**843.** *Stereochemistry of cycloHexane Derivatives.   Part V.*   Infrared Spectra and Conformations of Stereoisomeric* 1 : 2-*Diols.*

By A. R. H. COLE and P. R. JEFFERIES.

Infrared spectra in the hydroxyl stretching region of *p*-menthane-1 : 2-, -2 : 3-, and -3 : 4-diol and a variety of 1-alkyl*cyclo*hexane-*cis*- and -*trans*-1 : 2-diols has provided evidence on stabilities of different conformations. Distinction between secondary and tertiary free hydroxyl absorptions in the secondary-tertiary glycols has indicated hydrogen-bonding rules.   Secondary hydroxyl groups form intramolecular hydrogen bonds more readily than tertiary, and axial groups more readily than equatorial.   Kuhn's Δν values have been obtained and interpreted in terms of conformational arguments. The structures have been assigned to two *cis-p*-menthane-1 : 2-diols.

IT is now accepted [1-3] that at ordinary temperatures the preferred form for a mono-substituted *cyclo*hexane derivative will be the chair form in which the substituent is equatorial, and that this preference is due to repulsive forces between non-bonded atoms which will be the greater the larger is the substituent.   In *trans*-1 : 2-, *cis*-1 : 3-, and *trans*-1 : 4-disubstituted *cyclo*hexanes both groups can usually adopt an equatorial position with consequent conformational stabilization,[2] whereas in the complementary *cis*-1 : 2-, *trans*-1 : 3-, and *cis*-1 : 4-isomers, which have one equatorial and one axial group, the distribution of the two conformations will depend on the relative sizes of the groups. Menthol (I) is better represented as (II), with all substituents equatorial.   However, the most stable conformation of *neoiso*menthol (III) could be (IV) or (IVA) or a significant mixture of the two, since the tendency of the larger *iso*propyl group to be equatorial might be equalled or overcome by the combined effects of the hydroxyl and the methyl group. It is deduced below that *neoiso*menthol exists almost entirely as (IV), in agreement with the purely chemical evidence of Eliel.[4]

(I)   (II)   (III)   (IV)   (IVA)
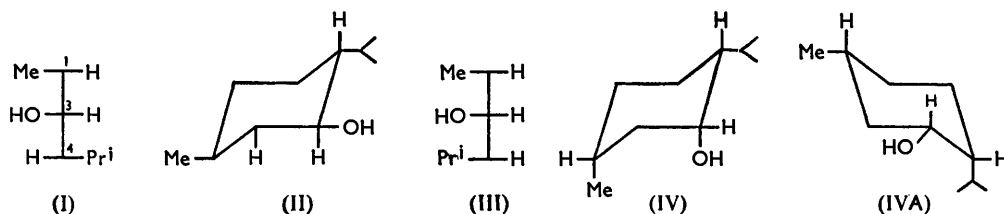
The present work is concerned with the conformations adopted by a series of 1 : 2-diols based on *cyclo*hexane and containing a range of other substituents.   By using infrared absorption spectra to study intramolecular hydrogen-bonding, we have found a direct experimental method of determining the nature of these conformations at room temperature in carbon tetrachloride solution.

Kuhn [5] described infrared measurements on a series of cyclic diols with varying ring sizes, and correlated (*a*) the separation Δν between the free hydroxyl stretching band (near 3630 cm.$^{-1}$) and the band due to intramolecular hydrogen bonds (near 3590 cm.$^{-1}$) with (*b*) the distance between the hydroxyl groups.   In general, the closer are the two groups the more readily is the hydrogen bond formed and the larger the value of Δν.   We have found it profitable to examine closely the intensities of the free and hydrogen-bonded hydroxyl absorption and the frequencies of the free hydroxyl groups as well as the Δν values, while keeping the ring size constant.

* Part IV, preceding paper.

[1] Rasmussen, *J. Chem. Phys.*, 1943, **11**, 249;   Kohlrausch and Wittek, *Z. phys. Chem.*, 1941, **48**, B, 177;   Hassel and Viervoll, *Acta Chem. Scand.*, 1947, **1**, 149;   Aston, Schumann, Fink, and Doty, *J. Amer. Chem. Soc.*, 1941, **63**, 2029;   Beckett, Pitzer, and Spitzer, *ibid.*, 1947, **69**, 2488.
[2] Hassel, *Research*, 1950, **3**, 504.
[3] Barton, *Experientia*, 1950, **6**, 316;   Barton, Hassel, Pitzer, and Prelog, *Nature*, 1953, **172**, 1096; Orloff, *Chem. Rev.*, 1954, **54**, 347.
[4] Eliel, *Experientia*, 1953, **9**, 91.
[5] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492;   1954, **76**, 4323.

RESULTS AND DISCUSSION

The frequencies and peak intensities of the free- and bonded-hydroxyl absorption bands and the values of $\Delta\nu$ are given in the Table, with an indication of the configuration and conformation of the hydroxyl group responsible for each band.

Absorption Frequencies.—It should be noted that $\Delta\nu$ is, not the difference between the frequencies listed under Free OH and Bonded OH in the Table, but the amount by which the bonded type is lowered from its own unbonded frequency. Although Bellamy [6] doubts that they can be so distinguished, experience in this laboratory [7] shows that in carbon tetrachloride solution primary alcohols absorb near 3642 cm.$^{-1}$ ($\varepsilon \sim 70$), secondary near 3629 cm.$^{-1}$ ($\varepsilon \sim 50$—60, axial slightly higher frequency than equatorial), and tertiary near 3618 cm.$^{-1}$ ($\varepsilon \sim 45$). No primary alcohols are included in the present study, but for interpretation of the results in Table 1 it is necessary to be able to distinguish between the secondary and tertiary groups. Menthol (II) absorbs at 3628 cm.$^{-1}$, *iso*menthol at 3627

Infrared spectra in the region of hydroxyl stretching absorption.
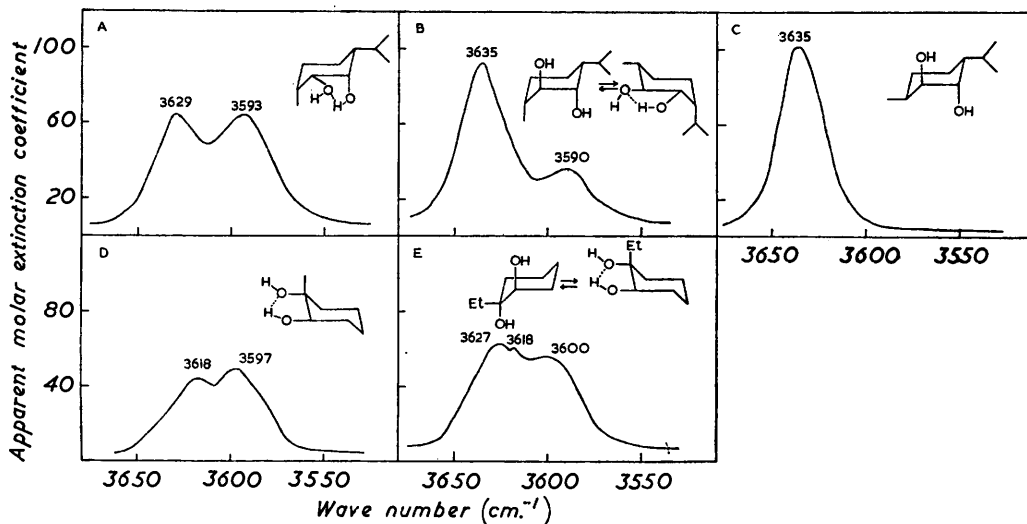
A, cis-2-*Hydroxy*neoisomenthol.
B, trans-2-*Hydroxy*neoisomenthol.
C, trans-2-*Hydroxy*neomenthol.
D, 1-*Methyl*cyclohexane-trans-1 : 2-*diol*.
E, 1-*Ethyl*cyclohexane-trans-1 : 2-*diol*.

cm.$^{-1}$, *neo*menthol and *neoiso*menthol at 3632 cm.$^{-1}$, while guaiol [7] and a number of tertiary hydroxy-steroids [8] absorb near 3618 cm.$^{-1}$. We have therefore taken the frequencies 3629 and 3618 cm.$^{-1}$ as standard free-hydroxyl frequencies in the calculation of $\Delta\nu$ values. Now, 1-methyl*cyclo*hexane-*cis*-1 : 2-diol absorbs at 3628 cm.$^{-1}$ (free) and 3584 cm.$^{-1}$ (bonded), indicating that the secondary hydroxyl group is free and therefore the tertiary bonded. Thus the value of $\Delta\nu$ is $3618 - 3584 = 34$ cm.$^{-1}$ not $3629 - 3584 = 45$ cm.$^{-1}$ as might appear at first sight from the Table. Some of the secondary hydroxyl groups in the *p*-menthane-2 : 3-diol stereoisomers absorb slightly above 3629 cm.$^{-1}$, particularly in those compounds which form hydrogen bonds fairly readily (*e.g.*, *cis*- and *trans*-2-hydroxy-menthol), and this high frequency may be related to the stability or rigidity of the cyclic bonded system. However, even with these we have used 3629 cm.$^{-1}$ as the free secondary hydroxyl frequency for the purposes of calculating $\Delta\nu$.

Relation between Spectra and Conformations.—Typical examples of the spectra are shown in the Figure and are keyed to the Table by letters. Where the conformation favours hydrogen bonding (Fig. A), the intensities of the free and the bonded absorption

[6] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 86.
[7] (*a*) Allsop, Cole, White, and Willix, (*b*) Cole and Thornton, unpublished results.
[8] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2820.

are approximately equal (ε 50—60). Conformations which do not favour hydrogen bonding will thus be identified by increased intensity of the free-hydroxyl band and a decrease in that of the bonded-hydroxyl band (Figs. B and C).

Structures, hydroxyl frequencies, intensities, and band separations of 1 : 2-diols (cm.$^{-1}$, carbon tetrachloride solutions). Values of ε$_{max.}$ are in parentheses.

Spectral type [a]	Compound	Structure and conformation	Free OH	Free type [b]	Bonded OH	Bonded type [b]	Δν
A	*cyclo*Hexane-*cis*-1 : 2-diol ...	VI; R = H	3626 (60)	e(?), s	3588 (60)	a(?)s	41
A	1-Methyl*cyclo*hexane-*cis*-1 : 2-diol	VI; R = Me	3628 (50)	e, s	3584 (52)	a, t	34
A	1-Ethyl*cyclo*hexane-*cis*-1 : 2-diol	VI; R = Et	3628 (60)	e, s	3583 (63)	a, t	35
A	1-*iso*Propyl*cyclo*hexane-*cis*-1 : 2-diol	VI; R = Pr^i	3629 (61)	e, s	3582 (63)	a, t	36
A	*cis*-2-Hydroxymenthol	XII; R^1 = Me, R^2 = H	3639 (58)	e(?), s	3583 (61)	a(?)s	46
A	*cis*-2-Hydroxy*iso*menthol	XII; R^1 = H, R^2 = Me	3637 (69)	e(?), s	3583 (71)	a(?)s	46
A	*cis*-2-Hydroxy*neo*menthol	XIII; R^1 = Me, R^2 = H	3633 (60)	e(?)s	3583 (62)	a(?)s	46
A	*cis*-2-Hydroxy*neoiso*menthol	XIII; R^1 = H, R^2 = Me	3629 (64)	e(?)s	3593 (64)	a(?)s	36
A	*cis*-*p*-Menthane-3 : 4-diol	XIV	3627 (61)	e, s	3581 (61)	a, t	37
A	1-Hydroxycarvomenthol (m. p. 49°)	VII	3628 (67)	e, s	3586 (58)	a, t	32
D	1-Hydroxy*neoiso*carvomenthol (m. p. 72·5°)	VIII	3618 (55)	e, t	3580 (67)	a, s	49
A	*trans*-*cyclo*Hexane-1 : 2-diol	VA; R = H	3631 (62)	e, s	3600 (75)	e, s	29
D	1-Methyl*cyclo*hexane-*trans*-1 : 2-diol	VA; R = Me	3618 (44)	e, t	3597 (50)	e, s	32
E	1-Ethyl*cyclo*hexane-*trans*-1 : 2-diol [c]	V, VA; R = Et	3627 3618 }(~62)	e, t a, s a, t }	3600 (56)	e, s	29
C	1-*iso*Propyl*cyclo*hexane-*trans*-1 : 2-diol	V; R = Pr^i	3625 (88)	a, s; a, t	—	—	—
A	*trans*-2-Hydroxymenthol	XV; R^1 = Me, R^2 = H	3639 (46)	e, s	3590 (60)	e, s	39
A	*trans*-2-Hydroxy*iso*menthol	XV; R^1 = H, R^2 = Me	3631 (56)	e, s	3590 (65)	e, s	39
C	*trans*-2-Hydroxy*neo*menthol	XVI	3635 (100)	a, s	—	—	—
B	*trans*-2-Hydroxy*neoiso*menthol [c]	IX, IXA	3635 (93)	a, s; (e, s)	3590 (36)	e, s	39
C	*trans*-*p*-Menthane-3 : 4-diol	XVII	3629 (100)	a, s; a, t	—	—	—
D	1-Hydroxy*iso*carvomenthol	XVIII	3618 (52)	e, t	3597 (68)	e, s	32
C	1-Hydroxy*neo*carvomenthol	XIX	3624 (84)	a, s; a, t	—	—	—

|			R^1	R^2	R^3	R^4
	*iso*Menthol	X :	H	Me	OH	H
	*neo*Menthol	X :	Me	H	H	OH
	Carvomenthol	XI :	Me	H	H	OH
	*neo*Carvomenthol	XI :	Me	H	OH	H
	*iso*Carvomenthol	XI :	H	Me	H	OH
	*neoiso*Carvomenthol	XI :	H	Me	OH	H

[a] See Figure. [b] e = equatorial, a = axial, s = secondary, t = tertiary. [c] Mixture of two conformations.

All the *cis*-1 : 2-diols show strong absorption due to hydrogen bonding (*e.g.*, curve A), since in all of them one hydroxyl group is equatorial and one axial and they are sufficiently close to form a hydrogen bond regardless of the conformation of the molecule. The absence of hydrogen bonding in 1-*iso*propyl*cyclo*hexane-*trans*-1 : 2-diol shows that in the competition to occupy the equatorial position the *iso*propyl group is able to overcome completely the tendency of the two hydroxyl groups plus the energy of stabilization due to the hydrogen-bond formation. The conformation of this compound must therefore be substantially (V; R = Pr^i). The frequency of the combined secondary and tertiary free hydroxyl groups is 3625 cm.$^{-1}$ (components not resolved), which lies between the individual frequencies given above, and the peak intensity is 88.
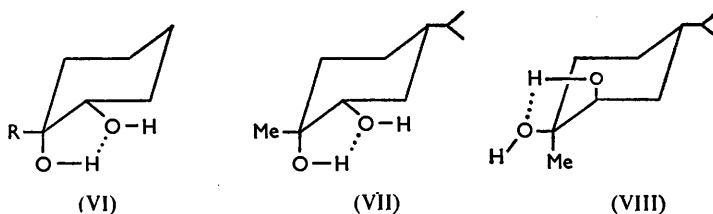
In 1-methyl*cyclo*hexane-*trans*-1 : 2-diol (Fig. D) the hydrogen bonding indicates that the two hydroxyl groups prevail over the methyl group (which is of course smaller than *iso*propyl), so that this compound exists as (VA; R = Me). The tertiary hydroxyl group is free (3618 cm.$^{-1}$) and the absence of absorption at 3629 cm.$^{-1}$ (free secondary) shows that none of the form (V; R = Me) is present. This preference of the secondary group to form the intramolecular hydrogen bond is borne out in a number of other compounds in this series (see Table) and allows us to state a first hydrogen-bonding rule, *viz.*, in *cyclo*hexane-*trans*-1 : 2-diols, where both hydroxyl groups are equatorial, a secondary group is involved in intramolecular hydrogen bonding in preference to a tertiary.

The intermediate case of 1-ethyl*cyclo*hexane-*trans*-1 : 2-diol (Fig. E) shows the presence of both conformations (V and VA; R = Et), demonstrating that they have about equal energies. The form (VA; R = Et) would be somewhat stabilized by the hydrogen-bond formation, whereas the alternative (V; R = Et) has its largest substituent group equatorial. The two free-hydroxyl bands are just resolved (3627, 3618 cm.$^{-1}$) and there is considerable hydrogen bonding. By analogy with 1-methyl*cyclo*hexane-*trans*-1 : 2-diol it might be expected that the secondary hydroxyl group would form the hydrogen bond, leaving the tertiary one free (3618 cm.$^{-1}$). The free secondary absorption (3627 cm.$^{-1}$) must be due to the diaxial form (V; R = Et).

1-Methyl*cyclo*hexane-*cis*-1 : 2-diol differs from the *trans*-compound in having its tertiary hydroxyl group bonded (free secondary 3628 cm.$^{-1}$). It must therefore be represented as (VI; R = Me). Similarly, 1-ethyl- (VI; R = Et) and 1-*iso*propyl-*cyclo*hexane-*cis*-1 : 2-
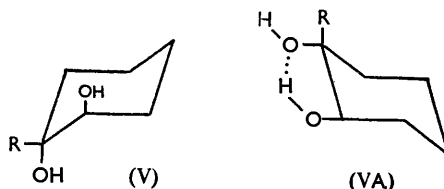

diol (VI; R = Pr^{i}) and 1-hydroxycarvomenthol (VII) all have free secondary hydroxyl (equatorial) and bonded tertiary (axial) groups. However, 1-hydroxy*neoiso*carvomenthol (VIII) has a free tertiary (3618 cm.$^{-1}$) and a bonded secondary group; here the tertiary hydroxyl group is equatorial and the secondary axial. Hence a second hydrogen-bonding rule can be stated, *viz.*, in *cyclo*hexane-*cis*-1 : 2-diols, where one hydroxyl group is equatorial and one axial, the latter is involved in intramolecular hydrogen bonding in preference to the former, regardless of whether they are secondary or tertiary.


Bonded types deduced from this and the previous rule are shown in the Table with queries, but little doubt remains.

In addition to the case of 1-ethyl*cyclo*hexane-*trans*-1 : 2-diol, mixed conformations are found for *trans*-2-hydroxy*neoiso*menthol (IX, IXA) (Fig. B). Without carrying out an accurate band separation we estimate from the relative intensities of the free- and the bonded-hydroxyl absorption that the proportion of (IXA) is ~20%. Therefore, since an *iso*propyl group can hold 80% of the molecules of this compound in conformation (IX) against the combined influences of a methyl group, two hydroxyl groups, and one hydrogen bond, it may safely be deduced that *neoiso*menthol (with one less axial hydroxyl group and no hydrogen bond) is represented by (IV) rather than (IVA). The other conformations in the Table are deduced similarly. Those for the carvomenthols confirm Bose's

chemical evidence [9] (considerable doubt hitherto attended the assignment for *neoiso*-carvomenthol).   For *cis-p*-menthane-3 : 4-diol the present work does not assign the configuration of the 1-methyl group.   For *trans*-2-hydroxymenthol there is no proof that the 3-hydroxyl group forms the hydrogen bond but it is thus reported here since it would


(IX)   (IXA)   (X)   (XI)
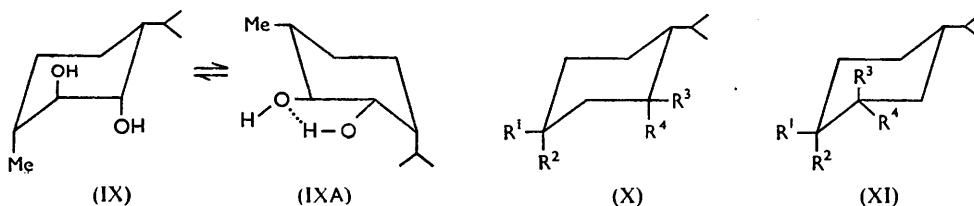
probably assume the position remote from the bulky *iso*propyl group.   Although the configuration of the 1-methyl group in *trans-p*-methane-3 : 4-diol is not known, the absence of hydrogen bonding indicates that the methyl group is equatorial since if it were axial

(XII)   (XIII)   (XIV)
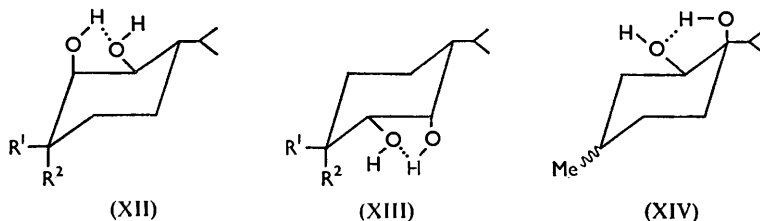
both conformations would be expected (cf. *trans*-2-hydroxy*neoiso*menthol); the methyl group is thus *trans* to the *iso*propyl group.   The similarity of the spectra of 1-hydroxy*iso*-carvomenthol and 1-methyl*cyclo*hexane-*trans*-1 : 2-diol provides further evidence for the structure proposed in the previous paper.
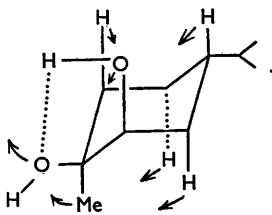
The Significance of $\Delta\nu$.—The frequency difference $\Delta\nu$ for 1-hydroxycarvomenthol and 1-hydroxy*neoiso*carvomenthol further supports the configurations.   In the previous paper the difficulty associated with chemical distinction between the two *cis-p*-menthane-1 : 2-

(XV)   (XVI)   (XVII)

(XVIII)   (XIX)
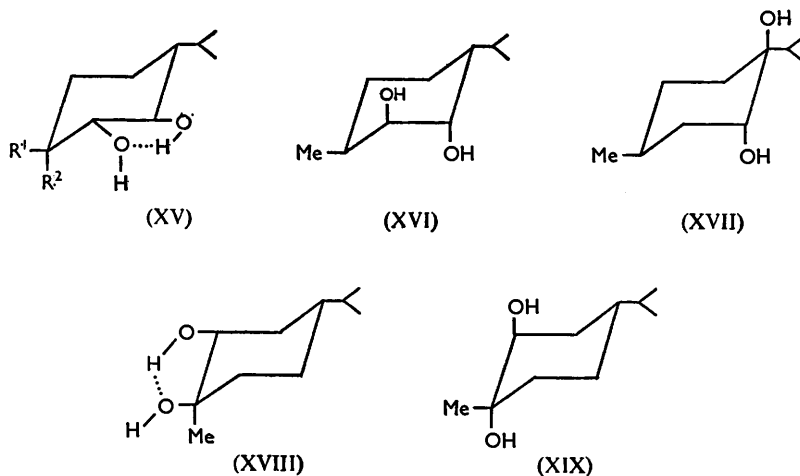
diols (m. p. 49° and 72·5° respectively) was pointed out.   The most stable conformation of 1-hydroxycarvomenthol is clearly (VII).   1-Hydroxy*neoiso*carvomenthol is form (VIII) since it involves substitution of an equatorial hydroxyl group into the established most stable configuration of *neoiso*carvomenthol.   The isomer, m. p. 49° ($\Delta\nu$ 32 cm.$^{-1}$), has a

[9] Bose, *Experientia*, 1952, **8**, 458.

spectrum corresponding closely to that of 1-methyl*cyclo*hexane-*cis*-1 : 2-diol (VI; R = Me) ($\Delta\nu$ 34 cm.$^{-1}$) and so must be 1-hydroxycarvomenthol (VII). The isomer, m. p. 72·5°, which shows an entirely different spectrum ($\Delta\nu$ 49 cm.$^{-1}$) is therefore 1-hydroxy*neoiso*-carvomenthol (VIII). The large value of $\Delta\nu$ for the latter is required by conformation (VIII) since Kuhn [5] has shown that the magnitude of $\Delta\nu$ is inversely proportional to the ease of hydrogen-bond formation and is larger if the hydroxyl groups are close together. He attributes the fact that the value for *cyclo*hexane-*cis*-1 : 2-diol is higher than that of the *trans*-isomer to rotation of the hydroxyl groups towards each other, known to be easier for *cis*- than for *trans*-diols since in the former it is assisted by interactions (repulsions) between axial groups,[10] but opposed in the latter. The situation in (VIII) corresponds to the replacement of an axial hydrogen atom by a methyl group which causes much more rotation of the 1-hydroxyl group (cf. XX) with a corresponding increase in $\Delta\nu$. It is of interest to note that $\Delta\nu$ for the compound (VIII) is greater than that of any other studied in this investigation.

A similar argument can be put forward on the basis of periodate oxidation rates which also depend on the distance separating the hydroxyl groups.[11] One would expect 1-hydroxy*neoiso*carvomenthol with the smaller separation of hydroxyl groups to be oxidised significantly faster than 1-hydroxycarvomenthol. The values for k_2 given in the previous paper are 8·8 and 6·5 respectively. The formation of a mono-*p*-nitrobenzoate from (VII) under conditions affording the diester of (VIII) agrees with the presence of a tertiary hydroxyl which is axial in the former and equatorial in the latter.

In 1-ethyl*cyclo*hexane-*trans*-1 : 2-diol (VA; R = Et) ($\Delta\nu$ 29 cm.$^{-1}$) the repulsion between the 1-ethyl group and the axial groups would be greater than for the 1-methyl-*trans*-compound (VA; R = Me) ($\Delta\nu$ 32 cm.$^{-1}$). In these molecules the repulsion moves the tertiary away from the secondary hydroxyl group, thereby weakening the hydrogen bonding and decreasing $\Delta\nu$. The limiting case is that of 1-*iso*propyl*cyclo*hexane-*trans*-1 : 2-diol where the repulsion is sufficient to invert the molecule and so prevent all hydrogen bonding.

A slightly different effect is responsible for the lower value of $\Delta\nu$ in *cis*-2-hydroxy*neoiso*-menthol (XIII; R^1 = H, R^2 = Me) ($\Delta\nu$ 36 cm.$^{-1}$) than in the other *cis*-2-hydroxy-isomers of the menthol series for which $\Delta\nu$ = 46 cm.$^{-1}$. In *cis*-2-hydroxy*neoiso*menthol the axial 1-methyl group (R^2) will repel the hydrogen of the axial 3-hydroxyl group, orienting it away from the 2-hydroxyl group. The hydrogen bond is lengthened, and therefore weakened, relative to that in the other three compounds in which there are only axial hydrogen atoms on the same side of the molecule as the axial hydroxyl group.

(XX)

EXPERIMENTAL

The diols used in this work were pure samples available from previous studies.[11,12]

The infrared spectra were recorded on a Grubb–Parsons single-beam spectrometer, Model S.3.A equipped with a Perkin–Elmer thermocouple, light-chopper, and No. 81 amplifier. A prism of calcium fluoride was employed and the spectral slit width at 3620 cm.$^{-1}$ was *ca.* 6 cm.$^{-1}$. By using the water-vapour absorption in the background of each spectrum as calibration, frequencies could be measured with an accuracy of ± 1 cm.$^{-1}$. Measurements were made on carbon tetrachloride solutions in 3·3 and 10 mm. cells, and since the concentrations were less than 0·01M, no intermolecular hydrogen bonding was encountered. Solutions were made up by weight and molar concentrations calculated from the density. Spectral intensities, expressed as apparent molar extinction coefficient, $\varepsilon = (1/cl) \log_{10}[I_0/I]$, are estimated to be accurate to 5—10%; no corrections for finite slit width have been made, nor has band overlap been taken into account in quoting values of $\varepsilon_{max.}$ in the Table. Strictly, the integrated band area should be used as the measurement of the concentration of a particular species, but this was not

[10] Hassel and Ottar, *Acta Chem. Scand.*, 1947, **1**, 929; Angyal and Macdonald, *J.*, 1952, 686.
[11] Jefferies, Macbeth, and Milligan, *J.*, 1954, 705.
[12] Macbeth and Robertson, *J.*, 1953, 895, 3512; 1954, 701.

considered necessary for the present purpose. The deductions of conformation depend only on relative intensities of the absorption bands due to free and bonded hydroxyl groups, and these are much more accurate than the absolute measurements.

DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF WESTERN AUSTRALIA,
    NEDLANDS, WESTERN AUSTRALIA.
DEPARTMENT OF ORGANIC CHEMISTRY, THE UNIVERSITY OF ADELAIDE,
    ADELAIDE, SOUTH AUSTRALIA.   [*Received, May 15th,* 1956.]