191. *New Syntheses of Heterocyclic Compounds. Part VII. 9-Amino-6 : 8-dimethyl-7 : 10-diazaphenanthrenes.*

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A new method for the synthesis of some 9-amino-6 : 8-dimethyl-7 : 10-diazaphenanthrenes from *o*-nitroaryl aldehydes has been developed.

Condensation of *o*-nitrobenzaldehyde with β-aminocrotononitrile and ethyl β-aminocrotonate led to the formation of *ethyl* 3-*cyano*-4-o-*nitrophenyl*-2 : 6-*dimethyl*-1 : 4-*dihydropyridine*-5-*carboxylate* (III; R = CO_2Et). Oxidation of this gave *ethyl* 3-*cyano*-4-o-*nitrophenyl*-2 : 6-*dimethylpyridine*-5-*carboxylate* (IV; R = CO_2Et), hydrolysed to the corresponding *acid* (IV; R = CO_2H), and decarboxylated to 3-*cyano*-4-o-*nitrophenyl*-2 : 6-*dimethylpyridine* (IV; R = H). Reduction of this compound was accompanied by cyclisation and formation of 9-*amino*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene* (VIII; R = H). The constitution assigned to this compound was confirmed by reaction with nitrous acid to give 9-*hydroxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene* (VII), identical with the *lactam* formed by reduction of *ethyl* 4-o-*nitrophenyl*-2 : 6-*dimethylpyridine*-3-*carboxylate* (VI; R = H).

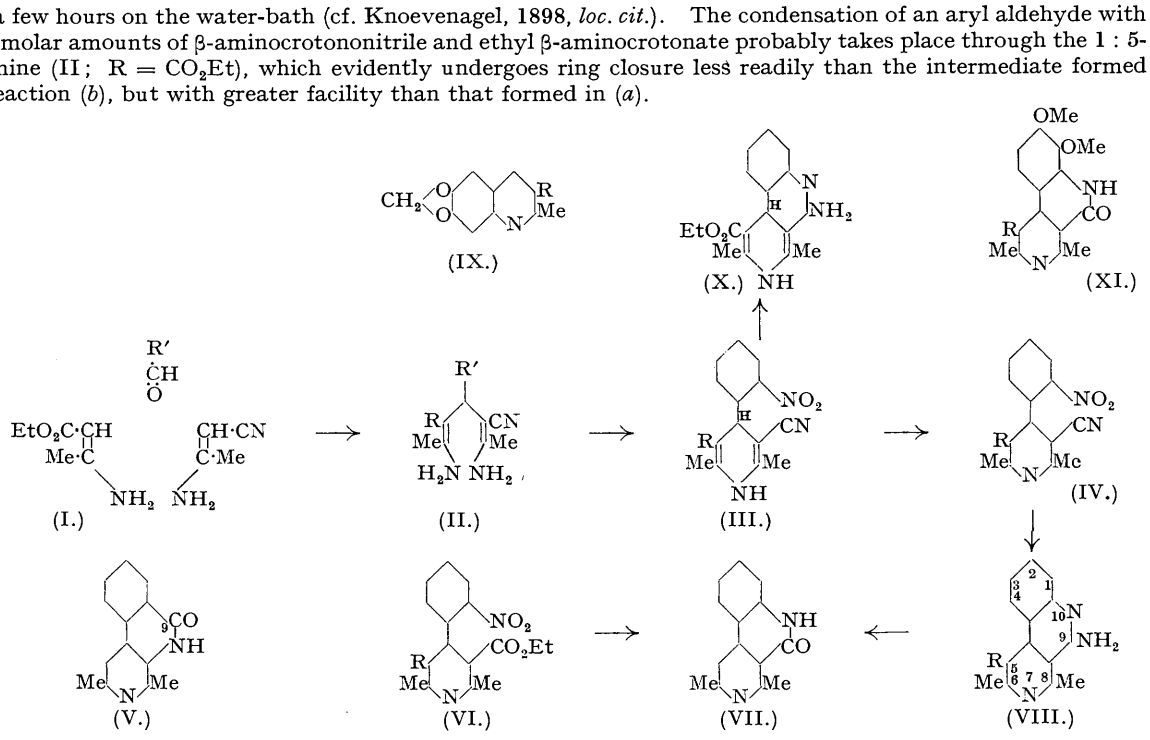
The synthesis has been applied to 6-nitropiperonal and to 2-nitrovanillin, leading to the formation of 9-*amino*-2 : 3-*methylenedioxy*- and 9-*amino*-1 : 2-*dimethoxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene* respectively.

EARLIER work on the relationship between structure and biological activity in the diazaphenanthrene (benznaphthyridine) series (Part V, Petrow, this vol., p. 200; see also footnote on nomenclature, *ibid.*, p. 201) has now been extended to some derivatives of the hitherto unknown 7 : 10-diazaphenanthrene. These were prepared by a method involving several novel features. In the first place, a new extension of Hantzsch's collidine synthesis has been developed whereby 3-*cyano*-4-o-*nitrophenyl*-2 : 6-*dimethylpyridines* (*e.g.*, IV; R = H) are obtained. Secondly, the interesting observation has been made that reduction of these compounds is accompanied by cyclisation and formation of the 9-*amino*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrenes* (*e.g.*, VIII; R = H). Although rearrangements of this type have been employed in the pyridine and quinoline series (Meyer, *Zentr.*, 1908, ii, 591; Pschorr, *Ber.*, 1898, **31**, 1289; Tröger and Köppen-Kastrop, *J. pr. Chem.*, 1922, **104**, 335; Gabriel, *Ber.*, 1918, **51**, 1500), the literature apparently records only one instance of its application to the synthesis of an aminonaphthyridine, *viz.*, the condensation of cyanoacetic ester with 6 : 6′-diamino-3 : 4 : 3′ : 4′-tetramethoxybenzophenone leading to the formation of an 8-amino-1-hydroxy-3 : 4 : 5 : 6-diveratro-2 : 7-naphthyridine (Lawson, Perkin, and Robinson, *J.*, 1924, **125**, 630).

The well-known synthesis of pyridine derivatives by Hantzsch's method from two molecules of ethyl acetoacetate, one molecule of an aldehyde, and ammonia, was shown by Knoevenagel (*Ber.*, 1898, **31**, 738, cf. Beyer, *ibid.*, 1891, **24**, 1662) to take place through the intermediate formation of ethyl β-aminocrotonate. Further study of the reaction revealed that one molecule of ethyl acetoacetate could be replaced by such ketomethylene compounds as acetaldehyde (Michael, *Ber.*, 1885, **18**, 2020), desoxybenzoin (Knoevenagel, *Annalen*, 1894, **281**, 74), and β-diketones and their ammonia derivatives (Knoevenagel and Ruschaupt, *Ber.*, 1898, **31**, 1025). An extension of what is essentially the same reaction was independently discovered by Meyer (*J. pr. Chem.*, 1895, **52**, 101), who replaced the ethyl β-aminocrotonate by β-aminocrotononitrile. In this way a wide variety of dicyanodihydropyridines was prepared by Mohr (*ibid.*, 1897, **56**, 124), and by Meyer (*ibid.*, 1908, **78**, 507; 1915, **92**, 175).

It appeared from these observations that a mixed Hantzsch–Knoevenagel reaction between an aldehyde, β-aminocrotononitrile, and ethyl β-aminocrotonate (I; see scheme) might be expected to occur with formation of a 4-*substituted ethyl* 3-*cyano*-2 : 6-*dimethyl*-1 : 4-*dihydropyridine*-5-*carboxylate* (*e.g.*, III; R = CO_2Et). Experimental study has now shown this to be the case. Slow condensation took place in the expected manner on heating the components in a solvent such as alcohol, with steady evolution of ammonia over periods of up to 60 hours. Occasionally reaction did not appear to proceed to completion with consequent difficulty in isolating the product. This was easily overcome by heating the reaction mixture, after removal of solvent, with acetic anhydride. These results may be interpreted by considering the reaction between an aldehyde and (*a*) β-aminocrotononitrile, or (*b*) ethyl β-aminocrotonate. Mohr (*loc. cit.*) has shown that in reaction (*a*) the 1 : 5-diamine (II; R = CN) is initially formed. Conversion of this compound into a dihydropyridine such as (III; R = CN) fails to take place on heating, but occurs readily on treatment with acidic reagents such as acetic anhydride. In contrast to this, reaction (*b*) proceeds to completion on simply heating the components

for a few hours on the water-bath (cf. Knoevenagel, 1898, *loc. cit.*). The condensation of an aryl aldehyde with equimolar amounts of β-aminocrotononitrile and ethyl β-aminocrotonate probably takes place through the 1 : 5-diamine (II; R = CO_2Et), which evidently undergoes ring closure less readily than the intermediate formed in reaction (*b*), but with greater facility than that formed in (*a*).



The above reaction has been successfully applied to a number of aromatic aldehydes (see Experimental), and the hitherto unknown ethyl cyanodihydropyridinecarboxylates obtained in yields varying from 15 to 70%. These products have been oxidised to the pyridines by dilute nitric acid in alcohol, or better by chromic acid in acetic acid (cf. also Part VIII, following paper).

When *o*-nitrobenzaldehyde was employed in this new synthesis, *ethyl* 3-*cyano*-4-o-*nitrophenyl*-2 : 6-*dimethyl*-1 : 4-*dihydropyridine*-5-*carboxylate* (III; R = CO_2Et) was obtained in 22% yield. Oxidation gave *ethyl* 3-*cyano*-4-o-*nitrophenyl*-2 : 6-*dimethylpyridine*-5-*carboxylate* (IV; R = CO_2Et), hydrolysed by one molecular proportion of potassium hydroxide in 50% alcohol to the corresponding *acid* (IV; R = CO_2H). On heating this acid above its melting point smooth decarboxylation occurred to give 3-*cyano*-4-o-*nitrophenyl*-2 : 6-*dimethylpyridine* (IV; R = H), characterised by its *picrate*. Reduction of the pyridine (IV; R = H) with reduced iron in aqueous alcohol containing a trace of hydrochloric acid was, in general, accompanied by rearrangement and formation of 9-*amino*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene* (VIII; R = H). The product occasionally contained some uncyclised material, as shown by a positive primary amine test on diazotisation and coupling with alkaline β-naphthol. In these instances the crude reduction product was heated under reflux with sodium ethoxide to complete conversion of the cyano-amine into (VIII; R = H), which no longer gave the diazo-test (cf. however the behaviour of 8-amino-1-hydroxy-3 : 4 : 5 : 6-diveratro-2 : 7-naphthyridine on diazotisation, reported by Lawson, Perkin, and Robinson, *J.*, 1924, **125**, 652). The constitution assigned to (VIII; R = H) was confirmed by preparation of a *benzoyl* derivative, and by reaction with nitrous acid, which gave 9-*hydroxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene* (VII) in nearly quantitative yield. The formulation assigned to (VII) followed from its independent synthesis in the following way. Ethyl 4-*o*-nitrophenyl-2 : 6-dimethylpyridine-3 : 5-dicarboxylate (VI; R = CO_2Et) (Hinkel, Ayling, and Morgan, *J.*, 1931, 1837; cf. Lepetit, *Ber.*, 1887, **20**, 1341) was partially hydrolysed by one molecular proportion of potassium hydroxide in 50% alcohol to 3-*carbethoxy*-4-o-*nitrophenyl*-2 : 6-*dimethylpyridine*-5-*carboxylic acid* (VI; R = CO_2H). Decarboxylation of this acid-ester by heating above its melting point furnished the oily *ethyl* 4-o-*nitrophenyl*-2 : 6-*dimethylpyridine*-3-*carboxylate* (VI; R = H), characterised by its well-defined *picrate*. Reduction of this compound was accompanied by lactamisation and formation of 9-hydroxy-6 : 8-dimethyl-7 : 10-diazaphenanthrene (VII), identical in melting point and mixed melting point with the compound formed by the action of nitrous acid on (VIII; R = H).

6-Nitropiperonal condensed normally with β-aminocrotononitrile and ethyl β-aminocrotonate, and the resulting *ethyl* 3-*cyano*-4-(2′-*nitro*-4′ : 5′-*methylenedioxyphenyl*)-2 : 6-*dimethyl*-1 : 4-*dihydropyridine*-5-*carboxylate* was converted into 9-*amino*-6 : 8-*dimethyl*-2 : 3-*methylenedioxy*-7 : 10-*diazaphenanthrene*. An aminodiazaphenanthrene was not obtained when 6-aminopiperonal was employed in place of the nitro-aldehyde. Two substances were isolated from the complex reaction product after preliminary fractionation followed by treatment with acetic anhydride. The less soluble of the two was identified as 3-*cyano*-6 : 7-*methylenedioxy*-2-*methylquinoline* (IX; R = CN) by its direct synthesis from 6-aminopiperonal and β-aminocrotononitrile (cf.

Meyer, *J. pr. Chem.*, 1914, **90**, 1). The more soluble compound was the corresponding *ethyl* 6 : 7-*methylenedioxy*-2-*methylquinoline*-3-*carboxylate* (IX; R = CO_2Et), also obtained by the Friedländer method from 6-aminopiperonal and ethyl β-aminocrotonate. 6-Acetamidopiperonal failed to react in the synthesis and was largely recovered unchanged.

Although the condensation product of 2-nitrovanillin with β-aminocrotononitrile and ethyl β-aminocrotonate failed to crystallise, yet after acetylation *ethyl* 3-*cyano*-4-(2′-*nitro*-4′-*acetoxy*-3′-*methoxyphenyl*)-2 : 6-*dimethyl*-1 : 4-*dihydropyridine*-5-*carboxylate* was readily isolated in 66% yield. Oxidation gave the corresponding *pyridine* derivative, also obtained together with an isomeric *nitro*-compound, by nitration of *ethyl* 3-*cyano*-4-(4′-*acetoxy*-3′-*methoxyphenyl*)-2 : 6-*dimethylpyridine*-5-*carboxylate*, prepared as above from vanillin. Previous experience in a related field (forthcoming publication) had shown that the decarboxylation of 4-hydroxyphenylpyridine-3-carboxylic acids was very unsatisfactory. *Ethyl* 3-*cyano*-4-(2′-*nitro*-4′-*hydroxy*-3′-*methoxyphenyl*)-2 : 6-*dimethylpyridine*-5-*carboxylate* was therefore prepared by hydrolysis of the above acetyl derivative, followed by methylation with methyl sulphate to the 4′-*methoxy*-derivative, and conversion of the latter without difficulty into 9-*amino*-1 : 2-*dimethoxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene*. The constitution assigned to this compound was supported by the action of nitrous acid on it to give 9-*hydroxy*-1 : 2-*dimethoxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene* (XI; R = H) in nearly quantitative yield.

Reduction of (III; R = CO_2Et) with reduced iron in faintly acid alcoholic solution gave a *product*, $C_{17}H_{19}O_2N_3$, which failed to give a positive primary amine test on diazotisation followed by coupling with alkaline β-naphthol, and must therefore be assigned the constitution of *ethyl* 9-*amino*-6 : 8-*dimethyl*-7 : 13-*dihydro*-7 : 10-*diazaphenanthrene*-5-*carboxylate* (X). Reduction of the appropriate pyridinecarboxylic esters (*e.g.*, IV; R = CO_2Et) likewise gave *ethyl* 9-*amino*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene*-5-*carboxylate* (VIII; R = CO_2Et), and *ethyl* 9-*amino*-2 : 3-*methylenedioxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene*-5-*carboxylate*, cyclisation of the intermediate amino-nitriles occurring in preference to lactamisation between the amino- and available carbethoxy-groupings. Reduction of ethyl 3-cyano-4-(2′-nitro-3′ : 4′-dimethoxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate, on the other hand, led to the almost exclusive formation of the *lactam* (XI).

In Part V of this series (Petrow, *loc. cit.*) it was shown that the Schmidt rearrangement of 1 : 3-dimethyl-2-azafluorenone leads to a hydroxydimethyldiazaphenanthrene represented by either (V) or (VII). The constitution of 9-hydroxy-1 : 3-dimethyl-2 : 10-diazaphenanthrene (V) was assigned to this product, as oxidation of 1 : 3 : 9-trimethyl-2 : 10-diazaphenanthrene gave a hydroxydimethyl-2 : 10-diazaphenanthrene identical with it in melting point and mixed melting point. A direct comparison of the two sets of compounds derived from 2 : 10- and 7 : 10-diazaphenanthrene has now been made, and the results confirm the conclusions put forward in the earlier communication.

Experimental.

M. ps. are corrected. Microanalyses are by Drs. Weiler and Strauss, Oxford.

Ethyl 3-*Cyano*-4-*o*-*nitrophenyl*-2 : 6-*dimethyl*-1 : 4-*dihydropyridine*-5-*carboxylate* (III; R = CO_2Et).—*o*-Nitrobenzaldehyde (225 g.), β-aminocrotononitrile (125 g.), ethyl β-aminocrotonate (195 g.), and absolute alcohol (500 ml.) were heated under reflux for 70—80 hours; evolution of ammonia had then ceased. Light petroleum (300 ml., b. p. 40—60°) was added to the cooled mixture and, after several days at 0°, the crystalline product was collected and crystallised twice from aqueous methyl alcohol (charcoal). The *ester* formed lemon-yellow needles, m. p. 191·5—192·5° (Found: C, 62·5; H, 5·3; N, 12·7. $C_{17}H_{17}O_4N_3$ requires C, 62·4; H, 5·2; N, 12·8%). Yield, 107·5 g.

Ethyl 3-*Cyano*-4-*o*-*nitrophenyl*-2 : 6-*dimethylpyridine*-5-*carboxylate* (IV; R = CO_2Et).—The finely powdered dihydrobase (10 g.), suspended in absolute alcohol (40 ml.) was treated with dilute nitric acid (40 ml.; 1 part conc. acid : 7 parts water) on the water-bath. Vigorous reaction occurred and the material went into solution. The *product* was obtained crystalline by careful addition of dilute ammonium hydroxide in excess to the hot mixture. It formed glittering white needles from aqueous methyl alcohol, m. p. 115·5—116·5° (Found: C, 62·9; H, 4·6; N, 13·1. $C_{17}H_{15}O_4N_3$ requires C, 62·8; H, 4·6; N, 12·9%). Yield, 8·2 g. (85%).

3-*Cyano*-4-*o*-*nitrophenyl*-2 : 6-*dimethylpyridine*-5-*carboxylic Acid* (IV; R = CO_2H).—The corresponding ester (75 g.), potassium hydroxide (13·5 g.), absolute alcohol (150 ml.), and water (150 ml.) were heated under reflux for 80 hours. The alcohol was removed on the water-bath, the residue was diluted with water, and the filtered solution and washings were acidified by dropwise addition with stirring of dilute sulphuric acid (from 4·5 g. conc. acid). The precipitated acid formed a gelatinous mass which became crystalline on standing. It was collected, washed with water, and dried. Yield 20·3 g. (89%) of a *product*, m. p. 227—229°, which was pure enough for decarboxylation. It formed cubic crystals from aqueous alcohol, m. p. 232—233° (decomp.) (Found: C, 60·3; H, 3·8; N, 14·1. $C_{15}H_{11}O_4N_3$ requires C, 60·6; H, 3·7; N, 14·1%).

3-*Cyano*-4-*o*-*nitrophenyl*-2 : 6-*dimethylpyridine* (IV; R = H).—The corresponding acid (8·4 g.) was heated in a metal-bath at 250—270° for 4—5 minutes; evolution of carbon dioxide had then ceased. The *product* was isolated by distillation under reduced pressure or by conversion into the picrate. It formed squat yellow needles from aqueous alcohol, m. p. 160·5—161·5° (Found: C, 66·5; H, 4·3; N, 16·4. $C_{14}H_{11}O_2N_3$ requires C, 66·4; H, 4·3; N, 16·6%). Yield, 5·9 g. (80%). The *picrate* formed squat yellow needles from spirit, m. p. 216·5—217·5° (Found: N, 17·7. $C_{14}H_{11}O_2N_3,C_6H_3O_7N_3$ requires N, 17·4%).

9-*Amino*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene* (VIII; R = H).—Crude 3-cyano-4-*o*-nitrophenyl-2 : 6-dimethylpyridine (2·8 g.), reduced iron (5·0 g.), water 5 ml.), spirit (30 ml.), and three drops of concentrated hydrochloric acid were heated under reflux for 2 hours. The mixture turned dark crimson and became gelatinous, but cleared after *ca.* 1½ hours. The mixture was filtered and the iron residues were thoroughly extracted with boiling spirit. The filtrate and washing were taken to dryness (m. p. 180—184°), and, as the primary amine test by diazotisation was still faintly positive, the product was heated under reflux with sodium ethoxide (1·2 g. of sodium in 50 ml. of alcohol) for 45 minutes. Water was added, the alcohol removed on the water-bath, and the *product* (m. p. 193—195°) crystallised from alcohol–ligroin (charcoal). It formed faintly yellow needles, m. p. 197—198° (Found: C, 75·3; H, 5·9; N, 19·0. $C_{14}H_{13}N_3$ requires C, 75·3; H, 5·8; N, 18·8%). Yield, 35—45%. The *picrate* separated from alcohol in pale yellow needles, m. p. 254—255° (decomp.) (Found: N, 18·7. $C_{14}H_{13}N_3,C_6H_3O_7N_3$ requires N, 18·6%). The base and picrate gave depressions of m. p. in admixture with the corresponding derivatives from 2 : 10-diazaphenanthrene described in Part V

(*loc. cit.*). 9-*Benzamido*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene*, obtained in nearly quantitative yield by treating the amino-compound (500 mg.) in pyridine (2·5 ml.) with benzoyl chloride (300 mg.) under reflux for 30 minutes, formed a felted mass of sparingly soluble silky white needles from spirit, m. p. 230—230·5° (Found : C, 76·9; H, 5·3; N, 13·2. $C_{21}H_{17}ON_3$ requires C, 77·2; H, 5·2; N, 12·8%).

9-*Hydroxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene* (VII).—(*a*) A solution of 9-amino-6 : 8-dimethyl-7 : 10-diazaphenanthrene (1·3 g.) in concentrated hydrochloric acid (3 ml.) and water (7 ml.) was cooled to 0° and a solution of sodium nitrite (700 mg.) in a little water slowly added with stirring. Rapid evolution of gas occurred and separation of crystalline material began after 1 minute. After 1 hour at room temperature, the mixture was heated on the water-bath for 30 minutes, made alkaline with ammonia, and the precipitated *base* collected and crystallised from spirit (charcoal). It separated in silky needles, m. p. 310—311° (Found : C, 74·8; H, 5·3; N, 12·6. $C_{14}H_{12}ON_2$ requires C, 75·0; H, 5·4; N, 12·5%). Yield, >90%. The compound gave a depression of m. p. in admixture with the corresponding 2 : 10-diazaphenanthrene compound described in Part V (*loc. cit.*).

(*b*) Ethyl 4-*o*-nitrophenyl-2 : 6-dimethyl-1 : 4-dihydropyridine-3 : 5-dicarboxylate was prepared by the method of Hinkel, Ayling, and Morgan (*loc. cit.*). For oxidation, the finely powdered ester (22 g.) was added to chromic acid (4·1 g.) dissolved in a little water and glacial acetic acid (120 ml.), and the mixture heated on the water-bath for 10—15 minutes. The ester (VI; R = CO_2Et), precipitated in crystalline form by addition of dilute ammonia in slight excess, formed pale yellow needles from aqueous methyl alcohol, m. p. 92·5—93·5° (Found : C, 61·4; H, 5·4. Calc. for $C_{19}H_{20}O_6N_2$: C, 61·3; H, 5·4%) (Hinkel *et al.*, *ibid.*, p. 1839, give m. p. 75°). Yield, 19·7 g. 3-*Carbethoxy*-4-*o*-*nitrophenyl*-2 : 6-*dimethylpyridine*-5-*carboxylic acid* (VI; R = CO_2H), spear-head crystals from aqueous methyl alcohol, m. p. 216—217° (Found : C, 59·4; H, 4·7; N, 8·3. $C_{17}H_{16}O_6N_2$ requires C, 59·3; H, 4·7; N, 8·1%), was obtained by hydrolysis of the diethyl ester with 1 mol. of potassium hydroxide (10% solution in 50% alcohol) for 60 hours under reflux. Ethyl 4-*o*-nitrophenyl-2 : 6-dimethylpyridine-3-carboxylate (VI; R = H) was obtained in 70% yield as a pale yellow oil when the above acid-ester was heated for 5 minutes at 250—260°, and the product distilled under reduced pressure. The *picrate* separated from alcohol in fairly soluble bright yellow needles, m. p. 172—173° (Found : N, 13·5. $C_{16}H_{16}O_4N_2,C_6H_3O_7N_3$ requires N, 13·2%). The nitro-ester (3 g.) was reduced with reduced iron (6 g.), water (5 ml.), spirit (25 ml.), and 3 drops of concentrated hydrochloric acid for 50 minutes under reflux. The mixture was filtered and the iron residues were thoroughly extracted under reflux with successive large volumes of spirit. The filtrate and washings were taken to dryness and heated at 170° for 1 hour. This product, m. p. 310°, gave slightly low analyses for carbon (C, 74·5%). After sublimation at 270—280°/11 mm. and refluxing with acetic anhydride, 9-hydroxy-6 : 8-dimethyl-7 : 10-diazaphenanthrene (VII) formed silky white needles from spirit, m. p. 310—311° (Found : C, 74·7; H, 5·6; N, 12·4%), not depressed in admixture with the product obtained by method (*a*) above. Yield, 25%.

Ethyl 3-*Cyano*-4-(2′-*nitro*-4′ : 5′-*methylenedioxyphenyl*)-2 : 6-*dimethyl*-1 : 4-*dihydropyridine*-5-*carboxylate*.—6-Nitropiperonal (115 g.), β-aminocrotononitrile (50 g.), ethyl β-aminocrotonate (78 g.), and absolute alcohol (400 ml.) were heated under reflux for 50 hours. The alcohol was removed under reduced pressure, the residue heated under reflux with 3 vols. of acetic anhydride for 10 minutes, and the mixture decomposed with water. The sticky brown product was collected, dried, heated under reflux with 5 vols. of benzene, and left at 0° for several days. The *product* was collected and crystallised twice from benzene (charcoal) and finally from methyl alcohol. It formed lemon-yellow octahedra, m. p. 224·5—225·5° (Found : C, 58·2; H, 4·6; N, 11·3. $C_{18}H_{17}O_6N_3$ requires C, 58·2; H, 4·6; N, 11·3%). Yield, 35 g. (18%).

Ethyl 3-*cyano*-4-(2′-*nitro*-4′ : 5′-*methylenedioxyphenyl*)-2 : 6-*dimethylpyridine*-5-*carboxylate*, glittering needles from alcohol, m. p. 153—154° (Found : C, 58·7; H, 4·4; N, 11·3. $C_{18}H_{15}O_6N_3$ requires C, 58·5; H, 4·1; N, 11·4%), was prepared by suspending the finely powdered dihydro-ester (35 g.) in glacial acetic acid (90 ml.), adding a solution of chromic acid (7·5 g.) in a little water, and heating with shaking on a water-bath until a clear solution was obtained. Yield, 30 g. (85%).

3-*Cyano*-4-(2′-*nitro*-4′ : 5′-*methylenedioxyphenyl*)-2 : 6-*dimethylpyridine*.—The foregoing ester was hydrolysed and the crude acid (m. p. 145°) decarboxylated. The *product* formed faintly coloured plates from aqueous methyl alcohol, m. p. 173—174° (Found : C, 60·7; H, 3·8; N, 14·3. $C_{15}H_{11}O_4N_3$ requires C, 60·6; H, 3·7; N, 14·1%). By reduction it gave 9-*amino*-2 : 3-*methylenedioxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene*, glittering needles from aqueous alcohol, m. p. 228—228·5° (Found : C, 67·2; H, 4·9; N, 16·0. $C_{15}H_{13}O_2N_3$ requires C, 67·4; H, 4·9; N, 15·7%).

6-*Aminopiperonal Series*.—(*a*) 6-Aminopiperonal (10 g.), β-aminocrotononitrile (5 g.), ethyl β-aminocrotonate (8 g.), and absolute alcohol (25 ml.) were heated under reflux for 30 hours; evolution of ammonia had then ceased. After being allowed to cool, the product was collected (m. p. 150—170°, yield 12 g.) and crystallised from aqueous alcohol. The less soluble fraction (m. p. 185—195°) was heated under reflux with acetic anhydride for 15 minutes, the mixture decomposed with water, and the insoluble fraction crystallised from benzene–light petroleum. 3-*Cyano*-6 : 7-*methylenedioxy*-2-*methylquinoline* (IX; R = CN) formed small needles, m. p. 214—215° (Found : C, 68·2; H, 4·2; N, 13·1. $C_{12}H_8O_2N_2$ requires C, 67·9; H, 3·8; N, 13·2%). The more soluble fraction, m. p. 150—152°, after sublimation under reduced pressure and treatment with acetic anhydride, gave *ethyl* 6 : 7-*methylenedioxy*-2-*methylquinoline*-3-*carboxylate* (IX; R = CO_2Et), dazzling white plates from benzene–light petroleum, m. p. 159—160° (Found : C, 65·1; H, 5·1; N, 5·6. $C_{14}H_{13}O_4N$ requires C, 64·9; H, 5·0; N, 5·4%).

(*b*) 3-Cyano-6 : 7-methylenedioxy-2-methylquinoline, m. p. 214—215° (Found : N, 13·3%), not depressed in admixture with a sample prepared by method (*a*), was obtained in 60% yield by heating aminopiperonal (2·3 g.), β-aminocrotononitrile (2·3 g.), and absolute alcohol (10 ml.) for 40 hours under reflux.

(*c*) Ethyl 6 : 7-methylenedioxy-2-methylquinoline-3-carboxylate, m. p. 162—163° (Found : N, 5·6%), not depressed in admixture with a sample prepared by method (*a*), was obtained in 58% yield by heating aminopiperonal (1·65 g.), ethyl β-aminocrotonate (2·58 g.), and absolute alcohol (5 ml.) for 40 hours under reflux.

Ethyl 3-*Cyano*-4-(2′-*nitro*-4′-*acetoxy*-3′-*methoxyphenyl*)-2 : 6-*dimethyl*-1 : 4-*dihydropyridine*-5-*carboxylate*.—2-Nitrovanillin (400 g.) (Raiford and Sloesser, *J. Amer. Chem. Soc.*, 1928, **50**, 2559), β-aminocrotononitrile (167 g.), ethyl β-aminocrotonate (262 g.), and absolute alcohol (1000 ml.) were heated under reflux for 74 hours. The product, after removal of solvent, was heated under reflux with acetic anhydride (1200 ml.) for 45 minutes, and the cooled product poured into water (7000 ml.) and shaken until decomposition was complete. The granular precipitated material was collected and crystallised from dilute acetic acid. The *ester* formed golden-yellow leaflets, m. p. 175—177° (Found : C, 57·2; H, 4·8; N, 11·2. $C_{20}H_{21}O_7N_3$ requires C, 57·8; H, 5·1; N, 10·1%). Yield, 560 g. (68%).

Ethyl 3-*cyano*-4-(2′-*nitro*-4′-*acetoxy*-3′-*methoxyphenyl*)-2 : 6-*dimethylpyridine*-5-*carboxylate*, pearly needles, m. p. 112—113° (Found : C, 57·7; H, 4·5; N, 10·0. $C_{20}H_{19}O_7N_3$ requires C, 58·1; H, 4·6; N, 10·2%), was prepared by gradually treating a hot solution of the above dihydro-base (120 g.) in glacial acetic acid (300 ml.) with chromic acid (25 g.) in water (100 ml.), and when oxidation was complete adding water to the hot mixture until crystallisation commenced. Yield, 64%.

Ethyl 3-*Cyano*-4-(2′-*nitro*-4′-*hydroxy*-3′-*methoxyphenyl*)-2 : 6-*dimethylpyridine*-5-*carboxylate*.—The foregoing acetyl derivative (80 g.), potassium hydroxide (20 g.), water (100 ml.), and alcohol (100 ml.) were heated under reflux for 40 minutes. The alcohol was removed on the water-bath, the mixture diluted to 400—500 ml., and the *base* precipitated

with glacial acetic acid (20 ml.). It formed squat glittering needles from aqueous methyl alcohol, m. p. 187·5—188·5° (Found : C, 58·6; H, 4·8; N, 11·0. $C_{18}H_{17}O_6N_3$ requires C, 58·2; H, 4·6; N, 11·3%). Yield, nearly quantitative. A solution of the substance in dilute alcohol gave a purple coloration with ferric chloride solution.

Ethyl 3-Cyano-4-(2′-nitro-3′ : 4′-dimethoxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate.—A solution of the above hydroxy-compound (37 g.) in potassium hydroxide (6·5 g.) and water (300—400 ml.) was treated at room temperature with shaking with methyl sulphate (12·6 g.) added over 45 minutes. After 24 hours at room temperature the product was collected. Passage of carbon dioxide through the filtrate precipitated unchanged material (*ca.* 10%). The *dimethoxy*-compound formed octahedra from aqueous alcohol, m. p. 131·5—132·5° (Found : C, 59·2; H, 5·0; N, 10·8. $C_{19}H_{19}O_6N_3$ requires C, 59·2; H, 4·9; N, 10·9%). Yield, 80%.

3-Cyano-4-(2′-nitro-3′ : 4′-dimethoxyphenyl)-2 : 6-dimethylpyridine.—The foregoing ester was hydrolysed and the crude acid (m. p. 195—205°) decarboxylated. The *product* formed glittering needles from benzene–ligroin, m. p. 182—183° (Found : C, 61·5; H, 5·1; N, 13·7. $C_{16}H_{15}O_4N_3$ requires C, 61·3; H, 4·8; N, 13·4%). The *picrate* formed rather soluble bright yellow needles from absolute alcohol, m. p. 190·5—191·5° (Found : N, 15·1. $C_{16}H_{15}O_4N_3,C_6H_3O_7N_3$ requires N, 15·5%).

9-Amino-1 : 2-dimethoxy-6 : 8-dimethyl-7 : 10-diazaphenanthrene, glittering faintly yellow needles from benzene–ligroin, m. p. 183—184° (Found : C, 67·3; H, 6·0; N, 14·9. $C_{16}H_{17}O_2N_3$ requires C, 67·9; H, 6·0; N, 14·8%), was prepared by reduction of the foregoing nitro-compound. It was fairly soluble in water. On treatment with nitrous acid in hydrochloric acid solution it yielded *9-hydroxy-1 : 2-dimethoxy-6 : 8-dimethyl-7 : 10-diazaphenanthrene* (XI; R = H), glittering plates from spirit, m. p. 242·5—243·5° (Found : C, 67·5; H, 5·8; N, 9·6. $C_{16}H_{16}O_3N_2$ requires C, 67·6; H, 5·6; N, 9·9%).

Ethyl 3-cyano-4-(4′-hydroxy-3′-methoxyphenyl)-2 : 6-dimethyl-1 : 4-dihydropyridine-5-carboxylate, faintly yellow spear-shaped crystals from aqueous alcohol, m. p. 161—162° (Found : C, 65·5; H, 6·3; N, 8·7. $C_{18}H_{20}O_4N_2$ requires C, 65·9; H, 6·1; N, 8·5%), was prepared from vanillin. Yield, 62%.

Ethyl 3-cyano-4-(4′-acetoxy-3′-methoxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate, glistening plates from aqueous methyl alcohol, m. p. 165—166° (Found : C, 65·3; H, 5·6; N, 8·2. $C_{20}H_{20}O_5N_2$ requires C, 65·2; H, 5·4; N, 7·6%), was prepared by acetylation of the foregoing hydroxy-compound followed by oxidation with chromic acid. Yield, 80%.

Nitration of Ethyl 3-Cyano-4-(4′-acetoxy-3′-methoxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate.—The ester (10 g.) was added with mechanical stirring to fuming nitric acid (40 g.) cooled in ice-salt, over a period of 30 minutes. The product was poured on ice, made alkaline with ammonia, and the precipitated material collected and crystallised from aqueous methyl alcohol. The less soluble fraction gave *ethyl 3-cyano-4-(?′-nitro-4′-acetoxy-3′-methoxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate*, flat pearly plates, m. p. 177—178° (Found : C, 57·8; H, 4·8; N, 10·2. $C_{20}H_{19}O_7N_3$ requires C, 58·1; H, 4·6; N, 10·2%). Yield, 10%. The more soluble fraction gave ethyl 3-cyano-4-(2′-nitro-4′-acetoxy-3′-methoxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate, pearly needles, m. p. 112—113° (Found : C, 57·8; H, 4·8; N, 10·1%), not depressed in admixture with the compound prepared from 2-nitrovanillin (above). Yield, 10%.

Ethyl 3-cyano-4-(4′-hydroxy-3′-methoxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate, prismatic needles from alcohol–ligroin, m. p. 132·5—133·5° (Found : C, 66·4; H, 5·5; N, 8·7. $C_{18}H_{18}O_4N_2$ requires C, 66·3; H, 5·5; N, 8·6%), was prepared by hydrolysis of the corresponding acetyl derivative (20 g.), with potassium hydroxide (7 g.) and water (60 ml.) under reflux for 1 hour, followed by precipitation of the base with acetic acid (7 ml.).

Ethyl 3-cyano-4-(3′ : 4′-dimethoxyphenyl)-2 : 6-dimethyl-1 : 4-dihydropyridine-5-carboxylate, faintly yellow rhombic crystals from aqueous alcohol or ligroin, m. p. 166—167·5° (Found : C, 66·4; H, 6·5; N, 8·0. $C_{19}H_{22}O_4N_2$ requires C, 66·7; H, 6·4; N, 8·2%), was prepared from veratraldehyde followed by heating with acetic anhydride. Yield, 36%. Oxidation with chromic acid gave *ethyl 3-cyano-4-(3′ : 4′-dimethoxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate*, flat glittering needles from aqueous alcohol, m. p. 148—149° (Found : N, 8·3. $C_{19}H_{20}O_4N_2$ requires N, 8·2%).

Ethyl 3-Cyano-4-(3′ : 4′-methylenedioxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate.—As the product obtained from piperonal failed to crystallise, even after heating with acetic anhydride, it was oxidised with chromic acid without further treatment. Tedious fractionation from aqueous methyl alcohol and finally from benzene–ligroin, gave *ethyl 3-cyano-4-(3′ : 4′-methylenedioxyphenyl)-2 : 6-dimethylpyridine-5-carboxylate*, glistening needles, m. p. 132·5—133·5° (Found : C, 66·5; H, 5·1; N, 8·9. $C_{18}H_{16}O_4N_2$ requires C, 66·7; H, 4·9; N, 8·6%). Yield, 10%. 2 : 4-Dinitrobenzaldehyde failed to react with β-aminocrotononitrile and ethyl β-aminocrotonate, and was recovered unchanged.

Ethyl 9-amino-6 : 8-dimethyl-7 : 13-dihydro-7 : 10-diazaphenanthrene-5-carboxylate (X), faintly yellow needles from alcohol–light petroleum, m. p. 164—165·5° (Found : C, 68·3; H, 6·3; N, 14·0. $C_{17}H_{19}O_2N_3$ requires C, 68·7; H, 6·4; N, 14·1%), was prepared by reduction of (III; R = CO_2Et) (1·4 g.) with reduced iron (2·5 g.), water (2·5 ml.), alcohol (6 ml.), and one drop of concentrated hydrochloric acid for 1 hour under reflux. Yield, 25%.

Ethyl 9-amino-6 : 8-dimethyl-7 : 10-diazaphenanthrene-5-carboxylate (VIII; R = CO_2Et), prepared by reduction of (IV; R = CO_2Et), formed faintly yellow needles from benzene–ligroin, m. p. 191·5—192·5° (Found : C, 68·6; H, 5·6; N, 14·3. $C_{17}H_{17}O_2N_3$ requires C, 69·2; H, 5·8; N, 14·2%). Yield, 25%.

Ethyl 9-amino-2 : 3-methylenedioxy-6 : 8-dimethyl-7 : 10-diazaphenanthrene-5-carboxylate formed pale yellow platelets, m. p. 239—240° (Found : C, 63·7; H, 5·1; N, 12·9. $C_{18}H_{17}O_4N_3$ requires C, 63·7; H, 5·0; N, 12·4%).

9-Hydroxy-5-cyano-1 : 2-dimethoxy-6 : 8-dimethyl-7 : 10-diazaphenanthrene (XI; R = CN), formed faintly straw-coloured silky needles, m. p. 301—302° (Found : C, 66·0; H, 4·8; N, 13·9. $C_{17}H_{15}O_3N_3$ requires C, 66·0; H, 4·9; N, 13·6%), very sparingly soluble in the usual solvents, more soluble in boiling glacial acetic acid, and readily soluble in hot nitrobenzene.

The author thanks the Therapeutic Research Corporation of Great Britain Limited for a grant and for certain facilities. The work was carried out during the period July, 1944—July, 1945, when Queen Mary College was at Cambridge, and the author acknowledges with gratitude the facilities placed at his disposal at the University Chemical Laboratory, Cambridge.

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