Helicity

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Control of the Helicity of Poly(phenylacetylene)s: From the Conformation of the Pendant to the Chirality of the Backbone**

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Dedicated to Professor Pelayo Camps on the occasion of his 65th birthday

Since the seminal work of Percec and co-workers,[1a] the design, synthesis, and applications of helical polymers with a controlled helix sense has become a field of major interest in recent years.[1b,c,2] The possibility of controlling and switching the helicity of these polymers by an external agent[2,3] (e.g. temperature,[3a,b] solvent,[3c–e] light[3f,g]) makes them suitable[4] for several applications.[1b,c,2]

We now present a novel reversible way to control the helicity of poly(phenylacetylene)s with phenylglycine methyl ester pendant groups (poly-(*R*)-**1** and poly-(*S*)-**1**; Figure 1). We show herein that the manipulation of the conformational equilibrium of the pendant allows one to choose the right- or left-handed sense of the helix. This phenomenon is achieved by complexation with appropriate metal cations or by solvent polarity effects[2,5] and is based on the characteristics of the conformational equilibrium of the pendants. We performed variable-temperature circular dichroism (CD) experiments in a variety of solvents, atomic force microscopy (AFM) on highly oriented pyrolytic graphite (HOPG), NMR, IR, and Raman spectroscopy, and theoretical calculations (MM (MMFF94), DFT (B3LYP), PCM).

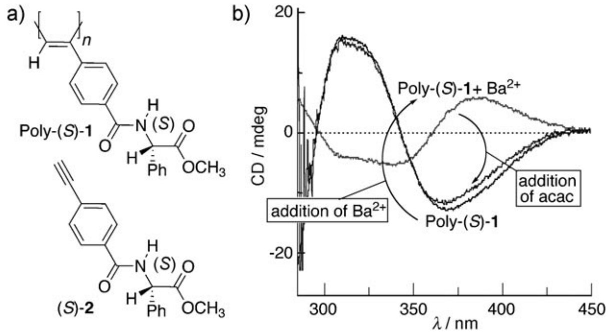

Figure 1. a) Structure of poly-(*S*)-**1** and monomer (*S*)-**2**. b) CD spectra of poly-(*S*)-**1** taken before and after the addition of $Ba(ClO_4)_2$ and recovery of the original helicity after the addition of acac ($CHCl_3$).

(*R*)- and (*S*)-Phenylglycine methyl esters were chosen as suitable pendants for the planned studies. Accordingly, poly-(*R*)-**1** and poly-(*S*)-**1** (Figure 1) were prepared by following known procedures[5a] with $[Rh(nbd)Cl]_2$ (nbd = 2,5-norbornadiene) as catalyst from monomer **2** and obtained with stereoregular *cis-transoid*[5] backbones as shown by the chemical shifts of the vinyl protons ($\delta = 5.7$–5.8 ppm) and Raman resonances (1553, 1343, 1003 cm^{-1}) (see the Supporting Information for experimental details and spectroscopic data). Poly-(*R*)-**1** adopts a right-handed helical conformation and poly-(*S*)-**1** a left-handed one[5a] in $CHCl_3$ (positive and negative Cotton effects, respectively, at 375 nm; Figure 1), and the polymers have positive and negative dihedral angles, respectively ($180° < \omega 1 < 0°$ and $180° > \omega 1 > 0°$, Figure 2c), between vicinal double bonds.

CD spectra of the two polymers after addition of a series of perchlorates of mono- and divalent metal cations (Li^+, Na^+, Ag^+, Mg^{2+}, and Ba^{2+}) showed, in all cases, that inversion of the helicity had taken place (opposite CD signs); Ba^{2+} gave the strongest response. The addition of acetylacetone (acac) reversed the helicity, causing the recovery of the original CD spectra in all cases.[6]

To reveal the mechanism beyond this inversion of helicity, a series of studies were performed:

1) AFM (HOPG)[7] gave important insights into the helicity and morphology of poly-(*R*)-**1** (see the Supporting Information for details). The images show two types of structures (Figure 2): individual and associated chains.

The single chains, packed parallel one after another, display a left-handed (counterclockwise) pendant disposition[3b] (Figure 2a,d) with the periodic oblique strips forming angles close to 45° (i.e. $\omega 1 \approx +148°$, Figure 2c). This value justifies the right-handedness of the backbone (Figure 2d) and allows intrachain hydrogen bond formation between the *n*th and $(n+2)$th amide groups (essential to stabilize the helical structure).[8] AFM also shows multistranded left-handed helices, in which interchain hydrogen bonds are likely to play a main role[9] (Figure 2b). The AFM images show, after the partial addition of $Ba(ClO_4)_2$ (1.0 equiv), the coexistence of both senses of handedness (see the Supporting Information).

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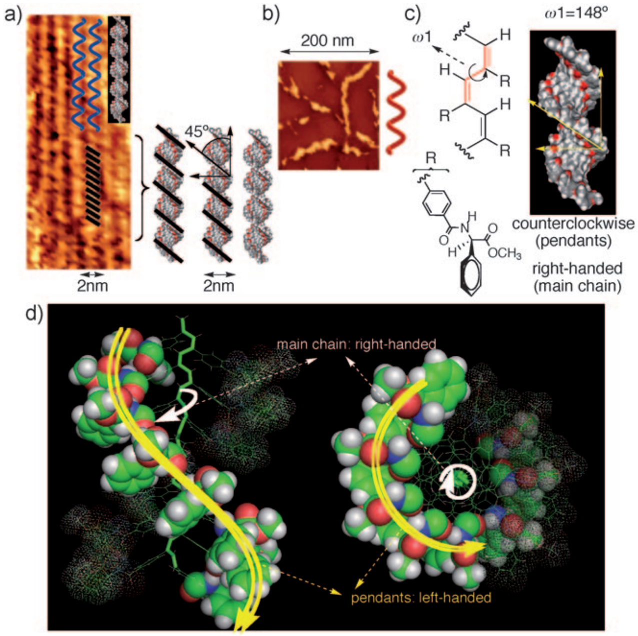

Figure 2. a) AFM image of poly-(*R*)-**1** showing single chains. b) AFM image showing multistranded helices. c) Side view of poly-(*R*)-**1** in right-handed and anticlockwise helical array of the main chain and pendants, respectively. d) Side (left) and top (right) views of poly-(*R*)-**1** showing the main chain as a tube (green) and the pendants as solid and dotted spheres.

2) DFT calculations[10] [B3LYP/6-31 + G(d,p)] were performed on (*R*)-methyl 2-benzamido-2-phenylacetate (**3**) as a model of the chiral pendant (Figure 3 a). Sp1, sp2, and ap are the main conformers generated by rotation around the $\omega 2$ and $\omega 3$ bonds; sp1 is the most stable one (2.50 and 1.11 kcal mol^{-1} for sp2 and ap, respectively). The complexes were also studied at the B3LYP/lanl2dz level using Ba^{2+} as metal cation. In all cases, the initial conformations evolved to the sp2-Ba form, in which Ba^{2+} coordinates to the ester and amide carbonyl groups (Figure 3 a).

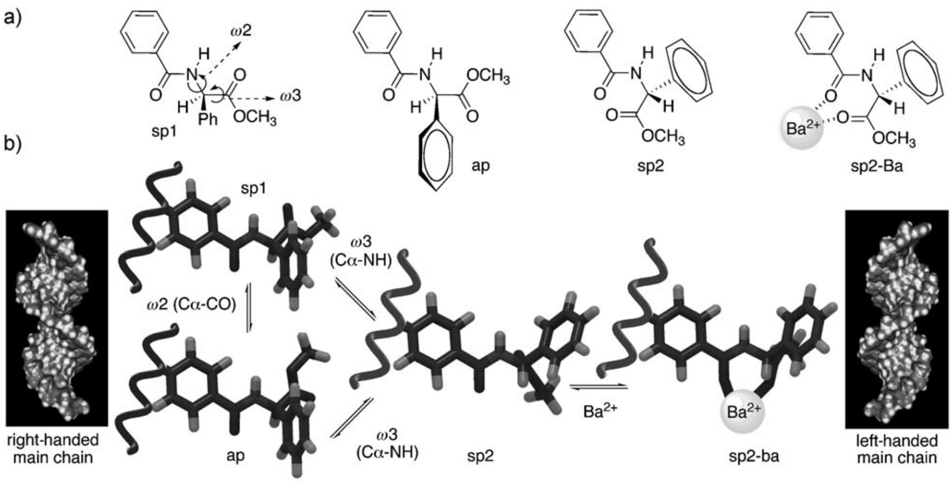

Figure 3. a) Main conformers of the model of the chiral pendant (**3**). b) Partial view of the mechanism for the inversion of helicity of poly-(*R*)-**1**.

When the pendant is incorporated in the main framework, MMFF94 calculations[10,11] on poly-(*R*)-**1** show that the right-handed form ($\omega 1 = +148°$) with sp1 pendants (right-handed/sp1) is the most stable one [by 27.87 and 4.50 kcal mol^{-1} relative to right-handed/sp2 and left-handed/sp1 ($\omega 1 = -148°$), respectively]. However, when Ba^{2+} is incorporated, the left-handed/sp2-Ba form becomes more stable than the right-handed/sp2-Ba form (5.41 kcal mol^{-1}).

3) Variable-temperature CD, ^{13}C NMR spectrscopy, and FTIR spectroscopy corroborated the presence of the equilibria: a) when temperature drops, the CD band of poly-(*R*)-**1** intensifies owing to the increase of the number of pendants adopting the sp1 conformation. As the CD spectra is the average between the contributions of the right-handed and left-handed segments present in the polymer chain [pendants in sp1 (positive CD) and pendants in sp2 (negative CD), respectively], an increment in the number of pendants in the most stable conformation (sp1) produces an increment in the intensity of the CD band;[12] b) a noticeable deshielding on the amide/ester carbonyl groups after Ba^{2+} addition[13] is observed, pointing to those groups as coordination sites [1.0/0.3 and 8.3/7.2 ppm for (*R*)-**2** and poly-(*R*)-**1**, respectively]; c) the FTIR spectroscopic experiments on poly-(*R*)-**1** and (*R*)-**2** indicate that the original C=O/NH association through hydrogen bonding is disturbed by the addition of the divalent cation: the carbonyl groups are now associated preferentially with the metal and, correspondingly, their association to the NH groups diminishes (see the Supporting Information).

The mechanistic scenario (Figures 3 b and 4) that results from the aforementioned studies foresees an equilibrium for the pendants whereby, in the absence of Ba^{2+}, sp1 predominates over ap and sp2. This conformational preference of the pendants is transmitted to the polyene backbone, which adopts the most stable right-handed form (Figure 4 b). The addition of Ba^{2+} makes sp2-Ba the most stable conformation, and the backbone is now forced to switch to the left-handed form, which now becomes more stable (Figure 4 c,d).[14] Therefore, it is the shift in the conformational equilibria of the pendant that causes the change in helicity.

Complementary experiments demonstrating this mechanism can be obtained by changing the polarity of the solvent. For polymers with long alkyl chains attached to alanine pendants, it has been proposed that the intramolecular hydrogen-bonding network that stabilizes the helix in nonpolar solvents is weakened or switched off in polar solvents, resulting in the formation of a different or even opposite helical conformation.[3d] The disappearance of hydrogen bonds does not fully explain the reversal of the helix sense, and the

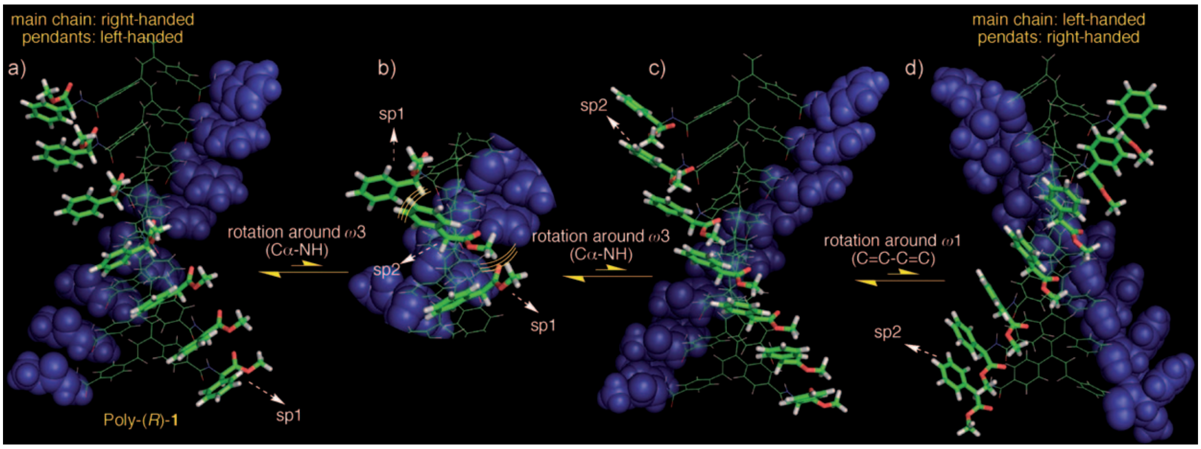

Figure 4. Proposed mechanism for the inversion of helicity of poly-(*R*)-**1**. a) Main chain in right-handed helix with pendants in left-handed sense. The pendants are in sp1 conformation (the most stable one in the absence of Ba^{2+} or in nonpolar solvents). b) When a pendant shifts to sp2 (i.e. after addition of Ba^{2+} or by a change of polarity), its steric hindrance with the neighboring pendants in sp1 form initiates the inversion of both the helicity of the main chain and the sense of the pendant ("domino effect"). c) The inversion progresses as the number of pendants in sp2 increases. d) When the majority of the pendants are in the sp2 conformation (the most stable conformation in the presence of Ba^{2+} or in polar solvents), the main chain is a left-handed helix and the pendants present a right-handed sense.

conformational change induced in the pendant by the polarity of the solvent is the main factor.

In fact, when trifluoroacetic acid (TFA)[15] is added to poly-(*S*)-**1** dissolved in two solvents inducing opposite helicity (namely, $CHCl_3$ for the left-handed form and CH_3CN for the right-handed form), the Cotton effect dramatically diminishes but does not generate the opposite helix. Therefore, although the disappearance of the intramolecular hydrogen bonds may destroy the helix, it does not by itself justify the helical inversion.

The central role of the conformation of the pendants in the inversion of the helix is demonstrated in the following experiments. Thus, the CD bands of poly-(*S*)-**1** move from negative to positive $\Delta\varepsilon$ (at 375 nm) when going from more polar (i.e. DMSO) to less polar solvents (i.e. $CHCl_3$, Figure 5a): a left-handed helix predominates in $CHCl_3$, CH_2Cl_2, 1,4-dioxane, and THF, and the right-handed in acetone, CH_3CN, and DMSO. There is a good correlation among the intensity/sign of the CD bands, the difference of energy of sp1/sp2 [PCM-B3LYP/6-31+G(d,p)],[10] and the polarity of the solvents (Debye solvent polarizability function)[16] (Table 1): as the sp1 conformer of the pendant is less polar than the sp2 (2.77 versus 3.47 D, B3LYP/lanl2dz), sp1 predominates in low/medium polarity solvents and induces a preference for the left-handed helicity. In contrast, the stabilization of the more polar sp2 conformer by high polarity solvents switches the preference to the right-handed helicity (Figure 5b).

Additional evidence for the postulated control of the helix sense was obtained from the following experiments: a) the addition of Ba^{2+} to a solution of poly-(*S*)-**1** in $CHCl_3$ (left-handed helix) reverses its helicity (sp1 in the pendant shifts to sp2), b) analogous addition of Ba^{2+} to the same polymer in CH_3CN (right-handed helix) does not reverse the helicity but produce an increase of the original helix as shown by the increase in intensity of the CD bands. Again, this result can be explained by the conformation of the pendant: in MeCN, sp2 is already the main conformer and the addition of Ba^{2+} can only increase its population over sp1.

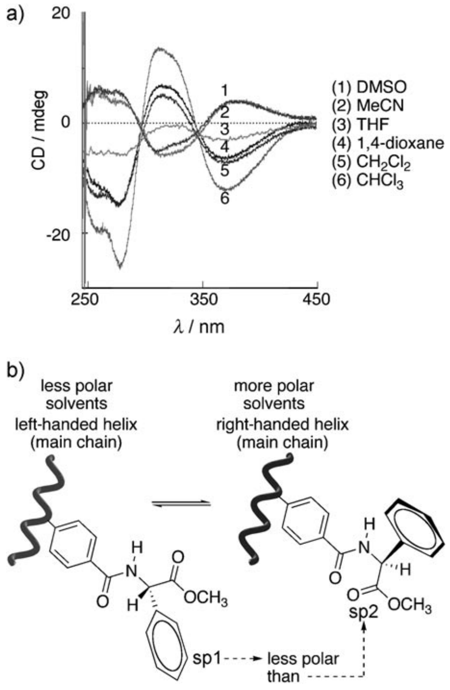

Figure 5. a) CD spectra of poly-(*S*)-**1** in solvents of diverse polarity. b) Conformational equilibrium and solvent dependence.

In summary, in this work we have demonstrated that the conformation of the chiral pendant determines the helix sense of the polymer. Its modification by complexation with appropriate metal cations (e.g. Ba^{2+}) or by changing the polarity of the solvent allows selection and reversal of the helix sense. This knowledge of the mechanism that controls the left- or right-handed sense of the polymer opens new perspectives for future applications.

Table 1: CD data ($\Delta\varepsilon$ values) of poly-(S)-**1**, Debye solvent polarizability function, and relative energies[a] for the main conformers[b] of **3** in a selection of solvents of diverse polarity.

	$CHCl_3$	THF	Acetone	CH_3CN	DMSO
$\Delta\varepsilon$ (375 nm)	-11.25	-2.57	$+3.21$	$+3.28$	$+3.39$
$(\varepsilon-1)/(\varepsilon+2)$	0.156	0.68	0.86	0.92	0.93
sp1	0.00	0.00	0.00	0.07	0.00
sp2	0.37	0.25	0.10	0.00	0.02

[a] PCM/B3LYP/6-31+G(d,p); in $kcal\,mol^{-1}$. [b] For the ap conformer, the calculated energy values are 2.17, 2.07, 1.93, 1.87, and 1.98 in the series.

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