STRUCTURE OF A THIOCHROME TRANSFORMATION PRODUCT

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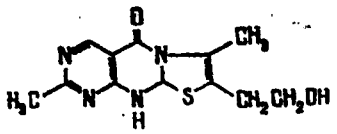
Thiochrome (I) — a natural catabolite of vitamin B_1 [1] — may, under certain conditions, take part in reversible redox reactions in biological systems [2] and, apparently, undergo other transformations. Thus, on chromatograms of the preparation that has been stored for a long time an additional fluorescent spot always appears [3] [R_f in the butan-1-ol–ethanol–water (2:1:1) system 0.75)]. The structure of this product (II) has hitherto remained unknown. Since the oxidation of thiamine to thiochrome is important in the metabolism of the vitamin itself [4], it appeared to us to be of interest to determine the nature of the product of the further transformation of thiochrome itself.

We isolated compound (II) in the individual form by column chromatography on silica gel L 100/250 μ (with methanol as eluent) in the form of light yellow crystals with mp 125-127°C (chloroform–ether), $C_{12}H_{14}N_4O_2S$, M^+ 278.

^{1}H NMR spectrum (D_2O, pD = 3.4, 32°C, internal standard TSP, δ, ppm): 2.44 (s, 3 H, 7-CH_3); 2.69 (s, 3 H, 2-CH_3); 2.98 (t, 2 H, α-CH_2, J = 7.6 Hz); 3.82 (t, 2 H, β-CH_2, J = 7.6 Hz); 6.98 (s, 1 H, H-9a); 8.57 (s, 1 H, H-4). The IR spectrum of (II) ($CHCl_3$) showed characteristic absorption bands due to the stretching vibrations of the bonds: O–H (3635 cm^{-1}); N–H (3288 cm^{-1}); 9a-C–H (3055 cm^{-1}); C–H in CH_3 groups (2965 cm^{-1}, ν_{as}, and 2890 cm^{-1}, ν_s); C–H in CH_2 groups (2938 cm^{-1}, ν_{as}, and 2863 cm^{-1}, ν_s); C=O (1677 cm^{-1}, C=N and C=C (1588, 1550, 1535 cm^{-1}), C–N (1250 cm^{-1}), and C–O (1054 cm^{-1}), and to deformation vibrations of C–H bonds in CH_3 groups at 1442 cm^{-1} (δ_{as}) and 1378 cm^{-1} (δ_s). In the UV spectrum, a strong long-wave absorption band ($\lambda_{max}^{C_2H_5OH}$ 347 nm) was hypsochromically shifted by 22 nm in comparison with the corresponding band in the initial compound (I), which indicated a disturbance of conjugation in the total chromophoric system. Fluorescence spectrum (H_2O): λ_{max}^{exc} 350 nm, $\lambda_{max}^{emission}$ 440 nm.

The combination of spectral characteristics mentioned above gives grounds for characterizing the thiochrome transformation product as 8-(2-hydroxyethyl)-2,7-dimethyl-5-oxo-5,6,9a,10-tetrahydrothiazolo[2,3-a]pyrimido[4,5-d]pyrimidine



Compound (II) was also obtained by independent synthesis in which (I) was oxidized by Beckman's mixture (70°C, 1.5 h, yield 47%). The substance synthesized and that isolated chromatographically were identical (mixed melting point).

Preliminary trials have shown that compound (II), unlike (I), possesses a pronounced biological activity. Thus, it suppresses the activity of the main enzyme of the pentise phosphate cycle, transketolase in mouse liver and blood by 26 and 41%, respectively (12 h). In the sphere of lipid metabolism, compound (II) has a substantial influence (72 h) on the amount of fatty acids in the rat liver: the amounts of 18:2 and 20:4 acids fall (19% and 30%, respectively) and the amounts of 16:1 and 18:1 acids rise (91% and 30%, respectively), with the simultaneous increase in the level of total lipids (26%) and phospholipids (69%) and a fall in the amount of cholesterol (35%).

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