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SECO-, *NOR-*, NORMAL AND REARRANGED LABDANES FROM *HAPLOPAPPUS PARVIFOLIUS*

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Key Word Index—*Haplopappus parvifolius*; Compositae; diterpenes; labdanes; *seco*-labdanes; *nor*-labdanes; rearranged labdanes; new carbon skeleton.

Abstract—The aerial parts of *Haplopappus parvifolius* afforded 30 new diterpenes including 21 labdane derivatives, four *nor*-diterpenes, three rearranged ones, four *seco*-labdanes and one with a new carbon skeleton whose structure was established by partial synthesis. All structures were elucidated by high field NMR spectroscopy and other spectroscopic techniques. Biogenetic relationships are discussed briefly.

INTRODUCTION

The large genus *Haplopappus* with *ca* 160 species (Compositae) is the most cytologically variable genus in the tribe Astereae [1]. So far limited studies have also indicated that the chemistry is not very uniform [2 and lit. cited therein]. In continuation of our investigations of the chemistry of Chilean Compositae we now have studied *H. parvifolius* (DC.) A. Gray.

RESULTS AND DISCUSSION

Aerial parts of *H. parvifolius* afforded, in addition to 13-*epi*-manoyloxide (**1**) [3], isomanool [4] and the carotane derivative **32** [5], a very complex mixture of compounds which could only be separated by repeated TLC and HPLC and which often still gave mixtures. Changing of TLC and HPLC conditions finally afforded 30 new diterpenes, the labdane derivatives **2**–**22**, the *nor*-diterpenes **23**, **30** and **31**, the *seco*-diterpenes **24**, **25** and **28**, the *seco-nor*-labdane **27** and the tetracyclic diterpene **26** with a new carbon skeleton.

The configuration of compound **1** followed from its ^{13}C NMR which showed the characteristic shift of C-17 (δ32.6) instead of δ28.7 for the 13-*epi* isomer. The optical rotation showed that we were dealing with normal labdanes. We therefore propose that all the isolated diterpenes belong to this series.

The ^{1}H NMR spectra of **2** and **3** (Table 1) differed only in the chemical shifts of several signals indicating the presence of isomers. Compound **2** showed NOEs of H-16 and H-17 with H-14 (5 and 8%, respectively), while H-20 gave a NOE with H-17 (12%). An effect between H-18 and H-6 (8%) allowed the assignment of the olefinic protons which required the presence of a 6,7-double bond. In the case of **3** the NOEs indicated the presence of a 8-*epi* isomer of **2** [H-17 with H-7 (6%) and H-11α (7%), H-16 with H-14 (6%), H-18 with H-6 (10%) and H-5 (6%), H-11α with H-17 (4%) and H-16 (4%)].

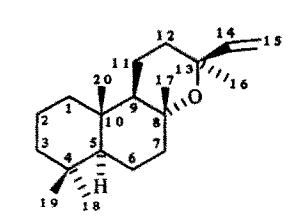
The carbinols **4** and **5** could be separated only by TLC on $AgNO_3$ coated silica gel. The ^{1}H NMR (Table 1) of the higher R_f compound **4** showed the presence of an olefinic methyl (δ1.69) while the isomer **5** displayed a pair of broadened singlets at δ4.90 and 4.88 typical for a 8(17)-double bond. Accordingly, the ^{1}H NMR spectrum was in part very close to that of a corresponding labdanolic acid from a *Gutierrezia* species [6].

The ^{1}H NMR spectrum of **6** (Table 1) showed in part similarities with that of **5**. However, the molecular formula showed that this compound had two hydrogens less. Spin decoupling indicated that the broadened singlet at δ2.50 was due to H-5. The drastic downfield shift of this double doublet required an axial oxygen function at C-9. The resulting structure **6** is close to a 15-oic acid [7]. Accordingly, the ^{1}H NMR data resembled those of **6**.

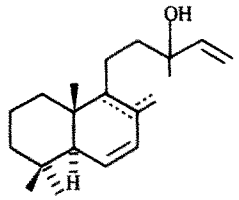
The ^{1}H NMR spectra of **7**–**9** (Table 2) were similar, differing only in the signals of the ester group and in the case of **7** by the chemical shift of the proton under the oxygen function. Accordingly, compound **7** was the free alcohol while compound **8** was the corresponding acetate. As already indicated by the molecular formula of **9** ($C_{24}H_{38}O_3$), in this case the alcohol **7** was esterified with *n*-butyric acid. Due to the neighbouring chiral centre the signals of the α-protons exhibited a pair of double triplets and even the signals of the β-protons were not simply a triplet of quartets. Spin decoupling showed that compounds **7**–**9** were labdanes with a 9,13-ether bridge with Δ^7 and Δ^{14} double bonds and an α-orientated oxygen function at C-6. Accordingly, the ^{1}H NMR spectrum of **7** was close to that of 6-hydroxygrindelic acid [8].

The ^{1}H NMR spectrum of **10** (Table 2) showed that we were dealing with a conjugated ketone closely related to **7**. In agreement with the molecular formula ($C_{20}H_{30}O_3$), a 5-hydroxy group was proposed. This was supported by the downfield shift of the methyl singlets of H-18–H-20.

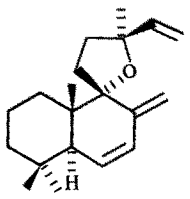
The ^{1}H NMR spectrum of **11** (Table 2) indicated the presence of a labdane with an acetoxy group. Spin decoupling showed that the latter was at C-6, allylic to a 7,8-double bond. Furthermore, an allylic coupling of H-7 with both H-9 and H-17 indicated that no ether ring between C-9 and C-13 was present. The observed coupling $J_{5,6}$ and $J_{6,7}$ required a 6β-acetoxy group.



1 **2** Δ^6 **3** Δ^6 8-*epi*



4 Δ^8 **5** $\Delta^{8(17)}$



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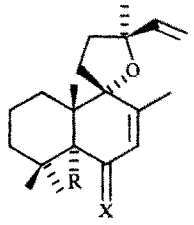
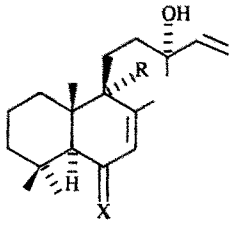
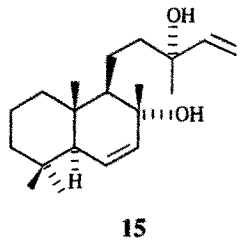


	7	**8**	**9**	**10**
X	αOH,H	αOAc,H	αO*n*Bu,H	=O
R	H	H	H	OH





15

	11	**12**	**13**	**14**
X	βOAc,H	αO*n*Bu,H	=O	=O
R	H	H	H	OH

The ^{1}H NMR spectrum of **12** (Table 2) differed from that of **11** mainly by the replacement of the acetoxy signal by those of a *n*-butyryloxy group and by the changed coupling $J_{5,6}$ indicating the presence of a 6α-butyryloxy derivative of **11**. The ^{13}C NMR spectrum (Table 3) also supports the structure.

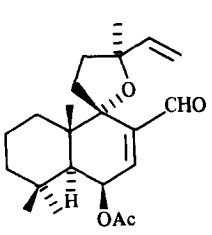
The ^{1}H NMR data of **13** (Table 2) show that again a 6-keto labdane was present. In agreement with the molecular formula ($C_{20}H_{32}O_2$) 6-oxo-isomanool was, therefore, proposed. The ^{13}C NMR data further support this structure (Table 3). The observed positive Cotton-effect at 333 nm again shows that we were dealing with normal labdanes if the effect was compared with the results on 6-oxo-grindelic acid [9]. Comparison of the ^{1}H NMR spectrum of **14** with that of **13** (Table 2) showed that in that of the former no H-9 signal was visible. Accordingly, a 9-hydroxy group was proposed. This was supported by the missing couplings of H-7 and H-17. The molecular formula also required a third oxygen function. The configuration at C-9 followed from the downfield shift of H-5.

The ^{1}H NMR spectrum of **15** (Table 4) indicated that again an isomanool derivative was present. Signals at δ1.62, 5.64 and 5.70 were due to H-5, H-6 and H-7. Thus, the diol **15** most likely was formed by an ene-reaction of isomanool with oxygen followed by reduction of the hydroperoxide. The ^{13}C NMR spectrum supports the structure (Table 3).

The ^{1}H NMR spectrum of **16** (Table 4) showed the presence of an aldehyde and an acetoxy group. Comparison of the data with those of related grindelic acid derivatives [8] led to the structure. The configuration at C-6 followed from the coupling $J_{5,6}$.

The ^{1}H NMR data of **17** (Table 4) were in part similar to those of **16**. However, H-7 showed an allylic coupling requiring a proton at C-9 and the acetoxy was replaced by a hydroxy group. A broadened signal at δ4.54 was changed to a double triplet by deuterium exchange. Spin decoupling showed that an addition to a vicinal, a homoallylic coupling with H-9 was present. The coupling $J_{5,6}$ required a 6α-hydroxy group. The ^{13}C NMR spectrum also agreed with the structure (Table 3).

The ^{1}H NMR spectrum of **19** (Table 4) again showed five methyl singlets and the double doublets of a vinyl group. Accordingly, a labdane derivative was very likely. A singlet at δ2.03 was due to an acetoxy methyl while the methyl singlet at δ1.73 should be that of an olefinic methyl. As no signal of an olefinic proton was visible and as typical H-11 signals around δ2.3 were present, a ditertiary double bond had to be proposed. This was established by the ^{13}C NMR spectrum (Table 3) which further indicated the presence of one tertiary and two



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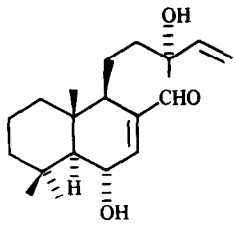

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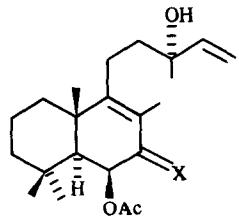
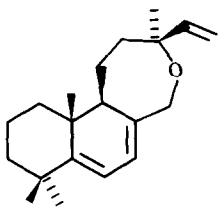


18 19

X =O βOH,H



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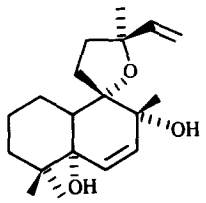

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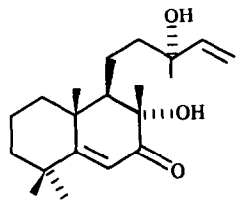

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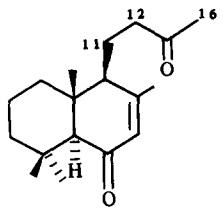

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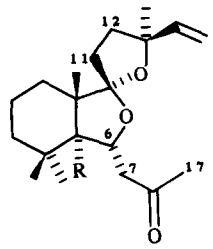
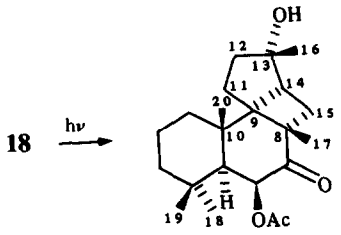


24 R = H

25 R = OH



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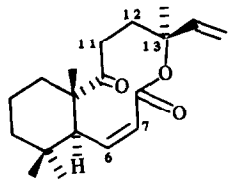

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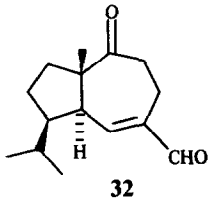


32

secondary oxygen bearing carbons. Proton signals at δ5.24 and 3.63 supported the presence of two oxygen bearing methin carbons. Spin decoupling showed that a 6-acetoxy-7-hydroxy derivative was present. The couplings required β-orientation of these groups as H-5 was not deshielded (δ1.53 *d*). A NOE between H-5 and H-6 (7%) as well as between H-19, H-20 (5%) and OAc (3%) established the proposed configuration.

The ^{1}H NMR spectrum of **18** (Table 4) was in part close to that of **19**. However, in addition to shift differences the H-7 signal was missing and that of H-6 was shifted, downfield, now being a doublet. As already indicated by the molecular formula ($C_{22}H_{34}O_4$) all data, therefore, agreed with the 7-keto derivative of **19**. The ketone gave a negative Cotton-effect at 330 nm.

The molecular formula of **20** ($C_{20}H_{30}O$) and the presence of three double bonds required a tricyclic diterpene. Spin decoupling showed that the low field signals in the ^{1}H NMR spectrum (Table 4) required in addition to the Δ^{14} double bond a 5,7-diene. The signals at δ4.31 *dt* and 4.16 *d* were due to H-17 as the triplet splitting result

Table 1. ^{1}H NMR spectral data of compounds **2–6** (400 MHz, $CDCl_3$, δ-values)

H	2	3	4†	5	6	Multiplicity
5	1.95	1.45	1.94	1.94	2.50	*dd*
6	5.62	5.75	5.82	6.15	6.11	*dd*
7	5.67 *dd*	5.58	5.70	5.72	5.81	*br d*
9	1.88	*	—	1.84	—	*br d*
14	6.04	5.71	5.95	5.94	5.90	*dd*
15c	4.99	4.96	5.10	5.08	4.85	*dd*
15t	5.00	5.19	5.24	5.23	5.04	*dd*
16	1.18	1.32	1.32	1.31	1.31	*s*
17	1.35	1.33	1.70	4.90 *br s*	4.99 *br s*	*s*
17′				4.88 *br s*	4.89 *br s*	*s*
18	0.90	0.92	0.95	0.94	0.99	*s*
19	0.82	0.90	0.81	0.83	0.85	*s*
20	0.78	0.84	0.93	0.68	0.73	*s*

*Overlapped multiplet.

†H-11 2.15 *dt* and 1.99 *dt*.

J [Hz]: 5,6 = 3; 5,7 ~ 2; 6,7 = 10; 9,11 = 8; 14,15c = 10; 14,15t = 17; 15c,15t = 1.5; compound 4; 11,11′ = 11,12 = 11′,12′ = 12; 11,12′ = 11′,12 = 5.

Table 2. ^{1}H NMR spectral data of compounds **7–14** (400 MHz, $CDCl_3$, δ-values)

H	7	8	9*	10	11	12	13†	14
5	2.05 *d*	2.14 *d*	2.14 *d*	—	1.29 *d*	1.47 *d*	2.03 *s*	2.19 *s*
6	4.04 *br d*	5.36 *ddq*	5.37 *ddq*	—	5.41 *br dd*	5.46 *ddq*	—	—
7	5.47 *dq*	5.33 *br s*	5.31 *br s*	5.92 *q*	5.50 *ddq*	5.21 *dq*	5.73 *dq*	6.07 *q*
14	6.01 *dd*	6.02 *dd*	6.02 *dd*	5.91 *dd*	5.90 *dd*	5.91 *dd*	5.92 *dd*	5.89 *dd*
15*c*	4.96 *dd*	4.95 *dd*	4.95 *dd*	4.94 *dd*	5.05 *dd*	5.07 *dd*	5.09 *dd*	5.13 *dd*
15*t*	5.15 *dd*	5.17 *dd*	5.17 *dd*	5.18 *dd*	5.20 *dd*	5.21 *dd*	5.23 *dd*	5.25 *dd*
16	1.31 *s*	1.31 *s*	1.31 *s*	1.26 *s*	1.29 *s*	1.28 *s*	1.31 *s*	1.32 *s*
17	1.74 *t*	1.73 *t*	1.72 *t*	1.94 *d*	1.73 *q*	1.71 *q*	1.91 *t*	2.08 *d*
18	1.15 *s*	0.98 *s*	0.97 *s*	1.47 *s*	1.08 *s*	0.95 *s*	1.14 *s*	1.29 *s*
19	1.04 *s*	0.95 *s*	0.95 *s*	1.09 *s*	1.00 *s*	0.92 *s*	1.11 *s*	1.12 *s*
20	0.86 *s*	0.90 *s*	0.91 *s*	1.04 *s*	0.94 *s*	0.84 *s*	0.83 *s*	1.11 *s*
OAc	—	2.03 *s*	—	—	2.02 *s*	—	—	—

*OCOR 2.28 and 2.24 *dt*, 1.66 *m*, 0.95 *t*.

†H-9 2.02 *br d*.

J [Hz]: 14,15c = 10; 14,15t = 17; 15c,15t ~ 1.5; compounds **7–9**: 5,6 = 10; 6,7 = 2.5; 6,17 = 7,17 = 1; compound **10**: 7,17 = 1.5; compound **11**: 5,6 = 4; 6,7 = 5; 6,17 = 7,17 = 9,17 ~ 1; compound **12**: 5,6 = 10; 6,7 ~ 2; 6,17 = 7,17 ~ 1.5; OCOR: 2,2′ = 15; 2,3 = 3,4 ~ 7.5; compound **13**: 7,9 = 7,17 ~ 1.5; compound **14**: 7,17 = 1.5.

from coupling with H-7 and H-9. In agreement with the molecular formula a 13,17-ether bridge was present. The very small amount did not allow the assignment of all ^{13}C NMR signals. However, signals at δ68.5 and 74.0 agreed with the proposed ether ring and six signals at δ145.7, 143.2, 143.0, 121.3, 119.4 and 115.0 are due to the olefinic carbons. The observed NOE also supported the structure and the stereochemistry [H-19 with H-20 (5%), H-18 with H-6 (8%), H-17′ with H-7 (4%), H-16 with H-14 (4%)].

Compound **21** (molecular formula $C_{20}H_{32}O_3$) showed in its ^{13}C NMR spectrum four signals for oxygen bearing carbons (Table 3) while the ^{1}H NMR spectrum displayed a pair of doublets at δ5.93 and 5.71 due to a 6,7-double bond. Chemical shifts in the ^{13}C NMR spectrum indicated an oxygen function at C-9. Thus, a 9,13-ether bridge was most probable, especially as H-17 showed a *W*-coupling with a hydroxy group. NOEs allowed the assignment of the methyl singlets and the olefinic protons [H-18 with H-6 (8%), H-19 with H-20 (7%), H-16 with H-14 (5%) and H-15 *t* (3%), H-17 with H-7 (8%)]. Most likely a hydrogen bond between 8-OH and the ether oxygen was present leading to a boat conformation of the cyclohexene ring; therefore no NOE between H-17 and H-20 was observed.

The ^{1}H and ^{13}C NMR data of **22** (Tables 3 and 4) indicated that a sclareol derivative with a 5,6-double bond and a 7-keto group was present. Accordingly, H-6 was a singlet (δ6.02) and the signals of H-18, H-19 and H-20 were shifted downfield. As expected C-5 was at very low fields (δ179.9), while C-7 showed a signal at 203.7, probably somewhat more downfield than usual due to a hydrogen bond with the 8-hydroxy group.

The ^{1}H NMR spectrum (Table 5) of the diketone **23**

Table 3. ^{13}C NMR spectral data of compounds **12, 13, 15, 17, 19, 21–23** and **26–29*** (100.6 MHz, $CDCl_3$, δ-values)

C	12	13	15	17	19	21	22	23	26	27	28	29
1	43.2	43.1	41.2	43.4	41.6	35.6	40.1	41.2	41.7	31.9	40.4	29.2
2	18.5	18.1	18.1	18.2	19.0	18.0	19.3	18.0	18.3	17.7	19.0	20.0
3	44.6	44.5	45.9	44.0	42.9	36.8	43.7	45.9	45.1	41.9	41.9	43.7
4	40.3	43.3	32.7	39.8	33.1	34.4	37.6	37.9	34.9	33.8	34.7	33.5
5	53.6	62.5	55.1	56.7	47.8	75.5	179.9	55.1	52.5	48.0	86.8	142.7
6	72.1	200.2	127.3	69.1	72.4	126.9	119.3	127.3	72.1	141.9	106.0	125.0
7	122.6	128.4	134.3	153.6	73.6	137.7	203.7	134.3	210.1	124.8	142.5	137.6
8	129.0	158.8	70.9	143.6	124.1	86.1	76.1	70.9	65.3	164.3	106.4	131.8
9	54.2	56.5	58.0	50.0	145.5	91.7	56.7	58.0	45.4	212.6	63.2	120.8
10	33.0	32.2	37.9	33.1	39.6	56.7	41.5	32.8	38.2	53.1	51.6	124.4
11	18.2	21.3	18.0	20.6	22.3	22.5	17.4	18.1	26.4	35.7	23.4	28.4
12	38.8	38.6	36.8	38.9	39.0	30.6	39.0	36.8	33.0	34.3	36.0	39.9
13	73.4	73.3	73.6	73.2	73.5	73.4	73.7	73.6	81.2	81.6	73.2	72.7
14	144.9	144.6	145.0	144.7	144.7	144.7	145.1	145.0	47.9	142.8	145.2	145.1
15	111.9	112.2	111.8	111.6	112.0	112.0	111.9	111.8	29.5	113.3	111.6	111.3
16	27.5	27.7	27.5	28.2	27.5	26.4	28.6	27.5	24.2	22.7	27.2	28.0
17	21.5	21.3	29.4	195.4	21.1	23.3	29.3	29.4	19.2	—	26.3	15.4
18	35.5	33.4	32.5	36.3	33.1	28.4	32.1	32.5	32.7	33.8	27.3	} 31.9
19	22.5	22.0	21.8	22.3	23.4	23.1	23.5	21.8	23.2	21.7	23.4	
20	14.7	14.6	14.2	15.2	17.5	19.3	20.4	14.3	17.0	17.4	17.2	15.2
OCOR	173.3	—	—	—	171.0	—	—	—	170.3	—	—	—
	37.0				21.6				21.3			
	20.8											
	12.7											

*Assigned by DEPT and by comparison with the data of related compounds, a few signals may be interchangeable.

Table 4. ^1H NMR spectral data of compounds **15–22** (400 MHz, $CDCl_3$, δ-values)

H	15	16	17*	18	19	20†(C_6D_6)	21‡	22
5	1.62 *br s*	2.20 *d*	1.15 *d*	1.71 *d*	1.52 *d*	—	—	—
6	5.64 *dd*	5.84 *dd*	4.54 *m*	5.76 *d*	5.24 *t*	5.92 *d*	5.71 *d*	6.02 *s*
7	5.70 *br d*	6.52 *d*	6.59 *t*	—	3.63 *br s*	5.84 *dd*	5.93 *d*	—
14	5.94 *dd*	5.83 *dd*	5.87 *dd*	5.92 *dd*	5.91 *dd*	5.84 *dd*	5.87 *dd*	5.88 *dd*
15c	5.07 *dd*	4.85 *dd*	5.04 *dd*	5.13 *dd*	5.08 *dd*	5.18 *dd*	5.08 *dd*	5.08 *dd*
15t	5.23 *dd*	4.99 *dd*	5.23 *dd*	5.26 *dd*	5.22 *dd*	5.23 *dd*	5.21 *dd*	5.26 *dd*
16	1.29 *s*	1.31 *s*	1.28 *s*	1.34 *s*	1.29 *s*	1.34 *s*		
17	1.18 *s*	9.47 *s*	9.44 *s*	1.80 *s*	1.73 *s*	4.31 *dt* 4.16 *d*	1.28 *s* 1.31 *s*	1.26 *s* 1.32 *d*
18	0.91 *s*	1.13 *s*	1.15 *s*	1.03 *s*	0.98 *s*	1.21 *s*	1.18 *s*	1.25 *s*
19	0.88 *s*	1.02 *s*	1.09 *s*	1.39 *s*	1.24 *s*	1.15 *s*	0.98 *s*	1.12 *s*
20	0.83 *s*	1.00 *s*	0.85 *s*	1.02 *s*	0.97 *s*	0.90 *s*	0.95 *s*	1.16 *s*
OAc	—	2.09 *s*	—	2.05 *s*	2.03 *s*	—	—	—

*H-9 1.96 *m*, H-6 + D_2O *dt* ($J = 10 + 2$).

†H-9 2.25 *br d* ($J = 11$ Hz).

‡OH 2.87 *q* ($J = 1$ Hz).

J [Hz]: 14,15c = 10; 14,15t = 17; 15c,15t ~ 1.5; compound **15**: 5,6 = 2.5; 6,7 = 10; compound **16**; 5,6 = 6; 6,7 = 4; compound **17**: 5,6 = 10; 6,7 = 6,9 = 7,9 ~ 2; compound **18**: 5,6 = 3; compound **19**: 5,6 = 6,7 = 1.5; compound **20**: 6,7 = 5; 7,9 = 1; 7,17 = 9,17 ~ 1; 17,17′ = 14; compound **21**: 6,7 = 9.5; compound **22**: 17,OH = 1.

required, in agreement with the molecular formula ($C_{18}H_{28}O_2$), the presence of a *nor*-labdane closely related to **13**. Accordingly, the protons of the decalin part were similar while the signals of H-11, H-12 and H-16 were typical for the side chain.

The ^1H NMR spectrum of **24** (Table 5) was in part very similar to that of strictanonic acid [8] where the vinyl group is replaced by a CH_2CO_2H group. All data, therefore, agree with the proposed structure. The ^1H NMR data of **25** (Table 5) differ from those of **24** by the absence of a 5,6-coupling and some shift differences. In agreement with the molecular formula ($C_{20}H_{32}O_4$) a

Table 5. ^{1}H NMR spectral data of compounds **23–31** (400 MHz, $CDCl_3$, δ-values)

H	23*	24	25	26† (C_6D_6)	27‡	28	29§ (C_6D_6)	30	31‖
5	2.04 *s*	1.85 *d*	—	2.43 *d*	2.87 *d*	—	—	—	6.66 *d*
6	—	4.28 *dt*	4.61 *dd*	6.28 *d*	5.99 *dd*	4.98 *d*	7.21 *s*	6.97 *d*	6.92 *d*
7	5.72 *dq*	2.76 *dd* 2.64 *dd*	2.95 *dd* 2.70 *dd*	—	5.79 *d*	6.31 *d*	—	7.15 *br d*	—
14	—	6.04 *dd*	6.00 *dd*	2.19 *ddd*	6.18 *dd*	5.91 *dd*	5.86 *dd*	6.04 *dd*	5.86 *dd*
15c	—	5.01 *dd*	4.99 *dd*	1.82 *dd* (α)	5.14 *d*	5.04 *dd*	5.04 *dd*	5.17 *dd*	5.05 *dd*
15t	—	5.19 *dd*	5.17 *dd*	0.93 *dd* (β)	5.18 *d*	5.22 *dd*	5.28 *dd*	5.32 *dd*	5.13 *dd*
16	2.18 *s*	1.18 *s*	1.21 *s*	1.26 *s*	1.61 *s*	1.28 *s*	1.36 *s*	1.35 *s*	1.41 *s*
17	1.90 *t*	2.21 *s*	2.19 *s*	0.96 *s*	—	1.55 *s*	1.19 *s*	2.14 *s*	2.25 *s*
18	1.13 *s*	1.00 *s*	1.19 *s*	1.13 *s*	0.87 *s*	0.97 *s*	1.36 *s* (6H)	1.27 *s* (6H)	1.70 br s
19	1.16 *s*	0.98 *s*	1.11 *s*	1.28 *s*	1.08 *s*	0.99 *s*			
20	0.87 *s*	0.92 *s*	0.93 *s*	0.83 *s*	1.12 *s*	1.04 *s*	2.20 *s*	—	—

*H-9 2.08 *br d* (J = 7 Hz); H-11 1.84 and 1.65 *m*, H-12, 2.70 and 2.54 *ddd* (J = 17, 10, 5 Hz).

†H-11α 1.44 *m*.

‡H-11 3.30 *br dd* and 1.94 *ddd*, H-12 2.78 *br dd* and 1.63 *m*.

§H-1 2.82 and 2.76 *dt*, H-2 1.80 *m*, H-3 1.59 *m*, H-11 2.53 *br t*, H-12 1.75 *m*.

‖H-1 2.55 *dd*, H-2 2.10 *m*, H-3 5.21 *tqq*, H-11 2.73 and 2.63 *dt*, H-12 1.95 and 1.82 *dt*.

J [Hz]: 14,15c = 10; 14,15t = 17; 15c,15t ~ 1.5; compound **23**: 7,9 = 7,17 = 9,17 ~ 1.5; compound **24**: 5,6 = 6,7 = 10; 6,7′ = 2.5; 7,7′ = 15; compound **25**: 6,7 = 8.5; 6,7′ = 3.5; 7,7′ = 16; compound **26**: 5,6 = 9; 12,14 = 1.5; 14,15α = 11; 14,15β = 5.5; 15α,15β = 14; compound **27**: 5,6 = 10; 6,7 = 12; 11,11′ = 15; 11,12 = 12; 11′,12 = 7; 11′,12′ = 1.5; 12,12′ = 13; compound **28**: 6,7 = 6.5; compound **29**: 1,1′ = 1,2 = 1′,2′ = 13; 1,2′ = 1′,2 = 5.5; 11,12 = 6.5; compound **30**; 6,7 = 8; compound **31**: 1,2 = 8 and 10; 2,3 = 7; 3,18 = 3,19 = 1.5; 5,6 = 8.5; 11,11′ = 16.5; 11,12 = 11,12′ = 11′,12 = 11′,12′ = 5; 12,12′ = 13.

5-hydroxy derivative of **24**, which we have named haploparvone, was present.

The ^{1}H NMR spectrum of **26** (Table 4) differed completely from all the others. The molecular formula was $C_{22}H_{34}O_4$ and the ^{1}H NMR spectrum displayed in addition to an acetoxy methyl, five methyl singlets and no olefinic proton signals. A doublet at δ6.28 in benzene-d_6 was coupled with a doublet at δ2.43 which most likely was due to H-5. Accordingly, a 6-acetoxy derivative with a 7-keto group of a so far unknown diterpene skeleton was proposed. This assumption was supported by the ^{13}C NMR spectrum which displayed signals for a keto carbon (δ210.1), an acetoxy group (δ170.3 and 21.3) and an oxygen bearing carbon (δ81.2). The molecular formula requires the presence of four rings, none of them being an ether ring. As far as we know tetracyclic diterpenes with five methyl groups have not been reported. Extended NOEs finally showed together with spin decoupling and the ^{13}C NMR data that the diterpene **26** with a new carbon skeleton was present which we have named haplopane. Most important are the NOEs between H-18, H-5 (6%) and H-6 (7%), between H-19, H-18 (4%), H-20 (6%) and acetoxy methyl (2%), between H-16, H-11 (6%) and H-15′ (4%), between H-5, H-6 (5%) and H-14 (5%) as well as between H-15 and H-6 (3%). The resulting structure **26** most likely is the result of a photochemically induced 2+2-cycloaddition of the ketone **18**. Indeed, irradiation of **18** in petrol with UV light afforded nearly quantitatively only one adduct which was identical with **26**. Inspection of models shows that the isolated adduct is by far the most preferred one as addition from the β-face is hindered by the C-10 methyl and a bonding of C-15 with C-9 and C-14 with C-8 is very unlikely due to steric strain in the transition state. The coupling of H-5 was 9 Hz requiring a boat conformation of ring B, most likely due to sterical hindrance of the axial acetoxy group at C-6. This conformation also followed from the NOEs of H-18 with both H-5 and H-6.

The molecular formula of **27** ($C_{19}H_{28}O_3$) indicated the presence of a *nor*-diterpene. The ^{1}H NMR spectrum (Table 5) only displayed four methyl singlets indicating that one methyl of the labdane precursor was missing, most likely that at C-8 if the chemical shifts of the remaining were considered. In addition to the typical signals of H-14 and H-15 a further double bond was present as followed from the signals at δ5.99 and 5.79. The former was coupled with a signal at δ2.87 which most likely was due to H-5. Signals at δ3.30, 2.78 and 1.94 required a neighbouring keto group while the downfield shifted methyl singlet at δ1.61 may be due to a methyl on an acyloxy bearing tertiary carbon. The ^{13}C NMR spectrum (Table 3) showed the presence of a saturated keto group (δ212.6), four olefinic protons and of a lactone carbonyl (δ164.3). All data, therefore, agree best with structure **27**, which was also supported by the observed NOEs [H-18 with H-5 (8%), H-19 with H-6 (10%), H-17 with H-14 (4%) and H-15t (6%), H-6 with H-19 (5%) and H-20 (3%), H-11 with H-5 (5%) and H-12 with H-14 (4%)]. The resulting conformation explains the chemical shift of H-6 as the lactone carbonyl is out of plane and H-12 is deshielded by the latter. Most likely the ketone **27**, which we have named haploparviolide, is formed by oxidative degradation of **4**.

The molecular formula of **28** ($C_{20}H_{32}O_3$) and its ^{13}C NMR spectrum (Table 3) which shows signals of three oxygen bearing carbons and of four olefinic carbons, required a tricyclic compound. The ^{1}H NMR spectrum shows a pair of doublets at δ6.31 and 4.98 with a 6.5 Hz coupling. The shifts and the coupling agree with the presence of an enol ether. This is supported by the ^{13}C NMR signals at δ106.0 and 142.5. A signal at δ106.4 requires a ketal carbon while two further singlets at δ86.8

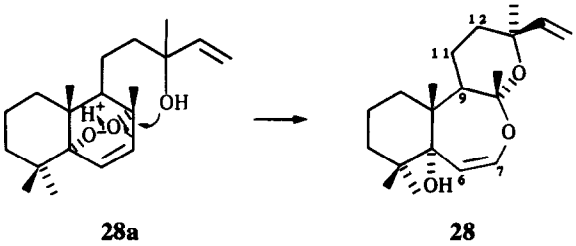
and 73.2 were due to two further oxygen-bearing carbons. All data, therefore, agree with the presence of the enol ether **28**. NOEs support the structure and the stereochemistry [H-6 with H-18 (5%) and H-7 (7%), H-16 with H-14 (5%) and H-15t (5%), H-17 with H-19 (5%), H-14 (3%) and H-15t (3%)]. Obviously, the enol ether **28** is formed by oxidative attack of a labdane 5,7-diene, perhaps via the endoperoxide **28a** as shown in Scheme 1.

The spectral data of **29** (Tables 3 and 5) indicated the presence of an aromatic compound with only one free position. In benzene-d_6 all ^{1}H signals could be assigned by spin decoupling leading to a tetralin derivative with four methyl groups, two of them being aromatic, and a 3-hydroxy-3-methyl-pent-4-ene side chain. The NOE of H-11 with H-17 and not with H-1 or H-20 required the proposed positions of the substituents. A compound with an identical substitution pattern, with a CH_2CO_2H instead of a vinyl group, has been reported from a *Grindelia* and a *Chrysothamnus* species [10]. Of course several NMR data are very similar to those of **29**.

The molecular formula of **30** was $C_{19}H_{28}O$ indicating the presence of a *nor*-diterpene. Again the ^{1}H NMR spectrum (Table 5) showed that an aromatic compound was present which, however, only had four substituents. Two aromatic protons showed a vicinal coupling. Again the data required a tetralin derivative with two geminal methyls at C-4. The position of third methyl and the side chain followed from the observed NOE between H-20, H-11 (4%) and H-1 (3%).

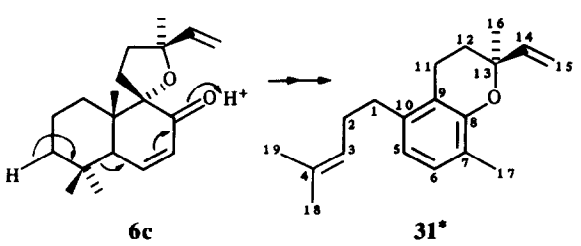
The ^{1}H NMR spectrum of **31** (Table 5) shows again the presence of an aromatic compound with four substituents. The nature of these substituents followed from the ^{1}H NMR signals which could be assigned by spin decoupling. The chemical shifts of the aromatic protons required a phenyl ether substituent. A coupling of H-17 with H-6 and H-1 with H-5 indicated the proposed substition. Most likely the compounds **29** and **30** are derived from **6**. As shown in Scheme 2 protonation of the ether oxygen would lead to **6a** which could be transformed to the triene **6b**. Protanation at C-17 could induce the required Wagner–Meerwein-rearrangements of either methyls and/or the side chain (see also [10]). In the case of **30** the missing methyl group may be eliminated by oxidation. The formation of **31** probably requires a different precursor. Several possibilities can be considered. Perhaps in this case compound **6** is first degraded to the corresponding 8-keto derivative **6c** which could be transformed to a *seco* compound which then, as discussed for **29** and **30**, could lead to the aromatic compound (Scheme 3).

The overall picture on the chemistry of this species shows that metabolism is characterized by an unusual



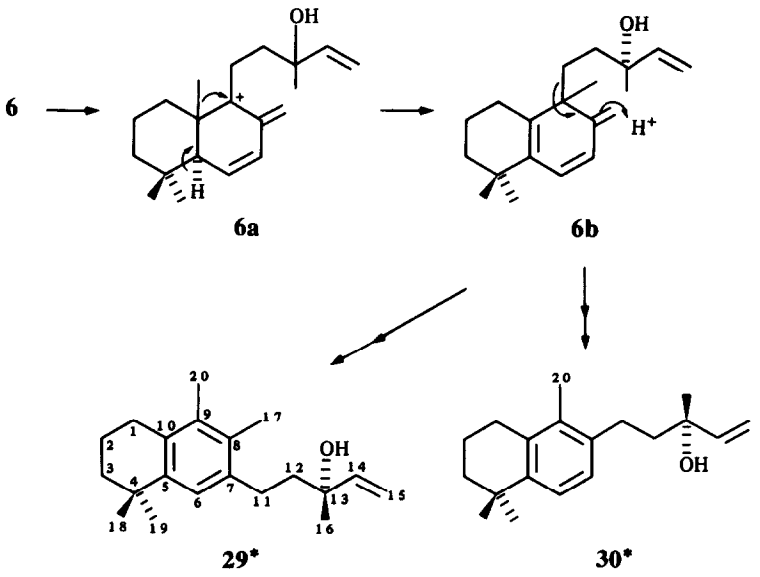
28a **28**

Scheme 1.



6c **31***

Scheme 3.



29* **30***

* numbering as in the labdane precursors

Scheme 2.

degree of oxidative transformations and rearrangements though nearly all compounds are biogenetically closely related. Sclareol, which itself was not isolated, may be the common precursor. So far none of the investigated *Haplopappus* species showed a similar picture. Other labdanes have been reported from four *Haplopappus* species [2, 6, 11], but they are also relatively common in other genera of the subtribe Solidaginae. Further chemical and taxomonic studies may show whether the genus can be separated into more uniform genera.

EXPERIMENTAL

Aerial parts (280 g, voucher Niemeyer 89129, collected in the region de Coquimbo, Chile, September 1990) were extracted with MeOH–Et_2O–petrol (1:1:1). The extract was sepd as reported previously [12] by medium pressure chromatography, repeated TLC (T1: Et_2O–petrol, 1:3; T2: Et_2O–petrol, 2:3; T3: Et_2O–petrol, 3:1; T4: Et_2O–petrol, 1:1) and HPLC (always RP 8, flow rate 3 ml min^{-1}; H1: MeOH; H2: MeOH–H_2O, 9:1; H3: MeOH–H_2O, 3:1). The following compounds were isolated (conditions of final purification in parentheses): 2 mg **1** (H1, R_t 4.8 min), 10 mg **2** (H1, R_t 3.7 min), 2 mg **3** (H1, R_t 4.2 min), 15 mg **4** (T1, $AgNO_3$ coated, ×2, R_f 0.65), 15 mg **5** (T1, $AgNO_3$ coated, ×2, R_f 0.58), 2 mg **6** (H1, R_t 3.1 min), 2 mg **7** (H2, R_t 6.0 min), 1.5 mg **8** (H1, R_t 1.4 min), 1.5 mg **9** (H1, R_t 2.3 min), 2 mg **10** (T1, R_f 0.63), 350 mg **11** (H2, R_t 5.2 min), 20 mg **12** (H2, R_t 8.4 min), 700 mg **13** (H2, R_t 2.4 min), 2 mg **14** (T2, R_f 0.41), 6 mg **15** (H2, R_t 4.5 min), 2 mg **16** (H2, R_t 6.7 min), 10 mg **17** (T3, ×2, R_f 0.53), 50 mg **18** (H2, R_t 2.4 min), 50 mg **19** (H2, R_t 1.6 min), 2 mg **20** (H1, R_t 2.9 min), 3 mg **21** (T4, R_f 0.42), 4 mg **22** (H3, R_t 8.5 min), 3 mg **23** (T2, ×2, R_f 0.52), 4 mg **24** (H1, R_t 5.2 min), 4 mg **24** (H1, R_t 5.2 min), 2 mg **25** (T1, R_f 0.54), 7 mg **26** (T4, R_f 0.55), 4 mg **27** (H2, R_t 2.3 min), 14 mg **28** (H2, R_t 4.4 min), 20 mg **29** (H1, R_t 8.3 min), 4 mg **30** (H2, R_t 6.8 min), 4 mg **31** (H1, R_t 2.5 min), 3 mg **32** (H2, R_t 1.6 min), *iso*-manool (H2, R_t 14.1 mın).

6,7-*Dehydro*-13-epi-*manoyloxid* (**2**). MS *m/z* (rel. int.): 288.245 $[M]^+$ (10) (calc. for $C_{20}H_{32}O$: 288.245), 273 $[M-Me]^+$ (100), 255 $[273-H_2O]^+$ (5), 125 (40), 95 (28), 81 (82), 69 (44).

6,7-*Dehydro*-8,13-bis-epi-*manoyloxid* (**3**). MS *m/z* (rel. int.): 288.245 $[M]^+$ (6) (calc. for $C_{20}H_{32}O$: 288.245), 273 $[M-Me]^+$ (47), 91 (60), 81 (97), 69 (100).

13-*Hydroxy-labda*-6,8,14-*triene* (**4**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH). MS *m/z* (rel. int.): 288.245 $[M]^+$ (14) (calc. for $C_{20}H_{32}O$: 288.245), 270 $[M-H_2O]^+$ (5), 255 $[270-Me]^+$ (11), 217 (9), 187 (56), 133 (35), 119 (100).

13-*Hydroxy-labda*-6,8(17),14-*triene* (**5**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH). MS *m/z* (rel. int.): 288.245 $[M]^+$ (12) (calc. for $C_{20}H_{32}O$: 288.245), 270 $[M-H_2O]^+$ (9), 255 $[270-Me]^+$ (24), 217 (7), 187 (44), 133 (40), 119 (100), 81 (28), 71 (30), 69 (36).

9α,13-*Epoxy-labda*-6,8(17),14-*triene* (**6**). MS *m/z* (rel. int.): 286.230 $[M]^+$ (21) (calc. for $C_{20}H_{30}O$: 286.230), 271 $[M-Me]^+$ (26), 203 (54), 187 (80), 81 (100).

6α-*Hydroxy*-9α,13-*epoxy-labda*-7,14-*diene* (**7**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH). MS *m/z* (rel. int.): 304.240 $[M]^+$ (14) (calc. for $C_{20}H_{32}O_2$: 304.240), 286 $[M-H_2O]^+$ (6), 271 $[286-Me]^+$ (5), 186 (40), 180 [RDA]$^+$ (100), 151 (52), 81 (50), 69 (51). $[\alpha]_D^{24°}$ −45 ($CHCl_3$; *c* 0.24).

6α-*Acetoxy*-9α,13-*epoxy-labda*-7,14-*diene* (**8**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1255 (OAc). MS *m/z* (rel. int.): 346.251 $[M]^+$ (16) (calc. for $C_{22}H_{34}O_3$: 346.251), 286 $[M-HOAc]^+$ (20), 249 (22), 222 (100), 180 (83), 109 (85), 81 (98), 69 (87).

6α-*Butyryloxy*-9α,13-*epoxy-labda*-7,14-*diene* (**9**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725 (CO_2R). MS *m/z* (rel. int.): 374.282 $[M]^+$ (25) (calc. for $C_{24}H_{38}O_3$: 374.282), 286 $[M-RCO_2H]^+$ (40), 271 [286 −Me]$^+$ (11), 250 (77), 187 (48), 180 (100), 149 (88), 109 (63), 94 (78), 81 (72), 69 (75).

5α-*Hydroxy*-9α,13-*epoxy-labda*-7,14-*diene*-6-*one* (**10**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3470 (OH), 1700 (C=O). MS *m/z* (rel. int.): 318.219 $[M]^+$ (6) (calc. for $C_{20}H_{30}O_3$: 318.219), 207 (31), 151 (70), 137 (72), 123 (77), 109 (90), 81 (87), 69 (100).

6β-*Acetoxy*-13-*hydroxy-labda*-7,14-*diene* (**11**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1745, 1255 (OAc). MS *m/z* (rel. int.): 288.245 [M −HOAc]$^+$ (20) (calc. for $C_{20}H_{32}O$: 288.245), 273 $[288-Me]^+$ (21), 262 $[M-Me_2C(OH)CH=CH_2]^+$ (82), 232 (50), 220 (74), 202 (80), 187 (85), 133 (84), 119 (100), 95 (87), 71 (76), 69 (92). $[\alpha]_D^{24°}$ −97 ($CHCl_3$; *c* 1.07).

13-*Hydroxy*-6α-*butyryloxy-labda*-7,14-*diene* (**12**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1735 (CO_2R). MS *m/z* (rel. int.): 288.245 [M −RCO_2H]$^+$ (60) (calc. for $C_{20}H_{32}O$: 288.245), 273 $[288-Me]^+$ (12), 255 $[273-H_2O]^+$ (54), 202 (64), 187 (88), 133 (76), 119 (100), 81 (72), 71 (88), 69 (74). $[\alpha]_D^{24°}$ +130 ($CHCl_3$; *c* 1.41).

13-*Hydroxy-labda*-7,14-*diene*-6-*one* (**13**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1680 (C=CC=O). MS *m/z* (rel. int.): 304.240 $[M]^+$ (5) (calc. for $C_{20}H_{32}O_2$: 304.240), 286 $[M-H_2O]^+$ (55), 271 $[286-Me]^+$ (13), 219 $[M-CH_2C(OH)(Me)CH=CH_2]^+$ (63), 218 [M $-Me_2C(OH)CH=CH_2]^+$ (76), 203 $[218-Me]^+$ (58), 162 (56), 148 (58), 135 $[C_9H_{11}O]^+$ (100), 110 (70), 95 (68), 81 (66), 71 (77), 69 (76). CD (MeOH): $\Delta\varepsilon_{330}$ +0.33.

9α,13-*Dihydroxy-labda*-7,14-*dien*-6-*one* (**14**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1687 (C=CC=O). MS *m/z* (rel. int.): 320.235 $[M]^+$ (4) (calc. for $C_{20}H_{32}O_3$: 320.235), 302 $[M-H_2O]^+$ (8), 287 [302 $-Me]^+$ (4), 221 (20), 203 (22), 109 (60), 81 (82), 69 (100).

8α,13-*Dihydroxy-labda*-6,14-*diene* (**15**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 288.245 $[M-H_2O]^+$ (48) (calc. for $C_{20}H_{32}O$: 288.245), 273 $[288-Me]^+$ (100), 245 (52), 205 (52), 177 (74), 135 (86), 123 (90), 121 (94), 109 (96), 107 (86), 95 (90), 81 (98), 71 (88), 69 (88).

6β-*Acetoxy*-9α,13-*epoxy-labda*-7,14-*dien*-17-*al* (**16**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2740, 1690 (C=CCHO), 1745 (OAc). MS *m/z* (rel. int.): 302.225 $[M-HOAc]^+$ (6) (calc. for $C_{20}H_{30}O_2$: 302.225), 287 $[302-Me]^+$ (12), 258 $[287-CHO]^+$ (26), 243 $[258-Me]^+$ (66), 236 (64), 194 (62), 185 (55), 177 (65), 109 (74), 95 (62), 81 (100), 69 (88).

6α,13-*Dihydroxy-labda*-7,14-*dien*-17-*al* (**17**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 2740, 1705 (C=CCHO). MS *m/z* (rel. int.): 302.225, $[M-H_2O]^+$ (12) (calc. for $C_{20}H_{30}O_2$: 302.225), 287 [302 $-Me]^+$ (10), 203 (42), 151 (74), 123 (77), 109 (94), 95 (80), 81 (97), 71 (86), 69 (100). $[\alpha]_D^{24°}$ +35 ($CHCl_3$; *c* 0.96).

6β-*Acetoxy*-13-*hydroxy-labda*-8,14-*dien*-7-*one* (**18**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1760 (OAc), 1680 (C=CC=O). MS *m/z* (rel. int.): 362.246 $[M]^+$ (2) (calc. for $C_{22}H_{34}O_4$: 362.246), 320 [M −ketene]$^+$ (21), 302 $[M-HOAc]^+$ (37), 238 (100), 221 (48), 203 (98), 175 (86), 161 (87), 137 (88), 109 (96), 81 (97), 69 (99). CD (MeOH): $\Delta\varepsilon_{330}$ −0.67. Compound **18** (20 mg) in 20 ml petrol was irradiated for 1 hr with a UV lamp. After evapn the residue gave by HPLC (H2) 17 mg **26**, identical with the natural product (^1H NMR, ^{13}C NMR).

6β-*Acetoxy*-7β,13-*dihydroxy-labda*-8,14-*diene* (**19**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1740, 1250 (OAc). MS *m/z* (rel. int.): 304.240 $[M-HOAc]^+$ (68), 289 $[304-Me]^+$ (24), 271 $[289-H_2O]^+$ (27), 233 (56), 222 (86), 205 (89), 164 (100), 135 (88), 109 (84), 81 (85), 69 (85). $[\alpha]_D^{24°}$ +30 ($CHCl_3$; *c* 4.40).

13,17-*Epoxy-labda*-5,7,14-*triene* (**20**). MS *m/z* (rel. int.): 286.214 $[M]^+$ (38) (calc. for $C_{20}H_{30}O$: 286.214), 271 $[M-Me]^+$ (9), 257 $[M-CH=CH_2]^+$ (6), 201 (28), 187 (34), 173 (62), 105 (60), 81 (100).

9α,13-*Epoxy*-5α,8α-*dihydroxy-labda*-6,14-*diene* (**21**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH). MS *m/z* (rel. int.): 320.235 $[M]^+$ (3) (calc. for $C_{20}H_{32}O_3$: 320.235), 302 $[M-H_2O]^+$ (5), 177 (36), 151 (54), 123 (58), 109 (67), 81 (66), 69 (100).

8α,13-*Dihydroxy-labda*-5,14-*dien*-7-*one* (**22**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH). 1675 (C=CC=O). MS *m/z* (rel. int.): 320.235 $[M]^+$ (0.5) (calc. for $C_{20}H_{32}O_3$: 320.235), 302 $[M-H_2O]^+$ (3), 287 $[302-Me]^+$ (4.5), 259 (32), 165 (54), 164 (100), 149 (62), 81 (44), 69 (41).

6-*Oxo*-14,15-nor-*labda*-7-*ene* (**23**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725 (C=O), 1680 (C=CC=O). MS *m/z* (rel. int.): 276.209 $[M]^+$ (9) (calc. for $C_{18}H_{28}O_2$: 276.209), 261 $[M-Me]^+$ (7), 219 $[M-CH_2COMe]^+$ (24), 203 $[261-Me_2CO]^+$ (23), 135 (100), 109 (76), 91 (73), 81 (69), 69 (98).

Haploparvone (**24**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725 (C=O). MS *m/z* (rel. int.): 320.235 $[M]^+$ (5) (calc. for $C_{20}H_{32}O_3$: 320.235), 305 $[M-Me]^+$ (3), 262 $[M-Me_2CO$, McLafferty$]^+$ (11), 247 $[262-Me]^+$ (10), 194 (15), 177 (30), 161 (32), 136 (34), 109 (46), 95 (44), 84 (100), 81 (53), 69 (55). $[\alpha]_D^{24°}-12$ ($CHCl_3$; *c* 0.30).

5α-*Hydroxyhaploparvone* (**25**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3470 (OH), 1725 (C=O). MS *m/z* (rel. int.): 336.230 $[M]^+$ (18) (calc. for $C_{20}H_{32}O_4$: 336.230), 318 $[M-H_2O]^+$ (6), 249 (88), 151 (86), 140 (90), 109 (98), 95 (68), 81 (98), 69 (100).

6β-*Acetoxy*-13α-*hydroxyhaplopan*-7-*one* (**26**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1755, 1250 (OAc), 1715 (C=O). MS *m/z* (rel. int.): 362.246 $[M]^+$ (1.5) (calc. for $C_{22}H_{34}O_4$: 362.246), 320 $[M-$ketene$]^+$ (17), 302 $[M-HOAc]^+$ (20), 197 (34), 178 (33), 151 (46), 109 (74), 81 (73), 69 (100).

Haploparviolide (**27**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730 (C=CC=O), 1715 (C=O). MS *m/z* (rel. int.): 304.204 $[M]^+$ (8) (calc. for $C_{19}H_{28}O_3$: 304.204), 195 (22), 163 (42), 109 (68), 95 (57), 81 (94), 69 (100).

5α-*Hydroxy*-7,8-*epoxy*-7,8-seco-6,7-*dehydro*-13-epi-*manoyl-oxide* (**28**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1645 (C=C–O). MS *m/z* (rel. int.): 320.235 $[M]^+$ (18) (calc. for $C_{20}H_{32}O_3$: 320.235), 302 $[M-H_2O]^+$ (6), 249 $[M-MeC(OH)CH=CH_2]^+$ (100), 220 $[M-MeCH_2C(Me,OH)CH=CH_2]^+$ (92), 202 $[220-H_2O]^+$ (18), 177 (52), 159 (95), 81 (67). $[\alpha]_D^{24°}+10$ ($CHCl_3$; *c* 0.94).

1,1,5,6-*Tetramethyl*-4-[3-*hydroxy*-3-*methyl-pent*-(4)-*enyl*]-*tetralin* (**29**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH). MS *m/z* (rel. int.): 286.230 $[M]^+$ (66) (calc. for $C_{20}H_{30}O$: 286.230), 271 $[286-Me]^+$ (100), 253 $[271-H_2O]^+$ (98), 215 $[M-MeC(OH)CH=CH_2]^+$ (60), 201 $[M-CH_2C(OH)(Me)CH=CH_2]^+$ (63), 185 (69), 173 (63), 119 (100), 81 (45), 71 (40), 69 (37). $[\alpha]_D^{24°}+20$ ($CHCl_3$; *c* 0.83).

1,1,5-*Trimethyl*-6-(3-*hydroxy*-3-*methyl-pent*-4-*enyl*)-*tetralin* (**30**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH). MS *m/z* (rel. int.): 272.214 $[M]^+$ (68) (calc. for $C_{19}H_{28}O$: 272.214), 257 $[M-Me]^+$ (80), 254 $[M-H_2O]^+$ (59), 239 $[257-H_2O]^+$ (100), 201 $[M-MeC(OH)CH=CH_2]^+$ (78), 187 $[M-C_6H_{11}O]^+$ (78), 171 (73), 81 (70), 71 (70), 69 (59). $[\alpha]_D^{24°}+18$ ($CHCl_3$; *c* 0.26).

2,8-*Dimethyl*-2′-*vinyl*-5-[4-*methyl-pent*-3-*enyl*]-*chromane* (**31**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1610 (aromatic). MS *m/z* (rel. int.): 270.198 $[M]^+$ (84) (calc. for $C_{19}H_{26}O$: 270.198), 202 $[M-$isoprene$]^+$ (22), 201 $[M-CH_2CH=CMe_2]^+$ (100), 187 $[202-Me]^+$ (20), 159 (34), 145 (26), 91 (9), 69 (14).

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REFERENCES

1. Grau, J. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L. eds), p. 539. Academic Press, London.
2. Zdero, C., Bohlmann, F. and Niemeyer, H. M. (1990) *Phytochemistry* **29**, 326.
3. Hosking, J. R. and Brandt, C. W. (1935) *Chem. Ber.* **68**, 1311.
4. Bohlmann, F., Zdero, C., Hoffmann, E., Mahanta, P. K. and Dorner, W. (1978) *Phytochemistry* **17**, 1917.
5. Misra, L. N., Jakupovic, J., Bohlmann, F. and Schmeda-Hirschmann, G. (1985) *Tetrahedron* **41**, 5353.
6. Jakupovic, J., Baruah, R. N., Zdero, C., Eid, F., Pathak, V. P., Chau-Thi, T. V., Bohlmann, F., King, R. M. and Robinson, H. (1986) *Phytochemistry* **25**, 1873.
7. Timmermann, B. N., Luzbetak, D., Hoffmann, J. J., Jolad, S. D., Schram, K. H., Bates, R. B. and Klenck, R. E. (1983) *Phytochemistry* **22**, 523.
8. Bohlmann, F., Ahmed, M., Borthakur, N., Wallmeyer, M., Jakupovic, J., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 167.
9. Adinolfi, M., Della Greca, M. and Mangoni, L. (1988) *Phytochemistry* **27**, 1878.
10. Timmermann, B., Hoffman,, J. J., Jolad, S. D., Schram, K., Klenck, R. and Bates, R. (1982) *J. Org. Chem.* **47**, 4115.
11. Bohlmann, F., Fritz, U., Robinson, H. and King, R. M. (1979) *Phytochemistry* **18**, 1749.
12. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.