

THE DIRECT INTRODUCTION OF THE DIAZONIUM GROUP INTO AROMATIC NUCLEI—VI

REACTION MECHANISMS

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Abstract—Mechanisms are put forward to explain the formation of diazonium salts by the direct interaction of nitrous acid derivatives with aromatic compounds under a variety of conditions.

SINCE the preliminary communication¹ considerable work has been done,²⁻⁷ and we feel the investigation has now reached a stage where sufficient data is available to make speculation about possible reaction mechanisms worthwhile. The purpose of the present paper is to collect together all the relevant data, largely from work already described in previous papers in this series or from earlier work and to show that all the results so far obtained can be explained in terms of very simple reaction mechanisms. Three rather different procedures have been used to introduce the diazonium group into aromatic compounds. Phenols and tertiary amines have been treated with nitrous acid in dilute aqueous or alcoholic media;^{2,4,6,7} phenol ethers and poly-alkylbenzenes have been treated with nitrous acid in strongly acidic media such as concentrated sulphuric acid;^{2,5,8} finally deactivated compounds such as nitro-derivatives have been treated with nitrous acid and catalytic amounts of mercuric ions in concentrated sulphuric acid.³ Evidence has already been given to show that in the last case mercuration is the initial reaction. The first point to establish is that all these reactions proceed via nitroso-compounds.

(i) Evidence that nitroso-compounds are invariably intermediates

It has previously been shown that, with each of the above methods for introducing the diazonium group, nitroso-compounds occur among the reaction products and that the nitroso-compound so formed when returned to a similar reaction system is converted into a diazonium salt. This does not establish that all the diazonium salt is formed in this way, for the route via the nitroso-compound might only be of minor importance and some as yet unknown direct route be the chief mechanism. We now have evidence for all three methods that *all* the diazonium salt is formed via the nitroso-compound. *p*-Cresol is converted into the corresponding diazonium salt by buffered nitrous acid in 77% yield.⁶ If cupric ions are added to this solution the

¹ J. M. Tedder, *Tetrahedron* 1, 270 (1957).

² J. M. Tedder, *J. Chem. Soc.* 4003 (1957).

³ J. M. Tedder and G. Theaker, *J. Chem. Soc.* 4008 (1957).

⁴ J. M. Tedder and G. Theaker, *Chem. & Ind.* 1485 (1957).

⁵ J. M. Tedder, *J. Amer. Chem. Soc.* 79, 6090 (1957).

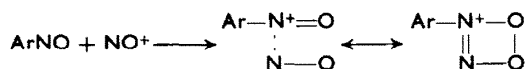
⁶ J. M. Tedder and G. Theaker, *J. Chem. Soc.* 2573 (1958).

⁷ J. M. Tedder and G. Theaker, *J. Chem. Soc.* In press.

⁸ E. J. Bourne, M. Stacey, J. C. Tatlow and J. M. Tedder, *J. Chem. Soc.* 1695 (1952).

formation of the diazonium salt is almost completely suppressed. The cupric ions trap the nitroso-compound as a chelate and prevent it from being converted into the diazonium salt, as it rapidly is by such solutions in the absence of copper. These facts clearly establish the nitroso-compound as an essential intermediate in this case.

The reactions carried out in strongly acid media are more complicated. At first we assumed that the diazonium salt was actually formed in the strong acid solution, but it has now been found that no diazonium salt is formed until the reaction mixture is poured into water. All the reactions in strong acid media are accompanied by very intense red-brown colours. We believe that these colours are due to a complex ion formed between the nitroso-compound and the nitrosionium ion.



Such colours can be produced by adding nitrosobenzene to concentrated solutions of sodium nitrite in sulphuric acid. Similar complexes have been proposed for nitrosoamines.⁹ These complexes may be important in protecting the nitroso-group from further reaction in the concentrated sulphuric acid.¹⁰ The reaction procedures used to prepare diazonium salts from mesitylene² (a typical strong acid preparation) and from *p*-nitroanisole³ (a mercury catalysed reaction) have been repeated exactly as before, only instead of pouring the reaction mixtures into crushed ice, they were poured into cold sulphamic acid solution. In both cases only traces of diazonium salt were detected. In the latter example an 88% yield of crude 2-nitroso-4-nitroanisole was isolated (cf. a 75% yield of diazonium salt when poured into water).³ In the former case the yield of diazonium salt was reduced to less than 15% (cf. a 78% yield when poured into water²) but the nitrosomesitylene could not be isolated from the nitrobenzene used as solvent. Not only do these results show that the nitroso-compound is an essential intermediate in the preparation of diazonium salts by either of these procedures, but clearly the mercuration procedure³ could be adapted for the preparation of nitroso-compounds. It also seemed likely that the yields of diazonium salt could be improved by pouring the acid solutions into nitrous acid instead of water. This has been confirmed with *p*-nitroanisole when the yield was raised from 72.5% when poured into water, to 79.0% when poured into nitrous acid.

(ii) *The mechanisms of the nitrosations*

It is not the purpose of the present paper to draw any definite conclusions as to the exact mechanisms of the nitrosation steps. However certain inferences can be drawn from the data already available. Phenols and tertiary amines are nitrosated in very weakly acidic media, if diazonium salts are desired as the end products, and under these conditions only a limited number of nitrosating species are available. The most likely are HNO_2 , N_2O_3 and NOCl . Less likely is H_2NO_2^+ and NO^+ can be discounted in such weakly acidic systems. On the basis of the work of Ingold, Hughes and their collaborators¹¹ N_2O_3 is the strongest candidate as the effective species, since in *qualitative* experiments chloride ion appears to have very little

⁹ C. C. Addison, N. Hodge and J. C. Sheddon, *Chem. & Ind.* 1338 (1953).

¹⁰ E. Bamberger, H. Büsdorf and H. Sand, *Ber. Dtsch. Chem. Ges.* 31, 1513 (1898).

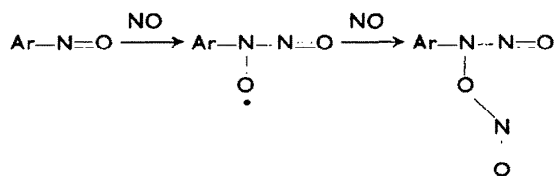
¹¹ E. D. Hughes, C. K. Ingold and J. H. Ridd, *J. Chem. Soc.* 88 (1958).

accelerating effect. On the other hand nitrosation by ethyl nitrite and hydrogen chloride in anhydrous ethanol^{4,6} probably involves molecular NOCl.

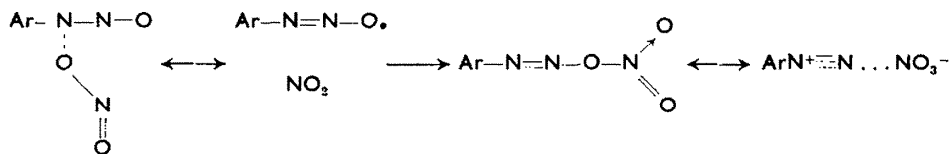
The reactions in more strongly acidic media^{2,3,5,8} almost certainly involve nitrosation by the nitrosonium ion¹² and all the results so far obtained are consistent with such an hypothesis. In the mercury catalysed reaction the nitrosonium ion is probably also the species which displaces the mercuric ion, since this replacement will only occur in strongly acidic media.

(iii) *The conversion of the nitroso-compound into the diazonium salt*

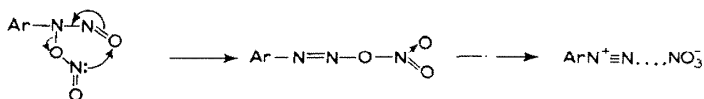
Whereas there are three very different conditions for the nitrosation, the conversion of the nitroso-compound into the diazonium salt always occurs in dilute nitrous acid in all the procedures developed so far. Bamberger showed that nitric oxide will convert nitrosobenzene into benzene diazonium nitrate and later that sodium nitrite in acetic acid will do the same.¹³ He was unable to establish the stoichiometry of the reaction definitely, but recently Havinga and his co-workers have shown that three moles of nitrite are necessary in the acetic acid system.¹⁴ We have found that nitrosobenzene in nitrobenzene solutions absorbs almost exactly two moles of nitric oxide; unfortunately the yield of azo-dye obtained by coupling the resulting diazonium salt was not quantitative (75%) so that the stoichiometry of this reaction is still not completely established. However, if just two moles of nitric oxide are assumed to be involved as suggested by the above result, a simple addition mechanism seems probable.



To be followed by either a dissociation and readdition;



or an intramolecular rearrangement.

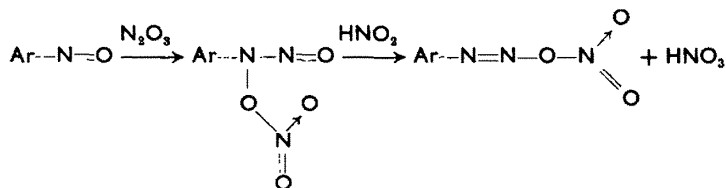


In solution the reactive entity is likely to be dinitrogen trioxide instead of nitric oxide and this would readily explain the difference in the observed stoichiometry.

¹² C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Jones, G. J. Minkoff and R. I. Reed, *J. Chem. Soc.* 2628 (1950).

¹³ E. Bamberger, *Ber. Dtsch. Chem. Ges.* 30, 506 (1877); *Ibid.* 51, 634 (1918).

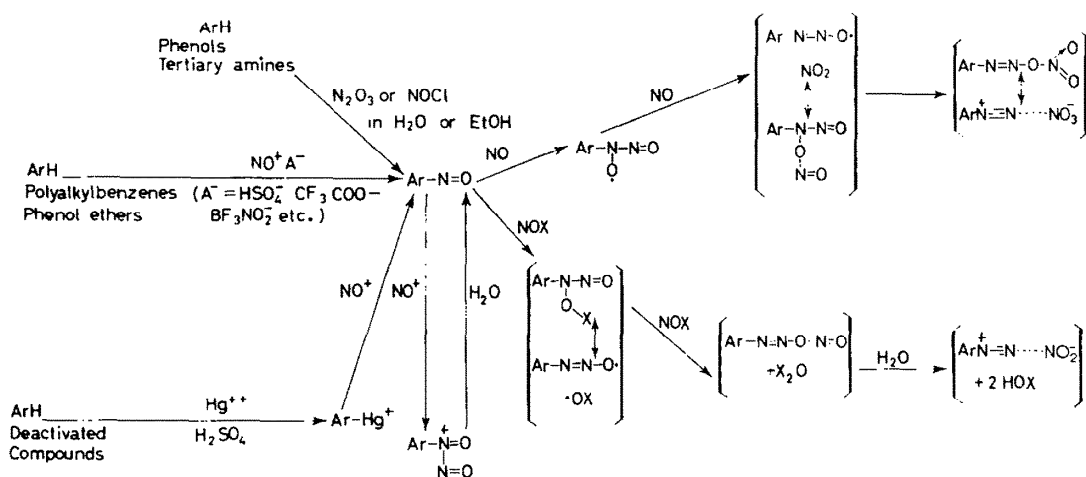
¹⁴ A. Kraaijeveld and E. Havinga, *Rec. Trav. Chim.* 73, 549 (1954).



Clearly similar mechanisms can be visualised for a variety of nitrosyl derivatives NOX.

(iv) Conclusions

We believe we have established unequivocally the two stage nature of the reaction involving a nitroso-intermediate. There appear to be several mechanisms leading to the formation of the nitroso-compounds and similarly a number of closely related mechanisms for the conversion of the nitroso-compound into the diazonium salt. It has not been possible so far to attempt thorough investigations to elucidate the exact details of these steps; however, our present qualitative ideas about these mechanisms have proved of the utmost value when attempting to extend the reaction and for this reason we are presenting them now. They are summarised in the following scheme.



X = NO₂, Cl, Br etc.

HOX will tend to oxidise any HNO₂ present.

EXPERIMENTAL

Experiments to halt the reaction at the nitroso-stage

(a) *p*-Cresol nitrosated in the presence of cupric ions. *p*-Cresol (1.08 g) was dissolved in acetone (50 cc) and the solution diluted with water (100 cc). Sodium nitrite (10 g) were dissolved and cupric acetate (10 g) were added. Not all the cupric acetate dissolved. The mixture was cooled to 0° and 2 N HCl (20 cc) were added. After 20 hr a 50 cc portion was withdrawn and the excess nitrous acid removed by the addition of sulphamic acid solution. The solution, which was an intense purple colour, was extracted with light petroleum (b.p. 60–80°) and the aqueous layer treated with a slight excess of 2 N NaOH solution. The copper hydroxide was removed by filtration and the clear yellow liquid rendered just acid. Excess resorcinol was added and the solution was made alkaline and left

for an hour before reacidification. A trace of dye (0.01 g) was precipitated (cf. 0.51 g in the absence of copper ions).

(b) *Mesitylene treated with sodium nitrite and sulphuric acid in nitrobenzene and then poured into sulphamic acid solution.* Sodium nitrite (4.2 g) was dissolved in concentrated sulphuric acid (10 cc). Nitrobenzene (10 cc) was added to the cooled paste. Mesitylene (1 cc) was added at 20° and the mixture frequently stirred by hand during a 4 hr reaction.³ The mixture was then treated with sulphamic acid (7 g) poured into a solution of sulphamic acid (7 g) in ice/water (200 g) and ether extracted (green solution). The aqueous portion was coupled with excess β -naphthol. Yield of crude mesitylene-azo- β -naphthol, red solid, m.p. 127–131°, was 0.32 g (15% theory). Attempts to isolate the nitrosomesitylene from the ethereal/nitrobenzene solution were not successful. However, presence of nitroso-compound was established qualitatively (Liebermann test).

(c) *Preparation of 2-nitroso-4-nitroanisole.* *p*-Nitroanisole (3.06 g) was dissolved in concentrated sulphuric acid (15 cc) containing mercuric oxide (0.043 g) at 20°. A solution of sodium nitrite (6.90 g) in concentrated sulphuric acid (30 cc) was added evenly during 3 hr at 20°. After 3 hr further reaction at 20° the mixture was treated with sulphamic acid (10 g) and the whole poured carefully into ice/water (500 g) containing sulphamic acid (10 g). The buff coloured precipitate was filtered off (3.20 g 88%, m.p. 109–112°). (The filtrate was tested for the presence of diazonium salt—only a trace was detected). The crude nitroso-compound was recrystallised three times from aqueous acetic acid (plus charcoal) as pale yellow plates, m.p. alone, or in admixture with pure 2-nitroso-4-nitroanisole,⁹ 123–124°. The u.v. spectrum was compared with that of the authentic material and found identical; the spectrum of the crude material indicated that it was 90.0% 2-nitroso-4-nitroanisole.

Improving the yield of 2-diazo-4-nitroanisole by pouring the reaction products into nitrous acid

p-Nitroanisole was treated with mercuric oxide and sodium nitrite in concentrated sulphuric acid as above, (c). After 3 hr reaction at 20°, aliquots (ca. 2.0 g) were removed and treated as follows:—

(a) reaction mixture poured into ice/water (100 g), treated immediately with a slight excess of sulphamic acid solution, neutralised with sodium acetate and coupled with an excess of a standard solution of 3-methyl-1-*p*-sulphophenyl-5-pyrazolone solution containing sodium acetate.³ After a suitable period for completion of coupling, the excess of pyrazolone was back-titrated with standard *p*-nitrobenzene diazonium-chloride solution using the sodium salt of H-acid solution as external indicator. Yield of diazonium salt as above was 72.5%.

(b) mixture poured into ice/water containing sodium nitrite (2 g) and reaction allowed to proceed for 30 min. A slight excess of sulphamic acid was then added and the yield estimated as above. Yield of diazonium salt was 79.0%.

Reaction of nitric oxide with nitrosobenzene

Purified nitrosobenzene (approx 0.2 g) was added to nitrobenzene (20 ml) saturated with nitric oxide and contained in a 50 ml conical reaction vessel attached to a simple low pressure "hydrogenation" apparatus containing pure nitric oxide in the storage burette. The reaction was carried out with stirring at 20° for up to 25 hr, until no more gas was absorbed, the reaction vessel being covered with dark paper. From two experiments, the absorption of nitric oxide by nitrosobenzene was 2.21 and 1.88 moles per mole. The reaction mixture was then poured into water (100 cc) and the nitrobenzene separated and the aqueous solution coupled with excess β -naphthol. The yield of crude benzene-azo- β -naphthol, m.p. 122–4°, was 0.383 g (from nitrosobenzene (0.22 g) and 2.21 moles/mole nitric oxide) equivalent to a 75% yield.

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