193. *The Intramolecular Nature of the Benzidine Rearrangement.*

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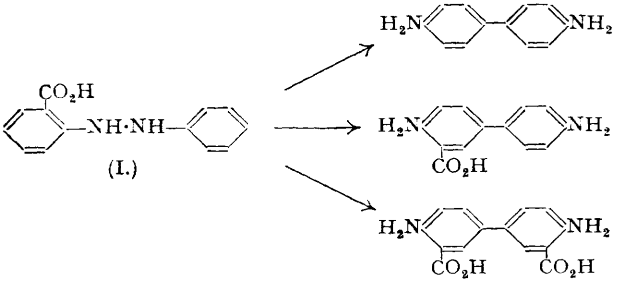
By a study of the rearrangement of unsymmetrical hydrazobenzenes, confirmation of the intramolecular nature of the benzidine rearrangement has been obtained.

Although there have been many formulations of the mechanism of the benzidine rearrangement (cf. Dewar, "Electronic Theory of Organic Reactions," Oxford, 1949, pp. 235 *et seq.*), there had hitherto only been one investigation (Ingold and Kidd, *J.*, 1933, 984) which determined whether the reaction was inter- or intra-molecular.

Ingold and Kidd rearranged a mixture of 2 : 2′-dimethoxy- and 2 : 2′-diethoxy-hydrazobenzene, and thermal analysis indicated that the only products were 3 : 3′-dimethoxy- and 3 : 3′-diethoxy-benzidine. Apparently no 3-methoxy-3′-ethoxybenzidine was formed in this mixed rearrangement and it was concluded that the reaction was intramolecular. As the above work depends for its conclusions on mixed melting points, it was decided to perform some experiments whereby a chemical separation of possible products could be attempted.

Accordingly, the various carboxy-substituted hydrazobenzenes were rearranged, and the products examined. If one considers the rearrangement of 2-*carboxyhydrazobenzene* (I), the possible products are benzidine (II), 3-*carboxybenzidine* (III), and 3 : 3′-dicarboxybenzidine (IV).



(I.) (II.) (III.) (IV.)

If the reaction is intermolecular, the principal products should be (II) and (IV) as a large difference in reactivity would be expected between the two fragments formed by an N–N fission, whereas (III) only would be formed by an intramolecular reaction. Thus the presence of (II), provided that decarboxylation does not occur, should indicate an intermolecular reaction.

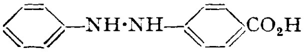
Now (II) can readily be chemically separated from (III) and (IV) owing to its non-solubility in sodium hydroxide, and thus its presence can be readily demonstrated. Furthermore, the alkali-soluble fraction will be either pure (III) or a mixture of (III) and (IV), and these two possibilities can be differentiated by both a nitrogen estimation and a determination of the acid equivalent.

The 2-, 3-, and 4-*carboxyhydrazobenzenes* were prepared by first condensing the appropriate primary amino-acid with nitrosobenzene to form the corresponding *carboxyazobenzene*. It may be noted that when either anthranilic acid or ethyl anthranilate was used, very poor yields of the azo-compound were obtained owing, apparently, to the sterically interfering *ortho*-group. These azo-compounds were then reduced to their hydrazo-analogues by means of zinc dust and sodium hydroxide, but the latter compounds were not isolated but were immediately rearranged by warming with added excess of dilute hydrochloric acid. After removal of any azo-compound by filtration, the reaction mixture was made alkaline and extracted with ether in order to isolate any benzidine formed. The alkaline solution was then weakly acidified and the amino-acids were precipitated by addition of glacial acetic acid.

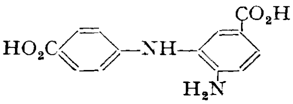
It was found that a small yield of benzidine was obtained from the rearrangement of 2-carboxyhydrazobenzene (I), indicating the possibility of an intermolecular action. However, the amino-acid gave analyses (both for nitrogen and for acid equivalent) for the mono-acid (III) and not the di-acid (IV), indicating that the benzidine had been formed by a partial decarboxylation of (III) during the course of the reaction. As the results are not conclusive it was desirable to obtain further information from the behaviour of the other isomers.

When 3-carboxyhydrazobenzene was rearranged under the same conditions, no benzidine could be isolated from the reaction mixture and the amino-acid gave analyses corresponding to pure 2-*carboxybenzidine*. This clearly indicates that an intramolecular reaction is involved and the benzidine formed during the rearrangement of (I) has only resulted by decarboxylation occurring during the reaction.

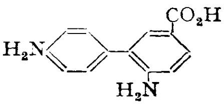
It is also of interest that when 4-carboxy- and 4-carbethoxy-hydrazobenzene (as V) were rearranged, large yields of benzidine were obtained. If one assumes an intermolecular rearrangement, then by application of the rules enunciated by Dewar (*op. cit.*, p. 234), the main products should be benzidine (II) and 4′ : 5-dicarboxysemidine (VI) along with some 5-carboxydiphenyline (VII). The amount of benzidine formed from the acid corresponded to a 74% yield if intermolecular reaction were assumed. However, the amino-acid fraction was found to be pure (VII) (nitrogen analysis and acid equivalent) and no indication of the presence of the dicarboxylic amino-acid (VI) was obtained. Thus the benzidine has once again merely resulted from a decarboxylation and not from an intermolecular reaction. This is substantiated by the fact that a gas was evolved during the rearrangement.



(V.)



(VI.)



(VII.)

In order to obtain further evidence, it was intended to investigate compounds containing a hydroxyl group in place of the carboxyl group; so once again there would be an alkali-solubilising group present which would allow the separation of any benzidine that may be formed.

However, many difficulties were encountered in this work. Owing to their ease of preparation benzeneazo-β-naphthol and 4-hydroxyazobenzene were used as starting materials. When the reduction of these compounds was attempted by the method used above, fission of the $-N{=}N-$ bond took place and appreciable amounts of aniline were isolated in each case. Catalytic reduction in the presence of Adams's catalyst (cf. Strel'tsova and Zelinskii, *Bull. Acad. Sci. U.R.S.S.*, 1941, 401) gave the same results, two moles of hydrogen being absorbed; when the reduction was stopped when only one mole of hydrogen had been adsorbed, unchanged azo-compound and aniline were isolated. However, when zinc and ammonium chloride in benzene–aqueous alcohol were used (cf. Krolik and Lukaschevich, *Chem. Abs.*, 1949, **43**, 5774) reduction appeared to take place, since the solution became colourless. Dilute hydrochloric acid was then added in order to rearrange any substituted hydrazobenzene formed and, after evaporation of the benzene and alcohol, the reaction mixture was made alkaline and extracted with ether to remove any bases formed. Evaporation of this extract yielded an almost negligible amount of substance, in both cases, which did not give any tests for benzidine (insolubility of sulphate and immediate formation of dibenzylidene derivative in alcoholic solution) or aniline (diazotisation test). This result indicates that fission of the $-N{=}N-$ linkage had not occurred during this method of reduction, since aniline was not formed. In addition, the rearrangement had not produced benzidine, thus confirming the findings obtained with the carboxy-compounds. When the aqueous solution was made slightly acidic, and excess of sodium hydrogen carbonate added, the rearrangement product was precipitated. Owing to its rapid oxidation, it could not be obtained pure even though the whole reaction had been performed in an atmosphere of nitrogen.

In order to prevent oxidation of the rearrangement product (an amino-phenol) it was decided to use the benzhydryl ethers of benzeneazo-β-naphthol and 4-hydroxyazobenzene and to remove the protecting benzhydryl group by hydrogenolysis after rearrangement. The latter benzhydryl ether was readily obtained by treatment with diphenyldiazomethane in dry benzene, but the benzeneazo-β-naphthol was recovered unchanged when similarly treated. It was found that although the above ether was readily reduced, the solution rapidly darkened during rearrangement and, as the product appeared to resist hydrogenolysis, this method of approach was abandoned.

Our work thus confirms Ingold and Kidd's postulation that this reaction is intramolecular. Since this work was completed, Wheland and Schwartz (*J. Chem. Physics*, 1949, **17**, 425) have obtained confirmatory evidence by a study of the rearrangement of an unsymmetrical hydrazobenzene by using ^{14}C as a radioactive tracer.

EXPERIMENTAL.

(M. p.s are uncorrected. Analyses are by Messrs. N. Lottkowitz and N. Gamble.)

Carboxy-substituted Compounds.—Preparation of azo-compounds. Freshly prepared nitrosobenzene (Vogel, " A Text Book of Practical Organic Chemistry," Longmans, 1948, p. 603) was condensed with the appropriate amino-compound in ethyl alcohol and glacial acetic acid under the conditions described by Wieland (*Ber.*, 1915, **48**, 1098). The reaction mixture was concentrated to obtain an additional amount of azo-compound. With 2-carboxyazobenzene it was necessary to evaporate the reaction mixture to dryness and dissolve the residue in benzene. Unchanged anthranilic acid was removed by extraction with dilute hydrochloric acid, and crude 2-carboxyazobenzene with aqueous sodium hydrogen carbonate. The latter product was precipitated by acidification of the carbonate solution and, after being extracted with ether, was crystallised from light petroleum (b. p. 60—90°).

The following table summarises the pertinent data for these compounds:

Substituted azobenzene.	Yield, %.	M. p.	Crystal form.	Solvent.	N (found), %.
2-*Carboxy-*	11	91—92°	Yellow needles	Light petroleum (b. p. 60—90°)	12·3
3- ,, ...	21	169	Light orange prisms	Alcohol	12·7
4- ,, ...	56	247	Orange plates	Alcohol	12·2

$C_{13}H_{10}O_2N_2$ requires N, 12·4%.

4-Carbethoxyazobenzene (m. p. 87°; 27% yield) was also prepared by the above method. Wieland (*loc. cit.*) gives m. p. 86—87°.

Reduction of the substituted azobenzene and rearrangement of the hydrazobenzene formed. The azobenzene (5 g.), dissolved in 2·5N-sodium hydroxide solution (50 ml.), was heated (0·75 hour) in a boiling water-bath with zinc dust (7 g.). The colourless solution was decanted and 2·5N-hydrochloric acid (150 ml.) added, whereupon a precipitate was obtained. Heating was continued (1 hour) and any solid present (identified as azo-compound formed by atmospheric oxidation) was filtered off. The solution was then basified and extracted with ether. The benzidine thus obtained was identified as its dibenzylidene derivative (m. p. and mixed m. p. 233°). The alkaline solution was acidified with acetic acid, the amino-acid fraction then being precipitated. It was purified by dissolution in hot dilute hydrochloric acid (charcoal) and precipitated as colourless micro-crystals by addition of excess of sodium acetate. If any zinc salts were present, they were removed by heating the solid with sodium hydrogen carbonate solution and the amino-acid was precipitated by addition of acetic acid. When 4-carbethoxyazobenzene was used, the reduction was carried out in alcoholic sodium hydroxide. Simultaneous hydrolysis took place, for the amino-acid obtained by rearrangement was identical with the product formed from 4-carboxyazobenzene.

The results obtained are summarised below :

Initial compound.	Azo-compound recovered, g.	Wt. of benzidine, g.	Wt. of amino-acid, g.	M. p. of amino-acid.	Acid equiv.	N (found), %.
2-Carboxy-	—	0·13	0·4	207—208°(d.)	232, 232	12·3
3-Carboxy- ...	—	—	2·5	269°(d.)	223, 226	12·7
4-Carboxy-	0·61	1·51	0·9	236—237°(d.)	224, 238	12·5
4-Carbethoxy-...	0·68	1·37	1·61	236—237°(d.)	224, 238	12·5

$C_{13}H_{12}O_2N_2$ requires N, 12·3%; equiv., 228. $C_{14}H_{12}O_4N_2$ requires N, 10·3%; equiv., 136.

Benzhydryl Ether of 4-*Hydroxyazobenzene*.—4-Hydroxyazobenzene (8·2 g.) was dissolved in dry benzene (160 ml.), and a solution of diphenyldiazomethane (9 g.) in benzene added. The solution was kept for 18 hours at 32° and then concentrated to 25 ml. The *ether* obtained (8·3 g.) crystallised from ethyl alcohol as yellow needles, m. p. 127° (Found : N, 8·0. $C_{25}H_{20}ON_2$ requires N, 7·7%).

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