[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

1,3-Diaxial Hydrogen Bonding and the Intramolecular Assistance of Solvolysis

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The infrared spectra of some polycyclic 1,3-diols and 1,3-diol monoacetates, compounds I–VI, have been studied in the O—H stretching region under high resolution. Intramolecular hydrogen bonds from hydroxyl hydrogens to the ether oxygen of the acetate groups[2a] appear to be present in those monoacetates in which both groups are axial. In the diaxial diols the spectra indicate probable equilibrium between two different intramolecularly bonded species. The mechanism of hydroxyl participation in the solvolysis of the diaxial monoacetates is discussed.

In six-membered ring 1,3-diol monoesters which have the two functional groups rigidly held in the *cis*-diaxial relationship to one another, the ester group undergoes base-catalyzed methanolysis with surprising ease. This assistance by the hydroxyl group in facilitating solvolysis in such compounds was discovered independently by Henbest and Lovell[2] and by workers in these laboratories,[3] and accordingly may be called the "Henbest-Kupchan effect." Henbest and Lovell have also observed the infrared spectra of several 1,3-diaxial hydroxyesters in the cholestane and coprostane series.[2b] These spectra provide evidence for intramolecular hydrogen bonding of the hydroxyl hydrogen to the weakly basic alcohol oxygen of the ester group, and Henbest and Lovell suggest that this hydrogen bond formation is the factor responsible for the increased solvolysis rate of these compounds.

The importance of this unusual type of hydrogen bonding prompted us to study, at high resolution, the infrared spectra in the O—H region of some 1,3-diols and 1,3-hydroxyacetates of the bicyclononane and bicyclononene series (compounds I–VI).

EXPERIMENTAL

All of the compounds used in this study were prepared, purified, and characterized by methods described elsewhere.[4] The carbon tetrachloride solvent was used directly from freshly opened bottles of Merck and Co. reagent grade material; it contained negligible amounts of hydroxylic impurities. The spectra were determined using a Perkin-Elmer Model 112 single-beam double-pass spectrometer with calcium fluoride prism calibrated against ammonia and water vapor. Assignments are considered to be accurate to ±3 cm.$^{-1}$ for sharp bands. Most of the compounds were studied both at 0.05M, using 1 mm. path length, and at 0.005M, using 10 mm. path length. Compounds II and IV were not soluble to the extent of 0.05M in carbon tetrachloride, and so were studied only at the lower concentration. Spectra in the 1700 cm.$^{-1}$ region were determined for some of the compounds as approximately 0.01M solutions in carbon tetrachloride.

All band maxima observed between 3100 and 3750 cm.$^{-1}$ are given following the names of the compounds below. Frequencies are given in cm.$^{-1}$, and the letters following the frequencies describe the bands as follows: s, strong; m, medium; w, weak; sh, shoulder; c, concentration-dependent band (intensity decreases upon dilution).

1β,6-*endo*-Dimethyl-6-*exo*-hydroxy-9α-acetoxy-2,3-(1′-methoxy-7′,8′-dihydro-6′,5′-naphtho)-Δ^2-bicyclo[3,3,1]-nonene[4b] (1), m.p. 131–132°, $\nu_{\max}$ 3594 (s), 3480 (w).

1β,6-*endo*-Dimethyl-6-*exo*-9α-dihydroxy-2,3-(1′-methoxy-7′,8′-dihydro-6′,5′-naphtho)-Δ^2-bicyclo[3,3,1]nonene[4a] (II), m.p. 150.5–151°, $\nu_{\max}$ 3628 (sh, m), 3607 (m), 3500 (s), 3300 (c).

1β,6-*endo*-Dimethyl-6-*exo*-hydroxy-9α-acetoxy-2,3-(1′-methoxy-5′β,6′β,7′,8′-tetrahydro-6′,5′-naphtho)-bicyclo-[3,3,1]nonane[4b] (III), m.p. 197–198°, $\nu_{\max}$ 3593 (s), 3482 (w).

1β,6-*endo*-Dimethyl-6-*exo*-9α-dihydroxy-2,3-(1′-methoxy-5′β,6′β, 7′,8′-tetrahydro-6′,5′-naphtho)-bicyclo[3,3,1]nonane[4a] (IV), m.p. 212–218°, $\nu_{\max}$ 3628 (sh, m), 3609 (m), 3510 (s), 3530 (c).

1β,6-*endo*-Dimethyl-6-*exo*-hydroxy-9β-acetoxy-2,3-(1′-methoxy-7′,8′-dihydro-6′,5,-naphtho)-Δ^2-bicyclo[3,3,1]-nonene[4b] (V), m.p. 195–198°, $\nu_{\max}$ 3608(m), 3450 (c).

1β,6-*endo*-Dimethyl-6-*exo*-9β-dihydroxy-2,3-(1′-methoxy-7′, 8′-dihydro-6′, 5′-naphtho)-Δ^2-bicyclo [3,3,1]nonene[4a] (VI), m.p. 185–186.5°, $\nu_{\max}$ 3618 (m), 3588 (m), 3300 (c).

DISCUSSION

The 1,3-diol monoacetates. The high resolution infrared spectra of the diaxial 1,3-hydroxy acetates I and III provide strong evidence in favor of intramolecular hydrogen bonding involving the hydroxyl group. Both compounds have a single strong O—H stretching absorption band at 3593–3594 cm^{-1}. The intensity of this bond is independent of concentration, and even at the maximum concentration used, 0.05M, there is no appearance of a concentration-dependent band attributable to intermolecular hydrogen bonding. In contrast the spectrum of the axial-equatorial hydroxy acetate V, which cannot be intramolecularly hydrogen bonded, has a sharp peak at 3607 cm.$^{-1}$ and a broad band at about 3450 cm.$^{-1}$, increasing in relative intensity with increasing concentration, characteristic of intermolecularly associated hydroxyl (Fig. 1).

A weak band at about 3480 cm.$^{-1}$ also appears in the spectra of compounds I and III. However, this band is not due to a hydrogen-oxygen stretch-

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[1] Allied Chemical and Dye Company Fellow, 1958–1959.

[2] (a) H. B. Henbest and B. J. Lovell, *Chem. and Ind.*, 278 (1956); (b) H. B. Henbest and B. J. Lovell, *J. Chem. Soc.*, 1965 (1957).

[3] S. M. Kupchan and W. S. Johnson, *J. Am. Chem. Soc.*, **78**, 3864 (1956).

[4] (a) W. S. Johnson, J. Ackerman, J. F. Eastham, and H. A. DeWalt, Jr., *J. Am. Chem. Soc.* **78**, 6302 (1956); (b) W. S. Johnson, J. J. Korst, R. A. Clement, and J. Dutta, *J. Am. Chem. Soc.*, **82**, 614 (1960).

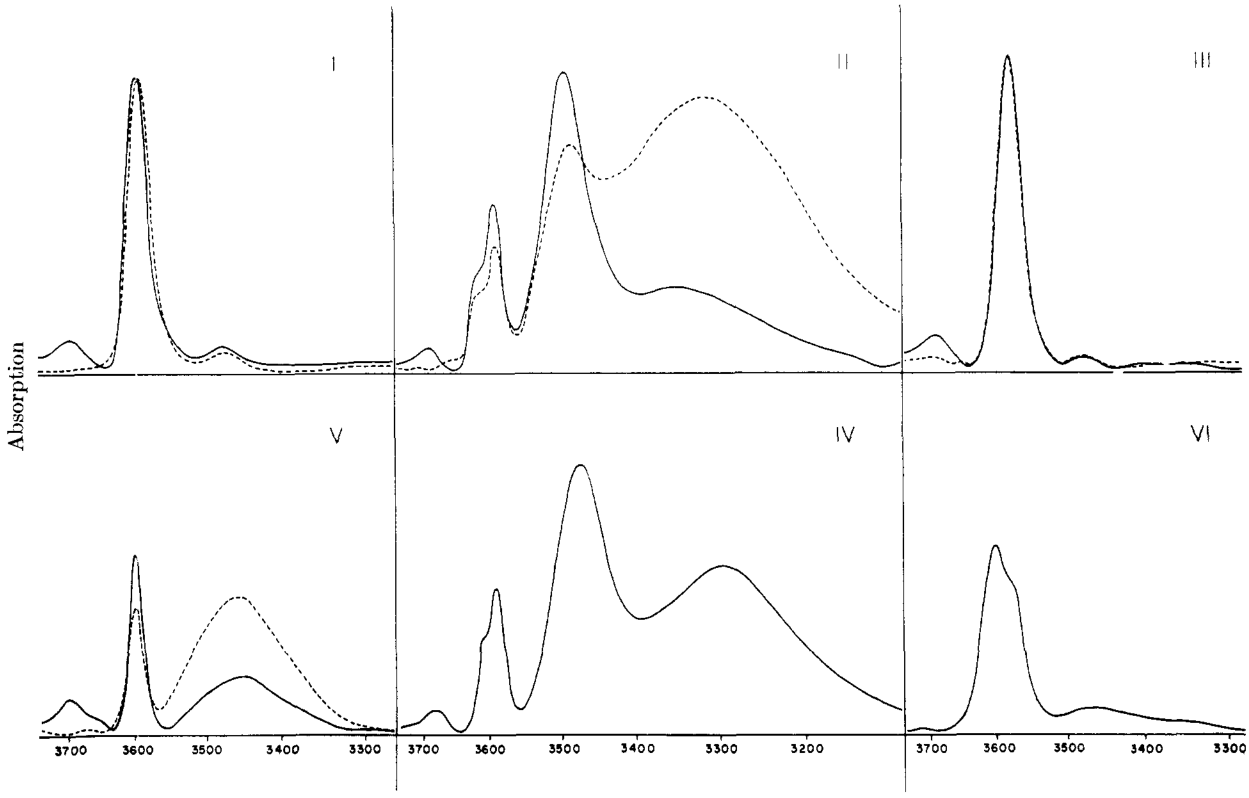
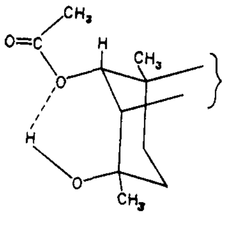


Fig. 1. Infrared spectra in the hydroxyl region. Solid lines, 0.005 *M;* broken lines, 0.05 *M,* in carbon tetrachloride

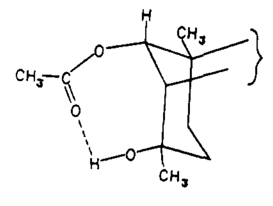
ing absorption, for when compound I was partially deuterated at the hydroxyl group by exchange with deuterium oxide in dioxane, the 3480 cm.$^{-1}$ band was not shifted. In contrast, the 3593 cm.$^{-1}$ O—H band exhibited a normal shift to 2637 cm^{-1}. The 3480 cm.$^{-1}$ band probably represents the first overtone of the strong carbonyl absorption at 1730 cm^{-1}.

The shift, $\Delta\nu$, of band position on hydrogen bond formation is approximately proportional to ΔH for the hydrogen bonding reaction.[5] The band at 3593 cm.$^{-1}$ in compounds I and III must therefore represent a very weakly bonded hydroxyl group, as $\Delta\nu$ is only 15 cm.$^{-1}$ from the position of the unassociated band (in compound V). The shift seems too small for a hydrogen bond to the carbonyl oxygen of the acetate group.[6] We believe that it indicates hydrogen bonding to the ether oxygen, as shown in structure A. As suggested by Henbest and Lovell for other compounds,[2b] hydrogen bonding to the more weakly basic ether oxygen atom probably takes place in I and III because of the large entropy effect favoring the six-membered ring hydrogen bonded system in A over the eight-membered ring system in B.

Further evidence for hydrogen bonding to the ether oxygen rather than to the carbonyl oxygen is given by the spectra of compounds I and III in the 1700 cm.$^{-1}$ region. Intramolecular hydrogen bonding to carbonyl oxygen is known to lower the frequency of C=O stretching bands.[7] Compounds I and III, however, are observed to have carbonyl bands at unusually high frequencies. Compound V, which cannot be intramolecularly hydrogen bonded to either oxygen of the acetate group, has a broad carbonyl band centered at 1730 cm.$^{-1}$, while compounds I and III show sharp C=O bands near 1745 cm^{-1}.



A



B

Henbest has suggested that the intramolecular assistance of solvolysis in 1,3-diaxial hydroxy acetates involves an intramolecular solvation in the collapse (see arrows, formula C) of the reversibly formed adduct C between the ester and nucleophile (N$^-$). An alternative mechanism is conceivable, however, in view of the likely facile

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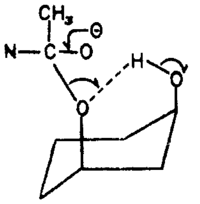
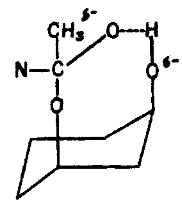
(5) R. M. Badger, *J. Chem. Phys.,* **8,** 288 (1940).

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

(7) L. J. Bellamy, *The Infrared Spectra of Complex Molecules,* 2nd Edition, Methuen and Co., London, 1958, p. 142.


C

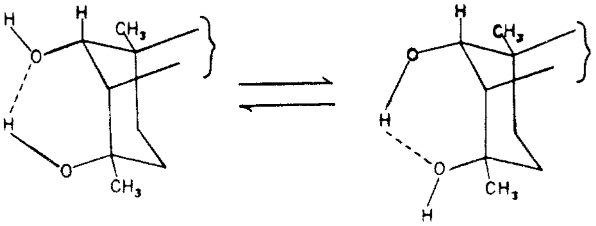

D

interconversion between structures A and B.[8] Hydrogen bonding to the carbonyl oxygen in species B would strongly polarize the $C=O$ group and render it more susceptible to nucleophilic attack, by a sort of intramolecular acid catalysis (see formula D). Form B rather than A thus may be important in facilitation of solvolysis. In any case, the hydrogen bond to the ether oxygen in species A, prior to the solvolysis of the acetate group, seems too weak to have a significant influence on the rate of solvolysis. Which ever species is the important one in solvolysis, it seems likely that the hydrogen bond will become much stronger in the transition state, and that the increase in hydrogen bond energy in passing from the ground state to the transition state decreases the energy of activation for the reaction, thereby increasing the rate of solvolysis.

It may be possible to distinguish between the two mechanisms by appropriate kinetic measurements comparing the facilitation of 1,3-diaxial systems with eclipsed 1,2-systems wherein the entropy as well as enthalpy factors would favor the hydrogen to carbonyl oxygen interaction.

The 1,3-diols. The diols II and IV present very similar, and quite complicated, infrared spectra in the 3100–3800 cm.$^{-1}$ region (Fig. 1). Both show the following features: (a) a concentration-dependent band at about 3300 cm.$^{-1}$ which can be ascribed to intermolecular hydrogen bonding; (b) a strong concentration-independent band at about 3500 cm.$^{-1}$, in an appropriate position for an intramolecular hydrogen bond of moderate strength; and (c) two sharp, closely spaced bands, one at about 3608 and the other at about 3628 cm.$^{-1}$ The last two bands are in the right region for non-bonded hydroxyl groups. However, it seems quite unlikely that there are any substantial numbers of molecules of II or IV present which are not intramolecularly bonded, as even in the case of the weakly bonded acetates I and III no free hydroxyl vibrations are observed. We attribute the 3628 and 3608 cm.$^{-1}$ bands to secondary and tertiary hydroxyl groups, respectively, which are acting as bases in intramolecular hydrogen bond formation. The lower frequency band can be attributed to the tertiary hydroxyl, as in the nonbonded compound V the tertiary hydroxyl also absorbs at 3608 cm.$^{-1}$ It is well established that secondary hydroxyl groups absorb at higher frequencies than tertiary hydroxyls,[9] and Cole has recently shown that axial secondary hydroxyls absorb about 20 cm.$^{-1}$ higher than axial tertiary hydroxyls in triterpenoids.[10]

Our assignment implies the following equilibrium in diols II and IV:


E F

The relative intensities of the O—H bands suggest that the equilibrium constant for the reaction $E \rightleftharpoons F$ lies in the neighborhood of 2. The ring formed by the hydrogen bond is six-membered in both E and F, so no large entropy effect is expected. The position of the equilibrium reflects the fact that the secondary hydroxyl is slightly more acidic, and less basic, than the tertiary hydroxyl group.[9] The bonded hydroxyl groups in forms E and F together contribute to the strong, broad peak at about 3500 cm.$^{-1}$ Finally, the presence of a concentration-dependent band at much lower frequency is not inconsistent with complete intramolecular hydrogen bonding in the diols, as that hydroxyl hydrogen which is not intramolecularly hydrogen bonded is available for intermolecular association.

One of the hydroxyl groups in compound VI is equatorial to ring A, which precludes intramolecular hydrogen bonding between the hydroxyl groups. It is somewhat surprising, then, to find that this compound has an absorption band at 3588 cm.$^{-1}$, indicating weak intramolecular hydrogen bonding. Probably the equatorial (secondary) hydroxyl group is partly or wholly intramolecularly hydrogen-bonded to the π-electrons of the double bond in ring B.[11]

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[8] The spectra give no indication of the presence of structure B, but an amount of B less than 1% of A at equilibrium cannot be excluded.

[9] L. P. Kuhn, *J. Am. Chem. Soc.*, **74**, 2492 (1952).

[10] A. R. H. Cole, P. R. Jefferies, and G. T. A. Müller, *J. Chem. Soc.*, 1222 (1959).

[11] A number of instances of intramolecular hydrogen bonding to olefinic double bonds have been reported recently, including some closely related analogs such as *epi*-cholesterol. See P. von R. Schleyer, D. S. Trifan, and R. Backskai, *J. Am. Chem. Soc.*, **80**, 6691 (1958); A. W. Baker and A. T. Shulgin, *J. Am. Chem. Soc.*, **81**, 5358 (1958); R. West, *J. Am. Chem. Soc.*, **81**, 1614 (1959).