370. p-*Aminodimethylaniline. Part V.* The Effect of Substituents on the Azo-coupling Efficiency of the Diazonium Compounds.*

By John H. Gorvin.

In Part I (*J.*, 1941, 613) Ayling, Gorvin, and Hinkel showed that the low coupling power of diazotised *p*-aminodimethylaniline with amines and phenols is a consequence of electron-release by the NMe_2 group. It has now been demonstrated that, whereas a single *m*-substituent either exerts no influence (Cl) or reduces the coupling power (NO_2), an *o*-substituent markedly increases the efficiency of the reaction whether or not a *m*-substituent is at the same time present. Diazo-compounds of this type show a general tendency to couple under the strongly acid conditions of Schoutissen (*J. Amer. Chem. Soc.*, 1933, **55**, 4541).

The reaction of diazotised *p*-aminodimethylaniline with an amine or a phenol is a " coupling-decomposition " process (Ayling, Gorvin, and Hinkel, Part I, *J.*, 1941, 613) in which the yield of product depends on the relative rates of two simultaneous reactions. The effect of nuclear substituents on the efficiency of the process must therefore be considered in relation both to the stability of the diazo-compound (Part IV, preceding paper) and to its rate of coupling. An *o*-substituent, by impeding the mesomerism of the dimethylamino-group, will increase the tendency to passage into un-ionised forms : thus in a weakly acidic medium of given pH the coupling reaction is facilitated under conditions of reduced stability. Consequently the absolute rate of azo-coupling should be increased and the " coupling-decomposition " process at this pH completed more rapidly. A *m*-substituent on the other hand will not appreciably modify the influence of the dimethylamino-group : hence the *m*-substituted bases should resemble *p*-aminodimethylaniline both in the duration of the process at a given pH and in the absolute rate of coupling of their diazo-compounds.

The effect of a substituent on the absolute rate of decomposition is less clear, since it depends on the particular mechanism involved. It appears (Part IV) that diazotised *p*-aminodimethylaniline and its *m*-substituted derivatives, in which the ionic form is stabilised, decompose in weakly acidic solutions to a large extent by homolysis of the un-ionised diazo-compound. Grieve and Hey (*J.*, 1934, 1797; 1935, 689; cf. Hey and Waters, *J.*, 1948, 882) state that the rate of such a process is essentially independent of the nuclear substituent. Although Huisgen and Horeld (*Annalen*, 1949, **562**, 137) suggest an alternative interpretation of certain evidence of Grieve and Hey, they do not claim that substituent groups markedly affect the rate of actual homolysis, the driving force of which they, like Saunders and Waters (*J.*, 1946, 1154), consider to be the elimination of nitrogen. The assumption, if justified (cf. Ambrose and Brady, *J.*, 1950, 1245), suggests the corollary that all diazo-solutions in which decomposition is determined purely by homolysis will possess minimum stabilities of the same order of magnitude, although this minimum, which corresponds to maximum production of un-ionised forms, may

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* Part IV, preceding paper.

occur at slightly different pH values according to the substituents in the ring. In the present case, however, the validity of the assumption is of little moment, for in the diazohydroxides in question the dimethylamino-group can exert its full mesomeric effect independently of the *m*-substituent; thus it seems reasonable to assume that the un-ionised diazohydroxides (or acetates) derived from *p*-aminodimethylaniline and from its *m*-substituted derivatives will possess the same absolute rate of decomposition.

From the foregoing it was expected that the yield of azo-compound would be unaffected by the presence of a *m*-substituent in so far as the latter exerted no direct effect on the diazo-group.

It was shown in Part IV that homolytic fission may play a less prominent rôle with the *o*-substituted derivatives than with those compounds in which the full stabilising effect of the dimethylamino-group is apparent; in these instances heterolysis of the ion may become more prominent than homolysis of the diazohydroxide. In view of the uncertainty on this point it can only be stated that the probability of the diazo-compound, in whatever form, undergoing decomposition in a given time is greater for the *o*-substituted compounds than for diazotised *p*-aminodimethylaniline over the usual pH range. The efficiency of coupling will therefore depend on the degree to which the decrease in stability caused by the presence of the *o*-substituent is outweighed by the increase in coupling activity resulting from the same cause.

In the present work the effect of a *m*-substituent was studied in 4-amino-3-chloro-*NN*-dimethyl- and 4-amino-*NN*-dimethyl-3-nitro-aniline. The *ortho*-effect was investigated in 4-amino-2-chlorodimethylaniline and, in presence of a *m*-substituent, in the 4-amino-3-chloro-2-nitro-, 4-amino-2-chloro-3-nitro-, 4-amino-2-chloro-5-nitro-, and 4-amino-2 : 5-dinitro-derivatives of dimethylaniline (cf. Ayling, Gorvin, and Hinkel, Parts II and III, *J.*, 1942, 755; 1946, 530). The yields obtained in a series of coupling reactions in weakly acid solution are set out in the Table and may be compared with yields obtained under the same conditions with the unsubstituted base (cf. Part I) and with *p*-toluidine. In agreement with the foregoing conclusions, diazotised 4-amino-3-chlorodimethylaniline differed little from the unsubstituted compound in the yields of azo-compound obtained. Diazotised 4-amino-2-chlorodimethylaniline however showed significant increments in the yields obtained, and the *ortho*-effect was

The effect of substituents on the coupling efficiency of diazotised p-*aminodimethylaniline.*

Amine or phenol coupled.	Mean yields (%) and colour of azo-compound. Substituent in *p*-aminodimethylaniline,			
	none.	3-Cl.	3-NO_2.	2-Cl.
β-Naphthol	93 blue-black	88 dull red	48·5 [2] purple	95 [4] red
α-Naphthylamine	91 dull red	—	64 dull red	100 bright red
β-Naphthylamine	84 dark red	73 dark red	51 purple	95 red
Naphthionic acid	44 purple-brown	31 purple-brown	* [3]	72 dull red
Anthranilic acid	37 brown	35 purple-brown	*	69 brown
Dimethylaniline	<20 orange	* [1]	*	77 orange

Amine or phenol coupled.	Mean yields (%) and colour of azo-compound. Substituent in *p*-aminodimethylaniline.				
	3-Cl-2-NO_2.	2-Cl-3-NO_2.	2-Cl-5-NO_2.	2 : 5-$(NO_2)_2$.	*p*-$C_6H_4Me{\cdot}NH_2$.
β-Naphthol	93·5 dull red	97 bright red	91 purple	—	89 bright red
α-Naphthylamine	100 dull red	95 dull red	99 purple	100 purple	93·5 dull red
β-Naphthylamine	90 deep red	100 bright red	99 purple	100 purple-red	95·5 bright orange
Naphthionic acid	90—100 dark red	86 dark red	81 dark red	90—100 purple-red	—
Anthranilic acid	86 orange-brown	92 yellow-brown	81 brown	86 yellow-brown	77 yellow-brown
Dimethylaniline	92 bright red	92 bright red	79 dark red	95·5 purple-red	93·5 orange

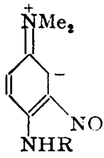
* No pure azo-compound isolated.

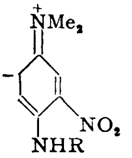
[1] *m*-Chlorodimethylaniline produced in >40% yield. [2] *m*-Nitrodimethylaniline produced in 12·5% yield. [3] *m*-Nitrodimethylaniline produced in 27% yield. [4] Weighed as red-orange hydrochloride.

even more striking in the case of 4-amino-3-chloro-2-nitrodimethylaniline. There can be no doubt that in these instances the increased coupling activity due to the *o*-substituent more than neutralised the reduction in stability of the reacting solution. These examples bear a close analogy to the elimination by an *o*-substituent of the inhibiting influence of the dimethylamino-group on the alkaline hydrolysis of ethyl benzoate (Westheimer and Metcalf, *J. Amer. Chem. Soc.*, 1941, **63**, 1339).

The introduction of a *m*-nitro-group into diazotised *p*-aminodimethylaniline resulted most unexpectedly in a considerable diminution of the coupling efficiency; whereas a possible slight increase in coupling power might have been expected in view of the negative character of the nitro-group, the actual yields obtained were the poorest in the series and reaction proceeded sluggishly with considerable decomposition. Reductive elimination of the diazo-group proceeded in the usual way (Part IV). In a typical coupling reaction with β-naphthol the azo-compound (48·5%) was accompanied by an amount of *m*-nitrodimethylaniline (12·5%) equivalent to the decomposition of just under half of the original diazo-compound calculated on the basis of Table II (Part IV). In the naphthionic acid coupling no azo-compound could be isolated from the resulting tar but on steam-distillation *m*-nitrodimethylaniline (27%) was recovered. It appears therefore that β-naphthol and naphthionic acid, which do not separate from the coupling mixture as a liquid phase, and which contain no aliphatic groups, have little or no effect on the free radical decomposition of the uncoupled diazo-compound. The present case resembles those previously discussed in that the substitution of an *o*-group greatly improved the coupling efficiency; the yields obtained with the 2-chloro-3-nitro-, 2-chloro-5-nitro- and 2 : 5-dinitro-derivatives were excellent and the reactions were complete within a short time. Comparison of yields obtained with the diazotised 4-amino-2-chloro-, 4-amino-2-chloro-3-nitro-, and 4-amino-2-chloro-5-nitro-amines indicates in general slightly higher coupling efficiency in the last two compounds; it would seem that, in the *o*-substituted if not in the unsubstituted compound, a *m*-nitro-group is able to cause some withdrawal of electrons from the adjacent diazo-group.

All the *o*-substituted compounds coupled normally with dimethylaniline. The diazotised 4-amino-3-chloro- and 4-amino-3-nitro-compounds however gave no isolable azo-compound. Homolytic decomposition is favoured by the withdrawal of the weakly coupling diazohydroxide from solution by the dimethylaniline (cf. Part IV); in the attempted coupling of the *m*-chloro-diazo-compound at least 40% was reduced to *m*-chlorodimethylaniline.


(I.)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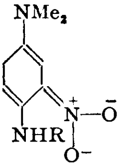
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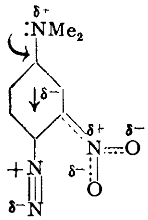
(IV.)

The anomalous behaviour of diazotised 4-amino-*NN*-dimethyl-3-nitroaniline may be related to the indirect interaction between a positive group and a negative group *meta* to it which is apparent in colour (*e.g.*, of *m*-nitroaniline) and in certain substitution reactions in which the 6-position is deactivated to the advantage of the 2-position (cf. Dewar, *J.*, 1949, 468; Kleene, *J. Amer. Chem. Soc.*, 1949, **71**, 2259; Kobe and Hudson, *Ind. Eng. Chem.*, 1950, **42**, 356). The 2-nitration of *m*-halogenodimethylanilines (Hodgson and Nicholson, *J.*, 1941, 766) indicates the effect to be a function of the two groups alone. The 2-chlorination of 4-acetamido-*NN*-dimethyl-3-nitroaniline (Part III) is analogous; it may be explained by assuming that resonance structures (I) and (II) are compounded with (III) (de la Mare, *J.*, 1949, 2874). Such interaction of the nitro-group with the ring necessitates movement of the oxygen atoms into the plane of the ring (Pauling, "The Nature of the Chemical Bond," Cornell, 1945); these carry fractional negative charges relayed indirectly from the dimethylamino-group and in the case of diazotised 4-amino-*NN*-dimethyl-3-nitroaniline (IV) will set up an electrical and steric barrier to the approach of coupling reagents. An *o*-substituent in addition to inhibiting the direct influence of the dimethylamino-group on the *p*-position will largely restore the *m*-nitro-group to a state of free rotation.

In the diazonium compounds of *p*-aminodimethylaniline and its derivatives salt formation at the dimethylamino-group should produce bivalent ions of high coupling activity comparable with the *p*-nitrobenzenediazonium cation. The coupling of some of these compounds in strong acid under the conditions of Schoutissen (*J. Amer. Chem. Soc.*, 1933, **55**, 4541) was therefore examined. Evidence of reaction was obtained in each case. Comparison of the yields of azo-compound obtained after 24 hours showed that diazotised *p*-aminodimethylaniline (49%) reacted more slowly than *p*-nitroaniline (100%); the value of this comparison is reduced by uncertainty in regard to the degree of salt-formation of the NMe_2 group in the medium. Substituents in diazotised *p*-aminodimethylaniline exert a complex effect on this reaction since they modify both the basicity of the NMe_2 group and the extent of withdrawal of electrons from the diazo-group. Yields obtained were as follows: *m*-nitro, 7%; *m*-chloro, 46%; 2-chloro-3-nitro, 100%; 2 : 5-dinitro, 49%. The non-coupling diazo-compound in these reactions appeared to remain unchanged; no evolution of nitrogen was apparent.

EXPERIMENTAL.

Coupling in Weak Acid.—The azo-coupling experiments were carried out as far as possible by a standardised procedure essentially similar to that described (Part I, p. 619) for the reaction of diazotised *p*-aminodimethylaniline with amines (β-naphthol couples satisfactorily under these conditions). The diazo-solutions were normally prepared from 0·5 g. of the base in a mixture of hydrochloric acid (1 c.c.; *d* 1·2) and water (10 c.c.), except that for 4-amino-*NN*-dimethyl-3-nitroaniline a larger amount (2 c.c.) of acid served to prevent the separation of a trace of dark amorphous material in the diazotisation. In coupling experiments with dimethylaniline, and α- and β-naphthylamine, the base (1 molar equivalent) was dissolved in hydrochloric acid (1 c.c.) and water, the diazo-solution was added, and excess of mineral acid neutralised with aqueous sodium acetate solution. β-Naphthol, naphthionic acid, and anthranilic acid were dissolved in the form of sodium salts and the requisite amount of aqueous sodium acetate was added to the solutions before the addition of the diazo-compound. The coupling experiments were set aside for periods ranging from 2 days for rapidly coupling compounds to 5 days for the more sluggish.

The method of isolation of the azo-compound depended to some extent on the coupling components. Care was taken to eliminate any unchanged amine or phenol from the dye by suitable adjustment of pH. Wherever necessary the azo-compound was dissolved in concentrated hydrochloric or sulphuric acid, and the solution filtered; reprecipitation could then be brought about at a pH value sufficiently low to ensure that simple amines, including the products of reductive elimination of the diazo-group, remained in solution. The purified azo-compound was dried to constant weight *in vacuo* over sulphuric acid. Most of the coupling experiments were repeated at least once to ensure that the yields were reasonably reproducible; the theoretical conclusions are however drawn from the general effect of five or six different coupling reactions for each diazo-compound, rather than from individual yields, and it is possible that by careful attention to the conditions the yield from any given coupling-reaction might be increased. Although reprecipitation improved the products of the more sluggish couplings, yet owing to some contamination by tarry products these were less pure than the dyes obtained in high yield.

The yields of deamination product recorded in the Table were obtained by procedures similar to those described in Part IV, involving steam-distillation of the reaction mixture. In the case of the coupling of diazotised 4-amino-3-chlorodimethylaniline with dimethylaniline the steam-distillate therefore contained a mixture of dimethylaniline and *m*-chlorodimethylaniline. This was extracted with ether and the dried (Na_2SO_4) extract evaporated. The weighed oil was then fractionally precipitated from ethanol with picric acid. Dimethylaniline picrate, m. p. 163—164°, came out first and was thus partly removed. Later crops were mixtures and subsequently the pure *m*-chlorodimethylaniline picrate, m. p. 145° (cf. Fieser and Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 383), appeared. By recovery of the base from mixtures and further treatment with picric acid, a yield of 40% of the pure picrate was obtained; this figure is of course a minimum value for the reaction owing to experimental losses. In the distillation flask remained a hard, brittle resin amounting to 45% of the original base diazotised; this was probably a mixture of two azo-compounds derived from dimethylaniline and *m*-chlorodimethylaniline respectively, together with products of free radical reactions.

Coupling in Concentrated Acid.—The base (0·002 mol.) was dissolved in concentrated sulphuric acid (1·5 c.c.) at 0° and mixed with a solution of sodium nitrite (0·145 g.) in sulphuric acid (1·5 c.c.). Phosphoric acid (6 c.c.; *d* 1·7) was added below 0°. After 30 minutes powdered urea (0·2 g.) was added. After a further 30 minutes a solution of β-naphthol (1 g., excess) in glacial acetic acid (3 c.c.) was introduced and the mixture vigorously shaken. A gradually increasing red colour was apparent, its intensity being least with 4-amino-*NN*-dimethyl-3-nitroaniline. After 24 hours at room temperature the mixture was poured into water; the precipitated solid was filtered off and washed with water. It was then set aside overnight with excess of 5% aqueous sodium hydroxide and filtered again. The azo-compounds obtained corresponded in their properties to those produced in the weak acid coupling. Diazotised 4-amino-2-chlorodimethylaniline appeared to couple rapidly but the yield was not recorded owing to the difficulty of filtering the semi-solid mixture of azo-compound with excess of β-naphthol obtained on pouring of the solution into water.

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