Unusual Reactions of Aryl Diazonium Sulphonates Possessing *ortho*-t-Amino-substituents

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Aryl diazonium sulphonates with an *ortho*-t-amino-substituent cyclise on treatment with sulphur dioxide to give triazines and benzimidazolium sulphonates. Hot aqueous sodium hydroxide causes loss of nitrogen from these heterocycles with formation of the corresponding t-amino-aryls and -lactams. A reaction mechanism involving the t-amino-group is postulated.

AROMATIC compounds with an *ortho*-t-amino-substituent often react in an unusual way undoubtedly owing to the influence of the t-amino-group. For instance, Spiegel and Kaufmann [1] reported that reduction of 2,4-dinitrophenylpiperidine gave not only the expected amino-compound but also the benzimidazole (XVI; R = NO_2, $n = 4$). Other examples in which the 'tertiary nitrogen' plays a key-part are the cyclisation of *N*-acylaminophenyl heterocycles with peracids [2] or polyphosphoric acid [3] and also that of *N*-*o*-aminophenyl heterocycles with hydroxylamine and chloral hydrate [4] to give benzimidazoles. Moreover, alloxan which reacts normally with *p*-aminodimethylaniline to give an anil, cyclises with the *ortho*-isomer to a quinoxaline [5] and with *o*-aminodiethylaniline to a benzimidazolium structure.[6]

We now report yet another case of the 't-amino-group effect' which leads to unexpected reactions in aromatic diazo-compounds.

When an alkaline solution of *o*-piperidinobenzenediazonium chloride (I; B = $C_5H_{10}N$) is treated for a short time with sulphur dioxide the stable, yellow diazosulphonate (II; B = $C_5H_{10}N$) is obtained which is analogous to the intermediate produced from aniline in the well known aryl hydrazine preparation.[7] If, however, the alkaline solution was acidified by the passage of sulphur dioxide for a sufficiently long period, or sulphur dioxide was passed briefly through an aqueous suspension of the purified diazosulphonate (II), a mixture of two substances was deposited. The major constituent was sparingly soluble in ethanol and, on the evidence of analytical and spectral data, was assigned the benzimidazolium structure (X). Its ultraviolet spectrum had $\lambda_{max.}$ 206·0, 245·4, 269·6, and 276·4 mμ (log ε, 4·01, 3·50, 3·52, and 3·51), data which closely resemble those of the parent imidazole hydrochloride (XVI; R = H, $n = 4$), namely, $\lambda_{max.}$ 206·0, 243·4, and 282·0 mμ (log ε, 4·42, 3·66, 3·73, and 3·77), while its infrared spectrum showed bands at 3500—3390 (hydrate), 1630 (C:N), and 775—770 cm.$^{-1}$ (*o*-disubstituted benzene). The n.m.r. spectrum in deuteriopyridine absorbed at τ 8·30 (complex quintet: $CH_2{\cdot}CH_2$ at *a*), 7·00 (broad triplet: CH_2 at *c*), 6·22 (broad triplet: CH_2 at *b*), 1·7—2·8 (4 aromatic protons) and 2·20 (NH removed by D_2O). The benzimidazolium sulphonate (X) was also produced by addition of a catalytic amount of hydrochloric acid to a warm ethanolic solution of the diazosulphonate (II; B = $C_5H_{10}N$). The second component could not be purified sufficiently for analysis but as it gave the triazine (XI) on treatment with sodium hydroxide (cf. below) we ascribe to it structure (VIII; $n = 4$).

From the filtrate of the reaction mixture the expected reduction product namely the hydrazine sulphonic acid (IV; B = $C_5H_{10}N$) separated on cooling. This assignment agreed with its infrared spectrum which had bands at 3250 (NH) and 770 cm.$^{-1}$ (*ortho*-disubstitution) and its n.m.r. spectrum which showed two sets of aliphatic protons at τ 6·40 (4H as a broad triplet) and at τ 8·1 (6H) indicating an intact piperidine ring. Chemical evidence for the structure was obtained by warming this hydrazine (IV) with cyclohexanone which produced the tetrahydrocarbazole [8] (XVII) by an indole cyclisation.

Formation of the products (VIII; $n = 4$) and (X) from the diazosulphonate (II; B = $C_5H_{10}N$) can be rationalised by involving the t-amino-group in the intermediate stages as set out in Scheme 1 [(II) ⟶ (III) ⟶ (V) ⟶ (X)]. Interaction between the diazo-group and the t-amino-nitrogen leads to the dipolar ion (III) which finds its analogy in the adduct $Ph\overset{+}{N}(Me_2),N(CO_2Et){\cdot}\overset{-}{N}{\cdot}CO_2Et$ formed from dimethylaniline and an azodicarboxylic ester as described by Kenner [9] and Huisgen.[10] A 1 : 6-proton abstraction from the α-methylene group as shown in the Scheme [(III) ⟶ (V)] (or possibly by an intermolecular process) produces the mesomeric immonium ion (V) ⟷ (VI) which by a 1 : 6- [(VI) ⟶ (VIII)] or a 1 : 5-cyclisation [(VII) ⟶ (IX)] can yield the triazine (VIII) and the benzimidazole (IX), respectively. The latter attains greater stability by spontaneous aromatisation to give (X).

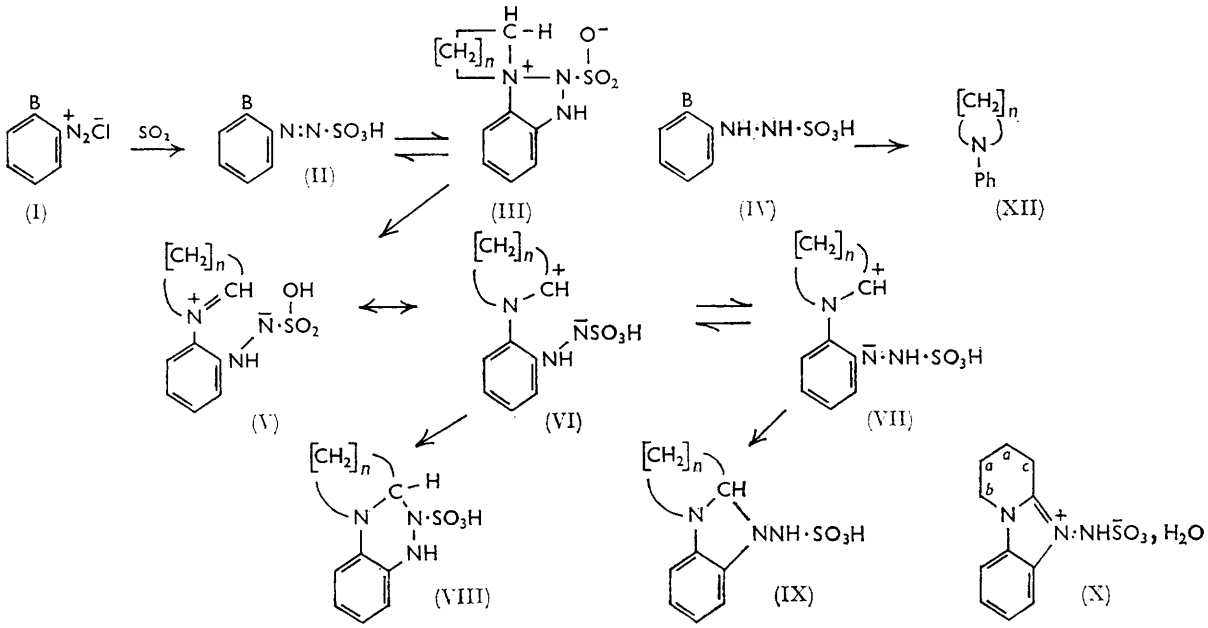
The 't-amino-group effect' in these diazonium reactions is clearly demonstrated by the failure of *o*-cyclohexylbenzenediazonium hydrochloride to behave in an analogous way.

[1] L. Spiegel and H. Kaufmann, *Ber.*, 1908, **41**, 682.
[2] O. Meth-Cohn and H. Suschitzky, *J. Chem. Soc.*, 1963, 4666.
[3] R. Garner and H. Suschitzky, *J. Chem. Soc.* (*C*), 1966, 1572; O. Meth-Cohn and H. Suschitzky, *J. Chem. Soc.*, 1964, 2609.
[4] R. Garner and H. Suschitzky, *Chem. Comm.*, 1967, 129.
[5] F. E. King and J. W. Clark-Lewis, *J. Chem. Soc.*, 1951, 3080.
[6] J. W. Clark-Lewis, J. A. Edgar, J. S. Shannon, and M. J. Thompson, *Austral. J. Chem.*, 1964, **17**, 877.
[7] E. Fischer, *Annalen*, 1877, **190**, 71.
[8] D. P. Ainsworth and H. Suschitzky, *J. Chem. Soc.* (*C*), 1967, 315.
[9] G. W. Kenner and R. J. Stedman, *J. Chem. Soc.*, 1952, 2081.
[10] R. Huisgen and F. Jakob, *Annalen*, 1954, **590**, 37.

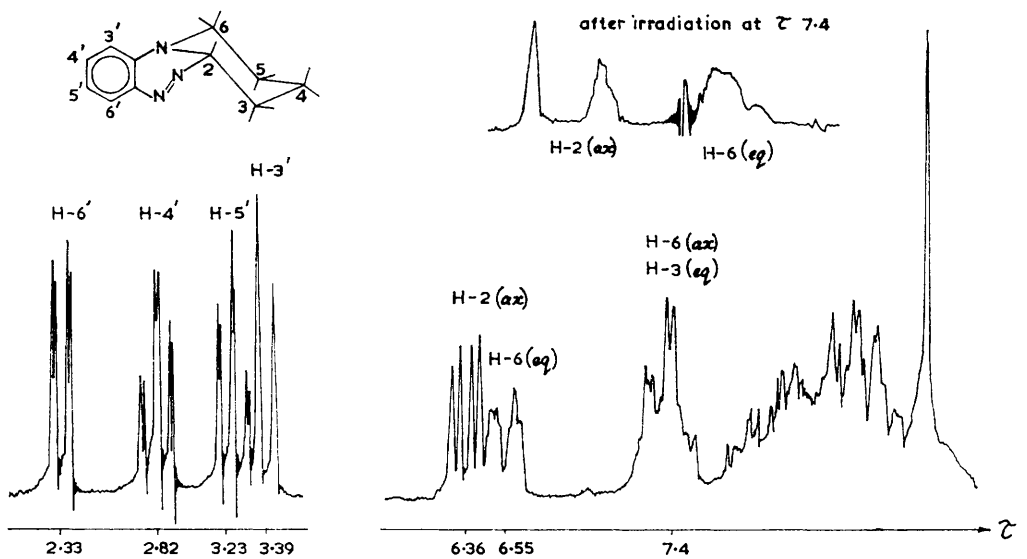
Hot, aqueous sodium hydroxide converted the product (VIII; $n = 4$) into a red oil which was chromatographed to give *N*-phenylpiperidine (XII; $n = 5$) and an orange, crystalline solid, $C_{11}H_{13}N_3$.

Its structure was established as the 1,2,4-triazine (XI) from a study of its n.m.r. spectrum (see Figure) and it was presumably formed by a β-elimination from the intermediate (VIII; $n = 4$). Double resonance (see Figure) confirmed the assignment of the aliphatic protons indicated. Its mass spectrum showed a strong molecular ion peak (187) and fragmentation peaks at *m/e* 172 and 159 corresponding to the benzimidazole (XVI; R = H, $n = 4$) and the unstable species (XVIII), respectively. *N*-Phenylpiperidine (XII; $n = 5$) one of the reaction products is derived from the triazine (XI) since the latter lost nitrogen readily on heating.

Treatment of the benzimidazole (X) with hot, aqueous sodium hydroxide produced *N*-phenylpiperidone (XV; $n = 4$) by the postulated route (X) ⟶ (XIII) ⟶ (XV). This reaction sequence is in agreement with the known action of hydroxy-ions on benzimidazolium salts [11] which leads to ring fission [(XIII) ⟶ (XIV)]. Subsequent loss of the hydrazinosulphonic acid group



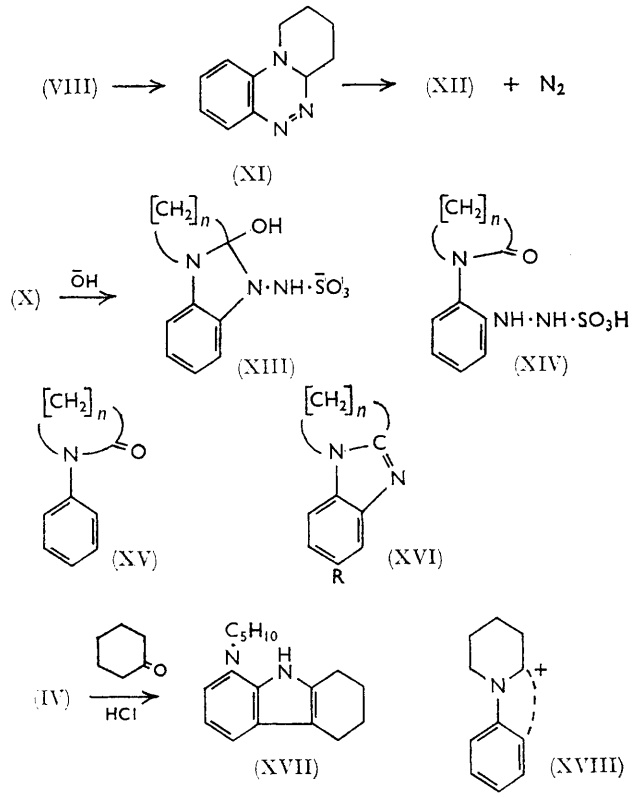
SCHEME 1



N.m.r. spectrum of the triazene (XI) at 100 Mc./sec. in $CDCl_3$ solution ($J_{3'4'} = J_{4'5'} = J_{5'6'} = 7{\cdot}5$ c./sec.; $J_{3'5'} = 1{\cdot}5$ c./sec.; $J_{4'6'} = 1{\cdot}8$ c./sec.; $J_{2\alpha,3\alpha} = 10{\cdot}9$ c./sec.; $J_{2\alpha,3\epsilon} = 4{\cdot}25$ c./sec.; $J_{6\alpha,6\epsilon} = 12$ c./sec.)

[11] O. Meth-Cohn, *J. Chem. Soc.*, 1964, 5245.

[(XIV) ⟶ (XV)] is feasible under the reaction conditions since we found that the hydrazosulphonate (IV) as well as *m*-chlorophenylhydrazine sulphonic acid gave phenylpiperidine and chlorobenzene, respectively, in hot sodium hydroxide solution. The dry benzimidazolium compound (X; $n = 4$) was heated to give the corresponding benzimidazole (XVI; R = H, $n = 4$); a similar result was obtained by electron impact (cf. above).



SCHEME 2

Diazonium salts with other t-amino-substituents (I; B = NMe_2, NEt_2, C_4H_8N, $C_6H_{12}N$, and morpholino) behaved similarly.

The diazonium salts (I) could also be converted into the corresponding *N*-phenyl heterocycle (XII) and *N*-phenyl lactam, without isolation of intermediates, by treatment with sulphur dioxide followed by heating the reaction mixture with sodium hydroxide.

EXPERIMENTAL

Preparation of the Diazosulphonates (II; B = t-Amine).—In a typical example a solution of 2-piperidinoaniline (8·9 g.) in hydrochloric acid (17·5 ml.) and water (10 ml.) was diazotised at 0° with an aqueous solution (15 ml.) of sodium nitrite (5 g.). The diazotised mixture was added dropwise with stirring to a solution of sodium carbonate (5 g.) and sodium sulphite (32·5 g.) in water (50 ml.) at 0° when an orange precipitate formed. The suspension was warmed to 40° until it became clear and then a stream of sulphur dioxide gas was passed through for a few minutes to produce a dense yellow precipitate. This was filtered off, washed with water, and crystallised from ethanol to give the *o-piperidinobenzenediazosulphonate* (8·6 g.) as yellow needles, m. p. 98—99° (Found: C, 45·8; H, 6·0; N, 14·7. $C_{11}H_{15}N_3O_3S,H_2O$ requires C, 46·0; H, 6·0; N, 14·6%). The n.m.r. spectrum (deuteriopyridine) showed resonances at τ 0·67 (3OH protons), 2·2—3·2 (4 aromatic H), 6·80 ($CH_2{\cdot}N{\cdot}CH_2$; 4H), and 8·52 ($[CH_2]_3$; 6H).

Other diazosulphonates were prepared similarly but not isolated.

Reaction of the Diazosulphonates (II; B = t-Amine) *with Sulphur Dioxide.*—(*a*) In a typical example an aqueous suspension of the piperidino-compound (II; B = $C_5H_{10}N$) (8 g.) was treated at 70° with sulphur dioxide for 0·5 hr. The yellow solid which separated (6 g.) was filtered off (filtrate A) and left, after extraction with ethanol, the *benzimidazolium sulphamate* (X) (3 g.), m. p. 304—306° (decomp.) (Found: C, 46·05; H, 5·2; N, 14·8; S, 11·0. $C_{11}H_{13}N_3O_3S,H_2O$ requires C, 46·3; H, 5·3; N, 14·7; S, 11·25%).

The ethanolic extract produced the impure triazine (VIII; $n = 4$) which on warming with 4N-sodium hydroxide solution gave an oil from which the yellow *triazine* (XI) was extracted with benzene. It had m. p. 71—72° (Found: C, 71·0; H, 7·05; N, 22·0. $C_{11}H_{13}N_3$ requires C, 70·6; H, 7·0; N, 22·4%).

The triazine (XI) decomposed when heated at 100° to give *N*-phenylpiperidine and tar.

From the filtrate (A) *2-piperidinophenylhydrazine sulphonic acid* was obtained slowly on cooling, m. p. 316° (water) (Found: C, 46·2; H, 6·1; N, 14·65. $C_{11}H_{17}N_3O_3S,H_2O$ requires C, 45·7; H, 6·6; N, 14·6%).

When a mixture of the hydrazine (3 g.), water (20 ml.), hydrochloric acid (10 ml.), and cyclohexanone (1·1 g.) was heated on a water-bath for 2 hr. 1,2,3,4-tetrahydro-8-piperidinocarbazole hydrochloride (XVII), m. p. 268° (1·2 g.), was obtained.[7] On heating the hydrazine (4 g.) with 4N-sodium hydroxide, nitrogen was evolved and *N*-phenylpiperidine, b. p. 88—90°/0·5 mm. separated as an oil (70%).

Similarly *m*-chlorophenylhydrazine sulphonic acid gave chlorobenzene on treatment with hot sodium hydroxide.

Other benzimidazolium sulphamates were made similarly from the corresponding diazosulphonates (II). The *pyrrolidine sulphamate* had m. p. 304—306° (Found: C, 44·85, H, 4·9, N, 15·4; S, 11·8. $C_{10}H_{11}N_3O_3S,H_2O$ requires C, 44·6; H, 4·8; N, 15·5; S, 11·8%) and the *perhydroazepino-compound* had m. p. 289—290° (Found: C, 48·3;

Products from *o*-t-amino-substituted diazosulphonates (II) on treatment with sulphur dioxide and hot sodium hydroxide

B in (II)	Products (%)	
C_4H_8N		*N*-Phenylpyrrolidone (55)
$C_5H_{10}N$	*N*-Phenylpiperidine (16)	*N*-Phenylpiperidone (9)
$C_6H_{12}N$		*N*-Phenylcaprolactam (40)
Morpholino	*N*-Phenylmorpholine (22)	
4-Me-1-piperazinyl	*N*-Methyl-*N*-phenylpiperazine (42)	
Me_2N	*N*-Dimethylaniline (34)	*N*-Methylformanilide (21)
		N-Methylaniline (24)
Et_2N	*N*-Diethylaniline (5)	*N*-Acetyl-*N*-ethylaniline (28)
		N-Ethylaniline (21)

H, 5·8; N, 13·95; S, 10·35. $C_{12}H_{15}N_3SO_3,H_2O$ requires C, 48·18; H, 5·7; N, 14·0; S, 10·7%).

(*b*) When the diazosulphonates (II) were treated with sulphur dioxide as described in (*a*) and this was followed by heating the reaction mixture with aqueous 4N-sodium hydroxide, nitrogen was evolved and an oil was obtained. Purification and separation on alumina with benzene gave the products listed in the Table.

Reaction of the Benzimidazolium Compounds.—(a) *With sodium hydroxide.* On heating a benzimidazolium sulphamate (3 g.) with aqueous 4N-sodium hydroxide (25 ml.) on a water-bath for 5 min., nitrogen was evolved and an oil separated which was chromatographed on alumina with benzene to give the corresponding lactam in high yield (see Table).

(*b*) *Thermolysis.* When the title compounds were heated dry the corresponding benzimidazoles (XVI; R = H) slowly sublimed.

Reaction of 2-Cyclohexylaniline.—When 2-cyclohexylaniline [12] was diazotised and then treated with sulphur dioxide followed by sodium hydroxide only cyclohexylbenzene [12] was obtained.

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[12] D. A. Denton, R. K. Smalley, and H. Suschitzky, *J. Chem. Soc.*, 1964, 2421.