The Role of Chlorine position in the Electronic Circular Dichroism of Chlorophenyl-Ethanol Investigated by Vibronic Calculations

Daniel Aranda,[a,b] and Fabrizio Santoro*[a]

Abstract: (R)-1-phenyl-ethanol (PhEtOH) and the different isomers of (R)-1-(chlorophenyl)ethanol (ClPhEtOH) exhibit very interesting electronic circular dichroism (ECD) in methanol. In all cases, the spectrum shows clear vibronic features but it is monosignated and negative for PhEtOH and meta-ClPhEtOH, positive for the ortho isomer and bisignated for the para isomer. We used computational chemistry to rationalize this behavior adopting CAM-B3LYP/def2-TZVP, describing the bulk solvent effects with polarizable continuum models and solute-solvent specific interactions with clusters comprising the solute and two solvent molecules. We adopted harmonic vibronic models to compute the ECD spectral shapes of all stable conformers and we obtained the room-temperature spectra by Boltzmann average. Simulated spectra are in very good agreement with experiment and allow us to rationalize their difference in terms of the relevance of Franck-Condon (FC) and Herzberg-Teller (HT) intensity-borrowing contributions, modulated by the substituent effect. The bisignated shape of the spectrum of para-ClPhEtOH arises from the competition of opposite-sign FC and HT bands, promoted by different vibrational modes. Due to the challenges we document in computing its ECD spectrum, para-ClPhEtOH represents a good test-case to help the development of novel methodologies for an improved description of weak vibronic ECD spectra of flexible systems in explicit solvents.

Keywords: Lb benzene transition, Franck Condon and Herzberg Teller mechanisms, vertical harmonic models with Duschinsky mixings, assignment of the main vibronic progressions, effect of soft modes, specific solute-solvent interactions

Introduction

The electronic circular dichroism (ECD) spectra of many organic molecules, especially in low polarity solvents, are characterized by clear vibronic progressions. They carry information on the molecule and electronic states involved in the transition. For weak electronic transitions, vibrations can trigger intensity-borrowing from close strongly-absorbing states, leading to ECD spectra that exhibit a typical “forbidden” character with alternating signs.[1] The ECD response of the ^1L_b transition of chiral benzene derivatives falls into this category. Its interpretation has been traditionally faced with simplified approaches as the sector and benzene chirality rules.[2,3] Semiempirical rules have actually allowed great progress in the ECD community and here we mention also those developed by Harada and Nakanishi, like the benzoate[4] and dibenzoate sector rules. [5] The latter was afterwards renamed “exciton chirality rule”[6] and has been extensively used to characterise the absolute configuration of natural products.[7-17]

Notwithstanding the utility of these rules, in principle, a vibronic analysis is required to get a robust interpretation of weak ECD spectra with alternating signs, and use them for assigning absolute configurations. Actually, recent progress in computational methods have made the computation of vibronically resolved electronic spectra rather standard.[18,19] These methods also provide the possibility to address the ECD of forbidden transitions, in the limit where the electronic states couplings, responsible for the intensity borrowing, are weak and the energies of the coupled states are separated enough to allow the description of their effect within first-order perturbation theory (Herzberg-Teller, HT, mechanism). The most popular available techniques are suitable for rigid systems, i.e. molecules whose potential energy surfaces can be adequately described within the harmonic approximation. By definition, molecules with chiral centres do not fall in this category since the tetrahedral carbon forms four single bonds, characterized by easy rotations. However, a rather straightforward generalization for these cases is possible when the electronic-density changes due to the transition mainly involves the rigid moiety of the molecule (e.g. the benzene ring). First, the ECD spectrum is computed for each stable conformer, characterized by different rotations of the flexible torsions around the stereogenic centre. Second, its Boltzmann average is calculated. Few years ago[20] we showed that this approach can shed light on the ECD shapes of the ^1L_b band of phenylethanes substituted in position 1 with different alkyl groups, in hexane or heptane.

(R)-1-Phenyl-ethanol (PhEtOH) and the family of ortho- (o-) meta- (m-) and para- (p-) (R)-1-(chlorophenyl)ethanol (ClPhEtOH) molecules (Scheme 1) are characterized by very interesting ECD spectra in methanol, in the region of the ^1L_b benzene transition (see Figure 1).[21,22] PhEtOH and the o- and m-ClPhEtOH exhibit a monosignated spectrum with very clear

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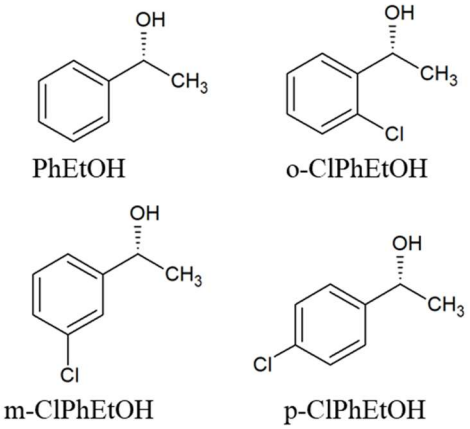
vibronic progressions and an overall sign depending on the chlorine position, whereas p-ClPhEtOH has a bisignated ECD with two weak positive peaks at low energy, followed by a number of negative ones at higher energies. Each of these compounds is characterized by three flexible dihedrals, namely, the rotation of the phenyl (θ_{Ph}), the OH (θ_{OH}) and the methyl (θ_{Me}) groups (Figure 2) which are expected to have a remarkable impact on the ECD response.



SCHEME 1. Molecular structures of the systems studied in this work: (1) PhEtOH, (2) o-ClPhEtOH, (3) m-ClPhEtOH, and (4) p-ClPhEtOH.

Conformational search is not always an easy task, and it can become very complicated in molecules like PhEtOH. In fact, the quaternary carbon brings a polar -OH able to establish specific and potentially strong interaction with one or several molecules of polar solvents. Such interactions could alter the conformational populations and even the ECD response of each single conformer and, therefore, its thermal average. A full description of the possible conformational diversity in these cases can only be obtained with long-enough Molecular Dynamics (MD) trajectories using reliable force fields. However classical MD reveals not adequate when, like in our case, vibronic peaks need to be described, since they arise from the quantum nature of molecular vibrations. In addition, investigating the ECD of chiral anthryl-ethanol we recently showed[23,24] that, in principle, when the potential energy surface (PES) separating the different conformers is rather flat, even off-equilibrium structures can modulate the ECD signal.

A full account of all these possible effects is not yet at hand with available methodologies. It may become possible in the near future with novel methodologies. Among those, we recently proposed a method we named the Adiabatic MD generalized Vertical Hessian (Ad-MD|gVH) that combines MD and vibronic models,[25] but extensions are needed to include HT transitions and how they are modulated by solute-solvent interactions.

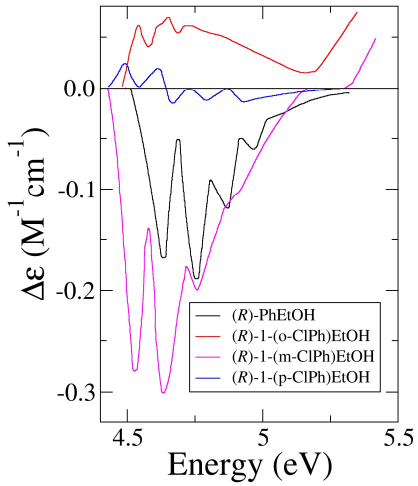


FIGURE 1. Experimental ECD spectra of (R)-1-phenylethanol (PhEtOH) and the (R)-1-(chlorophenyl)ethanol compounds reproduced from references 21 and 22.

As a necessary intermediate step for this further development, in this contribution we investigate to what extent it is possible to simulate and interpret the ECD of 1-(chlorophenyl)-ethanol series by applying the standard vibronic approach. As mentioned above, it obtains the spectrum from the Boltzmann average of the independent contributions of the different stable conformers. Solvent effects will be mimicked either with a polarizable continuum or adopting small clusters embedded in a polarizable continuum. We show that, despite its approximations, this approach provides a good agreement with experiment for all the 4 investigated species. This allows us a detailed analysis of the role of the chlorine position in determining the sign, intensity and shape of the ECD response, and a critical comparison with the predictions of qualitative sector and benzene-chirality rules.[2,3] On the other side, especially for the most challenging p-ClPhEtOH, we critically highlight that the ECD results depend on a delicate balance of the internal flexibility, how it is modulated by specific solute-solvent interactions, and even by the solvent dynamical effects. Therefore, we propose para-ClPhEtOH as a very interesting case to test new methodologies.

Materials and Methods

Electronic structure calculations were performed adopting the Gaussian16 package of programs[26] with CAM-B3LYP/Def2-TZVP[27-29] since previous studies on similar systems and using a similar level of theory provided very good agreement with the experiments.[20,23,24,30,31] Solvent effects were included with the Polarizable Continuum Model (PCM).[32] As a standard choice, for computational convenience we used the equilibrium solvation (EqSolv) regime for which analytical Hessians are available. However, for some specific cases, spectra were also computed numerically with the non-equilibrium solvation (NonEqSolv) regime. Comparison between the two regimes allows us to investigate possible dynamical solvent effects.

ECD vibronic spectra were computed at room temperature with the FCclasses 3 code[33-38] in the harmonic approximation, adopting the Vertical Hessian (VH) model in curvilinear internal coordinates.[35] In VH both the ground and excited state potential energy surfaces (PES) are quadratically expanded at the

equilibrium geometry of the initial state of the transition (the ground state).[36] We included both Franck-Condon (FC) and HT contributions, computing the transition dipoles derivatives at the ground-state equilibrium geometry (HTi formalism).[33,37]
HT effects contribute with new terms to the spectrum intensity. It is therefore useful to define a generalized rotatory strength R^{FCHT} that corresponds to the integrated intensity of the spectrum. R^{FCHT} is the sum of the standard FC contribution (R^{FC}) and a HT contribution (R^{HT}),[39]

$$R^{FCHT} = R^{FC} + R^{HT} = \mathrm{Im}\left[\vec{\mu}_0 \cdot \vec{m}_0\right] + \sum_\alpha \frac{\hbar \cot(\beta\hbar\omega_\alpha)}{2\omega_\alpha} \mathrm{Im}\left[\left(\frac{\partial \vec{\mu}}{\partial Q_\alpha}\right)_0 \left(\frac{\partial \vec{m}}{\partial Q_\alpha}\right)_0\right] \quad (1)$$

Here, $\vec{\mu}$ and $\vec{m}$ are respectively the electric and magnetic transition dipole moments between the ground and excited electronic states (integrated over the electronic coordinates), the subscript 0 indicates that values are taken at the ground-state equilibrium geometry, $\beta = 1/K_B T$, T is the temperature and K_B the Boltzmann constant. R^{HT} is a sum of contributions over the ground-state normal coordinates Q_α , whose strength and sign depend on the derivatives of $\vec{\mu}$ and $\vec{m}$ with respect to Q_α , on its frequency ω_α , and on its average quantum number .

For obtaining fully-converged vibronic spectra we used the time-dependent formalism described in ref.[37] whereas for the assignment of the main vibronic bands we employed the time-independent pre-screening method reported in ref.[33,34] For clusters of the solute + 2 methanol molecules, the harmonic PES were generated using energy gradients and Hessians of the whole cluster in PCM and projecting out the solvent degrees of freedom as we did in ref. 25. This approach allows us to obtain normal coordinates that involve only the solute degrees of freedom but, at the same time, “feel” the electronic effects due to existence of the explicit solvent molecules. The Cartesian coordinates of all the ground state optimised structures are given in the Supporting Information (SI).

Results and Discussion

1. DIFFERENT CONFORMERS IN GAS PHASE AND SOLUTION WITH PCM

1.1. Conformational analysis.

We consider here R enantiomers of PhEtOH and their monochloro-derivatives. Stable conformers can exist for different values of the three dihedrals θ_{Ph}, θ_{OH} and θ_{Me}. In ref. 30, a conformational search of PhEtOH in gas phase was performed by exploring the PES along all the three flexible dihedrals. Five different stable conformers (M01-M05) were located at CAM-B3LYP/TZVP level of theory. Here, those conformers were used as starting geometries and re-optimised in gas phase using CAM-B3LYP in combination with the basis set def2-TZVP. We chose this larger basis set because it was shown to improve the comparison with experiment of the ECD of diphenyl-methanols.[31]
The stable minima we obtained are shown in Figure 2 together with the values of θ_{Ph} and θ_{OH}; θ_{Me} was omitted because its effect is less relevant.[30] At this level of theory, only four different conformers were found, since the optimization of M03 collapses into the M05 minimum. This suggests that the energetic barrier between the two conformers with the TZVP basis set is very shallow so that it may disappear as a result of small changes of the computational settings.
To account for the bulk solvent effects, the initial conformers of PhEtOH were optimised also in methanol by using the PCM model. In the following we refer to these calculations with the label “PCM-only”. For the different isomers of ClPhEtOH, we assumed that the effect of the chlorine atom is only to distort the minima found for PhEtOH. However, we accounted for the possibility that M03 and M05 give rise to different stable conformers. In practice for p-ClPhEtOH five optimizations were performed after replacing the corresponding aromatic hydrogen by Cl. At variance, since in the phenyl ring there are two distinguished ortho and meta positions, for o-ClPhEtOH and m-ClPhEtOH 10 different initial structures were considered. They were obtained by placing the chlorine atom on the same molecular side of either H1 (Figure 2) or OH (conformers 1-5 and 6-10 respectively, see Figure S1 in SI for an example).
Tables 1-4 report the values of the flexible dihedrals for all the stable structures of PhEtOH, o-, m- and p-ClPhEtOH and their Boltzmann populations computed from the free energy at 25ºC. For all the molecules, both in gas phase and PCM, the most stable conformer is M01 type (θ_{OH} ~ -60º and θ_{Ph} ~ -23º). This θ_{Ph} value is coherent with a general criterion for substituted benzenes. It states that, if there is only one benzylic hydrogen atom, the preferred conformation tends to be one on which the aromatic ring and the hydrogen are eclipsed or almost eclipsed.[2] M01 conformers represent about 70% of the total population in gas phase and ~60% in PCM (considering that for o-ClPhEtOH and m-ClPhEtOH conformers 1 and 6 are both M01-type). Despite the major role of M01, it is important to notice that the four molecules have 3-4 (6-8 for o-ClPhEtOH and m- ClPhEtOH) different conformers that are populated at room temperature and contribute to the spectrum.
For the sake of simplicity, since now on we introduce a shorter notation where p- m- and o-M0X (X=1,5) represent the M0X conformer of p-, m- and o-ClPhEtOH respectively. As expected, the chlorine atom has an important steric effect for o-ClPhEtOH: all the conformers where the Cl is close to the OH group, i.e. o-M06 to o-M10, are barely populated. This effect vanishes for m-ClPhEtOH in gas phase and, in fact, equivalent conformers up to a rotation of the aromatic ring (i.e., M0X and M0(X+5)), are equally populated. Such a symmetry is broken in methanol (PCM), because the isomers with both chlorine and hydroxyl groups on the same side have larger electric dipoles and therefore are more stable. Finally, p-M0X conformers closely resemble the ones found for PhEtOH. This is particularly true for θ_{OH} and θ_{Ph} values of M01, M02 and M04, both in gas phase and with PCM-only model. Nevertheless, some differences can be ascribed to the presence of the Cl atom. First, in the gas phase, p-M03 (θ_{OH} = -176º, θ_{Ph} = 72º) of ClPhEtOH is a stable conformer. Second, the populations of M01, M02 and M04 type of conformers change remarkably from PhEtOH to p-ClPhEtOH. This indicates that the long-range electronic effect of the Cl atom is not fully negligible.

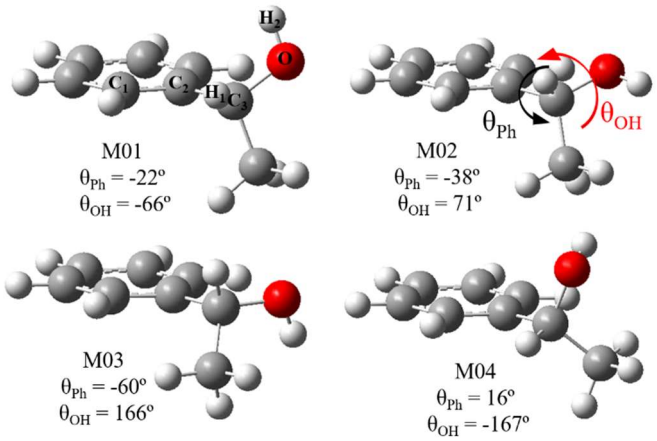


FIGURE 2. PhEtOH stable conformers in gas phase for different values of the dihedral angles θ_{Ph} (defined as C1-C2-C3-H1, i.e., rotation along C2-C3 bond) and θ_{OH} (defined as H2-O-C3-H1, i.e., rotation along O-C3 bond).

1.2. ECD vibronic spectra with the PCM-only model.

1.2.1. Spectra within equilibrium solvation regime.

In first place we analyse the results obtained in the equilibrium solvation regime (EqSolv). Figure 3 compares the FCHT Boltzmann-weighted vibronic spectra for the four molecules, with the experimental results digitalized from refs. 21 and 22. The computed spectra are in good agreement for PhEtOH, o-ClPhEtOH and m-ClPhEtOH. In fact, their signs and shapes, i.e. the pattern of the vibronic progressions, are overall nicely reproduced, in particular for o-ClPhEtOH. The position of the spectra is blue-shifted by ~0.55-0.60 eV. An overestimation of the vertical excitations is expected for CAM-B3LYP and these values are in line with what already published for α-alkyl-phenylethanes[20] and for PhEtOH.[30] Table S1 in the SI shows that extension of the basis set up to aug-cc-pVTZ decreases the computed vertical excitation by only 0.02-0.03 eV. At variance, adopting B3LYP the vertical excitation is red-shifted by 0.12-0.18 eV. As we show below, HT contributions are very important for the investigated spectra. They depend on the mixing with higher excited states which can have different characters. Since CAM-B3LYP is known to give a more balanced description of different kind of excited states we selected this functional for our study.

Some discrepancies appear when considering finer details of the spectra like the relative intensities of the first and second vibronic peaks of PhEtOH and m-ClPhEtOH but, on the balance, the results are satisfactory. On the other hand, the computations for p-ClPhEtOH fail to reproduce the observed bisignated progression and predict, instead, an almost unstructured negative band. To rationalize these results it is necessary to analyse the spectra of the individual conformers reported in the SI (Figures S2-S5, EqSolv panels).

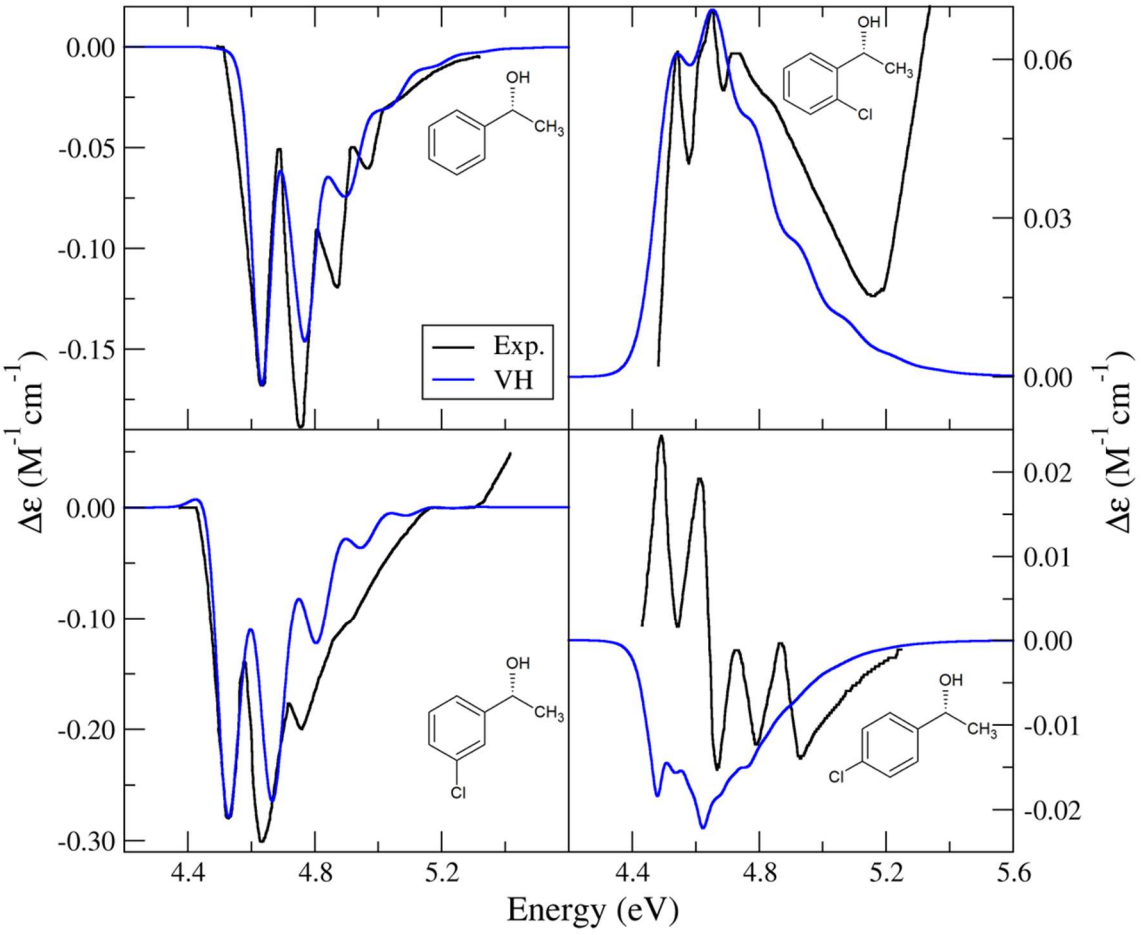


FIGURE 3. Calculated and experimental ECD spectra of the R enantiomers of PhEtOH (top left), o-ClPhEtOH (top right), m-ClPhEtOH (bottom left) and p-ClPhEtOH (bottom right) in methanol. The experimental results were reproduced from references 21 and 22. The VH spectra were computed with the PCM-only model, scaled by a factor of 0.46, 0.48, 0.75 and 0.05, and shifted by -0.596, -0.565, -0.584 and -0.550 eV, respectively. A half-width at half maximum of 0.03 eV for all the systems.

All the relevant conformers of PhEtOH (Table 1) and m-ClPhEtOH (Table 3) at room temperature have a negative rotatory strength and vibronic spectra similar to the experimental one. o-ClPhEtOH exhibits conformers with positive and negative rotatory strength of the same intensity but, interestingly, those with negative rotatory strength correspond to structures that are not populated at room temperature. Therefore, after Boltzmann averaging, the spectrum is positive.

For p-ClPhEtOH, all the conformers have negative rotatory strength, and the most populated are p-M01 (56% weight) and p-M02 (32% weight). The former has an unstructured shape. This is due to a long progression of mode ν_1 which has a low frequency (~30 cm^{-1}) and a large dimensionless shift $|\Delta_1|$ ~ 2.4. It corresponds to the rotation of the 1-hydroxyethyl group with respect to the aromatic ring, i.e., a change of θ_{Ph} angle (see Figure S6). Additionally, ν_1 displays large transition dipole derivatives for both p-M01 and p-M02 and therefore it is strongly involved in the HT intensity-borrowing mechanism.

Hindered rotations are, by definition, strongly anharmonic and their description with harmonic models, even if built up with curvilinear internal coordinates, can give rise to artefacts.

1.2.2. Reduced-dimensionality vibronic spectra.

To investigate in further detail the effect of this anharmonic vibration, we computed the ECD spectrum of all the conformers of p-ClPhEtOH using a reduced dimensionality model where θ_{Ph} (and therefore ν_1) is projected out from the vibrational space. To that end, we used the novel procedure available in FCclasses 3 and presented in ref. 25. Figure 4 shows the ECD spectra in reduced dimensions. For the EqSolv model, p-M01 and p-M02 spectral shape remarkably changes with respect to the full dimension results. In particular, neglecting ν_1 , p-M01 shows a spectrum which resembles the experimental spectrum in the lowest energy region. At variance, p-M02 intensity remarkably decreases and its shape loses its well-defined structure. Finally, p-M04 spectrum is almost unaffected except for a small change of the intensity.

The averaged spectrum is very different from the one obtained in full-dimensions: it is bisignated and somewhat similar to the experimental one. These drastic differences and the improved agreement with experiment strongly suggest that the contribution of the floppy mode ν_1 is not correctly treated in the harmonic approximation.

1.2.3. Solvent dynamical effects on ECD vibronic spectra.

In this section we investigate if the predictions of the spectra depend on solvent dynamical effects. To that end we computed the NonEqSolv spectra of all the conformers of the four molecules and compared them with the EqSolv ones. The spectra of PhEtOH, o-ClPhEtOH and m-ClPhEtOH are similar and, in some cases, they even improve the good agreement with experiment already achieved with EqSolv. They are reported in Figures S2-S4 in SI, while here we focus on the more challenging p-ClPhEtOH.

NonEqSolv spectra of p-M01 and p-M02 (Figure 4, bottom left panel) are bisignated and dramatically different from the ones obtained with EqSolv (see Figure S5 for a more direct comparison). In particular, p-M01 spectrum nicely matches with the behaviour observed in the experiments. However, because of the much larger intensity, p-M02 conformer dominates the spectral shape in the low energy region. Therefore, after Boltzmann average, we obtain a spectrum totally negative.

In Figure 4 we report also the NonEqSolv spectra obtained after projecting out the ν_1 mode. As observed in the EqSolv results, this procedure leads to large changes for p-M01 and p-M02, whereas p-M04 spectrum remains almost unaltered, except for the intensity. The most remarkable effect on the spectral shapes of p-M01 and p-M02 is that they both become monosignated and positive. This is due to the fact that, as previously highlighted, ν_1 mode largely contributes to the HT term of the rotatory strength.

The largest dependence of the p-ClPhEtOH on the details of the computational model is mainly related to its weak rotatory strength and the consequentially strong HT effects. In this situation, the experimental spectral shape is expected to arise from a delicate balance of many factors. It is realistic to imagine that such balance can be further altered by specific solute solvent interactions. In order to qualitatively investigate their possible effect, in the following section we consider clusters made up by the system and two explicit methanol molecules.

2. CLUSTER MODELS WITH EXPLICIT SOLVENT MOLECULES

A complete description of specific solute-solvent interactions on the ECD spectral shape requires a combination of MD simulations, using accurate force fields, and methods for the computation of vibronical spectra. As a necessary preliminary step for these more sophisticated approaches, here we decided to study clusters of the investigated PhEtOH derivatives with two methanol molecules, which act respectively as a hydrogen donor or an acceptor in H-bonds with the OH group of the dye. First, the effect of the explicit solvent molecules on the relative stabilities of the conformers will be analysed and afterwards the ECD spectra will be presented.

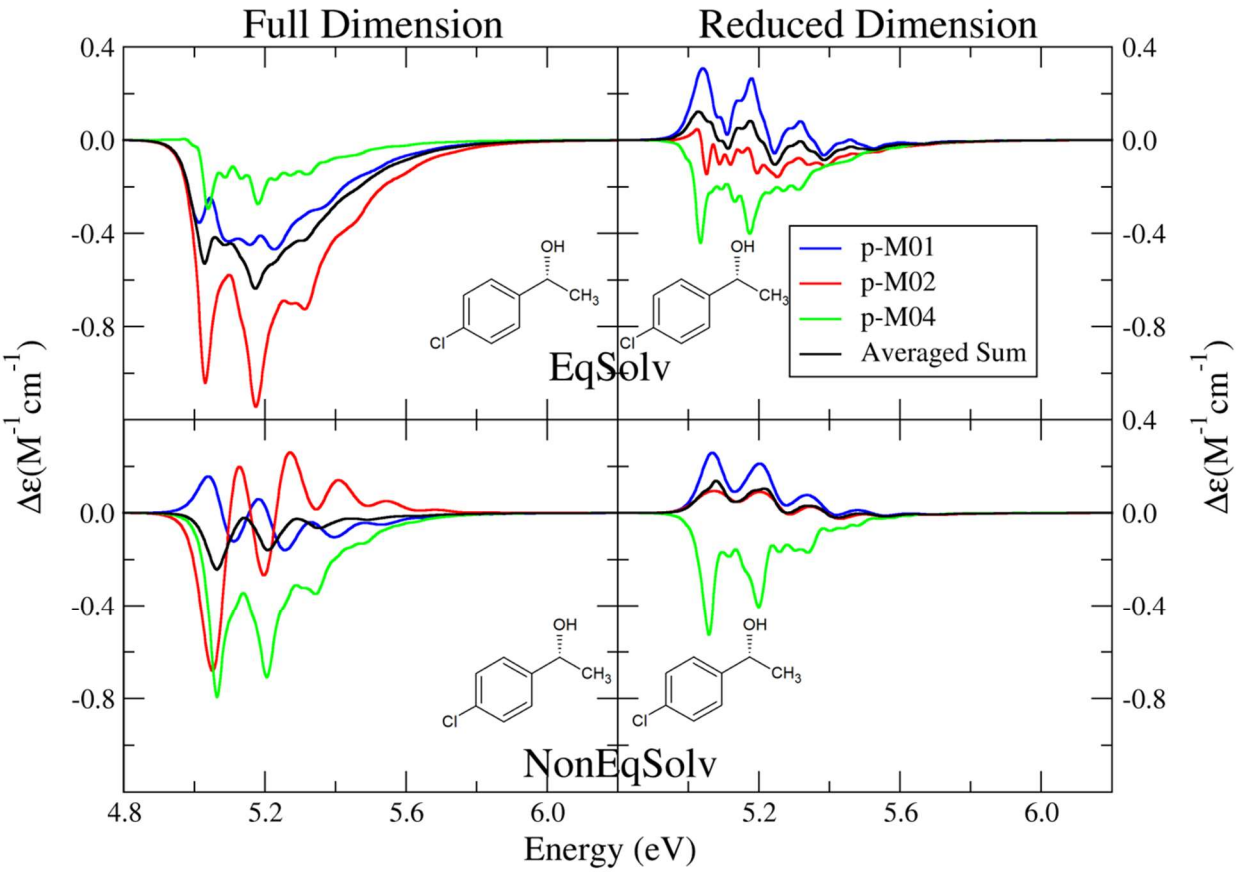


Figure 4. Full (left) and reduced (right) dimensionality ECD spectra (not including Boltzmann weights) of the R enantiomers of p-ClPhEtOH, i.e. p-M0X (X=1,2,4) conformers, and their averaged sum (black) computed with the PCM-only model and EqSolv (top) and NonEqSolv solvation (bottom) regimes. The spectra were convoluted with a Gaussian function of half-width at half maximum of 0.03 eV at T=298.15K.

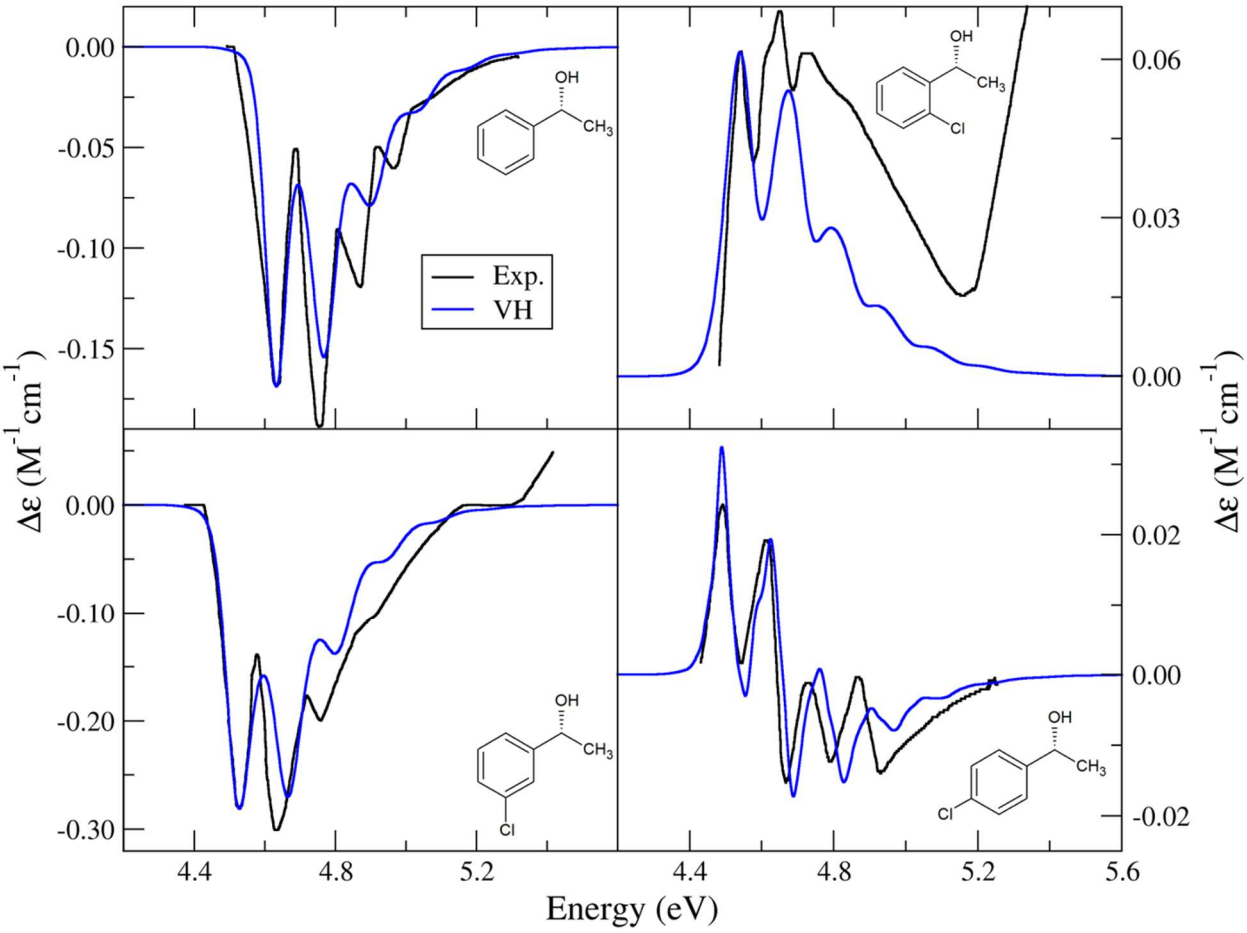


FIGURE 5. Calculated (cluster with 2 explicit solvent molecules in PCM) and experimental ECD spectra of the R enantiomers of PhEtOH (top left), o-ClPhEtOH (top right), m-ClPhEtOH (bottom left) and p-ClPhEtOH (bottom right). The experimental results were reproduced from references 21 and 22. The computed spectra were scaled (multiplied) by a factor of 0.30, 0.23, 0.57 and 0.16, and shifted by -0.605, -0.569, -0.576 and -0.560 eV, respectively. A half-width at half maximum of 0.03 eV was used for all the systems except for p-ClPhEtOH (0.01 eV).

2.1. Effect of the explicit solvent molecules on the conformational analysis.

In the exploratory spirit of the present analysis we simplified the challenging conformational search by simply assuming that the conformational space can be acceptably spanned by (i) starting from the same initial geometries (5 for PhEtOH and p-PhEtOH and 10 for m- and o-ClPhEtOH) considered without explicit solvent molecules, (ii) adding two methanol molecules according to chemical intuition and (iii) performing new geometry optimizations. The results are shown in Tables 1-4 and compared with those obtained with PCM-only model. The molecular structures of some of the clusters are shown in Figure S12 in the SI.

Inspection of θ_{OH} and θ_{Ph} values (Tables 1-4) indicate that, even considering two explicit methanol molecules, the most stable conformers for all molecules belong to M01 type. Rather indeed, its relative population raises from 0.56-0.61 to 0.62-0.84. The opposite effect is observed for the M02-type of conformers (θ_{OH} ~ 60º, θ_{Ph} ~ -30º) whose population largely decreases. Specifically, p-M02 population changes from 32% (PCM-only) to 3% (cluster model). Furthermore, some structural changes are observed and, more importantly, M03 (θ_{OH} ~ -170º, θ_{Ph} ~ 60-70º) and M05 (θ_{OH} ~-170º to 170º, θ_{Ph} ~ -10 to 10º) type of initial structures do not collapse on each other. They actually lead to different and stable minima, enriching the conformational space of the studied molecules.

2.2 ECD vibronic spectra of the cluster models

The Boltzmann average of the ECD spectra of the different conformers + 2 methanol molecules in PCM is compared with the experimental results in Figure 5. For completeness, the spectra of the individual conformers are shown in the SI (Figures S7-S10). Inclusion of two methanol molecules lead to results that are now in very good agreement with experiment for all the four molecules studied. In particular, and at variance with the PCM-only model, the cluster model is able to reproduce very nicely the ECD spectrum of p-ClPhEtOH. This is due to the fact that the EqSolv spectra of p-M01 and p-M02 are dramatically changed (see Figure 6) with respect to the predictions of the previous model. On the contrary, the spectral shape of p-M04 remains almost unaltered. More specifically, p-M01 becomes bisignated and very similar to the experimental shape. On the other hand, p-M02 has virtually no longer an effect on the average spectrum due to both the large reduction of the intensity and the decrease of population. Additionally, p-M05, not stable according to PCM-only model, is the second more populated conformer and provides almost

identical spectrum to p-M01, contributing also to the characteristic bisignated shape.

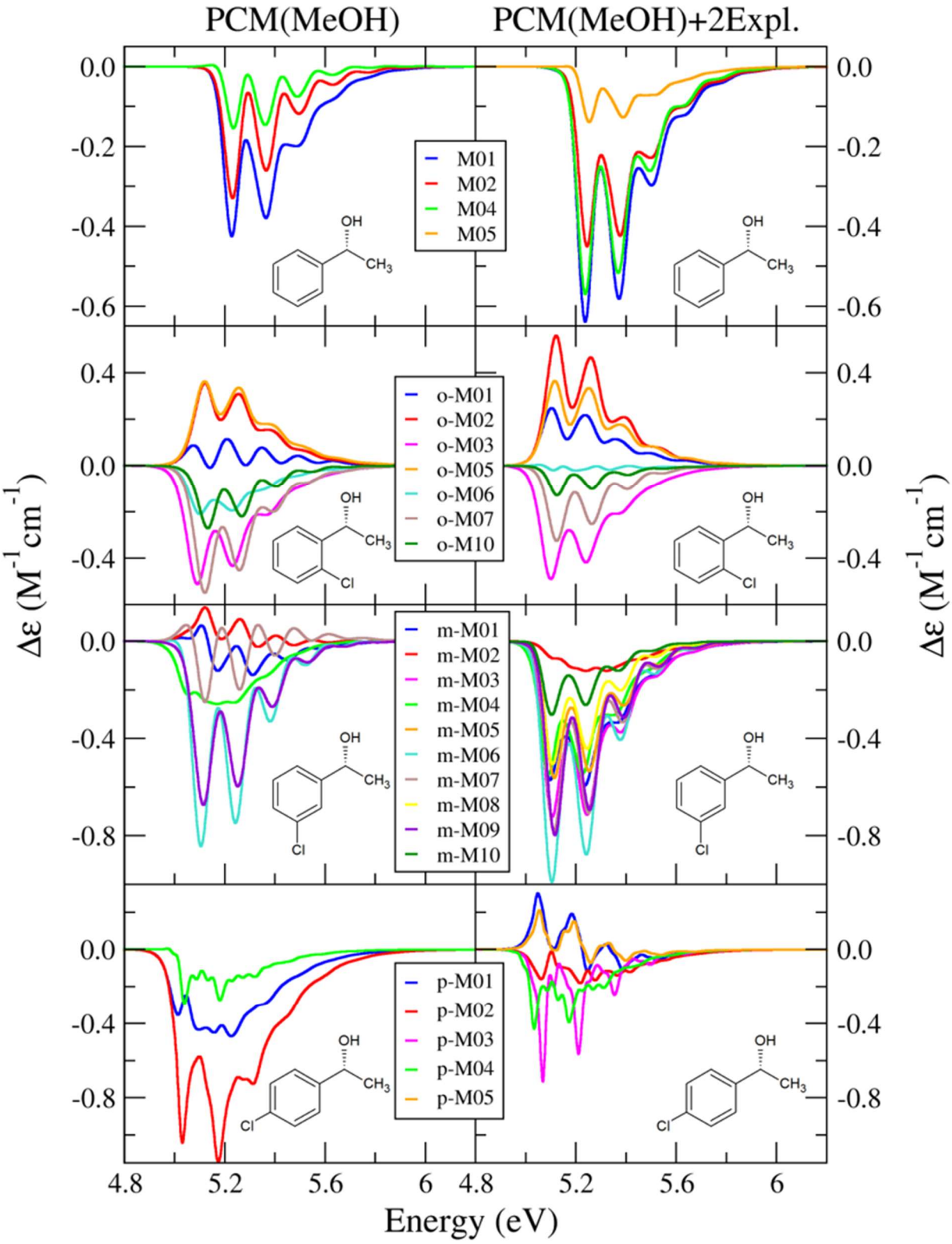


FIGURE 6. ECD spectra of the R enantiomer of PhEtOH and the isomers of ClPhEtOH (Boltzmann weights not included) for the model PCM-only (left) and for the cluster model in PCM (right) within the EqSolv regime. From top to bottom: PhEtOH (M0X), o-ClPhEtOH (o-M0X), m-ClPhEtOH (m-M0X) and p-ClPhEtOH (p-M0X).

Moving from the PCM-only to the cluster model we notice a change on the dimensionless shifts of ν_1 : p-M01 and p-M02 show much smaller values than the ones observed with PCM-only (see Table S1). Moreover for p-M01 the contribution to R^{HT} of ν_1 mode goes from -0.08 in PCM-only to +0.01 in the cluster model (10^{-40} cgs units) and from -0.09 to -0.04 for p-M02. We conclude that

specific solute-solvent interaction can play a relevant role to reproduce the properties of flexible motions like the rotation along θ_{Ph}. For PhEtOH and all the other ClPhEtOH isomers, the results are very similar to what predicted with PCM-only model. In fact, their thermally populated conformers show in general similar shapes.

2.2.1 Effect of specific solute-solvent interactions on Franck-Condon and Herzberg-Teller contributions.

Further insight on the impact of the specific solute-solvent interactions on the spectra, can come from the analysis of the R^{FC} and R^{HT} contributions to the intensity (Tables 5-8). Here we focus on the most populated conformers, i.e. the M01 type.

Interestingly, for PhEtOH and its m-chloro derivative, R^{HT} is in overall small: less than 5% of the total intensity R^{FCHT}. In the case of o-ClPhEtOH it represents about 1/3 of the total intensity while for p-ClPhEtOH R^{FCHT} is about 1/4 of R^{FC}. This is due to the fact that, differently to PhEtOH and the o- and m- chloro derivatives, in p-ClPhEtOH R^{HT} has an opposite sign with respect to R^{FC}. FC and HT intensities thus partially cancel out giving rise to the bisignated feature of the spectrum.

It is important to emphasize that the effect of the solvent on the conformer spectra is not limited to the total intensity since also the spectral shape can be altered (Figure 6). This is particularly true for the most populated conformers m-M01 and p-M01, while moderate changes are also observed on o-M01. On the contrary, M01 spectrum of the unsubstituted PhEtOH is almost identical but its overall intensity increases. In summary, the solute-solvent interactions play a very important role affecting both the relative stability of the conformers and the transition dipoles and their derivatives which ultimately determine the spectrum.

To conclude, Figure S11 compares the EqSolv and NonEqSolv spectra of p-M01 cluster model. NonEqSolv spectrum is completely positive, in disagreement with the experimental behaviour. This is a further indication that in cases where the ECD spectrum is the result of a very subtle equilibrium between electronic and solvents effects, it can be very complicated to reproduce the experimental behaviour with simplified approaches like the standard one here presented. These findings evidence the necessity for new methodological developments.

3. EFFECT OF THE CHLORINE

The ECD of the ^1L_b band of benzene derivatives is usually interpreted on the grounds of qualitative rules like the sector and benzene-chirality ones.[2,3,40] They successfully predict the ECD sign and therefore the absolute configuration of a number of related molecules[21,22,42-48] but some exceptions have been documented like (R)-methylmandelate,[49] (R)-1-indancarboxylate,[50] and (R)- α-isopropylphenylethane.[20]

Sector rule predicts that the ECD of R enantiomer of PhEtOH is dominated by HT effects and is negative, according to the preferred position of the benzylic hydrogen and the sectors where the OH and CH_3 groups are located. For ClPhEtOH one can use the benzene-chirality rule. In substituted benzenes FC intensity is allowed due to what is sometimes defined as "spectroscopic moment" or induced moment of the substituent.[2,40,41] Chlorine substituent falls in the category defined as "positive" since it increases the oscillator strength of the transition with respect to PhEtOH.

In summary it is assumed that for all isomers of ClPhEtOH the HT contribution has the same sign as in the parent PhEtOH compound. At variance, the FC contribution has the same sign of HT one for meta isomer and opposite sign for ortho and para. As a consequence, for the latter two isomers the overall ECD sign can be inverted respect to the unsubstituted compound,[2,40] if the FC contribution is dominant. Therefore, in principle the rule cannot predict the sign of o- and p-ClPhEtOH. Notwithstanding this, experimental observations report that, in several compounds, o- and p- isomers with positive substituents exhibit a sign opposite to the m- derivative and the unsubstituted compound.[2,40]

In the specific case of PhEtOH and its ClPhEtOH, the predictions of these qualitative rules are in line with the negative sign of PhEtOH and m-ClPhEtOH observed in experiments. The positive sign of o-ClPhEtOH also follows the expectations, while of course the bisignated shape exhibited by p-ClPhEtOH is too complicated to be covered by these simple rules. It is however noteworthy that the integrated ECD intensity of by p-ClPhEtOH is indeed positive. Electronic structure calculations have been proven to be an important tool to overcome the limitations of these qualitative rules.[30,51] For the molecules under consideration, our computations on the cluster models reproduce almost quantitatively the shape of the experimental spectra. Therefore, they can be used to revisit the interpretation of the effect of the chlorine position on the ECD spectra. In particular thanks to Eq.1 we can explicitly define the FC and HT contributions to the intensity, R^{FC} and R^{HT}, respectively.

The analysis of the computed R^{FC} and R^{HT} for the cluster model (Tables 5-8) support several predictions of the benzene chirality rule. For the most populated conformers (M01 type), R^{FC} is negative for PhEtOH and m-ClPhEtOH, whereas it is positive for o-ClPhEtOH and p-ClPhEtOH. Moreover, in agreement with the rule R^{HT} is negative for PhEtOH and its m- and p- isomer. However, it is positive for o-ClPhEtOH. This contradicts the rule, although for this isomer R^{HT} values are very small (at least for the model with explicit solvent molecules). Looking at the absolute values of R^{FC} and R^{HT}, the ECD of PhEtOH is mainly ruled by the FC contribution and this contradicts the assumption that HT terms are dominant. It is also noteworthy that the computed R^{FC} and R^{HT} values are very sensitive to the molecular model adopted. The model PCM-only (also reported on Tables 5-8), which do not reproduce the p-ClPhEtOH experimental spectrum, would indicate more violations of the qualitative rules.

Besides the above conclusions, for all cases, our calculations allow us to gain a more complete picture of the physical factors that rule the ECD spectrum. For instance, they show that the sign of overall R^{HT} is itself the result of a balance among the contributions of the different vibrational modes which, in all investigated cases, are both positive and negative. For p-M01, for instance, R^{HT} would be 5 times larger if the contributions of the individual modes had all the same sign.

The moderate HT contribution ($|R^{FC}|>|R^{HT}|$) in PhEtOH and in the o- and m- isomers of ClPhEtOH explains why their ECD shapes are similar. As a matter of fact, the dominant FC vibronic progressions of these three molecules mainly involve the same vibrational modes, shown in Figure S12. They are collective hydrogen bendings of the aromatic and chiral groups, with frequencies ~1060, ~1120 and ~1240 cm^{-1}, and a ring breathing with frequency around 1050 cm^{-1} corresponding to the well-known trigonal deformation labelled as mode 12 in Wilson nomenclature.

3.1 Analysis of the transitions with Natural Transition Orbitals

A closer analysis of the electronic transition responsible for the observed ECD signals can be obtained looking at the natural transition orbitals (NTOs)[52] which are shown in Figure 7. Kohn-Sham molecular orbitals are reported in Figure S13 and are very similar to the NTOs. ^1L_b state can be expressed in terms of two transitions, namely $\pi_2 \rightarrow \pi_4^*$ and $\pi_3 \rightarrow \pi_5^*$ in the nomenclature of benzene orbitals. The chlorine affects their respective weights: in PhEtOH they are almost equal while their ratio is about 60/40 for

o-M01 and m-M01 and 70/30 for p-M01. The presence of the chlorine induces a rotation of the orbitals along an axis perpendicular to the molecular plane as the chlorine position moves from ortho- to meta- and para-positions. This is particularly evident for π_2 which appears to be strongly mixed with chlorine 3p orbital.

In benzyl derivatives, the electric transition dipole moment of the ^1L_b transition is expected to be mostly in the molecular plane and the magnetic transition dipole mostly perpendicular to it.[2] The existence of an ECD signal in the investigated molecules must arise from a tilting of $\vec{\mu}$ and/or $\vec{m}$ that creates an out-of-plane component of the $\vec{\mu}$ and/or an in-plane component of $\vec{m}$ so that the two vectors are not orthogonal anymore. Data in Table 9 show that, apart from PhEtOH, where the two phenomena have similar magnitude, in the isomers of ClPhEtOH the second effect, i.e. the deviation of $\vec{m}$ toward the plane, is much more evident. Notwithstanding this, in-plane and out-of-plane contributions to the rotatory strength have actually similar magnitudes (Table 9). It is noteworthy that, in all the cases except in o-M01, the in-plane and out-of-plane contribution have different signs and partially cancel out. In particular, for p-M01 both terms have very similar absolute values resulting in a small total rotatory strength making possible strong HT effects.

3.2 Assignment of the vibronic peaks of the ECD spectrum of p-M01

The results presented in section 2 showed that PhEtOH and p-ClPhEtOH spectra are dominated by the contribution of the M01 conformer. Although M01 structure is very similar in both molecules, the ECD spectra are very different. These discrepancies must be related to the presence of the Cl atom. At variance with other M01 type conformers, M01 in p-ClPhEtOH exhibits an important HT contribution to the rotatory strength with sign opposite to the FC one. Combined with the smaller value of R^{FC} discussed at the end of the last section, this leads R^{FCHT} to be remarkably smaller than R^{FC} (Table 8). In order to better distinguish FC and HT contributions we computed a vibronic ECD spectrum of p-M01 including only the contribution of the transition dipole derivatives (HT spectrum). In Figure 8 we compare the FC spectrum, the HT one, their sum FC+HT and the full FCHT spectrum, i.e. the one discussed in the previous sections, obtained accounting simultaneously for FC and HT terms in the transition dipoles. It is noteworthy that the sum of FC and HT spectra is not expected to be exactly equal to the FCHT one since interferential effects take place in the latter.[33,34,38] However Figure 8 shows that these effects are small and FC+HT and FCHT spectra are rather similar. The FC spectrum is positive while the HT spectrum is mainly negative (except for the lowest energy band). This causes partial cancelations in most of the spectral range. At large energies, the HT dominates over the FC contribution, making the whole FCHT spectrum negative.

Interestingly, the main FC and HT progressions are shifted in frequency, so that the negative HT peaks correspond to minima in the positive FC spectrum, making the overall FCHT spectrum acquire the observed characteristic bisignated shape.

On balance, the results show that, like for simpler α-alkyl-phenylethane,[20] also in p-ClPhEtOH the spectral shape basically arises from the competition between the FC and HT vibronic progressions. We can however notice some interesting differences. The lower panel of Figure 8 provides an assignment of the main vibronic transitions for the FCHT spectrum of p-M01. The positive FC progression is mainly due to excitations of mode ν_{27}, an in-plane breathing mode of the ring, combined with excitations of a low-frequency mode ν_3, mainly an out-of-plane distortion of the ring. Interspersed with these transitions there are other progressions which are mainly due to HT effects and carry on the opposite sign. The first group of these bands is blueshifted with respect to the 0-0 transition by ~500 cm^{-1} (~0.06 eV). The most intense among them is the fundamental of mode ν_{11} (11^1), a concerted out-of-plane motion of the four CH phenyl bonds (see Figure S14). These transitions strongly decrease the FC intensity (Figure 8), bringing the intensity of the FCHT spectrum close to zero. An analogous phenomenon was observed in simple α-isopropylphenylethane, and it was theoretically reproduced in ref. 20 showing that it is triggered by a similar vibrational mode. However, in that molecule the intensity of this first negative band was by far stronger. Both α-isopropylphenylethane and p-ClPhEtOH show further negative bands at higher energies. However, only in p-ClPhEtOH the second negative band (at 5.25 eV) is much more intense than the first one. Such band is dominated in fact by the fundamental of a second HT-active mode ν_{40} (1576 cm^{-1}), an asymmetric in-plane distortion of the ring that plays essentially no-role in α-isopropylphenylethane. It is therefore likely that ν_{40} couples the ^1L_b transition with a strongly absorbing higher-energy state remarkably affected by the chlorine substituent.

Conclusion

In this contribution we carried out a computational investigation of the weak ECD spectra arising from the ^1L_b transition of (R)-PhEtOH and the ortho-, meta- and para-isomers of (R)-1-(ClPh)EtOH in methanol solution. We adopted TD-DFT and described the solvent effects with PCM and/or cluster models including the solute and two explicit solvent molecules in PCM. The spectral shapes of stable conformers were computed at vibronic level in harmonic approximation including FC and HT contributions and then averaged according to Boltzmann populations. The experimental spectra of PhEtOH and the meta and ortho isomers of ClPhEtOH are monosignated, the former two being negative and the latter positive, whereas p-ClPhEtOH exhibits a characteristic bisignated shape. Our computations reproduce very nicely the signs and spectral shape of all four compounds and allow us to individuate the vibrational modes responsible for the main progressions. In particular, the modes responsible for the positive and negative bands of the ECD of p-ClPhEtOH were carefully described and their nature critically compared with those responsible for bisignated spectra in α-alkylphenylethanes studied few years ago.[20]

On the grounds of the good agreement with experiment we used our calculations to revisit the interpretation of the spectra of ClPhEtOH provided by sector and benzene-chirality rules, separately discussing the relevance of FC and HT contributions. The predictions for ortho and meta isomers were substantially confirmed. The bisignated ECD shape of the para isomer is too complex to be fully described by these simple models. Besides this, our computations indicate that the FC contribution to the spectrum of PhEtOH is larger than expected, and they unveil that, in all systems, the HT contributions comprise both positive and negative terms, depending on the promoting vibrational modes.

From a computation point of view, the correct reproduction of the spectral shape of p-ClPhEtOH was more challenging than for the other isomers. In fact, we showed that the predicted spectral shape is rather sensitive to different possible settings of the computational method, like the treatment of low frequency modes, the inclusion of explicit solvent molecules or the choice of the equilibrium or non-equilibrium solvation regimes. At variance,

these options all produce similar spectra (always in good agreement with experiments) for PhEtOH and the ortho and meta isomers of ClPhEtOH. A careful analysis evidences that such sensitivity is also connected to the coupling between the movements of the solvent molecules and the three hindered rotations of the chiral ethanol group. These modes are intrinsically connected to the chiral response of the system and are strongly anharmonic, and therefore in principle not suited for a harmonic treatment. The above observations highlight the need for new methodologies able to combine MD simulations to fully describe the richness of solvent interactions with flexible solutes and vibronic models to compute the spectral shapes. In this spirit, for instance, we recently introduced a novel method, Ad-MD|gVH.[25] The results obtained in this contribution indicate that the PhEtOH derivatives and, in particular, the para isomer of ClPhEtOH stand as optimal training pools for these new computational developments in the field.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's website. Spectra of individual conformers with the model PCM-only, and with the cluster model in PCM, using equilibrium solvation and non-equilibrium solvation regimes. Displacement vectors for the most relevant vibrational modes, molecular orbitals. Cartesian coordinates of the cluster model structures.

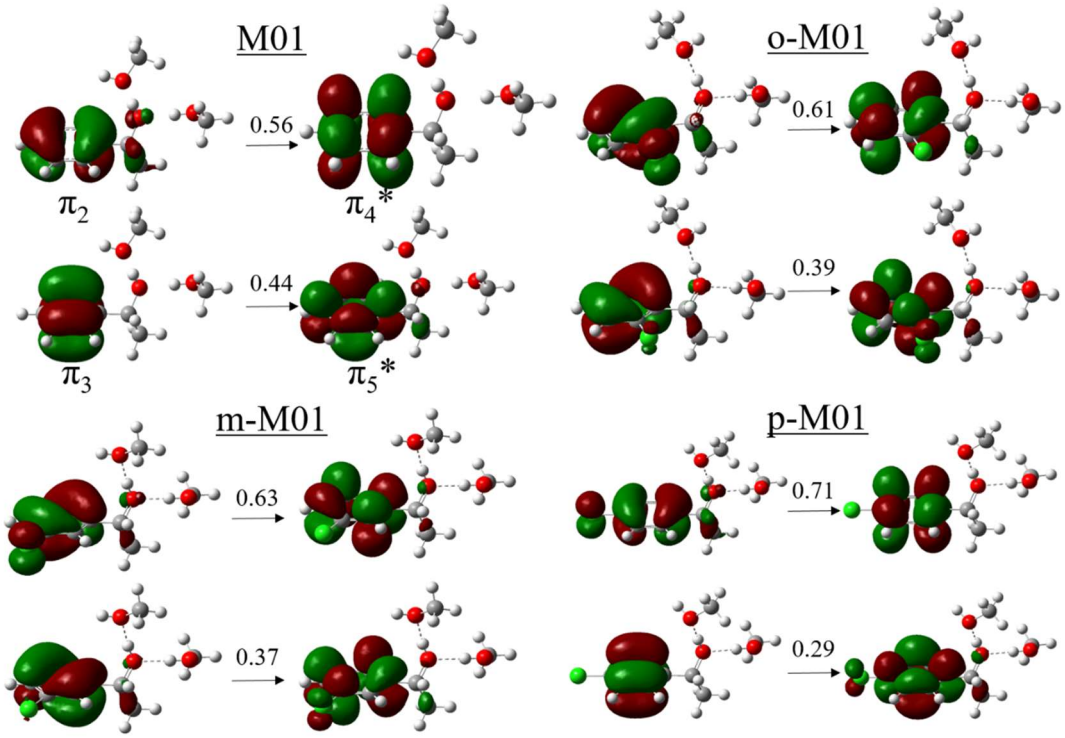

FIGURE 7. Natural transition orbitals for the L_b excited state of the conformers of PhEtOH (M01, top left), o-PhEtOH (o-M01, top right),), m-PhEtOH (m-M01, bottom left), and p-PhEtOH (p-M01, bottom right). The weight of each transition to the total of the state is shown.

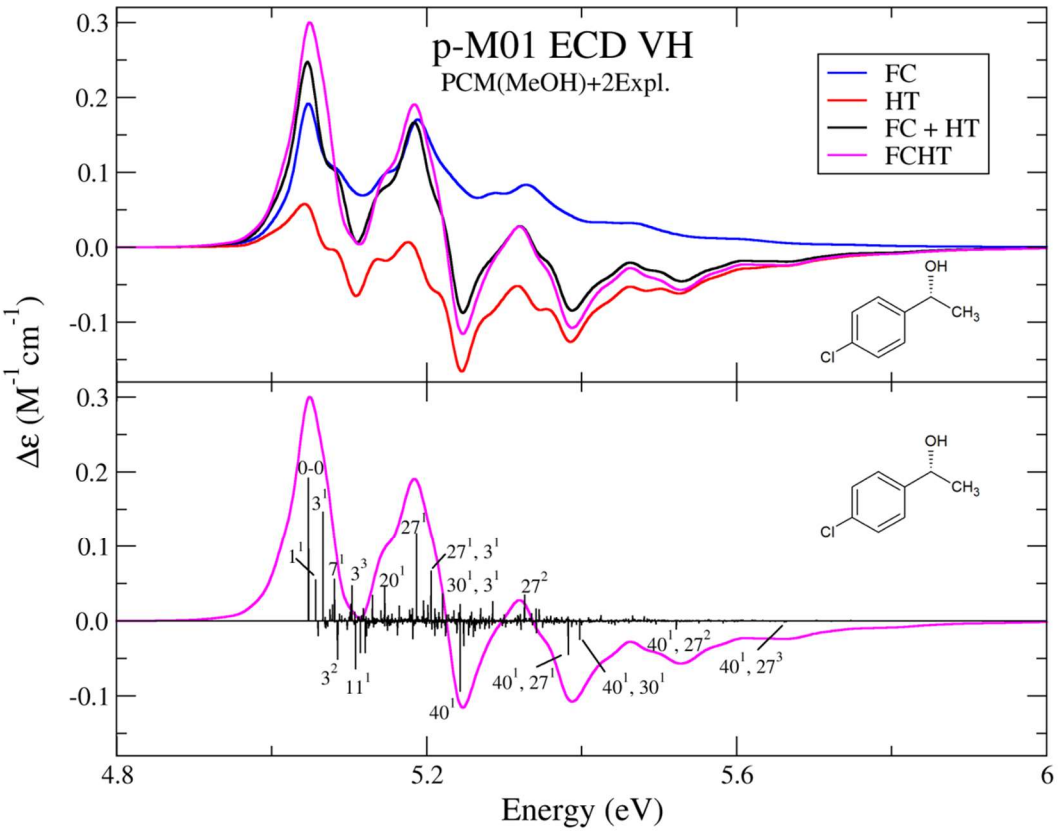

Figure 8. Top: Spectra of the M01 conformer of p-PhEtOH (p-M01) obtained accounting for only the Franck-Condon (FC) or Herzberg-Teller (HT) contributions. The sum of FC and HT spectra (FC+HT) is compared with the spectrum obtained by including both contributions simultaneously (FCHT) and already discussed in the previous sections. Bottom: FCHT spectrum of p-M01 with stick transitions and labels to the vibrational modes involved on the most relevant ones.

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Table 1. Conformational analysis for PhEtOH in gas phase, PCM and PCM including two explicit solvent molecules. The values of θ_{Ph} and θ_{OH} are expressed in degrees. The population is not shown for conformers already obtained from others initial structures.

	Gas Phase[1]		**Gas Phase[2]**			**PCM(MeOH)**			**2 Explicit MeOH+ PCM**		
Conformer	θ_{OH}	θ_{Ph}	θ_{OH}	θ_{Ph}	Pop.	θ_{OH}	θ_{Ph}	Pop.	θ_{OH}	θ_{Ph}	Pop.
M01	-65	-19	-66	-22	0.65	-62	-23	0.61	-61	-22	0.84
M02	70	-37	71	-38	0.13	68	-28	0.27	50	-30	0.07
M03	-175	74	-167	-164	-	162	-47	-	168	-9	-
M04	170	-69	166	-60	0.06	162	-47	0.12	160	-42	0.07
M05	-169	10	-167	-164	0.17	162	-47	-	167	-7	0.02

[1]Data obtained with the CAM-B3LYP/TZVP level of theory in ref. 16. [2]CAM-B3LYP/def2-TZVP.

Table 2. Conformational analysis for o-ClPhEtOH in gas phase, PCM and PCM including two explicit solvent molecules. The values of θ_{Ph} and θ_{OH} are expressed in degrees. The population (Pop) is not shown for conformers already obtained from others initial structures.

		Gas Phase			**PCM(MeOH)**			**2 Explicit MeOH+ PCM**		
Cl on the side of:	Conformer	θ_{OH}	θ_{Ph}	Pop.	θ_{OH}	θ_{Ph}	Pop.	θ_{OH}	θ_{Ph}	Pop.
H1	o-M01	-56	-34	0.69	-56	-35	0.55	-50	-35	0.77
H1	o-M02	68	-40	0.2	66	-37	0.26	64	-36	0.07
H1	o-M03	-171	38	0.01	-148	38	0.03	-180	38	0.01
H1	o-M04	151	-43	0.07	155	-40	0.11	159	-38	0.14
H1	o-M05	151	-43	-	155	-40	-	159	-38	-
OH	o-M06	-66	-7	0	-59	-7	0.01	-58	-7	0
OH	o-M07	179	-11	0.02	69	-7	0	56	-8	0
OH	o-M08	179	-11	-	176	-12	-	143	-9	-
OH	o-M09	179	-11	-	175	-12	-	143	-9	-
OH	o-M10	179	-11	-	175	-12	0.03	141	-9	0

Table 3. Conformational analysis for m-ClPhEtOH in gas phase, PCM and PCM including two explicit solvent molecules. The values of θ_{Ph} and θ_{OH} are expressed in degrees. The population is not shown for conformers already obtained from others initial structures.

		Gas Phase			**PCM(MeOH)**			**2 Explicit MeOH+ PCM**		
Cl on the side of:	Conformer	θ_{OH}	θ_{Ph}	Pop.	θ_{OH}	θ_{Ph}	Pop.	θ_{OH}	θ_{Ph}	Pop.
H1	m-M01	-63	-24	0.33	-59	-25	0.25	-57	-23	0.45
H1	m-M02	70	-40	0.09	68	-31	0.12	52	-16	0.02
H1	m-M03	-173	9	0.04	158	-45	-	164	-27	0.03
H1	m-M04	164	-60	0.04	158	-45	0.04	162	-47	0.03
H1	m-M05	164	-60	-	158	-45	-	167	-11	0.02
OH	m-M06	-63	-25	0.35	-59	-27	0.34	-57	-27	0.17
OH	m-M07	71	-40	0.09	68	-36	0.23	66	31	0.1
OH	m-M08	-177	74	0.03	160	-51	-	165	-24	0.08
OH	m-M09	163	-60	0.04	160	-51	0.04	162	-48	0.05
OH	m-M10	163	-60	-	160	-51	-	167	-12	0.05

Table 4. Conformational analysis for p-ClPhEtOH in gas phase, PCM and PCM including two explicit solvent molecules. The values of θ_{Ph} and θ_{OH} are expressed in degrees. The population is not shown for conformers already obtained from others initial structures.

	Gas Phase			**PCM(MeOH)**			**2 Explicit MeOH+ PCM**		
Conformer	θ_{OH}	θ_{Ph}	Pop.	θ_{OH}	θ_{Ph}	Pop.	θ_{OH}	θ_{Ph}	Pop.
p-M01	-63	-22	0.69	-60	-24	0.56	-56	-22	0.71
p-M02	70	-40	0.18	68	-31	0.32	51	-15	0.03
p-M03	-176	72	0.06	160	-47	-	-175	51	0.06
p-M04	164	-62	0.07	160	-47	0.12	165	-48	0.04
p-M05	164	-62	-	160	-47	-	166	-15	0.16

Table 5. Rotatory Strengths (in 10^{-40} cgs) obtained for the different PhEtOH conformers including either only the FC contribution (FC) or both the FC and HT (FCHT) contributions.

	PCM(MeOH)				**2 Explicit MeOH+ PCM**			
Conformer	Pop.	R^{FC}	R^{HT}	R^{FCHT}	Pop.	R^{FC}	R^{HT}	R^{FCHT}
M01	0.61	-0.697	0.205	-0.492	0.84	-0.675	-0.035	-0.710
M02	0.27	-0.330	0.038	-0.292	0.07	-0.451	-0.093	-0.544
M03	-	-	-	-	-	-	-	-
M04	0.12	-0.611	0.482	-0.129	0.07	-0.641	0.019	-0.622
M05	-	-	-	-	0.02	-0.172	0.010	-0.162

Table 6. Rotatory Strengths (in 10^{-40} cgs) for the different o-ClPhEtOH conformers including either only the FC contribution (FC) or both the FC and HT (FCHT) contributions.

	PCM(MeOH)				**2 Explicit MeOH+ PCM**			
Conformer	Pop.	R^{FC}	R^{HT}	R^{FCHT}	Pop.	R^{FC}	R^{HT}	R^{FCHT}
o-M01	0.55	0.020	0.104	0.124	0.77	0.235	0.076	0.311
o-M02	0.26	0.395	0.052	0.447	0.07	0.614	0.009	0.623
o-M03	0.03	-0.430	-0.234	-0.664	0.01	-0.447	-0.184	-0.631
o-M04	0.11	0.387	0.115	0.502	0.14	0.372	0.099	0.471
o-M05	-	-	-	-	-	-	-	-
o-M06	0.01	-0.232	-0.056	-0.288	0.00	-0.064	0.04	-0.024
o-M07	0.00	-0.525	-0.098	-0.623	0.00	-0.302	-0.017	-0.319
o-M08	-	-	-	-	-	-	-	-
o-M09	-	-	-	-	-	-	-	-
o-M10	0.03	-0.201	-0.062	-0.263	0.00	-0.139	0.021	-0.118

Table 7. Rotatory Strengths (in 10^{-40} cgs) for the different m-ClPhEtOH conformers including either only the FC contribution (FC) or both the FC and HT (FCHT) contributions.

	PCM(MeOH)				**2 Explicit MeOH+ PCM**			
Conformer	Pop.	R^{FC}	R^{HT}	R^{FCHT}	Pop.	R^{FC}	R^{HT}	R^{FCHT}
m-M01	0.25	-0.792	0.665	-0.127	0.45	-0.848	-0.007	-0.855
m-M02	0.12	-0.450	0.528	0.078	0.02	-0.153	-0.059	-0.212
m-M03	-	-	-	-	0.03	-0.946	-0.016	-0.962
m-M04	0.04	-0.451	-0.23	-0.681	0.03	-0.744	-0.002	-0.746
m-M05	-	-	-	-	0.02	-0.716	0.039	-0.677
m-M06	0.34	-1.739	0.927	-0.812	0.17	-1.167	0.104	-1.063
m-M07	0.23	-1.119	1.073	-0.046	0.10	-0.916	0.065	-0.851
m-M08	-	-	-	-	0.08	-0.628	0.091	-0.537
m-M09	0.04	-0.829	0.099	-0.730	0.05	-0.904	0.073	-0.831
m-M10	-	-	-	-	0.05	-0.393	0.074	-0.319

Table 8. Rotatory Strengths (in 10^{-40} cgs) for the different p-ClPhEtOH conformers including either only the FC contribution (FC) or both the FC and HT (FCHT) contributions.

	PCM(MeOH)				**2 Explicit MeOH+ PCM**			
Conformer	Pop.	R^{FC}	R^{HT}	R^{FCHT}	Pop.	R^{FC}	R^{HT}	R^{FCHT}
p-M01	0.56	0.096	-0.954	-0.858	0.71	0.193	-0.148	0.045
p-M02	0.32	-0.241	-1.422	-1.663	0.03	0.037	-0.332	-0.295
p-M03	-	-	-	-	0.06	-0.392	-0.062	-0.454
p-M04	0.12	-0.636	0.314	-0.322	0.04	-0.569	0.104	-0.465
p-M05	-	-	-	-	0.16	0.170	-0.116	0.054

Table 9. Angle of the electric and magnetic transition dipole moment with the direction perpendicular to the phenyl ring (φ). Decomposition of the Rotatory strengths in in-plane and out-of-plane contributions (in 10^{-40} cgs). Calculations for M01 conformers of PhEtOH and the different isomers of ClPhEtOH with two explicit methanol molecules in PCM.

	M01		o-M01		m-M01		p-M01	
	μ	m	μ	m	μ	m	μ	m
φ (deg)	97.7	6.2	89.0	130.9	91.7	8.1	92.4	22.0
	Rotatory strength (10^{-40} cgs)							
In plane	1.095		0.085		-1.467		-1.546	
Out-of-plane	-1.775		0.148		0.634		1.737	
Sum	-0.68		0.23		-0.83		0.19	

Graphical Abstract