Wallach Transformation Rates of Substituted Azoxybenzenes

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Substituents studied cause a 10^5-fold change in azoxybenzene Wallach transformation rates in 90% sulfuric acid at 30°, but nitro groups while causing greatly reduced reactivity in 83% acid actually produced enhanced reactivity relative to unsubstituted azoxybenzene in 100% sulfuric acid. These and other substituent effects are interpreted in terms of reversible nucleophilic attack by bisulfate on the conjugate acids followed by proton transfer and a slower irreversible process in which the N–O bond is broken.

In aqueous sulfuric acid azoxybenzene itself and a variety of substituted azoxybenzenes transform into the corresponding hydroxyazobenzenes.[1-4] The reaction is called the Wallach transformation after an early investigator.[5] The hydroxyl group generally appears in a *para* position of the product, though strenuous conditions or blocking both *para* positions results in *o*-hydroxyazobenzenes.[6] When dilute solutions are used, the Wallach process is not accompanied significantly by side reactions and is thus suited to kinetic study.

Buncel and Lawton have carefully examined the apparent first-order kinetics of the Wallach transformation of azoxybenzene in 65–96% sulfuric acid–water solvents and demonstrated a higher dependence of the rate constants on acid strength than is necessary solely for the conversion of azoxybenzene into its conjugate acid.[7] To account for rate constant variations, they enlarged upon Gore's proposed reaction sequence[8] and suggested that a second proton is transferred to the already protonated oxygen of the azoxybenzene conjugate acid as, or before, the N–O bond breaks. Cleavage of the N–O bond was proposed as the rate-limiting process leading to the dication, **1**, the charge delocalization possibilities of which make it an attractive intermediate. The scheme was completed by attacking **1** with water followed by proton loss and aromatization.

$$C_6H_5\overset{+}{N}\equiv\overset{+}{N}C_6H_5$$

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The Gore–Buncel–Lawton (GBL) mechanism is consistent with other known features of the Wallach transformation of azoxybenzene. Significant among these are recovered starting material has not undergone oxygen exchange with the solvent and the nitrogens have not become equivalent;[9-11] the hydroxyl oxygen of the product is not usually that present in the reactant;[10,11] the entering oxygen function shows no preference for one ring over the other.[9,12] With unsymmetrically substituted azoxybenzenes, however, a strong preference by the entering oxygen for one ring has been observed in several cases even when both *para* positions are open.[3,6]

On the other hand, several factors militating against the GBL mechanism are as follows. (a) In 83–98% sulfuric acid log *k* for azoxybenzene transformation increases much less rapidly than the function $-J_0$ (or $-C_0$)[13] in contrast to expectation by analogy with di- and triarycarbinol ionization[14] if the N–O bond breaks to form **1** as a proton is transferred to the conjugate acid of azoxybenzene. (b) If, instead of concerted proton transfer and N–O bond cleavage, a species with a doubly protonated azoxy oxygen precedes the formation of **1**, then log *k* and $-H_0$[15] should be parallel functions of the acidity of the medium. This parallelism is also not found for azoxybenzene in 83–98% acid solutions though it is approximated above 99% (Figure 1). (c) Lower ionic mobilities in sulfuric acid[16] than in water indicate a diffusion-controlled bimolecular reaction rate limit perhaps as low as one-tenth that for water,[17] and this limit combined with the probably extremely low basicity of azoxybenzene conjugate acid allows only a marginal possibility that proton transfer to the conjugate acid could occur fast enough to permit observed Wallach reaction rates. (d) Potassium bisulfate (0.48 *M*) in 99.8% acid produced a 1.5-fold rate enhancement. As bisulfate should reduce sulfuric acidium ion and disulfuric acid concentrations and hence reduce $-H_0$ as does potassium sulfate in fuming sulfuric acid,[18] a rate decrease rather than the observed increase would be predicted from the GBL mechanism.

Scheme I avoids these objections and therefore constitutes, the authors believe, a more plausible mechanism for the Wallach transformation. A conceivable defect of this reaction scheme results from the environmental nonequivalence of the aromatic rings of **2** which might thence be expected to show different sensitivities to nucleophilic attack in contradiction to observations that the hydroxyl group of the product from azoxybenzene appears equally in either ring. The artificiality of this defect is shown, however, by the observation that bromide ion is liberated at about the same rate from either 4- or 4′-bromoazoxybenzene in the alcoholic alkali at 117°.[19] Both rings must in fact be considerably

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[1] L. C. Behr, E. G. Alley, and O. Levand, *J. Org. Chem.*, **27**, 65 (1962).

[2] C.-S. Hahn and H. H. Jaffé, *J. Amer. Chem. Soc.*, **84**, 946 (1962).

[3] P. H. Gore and G. K. Hughes, *Aust. J. Sci. Res., Ser. A*, **3**, 136 (1950).

[4] E. Müller, "Die Azoxyverbindungen," F. Enke Verlag, Stuttgart, 1936.

[5] O. Wallach and E. Belli, *Chem. Ber.*, **13**, 525 (1880).

[6] J. Singh, P. Singh, J. L. Boivin, and P. E. Gagnon, *Can. J. Chem.*, **41**, 499 (1963).

[7] E. Buncel and B. T. Lawton, *ibid.*, **43**, 862 (1965).

[8] P. H. Gore, *Chem. Ind.* (London), 91 (1959).

[9] M. M. Shemyakin, V. I. Maimind, and B. K. Vaichunaite, *ibid.*, 755 (1958).

[10] M. M. Shemyakin, T. E. Agadzhanyan, V. I. Maimind, and R. V. Kudryatsev, *Izv. Acad. Nauk SSSR, Ser. Khim.*, 1339 (1963) [*Chem. Abstr.*, **59**, 12619b (1963)]; M. M. Shemyakin, V. I. Maimind, and T. E. Agadzhanyan, *Chem. Ind.* (London), 1123 (1961).

[11] S. Oae, T. Fukumoto, and M. Yamagami, *Bull. Chem. Soc. Jap.*, **36**, 601 (1963).

[12] L. C. Behr and E. C. Hendley, *J. Org. Chem.*, **31**, 2715 (1966).

[13] M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957).

[14] N. C. Deno, J. J. Jaruzelski, and A. Schriesheim, *J. Amer. Chem. Soc.*, **77**, 3044 (1955).

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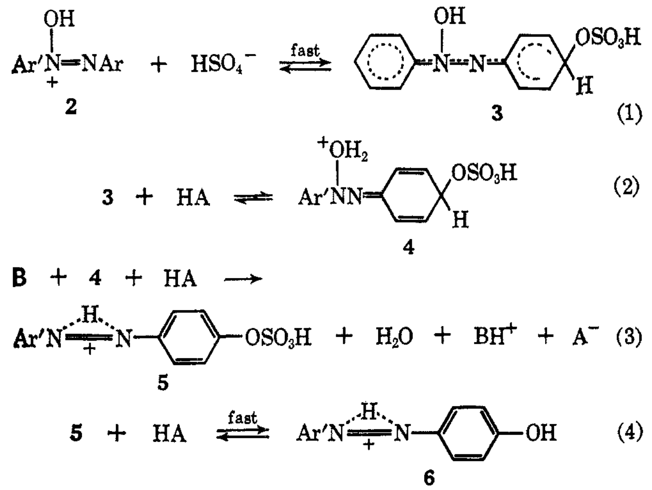
[16] R. J. Gillespie and E. A. Robinson, *Advan. Inorg. Chem. Radiochem.*, **1**, 385 (1959).

[17] M. Eigen, W. Kruse, G. Maass, and L. DeMaeyer, *Progr. Reaction Kinetics*, **2**, 285 (1964).

[18] F. A. Long and M. A. Paul, *Chem. Rev.*, **57**, 935 (1957).

[19] E. C. Hendley, unpublished results.

SCHEME I



activated toward nucleophilic attack for the *p*-bromoazoxybenzenes to yield bromide nearly as readily as *p*-nitrobromobenzene.

In reactions 2, 3, and 4, HA may be any acid in the system, but catalytic constants for the different acids probably differ. In fuming acid, for example, all of the azoxybenzenes studied were converted completely to **5** (or **6** in the case of 3,3′-dinitroazoxybenzene) too rapidly to follow ($t_{1/2} < 10$ sec) indicating that sulfuric acidium ion or disulfuric acid or both are very much stronger catalysts than either sulfuric acid or hydronium ions. Compounds **5** and **6** are drawn according to Jaffé and Gardner.[20] The identity of **5** in the case of azoxybenzene is indicated by cryoscopic and conductivity studies of 100% sulfuric acid solutions that show the formation of 4.2 ± 0.2 particles,[21] approximately two of which were bisulfate ions, per molecule of azoxybenzene. Further support for this assignment comes from the identical visible spectra of the benzenesulfonate of *p*-hydroxyazobenzene[22] in ethanol–water containing about 70% sulfuric acid and azoxybenzene or *p*-hydroxyazobenzene in 5% fuming acid [λ_{max} 425 mμ (log ϵ 4.41)].

Reaction 3, in which B functions as the acceptor of the ring proton, may consist of several steps, but it would seem likely that loss of water and aromatization of **4** are essentially concerted and may be the rate-limiting step. It is quite possible also that the basicity of **3** is so low that its protonation is the rate-limiting step and need not be reversible. In either case Scheme I leads to some predictions of substituent effects on Wallach reaction rates that differ from the effects to be expected from the GBL mechanism.

Rate constants of some substituted azoxybenzenes are shown in Table I. In 90% sulfuric acid the substituents cause a 10^5-fold reactivity range. Primed numbers designate substituent positions on the ring nearest the oxygen-bearing nitrogen (β isomers[23]).

Conjugate acid pK_a's in Table I are for sulfuric acid–water rather than the acid–water–ethanol systems used by Hahn and Jaffé.[24] Hammett equation correlations do not hold well for either the pK_a's or rate constants, but rough Wallach reaction constants, ρ, of −3.3 for the α isomers and −0.7 for the β isomers may be calculated from the rate constants in 90% sulfuric acid.

TABLE I

WALLACH TRANSFORMATION RATE CONSTANTS OF AZOXYBENZENES AT 30°

(sec^{-1} × 10^7)

	% H_2SO_4^{a}			
Substituents	83.6	90.0	98.0	−pK_a^{b}
3,3′-Dinitro	. . .	0.25	18	8.01
4-Nitro	. . .	3.5	320	6.18
3-Nitro	0.28	6.5	684	6.33
4′-Nitro	. . .	300	33,300	6.21
3′-Nitro	9.0	450	38,000	6.47
None	200^c	1280^c	9,170	5.13^d
3,3′-Dimethoxy	110^e	1350	. . .	5.15
4-Bromo	467^f	2920	. . .	5.03
4′-Bromo	. . .	3270	. . .	5.35
4-Hydroxy	6120	33,000	. . .	5.21

^{a} ±0.3%. ^{b} ±0.07 at 25°. ^{c} Interpolated from ref 7. ^{d} Reference 7 gives 5.15 ± 0.05. ^{e} 84.3%. ^{f} 85.5%.

Scheme I for the Wallach transformation presents the opportunity for substituents to alter reaction rates both by changing nucleophilic sensitivity of **2** and by changing the basicity of **3**. Since a given substituent usually affects these properties oppositely, neither Hammett equation nor basicity correlations of the rate constants are to be expected if both factors are operating strongly.

In the less acidic solvents the rate constants in Table I indicate a predominance of basicity in governing the rates as evidenced by the Hammett ρ value of about −3.3 for the α isomers, but in 98% acid where the availability of nucleophiles is much lower the greater reactivities of the less basic 3′- and 4′-nitroazoxybenzenes compared to azoxybenzene reveal a strong dependence of the rate on nucleophilic sensitivity. Similar conclusions are derivable from the facts that, while log k for azoxybenzene does not increase as much as $-H_0$ on going from 83 to 90% acid, log k for 3′-nitroazoxybenzene closely parallels the function $-J_0$ which rises even more rapidly than $-H_0$.

In considering substituent effects on basicity *vis-à-vis* nucleophilic sensitivity it has been assumed that basicity of the conjugate acids takes the same order as basicities of the azoxybenzenes. That this assumption is not fully accurate might be indicated by the high reactivites of *p*-bromo- and *p*-hydroxyazoxybenzenes that are not matched by corresponding increases of their pK_a's relative to azoxybenzene. On the other hand, however, were it not for the dependence of the rates on solvent acidity, these enhanced reactivities and the reduced reactivities of the nitroazoxybenzenes might all be best explained by substituent capacity for stabilizing a nascent positive charge as the N–O bond breaks.

A less equivocal feature of the data in Table I is that β isomers are more reactive than the corresponding α isomers. The reactivity difference for the *p*-bromoazoxybenzenes, though small, is reproducible and has

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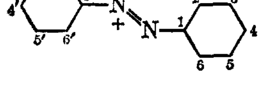
(20) H. H. Jaffé and R. W. Gardner, *J. Amer. Chem. Soc.*, **80**, 319 (1958).

(21) G. E. Eastman, M.S. Thesis, Mississippi State University, 1963.

(22) E. Grandmougin and H. Freimann, *J. Prakt. Chem.*, **78**, 384 (1908).

(23) Monosubstituted azoxybenzenes are numbered herein according to the following structure such that 4- and 4′-bromo(nitro)azoxybenzene correspond, respectively, to the α and β isomers of Angeli [*Atti Accad. Lincei*, **19**, 793 (1910)].



(24) C. S. Hahn and H. H. Jaffé, *J. Amer. Chem. Soc.*, **84**, 949 (1962).

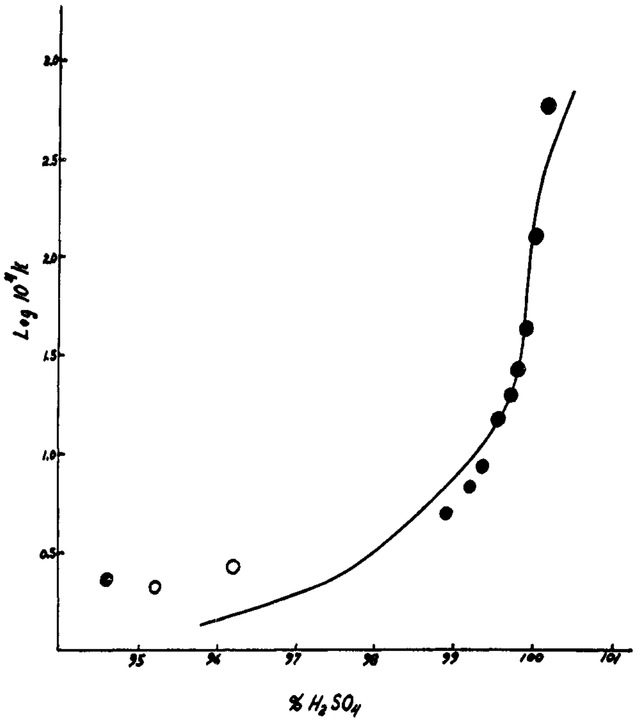


Figure 1.—Variation of Wallach transformation rates of azoxybenzene at 25° with sulfuric acid composition. Open circles are data from ref 7.

been reported by others in a different solvent.[25] These rate differences are most readily comprehensible from the greater basicity of **3** with bisulfate at the 4 position rather than greater susceptibility to nucleophilic attack at this position compared to the 4′ position.

In Figure 1 the solid curve is the function $-(H_0 + 8.85)$ using Paul and Long's values of H_0 which extend into fuming acid.[18] The reactivity of azoxybenzene is seen to increase at least as rapidly as $-H_0$ around 100% acid.

The Wallach transformation rate for 3′-nitroazoxybenzene also climbs very rapidly as the solvent approaches 100% acid. The rate increase is even more rapid with the nitro substituent since the rate constant ratio of 3′-nitroazoxybenzene to azoxybenzene which is about four in 98.3% acid reaches ten in 99.6% acid.

Related mechanistic inferences are derivable from the Arrhenius activation energies and absolute rate theory entropies of activation presented in Table II. The activation requirement is greatest when the oxygen function enters the 4′ position. The activation entropy is least where the oxygen function must enter at a somewhat obstructed position as in 3,3′-dinitroazoxybenzene. Neither of these observations would be anticipated from a mechanism employing nucleophilic attack after the rate-limiting step, but both are consistent with the reaction sequence that we have proposed.

The question of interconversion of α and β isomers under Wallach reaction conditions was necessarily considered in this work when the isomers were found to transform at different rates. It seems clear that in azoxybenzene the oxygen does not move from one nitrogen to the other,[9] but several reports exist of 4′-nitroazoxybenzene isomerizing to 4-nitroazoxybenzene (α isomer) in sulfuric acid,[8,10] or even in acetic acid containing chromic oxide.[4] Though the isomerization appears to be acid catalyzed, the 4-nitroazoxybenzene isolated had not undergone oxygen exchange with the solvent in contrast to the 4-hydroxy-4′-nitroazobenzene also isolated.[10]

The β isomers of *m*- and *p*-nitroazoxybenzene react too fast to expect distinguishable accumulations of them during the Wallach transformation of the α isomers unless isomerization were greatly faster than the Wallach reaction, a possibility eliminated by lower uniform rate constants observed from 5 to 90% reaction for 3- and 4-nitroazoxybenzene. Since 4-bromoazoxybenzene transforms at nearly the rate for 4′-bromoazoxybenzene, however, evidence for α → β isomerization was sought by recovering the remaining azoxy material after about half the initial 4-bromoazoxybenzene had undergone a Wallach reaction. The material isolated contained less than observable (2%), if any, 4′-bromoazoxybenzene. Purity of the recovered starting material was estimated from its infrared spectrum and melting point.

Carefully purified 3′-nitroazoxybenzene (mp 93–93.5°) gave uniform Wallach transformation rate constants over the range 7–96% reaction. An infrared spectrum of material recovered after 90% reaction indicated that no more than 3% of the starting material could have isomerized to the less reactive α isomer. *p*-Bromoazoxybenzene recovered after about 30% Wallach reaction of 4′-bromoazoxybenzene had occurred contained no more than 5%, if any, 4-bromoazoxybenzene. On the basis of these experiments we have assumed that α ↔ β isomerization is not significant for any of the compounds studied except 4′-nitroazoxybenzene where the minimum amount of 4-nitroazoxybenzene appearing during the Wallach reaction of several preparations was about 50%.

The procedure used to follow Wallach transformation rates does not allow a distinction between the cases of concurrent β → α isomerization and initial presence of α isomer in the 4′-nitroazoxybenzene because light transmittance at 262 mμ where the 4′ isomer shows a maximum absorption is obscured by the product 4-hydroxy-4′-nitroazobenzene. Kinetically the latter case is analogous to that treated by Brown and Fletcher.[26] The former case may be described as

$$\begin{tikzcd}
A' \arrow[rr, "k_1"] \arrow[dr, "k_3"'] & & A \arrow[dl, "k_2"] \\
& P &
\end{tikzcd}$$

where A′ and A are 4′- and 4-nitroazoxybenzene and P is the Wallach product 4-hydroxy-4′-nitroazoxyben-

TABLE II

ACTIVATION PARAMETERS IN 90% SULFURIC ACID

Substituents	E_a (±1 kcal/mol)	ΔS^* (±2 eu)
None	22[a]	0[a]
3′-Nitro	19	0
3-Nitro	26	2
3,3′-Dinitro	22	−6

[a] Calculated from data in ref 7.

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(25) C. S. Hahn, K. W. Lee, and H. H. Jaffé, *J. Amer. Chem. Soc.*, **89**, 4975 (1967).

(26) H. C. Brown and R. S. Fletcher, *ibid.*, **71**, 1845 (1949).

zene. Time dependence of the concentration of P under the pseudo-first-order conditions, in which the constants may contain acid concentration and catalytic constants, is given by the equation

$$\frac{P}{P_\infty} = \frac{k_3}{k_1 + k_3}(1 - e^{-k_3t}) + \left[\frac{k_1}{(k_1 - k_2)(k_1 + k_3)}\right][k_1(1 - e^{-k_2t}) - k_2(1 - e^{-k_1t})]$$

where P_∞ is the concentration of P at "infinite" time. The value of k_1 at 30° in 90% acid was calculated to 4.2 × 10^{-5}, k_3 was 3.2 ± 0.2 × 10^{-5}, and k_2 was determined independently with 4-nitroazoxybenzene as 3.55 ± 0.09 × 10^{-7} sec^{-1}. If all α isomer is assumed present initially the value calculated for the equivalent of k_3 was 2.8 ± 0.2 × 10^{-5} sec^{-1}. The average of these values is given in Table I.

Experimental Section

Azoxybenzenes.—The various azoxybenzenes were prepared by reaction of the appropriately substituted azobenzene with peracetic acid[4] or through the appropriate indazole oxide.[27] Preparations and properties of these materials have been described previously in articles referred to in footnotes to Table III. Purification was achieved by recrystallization from ethanol or hexane and by chromatography on a silicic acid column. Identification of the Wallach transformation products are also described by references listed as footnotes to Table III.

TABLE III

AZOXYBENZENE ABSORPTION MAXIMA IN VARIOUS SOLVENTS

[λ_{max} in mμ (log ϵ)]

Substituents[l]	Acidic ethanol	90% H_2SO_4[a]	Fuming acid	Wallach product in "47%" H_2SO_4[a]
3,3′-Dinitro[d]	313 (4.16)	364 (4.10)	420[b]	439 (4.44)
4-Nitro[e]	338 (4.25)[i]	385 (4.20)	430 (4.49)	473 (4.63)
3-Nitro[j]	310 (4.11)[i]	376 (4.07)	414 (4.49)	459 (4.61)
4′-Nitro[e]	341 (4.23)[i]	390 (4.15)	430 (4.49)	473 (4.63)
3′-Nitro[j]	326 (4.17)[i]	390 (4.16)	414 (4.49)	459 (4.61)
None[f]	323 (4.18)[i]	390 (4.16)	425 (4.40)	464 (4.54)
3,3′-Dimethoxy[g]	320 (4.12)	380 (4.06)	425[c]	495 (4.51)
4-Bromo[k]	334 (4.23)	398 (4.18)	454 (4.49)	473 (4.64)
4′-Bromo[k]	327 (4.07)	392 (4.06)	454 (4.49)	473 (4.64)
4-Hydroxy[h]	353 (4.24)	406 (4.21)	428 (4.46)	478 (4.50)

[a] Conjugate acids. [b] Observed as a shoulder in 15% fuming sulfuric acid. [c] A more slowly developing peak appeared at 503 mμ. [d] K. Brand and J. Mahr, *J. Prakt. Chem.*, **131**, 97 (1931). [e] D. Brown, M.S. Thesis, Mississippi State University, 1963. [f] Eastman Organic Chemicals Co. White Label grade. [g] T. Rotarski, *Chem. Ber.*, **41**, 865 (1908). [h] A. Angeli, *Atti Accad. Naz. Lincei*, **23**, I, 557 (1914). [i] A. Risaliti and A. Monti, *Gazz. Chim. Ital.*, 91, 299 (1961). [j] Reference 1. [k] Reference 27. [l] Respective registry no. follow: 1230-85-9; 4504-08-9; 16054-46-9, 13921-68-1, 16054-44-7, 495-48-7, 13556-81-5, 16054-48-1, 16109-68-5, 16054-49-2.

Spectra.—Visible and ultraviolet absorption maxima pertinent to this work are reported in Table III. The spectra were obtained with Perkin-Elmer Model 202 or Beckman Model DU spectrophotometers. Kinetics of reactions in greater than 99.5% sulfuric acid were followed with a Coleman Junior spectrophotometer set to 464 mμ. Infrared spectra were measured with Perkin-Elmer Model 137B or 521 spectrophotometers using potassium bromide wafers or carbon tetrachloride solutions in matched sodium chloride cells.

Kinetics Measurements.—Approximately 10^{-4} *M* solutions of the azoxybenzenes were prepared and immersed in baths thermostated to ±0.1°. At intervals 5-ml aliquots were withdrawn and emptied into a chilled quenching solution composed of sulfuric acid–water–ethanol in the percentages by weight of 47:30:23. The solution was diluted to 50 ml and served to convert the Wallach products into their conjugate acids without substantially protonating any unreacted azoxybenzene. The reactions were usually followed by observing the rate of Wallach product formation, but satisfactory results were also obtainable in most cases by following the disappearance of the azoxybenzene as shown in Table IV. With this procedure the contribution of the azoxybenzene to absorbance at the wavelength of maximum absorbance by the Wallach product was negligible. In solvents of more than 99.5% sulfuric acid the reactions were followed by the absorbance changes at 464 mμ of the reacting solutions directly. Temperatures of these runs were in the range 25.0 ± 0.5°. A typical experiment of this latter type gave the results shown in Table V. The precision of these procedures gave average values for rate constants from which single points showed mean deviations of about 5% and did not exceed 10% even in the fastest reaction over the range 10–90% reaction. Sulfuric acid concentrations were ascertained by titration with standard aqueous sodium hydroxide to the thymol blue end point or in the vicinity of 100% acid by freezing point.

TABLE IV

REACTION RATE OF 4′-BROMOAZOXYBENZENE IN 90.6% SULFURIC ACID AT 30°

(4.8 × 10^{-5} *M*)

Time, sec	327 mμ	473 mμ	10^4k, sec^{-1} from 327 mμ	10^4k, sec^{-1} from 473 mμ
300[a]	0.790	0.244	. . .	. . .
840	0.681	0.567	3.3	3.6
1,860	0.539	0.976	3.0	3.3
2,700	0.428	1.226	3.2	3.2
4,020	0.295	1.518	3.6	3.2
6,969	0.194	1.865	3.3	3.2
12,240	0.135	2.070	3.1	4.0[b]
86,460	0.118	2.085	. . .	. . .
		Av	3.3 ± 0.2	3.3 ± 0.1

[a] To allow thermal equilibration this point was taken as zero time. [b] This value was excluded from the average. It corresponds to more than 99% reaction.

TABLE V

REACTION RATE OF 3′-NITROAZOXYBENZENE IN 99.6% SULFURIC ACID AT 25°

Time, sec	Absorbance at 464 mμ	10^2k, sec^{-1}
50	0.468	(1.47)[a]
60	0.513	1.36
70	0.550	1.30
80	0.588	1.31
90	0.620	1.31
140	0.737	1.36
250	0.824	1.35
300	0.832	(1.23)[a]
500	0.850	. . .
	Av	1.33 ± 0.03[b]

[a] Not included in the average. [b] Five additional points are included in the average.

pK_a Determinations.—Solutions containing weighed amounts of the azoxybenzene in solvents of known sulfuric acid content were examined for absorbance at the wave lengths corresponding to maximum absorption by the azoxybenzene and its conjugate acid as shown in Table III. Molar extinction coefficients for the azoxybenzene were measured in slightly acidic ethanol. Coefficients for the conjugate acids were determined in 83% sulfuric acid except for the nitroazoxybenzenes where 95% acid was used. The concentration of each species was then calculated by simultaneous solution for its contribution to the absorbance at each wavelength. A tenfold or greater range in the ratio of

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(27) L. C. Behr, *J. Amer. Chem. Soc.*, **76**, 3672 (1954).

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

$$10^5[\mathrm{A}] = 5.99 \text{ (at 353 m}\mu) - 2.18 \text{ (at 406 m}\mu)$$

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

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

The results obtained using the Jørgenson and Hartter values[15] of H_0 are shown in Table VI.

Table VI

pK_a Determination of 4-Hydroxyazoxybenzene

% H_2SO_4	$-H_0$	Absorbance 406 mμ	Absorbance 353 mμ	10^5 [A]	10^6 [HA$^+$]	$-$pK_a
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[1]

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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[2,3] 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[3] 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."[4]

Recently, Condon[5] 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 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 pa$_H$.[6] This error is

Table I

pK_a 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-*t*-Butylpyridine	4.56	4.99	5.04	5.42	5.65	5.74	5.90
2,6-Di-*t*-butylpyridine	3.50	4.32	4.73	4.96	5.06	5.24	5.02

Table II

pK_a 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-*t*-Butylpyridine	4.16	4.76	4.97	5.28	5.61	5.65	5.80
2,6-Di-*t*-butylpyridine	2.83	3.65	4.06	4.77	4.81	4.87	4.91

Table III

pK_a 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-*t*-Butylpyridine	4.26	4.60	5.08	5.56	5.61	5.79
2,6-Di-*t*-butylpyridine	...	(<2.5)	3.85	4.61	4.84	4.88

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[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).

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