106. *Absorption Spectra of Acridines. Part I. Some Aminoacridines.*

By D. P. Craig and L. N. Short.

The outstanding antiseptic properties of certain acridines have stimulated efforts to relate their physical properties to their biological action. Albert and his collaborators have synthesised many such compounds and have examined particularly the mono- and di-aminoacridines, which are the most active antiseptic agents. In the hope that further light might be shed on the structure of these compounds, their absorption spectra have been examined in the visible and the ultra-violet region. The results confirm the observation that the *ring* nitrogen atom is the most basic nitrogen in the compounds examined and suggest that imine forms are not present in significant amount under the conditions studied.

Previous spectrographic work in the acridine series by Charlampowiczowna and Marchlewski (*Bull. Acad. Polonaise*, 1930, *A*, 376), Radulescu and Ostrogovitch (*Ber.*, 1931, **64**, 2233), Dima and Pogangeanu (*Bull. Sect. Sci. Acad. Roumanie*, 1938, **21**, 38), and others has shown that the absorption of acridine in the ultra-

Ultra-violet absorption of acridines in dioxan.

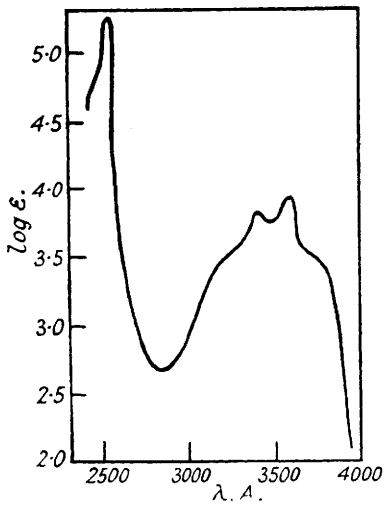


Fig. 1.—*Acridine.*

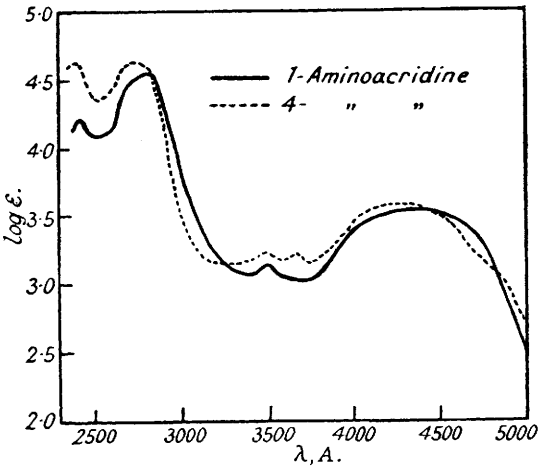


Fig. 2.—1-*Aminoacridine* (*full line*). 4-*Aminoacridine* (*broken line*).

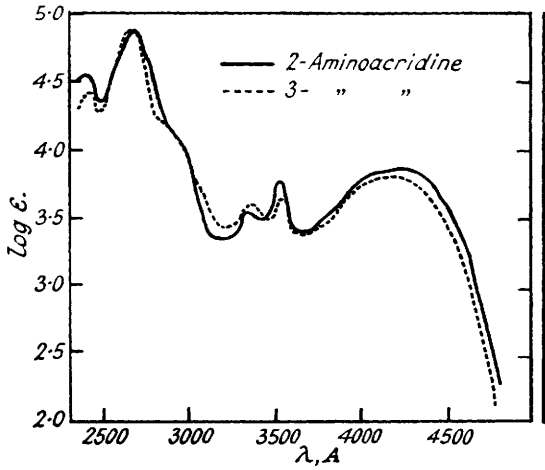


Fig. 3.—2-*Aminoacridine* (*full line*). 3-*Aminoacridine* (*broken line*).

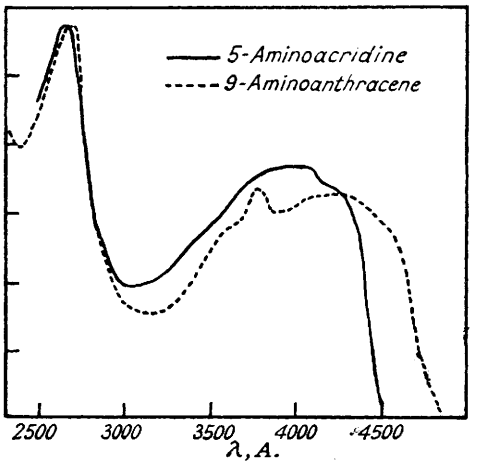


Fig. 4.—5-*Aminoacridine* (*full line*). 9-*Aminoanthracene* (*broken line*).

violet is almost exactly the same as that of anthracene and phenazine, indicating that the behaviour of nitrogen in the resonating ring system is spectrographically similar to that of ⁻CH⁼. It will be seen that the same feature is evident in the very similar spectra of 5-aminoacridine and 9-aminoanthracene, in which the amino-groups are similarly situated (see Fig. 4).

Previous studies have shown that the ultra-violet absorption spectra of benzene, naphthalene, and anthracene are very similar to those of pyridine, quinoline, and acridine, respectively. It is to be expected, there-

fore, that the effect of introducing an amino-group into the acridine nucleus will depend on the position of this group with regard to the 5- and the 10-position in the nucleus; *e.g.*, a 1-amino-group bears the same relation to the 10-position as a 4-amino-group does to the 5-position, so 1- and 4-aminoacridine should be spectrographically equivalent. A similar argument requires equivalence between 2- and 3-aminoacridines. Figs. 2 and 3 show that the absorption spectra have the expected identity in the spectral region examined.

The spectrum of 5-aminoacridine shows marked differences from those of its isomerides. However, it is practically identical with that of 9-aminoanthracene, a fact in keeping with the similar spectrographic behaviour of $-CH=$ and $-N=$ in a resonating system.

A problem of great interest was to determine whether the ring nitrogen or the amino-nitrogen atom accepted the first proton during salt formation, and the curves (Figs. 5—7) of the visible range show the important spectral changes which occur in the monosubstituted compounds as they are converted into the mono- and di-acid bases.

*Visible absorption spectra of monoaminoacridines.**

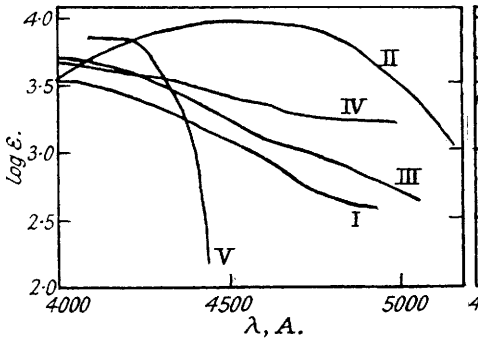


FIG. 5.—*At pH* 11.

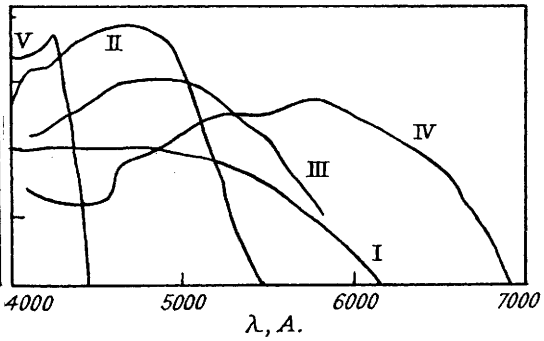


FIG. 6.—*At pH* 3.

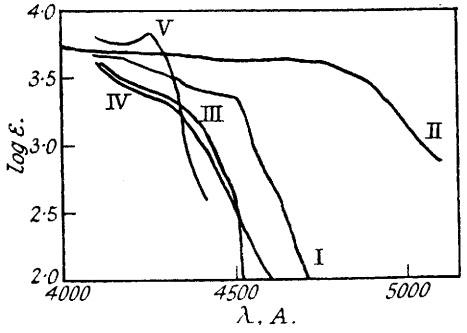


FIG. 7.

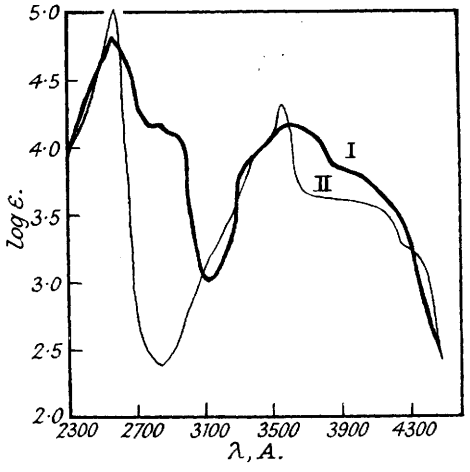


FIG. 8.

FIG. 7.—*In* 5N-*hydrochloric acid.*
FIG. 8.—I = *Monobasic ion of* 2 : 5-*diaminoacridine in water.* II = *Acridinium ion in* 5N-*hydrochloric acid.*

Electrometric studies (Albert and Goldacre, J., 1943, 454) show that at pH 3 the isomerides exist as monobasic ions. The spectra in Fig. 6 show that the visible absorption band of all except 5-aminoacridine has moved toward longer wave-lengths as compared with the undissociated bases shown in Fig. 5. Now the conversion of $-NH_2$ into $-NH_3^{\oplus}$ removes the possibility of interaction between the nitrogen atom and the ring structure, so if the first proton had gone to this nitrogen we should have expected a reversion to the acridine spectrum. No such reversion is to be seen in the monobasic ions, and it is concluded that the ring nitrogen accepts the first proton and is therefore the more basic. However, at a lower pH value those isomerides (*i.e.*, all except the 5-isomeride) which form dihydrochlorides must undergo the $-NH_2$ to $-NH_3^{\oplus}$ change and should revert to the acridinium ion spectrum. This is shown in Fig. 7, in which there is seen to be a marked shift of the absorption maxima toward shorter wave-lengths.

The spectrum of 5-aminoacridine stands apart from those of the other isomerides. There is practically no change throughout the range of attainable pH values, and there is certainly no suggestion of a reversion

* In Figs. 5, 6, and 7, curves I, II, III, IV, and V relate respectively to 1-, 2-, 3-, 4-, and 5-aminoacridine.

to the acridinium ion spectrum. It seems clear that at no time is the amino-group in this compound converted into $^{-}NH_3^{\oplus}$, a conclusion reached also from electrometric studies (Albert and Goldacre, *loc. cit.*). The spectrum of 2-aminoacridine shows clearly that in 5N-hydrochloric acid there is partial formation of a dihydrochloride. The curve for the 2-compound in Fig. 7 is that appropriate to a mixture of the monobasic ion (Fig. 6) and the acridinium ion to which the dihydrochloride would tend.

Chemical evidence (Albert and Ritchie, J., 1943, 458) suggests that the imino-form of 5-aminoacridine may play a part in certain reactions of that compound. The spectrographic evidence is inconclusive on the point, but it is noteworthy that the strong similarity between the absorptions of 5-aminoacridine and of 9-amino-

FIG. 9.

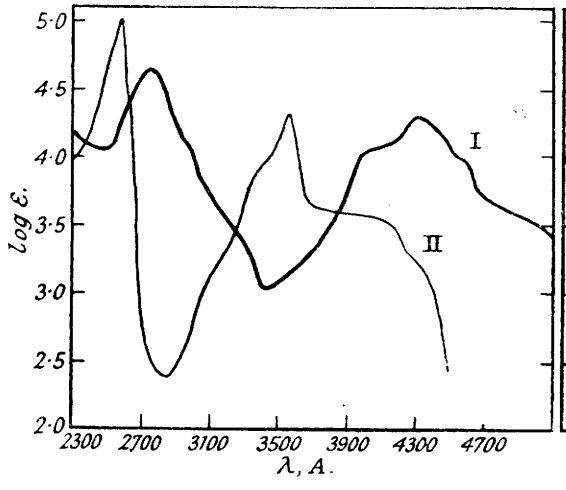
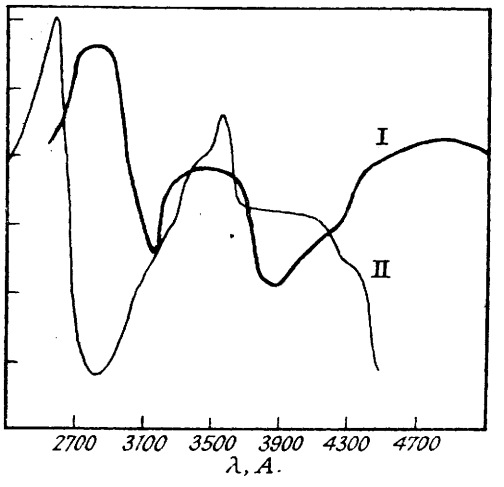


FIG. 10.



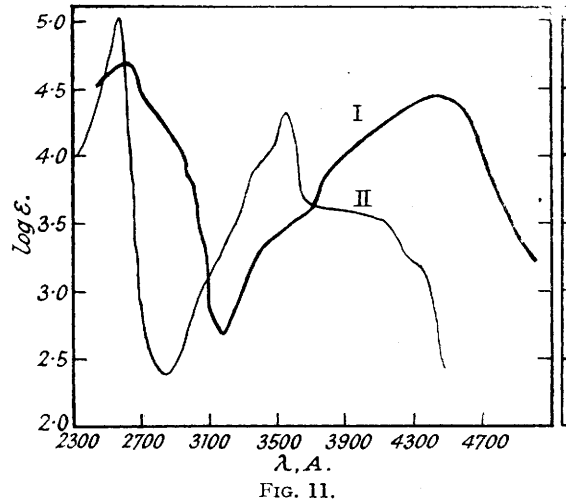


FIG. 11.

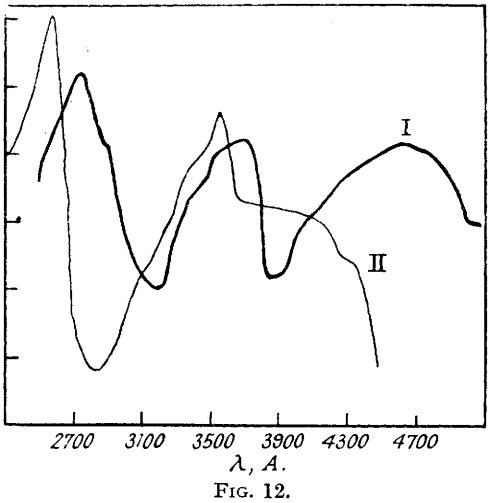


FIG. 12.

FIG. 9.—I = *Monobasic ion of* 2 : 6-*diaminoacridine in water.* II = *Acridinium ion in* 5N-*hydrochloric acid.*
FIG. 10.—I = *Monobasic ion of* 2 : 7-*diaminoacridine in water.* II = *Acridinium ion in* 5N-*hydrochloric acid.*
FIG. 11.—I = *Monobasic ion of* 2 : 8-*diaminoacridine in water.* II = *Acridinium ion in* 5N-*hydrochloric acid.*
FIG. 12.—I = 2-*Amino*-10-*methylacridinium ion in water.* II = *Acridinium ion in* 5N-*hydrochloric acid.*

anthracene suggests that the imine form plays an insignificant part under the conditions of the comparison. The possibility that 9-aminoanthracene is itself more correctly formulated as the imine of anthrone cannot, however, be entirely ruled out.

It was thought that 2-aminoacridine also might exist in the imine form, but this seems unlikely in view of the spectral evidence (Fig. 3) that its absorption is almost identical with that of the 3-isomeride, which cannot be formulated analogously.

The effect of adding a second amino-group to the 2-aminoacridinium ion is seen in Figs. 8—11; for purpose of comparison the absorption of 2-amino-10-methylacridinium chloride is shown in Fig. 12.

Experimental.—The ultra-violet absorption spectra were determined by means of a Hilger spectrograph and a Hilger rotating sector spectrophotometer. The light source was a condensed iron spark. The visible spectra were examined by using a Hilger–Nutting absorption spectrophotometer with a " Pointolite " light source.

The selection of dioxan as solvent for the spectra of free bases in neutral solution was suggested by the requirements of ultra-violet transparency, low dielectric constant, and non-hydroxylic nature. The dioxan was rendered acid-free immediately before use.

The visible spectra were obtained from aqueous solutions buffered to the required pH values as follows : pH 3. Potassium hydrogen phthalate and hydrochloric acid in 67% methyl alcohol—read pH 3 against glass electrode (uncorrected for effect of alcohol). pH 11. Alkaline phosphate buffer in 30% methyl alcohol.

The characteristics of the absorption spectra are shown in the table.

Substance.	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$	$\lambda_{max.}$, A.	log $\varepsilon_{max.}$	Inflexion at
Acridine	2520	5·24	3470	3·90	—	—	—
1-Aminoacridine	2790	4·55	3600	3·15	4340	3·55	—
2-Aminoacridine	2680	4·80	3450	3·60	4180	3·85	—
3-Aminoacridine	2670	4·90	3450	3·60	4140	3·82	—
4-Aminoacridine	2740	4·60	3600	3·25	4290	3·60	—
5-Aminoacridine	2660	4·88	3900	3·85	—	—	—
9-Aminoanthracene	2690	4·88	4050	3·55	—	—	—
2 : 5-Diaminoacridine ion	2550	4·80	3600	4·15	—	—	2850, 4100 A.
2 : 6-Diaminoacridine ion	2750	4·62	—	—	4300	4·30	4000 A.
2 : 7-Diaminoacridine ion	2850	4·80	3450	3·90	4850	4·12	—
2 : 8-Diaminoacridine ion	2600	4·70	—	—	4450	4·45	3500 A.
2-Aminoacridine *N*-methobromide	2760	4·60	3700	4·12	4650	4·10	—

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