268. *Some Halogeno-derivatives of* 2 : 3-*Benzacridine.*

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A method is described which affords 3-chloro-2-naphthoic acid from 3-hydroxy-2-naphthoic acid in good yield. 3-Chloro-2-naphthoic acid was condensed with *o*-, *p*-, and *m*-chloroaniline, and the resulting anilino-acids were cyclized to 5 : 9-, 5 : 7-, and a mixture of 5 : 6- and 5 : 8-*dichloro*-2 : 3-*benzacridine*, respectively. The 5 : 6- and 5 : 8-dichloro-isomers were identified by the fact that, when heated with phosphorus pentachloride, the latter yielded 1 : 5 : 8-*trichloro*-2 : 3-*benzacridine* (IV; R = H, R′ = Cl) which was prepared unambiguously by condensing 1-chloro-2-naphthylamine with 2 : 4-dichlorobenzoic acid and cyclizing the product with phosphorus oxychloride. The orientation of the 5 : 8- and 5 : 6-dichloro-compounds differs from the usual finding that, with such pairs of isomers obtained by the cyclization of 3′-substituted diphenylamine-2-carboxylic acid derivatives, the 5 : 6-isomer has the lower m. p. 7-*Chloro*-2 : 3-*benzacridone* is converted into 1 : 5 : 7-*trichloro*-2 : 3-*benzacridine* (V) by treatment with phosphorus oxychloride containing an excess of phosphorus pentachloride.

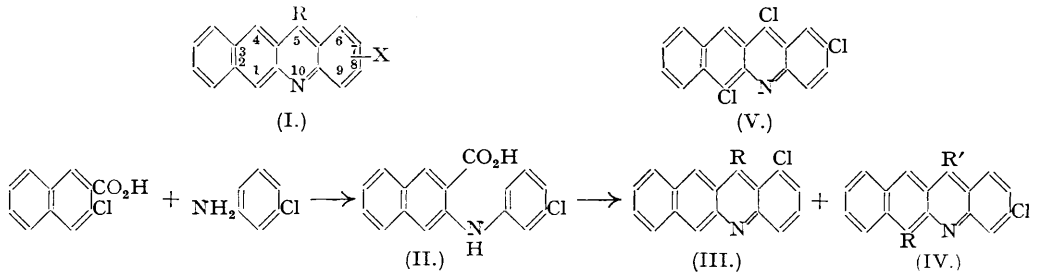
Dobson, Hutchison, and Kermack (*J.*, 1948, 123) have shown that, whereas derivatives of angular 3 : 4-benzacridine carrying a basic side chain in position 5 and a chlorine atom in position 8 of the acridine nucleus possess appreciable antimalarial activity (*Plasmodium gallinaceum* infections in chicks), the corresponding angular 1 : 2-isomer was completely inactive. Since 8-chloro-5-(dialkylaminoalkylamino)acridines are active, it is clear that a benzene ring fused at the 1 : 2-positions has a strong dystherapeutic effect, while the antimalarial activity persists when a benzene ring is fused at the 3 : 4-positions. A benzene ring at the 2 : 3-positions leads to linear as opposed to angular benzacridine derivatives, and the chemotherapeutic efficiency of this linear type is of evident interest. Bachman and Cowen (*J. Org. Chem.*, 1948, **13**, 89) have prepared 5-chloro-2 : 3-benzacridine (I; R = Cl, X = H) and its 7-methoxy-derivative by cyclizing 3-anilino- and 3-(*p*-anisidino)-2-naphthoic acid with phosphorus oxychloride. They replaced the 5-chlorine atom of these compounds by 6′-methoxy-8′-quinolylamino- and diethylaminopropylamino-side chains and state that the resulting bases are quite inactive. Certain acridine derivatives, though inactive or only slightly active when no chlorine atom (or equivalent atom or group) is present in the molecule, become highly active when a chlorine atom is introduced into position 8 of the acridine nucleus without further alteration of the molecular structure. It was therefore considered desirable to attempt the preparation of derivatives of 2 : 3-benzacridine carrying a basic side chain in position 5 and a chlorine atom in position 8 (or 6, 7, or 9). Preparation of the required intermediates, 5 : 6-, 5 : 7-, 5 : 8-, and 5 : 9-*dichloro*-2 : 3-*benzacridine*, is described in the present paper.

The general scheme followed involved the preparation of 3-(o-*chloroanilino*)-, 3-(m-*chloroanilino*)-, and 3-(p-*chloroanilino*)-2-*naphthoic acid*, and their cyclization with phosphorus oxychloride. Bachman and Cowen (*loc. cit.*) and Albert, Brown, and Duewell (*J.*, 1948, 1284) obtained 3-anilino-2-naphthoic acid in 45% and 10% yield respectively by refluxing a mixture of aniline and 3-hydroxy-2-naphthoic acid, and hydrolysing the resulting 3-anilino-2-naphthanilide with alcoholic potassium hydroxide. When this method was applied to *m*-chloroaniline, much tarring took place, and the reaction mixture set to a solid black mass from which no crystalline product could be isolated on hydrolysis. The synthesis of the required compound was therefore attempted by the Ullmann condensation of 3-chloro-2-naphthoic acid with *m*-chloroaniline.

When 3-hydroxy-2-naphthoic acid was heated with phosphorus pentachloride according to the method recommended by Hosaeus (*Ber.*, 1893, **26**, 668), much tarring took place and the product, which was very difficult to purify, yielded 3-chloro-2-naphthoic acid in only 25% yield. Strohbach's method (*Ber.*, 1901, **34**, 4160), in which 3-chloro-2-naphthoyl chloride was distilled under reduced pressure, afforded a very pure product but in very small yield owing to extensive charring. It was eventually found that a 73% yield of 3-chloro-2-naphthoic acid could be obtained by heating a mixture of phosphorus pentachloride and 3-hydroxy-2-naphthoic acid in phosphorus oxychloride as solvent, with a trace of trimethylhexadecylammonium bromide ("Cetavlon") which prevented tarring and so improved the yield considerably (cf. U.S.P. 2,394,279/1946).

3-Chloro-2-naphthoic acid was condensed with *m*-chloroaniline in amyl alcohol in the presence of anhydrous potassium carbonate and copper bronze. The yield of 3-(m-*chloroanilino*)-2-*naphthoic acid* (II) was only 12% but was increased to 72% on the addition of a trace of potassium iodide to the reaction mixture. A similar beneficial effect was found in the analogous condensations of 3-chloro-2-naphthoic acid with *o*- and *p*-chloroaniline.

3-(o-*Chloroanilino*)- and 3-(p-*chloroanilino*)-2-*naphthoic acid* were cyclized smoothly by phosphorus oxychloride, to yield 5 : 9- (I; R = Cl, X = 9-Cl) and 5 : 7-*dichloro*-2 : 3-*benzacridines* (I; R = Cl, X = 7-Cl), respectively. Cyclization of (II) may afford either 5 : 6-(III; R = Cl) or 5 : 8-*dichloro*-2 : 3-*benzacridine* (IV; R′ = Cl, R = H). A mixture of these dichlorobenzacridines was indeed obtained, the components being separated by fractional crystallisation followed by chromatography on alumina. The problem of the identification of isomers (m. p. 231—232° and 180·5°) then presented itself. In order to obtain a definite derivative of 5 : 8-*dichloro*-2 : 3-*benzacridine*, 1-bromo-2-naphthylamine was condensed with 2 : 4-dichlorobenzoic acid in the presence of anhydrous potassium carbonate, copper bronze, and a trace of potassium iodide. When amyl alcohol was used as solvent, no 4-*chloro*-2-(1-*bromo*-2-*naphthylamino*)*benzoic acid* was isolated; instead, there was obtained a considerable yield of *p*-chlorobenzoic acid, formed evidently by the removal of a chlorine atom from 2 : 4-dichlorobenzoic acid. A similar removal of chlorine from a derivative of *o*-chlorobenzoic acid during



an Ullmann condensation has been reported by Goldberg and Kelly (*J.*, 1946, 102), who isolated *p*-nitrobenzoic acid in experiments with 2-chloro-4-nitrobenzoic acid (cf. Albert and Linnell, *J.*, 1936, 1614). Bachman and Wetzel (*J. Org. Chem.*, 1946, **11**, 454), from the product of the condensation of 4-methoxy-1-naphthylamine hydrochloride with 2 : 4-dichlorobenzoic acid, isolated a product, melting range 225—242°, which was soluble in sodium hydrogen carbonate and contained chlorine but no nitrogen; this compound may have been *p*-chlorobenzoic acid (m. p. 241—243°). When, as recommended by Goldberg and Kelly, *iso*propyl alcohol was used in the present experiment, a small quantity of *p*-chlorobenzoic acid was still obtained but some of the desired naphthylaminobenzoic acid was also isolated. The yield however was poor. Bromination of 4-chloro-2-(2-naphthylamino)benzoic acid gave a monobromo-derivative identical with the small quantity of acid obtained by the Ullmann condensation; the bromine atom had thus entered the α-position of the naphthalene nucleus. On cyclization with phosphorus oxychloride the bromo-acid yielded two products—a pale pink compound, m. p. 241—242°, which proved to be the desired 5 : 8-*dichloro*-1-*bromo*-2 : 3-*benzacridine* (IV; R = Br), and a small amount of a dark red crystalline product, m. p. 264—265°, which analysed as, and was later shown to be, 1 : 5 : 8-*trichloro*-2 : 3-*benzacridine* (IV; R = R′ = Cl).

The identity of the latter compound was proved by synthesis: Ullmann condensation of 1-chloro-2-naphthylamine with 2 : 4-dichlorobenzoic acid in *iso*propyl alcohol gave small yields of 4-*chloro*-2-(1-*chloro*-2-*naphthylamino*)*benzoic acid* and *p*-chlorobenzoic acid, and the former

product was cyclized to the 1 : 5 : 8-trichloro-compound described above. The identification of this compound demonstrated that during the treatment with phosphorus oxychloride replacement of the bromine by chlorine must have occurred, this being perhaps analogous to the formation of 5-chloro-6-aminoquinoline from 5-bromo-6-aminoquinoline when the latter is heated in a sealed tube with concentrated hydrochloric acid (Kern, Diss., Freiberg, 1907, 7).

In order to utilize 5 : 8-dichloro-1-bromo-2 : 3-benzacridine for the identification of the dichloro-2 : 3-benzacridines, attempts were made to remove the bromine atom. The compound was treated with reducing agents, such as stannous chloride and concentrated hydrochloric acid, and phosphorus and hydriodic acid. The former reagent merely hydrolysed it to the corresponding 8-*chloro*-1-*bromo*-2 : 3-*benzacridone*, and the latter yielded a compound which may have been 8-chloro-1-bromo-2 : 3-benzacridine. In view of the ready removal of bromine from such compounds as 1-bromo-2-naphthylamine (in the presence of acid reducing agents) this difficulty in removing the bromine atom is somewhat surprising. Attempts to introduce bromine into the chloroacridones obtained from 5 : 6- and 5 : 8-dichlorobenzacridine, in the hope that the bromine would enter position 1, were unsuccessful. However, on treating the dichloro-compounds with a suitable proportion of phosphorus pentachloride, chlorination took place. The isomer, m. p. 180·5°, yielded 1 : 5 : 8-trichloro-2 : 3-benzacridine and so was 5 : 8-dichloro-2 : 3-benzacridine. The isomer, m. p. 131—132°, yielded no trichloro-derivative, but various crystalline compounds were isolated which gave analytical data suggesting the presence of five chlorine atoms in the molecule; it was concluded that this was the 5 : 6-dichloro-isomer.

Lehmstedt and Schrader (*Ber.*, 1937, **70**, 838) obtained mixtures of 6- and 8-substituted 5-chloroacridines by the cyclization of 3'-substituted diphenylamine-2-carboxylic acids with phosphorus oxychloride. In every case the compound with the lower melting point proved to be the 6-substituted 5-chloro-isomer and that with the higher melting point the 8-substituted 5-chloro-isomer. Similar results have been quoted by Bradbury and Linnell (*J.*, 1942, 377) and it seemed as if the principle held that the 5 : 8-isomer had always a higher melting point than the 5 : 6-isomer. However, Dauben (*J. Amer. Chem. Soc.*, 1948, **70**, 2420) on cyclizing 2-(*m*-chloroanilino)-5-methoxybenzoic acid with phosphorus oxychloride isolated a pure compound, m. p. 182°, which was evidently the 5 : 6-dichloro-isomer, as 5 : 8-dichloro-3-methoxyacridine (m. p. 162°) is a well-known compound prepared by Mauss and Mietzch during the synthesis of mepacrine. From this and the present case, it is clear that the above-mentioned generalisation is not of universal validity.

A chlorination process similar to that described for 5 : 6- and 5 : 8-dichlorobenzacridine took place when 7-chloro-2 : 3-benzacridone was treated with excess of phosphorus pentachloride in phosphorus oxychloride. The resultant dark-red trichlorobenzacridine was probably, by analogy, 1 : 5 : 7-*trichloro*-2 : 3-*benzacridine*. This was confirmed by condensing 1-chloro-2-naphthylamine with 2 : 5-dichlorobenzoic acid and cyclizing the intermediate acid with phosphorus oxychloride.

When heated with acid, the 5-chloro-2 : 3-benzacridine derivatives described above are readily converted into the corresponding acridones, the melting points of which are above 360°, except that of 9-*chloro*-2 : 3-*benzacridone* (m. p. 271—272°). These chloro-acridines and -acridones give characteristic colours with concentrated sulphuric acid (see Table); it will be

2 : 3-Benzacridine.	Colour in H_2SO_4.	2 : 3-Benzacridone.	Colour in H_2SO_4.
5 : 6-Dichloro-	Purple	6-Chloro-	Red
5 : 7- ,,	,,	7- ,,	,,
5 : 8- ,,	,,	8- ,,	,,
5 : 9- ,,	,,	9- ,,	,,
1 : 5 : 8-Trichloro-	Blue	1 : 8-Dichloro-	Purple
1 : 5 : 7- ,,	,,	8-Chloro-1-bromo-	Pale yellow
5 : 8-Dichloro-1-bromo-	Pale yellow		

observed that 5 : 8-dichloro-1-bromo-2 : 3-benzacridine and the corresponding acridone give only a yellowish colour whereas the other compounds give purple, blue, or red solutions. The bromo-derivative also differs from its chloro-analogues in that it gives no fluorescence in benzene, whereas the others give solutions with a brilliant green fluorescence.

Experimental.

3-*Chloro*-2-*naphthoic Acid.*—Dried 3-hydroxy-2-naphthoic acid (30 g.) was slowly stirred into a mixture of phosphorus pentachloride (100 g.), phosphorus oxychloride (50 c.c.), and a trace of "Cetavlon." The reaction was exothermic. The mixture was heated under reflux for 6 hours in an

oil-bath at 160—170°, the phosphorus oxychloride removed by distillation, and the dark brown oily residue poured into water. The mixture was warmed slightly on the steam-bath to hydrolyse the acid chloride, 3-chloro-2-naphthoic acid being formed as a pale yellow solid, which was filtered off, purified by extraction with aqueous ammonia and reprecipitation with hydrochloric acid, and recrystallised from aqueous alcohol as pale yellow needles, m. p. 216° (26·5 g.).

3-(o-*Chloroanilino*)-2-*naphthoic Acid.*—A mixture of 3-chloro-2-naphthoic acid (5 g.), *o*-chloroaniline (3·25 g.), anhydrous potassium carbonate (3·75 g.), copper bronze (0·15 g.), potassium iodide (0·05 g.), and amyl alcohol (40 c.c.) was heated under reflux for 6 hours in an oil-bath at 150°. The solution became very dark and on cooling deposited a small amount of solid which was filtered off, washed thoroughly with acetone, and extracted with 2N-sodium carbonate. The extract on acidification with hydrochloric acid yielded a small amount of yellow 3-hydroxy-2-naphthoic acid which on recrystallisation from aqueous alcohol melted at 220°. The amyl-alcoholic filtrate and acetone washings were steam-distilled, and the residual black oil was thoroughly extracted with hot potassium carbonate solution. On acidification of the hot extract with glacial acetic acid, a canary-yellow solid separated. This was filtered off, and the filtrate acidified with hydrochloric acid. A small quantity of pale yellow 3-chloro-2-naphthoic acid was precipitated which crystallised from aqueous alcohol as needles, m. p. 216°. The canary-yellow 3-(o-*chloroanilino*)-2-*naphthoic acid* after several crystallisations from alcohol melted at 228—230° (4·5 g.) (Found : C, 68·2; H, 4·0; N, 4·85. $C_{17}H_{12}O_2NCl$ requires C, 68·6; H, 4·05; N, 4·75%).

3-(p-*Chloroanilino*)-2-*naphthoic Acid.*—A mixture of 3-chloro-2-naphthoic acid (5 g.), *p*-chloroaniline (3·25 g.), anhydrous potassium carbonate (3·75 g.), copper bronze (0·15 g.), potassium iodide (0·05 g.), and amyl alcohol (40 c.c.) similarly gave 3-(p-*chloroanilino*)-2-*naphthoic acid* as a bright yellow solid which crystallised from benzene as needles, m. p. 245° (4·5 g.) (Found : C, 68·2; H, 4·5; N, 4·6%).

3-(m-*Chloroanilino*)-2-*naphthoic Acid.*—This *acid*, prepared as in the previous case, but from *m*-chloroaniline, was obtained as a canary-yellow solid which crystallised from alcohol as needles, m. p. 227—229° (Found : C, 67·5; H, 4·3; N, 4·4. $C_{17}H_{12}O_2NCl,\frac{1}{2}C_2H_6O$ requires C, 67·5; H, 4·7; N, 4·4%).

5 : 9-*Dichloro*-2 : 3-*benzacridine.*—A mixture of 3-(*o*-chloroanilino)-2-naphthoic acid (6 g.) and phosphorus oxychloride (60 c.c.) was heated under reflux in an oil-bath at 150° for 2 hours. The solution became dark purple, and after removal of the oxychloride, the dark purple, oily residue was poured into a mixture of ice, chloroform, and concentrated ammonia solution. The orange chloroform layer, which exhibited a green fluorescence, was washed, dried (Na_2SO_4), and freed from solvent. The orange-red solid residue, after crystallising from dry benzene, yielded 5 : 9-*dichloro*-2 : 3-*benzacridine* as rods, m. p. 203° (4 g.) (Found : C, 66·7; H, 2·8; N, 5·0. $C_{17}H_9NCl_2,\frac{1}{2}H_2O$ requires C, 66·45; H, 3·2; N, 4·6%).

9-*Chloro*-2 : 3-*benzacridone.*—5 : 9-Dichloro-2 : 3-benzacridine was heated on the steam-bath with 3N-hydrochloric acid for ½ hour. The reddish colour of the acridine changed to the orange-yellow of the acridone. The latter was filtered off, washed, and crystallised, first from alcohol and then from benzene, as yellow crystals, m. p. 271—272° (Found : C, 72·2; H, 3·6; N, 4·8. $C_{17}H_{10}ONCl$ requires C, 73·0; H, 3·6; N, 5·0%).

5 : 7-*Dichloro*-2 : 3-*benzacridine.*—3-(*p*-Chloroanilino)-2-naphthoic acid (5 g.) and phosphorus oxychloride similarly gave 5 : 7-*dichloro*-2 : 3-*benzacridine* as an orange solid which after several crystallisations from benzene melted at 227—228° (3·5 g.). When this compound was dried for 6 hours *in vacuo* at 70° over phosphoric oxide, the melting point rose to 239—240° (decomp.) (Found : C, 68·95; H, 2·9; N, 4·8. $C_{17}H_9NCl_2$ requires C, 68·45; H, 3·0; N, 4·7%).

7-*Chloro*-2 : 3-*benzacridone.*—5 : 7-Dichloro-2 : 3-benzacridine was heated on the steam-bath for ½ hour with 2N-hydrochloric acid. The resulting 7-*chloro*-2 : 3-*benzacridone* was filtered off, washed with water, and recrystallised from alcohol, in which it dissolved giving a yellow solution with a brilliant green fluorescence. It had m. p. >360° (Found : C, 70·5; H, 3·4; N, 4·3. $C_{17}H_{10}ONCl,\frac{1}{2}H_2O$ requires C, 70·7; H, 3·8; N, 4·8%).

Action of Phosphorus Pentachloride on 7-*Chloro*-2 : 3-*benzacridone.*—A mixture of 7-chloro-2 : 3-benzacridone, phosphorus oxychloride, and excess of phosphorus pentachloride was heated under reflux at 150° for 2 hours and the dark-red product worked up as described previously. 1 : 5 : 7-*Trichloro*-2 : 3-*benzacridine* was isolated as a dark red solid which crystallised from light petroleum (b. p. 60—80°) as needles m. p. 265—266° (Found : C, 61·4; H, 2·3; N, 4·2. $C_{17}H_8NCl_3$ requires C, 61·35; H, 2·4; N, 4·2%).

5-*Chloro*-2-(1-*chloro*-2-*naphthylamino*)*benzoic Acid.*—A mixture of 1-chloro-2-naphthylamine (2·5 g.), 2 : 5-dichlorobenzoic acid (2·7 g.), anhydrous potassium carbonate (2 g.), *iso*propyl alcohol (30 c.c.), copper bronze (0·1 g.), and a trace of potassium iodide was heated under reflux at 150° for 6 hours. The greenish solution was then filtered, the *iso*propyl alcohol removed by steam-distillation, and the residual oil extracted with dilute aqueous ammonia. On acidification of the extract with glacial acetic acid, a greenish-yellow precipitate was obtained, which after crystallisation from benzene yielded 5-*chloro*-2-(1-*chloro*-2-*naphthylamino*)*benzoic acid*, as yellow needles, m. p. 266—267° (1·2 g.) (Found : C, 61·35; H, 3·2. $C_{17}H_{11}O_2NCl_2$ requires C, 61·45, H, 3·3%).

1 : 5 : 7-*Trichloro*-2 : 3-*benzacridine.*—A mixture of 5-chloro-2-(1-chloro-2-naphthylamino)benzoic acid (1 g.) and phosphorus oxychloride (10 c.c.) was heated under reflux at 150° for 2 hours and the dark-red product worked up as described previously. 1 : 5 : 7-Trichloro-2 : 3-benzacridine (cf. above) crystallised from light petroleum (b. p. 60—80°) as dark red needles, m. p. 265—266° (Found : C, 61·2; H, 2·4; N, 4·2%).

5 : 6- *and* 5 : 8-*Dichloro*-2 : 3-*benzacridine.*—3-(*m*-Chloroanilino)-2-naphthoic acid (4 g.) and phosphorus oxychloride (40 c.c.) were heated under reflux at 180° for 2 hours. After removal of the excess of phosphorus oxychloride the dark-purple oily residue was poured into a mixture of ice, chloroform, and concentrated aqueous ammonia. The orange chloroform layer, which exhibited a green fluorescence, was washed with water and dried (Na_2SO_4), and the solvent removed. The reddish-orange solid (3·5 g.) which remained was fractionally crystallised from dry benzene, to give (i) light orange needles, m. p. 210—220°, (ii) deep-orange crystals, m. p. 180—200°, (iii) orange-red crystals, m. p. 150—165°, and (iv) a dark-brown amorphous mass. Fraction (i), after several crystallisations from

light petroleum (b. p. 60—80°), gave 5 : 6-*dichloro*-2 : 3-*benzacridine* as long, pale orange needles, m. p. 231—232° (decomp.) (3·5 g.) (Found : C, 68·5; H, 3·1; N, 4·8. $C_{17}H_9NCl_2$ requires C, 68·4; H, 3·0; N, 4·7%). The remaining material was dissolved in 1 : 1 benzene–light petroleum (b. p. 60—80°) and chromatographed on alumina. A light orange band passed quickly down the column and was collected as an orange solution with a green fluorescence. On reducing the volume of this solution a further quantity of 5 : 6-dichloro-2 : 3-benzacridine, m. p. 231—232° crystallised. A reddish-orange band was strongly adsorbed at the top of the column. When the light-orange band had been completely washed through, the column was extruded and extracted with hot benzene. The solvent was then removed and the resulting 5 : 8-*dichloro*-2 : 3-*benzacridine* crystallised from light petroleum (b. p. 60—80°) as reddish-orange needles, m. p. 180·5° (Found : C, 68·4; H, 3·2; N, 4·8. $C_{17}H_9NCl_2$ requires C, 68·4; H, 3·0; N, 4·7%).

6-*Chloro*-2 : 3-*benzacridone*.—5 : 6-Dichloro-2 : 3-benzacridine was heated on the steam-bath with 2N-hydrochloric acid for ½ hour. The resulting yellowish-orange 6-*chloro*-2 : 3-*benzacridone*, crystallised several times from alcohol in which it gave a bright-green fluorescence, had m. p. > 360° (Found : C, 72·5; H, 3·5. $C_{17}H_{10}ONCl$ requires C, 73·0; H, 3·6%).

8-*Chloro*-2 : 3-*benzacridone*.—5 : 8-Dichloro-2 : 3-benzacridine similarly gave 8-*chloro*-2 : 3-*benzacridone* as an orange solid which, crystallised from alcohol, had m. p. 360° (Found : N, 4·7. $C_{17}H_{10}ONCl$ requires N, 5·0%).

4-*Chloro*-2-(2-*naphthylamino*)*benzoic Acid* (Dobson, Hutchison, and Kermack, *J.*, 1948, 123).—β-Naphthylamine (5·7 g.), potassium 2 : 4-dichlorobenzoate (9·2 g.), amyl alcohol (30 c.c.), copper bronze (0·1 g.), and potassium iodide (0·05 g.) were heated under reflux at 150° for 6 hours. On cooling, the dark purple oily solid which separated was filtered off and washed thoroughly with acetone; all the purple material dissolved, leaving behind a small amount of greenish-white solid, which on purification was identified as *p*-chlorobenzoic acid, m. p. 240°. The amyl-alcoholic filtrate and the acetone washings were steam-distilled, and the black tarry residue thoroughly extracted with dilute aqueous ammonia. (Extraction of the considerable residue with dilute hydrochloric acid yielded β-naphthylamine, m. p. 112°.) The hot ammoniacal extract was acidified with acetic acid, a purplish solid being precipitated. Treated with charcoal in aqueous alcohol solution and further crystallised from benzene, this gave 4-chloro-2-(2-naphthylamino)benzoic acid as pale yellow needles, m. p. 231—232° (9·5 g.).

4-*Chloro*-2-(1-*bromo*-2-*naphthylamino*)*benzoic Acid*.—(*a*) 1-Bromo-2-naphthylamine (6·6 g.), 2 : 4-dichlorobenzoic acid (5·7 g.), anhydrous potassium carbonate (4·06 g.), copper bronze (0·1 g.), potassium iodide (0·5 g.), and *iso*propyl alcohol (50 c.c.) were heated under reflux for 6 hours at 150°. On cooling, the greenish solid was filtered off, washed with acetone and extracted with 2N-sodium carbonate, which removed *p*-chlorobenzoic acid, m. p. 241—243°. Steam-distillation of the *iso*propyl-alcoholic filtrate left a black oily residue which was thoroughly extracted with potassium carbonate. Acidification of the extract, with acetic acid, afforded a purplish solid (0·5 g.), which was recrystallised several times from aqueous alcohol and benzene and finally yielded 4-*chloro*-2-(1-*bromo*-2-*naphthylamino*)*benzoic acid* as pale yellow rectangular plates, which softened at 262° and melted at 272° (0·2 g.) (Found : C, 54·3; H, 3·0; N, 3·6. $C_{17}H_{11}O_2NClBr$ requires C, 54·2; H, 2·9; N, 3·7%).

(*b*) 4-Chloro-(2-naphthylamino)benzoic acid (10 g.) was dissolved in cold glacial acetic acid, and bromine (5·35 g.) in the same solvent was slowly stirred in. After a few minutes a pale yellow solid separated, and after ½ hour was filtered off, washed, and crystallised several times from alcohol, giving pale yellow rectangular plates which softened at 262° and melted at 272°. A mixed m. p. with the acid prepared in (*a*) was not depressed.

4-*Chloro*-2-(1-*chloro*-2-*naphthylamino*)*benzoic Acid*.—1-Chloro-2-naphthylamine (5 g.), 2 : 4-dichlorobenzoic acid (5·4 g.), anhydrous potassium carbonate (3·88 g.), copper bronze (0·1 g.), potassium iodide (0·05 g.), and *iso*propyl alcohol (50 c.c.) were heated under reflux for 6 hours at 150°. The solution became greenish-blue, and on cooling, the greenish-white solid which separated was filtered off, washed with acetone, and extracted with hot dilute aqueous ammonia, which removed *p*-chlorobenzoic acid, m. p. 241—243°. The *iso*propyl-alcoholic filtrate and acetone washings were steam-distilled. A white solid, m. p. 56°, which solidified in the condenser was identified as unchanged 1-chloro-2-naphthylamine. The black oily residue was first extracted with dilute hydrochloric acid, which removed unchanged 1-chloro-2-naphthylamine, m. p. 56°. The oily material, insoluble in dilute hydrochloric acid, was extracted with dilute aqueous ammonia. Most of it dissolved, leaving only a small amount of black oil. On acidification of the hot extract with acetic acid, a yellow solid separated. (The filtrate on addition of hydrochloric acid yielded a further quantity of *p*-chlorobenzoic acid.) The yellow solid—4-*chloro*-2-(1-*chloro*-2-*naphthylamino*)*benzoic acid*—crystallised from aqueous alcohol as rectangular tetrahedra, and from benzene as long needles, which softened at 230° and melted at 255°. After drying at 80° over phosphoric oxide for 3 hours this compound, melted from 235° to 245° (Found : C, 61·5; H, 3·25; N, 4·4. $C_{17}H_{11}O_2NCl_2$ requires C, 61·45; H, 3·3; N, 4·2%).

1 : 5 : 8-*Trichloro*-2 : 3-*benzacridine*.—4-Chloro-2-(1-chloro-2-naphthylamino)benzoic acid (1 g.) and phosphorus oxychloride (10 c.c.) were heated under reflux for 2 hours at 150°. The solution became deep red and finally purplish-brown. On removal of the excess of oxychloride, and pouring of the residue into a mixture of ice, chloroform, and concentrated aqueous ammonia, the chloroform layer became deep red and an orange-green fluorescence was observed. This layer was washed with water and dried (Na_2SO_4), and the chloroform removed. A deep-red solid was obtained which after 4 crystallisations from benzene and light petroleum (b. p. 60—80°) melted from 190° to 230°. It was dissolved in 1 : 1 benzene–light petroleum (b. p. 60—80°) and chromatographed on alumina. A deep-red band passed quickly down the column, leaving a yellow band strongly adsorbed on the alumina. The red-band was collected as a yellow-orange fluorescent solution, from which, on concentration, a deep-red solid crystallised having m. p. 257—259°. Recrystallisation from light petroleum yielded 1 : 5 : 8-*trichloro*-2 : 3-*benzacridine* as long red rods m. p. 262—263° (0·6 g.) (Found : C, 61·05; H, 2·45; N, 4·4. $C_{17}H_8NCl_3$ requires C, 61·35; H, 2·4; N, 4·2%). The yellow band which was more strongly adsorbed on the column was washed through with benzene and collected as a yellow, non-fluorescent solution. On concentration a very small quantity of an orange-pink solid crystallised which after recrystallisation

from light petroleum (b. p. 40—60°) melted at 238° (Found : C, 59·7; H, 2·3%). The analytical figures suggest that this material is an isomeric trichlorobenzacridine. It may have been formed from a trace of an isomer present in the original 1-chloro-2-naphthylamine.

1 : 8-*Dichloro*-2 : 3-*benzacridone*.—1 : 5 : 8-Trichloro-2 : 3-benzacridine was heated on the steam-bath with 2N-hydrochloric acid for ½ hour. A yellow solid was formed which dissolved in hot alcohol, giving a yellow solution with a brilliant green fluorescence. On cooling 1 : 8-*dichloro*-2 : 3-*benzacridone* separated as yellow needles which, after several recrystallisations from alcohol, melted at 349—350° (Found : C, 64·55; H, 2·6; N, 4·3. $C_{17}H_9ONCl_2$ requires C, 64·95; H, 2·85; N, 4·5%).

5 : 8-*Dichloro*-1-*bromo*-2 : 3-*benzacridine*.—4-Chloro-2-(1-bromo-2-naphthylamino)benzoic acid (2 g.) and phosphorus oxychloride (20 c.c.) were heated under reflux at 150° for 2 hours. The solution became dark-purple and, on cooling, green. Treated as recorded previously, this gave a scarlet fluorescent chloroform layer and thence a scarlet solid, which was triturated with small amounts of cold benzene. Most of the deep-red material dissolved, leaving a pale pink residue. This residue was dissolved in benzene, and the solution was heated with charcoal and reduced in volume; 5 : 8-*dichloro*-1-*bromo*-2 : 3-*benzacridine* crystallised as a pale pink solid which after several recrystallisations from benzene–ether melted at 241—242° (1·2 g.) (Found: C, 54·3; H, 1·9; N, 3·4. $C_{17}H_8NCl_2Br$ requires C, 54·1; H, 2·1; N, 3·7%). On evaporation of the dark red benzene solution, a small quantity of a dark red solid was obtained having m. p. 170—190°. This was dissolved in 1 : 1 benzene–light petroleum and chromatographed on alumina. A red band passed quickly down the column and was collected as a yellowish-orange solution with a green fluorescence; on concentration, deep-red, rod-shaped crystals separated, which after several crystallisations from light petroleum (b. p. 40—60°) melted at 264—265° (Found : N, 4·3. $C_{17}H_8NCl_3$ requires N, 4·2%). This compound did not depress the m. p. of authentic 1 : 5 : 8-trichloro-2 : 3-benzacridine m. p. 263—264°, described above.

8-*Chloro*-1-*bromo*-2 : 3-*benzacridone*.—5 : 8-Dichloro-1-bromo-2 : 3-benzacridine was heated on the steam-bath with 2N-hydrochloric acid for ½ hour. The buff-coloured solid which formed was filtered off, washed, and dissolved in hot alcohol, giving a yellow solution with only a faint green fluorescence. On cooling, 8-*chloro*-1-*bromo*-2 : 3-*benzacridone* crystallised as buff-coloured needles, m. p. > 360° (Found : C, 56·6; H, 2·6; N, 4·2; $C_{17}H_{19}ONClBr$ requires C, 56·9; H, 2·5; N, 3·9%).

8-*Chloro*-1-*bromo*-2 : 3-*benzacridine*.—8-Chloro-1-bromo-2 : 3-benzacridone (0·5 g.), red phosphorus (1 g.), and hydriodic acid (10 c.c.) were heated on the water-bath for 3 hours and then poured into water. The dark-red solid was filtered off, washed with water, and extracted with alcohol; concentration gave an orange solid which was extracted with acetone; this solution was treated with charcoal and then reduced in volume. A pale yellow solid, probably 8-*chloro*-1-*bromo*-2 : 3-*benzacridine*, separated which after several crystallisations from acetone melted at 212—213° (Found : C, 58·8; N, 2·6; $C_{17}H_9NClBr$ requires C, 59·6; N, 2·6%). This compound in contrast to the original acridone, is readily soluble in organic solvents and in dilute acids.

Action of Phosphorus Pentachloride on 5 : 8-*Dichloro*-2 : 3-*benzacridine*.—(*a*) 5 : 8-Dichloro-2 : 3-benzacridine (0·5 g.), phosphorus pentachloride (0·7 g., 2 moles), and phosphorus oxychloride (5 c.c.) were heated under reflux for 2 hours at 150°, and treated as usual. The rose-red solid residue (m. p. 240—244°) from the chloroform was dissolved in light petroleum (b. p. 60—80°) and chromatographed on alumina. A red band passed quickly through the column. Six 100-c.c. fractions—orange fluorescent solutions—were collected and reduced in volume. The first two fractions yielded deep-red, rod-shaped crystals which after several recrystallisations from the same solvent melted at 262—263° (Found : C, 60·9; H, 2·8. Calc. for $C_{17}H_8NCl_3$: C, 61·35; H, 2·4%). This compound did not depress the m. p. of authentic 1 : 5 : 8-trichloro-2 : 3-benzacridine. The next four fractions from the chromatogram also yielded red solids, lighter in colour than the 1 : 5 : 8-trichloro-compound and melting over the range 200° to 240°. No purification was effected by crystallisation.

(*b*) The experiment was repeated using three moles of phosphorus pentachloride, and the product worked up as in previous experiments. The chloroform became only faintly coloured and on removal of the solvent a pink solid was obtained, which after trituration with cold benzene and recrystallisation from light petroleum (b. p. 60—80°) was obtained as pale pink needles which melted to a deep-red liquid at 205°. This material gave analytical data suggesting its formulation as a *perchloride* of a trichlorobenzacridine (Found : C, 50·05; H, 2·0; N, 3·2. $C_{17}H_8NCl_5$ requires C, 50·55; H, 2·0; N, 3·5%).

Action of Phosphorus Pentachloride on 5 : 6-*Dichloro*-2 : 3-*benzacridine*.—Three experiments were carried out with 5 : 6-dichloro-2 : 3-benzacridine, similar to those described above, using 1, 2, and 3 moles of phosphorus pentachloride, respectively. In the first, no reaction took place, and the original dichloroacridine was recovered. With 2 moles, a pale pink solid was obtained which after several crystallisations from light petroleum yielded pale pink rectangular tetrahedra which became deep red at 175—180° and melted sharply at 183° (Found : C, 50·15; H, 2·1. $C_{17}H_8NCl_5$ requires C, 50·55; H, 2·0%). The analytical data suggest that this compound may also be a *perchloride* of a trichlorobenzacridine. With 3 moles of phosphorus pentachloride the only pure product isolated was a small amount of a dark red solid, m. p. 185°, insufficient for analysis.

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