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# Chiral Coalition in Helical Sense Enhancement of Copolymers: the Role of the Absolute Configuration of Comonomers Promoting the Helical Scaffold

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*Chiral Communication, Helical Polymers, poly(phenylacetylene)s, Chiral Conflict, Sergeants and Soldiers effect.*

**ABSTRACT:** Both the role of the absolute configuration and the tendency of a chiral monomer to promote a certain helical scaffold in a polyphenylacetylene (PPA) —that depends on the conformational composition at the pendant group— have been evaluated to study the communication between two chiral monomers within a copolymer chain. 19 different PPA copolymer series —47 copolymers altogether— were prepared to explore the existence of a chiral to chiral communication mechanism in helical copolymers. From the data obtained, we found that communication between two different chiral monomers within a copolymer chain emerge when the two monomers exhibit two special features: (a) a different conformational composition —one chiral monomer must exist in a single low energy conformation ("chiral Sergeant") and the other must present an equilibrium between two different conformers ("chiral Soldier")—, and (b) both chiral monomers must promote a similar scaffold in the PPA, either *cis-cisoidal* or *cis-transoidal*. In the selected systems, the chiral Soldier includes the 4-ethynylanilide (*para* position) of either (*R*)- or (*S*)-2-methoxy-2-phenylacetic acid [(*R*)- or (*S*)-1], pendants characterized by their conformational flexibility once polymerized (equilibrium between *synperiplanar* and *antiperiplanar* conformations). The chiral Sergeant contains the same chiral groups but linked to the backbone in *meta* position [3-ethynylanilide of (*R*)- or (*S*)-2-methoxy-2-phenylacetic acid, (*R*)- or (*S*)-2] and is selected on the basis of its restricted *antiperiplanar* conformation. Incorporation of a very small amount (1%) of the Sergeant [either (*R*)- or (*S*)-2] to a chain composed just by the Soldier transforms the originally axially racemic chain into a helix with strong sense preference (either *M* or *P*) that is determined by the absolute configuration of the Soldier. For instance, both poly-[(*R*)-1<sub>0.9</sub>-*co*-(*R*)-2<sub>0.1</sub>] and poly-[(*R*)-1<sub>0.9</sub>-*co*-(*S*)-2<sub>0.1</sub>] adopt *M* helical structures due to the absolute configuration of the soldier, although the extent of the chiral amplification induced by the Sergeant is different as a consequence of a different communication mechanism between the (*R*)-Sergeant/(*R*)-Soldier and the (*S*)-Sergeant/(*R*)-Soldier.

## INTRODUCTION

The helical structure adopted by many biomolecules and its relationship with their function<sup>1</sup> has inspired the scientific community to develop new non natural helical materials such as foldamers,<sup>2</sup> supramolecular helices<sup>3</sup> or helical polymers.<sup>4</sup>

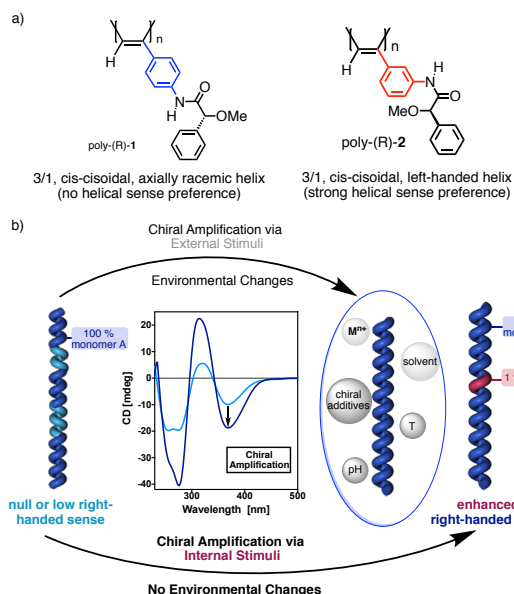
Studies on the folding of these helical materials have lead to the identification of the most relevant parameters that determine the formation of a helix and allowed the formulation of several mechanisms that explain the chiral amplification observed. Among them, the Sergeants and Soldiers effect,<sup>5</sup> the Majority rule<sup>6</sup> or the Domino effect<sup>7</sup> are particularly important.

The Sergeants and Soldiers effect, first described in polyisocyanates,<sup>8,9</sup> shows that the introduction of a small amount of a chiral monomer (Sergeant) within a polymer formed by an achiral monomer (Soldier) is able to induce an excess of the screw sense in the copolymer chain that depends on the *R/S* configuration of the Sergeant. It was also found that when the two monomers forming the copolymer are enantiomers in a 1/1 ratio, the copolymer is —as expected— axially racemic. However, the presence of a slight excess of one of the enantiomers [e.g., 51% (*R*) monomer and 49 % (*S*) or *vice versa*] produces the adoption of a single handed helical structure in the whole chain, a phenomenon known as the Majority rule.<sup>6,10,11</sup> It means that the major enantiomer determines the final helical sense.

The above mechanisms are based on the interaction between a chiral monomer and an achiral one (Sergeants and Soldiers effect) or between two chiral monomers that are enantiomers (Majority rule). Another case of chiral communication named chiral Conflict<sup>8</sup> was described in copolymers formed by two chiral components that induce opposite helical sense and are in close ratio, resulting in an axially racemic structure.

Herein we described a novel helical enhancement mechanism based on the interaction between two non-enantiomeric chiral monomers, where a chiral monomer (chiral Sergeant) will induce a preferred conformation on the other chiral monomer (chiral Soldier) resulting in a helical sense enhancement of the copolymer. This outcome is opposite to that originated from chiral conflict, where no interaction between the different chiral monomers is observed.

We will show in this paper that this chiral to chiral Sergeants and Soldiers effect allows the conversion of a chiral polymer with very low helical sense preference [poly-(*R*)-1] into a strongly biased one by introduction in the chain of a minute amount [i.e., <10%] of a selected chiral monomer [(*R*)-2], where the parent homopolymers (poly-1 and poly-2, Figure 1a) promote similar helical structures —both 3/1, *cis-cisoidal*; although poly-1 yields an axially racemic chain (no helical sense preference) while poly-2 induces a strong helical sense—.



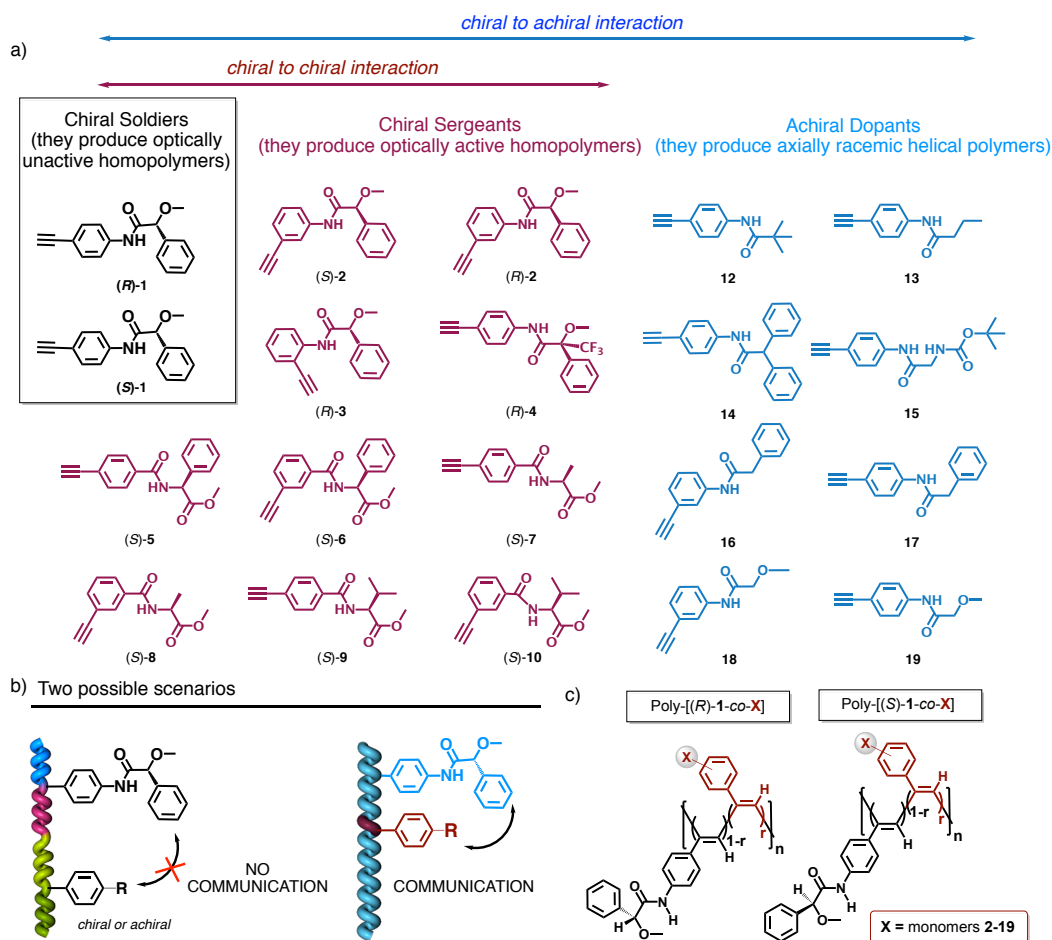
**Figure 1.** (a) Structures of poly-(R)-1 and poly-(R)-2 homopolymers. (b) Schematic illustration of the chiral amplification process of a helical polymer based on a chiral to chiral Sergeants and Soldiers effect vs. the amplification based on external stimuli.

This internal doping of the helically “poor” polymer with a tiny amount of the chiral Sergeant should be useful to optimize materials and chemical processes where the helical sense preference is directly related to its function, such as applications in chiral stationary phases,<sup>9</sup> asymmetric synthesis<sup>10</sup> or chiral recognition.<sup>11</sup> An additional advantage of this approach is that there is no need to resort to external stimuli (e.g., pH, solvents, temperature) and therefore no interferences with the application are expected (Figure 1b).

## RESULTS AND DISCUSSION

For the study of the helical sense enhancement based on chiral to chiral communication mechanism between chiral monomers, we prepared a series of PPA type copolymers composed by the combination of two chiral units in different ratios.

One of the monomeric components is formed by monomer (R)-1, which contains (R)-2-methoxy-2-phenylacetic acid [(R)-MPA] bonded to the PPA backbone in *para*-position for its enantiomeric form (S)-1]. This monomer, although chiral, produces a *cis-cisoidal* axially racemic helix (mixture of left and right-handed helices originated by its conformational composition) and where any helical amplification can be easily detected (active CD, Figure 2a). For these reasons, this monomer was selected as the chiral Soldier.<sup>12</sup>



**Figure 2.** (a) Structure of monomers used as chiral Soldiers, chiral Sergeants and achiral dopants. (b) Presence or absence of chiral to chiral communication in helical copolymers. (c) Copolymer series poly-[(R)-1-co-X] and poly-[(S)-1-co-X], where X are monomers 2-19 used as chiral Sergeants and achiral doping agents.

The other chiral component was selected taking into account both the conformational behavior of the monomers and the dynamic helical behavior of the corresponding homopolymers. Monomers (**2-10**) with a preponderant conformer in their structure are known to produce polymers with a defined helical structure, and therefore it was expected that they should work well as chiral Sergeants.<sup>17,21</sup> Moreover, two main groups can be distinguished in **2-10**, attending to the secondary structure adopted by the corresponding homopolymers:

a) Monomer **2** generates a *cis-cisoidal* helical scaffold similar in elongation to poly-**1**.

b) Monomers **3** to **10** produce *cis-transoidal* helical scaffolds that are more stretched than the one obtained from poly-**1**.

In this way, a series of PPA copolymers — i.e., poly-[(*R*)-**1-co-(R)-X**]<sub>n</sub> and poly-[(*S*)-**1-co-(R)-X**]<sub>n</sub>, X = **2** to **10**, a total of 34—, containing both enantiomers of chiral soldier **1**, were prepared using a rhodium (I) catalyst (Figure 2). Ten chiral homopolymers [poly-(**1-10**), Figure 1a and Figure 3] were also prepared and used as references.<sup>14,15</sup>

CD studies of the different copolymer series (0.3 mg/mL in THF) revealed that only poly-[(*R*)-**1-co-(R)-2**]<sub>n</sub> and poly-[(*S*)-**1-co-(R)-2**]<sub>n</sub>, both made from monomers that generate *cis-cisoidal* homopolymers (poly-**1** and poly-**2**, Figure 1a) showed helical sense amplification, associated to the interaction between monomers **1** and **2** (Figure 4a).

On the contrary, the other copolymer series — poly-[(*R*)-**1-co-(R)-X**]<sub>n</sub>, X = **3** to **10**—, made from monomers producing different helical scaffolds (poly-**1** = *cis-cisoidal*; poly-(**3-10**) = *cis-transoidal*), showed a decrease in the CD signal when the amount of Sergeant component (**3-10**) is reduced within the copolymer series — see Figure 4b for poly-[(*R*)-**1-co-(S)-7**]<sub>n</sub>, and S18 to S45 for the series involving monomer (*R*)-**1** and monomers **3-6**, **8-10**—, proving that no helical amplification is present, and therefore the absence of an efficient communication between chiral monomers **3-10** and chiral monomer **1**.

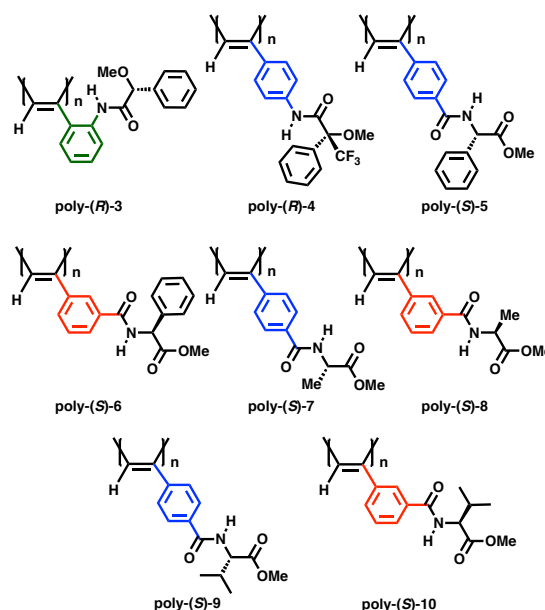
In addition, in order to demonstrate that the helical sense enhancement shown in poly-[(*R*)-**1-co-(R)-2**]<sub>n</sub> and poly-[(*S*)-**1-co-(R)-2**]<sub>n</sub> is due to a chiral to chiral communication within a stereoregular *cis-cisoidal* copolymer chain (poly-**1** and poly-**2**), we prepared a series of *cis-cisoidal* stereoregular PPA type copolymers [poly-[(*R*)-**1-co-(R)-X**]<sub>n</sub>, X = **12** to **19** (a total of 34), composed by the combination of the chiral soldier [(*R*)-MPA] and an achiral monomer (monomers **12-19**) in different ratios (Figure 2).<sup>22</sup>

CD experiments on poly-[(*R*)-**1-co-X**] and poly-[(*S*)-**1-co-X**]<sub>n</sub>, X = **12-19** (0.3 mg/mL in THF) showed a null CD and therefore the presence of an axially racemic helix, which indicates that there is no communication between those monomeric units — see Figure 4c for poly-[(*R*)-**1-co-(S)-13**]<sub>n</sub> series and S52 for those copolymer series involving monomer (*R*)-**1** and monomers **12**, **14-15**—.

Summing up, these studies indicate that a chiral to chiral communication mechanism is observed only in PPA copolymers comprising two features: a) the comonomers must display different dynamic conformational behaviors — e.g., monomer **1** with different conformers in equilibrium (*sp/ap*) and monomer **2** with a preferred single conformation (*ap*)— and b) that the homopolymers arising from those comonomers must show similar helical scaffolds (e.g., *cis-cisoidal*).

In order to better analyze this communication mechanism, we decided to study the different copolymer series resulting from all the combinations between monomers [(*R*)-**1**/(*S*)-**1** and [(*R*)-**2**/(*S*)-**2**], namely [poly-[(*R*)-**1-co-(R)-2**]<sub>n</sub>], [poly-

[(*S*)-**1-co-(R)-2**]<sub>n</sub>], [poly-[(*R*)-**1-co-(S)-2**]<sub>n</sub>] and [poly-[(*S*)-**1-co-(S)-2**]<sub>n</sub>].



**Figure 3.** Additional chiral homopolymers employed in this study.

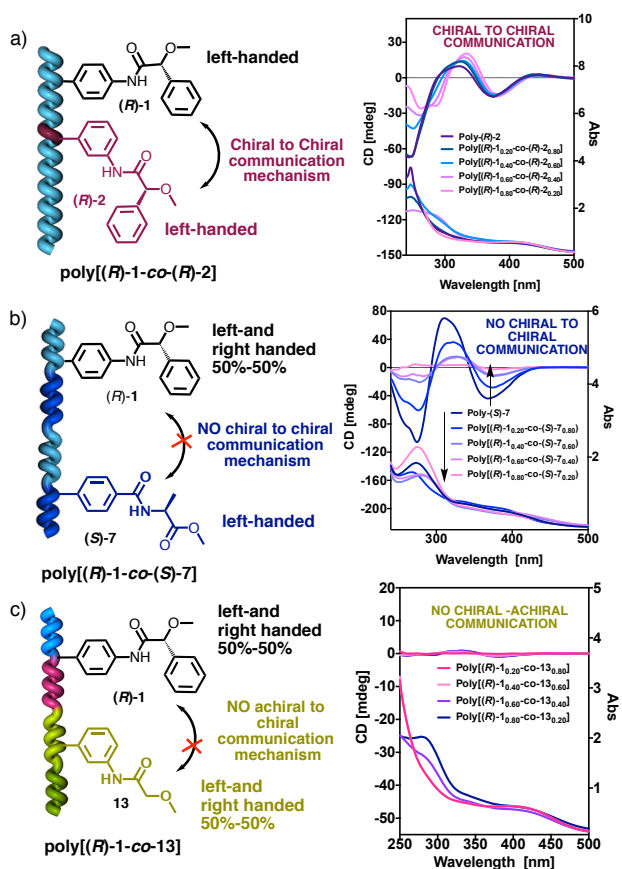
The results from the poly-[(*R*)-**1-co-(R)-2**]<sub>n</sub> and poly-[(*S*)-**1-co-(R)-2**]<sub>n</sub> series are describe next, while those on the complementary poly-[(*R*)-**1-co-(S)-2**]<sub>n</sub> and poly-[(*S*)-**1-co-(S)-2**]<sub>n</sub> series can be found in S66.

The CD spectra of poly-[(*R*)-**1-co-(R)-2**]<sub>n</sub> series (0.3 mg/mL THF) (Figure 5a) show for all those copolymers the same left-handed helical sense associated to a negative first Cotton effect. It is remarkable that the intensity of the band — and therefore the excess of left-handed sense — is quite similar in all the series independently of monomer ratios. This indicates that a very effective chiral amplification phenomenon is in operation with remarkably small amounts of the chiral Sergeant [(*R*)-**2**].

More precisely, the presence of just 1% of (*R*)-**2** in the copolymer is enough to get 35% of the maximum helicity (Figure 5c), while incorporation of 10% of (*R*)-**2** — i.e., poly-[(*R*)-**1-co-(R)-2**]<sub>n</sub> — induces the same helicity in the copolymer as that of the pure homopolymer [poly-(*R*)-**2**] (Figure 5a). Moreover, if the CD spectra are measured at -10°C, this helical amplification is even better and 1% of (*R*)-**2** is enough to make the whole copolymer chain to attain 70% of the maximum helicity (Figure 5c). The high effectiveness of this communication between Sergeants and Soldiers is related to the structure of (*R*)-**1** and (*R*)-**2** and their mutual interactions within the chain.

An explanation of those results can be envisioned considering the role played by the conformation of the pendants in the helical structure of the parent homopolymers [poly-(*R*)-**1** and poly-(*R*)-**2**], and their response to the addition of mono and divalent ions.<sup>16a,b</sup>

In poly-(*R*)-**2**, the pendants adopt a preferred antiperiplanar conformation — *ap*, between carbonyl and methoxy groups — responsible for inducing a left-handed helix in the polyene backbone. For its part, poly-(*R*)-**1** exhibits an axially racemic helix associated to 1:1 *anti*- and *synperiplanar* conformations in the pendant groups.<sup>1,13a,16b</sup>



**Figure 4.** (a) Helical sense enhancement in poly-[(*R*)-1-*r*-co-(*R*)-2]<sub>*r*</sub> series. (b) Helical sense decay in poly-[(*R*)-1-*r*-co-(*S*)-7]<sub>*r*</sub> series. (c) Macroscopically racemic poly-[(*R*)-1-*r*-co-13]<sub>*r*</sub> series.

Thus, in the poly-[(*R*)-1-*co*-(*R*)-2]<sub>*r*</sub> series, the virtually static Sergeant [(*R*)-2] adopts a fixed *ap* conformation — virtually identical to the one in poly-(*R*)-2— and commands the highly dynamic Soldier [(*R*)-1] to adopt an *ap* conformation, promoting a left-handed helical structure similar to the one in the poly-(*R*)-2 homopolymer (see S74 and S75 for structural studies).

This hypothesis is verified by addition of divalent metal ions (i.e., Ba<sup>2+</sup>) to poly-[(*R*)-1-*co*-(*R*)-2]<sub>*r*</sub>. The ions chelate to the chiral Soldiers [(*R*)-1],<sup>16</sup> promoting the synperiplanar (*sp*) conformation of the pendants and, as a consequence, the expected helical inversion (see S69 for detailed explanation).

In order to further examine the role of the chirality in the communication, we carried out analogous studies on the diastereomeric copolymer series, poly-[(*S*)-1-*co*-(*R*)-2]<sub>*r*</sub> where the (*R*)-1 chiral Soldier was replaced by its (*S*)-1 enantiomer. CD spectra of poly-[(*S*)-1-*co*-(*R*)-2]<sub>*r*</sub> series are shown in Figure 5d. As before, all the copolymers are CD active, and the intensity of the bands prove that chiral amplification processes are in action. Intriguingly, inversion of the CD traces — from negative (left-handed helix) to positive (right-handed helix)— is observed when the ratio of the Sergeant [(*R*)-2] falls below 30% (Figure 5d), following the “abnormal” Sergeants and Soldiers effect.<sup>17</sup>

This suggests that the chiral Sergeant [(*R*)-2] shifts the original 1:1 *sp/ap* equilibrium in the chiral Soldier [(*S*)-1] to a preferred *ap* conformation that favors the right-handed helical sense and triggers the helical inversion as the Sergeant ratio diminishes in the copolymer series.

More precisely, the CD traces are negative (dominant left-handed helix) at high percentages of (*R*)-2 and positive (dominant right-handed helix) at low (*R*)-2 ratios, indicating that the Sergeant commands the Soldiers to adopt the opposite helical sense [Sergeants= left-handed, Soldiers= right-handed]. From a quantitative point of view, the chiral amplification is better in poly-[(*S*)-1-*co*-(*R*)-2]<sub>*r*</sub> than in poly-[(*R*)-1-*co*-(*R*)-2]<sub>*r*</sub>. In fact, the maximum helicity is now obtained with just 10% of the chiral (*R*)-2 Sergeant, while 1% of the chiral (*S*)-1 Soldier is enough to obtain a 60% of the maximum helicity (Figures 5d,e). Moreover, these values are improved at low temperature: at -10°C, 1% of (*R*)-2 is enough to get 71% of the maximum helicity (Figure 5f).

As above, CD studies with the poly-[(*S*)-1-*co*-(*R*)-2]<sub>*r*</sub> series showed that the (*S*)-1 pendant is in *ap* conformation. Addition of divalent metal ions produced helical inversion — due to the *ap* to *sp* conformational change— confirming that in this series the (*S*)-1 chiral soldier adopts a favored *ap* conformation when is commanded by the (*R*)-2 Sergeant (see S70).

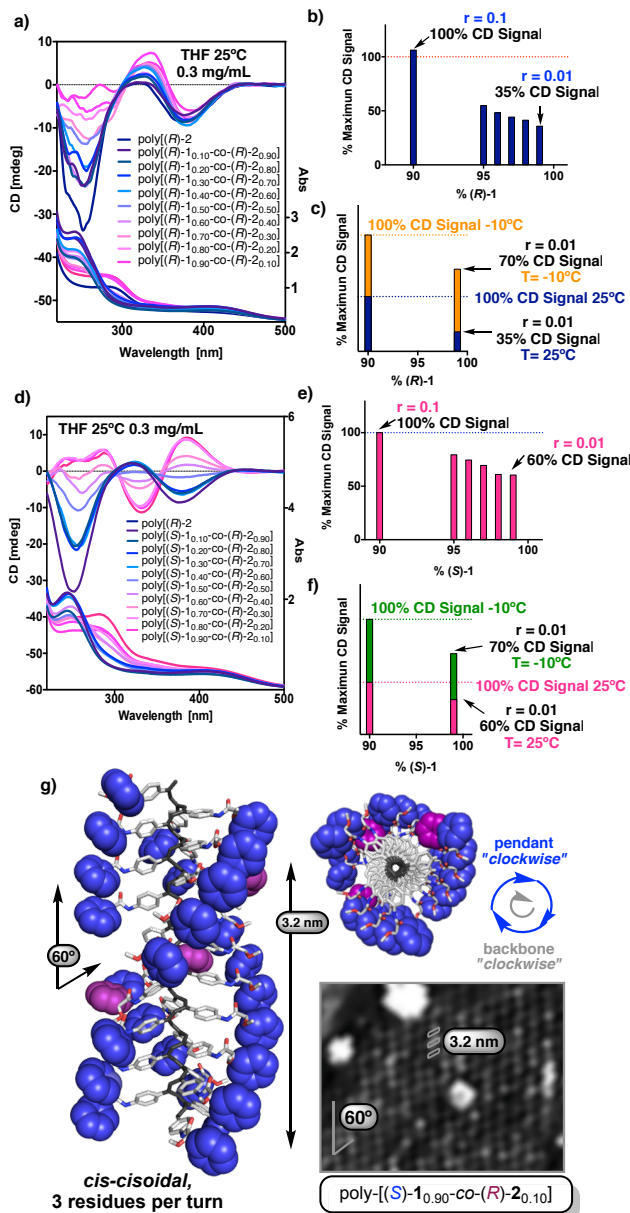
As a result, a left-handed helix can be induced in the axially racemic poly-(*R*)-1 by synthesizing a copolymer with a very small amount of either (*R*)-2 [e.g., poly-[(*R*)-1-*co*-(*R*)-2]<sub>*r*</sub> (*r* > 0.9)] or (*S*)-2 [e.g., poly-[(*R*)-1-*co*-(*S*)-2]<sub>*r*</sub> (*r* > 0.9)].

Alternatively, the axially racemic poly-(*S*)-1 can be compelled to adopt a right-handed helix by doping the polymer with (*R*)-2 or (*S*)-2 [e.g., right-handed helix in poly-[(*S*)-1-*co*-(*R*)-2]<sub>*r*</sub> (*r* > 0.9) and poly-[(*S*)-1-*co*-(*S*)-2]<sub>*r*</sub> (*r* > 0.9)].

The secondary structure of the chiral amplified poly-[(*S*)-1-*co*-(*R*)-2]<sub>*r*</sub> was analyzed in the solid state. Thus, a dilute solution of poly-[(*S*)-1-*co*-(*R*)-2]<sub>*r*</sub> was spin coated onto a HOPG substrate and submitted to AFM studies.<sup>14d</sup> The high resolution images obtained from the well-ordered monolayers allowed us to measure the helical pitch (3.2 nm), packing angle (60°) and helical sense described by the pendants (right-handed), indicating that the copolymer displays a *cis-cisoidal* helix (Figure 5g).

These data are in very good agreement with those found when poly-(*S*)-1 homopolymer is amplified towards a right-handed helix by addition of a monovalent metal ion (external stimulus),<sup>15d</sup> indicating that the internal doping leads to the same helix in the copolymer (see S70 for further explanation).

The chiral communication mechanism between chiral monomers was quantified using Green’s and Sato’s theories. The experimental results show that copolymers poly-[(*R*)-1-*co*-(*R*)-2]<sub>*r*</sub> follow Green’s original theory (Figure 5a),<sup>18</sup> while in the poly-[(*S*)-1-*co*-(*R*)-2]<sub>*r*</sub> copolymer series, the “abnormal” Sergeants and soldiers effect was found (Figure 5d).<sup>17</sup>



**Figure 5.** (a) CD studies for (a) [poly-[(*R*)-1-*co*-(*R*)-2]<sub>1-*r*</sub>] and (d) [poly-[(*S*)-1-*co*-(*R*)-2]<sub>1-*r*</sub>] copolymer series. Plot of *g*-values for (b) poly-[(*R*)-1-*co*-(*R*)-2]<sub>1-*r*</sub>] and (e) [poly-[(*S*)-1-*co*-(*R*)-2]<sub>1-*r*</sub>] copolymer series. Highlight of the *g*-value in a range of 90 to 99% of the chiral soldier (c) (*R*)-1 and (f) (*S*)-1 at room temperature and -10°C. (g) AFM images and 3D-models of poly-[(*S*)-1<sub>0.90</sub>-*co*-(*R*)-2<sub>0.10</sub>].

To determine the communication mechanism between chiral monomers, we applied Sato's model, a variation of the one dimensional Ising model developed by Green, which takes into account that the degree and the direction of the helical sense induction depend on the nature of the neighboring monomer units.

Thus, two different energy preferences ( $\Delta G_i$ ) are considered related to the presence of a chiral sergeant followed in sequence either by another chiral Sergeant ( $\Delta G_{ss}$ ) or by a chiral Soldier ( $\Delta G_{s}$ ):

$$g_{ss} = \tanh(-N\Delta G/RT) \cdot g_{ss} \quad (1)$$

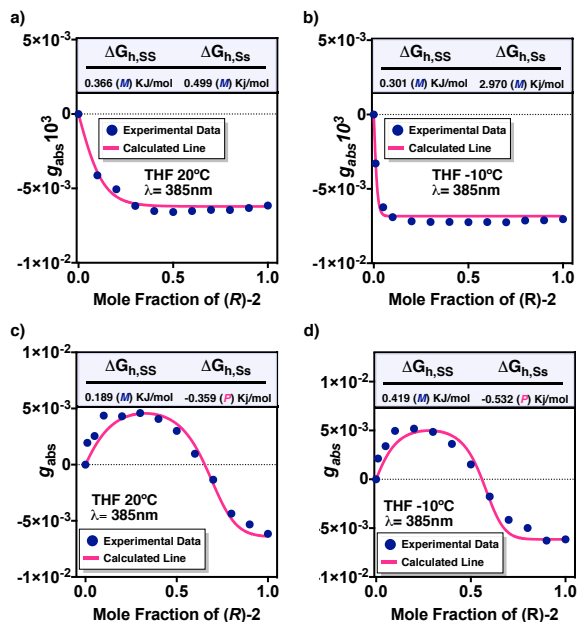
$$\Delta G_i = x \cdot \Delta G_{ss} + x(1-x) \cdot \Delta G_{s} \quad (2)$$

where  $g_{ss}$  represents Kuhn's dissymmetry factor ( $=[\theta]/3300/\epsilon$ ) and  $g_{s}$  correspond to the  $g_{ss}$  of the optically active parent homopolymer.  $\Delta G_i$  is the free energy difference per monomeric unit between both possible helical senses adopted by the polyene backbone (*P/M*).  $\Delta G_{ss}$  correspond to the  $\Delta G$  of a chiral Sergeant (Sergeant = *S*) interacting with another chiral Sergeant followed in sequence along the polymer chain, while  $\Delta G_{s}$  denotes the free energy of a chiral Sergeant interacting with a neighboring in sequence chiral soldier (Soldier = *s*).  $\Delta G_{ss}$  and  $\Delta G_{s}$  are, in accordance to Sato's model, competing energy contributions that determine the adoption of a preferred handed helical structure. The  $g_{ss}$  obtained at 20°C was plotted against the mole fraction of the chiral Sergeant monomer and subjected to a nonlinear, least-squares fitting of the parameters  $\Delta G_{ss}$ ,  $\Delta G_{s}$  and  $g_{ss}$  using equations 1 and 2 (Figures 6a and 6c). The parameters could be converged successfully affording  $\Delta G_{ss}$  and  $\Delta G_{s}$  values.

In the poly-[(*R*)-1-*co*-(*R*)-2]<sub>1-*r*</sub>] copolymer series, positive values of  $\Delta G_{ss} + 0.366$  and  $\Delta G_{s} + 0.499$  kJ/mol indicate that the same left-handed helical structure (*M* helix) is induced by both, the chiral Sergeant [(*R*)-2] and chiral Soldier [(*R*)-1] once is activated.

On the contrary, opposite sign values of  $\Delta G_{ss}$  and  $\Delta G_{s}$  — +0.189 and -0.359 — were obtained for the poly-[(*S*)-1-*co*-(*R*)-2]<sub>1-*r*</sub>] copolymer series, indicating that the chiral Soldier [(*S*)-1] tends to induce the opposite *P* helix once is activated by the chiral Sergeant [(*R*)-2], which induces a *M* helix in the copolymer.

Interestingly, the same studies carried out at lower temperatures showed  $\Delta G_{s} = 2.970$  KJ/mol for the poly-[(*R*)-1-*co*-(*R*)-2]<sub>1-*r*</sub>] copolymer series, being six times higher than the value obtained at 20°C, while  $\Delta G_{ss}$  remains almost unaltered (0.301 KJ/mol). This fact indicates that the communication between chiral monomers within this copolymer series is more fluent when the temperature decreases. On the contrary, identical studies on poly-[(*S*)-1-*co*-(*R*)-2]<sub>1-*r*</sub>] copolymer series showed slight variations on  $\Delta G_{ss}$  and  $\Delta G_{s}$ , with the temperature (Figures 6c and 6d), indicating that the communication mechanism between chiral monomers depends largely on the absolute configuration of the chiral Soldier (Figures 6c and 6d).

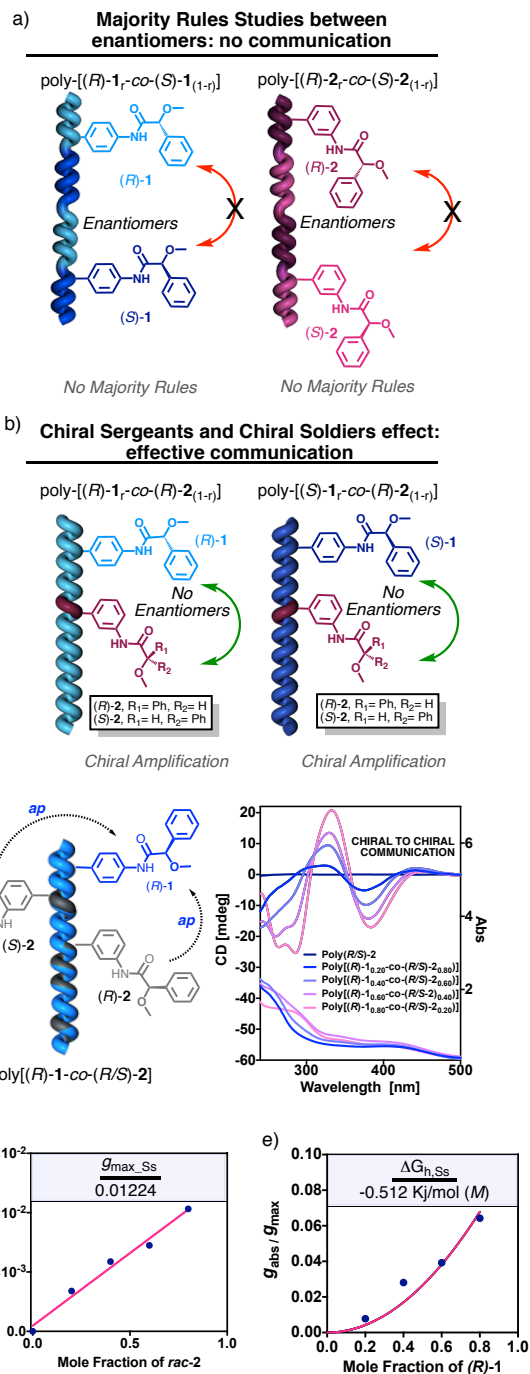


**Figure 6.** Plots of  $g_{\text{abs}}$  values at indicated wavelength of poly- $[(R)1_r\text{-co-}(R)\text{-}2]_{1-r}$  against copolymer composition in THF at (a) 20°C and (b) -10°C, and their corresponding regression lines based on equations (1) and (2) to obtain the free energy parameters  $\Delta G_{h,SS}$  and  $\Delta G_{h,Ss}$ . Identical studies for poly- $[(S)1_r\text{-co-}(R)\text{-}2]_{1-r}$  at (c) 20°C and (d) -10°C.

Finally, to fulfill the chiral to chiral communication studies of this work, we checked the presence/absence of the Majority rules phenomenon in these systems. In this regard, poly- $[(R)1_r\text{-co-}(S)\text{-}1]_{1-r}$  and poly- $[(R)2_r\text{-co-}(S)\text{-}2]_{1-r}$  copolymer series composed by enantiomers (i.e., neither Sergeants nor Soldiers) were prepared. CD experiments indicated that Majority rules are not operative in these systems (i.e., there is not communication between enantiomers; see full details in SI and Figure 7).

The lack of majority rules allows us to propose a particularly interesting case, represented by copolymers where one monomer is racemic  $-(R/S)\text{-}2$  (the Sergeant) and the other is chiral  $-(R)\text{-}1$  (the Soldier). From the studies detailed above, we knew that both Sergeants,  $(R)\text{-}$  and  $(S)\text{-}2$ , induce the same *ap* conformation in the chiral soldier  $[(R)\text{-}1]$ . As a result, copolymers with a large ratio of monomer  $(R)\text{-}1$  adopt a left-handed helix. Thus, all copolymers with a  $[\text{poly-}[(R)1_{0.8}\text{-co-}(R/S)\text{-}2]_{0.2}]$  composition should adopt the same left-handed helical structure (Figure 7b). In fact, CD spectra of poly- $[(R)1_{0.8}\text{-co-}(R/S)\text{-}2]_{0.2}$  copolymer series showed as expected a negative Cotton effect (Figure 7c) similar to the one obtained for poly- $[(R)1_{0.8}\text{-co-}(R)\text{-}2]_{0.2}$  (Figure 5a) and poly- $[(R)1_{0.8}\text{-co-}(S)\text{-}2]_{0.2}$  (Figure 5d), indicating that both enantiomers of monomer **2** give the same order to monomer  $(R)\text{-}1$ , i.e., the adoption of a preferred *ap* conformation.

With this CD data on hand, we carried out the theoretical evaluation of the contribution of the Soldier to the CD spectra ( $g_{\text{max, Soldier}}$  or  $g_{\text{max, S}}$ ). In this special case,  $g_{\text{max, Sergeant}}$  is null due to the presence of a racemic mixture of the Sergeant and therefore  $g_{\text{obs}}$  is proportional to the  $g_{\text{max, Soldier}}$  (equation 3).

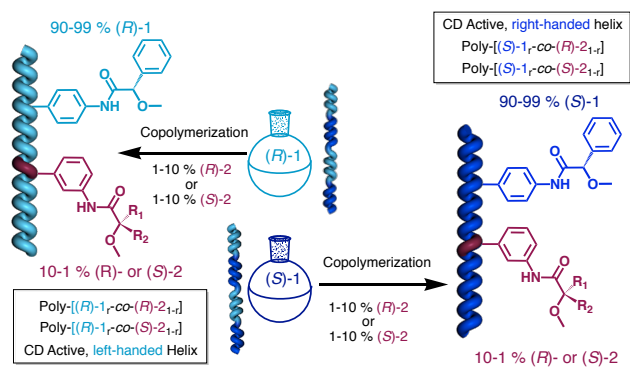


**Figure 7.** (a) Schematic representation indicating the absence of Majority rules in poly- $[(R)1_r\text{-co-}(S)\text{-}1]_{1-r}$  and poly- $[(R)2_r\text{-co-}(S)\text{-}2]_{1-r}$  series (no communication). (b) Idem showing the presence of chiral to chiral communication in the  $[\text{poly-}[(R)1_r\text{-co-}(R)\text{-}2]_{1-r}]$ ,  $[\text{poly-}[(R)1_r\text{-co-}(S)\text{-}2]_{1-r}]$ ,  $[\text{poly-}[(S)1_r\text{-co-}(S)\text{-}2]_{1-r}]$  and  $[\text{poly-}[(S)1_r\text{-co-}(R)\text{-}2]_{1-r}]$  series. (c) Helix sense enhancement of a macroscopically racemic polymer  $[(R)\text{-}1]$  by a racemic mixture of a chiral Sergeant ( $2_{\text{rac}}$ ). Plots of (d)  $g_{\text{obs}}$  and  $g_{\text{obs}}/g_{\text{max}}$  values at indicated wavelength of poly- $[(R)1_r\text{-co-}(R/S)\text{-}2]_{1-r}$  against copolymer composition in THF at -10°C, and their corresponding regressions to obtain  $g_{\text{max}}$  and the free energy parameters  $\Delta G_{h,SS}$ .

$$g_{\text{obs}} = x \cdot g_{\text{max, Soldier}} + (1-x) g_{\text{max, Sergeant}} = x \cdot g_{\text{max, Soldier}} \quad (3)$$

Thus, plotting  $g_{\text{obs}}$  against the mole fraction of the chiral Sergeant monomer should produce (after linear regression) the  $g_{\text{max, Soldier}}$  value. The values obtained ( $g_{\text{max, Soldier}} = -0,01224$ ) for

the poly-[(*R*)-**1**<sub>0.5</sub>-*co*-(*R/S*)-**2**<sub>0.2</sub>] series (Figure 7d), fit perfectly on the equation of a straight line, indicating that the CD contribution of the chiral Soldier is always the same due to the adoption of a specific conformation (*ap*) once the Sergeant is introduced within the copolymer chain.



**Figure 8.** Chiral amplification of a chiral helical polymer with low screw sense excess by copolymerization with the two enantiomers of an appropriate chiral doping agent.

For its part,  $\Delta G_{ss}$  depends only on  $\Delta G_{ss}$ , ( $\Delta G_{ss}$  is null, racemic Sergeant). Combination of equations (2) and (3) should allow to obtain  $\Delta G_{ss}$  by plotting  $g_w/g_{ss}$  against the mole fraction of (*R*)-**1**. The value obtained ( $\Delta G_{ss} = -0.512$  KJ/mol; Figure 7e) shows that in poly-[(*R*)-**1**<sub>1</sub>-*co*-(*R/S*)-**2**<sub>0.2</sub>], the *M*-helix is more favorite by just 0.512 KJ/mol when a chiral Sergeant (*R* or *S*)-**2** is adjoined by a chiral soldier [(*R*)-**1**].

## Conclusions

In conclusion, we report here a chiral amplification procedure based on chiral Sergeant to chiral Soldier communication. Using this novel approach is possible to induce a single handed helical structure on a dynamic axially racemic polyphenylacetylene by doping the chain with a very small amount (1-10%) of an adequately selected chiral monomer (that acts as Sergeant) (Figure 8). In our examples, the chiral Sergeant has a fairly restricted conformational mobility that fixes a preferred conformation on the highly dynamic chiral Soldier independently on the absolute configuration of the Sergeant, although the extent of this communication is different in both copolymer series, indicating the importance of the chirality of the two counterparts in this chiral to chiral communication mechanism. Moreover, both the chiral Sergeant and the chiral Soldier should produce a similar helical scaffold in their corresponding homopolymers (e.g. *cis-cisoidal*) to transmit the order between monomers more effectively. Thus, either *M* or *P* helical senses can be induced depending on the absolute configuration of the chiral Soldier (Figure 8).

Thus, a *M* helical sense will be induced in both poly-[(*R*)-**1**<sub>1</sub>-*co*-(*R*)-**2**<sub>0.2</sub>] and poly-[(*R*)-**1**<sub>1</sub>-*co*-(*S*)-**2**<sub>0.2</sub>] copolymer series, because the two different configurations of the Sergeant command the same conformation on the chiral Soldier [(*R*)-**1**]. The same effect is observed in the poly-[(*S*)-**1**<sub>1</sub>-*co*-(*R*)-**2**<sub>0.2</sub>] and poly-[(*S*)-**1**<sub>1</sub>-*co*-(*S*)-**2**<sub>0.2</sub>] copolymer series, although the helical sense induced in the copolymer is the *P* helix due to the enantiomeric configuration of the chiral soldier [(*S*)-**1**].

In addition to this remarkable chiral enhancement, the resulting well-ordered polymer maintains its dynamic character and tunability. So, when submitted to appropriate stimuli (e.g., metal coordination), it can undergo further helical inversion or nanostructuration (see S76).

We think this approach can open new perspectives in the preparation of functional polymers with precise stereo-

chemical characteristics and suggests that polymers now considered useless as macroscopically helical materials, because of their low sense preference, could be improved by this procedure to form a single preponderant *P/M* helix.

## ASSOCIATED CONTENT

### Supporting Information

Materials and methods, synthesis and characterization of monomers, synthesis and characterization copolymers, conformational studies, AFM studies, nanostructuration studies and supporting references.

The Supporting Information is available free of charge on the ACS Publications website.

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## ABBREVIATIONS

PPA, poly(phenylacetylene); AFM, Atomic Force Microscopy; CD, Circular Dichroism; MPA, methoxyphenylacetic acid

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