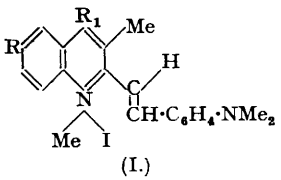
6. *Novel Types of Styrylquinolinium Compounds.*

By VLADIMIR A. PETROW.

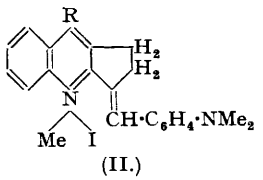
A new method has been developed for the synthesis of compounds related to 2-*p*-dimethylaminostyrylquinoline methochloride. Products derived from 3-methylquinoline, dihydro-β-quinindene, tetrahydroacridine, and phenanthridine have been prepared for examination as bactericides and trypanocides.

THE early observations of Browning, Cohen, Ellingworth, and Gulbransen (*Proc. Roy. Soc.*, 1924, *B*, **96**, 317) on the bactericidal action of the cyanine dyes led these workers to undertake a systematic study of the related styrylquinolinium compounds. These were found to possess strong antiseptic activity *in vitro* towards both *Staphylococcus aureus* and *B. coli*, not appreciably decreased by the presence of serum (*ibid.*, 1926, *B*, **100**, 293). Although attempts to increase their antiseptic power by the introduction of a further basic group at C_6 in the quinoline nucleus were not successful, yet these diamino-bases were shown in 1929 to constitute a new type of trypanocidal agent (*ibid.*, *B*, **105**, 99). The 4 : 4′-diamino-analogues were investigated by Ashley, Browning, Cohen, and Gulbransen (*ibid.*, 1933, *B*, **113**, 293) but were found to be less effective therapeutically. Styryl derivatives of 4-amino-5 : 6-benzoquinoline are claimed as bactericidal in G.P. 440,008.

In the course of investigations for new chemotherapeutic agents the observations of Browning *et al.* have been extended to embrace the novel types (I)—(IV). Condensation of *p*-dimethylaminobenzaldehyde and



(I.)



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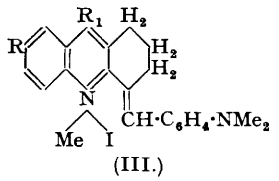

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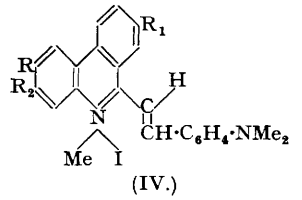

(IV.)

p-nitrobenzaldehyde with 1 : 2 : 3 : 4-tetrahydroacridine and 1 : 2 : 3 : 4-tetrahydro-6 : 7-benzacridine readily took place in the presence of anhydrous zinc chloride (cf. Borsche, *Annalen*, 1910, **377**, 110), but these *benzylidene* derivatives could not be converted into the methosulphates owing probably to steric hindrance. For instance, when 1-p-*dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydroacridine* was boiled with methyl sulphate in nitrobenzene solution, the mixture immediately became intensely purple, yet the product which separated was a yellow water-soluble substance which regenerated the benzylidene compound on treatment with ammonia. Similar loose molecular complexes have been described by Browning, Cohen, Couper, and Gulbransen (*Proc. Roy. Soc.*, 1931, *B*, **109**, 51). When Köenig's method (*J. pr. Chem.*, 1912, **86**, 172) was used and the corresponding methiodides heated with *p*-dimethylaminobenzaldehyde in aqueous-alcoholic solution in the presence of piperidine, moderate yields of (I) and (II) were obtained, the procedure failing for (III) and (IV). The use of higher alcohols as solvents and even fusion of the components at temperatures up to 200° failed to give compounds of the latter two types. It was ultimately found that the desired condensations could be achieved and compounds of all four types obtained in excellent yields by adding intimate equimolecular mixtures of the requisite methiodides with *p*-dimethylaminobenzaldehyde to boiling acetic anhydride. Separation of the styryl and the benzylidene compounds from the hot solution in an essentially pure condition usually occurred after 4—10 minutes' vigorous refluxing.

2 : 3-Dimethylquinoline methiodide readily condensed with *p*-dimethylaminobenzaldehyde to give 2-p-*dimethylaminostyryl*-3-*methylquinoline methiodide* (I; R = R_1 = H). Condensation of isatin with methyl ethyl ketone in aqueous ammonia gave 2 : 3-*dimethylquinoline*-4-*carboxyamide* (cf. G.P. 290,703), converted smoothly into 4-*amino*-2 : 3-*dimethylquinoline* by hypobromite oxidation. Both 4-*amino*-2 : 3-*dimethylquinoline methiodide* and its *acetyl* derivative failed to condense with *p*-dimethylaminobenzaldehyde to give (I; R = H, R_1 = NH_2 or NHAc) under a wide variety of conditions. The lesser reactivity of the related 4-aminoquinaldine methiodide, compared with quinaldine methiodide, had previously been noted by Browning *et al.* (1933, *loc. cit.*), who used fusion in the presence of piperidine for the analogous condensation. Reaction of 5-nitroisatin with methyl ethyl ketone in the presence of aqueous ammonia gave 6-*nitro*-2 : 3-*dimethylquinoline*-4-*carboxyamide*. Attempts to hydrolyse the amide to the acid, from which 6-amino-2 : 3-dimethylquinoline might be obtained for conversion into (I; R = NH_2, R_1 = H), were not successful. Reduction of the nitro-amide gave the corresponding 6-*amino*-2 : 3-*dimethylquinoline*-4-*carboxyamide*, which on dry distillation

with or without soda-lime, led surprisingly to 4-*cyano*-6-*amino*-2 : 3-*dimethylquinoline* in high yield in place of the expected 6-amino-2 : 3-dimethylquinoline.

3-p-*Dimethylaminobenzylidenedihydro*-β-*quinindene methiodide* (II; R = H) was obtained in good yield from dihydro-β-quinindene methiodide. Attempts to prepare (II; R = NH_2) from 9-*aminodihydro*-β-*quinindene methiodide* or its *acetyl* derivative were unsuccessful, no evidence of reaction being observed. Condensation of 5-nitroisatin with *cyclo*pentanone in the presence of ammonia gave a low yield of a product which could not be identified.

1-p-*Dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydroacridine methiodide* (III; R = R_1 = H) and its 7-substituted derivatives were obtained from the methiodides of the corresponding tetrahydroacridines prepared by the method of Petrow (J., 1942, 693). 5-*Amino*-1 : 2 : 3 : 4-*tetrahydroacridine methiodide* failed to condense with *p*-dimethylaminobenzaldehyde. The *acetyl* derivative gave evidence of reaction but a product could not be isolated.

The 9-p-*dimethylaminostyrylphenanthridinium methiodides* (IV) were prepared from the corresponding 9-methylphenanthridine methiodides. 2-*Nitro*-4-*methyldiphenyl* was prepared from the corresponding nitrotoluidine by the Gomberg reaction as improved by Elks, Haworth, and Hey (J., 1940, 1285), the derived 2-*acetamido*-4-*methyldiphenyl* readily undergoing ring closure with phosphorus oxychloride to give 2 : 9-*dimethylphenanthridine*. Difficulty was experienced in preparing 7-*amino*-9-*methylphenanthridine*. Cyclisation of 4'-nitro-2-acetamidodiphenyl gave 7-nitro-9-methylphenanthridine in only 4% yield (cf. Morgan and Walls, J., 1932, 2227) for reasons discussed by these authors in a later publication (J., 1938, 390). It was ultimately found that the deactivating influence of the 4'-nitro-group could be circumvented by reduction to 4'-*amino*-2-*acetamidodiphenyl*, followed by protection of the amino-group by benzoylation. The resulting 4'-*benzamido*-2-*acetamidodiphenyl*, cyclised by phosphorus oxychloride to 7-*benzamido*-9-*methylphenanthridine* in 62% yield, was smoothly hydrolysed to 7-*amino*-9-*methylphenanthridine* * by syrupy phosphoric acid.

During the preparation of compounds of types (II) and (III) it was observed that the purity of the product was related to the time of heating of the components in acetic anhydride. Numerous experiments were required before optimum conditions were elaborated and analytically pure products obtained. The nature of the secondary change taking place was fully investigated only in the case of tetrahydroacridine methiodide. When an equimolecular mixture of tetrahydroacridine methiodide and *p*-dimethylaminobenzaldehyde was added to boiling acetic anhydride, rapid solution occurred. Separation of bright red crystals of the *benzylidene* compound took place after 4 minutes and was complete after 6 minutes. When the time of heating was prolonged to 1½ hours, a new *product* was obtained, separating in brilliant dark green needles and giving consistent analytical results corresponding to $C_{22}H_{23}N_2I$ (loss of methylene) or $C_{22}H_{21}N_2I$ (loss of methane). Incontrovertible evidence that the formation of this substance involved the loss of the methyl group attached to the ring nitrogen was furnished by the production of the identical product from *tetrahydroacridine ethiodide*. Its formulation as 1-p-*dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydroacridine hydriodide* followed from the observation that the corresponding *chloride* passed quantitatively on warming with a large volume of water into 1-p-*dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydroacridine*, identical in every respect with the material obtained by direct combination, and reconverted into the hydriodide identical with the dark green product above. As the ultraviolet absorption spectra of the green and the red iodide were nearly identical, it may be inferred that they are similarly constituted. The alternative formulation, a structure analogous to the pale yellow methiodide $C_9H_6{\cdot}CH{:}CH{\cdot}C_6H_4{\cdot}NMe_3I$, obtained by Rupe, Hagenbach, and Collin (*Helv. Chim. Acta*, 1935, **18**, 1400) by condensation of quinaldine with *p*-dimethylaminobenzaldehyde methiodide, cannot account for the intense colour—due to a resonance effect—of the green hydriodide and for the observed similarity of the absorption spectra, and can thus be ruled out.

The mechanism of the reaction between quinaldine alkiodides and *p*-dimethylaminobenzaldehyde in the presence of piperidine has been studied by Mills and Raper (J., 1925, **127**, 2466), who proved that the styryl compounds were formed through the intermediate formation of methylene bases which condensed with the *p*-dimethylaminobenzaldehyde to give compounds of the " allene " type, from which the styryl derivatives were obtained by addition of halogen hydride. Whilst this mechanism cannot be excluded in the formation of (I) and (IV) in acetic anhydride solution, an alternative mechanism must a priori be postulated to occur in the formation of (II) and (III). It is tentatively suggested that the condensations described in the present communication proceed through the intermediate formation of alkine-bases, which, as shown by Benrath (*J. pr. Chem.*, 1906, **73**, 387), can undergo dehydration under these experimental conditions.

The ultra-violet absorption curves of (II) and (III) over the range 2000—6000 A., kindly examined by Glaxo Laboratories Ltd., resemble closely that of 2-*p*-dimethylaminostyrylquinoline methiodide, a substance with photosensitising properties. Both dihydro-β-quinindene methiodide and tetrahydroacridine methiodide also form highly coloured products with *p*-nitrosodimethylaniline. The preparation of cyanine dye analogues from bases containing active homocyclic methylene groups has not hitherto been described in the literature, and compounds (II) and (III) furnish the first examples of this type.

The pharmacology of the above compounds, as methochlorides, will be reported in detail elsewhere.

* (*Added in proof.*) Since the above was submitted for publication the author has learnt that Dr. L. P. Walls has prepared 7-amino-9-methylphenanthridine by a somewhat different method, the results being incorporated in Provisional British Patent Application No. 52/1944.

Experimental.

Melting points are corrected.

Benzylidene Derivatives of Tetrahydroacridine.—These were prepared by heating equimolecular amounts of the reactants in the presence of a little anhydrous zinc chloride at 120—130° for 2—3 hours. 1-p-*Nitrobenzylidene*-1 : 2 : 3 : 4-*tetrahydroacridine* formed orange octahedra from acetone–methyl alcohol, m. p. 145—146° (Found : C, 76·2; H, 5·4; N, 8·6. $C_{20}H_{16}O_2N_2$ requires C, 76·0; H, 5·1; N, 8·9%). 1-p-*Nitrobenzylidene*-1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*benzacridine* formed golden-yellow octahedra from benzene, m. p. 220—221° (Found : C, 78·6; H, 5·0; N, 7·1. $C_{24}H_{18}O_2N_2$ requires C, 78·7; H, 4·9; N, 7·7%). 1-p-*Dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydroacridine* formed pale yellow, prismatic plates from aqueous acetone, m. p. 133—134° (Found : C, 84·0; H, 7·0; N, 9·1. $C_{22}H_{22}N_2$ requires C, 84·1; H, 7·0; N, 8·9%). 1-p-*Dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*benzacridine* formed golden-yellow needles from acetone, m. p. 211·5° (Found : C, 86·1; H, 6·6; N, 8·0. $C_{26}H_{24}N_2$ requires C, 85·7; H, 6·6; N, 7·7%). Methosulphates could not be obtained from these compounds (see p. 18).

Styryl Compounds.—The general method of preparation was as follows : An intimate, very finely powdered mixture of 0·1 g.-mol. of the methiodide and 0·12 g.-mol. of *p*-dimethylaminobenzaldehyde was added in one portion to boiling acetic anhydride [1000 ml. for (I), (II), and (III), and 1500 ml. for (IV)], and vigorous refluxing continued for 5—6 minutes [(I), (II), and (III)] or 10 minutes (IV). After cooling to room temperature, the product, which usually separated in the pure state, was collected and crystallised from a large volume of spirit where necessary. Yields are given in parentheses. The methochlorides were prepared by heating the finely powdered methiodides in methyl-alcoholic suspension with freshly precipitated silver chloride for 1—3 hours, and were crystallised from methyl alcohol or ether–methyl alcohol. 2-*p*-Dimethylaminostyrylquinoline methiodide had m. p. 269—270° (decomp.) (Found : I, 30·5. Calc. for $C_{20}H_{21}N_2I$: I, 30·5%). Rupe, Hagenbach, and Collin (*loc. cit.*) give m. p. 254° (decomp.).

2-p-*Dimethylaminostyryl*-3-*methylquinoline methiodide* (I; R = R_1 = H). (*a*) 2 : 3-Dimethylquinoline methiodide (2 g.) (Rohde, *Ber.*, 1889, **22**, 271) in absolute alcohol (75 ml.) was treated with *p*-dimethylaminobenzaldehyde (1 g.) and piperidine (1 ml.) for 1½ hours under reflux. The *product* formed small purplish needles from spirit, m. p. 255—255·5° (decomp.) (Found : C, 58·6; H, 5·4; N, 6·5; I, 29·5. $C_{21}H_{23}N_2I$ requires C, 58·6; H, 5·4; N, 6·5; I, 29·5%). Yield, 70%. (*b*) The *product* (93%) obtained by the acetic anhydride method was identical with the material obtained above (Found : C, 58·7; H, 5·4; N, 6·5; I, 29·5%). The *methochloride* formed dark purple needles, m. p. 245° (decomp.) (Found : Cl, 11·0. $C_{21}H_{23}N_2Cl$ requires Cl, 10·5%).

2 : 3-*Dimethylquinoline*-4-*carboxyamide.*—This *compound*, acicular plates from aqueous alcohol, m. p. 287—288° (Found : N, 14·3. $C_{12}H_{12}ON_2$ requires N, 14·0%), was prepared by heating isatin (12 g.), methyl ethyl ketone (18 ml.), and aqueous ammonia (80 ml., *d* 0·880) in a pressure bottle for 8 hours at 100°. The product (m. p. *ca.* 235°, yield 15 g.) was used direct.

4-*Amino*-2 : 3-*dimethylquinoline.*—The corresponding crude finely powdered amide (17·5 g.) was added in one portion with mechanical stirring to an ice-cold solution of bromine (15 g.) in 10% potassium hydroxide solution (250 ml.). After 45 minutes a further quantity of the potassium hydroxide solution (150 ml.) was added to the clear solution. After 5 minutes the mixture was heated at 100° for 30 minutes and boiled for 2—3 minutes. After standing overnight at 0°, the crude amine was collected. Yield, 15 g. 4-*Amino*-2 : 3-*dimethylquinoline*, purified *via* the hydrochloride, formed silky needles from aqueous acetone, m. p. 188·5—189·5° (Found : C, 76·3; H, 7·1; N, 16·4. $C_{11}H_{12}N_2$ requires C, 76·8; H, 7·0; N, 16·2%). The *methiodide* formed white needles from water, m. p. >310° (Found : I, 40·6. $C_{12}H_{15}N_2I$ requires I, 40·5%), stable to sodium bicarbonate. 4-*Acetamido*-2 : 3-*dimethylquinoline*, octahedra from aqueous methyl alcohol, m. p. 216—217° (Found : C, 72·9; H, 6·6; N, 13·2. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·5; N, 13·1%), was prepared by heating the base (4 g.), redistilled acetic anhydride (4 ml.), and dry pyridine (8 ml.) for 30 minutes. The *methiodide* formed octahedra or silky needles from water, m. p. 295—296° (decomp.) (Found : I, 35·8. $C_{14}H_{17}ON_2I$ requires I, 35·7%).

6-*Nitro*-2 : 3-*dimethylquinoline*-4-*carboxyamide*, prepared from 5-nitroisatin as above, separated from alcohol in pale yellow needles, m. p. 278—280° (Found : C, 58·5; H, 4·7; N, 17·0. $C_{12}H_{11}O_3N_3$ requires C, 58·8; H, 4·5; N, 17·1%).

6-*Amino*-2 : 3-*dimethylquinoline*-4-*carboxyamide*, pale yellow needles from water, m. p. 293·5—294·5° (decomp.) (Found : C, 67·0; H, 6·1; N, 19·5. $C_{12}H_{13}ON_3$ requires C, 67·0; H, 6·1; N, 19·5%), was prepared by reducing the crude nitro-amide (5 g.) in water (7 ml.) and spirit (18 ml.) to which a few drops of hydrochloric acid had been added, with reduced iron (7·5 g.) for 1½ hours on the water-bath.

4-*Cyano*-6-*amino*-2 : 3-*dimethylquinoline*, separating from aqueous acetone in pale yellow needles, m. p. 218·5—219·5° (Found : C, 73·1; H, 6·1; N, 21·1. $C_{12}H_{11}N_3$ requires C, 73·1; H, 5·6; N, 21·3%), was obtained (60—70% yield) by dry distillation of the amino-amide at atmospheric pressure. The *acetyl* derivative formed silky yellow needles from aqueous acetone, m. p. 238—239° (Found : C, 70·1; H, 5·6; N, 17·9. $C_{14}H_{13}ON_3$ requires C, 70·3; H, 5·4; N, 17·6%).

3-p-*Dimethylaminobenzylidenedihydro-β-quinindene Methiodide* (II; R = H).—(*a*) Dihydro-β-quinindene methiodide (6·0 g.), m. p. 212—213° (Borsche, *Annalen*, 1910, **377**, 121 gives m. p. 207°), *p*-dimethylaminobenzaldehyde (3 g.), absolute alcohol (80 ml.), and piperidine (2 ml.) were heated under reflux for 1 hour. The *product* formed brilliant blue needles, m. p. 235—236° (decomp.) (Found : N, 5·9; I, 28·3. $C_{22}H_{23}N_2I$ requires N, 6·3; I, 28·7%). Yield, 68%. (*b*) The product (95%), m. p. 238·5° (decomp.), obtained by the acetic anhydride method, was identical with the material obtained above (Found : C, 59·7; H, 5·4; N, 6·5; I, 28·9. $C_{22}H_{23}N_2I$ requires C, 59·7; H, 5·2; N, 6·3; I, 28·7%). The *methochloride* formed brilliant dark blue needles, m. p. 232° (decomp.) (Found : Cl, 10·0. $C_{22}H_{23}N_2Cl$ requires Cl, 10·1%).

9-*Aminodihydro-β-quinindene methiodide* formed needles from water, m. p. >320° (Found : I, 38·9. $C_{13}H_{15}N_2I$ requires I, 39·0%), stable to sodium bicarbonate. The *acetyl* derivative formed cubic crystals from water, m. p. 294—295° (decomp.) (Found : I, 34·6. $C_{15}H_{17}ON_2I$ requires I, 34·5%).

Condensation of Nitroisatin with cyclo*Pentanone.*—*cyclo*Pentanone (8 ml.) was added to nitroisatin (12 g.) dissolved in aqueous ammonia (80 ml., *d* 0·880), and the mixture heated for 8 hours at 100°. The black tarry mass was collected and extracted with a large volume of boiling spirit (charcoal), which on concentration deposited yellow plates (3·5 g.), m. p. 310—311° (decomp.), from alcohol (Found : C, 69·5, 69·5; H, 5·9, 5·8; N, 19·7, 19·8%).

1 : 2 : 3 : 4-*Tetrahydroacridine Derivatives.*—1-p-*Dimethylaminobenzylidene*-1 : 2 : 3 : 4-*tetrahydroacridine methiodide* (III, R = R_1 = H) (84%) formed brilliant scarlet needles, m. p. 236·5—237·5° (decomp.) (Found : C, 60·4; H, 5·5; N, 6·1; I, 28·0. $C_{23}H_{25}N_2I$ requires C, 60·5; H, 5·5; N, 6·1; I, 27·9%). The *methochloride* formed squat red rods, m. p. 230·5—231·5° (decomp.) (Found : Cl, 10·0. $C_{23}H_{25}N_2Cl$ requires Cl, 9·7%). 7-*Methyltetrahydroacridine methiodide* crystallised in pale yellow needles from water, m. p. 240—241° (decomp.) (Found : I, 37·5. $C_{15}H_{18}NI$ requires I, 37·5%). 1-p-*Dimethylaminobenzylidene*-7-*methyltetrahydroacridine methiodide* (III; R = CH_3, R_1 = H) (81%), formed red octahedra with a brilliant red reflex, m. p. 231·5—232·5° (decomp.) (Found : C, 61·3; H, 5·8; N, 6·1; I, 27·0. $C_{24}H_{27}N_2I$ requires C, 61·3; H, 5·7; N, 6·0; I, 27·0%). The *methochloride* separated in dark red octahedra with a green reflex, m. p. 219—220° (decomp.) (Found : Cl, 9·2. $C_{24}H_{27}N_2Cl$ requires Cl, 9·4%). 7-*Methoxytetrahydroacridine methiodide* formed yellow needles, from water, m. p. 247—248° (decomp.) (Found : I, 35·7. $C_{15}H_{18}ONI$ requires I, 35·8%). 1-p-*Dimethylaminobenzylidene*-7-*methoxytetrahydroacridine methiodide* (III; R = OMe, R_1 = H) (45%)

(600 ml. of acetic anhydride used) formed brilliant red needles with a golden reflex, m. p. 220—221° (decomp.) (Found : C, 58·9; H, 5·6; N, 5·8; I, 26·9. $C_{24}H_{27}ON_2I$ requires C, 59·3; H, 5·6; N, 5·8; I, 26·2%). The *methochloride* formed dark red octahedra, m. p. 208—209° (decomp.) (Found : Cl, 8·5. $C_{24}H_{27}ON_2Cl$ requires Cl, 9·0%). *7-Chlorotetrahydroacridine methiodide* formed pale yellow needles, m. p. 268—269° (decomp.) (Found : N, 4·0. $C_{14}H_{15}NClI$ requires N, 3·9%). *7-Chloro*-1-p-*dimethylaminobenzylidenetetrahydroacridine methiodide* (III; R = Cl, R_1 = H) (95%) crystallised in brilliant dark green plates, m. p. 229—230° (decomp.) (Found : C, 56·3; H, 4·8; N, 5·8. $C_{23}H_{24}N_2ClI$ requires C, 56·3; H, 4·9; N, 5·7%), and the *methochloride* in squat red needles, m. p. 215·5—216·5° (decomp.) (Found : Cl, 18·1. $C_{23}H_{24}N_2Cl_2$ requires Cl, 17·8%). *7-Azo*-1 : 2 : 3 : 4-*tetrahydroacridine*, obtained in 5% yield during the reduction of 7-nitrotetrahydroacridine, formed orange micro-crystals from nitrobenzene, m. p. 280—281° (decomp.) (Found : C, 79·6; H, 6·0; N, 14·1. $C_{26}H_{24}N_4$ requires C, 79·6; H, 6·1; N, 14·3%). *7-Acetamidotetrahydroacridine methiodide* formed pale yellow needles from water, m. p. 268—269° (decomp.) (Found : I, 33·3. $C_{16}H_{19}ON_2I$ requires I, 33·3%). 1-p-*Dimethylaminobenzylidene-7-acetamidotetrahydroacridine methiodide* (III; R = NHAc, R_1 = H) was obtained in 30—50% yield by adding the methiodide (above) (8 g.) and *p*-dimethylaminobenzaldehyde to boiling acetic anhydride (400 ml.) to which a few drops of piperidine had been added. After 10 minutes' very vigorous refluxing the solution was filtered, and on cooling deposited the *benzylidene* derivative in brilliant red needles with a green reflex, m. p. 241·5—242·5° (decomp.) (Found : C, 58·1; H, 5·8; N, 8·1; I, 24·3. $C_{25}H_{28}ON_3I$ requires C, 58·5; H, 5·5; N, 8·2; I, 24·8%). The *methochloride* formed intense purple octahedra with a golden reflex, m. p. 202—203° (decomp.) (Found : Cl, 8·8. $C_{25}H_{28}ON_3Cl$ requires Cl, 8·4%). *5-Aminotetrahydroacridine methiodide* separated from water in faintly yellow needles, m. p. 300—301° (decomp.) (Found : I, 36·8. $C_{14}H_{17}N_2I$ requires I, 37·3%), stable to sodium bicarbonate. The *acetyl* derivative formed pale yellow octahedra from water, m. p. 240—241° (decomp.) (Found : I, 33·8. $C_{16}H_{19}ON_2I$ requires I, 33·3%). 1-p-*Dimethylaminobenzylidenetetrahydroacridine hydriodide*, brilliant dark green needles, m. p. 263—264° (decomp.) (Found : C, 59·8; H, 5·0; N, 6·6; I, 28·7. $C_{22}H_{22}N_2,HI$ requires C, 59·7; H, 5·2; N, 6·3; I, 28·7%), was obtained by adding tetrahydroacridine methiodide (33 g.) and *p*-dimethylaminobenzaldehyde (18 g.) to acetic anhydride (1500 ml.) and heating under reflux for 1½ hours. Yield, 13·5 g. The hydriodide was also obtained under identical conditions from *tetrahydroacridine ethiodide*, yellow needles from absolute alcohol, m. p. 224—225° (decomp.) (Found : I, 37·4. $C_{15}H_{18}NI$ requires I, 37·5%). The *hydrochloride*, nearly black octahedra from ether–methyl alcohol, m. p. 232—233° (decomp.) (Found : Cl, 10·0. $C_{22}H_{22}N_2,HCl$ requires Cl, 10·0%), passed on heating with 70 vols. of water under reflux into 1-p-*dimethylaminobenzylidenetetrahydroacridine*, m. p. 133—134° (Found : C, 84·1; H, 6·8; N, 9·6. $C_{22}H_{22}N_2$ requires C, 84·1; H, 7·0; N, 8·9%), identical with the material described above obtained by direct interaction. After addition of a few drops of hydriodic acid (*d* 1·7) to the solution of the benzylidene derivative in boiling acetic anhydride, the characteristic dark green needles of the hydriodide separated on cooling, identical with the compound described above.

Phenanthridine Derivatives.—9-p-*Dimethylaminostyrylphenanthridine methiodide* (IV; R = R_1 = R_2 = H) (74%), dark red needles with a green reflex, m. p. 236·5—237·5° (decomp.) (Found : C, 61·8; H, 4·9; N, 6·1; I, 27·2. $C_{24}H_{23}N_2I$ requires C, 61·8; H, 4·9; N, 6·0; I, 27·3%), was prepared from 9-methylphenanthridine methiodide, m. p. 270—271° (decomp.) (Found : I, 37·9. Calc. for $C_{14}H_{15}NI$: I, 37·9%) (Pictet and Hubert give 246—247°, *Ber.*, 1896, **29**, 1185). The *methochloride* formed dark purple needles with a green reflex, m. p. 239—240° (decomp.) (Found : Cl, 9·5. $C_{24}H_{23}N_2Cl$ requires Cl, 9·5%). 5-Nitro-2-*p*-toluenesulphonamidodiphenyl was prepared by the method of G.P. 163,516. For hydrolysis the nitro-derivative (5 g.) was added to a mixture of concentrated sulphuric acid (10 ml.) and glacial acetic acid (10 ml.), warmed until solution was complete, and poured into ice-water (200 ml.) (cf. Bell, J., 1928, 2773). Reduction of 3-nitro-9-methylphenanthridine by the method of Morgan and Walls (1932, *loc. cit.*) gave a high-melting yellow product, so the following procedure was adopted : Finely powdered 3-nitro-9-methylphenanthridine (10 g.), suspended in concentrated hydrochloric acid (50 ml.), was treated with stannous chloride (27·5 g.) in concentrated hydrochloric acid (30 ml.), reaction being completed by heating for 30 minutes on the water-bath. After 12 hours at 0° the product was collected, the regenerated base refluxed with acetic anhydride (50 ml.) for 20 minutes, diluted to 250 ml., and the filtered solution made alkaline with ammonia. The acetyl derivative was crystallised once from spirit. Yield, 6·6 g. 3-Acetamido-9-methylphenanthridine methiodide formed very pale yellow needles from water, m. p. 268·5—269·5° (decomp.) (Found : I, 32·6. Calc. for $C_{17}H_{17}ON_2I$: I, 32·4%) (no m. p. is given by Morgan and Walls, J., 1938, 394).

3-*Acetamido*-9-p-*dimethylaminostyrylphenanthridine methiodide* (IV; R = NHAc, R_1 = R_2 = H) (80%) formed dark crimson-brown needles, m. p. 267·5—268·5° (decomp.) (Found : C, 59·5; H, 5·1; N, 8·1; I, 24·4. $C_{26}H_{26}ON_3I$ requires C, 59·4; H, 5·3; N, 8·0; I, 24·2%). The *methochloride*, intense mauve needles with a brassy reflex, m. p. 264·5—265·5° (decomp.) (Found : Cl, 8·0. $C_{26}H_{26}ON_3Cl$ requires Cl, 8·2%), was hydrolysed by heating the compound (8 g.) with concentrated hydrochloric acid (40 ml.) and water (40 ml.) for 1 hour under reflux, evaporating the solution to dryness on the water-bath, and crystallising the residue from absolute alcohol, the *amino-methochloride hydrochloride* being obtained in small brown needles (Found : Cl, 16·7. $C_{24}H_{25}N_3Cl_2$ requires Cl, 16·7%).

Reduction of 4'-nitro-2-acetamidodiphenyl (10 g.) (Bell, J., 1927, 95), suspended in spirit (40 ml.) and water (10 ml.), with reduced iron (15 g.) and a trace of hydrochloric acid for 1½ hours on the water-bath gave 4'-*amino*-2-*acetamidodiphenyl*, cubes from alcohol–light petroleum, m. p. 118·5—119·5° (Found : C, 74·3; H, 6·3; N, 12·4. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2; N, 12·4%). 4'-p-*Toluenesulphonamido*-2-*acetamidodiphenyl* formed octahedra from aqueous methyl alcohol, m. p. 201—202° (Found : S, 8·4. $C_{21}H_{20}O_3N_2S$ requires S, 8·4%). Attempts at ring closure with phosphorus oxychloride did not give satisfactory results. 4'-*Benzamido*-2-*acetamidodiphenyl*, dazzling white plates from spirit, m. p. 216—217° (Found : C, 76·4; H, 5·4; N, 8·6. $C_{21}H_{18}O_2N_2$ requires C, 76·4; H, 5·5; N, 8·5%), was cyclised to 7-*benzamido*-9-*methylphenanthridine*, pale yellow needles from methyl alcohol, m. p. 214—215° (Found : C, 77·8; H, 5·4; N, 8·3. $C_{21}H_{16}ON_2,CH_3\cdot OH$ requires C, 76·7; H, 5·8; N, 8·1%. The material dried in a vacuum at 135° gave C, 81·2; H, 5·2; N, 9·1. $C_{21}H_{16}ON_2$ requires C, 80·8; H, 5·1; N, 9·0%). The *picrate* formed a felted mass of pale yellow micro-needles from spirit, m. p. 277° (decomp.) (Found : N, 13·0. $C_{21}H_{16}ON_2,C_6H_3O_7N_3$ requires N, 12·9%). 7-*Amino*-9-*methylphenanthridine*, needles from spirit, m. p. 232·5—233·5° (Found : C, 80·4; H, 6·1; N, 13·8. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·5%), was prepared by hydrolysis of the benzamido-derivative with 2 parts of syrupy phosphoric acid for 1½ hours at 200—210°. 7-*Acetamido*-9-*methylphenanthridine*, obtained as a felted mass of faintly yellow needles from aqueous alcohol, m. p. 248—249° (Found : C, 76·8; H, 5·8; N, 11·3. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%), formed a *methiodide*, orange silky needles from water, m. p. 278—279° (Found : I, 32·0. $C_{17}H_{17}ON_2I$ requires I, 32·4%). 7-*Acetamido*-9-p-*dimethylaminostyrylphenanthridine methiodide* (IV; R = R_2 = H, R_1 = NHAc) (80%) formed small dark green needles, m. p. 270—271° (decomp.) (Found : C, 59·2; H, 5·3; N, 7·8; I, 24·6. $C_{26}H_{26}ON_3I$ requires C, 59·4; H, 5·3; N, 8·0; I, 24·2%). The *methochloride* crystallised in brilliant dark green needles, m. p. 276—277° (decomp.) (Found : Cl, 7·8. $C_{26}H_{26}ON_3Cl$ requires Cl, 8·2%). The *amino-methochloride hydrochloride* formed a brown microcrystalline powder from ether–alcohol (Found : Cl, 16·6. $C_{24}H_{25}N_3Cl_2$ requires Cl, 16·7%). 2-*Nitro*-4-*methyldiphenyl* was prepared in 51% yield from *m*-nitro-*p*-toluidine by the method of Elks, Haworth, and Hey (*loc. cit.*) and formed a pale yellow oil with a faint odour of bitter almonds, b. p. 208°/11 mm. (Found : C, 73·0; H, 5·2; N, 7·0. $C_{13}H_{11}O_2N$ requires C, 73·2; H, 5·2; N, 6·6%). 2-*Amino*-4-*methyldiphenyl*, obtained from the

nitro-compound in 83% yield by reduction with reduced iron in aqueous alcohol, b. p. 183°/11 mm. (Found : C, 85·4; H, 7·3; N, 8·0. $C_{13}H_{13}N$ requires C, 85·2; H, 7·1; N, 7·7%), formed an *acetyl* derivative, plates from aqueous methyl alcohol, m. p. 150·5—151·5° (Found : C, 79·7; H, 6·6; N, 6·5. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%), cyclised by phosphorus oxychloride to 2 : 9-*dimethylphenanthridine*, octahedra from light petroleum, m. p. 104·5—105·5°, b. p. 240°/14 mm. (Found : C, 87·0; H, 6·4; N, 6·9. $C_{15}H_{13}N$ requires C, 87·0; H, 6·3; N, 6·8%). Yield, 73%. 2 : 9-*Dimethylphenanthridine methiodide* formed yellow micro-needles from water, m. p. 261—262° (decomp.) (Found : I, 36·6. $C_{16}H_{16}NI$ requires I, 36·4%). 9-p-*Dimethylaminostyryl*-2-*methylphenanthridine methiodide* (IV; R = R_1 = H, R_2 = CH_3) (83%) formed small purplish needles with a greenish-brown reflex, m. p. 246—247° (decomp.) (Found : C, 62·2; H, 5·4; N, 6·1; I, 26·9. $C_{25}H_{25}N_2I$ requires C, 62·5; H, 5·2; N, 5·8; I, 26·5%). The *methochloride* formed permanganate-like crystals, m. p. 240—240·5° (decomp.) (Found : Cl, 8·7. $C_{25}H_{25}N_2Cl$ requires Cl, 9·1%).

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