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KAURENE DERIVATIVES FROM *LASIANTHEA FRUTICOSA*, REVISION OF STEREOCHEMISTRY OF RELATED COMPOUNDS

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Key Word Index—*Lasianthea fruticosa*; Compositae; kaurene derivatives.

Abstract—Two new kaurene diterpenes, 12α-angeloyloxy and 12α-senecioyloxy-9,11-dehydro-*ent*-kaur-16-en-19-oic acids, have been isolated from *Lasianthea fruticosa*. The structures and stereochemistry of the compounds were determined on the basis of spectroscopic techniques and minor chemical transformation. The stereochemistry of a few similar compounds has been revised.

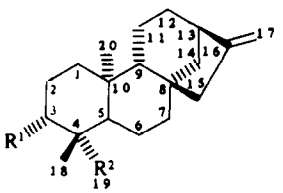
INTRODUCTION

Lasianthea fruticosa R. Becker is a common shrub native in Central America [1]. A sesquiterpene named lasidiol angelate was reported earlier from this plant by Wiemer *et al.* [2]. More recent investigation on this plant by Khan *et al.* [3] afforded five kaur-16-ene diterpenes.

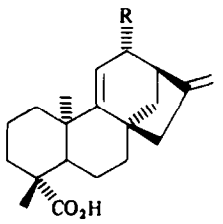
RESULTS AND DISCUSSION

The extract of the aerial parts of *L. fruticosa* yielded in addition to germacrene D, **1** [4], **2** [4], **3** [5], **4** [6] and **5** [7], the new diterpenes **6** and **7**. Surprisingly we could not detect the presence of the sesquiterpene lasidiol angelate.

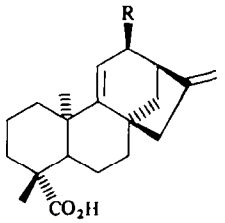
The structure of compounds **6** and **7** followed from the ^{1}H NMR spectral data (Table 1) of the methyl esters **6a** and **7a** obtained upon addition of diazomethane. The spectral data of **6a** differed from those of **7a** only by the signals of the angelate and senecioate ester groups, respectively. Otherwise the spectra of both compounds were similar to that of **5a**. In the case of **6a**, a double doublet at δ5.08 (J = 2.5, 4.5 Hz) which coupled with the olefinic signal at δ5.36 (H-11, J = 1, 4.5 Hz) indicated that the ester group is at C-12. In compounds **11** and **12** [8, 9] a β-configuration for the oxygen function was assigned at C-12, based mainly on the downfield shift of H-17 [8]. On the other hand the epimeric 12-oxykaur-16-enes occurred



	1	2	3	4
R^1	H	H	H	OAng
R^2	CH_2OH	CHO	CO_2H	CO_2H



	5	6	7	8	9	10
R	H	OAng	OSen	OMe	OH	OEt



	11	12
R	OH	OEt

3a–7a are the methyl esters

Table 1. ^{1}H NMR spectral data of compounds **6a**, **7a** and **8** (400 MHz, $CDCl_3$, TMS as int. standard)

H	6a	7a	8
1α	1.91 *m*	*	1.96 *br d*
1β	1.23 *br ddd*	1.22 *m*	1.22 *br ddd*
2α	1.83 *ddddd*	*	1.86 *m*
2β	1.50 *m*	†	1.51 *br d*
3α	2.15 *br d*	2.15 *br d*	2.15 *br d*
3β	1.01 *ddd*	1.00 *ddd*	1.02 *ddd*
5	1.61 *dd*	1.61 *dd*	1.62 *dd*
6α	2.50 *m*	2.49 *m*	2.50 *dddd*
6β	1.87 *m*	*	1.87 *m*
7α	1.52 *m*	†	1.46 *br dd*
7β	2.01 *m*	*	2.03 *ddd*
11	5.36 *dd*	5.32 *dd*	5.37 *dd*
12	5.08 *dd*	5.02 *dd*	3.44 *dd*
13	2.91 *br s*	2.89 *br s*	2.95 *br s*
14α	1.70 *dd*	1.68 *dd*	1.66 *dd*
14β	1.45 *dd*	1.42 *dd*	1.37 *dd*
15α	2.15 *br d*	2.15 *br d*	2.12 *br ddd*
15β	2.43 *br d*	2.43 *br d*	2.41 *br d*
17	4.96 *br s*	4.96 *br s*	4.91 *br s*
17′	5.16 *br s*	5.16 *br s*	5.01 *br s*
18	1.18 *s*	1.19 *s*	1.24 *s*
20	0.96 *s*	0.98 *s*	1.08 *s*
CO_2Me	3.68 *s*	3.66 s	3.41 *s* (OMe)
OR			
3′	6.01 *qq*	5.68 *qq*	
4′	1.95 *dq*	1.88 *d*	
5′	1.87 *dq*	2.17 *d*	

*1.75–2.05 *m*.

†1.45–1.55 *m*.

J [Hz]: 1α,1β = 1β,2α = 2α,2β = 2α,3β = 3α,3β = 13; 1α,2α = 1β,2β = 2α,3α = 2β,3β = 4; 5,6α = 11.5; 5,6β = 8.5; 6α,6β = 7α,7β = 14; 6α,7β = 6β,7α = 6β,7β = 9.5; 11,12 = 4.5; 11,13 = 1; 12,13 = 2.5; 14α,14β = 11; 14α,15β = 3; 15α,15β = 16; 15α,17 = 15α,17′ = 2.5; OAng: 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.5; OSen: 2′,4′ = 2′,5′ = 1.5.

Table 2. ^{13}C NMR spectral data of **6a** and **8** (100 MHz, $CDCl_3$, δ-values)

C	6a	8
1	38.23 *t*	38.17 *t*
2	18.44 *t*	18.35 *t*
3	29.12 *t*	29.03 *t*
4	43.08 *s*	43.43 *s*
5	44.85 *t*	43.81 *d*
6	20.08 *t*	20.07 *t*
7	40.52 *t*	40.60 *t*
8	44.84 *s*	44.66 *s*
9	161.81 *s*	160.28 *s*
10	38.93 *s*	38.94 *s*
11	114.13 *d*	115.42 *d*
12	74.06 *d*	81.79 *d*
13	46.09 *d*	46.17 *d*
14	46.17 *t*	40.60 *t*
15	46.94 *t*	47.17 *t*
16	151.36 *s*	153.00 *s*
17	109.59 *t*	108.12 *t*
18	28.1 *q*	28.22 *q*
19	177.76 *s*	182.98 *s*
20	23.1 *q*	23.41 *q*
CO_2Me	51.3 *q*	56.53 *q* (OMe)
OR		
1′	167.79 *s*	
2′	128.54 *s*	
3′	136.64 *d*	
4′	20.63 *q*	
5′	15.70 *q*	

[9]. For this reason we carefully checked the stereochemistry of the compounds by a NOE experiment. As from the NOE effects of compound **6a** no clear decision was possible, it was hydrolysed by KOH in methanol solution to produce the 12-hydroxy derivative. After usual work-up we obtained a mixture of the corresponding hydroxy (**9**) and methoxy (**8**) compounds (1:1). The multiplicity and the couplings of H-12 signal in the ^{1}H NMR spectrum of **8** indicated the same stereochemistry as in compounds **6a** and **7a**. Compound **8** was probably formed during acidic work-up of the reaction mixture by addition of methanol from the α-side to the allylic cation. The NOE experiment was performed on methoxy compound **8**. Irradiation of H-12 gave a NOE with one of the exomethylene proton (3%) indicating that the ester group at C-12 is α-oriented. Conversely, irradiation of the same exomethylene proton showed an effect with H-12 (4%) and H-13 (4%) and the remaining exomethylene proton (12%). As the splitting of H-12 in the spectra of our compounds and in those of **11** and **12** were identical, the stereochemistry at C-12 in the latter compounds should be revised to compounds **9** and **10**, respectively.

EXPERIMENTAL

The aerial parts of *L. fruticosa* (1 kg, collected in March 1989 in Rincon de la Vieja, Costa Rica, voucher deposited at the National Herbarium of Costa Rica) were extracted with MeOH–Et_2O–petrol (1:2:1) at room temp. for 24 hr. After removing the fatty materials by MeOH treatment, the extract was first separated by CC (silica gel) using solvent mixts comprising petrol, Et_2O and MeOH with increasing polarities. The compounds were further sepd and purified by repeated TLC. The extract yielded 300 mg germacrene D, 500 mg **1**, 500 mg **2**, 6 g **3**, 200 mg **4**, 2 g **5**, 2 g **6** and 200 mg **7**. The structures of the known compounds were determined by comparing their spectral data with those of reference compounds.

12α-*Angeloyloxy*-9,11-*dehydro*-ent-*kaur*-16-*en*-19-*oic acid* (**6**). (Isolated as its methyl ester **6a**); oil, R_f 0.70 (E-PE, 1:4); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (CO_2R); MS *m/z* (rel. int.): 412 $[M]^+$ (8) (calc. for $C_{26}H_{36}O_4$: 412.262), 297 $[M-Me]^+$ (3), 353 $[M-CO_2Me]^+$ (4), 330 $[M-O{=}C{=}C(Me)-CH{=}CH_2]^+$ (54), 329 $[M-C_5H_7O]^+$ (7), 313 $[M-C_5H_7O_2]^+$ (12), 312 $[M-C_5H_8O_2]^+$ (7), 297 $[312-Me]^+$ (10), 83 $[C_5H_7O]^+$ (100); $[\alpha]_D^{24°}$ +123 ($CHCl_3$; *c* 2.5).

12α-*Senecioyloxy*-9,11-*dehydro*-ent-*kaur*-16-*en*-19-*oic acid* (**7**). (Isolated as its methyl ester **7a**); oil; R_f 0.63 (E-PE, 1:4); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (CO_2R); MS *m/z* (rel. int.): 412 $[M]^+$ (3) (calc. for $C_{26}H_{36}O_4$: 412.262), 353 $[M-CO_2Me]^+$ (1), 330 $[M-O{=}C{=}C{=}C(Me)_2]^+$ (56), 329 $[M-C_5H_7O]^+$ (2), 313 $[M-C_5H_7O_2]^+$ (5), 312 $[M-C_5H_8O_2]^+$ (4), 297 $[312-Me]^+$ (4), 83 $[C_5H_7O]^+$ (100); $[\alpha]_D^{24°}$ +76.6 ($CHCl_3$; *c* 0.3).

Compound **6** was hydrolysed with KOH in MeOH soln at 60°

for 1 hr. Usual work-up afforded a mixt. of corresponding 12-hydroxy and methoxy compounds (1:1). On TLC separation we obtained compounds **8** and **9**. Our spectral data of compound **9** were identical to those of the 12-hydroxy compound reported from *Montanoa pteropoda* [8].

12α-*Methoxy*-9,11-*dehydro*-ent-*kaur*-16-*en*-19-*oic acid* (**8**). Oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1695; MS *m/z* (rel. int.): 330 $[M]^+$ (100) (calc. for for $C_{21}H_{30}O_3$: 330.219), 315 $[M-Me]^+$ (28), 298 $[M-HOMe]^+$ (12), 283 $[298-Me]^+$ (12).

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SESQUITERPENE LACTONES FROM *ARTEMISIA RUTIFOLIA*

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Key Word Index—*Artemisia rutifolia*; Compositae; sesquiterpene lactones; guaianolides; germacranolide; eudesmane derivative.

Abstract—The polar fractions of *Artemisia rutifolia* afforded three new guaianolides, a germacranolide and a trihydroxycostic acid methyl ester. Structures were elucidated by high field NMR techniques.

INTRODUCTION

In our previous study of *Artemisia rutifolia* Steph. ex Spreng [1], we obtained from this plant a very polar mixture of lactones, the structures of which were not elucidated. We have re-investigated this fraction from plant material collected in Bulgan-Aimack in Mongolia.

RESULTS AND DISCUSSION

In addition to compounds isolated previously [1], we isolated the guaianolides **1**–**3**, the germacranolide **4** and the eudesmane derivative **5** from the polar column chromatography fractions.

The ^{1}H NMR spectrum of **1** (Table 1) indicated the presence of a guaianolide with a 2,3-double bond by a pair of doublets at δ5.61 and 5.94. As these protons showed no further vicinal couplings, C-1 and C-4 are quarternary. All data agreed with the proposed structure. The stereochemistry was determined by NOED. Clear effects were observed between H-6 and H-15 (5%) but not between H-6 and OH-1, between H-7 and H-5 (6%) as well as between H-15, H-6 (10%) and H-3 (6%).

The ^{1}H NMR spectrum of **2** (Table 1) was similar to that of **1**. However, the exomethylene proton signals were replaced by a singlet at δ1.45 indicating a 10-hydroxyguaianolide. The configuration at C-10 was proposed by comparison with the spectra of similar guaianolides and from biogenetic considerations as several 10α-hydroxyguaianolides were isolated from this species [1].

The ^{1}H NMR spectra of **3** and its acetate **3a** (Table 1) showed that a guaianolide was again present. Spin decoupling indicated a 12,6α-olide with oxygen functions at C-2, C-5 and C-10. Comparison of the chemical shifts of **3** and **3a** with those of related lactones led to the assignment of the configurations at the chiral centres. The