LIV.—*Studies in the Acridine Series. Part I.*

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THIS paper is the first instalment of a series of communications describing the results of an examination of various acridine and azine compounds, which has been undertaken with the view of elucidating the constitution of the anhydrous bases obtained from quaternary ammonium compounds in which the quinquivalent nitrogen atom is a member of a ring attached to a benzene or naphthalene residue, this nucleus containing a substituent amino- or hydroxy-group in the meta- and para-positions relatively to the basic nitrogen atom and the remaining member of the heterocyclic ring respectively. The following substances have this configuration :

To the base obtained from the former salt the two following formulæ have been assigned,

and

the latter being remarkable in that a linking is supposed to occur between the substituent groups in the meta-position, whilst the ammonium nitrogen atom is represented as remaining quinquivalent after the removal of acid.

Corresponding with these formulæ for free aposafranin, aposafranine must be formulated either as

or

The question as to whether the ortho- or the para-quinonoid formula was the more correct aroused considerable discussion some six or seven

* We have adopted the numbering given in Richter's *Lexikon*, whereas Ullmann describes the compound as 6-amino-2:7-dimethylacridine methiodide.

years ago, the para-quinonoid structure being defended by O. Fischer and E. Hepp (*Ber.*, 1895, 28, 2283, and 29, 361), and also by G. F. Jaubert (*Ber.*, 1896, 29, 414), whilst Nietzki regarded the safranine bases as being ortho-quinonoid, not merely in their salts, but also in the free state (*Ber.*, 1896, 29, 1445).

Kehrmann at first held an intermediate view, supposing that the aposafranine salts are ortho-quinonoid derivatives, whereas the para-quinonoid structure results when the acid is withdrawn (*Annalen*, 1896, 290, 257). Fischer and Hepp, who treated rosindone with phosphorus pentachloride, obtained phenylchloronaphthaphenazonium chloride and not a dichloride having the structure

(*Ber.*, 1897, 30, 1827), but they pointed out at the same time that such an agent as phosphorus pentachloride might effect intramolecular change. Shortly afterwards, Kehrmann accepted Nietzki's view that aposafranone is an internal anhydride, but at the same time he showed that phenylphenazonium salts readily give aposafranone when treated with alkali in presence of air, or aposafranine when the alkali is replaced by ammonia (*Ber.*, 1897, 30, 2620). Fischer and Hepp subsequently (*Ber.*, 1898, 31, 299) concurred with the other investigators, with the exception of Jaubert, in accepting the ortho-quinonoid formula, and since this period aposafranone and the base, aposafranine, have generally been represented as meta-anhydrides.

One of the present authors has never accepted this view because aposafranone is practically insoluble in water and gives salts which are hydrolysed with great readiness. Were aposafranone really an internal anhydride of a phenol containing a powerful quaternary ammonium hydroxide group, then it should be comparable with the hydroxyphenyltrimethylammonium hydroxides which are readily soluble and very alkaline, and moreover give stable salts with acids.*

The conversion of an aposafranine salt into an anhydro-base of para-quinonoid structure is not only possible, but indeed probable, if the hydroxyl radicle of the ammonium group is assumed to migrate to the para-nitrogen atom. The product would, however, be a substituted hydroxylamine and would immediately lose the elements of water, so that the intermediate product (formula II.) in the following scheme might not be sufficiently stable to admit of isolation.

* The examination of such hydroxides and the determination of their electrical conductivity is now being undertaken in the laboratory of the East London Technical College.—J. T. H.

If, however, the nitrogen atom of the ring were replaced by a methenyl group, the intermediate product, II., might be possible, especially since carbinol bases are produced by the action of alkalis on quaternary acridinium iodides (H. Decker, *J. pr. Chem.*, 1892, 45, 161; A. Bernthsen, *Ber.*, 1892, 25, 1746; A. Hantzsch, *Ber.*, 1899, 32, 275).

We consequently started with 3:7-dimethyl-8-acetaminoacridine (Ullmann, *Ber.*, 1903, 36, 1025), which was converted into a methiodide. By precipitating the iodide with ammonia, a carbinol base was obtained from which the acetyl group was removed by boiling with dilute sulphuric acid and reprecipitation with ammonia. The product of hydrolysis was a carbinol base, $\text{C}_{16}\text{H}_{18}\text{ON}_2$, which can only have the constitution

This base, when heated at about 200° , loses the elements of water; the resulting anhydro-base, $\text{C}_{16}\text{H}_{16}\text{N}_2$, redissolves in acids furnishing salts identical with those produced by the carbinol base, the hydrochloride, for example, being $\text{C}_{16}\text{H}_{17}\text{N}_2\text{Cl}$. It is noteworthy that the base, although containing two nitrogen atoms, is only monacidic, a property which it shares with aposafranine.

8-Amino-3:7-dimethylacridine.—This colouring matter has already been described by Ullmann (*Ber.*, 1903, 36, 1025), who obtained it by the action of *p*-toluidine on tetra-aminoditolylmethane. Our material was prepared by the method indicated by H. Terrisse and G. Darier (D.R.-P. 107,517).

The methylene derivative of *m*-tolylenediamine, obtained by the action of 40 per cent. formaldehyde solution on this diamine suspended in water, was dissolved in six parts by weight of fused *p*-toluidine, three parts of *p*-toluidine hydrochloride being then added and the mixture heated for 3 hours at 160° . The excess of *p*-toluidine was then removed in a current of steam, the residue was digested with hot water, the extract filtered after cooling, and the sparingly soluble nitrate of the base precipitated by the addition of potassium nitrate.

The base, which was liberated from this salt by ammonia, was dried and extracted with toluene. The residue usually melted above 240° , whilst the purified colouring matter, after recrystallising from alcohol, melted at 245° (compare Terrisse and Darier).

The acetylation was carried out according to Ullmann's method; but the melting point of our product was somewhat higher than that given by this investigator.

The acetylated base was heated in a sealed tube for 4 hours at 110 – 120° with five times its weight of methyl alcohol and one and a half molecular proportions of methyl iodide. The methyl-alcoholic solution was filtered and allowed to crystallise; the salt, which separated in small, very dark needles, was fairly soluble in water, the solubility being comparable with that of acridinium methiodide; it had no definite melting point.

0.1166 gave 0.0671 AgI. $I = 31.1$.

$C_{18}H_{19}ON_2I$ requires $I = 31.3$ per cent.

8-Amino-5-hydroxy-3:7:10-trimethyldihydroacridine.—A solution of the foregoing methiodide, when left in contact with dilute ammonia, did not yield a carbinol base corresponding with the acetamino-compound owing to the ease with which the acetyl group was hydrolysed. The precipitate was therefore collected, washed, and boiled for 3 or 4 hours with 25 per cent. sulphuric acid to ensure the complete hydrolysis of the acetamino-group. The filtered dark-red solution was then poured into ammonia solution, the precipitate being dried in the air and extracted with dry acetone. After the addition of benzene, the extract was allowed to evaporate slowly, when pale reddish, microscopic needles were obtained; these appeared to melt at 210° , but in all probability the apparent melting was really nothing more than the removal of the elements of water.

0.0879 gave 0.2434 CO_2 and 0.0572 H_2O . $C = 75.5$; $H = 7.3$.

0.1209 „ 11.9 c.c. nitrogen at 18.5° and 763 mm. $N = 11.3$.

$C_{16}H_{18}ON_2$ requires $C = 75.6$; $H = 7.1$; $N = 11.0$ per cent.

On keeping this substance, it darkens considerably; this change may be due either to a gradual oxidation resulting in an acridone, or possibly to the removal of the elements of water. The carbinol dissolves readily in acetone and the alcohols, is somewhat soluble in benzene, but practically insoluble in petroleum. The solutions of this substance darken very considerably on the addition of acids.

The first attempts to remove the elements of water were made by heating the dry substance in a bath of aniline vapour at 184° . The product, although much darker, did not give analytical numbers agreeing with those required for the formula $C_{16}H_{16}N_2$. We therefore

resorted to the following method, by means of which the desired result was obtained. A solution of this substance in nitrobenzene was heated for several hours just below the boiling point of the solvent. The liberation of water was rendered very evident by the crackling sound produced; eventually, the hot solution was filtered, and when cold treated with excess of light petroleum. The dark red precipitate produced was collected, washed with light petroleum, and dried.

Analysis of this substance proved conclusively that one molecule of water had been removed from the carbinol base.

0.1138 gave 0.3370 CO_2 and 0.0702 H_2O . $\text{C} = 80.8$; $\text{H} = 6.9$.

0.1062 „ 10.8 c.c. nitrogen at 15° and 769 mm. $\text{N} = 12.0$.

$\text{C}_{16}\text{H}_{16}\text{N}_2$ requires $\text{C} = 81.3$; $\text{H} = 6.8$; $\text{N} = 11.9$ per cent.

The anhydro-base did not melt below 250° , and for this reason we think that the ill-defined melting point (210°) observed in the case of the carbinol base is not really caused by fusion, but rather by the removal of the elements of water.

This anhydro-base differs markedly from the carbinol in that it is practically insoluble in acetone or benzene, although its solutions in acids are identical in colour with those of the latter base.

A solution of the carbinol base in excess of hydrochloric acid was evaporated on the water-bath, the resulting crystals being recrystallised. The intensely dark red salt thus obtained showed that the base was apparently monacidic towards hydrochloric acid.

0.1150 gave 0.0609 AgCl . $\text{Cl} = 13.1$.

0.1332 „ 0.0728 AgCl . $\text{Cl} = 13.5$.

$\text{C}_{16}\text{H}_{17}\text{N}_2\text{Cl}$ requires $\text{Cl} = 13.0$ per cent.

This salt is easily soluble in water to a dark red solution.

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