[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Position of the Proton in Substituted Azobenzene Molecules

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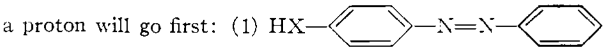
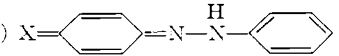
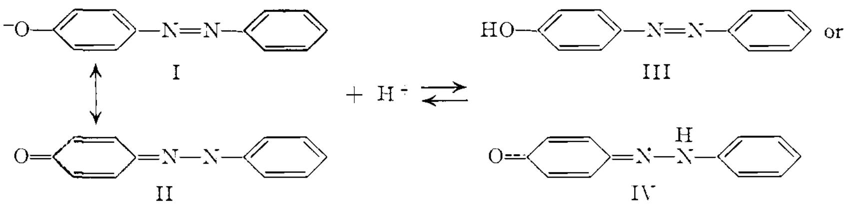
RECEIVED MAY 28, 1954

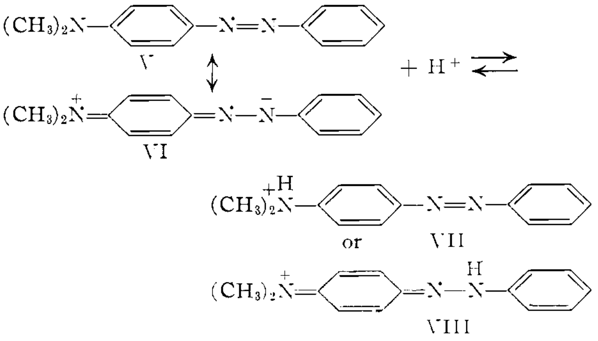
If X is a basic substituent, such as $-N(CH_3)_2$ or $-O^-$, in azobenzene derivatives, there are two views possible as to where a proton will go first: (1)  or (2)  On the basis of pK data, it can be concluded unequivocally that the benzenoid structure is the correct one, at least in aqueous solutions, and that the relative basicities of possible competing groups lie in the order: $O^- >$ pyridine N $> -N(CH_3)_2 >$ —N=N—

Introduction

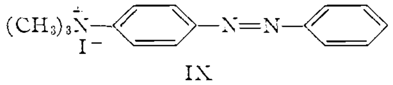
During the past few years, a substantial number of studies have been carried out in this Laboratory of the complexes between azobenzene derivatives and proteins. In the course of this work, it has been desirable on several occasions to know the basicity of various substituents, in particular relative to the azo group.

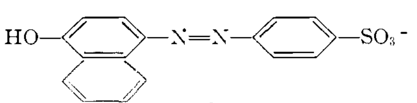
The protonic equilibria of dialkylaminoazobenzenes and of hydroxyazobenzenes have been studied for many years, much attention having been paid especially to parallel spectroscopic changes. Two viewpoints are possible as regards the structure of the participating ions. For hydroxyazobenzene in alkaline solution ($pH > 10$), structures I and II represent resonance forms contributing to the hybrid and are experimentally indistinguishable; addition of a proton, however, may lead to either III or IV, which are genuine tautomers. Similarly, with 4-dimethylaminoazobenzene in neutral or slightly acid solution ($pH > 5$), formulas V and VI represent the structures contributing to the resultant hybrid; addition of a proton may lead to either VII or VIII, which are fundamentally different and should be distinguishable.

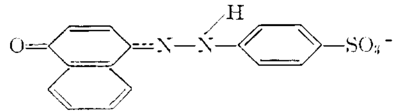




An examination of the literature reveals that quinoid forms such as IV and VIII are preferred by most investigators, particularly for naphthol derivatives. The choice has been made by some largely because of an intuitive attraction to a quinoid structure for a strongly colored compound. There exists in addition, however, good evidence for this choice in several spectroscopic studies.[1,2] Thus, as was shown by Hantzsch[2] and many others, the methiodide IX corresponding to VII has a spectrum (λ_{max} 315, 425 mμ) analogous to that of azobenzene (λ_{max} 313, 448 mμ) and not at all like that of 4-dimethylaminoazobenzene in mildly acidic ($pH \sim 2$) aqueous solution (λ_{max} 510 mμ). The existence of VII as the acidic form thus seems unlikely. Likewise optical evidence points frequently toward the hydrazone-type structure IV at least for naphtholazobenzenes.[3] For example, Müller, Blangey and Fierz-David[3b] showed that Orange I in neutral solution, for which either X or XI may be drawn, has an absorption spectrum (λ_{max} 470 mμ) which is very similar to the N-methyl derivative (λ_{max} 466 mμ) but not comparable to the O-methyl derivative (λ_{max} 402 mμ). The O-methyl and N-methyl derivatives (XII and


IX


X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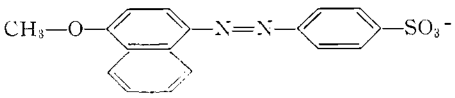
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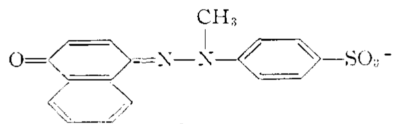
XIII

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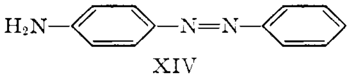
(1) J. T. Hewitt, *Analyst*, **33**, 85 (1908).

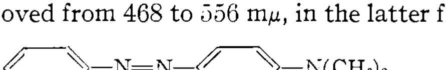
(2) A. Hantzsch and F. Hilscher, *Ber.*, **41**, 1171 (1908); A. Hantzsch and A. Burawoy, *ibid.*, **63**, 1760 (1930).

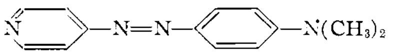
(3) (a) A. Burawoy, A. G. Salem and A. R. Thompson, *J. Chem. Soc.*, 4793 (1952); (b) J. B. Müller, L. Blangey and H. E. Fierz-David, *Helv. Chim. Acta*, **35**, 2579 (1952); (c) J. N. Ospenson, *Acta Chem. Scand.*, **5**, 491 (1951). Citations of most of the earlier literature will be found in these references.

XIII, respectively) were prepared by presumably unequivocal means. It seems reasonable, therefore, to assign structure XI to Orange I in neutral solution.

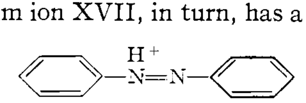
The optical data do not always lead to such clear-cut interpretations, however. It is apparent in many cases that relatively small changes in the structure of a substituent, changes which should have only minor effects on the resonance structures, produce major shifts in absorption spectra, equivalent in magnitude to those used to choose between formulas such as X and XI. Thus 4-aminoazobenzene (XIV) possesses an absorption maximum at 380 mμ in neutral aqueous solution; replacement of the two amino hydrogen atoms by methyl groups, leading to V, shifts the spectrum peak to 450 mμ. Even more striking are the major shifts produced when one proton is added to pyridine-2-azo-*p*-dimethylaniline (XV) or to pyridine-4-azo-*p*-dimethylaniline (XVI). In the former molecule λ_{max} is moved from 468 to 556 mμ, in the latter from 475 to 553 mμ. The first proton in each case undoubtedly goes to the pyridine nitrogen as will be shown later; although it should have little effect on resonance between structures corresponding to V and VI, the proton produces major shifts in the spectra.


XIV


XV


XVI

The assignment of structure VIII to the singly charged cation of 4-dimethylaminoazobenzene and of XI to the mono-anion of Orange I has seemed to us somewhat unreasonable from a qualitative consideration of the relative basicity of the groups involved.[4] Dimethylanilinium ion dissociates with a *pK* of 5.1.[5] An electrophilic substituent such as —N=N— in the *para* position would be expected to decrease the basicity of the aniline nitrogen; if $-NO_2$ is considered as roughly comparable in electrophilic character to —N=N—, the *pK* of the dimethylanilinium ion might be as low as 3 (the observed *pK* of *p*-nitrodimethylanilinium ion). The azobenzenium ion XVII, in turn, has a *pK* of −2.5, as will be shown in the Experimental section. A $(CH_3)_2N$- substituent might raise this *pK* about 1–2 units, perhaps even to 0.0. The observed *pK* of the mono-cation of 4-dimethylaminoazobenzene is 3.5. These results favor structure VII rather than VIII.


XVII

Similarly, in the hydroxy-substituted series phenol has a pK_a of 9.9; the —N=N— group should increase the acidity of the -OH substituent by about 2–3 *pK* units, if one may judge from *p*-nitrophenol (pK_a 7.0). The observed pK_a's of 4-hydroxyazobenzene and of the benzeneazonaphthols such as Orange I are near 8. Thus the acidity constant is in good agreement with structure X. Nevertheless structure XI cannot be ruled out unequivocally.

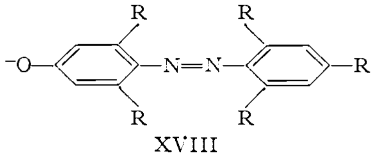
It seemed desirable, therefore, to determine the *pK*'s of a number of related substituted azobenzenes, so as to be able to settle this question convincingly. The measurement of acidity constants, rather than the accumulation of additional absorption spectra, seemed preferable because the former reflects only the energy of the ground state of the molecule (in its acidic and basic forms). On the other hand, the absorption spectrum may respond to influences on both the ground and excited states of the molecule. Despite recent theoretical work on the nature of these states in azobenzene compounds[6] and on charge distributions in analogous stilbene derivatives,[7a,b] it would be difficult to predict with confidence whether the introduction of a particular substituent has a greater effect on the lower- or the higher-energy state.

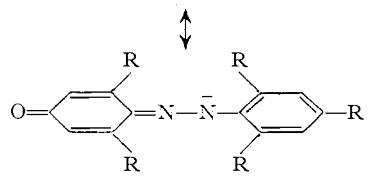
Results

Acidity constants have been determined over the range of *p*H from 10 to 1 in aqueous solution and in sulfuric acid solutions from approximately 0.3 to 18 *M*. The methods used are described in the Experimental section. The results have been assembled in Table I in a form which facilitates comparison of corresponding *pK*'s.

Discussion

The results assembled in Table I consistently support the benzenoid type of structure (*i.e.*, VII and X) and in several cases seem to rule out the quinoid alternative unequivocally. Thus, comparing the *pK*'s of compounds 2 and 3 in the *p*H region of 8–9, we can make the following prediction. If the anion in basic solution (above *p*H 10) is represented by the two resonance forms XVIII and XIX, then the following alternatives exist. (1) If the proton which goes on as the acidity is increased be-


XVIII


XIX

R = H (no. 2)

R = CH_3 (no. 3)

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[4] Similar doubts have been expressed by H. H. Jaffe, *J. Chem. Phys.*, **21**, 415 (1953), on the basis of comparative values of Hammett ρ-constants.

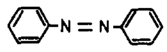
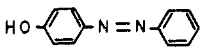
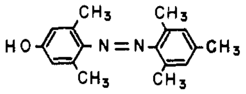
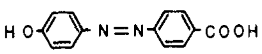
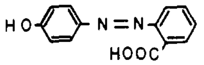
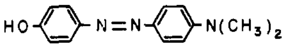
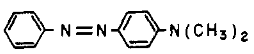
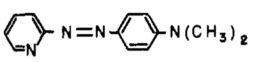
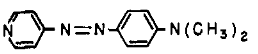
[5] N. F. Hall, THIS JOURNAL, **52**, 5115 (1930).

[6] P. P. Birnbaum, J. H. Linford and D. W. G. Style, *Trans. Faraday Soc.*, **49**, 735 (1953).

[7] (a) C. A. Coulson and J. Jacobs, *J. Chem. Soc.*, 1983 (1949); (b) R. N. Beale and E. M. F. Roe, THIS JOURNAL, **74**, 2302 (1952); *J. Chem. Soc.*, 2755 (1953).

Table I

Acidity Constants (pK_a) for Azobenzene Derivatives at 25°.

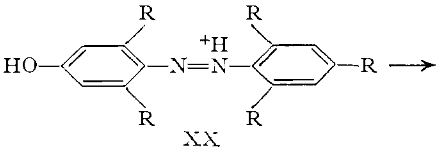
No.	Compound	pH Range -4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9
1				-2.48											
2					-0.93									8.2	
3					-1.30										9.1
4				-1.64										7.9	
5					-1.26									8.2	
6				-1.81					3.4						8.6
7		-4.37							3.5						
8								2.0[a]		4.5[a]					
9									3.4			5.8			

[a] Taken from I. M. Klotz and W.-C. L. Ming, This Journal, **75**, 4159 (1953).

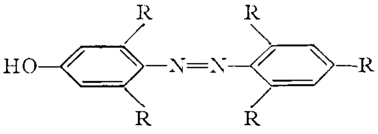
comes attached to the oxygen, the replacement of H by CH_3 should produce no direct steric effect, but may interfere with resonance between the azo group and the left-hand benzene ring. Such an interference would tend to increase the negative charge and hence the basicity of the oxygen. Thus if the proton goes to the oxygen, pK_a should be increased when R is changed from H to CH_3. (2) If H^+ goes to the azo nitrogen, the presence of four CH_3 groups *ortho* to the azo group should cause some direct steric interference toward the approach of the proton. It is possible, however, that such interference would be minor when the approaching ion is so small. Steric interference with resonance between the —N=N— and benzene ring also would tend to decrease the basicity of the charged $-\bar{N}-$ in XIX, although again one might argue that this effect should be small. In any event, according to this second alternative, replacement of H atoms by CH_3 groups (*ortho* to the —N=N—) should either lower pK_a or leave it unchanged.

Experiment shows (Table I) that the pK_a of the conjugate acid of compound 3 (XVIII ↔ XIX) in dilute aqueous alkali is higher than that of compound 2 by almost a full unit. The increase in pK_a as H is replaced by CH_3 is consistent only with the benzenoid structure.

The pK_a's in sulfuric acid solutions also fit this interpretation although they do not in themselves permit one to rule out the quinoid structure. Since the pK's near 8 refer to the dissociation of a proton from the oxygen, those in sulfuric acid refer to the dissociation



XX



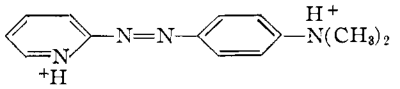
XXI

R = H (no. 2)
R = CH_3 (no. 3)

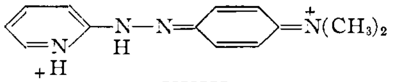
Compared to the pK_a of −2.48 for the parent compound, it is reasonable to expect a pK_a near −1 for the hydroxy-substituted derivatives XX and XXI, since the resonance of the HO– with the ring increases the basicity of the right-hand azo nitrogen. Furthermore, it is reasonable to expect compound 3 to be a somewhat weaker base than compound 2 because of the steric effect of the *o*-methyl groups. The observed shift in pK_a from −0.93 to −1.30 when four methyl groups are introduced is thus predicted.

Further evidence for the benzenoid structure is available from an examination of the pK's of compounds 4 and 5 in Table I. It is necessary to keep in mind that the pK of the carboxyl group is near 4, so that at pH's near 8, it is entirely in the form of the anion, $-COO^-$. Under such circumstances, if the first proton becomes attached to the azo nitrogen, it seems reasonable to expect that (1) the shift of a $-COO^-$ ion from the *para* to the *ortho* position should increase the stability of the conjugate acid by a very substantial amount and (2) that compound 5 should have a markedly higher pK_a than compound 2, in which there is no negative charge in the neighborhood of the azo nitrogen. Hydrogen bonding possibilities in the *ortho* compound ought to accentuate these effects even further.[8] Actually, compounds 2 and 5 have essentially identical pK's in the region near pH 8, and the difference between 4 and 5 is inconsequential. Such behavior again can be understood only on the basis of the benzenoid type of structure.

A definite decision also appears possible for the 4-dimethylaminophenyl azo compounds by a comparison of the pK_a's in aqueous solution ($pH > 0$) of compounds 7, 8, 9. With the last two, there is little doubt that the first proton which is attached as the pH decreases from near 7, should be placed on the pyridine nitrogen. Only on this basis can one justify the rise of the least acidic pK_a from 3.5 in compound 7 to 4.5 and 5.8 in compounds 8 and 9, respectively. If these latter pK's were attributed to either the azo or dimethylamino nitrogen, it would be difficult to understand why the insertion of an electron-attracting pyridine nitrogen, as one goes from compound 7 to 8 or 9, should increase the basicity of the —N=N— or $-N(CH_3)_2$ group. The pK_a near 5 must refer then to the pyridinium ion. The second proton, as one goes to more acid solution, should be taken up, therefore, at one of the two remaining positions to give XXII or XXIII, analogous to VII and VIII, respectively. The pK_a of the reference compound (no. 7 in Table I), in which a benzene ring replaces the pyridine, is 3.5. It is difficult to believe that the introduction of the positively charged pyridinium nitrogen only one carbon atom removed from the nitrogen holding the second proton, as would be required by structure XXIII, should decrease pK_a by only 1.5 units. In an analogous situation, 2-aminopyridine, the first proton has a pK_a of 6.63 in water[9] and the second cannot be put on even at pH's as low as 2. Thus a positively charged nitrogen one carbon atom removed from the potentially basic second nitrogen lowers the pK by an unknown amount but more than 3 units. Furthermore, it is equally unlikely that for compound 9 in which the pyridinium nitrogen would be removed by three atoms from the azo nitrogen according to the structure analogous to XXIII, the pK_a should be 3.4, not appreciably different from the reference compound (no. 7).[10]



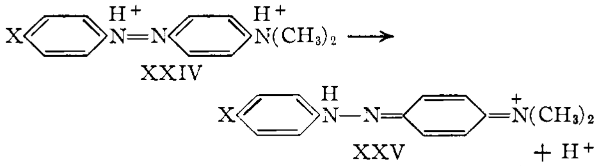
XXII



XXIII

On the other hand, structure XXII would account well for the facts. The drop in pK_a of the dimethylamino nitrogen from 3.5 to 2.0 on introduction of the pyridinium nitrogen (*cf.* compound 7 and 8, Table I) is reasonable. Likewise the shift of the pyridinium charge from the *ortho* to the *para* position (relative to the azo group) places the positive charge approximately 12 Å. away from the ionizing dimethylammonium group and hence the effect on the pK_a of the latter is undetectable. There are good indications from the pK's of crystal violet[11] that positively charged ammonium groups separated by approximately 12 Å. are without appreciable influence on each other's dissociation characteristics.

Other pK_a's also strengthen the conclusion that the benzenoid structure is to be preferred to the quinoid structure for the substituted azobenzenes. With compound 6 of Table I it has been observed that the pK_a of the phenolic hydroxy group is 8.6, about 0.4 unit higher than with compound 2. Evidently the added $-N(CH_3)_2$ substituent has only a minor effect in the direction, as might be expected from a survey of pertinent resonance forms, of decreasing the extent of double bond formation of the HO- group with the ring. Conversely, one would expect a diametrically opposite HO- group to have only a very small effect on the basic properties of the dimethylamino nitrogen. According to the quinoid viewpoint, however, the pK_a's in sulfuric acid of compounds 6 and 7 refer to the dissociation



X = H (no. 7)
X = OH (no. 6)

It is difficult to understand, therefore, why pK_a

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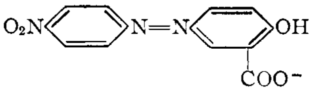
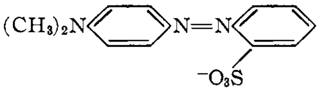
[8] In the analogous situation with phenol, the shift of the $-COO^-$ group from the *para* to the *ortho* position raises the pK by over 3 units (C. T. Abichandani and S. K. K. Jatkar, *J. Indian Inst. Sci.*, **21A**, 417 (1938); *C. A.*, **33**, 3662 (1939)). Likewise we have found that



has a pK of 11.0, which may be compared with 8.2 for compound 2 (Table I). It is apparent that a carboxy anion *ortho* to the phenolic oxygen has a pronounced effect on the basicity of the latter, yet *ortho* to the azo group the carboxy anion produces only a minor change.

[9] L. C. King and E. Stern, private communication. See also J. P. Wibaut, in "Progress in Organic Chemistry," Volume 2 edited by J. W. Cook, Academic Press, Inc., New York, N. Y., 1953, for similar results in an ethanol–water mixture.

[10] A similar situation exists with *o*- and *p*-methyl orange, with



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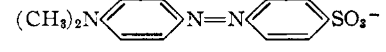
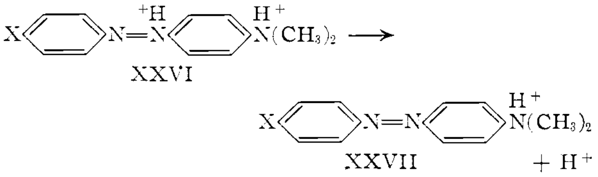


pK's of 3.47 and 3.40, respectively (A. Thiel, A. Dassler and F. Wülfken, *Fortsch. Chem. Physik u. physik. Chem.*, **18**, No. 3 (1924)). It is difficult to believe that the shift of the sulfonate group from the *para* to the *ortho* position should have so little effect on the base strength of the azo group.

[11] E. Q. Adams, THIS JOURNAL, **38**, 1503 (1916).

changes from −4.37 to −1.81 when X is changed from H to OH. On the other hand, if the dissociation in sulfuric acid refers to the reaction


XXVI

XXVII

X = H (no. 7)
X = OH (no. 6)

then when X is made OH a base-strengthening effect is in line with the expected resonance effect of an hydroxy group *para* to an —N=N— substituent.

All of the compounds in Table I contain only monocyclic systems. One might inquire then whether similar conclusions are justified for the benzeneazonaphthols. With the backlog of information available from the above considerations, it seems most pertinent to examine the acid–base properties of these compounds. In the course of other studies of spectroscopic changes of Orange I (X and XI), we have found[12] that pK_a is near 8, essentially the same as for the corresponding benzene compound (no. 2, Table I). There seems little reason to doubt, therefore, that structure X, rather than XI, is the correct one for Orange I.

On the other hand, it should be emphasized that all of the information obtained here refers to aqueous solution. A corresponding state of affairs may not be assumed to exist in non-aqueous media.

In water solution, however, the conclusion seems inescapable that the uptake of protons leads to a benzenoid rather than a quinoid structure and that the relative basicities of the possible competing groups lie in the order: $^-$O > pyridine N > $-N(CH_3)_2$ > —N=N—.

Experimental

Materials.—The azo compounds were prepared by the following procedures. Azobenzene from a commercial source was recrystallized from alcohol–water mixtures and dried over P_2O_5 *in vacuo*. 4-Hydroxyazobenzene, also from a commercial source, was recrystallized from 95% ethanol; m.p. 151–153° (lit.[13] 152°). A sample of 4-hydroxy-2,2′,4′,6,6′-pentamethylazobenzene was obtained through the kindness of Dr. W. R. Brode.[14] 4-Hydroxy-4′-dimethylaminoazobenzene was prepared by coupling the diazonium salt of *p*-aminophenol with dimethylaniline. The product, recrystallized from 95% ethanol, melted with decomposition at 200–201° (lit.[15] 203–204°). Samples of pyridine-2-azo-*p*-dimethylaniline and of pyridine-4-azo-*p*-dimethylaniline were kindly supplied by Dr. E. V. Brown.[16] 2-Carboxy-4′-hydroxyazobenzene was prepared by Mr. S. Preis following the procedure of Borsche, Müller and Bodenstein.[17] The material purified from methanol–ether mixtures melted at 202–205° (lit.[17] 206–207°). 4-Carboxy-4′-hydroxyazobenzene was prepared by the same procedure and recrystallized from acetic acid; m.p. 273° dec. (lit.[18] 266° dec.). 4-Dimethylaminoazobenzene from a commercial source was purified from ethanol–water mixtures; m.p. 119–120° (lit.[19] 117°).

Phosphate or borate salts, together with sodium hydroxide, were used to prepare buffers in the *p*H region around 8. Buffers near *p*H 4 were prepared from acetate or glycine solutions, adjusted with hydrochloric acid. All of these materials, as well as the sulfuric acid used for the very low *p*H's, were of reagent grade.

Methods.—All of the dissociation constants were determined by optical methods. In general, spectra were taken over a range of *p*H's on both sides of the *pK*. The optical density at the wave length of maximum absorption of either the acid or conjugate base (in some cases of both) was then plotted as a function of *p*H. The *p*H of the mid-point in such a curve was taken as *pK*.

The experiments in sulfuric acid were similar to those of Rogers, Campbell and Maatman.[20] It was our experience, however, that several of the azo compounds were unstable in concentrated sulfuric acid solutions in the presence of light. For this reason solutions of such dyes were made up in flasks painted black. With precautions taken to protect the solutions from light, the dyes were stable.

Computations of *pK* in aqueous sulfuric acid were carried out by the method used by Rogers, Campbell and Maatman,[20] as well as by the graphical procedure described above. Essentially the same results were obtained by both methods. Furthermore, with dimethylaminoazobenzene our *pK* of −4.37 agrees well with that of −4.50 obtained by these workers.[20] All computations in sulfuric acid were based on the extended *p*H scale of Michaelis and Granick.[21]

The primary source of error in our experiments is due to uncertainties in temperature. No efforts were made to maintain the solutions at constant temperature. For this reason most of the *pK*'s are listed only to 0.1 unit and refer to 25 ± 3°. The spectrophotometric method is inherently capable of much greater precision, but for the purpose of the present investigation the uncertainty is from one to several orders of magnitude smaller than the differences in ionization constant which provide criteria for a choice between alternative structures.

Acknowledgment.—These investigations were aided by a grant from the Rockefeller Foundation and by a contract between the Office of Naval Research, Department of the Navy, and Northwestern University, NR 124 054.

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[12] See also K. H. Slotta and W. Franke, *Ber.*, **64**, 86 (1931).

[13] "Dictionary of Organic Compounds," edited by I. M. Heilbron and H. M. Bunbury, Vol. 2, Oxford University Press, New York, N. Y., 1936, p. 230.

[14] W. R. Brode, J. H. Gould and G. M. Wyman, This Journal, **75**, 1856 (1953).

[15] J. T. Hewitt and W. Thomas, *J. Chem. Soc.*, **95**, 1295 (1909).

[16] R. W. Faessinger and E. V. Brown, This Journal, **73**, 4606 (1951).

[17] W. Borsche, W. Müller and C. A. Bodenstein, *Ann.*, **472**, 201 (1929).

[18] A. Angeli and B. Valori, *Atti accad. Lincei*, **22**, 1, 132 (1913); *C. A.*, **7**, 2223 (1913).

[19] Reference 13, Vol. 1, page 562.

[20] M. T. Rogers, T. W. Campbell and R. W. Maatman, This Journal, **73**, 5122 (1951).

[21] L. Michaelis and S. Granick, *ibid.*, **64**, 1861 (1942).