Conformational Flexibility in Terpenes: Vibrational Circular Dichroism (VCD), Infrared and Raman Study of *S*-(−)-Perillaldehyde

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S-(−)-Perillaldehyde (4-isopropenylcyclohex-1-ene-1-carbaldehyde) is a secondary metabolite and an atmospheric pollutant obtained from the oxidation of other terpenes, as limonene and α-pinene, among others. For the first time, a study of the molecular structure and the infrared and Raman spectra of this chemical is presented. Theoretical calculations reveal the existence of two conformers depending on the position of the isopropenyl group (axial and equatorial) and twelve rotamers (six equatorials and six axials), being three of these equatorial rotamers the most stable (ca. 93%). A complete and reliable assignment of the IR and Raman spectra of the title compound is made, taking into account these three last rotamers, and the results are used to carry out a detailed interpretation, for the first time to our knowledge, of the VCD spectrum of this compound in the 1500−900 cm^{-1} region.

1. Introduction

Terpenes are the main components in essential oils and show a great diversity in structure and bioactivity.[1−8] In addition, they are atmospheric pollutants.[9−11] Hence, a deep knowledge of the molecular structure and possible conformers of this type of compounds would be desirable.[12,13] The title molecule, *S*-(−)-perillaldehyde (4-isopropenylcyclohex-1-ene-1-carbaldehyde, Figure 1), is found in the perennial herb perilla, being the most common species *Perilla frutescens* var. japonica or shiso.[13] Chemically, it is a monoterpene containing an aldehyde functional group.

In the literature, works dealing with the vibrational study of terpenes are scarce, and for perillaldehyde, to the best of our knowledge, there are no works dealing with its molecular structure and vibrational spectra. About the VCD spectrum of the title species, one work dealing with its NIR-VCD spectrum is found[14] where bisignate couplets are observed and ascribed to overtones associated with C−H stretching vibrations. In that work, the presence of such couplets is interpreted in terms of normal-mode versus local-mode behavior.

In the present work, a study of the molecular structure, IR, Raman and VCD spectra of *S*-(−)-perillaldehyde is presented for the first time. For this task, a systematic and detailed study has been carried out starting from a theoretical investigation of the molecular structure, possible conformers and rotamers and the relative abundance of these in the gas phase (Figure 2 and Figure 3), according to the Boltzmann distribution. Later, the IR and Raman spectra were recorded and the complete assignment of them was done by taking into account the three most stable rotamers (i.e., the three most stable equatorial rotamers). For this task, DFT/B3LYP/cc-pVDZ theoretical calculations combined with the scaled quantum mechanical force field (SQMFF) methodology by Pulay et al.[15] was applied in the vibrational analysis of the title compound. Finally, the VCD spectrum of this chemical was recorded and, once the vibrational analysis was carried out, a detailed and reliable interpretation of it was done.

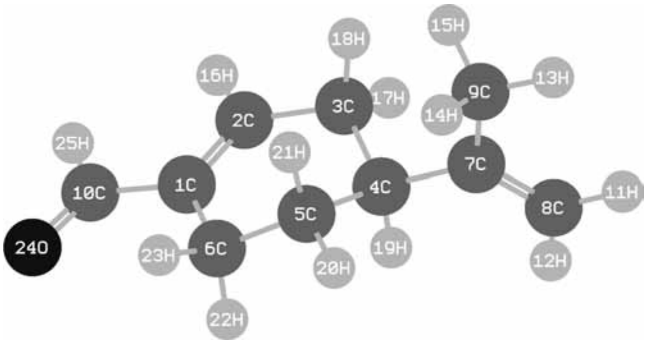

Figure 1. Molecular structure and atom numbering adopted in this study for the *S*-(−)-perillaldehyde, where the C4 is a chiral atom.

2. Experimental Details

Commercial *S*-(−)-perillaldehyde samples (99%) were purchased from Sigma-Aldrich. The recording of the IR, Raman and VCD spectra have been carried out in the liquid phase without performing any previous treatment and purification.

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

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

The VCD spectra of the *S*-(−)-perillaldehyde in the liquid phase were recorded by using a JASCO FVS-4000 FTIR spectrometer equipped with a InSb detector (4000−1900 cm^{-1}) and a MCTV detector (2000−800 cm^{-1}). All spectra were recorded in the neat liquid phase by using a standard cell equipped with BaF2 windows, with a resolution of 2−4 cm^{-1}, with a spacer between 6−50 μm and 4000−16000 scans.

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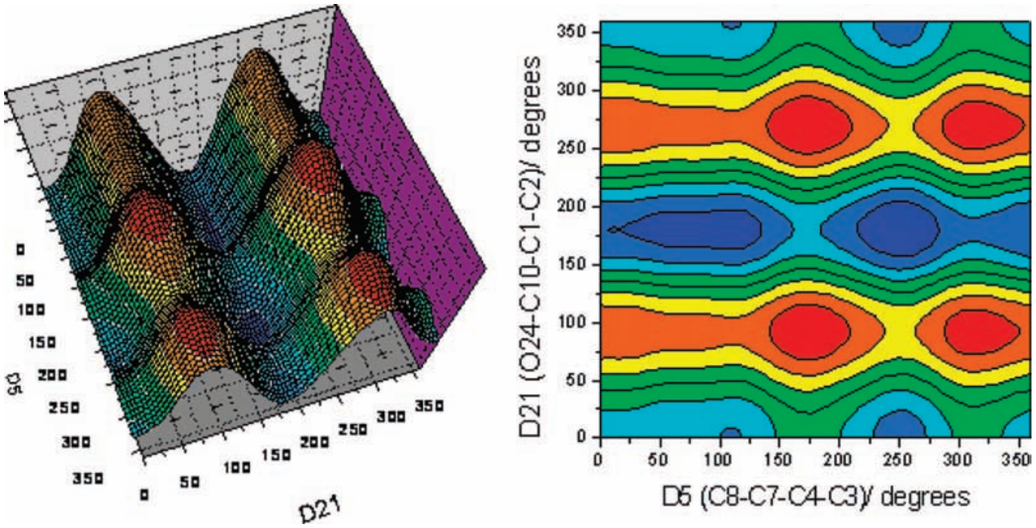
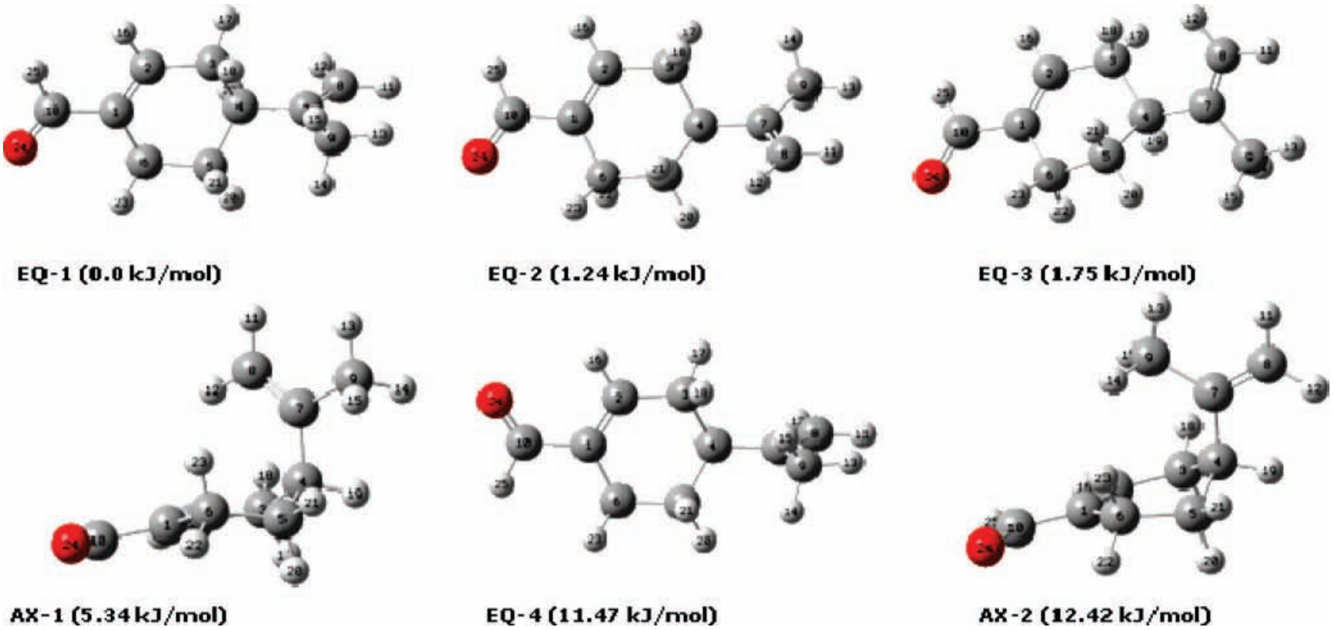


Figure 2. Two-dimensional potential energy surface (PES) calculated along the D5 (C8−C7−C4−C3) and D21 (O24−C10−C1−C2) dihedral angles at the B3LYP/cc-pVDZ level of the *S*-(−)-perillaldehyde. Twelve equilibrium conformations calculated at the B3LYP/6-31G** and B3LYP/cc-pVDZ levels of the *S*-(−)-perillaldehyde.



EQ-1 (0.0 kJ/mol) EQ-2 (1.24 kJ/mol) EQ-3 (1.75 kJ/mol)

AX-1 (5.34 kJ/mol) EQ-4 (11.47 kJ/mol) AX-2 (12.42 kJ/mol)

Figure 3. Structure of the six most stable conformers of the *S*-(−)-perillaldehyde at the B3LYP/cc-pVDZ level of theory. Relative energies taking account of the ZPE corrections are shown for each one.

The IR and VCD spectra of the *S*-(−)-perillaldehyde in the liquid phase are shown in Figure 4 and the IR and Raman spectra in Figure 1S.

3. Computational Details and Methods

All the theoretical calculations using the DFT/B3LYP method were carried out with the Gaussian03 software package.[16]

In a first step, a fixed scan of the potential energy surface (PES), for 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 respect to the ring) and O24−C10−C1−C2 (rotation of the carbaldehyde moiety respect to the ring). In this stage, only the torsional angles above were varied, keeping fixed the rest of the structural parameters (Figure 2). Afterward, the twelve (six equatorial and six axial) obtained equilibrium structures were reoptimized at the B3LYP/cc-pVDZ level of theory, the relative energies with the zero point correction (ZPE) were calculated and the molecular statistical Boltzmann populations of those rotamers obtained. To accomplish the analysis of the experimental spectra, the harmonic IR, Raman and VCD spectra of the three most stable rotamers of equatorial conformation found for the *S*-(−)-perillaldehyde were calculated at the same level of theory. In the calculation of the VCD spectrum, Stephens' theory[17] is used as implemented in Gaussian03. The quantum chemical calculations carried out give access to the most stable conformations expected to be detected experimentally and, in addition, to the harmonic spectra that are useful in the analysis of the experimental spectra.

To facilitate the complete assignment and reproduction of the IR and Raman spectra, Pulay's SQMFF methodology[15] was implemented starting from values of the scaling factors related to the molecular force constants calculated at the B3LYP/cc-pVDZ level equal to 1.000. The theoretical frequency values of each of the three above-mentioned rotamers were fitted as far as possible to those experimental ones using MOLVIB

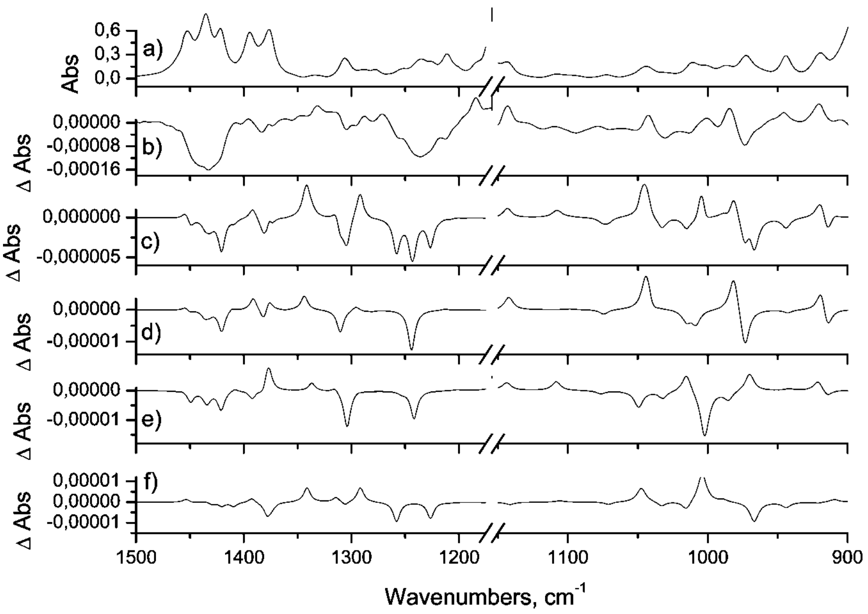


Figure 4. Experimental and theoretical VCD spectra of *S*-(−)-perillaldehyde: (a) Experimental IR spectrum directly obtained from the JASCO VCD spectrometer (16 cm^{-1} of resolution). (b) Experimental spectrum (neat liquid, 7000 scans, 4 cm^{-1} of resolution, spacer of 15 μm and baseline corrected). (c) 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. (d), (e), (f) Predicted scaled spectra of the rotamers EQ-1, EQ-2 and EQ-3 respectively (using JASCO software,[20] pitch = 1 cm^{-1}, fwhm = 8 cm^{-1}).

program.[18,19] With the results from the previous vibrational analysis, the predicted VCD spectrum from the same level of theory and the aid the MakeVCD program by JASCO Inc.[20] the experimental VCD spectrum of *S*-(−)-perillaldehyde has been completely reproduced and correctly interpreted.

3. Results and Discussion

3.1. 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,[21] as perillaldehyde due to its isopropenyl group. The fixed scan at the B3LYP/6-31G** level of these two conformers revealed the existence of six rotamers for each one of them, mainly depending on the rotation of the isopropenyl group around the C_4-C_7 simple bond and on the rotation of the carbaldehyde group around the C_1-C_{10} bond (Figure 2).

In Figure 3 are displayed the six most stable equilibrium structures of *S*-(−)-perillaldehyde optimized at the B3LYP/cc-pVDZ level, along with their relative energies calculated at the same level of theory and with the zero point correction (ZPE). The notation that is employed in Figure 3 uses the terms EQ and AX for the equatorial and axial positions of the isopropenyl group respectively and the notation of the D5 (C8−C7−C4−C3) and D21 (O24−C10−C1−C2) dihedral angles values, respectively. In Table 1S the molecular parameters (in terms of Z-matrix) of the twelve conformers are shown. For the six equatorial rotamers, the torsion of the isopropenyl (D5) and carbaldehyde (D21) groups show values 251.5° and 180° (EQ-1), 111.0° and 180° (EQ-2), 21.7° and 180° (EQ-3), 250.9° and 0° (EQ-4), 111.4° and 0° (EQ-5) and 22.1° and 0° (EQ-6), respectively. In the case of the six axial rotamers, these values are 18.7° and 180° (AX-1), −132.7° and 180° (AX-2), 136.5° and 180° (AX-3), 19.6° and 0° (AX-4), −134.5° and 0° (AX-5), and 138.3° and 0° (AX-6), respectively. As can be seen in Table 1S, the differences existing among the rest of the geometrical parameters for the different rotamers are very small.

TABLE 1: Calculated Electric Dipole Moments (μ), Relative Energies without ZPE Correction (ΔE_e), Relative Energies with ZPE Correction (ΔE_0) and the Corresponding Populations of the Three Equatorials Conformers and the Three Axial Conformers of the *S*-(−)-Perillaldehyde at the B3LYP/cc-pVDZ Level of Theory

	gas phase			
conformer	μ (Debye)	ΔE_e (kJ/mol)	ΔE_0 (kJ/mol)	% population[a]
EQ-1	3.2	0.00	0	44.49
EQ-2	3.4	1.08	1.24	27.00
EQ-3	3.1	1.86	1.75	21.92
AX-1	3.5	5.63	5.34	5.15
EQ-4	3.0	12.08	11.47	0.43
AX-2	3.1	12.92	12.42	0.30
EQ-5	2.9	12.95	12.63	0.27
AX-3	3.7	13.79	13.39	0.20
EQ-6	3.2	14.06	13.50	0.19
AX-4	3.6	17.19	16.90	0.05
AX-5	2.7	24.79	24.50	0.00
AX-6	3.2	25.51	25.22	0.00

[a] Boltzmann population from ΔE_0 taking $T = 298.16$ K.

The three most stable equatorial conformations are under 2 kJ/mol (being EQ-2 1.24 kJ/mol and EQ-3 1.75 kJ/mol higher in energy than EQ-1) and the next three conformations are over 5 kJ/mol (being AX-1 5.34 kJ/mol, EQ-4 11.47 kJ/mol and AX-2 12.42 kJ/mol higher in energy than EQ-1). The six next conformers are in the energy range between 12.50 and 25.30 kJ/mol (EQ-5 at 12.63 kJ/mol, AX-3 at 13.39 kJ/mol, EQ-6 at 13.50 kJ/mol, AX-4 at 16.90 kJ/mol, AX-5 at 24.50 kJ/mol and AX-6 at 25.22 kJ/mol). From the calculated energies at the B3LYP/cc-pVDZ level of theory with the ZPE correction, and if the Boltzmann distribution is supposed to be a good approach, we obtain that at room temperature (298 K) more than 93% of the total population are due to the three most stable equatorial rotamers, Table 1 (around 44.5% of EQ-1, 27% of EQ-2 and 22% of EQ-3). It means that all of these three equatorial rotamers should be detected experimentally at room temperature.

TABLE 2: Experimental IR and Raman Bands of *S*-(−)-Perillaldehyde in the Liquid Phase[a]

IR liquid	relative intensity	Raman liquid	relative intensity	IR liquid	relative intensity	Raman liquid	relative intensity
3082	w	3084	vw	1097	w	1099	vw
3073	w	3073	vw	1073	w	1070	vw
3046	w	3048	vw	1045	w	1042	vw
3020	w			1031	w		
2990	w	2990	m	1011	w	1009	vw
		2980	sh	1001	w	1001	vw
2968	w			987	w		
2933	m	2935	sh	972	w	973	vw
2918	m	2918	m	944	w	945	vw
2896	m			920	w	921	vw
2889	m	2887	m			889	vw
2875	sh	2875	sh	881	m	881	vw
2863	w			841	w	841	vw
		2849	w	815	w	815	vw
		2824	w			809	sh
2754	w			797	w	794	vw
2718	w	2726	vw	791	w	773	w
1685	vs	1683	m	771	m		
1645	s	1645	vs	708	w		
		1607	vw	692	m	692	w
		1577	vw			630	vw
1452	m	1453	vw	579	w	578	vw
1435	m	1434	w	548	w		
1421	m	1422	w	537	w	538	vw
1394	m	1396	w	523	w	522	vw
1376	m	1377	vw	503	w		
		1354	vw			486	vw
1334	w	1331	vw	465	w		
1306	w	1305	vw	448	w	449	vw
		1295	vw			430	vw
1287	w			421	w	420	vw
1277	w	1278	vw			332	vw
1252	w					315	vw
1239	w					298	vw
1226	w					279	vw
1211	w					236	vw
1182	w					194	vw
1166	m	1166	w			159	vw
1143	w	1143	vw				
1109	w	1109	vw				

[a] vs = very strong, s = strong, m = medium, w = weak, vw = very weak, sh = shoulder.

3.2. Vibrational Study. ***Theoretical and Experimental Data.*** As mentioned above, works dealing with the molecular structure and vibrational spectra of terpenes are scarce in the literature. Nevertheless, the molecular structure and vibrational spectra of the cyclohexene molecule have been studied from both the theoretical and experimental points of view[22−31] and there is a work dealing with the IR spectrum of isopropenyl group in different molecular systems.[32]

Perillaldehyde 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*-(−)-perillaldehyde are displayed in Figure 1S and experimental data of them (wavenumbers 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 most stable equatorial rotamers (EQ-1, EQ-2 and EQ-3). In Table 3S are shown the theoretical scaled and experimental wavenumbers of the three most stable equatorial conformers (in Table 3 is shown only the spectral range relevant in the discussion below). For obtaining the scaled wavenumbers, the SQMFF methodology by Pulay et al.[15] was used. Thus, the Cartesian Hessian matrix obtained from the DFT calculations was transformed into a new Hessian in terms of Pulay's natural internal coordinates.[15] Afterward, using the MOLVIB program[18,19] the theoretical wavenumbers were fitted to the experimental ones by means of a refinement process of the scale factors (with the starting values equal to 1.000) associated with the force constants expressed in natural internal coordinates. In the refinement procedure, experimental bands mainly coming from IR spectrum in liquid phase were taken into account. When the IR bands were not present in the liquid phase, Raman bands were used.

The predicted theoretical spectra after the scaling procedure, taking into account the relative population of the three most stable equatorial rotamers in gas phase, are displayed in Figure 1S. In Table 5S the description of every normal modes is shown from the potential energy distribution (PED) matrix.

In Table 4 are shown the sets of refined scaling factors for each of the most stable rotamers of the equatorial conformer of *S*-(−)-perillaldehyde as well as the set of their mean values obtained in the refinement procedure for the B3LYP/cc-pVDZ level of theory. These results are in good agreement with those obtained in our study on the carvone molecule (5-isopropenyl-2-methylcyclohex-2-en-1-one),[33] a similar terpenoid. The root-mean-square (rms) obtained for the difference between the experimental and theoretical (after the refinement) wavenumber values of *S*-(−)-perillaldehyde using these scaling factors is 5.52

TABLE 3: Theoretical (B3LYP/cc-pVDZ), Scaled and Experimental Vibrational Wavenumbers of *S*-(−)-Perillaldehyde in the Spectral Region 900−1500 cm^{-1} and Theoretical (B3LYP/cc-pVDZ) Vibrational Wavenumbers[a]

mode	EQ-1 (theo)	EQ-1 (scal)	exp	EQ-2 (theo)	EQ-2 (scal)	exp	EQ-3 (theo)	EQ-3 (scal)	exp
1	3220.9	3094.0	3073	3235.1	3106.9	3082	3231.9	3104.5	3082
2	3131.7	3008.4		3145.4	3020.5	3020	3144.9	3020.8	3020
3	3130.9	3007.4		3132.6	3008.5		3133.9	3010.5	
18	1470.6	1454.2	1452	1473.7	1456.2	1452	1479.7	1453.4	1452
19	1466.9	1450.5	1452	1466.2	1449.3	1452	1464.9	1448.4	1452
20	1452.4	1436.2	1435	1452.9	1435.6	1435	1450.9	1434.7	1435
21	1448.2	1432.1	1435	1449.3	1433.3	1435	1445.9	1429.9	1435
22	1437.1	1420.5	1421	1438.4	1421.0	1421	1436.7	1420.4	1421
23	1429.2	1411.0		1429.1	1408.8		1429.1	1409.3	
24	1410.1	1390.8	1394	1410.7	1391.7	1394	1411.2	1392.0	1394
25	1399.0	1381.4	1376	1400.8	1381.9	1376	1402.3	1383.8	1376
26	1395.4	1376.0	1376	1396.6	1377.7	1376	1396.2	1378.1	1376
27	1378.5	1360.9		1393.6	1376.1	1376	1392.3	1373.8	1376
28	1359.9	1343.1	1354	1353.3	1336.1	1334	1356.2	1340.6	1334
29	1325.2	1309.7	1306	1330.7	1314.6	1306	1329.7	1313.6	1306
30	1311.5	1295.2	1295	1319.0	1303.4	1306	1321.4	1305.1	1306
31	1304.2	1287.3	1287	1310.0	1293.8	1295	1306.6	1291.0	1295
32	1297.0	1280.9	1277	1268.3	1252.7	1252	1272.2	1257.6	1252
33	1258.7	1243.4	1239	1256.2	1241.1	1239	1241.8	1226.0	1226
34	1227.6	1212.6	1211	1216.9	1201.4	1202	1223.5	1208.7	1211
35	1179.4	1160.9	1166	1182.7	1164.2	1166	1184.0	1165.8	1166
36	1155.4	1141.8	1143	1156.9	1143.2	1143	1154.3	1140.8	1143
37	1116.3	1098.5	1097	1126.3	1108.3	1109	1123.4	1106.0	1109
38	1086.6	1074.1	1073	1089.1	1076.0	1073	1083.1	1070.7	1073
39	1057.2	1043.7	1045	1062.7	1049.1	1045	1061.6	1047.2	1045
40	1054.5	1039.3	1045	1047.7	1032.0	1031	1048.6	1032.9	1031
41	1025.9	1015.2	1011	1025.5	1015.2	1011	1026.3	1015.1	1011
42	1023.5	1008.4	1011	1016.7	1001.9	1001	1017.9	1003.8	1001
43	993.7	981.0	987	998.4	985.1	987	1002.7	988.8	987
44	988.4	973.4	972	984.0	969.9	972	980.7	966.6	972
45	953.8	942.8	944	954.1	941.7	944	955.4	943.9	944
46	929.6	918.7	920	931.4	921.0	920	932.1	921.1	920
47	924.0	914.5	920	924.3	914.5	920	919.1	909.6	920

[a] See Table 2. See Table 2S in the Supporting Information for the complete assignment.

TABLE 4: Set of Scaling Factors Obtained for the *S*-(−)-Perillaldehyde at the B3LYP/cc-pVDZ Level of Theory

	scaling factor			
mode	EQ-1	EQ-2	EQ-3	mean value
C═C stretching	0.905	0.899	0.902	0.902
C−C stretching	0.967	0.959	0.957	0.961
C−H stretching	0.927	0.921	0.920	0.923
XYZ bending	0.986	1.032	1.008	1.009
torsions of single bonded systems	0.999	0.947	0.996	0.981
XY−H bendings	0.983	0.974	0.976	0.977
out-of-plane modes	0.978	0.981	0.983	0.980
H−X−H bending	0.977	0.977	0.980	0.978
torsions of conjugated systems	0.926	0.951	0.943	0.940
C═O stretching	0.889	0.890	0.891	0.890

cm^{-1}, the individual rms for each rotamer being 6.09 cm^{-1} (EQ-1), 5.39 cm^{-1} (EQ-2) and 5.08 cm^{-1} (EQ-3).

Vibrational Assignment. *S*-(−)-Perillaldehyde displays rather complex IR and Raman spectra (Figure 1S). For clarity, the vibrational assignment is discussed dividing the complete mid-IR spectral range into several zones and only relevant features are discussed. The whole information can be obtained by the reader from the Supporting Information.

C−H Stretching Region. This region is very complex even for the cyclohexene molecule,[22−31] where Fermi resonances between methylene C−H bond stretchings and combinations involving low-wavenumber modes are described for this region.[31] In addition, it is described in the literature[34−36] that the IR experimental band corresponding to the C−H stretching of the aldehyde moiety is affected by Fermi resonances, the corrected value proposed in the literature being for the wavenumber of this normal mode in the acetaldehyde molecule 2750 cm^{-1}.[35] In the *S*-(−)-perillaldehyde, this band appears at 2718 cm^{-1} in the IR spectrum and at 2726 cm^{-1} in the Raman. Our scaling calculation predicts this band in the three most stable rotamers (EQ-1, EQ-1 and EQ-3) at 2751 cm^{-1}.

From the performance of the SQMFF methodology (see Table 3), the band appearing at 3073 cm^{-1} (IR and Raman) is assigned to the normal mode 1 of EQ-1 (described as the asymmetric C−H stretching of the vinyl group from the PED). Normal mode 1 of EQ-2 and EQ-3 (with the same description) is ascribed to the experimental band at 3082 cm^{-1} (IR) and 3084 cm^{-1} (Raman). This feature is a first example in the experimental detection of different rotamers of *S*-(−)-perillaldehyde in the neat liquid. Another example showing the presence of the three conformers is the normal mode 12, which is assigned to the bands at 2896 cm^{-1} (EQ-1, described as C−H stretchings involving the chiral carbon), 2875 cm^{-1} (EQ-2, described as the asymmetric C−H stretching of a methylene group) and 2889 cm-1 (EQ-3, with the same description as in EQ-2). These changes in the description from the PED of the same normal mode are general and they appear along all the vibrational spectral range. They also are common for the same type of terpenoids like limonene and carvone.[33]

Because of the great overlapping present in this zone, some normal modes that should appear there could not be assigned (see Tables 2 and 3S). In addition, there are experimental bands that cannot be assigned to the fundamentals which could be due to overtones and/or combination bands.

Intermediate Vibrations Spectral Region. This is the spectral zone from 1700 to 400 cm^{-1}. In Table 2 is shown only the relevant part in the study of the VCD spectrum of *S*-(−)-perillaldehyde. The band with the highest wavenumber in this zone, observed at 1685 cm^{-1} (IR) and 1683 cm^{-1} (Raman), is assigned to the C═O bond stretching of the carbaldehyde group in all the rotamers (normal mode 15), with a contribution around 80% from the PED matrix. The band observed at 1645 cm^{-1} (IR and Raman) is assigned to the normal modes 16 and 17, which are described as the C═C bond stretching vibrations of the vinyl group (mode 16) and in the ring (mode 17). In both cases these movements appear mixed with others in all the three rotamers, as obtained from the PED (Table 4S).

The rest of the normal modes in this region present a complex description from the PED matrix 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 assignment of the carvone and limonene molecules.[33]

As can be seen in Table 4S, 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, this is the case of normal modes 52 and 53 (Table 4S): normal mode 52 for EQ-1 is described as 63% of vinyl torsion, the same description as normal mode 53 for EQ-3 (see Table 4S). However, for EQ-2 these two normal modes present a mixed description between normal modes 52 in EQ-3 and 53 in EQ-1.

Low-Frequency Vibrations Region. The third region under study corresponds to vibrations below 400 cm^{-1}. As in the previous region, normal modes present a complex description from the PED matrix analysis (see Table 4S), where waggings, rockings, torsions of the substituent groups and ring deformations appear mixed in some extent and, as in the previous regions, there are normal modes that present different descriptions. As an example, from the PED matrix, it is observed that normal mode 67 in EQ-1 (scaled value at 136.0 cm^{-1}) and EQ-2 (scaled value at 141.0 cm^{-1}) present the same description as normal mode 66 in EQ-3 (scaled value at 146.6 cm^{-1}). In this way, normal mode 67 in EQ-3 (scaled value at 143.2 cm^{-1}) presents the same description as normal mode 66 in EQ-1 (scaled value at 147.4 cm^{-1}) and EQ-2 (experimental value at 159 cm^{-1}; scaled value at 152.7 cm^{-1}).

3.3. Vibrational Circular Dichroism (VCD) Spectrum. Once the vibrational analysis has been made and the IR and Raman spectra of perillaldehyde have been completely assigned and reproduced applying the SQMFF methodology to the molecular force field calculated at DFT/B3LYP/cc-pVDZ level, the VCD spectrum of *S*-(−)-perillaldehyde can be reproduced and analyzed. Thus, the VCD spectrum of the target species has been analyzed in the region 4000−900 cm^{-1}. Because of the presence of possible artifacts due to infrared absorptions higher than suitable in the neat liquid sample, only the zone between 1500 and 900 cm^{-1} has been analyzed in this work (Figure 4). Concerning the VCD spectrum in solution, a work on the limonene molecule[33] reveals that the solvent could influence the VCD spectra changing the signs of the rotator strength of some normal modes.

In Table 2S are shown the theoretical (B3LYP/cc-pVDZ) dipole and rotatory strengths for the three equatorial rotamers (EQ-1, EQ-2 and EQ-3) of *S*-(−)-perillaldehyde experimentally detected as obtained from Gaussian03 output. In Figure 4 are displayed the predicted VCD spectra of every individual rotamer, once the vibrational wavenumbers were scaled following the SQMFF procedure, along with the sum spectrum obtained by the addition of those theoretical spectra weighted taking into account their contributions according to the Boltzmann′s population theoretically obtained. To better reproduce the experimental spectra, the population theoretically obtained could have been conveniently changed, but our aim is to check the suitability of the procedure chosen in reproducing experimental results and for this reason it has not been made.

Interpretation of the VCD spectral features of highly complex chemical species is a difficult task and our study shows that a previous reliable vibrational analysis from IR-Raman experimental data and theoretical calculations could help in the interpretation of VCD spectra.

In addition, some VCD bands change shape on going from a rotamer to another (Figure 4). This fact is due to changes in the sign and absolute value of the rotator strength of the same normal modes among the different rotamers (Table 2S) and can be used in the experimental detection of conformers. As an example, normal mode 39, assigned to the experimental band at 1045 cm^{-1}, has a value of its rotator strength of 31.25×10^{-44} esu^2 cm^2 in EQ-1, -14.54×10^{-44} esu^2 cm^2 in EQ-2 and 17.95×10^{-44} esu^2 cm^2 in EQ-3. In this case, the description of the normal mode from the PED is essentially the same in the three rotamers, being the methyl rocking of the isopropenyl group the predominant one (Tables 3 and 4S). The same is found for normal mode 41, assigned to the experimental band at 1011 cm^{-1} and described as the wagging of the C═O group, with a pattern (−, +, −) for EQ-1, EQ-2 and EQ-3, respectively (see Table 4S). These two examples can illustrate the helpfulness of VCD spectrum in detecting conformers combined with IR and Raman techniques. Experimental IR and Raman bands around 1000 cm^{-1} are assigned to normal modes 41, 42, 43 and 44 of all the rotamers and bands around 1050 cm^{-1} to normal modes and 39 and 40. The spectral VCD profile is reproduced by taking into account the three rotamers and the changes in the rotator strength for every one. Hence, the experimental VCD profile around 1000 cm^{-1} reveals clearly the presence of the minor rotamer EQ-3 by simple comparison with predicted spectra of each one and with the sum spectrum.

Another example is the broad experimental band with three negative ΔA signals at 1255, 1235 and 1210 cm^{-1}. This feature is reproduced theoretically by our calculations with three negative bands at 1257, 1242 and 1226 cm^{-1}, corresponding two bands at 1257 and 1226 cm^{-1} to EQ-3 (normal modes 32 and 33; see Table 4S for description), one band at 1241 cm^{-1} to EQ-2 (normal mode 33) and another one at 1243 cm^{-1} to EQ-1 (normal mode 33).

In addition, taking into account the three most stable rotamers, a positive theoretical couplet is predicted near 1300 cm^{-1} and two negative experimental ones are reproduced centered at 915 and 1385 cm^{-1}.

Finally, some bands appearing in the recorded VCD spectrum are not predicted from the theoretical calculations after the scaling procedure. Although, for a better knowledge of their nature, these bands should be compared with similar ones in molecular systems with a comparable structure, they could be due to overtones or combination bands that cannot be predicted by our theoretical calculations because they are done in the harmonic approximation.

4. Conclusion

A systematic, detailed, reliable and complete structural and vibrational study of the most stable conformers and rotamers of *S*-(−)-perillaldehyde has been made. The analysis of IR and Raman spectra concludes the presence of the three most stable rotamers of the equatorial conformer of the *S*-(−)-perillaldehyde in the liquid phase.

Concerning the relative population and the IR and Raman spectra, there is a good agreement between the observed and theoretical spectra.

In light of the vibrational analysis, the interpretation of the VCD spectrum of the title species is made in the wavenumber range 1500−900 cm^{-1}, revealing its great complexity. To reproduce the VCD experimental spectrum, and in agreement with the vibrational analysis, the three most stable equatorial rotamers must be taken into account. Depending on the normal modes involved, different VCD band types can be described.

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Supporting Information Available: Calculated equilibrium structures of *S*-(−)-perillaldehyde at B3LYP/cc-pVDZ levels for the six equatorial conformers (EQ-1, EQ-2, EQ-3, EQ-4, EQ-5 and EQ-6) and the six axial conformers (AX-1, AX-2, AX-3, AX-4, AX-5 and AX-6) (Table 1S), theoretical (B3LYP/cc-pVDZ) vibrational wavenumbers, infrared intensities, Raman activities, dipole strengths and rotatory strengths for the three equatorial rotamers (EQ-1, EQ-2 and EQ-3) detected experimentally of *S*-(−)-perillaldehyde (Table 2S), experimental and theoretical (B3LYP/cc-pVDZ) vibrational wavenumbers (Table 3S), the potential energy distribution (PED) coming from the output of the MolVib program for the three equatorial conformers (EQ-1, EQ-2, EQ-3) of the *S*-(−)-perillaldehyde (Table 4S) and experimental IR and Raman spectra compared with predicted scaled spectrum for the *S*-(−)-perillaldehyde (Figure 1S). This material is available free of charge via the Internet at http://pubs.acs.org.

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