# 78. *Nitrosoacylarylamines. Part IV. The Action of Some Nitrosoacylarylamines on Pyridine.*

By J. W. Haworth, I. M. Heilbron, and D. H. Hey.

The action of nitrosoacetanilide on pyridine is shown to give rise to a mixture of α-, β- and γ-phenylpyridine in a total yield of about 60%. The three isomerides are separated by fractional crystallisation of the picrates from acetone. Attention is drawn to the related reactions between benzenediazohydroxide, phenylazotriphenylmethane, and dibenzoyl peroxide and pyridine, all of which give in similar manner mixtures of phenylpyridines. Attempts to nitrosate α-acetamidopyridine, with the view to obtaining a single isomeride on reaction with benzene, were unsuccessful. Whereas it is known that dinitrosodiacetyl-1 : 4-phenylenediamine reacts with benzene to give *p*-terphenyl, it reacts differently with pyridine to give a product containing α- and γ-4-acetamidophenylpyridine.

Attention has been drawn elsewhere (Hey and Waters, *Chem. Reviews*, 1937, **21**, 169) to the fact that the reactions of the diazohydroxides, nitrosoacylarylamines, arylazotriarylmethanes, and diacyl peroxides have many features in common. In each case reaction can take place (a) with an aromatic compound $C_6H_5R$ to give a biaryl compound in which the normal laws of aromatic substitution are not obeyed, (b) with a non-aromatic hydrogen-containing solvent R′H, resulting in abstraction of hydrogen from that solvent, and (c) with a non-aromatic halogen-containing solvent R′Hal, resulting in abstraction of halogen from that solvent, facts which are best explained on the basis of the intervention of reactive aryl radicals :

$$\begin{array}{lll} \mathrm{Ph} + \mathrm{C_6H_5R} \longrightarrow o\text{- and } p\text{- } \mathrm{Ph{\cdot}C_6H_4R} & \ldots\ldots & \text{(a)} \\ \mathrm{Ph} + \mathrm{R'H} \longrightarrow \mathrm{C_6H_6} & \ldots\ldots & \text{(b)} \\ \mathrm{Ph} + \mathrm{R'Hal} \longrightarrow \mathrm{PhHal} & \ldots\ldots & \text{(c)} \end{array}$$

Reactions between benzenediazohydroxide and pyridine (Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1924, **46**, 2339), phenylazotriphenylmethane and pyridine (Wieland *et al.*, *Annalen*, 1934, **514**, 155), and dibenzoyl peroxide and pyridine (Overhoff and Tilman, *Rec. Trav. chim.*, 1929, **48**, 993) have already been described. In the benzenediazohydroxide reaction the product is stated to be " phenylpyridine, m. p. 54—55°." Since, of the three isomeric phenylpyridines, only γ-phenylpyridine (m. p. 74°; Forsyth and Pyman, J., 1926, 2923) is solid, the product isolated in this instance is probably impure γ-phenylpyridine. In the reactions with phenylazotriphenylmethane and with dibenzoyl peroxide the products are stated to consist of mixtures of the α- and the γ-isomeride.

The corresponding reaction with nitrosoacetanilide is now described, which, in reaction with pyridine, gives a mixture of all three isomeric phenylpyridines in a total yield of 60%. The three isomerides are separated by fractional crystallisation of their picrates from acetone.

With a view to obtaining single isomerides attempts were made to effect the reverse process by utilising a nitrosoacetamidopyridine and benzene. It was found, however, that neither α-acetamidopyridine nor its methiodide nor methyl methosulphate could be nitrosated. This may be due to the fact that α-acetamidopyridine reacts in the tautomeric form $\cdot\mathrm{NH}\cdot\overset{|}{\mathrm{C}}\!:\!\mathrm{N}\cdot\mathrm{CO}\cdot\mathrm{CH_3}$, thus simulating the difficult diazotisation of α-aminopyridine in which the tautomerism $\cdot\mathrm{N}\!:\!\overset{|}{\mathrm{C}}\cdot\mathrm{NH_2} \rightleftharpoons \cdot\mathrm{NH}\cdot\overset{|}{\mathrm{C}}\!:\!\mathrm{NH}$ is present.

In a previous communication (this vol., p. 368) it was shown that *p*-benzamidoacetanilide formed a mononitroso-derivative, which reacted with benzene to give 4-benzamidodiphenyl. In similar manner *p*-benzamidonitrosoacetanilide reacts with pyridine to give a mixture of *p*-benzamidophenylpyridines.

Whereas dinitrosodiacetyl-1 : 4-phenylenediamine reacts with benzene to give *p*-terphenyl (France, Heilbron and Hey, J., 1938, 1371), with pyridine the product consists of regenerated diacetyl-1 : 4-phenylenediamine and a mixture of *p*-acetamidophenylpyridines, from which both α- and γ-4-aminophenylpyridine are obtained on hydrolysis. No indication was obtained of the formation of any dipyridylbenzene in this reaction.

The formation of all three isomerides in the reaction between nitrosoacetanilide and pyridine may be regarded as contributory evidence for the participation of free aryl radicals in this reaction (cf. Hey and Waters, *loc. cit.*), which follows a non-ionic course, since, if ions were involved, the formation of only the α- and the γ-isomeride would be expected by any mechanism involving addition to the tertiary nitrogen atom, followed by a tautomeric change or migration reaction.

## EXPERIMENTAL.

*Action of Nitrosoacetanilide on Pyridine.*—Nitrosoacetanilide (60 g.) was added (20 g. during 4 hours per day) to pyridine (500 c.c.). The nitrosoacetanilide dissolved, nitrogen was evolved, and the solution darkened. Finally, after standing overnight, the pyridine was removed by distillation, and the residue collected at 150—180°/10—20 mm. (34 g.) as a yellow oil, from which, when cold, some γ-phenylpyridine separated. The whole of the product, dissolved in alcohol, was added to a hot solution of picric acid (39 g.) in alcohol (530 c.c.). The mixture was boiled and filtered hot from a yellow picrate (A) (21 g.). A further quantity of picrate (B) (49 g.) separated from the filtrate when cold. Systematic fractional crystallisation from acetone yielded from (A) mainly γ-phenylpyridine picrate (9 g.) in hard orange needles, m. p. 195—196°, and from (B) mainly α-phenylpyridine picrate (21 g.) in large yellow rhombic prisms, m. p. 175—176°, together with some β-phenylpyridine picrate (9 g.) in long silky yellow needles, m. p. 159—160°. The mother-liquors from the various fractions yielded a further 14 g. of mixed picrates. The m. p.'s of the picrates were not depressed on admixture with the corresponding products obtained from the reaction between diazotised aniline and pyridine (this vol., p. 352).

*Attempted Nitrosation of α-Acetamidopyridine.*—Nitrous fumes were passed for 4 hours into a solution of α-acetamidopyridine (4 g.) in a mixture of glacial acetic acid (50 c.c.) and acetic anhydride (20 c.c.). α-Acetamidopyridinium nitrate (4·3 g.) separated as a water-soluble white precipitate, m. p. 187—188° (decomp.) both alone and on admixture with a specimen [m. p. 190° (decomp.)] prepared by the gradual addition of concentrated nitric acid to a solution of α-acetamidopyridine in glacial acetic acid. Plazek and Sucharda (*Ber.*, 1928, **61**, 1814) record m. p. 190°. Further treatment with nitrous fumes of a suspension of the nitrate in glacial acetic acid produced no change.

*Attempted Nitrosation of α-Acetamidopyridine Methiodide.*—The methiodide was prepared by boiling α-acetamidopyridine (10 g.), acetone (30 c.c.), and methyl iodide (20 c.c.) under reflux for 1 hour. The product (18 g.), which separated on cooling, was boiled in alcoholic solution with charcoal; the pure methiodide, which separated from the filtered solution, melted at 176° (Found: C, 34·7; H, 3·7. Calc. for $C_8H_{11}ON_2I$: C, 34·5; H, 3·9%). Renshaw and Shand (*J. Amer. Chem. Soc.*, 1932, **54**, 1475) give m. p. 177°. Nitrous fumes were passed for 4 hours into an ice-cold solution of the methiodide (0·5 g.) in a mixture of glacial acetic acid (80 c.c.) and acetic anhydride (20 c.c.). The only action which took place was the liberation of iodine and there was no indication of the formation of any nitroso-compound. Similar attempted nitrosation of α-acetamidopyridine methyl methosulphate (prepared as a hygroscopic solid by refluxing methyl sulphate with α-acetamidopyridine in benzene solution) also gave no indication of the formation of a nitroso-derivative.

*Action of* p-*Benzamidonitrosoacetanilide on Pyridine.*—The nitroso-compound of *p*-benzamidoacetanilide (8 g.), prepared as previously described (this vol., p. 368), was added gradually during 2 hours to pyridine (200 c.c.) at 80°. The nitroso-compound dissolved slowly with evolution of nitrogen. After being heated for a further 2 hours at 80°, the solution was evaporated to small bulk. The product (4·5 g.) which separated was boiled under reflux with alcohol and charcoal. After filtration and concentration a mixture of *p*-benzamidophenylpyridines was obtained, m. p. 204—214° (Found: C, 78·8; H, 5·2. $C_{18}H_{14}ON_2$ requires C, 78·8; H, 5·1%). Owing to the limited quantity of material available and its sparing solubility in most organic solvents a separation of the isomerides was not attempted.

*Action of Dinitrosodiacetyl-*1 : 4-*phenylenediamine on Pyridine.*—Dinitrosodiacetyl-1 : 4-phenylenediamine (25 g.) (France, Heilbron, and Hey, *loc. cit.*) was added during 2 hours to pyridine (500 c.c.) at 40—50°; it dissolved with evolution of nitrogen. After being heated at 70—80° for 2 hours, the solution was cooled. Some diacetyl-1 : 4-phenylenediamine (6·2 g.) separated, m. p. and mixed m. p. 302° after purification by sublimation in a vacuum. The filtrate was evaporated to small bulk, and addition of acetone precipitated a further quantity (4·2 g.) of diacetyl-1 : 4-phenylenediamine. The acetone–pyridine filtrate was evaporated to dryness; the residue, on high-vacuum distillation, yielded a mixture of *p*-acetamidophenylpyridines (4 g.,), which, after crystallisation first from benzene, then from benzene–light petroleum (b. p. 60—80°), and finally three times from hot water, was obtained in colourless needles, m. p. 123—126° (Found : C, 73·8; H, 5·6. $C_{13}H_{12}ON_2$ requires C, 73·6; H, 5·7%). Hydrolysis with boiling concentrated hydrochloric acid, followed by basification and extraction with ether, gave γ-4-aminophenylpyridine, m. p. 228—230° (Found : C, 77·3; H, 5·8. Calc. for $C_{11}H_{10}N_2$ : C, 77·6; H, 5·9%), which separated from the ethereal extract on concentration, and α-4-aminophenylpyridine, m. p. 97—98° (Found : C, 77·9; H, 6·3%), which was obtained on evaporation of the extract to dryness and purified by vacuum sublimation and crystallisation from light petroleum (b. p. 40—60°). Neither base showed any depression in m. p. on admixture with authentic specimens prepared by the reduction of the appropriate nitro-compounds (Forsyth and Pyman, J., 1926, 2912; Haworth, Heilbron, and Hey, this vol., p. 349).

The authors thank Imperial Chemical Industries Ltd. (Dyestuffs Group) for grants and gifts of chemicals, and Messrs. James Woolley, Sons, and Co. Ltd. for the award of a scholarship to one of them (J. W. H.).

THE UNIVERSITY, MANCHESTER. [*Received, January 8th,* 1940.]