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coumarin, a 5,6,7-Trioxxygenated
Coumarin from *Pterocaulon virgatum***

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5-(3-METHYL-2-BUTENYLOXY)-6,7-METHYLENEDIOXY- COUMARIN, A 5,6,7-TRIOXYGENATED COUMARIN FROM *PTEROCAULON VIRGATUM*

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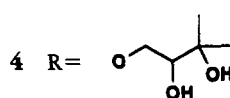
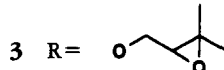
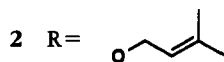
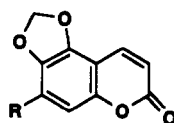
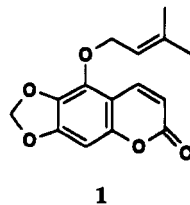
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ABSTRACT.—The coumarin **1** [5-(3-methyl-2-butenyloxy)-6,7-methylenedioxy-6-methoxycoumarin] and the recently reported 5-methoxy-6,7-methylenedioxy-6-methoxycoumarin, have been isolated from a petroleum ether extract of *Pterocaulon virgatum*. The structure of **1** was determined on the basis of X-ray crystallographic analysis and spectroscopic data.

Pterocaulon virgatum (L.) DC. (Compositae) has been used in Argentine traditional medicine as a digestive, an insecticide, an emmenagogue, and as a snakebite remedy (1–4). In our previous work we have reported the isolation and identification of five flavonoids (5), the 3,4-dicaffeoylquinic acid content (6), and two coumarins (7) from the aerial parts of *P. virgatum*. The present study describes the isolation of the coumarin **1** and the recently reported 5-methoxy-6,7-methylenedioxy-6-methoxycoumarin from the same plant material. Coumarin **1** was previously isolated from *P. balansae*, but was erroneously assigned structure **2** (8). The structures were elucidated by uv, ir, eims, ^1H -nmr, and ^{13}C -nmr spectroscopy. The structure of **1** was confirmed by X-ray crystallographic analysis.

The petroleum ether extract of the aerial parts of *P. virgatum* was subjected to cc over Si gel to give coumarin **1** and 5-methoxy-6,7-methylenedioxy-6-methoxycoumarin.

Coumarin **1** exhibited an ir absorption band at 1720 cm^{-1} , indicating the presence of a lactone carbonyl typical of a coumarin (9). The uv spectrum was consistent with a coumarin oxygenated at C-7 (10). There was no bathochromic



shift on adding NaOH, suggesting that it is a non-phenolic coumarin (11). The ^1H -nmr spectrum of **1** showed a pair of doublets at δ 6.20 and 7.95 (1H each, $J=9.8\text{ Hz}$), assigned to the vinylic protons H-3 and H-4, respectively. The deshielded nature of the latter proton suggested that there is an oxygen function at the C-5 position (12). The aro-

matic singlet signal at δ 6.53 must be assigned to H-8. The reduction of the peak height of the doublet for H-4, with respect to that of H-3, is evidence of a long-range coupling over five bonds in a rigid zig-zag pattern, well documented in bicyclic aromatic systems (13,14). The signal at δ 6.03 (2H, s) was assigned to methylene protons in a O-CH₂-O group. The remaining signals at δ 4.85 (2H, d, $J=7.4$ Hz), δ 5.48 (1H, t, $J=7.4$ Hz) and δ 1.83 and 1.78 (3H each, each s) were attributed to a 3,3-dimethylallyloxy substituent, which could be placed at C-5 or C-7. The eims of coumarin **1** showed a peak corresponding to the $[M^+]$ at m/z 274 for C₁₅H₁₄O₅. The base peak at m/z 206 $[M^+ - 68]$ reflected the facile loss of the ion $[C_5H_8]^+$. The ¹³C-nmr spectrum was assigned to the corresponding carbons based on ¹H-decoupling spectra and the DEPT pulse sequence (Experimental).

Combining all these structural requirements, the regioisomers **1** and **2** were the only two possibilities for the structure of the compound isolated. Earlier, the isolation of a coumarin assigned structure **2**, was reported from a related *Pterocaulon* species, namely, *P. balansae* (8). To determine unambiguously the structure of the isolate, X-ray diffraction analysis (15) was employed which showed that the coumarin isolated here corresponded to structure **1**. The X-ray crystallographic structure of the natural product, showing the atomic numbering system, is given in Figure 1.¹

It is worth noting that literature reports concerning the structure of several related compounds are ambiguous. The lack of full spectroscopic and physi-

cal data thereby impedes a correct analysis of the different structural assignments. A coumarin assigned structure **3** was first isolated from *Pteronia glabrata* (16). A few years later, it was isolated a second time from *Pterocaulon balansae* and *P. lanatum*, together with two closely related coumarins, which were assigned the structures **2** and **4**, respectively (8). In both cases, the positioning of the O-substituents on the coumarin nucleus was established by the C₆H₆-d₆/CDCl₃-induced shift observed for the methylenedioxy and methoxy signals in the ¹H-nmr spectrum (17). The first reported synthesis of coumarin **3** (no data given) was established by epoxidation of synthetically obtained **2** (18). However, the spectroscopic data of the synthetic coumarin **2** differed markedly from the isolate (¹H nmr; $\Delta\delta$ max=0.38) (8). Magalhaes *et al.* (19) synthesized coumarins **2-4** and concluded that since the spectroscopic properties of these compounds differed from the coumarins that they had isolated from *P. balansae* and/or *P. lanatum* (8), it is probable that the isolates have different structures. However, no other structures were proposed. An examination of the spectroscopic and physical data reported (19) for the coumarin designated as **2**, isolated from *P. balansae* (8), showed them to match very well (¹H nmr; $\Delta\delta$ max=0.09) with those we obtained for **1** [5-(3-methyl-2-butenyloxy)-6,7-methylenedioxy coumarin]. Therefore, the previously reported (8) structure **2** for the *P. balansae* coumarin must have structure **1**.

5-Methoxy-6,7-methylenedioxy coumarin was isolated from *Pterocaulon virgatum* as colorless crystalline needles, mp 192–194° (MeOH). The spectral data (uv, ¹H-nmr, ¹³C-nmr, and eims) were identical with the data published for this compound (20). This is the second report of the occurrence of this natural coumarin, and the first time that it has been isolated from the genus *Pterocaulon*.

¹Atomic coordinates, thermal parameters, bond distances and angles, and observed and calculated structure factors have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.

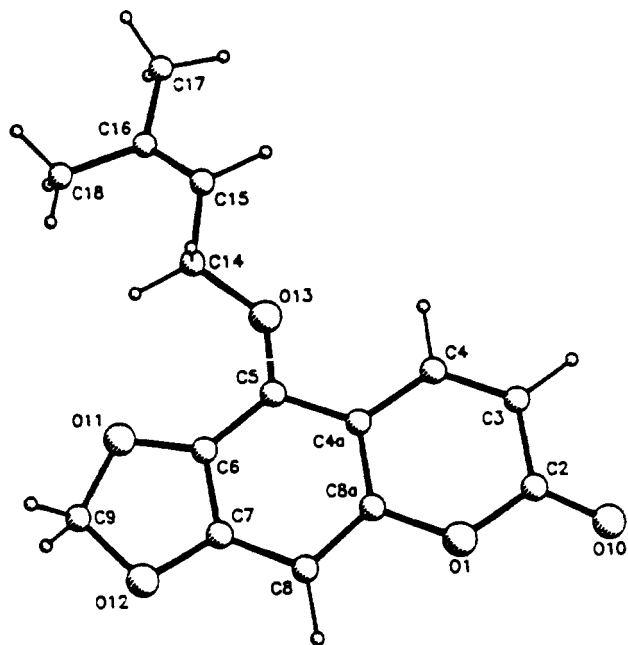


FIGURE 1. X-ray crystallographic structure and atomic numbering system of 5-(3-methyl-2-butenyloxy)-6,7-methylenedioxycoumarin [1].

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The ^1H - and ^{13}C -nmr spectra were recorded on a Varian T60 (60 MHz) and a Varian FT80 (20 MHz), respectively, in CDCl_3 , using TMS as internal standard. The ir spectra (KBr) were taken on a Bruker IFS 25. The uv spectra (MeOH) were determined on a Shimadzu model UV-240. The mass spectra were measured at 70 eV, using a Varian MAT 2A Data System 166. Mps were determined with a Mettler PF2 melting point apparatus and are uncorrected.

PLANT MATERIAL.—*Pterocaulon virgatum* was collected by Prof. A. Schultz from the Experimental Station INTA, Concepción del Uruguay, Entre Rios, Argentina, during November 1989. A voucher specimen is deposited at the Botanical Museum "Juan A. Dominguez" in Buenos Aires, Argentina.

EXTRACTION AND ISOLATION.—Dried and powdered aerial parts of *P. virgatum* (950 g) were extracted at room temperature with 25% aqueous MeOH. The MeOH was removed under reduced pressure and the aqueous layer was partitioned with petroleum ether, CHCl_3 , Et_2O , and EtOAc . The petroleum ether extract (4.0 g) was subjected to cc on Si gel, eluted successively with a petroleum ether/ EtOAc solvent mixture of increasing polarity. Fractions 6–13 afforded compound 1

while fractions 27–36 yielded 5-methoxy-6,7-methylenedioxycoumarin. Following repeated recrystallizations from MeOH, [5-(3-methyl-2-butenyloxy)-6,7-methylenedioxycoumarin] [1] (53 mg) and 5-methoxy-6,7-methylenedioxycoumarin (69 mg) were obtained.

5-(3-Methyl-2-butenyloxy)-6,7-methylenedioxycoumarin [1].—Colorless prisms, mp 128–129°; ir (KBr) ν_{max} 3052, 2972, 1724, 1628, 1564, 1508, 1428, 1388, 1300, 1244, 1196, 1092, 1044, 932, 820, 788 cm^{-1} ; uv (MeOH) λ_{max} 335 sh, 315, 257 sh, 235 nm; eims (70 eV) m/z 274 (M^+ , 10), 206 ($\text{M}^+ - \text{R}$, 100), 178 ($\text{M}^+ - \text{R} - \text{CO}$, 21), 69 (R^+ , 45); ^1H nmr (60 MHz, CDCl_3) δ 1.78 and 1.83 (3H each, s, Me_2), 4.85 (2H, d, $J=7.4$ Hz, OCH_2), 5.48 (1H, t, $J=7.4$ Hz, CH), 6.02 (2H, s, OCH_2O), 6.20 (1H, d, $J=9.8$ Hz, H-3), 6.53 (1H, s, H-8), 7.95 (1H, d, $J=9.8$ Hz, H-4); ^{13}C nmr (CDCl_3) δ 161.25 (s, C-2), 152.55 (s, C-8a), 151.64 (s, C-7), 139.70 (s, C-3'), 139.04 (d, C-4), 137.28 (s, C-5), 132.37 (s, C-6), 119.55 (d, C-2'), 111.63 (d, C-3), 107.37 (s, C-4a), 101.92 (t, OCH_2O), 92.40 (d, C-8), 68.90 (t, C-1'), 25.75 and 18.15 (each q, Me_2).

5-Methoxy-6,7-methylenedioxycoumarin.—Colorless crystalline needles mp 192–194° [lit. (19) 200–202°].

X-RAY CRYSTALLOGRAPHIC DATA FOR 5-(3-METHYL-2-BUTENYLOXY)-6,7-METHYLENEDIOXYCOUMARIN [1].— $\text{C}_{15}\text{H}_{14}\text{O}_5$, Mol wt = 274.27,

monoclinic, $P2_1/n$, $a=9.130$ (1), $b=7.826$ (1), $c=18.967$ (2) Å, $\beta=103.79$ (1)°, $V=1316.2$ (2) Å³, $Z=4$, $D_x=1.38$ g·cm⁻³, $CuK\alpha$, $\lambda=1.54178$ Å, $\mu=8.8$ cm⁻¹, $F(000)=576$, $T=291$ K, $R=0.059$ for 2031 observed reflections. DM not measured. Parallelepiped crystal with dimensions $0.2 \times 0.2 \times 0.4$ mm. Lattice parameters refined using 25 reflections in the range $25^\circ \leq 2\theta \leq 50^\circ$. HUBER diffractometer, graphite monochromatized $CuK\alpha$ radiation. 2372 $hkl \pm 1$ independent reflections with $\sin\theta/\lambda \leq 0.600$ Å⁻¹, 2031 with $I \geq 2.5\sigma(I)$. Standard reflection $(-3,3,0)$ checked every 50 reflections: no significant deviation. Structure solved by direct methods using SHELX86 (21), H atoms in computed positions, except the two methyl groups from difference Fourier synthesis. Anisotropic least squares refinement SHELX76 (22) using F; H isotropic with common refined temperature factor ($B=8.2$ Å²); $w=1/(\sigma^2+0.03F^2)$, $R=0.059$, $R_w=0.074$, $S=0.58$ for 2031 observed reflections. Final maximum shift to error=0.17. Maximum and minimum heights in final difference Fourier synthesis=0.32 and -0.34 e.Å⁻³. Atomic scattering factors from International Tables (23).

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