

## DITERPENOIDS FROM *SIDERITIS VAROI*\*

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**Key Word Index**—*Sideritis varoi*; Labiatae; *ent*-13-*epi*-manoyl oxides;  $^{13}\text{C}$  NMR.

**Abstract**—From the aerial parts of *Sideritis varoi*, the previously known, *ent*-kaurenic compounds linearol, sidol, isolinearol, isosidol, 3-acetilleucanthol, 18-acetilleucanthol and siderol, as well as ribenol and andalusol, have been isolated. In addition, *ent*-8 $\alpha$ -hydroxy-13(16),14-labdadien-18-al (6-deoxiandalusol), *ent*-12 $\alpha$ -hydroxy-13-*epi*-manoyl oxide (varol), *ent*-3 $\beta$ ,12 $\alpha$ -dihydroxy-13-*epi*-manoyl oxide (varodiol) and three natural acetates of the last product, have also been obtained from the same source. The structures of these new diterpenoids have been established by chemical and spectroscopic means.

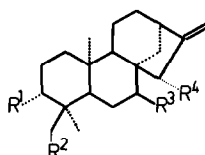
### INTRODUCTION

We are making a systematic investigation of the diterpenoid content of the endemic *Sideritis* species growing in Andalusía (southern Spain). This genus presents many classification problems, as the presence of hybrids is very common. Thus, *Sideritis varoi* Soc. is an established hybrid from *S. lagascana* Willk. and *S. leucantha* Cav. var. *incana* Font Quer [1]. This plant was previously classified as *S. leucantha* Cav. var. *paucidentata* [2]. In addition to botanical considerations, we have found several *ent*-kaurenoids which are characteristic of *S. lagascana* [3] and *S. leucantha* Cav. [4].

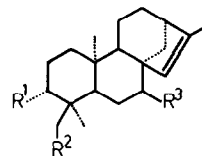
The hybrid *S. varoi* Soc. grows over extensive areas of gypsum-rich soils. Elsewhere, the pure *S. leucantha* Cav. var. *incana* is reduced to very restricted areas.

### RESULTS AND DISCUSSION

*S. varoi* contained seven known *ent*-kaurenoids: *ent*-3 $\beta$ ,7 $\alpha$ -dihydroxy-18-acetoxykaur-16-ene (linearol, 1), *ent*-7 $\alpha$ ,18-dihydroxy-3 $\beta$ -acetoxykaur-16-ene (sidol, 2), *ent*-3 $\beta$ ,7 $\alpha$ -dihydroxy-18-acetoxykaur-15-ene (isolinearol, 3), *ent*-7 $\alpha$ ,18-dihydroxy-3 $\beta$ -acetoxykaur-15-ene (isosidol, 4), *ent*-7 $\alpha$ ,15 $\beta$ ,18-trihydroxy-3 $\beta$ -acetoxykaur-16-ene (3-acetilleucanthol, 5), *ent*-3 $\beta$ ,7 $\alpha$ ,15 $\beta$ -trihydroxy-18-acetoxykaur-



	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>
1	OH	OAc	OH	H
2	OAc	OH	OH	H
5	OAc	OH	OH	OH
6	OH	OAc	OH	OH

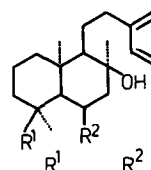


	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>
3	OH	OAc	OH
4	OAc	OH	OH
7	H	OH	OAc

16-ene (18-acetilleucanthol, 6) and *ent*-18-hydroxy-7 $\alpha$ -acetoxykaur-15-ene (siderol, 7). Compounds 1–4 were isolated for the first time from *S. leucantha* Cav. and *S. linearifolia* Lam. [4] and later they were also isolated, *inter alia*, from *S. lagascana* Willk. [3]. The physical and spectroscopic properties of 1–7 were identical with those reported in the literature [4–6].

*S. varoi* also contained two *ent*-labda-13(16),14-dienes of known structure, *ent*-6 $\alpha$ ,8 $\alpha$ ,18-trihydroxylabda-13(16),14-diene (andalusol, 8) and *ent*-8 $\alpha$ ,18-dihydroxylabda-13(16),14-diene (6-deoxiandalusol, 9) [7, 8] as well as a new *ent*-labda-13(16),14-diene (10).

The new labdiene was found to have a molecular formula  $\text{C}_{20}\text{H}_{32}\text{O}_2$ , and its UV spectrum showed a maximum at 226 nm. Its IR spectrum showed hydroxyl ( $3440\text{ cm}^{-1}$ ) and carbonyl ( $1720\text{ cm}^{-1}$ ) absorptions. Its  $^1\text{H}$  NMR spectrum (see Experimental) contained a singlet signal at  $\delta$  9.1 (1H), which was attributed to an equatorial formyl group situated at a quaternary carbon, as well as an



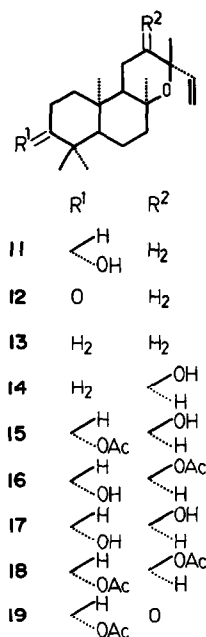
	R <sup>1</sup>	R <sup>2</sup>
8	$\text{CH}_2\text{OH}$	OH
9	$\text{CH}_2\text{OH}$	H
10	CHO	H

\*Part 11 in the series "Terpenic Components of Spanish Labiatae". For part 10 see A. García-Granados, A. Parra, A. Peña and O. Socorro, *An. Quim.* (in press).

$A_2B_2X$  system similar to that shown by **8** and **9** [7, 8], and three methyl singlet signals at  $\delta$  1.08, 0.97 and 0.83 (3H each). The rotatory power of **10** was very similar to that previously described for **9**, the structure of which was firmly established [8]. The correlation of these data with those reported for **9**, allowed the structural assignment of **10** as 6-deoxyandalusal, this being the first aldehydic compound found in an Iberian *Sideritis*. Sodium borohydride reduction of **10** gave **9**, and Jones' oxidation of **9** led to **10**.

Five *ent*-13-epi-manoyl oxides were also isolated from this plant. That of least mobility (TLC) was identified as *ent*-3 $\beta$ -hydroxy-13-epi-manoyl oxide (ribenol **11**) [9]. Its physical and spectroscopic data were in agreement with those described for ribenol. On the other hand, Jones' oxidation gave the ketone, **12**, which showed methyl singlet signals that were not in agreement to those described for a similar ketone (**9**). Wolff-Kishner reduction of ketone **12** gave, as the main product, *ent*-13-epi-manoyl oxide, **13**, identified through its physical constants. Compound **11** was positively identified by comparison with authentic ribenol isolated from *S. canariensis* [9].

Compound **14** had a molecular formula of  $C_{20}H_{34}O_2$ . The chemical shifts of the five singlet methyl groups ( $\delta$  1.15, 1.12, 0.82, 0.74 and 0.69; 3H each) as well as an ABX system similar to that found in product **12**, suggested a 13-epi-manoyl structure. A signal at  $\delta$  4.0 (1H, *dd*,  $J_1 = 3$  and  $J_2 = 4.5$  Hz) was attributable to an equatorial proton geminal to a hydroxyl group, and with two other vicinal proton couplings. In addition, the high chemical shift of this proton indicated the presence of a hydroxyl group at C-7 or C-12, but data from **15** and **16**, two other natural products isolated from *S. varoi*, allowed us to reject the C-7 position, and a structure of *ent*-12 $\alpha$ -hydroxy-13-epi-manoyl oxide was assigned to **14** for which we suggest the trivial name of varol. Its enantiomer had been previously described [10], which confirmed the *ent*-configuration for **14**.



The natural products **15**–**17** gave the same diacetate, **18**, on acetylation with hot acetic anhydride–pyridine. Compound **15** had a molecular formula of  $C_{22}H_{36}O_4$ , and its IR spectrum contained bands at 3450, 1720 and  $1250\text{ cm}^{-1}$ . The  $^1\text{H}$  NMR spectrum showed an axial proton at  $\delta$  4.5 (1H, *dd*,  $J_1 = 17$  and  $J_2 = 9$  Hz), geminal to an acetoxyl group. This equatorial acetoxyl group had to be placed between a tetrasubstituted  $sp^3$  group carbon atom and a methylene grouping. On the other hand, a signal, (1H, *dd*,  $J_1 = 3$  and  $J_2 = 4.5$  Hz) similar to that found in **14**, was present. These data and the rest of the signals (see Experimental), were compatible with the structure of *ent*-3 $\beta$ -acetoxyl-12 $\alpha$ -hydroxy-13-epi-manoyl oxide for **15**. Oxidation of this product by Jones' reagent gave a ketone, **19**, that showed a negative Cotton effect, in accord with the location of the hydroxyl group of **15** at C-12. The  $^{13}\text{C}$  NMR spectrum (see Table 1) of the diacetate, **18**, obtained from **15**, provided conclusive proof of the structure proposed for **15**. The diacetate, **18**, was shown to be identical with a minor product also isolated from this plant. Hence, product **18** is a natural diacetate.

The chemical shifts for the carbons of ring A of product **18** were consistent with those published for products with similar structures in this ring (**11**, **12**). For this product, a chair conformation for ring C was deduced from a consistent  $\gamma$ -effect observed for C-9 ( $\Delta\delta = -8.5$  for 13-epi-manoyl oxide and  $\Delta\delta = -5.7$  for a manoyl oxide skeleton). It was also consistent with the proposed axial configuration for C-12 [13].

From the  $^{13}\text{C}$  NMR spectrum of **18**, the C-13 configu-

Table 1.  $^{13}\text{C}$  NMR chemical shifts of compound **18** and reference compounds

Carbon No.	18	13*	20†
1	37.09	39.4	39.0
2	23.88	18.7	18.6
3	80.65	42.2	42.1
4	37.86	33.4	33.1
5	55.42	56.5	56.4
6	19.40	19.9	19.9
7	42.44	43.1	43.2
8	79.96	76.1	74.8
9	49.98	58.5	55.7
10	35.88	39.6	36.9
11	21.64	15.9	15.4
12	71.32	34.6	35.8
13	36.03	73.3	73.0
14	146.61	147.8	147.8
15	111.03	109.5	110.1
16	27.96	32.7	28.5
17	23.49	24.0	25.5
18	16.29	21.3	21.3
19	27.08	33.3	33.4
20	15.81	15.9	15.3
$\text{CH}_3\text{COO}-$	21.30	—	—
	21.30		
$\text{CH}_3\text{COO}-$	170.60	—	—
	171.60		

The  $^{13}\text{C}$  chemical shifts are given in  $\delta$ -values (ppm) relative to TMS.

\* See ref. [14].

† See refs. [11, 12].

ation of this product was also deduced. Thus, the chemical shift of the C-17 atom was more in accord with a 13-epi-manoyl oxide skeleton. On the other hand, the axial acetoxyl group at C-12 produced a  $\gamma$ -gauche effect on C-16 ( $\Delta\delta = -4.7$ ) in accord with the C-13 epiconfiguration. In the same manner, a moderate anti-periplanar  $\gamma$ -effect on C-14 ( $\Delta\delta = -1.2$ ) was consistent with the relative C-12 and C-13 configurations for **18**.

The *ent*-configuration for **15** was deduced from the negative Cotton effect of the ketonic product, **19**. The new compound, **15**, was thus *ent*-3 $\beta$ -acetoxyl-12 $\alpha$ -hydroxy-13-epi-manoyl oxide.

Another natural product, **16**, was an isomeric acetate of **15**. Acetylation of **16** also produced the diacetate **18**. In this case, the acetoxyl group was situated at C-12, and in its  $^1\text{H}$  NMR spectrum there were signals of an axial proton geminal to a hydroxyl group ( $\delta$  3.10; 1H, *dd*,  $J_1 = 7$  and  $J_2 = 9$  Hz) and an equatorial proton geminal to an acetoxyl group ( $\delta$  5.20; 1H, *dd*,  $J_1 = 3$  and  $J_2 = 4.5$  Hz). From the overall data, the structure of *ent*-3 $\beta$ -hydroxy-12 $\alpha$ -acetoxyl-13-epi-manoyl oxide was proposed for **16**.

The most polar *ent*-13-epi-manoyl oxide (**17**) isolated from *S. varoi* had a molecular formula of  $\text{C}_{20}\text{H}_{34}\text{O}_3$ . On acetylation, the above described diacetate, **18**, was obtained. Thus, the new diterpenoid was *ent*-3 $\beta$ ,12 $\alpha$ -dihydroxy-13-epi-manoyl oxide, for which we propose the trivial name of varodiol.

#### EXPERIMENTAL

Mps (Kofler apparatus) are uncorr.  $^1\text{H}$  NMR: 60 or 90 MHz (as indicated),  $\text{CDCl}_3$  with TMS as int. standard;  $^{13}\text{C}$  NMR: 25.2 MHz,  $\text{CDCl}_3$  (which also provided the lock signal) with TMS as int. reference. Assignments of  $^{13}\text{C}$  chemical shifts were made with the aid of off-resonance and noise-decoupled  $^{13}\text{C}$  NMR spectra. MS: Hewlett-Packard 5930 A instrument or a Micromass VG model. ZAB-2F operating in a low resolution mode (70 eV e. e. direct inlet). CC: Si gel Merck 7729 (less than 0.08 mm).

Plant material was collected in June 1979 near Cullar-Baza (Granada) and voucher specimens were deposited in the Herbarium of the Faculty of Pharmacy (Granada University).

**Extraction and isolation of the diterpenoids.** Dried and finely powdered *Sideritis varoi* plants (5 kg) were extracted with hexane (9 l) in a Soxhlet. The extract was concd *in vacuo* to 1.5 l. and repeatedly extracted with 90% aq. MeOH (6  $\times$  300 ml). The MeOH extracts were concd to 0.5 l, diluted with  $\text{H}_2\text{O}$  (3 l) and extracted with  $\text{MeCl}$  (6  $\times$  250 ml). The  $\text{CHCl}_3$  extracts were dried with  $\text{MgSO}_4$ , filtered and concd *in vacuo* to leave a yellowish residue (82 g), which was stepwise chromatographed through a Si gel column eluted with  $\text{CH}_2\text{Cl}_2$ - $\text{Me}_2\text{CO}$  mixtures of increasing polarity. The homogeneous fractions were repeatedly chromatographed through Si gel columns with 10%  $\text{AgNO}_3$ , and eluted with  $\text{CH}_2\text{Cl}_2$ - $\text{Me}_2\text{CO}$  mixtures of increasing polarity, yielding the following compounds in order of elution: diacetylvarodiol (**18**) 60 mg, ribenol (**11**) 1.3 g, varol (**14**) 600 mg, 6-deoxyandalusal (**10**) 600 mg, 12-acetylvarodiol (**16**) 900 mg, siderol (**7**) 200 mg, 3-acetylvarodiol (**15**) 850 mg, linearol (**1**) 150 mg, isolarol (**3**) 200 mg, 6-deoxyandalusol (**9**) 900 mg, varodiol (**17**) 3 g, sidol (**2**) 100 mg, isosidol (**4**) 50 mg, 18-acetylleucanthol (**6**) 250 mg, 3-acetylleucanthol (**5**) 250 mg and andalusol (**8**) 2 g.

**6-Deoxyandalusal (10).** A syrup;  $[\alpha]_D = -17^\circ$  ( $\text{CHCl}_3$ ; *c* 0.1);  $\text{IR } \nu_{\text{max}}^{\text{neat}} \text{ cm}^{-1}$ : 3440, 3140, 2980, 2930, 2860, 1725, 1650, 1465, 1395, 1255, 1160, 1120, 1090, 1080, 1035, 1000, 970, 940, 905;  $\text{UV } \lambda_{\text{max}}^{\text{hexane}} \text{ nm}$ : 226 (10800);  $^1\text{H}$  NMR (60 MHz):  $\delta$  9.20 (1H, *s*, H-18), vinyl group (ABX system,  $\delta_A = 5.10$ ,  $\delta_B = 5.38$ ,  $\delta_X = 6.35$ ,

$J_{AX} + J_{BX} = 29$  Hz, H-14 and 2H-15 protons), 5.01 (2H, *s*, 2H-16), C-Me singlets at  $\delta$  1.08, 0.97 and 0.83; MS  $m/z$  (rel. int.): 291 (1), 255 (1), 220 (0.5), 202 (0.5), 192 (1), 187 (1), 177 (8), 159 (18), 149 (8), 147 (8), 145 (8), 135 (14), 133 (14), 131 (14), 121 (25), 107 (45), 93 (70), 81 (100).

**3-Oxo-ent-13-epi-manoyl oxide (12).** 100 mg ribenol (**11**) gave 93 mg ketone, **12**, by Jones' oxidation. Mp  $87-89^\circ$ ;  $[\alpha]_D = -61.4^\circ$  ( $\text{CHCl}_3$ ; *c* 1);  $\text{IR } \nu_{\text{max}}^{\text{KBr}} \text{ cm}^{-1}$ : 3100, 2980, 2940, 2880, 1705, 1640, 1455, 1410, 1390, 1375, 1100, 1085, 1075, 1010, 990, 960, 915, 840;  $^1\text{H}$  NMR (60 MHz): vinyl group (ABX system,  $\delta_A = 4.77$ ,  $\delta_B = 5.02$ ,  $\delta_X = 5.97$ ,  $J_{AX} + J_{BX} = 28$  Hz, H-14 and 2H-15 protons),  $\delta$  2.2-2.6 (2H, *m*, 2H-2 protons), C-Me singlets at  $\delta$  1.98, 1.80, 1.20, 1.09 and 1.04; MS  $m/z$  (rel. int.): 305  $[\text{M} + 1]^+$  (0.5), 304  $[\text{M}]^+$  (0.5), 289 (15), 277 (1), 271 (3), 259 (0.5), 253 (1), 243 (1), 234 (1), 229 (1), 206 (8), 191 (6), 177 (5), 163 (8), 149 (14), 135 (19), 121 (22), 119 (21), 109 (57), 107 (59), 95 (70), 93 (70), 91 (62), 81 (100).

**Reduction of ketone 12.** To a soln of **12** (50 mg) in diethylene glycol (5 ml),  $\text{N}_2\text{H}_4$  (0.5 ml) was added and the mixture refluxed for 90 min (temp.  $130^\circ$ ). After the addition of KOH pellets (200 mg) refluxing was continued for 45 min when the temp. reached  $220^\circ$  after which refluxing was continued for a further 2 hr. *Ent*-13-epi-manoyl oxide (**13**) (20 mg) was isolated, mp  $97-99^\circ$ ;  $[\alpha]_D = -36^\circ$  ( $\text{CHCl}_3$ ; *c* 1);  $\text{IR } \nu_{\text{max}}^{\text{KBr}} \text{ cm}^{-1}$ : 3070, 2960, 2930, 2860, 1635, 1190, 1070, 985, 950, 910, 830;  $^1\text{H}$  NMR (60 MHz): vinyl group (ABX system,  $\delta_A = 4.75$ ,  $\delta_B = 5.05$ ,  $\delta_X = 5.95$ ,  $J_{AX} + J_{BX} = 29$  Hz), C-Me singlets at  $\delta$  1.15, 1.03, 0.85, 0.77 and 0.71.

**Ent-12 $\alpha$ -13-epi-manoyl oxide (varol) (14).** Mp  $138-140^\circ$ ;  $[\alpha]_D = -37.5^\circ$  ( $\text{CHCl}_3$ ; *c* 1);  $\text{IR } \nu_{\text{max}}^{\text{KBr}} \text{ cm}^{-1}$ : 3410, 3080, 2980, 2915, 1640, 1460, 1390, 1375, 1260, 1240, 1090, 1080, 1020, 1000, 960, 950, 910, 835, 780;  $^1\text{H}$  NMR (60 MHz): vinyl group (ABX system,  $\delta_A = 4.80$ ,  $\delta_B = 5.05$ ,  $\delta_X = 6.05$ ,  $J_{AX} + J_{BX} = 29$  Hz, H-14 and 2H-15 protons),  $\delta$  4.0 (1H, *dd*,  $J_1 = 3$ ,  $J_2 = 4.5$  Hz, H-12), C-Me singlets at  $\delta$  1.18, 1.15, 0.82, 0.74 and 0.71; MS  $m/z$  (rel. int.): 306  $[\text{M}]^+$  (0.2), 291 (2), 273 (2), 262 (1), 236 (2), 235 (2), 221 (4), 217 (2), 207 (1), 192 (100), 177 (95), 149 (30), 137 (25), 136 (27), 123 (70), 114 (20), 109 (33), 107 (32), 95 (47), 81 (61).

**Ent-3 $\beta$ -acetoxyl-12 $\alpha$ -hydroxy-13-epi-manoyl oxide (3-acetylvarodiol) (15).** A syrup;  $[\alpha]_D = -24.0^\circ$  ( $\text{CHCl}_3$ ; *c* 1);  $\text{IR } \nu_{\text{max}}^{\text{neat}} \text{ cm}^{-1}$ : 3450, 3075, 1735, 1660, 1450, 1380, 1250, 1100, 1090, 1050, 1030, 990, 960, 940, 920, 860;  $^1\text{H}$  NMR (60 MHz): vinyl group (ABX system,  $\delta_A = 4.80$ ,  $\delta_B = 5.04$ ,  $\delta_X = 6.02$ ,  $J_{AX} + J_{BX} = 29$  Hz, H-14 and 2H-15 protons),  $\delta$  4.42 (1H, *dd*,  $J_1 = 7$ ,  $J_2 = 9$  Hz, H-3), 4.02 (1H, *m*,  $W_{1/2} = 7$  Hz, H-12), 2.02 (3H, *s*, -OAc), C-Me singlets at  $\delta$  1.19, 1.13, 0.81 (6H) and 0.75; MS  $m/z$  (rel. int.): 364  $[\text{M}]^+$  (0.1), 349 (0.2), 346 (0.1), 321 (3), 307 (1), 293 (2), 271 (1), 250 (2), 234 (1), 225 (4), 217 (4), 199 (5), 175 (100), 165 (15), 147 (50), 135 (24), 121 (20), 107 (16), 93 (32), 81 (40).

**Ent-3 $\beta$ -hydroxy-12 $\alpha$ -acetoxyl-13-epi-manoyl oxide (12-acetylvarodiol) (16).** A syrup;  $[\alpha]_D = -57.3^\circ$  ( $\text{CHCl}_3$ ; *c* 1);  $\text{IR } \nu_{\text{max}}^{\text{neat}} \text{ cm}^{-1}$ : 3450, 3085, 2980, 2935, 2880, 1735, 1650, 1450, 1380, 1250, 1095, 1075, 1040, 1020, 990, 955, 935, 915, 850, 830;  $^1\text{H}$  NMR (60 MHz): vinyl group (ABX system,  $\delta_A = 4.80$ ,  $\delta_B = 5.02$ ,  $\delta_X = 5.90$ ,  $J_{AX} + J_{BX} = 29$  Hz, H-14 and 2H-15 protons),  $\delta$  5.22 (1H, *m*,  $W_{1/2} = 7$  Hz, H-12), 3.09 (1H, *dd*,  $J_1 = 7$ ,  $J_2 = 9$  Hz, H-3), 2.0 (3H, *s*, -OAc), C-Me singlets at  $\delta$  1.17, 1.01, 0.91, 0.70 and 0.67; MS  $m/z$  (rel. int.): 364  $[\text{M}]^+$  (0.1), 349 (0.2), 304 (0.3), 299 (0.3), 297 (0.3), 288 (0.2), 271 (0.3), 260 (0.2), 234 (0.5), 208 (12), 190 (28), 175 (28), 161 (4), 147 (26), 135 (24), 120 (50), 105 (50), 93 (68), 81 (100).

**Ent-3 $\beta$ , 12 $\alpha$ -dihydroxy-13-epi-manoyl oxide (varodiol) (17).** Mp  $136-138^\circ$ ;  $[\alpha]_D = 42.3^\circ$  (EtOH; *c* 1);  $\text{IR } \nu_{\text{max}}^{\text{KBr}} \text{ cm}^{-1}$ : 3485, 3080, 3000, 2980, 2940, 2875, 1640, 1450, 1415, 1380, 1080, 1050, 1015, 995, 960, 915, 840;  $^1\text{H}$  NMR (90 MHz): vinyl group (ABX system,  $\delta_A = 4.85$ ,  $\delta_B = 5.0$ ,  $\delta_X = 6.05$ ,  $J_{AX} + J_{BX} = 29.5$  Hz, H-14 and 2H-15 protons);  $\delta$  4.03 (1H, *t*,  $J = 3.3$  Hz, H-12); 3.22 (1H, *dd*,  $J_1 = 7$ ,  $J_2 = 8.6$  Hz, H-3); C-Me singlets at  $\delta$  1.21, 1.16, 0.94 and 0.72

(6H); MS  $m/z$  (rel. int.): 322  $[M]^+$  (0.1), 320 (0.2), 307 (0.2), 305 (0.3), 279 (6), 251 (1), 208 (18), 190 (60), 175 (80), 161 (10), 147 (40), 135 (20), 121 (40), 120 (35), 119 (30), 114 (15), 109 (40), 107 (60), 105 (50), 95 (60), 93 (70), 91 (80), 81 (100).

Ent-3 $\beta$ , 12 $\alpha$ -diacetox-13-*epi*-manoyl oxide (diacetylvarodiol) (18). 500 mg varodiol (17) was acetylated in hot Ac<sub>2</sub>O–pyridine, and 460 mg diacetylvarodiol was isolated. Compound 18 was also obtained by acetylation of 15 and 16, and proved identical with a natural diacetate isolated from this plant. Mp 156–158°;  $[\alpha]_D^{25} = -17.3^\circ$  (CHCl<sub>3</sub>;  $c$  1); IR  $\nu_{\max}^{KBr}$  cm<sup>-1</sup>: 3100, 2980, 1740, 1650, 1380, 1250, 1080, 1050, 1020, 995, 970, 950, 910, 850; <sup>1</sup>H NMR (60 MHz): vinyl group (ABX system,  $\delta_A = 4.75$ ,  $\delta_B = 5.0$ ,  $\delta_X = 5.90$ ,  $J_{AX} + J_{BX} = 29$  Hz, H-14 and 2H-15 protons),  $\delta$  5.15 (1H, *br s*,  $W_{1/2} = 6$  Hz, H-12), 4.35 (1H, *dd*,  $J_1 = 7$ ,  $J_2 = 8$  Hz, H-3), 2.03 (3H, *s*, -OAc), 1.95 (3H, *s*, -OAc), C-Me singlets at  $\delta$  1.19, 1.04, 0.83 0.80 and 0.71; MS  $m/z$  (rel. int.): 406  $[M]^+$  (0.5), 391 (1), 346 (1), 331 (4), 320 (2), 313 (1), 286 (1), 276 (4), 250 (27), 190 (100), 175 (6), 147 (27), 135 (22), 121 (20).

Ent-3-acetox-12-oxo-13-*epi*-manoyl oxide (19). A syrup;

$$[\alpha]_D^{25} = \frac{589}{-49.6} - \frac{579}{-49.1} - \frac{546}{-53.6} - \frac{434}{-100.9} - \frac{365}{-200} \quad (\text{CHCl}_3; c \text{ 0.56});$$

$$[\alpha]_D^{25} = \frac{334}{-348} - \frac{302}{0} - \frac{289}{+35.7} - \frac{265}{0} - \frac{253}{0} \quad (\text{CHCl}_3; c \text{ 0.056});$$

IR  $\nu_{\max}^{neat}$  cm<sup>-1</sup>: 3090, 1725, 1700, 1250, 725; <sup>1</sup>H NMR (60 MHz): vinyl group (ABX system,  $\delta_A = 5.0$ ,  $\delta_B = 5.22$ ,  $\delta_X = 6.18$ ,  $J_{AX} + J_{BX} = 29$  Hz, H-14 and 2H-15),  $\delta$  4.55 (1H, *dd*,  $J_1 = 7$ ,  $J_2 = 9$  Hz, H-3), 2.05 (3H, *s*, -OAc), C-Me singlets at  $\delta$  1.31, 1.19, 0.90, 0.85 and 0.80; MS  $m/z$  (rel. int.): 362  $[M]^+$  (0.7), 319 (3), 264 (2), 259 (9), 250 (14), 235 (4), 204 (7), 190 (71), 175 (52), 161 (8), 147 (19), 136 (16), 135 (15), 121 (22), 107 (15), 93 (15), 81 (19).

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