PRODUCTION OF FLAVOLIGNINS OF HERBACETIN WITH THE AID OF PEROXIDASE

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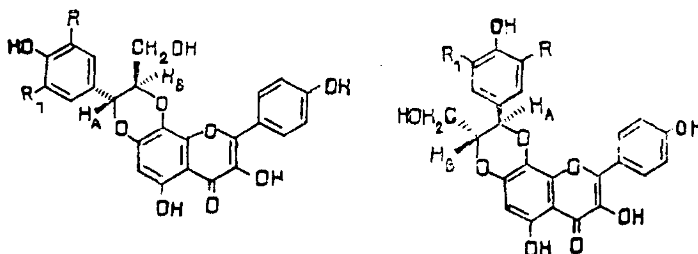
UDC 547.972

Flavolignins – (in particular, silybin and other components of the fruit of the blessed milk thistle (Silybum marianum Gaertn.)) are original biologically active compounds used in medical practice as effective hepatoprotectant drugs [1-3].

The production of silybin by the oxidative coupling of taxifolin and coniferyl alcohol with the aid of horseradish peroxidase has been reported previously [4]. It appeared of interest to obtain the flavolignan rhodiolin by an analogous method; we have isolated this flavolignan previously from the rhizomes of roseroot stonecrop (Rhodiola rosea L., family Crassulaceae) [5]. As the initial compounds we used herbacetin (3,4'5,7,8-pentahydroxyflavone) and p-coumaryl, coniferyl, or sinapyl alcohol. The oxidative coupling of herbacetin and the phenylpropanoids was effected with the aid of horseradish peroxidase (Reanal, Budapest).

Thus, from herbacetin we have obtained rhodiolin (II), and also the flavolignans (I) and (III), which we have called demethoxyrhodiolin and methoxyrhodiolin, respectively.



Demethoxyrhodiolin (Ia). $R=R_1=H$ I b, $R=R_1=H$
Rhodiolin (IIa). $R=OCH_3$; $R_1=H$ II b, $R=OCH_3$; $R_1=H$
Methoxyrhodiolin (IIIa). $R=R_1=OCH_3$ III b, $R=R_1=OCH_3$

To identify the substances obtained and to establish their structures we made use of the results of UV, PMR, and mass spectroscopies and also a direct comparison with an authentic sample of rhodiolin.

Demethoxyrhodiolin (I) – yellow crystals with the composition $C_{24}H_{18}O_9$, M+ 450 (4%), mp 239-240.5°C (aqeous ethanol)., λ_{max}^{EtOH} 278, 331, 377.

Rhodiolin (II) – yellow crystals with the composition $C_{25}H_{20}O_{10}$, M+ 480 (14%), mp 235-237°C (MeOH), λ_{max}^{EtOH} 281, 333, 384.

Methoxyrhodiolin (III) – yellow acicular crystals with the composition $C_{26}H_{22}O_{11}$, M+ 510 (20%), mp 246-247°C (aqueous ethanol), λ_{max}^{EtOH} 279, 331, 382.

The mass spectra of compounds (I-III) enabled the empirical formulas of their molecules to be established and also the presence in them of a residue of p-coumaryl, coniferyl, or sinapyl alcohol, respectively: the peaks of ions with m/z 150 (in compound (I)), 180 (in compound (II)), and 210 (in compound (III)). In the PMR spectra of compounds (I-III) all the signals of the protons corresponding to the herbacetin residue were clearly distinguishable, and its link with the hydroxycinnamyl alcohols must have taken place through the oxygen.

The absence of a bathochromic shift of the short-wave band in the UV spectra of compounds (I-III) with sodium acetate indicated that the 7-OH group in herbacetin had been

All-Union Scientific-Research Institute of Medicinal Plants Scientific Production Combine, Moscow. Translated from Khimiya Prirodnykh Soedinenii, No. 6, p. 880-881, November-December, 1990. Original article submitted February 19, 1990.

 0009-3130/90/2606-0710$12.50 © 1991 Plenum Publishing Corporation

substituted, while the negative reaction with p-benzoquinone (gossypetone test) indicated the substitution of the 8-OH group. The substitution of the 8-OH group in these compounds was also confirmed by the fact that their spots on Silufol plates did not become blue during storage [5]. Consequently, in compounds (I-III), the hydroxycinnamyl alcohol residue was attached to the 7,8-dihydoxy grouping of herbacetin with the formation of a 1,4-dioxane ring [5].

In the light of the doublet signal at δ 5.2 ppm (J = 8 Hz) observed in the spectrum of compound (I-III) and assigned to the H benzyl proton, it can be stated that the relative configuration f the substituents in the dioxane fragment is transoid. In view of the fact that the question of the position isomerism of these substituents remains open, demethoxyrhodiolin, rhodiolin, and methoxyrhodiolin may, with equal probability correspond to structures (Ia), (IIa), and (IIIa) or to (Ib), (IIb), and (IIIb), respectively.

Thus, three flavolignans have been obtained by the oxidative coupling with the aid of peroxidase of herbacetin and cinnamyl alcohols, two of them (I and III) being new.

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