total volume of effluent showed transient maxima, presumably as a result of displacement of the less strongly adsorbed substrate by the more strongly adsorbed one.[26]

Chromatography on plain silicic acid. The procedure was the same as with impregnated silicic acid except that a total of 5.5 g. of plain adsorbent was used instead. Data are also to be found in Table I.

Chromatography on alumina. Into a 2.5×11.5 cm. column of alumina (packed and prewashed as for silicic acid) was passed 200 ml. of isooctane solution *ca.* $5 \times 10^{-5}M$ in each of V and VI. The column was then eluted with 2% (by volume) acetone in isooctane and the effluent was analyzed as previously. Nearly all of V had been eluted before VI began to appear.

This procedure was repeated for use of I and IV except that the size of the column was 2.5×20 cm., 10 ml. of solution *ca.* $5 \times 10^{-3}M$ in each substrate was used, and elution was conducted with 300 ml. of isooctane. I attained a maximum concentration in the effluent at a cumulative volume of 150 ml. and dropped to an immeasurably low value at 250 ml. Meanwhile no concomitant effusion of IV was evident.

EUGENE, ORE.

(26) Ref. 14, pp. 225–6.

[CONTRIBUTION FROM THE CANCER RESEARCH LABORATORY, UNIVERSITY OF FLORIDA]

Physical Properties of Aminoazobenzene Dyes. VI. Intramolecular Hydrogen Bonding and Tautomerism in 4-Hydroxyazobenzene Derivatives and Higher Homologs[1]

EUGENE SAWICKI[2]

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The phenylhydrazone ⇄ azo dye tautomerism of 2′-methyl-, 4′-methyl-, 2′-methoxycarbonyl-, 4′-ethoxycarbonyl-, and unsubstituted derivatives of 4-phenylazo-1-naphthol and 5-phenylazo-8-hydroxyquinoline has been studied in alcoholic solution. In 5-(2′-methoxycarbonylphenylazo)-8-hydroxyquinoline the intramolecular hydrogen bond between the methoxycarbonyl ketonic oxygen and the azonium hydrogen involved in the 6-membered ring of the phenylhydrazone tautomer was of the same order of energy as the intramolecular hydrogen bond between the heterocyclic nitrogen and the hydroxyl hydrogen in the 5-membered ring of the azo tautomer. The 2′- and 4′-electron donor and electron attractor substituents studied in this paper were found to have similar qualitative effects on the tautomerism of 4-phenylazo-1-naphthol in alcohol and the tautomerism of the monocationic salt of 4-dimethylaminoazobenzene.

4-Hydroxyazobenzene has been shown to exist in alcohol in the azo form, λ_{max} 350 mμ.[3] Shingu[4] has shown that electron attractor substituents in the benzene ring of 1-phenylazo-4-naphthols increase the relative proportion of the phenylhydrazone tautomer while electron donor substituents in the 4′-position of the benzene ring increase the proportion of the azo tautomer. Each of these tautomers has a characteristic absorption spectrum with the azo tautomer absorbing at shorter wavelengths.[3] In this respect the 2′,4′-dinitro derivative of 4-hydroxyazobenzene acts like the 2,4-dinitrophenylhydrazone of *p*-benzoquinone in that it shows evidence of quinonoid character by its ability to undergo the Diels-Alder reaction with cyclopentadiene.[5] The discovery of the existence of a tautomeric equilibrium in solution between 4-phenylazonaphthol (I) and naphthoquinone monophenylhydrazone (II) by Kuhn and Bär[3] has been confirmed spectrally by Burawoy and Thompson,[6] Ospenson,[7] Badger and Buttery,[8] and Hadzi.[9] Ospenson has also given spectral evidence that 4-phenylazo-1-anthrol exists in alcohol almost completely in the phenylhydrazone form. From a study of the spectrum of 9-phenylazo-10-anthrol and appropriate derivatives in alcohol, Shingu[4] has concluded that the compound exists in solution only as anthraquinone monophenylhydrazone. These results parallel the reduction potentials[10] in alcohol of *p*-benzoquinone, $0.71v$; 1,4-naphthoquinone, $0.49v$; 1,4-anthraquinone, $0.40v$; and 9,10-anthraquinone, $0.15v$. *p*-Benzoquinone is the least stable of the *p*-quinones and the equilibrium Ph—NH—N═Ar═O ⇄ Ph—N═N—Ar—OH is displaced completely to the right; 9,10-anthraquinone is the most stable of these quinones and the equilibrium is displaced completely to the left.

The spectral data of Badger and Buttery[8] indicate that 4-phenylazo-1-naphthol exists in absolute alcohol solution as an equilibrium mixture of the

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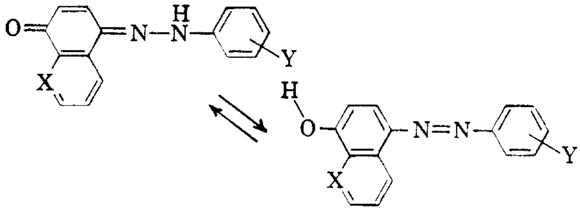
azo and the phenylhydrazone tautomers, the former in slight excess. These authors have found that 5-phenylazo-8-hydroxyquinoline exists almost entirely in the azo form. This shift in the equilibrium has been attributed to the presence of a weak intramolecular hydrogen bond between the heterocyclic nitrogen and the hydroxyl hydrogen. This, of course, would tend to stabilize the azo tautomer. Badger and Buttery's results are confirmed and extended in Figure I and Table I.

TABLE I

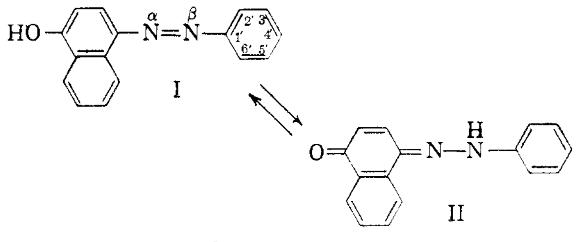
PHENYLHYDRAZONE ⇄ PHENYLAZO TAUTOMERS

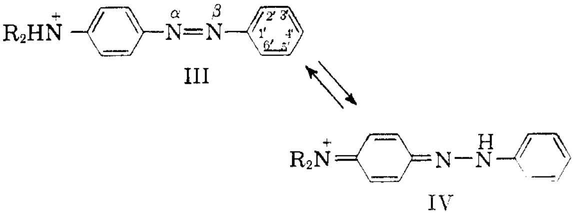


X	Y	$\lambda_{max}(\epsilon \times 10^{-3})$ P	A	P_ϵ/A_ϵ	DAB[a] Deriv.	C_ϵ/A_ϵ[b]
N	4'-CH_3	~(465)[c](4.8)	387(24.4)	0.20		
CH	2'-CH_3	~(465)(4.25)	403(17.7)	0.24	2'-CH_3	0.29
N	2'-CH_3	~(465)(5.7)	388(21.9)	0.26		
	H	(462)(5.5)	387(21.1)	0.26		
	4'-$COOC_2H_5$	~(465)(8.4)	402(23.7)	0.33		
CH	4'-CH_3	~(465)(10.5)	407(23.9)	0.44	4'-CH_3	2.6
	H	464(11.5)	409(15.4)	0.74	H	3.6
N	2'-$COOCH_3$	460(16.1)	395(14.4)	1.1		
CH	4'-$COOC_2H_5$	465(33.6)	~400[d](8.45)	~4	4'-$COOC_2H_5$	~6–8[e]
	2'-$COOCH_3$	466(31.9)	~400[d](5.00)	~6	2'-$COOCH_3$	13.1

[a] DAB is 4-Dimethylaminoazobenzene. [b] Reference 11. [c] Wave length values in parentheses are shoulders. [d] Not a λ_{max} or a definite shoulder. The main band at 465–466 mμ is unsymmetrical, sloping more gradually on the short wave length side. [e] Predicted value.

The P_ϵ/A_ϵ ratio in Table I gives an approximate idea of the relative proportion of phenylhydrazone to azo tautomer present in solution. P_ϵ is the molar extinction coefficient at the wave length maximum (or shoulder) of the phenylhydrazone tautomer; A_ϵ is the molar extinction coefficient at the wave length maximum of the azo tautomer. The ratio is approximate mainly because of the varying electronic and steric effects of diverse substituents. In 4-phenylazo-1-naphthol the presence of a 2'-methyl and/or an 8-aza group decreases the P_ϵ/A_ϵ ratio considerably (Table I). This effect of a 2'-methyl group is in line with the fact that the presence of this group in the 4-aminoazobenzene dyes has been shown to have a base-weakening effect on the adjacent β-nitrogen.[11] The same order of decrease is caused by the stabilization of the azo tautomer through the formation of an intramolecular hydrogen bond between the 8-aza nitrogen and the hydroxyl hydrogen. The electron donor 4'-methyl group decreases the P_ϵ/A_ϵ ratio while the electron attractor 4'-ethoxycarbonyl group increases this ratio in 4-phenylazo-1-naphthol (Table I). This agrees with Shingu's results.[4] The substitution of an 8-aza group in these compounds and the consequent intramolecular hydrogen bonding has a buffering action on the equilibrium so that both the methyl and ethoxycarbonyl groups have a much weaker effect (Table I). The striking effect of analogous substitutions in the 2'- and 4'-positions on the I ⇄ II tautomerism of 4-phenylazo-1-naphthol in 95% ethanol and the III ⇄ IV tautomerism of 4-dimethylaminoazobenzene in 50% alcoholic 1*N* hydrochloric acid is noticeably similar.





It has been shown[11] that in the monocationic salts of 4-aminoazobenzene derivatives the presence of a 2'-carboxy group considerably increases the proportion of the C tautomer (IV) involving proton addition to the β-nitrogen as compared to the A tautomer (III). This increase has been mainly attributed to the stabilization afforded by the in-

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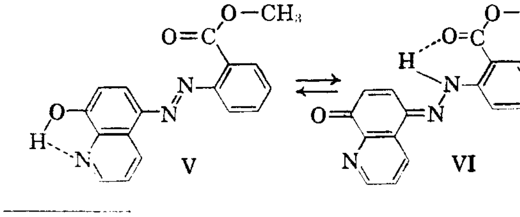
(11) E. Sawicki, *J. Org. Chem.*, 21, 605 (1956).

tramolecular hydrogen bonding involving the azonium hydrogen and the carboxy ketonic oxygen. In these monocationic salts the C_ϵ/A_ϵ ratio was found to give an approximate idea of the ratio of C to A tautomers present in acid solution. C_ϵ is the molar extinction coefficient at the long wave length maximum of the C tautomer; A_ϵ is the molar extinction coefficient at the long wave maximum of the A tautomer (e. g. III). As the I $\rightleftarrows$ II tautomeric system has evident geometrical and electronic differences from the III $\rightleftarrows$ IV tautomeric system one could not expect a strictly similar effect of all types of analogous substitutions on these two tautomeric systems. Just as in the 4-aminoazobenzene cationic salts the substitution of a 2′-methoxycarbonyl group into 4-phenylazo-1-naphthol strongly increases the P_ϵ/A_ϵ ratio. Part of this increase must be due to the electron attracting properties of the methoxycarbonyl group but the intramolecular hydrogen bond, involving a 6-membered ring, must also tend to stabilize the phenylhydrazone tautomer. An electron attracting substituent in the 4′-position of 4-aminoazobenzene causes an increase in the stability of the IV form, *i. e.*, the C_ϵ/A_ϵ ratio becomes larger. On the other hand an electron-donor substituent, such as the methyl, methoxy, or methylthio group, in the 4′-position decreases the C_ϵ/A_ϵ ratio.[12] This corresponds with somewhat similar effects of electron donor and electron acceptor substituents on the P_ϵ/A_ϵ ratio of 4-phenylazo-1-naphthol.[4]

In 5-(2′-methoxycarbonylphenylazo)-8-hydroxyquinoline the intramolecular hydrogen bond, involving a 5-membered ring, in the azo tautomer (V) is pitted against the intramolecular hydrogen bond, involving a 6-membered ring, of the phenylhydrazone tautomer (VI). The spectrum of 5-(2′-methoxycarbonylphenylazo)-8-hydroxyquinoline consists of two broad bands, with maxima at 395 mμ (associated with the azo tautomer, V) and 460 mμ (associated with the phenylhydrazone tautomer, VI. The relative intensities of these bands as compared to the relative intensities of the analogous bands in 5-phenylazo-8-hydroxyquinoline, 4-phenylazo-1-naphthol, and 4-(2′-methoxycarbonylphenylazo)-1-naphthol indicate that the intramolecular hydrogen bond involved in the 6-membered ring is somewhat stronger than the intramolecular hydrogen bond in the 5-membered ring (Fig. 1).


V VI

EXPERIMENTAL[13]

5-(2′-Methoxycarbonylphenylazo)-8-hydroxyquinoline. All the compounds were essentially prepared by the following procedure. A diazotized solution of methyl anthranilate in aqueous hydrochloric acid was added to a stirred cold solution of 8-hydroxyqinoline in methanol. Enough potassium acetate was added to neutralize the hydrochloric acid. The mixture was kept below 5° for 12 hr. after which the mixture was filtered and washed thoroughly with water. Several crystallizations from methyl Cellosolve (2-methoxyethanol) gave an 80% yield of the dye, m.p. 164°.

Anal. Calcd. for $C_{17}H_{13}N_3O_3$. N, 13.7. Found. N, 13.5.

4-Phenylazo-1-naphthol,[14] m.p. 205° dec., 4-*o*-tolylazo-1-naphthol,[15] m.p. 146°, 4-*p*-tolylazo-1-naphthol,[15] m.p. 205–206° dec., 4-(4′-ethoxycarbonylphenylazo)-1-naphthol,[16] m.p. 247–248° dec., 5-*o*-tolylazo-8-hydroxyquinoline,[17] m.p. 181°, 5-*p*-tolylazo-8-hydroxyquinoline,[18] m.p. 191°, and 5-phenylazo-8-hydroxyquinoline,[19] m.p. 185–186°, were crystallized to constant melting point.[5]

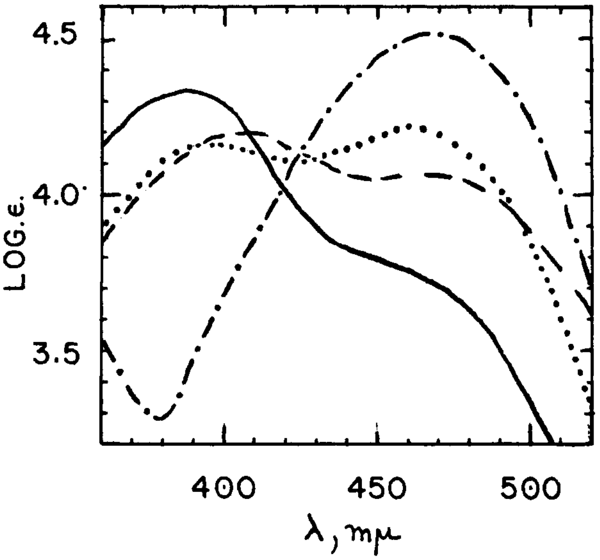


FIG. 1. VISIBLE ABSORPTION SPECTRA: 5-phenylazo-8-hydroxyquinoline (———); 4-phenylazo-1-naphthol (- - - -); 5-(2′-methoxycarbonylphenylazo)-8-hydroxyquinoline (......); and 4-(2′-methoxycarbonylphenylazo)-1-naphthol (-·-·-·)

5-(4′-Ethoxycarbonylphenylazo)-8-hydroxyquinoline. This compound was crystallized several times from xylene to give orange cotton-like needles, m.p. 215–216°.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$. N, 13.1. Found: N, 13.0.

4-(2′-Methoxycarbonylphenylazo)-1-naphthol. Several crystallizations from xylene gave orange crystals, m.p. 222°.

Anal. Calcd. for $C_{18}H_{14}N_2O_3$. N, 9.2. Found: N, 9.4.

Absorption spectral data. The spectra of all compounds were determined in commercial 95% ethanol containing 0.2% dioxane with a Beckman Model DU spectrophotometer. The dioxane was found to be necessary to facilitate solution of the dyes.

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(13) All melting points are uncorrected.

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