654. *Mechanism of Benzidine and Semidine Rearrangements. Part X.*[1] *Substrate-isotope Effects on Kinetics and Products of Acid Rearrangement of the Hydrazobenzenes.*

By D. V. Banthorpe and E. D. Hughes.

Hydrazobenzene, its 4,4′-dideutero-derivatives, and a derivative *C*-deuterated everywhere except in 4,4′-positions, have been rearranged with acid in aqueous dioxan and in aqueous and anhydrous ethanol; and comparisons have been made of the rearrangement rates and product proportions. The products are benzidine 76—72%, and diphenyline 24—28%, the small variation depending on the solvent. Neither in *para*- nor in *ortho*-positions does deuteration make a detectable difference either to reaction rates or to product ratios. The aromatic proton losses are concluded to occur after the activation barrier for rearrangement has been surmounted, and after the mechanism has decisively branched towards the individual products.

Hammond and Grundemeier [2] were the first to replace selected aromatic hydrogen atoms in a hydrazo-compound by deuterium, and to note the effect of so doing on the acid-rearrangement rate and on the proportions of products. They prepared hydrazobenzene deuterated in the 4,4′-positions, and reported that its rate of rearrangement in ethanolic hydrogen chloride at 0° was reduced by about 10%, but that the proportions of the products (benzidine 70%, and diphenyline 30%) [3] were unchanged by the deuteration.

This work has been revised, because our experience, gained in the work of Part IX,[1] made it appear experimentally incomplete; but, let us say at once, our results support Hammond and Grundemeier's main conclusions. The work has also been extended, in order to complete the evidence obtainable by this method, to include a study of hydrazobenzene deuterated in 2,2′-positions.

One minor conclusion by Hammond and Grundemeier can be discounted immediately,

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[1] Parts I—IX, *J.*, 1962, 2386—2444, and the two preceding papers.

[2] Hammond and Grundemeier, *J. Amer. Chem. Soc.*, 1955, **77**, 2444.

[3] Carlin, Nelb, and Odioso, *J. Amer. Chem. Soc.*, 1951, **73**, 1002.

because the evidence for so doing is contained in their paper. This is the alleged loss of rate by about 10% on 4,4'-deuteration. For their figures show that the drop of 10% occurred in the first-order rate-constants of substrate disappearance in a series of runs in which the acidity was not held constant. The series consisted of six runs with undeuterated, followed by two with deuterated material; and the concentration of acid was reduced by 5% on passing from the undeuterated substrate to the deuterated. In view of the quadratic character of the acid dependence,[4] this neglected change of acidity accounts for the rate difference.

We have, however, some real difficulties with Hammond and Grundemeier's experimental record. First, they introduced aromatic deuterium by transference from hypophosphorous acid, which had been deuterated by hot evaporation with deuterium oxide, a method of preparation which we could not repeat (cf. Part IX, Section 4.1). Secondly, they reported their deuterated hypophosphorous acid as having 60% of the theoretical content of deuterium, but we could not repeat their analysis, because the infrared band on which it depended was not visible in the spectrum of our 100%-deuterated material (*loc. cit.*). Thirdly, if we nevertheless accept 60% as the deuterium content of the hypophosphorous acid with which those authors converted *p*-nitroaniline into a deuterated nitrobenzene, and if we assume no entry at all of protium from uncontrolled sources, then the reported 50% of one atom of deuterium in the formed nitrobenzene (or 44% according to another analysis) seems to leave too little margin for the considerable primary isotope effect expected (*loc. cit.*) to attend the transference of phosphorus-bound hydrogen. Fourthly, if we nevertheless accept 50% as the degree of *para*-deuteration of the nitrobenzene, and if we assume no loss of deuterium in the subsequent steps of conversion into the hydrazobenzene, for which no deuterium analysis is reported, this material would have contained only 25% of the required 4,4'-dideutero-derivative, accompanied by 50% of the monodeutero-compound, and 25% of the completely undeuterated form, a 4-fold dilution of the desired substrate, which much weakens the power of the method. Fifthly, a lack in the kinetic record further weakens the evidence for or against an isotope effect on rate. For the object is to discover whether or not the 4,4'-dideutero-compound reacts more slowly than other forms: if it did, it would react last, and its rate of reaction might not be picked up, except late in runs kinetically followed to over 75% of reaction. Hence the extent of reaction to which the kinetics were followed is an indispensable datum; but it is not recorded. Sixthly, the spectroscopic analyses for benzidine and diphenyline were made when 6% of a third component, *viz.*, unconverted hydrazobenzene, should have been present, so creating a disturbance to composition of the order of the change being looked for. Finally, having on all these grounds decided to revise the work, we found that we could not repeat the author's analytical procedure, particularly their method of sampling for kinetic and product analyses. For, in our experiments in ethanol at their acidities, amine hydrochlorides crystallised at a somewhat early stage of reaction, and fair sampling then became impossible. It therefore seemed to us that, even if the conclusions were right, better support would not come amiss, and accordingly that total repetition was desirable.

(1) *Choice and Preparation of Deuterated Hydrazobenzenes.*—As to the extension to *ortho*-deuterated compounds, the simplest that we could have used is 2,6:2',6'-tetradeuterohydrazobenzene, but, for convenience in preparation, we actually employed 2,3,5,6,2',3',5',6'-octadeuterohydrazobenzene. This is *meta*- as well as *ortho*-deuterated, but the *m*-deuterium can play no part in the rearrangement, and its secondary isotope effect can safely be assumed to be negligible.

It is known that 1,3,5-trideuterobenzene can be prepared in a spectroscopically pure state by boiling aniline hydrochloride with an excess of deuterium oxide, repeatedly to total exchange, and then deaminating the deuterated amine.[5] By similarly exchanging

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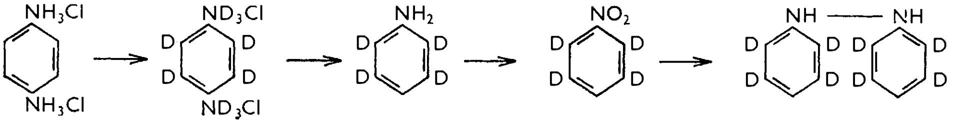
[4] Hammond and Shine, *J. Amer. Chem. Soc.*, 1950, **72**, 220.

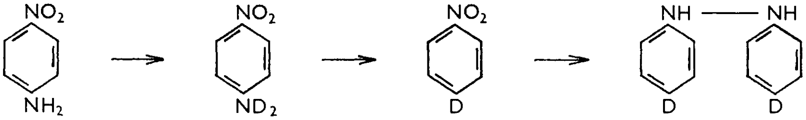
[5] Best and Wilson, *J.*, 1946, 239.

the hydrogen of *p*-phenylenediamine dihydrochloride with deuterium oxide, diazotising the perdeutero-diamine, and reducing the formed *p*-aminotetradeuterobenzenediazonium ion with hypophosphorous acid, we obtained 2,3,5,6-tetradeuteroaniline. This was diazotised to give the tetradeuterobenzenediazonium cobaltinitrite, which was converted with copper sulphate and cuprous oxide into 2,3,5,6-tetradeuteronitrobenzene.[6] This last product was reduced with zinc and alkali to the octadeuterohydrazobenzene, the overall yield of which, calculated on the *p*-phenylenediamine, was 18%.



The deuterium content of the deuterated *p*-phenylenediamine was 100%, but that of the final octadeuterohydrazobenzene was only 80% of the theoretical. The mode of incursion of the unwanted protium was not elucidated, but our preliminary experiments contributed a certain amount of information on the point. It was shown that no exchange of nuclear hydrogen with solvent hydrogen occurs in aniline under the conditions of acidity in which the tetradeuteroaniline was produced. It was also shown that no such exchange takes place in the conditions of the reduction of the tetradeuteronitrobenzene. The remaining possibilities are the reaction of the diazonium cobaltinitrite with cupric ion and cuprous oxide, a reaction that probably involves single-electron transfers, and the reduction of *p*-aminobenzenediazonium ion with hypophosphorous acid. Such exchange does not accompany the similar reduction of the *p*-nitrobenzenediazonium ion (see below), but the much greater stability of the *p*-aminobenzenediazonium ion might allow attack by a free-radical reagent on nuclear hydrogen to become competitive with that on the diazo-position.

The preparation of 4,4'-dideuterohydrazobenzene was accomplished essentially by Hammond and Grundemeier's method,[2] with the modification that the starting material, *p*-nitroaniline, was first deuterated in the amino-group by exchange with deuterium ethoxide, and then converted with sodium nitrite and dideuterosulphuric acid in deuterium oxide into the *p*-nitrophenylhydrazinium ion, which was reduced in the solution in which it was formed by protium-free trideuterohypophosphorous acid. The resulting *p*-deuteronitrobenzene was reduced with zinc and alkali to 4,4'-dideuterohydrazobenzene, the overall yield of which, calculated on *p*-nitroaniline, was 29%. It had 100% of the theoretical content of deuterium.



(2) *Rate of Acid Rearrangement of Hydrazobenzene and of its* 2,3,5,6,2',3',5',6'-*Octadeutero- and its* 4,4'-*Dideutero-derivative.*—It had to be determined whether the rates of acid-catalysed rearrangement of these *o*- and *p*-deuterated hydrazobenzenes were any different from that of hydrazobenzene itself in like conditions. This was checked in " 90% " aqueous ethanol as solvent, and with hydrogen chloride as the catalysing acid. The result was, as Table 1 shows, that the *ortho*- and *para*-deuteration made no kinetic difference. As one of the forms was not isotopically pure, it should be recorded that all runs, of which the first-order rate constants are given, were shown accurately to obey the first-order rate-law, as far as the runs were followed, which in all cases was to more than 90% of reaction.

(3) *Products of Acid Rearrangement of Hydrazobenzene and of its* 2,3,5,6,2',3',5',6'-*Octadeutero- and its* 4,4'-*Dideutero-derivative.*—We agree with Carlin *et al.*[3] and with Hammond *et al.*[2] that the acid rearrangement of hydrazobenzene gives just two products,

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[6] Večera, Petranek, and Gasparič, *Coll. Czech. Chem. Comm.*, 1957, **22**, 1603.

TABLE 1.

First-order rate-constants, k_1 in sec.$^{-1}$, of rearrangement of hydrazobenzene and of its 2,3,5,6,2′,3′,5′,6′-octadeutero- and 4,4′-dideutero-derivative, each initially 0·004M, in " 90% " aqueous ethanol in the presence of 0·2N-hydrogen chloride at 0·0°.

	10^3k_1	Mean
Hydrazobenzene	0·113, 0·111	0·112
80% 2,3,5,6,2′,3′,5′,6′-Octadeutero-	0·115	0·115
100% 4,4′-Dideutero-	0·112, 0·116	0·114

TABLE 2.

Proportions of products, benzidine (I) and diphenyline (II), formed by rearrangement in aqueous or anhydrous organic solvents in the presence of acids, from hydrazobenzene, and from its 2,3,5,6,2′,3′,5′,6′-octadeutero- and its 4,4′-dideutero-derivative.

		Products (mol. %)		
Substrate	Method	I	II	Total
(A) *In " 60% " aqueous dioxan with* 0·3M-*perchloric acid,* 25°.				
Hydrazobenzene	Spec.	76·7	23·0	99·7
,,	Spec.	76·9	24·1	101·0
,,	Grav.	75·4	—	—
,,	Grav.	76·6	—	—
	Mean	76·4	23·6	100·0
80% 2,3,5,6,2′,3′,5′,6′-Octa-D	Spec	77·0	22·5	99·5
,,	Grav.	75·4	—	—
	Mean	76·2	22·5	98·7
100% 4,4′-Di-D	Spec.	75·5	24·0	99·5
,,	Grav.	75·8	—	—
	Mean	75·7	24·0	99·7
(B) *In " 95% " aqueous ethanol with* 0·1M-*hydrogen chloride at* 25°.				
Hydrazobenzene	Spec.	72·9	27·7	100·6
,,	Spec.	73·2	26·5	99·7
,,	Spec.	73·6	23·7	97·3
,,	Grav.	71·3	—	—
,,	Grav.	71·9	—	—
	Mean	72·4	26·0	98·4
80% 2,3,5,6,2′,3′,5′,6′-Octa-D	Spec.	72·7	27·3	100·0
,, ,,	Spec.	71·3	26·4	97·7
,, ,,	Grav.	70·0	—	—
	Mean	71·3	26·9	98·2
100% 4,4′-Di-D	Spec.	74·0	25·0	99·0
,,	Grav.	72·4	—	—
	Mean	73·2	25·0	98·2
(C) *In " 100% " ethanol with* 0·1M-*hydrogen chloride at* 0°.				
Hydrazobenzene	Spec.	72·4	28·4	100·8
,,	Grav.	73·5	—	—
	Mean	73·0	28·4	101·4
80% 2,3,5,6,2′,3′,5′,6′-Octa-D	Spec.	71·1	28·9	100·0
,, ,,	Grav.	71·9	—	—
	Mean	71·5	28·9	100·4
100% 4,4′-Di-D Mean	Spec.	72·0	27·3	99·3

4,4′-ring-coupled benzidine and 2,4′-ring-coupled diphenyline. We could not find any of the other products, *viz.*, *o*-benzidine, *o*- and *p*-semidine, and disproportionation products, which Večera, Petranek, and Gasparič claim [6] to have detected by paper chromatography, not even when we used their methods, which, we agree, are usually capable of detecting by-products present to the extent of 0·5% in products of benzidine-type rearrangements.

We have used Carlin's method of spectroscopic determinaton of benzidine and diphenyline, and, as a check, we have determined benzidine by the gravimetric method employed for product analysis in most of the earlier papers of this series. Our figures, given in Table 2, are in fairly good agreement with those of the previous authors. We have used three solvents, "60%" aqueous dioxan, "95%" aqueous ethanol, and "100%" ethanol, and have found proportions of benzidine falling from about 76% to 72%, and of diphenyline rising from about 24% to 28%, towards the more anhydrous media.

The determinations of individual rearrangement products were independent, and hence the deviations of their sum from 100% give some idea of the analytical error. Our impression is that our mean figures are good to 1%, though individual analyses are occasionally in error by 2%.

The most important result in Table 2 is the evidence it offers that, to within the limits of analytical accuracy, neither *ortho*- nor *para*-deuteration of the hydrazobenzene changes the ratio of the 4,4′- to the 2,4′-ring-coupled products.

Bearing in mind the evidence in Part IX (preceding paper) that the loss of at least one of the two aromatic protons that must be lost to permit internuclear coupling in benzidine rearrangements is an activated process, the conclusion follows that, in the rearrangement of hydrazobenzene, no activated proton-loss occurs where a bifurcation of mechanism towards separate products would create kinetically competing processes. The results of Section 2 of this paper show further that such proton losses must occur beyond the main activation barrier for rearrangement, and, indeed, further beyond in terms of reduced energy than the activation energy of proton loss. This will be discussed further in Part XIII.

EXPERIMENTAL

(4.1) *2,3,5,6,2′,3′,5′,6′-Octadeuterohydrazobenzene.*—*p*-Phenylenediamine dihydrochloride (21 g.) was dissolved in deuterium oxide (75 g.), the solvent was pumped off at 25°/1·0 mm., and the process was repeated with fresh deuterium oxide. The *N*-deuterated salt thus formed was heated in a sealed tube under nitrogen with deuterium oxide (100 g.) at 105° for 72 hr., the solvent was pumped off, and the process was repeated. Examination of the finally recovered salt by infrared absorption showed that it contained no detectable protium, *i.e.*, not above 1%.

This *N*- and *C*-deuterated salt was next isotopically normalised with respect to the hydrogen of the amino-groups by dissolving it in a large volume of water and pumping off the solvent at 20°. It was shown that this procedure did not disturb any of the aromatically bound deuterium.

The resulting *C*-deuterated salt was now deaminated by dissolving it (20 g.) in concentrated hydrochloric acid (15 ml.) and water (600 ml.), diazotising it at 0° with sodium nitrite (7·7 g.) in water (50 ml.) added in 45 min. (during which much frothing occurred), and then adding concentrated (*ca.* 100%) hypophosphorous acid (85 ml.). The solution was stirred at 0° for 7 hr., and thereafter kept at 0° for 48 hr. It was then made alkaline and extracted with ether; and, from the dried extract, 2,3,5,6-tetradeuteroaniline hydrochloride was precipitated by passing in hydrogen chloride (yield, 6·1 g., 42%).

The tetradeuteroaniline salt (6·1 g.) was converted into tetradeuteronitrobenzene by Hodgson and Marsden's method [7] of preparing the diazonium cobaltinitrite and decomposing this solid substance with a solution in water of sodium nitrite and cupric sulphate, together with suspended cuprous oxide, at 20°. The basified solution was distilled in steam, and the tetradeuteronitrobenzene was collected in ether, and redistilled (yield 3·3 g., 60%).

This substance was converted into the corresponding hydrazobenzene by reduction with

[7] Hodgson and Marsden, *J.*, 1944, 22.

zinc dust in refluxing aqueous-ethanolic sodium hydroxide, following the procedure given by Cohen.[8] The product, crystallised three times from light petroleum–ethanol, had m. p. 129° (yield, 70%).

(4.2) 4,4′-*Dideuterohydrazobenzene.*—*p*-Nitroaniline (13·8 g.) was first deuterated by exchange with respect to the hydrogen of its amino-group, by dissolving the amine in 10 mol. of deuterium ethoxide (100% EtOD), pumping off the solvent, and repeating the procedure with fresh deuterium ethoxide. The nitro-dideuteroamine thus produced was then diazotised with sodium nitrite in a mixture of deuterium oxide (50 ml.) and dideuterosulphuric acid (13 ml.), and the diazonium salt was reduced with trideuterohypophosphorous acid (20 ml.), much as described for an analogous case in Section 4.2 of Part IX. The resulting *p*-deuteronitrobenzene (5·1 g., 41%) was reduced by Cohen's method [8] with zinc and alkali to the hydrazo-compound.

(4.3) *Deuterium Analyses.*—Routine checks on the completeness of replacement of protium in inorganic chemical reagents were made by nuclear magnetic resonance, and in organic chemical products by measurements of infrared absorption. The infrared method was used in order to obtain an approximate idea of the rate of hydrogen exchange of *p*-phenylenediamine dihydrochloride with deuterium oxide, and to show the completeness of the exchange (by disappearance of the band at 12·1 μ) under the conditions used preparatively. Analyses of the final hydrazobenzenes were by mass-spectrometer.

(4.4) *Kinetics.*—The runs were quenched with Bindschedler's Green, excess of which was titrated with titanous chloride to visual end-points.

(4.5) *Products.*—Product analyses were made, after 12 half-lives, by two methods, the first, Carlin, Nelb, and Odioso's spectrophotometric method. A sample (2·0 ml.) of the rearranged solution was added to ethanol (5 ml.) containing sodium ethoxide (0·5N), and this mixture was suitably diluted. Optical densities were then measured at 245, 270, and 285 mμ, and the composition was calculated by using the known extinction coefficients at these wavelengths. Three components, had all been present, could thus have been determined, but, as expected, no appreciable quantity of the hydrazo-compound could be detected. The sum of the determined concentrations of benzidine and diphenyline usually amounted to more than 98% of the theoretical (cf. Table 2).

A gravimetric check was usually carried out with the remainder of the solution. The method was essentially the first step of that employed to determine the proportions of products of benzidine rearrangements in the naphthalene series (Part I [1]). Benzidine sulphate was precipitated to give a 99—100% recovery of benzidine from " 60% " aqueous dioxan, " 95% " aqueous ethanol, or " 100% " ethanol at 0°, in solutions up to 0·3N in acid. Diphenyline was not appreciably co-precipitated under the conditions. However, diphenyline could not be satisfactorily determined by an extension of the procedure on the lines of that worked out in the naphthalene series (Part I).

The agreement between spectrophotometric and gravimetric analyses, and the fact that the agreement was unimpaired by deuteration, even in up to 4/5 of the nuclear positions, confirms our expectation that such deuteration would not modify optical band-intensity at a given wavelength of absorption in the near-ultraviolet region to any serious extent. The second difference (over combining states and isotopic forms) of zero-point energy would produce a short-wave shift of band-origin, and the difference (over isotopic forms) of upper-state vibrational energy would create a compression to long waves of band development relative to the band origin, each of these countervailing shifts being of the order 1—2 mμ in the regions of our measurements.

In the experiments in 100% ethanol, precipitation of amine hydrochlorides usually occurred in the course of the kinetic runs. Water (5 ml.) was therefore added to the total material (100 ml.) of the spent runs made for product determinations, and the resulting solutions were analysed as before.

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[8] Cohen, " Practical Organic Chemistry," Macmillan, London, 1949, p. 162.