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TWO NEW COUMARINS FROM *HAPLOPHYLLUM PTILOSTYLUM*

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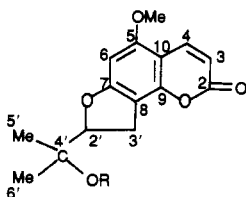
ABSTRACT.—Two new coumarins, ptilostin [**1**] and ptilostol [**2**], were isolated from the aerial parts of *Haplophyllum ptilostylum* (Rutaceae) together with two known lignans, justicin B and isodaurinol. The structures of the new and the known compounds were established by spectral data.

As a part of our continuing investigations of the genus *Haplophyllum* (1–3) we studied the aerial parts of *Haplophyllum ptilostylum* Spach (Rutaceae) and obtained two new coumarins, ptilostin [**1**] and ptilostol [**2**], in addition to a well known cytotoxic lignan, justicin B (2,4,5), and isodaurinol (6). No alkaloids were found in this extract.

The hreims of the new coumarin ptilostin [**1**] indicated the molecular formula $C_{20}H_{24}O_5$ (m/z 344.1618, calcd 344.1623). The ir spectrum showed the presence of aromatic (3040, 1620, 1560, 1500 cm^{-1}) and carbonyl (1710 cm^{-1}) absorbancies. The uv spectrum indicated an angular furanocoumarin structure (322 and 224 nm). The 1H -nmr spectrum of **1** showed aromatic proton signals at δ 7.97 (1H, d, $J=10$ Hz, H-4), 6.25 (1H, d, $J=10$ Hz, H-3); the chemical shift of the former signal indicated the presence of an oxygen function at C-5 (7–10). The diamagnetic shift observed for H-6 is due to the β effect induced by the two vicinal oxygen functionalities (7,11). The MeO group at C-5 appeared at δ 3.90 (3H, s), indicating the angular furanocoumarin structure of **1** (12,13). The presence of

the MeO group at C-5 was proven by an nOe experiment; irradiation of the MeO caused enhancement of the H-4 and H-6 signals. The tetrahydrofuran ring was indicated by the signals at δ 5.08 (1H, br t, $W_{1/2}=7$ Hz, H-2'), 3.72 (1H, dd, $J=6$ Hz and 12 Hz) and 3.48 (1H, dd, $J=7$ Hz and 12 Hz) (H-3'), and at δ 1.60 (3H, s) and 1.58 (3H, s) (Me-5' and Me-6'). The prenyloxy side chain was observed at δ 4.65 (2H, br d, $J=7$ Hz, H-1''), 5.47 (1H, dt, $J=7$ Hz and 1 Hz, H-2''), and 1.73 (3H, s) and 1.77 (3H, s) (Me-4'' and Me-5''). Spin decoupling experiments showed the relation between H-2' and H-3', as well as between H-1'' and H-2''. The ^{13}C -nmr spectrum and APT and SFORD experiments indicated the presence of five Me quartets, two methylene triplets, five methine doublets, and eight carbon singlets for twenty carbon atoms. The ^{13}C -nmr spectrum indicated an α -pyrone carbonyl signal at 161.6 ppm; all other signals were in agreement with the given structure. Mass degradation also showed the structure clearly; the base peak at m/z 275 $[M-C_5H_9]^+$ indicated the presence of a prenyl side chain; other fragments were typical for coumarin degradation (see Experimental).

The second new compound, ptilostol [**2**], was 5-methoxycolumbianetin. The hreims indicated the molecular formula $C_{15}H_{16}O_5$ (m/z 276.0998, calcd 276.0997). The absorbancies of the ir spectrum (3045, 1710, 1620, 1560, 1510 cm^{-1}) and the uv spectrum (320 and 226 nm) were similar to those of **1** with the exception of an OH signal at 3450 cm^{-1}



- 1** $R = \overset{1''}{CH_2}-\overset{2''}{CH}=\overset{3''}{C}(\overset{4''}{Me})(\overset{5''}{Me})$
2 $R = H$

in the ir spectrum of the latter compound. The ^1H -nmr spectrum was also quite similar to that of **1** except for the prenyl side chain; the aromatic proton signals at δ 7.97 (1H, d, $J=10$ Hz, H-4), 6.22 (1H, d, $J=10$ Hz, H-3), 6.45 (1H, s, H-6) together with the MeO signal at δ 3.90 (3H, s) indicated a 5-methoxylated compound. The tetrahydrofuran ring was determined from the signals at δ 4.65 (1H, dd, $J=7$ Hz and 2.5 Hz, H-2'), 2.82 (1H, dd, $J=7$ Hz and 10 Hz), and 2.35 (1H, br d, $J=10$ Hz) (H₂-3'), and the signal at δ 1.36 (6H, s) indicated the Me-5' and Me-6'. The relationship between H-2' and H-3' was shown by spin decoupling experiments. The ^{13}C -nmr spectrum of **2** was in agreement to that of **1** except for the lack of the prenyl signals. The two known lignans, justicin B and isodaurinol, were identified by comparing their spectral data to those of literature values and by tlc comparison with authentic samples.

EXPERIMENTAL

PLANT MATERIAL.—The aerial parts of *H. pilostylum* were collected from southern Turkey (Ermenek) in June 1992 and identified by Prof. Dr. E. Tuzlaci (Istanbul). A voucher specimen is deposited in the Herbarium of the Faculty of Pharmacy, University of Marmara (Mare 3742).

EXTRACTION AND SEPARATION.—The dried and powdered plant material (870 g) was extracted in a Soxhlet apparatus with MeOH. The extract was evaporated to dryness under a vacuum to yield 133 g of a residue. Half of the residue was fractionated in a Si gel column (5×90 cm) eluted with petroleum ether, and a gradient of Et₂O was added up to 100%, followed by EtOH up to 100%. The compounds were obtained in the following order: ptilostin [**1**] (20 mg), ptilostol [**2**] (10 mg), justicin B (15 mg), and isodaurinol (10 mg).

Ptilostin [1].— $[\alpha]_{\text{D}} + 30.4$ (MeOH, $c=0.1$); uv (MeOH) λ max 322 (log ϵ 4.10), 224 (log ϵ 4.00); ir (CHCl₃) ν max 3040, 2985, 2910, 2850, 1710, 1620, 1560, 1500, 1465, 1430, 1360, 1330, 1280, 1260, 1180, 1140, 1120, 1080, 1030 cm^{-1} ; ^1H nmr (CDCl₃) δ 7.97 (1H, d, $J=10$ Hz, H-4), 6.25 (1H, d, $J=10$ Hz, H-3), 6.44 (1H, s, H-6), 5.47 (1H, dt, $J=7$ Hz and 1 Hz, H-2'), 5.08 (1H, br t, $W_{1/2}=7$ Hz, H-2'), 4.65 (2H, br d, $J=7$ Hz, H-1'), 3.72 (1H, dd, $J=6$ Hz and 12 Hz), 3.48 (1H, dd, $J=7$ Hz and 12 Hz) (H₂-3'), 3.90

(3H, s, OMe), 1.60 (3H, s), 1.58 (3H, s) (Me-5' and Me-6'), 1.73 (3H, s), 1.77 (3H, s) (Me-4'' and Me-5''); ^{13}C nmr (CDCl₃) δ 161.6 (C-2), 111.3 (C-3), 138.7 (C-4), 154.8 (C-5), 93.2 (C-6), 145.7 (C-7), 131.6 (C-8), 151.5 (C-9), 102.4 (C-10), 65.9 (C-2'), 26.1 (C-3'), 66.2 (C-4'), 17.6 (C-5'), 16.6 (C-6'), 66.2 (C-1''), 119.2 (C-2''), 145.0 (C-3''), 25.6 (C-4''), 25.2 (C-5''); eims m/z (rel. int.) $[\text{M}]^+$ 344 (5), $[\text{M}-29]^+$ 315 (10), $[\text{M}-\text{C}_6\text{H}_5]^+$ 275 (100), 253 (25), 208 (20), 192 (25), 155 (18), 110 (38), 96 (58), 70 (74), 56 (98); hreims m/z 276.0998 (calcd 276.0997).

Ptilostol 2.— $[\alpha]_{\text{D}} + 29.8$ (MeOH, $c=0.1$); uv (MeOH) λ max 320 (log ϵ 4.10), 226 (log ϵ 4.00); ir (CHCl₃) ν max 3450, 3045, 2940, 3450, 3045, 2940, 2850, 1710, 1620, 1560, 1510, 1460, 1420, 1380, 1350, 1275, 1250, 1180, 1150, 1100, 1020 cm^{-1} ; ^1H nmr (CDCl₃) δ 7.97 (1H, d, $J=10$ Hz, H-4), 6.22 (1H, d, $J=10$ Hz, H-3), 6.45 (1H, s, H-6), 3.90 (3H, s, OMe), 4.65 (1H, dd, $J=7$ Hz and 2.5 Hz, H-2'), 2.82 (1H, dd, $J=7$ Hz and 10 Hz), 2.35 (1H, br d, $J=10$ Hz) (H₂-3'), 1.36 (6H, s) (Me-5' and Me-6'), ^{13}C nmr (CDCl₃) δ 161.8 (C-2), 108.5 (C-3), 141.5 (C-4), 154.7 (C-5), 93.3 (C-6), 145.6 (C-7), 131.7 (C-8), 151.5 (C-9), 102.5 (C-10), 65.9 (C-2'), 27.1 (C-3'), 65.9 (C-4'), 18.2 (C-5'), 17.1 (C-6'); eims m/z (rel. int.) $[\text{M}]^+$ 276 (50), $[\text{M}-29]^+$ 247 (20), 217 (100), 203 (40), 175 (20), 144 (10); hreims m/z 344.1618 (calcd 344.1623 for C₂₀H₂₄O₃).

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