56. *Evidence for the Structural Isomerism of Hantzsch's Aryl* syn- *and* anti-*Diazotates.*

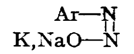
By Herbert H. Hodgson and Ewart Marsden.

In view of the fact that Hantzsch's aryl *syn*- and *anti*-diazosulphonates and aryl *syn*- and *anti*-diazocyanides are probably structural and not stereo-isomers, the evidence for the stereo- or structural isomerism of the aryl *syn*- and *anti*-diazotates is now examined. It is concluded from experimental evidence : (*a*) that the solid *syn*(normal)-diazotates are represented by the formula $\mathrm{Ar{\cdot}N{:}N{\cdot}OM}$ (where M is a metal), and in aqueous solution hydrolyse to give an equilibrium mixture, $\mathrm{Ar{\cdot}N{:}N{\cdot}OH \rightleftharpoons Ar{\cdot}\overset{+}{N}{\equiv}N{:}\}\overset{-}{O}H}$, the diazohydroxide being the coupling compound; (*b*) that the *anti*(or *iso*)-diazotates are either nitrosoamines, $\mathrm{Ar{\cdot}\overset{-}{N}(NO)\}\overset{+}{M}}$, or equilibrium mixtures in alkaline solution of the ionised normal diazotate and nitrosoamine,

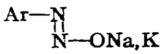
$$\mathrm{Ar{\cdot}N{=}N{\cdot}\overset{-}{O}\}\overset{+}{M} \rightleftharpoons Ar{\cdot}\overset{-}{N}(NO)\}\overset{+}{M}.}$$

It is well known that when a mineral acid solution of a diazonium salt is treated gradually with sodium or potassium hydroxide in the cold, a marked change occurs in the properties of the diazo-compound as the acidity of the solution diminishes, and that change persists until the solution is markedly alkaline, although heat is sometimes necessary to consummate the final conversion. Three broad zones can clearly be distinguished, *viz.*, acid up to *ca.* pH 3·5, where diazonium salts can exist, neutral from *ca.* pH 6·5—8·0, where the so-called normal or *syn*-diazotates (hereinafter styled *n*-diazotates) are formed, and alkaline above pH 8·0, where *iso*- or *anti*-diazotates make their appearance. Whereas the constitution of the diazonium salts has long been settled in favour of Blŏmstrand's formula, $\mathrm{Ar{\cdot}\overset{+}{N}{\equiv}N{:}\}\overset{-}{X}}$, the structures of the *syn*- and *anti*-diazotates still await determination, despite discussion extending from 1866 to 1931 and recently revived by Farrar and Gulland (J., 1944, 368). The alternative points of view are :

(a) *Stereoisomeric*, due to Hantzsch (*Ber.*, 1894, **27**, 1702), whereby the isomers differ only in geometrical arrangement :



Normal or *syn*-diazotates

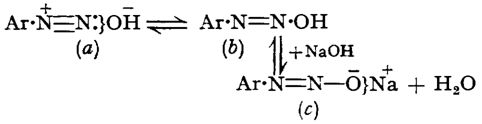


iso- or *anti*-Diazotates

(b) *Structural*, wherein many different versions occur, of which the most important are : (1) that the *n*-diazotates are obtained from a diazohydroxide $\mathrm{Ar{\cdot}N{:}N{\cdot}OH}$, and the *iso*-diazotates are derived from the isomeric (tautomeric) nitrosoamine, $\mathrm{Ar{\cdot}\underset{NO}{\underset{|}{N}}{-}H}$ (cf. Schraube and Schmidt, *Ber.*, 1894, **27**, 514 ; v. Pechmann and Frobenius, *ibid.*, p. 672 ; Bamberger, *ibid.*, p. 679) ; (2) the structure, $\mathrm{Ar{\cdot}\underset{O}{\underset{\downarrow}{N}}{=}N{-}}$, originally proposed rather speculatively by Bamberger and later supported with fresh evidence by Angeli (*Gazzetta*, 1921, **51**, i, 35 ; *Ber.*, 1926, **59**, 1400), for the *n*-diazotate ion, with the structure $\mathrm{Ar{\cdot}N{=}N{-}\overset{-}{O}}$ for the *iso*diazotate ion.

With respect to Hantzsch's stereochemical theory of the diazotates, Taylor and Baker (Sidgwick's " Organic Chemistry of Nitrogen," 1937, p. 417) state that the strongest evidence in its support is derived from the study of the two forms of the diazocyanides and the diazosulphonates, which until recently have been regarded as stereoisomers. It seemed logical, state Taylor and Baker (*ibid.*, p. 419), to assign the isomerism to a cause which was common to all three classes, and the only possible one was geometrical isomerism ; they concluded, however, that without direct experimental evidence, Hantzsch's view remained a probable assumption and could not be taken as firmly established. Recently, however, Hodgson and Marsden (J., 1943, 470) have submitted experimental evidence indicating that Hantzsch's so-called *syn*- and *anti*-diazosulphonates were not geometrical but structural isomers, *viz.*, diazosulphites and diazosulphonates respectively, and later (J., 1944, 395) that the so-called *syn*- and *anti*-diazocyanides have the *iso*nitrile and the nitrile structure respectively. Thus geometrical isomerism in two of the three classes concerned is now invalid, and the analogy on which the stereochemical structures for the diazotates was based not only disappears, but must be used for a structural representation of the *n*- and *iso*-diazotates. Such a point of view will now be explored.

Normal or syn-*Diazotates*.—From the fact that only the *n*-diazotates couple with phenols and amines their structure can be settled from a study of the equilibria :



$$\underset{(a)}{\mathrm{Ar{\cdot}\overset{+}{N}{\equiv}N\!:\!\}\overset{-}{O}H}} \rightleftharpoons \underset{(b)}{\mathrm{Ar{\cdot}N{=}N{\cdot}OH}} \xrightleftharpoons{+\mathrm{NaOH}} \underset{(c)}{\mathrm{Ar{\cdot}N{=}N{-}\overset{-}{O}\}\overset{+}{N}a}} + \mathrm{H_2O}$$

which can be assumed to exist in the solution prior to coupling with an alkaline phenol. The anion (*c*) of the sodium salt can be rejected forthwith as the coupling reagent, since it is negatively charged and would be repelled from the *o*- and *p*-positions of the phenol; in fact, coupling can be retarded and almost prevented by increase of alkaline concentration. Choice of coupling reagent lies therefore between (*a*) and (*b*), and Conant and Tischler (" The Chemistry of Organic Compounds," The Macmillan Co., New York, 1939, p. 382) state that it is (*b*) which couples (cf. also Conant and Peterson, *J. Amer. Chem. Soc.*, 1930, **52**, 1220; Hodgson, *J. Soc. Dyers and Col.*, 1942, **58**, 228; Hodgson and Marsden, *ibid.*, 1944, **60**, 16, 120).

In further support of the above theory of coupling it has been found that *p*-nitrobenzeneazo-*N*-bromocarbonamide rapidly couples with either α- or β-naphthylamine in chloroform or benzene, *i.e.*, under conditions where a diazonium ion could not exist (cf. Hodgson and Marsden, J., 1944, 395). In solution, therefore, the so-called *n*-diazotates are equilibrium hydrolysis mixtures of ionised and un-ionised compounds :

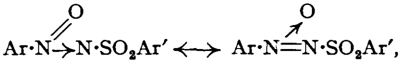
$$\mathrm{Ar{\cdot}N{=}N{-}\overset{-}{O}\}\overset{+}{N}a} + \mathrm{H_2O} \rightleftharpoons \mathrm{Ar{\cdot}N{=}N{\cdot}OH} + \mathrm{NaOH}$$

and in the solid state they have the configurations of an ordinary alkali salt capable of ready hydrolysis by water. This follows experimentally from the fact that the *n*-diazotates couple at once with α- or β-naphthol and with α- or β-naphthylamine when the latter compounds in finely divided form are stirred into an aqueous solution of the diazotate prepared by Bamberger's directions (*Ber.*, 1896, **29**, 461). Further, when the solid sodium salt of β-naphthol is added to the aqueous solution of the *n*-diazotate or when their solutions are mixed in either order, coupling occurs forthwith.

The previous data indicate that the formula of a *n*-diazotate is Ar·N═N·ONa, and confusion as to which is the real coupling reagent has led to this formula being assigned to the *iso*diazotate. It is only when the pH value of the solution is sufficiently high, *i.e.*, when hydrolysis to Ar·N═N·OH is prevented, that coupling is inhibited. This formula for the diazotate is also supported by the theories of Wistar and Bartlett (*J. Amer. Chem. Soc.*, 1941, **63**, 413) and Hauser and Breslow (*ibid.*, p. 418), which claim that the coupling reagent is the diazonium ion, from which it must follow that the relevant anion is either the hydroxyl group (in alkaline or neutral solution) or the anion of the weak acid employed in their buffer solutions. In no case could an anion of the Angeli type, $\mathrm{R{-}\underset{\substack{\downarrow\\ O}}{N}{=}\overset{-}{N}}$, be visualised.

The counter arguments to Angeli's theory are collected together by Saunders (" The Aromatic Diazo-compounds," 1936, p. 209) and are very imposing : they include the oxidation of *n*-diazotates to salts of phenylnitroamine, which would be impossible on Angeli's constitution.

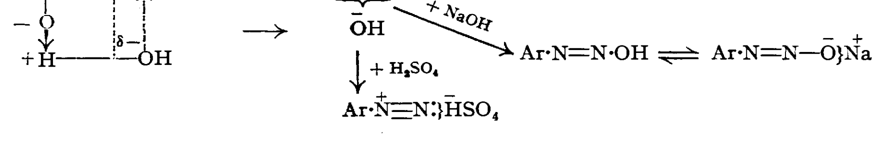
Farrar and Gulland (*loc. cit.*), however, have prepared azoxysulphones,



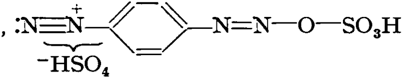
$$\mathrm{Ar{\cdot}\overset{O}{N}{\rightarrow}N{\cdot}SO_2Ar'} \longleftrightarrow \mathrm{Ar{\cdot}N{=}\overset{O}{\overset{\nearrow}{N}}{\cdot}SO_2Ar'},$$

which, like Angeli's azoxycarbonamides (cf. Angeli, *Gazzetta*, 1917, **47**, I, 215; Pieroni, *ibid.*, 1922, **52**, II, 32), are readily hydrolysed by dilute alkali to *n*-diazotates. In addition, distillation of the azoxysulphones with 50% sulphuric acid affords considerable quantities of phenol, which indicates that a diazonium salt is an intermediate in the hydrolysis; further, when phenyl-*p*-tolylazoxysulphone is dissolved in ice-cold concentrated sulphuric acid, the solution on dilution with water exhibits the reactions of benzenediazonium sulphate. Farrar and Gulland state that, if it is accepted that the products of hydrolysis of all these azoxy-compounds are true *n*-diazotates, either these must be denoted by the Angeli formula above, or a transfer of oxygen from one nitrogen to the other must be postulated to give the formula Ar·N═N·ONa. They also state that there is neither analogy nor experimental support for this migration, but in any recognition of the Angeli theory recourse must be made to such a transfer, as in the explanation of the facile oxidation of *n*-diazotates to arylnitroamines.

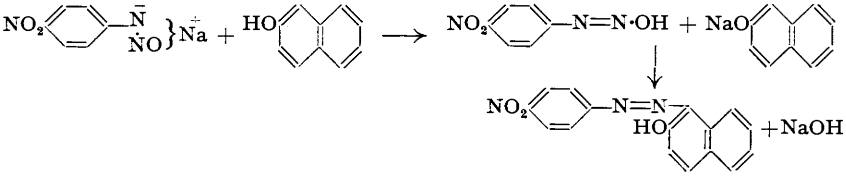
It has long been known (Wallach and Belli, *Ber.*, 1880, **13**, 525; *Annalen*, 1882, **215**, 218) that azoxybenzene itself isomerises in concentrated sulphuric acid to hydroxyazobenzene, thereby indicating easy detachment of the oxygen atom by an acid, a reaction which can readily explain Farrar and Gulland's results with the azoxy-sulphones, where the mechanism of hydrolysis would appear to be a two-point attack by water as in the scheme :



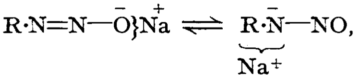
the resulting ephemeral diazonium hydroxide becoming diazonium sulphate in the acid hydrolysis and *n*-diazotate in the alkaline hydrolysis. In this respect the azoxysulphones behave like azoxycarbonamides in having the very stable N—S and N—C bonds in the parent diazosulphonate and diazo-carbonamide weakened by the dipolar $\overset{+}{N}$—$\overset{-}{O}$ group, which sets up adjacent positive charges at the N—S and N—C bonds respectively, with consequent destabilisation and rupture by hydrolysis (compare Pauling on the adjacent charge rule, "Nature of the Chemical Bond," Cornell Univ. Press, 1940, pp. 199, 210). The diazosulphonates and diazosulphides, like the diazocarbonamides and diazocyanides, will not couple with alkaline β-naphthol.

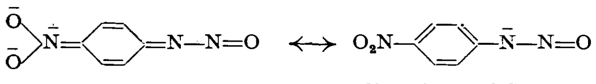
The acceptance of Angeli's formula for the *n*-diazotate, however, would involve facile migration of the oxygen from one nitrogen to the other and back according to circumstances, *i.e.*, tautomeric oxygen. Now the formula Ar·N=N·OH must be postulated for the hydroxide before conversion into the *n*-diazotate, whether it couples as such (Conant and Peterson, *loc. cit.*) or as the diazonium hydroxide (Wistar and Bartlett, *loc. cit.*). Further, if the sodium and silver salts of *p*-nitrodiazobenzene are treated with methyl iodide, the former give *p*-nitro-*N*-nitrosomonomethylaniline, and the latter the methyl ether of *p*-nitrobenzenediazohydroxide, $NO_2{\cdot}C_6H_4{\cdot}N{=}N{\cdot}O{\cdot}CH_3$, which shows the reactions of a diazo-compound by giving a diazoamino-compound with aniline and by coupling with phenol. In both cases the oxygen is attached to the outer and not to the inner nitrogen, and indicates a coupling mechanism involving scission at the N—O bond. Additional evidence of like import is given by the *N*-nitrosoacylarylamines, which behave like *n*-diazotates (cf. Grieve and Hey J., 1935, 689; Hodgson and Marsden, J., 1943, 285) and couple following alkaline hydrolysis to the normal diazotate (Bamberger and Muller, *Annalen*, 1900, **313**, 126). A still more striking example is afforded by the mono-coupling of tetrazotised *p*-phenylenediamine with β-naphthol in concentrated sulphuric acid solution, which must take place at the N—O link of the structure, 

(Schoutissen, *J. Amer. Chem. Soc.*, 1933, **55**, 4541), and should finally dispose of any doubt as to whether coupling occurs at the second nitrogen to which an oxygen atom had previously been attached. Conversion of these compounds into alkali *n*-diazotates would involve the reverse migration of oxygen from the outer to the inner nitrogen if Angeli's formula be postulated for the *n*-diazotate, and such facile migration in either direction appears to introduce an unnecessary complication for an otherwise simple reaction. Similarly, the more involved mechanisms put forward by Angeli to explain coupling and diazo-ether formation fall into the same category. The coupling of the sodium salt of the *p*-nitrophenylnitrosoamine caused by β-naphthol alone to form *p*-nitrobenzeneazo-β-naphthol could only take place *via* the sequence of changes :



thereby proving that the oxygen of the coupling reagent is attached to the outer nitrogen.

iso*Diazotates.*—This term has been used to refer to (*a*) those solutions of diazo-compounds which, owing to their high pH value, couple either very slowly or not at all with phenols and naphthols, and (*b*) nitrosoamines which in the cases of some amines, *e.g.*, *p*-nitroaniline, are made immediately by the action of alkali hydroxides on the diazonium salts, and in other cases, *e.g.*, aniline, require very concentrated (sometimes 60%) potassium hydroxide solution at about 140°. Solutions (*a*), with no or little coupling ability, are probably equilibrium mixtures of the sodium nitrosoamine and *n*-diazotate,  $R{\cdot}N{=}N{-}\overset{-}{O}\}\overset{+}{Na} \rightleftharpoons \underbrace{R{\cdot}\overset{-}{N}{-}NO}_{Na^+}$, in which the nitrosoamine greatly predominates. Compounds (*b*) are either the alkali nitrosoamines, which in alkaline solutions retain their structure; or are ion-pairs (cf. Hammett, "Physical Organic Chemistry," 1940, p. 40 *et seq.*), whose normal condition is that of the *n*-diazotate but which under the influence of heat and caustic alkali have been converted into the nitrosoamines. Both types react with methyl iodide to give *N*-nitrosomethylarylamine, but 1-chloro-2 : 4-dinitrobenzene in boiling benzene failed to react with the nitrosoamine from *p*-nitroaniline, thereby indicating the intensity of the electrostatic attraction. Incidentally, Wojciechowski (*Rocz. Chem.*, 1934, **14**, 739) reports that he was unable to get potassium *p*-chlorobenzene*iso*diazotate (nitrosoamine) free from caustic alkali, and our experience appears to indicate that the presence of a slight amount of caustic alkali is essential for the preservation of the *iso*diazotate. Some of the nitrosoamines, *e.g.*, from *p*-nitroaniline and *p*-chloroaniline, are highly coloured, and this may be ascribed to resonance between ionic structures (cf. Pauling, "Nature of the Chemical Bond," 1940, Chap. IV, p. 124),



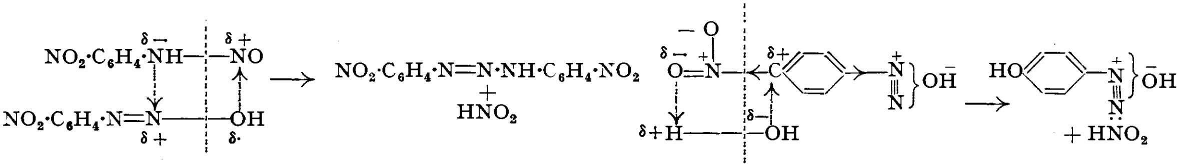
Potassium benzene*iso*diazotate prepared according to the directions of Schraube and Schmidt (*loc. cit.*) was colourless initially but became brown rapidly and progressively; this is due possibly to incipient hydrolysis by atmospheric moisture with resultant generation of *n*-diazotate, which in turn would be in equilibrium with diazonium hydroxide, whose decomposition to phenol with subsequent coupling by the *n*-diazotate would produce the coloured azo-compound shown by the colour change above. Solid sodium and potassium *p*-nitrobenzene*iso*diazotates (nitrosoamines) are formed with the greatest ease and are soluble in water, but are reprecipitated therefrom by caustic alkali. If solutions of these compounds are treated with alkaline β-naphthol, no coupling occurs for a considerable time, and the same negative result is obtained when aqueous solutions of the nitrosoamines are treated with an aqueous solution of sodium β-naphthoxide or phenoxide or of disodioresorcinol. If, however, finely powdered α- or β-naphthol, or phenol, or resorcinol, or their solutions in water, are shaken with a solution of the sodium *iso*diazotate (whether from *p*-nitroaniline, or aniline, or *p*-chloroaniline), coupling occurs rapidly and can only be due to the sequence of reactions indicated previously.

Orton (J., **1903**, **83**, 796) found that in alcoholic solution Schraube and Schmidt's nitrosoamines coupled at once with sodium β-naphthoxide, owing to removal of the nitrosoamine sodium or potassium by the alcohol.

It is thus apparent why the usual coupling test failed with the *iso*diazotates, since the effect of the excess of alkali present was to retain them in the nitrosoamine form or as the *n*-diazotate ion. The coupling reaction with β-naphthol alone, indicates that the coupling reagent is the diazohydroxide in accordance with the view of Conant and Peterson (*loc. cit.*).

When a solution of β-naphthol in sodium carbonate is added to an aqueous solution of the *iso*diazotate (either from *p*-nitroaniline, aniline, or *p*-chloroaniline), coupling is delayed for several minutes, in contrast to the complete prevention of coupling which occurs when caustic alkaline solutions are used (in one experiment no coupling occurred for 3 weeks) and to the immediate coupling which occurred when the free β-naphthol was used. It was this prevention of coupling in solution of $\text{pH} > 8$ which led to the view that an *anti*-diazotate existed which would not couple, and on account of this negative property it was regarded as the more stable form, whereas with many of the *anti*-diazotates considerable heat is required to effect their transformation from the *syn*-form.

Bucherer and Fröhlich (*J. pr. Chem.*, **1931**, **132**, 72), in a study of the action of weak acids (carbonic, boric, acetic, oxalic, and sodium bicarbonate) on the *anti*-diazotate (nitrosoamine) from *p*-nitroaniline, have concluded that the *syn*-diazotate is first formed, which is then partly hydrolysed to nitrous acid and *p*-nitroaniline, and also has its nitro-group replaced in part by hydroxyl, since the products of reaction were 4 : 4′-dinitrodiazoaminobenzene, *p*-hydroxydiazobenzene (20%), and nitrous acid. A somewhat modified mechanism would appear, however, to explain their results more simply and to avoid the assumption of an intermediate formation of *p*-nitroaniline, *viz*, that the unstable free nitrosoamine first liberated will begin to isomerise to an equilibrium mixture of the diazo- and the diazonium hydroxide, the diazohydroxide then coupling with unchanged nitrosoamine to form the 4 : 4′-dinitrodiazoaminobenzene, and the diazonium hydroxide *via* a two-point attack by water giving the *p*-hydroxydiazobenzene as follows :



An aqueous solution of the sodium nitrosoamine from *p*-nitroaniline slowly decomposes with evolution of nitrogen to form complex mixtures containing azo-phenolic compounds.

The Analogy with the Oximes.—Hantzsch reared the whole of his theory on the fundamental proposition that the difference between the oximes and the diazo-compounds lies merely in the substitution of nitrogen for carbon, and that the series of normal and *iso*diazo-compounds must in consequence be derived from the stereoisomeric diazohydroxides. Modern electronic theory was of course unknown in Hantzsch's period of activity, although he was still alive when the theory had attained considerable importance, but had passed away before the theory of resonance was developed by Pauling. On these theories, the electrons on the carbon atoms in the oxime are all employed in covalencies, whereas there is a lone pair in the corresponding nitrogen atom of the diazo-compound, which fact alone renders invalid the Hantzsch stereochemical analogy. Even if the diazohydroxides could be prepared, they could not exist in rigid structures like the oximes, since there would be easy resonance with all its consequences.

Conclusions.—(1) Hantzsch's stereo-formulation of the diazotates will not explain : (*a*) The endothermic character of the *iso*(*anti*)-forms from diazotised aniline, *o*- and *p*-toluidines, and the contrasting ready formation in the cold from diazotised *p*-nitroaniline.

(*b*) The non-existence of stereoisomeric diazo-ethers.

(*c*) The reaction of the *syn*-form with sodium stannite, and the stability of the *anti*-form towards this reagent (Hantzsch and Voch, *Ber.*, **1903**, **36**, 2065).

(*d*) The fact that the *cis*(*syn*)-compound is the stronger of the *cis*- and *trans*-cinnamic acids and of the *cis*- and *trans*-benzaldoximes, whereas the opposite is the case with the hypothetical *syn*- and *anti*-diazohydroxides, known only in their salts.

(*e*) Coloured *anti*- and colourless *syn*-diazotates.

(*f*) The rapid coupling of the *syn*- and the non-coupling of the *anti*-diazotates, since it is an N—O link which must be broken in each case.

(*g*) The ephemeral existence of hydrogen compounds of the *iso*diazotates, and the formation of anhydrides from *n*-diazotates by the action of acids.

(2) Euler's view (*Ber.*, **1903**, **36**, **2503**, **3835**) that alkaline hydrolysis of the diazo-ethers gives the *n*-diazotates is correct, since only the *n*-diazotates couple readily in the presence of alkali.

(3) All the above difficulties are removed when the *n*-diazotate is formulated as $\mathrm{Ar{\cdot}N{=}N{\cdot}ONa,K}$, where the metal has partial ionic structure and is readily hydrolysed, and the *iso*diazotate is regarded as an ion-pair with the nitrosoamine structure. Hydrolysis of the *n*-diazotate gives the coupling reagent, $\mathrm{Ar{\cdot}N{=}N{\cdot}OH}$, which is also liberated from the nitrosoamine by such weak acids as phenol, resorcinol, and β-naphthol. Moreover, the solid *n*-diazotates usually have water of crystallisation which may be ascribed to their partial ionic structure, the alkali metal being hydrated, whereas the *iso*diazotates crystallise with less water or none owing to the much stronger electrostatic attraction between the ions of the ion-pair. This formulation explains why sodium stannite reduces the *n*-diazotates to hydrocarbons but does not attack the *iso*diazotates, since in alkaline solution the *n*-diazotate will hydrolyse into an equilibrium mixture of the diazonium and the diazo-hydroxides, the former of which will be reduced by the stannite. On the other hand, an ion-pair will be preserved in the alkaline solution (cf. Saunders, *op. cit.*, p. 86) and so resist attack by the stannite.

(4) Angeli's formula, $\mathrm{Ar{\cdot}}\underset{\substack{\downarrow\\ \mathrm{O}}}{\mathrm{N}}\mathrm{{\cdot}N}$—, for the *n*-diazotate ion requires facile migration of the oxygen from the nitrogen in both directions according to circumstances, and this is highly improbable; further, all the reactions for the Angeli-formulated compound require much more complicated representation than would seem to be warranted. The conversions of the azoxycarbonamides and azoxysulphones (Farrar and Gulland, *loc. cit.*) into diazo-compounds can be explained by a simple hydrolytic mechanism.

The authors thank Imperial Chemical Industries, Ltd., Dyestuffs Division, for gifts of chemicals.

TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, October 6th*, **1944**.]