Organic and Biological Chemistry

Intramolecular Hydrogen Bonding in Aliphatic Hydroxy Ketones[1]

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Abstract: For a given class of compounds, the infrared spectral shift ($\Delta\nu$) produced by a six-membered intramolecular hydrogen bond is normally far greater than a $\Delta\nu$ due to a five-membered chelate ring. Aliphatic hydroxy ketones are a marked exception to this generalization (Table I and Figures 1A and 1B). This discrepancy prompted the investigation reported here. Prior studies of hydrogen bonding to ketones suggested the presence of multiple proton-acceptor sites: the n and π electrons of oxygen (designated n-O and π-O, respectively). In analogy with olefins, it is also conceivable that the π electrons of carbon (π-C) can function as additional, weaker sites. The spectral results obtained with restricted intramolecular systems are in accord with these three possibilities. The bonded peaks of α-hydroxy ketones are symmetrical and usually have $\Delta\nu$'s about 130 cm^{-1} (Figure 1A). The most probable conformation for these molecules is that with both C–O bonds eclipsed, thereby permitting optimum hydrogen bonding between the hydroxyl hydrogen and the n-O electrons, the most basic site in the carbonyl group. Acyclic β-hydroxy ketones (**41**) generally possess asymmetrical bonded peaks (Figure 1B). These were decomposed by a digital computer program into two symmetrical component bands (Figure 2)—the more intense component with a $\Delta\nu$ of about 40 cm^{-1}, and the less intense component with a $\Delta\nu$ of about 90 cm^{-1}. On the basis of the magnitudes of the $\Delta\nu$'s, the probable assignments to OH$\cdots\pi$-O and OH$\cdots$n-O hydrogen bonds, respectively, were made. In semicyclic β-hydroxy ketones (**42**), because of geometrical constraints, only one type of hydrogen bond (either OH$\cdots\pi$-O or OH$\cdots$n-O) occurs in a given molecule. The $\Delta\nu$'s could be related to the dihedral angle (designated φ) between the C–O and C–CH$_2$OH groups. When $\varphi \sim 0°$ hydrogen bonding to the π-O electrons occurs exclusively and the $\Delta\nu$ is $\sim$60 cm^{-1}. When $\varphi \sim 60°$ the proton-acceptor site appears to be the n-O electrons, and $\Delta\nu$ is $\sim$90 cm^{-1}. When φ is further increased to $\sim$120° hydrogen bonding to either site on oxygen is not possible, and only the weaker interaction with the π-C electrons can be observed. This situation is illustrated by cyclic β-hydroxy ketones (**43**) whose spectra display only very small spectral shifts ($\Delta\nu \sim$ 10–20 cm^{-1}). The olefinic analogs of **43** exhibit much larger $\Delta\nu$'s revealing the π-C electrons of a C=C double bond to be more basic than those of a carbonyl. This is reasonable, since one would expect the π electrons of a carbonyl group to be polarized toward the oxygen atom.

Infrared spectral features characteristic of intramolecular hydrogen bonding are very dependent on the size of the chelate ring.[3,4] Usually the behavior of the stretching vibration of the proton donor, such as the hydroxyl group, is studied. Two infrared bands, free and bonded, are indicative of the occurrence of intramolecular hydrogen bonding. The separation ($\Delta\nu$) between these two bands is particularly sensitive to the size of the hydrogen-bonded ring. With nearly all proton-acceptor groups, a compound with a six-membered hydrogen-bond ring produces a larger $\Delta\nu$ than an analogous compound with a five-membered hydrogen-bond ring. Table I gives typical examples of this phenomenon with OH, OCH$_3$, and N(CH$_3$)$_2$ groups as proton acceptors. Hydroxy ketones are almost unique in behaving anomalously in this respect, since an increase in the ring size from five to six results in a marked decrease in $\Delta\nu$ (Table I; also compare Figures 1A and 1B).

Table I. Spectral Shifts as a Function of Ring Size for Intramolecular Hydrogen Bonds

Compound	$\Delta\nu$, cm^{-1} $n = 2$	$n = 3$
HO(CH$_2$)$_n$OH[a]	26	76
HO(CH$_2$)$_n$OCH$_3$[a]	31	87
HO(CH$_2$)$_n$N(CH$_3$)$_2$[b]	138	327
HO(CH$_2$)$_{n-1}$COCH$_3$[c]	134	46

[a] A. B. Foster, A. H. Haines, and M. Stacey, *Tetrahedron*, **16**, 177 (1961); *cf.* L. P. Kuhn, *J. Am. Chem. Soc.*, **74**, 2492 (1952); L. P. Kuhn and R. A. Wires, *ibid.*, **86**, 2161 (1964), and F. T. Wall and W. F. Claussen, *ibid.*, **61**, 2679 (1939). [b] J. H. Raubitschek, A.B. Thesis, Princeton University, 1964; *cf.* N. Mori, E. Nakamura, and Y. Tsuzuki, *Bull. Chem. Soc. Japan*, **40**, 2191 (1967), and A. M. de Roos and G. A. Bakker, *Rec. Trav. Chim.* **81,** 219 (1962). [c] This study.

Although a reasonable number of examples of intramolecular hydrogen bonding in aliphatic hydroxy ketones have been reported,[5-22] the literature is in a

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[1] Paper XIX of a series on hydrogen bonding; XVII, L. Joris, P. von R. Schleyer, and R. Gleiter, *J. Am. Chem. Soc.*, **90**, 327 (1968); XVIII, L. Joris and P. von R. Schleyer, *Tetrahedron*, in press.

[2] National Science Foundation Cooperative Fellow, 1963–1964; National Institutes of Health Predoctoral Fellow, 1967–1968; Ph.D. Thesis, Princeton University, 1968.

(3) 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.

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

(5) J. Fajkoš, J. Joska, J. Pitha, and F. Sorm, *Collection Czech. Chem. Commun.*, **28**, 2337 (1963).

(6) M. K. Birmingham, H. Traikov, and P. J. Ward, *Steroids*, **1**, 463 (1963).

(7) C. Duculot, *Compt. Rend.*, **241**, 1738, 1925 (1955).

(8) M. St. C. Flett, *Spectrochim. Acta*, 10, 21 (1957).

(9) W. Lüttke and H. Marsen, *Z. Elektrochem.*, **57**, 680 (1953).

(10) J. C. Sheehan, R. C. O'Neill, and M. A. White, *J. Am. Chem. Soc.*, **72**, 3376 (1950).

(11) Y. Mazur and M. Nussin, *Tetrahedron Letters*, **22**, 817 (1961).

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

(13) G. Eglinton, J. Martin, and W. Parker, *ibid.*, 1243 (1965).

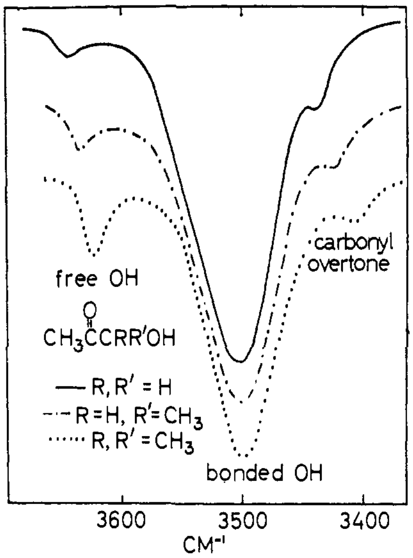

Figure 1A. Hydroxyl region infrared spectra of acyclic α-hydroxy ketones.

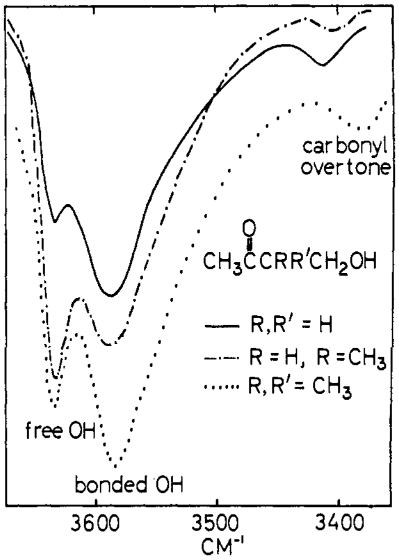

Figure 1B. Hydroxyl region infrared spectra of acyclic β-hydroxy ketones.

state of confusion because carbonyl overtones sometimes have been mistaken for bonded peaks. There has been no systematic attempt to relate the magnitudes of the $\Delta\nu$'s observed with configuration and conformation. Furthermore, it has been suggested by some authors[23,24] but not accepted by others,[25] that there are multiple bonding sites in the carbonyl group. We present the results of our investigation of the behavior of hydroxy ketone hydrogen bonding designed to clarify these problems.

Results and Discussion

Figures 1A and 1B show infrared spectra of typical acyclic α- and β-hydroxy ketones. All of these spectra exhibit three maxima in the OH stretching region, 3700–3200 cm^{-1}: the free OH absorption (3638–3621 cm^{-1}), the hydrogen-bonded OH absorption (3596–3494 cm^{-1}), and the first overtone of the fundamental carbonyl stretching vibration (3450–3400 cm^{-1}). It is this last feature which we will discuss in detail first. A carbonyl overtone will normally be observable in the ir spectra of molecules possessing a fundamental carbonyl stretching absorption. In Figures 1A and 1B these overtones are seen as small "bumps" on the low-frequency wings of the more intense OH-bonded peaks. In these spectra, this feature presents no difficulty in assignment, but such is not always the case.

The Carbonyl Overtone. Unless caution is exercised, the carbonyl overtone may be mistaken for an intramolecular bonded OH peak; this error has already been made several times in the literature. Carbonyl overtones fall near 3400 cm^{-1}, *i.e.*, in the spectral region normally associated with bonded OH peaks. Furthermore, the extinction coefficients of overtones, like those of intramolecular hydrogen-bond absorptions, are concentration independent.

Three characteristics serve to identify carbonyl overtones. The carbonyl overtone is found at approximately twice the frequency of the carbonyl fundamental stretching absorption (Table II). The carbonyl overtone will always be a relatively weak absorption, whereas intramolecular bonded OH peaks usually are much more intense. The width of the absorption band provides an unambiguous distinction between carbonyl overtones and OH-bonded peaks. A bonded OH peak is broad with a band width roughly proportional to $\Delta\nu$[26]; by comparison, a carbonyl overtone is relatively narrow. For example, the 3436-cm^{-1}, intramolecular-bonded OH absorption of α-(2-pyridyl)ethanol[27] has a band width of 126 cm^{-1},[28] whereas carbonyl overtones near 3440 cm^{-1} were found in this study to have band widths of about 25 cm^{-1}.[28] By measuring the band width, absorptions can be assigned reliably to either of these two causes.

If one desires to distinguish conclusively between carbonyl overtones and hydroxyl peaks, the effect on the infrared spectrum when the OH bond is transformed into an OD bond should be studied. After complete deuterium exchange the OH bands will be absent and in their place OD bands will appear at distinctively lower frequencies. The carbonyl overtone will be unaffected by deuterium exchange and there will be no OD band corresponding to this absorption. Using this technique Stolow[18] conclusively demonstrated that the absorptions at *ca.* 3400 cm^{-1} in 4-hydroxycyclohexanone and in 4-hydroxy-4-phenylcyclohexa-

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(14) F. Dalton, J. I. McDougall, and G. D. Meakins, *J. Chem. Soc.*, 4068 (1963).

(15) J. Pitha, J. Plešek, and M. Horák, *Collection Czech. Chem. Commun.*, **26**, 1209 (1961).

(16) W. von E. Doering and A. A.-R. Sayigh, *J. Org. Chem.*, **26**, 1365 (1961).

(17) J. Rigaudy and P. Courtot, *Compt. Rend.*, **248**, 3016 (1959).

(18) R. D. Stolow, *J. Am. Chem. Soc.*, **84**, 686 (1962).

(19) R. N. Jones, P. Humphries, F. Herling, and K. Dobriner, *ibid.*, **74**, 2820 (1952).

(20) G. Hite, E. E. Smissman, and R. West, *ibid.*, **82**, 1207 (1960).

(21) O. R. Wulf and U. Liddel, *ibid.*, **57**, 1464 (1935).

(22) P. Colard, I. Elphimoff-Felkin, and M. Verrier, *Bull. Soc. Chim. France*, 516 (1961).

(23) (a) H. Fritzsche, *Spectrochim. Acta*, **21**, 799 (1965); (b) H. Fritzsche, *Z. Physik. Chem.* (Neue Folge), **43**, 154 (1964).

(24) A. T. Shulgin and H. O. Kerlinger, *Chem. Commun.*, 249 (1966).

(25) E. Ōsawa, K. Kitamura, and Z. Yoshida, *J. Am. Chem. Soc.*, **89**, 3814 (1967).

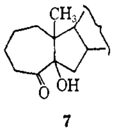
(26) Reference 4, p 94.

(27) L. Joris, unpublished result.

(28) Measured at half the absorbance maximum.

Table II. Infrared Spectroscopic Properties of Aliphatic Hydroxy Ketones^{a}

Compound	ν_{free}	ν_{bonded}	$\Delta\nu$	$A_b/A_f{}^{b}$	Carbonyl overtone ν	Carbonyl overtone Rel absorb.^{c}	$\nu_{C=O}$
		α-Hydroxy Ketones					
Acetol (**1**)	3638	3504 (3501)^{d}	134	15	3439^{e}	0.06^{e}	1728
Acetoin (**2**)	3628 (3616)^{7}	3496 (3481)^{7}	132 (135)^{7}	8	3420^{e}	0.06^{e}	1722
3-Hydroxy-3-methyl-2-butanone (**3**)	3621	3498	123	4	3408^{e}	0.06^{e}	1715
2-Hydroxyacetophenone (**4**)		3491	...		3367^{e}	0.06^{e}	1692
Benzoin (**5**)	(3623)^{8}	3475 (3480,^{8} 3472^{9})	(143)^{8}		3351^{e}	0.06^{e}	1687
Adipoin (**6**)		3497 (3484,^{10} 3500^{d})			3419^{e}	0.06^{e}	1721
A-Homo-B-norcholestan-6β-ol-5-one^{11} (**7**)	(3495)						
Cholestan-5β-ol-6-one (**8**)		(3505,^{11} 3480^{d})					
Cholestan-5α-ol-6-one (**9**)	(3615,^{11} 3614^{d})	(3602)^{d}	(12)^{d}	(3.7)^{d}			
Cholestan-5α-ol-4-one^{d} (**10**)	(3615)	(3603)	(12)	(3.3)			
3-*endo*-Hydroxybicyclo[2.2.1]heptan-2-one (**11**)		3569			3488	0.08	1757
		β-Hydroxy Ketones					
4-Hydroxy-2-butanone (**12**)	3635 (3637)^{d}	3589^{f} (3580)^{d}	46^{f} (47)^{d}	1.5 (1.6)^{d}	3414^{e}	0.1^{e}	1714
4-Hydroxy-3-methyl-2-butanone (**13**)	3637	3593^{f}	44^{f}	0.8	3406^{e}	0.05^{e}	1711
4-Hydroxy-3,3-dimethyl-2-butanone (**14**)	3638	3586^{f}	52^{f}	1.5	3406^{e}	0.05^{e}	
Diacetone alcohol (**15**)	3614	3535	79	6.0	3404^{e}	0.05^{e}	1711
2-Hydroxymethylcyclohexanone (**16**)	3640 (3641)^{d}	3583 (3586)^{d}	57 (55)^{d}	4.0 (3.9)^{d}	3390^{e}	0.08^{e}	1706
3-Hydroxymethylcamphor (**17**)	3631	3552	83	0.5	3443^{e}	0.06^{e}	1735
2-Hydroxymethylcyclopentanone (**18**)	3634, 3626 sh	3547	87	0.8	3446^{e}	0.06^{e}	1737
Methylicterogenin^{12} (**19**)	(3635)	(3518)	(117)	(1.4)			
Methylhederagonate^{12} (**20**)	(3630 sh)	(3602,^{g} 3540)	(28, 90)				
6-*endo*-Hydroxycamphor^{h} (**21**)	3620	3606	14	2.0	3474	0.06	
2-*exo*-Hydroxybornan-7-one (**22**)	3633 sh	3615	18		3550	0.06	1777
2β-Hydroxybicyclo[3.1.1]heptan-2-one (**23**)	3617	3598	19	1.0	3542	0.05	1784
2-Hydroxy-1,5-dimethylbicyclo[3.3.1]-nonan-9-one^{13} (**24**)	(3630)						
4,4-Dimethyl-5α-cholestan-3-one^{q} (**25**)	(3632)						
10α-Hydroxy-9β-methyl-3-decalone (**26**)	3619^{h}	3605^{h} (3607)^{14,i}	14	5.6	3416 (3420)^{14}	0.07 (0.38)^{14,j}	(1719, 1712 sh)^{14,k}
Cholestan-5α-ol-3-one (**27**)	(3620)^{d}	(3606)^{d,14,i}	(14)^{d}	(7.8)^{d}	(3424)^{14}		
trans-2-Decalon-9-ol (**28**)	3615^{b} (3622 sh)^{14}	3608^{h} (3609)^{14,i}	17	5.0	3418	0.07	
5α-Hydroxyergosta-7,22-dien-3-one^{14} (**29**)		(3608,^{i} 3594^{l})					(1722)
10β-Hydroxy-6α-isopropyl-9β-methyl-3-decalone (**30**)		3610^{m}			3409	0.06	1721
10β-Hydroxy-4β-methyl-9β-methyl-3-decalone (**31**)		3615^{m}			3414	0.06	
10β-Hydroxy-9β-methyl-3-decalone (**32**)		3610^{m} (3610)^{14,i}			3420 (3422)^{14}	0.08 (0.35)^{14,j}	1719 (1719, 1714 sh)^{14,h}
5β-Hydroxycholestan-3-one (**33**)	(3620)^{d}	(3611,^{14,i} 3609^{d})	(11)^{d}	(4.2)^{d}	(3424)^{14}	(0.22)^{14}	(1719)^{14}
cis-2-Decalon-9-ol (**34**)		3602^{m}			3412	0.07	
35, R = H^{15,n}		(3602)^{i}			(3395)^{o}	(0.46)	
36, R = CH$_3$^{15,n}		(3602)^{i}			(3393)^{o}	(0.46)	(1713)^{p}
37, R = C$_2$H$_5$^{15,n}		(3604)^{i}			(3392)^{o}	(0.46)	



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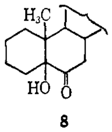

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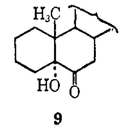

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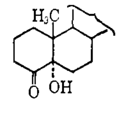

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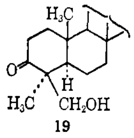

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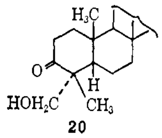

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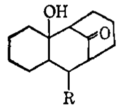

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^{a} Frequencies are in cm^{-1}; measured in dilute CCl$_4$ solution unless otherwise noted. ^{b} (Maximum absorbance of the bonded peak)/(maximum absorbance of the free peak). ^{c} (Maximum absorbance of the carbonyl overtone)/(maximum OH absorbance). ^{d} M. Ōki, H. Iwamura, J. Aihara, and H. Iida, Twentieth Annual Meeting of the Chemical Society of Japan, Tokyo, March 1967, Abstract No. III, p 128. ^{e} The bonded OH peak overlaps part of the carbonyl overtone. The band parameters listed refer to the "resolved" carbonyl overtone. ^{f} The bonded peak is asymmetrical and was resolved into two symmetrical components. See Table III for the results. ^{g} Assigned to a free OH peak in ref 12, but more likely is a bonded OH absorption; free OH absorptions of primary alcohols almost always occur at frequencies higher than 3625 cm^{-1}. ^{h} Spectrum composed of overlapping absorptions; these were resolved by means of a computer program.^{35} The spectral results listed refer to the resolved spectrum. ^{i} Originally assigned to a free OH absorption, but probably is due to a bonded OH (see text). ^{j} The apparent intensity of the carbonyl overtone listed probably includes a contribution from the overlapping OH absorption of dimer. ^{k} The shoulder of the carbonyl absorption was attributed to the stretching vibration of a carbonyl group, which was serving as a proton acceptor in intermolecular hydrogen bonding. ^{l} Hydrogen bonding to the π electrons of a C=C bond. ^{m} Tentative assignment. ^{n} Stereochemistry has not yet been determined. ^{o} Originally assigned to a bonded OH peak^{15} but more likely is a carbonyl overtone (see text). ^{p} Measured in CHCl$_3$ solution. ^{q} M. Fétizon, M. Golfier, and J. Rens, *Bull. Soc. Chim. France*, 2680 (1967).

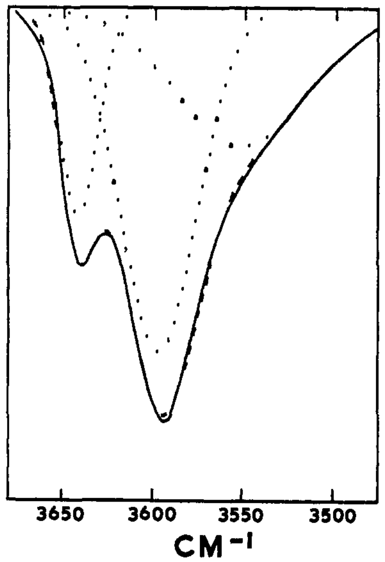

Figure 2. Experimental OH absorption of 4-hydroxy-2-butanone, ——; component bands calculated by computer, ... ; sum of the calculated component bands, - - - -. The close agreement between this calculated sum and the actual spectrum is evident.

none were carbonyl overtones and not bonded OH peaks as had been previously suggested.[16] Similar errors in assignment, not commented on previously, exist in the literature. Eglinton[29] erroneously listed the position of the intramolecular bonded peak in 4-hydroxy-2-butanone as 3430 cm^{-1}. This band (which we find at 3414 cm^{-1} (Figure 1B)) is actually the carbonyl overtone. The major band at 3587 cm^{-1} due to intramolecular hydrogen bonding was not referred to.[29] Bands near 3400 cm^{-1} in **35**–**37** which were originally assigned to bonded OH peaks[16] are almost certainly carbonyl overtones. All axial-β-hydroxycyclohexanones, **24**–**37** (Table I), have carbonyl overtones near 3400 cm^{-1} and no intramolecular bonded OH absorption below 3600 cm^{-1}.[30] The absorption at 3469 cm^{-1} ($\Delta\nu$ = 161 cm^{-1}) in the spectrum of 5β-B-norcholestan-6α-ol-3-one was assigned to a bonded OH.[5] However, a frequency shift of this magnitude is not at all consistent with the proposed structure of the compound. From a molecular model of 5β-B-norcholestan-6α-ol-3-one, the estimated minimum O–O distance is about 3.8 Å. This distance is greater than the expected O–O distance limit of 3.4 Å for hydrogen bonding.[31] It appears inconceivable that a $\Delta\nu$ of 161 cm^{-1} could be produced when the oxygens are 3.8 Å apart. The 3469-cm^{-1} band may well be a carbonyl overtone.

It also is probable that carbonyl overtones have been mistaken for bonded OH peaks in other types of alcohols containing carbonyl functions, *i.e.*, hydroxy esters and aromatic hydroxy ketones.[3] Assignments of absorptions with frequencies approximately double those of carbonyl stretching frequencies to hydrogen-bonded OH groups should be supported by relative band intensity and half band width data. Assignments in the literature where such information is absent might well be regarded with suspicion.[32]

Free and Bonded Peaks of α- and β-Hydroxy Ketones. β-Hydroxy ketones can form a six-membered hydrogen-bond ring, while only a five-membered ring can form in α-hydroxy ketones. Despite this fact, the $\Delta\nu$'s of CH_3COCR_2OH (R = H or CH_3) vary from 123 to 134 cm^{-1} (Figure 1A) but the $\Delta\nu$'s of $CH_3COCR_2CH_2OH$ (R = H or CH_3), instead of being larger (compare Table I), are actually smaller, and range from 44 to 52 cm^{-1} (Figure 1B).

An additional unusual feature of the bonded peaks of the β-hydroxy ketones is their marked asymmetry (Figure 1B). α-Hydroxy ketones, in contrast, give symmetrical bonded bands (Figure 1A), behavior ordinarily expected. A Lorentz mathematical function describes adequately the shape of symmetrical infrared OH bands, whether these are free or bonded.[33] When such bands are observed experimentally not to be symmetrical, it is usually considered that they are made up of a composite of two or more component bands, each of which is assumed to be symmetrical.[23,25,34] Accordingly, the spectra of the β-hydroxy ketones were decomposed by means of a computer program[35] into symmetrical "Lorentzian" components. The sum of two calculated components almost exactly reproduces the experimental bonded OH absorption band (Figure 2).

When regarded in this way, the β-hydroxy ketone bonded peaks are composed of two bands. The more intense components are found at higher frequencies ($\Delta\nu \sim$ 35–50 cm^{-1}) while minor components have the larger $\Delta\nu$'s ($\sim$90 cm^{-1}). Table III summarizes the data so obtained for the β-hydroxy ketones whose spectra are shown in Figures 1B and 2.

Table III. Resolution of Spectra of β-Hydroxy Ketones into Symmetrical Components

Compound	Peak posn, cm^{-1}	Rel absorb.	Half band width[a] cm^{-1}	$\Delta\nu$, cm^{-1}
4-Hydroxy-2-butanone (**12**)	3637	0.6	14	. .
	3594	1.0	30	43
	3547	0.4	51	90
4-Hydroxy-3-methyl-2-butanone (**13**)	3638	0.9	10	. .
	3601	1.0	45	37
	3548	0.4	68	90
	3638	0.9	15	. .
4-Hydroxy-3,3-dimethyl-2-butanone (**14**)	3587	1.0	30	51
	3550	0.5	64	88

[a] Band width at half the absorbance maximum.

Multiple Proton-Acceptor Sites in the Carbonyl Group. It is conventional to regard the carbonyl group as being composed of a σ–π double bond, with the electrons

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(29) G. Eglinton in "Physical Methods in Organic Chemistry," J. C. P. Swartz, Ed., Holden-Day, Inc., San Francisco, Calif., 1964, p 67.

(30) Also see ref 13.

(31) L. P. Kuhn, P. von R. Schleyer, W. F. Batinger, Jr., and L. Eberson, *J. Am. Chem. Soc.*, **86**, 650 (1964), and references cited therein.

(32) B. E. Cross, R. H. B. Galt, and J. R. Hanson, *J. Chem. Soc.*, 2944 (1963).

(33) L. Joris, Ph.D. Thesis, Princeton University, 1968.

(34) (a) Z. Yoshida and E. Ōsawa, *J. Am. Chem. Soc.*, **87**, 1467 (1965); (b) M. Ōki, H. Hosoya, and H. Iwamura, *Bull. Chem. Soc. Japan*, **34**, 1391 (1961); (c) M. Ōki and H. Iwamura, *ibid.*, **39**, 470 (1966); (d) N. Mori, S. Omura, and Y. Tsuzuki, *ibid.*, **38**, 1631 (1965); (e) N. Mori, N. Kobayashi, and Y. Tsuzuki, *ibid.*, **38**, 2149 (1965).

(35) A modification of the Stone program was used [H. Stone, *J. Opt. Soc. Am.*, **52**, 998 (1962)]. A copy of this program and instructions for its use are provided in the Ph.D. Thesis of L. J., Princeton University, 1968.

polarized more toward the electronegative oxygen, and two nonbonding pairs of electrons on oxygen. There is some controversy concerning these nonbonding electrons, whether they are in unhybridized s and p orbitals[36] or whether hybridized sp or sp^2 orbitals are occupied[37] (Figure 3). The electron density of the π bond is concentrated above and below the R_2CO plane, while the n electron density is greatest in this plane, on either side of the oxygen atom (Figure 3).

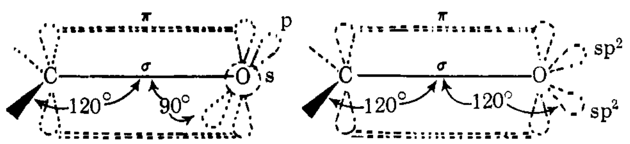


Figure 3. Idealized representations of the molecular orbitals of carbonyl functions for sp^2-hybridized (right) and for unhybridized oxygen (left).

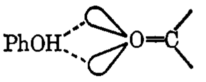
Since C=C double bonds, which have no n electrons, can form hydrogen bonds utilizing their π electrons,[3,4] it is reasonable to expect C=O bonds to be able to do this as well. The n electrons of the carbonyl oxygen atom, like the n electrons of an ether oxygen,[3,4] should also be good sites for proton interaction. Therefore, the carbonyl group should be capable of forming two types of hydrogen bonds involving the n and the π electrons.

An analogy exists between the carbonyl group and the nitrile function, the hydrogen-bonding properties of which have already been studied.[41] A nitrile group should also have π and n electron sites, the latter colinear with the CN bond and extending from the N atom. In intermolecular hydrogen bonding moderately strong hydrogen bonds are observed, *e.g.*, the phenol–benzonitrile interaction has $\Delta\nu = 153$ cm^{-1}. The n electrons are implicated as the proton acceptors in such cases.[41,42] Most hydroxynitriles capable of intramolecular hydrogen bonding, such as *o*-hydroxybenzonitrile ($\Delta\nu = 38$ cm^{-1}) and β-cyanoethanol ($\Delta\nu = 15$ cm^{-1}),[41] give much smaller spectral shifts. These compounds cannot form hydrogen bonds involving the n electrons on nitrogen, for this is geometrically impossible. The observed intramolecular association must then be to the π electrons of the CN triple bond.

The bonded peaks due to intermolecular nitrile–HOR association are symmetrical, despite the presence of two potential hydrogen-bonding sites. Were interaction with both sites taking place simultaneously, two bonded peaks would be observed. Evidently, the π site is too weak to compete with the stronger n site, and only the latter is utilized.

The experimental situation is more favorable with carbonyl groups, where there is evidence even in intermolecular studies for the presence of both n- and π-proton-acceptor sites. Fritzsche[23] observed asymmetrical OH-bonded peaks for intermolecular hydrogen bonding between phenol and ketones. This asymmetry was preserved in the first overtone band and also in the OD-bonded peak when C_6H_5OD was the proton donor; therefore Fermi resonance could not be the cause of this behavior. According to Fritzsche, the most reasonable explanation for the asymmetrical peaks was the presence of two different kinds of hydrogen bonds. Either rotational isomerism of the C–O bond in phenol or multiple proton-acceptor sites in ketones could, in principle, produce the asymmetrical bonded peaks. The former possibility was rejected by Fritzsche, since 2,6-dimethylphenol, expected to have but one minimum energy C–O rotamer, nevertheless showed asymmetrical bonded OH peaks when ketones were proton acceptors. In addition we found asymmetrical bonded OH peaks for the association of methanol with acetone, 2-butanone, acetophenone, cyclohexanone, and anthrone. Methanol has just one type of minimum energy rotamer. Hence, asymmetrical ROH–ketone bonded peaks are evidently a result of multiple bonding sites in the carbonyl groups.

Like simple ketones, quinones also produce asymmetrical bonded peaks with proton donors.[23] Fritzsche resolved these peaks mathematically into two symmetrical components, one at a higher and one at a lower frequency. Successive methyl substitution on the quinone ring decreased the relative absorbance of the low frequency component. Finally, in duroquinone, with methyls on both sides of both keto groups, this low-frequency component was completely gone: the remaining high frequency band was symmetrical. Undoubtedly, the methyl groups sterically prevented hydrogen bonding to the site responsible for the low-frequency component. The nonbonding electrons of oxygen should be more subject to such steric hindrance because they are in the plane of the molecule close to the methyl groups. On the basis of this reasoning, the low-frequency band (larger $\Delta\nu$) was assigned to a OH···O (nonbonding electron) hydrogen bond. For the high-frequency band (smaller $\Delta\nu$), Fritzsche suggested that either hydrogen bonding to the carbonyl π electrons or a bifurcated hydrogen bond, **38**,[43] was responsible.



38

Thus the intermolecular hydrogen bonding results did not unambiguously demonstrate the proton acceptor ability of the π electrons. An intramolecular hydrogen bond with a geometry analogous to **38** will almost never occur since there are not normally enough atoms in the chelate ring to permit a linear OH···O=C arrangement. Consequently, the asymmetrical bonded OH absorptions in β-hydroxy ketones, cannot result from bifurcated hydrogen bonds to nonbonding elec-

[36] G. Berthier and J. Serre in "The Chemistry of the Carbonyl Group," S. Patai, Ed., Interscience Publishers, New York, N. Y., 1966, Chapter 1, and references cited therein are in favor of an unhybridized carbonyl oxygen.

[37] Cook[38] and Schneider[39] suggested that the carbonyl oxygen is hybridized. The nmr spectra of protonated ketones was found to be more easily explained by assuming a hybridized oxygen,[40] but the evidence is not compelling.

[38] D. Cook, *J. Am. Chem. Soc.*, 80, 49 (1958).

[39] W. G. Schneider, *J. Chem. Phys.*, 23, 26 (1955).

[40] G. A. Olah, M. Calin, and D. H. O'Brien, *J. Am. Chem. Soc.*, **89**, 3586 (1967).

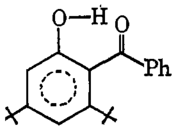
[41] A. Allerhand and P. von R. Schleyer, *ibid.*, **85**, 866 (1963); N. Mori, S. Ōmura, H. Yamakawa, and Y. Tsuzuki, *Bull. Chem. Soc. Japan*, 38, 1627 (1965).

[42] A. Loewenstein and Y. Margalit, *J. Phys. Chem.*, **69**, 4152 (1965).

[43] We, however, are very skeptical of suggestions of bifurcated hydrogen bonds, since no conclusive evidence of tricoordinate hydrogen has ever been presented. However, *cf.* J. Donohue in "Structural Chemistry and Molecular Biology: A Volume Dedicated to Linus Pauling by His Students, Colleagues, and Friends," A. Rich and N. Davidson, Ed., W. H. Freeman and Co., San Francisco, Calif., 1968, p. 450.

trons of the carbonyl oxygen, and the π electrons are implicated as the second bonding site.

The unusually high frequency of the bonded OH peak (3588 cm^{-1}) in 2,4-di-*t*-butyl-6-hydroxybenzophenone (**39**) was cited as evidence for a hydrogen bond to the carbonyl π electrons.[24] Normally intramolecular hydrogen bonds in 2-hydroxybenzophenones are very strong because of the contribution of resonance form **40**, which simultaneously increases both the proton-acceptor ability of the carbonyl group and the proton-donor ability of the hydroxyl group.[44] The absence of a bonded OH peak with a large $\Delta\nu$ in the spectrum of **39** indicates that the contribution of a resonance structure analogous to **40** is not significant. This is another example of steric inhibition of resonance; apparently, the bulky *t*-butyl group forces the benzoyl group out of the plane of the aromatic ring and into a conformation in which a hydrogen bond can form to the carbonyl π electrons.



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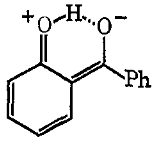

40

The $\Delta\nu$'s (37–51 cm^{-1}) of the more intense bonded OH component of β-hydroxy ketones are of a magnitude suggestive of hydrogen bonding to π electrons: a $\Delta\nu$ of 39–40 cm^{-1} was observed for hydrogen bonding to such electrons in an analogous system, $CH_2{=}CH(CH_2)_2OH$.[45] Because of the larger $\Delta\nu$'s ($\sim$90 cm^{-1}), we attribute the low-intensity bonded OH component in the spectra of β-hydroxy ketones to a OH···O (nonbonding electron) intramolecular hydrogen bond.

Recently, Ōsawa, Kitamura, and Yoshida[25] observed two ir bonded peaks due to the interaction of methanol with diphenylcyclopropenone, but they were reluctant to ascribe this behavior to simultaneous interaction of the proton donor with n and with π sites on the carbonyl group. It was pointed out that acetonitrile, which has both n and π electrons, gives a symmetrical bonded peak, while di-*t*-butyl ether, which has only n electrons, gives an asymmetrical one.[25] No alternative explanation was advanced for their two bonded bands.

Although acetonitrile could, in principle, form two types of intermolecular hydrogen bonds simultaneously, this behavior would not be expected if the two potential bonding sites were markedly different in proton-accepting strength. If association to the nitrogen lone pair greatly predominated over that to the π electrons, only one bonded band would be seen. The evidence from intramolecular hydrogen-bonding studies,[41] discussed above, suggests that this is likely the case.

We have studied the hydrogen bonding of alcohols and phenols to a number of ethers, *e.g.*, tetrahydrofuran, dioxane, anisole, diethyl ether, di-*n*-butyl ether, triethyl orthoformate, and triethyl orthoacetate. In every case, a symmetrical OH···O bonded peak is observed. We have also examined the behavior of di-*t*-butyl ether.[46] With phenol, two bonded peaks at about 3300 and 3430 cm^{-1} definitely are present.[25] This is exceptional behavior. Perhaps access to the highly hindered ether is restricted, and there are two average equilibrium conformations for hydrogen bonding, one somewhat better than the other. It is possible, for instance, that di-*t*-butyl ether exists in solution as a mixture of two different conformational isomers, each with different hydrogen-bonding capabilities.

The experimental observation of more than one bonded peak in a hydrogen-bonding spectrum would seem to be a reliable indication of more than one kind of association, but this need not necessarily be due to the presence of more than one type of hydrogen-bonding site. However, when uncrowded molecules, such as simple ketones, give multiple bonded peaks, the sum of the evidence makes it most reasonable to ascribe this behavior to interaction with n- and π-electron sites.

α-Hydroxy Ketones

The α-hydroxy ketones **1–8** gave bonded OH absorptions in a narrow frequency range, 3475–3505 cm^{-1} ($\Delta\nu$'s 120–140 cm^{-1}) (Table II). The rather small differences observed result from minor variations in the factors influencing the strengths of hydrogen bonds: the geometry of the chelate ring, the acidity of the proton-donating OH group, and the basicity of the carbonyl proton-acceptor function. These factors will now be considered as a function of alkyl substitution.

Proton-Donor Acidity of the OH Group. In aliphatic alcohols, α-alkyl groups produce a decrease in proton-donor ability, conveniently measurable by the spectral shifts observed in intermolecular hydrogen bonding.[4] With pyridine as the common proton acceptor, a progression in $\Delta\nu$ from primary to tertiary alcohols is seen: ethanol ($\Delta\nu$ = 282 cm^{-1}), 2-propanol ($\Delta\nu$ = 262 cm^{-1}), and *t*-butyl alcohol ($\Delta\nu$ = 245 cm^{-1}). The proton-donor acidities of the OH groups in the α-hydroxy ketones (CH_3COCR_2OH) **1–3** would be expected to follow a similar progression. This can be demonstrated experimentally. Keto alcohols **1–3** are not completely intramolecularly associated, and intermolecular hydrogen bonding to pyridine can be measured. The order of such intermolecular $\Delta\nu$'s is that expected: **1** (373 cm^{-1}) > **2** (358 cm^{-1}) > **3** (326 cm^{-1}), and the magnitude of the changes with alkyl substitution are proportionately as large as those with the simple alcohols. Of course, the presence of the carbonyl group is manifest by an increase of acidity of the adjacent OH groups, and the $\Delta\nu$'s of **1–3** are enhanced substantially.

Proton-Acceptor Basicity of the CO Group. The effect of alkyl substitution in the compounds CH_3COCR_2OH on the proton-acceptor ability of the CO group cannot easily be measured directly by intermolecular techniques. An external alcohol could associate with either oxygen atom of the keto alcohol, and the normal intramolecular hydrogen bonding would interfere further. However, simple ketones are free from these difficulties. Several authors have studied intermolecular hydrogen bonding to ketones, as a function of changes in substituents.[23,47] Most of the work-

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(44) A. Nyquist, *Spectrochim. Acta*, **19**, 1655 (1963), reported a bonded peak near 3100 cm^{-1} for 2-hydroxybenzophenone.

(45) P. von R. Schleyer, D. S. Trifan, and R. Bacskai, *J. Am. Chem. Soc.*, **80**, 6691 (1958); M. Ōki and H. Iwamura, *Bull. Chem. Soc. Japan*, **32**, 567 (1959); *cf.* M. Ōki, H. Iwamura, T. Onda, and W. Iwamura, *Tetrahedron*, **24**, 1905 (1968), and references cited therein.

(46) Kindly supplied by Professor R. West. Gas chromatography confirmed the high purity of this sample.

(47) (a) J. M. Widom, R. J. Philippe, and M. E. Hobbs, *J. Am. Chem. Soc.*, **79**, 1383 (1957); (b) T. Gramstad, *Spectrochim. Acta*, **19**, 476

ers did not consider the possibility of multiple bonding sites, and only data pertaining to the absorption of the greater intensity band were reported.[47] The behavior observed does not correspond to simple expectation. When attached to an sp^2-hybridized center, alkyl groups generally are electron donating in the order *t*-butyl > isopropyl > ethyl > methyl.[48,49] For this reason, successive α-methyl substitution on acetone would be expected to *increase* the $\Delta\nu$'s observed due to intermolecular hydrogen bonding. In fact, just the opposite is actually found.[23,47] For example, Hoeke and Koevoet reported the following $\Delta\nu$'s (*n*-BuOH) (in cm^{-1}): acetone (114), 2-butanone (92), 3,3-dimethyl-2-butanone (79).[47c] Other studies indicated the same trends, with somewhat smaller $\Delta\nu$ differences. No satisfying explanation has been offered for this behavior.

If the intramolecular hydrogen bonding in α-hydroxy ketones responds in a similar way to the intermolecular hydrogen bonding between alcohols and ketones, then one would expect that increasing alkyl substitution in the series of compounds CH_3COCR_2OH (**1–3**) would give rise to a slight decrease in the intramolecular $\Delta\nu$'s due both to the effect on the CO basicity and the OH acidity.

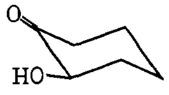
The geometrical changes produced by alkyl substitution in the same series of compounds should be minor. The C–C–OH angle should decrease somewhat as the H's are replaced by CH$_3$'s, the OH···OC distance should decrease, and the intramolecular $\Delta\nu$'s should therefore increase.[50] A fuller discussion of the geometry of hydrogen bonding of these compounds is presented below.

The successive methyl substitution in the series **1** ($\Delta\nu$ = 134 cm^{-1}), **2** (132 cm^{-1}), and **3** (123 cm^{-1}) produces only a slight decrease in spectral shift. Evidently the composite of the three effects discussed is responsible for this behavior. However, the bonded peaks for all three compounds have nearly the same frequency; the differences in $\Delta\nu$ are due mainly to the normal decrease in free peak position as one goes from primary to secondary to tertiary alcohols.

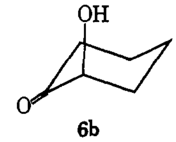
Terminal phenyl substitution in 2-hydroxyacetophenone (**4**) produces a decrease in bonded peak position (to 3491 cm^{-1} from 3504 cm^{-1} in **1**), which probably is the result of enhanced acidity of the alcohol function. (In intermolecular studies, $\Delta\nu$'s found with acetophenone are slighly less than those with acetone.[47]) This effect is more marked in benzoin (**5**) which had the lowest bonded peak position (3475 cm^{-1}) among the α-hydroxy ketones examined. The OH acidity enhancement produced by phenyl substitution is illustrated by the magnitudes of intermolecular spectral shifts to pyridine: ethanol, $\Delta\nu$ = 282 cm^{-1}; α-phenylethanol, $\Delta\nu$ = 310 cm^{-1}.

Hydrogen-Bonding Geometries of α-Hydroxy Ketones. Three of the α-hydroxy ketones **9–11** displayed spectra markedly different from those of **1–8**. The bonded OH peak of **11** was found at 3569 cm^{-1}, while **9** and **10** did not absorb at all below 3600 cm^{-1}. This abnormal behavior was due to the structural restrictions of these compounds, which prevent them from attaining the optimum hydrogen-bonding geometry.

This optimum geometry is easily determined by examining the spectra of rigid, conformationally fixed molecules. In adipoin (**6**), the hydroxyl group can either be equatorial (dihedral angle to the C=O group nearly 0°), **6a**, or axial (with about a 120° dihedral angle to the carbonyl), **6b**. The rigid steroids **7** and **8**, with equatorial hydroxyl groups, give $\Delta\nu$'s of the same magnitude as **6** and as the acyclic α-hydroxy ketones **1–5**. In contrast, the steroids **9** and **10**, with axial hydroxyls, show at best only very weak intramolecular hydrogen bonding.



6a



6b

This evidence clearly indicates the optimum geometry for hydrogen bonding in α-hydroxy ketones: OH and C=O groups in the same plane, as in **6a**. This is exactly what is expected from a consideration of distances and angles in various possible hydrogen-bonding conformations (Table IV). The best possible geometry is found with a dihedral angle between OH and C=O groups of 0°. Increasing this angle should decrease the strength of the intramolecular hydrogen bond and the spectral shift observed.

Table IV. Variation of Spectral Shifts with Hydrogen-Bonding Geometries for α-Hydroxy Ketones

	O–C–C–O dihedral angle, deg	O···O distance, Å	C=O···H angle, deg	O—H···O angle, deg	$\Delta\nu$, cm^{-1}
Ideal geometry	0	2.4–2.6[a]	90–120[b]	180[a]	...
Compd **6–8**	0	3.0[c]	90[c]	120[c]	~130
Compd **11**	60	3.4[c]	50–60[c]	120[c]	~60
Compd **9–10**	120	3.7[c]	40[c]	60[c]	$\leqq$12

[a] For a discussion of these estimates, see ref 31. [b] The optimum H···O=C angle angle should be the same as the angle between an axis of the orbital containing the pair of n electrons and the O–C bond, and would be 120° if the oxygen was hybridized and 90° if it was not. [c] Determined from measurements on Framework Molecular Models.

An experimental confirmation of this expectation is provided by 3-*endo*-hydroxybicyclo[2.2.1]heptan-2-one (**11**), where the dihedral angle is fixed at about a 60° value (see Table IV). The spectral shift for this compound is about 60 cm^{-1}, *i.e.*, about half the value found for compounds capable of attaining the optimum eclipsed geometry. When the dihedral angle is increased to 120°, the OH···O distances become too large for intramolecular hydrogen bonding (Table IV), and only very small spectral shifts ($\Delta\nu$ ~ 12 cm^{-1}) are observed in **9** and **10**. These small shifts may be due to hydrogen bonding to the π electrons of the C=O double bond.[3,45]

For most α-hydroxy ketones capable of attaining the optimum, coplanar arrangement, the proton-acceptor site is the n electrons of the carbonyl group.

(1963); (c) M. Hoeke and A. L. Koevoet, *Rec. Trav. Chim.*, **82**, 17 (1963).

(48) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 590.

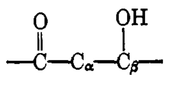
(49) *Cf.* C. D. Ritchie, *J. Phys. Chem.*, **65**, 2091 (1961).

(50) *Cf.* P. von R. Schleyer, *J. Am. Chem. Soc.*, **83**, 1368 (1961).

The symmetry of the bonded peaks observed for acyclic α-hydroxy ketones suggests that other hydrogen-bonding conformations are largely absent.

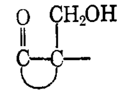
β-Hydroxy Ketones

Different types of β-hydroxy ketones were examined (Tables II, III, and V): acyclic **41** (**12–15**), semicyclic **42** (**16–20**), and cyclic **43** (**21–37**). Compounds in the last class are restricted conformationally, intramolecular hydrogen-bonding interactions, if present at all, are very weak, and these cyclic compounds will be considered separately later.



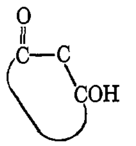
acyclic

41



semicyclic

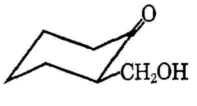
42



cyclic

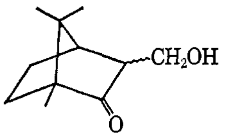
43

Geometries of Acyclic and Semicyclic β-Hydroxy Ketones. In α-hydroxy ketones the chief conformational problem was the assessment of the torsional angle between the C=O and C—O groups. β-Hydroxy ketones have an additional degree of freedom, and two dihedral angles, those between the C=O and C_α—C_β bonds (designated φ here) as well as between the OC—C_α and C_β—OH bonds, need to be determined. (It is assumed, because of the low barrier to rotation around C–OH bonds,[31] that the OH group will necessarily adopt the best arrangement for hydrogen bonding.) This task is simplified in the semicyclic compounds **42**, where it is possible to fix the O=C—C_α—C_β torsional angles (φ), at least within a narrow range of values.



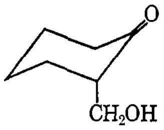
44

$\varphi \cong 0°$



45

$\varphi \cong 60°$ (*endo* and *exo*)

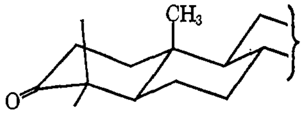


46

$\varphi \cong 120°$

In 2-methylcyclohexanone, the 2-methyl group is preferentially equatorial; at conformational equilibrium only 5% of the molecules are axial.[51] The CH_2OH group in 2-hydroxymethylcyclohexanone (**16**) should also be equatorial (**44**) rather than axial (**46**). Furthermore, a stronger hydrogen bond is possible in **44** than in **46**, due to the shorter O···HO distance, and this should further increase the preference for the equatorial arrangement (**44**). In fact, the *minimum* O···O distance in the axial conformation is about 3.4 Å,[52] which is the *maximum* distance said to be associated with hydrogen bonds in crystals.[4] It seems probable that little, if any, OH···O hydrogen bonding can occur in **46**. Several compounds in class **43**, such as **21** and **35–37**, have geometries similar to that expected for **46**; these model compounds show only very small spectral shifts (10–20 cm⁻¹) possibly attributable to OH···π-C but not to OH···O hydrogen bonding (see below).

The actual spectrum of **16** has a symmetrical bonded peak with $\Delta\nu$ = 57 cm⁻¹. This is assigned to conformation **44**, with a dihedral angle φ of about 0°. A φ of 120° (as in **46**) is associated with a very small spectral shift. However, compounds with intermediate dihedral angles (0° < φ < 120°) give larger spectral shifts. Both *endo* and *exo* isomers of 3-hydroxymethylcamphor (**45**) have φ's near 60°; a mixture of these isomers had $\Delta\nu$ = 83 cm⁻¹. 2-Hydroxymethylcyclopentanone (**18**) should have dihedral angle φ somewhat less than 60°; the spectral shift of this compound was 87 cm⁻¹.



47

At first, the spectral data for methylicterogenin (**19**) ($\Delta\nu$ = 117 cm⁻¹) and for methylhederagonate (**20**) ($\Delta\nu$ = 28, 90 cm⁻¹) reported by Cole and Müller[12] appear not to conform to these generalizations, for these molecules would seem to be axial (**46**) and equatorial (**44**) 2-hydroxymethylcyclohexanone derivatives, respectively. However, ring A of 4,4-dimethylcholestan-3-one (**47**) is known to have a flattened conformation, due to the presence of the keto group and the adverse *meta*-axial methyl–methyl repulsion.[53] The same flattening should be present in **19** and **20**, and the dihedral angles φ should approach the bisected value of **60**°, as a result. For this reason, the $\Delta\nu$'s for **19** and **20** are similar in value to those of **17** and **18**, rather than to that of **16**.

In summary, in semicyclic compounds of type **42**, $\Delta\nu$ varies with the O=C—CCH_2OH dihedral angle φ in an irregular way. When φ is near 0° (as in **16** and in acyclic examples to be considered later), $\Delta\nu$ is about 50–60 cm⁻¹. An increase in φ produces initially an increase in $\Delta\nu$; maximum values of about 100 ± 20 cm⁻¹ (**17–20**) are found in compounds with φ in the region near 60°. When φ reaches 120°, $\Delta\nu$ is very small (as in type **43** compounds). How are these variations to be explained?

In the semicyclic compounds under consideration, φ is fixed, more or less, but rotation about the exocyclic CCH_2OH bond can take place. A minimum energy conformation, considering both torsional and hydrogen-bonding factors, will be favored. With φ = 0° (**16** and **44**), an all-planar arrangement (Figure 4A) should be unlikely on both grounds. The O···O distance of about 2.0 Å is too short to permit hydrogen bonding.[4] In addition, the C–CH_2OH conformation is eclipsed. When this latter conformation is staggered, as in Figure 4B, a much more satisfactory situation results. The O···O distance is about 2.9 Å and hydrogen bonding can occur. However, this conformation is not ideal, for models indicate that the OH group has been moved away from optimum orientation toward the n electrons of the carbonyl oxygen atom, and yet the best possible arrangement with the π electrons on oxygen cannot be achieved. This "in-between" conformation results in intermediate $\Delta\nu$'s for compounds with φ's near 0°.

An increase in φ not only improves the geometry for n electron CO···HO interaction (see Figure 4C for

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(51) N. L. Allinger and H. M. Blatter, *J. Am. Chem. Soc.*, **83**, 994 (1961).

(52) Determined from measurements on framework molecular models.

(53) N. L. Allinger and M. A. DaRooge, *J. Am. Chem. Soc.*, **84**, 4561 (1962); E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," John Wiley and Sons, Inc., New York, N. Y., 1965, p 478.

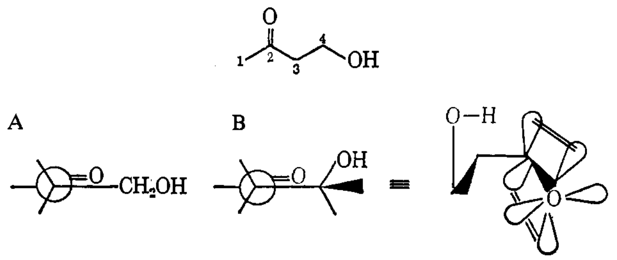
one possibility), but the O···O distances can then attain their optimum values of about 2.5–2.6 Å[4] at $\varphi \sim 30°$. Thus $\Delta\nu$ should increase as φ goes from 0 to 30° but should decrease slightly as φ goes from 30 to 60°. With $\varphi > 0°$ and with a staggered C–CH_2OH arrangement, there are two possible bonding conformations available for the OH group: on the same side as the C=O (Figure 4C, discussed above) and on the opposite side. In this latter conformation, no OH···O hydrogen bonding is possible, but the π electrons above the carbon atom of the C=O bond are an alternative site. The weak ($\Delta\nu$ = 28 cm^{-1}) additional band observed in **20** may be due to this alternative. Finally, when $\varphi = 120°$, as in the cyclic ketones (type **43**, see below), only this π-electron site above carbon is available, and the interactions observed are weak.

The acyclic β-hydroxy ketones **41** can, in principle, adopt a number of conformations. Three of the compounds examined, **12–14**, whose spectra are pictured in Figure 1B, gave two bonded peaks (Table III), while the fourth, diacetone alcohol **15**, gave only a single, symmetrical bonded absorption, with $\Delta\nu$ = 79 cm^{-1}. The two bonded peaks observed for **12–14** indicate the presence of two bonded conformations in those molecules. The higher frequency bonded peak corresponds in $\Delta\nu$ (from 37 to 51 cm^{-1}) to the value (57 cm^{-1}) observed for 2-hydroxymethylcyclohexanone (**16**); evidently, the conformations responsible for this interaction also correspond, *e.g.*, with $\varphi \sim 0°$. This follows expectation, for it is known that the most stable conformation of ethyl ketones is the one with methyl and C=O groups eclipsed.[54]

However, the difference in energy between the more stable conformations of ethyl ketones is relatively small,[54] and the barrier to rotation around R–CO bonds also is low.[55] Consequently, more than one conformation of **12–14** should be populated significantly; such a second conformation evidently gives rise to the bonded peaks at lowest frequencies ($\Delta\nu$ = 88–90 cm^{-1}) found in the spectra of these compounds. Spectral shifts of similar magnitude ($\Delta\nu$ = 83–87 cm^{-1}) are found for **17** and **18**, which have φ near 60°; it may be that such conformations are also adopted by **12–14**. Of course, the number of conformational variables in acyclic β-keto alcohols **41** is large, and one cannot determine the exact geometry of such a molecule from $\Delta\nu$ measurements alone.

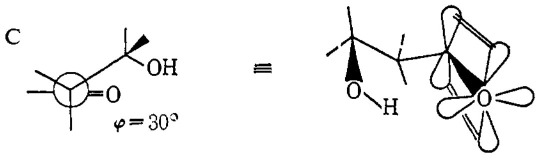
Diacetone alcohol **15** gives only the low-frequency bonded peak ($\Delta\nu$ = 79 cm^{-1}). When models are examined, a reason for this behavior is suggested. The usual conformation with $\varphi \cong 0°$ is destabilized because of a very unfavorable CH_3···O=C interaction. This can be relieved by twisting, and a conformation with $\varphi > 0°$ results. Since **15** is a tertiary alcohol, it is less acidic ($\Delta\nu$ intermolecular to pyridine = 302 cm^{-1}) than primary alcohols, such as **12** ($\Delta\nu$ to pyridine = 331 cm^{-1}). This variation in acidity (as well as the positions of the free peaks) helps to explain the spectral shift difference between the comparable bands of **15** ($\Delta\nu$ = 79 cm^{-1}) and of **12** ($\Delta\nu$ = 90 cm^{-1}).

Although it may be an oversimplification, it is convenient to attribute the two bonded bands in β-hydroxy ketones to interaction with two different bonding sites, the n and the π electrons of the carbonyl oxygen.



atoms O, C(2), C(3), C(4), and O are in a plane; O···O distance ~2.0 Å

substituents on bond C(2)–C(3) are eclipsed and substituents on bond C(3)–C(4) are staggered; O···O distance ~ 2.9 Å



substituents on bonds C(3)–C(4) and C(2)–C(3) are staggered; O···O distance ~2.6 Å

Figure 4. Representative conformations of β-hydroxy ketones.

In the introduction, a peculiarity in the behavior of hydroxy ketones was emphasized: as the number of carbon atoms between the two functional groups is increased from one to two, $\Delta\nu$, instead of rising in magnitude, actually appears to decrease. The reasons for this unique behavior can now be analyzed. The major factor responsible for the pronounced differences (compare Figures 1A and 1B) is the change in principal bonding site. α-Hydroxy ketones (Figure 1A) can form a planar chelate ring between the OH group and the n electrons on the carbonyl oxygen, but this is impossible for β-hydroxy ketones (Figure 1B). Instead, the latter populate most heavily a conformation in which intramolecular hydrogen bonding to an inferior site—the π electrons on the carbonyl oxygen—occurs. Hence, the major bonded peaks in the spectra of **12–14** (Figure 1B) are at very much higher frequencies than those of **1–3** (Figure 1A).

However, a second, lower frequency bonded band is present in the spectra of **12–14**, and other β-hydroxy ketones (*e.g.*, **17–20**) show this peak predominantly. Nevertheless, the spectral shifts associated with these second peaks, usually about 90 cm^{-1}, are inferior in magnitude to those of typical α-hydroxy ketones ($\Delta\nu \sim 130$ cm^{-1}), despite the presumption that the same bonding site, the n electrons on the carbonyl oxygen, is involved in both cases.

A part, but only a part, of this difference is due to a decrease in acidity as the carbonyl is moved farther away from the OH group. Two comparisons of intermolecular hydrogen-bonding propensities of α- and β-hydroxy ketones are available, with pyridine as the common proton acceptor. The primary alcohols **1** and **12** gave $\Delta\nu$'s of 373 and 331 cm^{-1}, respectively, while their derivatives **3** and **14** gave values of 326 and 302 cm^{-1}. In both cases, the difference in magnitude of the spectral shifts of the α-hydroxy ketones **1** and **2** and the β-hydroxy ketones **12** and **14** was only about 10% of the total value. On a similar basis, the

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(54) G. J. Karabatsos and N. Hsi, *J. Am. Chem. Soc.*, 87, 2864 (1965), and references cited therein.

(55) J. Dale, *Tetrahedron*, 22, 3373 (1966).

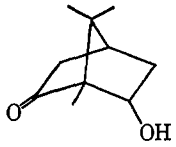
typical intramolecular $\Delta\nu \sim 130$ cm^{-1} of an α-hydroxy ketone would be expected to decrease only to about 115 cm^{-1} in β-hydroxy ketones, due to the decrease in OH acidity. This effect is not large enough to explain why typical β-hydroxy ketones have $\Delta\nu$'s near 90 cm^{-1}, instead of greater values.

Ordinarily, the increase in $\Delta\nu$ commonly observed (see Table I) when the size of hydrogen-bonding rings becomes larger is attributed to improvement of hydrogen-bonding geometry. However, this situation does not pertain in the hydroxy ketones. α-Hydroxy ketones preferentially adopt the planar conformation with the best possible geometry for hydrogen bonding to the carbonyl n electrons—the most basic proton-acceptor site. β-Hydroxy ketones cannot adopt such an all-planar conformation; not only are the torsional arrangements unfavorable but the O···C distance is too short to permit hydrogen bonding. As a consequence, β-hydroxy ketones are forced into other conformations with inferior intramolecular hydrogen-bonding geometries (see Figures 4A and 4B), and the resulting spectral shifts are smaller than those exhibited by α-hydroxy ketones.[56]

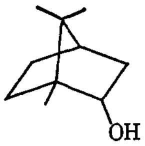
Geometries of Cyclic β-Hydroxy Ketones. In cyclic β-hydroxy ketones **21**–**37**, intramolecular hydrogen bonding is conceivable only to the π electrons on carbon since the hydroxyl group is too far from the carbonyl oxygen to permit association to this site. The π electron of the carbonyl group should be polarized with a greater density toward oxygen than toward carbon. For this reason, intramolecular hydrogen bonds in **21**–**37** are expected to be especially weak and, in fact, these molecules display no bands significantly below about 3600 cm^{-1}.

An unambiguous demonstration of intramolecular hydrogen bonding in compounds displaying such small spectral shifts, *i.e.*, 10–20 cm^{-1}, is inherently difficult because even saturated alcohols incapable of intramolecular hydrogen bonding often give rise to more than one OH band with frequency differences between these bands often as large as 20 cm^{-1}. The complex OH character of saturated alcohols is caused by conformational heterogeneity: the superposition of two or more symmetrical bands differing in frequency, each the absorption of an individual C–O rotamer.[57] Fortunately, certain characteristics serve to distinguish between weak hydrogen bonds and conformational heterogeneity. The former display enhanced intensity peaks at frequencies lower than expected on the basis of conformational heterogeneity. Hydrogen bonding is an attractive interaction, and therefore the conformation permitting association should be preferentially populated. It is useful to compare the spectrum of a compound suspected of having a weak intramolecular hydrogen bond with that of carefully chosen models, in which hydrogen bonding is not possible. In addition, an analysis of the spectrum in terms of the conformations expected to be present can be made.[58]

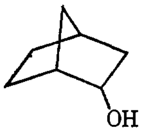
The complex OH spectrum of 6-*endo*-hydroxycamphor (**21**) was resolved by computer[35] into a major band at 3606 cm^{-1} and a minor band at 3620 cm^{-1}. By contrast the ideal model compound **50** and the slightly poorer model **51** show only singlet OH absorptions at 3627 and 3619 cm^{-1}, respectively. It appears therefore that the 3620-cm^{-1} band of **21** is a free peak and the 3606-cm^{-1} major band is a bonded peak. The $\Delta\nu$ of compound **21** is considerably smaller than that of its olefinic analog **52**,[59] thus confirming our expectation that an OH···π (carbon) interaction to a carbonyl group would be inferior to an analogous interaction to a C=C double bond.



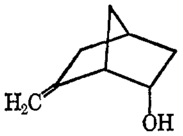
21
$\Delta\nu = 14$ cm^{-1}



50

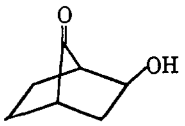


51

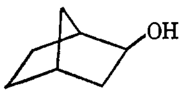


52
3621, 3543 cm^{-1}; $\Delta\nu = 78$ cm^{-1}

Evidence for hydrogen bonding in 2-*exo*-hydroxynorbornan-7-one (**22**) is not clear-cut. Two overlapping bands are observed, a shoulder at 3633 cm^{-1} and a major band at 3615 cm^{-1}, but the absorption frequency of the latter band is only 4 cm^{-1} lower than that of the model saturated alcohol **53**. On the other hand, the olefinic analog **54**[61] definitely shows evidence for hydrogen bonding. Because of this result, we shall tentatively assign the 3615-cm^{-1} absorption of **22** to a hydrogen bond, albeit a very weak one.



22
3633 sh, 3615 cm^{-1}
$\Delta\nu = 18$ cm^{-1}



53

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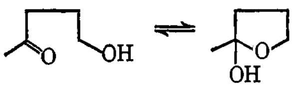
[56] To see whether or not this trend would continue, we examined the spectrum of 3-acetyl-1-propanol (**48**), a γ-hydroxy ketone. Unfortunately, this compound exists in a $\sim$3:1 equilibrium mixture (determined by nmr) with its cyclized, hemiketal form **49**, which also absorbs in the region of interest. The spectrum of the mixture had a free peak at 3639 cm^{-1}, a sharp bonded peak at 3605 cm^{-1} (evidently attributable to α-hydroxy ether hydrogen bonding in **49**), and a broad, rather weak band at about 3500 cm^{-1}, in addition to the carbonyl overtone at 3422 cm^{-1}. The 3500-cm^{-1} band, corresponding to a $\Delta\nu$ of about 140 cm^{-1}, was proabably due to OH··O=C association. As might be expected, the larger hydrogen-bonding ring of **48** permits more conformational degrees of freedom than is possible in β-hydroxy ketones, and an increase in spectral shift results. *Cf.* W. Lüttke, *Ber.*, **83**, 571 (1950); Yu. A. Pentin and I. S. Trubnikov, *Dokl. Akad. Nauk SSSR*, **146**, 107 (1962); *Chem. Abstr.*, **58**, 2341*d* (1963).



48 ≈75% **49** ≈25%

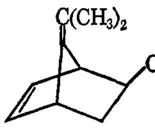
[57] L. Joris, P. von R. Schleyer, and E. Ōsawa, *Tetrahedron*, **24**, 4759 (1968), and references cited therein.

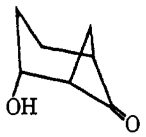
[58] Compare the approach in the analysis of OH···cyclopropane hydrogen bonding: L. Joris, P. von R. Schleyer, and R. Gleiter, *J. Am. Chem. Soc.*, 90, 327 (1968).

[59] We wish to thank Mr. W. A. Washburn[60] for supplying a sample of **52**.

[60] A.B. Thesis, Princeton University, 1967.

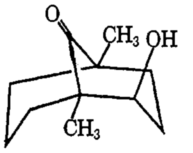
[61] Kindly supplied by Professor C. H. DePuy; *cf.* C. H. DePuy, I. A. Ogawa, and J. C. McDaniel, *J. Am. Chem. Soc.*, **83**, 1668 (1961).

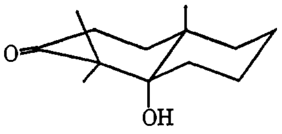

54


23

	54	23
ν_{max} (cm^{-1})	3620,3581	3617,3598
$\Delta\nu$ (cm^{-1})	39	19

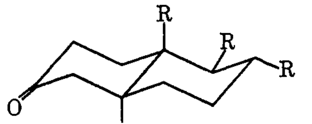
The presence of a hydrogen bond in 2β-hydroxybicyclo[3.1.1]heptan-2-one (**23**) is quite certain, since free OH peaks presumably have never been observed below 3600 cm^{-1}.


24

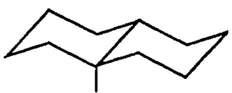

25

The singlet OH absorptions of 2-hydroxy-1,5-dimethylbicyclo[3.3.1]nonan-9-one (**24**) and cholestan-4,4-dimethyl-5α-ol-3-one (**25**) located near 3630 cm^{-1} reveal the absence of hydrogen bonding, although other 3-axial-hydroxycyclohexanones (**26–37**) with OH absorptions at lower frequencies (Table II), as will be discussed shortly, apparently have weak OH··· π interactions. The anomalous behavior of **24** and **25** is probably a result of the increased distance between the O—H and C=O groups caused by ring flattening; physical evidence indicates that the A ring of 4,4-dimethylcholestan-3-ones[53] and the rings of bicyclo[3.3.1]nonanes[62] exist in flattened chair conformations. In the latter case, the rings are flattened in order to relieve the adverse repulsion between the "bowsprit" hydrogens.

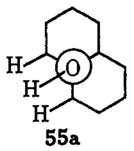
To analyze satisfactorily the OH spectra of **26–37**, which absorb in the 3615–3600-cm^{-1} region, the spectra of model saturated alcohols are needed for comparison. Suitable models were available only for **26–28** and **34**; hence, our discussion will be confined to these compounds.

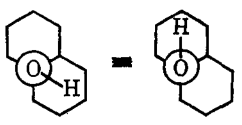

26–28

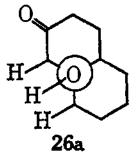
R = H or alkyl

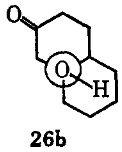

55

The OH spectra of **26–28** are quite similar, as expected from the correspondence of their structures, and were decomposed by computer into two symmetrical components—a major band at about 3605 cm^{-1} and a minor band, approximately 20% as intense, near 3620 cm^{-1} (Table V). The asymmetrical OH spectrum of *trans*-9-decalol (**55**) should approximate the free OH absorptions of **26–28**. In a previous study, we had assigned the 3613-cm^{-1} absorption of **55** to the C–O rotational isomer (rotamer) **55a** and the 3625-cm^{-1} absoption to rotamer **55b**.[57] Rotamers **55a** and **55b** should be analogous to **26a** and **26b**, respectively, since no interaction with the carbonyl group should be possible, and their absorption frequencies should also be similar. In **26–28**, the third type of C–O rotamer (**26c**) is of greatest interest, since it is the one in which hydrogen bonding may take place.


55a
3613 cm^{-1}


55b
3625 cm^{-1}


26a
3613 cm^{-1}


26b
3625 cm^{-1}

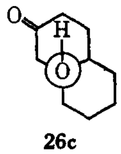

26c
~3600 cm^{-1}

Table V. Summary of Spectral Data for 2-Decalon-9-ols and Their Analogs

Compound	ν_{max}, cm^{-1}	$\Delta\nu$, cm^{-1}	Rel absorb.	$\Delta\nu^{1/2}$,[a] cm^{-1}
10α-Hydroxy-9β-methyl-3-decalone[b]	3619	14	0.2	15
(**26**)	3605		1.0	13
Cholestan-5α-ol-3-one[b,c] (**27**)	3620	14	0.1	..
	3606		1.0	
trans-2-Decalon-9-ol[b] (**28**)	3615	7	0.2	10
trans-9-Decalol[b,d] (**55**)	3608		1.0	12
	3625	12	1.0[e]	14
	3613		1.3[e]	14
cis-2-Decalon-9-ol (**34**)	3602	..	...	15
cis-9-Decalol[b,d] (**56**)	3621	13	1.0[e]	16
	3608		1.4[e]	13

[a] Band width at half the absorbance maximum. [b] Spectral data obtained from a computer resolution.[35] [c] Data from reference cited in footnote *d*, Table II. [d] Data from ref 57. [e] Statistically corrected for the presence of two equivalent rotamers.

The 3620-cm^{-1} band found in the spectra of **26–28** can be interpreted as the superposition of the absorptions of **26a** and **26b**.[63] The intense 3605-cm^{-1} band has previously been attributed to the overlap of the absorptions of **26c** and **26a**.[64] This seems reasonable, and it also appears likely that the 3605-cm^{-1} band is mostly due to rotamer **26c**, since the absorptions of **26a** and **26b** should be approximately equally weak in intensity. The relatively high intensity of the absorption of **26c** and the fact that its absorption frequency (~3600 cm^{-1}) is significantly lower than that of the analogous rotamer, **55b** (3625 cm^{-1}), of a model compound are both indicative of intramolecular hydrogen bonding.

The OH spectrum of *cis*-2-decalon-9-ol (**34**) is nearly symmetrical with an absorption maximum at 3602 cm^{-1}. The two minimum energy conformations of **34** are **34a** and **34b**. Hydrogen bonding is possible only in **34a**

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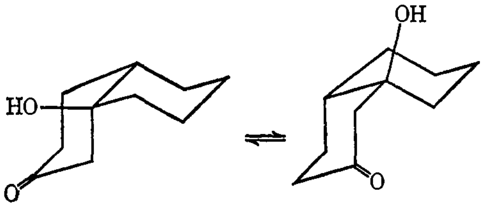
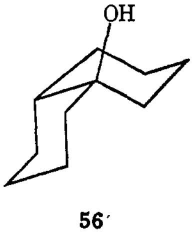
(62) W. A. C. Brown, G. Eglinton, J. Martin, W. Parker, and G. A. Sim, *Proc. Chem. Soc.*, 57 (1964).

(63) Our usual procedure of spectral decomposition[57] is to divide the asymmetrical absorption into the smallest possible number of symmetrical components needed to reproduce the original spectrum. For the alcohols being discussed, decomposition into two components produced good agreement between the calculated spectra (sum of the components) and the experimental one. These spectra could also have been decomposed satisfactorily into three bands but the solution obtained would not be a unique one, *i.e.*, there are many possible ways to decompose the narrow absorptions observed into three bands. Consequently, such decompositions are not very meaningful.

(64) See Table II, footnote *q*.



34a **34b**

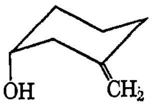


56′

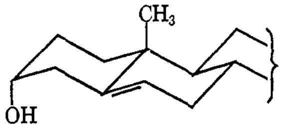
where the hydroxyl group is axial to the cyclohexanone ring; the hydroxyl group points away from the carbonyl function in **34b**.

The free OH absorption of **34** should be approximated by the OH absorption of *cis*-9-decalol (**56**). Spectral decomposition of the latter spectrum yielded the results shown in Table V. The absence of the relatively strong 3621-cm^{-1} band of **56** in the spectrum of **34** is good evidence for the occurrence of weak intramolecular hydrogen bonds in the latter.

The most appropriate olefinic analog for 3-axial-hydroxycyclohexanones is **57**. Unfortunately, spectral data for **57** have not been reported. However, data



57



58

are available for **58** (ν_{max} = 3620 cm^{-1}, 3588 cm^{-1}; $\Delta\nu$ = 32 cm^{-1}),[65] but this compound is a relatively poor model, since the geometrical relationships between the OH group and the π electrons found in **57** and **58** should be significantly different.

The only possible proton acceptor site in cyclic β-hydroxy ketones is the very weakly basic π electrons on the carbonyl carbon—even less basic than π electrons on a carbon atom in a C=C double bond. For this reason spectral shifts caused by hydrogen bonding in cyclic β-hydroxy ketones are very small, *i.e.*, <20 cm^{-1}. The observation of two OH absorptions with spectral shifts of this magnitude is not in itself an unambiguous demonstration of hydrogen bonding, since such spectra are also characteristic of conformational heterogeneity. However, by comparing the spectra of the cyclic β-hydroxy ketones with those of appropriate model saturated alcohols, a distinction between the two phenomena can be made.[65a]

Experimental Section

Infrared Spectral Measurements. The OH infrared spectra were recorded on a Perkin-Elmer 421 double beam grating spectrometer. Reagent grade CCl_4 was dried over P_2O_5, decanted, and used without further purification. Reagent grade pyridine was used without purification. Matched infrared silica cells 1 or 2 cm in length were used. The alcohol concentrations were 0.005 *M* or less to prevent dimerization; 10 mg of pyridine/ml of CCl_4 solution was employed for the intermolecular studies.

The carbonyl stretching frequencies were measured on a Beckman IR 12 spectrometer. The concentrations of hydroxy ketones were approximately 1.0 mg/ml of CCl_4; 3-mm path length NaCl cells were used.

All spectral measurements were performed at room temperature. The peak positions were found by determining the center of the band at various absorbances and averaging. Sharp peaks and broad peaks were measured with an accuracy of ±1 cm^{-1} and ±2 or ±3 cm^{-1}, respectively. The separation of the peaks, $\Delta\nu$, could be measured with an accuracy of ±2 cm^{-1} since the difference was dependent on the relative and not the absolute position of the peaks. The calibration of the instrument was checked daily against atmospheric water vapor; all frequencies reported were so corrected. Excellent reproducibility was observed. In the spectral decomposition by computer, the peak position of the more intense component was accurate to ±2 cm^{-1} and that of the minor component was accurate to ±4 or ±5 cm^{-1}.

Sources of Compounds. Compounds **1–6**, **12–13**, and **15** were commercially available and were distilled or recrystallized before use. Compounds **14**,[66] **17**,[67] and **18**[68] were prepared according to literature procedures. *exo*-2-Hydroxy-7,7-dimethoxybicyclo[2.2.1]-heptane, furnished by Dr. P. G. Gassman, was used for the preparation of **22**.[69] Dr. P. Yates[70] supplied samples of **11** and **23**. A sample of **21** was donated by Dr. P. J. Chapman.[71] Dr. J. A. Marshall donated samples of **26**,[72] **28**,[72] **30–32**, and **34**.[72]

2-Carbethoxycyclohexanone Ethylene Glycol Ketal. A mixture of 100 g of 2-carbethoxycyclohexanone[73] (0.6 mol), 40 g of ethylene glycol (0.64 mol), 200 ml of dry benzene, and 200 mg of *p*-toluenesulfonic acid were refluxed 10 hr with a Dean-Stark water separator. After the benzene was distilled off, the residue was dissolved in ether, and the solution was washed with a dilute sodium carbonate solution. Following removal of the ether, distillation of the residue afforded 115 g (92%) of 2-carbethoxycyclohexanone ethylene glycol ketal, bp 129° (11 mm). *Anal.* Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.73; H, 8.58.

2-Hydroxymethylcyclohexanone Ethylene Glycol Ketal. 2-Carbethoxycyclohexanone ethylene glycol ketal (60 g) was reduced by $LiAlH_4$ in the usual manner to yield 43 g (88%) of 2-hydroxymethylcyclohexanone ethylene glycol ketal, bp 119° (8 mm). *Anal.* Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 63.19; H, 9.27.

2-Hydroxymethylcyclohexanone (16). 2-Hydroxymethylcyclohexanone ethylene glycol ketal (10 g), 10 ml of ethanol, 8 ml of a saturated tartaric acid solution, and 1 ml of concentrated HCl were combined and were heated for 3 hr at 50°. The mixture was poured into 50 ml of water, and the resulting solution was made alkaline with sodium bicarbonate. After ether extraction and distillation of the solvent, the residue was distilled to yield 4 g (54%) of **16**,[74] bp

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(65) M. Ōki, H. Iwamura, T. Onoda, and M. Iwamura, *Tetrahedron*, **24**, 1905 (1968); also see ref 45.

(65a) Note Added in Proof. M. Ōki, H. Iwamura, J. Aihara, and H. Iida, *Bull. Chem. Soc. Japan*, **41**, 176 (1968), recently published in full (see Table II, footnote *d*) their results of infrared investigations of hydroxy ketones. While their data are in good agreement with ours, there is some disagreement in interpretation. The Japanese workers did not resolve the asymmetrical β-hydroxy ketone bands into components and they failed to consider the possibility that two different types of hydrogen bonds (OH···n-O and OH···π-O) might be present simultaneously in these compounds. The $\Delta\nu$ ~ 45 cm^{-1} bands of β-hydroxy ketones were assigned by these workers to a OH···n-O hydrogen bond in which the overlap is very poor. By contrast we have suggested that a OH···π hydrogen bond was responsible for this band.

(66) J. E. Dubois, *Ann. Chim.*, **12**, 406 (1951).

(67) H. Rupe, A. Akermann, and H. Takagi, *Helv. Chim. Acta*, **1**, 452 (1918).

(68) T. Takahashi, A. Kato, and S. Matsuoka, *Yakugaku Zasshi*, **79**, 1087 (1959); *Chem. Abstr.*, **54**, 4543*f* (1960).

(69) P. G. Gassman and J. L. Marshall, *J. Am. Chem. Soc.*, **88**, 2822 (1966).

(70) P. Yates and R. J. Crawford, *ibid.*, **88**, 1561 (1966).

(71) P. J. Chapman, G. Meerman, I. C. Gunsalus, R. Srinivasan, and K. L. Rinehart, Jr., *ibid.*, **88**, 618 (1966).

(72) J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964).

(73) H. R. Snyder, L. A. Brooks, and S. H. Shapiro in "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p 531.

(74) The synthesis of **16** according to the procedure of Olsen and Aalrust[75] was found to give a mixture of products, which we were unable to separate.

(75) S. Olsen and E. Aalrust, *Ann.*, **648**, 29 (1960).

97–99° (3.5 mm). The 3,5-dinitrobenzoate melted at 102–103°. *Anal.* Calcd for $C_{14}H_{14}O_7N_2$: C, 52.18; H, 4.38; N, 8.69. Found: C, 52.23; H, 4.50; N, 9.09.

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The Heat Capacity of Activation and Mechanism of the Hydrolysis of Methylallyl Chlorides

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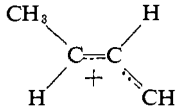
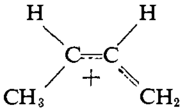
Abstract: Data from a careful study of the temperature dependence of the rate of hydrolysis in water of α-, β-, γ-*cis*-, and γ-*trans*-methylallyl chlorides are presented. The implications of these results together with the corresponding products are discussed in terms of the detailed mechanism.

The solvolysis of allylic types of halides has been widely studied and comprehensively reviewed by DeWolfe and Young.[2a] Various mechanisms have been postulated for the solvolysis of different allyl substrates in several solvent systems including normal bimolecular substitution (SN2), abnormal bimolecular substitution (SN2′), unimolecular substitution (SN1), and intramolecular isomerization *via* an ion-pair intermediate. In the silver ion assisted hydrolysis of α- and γ-methylallyl chlorides[2b] the reaction is presumed to proceed *via* a free carbonium ion in which the positive charge is delocalized over the allylic system. Since rotation about the partial double bond is unlikely, the carbonium ion can exist in either *cis* or *trans* geometry, depending on the geometry or conformation of the original substrate.


I (*trans*)


I (*cis*)

As a continuation of our studies on the temperature dependence of the enthalpy of activation of hydrolytic reactions in water, we have made a careful kinetic study of the hydrolysis of α-, β-, and γ-*cis*- and *trans*-methylallyl chlorides. We report here the thermodynamic activation parameters derived from this study and the products observed over the temperature range studied.

In previous publications we have concluded that the heat capacity of activation, $\Delta C_p^{\ddagger}$, is determined to an important degree by the temperature sensitivity of the structure of the solvation shell around the solute in the initial state.[3,4] The basic hypothesis is that this structure must be broken down in the activation process and the work so required makes a significant contribution to $\Delta F^{\ddagger}$.[4] As the temperature is raised the solvation shell around the solute becomes more mobile and the ground state becomes more like the transition state; thus $\Delta H^{\ddagger}$ decreases with rising temperature, and $d\Delta H^{\ddagger}/dT = (\Delta C_p^{\ddagger})$ is negative as observed. The actual value of $\Delta C_p^{\ddagger}$ will be related to the extent of solvent reorganization in the activation process, and empirically it would appear that $\Delta C_p^{\ddagger}$ may serve to distinguish between the SN1 and SN2 mechanisms for solvolysis in water[4] and in combination with $\Delta S^{\ddagger}$ in mixed solvents.[5] Thus $\Delta C_p^{\ddagger}$ generally has a value of −50 cal/mol deg for SN2 hydrolysis reactions of alkyl halides in water, and a corresponding value of −80 to −100 cal/mol deg for SN1 reactions. In this paper we show that this same generalization holds for the methyl-substituted allyl chlorides but must be applied with care if the reaction proceeds by two competing mechanisms.

Experimental Section

Materials. ***cis*-γ-Methylallyl Chloride.** 2-Butyn-1-ol was converted into *cis*-2-buten-1-ol according to the procedure of Georgoulous[6] modified to employ the Lindlar catalyst.[7] *cis*-γ-Methylallyl chloride (*cis*-crotyl chloride) was obtained by treatment of the latter alcohol with thionyl chloride.[2b] The chloride was finally purified by preparative gas chromatography using a 9 ft × 3/8 in. column of 15% β,β′-oxydipropionitrile on Chromosorb P (80–100 mesh), which is capable of separating the *cis* and *trans* isomers. A 6 ft × 0.25 in. column of the same material was used to check the purity of the final product on the F & M Model 700 gas chromatograph: injector, 100°; oven, 41°; detector, 197°; helium flow rate, 27 cc/min. The sample was found to contain none of the *trans* isomer within an estimated absolute experimental error of less than 0.3%. The purified compound was stored in a Parafilm-sealed flask at −20°.

***trans*-γ-Methylallyl Chloride (*trans*-Crotyl Chloride).** Material purchased as crotyl chloride from Columbia Organic Chemicals Co. was purified in the same way as the *cis* isomer. The final product contained 0.3% of the *cis* isomer and 0.04% α-methylallyl chloride.

α-Methylallyl Chloride. Material purchased as 3-chloro-1-butene from Columbia Organic Chemicals Co. was also purified by preparative gas chromatography. Since this compound isomerized readily to *trans*-γ-methylallyl chloride in the hot injector of the gas

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[1] National Research Council of Canada Postdoctorate Fellow.

[2] (a) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956); (b) W. G. Young, S. H. Sharman, and S. Winstein, *J. Amer. Chem. Soc.*, **82**, 1376 (1960).

[3] R. E. Robertson, *Suomen Kemistilehti, A*, **33**, 63 (1960).

[4] R. E. Robertson, *Progr. Phys. Org. Chem.*, **4**, 213 (1967).

[5] G. Kohnstam, *Advan. Phys. Org. Chem.*, **5** (1967).

[6] C. Georgoulous, *Ann. Chim.* (Paris), **6**, 5 (1961).

[7] H. Lindlar, *Helv. Chim. Acta*, **35**, 446 (1952).