883. *The Rearrangement of Aromatic* N-*Nitroamines. Part II.* Isotopic Test for Intramolecular Character in the Nitro-transfers from Side-chain to* ortho- *and* para-*Positions.*

By S. Brownstein, C. A. Bunton, and E. D. Hughes.

It was known from previous work that the main part of the rearrangement of *N*-nitroaniline in aqueous sulphuric acid, which produces 93% of *o*-nitroaniline and 7% of *p*-nitroaniline, is intramolecular. However, the previous work was not quantitative enough to exclude the possibility that the *para*-product and perhaps a little of the *ortho*-isomer might arise from a concurrent acidolysis of the *N*-nitro-group and subsequent *C*-nitration by the nitric acid formed. This possibility is now excluded by showing that no trace of a nitrogen-isotopic label contained in nitric acid introduced into the medium used for the rearrangement appears in either the *o*- or the *p*-nitroaniline. Both products are therefore formed exclusively by intramolecular mechanisms, concerning which a suggestion is made.

Bamberger showed that *N*-nitroaniline and similar nitro-amines undergo rearrangement under the influence of acids to form *C*-nitroanilines.[1] He suggested that the nuclear nitration of aniline derivatives that can easily form nitro-amines may proceed by intramolecular rearrangement of first-formed nitro-amines.[2] Holleman *et al.* cast doubt on this concept by showing that the *C*-nitroanilines are formed in different proportions by the rearrangement of *N*-nitroaniline, and by the direct nitration of aniline.[3] However, this work left some doubt, because the nitrations of aromatic amines are notable for the fact that the proportions of isomers formed vary markedly with the conditions, and the authors used essentially different conditions for their rearrangement and nitration. This hole in the evidence was plugged by Hughes and Jones, who obtained the following, quite different, proportions of isomers for rearrangement and for nitration in the same conditions, namely, in sulphuric acid monohydrate at its freezing-point:[4]

Rearrangement of *N*-nitroaniline	*ortho*, 93%;	*meta*, 0%;	*para*, 7%
Nitration of aniline	,, 6%;	,, 34%;	,, 59%

It was thus made clear that the nuclear substitution is not a rearrangement in disguise, as Bamberger thought. The complementary question of whether the rearrangement is a nuclear substitution in disguise had already been raised by Orton's demonstration that the

* Part I, *J.*, 1950, 2678.

[1] Bamberger, *Ber.*, 1893, **26**, 471, 485; 1894, **27**, 359.
[2] Bamberger, *Ber.*, 1894, **27**, 584; 1895, **28**, 399; Bamberger and Hoff, *Ber.*, 1897, **30**, 1248; *Annalen*, 1900, **311**, 91.
[3] Holleman, Hartogs, and Linden, *Ber.*, 1911, **44**, 704.
[4] Hughes and G. T. Jones, *J.*, 1950, 2678.

rearrangement of aromatic chloro-amines normally proceeds by an acidolysis to form chlorine, which then effects nuclear chlorination.[5] Bradfield and Orton looked into nitro-amine rearrangements from this point of view, and concluded that, for the most part, they were not analogous.[6] For although they are general-acid catalysed, and although nitro-amines are in general reversibly acidolysed to form nitric acid, the authors could not establish that nitric acid is "invariably and normally" formed when nitro-amines rearrange. Hughes and Jones supplemented this evidence by showing that, whilst in some such rearrangements free nitric acid is not formed fast enough, in others it is freely formed but does not nitrate the aromatic nucleus fast enough to be made responsible for the products of the rearrangements.[4] It thus appeared that typical nitro-amine rearrangements proceed mainly independently of successive acidolysis and nuclear nitration, and therefore by some intramolecular mechanism, presumably, in view of the acid catalysis, an intramolecular rearrangement of the ionic conjugate acid of the nitro-amine.

None of the work surveyed in the preceding paragraph was quantitative enough to yield any conclusions except with respect to a preponderating proportion of the product of a rearrangement, *i.e.*, the main bulk of the principal isomer formed by rearrangement. It helped the concept, that at least this much of the reaction is intramolecular, to note that principal isomers formed in aryl nitro-amine rearrangements are always *ortho*-nitroanilines. A theory of these rearrangements was proposed to the effect that the ionic conjugate acid of the nitro-amine passes its nitro-group to the *ortho*-position by way of a rearrangement of the nitro-amine to a nitrito-amine, in which the nitrito-group could then form a bridge between the nitrogen and the *ortho*-carbon atom, and so migrate to *ortho*-carbon.[7]

The two further questions which arose can be stated with specific reference to the prototype example, the rearrangement of *N*-nitroaniline. It yields 93% of *o*-nitroaniline. We can accept, on the evidence cited, the conclusion that most of this is produced by an intramolecular rearrangement. But is it all produced thus? And how does the 7% of *p*-nitroaniline arise? Two such small proportions of the total product as the last few units % of the *o*-nitroaniline, and the whole of the *p*-nitroaniline, might conceivably be formed, concurrently with the main intramolecular reaction, by successive acidolysis and nuclear nitration. The attraction of this idea is that, if it were true, we should be relieved of the necessity either to extend the already-mentioned theory of the *ortho*-rearrangement or to invent some other theory to cover the formation of the *para*-by-product. The difficulty with the hypothesis that the *p*-nitroaniline arises from acidolysis and nuclear nitration, is that one would then expect some *m*-nitroaniline to accompany the other isomers. Actually Holleman, Hartogs, and Linden reported the presence of about half as much *m*- as of *p*-nitroaniline, but Hughes and Jones, whose work is thought to have been more accurate, found no *m*-nitroaniline at all.

In order to answer definitely the above two questions it was necessary to study quantitatively the distribution, after rearrangement, of a nitrogen-isotopic label appropriately introduced among the reactants. *N*-Nitroaniline was rearranged in aqueous sulphuric acid in the presence of some nitric acid containing an enhanced proportion of ^{15}N. Obviously, any acidolytic nitric acid formed from the nitro-amine would mix with this labelled nitric acid, and any subsequent nuclear nitration would carry the label into the formed nitroanilines.

Hughes and Jones found that *N*-nitroaniline is rearranged smoothly and quantitatively in cold 84% aqueous sulphuric acid. We confirmed this, but found in preparatory experiments that by-products are formed when potassium nitrate is added. Evidently some nitrating or other reactions of the introduced nitric acid with either the nitro-amine or its

[5] Orton, *J.*, 1902, **81**, 490, 806; 1905, **87**, 389; 1907, **91**, 146; 1908, **93**, 725; *Rep. Brit. Assoc.*, 1912, 117.

[6] Bradfield and Orton, *J.*, 1929, 915.

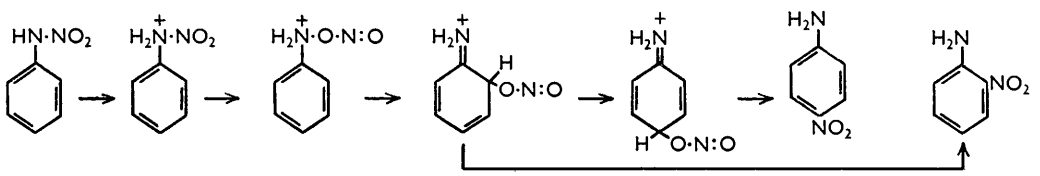
[7] Hughes, cited in Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, New York, 1953, p. 628; cf. Hughes and Ingold, *Quart. Rev.*, 1952, **6**, 51.

rearrangement products (reactions which were not necessarily involved in the rearrangement) were now running concurrently with the rearrangement. However, we found that this disturbance disappeared when we used more dilute acid, and, in particular, that, in 74% aqueous sulphuric acid at −20°, the rearrangement is smooth and quantitative, both in the absence and in the presence of added potassium nitrate.

These were therefore the conditions chosen for the experiments on the uptake in rearrangement of a nitrogen-isotopic label originally introduced in added potassium nitrate. The rearrangement product formed in such conditions was chromatographed on alumina. By far the most extensive deposit was *o*-nitroaniline. A pure sample of this, obtained by elution, was isotopically normal in nitrogen. Had 2% of the *o*-nitroaniline, equivalent to *ca.* 2% of the total rearrangement product, contained a nitro-group carried in from free nitric acid, this would have been noticeable in the mass-spectrographic analysis.

The *p*-nitroaniline was found concentrated in the tail of the chromatogram, and, as eluted, contained some residual *o*-nitro-isomer. In view of the isotopic normality of the latter, it was decided to analyse this *para*-concentrate directly, rather than to re-chromatograph it. First, as to the isomer proportions, analyses by freezing-point and by infrared spectrum agreed in giving the composition as 76% of *p*-nitroaniline plus 24% of *o*-nitroaniline. Then, as to isotopic composition, the normal nitrogen abundances were found. Had 1% of the *p*-nitroaniline, equivalent to 0·07% of total rearranged isomers, contained a nitro-group derived from free nitric acid, this would have been detected.

This work shows that the total products of the rearrangement of *N*-nitroaniline, including all the *o*-nitroaniline, and the by-product of *p*-nitroaniline, arise intramolecularly. In extension of the ideas relating to the *ortho*-rearrangement, the suggestion has been made that, just as, on the addition of a proton to the amino-nitrogen atom of the nitro-amine, the nitro-group, after becoming a nitrito-group, can bridge the amino-nitrogen and the *ortho*-carbon atom and can thus achieve transfer to the *ortho*-position, so, after the transfer, but before loss of the proton from the *ortho*-carbon atom, the same nitrito-group can alternatively bridge the *ortho*- and the *para*-carbon atom, and can thus accomplish the further step of transfer to the *para*-position: [8]



In principle, this hypothesis can be checked by means of the isotope effect of *ortho*-deuterium on the isomer ratio of the products of rearrangement, and experiments in this direction are being pursued.

Experimental

^{15}N-*Enriched Potassium Nitrate.*—This was prepared from ^{15}N-enriched ammonium chloride by carrying the ammonia from a basified solution in excess of oxygen over a platinum coil at 640° and trapping the oxides of nitrogen in potassium hydroxide. The abundance of ^{15}N in the nitrate was 2·95 atoms % in excess of normal. The proportion of nitrite, present as an impurity in the nitrate, was a few units per cent., which it was not considered necessary to remove. The nitrate also contained a little sulphate from the sulphuric acid used to neutralise the slight excess of alkali employed.

Rearrangement of N-*Nitroaniline.*—The nitro-amine (10 mmols.) was slowly added with stirring to a solution of potassium nitrate (0·75 mmol.), containing a ^{15}N-abundance of 2·95 atoms % in excess of normal, in aqueous sulphuric acid (25 ml.) containing 74% by weight of sulphuric acid at −20°. After stirring had been continued for a further 15 min., the solution was allowed to warm and was then diluted with ice-water (250 ml.). The product was extracted with chloroform, and the combined extracts were concentrated to about 10 ml., and then put

[8] Brownstein, Bunton, and Hughes, *Chem. and Ind.*, 1956, 981.

one-half on each of two alumina columns. Most of the *o*-nitroaniline (m. p. 68°) was washed out with 10 l. of benzene–light petroleum (30–70, v/v). The rest of the adsorbate was removed in benzene, and this eluate, after concentration, was put on a similar column. After development of the chromatogram with benzene (7 l.), this column was ejected and cut up, and the portions were extracted with acetone. A *p*-nitroaniline concentrate (m. p. 131°) was thus obtained, which was shown by both f. p. and infrared spectrum to contain 76% of the *p*-isomer.

Mass-spectrometric Analysis.—Measurements of the isotopic composition of nitrogen were made on nitrogen gas obtained from ammonia. From potassium nitrate, the ammonia was produced by reduction with Devarda's alloy. From *o*- or *p*-nitroaniline, or from mixtures of them, the ammonia was prepared as follows. To the sample (0·1 g.) were added glucose (1 g.), potassium sulphate (4 g.), some copper sulphate, and concentrated sulphuric acid (30 ml.). The mixture was digested until pale yellow (about 2 hr.), and thereafter for a further 15 min. After 50% potassium hydroxide (100 ml.) had been added, the liberated ammonia was collected in dilute sulphuric acid. This procedure converted both nitrogen atoms of the nitroanilines quantitatively into ammonia.

The ammonium sulphate was converted into nitrogen gas by treating its solution with one of sodium hypobromite in a vacuum.[9] The evolved nitrogen was analysed mass-spectrometrically.

The nitroanilines, isolated from the product of rearrangement of *N*-nitroaniline in aqueous sulphuric acid in the presence of ^{15}N-enriched potassium nitrate, had contents of ^{15}N slightly lower than that of a sample of nitrogen from a cylinder. The latter nitrogen being taken as normal, the recovered *o*-nitroaniline had a ^{15}N-abundance of −0·004 and −0·002 atom % excess, the former figure applying to a preliminary experiment on one-tenth of the scale of the final one. The figures obtained for the ^{15}N-abundance in the *p*-nitroaniline concentrate were −0·003 and −0·002 atoms % excess.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, July 25th*, 1958.]

[9] Rittenberg, "Preparation and Measurement of Isotopic Tracers," J. W. Edwards, Ann Arbor, Michigan, 1948, p. 36.