Organic and Biological Chemistry

Cyclopropane Rings as Proton-Acceptor Groups in Hydrogen Bonding[1]

Louis Joris,[2] Paul von R. Schleyer, and Rolf Gleiter

Contribution from the Department of Chemistry, Princeton University, Princeton, New Jersey 08540. *Received September 1, 1967*

Abstract: Can cyclopropane rings function as weak proton acceptors in hydrogen bonding? This problem has been investigated using infrared spectral techniques. Evidence for OH···cyclopropane hydrogen bonding seems quite conclusive. When 1,1-dimethylcyclopropane or dicyclopropylmethane are added to a solution of *p*-fluorophenol in CCl_4 new bands ($\Delta\nu$'s 43 and 35 cm^{-1}, respectively) indicative of intramolecular hydrogen bonding are formed. Intramolecular association involving hydroxyl groups and cyclopropane rings can also be demonstrated. While there is no evidence for hydrogen bonding in β-cyclopropylethanol itself, more rigid, properly oriented derivatives give well-defined, two-peak spectra. The best example is *endo-syn*-tricyclo[3.2.1.$0^{2,4}$]octan-8-ol (VII) with $\Delta\nu$ 35 cm^{-1}. The *anti* isomer XI as well as the model compound, 7-norbornanol (IX), show only the one peak expected of secondary alcohols. Cyclopropylcarbinols also show evidence for intramolecular hydrogen bonding, but the $\Delta\nu$'s are smaller (~15 cm^{-1}) and the interpretation of the spectra is less straightforward. In some cases, *e.g.*, 1-methylcyclopropylcarbinol, the free and bonded peaks are well separated, but in most instances computer decomposition of the observed band into component peaks is required. Saturated alcohols incapable of intramolecular hydrogen bonding also give complex spectra due to conformational heterogeneity; but the decomposed spectra show significant differences when compared with those of cyclopropylcarbinols. The latter display enhanced intensity peaks at lower frequencies than expected on the basis of conformational heterogeneity; these peaks are assigned to OH···cyclopropane hydrogen bonds. Conformation XIII, in which the C–O bond bisects the cyclopropane ring, appears to be unfavorable for intramolecular association. The spiro compound XV, with such an arrangement, has practically the same spectrum as that of a reference substance, XVII. The preferred hydrogen bonding conformation for cyclopropylcarbinols appears to be one (XII, XVIIIa, and XIXe) in which the O–H bond and a ring C–C bond are roughly parallel.

The π electrons in olefins, acetylenes, and aromatic compounds can function as proton-acceptor sites in both inter-[3] and intramolecular[4-10] hydrogen bonding. Many similarities exist between the properties of cyclopropane rings and unsaturated π-electron systems.[11] This paper concerns itself with the problem of whether or not the cyclopropane ring can function as a proton acceptor in hydrogen bonding.

Apparently Turnbull and Wallis were the first to recognize the possibility that the cyclopropane ring might participate in hydrogen bonding.[12] It was suggested that a contributing cause of the slow reaction of bromine with cyclopropaneacetic and -carboxylic acids could be the presence of intramolecular hydrogen bonds in those molecules. However, no evidence was cited to support this speculation and it seems quite unlikely that such hydrogen bonding could be important, especially in the aqueous acetic acid solvent employed.[13]

The cyclopropane ring, at best, can only be a very weak proton acceptor, and it is clear that a very sensitive and specific method must be employed to detect hydrogen bonding in such instances. Infrared spectroscopy is the method of choice.[15] This was first applied to a study of cyclopropylcarbinol by Schleyer, Trifan, and Bacskai.[5] Two overlapping peaks were observed in the OH stretching region; the more in-

(1) Paper XVII in a series on hydrogen bonding: XIV, W. F. Baitinger, Jr., P. von R. Schleyer, and K. Mislow, *J. Am. Chem. Soc.*, 87, 3168 (1965); XV, E. M. Arnett, T. S. S. R. Murty, P. von R. Schleyer, and L. Joris, *ibid.*, 89, 5955 (1967); XVI, D. Gurka, R. W. Taft, L. Joris, and P. von R. Schleyer, *ibid.*, 89, 5957 (1967).

(2) National Science Foundation Cooperative Fellow, 1963–1964; National Institutes of Health Predoctoral Fellow, 1967; Ph.D. Thesis, Princeton University, 1967.

(3) (a) R. West, *J. Am. Chem. Soc.*, 81, 1614 (1959); (b) Z. Yoshida and E. Ōsawa, *ibid.*, 88, 4019 (1966), and previous papers; (c) L. P. Kuhn and R. E. Bowman, *Spectrochim. Acta*, 23A, 189 (1967).

(4) Review: M. Tichý in "Advances in Organic Chemistry: Methods and Results," Vol. 5, R. A. Raphael, E. C. Taylor, and H. Wynberg, Ed., John Wiley and Sons, Inc., New York, N. Y., 1965, p 115.

(5) P. von R. Schleyer, D. S. Trifan, and R. Bacskai, *J. Am. Chem. Soc.*, 80, 6691 (1958).

(6) R. Piccolini, Ph.D. Thesis, University of California, Los Angeles, Calif., 1959; see R. Piccolini and S. Winstein, *Tetrahedron Letters*, No. 13, 4 (1959).

(7) (a) M. Ōki and H. Iwamura, *Bull. Chem. Soc. Japan*, 32, 567 (1959); (b) *ibid.*, 32, 950 (1959); (c) *ibid.*, 32, 955 (1959).

(8) M. Ōki and H. Iwamura, *ibid.*, 32, 1135 (1959).

(9) Y. Armand and P. Arnaud, *Ann. Chim.*, 9, 433 (1964).

(10) Conclusive evidence is available from a microwave study of the structure of allyl alcohol: A. N. Murty and R. F. Curl, Jr., *J. Chem. Phys.*, 46, 4176 (1967).

(11) Reviews: M. Y. Lukina, *Russ. Chem. Rev.*, 31, 419 (1962); W. Bernett, *J. Chem. Educ.*, 44, 17 (1967).

(12) J. H. Turnbull and E. S. Wallis, *J. Org. Chem.*, 21, 663 (1956).

(13) Because of their preference for a *cis* conformation, carboxylic acid groups do not function well as proton-donor groups in intramolecular hydrogen bonding.[14] We have found no evidence for hydrogen bonding in cyclopropanecarboxylic acid: a very dilute solution in CCl_4 shows only one O–H stretching vibration in the infrared, at 3537 cm^{-1}. Propionic acid, a model compound which cannot form an intramolecular hydrogen bond, has an OH absorption at 3535 cm^{-1}, and similar values have been found for the free peaks of other carboxylic acids.[14]

(14) M. Ōki and H. Iwamura, *Bull. Chem. Soc. Japan*, 35, 283 (1962); M. Ōki and M. Hirota, *ibid.*, 34, 374, 378 (1961); H. A. Lloyd, K. S. Warren, and H. M. Fales, *J. Am. Chem. Soc.*, 88, 5544 (1966), and references cited therein.

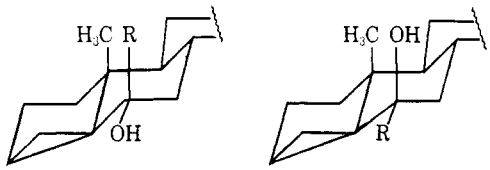
(15) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco, Calif., 1960.

tense band, at lower frequency, was assigned to an OH···cyclopropane intramolecular hydrogen bond. The spectral shift ($\Delta\nu$) was very small, 16 cm^{-1}, but the appearance of the spectrum was quite different from that of typical primary alcohols, which have the most intense portion of the peak at higher frequencies. Several additional examples of OH···cyclopropane hydrogen bonding have been claimed in the literature; these are summarized in Table I.

Table I. Spectroscopic Measurements Presented as Evidence for Intramolecular Hydrogen Bonding Involving the Cyclopropane Ring. Literature Examples

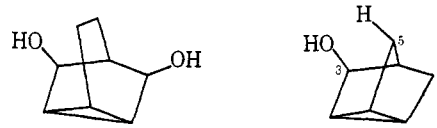
Compound	Free peaks,[a] cm^{-1}	Bonded peaks,[a] cm^{-1}	$\Delta\nu$, cm^{-1}
Cyclopropylcarbinol[5]	3631 sh	3615	16
3,5-Cyclocholestan-6α-ol[5,i] (Ia)	3628	3612 sh[b]	16
3,5-Cyclocholestan-6β-ol[5,i] (IIa)	3614[c]		
6β-Methyl-3,5-cyclocholestan-6α-ol[d,i] (Ib)	sh[e]	3616[e]	
6α-Methyl-3,5-cyclocholestan-6β-ol[d,i] (IIb)	3610[e]		
Cyclopropane-1,1-dimethanol[18]	3636	3614, 3567[f]	21, 69[f]
cis-Bicyclo[3.1.0]hexan-2-ol[g]	3616	3603	13
trans-Bicyclo[3.1.0]hexan-2-ol[g]	3615		
Tricyclo[2.2.2.0^{2,6}]octan-3,5-*exo*-*cis*-diol[h,i] (III)	3630	3572[i]	58[i]

[a] Tentatively assigned. [b] Questioned by Piccolini[6] on the grounds that the spectrum of Ia is similar to those of equatorial cyclohexanols with no proton acceptor functions. Therefore, the shoulder should be a free OH absorption. We agree with this suggestion (see text). [c] Assigned to a free peak because the peak position was close to those of saturated secondary alcohols. However, we are now of the opinion that the 3614-cm^{-1} absorption is a bonded peak (see text). [d] M. Davis, S. Julia, and G. H. R. Summers, *Bull. Soc. Chim. France*, 742 (1960). [e] The assignments were made on the basis of the assignments for Ia and IIa cited in ref 5 and are therefore questionable. [f] Hydrogen bonding of a 1,3-diol. [g] M. Hanack and H. Allmendinger, *Chem. Ber.*, **97**, 1669 (1964). [h] C. A. Grob and J. Hostynek, *Helv. Chim. Acta*, **46**, 2209 (1963). [i] It is dubious that such a large $\Delta\nu$ could be observed from a hydrogen bond to cyclopropane. Moreover, the spectrum of IV whose hydroxyl group has a similar geometry with respect to the cyclopropane ring has only an absorption at 3622 cm^{-1} [5] (see text). [j] The structures are as follows.



Ia, R = H
b, R = CH_3

IIa, R = H
b, R = CH_3



III IV

There are a number of problems associated with these assignments and some are challengable (Table I, footnotes). All of the compounds in Table I have the hydroxyl groups attached to positions α to the cyclopropane rings; the observed spectral shifts are quite small. The unambiguous demonstration of intramolecular hydrogen bonding in compounds displaying such small spectral shifts is inherently difficult because saturated alcohols incapable of hydrogen bonding often give not just one but two overlapping OH bands with frequency differences of magnitude similar to those observed in Table I.[6-8] These multiple peaks are ascribed to conformational heterogeneity,[16] a feature to be expected also in the α-hydroxycyclopropanes. The same problem arises in interpreting the spectra of allyl and benzyl alcohols, whose appearance is very similar to that of cyclopropylcarbinol.[4-9] In these former cases, convincing evidence for hydrogen bonding can be obtained by moving the OH group from the α to the β position; in both β-phenylethanol and 1-buten-4-ol spectral shifts are much larger ($\Delta\nu$'s 30–40 cm^{-1})[4] than would be expected on the basis of conformational heterogeneity. Unfortunately, this strategem does not work in the cyclopropane series. The OH spectrum of β-cyclopropylethanol is essentially the same as that of ethanol or other saturated primary alcohols.[17] Evidently the cyclopropane ring is a weaker proton acceptor than a double bond or a phenyl ring, and the interaction energy is insufficient to orient the molecule into a conformation favorable for intramolecular hydrogen bonding.

The problem that must be faced here is one common to the interpretation of many phenomena: recourse must be made to comparison of the behavior of some substance with that of a model. But the uncertainty that the model chosen may be inadequate is always present. Of the compounds in Table I, the results with cyclopropane-1,1-dimethanol were perhaps the most convincing for the existence of an OH···cyclopropane hydrogen bond.[18] This substance alone, out of some 50 saturated 1,3-diols examined, gave in addition to the usual free OH and OH···O bonded peaks, a third clearly visible maximum, which very probably is due to interaction with the cyclopropane ring.

This paper presents additional and more convincing evidence for OH···cyclopropane hydrogen bonding. The best cases, involving both intermolecular and intramolecular hydrogen bonding, will be described first, and then the more subtle α-hydroxycyclopropane systems will be analyzed. These results have pertinence as a measure of the ability of the cyclopropane ring to function as an electron donor. This ability is of current interest in other problems: the protonation of cyclopropane containing compounds and the structure of the resulting transition states or intermediates,[19] the interaction of other electrophilic reagents with cyclopropanes,[19] and the question of neighboring group participation involving cyclopropane rings (the interactions of cyclopropanes and carbonium ions).[20-22]

(16) To be discussed in detail in a future publication.
(17) C. Wintner, A.B. Thesis, Princeton University, 1959. Also see below.
(18) P. von R. Schleyer, *J. Am. Chem. Soc.*, **83**, 1368 (1961), where the spectrum is reproduced.
(19) R. L. Baird and A. A. Aboderin, *ibid.*, **86**, 252 (1964); A. A. Aboderin and R. L. Baird, *ibid.*, **86**, 2300 (1964); N. C. Deno and D. N. Lincoln, *ibid.*, **88**, 5357 (1966); H. Hart and R. H. Schlosberg, *ibid.*, **88**, 5030 (1966); G. J. Karabatsos, N. Hsi, and S. Meyerson, *ibid.*, **88**, 5649 (1966); G. J. Karabatsos, R. A. Mount, D. O. Rickter, and S. Meyerson, *ibid.*, **88**, 5651 (1966), and references cited in these papers. *Cf.* also C. C. Lee and L. Gruber, Abstracts, 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967, S81; G. J. Krabatsos J. L. Fry, and S. Meyerson, *Tetrahedron Letters*, 3735 (1967); and C. C. Lee and J. E. Kruger, *Tetrahedron*, **23**, 2539 (1967), and references cited therein.
(20) H. Tanida, T. Tsuji, and T. Irie, *J. Am. Chem. Soc.*, **89**, 1953 (1967).

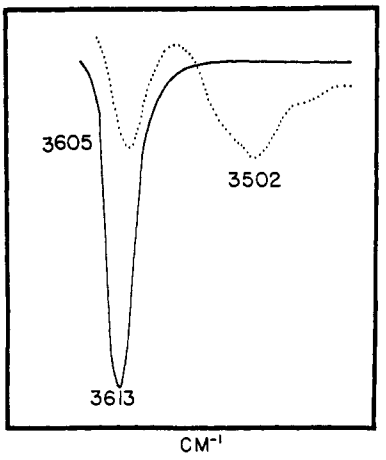


Figure 1A. Spectrum of 2 mg/ml of *p*-fluorophenol in 40% (vol) cyclohexane in CCl_4, ———; spectrum of 0.7 mg/ml of *p*-fluorophenol in 40% (vol) cyclohexene in CCl_4, ...

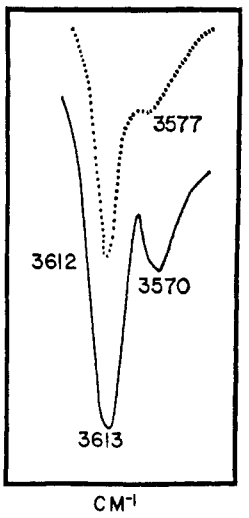


Figure 1B. Spectrum of 2.5 mg/ml of *p*-fluorophenol in 40% (vol) 1,1-dimethylcyclopropane in CCl_4, ———; spectrum of 0.9 mg/ml of *p*-fluorophenol in 40% (vol) dicyclopropylmethane in CCl_4, ...

Results and Discussion

Intermolecular Hydrogen Bonding. A very dilute solution of a hydroxylic proton donor in an inert solvent such as CCl_4 shows a single absorption (free peak) in the OH stretching region of the infrared. When a proton acceptor is added to this solution, the frequency of the free peak remains essentially the same, but, in addition, a new and usually much broader peak appears at a lower frequency, corresponding to the stretching vibration of a hydroxyl group participating in hydrogen bonding. This new peak, indicative of a specific interaction between proton donor and acceptor, is considered to be the best and least ambiguous evidence for the formation of a hydrogen bond.[15] The frequency difference ($\Delta\nu$) between the free and the bonded peaks is at least a rough measure of the strength of the hydrogen bond.[23]

When an "inert" substance incapable of acting as a proton acceptor in hydrogen bonding is added to the solution of hydroxylic proton donor, no new peak appears in the OH region of the infrared spectrum,[24] indicating the absence of a specific interaction.[15] It is known that the addition of saturated hydrocarbons to a solution of phenol in CCl_4 produces very little effect in the OH absorption peak at 3611 cm^{-1}.[24] Figure 1A provides a similar example: the spectrum of *p*-fluorophenol in a 40% solution of cyclohexane in CCl_4 shows only a free OH peak. In contrast, the spectrum of *p*-fluorophenol in 40% cyclohexene–CCl_4 solution (Figure 1A) has a bonded peak with a $\Delta\nu$ of 103 cm^{-1},[25] caused by the interaction of the OH group and the π electrons of the double bond.[3]

In a similar way, the ability of the cyclopropane ring to function as a proton acceptor in hydrogen bonding can be demonstrated convincingly by such intermolecular studies. The spectra of solutions of *p*-fluorophenol in dicyclopropylmethane–CCl_4 and in 1,1-dimethylcyclopropane–CCl_4 (Figure 1B) show clearly both free and bonded peaks. A comparison of the $\Delta\nu$'s with dicyclopropylmethane (35 cm^{-1}) and with 1,1-dimethylcyclopropane (43 cm^{-1}) to those with cyclohexene (103 cm^{-1}) indicates that olefins are better proton acceptor sites than are cyclopropane rings.[26]

Intramolecular Hydrogen Bonding. Best Cases. As mentioned above, larger $\Delta\nu$'s for intramolecular hydrogen bonding would be expected with β-hydroxy- than with α-hydroxycyclopropane derivatives. Although β-cyclopropylethanol itself does not form an intramolecular hydrogen bond, a molecule constrained in a conformation favorable for hydrogen bonding might give better results. We were intrigued by a report by Tanida, Tsuji, and Irie[20] that V absorbed at 3590 cm^{-1}, a position unexpectedly low for the free ν_{OH} of a secondary alcohol. VI, the epimer of V, was reported to have a band at 3576 cm^{-1}, reasonably assigned to an OH···π hydrogen bonding interaction,[20] but the low absorption position of V was not commented on. It seemed possible to us that this band was due to OH···cyclopropane hydrogen bonding. An examination of the saturated isomers VII and XI[27] fully confirmed this assignment (Figure 2A and Chart I).

(21) M. A. Battiste, C. L. Deyrup, R. E. Pincock, and J. Haywood-Farmer, *J. Am. Chem. Soc.*, **89**, 1954 (1967). References to the prior literature are summarized here.

(22) C. F. Wilcox, Jr., and R. G. Jesaitis, *Tetrahedron Letters*, 2567 (1967); K. B. Wiberg and G. R. Wenzinger, *J. Org. Chem.*, **30**, 2278 (1965); A. K. Colter and R. C. Musso, *ibid.*, **30**, 2462 (1965); J. Haywood-Farmer, R. E. Pincock, and J. I. Wells, *Tetrahedron*, **22**, 2007 (1966); M. A. Eakin, J. Martin, and W. Parker, *Chem. Commun.*, 955 (1967).

(23) The exact relationship is controversial. For leading references see S. Singh, A. S. N. Murthy, and C. N. R. Rao, *Trans. Faraday Soc.*, **62**, 1056 (1966); and K. F. Purcell and R. S. Drago, *J. Am. Chem. Soc.*, **89**, 2874 (1967); T. D. Epley and R. S. Drago, *ibid.*, **89**, 5770 (1967).

(24) Exceptions to this generalization are now known, but these should not affect the arguments of the present paper. See A. Allerhand and P. von R. Schleyer, *ibid.*, **85**, 371 (1963); M. Horák, J. Moravec, and J. Plíva, *Spectrochim. Acta*, **21**, 919 (1965).

(25) Literature value: 99 cm^{-1},[3a] $\Delta\nu$'s of 95,[3a] 96,[3c] and 99 cm^{-1} [3b] have also been reported for the phenol–cyclohexene hydrogen bond.

(26) The difference is probably not as great as is implied by this comparison. Kuhn and Bowman found that the magnitude of $\Delta\nu$ (phenol–olefins) is quite sensitive to the number of alkyl substituents.[3c] For example, isobutylene gave a $\Delta\nu$ of 96 cm^{-1} with phenol while monoalkyl-substituted olefins gave $\Delta\nu$'s of about 64 cm^{-1}. The proton-acceptor abilities of cyclopropane compounds might well be less sensitive to the number of substituents. Perhaps the closest comparison possible here is between 1,4-pentadiene (divinylmethane, $\Delta\nu_{phenol}$ 51 cm^{-1})[3c] and dicyclopropylmethane ($\Delta\nu_{p\text{-fluorophenol}}$ 35 cm^{-1}).

(27) Very kindly provided by Dr. Tanida.

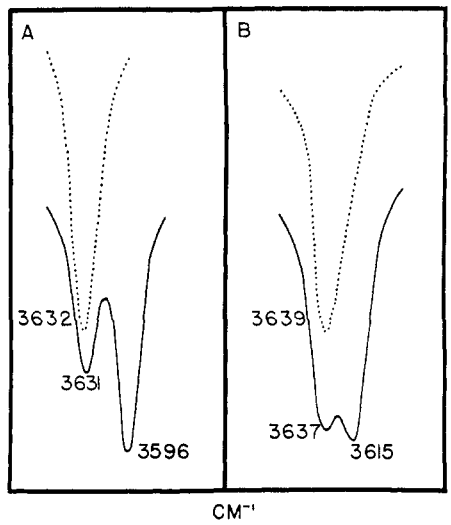
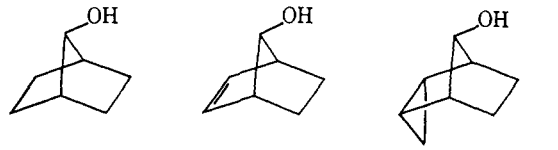


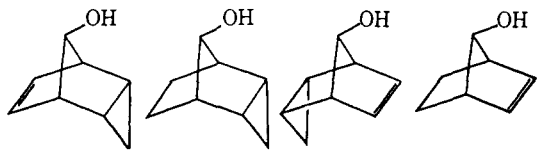
Figure 2. Spectra of alcohols in CCl_4 solution: (A) ———, VII; . . . . . , XI; (B) ———, 1-methylcyclopropylcarbinol; . . . . . , 1-methylcyclobutylcarbinol.

The OH spectrum of *endo-syn*-tricyclo[3.2.1.$0^{2,4}$]-octan-8-ol (VII), with two well-separated maxima at 3631 and 3596 cm^{-1} (Figure 2A), offers practically indisputable evidence for hydrogen bonding to the cyclopropane ring. The high-frequency or free band of VII is similar in position to that of the singlet absorptions of the *anti* isomer XI, 7-norbornanol (IX), and *anti*-7-norbornenol (X). The low frequency of the bonded band of VII corresponds in position to the absorption reported for V;[20] these bands are due to OH···cyclopropane hydrogen bonding. Finally, the similarity in position of the OH···π hydrogen bonded peaks in VI and in VIII should be noted. These 7-hydroxynorbornane derivatives seem to be close models for one another, furnishing a highly mutually consistent set of data.

Chart I. Free and Bonded Peak Positions, in cm^{-1}, of 7-Norbornanol Derivatives



	IX[28]	X[28]	XI
ν_{OH} free	3630 cm^{-1}	3630	3632



	V[20]	VII	VI[20]	VIII[28]
ν_{OH} free	not given	3631	not given	3624
bonded	3590 cm^{-1}	3596	3576	3574
$\Delta\nu$	not given	35	not given	50

The compounds in Chart I also provide a comparison between the proton-acceptor abilities of olefins and cyclopropane rings. The larger $\Delta\nu$ of VIII *vs.* VII and the lower bonded peak positions of VI *vs.* V show the superiority of the olefins as bases in hydrogen bonding, consistent with the conclusion based on the intermolecular studies. Of course, such comparisons are based on the assumption, which appears reasonable in this case, that these molecules have similar geometries.

It is interesting to contrast this behavior with that of carbonium ion processes in which a cyclopropane ring or double bond interacts with a positive charge.[20,21] The tosylate derivatives of X and XI have the proper orientation for the observation of anchimeric assistance during solvolysis. While the acceleration due to the participation of the double bond in X tosylate is very large (relative rate 10^{11} greater than that of IX tosylate) the acceleration in XI tosylate is even greater (10^{14}).[20,21] Thus, in this instance, the magnitude of the interaction involving the cyclopropane ring is more pronounced than that of the double bond,[29] a result contrary to that found in hydrogen bonding. Of course, hydrogen bonding is largely a ground-state phenomenon, in which the electron distributions in proton donor and acceptor are but little altered due to their mutual interaction. Participation, the involvement of a neighboring group in the process whereby a carbonium ion is generated, depends to a great extent on the nature of the transition state, in which the structure and electronic distribution are very much altered. Thus, carbonium ions and proton donors are quite different "electron density probes," and it is not necessarily expected that both give consistent results.

In one respect carbonium ions, proton donors, and other electrophilic agents might be quite similar: the preferred site of their interaction with the electrons of the cyclopropane ring could be the same. Accumulating evidence seems to indicate that this site is the "edge" along one of the bonds in the plane of the ring, rather than some location above the ring plane.[11,19-22] The marked participation found in the solvolysis of XI tosylate,[20,21] but not in other β-cyclopropylethyl tosylate derivatives[22,29] is in accord with this idea. Similarly, the pronounced evidence for hydrogen bonding in V and VII shows that the edge of the cyclopropane ring is a very good electron-donor site for the rigidity of the system prevents the hydroxyl group from reaching any other position.

The OH spectrum of 1-methylcyclopropylcarbinol (Figure 2B) has pronounced maxima at 3637 and 3615 cm^{-1} ($\Delta\nu$ 22 cm^{-1}). The appearance of this spectrum is rather similar to that of the analogously constituted molecule, cyclopropane-1,1-dimethanol, except for the absence of the OH···O peak in the latter.[18] 1-Methylcyclobutylcarbinol has a very similar structure, but the three-membered ring has been replaced by a four-membered one; in contrast, the OH spectrum (Figure 2B) shows only a single peak at 3639 cm^{-1}. Other 1-methylcycloalkylcarbinols and neopentyl-type alcohols give similar one-peak spectra. Therefore, the low-frequency (3615 cm^{-1}) band of 1-methylcyclopropylcarbinol is quite unusual and must result from hydrogen bonding to a polarizable bond in the cyclopropane ring. The four-membered ring does not appear to be able to function as a proton acceptor.

Among the various cyclopropylcarbinols whose spectra we have examined, 1-methylcyclopropylcarbinol

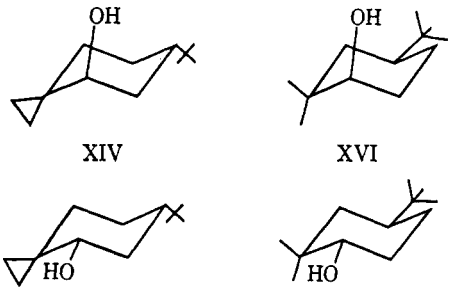
(28) L. P. Kuhn, R. E. Bowman, R. S. Bly, R. K. Bly, L. Joris, and P. von R. Schleyer, to be published; *cf.* R. K. Bly and R. S. Bly, *J. Org. Chem.*, **28**, 3165 (1963).

(29) This is rather exceptional. In other cases cyclopropane rings have proven to be inferior to olefins as neighboring groups.[22]

provides an especially well-resolved spectrum. This is very likely due to the steric effect of the methyl group which orients the hydroxyl group in conformations favorable for hydrogen bonding (discussed in detail below). This favorable C–OH conformation could either be adjacent to one of the ring C–C bonds (XII) or it could be over the ring (XIII); both conformations are possible in this instance.

XII XIII

These conformational possibilities are restricted in XIV (conformation: type XII) and in XV (type XIII). The spectra of these compounds were interpreted by comparison with the spectra of XVI and XVII, model substances incapable of hydrogen bonding which, however, should have steric environments similar to XIV and XV. Thus, any differences between the spectra of XIV and XVI and between XV and XVII should be due to the existence of OH···cyclopropane hydrogen bonding.



XIV XVI

XV XVII

As can readily be seen in Figure 3, the spectra of the equatorial isomers XV and XVII are quite similar, both in appearance and in position of the maxima. Such is not the case for the axial compounds XIV and XVI, which differ quite significantly in the position of the absorption maxima. This difference indicates the presence of an intramolecular hydrogen bond in XIV, but the absence of such an interaction in XV.

In order to confirm this conclusion, the spectra of XIV–XVII, all of which are unsymmetrical, were each decomposed by means of a digital computer curve resolution program[30] into two symmetrical bands. The data are summarized in Table II. Some differences are found between XV and XVII by this method but these differences are minor, and it seems likely that no appreciable amount of hydrogen bonding is occurring in XV. The differences in the spectra of XIV and XVI, apparent from Figure 3, are found, of course, in the results of spectral decomposition (Table II): the positions of the individual bands show an appreciable shift to lower frequencies in XIV, indicating the presence of an OH···cyclopropane hydrogen bond.

In XV the equatorial hydroxyl group lies over the cyclopropane ring in a bisected conformation (as in XIII). This rearrangement evidently is unfavorable for intramolecular hydrogen bonding. Edge interaction seems here also to be preferred. The hydroxyl group in XIV is in conformation of type XII, permitting interaction with the "τ" electrons of the C–C ring "bent" bonds.[11]

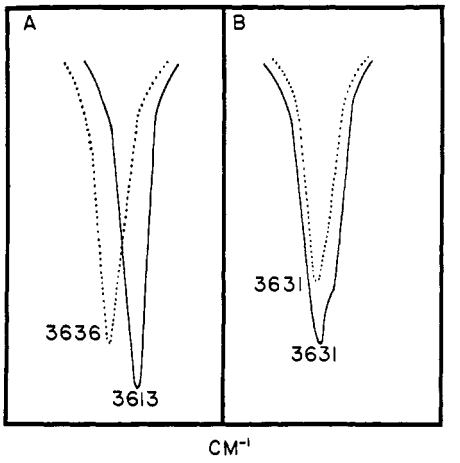


Figure 3. Spectra of alcohols in CCl_4 solution: (A) ———, XIV; ·····, XVI; (B) ———, XV; ·····, XVII.

Table II. Results of Computer Decomposition of Spectral Bands

Compound	ν_{max}, cm^{-1}	Rel absorbance	Band width,[a] cm^{-1}
XIV	3612	1.0	13.0
	3621	0.32	11.6
XVI	3625	0.39	14.2
	3636	1.0	14.4
XV	3616	0.46	16.0
	3632	1.0	19.2
XVII	3622	0.72	16.8
	3632	1.0	11.4
3,5-Cyclocholestan-6β-ol (IIa)	3616[b]	1.0[b]	15.0[b]
3,5-Cyclocholestan-6α-ol (Ia)	3613	0.35	19.2
	3632	1.0	14.4
3,5-Cycloergostan-6α-ol (Ia)	3613	0.37	18.4
	3631	1.0	12.0

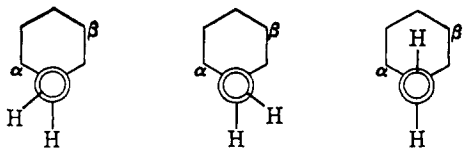
[a] At half-height. [b] One symmetrical peak.

The molecules XIV and XV can serve as reasonably good models for the interpretation of the spectra of the 6-hydroxy-3,5-cyclo steroids I and II, whose literature assignments have been questioned.[31] It would be expected that the poorer comparison might be between XIV and IIa, because of the presence of the axial methyl group in the latter. Despite this, the OH spectra of the two compounds resemble each other closely. 3,5-Cyclocholestan-6β-ol (IIa) has a symmetrical OH absorption with ν_{max} at 3616 cm^{-1}, while *trans*-6-*t*-butylspiro[2.5]octan-4-ol (XIV) gives a slightly asymmetrical band with ν_{max} at 3613 cm^{-1} (see Table II). Since we have already concluded that this 3613-cm^{-1} peak of XIV involves OH···cyclopropane hydrogen bonding, it seems likely that this type of interaction is also present in IIa. This requires revision of the original tentative assignment.[5,32]

(30) A modification of the Stone program was used: H. Stone, *J. Opt. Soc. Am.*, 52, 998 (1962). This is described in detail in the Ph.D. Thesis of L. J., Princeton University, 1967.

(31) See Table I, footnotes *b*, *c*, and *e*.

(32) And probably also those of the corresponding tertiary alcohol (Table I, footnotes *d* and *e*).



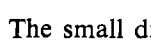
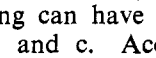
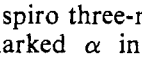
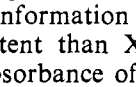
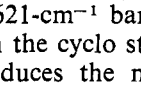
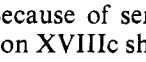
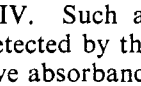
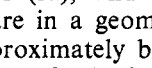
XVIIIa XVIIIb XVIIIc

The small differences in the spectra of XIV and IIa can be rationalized in terms of conformational heterogeneity.[16] Hydroxyl groups axial to a cyclohexane ring can have three conformational minima, XVIIIa, b, and c. According to our analysis[16] all three of these give about the same ν_{max}, *ca.* 3625 cm^{-1}.[33] When a spiro three-membered ring is attached to the position marked α in XVIIIa–c, only conformation XVIIIa should permit hydrogen bonding to the cyclopropane ring. However, since this interaction is attractive, conformation XVIIIa should be populated to a greater extent than XVIIIb and XVIIIc. Thus, the relative absorbance of the 3612-cm^{-1} band of XIV (conformation XVIIIa) is three times greater than that of the 3621-cm^{-1} band (conformations XVIIIb and XVIIIc). In the cyclo steroid IIa the axial angular methyl group reduces the number of available conformations. In XVIIIa–c the axial methyl would be at position β. Because of serious nonbonded interactions, conformation XVIIIc should not be populated significantly. We suggest that for this reason the OH spectrum of IIa apparently lacks the 3621-cm^{-1} component found in XIV. Such a component band would not easily be detected by the spectral resolution program, if its relative absorbance were small.

3,5-Cyclocholestan-6α-ol (Ia), 3,5-cycloergostan-6α-ol (Ia), and *cis*-6-*t*-butylspiro[2.5]octan-4-ol (XV) all are in a geometry (XIII) in which the C–O bond approximately bisects the cyclopropane ring. The spectra of all of these compounds, as well as that of the model XVII, are all quite similar, as is shown by the decomposition results (Table II). All have the major component band at higher frequencies (3631–3632 cm^{-1}), and a second weaker band at lower frequencies (3613–3616 cm^{-1} for both compounds Ia and XV; 3622 cm^{-1} for XVII). Examination of models shows that there are three different minimum energy conformations available to these compounds by rotation around the equatorial C–O bonds; these different conformations provide different environments for the OH group and would be expected to give rise to component spectral bands similar to those observed here.[6,16,33] There seems to be no need to postulate OH···cyclopropane hydrogen bonding in Ia, Ib,[32] and XV. We agree with Piccolini,[6] who attributed the doublet character of the spectrum of 3,5-cyclocholestan-6α-ol to conformational heterogeneity and not to hydrogen bonding. The original assignments[5,32] need to be revised.

Conformationally Flexible Cyclopropylcarbinols. The spectra of a number of cyclopropylcarbinols were examined. The OH peaks were generally unsymmetrical, and were decomposed by computer into two symmetrical components. The resulting data are summarized in Table III. For comparison, the spectra of a number of model compounds were taken and decomposed in a similar manner (Table IV). These model compounds include not only saturated alcohols incapable of forming intramolecular hydrogen bonds, but also allyl and benzyl type alcohols which are believed to be engaged in weak intramolecular hydrogen bonding.[4–10]

Table III. Summary of Spectral Data for Cyclopropylcarbinols and Analogs

Compound	ν_{max}, cm^{-1}	$\Delta\nu$, cm^{-1}	Rel absorbance	$\Delta\nu_{1/2}$,[a] cm^{-1}
Cyclopropylcarbinol	3633		1.0	26
	3616	17	1.1	18
				
trans-2-*t*-Butylcyclopropylcarbinol	3631		1.0	22
	3616	15	1.1	16
				
1-Methylcyclopropylcarbinol	3638		1.0	25
	3615	23	1.0	17
				
2,2,3,3-Tetramethylcyclopropylcarbinol	3629		...	21
				
1-Hydroxymethylnortricyclene	3634		1.0	16
	3619	15	1.0	21
				
1-Cyclopropylethanol	3626		1.0	24
	3615	11	2.3	16
				
1-(1-Hydroxyethyl)nortricyclene	3626		1.0	16
	3616	10	2.0	18
				
Cyclopropyldimethylcarbinol	3623		1.0	18
	3611	12	0.9	14
				

[a] Band width at half the absorbance maximum.

The primary alcohols of Table IV will be considered first. The first seven compounds form a set whose spectral features are similar: they give a more intense band at high frequencies (3637–3640 cm^{-1}) and a weaker band at lower frequencies (3625–3627 cm^{-1}). These features are typical of a large number of saturated primary alcohols of varied structure.[16] In contrast to these, the spectra of cyclopropylcarbinol, benzyl alcohol, and allyl alcohol show distinct differences: the high-frequency bands are now of lower relative intensity and the other bands have been displaced to lower frequencies (3616–3619 cm^{-1}). This shift and increase in relative intensity has been cited as evidence for intramolecular hydrogen bonding in benzyl and allyl alcohols.[4–9] By analogy, the similar spectral features of cyclopropylcarbinol can also be taken as evidence for intramolecular OH···cyclopropane hydrogen bonding.

The secondary alcohols of Table IV also form two groups, even though all the compounds give two bands

(33) For another interpretation see H. S. Aaron, C. P. Ferguson, and C. P. Rader, *J. Am. Chem. Soc.*, **89**, 1431 (1967), and references cited therein.

Table IV. Summary of Spectral Data for Comparison Alcohols

R	ν_{max}, cm^{-1}	$\Delta\nu$	Rel absorbance	$\Delta\nu_{1/2}$,[a] cm^{-1}
	Primary Alcohols (RCH_2OH)			
CH_3	3637		1.0	21
	3625	12	0.6	16
CH_3[7b]	3637		1.0	18
	3627	10	0.6	19
C_2H_5[7b]	3640		1.0	20
	3626	14	0.4	18
$(CH_3)_2CH$[7b]	3642		1.0	18
	3628	14	0.5	22
$(CH_3)_3C$[7b]	3642		1.0	21
	3632	10	0.17	18
Cyclobutyl	3638		1.0	22
	3625	13	0.8	20
1-Methylcyclobutyl	3640		1.0	18
	3626	14	0.4	21
C_6H_5[7b]	3636		1.0	24
	3617	19	1.7	17
Vinyl[7a]	3635		1.0	23
	3619	16	1.3	16
	Secondary Alcohols ($RCHOHCH_3$)			
CH_3	3627		1.0	19
	3616	19	0.5	19
CH_3[7b]	3627		1.0	14
	3617	10	0.6	26
C_2H_5[7b]	3629		1.0	20
	3615	14	0.3	27
Cyclopropyl	3626		1.0	24
	3615	11	2.3	16
C_6H_5[7b]	3627		1.0	21
	3616	11	3.8	16
	Tertiary Alcohols ($R(CH_3)_2COH$)			
CH_3	3616		...	18
CH_3[7b]	3617		...	15
C_2H_5[7b]	3617		...	20
Cyclopropyl	3623		1.0	18
	3611	12	0.9	14
C_6H_5[7b]	3621		1.0	15
	3607	14	2.1	15
	Primary Alcohols (RCH_2CH_2OH)			
Cyclopropyl	3638		1.0	18
	3622	16	0.7	19
Vinyl[7a]	3635		1.0	32
	3596	39	0.6	24
C_6H_5[8]	3636		1.0	18
	3626	10	0.3	17
	3606	30	1.1	24

[a] Band width at half the absorbance maximum.

at very nearly the same positions. The high-frequency components of the OH spectra of 2-propanol and 2-butanol are more intense, but this is markedly reversed in methylcyclopropylcarbinol and in α-phenylethanol where the low-frequency bands have the greater relative absorbances. The reference tertiary alcohols, *t*-butyl and *t*-amyl alcohols (Table IV), have but one peak, but dimethylcyclopropylcarbinol and dimethylphenylcarbinol both have two; the lower frequency one may possibly be due to intramolecular hydrogen bonding (see discussion below).

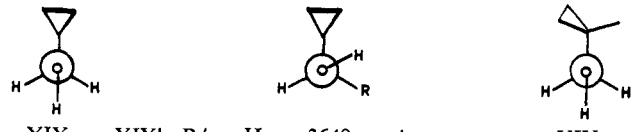
The last group of compounds in Table IV are β-substituted ethanols. The spectrum of β-cyclopropylethanol is identical with that of typical saturated primary alcohols and no intramolecular hydrogen bond is present. This behavior is in contrast to that of 3-buten-1-ol and β-phenylethanol which show distinct low-frequency peaks; the $\Delta\nu$'s are sufficiently large in magnitude to furnish quite unambiguous evidence for intramolecular hydrogen bonding.[4] The cyclopropane ring is a weaker proton acceptor than these π-electron systems. Evidently, the attraction of the OH group for the ring in β-cyclopropylethanol is insufficiently great to overcome the unfavorable entropy of cyclization, and no intramolecular hydrogen bond is observed. When a rigid system is employed, as in VII, an interaction giving a rather large $\Delta\nu$ is found.

With the exception of the β-substituted ethanols, it is clear from Table IV that the cyclopropane, the phenyl, and the vinyl derivatives give similar OH spectra and that these spectra differ significantly from those of typical saturated alcohols. These differences are attributed to intramolecular hydrogen bonding. Although conformational heterogeneity can also give rise to OH band multiplicity, the effects observed in the cyclopropylcarbinols, the allyl alcohols, and the benzyl alcohols of Table IV would appear to be too large to be explained on that basis. This conclusion agrees with that of other investigators.[4-9]

Analysis of the Conformations of Cyclopropylcarbinols. In the conformationally flexible cyclopropylcarbinols there are three possible minimum energy rotamers around the exocyclic C–C bond, and three rotamers around the C–O bond. Conceivably, the OH group could be in as many as 27 different environments. Actually, in the compounds of Table III many of the rotamers are identical. For example, for cyclopropylcarbinol itself there are five different conformations, XIXa–e, expected to be significantly populated. Each one of these conformations would be expected to give rise to an OH band. The observed spectrum should be a composite of all these bands. Obviously, such a spectrum is difficult to interpret unless simplifying assumptions are made.

The basic assumption is quite reasonable and it is supported by considerable success in application in other cases:[16] OH groups in similar environments will have similar OH absorption frequencies, even if these environments are in different molecules. Thus the OH absorption frequency is almost wholly influenced by the substituents *gauche* to an OH group. An analysis of the spectra of many saturated alcohols yielded the assignments for the various conformational types (XXa–c and XXIa–c), shown below.[16]

By analogy with saturated primary alcohols, conformations XIXa and XIXc of cyclopropylcarbinol, which differ only in the rotational arrangement around the C_1–C_1' bond, would be expected to absorb at about 3638 cm^{-1}. In these conformations, the OH group points away from the cyclopropane ring, and no hydrogen bonding should be possible. A similar situation exists in XIXd, but this conformation should give rise to a band at 3626 cm^{-1} since it is skew in character (like XXb). In XIXb and XIXf the OH group and the three-membered ring are in proximity, but these conformations evidently are not bonding ones. The close similarity of the spectra of XV and XVII (Figure 3B) suggests that the environments of the OH groups in both molecules are analogous in their effect on the OH absorptions. The conformers present in XV, namely, XIXb, XIXf, and XXb, are comparable in this sense to the conformers, XXc, XXIc, and XXb, respectively, present in XVII. On the basis of the analogy with XXc and XXIc, the frequency assignments for XIXb and XIXf were made.



XIXa ~3638 cm^{-1} | XIXb, R′ = H; ~3640 cm^{-1} f, R′ = CH_3 or CH_2R; ~3614 cm^{-1} | XIXc ~3638 cm^{-1}

XIXd, R′ = H; ~3626 cm^{-1}
g, R′ = CH_3; ~3640 cm^{-1}

XIXe ~3612 cm^{-1}

XXa ~3638 cm^{-1}

XXb, R′ = H; ~3626 cm^{-1}
c, R′ = CH_3; ~3640 cm^{-1}
R = H or alkyl

XXIa, R′ = H; ~3611 cm^{-1}
b, R′ = CH_3; ~3624 cm^{-1}

XXIc, R′ = CH_3 ~3614 cm^{-1}

The one conformation remaining, XIXe, is thus implicated as the one in which OH···cyclopropane hydrogen bonding is taking place, a conclusion in accord with theoretical and geometrical expectations. "Edge" interaction can best occur in this conformation, and the 3612-cm^{-1} band is assigned to it.

Based on these expectations the spectrum of cyclopropylcarbinol should be the composite of three bands: at ~3638 cm^{-1} (XIXa and XIXc), at ~3626 cm^{-1} (XIXd and possibly XIXb), and the bonding one at 3612 cm^{-1} (XIXe). However, in applying the computer band resolution program[30] it was decided to adopt the conservative position of decomposing each experimental spectrum into two bands, the minimum number needed to give symmetrical components. After all, by means of such computer resolution even a symmetrical band can be decomposed artificially into any number of symmetrical "components," but the meaning of these "components" is lost. The higher frequency band of cyclopropylcarbinol at 3633 cm^{-1} (Table III) could thus result from a synthesis of the 3638- and 3626-cm^{-1} components.

This type of analysis explains well the spectra observed for the cyclopropylcarbinol derivatives studied (Table III). Two of these compounds show significant spectral differences from that of the parent compound. 1-Methylcyclopropylcarbinol gives rise to an especially well-resolved spectrum (Figure 2) which has already been commented on. The 1-methyl group in this compound should do little to change the band positions in the conformers XIXa–c and XIXe but exerts an influence on the OH absorption of the remaining conformer XIXg (analogous to XIXd in cyclopropylcarbinol), which is shifted upward in frequency. Since the absorptions of the various conformers of 1-methylcyclopropylcarbinol all fall into either of two well-separated frequency ranges, *i.e.*, ~3640 and ~3612 cm^{-1}, the two component bands are clearly visible. In other words, the absence of the "middle" band at 3626 cm^{-1} found in cyclopropylcarbinol gives rise to the especially "clean" appearing spectrum (Figure 2B) for 1-methylcyclopropylcarbinol.

2,2,3,3-Tetramethylcyclopropylcarbinol has no OH···cyclopropyl bonded peak. The *cis*-2- and 3-methyl groups depopulate bonding conformation XIXe, as well as XIXa and XIXb, because of their adverse steric interaction. The single band observed at 3629 cm^{-1} evidently is the composite of the remaining conformations, XIXd and XIXc. An analogous situation is found in 3-hydroxynortricyclene (IV),[34] another molecule which apparently shows no evidence for OH···cyclopropane hydrogen bonding. This compound is of configurational type XII in which the available conformations are XIXc–e. Perhaps the bonding conformation, XIXe, in IV is rendered unfavorable because of the crowding of the *syn*-hydrogen across the ring at C_5.

The secondary and tertiary cyclopropylcarbinols of Tables III and IV represent borderline cases in which the presence of intramolecular OH···cyclopropane hydrogen bonding is more difficult to demonstrate. Secondary and tertiary saturated alcohols incapable of intramolecular hydrogen bonding usually have at least one conformer with an absorption band in the region 3611–3614 cm^{-1}. However, these frequencies are virtually the same as the one (3612 cm^{-1}) expected from an OH···cyclopropane hydrogen bond, and no experimental distinction between the two is possible. The only evidence for such intramolecular hydrogen bonding in 1-cyclopropylethanol and in 1-(1-hydroxyethyl)-nortricyclene, as discussed above, is the enhanced relative intensity of the low-frequency (3615–3616 cm^{-1}) over the high-frequency (3626 cm^{-1}) one, in comparison with the behavior of model compounds (Tables III and IV).

The observed spectrum of dimethylcyclopropylcarbinol was symmetrical with ν_{max} 3617 cm^{-1}, corresponding in position to that of *t*-butyl and *t*-amyl alcohols, in which, of course, intramolecular hydrogen bonding is not possible. However, the band of dimethylcyclopropylcarbinol was broader than normal and the peak maximum was somewhat flattened, suggesting the presence of more than one component band. Computer decomposition gave two bands of about equal absorbance (Table III), but this separation in itself can hardly be considered definitive evidence for intramolecular hydrogen bonding. For example, Armand and Arnaud found two bands, at 3621 and 3614 cm^{-1}, in the decomposed spectrum of methylethylisopropylcarbinol.[9] Furthermore, it might be expected that conformations such as XII in which a methyl must bisect the cyclopropane ring would be sterically unfavorable. Be this the case, then the only arrangements remaining are of type XIII, in which OH···cyclopropane hydrogen bonding appears not to be possible.

Conclusions

The cyclopropane ring seems to be capable of acting as a weak proton acceptor in both intra- and intermolecular hydrogen bonding. It appears from the available evidence that the preferred site for proton-donor interaction is the "edge" of the cyclopropane ring. Intramolecular hydrogen bonding can be demon-

(34) It should also be present in III. See discussion, Table I, footnote *i*.

strated in compounds in which a hydroxyl group is either α or β to a cyclopropane ring. However, the situation is often complicated because the magnitude of $\Delta\nu$ is not large and conformational heterogeneity as well as hydrogen bonding contribute to the appearance of the spectra observed. The use of model compounds and analysis of the spectra in terms of the components expected from the various conformations present facilitates interpretation of the difficult examples.[34a]

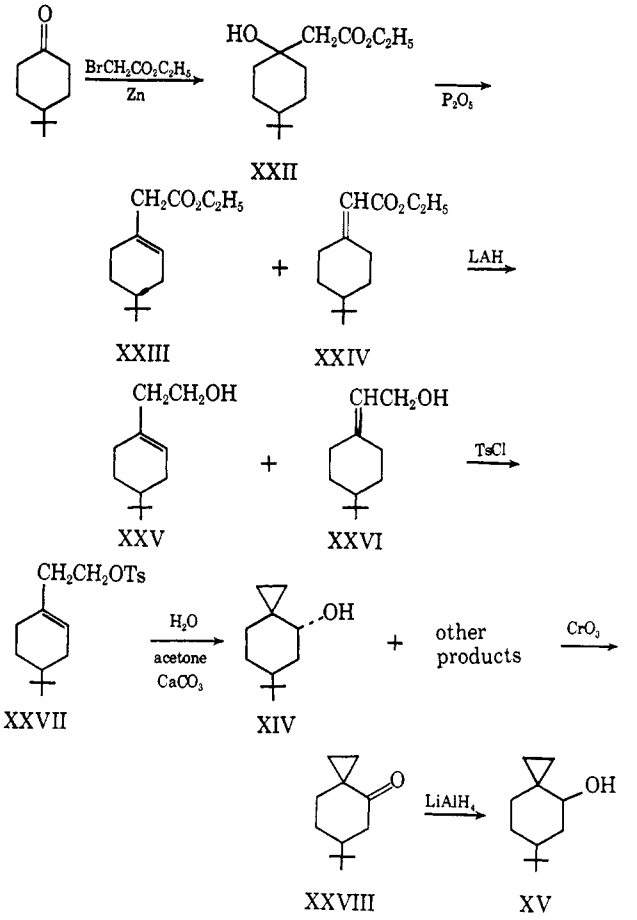
Experimental Section

Infrared Spectroscopic Technique. All infrared spectra were determined on a Perkin-Elmer 421 double beam grating spectrometer. For the intermolecular study where interference from water was especially serious, reagent grade CCl_4 was distilled from calcium hydride immediately before the solutions were made up. For the intramolecular studies, reagent grade CCl_4 was dried over P_2O_5, decanted, and used without further purification. The concentrations of alcohols varied from 0.5–1.0 mg/ml of CCl_4; 1-cm cells of infrared silica were used. The calibration of the instrument was checked daily against atmospheric water vapor; all frequencies reported were so corrected. Excellent reproducibility was observed.

Compounds. Cyclohexene and dicyclopropylmethane (Aldrich) were refluxed for 2 days over sodium and under nitrogen before a center distillation cut was taken. Cyclohexane was washed well with sulfuric acid, dried, and distilled from sodium under a nitrogen atmosphere. 1,1-Dimethylcyclopropane (Chemical Samples Co., >99% pure) was used without further purification. The following analytically pure compounds were kindly donated to us. We wish to thank the following persons especially: Dr. R. R. Sauers for 2-cyclopropylethanol;[35] Dr. E. L. Eliel[36] for XVII and XVI; Dr. H. Tanida[20] for VII and XI; Dr. W. J. A. VandenHeuvel for the steroids in Table II.[37,38] The remaining were available from other research programs at Princeton University. Cyclobutylcarbinol, 1-hydroxymethylnortricyclene, 1-(1-hydroxyethyl)nortricyclene, and 1-cyclopropylethanol were supplied by Mr. W. A. Washburn.[40] Dr. G. W. Van Dine[41] donated cyclopropylcarbinol, 2-*t*-butylcyclopropylcarbinol, and cyclopropyldimethylcarbinol. Mr. M. Hogan provided a sample of 1-methylcyclopropylcarbinol. Mr. C. Woodworth supplied a sample of 1-methylcyclobutylcarbinol.[42]

The syntheses of XV and XIV are illustrated in Chart II.

Chart II



Ethyl (4-*t*-Butyl-1-hydroxycyclohexyl)acetate (XXII). A Reformatsky reaction, according to the modification of Natelson and Gottfried,[43] using 50 g of 4-*t*-butylcyclohexanone,[44] 22 g of zinc foil, and 56 g of ethyl bromoacetate yielded 43 g (55%) of XXII, bp 124° (1.0 mm).

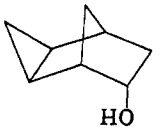
Ethyl (4-*t*-Butylcyclohexen-1-yl)acetate (XXIII). A mixture of of 43 g of XXII, 300 ml of benzene, and 48 g of P_2O_5 was refluxed for 3 hr. The flask was cooled; water was added, and the organic layer was separated. After removal of the benzene, distillation of the residue at 100–107° (0.6 mm) afforded 20 g (51%) of a mixture composed of 80% XXIII and 20% XXIV.

β-(4-*t*-Butylcyclohexen-1-yl)ethanol (XXV). Reduction of 85 g of the mixture of XXIV and XXIII with $LiAlH_4$ in the usual manner gave 65 g of a mixture of XXV and XXVI, bp 89–96° (0.6 mm), in 95% yield.

β-(4-*t*-Butylcyclohexen-1-yl)ethyl *p*-Toluenesulfonate (XXVII). The above mixture of alcohols (65 g) in 50 ml of dry pyridine was combined with 70 g of tosyl chloride in 80 ml of dry pyridine. After standing overnight in the refrigerator, the solution was poured into ice water and the crystals were filtered. Under these conditions the product was exclusively XXVII, mp 47°, as shown by nmr. β-(4-*t*-Butylcyclohexylidene)ethyl tosylate should be a highly reactive compound, and probably could be made only under special conditions. *Anal.* Calcd for $C_{19}H_{28}O_4S$: C, 67.83; H, 8.39. Found: C, 67.59; H, 8.65.

***trans*-6-*t*-Butylspiro[2.5]octan-4-ol (XIV).**[45] A mixture of 130 g of XXVII, 70 g of calcium carbonate, 300 ml of acetone, and 500 ml of water was heated at 70° for 11 days. The calcium carbonate was filtered, and then the solution was saturated with sodium chloride and extracted three times with 400 ml of ether. The solution was dried and the ether distilled. Fractional distillation of the residue yielded 28 g of a mixture containing predominantly XIV. By separating this mixture on a preparative glpc with a Carbowax

(34a) NOTE ADDED IN PROOF. We have recently been informed by Professor Z. Yoshida and by Professor M. Ōki of studies by their groups of inter- and intramolecular hydrogen bonding, respectively, to cyclopropane rings. The conclusions reached are in agreement with ours. Yoshida found $\Delta\nu$'s near 40 cm^{-1} and enthalpies of about −1.4 kcal/mol for interaction of phenol with cyclopropane rings. Ōki regards β-cyclopropylethanol to be a borderline case, but evidence for intramolecular association in β,β-dicyclopropylethanol is conclusive. A, studied by Ōki, provides a striking contrast to the behavior of VII. A, unlike VII (Figure 2A), gives no readily discernible second band, and only a low-frequency asymmetry. The hydroxyl group in A, unlike that in VII, is not symmetrically located relative to the cyclopropane ring, and this geometrical difference evidently is sufficient to make the OH···cyclopropane interaction in A inferior to that in VII.



A

(35) R. R. Sauers and R. W. Ubersax, *J. Org. Chem.*, **31**, 495 (1966).
(36) E. L. Eliel, S. H. Schroeter, T. L. Brett, F. J. Biros, and J.-C. Richer, *J. Am. Chem. Soc.*, **88**, 3327 (1966).
(37) W. J. A. VandenHeuvel, *J. Chromatog.*, **26**, 396 (1967).
(38) A sample of 3,5-cycloergostan-6α-ol was given to W. J. A. V. by Dr. M. J. Thompson.[39]
(39) M. J. Thompson, C. F. Cohen, and S. M. Lancaster, *Steroids*, **5**, 745 (1965).
(40) A. B. Thesis, Princeton University, 1967.
(41) (a) P. von R. Schleyer and G. W. Van Dine, *J. Am. Chem. Soc.*, **88**, 2321 (1966); (b) Ph.D. Thesis, Princeton University, 1967.
(42) *Cf.* P. von R. Schleyer and E. Wiskott, *Tetrahedron Letters*, 2845 (1967).
(43) S. Natelson and S. P. Gottfried, *J. Am. Chem. Soc.*, **61**, 970 (1939).
(44) S. Winstein and N. J. Holness, *ibid.*, 77, 5562 (1955).
(45) An analogous procedure was previously described for the preparation of 6-*t*-butylspiro[2.5]octan-5-ol.[46]
(46) M. Hanack and H.-J. Schneider, *Ann.*, **686**, 8 (1965).

column, a fraction composed of 90% XIV and 10% of an unidentified ketone was collected. The ketone was removed from XIV by "dry column" chromatography[47] on an alumina column with $CHCl_3$ as the eluent.

The *p*-nitrobenzoate of XIV melted at 113–114°. *Anal.* Calcd for $C_{19}H_{25}NO_4$: C, 68.86; H, 7.60: N, 4.23. Found: C, 68.53; H, 7.66; N, 4.15.

6-*t*-Butylspiro[2.5]octan-4-one (XXVIII). To 90 ml of pyridine cooled in an ice bath was carefully added 8 g of CrO_3; a yellow complex formed. To this mixture a solution of 8 g of XIV and 10 ml of pyridine was added. The reaction was stirred for a day at room temperature and then poured into 800 ml of water. The aqueous solution was extracted with ether. The ether extracts were washed with dilute HCl, dilute $NaHCO_3$ solution, and finally with water. The extracts were dried, and the ether was distilled. Distillation of the residue yielded 4 g (50%) of XXVIII, bp 57–57.5° (0.1 mm).

***cis*-6-*t*-Butylspiro[2.5]octan-4-ol (XV).** XXVIII (2.8 g) was reduced by 0.4 g of $LiAlH_4$ to yield 2 g (72%) of XV,[48] bp 77–77.5° (0.5 mm), mp 49–50°

The *p*-nitrobenzoate melted at 101–103°. *Anal.* Calcd for $C_{19}H_{25}NO_4$: C, 68.86; H, 7.60; N, 4.23. Found: C, 68.83; H, 7.41; N, 4.27.

Determination of Configuration of XV and XIV. A distinction between structures XV and XIV was made on the basis of the band shapes and the chemical shifts of the C*H*O– pmr absorption. As compared with equatorial protons, axial protons produce broader pmr bands.[49] The C-4 proton in XV appears as a quartet with a width of 18 cps[50] whereas the C-4 proton in XIV appears as an asymmetrical singlet with a width of 13 cps.[50] Therefore, the C-4 proton in XV is axial and that of XIV is equatorial. The C-4 proton in XIV occurs at a lower δ (2.97 ppm) due to the shielding anisotropy of the spiro cyclopropane ring[51] than the δ (3.63 ppm) of the C-4 proton in XV. $\Delta\nu(H_a-H_e)$ is approximately +42 cps.[52] Additional support for the configurational assignment of XV was provided by the stereochemical result for the $LiAlH_4$ reduction of a ketone analogous to XXVIII; 4-*t*-butyl-2,2-dimethylcyclohexanone when treated with $LiAlH_4$ produced an epimeric mixture containing 95% of the *trans* isomer of 4-*t*-butyl-2,2-dimethylcyclohexanol (XVII).[54]

Acknowledgments. We wish to thank the Whitehall Foundation who provided funds for the instrument upon which the spectral determinations were made. Computer time was provided by the Princeton University Computer Center, supported in part by National Science Foundation, Grant GP-579. This research was supported, in part, by the National Institutes of Health, Grant No. A107766, and the Petroleum Research Fund, administered by the American Chemical Society.

(47) See B. Loev and K. M. Snader, *Chem. Ind.* (London), 15 (1965), for a description of the method.

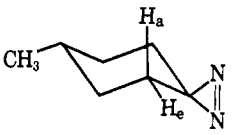
(48) The isomeric alcohol XIV was not detected by gas chromatography.

(49) N. C. Franklin and H. Feltkamp, *Angew. Chem. Intern. Ed. Engl.*, **4**, 774 (1965), and references cited therein. Following these authors the band widths are measured at one-fourth height.

(50) A trace of acid was added to the CCl_4 solution to remove coupling with the hydroxylic proton.

(51) The magnetic anisotropy of the cyclopropane ring is discussed in D. J. Patel, M. E. N. Howden, and J. D. Roberts, *J. Am. Chem. Soc.*, **85**, 3218 (1963).

(52) In a somewhat analogous system (XXIX), $\Delta\nu$ (H_a-H_e) was found to be +76 cps at 31° in CCl_4.[53]



XXIX

(53) J. J. Uebel and J. C. Martin, *ibid.*, **86**, 4618 (1964).

(54) J.-C. Richer, *J. Org. Chem.*, **30**, 324 (1965).

Transmission of Substituent Effects. Dominance of Field Effects[1]

C. F. Wilcox and C. Leung

Contribution from the Department of Chemistry, Cornell University, Ithaca, New York. *Received July 31, 1967*

Abstract: The dissociation constants of bicyclo[2.2.2]octane- and bicyclo[2.2.1]heptane-1-carboxylic acids substituted in the 4 position by $N(CH_3)_3$, CN, Br, CO_2CH_3, CO_2H, H, and CO_2^- groups have been measured. The results are in excellent agreement with expectations from a field effect model and in poor agreement with the classical inductive model. It is concluded from these results and other considerations that the purely inductive component of the total substituent effect is minor.

An old problem of organic chemistry is the interpretation of the electronic details of the processes by which substituents influence reactivity. From Ostwald's early investigations[2] of acidities of substituted carboxylic acids has developed several models to account for the varying acidity. Microscopic models based on simplified treatments of the electrostatic situation were initiated by Bjerrum[3] with his analysis of dissociation constants of dicarboxylic acids. He equated the statistically corrected ΔpK of a diacid to the simple Coulomb potential of one ionizable proton in the field of the other (eq 1). The effective dielectric

$$\Delta pK \text{ (statistically corrected)} = \frac{q_i q_j}{r_{ij} D_{eff}} \quad (1)$$

q_i = charge of proton 1
q_j = charge of proton 2
r_{ij} = distance between proton 1 and 2

(1) Based in part on the Ph.D. dissertation to be submitted to the Cornell Graduate School, July 1967. This material was presented at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967.

(2) W. Ostwald, *J. Prakt. Chem.*, **31**, 300 (1885); *Z. Physik. Chem.*, **3**, 170, 241, 369 (1889).

(3) N. Bjerrum, *ibid.*, **106**, 219 (1923).