CCCIX.—*The Tautomerism of Amidines. Part VII. Methylation of Benzenyl-*p*-nitrodiphenylamidine.*

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THE alkylation by alkyl salts of open-chain amidines, in which one of the nitrogen atoms is attached to an aryl group and the other to a non-aryl (hydrogen or alkyl) group, yields as main products compounds alkylated on the arylamine nitrogen atom, together with small quantities of the isomeric alkyl derivatives. For example, benzenylphenylmethylamidine (I or II) gives with methyl iodide methylphenylamidobenzenylmethylimidine (III) in 62% yield, and dimethylamidobenzenylphenylimidine (IV) in 4% yield (Pyman, J., 1923, **123**, 367).

In previous papers (Pyman, J., 1923, **123**, 3359; Forsyth and Pyman, J., 1926, 2502) one of us has expressed the view that results of this kind are due, not to the feebler basicity of the arylamino-group as compared with the alkylamino-group, as some previous investigators have supposed, but to the tendency of the aryl group to attract the double linking into the αβ-position. Thus, it was thought that benzenylphenylmethylamidine reacted in the form (I) to a much greater extent than in the form (II), owing to the influence of the phenyl group in the anilino-residue, and consequently gave (III) to a much greater extent than (IV), since the alkylation of open-chain amidines with alkyl salts leads to the attachment of the alkyl group to the nitrogen atom which is doubly linked to carbon (Pyman, J., 1923, **123**, 3359). Evidence that the structural effect is of greater importance than the relative basicities of the nitrogen atoms has been given in the papers quoted, and further evidence in favour of this view is afforded by the results of the present investigation.

$$\begin{tikzcd}
\text{(I.) } CPh(:NPh)\cdot NHMe \arrow[r, shift left] \arrow[d] & CPh(:NMe)\cdot NHPh \text{ (II.)} \arrow[l, shift left] \arrow[d] \\
\text{(III.) } CPh(:NMe)\cdot NMePh & CPh(:NPh)\cdot NMe_2 \text{ (IV.)}
\end{tikzcd}$$

Benzenyl-p-*nitrodiphenylamidine* (V or VI) gave on methylation with methyl iodide *benzenylmethylphenylamido*-p-*nitrophenylimidine* (VII) in 28·8% yield, and *benzenylmethyl*-p-*nitrophenylamidophenylimidine* (VIII) in 24·9% yield, together with 8·8% of unchanged material. Now, in benzenyl-*p*-nitrodiphenylamidine both nitrogen atoms are attached to phenyl groups, and the structural effect of the phenyl groups is thus balanced, but the two nitrogen atoms, which are present as anilino- and *p*-nitroanilino-residues respectively, differ considerably in basicity, for aniline has $K = 4{\cdot}6 \times 10^{-10}$ and *p*-nitroaniline $K = 1 \times 10^{-12}$. The results of the methylation thus show that the marked disparity between the yields of the two methyl derivatives, which is always observed when arylamine and alkylamine residues are in competition for a methyl group, has disappeared here on the elimination of the structural effect of a phenyl group attached to only one of the nitrogens, in spite of a considerable difference between the basicities of the two amino-residues. Further, it is noteworthy that the isomeride isolated in rather larger quantity is that in which the methyl group has become attached to the more basic nitrogen atom. This agrees with the results of alkylating open-chain amidines such

$$\begin{tikzcd}
\text{(V.) } CPh(:NPh)\cdot NH\cdot C_6H_4\cdot NO_2 \arrow[r, shift left] \arrow[d] & CPh(:N\cdot C_6H_4\cdot NO_2)\cdot NHPh \text{ (VI.)} \arrow[l, shift left] \arrow[d] \\
\text{(VII.) } CPh(:N\cdot C_6H_4\cdot NO_2)\cdot NMePh & CPh(:NPh)\cdot NMe\cdot C_6H_4\cdot NO_2 \text{ (VIII.)}
\end{tikzcd}$$

as benzenylmethylamidine, $NMe{:}CPh{\cdot}NH_2 \rightleftharpoons NHMe{\cdot}CPh{:}NH$, in which neither of the nitrogen atoms is attached to a phenyl group (Pyman, *loc. cit.*). The constitutions of the two methylated amidines (VII) and (VIII) were determined by synthesising them from the appropriate methylated amines, and in the course of this work various known methods for the preparation of amidines have been compared, and are referred to below.

EXPERIMENTAL.

Benzenyl-*p*-nitrodiphenylamidine was prepared by several of the available methods.

A. After Gerhardt (*Annalen*, 1858, **108**, 214). Benzanilide-iminochloride (53 g.) and *p*-nitroaniline (33 g.) in dry ether (1 l.) were kept for 4 days. The deposit (22 g.; m. p. 165—195°) was dissolved in hot alcohol (300 c.c.) and kept; the crystals (7·5 g.; m. p. 245—250°) which separated were dissolved in hot alcohol (150 c.c), and when the solution was basified with ammonia, the amidine separated (5·5 g.; m. p. 183°; yield 7%).

B. After Sen and Rây (J., 1926, 646). Benzanilide (10 g.), *p*-nitroaniline (7 g.), and phosphorus trichloride (170 g.) were heated under reflux for 4 hours in an oil-bath at 120—130°, and the amidine was isolated in 15% yield (2·38 g.; m. p. 180—182°).

C. After Hill and Rabinowitz (*J. Amer. Chem. Soc.*, 1926, **48**, 732). Benzanilide (10 g.), *p*-nitroaniline (7 g.), phosphorus trichloride (7 g.), and sodium-dried benzene (44 c.c.) were heated for 5 hours at 100°; the amidine was obtained in 8% yield (1·33 g.; m. p. 182°).

D. After Hill and Cox (*ibid.*, p. 3214). This proved to be by far the best method. To a well-cooled suspension of phosphorus pentachloride (11 g.) in sodium-dried benzene (50 c.c.), benzanilide (10 g.) was added, followed by *p*-nitroaniline (7 g.), and the mixture heated under reflux for 3 hours on the water-bath. The solvent was distilled off, the residue was well ground with aqueous ammonia, and the paste filtered. The precipitate was thoroughly extracted by grinding with cold alcohol and water, and the residue was crystallised from alcohol, the amidine being isolated in 61% yield (9·1 g. of m. p. 182—183° + 0·75 g. of m. p. 179—180°). In a repetition of this experiment with 40 g. of benzanilide, the amidine was isolated in 75% yield (48·7 g.; m. p. 182°).

Benzenyl-p-*nitrodiphenylamidine* (V or VI) crystallises from alcohol in long, lemon-yellow needles, m. p. 184° (corr.) (Found: C, 71·8; H, 5·1. $C_{19}H_{15}O_2N_3$ requires C, 71·9; H, 4·5%). It is insoluble in hot or cold water or in chloroform, but moderately soluble in hot alcohol or ether. On grinding the base with concentrated hydrochloric acid, a colourless, crystalline *hydrochloride*, m. p. 261°, is obtained, from which the amidine can be regenerated by treatment with ammonia. This hydrochloride is very sparingly soluble in hot water, and when boiled with alcohol containing hydrochloric acid yields *p*-nitrobenzanilide (m. p. crude, 194°; purified, 199°; mixed with a known specimen of m. p. 200°, 200°). In an attempt to prepare a picrate from the amidine and picric acid in hot alcohol, *p*-nitrobenzanilide was again deposited.

Benzenylmethylphenylamido-p-*nitrophenylimidine* (VII).—*p*-Nitrobenzanilide-iminochloride (9 g.), which had been completely freed from hydrogen chloride by keeping in an evacuated desiccator over sodium hydroxide, and monomethylaniline (3·5 g.) in dry ethereal solution were kept over-night, and the solvent distilled. The residue was extracted with hot 2% hydrochloric acid (250 c.c.), which left crude *p*-nitrobenzanilide undissolved (7·2 g.; m. p. 190°; mixed m. p. with a known specimen, 195°). The extract deposited a further 0·26 g. of the same compound on cooling, and the filtrate from this was basified and extracted with ether. The ether residue (3·65 g.) was separated by means of light petroleum into monomethylaniline (1·18 g.; b. p. 193°) and crude amidine (2·3 g.; m. p. 120—128°; yield 19%). It is essential to free the iminochloride from hydrogen chloride before attempting the condensation with monomethylaniline, for otherwise the amidine is not formed. Consequently, it is not surprising to find that this amidine cannot be prepared by the method of Hill and Cox.

Benzenylmethylphenylamido-p-*nitrophenylimidine* crystallises from alcohol in pale yellow plates, which in thin layers have a silvery lustre, m. p. 138° (corr.) (Found: C, 72·5; H, 5·4; N, 12·8. $C_{20}H_{17}O_2N_3$ requires C, 72·5; H, 5·1; N, 12·6%). It is insoluble in hot or cold water, chloroform, or benzene, moderately soluble in cold alcohol, and readily soluble in ether or hot alcohol. The *picrate* separates from alcohol in yellow plates, m. p. 206° (corr.). It is almost insoluble in water or cold alcohol, and explodes when heated in a flame. The *hydrochloride* and *hydriodide* separated from water as gums which could not be crystallised.

Benzenylmethyl-p-*nitrophenylamidophenylimidine* (VIII) could not be isolated from the products of interaction of benzanilideiminochloride (free from hydrogen chloride) with *p*-nitromonomethylaniline in cold or hot dry ether, but was readily prepared by the method of Hill and Cox. Benzanilide (5 g.) was added to a well-cooled suspension of phosphorus pentachloride (5·5 g.) in sodium-dried benzene (25 c.c.). After thorough shaking, *p*-nitromonomethylaniline (3·8 g.) was added, and the mixture heated under reflux for 3 hours on a steam-bath. The solvent was distilled off, and the residue extracted several times with hot water (1 l. in all), which left very crude benzanilide (0·85 g.; m. p. 140°) undissolved. On being cooled, the extract deposited a yellow product (2·25 g.; m. p. 140—170°) which gave on crystallisation from alcohol the amidine hydrochloride (0·75 g.; m. p. 218—220°), the mother-liquors containing *p*-nitromonomethylaniline. The filtrate from the yellow product was basified with ammonia and extracted with ether, which removed an orange syrup (5·25 g.). This was mixed with concentrated hydrochloric acid and a little alcohol, and filtered from more amidine hydrochloride (3·8 g.; m. p. 216—219°). A further small quantity of this was obtained from the filtrate, and all crops were combined and crystallised from alcohol, 2·78 g. of the pure salt being obtained (yield, 29%).

Benzenylmethyl-*p*-nitrophenylamidophenylimidine was obtained as a pale yellow syrup, which did not crystallise. It is insoluble in cold or hot water or in chloroform, but readily soluble in alcohol or ether. It yields well-crystallised salts. The *hydrochloride* crystallises from alcohol in colourless, rhombic prisms, containing 1EtOH which is not lost at 100°, and melts and effervesces at 226° (corr.) (Found: C, 64·0; H, 5·9. $C_{20}H_{17}O_2N_3,C_2H_6O,HCl$ requires C, 63·9; H, 5·8%). It is sparingly soluble in cold water, moderately soluble in cold alcohol, and very readily soluble in hot alcohol. The *hydriodide* crystallises from alcohol in pale yellow, anhydrous, rhombic prisms, m. p. 225° (corr.) (Found: C, 52·3; H, 4·5. $C_{20}H_{17}O_2N_3,HI$ requires C, 52·3; H, 3·9%). It is very sparingly soluble in cold water, alcohol, or acetone, but readily soluble in hot alcohol or acetone. The *picrate* crystallises from alcohol in yellow needles, m. p. 194° (corr.). It is sparingly soluble in hot water or cold alcohol, but readily soluble in hot alcohol.

*Methylation of Benzenyl-*p*-nitrodiphenylamidine by Methyl Iodide.*—Benzenyl-*p*-nitrodiphenylamidine (35 g.) and methyl iodide (35 c.c.) were heated under pressure for 3 hours at 100°. The partly crystalline product was mixed with acetone, and crude benzenylmethyl-*p*-nitrophenylamidophenylimidine hydriodide (13·8 g.; m. p. 220°) was collected. The filtrate was concentrated, basified with ammonia, and extracted with ether. The ether residue (27·3 g.) was crystallised from alcohol (220 c.c.), which deposited benzenylmethylphenylamido-*p*-nitrophenylimidine (10·2 g.; m. p. 136°) on keeping for 1 hour, whilst the filtrate deposited crude benzenyl-*p*-nitrodiphenylamidine (4·1 g.; m. p. 163°) on keeping over-night. The final mother-liquor was evaporated to a syrup and mixed with concentrated hydrochloric acid (10 c.c.) and a little acetone, whereupon benzenyl-*p*-nitrodiphenylamidine hydrochloride (0·43 g.; m. p. 249°) separated. The filtrate from this was deprived of acetone, dissolved in dilute hydrochloric acid, and mixed with sodium iodide, crude benzenylmethyl-*p*-nitrophenylamidophenylimidine hydriodide (0·71 g.; m. p. 197°) being then deposited. The filtrate was basified and extracted with ether, which gave a semi-solid residue (10·3 g.). This was crystallised from alcohol and gave crude *p*-nitromonomethylaniline (0·82 g.; m. p. 150°), but no other crystalline material could be isolated from the filtrate. When the various crude products were purified by the methods described earlier in this paper, benzenylmethyl-*p*-nitrophenylamidophenylimidine hydriodide was obtained in 24·9% yield (11·36 g. of m. p. 225° + 0·76 g. of m. p. 224°), benzenylmethylphenylamido-*p*-nitrophenylimidine in 28·8% yield (9·71 g. of m. p. 138° + 0·37 g. of m. p. 137°), and benzenyl-*p*-nitrodiphenylamidine was recovered unchanged in 8·8% yield (2·67 g. of m. p. 181° + 0·41 g. of m. p. 178°).

One of us (C. C.) is indebted to the Department of Scientific and Industrial Research for a grant which he desires gratefully to acknowledge.

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[*Received, August* 9*th*, 1927.]