

## FURTHER 6,12-CIS-GERMACRANOLIDES AND EUDESMANOLIDES FROM MONTANOA SPECIES

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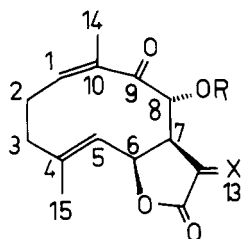
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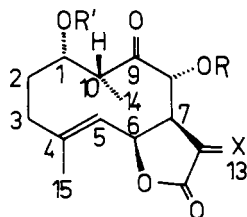
**ABSTRACT.**—The aerial parts of *Montanoa bibiscifolia* afforded, in addition to known compounds, twelve new germacranolides, all being 6,12-*cis*-lactones, as well as a new type of sesquiterpene lactone, obviously closely related to one of the germacranolides. Furthermore, a new prostaglandin-like compound was found together with one previously known. From *Montanoa dumicola* two 6,12-*cis*-germacranolides, as well as two 6,12-*cis*-eudesmanolides and a geranyl phloracetophenone derivative, were isolated. The structures and the stereochemistry of all compounds were elucidated by their pmr spectral data. Biogenetic relationships are discussed briefly.

*Montanoa bibiscifolia* (Benth.) Sch. Bip. (Compositae, tribe Heliantheae, subtribe Montanoinae) has been studied previously leading to the isolation of three *trans,trans*-germacra-1(10),4-dien-*cis*-6,12-olides (1), which at that time were rare and reported simultaneously from only an *Ursinia* species (2). Similar lactones are also present in *Montanoa pteropoda* and *Montanoa atriplicifolia* (3). We have studied again *M. bibiscifolia*, now collected in Costa Rica along with *Montanoa dumicola* Klatt. In addition to one of the lactones isolated previously, seventeen new ones were identified.

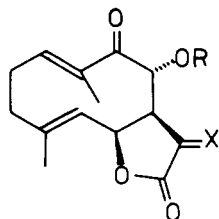
The aerial parts of *M. bibiscifolia* from Costa Rica afforded, after careful separation of the extract, in addition to widespread compounds (see Experimental), the epoxy angelate **13** (1), together with the germacranolides **1-12**, the lactone **14**, and the prostaglandin-like compounds **21** (4) and **22**. The structure of **13** clearly followed from



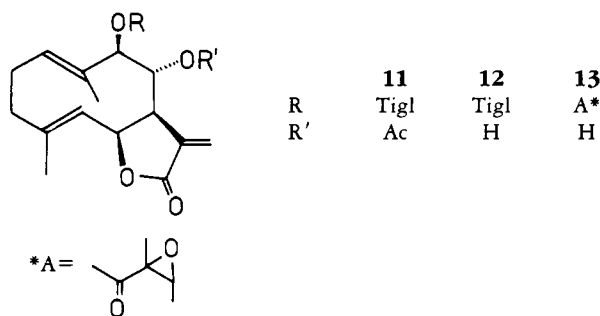
	<b>1</b>	<b>2</b>	<b>3</b>
R	A*	epiA*	A*
X	=CH <sub>2</sub>	=CH <sub>2</sub>	βMe, H



	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>
R	A*	epiA*	A*	A*
R	Me	Me	H	Me
X	=CH <sub>2</sub>	=CH <sub>2</sub>	=CH <sub>2</sub>	βMe, H



	<b>8</b>	<b>9</b>	<b>10</b>
R	A*	epiA*	A*
X	=CH <sub>2</sub>	=CH <sub>2</sub>	βMe, H

TABLE 1. Pmr Spectral Data of **8-12** (400 MHz, CDCl<sub>3</sub>, TMS as Internal Standard)<sup>a</sup>

	<b>8</b>	<b>9</b>	<b>10</b>	<b>11</b>	<b>12</b>
H-1 . . . . .	6.42 br dd	6.47 br d	6.54 br dd	5.48 ddq	5.33 br dd
H-2 . . . . .	} 2.60 m	2.60 m	2.60 m	2.24 m	2.19 m
H-2' . . . . .					
H-3 . . . . .	2.46 ddd	2.47 ddd	2.49 ddd	2.32 ddd	2.28 ddd
H-3' . . . . .	2.37 ddd	2.35 ddd	2.35 ddd	2.08 ddd	2.00 ddd
H-5 . . . . .	} 5.14 m	5.11 br d	5.19 br d	5.17 br d	4.95 br d
H-6 . . . . .			5.15 dd	5.05 dd	5.12 dd
H-7 . . . . .	3.46 dddd	3.52 dddd	3.19 ddd	3.20 br dd	3.18 br dd
H-8 . . . . .	5.79 br d	5.82 br d	5.83 d	5.31 dd	4.08 dd
H-9 . . . . .	—	—	—	5.09 br d	4.73 d
H-11 . . . . .	—	—	2.92 dq	—	—
H-13 . . . . .	6.48 d	6.49 d	} 1.43 d	6.25 d	6.40 br s
H-13' . . . . .	5.99 d	6.05 d			5.57 d
H-14 . . . . .	1.77 br s	1.78 br s	1.74 br s	1.64 d	1.62 br s
H-15 . . . . .	1.56 br s	1.57 br s	1.59 d	1.71 d	1.69 br s
OCOR . . . . .	3.07 q	3.09 q	3.10 q	6.77 qq	6.89 qq
	1.26 d	1.44 d	1.28 d	1.76 br d	1.70 br d
	1.55 s	1.55 s	1.60 s	1.74 br s	1.82 br s

<sup>a</sup>J (Hz): Compounds **8-10**: 1,2=11; 2,3=6; 2,3'=11; 2',3=2; 2',3'=7; 3,3'=12; 5,6=10; 6,7=6.5; 7,8=9; 7,13=2.7; 7,13'=2.4 (compound **10**: 5,6=11.5; 5,15=1; 6,7=8.5; 7,8=11.5; 7,11=8.5; 11,13=8); compounds **11** and **12**: 1,2=9; 1,2'=7.5; 1,14=1; 2,3=2',3=3.5; 2,3'=7; 2',3'=11; 3,3'=12; 5,6=11; 6,7=6; 7,8=8; 7,13=7,13'=1; 8,9=9.5.

the pmr spectral data, which agreed nicely with those reported for this lactone (**1**). Accordingly, the structures of **11** and **12** could be easily deduced from the very similar pmr spectra (Table 1). The signals of the ester part showed that the epoxy angelate residue was replaced by a tiglate in **12**, while **11** was the corresponding 8-O-acetate. Spin decoupling allowed the assignment of all signals; only those of H-2 were an overlapped multiplet.

The pmr spectra of **8** and **9** (Table 1) are very similar. The presence of epimeric epoxy angelates followed from the typical quartets at  $\delta=3.07$  and 3.09, the doublets at 1.26 and 1.44 as well as from the singlet at 1.55, respectively. The ir spectrum of **8** indicated, in addition to a  $\gamma$ -lactone and an ester carbonyl, the presence of a further carbonyl group. As the H-8 signal in the spectrum of **8** was shifted downfield, a keto group at C-9 could be proposed, especially as the broadened signal at 6.42 was most likely due to H-1. However, as followed from the ir band, the keto group was not in plane with the double bond. Though several other signals were broadened, too, spin decoupling allowed the assignment of all signals. The stereochemistry at C-6-C-8 followed from the couplings observed, while the *E*-configuration of the 1,10-double bond

could be deduced from the chemical shift of H-1. The couplings observed agreed best with a conformation with 4-methyl below and 10-methyl above the plane. Also, the chemical shift of H-7 supported this assumption. The stereochemistry of the epimeric esters could not be elucidated. All data therefore indicated that **8** was the 9-keto derivative of the known 9-acetoxy derivative (**1**).

The pmr spectrum of **10** (Table 1) indicated that an epoxy angelate was again present. However, the signals of the exomethylene protons were replaced by a methyl doublet at 1.43 and a doublet quartet at 2.92, indicating that we were dealing with a 11,13-dihydro derivative. From the observed coupling  $J_{7,11}$ , the  $\beta$ -orientation of the 11-methyl was deduced. Surprisingly, the spectrum of **10** indicated that a stable conformation was present while in the case of **8**, obviously a flexible system had to be assumed. Accordingly, all signals could be assigned easily by spin decoupling. The stereochemistry obviously was the same as in **8**.

The pmr spectra of **1** and **2** (Table 2) indicated that a second pair of lactones was present differing only in the stereochemistry of the epoxy angelate residue, while the mass spectra showed that **1** and **2** were isomers of **8** and **9**. The ir spectra showed a band for a conjugated ketone at  $1695\text{ cm}^{-1}$  while in the pmr spectra, the H-1 signal was shifted upfield if compared with the chemical shift in **8** in agreement with a *Z*-configured 1,10-double bond. The nOe difference spectra of **2** also led to the preferred conformation with the 4-methyl below and the 10-methyl above the plane, as strong effects were visible between H-8 and H-14 as well as between H-6 and H-15. The chemical shift of H-7 again required a 9-keto group below the plane, and the couplings  $J_{5,6}$  and  $J_{6,7}$  indicated that the conformation of **1** and **2** differed from that of **8** and **9**. As usual in melampolides, the cd-values were not clear. Again the stereochemistry of the epimeric epoxy angelates could not be established.

The pmr spectrum of **3** (Table 2) clearly showed that again a 11,13-dihydro derivative was present, obviously derived from **1** or **2** as followed from the results of spin decoupling which led to the assignment of all signals, only those of H-3 and H-2 $\beta$  being overlapped multiplets. The stereochemistry at C-11 again was proposed from the coupling  $J_{7,11}$ . If the couplings and chemical shifts of **3** are compared with those of **1**, it is obvious that small changes in the conformation are induced by introduction of a saturated C-11 carbon.

The lactone **4** showed no molecular ion by electron imp-act, but chemical ionization gave a clear  $M+1$  ion corresponding to  $C_{21}H_{28}O_7$  as a molecular formula. Inspection of the pmr spectrum (Table 2) indicated that an epoxy angelate again was present with a methyl ether group (3.33 s). The last oxygen function again must be a keto group, as a doublet quartet (3.12) obviously was the signal of H-10 as irradiation collapsed the methyl doublet at 0.96 to a singlet and a threefold doublet at 3.66 to a double doublet. As the latter signal most likely was due to the proton under the methoxy group, and the low field doublet at 5.78 was coupled with H-7 and therefore was the H-8 signal, the substitution pattern at C-1 and C-6-C-9 was settled. However, the stereochemistry at C-1 and C-10 had to be established while that at C-6 through C-8 obviously was the same as in all other lactones as followed from the coupling. The nOe difference spectra and the coupling allowed the assignment of the stereochemistry and the preferred conformation. Irradiation of H-15 gave a nOe of H-6; that of H-10, of H-8; that of methoxy, of H-1 and H-10; that of H-1, of H-3 $\beta$ , H-5, and H-8; that of H-5, of H-1, H-3 $\beta$ , and H-8; and that of H-8, of H-1, H-5, and H-10. These data require a conformation with the 4-methyl below the plane and the methoxy as well as the 10-methyl group *quasi*-equatorial, and the 9-keto group  $\alpha$ -oriented. All data, especially the coupling of H-1, nicely agreed with this assumption; a 1 $\beta$ -methoxy group would require a large coupling  $J_{1\alpha,2\beta}$ . The pmr data of **5** (Table 2) again were nearly identical

TABLE 2. Pmr Spectral Data of 1-7 (400 MHz, CDCl<sub>3</sub>, TMS as Internal Standard)<sup>a</sup>

	1	2	3	4	5	6	7		
H-1	5.72	5.71 ddq	5.67 brdd	3.66ddd	3.67 ddd	3.96 brs <sup>b</sup>	3.67 brdd		
H-2	2.45 br ddd	2.48 br ddd	2.65 br ddd	1.62 dddd	1.63 dddd	1.85 m	1.72 m		
H-2'	}	}	}	1.51 brd	1.51 brd	}	1.56 m		
H-3				2.17 m	2.20 m		2.07 ddd	2.10 m	2.14 m
H-3'				1.67 brt	1.60 m		2.13 ddd	5.46 brd	5.20 m
H-5	5.19 brd	5.16 brd	4.94 brd	5.35 brd	5.35 brd	5.15 dd	3.65 m		
H-6	5.14 br dd	5.11 br dd	5.13 br dd	5.20 dd	5.22 dd	3.97 dddd	6.00 d		
H-7	3.89 dddd	3.89 dddd	3.39 ddd	4.11 dddd	4.09 dddd	5.61 d	—		
H-8	5.58 d	5.53 d	5.29 d	5.78 d	5.73 d	3.04 dq	—		
H-10	—	—	—	3.12 dq	3.18 dq	—	2.79 dq		
H-11	—	—	3.06 dq	—	—	—	—		
H-13	6.29 brs	6.23 brs	}	6.39 d	6.37 d	6.33 dd	}		
H-13'	5.75 brs	5.77 brs		5.76 d	5.75 d	5.74 dd		1.35 d	
H-14	1.95 brs	1.95 brs	2.22 brs	0.96 d	0.96 d	1.15 d	0.94 d		
H-15	1.54 brs	1.52 brs	1.52 brs	1.44 d	1.44 d	1.50 s	1.49 brs		
OCOR	3.06 q	3.03 q	3.03 q	3.05 q	3.09 q	3.07 q	3.08 q		
	1.28 d	1.24 d	1.22 d	1.26 d	1.25 d	1.24 d	1.28 d		
	1.49 s	1.53 s	1.54 s	1.53 s	1.51 s	1.49 s	1.55 s		
OMe	—	—	—	3.33 s	3.36 s	—	—		

<sup>a</sup>J (Hz): Compounds 1-3: 1, 2=1, 2'=8, 5; 2, 2'=13; 2, 3'=13; 2, 3'=10; 1, 14=1; 5, 6=7, 5; 6, 7=6; 7, 8=11; 7, 13=1 (compound 3: 1, 2=7; 1, 2'=9; 5, 6=6; 7, 8=11; 7, 11=11, 13=7, 5); compounds 4 and 5: 1, 2=6; 1, 2'=5; 1, 10=3; 2, 2'=2, 3=13; 2, 3'=2, 3'=5; 3, 3'=13; 5, 6=9; 5, 15=1; 6, 7=8; 7, 8=11; 7, 13=7, 13'=2; 10, 14=7; compound 6: 1, 10=3; 5, 6=6, 7=8; 7, 8=11, 5; 7, 13=7, 13'=1, 7; 10, 14=7, 5; compound 7: 1, 2=7; 1, 10=2, 5; 7, 8=11; 7, 11=10; 10, 14=6, 5; 11, 13=8.

<sup>b</sup>Half-width 14 Hz (in CDCl<sub>3</sub>/C<sub>6</sub>D<sub>6</sub> 3:62).

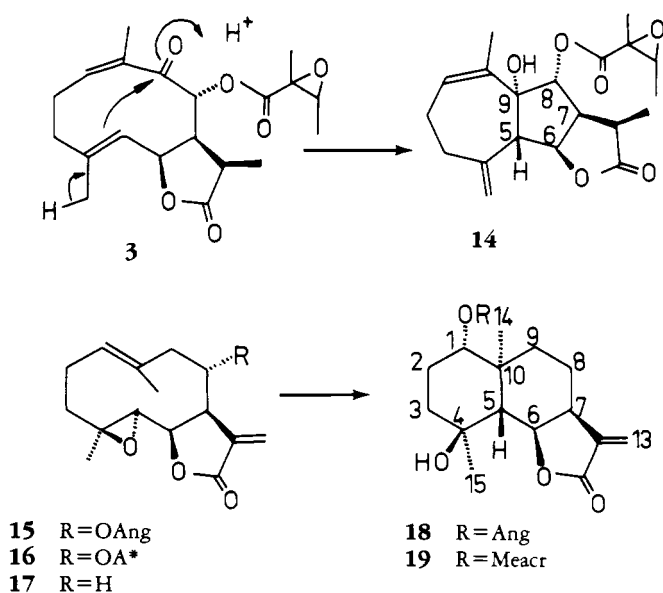
with those of **4**, indicating that also these lactones differed only in the configuration of the epoxy angelate residue.

The molecular formula of **6** again could be determined only indirectly by the  $M+1$  ion from the cims spectrum. However, the presence of an epoxy angelate followed from the pmr spectrum (Table 2), while the ir spectrum required a hydroxy and an additional carbonyl group. Accordingly, all data only agreed with  $C_{20}H_{26}O_7$  as a molecular formula. While in the pmr spectrum in  $CDCl_3$  some signals were overlapped, addition of  $C_6D_6$  led to a spectrum that could be assigned completely by spin decoupling. The similarity of the signals to those of **4** and **5** was obvious; however, the methyl ether singlet was absent. A broadened signal at 3.96 and 3.62 respectively after addition of  $C_6D_6$  obviously was that of H-1, which now was located on a hydroxy group bearing carbon. Accordingly, addition of  $D_2O$  sharpened this signal. All data therefore agreed with the presence of a 1-O-desmethyl derivative of **4** or **5**.

The lactone **7** was most likely a 11,13-dihydro derivative of **4** or **5**. Accordingly, the signals of the exomethylene protons were replaced by a methyl doublet at 1.35 and a doublet quartet at 2.79, which, however, showed a 10 Hz coupling of  $J_{7,11}$ . Inspection of a model indicated that the corresponding angle may be exactly zero degree. Therefore, the same stereochemistry at C-11 as in **3** and **10** was proposed.

Cims of **14** indicated that the molecular formula most likely was  $C_{20}H_{26}O_6$ . In agreement with this assumption, the eims spectrum showed  $m/z$  246 ( $M-RCO_2H$ ). As the pmr spectrum (Table 3) clearly showed that again an epoxy angelate was present, the proposed molecular formula was very likely. Furthermore, the ir spectrum indicated the presence of a hydroxy group and a saturated  $\gamma$ -lactone ( $1790\text{ cm}^{-1}$ ). Accordingly, the nature of all oxygen functions was established. The pmr spectrum further showed that again a 11,13-dihydro derivative was present which had only one olefinic methyl group, while the second one was replaced by an exomethylene group. Furthermore, spin decoupling showed that a doublet at 5.20 was due to H-8. Accordingly, no proton was at C-9 though a 9-keto group was unlikely following the chemical shift of H-8 and the ir spectrum. Further, spin decoupling, especially in  $C_6D_6$ , allowed the assignment of all signals leading to sequence from C-1 to C-8 as allylic couplings of H-3 and H-5 with H-15 allowed to connect the sequences C-1 through C-3 and C-5 through C-8. Also as an allylic coupling between H-14 and H-1 as well as with H-2 could be detected, the only missing link was C-9 which, however, must bear the hydroxy group and had to be connected with C-5 as obviously this carbon was secondary. Thus, the structure **14** was settled except for some stereochemical details that could be solved by nOe difference spectroscopy. Irradiation of H-6 especially showed clear effects with H-15 and that of H-8 with H-5, H-13, and H-14, indicating that H-5 and H-13 were  $\beta$ -oriented. Inspection of a model further showed that a  $9\alpha$ -hydroxy group had to be assumed, as only this stereochemistry was in agreement with the observed nOe and couplings. Most likely **3** was the precursor of **14**, which probably was formed as shown in Scheme 1. Accordingly, **14** may be an artifact. As, however, the corresponding lactones derived from **1** and **2** were not present, this possibility is not very likely. The same problems arise with the lactones **4-7**, which could be artifacts formed by addition of MeOH or  $H_2O$  to **1**, **2**, and **3**, respectively. Again, the absence of corresponding addition products derived from **8-10** does not favor such an assumption. For **14** without oxygen functions at C-8 and C-9, we propose the name montahibisciolide.

The structure of **22** could be deduced easily from the pmr spectral data (see Experimental) which showed that **22** was the 14-hydroxy derivative of **21** (**4**). Accordingly, the H-13 signal was a double doublet, and an additional low field double doublet at 4.52 collapsed to a doublet on irradiation of H-13. The stereochemistry at C-13 and C-14 could not be determined.



SCHEME 1.

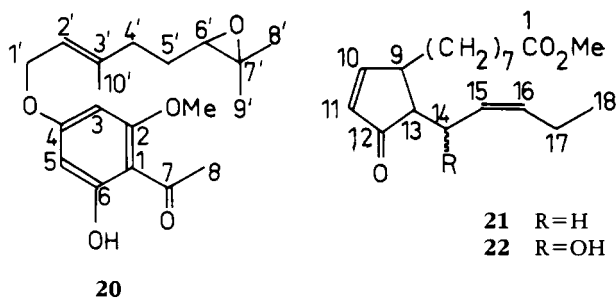
TABLE 3. Pmr Spectral Data of **14** (400 MHz, TMS as Internal Standard)<sup>a</sup>

	C <sub>6</sub> D <sub>6</sub>	CDCl <sub>3</sub>
H-1 . . . . .	5.31 ddq	5.70 ddq
H-2 . . . . .	1.79 dddq	{ 1.68 m 2.11 m
H-3 . . . . .	2.41 ddd br	2.53 m
H-3' . . . . .	2.19 ddd br	2.11 m
H-5 . . . . .	2.64 d br	2.88 d br
H-6 . . . . .	4.82 dd	5.19 dd
H-7 . . . . .	2.61 ddd	3.09 m
H-8 . . . . .	5.20 d	5.31 d
H-11 . . . . .	2.34 dq	2.94 dq
H-13 . . . . .	1.31 d	1.38 d
H-14 . . . . .	1.58 dd	1.68 s br
H-15 . . . . .	5.11 s br	5.19 s br
H-15' . . . . .	5.05 s br	5.13 s br
OCOR . . . . .	2.58 q 1.12 d 1.37 s	3.11 q 1.36 d 1.58 s
OH	2.08 s br	2.40 s br

<sup>a</sup>J (Hz): 1,2=2,3=6; 1,14=2,14=1.5; 2,3'=5; 3,3'=16; 5,6=7.5; 6,7=9.5; 7,8=8; 7,11=11.5; 11,13=8.

The aerial parts of *M. dumicola* afforded several widespread compounds (5), while the polar fractions gave small amounts of the germacranolides **15** and **16**, the eudesmanolides **18** and **19**, and the unusual geranyl derivative **20**.

The pmr spectra (Table 4) of **15** and **16** were close to that of parthenolide (**17**), but showed mostly very broad signals that could be assigned only in part. However, in C<sub>6</sub>D<sub>6</sub> at an elevated temperature, nearly all signals could be assigned by spin decoupl-

TABLE 4. Pmr Spectral Data of **15** and **16** (400 MHz, TMS as Internal Standard)<sup>a</sup>

	<b>15</b> , C <sub>6</sub> D <sub>6</sub> (70°)	<b>16</b> , C <sub>6</sub> D <sub>6</sub> (70°)	<b>15</b> , CDCl <sub>3</sub> <sup>b</sup>	<b>16</b> , CDCl <sub>3</sub> <sup>b</sup>
H-1 . . . . .	4.99 dd br	5.00 dd br	5.29 m	5.29 m
H-2 . . . . .	2.59 d br	2.61 d br		
H-2' . . . . .	1.85 m	1.85 m		
H-3 . . . . .	1.75 ddd	1.74 ddd		
H-3' . . . . .	0.94 m	0.94 m		
H-5 . . . . .	2.85 d	2.70 d		
H-6 . . . . .	3.75 dd	3.72 dd	4.07 dd	4.06 dd
H-7 . . . . .	2.73 dd br	2.78 dd br	3.18 m	3.24 m
H-8 . . . . .	5.33 ddd	5.24 m	5.44 m	5.45 m
H-9 . . . . .	1.85 m	1.85 m		
H-13 . . . . .	6.18 s br	6.24 s br	6.27 s br	6.37 s br
H-13' . . . . .	5.19 s br	5.36 s br	5.62 s br	5.77 s br
H-14 . . . . .	1.37 s br	1.38 s br	1.83 s br	1.83 s br
H-15 . . . . .	0.89 s	0.88 s	1.30 s	1.30 s
OCOR . . . . .	5.78 qq 1.99 dq 1.83 q	2.61 q 1.20 d 1.39 s	6.08 qq 1.96 dq 1.80 dq	2.99 q 1.27 s 1.48 s

<sup>a</sup>J (Hz): 1,2=6; 1,2'=11; 2,2'=14; 2,3=2',3=3.5; 3,3'=13; 5,6=9.5; 6,7=5.5; 7,8=6; 8,9=3.5; 8,9'=11; OAng: 3',4'=7; 3',5'=4',5'~1.5; OE pang: 3',4'=5.

<sup>b</sup>Remaining signals not assigned multiplets.

ing. Irradiation of the broadened double doublets at  $\delta=2.73$  in the spectrum of **15** showed that we were dealing with the signal of H-7 because the broadened singlets of 6.18 and 5.19, obviously the signals of H-13, were sharpened, while the double doublet at 3.75 collapsed to a double (H-6), and the threefold doublet at 5.33 was changed to a double doublet (H-8). Furthermore, the broad doublet at  $\delta=4.99$  obviously was due to H-1, as its irradiation caused the expected changes of the signal of the olefinic methyl and of the signals of two allylic protons ( $\delta=1.85$  and 2.59). A doublet at  $\delta=2.85$  was coupled with H-6, thus indicating the presence of an 4,5-epoxide.

Inspection of a model led to the proposed stereochemistry when the observed couplings were considered. The nature of the ester groups in **15** and **16** followed directly from the typical pmr signals.

The signals in the pmr spectra of **18** and **19** (Table 5) could be assigned, too, by spin decoupling, though some signals were overlapping multiplets. Again, the presence of an angelate and a methacrylate, respectively, could be deduced from the typical pmr signals, and the relative position of the oxygen functions followed from the results of spin decoupling and the chemical shifts. The stereochemistry, however, could be established only by nOe difference spectroscopy. Irradiation of the H-15 signal caused nOe of H-6 and H-14, while saturation of the H-1 signals gave clear effects of H-5 and

of the angelate methyl. Irradiation of H-7 showed nOe with H-14, too, and H-6 with H-8 $\alpha$ , H-14, and H-15. These results showed that a eudesmanolide was present with a 6 $\beta$ , 12-lactone ring and a 10 $\alpha$ -methyl group. Eudesmanolides with this configuration at C-10 have been observed from several genera belonging to the subtribe Ecliptinae (tribe Heliantheae) (6,7). Most likely **18** is formed via the epoxide **15** as shown in Scheme 1.

TABLE 5. Pmr Spectral Data of **18** and **19** (400 MHz, CDCl<sub>3</sub>, TMS as Internal Standard)<sup>a</sup>

	<b>18</b>	<b>19</b>
H-1 . . . . .	4.61 dd	4.59 dd
H-5 . . . . .	1.49 d	1.50 d
H-6 . . . . .	4.97 dd	4.98 dd
H-7 . . . . .	3.28 dddd	3.28 dddd
H-8 . . . . .	1.97 m	1.98 m
H-9 $\alpha$ . . . . .	1.49 ddd	1.48 ddd
H-9 $\beta$ . . . . .	1.26 ddd br	1.26 ddd br
H-13 . . . . .	6.34 d	6.35 d
H-13' . . . . .	5.56 d	5.56 d
H-14 . . . . .	1.00 s	1.01 s
H-15 . . . . .	1.40 s	1.41 s
OCOR . . . . .	6.06 qq 1.97 dq 1.86 dq	6.06 s br 5.56 s br 1.93 s br

<sup>a</sup>J (Hz): 1,2=4; 1,2'=5,6=11; 6,7=7.5; 7,13=3.5; 7,13'=3; 7,8=7,8'~4; 8,9=6; 8,9'=8',9'=3.5; 8',9=9,9'=13; OAng: 3',4'=7; 3',5'=4',5'~1.5.

The structure of **20** followed from the molecular formula C<sub>19</sub>H<sub>26</sub>O<sub>5</sub> and from the pmr spectrum (see Experimental). The presence of a phloracetophenone derivative was deduced from the typical pmr signals and from the corresponding fragments *m/z* 182 (C<sub>9</sub>H<sub>10</sub>O<sub>4</sub>) and 167 (182-Me), while the nature of the side chains followed from the pmr data. Spin decoupling again allowed the assignment of all signals. The presence of a geranyl-6',7'-epoxide derivative followed from the signals of H-1' and H-2' and from those of H-5' and H-6'. Also the methyl signals required a 6',7'-epoxide. The relative position of the two ether residues could only be determined by nOe difference spectroscopy. Irradiation of the methoxy signals again gave a clear nOe of H-3, while saturation of the H-1' doublet caused a positive nOe of H-5 and a negative one of H-3.

The chemistry of the genus *Montanoa* supports the separation of this genus as a new subtribe (8) from the subtribe Verbesinae where it was placed previously (9), inasmuch as similar sesquiterpene lactones have not been reported from any member of the Verbesinae.

## EXPERIMENTAL

MATERIALS AND METHODS.—Air-dried plant material, collected in Costa Rica, was extracted with Et<sub>2</sub>O-MeOH, 1:1, at room temperature for 24 h. Pmr spectra were recorded at 400 MHz (Bruker WM 400) with TMS as internal standard and mass spectra with a Varian MAT 711, 70 eV, direct inlet. The crude extract (5.3 g) of the aerial parts of *M. hibiscifolia* (500 g, voucher 1/83, deposited in the Institute for Organic Chemistry, Technical University of Berlin), was separated by cc (Siegel) into six fractions: 1 (petrol, 2 (Et<sub>2</sub>O-petrol, 1:10), 3 (Et<sub>2</sub>O-petrol, 1:3), 4 (Et<sub>2</sub>O-petrol, 1:1), 5 (Et<sub>2</sub>O) (standing in a small amount of Et<sub>2</sub>O gave 20 mg of amorphous material) and 6 (Et<sub>2</sub>O-MeOH, 3:1). Tlc (Si gel PF 254, petrol) of fraction 1 gave 3 mg of germacrene D, 3 mg of caryophyllene and 2 mg of  $\delta$ -cadinene. Tlc of fraction 2



(Et<sub>2</sub>O-petrol, 1:3) afforded 4 mg of β-amyirin palmitate, 4 mg of β-amyirin acetate, 4 mg of amyirin, 5 mg of phytol, and 5 mg of lupeol (all identified by comparing their 400 MHz-pmr spectra with those of authentic material). Tlc of fraction 3 (C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O, 2:2:1) gave 35 mg of **21** (identical with an authentic sample) and 5 mg of **22**. Tlc of fraction 4 (Et<sub>2</sub>O-petrol, 4:1, then C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O, 5:5:1, four developments) afforded 7 mg of **4**, 6 mg of **5**, 3 mg of **1**, and 4 mg of **2**. Tlc of fraction 5 (soluble part, C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O, 1:1:1, developed two times, then C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O, 5:5:1, developed six times) gave 8 mg of **1**, 40 mg of **2**, 4 mg of **11**, 27 mg of **12**, 4 mg of **3**, and 3 mg of **7**, while the amorphous residue of fraction 5 by tlc (C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O, 1:1:1, developed two times and C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O, 5:5:1, six developments) afforded 10 mg of **8**, 1 mg of **9**, and 5 mg of **10**. Tlc of fraction 6 (C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O, 5:5:1, six developments) gave 3 mg of **6**, 6 mg of **14** [further purified by hplc (RP 8, MeOH-H<sub>2</sub>O, 3:2)] and 15 mg of **13**, its pmr spectral data fully agree with those reported (1).

The crude extract (9 g) of the aerial parts of *M. dumicola* (National Herbarium of Costa Rica, No. 62829, collected near Santiago de Puriscal, Costa Rica) was separated by cc (Si gel) and the polar fraction (Et<sub>2</sub>O and Et<sub>2</sub>O-MeOH, 4:1) was separated by tlc (Si gel PF 254, C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O, 9:9:2) affording three zones. Repeated tlc (C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>, 1:1, three developments) of the first zone (Rf 0.50) gave 9 mg of **18** (less polar) and 1 mg of **19**. The second zone (Rf 0.25) on repeated tlc (C<sub>6</sub>H<sub>6</sub>-CH<sub>2</sub>Cl<sub>2</sub>, 1:1, several developments) gave 2.5 mg of **20**, while the most polar zone (Rf 0.15) on hplc (RP 8, MeOH-H<sub>2</sub>O, 7:3) afforded 4 mg of **16** and 4 mg of **15**. Probably due to the small amounts, several of the lactones could not be induced to crystallize, though they were homogeneous by tlc and pmr.

8α-(2',3'-Epoxy-2'-methylbutyryloxy)-9-oxo-germacra-4E.1(10)Z-dien-6β,12-olide (**1**): ir (CCl<sub>4</sub>) 1785 (γ-lactone), 1740 (CO<sub>2</sub>R), 1695 cm<sup>-1</sup> (C=CC=O); ms *m/z* (rel. int., %) (ci, isobutane) 361 (M+1<sup>+</sup>, 5), 245 (361-RCO<sub>2</sub>H, 100); cd (MeCN) Δε<sub>328</sub>+0.15; Δε<sub>292</sub>-0.25; Δε<sub>272</sub>+0.2 (compared to Δε<sub>292</sub>).

2',3'-Epimeric ester **2**: Colorless crystals, mp 141-142°; ir (CHCl<sub>3</sub>) 1770 (γ-lactone), 1740 (CO<sub>2</sub>R), 1690 cm<sup>-1</sup> (C=CC=O); ms *m/z* (rel. int., %) (ci, isobutane) 361 (M+1, 7), 245 (361-RCO<sub>2</sub>H, 100), 227 (245-H<sub>2</sub>O, 60), 117 (RCO<sub>2</sub>H+1, 51); cd (MeCN) Δε<sub>328</sub>+0.35; Δε<sub>292</sub>-0.09; Δε<sub>275</sub>+0.09.

11α,13-Dihydro derivative of **1** (**3**): ir (CHCl<sub>3</sub>) 1765 (γ-lactone), 1740 (CO<sub>2</sub>R), 1680 cm<sup>-1</sup> (C=CC=O); ms *m/z* (rel. int., %) (ci, isobutane) 363 (M+1, 24), 247 (363-RCO<sub>2</sub>H, 100), 229 (247-H<sub>2</sub>O, 48), 117 (RCO<sub>2</sub>H+1, 8).

8α-(2',3'-Epoxy-2'-methylbutyryloxy)-1α-methoxy-9-oxo-10αH-germacra-4E-en-6β,12-olide (**4**): ir (CHCl<sub>3</sub>) 1770 (γ-lactone), 1725 cm<sup>-1</sup> (CO<sub>2</sub>R, C=O); ms *m/z* (rel. int., %) (ci, isobutane) 393 (M+1, 50), 361 (393-MeOH, 60), 277 (393-RCO<sub>2</sub>H, 100), 245 (277-MeOH, 100).

2',3'-Epimeric ester **5**: ir (CCl<sub>4</sub>) 1780 (γ-lactone), 1740 (CO<sub>2</sub>R), 1725 cm<sup>-1</sup> (C=O); ms *m/z* (rel. int., %) (ci, isobutane) 393 (M+1, 25), 361 (393-MeOH, 11), 277 (393-RCO<sub>2</sub>H, 8), 245 (277-MeOH, 100).

8α-(2',3'-Epoxy-2'-methylbutyryloxy)-1α-hydroxy-9-oxo-10αH-germacra-4E-en-6β,12-olide (**6**): ir (CCl<sub>4</sub>) 3520 (OH), 1780 (γ-lactone), 1745 (CO<sub>2</sub>R), 1725 cm<sup>-1</sup> (C=O); ms *m/z* (rel. int., %) (ci, isobutane) 379 (M+1, 15), 361 (379-H<sub>2</sub>O, 19), 263 (379-RCO<sub>2</sub>H, 100), 245 (263-H<sub>2</sub>O, 45).

11α,13-Dihydro derivative of **4** (**7**): ir (CHCl<sub>3</sub>) 1790 (γ-lactone), 1730 cm<sup>-1</sup> (CO<sub>2</sub>R, C=O); ms *m/z* (rel. int., %) (ci, isobutane) 395 (M+1, 16), 377 (395-H<sub>2</sub>O, 8), 363 (395-MeOH, 7), 279 (395-RCO<sub>2</sub>H, 20), 247 (279-MeOH, 18), 117 (RCO<sub>2</sub>H+1, 100).

8α-(2',3'-Epoxy-2'-methylbutyryloxy)-9-oxo-germacra-4E.1(10)E-dien-6β,12-olide (**8**): ir (CHCl<sub>3</sub>) 1770 (γ-lactone), 1730 cm<sup>-1</sup> (CO<sub>2</sub>R, C=O); ms *m/z* (rel. int., %) (ci, isobutane) 361 (M+1, 10), 245 (361-RCO<sub>2</sub>H, 20), 117 (RCO<sub>2</sub>H+1, 91), 99 (117-H<sub>2</sub>O, 100); cd (MeCN): Δε<sub>328</sub>+0.29; Δε<sub>262</sub>-1.36.

2',3'-Epimeric ester **9**: ir (CHCl<sub>3</sub>) 1765 (γ-lactone), 1730 cm<sup>-1</sup> (CO<sub>2</sub>R, C=O); ms *m/z* (rel. int., %) (ci, isobutane) 361 (M+1, 5), 245 (361-RCO<sub>2</sub>H, 61), 227 (245-H<sub>2</sub>O, 100), 117 (RCO<sub>2</sub>H+1, 85).

11α,13-Dihydro derivative of **8** (**10**): Colorless crystals, mp 142-143°; ir (CHCl<sub>3</sub>) 1775 (γ-lactone), 1750 (CO<sub>2</sub>R), 1730 cm<sup>-1</sup> (C=O); ms *m/z* (rel. int., %) (ci, isobutane) 363 (M+1, 0.3), 247 (363-RCO<sub>2</sub>H, 0.3), 117 (RCO<sub>2</sub>H+1, 100); cd (MeCN): Δε<sub>328</sub>+1.69; Δε<sub>260</sub>-13.0.

8α-Acetoxy-9β-tigloyloxy-germacra-4E.1(10)E-dien-6β,12-olide (**11**): ir (CHCl<sub>3</sub>) 1760 (γ-lactone), 1750 (CO<sub>2</sub>R), 1710 cm<sup>-1</sup> (C=O); ms *m/z* (rel. int., %) (ci, isobutane) 389 (M+1, 45), 329 (389-HOAc, 50), 289 (389-RCO<sub>2</sub>H, 33), 229 (329-RCO<sub>2</sub>H, 100).

8α-Hydroxy-9β-tigloyloxy-germacra-4E.1(10)E-dien-6β,12-olide (**12**): ir (CHCl<sub>3</sub>) 3480 (OH), 1770 (γ-lactone), 1715, 1650 cm<sup>-1</sup> (C=CCO<sub>2</sub>R); ms *m/z* (rel. int., %) 346.178 (M<sup>+</sup>, 0.6) (calc. for C<sub>20</sub>H<sub>26</sub>O<sub>5</sub>: 346.178), 246 (M-RCO<sub>2</sub>H, 5), 228 (246-H<sub>2</sub>O, 5), 218 (246-CO, 5.5), 83 (C<sub>4</sub>H<sub>7</sub>-CO<sup>+</sup>, 100); cd (MeCN): Δε<sub>260</sub>-0.79.

8α-(2',3'-Epoxy-2'-methylbutyryloxy)-9α-hydroxy-montabibisciolide (**14**): ir (CCl<sub>4</sub>) 3600 (OH), 1790 (γ-lactone), 1740 cm<sup>-1</sup> (CO<sub>2</sub>R); ms *m/z* (rel. int., %) 246.126 (M-RCO<sub>2</sub>H, 39) (calc. for C<sub>15</sub>H<sub>18</sub>O<sub>3</sub>: 246.126), 228 (246-H<sub>2</sub>O, 26), 218 (246-CO, 63), 55 (100); ci (isobutane) 363 [M+1]<sup>+</sup> (7), 345 [363-H<sub>2</sub>O]<sup>+</sup> (24), 247 [363-RCO<sub>2</sub>H]<sup>+</sup> (100), 229 [247-H<sub>2</sub>O]<sup>+</sup> (91); cd (MeCN): Δε<sub>275</sub>-0.15.

8 $\alpha$ -(*Angeloyloxy*)-4 $\beta$ ,5 $\alpha$ -epoxygermacra-1(10)*E-en*-6 $\beta$ ,12-olide (**15**): Colorless crystals, mp 153°; ir (CCl<sub>4</sub>) 1780 ( $\gamma$ -lactone), 1715 cm<sup>-1</sup> (C=CCO<sub>2</sub>R); ms *m/z* (rel. int., %) 346 (M, 0.1), 246.126 (M-RCO<sub>2</sub>H, 10) (calc. for C<sub>15</sub>H<sub>18</sub>O<sub>3</sub>: 246.126), 83 (C<sub>4</sub>H<sub>7</sub>CO, 100), 55 (83-CO, 83).

$$[\alpha]_{24}^{\lambda} = \frac{589}{-41.4} \quad \frac{578}{-44.3} \quad \frac{546}{-59.3} \quad \frac{436 \text{ nm}}{-80.7} \quad (c=0.4, \text{CHCl}_3)$$

8 $\alpha$ -(2',3'-Epoxy-2'-methylbutyryloxy)-4 $\beta$ ,5 $\alpha$ -epoxygermacra-1(10)*E-en*-6 $\beta$ ,12-olide (**16**): Colorless oil; ir (CCl<sub>4</sub>) 1780 ( $\gamma$ -lactone), 1730 cm<sup>-1</sup> (CO<sub>2</sub>R); ms *m/z* (rel. int., %) 246.126 (M-RCO<sub>2</sub>H, 6) (calc. for C<sub>15</sub>H<sub>18</sub>O<sub>3</sub>: 246.126), 99 (RCO<sup>+</sup>, 10), 71 (99-CO, 42), 55 (100), [ $\alpha$ ]<sub>D</sub> = -27 (CHCl<sub>3</sub>, c=0.3).

1 $\alpha$ -*Angeloyloxy*-4 $\beta$ -hydroxy-10-*epi-eudesman*-6 $\beta$ ,12-olide (**18**): Colorless oil; ir (CCl<sub>4</sub>) 3580 (OH), 1785 ( $\gamma$ -lactone), 1720, 1650 cm<sup>-1</sup> (C=CCO<sub>2</sub>R); ms *m/z* (rel. int., %) 333.170 (M-Me, 1) (calc. for C<sub>19</sub>H<sub>25</sub>O<sub>5</sub>: 333.170), 248 (M-RCO<sub>2</sub>H, 2), 233 (248-Me, 2), 230 (248-H<sub>2</sub>O, 2), 215 (230-Me, 2), 83 (C<sub>4</sub>H<sub>7</sub>CO, 100), 55 (83-CO, 42).

$$[\alpha]_{24}^{\lambda} = \frac{589}{+24.5} \quad \frac{578}{+26.0} \quad \frac{546}{+30.4} \quad \frac{436 \text{ nm}}{+60.5} \quad (\text{CHCl}_3, c=0.8)$$

1 $\alpha$ -*Methacryloxy*-4 $\beta$ -hydroxy-10-*epi-eudesman*-6 $\beta$ ,12-olide (**19**): Colorless oil; ir (CCl<sub>4</sub>) 3580 (OH), 1780 ( $\gamma$ -lactone), 1725, 1635 cm<sup>-1</sup> (C=CCO<sub>2</sub>R); ms *m/z* (rel. int., %) 319.154 (M-Me, 1) (calc. for C<sub>18</sub>H<sub>23</sub>O<sub>5</sub>: 319.154), 248 (M-RCO<sub>2</sub>H, 2), 233 (248-Me, 2.5), 230 (248-H<sub>2</sub>O, 2.5), 215 (230-Me, 4), 187 (215-CO, 4.5), 69 (C<sub>3</sub>H<sub>5</sub>CO, 100).

2-*O-Methyl-4-O-[6',7'-epoxy-6',7'-dihydrogeranyl]-phloracetophenone* (**20**): Colorless oil; ir (CCl<sub>4</sub>) 3500-2700, 1620, 1600 cm<sup>-1</sup> (hydrogen bonded PhCO); uv  $\lambda$  max (MeOH) 286 nm; ms *m/z* (rel. int., %) 334.178 (M<sup>+</sup>, 0.3) (calc. for C<sub>19</sub>H<sub>26</sub>O<sub>5</sub>: 334.178), 333 (M-H, 1), 315 (333-H<sub>2</sub>O, 1), 291 (M-C<sub>3</sub>H<sub>7</sub>, 0.5), 273 (291-H<sub>2</sub>O, 1), 182 (2-O-methylphloracetophenone, 22), 167 (182-Me, 44), 71 (C<sub>4</sub>H<sub>7</sub>O, 100); pmr (CDCl<sub>3</sub>)  $\delta$  5.93 d (H-3), 6.06 d (H-5), 2.61 s (H-8), 4.55 d br (H-1'), 5.51 t br (H-2'), 2.27 dt (H-4<sub>1</sub>'), 2.19 dt (H-4<sub>2</sub>'), 1.69 ABq (H-5'), 2.72 t (H-6'), 1.31 s (H-8'), 1.27 s (H-9'), 1.76 s br (H-10'), 3.85 s (OMe) [J (Hz): 3,5=2.2; 1',2'=4<sub>1</sub>',5'=4<sub>2</sub>', 5'=5,6~7; 4<sub>1</sub>',4<sub>2</sub>'=14].

*Methyl-13-hydroxy-14-desoxy chromomoroate* (**22**): Colorless oil; ir (CCl<sub>4</sub>) 3460 (OH), 1740 (CO<sub>2</sub>R), 1710 cm<sup>-1</sup> (C=CC=O); ms *m/z* (rel. int., %) 322.214 (M<sup>+</sup>, 1) (calc. for C<sub>19</sub>H<sub>30</sub>O<sub>4</sub>: 322.214), 304 (M-H<sub>2</sub>O, 2), 238 (M-OCHCH=CH<sub>2</sub>, McLafferty, 8), 207 (238-OMe, 8), 55 (100); pmr (CDCl<sub>3</sub>)  $\delta$  2.30 t (H-2), 1.2-1.6 m (H-3-H-8), 2.54 dddd (H-9), 7.68 dd (H-10), 6.14 dd (H-11), 2.10 dd (H-13), 4.52 dd (H-14), 5.40 dddd (H-15), 5.58 ddd (H-16), 2.16 dddq (H-17), 2.06 dddq (H-17'), 0.97 t (H-18), 3.67 s (OMe) [J (Hz): 2,3=7.5; 8,9=6; 8',9=8; 9,10=2.5; 9,11=9, 13=2; 10,11=5.5; 13,14=14,15=9; 15,16=11; 15,17=15,17'=1.5; 16,17=16,17'=7.5; 17,17'=15; 17,18=17',18=7.5].

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