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THE MOLECULAR STRUCTURE OF MANILADIOL FROM *BACCHARIS SALICINA*†

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Key Word Index—*Baccharis salicina*; asteraceae; flavonoid; triterpene; maniladiol; ^{1}H and ^{13}C NMR; molecular structure.

Abstract—From the chloroform extract of *Baccharis salicina,* maniladiol, oleanolic acid, 5, 7, 3′-trihydroxy-3, 6, 4′-trimethoxyflavone (centaureidin) and 5, 7-dihydroxy-3, 6, 3′, 4′-tetramethoxyflavone were isolated. The structure and stereochemistry of maniladiol were confirmed by single crystal X-ray diffraction as olean-12-ene-3β,16 β-diol, which unambiguously established the configuration of the hydroxyl group at C-16 as 16β-OH. © 1998 Elsevier Science Ltd. All rights reserved

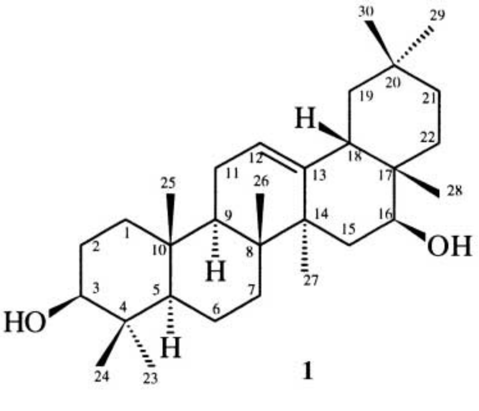
INTRODUCTION

Maniladiol (**1**) is a less common pentacyclic triterpene diol of the oleanane-type which was first isolated from *Manila elemi* (*Canarium luzoricum*, Burseraceae) [1] and more recently from members of the Asteraceae family: *Baccharis myrsinites* [2], *B. heterophylla* [3] and *Helianthus annuus* [4]. It is also a constituent of *Aucoumea klaineana* (Burseraceae) [5], *Gymnosporia trilocularis* (Celastraceae) [6] and several taxa of the Cactaceae [7]. It is also claimed to be a constituent of several *Erythrina* species (Leguminosae) [8–10].

RESULTS AND DISCUSSION

In previous papers we have reported the isolation of sesquiterpene lactones [11] and the crystal structure of the flavonol centaureidin from *Baccharis salicina* [12]. Further analysis of the dichloromethane extract of this plant afforded, besides centaureidin, the known 5, 7-dihydroxy-3, 6, 3′, 4′-tetramethoxyflavone [13], and two pentacyclic triterpenes of the oleanane-type, oleanolic acid and a second one which was identified as maniladiol (**1**). The characterization and identification of maniladiol (**1**) was based on a comparison of the ^{1}H and ^{13}C NMR data with those reported in the literature [3, 5, 6]. The ^{1}H and ^{13}C NMR data (Table 1) of **1** were in good agreement with those reported from the compound isolated from *B. heterophylla* [3], *A. klaineana* [5] and *G. trilocularis* [6], but they differed from those reported for the compound isolated from *Erythrina* species, mainly for H-16 and the carbons in the D-ring [8–10]. The corresponding 3-epimer of maniladiol has been isolated from *Canarium album* [14], and the NMR data for the D-ring were very similar to those of compound **1**.

Since no complete high resolution NMR data are available for compound **1**, we have included all our assignments, which were confirmed by 1D and 2D experiments (DEPT, COSY, NOESY, HMQC and



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†In memory of Dr Lydia Rodríguez-Hahn (1932–1998).

Table 1. ^{1}H-NMR (500 MHz) and ^{13}C-NMR (125 MHz) data for maniladiol (**1**) in $CDCl_3$

δ	C	H	HMBC correlations: ^2J, (^3J)
1	38.58 *t*	1.64, 0.98	(H-25)
2	27.19 *t*	1.62, 1.58	
3	78.97 *d*	3.22 *dd* (11.5, 4.5)	H-2, (H-1, H-23, H-24)
4	38.77 *s*	-	H-5, H-23, H-24
5	55.15 *d*	0.74 *dd* (11.5, 1.5)	(H-1, H-7, H-23, H-24, H-25)
6	18.33 *t*	1.58, 1.41 *dt* (15.5, 12.0)	
7	32.63 *t*	1.54, 1.33	(H-26)
8	39.86 *s*	-	H-7, H-9, H-26, (H-27)
9	46.82 *d* $^{(a)}$	1.51 *dd* (11.0, 6.5)	(H-7, H-12, H-25, H-26)
10	37.31 *s*	–	H-5, H-9, H-25
11	23.51 *t*$^{(b)}$	1.92 *ddd* (18.5, 11.0, 3.5),1.86 *ddd* (18.5, 7.0, 4.0)	H-12
12	122.33 *d*	5.25 *t* (3.5)	H-11, (H-18)
13	143.54 *s*	–	(H-11, H-15, H-18, H-23)
14	43.78 *s*	–	H-27, (H-12, H-18, H-26)
15	35.58 *t*$^{(c)}$	1.67 *dbr* (13.0), 1.31 *dd* (13.0, 5.0)	(H-27)
16	66.01 *d*	4.20 *dd* (11.5, 5.0)	(H-15, H-18, H-28)
17	36.87 *s*$^{(c)}$	–	H-28
18	49.06 *d*	2.15 *dd* (14.0, 4.5)	H-19, (H-12, H-22, H-28)
19	46.53 *t*$^{(a)}$	1.68 *t* (14.0), 1.06 *ddd* (13.5, 4.5, 2.5)	H-18, (H-21, H-29, H-30)
20	30.90 *s*	–	H-29, H-30, (H-22)
21	34.15 *t*	1.36, 1.15	(H-29, H-30)
22	30.54 *t*	1.83, 1.20	(H-28)
23	28.07 *q*	1.00 *s*	(H-3, H-24)
24	15.57 *q*	0.79 *s*	(H-3, H-5)
25	15.54 *q*	0.94 *s*	(H-5)
26	16.83 *q*	0.99 *s*	(H-9)
27	27.11 *q*	1.22 *s*	(H-15)
28	21.46 *q*	0.80 *s*	(H-16)
29	33.23 *q*	0.89 *s*	
30	23.95 *q*$^{(b)}$	0.90 *s*	(H-21, H-29)

(a), (b), (c) assignments reversed in Ref [6].

HMBC). Furthermore, because the reported stereochemistry for maniladiol (**1**) and its C-16-epimer has been ambiguous [6, 15], it was of interest to obtain suitable crystals of **1** for single crystal X-ray analysis. Single crystal X-ray diffraction of compound **1**, isolated from *B. salicina,* confirmed the β-configuration of the hydroxy group at C-16. The data also suggested that the configuration of C-16 for the triterpenes isolated from *Erythrina* species [8–10] must be revised from C-16 βOH to C-16 αOH.

The crystal structure of maniladiol (1)

The crystal structure of **1** is illustrated in Fig. 1, in which the C12=C13 double bond, the *cis*-fusion of the D and E rings, the β-methyl group at C-17, and the β-OH groups at C-3 and C-16 are evident. A search of the Cambridge Structural Database (CSD) [16] for the skeleton found in this molecule revealed that the crystal structures of two compounds have been reported with the same skeleton, having a β-OH group at C-3, a β-C substituent at C-17 and a β-O substituent at C-16. Gymnemagenin [17] has an OH group at C-16 and a hydroxymethyl group at C-17, while 3β,16β-dimethoxy-olean-12-en-28-21β-olide has methoxy and lactone substituents, respectively, at these sites [18]. Also, echinocystic acid diacetate [19] and protoaescigenin-21-tiglate-22-acetate benzene solvate [20] have similar structures, with the O-subsituent at C-16 α-oriented. Both OH groups of compound **1** are involved in intermolecular hydrogen bonds, with O···O distances 2.689(3) and 2.797(3) Å.

EXPERIMENTAL

Plant material

Baccharis salicina T. and G. was collected on April, 1981 on highway 357, 0.2 miles west of intersection with highway 286, near Corpus Christi, Texas (Malcolm-Vargas; voucher deposited at the Herbarium of Louisiana State University).

Extraction and isolation

The air dried plant material (370 g) was extracted with CH_2Cl_2. CC of the crude extract (16.3 g) on silica gel using CH_2Cl_2 and mixtures of CH_2Cl_2–Me_2CO (9:1, 8:2, 6:4) provided 30 fractions. Fractions 5–6 were combined and further purified by CC on silica gel affording 65 mg of maniladiol (**1**), mp 204–205° (lit. [6], 213–214°) and 6 mg of 5,7-dihydroxy-3,6,3′,4′-tetramethoxy, mp 150–152° (lit. [13], 152–153°). Fractions 11–15 were identified as a mixture of oleanolic acid and centaureidin mp 182–184°. Fractions 16–20 were combined and rechromatographed on silica gel affording further amounts of oleanolic acid identified by comparison with an authentic commercially available sample (Aldrich) and centaureidin.

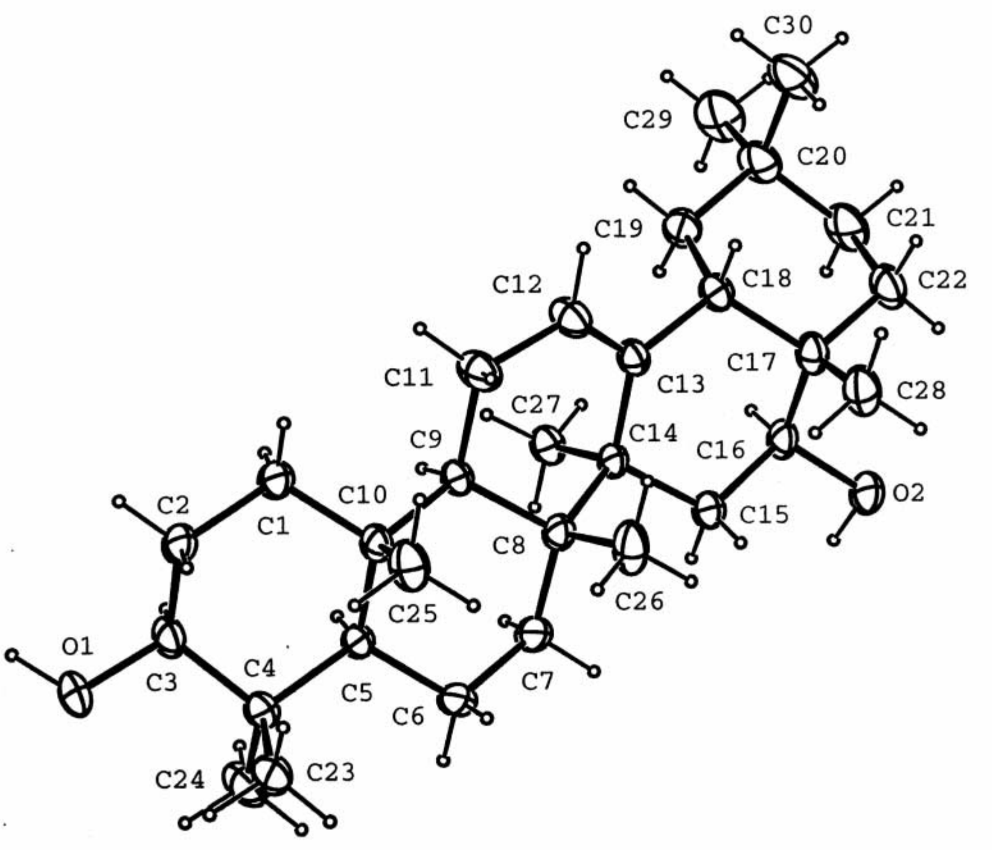

Fig. 1. The molecular strucutre of maniladiol (**1**).

Table 2. Positional parameters and their estimated s.d.s for maniladiol (**4**)

Atom	x	y	z	B_{eq} (Å^2)
O1	0.4042(1)	0	0.4006(1)	5.63(5)
O2	0.0863(1)	−0.2809(2)	−0.4503(1)	5.58(5)
C1	0.4345(1)	0.0187(2)	0.2128(2)	4.44(6)
C2	0.4607(2)	0.0214(3)	0.3212(2)	4.71(7)
C3	0.3804(1)	−0.0093(3)	0.2994(1)	4.59(6)
C4	0.3409(1)	−0.1218(3)	0.2476(2)	4.55(6)
C5	0.3180(1)	−0.1241(2)	0.1389(1)	3.89(5)
C6	0.2709(2)	−0.2267(3)	0.0690(2)	5.34(7)
C7	0.2244(2)	−0.2067(3)	−0.0504(2)	5.47(7)
C8	0.2898(1)	−0.1672(2)	−0.0541(2)	4.09(6)
C9	0.3483(1)	−0.0718(2)	0.0302(1)	3.76(5)
C10	0.3953(1)	−0.0907(2)	0.1520(1)	3.74(5)
C11	0.4145(2)	−0.0287(4)	0.0279(2)	6.01(8)
C12	0.3795(1)	−0.0329(3)	−0.0836(2)	5.17(7)
C13	0.03003(1)	−0.0770(2)	−0.1762(1)	3.80(5)
C14	0.2333(1)	−0.1205(2)	−0.1765(1)	3.60(5)
C15	0.1721(2)	−0.2105(3)	−0.2655(2)	4.45(6)
C16	0.1424(2)	−0.1920(2)	−0.3751(2)	4.41(6)
C17	0.2234(1)	−0.1748(3)	−0.3565(2)	4.47(6)
C18	0.2753(1)	−0.0718(2)	−0.2830(1)	4.10(6)
C19	0.2267(2)	−0.0350(3)	−0.3470(2)	5.28(7)
C20	0.1993(2)	0.0463(3)	−0.4554(2)	5.77(8)
C21	0.1418(2)	−0.0528(4)	−0.5286(2)	6.8(1)
C22	0.1899(2)	−0.1590(3)	−0.4697(2)	5.83(8)
C23	0.4051(2)	−0.2122(3)	0.3305(2)	6.19(8)
C24	0.2518(2)	−0.1313(4)	0.2128(2)	7.2(1)
C25	0.4762(2)	−0.1716(3)	0.2211(2)	5.55(8)
C26	0.3521(2)	−0.2610(3)	−0.0262(2)	6.56(9)
C27	0.1692(1)	−0.0270(3)	−0.2098(2)	4.45(6)

*X-ray data of maniladiol (***1***)*

X-Ray data for (**1**. CH_2Cl_2). A colorless crystal of dimensions $0.20 \times 0.40 \times 0.45$ mm was used for data collection on an Enraf-Nonius CAD4 diffractometer equipped with CuKα radiation (λ = 1.54184 Å), and a graphite monochromator. Crystal data are: $C_{30}H_{50}O_2$. CH_2Cl_2, $M_r = 527.7$, monoclinic space group C2, a = 21.298(6), b = 12.322(4), c = 17.438(5) Å, b = 136.74(2)°, V = 3136(3) Å^3, Z = 4, $d_c = 1.117$ g cm^{-3}, T = 20°C. Intensity data were measured by ω-2θ scans of variable rate. Two quadrants of data were collected within the limits $2 < \theta < 75°$. Data reduction included corrections for background, Lorentz, polarization, and absorption effects. Absorption corrections (μ = 20.5 cm^{-1}) were based on ψ scans, with minimum relative transmission coefficient 78%. Of 6464 unique data, 5338 had $I > 3\sigma(I)$ and were used in the refinement. The structure was solved by direct methods and refined by full-matrix least squares, treating nonhydrogen atoms anisotropically, except for the C atom of the solvent molecule, which was fixed with an isotropic displacement parameter. The displacement parameters of the solvent atoms are quite large (U = 30–50 Å^2) likely as a result of unresolved disorder. The Enraf-Nonius MolEN programs [21] were used for all calculations. Most hydrogen atoms were visible in difference maps but were placed in calculated positions during refinement. Convergence was achieved with $R = 0.069$, $R_w = 0.103$, and $GOF = 3.245$. A model with the reverse absolute configuration was refined under identical circumstances, yielding $R = 0.070$, $R_w = 0.105$, and $GOF = 3.305$. The crystal structure is illustrated in Fig. 1, and the coordinates of the triterpene are tabulated in Table 2.

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