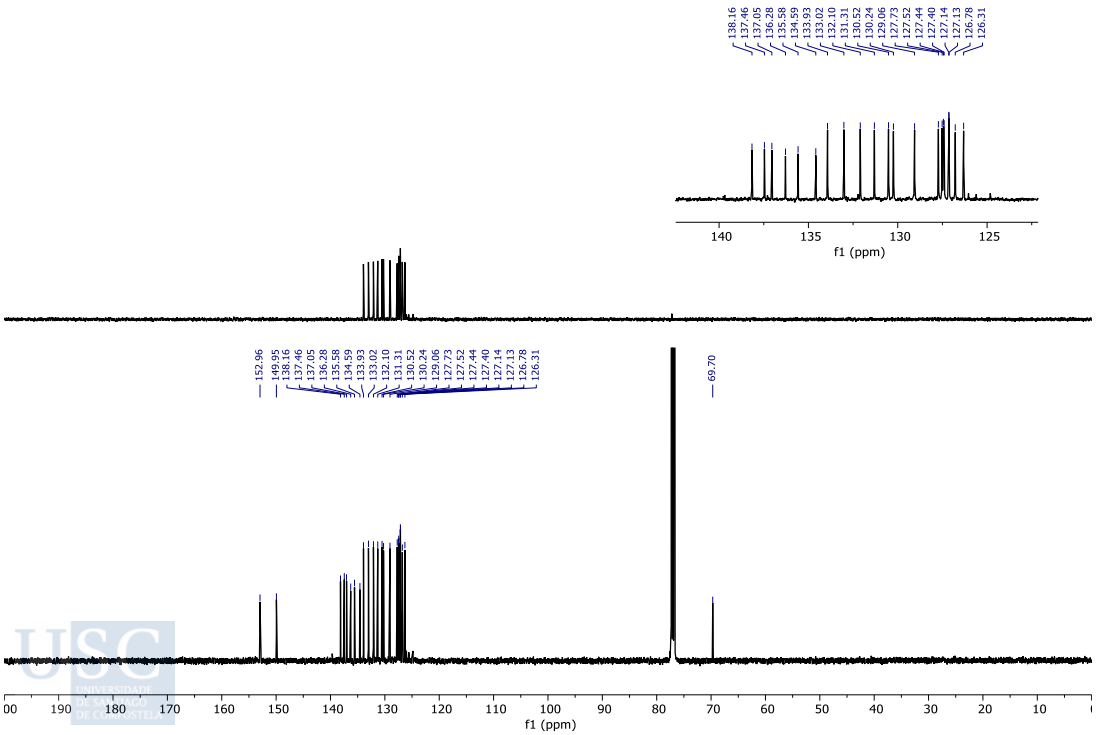


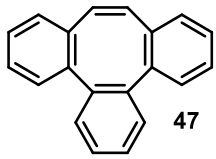


62

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

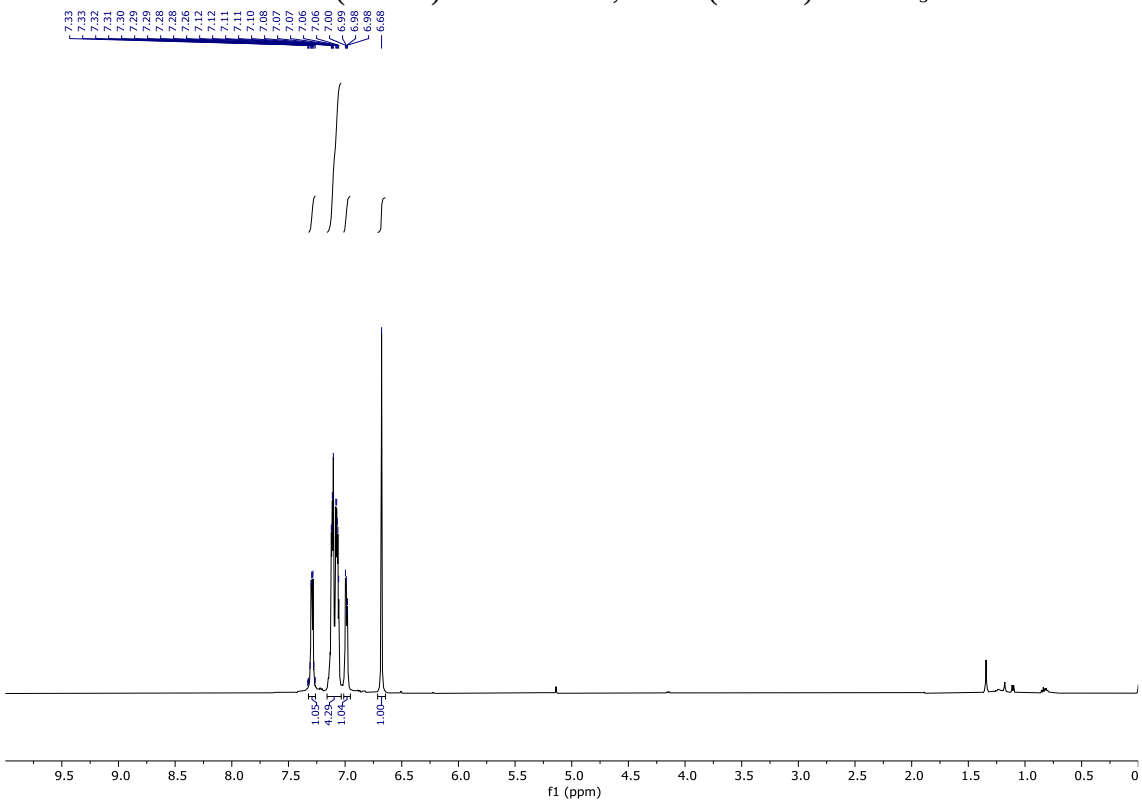


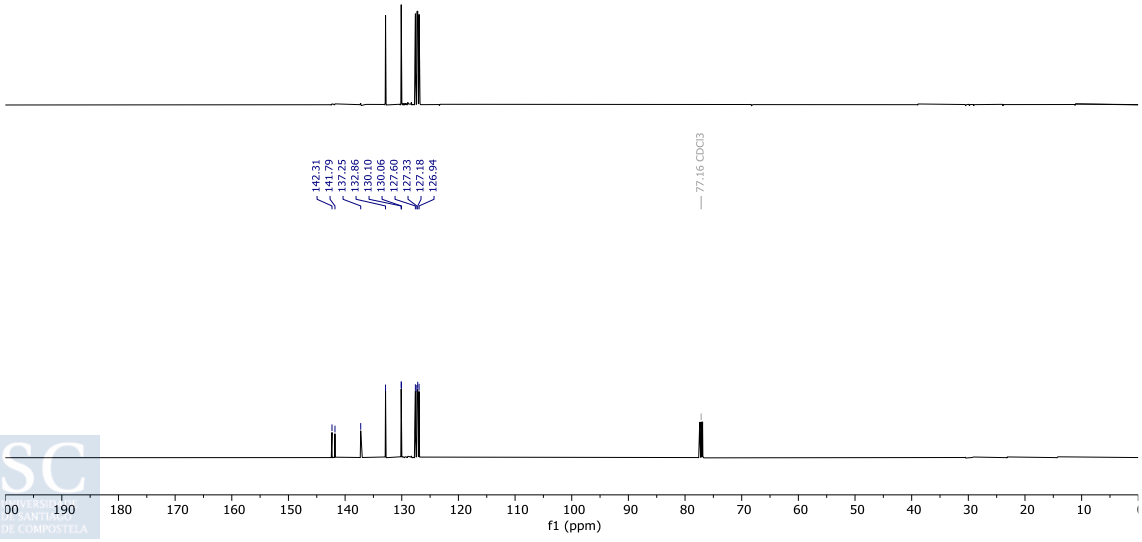


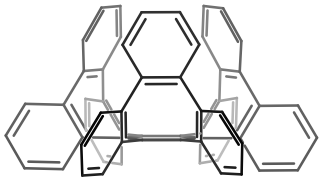


47

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in $CDCl_3$

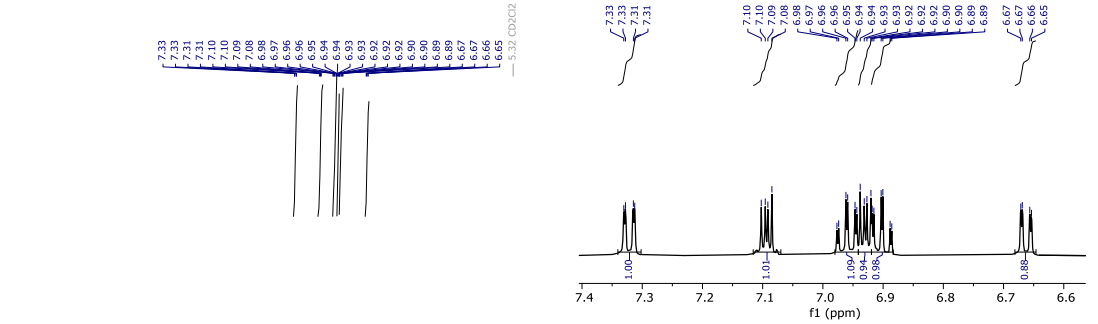


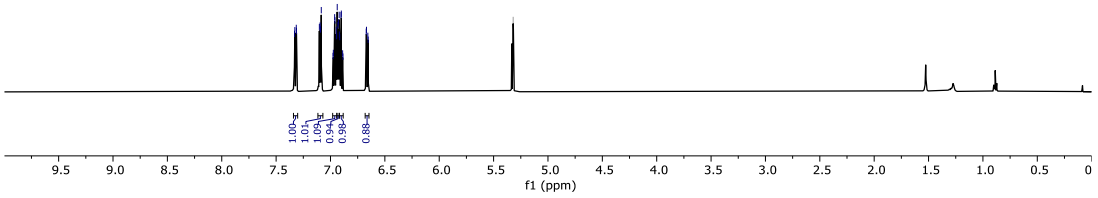


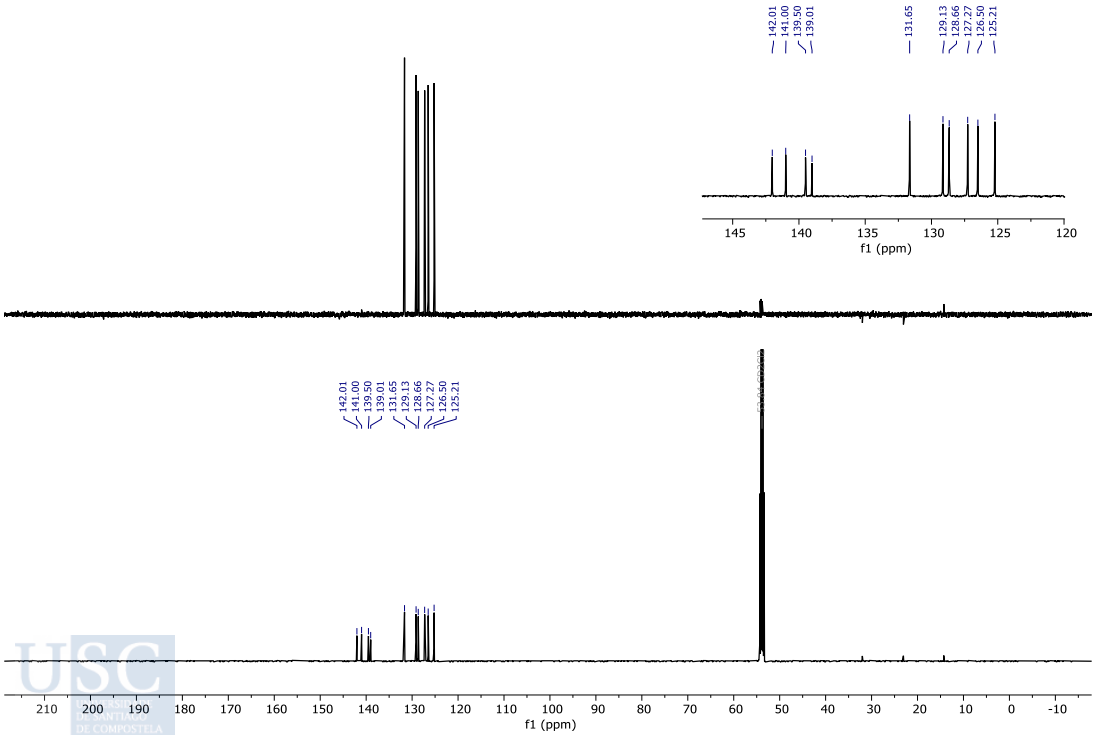


α,α,α–**73a**

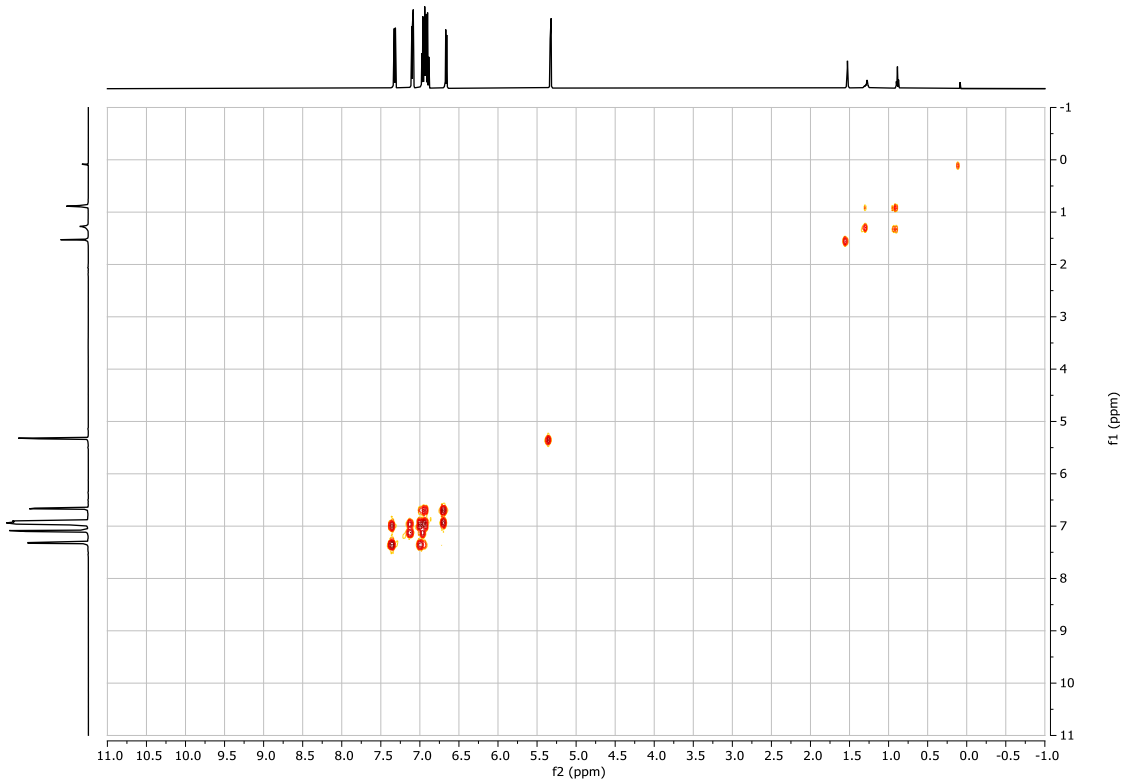
^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in CD_2Cl_2







COSY



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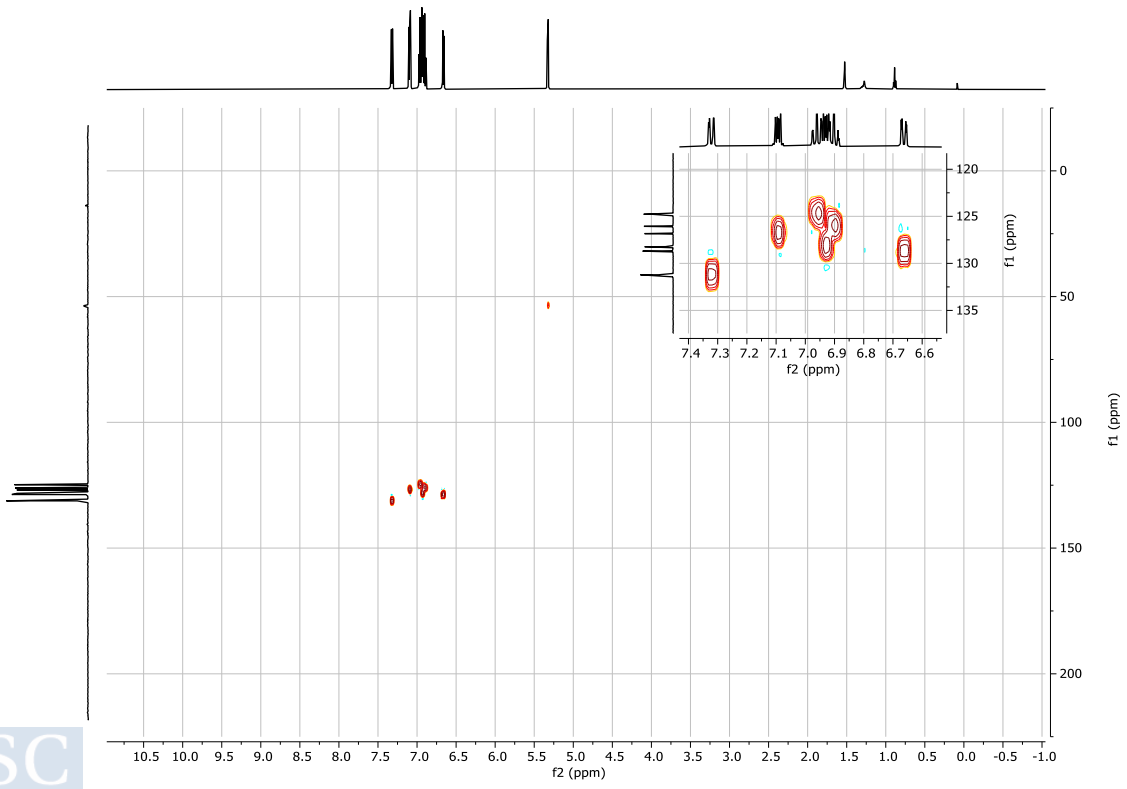

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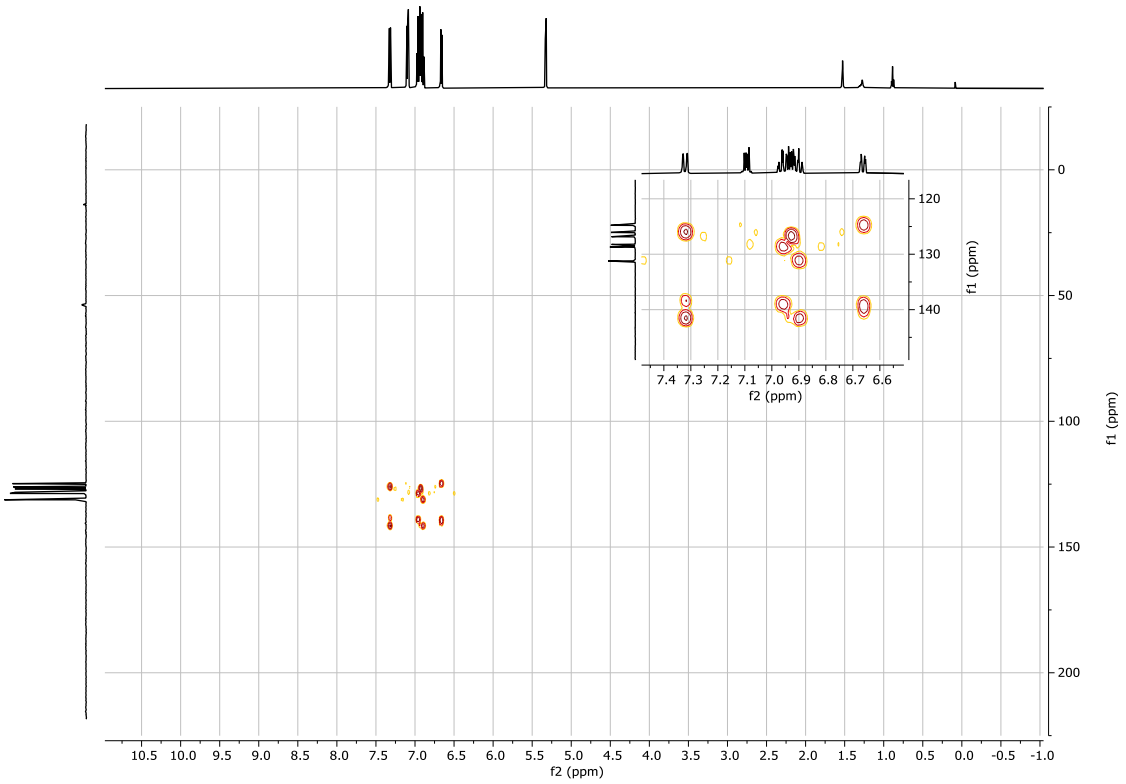
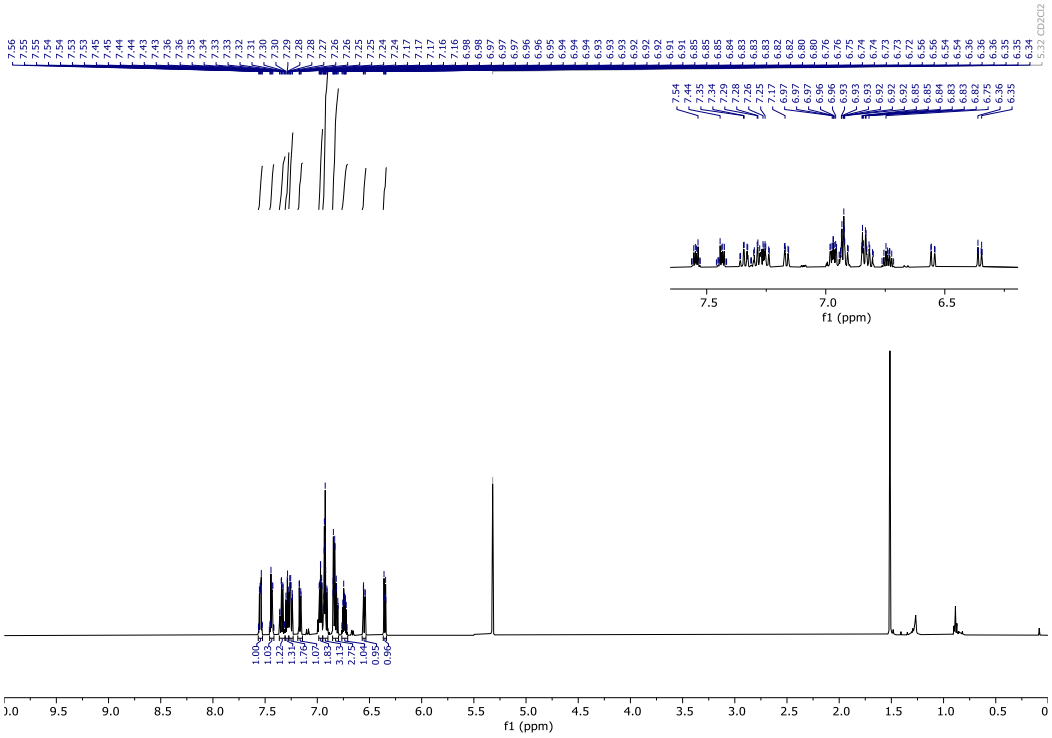
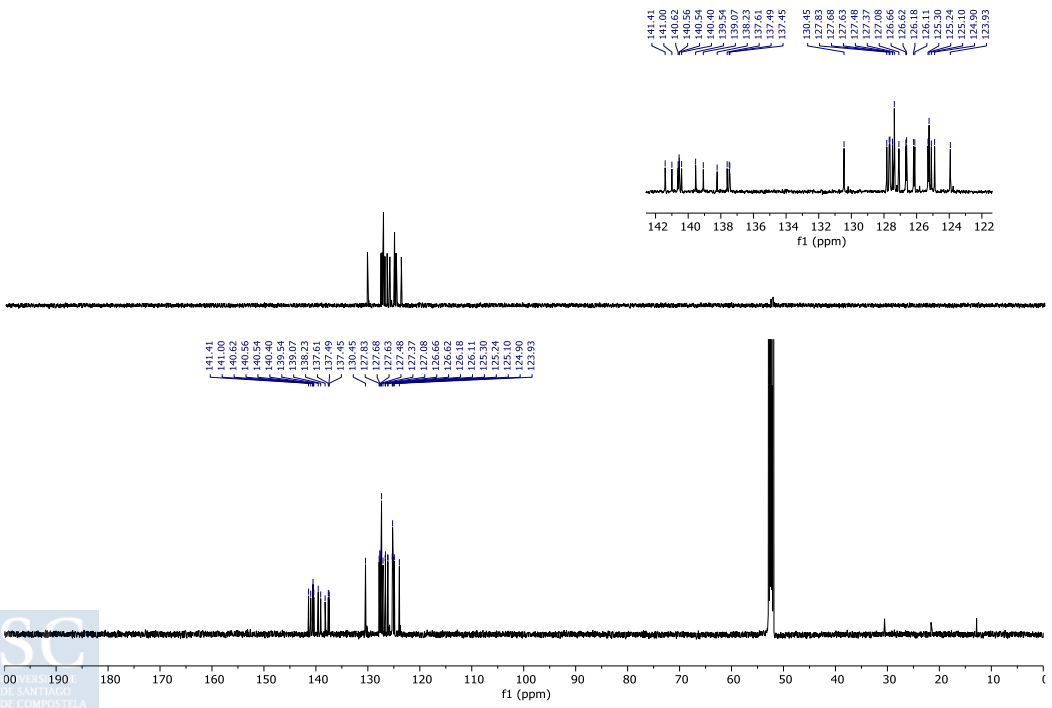


α,α,β–**73b**

^{1}H-NMR (500 Hz) and ^{13}C-NMR, DEPT (126 Hz) in CD_2Cl_2





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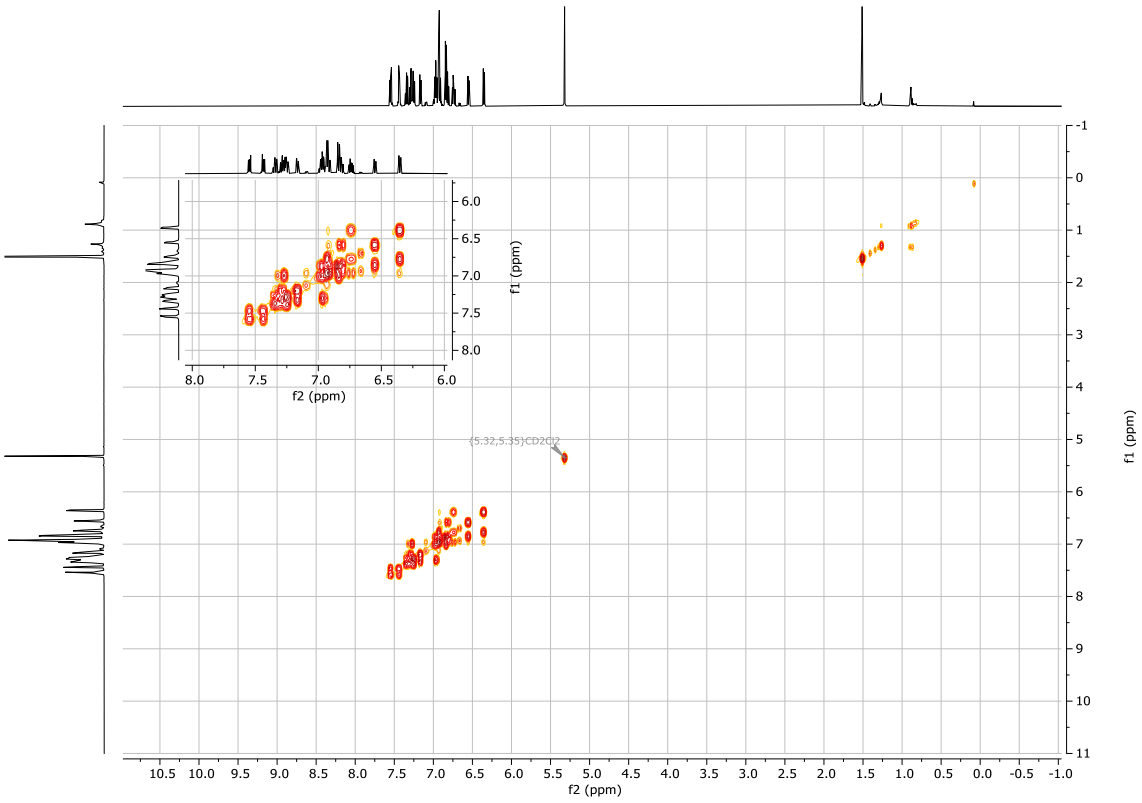

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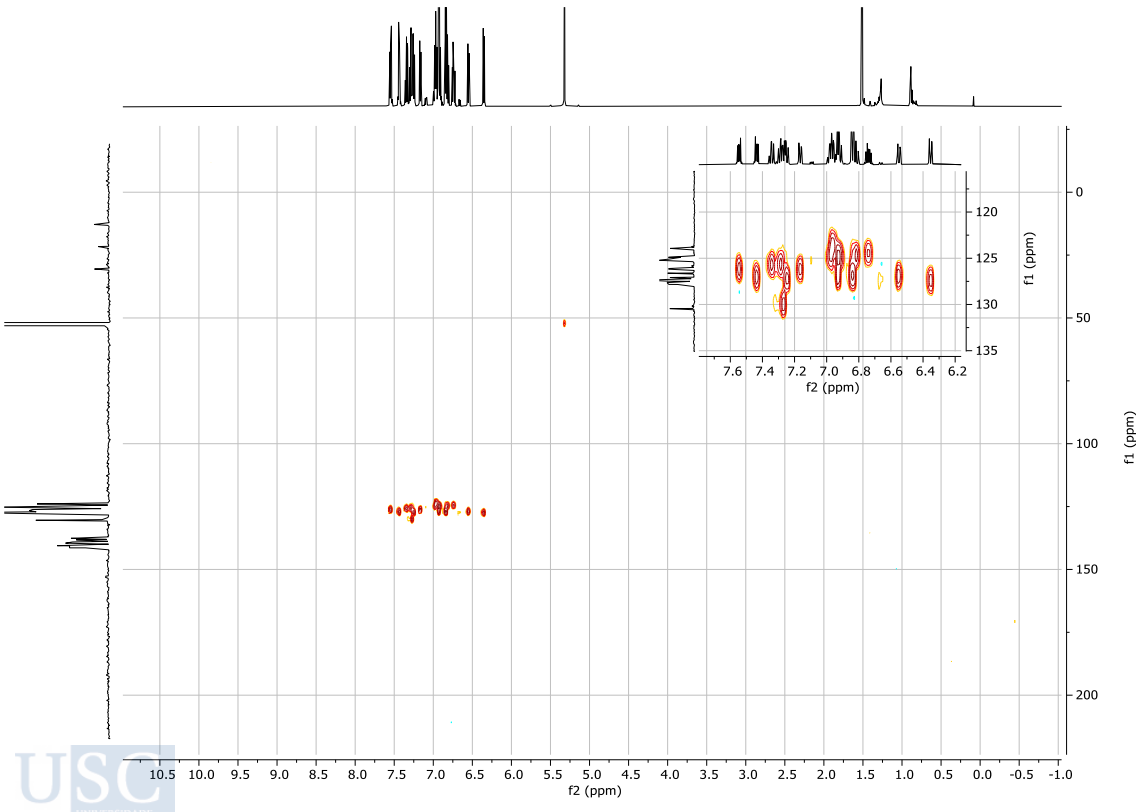

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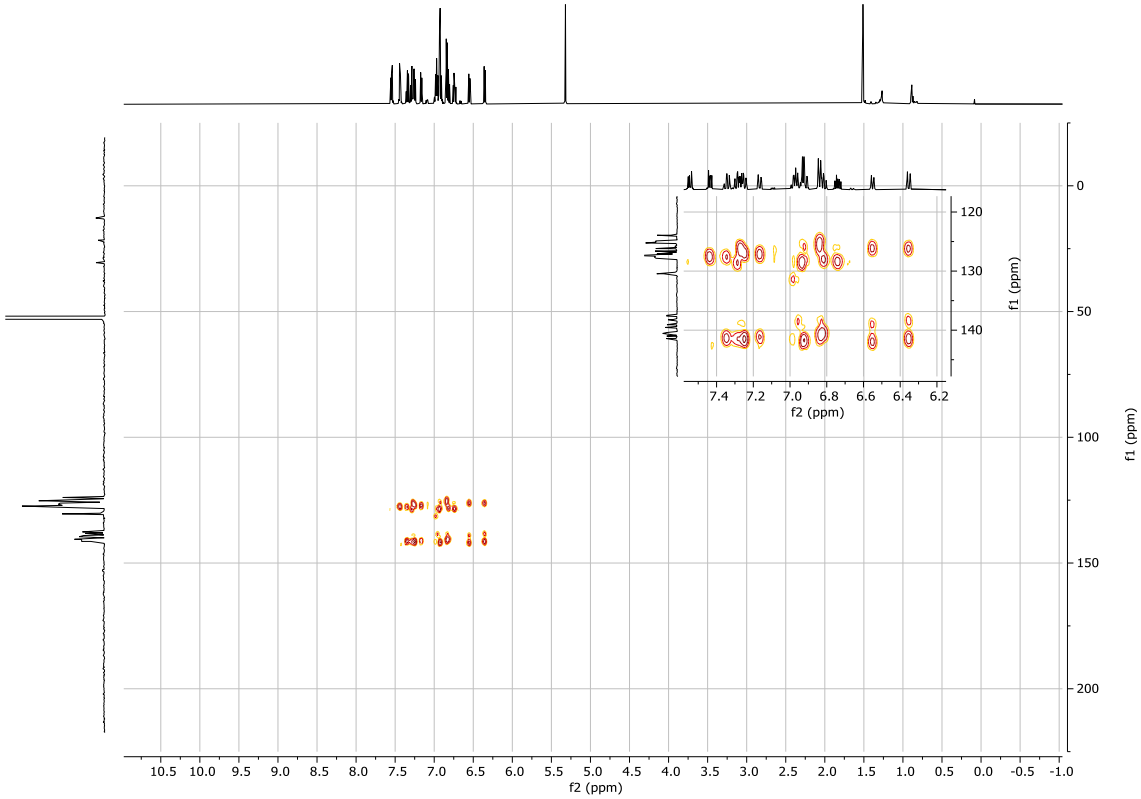
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f1 (ppm)
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50
100
150
200
7.4 7.2 7.0 6.8 6.6 6.4 6.2
120
130
140

Annex II: List of Publications

Results discussed in section 6.2.3 have been published in the following journal:

Title	*Nonplanar Tub-Shaped Benzocyclooctatetraenes via Halogen-Radical Ring Opening of Dihydrobiphenylenes*
Authors	Jesús Bello-García, Damián Padín, Jesús A. Varela and Carlos Saá
Citation	*Org. Lett*. 2021, 23, 5539–5544
DOI	10.1021/acs.orglett.1c01881
Personal contribution	Experimental procedures, preliminary DFT calculations, results discussion and preliminary manuscript
Journal Information	Print Edition ISSN:1523-7060 Web Edition ISSN: 1523-7052
2 Year Impact Factor 2022	5.2
Quartile 2022-2023	Q1

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Homo and Hetero Molecular 3D Nanographenes Employing a Cyclooctatetraene Scaffold

Author: Javier Urieta-Mora, Marcel Krug, Wiebke Alex, et al
Publication: Journal of the American Chemical Society
Publisher: American Chemical Society
Date: Mar 1, 2020

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Will you be translating?	No
Title of new work	Polycyclic Aromatic Hydrocarbons (PAHs) containing Biphenylenes and Cyclooctatetraenes Units
Institution name	Universidade de Santiago de Compostela
Expected presentation date	Feb 2024
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Title of new work	Polycyclic Aromatic Hydrocarbons (PAHs) containing Biphenylenes and Cyclooctatetraenes Units
Institution name	Universidade de Santiago de Compostela
Expected presentation date	Feb 2024
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Requestor Location	Universidade de Santiago de Compostela Rua de Jenaro de la Fuente s/n Santiago de Compostela, 15705 Spain Attn: Universidade de Santiago de Compostela
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Polycyclic aromatic hydrocarbons (PAHs) are a family of organic compounds presents around us from oil to interstellar space, that can be considered as well-defined graphene fragments. Defective PAHs with non hexagonal rings have emerge as improved scaffolds due to their ability to modify the properties of their planar analogous. The synthesis of both systems generally requires regioselective rings fusions, where metal-catalysed annulations have become one of the most attractive strategies.

Throughout this PhD thesis, 1,3- cyclohexadiene nuclei, presents in dihydrobiphenylenes systems, will be explored towards annulated systems containing biphenylenes units through oxidative process. Moreover, synthesis and reactivity of strained alkynes species (COTynes) for the formation of PAHs with COT units will also be adressed.