

*Aromatic Azo-compounds. Part V.\* The Absorption Spectra of  
N-Substituted 4-Aminoazobenzenes and their Mono-acid Salts.*

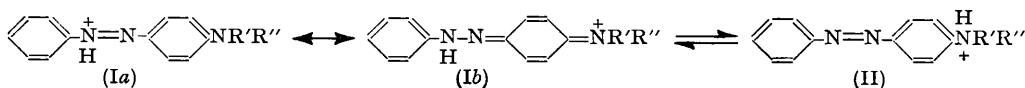
By G. M. BADGER, R. G. BUTTERY, and G. E. LEWIS.

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The absorption spectra of 4-aminoazobenzenes and of some *N*-substituted derivatives have been studied in neutral and in acid solutions. In general, the mono-acid salts show two absorption bands, one in the region 5000—5400 Å (*Q* band) and the other at 3200 Å (*K'* band). The results support the view that the salt cations exist in solution as an equilibrium mixture of two tautomeric forms, in which the proton is attached to the azo-linkage and to the amino-group, respectively. The ionisation constants of these aminoazobenzenes have also been determined from the spectra.

4-DIMETHYLAMINOAZOBENZENE ("Butter Yellow") is of considerable interest in carcinogenesis as it produces a high percentage of liver tumours in rats (for reviews see Badger and Lewis, *Brit. J. Cancer*, 1952, **6**, 270; Miller and Miller, "*Adv. Cancer Res.*," 1953, **1**, 339). Many related compounds are also carcinogenic, and it has been suggested that their activity is associated with an optimum degree of electron density at the azo-linkage (Pullman, *Compt. rend.*, 1946, **222**, 1501; 1947, **224**, 1773; Pullman and Pullman, *Rev. Sci.*, 1946, **84**, 145). In order to study this hypothesis experimentally the rates of peracid oxidation of substituted azobenzenes were determined (Badger and Lewis, *J.*, 1953, 2147). The effects of the various substituents were additive, and there was a strong correlation between the observed effect on the rate of oxidation and the magnitude of the Hammett  $\sigma$  constant for that substituent. Moreover, although further work was clearly required, the results were not inconsistent with the Pullman hypothesis.

Unfortunately, the reactivity of the amino-group itself towards peracids prevents the use of this technique with aminoazobenzenes (which are the most interesting derivatives in carcinogenesis). The present studies attempt to elucidate the relative effects of amino- and of substituted amino-groups on the azo-linkage.



It has long been maintained that hydrogen ions add to aminoazo-compounds at the azo-linkage (Ia) and that the observed deepening in colour is due to the contributing resonance structure (Ib) (Hantzsch and Hilscher, *Ber.*, 1908, **41**, 1171; Hantzsch, *ibid.*, 1919, **52**, 509; Kehrmann, *ibid.*, 1915, **48**, 1933; Bury, *J. Amer. Chem. Soc.*, 1935, **57**, 2115; Lewis and Calvin, *Chem. Reviews*, 1939, **25**, 273). In the absence of complicating factors, therefore, it was expected that the primary ionisation constants of a series of aminoazo-compounds would be an accurate measure of the relative electron densities at the azo-linkage. Rogers, Campbell, and Maatman (*J. Amer. Chem. Soc.*, 1951, **73**, 5122) have already found that there is a linear relationship between the Hammett  $\sigma$  constants and both the primary and secondary ionisation constants of 4'-substituted 4-dimethylaminoazobenzenes.

Following these authors' method we have evaluated the primary ionisation constants of 4-aminoazobenzene, and of various *N*-substituted derivatives, by examination of their absorption spectra in the region 3500—5000 Å at various acidities. The solvent employed was 50% (v/v) aqueous ethanol, and the optical-density measurements used in the calculations were taken in the 3800—4300-Å region. The results are given in Table I, together with the sulphuric acid concentration necessary to convert the free base into the mono-acid salt.

Except for the methylamino- and dimethylamino-derivatives, the results are in qualitative agreement with electronic theory. The lower ionisation constants produced

\* Part IV, *J.*, 1953, 2156.

by *N*-methyl-substitution, however, seem to be inconsistent with the high basicity of dimethylaniline compared with aniline (Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3472). This inconsistency raised doubts as to the validity of this method for determining relative electron densities at the azo-linkage. In this connection Hantzsch and Burawoy

TABLE I. Ionisation constants of *N*-substituted 4-aminoazobenzenes.

<i>N</i> -Substituent(s)	$pK_a$	Required acidity, N	<i>N</i> -Substituent(s)	$pK_a$	Required acidity, N
Ph	0.48 ± 0.03	6.8	H	2.30 ± 0.02	1.7
Me, CH <sub>2</sub> Ph	1.64 ± 0.04	5.0	Et	2.45 ± 0.02	1.7
Me, CH <sub>2</sub> ·CH <sub>2</sub> ·OH	2.01 ± 0.03	3.1	Me, Et	2.48 ± 0.03	1.7
2Me	2.21 ± 0.02	1.7	2Et	3.05 ± 0.03	0.85
Me	2.23 ± 0.03	1.7			

(*Ber.*, 1930, **63**, 1760) suggested that the salt cations exist in solution as an equilibrium mixture of the tautomeric forms (I) and (II) in which the proton is attached to the azo-linkage and to the amino-group, respectively. Spectrographic data were cited to support this suggestion, but as further information seemed desirable the present studies were extended to cover the range 2200—6600 Å in both neutral and acid solution. The results are collected in Table 2.

TABLE 2. Wave-lengths (Å) of the maxima and corresponding intensities ( $\times 10^{-3}$ ) in parentheses in the absorption spectra of azobenzenes and their mono-acid salts in aqueous ethanol.

Compound	Free base	Mono-acid salt	
	<i>K</i> band	<i>K'</i> band	<i>Q</i> band
Azobenzene	3200 (21.1)	—	—
Azoanisole	3500 (16)	—	5000 (43)
4-Phenylaminoazobenzene	4200 (28)	—	5400 (61)
4-( <i>N</i> -Methylbenzylamino)azobenzene	4200 (27)	3200 (9)	5300 (41)
4-( <i>N</i> -Methyl-2-hydroxyethylamino)azobenzene	4200 (26)	3200 (7)	5200 (47)
4-Dimethylaminoazobenzene	4200 (24)	3200 (10)	5200 (34)
4-Methylaminoazobenzene	4100 (23)	3200 (8)	5100 (39)
4-Aminoazobenzene	3800 (22)	3200 (18)	5000 (11)
4-Ethylaminoazobenzene	4100 (24)	3200 (13)	5100 (29)
4-( <i>N</i> -Ethylmethylamino)azobenzene	4300 (25)	3200 (15)	5300 (22)
4-Diethylaminoazobenzene	4400 (29)	3200 (20)	5200 (10)

Azobenzene has a strong absorption band (*K* band) at 3200 Å in neutral solution, and the spectra of aminoazobenzenes were found to be similar except that the *K* band is displaced bathochromically by about 600—1200 Å. On acidification, the *K* band was replaced by a band in the 5000—5400 Å region (*Q* band) and another at the constant wave-length of 3200 Å (*K'* band).

As Rogers, Campbell, and Maatman (*loc. cit.*) have shown, addition of the proton to the amino-group should result in the spectrum of the mono-acid salt being similar to that of azobenzene. 4-Dimethylaminoazobenzene methiodide has virtually the same absorption spectrum as azobenzene (Hantzsch and Hilscher, *loc. cit.*; Hantzsch and Burawoy, *loc. cit.*; Pongratz, Markgraf, and Mayer-Pitsch, *Ber.*, 1938, **71**, 1287). It is noteworthy that the *K'* bands of the mono-acid salts invariably occur at 3200 Å, the wave-length of the characteristic *K* band of azobenzene. In agreement with Hantzsch and Burawoy (*loc. cit.*), it seems that the *K'* band is associated with the ammonium form of the cation (II) and that the *Q* band is derived from the azonium form (I). In support of this, the mono-acid salt of 4 : 4'-azoanisole, which presumably exists only in the azonium form, shows an intense *Q* band at 5000 Å, but no peak at 3200 Å. It seems, then, that the cations are present as an equilibrium mixture in solution, the relative intensities of the *Q* and *K'* bands giving the approximate proportions of the two tautomers present.

The influence of a substituent at the amino-nitrogen atom on the position of the equilibrium will depend on its size and its electronic effect. Although electronic effects should be straightforward, and either increase or decrease the basicity, large substituents could hinder both the entrance of the hydrogen ion to the amino-nitrogen and the tendency

of the amino-group to assume coplanarity with the rest of the molecule. A comparison of the extinction coefficients of the *K'* and *Q* bands (Table 2) with the basicities (Table 1) shows that there is a general increase in the tendency for salts to exist in the ammonium form as the ionisation constants increase. The primary ionisation constants do not measure the relative electronic effects of amino- and substituted amino-groups on the azo-linkage, but merely the over-all basicity.

The published spectra of some methyl-4-dimethylaminoazobenzenes are interesting. Miller, Sapp, and Miller (*J. Amer. Chem. Soc.*, 1948, **70**, 3458) found that 4-dimethylamino-3-methylazobenzene has no absorption peak in the 5000-Å region in acid solution, but a very intense *K'* band at 3200 Å. This is because the 3-methyl group prevents the dimethylamino-group becoming coplanar with the ring system so that its tautomeric effect at the azo-linkage is restricted. In these circumstances the proton undoubtedly adds on to the amino-group in preference to the azo-nitrogen atom. Price and Lincoln (*J. Amer. Chem. Soc.*, 1951, **73**, 5838) attribute a much lower  $\sigma$  constant ( $-0.360$ ) to the 4-dimethylamino-3-methyl group combination than to the 4-dimethylamino-group alone ( $-0.720$ ).

Miller, Sapp, and Miller (*loc. cit.*) also showed that there is a marked difference between the spectra of 4-dimethylamino-2-methylazobenzene and that of 4-dimethylamino-2'-methylazobenzene. The former shows an intense *Q* band and a much weaker peak at 3200 Å; but the latter has an intense *K'* band at 3200 Å and a much weaker *Q* band. It has been shown (Badger and Lewis, *J.*, 1953, 2147; Badger and Buttery, *J.*, 1953, 2156) that *o*-methyl groups afford considerable steric hindrance at the nearer azo-nitrogen atom, and the preferential attachment of the hydrogen ion to the amino-group in 4-dimethylamino-2'-methylazobenzene, as shown by its spectrum in acid solution, is satisfactorily explained on this basis. With 4-dimethylamino-2-methylazobenzene there is no steric hindrance with the azo-nitrogen atom in question and the attack of the proton is therefore unhindered. This results in the predominant formation of the azonium cation, and hence the intense *Q* band observed.

#### EXPERIMENTAL

**4-Aminoazobenzene.**—This was prepared from diazoaminobenzene (Vogel, "Textbook of Practical Organic Chemistry," Longmans Green and Co., 1948, p. 599), and had m. p. 125°.

**4-Methyl- and 4-Ethyl-aminoazobenzene.**—These were prepared by the action of the appropriate alkyl halide on 4-aminoazobenzene (Berju, *Ber.*, 1884, **17**, 1401). They had m. p. 88° and 87°, respectively.

**Phenylaminoazobenzene.**—This was formed by coupling benzenediazonium chloride with diphenylamine (Witt, *Ber.*, 1879, **12**, 259). It had m. p. 82°.

**NN-Disubstituted Aminoazobenzenes.**—In each case these were prepared from benzenediazonium chloride and the appropriate disubstituted aniline (Miller and Miller, *J. Exptl. Med.*, 1948, **87**, 139). The melting points agreed with those recorded by Miller and Miller.

**Chromatography.**—All compounds were purified by passage through alumina, and finally recrystallised from benzene-light petroleum.

**Solvent.**—The aqueous ethanol used throughout was prepared from equal volumes of distilled water (or sulphuric acid of the requisite concentration) and absolute alcohol which had been refluxed over solid sodium hydroxide and subsequently fractionated.

**pH Measurements.**—These were made with a Cambridge bench type pH meter. In highly acidic solutions the total concentration of sulphuric acid was used as a guide to the approximate pH (Michaelis and Granick, *J. Amer. Chem. Soc.*, 1942, **64**, 1861).

**Absorption Spectra.**—All spectra were determined with a Hilger "Uvispek" spectrophotometer. The concentration of azo-compound in each case was  $0.5 \times 10^{-4}$ M.

**Ionisation Constants.**—These were calculated from optical-density measurements, after Beer's law had been checked. The acidities necessary to complete the addition of the first hydrogen ion were determined by plotting optical densities against pH.

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