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Intramolecular Hydrogen Bonds. VIII.[1] Isomeric Hydroxycyclohexylcarbinols and Bis-hydroxymethyl-cyclohexanes

By Nobuo Mori and Yojiro Tsuzuki

Department of Chemistry, Tokyo College of Science, Kagurazaka, Shinjuku-ku, Tokyo

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The preferential direction of intramolecular hydrogen bonding in isomeric hydroxycyclohexylcarbinols in dilute carbon tetrachloride solutions has been investigated by infrared spectroscopy. The 1-hydroxy isomer contains a tertiary hydroxyl group predominantly bonded to the oxygen atom of a primary hydroxyl, while the *cis*- and *trans*-2-hydroxy isomers contain a primary hydroxyl group mainly bonded to the oxygen atom of a secondary hydroxyl; the other isomers are internally unbonded. On the other hand, bis-hydroxymethyl-cyclohexanes other than the 1, 1- and 1, 2-isomers are unbonded. These findings can be explained in terms of the acidity of the hydroxyl groups and the steric effect on the orientation of the groups.

The direction and extent of intramolecular hydrogen bonding is particularly sensitive to changes in molecular structure and conformation. In intramolecularly hydrogen-bonded diol systems, the direction of the bonding of one hydroxyl group to another depends on the acidity and/or the basicity of the groups as well as on the steric environment around them; the steric requirement for the orientation of the groups often appears to be more influential than their acidity. For example, when the diols are those which contain a tertiary and a primary hydroxyl group in the 1, 2-position, the steric crowding about the tertiary hydroxyl group causes its hydrogen atom to be directed towards the primary hydroxyl group, resulting in hydrogen-bond formation with the oxygen atom of the latter,[2] although the former group is more basic or proton-accepting than the latter.[3] In *cis*-cyclohexane-1, 2-diols the so-called 1, 3-diaxial steric interaction being exercised on an axial hydroxyl group causes its hydrogen atom to be directed out of the cyclohexane ring; then the hydrogen atom is bonded with the oxygen atom of an equatorial hydroxyl.[2]

In the present investigation, such a preferential direction of hydrogen bonding has been investigated in hydroxycyclohexylcarbinols by means of infrared spectroscopy. Further, this investigation has dealt with the intramolecular hydrogen bonding in bis-hydroxymethyl-cyclohexanes.

Experimental

Samples.—Hydroxycyclohexylcarbinols were prepared in the usual manner by reducing the corresponding hydroxycyclohexane-carboxylates[4] with lithium aluminum hydride in ether. Bis-hydroxymethyl-cyclohexanes were similarly synthesized from the diethyl esters of cyclohexane-dicarboxylic acids.[5,6] They were purified through recrystallizations or redistillations; their physical constants closely agreed with those reported in the literature (see Table I).

Infrared Measurements.—The hydroxyl stretching region was measured by a method previously described,[4] using lithium fluoride optics with carbon tetrachloride solutions in concentrations of 0.004 mol./l. or less at ca. 25°C. Such a concentration was sufficiently low to avoid any intermolecular hydrogen bonding.

Results and Discussion

The data of the observed apparent hydroxyl bands are summarized in Table I, together with the physical constants of the samples.

In cyclohexane systems, characteristic unbonded hydroxyl frequencies[3,13,14] are 3635—3640 cm^{-1} for primary hydroxyl groups, 3627—3632 cm^{-1} and 3623—3630 cm^{-1} for axial and equatorial secondary hydroxyl respectively, and 3613—3619 cm^{-1} for tertiary hydroxyl; each frequency is that of the apparent band peak, which is practically assigned to the hydroxyl group in the sterically-most-preferable one of the three orientations around the C–O axis.[15] In practice for the exact assignment of an apparent free hydroxyl band one should also take account of an additional weaker absorption due to the hydroxyl group in the

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[1] Part VII: N. Mori, Y. Tanaka and Y. Tsuzuki, This Bulletin, **39**, 1490 (1966).

[2] L. P. Kuhn, *J. Am. Chem. Soc.*, **80**, 5950 (1958).

[3] L. P. Kuhn, ibid., **74**, 2492 (1952).

[4] N. Mori, S. Omura, N. Kobayashi and Y. Tsuzuki, This Bulletin, **38**, 2149 (1965).

[5] G. H. Haggis and L. N. Owen, *J. Chem. Soc.*, **1953**, 399.

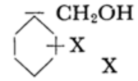
[6] G. H. Haggis and L. N. Owen, ibid., **1953**, 404.

[13] A. R. H. Cole, G. T. A. Müller, D. W. Thornton and R. L. S. Willix, *J. Chem. Soc.*, **1959**, 1218.

[14] A. R. H. Cole, P. R. Jefferies and G. T. A. Müller, ibid., **1959**, 1222.

[15] M. Oki and H. Iwamura, This Bulletin, **32**, 950 (1959).

TABLE I. SUMMARY OF THE COMPOUNDS AND THEIR INFRARED DATA

No.		B. p. °C/mmHg (M. p. °C)	n_D	ν_{OH} cm^{-1}	log I_0/I	$\Delta\nu_{1/2}$ cm^{-1}
I	1-OH	(76.5[7])		3638 3586	0.22 0.29	90
II	*cis*-2-OH	125—126/7[8] (49—51)		3642 (sh.) 3628 3538	 0.74 0.57	35 58
III	*trans*-2-OH	125—126/7[8]	1.4835(25°C)	3638 (sh.) 3623 3535	 0.81 0.96	44 60
IV	*cis*-3-OH	132/9[9]	1.4890(23°C)	3637 3622	0.64 0.75	36
V	*trans*-3-OH	134—136/6[9,10]	1.4874(25°C)	3638 3628	0.58 0.72	40
VI	1-CH_2OH[11]			3640 3550		
VII	*cis*-2-CH_2OH[3,12]			3633 3496		
VIII	*trans*-2-CH_2OH[3,12]			3631 3479		
IX	*cis*-3-CH_2OH	(59[5])		3640	1.68	24
X	*cis*-4-CH_2OH	154/9[6]	1.4868(20°C)	3635	1.03	30
XI	*trans*-4-CH_2OH	(66—66.5[6])		3637	1.17	28

other less-preferable orientations; this absorption appears generally as a broadening of the band, centered at a frequency lower by 10—15 cm^{-1} than the apparent peak frequency.[15] In fact, 1, 3- and 1, 4-bis-hydroxymethyl-cyclohexanes (IX—XI), which are internally unbonded, show only one sharp band, at ca. 3637 cm^{-1} somewhat broadened on the lower frequency side. 3-Hydroxycyclohexylcarbinols (IV and V) which are also internally unbonded show two band-peaks at ca. 3637 and 3625 cm^{-1}; the higher intensity of the lower frequency-free secondary hydroxyl band (see the table) may be attributed to such an absorption of the free primary hydroxyl group overlapped with the band. However, when the free secondary hydroxyl band is much stronger than the free primary hydroxyl, as is observed in the spectra (cf. Fig. 2) of 2-hydroxycyclohexylcarbinols (II and III), such an absorption of the primary hydroxyl group, overlapped with the stronger band, is practically negligible, especially for the purpose of confirming the preferential direction of hydrogen bonding.

In this paper, the term "free hydroxyl group" includes both the hydroxyls which contain an unbonded hydrogen atom (i. e., those not participating in any hydrogen bond) and the hydroxyls whose oxygen atom is bonded to the hydrogen atom of another hydroxyl, since the bonding of the oxygen atom of a free hydroxyl group to the hydrogen atom of another hydroxyl has, in general, little effect upon the frequency of the free hydroxyl.[2,3]

1-Hydroxycyclohexylcarbinol (I).—The resolution of the observed spectrum is far from complete, in spite of the relatively wide spacing of 52 cm^{-1} between the band-peaks (3638 and 3586 cm^{-1}), so its graphical separation has been examined by a method previously described.[1,4] This method, shown in Fig. 1, assumes, for convenience, that the individual band-components are symmetric; after subtracting two strong, substantially symmetric bands from the spectrum, a weak broad band remains with a peak frequency

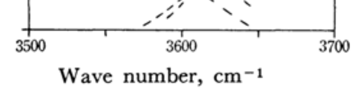


Fig. 1. Infrared spectrum of 1-hydroxycyclohexylcarbinol (I):
Apparent: ——; Separated: ----

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7) M. Mousseron, *Compt. rend.*, **224**, 1230 (1947).

8) H. B. Henbest and B. B. Millward, *J. Chem. Soc.*, **1960**, 3575.

9) D. S. Noyce and D. B. Denney, *J. Am. Chem. Soc.*, **74**, 5912 (1952).

10) H. L. Goering and C. Serres, ibid., **74**, 5908 (1952).

11) P. von R. Schleyer, ibid., **83**, 1368 (1961).

12) L. P. Kuhn, P. von R. Schleyer, W. F. Baitinger and L. Eberson, ibid., **86**, 650 (1964).

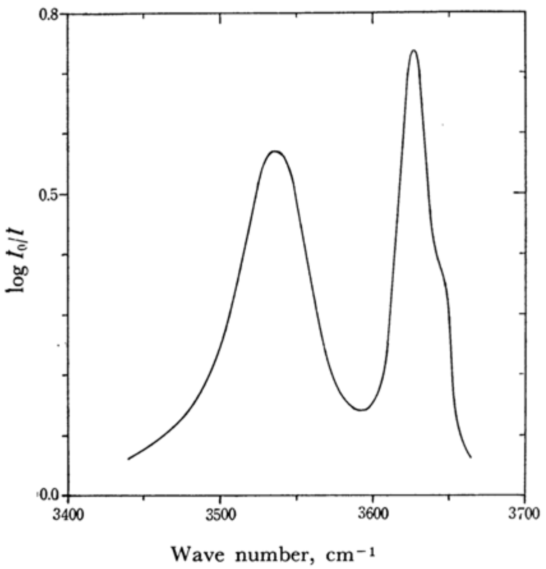
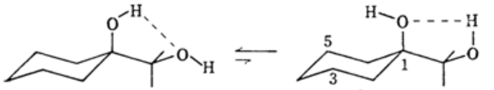


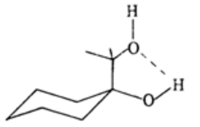
Fig. 2. Infrared spectrum of *cis*-2-hydroxycyclohexylcarbinol (II).

of 3615 cm^{-1}. The resulting band absorbances (and half-band widths in cm^{-1}) are 0.17 (38) for the 3638 band, 0.04 (30) for the 3615 band, and 0.25 (36) for the 3586 band. The separated weak band seems to be due to an additional absorption, (which will be assigned later), rather than to the intrinsic unsymmetry of the strong bands.

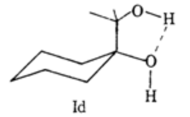
This carbinol may take the four interconvertible, internally bonded chair-forms Ia—Id, in which all the valence bonds of any two adjacent atoms are fully staggered:



Ia Ib



Ic



Id

In assigning the bands to the hydroxyl groups in these forms, one must first take the thermodynamical stability and the population of these forms into account. The difference in free energy between equatorial and axial hydroxyl groups lies in a range of -0.4 to -0.9 kcal./mol.[16]; for the hydroxymethyl group the difference is unknown, but it is expected to be nearly equal to the -1.5 to -1.9 kcal./mole given for the methyl.[16] Since the difference of -1 kcal./mole (the difference between the two averaged values) at 25°C corresponds to an equilibrium constant of ca. 5.3, as calculated using the van't Hoff isotherm, the carbinol may exist predominantly in a chair form containing the hydroxyl group in the axial position. The preference of the axial hydroxyl-containing form holds even when the hydrogen bonding is present, since no large entropy and enthalpy effect may be expected on the equilibrium between the bonded forms. Of the axial hydroxyl-containing forms, Ia and Ib, the preferable one may be Ia, in which the tertiary hydroxyl group is bonded to the oxygen atom of the primary hydroxyl, in spite of the former being more basic or proton-accepting than the latter. The reason is that the axial hydrogens on C_3 and C_5 in Ib may sterically repel the hydrogen of the tertiary hydroxyl group, causing it to be directed out of the cyclohexane ring and then towards the primary hydroxyl, as in Ia. The repulsion can then be removed by going to Ia. This expectation agrees well with the infrared data; the strong bands at 3638 and 3586 cm^{-1} are predominantly due to the free primary hydroxyl group and the bonded axial tertiary hydroxyl group respectively in Ia. The latter frequency agrees well with the 3586 cm^{-1} of the bonded tertiary hydroxyl group in 1, 1-diethylethyleneglycol.[2] On the other hand, the free tertiary hydroxyl group and the bonded primary hydroxyl group in Ib may together principally contribute to the weak band at 3615 cm^{-1}; this is supported by the fact that the frequency agrees with that of ordinary free tertiary hydroxyl groups and with the 3612 cm^{-1} of the bonded primary hydroxyl groups in ethyleneglycols.[2,3]

Further, the separation by 29 cm^{-1} between the free and the bonded tertiary hydroxyl band agrees with the 32 cm^{-1} of ethyleneglycol and 1, 1-diethylethyleneglycol,[2] but it is lower than either the 50 cm^{-1} of 1, 1,-diisopropylethyleneglycol[2] or the ca. 80 cm^{-1} of 1, 1-di-*t*-butylethyleneglycol.[2] Such a lowering in frequency resulting from the 1, 1-disubstitution may chiefly be attributed to the so-called Thorpe-Ingold effect,[17] which results in the decrease in valence angle between the other two bonds of C_1; therefore, the above fact suggests that the cyclohexane ring does not suffer from such an effect, and that, at the same time, the steric repulsion between the hydroxyl group on C_1 and the axial hydrogens on C_3 and C_5 is not so high as to change the valence angle of C_1 to any significant extent.

2-Hydroxycyclohexylcarbinols (II and III).—As Fig. 2 shows, the spectra are of a completely-resolved doublet with peak-frequencies of 3625 and 3536 cm^{-1}; the higher frequency band has a weak shoulder, centered at ca. 3640 cm^{-1}. An

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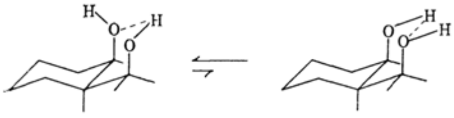
[16] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., New York, N. Y. (1962), p. 236.

[17] R. M. Beesley, C. K. Ingold and J. F. Thorpe, *J. Chem. Soc.*, **107**, 1030 (1915); C. K. Ingold, ibid., **119**, 305 (1921); see also Refs. 3 and 12.

examination of the rough graphical separation shows that the absorbance of the shoulder separated from the spectrum is about 0.19 for II and 0.17 for III.

For *cis*-carbinol II, the axial hydroxyl-containing forms, IIa and IIb, may similarly be preferable to the equatorial hydroxyl-containing forms. The steric environment around the hydroxyl groups included in the hydrogen bond may be essentially the same in both IIa and IIb, so the difference in acidity between the hydroxyl groups may be considered to be a major factor in deciding the direction of hydrogen bonding; therefore, IIa, in which the less basic primary hydroxyl group is bonded to the oxygen atom of the more basic secondary hydroxyl, should be more favorable than IIb. Accordingly, the strong band at 3628 cm^{-1} may primarily be assigned to the free secondary axial hydroxyl group in IIa, while the weak absorption at 3642 cm^{-1} may primarily be assigned to the free primary hydroxyl in IIb. The strong band at 3538 cm^{-1} is mainly due to the bonded primary hydroxyl group in IIa, together with a minor proportion of the bonded secondary hydroxyl in IIb.

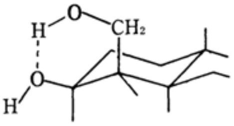


IIa IIb

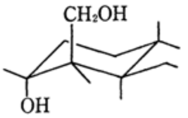
As for *trans*-carbinol III, only the diequatorial forms, IIIa and IIIb, are possible for hydrogen bonding for the following reasons: (1) any diaxial form should be unfavorable for hydrogen bonding in view of the distance between the hydroxyl groups, and in view of the fact that any such form includes 1, 3-diaxial interactions between the axial hydrogens and the groups, while (2) the diequatorial forms include only the so-called skew interaction between the groups, an interaction which is much lower in energy than the 1, 3-diaxial interaction, and they acquire in addition the stabilization resulting from the hydrogen bond. In IIIa and IIIb, the nature of the hydroxyl groups may similarly be a major factor in controlling the equilibrium between the forms. Accordingly, the strong bands at 3623 and 3535 cm^{-1} may mostly be due to the free secondary hydroxyl group and the bonded primary hydroxyl group in IIIa, while the weak shoulder at 3638 cm^{-1} may be due to the free primary hydroxyl in IIIb.

IIIa IIIb

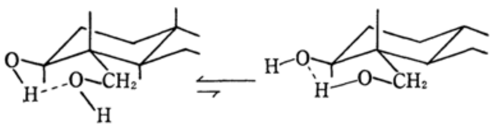
As has been mentioned above, the expected preferential direction of hydrogen bonding of the primary hydroxyl group toward the oxygen atom of the secondary hydroxyl agrees very well with the infrared data. In this connection, there has been an interesting report[18] on the direction of hydrogen bonding in some triterpenoid 3, 24-diols. Urs-12-ene-3β, 24-diol (A) has the primary hydroxyl group bonded to the oxygen atom of the equatorial secondary hydroxyl, the 3α-isomer with the diaxial structure (B) contains no hydrogen bonding, and methyl hederagenin with the diequatorial structure prefers form C to D. It is surprising that the hyderogen bonding in methyl hederagenin is opposite in preferential direction to those in carbinols II and III, the reason for this is not clear at the present time.



A



B



C D

3-Hydroxycyclohexylcarbinols (IV and V).—These are internally unbonded. The diaxially fixed structure of *cis*-3-hydroxycyclohexylcarbinol is known[19] to show a bonded hydroxyl band at 3460 cm^{-1}; this fact is not necessarily inconsistent with the absence of bonding in *cis*-carbinol IV for the following reason: the stabilization due to hydrogen bonding in the diaxial conformation can not be sufficient to overcome the instabilization due to the steric repulsion between the diaxial atoms and groups, in view of the fact that the difference in free energy between the diequatorial and the unbonded diaxial conformation is expected to be of the relatively high value of ca. −2.4 kcal./mol.[20] (corresponding to an equilibrium constant of 56), while the ordinary OH–O type intramolecular hydrogen bonding to form a seven-membered ring results in a large decrease in entropy of −10

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18) A. R. H. Cole and G. T. A. Müller, *J. Chem. Soc.*, **1959**, 1224.

19) J. Tadanier, *J. Org. Chem.*, **28**, 1744 (1963).

20) Approximated by adding the corresponding values for a hydroxyl and a hydroxymethyl group, since such summations have been verified to be approximately correct in some cases.[21,22]

21) S. J. Angyal and D. J. McHugh, *Chem. & Ind.*, **1956**, 1147.

22) N. L. Allinger and M. A. Miller, *J. Am. Chem. Soc.*, **83**, 2145 (1961); E. L. Eliel and H. Haubenstock, *J. Org. Chem.*, **26**, 3503 (1961).

e. u., with an enthalpy of 2.7 kcal./mol.[23] In other words, the bonded diaxial form, if any, exists in a population so low as to make it impossible to observe its spectral band. In fact, intramolecular hydrogen bonding is present when the difference in free energy is relatively low, e. g., such as the −1.9 kcal./mol.[21] for *cis*-cyclohexane-1, 3-diol, which is known to be hydrogen-bonded.[3]

Bis-hydroxymethyl-cyclohexanes (VI—XI).—The 1, 3- and 1, 4-isomers are internally unbonded, while the 1, 1- and 1, 2-isomers are bonded. The absence of bonding in the *cis*-1, 3-isomer IX can be explained by essentially the same reason as that mentioned in the case of *cis*-3-hydroxycyclohexylcarbinol IV; in this case, however, the difference in free energy between the diequatorial and the diaxial form should be much higher. In the case of the *cis*-1, 4-isomer X, on the other hand the most important factor may be that this compound can not take the boat or twist conformation required for ordinary hydrogen bondings between 1- and 4-*cis* groups.[24]

The authors are thankful to Mr. Teruo Kajiura and Mr. Tadao Tamura of the Government Chemical Industrial Research Institute of Tokyo for the infrared measurements.

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[23] L. P. Kuhn and R. A. Wires, *J. Am. Chem. Soc.*, **86**, 2161 (1964).

[24] R. D. Stolow, P. M. McDonagh and M. M. Bonaventure, ibid., **86**, 2165 (1964), and references cited therein.