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TWO ISOMERIC GLYCOSIDE SESQUITERPENES FROM *MACHAERANTHERA TANACETIFOLIA*

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Key Word Index—*Machaeranthera tanacetifolia*; Asteraceae; β-eudesmol glycosides; tetracyclic diterpenoid; kaurenoic acid.

Abstract—From the aerial parts of *Machaeranthera tanacetifolia* the known 12-hydroxy-*ent*-kauren-16-en-19-oic acid and the two previously unknown (−)-11-*O*-α-D-arabinopyranosyl-β-eudesmol and (+)-11-*O*-β-L-arabinopyranosyl-β-eudesmol were isolated. The structure elucidation of these compounds was based on spectroscopic and chemical evidences. (+)-11-*O*-β-L-Arabinopyranosyl-β-eudesmol was fully characterized by X-ray analysis of its peracetate derivative. According with these results, we propose that the previously reported (+)-11-*O*-α-L-arabinopyranosyl-β-eudesmol and 11-*O*-α-D-arabinopyranosyl-β-eudesmol are identical to (+)-11-*O*-β-L-arabinopyranosyl-β-eudesmol.

INTRODUCTION

In an earlier study of *Machaeranthera tanacetifolia* (H.B.K.) Ness the presence of (+)-11-*O*-α-L-arabinopyranosyl-β-eudesmol was reported [1]. Since the data presented there showed inconsistencies to support the proposed structure, and as part of our systematic phytochemical study of the Compositae of the Northern region of Mexico [2, 3], we decided to reinvestigate this species.

RESULTS AND DISCUSSION

Chromatographic separation of the hexane extract of the aerial parts of *M. tanacetifolia* afforded the known 12-α-hydroxy-*ent*-kaur-16-en-19-oic acid (**1**) and the glycoside **2**, while the glycoside **3** was obtained by CC from the EtOAc extract. Although **1** have been isolated from *Stevia eupatoria* [4], this is the first report to our knowlegde on the isolation of **1** from *Machaeranthera* genus.

Compound **2** was obtained as white crystals mp 99–102°C, $[\alpha]_D = -13$. It showed characteristic IR absorption bands at 3596 (OH), 1642 (C=C) and 1076 (glycosidic linkage) cm^{-1}. The molecular formula $C_{20}H_{34}O_5$ was deduced from the ^{13}C NMR spectrum and the EIMS mass spectrum showing an $[M-C_5H_9O_5$ ion at m/z 205 and an $[M-C_{20}H_{25}$ ion at m/z 149 which resulted from the cleavage of the glycoside bond. The structure of **2** was deduced primarily by ^1H and ^{13}C NMR, with the aid of COSY and HETCOR spectra where the β-eudesmol and the α-arabinopyranoside groupings were evident [5, 6] (Table 1).

The resonance in ^{13}C NMR of a C—O bonded saturated quaternary carbon at δ 80.8 led us to propose the glycoside link at C-11 of the β-eudesmol. The coupling constant ($J = 6.0$) of the anomeric proton at δ 4.52 in the ^1H NMRspectrum is in agreement with an α-D orientation of the arabinopyranoside residue [7]. Therefore we propose that **2** is the (−)-11-*O*-α-D-arabinopyranosyl-β-eudesmol.

Compound **3** was isolated as white crystals mp 129–130°C, $[\alpha]_D = +37$. The FABMS spectrum and the spectroscopic data (IR, ^1H and ^{13}C NMR) clearly showed that **3** is a diaestereoisomer of **1** (Table 1). Since that the ^1H NMR spectrum of **3**, obtained in $CDCl_3$, showed two overlapped signals at δ 4.43 assigned to one of the vinylic protons of the β-eudesmol group and to the anomeric proton of the sugar moiety, we decided to acquire the ^1H NMR spectrum in C_6D_6, where the vinilyc proton now appeared at δ 4.61 while the anomeric proton appeared as a doublet signal at δ 4.23 ($J = 6.5$ Hz). These results led us to propose the (+)-11-*O*-β-L-arabinopyranosyl-β-eudesmol structure for **3**. The presence of both stereoisomers in *M. tanacetifolia* made it necessary to

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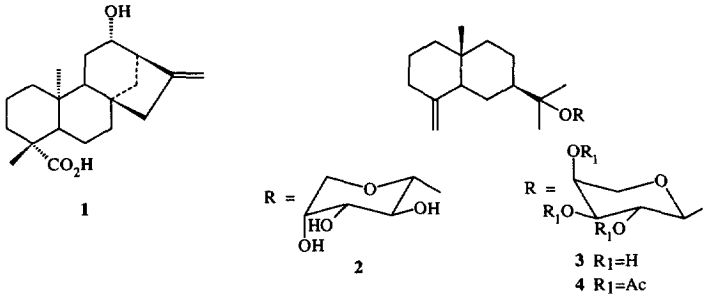

establish unequivocally the configuration of either **2** or **3**. This was achieved by a single-crystal X-ray analysis of the peracetate of **3** (**4**). The results (Fig. 1) confirmed the identity of **3** as (+)-11-*O*-β-L-arabinopyranosyl-β-eudesmol, therefore product **2** is the (−)-11-*O*-α-D-arabinopyranosyl-β-eudesmol. Besides the previous report of a phytochemical study of *M. tanacetifolia* [1], there is another report which deals with the identification of 11-*O*-α-D-arabinopyranosyl-β-eudesmol as a component of a mixture of sesquiterpene glycosides isolated from *Lessingia glandulifera* [6] However, the ^{1}H NMR data available in both reports showed that the signal of the anomeric proton (δ 4.43, J = 5–6 Hz) is overlaped with the signal of one of the vinylic protons of the β-eudesmol residue, then according with our findings, in both cases the compound is the same and corresponds to the (+)-11-*O*-β-L-arabinopyranosyl β-eudesmol.

Table 1. ^{1}H-NMR Chemical shift in ppm and coupling constants (J, Hz) for compounds **2**, **3** and **4**

H	2	3	3*	4
3	2.30 *brd*	2.30 *brd*	2.66 *brd*	2.30 *brd*
12	1.24 *s*	1.22 *s*	1.26 *s*	1.16 *s*
13	1.23 *s*	1.22 *s*	1.22 *s*	1.22
14	0.69 *s*	0.69 *s*	0.796 *s*	0.69 *s*
15a	4.71	4.71	4.83	4.71
15b	4.42	4.43	4.61	4.43
1′	4.50 *d*	4.45 *d*	4.23 *d*	4.45 *dd*
2′	3.66 *m*	3.67 *m*	3.87 *m*	5.16 *dd*
3′	3.69 *m*	3.67 *m*	3.65 *m*	5.05 *dd*
4′	3.92 *m*	3.92 *m*	3.87 *m*	5.24 *m*
$5'_{ax}$	3.53 *dd*	3.50 *dd*	3.25 *dd*	3.63 *dd*
$5'_{eq}$	3.89 *m*	3.87 *m*	3.87 *m*	3.98 *dd*
1′, 2′	5.7	5.1	6.5	7.0
2′, 3′				10.6
3′, 4′				3.9
4′, $5'_{ax}$	3.6	2.0	2.5	1.6
4′, $5'_{eq}$				2.6
$5'_{ax}$, $5'_{eq}$	14.1	11.1	13.1	13.0

* In C_6D_6.

EXPERIMENTAL

Plant material

Aerial parts of *Machaeranthera tanacetifolia* were collected in San Lucas, Durango, México, in August 1990. A voucher specimen (M. Martínez 72) is deposited at the Herbarium of Instituto de Biología, Universidad Nacional Autónoma de México.

Isolation of the constituents of M. tanacetifolia

Dried and ground plant material (413 g) was successively extracted with hexane and EtOAc at room temperature. The extracts were concentrated under vacuum. The hexane extract when chromatographed over silica gel column eluted with mixts of hexane–EtOAc of increasing polarity gave 12-α-hydroxy-*ent*-kaur-16-en-19-oic acid (**1**) [4] (hexane : EtOAc, 8 : 2) and (−)-11-*O*-α-(D)-arabinopyranosyl-β-eudesmol (**2**) (hexane : EtOAc, 1 : 2). Chromatography of the EtOAc extract on silica gel using hexane with increasing proportions of EtOAc gave (+)-11-*O*-β-(L)-arabinopyranosyl-β-eudesmol (**3**) (hexane : EtOAc, 1 : 2).

(−)-11-O-α-D-*arabinopyranosyl-β-eudesmol* (**2**). White crystals, mp 99–102° $[\alpha]_D = -13°$ [*c* 0.042; MeOH]. IR ($CHCl_3$) cm^{-1}: 3596 (OH), 1642 (C=C), 1076 (C—O). EIMS 70 eV *m/z* (rel int.): 297 (1), 296 (7.8), 281 (10.6), 205 [M − arabinose]$^+$ (50), 149 [M − β-eudesmol]$^+$ (50), 133 (99), 115 (45), 109 (100) $\{C_8H_{13}^+\}$, 73 (83). ^{1}H and ^{13}C-NMR see Tables 1 and 2.

(+)-11-O-β-L-*arabinopyranosyl-β-eudesmol* (**3**). White crystals, mp 120–123°. $[\alpha]_D = +37°$ [*c* 1.16; MeOH]. IR ($CHCl_3$) cm^{-1}: 3594 (OH), 1644 (C=C), 1076 (C—O). FABMS *m/z* (rel int.): 377 [M + Na]$^+$, 393 [M + K]$^+$, 355 [M + 1]$^+$, 307 (30), 289 (25), 265 (28), 205 (100), 203 (47), 154.13 (100), 149 (60), 136.13 (100), 133 (65), 109.12 (100), 95.1 (100), 73.03 (75), 55.07 (67), 41.06 (60). ^{1}H and ^{13}C-NMR see Tables 1 and 2.

Peracetate of (+)-11-O-β-L-*arabinopyranosyl-β-eudesmol* (**4**). (+)-11-*O*-β-L-arabinopyranosyl-β-eudesmol (**3**) (45 mg) was acetylated with acetic anh. and pyridine yielding **4** (35 mg) which was recrystallized from hexane–EtOAc, affording white crystals

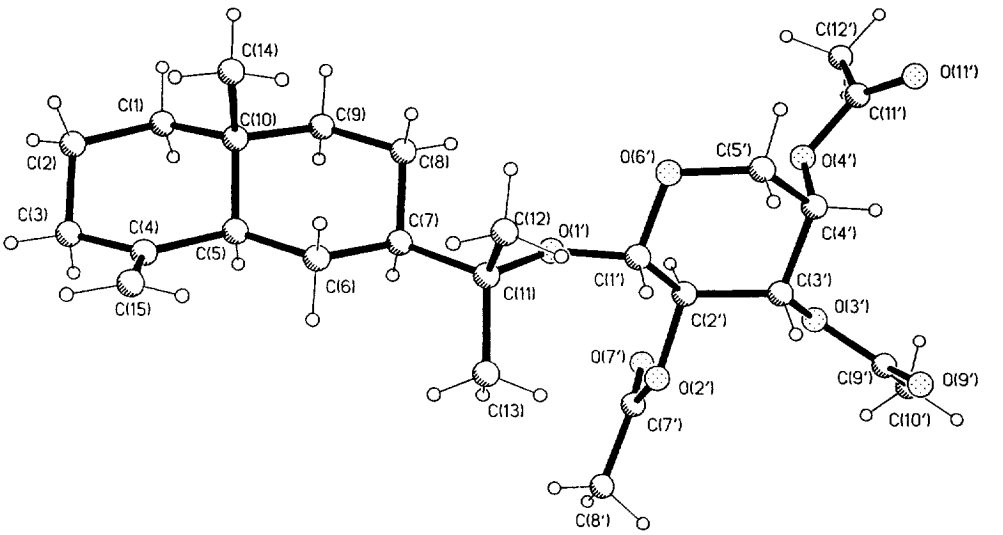

Fig. 1. Perspective view of the molecular structure of **4**

Table 2. ^{13}C-NMR Chemical shift in ppm for compounds **2**, **3** and **4**

Carbon	2	3	4
1	41.0	41.0	41.2
2	22.2	22.2	22.2
3	36.8	36.8	36.8
4	151.0	151.1	151.0
5	49.7	49.8	49.8
6	24.9	25.0	24.6
7	48.3	48.2	48.6
8	23.4	23.4	22.8
9	41.7	41.8	41.8
10	35.5	35.9	35.9
11	80.8	80.6	80.2
12	23.6	23.7	23.4
13	24.2	24.1	24.5
14	16.3	16.3	16.3
15	105.3	105.4	105.3
1′	95.5	96.9	95.3
2′	71.6	71.4	69.8
3′	72.6	72.9	70.5
4′	67.3	67.7	67.9
5′	64.2	64.7	62.7
COMe			170.3
			170.1
			169.1
COMe			20.8
			20.7
			20.5

mp 139°. IR ($CDCl_3$): 1741 (C=O), 1055 (C—O). EIMS 70 eV *m/z* (rel int.): 259 (100), 157 (55), 139 (86.9), 109 (50), 43 (56.9). ^{1}H and ^{13}C-NMR see Tables 1 and 2.

X-ray data of compound **4**

Orthorhombic crystal system, space group $P2_12_12_1$ with $a = 6.028(1)$ Å, $b = 11.954(1)$ Å, $c = 37.867(3)$ Å, $V = 2728.6(4)$ Å^3, $Z = 4$, $D_{calc} = 1.170$ g cm^{-3}. Diffraction measurements were made on a Siemens P4 diffractometer using Cu–K_α radiation. ($\lambda = 1.54178$ Å). Of 2025 reflexions collected, 1047 were observed ($F > 4\sigma$), and corrected for background Lorenz-polarization effect and absorption correction (face-indexed numerical, min/max transmission 0.721/0.982). The structure was solved by directed methods and refined by full-matrix least-squares [8] with anisotropic temperature factor for the non-hydrogen atoms. The hydrogen atoms were included at idealised position, with a fixed temperature factor $U = 0.08$ Å^2. The final $R = 6.66\%$, $Rw = 7.04\%$ for 308 parameters. The final difference Fourier map showed the maximum and minimum values 0.19 eÅ^{-3}/−0.22 eÅ^{-3}. The view of molecule X and the atomic numbering in Fig. 1 show *trans* junction of the sesquiterpene skeleton with a torsion angle between H(5)—C(5)—C(10)—C(14) 179.3 (7)°, and a β-orientation for the substituent at C(7). The sugar moiety presents a chair conformation and according with the CPIs rule the configuration of the carbon atoms C(1)′, C(2)′, C(3)′ and C(4)′ are *S*, *R*, *S* and *S* respectively, therefore the sugar group correspond to a β-L-arabinopyranoside [9]. List of atomic coordinates, thermal parameters, bond lengths and angles, the torsion angles and the calculated and observed factors have been deposited at the Cambridge Crystallographic Data Centre, U.K.

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