5-HYDROXYINDOLE ISOMERS WITH QUINONIMINE PROPERTIES

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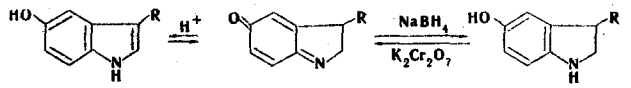
The structure of 5-hydroxyindole (I) permits the possibility of the existence of an isomer (II) that has the quinonimine structure:



I II III

a $R = CH_2CH_2NH_2$; b $R = CH_2CH(NH_2)COOH$; c $R = CH_2CH_2\overset{+}{N}(CH_3)_3Cl^-$

In our previous paper [1] it was demonstrated that 5-hydroxyindoles in acidic media are extremely easily hydrogenated over a palladium catalyst to give indolines. It may have been supposed that the anomalous ease with which this reaction proceeds is due to the ability of 5-hydroxyindoles to undergo reversible isomerization to quinonimines II. These results served as a starting point in a search for the quinoid isomer of serotonin (IIa) and its analogs (IIb,c). Sufficiently convincing proof of the formation of compounds of the II type during the oxidation of 5-hydroxyindoles (III) with potassium dichromate in acid media was obtained.

A solution of 75 mg of potassium dichromate in 50 ml of 0.001 N H_2SO_4 was added at 5°C to a solution of 100 mg of IIIa in 400 ml of 0.001 N H_2SO_4. The resulting solution had an absorption maximum at 275 nm in the same region as the starting indoline but with a much higher extinction. The product of the oxidation of p-aminophenol has a similar spectrum. When the reaction is carried out in the optical cell of a spectrophotometer, a sharp increase in the lifetime of the absorption band with λ_{max} 275 nm (Fig. 1) is observed after $K_2Cr_2O_7$ is added to the solution of indoline IIIa. Moreover, the spot of dihydroserotonin (R_f 0.94, paper, 2 N HCl) vanishes on the chromatogram, and the serotonin spot is also absent.

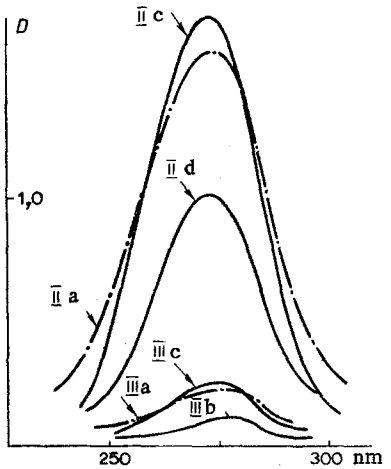


Fig. 1. UV spectra of 5-hydroxyindolines ($c = 4 \cdot 10^{-4}$ M for IIIa,c; $c = 1.2 \cdot 10^{-4}$ M for IIIb) and quinonimines IIa-c.

The product of the oxidation of dihydroserotonin was adsorbed on KB-$4N_2$ (H^+) ion-exchange resin, the resin was washed with cold 0.001 N hydrochloric acid, and the quinone was removed with 30 ml of 0.5% hydrochloric acid. Compound IIa is stable at room temperature for 1-2 h in pure dilute solution.

Crude solid quinonimine IIa was obtained by lyophilic drying of an acid solution of it. The gray hygroscopic powder could be stored at −40° for 20-30 min; a solution of it in 0.001 N H_2SO_4 had the spectrum of the starting compound and gave the same reactions.

Quinonimines IIc,b are also formed in the oxidation of bufotenidine (IIIc) and 5-hydroxydihydrotryptophan (IIIb), as

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attested to by the increase in the optical density of the solution at 275 nm after the addition of the oxidizing agent (see Fig. 1). The action of excess sodium borohydride leads to a sharp reduction in the optical density of solutions of these quinonimines at 275 nm.

The structure of the quinonimine formed in the oxidation of dihydroserotonin is confirmed by the fact that IIa is isomerized to serotonin Ia on standing in dilute acid solution for 24 h. A colored spot with R_f 0.45 in 2 N HCl appears on the chromatograms, just as in the case of serotonin, and the long-wave maximum (λ_{max} 295 nm) peculiar to serotonin is observed in the UV spectrum. Dihydroserotonin is absolutely stable under these conditions.

Concentrated solutions of quinonimine IIa are unstable. Their spectra change when the solutions are allowed to stand for a long time, and the spot of indoline IIIa (yellow color with Erlich's reagent, R_f 0.94) is detected on the chromatograms. Dimerization and polymerization of the quinonimine, similar to the reactions of quinones in alkaline media, apparently occur under these conditions.

A sharp decrease in the optical density of the band with λ_{max} 275 nm is observed when sodium borohydride is added to an acid solution of quinone IIa. The bright-yellow spot of dihydroserotonin (Erlich's reagent) with R_f 0.94 in 2 N HCl is observed on the chromatogram. Serotonin itself is not reduced under similar conditions.

The results of this study open up new approaches to the synthesis of serotonin derivatives and make it possible to take a fresh look at the mechanism of the biological action of these substances.

LITERATURE CITED

1. M. F. Petrova, N. S. Kaverina, and L. S. Yaguzhinskii, Khim. Geterotsikl. Soedin., 1058 (1971).