

XXV.—*The Formation of 2-Methylbenziminazoles.*

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THE nitration of diacetyl-*m*- and -*p*-phenylenediamine has been studied by Barbaglia (*Ber.*, 1874, **7**, 1258), Biedermann and Ledoux (*ibid.*, p. 1533), Ladenburg (*Ber.*, 1884, **17**, 150), and Bülow and

Mann (*Ber.*, 1897, **30**, 986), but the nitration of diacetyl-*o*-phenylenediamine does not appear to have been recorded hitherto. This nitration gives in good yield 4-nitrodiaacetyl-*o*-phenylenediamine, the orientation of which was determined by reduction, followed by acetylation, 1 : 2 : 4-triacetamidobenzene being obtained identical with the products of reduction and subsequent acetylation of 4-nitrodiaacetyl-*m*-phenylenediamine and 3-nitrodiaacetyl-*p*-phenylenediamine.

4-Nitrodiaacetyl-*o*-phenylenediamine was obtained by Ladenburg (*loc. cit.*) by the action of acetic anhydride on 4-nitro-*o*-phenylenediamine. Heim's suggestion (*Ber.*, 1888, **21**, 2307) that Ladenburg's compound was 5-nitro-2-methylbenziminazole is unfounded, since a repetition of Ladenburg's work gave 4-nitrodiaacetyl-*o*-phenylenediamine identical with the product obtained as described above. The melting point recorded by Ladenburg (227°) is, however, low.

On reduction, 4-nitrodiaacetyl-*o*-phenylenediamine gives an amino-compound which reacts normally with nitrous acid to give a diazo-compound, whereas the isomeric 4-aminodiaacetyl-*m*-phenylenediamine and 3-aminodiaacetyl-*p*-phenylenediamine both react with nitrous acid to give 5-acetamido-1 : 2 : 3-benzotriazole, thus showing the equivalence of the 5- and the 6-position in the benzotriazole system (compare Bülow and Mann, *loc. cit.*). On boiling mono- or di-acetyl-*o*-phenylenediamines with 3—4*N*-hydrochloric acid for several minutes, the corresponding 2-methylbenziminazoles are formed in good yield (compare Bistrzycki and Ulfers, *Ber.*, 1892, **25**, 1992; Waljaschko and Boltina, *J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1780). The first stage of ring closure of diacetyl-*o*-phenylenediamine is hydrolysis to the monoacetyl compound, since *o*-aminoacetanilide has been isolated from the reaction mixture (compare Baxter and Fargher, *J.*, 1919, **115**, 1373).

It appears, therefore, that hydrolysis of the diacetyl compound is favourable to rapid ring closure; this explains the difficulty of obtaining 2-methylbenziminazole from *o*-phenylenediamine by treatment with acetic anhydride (compare Ladenburg, *loc. cit.*; Heim, *loc. cit.*; Borsche and Rantscheff, *Annalen*, 1911, **379**, 150). 2-Methylbenziminazole was, however, obtained by boiling *o*-phenylenediamine with a mixture of acetic anhydride (0.5 g.-mol.) and 3—4*N*-hydrochloric acid: it is assumed that acetylation followed by ring closure occurred. Treatment of *o*-phenylenediamine with acetic anhydride (0.5 g.-mol.) gave a mixture of diacetyl-*o*-phenylenediamine and unchanged material; excess of acetic anhydride gave diacetyl-*o*-phenylenediamine only.

5-Amino-2-methylbenziminazole, isolated as the dihydrochloride or as the hydrochloride of the acetyl derivative, was formed by the

reduction of 5-nitro-2-methylbenziminazole and by the action of boiling 3*N*-hydrochloric acid on (i) 4-aminodiacetyl-*o*-phenylenediamine, (ii) 1:2:4-triacetamidobenzene, further de-acetylation having occurred, (iii) 4-aminodiacetyl-*m*-phenylenediamine and 3-aminodiacetyl-*p*-phenylenediamine. Case (iii) not only indicates the intermediate formation of these two bases in case (ii) but also confirms the work of Gallinek (*Ber.*, 1897, **30**, 1912) showing the identity of the 5- and the 6-position in the benziminazole system.

5-Acetamido-2-methylbenziminazole hydrochloride, m. p. 325°, has solubilities and a crystalline form similar to those of the compound, m. p. 324°, described without analytical data by Gallinek (*loc. cit.*) as the base. On treatment of its aqueous solution with ammonia, the base, m. p. 250°, separated (compare Kym, D.R.-P. 288190).

In similar experiments with 4-hydroxy- and 4-acetoxy-diacetyl-*o*-phenylenediamine, red amorphous solids but no benziminazole derivatives were isolated.

These reactions are being extended to derivatives of 3:4-diaminophenylarsinic acid.

EXPERIMENTAL.

o-Aminoacetanilide was obtained by adding a mixture of *o*-nitroacetanilide (180 g.) and iron powder (110 g.) to boiling water (1 l.) containing 50 c.c. of glacial acetic acid, a few drops of amyl alcohol being added from time to time to overcome the otherwise troublesome frothing. After being neutralised to litmus, filtered, and concentrated to small bulk, the solution deposited the amino-compound in 90% yield as white, hexagonal plates, m. p. 133° (Found: N, 18.7. Calc.: N, 18.7%).

Diacetyl-*o*-phenylenediamine was obtained by addition of acetic anhydride (200 c.c.) to the filtrate from the above reduction mixture. It separated as white, hexagonal prisms, m. p. 184°, and the yield, including material recovered from the mother-liquor, was 90% of the theoretical (Found: N, 14.6. Calc.: N, 14.6%).

Diacetyl-*m*-phenylenediamine and diacetyl-*p*-phenylenediamine were obtained in good yield from *m*-phenylenediamine hydrochloride and *p*-aminoacetanilide hydrochloride solutions respectively by treatment with sodium acetate and acetic anhydride in slight excess.

Nitration of the Three Diacetylphenylenediamines.—The compound (64 g.) was dissolved at 20° in sulphuric acid (240 c.c.) and nitrated at 5—10° with a mixture of nitric acid (*d* 1.42; 22 c.c.) and sulphuric acid (24 c.c.). When the product was poured into ice-water the nitro-compound was precipitated in 90% yield.

4-Nitrodiaacetyl-*m*-phenylenediamine, m. p. 246°, formed white needles from 50% acetic acid (compare Barbaglia, *loc. cit.*), and

3-nitrodiacetyl-*p*-phenylenediamine, m. p. 185°, pale yellow needles from alcohol (compare Ladenburg, *loc. cit.*). 4-Nitrodiacetyl-*o*-phenylenediamine formed white or pale yellow prisms, m. p. 255°, from 50% acetic acid. It is sparingly soluble in hot water, more readily soluble in alcohol or hot glacial acetic acid (Found : N, 17.7. Calc. : N, 17.7%). It was also obtained by reducing 2 : 4-dinitroaniline with ammonium sulphide (compare Heim, *loc. cit.*) and boiling the resulting 4-nitro-*o*-phenylenediamine, m. p. 197—198°, with an excess of acetic anhydride; no trace of 5-nitro-2-methylbenziminazole was detected even after several hours' boiling.

Reduction of the Three Nitrodiacetylphenylenediamines.—The compound (44 g.) mixed with iron powder (88 g.) was reduced by the method described for the preparation of *o*-aminoacetanilide. The filtrate on concentration deposited the amino-compound, the total yield in each case (including material recovered from mother-liquors) being almost quantitative.

2-Aminodiacetyl-*m*-phenylenediamine, m. p. 250°, formed white prisms from water. It is moderately easily soluble in cold water and in alcohol (Found : N, 20.4. $C_{10}H_{13}O_2N_3$ requires N, 20.3%). 3-Aminodiacetyl-*p*-phenylenediamine, m. p. 231—232°, has been described by Bülow and Mann (*loc. cit.*). 4-Aminodiacetyl-*o*-phenylenediamine, m. p. 205°, forms white prisms from water. It resembles the above isomerides in solubility (Found : N, 20.1%). 1 : 2 : 4-Triacetamidobenzene, which crystallises from hot water in needles, m. p. 239°, was obtained by adding sodium acetate and acetic anhydride to an acid solution of any of the three aminodiacetylphenylenediamines and also by adding acetic anhydride to the filtrates obtained in the reduction of the nitrodiacetylphenylenediamines. Concentration of the solutions was necessary to obtain good yields and the "mixed melting points" were undepressed (Found for specimens prepared by the six methods mentioned : N, 16.9, 16.8, 16.9, 16.8, 16.8, 16.8. Calc. : N, 16.9%).

*Action of Nitrous Acid on 4-Aminodiacetyl-*o*-phenylenediamine.*—This amine in the presence of 2—3 molecules of mineral acid gave a diazo-solution which reacted with sodium arsenite (Lewis and Cheetham, *J. Amer. Chem. Soc.*, 1921, **43**, 2119), 3 : 4-diacetamidophenylarsinic acid being produced in good yield.

2-Methylbenziminazole.—(i) *o*-Phenylenediamine (1.1 g.), hydrochloric acid (15% ; 10 c.c.), and acetic anhydride (1 c.c.) were boiled together under reflux for 20 minutes. On addition of sodium hydroxide solution until the mixture was faintly acid to litmus, 2-methylbenziminazole separated in 60% yield. It crystallised in white prisms, m. p. 176°, from hot water and was readily

soluble in mineral acids and in excess of caustic alkali (Found : N, 21.4. Calc. : N, 21.2%).

(ii) *o*-Aminoacetanilide (5 g.) or diacetyl-*o*-phenylenediamine (5 g.), on refluxing for 15 minutes with 10% hydrochloric acid (25 c.c.), gave in each case a 78% yield of the ring compound (Found : N, 21.4, 21.4%).

(iii) Diacetyl-*o*-phenylenediamine (1 g.), after boiling with 2—3*N*-hydrochloric acid (5 c.c.) for 1 minute, gave on neutralisation a mixture of prisms and hexagonal plates which, by fractional crystallisation from hot water, was shown to consist of *o*-aminoacetanilide (0.2 g.; m. p. 134°. Found : N, 18.8%) and 2-methylbenziminazole (0.2 g.; m. p. 176°. Found : N, 21.2%).

(iv) Acetic anhydride (0.5 c.c.; $\frac{1}{2}$ mol.) was added to *o*-phenylenediamine (1.1 g.). When vigorous reaction had ceased, the mixture was warmed in the water-bath for 1 minute. The solution on cooling deposited a mixture of diacetyl-*o*-phenylenediamine, m. p. 186°, and *o*-phenylenediamine, m. p. 102°, which was separated by fractionation from hot water, in which the latter is more soluble.

5-Nitro-2-methylbenziminazole.—(i) 4-Nitrodiaacetyl-*o*-phenylenediamine (47 g.) was boiled for not less than 1 hour with 25% sodium hydroxide solution (250 c.c.). On addition of hydrochloric acid until the precipitate first formed redissolved, and treatment of the filtered solution with sodium acetate until it was no longer acid to Congo-red, 5-nitro-2-methylbenziminazole was formed (20 g.; 55%).

Treatment for shorter periods with hot alkali causes the product to acquire a yellow colour which is difficult to remove.

(ii) 4-Nitrodiaacetyl-*o*-phenylenediamine (11 g.), after refluxing for 15 minutes with hydrochloric acid (10%; 10 c.c.), gave, on addition of sodium acetate, 5-nitro-2-methylbenziminazole (6 g.; 80%), which was obtained quite white by repeated crystallisation from water. Treatment lasting only 1 to 3 minutes gave the same product, but it was sometimes accompanied by a small amount of 4-nitro-*o*-phenylenediamine, m. p. 199°.

5-Nitro-2-methylbenziminazole made by the above methods or by the methods of Heim (*loc. cit.*) and of Fischer and Hess (*Ber.*, 1903, **36**, 3970) consisted of white, staggered plates, m. p. 221°, readily soluble in hot water, mineral acids and caustic alkalis. It is unacted upon by nitrous acid, or by sulphuric acid at 90° (Found : N, 23.9. Calc. : N, 23.7%).

5-Acetamido-2-methylbenziminazole.—(i) Any one of the three aminodiaacetylphenylenediamines described above (1 g.), after refluxing for 20 minutes with 4*N*-hydrochloric acid (10 c.c.), gave, on cooling, neutralisation, and addition of acetic anhydride (1 c.c.),

characteristic crystals of 5-acetamido-2-methylbenziminazole hydrochloride in 75% yield.

(ii) 1 : 2 : 4-Triacetamidobenzene (10 g.) was boiled under reflux for 30 minutes with 4*N*-hydrochloric acid (40 c.c.). The filtered solution on neutralisation to litmus and addition of acetic anhydride (10 c.c.) gave the above-mentioned hydrochloride in 80% yield.

(iii) 5-Nitro-2-methylbenziminazole (5 g.) mixed with iron powder (10 g.) was reduced by the general method described under *o*-aminoacetanilide. On addition of acetic anhydride (10 c.c.) to the filtrate from the neutralised reaction mixture 5-acetamido-2-methylbenziminazole separated.

The hydrochloride consists of stout, white, irregular, hexagonal plates, *m. p.* 325°, but is sometimes obtained as prismatic needles which rapidly change to the plates. It is sparingly soluble in cold water (Found: N, 18.4; Cl, 15.7. Calc.: N, 18.6; Cl, 15.7%). 5-Acetamido-2-methylbenziminazole is obtained by treatment of a warm aqueous solution of its hydrochloride with ammonia. It forms white prisms, *m. p.* 250°, is insoluble in cold water but readily soluble in mineral acids and in excess of caustic alkalis (Found: N, 22.2. Calc.: N, 22.2%). Treatment with concentrated hydrochloric acid gives the hydrochloride.

5-Amino-2-methylbenziminazole Dihydrochloride.—(i) 1 : 2 : 4-Triacetamidobenzene (40 g.) was treated as described under 5-acetamido-2-methylbenziminazole (ii). The filtered solution was evaporated to dryness under reduced pressure, and the residue crystallised from boiling concentrated hydrochloric acid, a 50% yield of the pure dihydrochloride being obtained.

(ii) 5-Acetamido-2-methylbenziminazole (2 g.) was heated under reflux for 1 hour with concentrated hydrochloric acid (4 c.c.). On cooling, 5-amino-2-methylbenziminazole dihydrochloride separated in white prisms, readily soluble in water (Found: N, 19.2; Cl, 32.6. Calc.: N, 19.1; Cl, 32.3%). The free base cannot readily be obtained owing to its solubility in water (compare Gallinek, *loc. cit.*).

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