How to cite: *Angew. Chem. Int. Ed.* **2026**, *65*, e25713
doi.org/10.1002/anie.202525713

Photocatalysis

Accessing Molecular Complexity from Methane and Other Gaseous Alkanes via Photocatalytic Cascade Cyclization

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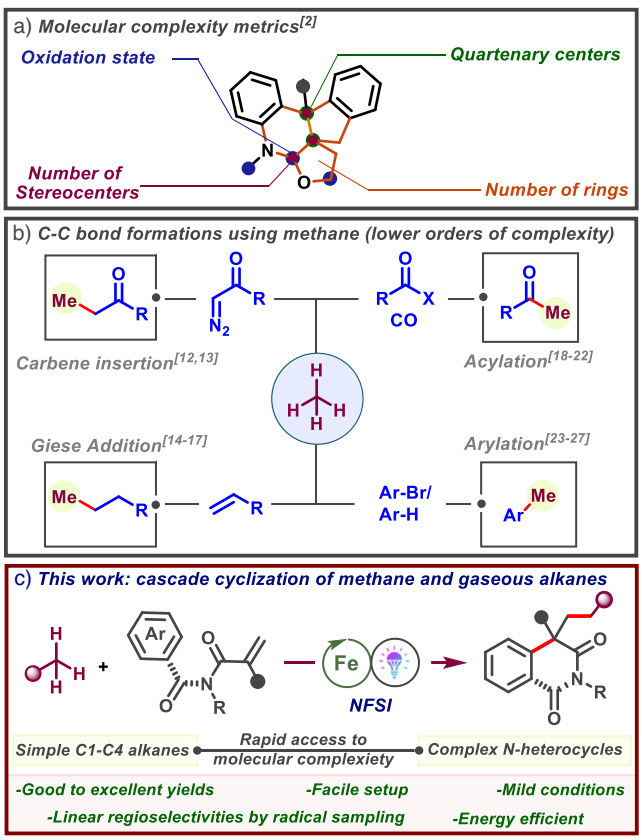
Abstract: The direct transformation of simple and abundant feedstocks into structurally complex molecules remains a central challenge in modern organic synthesis. Herein, we report a method for the oxidative cascade cyclization of *N*-aryl and *N*-benzoyl acrylamide derivatives, promoted by methane and other gaseous alkanes. This transformation is enabled by a readily available iron catalyst in combination with *N*-fluorobenzenesulfonimide (NFSI) as the oxidant, proceeding under mild conditions to afford a diverse array of *N*-heterocyclic frameworks in high yields. Late-stage functionalization studies highlight the utility of methane in the synthesis of biologically relevant scaffolds. Moreover, the Fe/NFSI system facilitates a radical sampling regime that enables the selective functionalization of less reactive primary C─H bonds. Overall, this work establishes a sustainable and versatile platform for constructing molecular complexity directly from gaseous alkanes.

The efficient generation of molecular complexity is a central goal in synthetic chemistry.[1–3] As noted by Sarpong, molecular complexity is assessed based on parameters such as the number of rings, quaternary centers, stereocenters, and oxidized carbon atoms (Scheme 1a).[2] In this context, the direct generation of molecular complexity from simple and abundant feedstocks is highly desirable, offering significant advantages in terms of sustainability, atom economy and step efficiency. Methane, the simplest alkane and a potent greenhouse gas, is one of the most abundant carbon feedstocks on the planet.[4,5] Thus, its efficient conversion into complex organic molecules would represent one of the most transformative avenues in organic synthesis.[6,7] However, the inertness of C─H bonds (BDE~105 kcal/mol, pKa~50) in methane makes its functionalization highly challenging. Consequently, strategies for efficient methane functionalization remain scarce.[8–12] Key advances in C─C bond formations with methane include carbene insertions,[12,13] addition to Michael acceptors,[14–17] acylations,[18–22] and arylations[23–27] (Scheme 1b). Nevertheless, methods to directly achieve molecular complexity (as defined above) from methane and other gaseous (C2-C4) alkanes remain elusive.



Scheme 1. Overview of the work. a) Molecular complexity metrics. b) Previous C─C bond forming reactions employing methane. c) This work: radical cascade cyclization promoted by methane and other gaseous alkanes.

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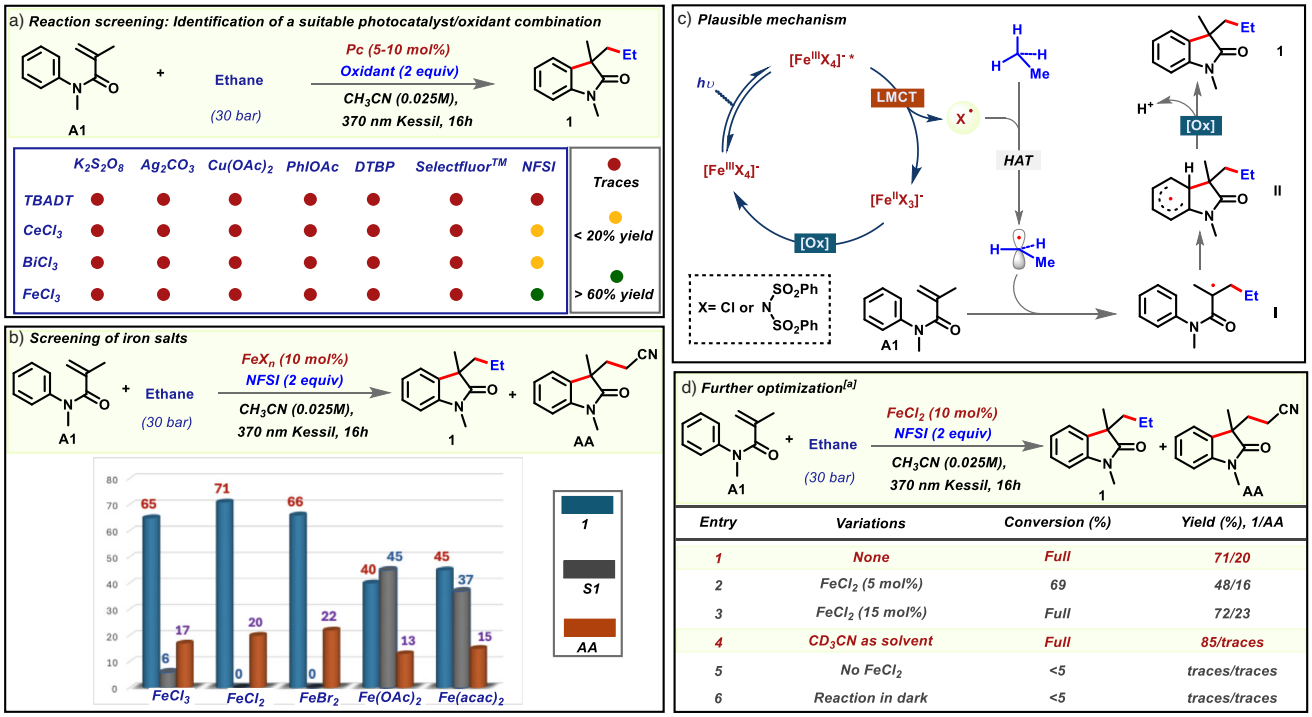
Additional supporting information can be found online in the Supporting Information section



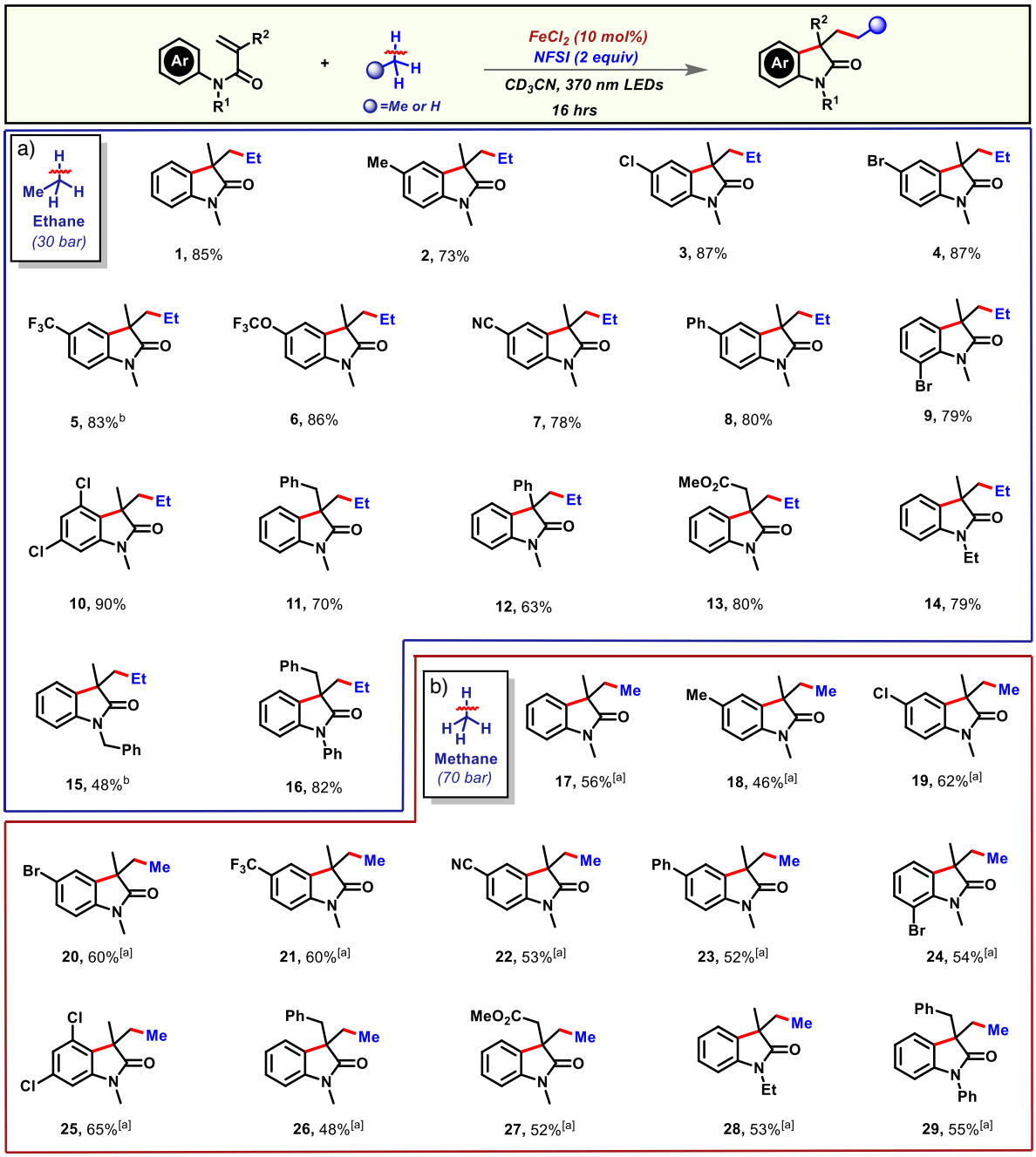
Entry	Variations	Conversion (%)	Yield (%), 1/AA
1	None	Full	71/20
2	$FeCl_2$ (5 mol%)	69	48/16
3	$FeCl_2$ (15 mol%)	Full	72/23
4	CD_3CN as solvent	Full	85/traces
5	No $FeCl_2$	<5	traces/traces
6	Reaction in dark	<5	traces/traces

Scheme 2. Optimization studies: a) screening of photocatalyst (Pc)/oxidant combinations and b) screening of iron salts. c) Proposed mechanism. d) Optimization of the $FeCl_2$/NFSI system. [a] Reaction conditions: **A1** (0.2 mmol), ethane (30 bar), Pc (10 mol%), NFSI (0.4 mmol), MeCN (0.025 M) at rt and 1200 rpm and irradiation by a 370 nm 44 W Kessil LED lamp. Yields refer to isolated products. AA = Acetonitrile addition.

Radical cascade cyclizations are powerful synthetic strategies that enable rapid access to complex molecular frameworks from simple precursors.[28–34] By allowing the formation of multiple bonds in a single step, they provide facile access to polycyclic or highly functionalized cores.[35–38] Traditionally, these cyclizations have relied on pre-functionalized substrates and often require harsh conditions, typically involving peroxide-based initiators. These radical precursors are often costly and require prior preparation, thereby compromising both the atom economy and the sustainability of the process. In this context, the development of cascade cyclizations directly using methane, and other gaseous alkanes, could unlock new avenues in sustainable synthesis and next-generation molecular design. Such a method would represent a strategic platform for accessing complex molecular frameworks from simple, abundant feedstocks.

We hereby report an Fe-catalyzed oxidative cascade cyclization of a range of *N*-aryl acrylamide derivatives promoted by gaseous alkanes (Scheme 1c). The reaction exhibits broad substrate scope and high yields, enabling access to a variety of complex *N*-heterocyclic frameworks. Subsequent derivatizations highlight the potential of this methodology to convert methane and ethane into biologically relevant molecules. Furthermore, we describe how the combination of Fe and *N*-fluorobenzenesulfonimide (NFSI) unlocks a unique radical sampling regime that allows selective C–H functionalization of primary positions in propane, *n*-butane, and isobutane.

We began our study by exploring the cascade cyclization of acrylamide **A1** promoted by ethane (30 bar) in acetonitrile using a 370 nm Kessil lamp. Initially, it was crucial to identify a suitable combination of photocatalyst and oxidant. The optimal oxidant must be capable of oxidizing both the aryl radical intermediate, formed following the radical addition and cyclization steps, and the reduced photocatalyst, thereby ensuring efficient regeneration of the catalytic cycle. Thorough evaluation of a variety of HAT photocatalysts with a range of oxidants was carried out (Scheme 2a). Tetrabutylammonium decatungstate (TBADT) failed to deliver product **1** with any of the oxidants under study. Common indirect HAT photocatalysts failed to deliver compound **1** with all oxidants tested, except NFSI. When NFSI was used in combination with $CeCl_3$ or $BiCl_3$, the yields of **1** remained below 20%. Remarkably, the use of $FeCl_3$ led to a significant improvement, affording **1** in 63% yield. Further screening of several Fe salts revealed the superior catalytic activity of $FeCl_2$, which led to **1** in 71% yield along with 20% of acetonitrile activation product **AA** (Scheme 2b). Interestingly, other Fe salts such as $FeBr_2$, $Fe(OAc)_2$, and $Fe(acac)_2$ proved also effective, although they led to diminished yield and selectivity. This was surprising as these catalytic systems would not generate chlorine radicals capable of carrying out HAT on ethane. This suggested that sulfonimidyl radical (BDE = 107 kcal/mol) may also act as a potential HAT agent in these cases.[39–43] EPR and UV–vis spectroscopic analysis of a mixture of $FeCl_2$ and NFSI revealed the formation of LMCT active Fe^{3+} species (See Supporting Information). These Fe^{3+} species, upon photoexcitation, would undergo LMCT to generate either chlorine or sulfonimidyl radicals (Scheme 2c).[44–49] These radicals then undergo HAT with ethane to generate

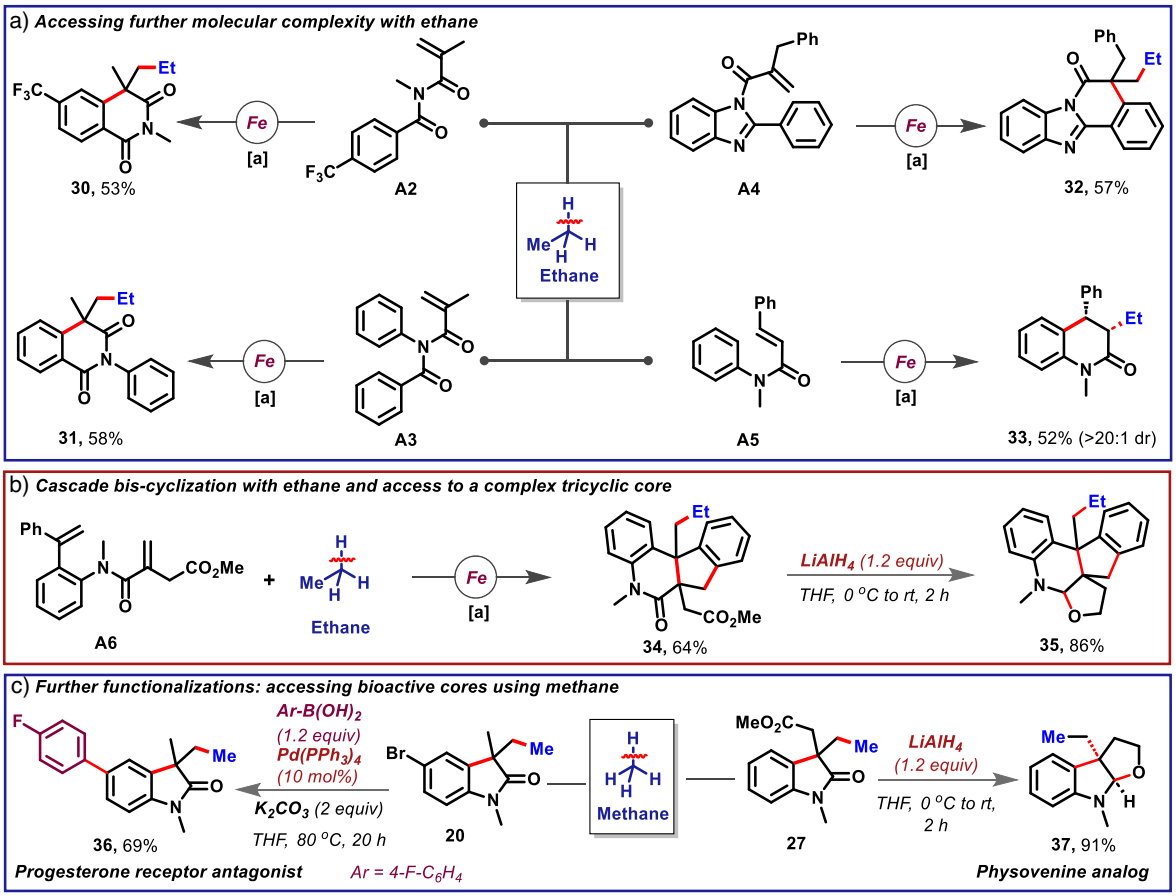


Scheme 3. Radical cyclizations promoted by a) ethane and b) methane. Reactions were run at 0.2 mmol scale using conditions in Scheme 1c, entry 4, unless otherwise noted. Yields refer to isolated products. Regiosiomeric ratio shown in brackets; structure of the major isomer is depicted. [a] 15 mol% $FeCl_2$, CD_3CN (0.0125 M).

the key ethyl radical, which would add onto the acrylamide **A1,** forming the stabilized α-carbonyl radical species **I**. The ensuing dearomative cyclization would form **II,** which upon oxidation and subsequent deprotonation delivers product **1**. The oxidation of the low valent Fe^{2+} regenerates the active Fe^{3+}catalyst.

Next, we further optimized the reaction by using $FeCl_2$ as a photocatalyst (Scheme 2d). Decreasing the catalyst loading to 5 mol% was found to be deleterious, whereas no significant change in product yield was observed upon increasing the loading of $FeCl_2$. The use of CD_3CN instead of CH_3CN as solvent circumvented the solvent activation, selectively leading to **1** in a remarkable 85% yield. Finally, control experiments showed that the reaction does not proceed either in the absence of $FeCl_2$ or light.

Having established optimized conditions, we next explored the scope of the ethane-promoted cascade cyclization (Scheme 3a). *N*-aryl acrylamides bearing electronically diverse *para*-substituents underwent facile cyclization to deliver the corresponding products **2–7** in high



Scheme 4. Radical a) cyclization and b) bis-cyclization of different acrylamide derivatives promoted by ethane. c) Transformation of methane-derived products into bioactive compounds. Conditions: [a] **A2-A6** (0.2 mmol), ethane (30 bar), $FeCl_2$ (10 mol%), NFSI (0.4 mmol), MeCN (0.025 M) at rt and 1200 rpm and irradiation by a 370 nm 44 W Kessil LED lamp.

yields. Substitutions were also tolerated at the *ortho*- and *meta*-positions as illustrated by the formation of products **9** and **10**. Furthermore, the reaction accommodated a range of alkene substituents, including benzyl, phenyl, and ester groups, affording products **11**–**13** in excellent yields. Variation of the *N*-protecting group was likewise feasible, with ethyl (**14**), benzyl (**15**), and phenyl (**16**) derivatives obtained efficiently. Notably, no by-products arising from functionalization of activated C─H bonds in compounds such as **11**, **13**, **15**, and **16** were detected.

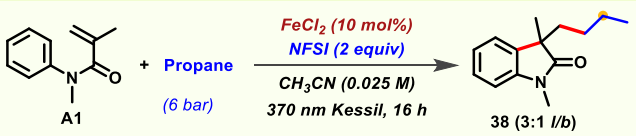
Importantly, our photocatalytic cascade cyclization was also amenable for methane, the major component of natural gas and the most unreactive alkane (BDE = 105 kcal/mol). A higher reaction pressure of 70 bar, more diluted conditions and a slightly higher loading of $FeCl_2$ was required to efficiently promote the reaction (see Supporting Information for optimization details). Under these conditions, a range of *N*-aryl acrylamides underwent cascade cyclization providing the corresponding products **17–29** in remarkably good yields (Scheme 3b).

The present protocol offers an excellent platform to expand the use of the two main components of natural gas in the synthesis of a more diverse range of complex polycyclic structures. To illustrate this, we extended this cascade cyclization strategy to different types of substrates (Scheme 4). Cyclization of acrylamide derivative **A2** with ethane furnished isoquinoline-1,3-dione **30**. Substrate **A3** underwent selective cyclization at the benzoyl moiety over the phenyl group, delivering compound **31** in good yield. Benzimidazole-tethered acrylamide **A4** smoothly afforded imidazo[2,1-a]isoquinolin-6(5*H*)-one **32**. Cinnamyl amide **A5** also proved to be an efficient substrate, yielding dihydroquinolin-2(1*H*)-one **33** with excellent diastereoselectivity. Notably, a bis-cyclization was also achieved under standard conditions. Dialkenyl derivative **A6** underwent double cyclization to form indeno[2,1-c]quinolinone **34**, which, upon reduction with $LiAlH_4$, furnished the complex alkaloid-like tricyclic furo[2,3-b]indeno[2,1-c]quinoline **35**. Furthermore, methane-derived indolinones **20** and **27** were transformed into biologically relevant progesterone receptor agonist **36**[50] and Physovenine analog **37**,[51] respectively. Collectively, all these examples exemplify the streamlined access to molecular complexity from inert gaseous alkanes and underscore the potential of the methodology for the effective use of natural gas main components.

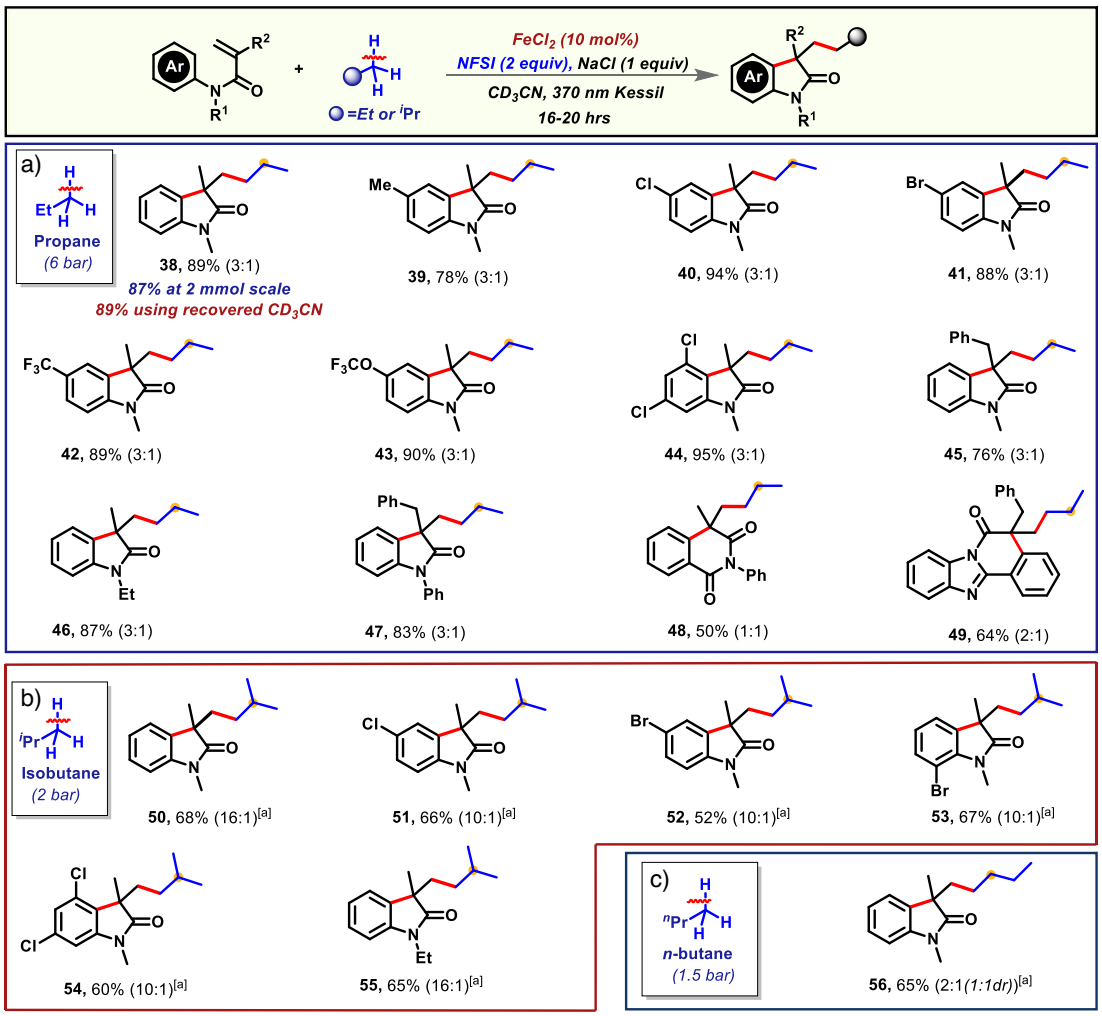
Having achieved efficient oxidative cyclization with methane and ethane, we attempted the logical extension of this method to the use of C3 and C4 gaseous alkanes. Surprisingly, the cascade cyclization of propane (BDE = 99 kcal/mol) was found to be more challenging than that

of ethane (BDE = 102 kcal/mol) or methane (BDE = 105 kcal/mol). The reaction of propane (6 bar) with acrylamide **A1** in CH_3CN led to product **38** in only 25% yield, while 47% of unreacted **A1** was recovered (Table 1, entry 1). We hypothesized that the low conversion could be due to an inefficient regeneration of the photocatalytically active [Fe(III)]-Cl species. To address this, we screened a variety of halide sources as additives to improve the reaction profile (Table 1, entries 2–7). Among the different additives tested, NaCl (1 equiv) proved to be the most effective, leading to full conversion and affording product **38** in 62% yield, along with 31% of the acetonitrile activation product **AA** (Table 1, entry 7). Notably, when CD_3CN was used as the solvent, the yield of **38** increased significantly up to 89%, while the formation of **AA** was suppressed (Table 1, entry 8). Interestingly, selective functionalization at the primary position over the secondary one was observed, resulting in the preferred installation of an *n*-propyl group rather than an isopropyl group. This selectivity is reflected in the formation of product **38** as a 3:1 linear:branched (l:b) mixture. Notably, this linear selectivity contrasts with the branched selectivity observed in previous reports on propane functionalization.[14–17,20–26]

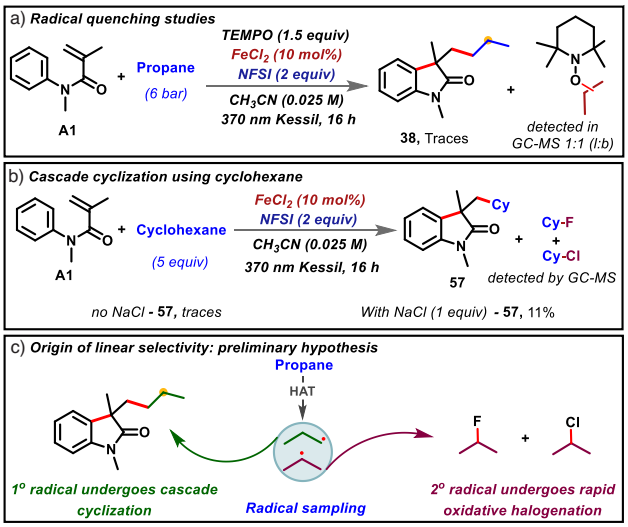
Table 1: Reaction optimization of the cascade cyclization with propane.



Entry	Additive (1 equiv)	Conversion (%)	Yield (%), (38/AA)
1	None	53	25/12
2	LiCl	76	53/15
3	LiBr	62	36/14
4	LiF	67	40/20
5	NaCl	full	62/31
6	TBACl	72	42/22
7	TMSCl	57	29/14
8	NaCl, CD_3CN as solvent	full	89/traces



Scheme 5. Radical cyclizations promoted by a) propane, b) isobutane and c) *n*-butane. Reactions run at 0.2 mmol scale using conditions shown in Table 1, entry 9, unless otherwise noted. Yields refer to isolated products. Regiosiomeric linear:branched (l:b) ratio shown in brackets; structure of the major isomer is depicted. [a] 3 equiv of NFSI.



Scheme 6. Preliminary insights into the origin of linear selectivity: a) radical quenching experiments, b) reaction outcome using cyclohexane, and c) proposed origin of linear selectivity.

Under these modified reaction conditions, a range of *N*-aryl acrylamides were reacted with propane to deliver products **38–49** in good to excellent yields with linear selectivity (up to l:b = 3:1) in almost all cases (Scheme 5a). The reaction was found to be scalable, as demonstrated with the 2 mmol scale synthesis of **38**. It is also important to note that CD_3CN could be easily recovered and reused without erosion in yields.

We next tried the cascade cyclization with isobutane (Scheme 5b). This reaction was found to be even more challenging and required a higher loading of NFSI to achieve productive yields (see Supporting Information for optimization details). Under these conditions, product **50** was obtained in 68% yield with a remarkable linear selectivity (l:b = 16:1). A range of *N*-aryl acrylamides underwent cyclization with isobutane to afford products **51–55** in good yields with linear selectivity in all cases (l:b = 10:1–16:1). Finally, cyclization of acrylamide **A1** could be also performed with *n*-butane, which was also found be selective toward the linear isomer furnishing product **56** as a 2:1 l:b mixture.

The observed linear selectivity in the reactions involving propane, isobutane, and *n*-butane deserved further attention. Therefore, we carried out some preliminary mechanistic studies to get some insights into the factors behind this selectivity (Scheme 6). The reaction using propane was quenched by TEMPO, and the propyl-TEMPO adduct was observed in GC-MS as a 1:1 (l:b) mixture (Scheme 6a). This suggests that both *n*-propyl and isopropyl radicals are initially generated in equal amounts, and the linear selectivity likely originates during subsequent steps. Next, we studied the cascade cyclization using an alkane having all secondary carbons (cyclohexane). The cascade cyclization with cyclohexane failed to proceed in the absence of NaCl, and only 11% of product **57** was obtained in the presence of 1 equiv of NaCl (Scheme 6b). Importantly, GC-MS analysis of these reactions showed significant formation of chlorocyclohexane and fluorocyclohexane.

Based on these observations, we hypothesized that the linear selectivity observed could be due to a radical sampling process (Scheme 6c).[52,53] The propensity of secondary and tertiary alkyl radicals to undergo rapid oxidative fluorination selectively over their primary counterparts has been well documented.[54–56] Accordingly, in the presence of NFSI, the secondary isopropyl radicals would be more prone to fluorination, whereas the primary *n*-propyl radicals would preferentially engage in the cascade cyclization pathway. In analogy, a selective radical ligand transfer (RLT)[57,59] from Fe-Cl species to the secondary radicals could explain the formation of the chlorination side product. This competing pathway would deplete the chloride ligands on Fe, and this could be the reason behind the necessity of NaCl as a chloride reservoir when alkanes bearing secondary or tertiary C–H bonds are used.

In summary, we report an efficient protocol for cascade cyclizations of methane and other gaseous alkanes with *N*-aryl and *N*-benzoyl acrylamides. The reaction proceeds under mild conditions, delivers consistently high yields, and exhibits broad functional group tolerance. The operational simplicity and scalability of the method highlight its potential as a practical platform for constructing molecular complexity directly from gaseous alkanes. An oxidative radical sampling regime was observed in the case of propane, *n*-butane, and isobutane, which led to the selective functionalization of aliphatic primary positions. Detailed mechanistic studies on this radical sampling regime are underway. We anticipate that this study will inspire others to explore cascade cyclizations of gaseous alkanes to access higher orders of complexity by using various coupling partners.

Supporting Information

Data relating to the materials and methods, optimization studies, experimental procedures and compound characterization. The authors have cited additional references within the Supporting Information.[60–72]

Acknowledgements

Financial support from the European Research Council (ERC-CoG 863914-BECAME), the Agencia Estatal de Investigación (PID2023-151875NB-I00), the Xunta de Galicia (ED431C 2022/27); Centro de investigación do Sistema universitario de Galicia accreditation 2023–2027, (ED431G 2023/03) and the European Regional Development Fund (ERDF) is gratefully acknowledged. A.M.N. thanks the European Union's Horizon Europe research and innovation program for a Marie Skłodowska-Curie postdoctoral fellowship (MePhoCat, No.101150274). J.M.M. thanks Xunta de Galicia for a predoctoral fellowship (ED481A-2024–112).

Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Cascade cyclization • Gaseous alkanes • Iron • Molecular complexity • Radical sampling

[1] K. C. Nicolaou, C. R. H. Hale, C. Nilewski, H. A. Ioannidou, *Chem. Soc. Rev.* **2012**, *41*, 5185, https://doi.org/10.1039/c2cs35116a.

[2] T. I. Oprea, C. Bologa, *J. Med. Chem.* **2023**, *66*, 12710–12714, https://doi.org/10.1021/acs.jmedchem.3c01507.

[3] B. A. Wright, R. Sarpong, *Nat. Rev. Chem.* **2024**, *8*, 776–792, https://doi.org/10.1038/s41570-024-00645-8.

[4] R. A. Kerr, *Science* **2010**, *328*, 1624–1626, https://doi.org/10.1126/science.328.5986.1624.

[5] J. Cooper, L. Stamford, A. Azapagic, *Energy Technol.* **2016**, *4*, 772–792, https://doi.org/10.1002/ente.201500464.

[6] N. J. Gunsalus, A. Koppaka, S. H. Park, S. M. Bischof, B. G. Hashiguchi, R. A. Periana, *Chem. Rev.* **2017**, *117*, 8521–8573, https://doi.org/10.1021/acs.chemrev.6b00739.

[7] E. McFarland, *Science* **2012**, *338*, 340–342, https://doi.org/10.1126/science.1226840.

[8] A. Caballero, P. J. Pérez, *Chem. Soc. Rev.* **2013**, *42*, 8809, https://doi.org/10.1039/c3cs60120j.

[9] A. Pulcinella, D. Mazzarella, T. Noël, *Chem. Commun.* **2021**, *57*, 9956–9967, https://doi.org/10.1039/D1CC04073A.

[10] A. Velasco-Rubio, P. Martínez-Balart, A. M. Álvarez-Constantino, M. Fañanás-Mastral, *Chem. Commun.* **2023**, *59*, 9424–9444, https://doi.org/10.1039/D3CC02790B.

[11] L. Chang, S. Wang, Q. An, L. Liu, H. Wang, Y. Li, K. Feng, Z. Zuo, *Chem. Sci.* **2023**, *14*, 6841–6859, https://doi.org/10.1039/D3SC01118F.

[12] A. Caballero, E. Despagnet-Ayoub, M. M. Díaz-Requejo, A. Díaz-Rodríguez, M. E. González-Núñez, R. Mello, B. K. Muñoz, W. S. Ojo, G. Asensio, M. Etienne, P. J. Pérez, *Science* **2011**, *332*, 835–838, https://doi.org/10.1126/science.1204131

[13] A. Olmos, R. Gava, B. Noverges, D. Bellezza, K. Jacob, M. Besora, W. M. C. Sameera, A. Caballero, M. Etienne, F. Maseras, G. Asensio, P. J. Pérez, *Angew. Chem. Int. Ed.* **2018**, *57*, 13848–13852, https://doi.org/10.1002/anie.201807448.

[14] G. Laudadio, Y. Deng, K. Van der Wal, D. Ravelli, M. Nuño, M. M. Fagnoni, D. Guthrie, Y. Sun, T. Noël, *Science* **2020**, *369*, 92–96, https://doi.org/10.1126/science.abb4688.

[15] G. B. Panetti, Q. Yang, M. R. Gau, P. J. Carroll, P. J. Walsh, E. J. Schelter, *Chem. Catal.* **2022**, *2*, 853–866, https://doi.org/10.1016/j.checat.2022.02.013.

[16] Z.-Y. Dai, S.-Q. Zhang, X. Hong, P.-S. Wang, L.-Z. Gong, *Chem. Catal.* **2022**, *2*, 1211–1222, https://doi.org/10.1016/j.checat.2022.03.020.

[17] P. Martínez-Balart, Á. Velasco-Rubio, S. Barbeira-Arán, H. Jiménez-Cristóbal, M. Fañanás-Mastral, *Green Chem.* **2024**, *26*, 11196–11205, https://doi.org/10.1039/D4GC04176C.

[18] R. A. Periana, O. Mironov, D. Taube, G. Bhalla, C. J. Jones, *Science* **2003**, *301*, 814–818, https://doi.org/10.1126/science.1086466.

[19] M. V. Kirillova, M. L. Kuznetsov, P. M. Reis, J. A. da Silva, J. J. da Silva, A. J. Pombeiro, *J. Am. Chem. Soc.* **2007**, *129*, 10531–10545, https://doi.org/10.1021/ja072531u.

[20] F. Raymenants, T. M. Masson, J. Sanjosé-Orduna, T. Noël, *Angew. Chem. Int. Ed.* **2023**, *62*, e202308563, https://doi.org/10.1002/anie.202308563.

[21] L. Wang, X.-F. Wu, *Nat. Commun.* **2025**, *16*, 4663, https://doi.org/10.1038/s41467-025-58472-4.

[22] A. M. Nair, S. Barbeira-Arán, J. M. Malga, M. Fañanás-Mastral, *Cell Rep. Phys. Sci.* **2025**, *6*, 102912, https://doi.org/10.1016/j.xcrp.2025.102912.

[23] A. Hu, J.-J. Guo, H. Pan, Z. Zuo, *Science* **2018**, *361*, 668–672, https://doi.org/10.1126/science.aat9750.

[24] P. C. Tiwari, A. Pulcinella, E. Hodžić, T. Noël, *ACS Cent. Sci.* **2025**, *11*, 910–917, https://doi.org/10.1021/acscentsci.5c00468.

[25] A. M. Nair, P. Martínez-Balart, S. Barbeira-Arán, M. Fañanás-Mastral, *Angew. Chem. Int. Ed.* **2025**, *64*, e202416957, https://doi.org/10.1002/anie.202416957.

[26] A. Pulcinella, P. C. Tiwari, A. Luridiana, K. Yamazaki, D. Mazzarella, A. K. Sadhoe, A. I. Alfano, E. H. Tiekink, T. A. Hamlin, T. Noël, *Angew. Chem. Int. Ed.* **2025**, *64*, e202413846, https://doi.org/10.1002/anie.202413846.

[27] B. Shao, A. L. Bagdasarian, S. Popov, H. M. Nelson, *Science* **2017**, *355*, 1403–1407, https://doi.org/10.1126/science.aam7975.

[28] S. P. Pitre, N. A. Weires, L. E. Overman, *J. Am. Chem. Soc.* **2019**, *141*, 2800–2813, https://doi.org/10.1021/jacs.8b11790.

[29] U. Wille, *Chem. Rev.* **2013**, *113*, 813–853, https://doi.org/10.1021/cr100359d.

[30] M. Latrache, N. Hoffmann, *Chem. Soc. Rev.* **2021**, *50*, 7418–7435, https://doi.org/10.1039/D1CS00196E

[31] B. Zhang, A. Studer, *Chem. Soc. Rev.* **2015**, *44*, 3505–3521, https://doi.org/10.1039/C5CS00083A.

[32] G.-A. Coppola, S. Pillitteri, E. Van der Eycken, S.-L. You, U.-K. Sharma, *Chem. Soc. Rev.* **2022**, *51*, 2313–2382, https://doi.org/10.1039/D1CS00510C.

[33] H.-M. Huang, D. J. Procter, *J. Am. Chem. Soc.* **2016**, *138*, 7770–7775, https://doi.org/10.1021/jacs.6b04086.

[34] Y. Jiang, R. E. McNamee, P. J. Smith, A. Sozanschi, Z. Tong, E. A. Anderson, *Chem. Soc. Rev.* **2021**, *50*, 58–71, https://doi.org/10.1039/D0CS00768D.

[35] W. Kong, N. Fuentes, A. García-Domínguez, E. Merino, C. Nevado, *Angew. Chem. Int. Ed.* **2015**, *54*, 2487–2491, https://doi.org/10.1002/anie.201409659.

[36] P. Wu, G. Goujon, S. Pan, B. Tuccio, B. Pégot, G. Dagousset, E. Anselmi, E. Magnier, C. Bolm, *Angew. Chem. Int. Ed.* **2024**, *63*, e202412418, https://doi.org/10.1002/anie.202412418.

[37] K. Muralirajan, R. Kancherla, J. A. Bau, M. R. Taksande, M. Qureshi, K. Takanabe, M. Rueping, *ACS Catal.* **2021**, *11*, 14772–14780, https://doi.org/10.1021/acscatal.1c04053.

[38] W.-T. Wei, M.-B. Zhou, J.-H. Fan, W. Liu, R.-J. Song, Y. Liu, M. Hu, P. Xie, J.-H. Li, *Angew. Chem. Int. Ed.* **2013**, *52*, 3638–3641, https://doi.org/10.1002/anie.201210029.

[39] M. Mandal, J. A. Buss, S.-J. Chen, C. J. Cramer, S. S. Stahl, *Chem. Sci.* **2024**, *15*, 1364–1373, https://doi.org/10.1039/D3SC03597B.

[40] H. Hu, S.-J. Chen, M. Mandal, S. M. Pratik, J. A. Buss, S. W. Krska, C. J. Cramer, S. S. Stahl, *Nat. Catal.* **2020**, *3*, 358–367, https://doi.org/10.1038/s41929-020-0425-1.

[41] J. A. Buss, A. Vasilopoulos, D. L. Golden, S. S. Stahl, *Org. Lett.* **2020**, *22*, 5749–5752, https://doi.org/10.1021/acs.orglett.0c02239.

[42] Z. Lu, M. Ju, Y. Wang, J. M. Meinhardt, J. I. Martinez Alvarado, E. Villemure, J. A. Terrett, S. Lin, *Nature* **2023**, *619*, 514–520, https://doi.org/10.1038/s41586-023-06131-3.

[43] Z. Lu, J. Putziger, S. Lin, *Nat. Chem.* **2025**, *17*, 365–372, https://doi.org/10.1038/s41557-025-01749-4.

[44] F. Julia, *ACS Catal.* **2025**, *15*, 4665–4680, https://doi.org/10.1021/acscatal.4c07962.

[45] A. R. Gogoi, Á. Rentería-Gómez, T. D. Tan, J. W. Ng, M. J. Koh, O. Gutierrez, *Nat. Synth.* **2025**, *4*, 1036–1055, https://doi.org/10.1038/s44160-025-00860-1.

[46] K.-J. Bian, S.-C. Kao, D. Nemoto, Jr., X.-W. Chen, J. G. West, *Nat. Commun.* **2022**, *13*, 7881, https://doi.org/10.1038/s41467-022-35560-3.

[47] K.-J. Bian, S. Yu, Y. Chen, Q. Liu, X. Chen, D. Nemoto, Jr., S.-C. Kao, A. A. Marti, J. G. West, *Nat. Commun.* **2025**, *16*, 7906, https://doi.org/10.1038/s41467-025-63203-w.

[48] S.-C. Kao, K.-J. Bian, X.-W. Chen, Y. Chen, A. A. Martí, J. G. West, *Chem. Catal.* **2023**, *3*, 100603, https://doi.org/10.1016/j.checat.2023.100603.
[49] When iron chloride serves as the photocatalyst, chlorine radical is likely the primary species responsible for alkane activation. Nevertheless, the involvement of a sulfonimidyl radical as HAT agent cannot be fully excluded, particularly when other iron salts are employed instead of iron chloride.
[50] S. Alluri, H. Feng, M. Livings, L. Samp, D. Biswas, T. M. Lam, E. Lobkovsky, A. K. Ganguly, *Tetrahedron Lett.* **2011**, *52*, 3945–3948, https://doi.org/10.1016/j.tetlet.2011.05.120.
[51] B. W. Boal, A. W. Schammel, N. K. Garg, *Org. Lett.* **2009**, *11*, 3458–3461, https://doi.org/10.1021/ol901383j.
[52] K. Chen, Q. Zeng, L. Xie, Z. Xue, J. Wang, Y. Xu, *Nature* **2023**, *620*, 1007–1012, https://doi.org/10.1038/s41586-023-06347-3.
[53] M. Wang, Y. Huang, P. Hu, *Science* **2024**, *383*, 537–544, https://doi.org/10.1126/science.adj9258.
[54] S. D. Halperin, H. Fan, S. Chang, R. E. Martin, R. Britton, *Angew. Chem. Int. Ed.* **2014**, *53*, 4690–4693, https://doi.org/10.1002/anie.201400420.
[55] J. G. West, T. A. Bedell, E. J. Sorensen, *Angew. Chem. Int. Ed.* **2016**, *55*, 8923–8927, https://doi.org/10.1002/anie.201603149.
[56] S. Bloom, C. R. Pitts, R. Woltornist, A. Griswold, M. G. Holl, T. Lectka, *Org. Lett.* **2013**, *15*, 1722–1724, https://doi.org/10.1021/ol400424s.
[57] D. T. Nemoto, Jr., K.-J. Bian, S.-C. Kao, J. G. West, *Beilstein J. Org. Chem.* **2023**, *19*, 1225–1233, https://doi.org/10.3762/bjoc.19.90.
[58] K.-J. Bian, D. Nemoto, Jr., X.-W. Chen, S.-C. Kao, J. Hooson, J. G. West, *Chem. Sci.* **2024**, *15*, 124–133, https://doi.org/10.1039/D3SC05231A.
[59] K.-J. Bian, D. Nemoto, Jr., S.-C. Kao, Y. He, Y. Li, X.-S. Wang, J. G. West, *J. Am. Chem. Soc.* **2022**, *144*, 11810–11821, https://doi.org/10.1021/jacs.2c04188.
[60] Y. Guo, S. Ma, L. Shi, L. Liu, X. Lei, P. Jiao, *Org. Chem. Front.* **2023**, *10*, 2257–2262, https://doi.org/10.1039/D3QO00181D.
[61] X. Sun, J. P. Zhu, Q. C. Qiu, Y. L. He, D. R. Hu, X. L. Li, G. P. Lu, Y. H. Yuan, X. F. Zhang, X. Xu, M. Yu, B. Wu, *Org. Biomol. Chem.* **2022**, *20*, 8042–8048, https://doi.org/10.1039/d2ob01256a.
[62] P. Xu, H. Xu, S. Wang, T. Z. Hao, S. Y. Yan, D. Guo, X. Zhu, *Org. Chem. Front.* **2023**, *10*, 2013–2017, https://doi.org/10.1039/D3QO00126A.
[63] Y. Z. Wang, W. J. Lin, H. C. Liu, W. Yu, *Org. Chem. Front.* **2022**, *9*, 2164–2168, https://doi.org/10.1039/D2QO00127F.
[64] J. L. Couto, M. M. Hornink, V. R. Nascimiento, L. H. Andrade, *Eur. J. Org. Chem.* **2022**, *2022*, e202200962, https://doi.org/10.1002/ejoc.202200962.
[65] W. Yan, Z. Qu, F. Zhao, G. J. Deng, G. J. Mao, H. Huang, *Adv. Synth. Catal.* **2023**, *365*, 612–617, https://doi.org/10.1002/adsc.202201234.
[66] L. Huang, J. Sun, B. Sun, S. Song, J. Li, *Chem. Commun.* **2024**, *60*, 4818–4821, https://doi.org/10.1039/D4CC00916A.
[67] S. S. Jiang, Y. T. Xiao, Y. C. Wu, S. Z. Luo, R. J. Song, J. H. Li, *Org. Biomol. Chem.* **2020**, *18*, 4843–4847, https://doi.org/10.1039/D0OB00877J.
[68] Q. Gui, L. Hu, C. X, , J. Liu, Z. Tan, *Asian J. Org. Chem.* **2015**, *4*, 870–874, https://doi.org/10.1002/ajoc.201500217.
[69] Z. Xie, P. Li, Y. Hu, N. Xu, L. Wang, *Org. Biomol. Chem.* **2017**, *15*, 4205–4211, https://doi.org/10.1039/C7OB00779E.
[70] Z. Li, X. Cui, L. Niu, Y. Ren, M. Bian, X. Yang, B. Yang, Q. Yan, J. Chao, *Adv. Synth. Catal.* **2017**, *359*, 246–249, https://doi.org/10.1002/adsc.201601001.
[71] O. Suarez-Castillo, M. Melendez-Rodriguez, L. R. Castelan-Duarte, M. Sanchez-Zavala, E. Rivera-Becerril, M. S. Morales-Rios, P. Joseph-Nathan, *Tetrahedron* **2009**, *20*, 2374–2389, https://doi.org/10.1016/j.tetasy.2009.09.017.
[72] R. Gao, X. Luan, Z. Xie, L. Yang, Y. Pei, *Org. Biomol. Chem.* **2019**, *17*, 5262–5268, https://doi.org/10.1039/C9OB00492K.

Manuscript received: November 20, 2025
Revised manuscript received: December 09, 2025
Manuscript accepted: December 10, 2025
Version of record online: December 19, 2025