LXXVII.—*The Influence of Nitro-groups on the Reactivity of Substituents in the Benzene Nucleus. Part VI. The Elimination of Halogen during the Reduction of Halogenated Nitro-compounds.*

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THE elimination of halogen from the benzene nucleus during the reduction of halogenated nitro-compounds has been frequently observed. Zincke and Sintenis observed that 4-bromo-*m*-dinitrobenzene was reduced to *m*-phenylenediamine by tin and hydrochloric acid (*Ber.*, 1872, **5**, 792), and 4-bromo-*m*-phenylenediamine remained unknown until Morgan employed iron filings with a little hydrochloric acid as reducing agent (*T.*, 1900, **77**, 1202). A number

of other instances were quoted by Blanksma (*Rec. trav. chim.*, 1905, **24**, 320), who concluded that elimination of halogen occurred only when this substituent was in the ortho- or para-position to the nitro-group. Further, such elimination was facilitated by the presence of hydroxyl-, amino-, or methyl groups in the meta-position to the nitro-group. For example, 2:4:6-tribromonitrobenzene furnishes 2:4-dibromoaniline, but *m*-toluidine is obtained from 2:4:6-tribromo-*m*-nitrotoluene. Loring Jackson and Calvert had previously shown that 2:4:6-tribromo-*m*-phenylenediamine was converted into *m*-phenylenediamine by treatment with tin and hydrochloric acid (*Amer. Chem. J.*, 1896, **18**, 466), and Blanksma concurred in the view expressed by them that nitro-compounds of the type in question do not lose halogen until the nitro- has been converted into an amino-group.

It is obvious, however, that qualitative evidence of this character does not exclude the possibility that some halogen may be eliminated in the first stages of the reaction. Especially is this the case in view of the known reactivity of halogen in the ortho- or para-position to a nitro-group. It is also conceivable that some elimination may occur during the passage of the intermediate hydroxyl-amino- into the amino-compound. Thus Bamberger has explained the introduction of chlorine often observed in the course of reduction with tin and hydrochloric acid by the following scheme of reactions (*Ber.*, 1895, **28**, 201; 1898, **31**, 1504; compare also Blanksma, *Rec. trav. chim.*, 1906, **25**, 765):

There seemed just a possibility that, during the reduction of, for example, 2-iodo-3-nitrotoluene, the following reaction might occur:

Admittedly the product (I) corresponds with that from which *p*-chloroaniline is produced according to Bamberger's scheme, and would therefore most probably rearrange into 2-iodo-*m*-toluidine, but the possibility of its reduction in the manner indicated to (II)

needs consideration. Flürscheim and Simon, in the course of experiments on the preparation of azoxy-compounds by the acid reduction of nitro-derivatives, showed that when 4-bromo-*m*-dinitrobenzene is reduced with a small proportion of stannous chloride, no hydrochloric acid being present, ionic bromine is not produced. They therefore accepted the view of Jackson and Calvert already mentioned. But, as their product consisted of approximately 80 per cent. of azoxy-compound and 20 per cent. of amine hydrochloride (T., 1908, **93**, 1481),

it is evident that the reduction of most of the material did not pass beyond the hydroxylamino-stage, and therefore that further evidence is desirable before this possibility is definitely ruled out in the general case. It may be mentioned that in the course of the present work an experiment on somewhat similar lines, in which hydrochloric acid was employed, showed that the proportion of ionic iodine produced from 2-iodo-3-nitrotoluene was also negligible.

It appeared that more conclusive evidence on the whole matter might be gained by a quantitative comparison of the amounts of iodine eliminated from corresponding nitro-, hydroxylamino-, and amino-compounds during their reduction under conditions as closely comparable as possible. A discussion of the methods employed will be found in the experimental portion of this paper. The following table summarises the results obtained by the gradual addition of alcoholic solutions of equivalent quantities of nitro- or hydroxylamino- or amino-derivative, respectively, at a definite rate to a constant quantity of stannous chloride and hydrochloric acid at 86.5° :

Orientation of Substituents.			Nature of Substituent X.		
Me.	I.	X.	NO ₂ .	NH.OH.	NH ₂ .
—	2	4	0	trace	trace
—	2	5	— *	8.4	12.65
—	2	3	4.9	14.8	21.5
1	3	6	9.2	11.2	13.1
1	2	5	19.5	33.6	36.1
1	4	3	21.1	42.3	— †
1	2	3	45.2	57.9	64.2

* *p*-Iodonitrobenzene was not sufficiently soluble for the purposes of these experiments.

† 4-Iodo-*m*-toluidine is described as liberating iodine on exposure to heat, or light, or air. Its "reduction" was therefore not undertaken.

The consistent increase in the values observed in each series, according as nitro-, hydroxylamino-, or amino-derivative was reduced, is at once explicable in terms of the view of Jackson and Calvert, since under the experimental conditions the proportion of reducing agent available for the removal of iodine is progressively greater in this order. The favourable influence of the methyl group in the meta-position to the nitro-group, commented on by Blanksma, is also very noticeable. Since the opposite effect is observed when the reactivity of substituents is due to an ortho-nitro-group (Kenner, T., 1914, **105**, 2717; Kenner and Parkin, T., 1920, **117**, 852), the probability is increased that the reactions now considered do not belong to this category. The results do not definitely disprove the view that halogen may be eliminated from the hydroxylamine, but this is rendered very doubtful by the outcome of an experiment with 4-iodo-5-nitro-*m*-xylene. This compound was chosen because the data already supplied indicated that a very considerable proportion of iodine would be removed during its reduction, and therefore that if this occurred to any extent prior to formation of the amino-group, the amount eliminated might be greater than the proportion of amino-compound formed, if an insufficiency of reducing agent for both reactions were employed. Actually, however, 61.1 per cent. of the total iodine was converted into the ionic form, and after allowing for this, a quantity of reducing agent remained unaccounted for, which would suffice for the formation of 61.8 per cent. of amino-compound.

Our experiments may therefore be said further to support the view that the removal of halogen in the reactions and conditions under consideration does not precede the formation of the amino-group. It has been previously pointed out that the first stage in the reduction of a nitro-group probably consists in the formation of a transitory molecular compound of hydrogen or of the reducing agent with the nitro-group (Burton and Kenner, T., 1921, **119**, 1047). According to the view advocated in this series of papers, however, the formation of such a product in the case, for example, of *o*-iodonitrobenzene represents the necessary preliminary stage to the elimination of iodine, so that the system (III) may decompose with formation either of nitrobenzene or of *o*-iodonitrosobenzene :

The former will be facilitated by increased mobility of the halogen atom and by the use of a very mild reducing agent, corresponding with a potential difference insufficient for the electrochemical reduc-

tion of the nitro-group. Hence it is that picryl chloride may be reduced to trinitrobenzene by the action of various metals in neutral organic solvents (Meyer, D.R.-P. 234726). In general, however, the halogen is insufficiently mobile, and the reducing agent, usually stannous chloride, is too powerful. As a result, the reaction proceeds almost entirely, if not entirely, in the direction of formation of nitroso- and eventually of amino-compound. The non-elimination of halogen during the transition from the hydroxylamino- to the amino-derivative must be ascribed to the rapidity with which the product (I) assumes the aminic form, a reaction which will probably be much accelerated by the presence of strong acid.

Considering the removal of halogen from the amino-compound, it will be noted, first, that apart from hydrogen the amino-group does not render *o*-substituents reactive, and secondly, that the removal occurs in strongly acid solution and hence, in all probability, from the salt of the base rather than from the base itself. It is a confirmation of this that the preparation of such halogenated amines from the nitro-compounds is usually best achieved by the use either of ferrous sulphate and ammonia (compare, for example, Wheeler and Liddle, *Amer. Chem. J.*, 1909, **42**, 441), or of zinc and acetic acid (compare, for example, Jackson and Calvert, *loc. cit.*), or, as already mentioned, of iron and a little hydrochloric acid; in other words, under such conditions that salt-formation is largely prevented. Accepting, therefore, the view that halogen is eliminated from the salt of the base, it is then noteworthy that the effect of salt-formation on the amino-group is to confer meta-directive properties which, if perhaps not as pronounced as in the case of the nitro-group, are nevertheless quite definite. Thus, whilst the claim of Noelting and Collin (*Ber.*, 1884, **17**, 261) that the nitration of aniline in strong sulphuric acid solution results almost exclusively in the formation of *m*-nitroaniline has been shown to have been exaggerated (Holleman, Hartogs, and van den Linden, *Ber.*, 1911, **44**, 704), it is true that the meta- and para-derivatives are formed in almost equal proportions. Vorländer, who showed that nitration of phenyltrimethylammonium nitrate, as well as bromination of the bromide, yielded a meta-derivative as sole product, also concluded that "the meta-directive influence of the ammonium group is not limited to the quaternary trimethylammonium-, but is similarly exhibited by primary, secondary, and tertiary ammonium-groups as soon as the aniline derivatives are present in strongly acid solution" (*Ber.*, 1919, **52**, [B], 268). This is perhaps best illustrated by the work of Tingle and Blanck* (*Amer. Chem. J.*,

* These workers also showed that it is not possible to obtain anything but dark-coloured products from the action of strong nitric acid on aniline nitrate.

1906, **36**, 605), who showed that meta-derivatives were produced by the nitration of formanilide, acetanilide, monomethyl-, dimethyl-, and diethyl-anilines respectively in sulphuric acid solution, although they were unable to confirm this in the case of benzanilide (compare Hübner, *Annalen*, 1881, **208**, 278).

The reaction in question is therefore comparable with those depending on the mobility of substituents in the ortho- or para-positions to nitro- or other meta-directive groups. When, further, it is remembered that stannous chloride has a great tendency to form the double compounds with the amine hydrochlorides which, by analogy with the view adopted in the case of nitro-groups, should represent the intermediate stage in the reactions now under discussion,

it would appear that a fairly complete basis for their comprehension has been reached, and one that may be tested by further experiment. An explanation of the influence of substituents is less easy to discover. The effect of substituents is probably the resultant of their influence in several directions. Thus, they will modify the strength of the base, and hence the completeness of salt-formation; the readiness with which the necessary additive compound of salt with stannous chloride is produced will be affected; and they will influence the mobility of the halogen atom in the manner previously discussed in this series of papers. Of these effects, the first is probably the most important, if salt-formation be fundamental to the occurrence of the reaction, and it is perhaps significant, in connexion with the favourable influence of the methyl, hydroxyl, and amino-groups in the meta-position to the amino-group, that in this position an increase in the basicity, or capacity for salt-formation, of the amino-group would be anticipated (compare Flürscheim, T., 1909, **95**, 725). Thus, *m*-toluidine is a stronger base than aniline, whereas *o*-toluidine is weaker. *p*-Toluidine is even stronger than *m*-toluidine in this respect, and therefore it will be desirable to study quantitatively the behaviour of its 3-iodo-derivative. One of us is, however, prevented from further participation in this work, and our results are therefore communicated in their present form.

EXPERIMENTAL.

The nitro- and amino-compounds used in the following experiments had all been previously described, with the exception of 6-iodo-*m*-toluidine. This base was prepared by the reduction of 2-iodo-5-nitrotoluene either by means of ferrous sulphate and

ammonia at 100°, or in glacial acetic acid solution by means of stannous chloride and hydrochloric acid. It crystallises from alcohol in colourless plates, m. p. 46° (Found : N = 6·12. C_7H_8NI requires N = 6·01 per cent.). The *hydrochloride* consists of colourless needles, and the *acetyl* derivative of colourless prisms, m. p. 147—148° (Found : N = 5·14. $C_9H_{10}ONI$ requires N = 5·09 per cent.). All efforts to obtain the base, m. p. 98—99°, described by Artmann (*Monatsh.*, 1905, **25**, 943) as resulting from the action of ferrous sulphate and ammonia on 2-iodo-5-nitrotoluene were unsuccessful.

Determination of the Proportion of Halogen Eliminated.—In the case of the nitro-compounds, the solutions for reduction were prepared by dissolving the iodonitrobenzene (10 grams), or an equivalent amount of iodonitrotoluene, in a mixture of absolute alcohol (100 c.c.) and water (10 c.c.).

The hydroxylamine solutions were prepared by reduction at the boiling point of exactly similar solutions of the nitro-derivatives in presence of ammonium chloride (0·8 gram) by gradual addition of zinc dust (14 grams) (compare Bamberger and Baudisch, *Ber.*, 1909, **42**, 3581), and filtering the colourless solutions obtained. These were then preserved from oxidation in an atmosphere of carbon dioxide.

Solutions of the amino-derivatives were made up from quantities of the bases equivalent to the above amounts of nitro-compounds, using the same quantities of alcohol and water.

The reduction experiments were carried out in a flask fitted with a cork carrying a reflux condenser, a thermometer reaching to the bottom of the flask, and a dropping-funnel. A solution of crystallised stannous chloride (23 grams, 94·6 per cent. purity) in concentrated hydrochloric acid (26·4 grams) was placed in the flask, and the whole heated to 86·5°, and maintained at this temperature by means of a water-bath. The solution for reduction was added at the rate of 5 c.c. every five minutes. Five minutes after the last addition, the solution was cooled, and made up to 500 c.c. One-tenth of this was rendered strongly alkaline with sodium hydroxide solution and extracted with ether. The aqueous solution was neutralised with sulphuric acid and treated with 10 per cent. sodium nitrite solution (10 c.c.) and dilute sulphuric acid (1·5N, 10 c.c.). The iodine liberated was then removed in a current of steam, and estimated by Jannasch's method (*Z. anorg. Chem.*, 1893, **1**, 144, 245) by absorption in alkaline hydrogen peroxide solution, followed by precipitation as silver iodide. It was found that unless neutralisation was performed before the treatment with nitrous acid, the precipitate contained an appreciable amount of

silver chloride. As a precaution, the silver iodide was therefore in every case washed with dilute ammonia until its weight was constant. The results obtained are shown in the table in the theoretical portion of this paper.

The conditions of reduction above described were chosen for the following reasons. The instability of the hydroxylamino-solutions renders their gradual addition to a hot solution of the reducing agent preferable to the inverse order of addition, and hence decides the mode of addition throughout. A consideration of the quantity of reducing agent to be employed at once shows that rigidly comparable experiments are not realisable, and that a compromise has to be made on this point. For very soon after the first addition of nitro- or hydroxylamino-solution has been made, amino-compound is present and is exposed to the action of the solution. For this reason it was decided not to employ quantities of stannous chloride proportional to those theoretically required for complete reduction and iodine elimination in each case, but the same quantity throughout. Further, this quantity was less than that theoretically necessary both for reduction and elimination of halogen, because this seemed to offer a greater prospect of detecting any formation of ionic iodine which might occur prior to the formation of amine. Finally, the impossibility of attaining rigidly comparable conditions of reduction seemed to render superfluous the precautions usual to ensure constancy of temperature in physico-chemical measurements.

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