

conjugate acid to azoxybenzene gave agreement to within an average deviation from the mean  $pK_a$  value of  $\pm 0.07$ . The equations for 4-hydroxyazoxybenzene are

$$10^6[A] = 5.99 \text{ (at 353 m}\mu\text{)} - 2.18 \text{ (at 406 m}\mu\text{)}$$

$$10^6[HA^+] = 6.32 \text{ (at 406 m}\mu\text{)} - 0.464 \text{ (at 353 m}\mu\text{)}$$

where A and  $HA^+$  are the azoxybenzene and its conjugate acid.

The results obtained using the Jørgenson and Hartter values<sup>15</sup> of  $H_0$  are shown in Table VI.

TABLE VI

pK <sub>a</sub> DETERMINATION OF 4-HYDROXYAZOXYBENZENE								
%	H <sub>2</sub> SO <sub>4</sub>	-H <sub>0</sub>	—Absorbance—		10 <sup>6</sup>	10 <sup>6</sup>	-pK <sub>a</sub>	
			406 mμ	353 mμ	[A]	[HA <sup>+</sup> ]		
67.6	5.44	0.638	0.635	2.42	3.75	5.26		
63.8	4.80	0.361	0.812	4.08	1.90	5.13		
60.0	4.46	0.203	0.912	5.03	0.86	5.23		
							Av	5.21 ± 0.05

## Solvent Effects on the Basicity of Sterically Hindered Pyridines<sup>1</sup>

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The  $pK_a$  values of pyridine, 2-*t*-butylpyridine, and 2,6-di-*t*-butylpyridine have been measured in aqueous solutions of methanol, ethanol, and 2-propanol at concentrations of alcohol ranging up to 70 vol %. The data support the conclusion that the base weakening effect of the alkyl groups in 2,6-di-*t*-butylpyridine is due to steric inhibition of solvation.

The introduction of an alkyl substituent into the *meta* or *para* position of aromatic bases results in an increase in the strength of the base, a result which may be attributed to the electron-releasing inductive effect of the alkyl group. The same effect has been noted for the substitution of alkyl groups in the *ortho* position of pyridine, with one exception. Brown and Kanner<sup>2,3</sup> found 2,6-di-*t*-butylpyridine to be a weaker base than pyridine itself. They attributed the base-weakening effect to steric strain involving the bound proton, postulating<sup>3</sup> that "the steric requirements of a lone pair on the nitrogen atom are less than the steric requirements of a lone pair bonding a proton to the nitrogen atom."<sup>4</sup>

Recently, Condon<sup>5</sup> has analyzed the  $pK_a$  data for a number of highly hindered bases and arrived at the conclusion that the base-weakening effect of the *ortho* di-*t*-butyl groups is due to steric inhibition of solvation.

The purpose of this research was to attempt to test these two explanations by investigating the effect of solvent variation of the basicity of sterically hindered pyridines. Brown and Kanner presented data showing that the  $pK_a$  value for most 2,6-dialkylpyridines could be calculated from that of the monosubstituted pyridines and pyridine itself by assuming additivity of substituent effects. The  $pK_a$  value for 2,6-di-*t*-butylpyridine in 50% ethanol deviated from that calculated on the additivity assumption by 1.4 pK units. This deviation of 1.4 pK units was taken by Brown and Kanner to be a measure of the steric hindrance toward the proton. If their interpretation is correct, then it would be expected that the deviation of the  $pK_a$  of 2,6-di-*t*-butylpyridine from that calculated by simple additivity would be independent of variations in the solvent system. On the other hand, if Condon's explanation of steric inhibition of solvation is correct, the deviation should depend on the steric requirements of

the solvent, and thus vary with variations in the solvent system.

Accordingly we have measured the  $pK_a$  values of pyridine, 2-*t*-butylpyridine, and 2,6-di-*t*-butylpyridine in aqueous methanol and aqueous ethanol at alcohol concentrations ranging from 2 to 70% and in aqueous 2-propanol at alcohol concentrations up to 50 vol %.

### Results

The results obtained are shown in Tables I, II, and III, which give the  $pK_a$  values of the pyridines as a

TABLE I  
pK<sub>a</sub> VALUES OF PYRIDINE AND SUBSTITUTED PYRIDINES  
IN AQUEOUS METHANOL SOLUTIONS

	Vol % alcohol						
	70	50	40	30	20	10	2
Pyridine	3.72	4.47	4.66	4.91	5.12	5.16	5.21
2- <i>t</i> -Butylpyridine	4.56	4.99	5.04	5.42	5.65	5.74	5.90
2,6-Di- <i>t</i> -butylpyridine	3.50	4.32	4.73	4.96	5.06	5.24	5.02

TABLE II  
pK<sub>a</sub> VALUES OF PYRIDINE AND SUBSTITUTED PYRIDINES  
IN AQUEOUS ETHANOL SOLUTIONS

	Vol % alcohol						
	70	50	40	30	20	10	2
Pyridine	3.66	4.39	4.65	4.87	5.09	5.12	5.18
2- <i>t</i> -Butylpyridine	4.16	4.76	4.97	5.28	5.61	5.65	5.80
2,6-Di- <i>t</i> -butylpyridine	2.83	3.65	4.06	4.77	4.81	4.87	4.91

TABLE III  
pK<sub>a</sub> VALUES OF PYRIDINE AND SUBSTITUTED PYRIDINES  
IN AQUEOUS 2-PROPANOL SOLUTIONS

	Vol % alcohol					
	50	40	30	20	10	2
Pyridine	4.28	4.34	4.65	4.96	5.09	5.17
2- <i>t</i> -Butylpyridine	4.26	4.60	5.08	5.56	5.61	5.79
2,6-Di- <i>t</i> -butylpyridine	...	(<2.5)	3.85	4.61	4.84	4.88

function of solvent composition. No ionic strength corrections have been made. These would be the same for all three pyridine bases for given solvent composition. This correction would be of the order of 0.05–0.1 pK units. The pH was determined with a glass electrode, introducing an error in the  $pK_a$  which is equivalent to the difference in pH and  $pH_0$ .<sup>6</sup> This error is

(6) See R. G. Bates, M. Paabo, and R. A. Robinson, *J. Phys. Chem.*, **67**, 1833 (1963).

(1) Based on a thesis submitted by M. Özcan in partial fulfillment of the requirements for the Master of Science degree.

(2) H. C. Brown and B. Kanner, *J. Amer. Chem. Soc.*, **75**, 3865 (1953).

(3) H. C. Brown and B. Kanner, *ibid.*, **88**, 986 (1966).

(4) For other approaches to the problem of the relative steric requirements of a nonbonding electron pair on nitrogen compared with proton on nitrogen, see N. L. Allinger and J. C. Tai, *ibid.*, **87**, 1227 (1965); N. L. Allinger, J. G. D. Carpenter, and F. M. Karkowski, *ibid.*, **87**, 1232 (1965); J. B. Lambert, R. G. Keske, R. E. Carhart, and A. P. Jovanovich, *ibid.*, **89**, 3761 (1967).

(5) F. E. Condon, *ibid.*, **87**, 4494 (1965).

indeterminate, but constant for a fixed buffer and solvent composition. The precision of the  $pK_a$  values is  $\pm 0.05 pK_a$  units or better, the accuracy is estimated to be  $\pm 0.2 pK_a$  units. In drawing their conclusion that 2,6-di-*t*-butylpyridinium ion exhibits steric strain involving the acidic proton, Brown and Kanner assumed that the inductive effect and any effect of interference with solvation would be additive for the two *ortho t*-butyl groups. The deviation from additivity was then taken as a measure of the increase in steric strain on protonating 2,6-di-*t*-butylpyridine.

Our data permit an examination of the solvent effect on the deviation of the  $pK_a$  of 2,6-di-*t*-butylpyridine from that calculated by additivity. These deviations are calculated as shown in the following example.

In 30% 2-propanol the first *t*-butyl group increases the  $pK_a$  value by 0.43 units over the 4.65 value of pyridine. If the second *t*-butyl group were to have the same effect, one would calculate the expected  $pK_a$  of 2,6-di-*t*-butylpyridine as follows: expected  $pK_a = 4.65 + 0.43 + 0.43 = 5.51$ . The measured  $pK_a$  is 3.85. The deviation between the value expected based on additivity and the measured value is 1.66  $pK_a$  units. The deviations from additivity calculated in this fashion for the solvent compositions studied are given in Table IV. It can easily be seen that the deviation is not

TABLE IV  
DIFFERENCES BETWEEN  $pK_a$  VALUES CALCULATED ON THE BASIS OF ADDITIVITY AND MEASURED  $pK_a$  VALUES FOR 2,6-DI-*t*-BUTYLPYRIDINE IN VARIOUS SOLVENTS

Alcohol, %	In aqueous methanol	In aqueous ethanol	In aqueous 2-propanol
2	1.57	1.51	1.53
10	1.08	1.31	1.29
20	1.08	1.32	1.55
30	0.98	0.92	1.66
40	0.69	1.23	>2
50	1.19	1.48	...
70	1.90	1.83	...

constant, varying between a low of 0.69 in 40% methanol to more than 2  $pK_a$  units in 40% 2-propanol. This variation shows that the deviation cannot be interpreted simply in terms of the steric strain between the two *ortho t*-butyl groups and the acidic proton since this steric strain would be independent of solvent. The deviation is solvent dependent and indicates that steric inhibition of solvation as proposed by Condon provides a better explanation of the data. The deviations at 2% alcohol composition are all the same within experimental error, as is required by the approach of all of the solvents at low alcohol composition to the same composition, *i.e.*, pure water.

The steric interference with solvation of even a single *ortho* butyl group shows up clearly if the data are compared in a different fashion. For a given concentration of alcohol it might be anticipated that the effects of dielectric constant, basicity of the alcohol, and sorting of solvent molecules for selective solvation would be about the same for aqueous methanol, ethanol and 2-propanol provided that no specific steric interference of solvation occurs. Table V shows the difference in  $pK_a$  values in methanol and ethanol at a fixed alcohol concentration. For any fixed alcohol concentration the effect of a change in solvent is greatest for the 2,6-di-*t*-

TABLE V  
SOME CHANGES IN  $pK_a$  VALUES WITH A CHANGE IN ALCOHOL AT A CONSTANT PER CENT ALCOHOL

Alcohol, %	$pK_a(\text{MeOH}) - pK_a(\text{EtOH})$		
	Pyridine	2- <i>t</i> -Butylpyridine	2,6-Di- <i>t</i> -butylpyridine
70	0.06	0.40	0.67
50	0.08	0.23	0.67
40	0.01	0.07	0.67
30	0.04	0.14	0.20
20	0.03	0.04	0.25
10	0.04	0.09	0.37
2	0.03	0.10	0.11

  

Alcohol, %	$pK_a(\text{MeOH}) - pK_a(2\text{-PrOH})$		
	Pyridine	2- <i>t</i> -Butylpyridine	2,6-Di- <i>t</i> -butylpyridine
50	0.19	0.73	...
40	0.32	0.44	>2.2
30	0.26	0.34	1.11
20	0.16	0.09	0.45
10	0.07	0.13	0.40
2	0.04	0.11	0.14

butylpyridine, but is appreciable even for 2-*t*-butylpyridine. With increasing alcohol concentration these differences increase. The effect is greater if the comparisons are made using methanol and 2-propanol, as would be anticipated if the origin is a steric inhibition of solvation. These data thus strongly support the suggestion of Condon that even a single *ortho* butyl group gives rise to steric hindrance to solvation.

### Experimental Section

**Materials.**—Pyridine was obtained from the Fisher Scientific Co. An analysis by gas chromatography revealed only a trace of water present, and accordingly the compound was used as received.

2-*t*-Butylpyridine was prepared by the method of Ziegler and Zeiser.<sup>7,8</sup> Final purification was achieved using temperature-programmed gas chromatography. The column used was packed with Carbowax supported on crushed firebrick. The column temperature started at 110° and was increased at a rate of 1°/min during operation.

2,6-Di-*t*-butylpyridine was prepared by Dr. Jacques Volgts in Professor Herbert C. Brown's laboratory at Purdue University. We are indebted to Professor Brown for a gift of this compound. It was purified by gas-liquid partition chromatography using conditions described above.

The methanol used was obtained from the Fischer Scientific Co. and was their reagent grade material. The ethanol used was A.P.I. absolute alcohol. The 2-propanol was Baker Analyzed reagent grade material.

**Procedure.**—Measurements of  $pK_a$  values were made by a spectrophotometric procedure.<sup>9</sup> A Cary Model 11 recording spectrophotometer was used for all spectral measurements. A 10-cm path length was used; the solutions contained the pyridine bases at a concentration of  $2 \times 10^{-5} M$ . The spectra of the acidic and basic forms of the pyridines were obtained in 0.1 *N* HCl and 0.1 *N* NaOH, respectively, in each solvent. Spectra were also obtained with the pyridines in buffer solutions made with acetic acid and sodium acetate or chloroacetic acid and sodium chloroacetate. All pH measurements were made with a Beckman Zeromatic pH meter which was calibrated with standard buffer solutions before each series of measurements. The temperature of the measurements was 24°.

**Registry No.**—Pyridine, 110-86-1; 2-*t*-butylpyridine, 5944-41-2; 2,6-di-*t*-butylpyridine, 585-48-8.

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(9) E. B. Hughes, H. H. G. Jellinek, and B. A. Ambrose, *J. Phys. Chem.*, **53**, 410 (1949).