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SECO-LABDANES AND OTHER CONSTITUENTS FROM *OPHRYOSPORUS FLORIBUNDUS*

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Key Word Index—*Ophryosporus floribundus*; Compositae; diterpenes; *ent*-labdanes; *seco-ent*-labdanes; geranylgeraniol derivatives; sesquiterpenes lactones; *p*-hydroxyacetophenone derivatives; flavanones.

Abstract—The extract of the aerial parts of *O. floribundus* afforded in addition to known compounds 17 new diterpenes, including eight *seco-ent*-labdanes with a very rare carbon skeleton. The structures were elucidated by high field NMR spectroscopy and a few chemical transformations.

INTRODUCTION

The genus *Ophryosporus* (Compositae, tribe Eupatorieae) with 37 species is restricted entirely to South America. Previously it was placed in the subtribe Piqueriinae, but is now in the Critoniinae of the *Koanophyllum* group [1]. So far five species have been studied chemically. Most widespread are prenylated *p*-hydroxyacetophenones [2–5], phenyl propane [2, 5] and labdane derivatives [2, 3], but flavanoids [2, 3, 6], triterpenes [5] and an umbelliferone derivative have also been isolated [5]. Only one species gave germacranolides [4]. We now have studied *O. floribundus* (DC.) K. et R. This species previously was part of the genus *Piqueria* which now only has seven species, as many species have been transferred to other genera [1]. The results are discussed in this paper.

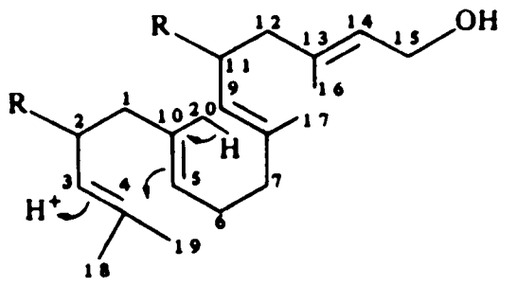
RESULTS AND DISCUSSION

The extract of the aerial parts of *O. floribundus* contained a very complex mixture of diterpenes, sesquiterpenes and *p*-hydroxyacetophenone derivatives. Eventually, the geranylgeraniol derivatives **2** and **3**, the *seco-ent*-labdanes **4**–**11**, the *ent*-labdanes **12**–**16**, **17** [7], **18**, **19** [2], **20** and **21** [2], the costic acid derivatives **22** [8], **23** [9], **24** [10], **25** [11], **26** [12] and **27** [9], the eudesmanolide **28** [13], the germacranolides **29** [14] and **30** [15], the *p*-hydroxyacetophenone derivatives **31** [16], **32** [17], **33** [18], **34** [19], **36** [20], **37** [17], **38** [18] and **39** [21], the chromene **35** [22], the flavanones **40** and **41** [23], ilicic acid [24], bicyclogermacrene, germacrene D, nerolidol, *p*-hydroxyacetophenone, taraxasteryl acetate and carabrone [25] were isolated.

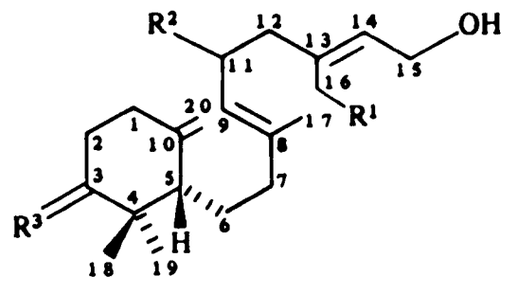
The structure of **2** followed from its ^{1}H NMR spectrum and from that of the corresponding triacetate **2Ac** (Table 1). Spin decoupling with both compounds allowed the assignment of nearly all signals. As H-3 was coupled with H-2 and two olefinic methyls the position of one oxygen function was established. Similarly, the sequence H-9, H-11, H-12, H-14 and H-15 could be established. Accordingly, no function was at C-6 or C-7. The configuration of the double bonds followed from the chemical shifts which were compared with those of similar diterpenes. Furthermore, clear NOEs between H-14 and H-12 (4%) as well as between H-1 and H-5 (4%) were observed which also require the proposed configurations. The stereochemistry at C-2 and C-11 could not be determined.

The ^{1}H NMR spectrum of **3Ac** (Table 1) was in part similar to that of **2Ac**. However, the signals at δ6.89 *s* (2H), 6.60 *tq* and 1.37 *s* (6H) indicated a difference at C-1–C-4. The only explanation for this difference was the presence of a cross conjugated ketone which followed from the IR band at 1665 cm^{-1}. The coincidence of the H-2 and H-3 signals requires a *trans*-double bond as has been shown in the case of a corresponding nerolidol derivative [26]. Again, the position of the secondary acetoxy group was established by spin decoupling.

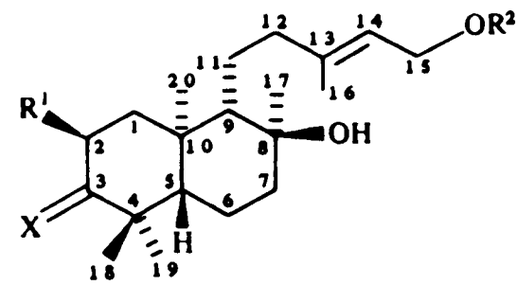
The main diterpene was compound **5** which could only be isolated after acetylation of the most polar fraction affording the monoacetate **5Ac**, the diacetate **5Ac$_2$** and the triacetate **5Ac$_3$**. Saponification of the latter gave the original triol, its ^{1}H NMR spectrum being identical with that of the main constituent in the mixture. In the ^{1}H NMR spectra of **5** and **5Ac$_3$** (Table 2) most signals could be assigned by spin decoupling. Notably, the whole sequence of the side chain clearly could be deduced from these experiments. In agreement with the mass spectrum therefore, a monocyclic diterpene with an additional exomethylene group in the ring part was present. The proposed structure was further supported by the ^{13}C NMR data of **5Ac$_3$**. The only two doublets (δ53.5 and 69.5) and the number of triplets required, together with the ^{1}H NMR data the proposed carbon skeleton. The configuration of the double bonds followed from the NOE's [H-17 with H-11 (7%) and H-14 with H-12 (4%)]. Thus, compound **5** was a *seco*-labdane derivative formed by cyclization of the 16-hydroxy derivative of **2**. Further cyclization should give the labdanes (see below). This type of diterpene seems to be very rare. Compound **5** is related to trixagol, a diterpene alcohol isolated from a member of the Scrophulariaceae [27]. An isomeric tertiary alcohol is present in a *Helipterum* species [28].



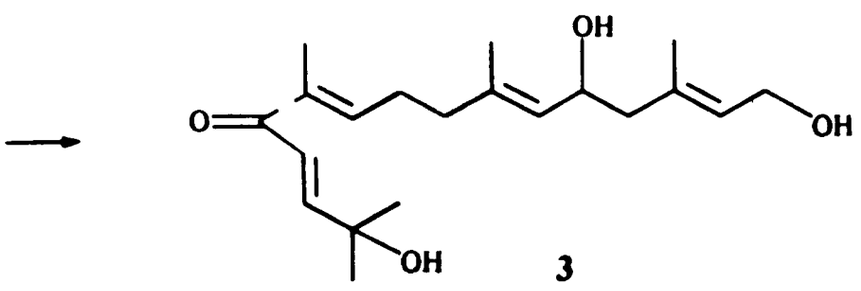
1 R = H
2 R = OH*



	4	**5**	**6**	**7**	**8***
R^1	H	OH	OH	H	H
R^2	OH	OH	H	OH	OH
R^3	H_2	H_2	H_2	=O	αOH,H



	12	**13**	**14**	**15**	**16**	**17**
X	O	βOH,H	βOH,H	βOAc,H	βOH,H	H_2
R^1	H	OH	H	H	H	H
R^2	H	H	H	H	Ac	H



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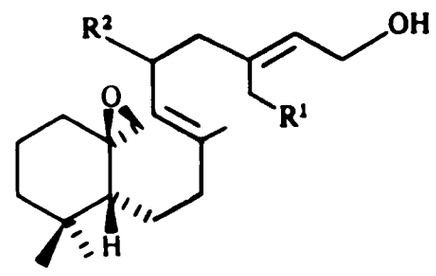
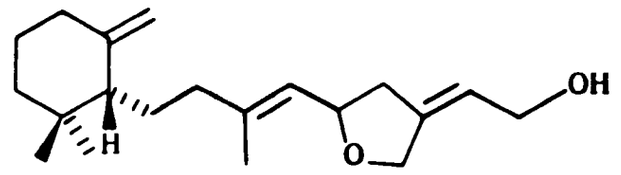
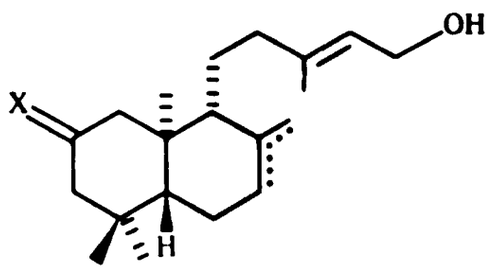


	9	**10**
R^1	H	OH
R^2	OH	H



11



18 X = βOH,H, $\Delta^{8(17)}$
19 X = O, $\Delta^{8(17)}$
20 X = βOH,H, Δ^{7}
21 X = αOH,H, $\Delta^{8(17)}$

* For comparison numbering as in labdanes
2 Ac and **5** Ac_3 are the triacetates, **3** Ac, **5** Ac_2, **7** Ac, **8** Ac_2, **9** Ac, **13** Ac and **14** Ac_2 the diacetates and **5** Ac, **8** Ac and **12** Ac the 15-*O*-acetates

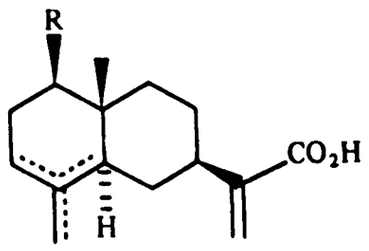
The ^{1}H NMR spectrum of **4** (Table 2) indicated that it is the 16-desoxy derivative of **5**. Accordingly, the broadened doublet for H-16 in the spectrum of **5** was replaced by a second olefinic methyl signal. Similarly, the spectrum of **6** (Table 2) showed that the 11-desoxy derivative of **5** must be present, as the H-9 signal now was a broadened triplet while those of H-11 and H-12 collapsed to a broadened singlet.

The ^{1}H NMR spectra of **7** and **7**Ac (Table 2) were in part similar to that of **4**. However, downfield shifted three-fold doublets at *ca* δ2.5 as well as the mass spectrum indicated the presence of a keto derivative of **4**. As the chemical shifts and splittings of H-20 were not much influenced, the keto group was at C-3 and not at C-1. The observed positive Cotton effect indicated the proposed absolute configuration of the ketone. Thus, the *seco*-diterpenes probably belong to the *ent*-series if the nomenclature of the labdanes is used (see below).

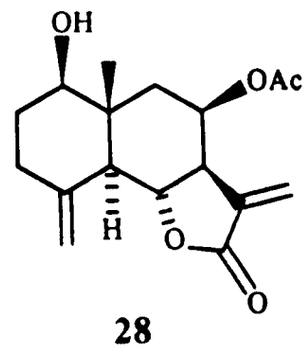
The ^{1}H NMR spectrum of **8**Ac and **8**Ac_2 (Table 2) showed that we were dealing with the corresponding 3-hydroxy derivative of **4**. The observed coupling required a 3α-orientation of the latter. Again, the position followed from the unchanged signals of the exomethylene protons.

The NMR spectrum of **9** and **9**Ac (Table 2) differed from that of **4** by the absence of exomethylene proton signals. They were replaced by those of epoxide protons (δ2.58 *br d* and 2.49 *d*). A *W*-coupling of the former with H-1 required the proposed stereochemistry as followed from inspection of a model. The presence of the corresponding 10,20-epoxide of **6** clearly followed from the ^{1}H NMR spectrum of **10**. Again a *W*-coupling of H-20 was present indicating identical stereochemistry.

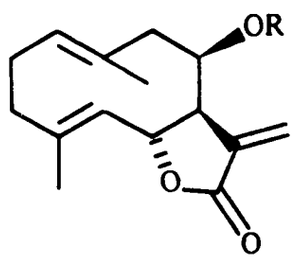
The molecular formula of compound **11** ($C_{20}H_{32}O_2$) required an additional double bond equivalent when compared with that of **4**. Comparison of the spectra of **4** and **11** (Table 2) showed that an ether ring between C-11 and C-16 was most likely; this was established by spin decoupling. The proton under the oxygen group (H-11) showed couplings with the signal at δ5.23 and the highly broadened doublets at δ2.66 and 2.31. The latter showed



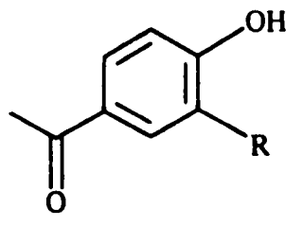
	22	23	24	25	26	27
R	H	OH	H	OH	H	OH
	Δ^3	Δ^3	Δ^4	Δ^4	$\Delta^{4(15)}$	$\Delta^{4(15)}$



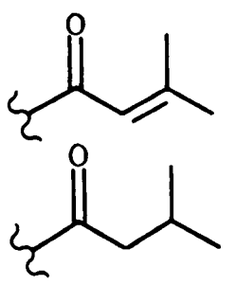
28



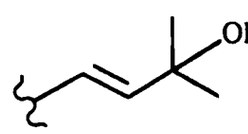
29 R = H
30 R = Ac



31 R = Ac

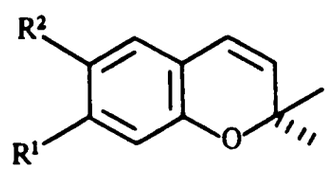


32 R =

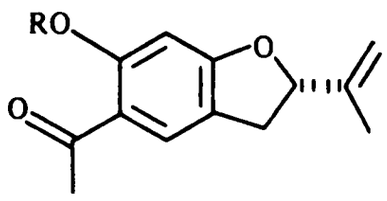


33 R =

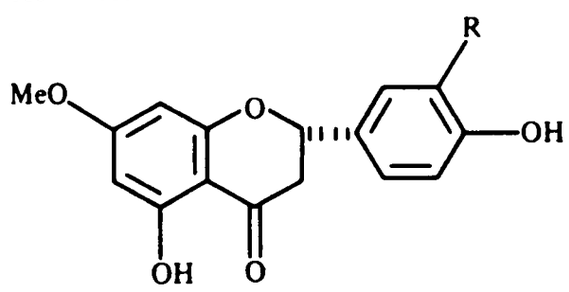
34 R =



	35	36	37
R^1	OMe	H	OH
R^2	OMe	Ac	Ac



38 R = H
39 R = Me



40 R = H
41 R = OH

allylic and homoallylic couplings with H-14 and H-15. The picture was nearly identical with that of a partially related 5-methyl coumarin with a terpene residue [29] where the structure was established by total synthesis [30].

The structure of ketone **12** followed from the ^{1}H NMR spectrum and of that of the corresponding acetate **12Ac** (Table 3). Most signals were close to those of **16** [7]. However, the presence of a 3-keto derivative was indicated by the changed chemical shifts of H-18 and H-19 and by the three-fold doublets at δ2.59 and 2.38. The configuration and assignment of the methyl signals was made from the observed NOEs of **12Ac** [H-20 with H-17 (5%), H-19 (5%), H-11 (6%), H-1α (3%) and H-2α (5%); H-9 with H-12 (3%), H-12′ (2%) and H-5 (7%); H-19 with H-20 (7%), H-18 (4%) and H-2α (3%); H-16 with H-15 (4%)]. The observed positive Cotton effect indicated the presence of an *ent*-labdane.

The diterpene **13** was isolated as its diacetate **13Ac**. Its mass spectrum indicated that a diterpene with four oxygen functions was present. Inspection of the ^{1}H NMR spectrum (Table 3) showed that in addition to functions at C-8 and C-15, two further functions must be present at C-2 and C-3 as followed from spin decoupling. The observed *J*-values required the proposed stereochemistry at C-2 and C-3. Both the tertiary hydroxyl group at C-8 and the sterically hindered hydroxyl group at C-3 were not acetylated. The tetrol **13** is closely related to the corresponding anhydro derivative from *O. heptantus* [3].

The ^{1}H NMR spectra of **14Ac$_2$**, **15** and **16** (Table 3) indicated that these diterpenes were all derived from triol **14**, differing only in the degree of acetylation. As followed

from the chemical shifts in compound **14Ac$_2$** the 3- and 15-hydroxy group were acetylated while in the diterpenes **15** and **16** a 3- and the 15-*O*-acetate, respectively, were present. Thus, mild acetylation of **14** gave the monoacetate **16**.

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

H	2	2Ac	3Ac
1	2.05 *m*	2.29 *dd*	—
1′		2.11 *dd*	—
2	4.36 *ddd*	5.62 *dd*	6.89 *s*
3	5.13 *br d*	5.09 *br d*	
5	5.17 *br t*	5.12 *br t*	6.60 *tq*
6	2.05 *m*	2.05 *m*	2.37 *m*
7			2.18 *m*
9	5.18 *br d*	5.11 *br d*	5.13 *br d*
11	4.48 *ddd*	5.66 *ddd*	5.59 *ddd*
12	2.23 *dd*	2.37 *dd*	2.37 *m*
12′	2.14 *dd*	2.18 *dd*	2.18 *m*
14	5.50 *br t*	5.36 *br t*	5.37 *br t*
15	4.16 *d*	4.55 *d*	4.54 *d*
16	1.72 *br s*	1.73 *br s*	1.72 *d*
17	1.70 *br s*	1.72 *d*	
18	1.66 *br s*	1.70 *br s*	1.37 *s*
19	1.65 *br s*	1.70 *br s*	
20	1.67 *br s*	1.63 *br s*	1.83 *d*
OAc	—	2.04 *s*	2.03 *s*
		2.01 *s*	2.00 *s*
		1.99 *s*	

J [Hz]: 5,6 = 7; 9,11 = 8; 11,12 = 8; 11,12′ = 6; 12,12′ = 14; 14,15 = 7; compounds **2** and **2Ac**: 1,1′ = 14; 1,2 = 9; 1′,2 = 3.5; 2,3 = 8; compound **3Ac**: 5,20 = 1.5.

The diterpenes **18**–**21** all were 8-anhydro derivatives. The ^{1}H NMR spectra of **18** and **20** (Table 3) clearly showed that labdanes were present with oxygen functions at C-2 and C-15. The observed negative Cotton-effect of **19** indicated that we were dealing again with *ent*-labdanes. The observed couplings in the spectra of **18** and **20** clearly showed that both compounds had a 2β-hydroxy group. While in the spectrum of diol **18**, exomethylene proton signals were visible, in that of **20** these signals were replaced by those of an olefinic methyl (H-17) and an olefinic proton (H-7). Thus, diols **18** and **20** were isomers. The 13-*Z*-isomer of the latter has already been prepared by reduction of the corresponding natural occurring 15-oic acid with established configuration of the double bond [31]. The ^{1}H NMR spectra differ in the expected manner supporting the configuration of the 13,14-double bond.

The complex chemistry of *O. floribundus* agrees in part with that of the five other species so far investigated. The occurrence of *ent*-labdanes seems to be especially characteristic, though in two species (*O. angustifolius* [5] and *O. triangularis* [4]) they appear to be absent. They are also reported from *Koanophyllon* species [32–34], a genus closely related to *Ophryosphorus* [1] while in *Eupatoriastrum*, also placed in the *Koanophyllon* group, germacranolides are present [35] which were also isolated from *O. triangularis* [4] and from the species studied here. Obviously, *p*-hydroxyacetophenone derivatives such as **31**–**39** are typical of *Ophryosporus*, though these compounds are also present in many other genera of the Eupatorieae. Our results clearly show that this species has no relationships to the genus *Piqueria* where it had been placed previously.

EXPERIMENTAL

Aerial parts (680 g, collected in Questa Cardones, Region de Tarapaca, Chile, in May 1989, voucher Niemeyer 8953, depos-

Table 2. ^{1}H NMR spectral data of compounds **4**–**7**, **9**–**11**, **5Ac**, **5Ac$_2$**, **5Ac$_3$**, **7Ac**, **8Ac**, **8Ac$_2$** and **9Ac** (400 MHz, $CDCl_3$, δ-values)

H	4	5	5Ac	5Ac$_2$	5Ac$_3$	6	7*
5	*	*	*	*	1.67 *dd*	1.68 *dd*	*
6	*	1.56 *m*	*	*	1.54 *m*	1.53 *m*	*
		1.46 *m*			1.43 *m*	1.43 *m*	
7	2.05 *m*	2.02 *m*	2.05 *m*	2.03 *m*	2.06 *m*	2.00 *m*	*
		1.96 *br ddd*			1.97 *br ddd*		
9	5.17 *dq*	5.23 *dq*	5.21 *dq*	5.16 *dq*	5.08 *dq*	5.11 *br t*	5.14 *dq*
11	4.52 *ddd*	4.54 *ddd*	4.55 *ddd*	4.55 *ddd*	5.64 *ddd*		4.49 *ddd*
12	2.24 *dd*	2.35 *br dd*	2.37 *dd*	2.31 *d*	2.40 *dd*	2.16 *br s*	2.22 *dd*
12′	2.17 *dd*	2.18 *dd*	2.33 *dd*		2.32 *dd*		2.14 *dd*
14	5.52 *br t*	5.72 *br t*	5.51 *br t*	5.66 *br t*	5.59 *br t*	5.65 *br t*	5.50 *br t*
15	4.19 *d*	4.25 *dd*	4.68 *d*	4.69 *d*	4.64 *d*	4.22 *d*	4.18 *d*
		4.19 *dd*					
16	1.73 *br s*	4.25 *br d*	4.28 *d*	4.69 *s*	4.68 *d*	4.18 *br s*	1.72 *br s*
		4.11 *br d*	4.16 *d*		4.64 *d*		
17	1.68 *d*	1.69 *d*	1.68 *d*	1.67 *d*	1.69 *d*	1.60 *br s*	1.64 *d*
18	0.91 *s*	0.92 *s*	0.91 *s*	0.92 *s*	0.91 *s*	0.91 *s*	1.20 *s*
19	0.83 *s*	0.84 *s*	0.84 *s*	0.84 *s*	0.83 *s*	0.83 *s*	1.04 *s*
20	4.76 *br s*	4.77 *br s*	4.76 *br s*	4.76 *br s*	4.75 *br s*	4.76 *br s*	4.93 *br s*
	4.54 *d*	4.54 *d*	4.54 *d*	4.54 *d*	4.58 *d*	4.54 *d*	4.84 *d*
OAc	—	—	2.06 *s*	2.08 *s*	2.07 *s*	—	—
				2.06 *s*	2.05 *s*		

Table 2. *Continued*

H	7Ac†	8Ac‡ (C_6D_6)	$8Ac_2$§	9	9Ac	10	11
5	*	1.76 *m*	*	*	1.11 *dd*	*	1.67 *dd*
6	*	1.67 *m* 1.76 *m*	*	1.45 *m* 1.25 *m*	1.43 *m* 1.21 *m*	1.43 *m* 1.28 *m*	1.46 *m*
7	*	2.22 *m* 1.96 *m*	2.05 *m*	2.05 *m* 1.93 *m*	2.05 *m* 1.92 *br ddd*	2.03 *m* 1.92 *m*	1.97 *m* 1.76 *br ddd*
9	5.06 *dq*	5.32 *dq*	5.07 *dq*	5.17 *dq*	5.10 *dq*	5.10 *br t*	5.23 *dq*
11	5.63 *ddd*	4.47 *ddd*	5.64 *ddd*	4.51 *dddd*	5.65 *ddd*		4.58 *ddd*
12	2.36 *dd*	2.25 *dd*	2.37 *dd*	2.25 *dd*	2.37 *dd*	2.18 *br s*	2.66 *br dd*
12′	2.14 *dd*	2.13 *dd*	2.18 *dd*	2.17 *dd*	2.18 *dd*		2.71 *br dd*
14	5.36 *br t*	5.49 *tq*	5.36 *br t*	5.50 *br t*	5.37 *br t*	5.63 *br t*	5.56 *ttt*
15	4.55 *d*	4.63 *dd* 4.58 *dd*	4.55 *d*	4.18 *d*	4.55 *d*	4.21 *br d*	4.08 *br d*
16	1.73 *br s*	1.58 *br s*	1.72 *br s*	1.73 *br s*	1.73 *br s*	4.17 *br s*	4.51 *br d* 4.30 *br d*
17	1.66 *d*	1.61 *d*	1.69 *d*	1.68 *d*	1.70 *d*	1.58 *br s*	1.70 *br*
18	1.19 *s*	1.05 *s*	1.02 *s*	1.06 *s*	1.05 *s*	1.05 *s*	0.90 *s*
19	1.05 *s*	0.87 *s*	0.73 *s*	0.86 *s*	0.85 *s*	0.85 *s*	0.83 *s*
20	5.02 *br s* 4.81 *d*	4.95 *br s* 4.72 *br s*	4.77 *br s* 4.56 *br s*	2.58 *br d* 2.49 *d*	2.61 *br d* 2.49 *d*	2.62 *br d* 2.49 *d*	4.76 *br s* 4.54 *d*
OAc	2.04 *s* 2.00 *s*	1.72 *s*	2.03 *s* 1.99 *s*	—	2.05 *s* 2.01 *s*	—	—

*Overlapped multiplets.
†H-1 2.46 *m*, H-2 2.62 and 2.30 *ddd*.
§H-3 3.18 *dd*.
‡H-3 3.39 *dd*.
J [Hz]: 9, 11 = 8; 9,17 = 1.5; 11,12 = 8; 11,12′ = 6; 12,12′ = 13.5; 14,15 = 7; 20,20′ = 1.5; compounds **5**, **5**Ac, $5Ac_2$ and $5Ac_3$: 16,16′ = 12.5; compounds **5** and $5Ac_3$: 5,6 = 11; 5,6′ = 3; 6,7 = 10; 6′,7 = 4; 7,7′ = 14; compounds **7** and **7**Ac: 1,2 = 8; 1′,2 = 11; 1, 2′ = 4; 1′, 2′ = 4; 2,2′ = 14; compounds **8**Ac and $8Ac_2$: 2,3 = 9; 2′,3 = 4; compounds **9**, **10** and **9**Ac: 1,20 = 0.5; 5, 6 = 8; 5,6′ = 4; 6,7 = 4; 6′,7 = 9; 7,7′ = 14; 20, 20′ = 4.5; compound **11**: 12,14 = 14,16 ~ 2.

ited in the Herbarium of the University of Chile, Santiago) were extracted with MeOH–Et_2O–petrol (1:1:1) at room temp. The extract obtained was defatted with MeOH and first sepd by CC (silica gel) into 7 crude frs, 1: petrol; 2: Et_2O–petrol, (4:1); 3 and 4: Et_2O–petrol, (1:1); 5: Et_2O–petrol, (3:1); 6: Et_2O; 7: Et_2O–MeOH, (9:1). Fr. 1 gave 300 mg germacrene D and 200 mg bicyclogermacrene by TLC. Fr. 2 was sepd by medium pressure chromatography (MPC) (silica gel, ϕ 30–60 μm, Et_2O–petrol, (20:1–1:1)). After monitoring by TLC the eluates were combined into 11 frs (2/1–2/11). Fr. 2/1 gave 200 mg taraxasteryl acetate, 2/2 200 mg spathulenol, 2/3 150 mg **37** and 2/4 a mixt. of 30 mg nerolidol and 100 mg **38** (sepd by TLC). Fr. 2/5 afforded 700 mg **38** and 2/6 200 mg **36**. Fr. 2/7 gave 300 mg **35**, 2/8 250 mg **33**, fr. 2/9 400 mg **39**, fr. 2/10 200 mg **32** and fr. 2/11 a mixt. of 500 mg **22**, 100 mg **24** and 1 g **26** (5% sepd by TLC). CC fr. 3 gave 6 g **32** and CC fr 4, 4 g **32** and 2 g **40** (1% sepd by TLC). CC fr 5 was sepd again by MPC [Et_2O–petrol, (9:1)–Et_2O] affording 8 crude frs (after monitoring by TLC). Fr 5/1 gave 200 mg **32**, 5/2 was a mixt. which gave by HPLC [MeOH–H_2O, (17:3) RP 8, flow rate, 3 ml min^{-1}, *ca* 100 bar] 100 mg **31**, 60 mg **29**, 100 mg **40**, 50 mg **32**, 20 mg **30**, 45 mg **16** (R_t 7.8 min), 40 mg **19**, 250 mg **21**, 100 mg **4** (R_t 15.7 min) and 3 mg **11** (R_t 21.1 min). Fr. 5/3 gave 200 mg *p*-hydroxyacetophenone and 5/4 150 mg **41**. Fr. 5/5 gave by HPLC (MeOH–H_2O, 17:3) 2 mg carabrone, 20 mg **29**, 40 mg **16**, 500 mg **19** and 250 mg **21**. Fr. 5/6 gave 700 mg **34** and 5/7 a mixt. which was first sepd into acidic and neutral compounds ($NaHCO_3$). HPLC of the neutral part (MeOH–H_2O, 17:3) gave 2 mg **28**, 2 mg **15** (R_t 3.0 min) and 5 mg **17**. HPLC of the acidic part (MeOH–H_2O, 4:1) gave 2 mg **23**, 10 mg **25** and 10 mg **27**. Fr. 5/8 gave by HPLC (MeOH–H_2O, 17:3), 2 mg **9** (R_t 2.7 min) and 3 mg **10** (R_t 3.7 min). CC fr. 6 gave by HPLC (MeOH–H_2O, 17:3) 10 mg **12** (R_t 0.9 min), a mixt. of 2 mg **7** and 8 mg **2** (sepd by repeated HPLC [MeOH–H_2O, (4:1), R_t 3.8 and 4.3 min, respectively], a mixt. which gave by repeated HPLC (MeOH–H_2O, 4:1) 5 mg **9** (R_t 5.7 min) and 10 mg **15** (R_t 6.5 min), 10 mg **18** (R_t 4.0 min), 5 mg **20** (R_t 4.6 min), 400 mg **4** and 2 mg **6** (R_t 7.5 min). CC fr. 7 contained no acetates (^{1}H NMR). Acetylation (Ac_2O, 1.5 hr, 70°) gave a mixt. which was sepd by CC into two frs. The first gave 4 g $5Ac_3$ [HPLC MeOH–H_2O, (9:1), R_t 11.7 min]. The polar fr. gave by HPLC (MeOH–H_2O, 9:1) 5 mg ilicic acid, a mixt (R_t 1.4 min) of 10 mg **3**Ac and 30 mg **13**Ac (sepd by TLC in Et_2O–petrol, 3:1), 2 mg **12**Ac (R_t 1.9 min), 4 mg **8**Ac (R_t 2.5 min), 35 mg **16** (R_t 2.8 min), 80 mg **14**Ac (R_t 3.5 min), 4 mg $8Ac_2$ (R_t 3.9 min) 50 mg **5**Ac (R_t 2.5 min), 100 mg $5Ac_2$ (R_t 6.1 min) and 500 mg $5Ac_3$ (R_t 11.7 min). Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material.

5,13-*Dihydroxygeranylgeraniol* (**2**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 304 $[M-H_2O]^+$ (0.1), 289.217 [304 − Me]$^+$ (0.4) (calc. for $C_{19}H_{29}O_2$: 289.217), 271 $[289-H_2O]^+$ (0.5), 235 (3.5), 205 (3.5), 191 (5.5), 135 (32), 85 $[C_5H_9O]^+$ (100), 69 (69). Acetylation (Ac_2O–$CHCl_3$; DMAP, 2 hr, 70°) gave the triacetate **2**Ac, gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745 (OAc); MS *m/z* (rel. int.): 448.283 $[M]^+$ (0.2) (calc. for $C_{26}H_{40}O_6$: 448.283), 388 [M − HOAc]$^+$ (0.5), 328 [388 − HOAc]$^+$ (3.5), 268 [328 − HOAc]$^+$ (4), 219 (12), 201 (26), 135 (93), 127 (66), 85 $[C_5H_9O]^+$ (100).

5,15-*Dihydroxy*-12-*oxo*-14,15-*dihydro*-13,14E-*dehydrogeranylgeraniol* (**3**). Isolated as diacetate 3Ac, gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1740, 1240 (OAc), 1665, 1620 (C=CCOC=C); MS *m/z* (rel. int.): 420 $[M]^+$ (0.4), 360.230 [M

Table 3. ^{1}H NMR spectral data of compounds **12**, **15**, **16**, **18**, **20**, **12Ac**, **13Ac** and **14Ac** (400 MHz, $CDCl_3$, δ-values)

H	12	12Ac	13Ac*	14Ac	15	16	18†	20
2	2.59 *ddd*	2.58 *ddd*	5.22 *ddd*	‡	‡	‡	3.88 *tt*	3.86 *tt*
2′	2.38 *ddd*	2.37 *ddd*		‡	‡	‡		
3	—	—	3.48 *d*	4.64 *t*	4.65 *t*	3.41 *t*	1.15 *t*	1.12 *t*
							1.77 *ddd*	1.75 *dd*
5	1.42 *m*	1.38 *m*	1.46 *dd*	1.40 *m*	1.45 *m*	1.42 *m*	1.08 *dd*	1.15 *dd*
9	1.14 *t*	1.11 *t*	1.16 *t*	1.14 *t*	1.14 *t*	1.13 *t*	1.63 *br d*	1.68 *m*
12	2.15 *ddd*	2.15 *m*	2.10 *m*	2.13 *m*	2.10 *m*	2.10 *m*	2.16 *ddd*	2.24 *ddd*
12′	2.06 *ddd*	2.08 *m*					1.82 *ddd*	1.96 *m*
14	5.43 *tq*	5.32 *tq*	5.33 *tq*	5.34 *tq*	5.44 *tq*	5.34 *tq*	5.39 *tq*	5.42 *tq*
15	4.16 *dd*	4.60 *dd*	4.60 *dd*	4.51 *dd*	4.18 *dd*	4.60 *dd*	4.16 *d*	4.16 *d*
	4.12 *dd*	4.54 *dd*	4.54 *dd*	4.55 *dd*	4.13 *dd*	4.55 *dd*		
16	1.69 *br s*	1.70 *br s*	1.70 *br s*	1.72 *br s*	1.70 *br s*	1.71 *br s*	1.68 *br s*	1.69 *br s*
17	1.19 *s*	1.18 *s*	1.12 *s*	1.14 *s*	1.14 *s*	1.13 *s*	4.87 *q*	1.70 *br s*
							4.55 *q*	
18	1.09 *s*	1.08 *s*	1.01 *s*	0.86 *s*	0.87 *s*	0.96 *s*	0.94 *s*	0.92 *s*
19	1.02 *s*	1.00 *s*	0.87 *s*	0.85 *s*	0.86 *s*	0.82 *s*	0.85 *s*	
20	0.97 *s*	0.95 *s*	0.90 *s*	0.82 *s*	0.82 *s*	0.81 *s*	0.72 *s*	0.80 *s*
OAc	—	2.04 *s*	2.10 *s*	2.08 *s*	2.09 *s*	2.05 *s*	—	—
			2.05 *s*	2.05 *s*				

*H-1α 1.63 *dd*, H-1β 1.56 *t*, H-6α 1.30 *dddd*, H-6β/7β 1.38 *m*, H-7α 1.88 *dt*, H-11 1.56, 1.38 *m*.

†H-6 1.30 *dq*, H-6′ 1.70 *m*, H-7 2.41 *ddd*, H-7′ 1.97 *br dt*.

‡Obscured multiplets.

J [Hz]: 9,11 = 4; 11,12 = 5; 11′,12 = 10; 11,12′ = 10; 11′,12′ = 5; 12,12′ = 15; 14,15 = 7; 14,16 = 1.5; 15,15′ = 13; compounds **12** and **12Ac**: 1,1′ = 13; 1,2 = 6.5; 1,2′ = 6; 1′,2 = 11.5; 1′,2′ = 3; 2,2′ = 15.5; compound **13Ac**: 1,1′ = 1,2 = 12; 1′,2 = 4; 2,3 = 2; 5,6 = 12; 5,6′ = 2.5; 6,6′ = 6,7 = 12.5; 6,7′ = 6′,7 = 3; 7,7′ = 12; compounds **14Ac**, **15** and **16**; 2,3 = 2′,3 = 2.5; compound **18**: 1,2 = 2,3 = 4; 1′,2 = 2,3′ = 11.5; 3,3′ = 12; 5,6 = 6,6′ = 6,7 = 7,7′ = 13; 5,6′ = 2.5; 6′,7 = 5; 6′,7′ = 2.5; 9,11 = 10; 7′,17 = 9,17 = 17,17′ = 1.

$-HOAc]^+$ (3) (calc. for $C_{22}H_{32}O_4$: 360.230), 342 $[360-H_2O]^+$ (2), 300 $[360-HOAc]^+$ (7), 285 $[300-Me]^+$ (5), 282 $[300-H_2O]^+$ (3), 233 (66), 205 (30), 133 (82), 95 (100), 81 (97).

11,15-*Dihydroxy*-9,10-seco-ent-*labda*-8E,13E, 10(20)-*triene* (**4**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 306 $[M]^+$ (0.2), 288.245 $[M-H_2O]^+$ (1.5) (calc. for $C_{20}H_{32}O$: 288.245), 273 $[288-Me]^+$ (2.5), 220 (8), 205 (20), 203 (29), 177 (76), 109 (66), 97 (86), 95 (91), 81 (99), 69 (100).

11,15,16-*Trihydroxy*-9,10-seco-ent-*labda*-8E,13Z,10(20)-*triene* (**5**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH); MS *m/z* (rel. int.): 304.240 $[M-H_2O]^+$ (1.5) (calc. for $C_{20}H_{32}O_2$: 304.240), 289 $[M-Me]^+$ (1.6), 286 $[M-H_2O]^+$ (1.3), 271 $[289-H_2O]^+$ (3), 203 $[304-CH_2C(CH_2OH)=CHCH_2OH]^+$ (31), 177 (46), 121 (43), 109 (65), 95 (80), 81 (96), 69 (100). Acetylation gave the triacetate $\mathbf{5Ac_3}$, gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3080, 1650 ($C=CH_2$), 1750, 1250 (OAc); MS *m/z* (rel. int.): 448.282 $[M]^+$ (0.3) (calc. for $C_{26}H_{40}O_6$: 448.282), 388 $[M-HOAc]^+$ (4), 328 $[388-HOAc]^+$ (11), 268 $[328-HOAc]^+$ (28), 221 $[C_{15}H_{25}O]^+$ (20), 203 $[C_{15}H_{23}]^+$ (100), 177 (42), 135 (46), 109 (57), 81 (68); ^{13}C NMR ($CDCl_3$, C-1–C-20): δ 37.9 *t*, 23.6 *t*, 40.6 *t*, 34.8 *s*, 53.5 *d*, 24.2 *t*, 36.2 *t*, 135.3 *s*, 127.2 *d*, 149.1 *s*, 69.5 *d*, 32.4 *t*, 141.6 *s*, 122.4 *d*, 60.1 *t*, 61.7 *t*, 16.9 *q*, 28.3 *q*, 26.2 *q*, 109.0 *t*; OAc 21.9 *q*, 20.8 *q* (2×), 170.6 *s*, 170.1 *s* (2×); $[\alpha]_D^{24°}$ +6 ($CHCl_3$; *c* 1.17). Partial acetylation gave the monoacetate **5Ac** and the diacetate $\mathbf{5Ac_2}$ (^{1}H NMR see Table 2).

15,16-*Dihydroxy*-9,10-seco-ent-*labda*-8E,13Z,10 (20)-*triene* (**6**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610, 3420 (OH); MS *m/z* (rel. int.): 306.256 $[M]^+$ (0.2) (calc. for $C_{20}H_{34}O_2$: 306.256), 288 $[M-H_2O]^+$ (1), 273 $[288-Me]^+$ (3.5), 255 $[273-H_2O]^+$ (2), 220 (3.5), 205 (3), 203 (3.5), 177 (14), 109 (42), 95 (42), 81 (100), 69 (76).

11,15-*Dihydroxy*-9,10-seco-ent-*labda*-8E,13E,(20)-*triene*-3-*one* (**7**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1710 (C=O); MS *m/z* (rel. int.): 302.225 $[M]^+$ (0.5) (calc. for $C_{20}H_{32}O_3$: 302.225), 235 (4.5), 217 (5), 191 (10), 135 (20), 97 (68), 69 (83), 68 (100). Acetylation gave the diacetate **7Ac**, gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (OAc), 1720 (C=O); MS *m/z* (rel. int.): 404.256 $[M]^+$ (2) (calc. for $C_{24}H_{36}O_5$: 404.256), 344 $[M-HOAc]^+$ (1), 284 $[344-HOAc]^+$ (8), 235 (100), 217 (61), 191 (64), 133 (61), 97 (91), 69 (80), 68 (90); CD (MeOH): $\Delta\varepsilon_{294}$ +0.15.

3α,11,15-*Trihydroxy*-9,10-seco-ent-*labda*-8E,13E,10(20)-*triene* (**8**). Isolated as monoacetate **8Ac**; gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1750, 1240 (OAc); MS *m/z* (rel. int.): 304.240 $[M-HOAc]^+$ (2) (calc. for $C_{20}H_{32}O_2$: 304.240), 289 $[304-Me]^+$ (5), 271 $[289-H_2O]^+$ (3), 235 (14), 219 (22), 201 (30), 175 (70), 135 (78), 121 (64), 97 (88), 69 (80), 68 (100); $[\alpha]_D^{24°}$ −16 ($CHCl_3$; *c* 0.38). Diacetate $\mathbf{8Ac_2}$; gum; ^{1}H NMR see Table 1.

11,15-*Dihydroxy*-10β,20-*epoxy*-9,10-seco-ent-*labda*-8E,13E-*diene* (**9**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH); MS *m/z* (rel. int.): 237.185 $[M-CH_2C(Me)=CHCH_2OH]^+$ (4) (calc. for $C_{15}H_{25}O_2$: 237.185), 219 (8), 201 (12), 135 (42), 109 (72), 97 (92), 69 (100), 68 (95). Acetylation gave diacetate **9Ac**, gum; MS *m/z* (rel. int.): 346.251 $[M-HOAc]^+$ (calc. for $C_{22}H_{34}O_3$: 346.251), 286 $[346-HOAc]^+$ (4), 237 (18), 219 (51), 201 (36), 109 (70), 97 (100), 81 (76), 69 (80).

15,16-*Dihydroxy*-10β,20-*epoxy*-9,10-seco-ent-*labda*-8E,13Z-*diene* (**10**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH); MS *m/z* (rel. int.): 304.240 $[M-H_2O]^+$ (0.7) (calc. for $C_{20}H_{32}O_2$: 304.240), 236 (4), 219 (6), 135 (37), 109 (60), 95 (51), 81 (100), 69 (68).

15-*Hydroxy*-11,16-*epoxy*-9,10-seco-ent-*labda*-8E,13Z,10(20)-*triene* (**11**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 3080, 1650 ($C=CH_2$); MS *m/z* (rel. int.): 304.240 $[M]^+$ (6) (calc. for $C_{20}H_{32}O_2$: 304.240), 289 $[M-Me]^+$ (5), 271 $[289-H_2O]^+$ (8), 203 (20), 177 (32), 153 (54), 109 (88), 95 (88), 81 (98), 69 (100).

8β,15-*Dihydroxy*-ent-labda-13E-*en*-3-*one* (**12**). Crystals, mp 134°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 1705 (C=O). Acetylation gave

monoacetate **12**Ac; gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1745, 1240 (OAc), 1710 (C=O); MS *m/z* (rel. int.): 364 $[M]^+$ (0.5), 304.240 $[M-HOAc]^+$ (7) (calc. for $C_{20}H_{32}O_2$: 304.240), 289 $[304-Me]^+$ (8), 286 $[304-H_2O]^+$ (26), 206 (46), 205 (46), 191 (42), 140 (100), 135 (68), 81 (98); CD (MeOH): $\Delta\varepsilon_{312}$ −0.07, $\Delta\varepsilon_{281}$ +0.1.

2*β*,3*β*,8*β*,15-*Tetrahydroxy*-ent-labda-13*E*-*ene* (**13**). Isolated as 2-*O*-15-*O*-diacetate **13**Ac; gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1755, 1255 (OAc); MS *m/z* (rel. int.): 364.261 $[M-HOAc]^+$ (2) (calc. for $C_{22}H_{36}O_4$: 364.261), 346 $[364-H_2O]^+$ (3), 286 $[346-HOAc]^+$ (2), 265 (5), 229 (5), 206 (24), 135 (100), 81 (28); ^{13}C NMR ($CDCl_3$, C-1–C-20): 44.4 *t*, 70.6 *d*, 76.6 *d*, 40.1 *s*, 48.0 *d*, 21.0 *t*, 42.4 *t*, 73.8 *s*, 60.5 *d*, 37.3 *s*, 23.1 *t*, 38.3 *t*, 143.2 *s*, 118.2 *d*, 61.4 *t*, 16.5 *q*, 28.4 *q*, 23.8 *q*, 19.7 *q*, 16.7 *q*; OAc 21.5 *q*, 21.4 *q*, 170.2 *s*, 171.2 *s*; $[\alpha]_D^{24°}$ −17 ($CHCl_3$; *c* 0.67).

3*β*,8*β*,15-*Trihydroxy*-ent-labda-13E-*ene* (**14**). Isolated as 15-*O*-acetate **16**; gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1750, 1240 (OAc); MS *m/z* (rel. int.): 306.256 $[M-HOAc]^+$ (12) (calc. for $C_{20}H_{34}O_2$: 306.256), 288 $[306-H_2O]^+$ (28), 207 (76), 190 (93), 175 (93), 135 (92), 81 (100); $[\alpha]_D^{24°}$ −19 ($CHCl_3$; *c* 3.27). Identical with isolated acetate **16**. Diacetate **14**Ac_2; gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1750 (OAc); MS *m/z* (rel. int.): 348.266 $[M-HOAc]^+$ (6) (calc. for $C_{22}H_{36}O_3$: 348.266), 330 $[348-H_2O]^+$ (9), 288 $[348-HOAc]^+$ (6), 270 $[288-H_2O]^+$ (7), 190 (100), 175 (91), 135 (88), 121 (75), 95 (77), 81 (96), 69 (88).

3*β*-*Acetoxy*-8*β*,15-*dihydroxy*-ent-labda-13-*ene* (**15**). Crystals, mp 151°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1750, 1255 (OAc); MS *m/z* (rel. int.): 348.266 $[M-H_2O]^+$ (0.3) (calc. for $C_{22}H_{36}O_3$: 348.266), 333 $[348-Me]^+$ (0.5), 330 $[348-H_2O]^+$ (0.3), 288 $[348-HOAc]^+$ (2), 273 (3), 255 (2.5), 190 (77), 175 (76), 135 (50), 121 (44), 95 (50), 81 (82), 69 (100), $[\alpha]_D^{24°}$ −44 ($CHCl_3$; *c* 0.52).

2*β*,15-*Dihydroxy*-ent-labda-8(17), 13E-*diene* (**18**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 3080, 1650 (C=CH_2); MS *m/z* (rel. int.): 306.256 $[M]^+$ (1) (calc. for $C_{20}H_{34}O_2$: 306.256), 291 $[M-Me]^+$ (6), 273 $[291-H_2O]^+$ (15), 255 $[273-H_2O]^+$ (10), 135 (82), 121 (46), 95 (50), 81 (76), 69 (100); $[\alpha]_D^{24°}$ −24 ($CHCl_3$; *c* 0.18).

2*β*,15-*Dihydroxy*-ent-labda-7,13E-*diene* (**20**). Gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH); MS *m/z* (rel. int.): 306.256 $[M]^+$ (0.5) (calc. for $C_{20}H_{34}O_2$: 306.256), 291 $[M-Me]^+$ (2.5), 288 $[M-H_2O]^+$ (1.5), 273 $[288-Me]^+$ (4.5), 220 $[M-Me_2C{=}CHCH_2OH]^+$ (93), 135 (58), 107 (60), 93 (61), 81 (100), 69 (56).

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