69. *New Trypanocides. Part I. Quaternary Salts derived from 2 : 7-Diaminophenanthridine and the Attempted Preparation of Quaternary Salts from 2 : 7-Diamino-9-anilinophenanthridine.*

By M. Davis.

2 : 7-Diamino- and 2 : 7-di(ethoxycarbonylamino)-10-methylphenanthridinium salts have been prepared by two routes. 2 : 7-Diamino-9-anilino- and -9-*p*-aminoanilino-phenanthridine have been prepared from 9-chloro-2 : 7-dinitrophenanthridine. Attempts to convert the last two bases into quaternary derivatives analogous to Dimidium and Trimidium salts were unsuccessful.

Although the trypanocidal activity of many 9-substituted phenanthridinium salts has been studied in detail, the examination of similar compounds containing a 9-anilino-group or without a 9-substituent has until recently been neglected. The synthesis of 2 : 7-diamino- (IX; R = H) and 2 : 7-di(ethoxycarbonylamino)-10-methylphenanthridinium salts (IX; R = CO_2Et) was therefore undertaken, and the intermediates made available in this work were employed in attempts to obtain 9-anilino- and 9-*p*-aminoanilino-derivatives (XIII; R = H and NH_2) analogous to the well known 9-phenyl- (Dimidium) and 9-*p*-aminophenyl- (Trimidium) compounds (XIV; R = H and NH_2). When this work was almost finished, a communication by Caldwell and Walls [1] described 2-, 3-, 5-, and 7-amino-10-methylphenanthridinium salts; all of these except the 5-amino-isomer had but slight trypanocidal activity.

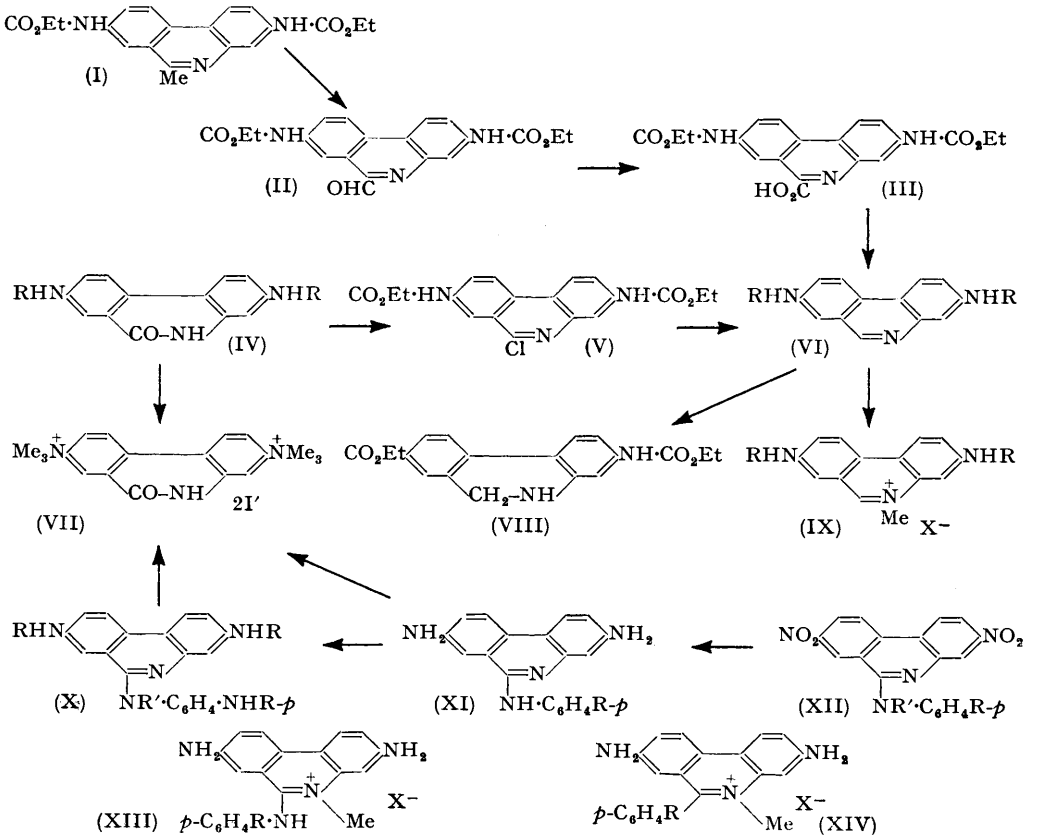
2 : 7-Diamino- and 2 : 7-dinitro-phenanthridine are not described in the literature and their synthesis was unsuccessfully attempted by Ritchie.[2] However, 2 : 7-dinitrophenanthridone has been prepared from 2 : 7-dinitrofluorenone by the Schmidt reaction [3] and application of this reaction to 2 : 7-diaminofluorenone [4] gave 2 : 7-diaminophenanthridone (IV; R = H), which was converted into 2 : 7-di(ethoxycarbonylamino)phenanthridone (IV; R = CO_2Et) and then treated with phosphorus oxychloride, yielding 9-chloro-2 : 7-di(ethoxycarbonylamino)phenanthridine (V). Dehalogenation over Raney nickel in alkaline solution proceeded readily, but the 2 : 7-di(ethoxycarbonylamino)phenanthridine (VI; R = CO_2Et) formed was always accompanied by some of the highly fluorescent 9 : 10-dihydro-derivative (VIII) which on one occasion, when the reaction was effected under pressure, was the sole product.

2 : 7-Di(ethoxycarbonylamino)phenanthridine was also prepared by an alternative route used by Caldwell and Walls [1] to make the mononitrophenanthridines. 2 : 7-Di-(ethoxycarbonylamino)-9-methylphenanthridine [5] (I) failed to condense with formaldehyde to form the dihydroxy*iso*propyl derivative,[6] but was readily oxidised to the 9-aldehyde [7] (II) by selenium dioxide in dioxan. Further oxidation with potassium permanganate in aqueous pyridine furnished the 9-carboxylic acid (III), which was decarboxylated in boiling nitrobenzene. Hydrolysis with aqueous sulphuric acid then yielded 2 : 7-diaminophenanthridine (VI; R = H).

Attempts to dehalogenate 9-chloro-2 : 7-dinitrophenanthridine [8] proved unsuccessful. Catalytic reduction over Raney nickel in alkaline solution resulted in an intractable mixture. On one occasion after reduction over platinum oxide in dioxan a small amount of what appeared to be 2 : 7-diamino-9-chlorophenanthridine or its 9 : 10-dihydro-derivative was isolated. 9-Chloro-2 : 7-dinitrophenanthridine failed to react with toluene-*p*-sulphonhydrazide in boiling chloroform or toluene [8] and was hydrolysed to 2 : 7-dinitrophenanthridone when heated with cuprous oxide–acetic anhydride in pyridine.[9]

[1] Caldwell and Walls, *J.*, 1952, 2156.
[2] Ritchie, *J. Proc. Roy. Soc. New South Wales*, 1945, **78**, 177.
[3] Walls, *J.*, 1935, 1407.
[4] Schmidt, Retzlaff, and Haid, *Annalen*, 1912, 390, 224; Barker and Barker, *J.*, 1954, 870.
[5] Walls, *J.*, 1947, 71.
[6] *Idem*, *J.*, 1934, 107.
[7] Caldwell, *J.*, 1952, 2039.
[8] Albert, Brown, and Duewell, *J.*, 1948, 1292.
[9] Edwards and Stewart, *Chem. and Ind.*, 1952, 472.

2 : 7-Di(ethoxycarbonylamino)phenanthridine formed a sparingly soluble methiodide (IX; R = CO_2Et, X^- = I^-). The more soluble metho(methyl sulphate) (IX; R = CO_2Et, X^- = $MeSO_4^-$) was obtained by brief treatment with methyl sulphate in nitrobenzene at 150°; at higher temperatures considerable decomposition occurred. Hydrolysis of the urethane groups was effected in aqueous sulphuric acid at 140°, the diamine being isolated most readily as the sparingly soluble iodide (IX; R = H, X^- = I^-). For biological testing it was converted into the more soluble chloride.



With the exception of 9-picrylaminophenanthridine,[10] no 9-anilinophenanthridine appears to have been described, although 9-amino-, 9-alkylamino-, and 9-dialkylamino-phenanthridines are well known.[11] By virtue of its amidine-like structure, 9-anilino-phenanthridine can theoretically exist in two tautomeric forms. Recent evidence [12] suggests that *N*-heteroaromatic amines of this type normally exist in the " amino "-form (as XI) and this structure is assumed throughout the present paper.

9-Chloro-2 : 7-dinitrophenanthridine condensed readily with *p*-nitroaniline to form the weakly basic 2 : 7-dinitro-9-*p*-nitroanilinophenanthridine (XII; R = NO_2, R′ = H) which yielded an acetyl derivative (XII; R = NO_2, R′ = Ac) only on prolonged boiling with acetic anhydride and pyridine. Neither the trinitro-base nor its acetyl derivative could be made to form a quaternary salt with methyl iodide, methyl sulphate, or methyl toluene-*p*-sulphonate. Morgan and Walls [13] were unable to quaternise the acetyl derivative of 9-aminophenanthridine, which observation led them to suggest that it was in fact the

[10] Morgan and Stewart, *J.*, 1938, 1304.
[11] Walls, *J.*, 1938, 389; cf. Finkelstein and Linder, *J. Amer. Chem. Soc.*, 1951, **73**, 302.
[12] Angyal and Angyal, *J.*, 1952, 1461; Angyal and Werner, *ibid.*, p. 2911; Goulden, *ibid.*, p. 2939; Short, *ibid.*, p. 4584.
[13] Morgan and Walls, *J.*, 1932, 2227.

acetyl derivative of the tautomeric imino-form. Failure to quaternise 2 : 7-dinitro-9-*p*-nitrophenylphenanthridine has also been recorded.[14]

Reduction of the derivative (XII; R = NO_2, R′ = H) with stannous chloride yielded 2 : 7-diamino-9-*p*-aminoanilinophenanthridine (XI; R = NH_2) which formed both a triacetyl (X; R = Ac, R′ = H) and a tetra-acetyl derivative (X; R = Ac, R′ = Ac). The tetra-acetyl derivative failed to react with methyl iodide in boiling methanol, but with the same reagents at 110° in a sealed tube degradation unexpectedly occurred to 2 : 7-bis-dimethylaminophenanthridone bismethiodide (VII). The same salt was obtained under similar conditions from both the triacetyl derivative (X; R = Ac, R′ = H) and the free base (XI; R = NH_2). For comparison, an authentic specimen of the bismethiodide (VII) was prepared from 2 : 7-diaminophenanthridone and identity was confirmed by examination of the ultraviolet absorption spectra. It is unlikely that degradation was preceded by formation of an unstable 10-methiodide since subsequent decomposition should then have led to the corresponding 10-methylphenanthridone. Thus Morgan and Walls [15] found that 9-dimethylaminophenanthridine 10-methiodide was decomposed by hot water into 10-methylphenanthridone.

Parallel experiments were carried out with 2 : 7-diamino-9-anilinophenanthridine (XI; R = H), prepared from 9-chloro-2 : 7-dinitrophenanthridine by condensation with aniline followed by reduction with stannous chloride. When its triacetyl derivative was heated with methyl iodide–methanol at 110°, the salt (VII) was again formed, but under milder conditions a crystalline iodide was obtained which apparently contained 0·8 *N*-methyl group. Hydrolysis of the acetyl groups, however, resulted in the recovery of the original 2 : 7-diamino-9-anilinophenanthridine.

To prevent the hydrolysis of the acetamido-groups which occurred in the degradation with methyl iodide, the amino-groups of the base (XI; R = NH_2) were protected by conversion into the urethanes. When 2 : 7-di(ethoxycarbonylamino)-9-*p*-ethoxycarbonylaminoanilinophenanthridine (X; R = CO_2Et, R′ = H) was boiled with methyl iodide in ethanol, a crystalline salt was obtained which appeared to be the hydriodide of the methylated compound (X; R = CO_2Et, R′ = Me). It was converted into the free base, which was treated further with methyl iodide at 110°, but the product was a mixture, the *N*-methyl content of which had not increased. Experiments with other alkylating agents were equally unsatisfactory.

An alternative approach to the required quaternary salts was then considered, involving the preliminary quaternisation of 9-chloro-2 : 7-dinitro- or 9-chloro-2 : 7-di(ethoxycarbonylamino)-phenanthridine and subsequent condensation with aniline or *p*-nitroaniline. In the quinoline series it is known that the reactivity of a halogen in the 2- or the 4-position is increased by quaternisation, which takes place under mild conditions.[16,17] Thus 2-iodo- and 4-chloro-quinoline methiodide readily form the 2- and the 4-anilino-derivative, respectively.[16,18] 9-Chloro-2 : 7-dinitrophenanthridine, on the other hand, was unaffected by methyl sulphate or methyl iodide in boiling benzene or toluene, and even by fusion with methyl toluene-*p*-sulphonate. Heating with methyl iodide in methanol caused hydrolysis to 2 : 7-dinitrophenanthridone. When 9-chloro-2 : 7-di(ethoxycarbonylamino)phenanthridine was heated with dry methyl iodide at 110°, the 9-chloro-group was replaced by iodine, but without concomitant quaternisation.

In a final attempt to obtain a quaternary salt, the 9-chloro-compounds were heated with tertiary bases, Morgan and Walls [15] having shown that 9-chlorophenanthridine itself condensed with trimethylamine to form trimethylphenanthrid-9-ylammonium iodide. 9-Chloro-2 : 7-di(ethoxycarbonylamino)phenanthridine was unaffected by alcoholic trimethylamine at 130—140° and gave no quaternary salt with boiling dimethylaniline, while 9-chloro-2 : 7-dinitrophenanthridine crystallised unchanged from boiling dimethylaniline.

[14] Walls and Whittaker, *J.*, 1950, 42.
[15] Morgan and Walls, *J.*, 1938, 396.
[16] Alekseeva, *J. Gen. Chem.* (*U.S.S.R.*), 1940, **10**, 263.
[17] Bergstrom, *Chem. Rev.*, 1944, **35**, 199, 211; Bahner, Easley, Pickens, Lyons, Norton, Walden, and Biggerstaff, *J. Amer. Chem. Soc.*, 1951, **73**, 3499.
[18] Brydowna, *Roczniki Chem.*, 1932, **12**, 89.

The author thanks Mrs. R. Stone for the following biological results: 2 : 7-Diamino-10-methylphenanthridinium chloride (IX; R = H, X^- = Cl^-) was inactive against *T. rhodesiense* and was effective, but not curative, against *T. congolense*. 2 : 7-Di(ethoxycarbonylamino)-10-methylphenanthridinium methyl sulphate (IX; R = CO_2Et, X^- = $MeSO_4^-$), 2 : 7-di(ethoxycarbonylamino)-9-*p*-ethoxycarbonylaminoanilinophenanthridine monohydrochloride, 2 : 7-diamino-9-anilinophenanthridine hydrochloride, and 2 : 7-diamino-9-*p*-aminoanilinophenanthridine hydrochloride were inactive against both organisms.

Experimental

2 : 7-*Diaminophenanthridone*.—A solution of 2 : 7-diaminofluorenone (31·3 g.) in concentrated sulphuric acid (250 ml.) was mechanically stirred and cooled to −30°. Sodium azide (21·8 g.) in water (75 ml.) was slowly added during 1·25 hr., at <0°, and water (75 ml.) was then added during the next 0·75 hr. The solution was poured on ice and aqueous ammonia (*d* 0·88), and the product was filtered off. Crystallisation from nitrobenzene gave 2 : 7-*diaminophenanthridone* (26 g., 78%) in thin prisms, m. p. 310—312° (decomp.) (Found: C, 69·0; H, 5·3; N, 18·3. $C_{13}H_{11}ON_3$ requires C, 69·3; H, 5·0; N, 18·65%). Heating the base (1 g.) with methyl iodide in methanol at 115° for 24 hr. afforded 2 : 7-*bisdimethylaminophenanthridone bismethiodide dihydrate* (2·6 g., 98%), yellow needles (from water), m. p. 330—334° (decomp.), which gave successively the monohydrate and the anhydrous salt when dried at 110°; the latter rapidly re-formed the dihydrate in air [Found (after drying at 100°): C, 38·9; H, 5·0; N, 7·0; I, 40·85; H_2O, 3·8; regain in air of anhydrous salt, 5·9. $C_{19}H_{25}ON_3I_2,H_2O$ requires C, 39·1; H, 4·7; N, 7·2; I, 43·5; H_2O, 3·1. $C_{19}H_{25}ON_3I_2,2H_2O$ requires H_2O, 6·0%] [$\lambda_{max.}$ in 0·1N-HCl at 336 (ε 8200), 325 (ε 9700), and 260 mμ (ε 23,300); inflexion at 269 mμ (ε 14,200)].

2 : 7-*Di(ethoxycarbonylamino)phenanthridone*.—2 : 7-Diaminophenanthridone (24·3 g.), ethyl chloroformate (25·8 ml.), and diethylaniline (43 ml.) were boiled in dry ethanol (700 ml.) for 3 hr. The cooled mixture was filtered, giving 2 : 7-*di(ethoxycarbonylamino)phenanthridone* which formed prisms, m. p. >360°, from dioxan (Found: C, 61·5; H, 5·4; N, 11·4. $C_{19}H_{19}O_5N_3$ requires C, 61·7; H, 5·2; N, 11·4%). The uncrystallised material (33·6 g., 84%) was pure enough for conversion into the chloro-compound.

9-*Chloro*-2 : 7-*di(ethoxycarbonylamino)phenanthridine*.—2 : 7-Di(ethoxycarbonylamino)phenanthridone (11·2 g.) was boiled with phosphorus oxychloride (55 ml.) for 30 min., and the mixture was then slowly poured into excess of aqueous ammonia and ice. The product was filtered off, washed with water, and added to boiling 2-ethoxyethanol, and the resulting solution was immediately diluted with water until cloudy; this gave 9-*chloro*-2 : 7-*di(ethoxycarbonylamino)phenanthridine* [7·95 g. (67%), m. p. 250—252° (decomp.)], which separated in needles, m. p. 252—254° (decomp.), from a large volume of ethanol (Found: Cl, 8·85. $C_{19}H_{18}O_4N_3Cl$ requires Cl, 9·15%).

2 : 7-*Di(ethoxycarbonylamino)*-9-*formylphenanthridine*.—2 : 7-Di(ethoxycarbonylamino)-9-methylphenanthridine (10 g.) and selenium dioxide (3·05 g.) in dioxan (400 ml.) and water (10 ml.) were boiled under reflux for 7 hr. and the solution was then filtered through alumina, which was washed with hot dioxan. The combined dioxan solutions when concentrated gave the aldehyde (7·45 g., 71%), m. p. 250—262° (decomp.), pure enough for further oxidation. For the pure aldehyde Caldwell [7] gave m. p. 270—275° (decomp.).

2 : 7-*Di(ethoxycarbonylamino)phenanthridine*-9-*carboxylic Acid*.—The foregoing aldehyde (12 g.) in pyridine (157 ml.) was heated to 50—55° and mechanically stirred whilst potassium permanganate (3·7 g.) in water (74·2 ml.) was added during 1·5 hr. After a further 1·5 hr. at 50—55°, the mixture was boiled and filtered, and the black residue was extracted successively with hot pyridine (2 × 150 ml.) and aqueous potassium carbonate (3 × 150 ml.). The pyridine extracts were combined with the original filtrate and concentrated under reduced pressure to 150 ml.; the carbonate extract was then added and the mixture was boiled and filtered. The residue after further extraction with potassium carbonate solution was unchanged aldehyde (2·85 g.). The combined solutions were added to acetic acid containing a small amount of dilute hydrochloric acid. The orange-red acid which separated was filtered off, washed with water, and purified by dissolution in hot N-aqueous ammonia, filtration (the insoluble residue contained more unchanged aldehyde), and addition of the filtrate to acetic acid. The reprecipitated *acid* (5·3 g., 56% allowing for recovered aldehyde) was washed with water and dried at 100° (Found: C, 60·0; H, 5·1; N, 10·6. $C_{20}H_{19}O_6N_3$ requires C, 60·45; H, 4·8; N, 10·6%).

2 : 7-*Di(ethoxycarbonylamino)phenanthridine*.—(*a*) The foregoing acid (5 g.) in nitrobenzene (25 ml.) was boiled for 2 min. and the solution was then cooled, mixed with ether, and filtered.

The solid was crystallised from aqueous pyridine, giving 2 : 7-*di*(*ethoxycarbonylamino*)*phenanthridine* [3·2 g. (72%), m. p. 250—253° (decomp.)] which formed blades, m. p. 252—254° (decomp.), from alcohol (Found : C, 64·3; H, 6·05; N, 11·9. $C_{19}H_{19}O_4N_3$ requires C, 64·6; H, 5·4; N, 11·9%. (*b*) A suspension of 9-chloro-2 : 7-di(ethoxycarbonylamino)phenanthridine (4 g.) in hot alcohol (400 ml.) containing potassium hydroxide (1 g.) and Raney nickel was shaken with hydrogen. When the uptake slackened fresh catalyst was added and the suspension was reheated. When the mixture began to fluoresce (owing to formation of the 9 : 10-dihydro-compound), it was heated and filtered and the solid was extracted with hot pyridine (2 × 75 ml.). The filtrate and the extracts were combined and concentrated; the residue was diluted with water and filtered. The product was crystallised from nitrobenzene and from aqueous pyridine, giving 2 : 7-di(ethoxycarbonylamino)phenanthridine (2·1 g., 58%), m. p. 253—256° (decomp.) (Found : C, 64·9; H, 5·9; N, 11·6%). On one occasion; when the chloro-compound (4 g.) was similarly reduced under pressure, the product (2·85 g.; m. p. 190—192°) was 2 : 7-*di*(*ethoxycarbonylamino*)-9 : 10-*dihydrophenanthridine*, m. p. 192—194° (after recrystallisation from aqueous alcohol) (Found : C, 64·2; H, 5·9; N, 11·6. $C_{19}H_{21}O_4N_3$ requires C, 64·2; H, 6·0; N, 11·8%). Its solutions are colourless with an intense violet fluorescence. The *acetyl derivative* (Found : C, 63·6; H, 6·1; N, 10·7. $C_{21}H_{23}O_5N_3$ requires C, 63·5; H, 5·8; N, 10·6%) formed feathery needles, m. p. 230—232°, from alcohol, and showed no fluorescence in solution.

2 : 7-*Diaminophenanthridine*.—2 : 7-Di(ethoxycarbonylamino)phenanthridine (0·5 g.) in concentrated sulphuric acid (1·2 ml.) and water (1 ml.) was heated at 160° for 30 min. The solution was basified and the base was filtered off, and recrystallised from water, giving 2 : 7-*diaminophenanthridine*, yellow needles, m. p. 208—210° (decomp.) (Found : C, 74·5; H, 5·3. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3%).

2 : 7-*Di*(*ethoxycarbonylamino*)-10-*methylphenanthridinium Methyl Sulphate*.—2 : 7-Di(ethoxycarbonylamino)phenanthridine (3·2 g.) in redistilled nitrobenzene (50 ml.) was maintained at 150° whilst redistilled methyl sulphate (3·2 ml.) was added. After 1 min. the mixture was cooled, diluted with ether, and filtered, and the product was washed with ether. The *metho*(*methyl sulphate*) (4·15 g., 92%) formed orange needles, decomp. >280°, from alcohol (green fluorescent solution) (Found : N, 8·8. $C_{21}H_{25}O_8N_3S$ requires N, 8·8%). Treatment of an aqueous solution of the salt with potassium iodide afforded the corresponding *methiodide* (also obtained directly from the original base with methyl iodide–methanol), which crystallised from alcohol (green fluorescent solution) in yellow needles, decomp. >260° (Found : I, 25·4. $C_{20}H_{22}O_4N_3I$ requires I, 25·6%).

2 : 7-*Diamino*-10-*methylphenanthridinium Iodide*.—The foregoing metho(methyl sulphate) (4·15 g.) in concentrated sulphuric acid (20 ml.) and water (15 ml.) was heated at 140° for 45 min. The solution was poured into water, neutralised to pH 7 with aqueous ammonia, and filtered hot, and the filtrate was treated with solid potassium iodide and cooled. The quaternary iodide (2·75 g., 90%) was filtered off, washed with cold water and alcohol, and dried at 100°. The same *iodide* was similarly prepared from 2 : 7-di(ethoxycarbonylamino)-10-methylphenanthridinium iodide, and formed red needles, m. p. 288—290° (decomp.) (Found : N, 11·8; I, 35·7. $C_{14}H_{14}N_3I$ requires N, 11·95; I, 36·15%), from water. Boiling its aqueous solution with freshly prepared silver chloride afforded the corresponding *chloride* (Found : N, 14·5; Cl, 12·2; loss of wt. at 100°/15 mm., 9·4; regain in air, 9·3. $C_{14}H_{14}N_3Cl,1{\cdot}5H_2O$ requires N, 14·7; Cl,12·4; H_2O, 9·4%) which formed red prisms, m. p. 278—280° (decomp.), from alcohol.

9-*Anilino*-2 : 7-*dinitrophenanthridine*.—9-Chloro-2 : 7-dinitrophenanthridine (2 g.) and aniline (9 ml.) were boiled under reflux for 1 hr.; the mixture was then cooled and diluted with ether. The product was filtered off, washed with ether, extracted with boiling water, and crystallised from acetone, giving 9-*anilino*-2 : 7-*dinitrophenanthridine* (2·2 g., 93%) in orange prisms or needles, m. p. 316—318° (Found : C, 63·4; H, 3·4; N, 15·5. $C_{19}H_{12}O_4N_4$ requires C, 63·3; H, 3·3; N, 15·55%).

2 : 7-*Dinitro*-9-p-*nitroanilinophenanthridine*, similarly prepared at 180—200° in 93% yield, formed orange needles, decomp. 350—360° (Found : C, 56·6; H, 3·0; N, 17·0. $C_{19}H_{11}O_6N_5$ requires C, 56·3; H, 2·7; N, 17·3%), from nitrobenzene. Treatment of the base with boiling acetic anhydride–pyridine gave the *acetyl derivative*, which crystallised from chloroform in needles, decomp. 300—304° (Found : N, 15·4. $C_{21}H_{13}O_7N_5$ requires N, 15·65%).

2 : 7-*Diamino*-9-*anilinophenanthridine*.—9-Anilino-2 : 7-dinitrophenanthridine (2·2 g.) was added to a hot solution of stannous chloride dihydrate (20 g.) in concentrated hydrochloric acid (20 ml.); the solution was boiled for 30 min., cooled, and then cautiously poured into concentrated aqueous sodium hydroxide. Crystallisation of the base from aqueous acetone gave

2 : 7-*diamino*-9-*anilinophenanthridine* (1·45 g., 79%) in yellow plates, m. p. 225—226° (decomp.) (Found : C, 75·9; H, 5·9; N, 18·2. $C_{19}H_{16}N_4$ requires C, 76·0; H, 5·3; N, 18·7%). The *hydriodide* formed orange needles, m. p. 224—226° (decomp.), from water (Found : N, 12·6; I, 29·05. $C_{19}H_{16}N_4,HI,H_2O$ requires N, 12·55; I, 28·5%). The *triacetyl derivative*, prepared with acetic anhydride–pyridine at 100° and crystallised from pyridine–ether, had m. p. 300—304° (Found : C, 70·0; H, 5·4; N, 12·9. $C_{25}H_{22}O_3N_4$ requires C, 70·4% H, 5·2; N, 13·1%).

2 : 7-*Diamino*-9-p-*aminoanilinophenanthridine*, similarly prepared in 90% yield, separated from aqueous acetone in yellow plates, m. p. 244—245° (decomp.) (Found : C, 72·3; H, 5·3; N, 21·4. $C_{19}H_{17}N_5$ requires C, 72·4; H, 5·4; N, 22·2%). The *triacetyl derivative*, prepared with acetic anhydride–pyridine at 100°, separated from acetone in needles, m. p. 328—329° (decomp.) (Found : C, 66·7; H, 5·3; N, 15·6; loss of wt. at 100°/15 mm., 2·5; regain in air, 2·5. $C_{25}H_{23}O_3N_5,0·5H_2O$ requires C, 66·7; H, 5·4; N, 15·55; H_2O, 2·0%). The *tetra-acetyl derivative*, formed when the base was boiled with acetic anhydride–pyridine, crystallised from aqueous pyridine in prisms, decomp. *ca.* 360° (Found : C, 63·1; H, 5·8; N, 13·5; loss of wt. at 100°/20 mm., 6·8. $C_{27}H_{25}O_4N_5,2H_2O$ requires C, 62·3; H, 5·6; N, 13·45; H_2O, 6·9%). The anhydrous compound re-formed the dihydrate in air.

2 : 7-*Di*(*ethoxycarbonylamino*)-9-p-*ethoxycarbonylaminoanilinophenanthridine*.—2 : 7-Diamino-9-*p*-aminoanilinophenanthridine (0·31 g.) in alcohol (50 ml.) was treated with diethylaniline (0·75 g.) and ethyl chloroformate (0·55 g.) and heated for 2 hr. under reflux at 100°. The solution was concentrated, the residual oil diluted with water and slightly acidified with hydrochloric acid, and the *hydrochloride* filtered off. Crystallisation from alcohol–ether gave yellow needles, m. p. 211—213° (decomp.) (Found : C, 56·8; H, 6·7; N, 12·25; Cl, 5·8; H_2O, 3·55. $C_{28}H_{29}O_6N_5,HCl,H_2O$ requires C, 57·4; H, 5·5; N, 11·9; Cl, 6·1; H_2O, 3·1%), partially hydrolysed by water with precipitation of the base. Crystallisation of the *base* from alcohol afforded needles, m. p. 238—242° (Found : C, 62·7; H, 5·6; N, 13·0. $C_{28}H_{29}O_6N_5$ requires C, 63·3; H, 5·5; N, 13·2%).

Reaction of Triacetyl-2 : 7-*diamino*-9-*anilinophenanthridine with Methyl Iodide*.—(*a*) The triacetyl derivative (0·6 g.), excess of methyl iodide, and methanol were heated under reflux for 18 hr., and the solution was then cooled. After 3 days the product (0·63 g.) was filtered off and crystallised from alcohol, giving yellow plates, m. p. 330—340° (decomp.) (Found : N, 10·5; I, 22·3; *N*-Me, 2·0. $C_{26}H_{25}O_3N_4I$ requires N, 9·85; I, 22·3; *N*-Me, 2·6%). When the salt was hydrolysed with boiling concentrated hydrochloric acid, iodine was evolved and 2 : 7-diamino-9-anilinophenanthridine, m. p. 224—226° (decomp.) (Found : C, 75·9; H, 5·4%), was recovered. Its m. p. was not depressed when it was mixed with an authentic specimen.

(*b*) The triacetyl derivative (0·4 g.) in excess of methyl iodide and methanol was heated for 18 hr. in a sealed tube at 110°. The product was filtered off and crystallised from water, yielding 2 : 7-bisdimethylaminophenanthridone bismethiodide dihydrate in yellow needles, m. p. 330° (decomp.) (Found : C, 38·7; H, 5·0; N, 7·35; I, 43·6; H_2O, 7·3; *N*-Me, 14·2; regain in air of anhydrous salt, 6·0. Calc. for $C_{19}H_{25}ON_3I_2,2H_2O$: C, 38·0; H, 4·85; N, 7·0; I, 42·3; H_2O, 6·0; *N*-Me, 15·0%).

Reaction of 2 : 7-*Diamino*-9-p-*aminoanilinophenanthridine and its Acetyl Derivatives with Methyl Iodide*.—(*a*) 2 : 7-Diamino-9-*p*-aminoanilinophenanthridine (0·35 g.) with methyl iodide–methanol at 115° gave 2 : 7-bisdimethylaminophenanthridone bismethiodide dihydrate (0·25 g.), m. p. 320—330° (decomp.) (Found : C, 38·4; H, 5·0; N, 7·0; I, 41·65; H_2O, 4·3; regain in air of anhydrous salt, 5·5%) [$\lambda_{max.}$ in 0·1N-HCl at 336 (ε 8300), 325 (ε 9830), and 260 mμ (ε 23,650); infl. at 269 mμ (ε 14,900)].

(*b*) The same salt, m. p. 310—325° (decomp.) (Found : N, 7·4; I, 43·5%), was obtained from the triacetyl derivative at 140°.

(*c*) The tetra-acetyl derivative was recovered substantially unchanged from boiling methyl iodide–methanol after 20 hr. At 110° the phenanthridone bismethiodide was formed, having m. p. 345° (decomp.) (Found : C, 37·9; H, 4·6; N, 7·45; I, 43·6%).

Reaction of 2 : 7-*Di*(*ethoxycarbonylamino*)-9-p-*ethoxycarbonylaminoanilinophenanthridine with Methyl Iodide*.—The trisurethane (0·53 g.) and anhydrous sodium carbonate (0·05 g.) were boiled for 13 hr. with excess of methyl iodide in alcohol. The red solution was evaporated and the residue was crystallised twice from acetone–ether, yielding 2 : 7-*di*(*ethoxycarbonylamino*)-9-(N-*methyl*-p-*ethoxycarbonylaminoanilino*)*phenanthridine hydriodide*, m. p. 250—255° (decomp.) (Found : C, 10·3; I, 18·4; OEt, 20·1; *N*-Me, 1·2. $C_{29}H_{31}O_6N_5,HI$ requires N, 10·4; I, 18·8; OEt, 20·1; *N*-Me, 2·2%). The *base*, purified from aqueous alcohol, appeared to be amorphous; it had m. p. 210—220° (decomp.) (Found : C, 63·4; H, 5·8; N, 12·5. $C_{29}H_{31}O_6N_5$ requires C, 63·8; H, 5·7; N, 12·8%).

Reduction of 9-*Chloro*-2 : 7-*dinitrophenanthridine.*—The dinitro-compound (0·25 g.) and platinum oxide (0·1 g.) in dioxan (50 ml.) were shaken with hydrogen at atmospheric temperature and pressure; the uptake was 160 ml. in 30 min. The yellow solution (green fluorescence) was filtered and evaporated and the residue was crystallised from acetone–benzene, giving yellow prisms, decomp. >200° (Found : N, 16·9; Cl, 14·3. Calc. for $C_{13}H_{10}N_3Cl$: N, 17·2; Cl, 14·6. Calc. for $C_{13}H_{12}N_3Cl$: N, 17·1; Cl, 14·3%). The diamino-chloro-compound was soluble in dilute hydrochloric acid and was precipitated unchanged by alkali.

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