CXXI.—*Halides of the Acridines and Naphthacridines.*

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IN the first memoir published on acridine, Graebe and Caro (1871, *Annalen*, 158, 265) describe a di-iodide of acridine hydriodide, but subsequent inquiry has not increased our knowledge of compounds formed by the addition of halogens to acridines. In the course of further work on these bases, we have observed that such addition takes place readily, giving rise to a series of well-defined crystalline substances. A preliminary account of some of these was communicated to the British Association at the Southport meeting (*Chem. News*, 1903, 88, 273). The compounds are obtained by bringing the halogen into contact with the base, either directly or in solution in an organic solvent; being sparingly soluble in these media they separate immediately, usually in the state of minute crystals, possessing characteristic colours. They are unstable in the presence of water, especially the chlorine compounds and all the compounds derived from acridine itself. The fluorescence exhibited by the acridines when in solution, which depends on the presence of the acridine fluorophore (Jourdan, *Ber.*, 1885, 18, 1447; R. E. Meyer, *Zeit. physikal. Chem.*, 1897, 24, 468), is absent except in three instances.

Chlorine, bromine, and iodine compounds were prepared of the following acridines: acridine, 5-methylacridine, hexamethylacridine,* α -naphthacridine (Senier and Goodwin), and β -naphthacridine (Reed). In most instances, the combination took place in the proportion of two atoms of halogen to one molecule of base, but compounds were also obtained containing one, three, or four atoms of the halogen.

Whether these substances are addition or substitution compounds cannot be decided from the results of elementary analysis. That they are not substitution derivatives is shown, however, by their instability,

* In a paper by Mr. Goodwin and one of us (*Trans.*, 1902, 81, 285), the position of the methyl groups in hexamethylacridine is given according to Graebe's notation as 1:2:4 and 5:6:8. It should be 1:2:4 and 5:7:8 or, according to the notation now generally adopted, 1:3:4 and 6:7:9.

by the small number of halogen atoms which they contain, and by their behaviour with water and alkalis. Instability, which is not generally a character of substitution derivatives, is seen in the fact that, in the presence of water, these compounds decompose, gradually yielding the base and free halogen. In the case of the dichlorine compound of acridine, this was particularly noticed when an attempt was made to prepare a series of salts and double salts in aqueous solutions. These, on analysis, turned out to be salts and double salts of the base itself. Further, this dichlorine compound, the most unstable of the series, was proved to lose chlorine gradually on prolonged exposure to the air. Higher derivatives, too, might be expected if substitution were supposed to take place in the benzene or naphthalene rings for in all the experiments an excess of halogen was employed. That such do not form is seen, notably in the case of the chlorine compound of β -naphthacridine, where only one chlorine atom is found in combination with one molecule of base. Moreover, hexamethylacridine combines with three halogen atoms, although there are only two hydrogen atoms in the benzene rings capable of being replaced. That substitution does not take place in the 5-position in the acridine ring is shown by the fact that on treatment with water or alkalis, acridones are not formed, but the original bases are regenerated. This was proved to be true both of the bromine compound of hexamethylacridine and of the chlorine and bromine compounds of β -naphthacridine.

The compounds now being described are therefore regarded as acridine halides or products of the direct addition of halogens to acridines. Moreover, this addition only affects the acridine ring. Were it otherwise, addition could take place only in pairs of atoms, but uneven numbers are found to combine; again, compounds containing a larger number of halogen atoms ought to be formed, for the addition of two monadic radicles to the benzene ring renders further addition easier, a fact usually explained by assuming the disruption of the supposed centric bonds.

Adopting this view, there are two possible monomolecular formulæ available for the dihalides, the acridine ring of which might be thus represented:

The first formula is of the type proposed by Bernthsen and Bender (*Ber.*, 1883, 16, 1802) for the non-fluorescent acridine dihydrides (dihydroacridines) which the dihalides much resemble. This formula is

adopted for the non-fluorescent dihalides. The second formula, with its para-linking, showing the acridine fluorophore, is suggested for those dihalides which unmistakably exhibit fluorescence. This formula belongs to the type employed by Bernthsen and Bender for such other di-addition fluorescent compounds as acridinium salts, acridine alkhalides, and acridine alkydroxides. Several attempts were made, having in view Jourdan's experiments with acridones, to prepare, in presence of catalysts, both these forms from the same base and halogen, and also to convert the one form into the other, but these experiments were not successful. The acridine ring of the one tetra- α halide obtained, a non-fluorescent tetrabromide, can only have the following monomolecular formula :

Now between acridine itself and the dihalides, as also between the dihalides and the tetra- α -halides, intermediate dimolecular compounds may be imagined, which would explain the existence of the products containing one and three atoms of halogen respectively in proportion to one molecule of base. These substances would thus become diacridine dihalides and diacridine hexa- α -halides, and the whole process of halogenation may be represented as shown on p. 1199.

The uppermost dimolecular formula conforms to the type used by Bernthsen and Bender (*Ber.*, 1883, 16, 1971) for Graebe and Caro's "insoluble hydroacridin," and by Graebe and Lagodzinski (*Annalen*, 1893, 276, 35) to explain the constitution of the dimolecular acridone biacridonyl. Recently, also, the middle type has been employed by Möhlau and Haase (*Ber.*, 1902, 35, 4164) for the compound naphth-acrihydridine, the *isonaphthacridine* discovered by Morgan (*Trans.*, 1898, 73, 536).

An interesting relation between these halides and Morgan's *isonaphthacridine* is seen in their behaviour towards acetone. By prolonged boiling with the solvent, they gradually lose their halogen, just as *isonaphthacridine*, when similarly treated, gradually loses hydrogen. When dodecamethylacridine hexabromide is boiled with acetone, it first forms the scarlet dodecamethylacridine dibromide. This scarlet dimolecular acridine dihalide, by further treatment with acetone, is converted by loss of bromine into the monomolecular base, just as, in similar circumstances, Morgan's *isonaphthacridine*, which Möhlau regards as a dimolecular naphthacridine dihydride, is converted by loss of hydrogen into the monomolecular naphthacridine.

Attempts were made to obtain additional support for these proposed formulæ by determining the molecular weights of the compounds, but their instability and the difficulty of obtaining suitable solvents rendered these unsuccessful.

The compounds described below are mostly insoluble in light petroleum, benzene, toluene, ether, or carbon disulphide, but dissolve in chloroform and glacial acetic acid; in many cases, they are decomposed by acetone. Fluorescence is only regarded as affecting constitution when unmistakably present; for a trace of water in the solvent, or a certain amount of decomposition, often produced a faint fluorescence, which, when greater care was taken, did not appear. The halogen determinations were made by Carius' method, except in the case of the

halides of acridine itself, where it was found preferable to decompose the compounds with alcoholic potassium hydroxide and determine the halogen in this solution.

Acridine Halides.

A small quantity of acridine was dissolved in dry ether, chloroform, or carbon disulphide, and a stream of dry chlorine introduced until saturation was effected. A canary-yellow precipitate gradually appeared, which soon formed a thick paste; the crystals were filtered off, well-washed with dry ether and then kept for an hour in a vacuum over potassium hydroxide. The substance may be recrystallised from glacial acetic acid, but it is very unstable, and slowly loses chlorine; it melts at 240° without decomposition. Solutions in glacial acetic acid and chloroform exhibit slight fluorescence, but this is probably due to a decomposition resulting in the separation of acridine.

0.2546 gave 0.2786 AgCl. Cl = 27.04.

$\text{C}_{13}\text{H}_9\text{NCl}_2$ requires Cl = 28.37 per cent.

A solution of acridine in chloroform was added to excess of a solution of bromine in chloroform, and the yellow precipitate which formed was separated and recrystallised from glacial acetic acid. It does not fluoresce in solution. Its melting point is $186-188^\circ$.

0.2388 gave 0.2660 AgBr. Br = 47.4.

$\text{C}_{13}\text{H}_9\text{NBr}_2$ requires Br = 47.2 per cent.

Acridine was placed in a closed apparatus over bromine and left for two days; the excess of bromine was then removed by spontaneous evaporation, and the residue was well washed with chloroform and finally with ether. No fluorescence was observed. The compound melts with decomposition at 220° .

0.3202 gave 0.4794 AgBr. Br = 63.7.

$\text{C}_{13}\text{H}_9\text{NBr}_4$ requires Br = 64.2 per cent.

A solution of acridine in chloroform was added to an excess of a solution of iodine in the same solvent, and the precipitate which formed was well washed with dry ether. The crystals, which melt at 145° , are green by reflected light, but no fluorescence could be detected.

0.2858 gave 0.3164 AgI. I = 59.8.

$\text{C}_{13}\text{H}_9\text{NI}_2$ requires I = 58.66 per cent.

5-Methylacridine Halides.

An excess of dry chlorine was passed into a solution of the base in chloroform, when a bright yellow precipitate slowly separated. As a suitable solvent could not be found, the substance was accordingly well washed with ether and dried in a vacuum over solid potassium hydroxide. It melts with decomposition at about 280° , and its solutions do not exhibit fluorescence until they are very much diluted, when traces could be detected, but this may well be due to decomposition.

0.2149 gave 0.2327 AgCl. Cl = 26.7.

$\text{C}_{14}\text{H}_{11}\text{NCl}_2$ requires Cl = 26.8 per cent.

A solution of bromine in chloroform was added in excess to a chloroform solution of the base, when red crystals slowly precipitated; these were washed with ether, separated, and shaken with carbon disulphide until no more bromine could be removed, then washed again with ether and dried in a vacuum over solid potassium hydroxide. The substance decomposes at about 261° without melting. No fluorescence was observed even in very dilute solutions.

0.2293 gave 0.2438 AgBr. Br = 45.24.

$\text{C}_{14}\text{H}_{11}\text{NBr}_2$ requires Br = 45.3 per cent.

The red crystals are nearly insoluble in chloroform, but dissolve in glacial acetic acid, from which, however, they do not crystallise unchanged. Yellow crystals instead are obtained, which were found

to contain a smaller proportion of bromine. Three specimens analysed gave respectively Br = 42.55, 42.9, 40.94 per cent.

On mixing together concentrated chloroform solutions of the base and iodine containing excess of the latter reagent, dark green needles separated, which were collected, washed with ether, and recrystallised from a little glacial acetic acid. The solution in this solvent is strongly fluorescent, being brownish-red when hot and bluish-green when cold. The substance melts between 180° and 210°.

0.184 gave 0.1906 AgI. I = 55.9.

$\text{C}_{14}\text{H}_{11}\text{NI}_2$ requires I = 56.8 per cent.

Hexamethylacridine Halides.

All the materials being carefully dried, a stream of chlorine was passed through some ether in a flask until it was saturated; another portion of ether containing hexamethylacridine, partly in solution and partly in suspension, was slowly dropped into it, the stream of chlorine being continued throughout. A red precipitate gradually separated, which was collected, well washed with ether, and dried in a vacuum.

The compound, which melts at 216°, is soluble in ethyl acetate and acetone, but the latter gradually decomposes it; its solutions show no fluorescence.

0.1595 gave 0.1348 AgCl. Cl = 20.8.

$\text{C}_{19}\text{H}_{21}\text{NCl}_2$ requires Cl = 21.23 per cent.

Dodecamethyldiacridine Hexabromide,

A small quantity of hexamethylacridine was dissolved in chloroform and added to an excess of a solution of bromine in the same solvent. A brown precipitate was obtained, which was washed with ether by decantation and then recrystallised from glacial acetic acid; it consists of brownish-yellow crystals, which show no fluorescence in solution, and melt at about 287°.

0.1581 gave 0.1798 AgBr. Br = 48.39.

$(\text{C}_{19}\text{H}_{21}\text{NBr}_3)_2$ requires Br = 47.70 per cent.

It was found difficult to remove the last traces of uncombined bromine from this compound, and unless great care was taken the bromine numbers obtained on analysis ranged from 50 to 53 per cent.

The compound is identical with that described as tribromohexamethylacridine by one of us with Mr. Goodwin (*loc. cit.*), which gave 47.33 per cent. of bromine.

When the brownish-yellow compound last described is boiled with acetone, it undergoes decomposition and becomes converted into a scarlet, crystalline compound with the loss of two-thirds of its bromine. The product is best obtained by boiling the brown compound for about 10 minutes with three successive portions of acetone. In this reaction, hexamethylacridine was found in the acetone washings, showing that part of the hexabromide had lost the whole of its halogen. The dibromide is sparingly soluble in chloroform, but in glacial acetic acid it dissolves more readily than the brown dodecamethyldiacridine hexabromide. Its solutions do not exhibit fluorescence, and it has no definite melting point.

0.1494 gave 0.0837 AgBr. Br = 23.17.

(C₁₉H₂₁NBr)₂ requires Br = 23.32 per cent.

Chloroform solutions of iodine and hexamethylacridine were mixed, the former in excess, when a precipitate was obtained consisting of brownish-red prisms, which were well washed with ether, dried for 48 hours in a vacuum over solid potassium hydroxide, and finally recrystallised from acetone. The solvent in this instance exerted no decomposing influence; the crystals, which melted at about 275°, exhibited no fluorescence.

0.2059 gave 0.2264 AgI. I = 59.4.

(C₁₉H₂₁NI₃)₂ requires I = 59.0 per cent.

α-Naphthacridine Halides.

An excess of dry chlorine was passed into a solution of α -naphthacridine in carbon disulphide, when the compound separated in small quantity as a bright yellow precipitate. It dissolves in chloroform and is very soluble in glacial acetic acid, but it was not found possible to recrystallise it. It melts indefinitely at about 158° . Its solutions exhibited no trace of fluorescence.

0.2558 gave 0.1900 AgCl. Cl = 18.33.

$C_{21}H_{13}NCl_2$ requires Cl = 20.2 per cent.

The preparation analysed was not a good one, but there can be no doubt that the compound is a dichloride that had already lost some of its chlorine.

Di-α-naphthacridine Hexabromide,

A small quantity of α -naphthacridine was dissolved in a little chloroform and added to an excess of bromine in ethereal solution. A yellow precipitate was obtained which was recrystallised from glacial acetic acid, the solutions showing no fluorescence. When heated, the compound begins to soften at about 220° and melts with decomposition at 234° . It is insoluble in chloroform and sparingly soluble in glacial acetic acid.

0.1486 gave 0.1584 AgBr. Br = 45.3.

$(C_{21}H_{13}NBr_3)_2$ requires Br = 46.2 per cent.

Di-α-naphthacridine Hexaiodide,

Considerable difficulty was experienced in bringing about combination between α -naphthacridine and iodine. The base, recrystallised from toluene, was dissolved in carbon disulphide and mixed with iodine in the same solvent, when a dark brown, almost black, precipitate was obtained, which was well washed with carbon disulphide, and dried in a vacuum over solid potassium hydroxide. The product dissolves in glacial acetic acid; the solution is not fluorescent.

0.2168 gave 0.2322 AgI. I = 57.87.

$(C_{21}H_{13}NI_3)_2$ requires I = 57.7 per cent.

β-Naphthacridine Halides.

About half a gram of Reed's β -naphthacridine was dissolved in a little chloroform and the solution dropped slowly into a saturated solution of chlorine, in chloroform, through which chlorine was passing. A bright yellow, crystalline compound was formed, which when recrystallised from glacial acetic acid, separated in pale yellow needles. The crystals, which give strongly fluorescent solutions, do not melt below 300° .

0.2578 gave 0.1113 AgCl. Cl = 10.8.

$(\text{C}_{21}\text{H}_{13}\text{NCl})_2$ requires Cl = 11.26.

Di-β-naphthacridine Hexabromide,

To an ethereal solution of bromine was added about 0.25 gram of Reed's β -naphthacridine dissolved in chloroform. A voluminous yellow precipitate appeared which was separated, well washed with ether, and dried in a vacuum over solid potassium hydroxide. Traces of fluorescence were observed in the chloroform and glacial acetic acid solutions, but these were probably due to admixture with the base. The compound had no definite melting point.

0.1310 gave 0.1450 AgBr. Br = 47.1.

$(\text{C}_{21}\text{H}_{13}\text{NBr}_3)_2$ requires Br = 46.2 per cent.

A chloroform solution of Reed's β -naphthacridine was added to a cold, nearly saturated solution of iodine in the same solvent. A dark precipitate formed which was separated, washed well with ether, and recrystallised from glacial acetic acid, when it left a small, black residue. The solution yielded dark green crystals, which melt at $270\text{--}273^\circ$ after softening at about 260° . The solution in glacial acetic acid is strongly fluorescent.

0.1375 gave 0.1184 AgI. I = 46.5.

$\text{C}_{21}\text{H}_{13}\text{NI}_2$ requires I = 47.65 per cent.

Another analysis gave I = 51.02 per cent.

1206 LAPWORTH: REACTIONS INVOLVING THE ADDITION OF

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