The Basicities of the Monoxides and Dioxides of *p*-Dimethylaminoazobenzene

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The three monoxides and two dioxides of *trans*-dimethylaminoazobenzene were synthesized, the assignments of various isomers were rechecked, and previous literature assignments were corrected. The basicities of these compounds were determined spectrophotometrically and potentiometrically. It was demonstrated that, in each compound, the first protonation occurs at the dimethylamino or oxidodimethylamino [$(CH_3)_2\overset{+}{N}O$] group in dilute acid, while protonation of the azo or azoxy group takes place only at fairly high concentration of sulfuric acid. The basicity data were analyzed by use of the Hammett equation, and the results were incorporated into previously established Hammett correlations. Estimates of the tautomeric equilibrium constants between the two first conjugate acids of each compound were obtained. The basicities of the same compounds in the first excited singlet states were estimated by use of the Förster cycle, and the tautomeric equilibrium constants in these states were derived. In several cases a reversal of the direction of the equilibrium between ground and excited states is demonstrated.

Derivatives of *p*-dimethylaminoazobenzene (DMAB, butter yellow) are of interest because of their well-known carcinogenic activity.[2] Previous papers from this laboratory have reported a considerable body of information concerning acid–base reactions of DMAB, of azoxybenzene, and of derivatives of both compounds.[3] The monoxides and dioxides of DMAB were first prepared by Anderson[4] and by Pentimalli;[5] polarographic reduction potentials on these were obtained and discussed by Costa and Puxeddu.[6] We have now undertaken a study of the basicities and of the electronic absorption spectra of the oxides of DMAB. In this study we were forced to reexamine the isomer assignments of the various products. We were further able to relate the basicities obtained in this work into the general framework of the acid–base reactions of azo- and azoxybenzene derivatives, as it has been developed in previous papers from this laboratory.[3,7] After this work was complete, there appeared a careful study of the various oxidation processes of DMAB and of the interrelation of the oxidation products.[8]

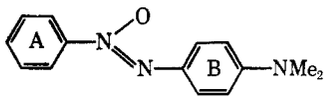
Results and Discussions

Syntheses and Isomer Assignments.—Oxidation of DMAB by perbenzoic acid in chloroform at reduced temperature yields *p*-phenylazo-N,N-dimethylaniline oxide [*p*-(oxido-N,N-dimethylamino)azobenzene] (**1**).[5,9] The *p*-dimethylaminoazoxy compounds, N,N-dimethyl-*p*-(phenyl-ONN-azoxy)aniline, the α isomer (**2**), and N,N-dimethyl-*p*-(phenyl-NNO-azoxy)aniline, the β isomer (**3**), were prepared by condensation of N-phenylhydroxylamine with N,N-dimethyl-*p*-nitrosoaniline in basic media and separated by column chromatography on neutral alumina.[4]

Oxidation of DMAB with hydrogen peroxide in glacial acetic acid at moderate temperatures yields a mixture of dioxides (and possibly other compounds). Column chromatography, in our hands, failed to yield pure products; however, one pure dioxide, mp 145°, was obtained by fractional crystallization of the reaction product from tetrahydrofurane. Oxidation under similar conditions of the monoxide of mp 121.5° yielded the other of the two oxides, mp 150°. These synthetic routes are summarized in Scheme I.

Anderson[4] originally assigned the monoxide of mp 122° to structure **2**, and the isomer of mp 126° to structure **3**, on the basis of uv absorption spectra. The spectral difference between the two compounds were quite small, and the argument is based on the assumption that all α and all β isomers show similar shifts of absorption bands, independent of the nature of the substituent present. The assumption does not seem *a priori* valid, and consequently Anderson's assignments are not convincing.

Pentimalli used Anderson's assignments of the monoxides. To confirm this assignment, he treated both compounds with bromine and found that under a standard set of very mild conditions only the compound of mp 122° was brominated. He concludes that this finding confirms Anderson's assignment of this compound as the β isomer (**3**). In our opinion, Pentimalli's



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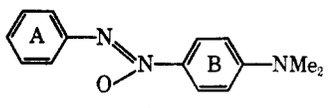

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bromination experiment, on the contrary, argues for the opposite assignment. Following the work of Angeli,[10] it may be assumed that a ring adjacent to the NO side of the azoxy group is very difficult to brominate. In other words, ring A of **2** and ring B of **3** may be as-

(1) U. S. Public Health Service Predoctoral Fellow.

(2) J. A. Miller and E. C. Miller, *Advan. Cancer Res.*, **1**, 339 (1953); J. A. Miller, E. C. Miller, and G. C. Finger, *Cancer Res.*, **17**, 387 (1957); *cf.* C. Hansch and T. Fujita, *J. Amer. Chem. Soc.*, **86**, 1616 (1964).

(3) (a) S. J. Yeh and H. H. Jaffé, *ibid.*, **81**, 3283 (1959); (b) C. S. Hahn and H. H. Jaffé, *ibid.*, **84**, 949 (1962); (c) M. Isaks and H. H. Jaffé, *ibid.*, **86**, 2209 (1964).

(4) A. Anderson, *J. Chem. Soc.*, 1722 (1952).

(5) L. Pentimalli. *Tetrahedron*, **5**, 27 (1959).

(6) G. Costa and A. Puxeddu, *Gazz. Chim. Ital.*, **89**, 1050 (1959).

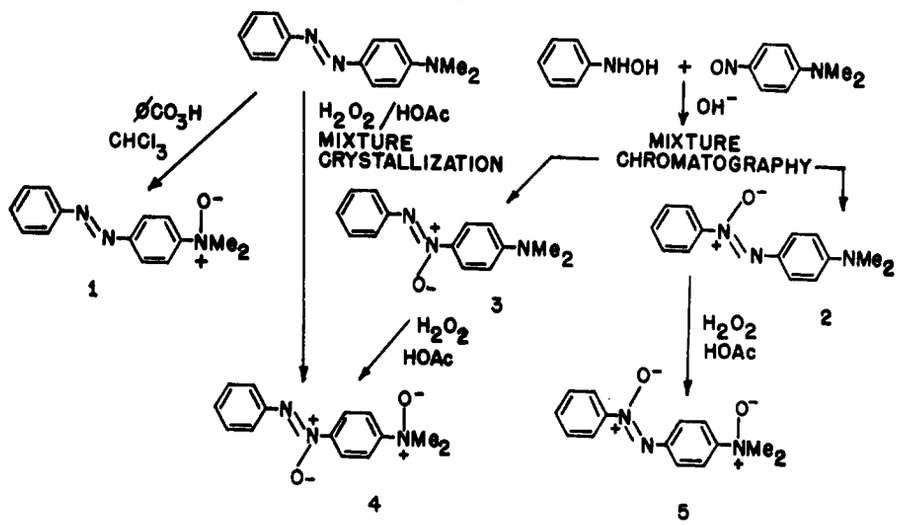
(7) (a) S. J. Yeh and H. H. Jaffé, *J. Amer. Chem. Soc.*, **81**, 3279 (1959); (b) J. H. Collins and H. H. Jaffé, *ibid.*, **84**, 4708 (1962).

(8) A. F. Douglas, P. H. Gore, and J. W. Hooper, *J. Chem. Soc.*, 674 (1967).

(9) International rules for nomenclature provide no name for the "dimethylamine oxide" [$(CH_3)_2\overset{+}{N}O$] group as a substituent, but require naming the compound as an amine oxide. Since, in this work, we will be interested in the effect of this group as a substituent on an aromatic compound, we propose to use the name N-oxido-N,N-dimethylamino, or simply oxidodimethylamino for this group. Upon protonation, the group $(CH_3)_2\overset{+}{N}OH$ is readily named N-hydroxy-N,N-dimethylammonio.

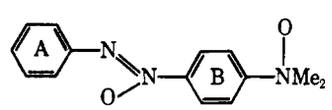
(10) A. Angeli, *Atti Accad. Naz. Lincei. Mem. Classe Sci. Fis. Mat. Nat. Sez. I.ª*, **24**, 1190 (1915).

SCHEME I



sumed to resist bromination. Ring B of **2** and ring A of **3** are similar, except for the presence of the strongly activating dimethylamino substituent in the former. Hence, if only one of the two compounds is brominated under a given set of conditions, we must conclude that this is **2**.

Angeli studied the bromination of the oxidation product (by hydrogen peroxide in glacial acetic acid) of DMAB, to elucidate its structure, which should have been **4** or **5**. The brominated material was reduced



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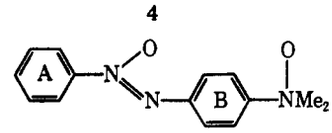

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with tin and hydrochloric acid, and benzoylated. The only brominated product isolated was benzoyl *p*-bromoaniline. This product can arise only from bromination of ring A of **4**, since ring A of **5** should not brominate. Thus, the oxidation product of DMAB, mp 145°, is **4**. The syntheses by Pentimalli of **4** and **5** from **3** and **2**, respectively, repeated in this work for **5** complete the stereochemistry and the relations between the compounds in Scheme I.

Finally, the interpretation of the basicities obtained in this work corroborate the assignments made here, as will be discussed below.

Unfortunately, the recent work of Douglas, Gore, and Hooper[8] is based on the Anderson–Pentimalli assignments. Consequently, many of the structures they give refer to the wrong isomer. It seems possible that the α–β rearrangements reported by these authors are only apparent because of the wrong assignments of isomers.

Basicities and Spectra.—The basicities of compounds **1**–**5** were determined and are expressed throughout as the pK_a of the conjugate acids. Each compound presents two separate and distinct pK's. In the cases of compounds **1**, **4**, and **5**, the pK corresponding to the first basicity (pK_2) produced no significant change in the uv absorption spectra, and consequently use

TABLE I

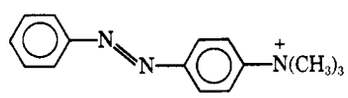
THE BASICITIES (AS pK_a's OF THE CONJUGATE ACIDS) OF THE OXIDES OF DMAB

No.	Compound	pK_{a2}[a]	pK_{a1}[a]
	p-Dimethylaminoazobenzene	2.96 ± 0.03	−5.34 ± 0.02
1	*p*-Oxidodimethylaminoazobenzene	4.11 ± 0.02	−4.65 ± 0.04
2	α-*p*-Dimethylaminoazoxybenzene	1.93 ± 0.05	−8.51[b]
3	β-*p*-Dimethylaminoazoxybenzene	2.62 ± 0.04	−8.02 ± 0.03
4	β-*p*-Oxidodimethylaminoazoxybenzene	4.03 ± 0.03	−8.00 ± 0.05
5	α-*p*-Oxidodimethylaminoazoxybenzene	3.71 ± 0.04	−8.41 ± 0.03

[a] Uncertainties given are standard deviations of at least five and usually more measurements. [b] Extrapolated value; see text.

had to be made of a titration method. All other pK's were determined spectrophotometrically. The results are summarized in Table I.

Since all compounds have two basic centers, it is essential to identify the site of protonation in each step of basicity, *i.e.*, the structure of the conjugate acid. This is most easily done by a comparison of the uv absorption spectra of the compounds in solution of different acidity with each other and with certain reference compounds. All spectral data are summarized in Table II. The uv spectrum of **1** is extremely similar to the spectra of azobenzene and of the other azobenzene derivatives carrying a quaternized ammonio substituent, *e.g.*, N,N,N-trimethylammonioazobenzene, **6** (*cf.* Figure 1). This



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is, of course, due to the well-known fact that a quaternary ammonio substituent has no significant effect on the spectra of aromatic compounds in which it is substituted. Thus, the oxidodimethylamino group $[(CH_3)_2N\rightarrow O]$ behaves as a quaternary ammonio group, which is not unexpected. The spectrum of the first conjugate acid of **1** again is almost identical with that of the free base (and with those of azobenzene and of **6**). This fact leads to the conclusion that the first protonation occurs completely at the oxidodimethyl-

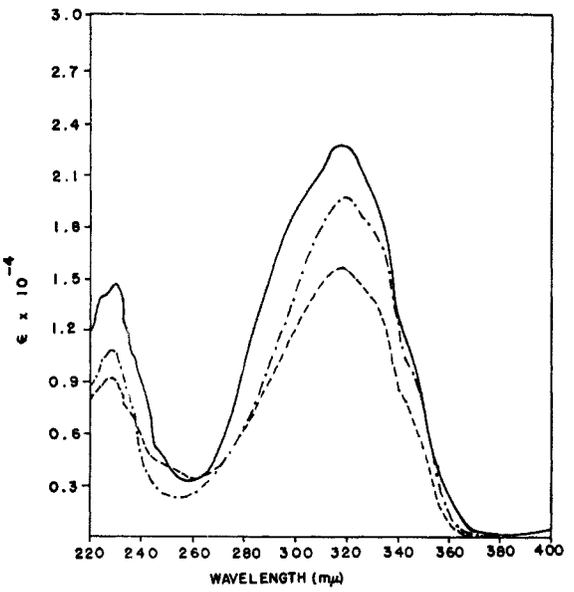


Figure 1.—Spectra of azobenzene (———), N,N,N-trimethylammonioazobenzene (– – – –), and p-phenylazo-N,N-dimethylaniline oxide (– · – ·).

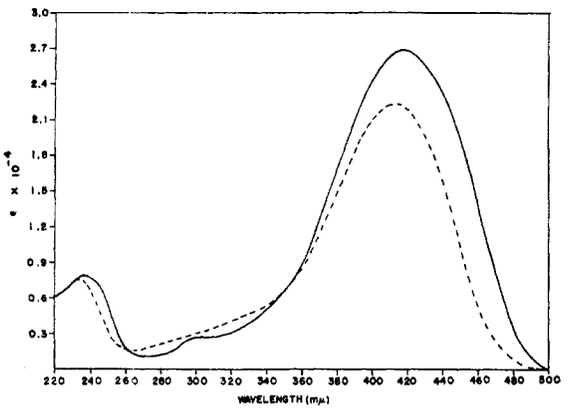


Figure 2.—Spectra of the first conjugate acid (BH^+) of azobenzene (———) and of the second conjugate acid (BH_2^{2+}) of p-phenylazo-N,N-dimethylaniline oxide (– – – –).

amino group (*i.e.*, at the N-oxido oxygen atom), and that the hydroxydimethylammonio group also behaves as a normal quaternary ammonio group.

In the second protonation of **1** (Figure 2), the spectrum changes drastically, giving a strong band at 420 mμ. This spectrum is almost identical with those of the conjugate acids of azobenzene and of **6**, and thus the second protonation of **1** occurs at the azo linkage.

The situation is quite similar for compounds **4** and **5**. The spectra of both compounds in 95% ethanol (325 and 320 mμ) resemble closely that of azoxybenzene (*cf.* Figure 3). Again the oxidodimethylamino group does not significantly affect the spectrum of the parent compound. The spectra of the first conjugate acids of **4** and **5** also closely approximate those of the free bases, again showing that protonation occurs at the oxidodimethylamino group exclusively. The spectra of the second conjugate acids of **4** and **5** (376 and 384 mμ) are shifted bathochromically relative to free base and first conjugate acid, and now resemble closely the spectrum of the first conjugate acid of azoxybenzene (Figure 4). Actually, the bathochromic shifts occuring upon protonation are 58 mμ for **4**, 59 mμ for **5**, and 62 mμ for azoxybenzene.

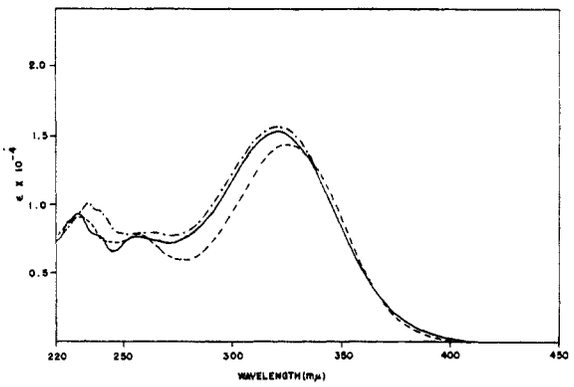


Figure 3.—Spectra of azoxybenzene (———), α-p-oxidodimethylaminoazoxybenzene (– – – –), and β-p-oxidodimethylaminoazoxybenzene (– · – ·).

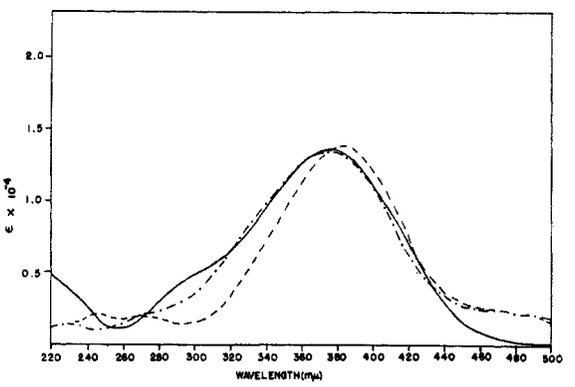


Figure 4.—Spectra of the first conjugate acid (BH^+) of azoxybenzene (———), of the second conjugate acid (BH_2^{2+}) of α-p-oxidodimethylaminoazoxybenzene (– – – –), and of the second conjugate acid (BH_2^{2+}) of β-p-oxidodimethylaminoazoxybenzene.

TABLE II
ULTRAVIOLET ABSORPTION SPECTRA OF AZOBENZENE, AZOXYBENZENE, OXIDIZED FORMS, AND ACID FORMS

		$^1B \leftarrow {}^1A$		$^1H \leftarrow {}^1A$		$^1W \leftarrow {}^1A$		$^1G \leftarrow {}^1A$	
		λ,	ε ×	λ,	ε ×	λ,	ε ×	λ,	ε ×
No.	Compound	mμ	10^{-4}	mμ	10^{-4}	mμ	10^{-4}	mμ	10^{-4}
	Azobenzene	314	2.26	230	1.45	420	0.076		
	Azobenzene conjd acid	418	2.69	236	0.80	300	0.30		
	Azoxybenzene	322	1.54	235	0.92			260	0.78
	Azoxybenzene conjd acid	376	1.35	232	0.34			290	0.40
1	p-Phenylazo-N,N-dimethylaniline oxide	318	1.97	228	1.08	440	0.06		
	1st conjd acid	320	1.53	228	0.99				
	2nd conjd acid	413	2.24	234	0.75				
2	α-p-Dimethylamino-azoxybenzene	395	2.42	246	1.16			320	0.92
								308	
	1st conj acid	326	1.31	241	1.01			250	0.92
3	β-p-Dimethylamino-azoxybenzene	418	2.90	260	1.26				
	1st conjd acid	315	1.48	225	0.98			259	0.98
	2nd conjd acid	366	1.31						
4	β-p-Oxidodimethyl-aminoazoxy-benzene	322	1.60	230	0.91			261	0.80
	1st conjd acid	318	1.30	290	0.46				
	2nd conjd acid	376	1.33	230	0.14			272	0.20
5	α-p-Oxidodimethyl-aminoazoxy-benzene	327	1.44	234	1.01			256	0.80
	1st conjd acid	326	1.33	236	0.92				
	2nd conjd acid	383	1.38	246	0.20				

The spectra of compounds **2** and **3** in 95% ethanol are shown in Figure 5. They are considerably bathochromically shifted relative to azoxybenzene, owing to the

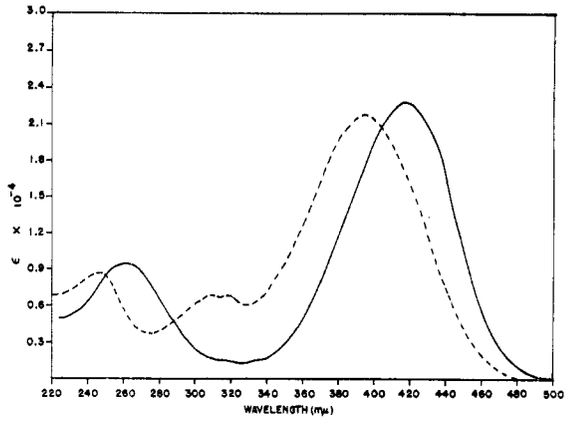


Figure 5.—Spectra of α- (- - - -) and β-*p*-dimethylaminoazoxybenzenes (———) in 95% ethanol

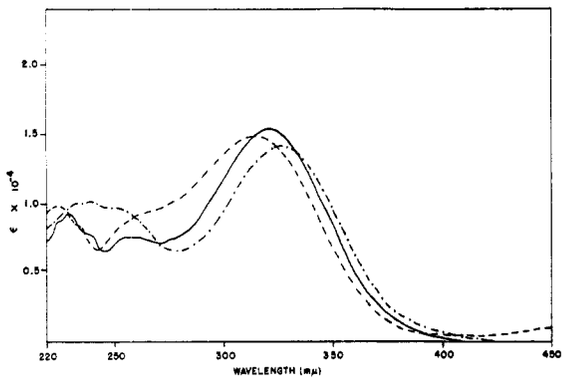


Figure 6.—Spectra of azoxybenzene (———), of the first conjugate acid (BH^+) of β-*p*-dimethylaminoazoxybenzene (- - - -), and of the first conjugate acid (BH^+) of α-*p*-dimethylaminoaxozybenzene (- · - · -).

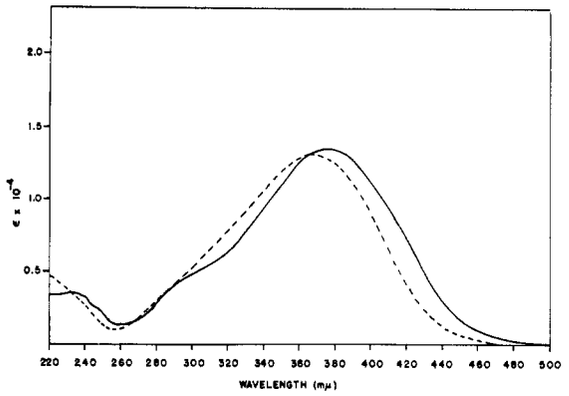


Figure 7.—Spectra of the first conjugate acid (BH^{2+}) of azoxybenzene (———) and of the second conjugate acid (BH_2^{2+}) of β-*p*-dimethylaminoazoxybenzene (- - - -).

effect of the free dimethylamino group. In slightly acidic solution, the spectra shift strongly hypsochromically and now closely resemble the spectrum of azoxybenzene (Figure 6) indicating that protonation has occurred on the dimethylamino group. The spectrum of the second conjugate acid of **3** (Figure 7) now closely resembles that of the conjugate acid of azoxybenzene. Compound **2** in strongly acidic solution was unstable and the spectrum of the second conjugate acid of **2** could not be observed. The second pK therefore could not be determined, and the value listed in Table I is a derived value as discussed below.

Thus we have seen that, in all of the compounds treated, the dimethylamino or oxidodimethylamino group protonates exclusively first, and the azo or azoxy group protonates at much higher acidity.

Application of the Hammett Equation.—Since we have previously examined the basicities of long series of azo and azoxy compounds, it is of interest to see how the new measurements reported fit in with the other material.

First, compound **1**, in its second protonation, is an azobenzene substituted by a hydroxydimethylammonio group. From $\rho = 2.20$ and $pK_0 = -2.90$[7a] we calculate a σ of 0.795 for this group. Further estimates of this same constant may be obtained from the second protonation of **4** and **5** and ρ values for protonation of azoxy compounds,[3b] $\rho_\beta = 1.735$, $\rho_\alpha = 2.508$, and $pK_0 = -6.45$, leading to 0.90 and 0.795, respectively. ρ_β is the least certain of the ρ values used, and its standard deviation exceeds 10% of its absolute value; consequently the value of 0.90 for *o*-hydroxydimethylammonio is least reliable, and the other two values agree fortuitously well. We may accept a value of about 0.80 for this constant. This is not significantly different from the σ values for other quarternary ammonio groups: *p*-NMe_3^+, 0.82; *p*-$NHMe_2^+$, 0.82. The second protonation of compound **3** provides an estimate of σ (*p*-$NHMe_2^+$), again +0.90 and again a little higher than expected since it uses the same low ρ_β of 1.735. This type of argument now permits us to calculate pK_1 of **2**, which was experimentally unaccessible. Using $\rho_\alpha = 2.508$, $pK_0 = -6.45$, and σ (*p*-$NHMe_2^+$) = −0.82 gives pK_1 = −8.51.

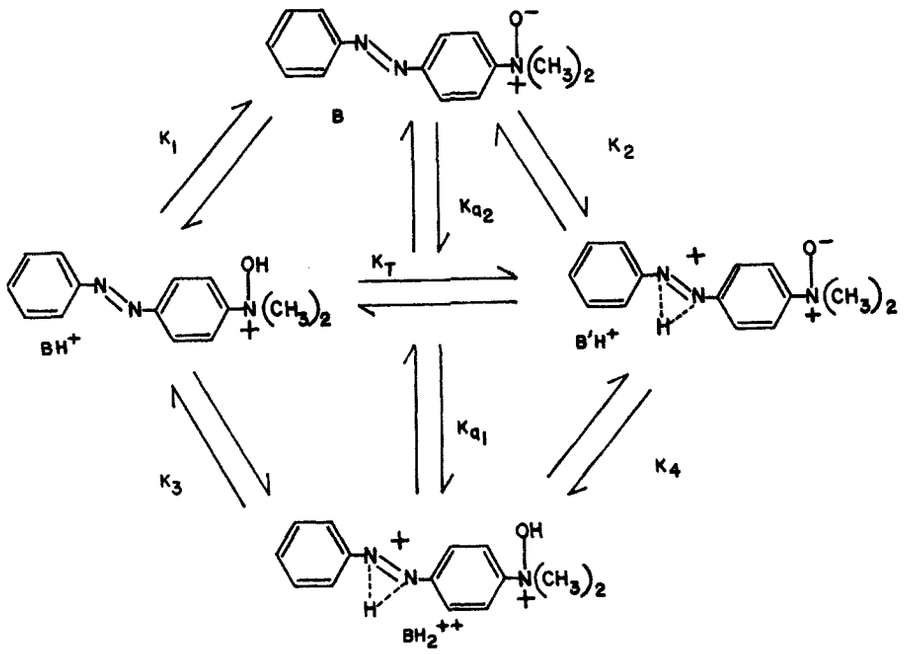
The σ values calculated for the *p*-hydroxydimethylammonio group in the preceding paragraph provide corrobatory evidence for the isomer assignment above. If the assignment were reversed, in accordance with the suggestions of Anderson and Pentimalli, σ values of 0.63 and 1.13 would result; the lack of agreement of these values with one another and with the value of 0.795 obtained from **1** strongly suggest that their assignment is inconsistent.

It now seems of interest to attempt to apply the Hammett equation to the protonation of the dimethylamino group (compounds **2** and **3**) and the oxidodimethylamino group (compounds **1**, **4**, and **5**). Unfortunately, very little information is available on substituent effects on the basicity of dimethylaniline oxide. From the pK's of **2** and **3**, together with the known application of the Hammett equation to dimethylanilines, we can calculate σ values for *p*-phenylazoxy-ONN-**2**, and *p*-phenylazoxy-NNO-**3**. The values so obtained are 0.78 and 0.56, respectively.

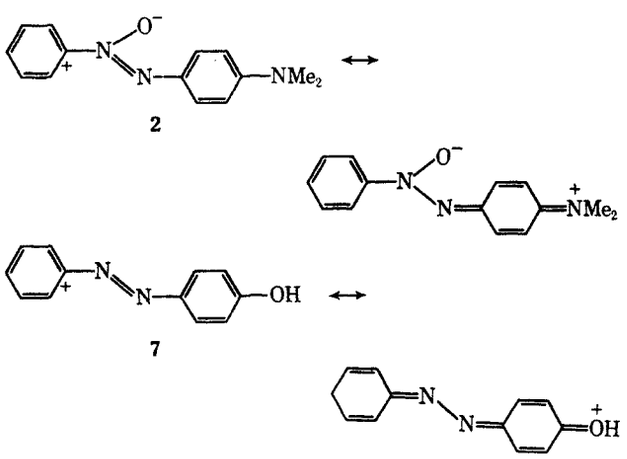
For the *p*-phenylazo group, Hammett originally reported a σ^- value of 0.64. The data of Yeh and Jaffé[11] on phenylazophenols lead to a value of 0.70.[11] Application of the values so obtained to the basicities of the substituted dimethylaniline oxides is not straightforward. The values given above are σ^- values. In *p*-phenylazophenol, **7**, and in **2**, quinoid resonance structures may be expected to make significant contributions, more so in **2** than in **7**, because a charge separa-

(11) S. J. Yeh and H. H. Jaffé, *J. Amer. Chem. Soc.*, **81**, 3287 (1959).

SCHEME II



tion exists in any form of 2, but not in the "normal" form of 7. No such resonance can be written for 3, and consequently the σ^- and σ values should be the same.



According to the data for the pK_2 of 1, 4, and 5 in Table I, σ (p-C_6H_5-NN) > σ (p-C_6H_5-NNO) > σ (p-C_6H_5-ONN), although all values are very close. Unfortunately, the aniline oxides are not very sensitive to substituent effects, and any further refinement of these arguments must await carefully collected data on some other reaction series, preferably one which is more sensitive to substituent effects.

Tautomeric Equilibria.—Although we have concluded above from spectroscopic evidence that, in each compound, the first protonation occurs at the dimethylamino or oxidodimethylamino group, it is of interest to attempt to obtain estimates of the equilibrium constants for the equilibria between the two tautomers of the first conjugate acid of the compounds under investigation. The equilibrium is shown in Scheme II. In this scheme we will call the ammonium or hydroxyammonium form BH^+, the azonium or azoxonium form $B'H^+$; K_{a1} and K_{a2} are our measured basicities. The seven equilibrium constants in this scheme are interrelated, and only three are independent. The desired K_t can be obtained from any one of several relations, *e.g.*,

$$K_t = [B'H^+]/[BH^+] = K_1/K_2 = K_4/K_3 \quad (1)$$

$$K_1K_3 = K_2K_4 \quad (2)$$

As a working hypothesis, we will assume that

$$K_{a1} = K_3,\ K_{a2} = K_1 \quad (3)$$

and test this hypothesis later. The K_2 for 1, 4, and 5 is the azo or azoxy protonation of an azo- or azoxybenzene bearing an oxidodimethylamino substituent. Assuming the σ value for this substituent to be about equal to that of other quaternary ammonio groups, we may estimate these K_2 values as given in Table III. The values of K_4 cannot readily be estimated independently, since they involve protonation of the oxidodimethylamino group, about which virtually no information is available, as discussed above, and hence were estimated from eq 2.

TABLE III

pK AND K_t VALUES FOR EQUILIBRIUM SCHEME

No.	Compound	pK_1	pK_2	pK_3	pK_4	K_t
	p-Dimethylaminoazobenzene	4.4_2	5.2_7	-4.4_3	-5.2_1	7.0_8
1	p-Oxidodimethylaminoazobenzene	4.1_1	-4.8_0	-4.6_5	4.2_6	$1.2_3 \times 10^{-9}$
2	α-p-Dimethylaminoazoxybenzene	1.9_3	-2.1_9	-8.4_7	-4.3_5	$7.5_9 \times 10^{-5}$
3	β-p-Dimethylaminoazoxybenzene	2.6_2	-6.0_7	-8.0_2	$+0.6_7$	$2.0_4 \times 10^{-9}$
4	β-p-Oxidodimethylaminoazoxybenzene	4.0_3	-7.8_7	-8.0_0	$+3.9_0$	$1.2_6 \times 10^{-12}$
5	α-p-Oxidodimethylaminoazoxybenzene	3.7_1	-8.5_1	-8.4_1	$+3.8_1$	$6.0_3 \times 10^{-13}$

From the K_2 and K_4 values so obtained, we can now readily calculate K_t, as listed in Table III. These values are seen to be rather extreme. We can now reassess our approximation made in eq 3. Using

$$K_{a2} = \frac{[B][H^+]}{([BH^+] + [B'H^+])} = \frac{[B][H^+]}{[BH^+](1 + K_t)} = \frac{K_1}{1 + K_t}$$

since the K_t values which we find are very small with respect to **1**, eq 3 is verified. Thus the data obtained here are consistent with the spectroscopic findings. Of course, the K_t values are extremely crude, and not much significance should be attached to them except for the order of magnitude.

Equilibrium Constants in Singlet Excited State.—It has been demonstrated in recent years that excited-state equilibrium constants, pK^*'s, can be obtained for acid–base reactions.[12] The simplest method for obtaining such data is through application of the Förster cycle[13] to the absorption spectra of the conjugate acid–base pair. Using this method, pK_1^* and pK_3^* were determined for the compounds in this study. The requisite spectroscopic data are taken from Table II. Azo- and azoxybenzene are included for comparison. (pK_1^* values could not be calculated for α-*p*-dimethylaminoazoxybenzene since no ground-state pK_{a1} and no spectroscopic information on the second conjugate acid is available.)

Since the Förster cycle depends on spectroscopic data for the various chemical species involved in the equilibrium scheme (Scheme II), pK^*'s estimated actually refer to the individual partial equilibrium constants, not to the directly observable pK_a's. Thus, for compounds **1**, **4**, and **5**, where the first protonation step in the ground state is, to an excellent approximation, expressed purely as K_1, the insensitivity of the uv spectra leads to K_1^* values equal to the ground-state values. Upon second protonation of these compounds, which in the ground state corresponds to K_3, a strong bathochromic shift is observed, which leads to the K_3^* values reported in Table IV.

TABLE IV
CALCULATIONS OF pK_{a1}^* AND pK_{a2}^*

No.	Compound	pK_3^* ΔpK_a	pK_{a2}	pK_3^*	pK_1^* ΔpK_a	pK_{a1}	pK_1^*
	Azobenzene				16.6	−2.9	13.7
	Azoxybenzene				10.5	−6.5	4.1
1	*p*-Oxidodimethylamino-azobenzene	0.0	4.1	4.1	14.8	−4.7	10.2
2	α-*p*-Dimethylaminoazoxy-benzene	−13.0	1.9	−11.1			
3	β-*p*-Dimethylaminoazoxy-benzene	−18.2	2.6	−15.6	10.7	−8.0	2.7
4	β-*p*-Oxidodimethylamino-azoxybenzene	0.0	4.0	4.0	10.0	−8.0	2.0
5	α-*p*-Oxidodimethylamino-azoxybenzene	0.0	3.7	3.7	9.8	−8.4	1.4

In the ground state we were able to equate pK_{a1} with pK_3 and pK_{a2} with pK_1. If we attempt to do the same in the excited state, we are led to the contradictory finding that the first pK of the second conjugate acid in these compounds is larger than the second pK. The most probable cause for this reversal may be a change in sign of pK_t between ground and excited states. Thus we must try to estimate K_t^*. To do so, estimation of K_2^* and/or K_4^* would be sufficient.

For compound **1**, K_4^* of the equilibrium scheme (II) refers to protonation of the amino oxide group. It has been shown that this reaction yields identical pK values for ground and excited states and consequently pK_4^* = pK_4. Using eq 1 and 2, pK_2^* = +10.42, $K_t^* = 2.04 \times 10^6$. From these data it is seen that, in the excited state, *p*-oxidodimethylaminoazobenzene protonates first virtually exclusively at the azo group, and only at higher acidity at the oxidodimethylamino group, while the order is just the reverse in the ground state.

For compounds **4** and **5**, again it can be presumed that pK_4 = pK_4^*, values for pK_2^* and K_t^* can be determined as above, and similar conclusions are drawn.

In contrast to the findings for the last three compounds, for α- (**2**) and β-*p*-dimethylaminoazoxybenzene (**3**), a considerable change in basicity occurs between the ground and excited state for both the first and second ionization constant.

It has already been shown that initial protonation of both isomers occurs at the dimethylamino group. Since the unshared electron pair on the nitrogen atom of this group is in conjugation with the aromatic portion of the molecule, the electron distribution about the nitrogen atom will be directly affected by the transition.

Since K_{a1}^* is not known for the α isomer, K_t^* cannot be determined. However, for the β isomer, K_t^* value can be calculated through use of the Hammett equation and the equilibrium scheme (II). It is seen that K_2^* represents protonation of the azoxy group in the system under investigation. An evaluation of excited-state acidity constants for a series of β-azoxybenzenes and determination of the pK^*–σ relationship for this series of compounds is given later in this paper. From these data, $\rho^* = 1.97$, log $K_0^* = -2.86$, σ [N(CH$_3$)$_2$] = −0.83, and log $K_2^* = -4.50$; $K_t^* = 1.20 \times 10^{20}$.

Since the first protonation of all of our compounds in the ground state occurs on the dimethylammonio or oxidodimethylammonio group, at the time of second protonation we deal with azo and azoxy compounds bearing the nonconjugated, purely inductive substituents dimethylammonio and hydroxydimethylammonio. Consequently the values of ΔpK_3 obtained for compound **1** should resemble ΔpK_a for azobenzene, and ΔpK_3 for the other compounds should resemble ΔpK_a for azoxybenzene. These similarities are well borne out by the data in Table IV.

The tremendous change in the equilibrium upon excitation of the azo and azoxy compounds in this study is aptly shown by comparison of K_t values in Tables III and V. The equilibrium between the two forms of the conjugate acids shifts from the ammonium or hydroxyammonium form in the ground state to the hydroxyazonium or azonium form in the excited state for **1** and **3**. For compounds **4** and **5**, although the equilibrium is not shifted, the change in K_t is still quite large.

TABLE V
pK^* AND K_t^* FOR THE EQUILIBRIUM SCHEME

No.	Compound	pK_1^*	pK_2^*	pK_3^*	pK_4^*	K_t^*
1	*p*-Oxidodimethylamino-azobenzene	4.1	9.8	10.1	3.8	2.0×10^6
3	β-*p*-Dimethylamino-azoxybenzene	−15.6	+4.5	2.7	−17.4	1.2×10^{20}
4	β-*p*-Oxidodimethylamino-azoxybenzene	4.0	2.1	2.0	3.9	1.3×10^{-2}
5	α-*p*-Oxidodimethylamino-azoxybenzene	3.7	1.3	1.4	3.8	3.8×10^{-3}
	p-Dimethylaminoazo-benzene	−9.6	7.8	10.8	−15.6	2.0×10^{26}

(12) (a) H. H. Jaffé, D. L. Beveridge, and H. L. Jones, *J. Amer. Chem. Soc.*, **86**, 2932 (1964); (b) W. Bartok, P. J. Lucchesi, and N. S. Snider, *ibid.*, **84**, 1842 (1962); (c) J. C. Haylock, S. F. Mason, and B. E. Smith, *ibid.*, **85**, 4897 (1963).

(13) (a) T. Förster, *Z. Elektrochem.*, **54**, 42 (1950); (b) A. Weller, *Progr. Reaction Kinetics*, **1**, 189 (1961); (c) E. L. Wehry and L. B. Rogers in "Fluorescence and Phosphorescence," D. M. Hercules, Ed., Interscience Publishers, New York, N. Y., 1966, pp 125–140.

TABLE VI

CALCULATION OF pK^* FOR MONOSUBSTITUTED AZOBENZENES

Designation	Substituent	B λ^a	B ν^b	BH$^+$ λ^a	BH$^+$ ν^b	$\Delta\nu^b$	ΔpK	pK_1	pK_1*	σ	σ^+	σ^-
a	H	314	318	419	239	79	16.6	−2.90	13.7	0		
b	4-OC_2H_5	348	287	468	214	73	15.2	−1.28	13.9	−0.24	−0.778	
c	4-OCH_3	348	287	469	213	74	15.4	−1.36	14.0	−0.268	−0.778	
d	4-CH_3	332	301	438	228	73	15.2	−2.35	12.8	−0.170	−0.311	
e	3-CH_3	322	311	420	238	73	15.2	−2.70	12.5	−0.069		
f	4-Br	328	305	440	227	78	16.2	−3.47	12.8	+0.232	+0.150	
g	3-Br	322	311	420	238	73	15.2	−3.83	11.4	+0.391		
h	4-$COCH_3$	328	305	420	238	67	13.9	−3.98	10.0	+0.502		+0.874
i	4-CN	326	307	418	239	68	14.1	−4.52	9.6	+0.660		+1.000
j	3-NO_2	316	316	412	243	73	15.2	−4.63	10.6	+0.710		
k	4-NO_2	334	299	420	238	61	12.7	−4.70	8.0	+0.778		+1.27
l	4-$N^+OH(CH_3)_2$	318	314	412	243	71	14.8	−4.65	10.1	+0.795		
m	4-OH	346	289	460	217	72	15.0	−1.02	14.0	−0.37	−0.92	

[a] Millimicrons. [b] Reciprocal centimeters × 10^{-2}.

TABLE VII

CALCULATION OF pK^* FOR MONOSUBSTITUTED AZOXYBENZENES

Designation	Substituent	B λ^a	B ν^b	BH$^+$ λ^a	BH$^+$ ν^b	$\Delta\nu^b$	ΔpK	pK_1	pK_1*	σ	σ^+	σ^-
					α Isomer							
a	H	322	311	383	262	49	10.3	−6.45	3.8	0		
b	$-CH_3$	340	294	394	254	40	8.4	−6.04	2.4	−0.170	−0.311	
c	$-OCH_3$	360	277	442	226	51	10.7	−6.10	4.6	−0.268	−0.778	
d	$-OC_2H_5$	358	279	425	234	45	9.4	−6.04	3.3	−0.24	−0.778	
e	$-NO_2$	356	281	372	269	12	2.5	−9.83	−7.3	+0.778		+1.27
f	−Br	334	299	394	254	45	9.4	−7.01	2.4	+0.232	+0.150	
g	$-N^+OH(CH_3)_2$	326	307	385	260	47	9.9	−8.41	1.5	+0.795		
					β Isomer							
h	$-CH_3$	344	291	394	254	37	7.8	−6.16	1.6	−0.170	−0.311	
i	$-OCH_3$	364	275	450	222	53	11.1	−6.15	5.0	−0.268	−0.778	
j	−Cl	332	301	405	247	54	11.2	−6.96	4.3	+0.227	+0.114	
k	−Br	336	297	390	256	41	8.5	−6.94	2.6	+0.232	+0.150	
l	$-N^+OH(CH_3)_2$	318	314	376	266	48	10.0	−8.00	2.0	+0.795		
m	$-N^+H(CH_3)_2$	315	317	375	270	47	9.8	−8.02	1.8	+0.820		

[a] Millimicrons. [b] Reciprocal centimeters × 10^{-2}.

The results of these calculations are subject to a considerable amount of error. Use of the Förster cycle involves a number of assumptions and therefore, only approximate results can be obtained. In determining pK^*'s the λ_{max} was taken from the absorption spectra of compounds under study; the absorption bands, in many instances, are broad; and values of λ_{max} may be uncertain by several millimicrons. Some pK's were estimated on the basis of the Hammett equation with approximate values for substituent effects. However, the differences in K_t between ground and excited states are so large that even errors of a power of ten or more would not invalidate the qualitative conclusions drawn.

Application of the Hammett Equation to the Excited-State Equilibria.—Considerable work has been done in this laboratory over the past few years in the application of the Hammett equation to evaluate substituent effects on the ionization constant of the conjugate acid of azo- and azoxybenzenes and in its application to excited-state pK's. We have extended this work in an attempt to fit the data obtained in this work into pK^*–σ correlations.

Jaffé and Jones,[14] in an exhaustive literature survey of series of compounds for which excited-state pK values had been determined, have obtained fair results in the correlation, with exalted σ values usually required; this work included the azo and azoxy series.

These two series were reexamined with the inclusion of data for compounds from this study. Table VI gives all calculations for the azobenzene series.

The best fit of pK^* *vs.* σ was obtained when σ values were used in place of σ^+ values for electron-donating groups and σ^- values were used for electron-withdrawing substituents. This conclusion is just the contrary of the finding of Yeh and Jaffé,[7a] who have shown in the ground state that σ^+ and normal σ values were required. These data indicate that in the ground state the azo group acts as an electron-withdrawing group, while in the excited state the group behaves as an electron donor. A similar behavior has also been noted in the ground states of *cis*-azobenzenes.[15]

For the azoxybenzene series a plot of pK^* *vs.* σ was made using data from this study combined with those of Hahn and Jaffé.[3b] Results of the calculations are given in Table VII.

Although the points are more scattered than those for the azobenzene series, the correlation still is significant. The use of σ and σ^- substituent values give a better fit than use of σ^+ in the azoxybenzenes examined, in agreement with the fit demonstrated with azobenzenes. Sta-

(14) H. H. Jaffé and H. L. Jones, *J. Org. Chem.*, **30**, 964 (1965).

(15) J. H. Collins and H. H. Jaffé, *J. Amer. Chem. Soc.*, **84**, 4708 (1962).

tistical data for the correlations found are given in Table VIII.

TABLE VIII

REACTION CONSTANTS FOR pK* FOR MONOSUBSTITUTED AZO- AND AZOXYBENZENES

	Azobenzenes		Azoxybenzenes	
			α isomer	β isomer
	σ^-	$\sigma^\pm$	σ^-	σ^-
ρ^* [a]	3.42	2.54	5.15	1.97
r [b]	0.983	0.973	0.803	0.516
s [c]	0.389	0.479	2.41	1.46
s_0 [d]	0.206	0.189	1.56	0.853
Log K_0* [e]	−12.93	−12.19	−0.001	−2.86
n [f]	13	13	6	6

[a] The reaction constant in the excited state. [b] The correlation coefficient. [c] The standard deviation of the data. [d] The standard deviation of the reaction constant. [e] The intercept with the $\sigma = 0$ axis. [f] The number of points in the regression line.

neutralized with dilute NaOH, and the product extracted with chloroform. The solvent was evaporated, and the resulting material was recrystallized from dry THF and dried *in vacuo* over P_2O_5.

Elemental analysis and melting points of these compounds are given in Table IX.

pK **Measurements.**—Values for pK_a for compounds **2** and **3** were determined spectrophotometrically[16] using a standard NaOAc–HCl buffer. Spectra in neutral and acid solutions were recorded using a Cary Model 11 spectrophotometer. Titration curves at selected wavelengths (ϵ *vs.* pH) were determined using a Beckman Model DU quartz spectrophotometer.

For compounds **1**, **4**, and **5**, it was found that formation of the conjugate acid did not result in a significant change in the uv spectra. The acid solution was added in a stepwise manner to a solution of base of accurately known concentration. The pH of the solution was measured using a Beckman Zeromatic pH meter after each addition of acid. The pK was determined from the relationship

$$pK_a = pH + \log\left[\frac{C_{HA} - [H^+]}{(C_B + C_{HCl}) + [H^+]}\right]$$

TABLE IX

ANALYSES AND MELTING POINTS OF MONOXIDES AND DIOXIDES OF *p*-DIMETHYLAMINOAZOBENZENE

Compound	Mp found	Lit. mp	% C		% H		% N	
			Calcd	Found	Calcd	Found	Calcd	Found
p-Oxidodimethylaminoazobenzene	145	126–127	69.68	70.16[a]	6.27	6.31	17.42	17.27
α-*p*-Dimethylaminoazoxybenzene	121–121.5	121.5	69.68	69.81	6.27	6.36	17.42	17.49
β-*p*-Dimethylaminoazoxybenzene	126–126.5	126.2–126.6	69.68	69.61	6.27	6.54	17.42	17.59
β-*p*-Oxidodimethylaminoazoxybenzene	145–145.5	125–126	65.35	65.61[a]	5.88	6.06	16.34	16.83
α-*p*-Oxidodimethylaminoazoxybenzene	150	117–118	65.35	65.30	5.88	5.93	16.34	16.26

[a] Values corrected for H_2O by Karl Fisher.

Experimental Section

Compounds.—*p*-Phenylazo-N,N-dimethylaniline oxide (**1**) was prepared by oxidation of *p*-dimethylaminoazobenzene (DMAB) with an equimolar amount of freshly prepared perbenzoic acid at reduced temperature.[5] Neutralization of the reaction mixture with Na_2CO_3 yielded a solid, orange product. The compound was recrystallized from THF, which had been distilled over $LiAlH_4$, and dried *in vacuo* over P_2O_5.

α- and β-*p*-dimethylaminoazoxybenzene were prepared through the condensation of N-phenylhydroxylamine with N,N-dimethyl-*p*-nitrosoaniline (at a 2:1 mole ratio) in a slightly basic medium.[4] N,N-Dimethyl-*p*-nitrosoaniline was obtained from Eastman Kodak and was recrystallized from petroleum ether: mp 84.5–85°. N-Phenylhydroxylamine was prepared by the reduction of nitrobenzene with aqueous ammonium chloride and zinc dust. The product was recrystallized from ethyl ether, rapidly dried *in vacuo*, and used immediately.

Initial separation of the desired compounds from tars in the reaction products was accomplished by recrystallization from *n*-heptane. Isomers were separated on a 1 × 15 in. column of neutral Al_2O_3 using benzene as the solvent. With benzene as the eluent a light orange fraction was recovered. The benzene was removed *in vacuo*, and the yellow needles of α-*p*-dimethylaminoazoxybenzene (**2**) that formed were recrystallized to a constant melting point from dry THF and dried *in vacuo* over P_2O_5.

The dark orange fraction was rechromatographed using 98% benzene–2% ether solution as the eluent. Two small fractions were rapidly eluted while the last large band yielded orange crystals which were recrystallized from dry THF and dried *in vacuo* over P_2O_5. These crystals were identified as β-*p*-dimethylaminoazoxybenzene (**3**).

β-*p*-Oxidodimethylaminoazoxybenzene (**4**) was prepared by treating DMAB with 34% H_2O_2 in glacial acetic acid at 40°.[5] The reaction was continued until the color of the reaction mixture changed from dark red to yellow. Treatment of the solution with dilute sulfuric acid and ice yielded a product as orange leaves. The solid material was recovered and dissolved in a Na_2CO_3 solution. When cooled to 0°, yellow crystals formed. The product was recrystallized from dry THF and dried *in vacuo* under P_2O_5.

α-*p*-Oxidodimethylaminoazoxybenzene (**5**) was prepared by treating α-*p*-dimethylaminoazoxybenzene with 34% H_2O_2 at 40° for 48 hr in glacial acetic acid.[5] The reaction mixture was

The pK_{a1}'s of all compounds were determined in mixtures of aqueous H_2SO_4 and 20% ethanol, using the H_0 acidity scale of Jaffé and Gardner[17] and Yeh and Jaffé.[18]

In the presence of concentrated sulfuric acid, azoxybenzenes undergo the Wallach rearrangement, resulting in the formation of the corresponding hydroxyazo compounds. The following method of sample preparation was used to reduce to a minimum the heat evolved in making up a solution of the organic base in sulfuric acid and the consequent Wallach rearrangement. The acid solution (40 ml) was pipetted into a 50-ml volumetric flask. Ethanol was slowly added to the acid solution, with cooling, up to the neck of the flask, leaving 2–3 ml to be added to the mark. The acid–alcohol solution was chilled to a predetermined temperature, and 2 ml of a stock solution of the base was pipetted into the chilled solution with constant agitation and then brought to the mark with alcohol. The heat of mixing of the base solution and alcohol brought the temperature of the solution to 25 ± 0.1°. Absorption at selected wavelengths was measured using a Beckman Model DU quartz spectrophotometer; pK_{a1}'s were calculated from the resulting titration curves (ϵ *vs.* H_0).

It was not possible to determine the pK_a of α-*p*-dimethylaminoazoxybenzene experimentally. This compound was very unstable in the presence of solutions of 90–100% sulfuric acid, and all uv spectra obtained on solutions in this acid region showed considerable concentration of rearrangement product.

Registry No.—**1**, 2747-31-1; **2**, 13921-71-6; **3**, 3291-89-2; **4**, 14135-50-3; **5**, 13921-67-0; Table VI—a, 103-33-3; b, 7466-38-8; c, 2396-60-3; d, 949-87-1; e, 17478-66-9; f, 4418-84-2; g, 4171-34-0; h, 4827-16-1; i, 1837-93-0; j, 4827-19-4; k, 2491-52-3; l, 17478-72-7; m, 1689-82-3; Table VII—a, 495-48-7; b, 17310-79-1; c, 17478-75-0; d, 17478-76-1; e, 4504-08-9; f, 16054-48-1; g, 17478-37-4; h, 17310-78-0; i, 17478-80-7; j, 17478-82-9; k, 16109-68-5; l, 17478-38-5; m, 17476-14-7.

(16) L. A. Flexser, L. P. Hammett, and A. Dingwall, *J. Amer. Chem. Soc.*, **57**, 2103 (1935).
(17) H. H. Jaffé and R. W. Gardner, *ibid.*, **80**, 319 (1958).
(18) S. J. Yeh and H. H. Jaffé, *ibid.*, **81**, 3274 (1959).