

## Raman Optical Activity of Menthol and Related Molecules

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Raman circular intensity difference spectra between 80 and 2 000  $\text{cm}^{-1}$  of (-)-menthol, (-)-menthylamine, (-)-menthyl chloride, (-)-isopulegol, (-)-menthone, (-)-3,3-dimethylcyclohexanol, (+)-pulegone, (-)-limonene, and (+)-carvone are presented. Several stereochemical correlations are pointed out involving, in particular, bands characteristic of the isopropyl and *gem*-dimethyl groups, methyl torsions, and out-of-plane olefinic hydrogen deformations.

A SMALL difference in the intensity of Raman scattering from chiral molecules in right and left circularly polarized incident light provides a measure of vibrational optical activity.<sup>1-11</sup> At this early stage in the development of the subject it is of interest to compare the Raman optical activity spectra of series of related compounds to see what common features emerge. Here the spectra of menthol and some related molecules are presented. This article is a continuation of the series started by refs. 7 and 8, where a more detailed introduction to Raman optical activity can be found.

### EXPERIMENTAL

The instrument used has been described previously.<sup>3,7</sup> The samples were studied as near saturated solutions or neat liquids. The instrumental conditions were as follows: laser wavelength 488.8 nm, laser power 3 W, slit width 10  $\text{cm}^{-1}$ , scan speed 1  $\text{cm}^{-1} \text{min}^{-1}$ . As before,<sup>3,7</sup> only the depolarized Raman circular intensity sum ( $I_z^R + I_z^L$ ) and difference ( $I_z^R - I_z^L$ ) spectra between 100 and 2 000  $\text{cm}^{-1}$  were recorded, the difference spectra being presented on a scale that is linear within each decade range but logarithmic between decade ranges. S and W indicate strongly and weakly polarized bands; all other bands are effectively depolarized.

### DISCUSSION

Figures 1-9 show the depolarized Raman circular intensity sum and difference spectra of, respectively, (-)-menthol, (-)-menthylamine, (-)-menthyl chloride, (-)-isopulegol, (-)-menthone, (-)-3,3-dimethylcyclohexanol, (+)-pulegone, (-)-limonene, and (+)-carvone.

The first three Raman circular intensity difference (c.i.d.) spectra in the region 1 100-1 400  $\text{cm}^{-1}$  are very similar: neglecting an extra positive c.i.d. at 1 210  $\text{cm}^{-1}$  in Figure 3, the positions and signs of the c.i.d.s are the same although relative intensities are variable. This correlation is gratifying because (-)-menthol, (-)-menthylamine, and (-)-menthyl chloride have the same basic skeletons with the same absolute configurations and are expected to have similar conformations. Definite band assignments in this spectral region are difficult due to the large number of CH and CH<sub>2</sub> deformation and C-C stretching vibrations which contribute here. However, the isopropyl group, which is present in all three molecules, gives rise to group frequencies in this region: two bands, at *ca.* 1 170 and 1 140  $\text{cm}^{-1}$ , arise from an interaction between the rocking modes of the two isopropyl methyl groups together with C-C stretches.<sup>12</sup> These bands are seen most clearly in

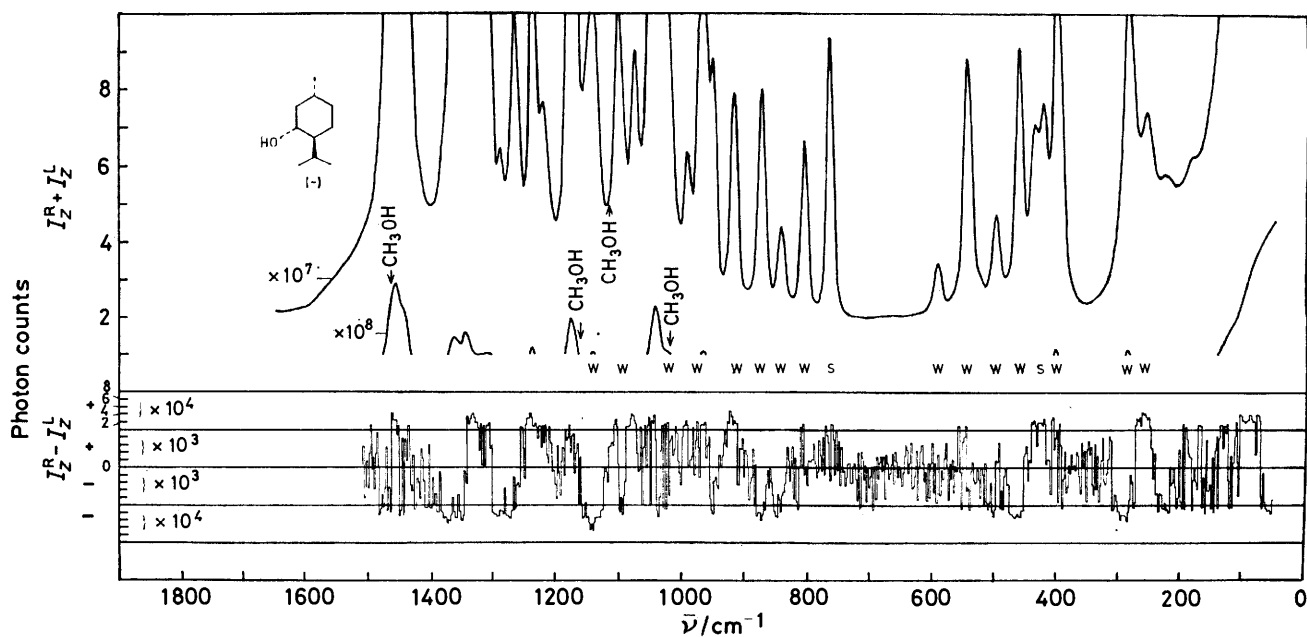


FIGURE 1 The depolarized Raman circular intensity sum and difference spectra of (-)-menthol in methanol

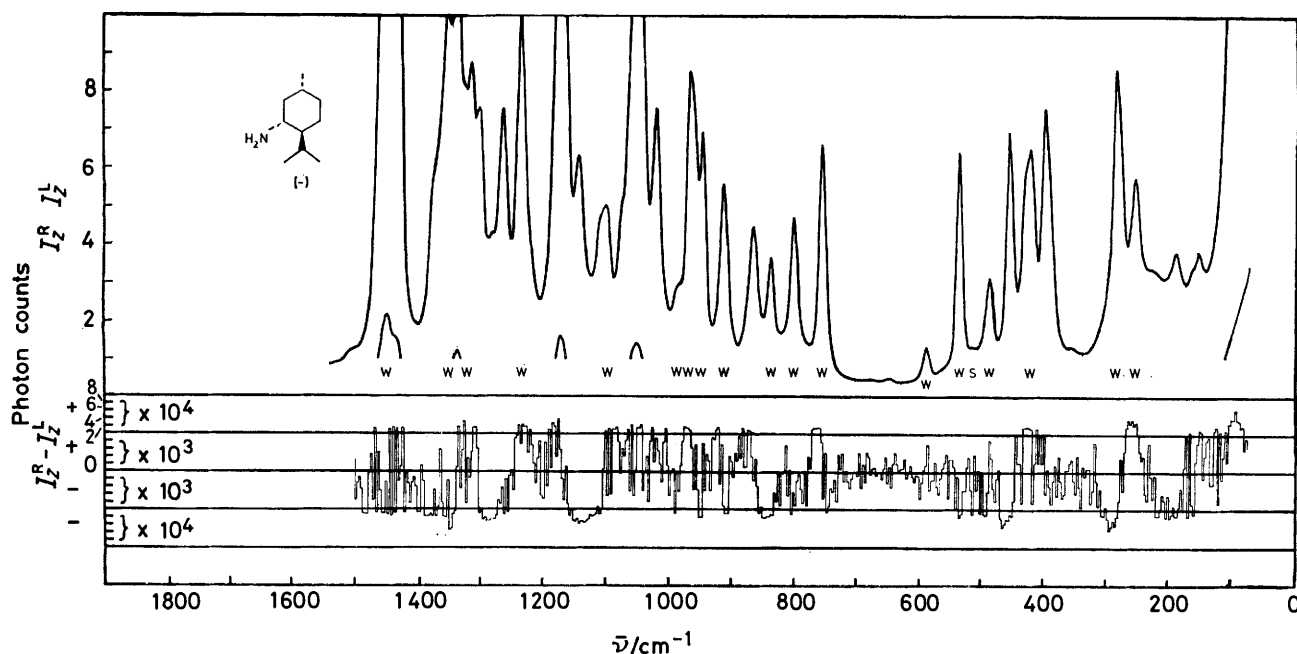


FIGURE 2 The depolarized Raman circular intensity sum and difference spectra of neat (-)-menthylamine

(-)-menthyl chloride (Figure 3) at 1175 and 1145  $\text{cm}^{-1}$ , and are associated with a c.i.d. couplet. This couplet, with the same sign, is also present in (-)-menthylamine (Figure 2) and in (-)-menthol (Figure 1), although in the last case the higher frequency component has all but disappeared. The appearance of a couplet may be due to a mechanism, described elsewhere,<sup>3,7,8</sup> which involves the coupling of two local group vibrational modes (in this case the methyl rocking deformations) by

a chiral perturbation. Lending strength to this assignment is the absence of any such couplet in the c.i.d. spectrum of (-)-isopulegol (Figure 4) in which the isopropyl group has been replaced by an isopropenyl group. Features appearing in the same region in the Raman c.i.d. spectrum of (-)-menthone (Figure 5) also probably originate in the isopropyl methyl rocking vibrations, but now the stereochemical environment of the isopropyl group is rather different on account of the adjacent  $sp^2$ -

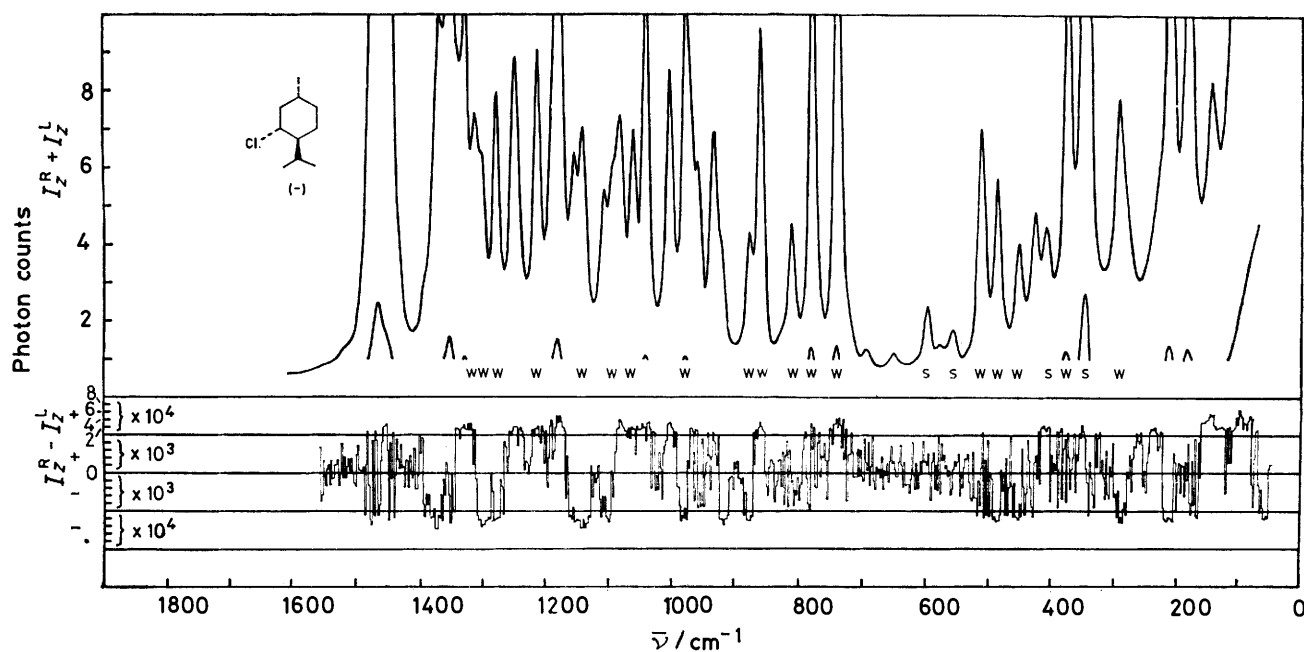


FIGURE 3 The depolarized Raman circular intensity sum and difference spectra of neat (-)-menthyl chloride

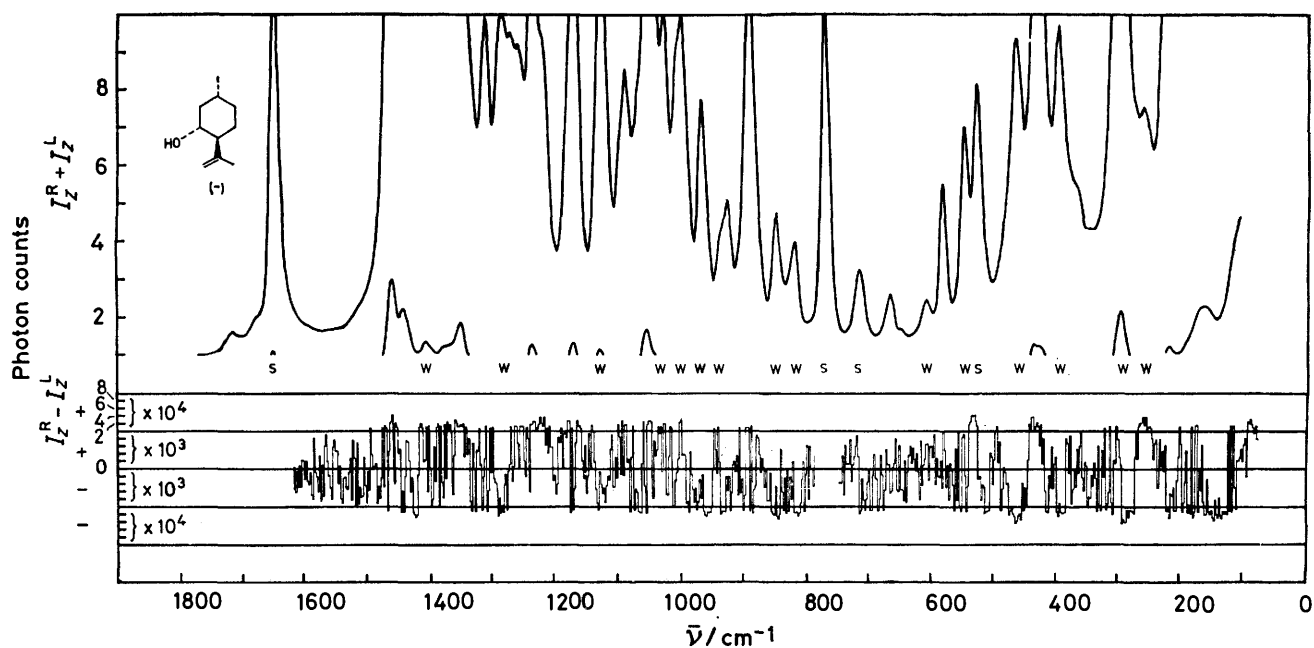


FIGURE 4 The depolarized Raman circular intensity sum and difference spectra of neat (—)-isopulegol

hybridized carbon atom in the ring, so no direct correlations with the first three examples can be made.

The *gem*-dimethyl group also gives rise to two characteristic bands at slightly higher frequencies than the isopropyl group.<sup>12</sup> The Raman optical activity spectra indicate that the situation is more complex than the isopropyl case with both bands sometimes producing c.i.d.s of the same sign. This is probably due to the increased participation of C-C stretching in the *gem*-

dimethyl modes which are centred around a quaternary carbon atom. In (—)-3,3-dimethylcyclohexanol (Figure 6), for example, the two *gem*-dimethyl bands are probably those at just under 1200 cm<sup>-1</sup> and at 1175 cm<sup>-1</sup>: both show a positive Raman optical activity. This is balanced by a negative effect associated with a Raman band at 1240 cm<sup>-1</sup> which could originate in stretching of the C-C bonds around the quaternary carbon atom. Previously published Raman c.i.d. spectra

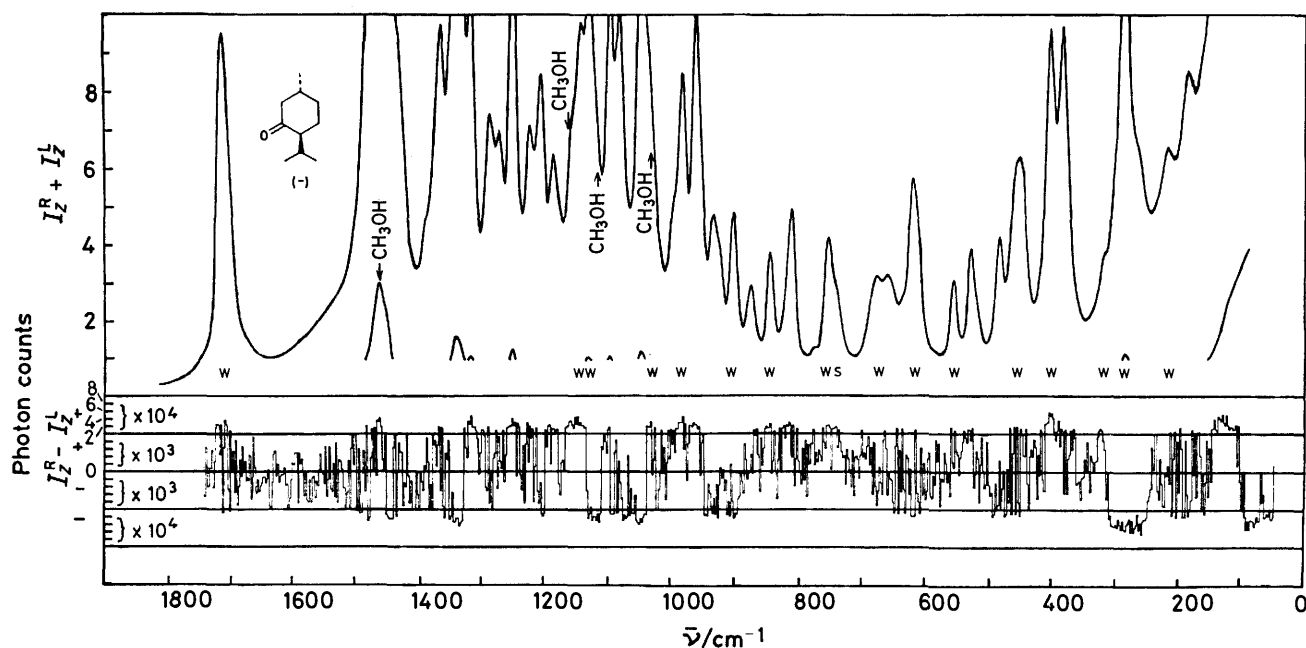


FIGURE 5 The depolarized Raman circular intensity sum and difference spectra of (—)-menthone in methanol

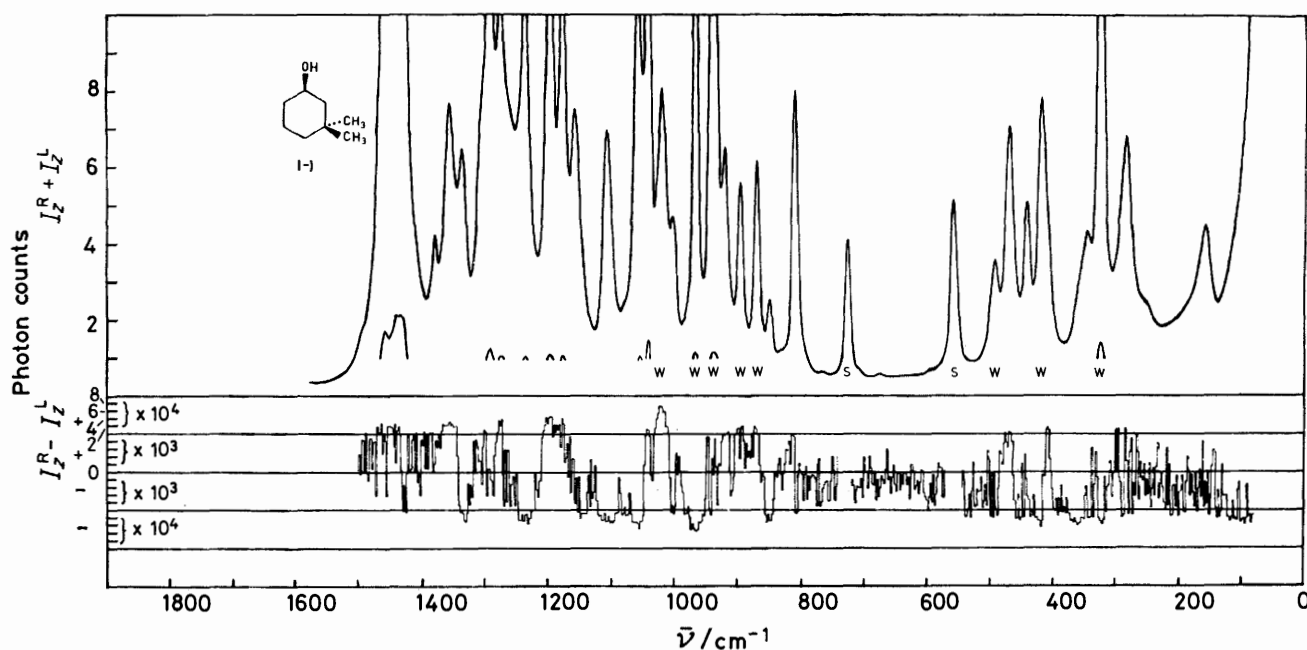


FIGURE 6 The depolarized Raman circular intensity sum and difference spectra of neat (—)-3,3-dimethylcyclohexanol

of camphor and related molecules<sup>7</sup> contain additional examples, although these were not pointed out at the time: camphor itself, for instance, shows a c.i.d. couplet associated with the Raman bands at 1190 and 1175  $\text{cm}^{-1}$  which were assigned in an earlier i.r. study of camphor to the *gem*-dimethyl group.<sup>13</sup>

Several of the Raman c.i.d. spectra presented here show large effects in the 1300–1400  $\text{cm}^{-1}$  region.

Some of these features almost certainly originate in CH deformations at tertiary carbon atoms.<sup>12</sup> The large negative c.i.d. at 1345  $\text{cm}^{-1}$  in (+)-pulegone (Figure 7) might be an example: this molecule contains only one  $\text{R}_3\text{C-H}$  group. It is worth noting that a large negative c.i.d. occurs at 1340  $\text{cm}^{-1}$  in (+)-3-methylcyclohexanone (Figure 7 of ref. 7) which might have a similar origin.

The Raman c.i.d. spectrum of (—)-3,3-dimethylcyclo-

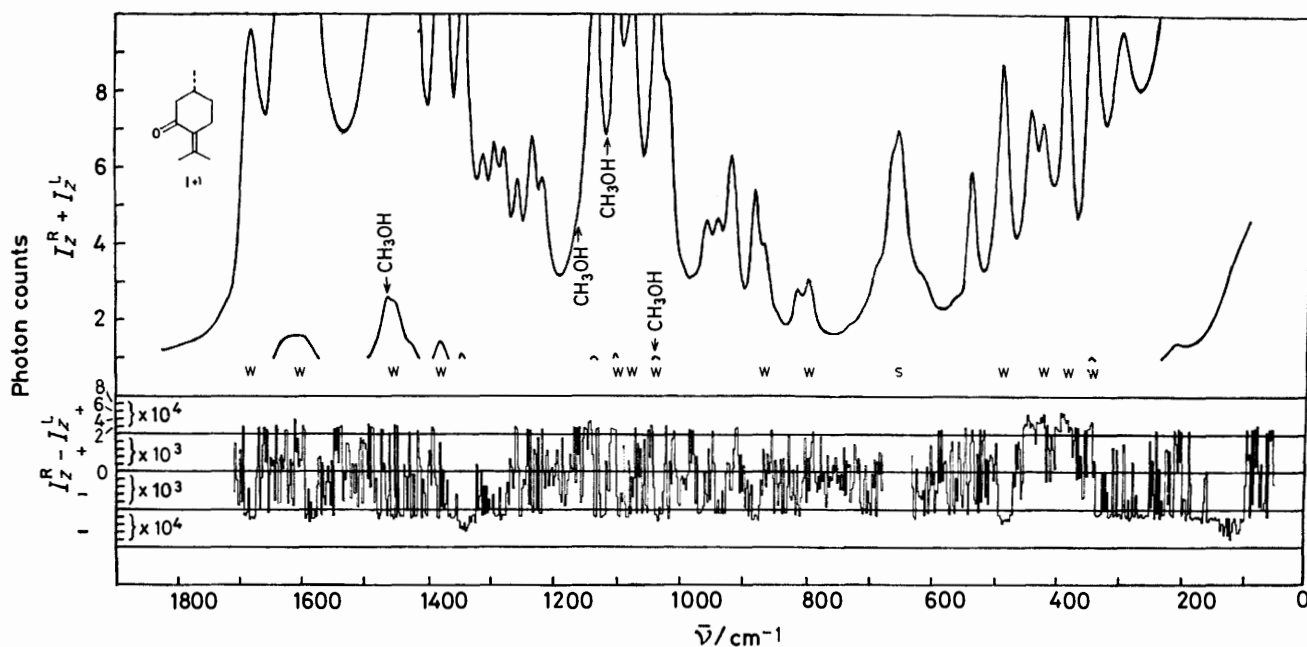


FIGURE 7 The depolarized Raman circular intensity sum and difference spectra of (+)-pulegone in methanol



ment of the methyl group attached to the ring in (–)-menthone (Figure 5) should be very similar to that in (+)-3-methylcyclohexanone. The large negative c.i.d. in a weak Raman band in (–)-menthone at *ca.* 260  $\text{cm}^{-1}$  (which merges with a large negative effect in a much stronger Raman band at slightly higher frequency) correlates with the negative effect in (+)-3-methylcyclohexanone since the two molecules have the same absolute configuration in the region of the ring methyl group. The weak, depolarized Raman bands at *ca.* 260  $\text{cm}^{-1}$  showing large positive c.i.d.s in (–)-menthol (Figure 1) and (–)-menthylamine (Figure 2) might also originate in torsions of the ring methyl group. The Raman band shoulders at *ca.* 260 and 230  $\text{cm}^{-1}$  showing small positive c.i.d.s in (–)-menthyl chloride (Figure 3) might have similar origins. The corresponding methyl torsion Raman band in (–)-isopulegol (Figure 4) might be that at *ca.* 260  $\text{cm}^{-1}$ , which again shows a positive c.i.d. The Raman optical activity spectrum of (–)-limonene (Figure 8) shows a large negative effect associated with a broad, weak, Raman band at *ca.* 250  $\text{cm}^{-1}$ ; that of (+)-carvone (Figure 9) shows a large positive effect associated with a Raman band of similar shape at the same frequency. These effects might originate in torsions of the isopropenyl methyl groups since the opposite signs correlate with the opposite absolute configurations of the structural features common to both molecules,<sup>15</sup> and might be generated through an 'inertial' mechanism discussed elsewhere.<sup>17</sup> As mentioned above, the Raman band with a positive c.i.d. at 260  $\text{cm}^{-1}$  in (–)-isopulegol (Figure 4) is assigned to the torsion of the ring methyl group rather than to the isopropenyl methyl group. If this assignment is correct, the absence of correlatable optical activity in the torsion of the isopropenyl methyl group in (–)-isopulegol might be attributed to intramolecular hydrogen bonding (between the OH group and the  $\pi$ -electrons) holding the isopropenyl group in a very different conformation to that in limonene and carvone. Although this is speculative, it is worth noting that the i.r. spectrum of isopulegol in the OH stretching region indicates that intramolecular hydrogen bonding exists in a large proportion of the molecules.

It was mentioned above that CH deformations at tertiary carbon atoms, and also  $\text{CH}_2$  deformations, can show large optical activity, although the complexity of the Raman and Raman c.i.d. features in the appropriate spectral region can make it difficult to extract useful stereochemical information. On the other hand, olefinic CH and  $\text{CH}_2$  deformations give rise to bands that are sufficiently well defined to be of diagnostic value in conventional i.r. and Raman spectroscopy,<sup>12,13</sup> and we have found a number of examples of c.i.d.s in the corresponding Raman bands. Most of these are presented elsewhere,<sup>18</sup> but examples occur in two of the spectra presented here, (–)-limonene (Figure 8) and (+)-carvone (Figure 9). The vinylidene  $\text{CH}_2$  out-of-plane, in-phase vibration in (–)-limonene is assigned to the strong, weakly polarized, Raman band at 888  $\text{cm}^{-1}$

(following an earlier assignment of an i.r. band at this frequency in limonene<sup>13</sup>), which shows a small negative c.i.d. And at 885  $\text{cm}^{-1}$  in the Raman spectrum of (+)-carvone a strong, weakly polarized, Raman band generates a small positive c.i.d. which correlates with the corresponding negative effect in (–)-limonene because in the two molecules the vinylidene  $\text{CH}_2$  groups are in equivalent stereochemical environments but with opposite absolute configurations. The out-of-plane olefinic CH deformation of a trisubstituted double bond occurs in the region 790–840  $\text{cm}^{-1}$ .<sup>12</sup> There are several clear examples elsewhere of Raman c.i.d.s associated with this mode.<sup>18</sup> This band occurs at 802  $\text{cm}^{-1}$  in limonene;<sup>13</sup> it is present in Figure 8 as a shoulder on a Raman band at slightly lower frequency, and is associated with a positive c.i.d. There is a hint of a small negative effect at the same frequency in (+)-carvone (Figure 9), although a direct correlation between limonene and carvone is not expected on account of the adjacent carbonyl group in the latter.

Although we will not speculate on their origins, other definite Raman optical activity correlations can be seen in the spectra of (–)-limonene and (+)-carvone. Note particularly the region at *ca.* 510  $\text{cm}^{-1}$  where three Raman bands at almost identical frequencies in the two molecules produce the same c.i.d. pattern but with opposite signs: from the lower frequency end the relative signs in (–)-limonene are positive-negative-negative. The additional Raman c.i.d. structure shown by (+)-carvone between *ca.* 550 and 720  $\text{cm}^{-1}$  could originate in carbonyl deformation vibrations.<sup>3,7</sup> Also worth mentioning are the effects at *ca.* 1 010, 1 250, and 1 325  $\text{cm}^{-1}$ , all of which have opposite signs in the two molecules.

With the exception of (–)-isopulegol and (–)-3,3-dimethylcyclohexanol, all of the absolute configurations shown were taken from ref. 19. That of (–)-3,3-dimethylcyclohexanol was provided by Professor H. S. Mosher, and that of (–)-isopulegol was deduced by assuming that the positive Raman optical activity in the band at *ca.* 260  $\text{cm}^{-1}$  in both (–)-menthol and (–)-isopulegol originates in the torsion of the ring methyl group (other features at low frequency also correlate). Because of an error, the absolute configuration of (–)-menthyl chloride shown in Figure 3 is incorrectly assigned to the (+)-isomer in ref. 19. This was noticed because it is clear from the correlation of many Raman optical activity features in Figures 1 and 3 that (–)-menthol and (–)-menthyl chloride must have the same absolute configuration. This indicates that correlations of absolute configuration from Raman optical activity data are reliable.

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