Phytochemistry, Vol. 27, No. 7, pp. 2235 2240, 1988.
Printed in Great Britain.

0031-9422/88 $3.00+0.00
Pergamon Press plc.

GUAIANOLIDES AND HOMODITERPENES FROM *HELIOPSIS HELIANTHOIDES*

J. JAKUPOVIC, A. SCHUSTER, T. V. CHAU-THI, F. BOHLMANN and X. A. DOMINGUEZ*

Institute of Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, F.R.G.; *Instituto Tecnologico de Estudios Superiores de Monterrey, N. L. 64849, Mexico

(*Revised received* 27 *November* 1987)

Key Word Index—*Heliopsis helianthoides*; Compositae; sesquiterpene lactones; guaianolides; germacranolides; homogeranylnerol derivatives; sesquiterpenes; daucane derivatives; tremetone derivative.

Abstract—Investigation of the aerial parts of *Heliopsis helianthoides* afforded in addition to known compounds 13 new guaianolides, one germacranolide, three derivatives of homogeranylnerol, one daucane and one tremetone derivative. The structures were elucidated by high field NMR spectroscopy. The chemotaxonomic significance of the results is discussed briefly.

INTRODUCTION

The North American genus *Heliopsis* (Compositae, tribe Heliantheae) was traditionally placed in the subtribe Zinniinae [1, 2] but later it was transferred to the Ecliptinae [3]. So far only a few species have been studied chemically [4–9]. In addition to highly unsaturated amides some lignanes were isolated. Also from *H. helianthoides* such compounds have been reported [6]. We have now re-examined the polar parts of an extract of the aerial parts from a sample of this plant collected in Mexico. The results are discussed in this paper.

RESULTS AND DISCUSSION

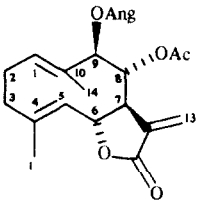
Polar fractions of the aerial parts afforded zoapatanolide A and B [10], the germacranolide **1**, the guaianolides **2a**–**2c**, **3a**–**3c**, **4a**–**4d**, **5a** and **5b**, **6** and the known epoxyangelate **4e** [11]. Furthermore, the geranylnerol derivatives **7a**–**7c**, the tremetone derivative **11** and 5,3′-dihydroxy-3,6,7,8,4′-pentamethoxyflavone [12] were isolated. The root extract afforded lasidiol angelate [13], the isomeric angelate **10a** [14] and the corresponding keto derivative **10b** and 5-hydroxymethyl furfural as well as the labdane diol **8** [15] and its degradation product **9** [16].

The stucture of **1** was deduced from the ^{1}H NMR data (Table 1) which were close to those of the corresponding desacetyl derivative [11]. As expected the chemical shifts of H-8 and H-9 were different.

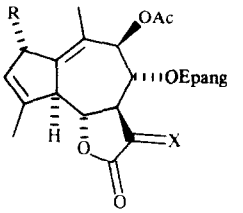
The ^{1}H NMR spectrum of **2b** (Table 1) and spin decoupling clearly showed that a guaianolide was present which had the ester groups at C-8 and C-9. The relative position of the ester groups most probably was the same as that in the corresponding epoxide **3c** where the position was established by NOE (see below). The ^{1}H NMR spectrum of **2c** (Table 1) showed that it was a 2-hydroxy derivative of **2b**. The configuration at C-2 followed from a clear NOE of H-2 with H-6. The ^{1}H NMR data of **2a** (Table 1) indicated that a 11β,13-dihydro derivative of **2b** was present. From the coupling of H-11 and the chemical shift of H-13 the configuration at C-11 was deduced. The ^{1}H NMR spectrum of **3c** (Table 1) was similar to that of **2c**. However, the 2,3-double bond was epoxidized as followed from the signals of H-3 and H-15. The stereochemistry was established by NOE. Clear effects were obtained between H-15, H-3 and H-6, between H-14, H-2 and OAc as well as betweeen H-2, H-3, H-6 and H-14. The NOE between H-14 and the acetate methyl group also established the relative position of the ester groups. Inspection of the ^{1}H NMR spectrum of **3a** (Table 1) showed that this guaianolide was a 2-desoxy derivative of **3c**. Accordingly, a pair of broadened doublets at δ2.72 and 2.50 for H-2 was now assigned by spin decoupling. The chemical shift of H-9, if compared with that of **3c**, indicated that the ester groups had most likely the same relative position as found in **3c**.

The ^{1}H NMR data of **3b** (Table 1) showed that a diangelate was present. The similarity of the spectrum with that of **3c** further showed that both had the same stereochemistry. As H-8 was shifted upfield in the spectrum of **3b** the angeloyloxy groups were at C-2 and C-9.

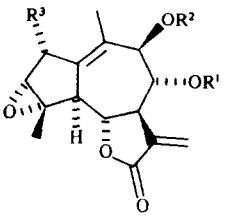
The ^{1}H NMR spectrum of **4d** (Table 2) was in part similar to that of **2c**. However, a pair of low field doublets at δ6.39 and 6.10 and the chemical shift of H-15 (δ1.48, *s*) showed that an isomer with a 2.3-double bond must be present. The observed NOE allowed the assignment of the stereochemistry. Thus, H-15 gave clear effects with H-6 and H-3. Furthermore, a NOE between the epoxyangelate methyl (H-5′) and H-13′ showed that the acetoxy group was at C-9. The spectral data of **4e** [11] differed clearly from those of **4d**. In addition to the inversed position of the ester groups, an epimeric situation at C-4 was also present which typically caused an upfield shift of H-5 due to the missing deshielding effect of the 4-hydroxy group. The ^{1}H NMR spectra of **4a** and **4b** (Table 2) also were similar to that of **4e**. However, the signals of the epoxyangelate residue were replaced by those of an angelate. A small downfield shift of H-9 in the spectra of **4a** and **4b** indicated that the angeloyloxy group was at C-9. The chemical shifts of H-5 differed in the spectra of **4a** and **4b**. Accordingly, these lactones were epimeric at C-4,



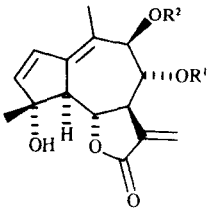
1



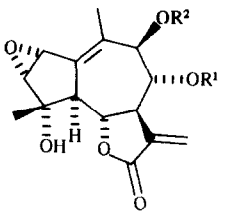
	2a	2b	2c
R	H	H	OH
X	αMe,H	CH_2	CH_2



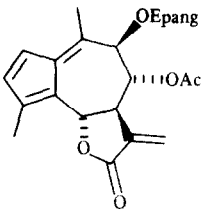
	3a	3b	3c
R¹	Epang	H	Epang
R²	Ac	Ang	Ac
R³	H	OAng	OH



	4a	4b	4c	4d	4e
R¹	Ac	Ac	H	Epang	Ac
R²	Ang	Ang	Ang	Ac	Epang
		4epi			4epi



	5a	5b
R¹	Ac	Ang
R²	Ang	Ac



6

4a being the 4α-hydroxy isomer as followed from the down field shift of H-5. The spectrum of **4c** (Table 2) showed that we were dealing with the desacetyl derivative of **4a** which we have named heliopsolide. Accordingly, the H-8 signal was shifted upfield.

The ^{1}H NMR spectra of **5a** and **5b** (Table 2) indicated that isomers were present which only differed in the relative position of the ester groups which followed in the case of **5b** from a clear NOE between the angeloyl methyl group and H-13′. Further effects between H-14, H-6, H-3 and OAc as well as between H-6, H-8 and H-14 led to the proposed stereochemistry. A small, but very clear NOE between H-6 and the acetate methyl group indicated a somewhat unusual conformation at **5b** which also followed from the slightly changed couplings of H-8 indicating that the angle between H-8 and H-9 is not *ca* 180°. Probably this is due to steric hindrance of the ester groups at C-8 and C-9. The observed NOE with **5a** indicated identical stereochemistry at all chiral centres. The ^{13}C NMR spectrum of **5b** (see Experimental) agreed well with the proposed structure.

The yellow colour, the UV spectrum and the chemical shifts in the ^{1}H NMR spectrum of **6** (Table 2) indicated the presence of a fulvene. Spin decoupling allowed the assignment of all signals. Furthermore the fulvene **6** was formed from **2c** after it had stood in chloroform containing traces of acid. Accordingly, it cannot be excluded that **6** is an artifact. Fulvenes recently have been reported from two different Compositae [17, 18].

The ^{1}H NMR spectral data of **7c** (Table 3) were in part close to those of homogeranylnerol derivatives isolated previously [19]. In addition to signals of an olefinic methyl and an acetate methyl group those of an isopropyl group and of two methyls on oxygen bearing carbons (δ1.29 and 1.38, *s*) were visible. Furthermore, typical signals of exomethylene protons (δ4.90 and 4.81 *br s*) indicated an additional equivalent of a methyl group. Low field signals at δ4.10 *br dd*, 2.99 *dd* and 2.72 *dd*

Table 1. ^{1}H NMR spectral data of **1**, **2a–2c** and **3a–3c** (400 MHz, $CDCl_3$, δ-values)

H	1†	2a‡	2b	2c	3a	3b	3c
2	*	3.08 *br d* 2.98 *br d*	3.08 *br d* 2.98 *br d*	5.11 *br s*	2.72 *br d* 2.50 *br d*	5.85 *br s*	4.71 *br d*
3	*	5.57 *br s*	5.58 *br s*	5.71 *br s*	3.42 *br s*	3.70 *br s*	3.56 *br d*
5	4.70 *br d*	3.36 *br d*	3.48 *br d*	3.58 *br d*	3.22 *br d*	3.40 *br d*	3.37 *br d*
6	4.94 *dd*	3.68 *dd*	3.66 *dd*	3.53 *dd*	3.66 *dd*	3.64 *dd*	3.60 *dd*
7	3.11 *dddd*	2.42 *br ddd*	3.36 *m*	3.38 *m*	3.35 *dddd*	3.08 *dddd*	3.34 *m*
8	5.35 *br dd*	5.08 *br dd*	5.28 *br dd*	5.28 *br dd*	5.21 *br dd*	3.78 *ddd*	5.24 *br dd*
9	5.42 *br d*	5.58 *br d*	5.56 *br d*	5.56 *br d*	5.52 *br d*	5.42 *br d*	5.45 *br d*
13	6.32 *d*	1.33 *d*	6.15 *d*	6.15 *d*	6.16 *d*	6.26 *d*	6.17 *d*
13′	5.72 *d*		5.52 *d*	5.54 *d*	5.51 *d*	6.24 *d*	5.54 *d*
14	1.57 *br s*	1.62 *br s*	1.62 *br s*	1.85 *br s*	1.60 *br s*	1.62 *br s*	1.81 *br s*
15	1.78 *br s*	1.92 *br s*	1.95 *br s*	2.00 *br s*	1.69 *s*	1.70 *s*	1.70 *s*
OAc	2.01 *s*	2.11 *s*	2.12 *s*	2.12 *s*	1.99 *s*	—	2.11 *s*
OR	6.21 *br q*	3.11 *q*	3.12 *q*	3.11 *q*	3.12 *q*	6.19, 6.14 *qq*	3.12 *q*
	2.00 *br s*	1.55 *s*	1.56 *s*	1.55 *s*	1.54 *s*	2.03, 2.01 *dq*	1.57 *s*
	1.88 *br s*	1.42 *d*	1.43 *d*	1.42 *d*	1.42 *d*	1.96, 1.90 *dq*	1.44 *d*
							2.02 *br d*

*Obscured; †H-1 5.34 *m*; ‡H-11 2.53 *dq*.

J[Hz]: Compound **1**: 5,6 = 8,9 = 9.5; 6,7 = 7,8 = 7.5; 7,13 = 3.5; 7,13′ = 3; compounds **2a–2c**,**3a–3c**: 5,6 = 6,7 = 7,8 = 8,9 ≈ 10; compound **2a**: 2,2′ = 21; 7,11 = 12; 11, 13 = 7; compounds **2b**, **2c**, **3a–3c**: 7,13 = 7,13′ = 3; compound **2b**: 2,2′ = 21; compound **3a**: 2,2′ = 18; compound **3c**: 2,3 = 1.5; 2,OH = 11.

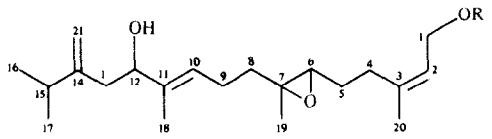
Table 2. ^{1}H NMR spectral data of **4a–4d**, **5a**, **5b** and **6** (400 MHz, $CDCl_3$, δ-values)

H	4a	4b	4c	4d	5a	5b	6
2	6.39 *d*	6.41 *d*	6.37 *d*	6.39 *d*	3.96 *d*	3.94 *d*	6.40 *br d*
3	6.08 *d*	6.02 *br d*	6.06 *br d*	6.10 *br d*	3.54 *d*	3.54 *d*	6.23 *d*
5	3.08 *br d*	2.86 *br d*	2.98 *br d*	3.10 *br d*	2.76 *dq*	2.76 *dq*	—
6	4.31 *dd*	4.20 *dd*	4.07 *dd*	4.50 *dd*	4.78 *dd*	4.81 *dd*	5.68 *dq*
7	3.25 *dddd*	3.35 *dddd*	2.95 *m*	3.24 *dddd*	3.06 *dddd*	3.10 *dddd*	3.28 *dddd*
8	5.42 *dd*	5.33 *dd*	3.93 *ddd*	5.41 *dd*	5.33 *dd*	5.40 *dd*	5.52 *dd*
9	5.67 *br d*	5.64 *br d*	5.54 *br d*	5.54 *br d*	5.41 *br d*	5.35 *br d*	5.14 *d*
13	6.26 *d*	6.21 *d*	6.33 *d*	6.31 *d*	6.29 *d*	6.29 *d*	6.28 *d*
13′	5.66 *d*	5.55 *d*	6.32 *d*	5.83 *d*	5.77 *d*	5.73 *d*	5.57 *d*
14	1.80 *br s*	1.80 *br s*	1.81 br *s*	1.83 *d*	2.03 *d*	2.01 *d*	2.32 *br s*
15	1.49 *s*	1.60 *s*	1.51 *s*	1.48 *s*	1.27 *s*	1.28 *s*	2.22 *br d*
OAc	2.03 *s*	2.04 *s*	—	2.10 *s*	2.13 *s*	2.05 *s*	2.03 *s*
OR	6.27 *qq*	6.28 *qq*	6.23 *br q*	3.11 *q*	6.17 *qq*	6.23 *qq*	3.21 *q*
	2.02 *dq*	2.05 *dq*	2.05 *br d*	1.59 *s*	2.00 *dq*	2.01 *dq*	1.56 *s*
	1.90 *dq*	1.90 *dq*	1.97 *br s*	1.41 *d*	1.81 *dq*	1.90 *dq*	1.47 *d*
			2.59 *d* (OH)				

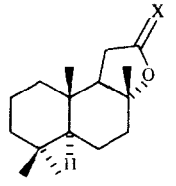
J[Hz]: 7,13 = 3.5; 7,13′ = 3; compounds **4a–4d**: 2,3 = 5.5; compound **4a**: 5,6 = 11; 6,7 = 7,8 = 10; 8,9 = 8; compound **4b**: 5,6 = 6,7 = 10.5; 7,8 = 10; 8,9 = 9; compound **4c**: 5,6 = 6,7 = 10.5; 7,8 = 10; 8,9 = 7.5; 8, OH = 4; compound **4d**: 5,6 = 11; 6,7 = 10; 7,8 = 8.5; 8,9 = 6.5; compounds **5a**/**b**: 2,3 = 3; 5,6 = 11; 5,14 = 2.5; 6,7 = 10; 7,8 = 8; 8,9 = 9 = 4; compound **6**: 2,3 = 5; 6, = 10.5; 6,15 = 2; 7,8 = 8.5; 8,9 = 2.5.

agreed with the presence of an allylic hydroxy and two epoxide groups. Spin decoupling allowed the assignment of all signals and the resulting sequences indicated the position of the oxygen functions. The stereochemistry was deduced from NOE. Thus, clear effects were obtained between H-10 and H-12, between H-2 and H-20, between H-6, H-8 and H-5 while no effect was obtained between H-19 and H-6. The ^{1}H NMR signals of **7b** (Table 3) were nearly identical to those of **7c**. The absence of the acetate methyl signal and the upfield shift of H-1 clearly indicated that **7b** was the desacetyl derivative of **7c**. The ^{1}H NMR spectrum of **7a** (Table 3) again was in part similar to that of **7c**. However, the absence of one epoxide group followed from the additional olefinic methyl signal (δ1.79 *br s*). Thus, **7a** was a precursor of **7c**. The ^{13}C NMR data of the latter also agreed with the structure. All signals could be assigned by a 2D ^{1}H ^{13}C COSY spectrum.

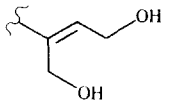
The structure of **10b** followed from its ^{1}H and ^{13}C NMR data (see Experimental). The ^{1}H NMR spect-



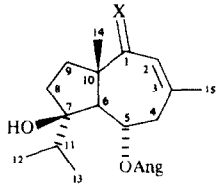
7a R = Ac
7b R = H, 2,3 epoxide
7c R = Ac, 2,3 epoxide



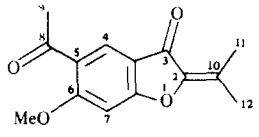
8 X = H,



9 X = O



10a X = H_2
10b X = O



11

rum was in part similar to that of the known 1-desoxo derivative **10a** [14]. Due to the keto group at C-1 the H-2 signal was shifted downfield and the vicinal couplings were missing. Clear NOE between H-13 and H-6 as well as between H-14, H-5 and H-4 indicated identical stereochemistry for both angelates.

The molecular formula and the ^{1}H NMR signals of **11** (see Experimental) showed that the methyl ether of a keto derivative of tremetone must be present. The positions of the keto group followed from the chemical shift of H-4 (δ8.17) while those of H-11 and H-12 showed that the 10,11-double bond of a tremetone derivative was shifted into conjugation.

The new results on the chemistry of *H. helianthoides* are of interest as very similar sesquiterpene lactones have been reported from *Balsamorhiza* [11], *Berlandiera* [20, 21] and *Blainvillea* species [22] which all have been placed in the subtribe Ecliptinae [3]. Furthermore, labdane derivatives like **8** and **9** are present in *Silphium* [15] and *Lindheimera* species [16] also belonging to the Ecliptinae. Finally, geranylnerol derivatives have been reported from *Balsamorhiza* [11] and *Blainvillea* species [22] which most likely are precursors of the homo diterpenes **7a**–**7c**. Tremetone derivatives are less characteristic but they also have been reported from many genera of the same subtribe.

EXPERIMENTAL

Air-dried aerial parts of *H. helianthoides* (L.) Sweet. (200 g, collected near Monterrey, N. L. in May 1987, voucher Domin-

Table 3. ^{1}H NMR spectral data of **7a**–**7c** and ^{13}C NMR data of **7c** ($CDCl_3$, δ-values)

H	7a	7b	7c	C	7c
1	4.59 *br d*	3.79 *br dd*	4.33 *dd*	1	62.8 *t*
		3.70 *br dd*	4.08 *dd*	2	60.8 *d*
2	5.40 *br t*	2.99 *dd*	2.92 *dd*	3	60.7 *s*
4	2.25 *m*	1.6-1.8 *m*	1.6–1.8 *m*	4	29.7 *t*
5	1.65 *m*			5	24.8 *t*
6	2.72 *dd*	2.80 *dd*	2.72 *dd*	6	62.8 *d*
8	1.65 *m*	1.65 *m*	1.65 *m*	7	60.5 *s*
	1.51 *ddd*	1.55 *m*	1.50 *ddd*	8	38.1 *t*
9	2.10 *m*	2.10 *m*	2.11 *m*	9	23.2 *t*
10	5.42 *br t*	5.41 *br d*	5.42 *br t*	10	124.9 *d*
12	4.10 *br dd*	4.10 *br dd*	4.10 *br dd*	11	137.2 *s*
13	2.31 *br dd*	2.32 *br dd*	2.32 *br dd*	12	76.6 *d*
	2.20 *br dd*	2.19 *br dd*	2.19 *br dd*	13	41.3 *t*
15	2.26 *br qq*	2.26 *br qq*	2.25 *br qq*	14	152.5 *s*
16	1.07 *d*	1.06 *d*	1.06 *d*	15	33.1 *d*
17	1.04 *d*	1.03 *d*	1.03 *d*	16	21.5 *q*
18	1.05 *br s*	1.64 *br s*	1.64 *br s*	17	21.9 *q*
19	1.28 *s*	1.29 *s*	1.29 *s*	18	11.6 *q*
20	1.79 *br* s	1.38 *s*	1.34 *s*	19	16.5 *q*
21	4.91 *br s*	4.91 *br s*	4.90 *br s*	20	21.8 *q*
	4.83 *br s*	4.82 *br s*	4.81 *br s*	21	109.6 *t*
OAc	2.05 *s*	—	2.10 *s*	OAc	170.7 *s*, 20.7 *q*

J[Hz]: 5,6 = 6; 8,8′ = 13.5; 8′,9 = 6.5; 8′,9′ = 8; 9,10 = 7; 12,13 = 4; 12,13′ = 9; 13,13′ = 14; 15,16 = 15,17 = 7; compound **7a**: 1,2 = 7; compound **7b**: 1,1′ = 12; 1,2 = 1′,2 = 6; compound **7c**: 1,1′ = 12; 1,2 = 4.5; 1′,2 = 6.5.

guez 7910, deposited in the Herbarium of the Instituto Technologico de Monterrey, Mexico) were extracted and worked-up as reported elsewhere [23]. Two crude CC fractions (Et_2O–petrol (1:1) and Et_2O–MeOH (9:1) were combined. Flash chromatography of the first fraction (silica gel, ϕ 30–60 μm) gave 210 mg **7a**, 300 mg **7c** and a mixture. HPLC [MeOH–H_2O, (3:1) RP 8, *ca* 100 bar] gave 20 mg **7a** and a mixture which by TLC gave two bands (1/3/1 and 1/3/2). HPLC (1/3/1, MeOH–H_2O (4:1) afforded 2 mg **1** (R_t 5.5 min) and 8 mg **11** (R_t 6.5 min). HPLC of 1/3/2 [MeOH–H_2O (7:3)] gave 2 mg **3b** (R_t 7.6 min), 3 mg **2a** (R_t 8.4 min) and 30 mg **2b** (R_t 9.6 min). Flash chromatography of the second CC fraction gave four mixtures (2/1–2/4). TLC of 2/1 (Et_2O–petrol (3:2) gave 5 mg **4b** (R_f 0.6), 20 mg **4a** (R_f 0.5), 6 mg **4d** (R_f 0.45) and a mixture which gave by TLC (Et_2O) 30 mg **5a** (R_f 0.35) and 20 mg **5b** (R_f 0.3). HPLC of 2/2 [MeOH–H_2O (7:3)] afforded 10 mg **3c** (R_t 5.7 min.) and 15 mg zoapatanolide A. From fraction 2/3 30 mg crystalline zoapatanolide B was obtained. The mother liquor gave by TLC [Et_2O–petrol (7:3)] 5 mg **3a** (R_f 0.5), 15 mg **2a** (R_f 0.43), 20 mg zoapatanolide A, 3 mg crude **4c** (purified by HPLC, MeOH–H_2O, (3:2), R_t 6.3 min) and 15 mg zoapatanolide B. TLC of 2/4 [toluene–CH_2Cl_2–Et_2O (2:2:1)] afforded 20 mg 3,6,7,8,4′-pentamethoxy-5,3′-dihydroxyflavone, 10 mg **4e**, 30 mg zoapatanolide A, 10 mg **7b** (R_f 0.3) and 20 mg zoapatanolide B. An extract of 60 g roots gave three CC fractions [1:Et_2O–petrol (1:1); 2: Et_2O and 3: Et_2O–MeOH (9:1)]. TLC of 1 [Et_2O–petrol (1:1)] gave 10 mg **10b** (R_f 0.42) and a mixture which gave by HPLC [MeOH–H_2O (17:3)] 5 mg lasidiol angelate, 2 mg **10a**, 3 mg tremetone and 5 mg **9**. TLC of 2 [Et_2O–petrol (3:1)] gave 10 mg **10b** and 20 mg 5-hydroxymethylene furfural while TLC of 3 gave 10 mg **8**.

Known compounds were identified by comparing their 400 MHz ^{1}H NMR spectra with those of authentic materials.

8α-*Acetoxy*-9β-*angeloyloxy-germacra*-1E,4E, 11 (13)-*trien*-12,6α-*olide* (**1**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.). 388.189 $[M]^+$ (19) (calc. for $C_{22}H_{28}O_6$: 388.189), 346 (1), 246 (5), 228 (4.5), 213 (4), 83 (100); $[\alpha]_D^{24}$ +24 ($CHCl_3$; *c* 0.15).

9β-*Acetoxy*-8-O-[2,3-*epoxy*-2-*methylbutyryl*]-8-*desacetyl*-11β,13-*dihydrozuzubergenin* (**2a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1785 (γ-lactone), 1750 (CO_2R); MS *m/z* (rel. int.): 404.184 $[M]^+$ (6) (calc. for $C_{22}H_{28}O_7$: 404.184), 344 (7), 288 (10), 228 (100); $[\alpha]_D^{24}$ +37 ($CHCl_3$; *c* 0.1).

9β-*Acetoxy*-8-O-[2,3-*epoxy*-2-*methylbutyryl*]-*desacetyl zuzubergenin* (**2b**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1750 (CO_2R); MS *m/z* (rel. int.): 402.168 $[M]^+$ (3) (calc. for $C_{22}H_{26}O_7$: 402.168), 342 (2), 286 (8), 226 (100); $[\alpha]_D^{24}$ −156 ($CHCl_3$; *c* 0.1).

9β-*Acetoxy*-2α-*hydroxy*-8-O-[2,3-*epoxy*-2-*methylbutyryl*]-*desacetyl zuzubergenin* (**2c**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1750 (CO_2R); MS *m/z* (rel. int.): 418.163 $[M]^+$ (0.1) (calc. for $C_{22}H_{26}O_8$: 418.163), 224 (100).

9β-*Acetoxy*-8α-[2,3-*epoxy*-2-*methylbutyryloxy*]-*ludartin* (**3a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1750 (CO_2R); MS *m/z* (rel. int.): 418.163 $[M]^+$ (1.5) (calc. for $C_{22}H_{26}O_8$: 418.163), 376 (2), 358 (2), 260 (64), 242 (22), 135 (100), 116 (80); $[\alpha]_D^{24}$ +11 ($CHCl_3$; *c* 0.1).

2α,9β-*Diangeloyloxy*-8α-*hydroxyludartin* (**3b**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1730 (C=CCO_2R); MS *m/z* (rel. int.): 458.194 $[M]^+$ (4) (calc. for $C_{25}H_{30}O_8$: 458.194), 359 (2), 358 (1), 83 (100); $[\alpha]_D^{24}$ +6 ($CHCl_3$; *c* 0.1).

2α-*Hydroxy*-9β-*acetoxy*-8α-[2,3-*epoxy*-2-*methylbutyryloxy*]-ludartin (**3c**). Colourless crystals, mp 212–13°; MS *m/z* (rel. int): 434.158 $[M]^+$ (0.2) (calc. for $C_{22}H_{26}O_9$: 434.158), 374 (24), 258 (30), 151 (100).

Heliopsolide-8-O-*acetate* (**4a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1750 (OAc), (C=CCO_2R); MS *m/z* (rel. int.): 302.115 $[M-AngOH]^+$ (10) (calc. for $C_{17}H_{18}O_5$: 302.115), 260 (14), 242 (12), 83 (100).

4-*Epi-Helipsolide*-8-*O*-*acetate* (**4b**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1745 (OAc), 1730 (C=CCO_2R); MS *m/z* (rel. int.): 302.115 $[M-AngOH]^+$ (11) (calc. for $C_{17}H_{18}O_5$: 302.115), 260 (12), 242 (13), 224 (7), 83 (100); $[\alpha]_D^{24}$ +10 ($CHCl_3$; *c*. 0.39).

Heliopsolide (**4c**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1730 (C=CCO_2R); MS *m/z* (rel. int.): 342.146 $[M-H_2O]^+$ (2) (calc. for $C_{20}H_{22}O_5$: 342.147), 324 (2), 242 (7), 224 (5), 83 (100).

9-O-*Acetyl*-8-O-[2,3-*epoxy*-2-*methylbutyryl*]-*desacyl-heliopsolide* (**4d**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 400.152 $[M-H_2O]^+$ (1) (calc. for $C_{22}H_{24}O_7$: 400.152), 358 (6.5), 242 (100).

2α,3α-*Epoxyheliopsolide*-8-*O*-*acetate* (**5a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1750 (OAc), 1725 (C=CCO_2R); MS *m/z* (rel. int.). 358.142 $[M-HOAc]^+$ (6) (calc. for $C_{20}H_{22}O_6$: 358.142), 258 (7), 83 (100).

2α,3α-*Epoxy*-9-O-*acetyl*-8-O-*angeloyl-desacyl-heliopsolide* (**5b**). Colourless oil; IR$_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1750 (OAc), 1725 (C=CCO_2R); MS *m/z* (rel. int.): 358.142 $[M-HOAc]^+$ (5) (calc. for $C_{20}H_{22}O_6$: 358.142), 258 (10), 83 (100); $[\alpha]_D^{24}$ −34 ($CHCl_3$; *c* 0.59); ^{13}C NMR ($CDCl_3$): δ123.1 *t*, 48.8, 54.1, 54.3, 61.8, 72.9 74.5, 75.5 *d*, 166.0, 135.3, 135.7, 131.2, 76.8 *s*, 20.0, 21.1 *q*; OAc: 168.9 *s*, 20.9 *q*; OAng: 168.5 *s*, 126.4 *s*, 141.3 *d*, 16.0, 20.5 *q*.

1-*Acetoxy*-12-*hydroxy*-6,7-*epoxysmallantha*-2Z,10E,14 (21)-*triene* (**7a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1750 (OAc); MS *m/z* (rel. int.): 318.256 $[M-HOAc]^+$ (0.5) (calc. for $C_{21}H_{34}O_2$: 318.256), 300 (0.8), 235 (30), 97 (91), 81 (100).

1,12-*Dihydroxy*-2,3,6,7-*bisepoxysmallantha*-10E,14 (21)-*diene* (**7b**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); CIMS *m/z* (rel. int.): 335 $[M-H_2O]^+$ (100), 317 (41), 237 (58), 221 (66); $[\alpha]_D^{24}$ −29 ($CHCl_3$; *c* 0.14).

1-*Acetoxy*-12-*hydroxy*-2,3,6,7-*bisepoxysmallantha*-10E,14(21)-*diene* (**7c**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590 (OH), 1740 (OAc); MS *m/z* (rel. int.): 394.272 $[M]^+$ (0.4) (calc. for $C_{23}H_{38}O_5$: 394.272), 376 (1.3), 233 (20), 97 (100), 81 (91).

5α-*Angeloyloxy*-7β-*hydrohydauca*-2-en-l-one (**10b**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3460 (OH), 1710 (C=CCO_2R), 1660 (C=CC=O); MS *m/z* (rel. int.). 334.214 $[M]^+$ (0.3) (calc. for $C_{20}H_{30}O_4$: 334.214), 291 (9), 234 (14), 191 (21), 83 (100); ^{1}H NMR ($CDCl_3$): δ5.98 (*ddq*, H-2, J = 1, 1, 1 Hz), 2.99 (*br dd*, H-4, J = 5, 16), 2.37 (*ddd*, H-4′, J = 1, 2.5, 16), 5.71 (*ddd*, H-5, J = 2.5, 5, 9.5), 2.44 (*d*, H-6, J = 9.5), 1.55 (*m*, H-11), 0.94 (*d*, H-12, J = 6.5), 0.87 (*d*, H-13, J = 6.5), 1.38 (*s*, H-14), 2.01 (*br s*, H-15); OAng: 6.15 *qq*, 2.02 *dq*, 1.89 *dq*; ^{13}C NMR ($CDCl_3$; C-1–C-15): δ208.4, 128.8, 149.5, 37.0, 69.8, 50.4, 84.3, 38.4, 31.3, 55.3, 36.4, 17.9, 18.3, 28.0, 17.3; OAng: 167.8, 127.3, 139.8, 15.8, 20.5.

5-*Acetyl*-2-*isopropylidene*-6-*methoxy-benzofuran*-3-*one* (**11**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1660, 1610 (PhCO); MS *m/z* (rel. int.): 246.089 $[M]^+$ (68) (calc. for $C_{14}H_{14}O_4$: 246.089), 231 (100), 216 (7); ^{1}H NMR ($CDCl_3$): δ8.17 (*s*, H-4), 6.69 (*s*, H-7), 2.59 (*s*, H-9), 2.36 (*br s*, H-11), 2.09 (*br s*, H-12), 4.00 (*s*, OMe).

Acknowledgement—X.A.D. thanks CONACYT of Mexico for a research grant PCECBNA-031053.

REFERENCES

1. Hoffmann, O. (1890) in *Die Natürlichen pflanzenfamilien* Vol. 4 (Engler, A. and Prantl, K., eds), p. 225.
2. Stuessy, T. F. (1977) *The Biology and Chemistry of the*

Compositae (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds), p. 632. Academic Press, London.
3. Robinson, H. (1981) *Smithsonian Contr. Botany* **51**, 48.
4. Burden, R. S., Crombie, L. and Whitney, D. A. (1968) Tetrahedron *Letters* 1035.
5. Johns, T., Graham. T. and Towers, G. H. N. (1982) *Phytochemistry* **21**, 2737.
6. Bohlmann, F., Gerke, T., Ahmed, M., King, R. M. and Robinson, H. (1983) *Liebigs Ann. Chem.* 1202.
7. Jacobsen, M. (1951) *J. Am. Chem. Soc.* **73**, 100.
8. Jacobsen, M. (1957) *J. Am. Chem. Soc.* **79**, 356.
9. Bohlmann, F., Lonitz, M. and Knoll, K. H. (1978) *Phytochemistry* **17**, 330.
10. Quijano, L., Calderon, J. S., Gomez, F. and Rios, T. (1982) *Phytochemistry* **21**, 2041.
11. Bohlmann, F., Misra, R. N., Jakupovic, J., King, R. M. and Robinson, H. (1985) *Phytochemistry* **24**, 2039.
12. Fang, N., Leidig, M. and Mabry, T. J. (1986) *Phytochemistry* **25**, 927.
13. Wiemer, D. F. and Ales, D. C. (1981) *J. Org. Chem.* **46**, 5449.
14. Miski, M., Ulubelen, A. and Mabry, T. J. (1983) *Phytochemistry* **22**, 2231.
15. Bohlmann, F. and Jakupovic, J. (1979) *Phytochemistry* **18**, 1987.
16. Herz, W., Watanabe, K., Kulanthaivel, P. and Blount, J. F. (1985) *Phytochemistry* **24**, 2645.
17. Barrero, A. F., Sanchez, J. F., Zefra, M. J., Barron, A. and San Feliciano, A. (1987) *Phytochemistry* **26**, 1531.
18. Zdero, C., Bohlmann, F., King, R. M. and Robinson, H. (1988) *Phytochemistry* **27** (in press).
19. Bohlmann, F., Jakupovic, J., Schuster, A., King, R. M. and Robinson, H. (1985) *Phytochemistry* **24**, 1315.
20. Herz, W., Bhat, S. V. and Srinivasan, A. (1973) *J. Org. Chem.* **38**, 4218.
21. Fischer, N. H., Leonard, C., Lee, I. Y. and Le Van, N. (1982) *J. Heterocycl. Chem.* **19**, 181.
22. Singh, P., Bhala, M. and Jakupovic, J. (1988) *Phytochemistry* **27**, 609.
23. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.