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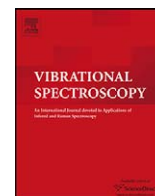


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Conformational landscape in chiral terpenes from vibrational spectroscopy and quantum chemical calculations: S-(+)-carvone

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ABSTRACT

S-(+)-carvone (5-isopropenyl-2-methylcyclohex-2-en-1-one) is the primary component in the oil of caraway. Different experimental and theoretical works reveal that there are two possible conformers in which the isopropenyl group can be in equatorial or axial position. For each one, three rotamers were found theoretically, with the equatorial rotamers around 95% of the whole statistical population. In the current work, from a complete assignment of the IR and Raman spectra and the results obtained from the study of the VCD spectrum of the title compound, the three most stable rotamers have been detected experimentally in the liquid phase for the first time. The present work reveals that IR, Raman and VCD are helpful complementary techniques to characterize flexible systems, as terpenes, which present several conformers.

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1. Introduction

Terpenes are one of the main groups of secondary metabolites in nature (nearly 23,000 have been described), showing a great diversity in structure and activity. They are found as the main components in essential oils and are implicated in almost every interaction existing between plant and animal, plant and plant or plant and microorganisms, showing activity as phytoalexins, insect antifeedants, defence agents, pheromones, signal molecules, etc. [1,2]. In addition, these compounds have important uses as flavourings and perfumes as well as in the production of solvents and adhesives showing, likewise, important biomedical applications and being consumed by humans in their daily diet.

In particular, monoterpenes are components of citrus fruits, olive oil, cherries, spearmint dill, caraway, apricots, grapes and herbs. They show antitumor, antimicrobial and antioxidant activities [1,3–7] and their properties have given rise to works dealing with the study of the relationship molecular structure/activity (see, for example [3,8]). In addition, they are atmospheric pollutants [9,10]. From this point of view, a deep knowledge of the

molecular structure and possible conformers of this type of compounds would be desirable.

The title molecule, S-(+)-carvone (5-isopropenyl-2-methylcyclohex-2-en-1-one, Fig. 1), is the main component in the caraway seed oil while its R-(−)-enantiomer is a component of spearmint. The molecular structure of carvone has been investigated by Egawa et al. [11] by means of gas electron diffraction (G.E.D.) with the aid of MP2/6-31G** and B3LYP/6-31G** calculations and IR spectroscopy. In this study, three stable rotamers with the isopropenyl group in the equatorial position were predicted theoretically as the main structures in the gas phase at 401 K, at the B3LYP level (the three stable axial rotamers are around 7% of the statistical population). However, only the two most stable equatorial rotamers were detected experimentally. Later, in order to detect the third equatorial rotamer in the gas phase, Egawa and Mineyama [12] measured the resonance enhanced multiphoton ionization (REMPI) spectrum of carvone in a supersonic free jet. With the aid of MP2 and CIS calculations the positions of the peaks were assigned and the authors concluded that this compound has three stable rotamers of the equatorial conformer in the S_0 electronic state, though the agreement between experimental and theoretical patterns was not perfect.

In the literature, works dealing with the vibrational study of terpenes are scarce, and for carvone only the above-mentioned by Egawa and Mineyama [12], aimed to support their G.E.D. data, and

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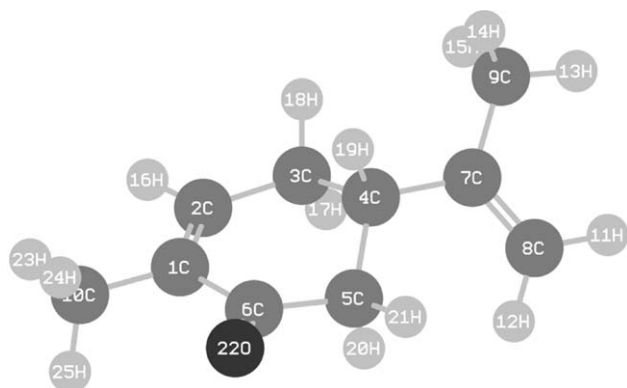


Fig. 1. Molecular structure and atom numbering adopted in this study for the S-(+)-carvone, where the C4 is a chiral atom.

another by Hoffmann [13] have been found. In this last study, an assignment of the vibrational bands to normal modes was proposed using data from recorded IR and Raman spectra in liquid phase combined with theoretical calculations at B3PW91/6-31G* level [13] and a frequency scaling. Experimental spectra are reproduced taking into account only the contributions of the two most stable equatorial rotamers (named in this work CE1 and CE2). In addition, in this work by Hoffmann [13], a comparison between experimental and predicted VCD spectra, at the B3PW91/6-31G* level together with frequency scaling, was carried out for S-(+)-carvone. It is asserted by the author that the addition to theoretical spectrum of the third equatorial rotamer (named CE3), as well as the three axial rotamers, does not further improve the reproduction of the experimental one. In the light of the VCD results, no effort was made to assign bands of the CE3 rotamer.

This latter work is not the only one dealing with the VCD spectrum of carvone in the literature. Thus, in a previous study, the experimental spectrum of S-(+)-carvone was compared by Singh and Keiderling [14] with a theoretical one obtained from the fixed partial charge (FPC) model. Previously, the molecular geometry was calculated from a consistent force field (CFF) energy minimization routine. In this work, two rotamers were found for each axial and equatorial conformer and the experimental spectrum was attributed to one of the equatorial rotamers. Later, a study of its VCD spectrum in the near infrared and visible range was carried out by Abbate et al. [15]. Other references [16–18] report the instrumental developments and applications for these kinds of molecules. Likewise, its spectrum in the mid-IR region was recorded and only shown without any further discussion in two papers in which carvone is considered as a spectral standard [19,20].

In the present work, a reinvestigation of the IR, Raman and VCD spectra of S-(+)-carvone is presented, being the first time that the existence of the three stable rotamers in gas phase of the equatorial conformer, theoretically predicted and tentatively detected using G.E.D., is confirmed experimentally in the liquid phase. For this task, a systematic and detailed study has been carried out for S-(+)-carvone starting from a new theoretical investigation of the molecular structure, possible conformers and rotamers and their relative statistical population in the gas phase, according to the Boltzmann's distribution law. Later, the IR and Raman spectra were newly recorded and, for the first time, the complete assignment of them was done taking into account the three most stable rotamers (i.e., the three equatorial rotamers). For this task, a DFT/B3LYP/cc-pVDZ theoretical calculation together with the scaled quantum mechanical force field (SQMFF) methodology by Fogarasi and Pulay [21] was applied in the vibrational analysis of the title compound. Finally, the VCD spectrum of this chemical species was newly

recorded and, once the vibrational analysis was carried out, a detailed interpretation of it has been done, finding that VCD spectra is a helpful technique in the detection of different rotamers if it is used together with IR and Raman ones.

2. Experimental details

Commercial S-(+)-carvone samples (99%) were purchased from Sigma–Aldrich. The recording of the IR, Raman and VCD spectra has been carried out in the liquid phase without performing any previous purification.

A FT-IR Bruker Vector 22 spectrometer, equipped with a Global source and a DGTS detector, was used to record the IR spectrum in the liquid phase using a standard liquid cell equipped with CsI windows. The IR spectrum has been recorded in the 400–4000 cm^{-1} range with a resolution of 1 cm^{-1} and 200 scans.

The Raman spectrum of S-(+)-carvone has been recorded in the liquid phase using a Bruker RF100/S FT-Raman spectrometer equipped with a Nd:YAG laser (excitation line at 1064 nm) and a Ge detector cooled at liquid nitrogen temperature. The spectra were measured using a standard liquid cell with a resolution of 1 cm^{-1} and 200 scans.

The VCD spectra of the S-(+)-carvone were recorded using a JASCO FVS-4000 FTIR spectrometer equipped with InSb (4000–1900 cm^{-1} , CCl_4 solution) and MCTV (2000–800 cm^{-1} , neat liquid) detectors. All spectra were recorded using a standard cell equipped with BaF_2 windows, with a resolution of 2–8 cm^{-1} , pathlengths between 6 μm and 50 μm and 4000 scans and 16,000 scans.

The baseline correction for the VCD spectra has been made taking into account the two enantiomers (R and S carvone) and making the half-sum of the two VCD spectra. This half-sum means mathematical half-sum, which is $[\Delta A(R) + \Delta A(S)]/2$. With this expression we obtain the baseline that will be subtracted to the raw R and S spectra. This baseline so obtained should be equivalent to the racemate spectrum, and we checked this. Also Figure 1S shows a comparison between the half-sum corrected spectra.

3. Computational details and methods

All the theoretical calculations at the DFT/B3LYP level were carried out using Gaussian03 software package [22].

In the first step, a fixed scan of the potential energy surface (PES) of both axial and equatorial conformers was performed at the B3LYP/6-31G** level of theory along the torsions C8–C7–C4–C3 (rotation of the isopropenyl group with respect to the ring) and H23–C10–C1–C2 (rotation of the methyl group with respect to the ring), keeping constant the rest of structural parameters. The six obtained equilibrium structures, three equatorial and three axial, were then reoptimized at the B3LYP/cc-pVDZ level, the relative energies with the zero point correction (ZPE) were calculated and the molecular statistical Boltzmann populations obtained. In order to perform the analysis of the experimental spectra, the harmonic IR, Raman and VCD spectra of the three rotamers of equatorial conformation of S-(+)-carvone were predicted at the same level of theory. In the calculation of the VCD spectrum, Stephens' theory [23] is used as implemented in Gaussian03. Quantum Chemical calculations give us access to the expected most stable conformations that can be experimentally detected and, on the other hand, to the harmonic spectra which are a useful help in the analysis of experimental spectra.

In order to facilitate the complete assignment and reproduction of the IR and Raman spectra, Pulay's SQMFF methodology [21] was implemented starting from the molecular force field calculated at the B3LYP/cc-pVDZ level and using MOLVIB software [24,25] in such a way that the theoretical values of the wavenumbers of each of the three above mentioned rotamers were fitted to the

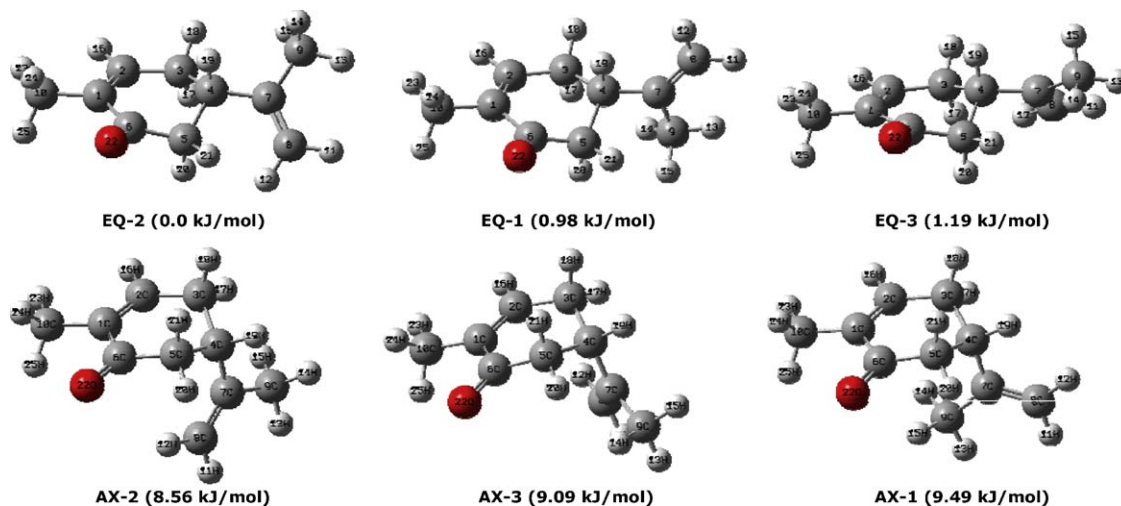


Fig. 2. Structure of the six stable conformers of the S-(+)-carvone obtained at the B3LYP/cc-pVDZ level of theory. Relative energies taking account the ZPE corrections are shown for each one.

experimental ones. With the results from the previous vibrational analysis, the predicted VCD spectrum from the same level of theory and the aid the MakeVCD software by JASCO Inc. [26] the experimental VCD spectrum of S-(+)-carvone was reproduced.

4. Results and discussion

4.1. Theoretical conformational analysis and molecular structure

It is well known that flexible six rings bearing a substituent group in a sp^3 carbon can exist as two conformers, with the group in equatorial or axial position [27], this is what happens for carvone in relation to its isopropenyl group. The fixed scan at the B3LYP/6-31G** level of these two conformers revealed the existence of three rotamers for each one of them, mainly depending on the rotation of the isopropenyl group around the C_4 – C_7 simple bond. The rotation of the methyl group around the C_1 – C_{10} simple bond gave rise to three equivalent conformations. It was found that the eclipsed position of the methyl hydrogen atoms gave the minimal energies in both the equatorial and the axial conformers.

In Fig. 2 are displayed the six optimized equilibrium structures of S-(+)-carvone at the B3LYP/cc-pVDZ level, along with their relative zero point corrected energies. In Table 1S are shown the molecular parameters (in terms of Z-matrix) of these six conformers. For the equatorial rotamers, the torsion angle of the isopropenyl group ($D_5 = C_8$ – C_7 – C_4 – C_3) has the values of 113.95° (EQ-1), 248.19° (EQ-2) and 12.98° (EQ-3). In the case of axial rotamers, these values are 117.31° (AX-1), 240.62° (AX-2) and 346.68° (AX-3). As can be seen in Table 1S, the differences among the rest of the geometrical parameters for the different rotamers are very small.

It was found that the equatorial conformations are more stable than the axial ones, in accordance with previous theoretical and experimental studies [11–13]. Thus, the three equatorial conformations have energies within 1.2 kJ mol^{-1} (with EQ-1 0.98 kJ mol^{-1} and EQ-3 1.19 kJ mol^{-1} higher in energy than EQ-2) and the three axial conformations are over 8 kJ mol^{-1} (with AX-2 8.56 kJ mol^{-1} , AX-3 9.09 kJ mol^{-1} and AX-1 9.49 kJ mol^{-1} higher in energy than EQ-2). From the calculated energies at the B3LYP/cc-pVDZ level of theory with the ZPE correction, and if the Boltzmann's distribution is supposed to be a good approach, we obtain that at room temperature (298 K) more than 95% of the total population are due to the three equatorial rotamers (Table 1, around 42% of EQ-2, 28% of EQ-1 and 26% of EQ-3). It means that all

of these three equatorial rotamers should be experimentally detected at room temperature, in accordance with reference [12].

4.2. Vibrational study

4.2.1. Theoretical and experimental data

As mentioned above, works dealing with the molecular structure and vibrational spectra of terpenes are scarce in literature. Nevertheless, the molecular structure and vibrational spectra of the cyclohexene molecule have been studied from both the theoretical and experimental points of view [28–37] and there is a work dealing with the IR spectrum of isopropenyl group in different molecular systems [38].

Carvone has $3N - 6 = 3 \times 25 - 6 = 69$ vibrational normal modes belonging to the unique irreducible representation (A) of its symmetry point group, C_1 . Recorded IR and Raman spectra of S-(+)-carvone are displayed in Fig. 3 and relevant data therefrom (frequencies and relative intensities) are collected in Table 2. In Table 2S are shown the theoretical (B3LYP/cc-pVDZ) vibrational wavenumbers, infrared intensities and Raman activities for the three equatorial rotamers (EQ-1, EQ-2 and EQ-3) experimentally detected of S-(+)-carvone. In Table 3 are shown the theoretical, scaled and experimental wavenumbers of the three equatorial rotamers. The scaled wavenumbers were obtained using the SQMFF methodology by Fogarasi and Pulay [21]. For this task, the Cartesian Hessian obtained from the DFT calculation was transformed into a new Hessian in terms of Pulay's natural

Table 1

Calculated dihedral angle C_8 – C_7 – C_4 – C_3 , electric dipole moments (μ), relative energies without ZPE correction (ΔE_e), relative energies with ZPE correction (ΔE_0) and the corresponding Boltzmann populations of the three equatorial conformers and the three axial conformers of S-(+)-carvone at the B3LYP/cc-pVDZ level of theory.

Conformer	Gas phase				
	$\tau_{(C_8-C_7-C_4-C_3)}$ (degrees)	μ (Debye)	ΔE_e (kJ mol^{-1})	ΔE_0 (kJ mol^{-1})	% population ^a
EQ-2	248.19	3.1	0.00	0.00	42.20
EQ-1	113.95	3.3	0.93	0.98	28.36
EQ-3	12.98	2.7	0.98	1.19	26.11
AX-2	240.62	3.5	7.88	8.56	1.33
AX-3	346.68	3.0	8.68	9.09	1.08
AX-1	117.31	3.0	9.06	9.49	0.91

^a Boltzmann population from ΔE_0 taking $T = 298.16 \text{ K}$.

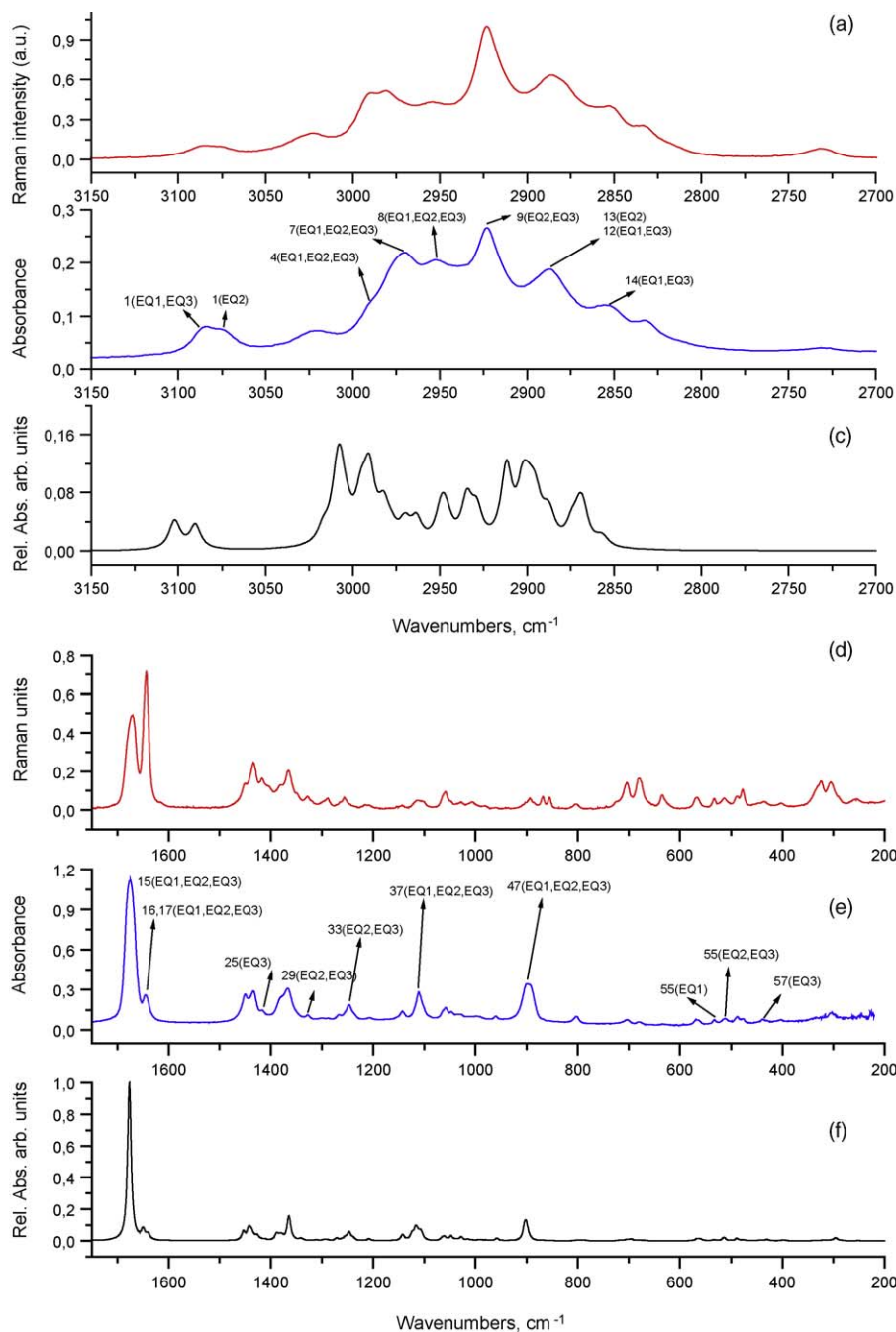


Fig. 3. Experimental IR and Raman spectra compared with predicted scaled spectrum for the S-(+)-carvone in the C–H stretching region (a) and in the intermediate region (d): (a and d) experimental Raman spectrum (resolution of 1 cm^{-1} and 200 scans); (b and e) experimental IR spectrum (resolution of 1 cm^{-1} and 200 scans); (c and f) sum of the predicted scaled IR spectra of the three most stable conformers (EQ-1, EQ-2 and EQ-3) taking into account their contributions according to Boltzmann's populations at 298.16 K (pitch = 1 cm^{-1} and FWHM = 8 cm^{-1}).

internal coordinates [21]. Afterwards, with MOLVIB software [24,25] the theoretical wavenumbers were fitted to the experimental ones by means of a refinement process of the scale factors associated with the natural internal coordinates. In the first step, we applied the Pulay's scale factors [39] to the calculated force field at the B3LYP/6-31G* level of theory to achieve the first assignment of our experimental spectra taking into account the three most stable rotamers (the equatorial ones). In order to carry out a more complete and reliable assignment of the IR and Raman spectra of carvone, in the second step we have calculated the vibrational spectra of these rotamers at the B3LYP/cc-pVDZ level and for each of them, one set of scaling factors was obtained comparing the

experimental and the theoretical spectra. In this new scaling procedure, all starting factors were set to 1.000 and refined to obtain the best fit to the experimental wavenumbers. If the assignment is done in a suitable way, scale factors for each rotamer must be consistent among them, as happened. Afterwards, we obtain an averaged set that reproduces in a suitable way (RMS around 5 cm^{-1}) the spectra of the three rotamers experimentally detected, and in Fig. 3a and b we present a weighted sum scaled spectrum using only the averaged set. In the refinement procedure, experimental bands mainly coming from IR spectrum of the liquid phase were taken into account. When the IR bands were not present Raman bands were used.

Table 2

Experimental IR and Raman bands of S-(+)-carvone in the liquid phase.

IR liquid	Relative intensity	Raman liquid	Relative intensity	IR liquid	Relative intensity	Raman liquid	Relative intensity
3085	W	3087	W	1058	M	1058	VW
3076	W	3077	VW	1048	W	–	–
3021	W	3023	W	1036	W	–	–
–	–	2989	M	1029	W	1029	VW
–	–	2981	M	1014	W	–	–
2971	M	–	–	–	–	1004	VW
2953	M	2954	M	998	W	–	–
–	–	2942	SH	–	–	981	VW
2923	M	2923	VS	960	W	–	–
2887	M	2886	S	901	M	–	–
2855	W	2853	M	894	M	894	VW
2832	W	2834	W	–	–	886	VW
2728	VW	2732	VW	–	–	868	VW
1794	W	–	–	855	W	855	VW
1676	VS	1671	M	841	W	–	–
1645	M	1643	S	803	W	804	VW
1450	M	1450	W	727	W	724	VW
1434	M	1434	W	704	W	704	W
1417	M	1418	W	680	W	680	W
–	–	1402	W	635	W	635	VW
–	–	1379	W	565	W	566	VW
1367	M	1365	W	533	W	533	VW
–	–	1349	VW	512	W	513	VW
1328	W	1328	VW	488	W	487	VW
–	–	1313	VW	477	W	477	W
1300	W	–	–	–	–	446	VW
1288	W	1289	VW	439	W	–	–
1267	W	–	–	–	–	431	VW
–	–	1255	VW	403	W	402	VW
1247	M	–	–	–	–	331	SH
–	–	1238	VW	–	–	324	W
–	–	1216	VW	–	–	304	W
1206	W	1205	VW	–	–	290	VW
–	–	1153	VW	–	–	255	VW
1143	W	1142	VW	–	–	171	W
1111	M	1113	VW	–	–	–	–
–	–	1063	VW	–	–	–	–

VS=very strong, S=strong, M=medium, W=weak, VW=very weak, and SH=shoulder.

Table 3Scaled and experimental vibrational wavenumbers of S-(+)-carvone in the most relevant spectral regions. **t.**

Exp.	EQ-1 ^a	EQ-2 ^a	EQ-3 ^a
3085	3102.9 (1)	–	3099.4 (1)
3076	–	3092.2 (1)	–
3021	3017.1 (2)	–	3014.8 (2)
3017	–	3009.7 (2)	–
1676	1676.2 (15)	1676.2 (15)	1676.3 (15)
1645	1649.4 (16)	1649.1 (16)	1650.6 (16)
–	1641.2 (17)	1640.8 (17)	1639.5 (17)
–	1389.3 (25)	1388.1 (25)	–
1402	–	–	1393.9 (25)
–	1338.6 (29)	–	–
1349	–	1346.4 (29)	–
1328	–	–	1329.2 (29)
1313	–	–	30, 1312.0 (30)
1300	1300.4 (30)	1298.6 (30)	–
1029	–	1029.4 (41)	1027.6 (41)
1014	1014.1 (41)	–	–
1004	–	1005.3 (42)	–
998	994.6 (42)	–	–
981	978.0 (43)	979.5 (43)	988.3 (42)
–	–	–	981.7 (43)
533	532.9 (55)	–	–
512	–	513.3 (55)	516.1 (55)
477	475.4 (57)	478.4 (57)	–
446	–	–	444.3 (57)
439	–	–	437.8 (58)
431	–	429.9 (58)	–
403	397.3 (58)	–	–

^a Scaled wavenumber value from the DFT calculations (normal mode).

The predicted theoretical spectra after the scaling procedure, taking into account the relative population of the three equatorial rotamers in gas phase, are displayed in Fig. 3. In Table 3S is shown the description from the potential energy distribution (PED) matrix of each normal mode.

The root mean square (r.m.s.) obtained for the difference between the experimental and theoretical (after the refinement) wavenumber values of S-(+)-carvone using these scaling factors is 4.95 cm⁻¹, with the individual r.m.s. for each rotamer 4.42 cm⁻¹ (EQ-1), 5.55 cm⁻¹ (EQ-2) and 4.89 cm⁻¹ (EQ-3).

4.2.2. Vibrational assignment

As can be seen, S-(+)-carvone displays rather complexes IR and Raman spectra. For clarity, the vibrational assignment is discussed dividing the complete mid-IR spectral range into several zones. For the discussion below, we will comment the most relevant features that improve the previous assignment by Hoffman [13].

4.2.2.1. C–H stretching region. This region is very complex even for the cyclohexene molecule [28–37] and Fermi resonances between methylene C–H bonds stretching and combinations involving low-wavenumber modes are described for this region [37]. One of these Fermi resonances in carvone spectra could be assigned to the experimental band observed at 2833 cm⁻¹ in its IR and Raman spectra, in accordance with that observed by us for limonene, where this band appears near 2836 cm⁻¹ in the IR and Raman spectra [40].

The four bands appearing at higher wavenumbers, 3085 cm⁻¹ (IR, Raman), 3076 cm⁻¹ (IR, Raman), 3021 cm⁻¹ (IR, Raman) and 3017 cm⁻¹ (IR) (Tables 2 and 3), are assigned to the C–H stretchings of the vinyl group and of the C–C double bond in the ring. These bands are appointed to the first two normal modes of the three equatorial rotamers, whose scaled values are: 3102.9 cm⁻¹ and 3017.1 cm⁻¹ for EQ-1, 3092.2 cm⁻¹ and 3009.7 cm⁻¹ for EQ-2 and 3099.4 cm⁻¹ and 3014.8 cm⁻¹ for EQ-3. The normal mode 3 is not observed and its scaled value is 3007.3 cm⁻¹ (EQ-1), 3005.3 cm⁻¹ (EQ-2) and 3007.7 cm⁻¹ (EQ-3).

As can be seen from the PED matrix (Table 3S), for rotamers EQ-1 and EQ-3 the normal modes 1 and 2 are described as the asymmetric and symmetric C–H stretching of the vinyl group, respectively, and the normal mode 3 is described as the C–H stretching of the double C–C bond in the ring. In the case of rotamer EQ-2 a change is produced, with the normal modes 1 and 3 described as the asymmetric and symmetric C–H stretchings of the vinyl group, respectively, and the normal mode 2 described as the C–H stretching of the double C–C bond in the ring. This is general and common along the vibrational spectral range. They are also common in the same type of terpenoids like limonene [40] and perillaldehyde [41].

This is the first time that the complete assignment of the IR and Raman spectra of the carvone molecule is made taking into account the three equatorial rotamers, in contrast with the previous work by Hoffman [13], where only two rotamers (EQ-2 and EQ-1) of those three were took into account.

Because of the great overlapping present in this zone, some normal modes that should appear there could not be assigned from the IR and Raman spectra. This is the case of normal modes 3, 4, 11 for all the rotamers (EQ-1, EQ-2 and EQ-3), 10 and 13 for EQ-1, 12 and 14 for EQ-2 and 13 for EQ-3. For these normal modes, we are only able to know the scaled wavenumbers values from the SQMFF procedure starting from the DFT theoretical calculations (see Table 3).

4.2.2.2. Intermediate vibrational region. This is the spectral zone from 1700 cm⁻¹ to 400 cm⁻¹. The band with the highest wavenumber in this zone, observed at 1676 cm⁻¹, is assigned to the C=O bond stretching of the carbonyl group in all the rotamers (normal mode 15), with a contribution around 75% from the PED. The band observed at 1645 cm⁻¹ is assigned to the normal modes 14 and 13, that are described as the C=C bond stretching vibrations of the vinyl group (mode 14) and in the ring (mode 13). In both cases these movements appear mixed with others in all the three rotamers, as obtained from the PED (Table 3S).

The rest of normal modes in this region present a complex description from the PED and are described as vibrations due to methylene groups, mixed in some extent with other vibrations due to the ring, carbonyl group, C–C bonds, and vibrations of the substituent isopropenyl and methyl groups, in good agreement with the previous assignment on cyclohexene molecule [27,29,31,36].

As can be seen in Table 3S, descriptions of some normal modes can change from one rotamer to another. There are different rearrangements of normal modes, similar to described above in the C–H stretching spectral region, depending on the rotamer. For example, we could comment, among others, the normal modes 45–47 for which the description from the PED matrix (Table 3S) is almost the same for EQ-1 and EQ-2: normal mode 45 is the vinyl wagging and normal modes 46 and 47 present a mixed description (C–C stretching, methyl rocking and C–H wagging of the chiral atom). Nevertheless, the vinyl wagging is normal mode 46 in EQ-3, being the mixed movements the normal modes 45 and 47.

In this zone we can find examples of the presence of the three conformers in the liquid phase. As can be seen in Table 3, normal

mode 42 is assigned to different experimental bands depending on the rotamer, i.e., at 998 cm⁻¹ (EQ-1, scaled value at 994.6 cm⁻¹), at 1004 cm⁻¹ (EQ-2, scaled value at 1005.3 cm⁻¹) and at 981 cm⁻¹ (EQ-3, scaled value at 981.7 cm⁻¹). In addition, normal mode 58 is assigned to the experimental bands at 403 cm⁻¹ (EQ-1, scaled value at 397.3 cm⁻¹), 431 cm⁻¹ (EQ-2, scaled value at 429.9 cm⁻¹) and 439 cm⁻¹ (EQ-3, scaled value at 437.8 cm⁻¹).

Finally, some experimental bands can be found that are only assigned to normal modes of rotamers that are in a minority, i.e. EQ-1 and EQ-3. Experimental bands that are only assigned to normal modes of EQ-1 are, for example, the band at 1238 cm⁻¹ (normal mode 33, scaled value at 1239.0 cm⁻¹), at 1014 cm⁻¹ (normal mode 41, scaled value at 1014.1 cm⁻¹), and at 533 cm⁻¹ (normal mode 55, scaled value at 532.9 cm⁻¹). In the same way, experimental bands that are only assigned to normal modes of EQ-3 are, for example, the band at 1402 cm⁻¹ (normal mode 25, scaled value at 1393.4 cm⁻¹), at 1328 cm⁻¹ (normal mode 29, scaled value at 1329.2 cm⁻¹), at 1313 cm⁻¹ (normal mode 30, scaled value at 1312.0 cm⁻¹) and at 446 cm⁻¹ (normal mode 57, scaled value at 444.3 cm⁻¹).

4.2.2.3. Low-frequency vibration region. The third region into study corresponds to vibrations below 400 cm⁻¹. As in the previous region, normal modes present a complex description from the PED analysis (Table 3S), where waggings, rockings, torsions of the substituent groups and of the ring, and ring deformations appear mixed to some extent. The only one normal mode with a pure description is that numbered as 66 which is the torsion of the methyl group attached to the ring in all the equatorial rotamers. This normal mode is not observed and its scaled values are (see Table 3S) 152.9 cm⁻¹ (EQ-1), 154.8 cm⁻¹ (EQ-2) and 152.3 cm⁻¹ (EQ-3).

4.3. Vibrational circular dichroism (VCD) spectrum

Interpretation of the VCD spectral features of medium size compounds, with additional conformational flexibility, as that studied in this work is a difficult and complicated task. Our study reveals that a previous vibrational analysis for them, from IR and Raman data and quantum chemical calculations (including SQMFF methodology) together with the availability of VCD experimental and theoretical data could result helpful for it and then for a better conformational landscape in flexible chiral molecules, as the terpene here studied.

Once the vibrational analysis has been made and the IR and Raman spectra of carvone have been assigned and reproduced applying the SQMFF methodology to the DFT/B3LYP/cc-pVDZ calculations accomplished for it, the VCD spectrum of neat liquid S-(+)-carvone is analysed and reproduced. Following the previous section, the spectral range analysed is divided into two regions for clarity.

4.3.1. C–H stretching region

In Fig. 4 is displayed the experimental VCD spectrum along with theoretical predicted ones for each rotamer and the sum spectrum taking into account scaled wavenumbers from the vibrational analysis and theoretical rotator strengths at the B3LYP/cc-pVDZ level. As can be seen, bearing in mind that theoretical calculations are done into the harmonic approximation and the value of the r.m.s. obtained in the wavenumber scaling procedure, the shape of the experimental spectrum is reproduced to a suitable extent.

An issue showing the complexity in the interpretation of VCD spectra of terpenes could be, for example, the change in the sign of the rotator strength of a normal mode depending of the rotamer. Thus, for instance, normal mode 1 in carvone, i.e., the asymmetric C–H stretching of the vinyl group, according to our normal mode

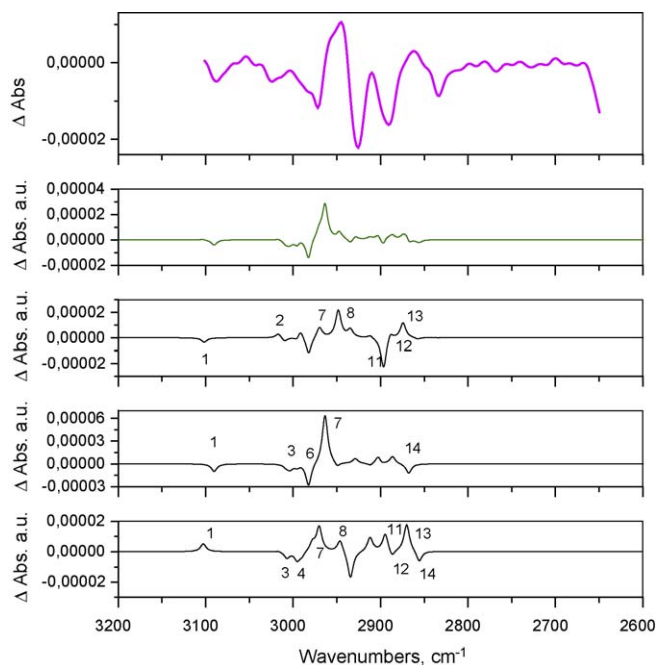


Fig. 4. Experimental and theoretical VCD spectra of S-(+)-carvone in the 3200–2600 cm^{-1} region: (a) experimental spectrum (CCl_4 solution, 5000 scans, 8 cm^{-1} of resolution, spacer of $100 \mu\text{m}$), baseline corrected VCD spectrum taking into account the R species; (b) sum of the predicted scaled spectra of the three most stable conformers (EQ-3c, EQ-2d and EQ-1e) taking into account their contributions according to Boltzmann's populations at 298.16 K. Parameters for the predicted VCD spectra: pitch = 1 cm^{-1} and FWHM = 8 cm^{-1} .

analysis in the three equatorial rotamers, shows a rotator strength value of $4.5663 \times 10^{-44} \text{ esu}^2 \text{ cm}^2$ in EQ-1, $-8.8639 \times 10^{-44} \text{ esu}^2 \text{ cm}^2$ in EQ-2 and $-3.0476 \times 10^{-44} \text{ esu}^2 \text{ cm}^2$ in EQ-3, that produce the shape of the spectrum in this region (Fig. 4 and Table 2S). In addition, the rearrangement of normal modes described above must be taken into account.

In this spectral region, normal modes that could not be observed in the IR and Raman spectra can be evidenced now. For example, the negative band at 3008 cm^{-1} in the VCD spectrum of S-(+)-carvone can be assigned to the normal mode 3 in all the rotamers (scaled values at 3007.1 cm^{-1} for EQ-1, at 3005.3 cm^{-1} for EQ-2 and at 3007.7 cm^{-1} for EQ-3). The description for this normal mode is the symmetric C–H stretching of the vinyl group for EQ-2 and the C–H stretching of the C–C double bond in the ring for EQ-1 and EQ-3.

Other normal mode that is evidenced for the three equatorial rotamers from the experimental VCD spectrum is the normal mode 4 (scaled values at 2995.5 cm^{-1} for EQ-1, at 2997.3 cm^{-1} for EQ-2 and at 2993.1 cm^{-1} for EQ-3, see Table 3 for description). The positive experimental band at 2989 cm^{-1} can be assigned to this normal mode 5. In the same way, there is a shoulder at 2910 cm^{-1} that can be assigned to the normal mode 10 (scaled values at 2912.4 cm^{-1} for EQ-1, at 2913.5 cm^{-1} for EQ-2 and at 2910.0 cm^{-1} for EQ-3). Other experimental band is the positive one at 2899 cm^{-1} , assigned to normal mode 11 (scaled values at 2895.0 cm^{-1} for EQ-1, at 2904.4 cm^{-1} for EQ-2 and at 2894.7 cm^{-1} for EQ-3).

In addition, to reproduce in a suitable way the experimental spectral profile of the $3090\text{--}2880 \text{ cm}^{-1}$ region, the three rotamers have to be taken into account, being this fact a proof of the presence of the three rotamers in the liquid phase, in accordance with the results from the vibrational analysis and the new bands that can be observed using the VCD technique.

Finally, in our vibrational analysis it is shown that in the region below 2850 cm^{-1} appears a Fermi resonance (centred at

2833 cm^{-1}). As our calculations are done under the harmonic approach, the VCD spectral below 2850 cm^{-1} cannot be reproduced.

4.3.2. Intermediate vibrational region

Because of the presence of possible artefacts due to the high infrared absorption in this region, higher than suitable to obtain a reliable VCD spectrum working with the neat liquid, only the $1500\text{--}900 \text{ cm}^{-1}$ zone, can be studied. In Fig. 5 is displayed the experimental spectrum along with the predicted spectra for each rotamer and the sum spectrum, taking into account previous results from our vibrational analysis, and theoretical rotator strengths at the B3LYP/cc-pVDZ level (see Table 2S).

As in the C–H stretching region, some VCD bands change its shape from a rotamer to another (Fig. 5), due to changes in the sign and absolute value of the rotator strength of the same normal mode in different rotamers (Table 2S). For example, normal mode 44, assigned to the experimental band at 960 cm^{-1} , have a value of its rotator strength of $13.40 \times 10^{-44} \text{ esu}^2 \text{ cm}^2$ in EQ-1, $7.17 \times 10^{-44} \text{ esu}^2 \text{ cm}^2$ in EQ-2 and $9.93 \times 10^{-44} \text{ esu}^2 \text{ cm}^2$ in EQ-3. Thus, an adequate theoretical reproduction of this band is only possible when the contributions of the three conformers are accounted.

Also in the C–H stretching region, the VCD spectrum gives us the possibility to detect experimentally a normal mode that could not be evidenced in the IR and Raman spectra. That is the case of normal mode 28 of EQ-2, that can be related to the negative VCD band observed at 1360 cm^{-1} .

The shape of the spectrum near 1300 cm^{-1} (normal modes 30 and 31) is reproduced only if the three rotamers and the shifting in the wavenumbers are taken into account, in agreement with our vibrational analysis and in contrast with the results by Hoffmann [13].

In our study, different couplets are theoretically predicted as due to the contribution of the three rotamers and not only to the contribution of two of them. An example is the couplet at

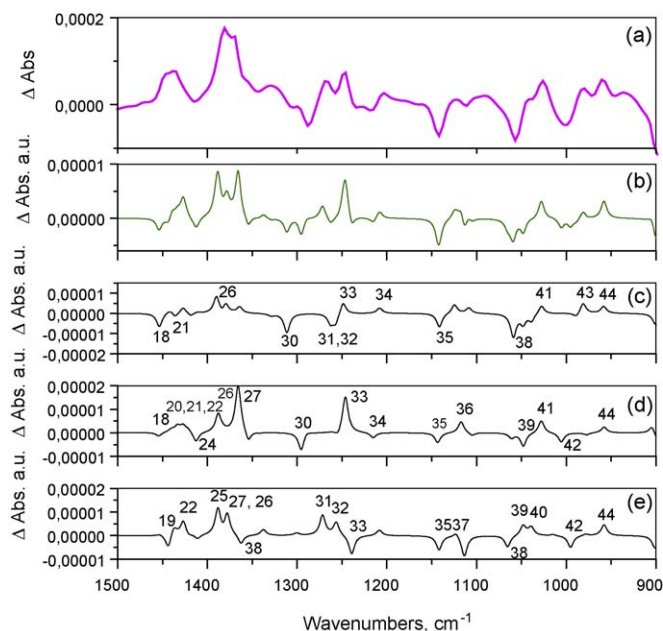


Fig. 5. Experimental and theoretical VCD spectra of S-(+)-carvone in the $1500\text{--}900 \text{ cm}^{-1}$ region: (a) experimental spectrum (neat liquid, 7000 scans, 4 cm^{-1} of resolution, spacer of $15 \mu\text{m}$), baseline corrected VCD spectrum taking into account the R species; (b) sum of the predicted scaled spectra of the three most stable conformers (EQ-1, EQ-2 and EQ-3) taking into account their contributions according to Boltzmann's populations at 298.16 K; (c–e) predicted scaled spectra of the conformers EQ-3, EQ-2 and EQ-1 respectively. Parameters for the predicted VCD spectra: pitch = 1 cm^{-1} and FWHM = 8 cm^{-1} .

1110 cm⁻¹ (normal modes 41 and 42). In this case, the rotational strength for the three rotamers is negative for normal mode 41 and positive for normal mode 42. Another couplet is centred at 1210 cm⁻¹ and, in this case, it is due to the same normal mode (mode 34) which changes the sign of the rotator strength in EQ-2 with respect to EQ-1 and EQ-3.

Finally, because of theoretical calculations are done in the harmonic approximation and in this approach overtones and combination bands have not sense, some bands appearing in the recorded VCD spectrum in the two regions into study which could be assigned to them, are not predicted from the theoretical calculations after the scaling procedure. In any case, for a better knowledge of their nature, these bands should be compared with those similar in molecular systems with a comparable structure.

5. Conclusions

A systematic and detailed structural and vibrational study of the most stable conformers and rotamers of S-(+)-carvone has been made. The analysis of the IR, Raman and VCD spectra concludes, for the first time, the presence of the three stable rotamers of the equatorial conformer of the S-(+)-carvone in the liquid phase.

As concerns the relative statistical population theoretically predicted and the IR, Raman and VCD spectra, there is a good agreement between observed and theoretical spectra.

The analysis of the VCD spectrum reveals a great complexity of it due to different factors. In order to reproduce the VCD experimental spectrum, and in agreement with the vibrational analysis, the three stable equatorial rotamers must be taken into account.

The present work reveals that IR, Raman and VCD are complementary techniques in order to characterize chiral flexible systems which present several conformers.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.vibspec.2009.08.007.

References

- [1] K.-H. Wagner, I. Elmadfa, *Ann. Nutr. Metab.* 47 (2003) 95.
- [2] V.M. Dembitsky, *Lipids* 41 (1) (2006) 1.
- [3] P.L. Crowell, Z. Ren, S. Lin, E. Vedejs, M.N. Gould, *Biochem. Pharmacol.* 47 (8) (1994) 1405.
- [4] G. Ruberto, M.T. Baratta, *Food Chem.* 69 (2000) 167.
- [5] P. McGeady, D.L. Wansley, D.A. Logan, *J. Nat. Prod.* 65 (7) (2002) 953.
- [6] H. Özer, M. Sökmen, M. Güllüce, A. Adigüzel, F. Şahin, A. Sökmen, H. Kiliç, Ö. Bariş, *J. Agric. Food Chem.* 55 (3) (2007) 937.
- [7] A. Wei, T. Shibamoto, *J. Agric. Food Chem.* 55 (5) (2007) 1737.
- [8] M. Chastrette, E. Rallet, *Flavour Frag. J.* 13 (1998) 5.
- [9] A. Calogirou, B.R. Larsen, D. Kotzias, *Atmos. Environ.* 33 (1999) 1423.
- [10] F.M.N. Nunes, M.C.C. Veloso, P.A. de, P. Pereira, J.B. de Andrade, *Atmos. Environ.* 39 (2005) 7715.
- [11] T. Egawa, Y. Kachi, T. Takeshima, H. Takeuchi, S. Konaka, *J. Mol. Struct.* 658 (2003) 241.
- [12] M. Mineyama, T. Egawa, *J. Mol. Struct.* 734 (2005) 61.
- [13] G.G. Hoffmann, *J. Mol. Struct.* 661–662 (2003) 525.
- [14] R.D. Singh, T.A. Keiderling, *J. Am. Chem. Soc.* 103 (9) (1981) 2387.
- [15] S. Abbate, G. Longhi, S. Boladjiev, D.A. Lightner, C. Bertucci, P. Salvadori, *Enantiomer* 3 (1998) 337.
- [16] E. Castiglioni, F. Lebon, G. Longhi, S. Abbate, *Enantiomer* 7 (2002) 161.
- [17] L.A. Nafie, R.K. Dukor, J.R. Roy, A. Rilling, X. Cao, H. Buijs, *Appl. Spectrosc.* 57 (2003) 1245.
- [18] X. Cao, R.D. Shah, R.K. Dukor, C. Guo, T.B. Freedman, L.A. Nafie, *Appl. Spectrosc.* 58 (2004) 1057.
- [19] E.D. Lipp, C.G. Zimba, L.A. Nafie, *Chem. Phys. Lett.* 90 (1982) 1.
- [20] C. Guo, R.D. Shah, R.K. Dukor, T.B. Freedman, X. Cao, L.A. Nafie, *Vib. Spectrosc.* 42 (2006) 254.
- [21] G. Fogarasi, P. Pulay, Ab initio calculation of force fields and vibrational spectra, in: J.E. Durig (Ed.), *Vibrational Spectra and Structure*, vol. 14, Elsevier, 1985 Chapter 3.
- [22] M.J. Frisch, et al., GAUSSIAN03, Revision B.04, Gaussian, Inc., Wallingford, CT, 2004.
- [23] J.R. Cheeseman, M.J. Frisch, F.J. Devlin, P.J. Stephens, *Chem. Phys. Lett.* 252 (1996) 211.
- [24] T. Sundius, *J. Mol. Struct.* 218 (1990) 321.
- [25] T. Sundius, *Vib. Spectrosc.* 29 (1–2) (2002) 89.
- [26] Jasco Spectra Manager for Windows™.
- [27] R.T. Morrison, R.N. Boyd, *Organic Chemistry*, 6th Edition, Prentice Hall, 1992, , ISBN: 0-13-643669-2.
- [28] N. Neto, C. Di Lauro, E. Castellucci, S. Califano, *Spectrochim. Acta A* 23 (1967) 1763.
- [29] F.R. Jensen, C.H. Bushweller, *J. Am. Chem. Soc.* 91 (21) (1969) 5774.
- [30] G. Davidovics, M. Monnier, J.P. Aycard, C. R. Acad. Sci. Paris C 285 (1977) 233.
- [31] R. Lauricella, J. Kéchayan, H. Bodot, *J. Org. Chem.* 52 (1987) 1577.
- [32] J. Haines, D.F.R. Gilson, *Can. J. Chem.* 67 (1989) 941.
- [33] V.E. Rivera-Gaines, S.J. Leibowitz, J. Laane, *J. Am. Chem. Soc.* 113 (26) (1991) 9735.
- [34] L. Lespade, S. Rodin, D. Cavagnat, S. Abbate, *J. Phys. Chem.* 97 (1993) 6134.
- [35] R.P. Johnson, K.J. DiRico, *J. Org. Chem.* 60 (1995) 1074.
- [36] C. Lapouge, D. Cavagnat, D. Gorse, M. Pesquer, *J. Phys. Chem.* 99 (1995) 2996.
- [37] S. Rodin-Bercion, L. Lespade, D. Cavagnat, J.C. Cornut, *J. Mol. Struct.* 526 (2000) 343.
- [38] Grimm A. Kolbe, *Spectrochim. Acta A* 24 (1968) 1697.
- [39] G. Rauhut, P. Pulay, *J. Phys. Chem.* 99 (1995) 3093; G. Rauhut, P. Pulay, Erratum: *J. Phys. Chem.* 99 (39) (1995) 14572.
- [40] F. Partal Ureña, J.R. Avilés Moreno, J.J. López González, *Tetrahedron Asym.* 20 (2009) 89–97.
- [41] F. Partal Ureña, J.R. Avilés Moreno, J.J. López González, *J. Phys. Chem. A* 112 (2008) 7887–7893.