233. *Tautomerism in the Solid State. Part II.**

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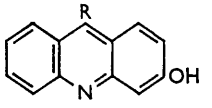
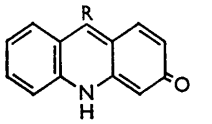
The colour changes undergone by 3-hydroxy-9-phenylacridine have been examined and are held to be related to lactim–lactam tautomerism.

KEHRMANN and MATUZINSKY [1] obtained 3-hydroxy-9-phenylacridine as yellow needles, m. p. 264°, which were converted instantaneously by pressing or rubbing into a red powder, m. p. 135°, and the authors suggested that this is the result of tautomeric change from the lactim (I; R = Ph) to the lactam form (II; R = Ph). It was reported that the compound crystallised from cold benzene in red crystals and from hot benzene in the yellow

(I)   (II)

form, and that the yellow form on storage became red and could be obtained by heating the red form above 135°. It was concluded that the red form is stable at room temperature and the yellow above 135°.

We have investigated these changes and our observations and conclusions differ materially from those of Kehrmann and Matuzinsky, although we confirm their suggestion that mild compression or friction can induce tautomeric changes in the solid state.

Comparison of the spectrum of 3-hydroxy-9-phenylacridine in various solvents with the spectra of the *O*- and the *N*-methyl ether shows that the compound exists in solution as a tautomeric equilibrium between the yellow lactim and the red lactam (I and II; R = Ph). The spectrum of the hydroxy-compound in contrast to those of the ethers varies considerably with change of solvent. In cyclohexane the compound exists as the lactim form with an ultraviolet spectrum similar to that of its *O*-methyl ether (Fig. 1), and in 20% aqueous ethanol as the lactam with a spectrum resembling that of the *N*-methyl ether (Fig. 2). In absolute ethanol the maxima of both forms are clearly visible (Fig. 3). These observations are similar to those made on 3-hydroxyacridine [2] (I and II; R = H) and certain hydroxyphenazines such as 2-hydroxy-1,3,4-trimethylphenazine.[3] Grinding these substances, however, effects no colour change. Incidentally, since the spectra of 3-hydroxy- and 3-hydroxy-9-phenyl-acridine are similar, the phenyl group in the latter cannot be coplanar with the acridine ring.[4]

At a fairly high temperature and under reduced pressure 3-hydroxy-9-phenylacridine sublimes and a fine-grained red film on a cooled silica plate was thus obtained. Heating the plate for one minute at 140° produced a corresponding film of the yellow form and, provided the change was sufficiently rapid, the grain size was still below the limits of a low-powered microscope. From these films qualitative spectra were obtained in which absorption maxima can be distinguished clearly. The curves obtained from the red film are shown in Fig. 4, curve (A) being obtained before and curve (B) after heating at 140°. The following points may be noted. The transition from the red to the yellow form is accompanied by the disappearance of the long-wave lactam absorption band and an inflexion at 290 mμ also in the position of a band characteristic of the lactam form. Both solid forms show a maximum between 358 and 360 mμ along with an inflexion or smaller maximum at 345 mμ, but this conveys little information since a feature of this type is observed both in lactim and lactam absorptions (Fig. 1 and 2). In both curves there is

* Part I, *J.*, 1961, 182.

[1] Kehrmann and Matuzinsky, *Ber.*, 1912, **45**, 3498; *Annalen*, 1917, **414**, 182.
[2] Albert and Short, *J.*, 1945, 760.
[3] John, *Z. angew. Chem.*, 1947, **59**, 188.
[4] Braude, Fawcett, and Webb, *J.*, 1954, 1049.

a maximum at 410 mμ, the intensity of which increases when the red form is changed to the yellow. This is indicative of the lactim form since the *O*-methyl ether absorbs in the 380—400 mμ region whereas the *N*-methyl ether has an absorption minimum in this region. It may be concluded from these results that the yellow form of 3-hydroxy-9-phenylacridine exists mainly or entirely in the lactim form, and the red form contains both the lactim and the lactam form. These conclusions are emphasised by the absorption curve

Ultraviolet absorption spectra.

FIG. 1. (A) *3-Hydroxy-9-phenylacridine (qualitative), and* (B) *O-methyl ether; in cyclohexane.*

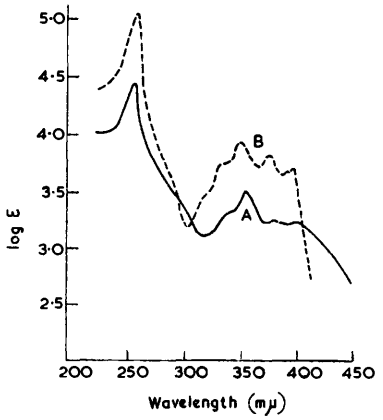


FIG. 2. (A) *3-Hydroxy-9-phenylacridine in 20% ethanol;* (B) *N-methyl derivative in n-hexane.*

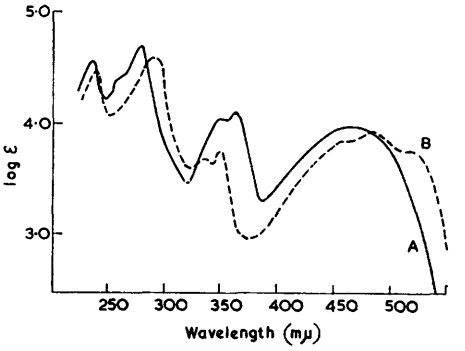


FIG. 3. (A) *3-Hydroxy-9-phenylacridine in absolute ethanol;* (B) *solid red form (qualitative).*

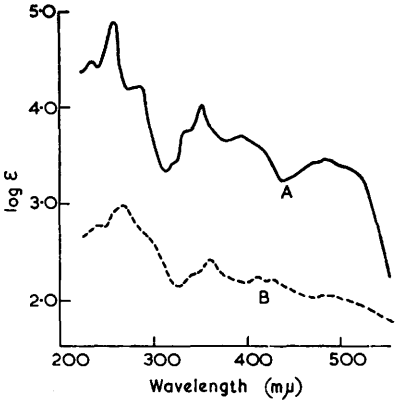
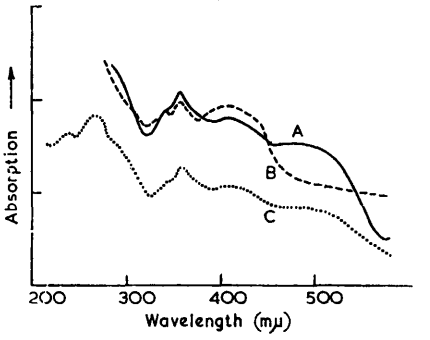


FIG. 4. *Qualitative spectra:* (A) *red film;* (B) *yellow film;* (C) *red film thinner.*



obtained from a thinner film of the red form (C) (Fig. 4) which shows a strong absorption at 268 mμ corresponding to lactim absorption at 260 mμ, and another at 240 mμ comparable to that of the lactam absorption of the *N*-methyl compound at 240 mμ in cyclohexane and 238 mμ in absolute ethanol. Also in harmony with our conclusions is the similarity of the spectrum of the red film and the spectrum of the hydroxyphenylacridine in absolute ethanol (Fig. 3).

It might be objected that the red sublimate is not the same substance as that obtained by grinding the yellow hydroxyphenylacridine. That the two are the same was shown by grinding the compound on to silica plates and examining the spectrum. The particle size in these films was much greater and the resultant scattering produced a pronounced levelling out of the spectrum. Nevertheless the " mixed " nature of the spectrum was

shown by its similarity to that of the sublimed red film. It therefore seems clear that the colour change which occurs when the yellow crystals of 3-hydroxy-9-phenylacridine are pressed or rubbed is due to tautomerism; that the mobile hydrogen atom is attached to the oxygen atom in the yellow solid; and that in the red solid a substantial proportion of the hydrogen atoms are attached to the nitrogen.

Further insight into the colour change was obtained from *X*-ray powder photographs which showed that the yellow form is crystalline and the red form is almost amorphous. Only one faint line could be seen in the photograph of the red form and this corresponded to a particularly intense line in the photograph of the yellow form. There can be little doubt therefore that grinding the yellow crystals of 2-hydroxy-5-phenylacridine results in tautomerisation and lattice disintegration.

The amorphous nature of the red compound implies that the red form should be metastable at all temperatures below the melting point of the compound and this is contrary to Kehrmann's view that the red substance is the pure lactam and is stable at room temperature. This discrepancy has to some extent been overcome by a re-investigation of Kehrmann's observations. We were unable to obtain any evidence that the yellow form becomes red when kept *in the dark*, nor were we able to obtain clean-cut red crystals from cold benzene solutions. We found, however, that the yellow form slowly becomes orange when kept *in light* and that by allowing a benzene solution to evaporate at room temperature a mixture of yellow crystals and red supercooled liquid is deposited. The supercooled liquid crystallises only very slowly, but the effect may be accelerated by heating and proceeds fairly rapidly at 130—140°. In addition to the yellow crystals and the red glass, slow evaporation may indeed produce " brick-red crystals with a metallic sheen," but one end of such a crystal may conform to this description while the other is pure yellow. Kehrmann's " red crystals " are in fact artefacts of yellow crystals covered by a layer of red supercooled liquid. There is thus no evidence of the existence of a crystalline, red modification of 3-hydroxy-9-phenylacridine.

The temperature, 135°, reported by Kehrmann as a transition temperature has little significance. Even at 100° the red form is converted into the yellow in two weeks. At temperatures above 135° the yellow form becomes red if ground or compressed, and the yellow colour is restored when the stress is removed. Grinding or compression thus produce a metastable state, a fact confirmed by the differential heating curve of 3-hydroxy-9-phenylacridine against sodium chloride which indicated that an exothermic change occurs in the region of the red ⟶ yellow transformation.

It is unusual for grinding to make a crystalline solid amorphous, as it is for tautomerism to occur so readily in the solid state. These two phenomena probably are closely connected, and it is suggested that the yellow crystals of 3-hydroxy-9-phenylacridine contain lattices in the lactim form in which the hydroxyl groups are engaged in short hydrogen bonds with the nitrogen atoms of adjacent molecules. Tautomeric changes occur by proton transfer along these bonds. Grinding causes local heating, giving rise to disordered oxygen–nitrogen hydrogen bonds, and leading to local melting. The melt then contains a mixture of the tautomers which will recrystallise only very slowly since the regular system of hydrogen bonds, which provided the mechanism for the original tautomeric changes, has now been destroyed. The crystals are thus converted progressively into a glass. In Part I of this series it is shown that hydrogen bonds of the type postulated are particularly liable to become disordered.

Experimental

Ultraviolet spectra were measured with a Unicam S.P. 500 spectrophotometer. M.p.s were determined, and thermal behaviour between room temperature and 350° was examined, by means of a Kofler hot-stage microscope. The heating curve of 3-hydroxy-9-phenylacridine against sodium chloride was obtained in an apparatus described in the Thesis of one of us.[5]

[5] Cairns-Smith, Thesis, Edinburgh, 1956, p. 114.

Thin films for spectroscopic examination were obtained by exposing in a vacuum of 0·4 mm. a silica plate (cooled by carbon dioxide–acetone) to the compound heated at 180—200° for 1—2 min.

3-*Hydroxy*-9-*phenylacridine*.—This compound was prepared by the recorded method [1] and chromatographed on alumina with chloroform as solvent and developer. A slow-moving upper red band and a fast-moving yellow band resulted. The latter on elution yielded a small amount of a substance, which is probably 1-hydroxy-9-phenylacridine since its ultraviolet spectrum resembled that of 4-hydroxyacridine.[2] The red band was removed by ethanol and yielded 3-hydroxy-9-phenylacridine, yellow needles (from benzene), m. p. 264° (lit.,[1] 264°) [*N*-methyl ether, m. p. 230° (lit., 231°)]. The hydroxy-compound (0·1 g.) in chloroform (3 ml.) was added in six portions to diazomethane in ether (prepared from 1 g. of *N*-nitrosomethylurea), and kept overnight at 0°. The solution was allowed to warm to room temperature and the solvent removed. The residue in chloroform was chromatographed on alumina and development with the same solvent gave a pale yellow band with a blue fluorescence, which yielded the O-*methyl ether*, a yellow green oil (0·4 g.); crystallised from absolute ethanol or light petroleum, this had m. p. 137—138° (Found: C, 84·3; H, 5·3; N, 4·9. $C_{20}H_{15}NO$ requires C, 84·2; H, 5·3; N, 4·9%).

Spectroscopic Measurements.—$\lambda_{max.}$ with log ε in parentheses and inflexions in italics were:

3-*Hydroxy*-9-*phenylacridine*: 258, *295*, 342, 356, 381, 402, *428* mμ in cyclohexane; 236, 259, 286, *322*, *338*, 352, 394, *410*, 483, *500* mμ (4·48, 4·89, 4·21, 3·39, 3·73, 3·99, 3·68, 3·58, 3·42, 3·35) in absolute ethanol; 236, *259*, 279, *355*, 365, 468 mμ (4·56, 4·42, 4·69, 4·05, 4·10, 3·98) in 20% aqueous ethanol.

3-*Methoxy*-9-*phenylacridine*: *239*, 260, *286*, *321*, 338, 352, 378, *393*, 398 mμ (4·52, 5·08, 3·70, 3·47, 3·76, 3·94, 3·84, 3·68, 3·71) in cyclohexane; 236, 258, *286*, 320, 335, 351, 380, *396* mμ (4·42, 5·07, 3·72, 3·47, 3·79, 4·02, 3·82, 3·67) in absolute ethanol.

10-*Methyl*-9-*phenylacridine*: 240, 294, 336, 351, *430*, 464, 490, *520* mμ in cyclohexane; 238, 288, 352, *363*, *450*, 478, 504 mμ (4·58, 4·69, 4·06, 4·03, 3·91, 4·07, 4·01) in absolute ethanol.

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