668. *Some Phenyl-pyridines and -quinolines.*

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Reaction of phenylazotriphenylmethane with pyridine gives a mixture of 2-, 3-, and 4-phenylpyridine in which, in contrast to the corresponding reactions with diazotised aniline, nitrosoacetanilide, or benzoyl peroxide, the 2-isomeride is present in smallest quantity. It is shown that derivatives of 3-aminopyridine and of 3-aminoquinoline behave like normal aromatic amines and can be converted into 3-phenylpyridines and 3-phenylquinolines, but the methods fail with 2-aminopyridines. In the reaction between 2-quinolylazotriphenylmethane and benzene the main products are triphenylmethane, triphenylmethyl peroxide, 2-triphenylmethylquinoline, and quinoline.

In previous communications (Heilbron, Hey, *et al.*, *J.*, 1940, 349, 355, 358, 1279) it has been shown that arylpyridines can be prepared by the action of aqueous solutions of diazonium salts on an excess of pyridine at temperatures between 20° and 70°. Similar results have been achieved by the action of a nitrosoacylarylamine on pyridine (Haworth, Heilbron, and Hey, *J.*, 1940, 372). When the above reactions were used with aniline as one of the starting compounds the three isomeric phenylpyridines were formed simultaneously. Overhoff and Tilman (*Rec. Trav. chim.*, 1929, **48**, 993) have shown that phenylpyridines can also be obtained by the action of benzoyl peroxide on pyridine, but they reported the formation of the 2- and 4-isomerides only. A re-

examination of this reaction has since shown that all three isomerides are formed simultaneously (Hey and Walker, *J.*, 1948, 2213). In similar manner Wieland *et al.* (*Annalen*, 1934, **514**, 155) have studied the reaction between phenylazotriphenylmethane and pyridine, and they, too, regarded the product as a mixture of the 2- and 4-isomerides only. This reaction has now been re-examined with the result that in this instance also all three isomerides are formed together. The correspondence thus revealed between all these reactions is in general agreement with the results which had been previously reported on the reactions between these four types of reagent and aromatic compounds (Grieve and Hey, *J.*, 1934, 1797; Hey, *ibid.*, p. 1966). The reaction between phenylazotriphenylmethane and pyridine, however, revealed an unexpected feature in that of the three isomeric phenylpyridines the 2-isomeride was formed in smallest quantity, whereas in the corresponding reactions with diazotised aniline, nitrosoacetanilide, or benzoyl peroxide the 2-isomeride constitutes the main product. The method of separation used, which involves the fractional crystallisation of the picrates, is not claimed as a quantitative method and reference to the actual weights of the picrates isolated may therefore be misleading, but the contrast cited above appears to be sufficiently well marked to deserve comment. The reason for this difference in behaviour, which is not at present clear, will form the subject of further investigation.

As methods for the preparation of individual arylpyridines, all the above reactions suffer from the disadvantage that a mixture of isomerides is formed from which the pure compounds can be isolated only by a tedious process such as the fractional crystallisation of the picrates. In the quinoline series the reaction products are even more complex (Hey and Walker, *loc. cit.*). This difficulty could be overcome in the reactions cited below if, instead of starting with aniline and pyridine ($R = C_6H_5$; $R' = C_5H_4N$), similar reactions could be carried out starting with an aminopyridine and benzene ($R = C_5H_4N$; $R' = C_6H_5$), thus:

$$\text{(i)} \quad R{\cdot}N_2OH + R'H \longrightarrow RR' + N_2 + H_2O$$

$$\text{(ii)} \quad R{\cdot}N(NO){\cdot}CO{\cdot}CH_3 + R'H \longrightarrow RR' + N_2 + CH_3{\cdot}CO_2H$$

$$\text{(iii)} \quad R{\cdot}N{:}N{\cdot}CPh_3 + R'H \longrightarrow RR' + N_2 + CHPh_3$$

No systematic attempts have been made to utilise this reverse procedure, although it has already been reported (Coates, Cook, Heilbron, Hey, Lambert, and Lewis, *J.*, 1943, 401) that, whereas a good yield of 3-pyridylquinolines can be obtained from the reaction between the diazonium chloride prepared from 3-aminoquinoline and pyridine, yet the reaction failed with both 2- and 4-aminoquinoline. In these examples, however, both R and R′ are heterocyclic nuclei. This distinction between the properties of the 3-amino-derivative on the one hand and of the 2- and 4-amino-derivatives on the other hand is not unexpected, since the latter are capable of imine–enamine tautomerism (cf. Steck and Ewing, *J. Amer. Chem. Soc.*, 1948, **70**, 3397). It has also been recorded (Haworth, Heilbron, and Hey, *J.*, 1940, 372) that attempts to nitrosate 2-acetamidopyridine failed, presumably for the same reason. From these facts it is obvious that the starting materials to be used in the reverse process must be chosen with discretion and that the best chances of success are likely to be achieved with pyridine or quinoline derivatives containing the amino-group at the 3-position.

It has now been confirmed that 2-aminopyridine and 5-nitro-2-aminopyridine are unsuitable starting materials, but both 2-chloro-3- and -5-acetamidopyridine were successfully nitrosated, and the subsequent reactions with benzene gave 2-*chloro*-3- and -5-*phenylpyridine* respectively in the normal manner. The nitroso-compounds prepared from these 3-acetamidopyridines showed considerably greater stability than nitrosoacetanilide; a similar contrast in properties has been reported between 3-nitroaminopyridine and nitroaminobenzene (Tschitschibabin and Kirssanov, *Ber.*, 1927, **60**, 2433). Further, 2-n-*butoxy*-5-*phenylpyridine* was prepared from diazotised 5-amino-2-*n*-butoxypyridine and benzene, and, the sodium acetate modification of the Gomberg reaction (cf. Elks, Haworth, and Hey, *J.*, 1940, 1284) being used, 2-chloro-5-aminopyridine gave 2-chloro-5-phenylpyridine. In the quinoline series 3-aminoquinoline was converted into 3-phenylquinoline through the agency of both 3-nitrosoacetamidoquinoline and 1-(3-quinolyl)-3 : 3-dimethyltriazen.

In view of the failures recorded above with 2-amino-derivatives of pyridine and quinoline, recourse was made to the use of 2-*quinolylazotriphenylmethane* in which imine–enamine tautomerism would not seem to be possible. It was therefore of interest to find that in reaction with benzene the product contained mainly triphenylmethane, triphenylmethyl peroxide, 2-*triphenylmethylquinoline*, and quinoline, and attempts to detect the presence of 2-phenylquinoline were unsuccessful. The formation of 2-triphenylmethylquinoline is comparable with the

formation of tetraphenylmethane in the decomposition of phenylazotriphenylmethane (cf. Hey, *loc. cit.*).

Experimental.

Reaction of Phenylazotriphenylmethane with Pyridine.—(*a*) At 65—70°. A solution of phenylazotriphenylmethane (21 g.) in dry pyridine (250 c.c.) was warmed on the water-bath. Nitrogen evolution commenced at 55° and was vigorous at 65°. The temperature was held at 65—70° until evolution of gas had ceased and the solution was then boiled under reflux for 2 hours The bulk of the pyridine was removed from the clear orange-red solution, and the dark viscous residue was distilled under reduced pressure. The main fraction was collected at 160—190°/17 mm. as an orange-yellow oil, which partly solidified, and a smaller fraction was collected at 220—260°/17 mm. The combined fractions (8·0 g.) were boiled with ethyl alcohol (60 c.c.) and from the hot solution a small quantity of tetraphenylmethane (0·2 g.) was filtered off which separated from benzene in needles, m. p. 273—276°, both alone and on admixture with an authentic specimen. The alcoholic filtrate deposited a crystalline solid (4·6 g.) on cooling, which on recrystallisation from alcohol gave triphenylmethane, m. p. 91—92°. The residual alcoholic filtrate was added to a hot solution of picric acid (4·5 g.) in alcohol (55 c.c.), and when cold the mixture of picrates was collected and dried (4·5 g.). Fractional crystallisation from acetone, as described by Haworth, Heilbron, and Hey (*J.*, 1940, 349), eventually gave 4-phenylpyridine picrate (1·1 g.) in hard yellow needles, m. p. and mixed m. p. 195—196°, 3-phenylpyridine picrate (0·5 g.) in bright yellow silky needles, m. p. and mixed m. p. 158—159°, and 2-phenylpyridine picrate (0·03 g.) in yellow prisms, m. p. and mixed m. p. 174—175°.

(*b*) At 20°. Phenylazotriphenylmethane (20 g.) was added to dry pyridine (200 c.c.) maintained at 20°. After 2 days the azo-compound had dissolved to give an orange-red solution and evolution of nitrogen was just perceptible. After 6 weeks the excess of pyridine was removed from the deep-red solution under reduced pressure, and the residue was collected in three fractions: (i) b. p. 100—155°/1 mm. (pale yellow oil); (ii) b. p. 155—165°/1 mm. (yellow oil which solidified), and (iii) b. p. 165—195°/1 mm. (orange-red oil which solidified). On working up these fractions as described above the following compounds were isolated: triphenylmethane (7·0 g.), m. p. 89—91°, tetraphenylmethane (<0·1 g.), m. p. 271—275°, 2-phenylpyridine picrate (0·2 g.), m. p. 172—174°, 3-phenylpyridine picrate (0·9 g.), m. p. 155—158°, and 4-phenylpyridine picrate (0·6 g.), m. p. 192—195°. The total weight of crude mixed picrates was 6·5 g.

2-Chloro-3- and -5-acetamidopyridine.—The nitration of 2-aminopyridine was carried out as described both by Phillips (*J.*, 1941, 12) and by Caldwell and Kornfeld (*J. Amer. Chem. Soc.*, 1942, **64**, 1696), and the 3-nitro-2-aminopyridine was separated from the 5-nitro-compound by prolonged distillation with steam. Both nitro-amines were converted into the nitro-2-hydroxypyridines and hence into the 2-chloro-nitropyridines as described by Phillips (*loc. cit.*) for the 5-nitro-compound. Both nitro-compounds were reduced with stannous chloride and hydrochloric acid to give 2-chloro-5-aminopyridine (m. p. 83°) and 2-chloro-3-aminopyridine (m. p. 80·5°) (cf. Tschitschibabin and Bylinkin, *J. Russ. Phys. Chem. Soc.*, 1940, **50**, 478; von Schickh, Binz, and Schulz, *Ber.*, 1936, **69**, 2593). Acetylation in the usual manner, followed by crystallisation, gave *2-chloro-5-acetamidopyridine*, m. p. 151—152° (from water) (Found: C, 49·2; H, 4·2. $C_7H_7ON_2Cl$ requires C, 49·3; H, 4·1%), and 2-chloro-3-acetamidopyridine, m. p. 90—91° [from light petroleum (b. p. 60—80°)] (cf. Schickh, Binz, and Schulz, *loc. cit.*).

2-Chloro-3- and -5-phenylpyridine.—A 15% solution of nitrosyl chloride in glacial acetic acid (25 c.c.) was added dropwise to a solution of 2-chloro-3-acetamidopyridine (5·0 g.) in a mixture of glacial acetic acid (35 c.c.) and acetic anhydride (15 c.c.), to which had been added fused potassium acetate (15 g.) and phosphoric oxide (0·5 g.), stirred at 0°. Stirring was continued for 10 minutes after the addition, after which the solution was poured on a mixture of ice and an excess of aqueous sodium carbonate. The nitroso-compound, which separated as a yellow oil, solidified and was collected, washed with ice-water, and dried [4·8 g.; m. p. 45—46° (decomp.)]. A solution of the 2-chloro-3-*N*-nitrosoacetamidopyridine (2 g.) in dry benzene (150 c.c.) was warmed on the water-bath until nitrogen was copiously evolved. The reaction was completed by several hours' boiling under reflux, after which the excess of benzene was removed under reduced pressure. The residual dark-brown viscous oil was boiled with ethyl alcohol and charcoal, filtered, and evaporated to dryness. *2-Chloro-3-phenylpyridine* and regenerated 2-chloro-3-acetamidopyridine were extracted from the residue with hot light petroleum (b. p. 40—60°) and further fractionation from the same solvent gave 2-chloro-3-phenylpyridine in yellow needles, m. p. 55—56° (Found: C, 68·95; H, 4·4. $C_{11}H_8NCl$ requires C, 69·65; H, 4·25%).

In a similar reaction starting with 2-chloro-5-acetamidopyridine (5 g.), the crude nitroso-compound (5·5 g.) was purified by extraction with cold ether, followed by filtration and evaporation under reduced pressure without the application of any heat. In this way any unchanged 2-chloro-5-acetamidopyridine, which is sparingly soluble in cold ether, was removed. The pure *2-chloro-5-N-nitrosoacetamidopyridine* (4·8 g.) was obtained as a yellow crystalline mass, m. p. 69—70° (decomp.) (Found: C, 42·5; H, 3·05; N, 20·3. $C_7H_6O_2N_3Cl$ requires C, 42·1; H, 3·0; N, 21·0%). A solution of the nitroso-compound (4·8 g.) in benzene (150 c.c.), treated as described above for the corresponding 3-*N*-nitrosoacetamido-compound, gave *2-chloro-5-phenylpyridine* (1·0 g.), which separated from light petroleum (b. p. 40—60°) in yellow needles, m. p. 65—66° (Found: C, 69·4; H, 4·2; N, 7·4. $C_{11}H_8NCl$ requires C, 69·65; H, 4·25; N, 7·4%).

Gomberg Reaction on 2-Chloro-5-aminopyridine using Sodium Acetate.—A solution of 2-chloro-5-aminopyridine (5 g.) in a mixture of concentrated sulphuric acid (7 c.c.) and water (50 c.c.) was diazotised at 0° with a concentrated solution of sodium nitrite (2·8 g.) in water. This solution of the diazonium sulphate was thoroughly stirred with benzene (100 c.c.) at room temperature and a solution of sodium acetate (40 g.; trihydrate) in water was added dropwise. The mixture was then warmed with stirring until a vigorous evolution of nitrogen took place. When cold, the mixture was filtered, the benzene layer separated, and the excess evaporated under reduced pressure. Extraction of the residue with light petroleum (b. p. 40—60°) gave 2-chloro-5-phenylpyridine, m. p. 63—64°, which showed no depression

on admixture with the product obtained as described above from 2-chloro-5-*N*-nitrosoacetamidopyridine and benzene.

Gomberg Reaction on 5-Amino-2-n-butoxypyridine.—A solution of 5-amino-2-*n*-butoxypyridine (8 g.), prepared from 2-chloro-5-nitropyridine, in concentrated hydrochloric acid (27·5 c.c.) and water (14 c.c.) was diazotised at −5° with aqueous sodium nitrite (3·8 g. in 9 c.c.) and added to benzene (100 c.c.) at 5°. Aqueous sodium hydroxide (30%) was added dropwise to the well-stirred mixture until it was alkaline to litmus, after which stirring was continued for 3 hours at 5—10° and for 24 hours at room temperature. The benzene layer was separated and washed with water. After removal of the solvent 2-n-*butoxy-5-phenylpyridine* was collected at 145—150°/2·5 mm. as a yellow oil (1·5 g.), which solidified when cooled below 20° (Found : C, 79·8; H, 7·8; N, 5·9. $C_{15}H_{17}ON$ requires C, 79·3; H, 7·5; N, 6·15%). The *picrate* separated from alcohol in yellow plates or from alcohol–acetone in yellow needles, m. p. 156° (Found : C, 55·4; H, 4·6; N, 12·1. $C_{15}H_{17}ON,C_6H_3O_7N_3$ requires C, 55·8; H, 4·4; N, 12·3%).

3-*Phenylquinoline.*—(*a*) *From 3-nitrosoacetamidoquinoline.* A 25% solution of nitrosyl chloride in acetic anhydride (24 c.c.) was added slowly to a mixture of 3-acetamidoquinoline (3·2 g.), fused potassium acetate (12 g.), and phosphoric oxide (0·5 g.) in a mixture of glacial acetic acid (20 c.c.) and acetic anhydride (5 c.c.) stirred at 0—12°. Stirring was continued for 40 minutes after the addition, after which the mixture was poured on crushed ice to which sufficient sodium carbonate was added to make the resulting solution alkaline. The 3-nitrosoacetamidoquinoline, which separated as a yellow oil that solidified, was collected, washed with ice-cold water, and dried [3·5 g.; m. p. 60—62° (decomp.)]. It was added to dry benzene (80 c.c.) and after storage overnight the solution was boiled under reflux for 4 hours. Excess of benzene and acetic acid was removed under reduced pressure and the oily residue was extracted several times with light petroleum (b. p. 40—60°). Evaporation of the solvent deposited a crystalline solid (1·1 g., m. p. 49—50°), which was contaminated with a red impurity, but repeated crystallisation from the same solvent gave 3-phenylquinoline in flat plates, m. p. 51—52° [picrate, m. p. 204—205° (uncorr.)].

(*b*) *From 1-3′-quinolyl-3 : 3-dimethyltriazen.* A solution of 3-aminoquinoline (1·8 g.) in water (5 c.c.) and concentrated hydrochloric acid (5 c.c.) was diazotised with a solution of sodium nitrite (0·9 g.) in water (5 c.c.) at 5—10°. The solid diazonium salt which separated was dissolved by the addition of ice-cold water and the yellow solution was added slowly with shaking to a mixture of a 33% aqueous solution of dimethylamine (2 g.) and aqueous sodium carbonate (5 g. in 20 c.c.). After ½ hour the orange-brown precipitate was collected and dried (2·0 g.; m. p. 85—95°). Extraction with light petroleum (b. p. 40—60°) left the triazen (1·6 g.), m. p. 80—90° (decomp.), which dissolved in cold concentrated hydrochloric acid to give a solution which gave a positive coupling action with alkaline β-naphthol. Evaporation of the light petroleum extract gave a product, m. p. 67·5—68° (picrate, m. p. 146—147°), which in hydrochloric acid solution did not couple with alkaline β-naphthol (Found : C, 63·6; H, 5·1; N, 20·6%). Dry hydrogen chloride was passed for 30 minutes into a boiling solution of the triazen (1·8 g.) in dry benzene (100 c.c.). The cooled solution was washed with 10% aqueous sodium hydroxide and the filtered benzene solution was dried. Removal of the solvent left a reddish oil from which 3-phenylquinoline was extracted with hot light petroleum (b. p. 40—60°), and identified as the picrate, m. p. and mixed m. p. 201—202° (uncorr.) (from alcohol).

2-*Quinolylazotriphenylmethane.*—Solutions of 2-quinolylhydrazine (11 g.), prepared as described by Perkin and Robinson (*J.*, 1913, **103**, 1978), in pyridine (200 c.c.) and of triphenylchloromethane (22 g.) in pyridine (100 c.c.) were mixed. A yellow precipitate separated and the mixture was boiled under reflux for 1½ hours, after which it was poured into water. The red gum which separated gave on trituration with ether a yellow amorphous powder (24 g.), which separated from alcohol in yellow needles (22·8 g.), which softened at 90° and finally melted at 157°. Further crystallisation from alcohol gave 2-*quinolylhydrazotriphenylmethane* in white needles, m. p. 163·5—164·5° *in vacuo* (Found : C, 80·4; H, 6·5; N, 9·45. $C_{28}H_{23}N_3,C_2H_6O$ requires C, 80·5; H, 6·5; N, 9·4%). Crystallisation from benzene–light petroleum gave the hydrazo-compound, m. p. 165° *in vacuo*, free from solvent of crystallisation (Found : C, 84·1; H, 5·5. $C_{28}H_{23}N_3$ requires C, 83·8; H, 5·7%). A solution of potassium ferricyanide (78 g.) in water (240 c.c.) was added to a partial solution of the hydrazo-compound (22 g.) in ether (550 c.c.) and the whole was stirred vigorously at 0—5° while 2N-sodium hydroxide (103 c.c.) was added during 20 minutes. The mixture became deep-red, and stirring was continued for 1½ hours. The ethereal layer was separated, washed with water, and dried. Evaporation of the solvent under reduced pressure gave an orange solid residue [16·0 g.; m. p. 97—99° (decomp.)]. Crystallisation from ether gave 2-*quinolylazotriphenylmethane* in small yellow prisms, m. p. 103° (decomp.) (Found : C, 83·5; H, 5·6. $C_{28}H_{21}N_3$ requires C, 84·1; H, 5·3%).

Reaction of 2-Quinolylazotriphenylmethane with Benzene.—A solution of the azo-compound (10 g.) in benzene (150 c.c.) was warmed to 70°. Evolution of nitrogen was vigorous and the solution darkened in colour. When evolution of gas had ceased the solution was boiled under reflux for 2 hours, after which the excess of benzene was removed and the residue on distillation under reduced pressure gave two fractions : (*a*) b. p. 180—190°/3·5 mm. (3·5 g.), and (*b*) b. p. 200—260°/3·5 mm. (2·1 g.). Fraction (*a*) gave triphenylmethane (1·75 g.), m. p. 90—91° after recrystallisation from alcohol, a small quantity of a solid, m. p. 159—160° after crystallisation, and quinoline (1·1 g.). Fraction (*b*) yielded a basic substance (1·3 g.), which on repeated crystallisation from alcohol–benzene gave 2-*triphenylmethylquinoline* in needles, m. p. 191—192° (Found : C, 90·6; H, 5·8. $C_{28}H_{21}N$ requires C, 90·5; H, 5·7%). In a second experiment with the azo-compound (5 g.) and benzene (50 c.c.) the temperature was maintained at 70° until evolution of nitrogen had ceased, after which the benzene was removed under reduced pressure. The residue was extracted with two portions (40 c.c.) of boiling ether. An insoluble residue (0·1 g.) of triphenylmethyl peroxide was obtained, which after crystallisation from alcohol–benzene melted at 186°. Distillation of the extracts gave (*a*) a yellow oil (0·6 g.), b. p. 70—100°/0·1 mm., (*b*) an orange-yellow oil (1·0 g.), b. p. 100—150°/0·1 mm., and (*c*) a viscous brown oil (1·7 g.), b. p. 150—230°/0·1 mm. Fraction (*a*) consisted mainly of quinoline, identified as its sparingly soluble picrate, m. p. and mixed m. p. 199—200°. Fraction (*b*) gave triphenylmethane (0·5 g.), m. p. 85—88° (from alcohol), and from the mother-liquor a further quantity of quinoline, isolated as picrate. Fraction (*c*) on crystallisation from benzene–alcohol gave 2-triphenylmethyl-

quinoline, m. p. 190—191°. In both experiments treatment of the mother-liquors with alcoholic picric acid gave mixtures of picrates from which no pure products, other than quinoline picrate, could be isolated.

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