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SESQUITERPENE LACTONES OF *MONTANOA GUATEMALENSIS* AND *MONTANOA TOMENTOSA* SUBSP. *XANTHIIFOLIA**

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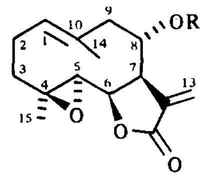
Key Word Index—*Montanoa guatemalensis*; *M. tomentosa* subsp. *xanthiifolia*; Asteraceae; Heliantheae; sesquiterpene lactones; germacranolides.

Abstract—New 4,5-epoxygermacra-12,6β-olides from *Montanoa guatemalensis* and a Guatemalan disjunct collection of *M. tomentosa* subsp. *xanthiifolia* are reported. These compounds were unlike those from the 10 other Mexican collections of *M. tomentosa* previous investigated.

INTRODUCTION

In continuation of our biochemical systematic analysis of *Montanoa* Cerv. (Asteraceae), the sesquiterpene lactones of *Montanoa guatemalensis* Robins. and Greenm. and a Guatemalan disjunct population of *M. tomentosa* subsp. *xanthiifolia* (Sch. Bip. in C. Koch) V. A. Funk were identified. Whereas other Mexican collections of *M. tomentosa* subsp. *xanthiifolia*, *tomentosa* and *rosei* (Rose ex Robins. and Greenm.) V. A. Funk almost exclusively produced 5α-hydroxyguaian-12,6α-olides [1; Quijano, L., personal communication], the Guatemalan collection of *M. tomentosa* subsp. *xanthiifolia* produced 4β,5α-epoxy-*trans*-germacra-1(10)-en-12,6β-olides and derivative compounds. The *M. tomentosa* subsp. *xanthiifolia* collection produced compounds **1**, **3**, **5** and **6** and the *M. guatemalensis* collection yielded **2** and **4**. Compounds **1** and **2** differ from structures reported earlier from *M. mollissima* Brongniart ex Groenland and *M. revealii* H. Robinson [2] only in the ester function at C-8. Like the earlier reported structures from *M. pteropoda* Blake [3, 4] and *M. hibiscifolia* (Benth.) Sch.-Bip. [4], the *M. tomentosa* subsp. *xanthiifolia* and *M. guatemalensis* *trans,trans*-germacra-1(10),4-dien-12,6β-olides co-occur with their 7α-hydroxy derivatives.



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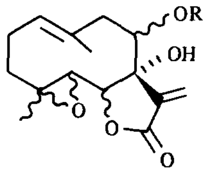
2 R = Epoxyang



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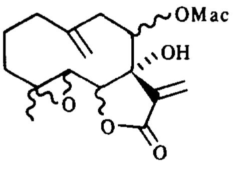
4 R = Epoxyang



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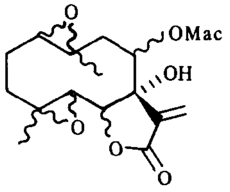

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Mac = Methacrylate
Epoxyang = Epoxyangelate

RESULTS AND DISCUSSION

The ^{1}H NMR spectrum of **1** ($C_{19}H_{24}O_5$, HRMS) displayed $J_{7,13} = 1$ Hz, $J_{5,6} = 10$ Hz and $J_{6,7} = 6$ Hz values, typical of germacra-12,6β-olides. Irradiation of a broad doublet of a doublet at δ3.22 (H-7) collapsed the pair of doublets at δ5.67 (H-13a) and 6.29 (H-13b) to singlets and the doublet of a doublet at δ4.07 (H-6) to a doublet ($J = 10$ Hz) and resolved the multiplet at δ5.27 (H-8) to a doublet of a doublet ($J_{8,9a} \approx 9$ Hz, $J_{8,9b} \approx 3$ Hz). Irradiation of the δ4.07 signal collapsed the H-7 signal to a broad doublet ($J = 5$ Hz) and a broad doublet at δ3.05 (H-5) to a broad singlet. Irradiation of a broad triplet at δ5.44 (H-1) sharpened a vinylic methyl signal at δ1.83 (H-14). A second vinylic methyl at δ1.89 and a pair of quartets at δ5.54 and 6.04 were assigned to the methacrylate. HRMS confirmed the presence of a molecular ion at m/z 332 ($C_{19}H_{24}O_5$), while the low resolution EIMS displayed peaks corresponding to the loss of methacrylic acid (m/z 246) and the m/z 69 (100.0, rel. int.) and m/z 41 (31.7) peaks typical of the methacrylate. ^{1}H NMR spectra (Table 1) and EIMS of **2** are identical to **1** in all respects except for signals associated with the C-8 ester function. An epoxyangelate (2,3-epoxy-2-methylbutyrate) moiety is indicated for compound **2**.

In the ^{1}H NMR spectrum (deuterochloroform) of **3** ($C_{19}H_{24}O_6$, HRMS) the H-13 signals appeared as singlets at δ5.74 and 6.27 (geminal coupling of less than 0.5 Hz

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*Part 5 in the series "*Montanoa*—Terpenes". For Part 4, see ref. [1].

Table 1. ^{1}H NMR signals for compounds **1–6** [200 MHz, TMS as int. standard, deuterochloroform, δ-values (ppm)]

H No.	**1**	**2**	**3**	**4**	**5**	**5** (deutero-benzene)	**6**
H-1	5.44 *br t* (7.5)†	5.43 *br t* (7.5)	5.65 *m*	5.64 *m*	*	*	3.14 *dd* (10.0, 8.0)
H-2	2.1–2.4	*	*	*	*	*	*
H-3	*	*	*	*	*	*	*
H-5	3.05 *br d* (10.0)	2.96 *br d* (9.5)	2.87 *d* (9.5)	2.80 *d* (9.5)	1.93 *d* (11.5)	1.72 *d* (11.5)	2.88 *d* (11.0)
H-6	4.07 *dd* (10.0, 5.0)	4.05 *dd* (5.5, 9.5)	3.88 *d* (9.5)	3.88 *d* (9.5)	4.48 *d* (11.5)	4.14 *d* (11.5)	3.87 *d* (11.0)
H-7	3.22 *br dd* (5.0, 8.0)	3.22 *tdd* (1.0, 6.0, 7.5)	—	—	—	—	—
H-8	5.27 *m*	5.28 *m*	5.16 *m*	5.20 *m*	5.07 *dd* (10.5, 2.0)	5.04 *d* (10.5, 2.0)	5.13 *dd* (11.5, 2.0)
H-9a	*	*	*	*	2.48 *dd* (14.0, 2.0)	2.36 *dd* (14.0, 2.0)	2.14 *dd* (11.5, 13.5)
H-9b	*	*	*	*	2.89 *dd* (10.5, 14.0)	2.80 *dd* (10.5, 14.0)	2.28 *dd* (13.5, 2.0)
H-13a	5.67 *d* (1.0)	5.72 *d* (1.0)	5.74	5.79	5.87	5.42	5.80
H-13b	6.29 *d* (1.0)	6.32 *d* (1.0)	6.27	6.37	6.41	6.15	6.24
H-14a	1.83 [3H] *br*	1.82 [3H] *br*	1.80 [3H] *br*	1.80 [3H] *br*	4.97 [2H] *br*	4.78 *br*	1.46 [3H]‡
H-14b	—	—	—	—	—	4.80 *br*	—
H-15	1.31	1.30	1.34	1.34	1.40	1.17	1.41 [3H]‡
H-2′	—	—	—	—	—	—	—
Me-2′	1.89 *br s*	1.47	1.88 *br*	1.47	1.97 *br s*	1.76 *qq* (1.5, 1.0)	1.82 *br*
H-3′a	5.54 *q* (1.5)	2.99 *q* (6.0)	5.48 *q* (1.5)	2.98 *q* (6.0)	5.67 *q* (1.5)	5.23 *q* (1.5)	5.64 *q* (1.5)
H-3′b	6.04 *q* (1.0)	—	6.05 *q* (1.0)	—	6.14 *q* (1.0)	5.95 *q* (1.0)	6.10 *q* (1.0)
Me-3′	—	1.31 *d* (6.0)	—	1.27 *d* (6.0)	—	—	—

*Obscured by other signals.
†Values in parentheses refer to J in Hz.
‡Interchangeable signals.

was evident in the slight splitting of these signals). When irradiated, the doublet at δ3.88 (H-6, $J = 9.5$ Hz) collapsed another doublet at δ2.87 (H-5). The doublet of a doublet at δ5.22 (H-8) was broadened due to the existence of more than one conformational isomer for **3** at 55°. The low resolution EIMS and CIMS fragmentation patterns reinforce the proposed formula for compound **3**. The similarity of the ^{1}H NMR spectra of **3** and **4** and the substitution of signals characteristic of an epoxyangelate moiety in **4** for the methacrylate signals present in the spectrum of **3** support the assigned structure for compound **4**. The low resolution EIMS results for **4** showed the expected sequence of losses of epoxyangelic acid (*m/z* 262) and water (*m/z* 244) as well as diagnostic fragments for epoxyangelate (*m/z* 71 and 43). The absence of H-7 in **3** and **4** restricts the use of ^{1}H NMR data in proposing stereochemistry at C-4–C-6 and C-8. Further, the absence of a cyclodecadiene system excluded the use of CD in the determination of stereochemistry. Co-occurrence of **1** with **3** and **2** with **4** suggests that **3** and **4** are merely the respective hydroxy derivatives of **1** and **2**, a relationship which parallels the situation reported for germacra-12,6β-olides in single collections of *M. pteropoda* and *M. hibiscifolia* [4].

The ^{1}H NMR spectral differences between **3** and **5** indicate that they are double bond isomers, differing in the migration of the 1(10)-double bond to an exocyclic position at C-10. The absence of the downfield H-1 signal and the Me-10 singlet and the presence of a two-proton broadened singlet at δ4.97 in the spectrum of **5** support the assigned C-10 exocyclic methylene. Also consistent with this assignment is the shift of the H-5 doublet $\Delta\delta$0.9 upfield and the H-6 doublet $\Delta\delta$0.4 downfield relative to their positions in the spectrum of compound **3**. The signals for H-13a and H-13b appeared as sharp singlets at δ5.87 and 6.41, respectively. Irradiation of a doublet of a doublet at δ5.07 (H-8) collapsed two upfield doublets of doublets at δ2.89 (H-9b; $J = 10.5$, 14.0 Hz) and 2.48 (H-9a; $J = 2.0$, 14.0 Hz) to doublets ($J = 14.0$ Hz). Irradiation of the H-9b signal collapsed the doublet of doublets at δ2.48 and 5.07 to doublets with equal coupling constants ($J = 2.0$ Hz). Finally, irradiation of the H-6 doublet at δ4.48 ($J = 11.5$) collapsed another doublet at δ1.93 (H-5). The low resolution EIMS of **5** displayed the same high mass fragmentation pattern as compound **3**: *m/z* 262 (3.3, rel. int.), 244 (16.7) and 226 (16.0).

There were two major differences between the ^{1}H NMR spectra of compounds **3** and **6**: (1) the H-1 broad doublet of a doublet was shifted from δ5.65 (**3**) to 3.14 where it was sharpened; (2) the Me-10 signal was shifted from δ1.80 (**3**) to 1.46, where it was also sharpened. The prominent high-mass EIMS peaks at *m/z* 278 $[\mathrm{M} - \mathrm{C_4H_6O_2}]^+$ and *m/z* 260 $[\mathrm{M} - \mathrm{C_4H_6O_2} - \mathrm{H_2O}]^+$ indicated that **6** ($\mathrm{C_{19}H_{24}O_7}$) differs from **3** by one oxygen. Epoxidation of the 1(10)-double bond of **3** yielded compound **6**, which is consistent with the above data.

EXPERIMENTAL

For general procedures see ref. [5]. NMR spectra were recorded on Hitachi–Perkin–Elmer R600A 60 MHz and Bruker 200 MHz FT spectrometers. Low resolution MS were obtained on a Hewlett–Packard Model 9585 GC/MS system and HRMS data on an AEl MS902 instrument.

M. tomentosa subsp. *xanthiifolia* (FL 2918, OS) was collected 1.7 miles N. of Rio Blanco on the road to Nebaj (Quiché, Guatemala) on 28 November 1978. The whole dried leaf, stem and head material (67.0 g) was extracted twice in $\mathrm{CH_2Cl_2}$ for 2 min and worked-up in the usual fashion [5], yielding 1.54 g syrup, 0.5 g of which was chromatographed by prep. TLC (silica gel; 0.5 mm × 20 cm × 20 cm; developed twice in $\mathrm{CHCl_3}$–$\mathrm{Me_2CO}$, 95:5) yielding a band containing **1** (8 mg) and a second band which, upon further prep. TLC yielded **3** (8 mg). CC over silica gel of the remaining syrup using first $\mathrm{CHCl_3}$ as eluant and then $\mathrm{CHCl_3}$ with increasing amounts of $\mathrm{Me_2CO}$ produced two fractions, 27 and 28, which upon further prep. TLC yielded **6** (15 mg) and **5** (10 mg), respectively.

M. guatemalensis (F3056, OS) was collected *ca* 6 km S. of Monte Verde (Puntarenas, Costa Rica) on 10 January 1980. The whole dried leaf, stem and head material (90.0 g) was worked-up according to the above procedure. CC of the crude syrup (1.2 g) over silica gel (eluant: $\mathrm{CHCl_3}$ followed by a $\mathrm{CHCl_3}$–$\mathrm{Me_2CO}$ mixture) yielded two sesquiterpene lactone-containing fractions: fraction 22 contained 15 mg **2** which was purified by additional prep. TLC; fraction 35 contained 11 mg **4**.

8α-Methacryloyloxy-4β,5α-epoxy-trans-*germacra*-1(10)-*en*-12,6*β-olide* (**1**). Colourless gum, UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 201 (ε1.3 × 10^4); IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1} 2940 (C–H), 2880 (C–H), 1775 (γ-lactone), 1715 (ester), 1645 (C=C), 1150, 1080 (C–O); MS *m/z* (rel. int.): 332 $[\mathrm{M}]^+$ ($\mathrm{C_{19}H_{24}O_5}$) (not observed), 246 $[\mathrm{M} - \mathrm{C_4H_6O_2}]^+$ (10.9), 231 (1.1), 188 (16.7), 163 (20.6), 148 (24.2), 147 (28.5), 69 (100.0), 41 (31.7). [Calc. for $\mathrm{C_{19}H_{24}O_5}$: 332.1624. Found: (MS) 332.1635. Calc. for $\mathrm{C_{15}H_{18}O_3}$: 246.1255. Found: (MS) 246.1256.]

8α-(2,3-*Epoxy-2-methylbutyryloyloxy*)-*4β,5α-epoxy*-trans-*germacra*-1(10),-*en*-12,6*β-olide* (**2**). Colourless gum, UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 206 (ε1.2 × 10^4); IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2970 (C–H), 2880 (C–H), 1770 (γ-lactone), 1715 (ester), 1420, 1325, 1145, 1085 (C–O), 1030, 985, 930, 875, 840; MS *m/z* (rel. int.): 362 $[\mathrm{M}]^+$ ($\mathrm{C_{20}H_{26}O_6}$) (not observed), 263 (0.5), 246 $[\mathrm{M} - \mathrm{C_5H_8O_3}]^+$, 231 $[\mathrm{M} - \mathrm{C_5H_8O_3} - \mathrm{Me}]^+$ (1.9), 215 (3.2), 188 (7.2), 163 (17.3), 148 (20.3), 147 (28.5), 69 (100.0), 41 (31.7).

7α-Hydroxy-8-methacryloyloxy-4,5-epoxy-trans-*germacra*-1(10)-*en*-12,6-*olide* (**3**). Colourless gum, UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 202 (ε2.38 × 10^4); IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2940 (C–H), 2870 (C–H), 1770 (γ-lactone), 1720, (ester), 1665 (C=C), 1625 (C–O), 1265, 1155; MS *m/z* (rel. int.): 348 $[\mathrm{M}]^+$ ($\mathrm{C_{19}H_{24}O_6}$) (not observed), 262 $[\mathrm{M} - \mathrm{C_4H_6O_2}]^+$ (2.6), 244 $[\mathrm{M} - \mathrm{C_4H_6O_2} - \mathrm{H_2O}]^+$ (2.3), 187 (3.1), 186 $[\mathrm{M} - \mathrm{C_4H_6O_2} - \mathrm{H_2O} - \mathrm{C_3H_6O}]^+$ (4.7), 162 (28.5), 83 (39.4), 69 (100.0), 55 (15.7), 41 (21.9); CIMS (isobutane): 349 $[\mathrm{M} + 1]^+$, 331 $[\mathrm{M} + 1 - \mathrm{H_2O}]^+$, 263 $[\mathrm{M} + 1 - \mathrm{C_4H_6O_2}]^+$, 245 $[\mathrm{M} + 1 - \mathrm{C_4H_6O_2} - \mathrm{H_2O}]^+$. [Calc. for $\mathrm{C_{19}H_{24}O_6}$: 348.1573. Found: (MS) 348.1583. Calc. for $\mathrm{C_{15}H_{18}O_4}$ $[\mathrm{M} - \mathrm{C_4H_6O_2}]^+$: 262.1204. Found: (MS) 262.1200. Calc. for $\mathrm{C_{15}H_{16}O_3}$ $[\mathrm{M} - \mathrm{C_4H_6O_2} - \mathrm{H_2O}]^+$: 244.1099. Found: (MS) 244.1119.]

7α-Hydroxy-8-(*2,3-epoxy-2-methylbutyryloyloxy*)-*4,5-epoxy*-trans-*germacra*-1(10)-*en*-12,6-*olide* (**4**). Colourless gum, UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 205 (ε1.6 × 10^4); IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3300, 2880 (C–H), 2370, 1770 (γ-lactone), 1730 (ester), 1660 (C=C), 1610 (C=O), 1440, 1380, 1325, 1260, 1140, 1115, 1075, 990, 870; MS *m/z* (rel. int.): 378 $[\mathrm{M}]^+$ ($\mathrm{C_{20}H_{26}O_5}$) (not observed), 279 $[\mathrm{M} - \mathrm{C_5H_7O_2}]^+$ (6.1), 262 $[\mathrm{M} - \mathrm{C_5H_8O_3}]^+$ (3.3), 244 $[\mathrm{M} - \mathrm{C_5H_8O_3} - \mathrm{H_2O}]^+$ (6.3), 233 (5.9), 229 $[\mathrm{M} - \mathrm{C_5H_8O_3} - \mathrm{H_2O} - \mathrm{Me}]^+$ (3.2), 215 (10.0), 187 (11.3), 186 (11.1), 183 (30.0), 182 (38.5), 167 (48.9), 162 (69.2), 149 (25.8), 109 (58.2), 99 (24.2), 71 $[\mathrm{C_4H_7O}]^+$ (47.8), 43 (100.0).

7α-Hydroxy-8-methacryloyloxy-4,5-epoxygermacra-10(14)-*en*-12,6-*olide* (**5**). Colourless gum, UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 207 (ε1.6 × 10^4); IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3500, 2870 (C–H), 1760 (γ-lactone), 1710 (ester), 1440, 1375, 1290, 1140, 1010; MS *m/z* (rel. int.): 348 $[\mathrm{M}]^+$ ($\mathrm{C_{19}H_{24}O_6}$) (not observed), 330 $[\mathrm{M} - \mathrm{H_2O}]^+$ (0.5), 262 $[\mathrm{M} - \mathrm{C_4H_6O_2}]^+$ (3.3), 244 $[\mathrm{M} - \mathrm{C_4H_6O_2} - \mathrm{H_2O}]^+$ (16.7), 235 (4.5), 226 (16.0), 211 (6.3), 186 (52.2), 173 (21.7), 105 (43.0), 69 (100.0), 41 (32.4).

7α-Hydroxy-8-methacryloyloxy-4,5,1,10-*diepoxygermacra*-12,6-*olide* (**6**). Colourless gum, UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 207 (7.0 × 10^3); IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1775, (γ-lactone), 1710 (ester), 1450, 1320, 1290, 1145, 995; MS *m/z* (rel. int.): 364 $[\mathrm{M}]^+$ ($\mathrm{C_{19}H_{24}O_7}$) (not observed), 278 $[\mathrm{M} - \mathrm{C_4H_6O_2}]^+$ (1.8), 260 $[\mathrm{M} - \mathrm{C_4H_6O_2} - \mathrm{H_2O}]^+$ (1.0), 235 (3.5), 219 (5.4), 165 (16.3), 152 (13.4), 125 (31.0), 95 (67.6), 69 $[\mathrm{C_4H_5O}]^+$ (100.0), 41 $[\mathrm{C_3H_5}]^+$ (18.7).

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