Acylarylnitrosamines. Part VII. Reactions of 3-Aminomethoxypyridines and 3-Amino-1-methylpyridones. The Preparation of 2-Methoxy-3-phenyl-, 4-Methoxy-3-phenyl-, and 2-Methoxy-5-phenylpyridine.*

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[Reprint Order No. 5654.]

Contrary to previous results obtained in the quinoline series [(Mrs.) Adams and Hey, *J.*, 1951, 1521] 5-acetamido-2-methoxypyridine, 3-acetamido-2-methoxypyridine, and 3-acetamido-4-methoxypyridine undergo normal nitrosation and the resulting nitroso-compounds react with benzene to give 2-methoxy-5-phenyl-, 2-methoxy-3-phenyl-, and 4-methoxy-3-phenylpyridine respectively. Similar reactions were not successful with the isomeric *N*-methylpyridones, although 1-methyl-5-phenyl-2-pyridone was obtained in poor yield from the dimethyltriazen prepared from 5-amino-1-methyl-2-pyridone on decomposition in benzene.

Numerous attempts have been made to prepare phenyl and pyridyl derivatives of both pyridine and quinoline by reaction of a *N*-nitrosoacetamido-pyridine or -quinoline, or of a diazotised amino-pyridine or -quinoline, with benzene or pyridine, but they have been successful only when the nitrosoacetamido- or amino-group is attached to the 3-position in the heterocyclic ring or, with one exception, to any position in the carbocyclic ring of quinoline. Thus, attempts to prepare 2-*N*-nitrosoacetamidopyridine as an intermediate for the preparation of 2-phenylpyridine were unsuccessful (Haworth, Heilbron, and Hey, *J.*, 1940, 372), and failures were reported with diazo-derivatives prepared from 2- and 4-aminoquinoline and their subsequent treatment with pyridine (Coates, Cook, Heilbron, Hey, Lambert, and Lewis, *J.*, 1943, 401). On the other hand, satisfactory yields of 3-phenyl- and 3-pyridyl-quinoline were obtained from derivatives of 3-aminoquinoline [Coates, Cook, Heilbron, Hey, Lambert, and Lewis, *loc. cit.*; (Mrs.) Adams, Hey, Mamalis, and Parker, *J.*, 1949, 3181]. Adams *et al.* also showed that, although 2-acetamido-5-chloropyridine could not be nitrosated, both 3- and 5-acetamido-2-chloropyridine underwent normal nitrosation and in subsequent reaction with benzene these nitroso-compounds gave 2-chloro-3- and 2-chloro-5-phenylpyridine respectively in the normal manner. It was noted that these nitroso-compounds were much more stable than nitrosoacetanilide. A successful reaction was also reported with diazotised 5-amino-2-*n*-butoxypyridine. The success achieved with derivatives of 3-amino-pyridine and -quinoline arises from the fact that these compounds, unlike the 2- and the 4-amino-derivatives, display the normal properties of aromatic amines (cf. Steck and Ewing, *J. Amer. Chem. Soc.*, 1948, **70**, 3397). The one example, referred to above, in which these reactions fail when the amino- or derived group is attached to the carbocyclic ring of quinoline, concerns 5-amino-6-methoxyquinoline (Coates, Cook, Heilbron, Hey, Lambert, and Lewis, *J.*, 1943, 406).

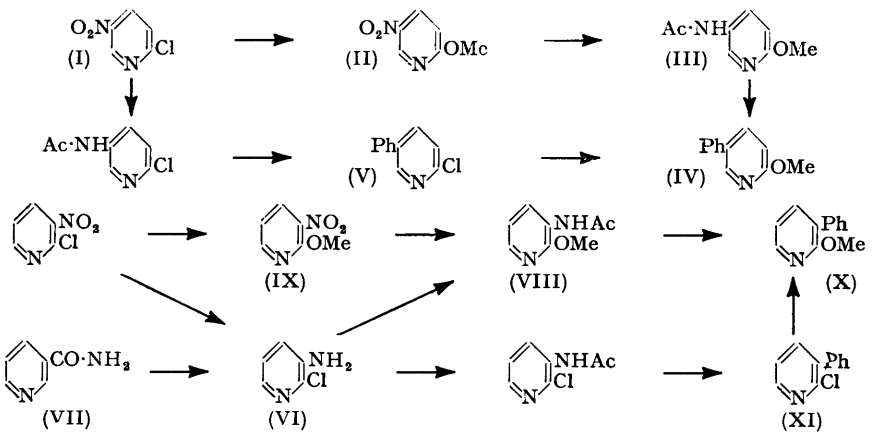
The use of derivatives of 3-aminopyridine for the preparation of 3-phenylpyridine has also been investigated by Rapoport, Look, and Kelly (*J. Amer. Chem. Soc.*, 1952, **74**, 6293). The product obtained in the nitrosation of 3-acetamidopyridine was not considered to be a suitable intermediate because it was soluble in water and difficult to isolate, and 3 : 3-dimethyl-1-3′-pyridyltriazen was found to be too stable, being recovered unchanged when refluxed in benzene in presence of glacial acetic acid or of hydrogen chloride. On the other hand, 3-*N*-nitroso*iso*butyramidopyridine was conveniently prepared, was easily extracted from dilute solution with ether or benzene, and on being warmed in benzene decomposed to give 3-phenylpyridine in 39% yield. Rapoport and Look subsequently (*ibid.*, 1953, **75**, 4605) used 3-*N*-nitroso*iso*butyramidopyridine for the preparation of 3 : 2′-nornicotyrine by reaction with ethyl pyrrole-1-carboxylate followed by hydrolysis and elimination of carbon dioxide.

In an investigation into the reactions of the isomeric *N*- and *O*-methyl derivatives of

* Part VI, *J.*, 1952, 4657.

3-amino-4-hydroxy-quinoline and -quinaldine it was found [(Mrs.) Adams and Hey, *J.*, 1951, 1521] that, contrary to expectation, normal behaviour was displayed in the *N*-methyl (or quinonoid) series, whereas the *O*-methyl (or benzenoid) series behaved abnormally. Thus, nitrosation of 3-acetamido-1-methyl-4-quinolone gave 1-methyl-3-*N*-nitrosoacetamido-4-quinolone, which with benzene gave 1-methyl-3-phenyl-4-quinolone, identical with a specimen prepared by the action of methyl iodide on 4-hydroxy-3-phenylquinoline and different from the product obtained from the action of sodium methoxide on 4-chloro-3-phenylquinoline. The same product was obtained from the action of 3 : 3-dimethyl-1-(1-methylquinol-4-on-3-yl)triazen on boiling in benzene in the presence of hydrogen chloride. Attempts to carry out similar reactions starting with 3-amino-4-methoxyquinoline were unsuccessful. Further, nitrosation of 3-acetamido-1 : 2-dimethyl-4-quinolone gave 1 : 2-dimethyl-3-*N*-nitrosoacetamido-4-quinolone, which gave 1-methylpyrazolo-(4′ : 5′-2 : 3)-4-quinolone in boiling benzene, whereas the attempted nitrosation of 3-acetamido-4-methoxyquinaldine again failed. This unexpected result made it desirable to study further reactions of this type. The present communication describes the results obtained with a series of methylated derivatives of 3-aminopyridine containing a hydroxyl group at position 2, 4, or 6.

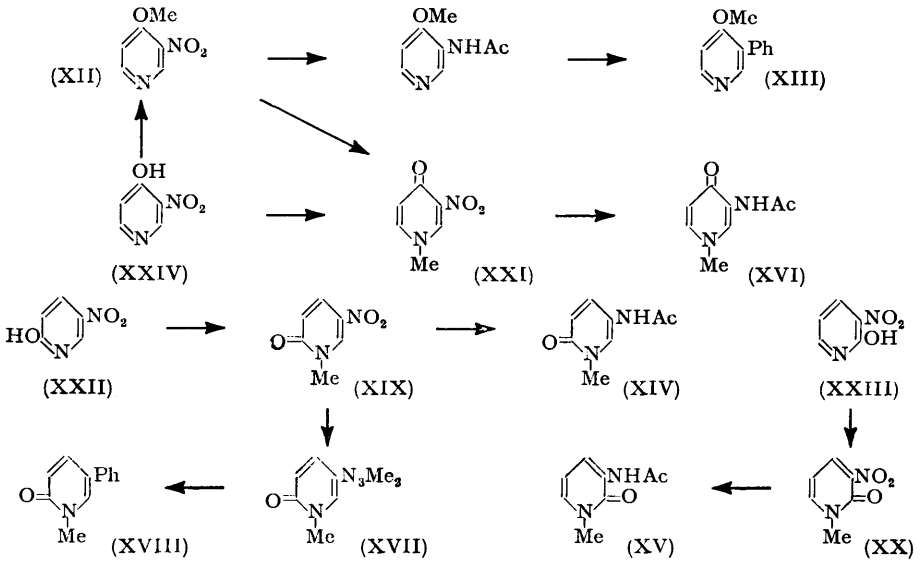
2-Chloro-5-nitropyridine (I) was converted successively into 2-methoxy-5-nitropyridine (II), 5-amino-2-methoxypyridine, and 5-acetamido-2-methoxypyridine (III). Nitrosation of the latter gave the *N*-nitroso-derivative, which when heated in benzene solution gave 2-methoxy-5-phenylpyridine (IV), the picrate of which was identical with that prepared



from the product of the reaction of sodium methoxide on 2-chloro-5-phenylpyridine (V). 3-Amino-2-chloropyridine (VI), prepared from nicotinamide (VII), was converted successively into 3-amino- and 3-acetamido-2-methoxypyridine (VIII), which was also prepared from 2-methoxy-3-nitropyridine (IX). Nitrosation of 3-acetamido-2-methoxypyridine (VIII) and decomposition in benzene solution gave 2-methoxy-3-phenylpyridine (X), the picrate of which was identical with that prepared from the product of the action of sodium methoxide on 2-chloro-3-phenylpyridine (XI). In a third series 3-amino-4-methoxypyridine, obtained by reduction of 4-methoxy-3-nitropyridine (XII), was successively acetylated and nitrosated, and the decomposition of 4-methoxy-3-*N*-nitrosoacetamidopyridine in benzene solution gave 4-methoxy-3-phenylpyridine (XIII). These reactions and interrelations are represented schematically in the appended formulæ.

In contrast to the above results 5-acetamido-1-methyl-2-pyridone (XIV), 3-acetamido-1-methyl-2-pyridone (XV), and 3-acetamido-1-methyl-4-pyridone (XVI) failed to undergo nitrosation, and attempted diazotisation of the corresponding amines and subsequent reaction with benzene also failed. The dimethyltriazen (XVII) prepared from 5-amino-1-methyl-2-pyridone gave 1-methyl-5-phenyl-2-pyridone (XVIII) in poor yield when boiled with benzene in presence of hydrogen chloride, but similar reactions with the triazens from 3-amino-1-methyl-2- and -4-pyridone failed. The three amino-1-methylpyridones

were prepared from the corresponding 1-methylnitropyridones (XIX, XX, and XXI), which in turn were obtained from the appropriate hydroxynitropyridine (XXII, XXIII, and XXIV) by methylation with methyl sulphate. The extreme solubility in water of these amines rendered their isolation difficult when the more conventional methods of reduction were used, but it was possible to prepare the free amines in high yield by the application of the hydrogen-transfer method of Linstead, Braude, Mitchell, Woolridge, and Jackman (*Nature*, 1952, **169**, 100) with palladium–charcoal and *cyclo*hexene.



The results of these experiments show that the abnormal behaviour revealed in the quinoline series is not reproduced in the pyridine series, for whereas 5-acetamido-2-methoxypyridine, 3-acetamido-2-methoxypyridine, and 3-acetamido-4-methoxypyridine give normal nitroso-derivatives which react with benzene to give the methoxyphenylpyridines, no success attended attempts to effect similar reactions with 5-acetamido-1-methyl-2-pyridone, 3-acetamido-1-methyl-2-pyridone, and 3-acetamido-1-methyl-4-pyridone. The failure with the *N*-methyl derivatives extended also to the reactions of the diazotised amines with benzene, with the exception of the triazen prepared from 5-amino-1-methyl-2-pyridone which, with benzene, gave 1-methyl-5-phenyl-2-pyridone in very poor yield.

The preparative work incidental to this investigation has resulted in the disclosure of discrepancies with regard to two compounds. It is now shown that 2-methoxy-3-nitropyridine (IX), prepared from 2-chloro-3-nitropyridine by the action of sodium in methanol, has m. p. 56—58°, whereas Magidson and Menshikov (*Trans. Sci. Chem. Pharm.-Inst., Moscow*, 1926, **16**, 23) reported m. p. 110° for this compound prepared by the action of methyl iodide on the silver salt of 2-hydroxy-3-nitropyridine. A recent repetition of the work of the latter authors by Gruber (*Canad. J. Chem.*, 1953, **31**, 1181) gave two products, (*a*) 2-methoxy-3-nitropyridine, m. p. 57—59°, and (*b*) 1-methyl-3-nitro-2-pyridone, m. p. 171—174°. Secondly, 3-acetamido-2-methoxypyridine (VIII), prepared from either 3-amino-2-chloropyridine (VI) or 2-methoxy-3-nitropyridine (IX), is now shown to have m. p. 88—90°. Schickh, Binz, and Schulz (*Ber.*, 1936, **69**, 2593) reported m. p. 163° for 3-acetamido-2-methoxypyridine prepared by acetylation of the amine with acetic anhydride at 200—220° in a sealed tube, but their compound is now shown to be the isomeric 3-acetamido-1-methyl-2-pyridone (XV).

Experimental

5-Acetamido-2-methoxypyridine (cf. Adams and Govindachari, *J. Amer. Chem. Soc.*, 1947, **69**, 1806).—A solution of 2-methoxy-5-nitropyridine (Friedman, Braitberg, Tolstoouhov, and Tisza, *ibid.*, p. 1204) (5·1 g.) in ethanol (100 c.c.) containing either Raney nickel (5 g.) or palladium

on carbon (5%; 1 g.) was shaken with hydrogen at room temperature and atmospheric pressure. After 30 min. absorption of the theoretical volume of hydrogen was complete. The solution was filtered and the solvent evaporated under reduced pressure. The residual amine, which was obtained in almost quantitative yield as a red oil (dipicrate, m. p. 127—128°; Adams and Govindachari, *loc. cit.*, give m. p. 128°), was acetylated with acetic anhydride containing two drops of perchloric acid. After removal of the excess of acetic anhydride under reduced pressure, the residue was made alkaline with ice-cold aqueous sodium hydroxide and extracted with ether. Evaporation of the ether from the dried (Na_2SO_4) extract left 5-acetamido-2-methoxypyridine (4·5 g.), which separated from benzene–light petroleum (b. p. 40—60°) in needles, m. p. 96—98° (Found: C, 57·4; H, 5·9. Calc. for $C_8H_{10}O_2N_2$: C, 57·8; H, 6·0%). Takahashi, Ichikawa, and Yatsuka (*J. Pharm. Soc. Japan.*, 1945, **65**, 2*A*, 14; *Chem. Abs.*, 1951, **45**, 8531) claim to have obtained this compound (m. p. 95°), together with an unidentified product, on boiling the amine with acetic anhydride.

2-*Methoxy*-5-*phenylpyridine*.—(*a*) A 15% solution of nitrosyl chloride in acetic anhydride (10 c.c.) was added dropwise to a well-stirred mixture of 5-acetamido-2-methoxypyridine (2 g.) in glacial acetic acid (14 c.c.) and acetic anhydride (6 c.c.) containing fused potassium acetate (6 g.) at 0—5°. Stirring was continued for 15 min. after the addition and the yellow mixture was then poured on crushed ice containing enough aqueous sodium carbonate to keep the mixture alkaline. With vigorous stirring the nitroso-compound separated as a yellow oil, which solidified (2·2 g.). It was collected, washed with ice-cold water and dried *in vacuo* over potassium hydroxide. A portion crystallised from dry ether (charcoal) in the cold was obtained in pale yellow needles, m. p. 51·5—52·5° (decomp.). A solution of 2-methoxy-5-*N*-nitrosoacetamidopyridine (2 g.) in dry " AnalaR " benzene (75 c.c.) was heated under gentle reflux for 24 hr. under moisture-proof conditions. Nitrogen was evolved and the solution became dark red. After removal of some of the solvent the solution was passed down a column of alumina, which was eluted with light petroleum (b. p. 40—60°). 2-Methoxy-5-phenylpyridine was obtained as a light yellow oil (0·74 g.), the *picrate* of which separated from benzene in yellow needles, m. p. 170—171° (Found: C, 51·8; H, 3·6. $C_{12}H_{11}ON,C_6H_3O_7N_3$ requires C, 52·2; H, 3·4%).

(*b*) Sodium (0·2 g.) in absolute methanol (15 c.c.), 2-chloro-5-phenylpyridine (0·38 g.), prepared as described by Adams, Hey, Mamalis, and Parker (*loc. cit.*), and a trace of copper powder were heated together in a sealed tube at 160° for 24 hr. The mixture was filtered and the methanol removed under reduced pressure. The residue was extracted with ether and dried (Na_2SO_4). The residue, on removal of the solvent, was converted into the picrate, which separated from benzene in yellow needles, m. p. 168—169°, which was not depressed on admixture with the picrate prepared by method (*a*).

3-*Amino*-2-*chloropyridine*.—It was found advantageous to convert nicotinamide into 3-amino-2-chloropyridine without the tedious isolation of 3-aminopyridine. A rapid stream of chlorine was passed into a solution of sodium hydroxide (18 g.) in water (200 c.c.) at 0° until an increase in weight of 11 g. was obtained. To this solution powdered nicotinamide (15 g.) was added with vigorous stirring. After 15 min. the clear solution was heated at 75° for 45 min. The mixture was made acid with concentrated hydrochloric acid (150 c.c.), and hydrogen peroxide (100-vol.; 18 c.c.) was added gradually with stirring at 70—80°. The mixture was concentrated under reduced pressure, made alkaline with aqueous sodium hydroxide, and extracted with ether. Evaporation of the dried (Na_2SO_4) extract left 3-amino-2-chloropyridine (9 g.), which was collected at 124°/12 mm. as a colourless oil which solidified. Recrystallisation from benzene gave needles, m. p. 79—80°. Schickh, Binz, and Schulz (*loc. cit.*) reported m. p. 79—80°. The *picrate*, prepared in benzene solution, separated in yellow needles, m. p. 169—171° (Found: C, 37·3; H, 2·2. $C_5H_5N_2Cl,C_6H_3O_7N_3$ requires C, 36·9; H, 2·2%).

3-*Acetamido*-2-*methoxypyridine*.—Acetic anhydride (20 c.c.) was added to 3-amino-2-methoxypyridine (4·6 g.), prepared from 3-amino-2-chloropyridine by the method of Schickh, Binz, and Schulz (*loc. cit.*), followed by 3 drops of perchloric acid. After being shaken and kept overnight, the mixture was neutralised with saturated aqueous sodium carbonate with the addition of crushed ice. The product was extracted with ether and dried (Na_2SO_4). Removal of the solvent left an oil which solidified. Crystallisation from dry ether (charcoal) gave 3-*acetamido*-2-*methoxypyridine* (4·5 g.) in hexagonal prisms, m. p. 88—90° (Found: C, 58·0; H, 6·1. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·0%) (cf. Schickh, Binz, and Schulz, *loc. cit.*).

2-*Methoxy*-3-*nitropyridine*.—2-Hydroxy-3-nitropyridine, m. p. 224—225° (3·3 g.), prepared from 2-hydroxypyridine (Binz and Maier-Bode, *Angew. Chem.*, 1936, **49**, 486; Bishop, Cavell, and Chapman, *J.*, 1952, 437) or from 2-amino-3-nitropyridine (Caldwell and Kornfeld, *J. Amer. Chem. Soc.*, 1942, **64**, 1695), was heated for 2 hr. at 110° under reflux with phosphorus penta-

chloride (6 g.) and phosphorus oxychloride (3 drops). After removal of phosphorus oxychloride under reduced pressure, the residue was treated with ice-cold water, and the product collected by filtration. Crystallisation from acetone (charcoal) gave 2-chloro-3-nitropyridine, m. p. 100—102° in almost quantitative yield. Tschitschibabin and Bylinkin (*J. Russ. Phys. Chem. Soc.*, 1920, **50**, 471) reported m. p. 101—102° for this compound. A solution of sodium (0·45 g.) in absolute methanol (20 c.c.) to which was added 2-chloro-3-nitropyridine (3 g.), was boiled under reflux for 1 hr. After removal of half of the methanol by distillation water was added and the precipitated *2-methoxy-3-nitropyridine* (2·5 g.) was collected, which crystallised from ether (charcoal) in needles, m. p. 56—58° (Found: C, 47·0; H, 4·0. $C_6H_6O_3N_2$ requires C, 46·75; H, 3·9%) (cf. Magidson and Menshikov, *loc. cit.*, and Gruber, *loc. cit.*).

3-Amino-2-methoxypyridine.—2-Methoxy-3-nitropyridine (0·55 g.) in methanol (20 c.c.) was hydrogenated in the presence of palladium on charcoal (0·2 g.). The reduction was complete in 30 min. After filtration the methanol was removed under reduced pressure and a small portion of the residual base was converted into the *picrate* in methanol solution. It separated from acetone in stout brown prisms, which became bright yellow on grinding, m. p. 155—156° (Found: C, 41·2; H, 3·3. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1%). The main bulk of the amine was acetylated with acetic anhydride containing a drop of perchloric acid. The resulting 3-acetamido-2-methoxypyridine separated from ether–light petroleum (b. p. 40—60°) in needles, m. p. 87—89°, which was not depressed on admixture with the product prepared as above from 3-amino-2-chloropyridine.

2-Methoxy-3-phenylpyridine.—(*a*) Nitrosyl chloride in acetic anhydride (8%; 23 c.c.) was added dropwise to a stirred mixture of 3-acetamido-2-methoxypyridine (2·5 g.), fused potassium acetate (7·5 g.), and phosphoric anhydride (0·25 g.) in glacial acetic acid (10 c.c.) and acetic anhydride (7·5 c.c.) at 0—5°. After 30 min. the mixture was poured on crushed ice containing sufficient aqueous sodium carbonate to make the mixture slightly alkaline. The 2-methoxy-3-*N* nitrosoacetamidopyridine separated as a yellow oil, which was extracted with "AnalaR" benzene and dried (Na_2SO_4). After filtration the solution was boiled gently under reflux under moisture-proof conditions. After the evolution of nitrogen had ceased the excess of benzene was removed under reduced pressure. The residue in a little benzene was passed down a column of alumina, which was then eluted with light petroleum (b. p. 40—60°). Evaporation of the eluate left 2-methoxy-3-phenylpyridine as a light yellow oil (0·9 g.). The *picrate* separated from benzene in yellow needles, m. p. 117—118° (Found: C, 52·6; H, 3·5. $C_{12}H_{11}ON,C_6H_3O_7N_3$ requires C, 52·2; H, 3·4%).

(*b*) A mixture of sodium (0·02 g.) in absolute methanol (10 c.c.) containing 2-chloro-3-phenylpyridine (0·1 g.), prepared as described by Adams, Hey, Mamalis, and Parker (*loc. cit.*), and copper powder (trace) was heated in a sealed tube at 150° for 10 hr. After filtration the methanol was removed by distillation and the residual 2-methoxy-3-phenylpyridine was converted into the picrate, which separated from benzene in yellow needles, m. p. 116—118°, undepressed on admixture with the compound prepared by method (*a*) above.

3-Amino-4-methoxypyridine.—A mixture of 4-methoxy-3-nitropyridine (5·1 g.) (Bremer, *Annalen*, 1937, **529**, 290) and Raney nickel (5 g., in suspension in ethanol) in methanol (100 c.c.) was shaken with hydrogen at atmospheric pressure and room temperature. After the rapid uptake of the required volume of hydrogen, the mixture was filtered and the alcohols were removed under reduced pressure. The amine was obtained as a red oil (4 g.), a portion of which was converted into the *picrate* in benzene solution. Recrystallisation from ethanol–acetone gave yellow-brown prisms, m. p. 162—163°, which gave a light yellow powder on grinding (Found: C, 40·7; H, 3·4. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1%). The free base (2·5 g.) was acetylated with acetic anhydride (10 c.c.) containing four drops of perchloric acid. Isolation of the acetyl derivative as described in previous examples gave *3-acetamido-4-methoxypyridine* (3·1 g.) in prismatic plates, m. p. 123—124°, from chloroform–light petroleum (b. p. 40—60°) (Found: C, 57·8; H, 6·0. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·0%).

4-Methoxy-3-phenylpyridine.—A 15% solution of nitrosyl chloride in acetic anhydride (7·5 c.c.) was added dropwise to a stirred mixture of 3-acetamido-4-methoxypyridine (1·5 g.), anhydrous potassium acetate (4·5 g.), and phosphoric anhydride (0·1 g.) in glacial acetic acid (11 c.c.) and acetic anhydride (5 c.c.) at 0—5°. After the addition stirring was continued for 15 min. and the mixture was then added to crushed ice containing an excess of a saturated solution of sodium carbonate. The nitroso-compound separated as a yellow oil which solidified (1·5 g.). A small portion was crystallised from ether (charcoal) by evaporation in the cold. *4-Methoxy-3-N-nitrosoacetamidopyridine* separated in light yellow crystals, m. p. 84° (decomp.) (Found: C, 49·3; H, 4·75. $C_8H_9O_3N_3$ requires C, 49·2; H, 4·6%). A solution of the nitroso-

compound (1·4 g.) in " AnalaR " benzene (60 c.c.) was filtered and then boiled gently under reflux for 20 hr. under moisture-proof conditions. Nitrogen was evolved and the solution became darker. After filtration the benzene was removed under reduced pressure and the residue in a little benzene was passed down a column of alumina, which was subsequently eluted with benzene–ether (2 : 1). Evaporation of the eluate left 4-methoxy-3-phenylpyridine as a light yellow oil (0·5 g.), which was converted into the *picrate* in benzene solution. It separated from acetone in yellow needles, m. p. 206—207° (Found : C, 52·1; H, 3·7. $C_{12}H_{11}ON,C_6H_3O_7N_3$ requires C, 52·2; H, 3·4%).

5-Amino-1-methyl-2-pyridone.—(*a*) Reduction of 1-methyl-5-nitro-2-pyridone (Räth, *Annalen*, 1930, **484**, 52) by conventional methods led to difficulties at the isolation stage as a result of the high solubility of the base in water (cf. Prill and McElvain, *Org. Synth.*, Coll. Vol. II, p. 421). The preparation of 5-amino-1-methyl-2-pyridone in aqueous solution was best effected as follows (cf. Jacobs and Heidelberger, *J. Amer. Chem. Soc.*, 1917, **39**, 1435) : a suspension of the nitro-compound (1·5 g.) in hot water (30 c.c.) containing aqueous ammonia (*d* 0·88; 6 c.c.) was added to a boiling solution of ferrous sulphate (24 g.) in water (70 c.c.). Ammonia (*d* 0·88; 12 c.c.) was added to the boiling solution in portions of 2 c.c. each. The hot mixture was filtered twice and the reddish-blue filtrate (having an intense blue fluorescence) was shown to contain 5-amino-1-methyl-2-pyridone, (i) by diazotisation and coupling with alkaline β-naphthol and (ii) by benzoylation (Schotten–Baumann) to *5-benzamido-1-methyl-2-pyridone*, which separated from ethanol (charcoal) in prisms, m. p. 149—151° (Found : C, 68·9; H, 5·4. $C_{13}H_{12}O_2N_2$ requires C, 68·4; H, 5·3%).

(*b*) The isolation of the free base was effected by means of the hydrogen-transfer method of Linstead, Braude, Mitchell, Woolridge, and Jackman (*loc. cit.*) as follows : a palladium–charcoal catalyst (5%; 1·1 g.; 0·0005 mole of Pd) and *cyclo*hexene (5 c.c.) were added to 1-methyl-5-nitro-2-pyridone (1·54 g.; 0·01 mole) in boiling methanol (60 c.c.), and the whole was boiled under reflux for 24 hr. The catalyst and the methanol were removed. The residue was dried *in vacuo* over potassium hydroxide, and purified by treatment with charcoal in methanol, followed by filtration. Evaporation of the solvent left the 5-amino-1-methyl-2-pyridone as a white hygroscopic wax-like solid with a violet tinge (1·35 g.). The base developed a deeper colour on standing and gave blue fluorescent solutions in water, methanol, and ethanol. It was moderately soluble in benzene but very sparingly soluble in ether. The *picrate*, prepared in methanol, separated in greenish-yellow needles, m. p. 204° (decomp. after darkening at 190°) (Found : C, 40·5; H, 3·3. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1%). Räth (*loc. cit.*) claimed to have obtained 5-amino-1-methyl-2-pyridone, m. p. 125—126° (decomp.), in a very small yield by the reduction of the nitro-compound with tin and hydrochloric acid.

1-Methyl-5-phenyl-2-pyridone.—The fluorescent aqueous filtrate obtained from 1-methyl-5-nitro-2-pyridone (1·5 g.) as described above was boiled to expel free ammonia, and most of the free sulphate was removed as barium sulphate. The volume of the resulting solution was reduced to 10 c.c., and at 0—5° sodium nitrite (0·56 g.) was added. To the diazotised solution was added a mixture of aqueous dimethylamine (25% solution; 3 c.c.) and sodium carbonate (1·2 g.) in water (16 c.c.) at 0°. The resulting mixture was stirred at room temperature for 1 hr. and then extracted repeatedly with benzene (5 × 100 c.c.). The dried ($MgSO_4$) benzene solution was concentrated to 100 c.c. and boiling under reflux was continued for 1 hr. while a stream of dry hydrogen chloride was passed in. Dilute aqueous sodium hydroxide (10%; 100 c.c.) was added and the benzene layer was separated, washed with water, and dried ($MgSO_4$). Removal of the benzene under reduced pressure left in poor yield a low-melting solid, which was converted into *1-methyl-5-phenyl-2-pyridone picrate* which separated from benzene in yellow needles, m. p. 133—134° (Found : C, 52·7; H, 3·65; N, 13·7. $C_{12}H_{11}ON,C_6H_3O_7N_3$ requires C, 52·2; H, 3·4; N, 13·5%).

5-Acetamido-1-methyl-2-pyridone.—(*a*) (cf. Haack and Rost, D.R.-P. 596,821). A mixture of 5-acetamido-2-methoxypyridine (0·9 g.) and freshly distilled methyl sulphate (0·7 g.) was warmed with a little water (4 or 5 drops) and made alkaline with 40% aqueous sodium hydroxide (0·5 c.c.). An excess of anhydrous potassium carbonate was added and the whole was extracted with acetone. The acetone solution was treated with charcoal and filtered. The residue obtained on evaporation separated from light petroleum (b. p. 40—60°) in needles, m. p. 74° (Found : C, 47·8; H, 7·0. $C_8H_{10}O_2N_2,2H_2O$ requires C, 47·5; H, 6·9%). The m. p. rose to 96—108° after recrystallisation from boiling benzene–light petroleum. After either product was dried *in vacuo* over potassium hydroxide at 60°, it melted at 147—149° with previous shrinking at 137°. The dried product had lost its crystalline form. In the air it reverted to the low-melting hydrated form.

(*b*) A mixture of acetic anhydride (10 c.c.) and dry 5-amino-1-methyl-2-pyridone (3·0 g.) was heated under reflux for 10 min. and then left overnight. The acetyl derivative was precipitated in almost quantitative yield by anhydrous ether. Crystallisation from benzene (charcoal) gave 5-*acetamido*-1-*methyl*-2-*pyridone* in needles, m. p. 74—76°, alone and admixed with the product prepared by method (*a*) above (Found: C, 47·9; H, 7·0. $C_8H_{10}O_2N_2,2H_2O$ requires C, 47·5; H, 6·9%). On storage *in vacuo* over potassium hydroxide, the water of crystallisation was lost and the amorphous *product* had m. p. 150—151° with previous shrinking at 142° (Found: C, 57·9; H, 6·2. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·0%).

Attempts to effect the nitrosation of 5-acetamido-1-methyl-2-pyridone by the method of France, Heilbron, and Hey (*J.*, 1940, 369) failed. Reactions of diazotised 5-amino-1-methyl-2-pyridone with benzene in presence of (*a*) sodium hydroxide (cf. Gomberg and Pernert, *J. Amer. Chem. Soc.*, 1926, **48**, 1372) and (*b*) sodium acetate (cf. Elks, Haworth, and Hey, *J.*, 1940, 1284) failed to yield any 1-methyl-5-phenyl-2-pyridone.

1-*Methyl*-3-*nitro*-2-*pyridone*.—A mixture of methyl sulphate (13·2 g.), 2-hydroxy-3-nitropyridine (14·8 g.), and a solution of potassium hydroxide (4 g.) in water (100 c.c.) was shaken for 20 min. and then left overnight at room temperature. The precipitated solid was collected, washed, and dried, and a further quantity was collected on concentration of the filtrate. Crystallisation from water gave 1-methyl-3-nitro-2-pyridone (14 g.) in yellow prismatic needles, m. p. 175—176° (Found: C, 46·8; H, 3·9. Calc. for $C_6H_6O_3N_2$: C, 46·75; H, 3·9%). Tschitschibabin and Konowalowa (*Ber.*, 1925, **58**, 1712) reported m. p. 175—176°, and Gruber (*loc. cit.*) m. p. 171—174° for this compound prepared by a similar method.

3-*Amino*-1-*methyl*-2-*pyridone*.—This base was prepared in aqueous solution by reduction of the nitropyridone with ferrous sulphate and ammonia as described above for the reduction of 1-methyl-5-nitro-2-pyridone. In addition, the free base was obtained by the hydrogen-transfer method as in the previous example. 3-Amino-1-methyl-2-pyridone thus prepared in almost quantitative yield was a white hygroscopic waxy solid having a greenish-blue tinge. It was soluble in water, methanol, ethanol, and acetone, sparingly soluble in benzene, and almost insoluble in ether. The solutions had a violet colour with a blue fluorescence. The *picrate* separated from methanol in greenish-yellow needles, m. p. 204° (decomp.) (Found: C, 41·2; H, 3·4. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1%). 3-Amino-1-methyl-2-pyridone was also obtained in poor yield by the action of sodium methoxide on 3-amino-2-chloropyridine at 160—180° in a sealed tube for 24 hr. (cf. Schickh, Binz, and Schulz, *loc. cit.*).

3-*Acetamido*-1-*methyl*-2-*pyridone*.—3-Amino-1-methyl-2-pyridone (1 g.) was boiled under reflux with acetic anhydride (4 c.c.) for 2 min. and the solution was left overnight at room temperature. Addition of ether precipitated 3-*acetamido*-1-*methyl*-2-*pyridone* (1 g.) which crystallised from dry benzene (charcoal) in long hygroscopic needles, m. p. 165—166° (Found: C, 57·5; H, 5·9; N, 17·0. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·0; N, 16·9%). This product was probably prepared by Schickh, Binz, and Schulz (*loc. cit.*) by the acetylation of 3-amino-2-methoxypyridine under drastic conditions, but they assigned to it the constitution 3-acetamido-2-methoxypyridine.

1-*Methyl*-3-*nitro*-4-*pyridone*.—This compound was prepared from 4-hydroxy-3-nitropyridine (4·7 g.) (Bremer, *loc. cit.*) as described above for 2-hydroxy-3-nitropyridine. 1-Methyl-3-nitro-4-pyridone (4·7 g.) crystallised from water in yellow monoclinic needles, m. p. 235° (Found: C, 47·0; H, 4·1. Calc. for $C_6H_6O_3N_2$: C, 46·75; H, 3·9%). It was identical with a sample prepared by Bremer's method by the isomerisation of 4-methoxy-3-nitropyridine, although Bremer reported m. p. 220°.

3-*Amino*-1-*methyl*-4-*pyridone*.—This base was prepared in aqueous solution by reduction of the nitro-compound with ferrous sulphate and ammonia, and the free base was prepared in almost quantitative yield by the hydrogen-transfer method as described above for the reduction of 1-methyl-5-nitro-2-pyridone. 3-*Amino*-1-*methyl*-4-*pyridone* thus obtained separated from acetone by cooling with solid carbon dioxide in light yellow needles which were very hygroscopic. After being dried *in vacuo* over potassium hydroxide it melted at 147—148° (Found: C, 57·1; H, 6·7. $C_6H_8ON_2$ requires C, 58·1; H, 6·45%). Absorption of water was rapid, which probably accounts for the poor analysis. The *picrate* separated from methanol in yellow needles, m. p. 209—210° (decomp.) (Found: C, 41·0; H, 3·1. $C_6H_8ON_2,C_6H_3O_7N_3$ requires C, 40·8; H, 3·1%).

3-*Acetamido*-1-*methyl*-4-*pyridone*.—3-Amino-1-methyl-4-pyridone (1 g.) was acetylated with acetic anhydride (5 c.c.) by boiling under reflux for 2 min. and then being kept overnight at room temperature. Addition of dry ether precipitated the product (1 g.) which was crystallised from benzene (charcoal). Two products were obtained in almost equal quantity, which were

separated by hand, (*a*) short feathery needles, m. p. 150—152° after recrystallisation from benzene, which proved to be 3-*diacetylamino*-1-*methyl*-4-*pyridone* (Found: C, 57·7; H, 5·7; N, 13·6. $C_{10}H_{12}O_3N_2$ requires C, 57·7; H, 5·8; N, 13·4%), and (*b*) long transparent needles, m. p. 185—186° after recrystallisation from benzene, which proved to be 3-*acetamido*-1-*methyl*-4-*pyridone* (Found: C, 57·75; H, 6·4; N, 16·9. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·0; N, 16·9%). Both products were soluble in water but were not capable of undergoing diazotisation unless previously hydrolysed with boiling hydrochloric acid.

Attempted Preparation of 1-*Methyl*-3-*phenyl*-2- *and* -4-*pyridone*.—Attempts to effect reactions between (*a*) the triazen prepared from diazotised 3-amino-1-methyl-2- or -4-pyridone and benzene, (*b*) nitrosyl chloride and 3-acetamido-1-methyl-2- or -4-pyridone, and (*c*) diazotised 3-amino-1-methyl-2- or -4-pyridone and benzene in the presence of aqueous sodium hydroxide or aqueous sodium acetate, were unsuccessful.

Thanks are accorded to the Education Department of the Punjab Government, Lahore, Pakistan, for a Scholarship awarded to Y. A.

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[*Received, August 25th*, 1954.]