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NEW 6-METHOXYFLAVONOLS FROM *CENTAUREA JACEA*

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Abstract—Two new flavonols were isolated from *Centaurea jacea* flowers and they have been shown to be 4′,5,7-trihydroxy-3,6-dimethoxyflavone and its 7-*O*-β-D-glucoside.

WE REPORT the isolation and structure determination of 4′,5,7-trihydroxy-3,6-dimethoxyflavone (Ia) and its 7-*O*-glucoside (Ib) from the flowers of *Centaurea jacea*. This species appears to be a rich source of flavonoids oxygenated at the 6 position; for example, the isolation of 3′,5,7-trihydroxy-3,4′,6-trimethoxyflavone 7-*O*-glucoside (centaurein),[1] and 4′,5,7-trihydroxy-3′,6-dimethoxyflavone 7-*O*-glucoside (jaceosid)[2] from the roots, and 4′,5,7-trihydroxy-3,3′,6-trimethoxyflavone 7-*O*-glucoside (jacein)[3] from the leaves of this same plant have been previously reported

When the residue obtained from methanol extracts of fresh flowers of *C. jacea* was chromatographed on polyamide[4] a flavonoid aglycone and glycoside were obtained as crystals. The glycoside was shown to be an *O*-β-D-glucoside of the aglycone by hydrolysis with β-glucosidase. The NMR spectrum of the trimethylsilyl ether of the glucoside indicated that the compound was a dimethyl ether-glucosyl derivative of 6-hydroxykaempferol: two methoxyl groups (3·80 δ and 3·87 δ); one glucosyl moiety (since the glucosyl H-1 signal was centered at 5·00 δ it cannot be attached at position 3)[4] and aromatic proton signals at 6·78 δ (singlet) for H-8 and two two-proton doublets at 7·00 δ and 8·06 δ ($J = 10$) for H-3′,-5′ and H-2′,-6′, respectively. The presence of three hydroxyl groups in the aglycone was confirmed by the formation of a triacetate. The assignment of an oxygen substituent to C_6 and not C_8 was confirmed by the u.v. spectral data for both the aglycone and the glycoside based on the fact that when flavones and flavonols contain a C_6 oxygen substituent and a free C_5 hydroxyl group, Band I shows, in the presence of $AlCl_3$–HCl, only about a 25 nm bathochromic shift (relative to the methanol spectrum) instead of the usual 40-60 nm shift.[4] The $AlCl_3$/HCl u.v. data for both natural products were in accord with the presence of an oxygen substituent at C_6.

Demethylation of the aglycone with pyridinium hydrobromide[5] produced a flavonol which had a free hydroxyl group at C_3. Thus, one of the methoxyl groups could be assigned to C_3. Similarly, demethylation (with concurrent deglucosylation) of the glucoside gave the same flavonol. (Both natural products appeared dark purple when viewed under u.v. light on chromatographic paper, whereas the demethylated flavonol appeared yellow-orange.)

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[2] H. WAGNER, L. HÖRHAMMER, R. HOER, T. MURAKAMI and L. FARKAS, *Tetrahedron Letters* 3411 (1969).
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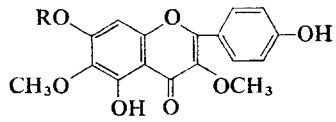
[4] T. J. MABRY, K. R. MARKHAM and M. B. THOMAS, "The Systematic Identification of Flavonoids", Springer-Verlag, New York (1970).
[5] See G. HOWARD and T. J. MABRY, *Phytochem.* **9**, 2413 (1970) for a description of the pyridinium hydrobromide procedure as developed by the senior author of the present paper.



Ia, R=H

Ib, R=glucosyl

Comparison of the u.v. data (a standard set of six spectra was recorded for each compound)[4] for the glucoside with those obtained for the aglycone indicated that the glucoside differed by having a substituent at the 7-position (i.e. Band II data in the presence of NaOAc); thus the glucosyl moiety must be attached at C_7. The only remaining question regarding the structure of the two 6-hydroxykaempferol derivatives concerned the position of the second methoxyl group. Since the u.v. data clearly established that both compounds contained free 4′ and 5 hydroxyl groups ($NaOCH_3$ and $AlCl_3$ spectral data), the second methoxyl group must be attached at C_6. Therefore, the two new flavonols from *C. jacea* can be assigned structures Ia and Ib.

EXPERIMENTAL

Centaurea jacea flowers were collected in July 1969 from a cultivated plot at the Drug Farm of the University of Texas in Austin. Polyamide then layer plates were developed in $CHCl_3$–MeOH–MeCOEt (12:2:1).[6] Two dimensional paper chromatograms were run on 3MM Whatman paper in TBA [*t*-BuOH–HOAc–H_2O (3:1:1)] and 15% aq. HOAc. u.v. spectra were measured using standard procedures.[4] NMR spectra of the trimethylsilyl ether of the glucoside and the aglycone acetate were measured in CCl_4 on a Varian A-60 spectrometer using tetramethylsilane as an internal standard. *Compound Ia:* 4′,5,7-*trihydroxy*-3,6-*dimethoxyflavone* showed the following properties: R_f (TBA) 0·85; R_f (HOAc) 0·13; U.V. λ_{max} (MeOH): 274, 295 sh, 340 nm, λ_{max} (NaOMe): 278, 325, 400 nm; λ_{max} ($AlCl_3$): 235 sh, 280, 305 sh, 370, 405 sh nm; λ_{max} ($AlCl_3$–HCl): same as $AlCl_3$; λ_{max} (NaOAc): 275, 320, 395 nm; λ_{max} (NaOAc–H_3BO_3): 270, 345 nm. The NMR spectrum of the acetate in CCl_4 (ppm) displayed the following signals: H-2′6′, 8·12 (d, $J = 10$); H-3′5′, 7·26 (d, $J = 10$); H-8, 7·26 (s); 3,6-methoxyls, 3·87, 3·82 (s); 4′,5,7-acetoxyl moieties, 2·33, 2·37, 2·51 (s) (δ-scale). *Compound Ib:* 4′,5,-dihydroxy-3,6-dimethoxyflavone 7-*O*-β-D-glucoside showed the following properties: R_f (TBA) 0·79; R' (HOAc) 0·53; u.v. λ_{max} (MeOH): 274, 335 nm; λ_{max} (NaOMe): 245 sh, 278, 305 sh, 402 nm; λ_{max} ($AlCl_3$): 235 sh, 282, 305 sh, 365, 410 sh nm; λ_{max} ($AlCl_3$–HCl): same as $AlCl_3$; λ_{max} (NaOAc): 273, 398 nm; λ_{max} (NaOAc–H_3BO_3): 272, 342 nm.

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