

323. The Attempted Rearrangement of Some Arylbenzimidinoquinolyl Ethers.

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Although *N*-phenylbenzimidino-8-quinolyl ether undergoes normal rearrangement to 8-benzanilidoquinoline, introduction of an *ortho*-halogen atom into the aryl group causes the ether to decompose at temperatures at which rearrangement might be expected to occur. A compound with halogen atoms in the quinoline nucleus underwent normal rearrangement.

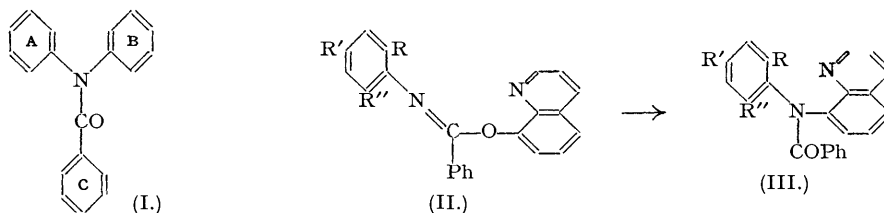
JAMISON and TURNER (*J.*, 1937, 1954) applied Chapman's diphenylamine synthesis to the preparation of substituted *N*-benzoyldiphenylamine-2-carboxylic acids, the salts of which, with optically stable bases, provided suitable material for the study of asymmetric transformation (*idem*, *J.*, 1938, 1646; 1940, 264). No study of the equilibria obtaining in the case of salts of optically labile bases with optically stable acids has yet been made, and in pursuit of this object the preparation of *N*-benzoyldiphenylamines with basic properties has now been attempted. It did not, however, prove possible to prepare compounds with basic substituents in either ring A or ring C (I), though a limited number of compounds containing a substituted quinoline nucleus in place of ring B were obtained.

The action of phosphorus pentachloride on benz-*m*-dimethylaminoanilide, 8-benzamidoquinoline, and *N*-benzoyl-*N'*-acetyl-*N'*-methyl-*p*-phenylenediamine in each case failed to give the desired iminochloride (or iminochloride hydrochloride).

p-Dimethylaminobenz-*o*-toluidide was obtained in very poor yield by an adaptation of Human and Mills's method (*Nature*, 1946, 158, 877).

Although 2-bromo-2'-nitro-*N*-benzoyl-4-methyldiphenylamine was prepared, its reduction to the 2'-amino-compound was unsatisfactory.

Phenylbenzimidinochloride reacted readily with the sodium derivative of 8-hydroxyquinoline to give *N*-phenylbenzimidino-8-quinolyl ether (II; R = R' = R'' = H) which rearranged at about 280° to 8-benzanilidoquinoline (III; R = R' = R'' = H). The rearrangement was also



successful when R = Me, R' = R'' = H; but when R was a halogen atom (*e.g.*, R = Cl, R' = R'' = H) the ether decomposed on heating at about 270°, while at lower temperatures some unchanged ether was recovered from the tarry product. The compounds (II; R = Br, R' = Me, R'' = H) and (II; R = Br, R' = R'' = Me) also decomposed when rearrangement

was attempted and thus behaved similarly to certain nitro-substituted imino-ethers investigated by Chapman (*J.*, 1927, 1743).

In the one compound investigated, the introduction of a halogen atom into the quinoline nucleus did not affect the rearrangement and *N*-phenylbenzimidino-5 : 7-dichloro-8-quinolyl ether passed smoothly into 5 : 7-dichloro-8-benzanilidoquinoline at 260°, but, as the ether was difficult to prepare and the product was only sparingly soluble, the use of 5 : 7-dichloro-8-hydroxyquinoline was not further explored.

EXPERIMENTAL.

Microanalyses are by Drs. Weiler and Strauss, Oxford; m. p.s are uncorrected.

Benz-m-dimethylaminoanilide.—*m*-Nitroaniline was methylated by Ullmann's method (*Annalen*, 1903, 327, 104), reduced with stannous chloride and hydrochloric acid, and the crude *NN*-dimethyl-*m*-phenylenediamine treated with benzoyl chloride in the presence of 10% aqueous sodium hydroxide. The resulting benzoyl compound (20 g.) was heated on the water-bath with phosphorus pentachloride (17.5 g.) until reaction ceased (3 hours); on being washed with light petroleum it set to a hard, deliquescent orange solid. This was filtered off quickly and added to an alcoholic solution of the sodium derivative of methyl salicylate in the presence of excess of sodium ethoxide. Normal working up gave a gum from which some crystals of the original benz-*m*-dimethylaminoanilide separated several weeks later. No other solid product could be isolated.

8-Benzamidoquinoline.—Quinoline was nitrated (Meigen, *J. pr. Chem.*, 1908, 77, 472) and the resulting mixture of 5- and 8-nitroquinolines separated through the nitrates (Dufton, *J.*, 1892, 61, 782). Reduction of 8-nitroquinoline by iron and 50% acetic acid (Dikshoorn, *Rec. Trav. chim.*, 1929, 48, 147) gave a poor yield, but 8-aminoquinoline was obtained almost quantitatively by employing iron and water in presence of a little acetic acid. Schotten-Baumann benzoylation gave 8-benzamidoquinoline in 90% yield. This was heated with a slight excess of phosphorus pentachloride, alone, or with phosphoryl chloride as solvent, and the resulting purple solid washed with light petroleum and added to an alcoholic solution of the sodium derivative of methyl salicylate. No crystalline product could be isolated.

N-Benzoyl-N'-acetyl-N'-methyl-p-phenylenediamine.—*N*-Methylacetanilide was prepared rapidly and in good yield by adding acetic anhydride (56 g.) to a mixture of methylaniline (54 g.), water (200 g.), and ice (100 g.). The whole was cooled in ice-water and stirred vigorously. After a few minutes the emulsion cleared and almost at once set to a thick paste. The acetyl compound was filtered off and a further crop obtained by adding a paste of sodium hydrogen carbonate (25 g.) to the filtrate; total yield 66 g., 88%; m. p. 100—101°. This was nitrated (Morgan and Grist, *J.*, 1918, 113, 688), and reduced with iron, water, and acetic acid to *p*-amino-*N*-methylacetanilide (yield 80—90% after one crystallisation from water). Benzoylation in pyridine solution gave *N*-benzoyl-*N'*-acetyl-*N'*-methyl-*p*-phenylenediamine, which crystallised from alcohol in long prisms, m. p. 203—204° (Found: C, 71.7; H, 5.7; N, 10.6. C₁₆H₁₆O₂N₂ requires C, 71.6; H, 6.0; N, 10.4%) (yield 66%). Phosphorus pentachloride reacted with the above compound to give a dark sticky mass which began to decompose during the attempt to remove phosphoryl chloride by distillation. It was washed with light petroleum and became hard but not crystalline. It showed none of the usual reactions of an iminochloride or iminochloride hydrochloride and was not investigated further.

p-Dimethylaminobenz-o-toluidide.—(a) *p*-Dimethylaminobenzoic acid (Willstätter and Kahn, *Ber.*, 1904, 37, 401) was treated with thionyl chloride, and *o*-toluidine added to the product. None of the required compound could be isolated. (b) The acid chloride was prepared from dimethylaniline (48.5 g.) and carbonyl chloride (10 g.) (Rivier and Richard, *Helv. Chim. Acta*, 1925, 8, 490), and *o*-toluidine (11 g.) added. 9 G. of the toluide, contaminated with di-*o*-tolylurea, were obtained, but crystallisation from a variety of solvents failed to give a sharply melting specimen. (c) (Method of Human and Mills, *loc. cit.*). Thionyl chloride (24 g.) was added gradually to *p*-dimethylaminobenzoic acid (33 g.) dissolved in pyridine (165 c.c.). After this had been stirred for 1 hour, a solution of *o*-toluidine (21 g.) in pyridine (16 c.c.) was added, and the mixture left overnight. It was poured into water, and the solid separated and dissolved in dilute hydrochloric acid. The insoluble di-*o*-tolylurea was filtered off, and the toluide precipitated by making the filtrate just alkaline with sodium hydroxide solution. The crude product was extracted with boiling benzene, and the extract dried and concentrated. It deposited 11 g. (22%) of the toluide, m. p. 138—140°. Two further crystallisations from benzene gave diamond-shaped, flattened prisms, m. p. 141—142° (Found: C, 75.3; H, 7.1; N, 10.4. C₁₄H₁₄ON₂ requires C, 75.6; H, 7.1; N, 11.0%). The picrate crystallised from alcohol in long, irregular, yellow prisms, m. p. 155° (Found: C, 55.5; H, 4.3. C₁₄H₁₄ON₂.C₆H₃O₇N₃ requires C, 54.7; H, 4.4%).

N-*o*-Bromo-*p*-tolylbenzimidino-*o*-nitrophenyl ether was obtained in 67% yield from benz-*o*-bromo-*p*-toluidideiminochloride and *o*-nitrophenol in presence of alcoholic sodium ethoxide. It crystallised from alcohol in six-sided yellow plates, m. p. 130—131° (Found: Br, 19.7. C₂₀H₁₅O₃N₂Br requires Br, 19.4%).

2-Bromo-2'-nitro-N-benzoyl-4-methyldiphenylamine.—The above ether rearranged on heating for 1 hour in a bath kept at 170—180°, and the amine crystallised from ethyl acetate in pale yellow rhombs, m. p. 152—153° (Found: C, 58.5; H, 4.5; Br, 20.15. C₂₀H₁₅O₂N₂Br requires C, 58.4; H, 3.7; Br, 19.4%).

N-Phenylbenzimidino-8-quinolyl Ether (II; R = R' = R'' = H).—8-Hydroxyquinoline (63 g.), dissolved in alcohol (500 c.c.) at 35°, and benzanilideiminochloride (94 g.), dissolved in dry ether (300 c.c.), were added in quick succession to a cooled solution of sodium (10 g.) in alcohol (500 c.c.). Sodium chloride separated at once. After 12 hours the ether and most of the alcohol were distilled off, and the residue poured into water. The solid was collected and crystallised from a large volume of alcohol; yield 105 g., 74%. *N-Phenylbenzimidino-8-quinolyl ether* was obtained as almost colourless, irregular, stout prisms, m. p. 154—155° (Found: C, 80.9; H, 5.0; N, 8.8. C₂₂H₁₆ON₂ requires C, 81.45; H, 5.0; N, 8.6%). This compound, like several other iminoquinolyl ethers, was a nose irritant.

8-Benzanilidoquinoline (III; R = R' = R'' = H).—The above ether (20 g.) was heated for 20 minutes

in a wide tube in a metal-bath kept at 280°. The reaction was strongly exothermic. Crystallisation from alcohol gave 14.5 g. (72%) of a brownish product, m. p. 129—131°. It was purified by recrystallisation from benzene and then from alcohol, 8-benzanilidoquinoline being obtained as colourless sheaves of needles, m. p. 130—131° (Found: C, 81.1; H, 5.0; N, 9.25. $C_{22}H_{16}ON_2$ requires C, 81.45; H, 5.0; N, 8.6%).

N-o-Tolylbenzimidino-8-quinolyl Ether (II; R = Me, R' = R'' = H).—This ether was prepared (47% yield) as described above by treating the sodium derivative of 8-hydroxyquinoline with benzotoluidideiminochloride. It crystallised from alcohol in rectangular plates, m. p. 115—116° (Found: C, 81.1; H, 5.3; N, 8.1. $C_{23}H_{18}ON_2$ requires C, 81.6; H, 5.4; N, 8.3%). On heating for 10 minutes in a bath at 280° it rearranged to give 8-benz-o-toluididoquinoline (III; R = Me, R' = R'' = H), which crystallised from alcohol in rhombohedra, m. p. 127—128° (Found: C, 81.3; H, 5.5; N, 8.5. $C_{23}H_{18}ON_2$ requires C, 81.6; H, 5.4; N, 8.3%).

N-o-Chlorophenylbenzimidino-8-quinolyl ether (II; R = Cl, R' = R'' = H) was obtained from benz-o-chloroanilideiminochloride and 8-hydroxyquinoline in 71% yield. It crystallised from acetone in pale yellow prisms, m. p. 133° (Found: C, 73.6; H, 4.0; N, 7.1; Cl, 9.3. $C_{22}H_{15}ON_2Cl$ requires C, 73.6; H, 4.2; N, 7.8; Cl, 9.9%). When heated in a bath kept at 280° or at 240° it decomposed.

N-o-Bromo-p-tolylbenzimidino-8-quinolyl ether (II; R = Br, R' = Me, R'' = H) was obtained in 62% yield from benz-o-bromo-p-toluidideiminochloride and 8-hydroxyquinoline. It was crystallised from alcohol and then from carbon tetrachloride and obtained as diamond-shaped prisms, m. p. 135.5° (Found: C, 66.3; H, 4.2; N, 6.6; Br, 19.5. $C_{23}H_{17}ON_2Br$ requires C, 66.2; H, 4.1; N, 6.7; Br, 19.15%). Rearrangement was attempted at 270—280° (vigorous decomposition) and at 240° and 220°, but without success.

N-5-Bromo-4-m-xylylbenzimidino-8-quinolyl Ether (II; R = Br, R' = R'' = Me).—Benz-5-bromo-4-m-xylidide was converted into benz-5-bromo-4-m-xylidideiminochloride, b. p. 248°/31 mm. (74% yield), which with 8-hydroxyquinoline gave a 66% yield of the ether, crystallising from alcohol in rectangular prisms, m. p. 116—117° (Found: C, 66.1; H, 4.5; N, 6.9; Br, 18.6. $C_{24}H_{19}ON_2Br$ requires C, 66.8; H, 4.4; N, 6.5; Br, 18.5%). It decomposed on heating at 260°.

N-Phenylbenzimidino-5 : 7-dichloro-8-quinolyl Ether.—5 : 7-Dichloro-8-hydroxyquinoline (36 g.) was partly dissolved in benzene (450 c.c.) and added to sodium ethoxide solution (4 g. of sodium in 150 c.c. alcohol); immediate precipitation of a mixture of 5 : 7-dichloro-8-hydroxyquinoline and its sodium derivative occurred. Benzanilideiminochloride (36 g.), dissolved in benzene (100 c.c.), was added, and the mixture left with occasional shaking for 40 hours, during which most of the solid disappeared. The remaining solid (18 g.) was filtered off: concentration of the filtrate gave 26 g. of mixed product. Further crops of 7 g., 3 g., and 3 g. severally were obtained by dilution with light petroleum. Lengthy fractional crystallisations from benzene and alcohol effected separation of the product into 5 : 7-dichloro-8-hydroxyquinoline (m. p. and mixed m. p. with authentic specimen, 182—183°) and *N*-phenylbenzimidino-5 : 7-dichloro-8-quinolyl ether (14 g.; 21%), which crystallised from alcohol in rods, m. p. 163° (Found: C, 67.0; H, 3.5; N, 7.0; Cl, 18.3. $C_{22}H_{14}ON_2Cl_2$ requires C, 67.2; H, 3.6; N, 7.1; Cl, 18.0%).

5 : 7-Dichloro-8-benzanilidoquinoline was obtained by heating the above ether for a few minutes at 260° (bath temp.). It crystallised from benzene in rhombs, m. p. 214—215° (Found: C, 67.4; H, 3.9; N, 7.2; Cl, 17.7. $C_{22}H_{14}ON_2Cl_2$ requires C, 67.2; H, 3.6; N, 7.1; Cl, 18.0%). It was sparingly soluble in alcohol, acetone, ethyl acetate, and benzene.

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