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Raman Optical Activity (ROA) as a New Tool to Elucidate the Helical Structure of Poly(phenylacetylene)s

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Abstract: Poly(phenylacetylene)s is a family of helical polymers constituted by conjugated double bonds that are fixed into specific helical structures due to supramolecular and/or steric interactions among pendant groups. Raman spectra of these polymers show a structural fingerprint of the polyene backbone which, in combination with its helical orientation, makes them great candidates to study their helical structure by Raman Optical Activity (ROA). Four different well-known poly(phenylacetylene)s adopting different scaffolds and ten different helical senses have been prepared. For all of these, Raman and ROA spectra were recorded which allows us to establish ROA spectrum/helical sense relationships: a righthanded orientation of the polyene backbone (P_{helix}) produces a triplet of negative ROA bands, whereas a M_{helix} produces a positive triplet ROA pattern. Raman and ROA spectra of each polymer exhibited the same profile and the sign of the ROA spectrum was opposite to the lowest energy ECD band, thus indicating a resonance effect. Resonance ROA appears then as a useful selective indicator of the helical sense of poly(phenylacetylene)s, especially for those showing an extra Cotton band in the ECD spectrum. In these cases, a wrong helical sense is assigned based on ECD, while ROA alerts of this misassignment.

Introduction

The generation of new functional materials based on helical polymers is directly related to the actuation on their helical structure —backbone elongation and helical sense—. Thus, to study the structure/function relationships of these materials is necessary to have capable tools to elucidate the secondary structure of these complex macromolecules. Nowadays, the structural elucidation of some helical polymers such as poly(phenylacetylene)s (PPAs)^[1-5] is still a challenge due to the co-habitation of different helices with different helical pitches and senses. For instance, PPAs are formed by two coaxial helices, an internal helix described by the polyene covalent backbone and an external helix described by the pendants, which can rotate either in the same or opposite senses depending on the dihedral angle between the conjugated double bonds (Figure 1).^[6,7]



Figure 1. (a) Main dihedral angles of a poly(phenylacetylene) and its folding into a helix. 3D model and schematic representation of PPAs showing two different scaffolds where the coaxial helices rotate in (b) the same *—ciscisoidal—* or (c) opposite direction *—cis-transoidal—*.

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As a result, to build up an approximate helical structure of a PPA, it is necessary to cross information from different structural and spectroscopic techniques each providing evidences of the multihelical supra-structure. To further hinder this structural research, many of the common techniques, such as Nuclear Magnetic Resonance (NMR) are not valid to characterize helical polymers due to their intrinsic repetitive structure. In PPAs, the helical structure is not defined by supramolecular interactions between different residues along the backbone as it happens for instance in peptides. Here, the helix is defined by steric interactions among pendants, which can originate many different possibilities depending on the dihedral angle between conjugated double bonds (ω_1 in Figure 1a). If the dihedral angle between conjugated double bonds is higher than 90° (i.e., $\omega_1 >$ 90°), the polymer adopts a *cis-transoidal* polyene configuration -internal and external helices rotate in opposite directions-(Figure 1c), while if $\omega_1 < 90^\circ$ the polymer adopts a *cis-cisoidal* direction— (Figure 1b). In a pioneering work, Simionescu et. al. reported and characterized all possible cis- and transstereoisomers found in a PPA, at the same time that developed a NMR method to determine the cis-content of cis-transoidal and cis-cisoidal poly(phenylacetylene)s.[8]

Solid-state structural techniques such as X-ray Diffraction (XRD),^[9-19] or Atomic Force Microscopy (AFM)^[20-28] can be used to provide insights of the helical pitch, length and helix width, although are silent about the features of the internal helix (Figure 2). Another restriction of AFM is that can provide structural information only when 2D crystals or self-assembled monolayers are available due to the need of getting high-resolution images. ^[20-28] Vibrational Circular Dichroism (VCD) has been also used to gain information about the orientation of the external helix in PPAs.^[30] In such case, the solvent used to perform the experiments will interact with the pendant groups of the PPA forming another supramolecular helix with the same orientation than that of the external part of the PPA helix. As a result, the solvent becomes VCD active, and its sign reflects the orientation of the external part of the helix (Figure 2).

Other techniques such as Differential Scanning Calorimetry (DSC) have also been used in the structural elucidation of poly(phenylacetylene)s.^[31-33] DSC provides information about the configuration of the polyene backbone —*cis-cisoidal* (*c-c*) and *cis-transoidal* (*c-t*)— associated to different and characteristic thermograms^[29] (Figure 2). Unfortunately, these studies are often limited by the poor definition of the thermograms and/or by the presence of peaks associated to conformational changes in the pendants, making the assignments unreliable.

Recently, it was also shown that combination of experimental and theoretical methods can be used to determine the secondary structure of some helical polymers different from PPAs, for instance by combining VCD,^[31-33] Electronic Circular Dichroism (ECD) simulations and MMFF94^[34] energy minimization. In this regard, lately, we found that it is possible to determine the *P/M* internal helical sense of a PPA from its ECD spectra (first Cotton effect). This conclusion is based on the correlations observed between experiments and time-dependent density functional theory (TD-DFT) which provides calculated ECD spectra of a series of PPAs with different and well-known helical scaffolds (Figure 2).^[35-36] Thus, a positive Cotton effect in the UV-vis absorption vinylic region corresponds to a *P* helical (internal) sense, while a negative Cotton effect indicates the presence of a *M* helix for the polyene skeleton. A detrimental point of this approach is that in some cases, this helical sense assignment is not straightforward. This is the case of PPAs featuring a particular rotation angle (i.e., ω_3) between the pendant groups and the main PA chain provoking a mixing of the two moieties molecular orbitals and an extra Cotton band, the so-called ω_3 rotation band, in the ECD spectrum. Contrary to the ω_1 and ω_2 ECD bands (i.e., mostly linked to the PA structure), the ω_3 feature responds to a synergy between the two PPA helices. It usually appears at higher wavelengths by which potentially overlaps the first Cotton effect in the ECD trace often causing wrong helical sense assignments. The structural nature (ω_3 angle rotation) of this extra band and the inherently electronic origin of the ECD feature further arise a complication in the structural assignments based on electronic effects.

Herein, Raman Optical Activity (ROA)^[37-45] is introduced as a novel technique to study the helical structure of PPAs. ROA is referred to the weak spectroscopic phenomenon resulting from subtracting the intensities of the Raman scattered radiation for right and left circularly polarized excitation light. Either by itself or by complementing other structural techniques, ROA will allow us to undoubtedly assign the internal sense of the helix of PPAs. The greater structural sensitivity of ROA will be crucial to clarify the assignment of the structure of these PPA polymers.



Figure 2. Combination of structural information obtained from a PPA by different structural techniques such as AFM, DSC, MM, DFT, ECD and VCD.

Results and Discussion

The Raman spectra of poly(phenylacetylene)s are strongly dominated by vibrations of the backbone chain -CC stretching of the Ph group of the cis-C-Ph moiety ca. 1580 cm⁻¹, CC stretching of cis-C=C ca. 1370 cm⁻¹, CH deformation mode of the cis-C-H ca. 1000 cm⁻¹, and CC stretching of the C-C moieties ca. 900 cm⁻¹. Moreover, the tunability of the chiral orientation of this chain into a P or M helical sense as well as the elongation ability (cis-cisoidal/compressed, cistransoidal/stretched) by using external stimuli^[47-51], make these polymers great candidates to study their folding by ROA spectroscopy (Scheme 1). Reversible interconversion between cis-cisoidal and cis-transoidal structures is also feasible in the solid state, where this motion can be translated at macroscopic length scales transforming the flexible PPA macromolecule into a nanomachine.^[52-53] In the following paragraphs we will explore the ability of ROA to go beyond ECD in order to elucidate the helical structure of PPAs bearing different pendant groups.



Scheme 1. Schematic representation of a PPA showing its helical rearrangements and the Raman bands associated to the polyphenylacetylene backbone.

1. Helix inversion and solvent polarity: poly-1. As the first example we chose the para-ethynylbenzamides of the (S)-Valine methyl ester. The PPA bearing this pendant (poly-1, Figure $3a)^{[51]}$ becomes a dynamic polymer whose helical sense can be inverted by the polar character of the solvent used (Figure 3b). Thus, in non-polar solvents such as DCM, the ECD spectrum shows a first negative Cotton effect at higher wavelengths (Figure 3c) which corresponds to an *M* helical structure of the polyene backbone induced by an antiperiplanar orientation of the carbonyl groups at the pendant (Figure 3c), indicating the presence of a *P* helix induced by the presence of a major synperiplanar conformation of the carbonyl groups at the pendant (Figure 3f).

DSC studies of poly-1 in polar and low-polar solvents show a classical thermogram for a *cis-transoidal* polyene backbone (ω_1 > 90°), where the helical scaffold is stabilized by H-bonds between amide groups in *i* and *i*+2 positions along the polymer chain (See ESI). TD-DFT calculations on the *M* helix of a *cis-transoidal* oligomer model (n= 10) of poly-1 shows a first negative Cotton effect which is coincident with the experimental ECD spectrum obtained in non-polar solvents. On the other hand, identical studies on a *P* helix of an oligomer model (n= 10) of poly-1

shows a first positive Cotton effect, which is also in agreement with the experimental observation.

Next, Raman and ROA studies in Figure 3 have been performed for poly-1 in both non-polar and polar solvents —DCM and DCM/MeOH in Figure 3d. As observed, the ROA spectra are monosignate with the same profile than their parent Raman spectra. In addition, the sign of every ROA spectrum is opposite to that of the lowest energy ECD band. These facts reveal that we are under resonance conditions in which an ECD/ROA sign inversion, coming from the opposite definition of ECD ($I_L - I_R$) and ROA ($I_R - I_L$) intensities, is observed. Resonance gives rise to a noticeable simplification of the two spectra,^[40-42] as only Raman bands due to vibrations of the active chromophore are enhanced.



Figure 3. (a) Structure of poly-1. (b) Poly-1 main conformers in low-polar and polar media. (c) ECD/UV and (d) Raman/ROA spectra of poly-1 in low-polar (DCM) and polar solvents (DCM/MeOH). 3D graphical representation of an oligomer (n= 16) *cis-transoidal* structure for poly-1 with a (e) *M* and (f) *P* helical sense of the polyene backbone. Calculated (g) ECD/UV and (h) Raman/ROA spectra for the two helical orientations of an oligomeric structure of poly-1.

The absence of pendant bands in the different Raman and ROA spectra clearly indicates that the PPA backbone is here the active chromophore with bands assigned to CC stretching of the

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Ph group of the *cis*-C-Ph moiety ca. 1580 cm⁻¹, CC stretching of *cis*-C=C ca. 1370 cm⁻¹ and CC stretching of the C-C moieties ca. 900 cm⁻¹. In this case, the excitation radiation at 532 nm used in the ROA experiments approaches, but does not match, the lowest energy ECD band. This means that, in terms of the physical description of these second order effects, we have an intermediate situation between the theory established for Strong-Resonance (SR) and Far-From-Resonance (FFR), or Near-Resonance (NR) theory.^[43] NR-ROA represents a higher level of description of the Raman optical activity which embraces the FFR theory when the vibrational Raman shifts are much smaller than the energy difference between the incident exciting light and the active electronic excited state.

Figure 3d shows how the ROA spectra is sensitive to the chiral orientation of the polyene backbone since almost mirror-like image spectra were obtained for this PPA dissolved in solvents with different polarity. This is ascribed to the presence of opposite helical senses of the same polyene backbone. Thus, in DCM —non-polar solvent— a full positive ROA spectrum was obtained which corresponds to negative pattern of the first polyene Cotton effect at 380 nm. Both the positive ROA and the negative ECD patterns consistently reveal *M* helical orientation of the PPA backbone. The opposite situation was found for poly-1 in a DCM/MeOH mixture —polar solvent—, where a negative ROA spectrum and a positive ECD signals were obtained both indicating a *P* helix.

DFT calculations^[54-62] on the *M* helix of a model oligomer (n= 10) of poly-1 shows a full positive ROA spectrum, matching the results obtained experimentally. On the other hand, ROA calculations on the *P* helix of a model oligomer (n= 10) of poly-1 shows a full negative spectrum such in the experimental measure, indicating an opposite orientation of the polyene backbone. Importantly, in this case, ECD and ROA predict the same helical sense of the polyene backbone. Here however, it must be emphasized that a strong ROA spectrum (Fig. 3h, M helix) goes with a weak ECD spectrum (Fig. 3g, P helix). This seemingly conflicting pattern reversion can be explained in the light of the TD-DFT calculations. At wavelengths below 350 nm the M helix presents three intense excitations, namely at 376 (f=0.237), 405 (f=0.215) and 451 (f=0.237) nm, while the P helix features only one at 411 (f=0.510) nm (See ESI). As a result, resonance at 532 nm is more efficiently established with the nearer band for the M helix at 451 nm than for the band of P helix at 411 nm.

2. Helix elongation and solvent polarity: *m*-poly-2. Next, we explore the ability of ROA to elucidate the helical structure of a PPA that bears the *meta*-ethynylbenzamide of the (*S*)-phenylglycine methyl ester as pendant group (*m*-poly-2) (Figure 4a).^[6] Interestingly, this polymer shows in non-polar solvents (DCM) a combination of two different *cis-transoidal* helical scaffolds in equilibrium —stretched and compressed— (Figure 4b) and oriented into the same *M* helical sense (two negative Cotton effects at the polyene region at ca. 365 and 442 nm). However, in polar solvents (DMSO) a single compressed *cis-transoidal M* helix is obtained (negative Cotton effect at 380 nm, Figure 4c).

Raman and ROA spectra are again dominated by bands assigned to the poly(phenylacetylene) backbone —CC stretching of the Ph group of the *cis*-C-Ph moiety ca. 1580 cm⁻¹, CC stretching of *cis*-C=C ca. 1370 cm⁻¹, CH deformation mode

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of the *cis*-C-H ca. 1000 cm⁻¹, and CC stretching of the C-C moieties ca. 900 cm⁻¹—. In this case, ROA spectra obtained for *m*-poly-**2** in polar and non-polar solvents are almost identical, showing a positive sign in the full spectra, opposite to the negative sign of the Cotton effect corresponding to the polyene bands in the ECD spectra of *m*-poly-**2**. Therefore, these results indicate that an *M* orientation for the polyene backbone produces a negative Cotton effect in the ECD spectrum, while ROA shows a full positive spectrum. TD-DFT and ROA calculations on the *M helix* of a model oligomer (n= 10) of *m*-poly-**2** corroborate the results obtained experimentally, a negative Cotton effect in the ECD spectrum for the polyene band and a full positive ROA spectrum. Again, such as in poly-**1** ECD and ROA, conclusions are fully coincident revealing the presence of a *M* helix in both cases.



Figure 4. (a) Structure of *m*-poly-2. (b) Schematic representation of the compressed and stretched *M* helical scaffolds obtained for *m*-poly-2. (c) ECD/UV and (d) Raman/ROA spectra of *m*-poly-2 in low-polar (DCM) and polar solvents (DMSO). 3D graphical representation of an oligomer (n=24) *cis*-transoidal structure for *m*-poly-2 with different *cis*-transoidal polyene backbones. Calculated (g) ECD/UV and (h) Raman/ROA spectra for the two helical orientations of an oligomeric structure of *m*-poly-2.

3. The ω_3 Cotton effect: *p*-poly-2. Let us go now with helical poly(phenylacetylene)s that show a more complicated ECD spectrum. Some PPAs adopt a kind of helical structure that generates three ECD bands with alternating signs. In such case,

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the first Cotton band is assigned to the polyene backbone and therefore it is a marker of the helical sense of the polymer. Occasionally, an extra Cotton effect appears at higher wavelengths as the result of a ω_3 rotation (Figure 5a).^[36] In these cases, the first Cotton effect is no longer associated to the polyene backbone and can lead to helical misassignment. Therefore, to elucidate the right helical sense of the polyene backbone it is necessary first to determine which ECD band corresponds to the main chain.



Figure 5. (a) Structure of *p*-poly-2. (b) *p*-poly-2 main conformers in low-polar and polar media. (c) ECD/UV and (d) Raman/ROA spectra of *p*-poly-2 in lowpolar (DCM) and polar solvents (DMSO). 3D graphical representation of an oligomer (n= 24) *cis-transoidal* structure for *p*-poly-2 with different *cistransoidal* polyene backbones. Calculated (g) ECD/UV and (h) Raman/ROA spectra for the two helical orientations of an oligomeric structure of *p*-poly-2.

Alternatively, we decided to test the reliability of ROA in a polymer that show such feature: the *para*-substituted isomer of poly-2 (*p*-poly-2).^[63] This polymer behaves in a similar manner than poly-1, that is, the two helical senses can be induced in the polymer by acting on the conformational composition of the pendant group through changes on the solvent polarity. Thus, in non-polar solvents (DCM), a *M cis-transoidal* helical structure of the polyene backbone is induced due to the presence of an

Looking at the ECD spectrum of *p*-poly-2 in DMSO, we can observe the presence of an extra band at ca. 460 nm, which is assigned to a rotation around the ω_3 bond, as aforementioned, and not intrinsically due to the polyene backbone. In this particular situation, the helical sense of the PPA is extracted from the second Cotton effect (390 nm), which has an opposite sign relative to the first one: this scenario can lead to helical sense misassignments if the first one is chosen to assign the helical sense of the PPA.

The mirror-like relationship of ROA experiments —ROA (+) in non-polar solvents and ROA (-) in polar solvents— evidences opposite orientations for the polyene backbones. Interestingly, in polar solvents (DMSO), the sign of the ROA spectrum is as expected from previous studies (see above), opposite to the second Cotton effect assigned to the polyene backbone, and not to the first one assigned to a ω_3 rotation. Moreover, the intensity of the ROA spectrum in DMSO is very weak in comparison with that obtained in DCM, indicating that the magnitude of the spectra is affected by the rotation of ω_3 , and therefore by the presence of an extra band in the ECD spectra. However, conversely to ECD, ROA is straightforward and is exclusively sensitive to the right sense of the polyacetylene helix.

4. Solvent donor vs solvent polarity effects: poly-3. Finally, to further test the reliability of ROA in the structural elucidation of PPAs, we choose one obtained from the polymerization of the of (R)- α -methoxy- α para-ethynylanilide the trifluoromethylphenylacetic acid as pendant group (poly-3, Figure 6).^[7] This polymer can adopt four different helical structures attending to the donor and polar character of the solvent. Thus, in the case of non-donor solvents a compressed helical structure is generated due to the presence of a major trans conformation for the amide moiety of the anilide group. In these non-donor solvents, the helical sense of the polymer can be tuned by changing the polar character of the solvent. In nonpolar/non-donor solvents, the carbonyl and the methoxy groups of the O=C-C-O moiety adopt a major antiperiplanar (ap) conformation, while in polar/non-donor solvents they adopt a preferred synperiplanar conformation (sp) (Figure 6b).

To carry out our structural studies on poly-**3**, we dissolved the polymer in chloroform —non donor/non-polar— and in a CHCl₃/DMSO mixture (4/1) —non donor/polar—. In these solvents, ECD studies showed the induction of opposite helical senses. Thus, while CHCl₃ induces a negative Cotton effect in the vinylic region and therefore an *M* helical sense of the polyene backbone, a positive Cotton effect is induced in DMSO which corresponds to a *P* right-handed helix (Figure 6c). ROA experiments show also spectra with opposite sign in these two media, indicating the presence of backbones with opposite helical senses (Figure 6d). As expected, the ROA spectra are opposite to the first Cotton effect observed in ECD, which corresponds to the polyene backbone [*P helix*: ECD (+)/ROA (-); *M helix*: ECD (-)/ROA (+)] (Figure 6 c-f).

In donor solvents, poly-**3** adopts a stretched helix due to the presence of a major *cis* conformation for the amide moiety of the anilide group (Figure 7a). Moreover, the helical sense of the polymer can be tuned by changing the polar character of the

solvent. Similar to non-donor media, in low-polar/donor solvents the O=C—C—O moiety adopts a major *antiperiplanar* (*ap*) conformation, while in polar/donor solvents it adopts a preferred *synperiplanar* conformation (*sp*) (Figure 7b).



Figure 6. a) Structure of poly-**3**. b) poly-**3** main conformers in non-donor solvents with low-polar and polar behavior. c) ECD/UV and (d) Raman/ROA spectra of poly-**3** in low-polar (CHCl₃) and polar solvents (CHCl₃/DMSO 4/1 v/v). 3D *cis-cisoidal* structures (n= 24) of poly-**3** with different (e) *M* and (f) *P* helical senses [CHCl₃ and CHCl₃/DMSO (4:1) respectively].

To study this case, UV, ECD, Raman and ROA studies were performed for poly-3 in THF (donor/low-polar) and a 1:1 CHCl3-DMSO mixture (donor/ polar). As expected, ECD spectra show mirror traces indicating the presence of helices with opposite helical senses (Figure 7a-b). Interestingly, in these ECD spectra it is possible to observe the presence of an extra feature around 450 nm which is more intense than the one observed previously in m-poly-2 (Figure 4c). ROA studies of poly-3 in donor solvents show a strong dependence with ω_3 . Thus, the ROA spectra show opposite sign to the first Cotton effect band which corresponds to a ω_3 rotation, and not to the polyene backbone (second Cotton effect at c.a. 380 nm). Intriguingly, the ROA spectra does not show the same pattern than those observed previously. In this particular case, ROA spectra do not show the C-C band at ca. 900 cm⁻¹, being absent in both cases, THF and a 1:1 CHCl₃-DMSO mixture (Figure 7b-c).

In order to remove the ω_3 effect in the ECD spectra, we played with different donor/non-polar mixtures. It was found that when poly-**3** is dissolved in a 1:1 CHCl₃/Dioxane mixture (donor/non-polar), the ECD spectra resemble the one obtained in THF (donor/non-polar) with the absence of the Cotton effect associated to ω_3 (Figure 8). ROA studies of poly-**3** in this solvent

mixture show a ROA trace with the three characteristic peaks of the main chain —*cis*-C—Ph, *cis*-C=C and the C—C— and opposite sign to the ECD band of the polyene backbone — ECD (+) at 380 nm / ROA trace (-)— which corresponds to an *P* helix (Figure 8).

This fact clearly indicates that rotation on ω_3 has a strong effect on the ECD and ROA spectra. In the ECD spectrum a new Cotton effect band is generated at higher wavelengths which makes difficult to assign the helical sense of the PPA. On the other hand, ROA shows a trace with the absence of the C—C band, indicating that the associated Cotton effect is not related to the helical sense of the main chain.



Figure 7. (a) Poly-3 main conformers in non-donor solvents with low-polar and polar parameters. (b) ECD/UV and (c) Raman/ROA spectra of poly-3 in donor-polar (CHCl₃/DMSO) and donor-low polar solvents (THF) (top and bottom spectra respectively). 3D *cis-transoidal* structures (n= 16) of poly-3 in (d) THF and (e) CHCl3/DMSO (1:1).



Figure 8. a) ECD spectra of poly-**3** in donor/non-polar solvents showing either four (THF) or three (CHCl₃/Dioxane) alternating Cotton effects. ROA spectrum of poly-**3** in (b) THF and (c) a CHCl₃/Dioxane mixture.

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Figure 9. ROA spectrum of a PPA with (a) a *P* helix without ω_3 interference, (b) an *M* helix without ω_3 interference, (c) a *P* helix with ω_3 interference, (d) an *M* helix with ω_3 interference

Conclusion

In conclusion, it was demonstrated through a good number of examples -4 polymers, 10 helical structures- that ROA is a powerful structural technique, which can be used in the helical sense assignment of PPAs. During these studies it was found that a ROA spectrum, working under resonance conditions, shows the three characteristic vibrational bands of the polyene backbone associated stretching modes of the cis-C-Ph, cis-C=C and C-C moieties, which can be correlated with the helical sense of the main chain attending to sign of the spectrum positive ROA/M_{helix}; negative ROA/P_{helix}— (Figure 9a-b). Moreover, it was also found that some PPAs produce in certain solvent conditions a ROA spectrum that lack the C-C band. This ROA spectrum is related to a rotation around the ω_3 and not to the polyene backbone which produces also an extra Cotton band in the ECD spectrum. In this case, the lack of the C-C band in the ROA spectrum is an alert sign which indicates that neither the ROA nor ECD -first Cotton band- are indicating the correct helical sense of the polymer (Figure 9c-d). To do a correct helical sense assignment in these cases it is necessary to look for a solvent where the three characteristic peaks of the polyene backbone appear in the ROA spectra.

Thus, the robustness of ROA in the helical sense elucidation of PPAs and its potential application in other families of helical polymers —with or without chromophores—has been clearly demonstrated along these studies.

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- [1] F. Freire, E. Quiñoá, R. Riguera, Chem. Commun., 2017, 53, 481-492.
- [2] F. Freire, E. Quiñoá, R. Riguera, Chem. Rev., 2016, 116, 1242-1271.
- [3] E. Yashima, N. Ousaka, D. Taura, K. Shimomura, T. Ikai, K. Maeda, *Chem. Rev.*, **2016**, *116*, 13752-13990.
- [4] E. Yashima, K. Maeda, H. Lida, Y. Furusho, K. Nagai, *Chem. Rev.* 2009, 109, 6102-6211.
- [5] J. Liu, J. W. Y. Lam, B. Z. Tang, B. Z. Chem. Rev. 2009, 109, 5799-5867.
- [6] R. Rodrígez, E. Quiñoá, R. Riguera, F. Freire, J. Am. Chem. Soc., 2016, 138, 9620-9628.
- S. Leiras, F. Freire, J. M. Seco, E. Quiñoá, R. Riguera, *Chem. Sci.* 2013, 4, 2735–2743.
- [8] C. I. Simionescu, V. Percec, S. Dumitrescu, J. Polym. Sci. Polym. Chem. Ed. 1977, 15, 2497-2509.
- [9] K. Nagai, K. Sakajiri, K. Maeda, K. Okoshi, T. Sato, E. Yashima, *Macromolecules* **2006**, *39*, 5371-5380.
- [10] M. Morimoto, K. Tamura, K. Nagai, E. Yashima, J. Polym. Sci., Part A: Polym. Chem. 2010, 48, 1383-1390.
- [11] T. Fukushima, H. Kimura, K. Tsuchihara, *Macromolecules* **2009**, *42*, 8619-8626.
- [12] K. Okoshi, T. Kajitani, K. Nagai, E. Yashima, *Macromolecules* 2008, 41, 258-261
- [13] Y. Mawatari, M. Tabata, T. Sone, K. Ito, Y. Sadahiro, *Macromolecules* 2001, 34, 3776-3782.
- [14] A. Motoshige, Y. Mawatari, R. Motoshige, Y. Yoshida, M. Tabata, J. Polym. Sci., Part A: Polym. Chem. 2013, 51, 5177-5183.
- [15] R. Motoshige, Y. Mawatari, A. Motoshige, Y. Yoshida, T. Sasaki, H. Yoshimizu, T. Suzuki, Y. Tsujita, M. Tabata, J. Polym. Sci., Part A: Polym. Chem. 2014, 52, 752-759.
- [16] V. Percec, J. G. Rudick, M. Peterca, M. Wagner, M. Obata, C. M. Mitchell, W-D. Cho, J. Am. Chem. Soc. 2005, 127, 15257-15264.
- [17] V. Percec, M. Peterca, J. G. Rudick, E. Aqad, M. R. Imam, P. A. Heiney, *Chem. Eur. J.* 2007, 13, 9572-9581.
- [18] V. Percec, E. Aqad, M. Peterca, J. G. Rudick, L. Lemon, J. C. Ronda, B. B. De, P. A. Heiney, E. W. Meijer, *J. Am. Chem. Soc.* 2006, *128*, 16365-16372.
- [19] V. Percec, J. G. Rudick, M. Peterca, E. Aqad, M. R. Imam, P. A. Heiney, J. Polym. Sci., Part A: Polym. Chem. 2007, 45, 4974-4987.
- [20] S. Sakurai, K. Okoshi, J. Kumaki, E. Yashima, E. J. Am. Chem. Soc. 2006, 128, 5650-5651.
- [21] S. Sakurai, K. Okoshi, J. Kumaki, E. Yashima, Angew. Chem. Int. Ed. 2006, 45, 1245-1248.
- [22] T. Nishimura, K. Takatani, S. Sakurai, K. Maeda, E. Yashima, Angew. Chem. Int. Ed. 2002, 41, 3602-3604.
- [23] S. Sakurai, A. Ohira, Y. Suzuki, R. Fujito, T. Nishimura, M. Kunitake, E. Yashima, J. Polym. Sci. Part A: Polym. Chem. 2009, 47, 4621-4640.
- [24] K. Okoshi, S. Sakurai, S. Ohsawa, J. Kumaki, E. Yashima, Angew. Chem. Int. Ed. 2006, 45, 8173-8176.
- [25] S. Sakurai, S. Ohsawa, N. Kanji, K. Okoshi, J. Kumaki, E. Yashima, Angew. Chem. Int. Ed. 2007, 46, 7605-7608.
- [26] S. Ohsawa, S. Sakurai, K. Nagai, M. Banno, K. Maeda, J. Kumaki, E. Yashima, J. Am. Chem. Soc. 2011, 133, 108-114.
- [27] S. Ohsawa, S. Sakurai, K. Nagai, K. Maeda, J. Kumaki, E. Yashima, *Polym. J.* **2012**, *44*, 42-50.
- [28] R. Rodríguez, S. Arias, E. Quiñoá, R. Riguera, F. Freire, *Nanoscale*, 2017, 9, 17752-17757
- [29] L. Liu, T. Namikoshi, Y. Zang, T. Aoki, Sh. Hadano, Y. Abe, I. Wasuzu, T. Tsutsuba, M. Teraguchi, T. Kaneko, J. Am. Chem. Soc., 2013, 135, 602-605.
- [30] B. Nieto-Ortega, R. Rodríguez, S. Medina, E. Quiñoá, R. Riguera, J. Casado, F. Freire, J. Ramírez, J. Phys. Chem. Lett. 2018, 9, 2266–2270.
- Y. Hase, K. Nagai, H. Iida, K. Maeda, N. Ochi, K. Sawabe, K. Sakajiri,
 K. Okoshi, E. Yashima, *J. Am. Chem. Soc.* **2009**, *131*, 10719-10732.
- [32] T. Kawauchi, J. Kumaki, A. Kitaura, K. Okoshi, H. Kusanagi, K. Kobayashi, T. Sugai, H. Shinohara, E. Yashima. *Angew. Chem. Int. Ed.* 2008, 47, 515-519.
- [33] H. Z. Tang, B. M. Novak, J. Polavarapu, P. L. He, Angew. Chem. Int. Ed. 2005, 44, 7298-7301.

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- [34] Y. Suzuki, J. Tabei, M. Shiotsuki, Y. Inai, F. Sanda, T. Masuda, *Macromolecules* **2008**, *41*, 1086-1093.
- [35] B. Fernández, R. Rodríguez, A. Rizzo, E. Quiñoá, R. Riguera, F. Freire, Angew. Chem., Int. Ed. 2018, 57, 3666-3670.
- [36] B. Fernández, R. Rodríguez, E. Quiñoá, R. Riguera, F. Freire, ACS Omega, 2019, 4, 5233-5240.
- [37] P. W. Atkins, L. D. Barron, Mol. Phys., 1969, 16, 453-466.
- [38] L. D. Barron, A. D. Buckingham, Mol. Phys., 1971, 20, 1111-1119.
- [39] L. A. Nafie, in Vibrational Optical Activity, Principles and Applications, John Wiley and Sons, Chichester, UK, 2011, pp. 133-137.
- [40] L. A. Nafie, Chem. Phys. 1996, 205, 309-322.
- [41] M. Vargek, T. B. Freedman, E Lee, L. A. Nafie, Chem. Phys. Lett. 1998, 287, 359-364
- [42] S. Luber, J. Neugebauer, M. Reiher, Chem. Phys. 2010, 132, 044113.
- [43] L. A. Nafie, Theor. Chem. Acc. 2008, 119, 39-55.
- [44] G. Li, J. Kessler, J. Cheramy, T. Wu, M. R. Poopari, P. Bouř, Y. Xu, Angew. Chem. Int. Ed. 2019, 58, 16495-16498.
- [45] M. G. Lizio, V. Andrushchenko, S. J. Pike, A. D. Peters, G. F. S. Whitehead, I. J. Vitórica-Yrezábal, S. T. Mutter, J. Clayden, P. Bouř, E. W. Blanch, S. J. Webb, *Chem. Eur. J.* **2018**, *24*, 9399-9408.
- [46] C. Mensch, C. Johannessen, ChemPhysChem, 2018, 19, 3134-3143.
- [47] M. Alzubi, S. Arias, R. Rodríguez, E. Quiñoá, R. Riguera, F. Freire, Angew. Chem. Int. Ed. 2019, 58, 13365-13369.
- [48] K. Cobos, E. Quiñoa, R. Riguera, F. Freire, J. Am. Chem. Soc. 2018, 140, 12239-12246.
- [49] S. Arias, F. Freire, M. Calderón, J. Bergueiro, Angew. Chem. Int. Ed., 2017, 56, 11420-11425.
- [50] R. Rodríguez, E. Quiñoá, R. Riguera, F. Freire, Small, 2019, 15, 1970070.
- [51] S. Arias, M. Núñez-Martínez, E. Quiñoá, R. Riguera, F. Freire, *Polym. Chem.*, 2017, 8, 3740-3745.
- [52] V. Percec, J. G. Rudick, M. Peterca, P. A. Heiney, J. Am. Chem. Soc. 2008, 130, 7503-7508.
- [53] V. Percec, M. Obata, J. G. Rudick, B. B, De, M. Glodde, T. K. Bera, S. N. Magonov, V. S. K. Balagurusamy, P. A. Heiney, J. Poly. Sci. A Polym. Chem, 2002, 40, 3509-3533.
- [54] M. J. Frisch, et al. Gaussian 09, Revision C.01, Gausian, INc. Wallingford CT, 2010.
- [55] A. D. Becke, J. Chem. Phys., 1993, 98, 5648-5652.
- [56] C. Lee, W. Yang, R. G. Parr, Phys. Rev. B, 1988, 37, 785-789.
- [57] Y. Tawada, T. Tsuneda, S. Yanagisawa, T. Yanai, K. Hirao, J. Chem. Phys, 2004, 120, 8425-8433.
- [58] P. C. Hariharan, J. A. Pople, Theor. Chim. Acta, 1973, 28, 213-222.
- [59] A. P. Scott, L. Radom, J. Phys. Chem. 1996, 100, 16502-16513.
- [60] E. Runge, E. K. U. Gross, *Phys. Rev. Lett.* **1984**, 52, 997-1000.
- [61] E. K. U. Gross, W. Kohn, Adv. Quant. Chem. 1990, 21, 255-294.
- [62] E. J. Heller, Y. Yang, L. Kocia, ACS Cent. Sci. 2015, 1, 40-49.
- [63] M. Alzubi, S. Arias, E. Quiñoá, R. Riguera, F. Freire, Chem. Commun., 2017, 53, 8573-8576

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