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Nuclear Magnetic Resonance Studies of Hydrogen Bonding in Hindered Phenols[1,2]

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Hydrogen bonding of the hindered phenols, 2-isopropyl-, 2,6-diisopropyl-, 2-t-butyl-, 2-methyl-6-t-butyl-, and 2,6-di-t-butylphenol, has been studied by observing the chemical shifts of –OH group protons. Room temperature dilution shifts in carbon tetrachloride of the phenolic –OH give dimerization constants K of 1.7, 1.3, 1.0, ≤ 0.05, and ≤ 0.05, respectively, for the five phenols. Association constants K_c for phenol–dioxane complexes were obtained from the phenolic –OH dilution shifts in 1,4-dioxane, employing general algebraic expressions derived for the purpose. The K_c's are in the same sequence as the K's but about tenfold larger, consistent with the greater ease with which a smaller molecule approaches the phenolic –OH. Observations of both the ethanolic and the phenolic –OH dilution shifts in ethanol–phenol solutions gave similar results, which were limited to a qualitative interpretation by the relatively strong polymerization of the ethanol. Several lines of evidence, including the temperature dependence of the –OH shifts in an equimolecular phenol–ethanol mixture and the dilution shifts of the 1:1 mixture in carbon tetrachloride, indicate that the stabler form of the complex has the phenolic hydrogen bonded to the ethanolic oxygen. N.m.r. dilution shifts for equimolecular mixtures in an inert solvent have useful features in the study of 1:1 complexes. The isopropyl C–H proton line exhibits relatively large downfield shifts, up to 30 c.p.s. at 60 Mc./sec., depending upon the other substituents.

Introduction

The main concern of this paper is hydrogen bonding in hindered phenols. The unusual properties of these hindered or "krypto" phenols were noted in 1945 by Stillson, Sawyer, and Hunt,[3] who pointed out that bulky o-substituents prevent the molecules from undergoing many of the characteristic reactions exhibited by simple phenols. The restricted access to the –OH group in such molecules should limit the degree of association through hydrogen bond formation and cause the equilibrium constants for polymer formation to exhibit a dependence upon the size of the o-substituents. In fact, such a dependence has been inferred from the infrared and ultraviolet spectra of several phenols by Coggeshall, Lang, and Saier.[4-6] It seems clear that the hindered and partially hindered phenols are not likely to form species larger than dimers, and this circumstance should in principle facilitate the analysis of their association behavior.

A comprehensive discussion of hydrogen bonding and of methods employed in its investigation is available,[7] as is a general treatment[8] of the nuclear magnetic resonance methods employed in our studies. It is well known that the formation of hydrogen bonds displaces the magnetic resonance of the protons involved

toward lower magnetic field, except in certain cases involving aromatic molecules.[8] When a molecule XH forms a hydrogen bond to a donor atom Y, the electronic structure, and consequently the magnetic susceptibility of the XH bond, are altered, leading to a change in the nuclear magnetic shielding. If the primary function of the Y atom is to produce a strong electric field in the vicinity of the XH bond, then a shift toward lower field upon hydrogen bond formation is quite reasonable.[8,9] The electric field deforms the electron distribution about the proton in the hydrogen bond, decreasing the electron density in its vicinity, and increasing its asymmetry. Both effects decrease the proton shielding.[9]

Another possible contribution to the chemical shift produced by association is the quenching of the intramolecular paramagnetic effects of neighboring-atom magnetic anisotropy,[8] which gives a downfield shift upon the formation of nonlinear hydrogen bonds, due to the loss of axial electric symmetry. The magnitude of proton shifts attending hydrogen bond formation, expressed in terms of the difference between the shifts for a pure substance in the liquid and in the gaseous state, usually amounts to less than 2.5 to 3 parts per million, although water and hydrogen fluoride which are, of course, very highly associated, have hydrogen bond shifts of 4.58 and 6.65 parts per million, respectively.[8]

In nuclear magnetic resonance experiments, chemical exchange usually prevents observation of separate resonances for both hydrogen-bonded and nonhydrogen-bonded states in the same medium,[10] although it is often possible to detect separate infrared frequencies for individual polymeric species. This reflects the different time scales of 10^{-13} sec. and 10^{-2} sec. required to average out differences in vibrational frequencies and differences in magnetic resonance frequencies, re-

(1) This paper has been taken in main from the Ph.D. thesis of B. G. Somers, University of Illinois, 1961.

(2) The work was supported in part by the Office of Naval Research. Also, acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

(3) G. H. Stillson, D. W. Sawyer, and C. K. Hunt, J. Am. Chem. Soc., 67, 303 (1945).

(4) N. D. Coggeshall, ibid., 69, 1620 (1947).

(5) N. D. Coggeshall and E. M. Lang, ibid., 70, 3283 (1948).

(6) N. D. Coggeshall and E. L. Saier, ibid., 73, 5414 (1951).

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

(8) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw–Hill Book Co., Inc., New York, N. Y., 1959.

(9) H. S. Gutowsky, Ann. N. Y. Acad. Sci., 70, 786 (1958); P. J. Frank and H. S. Gutowsky, Arch. Sci., 11, 216 (1958).

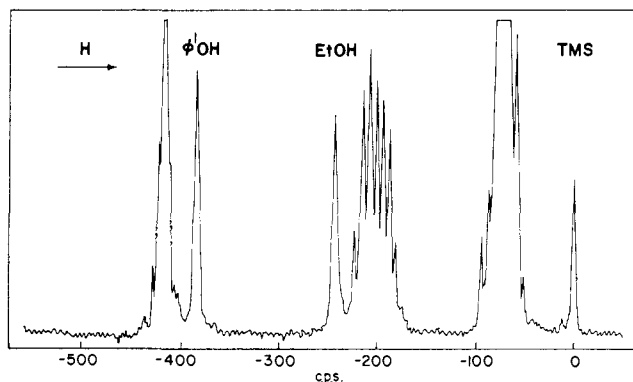(10) H. S. Gutowsky and A. Saika, J. Chem. Phys., 21, 1688 (1953).

Fig. 1.—The proton magnetic resonance spectrum of an equimolecular mixture of 2,6-diisopropylphenol and ethanol, observed at room temperature with a 60 Mc./sec. spectrometer.

spectively. However, in the hindered phenols proton exchange is decreased as well as the extent of association. Thus, it is possible to observe separate –OH proton resonances in solutions containing another hydrogen-bonding species besides a hindered phenol and to learn something about the relative degree of involvement in the hydrogen bonding of the different –OH groups. Furthermore, the very low probability of other than bimolecular complexes involving the hindered phenols makes it easier to estimate the chemical shift characteristic of the dimer proton and the equilibrium constant for dimer formation. In the work reported here, the latter approach was used with success to derive the equilibrium constants for dimer formation from concentration dependence measurements of the phenolic –OH proton shifts in solutions of several hindered phenols in carbon tetrachloride.

The association of the hindered phenols with smaller molecules such as ethanol and dioxane is also affected by the bulky o-substituents of the phenols, although one expects the effect to differ from that for association of like hindered molecules. For example, a small molecule of the right shape could hydrogen bond more readily with the –OH in the hindered phenol than could another molecule of the hindered phenol. This is borne out by the –OH proton shifts observed in solutions of the hindered phenols in ethanol and in dioxane. In addition, consideration of the direction, magnitude, and concentration dependence of the shifts of both the phenolic and ethanolic –OH protons indicates that a bimolecular complex is formed between ethanol and a hindered phenol. Moreover, the complex involves association of the phenolic –OH proton with the ethanol oxygen atom rather than the reverse.

Finally, the results suggest that dilution of equimolecular hindered phenol–ethanol mixtures with carbon tetrachloride may yield information regarding the bimolecular complexes, their hydrogen bond strength, and the shifts characteristic of their –OH protons. Similarly, the temperature dependence of the –OH shifts in these systems provides evidence bearing upon the relative stabilities of the phenol–ethanol complex and of the two types of dimer.

Experimental

The proton magnetic resonance spectra were measured with a Varian Associates Model V4300-2, 60 Mc./sec. high resolution n.m.r. spectrometer with a 12-in. electromagnet, regulated power supply, and superstabilizer. Spinning sample tubes of nominal 5 mm. o.d. were used to improve resolution. Sweep rates were calibrated by means of audiofrequency side bands of the internal reference tetramethylsilane (TMS), the use of which avoids bulk magnetic susceptibility corrections. Because the sweep rate varied considerably and rapidly, two audiooscillators were employed in order to place side bands on either side of the line whose position was to be measured and in reasonable proximity to it.

The audiofrequencies were monitored by a Hewlett–Packard Model 521C electronic counter. This calibration was usually satisfactory, but three or more measurements were averaged for most of the samples. The apparent shifts were not corrected for the intermolecular effects of high concentrations of aromatics on the resonance position of the TMS internal reference. These effects[11] are small compared with the shifts observed in the systems studied here.

For the measurements at elevated temperatures, the Varian Associates variable temperature accessories with a dewar probe insert were employed. Because of the necessity for spinning the sample, its temperature was not measured directly. Instead, each time the apparatus was assembled, a calibration curve was constructed by measuring the temperature of the air entering the dewar insert, with a copper–constantan thermocouple, and also the temperature of a liquid in a nonspinning sample tube located in the probe. The temperatures of the samples whose spectra were recorded were then inferred from this calibration data and the continuously monitored temperature of the air entering the insert.

Reagent grade ethanol and carbon tetrachloride were used without purification, but the carbon tetrachloride was stored in the dark and in brown bottles in order to minimize HCl formation. Measurements at several concentrations of ethanol in carbon tetrachloride agreed with those of Becker, Liddel, and Shoolery.[12] Eastman White Label 1,4-dioxane was passed through an alumina column in order to remove peroxide and water. Eastman White Label t-butylbenzene which had been distilled from calcium hydride was used. The hindered phenols 2-isopropylphenol, 2,6-diisopropylphenol, 2-t-butylphenol, 2-methyl-6-t-butylphenol, and 2,6-di-t-butylphenol, which were supplied by the Ethyl Corporation, were distilled in order to remove some colored material, presumably peroxide, present in small amounts, but the distillation was negligible in its influence upon the measured chemical shifts. The components of the solutions were transferred between rubber-stoppered serum bottles by means of a syringe in order to minimize the introduction of water and the solutions were weighed after the addition of each component in order to determine the concentrations.

Results and Discussion

Spectra and Their Interpretation.—Typical proton spectra are reproduced in Fig. 1 and 2 for equimolecular solutions of 2,6-diisopropylphenol and of 2-methyl-6-t-butylphenol, respectively, in ethanol at room temperature. The spectra are for a magnetic field sweep, increasing from left to right. The negative shifts given in c.p.s. correspond to downfield shifts from TMS. Assignment of the lines in the spectra is generally straightforward. In particular, the –OH lines are readily apparent from their concentration dependent shifts, and in the mixed solutions with two –OH lines the assignments are clear from the relative intensities and the known compositions of the solutions.

The lines of Fig. 1 are assigned as follows, reading from left to right: the phenyl proton lines (–415 c.p.s.), the phenolic hydroxyl line, the ethanolic hydroxyl line, a superposition of the methylene group lines of ethanol upon the septet due to the lone proton of the isopropyl group (–200 c.p.s.), the methyl group of ethanol, and the reference line of the internal TMS. The lines of Fig. 2 are, again reading from left to right: the phenyl proton lines, the phenolic hydroxyl line, the ethanolic hydroxyl line, the methylene lines of ethanol, the 2-methyl group line of the phenol, the methyl group line of the phenol followed closely by the methyl triplet of ethanol, and the TMS reference line.

At high ethanol concentration the triplet structure of the ethanolic –OH line is clearly discernible. Upon dilution or heating of the solution, the triplet structure is lost and, simultaneously, the methylene group multiplet is reduced to the four-line spectrum characteristic of a methylene group whose interaction with the –OH proton is averaged to zero owing to rapid exchange of the –OH proton. At elevated temperatures, both the ethanolic and phenolic –OH proton lines are broadened, but they do not coalesce at the maximum tempera-

(11) E. D. Becker, J. Phys. Chem., **63**, 1379 (1959).

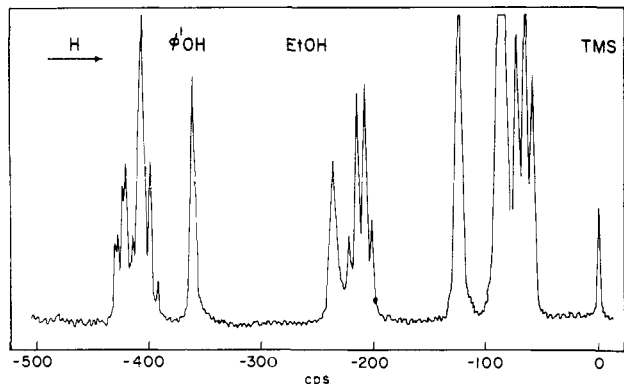(12) E. D. Becker, U. Liddel, and J. N. Shoolery, J. Mol. Spectry., **2**, 1 (1958).

Fig. 2.—The proton magnetic resonance spectrum of an equi-molecular mixture of 2-methyl-6-t-butylphenol and ethanol, observed at room temperature with a 60 Mc./sec. spectrometer.
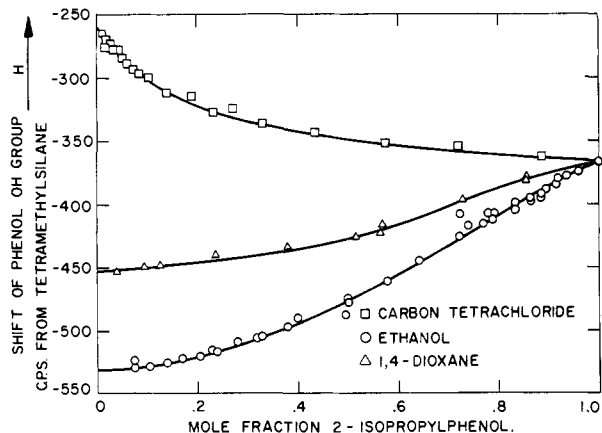

Fig. 3.—The proton shift of the phenolic –OH in 2-isopropyl-phenol, upon dilution,[13] observed at room temperature with a 60 Mc./sec. spectrometer.
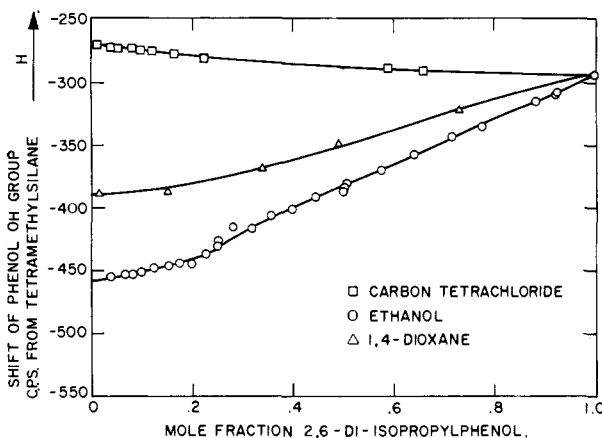

Fig. 4.—The proton shift of the phenolic –OH in 2,6-diiso-propylphenol, upon dilution,[13] observed at room temperature with a 60 Mc./sec. spectrometer.

ture attained in these experiments (ca. 180°). However, some of the samples, which were heated to approximately 230° in order to test the strength of the sample tubes, did exhibit coalesced lines.

Phenolic –OH Shifts upon Dilution.—The chemical shifts at room temperature of the phenolic –OH proton in 2-isopropylphenol, 2,6-diisopropylphenol, 2-t-butylphenol, 2-methyl-6-t-butylphenol, and 2,6-di-t-butylphenol are shown in Fig. 3–7, respectively, as a function of their concentration in carbon tetrachloride, ethanol, and dioxane. Upon dilution of the phenols with carbon tetrachloride, all of the –OH proton shifts are either upfield or negligible. An opposite
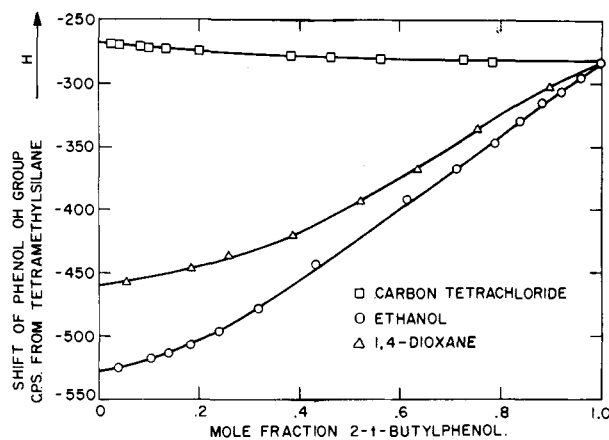

Fig. 5.—The proton shift of the phenolic –OH in 2-t-butyl-phenol, upon dilution,[13] observed at room temperature with a 60 Mc./sec. spectrometer.
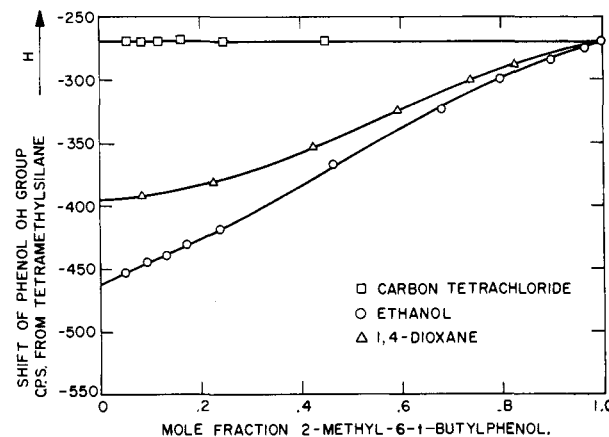

Fig. 6.—The proton shift of the phenolic –OH in 2-methyl-6-t-butylphenol, upon dilution,[13] observed at room temperature with a 60 Mc./sec. spectrometer.
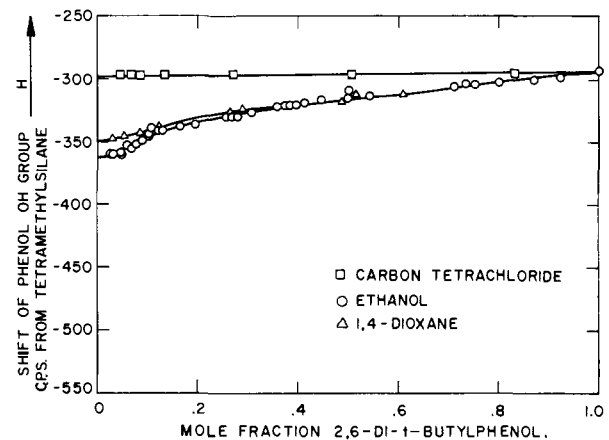
Fig. 7.—The proton shift of the phenolic –OH in 2,6-di-t-butylphenol, upon dilution,[13] observed at room temperature with a 60 Mc./sec. spectrometer.

effect is observed upon dilution with ethanol or with 1,4-dioxane; then the phenolic –OH exhibits a down-field shift. The largest difference between the line position in the pure phenol and that in an infinitely dilute solution of the phenol, in either ethanol or 1,4-dioxane, occurs in the case of 2-t-butylphenol, the smallest in the case of 2,6-di-t-butylphenol. Furthermore, the shifts in ethanol solution are significantly greater than those in 1,4-dioxane solution.[13]

(13) In Fig. 3–7, the concentration units for the carbon tetrachloride and the ethanol solutions are ordinary mole fractions. However, dioxane has

Dilution shifts of the phenolic –OH proton have been investigated by Batdorf,[14] by Gränacher and Diehl,[15,16] by Huggins, Pimentel, and Shoolery,[17] and by Davis, Pitzer, and Rao.[18] Gränacher[16] distinguishes three groups of solvents. A solvent of the first group is a good proton acceptor which forms stronger hydrogen bonds with phenol than with itself, thereby leading to significant, phenolic –OH downfield shifts. Examples are dioxane, ethyl ether, ethyl acetate, and to a lesser degree, acetone.[14,15] Solvents of the second group do not form hydrogen bonds and the phenolic –OH proton line is shifted very little upon initial dilution with these solvents. As dilution is continued, a pronounced upfield shift is observed owing to the decrease in the interphenolic hydrogen bonding. Solvents of this type are cyclohexane, carbon tetrachloride, and carbon disulfide. The solvents of the third group are chiefly aromatic compounds or others with whose π-electrons the phenol –OH proton can form a hydrogen bond. The π-electron ring currents produce upfield shifts in such cases.

Pure phenols with o-substituents forming at most weak intramolecular hydrogen bonds with the –OH group, $e.g.$, o-cresol and o-bromophenol,[19] exhibit large upfield shifts relative to unsubstituted phenol.[14] However, the –OH resonances undergo much larger downfield shifts upon dilution with acetone than does that of phenol. This behavior has been attributed to steric hindrance of hydrogen bonding in the substituted phenol, relative to phenol itself. Such hindrance should have less effect on the strength of the hydrogen bond formed between a phenol and the small acetone molecule than upon that formed with another phenol molecule. Our results are in general agreement with this conception, in that the –OH group resonances of the five hindered phenols studied are shifted upfield very extensively from that of phenol itself. Detailed analysis of the dilution shifts gives association constants which are qualitatively in keeping with the size, shape, and number of o-substituents.

Equilibrium Constants for Dimer Formation.— The dilution shifts for the carbon tetrachloride solutions are the easiest to analyze, as they should result very largely, if not entirely, from changes in the hydrogen bonding among the phenol molecules themselves. Furthermore, as noted previously, it is unlikely that association of the hindered phenols extends beyond dimer formation. With these assumptions, the equilibrium constant for dimer formation can be estimated from the limiting slope of the dilution shift and the total dilution shift,[17] $\Delta\nu = \nu_d - \nu_m$, where the subscripts d and m refer to dimer and monomer, respectively. For an open dimer, only one of the two –OH protons in it is involved directly in hydrogen bonding, although there is very likely an indirect effect upon the shift of the other. In such a system, with exchange averaging of the various shifts, ν_d is the average shift of the dimer protons and the observed frequency ν of the –OH protons is given by

$$\nu = \nu_d - (m/x)\Delta\nu \qquad (1)$$

where m is the number of moles of phenol monomer at equilibrium, and x is the total moles of phenol in all forms. Introduction into eq. 1 of the equilibrium constant $K = X_d/X_m^2$ in terms of the mole fractions X, and differentiation, leads us to

$$(d\nu/dX_p)_{x=0} = 2K\Delta\nu \qquad (2)$$

The quantity $(d\nu/dX_p)_{x=0}$ is the limiting rate of change, at infinite dilution, of the –OH proton shift with phenol mole fraction. Values for it are obtained readily from the curves plotted in Fig. 3, 4, and 5 and are listed in Table I. However, these values and eq. 2 give us only the product $K\Delta\nu$ and an independent value of $\Delta\nu$ is needed for the evaluation of K. As a first approximation we can assume complete dimerization of the pure phenol, which gives

$$\Delta\nu \cong \Delta\nu_p \equiv \nu_1 - \nu_0 \qquad (3)$$

where ν_1 and ν_0 are for pure and infinitely dilute phenol, respectively. The K's obtained in this way from the data in Table I show that corrections should be applied for the incomplete dimerization of the pure phenol.

TABLE I

DILUTION SHIFTS[a] AND DIMERIZATION CONSTANTS FOR HINDERED PHENOLS IN CARBON TETRACHLORIDE AT ROOM TEMPERATURE

Phenol	$(d\nu/dX)_0$	ν_0	ν_1	$\Delta\nu_p$	$\Delta\nu$	K
2-Isopropyl-	-568	-259	-366	-107	-135	1.7
2,6-Diisopropyl-	-92	-270	-294	-24	-36	1.3
2-t-Butyl-	-47	-269	-284	-15	-24	1.0
2-Methyl-6-t-butyl-	~ 0	-270	-270	~ 0	...	≤ 0.05
2,6-Di-t-butyl-	4	-298	-294	4	...	≤ 0.05

[a] The (negative) –OH proton shifts ν are in c.p.s. downfield from the internal reference TMS at 60 Mc./sec.

Successive approximations[1] lead to the values of K and $\Delta\nu$ given in Table I for 2-isopropylphenol, 2,6-diisopropylphenol, and 2-t-butylphenol. For the latter two compounds, dilution shifts calculated with these values of K and $\Delta\nu$ fit the observed concentration dependence in Fig. 4 and 5 within the experimental error, but for 2-isopropylphenol, the model is somewhat in error as the same computation predicts greater downfield shifts than are observed. This compound has the largest K, and the implication is that the deviations result from polymer formation. For 2-methyl-6-t-butylphenol and 2,6-di-t-butylphenol, the dilution shifts are too small to serve as a basis for estimating accurate values of K and $\Delta\nu$; in fact, the 4 c.p.s. dilution shift for 2,6-di-t-butylphenol is downfield rather than upfield, which indicates the presence of some shift-producing factor other than hydrogen bonding. Still, for these two compounds, an upper bound of 0.05 is set for K from the absence of any appreciable dilution shifts.

The equilibrium constants for dimerization obtained in this study are summarized in Table II along with

TABLE II

EQUILIBRIUM CONSTANTS FOR DIMER FORMATION FOR SEVERAL PHENOLS AT ROOM TEMPERATURE

Phenol	K	Phenol	K
p-Chloro-[a]	$9 + 4$	2,6-Diisopropyl-[b]	1.3 ± 0.5
m-Chloro-[a]	9 ± 4	2-t-Butyl-[b]	1.0 ± 0.5
o-Cresol[a]	8 ± 4	2,4-Di-t-butyl-[c]	0.96
Unsubstituted[a]	13 ± 7	2-Methyl-6-t-butyl-[b]	$\leq .05$
2-Isopropyl-[b]	1.7 ± 0.5	2,6-Di-t-butyl-[b]	$\leq .05$
2-t-Butyl-4-methyl-[c]	1.37	2-Chloro-[d]	$.02$

[a] Reference 17. [b] This research; the errors given are estimates. [c] Reference 6. [d] Reference 19; this is the equilibrium constant for $intra$molecular hydrogen bonding in a dilute solution of the phenol in CS_2.

two hydrogen bonding sites rather than one so it seems more appropriate to use a "site fraction" for the dioxane solutions. These are defined as $X_d' = 2n_d/(n_p + 2n_d)$ and $X_p' = n_p/(n_p + 2n_d)$, where subscripts d and p represent dioxane and phenol, and n is the number of moles.

(14) R. L. Batdorf, Ph.D. Thesis, University of Minnesota, 1955; quoted by J. A. Pople, W. G. Schneider, and H. J. Bernstein, ref. 8, p. 412.

(15) I. Gränacher and P. Diehl, $Arch.$ $Sci.$, **12**, Fasc. Special, Colloque Ampere, 238 (1959).

(16) I. Gränacher, $Helv.$ $Phys.$ $Acta$, **31**, 734 (1958).

(17) C. M. Huggins, G. C. Pimentel, and J. N. Shoolery, $J.$ $Phys.$ $Chem.$, **60**, 1311 (1956).

(18) J. C. Davis, K. S. Pitzer, and C. N. R. Rao, $ibid.$, **64**, 1744 (1960).

(19) E. A. Allan and L. W. Reeves, $ibid.$, **66**, 613 (1962).

results published on related systems for comparison. As expected, the association constants of the hindered phenols are significantly smaller than for the other phenols, the difference being about an order of magnitude for the monohindered phenols. And, of course, the dihindered phenols are associated even less, the decrease in K ranging from a factor of about $^1/_2$ for the isopropyl phenols to $^1/_{10}$ for the t-butyl. It is of interest that 2,6-diisopropylphenol has a larger K than the monohindered t-butylphenol, which agrees with our observation from molecular models that there is relatively little hindrance of the $-OH$ group in the 2-isopropylphenol. The most hindered phenols are the 2-methyl-6-t-butyl- and the 2,6-di-t-butyl-, for which the association constants are comparable with or less than the value of 0.02 found by Allan and Reeves[19] in their careful n.m.r. study of the weak *intra*molecular hydrogen bonding in 2-chlorophenol.

Hydrogen Bonding of Hindered Phenols with Dioxane and with Ethanol.—Ethanol and 1,4-dioxane are good proton acceptors and because of their small size should be capable of forming strong hydrogen bonds with hindered phenolic $-OH$ protons, even though the interphenol hydrogen bonding is relatively weak. In accord with this are the downfield, phenolic $-OH$ shifts, given in Fig. 3–7, found upon dilution of the hindered phenols with ethanol and dioxane and summarized in Table III. For ethanol, further evidence as to the nature of the bonding is given by the ethanolic $-OH$ shifts in the same solutions. These shifts, for solutions in the five hindered phenols, are shown in Fig. 8 except for solutions with a mole fraction of 2-isopropylphenol greater than 0.5, where the ethanolic $-OH$ line is obscured by the isopropyl C–H multiplet. In all cases, the dilution shift of the ethanolic $-OH$ is strongly upfield, indicating a decrease in the extent of hydrogen bonding. In fact, for all but the more dilute ethanol solutions, these upfield shifts are larger upon dilution with the phenols than with nonhydrogen bonding solvents such as carbon tetrachloride.[20] However, the limiting shifts at infinite dilution of the ethanol $-OH$ protons in solutions of the hindered phenols are all about -130 c.p.s., as summarized in Table III. Upon comparing this with the ethanolic $-OH$ limiting shifts of about -30 c.p.s. in nonhydrogen-bonding solvents,[20] we conclude that the ethanolic $-OH$ groups are in materially different limiting states in the two cases.
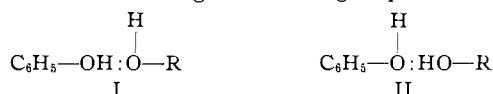
TABLE III

DIFFERENCES IN THE $-OH$ DILUTION SHIFTS[a] FOR SOLUTIONS OF HINDERED PHENOLS IN 1,4-DIOXANE AND IN ETHANOL AT ROOM TEMPERATURE

Phenol	Phenolic $-OH$ $\Delta\nu$ (diox.)[b]	K_c	Ethanolic $-OH$ $\Delta\nu$ (EtOH)[b]	ν_0	$\Delta\nu$ (C_6H_5OH)[b]
2-Isopropyl-	-195	14	-273	...	..
2,6-Diisopropyl-	-120	7.1	-188	-142	-99
2-t-Butyl-	-191	6.7	-259	-114	-71
2-Methyl-6-t-butyl-	-125	5.6	-192	-142	-99
2,6-Di-t-butyl-	-52	≤ 0.7	-65	-133	-90

[a] The (negative) $-OH$ proton shifts ν_0, at infinite dilution, are in c.p.s. downfield from the internal reference TMS at 60 Mc./sec. [b] The quantity $\Delta\nu$(S) is defined as ν_0(S) $- \nu_0$(CCl₄), where ν_0(S) is the proton shift of the $-OH$ group in question at infinite dilution in the solvent S. The ν_0(CCl₄) values for the phenolic $-OH$ shifts are given in Table I.

(20) See ref. 12. In addition, we checked the ethanolic $-OH$ shifts in carbon tetrachloride at several concentrations and also in t-butylbenzene. The upfield dilution shifts in the latter are somewhat larger than those in carbon tetrachloride over the entire concentration range, probably because of ring current effects from the aromatic ring. Similar effects upon the ethanolic $-OH$ shift would be expected in the phenol solutions, and, therefore, the $\Delta\nu$(C_6H_5OH) values in Table III should be reduced in magnitude by about 30 c.p.s.

The simplest interpretation of this result is that the phenol–ethanol complex involves bonding of the phenolic $-OH$ proton to the oxygen atom of an ethanol molecule. The upfield shift of the ethanolic $-OH$ line which occurs initially upon dilution with a hindered phenol is attributed to the breaking of the intermolecular ethanol–ethanol hydrogen bonds. This shift is compensated somewhat, upon further dilution, by the formation of phenol–ethanol complex so that the limiting, ethanolic $-OH$ shift is approximately 100 c.p.s. downfield from that found upon dilution with carbon tetrachloride. In support of this model, the curves shown in Fig. 3–7 for the concentration dependence of the phenolic $-OH$ shift in the 1,4-dioxane solutions are very similar to those in the ethanol solutions, and in the dioxane solutions the phenol $-OH$ must be bonded to an oxygen atom in the solvent. It is to be expected that size and shape effects should alter the relative stabilities of the two different complexes, I and II, formed by hydrogen bonding between two different molecules, each having an $-OH$ group. Our results

$$\underset{\text{I}}{\overset{\overset{\displaystyle H}{\overset{\displaystyle |}{}}}{C_6H_5-OH:O-R}} \qquad \underset{\text{II}}{\overset{\overset{\displaystyle H}{\overset{\displaystyle |}{}}}{C_6H_5-O:HO-R}}$$

indicate circumstances under which the relative stabilities differ appreciably and the usual assumption of equal stability may lead to erroneous conclusions.

The phenolic $-OH$ shifts in the dioxane solutions are smaller than those in the ethanol solutions by a quite uniform factor of about $^2/_3$, indicating that the hydrogen bonding is systematically weaker with dioxane[18] than with ethanol. The hydrogen bond shift, $\Delta\nu$(S), which we define as the difference ν_0(S) $- \nu_0$(CCl₄) between the infinite dilution shift ν_0 in the solvent S and that in the inert solvent carbon tetrachloride, is given in Table III for the dioxane and ethanol solutions. It has been suggested that these shifts can be correlated qualitatively with the relative hydrogen bond strengths of the complexes.[8,21] If this is so, then it appears that the hydrogen bonds in the bimolecular complexes of dioxane with 2-isopropylphenol and with 2-t-butylphenol are the strongest and of approximately the same strength. Next come 2,6-diisopropylphenol and 2-methyl-6-t-butylphenol, followed by the most severely hindered phenol, 2,6-di-t-butylphenol, which forms only very weak hydrogen bonds. The larger, phenolic $-OH$ hydrogen bond shifts in ethanol solution increase in the same order as do those in dioxane solution. However, in the ethanol solutions, the phenolic $-OH$ is probably not characteristic of a one-to-one phenol–ethanol complex. This complex with the structure I is capable certainly of association with other ethanol molecules, and such association may be an important cause of the larger phenolic $-OH$ shifts in ethanol compared with those in dioxane.

It is of interest to compare the dimerization constants in Table II for the hindered phenols with their hydrogen bond shifts in Table III. The main differences are for the 2-t-butyl- and the 2-methyl-6-t-butylphenols, which dimerize relatively less readily than they associate with dioxane or ethanol. Such differences are quite plausible in that the steric hindrance of dimer formation will differ from that of association of the phenol with the relatively small dioxane or ethanol molecules. A similar difference between the access to the $-OH$ group of a hindered phenol afforded an ethanol molecule and that afforded another phenol molecule has been observed by Coggeshall and Lang[5] in connection with their investigations of the ultraviolet spectra of several hindered phenols in ethanol solution.

(21) G. Korinek and W. G. Schneider, *Can. J. Chem.*, **35**, 1157 (1957).

Neither the dioxane molecule nor the ethanol molecule has ready access to the –OH group of 2,6-di-*t*-butylphenol, and the hydrogen bond shifts for this phenol are quite small in both dioxane and ethanol solutions. In this type of association, the 2,6-di-isopropylphenol and the 2-methyl-6-*t*-butylphenol molecules allow essentially equal access to the –OH group, which is considerably greater than that for the di-*t*-butylphenol. The monoalkylphenols, 2-isopropylphenol and 2-*t*-butylphenol, which exhibit relatively the same hydrogen bond shifts in dioxane or in ethanol solution, allow considerably freer access to the –OH group than do the other three phenol molecules. The dioxane molecule is considerably bulkier than the ethanol molecule, which no doubt is a major cause of the systematic differences between the phenolic –OH shifts in their solutions.

Phenol–Solvent Association Constants.—In principle, equilibrium constants for the solute–solvent association can be obtained readily from the dilution shifts if only simple 1:1 complexes are involved. For dilute solutions of a phenol in a proton-accepting solvent, this equilibrium may be written as

$$C_6H_5OH + :X \underset{\longleftarrow}{\overset{\longrightarrow}{\rightleftharpoons}} C_6H_5OH:X \qquad (4)$$
$$\quad m \qquad a \qquad\qquad c$$
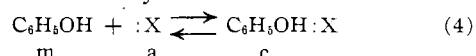
where m, a, and c refer to the monomeric phenol, the uncomplexed acceptor, and the hydrogen-bonded complex. In terms of mole fractions, the equilibrium constant for the association may be written as

$$K_c = X_c/X_m X_a \qquad (5)$$

and the shift ν of the phenolic –OH proton as[10]

$$\nu = (X_m/X_p)\nu_m + (X_c/X_p)\nu_c = \nu_m + (X_c/X_p)\Delta\nu \qquad (6)$$

where $X_p = X_m + X_c$ is the mole fraction of phenol in both forms; ν_m and ν_c are the phenolic –OH shifts in the monomer and complex, respectively; and $\Delta\nu = \nu_c - \nu_m$. Upon eliminating X_c from eq. 6 by introducing the definition of K_c, and rearranging the result, we obtain

$$1/(\nu - \nu_m) = (1/\Delta\nu) + (1/K_c\Delta\nu X_a) \qquad (7)$$

However, $X_a = 1 - X_p - X_c$ and for small X_p virtually all of the phenol exists as complex, so $X_c \cong X_p$. Thus, the final result is the following limiting expression for $X_p \rightarrow 0$

$$1/(\nu - \nu_m) = (1/\Delta\nu) + 1/K_c\Delta\nu(1 - 2X_p) \qquad (8)$$

The –OH shift ν_m for the monomeric phenol is at least approximately that found at infinite dilution in carbon tetrachloride solution (ν_0 in Table I). Therefore, by taking the experimental values of ν and X_p, and plotting $1/(\nu - \nu_m)$ vs. $1/(1 - 2X_p)$, one can evaluate K_c and $\Delta\nu$ from the intercept and slope at $X_p = 0$ of the resultant curve. An internal consistency check and/or iterative calculation can be made by comparing the value obtained for $\Delta\nu$ via eq. 8 with that employed in constructing the curve. *i.e.*, $\nu(X_p \rightarrow 0) - \nu_m$.
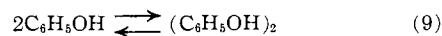
Application of this analysis to the data for the dioxane solutions gave the association constants listed in Table III. Comparison of these K_c's with the dimerization constants K in Table I reveals that they fall in the same sequence but that the former are about tenfold larger. The K_c's parallel the dilution shifts $\Delta\nu$-(diox.) reasonably well except that $K_c \cong 6.7$ for 2-*t*-butylphenol, which is about the same as the values for 2,6-diisopropyl- and 2-methyl-6-*t*-butylphenol, even though the dilution shifts for the latter are a good bit smaller. In the case of 2,6-di-*t*-butylphenol, very inconsistent $\Delta\nu$'s were obtained, probably because the data, shown in Fig. 7, do not extend to low enough phenol concentrations to give a very good limiting slope. For the other solutions, the $\Delta\nu$'s calculated

via eq. 8 are within 0 to 15 c.p.s. of the $\Delta\nu$(diox.) value assumed initially. At high phenol concentrations, the dimerization of the phenol competes with the phenol–solvent association. Indeed, the concentration dependence observed for the phenolic –OH shifts can be fitted reasonably well in terms of equilibrium constants K_c and K for the two reactions. However, there are too many adjustable parameters for a detailed analysis of this kind to be very meaningful here, especially as the measurements are not sufficiently accurate for the purpose nor do they extend to dilute enough solutions.
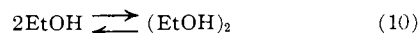
The phenol–ethanol solutions differ from the phenol–dioxane in that the solvent is itself strongly hydrogen bonded. Furthermore, as remarked in the preceding section, at low phenol concentrations the phenol molecules probably are hydrogen bonded to more than one ethanol molecule. Thus, it is not unexpected that the application of eq. 8 to the phenolic –OH dilution shifts in ethanol leads to generally unsatisfactory results. Similar problems arise in connection with the ethanolic –OH dilution shifts given in Fig. 8.

Dilution Shifts of 1:1 Phenol–Ethanol in Carbon Tetrachloride.—Some further, qualitative evidence concerning the nature of the hydrogen bonding in the phenol–ethanol complex is obtained from the –OH dilution shifts of an equimolar phenol–ethanol mixture. Such data are given in Fig. 9 for both the ethanolic and phenolic –OH resonances in 1:1 mixtures of ethanol with 2,6-di-*t*-butylphenol and with 2-isopropylphenol, diluted with carbon tetrachloride. At infinite dilution of the mixtures, the shift of the ethanolic –OH proton approaches that for solutions of ethanol alone in carbon tetrachloride. The infinite-dilution shift of the phenolic –OH proton in the mixture of 2,6-di-*t*-butylphenol with ethanol also approaches the limiting shift for an infinitely dilute solution of 2,6-di-*t*-butylphenol alone in carbon tetrachloride. On the other hand, the shift of the phenolic –OH proton in the mixture of 2-isopropylphenol with ethanol does not seem to approach that for infinite dilution of the phenol itself in carbon tetrachloride; instead the limit appears shifted downfield by about 100 c.p.s. No doubt this difference results in part from the fact that the phenolic –OH shifts are not available to low enough dilution. Also, it indicates that the phenol–ethanol complex is more stable than the phenol dimer.
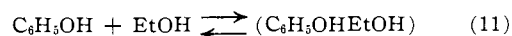
In the C_6H_5OH–CCl_4 and $EtOH$–CCl_4 systems, the –OH dilution shifts are governed by the dimerization equilibria

$$2C_6H_5OH \underset{\longleftarrow}{\overset{\longrightarrow}{\rightleftharpoons}} (C_6H_5OH)_2 \qquad (9)$$

and

$$2EtOH \underset{\longleftarrow}{\overset{\longrightarrow}{\rightleftharpoons}} (EtOH)_2 \qquad (10)$$

However, for the 1:1 C_6H_5OH–$EtOH$ in CCl_4 system, there is also the competing association reaction

$$C_6H_5OH + EtOH \underset{\longleftarrow}{\overset{\longrightarrow}{\rightleftharpoons}} (C_6H_5OHEtOH) \qquad (11)$$

Expressions similar to eq. 1–3 can be obtained relating the chemical shifts and their concentration dependences in the 1:1 equimolecular system to the K's for reactions 9–11. The data do not warrant a quantitative analysis, but, qualitatively, the apparent downfield displacement of the 2-isopropylphenol –OH shift, at infinite dilution of the 1:1 mixture, while the ethanolic –OH is relatively unaffected, requires that the phenol–ethanol complex be more stable than the phenol dimer and about as stable as the ethanol dimer. On the other hand, the data in Fig. 9 for the 2,6-di-*t*-butylphenol–ethanol system indicate at most a very weak phenol–ethanol complex.

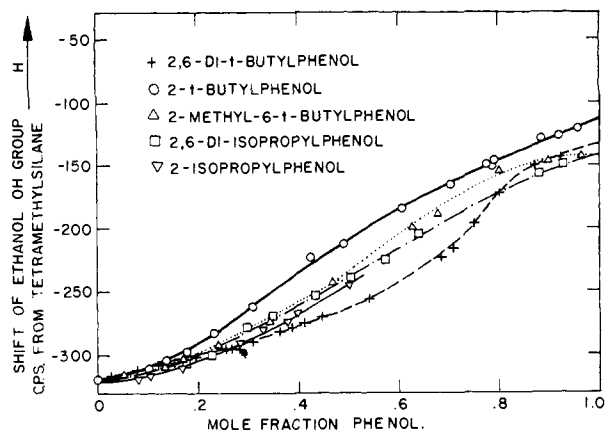Similar conclusions can be reached by comparing dilution shifts for the phenol–CCl_4, ethanol–CCl_4, and

Fig. 8.—The proton shift of the ethanolic –OH upon dilution in solutions of the hindered phenols, observed at room temperature with a 60 Mc./sec. spectrometer.

Fig. 9.—The proton shifts of the ethanolic and phenolic –OH upon dilution of 1:1 hindered phenol–ethanol mixtures in carbon tetrachloride, observed at room temperature with a 60 Mc./sec. spectrometer.

phenol–ethanol systems. However, for the latter the results are complicated by polymer formation, the effects of which are reduced in our experiments where the 1:1 mixture is diluted with an inert solvent. Indeed this approach has general utility in determining the relative stabilities of complexes by n.m.r. experiments.

Temperature Dependence of –OH Shifts in 1:1 Phenol-Ethanol Mixtures.—In the temperature range 25° up to 190° the lines of both the ethanolic and phenolic –OH protons in equimolecular mixtures of the several hindered phenols with ethanol exhibit upfield shifts with increasing temperature. These shifts are approximately linear functions of the temperature with the exception that the phenolic –OH shift in 2,6-di-*t*-butylphenol starts leveling off at temperatures greater than 100° and approaches a limiting value at 150°. This limiting value is the same within experimental error as the infinite-dilution shift of the phenol alone in carbon tetrachloride, –298 c.p.s., which is presumably characteristic of the monomer. The rates of change with temperature of the proton shifts of both –OH groups in each of the phenol–ethanol systems are given in Table IV, together with the temperature range over which they were measured. The upper limit of this range is not fixed by the limitations of the apparatus except in the case of 2,6-di-*t*-butylphenol. In all the other cases the lines were broadened and weak or were lost under the alkyl group signals before the instrumental limit of approximately 185° was reached.

TABLE IV

TEMPERATURE DEPENDENCE[a] OF THE PHENOLIC AND ETHANOLIC –OH SHIFTS IN EQUIMOLECULAR PHENOL-ETHANOL MIXTURES

	Phenolic –OH		Ethanolic –OH	
Phenol	C.p.s./deg.	Max. T, °C.	C.p.s./deg.	Max. T, °C.
2-Isopropyl-	0.86	94	0.69	94
2,6-Diisopropyl-	.68	130	0.82	110
2-*t*-Butyl-	.67	125	1.06	125
2-Methyl-6-*t*-butyl-	.70	128	0.68	93
2,6-Di-*t*-butyl-	.14[b]	192	1.38	154

[a] The measurements extended from 25° to the maximum temperature given. [b] This coefficient is not constant above 100°.

The measurements at higher temperatures are subject to considerable error not only because the temperature is difficult to measure accurately, but also because the small amount of oxygen present even in thoroughly de-gassed solutions causes oxidation of the ethanol at higher temperatures. The small amount of acid produced accelerates the proton exchange process and leads to broadened –OH proton lines. Some
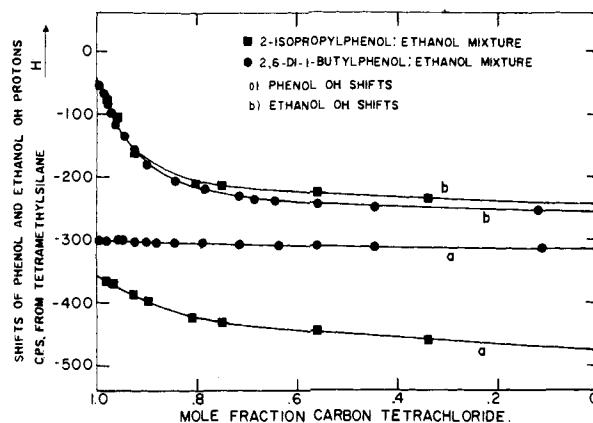
samples which had been heated above 230° in order to test the strength of the glass sample tubes, subsequently contained sufficient acid to cause coalescence of the separate ethanolic and phenolic –OH proton lines to a single line at room temperature whose position was the mean of those of the individual lines observed in a sample which had not previously been heated.

The temperature dependences observed depend upon ΔH for the association and complex formation and also upon the $\Delta \nu$'s involved. We have noted that for the phenolic –OH's there is a correlation between the $\Delta \nu$'s and the equilibrium constants. In accord with this are the temperature dependences of the phenolic –OH shifts, summarized in Table IV, which parallel the dimerization constants in Table II and the constants K_c in Table III for phenol–ethanol complex formation. Thus, the temperature dependence is largest for the 2-isopropylphenol and smallest, by a 6-fold factor, for 2,6-di-*t*-butylphenol.

For the ethanolic –OH, the temperature dependences in the 1:1 mixtures are in reverse order to those for the phenolic –OH. At first, this may seem anomalous. However, it is a natural consequence of the competing reactions 9–11. In the 2,6-di-*t*-butylphenol system where the phenol molecules are essentially inert, the ethanolic –OH temperature dependence results from the thermal dissociation of ethanol dimers (and polymers) per reaction 10, but in the 2-isopropylphenol system the phenol–ethanol complex is present in high concentration. Moreover, in this complex the ethanolic –OH shift is less than in the ethanol dimer (and polymer) because of the asymmetric nature of the hydrogen bonding in form I of the complex. Thus, the effect upon the ethanolic –OH shift of thermal dissociation of the complex, reaction 11, is canceled in part by dimerization of the liberated ethanol, reaction 10.

Shift of the $>$C–H Proton in Isopropylphenols.— In the course of the experiments it was noted that there are appreciable shifts (up to nearly 30 c.p.s.) in the isopropyl C–H proton line depending upon the other substituents. These shifts were measured in the pure liquids at room temperature to be –172, –199, and –184 c.p.s., respectively, at 60 Mc./sec., for isopropylbenzene, 2-isopropylphenol, and 2,6-diisopropylphenol, the shifts being downfield with respect to the internal TMS reference. The fact that the shift in 2,6-diisopropylphenol is virtually the average of those for isopropylbenzene and 2-isopropylphenol indicates that more than a simple, direct substituent effect is involved.

A likely explanation is that the downfield shifts result from electrostatic interactions[9] between the –OH and –CH(CH$_3$)$_2$ groups, which also affect the average rotational conformation of the isopropyl group with respect to the plane of the benzene ring. Thus, the stable form of the 2-isopropylphenol probably is that in which the C–H of the isopropyl group is in the plane of the ring and *cis* to the phenol oxygen. In the 2,6-diisopropylphenol one of the isopropyl groups could have this configuration, but the other would be rotated so that the C–H was *trans* to the oxygen. The latter

C–H has an environment similar to that in the two equivalent rotational forms of isopropylbenzene, which accounts for the intermediate shift.[22]

(22) This model is similar to that proposed to explain the CF$_3$ shifts and the F–CF$_3$ coupling constants in substituted 2-fluorobenzotrifluorides; see H. S. Gutowsky and V. D. Mochel, *J. Chem. Phys.*, in press.

Infrared and Nuclear Magnetic Resonance Hydrogen-Bonding Study of Dioxane and Pyridine in Aqueous Mixtures

BY A. FRATIELLO[1] AND J. P. LUONGO

An infrared study of the spectral behavior of all components of dioxane–water and pyridine–water mixtures was carried out. The frequency location of absorption bands studied for these components all exhibited a concentration dependence. High frequency shifts were observed for the –OH stretching band upon dilution in either solvent, indicating a reduction of the hydrogen bonding present in pure water. The low frequency shift noted for the C–O stretching mode of dioxane in aqueous mixtures was attributed to the occurrence of hydrogen bonding at the oxygen sites. High frequency displacement observed for the C–H stretching modes in both dioxane and pyridine in their aqueous mixtures could not be unambiguously interpreted. An attempt was made to correlate the infrared data with the results of nuclear magnetic resonance studies of these systems.

Introduction

Recent nuclear magnetic resonance studies[2] on dioxane–water and pyridine–water mixtures revealed a marked concentration dependence of the proton chemical shift of all the species involved. This indicated the presence of strong solvent interactions, interpreted as hydrogen bonding. Previous spectroscopic studies of these mixtures include infrared investigations of the water spectrum in dioxane[3,4a,b] and pyridine[4a,b] mixtures and extensive Raman investigation of the dioxane–water system.[5]

An infrared study of the spectral behavior of the organic components as well as the water in these mixtures was undertaken in an attempt to assign the interactions occurring to specific groups, particularly in the dioxane system for which the n.m.r. results could not unambiguously differentiate between interactions taking place at the dioxane oxygen or hydrogen sites.

Experimental

A Perkin-Elmer Model 421 grating spectrometer was used in this study. The abscissa scale was mechanically expanded 4× to increase the accuracy of the frequency determinations except when determining the position of the broad water –OH band, which was recorded at 1×. All solutions were studied in a 0.015-mm. CaF$_2$ cell.

Results

Dioxane.—The portion of the pure dioxane infrared spectrum which we investigated consists of three groups of absorptions: four bands which arise from the C–H stretching modes appear at ~2900 cm.$^{-1}$, four bands centered at ~1350 cm.$^{-1}$ result from C–H deformations, and three absorptions due to the C–O stretching in the 1100 cm.$^{-1}$ region.

Band position was determined as a function of concentration for all the absorptions mentioned above. For a series of solutions, ranging in concentration from 100 to

(1) Los Angeles State College, Los Angeles 32, Calif.
(2) A. Fratiello and D. C. Douglass, *J. Mol. Spectry.*, in press.
(3) W. Gordy, *J. Chem. Phys.*, **4**, 769 (1936).
(4) (a) E. Greinacher, W. Luttke, and R. Mecke, *Z. Elektrochem.*, **59**, 23 (1955); (b) J. Errera, R. Gaspart, and H. Sack, *J. Chem. Phys.*, **8**, 63 (1940).
(5) C. Fauconnier and M. Harrand, *Ann. Phys.*, Ser. *13*, **1**, 5 (1956).

12% dioxane in water, all the spectra were recorded on the same chart thereby permitting direct measurement of the absorption shifts. This is illustrated in Fig. 1a and 1b, wherein the band positions of the C–H and C–O stretching modes are shown for a 25% dioxane in water mixture and for 100% dioxane.

The band shifts measured in this way are listed in Table I and plotted in Fig. 2a, b, and c as a function of dioxane concentration. These shifts, designated by

TABLE I
DIOXANE FREQUENCY SHIFT DATA AT 25°

	C–O stretching, ν (cm.$^{-1}$)		
	1048	1083	1122
Dioxane, %	Δν	Δν	Δν
75	−2.9	−1.8	−0.6
50	−3.3	−1.8	−4.7
25	−3.3	−2.7	−5.8
12	−3.3	−3.0	−5.7

	C–H bending, ν (cm.$^{-1}$)			
	1253	1288	1365	1453
Dioxane, %	Δν	Δν	Δν	Δν
75	+0.7	+1.8	+1.9	+1.1
50	1.9	4.0	4.2	1.3
25	2.8	5.9	5.5	2.7
12	2.7	6.5	6.1	~2

	C–H stretching, ν (cm.$^{-1}$)			
	2853	2892	2915	2961
Dioxane, %	Δν	Δν	Δν	Δν
75	+6.3	+4.0	+4.0	+6
50	10	6.3	6.8	11
25	13	10	14	19
12	13	9	16	20

Δν, were obtained by subtracting the frequency location of the pure dioxane band from that of dioxane in an aqueous mixture. Thus, the high frequency shift is indicated by $\nu\uparrow$ and a low frequency shift by $\nu\downarrow$ in Fig. 2. Noticeable in Table I is the shift to lower frequency of the absorptions due to the C–O group upon dilution with water, whereas the bands arising from C–H stretching and bending shift to higher frequency.

Some of the observed shifts were very small, amounting to a few wave numbers, but in no case did the