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Hydrogen Bonding Studies. IX. The Thermodynamics of Hydrogen Bonding of Phenol to Ethers and Related Compounds¹

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RECEIVED MARCH 20, 1964

The enthalpy and free energy of interaction of phenol with eleven ethers, two sulfides, and one selenide have been determined by a near-infrared spectrophotometric method. Chain branching α to the oxygen atom increases the enthalpy of interaction, whereas aryl substitution decreases it. The cyclic ethers $(\text{CH}_2)_3\text{O}$, $(\text{CH}_2)_4\text{O}$, $(\text{CH}_2)_5\text{O}$, and 1,2-epoxyisobutane show about equal basicity toward phenol. The dialkyl sulfur and selenium compounds are much weaker bases toward phenol than analogous ethers. Implications of these findings are discussed.

The previous paper in this series¹ described a method for precise determination of the enthalpy of interaction of phenol with various hydrogen bond acceptors (bases) in carbon tetrachloride. In this method the absorbance of the first overtone of the free O-H stretching band of phenol, at 7220 cm^{-1} , is studied as a function of base concentration and temperature. This method has been used to determine the thermodynamics of interaction with phenol for a series of eleven ethers, and the compounds di-*n*-butyl sulfide, di-*t*-butyl sulfide, and di-*n*-butyl selenide. The results of this investigation are summarized in Table I.

TABLE I
THERMODYNAMICS OF INTERACTION OF PHENOL WITH BASES

	$-\Delta H$, kcal./mole	$p\Delta H$, ^a kcal./mole	$-\Delta F$, kcal./mole	$-\Delta S$, cal./deg. mole
Et_2O	5.41	0.06	1.29	13.8
<i>n</i> - Bu_2O	5.71	0.09	1.086	15.5
PhOEt	3.18	0.13	0.117	10.3
$(\text{PhCH}_2)_2\text{O}$	4.28	0.11	0.768	11.8
Ph_2O	2.06	0.17	-0.137	7.4
EIB ^b	5.26	0.13	1.214	13.6
$(\text{CH}_2)_3\text{O}$	5.16	0.06	1.634	11.8
$(\text{CH}_2)_4\text{O}$	5.29	0.08	1.651	12.2
$(\text{CH}_2)_5\text{O}$	5.19	0.08	1.155	13.5
EtO- <i>t</i> -Bu	6.52	0.06	1.400	17.2
<i>t</i> - Bu_2O	7.31	0.11	0.745	22.0
<i>t</i> - Bu_2S	4.87	0.20	0.041	12.2
<i>n</i> - Bu_2Se	3.69	0.33	0.423	14.9
<i>n</i> - Bu_2S	4.19	0.33	0.107	13.5

^a 90% confidence limits on precision calculated as in ref. 1. The value given is either the statistical or theoretical (calculated) limit, whichever is larger. ^b 1,2-Epoxyisobutane.

The phenol-diethyl ether data in Table I were published in the previous paper¹ and are included for comparison. The rest of the data in the table is new, except that preliminary data for the di-*n*-butyl chalcogenides appeared in a communication.² Most of the systems have not previously investigated thermodynamically, but the phenol-tetrahydropyran and phenol-tetrahydrofuran pairs have been studied by others with results which agree well with those in Table I.^{3,4}

Among the aliphatic ethers, the enthalpy of interaction with phenol increases from diethyl ether to ethyl *t*-butyl ether to di-*t*-butyl ether. The increasing base strength with chain branching α to the oxygen

atom was inferred from earlier measurements of the frequency shift of the phenol O-H bond upon hydrogen bonding⁵ and is in agreement with the well-known positive inductive effect of alkyl groups.⁶ The high base strength of di-*t*-butyl ether indicates a relatively low steric requirement for hydrogen bonding to phenol, for the same ether is nonbasic toward more hindered reagents such as N_2O_4 .⁷ That steric hindrance is a factor in the hydrogen bonding of phenol to di-*t*-butyl ether is indicated by the very large entropy and low free energy of hydrogen bonding found for this compound. A roughly linear relationship between ΔH and ΔF is expected in the absence of steric effects. Similar but small indications of steric hindrance to hydrogen bonding are provided by the data for ethyl *t*-butyl ether and di-*n*-butyl ether.

The enthalpies of interaction with phenol for the cyclic ethers $(\text{CH}_2)_3\text{O}$, $(\text{CH}_2)_4\text{O}$, and $(\text{CH}_2)_5\text{O}$ are approximately equal (within experimental error limits) and are close to the value obtained for diethyl ether. The unsubstituted three-membered ring ether could not be studied because of its volatility. In its place the compound 1,2-epoxyisobutane was investigated and found to have an enthalpy of interaction in the same range as the four- to six-membered ring ethers. Allowing for the effect of alkyl substitution, it seems likely that the intrinsic basicity toward phenol of oxygen in the three-membered cyclic ether is somewhat reduced, compared to open-chain or larger ring ethers.

In studies of the enthalpy of the charge-transfer interaction of cyclic ethers with iodine, Brandon, Searles, and Tamres found the basicity order $(\text{CH}_2)_3\text{O} > (\text{CH}_2)_4\text{O} > (\text{CH}_2)_5\text{O} > \text{propylene oxide}$.⁷ A similar order of basicity was found in studies of the equilibrium constants for complex formation of cyclic ethers with dinitrogen tetroxide.⁸ These differences in basicity have been attributed to rehybridization in these compounds leading to differing amounts of *s*- and *p*-character in the lone-pair orbitals on oxygen.⁷

Our results confirm the lowered basicity of the three-membered ring compounds but suggest that the previously observed basicity order for the four-, five-, and six-membered ring ethers may have been the result of steric rather than electronic differences. Inspection of models shows that the lone pairs on oxygen become progressively less available as the ring size is increased

(5) R. West, L. S. Whatley, and K. J. Lake, *J. Am. Chem. Soc.*, **83**, 761 (1961).

(6) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 70.

(1) Previous paper in this series: D. L. Powell and R. West, *Spectrochim. Acta*, **20**, 983 (1964).

(2) R. West, D. L. Powell, L. S. Whatley, M. K. T. Lee, and P. von R. Schleyer, *J. Am. Chem. Soc.*, **84**, 3221 (1962).

(3) H. Dunken and M. Fritzsche, *Z. Chem.*, **1**, 249 (1961).

(4) P. Pineau, Thesis, L'Universite de Bordeaux, 1961.

(7) M. Brandon, M. Tamres, and S. Searles, *J. Am. Chem. Soc.*, **82**, 2129 (1960).

(8) J. G. Whanger and H. H. Sisler, *ibid.*, **75**, 5188 (1953).

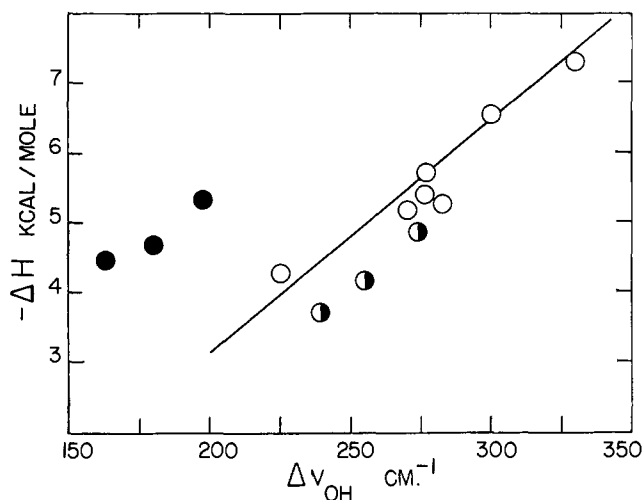


Fig. 1.—Enthalpy of hydrogen bonding with phenol vs. O-H frequency shift: O, ethers; ●, sulfur and selenium compounds; ●, carbonyl compounds; data from ref. 1.

from 4 to 5 to 6. The fact probably influences the base strength toward Lewis acids with high steric requirements such as I_2 and N_2O_4 , but is unimportant in interactions with an unhindered Lewis acid like phenol. The foregoing interpretation is strengthened by recent studies of n.m.r. spin coupling between C^{13} and protons in cyclic hydrocarbons, which indicate little difference in C-H orbital character *except* in cyclopropanes.⁹ Thus rehybridization in cyclic hydrocarbons seems to be slight, except in three-membered (or otherwise highly strained) rings.

Aryl substitution reduces the enthalpy of hydrogen bonding of ethers with phenol. Part of this reduction reflects the lowered basicity of an oxygen atom attached to an aryl group which exerts a weaker inductive effect than an alkyl group. However, the reduction in enthalpy probably also results from competitive hydrogen bonding to the very weakly basic π -electrons of the aromatic ring. Aryl-substituted ethers with phenol show two hydrogen-bonded O-H stretching bands in the infrared, indicating that hydrogen bonding does take place to both basic sites.⁵

Substitution of sulfur or selenium for oxygen greatly lowers the enthalpy of interaction with phenol. The observed basicity order, $O \gg S > Se$, is that expected for interaction of chalcogen compounds with "hard" Lewis acids such as proton donors.¹⁰ Chain branching is again important, and di-*t*-butyl sulfide is a stronger base than di-*n*-butyl sulfide.

A linear correlation between $-\Delta H$ and $\Delta\nu$, the frequency shift of the O-H stretching band for hydrogen-bonded systems, was originally proposed by Badger and Bauer.¹¹ The ethers show a fairly good linear correlation between $-\Delta H$ and $\Delta\nu$ for the phenol O-H band (Fig. 1), and the points for the sulfur and selenium compounds fall close to the line for ethers. However, significant deviations from the linear relationship are found for carbonyl compounds.² Apparently, the Badger-Bauer relationship does not hold perfectly when the hybridization of the oxygen atom hydrogen bonded to the proton is changed.¹²

(9) C. S. Foote, *Tetrahedron Letters*, 579 (1963).

(10) R. G. Pearson, *J. Am. Chem. Soc.*, **85**, 3533 (1963).

(11) R. M. Badger and S. M. Bauer, *J. Chem. Phys.*, **5**, 839 (1937); R. M. Badger, *ibid.*, **8**, 288 (1940).

Experimental

Procedure.—The spectra were all determined in carbon tetrachloride, using a Cary Model 14M spectrophotometer, a path length of 10 cm., and a slit width of 0.27 mm. The base and phenol concentrations were chosen on the basis of preliminary experiments so that after complex formation the concentration of free phenol would be about 0.01 to 0.02 *M*; for ethers, typical initial base concentrations were 0.2 *M*. Each solution was studied at seven or eight different temperatures spaced evenly over the interval from -5 to $+45^\circ$. A minimum of two (usually three) solutions were studied for each base.

The free phenol concentration was determined from the extinction coefficient of the free O-H first overtone band, found in previous studies to have the value $\epsilon = 3.4054 - 0.000434T$, where T is the absolute temperature. This concentration was used to determine the equilibrium constant for the reaction

$$K = \frac{(\text{phenol-base})}{(\text{free phenol})(\text{free base})}$$

Small corrections were made for the changes of density of the solutions with temperature and for the dimerization of phenol. Details of the method of calculation and of the manipulative technique are given in the previous paper.¹

Materials.—Mallinckrodt carbon tetrachloride from freshly opened bottles was used as the solvent; it was distilled from P_2O_5 into carefully dried receivers shortly before solutions were prepared. "Blank" spectra showed the amount of water present in the purified solvent to be negligible. Merck reagent grade phenol was twice fractionally crystallized and then vacuum distilled in a nitrogen atmosphere (b.p. 85.5–86.5, at 20 mm.) into a pressure equalized dropping funnel which was stored in a desiccator over P_2O_5 .

The purity of ethers and other bases was checked after purification by comparison of the boiling point and refractive index with literature values and also (for most compounds) by gas chromatography. Except where indicated, the bases were Eastman Kodak White Label materials. Di-*n*-butyl ether, ethyl *t*-butyl ether, trimethylene oxide (Aldrich), and 1,2-epoxyisobutane (K and K chemicals), after preliminary drying, were fractionally distilled from sodium. Tetrahydrofuran and tetrahydropyran were fractionally distilled from lithium aluminum hydride. In each case a heart cut with a narrow boiling range was taken for the hydrogen bonding studies. Diphenyl ether was fractionally crystallized and then distilled under vacuum. Phenyl ethyl ether and dibenzyl ether (Matheson Coleman and Bell) were fractionally distilled under vacuum. Di-*n*-butyl selenide was a sample kindly donated by Prof. P. von R. Schleyer; this compound and di-*n*-butyl sulfide were purified by fractional distillation. Di-*t*-butyl sulfide (Phillips Petroleum Co.) was fractionally distilled under vacuum.

Di-*t*-butyl Ether.—This compound was synthesized by the following improvement upon the method originally suggested by Erickson and Ashton.¹³ A suspension of 144 g. (0.52 mole) of freshly prepared silver carbonate in 400 ml. of ether was prepared and cooled to 0° under nitrogen while protecting the silver salt from direct light. Redistilled *t*-butyl chloride (93 g., 1.00 mole) was added dropwise from a separatory funnel to the stirred suspension while the reaction flask was maintained at 0° and shielded from light. After the addition, the flask was stirred for an additional 24 hr. in the dark at 0° during which time the suspended silver salts changed in color from pale yellow to brick-red. The solution was then filtered through a large sintered glass funnel, and the filtrate was distilled from sodium to yield 20 g. (31%) of product, b.p. 105° (747 mm.), lit. 106.5 – 107° (760 mm.).¹³

Success in this reaction depends upon shielding from light and air and also upon using carefully prepared silver carbonate. The silver carbonate was prepared as follows: A solution of 280 g. (1.65 mole) of silver nitrate in 500 ml. of water was prepared in a 5-l. flask, and deaerated by means of nitrogen passed into the solution through a fritted glass bubbler. The flask was enclosed in a cardboard "dark box" and cooled to 0° . A deaerated solution of 126 g. (1.50 moles) of sodium hydrogen carbonate in 2300 ml. of water was added dropwise through a tube extending

(12) The linear relationship is not expected to hold for major changes in the nature of the proton acceptor atom: cf. M. D. Joesten and R. S. Drago, *J. Am. Chem. Soc.*, **84**, 3817 (1962).

(13) J. L. E. Erickson and W. H. Ashton, *ibid.*, **63**, 1769 (1941).

through the dark box with continuous mechanical stirring and bubbling of nitrogen through the solution. The resulting pale yellow precipitate of silver carbonate was filtered with suction on a Büchner funnel and rapidly washed successively with 1.5 l. of cold water, 1 l. of ethanol, and 1 l. of diethyl ether, all under an atmosphere of nitrogen. The product was dried *in vacuo* over P_2O_5 in the dark; yield 208 g. (91%) of a light yellow powder with no dark inclusions.

Acknowledgments.—This work was supported by grants from the Petroleum Research Fund of the American Chemical Society and the Wisconsin Alumni Research Foundation. The authors also thank the Ordnance Materials Research Office for a grant for the purchase of equipment used in this research, and the Dow Chemical Company for a fellowship to D. L. P.

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Long-Range Effect of an Asymmetric Grouping on the Magnetic Equivalence of Methylene Group Protons

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RECEIVED FEBRUARY 14, 1964

Nuclear magnetic resonance spectra of seventeen *ortho*- or *meta*-substituted *N,N*-dimethylbenzylamines indicated a long-range effect of an asymmetric group in the *ortho* or *meta* side chain on the magnetic equivalence of the methylene group protons in the amine side chain. The protons were magnetically equivalent in the nine cases for which a plane of molecular symmetry existed and were nonequivalent for the eight cases for which there was no symmetry plane. A limited temperature range study of two amines and an *ortho*-substituted benzyl alcohol indicated some reduction in the observed chemical shift differences of the two methylene group protons, but at the highest temperatures investigated a chemical shift difference persisted. The possible importance of the observed long-range effect in structural studies is discussed briefly.

Introduction

In a recent publication, Snyder³ has given several examples and reviewed other cases in which an asymmetric atom or group affects magnetic nonequivalence in adjacent groups or atoms and has shown that the nonequivalence, as measured by the chemical shifts, is sensitive to the solvent used. Meyer, *et al.*,⁴ have reported nonequivalence of O-methylene protons in derivatives of 10-carbethoxy-1,1-dimethyldecahydro-naphthalene and postulated that steric interaction of the O-methylene group with the axial methyl group in the 1,1-dimethyl system gives rise to the observed magnetic nonequivalence. Gutowsky⁵ has given a general treatment for the analysis of such systems and Pople⁶ has discussed the type of spectrum that may appear for symmetrical and asymmetrical systems under various degrees of hindered rotation. In examining a number of substituted *N,N*-dimethylbenzylamines in this laboratory it was observed that magnetic nonequivalence of the benzylamine methylene protons, hereafter referred to as protons 1 and 2, was associated with the presence of an *ortho* or *meta* side chain bearing an asymmetric group. When the side chain had a plane of symmetry the 1,2-protons appeared equivalent. Since the chemical shift differences were small, only CCl_4 , $CHCl=CCl_2$, and $CDCl_3$ solutions were investigated. Several compounds were examined over a convenient temperature interval as this can give some indication of the relative importance of conformation *vs.* intrinsic asymmetry to the observed magnetic nonequivalence. The nonequivalence, as evidenced by chemical shift differences, was reduced but not eliminated at the highest temperatures investigated. An increase in the number of cases investigated and a

more extended temperature study are indicated before unambiguous conclusions can be drawn concerning the origin of the observed nonequivalence but, as many investigators may work with systems at room temperature which contain an asymmetric group, it was felt the long-range effects here reported will be of interest.

Results

The n.m.r. spectral data reported in Tables I and II and the examples reproduced in Fig. 1, 2, and 3 are referenced to tetramethylsilane as an internal standard. For subsequent reference protons 1,2 have been previously designated; protons 3 and 4 refer to protons on the α -carbon of the side chain attached to either the *ortho* or *meta* position of the *N,N*-dimethylbenzylamine; proton 5 is on the β -carbon of the side chain. In order to eliminate the possible effect of the nitrogen quadrupole, an *ortho*-substituted benzyl alcohol was examined over a temperature interval and data for this and for compounds XII and XIII are recorded in Table II. Data in Table I refer to 32° unless otherwise noted. In both Tables I and II the chemical shift is given to the nearest cycle per second as this properly indicates the precision of the measured values for the data taken on the Varian A-60 instrument. Coupling constants and differences in chemical shift for components of an AB or ABX system are expressed to the nearest 0.1 c.p.s. as this precision was necessary in the AB and ABX calculations by which the values of $\nu_{1,2}$, $\delta_{1,2}$, $J_{1,2}$, etc., were determined. The error in a single observation is undoubtedly several tenths of a cycle per second.

In Tables I and II and in Fig. 1, 2, 3, and 4 the numbered compounds, using A for the $-CH_2N(CH_3)_2$ group, B for the $-C(C_6H_5)_2OH$ group, and D for the $-CC_6H_5HOH$ group, are shown in Scheme I.

The symbols used in Tables I and II have the following meanings: $\nu_{1,2}$ are the chemical shifts of the 1,2-protons in the amine side chain—in case these are an AB system the two calculated values are shown,

(1) Tennessee Eastman Fellow, Duke University.

(2) National Defense Education Act Fellow, Duke University.

(3) E. I. Snyder, *J. Am. Chem. Soc.*, **85**, 2624 (1963).

(4) W. L. Meyer, A. S. Levinson, D. L. Davis, and V. L. Sawin, Abstracts, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963, p. 85Q.

(5) H. S. Gutowsky, *J. Chem. Phys.*, **37**, 2196 (1962).

(6) J. A. Pople, *Mol. Phys.*, **1**, 3 (1958).