267. *Contributions to the Chemistry of Phenanthridine. Part I. The Conversion of 9-(3′-Pyridyl)phenanthridines into their Quaternary Salts and the Preparation of Some Derivatives of Potential Biological Interest.*

By V. Petrow and W. R. Wragg.

9-(3′-*Pyridyl*)- (II; R = R′ = H), 3-*nitro*-9-(3′-*pyridyl*)- (II; R = NO_2, R′ = H), and 7-*nitro*-9-(3′-*pyridyl*)-*phenanthridine* (II; R = H, R′ = NO_2) have been obtained from the appropriate 2-*nicotinamidodiphenyls*. Conversion of the first two compounds into their mono-quaternary *salts* led to the formation of the py-N-*methylmethosulphates*, the constitution of which followed from their oxidation to the corresponding N-*methylpyridones*.* As expected, the *monomethiodide* derived from 9-(6′-*keto*-1′-*methyl*-1′ : 6′-*dihydro*-3′-*pyridyl*)*phenanthridine* (IV; R = H) possessed the anticipated properties of a phenanthridyl-*N*-methiodide.

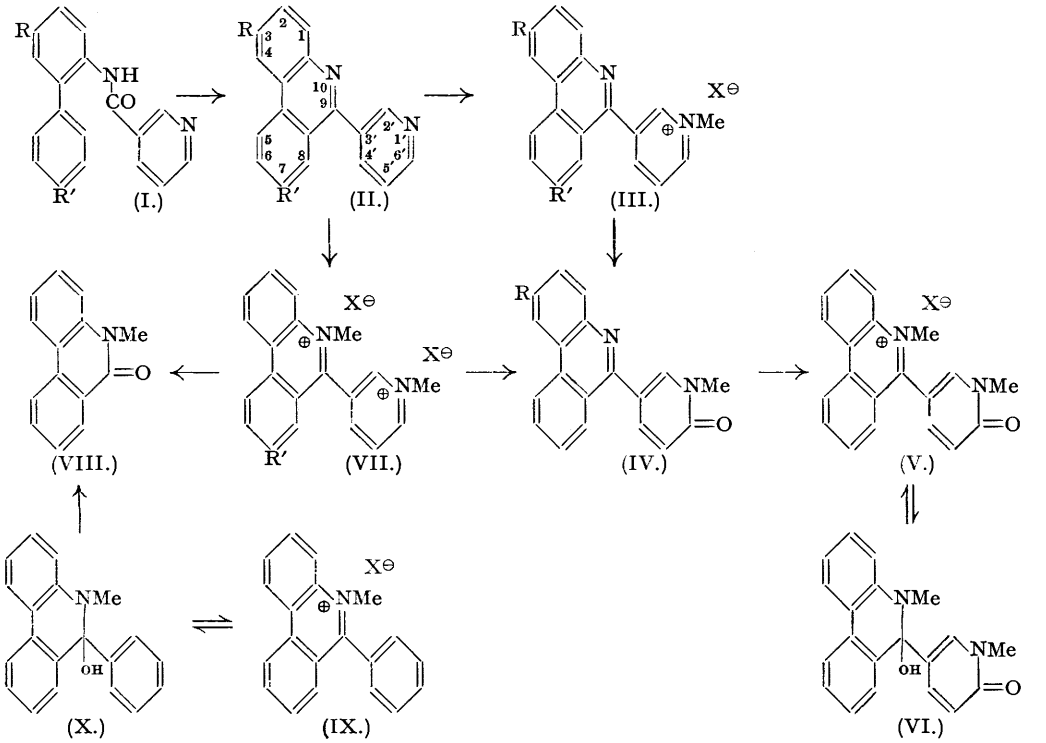
Treatment of 9-(3′-*pyridyl*)*phenanthridine* 1′ : 10-*dimethiodide* (VII; R′ = H, X = I) with excess of aqueous sodium hydroxide followed by potassium ferricyanide at room temperature gave (IV; R = H). Reaction with boiling alcoholic sodium hydroxide, however, resulted in

* These *N*-methylpyridones may clearly be either 2′- or 6′-pyridones. The question is irrelevant to the present investigation and the orientation of a 6′-pyridone has been *assumed* throughout.

loss of the pyridyl-1′-methiodide grouping and the production of 10-methyl-9-phenanthridone (VIII), also obtained by the action of alcoholic alkaline ferricyanide on 9-*phenylphenanthridine* 10-*methylmethosulphate* (IX; X = $MeSO_4$).

Reduction of the two nitro-9-(3′-pyridyl)phenanthridines (II; R = NO_2, R′ = H, and R = H, R′ = NO_2) and their py-N-*methylmethosulphates* gave the corresponding *amino*-compounds.

FOLLOWING recent work on the relationship between structure and biological activity in the phenanthridine series (Petrow, *J.*, 1945, 18; Walls, *ibid.*, p. 294), we have now synthesised some 9-(3′-pyridyl)phenanthridines. We required these for examination as trypanocides, and also, from their formal analogy to the pyridyl quinolines of Coates, Cook, Heilbron, Hey, Lambert, and Lewis (*J.*, 1943, 401), for study as spasmolytics.



Condensation of nicotinyl chloride hydrochloride with 2-aminodiphenyl in boiling chlorobenzene solution led to the formation of 2-*nicotinamidodiphenyl* (I; R = R′ = H) in 78% yield. 5-*Nitro*- (I; R = NO_2, R′ = H), and 4′-*nitro*-2-*nicotinamidodiphenyl* (I; R = H, R′ = NO_2) were similarly prepared from the appropriate diphenyls. Ring closure of these compounds failed to take place on heating them with phosphorus oxychloride alone, but was readily accomplished by using phosphorus oxychloride in nitrobenzene solution (B.P. 520, 273; cf. Walls, *loc. cit.*) giving 9-(3′-*pyridyl*)- (II; R = R′ = H) and 3-*nitro*-9-(3′-*pyridyl*)-*phenanthridine* (II; R = NO_2, R′ = H) in excellent yields. When 4′-nitro-2-nicotinamidodiphenyl (I; R = H, R′ = NO_2) was employed, however, ring closure appeared incomplete after 24 hours' heating, and the yield of 7-*nitro*-9-(3′-*pyridyl*)*phenanthridine* (II; R = H, R′ = NO_2) was only 37%. This result is a further illustration of the polar influence of the 4′-nitro-grouping in depressing the mobility of the 2′-hydrogen atom involved in ring closure (cf. Morgan and Walls, *J.*, 1938, 390; Petrow, *loc. cit.*).

Conversion of (II; R = R′ = H) into the mono-quaternary salt may clearly involve either the pyridyl or phenanthridyl basic centres. We have decided in favour of the former alternative on the following evidence. Reaction of 9-phenylphenanthridine, a compound structurally related to (II; R = R′ = H) but possessing only the phenanthridyl basic centre, with methyl sulphate, led to the formation of 9-*phenylphenanthridine* 10-*methylmethosulphate* (IX; X = $MeSO_4$), converted by one molar equivalent of sodium hydroxide into the *pseudo-base* (X). Although this reaction may also yield the methohydroxide, it has been assumed by earlier

workers that the product obtained is actually the pseudo-base where experimental evidence favours such a conclusion; pseudo-bases differ from the corresponding quaternary hydroxides in that they are relatively insoluble in water and soluble in non-hydroxylic solvents (*e.g.*, light petroleum). The pseudo-base reverted on treatment with 1·15 molar equivalents of hydrochloric acid to the quaternary salt, converted by potassium iodide into the normal *methiodide*. These model transformations serve to characterise systems such as (IX). The reactions of the monoquaternary salts obtained from (II) with, in the first place, alkali, and secondly potassium ferricyanide–sodium hydroxide, however, followed a different pattern which could be interpreted only by assuming that it was the pyridyl nitrogen which was involved in salt formation. Thus both 9-(3′-*pyridyl*)*phenanthridine* 1′-*methiodide* (III; R = R′ = H, X = I) and 3-*nitro*-9-(3′-*pyridyl*)*phenanthridine* 1′-*methylmethosulphate* (III; R = NO_2, R′ = H, X = $MeSO_4$) failed to give sparingly soluble pseudo-bases when treated with one molar proportion of aqueous sodium hydroxide. (III; R = R′ = H; X = I) was unchanged by heating with excess dilute sodium hydroxide for one minute. Treatment of a warm aqueous solution of (III; R = NO_2, R′ = H, X = $MeSO_4$) with a large excess of sodium hydroxide precipitated a red amorphous material, probably the pseudo-base, which on vacuum sublimation gave a very small yield of 3-*nitro*-9-(6′-*keto*-1′-*methyl*-1′ : 6′-*dihydro*-3′-*pyridyl*)*phenanthridine* (IV; R = NO_2), also obtained in good yield from (III; R = NO_2, R′ = H, X = $MeSO_4$) by hot alkaline ferricyanide oxidation, and characterised as its *hydrochloride*. Attempts to oxidise 9-(3′-pyridyl)phenanthridine 1′-methiodide (III; R = R′ = H, X = I) with potassium ferricyanide–sodium hydroxide at room temperature led to the separation of the very sparingly soluble *ferricyanide*. When the reaction was carried out at 80° (cf. Diesbach and Aeschbach, *Helv. Chim. Acta*, 1945, **28**, 1392) in the presence of benzene, oxidation occurred to give 9-(6′-*keto*-1′-*methyl*-1′ : 6′-*dihydro*-3′-*pyridyl*)*phenanthridine* (IV; R = H), characterised by conversion into the *hydrochloride* and the *thiopyridone* derivative.

Conversion of (IV; R = H) into the quaternary salt led to the formation of 9-(6′-*keto*-1′-*methyl*-1′ : 6′-*dihydro*-3′-*pyridyl*)*phenanthridine* 10-*methiodide* (V; X = I), a compound which now exhibited the typical reactions of the 9-phenyl-10-methylphenanthridinium system (IX). Thus with 1·05 molar equivalent of sodium hydroxide it passed into the *pseudo-base* (VI), converted by 1·1 molar equivalent of hydrochloric acid into the methochloride, which was transformed into the methiodide (V; X = I) with potassium iodide. Attempts to oxidise (V; X = I) with aqueous alkaline ferricyanide at 80° in the presence of benzene were unsuccessful, only the pseudo-base (VI) being isolated.

The conversion of 9-(3′-*pyridyl*)*phenanthridine* 1′ : 10-*dimethiodide* (VII; R′ = H, X = I) into (VI) would complete the series of reactions (II) to (VI) by two separate routes and supply further experimental evidence confirming these formulations. On treatment of (VII; R′ = H, X = I) with 50% alcoholic alkaline ferricyanide, however, 10-methyl-9-phenanthridone (VIII) was obtained in place of the expected (VI), the quaternary pyridyl group having been removed. The same product was also formed by employing 9-phenylphenanthridine-10-methylmethosulphate (IX; X = $MeSO_4$) in place of (VII; R′ = H, X = I). Attempts to oxidise (V; X = I) with 50% alcoholic alkaline ferricyanide, however, gave (VI) and not the phenanthridone (VIII). Further work showed that (VII; R′ = H, X = I) could be converted into (VIII) by simply refluxing it with 50% alcoholic dilute sodium hydroxide. Treatment of (VII; R′ = H, X = I) dissolved in a large excess of cold 2N-sodium hydroxide with potassium ferricyanide in very dilute solution, resulted in the loss of the quaternary group attached to the phenanthridyl nitrogen, the product isolated being (IV; R = H). Pictet and Patry (*Ber.*, 1893, **26**, 1966) have described the alkaline ferricyanide oxidation of phenanthridine 10-methiodide to 10-methyl-9-phenanthridone (VIII), and have also shown (*Ber.*, 1902, **35**, 2534) that steam distillation of phenanthridine 10-methohydroxide yields 10-methyl-9 : 10-dihydrophenanthridine and (VIII). Morgan and Walls (*J.*, 1938, 391) have obtained (VIII) by heating 9-dimethylaminophenanthridine 10-methiodide with water. The formation of (VIII) from (VII; R′ = H; X = I) and (IX; X = I) represents an extension of these observations, in that the elimination of a 9-aryl substituent is involved. This may take place by an oxidation of the tertiary C_9 alcohol (*e.g.*, X), or in the case of (VII; R′ = H; X = I) which yields (VIII) by simple treatment with alkali, by direct transference of hydrogen from the C_9 hydroxyl group to the quaternary pyridyl group.

3- (III; R = NH_2, R′ = H, X = Cl) and 7-*Amino*-9-(3′-*pyridyl*)*phenanthridine* 1′-*methochloride* (III; R = H, R′ = NH_2, X = Cl) were best prepared from the corresponding *methiodides*. These were obtained by reducing the appropriate nitro-9-(3′-pyridyl)phenanthridine 1′-monomethylmethosulphate with reduced iron in acidified aqueous solution followed

by treatment of the reduction liquor with potassium iodide. Catalytic methods led to nuclear reduction.

3- (II; R = NH_2, R′ = H) and 7-*Amino*-9-(3′-*pyridyl*)*phenanthridine* (II; R = H, R′ = NH_2), obtained from the corresponding nitro-compounds by reduction with stannous chloride, were characterised by preparation of the *acetyl* derivatives. These gelatinous compounds were obtained crystalline only after sublimation in a high vacuum. 7-Amino-9-(3′-pyridyl)phenanthridine (II; R = H, R′ = NH_2) was also obtained in 31% yield by catalytic reduction of the corresponding nitro-compound in glacial acetic acid with Adams's platinum oxide catalyst. When 2N-hydrochloric acid was substituted as solvent, however, simultaneous nuclear reduction invariably took place. As expected, attempts at the further reduction of the 7-amino-compound (II; R = H, R′ = NH_2) in methanol or glacial acetic acid were unsuccessful, whereas nuclear reduction again occurred in 2N-hydrochloric acid.

The spasmolytic activities of (II; R = R′ = H), (II; R = NH_2, R′ = H), and (II; R = H, R′ = NH_2) have been very kindly determined for us by Mr. R. Thorp (Wellcome Physiological Research Laboratories, Beckenham, Kent). The L.D.$_{50}$ of all three compounds, determined by intravenous injection in mice, was approximately 0·06 mg./g. Upon the isolated rabbit intestinal segment, a dilution of 1 : 100,000 of all three substances was about as effective as 1 : 50,000,000 of " trasentin " in relaxing the spasm caused by a 1 : 3,000,000 dilution of carbinoyl choline. Their spasmolytic activity was thus not of a high order.

The results of trypanocidal tests on (III; R = NH_2, R′ = H, X = Cl) and (III; R = H, R′ = NH_2, X = Cl) have already been reported (Wien, *Brit. J. Pharmacol.*, 1946, **1**, 65). At the time these were carried out we had not reached a decision as to the structure of the mono-quaternary salts, to which Dr. Wien provisionally ascribed the phenanthridyl *N*-methochloride formulation.

Experimental.

Semimicro-analyses are by Mr. S. Bance, B.Sc., A.R.I.C., Research Laboratories, May and Baker, Ltd. Melting points are corrected.

2-*Nicotinamidodiphenyl* (I; R = R′ = H).—Nicotinic acid (90 g.) was heated under reflux for 1 hour with thionyl chloride (250 c.c.), the mixture taken to dryness under reduced pressure on the water-bath, and the residue dissolved during 20 minutes in boiling chlorobenzene (1 l.). On addition of 2-aminodiphenyl (120 g.) in warm chlorobenzene (200 c.c.) a vigorous reaction occurred with evolution of hydrogen chloride and separation of a red oil which solidified. The solid product was collected, washed with ether, and crystallised from solution in methanol (1 l.) by addition of excess of aqueous ammonia. 2-*Nicotinamidodiphenyl* formed colourless octahedra from aqueous methanol (157 g.; 78%); m. p. 173—174° (Found: C, 78·8; H, 5·1; N, 10·4. $C_{18}H_{14}ON_2$ requires C, 78·8; H, 5·1; N, 10·2%).

5-*Nitro*-2-*nicotinamidodiphenyl* (I; R = NO_2, R′ = H).—Nicotinyl chloride hydrochloride (from 5 g. acid) dissolved in boiling chlorobenzene (35 c.c.), was treated with 5-nitro-2-aminodiphenyl (7 g.) for 5 minutes under reflux. After addition of pyridine (10 c.c.) and heating for 5 minutes, the mixture was cooled and the product precipitated with light petroleum (50 c.c.). The free base was obtained by crystallisation from alcohol (150 c.c.)–2N-ammonia (excess). 5-*Nitro*-2-*nicotinamidodiphenyl* formed long cream prisms from aqueous alcohol (8·6 g.; 83%); m. p. 160—161° (Found: C, 67·9; H, 4·2; N, 13·3. $C_{18}H_{13}O_3N_3$ requires C, 67·7; H, 4·0; N, 13·2%).

4′-*Nitro*-2-*nicotinamidodiphenyl* (I; R = H, R′ = NO_2).—Nicotinyl chloride hydrochloride (from 25 g. acid) in boiling chlorobenzene (200 c.c.) was treated with 4′-nitro-2-aminodiphenyl (35 g.) for 30 minutes under reflux. After addition of pyridine (30 c.c.) and a further 15 minutes heating, the product was precipitated with an equal volume of light petroleum (b. p. 100—120°). By solution in pyridine (400 c.c.; charcoal) and precipitation with excess of 2N-ammonia, 4′-*nitro*-2-*nicotinamidodiphenyl* was obtained, separating from pyridine–light petroleum (1 : 1) in small cream irregular prisms (40 g.; 77%); m. p. 226—227° (Found: C, 67·7; H, 4·0; N, 13·4. $C_{18}H_{13}O_3N_3$ requires C, 67·7; H, 4·0; N, 13·2%). Attempted preparations of this compound in pyridine at 100° instead of in boiling chlorobenzene yielded a product which could not readily be purified.

9-(3′-*Pyridyl*)*phenanthridine* (II; R = R′ = H).—Phosphorus oxychloride (30 c.c.), 2-nicotinamidodiphenyl (20 g.), and nitrobenzene (200 c.c.) were heated under reflux for 20 hours. The mixture was basified with concentrated ammonia at 0° and the nitrobenzene removed in steam. The solids were collected and dissolved in concentrated hydrochloric acid (200 c.c.; charcoal), and the base was precipitated with ammonia at 0°. 9-(3′-*Pyridyl*)*phenanthridine* formed colourless needles from light petroleum (b. p. 80—100°) (13·5 g.; 72%); m. p. 125—127° (Found: C, 84·0; H, 4·7; N, 11·2. $C_{18}H_{12}N_2$ requires C, 84·4; H, 4·7; N, 10·9%). With methyl sulphate (0·95 mol.) in boiling benzene for ½ hour it gave the 1′-methylmethosulphate, converted in aqueous solution into the 1′-*methiodide* (III; R = R′ = H, X = I), yellow elongated plates from methanol of indefinite m. p. 259—269° (Found: N, 7·2; I, 32·0. $C_{18}H_{12}N_2,CH_3I$ requires N, 7·0; I, 32·0%). The 1′-*methoferricyanide*, obtained by treating a warm aqueous solution of the 1′-methylmethosulphate with potassium ferricyanide, crystallised from aqueous methanol in irregular yellow plates, decomposing above 180° [Found: N, 16·2; Fe, 5·4. $(C_{19}H_{15}N_2)_3,Fe(CN)_6$ requires N, 16·4; Fe, 5·4%]. Reaction of (II; R = R = H; 5·1 g.) with methyl sulphate (7·6 c.c.; 4 mols.) in dry nitrobenzene (400 c.c.) at 170—180° for 30 minutes gave the 1′: 10-dimethyldimethosulphate. Removal of nitrobenzene in steam, followed by addition of potassium iodide (20 g.) to the residual aqueous liquor (250 c.c.), gave the corresponding 1′: 10-*dimethiodide* (VII; R′ = H, X = I). This salt formed golden irregular plates (8·8 g.; 82%)

from water; m. p. 237—242° with effervescence (preheated bath at 200°), resolidifying and melting again at 270—275° (Found: N, 5·2; I, 46·8. $C_{18}H_{12}N_2,2CH_3I$ requires N, 5·2; I, 47·0%).

3-Nitro-9-(3′-pyridyl)phenanthridine (II; R = NO_2, R′ = H).—Phosphorus oxychloride (200 c.c.), 5-nitro-2-nicotinamidodiphenyl (90 g.), and nitrobenzene (1·6 l.) were refluxed for 20 hours. The brown product which separated on cooling was boiled with pyridine (1 l.)–2N-ammonia (600 c.c.). *3-Nitro-9-(3′-pyridyl)phenanthridine* separated from pyridine in faintly yellow felted needles (80 g.; 94%); m. p. 250—252° (Found: C, 71·9; H, 3·8; N, 14·0. $C_{18}H_{11}O_2N_3$ requires C, 71·7; H, 3·7; N, 13·9%). The base (15 g.) was treated in nitrobenzene (400 c.c.) with methyl sulphate (4·5 c.c.; 0·95 mol.) at 170°, followed by precipitation with ether (300 c.c.). The *1′-methylmethosulphate* (86% yield) formed bulky colourless needles from methanol–ether; m. p. 210—212° (preheated bath) [Found N, 9·7; S, 7·5. $C_{18}H_{11}O_2N_3,(CH_3)_2SO_4$ requires N, 9·9; S, 7·5%].

7-Nitro-9-(3′-pyridyl)phenanthridine (II; R = H, R′ = NO_2), prepared (37% yield) in a similar manner to (II; R = NO_2; R′ = H) separated in felted buff needles from pyridine; m. p. 292—293° (Found: C, 71·8; H, 3·7; N, 14·0. $C_{18}H_{11}O_2N_3$ requires C, 71·7; H, 3·7; N, 13·9%). Reaction of (II; R = H, R′ = NO_2) in nitrobenzene at 170° with methyl sulphate (0·9 mol.) gave the *1′-methylmethosulphate* (III; R = H, R′ = NO_2, X = $MeSO_4$), small irregular plates from methanol–ether (78% yield); m. p. 251—253° (with previous softening) [Found: N, 9·8; S, 7·6. $C_{18}H_{11}O_2N_3,(CH_3)_2SO_4$ requires N, 9·9; S, 7·5%]. When the methyl sulphate was increased to 3 mols. the 1′: 10-*dimethyldimethosulphate* (VII; R′ = NO_2, X = $MeSO_4$) was obtained, small cream plates from methanol–ether; m. p. 256—258° (with previous softening) [Found: N, 7·5; S, 11·7. $C_{18}H_{11}O_2N_3,2(CH_3)_2SO_4$ requires N, 7·6; S, 11·6%]. The *1′-methopicrate* formed bright yellow irregular needles from acetone; m. p. 300—302° (Found: N, 15·4. $C_{18}H_{11}O_2N_3,C_7H_5O_7N_3$ requires N, 15·5%).

Model Experiments with Quaternary Salts of 9-Phenylphenanthridine.—Reaction of 9-phenylphenanthridine (Morgan and Walls, *J.*, 1931, 2451) in benzene with methyl sulphate (2 mols.) gave the *10-methylmethosulphate* (IX; X = $MeSO_4$) which separated from alcohol–ether in colourless prisms, m. p. 222—224° [Found: N, 4·0; S, 8·4. $C_{19}H_{13}N,(CH_3)_2SO_4$ requires N, 3·7; S, 8·4%]. The *10-methiodide* (IX; X = I) crystallised from water as well-defined bright yellow prisms which decomposed sharply at temperatures between 235 and 260°, depending on the rate of heating (Found: N, 3·7; I, 32·1. $C_{19}H_{13}N,CH_3I$ requires N, 3·6; I, 32·0%). The *pseudo-base* (X), precipitated from an aqueous solution of the 10-methylmethosulphate (IX; X = $MeSO_4$) by 1 mol. of N-sodium hydroxide, was extracted with ethyl acetate. It crystallised from light petroleum (b. p. 80—100°) in colourless prisms, m. p. 132—136° (Found: C, 83·8; H, 6·0; N, 5·0. $C_{20}H_{17}ON$ requires C, 83·6; H, 5·9; N, 4·9%). The pseudo-base (0·025 g.) dissolved in water (2 c.c.) containing N/10-hydrochloric acid (1 c.c.; 1·15 mol.), was treated with potassium iodide (0·3 g.), giving 9-phenylphenanthridine 10-methiodide (IX; X = I) identical with an authentic specimen.

9-(6′-Keto-1′-methyl-1′: 6′-dihydro-3′-pyridyl)phenanthridine (IV; R = H).—The yellow suspension obtained by treating a warm solution of 9-(3′-pyridyl)phenanthridine 1′-methiodide (8 g.) in water (400 c.c.) with potassium ferricyanide (20 g. in 50 c.c. water) was made alkaline by addition of 2N-sodium hydroxide (50 c.c.) and then vigorously stirred on the steam-bath for 40 minutes. Benzene (1 l.) was added to take up the product as it was formed. The red benzene layer was separated, washed with water (50 c.c.), and concentrated to 100 c.c. under reduced pressure. Addition of light petroleum precipitated *9-(6′-keto-1′-methyl-1′: 6′-dihydro-3′-pyridyl)phenanthridine* (4·1 g.; 70%), small buff prisms from chloroform–acetone; m. p. 211—212° (Found: C, 79·7; H, 5·0; N, 9·8. $C_{19}H_{14}ON_2$ requires C, 79·7; H, 4·9; N, 9·8%). A 57% yield of (IV; R = H) was also obtained by adding 2N-sodium hydroxide (2 c.c.) in one portion to a solution of 9-(3′-pyridyl)phenanthridine 1′-methiodide (0·4 g.) and potassium ferricyanide (1·6 g.) in 50% ethanol (40 c.c.), and refluxing the mixture for 30 minutes. The product was isolated by removing the ethanol under reduced pressure and extracting the residual suspension with benzene. Although (IV; R = H) was largely insoluble in boiling 2N-hydrochloric acid (0·13 g. in 4 c.c.), the *hydrochloride* was obtained by diluting a solution in warm concentrated hydrochloric acid (0·3 g. in 3 c.c.) with water (25 c.c.). Fawn hydrated needles separated which decomposed evolving hydrochloric acid gas above 205° (Found: C, 66·6; H, 5·3; N, 8·3; Cl, 10·3. $C_{19}H_{14}ON_2,HCl,H_2O$ requires C, 66·9; H, 5·0; N, 8·2; Cl, 10·4%). The *thiopyridone* derivative was obtained by refluxing the pyridone (IV; R = H; 0·57 g.) in chlorobenzene (20 c.c.) with finely powdered phosphorus pentasulphide (1·4 g.) for 1 hour. The hot reaction mixture was filtered and the insoluble material triturated with 2N-sodium hydroxide (40 c.c.). The brown insoluble residue (0·3 g.) was collected. It crystallised from alcohol (15 c.c.) in fawn prisms (0·1 g.), m. p. 182—197° (Found: N, 9·4; S, 10·8. $C_{19}H_{14}N_2S$ requires N, 9·3; S, 10·6%).

3-Nitro-9-(6′-keto-1′-methyl-1′: 6′-dihydro-3′-pyridyl)phenanthridine (IV; R = NO_2).—2N-Sodium hydroxide (20 c.c.) was added to the yellow suspension obtained when 3-nitro-9-(3′-pyridyl)phenanthridine 1′-methylmethosulphate (1 g.) in water (250 c.c.) at 60° was treated with potassium ferricyanide (3 g.). The mixture was then rapidly heated to boiling. After 15 minutes the suspension was cooled. The solid *product*, washed free from alkali, crystallised from pyridine (25 c.c.)–methanol (50 c.c.) as well-defined light brown needles (0·5 g.; 65%); m. p. 304—305° (Found: C, 68·8; H, 4·2; N, 12·8. $C_{19}H_{13}O_3N_3$ requires C, 68·9; H, 4·0; N, 12·7%). Sublimation of the red amorphous precipitate (2·2 g.) obtained by precipitating a warm aqueous solution (40 c.c.) of 3-nitro-9-(3′-pyridyl)phenanthridine 1′-methylmethosulphate (3·2 g.) with sodium hydroxide (15 c.c. of 50% w/v. solution), at 280°/0·02 mm. yielded a yellow crystalline sublimate (0·1 g.). After crystallisation from pyridine–light petroleum, (IV; R = NO_2) was obtained, m. p. 304—305°, not depressed in admixture with an authentic sample (Found: C, 68·9; H, 4·3; N, 12·6%). Although (IV; R = NO_2) was insoluble in boiling N-hydrochloric acid (0·1 g. in 4 c.c.), the *hydrochloride* was prepared by diluting a solution in hot concentrated hydrochloric acid. The salt separated in well-defined brown prisms which evolved hydrogen chloride above 140° and melted at 303—305° (Found: N, 11·2; Cl, 9·8. $C_{19}H_{13}O_3N_3,HCl$ requires N, 11·4; Cl, 9·7%). A mixed melting point of this hydrochloride and the corresponding base showed no depression.

9-(6′-Keto-1′-methyl-1′: 6′-dihydro-3′-pyridyl)phenanthridine 10-Methiodide (V; X = I).—9-(6′-Keto-1′-methyl-1′: 6′-dihydro-3′-pyridyl)phenanthridine (4·2 g.) was treated in xylene (150 c.c.) with

methyl sulphate (6 c.c.; 4 mols.) for 30 minutes. The gum which separated on cooling was dissolved in hot water (100 c.c.). Addition of potassium iodide (9 g.) gave the *methiodide*, golden prisms from water (2·9 g.); m. p. 240—243° (decomp.) (Found: N, 6·6; I, 29·7. $C_{19}H_{14}ON_2,CH_3I$ requires N, 6·5; I, 29·7%). The methiodide (0·4 g.) in ethanol (5 c.c.) was treated with N-sodium hydroxide (1 c.c.; 1·05 mol.). On dilution with water the *pseudo-base* (VI) was precipitated, forming irregular colourless prisms from aqueous alcohol (0·24 g.; 80%); m. p. 194—196° (Found: C, 75·3; H, 5·96; N, 8·9. $C_{20}H_{18}O_2N_2$ requires C, 75·5; H, 5·7; N, 8·8%). The pseudo-base (0·029 g.) dissolved in water (6 c.c.) containing N/10-hydrochloric acid (1 c.c.; 1·1 mol.) was treated with potassium iodide (0·3 g.), giving 9-(6′-keto-1′-methyl-1′ : 6′-dihydro-3′-pyridyl)phenanthridine 10-methiodide (V; X = I) identical with an authentic specimen.

Attempted Oxidations of 9-(3′-*Pyridyl*)*phenanthridine* 1′ : 10-*Dimethiodide* (VII; R′ = H, X = I).—(*a*) 2N-Sodium hydroxide (2 c.c.) was added to a boiling solution of 9-(3′-pyridyl)phenanthridine 1′ : 10-dimethiodide (0·54 g.) and potassium ferricyanide (1·6 g.) in 50% ethanol (40 c.c.). After 30 minutes the alcohol was removed and the insoluble precipitate crystallised from light petroleum (b. p. 80—100°); colourless needles of 10-methyl-9-phenanthridone (VIII) separated (0·12 g.; 57%); m. p. 108—110° (Pictet and Patry, *Ber.*, 1893, **26**, 1966, give m. p. 108°) (Found: N, 6·8. Calc. for $C_{14}H_{11}ON$: N, 6·7%). If the potassium ferricyanide were omitted in the above preparation the yield of (VIII) fell to 24%. When 9-phenylphenanthridine 10-methylmethosulphate was substituted for (VII; R′ = H; X = I) in the above alcoholic alkaline ferricyanide oxidation a 23% yield of (VIII) was obtained (Found: C, 80·5; H, 5·5%). The identity of this product was confirmed by a mixed melting point determination.

(*b*) Potassium ferricyanide (5·4 g.) was dissolved in a cold solution of the dimethiodide (VII; R′ = H, X = I) in 2N-sodium hydroxide (40 c.c.) diluted to 1 l. with water. After two days the collected precipitated solids were extracted with ethanol (10 c.c.). The white solid which separated from the filtered extract crystallised from benzene–light petroleum as almost white prisms (0·13 g.; 45%), m. p. 206—210°, identical with 9-(6′-keto-1′-methyl-1′ : 6′-dihydro-3′-pyridyl)phenanthridine (IV; R = H).

(*c*) A cold solution of the dimethiodide (VII; R′ = H, X = I) in water (500 c.c.) containing potassium ferricyanide (1·0 g.) was treated with N-sodium hydroxide (3 c.c.; 3 mol.). 1 C.c. of N-sodium hydroxide was added daily for 7 days by which time a stringy white precipitate had separated. This material (0·05 g.) was crystallised from aqueous alcohol and light petroleum giving 10-methyl-9-phenanthridone (VIII), m. p. 109—111°, mixed melting point with an authentic specimen 108—111°.

3-*Amino*-9-(3′-*pyridyl*)*phenanthridine* (II; R = NH_2, R′ = H).—3-Nitro-9-(3′-pyridyl)phenanthridine (4 g.) in concentrated hydrochloric acid (100 c.c.) was treated at the boiling point with stannous chloride (9 g.) in concentrated hydrochloric acid (25 c.c.), refluxing being maintained for a further 45 minutes. After being allowed to cool, the yellow stannichloride was collected and dissolved in water (40 c.c.), the base was liberated with 50% sodium hydroxide and extracted with chloroform (250 c.c.). After solution in 2N-hydrochloric acid (charcoal) and reprecipitation, it distilled at 230°/0·05 mm. and was crystallised from methanol (40 c.c.) and water (10 c.c.). 3-*Amino*-9-(3′-*pyridyl*)*phenanthridine monohydrate* formed pale yellow felted needles, m. p. 127—128° (decomp.) (Found: N, 14·7. $C_{18}H_{13}N_3,H_2O$ requires N, 14·5%). The anhydrous *base* formed light brown rectangular rods from benzene (1·2 g.; 33%); m. p. 165—166° (Found: C, 79·5; H, 4·6; N, 15·3. $C_{18}H_{13}N_3$ requires C, 79·7; H, 4·8; N, 15·5%). The *acetyl* derivative was prepared by heating the base (0·5 g.) and a little anhydrous sodium acetate in glacial acetic acid (5 c.c.) and acetic anhydride (5 c.c.) for 1½ hours. After sublimation at 260°/10 mm. it formed flat needles (0·3 g.); m. p. 253° (Found: C, 77·1; H, 4·9; N, 13·4. $C_{20}H_{15}ON_3$ requires C, 76·7; H, 4·8; N, 13·4%).

3-*Amino*-9-(3′-*pyridyl*)*phenanthridine* 1′-*Methochloride* (III; R = NH_2, R′ = H, X = Cl).—Reduced iron (5 g.) was added as rapidly as possible to a boiling aqueous solution (40 c.c.) of 3-nitro-9-(3′-pyridyl)-phenanthridine 1′-methylmethosulphate (4·27 g.), previously acidified (Congo-red) with 2N-sulphuric acid. After 30 minutes the mixture was filtered (charcoal) and treated with potassium iodide (5 g.). After 12 hours at 0° the solids were collected and crystallised from water (50 c.c.) and then from methanol. 3-*Amino*-9-(3′-*pyridyl*)*phenanthridine* 1′-*methiodide* (III; R = NH_2, R′ = H, X = I) formed light brown irregular plates of indefinite m. p. 180—240° (Found: C, 55·1; H, 4·3; N, 10·4; I, 30·8. $C_{18}H_{13}N_3,CH_3I$ requires C, 55·2; H, 3·9; N, 10·2; I, 30·8%). The *methochloride* (III; R = NH_2; R′ = H; X = Cl) formed brown rods from ethereal methanol, m. p. 256—257° (Found: N, 13·1; Cl, 11·3. $C_{18}H_{13}N_3,CH_3Cl$ requires N, 13·1; Cl, 11·1%). It gave positive primary amine tests.

7-*Amino*-9-(3′-*pyridyl*)*phenanthridine* (II; R = H, R′ = NH_2) formed a bright red stannichloride. The base separated from chlorobenzene in yellow rods (64% yield), m. p. 227—229° (Found: C, 79·5; H, 4·6; N, 15·2. $C_{18}H_{13}N_3$ requires C, 79·7; H, 4·8; N, 15·5%). The *acetyl* derivative, after sublimation at 290—300°/0·01 mm., formed felted colourless needles, m. p. 296—298° (Found: C, 76·5; H, 5·0; N, 13·4. $C_{20}H_{15}ON_3$ requires C, 76·7; H, 4·8; N, 13·4%).

7-*Amino*-9-(3′-*pyridyl*)*phenanthridine* 1′-*Methochloride* (III; R = H, R′ = NH_2, X = Cl).—The *methiodide* (III; R = H, R′ = NH_2, X = I) separated from water in light brown needles, m. p. 243—244° (decomp.) (Found: C, 55·4; H, 3·9; N, 10·3; I, 30·8. $C_{18}H_{13}N_3,CH_3I$ requires C, 55·2; H, 3·9; N, 10·2; I, 30·8%). The *methochloride* crystallised from ethereal methanol in orange plates, m. p. 265—267° (Found: N, 12·8; Cl, 11·2. $C_{18}H_{13}N_3,CH_3Cl$ requires N, 13·1; Cl, 11·1%); it gave positive tests for a primary amine.

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