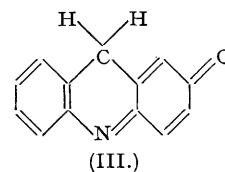
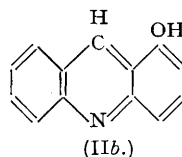
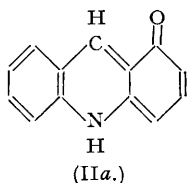
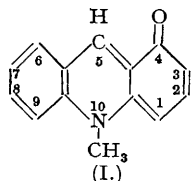


197. Absorption Spectra of Acridines. Part III. The Hydroxyacridines.

By ADRIEN ALBERT and L. N. SHORT.

The absorption spectra of the five isomeric monohydroxyacridines have been determined, and the tautomeric character of certain of these isomerides demonstrated. Comparison is made with the spectra of acridine and the five monoaminoacridines (Part I, Craig and Short, this vol., p. 419; Part II, Turnbull, *ibid.*, p. 441).

4-HYDROXYACRIDINE, when first prepared by Albert and Ritchie (J., 1943, 461), was a yellow substance giving yellow, green, and blue solutions in benzene, 90% and 20% aqueous alcohol, respectively, and it was suggested that the blue substance was a tautomer corresponding to the blue 10-methylacrid-4-one (I; Nitzsche, *Angew. Chem.*, 1939, 52, 517). This implies an amido-amidol prototropy involving the oxygen and nitrogen atoms as in (II, *a* and *b*), the equilibrium changing with the composition of the solvent. Similar tautomeric pairs can be written for the 2- and the 5-isomeride although these show little visible change in colour with changes of solvents.



Accordingly it was decided to investigate the ultra-violet and visible absorption spectra of the five hydroxyacridines, using as solvents absolute alcohol, 67% and 33% aqueous alcohols, and where solubility permitted, 20% aqueous alcohol (all v./v.). From knowledge of the dissociation constants of the isomerides (Albert and Goldacre, J., 1943, 454) it was plain that their spectra would not be distorted by anionic or kationic species in these solvents.

Inspection of the results (Figs. 1—5) shows that no significant alteration has taken place in the spectra of

FIG. 1.

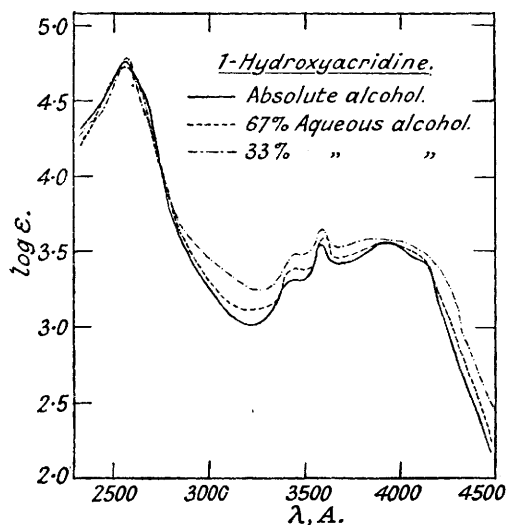


FIG. 2.

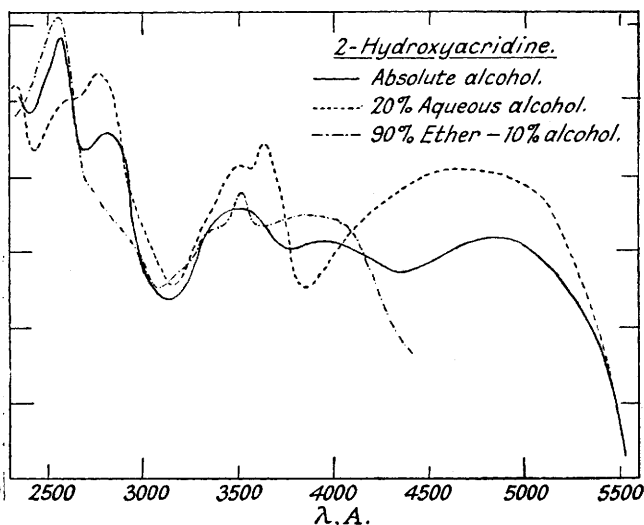


FIG. 3.

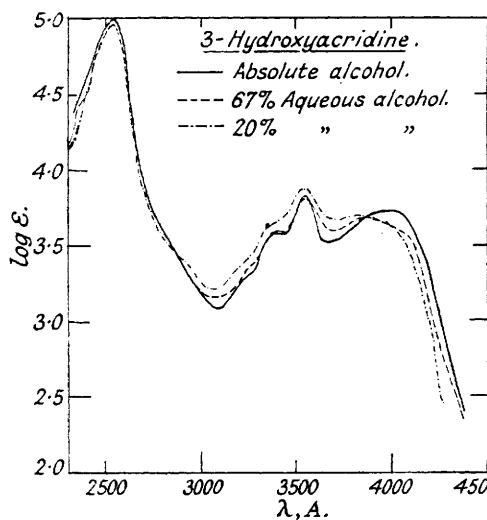


FIG. 5.

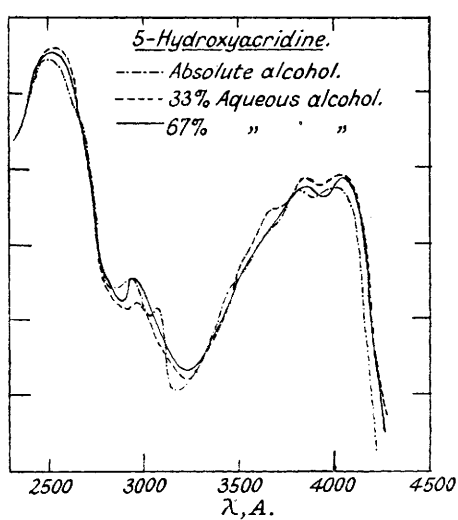
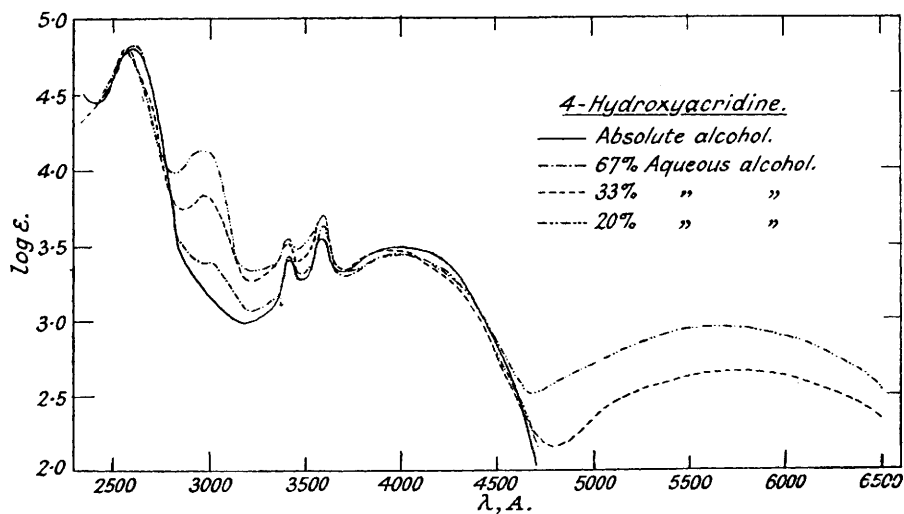


FIG. 4.



1- and 3-hydroxyacridine and this is in agreement with the fact that no tautomeric pairs of the type (II, *a* and *b*) can be written for these compounds. It is true that prototropy involving the 5-carbon atom is conceivable for these two isomerides and would involve keto-forms of the type (III). The latter class of compound, stabilised in the keto-form by substituting both hydrogens in the 5-position with alkyl groups, has been investigated by Kehrmann, Goldstein, and their collaborators (*Helv. Chim. Acta*, 1926, 9, 222; 1928, 11, 245, 478) and its members do not resemble 1- or 3-hydroxyacridine spectrographically or otherwise. These two isomerides are therefore assigned the orthodox formulæ for hydroxyacridines, as (II *b*).

4-Hydroxyacridine shows in dilute alcohol a marked shift in the ultra-violet in addition to the remarkable shift in the visible which suggested the present investigation. The spectrum obtained in absolute alcohol must be that of the pure enol because it so closely resembles the spectrum of 1-hydroxyacridine which is enolic (see Fig. 6). The altered spectrum obtained in 20% aqueous alcohol is accordingly due to the presence of the keto-form, the characteristic blue colour of which resembles the non-enolising ketone (I). This response to change in solvent is in agreement with experience that a rise in dielectric constant (in the present case from 24 in absolute alcohol to 67 in 20% alcohol) stabilises the ketonic form because the latter is more polar than the enolic form (Branch and Calvin, "The Theory of Organic Chemistry," New York, 1941, p. 296). In passing, it may be noted that the cation and anion of 4-hydroxyacridine are orange and red, respectively.

FIG. 6.

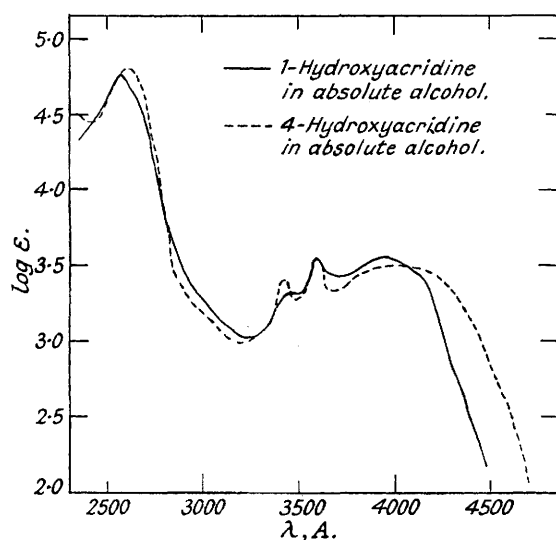
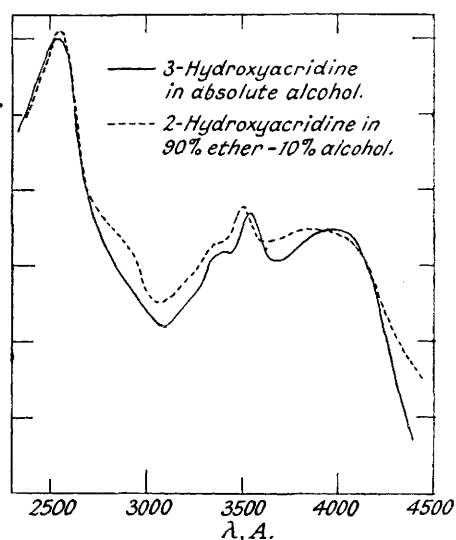


FIG. 7.



2-Hydroxyacridine gave what seemed to be a mixed spectrum in absolute alcohol, suggesting that its ketonic form is relatively more stable than that of the 4-isomeride. It was decided to reduce both the dielectric constant and the hydrogen-bonding properties of the solvent by the addition of as much ether as possible. In a 9 : 1 (v./v.) ether-alcohol mixture (dielectric constant = 6), a spectrum was obtained that must be that of the pure enol because of its close resemblance to that of 3-hydroxyacridine, which is always enolic (see Fig. 7). The radically different spectrum of 2-hydroxyacridine in 20% aqueous alcohol suggests that the latter solvent has shifted the equilibrium until the ketonic form is almost the only form present.

5-Hydroxyacridine ("acridone") showed no change comparable to those observed in the 2- and the 4-isomeride. In absolute alcohol a new band was developed at 3080 Å., the significance of which is not clear at present. The poor solubility of this substance in other solvents prevents a more searching investigation. None of its spectra corresponds to the other hydroxyacridines, and it is recalled that among the aminoacridines the 5-isomeride was also outstanding in this respect (Turnbull, *loc. cit.*). A preliminary investigation of the spectrum of anthrone and anthranol suggests that, in the solvents used in this study, 5-hydroxyacridine exists in the enolic rather than in the ketonic form. Nevertheless, 5-hydroxyacridine differs sharply from its isomerides in having a depressed acidic function; *e.g.*, it will not dissolve in *n*/10-sodium hydroxide (Albert and Goldacre, *loc. cit.*).

In conclusion it should be noted that the spectra of the enolic forms of 1-, 2-, 3-, and 4-hydroxyacridine closely resemble the spectra of the un-ionised molecules of the corresponding aminoacridines in aqueous methanol at pH 11 (Turnbull, *loc. cit.*), thus adding weight to the conclusion of Craig and Short (*loc. cit.*) that none of these un-ionised aminoacridines (which they examined in neutral dioxan) is to be represented as an imine.

Details of the chief bands of the hydroxyacridines are set out in the table, together with the corresponding values for acridine taken from Craig and Short (*loc. cit.*).

Summary of the chief bands of acridine and the hydroxyacridines (in A.).

Acridine.	Solvent.*	I.		II.		III.		IV.		V.		VI.	
		λ max.	log ϵ .	λ max.	log ϵ .	λ max.	log ϵ .	λ max.	log ϵ .	λ max.	log ϵ .	λ max.	log ϵ .
Unsubst.	A	2520	5.2	—	—	3390	3.8	3590	4.0	—	—	—	—
1-Hydroxy-	B	2570	4.75	—	—	3460	3.3	3600	3.55	3920	3.55	—	—
	C	2570	4.75	—	—	3460	3.4	3600	3.6	3920	3.55	—	—
	D	2570	4.75	—	—	3460	3.5	3600	3.65	3900	3.60	—	—
2-Hydroxy-	E	2550	5.05	—	—	3400	3.7	3510	3.9	3910	3.75	—	—
	B	2560	4.9	2820	4.3	3400	3.7	3500	3.6	3940	3.6	4630	3.6
	F	2600	4.4	2760	4.7	3400	3.8	3510	4.1	3630	4.2	4660	4.0
3-Hydroxy-	B	2540	5.0	—	—	3400	3.6	3540	3.85	3960	3.7	—	—
	C	2540	5.0	—	—	3400	3.6	3540	3.85	3860	3.7	—	—
	F	2540	5.0	—	—	3400	3.65	3540	3.9	3840	3.7	—	—
	B	2600	4.8	—	—	3410	3.4	3580	3.55	4000	3.5	—	—
4-Hydroxy-	C	2600	4.8	3000	3.4	3410	3.4	3580	3.65	4000	3.45	5700	2.6
	F	2580	4.8	2960	4.1	3410	3.5	3600	3.7	3980	3.45	5700	3.0
5-Hydroxy-	B	2510	4.7	2950	3.3	3080	3.1	3820	3.85	4020	3.85	—	—
	C	2530	4.8	2950	3.3	—	—	3860	3.9	4050	3.9	—	—
	D	2540	4.8	2960	3.1	—	—	3850	3.95	4040	3.95	—	—

* A = Dioxan; B = absolute alcohol; C = 67% aqueous alcohol; D = 33% aqueous alcohol; E = 90% ether-10% alcohol; F = 20% aqueous alcohol.

EXPERIMENTAL.

The ultra-violet absorption spectra were determined by means of a Hilger spectrograph fitted with a Hilger rotating sector spectrophotometer. The light source was a condensed iron spark. The long-wave portion of the spectrum of 4-hydroxyacridine was visually examined with a Hilger-Nutting absorption spectrophotometer using a "Pointolite" light source.

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