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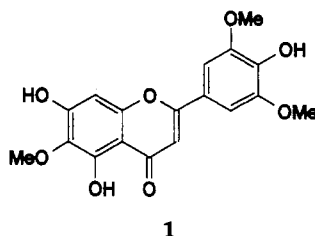
METHYLATED FLAVONES FROM *CONOCLIDIUM GREGGII*MARIANO MARTINEZ-VAZQUEZ,* HECTOR M. VAZQUEZ GARCIA,
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ABSTRACT.—Five known flavonoids were isolated from *Conoclidium greggii* (Compositae), including 5,7,4'-trihydroxy-6,3',5'-trimethoxyflavone [1], which showed inconsistencies in its spectral and physical data with those reported for this compound. The structure of **1** was unambiguously determined by a single crystal X-ray diffraction study. The five compounds isolated are new to this species.

A previous study of *Eupatorium greggii* Gray (1) reported the presence of β -farnesene. Recently, this species was reclassified to the *Conoclidium* genus (2). Since both genera are rich in secondary metabolites, mainly in flavonoid and sesquiterpene lactone derivatives (3), we decided to reinvestigate *Conoclidium greggii* Gray (Compositae).

Chromatographic separation of the hexane extract afforded lucidin dimethyl ether (4), nobelitin (5), and agestricin methyl ether (6), identified by comparison for their spectral data and physical constants with those reported for these compounds. It also provided gardenine A methyl ether, identified by comparison with an authentic sample (7), and 5,7,4'-trihydroxy-6,3',5'-trimethoxyflavone [1]. All five compounds isolated are new to this species.

The ms spectrum of **1** exhibited a molecular ion at m/z 360 (98%) for $C_{18}H_{16}O_8$ in accord with a flavone containing three OH and three MeO groups. The 1H -nmr spectrum (DMSO) showed, besides two one-proton singlets at 6.97 and 6.77 ppm assigned to H-8 and H-3 (8) (6.58 ppm and 6.56 ppm in $CDCl_3$) (9), respectively, one additional two-proton singlet at 7.28 ppm assigned to H-2' and H-6'. These assignments were supported by the observation of an nOe between the signal at 6.77 (H-3) and the signal at 7.28 ppm (H-2' and H-6'). Compound **1** also exhibited a singlet at 3.86 ppm for two MeO groups and another singlet at 3.72 for a third MeO



group. The relevant signals in the ^{13}C -nmr spectrum were at 93.73 (C-8), 104.23 (C-3), and 103.22 ppm (C-2' and C-6') (10).

A literature search revealed that **1** was previously isolated from *Artemisa* species (11,12) and *Conoclidium coelestinum* (8); however, these reports showed inconsistencies regarding the spectral and physical data of **1**. We therefore decided to establish the structure of **1** by a single crystal X-ray diffraction study. For this purpose, suitable crystals were obtained by slow crystallization from EtOAc. The molecular structure is shown in Figure 1, and the atomic coordinates for the non-hydrogen atoms are listed in Table 1. These results are in agreement with previous chemical studies on the genus *Conoclidium* (3,13).

EXPERIMENTAL

CRYSTAL DATA¹.—5,7,4'-Trihydroxy-

¹Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Center and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.

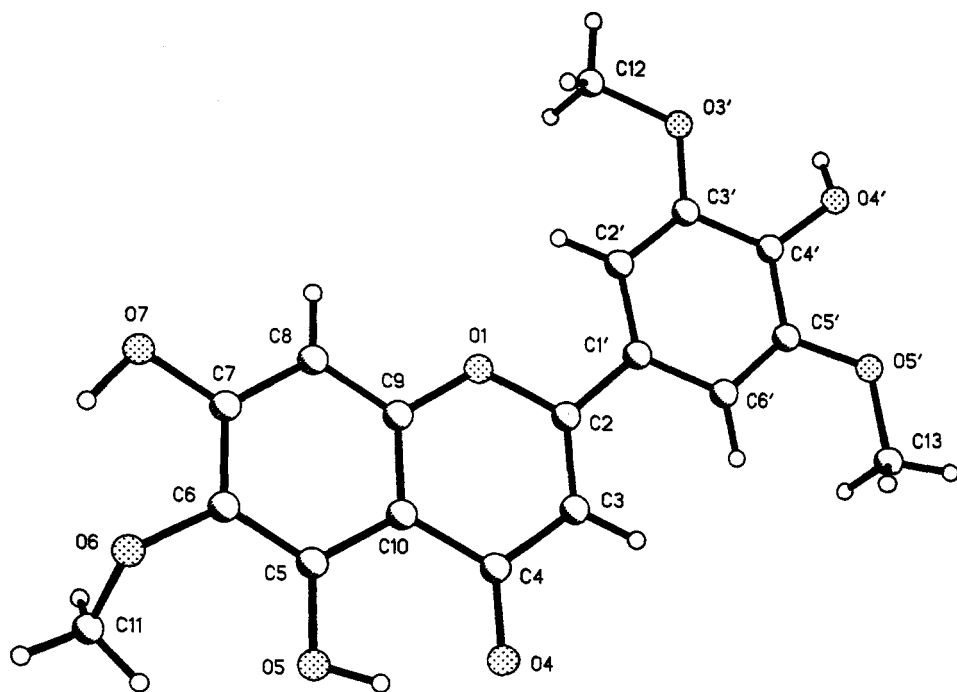


FIGURE 1. Molecular Stereostructure of 1.

6,3',5'-trimethoxyflavone-0.64 EtOAc [**1**], $C_{18}H_{16}O_8 \cdot 0.64 C_4H_8O_2$, $M = 416.71$, monoclinic, space group $P2_1/n$, $a = 8.402(5) \text{ \AA}$, $b = 15.476(9) \text{ \AA}$, $c = 14.346(9) \text{ \AA}$, $\beta = 90.00(5)$, $V = 1865.45 \text{ \AA}^3$, $D_c = 1.281 \text{ g/cm}^3$, $Z = 4$, $F(000) = 752$, $\mu(\text{CuK}\alpha) = 8.30 \text{ cm}^{-1}$, final $R = 8.3\%$ (266 parameters), $R_w = 10.5\%$ for 1929 unique reflections with $F \geq 3\sigma F$ in the range $3^\circ \leq 2\theta \leq 100^\circ$, residual electron density within $\pm 0.56 \text{ e \AA}^{-3}$.

DATA COLLECTION AND STRUCTURE REFINEMENT.—The intensity data were collected using a Nicolet P3/F four circles diffractometer using $\text{CuK}\alpha$ Ni-filtered radiation ($\lambda = 1.54178 \text{ \AA}$) operated in the $\theta:2\theta$ scanning mode with variable scan speed (4–29.3 deg/min) at room temperature. The data measured were corrected for background, Lorentz, and polarization effects, while crystal decay and absorption were negligible and no absorption corrections were applied. The structure was solved by direct methods using software provided by the diffractometer manufacturer. For structural refinements the nonhydrogen atoms were treated anisotropically. The hydroxyl hydrogens of **1** became evident from ΔF synthesis and their coordinates refined, the hydrogen atoms bonded to carbons atoms were included at idealized positions, all hydrogens with a fixed temperature factor $U = 0.06 \text{ \AA}^2$. The solvent molecule of EtOAc was found to be disordered.

GENERAL EXPERIMENTAL PROCEDURES.—Cc

was performed using Merck Si gel (70–230 mesh). Mp's were determined on a Fisher-Johns apparatus and are uncorrected. Ir spectra in CHCl_3 were obtained on a Nicolet 5SX spectrophotometer. Uv spectra were obtained on a Unicam SP-800 spectrophotometer. The nmr spectra were measured with TMS as the internal reference on Varian Associates XL-300GS spectrometer.

PLANT MATERIAL.—*C. greggi* was collected during August 1989 near La Escalera, Durango, Mexico. A voucher specimen (M. Martinez-68) was deposited at the Herbarium of Instituto de Biología, Universidad Nacional Autónoma de México. The dried and ground aerial parts (550 g) were successively extracted with hexane, EtOAc, and MeOH at room temperature. The extracts were concentrated under vacuum. From the hexane extract an amorphous solid precipitated, which after purification by recrystallization from hexane/EtOAc afforded 945 mg of gardenin A methyl ether (7).

Chromatography of the remaining hexane extract (7 g) on Si gel (210 g) using hexane with increasing proportions of EtOAc gave 1980 mg of lucidin dimethyl ether (4), 430 mg of nobilitin (5), 198 mg of agestricin methyl ether (6), and 24 mg of 5,7,4'-trihydroxy-6',3',5'-trimethoxyflavone [**1**].

5,7,4'-Trihydroxy-6',3',5'-trimethoxyflavone [**1**].—Mp 210–212° [lit. (11) 187–189°]; uv

TABLE 1. Atomic Coordinates ($\times 10^4$) and Temperature Factors ($\text{\AA}^2 \times 10^3$) for 5,7,4'-Trihydroxy-6,3',5'-trimethoxyflavone [1].

Atom	x	y	z	U
O-1	937 (4)	382 (2)	8757 (2)	43 (1) ^a
C-2	1765 (5)	483 (3)	9578 (3)	36 (2) ^a
C-3	1766 (6)	1240 (3)	10023 (3)	42 (2) ^a
C-4	924 (6)	1978 (3)	9708 (4)	42 (2) ^a
O-4	893 (5)	2678 (2)	10143 (3)	56 (1) ^a
C-5	-707 (7)	2566 (3)	8379 (4)	43 (2) ^a
O-5	-739 (5)	3348 (2)	8796 (3)	60 (2) ^a
C-6	-1446 (6)	2426 (3)	7541 (3)	36 (2) ^a
O-6	-2182 (4)	3095 (2)	7067 (2)	53 (1) ^a
C-7	-1380 (6)	1632 (3)	7119 (3)	42 (2) ^a
O-7	-2082 (5)	1486 (3)	6283 (3)	64 (2) ^a
C-8	-573 (6)	942 (3)	7517 (4)	45 (2) ^a
C-9	154 (6)	1081 (3)	8374 (4)	40 (2) ^a
C-10	109 (6)	1869 (3)	8824 (3)	38 (2) ^a
C-11	-3551 (7)	3465 (4)	7537 (4)	66 (2) ^a
C-12	2411 (9)	-2612 (4)	8254 (5)	74 (3) ^a
C-13	5073 (9)	-436 (5)	12359 (5)	92 (3) ^a
C-1'	2564 (6)	-322 (3)	9844 (3)	40 (2) ^a
C-2'	2520 (6)	-1042 (3)	9287 (4)	43 (2) ^a
C-3'	3341 (7)	-1772 (4)	9540 (4)	51 (2) ^a
O-3'	3424 (6)	-2535 (3)	9063 (3)	74 (2) ^a
C-4'	4251 (6)	-1786 (4)	10370 (5)	57 (2) ^a
O-4'	5113 (6)	-2486 (3)	10638 (4)	84 (2) ^a
C-5'	4239 (6)	-1075 (4)	10931 (4)	54 (2) ^a
O-5'	5116 (5)	-1132 (3)	11735 (3)	81 (2) ^a
C-6'	3427 (6)	-334 (4)	10689 (4)	47 (2) ^a
O-14	4928 (14)	5300 (7)	333 (7)	127 (4)
C-14	6335 (18)	5076 (8)	287 (9)	90 (4)
C-15	7080 (33)	5511 (16)	955 (17)	195 (10)
C-16	5493 (33)	5770 (13)	716 (13)	66 (6)
O-15	7750 (23)	4881 (11)	222 (12)	124 (8)

^aEquivalent isotropic U defined as one third of the trace of the orthogonalized U (i,j) tensor.

(MeOH) λ max nm (ϵ) 342 (33000), 273 (17000) [lit. (11) 348 (33300), 273 (17100)]; ir (CHCl₃) ν max cm⁻¹ 3511, 1659, 1616; ms (70 eV) m/z (rel. int.) [M]⁺ 360 (98), 345 (70), 342 (87), 317 (60), 314 (20), 139 (10), 69 (100) [lit. (11) [M]⁺ 360 (100), 359 (18), 345 (75), 342 (64), 331 (8), 317 (51), 167 (19), 139 (22), 111 (10), 178 (8), 181 (5)]; ¹H nmr see text [lit. (11) (TMS) ether derivative in CC14) 3.88 (2×MeO), 3.71 (MeO), 6.30 (H-3), 6.53 (H-8), 6.89 (H-2' and H-6')]; ¹³C nmr (75.4) (CDCl₃) 55.87 (2×MeO), 59.82 (MeO), 93.73 (C-8), 102.91 (C-10), 103.22 (C-2' and C-6'), 104.23 (C-3), 130.83 (C-6), 138.90 (C-4'), 138.93 (C-7), 147.35 (C-5), 152.30 (C-3'), 152.20 (C-5'), 158.30 (C-9), 163.43 (C-2), 181.83 (C-4).

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