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# Toward Ab Initio Anharmonic Vibrational Circular Dichroism Spectra in the Condensed Phase

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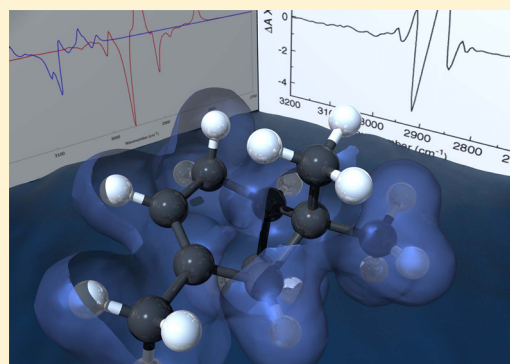
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## Supporting Information

**ABSTRACT:** The first implementation and calculation of anharmonic VCD rotational strengths for solvated systems is reported. Our approach, rooted in the polarizable continuum model (PCM) and in the second-order vibrational perturbation theory (VPT2), permits not only correction for anharmonicity in the signals associated with fundamental transitions but also calculation of rotational strengths of overtones and combination bands. This allows for a more physically consistent comparison between experiment and calculations together with the analysis of spectral regions dominated by anharmonic effects. The developed model is applied to a few test cases, and the computational outcomes are directly compared with experimental data.



**SECTION:** Spectroscopy, Photochemistry, and Excited States

Vibrational circular dichroism (VCD) has gained increasing interest as a valuable tool for assigning of absolute configurations and for obtaining information on the local environment of oscillating modes of molecular systems and on conformational ratios important in determining reactivities of biomolecules. VCD is therefore being increasingly utilized also as probe of the conformational structure of biopolymers,<sup>1</sup> and recently, it has been proposed also for the investigation of synthetic polymers.<sup>2,3</sup>

The use of VCD for structure assignment is however almost impossible without combining experimental measurements with quantum mechanical (QM) calculations, and therefore, the availability to the scientific community of computational codes for predicting the spectroscopic signals reliably and in a computationally viable manner has had a huge impact on the field of vibrational chiroptical spectroscopy.<sup>4</sup>

Another aspect of chiroptical spectroscopy that calls for reliable theoretical models and computational codes is the investigation of the effects of the molecular environment. Chiroptical measurements are only rarely carried out for isolated systems;<sup>5</sup> however, more commonly, the experiments are performed on solvated systems. Solvent effects can be very important, and there have been reports that not only the order of magnitude but also the sign of the properties can change with the polarity of the solvent. Accounting for solvent effects in the calculations is therefore crucial, especially in the determination of absolute configurations, and much effort has been put into this topic in recent years.<sup>6</sup>

One of the major limitations of currently available codes for calculating VCD rotational strengths of both isolated and especially solvated systems is that the common algorithms rely on the double harmonic approximation, that is, the effects due to the anharmonic character of the molecular vibrations responsible for the various bands are completely discarded. This means that, on one hand, only vibrational frequencies and rotational strengths of fundamental transitions can be calculated and, on the other hand, that calculated absolute values not only for frequencies but also for intensities can differ, even substantially, from experiments, thus making, in some cases, the assignment of the spectrum to a given configuration very difficult.

The only attempts to date to go beyond the double harmonic approximation for VCD calculations (other examples exist, such as ref <sup>7</sup> where only frequency values but not intensities are corrected for anharmonicity), both limited to isolated systems, are a very recent paper by some of the present authors<sup>8</sup> on a general formulation of VCD with the account of both mechanical and electric anharmonic effects and a previous work by Jørgensen and co-workers,<sup>9</sup> who extended to VCD the original work by Handy and co-workers<sup>10</sup> aimed at obtaining analytical formulations at the second-order vibrational perturbative (VPT2) level for computing IR bands by applying

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Van Vleck perturbation theory.<sup>11</sup> The paper by Jørgensen and co-workers,<sup>9</sup> was however limited to fundamental bands, whereas the approach developed in our group<sup>8</sup> permits calculation of VCD rotational strengths for fundamental, overtone, and combination bands. As already pointed out in ref 8, earlier attempts, such as those in refs 12 and 13, introduced various approximations to reduce the complexity of the anharmonic problem, such as considering independently the wave function and the property of interest and limiting the treatment beyond the harmonic level to only one of the terms.

By following the ref 8 in this Letter, we report on the formulation and first calculations of VCD anharmonic spectra obtained by extending the algorithms recently developed<sup>8</sup> to treat solvated systems described by means of the polarizable continuum model (PCM).<sup>14,15</sup> Due to the peculiarities of our approach, not only can a more physically consistent comparison between experiment and calculations be obtained, but also, spectral regions dominated by anharmonic effects become accessible to calculations.

As already pointed out above, the account for solvent effects is crucial in comparing calculated data and experiments. Therefore, even a very accurate QM modeling of vibrational frequencies and rotational strengths, accounting also for anharmonicity, may be insufficient to get a quantitative description of experimental spectra. Conversely, especially when a highly accurate QM modeling is exploited, the strategy to account for solvation should be as accurate as possible. Only in this way is a balanced model obtained, fully exploiting the potentialities of the two approaches.

A well-known method of coupling QM modeling and solvent effects is to exploit continuum solvation approaches, which in their current implementations have the capability of keeping the computational demand comparable to that of the corresponding calculation for the isolated system at a given QM level. In addition, the description of the molecular system that is obtained by using continuum models can be tailored to the various aspects/properties of the solvated systems under investigation. It has in fact already been amply demonstrated in the literature that peculiar aspects, such as equilibrium versus nonequilibrium solvation<sup>16,17</sup> and/or the account of local field effects,<sup>18</sup> not commonly included in the basic reaction field-based versions of such models, are to be invoked to obtain a physically consistent modeling of the solvated sample interacting with the radiation electromagnetic fields. In particular, in the special case of modeling chiroptical spectroscopies of solvated systems,<sup>6,19–23</sup> the basic reaction-field-based formulation of the PCM has been demonstrated to be insufficient to get a quantitative agreement between calculations and experiments.<sup>18,24,25</sup>

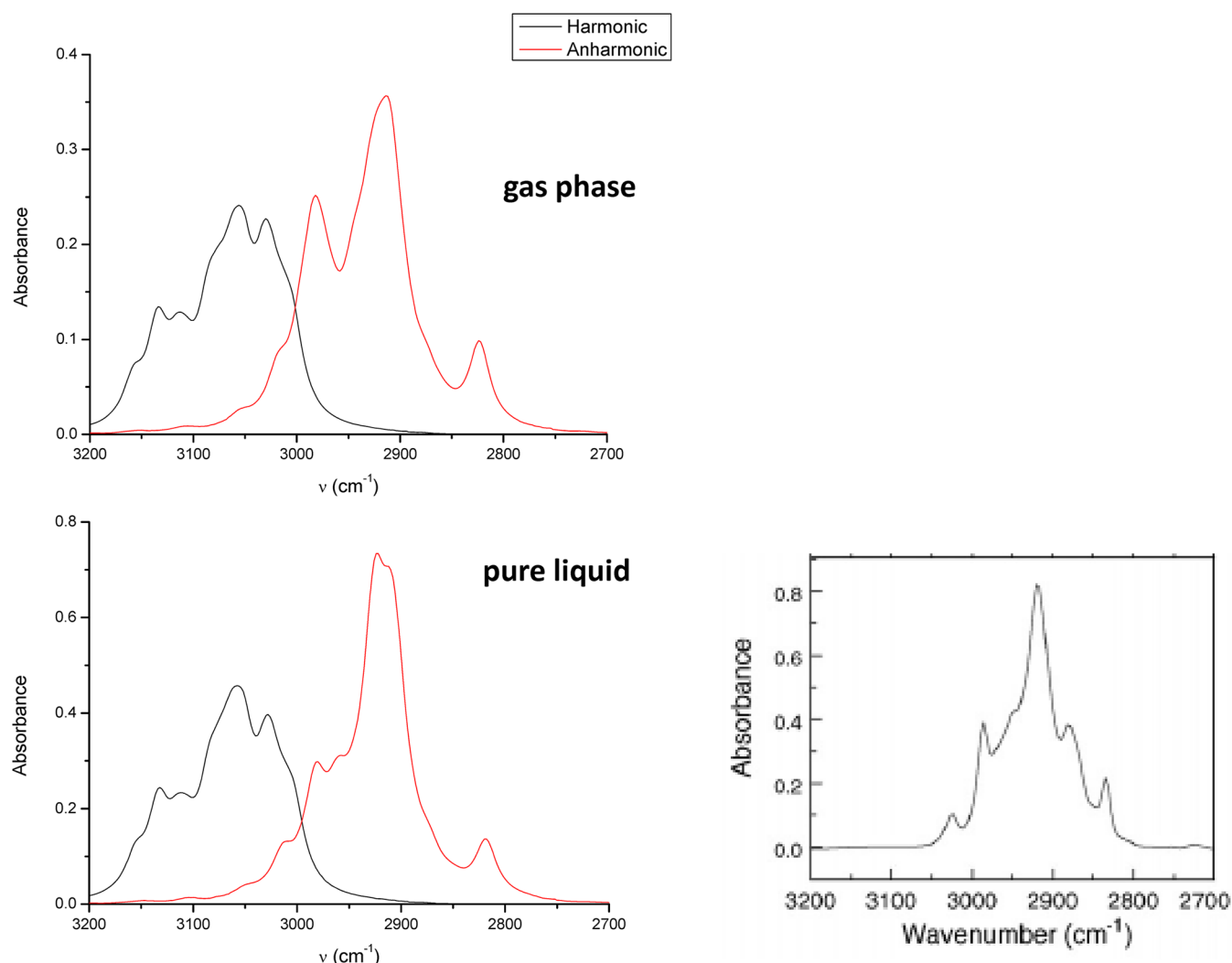
On the basis of the previous consideration, in this Letter, we present the first model able to couple a fully anharmonic treatment of VCD spectra (frequencies and rotational strengths) with a physically consistent picture of a solvated sample described by means of the PCM. The anharmonic treatment of frequencies by including PCM terms has already been reported in the literature by some of the present authors<sup>26</sup> (by also including vibrational nonequilibrium solvation terms<sup>17</sup>), whereas, here, for the first time, a full PCM anharmonic treatment of rotational strengths is reported. In particular, our model extends to VCD our recent work on IR intensities<sup>17</sup> and optical rotation<sup>20</sup> to step toward a fully coherent model for anharmonic spectroscopies of solvated systems, not only considering direct solvent effects on

molecular wave functions but also able to consider the indirect effect on the solute geometry and the so-called local field effects,<sup>18,27</sup> arising from the difference between the electromagnetic field acting on the molecule and the Maxwell field acting on the sample. In addition, in consideration of the time evolution of the solute electron density intrinsic to vibrational spectroscopic experiments, vibrational nonequilibrium effects<sup>16,17</sup> are included in our model, that is, a partition of the solvent polarization into a fast and a slow component is conceptually performed, so that the fast component will include the contribution due to the electronic and vibrational degrees of freedom, while the slow component will treat the effect of translations and rotations.<sup>16,17</sup> Once such partition is formulated; the analytical double differentiation of the nonequilibrium free energy yields molecular harmonic frequencies and normal modes of vibration. Further numerical differentiation permits evaluation of anharmonic effects on vibrational frequencies and IR intensities.<sup>17</sup> The further extension to VCD rotational strengths is obtained by reformulating the various quantities entering the definition so as to consider all of the previously mentioned solvent effects. The detailed formulas giving anharmonic rotational strengths for PCM solutes are given as Supporting Information.

To end this methodological introduction, we note that because we are using a purely continuum model, what is still lacking in the present approach is the consideration of specific solute–solvent interactions and solute–solute aggregation effects.<sup>19,28</sup> Whenever such interactions become important, a continuum-only description generally fails, and combinations with a discrete picture of some solvent molecules and/or extension of the definition of the solute have to be introduced, with an obvious increase in both computational cost and complexity. Another aspect to be underlined is that the present model only accounts for the electrostatic component of the solute–solvent interaction (and its coupling with the radiation field). Extension toward the inclusion of nonelectrostatic (dispersion, repulsion) terms would be necessary to gain a physically consistent modeling and is currently under development in our lab.

The potentialities of our methodology will be illustrated by the calculation of the VCD spectrum of (1R)-(+)- $\alpha$ -pinene (pure liquid) and (1R)-(+)-camphor in CCl<sub>4</sub> solution. These two systems are often used as test molecules in the development of theoretical/computational models for chiroptical properties and have the desirable feature of being semi-rigid systems, that is, they are safely described by means of a single minimum structure on the potential energy surface (PES). In addition, for such systems, VCD spectra in a wide range of wavenumbers have been experimentally measured by Nafie and co-workers,<sup>29</sup> so that a direct comparison between our calculated data and experiments is possible, especially in spectral ranges dominated by anharmonic effects.

Before focusing on the comparison between calculated and experimental VCD spectra, it is worth spending some words on evaluating the quality of the chosen QM level for the description of the two systems and their properties. The field of calculating anharmonic VCD for solvated systems is totally unexplored. Therefore, no benchmarking of QM models (DFT functionals and basis sets) has been reported, nor any evaluation of the quality of solvation models. For these reasons, we prefer to start our discussion on infrared spectra, for which at least some preliminary data have been reported in the literature. Once the quality of our approach has been assessed



**Figure 1.** Calculated anharmonic versus harmonic IR absorption spectra of  $\alpha$ -pinene in the gas phase and pure liquid phase. The experimental spectrum in the same range taken from ref 29 is also reported. Lorentzian broadening is exploited, with HWHM = 10  $\text{cm}^{-1}$ .

for IR, a similar quality should be obtained for VCD (by assuming of course the magnetic component of the property to be described at the same level as the electric one).

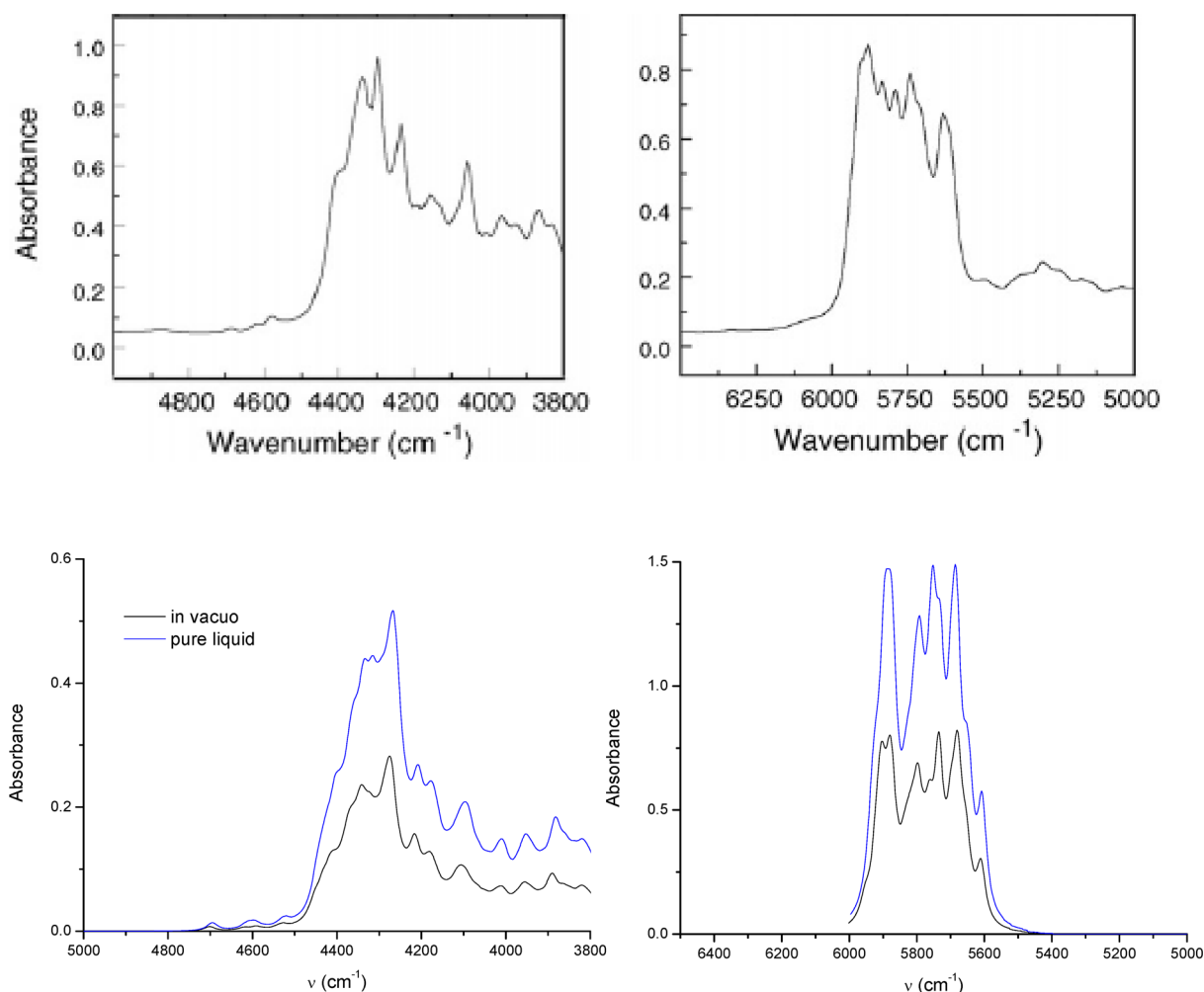
The combination of the B3LYP functional and the N07D<sup>30</sup> basis set for the evaluation of IR anharmonic spectra of organic molecules has been successfully tested<sup>31–33</sup> against both more accurate QM models for isolated systems and experimental data for isolated and solvated<sup>26</sup> systems described with the PCM. Therefore, such a combination has been applied in all calculations.

In Figure 1, calculated harmonic and anharmonic IR spectra of (1R)-(+)- $\alpha$ -pinene in the range between 2700 and 3200  $\text{cm}^{-1}$  are reported. Both the isolated system and the pure liquid are considered. The choice of focusing on such a spectral range is justified by the final aim of the Letter, that is, to evaluate the effects due to anharmonicity, which in principle dominates the spectral range shown in Figure 1. Such an assumption is in fact demonstrated by our calculations; harmonic and anharmonic spectra are markedly different, and it is especially worthy to note that anharmonic spectra cannot be simply obtained from harmonic ones by some scaling. Such a procedure, which roughly works for frequencies, does not work for intensities because anharmonic intensities cannot be obtained from harmonic ones by using a simple scaling procedure. However,

this is not the only conclusion that can be drawn by the reported spectra. In fact, calculated data in the gas phase and for the pure liquid differ sensitively, and once again, the difference is more evident for intensities than that for frequencies, such differences being even more marked for anharmonic spectra. Moving to the comparison with experimental findings, a very good description is obtained by using our methodology rooted in VPT2 and PCM, both as far as frequencies and relative intensities are concerned. As expected, a purely harmonic treatment of frequencies and IR intensities, even with the inclusion of solvation effects, is not able to reproduce correctly experimental data.

Such a better performance of VPT2-PCM to reproduce experimental IR spectra with respect to the gas phase is not limited to such a range but is also evident upon inspection of other spectral ranges. Figure S1 given in the Supporting Information shows the same comparison for the 800–1600  $\text{cm}^{-1}$  range.

The potentialities of our anharmonic models are further analyzed in Figure 2, which shows calculated anharmonic IR spectra of the same system in the spectral range between 3800 and 6500  $\text{cm}^{-1}$ , which is dominated by overtone and combination bands, which means that a purely harmonic approach is completely unable to describe such spectra. Overall,



**Figure 2.** Calculated anharmonic IR absorption spectra of  $\alpha$ -pinene in the gas phase and pure liquid phase. Experimental spectra in the same ranges taken from ref 29 are also reported. Lorentzian broadening is exploited, with HWHM = 16  $\text{cm}^{-1}$ .

the description of the experimental data is very good; calculated and experimental frequencies are very close, and the intensity pattern is described very well, especially if the huge experimental noise is considered. The differences between gas-phase and PCM results is again noticeable and once again more marked for relative intensities than that for frequencies. It is interesting to note that the dielectric permittivity that we used to describe pure  $\alpha$ -pinene is small, so that small differences between calculations in the gas phase and for the pure liquid are expected. Such an idea seems to be justified by the calculated frequency values, whereas IR intensities are more sensitive to the change in the environment.

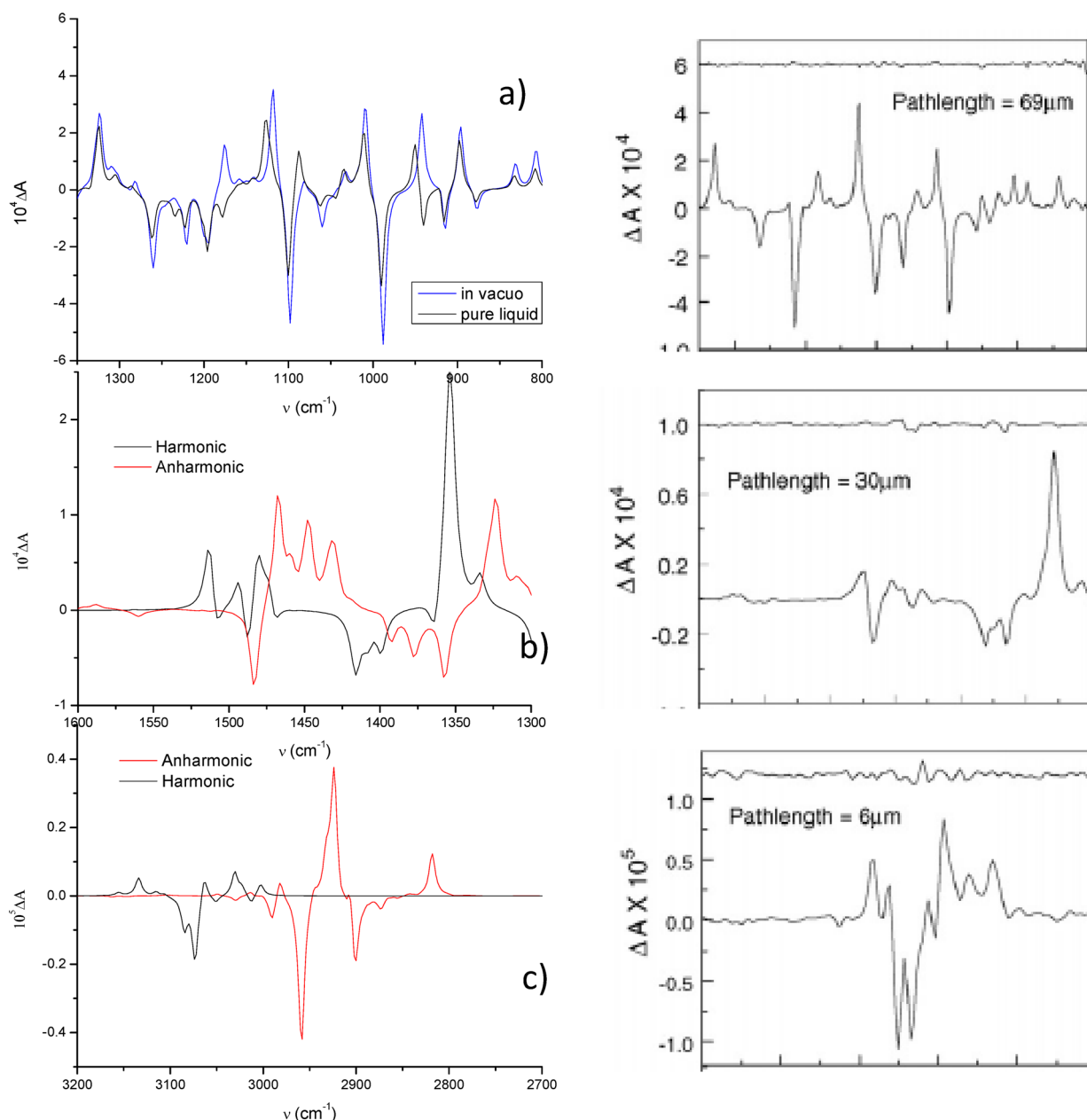
On the basis of the very good quality of the description of IR absorption spectra that has been obtained, the same QM level and solvation model has been applied to the calculation of VCD spectra (Figure 3 and S2 in the Supporting Information). Similar to IR, also for VCD, the introduction of anharmonic effects has a sensitive effect on calculated spectra, especially for the region above 2700  $\text{cm}^{-1}$ , involving anharmonic fundamental bands (see Figure 3c) and the regions above 3800  $\text{cm}^{-1}$  (Figure S2 in the Supporting Information), which are dominated by overtone and combination bands and, therefore, to which the harmonic approximation is not applicable. Also in the case of regions described fairly well within the double harmonic approximation, such as the one between 800 and

1600  $\text{cm}^{-1}$  (see panels a and b in Figure 3), the introduction of anharmonic terms in the evaluation of vibrational frequencies and in the expansion of transition moments can be appreciated, although the difference between harmonic and anharmonic spectra is, in this case, less pronounced.

The potentialities of our approach are further demonstrated by the application to another system, that is, (1R)-(+)-camphor in  $\text{CCl}_4$  solution (Figure 4). Also in this case, a good reproduction of frequencies and rotational strengths (sign and relative intensities) is obtained, therefore showing that the combination of a completely anharmonic treatment (electric and mechanical terms) of IR and VCD spectra, both in terms of frequencies and intensities, combined to a refined continuum solvation model rooted into the PCM also including local field and vibrational nonequilibrium effects, is a powerful method to study IR and VCD of optically active molecules also in spectral ranges dominated by anharmonic effects. The description that is obtained is very similar for all of the spectral ranges, and not only frequencies but also intensities vary, even markedly when the double harmonic approximation is abandoned.

To end this Letter, it is however worth noticing that the results presented here are preliminary; more extensive testing is surely required to fully assess the quality of the chosen QM level and the dependence of the quality of the description of solvation effects on PCM parameters (such as cavity size and





**Figure 3.** (a) Calculated anharmonic VCD spectra of  $\alpha$ -pinene in the gas phase and pure liquid phase in the 800–1350  $\text{cm}^{-1}$  range; (b) harmonic versus anharmonic VCD spectra of  $\alpha$ -pinene pure liquid in the 1300–1600  $\text{cm}^{-1}$  range; and (c) harmonic versus anharmonic VCD spectra of  $\alpha$ -pinene pure liquid in the 2700–3200  $\text{cm}^{-1}$  spectral range. Experimental spectra in the same ranges as those taken from ref 29 are also reported.

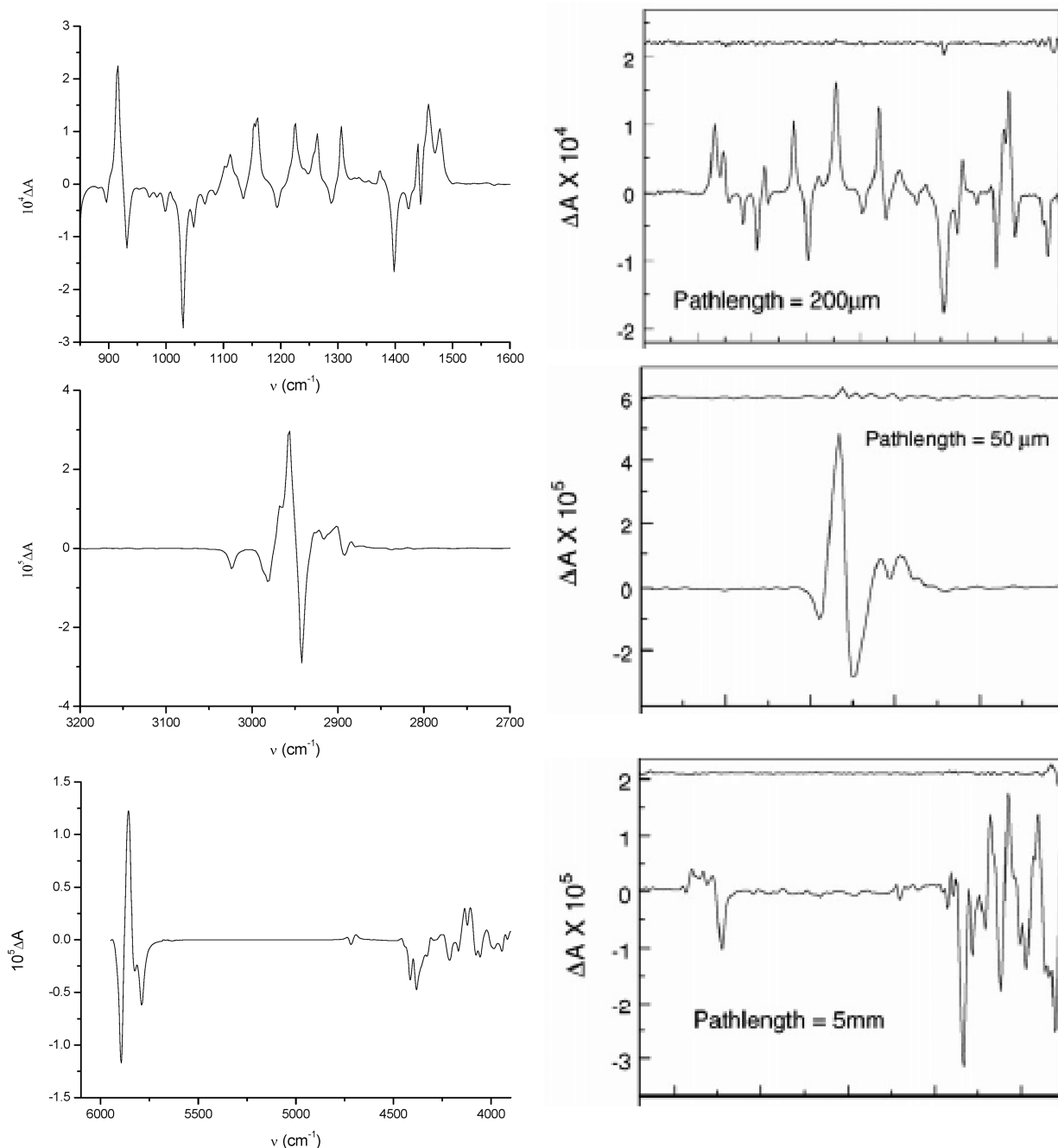
shape). In addition, further investigation is needed to develop proper anharmonic methods for considering resonances, not only on frequencies<sup>34,35</sup> but especially on band intensities.

## COMPUTATIONAL DETAILS

All DFT calculations were carried out with a development version of the Gaussian09 program<sup>36</sup> using the popular B3LYP exchange–correlation functional. Equilibrium geometries and VCD spectra were calculated using the N07D basis set,<sup>37</sup> which has been demonstrated to reliably reproduce absolute anharmonic frequencies for a large set of chemical systems.<sup>31–33</sup> Additional testing with more extensive basis sets (N07Ddiff and N07TDiff)<sup>37</sup> were also performed, giving very similar results.

Solvation effects were accounted for by using the PCM.<sup>14,15</sup> Molecular cavities were built by intersecting spheres centered on each of the atoms, with radii chosen according to G09 default settings. The static and optical dielectric permittivities of  $\text{CCl}_4$  were set to G09 default settings, whereas the following values were employed for pure  $\alpha$ -pinene:  $\epsilon_0 = 2.7$  and  $\epsilon_{\text{opt}} = 2.1462$ . All calculations in solution were preceded by a reoptimization of the molecular geometry in the presence of the polarizable continuum. Local field effects<sup>18</sup> and vibrational nonequilibrium effects<sup>16,17</sup> were included in the calculation. The evaluation of numerical derivatives was performed by setting the displacement equal to 1 pm for both the calculation of dipole and magnetic moment derivatives and cubic/quartic force field components.

The deperturbed VPT2 (DVPT2)<sup>34,35</sup> method is used to treat Fermi and accidental resonances. In such an approach, all



**Figure 4.** Calculated anharmonic VCD spectra of camphor in  $\text{CCl}_4$  solution. Experimental spectra in the same ranges taken from ref 29 are also reported. For drawing the spectrum in the lowest panel,  $\text{HWHM} = 16 \text{ cm}^{-1}$  is used.

terms defined as resonant by means of semiempirical thresholds are discarded. The so-called Martin parameters<sup>34</sup> were used to define the Fermi resonances. For frequencies, terms identified as resonant and consequently removed in the calculations are successively treated variationally. We have further assumed in the present paper that the Martin test is valid also in the case of anharmonic intensities. Further testing as well as the definition of resonance tests for intensities is surely required and is in fact under development in our lab.

Calculated spectra were plotted by assuming Lorentzian band shapes with  $\text{HWHM} = 4 \text{ cm}^{-1}$  if not stated elsewhere. In order to calculate absorbance and  $\Delta A$  values, path length and concentrations taken from ref 29 were used. For pure  $\alpha$ -pinene, a density equal to 0.858 was used to extract the concentration.

## ■ ASSOCIATED CONTENT

### Supporting Information

Formulas of anharmonic transition electric and magnetic dipoles for solvated systems described by means of the PCM. Calculated anharmonic versus harmonic IR absorption spectra of  $\alpha$ -pinene in the gas phase and pure liquid phase in the 800–1600  $\text{cm}^{-1}$  range. Calculated anharmonic VCD spectra of pure liquid  $\alpha$ -pinene in the 3800–6500  $\text{cm}^{-1}$  range. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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## Notes

The authors declare no competing financial interest.

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