400. *The Nitration of Phenanthridine.*

By A. G. CALDWELL and L. P. WALLS.

Nitration of phenanthridine in mixed acids yielded 1-, 2-, 3-, 4-, 5-, and 7-nitrophenanthridines, the last three constituting the bulk of the product, although analogy with quinoline and molecular-orbital calculations had indicated that the 1-nitro-compound would be a principal product.

The 1- and the 3-nitro-compound were identified by comparison with authentic specimens, which were prepared from the 9-methyl compounds by way of the aldehydes and carboxylic acids. The 2- and the 7-compound were reduced to the aminophenanthridines, which were identical with amines obtained from authentic carbethoxyamino-9-methyl compounds. The 4- and the 5-compound were identified by exclusion, but confirmation was obtained by oxidising them to the nitrophenanthridones.

The 2-, 3-, and 7-aminophenanthridinium salts had only very slight trypanocidal activity, and the 5-amino-salt was inactive.

5-Nitrophenanthridone was identical with a product formed in very small yield from 4-nitrophenanthraquinone by the Schmidt reaction, and 4-aminophenanthridone with that from fluorenone-4-carboxylic acid by the same reaction. Nitration of phenanthridone by nitric acid gives the 1- and the 3-nitrophenanthridone.

PRELIMINARY observations on the nitration of phenanthridine were made many years ago (Morgan and Walls, *J.*, 1932, 2229), and it is now possible to add more detail, including the identification by comparison with synthetic substances of the nitrophenanthridines thus produced. Interest in the phenanthridine series has increased in recent years, chiefly owing to the discovery of the nucleus in several classes of alkaloids, and of the notable chemotherapeutic properties of certain quaternary salts. It was important to settle the interesting question whether the characteristic trypanocidal activity of the aminophenanthridinium salts is dependent on the presence of a 9-substituent. The orientation of the nitro-compounds, and the relative proportions in which they arise are also of importance, for Longuet-Higgins and Coulson (*J.*, 1949, 978) have discussed the problem of the reactivity of the phenanthridine molecule in some detail from the point of view of molecular orbitals. There is a lack of data on the course of nitration of heterocyclic molecules (Schofield, *Quart. Reviews*, 1950, **4**, 393).

The nitration of phenanthridine is likely to be complex, for even if the 9-position is excluded from consideration on account of its marked reactivity towards nucleophilic reagents, there remain eight different positions available for attack by an electrophilic re-

agent. Longuet-Higgins and Coulson's calculations (I; the fractional numerals denote relative net charges at possible substitution positions) forecast that the 1- and the 5-position are the more probable positions of substitution under these conditions, although the 2-, 3-, 4-, and 7-positions might also be attacked, the differences between the relative net charges not being very great. On purely chemical grounds analogy might be sought in the nitration of quinoline and *iso*quinoline of both of which phenanthridine may be regarded as a derivative. In mixed acids quinoline affords roughly equal quantities of 5- and 8-nitro-quinolines (Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1940, **62**, 1643), corresponding to the 4- and the 1-position respectively in phenanthridine, but the position of nitration of quinoline depends on conditions, lithium nitrate in acetic anhydride giving the 7-compound only (Bacharach, Haut, and Caroline, *Rec. Trav. chim.*, 1933, **52**, 413), which corresponds to the 2-position in phenanthridine. Although there is an unsupported statement (Andersag, *Chem. Zentr.*, 1934, I, 3595) that nitration of *iso*quinoline gives the 5- and the 8-compound,
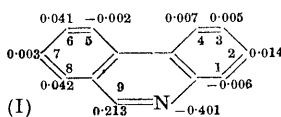
Le Fèvre and Le Fèvre (*J.*, 1935, 1475), using mixed acids, obtained a quantitative yield of a compound which was sub-sequently proved to be 5-nitro*iso*quinoline (Tyson, *J. Amer. Chem. Soc.*, 1939, **61**, 183). The quantitative yield of 5-nitro-*iso*quinoline has since been confirmed by Misani and Bogert (*J. Org. Chem.*, 1945, **10**, 358). The 5-position in phenanthridine is thus indicated, and chemical analogy, admittedly partial since no account is taken of the diphenyl link, therefore agrees with calculation in indicating 1-, 4-, and 5-nitrophenanthridines as likely products.

The early work had shown that phenanthridine is resistant to nitric acid alone, but nitration readily occurs in sulphuric acid solution, being restricted to mononitration only if exactly one equivalent of nitric acid is used. The product thus obtained was a complex mixture from which three nitro-compounds were isolated, A, m. p. 260—262°, B, m. p. 160—163°, and C, m. p. 156—158°, only B being obtained in good yield. Further examination of the nitration mixture has now revealed that three other nitro-compounds are present, namely, D, m. p. 194—195°, E, m. p. 187—188°, and F, m. p. 159—161°, and that B and C are formed in highest yield. The number of products and the circumstance that B and C are difficult to separate, have precluded quantitative assessment of the course of nitration, but certain generalisations may be advanced. The six products have all been identified by direct comparison with synthetic nitro- and amino-phenanthridines of known structures : B and C, formed in approximately equal amounts, are the 5- and the 4-derivative, and A, D, and E, all minor constituents of the mixture, are the 3-, 2-, and 1-derivative, respectively, whereas F, the 7-derivative, which is easily isolated, is formed in moderate yield. These results fall short of prediction chiefly in the very small yield of 1-nitrophenanthridine, which the molecular-orbital method had indicated as the probable main product. Nitration in sulphuric acid implies the prior addition of a proton to the nitrogen atom, and it is perhaps this circumstance, for which allowance has not been made in the molecular-orbital calculations, which causes the apparent divergence from theory. Schofield (*loc. cit.*) has discussed a similar divergence in quinoline and *iso*quinoline, and Longuet-Higgins and Coulson (*loc. cit.*) have advanced reasons why discrepancies between theory and experiment might be expected for electrophilic reactions.

For the preparation of authentic nitro- and amino-phenanthridines, the methyl group was eliminated from the appropriate nitro- or carbethoxyamino-9-methylphenanthridines by the method described by Ritchie (*J. Proc. Roy. Soc. N.S.W.*, 1945, **78**, 164) for phenan-thridine itself, namely, oxidation of the 9-methyl compound to the aldehyde by means of selenium dioxide, followed by permanganate oxidation to the 9-carboxylic acid, and decarboxylation. The 2-, 3-, and 7-carbethoxyamino- and 3-nitro-phenanthridine-9-aldehydes were available from earlier work (Caldwell, in the press) and the 6- and 8-carb-ethoxyamino- and 1-nitro-analogues have been prepared similarly. Diphenanthridinyl-ethylenes, obtained as by-products in the previous work, were again found in two examples.

The aldehydes were oxidised by permanganate in aqueous pyridine under mild conditions to the carboxylic acids, which were accompanied by small amounts of the corresponding phenanthridones (cf. Ritchie, *loc. cit.*). Stepan and Hamilton (*J. Amer. Chem. Soc.*, 1949,

71, 2438) describe 1-nitrophenanthridine-9-carboxylic acid as a yellow substance of m. p. 247—248°. Our product is almost colourless and is decarboxylated readily on melting at 170°, or in suitable boiling solvents (*e.g.*, glacial acetic acid), to give 1-nitrophenanthridine, m. p. 191—192°, identical with compound E. It is possible that Stepan and Hamilton's product was impure 1-nitrophenanthridone. 3-Nitrophenanthridine-9-carboxylic acid was decarboxylated particularly smoothly, so that when heated it showed no effervescence and gave only the melting point of 3-nitrophenanthridine, corresponding to compound A. The carbethoxyaminophenanthridine-9-carboxylic acids were also decarboxylated on melting, to give the carbethoxyaminophenanthridines, but use of this method involved the danger of thermal decomposition of the carbethoxyamino-group, and it was better in general to decarboxylate the amino-acids, which were readily obtained by mild alkaline hydrolysis of the carbethoxyamino-acids. An exception was 8-carbethoxyaminophenanthridine-9-carboxylic acid, which was smoothly decarboxylated below 100° to the carbethoxy-aminophenanthridine.

Reduction of the nitrophenanthridines obtained by direct nitration to the amines, required for comparison with the synthetic aminophenanthridines, presented some difficulty. Both compounds B and C in ethanol solution with hydrogen at normal temperature and pressure in the presence of palladium–charcoal gave mixtures indicative of reduction at other parts of the molecule in addition to the nitro-group. On use of iron powder and aqueous-alcoholic solutions of the nitro-compounds the products were hard to purify, particularly that from D. The action of iron powder on a hot aqueous suspension of the nitro-compound was satisfactory, and in this way aminophenanthridines were obtained from nitro-compounds A, D, and F, and equated with the synthetic 3-, 2-, and 7-amino-compounds.

Compound C gave a good yield of phthalic acid on oxidation with alkaline permanganate, and therefore must be 4-nitrophenanthridine, the nitro-group occupying the only available position in that ring. Compound B did not give an identifiable product on oxidation, but the amino-compound obtained from it by reduction was different from synthetic 6-, 7-, and 8-aminophenanthridines, and thus by exclusion must be 5-nitrophenanthridine. Direct proof of this assignment was obtained subsequently.

A nitrophenanthridine was obtained by Ritchie (*loc. cit.*, p. 177) by nitration of 10-acetyl-9 : 10-dihydrophenanthridine with nitric acid followed by simultaneous hydrolysis and oxidation, and identified with compound A; it was correctly assumed by Ritchie to have the nitro-group in the 3-position. A substance obtained similarly in poor yield by the action of mixed acids on the same dihydro-compound was thought to be 7-nitrophenan-thridine; it occurred in orange leaflets, m. p. 178°, and apparently does not correspond to our 7-nitrophenanthridine or to any other of our nitration products.

Phenanthridinium salts with an amino-group in the 2-, 3-, 5-, and 7-positions were prepared by conventional methods. Dr. L. G. Goodwin and his colleagues report that the 2-, 3-, and 7-compounds show slight trypanocidal activity, being less effective than the corresponding 9-alkyl compounds. The 5-compound is inactive. Substitution in the 9-position with an aryl group would appear to be a condition for significant trypanocidal activity.

It was first thought that the most convenient method of identification of the nitro-phenanthridines would be as the corresponding nitrophenanthridones. The literature describes only one method of oxidation of phenanthridines unsubstituted in the 9-position to phenanthridones, namely, by aqueous hypochlorite in the presence of a cobalt catalyst (Pictet and Patry, *Ber.*, 1893, **26**, 1962), but this method, which is very satisfactory for some quinoline derivatives, is unsuited to substances insoluble in water, and is liable to chlorinate the reactant or product (Sielisch and Sandke, *Ber.*, 1933, **66**, 433). The nitrophenanthrid-ines are resistant to many common oxidising agents, but a suitable one has been found in acid permanganate, which affords over 50% yields of 4-, 5-, and 7-nitrophenanthridones; 4-nitrophenanthridone was also obtained in minute yield by Pictet and Patry's method. Six nitrophenanthridones have previously been described, namely, the 1- (Stepan and Hamilton, *loc. cit.*), the 2- and 7- (Moore and Huntress, *J. Amer. Chem. Soc..*, 1927, **49**, 1327), the 3- (Walls, *J.*, 1935, 1406), and two nitration products of phenanthridone of

unknown orientation (Moore and Huntress, *loc. cit.*). The highest value recorded for the melting point of 7-nitrophenanthridone (292°) is much lower than ours (324—326°), but an explanation may be found in the earlier method of synthesis. The melting points of the nitrophenanthridones are much depressed by traces of impurity, and 7-nitrophenanthridone particularly is liable to further substitution, *e.g.*, chlorination (see Experimental), and it may be that the earlier preparation by Hofmann's reaction on 4'-nitrodiphenamic acid suffered slight bromination.

Nitration of phenanthridone might be expected to give the 1- and the 3-nitro-derivative, for the apposite ring is activated by a powerful *ortho-para*-orientating group, ·NH·COR (compare the ready *ortho-para*-nitration of arylurethanes, Dikshoorn, *Rec. Trav. chim.*, 1929, **48**, 527), whereas reactivity in the adjacent ring is depressed by a ·CO·NHR' group. The nitration product formed in small amount (the literature gives m. p. 253°), Stepan and Hamilton's compound (m .p. 257—258°), and that obtained as a by-product in the oxidation of 1-nitrophenanthridine-9-aldehyde have been shown to be identical, repeated crystallisation eventually yielding yellow plates, m. p. 265—267°. 3-Nitrophenanthridone as obtained by chromic acid oxidation of 9-methyl-3-nitrophenanthridine forms brick-red needles (Walls, *loc. cit.*) whereas the major nitration product, and that obtained as a by-product from the oxidation of 3-nitrophenanthridine-9-aldehyde, are cream-coloured. The chromic acid product could not be further purified by crystallisation, but chromatography of a pyridine solution on aluminium oxide was effective. 3-Nitrophenanthridone was strongly adsorbed, and on elution from the column was obtained in cream-coloured needles, m. p. 380—383°, identical with the nitration product. A dark red impurity was not adsorbed; it was not obtained pure, but may be mainly the diphenanthridinylethylene.

Caronna (*Gazzetta*, 1941, **71**, 483) reported the conversion of phenanthraquinone into phenanthridone by hydrazoic acid, and the application of this method to 4-nitrophenanthraquinone offered a means of identifying nitrophenanthridone B or C. Hydrazoic acid rapidly discharged the deep colour of the sulphuric acid solution of 4-nitrophenanthraquinone, vigorous effervescence occurring, but the main product was a mixture of nitrodiphenamic acids; a trace of nitrophenanthridone was also formed, and this was identical with nitrophenanthridone B and hence is the 5-compound. According to Stephenson (*J.*, 1949, 2620), diphenamic acid is also a product of the reaction with phenanthraquinone itself. This reaction of phenanthraquinones merits further study; the formation of phenanthridones involves the elimination of the elements of carbon monoxide, an unusual reaction under such mild conditions (cf. Gore and Hughes, *J. Amer. Chem. Soc.*, 1950, **72**, 5770). The production of phenanthridones and diphenamic acids from phenanthraquinones may be formally interpreted by an extension of the mechanism proposed by Smith (*J. Amer. Chem. Soc.*, 1948, **70**, 320) for the Schmidt reaction. The first step would be the formation of two pairs of *cis-trans*-azides (II; the NO_2-group being in the 4- or the 5-position), followed by a Beckmann type of rearrangement with evolution of nitrogen to yield respectively the cyclic amides (III) and (IV: two isomers). Hydrolysis of (III) would yield a mixture of nitrodiphenamic acids, whereas by loss of carbon monoxide one isomer (IV) would yield 4-nitroand the other 5-nitro-phenanthridone.

(II)   (III)   (IV)
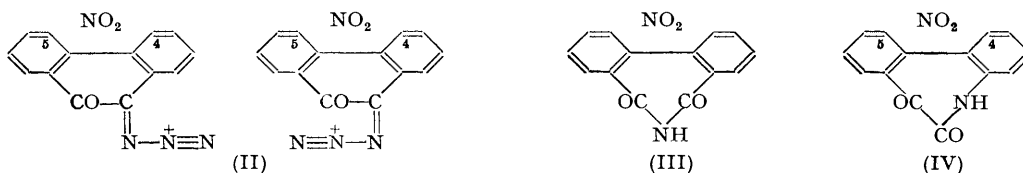
It was of interest to study the reaction between the readily accessible fluorenone-4-carboxylic acid and hydrazoic acid. Both ring-expansion to a phenanthridone and the conventional Schmidt replacement of a carboxy- by an amino-group occurred simultaneously, and 4-aminophenanthridone, identical with aminophenanthridone C, was isolated, but a mixture of presumed phenanthridonecarboxylic acids was also obtained.

The following table summarises information on the nitrophenanthridines and nitro-

phenanthridones; the figures in parentheses denote the percentage yields actually isolated in the nitration of phenanthridine.

Substitution position	Nitrophenanthridine, m. p.	Nitrophenanthridone, m. p.
1	190° (1)	265—267°
2	194—195 (6)	349 *
3	266—267 (3)	380—383
4	160·5—161·5 (26)	325—327
5	166—166·5 (21)	316—318
7	159—161 (11)	324—326

* Moore and Huntress, *loc. cit.*

EXPERIMENTAL

Nitration Experiments.—(i) Phenanthridine nitrate (37 g.) was added to concentrated sulphuric acid, and the crude mixture of nitro-compounds (35 g.) isolated as described previously (*J.*, 1932, 2229). The mixture was dissolved in boiling benzene (200 ml.), and the solution was cooled. 3-Nitrophenanthridine (A) crystallised in buff needles (1 g.), m. p. *ca.* 240—250°, which after successive recrystallisation from alcohol (750 ml.) and 2-ethoxyethanol formed fine, very pale yellow needles, m. p. 266—267°, not depressed on admixture with synthetic 3-nitrophenanthridine (Found : C, 69·35; H, 3·8; N, 12·0. Calc. for $C_{13}H_8O_2N_2$: C, 69·65; H, 3·6; N, 12·5%).

The benzene mother-liquor was evaporated to dryness, and the residue dissolved in boiling ethanol. On cooling, a mass of crystalline material formed, from which well-defined transparent brownish-yellow prisms, m. p. 158—160°, were separated by hand-sorting. This substance (5·5 g.), *viz.*, 5-nitrophenanthridine (B), was crystallised from benzene and then from ethanol, forming very pale yellow thick plates, m. p. 166—166·5° (Found : C, 69·6; H, 3·85; N, 12·3%). In the earlier publication (*loc. cit.*) it was stated that a third product was obtained in very small yield. It has now been found that crystallisation of the residue (28 g.), from which B had been sorted, from glacial acetic acid (56 ml.) afforded 4-nitrophenanthridine (C) in buff needles (6·5 g.), m. p. 158—160°, recrystallisation from alcohol yielding pale yellow stout needles, m. p. 160·5—161·5° (Found : C, 69·5; H, 3·4; N, 12·5%). The acetic acid mother-liquor slowly deposited 2-nitrophenanthridine (D) (2 g.), which on recrystallisation from alcohol formed colourless needles, m. p. 196—197° (Found : C, 69·6; H, 3·55; N, 12·6%).

The acetic acid mother-liquor was then diluted with water, and the crude solid collected, dried, and subjected again to the foregoing cycle of operations. Crystallisation from ethanol and hand-sorting afforded a further yield of B (2 g.), and crystallisation of the residue from acetic acid gave further C (2·5 g.). The acetic acid mother-liquor gradually deposited a fifth product (E) in small yield; crystallisation from alcohol gave stout acicular prisms, m. p. 187—188°, slightly raised by admixture with synthetic 1-nitrophenanthridine (Found : C, 70·1; H, 3·75; N, 12·45%).

Thus the original crude mixture (35 g.) had given A, B, C, D, and E in yields of approximately 1, 7·5, 9, 2, and <1 g., respectively; total 20·5 g. It was subsequently found that F (4 g.) was also present; the total yield was thus 24·5 g.

(ii) A solution of crude nitration product (23 g.) in benzene after removal of A was concentrated to 100 ml.; crude B (600 mg.), m. p. *ca.* 150—160°, slowly separated. Further concentration to 40 ml. and cooling gave pale yellow prismatic needles (6·7 g.), m. p. *ca.* 128—150°, a mixture of B and C, which could not be separated by crystallisation from alcohol or benzene. Fractional crystallisation from glacial acetic acid furnished the less soluble C (1·7 g.), m. p. 158—160°, and eventually crude B (1 g.) was isolated from the mother-liquor and purified by crystallisation from benzene. This method was not very satisfactory.

The benzene mother-liquor from which the B + C mixture had separated was evaporated to dryness, and the residue dissolved in ethanol (250 ml.). Addition of concentrated sulphuric acid (5 ml.) to the solution caused clumps of ill-defined crystals to separate, which were collected (4·2 g.) and converted into the base (2·9 g.), 7-nitrophenanthridine (F), m. p. 155—157°. Recrystallisation from ethanol afforded small cream-coloured needles, m. p. 158·5—160·5°, depressed by admixture with B or C (Found : C, 69·5; H, 3·35; N, 12·55%).

The alcoholic sulphuric acid mother-liquor on cooling deposited an oil, which soon crystallised, followed by cream-coloured needles. The latter, after recrystallisation from alcohol, although apparently homogeneous, was a mixture of the sulphates of B and C, the base derived from it having m. p. *ca.* 128—130°. It was clear that the attempt to separate the nitration mixture

through the sulphates was only successful in so far as the sulphate of 7-nitrophenanthridine is practically insoluble in alcohol. The method was not pursued further, effective separation being prevented by the formation of mixed crystals of B and C as bases and as sulphates.

2-, 3-, 4-, 5-, and 7-*Aminophenanthridines* were obtained by reduction of the nitro-compounds as follows : the nitrophenanthridine (200 mg.), iron powder (400 mg.), water (10 ml.), and 2N-acetic acid (0·2 ml.) were heated at 100° for 4 hours with frequent shaking. The iron–amine mixture was collected, dried, and extracted with boiling benzene. On cooling, the extract deposited crystals of the aminophenanthridine (80—150 mg.). The 2-, 3-, and 7-compounds were identical with synthetic specimens. Details are given in Table 3.

Phenanthridine-9-aldehydes.—These were prepared by the method already described for related compounds (Caldwell, *loc. cit.*), freshly prepared and sublimed selenium dioxide being used.

1-*Nitrophenanthridine*-9-*aldehyde* (30% yield, with recovery of 30% of starting material) crystallised from benzene–light petroleum (b. p. 60—80°) as fine cream-coloured needles, m. p. 203—204° (Found : C, 66·7; H, 3·15; N, 11·25. $C_{14}H_8O_3N_2$ requires C, 66·65; H, 3·2; N, 11·1%). The by-product, 1 : 2-*di*-(1-*nitro-9-phenanthridinyl*)*ethylene* (4%), was crystallised several times from pyridine to give fine orange-red needles, m. p. above 360° (Found : C, 71·65; H, 3·1; N, 11·4. $C_{28}H_{16}O_4N_4$ requires C, 71·2; H, 3·4; N, 11·85%).

6-*Carbethoxyaminophenanthridine*-9-*aldehyde*, obtained in 70% yield, formed pale yellow plates, m. p. 201—203°, from benzene (Found : C, 69·4; H, 4·65; N, 9·7. $C_{17}H_{14}O_3N_2$ requires C, 69·4; H, 4·8; N, 9·5%). 1 : 2-*Di*-(6-*carbethoxyamino-9-phenanthridinyl*)*ethylene* (7% yield) was identified by comparison with an authentic specimen synthesised from 6-carbethoxyamino-phenanthridine-9-aldehyde and 6-carbethoxyamino-9-methylphenanthridine (cf. Caldwell, *loc. cit.*). The pure compound formed small yellow plates, m. p. 295—300° (decomp.), from pyridine (Found : C, 73·2; H, 5·45; N, 10·2. $C_{34}H_{28}O_4N_4$ requires C, 73·35; H, 5·05; N, 10·05%). 8-*Carbethoxyaminophenanthridine*-9-*aldehyde* (60% yield) crystallised from benzene in bright yellow plates, m. p. 221—223° (effervescence) (Found : C, 69·5; H, 4·9; N, 9·6. $C_{17}H_{14}O_3N_2$ requires C, 69·4; H, 4·8; N, 9·5%).

Phenanthridine-9-carboxylic Acids.—The following general method was employed for the oxidation of the nitro- and carbethoxyamino-phenanthridine-9-aldehydes to the carboxylic acids : a solution of the aldehyde (2 g.) in pyridine (50—150 ml., according to solubility) was stirred at 40° during the gradual addition (30—45 minutes) of a solution of potassium permanganate (840 mg. for nitro-compounds; 800 mg. for carbethoxyamino-compounds) in water (16 ml.). The mixture was stirred for a further 30—60 minutes at the same temperature, heated to boiling, and filtered hot; the manganese dioxide was extracted with boiling pyridine and then potassium carbonate solution. The combined filtrates were much diluted with water, and then

TABLE 1. *Phenanthridine-9-carboxylic acids.*

Substituent	Colour (solvent)	M. p. (efferv.)	Formula	Found, %			Required, %		
				C	H	N	C	H	N
1-NO₂	Cream *	170°	$C_{14}H_8O_4N_2$	62·75	3·0	10·35	62·65	3·0	10·45
3-NO₂	Cream *	265—266 (no efferv.)	,,	63·15	2·95	10·65	,,	,,	,,
2-NH₂	Deep red (water)	183	$C_{14}H_{10}O_2N_2$	69·95	4·3	11·5	70·55	4·25	11·75
3-NH₂	Orange (water)	190	,,	70·8	4·5	11·85	,,	,,	,,
6-NH₂	Bright yellow (AcOH)	235	,,	70·2	4·2	11·9	,,	,,	,,
7-NH₂	Deep red (water)	202	,,	70·65	4·3	12·0	,,	,,	,,
2-NH·CO₂Et	Colourless (dioxan)	175 (rapid heating) 224—225 (slow heating)	$C_{17}H_{14}O_4N_2$	65·55	4·4	8·9	65·8	4·55	9·05
3-NH·CO₂Et	Yellow (AcOH)	193	,,	66·0	4·45	9·0	,,	,,	,,
6-NH·CO₂Et	Pale yellow *	193	,,	66·3	4·75	8·7	,,	,,	,,
7-NH·CO₂Et	Yellow (aq. dioxan)	192	,,	65·8	4·5	8·9	,,	,,	,,
8-NH·CO₂Et	Yellow *	105—110 Resolidification 158—160°	,,	65·65	4·6	9·15	,,	,,	,,

* Not recrystallised, but purified by reprecipitation from solution in aqueous potassium carbonate and dried at room temperature in a vacuum before analysis. Others dried at 100° in a vacuum.

evaporated to small volume to remove pyridine. The phenanthridone (usually 200—300 mg.) which separated was collected, and acidification of the filtrate gave the carboxylic acid (1·2—1·7 g.).

Oxidation of 8-carbethoxyaminophenanthridine-9-aldehyde under these conditions was very slow, so the temperature was raised to 50°, 750 mg. of the phenanthridone and 900 mg. of the carboxylic acid being obtained.

The carbethoxyaminophenanthridine-9-carboxylic acids, after hydrolysis for 5 minutes by boiling 2N-sodium hydroxide followed by neutralisation, gave the corresponding *amino-phenanthridine-9-carboxylic acids*.

The acids prepared by these procedures, which all formed needles, are listed in Table 1, and the carbethoxyaminophenanthridones, which all crystallised in colourless needles, in Table 2.

Decarboxylations.—Of the following methods of decarboxylation, that used in each case is indicated in Table 3. (i) The carboxylic acid was heated alone at a temperature 5—10° above

TABLE 2. *Carbethoxyaminophenanthridones.*

Position of substituent	Solvent	M. p. (efferv.)	Found, %		
			C	H	N
2-	Dioxan	*ca.* 250° (rapid heating)	67·55	5·15	9·95
3-	AcOH	285	68·1	4·95	10·0
6-	EtOH	280	68·25	4·95	10·05
8-	,,	295	68·4	4·8	9·95
		$C_{16}H_{14}O_3N_2$ requires	68·05	5·0	9·95

TABLE 3. *Phenanthridines.*

Substituent	Method of prepn.*	Description (of needles) (solvent)	M. p.	Formula	Found, %			Required, %		
					C	H	N	C	H	N
1-NO$_2$	a, c	Pale yellow (EtOH)	191—192° (shrinking 187)	$C_{13}H_8O_2N_2$	69·65	3·25	12·5	69·65	3·6	12·5
3-NO$_2$	a, c	White (aq. AcOH)	266—267	,,	69·75	3·7	12·45	,,	,,	,,
2-NH$_2$	b, e	Yellow, prismatic (C$_6$H$_6$)	144—145	$C_{13}H_{10}N_2$	80·25	4·95	14·35	80·35	5·25	14·45
3-NH$_2$	d, e	Pale yellow (C$_6$H$_6$)	152—153	,,	80·25	5·05	14·25	,,	,,	,,
4-NH$_2$	e	Yellow (C$_6$H$_6$)	115·5—117	,,	80·1	5·45	14·5	,,	,,	,,
5-NH$_2$	e	Pale yellow (C$_6$H$_6$)	143·5—144·5	,,	80·4	5·1	14·4	,,	,,	,,
6-NH$_2$	d	Colourless (aq. MeOH)	192—194	,,	80·6	5·25	14·25	,,	,,	,,
7-NH$_2$	b, e	Pale yellow (aq. MeOH)	203—204	,,	80·65	4·9	14·6	,,	,,	,,
8-NH$_2$	f	Pale yellow (C$_6$H$_6$)	208—210	,,	80·35	5·15	14·15	,,	,,	,,
2-NH·CO$_2$Et	g	Colourless, felted (EtOH)	227—229 (efferv.)	$C_{16}H_{14}O_2N_2$	72·3	5·35	10·35	72·15	5·3	10·5
3-NH·CO$_2$Et	g	Fine, colourless (EtOH)	221 (efferv.)	,,	72·15	5·35	10·7	,,	,,	,,
7-NH·CO$_2$Et	b	Colourless (MeOH)	205—206	,,	72·2	5·2	10·8	,,	,,	,,
8-NH·CO$_2$Et	h	Colourless (C$_6$H$_6$—light petroleum)	161—163	,,	72·35	5·25	10·7	,,	,,	,,

* (a) Nitration of phenanthridine. (b) Decarboxylation method (i). (c) Decarboxylation method (ii). (d) Decarboxylation method (iii). (e) Reduction of nitro-compound. (f) Hydrolysis of 8-carbethoxy-aminophenanthridine by 50% sulphuric acid at 150°. (g) Reaction of the aminophenanthridine with ethyl chloroformate in alcoholic solution. (h) Decarboxylation of 8-carbethoxyaminophen-anthridine-9-carboxylic acid in an oven at 95° for 2 hours.

its m. p. until effervescence ceased. The residue was dissolved in dilute (*ca.* 0·5N) acetic acid, and the solution was treated with charcoal, filtered, and made alkaline to precipitate the product. (ii) The carboxylic acid was boiled with glacial acetic acid for 5 minutes. The product was precipitated by dilution with water. (iii) A solution of the acid in quinoline (10 vols.) was boiled for 2—5 minutes. The quinoline was removed in steam, and the product worked up through dilute acetic acid as in (i).

*2-Carbethoxyamino-*10*-methylphenanthridinium Bromide.*—2-Carbethoxyaminophenanthridine (450 mg.) in nitrobenzene (4 ml.) was treated at 150° with methyl sulphate (0·5 ml.). After 5 minutes at 150° benzene was added, and the yellow solid collected and washed with acetone. The *bromide* (500 mg.), obtained by using potassium bromide in aqueous solution, crystallised from methanol as fine yellow needles, m. p. 252° (decomp.) (Found : N, 7·6; Br, 22·1. $C_{17}H_{17}O_2N_2Br$ requires N, 7·75; Br, 22·15%).

The 3-*carbethoxyamino*-analogue was prepared similarly and formed fine yellow needles, m. p. 242° (decomp.), from ethanol (Found : N, 7·65; Br, 22·1%); the 7-*carbethoxyamino*-isomer formed small bright yellow needles, m. p. 255° (decomp.), from methanol–ethyl acetate (Found : N, 7·65; Br, 21·85%).

*2-Amino-*10*-methylphenanthridinium Iodide.*—Hydrolysis of the carbethoxyamino-salt (450 mg.) with concentrated sulphuric acid (1·2 ml.) and water (1 ml.) at 140° for 25 minutes yielded, after dilution with water, neutralisation with ammonia, and addition of potassium iodide, the *amino-iodide* (400 mg.), which formed orange-red plates, m. p. 243—245°, from methanol (Found : C, 49·65; H, 3·8; N, 8·05; I, 38·35. $C_{14}H_{13}N_2I$ requires C, 50·0; H, 3·9; N, 8·3; I, 37·8%). The 3-*amino-iodide*, obtained similarly, crystallised from aqueous alcohol in fine orange needles, m. p. 255—257° (Found : N, 8·55; I, 37·6%), and the 7-*amino-iodide* formed orange-red needles, m. p. 250—251°, from aqueous alcohol (Found : N, 8·1; I, 37·65%).

*5-Acetamido-*10*-methylphenanthridinium Methyl Sulphate.*—5-Acetamidophenanthridine was obtained by warming the amine with acetic anhydride, dilution with water, and neutralisation with ammonia; the precipitated product crystallised from alcohol in colourless needles, m. p. 206° (Found : C, 76·0; H, 5·45; N, 11·5. $C_{15}H_{12}ON_2$ requires C, 76·15; H, 5·15; N, 11·85%). On addition of methyl sulphate (1·2 ml.) to a solution of this acetyl compound (3 g.) in nitrobenzene at 180°, the quaternary *salt* separated in light brown needles (3·7 g.), m. p. 215—220° (decomp.) (Found : N, 7·55; S, 9·25. $C_{17}H_{18}O_5N_2S$ requires N, 7·75; S, 8·85%).

*5-Amino-*10*-methylphenanthridinium chloride*, produced by hydrolysis of the foregoing salt by refluxing 5N-hydrochloric acid for 1 hour, cooling, and dilution with water, crystallised in orange needles, m. p. 233—234° (decomp.) (Found : C, 60·0; H, 6·05; N, 10·75; Cl, 13·8. $C_{14}H_{13}N_2Cl,1·5H_2O$ requires C, 60·05; H, 6·2; N, 10·8; Cl, 13·7%).

Oxidation of 4-Nitrophenanthridine.—The nitro-compound (1 g.) was heated at 100° with an aqueous solution of potassium permanganate (8·5 g.) until the latter was all consumed. The filtrate was evaporated to small bulk and acidified. Phthalic acid crystallised in colourless plates, m. p. 205° (efferv.), from which the anhydride, m. p. 132°, was obtained by sublimation.

1- and 3-Nitrophenanthridones.—Phenanthridone (5·5 g.) was nitrated by Moore and Huntress's method (*loc. cit.*). The crude product was extracted by boiling alcohol (8 × 200 ml.), and the extract, on cooling, deposited 1-nitrophenanthridone (400 mg.), which crystallised from glacial acetic acid in deep yellow acicular prisms, m. p. 265—267°, alone or in admixture with the product obtained by oxidation of 9-methyl-1-nitrophenanthridine (Found : C, 64·95; H, 3·55; N, 11·0. Calc. for $C_{13}H_8O_3N_2$: C, 65·0; H, 3·35; N, 11·65%). The alcohol-insoluble material (4·5 g.) crystallised from a large volume of boiling pyridine in cream-coloured needles, m. p. 380—384° (decomp.) (after immersion in a bath at 370°) (Found : C, 65·35; H, 3·35; N, 11·5%).

A solution of the brick-red product of oxidation of 9-methyl-3-nitrophenanthridine (1 g.) in pyridine (600 ml.) was percolated through a column of alumina, and eluted with pyridine until the eluate was no longer red. The pale yellow aluminium oxide was then removed from the column, and extracted with hot pyridine. On concentration of the extract and cooling, 3-nitrophenanthridone crystallised, identical with the sparingly soluble nitration product.

4-Nitrophenanthridone.—To a solution of 4-nitrophenanthridine (500 mg.) in hot 2N-sulphuric acid (10 ml.) was added potassium permanganate (1 g.), portionwise, as it reacted with effervescence. When all the permanganate had reacted, the precipitate of nitrophenanthridone and manganese dioxide was collected, washed with water, dried, and then extracted with boiling pyridine. Dilution of the extract with water precipitated 4-*nitrophenanthridone* (300 mg.), which crystallised from glacial acetic acid in almost white needles, m. p. 325—327° (Found : C, 65·25; H, 3·15; N, 11·85%). Alternatively, the reaction mixture could be warmed with 2N-hydrochloric acid to remove manganese dioxide.

5-Nitrophenanthridone.—(i) Oxidation of 5-nitrophenanthridine by potassium permanganate gave a *product* which crystallised from glacial acetic acid in buff-coloured prisms, m. p. 316—318° after earlier sintering (Found : C, 65·25; H, 3·3; N, 11·9%).

(ii) For the nitration of phenanthraquinone Schmidt and Spoun's method (*Ber.*, 1922, **55**,

1199) was used, the earlier method (Schmidt and Austin, *Ber.*, 1903, **36**, 3731) proving unsatisfactory. Sodium azide (2·6 g., 10 mols.) was added during 30 minutes with stirring to a solution of 4-nitrophenanthraquinone (1 g.) in concentrated sulphuric acid (10 ml.) at 10°. After 2 mols. of azide had been added the originally almost black solution had become colourless and the vigorous effervescence had subsided. After an hour, ice was added, and the white precipitate was collected and heated with water; the extract on cooling deposited white crystals of nitrodiphenamic acid I (800 mg.). The residue was then extracted with hot N-sodium hydroxide; on acidification of the extract nitrodiphenamic acid II (150 mg.) separated. The residue (*ca.* 20 mg.) crystallised from glacial acetic acid in buff prisms, m. p. 311—315°, depressed by admixture with 4-nitrophenanthridone, but raised by 5-nitrophenanthridone.

The nitrodiphenamic acids were purified by dissolving them in aqueous sodium carbonate (charcoal) and reprecipitation by acid. *Nitrodiphenamic acid* I crystallised from water, but tended to separate first as an oil; it formed clumps of white needles (possibly slightly contaminated with II), m. p. 205—209° (Found : C, 58·6; H, 3·45; N, 10·0. $C_{14}H_{10}O_5N_2$ requires C, 58·7; H, 3·55; N, 9·8%). *Nitrodiphenamic acid* II was sparingly soluble in water; it formed glistening talc-like crystals, m. p. 219—221° (Found : C, 58·85; H, 3·5%).

7-Nitrophenanthridone, obtained by oxidation of 7-nitrophenanthridine, formed bright yellow needles which melted over a range, *ca.* 285—305°. It was purified chromatographically in pyridine solution on alumina, impurities being strongly adsorbed. Concentration of the pyridine eluate caused yellow needles to separate, having m. p. 320—325°; recrystallisation from acetic acid gave a product, m. p. 324—326° (decomp.) (Found : C, 64·4; H, 3·1; N, 11·6. Calc. for $C_{13}H_8O_3N_2$: C, 65·0; H, 3·35; N, 11·65%). When the manganese dioxide was dissolved by hydrochloric acid extensive chlorination occurred; the product had m. p. *ca.* 305° (Found : C, 57·35; H, 3·25; N, 9·85; Cl, 10·4. Calc. for $C_{13}H_7O_3N_2Cl$: C, 56·8; H, 2·6; N, 10·2; Cl, 12·9%).

4-Aminophenanthridone.—(i) The nitro-compound (500 mg.) was suspended in ethanol (35 ml.) and reduced with hydrogen (10 atm.) in the presence of Adams's catalyst (50 mg.) at room temperature. The amino-compound was present as a suspension, and sufficient boiling ethanol was added to dissolve it; after filtration from catalyst, concentration, and cooling, the *amine* crystallised in buff needles (250 mg.), m. p. 319—323° with blackening (Found : C, 74·1; H, 5·05; N, 13·25. $C_{13}H_{10}ON_2$ requires C, 74·2; H, 4·8; N, 13·3%).

(ii) Fluorenone-4-carboxylic acid (3 g.) was dissolved in sulphuric acid (30 ml.), and the deep crimson solution was cooled and treated with sodium azide (1·5 g.) during 30 minutes. At the first additions vigorous effervescence occurred, and the colour of the solution was progressively discharged. After ½ hour water was added, and the pale solid thus precipitated was collected and washed with water (3 g.). Extraction with warm N-sodium hydroxide left a solid residue (1·1 g.), m. p. 295—305°, which was extracted with boiling sulphuric acid (400 ml.). On cooling, the *sulphate* crystallised in almost white needles (Found, for dried salt : C, 60·1; H, 4·1; N, 10·65; S, 6·2. $C_{13}H_{11}N_2O,0.5H_2SO_4$ requires C, 60·05; H, 4·25; N, 10·75; S, 6·15%). The base was liberated by heating the sulphate with dilute ammonia solution, and after crystallisation had the same m. p. and mixed m. p. as the product in (i).

5-Aminophenanthridone was prepared from 5-nitrophenanthridone by method (i) and crystallised from pyridine in small buff prisms, m. p. 330—334° (with blackening), depressed by the product described in (ii) above (Found : C, 74·2; H, 4·7; N, 13·15. $C_{13}H_{10}ON_2$ requires C, 74·2; H, 4·8; N, 13·3%).