99. *The Condensation of Acridone with Tertiary Aromatic Amines and the Ultraviolet Absorption Spectra of the Products.*

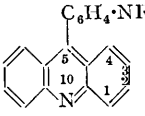
By R. M. Acheson and M. J. T. Robinson.

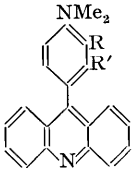
Acridone has been condensed with a number of aromatic amines, and the structures and ultraviolet absorption spectra of the products are discussed. It is suggested tentatively that the colours of 5-*p*-aminoarylacridinium ions are due to intramolecular charge-transfer phenomena.

Dimethylaniline was first condensed with acridone in the presence of phosphorus oxychloride by Ullmann,[1] who ascribed the correct structure to the product, 5-*p*-dimethylaminophenylacridine (I), proved, incidentally, by Gilman and Shirley.[2] Drozdov[3] later showed that acridone and phosphorus oxychloride may be replaced by 5-chloroacridine and aluminium chloride. This reaction has been used to prepare conveniently low-melting derivatives of acridones, but hitherto only with dimethyl- and diethyl-aniline; it has now been extended to several other substituted anilines and to naphthylamines. The general procedure used was to heat the amine with acridone and phosphorus oxychloride, or with 5-chloroacridine and aluminium chloride, in a sealed tube at 100° for between 2 hours and 2 weeks; the product was purified by chromatography.

The condensation failed with dimethyl-*p*-toluidine and dimethyl-*m*-nitroaniline, in which the *para*-position is blocked or very strongly deactivated respectively. All the other substituted anilines reacted in moderate to good yield to give products assumed to have structures (II—VIII) by analogy with the unsubstituted compound (I).

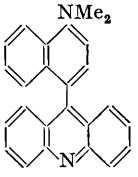
(I) : R = R′ = Me
(II) : R = R′ = CH_2Ph
(III) : R = R′ = Ph
(IV) : R = Me, R′ = NMe_2



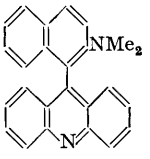


(V) : R = OMe, R′ = H
(VI) : R = H, R′ = Me
(VII) : R = H, R′ = Br
(VIII) : R = Me, R′ = H

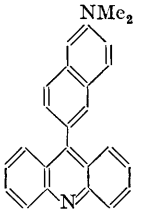
Dimethyl-α-naphthylamine gave, in addition to a good yield of a substance assumed to be 5-(4-dimethylamino-1-naphthyl)acridine (IX), a small amount of a very high-melting base which was practically insoluble in all non-acidic solvents: analyses of the hydrochloride of the latter indicated that it might be an isomer, but the quantities available were too small for further investigation.



(IX)



(X)



(XI)

	R	R′	R″	R‴
(XII) :	Br	H	H	H
(XIII) :	Br	H	Br	H
(XIV) :	Br	Br	H	Br
(XV) :	Br	Br	Br	Br

Dimethyl-β-naphthylamine and acridone gave isomeric products, (X) and (XI), when aluminium chloride and phosphorus oxychloride respectively were used. These tentative structure allocations are based on the assumption that positions 1 and 6 in the naphthylamine are the most reactive and on the absorption spectra.

In glacial acetic acid or acidified ethanol most 5-*p*-aminoarylacridines give highly coloured solutions which are considered to contain acridinium monocations (*e.g.*, XVI). This is supported by the observations that the condensation products of *N*-substituted

[1] Ullmann, *Ber.*, 1907, **40**, 4796.
[2] Gilman and Shirley, *J. Amer. Chem. Soc.*, 1950, **72**, 2181.
[3] Drozdov, *J. Gen. Chem.* (*U.S.S.R.*), 1936, **6**, 219.

acridones are similarly coloured quaternary salts,[4] that the solutions give an acridinium-ion colour and fluorescence when strongly acidified unless the basicity of the amino-group is very low (as in III), and that if the basicity of the acridine nucleus is lowered by several bromine substituents the colours are not observed since, presumably, the amino-group is then relatively more basic than the acridine nucleus. Preparation of the bromoacridines (XII—XV) has been described previously.[5]

Gleu and Schubert [4] suggested that the colour is a consequence of resonance between structures (XVI) and (XVII) as in the case of the triphenylmethane dyes. Albert and Goldacre,[6] however, found no significant difference between the basicity of acridine and its 5-*p*-dimethylaminophenyl derivative (I), and concluded that the ion (XVI) was not stabilised by " additional ionic resonance " in the ground state. This is doubtless because the planar configuration required by structure (XVII) is impossible; serious interference between carbon and hydrogen atoms begins to take place in 9-phenylanthracene when the planes of the ring systems are 57° apart.[7]

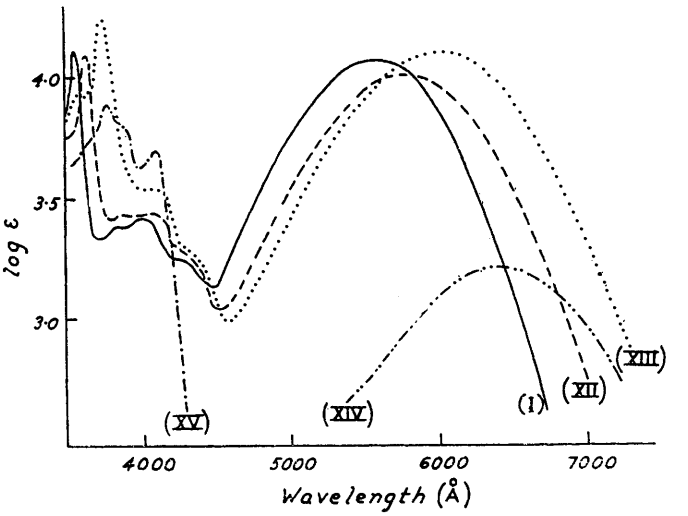
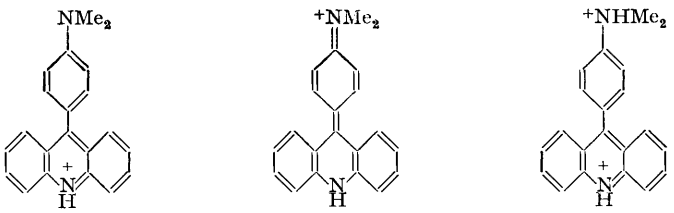


FIG. 1. 5-p-*Dialkylaminoaryl-acridine monocations.*

Albert [8] suggested that there might be resonance in an excited state, but he did not amplify this. Dr. L. E. Orgel personally has pointed out that the colour is perhaps best considered as due to a charge-transfer phenomenon,[9] an electron, initially largely localised



(XVI) (XVII) (XVIII)

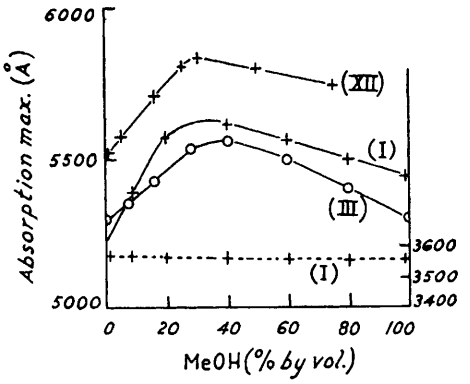
on the donor aminoaryl group, passing to the positively charged acridine ring system during light absorption. In agreement with this the ions such as (XVI) have been found to give one very broad, moderately intense band in the visible region (Fig. 1). In contrast the absorption of the dications and free bases decreases rapidly at > *ca.* 4500 Å.

[4] Gleu and Schubert, *Ber.*, 1940, **73**, 757.
[5] Acheson and Robinson, *J.*, 1953, 232.
[6] Albert and Goldacre, *J.*, 1943, 454; 1946, 706.
[7] Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127.
[8] Albert, " The Acridines," E. Arnold & Co., London, 1950, p. 133.
[9] Orgel, *Quart. Rev.*, 1954, **8**, 422.

The spectra of the acridines were measured in methanol or chloroform–methanol solutions. Sufficient mineral acid was added to develop the maximum colour as shown spectrophotometrically for the long-wavelength band for the monocations (Fig. 1, Table 2), and concentrated sulphuric acid was added until the dications were formed (Table 1). The maximum colour was observed when about three equivalents of acid had been added. It was relatively insensitive to further additions of acid, the extinction maximum only decreasing by 10% or less in the presence of 100 equivalents. At least 4% of sulphuric acid was needed to convert the compounds into their dications. Since the compounds (I—IV, XII, and XIII) give similar maximum intensities in the weakly acid solutions (Table 2), despite considerable differences in the relative basicities of the amino-group and the acridine nucleus, the formation of the monocations (cf. XVI) is probably virtually complete before the dications (cf. XVIII) are present in appreciable concentration.

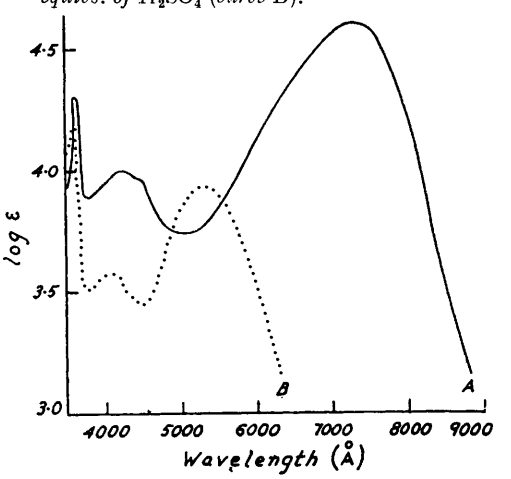
Chloroform–methanol was used for the compounds (I and XII—XV) because the last two were too sparingly soluble in methanol. The long-wavelength absorption bands of three monocations (of I, III, and XII; Fig. 2) were subject to very considerable solvent

FIG. 2. $\lambda_{max.}$ *for some acridine monocations in methanol–chloroform solutions.*



Full lines, scale on left; broken line, scale on right.

FIG. 3. 5-p-*Diphenylaminophenylacridine* (III) *in* 75% H_2SO_4 (*curve A*) *and in* MeOH + 5·3 *equivs. of* H_2SO_4 (*curve B*).



effects when passing from methanol to chloroform solutions, but the 3600 Å absorption band was only affected slightly by the solvent change in the one case examined. Since the solvent effects are considerable but similar up to 60% of chloroform in the compounds examined it is not very likely that the relative positions of the long-wave maxima of the monocations would be changed in another dissociating solvent. In a poorly dissociating solvent, for example, in methanol–chloroform rich in the latter, it is probable that ion pairs and higher aggregates are present and specific effects may be expected with individual compounds.

The absorption of the monocation of 1 : 3 : 7 : 9-tetrabromo-5-*p*-dimethylaminophenylacridine (XV) resembles that of 1 : 3 : 7 : 9-tetrabromoacridine in both neutral methanol and 3% methanolic sulphuric acid; a coloured monocation could not be detected at all. It is clear that in these compounds, in contrast to the other aminoarylacridines, the steric and the electrical effect of the bromine atoms prevent the initial formation of an acridinium ion. Under the usual conditions for the qualitative observation of these colour reactions (*i.e.*, solution in acidified ethanol or acetic acid) the tribromoacridine (XIV) gave no noticeable colour because its solubility is very low, the colour intrinsically weak, and the basicity of the nucleus low; a pale green colour is observed in formic–acetic acid.

The triphenylamine derivative (III) gave a coloured monocation in several solvents and a bathochromic shift with increase in the polarity of the solvent. In concentrated sulphuric acid the absorption and fluorescence resembled those of an acridinium ion, but the dark

bluish-green solution in 75% sulphuric acid showed a very intense band at much longer wavelengths (Fig. 3). This is probably due to some irreversible change, as dilution gave first a red and then a blue solution; the original acridine is not soluble in dilute sulphuric acid of these concentrations.

The variations in the long-wavelength absorption maxima of the monocations, with 5-*p*-dimethylaminophenylacridine (I) as a standard, are such as would be expected for charge-transfer spectra. Substituents which decrease the electron-donor character of the aminoaryl group, *i.e.*, replacement of *N*-methyl by *N*-benzyl (II) or *N*-phenyl (III) or the introduction of a bromine atom into the aryl group (VII), cause considerable hypsochromic shifts. Substituents which increase the electron-donor character of the aminoaryl group, *e.g.*, methoxyl (V), or increase the acceptor properties of the acridine nucleus, *e.g.*, bromine (XII—XIV), produce bathochromic shifts. The monocation derived from the hydrazine (IV) absorbs at shorter wavelengths than the standard (I). The small effect caused by the methyl substituent in the compound (VI) is unusual when compared with the large hypso- and batho-chromic effects of hindering methyl groups in unsymmetrical and symmetrical cyanine dyes respectively [10] and the compound may be of the intermediate classification predicted by Brooker. In agreement with this the extinction maxima of the long-wavelength band is less than that of the unhindered compound (I) as with the cyanines. The dyes studied by Brooker and his colleagues are all much more intensely coloured than the monocations of the compounds (I, II, IV—XIV), and because of the extreme steric hindrance in the latter additional ionic resonance is probably negligible in both the ground and the excited state.

The absorption of the monocation of the α-naphthylamine derivative (IX), in which a benzene ring has been fused on to the standard (I), is very weak and at short wavelengths. The dimethylamino-group cannot conjugate so effectively with the naphthalene ring as it can with the benzene ring in the analogue (I) and this appears to be more important than the usual bathochromic effect of an added benzene ring. There is also more hindrance between the two ring systems and hence a decrease in intensity. It is clear that no sharp distinction can be made between ordinary " resonance " and " charge-transfer " spectra, which are two ideal extremes, but the absorption of unhindered symmetrical cyanine dyes and of the aminoarylacridines respectively approximate closely to them.

TABLE 1. *Visible and near-ultraviolet absorption maxima of some* 5-p-*aminoarylacridines.*

	Free bases			Dications			
Compound	Solvent ‡	$\lambda_{max.}$ (Å) (log ε)		Solvent ‡	$\lambda_{max.}$ (Å) (log ε)		
I	M	3580 (4·02)	4040 (3·86)	Ms	3600 (4·20)	—	4130 (3·67)
II	M	3600 (3·90)	4100 (3·87)	Ms	3600 (4·17)	—	* 4100 (3·65)
III	—	—	—	S, 98%	3600 (4·26)	—	* 4200 (3·79)
IV	M	3600 (4·02)	3950 (3·92)	Ms	3600 (4·27)	—	* 4200 (3·83)
V	M	3600 (3·99)	3850 (3·84)	Ms	3600 (4·30)	—	* 4100 (3·82)
VI	M	3600 (3·74)	—	Ms	3600 (4·29)	—	* 4100 (3·74)
VII	M	3600 (4·05)	—	Ms	3600 (4·27)	—	* 4100 (3·68)
VIII	M	3580 (3·99)	3750 (3·89)	Ms	3590 (4·16)	—	* 4150 (3·74)
IX	M	3570 (4·11)	—	Ms	3600 (4·18)	—	* 4100 (3·76)
X	C	3600 (4·25)	4200 (3·14)	Ms	3600 (4·17)	—	* 4100 (3·66)
XI	C	3600 (4·12)	—	Ms	3600 (4·16)	* 3900 (3·65)	* 4100 (3·67)
I	C–M	3580 (3·93)	4050 (3·82)	C–Ms	3600 (4·23)	—	4020 (3·72)
XII	C–M	3650 (3·90)	4150 (3·72)	C–Ms	3530 (3·85)	3680 (4·21)	4180 (3·72)
XIII	C–M	3720 (4·15)	4380 (3·79)	C–Ms	3570 (4·08)	3810 (4·37)	4170 (3·81)
XIV	C–M	3760 (4·00)	4420 (3·74)	C–Ms	† [3700 (3·97)]	3840 (4·16)	4400 (3·53)
XV	C–M	3760 (3·90)	4580 (3·72)	S, 64%	3730 (3·75)	3900 (3·80)	4580 (3·44)

* = Broad, shallow, irregular maximum. † = Shoulder.

‡ M = methanol; C = chloroform; C–M = 1 vol. chloroform diluted to 2 vols. with methanol; S = sulphuric acid; s = solution 1·5M in sulphuric acid.

Provisional structures of the two isomers obtained from *N*-dimethyl-β-naphthylamine were deduced from the spectra of their monocations. One isomer (XI) in acidified methanol gave a very broad band of low intensity at long-wavelengths, but the other (X) absorbed at only slightly longer wavelengths than the corresponding dication (Tables 1 and 2). The

[10] Brooker, White, Sprague, Dent, and van Zant, *Chem. Rev.*, 1947, **41**, 325.

data also show that the isomer (X) is even more hindered than the α-naphthylamine derivative (IX) and must therefore have the most hindered structure. The possibility that the compound (X) was 5-(*N*-methyl-β-naphthylamino)acridine, formed by demethylation and subsequent *N*-substitution, was excluded by its stability to hot dilute sulphuric acid and by the similarity of its absorption spectra to those of the isomer (XI) in neutral and strongly acid solutions.

TABLE 2. *Visible and near-ultraviolet absorption maxima of the monocations of some 5-p-aminoarylacridines.*

Compound	Solvent ‡	10^4 Molality Solute	10^4 Molality H_2SO_4	$\lambda_{max.}$ (Å) (log ε)			
I	M	0·60	1·0	—	3550 (4·09)	* 3950 (3·37)	5440 (3·94)
II	M	0·58	1·0	—	3550 (4·14)	* 4000 (3·40)	5360 (4·05)
III	M	0·57	1·5	—	3570 (4·18)	* 4000 (3·62)	5300 (3·94)
IV	M	0·81	1·0	—	3580 (4·06)	* 4000 (3·59)	5300 (3·93)
V	M	0·73	1·0	—	3600 (4·23)	—	5610 (3·40)
VI	M	0·73	1·0	—	3600 (4·11)	* 4100 (3·61)	5450 (3·17)
VII	M	0·78	1·0	—	3600 (4·21)	* 4100 (3·61)	5210 (3·51)
VIII	M	3·30	8·0	—	¶	¶	† [4500—5500] (3·49–3·27)
IX	M	0·75	2·0	—	3600 (4·23)	* 4100 (3·74)	5000—5200 (2·70)
X	M	0·50	1·0	—	¶	* 4000 (3·67)	[5200 (2·17)] †
XI	M	3·64	5·0	—	¶	* 4000 (3·65)	6200 (2·56)
I	C–M	0·49	17·5	—	3560 (4·12)	* 4000 (3·41)	5590 (4·06)
XII	C–M	0·62	26	—	3640 (4·10)	* 4100 (3·44)	5790 (4·00)
XIII	C–M	0·56	57	3580 (3·88)	3750 (4·24)	† [4100 (3·54)]	6000 (4·10)
XIV	C–M	5·01	85	—	—	—	6410 (3·20)
XV	C–M	0·90	6000	—	3780 (4·02)	4090 (3·82)	—

* † ‡ See Table 1. ¶ Not measured.

An improved synthesis of 1 : 3 : 7-tribromo-5-chloroacridine is worthy of note. Methyl *N*-phenylanthranilate gave methyl 2′ : 4′ : 4-tribromodiphenylamine-2-carboxylate when treated with a slight excess of bromine in acetic acid. Its structure was proved by hydrolysis to the acid, which was not identical with 4 : 6 : 4′-tribromodiphenylamine-2-carboxylic acid [11] but reacted with phosphorus oxychloride to give the known 1 : 3 : 7-tribromo-5-chloroacridine.[5]

EXPERIMENTAL

Acridone.—Methyl *N*-benzoyldiphenylamine-2-carboxylate (5 g.) and 100% orthophosphoric acid (10 ml.) were heated at 200—210° for 10 min., cooled to 100°, and diluted with ethanol (20 ml.), and methyl benzoate was removed in steam. The residual acridone (88—93%) was washed with dilute alkali, water, and ethanol, and recrystallised from *m*-cresol–acetic acid.

Condensations of Acridone or 5-Chloroacridine with Tertiary Aromatic Amines.—Dimethylaniline and triphenylamine were purified commercial specimens. *NN*-Dibenzylaniline, prepared from aniline, benzyl chloride, and sodium acetate, was purified by crystallisation of the hydrochloride and the free base. *m*-Bromodimethylaniline was prepared by pyrolysis of its methiodide. All the other amines were obtained by methylating primary aromatic amines with methyl sulphate and 20% aqueous sodium hydroxide at 100°; they were purified by acetic anhydride at 140° (30 min.) and then fractionally distilled. β-Dimethylaminonaphthalene was stable to light and air for months after chromatographic purification, but otherwise became purple after a few hours. *NN*-Dimethyl-*o*-toluidine had d_4^{20} 0·929$_6$ (Ley and Pfeiffer [12] give d_4^{20} 0·9287 for *NN*-dimethyl-*o*-toluidine and d_4^{20} 0·9769 for *N*-methyl-*o*-toluidine. Acridone (0·5 g.) and phosphorus oxychloride (1·0 ml.), or 5-chloroacridine (0·5 g.) and aluminium chloride (1·0 g.), were heated with the appropriate amine (2·0 g.) in a sealed tube at 100° for between 2 hours and 2 weeks. The mixtures were worked up according to Ullmann.[1] The product, in benzene, was purified chromatographically on alumina (20 g., if the amine was volatile in steam; otherwise 50—100 g.). Properties of the *products* are reported in Table 3.

2′ : 4 : 4′-*Tribromodiphenylamine-2-carboxylic Acid.*—Bromine (1·65 ml., 3·3 mols.) in acetic acid (15 ml.) was added to methyl diphenylamine-2-carboxylate (2·27 g.; m. p. 59—60°) in

[11] Jamison and Turner, *J.*, 1937, 1954.
[12] Ley and Pfeiffer, *Ber.*, 1921, **54**, 376.

TABLE 3. *5-p-Aminoarylacridines prepared by condensing acridone with a tertiary aromatic amine in the presence of phosphorus oxychloride.*

Compound	Heating (days)	Yield (%)	Solvent [a]	M. p.	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
II	½	55	B–E	164—165° [b]	$C_{33}H_{26}N_2,C_6H_6$	88·7	6·2	88·6	6·1
III	1	50	B–E	192—193	$C_{31}H_{22}N_2,EtOH$	—	—	—	—
					$C_{31}H_{22}N_2$ [c]	88·1 [d]	5·3	88·1	5·3
IV	½	50	E	178·5—180	$C_{22}H_{21}N_3$	81·1	6·5	80·7	6·5
V	½	20	E	243·5—245	$C_{22}H_{20}ON_2$	80·3	6·0	80·4	6·1
VI	2½	65	B	235—237	$C_{22}H_{20}N_2$	84·6	6·3	84·6	6·5
VII	2½	10	B–E	255—257	$C_{21}H_{17}N_2Br$	66·8 [e]	4·7	66·9	4·5
VIII	2½	70	B–E	271—273	$C_{21}H_{18}N_2$	84·6	6·3	84·5	6·1
IX	1	80	B	261—262	$C_{25}H_{20}N_2$	86·0	5·8	86·2	5·7
X [f]	2	15	B	204—206	$C_{25}H_{20}N_2$	85·9	5·7	86·2	5·7
XI	14	75	B	309—310	$C_{25}H_{20}N_2$	85·9	5·8	86·2	5·7

[a] B = benzene; E = ethanol. [b] Partial melting and resolidification at 100—110°. [c] Dried at 140° for 1 hr.; colour changes from orange to pale yellow. [d] Loss in wt. at 100° in 4 hr.: Found, 10·2; Reqd., 9·9%. [e] Found: Br, 20·9. Reqd.: Br, 21·2%. [f] Only aluminium chloride, but not phosphorus oxychloride, and 5-chloroacridine reacted with dimethyl-β-naphthylamine to give this compound.

acetic acid (10 ml.). Needles separated after 2—3 min. and the mixture was poured into water (20 ml.). The precipitate crystallised from acetone, giving the *tribromo-ester* (3·8 g., 82%) in yellow needles, m. p. 112—113° (Found: C, 36·3; H, 2·3; Br, 52·3. $C_{14}H_{10}O_2NBr_3$ requires C, 36·2; H, 2·2; Br, 51·7%). This ester was not identical (mixed m. p. depressed) with *methyl 4 : 4′ : 6-tribromodiphenylamine-2-carboxylate* (prepared from the corresponding acid [11] with diazomethane in ether), which separated from methanol as yellow needles, m. p. 117—118° (Found: C, 35·7; H, 2·3%). Methyl 2′ : 4 : 4′-tribromodiphenylamine-2-carboxylate (1·0 g.), potassium hydroxide (0·5 g.), and methanol (10 ml.) were boiled for 2 hr. and the resulting solution was poured into N-hydrochloric acid (50 ml.). The precipitated *acid* (0·85 g.) crystallised from benzene–acetic acid (1 : 5) in yellow needles, m. p. 294—296° (Found: C, 35·0; H, 2·1. $C_{13}H_8O_2NBr_3$ requires C, 34·7; H, 1·8%). The acid was cyclised with phosphorus oxychloride, giving 1 : 3 : 7-tribromo-5-chloroacridine, m. p. and mixed m. p. 232—233°.

Some of the spectral data were obtained by Mr. F. Hastings under the supervision of Dr. F. B. Strauss.

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