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Hydrogen Bond Formation with Pyridines and Aliphatic Amines[1]

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The electron donor ability of a number of pyridine bases and aliphatic amines, as well as pyrrole, has been measured by both a calorimetric and a spectroscopic method. It was found that the abilities of the pyridines to form hydrogen bonds were related to their acidity constants by a linear equation, but this relationship did not seem applicable to the aliphatic bases. These results suggest that a quantitative relationship between hydrogen bonding ability and acidity constants of bases, such as the one proposed by Gordy and Stanford, is subject to some limitation. Steric hindrance and the effect of π-electrons in the pyridine ring appear to be among the factors causing discrepancies.

Introduction

Determinations of electron donor abilities in hydrogen bonding have been used as a qualitative measure of the relative basicities of molecules. It has been proposed by Gordy[3,4] that hydrogen bonding abilities and acidity constants of bases can be related quantitatively, a single equation being sufficient to represent a wide variety of electron donors. Because of the usefulness of such a relationship, it was thought of interest to determine the effect on the relationship of varying steric and electronic factors in two series of nitrogenous bases.

Two methods were employed in this study, one being the determination of the heat of mixing with chloroform, and the other being the determination of the frequency shift of the OD bond in the infrared spectrum of methanol-*d* solutions. The two methods served as independent checks of the results.

Experimental

Spectroscopic Method.—The infrared procedures followed were similar to those reported previously.[5,6] The position of the monomeric OD band in a 0.1 *M* solution of methanol-*d* in carbon tetrachloride was compared with the positions of the OD bands in 1.0 *M* solutions of methanol-*d* in the various nitrogen bases at 25°. A Perkin-Elmer model 12B spectrometer equipped with a rock salt prism was used for the majority of observations,[7] the OD absorption band being too broad in general for the higher resolution of a lithium fluoride prism to be of particular value.

The estimated probable accuracy in absorption band location is about ±5 cm.$^{-1}$, except for tri-*n*-butylamine, diethylamine and diisopropylamine where the asymmetry and breadth of the bands increased the error to ±10 cm.$^{-1}$. In determining the band centers, percentage transmission curves for the methanol-*d* were plotted manually from the recorded spectra of the solutions and of the solvent nitrogen compounds. The maximum difference was taken as the band position; but in cases where the band envelopes were unsymmetrical, the center was taken generally to be the frequency bisecting the area under the absorption band.

Calorimetric Method.—The apparatus and method employed for the heat of mixing determinations were essentially as described by Zellhoefer and Copley[8] with minor modifications. The hygroscopic nature, and in some cases the volatility, of the nitrogen bases necessitated sealing the sample in a thin-walled ampoule which was placed in a silver calorimeter containing a stoichiometric quantity (within 50 ± 0.2 mole % in all cases) of chloroform. Mixing was accomplished by crushing the ampoule.

Determinations of the heats of mixing were repeated until suitable checks were obtained. The small diameter of the calorimeter limited the size of the ampoule, and the total quantity of base plus chloroform was approximately 0.1 mole (range from 0.15 to 0.05 mole, with the smaller value applying usually to the high molecular weight bases). The temperature increase on mixing was of the order of 1° or less. The results are probably accurate to 3%, although for the volatile bases the error may be as high as 5%.

Materials.—Methanol-*d* was prepared by the method of Redlich and Pordes,[9] b.p. 65° (750 mm.). The amines listed in Table I were good quality commercial products which were dried over sodium metal or barium oxide and fractionally distilled at a high reflux ratio through a six-inch Fenske column[10] packed with glass helices. Only the middle cuts were used, the boiling points and refractive indices of which were in agreement with the literature values.[11] The quinoline was a synthetic product (Eastman Kodak Co.). The isoquinoline was purified by both fractional crystallization and distillation (m.p. 23.5°, lit. value 24.6°). Carbon tetrachloride and chloroform were purified in the manner described by Fieser.[12]

Results

The spectroscopic and calorimetric data are given in Table I. The calorimetric result for *n*-butylamine is in reasonable agreement with the value reported by Marvel, Copley and Ginsberg.[13] In the spectroscopic study the values for the OD frequency shifts observed in the present investigation average about 25 cm.$^{-1}$ larger than those reported by Gordy.[3] Part of this systematic difference lies in the choice of a reference OD frequency, the value of 2689 cm.$^{-1}$ for methanol-*d* in carbon tetrachloride being the reference chosen in this investigation whereas Gordy used the value of 2681 cm.$^{-1}$ for methanol-*d* in benzene. Some difference may arise also from the criteria employed in choosing the band center, this being true particularly in the case of broad and asymmetric bands.

The linear relationship obtained between the heats of mixing and the OD shifts (Fig. 1) supports the experimental results as this type of relationship has been observed previously.[3,6] The straight line of Fig. 1 was drawn using the method of least squares without including the data for triethylamine and tri-*n*-butylamine; the reason for their exclusion will be mentioned below. The equation for the

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(3) W. Gordy and S. C. Stanford, *J. Chem. Phys.*, **9**, 204 (1941).

(4) W. Gordy, *ibid.*, **9**, 215 (1941).

(5) W. Gordy, *J. Chem. Phys.*, **7**, 93 (1939).

(6) S. Searles and M. Tamres, THIS JOURNAL, **73**, 3704 (1951).

(7) The OD shifts in quinoline, isoquinoline, 2,4,6-collidine and *n*-propylamine were obtained with a Beckman IR 2-T spectrometer, using a lithium fluoride prism. We wish to thank Dr. Gordon Barrow for his assistance with these observations.

(8) G. F. Zellhoefer and M. J. Copley, THIS JOURNAL, **60**, 1343 (1938).

(9) O. Redlich and F. Pordes, *Monatsh.*, **67**, 203 (1936).

(10) F. P. Pingert, *Org. Syntheses*, **25**, 2 (1945).

(11) I. M. Heilbron and M. M. Bunbury, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1936.

(12) L. F. Fieser, "Experiments in Organic Chemistry," second ed., D. C. Heath, Boston, Mass., 1941, p. 365.

(13) C. S. Marvel, M. J. Copley and E. Ginsberg, THIS JOURNAL, **62**, 3109 (1940).

TABLE I

HYDROGEN BONDING AT 25° OF PYRROLE, PYRIDINES AND AMINES

	OD bond in CH_3OD solutions		Heat of mixing with $CHCl_3$, cal./mole of soln.		
Compound	Position, cm.$^{-1}$	Shift, cm.$^{-1}$		pK_a[b]	pK_a ref.
Carbon tetrachloride	2689[a]	reference			
Pyrrole	2528	161	145	...	..
Isoquinoline	2482	207	440	5.36	c
Quinoline	2472	217	485	4.94	d
Pyridine	2476	213	484	5.23	e
2-Picoline	2466	223	590	5.96	e
3-Picoline	2471	218	536	5.66	f
4-Picoline	2466	223	556	6.05	e
2,4-Lutidine	2454	235	773	6.79	e
2,6-Lutidine	2454	235	777	6.62	e
2,4,6-Collidine	2441	248	903	7.45	e
Benzylamine	2466	223	..	9.34	g
n-Butylamine	2454	235	714	10.61	g
n-Propylamine	2439	250	..	10.59	h
Di-*n*-butylamine	2449	240	810	11.31	g
Diethylamine	2421	268	886	10.98	g
Diisopropylamine	2431	258	935	11.05	g
Tri-*n*-butylamine	2446	243	438	9.93	g
Triethylamine	2400	289	870	10.78	i

[a] When using a sodium chloride prism, the Perkin-Elmer model 12B spectrometer gave a value of 2683 cm.$^{-1}$ for the position of the OD bond of methanol-*d* in carbon tetrachloride. In order to keep a constant reference of 2689 cm.$^{-1}$, the value obtained with the lithium fluoride prism, 6 cm.$^{-1}$, was added to the results with sodium chloride optics. [b] Negative logarithm of the acidity constant $[B][H^+]/[BH^+]$. [c] P. Karrer and H. Schmid, *Helv. Chim. Acta*, **29**, 1853 (1946). [d] A. Albert and R. Goldacre, *Nature*, **153**, 467 (1944). [e] A. Gero and J. J. Markham, *J. Org. Chem.*, 16, 1935 (1952). [f] R. G. Pearson and F. Williams, private communication. [g] N. F. Hall and M. R. Sprinkle, THIS JOURNAL, **54**, 3469 (1932). [h] "International Critical Tables," first ed., McGraw-Hill Book Co., New York, N. Y., 1929, Vol. 6, p. 264. [i] M. H. Dilke, D. D. Eley and M. G. Sheppard, *Trans. Faraday Soc.*, **46**, 261 (1950).

line is

$$\Delta H = 8.33\Delta\nu - 1240 \qquad (1)$$

where ΔH is the heat of mixing per mole of solution of equimolecular quantities of the nitrogen compound and chloroform, and $\Delta\nu$ is the shift (cm.$^{-1}$) produced by the nitrogen based on the OD band of methanol-*d*.

Discussion

The normal inductive effect of the methyl group on the ability of the pyridine bases to interact with chloroform and methanol-*d* is observed. This contrasts with the marked steric effects found by Brown and Barbaras[14] for the interaction of trimethylboron with pyridine and the picolines. The difference in the two studies may be accounted for by the different steric requirements of the electron acceptor molecules. Not only are the molecules of chloroform and methanol less bulky than that of trimethylboron, but the possible interfering atoms in chloroform and methanol are attached no closer than the second atom from the nitrogen; and the first atom, a hydrogen, is not so closely or rigidly bound to the nitrogen as in the case of boron addition compounds.

In the aliphatic series, the expected increase in electron donor ability is noted as one proceeds from the primary amines, *n*-propylamine and *n*-butylamine, to the secondary amines, diethylamine and diisopropylamine. However, the presence of three alkyl groups, ethyl or larger, causes a decrease in donor ability. This may be due to the folded carbon chain which may prevent sufficient close approach of the acceptor molecule.[15] The effect of the butyl group is much more pronounced than that of the ethyl. Thus for tri-*n*-butylamine, the markedly low calorimetric result with chloroform and low spectroscopic result with methanol-*d* may be due to steric interaction between the end of the four-carbon chain and the chloromethyl or methyl group of the acceptor molecule. Similar observations[6] have been reported for the interaction of di-*n*-butyl ether with these acceptor molecules.

Gordy and Stanford[3] have proposed an empirical linear relationship to correlate the acidity constants and hydrogen bonding abilities toward methanol-*d* for a wide variety of electron donor molecules. Their equation is

$$\Delta\mu = 0.0147\, pK_a + 0.194 \qquad (2)$$

where $\Delta\mu$ is the observed OD shift in microns and pK_a[16] is the negative logarithm of the acidity constant.

It may be seen (Fig. 2) that for the nitrogen bases a single equation does not seem applicable since the data appear to spread into two groups. The linear equation for the pyridine series is

$$\Delta\nu = 14.8\, pK_a + 136 \qquad (3)$$

or

$$\Delta\mu = 0.0242\, pK_a + 0.194$$

where the terms are the same as defined in the previous equations. A similar equation may be written relating pK_a to the heat of mixing with chloroform. Since the data for the amine series are less precise the dashed line (Fig. 2) may be subiect to appreciable error, but the statistical probability of the dashed and solid lines being coincident is of the order of 0.1%.

It may be that some systematic error could account for the difference in the correlation of hydrogen bonding abilities and pK_a's for the two series of nitrogen bases. Such an error might arise if the amines were more highly self-associated than the pyridines. This possibility was tested by determining the heats of mixing at 25° of *n*-heptane ($n^{20}D$ 1.3820) with *n*-butylamine and with 2,4,6-collidine. The results were −242 and −229 cal./mole for *n*-butylamine and 2,4,6-collidine, respectively. This small difference, which is within experimental error, is not sufficient to account for the appreciably greater heat of mixing per mole of solution observed for chloroform and 2,4,6-collidine than for chloroform and *n*-butylamine.

The data thus indicate that linear correlation between the ability of electron donors to enter into hydrogen bonding and their ability to accept a proton completely may not be general, although such

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[14] H. C. Brown and G. K. Barbaras, THIS JOURNAL, **69**, 1137 (1947)

[15] H. C. Brown, H. Bartholomay, Jr., and M. D. Taylor, *ibid.*, **66**, 435 (1944).

[16] Actually, the equation is $\Delta\mu = 0.0147 \log K_b + 0.194$. Their definition for K_b as the ionization constant of a base divided by the dissociation constant of water makes $\log K_b$ equal to pK_a.

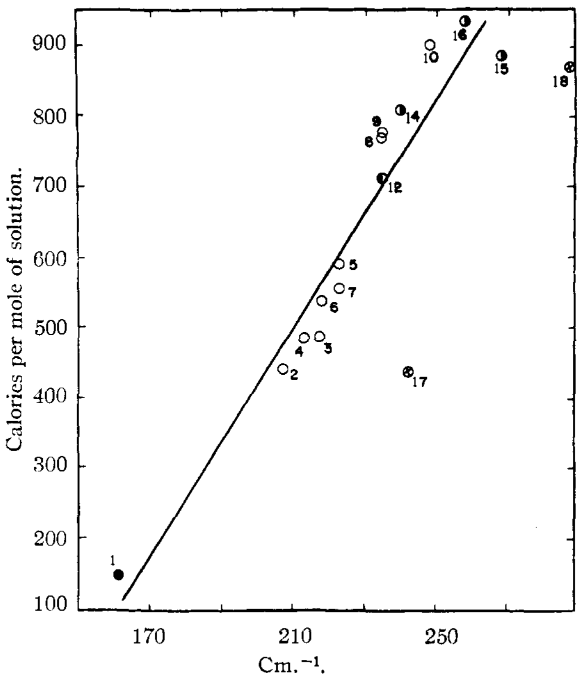

Fig. 1.—Heat of mixing at 25° of chloroform with nitrogen bases (50 mole %) *vs.* shift in vibrational frequency of OD band of methanol-*d* in nitrogen bases. The numbers correspond to the compounds listed in Table I: ●, pyrrole; ○, pyridines; ◐, primary aliphatic amines; ◑, secondary aliphatic amines; ⊗, tertiary aliphatic amines.

correlations may exist for closely related compounds. Consequently, determinations of acidity constants from studies of hydrogen bonding should be made with caution. Among the factors which can cause discrepancies are steric effects, as has been noted above, and solvation effects[17] which may be appreciably different for dissimilar bases.

It seems necessary to distinguish between the formation of a hydrogen bond in which there is principally an electrostatic attraction between a hydrogen atom and an electron rich area, and the formation of a covalent bond in which a proton shares an electron pair with another atom.[18] From the electrostatic viewpoint a hydrogen bond study, in which there is used the same electron acceptor agent and compounds containing the same electron donor atom, may be considered as a study of relative electron densities about that atom.[19,20] Since several of the pyridines are as good electron donors toward hydrogen bonding as some of the amines, this would suggest that the unshared electron pair on the nitrogen atom in the pyridine ring contributes to the electron density on the nitrogen. But these electrons may be less available for covalent bond formation because they partake of resonance in the ring, thereby contributing to resonance stabilization. This view has been expressed also by Albert, Goldacre and Phillips,[21] who have used the term "additional ionic resonance effect" in explaining the difference in the pK_a values for heterocyclic bases and saturated aliphatic amines.

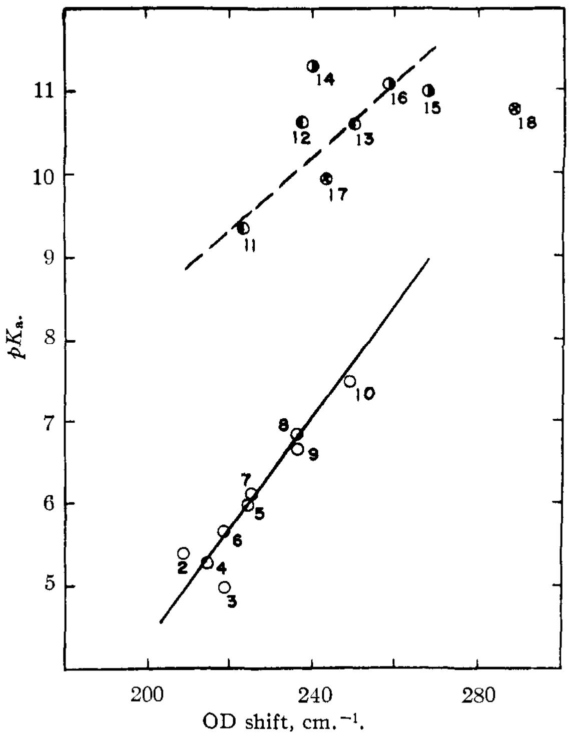

Fig. 2.—pK_a *vs.* shift in vibrational frequency of OD band of methanol-*d* in nitrogen bases. The numbers correspond to the compounds listed in Table I: ○, pyridines; ◐, primary aliphatic amines; ◑, secondary aliphatic amines; ⊗, tertiary aliphatic amines. Steric interferences are likely for compounds 14, 17 and 18, hence these were not included in determining the dashed line. Both lines were determined by use of the method of least squares.

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(17) M. M. Davis and H. B. Hetzer, *J. Research Natl. Bur. Standards*, **48**, 381 (1952), RP 2326.

(18) This distinction for reactions of the aromatic nucleus was pointed out recently by H. C. Brown and J. D. Brady, THIS JOURNAL, **74**, 3570 (1952).

(19) Professor R. S. Mulliken has suggested the term *electron density probe*.

(20) See H. D. Longuet-Higgins and C. A. Coulson, *Trans. Faraday Soc.*, **43**, 87 (1947), for calculated values of electron densities about the N-atom in several nitrogen bases.

(21) A. Albert, R. Goldacre and J. Phillips, *J. Chem. Soc.*, 2240 (1948).