Helical Structures

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Chiral Amplification and Helical-Sense Tuning by Mono- and Divalent Metals on Dynamic Helical Polymers**

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In memory of Rafael Suau

The controlled induction of a helix-sense bias in helical polymers[1] by external stimuli[1–4]—that is, the possibility of selecting a helix with a preferred handedness—has become a desirable goal[2,3] owing to the potential applications of these materials as chiral sensors, molecular devices,[5] chiro-optical switches, memory elements for information storage, chiral catalysts, and conductive materials, amongst others.[1–3] Since the pioneering work by Green et al.[6] on the amplification of chirality in polyisocyanates, helical polymers with chiral amplification properties have attracted much attention.[1–3,7]

Herein we report the synthesis and evaluation of a new and highly dynamic poly(phenylacetylene) (PPA) derivative that bears chiral pendants. This polymer incorporates the two aforementioned features (selective helix induction and chiral amplification) to give a material that acts as a sensor for the valence of metal cations. In the amplification of chirality reported herein, the external stimulus—the trigger—is provided by the selective coordination of the pendants with mono- or divalent metal cations (achiral agents) in such a way that the valence of the metal determines the right- or left-handed helical sense of the polymer and its chiroptical response.[8]

α-Methoxyphenylacetic acid (MPA), connected to the phenylacetylene moiety through a (C_6H_4)−NH−C(=O) amide bond, was the pendant of choice. This system was selected because: 1) the 1,2-(amide carbonyl–methoxy) moiety is an excellent chelating moiety for certain cations (as shown by CD and NMR spectroscopy studies)[9] and 2) metal chelation is known to switch the antiperiplanar/synperiplanar (*ap*/*sp*) conformational equilibrium of chiral MPA amides.[9]

In this way, the (*R*)- and (*S*)-MPA phenylacetylene monomers **1** and **2** (Figure 1 a) were prepared and we assessed their capacity to coordinate with mono- and divalent cations (Li^+, Ca^{2+}, Ba^{2+}, Mn^{2+}). The addition of divalent metal cations induced an inversion of the CD spectrum, indicating a conformational switch from the *ap* to the *sp* form. This inference was corroborated by optical rotation and by ^1H and

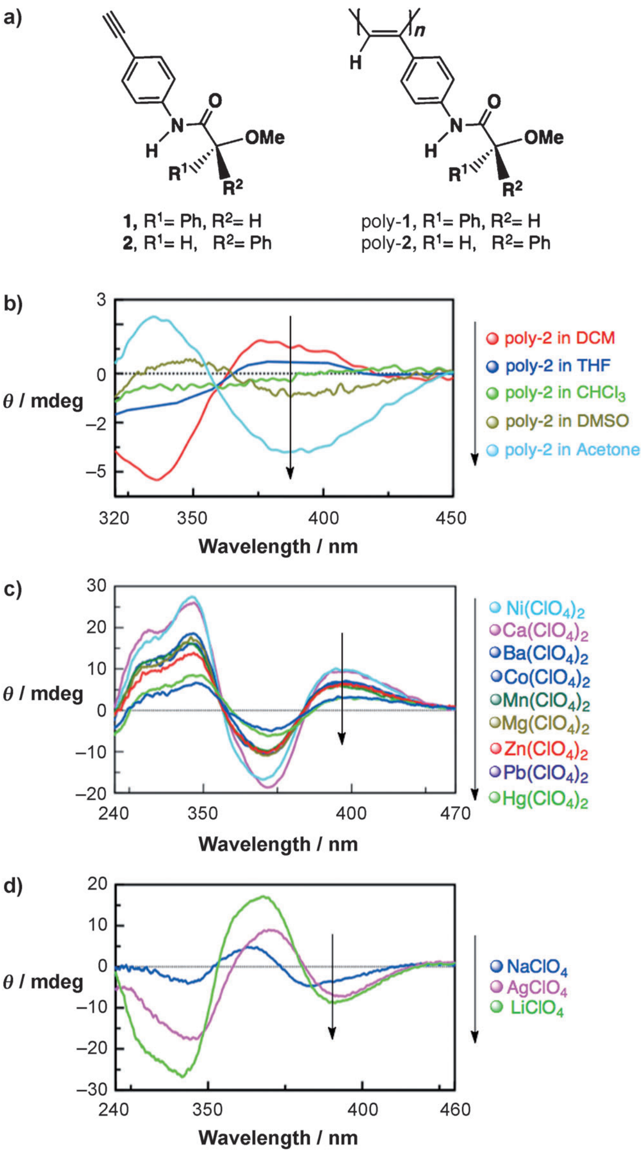

Figure 1. a) Structures of **1**, **2**, poly-**1**, and poly-**2**. b) CD spectra of poly-**2** in different solvents (0.1 $mg\,mL^{-1}$). Poly-**1** generates the corresponding mirror-image spectra. c) CD spectra of poly-**1** with divalent metal cations in $CHCl_3$.[14] d) CD spectra of poly-**1** with monovalent metal cations in $CHCl_3$.[14]

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^{13}C NMR spectroscopy (see full description of the behavior of the monomers in the Supporting Information).[10]

The addition of monovalent cations to **1** or **2** only led to a decrease in the intensity of the CD bands but not to an inversion, thus suggesting that a different type of coordination was operating. ^{1}H and ^{13}C NMR spectroscopy and optical rotation data are consistent with this interpretation.

With this information in hand, the two novel PPAs poly-(*R*)-MPA (poly-**1**) and poly-(*S*)-MPA (poly-**2**; Figure 1 a) were synthesized.[11] $[\{Rh(nbd)Cl\}_2]$ was employed as a catalyst (nbd = 2,5-norbornadiene), and the polymeric materials that were obtained had a high content of the *cis* isomer, as was concluded from the chemical shifts of the vinyl protons ($\delta = 5.7$–5.8 ppm) and Raman resonances (1567, 1340, 1003 cm^{-1}).[12] The material properties were subsequently verified.

The helicity of the polymers can be inferred from CD spectroscopy.[1,12] The small Cotton effects observed at 375 nm for poly-**1** and poly-**2** in a series of solvents (Figure 1 b) indicate that, in solution, these polymers have highly dynamic helices. Only in some solvents a slight predominance of one sense of helicity was observed and virtually none in $CHCl_3$, as shown by the absence of a CD effect.

Once evidence for the dynamic behavior had been obtained, we investigated whether this characteristic could be modulated by coordination with mono and divalent cations. Nine perchlorates[13] of divalent metals ($M(ClO_4)_2$; M = Mg^{2+}, Ca^{2+}, Mn^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+} , Ba^{2+}, Hg^{2+}, Pb^{2+})[14] were added to solutions of poly-**1** and poly-**2** in $CHCl_3$. CD, UV/Vis, and FTIR spectroscopy, and optical rotation studies indicated the formation of helical polymer–metal complexes (HPMCs), together with the modulation of the helicity of the polymer from the initial highly dynamic helix (no CD effect) to a final helix with a prevalent helical sense (strong positive Cotton effects at 375 nm after the addition of the salts for poly-**1**; negative for poly-**2**; Figure 1 c). Importantly, all the divalent cations tested induced the same sense of helicity, and the maximum responses were achieved with just 0.1(M^{2+})/1.0(monomer) (equiv/equiv) ratios.

On addition of monovalent cations ($MClO_4$; M = Li^{+}, Na^{+}, Ag^{+}),[15] the polymers adopted the opposite helical sense in all cases (negative Cotton effects at 375 nm for poly-**1**; positive for poly-**2**) at analogous monomer/metal ratios (Figure 1 d).

A relationship between cation size (ionic radius) and the observed selectivity bias was not found.

AFM images of poly-**1**/Ba^{2+} and poly-**1**/Ag^{+}[16] on highly oriented pyrolytic graphite (HOPG) provided important insights into the helicity and morphology of the HPMCs (Figure 2) and are in full agreement with the information obtained from CD spectroscopy.[17] With Ba^{2+}, the single chains were packed in a parallel manner, one after the other, to form a right-handed (clockwise) pendant disposition with the periodic oblique stripes forming 60.0° angles and a helical pitch of 3.23 nm (Figure 2 a). In the case of Ag^{+}, the chains were also aligned side-by-side but, in contrast to the previous case, showed a left-handed (counterclockwise) pendant disposition with the periodic oblique stripes forming 60.8° angles and a helical pitch of 3.21 nm (Figure 2 b).

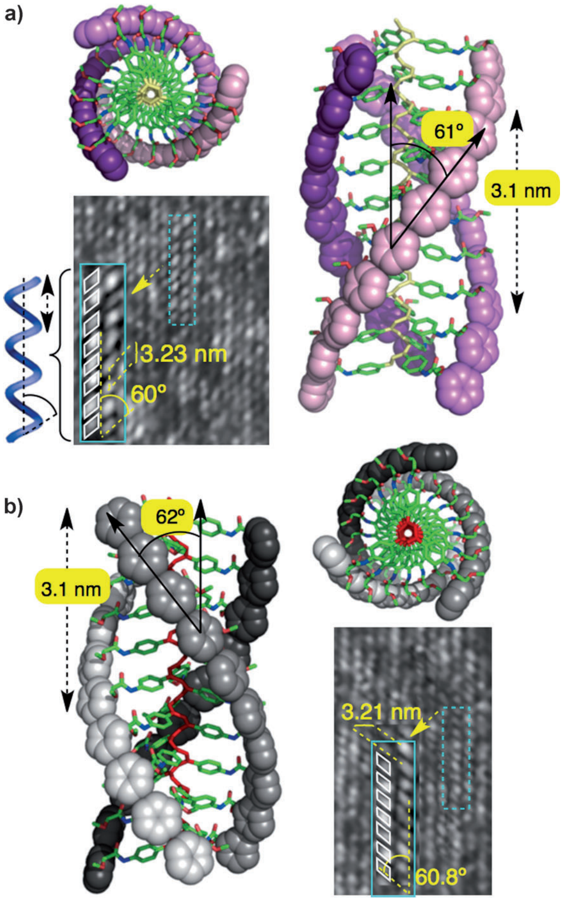

Figure 2. a) AFM image and top and side views of the 3/1 right-handed helix of poly-**1**/Ba^{2+}. b) AFM image and top and side views of the 3/1 left-handed helix of poly-**1**/Ag^{+}. The values depicted in the top and side views of the helices were obtained by MMFF94 calculations.

MMFF94[18] molecular mechanics calculations on the secondary structure of poly-**1** (28-mer) showed that a 3/1 right-handed helix resulted when the (*R*)-MPA pendants adopted *sp* conformations. On the other hand, a 3/1 left-handed helix of similar energy arose when (*R*)-MPA pendants adopted *ap* conformations. In both cases the angles formed by the oblique stripes and the helical pitches (61.0°/62.0° and 3.1/3.1 nm for *sp*/*ap* conformations, respectively) match the experimental values (Figure 2). These results imply internal angles close to +75° and −75° for *sp* and *ap* conformations, respectively, and explain the right- and left-handedness of the corresponding backbones. Moreover, these angles allow the formation of hydrogen bonds between the *n*th and (*n*+3)th amide bonds.

Consequently, the different behavior of the dynamic polymer in the presence of di- and monovalent cations can be attributed to the different conformations of the pendants favored by each type of cation (*sp* and *ap*, respectively, Figure 3).

IR spectra confirmed the different coordination modes of the cations according to their valence, as evidenced by the shifts of the C=O and OMe bands (see Δν values in Table 1). Thus, divalent cations coordinate to both the C=O and OMe

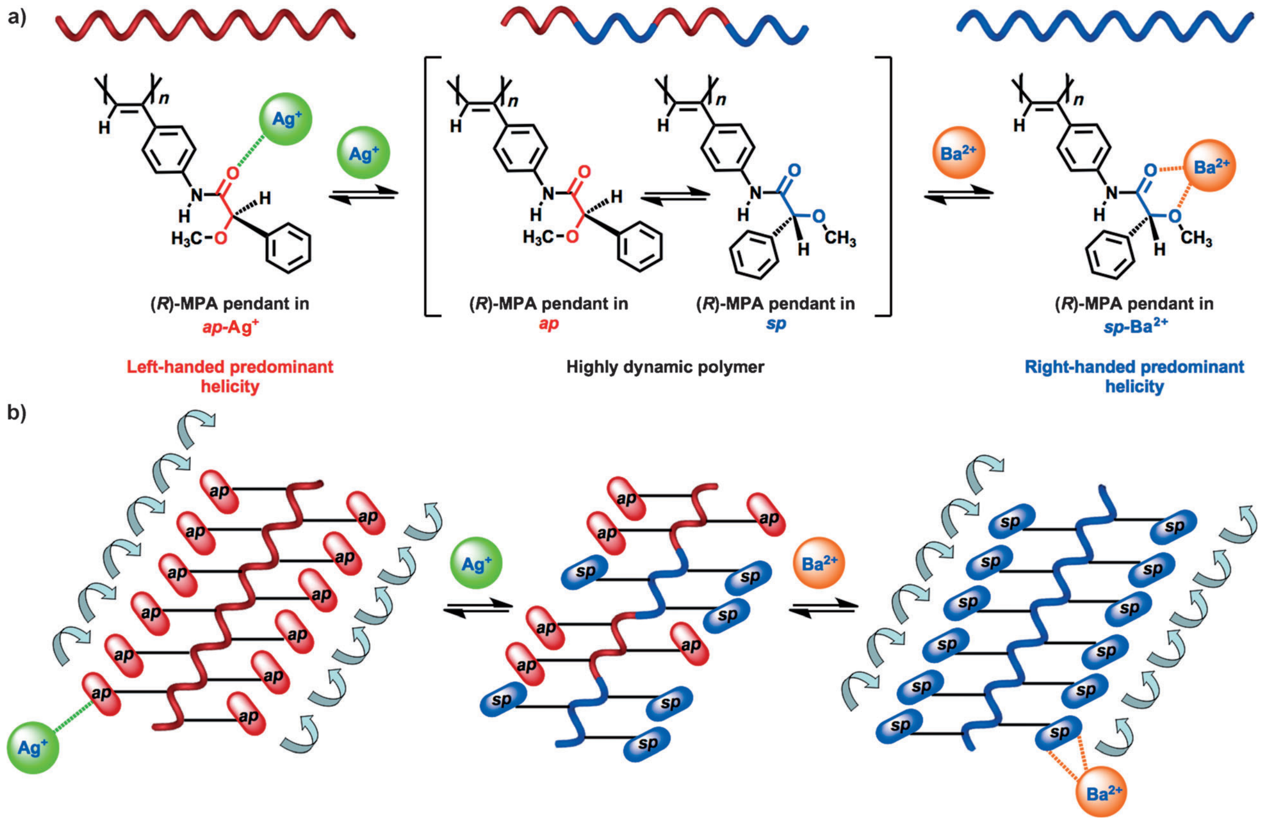

Figure 3. a) Selective modulation of the helicity induced by control of the conformation of the pendants by complexation with mono- and divalent cations (poly-**1**). b) Schematic representation of the amplification phenomenon indicating the *ap*/*sp* conformation of the pendants.

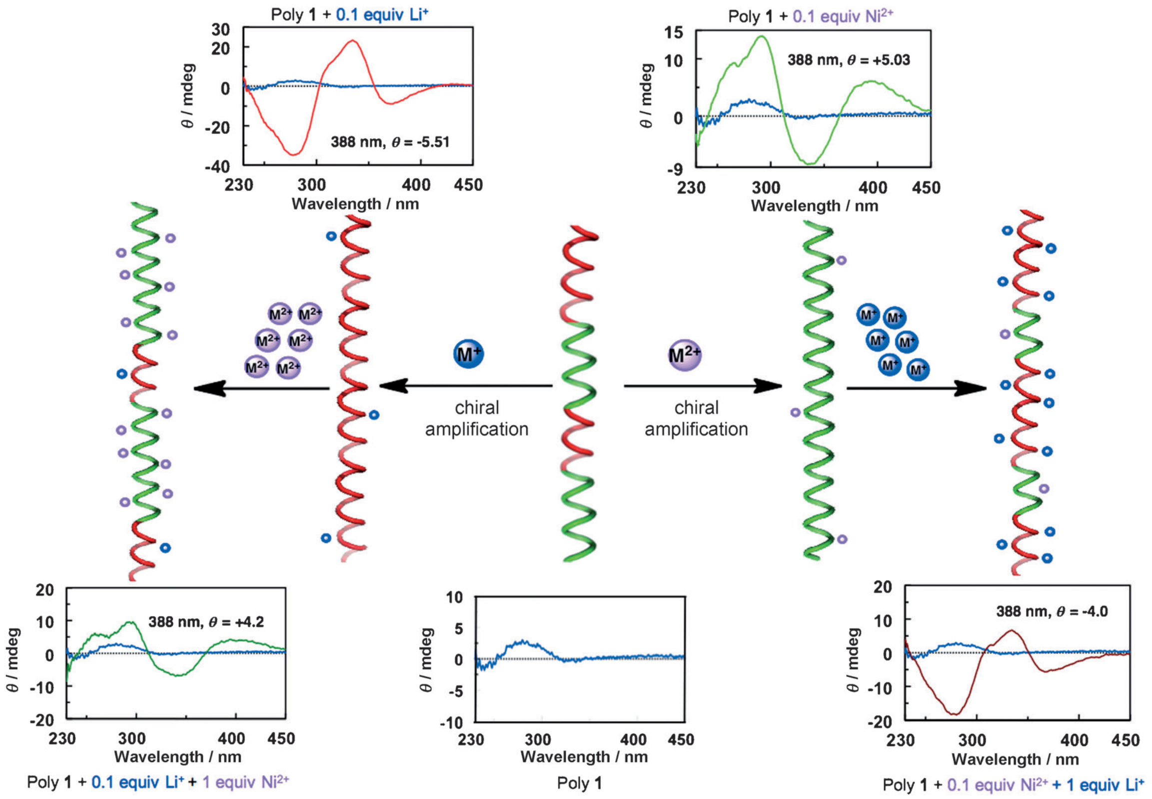

Figure 4. Chiral amplification and helix inversion (poly-**1**) by step-by-step addition: first M^+ (Li^+), second M^{2+} (Ni^{2+}) (left) and first M^{2+} (Ni^{2+}), second M^+ (Li^+) (right).

Table 1: Selected IR spectroscopy data of poly-**1** and poly-**1**/metal cation (KBr).

Polymer/M	ν CO [cm^{-1}]	ν OMe [cm^{-1}]	$\Delta\nu$ CO [cm^{-1}][a]	$\Delta\nu$ OMe [cm^{-1}][a]
Poly-**1**	1682	1099	0	0
Poly-**1**/Ag^{+}	1650	1099	32	0
Poly-**1**/Na^{+}	1672	1100	10	−1
Poly-**1**/Li^{+}	1669	1100	13	−1
Poly-**1**/Ba^{2+}	1665	1063	17	36
Poly-**1**/Ca^{2+}	1658	1074	24	25
Poly-**1**/Ni^{2+}	1638	1074	44	25

[a] $\Delta\nu = \nu$(poly-**1**)$-\nu$(poly-**1**/M).

groups (*sp* conformation), while monovalent cations only coordinate to the C=O unit (*ap* conformation, Figure 3a).

The low monomer/cation ratios required to achieve a maximum CD response (less than 0.1 in most cases) imply that chiral amplification phenomena are operating. The coordination of one cation to one pendant induces a preferred conformation (*sp* or *ap* depending on the valence), which is transmitted to the nearby pendant groups by a domino effect, thus leading to a more stable arrangement of the chain (Figure 3b). The low energy barrier between the left- and right-handed helices facilitates the dual behavior of the polymer, thus allowing its evolution to either one or the other helical sense according to the valence of the cation.

Additional experiments showed the versatility of the polymer. For example, once chiral amplification has been obtained with a cation (i.e. M^{2+} at a cation/monomer ratio of 0.1), addition of a cation belonging to the other valence type (M^{+}) at a higher concentration (cation/monomer ratio of 1.0) reverses the helicity (Figure 4). The opposite addition sequence (first monovalent, second divalent) works in the same way and the helicity induced by the cation present in excess prevails (Figure 4). Addition of mixtures of both types of cations to the polymer yielded the same final CD spectra as those obtained by step-by-step additions (see the Supporting Information).

The full reversibility of the processes was established using scavenger resins (Figure 5). In these experiments the CD spectrum of the dynamic polymer was recovered when the cation was removed after complexation by addition of the resin (see the Supporting Information). In this way, the characteristic CD properties of the polymer are recovered (no memory), and it can be reused for new complexation with other di- or monovalent cations.

In summary, we present herein a highly dynamic helical polymer (PPA) with a chiral pendant ((*R*)- or (*S*)-MPA), which shows no CD effect. The discriminating interaction of the polymer with mono- and divalent metals induces either left- or right-handed helical senses and opposite chiroptical responses.[19] This selective modulation (confirmed by AFM) is triggered by the initial control of the conformation of the pendants by complexation with the metal cations. This effect is further transmitted from the pendants to the main polymer backbone.

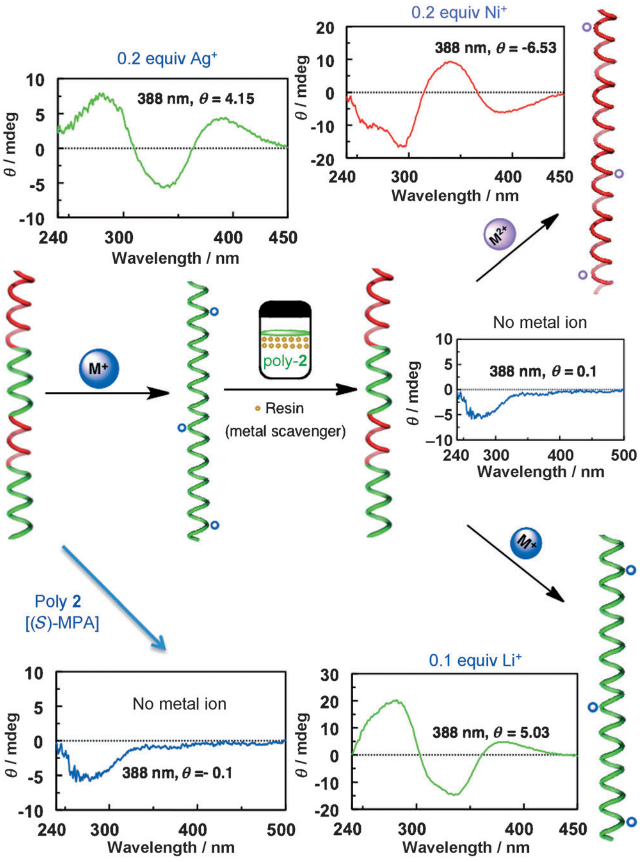

Figure 5. Reversible use of poly-**2** by means of scavenger resins. For examples with other metal cations and other addition sequences (i.e. 1st M^{2+}, 2nd resin, 3rd M^{+} or M^{2+}) see the Supporting Information.

The maximum intensities of the Cotton effects in the CD spectra are reached with less than 0.1 cation/monomer ratios, indicating that the chiral polymer amplifies the effect of metal-ion complexation (chiral amplification). This response of the polymer to the valence of the ion shows that the polymer acts as a mono- and divalent metal cation sensor.[20]

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Keywords: chiral amplification · helical structures · helix induction · metal cations · sensors

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[1] a) E. Yashima, K. Maeda, Y. Furusho, *Acc. Chem. Res.* **2008**, *41*, 1166–1180; b) E. Yashima, K. Maeda, H. Lida, Y. Furusho, K. Nagai, *Chem. Rev.* **2009**, *109*, 6102–6211; c) J. Liu, J. W. Y. Lam, B. Z. Tang, *Chem. Rev.* **2009**, *109*, 5799–5867; d) B. M. Rosen, C. J. Wilson, D. A. Wilson, M. Peterca, M. R. Imam, V. Percec, *Chem. Rev.* **2009**, *109*, 6275–6540; e) E. Schwartz, M. Koepf, H. J. Kitto, R. J. M. Nolte, A. E. Rowan, *Polym. Chem.* **2011**, *2*, 33–47.

[2] a) K. Maeda, E. Yashima, *Top. Curr. Chem.* **2006**, *265*, 47–88; b) E. Yashima, K. Maeda, *Helically Folding Polymers* in *Foldamers: Structure Properties and Applications* (Eds.: S. Hecht, I. Huc), Wiley-VCH, Weiheim, **2007**, chap. 11, pp. 331–366; c) E. Yashima, K. Maeda, *Macromolecules* **2008**, *41*, 3–12.

[3] T. Sierra, “Expression of Chirality in Polymers” in *Chirality at the Nanoscale: Nanoparticles, Surfaces, Materials and more* (Ed.:

D. B. Amabilino), Wiley-VCH, Weinheim, **2009**, chap. 5, pp. 115–190.

[4] a) S. Sakurai, K. Okoshi, J. Kumaki, E. Yashima, *J. Am. Chem. Soc.* **2006**, *128*, 5650–5651; b) K. Okoshi, S. Sakurai, J. K. Ohsawa, E. Yashima, *Angew. Chem.* **2006**, *118*, 8353–8356; *Angew. Chem. Int. Ed.* **2006**, *45*, 8173–8176; c) D. Pijper, M. G. M. Jongejan, A. Meetsma, B. L. Feringa, *J. Am. Chem. Soc.* **2008**, *130*, 4541–4552.

[5] B. L. Feringa, *Acc. Chem. Res.* **2001**, *34*, 504–513.

[6] a) M. M. Green, N. C. Peterson, T. Sato, A. Teramoto, R. Cook, S. Lifson, *Science* **1995**, *268*, 1860–1866; b) M. M. Green, J. W. Park, T. Sato, A. Teramoto, S. Lifson, R. L. B. Selinger, J. V. Selinger, *Angew. Chem.* **1999**, *111*, 3328–3345; *Angew. Chem. Int. Ed.* **1999**, *38*, 3138–3154, and references therein.

[7] This phenomenon has attracted a great deal of attention owing to the potential of this unique process in different fields of nanotechnology and nanoscience and to its possible relationship with the origin of homochirality in nature. See a) E. Yashima, K. Maeda, T. Nishimura, *Chem. Eur. J.* **2004**, *10*, 42–51; b) A. R. A. Palmans, E. W. Meijer, *Angew. Chem.* **2007**, *119*, 9106–9126; *Angew. Chem. Int. Ed.* **2007**, *46*, 8948–8968; c) M. M. J. Smulders, I. A. W. Filot, J. M. A. Leenders, P. van der Schoot, A. R. A. Palmans, A. P. H. J. Schenning, E. W. Meijer, *J. Am. Chem. Soc.* **2010**, *132*, 611–619.

[8] Kakuchi et al. have reported that the CD spectra of copolymers that had an initial predominant one-handed helical sense were inverted in the presence of metal cations. However, neither selectivity related to the valence of the cations (the polymers did not behave as valence sensors) nor amplification of chirality mechanisms and the helical senses of the copolymers (AFM images) were reported. See a) I. Otsuka, R. Sakai, T. Satoh, R. Kakuchi, H. Kaga, T. Kakuchi, *J. Polym. Sci. Part A* **2005**, *43*, 5855–5863; b) I. Otsuka, R. Sakai, R. Kakuchi, T. Satoh, T. Kakuchi, *Eur. Polym. J.* **2008**, *44*, 2971–2979.

[9] a) B. López, E. Quiñoá, R. Riguera, *J. Am. Chem. Soc.* **1999**, *121*, 9724–9725; b) R. García, J. M. Seco, S. A. Vázquez, E. Quiñoá, R. Riguera, *J. Org. Chem.* **2002**, *67*, 4579–4589; c) R. García, J. M. Seco, S. A. Vázquez, E. Quiñoá, R. Riguera, *J. Org. Chem.* **2006**, *71*, 1119–1130.

[10] There has been a recent example of the use of monomers in the study of helix inversion of helicates. See M. Albrecht, E. Isaak, M. Baumert, V. Gossen, G. Raabe, R. Fröhlich, *Angew. Chem.* **2011**, *123*, 2903–2906; *Angew. Chem. Int. Ed.* **2011**, *50*, 2850–2853.

[11] The synthesis, solubilities, stereoregularities, and description of the main conformers as well as helicity studies by CD spectroscopy in different solvents can be found in the Supporting Information.

[12] a) K. K. L. Cheuk, J. W. Y. Lam, J. Chen, M. L. Lai, B. Z. Tang, *Macromolecules* **2003**, *36*, 5947–5959; b) B. S. Li, K. K. L. Cheuk, L. Ling, J. Chen, X. Xiao, C. Bai, B. Z. Tang, *Macromolecules* **2003**, *36*, 77–85; c) J. W. Y. Lam, B. Z. Tang, *Acc. Chem. Res.* **2005**, *38*, 745–754; d) M. G. Mayershofer, O. Nuyken, *J. Polym. Sci. Part A* **2005**, *43*, 5723–5747; e) K. K. L. Cheuk, B. S. Li, J. W. Y. Lam, B. Z. Tang, *Macromolecules* **2008**, *41*, 5997–6005.

[13] Perchlorates showed appropriate solubility and the anions did not interfere with the polymers, as shown by the lack of response obtained by treatment with ammonium perchlorate.

[14] 0.2(M^{2+} or M^{1+})/1.0(monomer)(equiv/equiv) ratios taken from 10.0 mg mL^{-1} (MClO$_4$)$_n$(n=1 or 2)/THF and 0.1 mg mL^{-1} polymer/CHCl$_3$ solutions, respectively.

[15] KClO$_4$ and CsClO$_4$ were insoluble under the experimental conditions.

[16] 0.2(Ba^{2+})/1.0(monomer) and 0.5(Ag^{+})/1.0(monomer) (equiv/equiv) ratios.

[17] To our knowledge, this is the first time that images of both helical senses are reported for polyphenylacetylenes bearing short pendants. Usually, long alkyl chains are needed as pendants to favor the interaction with the HOPG surface. See reference [4a] and S. Sakurai, K. Okoshi, J. Kumaki, E. Yashima, *Angew. Chem.* **2006**, *118*, 1267–1270; *Angew. Chem. Int. Ed.* **2006**, *45*, 1245–1248.

[18] Calculations were performed with Spartan 08.

[19] This response is generated from a highly dynamic polymer in which both helical senses are initially present (no CD signal), so the phenomenon reported herein cannot be classified as belonging to the "helix inversion" type because there is not any "inversion" from a previous helicity.

[20] We recently reported a less dynamic polymer bearing another kind of pendant with a different connection to the phenylacetylene, where the addition of certain metal cations produced helix inversion from a previous predominant helical sense, but neither selectivity associated with the valence of the metals nor amplification of chirality were observed. Thus, that material did not behave as valence sensor. See I. Louzao, J. M. Seco, E. Quiñoá, R. Riguera, *Angew. Chem.* **2010**, *122*, 1472–1475; *Angew. Chem. Int. Ed.* **2010**, *49*, 1430–1433.