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GERMACRA-1(10),4-DIEN-*CIS*-6,12-OLIDES AND ELEMANOLIDES FROM *MONTANOA ATRIPLICIFOLIA**

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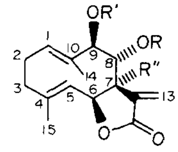
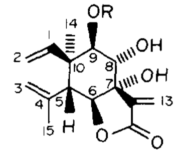
Abstract—The investigation of the aerial parts of *Montanoa atriplicifolia* afforded, in addition to known compounds, two pairs of isomeric *cis*-6,12-germacranolides and three elemanolides closely related to the germacranolides. All seven lactones had a 7-hydroxy group which may be characteristic for this genus The structures were elucidated by spectroscopic methods and a few chemical transformations.

INTRODUCTION

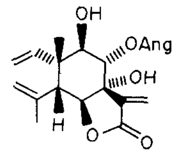
The genus *Montanoa* (tribe Heliantheae) was placed by Stuessy in the subtribe Verbesininae [1], but later transferred to the monogeneric subtribe Montanoinae [2]. To date four species have been studied chemically. All afforded 6,12-germacranolides [3–6] and three of them *ent*-kaurenic acid and derivatives [4, 7]. One species contained unusual diterpenes [8]. We have now investigated a species from Costa Rica, *M. atriplicifolia* (Pers.) Sch Bip. in Seeman The results are discussed in this paper.



	1	2	3	4	5	6
R	H	Ang	H	Sen	Epang	Epang
R'	Ang	H	Sen	H	Ac	Ac
R''	OH	OH	OH	OH	OH	H



7 R = Ang
8 R = Sen



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RESULTS AND DISCUSSION

The aerial parts of *M. atriplicifolia* afforded germacrene D, a mixture of triterpene acetates containing lupeyl and taraxasteryl acetates, *ent*-kaurenic acid and a mixture of sesquiterpene lactones which could be separated only by reversed phase HPLC. Finally, seven lactones were obtained, the germacranolides **1–4** and the related elemanolides **7–9**. All lactones had the same molecular formula, $C_{20}H_{26}O_6$. Two of the germacranolides were angelates and two were senecioates as followed from the typical ^1H NMR signals (Table 1). Each pair of isomeric lactones differed in the relative position of the ester group. The molecular formula indicated that most likely two hydroxyl groups were also present. One of these was obviously at C-7 as in all cases the exomethylene protons displayed singlets and the signal of H-6 was a doublet. The assignment of the latter followed from the results of spin decoupling, which further showed that **1–4** were *trans,trans*-germacra-1(10),4-dien-*cis*-6,12-olides closely related to the lactone, **5**, isolated from *M. hibiscifolia*, its structure being established by X-ray analysis [6]. All data, therefore, agreed with the structures **1–4**.

The ^1H NMR spectra of two lactones isolated from *M. pteropoda* [3] were identical with those of **5** and **6** [6]. Accordingly, the structures of the germacranolides from *M. pteropoda* have to be corrected (H-6β to H-6α).

The elemanolides, **7–9**, were closely related to the germacranolides, **1–3**. Accordingly, Cope rearrangement of **1** and **2** led to the elemanolides, **7** and **9**, identical with the natural compounds.

The ^1H NMR spectra of **7** and **9** (Table 1 indicated that **7** had an 8α-hydroxy group and **9** a 9β-hydroxy group, as followed from the downfield shift of H-13' in the spectrum of **7** if compared with that of **9** The differences in the couplings of H-5 in the spectra of the isomeric lactones showed that the two elemanolides had different preferred conformations, most probably influenced by the configuration at C-10. The large coupling of H-5 in the spectrum of **7** indicated a *trans*-diaxial orientation of the protons of C-5 and C-6 while the spectrum of **9** showed a small coupling of H-5. As the coupling of H-9 indicated an equatorial orientation of the oxygen functions at C-8 and C-9 for both isomers, the only explanation for the

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*Part 473 in the series "Naturally Occurring Terpene Derivatives" For Part 472 see Halim, A F, Zaghloul, A M, Zdero, C and Bohlmann, F (1983) *Phytochemistry* **22** (in press)

Table 1. ^{1}H NMR spectral data of **1–4** and **7–9** (400 MHz, $CDCl_3$, TMS as int. standard)

	1	**2**	**3**	**4**	**7**	**8**	**9**
H-1	5.25 *br dd*	5.50 *br d*	5.23 *ddq*	5.44 *br d*	5.83 *dd*	5.77 *dd*	5.63 *dd*
H-2-(2*c*)	2.23 *m*	2.1–2.4 *m*	2.22 *m*	2.1–2.4 *m*	5.14 *d*	5.12 *d*	5.10 *d*
H-2′-(2*t*)					5.01 *d*	4.99 *d*	4.99 *d*
H-3	1.89 *m*		1.90 *ddd*		5.04 *dq*	5.03 *br s*	5.15 *br s*
H-3′	2.32 *ddd*		2.33 *ddd*		4.77 *br s*	4.77 *br s*	5.06 *br s*
H-5	4.61 *br d*	5.03 *br d*	4.57 *br d*	5.02 *br d*	2.38 *d*	2.38 *d*	2.63 *d*
H-6	4.97 *d*	4.86 *d*	4.96 *d*	4.86 *d*	4.74 *d*	4.73 *d*	4.43 *d*
H-8	4.15 *br d*	5.14 *d*	4.11 *br d*	5.07 *d*	4.13 *br d*	4.07 *br d*	5.10 *d*
H-9	5.15 *d*	4.46 *br d*	5.02 *d*	4.41 *br d*	5.07 *d*	5.00 *d*	3.87 *br d*
H-13	6.48 *s*	6.34 *s*	6.47 *s*	6.35 *s*	6.45 *s*	6.44 *s*	6.33 *s*
H-13′	6.33 *s*	5.81 *s*	6.37 *s*	5.84 *s*	6.16 *s*	6.13 *s*	5.82 *s*
H-14	1.66 *d*	1.70 *br s*	1.64 *d*	1.68 *br d*	1.17 *s*	1.17 *s*	1.28 *s*
H-15	1.72 *d*	1.70 *br s*	1.72 *d*	1.70 *d*	1.79 *br s*	1.80 *br s*	1.83 *br s*
OH	3.05 *br s*	—	2.81 *s*	—	3.29 *br s*	3.34 *br s*	3.33 *br s*
	2.79 *br s*				3.04 *br s*	3.02 *br s*	3.00 *br s*
OR	6.10 *qq*	6.12 *qq*	5.70 *qq*	5.64 *qq*	6.15 *qq*	5.63 *qq*	6.10 *qq*
	1.97 *dq*	1.95 *dq*	2.16 *d*	2.13 *d*	1.99 *dq*	2.17 *d*	1.96 *dq*
	1.88 *dq*	1.86 *dq*	1.89 *d*	1.89 *d*	1.85 *dq*	1.91 *d*	1.83 *br s*

J (Hz): Compounds **1** and **3**: 1,2 = 8.5, 1,14 = 1.5, 2,3 = 3.5, 3,3′ = 12, 5,6 = 10, 5,15 = 1.4, 8,9 = 9; compounds **2** and **4**: 1,2′ = 11, 1,14 = 1.5, 5,6 = 11, 5,15 = 1.5, 8,9 = 9; compounds **7** and **8**: 1,2*c* = 11, 1,2*t* = 17.5, 3,3′ = 3, 15 = 1.5, 5,6 = 11.5, 8,9 = 10; compound **9**: 1,2*c* = 11, 1,2*t* = 17.5, 5,6 = 3.5, 8,9 = 10.5.

coupling of H-5 in **7** was a boat conformation. This could be favoured by the axial vinyl groups which had to be assumed to be in a chair conformation. An isomer with a 10*β*-methyl group would have only one axial vinyl group and, therefore, should be more stable in a chair conformation.

The different position of the ester group in **7**, compared with **9**, was due to *trans*-esterification. This reaction occurred during evaporation of the methanol–water solutions during work-up of the HPLC fractions and at first led to severe confusion. All germacranolide fractions obtained were mixtures, as followed from the ^{1}H NMR spectra. However, when the lactones were isolated from the different fractions by ether extraction pure compounds were isolated. The same *trans*-esterification of **1** and **2**, respectively, occurred by heating in benzene at 70°. Accordingly, we were dealing with a thermal reaction which always led to the formation of an equilibrium mixture. However, only the germacranolides, **1–4**, showed this unusual reaction, the elemanolides, **7–9**, were stable under the same conditions. Most likely, therefore, heating of **2** first led to a mixture of **1** and **2** which underwent Cope reaction from different conformers. Inspection of models showed that the observed coupling $J_{5,6}$ required conformations where the C-4 methyl was below the plane in both **1** and **2**. Most probably a double boat is the preferred conformation of **2** with the C-10 methyl above the plane. A chair boat may be the preferred conformation of **1** with the C-10 methyl below the plane, which may be influenced by a steric interference of the C-10 methyl and C-9 angeloxyloxy groups if the C-10 methyl is above the plane. Hence, Cope reaction of **1** would lead to **9** while **2** would be transformed to **7**. Conformers of **1** and **2** with the C-4 methyl group above the plane would lead to isomers of **7** and **9** which should display other ^{1}H NMR spectral data. Those of **8** showed only very small differences to those of **7** except for the signals of the ester residue which clearly showed the presence of a senecioate.

These additional results on the chemistry of the genus *Montanoa* showed that *cis*-6,12-germacranolides, especially those with a 7α-hydroxy group, may be characteristic for this genus. So far *cis*-6,12-germacranolides have only been reported from *Ursinia* species [9, 10], a genus which is not related at all to *Montanoa*.

EXPERIMENTAL

The air-dried aerial parts (530 g) collected December 1981, near San Pedro, Costa Rica (voucher 81/5), were extracted with Et_2O–petrol (1:2) and the extract obtained was separated first by CC (Si gel) and further by repeated TLC (Si gel) affording 10 mg germacrene D, 1 g of a triterpene acetate mixture containing lupeyl- and taraxasteryl acetate, 1 g *ent*-kaurenic acid and, with Et_2O–MeOH (1:1), 100 mg of a mixture of sesquiterpene lactones which could not be separated by TLC. HPLC (reversed phase, MeOH–H_2O, 3:2) afforded 15 mg **1**, 12 mg **2**, 6 mg **3**, 7 mg **4**, 6 mg **7**, 2 mg **8** and 8 mg **9**. Direct evaporation of the MeOH–H_2O fractions, containing **1–4** *in vacuo*, afforded mixtures of **1** and **2** or **3** and **4**. Repeated separations and extractions with Et_2O gave pure samples. The lactones could not be induced to crystallize.

9β-Angeloyloxy-7α, 8α-dihydroxy-trans,trans-*germacra*-1(10), 4-*dien*-cis-6,12-*olide* (**1**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1765 (γ-lactone), 1715, 1650 (C=CCO_2R), MS *m/z* (rel. int.): 362.173 $[M]^+$ (0.5) ($C_{20}H_{26}O_6$), 262 $[M - RCO_2H]^+$ (1), 244 $[262 - H_2O]$ (4), 229 $[244 - Me]^+$ (1), 83 $[C_4H_7CO]^+$ (100), 55 $[83 - CO]^+$ (92). CD (MeCN)$\Delta\varepsilon_{267}$ +0.76. 8 mg **1** in 0.5 ml C_6D_6 was heated in a sealed NMR tube initially at 70°. The ^{1}H NMR spectrum showed the presence of an equilibrium of **1** and **2**. Further heating at 200° for 15 min afforded a mixture of **7** and **8** (*ca* 1:1), identical with the natural lactones.

8α-Angeloyloxy-7α, 9β-dihydroxy-trans,trans-*germacra*-1(10), 4-*dien*-cis-6,12-*olide* (**2**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1770 (γ-lactone), 1710, 1645 (C=CCO_2R), MS *m/z* (rel. int.): 362.173 $[M]^+$ (0.2) ($C_{20}H_{26}O_6$), 83 $[C_4H_7CO]^+$ (100).

9β-Senecioyloxy-7α, 8α-dihydroxy-trans,trans-*germacra*-1(10), 4-*dien*-cis-6,12-*olide* (**3**) Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600 (OH), 1765 (γ-lactone), 1725, 1655 ($C=CCO_2R$), MS *m/z* (rel int) 362 173 $[M]^+$ (0 3) ($C_{20}H_{26}O_6$), 344 $[M-H_2O]^+$ (0 1), 262 $[M-RCO_2H]^+$ (1), 244 $[262-H_2O]^+$ (2), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (30)

8α-*Senecioyloxy*-7α, 9β-*dihydroxy*-trans,trans-*germacra*-1(10), 4-*dien*-cis-6,12-*olide* (**4**) Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3570 (OH), 1765 (γ-lactone), 1715, 1645 ($C=CCO_2R$), MS *m/z* (rel int) 362.173 $[M]^+$ (0 1) ($C_{20}H_{26}O_6$), 262 $[M-RCO_2H]^+$ (1), 244 $[262-H_2O]^+$ (3), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (32)

9β-*Angeloyloxy*-7α, 8α-*dihydroxy*-10-epi-*eleman*-cis-6, 12-*olide* (**7**) Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600 (OH), 1770 (γ-lactone), 1725, 1650 ($C=CCO_2R$), MS *m/z* (rel int) 362 173 $[M]^+$ (0 5) ($C_{20}H_{26}O_6$), 262 $[M-RCO_2H]^+$ (0 5), 244 $[262-H_2O]^+$ (1 5), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (44), CD (MeCN)$\Delta\varepsilon_{261}$ + 3 7

9β-*Senecioyloxy*-7α, 8α-*dihydroxy*-10-epi-*eleman*-cis-6, 12-*olide* (**8**) Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600 (OH), 1770 (γ-lactone), 1720, 1655 ($C=CCO_2R$), MS *m/z* (rel int) 362 173 $[M]^+$ (0 5) ($C_{20}H_{26}O_6$), 83 $[C_4H_7CO]^+$ (100)

8α-*Angeloyloxy*-7α,9β-*dihydroxy*-*eleman*-cis-6,12-*olide* (**9**) Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600 (OH), 1775 (γ-lactone), 1720, 1655 ($C=CCO_2R$), MS *m/z* (rel int) 362 173 $[M]^+$ (0 5) ($C_{20}H_{26}O_6$), 83 $[C_4H_7CO]^+$ (100), CD (MeCN)$\Delta\varepsilon_{263}$ + 2 3

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