29. *Synthesis of Diaminoacridines. Part I.*

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Various routes to 2 : 7-diaminoacridone have been investigated and three new syntheses described :* *viz.*, (i) condensation of the 4-nitro- or 4-acetamido- derivative of 2-chlorobenzoic acid with *p*-phenylenediamine or *p*-aminoacetanilide followed by *cyclo*dehydration, (ii) condensation of the 5-nitro- or 5-acetamido-derivative of 2-chlorobenzoic acid with *m*-phenylenediamine with subsequent *cyclo*dehydration and (iii) nitration of 2-nitroacridone, followed by reduction.

A number of 3′-nitro- and 3′-amino-diphenylamine-2-carboxylic acids bearing a further substituent in the carboxylated nucleus have been cyclised with sulphuric acid and in all cases it has been shown that in the 3′-nitro series ring closure takes place principally on the 2′-position (*ortho*-closure) and in the 3′-amino series cyclisation takes place almost exclusively on the 6′-position (*para*-closure).

General observations have been made on the influence of substituents in the carboxylated nucleus upon the ease of cyclisation of monosubstituted diphenylamine-2-carboxylic acids.

2 : 7-Diaminoacridine has been shown to possess high antibacterial activity and comparatively low tissue and systemic toxicity together with physical properties which recommend its use as a general antiseptic in place of proflavine (Albert, Dyer, and Linnell, *Quart. J. Pharm.*, 1937, **10**, 649; Ungar and Robinson, *J. Pharm. Exp. Ther.*, 1944, **80**, 217). The method reported for the preparation of the compound (Albert and Linnell, *J.*, 1936, 1614) leaves much to be desired because the intermediate compound, 5 : 4′-dinitrodiphenylamine-2-carboxylic acid, is difficult of access; it was accordingly thought desirable to investigate alternative synthetic routes.

The general literature relating to the Ullmann condensation between negatively substituted arylamines and 2-halogenobenzoic acids (Ullmann, *Annalen*, 1907, **355**, 312; Tuttle, *J. Amer. Chem. Soc.*, **1923**, **45**, 1906; Bogert and Hirschfelder, *Coll. Trav. Chim. Czeckoslov.*, 1930, **5/6**, **382**; Magidson and Trawin, *Ber.*, 1936, **69**, 537; Albert and Linnell, *J.*, 1936, 89 and 1614; Lehmstedt and Schrader, *Ber.*, 1937, **70**, 838) indicates that the presence of a negative substituent in either of the reactants, particularly in the arylamine nucleus, exerts an inhibiting influence upon the course of the condensation; attention was directed, therefore, to the interaction of the corresponding positively substituted arylamine with the negatively and with the positively substituted 2-halogenobenzoic acid. It was found that *p*-phenylenediamine readily reacts with 2-chloro-4-nitrobenzoic acid but under the usual conditions of the Ullmann reaction, *viz.* at *ca.* 140° in amyl alcohol, the diamine effects reductive dehalogenation of the chloronitrobenzoic acid with formation of *p*-nitrobenzoic acid in almost quantitative yield. At *ca.* 80°, however, in *iso*propyl alcohol, the normal Ullmann reaction takes place smoothly with production of *5-nitro-4′-aminodiphenylamine-2-carboxylic acid* in satisfactory yield; even at this abnormally lowered temperature appreciable amounts of *p*-nitrobenzoic acid are formed. At 100°, 120°, and 130° in amyl alcohol the ratios at which the normal Ullmann reaction and the reductive dehalogenation take place are approximately 60 : 40, 40 : 60, and 20 : 80 respectively. Similarly at 140°, *p*-aminodimethylaniline reacts vigorously with 2-chloro-4-nitrobenzoic acid with formation of *p*-nitrobenzoic acid, but the tendency to effect reductive dehalogenation would appear to be less than with *p*-phenylenediamine since, at 120°, a high yield of *5-nitro-4′-dimethylaminodiphenylamine-2-carboxylic acid* is obtainable. Interaction of *p*-phenylenediamine with 2-chloro-4-acetamidobenzoic acid gave analogous results; at 140° *p*-acetamidobenzoic acid is the principal product while at 100° the desired *4′-amino-5-acetamidodiphenylamine-2-carboxylic* acid is obtained in satisfactory yield.

Monoacylation of the diamine was found to inhibit the ability of the latter to effect dehalogenation; 2-chloro-4-acetamidobenzoic acid condenses smoothly with *p*-aminoacetanilide and even at elevated temperatures 5 : 4′-*di*(*acetamido*)*diphenylamine-2-carboxylic* acid is the sole reaction product. It is believed that the reductive dehalogenation (hydrogenolysis) of activated halogeno-aryls (compare Lehmstedt, *Ber.*, 1937, **70**, 1526) may serve as a useful method for obtaining the corresponding nonhalogenated aryl where other methods fail or cannot be employed (also compare the use of Raney nickel for this purpose, Schwenk *et al.*, *J. Org. Chem.*, 1944, **9**, 1).

An alternative route to 2 : 7-diaminoacridone is evidently available from suitable 4 : 3′-disubstituted diphenylamine-2-carboxylic acids provided that closure of the acridone ring can be effected at the 6′-position. Accordingly 2-chloro-5-nitrobenzoic acid was condensed with *m*-nitroaniline and with *m*-phenylenediamine to give 4 : 3′-dinitro- and *4-nitro-3′-aminodiphenylamine-2-carboxylic* acids respectively; in addition 2-chloro-5-acetamidobenzoic acid and *m*-phenylenediamine gave *3′-amino-4-acetamidodiphenylamine-2-carboxylic acid* in excellent yield. In this series, *i.e.* 5-substituted 2-chlorobenzoic acids, there appeared to be little tendency to undergo hydrogenolysis on treatment with the diamine and the temperature of the reaction accordingly is not critical.

2-Chloro-3-acetamidobenzoic acid failed to condense with aniline and *m*-phenylenediamine; under all the conditions used, from 100° to 140°, dehalogenation of the chloroacetamidobenzoic acid took place with formation of *m*-acetamidobenzoic acid. *m*-Nitroaniline similarly effected dehalogenation at 140°, and at 100° no reaction was observable. 2-Chloro-3-nitrobenzoic acid, however, condensed smoothly with aniline to yield *6-nitrodiphenylamine-2-carboxylic acid*.

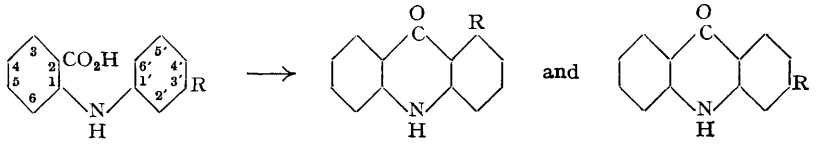
2-Chloro-6-acetamidobenzoic acid and 2-chloro-6-nitrobenzoic acid condensed with aniline to give

* British and U.S. Patent Specifications pending.

3-*acetamidodiphenylamine*-2-*carboxylic acid* and 3-*nitrodiphenylamine*-2-*carboxylic acid* respectively. The results of the condensation of the 3-acetamido- and the 3-nitro-derivative of 2-chlorobenzoic acid and of the 6-acetamido- and the 6-nitro-derivative of 2-chlorobenzoic acid with *m*-nitroaniline and *m*-phenylenediamine will be reported shortly.

cyclo*Dehydration of Substituted Diphenylamine*-2-*carboxylic Acids.*—Treatment of 5-nitro-4′-aminodiphenylamine-2-carboxylic acid with hot sulphuric acid (Jourdan, *Ber.*, 1885, **18**, 1444; Ullmann, *loc. cit.*) effected cyclisation with formation of 2-*nitro*-7-*aminoacridone* which on reduction yielded 2 : 7-diaminoacridone. Similarly, cyclisation and simultaneous hydrolysis of 5 : 4′-di(acetamido)diphenylamine-2-carboxylic acid gave 2 : 7-diaminoacridone and both of these methods constitute facile routes to the latter.

While 2′- and 4′-substituted diphenylamine-2-carboxylic acids can undergo cyclisation with formation in each case of only one product, the 3′-substituted diphenylamine-2-carboxylic acids may give rise to 4- or 2-substituted acridones according to whether the acridone ring closes on the 2′-position (*ortho*-closure) or the 6′-position (*para*-closure) respectively.



ortho-closure *para*-closure

Thus both the 2 : 6- and the 2 : 8-dinitro-derivative of 5-chloroacridine are simultaneously formed by the action of phosphoryl chloride on 5 : 3′-dinitrodiphenylamine-2-carboxylic acid (Albert and Linnell, *J.*, 1936, 89). Lehmstedt and Schrader (*Ber.*, 1937, **70**, 838) made quantitative measurements upon the directional cyclisation of a series of 3′-substituted diphenylamine-2-carboxylic acids and reported that the ratio of *ortho*- to *para*-closure is 75 : 25 when the 3′-substituent is NO_2 (negative) and 20 : 80 when the 3′-substituent is Me (positive). These authors believed that the same or a similar ratio would obtain with a 3′-amino substituent as with a 3′-nitro substituent but, later, this assumption was shown to be incorrect as 2- and 4-aminoacridones were obtained in the ration of *ca.* 8 : 1 by the cyclisation of 3′-aminodiphenylamine-2-carboxylic acid (Albert and Ritchie, *J.S.C.I.*, 1941, **60**, 120), *i.e.* *para*-closure largely predominates. The present work relates to the *cyclo*-dehydration of 3′-nitro- and 3′-amino-diphenylamine-2-carboxylic acids which have another substituent in the carboxylated nucleus and in all cases it has been shown that, while with the 3′-nitro- series *ortho*-closure largely predominates, with the 3′-amino- series *para*-closure takes place almost exclusively. Thus 3′-nitro-4-acetamidodiphenylamine-2-carboxylic acid yields principally 6-nitro-3-aminoacridone which on reduction gives 3 : 6-diaminoacridone, m. p. 314—316°, and 3 : 6-diaminoacridine, m. p. 254—256°; the constitution of the latter (not previously proved) was shown by its identity with the diaminoacridine obtained by nitration of 4-nitroacridone and reduction of the dinitroacridone thus obtained. On the other hand cyclisation of 3′-amino-4-acetamidodiphenylamine-2-carboxylic acid takes place with almost exclusive formation of 2 : 7-diaminoacridone, m. p. 358—360°, which on reduction yields 2 : 7-diaminoacridine identical with the diaminoacridine obtained by the nitration of 2-nitroacridone and reduction of the resulting dinitroacridone.

Similarly 3′ : 4-dinitro-diphenylamine-2-carboxylic acid cyclises into 3 : 6-dinitroacridone which on reduction gives 3 : 6-diaminoacridone, m. p. 314—316° (compare Albert and Linnell, *J.*, 1938, 22) whereas *cyclo*dehydration of 4-nitro-3′-aminodiphenylamine-2-carboxylic acid yields 7-*nitro*-2-*aminoacridone* which on reduction gives 2 : 7-diaminoacridone, m. p. 358—360°.

In the same manner 3′-nitro-5-acetamidodiphenylamine-2-carboxylic acid yields 6-nitro-2-aminoacridone which on reduction gives successively 2 : 6-diaminoacridone, m. p. 304—306°, and 2 : 6-diaminoacridine, m. p. 204—206°, while 3′-amino-5-acetamido-diphenylamine-2-carboxylic acid yields almost exclusively 2 : 8-diaminoacridone, m. p. 368—370°, which on reduction gives 2 : 8-diaminoacridine, m. p. 284—286°. Similarly, while 3′ : 5-dinitro-diphenylamine-2-carboxylic acid yields 2 : 6-dinitroacridone which on reduction leads to 2 : 6-diaminoacridone, m. p. 300—302°, and 2 : 6-diaminoacridine, m. p. 204—206°, 5-nitro-3′-amino-diphenylamine-2-carboxylic acid gives principally 8-nitro-2-aminoacridone which on reduction is convertible into 2 : 8-diaminoacridone, m. p. 366—368°, and 2 : 8-diaminoacridine, m. p. 284—286°.

The *cyclo*dehydration of diphenylamine-2-carboxylic acid bearing a single substituent in the carboxylated nucleus presents several anomalies. Diphenylamine-2-carboxylic acid itself readily undergoes cyclisation with sulphuric acid at 90—100° yielding in 30 minutes and 120 minutes almost quantitative yields of acridone and acridone-3-sulphonic acid respectively (Matsumura, *J. Amer. Chem. Soc.*, 1935, **57**, 1533); it has been found that avoidance of sulphonation may best be effected by the prolonged action of 70—75% sulphuric acid.* Ullmann (*loc. cit.*) failed to obtain 2-nitroacridone from 5-nitrodiphenylamine-2-carboxylic acid by the use of sulphuric acid and effected cyclisation with aluminium chloride and phosphorus pentachloride (compare also Albert and Linnell, *loc. cit.*). Repeated attempts to obtain 2- and 3-nitroacridones by the ring closure of 5- and 4-nitrodiphenylamine-2-carboxylic acids were unsuccessful, the only products isolated being nitroacridone-sulphonic acids; this would accord with the observations of Matsumura (*loc. cit.*) who obtained 2-nitroacridone-

* The "concentrated sulphuric acid" (Cohen, "Practical Organic Chemistry" (1930), p. 278) is evidently a mistranslation of "englische Schwefelsäure" from Graebe and Lagodzinski (*Ber.*, 1892, **25**, 1737).

7-sulphonic acid by the action of cold 20% fuming sulphuric acid on 5-nitrodiphenylamine-2-carboxylic acid. Similarly 4-acetamidodiphenylamine-2-carboxylic acid could not be converted into 3-aminoacridone, the only identifiable product being an aminoacridonesulphonic acid, presumably the 3 : 7-isomeride. On the other hand, 6-nitro-diphenylamine-2-carboxylic acid on treatment with sulphuric acid at 100° readily gave 1-nitroacridone which on reduction yielded 1-aminoacridone, whereas 6-acetamidodiphenylamine-2-carboxylic acid suffered almost total decarboxylation on treatment with the cyclising reagent. 3-Acetamidodiphenylamine-2-carboxylic acid gave 4-aminoacridone although in very small yield (*ca.* 5%); 3-nitrodiphenylamine-2-carboxylic acid could not be converted into 4-nitroacridone owing to loss of carbon dioxide. The formation of 1- and 4-aminoacridones from substituted 2-halogenobenzoic acids and aniline has not previously been recorded.

It would appear that substituents in the carboxylated nucleus may, according to their nature and orientation, deactivate the carboxyl group towards cyclisation or, alternatively, they activate the 7-(or 3-)position of the acridone first obtained and thus facilitate sulphonation in this position. This accords with the successful closure of 4′-substituted diphenylamine-2-carboxylic acids in which the activated 7-(or 3-)position is blocked and also of 3′-nitrodiphenylamine-2-carboxylic acids in which the presence of the nitro group would preclude easy sulphonation; but it does not explain the normal cyclisation of 3′-amino-4- and -5-acetamidodiphenylamine-2-carboxylic acids in which the presence of the amino group in the 8-(or 2-)position of the formed acridone would be expected to assist sulphonation at the 7-(or 3-)position.

Since the 3- and 7-positions in the acridone molecule are the predominantly activated positions towards nitrating and sulphonating agents while the 1- and the 9-positions are activated to a far lesser extent (Lehmstedt *et al.*, *Z. angew. Chem.*, 1928, **41**, 220; *Ber.*, 1927, **60**, 1370; 1931, **64**, 1232; 1931, **64**, 2381, 2386; Jensen, *J. Amer. Chem. Soc.*, 1927, **49**, 1049; Scherlin *et al.*, *Annalen*, 1935, **516**, 218; Matsumura, *J. Amer. Chem. Soc.*, 1935, **57**, 1533; 1938, **60**, 593) the possibility presented itself that 2 : 7-dinitroacridone could be obtained by the nitration of the easily accessible 2-nitroacridone. It was found that the latter nitrates smoothly in sulphuric acid solution with production of 2 : 7-dinitroacridone in almost theoretical yield; no 2 : 9-dinitroacridone could be separated from the crude reaction product. Reduction with stannous chloride effected quantitative formation of 2 : 7-diaminoacridone and further reduction of the crude diaminoacridone with sodium amalgam followed by oxidation of the resulting diaminoacridane gave 2 : 7-diaminoacridine in good yield. Since the m. p. of the crude product, 348—352°, was very little different from that of the recrystallised material, 354—356°, this is additional evidence for the absence of any but traces of the isomeric 2 : 9-dinitroacridone in the crude nitration product (2 : 9-diaminoacridine has m. p. 250°). This would appear to be the easiest method of preparing 2 : 7-diaminoacridine. Similarly, nitration of 4-nitroacridone yielded 3 : 6-dinitroacridone which was successively converted into 3 : 6-diaminoacridone and 3 : 6-diaminoacridine. The identity of the m. p. of the latter (254—256°) with that of the product obtained by the cyclisation of 3′ : 4-dinitrodiphenylamine-2-carboxylic acid followed by reduction (254—256°) would indicate that the m. p. of 322° for this compound given by Albert and Linnell (*loc. cit.*) is incorrect.

Cyclisation of 5-nitro-4′-dimethylaminodiphenylamine-2-carboxylic acid by the phosphoryl chloride method (Lesnianski, *Bull. Acad. Polonaise*, 1929, A, 81; Magidson and Grigorowski, *Ber.*, 1933, **66**, 866; Borsche, Runge, and Trautner, *ibid.*, 1933, **66**, 1315; Dirscherl and Thron, *Annalen*, 1933, **504**, 297) gave 5-*chloro*-2-*nitro*-7-*dimethylaminoacridine* which on acid hydrolysis yielded 2-*nitro*-7-*dimethylaminoacridone*; reduction of the latter with stannous chloride gave 2-*amino*-7-*dimethylaminoacridone* which was converted by sodium amalgam followed by oxygenation into 2-*amino*-7-*dimethylaminoacridine*.

4′-Dimethylamino- and 5-chloro-4′-dimethylamino-diphenylamine-2-carboxylic acids on cyclisation with phosphoryl chloride afforded in good yield 5-chloro-3-dimethylamino- and 5 : 8-dichloro-3-dimethylaminoacridine respectively. The presence of the 3-dimethylamino substituent exerts a strong stabilising influence upon the *meso*-halogen since both these compounds may be recrystallised without decomposition from boiling aqueous alcohol whereas 5-chloroacridine under similar conditions is rapidly converted into acridone (compare also the stabilisation of *meso*-halogens by a 3-methoxy group). 5-Chloro-3-dimethylamino- and 5 : 8-dichloro-3-dimethylamino-acridine reacted readily with ammonium carbonate in phenol solution with formation of 5-*amino*-3-*dimethylamino*- and 8-*chloro*-5-*amino*-3-*dimethylamino-acridine* respectively; both these diamines possess powerful antibacterial activity and low tinctorial values.

Experimental.

All m. ps. above 310° were determined on a Mason's block, the compound being inserted at *ca.* 20° below its m. p. All compounds for analysis were dried at 100—110°/1 mm. over phosphoric oxide.

General Procedure used for Ullmann Reactions.—The 2-halogenobenzoic acid was dissolved in 4 to 10 times its weight of rectified amyl alcohol (b. p. 132—136°), potassium carbonate added and the mixture stirred rapidly at the boiling point for ½ hour during which time *ca.* one-tenth of the solvent was allowed to distil off in order to remove most of the water and obtain the potassium salt of the acid in a voluminous state. The mixture was cooled, the arylamine and copper catalyst added and the stirring continued at the stated temperatures; the amyl alcohol was removed by distillation in steam, the residual liquid filtered from neutral material and whilst stirred at 80—100° adjusted to pH 4 with 5N-hydrochloric acid. The precipitated diphenylaminecarboxylic acid collected from the hot solution was usually purified by dissolution in a large volume of boiling water containing a slight excess of ammonia and the free acid reprecipitated from this boiling, *ca.* 5%, solution of the ammonium salt by adjustment to *p*H 4 and collection at the boiling point. This procedure effectively removed unchanged halogenobenzoic acids and by-products (*e.g.*, *p*-nitrobenzoic acid) with little loss of product. In some cases, particularly with nitrodiphenylamine-2-carboxylic acids, crystallisation of the potassium salt was found to be effective and economical. Formation of the diphenylaminecarboxylic acid in high yield, particularly when the reaction is conducted at low temperatures, appears to depend to a considerable extent upon

the physical state of the potassium salt of the halogenobenzoic acid and also upon the presence of a trace of water; a voluminous crystalline form of the potassium salt conduces to high yield and this is best obtained by the employment of amyl alcohol containing *ca.* 3% of water and then distilling off most of this water, together with that formed during the neutralisation, before the addition of the arylamine and the catalyst. For example, on three occasions when preformed anhydrous potassium 2-chloro-4-nitro-benzoate, ignited potassium carbonate and anhydrous amyl alcohol were stirred for 4 hours at 120° with *p*-phenylenediamine no reaction took place, the whole of the chloronitrobenzoic acid being recovered unchanged. In many cases the diphenylamine-2-carboxylic acids obtained were too highly coloured or too insoluble in aqueous alcohol for determination of their equivalents.

Series Derived from 4-Substituted 2-Chlorobenzoic Acids.

3'-Amino-5-acetamidodiphenylamine-2-carboxylic Acid.—2-Chloro-4-acetamidobenzoic acid (10 g.), potassium carbonate (7·5 g.), copper powder (0·2 g.), *m*-phenylenediamine (8 g.) and amyl alcohol (40 c.c.) were stirred at 150° (bath-temperature) for 1 hour. The crude *3'-amino-5-acetamidodiphenylamine-2-carboxylic acid* thus obtained (5·6 g.), m. p. 182—186°, was difficult to purify and was used as such (Found: N, 14·3. $C_{15}H_{15}O_3N_3$ requires N, 14·7%).

2 : 8-Diaminoacridone.—The foregoing material (2·6 g.) was dissolved in sulphuric acid (18 c.c.) and the solution heated to 100° for 1½ hours; water (10 c.c.) was added, the heating at 100° continued for a further ½ hour, the solution poured on to ice (100 g.) and basified with aqueous ammonia. Collection of the yellow precipitate and recrystallisation from aqueous pyridine gave 2 : 8-diaminoacridone (0·85 g.) in yellow needles, m. p. 368—370°. The identity of this product was established by reduction with sodium amalgam to 2 : 8-diaminoacridine (proflavine), m. p. 282—284° alone and in admixture with authentic material (Found: N, 20·3. Calc. for $C_{13}H_{11}N_3$: N, 20·1%).

3'-Nitro-5-acetamido-diphenylamine-2-carboxylic Acid.—2-Chloro-4-acetamidobenzoic acid (10 g.), *m*-nitroaniline (8 g.), potassium carbonate (7 g.), copper powder (0·2 g.) and amyl alcohol (40 c.c.) were stirred at 150° (bath temperature) for 2¼ hours. The crude product, after extraction three times with boiling water (300 c.c. each time), was recrystallised from aqueous alcohol and gave *3'-nitro-5-acetamidodiphenylamine-2-carboxylic acid* (6·2 g.) in yellow needles, m. p. 246—248° (Found: N, 13·3; *M*, by titration, 315. $C_{15}H_{13}O_5N_3$ requires N, 13·3%; *M*, 315).

2 : 6-Diaminoacridone.—The foregoing acid (6 g.) dissolved in sulphuric acid (45 c.c.) was heated to 100° for 1½ hours, water (15 c.c.) added, the solution heated at this temperature for a further ½ hour and poured on to ice (200 g.). The precipitate was collected, ground with aqueous ammonia and washed with hot water, *6-nitro-2-aminoacridone* (4·5 g.) being obtained as a dark powder, m. p. 352—356°. Recrystallisation from aqueous pyridine gave the pure compound in brown-yellow needles, m. p. 366—368° (Found: N, 16·9. $C_{13}H_9O_3N_3$ requires N, 16·5%).

The crude compound (3·5 g.) was added to a solution of stannous chloride crystals (40 g.) in hydrochloric acid (40 c.c.) and the solution heated on the water bath for 2½ hours. After cooling, the mixture was diluted with water (200 c.c.), poured into an excess of 5N-sodium hydroxide, the precipitate collected, redissolved in dilute hydrochloric acid, filtered (charcoal) and basified with 5N-sodium hydroxide. The yellow precipitate was collected and washed with water, 2 : 6-diaminoacridone being obtained (2·5 g.), m. p. 304—306° (sintering at 294°). Recrystallisation from aqueous pyridine gave the pure compound in yellow needles, m. p. 302—304° (lit. 306°) (Found: N, 18·3. Calc. for $C_{13}H_{11}ON_3$: N, 18·7%).

Reduction of the crude diaminoacridone with sodium amalgam gave 2 : 6-diaminoacridine which was obtained in brown needles from aqueous pyridine, m. p. 205—206° (Albert and Linnell, J., 1936, 89, give m. p. 213—216°) (Found: C, 74·1; H, 5·3; N, 20·1. Calc. for $C_{13}H_{11}N_3$: C, 74·6; H, 5·3; N, 20·1%).

4'-Amino-5-acetamidodiphenylamine-2-carboxylic Acid.—2-Chloro-4-acetamidobenzoic acid (10 g.), potassium carbonate (7·5 g.), copper powder (0·2 g.), *p*-phenylenediamine (8 g.) and amyl alcohol (40 c.c.) were stirred at 110° (bath temperature, *ca.* 100° internal temperature) for 2½ hours. The crude 4'-amino-5-acetamidodiphenylamine-2-carboxylic acid (5·1 g.), which had m. p. 214° (sintering at 194°), could not be effectively purified; acetylation with acetic anhydride in dilute aqueous sodium carbonate solution (see below) gave *4' : 5-di(acetamido)diphenylamine-2-carboxylic acid* which crystallised from aqueous alcohol in brown needles, m. p. 244—246° (Found: N, 12·7; *M*, by titration, 334. $C_{17}H_{17}O_4N_3$ requires N, 12·9%; *M*, 327).

2 : 7-Diaminoacridone.—Crude 4'-amino-5-acetamidodiphenylamine-2-carboxylic acid (4·2 g.) was heated to 100° with sulphuric acid (30 c.c.) for 1 hour, the solution cooled, water (10 c.c.) added, the solution reheated at this temperature for a further ½ hour and poured on to ice (250 g.). After basification with ammonia, the insoluble material was collected and purified by dissolution in dilute hydrochloric acid and reprecipitation with ammonia, 2 : 7-diaminoacridone being obtained (1·7 g.) as a yellow powder, m. p. 340—344°. Recrystallisation from dilute pyridine gave the pure compound in golden-brown plates, m. p. 358—360° (Found: N, 18·7. Calc. for $C_{13}H_{11}ON_3$: N, 18·7%).

5-Nitro-4-aminodiphenylamine-2-carboxylic Acid.—2-Chloro-4-nitrobenzoic acid (40 g.) was dissolved in *iso*propyl alcohol (325 c.c.) and potassium carbonate (40 g.) slowly added; after the addition of benzene (75 c.c.), the mixture was stirred and 150 c.c. of the ternary liquid distilled off, leaving the potassium salt as a voluminous crystalline precipitate. Copper powder (1 g.) and *p*-phenylenediamine (27 g.) were added, the mixture stirred whilst gently refluxed (internal temperature 79°) for 7 hours and then distilled in steam. The residual solution was filtered (charcoal) from insoluble black material (10 g.), the filtrate (vol. 750 c.c.) whilst being stirred at the boiling point adjusted to pH 4·0—4·5 with hydrochloric acid, the ochre microcrystalline precipitate of 5-nitro-4'-aminodiphenylamine-2-carboxylic acid (32 g.) collected from the hot liquor, washed with hot water and dried. It had m. p. 264—266° (decomp. with softening at 258°). Acidification of the cold filtrate (750 c.c.) with excess of hydrochloric acid precipitated crude *p*-nitrobenzoic acid which, after dissolution in dilute aqueous ammonia, filtering (charcoal) and reprecipitating with hydrochloric acid and recrystallisation from dilute alcohol, yielded pure *p*-nitrobenzoic acid (10 g.), m. p. and mixed m. p. 242—244° (Found: N, 8·5; *M*, 166. Calc.: N, 8·4%; *M*, 166). The crude nitro-aminodiphenylamine-2-carboxylic acid could not be purified by crystallisation. A sample (8 g.) was dissolved in boiling water (100 c.c.) and potassium carbonate (2·2 g.) and the filtered solution (charcoal) allowed to stand on ice overnight; the potassium salt (glistening crystals) was collected, dissolved in boiling water and the free acid precipitated with hydrochloric acid, pure *5-nitro-4'-amino-diphenylamine-2-carboxylic acid* (3·6 g.) being obtained as a light yellow crystalline powder, m. p. 282—284° (decomp.) (Found: C, 57·0; H, 4·2; N, 15·2. $C_{13}H_{11}O_4N_3$ requires C, 57·1; H, 4·0; N, 15·4%). The filtrate from the collection of the potassium salt gave the less pure acid (3·4 g.), m. p. 256—258° decomp. with softening at 252°.

Interaction between 2-chloro-4-nitrobenzoic acid and p-phenylenediamine at higher temperatures. 2-Chloro-4-nitrobenzoic acid (41 g.), potassium carbonate (31 g.), copper powder (1 g.), *p*-phenylenediamine (27 g.), amyl alcohol (390 c.c.) and water (5 c.c.) were submitted to the usual procedure at 130° (internal) for 4½ hours. The crude acid (40 g.), isolated by adjusting the cold liquor to pH 3 after the steam distillation, was purified by repeated precipitation at pH 4·0—4·5 of the boiling (*ca.* 5%) solution of the ammonium salt. This yielded 5-nitro-4'-amino-diphenylamine-2-carboxylic acid still contaminated with *p*-nitrobenzoic acid; the latter was removed by extraction with hot 80% alcohol in which the former is sparingly soluble. The residue (8·5 g.) gave, on crystallisation of the potassium salt and reprecipitation, pure 5-nitro-4'-amino-diphenylamine-2-carboxylic acid (5 g.), m. p. 282—284° (decomp.). The liquors from the

precipitation of the acid at pH 4·0—4·5 were combined, chilled, strongly acidified and the impure *p*-nitrobenzoic acid collected; this was treated with chromic acid in boiling acetic acid solution and yielded, on recrystallisation, pure *p*-nitrobenzoic acid (20 g.), m. p. and mixed m. p. 242—244° (Found: *M*, 166. Calc.: *M*, 166).

When the reaction was carried out for 3 hours at 120° (internal), 5-nitro-4′-amino-diphenylamine-2-carboxylic acid (15·5 g.), m. p. 266—270°, and pure *p*-nitrobenzoic acid (16 g.), m. p. 242—244° (Found: *M*, 167), were obtained. When the reaction was carried out at 100° (internal) for 5 hours, 5-nitro-4′-amino-diphenylamine-2-carboxylic acid (25 g.), m. p. 262—264°, and pure *p*-nitrobenzoic acid (13·5 g.) were obtained.

In three experiments in which preformed anhydrous finely ground potassium 2-chloro-4-nitrobenzoate (48 g.), ignited potassium carbonate (14·7 g.), *p*-phenylenediamine (27 g.), copper powder (1 g.) and anhydrous amyl alcohol (300 c.c.) were stirred at 120° (internal) for 5 hours, unchanged 2-chloro-4-nitrobenzoic acid (30—33 g.), m. p. and mixed m. p. 142—144°, was recovered (Found: Cl, 17·5; *M*, by titration, 201. Calc.: Cl, 17·6%; *M*, 201·5).

2-Nitro-7-aminoacridone and 2:7-Diaminoacridone.—Crude 5-nitro-4′-amino-diphenylamine-2-carboxylic acid (25 g.) was dissolved in sulphuric acid (250 c.c.), the solution heated at 100° for 2 hours and poured on to crushed ice (1200 g.). After 2 hours, the pasty yellow mass of sulphate was drained on porous glass and stirred with dilute ammonia (1200 c.c.); the deep maroon insoluble 2-nitro-7-aminoacridone was collected, washed and dried (17·5 g.; decomp. at 370—375° without melting). A sample was dissolved in boiling 95% pyridine and an excess of boiling water added to the filtered solution; after some time the *2-nitro-7-aminoacridone* separated in lustrous maroon prisms (decomp. 380°) (Found: C, 60·8; H, 3·7; N, 16·1. $C_{13}H_9O_3N_3$ requires C, 61·2; H, 3·5; N, 16·5%).

The foregoing crude compound (7 g.) was added to a solution of stannous chloride crystals (42 g.) in hydrochloric acid (42 c.c.) and the mixture heated on the water-bath for 1 hour when an almost clear solution was obtained. After some hours at 0°, the precipitate of the stannichloride complex was collected and stirred with cold 5N-sodium hydroxide (200 c.c.) for 1 hour. The insoluble material was separated, dissolved in dilute hydrochloric acid, traces of tin salts removed with hydrogen sulphide and the warm filtered solution (charcoal) basified with ammonia, 2:7-diaminoacridone being obtained as a pale yellow powder (5·7 g.); this was recrystallised from dilute pyridine to give the compound in glittering ochre tablets, m. p. 354—356° (Found: C, 69·1; H, 4·8; N, 18·8. Calc. for $C_{13}H_{11}ON_3$: C, 69·4; H, 4·9; N, 18·7%).

5-Nitro-4′-dimethylaminophenylamine-2-carboxylic acid. Potassium 2-chloro-4-nitrobenzoate (60 g.; 0·25 mol.), potassium carbonate (20 g.) and copper powder (1 g.) were stirred with amyl alcohol (400 c.c.) at 120°; freshly redistilled *p*-aminodimethylaniline (43 g.; 0·32 mol.) was added slowly over 20 minutes and the rapidly stirred mixture maintained at 120° ± 2° for 3 hours. The crude acid was isolated in the usual manner (vol. filtrate 400 c.c.), washed, dissolved in boiling water (225 c.c.) containing potassium carbonate (20 g.) and a solution of potassium chloride (15 g.) in boiling water (50 c.c.) added; the potassium salt separated after some hours at 0° in glistening black prisms. It was dissolved in boiling water (600 c.c.) and the acid precipitated at pH 4·0 with 5N-hydrochloric acid, *5-nitro-4′-dimethylamino-diphenylamine-2-carboxylic acid* being obtained (37 g.; m. p. 216—218°); a sample crystallised from dilute dioxan in small glistening black tablets, m. p. 226—228° (decomp.) (Found: C, 60·3; H, 5·1; N, 14·1, 14·2. $C_{15}H_{15}O_4N_3$ requires C, 59·8; H, 4·9; N, 14·0%). The acid (5 g.) dissolved completely in 0·5N-hydrochloric acid (100 c.c.) at the boiling point but suffered some decomposition.

In two runs in which the *p*-aminodimethylaniline was added all at once to the other reactants at 140° the reaction became very violent; the stirring was continued for 5 hours at 140° (internal) and the product precipitated at pH 3 in the cold. The crude product (40 g.) was crystallised twice from dilute acetic acid and gave *p*-nitrobenzoic acid (23 g.) in the form of glittering yellow needles, m. p. 240—242° alone and in admixture with an authentic specimen (Found: *M*, by titration, 165. Calc.: *M*, 166).

5-Chloro-2-nitro-7-dimethylaminoacridine. 5-Nitro-4′-dimethylamino-diphenylamine-2-carboxylic acid (30 g.) was refluxed with phosphorus oxychloride (320 c.c.) for 4 hours. The cooled mixture was poured on to an excess of powdered ice and then ammonia slowly added with rapid stirring until the liquor was just alkaline, the temperature of the mixture being kept below 2°. The *5-chloro-2-nitro-7-dimethylaminoacridine* (29 g.; m. p. 254—260°) was collected, well washed with water, drained, and dried under reduced pressure. A sample crystallised from aqueous alcoholic pyridine as a purple black powder, m. p. 278—282°, but was still impure (Found: N, 14·2; Cl, 9·3. $C_{15}H_{12}O_2N_3Cl$ requires N, 13·95; Cl, 11·8).

2-Nitro-7-dimethylaminoacridone. Crude 5-chloro-2-nitro-7-dimethylaminoacridine (28 g.) was heated to 100° with 3·3N-hydrochloric acid (2 l.) for 12 hours and the relatively insoluble dark ochre crystalline deposit of *2-nitro-7-dimethylaminoacridone hydrochloride* separated from the hot solution (Found, after drying at 100°/2 mm.: N, 12·9; Cl, 10·3. $C_{15}H_{13}O_3N_3$,HCl requires N, 13·1; Cl, 11·1%). The filtrate was made alkaline with ammonia and the precipitated acridone collected and washed. This was combined with the hydrochloride and refluxed for 1½ hours with 8% sodium carbonate (2 l.), collected, washed and dried. The crude *2-nitro-7-dimethylaminoacridone* (24 g.), was obtained as a dark brown powder, m. p. 344—346° (Found: N, 14·95. $C_{15}H_{13}O_3N_3$ requires N, 14·8%); it was too insoluble in organic solvents for recrystallisation.

2-Amino-7-dimethylaminoacridone.—2-Nitro-7-dimethylaminoacridone (20 g.) was added in small portions to a solution of stannous chloride crystals (120 g.) in hydrochloric acid (120 c.c.). The mixture was heated on the water-bath for 1½ hours, the clear dark solution cooled and slowly added to stirred cold 5N-sodium hydroxide (800 c.c.), the temperature being maintained at < 40°. The *2-amino-7-dimethylaminoacridone* was collected, washed, dissolved in boiling water (200 c.c.) and hydrochloric acid (50 c.c.) and the filtered solution run into stirred cold 2·5N-sodium hydroxide (800 c.c.); after separation and washing, the compound was obtained as an olive-yellow powder (16·8 g.; m. p. 310—314°). A sample crystallised from aqueous alcoholic pyridine in yellow-brown needles, m. p. 312—314° (Found: C, 70·9; H, 6·0; N, 16·9. $C_{15}H_{15}ON_3$ requires C, 71·1; H, 5·9; N, 16·6%).

2-Amino-7-dimethylaminoacridine.—A solution of 2-amino-7-dimethylaminoacridone (4 g.) in warm N-hydrochloric acid (75 c.c.) was added dropwise to stirred cold 0·5N-sodium hydroxide (400 c.c.). The fine yellow suspension was saturated with carbon dioxide, heated to 80° and 4% sodium amalgam (220 g.) added in 7 portions over 1½ hours, the carbon dioxide stream and stirring being continuous during this period and for a further 1 hour at 80°. Ferric chloride solution (5%; 5 c.c.) was added and a current of oxygen passed in with rapid stirring for 1 hour at 60°. The dark chocolate-brown microcrystalline powder (3·2 g.; m. p. 234—242°) was separated, dissolved in boiling water (110 c.c.) and N-hydrochloric acid (18 c.c.) and the crimson purple solution filtered and rapidly heated to 80°. A hot solution (150 c.c.; 80° C.) of ammonium chloride–sodium chloride (saturated at 15° with 2 parts ammonium chloride and 1 part sodium chloride) was added; after scratching and cooling, the 2-amino-7-dimethylaminoacridine hydrochloride (3 g.) separated in glittering black prisms. The free diamine was obtained as a dark brick-red powder (2·2 g.) from the aqueous solution by precipitation with cold dilute sodium hydroxide. When this (1 g.) was dissolved in pyridine (25 c.c.), alcohol (10 c.c.) and water (10 c.c.), the solution filtered and heated to the b. p. and boiling water (200 c.c.) added, the solution, after 2 days at 0°, gave *2-amino-7-dimethylaminoacridine* (0·68 g.) in black rhombs with a metallic lustre. When these were dried at 110°/2 mm. they gave a brick-red powder, m. p. 254—256° (Found: C, 75·6, 75·4; H, 6·3, 6·3; N, 17·9, 17·8. $C_{15}H_{15}N_3$ requires C, 75·8; H, 6·3; N, 17·7%). The monohydrochloride was soluble to the extent of *ca.* 3% in water at 20° giving a purple crimson solution.

5-Nitro-3'-aminodiphenylamine-2-carboxylic acid. 2-Chloro-4-nitrobenzoic acid (10 g.), *m*-phenylenediamine (7 g.), potassium carbonate (7·5 g.), copper powder (0·2 g.) and amyl alcohol were stirred together at 150° (bath temperature) for 1½ hours. The crude product (9·5 g.), m. p. > 300°, was reprecipitated at the boiling point from the 10% solution in dilute ammonia, but was still impure *5-nitro-3'-aminodiphenylamine-2-carboxylic acid* (Found: N, 15·2; *M*, by titration, 252. $C_{13}H_{11}O_4N_3$ requires N, 15·4%; *M*, 273). It was acetylated with acetic anhydride in 10% solution in cold aqueous sodium carbonate; the *5-nitro-3'-acetamido-diphenylamine-2-carboxylic acid* crystallised from aqueous alcohol in scarlet needles, m. p. 242—244° (Found: N, 13·2. $C_{15}H_{13}O_5N_3$ requires N, 13·3%).

2-Nitro-8-aminoacridone and 2 : 8-Diaminoacridone.—The foregoing crude nitroaminodiphenylamine-2-carboxylic acid (4·3 g.) was heated with sulphuric acid (30 c.c.) at 100° for 1¾ hours, poured on ice (200 g.) and the yellow precipitate collected. This was ground with aqueous ammonia, collected and washed, *2-nitro-8-aminoacridone* being obtained as a yellow-brown powder (3·5 g.). It was recrystallised from aqueous pyridine and obtained in brown needles, m. p. > 400° (Found: N, 16·7. $C_{13}H_9O_3N_3$ requires N, 16·5%).

The crude material (3 g.) was heated on the water bath with stannous chloride crystals (30 g.) and hydrochloric acid (30 c.c.) for 2 hours. After cooling, the precipitate was separated, stirred with excess of cold 5N-sodium hydroxide and the insoluble material collected, washed with water and dried, 2 : 8-diaminoacridone being obtained as a yellow powder (2·0 g.); recrystallisation from aqueous pyridine gave the compound in felted yellow needles, m. p. 368—370°. Reduction with sodium amalgam gave 2 : 8-diaminoacridine which crystallised from aqueous pyridine in yellow needles, m. p. 284—286° alone and in admixture with authentic material.

3' : 5-Dinitrodiphenylamine-2-carboxylic acid. 2-Chloro-4-nitrobenzoic acid (10 g.), *m*-nitroaniline (7 g.), potassium carbonate (7·5 g.), amyl alcohol (40 c.c.) and copper powder (0·2 g.) were stirred at 150° (bath temperature) for 2 hours. The crude product (3·5 g.) was crystallised twice from aqueous alcohol and gave 3' : 5-dinitrodiphenylamine-2-carboxylic acid in orange brown needles (2 g.), m. p. 262° (cf. Albert and Linnell, *loc. cit.*). Cyclisation of the crude acid (1·6 g.) with sulphuric acid (16 c.c.) at 100° for 1 hour gave 2 : 6-dinitroacridone which on reduction with stannous chloride and hydrochloric acid as described above yielded 2 : 6-diaminoacridone (1·1 g.); it crystallised from aqueous pyridine in yellow needles, m. p. 300—302°. When mixed with 2 : 8-diaminoacridone (m. p. 368—370°) prepared by cyclisation of 5-nitro-3'-aminodiphenylamine-2-carboxylic acid followed by reduction the m. p. was 300° with softening and sintering at 290°.

5 : 4'-Di(acetamido)diphenylamine-2-carboxylic acid.—2-Chloro-4-acetamidobenzoic acid (10 g.), *p*-aminoacetanilide, potassium carbonate (7·5 g.), copper powder (0·2 g.) and amyl alcohol (40 c.c.) were stirred at 145—150° (bath temperature) for 1 hour. The crude product (11 g.) was recrystallised from aqueous alcohol and gave *5 : 4'-di(acetamido)diphenylamine-2-carboxylic acid* (8 g.) in brown needles, m. p. 244—246° alone and in admixture with a sample prepared as described above. Cyclisation of the crude acid (11 g.) in the manner previously described for 4'-amino-5-acetamidodiphenylamine-2-carboxylic acid yielded 2 : 7-diaminoacridone (6 g.) which, on recrystallisation from aqueous pyridine, was obtained in brown leaves, m. p. 356—358°.

Series Derived from 5-Substituted 2-Chlorobenzoic Acid.

2-Chloro-5-nitrobenzoic Acid (cf. Hubner, *Annalen*, 1883, **222**, 195; Lehmstedt, *Ber.*, 1931, **64**, 2381).—*o*-Chlorobenzoic acid (100 g.) was dissolved in sulphuric acid (300 c.c.) and a solution of nitric acid (32 c.c.; *d*, 1·50) in sulphuric acid (68 c.c.) added with stirring at such a speed that the reaction temperature maintained itself at 50—55°. After some hours the mixture was added to an excess of ice and the precipitate collected, washed and dissolved in boiling water (3 l.). The solution was allowed to cool to 40° and the crystals of 2-chloro-5-nitrobenzoic acid (91 g.; m. p. 164—165°) collected and washed with water. The filtrate contained appreciable amounts of 2-chloro-5-nitro- and 2-chloro-3-nitro-benzoic acid which separated on freezing.

2-Chloro-5-acetamidobenzoic acid. The foregoing acid (100 g.), water (1 l.), hydrochloric acid (3 c.c.), and iron powder (100 g., "Pactèron No. 2") were stirred at 90—95° for 6 hours. The mixture was made just alkaline to phenolphthalein with 5N-sodium hydroxide and filtered whilst hot; adjustment to pH *ca.* 3 of the cooled filtrate precipitated 2-chloro-5-aminobenzoic acid (74 g.), m. p. 187—188° (Found: *M*, by titration, 169. Calc.: *M*, 171·5). The acid (20 g.) was dissolved in water (200 c.c.) and sodium carbonate (20 g.) and acetic anhydride (14 c.c.) added with stirring at such a speed that the temperature did not exceed 25°; after stirring for a further ¼ hour more acetic anhydride (4 c.c.) was added and the stirring continued for another ½ hour. Acidification to pH *ca.* 3 precipitated 2-chloro-5-acetamidobenzoic acid (24·6 g.; m. p. 215°). A sample crystallised from water in colourless prisms, m. p. 216° (Found: *M*, by titration, 213. Calc.: *M*, 213·5).

4-Nitro-3'-aminodiphenylamine-2-carboxylic acid. 2-Chloro-5-nitrobenzoic acid (10 g.), *m*-phenylenediamine (7 g.), potassium carbonate (7·5 g.), copper powder (0·2 g.) and amyl alcohol (40 c.c.) were stirred at 150° (bath temperature) for 1½ hours. The crude product when purified by reprecipitation from its hot solution in dilute ammonia yielded *4-nitro-3'-aminodiphenylamine-2-carboxylic acid* (7·8 g.), m. p. 300° (Found: N, 15·6; *M*, by titration, 265. $C_{13}H_{11}O_4N_3$ requires N, 15·4%; *M*, 273). The compound was difficult to purify and was characterised by acetylation in dilute sodium carbonate solution with acetic anhydride, *4-nitro-3'-acetamidodiphenylamine-2-carboxylic acid* being obtained which crystallised from aqueous alcohol in yellow needles, m. p. 292—294° (Found: N, 13·3; *M*, by titration, 318. $C_{15}H_{13}O_5N_3$ requires N, 13·3%; *M*, 315).

7-Nitro-2-aminoacridone and 2 : 7-diaminoacridone. The foregoing crude nitroaminodiphenylamine-2-carboxylic acid (3·7 g.) was heated with sulphuric acid (25 c.c.) at 100° for 1½ hours and poured on to ice. The insoluble material was separated, stirred with excess of dilute ammonia and collected; it could not be satisfactorily purified owing to its insolubility and was accordingly directly reduced. The material was added to a solution of stannous chloride crystals (20 g.) in hydrochloric acid (20 c.c.), the mixture heated on the water-bath for 1 hour, diluted with hot water and filtered (charcoal). Basification with 5N-sodium hydroxide precipitated 2 : 7-diaminoacridone which after dissolution in dilute hydrochloric acid, filtering with charcoal and reprecipitating amounted to 1 g. Recrystallisation from aqueous pyridine gave 2 : 7-diaminoacridone in greenish-brown leaves, m. p. 352—354° alone and in admixture with that obtained from the cyclisation and reduction of 5-nitro-4'-aminodiphenylamine-2-carboxylic acid of which the constitution follows from the method of synthesis (Found: N, 18·6. Calc.: N, 18·7%).

4 : 3'-Dinitrodiphenylamine-2-carboxylic acid. 2-Chloro-5-nitrobenzoic acid (10 g.), *m*-nitroaniline (7 g.), potassium carbonate (7·5 g.), copper powder (0·2 g.) and amyl alcohol (40 c.c.) were stirred at 155° (bath temperature) for 5 hours. The crude product, isolated in the normal manner, was recrystallised from aqueous alcohol and gave 4 : 3'-dinitrodiphenylamine-2-carboxylic acid (1·3 g.) in brown needles, m. p. 288—290° (Albert and Linnell, J., 1938, 22, record m. p. 229°) (Found: N, 13·9; *M*, by titration, 299. Calc. for $C_{13}H_9O_6N_3$: N, 13·9%; *M*, 303).

3 : 6-Diaminoacridone.—The foregoing acid (1·1 g.) and sulphuric acid (11 c.c.) were heated at 100° for 1 hour and the resulting dinitroacridone isolated in the usual manner. The crude product was heated on the water bath with a solution of stannous chloride crystals (10 g.) in hydrochloric acid (10 c.c.) for 1 hour, diluted with boiling water, filtered hot (charcoal), strongly basified with cold 5N-sodium hydroxide and the precipitate collected and washed. Recrystallisation

of this (0·6 g.) gave 3 : 6-diaminoacridone in brown needles, m. p. 314—316°; this m. p. was depressed when the substance was mixed with 2 : 7-diaminoacridone (m. p. 354°) obtained by cyclisation of 4-nitro-3′-aminodiphenylamine-2-carboxylic acid.

4 : 4′-*Dinitrodiphenylamine-2-carboxylic Acid and* 3 : 7-*Diaminoacridone.*—The acid was obtained by the method of Bogert and Hirschfielder (*loc. cit.*) and the crude material purified through the insoluble ammonium salt. It had m. p. 292° (lit. 293°) (Found: N, 14·1; *M*, by titration, 303. Calc. for $C_{13}H_9O_6N_3$: N, 13·9%; *M*, 303).

Cyclisation with sulphuric acid followed by reduction with stannous chloride–hydrochloric acid gave 3 : 7-diaminoacridone which crystallised in golden yellow needles from aqueous pyridine, m. p. 320° (Bogert and Hirschfielder give m. p. 325°).

3′-*Amino-4-acetamidodiphenylamine-2-carboxylic acid.* 2-Chloro-5-acetamidobenzoic acid (10 g.), *m*-phenylenediamine (8 g.), potassium carbonate (7 g.), copper powder (0·2 g.) and amyl alcohol (40 c.c.) were heated at 150° (bath temperature) for 1½ hours. The product isolated in the normal manner by precipitation was obtained in yellow-green needles (10 g.), m. p. 152—154° (Found: N, 14·3; *M*, by titration, 285. $C_{15}H_{15}O_3N_3$ requires N, 14·7%; *M*, 285. Acetylation with acetic anhydride in cold dilute sodium carbonate solution gave 4 : 3′-*di(acetamido)diphenylamine-2-carboxylic acid* in yellow-green needles, m. p. 264—265° (Goldstein *et al.*, *Helv. Chim. Acta*, 1927, **10**, 603, give m. p. 252°) (Found: N, 12·8; *M*, by titration, 315. $C_{17}H_{17}O_4N_3$ requires N, 12·9%; *M*, 327).

2 : 7-*Diaminoacridone and* 2 : 7-*Diaminoacridine.*—The foregoing 3′-amino-4-acetamidodiphenylamine-2-carboxylic acid (6 g.) was heated with sulphuric acid (42 c.c.) at 100° for 1½ hours, water (20 c.c.) added and the heating continued for a further ½ hour. The reaction mixture was cooled, poured into an excess of ammonia and the crude 2 : 7-diaminoacridone collected and washed (4·0 g.). This was purified by reprecipitation from its solution in dilute hydrochloric acid and then recrystallised from dilute pyridine, 2 : 7-diaminoacridone being obtained in clusters of green-brown needles, m. p. 354—356° (Found: N, 18·8. Calc.: N, 18·7%). Reduction with sodium amalgam followed by oxygenation in the same manner as described for the 3 : 6-isomeride gave 2 : 7-diaminoacridine (60%) which on crystallisation from dilute pyridine was obtained in orange-brown plates, m. p. 352—354° (Found: N, 20·4. Calc.: N, 20·1%).

3′-*Nitro-4-acetamidodiphenylamine-2-carboxylic acid.* 2-Chloro-5-acetamidobenzoic acid (11 g.), *m*-nitroaniline (8·6 g.), potassium carbonate (7·2 g.), copper powder (0·2 g.) and amyl alcohol (40 c.c.) were stirred at 150° (bath temperature) for 2 hours. The crude acid isolated was extracted with boiling water (3 × 300 c.c.) and the insoluble material recrystallised from dilute alcohol, 3′-*nitro-4-acetamidodiphenylamine-2-carboxylic acid* being obtained in clusters of orange needles (5 g.), m. p. 250° (Found: N, 13·4; *M*, by titration, 310. $C_{15}H_{13}O_5N_3$ requires N, 13·3%; *M*, 315).

6-*Nitro-3-amino- and* 3 : 6-*Diamino-acridone.*—The above acid (3·3 g.) was heated with sulphuric acid (23 c.c.) at 100° for 2 hours, water (10 c.c.) added and the heating continued for a further ½ hour. Water (100 c.c.) was added, the resulting solution basified with ammonia and the precipitated 6-*nitro-3-aminoacridone* (2·5 g.) collected; recrystallisation from dilute pyridine gave the compound in brown needles which, on drying at 100°, fell to a brick-red powder, m. p. 340—342° (Found: C, 61·0; H, 3·9; N, 16·5. $C_{13}H_9O_3N_3$ requires C, 61·2; H, 3·5; N, 16·5%).

The crude nitroaminoacridone (1·0 g.) was heated to 100° for 1 hour with hydrochloric acid (7 c.c.) and stannous chloride crystals (7 g.). After cooling, the insoluble stannichloride complex was collected, stirred with excess of cold 5N-sodium hydroxide and the 3 : 6-diaminoacridone separated and washed with water (0·8 g.). Recrystallisation from aqueous pyridine gave the pure compound in brown needles, m. p. 312—314° (Found: C, 69·1; H, 5·0; N, 18·8. Calc. for $C_{13}H_{11}ON_3$: C, 69·4; H, 4·9; N, 18·7%).

3 : 6-*Diaminoacridine.* The above 3 : 6-diaminoacridone (2 g.) was suspended in 60% ethyl alcohol (125 c.c.), 4% sodium amalgam (80 g.) added and the mixture stirred at room temperature for 6 hours during which time the suspension was kept saturated with carbon dioxide. The mixture was then heated to 60° and, whilst rapidly stirred, a current of air passed in for 2 hours at this temperature. After cooling, the insoluble material was collected, dissolved in dilute hydrochloric acid, the solution filtered (charcoal) and basified with ammonia. The precipitate was collected (1·5 g.) and recrystallised from dilute pyridine, 3 : 6-diaminoacridine being obtained in chocolate prisms, m. p. 254—256° (Found: C, 74·0; H, 5·3; N, 20·0. Calc. for $C_{13}H_{11}N_3$: C, 74·6; H, 5·3; N, 20·1%). Albert and Linnell, *loc. cit.*, record m. p. 322°.

Monosubstituted Diphenylamine-2-carboxylic Acids.

3-*Nitrodiphenylamine-2-carboxylic Acid.*—2-Chloro-6-nitrobenzoic acid (10 g.), aniline (20 c.c.), potassium carbonate (7 g.) and copper powder (0·5 g.) were stirred at 180° (bath temperature) for 1 hour. The crude acid (3·5 g.), recrystallised from aqueous methanol, gave the pure compound in yellow-brown prisms, m. p. 174° (Lehmstedt and Schrader, *Ber.*, **1937**, **70**, 1526, give m. p. 172°) (Found: *M*, by titration, 259. Calc. for $C_{13}H_{10}O_4N_2$: *M*, 258). Repeated attempts to obtain 4-nitroacridone from this by cyclisation with sulphuric acid were unsuccessful.

3-*Acetamidodiphenylamine-2-carboxylic Acid.*—2-Chloro-6-acetamidobenzoic acid (10 g.), aniline (7·6 c.c.), potassium carbonate (7 g.), copper powder (0·2 g.) and amyl alcohol (40 c.c.) were stirred at 145—150° (bath temperature) for 2 hours. The crude product was recrystallised from aqueous alcohol and gave 3-*acetamidodiphenylamine-2-carboxylic acid* (4 g.) in yellow needles, m. p. 160° (Found: N, 10·5; *M*, by titration, 273. $C_{15}H_{14}O_3N_2$ requires N, 10·4%; *M*, 270).

4-*Aminoacridone.*—Cyclisation of the above acid with concentrated sulphuric acid failed to yield 4-aminoacridone. The acid (2 g.) was heated with 75% sulphuric acid (20 c.c.) at 100° for 2 hours, water (6 c.c.) added and the heating continued for a further ½ hour. The crude material was a dark solid gum, insoluble in alkali; this was extracted with methanol, and from the solution, after some hours, the crystalline deposit was collected. Recrystallisation from the same solvent gave 4-aminoacridone (0·05 g.) in pale yellow needles, m. p. 290—292° alone and in admixture with that obtained by the cyclisation of 3′-nitrodiphenylamine-2-carboxylic acid followed by reduction (Found: N, 13·3. Calc. for $C_{13}H_{10}ON_2$: N, 13·3%).

4-*Acetamidodiphenylamine-2-carboxylic acid.* 2-Chloro-5-acetamidobenzoic acid (10 g.), aniline (7·6 g.), potassium carbonate (7 g.), copper powder (0·2 g.) and amyl alcohol (40 c.c.) were stirred at 150° (bath temperature) for 1½ hours. The crude product on recrystallisation from 50% alcohol (100 c.c.) gave 4-*acetamidodiphenylamine-2-carboxylic acid* as a mass of felted yellow needles (7·1 g.), m. p. 236—238° (Found: N, 10·6; *M*, by titration, 270. $C_{15}H_{14}O_3N_2$ requires N, 10·4%; *M*, 270).

3-*Aminoacridone-7(?)-sulphonic acid.* The foregoing acid (1·5 g.) was heated with sulphuric acid (15 c.c.) for 4 hours at 100°, water (5 c.c.) added and the heating continued for a further ½ hour. The solution was cooled, diluted with water (50 c.c.) and, after chilling, the precipitate collected; this was redissolved in dilute ammonia and reprecipitated at the boiling point by acidification to pH 2·0—2·5 with hydrochloric acid. The yellow microcrystalline precipitate which slowly separated was collected and dried (1·4 g.); analysis showed it to be an *aminoacridone sulphonic acid* probably the 3 : 7-isomeride (Found: N, 9·6; *M*, by titration, 298. $C_{13}H_{10}O_4N_2S$ requires N, 9·7%; *M*, 290).

It was not found possible to effect *cyclo*dehydration of 4-acetamidodiphenylamine-2-carboxylic acid with production of 3-aminoacridone; with 80% sulphuric acid, or with 100% sulphuric acid for a shorter time, the only alkali insoluble material obtained was 4-aminodiphenylamine-2-carboxylic acid.

4-*Nitrodiphenylamine-2-carboxylic acid.* 2-Chloro-5-nitrobenzoic acid (10 g.), potassium carbonate (7 g.), aniline

(20 c.c.) and copper powder (0·2 g.) were stirred at 180° (bath temperature) for 1½ hours. After removal of the aniline in steam, potassium chloride (10 g.) was dissolved in the boiling filtered solution (vol. 250 c.c.) which was then allowed to stand on ice. The scarlet needles of the potassium salt were collected, dissolved in boiling water and the solution acidified with dilute hydrochloric acid, 4-nitrodiphenylamine-2-carboxylic acid separating as a yellow-green crystalline mass (9·7 g.), m. p. 256—258° (Found: N, 11·1; *M*, by titration, 250. $C_{13}H_{10}O_4N_2$ requires N, 10·9%; *M*, 258). Attempted cyclisation of this compound with concentrated and with 70% and 90% sulphuric acid failed to yield 3-nitroacridone.

6-*Nitrodiphenylamine-2-carboxylic acid*. 2-Chloro-3-nitrobenzoic acid (10 g.), aniline (20 c.c.), potassium carbonate (7·5 g.) and copper powder (0·2 g.) were stirred at 160° (bath temperature) for 1 hour. After removal of the excess aniline in steam, the product was isolated in the usual manner in the form of an orange-yellow crystalline mass (11 g.). This, on recrystallisation from dilute alcohol, gave the pure compound in orange prisms, m. p. 195—196° (Found: N, 11·0. Calc. for $C_{13}H_{10}O_4N_2$: N, 10·9%) (cf. Tuttle, *loc. cit.*).

1-*Nitroacridone*.—The foregoing acid (2 g.) was heated with sulphuric acid (14 c.c.) for 1 hour at 100°, poured on to ice (60 g.) and, after standing, the yellow precipitate collected, washed with warm dilute ammonia and dried. The crude 1-nitroacridone (1·25 g.) crystallised from dilute pyridine in orange needles, m. p. 260—262° alone and in admixture with that obtained by the cyclisation of 2′-nitrodiphenylamine-2-carboxylic acid (Ullmann, *loc. cit.*) (Found: N, 11·8. Calc.: N, 11·7%).

Attempted Condensation of 2-Chloro-3-acetamidobenzoic Acid with m-*Phenylenediamine*.—2-Chloro-3-acetamidobenzoic acid (5 g.), *m*-phenylenediamine (4 g.), potassium carbonate (3·25 g.), copper powder (0·2 g.) and amyl alcohol (20 c.c.) were stirred at 150° (bath temperature) for 1½ hours. Isolation of the product in the usual manner yielded *m*-acetamidobenzoic acid (3·6 g.); it was recrystallised from aqueous alcohol (charcoal) and pure *m*-acetamidobenzoic acid obtained in colourless needles, m. p. 252° alone and in admixture with authentic material (Found: N, 8·1; *M*, by titration, 180. Calc.: N, 7·8%; *M*, 179).

Lowering the reaction temperature to 100° failed to effect the desired Ullmann condensation; dehalogenation took place with production of *m*-acetamidobenzoic acid in *ca.* 85% yield.

With *m*-nitroaniline and 2-chloro-5-acetamidobenzoic acid no reaction took place at temperatures in the region of 120°; at 150° (bath temperature) dehalogenation with production of *m*-acetamidobenzoic acid took place.

5-*Acetamidodiphenylamine-2-carboxylic acid*. 2-Chloro-4-acetamidobenzoic acid (10 g.), potassium carbonate (7·5 g.), copper powder (0·2 g.) and aniline (20 c.c.) were stirred at 180° (bath temperature) for 90 minutes. After removal of the aniline by distillation in steam, the crude product was isolated and recrystallised from aqueous alcohol giving 5-*acetamidodiphenylamine-2-carboxylic acid* (5 g.) as a mass of buff needles, m. p. 248—250° (Found: N, 10·5; *M*, by titration, 267. $C_{15}H_{14}O_3N_2$ requires N, 10·4%; *M*, 270).

2-*Aminoacridone-7-sulphonic acid*. A solution of the foregoing acid (1·5 g.) in sulphuric acid (15 c.c.) was heated at 100° for 1 hour; water (4 c.c.) was added, the mixture heated at 100° for a further 30 minutes to effect deacetylation, poured on to ice (50 g.) and the precipitate collected. This dissolved completely in dilute ammonia; the solution was filtered (charcoal) and adjusted to pH *ca.* 2 at the boiling point with hydrochloric acid. A microcrystalline precipitate of the aminoacridone sulphonic acid gradually separated (0·5 g.), m. p. > 400°, which would appear to be the 2 : 7-isomeride (Found: N, 9·7; *M*, by titration, 305. Calc. for $C_{13}H_{10}O_4N_2S$: N, 9·7%; *M*, 290).

5-*Nitrodiphenylamine-2-carboxylic acid* (cf. Ullmann, *loc. cit.*). 2-Chloro-4-nitrobenzoic acid (50 g.), potassium carbonate (50 g.), copper powder (1 g.), amyl alcohol (150 c.c.) and aniline (200 c.c.) were stirred at 140° for 4½ hours. After removal of the amyl alcohol and excess aniline in a current of steam, the filtered (charcoal) solution was evaporated to small volume and allowed to stand at 0°; the crystalline mass was drained (vol. filtrate, 180 c.c.), dissolved in boiling water (500 c.c.) and adjusted to pH 2 with hydrochloric acid. The yellow microcrystalline precipitate of 5-nitrodiphenylamine-2-carboxylic acid was collected and dried (yield 50—52 g.); this was sufficiently pure for further use. It crystallised from 95% alcohol in long yellow needles, m. p. 232—234°.

2-*Nitroacridone* (cf. Ullmann, *loc. cit.*; Albert and Linnell, *loc. cit.*). Anhydrous 5-nitrodiphenylamine-2-carboxylic acid (50 g.) was gently refluxed with phosphorus oxychloride (500 c.c.) for 4 hours. A portion (*ca.* one-third) of the oxychloride was removed by distillation under reduced pressure and the residue, while still hot, slowly mixed with powdered ice (2 kg.). Ammonia was added with rapid stirring until the solution was just alkaline (pH 9), the temperature being maintained below 3°. The precipitate was collected, washed and dried at 20° over potassium hydroxide, 5-chloro-2-nitroacridine (50 g.) being obtained as an olive-green powder; a sample crystallised from a large volume of benzene in long olive needles, m. p. 208° (Found: Cl, 13·6. Calc.: Cl, 13·7%). No tendency towards replacement of the nitro group by chlorine was observed under these experimental conditions; contrast Albert and Linnell (*loc. cit.*) who used less phosphorus oxychloride and, consequently, a higher temperature. The crude 5-chloro-2-nitroacridine was boiled with 3·3N-hydrochloric acid (1500 c.c.) for 3 hours, the insoluble nitroacridone collected, washed and extracted with boiling 2½% sodium carbonate solution for ½ hour. The insoluble yellow 2-nitroacridone was collected, washed and dried (44 g., m. p. > 400°).

2 : 7-*Dinitroacridone*.—Anhydrous 2-nitroacridone (72 g.; 0·3 mol.) was dissolved in sulphuric acid (300 c.c.; *d*, 1·82—1·84) by stirring at 25°. A solution of nitric acid (14·5 c.c.; 0·345 mol.; *d*, 1·5) in sulphuric acid (100 c.c.) was then added dropwise with rapid stirring over 15 minutes, the temperature being maintained at 25—30° during the addition. Stirring was maintained at this temperature for a further 2 hours, the temperature raised to 70° over ½ hour and maintained at 70—75° with stirring for a further ½ hour. The solution was poured on to crushed ice (2 kg.), the yellow precipitate collected, washed and extracted by boiling with 8% sodium carbonate solution (2 l.) for ¼ hour to remove any trinitroacridone which is soluble in sodium carbonate. The insoluble material was collected, washed and dried, 2 : 7-dinitroacridone being obtained as a fine yellow powder (73 g.), m. p. 360—366°. A sample was dissolved in boiling 95% pyridine and a large excess of boiling water added to the filtered solution; the 2 : 7-dinitroacridone slowly crystallised in almost quantitative amount in long golden-brown needles (Found: C, 55·0; H, 2·7; N, 15·0. Calc. for $C_{13}H_7O_5N_3$: C, 54·8; H, 2·5; N, 14·7%).

2 : 7-*Diaminoacridone*.—The foregoing crude dinitroacridone (76 g.) was added in small portions to a hot stirred solution of stannous chloride crystals (780 g.) in 10N-hydrochloric acid (780 c.c.) at such a rate that the internal temperature was maintained at 85—90°; the addition took *ca.* 30 minutes and at the end of this time an almost clear solution was obtained. The solution was stirred for a further 45 minutes at 90° and then allowed to stand at 0°; after some hours, the pasty mass was drained at the pump. The solid was added in portions to stirred cold 5N-sodium hydroxide (2 l.) and, after stirring for a further 1 hour, the insoluble yellow material was collected, dissolved in hot 2N-hydrochloric acid (1 l.) and residual traces of tin removed with hydrogen sulphide. The filtered solution was cooled, nearly neutralised with cold 5N-sodium hydroxide and then basified with excess of 2½% sodium carbonate solution with stirring. The insoluble material was collected, washed and dried at 20°, 2 : 7-diaminoacridone being obtained as a light yellow powder (58—60 g.; m. p. 348—352°). A sample crystallised from dilute pyridine in golden-brown leaves, m. p. 354—356° (Found: C, 69·1; H, 4·9; N, 18·8. Calc. for $C_{13}H_{11}ON_3$: C, 69·4; H, 4·9; N, 18·7%).

2 : 7-*Diaminoacridine*.—The above crude 2 : 7-diaminoacridone (20 g.) was dissolved in boiling N-hydrochloric acid

(375 c.c.) and the filtered solution run into rapidly stirred cold 0·5N-sodium hydroxide (1 l.) to precipitate the diaminoacridone as a fine bright olive-yellow powder. The suspension was saturated with carbon dioxide, heated to 80° and 4% sodium amalgam (1 kg.) added in 7 portions over a period of 1½ hours to the rapidly stirred suspension at 80—82°; stirring was continued at this temperature for a further 1½ hours, and the passage of carbon dioxide maintained throughout. Ferric chloride solution (5%, 20 c.c.) was added to the golden-yellow suspension and a fast stream of oxygen passed for 1½ hours with rapid stirring at 60—62°; the chocolate-brown suspension had then become crystalline. The 2 : 7-diaminoacridine (15·5 g.; m. p. 350—352°) was washed and dried at 25°. When crystallised from aqueous alcoholic pyridine, the pure compound was obtained in glittering golden leaves, m. p. 354—356° (shrinking at 350°) alone and in admixture with material obtained by cyclisation of 3′-amino-4-acetamidodiphenylamine-2-carboxylic acid followed by reduction (Found: C, 74·5; H, 5·0; N, 20·0. Calc. for $C_{13}H_{11}N_3$: C, 74·6; H, 5·3; N, 20·1%).

The crude diaminoacridine (15·5 g., 0·075 mol.), suspended in boiling water (425 c.c.), immediately gave a purple solution on addition of the theoretical amount of N-hydrochloric acid (75 c.c.). The filtered solution was heated quickly to 80° and the hot (80°) salting-out-solution (500 c.c.) added, followed by a further quantity (250 c.c.) when the solution had cooled to 60°. Crystallisation was facilitated by scratching and the mixture was set aside at 20° for several hours. 2 : 7-Diaminoacridine monohydrochloride was obtained as a mass of glistening black tablets having the appearance of grains of marcassite (16·5—17·0 g.). [The salting-out-solution was prepared by mixing 1 vol. of sodium chloride solution (saturated at 15°) with 2 vols. of ammonium chloride solution (saturated at 15°)]. The hydrochloride (1 g.) was dissolved in hot water (25 c.c.) and the red solution added to cold N-sodium hydroxide (50 c.c.) with stirring; the free diamine was precipitated as a pale yellow powder which, after collection, washing and drying at 10 mm., amounted to 0·8 g., m. p. 350—354° (Found: N, 20·1%). When recrystallised from dilute alcoholic pyridine the compound was obtained as glistening golden leaves, m. p. 354—356° (Found: N, 20·0, 20·2%). The monohydrochloride (1 g.) was dissolved in boiling 33% ethyl alcohol (40 c.c.) and 3N-alcoholic ammonia (6 c.c.) added to the boiling filtered red solution; after scratching whilst almost boiling for a few minutes, 2 : 7-diaminoacridine separated (0·67 g.) as a mass of glittering golden spangles, m. p. 354—356° (Found: N, 20·1%).

2- and 4-Nitroacridones and 2- and 4-Aminoacridones.—3′-Nitrodiphenylamine-2-carboxylic acid was prepared by the method described by Ullmann (*loc. cit.*) and by Lehmstedt and Schrader (*loc. cit.*). The acid (62 g.) was cyclised with sulphuric acid and the crude product (52 g.) separated into its components by fractional crystallisation from aqueous pyridine. From the less soluble fractions 2-nitroacridone (8·5 g.), m. p. >400°, was obtained and the more soluble fractions yielded 4-nitroacridone (35 g.), m. p. 362—364°. Reduction of these separately with stannous chloride followed by sodium amalgam gave 2-aminoacridone, m. p. 300—302°, and 2-aminoacridine, m. p. 222°, and also 4-aminoacridone, m. p. 292—294°, and 4-aminoacridine, m. p. 172—174° (Lehmstedt effected separation of the 2- and 4-nitroacridones through the corresponding 2- and 4-nitro-derivatives of 5-chloroacridine).

Nitration of 4-Nitroacridone.—*3 : 6-Dinitroacridone, 3 : 6-diaminoacridone and 3 : 6-diaminoacridine.* 4-Nitroacridone (39 g.) was nitrated in the same way as the 2-isomeride except that the addition of the nitrating mixture was made at 10° after which the solution was stirred for 2 hours at 20° and then ½ hour at 75°. A portion of the crude 3 : 6-dinitroacridone (44 g.) was recrystallised from aqueous pyridine and obtained in golden-brown plates, m. p. 388—390° (Found: N, 15·2. Calc.: N, 14·7%).

The crude 3 : 6-dinitroacridone (35 g.) was reduced with stannous chloride similarly to the 2 : 7-isomeride and gave 3 : 6-diaminoacridone as a yellow-brown powder (24 g.; m. p. 308—310°); this crystallised from aqueous pyridine in golden-brown needles, m. p. 314—316° alone and when mixed with the substance obtained by the cyclisation of 4 : 3′-dinitrodiphenylamine-2-carboxylic acid and subsequent reduction (Found: N, 18·8. Calc.: N, 18·7%).

Crude 3 : 6-diaminoacridone (4·7 g.) was dissolved in 60% ethanol (400 c.c.), 4% sodium amalgam (200 g.) added and carbon dioxide passed with stirring for 2 hours at room temperature and then for a further 1 hour at 60°. Ferric chloride solution (10%; 5 c.c.) was added and a current of air drawn through the rapidly stirred solution at 60° for 1½ hours. After the addition of alcohol (200 c.c.) the hot solution was filtered and most of the alcohol distilled away on the water bath; on adding ammonia (10 c.c., *d*, 0·880) 3 : 6-diaminoacridine separated in dark brown prisms (3·5 g.). Recrystallisation from aqueous alcohol gave the pure compound in brown prisms, m. p. 252—254° alone and in admixture with the diaminoacridine obtained by cyclisation of 3′-nitro-4-acetamidodiphenylamine-2-carboxylic acid and subsequent reduction (Found: N, 20·3. Calc.: N, 20·1%).

5-Amino- and 8-Chloro-5-amino-3-dimethylaminoacridine.

4′-Dimethylaminodiphenylamine-2-carboxylic Acid (cf. Drozdov, *J. Gen. Chem. Russ.*, 1939, **9**, 1373).—2-Chlorobenzoic acid (39 g.), potassium carbonate (40 g.), copper powder (1 g.), freshly distilled *p*-aminodimethylaniline (43 g.) and amyl alcohol (400 c.c.) were stirred at 140—145° (bath temperature) for 4 hours. The crude acid, isolated in the usual manner, was redissolved in boiling water (500 c.c.) containing a slight excess of potassium carbonate and reprecipitated at pH 4; the product (42 g.) was recrystallised from the minimum amount of alcohol (650 c.c.) and 4′-dimethylaminodiphenylamine-2-carboxylic acid (30 g.) obtained as a mass of olive-green needles, m. p. 224—226° (Found: *M*, by titration, 254. Calc.: *M*, 256).

5-Chloro-3-dimethylaminoacridine.—Anhydrous 4′-dimethylaminodiphenylamine-2-carboxylic acid (30 g.) was refluxed with phosphorus oxychloride (300 c.c.) for 4 hours and then *ca.* 100 c.c. of the oxychloride distilled off. The residue was mixed with excess of powdered ice and then ammonia and ice were added with rapid stirring until the liquor was alkaline to phenolphthalein, the temperature not being allowed to exceed 3°. The precipitated 5-chloro-3-dimethylaminoacridine was collected, drained on porous porcelain and dried under reduced pressure (30 g.); crystallisation from *cyclo*hexane (300 c.c.) gave the compound in long crimson needles, m. p. 158—160° (21 g.) (Found: N, 11·0; Cl, 13·6. Calc. for $C_{15}H_{13}N_2Cl$: N, 10·9; Cl, 13·8%).

5-Amino-3-dimethylaminoacridine. A solution of 5-chloro-3-dimethylaminoacridine (10 g.) in phenol (80 g.) was heated at 110° for 1 hour and then powdered ammonium carbonate (8 g.) added over 15 minutes with stirring; the solution was heated at 105° for a further 2 hours, cooled and poured into an excess of ether. The red precipitate was collected, refluxed for 1½ hours with methanol (800 c.c.) and the filtered solution evaporated to smaller volume (*ca.* 400 c.c.); on cooling, *5-amino-3-dimethylaminoacridine hydrochloride* (8·1 g.) separated in long crimson prisms, m. p. 360—362° (Found: N, 15·0; Cl, 12·7. $C_{15}H_{16}N_3Cl$ requires N, 15·3; Cl, 13·0%). This hydrochloride dissolved in water giving a pale red solution having pH *ca.* 6·6; the solubility at 20° was *ca.* 3%. The hydrochloride (3 g.) was shaken with 2·5N-sodium hydroxide (100 c.c.) and glass beads for 1 hour and the light yellow insoluble base collected and washed. Recrystallisation from dilute alcoholic pyridine gave *5-amino-3-dimethylaminoacridine* in stellate clusters of yellow needles, m. p. 256—258° (Found: C, 75·2; H, 6·3; N, 17·6. $C_{15}H_{15}N_3$ requires C, 75·9; H, 6·3; N, 17·7%). The base was very soluble in pyridine and almost insoluble in alcohol.

5-Chloro-4′-dimethylaminodiphenylamine-2-carboxylic acid (cf. Drozdov, *loc. cit.*). 2 : 4-Dichlorobenzoic acid (48 g.), potassium carbonate (41 g.), copper powder (1 g.), *p*-aminodimethylaniline (43 g.) and amyl alcohol (450 c.c.) were heated at 140° for 4 hours. The crude acid, isolated in the usual manner, was purified by reprecipitation and crystallisation

from the minimum amount of 96% alcohol; 5-chloro-4'-dimethylaminodiphenylamine-2-carboxylic acid was obtained in dark grey needles (36 g.). When recrystallised from the same solvent, it had m. p. 246—248° (Found: Cl, 12·0. Calc. for $C_{15}H_{15}O_2N_2Cl$: Cl, 12·2%).

5 : 8-*Dichloro-3-dimethylaminoacridine*. The foregoing acid (40 g.) was gently refluxed with phosphorus oxychloride (400 c.c.) for 4 hours and the resulting mixture, while still hot, slowly poured on to a large excess of powdered ice; ammonia was then added with stirring until the liquid was just alkaline, the temperature throughout being kept at $< 2°$ by the addition of ice. The precipitate was separated from the cold liquor (vol. *ca.* 5 litres), washed, drained on porous porcelain and dried under reduced pressure at 20° over potassium hydroxide; the crude product (37 g.) was a deep red-brown powder. This was recrystallised from boiling benzene (*ca.* 400 c.c.) and gave 5 : 8-dichloro-3-dimethylaminoacridine (26 g.) in scarlet prisms, m. p. 200—202° (Found: N, 9·7; Cl, 24·5. Calc. for $C_{15}H_{12}N_2Cl_2$: N, 9·6; Cl, 24·4%). The compound is dichroic and may be obtained in brown leaves. When recrystallised from benzene–alcohol (3 : 1), it was obtained in long crimson needles, m. p. 206—208° (Found: Cl, 24·0%); a further sample crystallised from boiling alcohol–benzene–water (60 : 35 : 5) in scarlet prisms, m. p. 206—208° (Found: N, 9·6; Cl, 24·2%).

8-*Chloro-5-amino-3-dimethylaminoacridine*.—5 : 8-Dichloro-3-dimethylaminoacridine (10 g.) was heated with phenol (100 g.) for 1 hour at 110°, powdered ammonium carbonate (10 g.) slowly stirred in and the resulting solution heated at 110° for 2 hours and poured into an excess of dry ether. The precipitate was collected, dissolved in methanol (1500 c.c.), the solution refluxed for 2 hours and the solvent distilled away until the residual volume was *ca.* 750 c.c.; on cooling, *8-chloro-5-amino-3-dimethylaminoacridine hydrochloride* (7·5 g.) separated in crimson needles, m. p. 368—370° (decomp.) (Found: N, 13·4; Cl, 22·8. $C_{15}H_{15}N_3Cl_2$ requires N, 13·7; Cl, 23·1%).

The hydrochloride (2 g.) was ground with 2N-sodium hydroxide (100 c.c.) and glass beads; the yellow base was collected, washed and recrystallised from dilute alcoholic pyridine giving *8-chloro-5-amino-3-dimethylaminoacridine* in long golden needles, m. p. 304—306° (Found: N, 15·7; Cl, 13·2. $C_{15}H_{14}N_3Cl$ requires N, 15·5; Cl, 13·1%).

The authors thank Mr. H. S. Turner, B.Sc., for preparing the 3-acetamido-, 3-nitro-, 6-acetamido- and 6-nitro-derivatives of 2-chlorobenzoic acid and Mr. Fairbairn and Mr. R. Selway for technical assistance and some of the analytical work.

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[*Received, November 7th*, 1945].