78. *Researches in the Phenanthridine Series. Part V. The Colour and Antiseptic Properties of Quaternary Salts.*

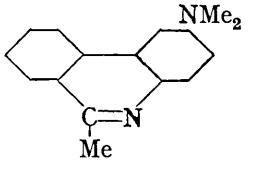
By Sir Gilbert Morgan and Leslie P. Walls, with a Note by C. H. Browning, R. Gulbransen, and J. V. M. Robb.

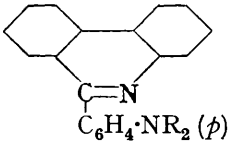
In Parts I and II the preparation was described of various phenanthridine compounds containing amino-groups, and of quaternary salts derived from them analogous to those of the acridine series. This work has now been amplified, particularly with a view to gaining information on the colour and antiseptic properties of phenanthridinium compounds.

By methylation of the corresponding compounds containing primary amino-groups the ditertiary amines, 3-dimethylamino-9-methyl- and 9-*p*-dimethylamino-phenyl-phenanthridine have been prepared, and from the latter the three possible quaternary salts have been obtained. The colours of the latter conform to a theory of benzenoid-quinonoid resonance. Further information on the mechanism of the conversion of acyl-*o*-xenylamines into phenanthridine compounds has led to the synthesis of two series based on 3(and 7)-amino-9-*p*-aminophenylphenanthridine, and certain quaternary salts derived from these triamines have unexpected trypanocidal properties. In addition, the antiseptic properties of thirty-one compounds, including a series of amino-compounds derived from 9-chloro- and 9-ω-chloromethyl-phenanthridine, are reported on by Professor C. H. Browning and his collaborators, and some are shown to be powerfully active both in peptone water and in a serum medium.

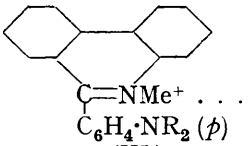
In Parts I and II (J., 1931, 2451; 1932, 2230) attention was drawn to the colour of certain quaternary salts of the series, which also contained primary amino-groups. Further information has been obtained by replacement of the latter by tertiary amino-groups, and by the study of other series of salts. At the same time a comprehensive series of salts has become available for the investigation of antiseptic properties. In addition, a number of derivatives of 9-chloro- and 9-ω-chloromethyl-phenanthridine have been prepared for the latter purpose.

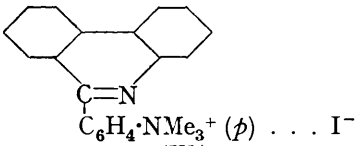
3-Amino-9-methylphenanthridine (J., 1932, 2228) was smoothly converted by methyl iodide into the dimethylamino-compound (I), but pure quaternary salts could not be obtained therefrom by further methylation.

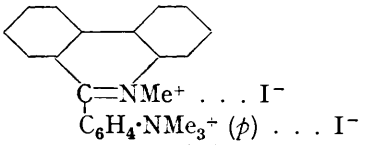
(I.) 

 (II.)

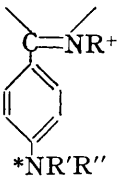
9-*p*-Aminophenylphenanthridine (II; R = H) (J., 1931, 2454) was similarly converted into a tertiary amine (II; R = Me), and from the latter all three possible quaternary salts were obtained: the red *hetero-N*-salt (III; R = Me), the white *ar-N*-salt (IV), and the diquaternary salt (V). Although the di-iodide (V) is yellow, the corresponding dichloride is white, the yellow colour being due possibly to a like cause to that of mercuric iodide. These constitutions were confirmed by methylation of 9-*p*-aminophenyl-10-methylphenanthridinium iodide (III; R = H), whereby (III; R = Me) and (V) alone were obtained.

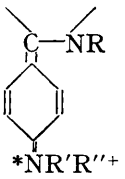

(III.)


(IV.)


(V.)

The colour relationships of the series derived from (II) may now be summarised. Bases, primary and tertiary, and acetyl derivatives are colourless or almost so, but monoacid salts and those with *hetero-N* alone quaternary are red. The appearance of colour is always associated with the possibility of valency tautomerism (involving electron displacements only), and thus is probably due to a like cause to that of the basic dyes of the acridine, cyanine and triphenylmethane series, namely, wave-mechanical resonance; the true structure of a coloured salt is intermediate between the benzenoid (VI) and the quinonoid (VII) forms (R = H or Me).

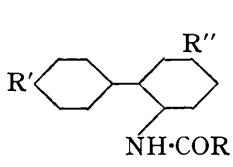
(VI.) 

 (VII.)

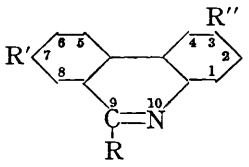
When *ar-N** is quaternary, this valency tautomerism is impossible; when R′ = H and R″ = CO·CH_3, it is largely suppressed. It follows that in the coloured monoacid salt, proton attaches itself to *hetero-N*.

In the synthesis of phenanthridine derivatives (IX) from acyl-*o*-xenylamines (VIII) with the agency of phosphorus oxychloride considerable resinification may occur, which is due probably to a side reaction involving elimination of the acyl group. The side reaction predominates when in (VIII) R = Me, R′ = NO_2, and R″ = H (or NO_2). When acetyl is replaced by a less readily removable group (R = C_6H_5 or *p*-C_6H_4·NO_2), the side reaction is suppressed and ring closure occurs, though very slowly. Appreciation of this factor has

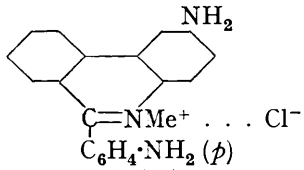
led to two series of derivatives, from which isomerides of chrysaniline have been prepared. 5-Nitro-2-*p*-nitrobenzamidodiphenyl (VIII; R = *p*-$C_6H_4{\cdot}NO_2$, R′ = H, R″ = NO_2) was converted into 3-nitro-9-*p*-nitrophenylphenanthridine (IX; R = *p*-$C_6H_4{\cdot}NO_2$, R′ = H, R″ = NO_2), which was readily reduced to the diamino-compound. Addition of methyl *p*-toluenesulphonate to the diacetyl derivative of the diamine converted it into a quaternary



(VIII.)

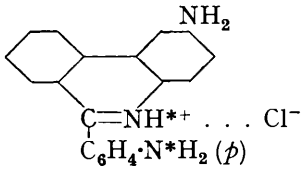


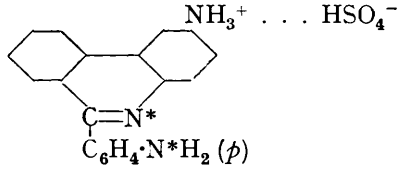
(IX.)



(X.)

(XI.)



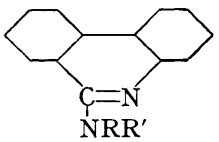


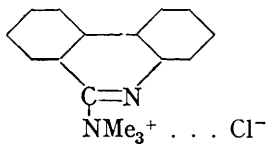
(XII.)

salt, which, after hydrolysis of the acetyl groups, yielded red 3-amino-9-*p*-aminophenyl-10-methylphenanthridinium chloride (X). The series corresponding to 7-amino-9-*p*-aminophenylphenanthridine was similarly prepared.

The colour relationships of these chrysaniline analogues conform to the foregoing postulates, except that, whereas the hydrobromide of 3-amino-9-*p*-aminophenylphenanthridine is red, the sparingly soluble sulphate is almost colourless. In a salt of this type, proton can attach itself to one of three possible basic centres: if it chooses the *hetero-N* (XI), the salt should be coloured, but if the attachment is to either primary amino-group (compare XII), the salt would probably be colourless. The sulphate may be of the latter type, but the hydrobromide of the former. The second stage of ionisation of sulphuric acid may be effective, however, so that in the colourless salt as in (V) two basic centres (indicated by * in XI and XII) are satisfied with consequent suppression of valency tautomerism. This alternative explanation is not supported by the fact that the sulphate of 7-amino-9-*p*-aminophenylphenanthridine, for which similar arguments should apply, is coloured.

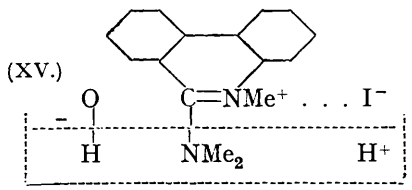
(XIII.)

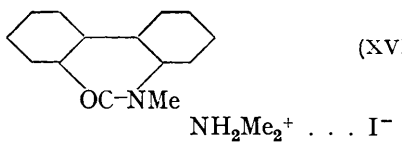




(XIV.)

(XV.)





(XVI.)

9-Chlorophenanthridine condensed with mono-, di- and tri-methylamine to yield respectively 9-methyl- (XIII; R = H, R′ = Me), 9-dimethyl- (XIII; R = R′ = Me) aminophenanthridine, and 9-phenanthridyltrimethylammonium chloride (XIV). The diamine (XIII; R = R′ = Me) was further methylated to 9-dimethylamino-10-methylphenanthridinium iodide (XV), which was unexpectedly unstable in hot aqueous solution; it was converted smoothly into *N*-methylphenanthridone (XVI), a hydrolysis which establishes its constitution.

9-ω-Chloromethylphenanthridine likewise condensed readily with trimethylamine, piperidine and pyridine with the formation of similar compounds.

Note on the Antiseptic Action of Certain Phenanthridine Compounds.†

The method of measuring antiseptic activity is that previously used by the authors (Browning and Gulbransen, *Brit. J. Exp. Path.*, 1921, **2**, 95; Browning, Cohen, Gaunt, and Gulbransen, *Proc. Roy. Soc.*, 1922, *B*, **93**, 329; Browning, Cohen, Ellingworth, and Gulbransen, *ibid.*, 1926, *B*, **100**, 293). Two media were employed : (a) a 0·7% solution of bacteriological peptone in 0·35% sodium chloride solution adjusted to a p_H of 7·2—7·8 and (b) sterile ox serum previously heated for several hours at 56° (only such specimens of serum were used as yielded good growths of *B. coli*). Each medium in 1 c.c. amounts, containing various concentrations of the substances to be tested, was inoculated with 0·1 c.c. of a 1 : 1000 dilution of a 24 hours' culture of *Staphylococcus aureus* or *B. coli*. The results were read after 48 hours at 37°, inhibition of growth being judged by absence of obvious turbidity of the originally clear medium and by sterility or very limited growth when a loopful of the mixture was subcultured on agar. The lowest concentration of each substance which produced this result, termed the " inhibitory concentration," has been ascertained. This value yields the most satisfactory indication of the antiseptic power of slowly acting bactericidal agents such as complex organic compounds usually are. It is employed in preference to the sterilising concentration for purposes of comparison of compounds, because inhibition of bacterial growth may be produced over a wide range of concentrations before the actual sterilising concentration is attained. Also in repeated tests the concentration of antiseptic at which inhibition first occurs tends to be more constant than that at which complete sterilisation is effected.

Thirty-one phenanthridine compounds were examined for antiseptic properties; appropriate references are given, numbers otherwise referring to the experimental section. Phenanthridine hydrochloride (1*;‡ Pictet and Ankersmit, *Ber.*, 1889, **22**, 3340) has only a moderate antiseptic action in aqueous medium, and this is diminished in serum. The activity of the molecule is not significantly increased by the simultaneous introduction of a methyl group into the 9-position and an amino-group (2) or dimethylamino-group (3) into the 3-position. Similarly, the presence of an amino-group attached to the 9-C atom as in 9-aminophenanthridine (24; J., 1932, 2230), or of a methylamino-group (25), or dimethylamino-group (26) does not markedly affect the antiseptic action. 9-Phenanthridyltrimethylammonium iodide (27) is also of the same order of potency as phenanthridine.

9-ω-Phenanthridylmethyltrimethylammonium iodide (29*) is similar to (1*) in aqueous medium, but as compared with the latter shows no weakening of action in serum. 9-ω-Phenanthridylmethyl-*N*-pyridinium chloride (30*) is among the most active members of the series for both organisms in serum as well as in aqueous medium. 9-ω-Piperidinomethylphenanthridine hydrochloride (31*), however, shows distinct weakening of action in serum as compared with peptone water medium.

In general the presence of a quaternary nitrogen atom as in phenanthridine methiodide (4*; Pictet and Ankersmit, *loc. cit.*) leads to distinct enhancement of action in serum. Antiseptic properties are not further greatly affected by the presence in addition of an amino-group in the 3-position as in 3-amino-9 : 10-dimethylphenanthridinium chloride (5; J., 1932, 2230) or of an acetamido-group (6 and 7).

The compounds in which an aminophenyl group is attached in the 9-position (8—23) exhibit certain definite relations between constitution and action.

These are well exemplified in the series which has in addition an amino-group in the 3-position. 3-Amino-9-*p*-aminophenylphenanthridine sulphate (18*) is only moderately antiseptic for either organism in peptone water medium and acts less well in serum, being practically equal to (1*). The corresponding quaternary chloride (20*) is very powerfully antiseptic for *Staphylococcus* both in peptone water and in serum and also for *B. coli* in serum. As compared with this, the acetamido-derivative (19*) is greatly reduced in action.

† Work done with the support of the Medical Research Council in the Department of Bacteriology and Pathology, the University and Western Infirmary, Glasgow.

‡ The compounds to the numbers of which an asterisk is attached are given in the table showing antiseptic values.

The series with an amino-group in the 7-position (21—23) possesses respectively activities of nearly the same order as those just mentioned, and shows the same relations between constitution and action. With the 9-aminophenyl compounds lacking substituents in the phenanthridine nucleus (8—14), the results are obscured by the very slight solubility of the phenanthridine salts (8* and 9) in peptone water—less than 1 : 40,000, although a solution of 1 : 1000 is obtained in serum; but the same relations hold here, the quaternary compounds being much the most active (cf. 8* and 10*) and the acetamido-derivative of the latter again being less strongly antiseptic. The 9-*o*-, -*m*- and -*p*-aminophenyl-10-methylphenanthridinium chlorides (13, 14, 10*; J., 1931, 2454) do not differ much in potency among themselves, the last being slightly the most active. The substitution of a dimethylamino- for an amino-group in the last-named causes no striking increase in antiseptic activity when the nitrogen atom is either tertiary (8*, 9) or quaternary (10* and 11* compared with 15* and 16*). On the other hand, the diquaternary compound (17*) is very weak, except in its action on *B. coli* in serum.

As regards the relations between chemical constitution and biological action, certain of the facts established in the present work have analogies in other series. Thus the enhanced antiseptic action of the quaternary salts of the series as compared with the analogous compounds in which the nitrogen atom is tervalent, was also observed with the less powerfully antiseptic members of the acridine series, *e.g.*, 9-phenylacridine and 2 : 7-tetraethyldiaminoacridine (Browning, Cohen, Gaunt, and Gulbransen, *loc. cit.*). Also the effect of acetylation of an amino-group in markedly diminishing antiseptic action has been paralleled in the acridine series (*loc. cit.*), and the same holds for acetylation of the amino-group in the benzene nucleus of quaternary salts of amino-derivatives of styryl- and anil-quinolines (Browning, Cohen, Ellingworth, and Gulbransen, *loc. cit.*). The failure of compounds containing a secondary or tertiary group to show distinct superiority over that containing the corresponding primary amino-group has also been observed in the acridine series, although with the styryl and anil compounds the introduction of methyl or ethyl radicals into the amino-group of the benzene nucleus tends to enhance their antiseptic properties, and a similar result follows in the triphenylmethane dyes.

All the compounds in the present work have been tested for chemotherapeutic action in mice infected experimentally with trypanosomes. Only Nos. 19 and 23 are effective, the latter in infections with *T. brucei* and *T. congolense*, the former sterilising *T. brucei* only (Browning, Morgan, Robb, and Walls, *J. Path. Bact.*, 1938, **46**, 203).

Table of Antiseptic Values.

Substance No.	Antiseptic action.* *Staphylococcus.* P.	S.	*B. coli.* P.	S.	Precipitation.† P.	S.	Substance No.	Antiseptic action.* *Staphylococcus.* P.	S.	*B. coli.* P.	S.	Precipitation.† P.	S.
1	4	<1	4	<1	4	<1	17	1	10	2	100	—	—
4	4	20	4	100	—	—	18	4	<1	2	<1	4	—
8	<1	<1	<1	1	40	2	19	<1	20	<1	4	4	4
10	40	100	2	100	—	—	20	200	100	4	100	—	—
11							29	10	10	1	10	—	—
15	200	200	10	40	—	—	30	40	40	10	40	—	—
16							31	40	4	4	2	2	—

* Antiseptic action : the numbers are the reciprocals ÷ 1000 of the lowest concentrations which suffice to produce inhibition of growth in 48 hours at 37°.

† Precipitation : the numbers are the reciprocals ÷ 1000 of the lowest concentrations (below 1 : 1000) which cause precipitation in the medium.

P = peptone water medium. S = ox serum previously heated at 56°.

Experimental.

3-*Amino*-9-*methylphenanthridine hydrochloride* (2) crystallised from a solution of the base (I) in dilute hydrochloric acid in minute yellow needles (Found : loss at 100°, 13·1; Cl, 12·4. $C_{14}H_{12}N_2,HCl,2H_2O$ requires H_2O, 12·85; Cl, 12·65%).

3-*Dimethylamino*-9-*methylphenanthridine* (I).—The product of the reaction between the primary amine (3 g.) and methyl iodide (6 g.) at 150° for 6 hours was extracted with hot dilute hydrochloric acid. The red extract was neutralised with potassium carbonate, and heated on

the steam-bath until a brown crystalline solid was formed; this was recrystallised from alcohol, forming large, transparent, brown prisms (2 g.), m. p. 146° (Found : C, 81·3; H, 6·75; N, 12·15. $C_{16}H_{16}N_2$ requires C, 81·35; H, 6·8; N, 11·85%). Evaporation of a solution of the *base* in dilute hydrochloric acid (1 equiv.) left a crystalline mass, which gave small red needles of the *hydrochloride* (3) from alcohol; the salt was very soluble in water, but sparingly so in alcohol (Found : Cl, 12·85. $C_{16}H_{16}N_2$,HCl requires Cl, 13·0%).

3-*Acetamido*-9 : 10-*dimethylphenanthridinium Chloride* (6).—When an aqueous solution of the methosulphate (J., 1932, 2230) was treated with potassium iodide, the *iodide* (7) crystallised in yellow needles (Found : I, 32·05. $C_{17}H_{17}ON_2I$ requires I, 32·4%). The iodide was refluxed in aqueous methyl alcohol with silver chloride for 4 hours; after filtration and evaporation to small bulk, ether was added, which precipitated the *chloride* (6) in pale yellow needles (Found : loss at 100°, 5·35; Cl, 11·1. $C_{17}H_{17}ON_2Cl,H_2O$ requires H_2O, 5·65; Cl, 11·15%).

9-p-*Aminophenylphenanthridine Hydrochloride* (8).—The base (II; R = H) was dissolved in hot dilute hydrochloric acid, and ammonia added until red prisms of the *monohydrochloride* separated (Found : Cl, 11·4. $C_{19}H_{14}N_2$,HCl requires Cl, 11·6%).

9-p-*Dimethylaminophenylphenanthridine* (II; R = Me).—The primary amine (3 g.) was methylated by methyl iodide (6 g.) at 150°. After 8 hours the product was extracted with dilute hydrochloric acid. Sodium carbonate was added to the hot solution, and after 1 hour on the steam-bath the precipitate was extracted with benzene. By evaporation of the solvent, the *tertiary amine* was obtained in buff prisms (2 g.), m. p. 179—181°, which were very soluble in benzene, but more sparingly so in alcohol (Found : C, 84·4; H, 5·95; N, 9·75. $C_{21}H_{18}N_2$ requires C, 84·55; H, 6·05; N, 9·4%). The *hydrochloride* (9) crystallised from water in hydrated orange-red transparent plates (Found for salt dried at 100° : Cl, 10·3. $C_{21}H_{18}N_2$,HCl requires Cl, 10·6%).

9-p-*Aminophenyl*-10-*methylphenanthridinium iodide* (11) was obtained in the usual way from the chloride (J., 1931, 2456) in ruby-red transparent prisms (Found : I, 30·1. $C_{20}H_{17}N_2I$ requires I, 30·8%).

9-p-*Acetamidophenyl*-10-*methylphenanthridinium chloride* (12), obtained from the methosulphate (*loc. cit.*), crystallised from its neutral aqueous solution in pale orange prisms (Found : loss at 100°, 9·25. $C_{22}H_{19}ON_2Cl,2H_2O$ requires H_2O, 9·05%. Found for dry salt : Cl, 9·7. $C_{22}H_{19}ON_2Cl$ requires Cl, 9·8%).

9-p-*Dimethylaminophenyl*-10-*methylphenanthridinium Iodide* (15) (III; R = Me).—When a solution of the relevant tertiary amine (II; R = Me) (2 g.) in nitrobenzene (20 c.c.) at *ca.* 180° was treated with methyl *p*-toluenesulphonate (1·4 g.; > 1 equiv.), the solution became dark red and heat was evolved. On cooling, there separated a white *p*-toluenesulphonate (0·5 g.), which was purified by crystallisation from alcohol and then converted into the iodide. The product, 9-*phenanthridyl*-p-*phenyltrimethylammonium iodide* (IV), crystallised from water or alcohol in white plates, m. p. 179° (decomp.), but the red melt resolidified and then melted at 235°; it had evidently been converted into its isomeride (III; R = Me) (Found for white iodide; C, 60·15; H, 4·65; N, 6·15; I, 28·8. $C_{22}H_{21}N_2I$ requires C, 60·0; H, 4·75; N, 6·35; I, 28·85%).

The red aqueous liquor left after steam distillation of nitrobenzene deposited, on cooling, orange prisms of 9-p-*dimethylaminophenyl*-10-*methylphenanthridinium* p-*toluenesulphonate* (compare III) (1·2 g.), which melted with loss of water at 120° and then set to a dark red glass (Found : C, 67·35; H, 6·15; N, 5·65; S, 6·35; loss at 100°, 6·85. $C_{29}H_{28}O_3N_2S,2H_2O$ requires C, 67·0; H, 6·15; N, 5·4; S, 6·15; H_2O, 6·9%). The *iodide* (16) formed small brick-red prisms, m. p. 238° (decomp.) (Found : C, 59·55; H, 5·1; N, 6·8; I, 28·55. $C_{22}H_{21}N_2I$ requires C, 60·0; H, 4·75; N, 6·35; I, 28·85%). The *chloride* (15), which was prepared from the iodide, was very soluble in water and alcohol, but crystallised from the former in hydrated ruby-red prisms, which had copper reflex (Found for salt dried at 100° : N, 8·25; Cl, 10·1. $C_{22}H_{21}N_2Cl$ requires N, 8·05; Cl, 10·2%).

When methyl sulphate was used as methylating agent, the salt that separated from the nitrobenzene was the diquaternary dimethosulphate, characterised by the *di-iodide* (17) (V), which crystallised from water in transparent, pale yellow prisms, m. p. 232—236° (decomp.) (Found : C, 48·1; H, 4·2; N, 4·85; I, 43·3. $C_{23}H_{24}N_2I_2$ requires C, 47·45; H, 4·1; N, 4·8; I, 43·65%). The same salt was obtained in high yield when a large excess of methyl *p*-toluenesulphonate was used. On cooling, the nitrobenzene filled with white deliquescent plates of the diquaternary di-*p*-toluenesulphonate, which was readily converted into the foregoing di-iodide. The white chloride obtained from this salt lost methyl chloride slowly at 100° to yield the red monochloride.

Methylation of 9-p-*Aminophenyl*-10-*methylphenanthridinium Iodide*.—The quaternary salt (2 g.) and methyl iodide (4 g.), after being heated at 180° for 7 hours, gave a product, from a hot aqueous extract of which a brick-red iodide separated on cooling (0·5 g.). It was characterised as 9-*p*-dimethylaminophenyl-10-methylphenanthridinium iodide by conversion into the orange prisms of the *p*-toluenesulphonate by means of silver *p*-toluenesulphonate. The aqueous mother-liquor from which the red iodide separated gave on evaporation characteristic crystals of the diquaternary di-iodide (V).

5-*Nitro*-2-p-*nitrobenzamidodiphenyl*, obtained by the condensation of 5-nitro-2-aminodiphenyl (10 g.) and *p*-nitrobenzoyl chloride (10 g.) in hot pyridine (40 c.c.), crystallised from glacial acetic acid in buff prisms (11·5 g.), m. p. 209° (Found : N, 11·4. $C_{19}H_{13}O_5N_3$ requires N, 11·55%).

3-*Nitro*-9-p-*nitrophenylphenanthridine*.—The foregoing compound (20 g.) was refluxed with phosphorus oxychloride (40 g.) for 30 hours. The product left after cautious decomposition with water crystallised from boiling pyridine in pale yellow, felted needles (11·5 g.), m. p. 294°, very sparingly soluble in all other solvents (Found : N, 12·35. $C_{19}H_{11}O_4N_3$ requires N, 12·15%). When the residue left after evaporation of pyridine was again treated with phosphorus oxychloride, a further yield (2 g.) was obtained.

3-*Amino*-9-p-*aminophenylphenanthridine* was obtained by reduction of the foregoing compound (11·5 g.) in alcoholic solution (350 c.c.) in an autoclave with hydrogen (5 atms.) at 50°, platinic oxide being used as catalyst. The almost colourless, prismatic needles (8·5 g.), m. p. 233°, were sparingly soluble in alcohol (Found : C, 79·6; H, 5·4; N, 14·95. $C_{19}H_{15}N_3$ requires C, 80·0; H, 5·25; N, 14·75%). The *hydrobromide* crystallised from its dark red aqueous solution in clusters of orange plates (Found : loss at 100°, 4·8; Br, 20·2. $C_{19}H_{16}N_3Br,H_2O$ requires H_2O, 4·7; Br, 20·85%). The sparingly soluble *sulphate* crystallised in cream-coloured needles (Found after drying at 100° : N, 10·8; S, 8·1. $C_{19}H_{15}N_3,H_2SO_4$ requires N, 10·95; S, 8·35%).

The dark red solution of the amine in glacial acetic acid was readily acetylated by acetic anhydride. The *diacetyl* compound crystallised in white felted needles, m. p. 327—328° (decomp.) (Found : C, 74·7; H, 5·25; N, 11·5. $C_{23}H_{19}O_2N_3$ requires C, 74·8; H, 5·15; N, 11·4%).

3-*Acetamido*-9-p-*acetamidophenyl*-10-*methylphenanthridinium chloride* (19) was prepared by methylation of the foregoing compound (5 g.) in hot nitrobenzene (100 c.c.) with methyl *p*-toluenesulphonate (3 g.). The quaternary salt crystallised from the aqueous liquor left after steam-distillation of nitrobenzene in clumps of pale orange needles. The *chloride* (4 g.) was salted out from the hot solution in small, pale yellow needles, sparingly soluble in water to a neutral solution (Found : N, 9·95; Cl, 8·1. $C_{24}H_{22}O_2N_3Cl$ requires N, 10·0; Cl, 8·45%).

3-*Amino*-9-p-*aminophenyl*-10-*methylphenanthridinium Chloride* (20) (X).—The foregoing salt (4 g.) was readily hydrolysed by boiling concentrated hydrochloric acid (20 c.c.). On neutralisation of the solution, the *quaternary* salt crystallised in transparent, red, prismatic needles (2·6 g.), fairly soluble in water (Found : C, 69·1; H, 5·35; loss at 100°, 2·4, 2·6. $C_{20}H_{18}N_3Cl,0·5H_2O$ requires C, 69·65; H, 5·5; H_2O, 2·6%. Found for salt dried at 100° : N, 12·6; Cl, 10·45. $C_{20}H_{18}N_3Cl$ requires N, 12·5; Cl, 10·6%).

The following compounds were prepared in substantially the same way as their isomerides.

4'-*Nitro*-2-p-*nitrobenzamidodiphenyl* crystallised from glacial acetic acid in white prisms, m. p. 208° (Found : N, 11·95. $C_{19}H_{13}O_5N_3$ requires N, 11·55%).

7-*Nitro*-9-p-*nitrophenylphenanthridine*.—The foregoing compound (28 g.) was dehydrated less readily than its isomeride, the yield after 30 hours' refluxing being 8 g.; by repeated re-treatment of the residue a further 8·5 g. were obtained. Almost white, felted needles, m. p. 327°, crystallised from pyridine (Found : N, 12·4. $C_{19}H_{11}O_4N_3$ requires N, 12·15%).

7-*Amino*-9-p-*aminophenylphenanthridine* crystallised from alcohol in pale yellow, transparent cubes, m. p. 212° (Found : C, 79·8; H, 5·3; N, 14·85. $C_{19}H_{15}N_3$ requires C, 80·0; H, 5·25; N, 14·75%). The red hydrochloride was extremely soluble in water, but the *sulphate* (21) was obtained in brick-red talc-like crystals (Found for salt dried at 100° : N, 10·95; S, 8·35. $C_{19}H_{15}N_3,H_2SO_4$ requires N, 10·95; S, 8·35%). The *diacetyl* compound crystallised from alcohol in solvated colourless prisms, m. p. 172—173° (Found after drying at 100° : N, 11·35. $C_{23}H_{19}O_2N_3$ requires N, 11·4%).

7-*Acetamido*-9-p-*acetamidophenyl*-10-*methylphenanthridinium* p-*toluenesulphonate* crystallised from water or alcohol in yellow felted needles, or in transparent prisms (Found : N, 7·7. $C_{31}H_{29}O_5N_3S$ requires N, 7·55%). The *chloride* (22) formed yellow prisms from alcohol, m. p. 231° (decomp.) (Found : C, 64·65; H, 5·7; N, 9·7; Cl, 7·8; loss at 100° 5·3. $C_{24}H_{22}O_2N_3Cl,1·5H_2O$ requires C, 64·5; H, 5·6; N, 9·4; Cl, 7·95; H_2O, 6·05%).

7-*Amino*-9-p-*aminophenyl*-10-*methylphenanthridinium chloride* (23) crystallised from water in ruby-red transparent plates, m. p. 262° (decomp.), but dependent on rate of heating (Found : C, 69·35; H, 5·3; 5·5; loss at 120°, 2·3. $C_{20}H_{18}N_3Cl,0{\cdot}5H_2O$ requires C, 69·65; H, 5·5; H_2O, 2·6%. Found for salt dried at 120° : N, 12·4; Cl, 10·4. $C_{20}H_{18}N_3Cl$ requires N, 12·5; Cl, 10·6%).

4′-*Nitro*-2-*benzamidodiphenyl*.—4′-Nitro-2-xenylamine (3 g.) and benzoic anhydride (3·5 g.) were heated at 150° for 1 hour. The product was lixiviated with hot dilute alkali; it then crystallised from alcohol in colourless acicular prisms (4 g.), m. p. 165·5° (Found : N, 8·85. $C_{19}H_{14}O_3N_2$ requires N, 8·8%).

7-*Nitro*-9-*phenylphenanthridine* was obtained by fractional crystallisation from glacial acetic acid of the product of 7 hours' reaction of the foregoing (3·5 g.) and phosphorus oxychloride. It crystallised in flocculent, pale yellow needles (0·8 g.), m. p. 237° (Found : N, 9·4. $C_{19}H_{12}O_2N_2$ requires N, 9·35%).

5 : 4′-*Dinitro*-2-*benzamidodiphenyl*, obtained from 5 : 4′-dinitro-2-xenylamine (Scarborough and Waters, J., 1927, 89) and benzoic anhydride by the method previously described, crystallised from nitrobenzene in white plates, m. p. 250° (Found : N, 12·0. $C_{19}H_{13}O_5N_3$ requires N, 11·55%). After prolonged heating with phosphorus oxychloride, the yield of 3 : 7-*dinitro*-9-*phenylphenanthridine* was very small; by fractional crystallisation of the product from glacial acetic acid and benzene it was obtained in flat yellow plates, m. p. 275—277° (Found : N, 12·4. $C_{19}H_{11}O_4N_3$ requires N, 12·2%).

9-*Methylaminophenanthridine* (XIII; R = H, R′ = Me).—The product of the reaction between 9-chlorophenanthridine (5 g.) and methylamine (10 g. of 33% alcoholic solution) at 180° for 5 hours was extracted with dilute sulphuric acid. On neutralisation of the extract the amine was obtained in quantitative yield; it crystallised from alcohol in colourless prismatic needles, m. p. 187° (Found : N, 13·55. $C_{14}H_{12}N_2$ requires N, 13·45%). The hydrochloride was very sparingly soluble in water, but the *sulphate* (25) crystallised in hydrated needles, the 2% aqueous solution of which had p_H 6—6·5 (Found for salt dried at 100° : S, 6·0. $C_{14}H_{12}N_2,0{\cdot}5H_2SO_4$ requires S, 6·2%). The *acetyl* compound was obtained quantitatively when the base was refluxed with acetic anhydride and fused sodium acetate; it crystallised from aqueous methyl alcohol in white plates, m. p. 155° (Found : N, 11·45. $C_{16}H_{14}ON_2$ requires N, 11·2%).

9-*Dimethylaminophenanthridine* (XIII; R = R′ = Me), prepared in the same way as the foregoing compound by means of dimethylamine, crystallised from a small volume of light petroleum (b. p. 60—80°) in colourless prisms, m. p. 61·5° (Found : N, 12·35. $C_{15}H_{14}N_2$ requires N, 12·6%). The *hydrochloride* (26) occurred in hydrated white needles, the 2% aqueous solution of which had p_H 4·5—5 (Found for salt dried at 100° : Cl, 13·5. $C_{15}H_{14}N_2,HCl$ requires Cl, 13·7%).

9-*Phenanthridyltrimethylammonium iodide* (27) (XIV) was obtained in moderate yield by the reaction between 9-chlorophenanthridine and alcoholic trimethylamine. When an aqueous extract of the product was treated with potassium iodide, the white salt crystallised, m. p. 234° (decomp.), p_H of 2% aqueous solution 5·5 (Found : I, 34·9. $C_{16}H_{17}N_2I$ requires I, 34·9%).

9-*Dimethylamino*-10-*methylphenanthridinium Iodide* (28) (XV).—9-Dimethylaminophenanthridine (2 g.) and methyl iodide (2 g.) were heated at 125° for 4 hours. When a hot aqueous extract of the product was cooled, the quaternary *iodide* crystallised in yellow needles (1·7 g.), m. p. 230° (efferv.) (Found : N, 7·55; I, 35·2. $C_{16}H_{17}N_2I$ requires N, 7·7; I, 34·9%). When the aqueous solution, which had a neutral reaction, was heated, smooth decomposition occurred slowly with separation of a non-basic colourless oil, which solidified on cooling to white needles, m. p. 112° alone or in admixture with *N*-methylphenanthridone (Graebe and Wander, *Annalen*, 1893, **276**, 245).

9-ω-*Phenanthridylmethyltrimethylammonium Iodide* (29).—When an aqueous extract of the product of the reaction between 9-ω-chloromethylphenanthridine and trimethylamine at 100° for 2 hours was treated with potassium iodide, the *iodide* was precipitated in colourless prisms, m. p. *ca.* 222° (decomp.), dependent on the rate of heating. Its aqueous solution was neutral (Found : I, 33·3. $C_{17}H_{19}N_2I$ requires I, 33·6%).

9-ω-*Phenanthridylmethyl*-N-*pyridinium chloride* (30), prepared similarly from pyridine, crystallised from water in colourless plates, decomp. *ca.* 250° (Found : N, 8·65; Cl, 10·85; loss at 100°, 5·45, 5·2. $C_{19}H_{15}N_2Cl,H_2O$ requires N, 8·2; Cl, 10·95; H_2O, 5·55%). The 2% aqueous solution had p_H 6·5. The corresponding nitrate, sulphate, and perrhenate were very sparingly soluble in water.

9-ω-*Piperidinomethylphenanthridine* (31).—9-ω-Chloromethylphenanthridine (4·5 g.) and

piperidine (6 g.) reacted at 100° with evolution of heat. The product (3·2 g.) crystallised from light petroleum (b. p. 60—80°) in pale yellow rhombs, m. p. 90—93° (Found: N, 10·3. $C_{19}H_{20}N_2$ requires N, 10·15%). The hydrochloride separated from aqueous solution (2% had p_H 5·5) in white prisms (Found: Cl, 10·75. $C_{19}H_{20}N_2,HCl,H_2O$ requires Cl, 10·75%).

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