357. *Chemotherapeutic Studies in the Acridine Series. Part II. 2-Amino, 2 : 5-, 2 : 7-, and 2 : 9-Diamino-acridines.*

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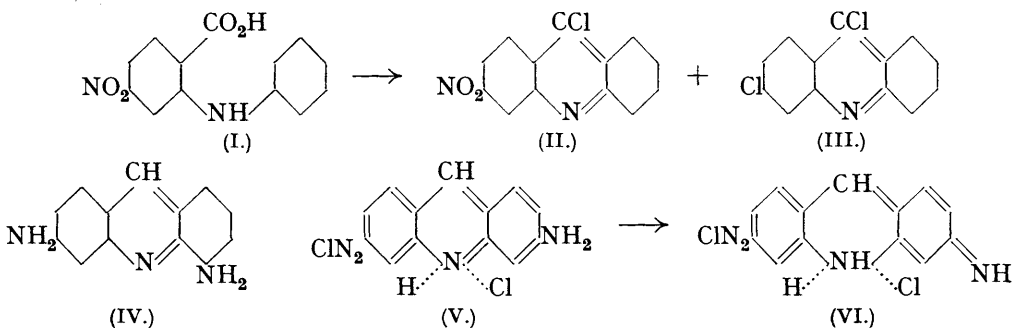
In furtherance of the plan of preparing the isomeric diaminoacridines, sodium 2-chloro-4-nitrobenzoate (Albert and Linnell, *J. Soc. Chem. Ind.*, 1936, **55**, 54T) was condensed with the appropriate amine to give 5 : 4′-*dinitrodiphenylamine-2-carboxylic acid*, 5 : 6′-*dinitrodiphenylamine-2-carboxylic acid*, and 5-nitrodiphenylamine-2-carboxylic acid (I), which, analogously with 5 : 5′-dinitrodiphenylamine-2-carboxylic acid (Part I, this vol., p. 89), lose carbon dioxide on gentle reduction to give 3 : 4′-*diaminodiphenylamine* (*bisacetyl* derivative), 3 : 2′-*diaminodiphenylamine* (*hydrochloride*), and 3-aminodiphenylamine (m. p. 75—76°) respectively. Sodium 2-chloro-4-nitrobenzoate and *o*-phenylenediamine similarly produced 5-*nitro*-6′-*aminodiphenylamine-2-carboxylic acid* (*hydrochloride*), which, however, did not lend itself to ring closure.

The above-mentioned dinitrodiphenylaminecarboxylic acids, treated with phosphorus oxychloride, followed by hydrolysis, gave excellent yields of 2 : 7-*dinitroacridone* and 2 : 9-*dinitroacridone* respectively. 5-Nitrodiphenylamine-2-carboxylic acid reacted with phosphorus oxychloride in a curious way; when the excess of chlorinating agent was extracted in the cold with light petroleum, 5-*chloro*-2-*nitroacridine* (II) resulted in good yield; but when it was removed by distillation from a glycerol bath, the nitro-group was largely replaced by chlorine, and up to 63% of 2 : 5-dichloroacridine (III) was produced. This unexpected reaction is reminiscent of the use of thionyl chloride (Meyer, *Monatsh.*, 1915, **36**, 723) at 190° to convert nitrobenzene quantitatively into chlorobenzene. The complete separation of the 2 : 5-dichloroacridine from the 5-chloro-2-nitroacridine could not be achieved by fractional crystallisation, and two *molecular* compounds, $C_{13}H_7NCl(NO_2) + C_{13}H_7NCl_2$ and $C_{13}H_7NCl(NO_2) + 2C_{13}H_7NCl_2$, were obtained, which, on hydrolysis, gave a mixture of 2-nitroacridone and 2-chloroacridone. This mixture was reduced with stannous chloride and the 2-aminoacridone was extracted with dilute acid, leaving 2-chloroacridone, which on treatment with phosphorus oxychloride furnished 2 : 5-dichloroacridine (III), m. p. 168—169° (corr.) (Magidson, *Ber.*, 1936, **69**, 404). The 2-aminoacridone displayed the properties ascribed to it by Tanasescu (*Bull. Soc. chim.*, 1934, **1**, 556), who obtained it indirectly by the reduction of 2-nitro-5-hydroxy-10-oxoacridine. On treatment with sodium amalgam in aqueous sodium hydroxide it yielded 2-aminoacridine (characterised as the *acetyl* derivative) more conveniently and in better yield (54%, calculated on the 2-nitroacridone) than did Scherlin's method (*Annalen*, 1935, **516**, 218) in which 2-nitro-

acridone was reduced in absence of air to 2-aminodihydroacridine, which was acetylated, oxidised, and deacetylated (30% yield).



Treatment of 2 : 5-dichloroacridine (III) with phenol and alcoholic ammonia yielded 2-*chloro-5-aminoacridine*, which, like the parent 5-aminoacridine (Lehmstedt, private communication), is not readily diazotisable, apparently functioning as the tautomeric acridonimine. Under somewhat similar conditions, 5-chloro-2-nitroacridine (II) gave 2 : 5-*diaminoacridine*.

Graduated reduction of 2 : 7- and 2 : 9-dinitroacridones produced in turn 2 : 7-*diaminoacridone*, 2 : 7-*diaminoacridine*, 2 : 9-*diaminoacridone*, and 2 : 9-*diaminoacridine* (IV). On testing Grandmougin's assumption (*Ber.*, 1913, **46**, 3425) that the intense violet colour produced when 2 : 8-diaminoacridine is cautiously diazotised is due to tautomeric change from the orange orthoquinonoid salts (V) to a violet paraquinonoid series (VI), it was found, as would be expected, that 2 : 6-diaminoacridine does, and 2-amino-, 2-*amino*-8-*acetamido*-, 3 : 7-diamino-, and 2 : 5-diamino-acridines (since the 5-group is not functional) do not give the violet coloration. The 2 : 7- and 2 : 9-diaminoacridines do not produce the violet colour : this suggests that here the 2-amino-group is the first to be diazotised.

The bactericidal properties of these aminoacridines will shortly be made known.

Experimental.

Dinitrodiphenylaminecarboxylic Acids.—Sodium 2-chloro-4-nitrobenzoate (4·5 g.), *p*-nitroaniline (4·2 g.; 1·5 mols.), and freshly precipitated copper (0·1 g.) were refluxed for an hour in nitrobenzene (20 ml.). After the product had been submitted to steam distillation, and the residue boiled with excess of aqueous sodium carbonate, the solution deposited a bright reddish-orange sodium salt, which, on treatment with hot 10% hydrochloric acid, gave (in 18% yield, this being the best obtainable by any modification) 5 : 4′-*dinitrodiphenylamine-2-carboxylic acid*; this crystallised from alcohol in brilliant orange-yellow needles, m. p. 252° (corr.), almost insoluble in light petroleum, dilute acids and hot water, sparingly soluble in chloroform and benzene, more soluble in ether, acetone, boiling glacial acetic acid (approx. 1 in 12; 1 in 17 is the best concentration for crystallisation) and alcohol (approx. 1 in 17, boiling) (Found : C, 51·3; H, 3·1; N, 14·2. $C_{13}H_9O_6N_3$ requires C, 51·5; H, 3·0; N, 13·9%). The almost colourless solution in sulphuric acid is rendered brilliant yellow by the addition of a trace of a nitrate. The *silver* salt is bright yellow-orange, soluble in aqueous ammonia, and almost insoluble in boiling water (Found : Ag, 26·3. $C_{13}H_8O_6N_3Ag$ requires Ag, 26·3%).

The synthesis of 5 : 6′-*dinitrodiphenylamine-2-carboxylic* acid proved still more difficult, and the best results (9% yield) were obtained by refluxing sodium 2-chloro-4-nitrobenzoate (4·5 g.), sodium carbonate (1·1 g.; 1 equiv.), freshly precipitated copper (0·1 g.), and *o*-nitroaniline (4·2 g.) in nitrobenzene (20 ml.) for 80 minutes. The product was cooled and diluted with benzene, and after filtration the solid was refluxed with chloroform, drained, taken up in boiling water, and filtered through decolourising carbon. Excess of sodium carbonate, added to the filtrate, precipitated a bright reddish-orange sodium salt. The free acid crystallised from alcohol in bright lemon-yellow needles, m. p. 239° (corr.), soluble in boiling alcohol (approx. 1 in 25) and boiling glacial acetic acid (a 1 in 25 solution deposits 90% on cooling); in other chemical and physical properties it was similar to the 5 : 4′-isomeride (Found : C, 51·9; H, 3·05; N, 14·3%).

5-Nitrodiphenylamine-2-carboxylic acid (I) was produced in unusually good yields (averaging

50%) when sodium 2-chloro-4-nitrobenzoate (4·5 g.) and precipitated copper (0·1 g.) were refluxed in aniline (20 ml.) for 2 hours and the product was acidified and washed with boiling water until only the required acid remained; m. p. 230·5° (corr.) after recrystallisation (1 in 5) from glacial acetic acid. It was soluble in boiling alcohol (approx. 1 in 13) and gave the above-described nitrate reaction. The scarlet sodium salt was not readily salted out. This acid was not formed when 4-nitroanthranilic acid and bromobenzene were heated with copper and alkali in various solvents.

In the preparation of these three nitrodiphenylamine-2-carboxylic acids, *p*-nitrobenzoic was regularly obtained as a by-product in 15—30% yield (calc. on the chloronitrobenzoic acid).

A mixture of *o*-phenylenediamine (3·25 g.; 1·5 mols.), sodium 2-chloro-4-nitrobenzoate (4·5 g.), sodium carbonate (1·1 g.), and precipitated copper (0·1 g.) was refluxed for an hour in *n*-butyl alcohol and the product was cooled and diluted with light petroleum. The cake obtained on filtration was dissolved in water and the solution was strongly acidified, filtered from tar, and treated with excess of sodium acetate, giving *5-nitro-6′-aminodiphenylamine-2-carboxylic acid monohydrochloride*, which formed golden spangles from butanol (1 in 20), m. p. 207° (corr., foaming), slightly soluble in hot water, sparingly in toluene and chloroform, and crystallised well from 30% alcohol (Found: C, 50·9; H, 4·2; N, 13·4; Cl, 11·0. $C_{13}H_{11}O_4N_3$,HCl requires C, 50·4; H, 3·9; N, 13·5; Cl, 11·5%). The colourless solution in sulphuric acid is unaffected by sodium nitrate. The sodium salt is not readily salted out. The dihydrochloride is white and fairly readily soluble. With nitrous acid it gives a white precipitate of the triazole and does not couple with phenols. With dilute hydrochloric acid and a trace of ferric chloride, a cherry-red colour (phenazine) is obtained on heating. With phenanthraquinone in glacial acetic acid, the phenanthrazonium betaine is deposited as creamy-white needles (from chloroform), m. p. 225° (corr.), which give the characteristic intense red colour with sulphuric acid, becoming yellow on dilution.

3 : 2′-*Diaminodiphenylamine.*—5 : 6′-Dinitrodiphenylamine-2-carboxylic acid (0·5 g.), stannous chloride (4·0 g.), and hydrochloric acid (15 ml., 10%) were gently warmed on the water-bath under reflux and the filtered liquid was made alkaline and shaken with ether. The extract was shaken with sodium hydroxide solution (rejected) and then with dilute hydrochloric acid, to which was finally added an equal volume of fuming hydrochloric acid; this caused the deposition of crystals of 3 : 2′-*diaminodiphenylamine dihydrochloride* in 70% yield. No amino-acid could be recovered from the alkaline liquors. The addition of benzene to a saturated solution of this salt in alcohol (1 in 50) slowly precipitated the hydrochloride in fine white crystals, very soluble in water and insoluble in butanol; they charred without melting at approx. 200° (Found: N, 15·6. $C_{12}H_{13}N_3$,2HCl requires N, 15·45%). The salt is very sensitive to iron, turning red (phenazine formation) even in the cold. The free base was deposited from all solvents as an oil which slowly solidified, m. p. 73°, and discoloured in the air. The isomeric 3 : 4′-diaminodiphenylamine, similarly obtained (yield, 85%), formed white crystals of low melting point, readily oxidising in the air to a pink product, and giving with a trace of ferric chloride a deep blue colour (indamine?), turning violet on keeping. Potassium dichromate gave a green precipitate soluble in sulphuric acid with a red coloration. 3 : 4′-*Bisacetamidodiphenylamine*, prepared by treating an ethereal solution of the base with acetic anhydride, formed cream-coloured needles from 30% alcohol (1 in 16), m. p. 186° (corr.), sparingly soluble in hot water, chloroform, benzene, toluene and ether, soluble without temperature gradient in alcohol and acetone (Found: N, 15·0. $C_{16}H_{17}O_2N_3$ requires N, 14·9%).

Dinitroacridones.—The use of sulphuric acid for ring closure caused sulphonation in every case and the following method was preferable: 5 : 4′-dinitrodiphenylamine-2-carboxylic acid (3 g.) and phosphorus oxychloride (18 ml.) were refluxed for ½ hour and the cooled product was poured into ice-water and basified. The precipitated 5-chloro-2 : 7-dinitroacridine was hydrolysed with boiling 10% hydrochloric acid, and the product exhausted with boiling sodium carbonate solution. After purification by solution in 1% alcoholic potassium hydroxide and reprecipitation with carbon dioxide, the 2 : 7-*dinitroacridone* was recrystallised from alcoholic pyridine, giving orange-needles, not melting at 350°, in 80% yield (Found: C, 55·1; H, 2·9; N, 14·3. $C_{13}H_7O_5N_3$ requires C, 54·7; H, 2·5; N, 14·7%). 2 : 7-Dinitroacridone is very sparingly soluble in the ordinary solvents, including boiling glacial acetic acid, but soluble in pyridine (approx. 1 in 120, boiling) and nitrobenzene. Unlike the 2 : 6- and the 2 : 8- isomeride, it is insoluble in alcoholic potassium hydroxide unless the alcohol is dilute; it then forms a port-wine red solution. To 20% aqueous sodium hydroxide it imparts a port-wine colour, without dissolving to any extent, whereas the 2 : 6- and the 2 : 8-isomeride impart a deep brown colour (cf. Part I).

2 : 9-*Dinitroacridone*, produced similarly, in 85% yield, formed brownish-orange crystals from alcoholic pyridine, m. p. 318—320°. It crystallised from boiling glacial acetic acid, but in its other properties behaved exactly as the 2 : 7-isomeride (Found : C, 55·0; H, 2·7; N, 14·65%).

2-Nitroacridone, similarly produced, gave an orange-red colour with alcoholic potassium hydroxide, contrasting with the port-wine colour given by the 2 : 6-, 2 : 7-, 2 : 8-, and 2 : 9-dinitro-analogues (*v.s.*, and Part I). Again, unlike these four compounds, it imparts no colour to 20% aqueous sodium hydroxide. The solubility in nitrobenzene is approx. 1 in 33.

Action of Phosphorus Oxychloride on 5-Nitrodiphenylamine-2-carboxylic Acid (I).—Phosphorus oxychloride (3 ml.) and 5-nitrodiphenylamine-2-carboxylic acid (0·5 g.) were refluxed together for ½ hour, chilled, and the excess of phosphorus oxychloride washed out with light petroleum. The sticky residue was treated with ice and 10% aqueous ammonia, giving yellow flakes of 5-*chloro*-2-*nitroacridine* (II) (80% yield), which separated from chloroform (1 in 18) in lemon-yellow hair-like crystals, m. p. 216° (corr.) (Found : N, 10·7; Cl, 13·7. $C_{13}H_7O_2N_2Cl$ requires N, 10·8; Cl, 13·7%), almost insoluble in dilute acids, but hydrolysed by boiling acids to 2-nitroacridone. Unlike 5-chloro-2 : 6-dinitroacridine (Part I), it was insoluble in cold 1% alcoholic potassium hydroxide. It crystallised well from toluene and benzene, and was slightly soluble in ether and alcohol without fluorescence. When the above reaction was repeated and the phosphorus oxychloride removed by distillation from a glycerol bath, 0·48 g. of a yellow solid was produced which gave two *fractions* when crystallised from benzene : yellow needles, soluble in benzene (approx. 1 in 15), m. p. 197—200° (corr.) [Found : N, 8·5. $C_{13}H_7NCl(NO_2) + C_{13}H_7NCl_2$ requires N, 8·3%], and bright yellow needles, soluble in benzene (approx. 1 in 10) and chloroform (approx. 1 in 7), m. p. 178—181° (corr.) [Found : N, 7·2; C, 62·2; H, 3·1. $C_{13}H_7NCl(NO_2) + 2C_{13}H_7NCl_2$ requires N, 7·4; C, 62·0; H, 2·8%]. These two compounds occur in the proportion of 1 mol. of the former to 1·7 mols. of the latter. The molecular compounds were hydrolysed with boiling dilute hydrochloric acid to a mixture of 2-chloroacridone and 2-nitroacridone. This mixture (1 g.) was treated in the cold with anhydrous stannous chloride reagent (*v.i.*; 30 ml.), and the stannichloride filtered off and decomposed with ice and sodium hydroxide. From the resultant mixture, 2-aminoacridone was extracted with hydrochloric acid, and the 2-chloroacridone remaining (0·5 g.), purified by solution in alcoholic potassium hydroxide and reprecipitation with acid, was converted into 2 : 5-dichloroacridine (0·5 g.) by refluxing with phosphorus oxychloride (3 ml.); it formed pale brownish-yellow crystals from benzene, m. p. 168—169° (corr.), very soluble in chloroform.

Anhydrous Stannous Chloride Reagent.—A mixture of hydrated stannous chloride (225 g.; 1 mol.), acetic anhydride (200 g.), and acetic acid (to produce 1 l.) was saturated with hydrogen chloride and used without filtration. It is a gentle, but effective, cold reducing reagent for nitro-groups.

meso*Amino-compounds.*—Phenylhydrazine crystals (0·11 g.), 2 : 5-dichloroacridine (0·3 g.), and amyl alcohol (1·3 ml.) were heated for 2 hours at 105° and the red hydrochloride (of chloroacridylphenylhydrazine) was filtered off (0·33 g.), dried, and reduced with zinc (0·5 g.) and acetic acid (2·5 ml.; 90%) in a boiling water-bath for 1 hour. The filtered solution gave with fuming hydrochloric acid creamy-white flakes of the hydrochloride of 2-*chloro*-5-*aminoacridine* (16% yield). The base formed lemon-yellow tufts, m. p. 272·5° (corr.), from 50% alcohol (Found : N, 12·0; Cl, 15·4. $C_{13}H_9N_2Cl$ requires N, 12·25; Cl, 15·5%), almost insoluble in boiling water and benzene, slightly soluble with fluorescence in ether and toluene, and very soluble in cold alcohol (with a blue-green fluorescence, turned green by a trace of alkali and violet by a trace of acid). The hydrochloride is soluble in water (violet fluorescence) and is not diazotised by the usual methods, but when a solution in glacial acetic acid is treated with sodium nitrite in sulphuric acid, a bright red solution is formed. An alternative process, giving 2-chloro-5-aminoacridine in 60% yield, consisted in dissolving 2 : 5-dichloroacridine (0·14 g.) in phenol (0·5 g.) by heating for ½ hour at 80°, cooling, and washing away the excess of phenol with ether. The residue of 2-chloro-5-phenoxyacridine hydrochloride (0·15 g.) was recrystallised from alcohol. This substance (1·62 g.) and alcohol saturated with ammonia at − 5° (20 ml.) were heated at 130° in a sealed tube for 3 hours. On cooling, crystals of 2-chloroacridone and a brown solution were obtained; the latter was evaporated, and the residue recrystallised from 50% alcohol, giving crystals, m. p. 272° (corr.) alone or mixed with those obtained as above.

Similarly 5-chloro-2-nitroacridine (0·45 g.), phenylhydrazine (0·18 g.), and amyl alcohol (2 ml.) gave the red hydrochloride of the *meso*phenylhydrazine derivative, which was reduced with zinc (0·8 g.) and acetic acid (3·5 ml.; 90%) for 1 hour in a boiling water-bath; after boiling with hydrochloric acid, filtering and cooling, the solution deposited light yellow flakes

of 2 : 5-*diaminoacridine hydrochloride*, which were washed with acetone and recrystallised from a little boiling water (13% yield) (Found for material dried in air at 120° : loss in a vacuum at 100°, 8·2. $C_{13}H_{11}N_3,HCl,H_2O$ requires H_2O, 7·35%. Found for material dried in a vacuum at 100° : C, 64·0; H, 5·2; N, 17·3. $C_{13}H_{11}N_3,HCl$ requires C, 63·5; H, 4·95; N, 17·1%).

The free base, which solidified soon after precipitation but did not readily crystallise, had m. p. 141° (corr.) and gave no depression with a sample, m. p. 140° (corr.), manufactured under D.R.-P. 364,033. The base is moderately soluble in hot and cold water, very soluble in butanol and alcohol (intense green fluorescence, lessened by traces of acid and unchanged by alkali), and almost insoluble in benzene, ether and chloroform. The hydrochloride is very soluble in boiling water to a supersaturated solution, from which it may be precipitated by seeding, or by the addition of hydrochloric acid, brine, or acetone. The light yellow aqueous solution fluoresces intense yellow-green, but only when dilute, and on diazotisation gives an orange solution which couples with β-naphthol (orange-red). The orange-yellow acetyl derivative is soluble in alcohol with bluish-green fluorescence (unchanged by alkali, but turning intense violet with a trace of acid) and decomposes without melting when heated.

2-Aminoacridone, obtained as above described and also (in 91% yield) by the direct reduction of 2-nitroacridone (1·5 g.) with anhydrous stannous chloride reagent (*v.s.*; 45 ml.), crystallised from dilute alcohol in pale yellow needles, m. p. 301—303° (corr.), almost insoluble in 20% aqueous sodium hydroxide, soluble in alcohol (violet fluorescence, turning intense yellow-green on the addition of a trace of acid), and in glacial acetic acid (intense green fluorescence). The hydrochloride gives an orange diazo-solution which couples with β-naphthol (scarlet).

In the same way, 2 : 7-dinitroacridone was reduced to the corresponding 2 : 7-*diaminoacridone* in 55% yield. Crystallised from 25% alcohol and from hot water (1 in 1700), this formed brownish-yellow, compact crystals, m. p. 352° (decomp.; bath at 345°), soluble (approx. 1 in 400) in alcohol, equally cold and boiling (the solubility in water and alcohol is uninfluenced by addition of alkali), very soluble in pyridine and glacial acetic acid, insoluble in all other solvents tried (Found : C, 68·7; H, 4·9; N, 18·0. $C_{13}H_{11}ON_3$ requires C, 69·3; H, 4·9; N, 18·6%). The hydrochloride gives a light brown solution in water, becoming orange on diazotisation and coupling with β-naphthol (port-wine red). The yellow sulphate is difficultly soluble in hot water. The intense yellow-green fluorescence of the base in alcohol is abolished by a trace of acid, and in glacial acetic acid there is only a trace of fluorescence. These fluorescences of the base, and the above colour reactions of the hydrochloride are also given by 3 : 7-diaminoacridone (Bogert, Hirschfelder, and Lauffer, *Coll. Czech. Chem. Comm.*, 1930, **2**, 385), specimens of which and of the corresponding acridine we have been enabled to examine through the kindness of the authors.

Similarly, 2 : 9-*diaminoacridone*, obtained from 2 : 9-dinitroacridone with anhydrous stannous chloride reagent in 77% yield, and precipitated from pyridine solution (1 in 50) with benzene, crystallised from water (1 in 5000) in lemon-yellow flocks, m. p. over 360°, soluble in alcohol (yellow-green fluorescence, unchanged by addition of acid) and glacial acetic acid (no fluorescence), slightly soluble in nitrobenzene, and almost insoluble in other solvents tried. As with the 2 : 7-isomeride, alkalis do not influence its solubility in water; yet it is very soluble in 1% alcoholic potassium hydroxide (Found : C, 68·9; H, 5·3; N, 18·1%). The brown aqueous solution of the hydrochloride fluoresces faintly green, and gives with nitrous acid a brown precipitate (triazole) and a yellow solution which couples with β-naphthol (deep red-brown). The hydrochloride gives no red colour with ferric chloride on warming, but a black precipitate such as the 2 : 6- and 2 : 7- isomerides produce, and the base forms no phenanthrazine.

2-Aminoacridine was obtained in 60% yield when 2-aminoacridone (0·4 g.), dissolved in *N*-hydrochloric acid (4·0 ml.), was added to *N*/2-sodium hydroxide (40 ml.) and treated during 1 hour, with stirring, at 80°, with sodium amalgam (40 g.; 2%); the mixture was then stirred for 2 hours, the mercury decanted, and air beaten into the hot liquid for 2 hours, no addition of ferric chloride being required. On cooling, the base was filtered off and dissolved in hydrochloric acid. The hydrochloride, precipitated with brine, gave on basification and recrystallisation from 35% alcohol brownish-orange needles, m. p. 219°, or from hot water bright yellow needles, m. p. 215° (both corr.; sealed tube). It is very soluble in butanol and chloroform; the alcoholic solution shows an intense yellow-green fluorescence. The yellowish-orange aqueous solution of the hydrochloride shows a slight green fluorescence, but only when dilute; it is diazotised to a yellow-orange solution which couples with β-naphthol (bright red). 2-*Acetamidoacridine* separates from dilute alcohol in pale yellow, sternutatory crystals, m. p. 236° (corr.; sealed tube) (Found : N, 12·05. $C_{15}H_{12}ON_2$ requires N, 11·9%), very soluble in alcohol (intense pure blue fluorescence). The hydrochloride gives an intense green fluorescence in water, and does not react with nitrous acid. The acetate is readily soluble.

2 : 7-Diaminoacridone, treated with sodium amalgam and ferric chloride, the product being precipitated as the sulphate precisely as the 2 : 6-isomeride (Part I), gave a 51% yield of 2 : 7-*diaminoacridine*, which after recrystallisation from alcohol (1 in 800), formed orange-yellow needles from boiling water, m. p. 355° (bath at 345°), slightly soluble in acetone and methanol and almost insoluble in benzene, xylene, ether, chloroform and nitrobenzene. The alcoholic solution fluoresces yellow-green (Found : C, 74·5; H, 5·25; N, 19·8. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3; N, 20·1%). The base is stable in air and stains the skin red. The sulphate is dull scarlet and sparingly soluble; the hydrochloride is red-brown and gives a deep red aqueous solution, entirely without fluorescence, which becomes orange-coloured on diazotisation, and couples with β-naphthol (violet). The fluorescences, stability, diazotisation, and coupling of the 3 : 7-isomeride (*v.s.*) were found to be almost identical.

The application of the above reduction method, the ferric chloride being omitted, to 2 : 9-diaminoacridone gave an 88% yield of 2 : 9-*diaminoacridine* (IV), bright yellow crystals from alcohol (1 in 250), m. p. 249° (corr.), sparingly soluble in hot water and light petroleum, but crystallising well from chloroform and benzene (Found : C, 74·9; H, 5·3; N, 20·0%). None of the solutions of the base or the hydrochloride shows any fluorescence. The scarlet sulphate is sparingly soluble in water and alcohol; the hydrochloride is readily soluble, and addition of sodium nitrite to the acidified orange-red solution produces a bright pink colour, and at this stage the solution will couple with β-naphthol (bright red); but excess of sodium nitrite gives a green precipitate, and the solution will no longer couple with phenols.

Partial Acetylation of Proflavine (Base).—2 : 8-Diaminoacridine monohydrochloride (from commercial proflavine; 2·5 g.) was stirred with glacial acetic acid (10 ml.), and acetic anhydride (2·5 ml.) added; the mixture was warmed until the contents solidified (cf. D.R.-P. 546,661) and then for 15 minutes in a boiling water-bath, treated with glacial acetic acid (20 ml.), warmed to 118°, and refluxed for 15 minutes. On cooling, filtering, and basifying the precipitate and washing it several times with boiling water, an almost quantitative yield of 2-*amino*-8-*acetamidoacridine* was obtained, which formed orange-yellow flakes (from 30% alcohol), m. p. 286° (corr.), almost insoluble in chloroform and benzene, slightly soluble in hot water, and very soluble in alcohol and butanol (Found : N, 16·8. $C_{15}H_{13}ON_3$ requires N, 16·7%). The alcoholic solution fluoresces an intense yellow-green. The hydrochloride, only sparingly soluble in boiling alcohol, but soluble in methanol (approx. 1 in 35), is precipitated from its solution in the latter by benzene in brilliant scarlet crystals, readily soluble in water to a reddish-orange solution (fluorescing green when dilute), which becomes orange-red on diazotisation and couples with β-naphthol (bright red). As with many other aminoacridines, ammonia does not precipitate the free base.

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