47. *The Bromination of Acridone.*

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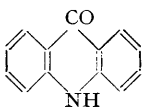
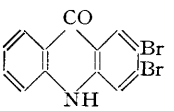
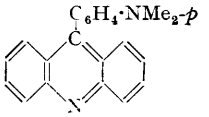
Re-investigation of the bromination of acridone has shown that the product is not 2 : 3-dibromoacridone as claimed by Tanasescu and Ramontianu (*Bull. Soc. chim.*, 1939, **6**, 486) but 3 : 7-dibromo- or 1 : 3 : 7 : 9-tetrabromoacridone according to the conditions. The structures of these bromoacridones have been proved by their identity with authentic specimens prepared by the cyclisation of diphenylamine-2-carboxylic acids. Vigorous bromination of 1 : 3 : 7 : 9-tetrabromoacridone gives an unidentified hexabromoacridone.

ALTHOUGH the nitration and sulphonation of acridone (I) have been fairly extensively investigated (Lehmstedt, *Ber.*, 1931, **64**, 2381; Matsumura, *J. Amer. Chem. Soc.*, 1935, **57**, 1533), little work has been done on the halogenation of acridone or its derivatives. Eckert and Steiner (*Sitzungsber. Akad. Wiss. Wien*, 1914, **123**, 1141) obtained octachloroacridone from acridone and 10-methylacridone and antimony pentachloride, and Tanasescu and Ramontianu (*loc. cit.*) have examined the chlorination of 10-hydroxyacridone and acridone, and claim that the bromination of acridone and 10-hydroxyacridone under conditions which they do not define gives the 2 : 3-dibromo-compounds (*e.g.*, II). Bromination of " 3-chloro-," and 10-hydroxy-2-nitroacridone effects only monosubstitution, which led these authors to claim that the disubstitution product obtained from acridone was (II), as


(I)


(II)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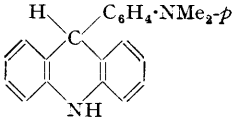
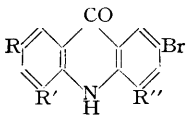

(IV)

in the other cases they considered the nitro- or chloro-group to occupy one of the substitutable positions. This argument is open to many objections. A chloro-, bromo-, or nitro-substituent, irrespective of position, will deactivate the substituted ring so that the bromine is expected to attack the unsubsituted ring first. The structure of the supposed " 3-chloro-10-hydroxyacridone " is incorrect; Lehmstedt (*Ber.*, 1932, **65**, 834) showed that the substance is 2-chloro-10-hydroxyacridone. It is also difficult to explain why the bromine should attack position 2 when nitration, which presumably proceeds through a similar cationoid attack, causes substitution only at positions 1, 3, 7, and 9.

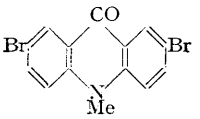
The bromination was therefore re-investigated. The general technique was to compare the products of bromination with bromoacridones of definite constitution. Direct mixed-melting point determinations were not suitable for this as the melting points are, with one exception, too high; the acridones were therefore converted into the lower-melting 5-chloroacridines with phosphorus oxychloride alone, or with the addition of a dialkylaniline into the 5-dialkylaminophenylacridines (*e.g.*, III). Gilman and Shirley (*J. Amer. Chem. Soc.*, 1950, **72**, 2181) have provided the only structural proof of (III) by its synthesis from (IV). The comparatively low-melting 5-*p*-dialkylaminophenylacridines have been recommended for the characterisation of acridones by Albert (" The Acridines," Arnold, 1950, p. 133) but this is now endorsed only if the original acridone is comparatively pure. Mixtures of these derivatives, prepared from inseparable mixtures of brominated acridones, could not be resolved by crystallisation in any case examined, as mixed crystals or lattice compounds were formed. Tedious chromatographic separations are necessary in order to separate sufficient quantities of pure materials from such mixtures for identification. Fractionation of the corresponding 5-chloroacridines appears to be preferable.

The brick-red precipitate obtained when bromine was added to a cold solution of acridone in acetic acid became yellow when warmed, kept, or treated with water or bases. It could not be obtained free from acetic acid, but an estimate of the " available bromine " was obtained in sulphuric–acetic acid solution by titration of the iodine liberated from potassium iodide. Somewhat less than half the original bromine was " available," so the

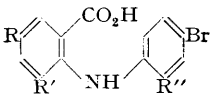
precipitate appeared to contain perbromides. 10-Bromoacridones are probably absent, as 10-methylacridone gives a similar red substance. When the acridone–bromine–acetic acid mixture was heated to 60—70° the red precipitate became yellow and gave a mixture of acridones which could not be separated by crystallisation before or after conversion into the corresponding 5-dialkylaminophenylacridines; in one instance the resulting mixture of acridines melted sharply at 238°, unchanged by recrystallisation. Authentic 3-bromo-5-*p*-dimethylaminophenylacridine also has m. p. 238° but a mixture melted at 217°. The formation of 3-bromoacridone (V) in the bromination of acridone was, however, proved by a tedious chromatographic separation of the mixed 5-dimethylaminophenylacridines on alumina. As only one orange band is formed colour reactions were devised, with pure acridines, whereby the elution of 3-bromo-5-*p*-dimethylaminophenylacridine could be detected; this compound was eventually isolated in a pure condition. 3 : 7-Dibromoacridone was also shown present in the bromination product by reaction with phosphorus oxychloride followed by fractional crystallisation of the resulting 5-chloroacridines; it was not possible to obtain pure 3-bromo-5-chloroacridine from this fractionation.



(V; R = R′ = R″ = H)
(VI; R = Br, R′ = R″ = H)
(VII; R = R′ = Br, R″ = H)
(VIII; R = R′ = R″ = Br)



(IX)



(X; R = R′ = R″ = H)
(XI; R = Br, R′ = R″ = H)
(XII; R = R′ = Br, R″ = H)
(XIII; R = R′ = R″ = Br)

Boiling acridone with bromine in acetic acid gives an excellent yield of 3 : 7-dibromoacridone (VI), proved identical with the cyclisation product of 4 : 4′-dibromodiphenylamine-2-carboxylic acid (XI) by comparison of lower-melting derivatives. Since the completion of this work Kruger (*J.*, 1952, 3648) prepared 3 : 7-dibromoacridone from the corresponding diamine, and showed it identical with an acridone bromination product by a comparison of the corresponding 5-diethylaminophenylacridines.

Further bromination of 3 : 7-dibromoacridone yields inseparable mixtures unless the reaction is continued until 1 : 3 : 7 : 9-tetrabromoacridone (VIII), best prepared by refluxing acridone with a large excess of bromine in acetic acid, is formed. Formation of 1 : 3 : 7-tribromoacridone (VII) in the bromination of 3 : 7-dibromoacridone (VI) can be shown if the reaction time is insufficient for tetrasubstitution. The least soluble fraction of the mixed bromoacridones in *m*-cresol was heated to 100° with phosphorus oxychloride and diethylaniline to convert all the unchanged 3 : 7-dibromoacridone into 3 : 7-dibromo-5-*p*-diethylaminophenylacridine. Impure 1 : 3 : 7-tribromo-5-chloroacridine remained after extraction with hot dilute acid, and after much purification proved identical with a specimen of known structure. The last separation depends on the fact that although acridone and its 3-bromo-, and 3 : 7-dibromo-, and many other derivatives will give the corresponding 5-dialkylaminophenylacridines with dialkylanilines and phosphorus oxychloride during 2 hours at 100°, 1 : 3 : 7-tribromo- and 1 : 3 : 7 : 9-tetrabromo-acridone give only the 5-chloroacridines under these conditions. These 5-chloroacridines nevertheless react readily with dimethyl- or diethyl-aniline in the presence of aluminium chloride (Drozdov, *Chem. Abstracts*, 1937, **31**, 4321) to give the corresponding 5-dialkylaminophenylacridines.

Further bromination of 1 : 3 : 7 : 9-tetrabromoacridone could only be effected in boiling bromine in the presence of aluminium bromide. An unidentified 1 : 3 : 7 : 9 : *x* : *x*-hexabromoacridone was formed and further substitution did not appear to take place.

10-Methylacridone readily gave 3 : 7-dibromo-10-methylacridone (IX), prepared also by the methylation of 3 : 7-dibromoacridone, with a small excess of bromine in boiling acetic acid. Only 1 : 3 : 7 : 9-tetrabromoacridone (VIII) could be isolated from a more vigorous bromination; demethylation is not unexpected by analogy with the results of Eckert and Steiner (*loc. cit.*).

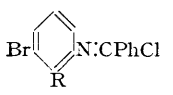
These results show that the structures given by Tanasescu and Ramontianu to many

of their halogenated acridones are erroneous, their " 2 : 3- " disubstituted derivatives being 3 : 7-derivatives, etc.

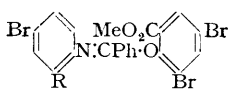
The acridones and their derivatives of known structure required for comparison were prepared from the appropriate diphenylamine-2-carboxylic acids or their derivatives. *p*-Bromoaniline with 2-chloro- and 5-bromo-2-chloro-benzoic acid gave, by the Ullmann reaction, 4'-bromo- (X) (Ullmann and Tedescu, *Annalen*, 1907, **355**, 351) and 4 : 4'-dibromodiphenylamine-2-carboxylic acid (XI). The latter could not be prepared from *p*-dibromobenzene and 5-bromoanthranilic acid. Refluxing phosphorus oxychloride cyclised both these acids to 5-chloroacridines, which with diethyl- and dimethyl-aniline gave the corresponding dialkylaminophenylacridines also required for comparison purposes.

Attempts were also made to prepare the tri- and tetra-bromo-acids (XII and XIII) by the Ullmann condensation. 3 : 5-Dibromoanthranilic acid (Freundler, *Compt. rend.*, 1909, **149**, 1137), in a Sandmeyer reaction, gave an excellent yield of 3 : 5-dibromo-2-chlorobenzoic acid. Unfortunately only reductive dehalogenation (cf. Goldberg and Kelly, *J.*, 1946, 102) to 3 : 5-dibromobenzoic acid took place when this acid was used in Ullmann condensations with 4-bromo- and 2 : 4-dibromo-aniline.

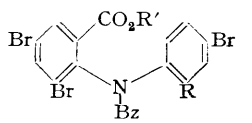
Jamison and Turner's adaptation (*J.*, 1937, 1954) of Chapman's diphenylamine synthesis (*J.*, 1927, 1743) is the only method available for the preparation of 1 : 3 : 7-tribromoacridone (VII), and is satisfactory in the case of 1 : 3 : 7 : 9-tetrabromoacridone (VIII)



(XIV; R = H)
(XV; R = Br)



(XVI; R = H)
(XVII; R = Br)



(XVIII; R = H, R' = Me)
(XIX; R = Br, R' = Me)
(XX; R = R' = H)

2' : 4'-Dibromobenzanilide, prepared by the bromination of benzanilide, and 4'-bromobenzanilide with phosphorus pentachloride gave the imidoyl chlorides (XV and XIV). These chlorides and the sodium derivative of methyl 3 : 6-dibromosalicylate gave the imidates (XVII and XVI) which at >200° rearranged to the methyl *N*-benzoyldiphenylamine-2-carboxylates (XIX and XVIII); neither the imidate nor its rearrangement product in the tetrabromo-series could be obtained crystalline. Pyrolysis of (XX), obtained by the partial hydrolysis of (XVIII), gave an excellent yield of 1 : 3 : 7-tribromoacridone (VII) (cf. Jamison and Turner, *loc. cit.*) but the simplest way of cyclising the *N*-benzoyl esters is by sulphuric acid at 160—200° : excellent yields of (VII and VIII) are thus obtained.

Methyl 3 : 5-dibromosalicylate was easily prepared by the iron-catalysed bromination of methyl salicylate, although this bromination is stated (Cahours, *Annalen*, 1894, **52**, 328; Kaufmann and Egner, *Ber.*, 1913, **46**, 3786) to give mixtures. Bromination of salicylic acid, contrary to previous reports (Robertson, *J.*, 1902, **81**, 1480; Leulier and Pinet, *Bull. Soc. chim.*, 1927, **41**, 1367), gave much 3-bromosalicylic acid and 2 : 4 : 6-tribromophenol as well as 3 : 5-dibromosalicylic acid.

Experimental

5-p-*Dialkylaminophenylacridines.*—*Method* 1. The acridone (1·0 g.), phosphorus oxychloride (2 ml.), and dimethyl- or diethyl-aniline (4 ml.) were heated to 100° (2—3 hr.), diluted with water (100 ml.), and basified and excess of amine was removed by steam. The residual solid was passed in benzene through a short alumina column, and recovered from the eluate.

Method 2. When method 1 was carried out on a very small scale the reaction product was dissolved in boiling 2N-hydrochloric acid and filtered into excess of aqueous sodium acetate, and the precipitate purified as before.

Method 3. The 5-chloroacridine (0·02—0·2 g.), aluminium chloride (0·1—0·5 g.), and dimethyl- or diethyl-aniline (1—2 ml.) were heated at 100° (4—6 hr.). The product was boiled with 2N-hydrochloric acid (20 ml.), and the yellow or orange residue collected, washed with hot dilute acid, water, and concentrated aqueous ammonia, dried, and chromatographed.

Detection of 3-*Bromoacridone* (V).—Bromine (1·64 g.) in acetic acid (20 ml.) was added to a cold solution of acridone (2·0 g.) in acetic acid (300 ml.), and the mixture left at room temperature until the bulky red solid immediately precipitated had become yellow. A clear solution was obtained on boiling and deposited microscopic yellow needles (1·4 g.) when cold. This mixture of acridones was converted into the corresponding 5-*p*-dimethylaminophenylacridines (method 1), which (0·7 g.) were adsorbed on alumina from a saturated solution in light petroleum (1 l., b. p. 60—80°). A single orange band was formed and eluted with light petroleum (b. p. 60—80°)–benzene (3 : 1). No visual separation of the mixture was observed, but when the colour reactions of the eluate indicated the presence of mainly 3-bromo-5-*p*-dimethylaminophenylacridine this was collected and evaporated. Repeated crystallisation of the residue from benzene, followed by ethanol, gave 3-bromo-5-*p*-dimethylaminophenylacridine as yellow needles, m. p. 237·5° alone or mixed with an authentic specimen (m. p. 239°) (Found: C, 66·6; H, 4·5. Calc. for $C_{21}H_{17}N_2Br$: C, 66·8; H, 4·5%).

A portion of the mixed bromoacridones with refluxing phosphorus oxychloride gave the 5-chloroacridines which after chromatographic purification (benzene–alumina) and fractional crystallisation from benzene–light petroleum (b. p. 60—80°) gave 3 : 7-dibromo-5-chloroacridine as the least soluble fraction, m. p. 218° alone or mixed with an authentic specimen. A more soluble fraction, m. p. 128—130°, appeared to be substantially 3-bromo-5-chloroacridine, m. p. 134—135°, mixed m. p. 130—133°.

3 : 7-*Dibromoacridone* (VI).—A mixture of bromine (4·1 g.), acridone (2·0 g.), and acetic acid (250 ml.) was boiled until the flocculent yellow precipitate became granular (10 min.), then filtered hot, and the residual yellow solid (2·4—2·8 g., 70—80%) washed with hot acetic acid. On crystallisation from *m*-cresol 3 : 7-*dibromoacridone* was obtained (80%) as yellow needles, m. p. > 340° (Found: C, 44·2; H, 2·3; Br, 44·3. $C_{13}H_7ONBr_2$ requires C, 44·3; H, 2·0; Br, 45·2%). 3 : 7-*Dibromo*-5-p-*dimethylaminophenylacridine* (method 2) crystallised from ethanol in yellow granules, m. p. 271—272°, and mixed m. p. 272° with an authentic specimen of m. p. 273—273·5° (Found: C, 55·5; H, 3·4. $C_{12}H_{16}N_2Br_2$ requires C, 55·3; H, 3·5%). 3 : 7-*Dibromo*-5-p-*diethylaminophenylacridine*, similarly prepared and purified, separated from ethanol in yellow plates, m. p. 274° alone or mixed with an authentic specimen (m. p. 274°) (Found: C, 57·4; H, 4·6. $C_{23}H_{20}N_2Br_2$ requires C, 57·0; H, 4·6%).

Detection of 1 : 3 : 7-*Tribromoacridone* (VII).—3 : 7-Dibromoacridone (5·9 g.), bromine (2·5 ml.), and acetic acid (50 ml.) were refluxed for 2·5 hours and the yellow solid (7·6 g.) was collected. It dissolved in boiling *m*-cresol (50 ml.) but from the refluxing solution yellow crystals separated during 1 hour. They were collected from the boiling solution, washed with acetic acid, and dried (2·5 g.). 3 : 7-Dibromoacridone was removed by treating this solid (0·5 g.) with diethylaniline and phosphorus oxychloride (2 hours at 100°) and extracting the product with hot 2N-hydrochloric acid. The residue (0·26 g.) was purified chromatographically, and repeated crystallisation from benzene then gave 1 : 3 : 7-*tribromo*-5-*chloroacridine* as yellow needles, m. p. 232—233°, which did not depress the m. p. of an authentic specimen (Found: C, 34·9; H, 1·3. $C_{13}H_5ClNBr_3$ requires C, 34·7; H, 1·1%. 1 : 3 : 7-*Tribromo*-5-p-*dimethylaminophenylacridine* (method 3) separated from benzene–ethanol as scarlet prisms, the less common crystal form, of m. p. 292—293° alone or mixed with an authentic specimen (Found: C, 47·2; H, 2·8. $C_{21}H_{15}N_2Br_3$ requires C, 47·2; H, 2·9%). 1 : 3 : 7-*Tribromo*-5-p-*diethylaminophenylacridine* (method 3) crystallised from benzene–ethanol in orange-red prisms, m. p. 260·5° alone or mixed with authentic specimen (Found: C, 48·8; H, 3·4; Br, 42·1. $C_{23}H_{19}N_2Br_3$ requires C, 49·1; H, 3·4; Br, 42·5%).

1 : 3 : 7 : 9-*Tetrabromoacridone* (VIII).—Acridone (1·0 g.), bromine (10 ml., in two portions, the second after 6 hours), and acetic acid (50 ml.) were refluxed for 18—24 hours and the precipitate was collected, washed, and dried (m. p. 307—308°; 2·1—2·2 g.). On crystallisation from *m*-cresol–acetic acid 1 : 3 : 7 : 9-*tetrabromoacridone* was obtained in pale yellow needles, m. p. 308—308·5° alone or mixed with an authentic specimen (Found: C, 30·6; H, 1·3; Br, 62·2. $C_{13}H_5ONBr_4$ requires C, 30·6; H, 1·0; Br, 62·5%).

1 : 3 : 7 : 9-*Tetrabromo*-5-*chloroacridine*.—This *acridine*, prepared from the acridone with phosphorus oxychloride, separated from benzene in pale yellow needles which rapidly changed to thick lemon-yellow prisms, m. p. 254—254·5°, unchanged on admixture with an authentic specimen (Found: C, 29·6; H, 0·8; Hal., 66·3. $C_{13}H_4ClNBr_4$ requires C, 29·5; H, 0·8; Hal., 67·2%). 1 : 3 : 7 : 9-*Tetrabromo*-5-p-*dimethylaminophenylacridine* (method 3) separated from benzene–ethanol in bright red needles, m. p. 309—310°, or m. p. 309° on mixture with an authentic specimen (Found: C, 41·1; H, 2·2; Br, 52·2. $C_{21}H_{14}N_2Br_4$ requires C, 41·1; H, 2·3; Br, 52·1%). 1 : 3 : 7 : 9-*Tetrabromo*-5-p-*diethylaminophenylacridine* (method 3) separated

from benzene as orange-red needles, m. p. 268° unchanged on admixture with an authentic specimen (Found : C, 43·0; H, 3·0; Br, 50·4. $C_{23}H_{18}N_2Br_4$ requires C, 43·0; H, 2·8; Br, 49·8%).

1 : 3 : 7 : 9 : x : x-*Hexabromoacridone*.—Thin aluminium foil (0·27—0·55 g.) was added in very small pieces to a mixture of acridone (1·0 g., 1 mol.) or 1 : 3 : 7 : 9-tetrabromoacridone (2·52 g., 1 mol.) and bromine (10 ml.), and the mixture refluxed for 2·5 hours to 5 days. Excess of bromine was then removed at 100° and the residual clear red gum treated with 2N-hydrochloric acid (50 ml.) with cooling. The bright yellow precipitate was collected, washed with hydrochloric acid, and dried (m. p. 346—347°; 3·35—3·42 g.), and on crystallisation from *m*-cresol gave 1 : 3 : 7 : 9 : x : x-*hexabromoacridone* as yellow prisms, m. p. 347° (Found : C, 23·8; H, 0·7. $C_{13}H_3ONBr_6$ requires C, 23·3; H, 0·4%).

Bromination of 10-*Methylacridone*.—(*a*) Bromine (0·9 g.) in acetic acid (11 ml.) was added to a hot solution of 10-methylacridone (0·5 g.) and sodium acetate (anhyd., 0·5 g., 2·5 mol.), and the mixture boiled gently until the flocculent yellow precipitate changed to yellow needles (5—10 min.). After cooling, 3 : 7-*dibromo*-10-*methylacridone* was collected, washed, dried (0·71 g.), and crystallised from ethanol as very pale yellow needles, m. p. 282—283° alone or mixed with an authentic specimen (Found : C, 46·0; H, 2·4; Br, 42·7. $C_{14}H_9ONBr_2$ requires C, 45·8; H, 2·5; Br, 43·6%).

(*b*) 10-Methylacridone (0·5 g.), anhydrous sodium acetate (8·0 g.), bromine (10 ml., in two portions, the second being added after 6 hr.), and glacial acetic acid (50 ml.) were refluxed (18 hr.), and the product (0·7 g.) was precipitated with water. Crystallisation from *m*-cresol gave 1 : 3 : 7 : 9-tetrabromoacridone, discoloured needles, m. p. 307—308°, mixed m. p. 308°.

5-*Bromo*-2-*chlorobenzoic Acid*.—5-Bromoanthranilic acid (10·9 g.) was diazotised (sodium nitrite, 5·0 g.) in hydrochloric acid (8N; 120 ml.) at 5—10°, and the solution poured into cuprous chloride (6·0 g.) in hydrochloric acid (40 ml.; *d* 1·16), and after 30 minutes at 18°, the precipitate was collected. Acidification of its solution in alkali (charcoal) precipitated 5-bromo-2-chlorobenzoic acid (10·0 g.), colourless needles (from water), m. p. 155—156° (Cohen and Raper, *J.*, 1904, **85**, 1267, give this m. p.).

4 : 4′-*Dibromodiphenylamine*-2-*carboxylic Acid*.—5-Bromo-2-chlorobenzoic acid (4·7 g.), *p*-bromoaniline (6·9 g.), potassium carbonate (5·5 g.), and " Naturkupfer C " (Kahlbaum, 0·1 g.) were refluxed in amyl alcohol (15 ml.) for 5 hours. The residue from steam-distillation was extracted with ether, decolorised with charcoal, partly acidified, boiled, and filtered into an excess of hydrochloric acid. The precipitated 4 : 4′-*dibromodiphenylamine*-2-*carboxylic acid* (4·0 g.) after one crystallisation from light petroleum (b. p. 60—80°) separated from benzene as yellow crystals, m. p. 232—234 (Found : N, 4·1. $C_{13}H_9O_2NBr_2$ requires N, 3·8%).

3-*Bromo*- and 3 : 7-*Dibromo*-5-p-*dialkylaminophenylacridine*.—4′-Bromodiphenylamine-2-carboxylic acid (X) (Ullmann and Tedescu, *Annalen*, 1907, **355**, 341) or 4 : 4′-dibromodiphenylamine-2-carboxylic acid (2·0 g.) was refluxed with phosphorus oxychloride (10 ml.) until hydrogen chloride was no longer evolved (1—2 hr.), dimethyl- or diethyl-aniline (4 ml.) added, refluxing continued for a further hour, and the product worked up as in method 1. The products, all formed in excellent yield, were crystallised once from amyl alcohol and twice from ethanol. 3-Bromo-5-*p*-dimethylaminophenylacridine separated as yellow laths, m. p. 239° (Polaczek, *Roczniki Chem.*, 1936, **16**, 76, gives m. p. 239—240°). 3 : 7-*Dibromo*-5-p-*dimethylaminophenylacridine* formed almost cubic yellow granules, m. p. 273—273·5° (Found : C, 55·5; H, 3·8; Br, 35·3%). Red, and violet-blue colours, which are discharged on shaking, are formed with 3-bromo- and 3 : 7-dibromo-5-*p*-dimethylaminophenylacridine respectively on treatment of their solutions in benzene (0·1 ml.)–amyl alcohol (0·5 ml.) with 2N-aqueous hydrochloric acid (1 ml.). 3-*Bromo*-5-p-*diethylaminophenylacridine* separated in orange-yellow prisms, m. p. 211° (Found : C, 68·4; H, 5·1; Br, 19·8. $C_{23}H_{21}N_2Br$ requires C, 68·2; H, 5·2; Br, 19·7%). 3 : 7-*Dibromo*-5-p-*diethylaminophenylacridine* crystallised in minute yellow plates, m. p. 274° (Found : C, 56·7; H, 4·4; Br, 33·8%).

3-*Bromo*-5-*chloroacridine*.—4′-Bromodiphenylamine-2-carboxylic acid (X) on cyclisation with boiling phosphorus oxychloride gave 3-bromo-5-chloroacridine, which separated from benzene–light petroleum (b. p. 60—80°) in pale yellow needles, m. p. 134—185° (*Chem. Zentr.*, 1936, 4466, gives m. p. 136°).

3 : 7-*Dibromo*-5-*chloroacridine*.—This *acridine*, prepared from the acridone with phosphorus oxychloride, separated from light petroleum (b. p. 60—80°) in pale yellow needles, m. p. 219° (Found : C, 42·1; H, 1·7. $C_{13}H_6NClBr_2$ requires C, 42·1; H, 1·6%).

3 : 7-*Dibromo*-10-*methylacridone*.—3 : 7-Dibromoacridone (1·0 g.), potassium hydroxide (3·0 g.), water (2 ml.), and ethanol (10 ml.) were heated with stirring until pasty. After cooling,

the bright greenish-yellow solid was collected and dried for 2 hours at 150°. It was then powdered and heated with methyl sulphate (3—4 ml.) at 100° for 1 hour, and after the addition of concentrated aqueous ammonia the pale yellow precipitate was collected (0·94 g., 90%). Crystallisation from ethanol gave 3 : 7-dibromo-10-methylacridone as pale yellow needles, m. p. 284° alone or mixed with a specimen prepared from 10-methylacridone (see above).

3 : 5-*Dibromo*-2-*chlorobenzoic Acid*.—3 : 5-Dibromoanthranilic acid (17·25 g.) suspended in hydrochloric acid (10N; 100 ml.) was diazotised (5—10°) with sodium nitrite (5·5 g.) and, after addition of urea (3 g.), poured into hydrochloric acid (50 ml.; 10N) containing cuprous chloride (6·4 g.). After 30 minutes the 3 : 5-dibromo-2-chlorobenzoic acid was collected and purified through hot aqueous alkali (charcoal); the *acid* (15·6 g.) separated from ethanol–water in colourless needles, m. p. 189—189·5° (Found: C, 27·3; H, 1·2. $C_7H_3O_2ClBr_2$ requires C, 26·8; H, 1·0%). The *amide* separated from aqueous ethanol as needles, m. p. 213—215° (Found: N, 4·2. $C_7H_2ONClBr_2$ requires N, 4·5%).

Unsuccessful Ullmann Condensations.—3 : 5-Dibromo-2-chlorobenzoic acid (8·0 g.), potassium carbonate (4·2 g.), 2 : 4-dibromoaniline (11·7 g.), and Fauconau's copper (0·1 g.; Fauconau, *Bull. Soc. chim.*, 1937, **4**, 58) were refluxed in *cyclo*hexanol (15 ml.) for 5 hours. The reaction product yielded 3 : 5-dibromobenzoic acid as needles, m. p. 214—215°, from ethanol; the amide crystallised from aqueous ethanol as needles, m. p. 185—186°. Cohen and Dutt (*J.*, 1914, **105**, 502) give m. p. 213—214° for the acid, and Sudborough (*J.*, 1895, **87**, 594) gives m. p. 187° for the amide. 3 : 5-Dibromobenzoic acid was the sole product obtained from 3 : 5-dibromo-2-chlorobenzoic acid, *p*-bromoaniline, potassium carbonate, and Naturkupfer C in either nitrobenzene or *cyclo*hexanol, with or without potassium iodide.

Methyl 3 : 5-*Dibromosalicylate*.—Bromine (77 ml.) in chloroform (100 ml.) was added to a mixture of methyl salicylate (64 ml.), chloroform (200 ml.), and iron powder (4 g.) with shaking so that a vigorous evolution of hydrogen bromide took place (5—10 min.). When the reaction slackened the mixture was refluxed from a steam-bath until the bromine vapour evolved contained only little hydrogen bromide (30—45 min.). After cooling, the semi-solid mass was shaken with sodium hydrogen sulphite (60 g.) in water (300 ml.) until almost colourless, and then washed by decantation with fresh aqueous bisulphite (10 g., in 500 ml. of water), followed by water. The heated mixture was then treated with boiling chloroform (300—400 ml.), and extraneous water removed in a heated separating funnel; on cooling, the filtered chloroform solution deposited methyl 3 : 5-dibromosalicylate as colourless prisms, m. p. 150—152° (105 g.). Repeated recrystallisation from ethanol raised the m. p. to 153° (recorded values are 148° to 156°).

N-p-*Bromophenylbenzimidoyl Chloride*.—4′-Bromobenzanilide (44 g.) and powdered phosphorus pentachloride (36 g.) were heated on a steam-bath (30 min.). Phosphorus oxychloride was removed *in vacuo*, and the residue treated with light petroleum (b. p. 60—80°; sodium-dried), which was then distilled off to remove the last traces of phosphorus chlorides. The residue was refluxed with more light petroleum (300 ml.; b. p. 60—80°) for 30 min., and the solution decanted from insoluble material and cooled to 0°. N-p-*Bromophenylbenzimidoyl chloride* separated as needles, m. p. 70° (39 g.) (Found: C, 52·7; H, 3·4; Hal., 40·0. $C_{13}H_9NClBr$ requires C, 53·0; H, 3·1; Hal., 39·2%).

Methyl N-*Benzoyl*-4 : 6 : 4′-*tribromodiphenylamine*-2-*carboxylate*.—4 : 6-Dibromo-2-carbomethoxyphenyl *N*-*p*-bromophenylbenzimidate (30 g.) rearranged to the diphenylamine at 200—210° (Jamison and Turner, *loc. cit.*, give 270°). The diphenylamine was obtained as colourless needles, m. p. 132—134° (86—94%) when the glassy reaction product crystallised from ethanol, and gave the acid, m. p. 218·5°, on mild alkaline hydrolysis.

1 : 3 : 7-*Tribromoacridone*.—(*a*) *N*-Benzoyl-4 : 6 : 4′-tribromodiphenylamine-2-carboxylic acid (5·0 g.) was heated at 300—350° and the product boiled with aqueous sodium hydroxide followed by water. It gave 1 : 3 : 7-tribromoacridone as pale yellow needles (from *m*-cresol), m. p. >340° (2·17 g.) (Found: C, 36·6; H, 1·8. Calc. for $C_{13}H_6ONBr_3$: C, 36·3; H, 1·4%). (*b*) Methyl *N*-benzoyl-4 : 6 : 4′-tribromodiphenylamine-2-carboxylate (1·0 g.) was heated with concentrated sulphuric acid (2·0 ml.) to 160—200°; on cooling, 1 : 3 : 7-tribromoacridone (0·66 g.) was precipitated.

1 : 3 : 7-*Tribromo*-5-*chloroacridine*.—1 : 3 : 7-Tribromoacridone (2·0 g.) and phosphorus oxychloride (5 ml.) were refluxed (90 min.) and the product poured into ice (100 g.), ammonia (100 ml.; *d* 0·880), and chloroform (125 ml.). The chloroform layer was boiled to dissolve all the solid; on cooling to 0°, 1 : 3 : 7-tribromo-5-chloroacridine crystallised (1·15 g.). It separated from benzene in pale yellow needles, m. p. 232—233° (Found: C, 35·0; H, 1·2%). 1 : 3 : 7-Tribromo-5-(4-dimethylaminophenyl)acridine (method 3) separated from benzene as yellow needles which change to red at about 200°, or occasionally as scarlet prisms; both forms have

m. p. 292—293°. 1 : 3 : 7-Tribromo-5-*p*-diethylaminophenylacridine, similarly prepared and purified, had m. p. 260° (Found : C, 49·5; H, 3·4%).

2′ : 4′-*Dibromobenzanilide*.—Benzanilide (49 g.), anhydrous sodium acetate (45 g.), bromine (26 ml.), and glacial acetic acid (300 ml.) were heated on a steam-bath for 18 hours and allowed to cool (cf. Chattaway and Clemo, *J.*, 1916, **109**, 91). The precipitate was collected and after being washed with a little acetic acid and much water crystallised from ethanol, to give 2′ : 4′-dibromobenzanilide as colourless needles, m. p. 138° (67 g.) (Wittig *et al.*, *Annalen*, 1929, **469**, 11, give m. p. 139°).

N-(2 : 4-*Dibromophenyl*)*benzimidoyl Chloride*.—2′ : 4′-Dibromobenzanilide (35·5 g.) and powdered phosphorus pentachloride (22·8 g.) were heated on a steam-bath for 30 minutes. The phosphorus oxychloride was removed as for (XIV), and the residue on crystallisation from light petroleum (b. p. 60—80°; sodium-dried) gave *N*-(2 : 4-*dibromophenyl*)*benzimidoyl chloride* as needles, m. p. 95·5° (31 g.) (Found: C, 41·8; H, 2·4. $C_{13}H_8NClBr_2$ requires C, 41·8; H, 2·2%).

1 : 3 : 7 : 9-*Tetrabromoacridone*.—A solution of the above chloride (13·2 g.) in dry ether (100 ml.) was added with shaking to a mixture of methyl 3 : 5-dibromosalicylate (10·9 g.) and a solution of sodium (0·8 g.) in dry ethanol (100 ml.). Next day the solvent was removed *in vacuo*, and after addition of water the semi-solid 4 : 6-dibromo-2-carbomethoxyphenyl *N*-(2 : 4-dibromophenyl)benzimidate was collected. Attempts to crystallise this material failed. The imidate (5 g.) was heated at 260° for 5 minutes to effect rearrangement to methyl *N*-benzoyl-4 : 6 : 2′ : 4′-tetrabromodiphenylamine-2-carboxylate, also obtained only as a glass. This (4·0 g.) was heated at 200° for 1 min. with concentrated sulphuric acid (10 ml.; *d* 1·84), and, on cooling, 1 : 3 : 7 : 9-tetrabromoacridone separated in minute pale yellow needles which were washed with sulphuric acid, acetic acid, and ethanol (yield, 2·1 g.). After crystallisation from *m*-cresol–acetic acid the acridone had m. p. 308—309° (Found : C, 30·6; H, 1·1%).

1 : 3 : 7 : 9-*Tetrabromo*-5-*chloroacridine*.—This was prepared from the acridone as before and separated from benzene as pale yellow needles changing to yellow prisms, m. p. 254° (Found : C, 29·9; H, 0·8%). 1 : 3 : 7 : 9-Tetrabromo-5-*p*-dimethylaminophenylacridine (method 3) separated from benzene–ethanol in scarlet needles, m. p. 308—309° (Found : C, 41·4; H, 2·4%). 1 : 3 : 7 : 9-Tetrabromo-5-*p*-diethylaminophenylacridine (method 3) separated from benzene as orange-red needles, m. p. 268—269°.

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