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Multipodal dynamic coordination involving cation- π interactions to control the structure of helical polymers

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A precise tuning of the four possible states of a helix (*P/M* helical sense and stretched/compressed helical backbone) is attained by controlling the complexation between Li^+ and a poly(phenylacetylene) that bears amide, ester and phenyl ring functionalities at the pendant group. Depending on the MeOH ratio that is present as cosolvent, different coordination sites are involved leading to complexes I-III, each one with a characteristic structure (tri-, bi-, unipodal) and associated helical state. This dynamic coordination allows the selective modification of the helical sense or the stretching/compression backbone of a helical polymer.

The control of the helical sense and elongation of helical polymers,¹ by the action of external stimuli,¹⁻⁴ has attracted the attention of the scientific community due to the potential interest of those materials in applications as sensors,² molecular devices,³ chiro-optical switches,⁴ memory elements and chiral catalysts.⁵ Poly(phenylacetylene)s⁶ are a family of helical polymers especially suited for those applications due to the wide range of substituents available and above all, their dynamic behaviour that allows a helical PPA to invert or amplify its helical sense, and even to modulate its elongation by the action of an external stimuli.⁷

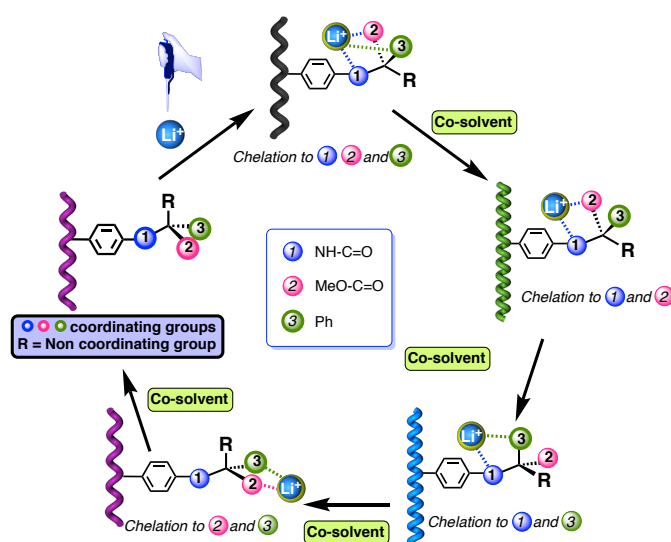
In our group we recently described that a poly(phenylacetylene) bearing the anilide of the (*R*)- α -methoxy- α -phenylacetic acid as pendant [poly-(*R*)-**1**], (null CD, axially racemic due to the 1:1 *sp/ap* conformational ratio),⁸ can be specifically shifted to adopt either the *P* or the *M* helical sense by addition—in CHCl_3 solution—of a small amount of a monovalent metal ion (Na^+ or Ag^+) that, depending on the amount of a crucial donor cosolvent (i.e., MeOH), chelates the

change in complexation/helical sense involves the control of the formation and cleavage of a cation- π interaction.

Herein, we describe a more sophisticated system where tuning the complexation of the metal ion with different groups in the pendants allows not only the control on the helical sense of the polymer but also on the elongation of the chain.

To this end, we devised a pendant comprising three complexation sites with different coordinating ability and located at adequate distance for chelation: two carbonyl groups and an aromatic ring for metal cation- π interaction).

This pendant should be able to complex the metal ion in different ways, generating complexes whose different structures and interactions with the vicinal pendants will determine a given helix for each one (Scheme 1).



Scheme 1. Potential structural changes (sense, elongation) in a helical polymer-metal complex due to the presence of different chelation modes.

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pendant in two different ways, each one promoting one helical sense in the backbone.⁹ From the structural point of view, this

In this paper, we demonstrate this successful idea using as pendants the benzamides of (*S*)-phenylglycine methyl ester [m-(*S*)-**2**],¹⁰ and (*S*)-phenylalanine methyl ester [m-(*S*)-**3**], where their amide, ester and phenyl ring functions act as complexing

sites (Figure 1). We will show also that selective conversion of the PPA into its complexes allows the preparation of the four different helical states, represented by the *P* and *M* helical senses and compressed/stretched skeleton.

Thus, 4-ethynylbenzamide of *L*-phenylglycine methyl ester and *L*-phenylalanine methyl ester were prepared and polymerized using $[\text{Rh}(\text{nbd})\text{Cl}]_2$ as catalyst (nbd = 2,5-norbornadiene) that gave the poly-(*S*)-2 and poly-(*S*)-3 PPAs in good yield (90 % and 93% respectively) and with a high content of the *cis* configuration of the double bonds (see SI for details).

CD studies of poly-(*S*)-2 and poly-(*S*)-3 in chloroform (0.3 mg/mL) show a preferred helical structure —helix I— associated to the presence of a preponderant *anti*-conformation (the two carbonyls oppositely oriented in the pendant group, Figure 2).¹⁰

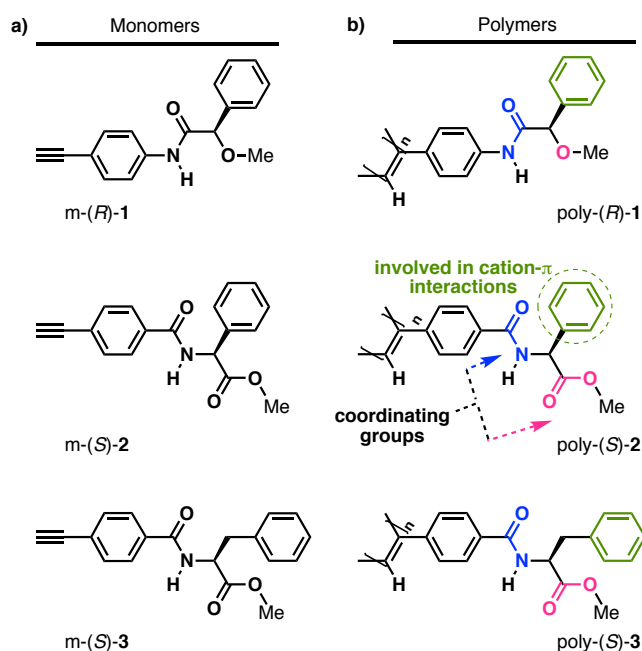


Figure 1. a) Structure of monomers *m*-(*S*)-1, *m*-(*S*)-2, *m*-(*S*)-3 and functional groups potentially involved in interaction with LiClO_4 .

Next, lithium perchlorate in MeOH (10 mg/mL) was added to a chloroform solution of poly-(*S*)-2 (or 3) (0.3 mg/mL) to prepare poly-(*S*)-2/ Li^+ /MeOH in a 1.0/0.5/133 mole ratio and poly-(*S*)-3/ Li^+ /MeOH in a 1.0/0.5/130 mole ratio.¹¹ In these conditions [i.e., poly-(*S*)-2 (or 3)/ Li^+ /MeOH = 1.0/0.5/<135], complex I— where the metal ion coordinates both carbonyl groups (amide and ester) as inferred from IR studies— is formed (Figure 2). Moreover, ^7Li NMR studies show a strong shielding of the ^7Li peak once poly-(*S*)-2 is present in the solution, resonating at -5.89 ppm, typical for a cation- π interaction¹² (similar results were obtained for the Li NMR of poly-3/ Li^+ complex I). This chemical shift also indicates that Li^+ ion interacts with a single phenyl ring.¹³ Thus, in complex I, the Li^+ ion chelate the two carbonyls in a *syn* orientation, establishing also an extra cation- π interaction with the aryl ring of the amino acid (Figure 2b). During the formation of this complex, a helical inversion is observed from helix I to helix II, due to the conformational

change produced at the pendant moiety, which places the bulkiest group in the opposite direction.

Next, complex I was titrated with different amounts of MeOH to study the dynamic coordination chemistry of the poly-(*S*)-2 (or 3)/ Li^+ system.

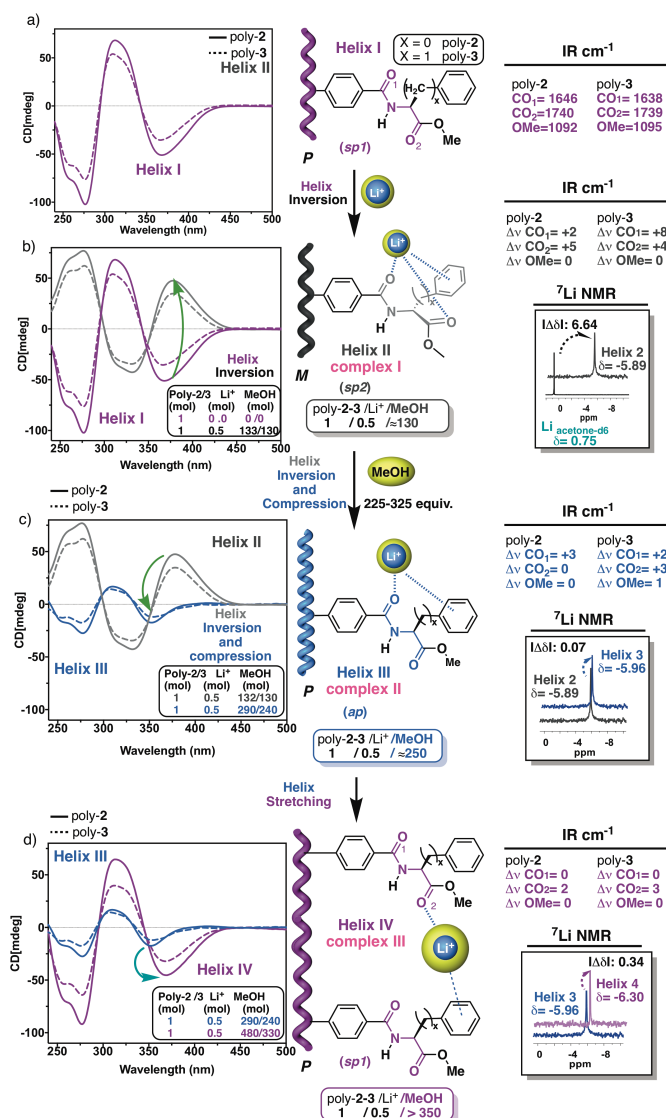


Figure 2. (a) CD spectra of poly-(*S*)-2 and poly-(*S*)-3 in CHCl_3 , showing the same *anti*-conformation at the pendant group (helix I). CD, IR and Li NMR studies demonstrating the dynamic coordination chemistry of a poly-(*S*)-2 (or 3)/ Li^+ /MeOH complex in a (b) 1.0/0.5/ \approx 130 ratio (helix II), (c) 1.0/0.5/ \approx 250 ratio (helix III) and (d) 1.0/0.5/ $>$ 350 ratio (helix IV).

Interestingly, it was found that when the amount of MeOH added to the poly-(*S*)-2 (or 3)/ Li^+ complex is in a poly-(*S*)-2

(mru)/MeOH ratio of 1/ (278-326) (mol/mol), and in a poly-(S)-**3**(mru)/MeOH ratio of 1/ (226-277) (mol/mol), a new helical inversion was produced associated to the evolution of complex I to a new complex II (Figure 2c). In complex II, the metal ion remains coordinated to the amide group—inferred from IR studies—and to the π system—determined by ^7Li NMR analysis: $\delta(^7\text{Li}) = -5.96$ ppm for poly-**2**/ Li^+ and -6.04 ppm for poly-**3**/ Li^+ ¹³ but the linkage with the ester group has disappeared (Figure 2). Thus, in complex II the metal ion has only two points for chelation and the complex adopts the anti-conformation producing a helical structure with the same helical sense as helix I. In fact, this second inversion clearly shows a hypsochromic shift observed both at the CD and UV spectra (Figure 2 and SI). Thus, complex II is structurally represented by a helix with the same sense as helix I, but a more compressed scaffold (Figure 2 and SI).

Finally, the addition of a larger amount of methanol—poly-(S)-**(2)**/ Li^+ /MeOH in a 1.0/0.5/>380 (mol/mol/mol) ratio, and poly-(S)-**(3)**/ Li^+ /MeOH in a 1.0/0.5/>330 (mol/mol/mol) ratio—, produced another structural change in the complex formed between the Li^+ ion and the pendant group. In this new mode of complexation (i.e., complex III), the metal ion “jumps” from the amide to the ester group, without altering the anti conformation at the pendant moiety, and therefore no helical inversion is observed (Figure 2d). On the other hand, examination of the CD and UV spectra indicate the stretching of the helix once complex III is formed (see Figure 2d and SI for details). This elongation is explained by the presence of a cation- π interaction [$\delta(^7\text{Li}) \approx -6.2$ ppm for poly-(**2** or **3**)/ Li^+] between vicinal amino acid groups (Figure 2d). In this way, the anti conformation will remain unaltered, while the constraint originated by the placement of the metal ions between neighbouring pendants is released via elongation of the polyene chain.

In order to demonstrate the generality of this sequential modification of a helix and the role of the different groups, we perform the same studies using a different PPA. In this case, we chose poly-(S)-**4**, bearing the benzamide of L-alanine methyl ester as pendant group that differs from the previously studied ones in the replacement of the Ph ring found in poly-(S)-**2** by a methyl group (Figure 3).

CD spectra of poly-(S)-**4** in CHCl_3 (0.3 mg/mL) shows a practically identical CD trace to the one adopted by poly-(S)-**(2-3)** (Figure 3a) indicating that the three polymers adopt the same helical structure (helix I).

Addition of LiClO_4 in MeOH (10 mg/mL) to the chloroform solution of poly-(S)-**4** (0.3 mg/mL) where poly-(S)-**4**/ Li^+ is in a 1.0/0.5 (mol/mol) ratio, produced a helical inversion with formation of a complex I, in a similar manner as that observed for poly-(S)-**(2 or 3)**/ Li^+ /MeOH in a 1.0/0.5/<135 (mol/mol/mol) ratio (Figure 2). In this case, the helix inversion observed in complex-I of poly-(S)-**4** is due to the adoption of a *syn* conformation at the pendant group, induced by the chelation of the two carbonyl groups with the monovalent metal ion and without cation- π interaction (Figure 3).

Ulterior additions of MeOH produce the inversion of the helical sense directly forming helix IV (Figure 3). Contrary to what was

observed in poly-(S)-**(2 or 3)**, the presence of helix III was not detected. This is related to the absence in poly-(S)-**4**, of the cation- π bonding, necessary to stabilize the complex leading to helix III (see complex II in Figure 2). Moreover, ^7Li NMR [$\delta(^7\text{Li}) \approx -2$ ppm] confirmed the absence of any cation- π interaction in all the poly-(**4**)/ Li^+ complexes.

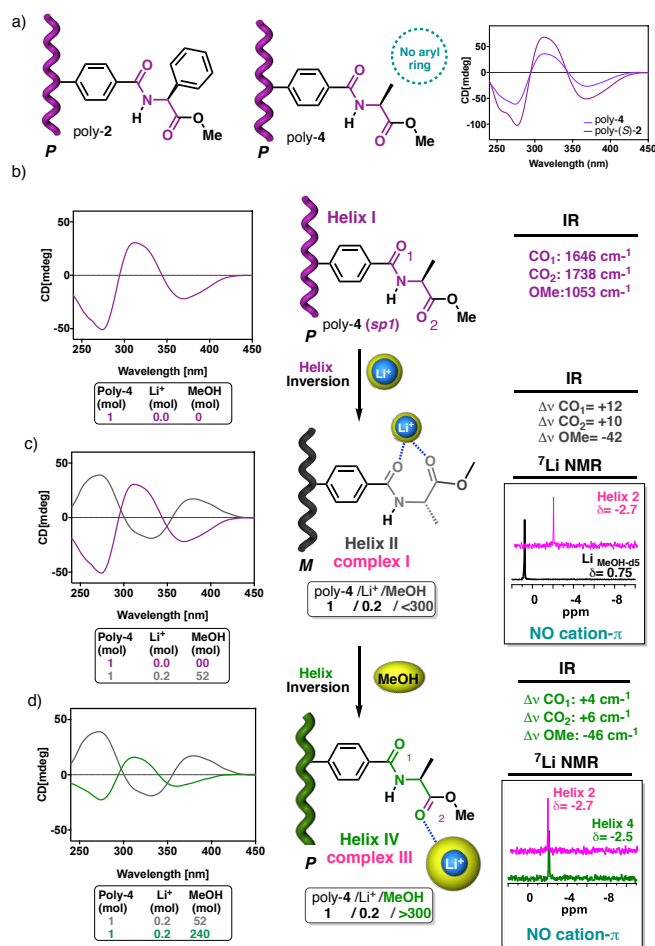


Figure 3. (a) CD spectra of poly-(S)-**2** and poly-(S)-**4** showing the anti-conformation at the pendant group (helix I). CD, IR and ^7Li NMR studies demonstrating the dynamic coordination chemistry of a poly-(S)-**(4)**/ Li^+ /MeOH complex in (b) a 1.0/0.0/0 ratio (helix I), (c) a 1.0/0.5/132 ratio (helix II) and (d) a 1.0/0.5/240 ratio (helix III).

In conclusion, it has been demonstrated that addition of low amounts of Li^+ salt to a polyphenylacetylene with pendants containing amide, ester and phenyl ring functions at precise distances, allows the sequential formation of three different complexes (complexes I-III) each one involving different coordination sites (amide, ester and cation- π) and structures (tri-, bi-, unipodal) that modify the helical sense or the stretching/compression of the original helix. The dynamic character of the complexation allows its manipulation by controlled addition of MeOH that debilitates some coordinations and favours others.

In this way, a single helical polymer can be forced to adopt any of the four forms of a helix (*P/M* sense and stretched/compressed backbone) by selection of the complexing state (uncomplexed polymer and complexes I-III).

We think that this approach can be extended to other dynamic helical polymers, where adequate selection of the pendant groups and metal ion could generate multiple helical structures via dynamic coordination chemistry.

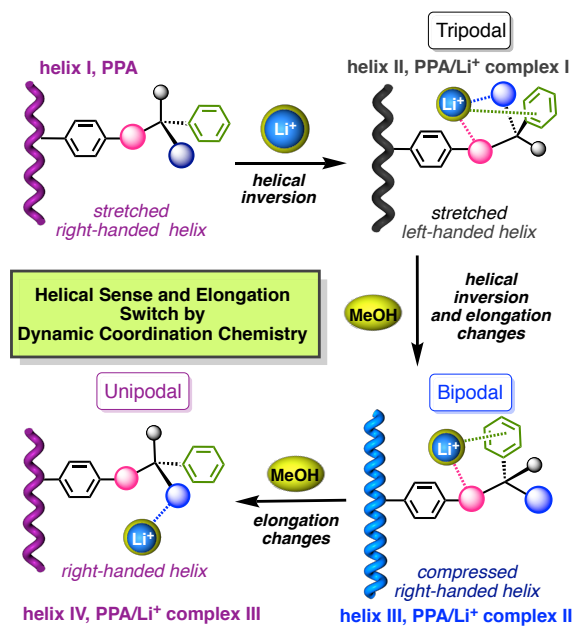
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Dynamic coordination, by means of multipodal metal complexes and cation- π interactions, controls the structure of helical polymers