Phytochemistry, Vol. 24, No. 3, pp 517–521, 1985.
Printed in Great Britain.

0031–9422/85 $3.00 + 0.00
Pergamon Press Ltd.

DITERPENOIDS FROM *SIDERITIS ARBORESCENS* SUBSP. *PAULII**

ANDRÉS GARCÍA-GRANADOS, ANTONIO MARTÍNEZ and M. ESTHER ONORATO

Departamento de Química Orgánica, Universidad de Granada, Spain

(*Received* 18 *June* 1984)

Key Word Index—*Sideritis arborescens*; Labiatae; *ent*-manoyl oxides; *ent*-13-epi-manoyl oxides.

Abstract—Several *ent*-labda-13(16),14-dienes, *ent*-13-epi-manoyl oxides and the new natural products *ent*-6α,8α-dihydroxylabda-13(16),14-diene, *ent*-18-hydroxy-15(16)-peroxylabd-13-ene, *ent*-16,18-dihydroxymanoyl oxide, *ent*-13-epi-16,18-dihydroxymanoyl oxide and *ent*-6α,16,18-trihydroxymanoyl oxide have been isolated from *Sideritis arborescens* subsp. *paulii*. The structures of these compounds have been established by spectroscopic means and chemical correlations.

INTRODUCTION

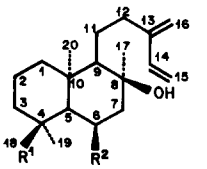
Sideritis arborescens Salzm. ex Bentham subsp. *paulii* (Pau) P. W. Ball ex Heywood is a plant which grows in restricted areas with acidic soil in west Andaluzia (southern Spain). Another plant named *Sideritis paulii* (Pau) P. W. Ball ex Heywood and collected in the middle of the Iberian peninsula was studied several years ago, although on that occasion only *ent*-7α,18-dihydroxykaur-15-ene, *ent*-3β,7α,18-trihydroxykaur-15-ene and *ent*-3β,7α,18-trihydroxy-15β,16β-epoxykaurane [1] were identified.

RESULTS AND DISCUSSION

Some diterpenoids isolated from *Sideritis paulii* have been previously characterized as *ent*-labda-13(16),14-dienes: *ent*-8α,18-dihydroxylabda-13(16),14-diene (6-deoxyandalusol, **1** [2]), *ent*-8α-hydroxylabda-13(16),14-dien-18-al (6-deoxyandalusal, **2** [3]), *ent*-8α-hydroxylabda-13(16),14-dien-18-oic acid (6-deoxyandalusoic acid, **3** [4]) and *ent*-6α,8α,18-trihydroxylabda-13(16),14-diene (andalusol, **4** [5]). Ribenol (*ent*-13-epi-3β-hydroxymanoyl oxide, **5** [6]) and the *ent*-kaurene siderol (*ent*-7α-acetoxy-18-hydroxykaur-15-ene, **6** [7]) were also isolated.

Another product (**7**) isolated from this subspecies of *S. arborescens* was found to have the molecular formula $C_{20}H_{34}O_2$ and a UV spectrum with a maximum at 226 nm. Its IR spectrum showed hydroxyl absorptions. The ^{1}H NMR spectrum (see Experimental) contained an A_2B_2X system similar to that shown by *ent*-labda-13(16),14-diene systems [2, 3] and a signal at δ3.86 (1H, *ddd*, $J_1 = 10$, $J_2 = 10$, $J_3 = 4$ Hz) and four methyl singlet signals at 1.21, 1.15, 0.99 and 0.825 (3H each). These spectroscopic data supported the idea of an *ent*-6α,8α-dihydroxylabda-13(16),14-dienic structure for product **7**. Acetylation of **7** gave a monoacetate product (**8**) with a ^{1}H NMR spectrum in which the signal due to a proton geminal to an acetoxy group was shifted downfield to δ5.07. As the structures of products **7** and **8** were confirmed by ^{13}C NMR experiments (see Table 1), we therefore concluded that **7** must be *ent*-6α,8α-dihydroxylabda-13(16),14-diene, a new natural product.

One compound isolated from the most polar fraction of diterpenoids was product **9** of molecular formula $C_{20}H_{34}O_3$. Its IR spectrum showed bands indicative of hydroxyl and double-bond functions. Its ^{1}H NMR spectrum (see Experimental) contained an ABX system similar to that found in manoyl oxide [3]. Signals arising from two AB systems (four doublets, 1H each, $J = 12$ Hz at δ2.95, 3.09, 3.32 and 3.44) and three methyl singlet signals (1.25, 0.75 and 0.725, 3H each) were observed. Comparison of the ^{1}H NMR spectra of products **9** and 6′-deoxyandalusol (**1**) indicated that one of these AB systems (doublets centred at 3.09 and 3.44) was attributable to a hydroxymethylene group at C-18. The other hydroxymethylene group (double doublet with signals centred at



	R^1	R^2
1	CH_2OH	H
2	CHO	H
3	COOH	H
4	CH_2OH	OH
7	CH_3	OH
8	CH_3	OAc
12	CH_2OAc	H
21	CH_2OAc	OAc
23	CH_3	H

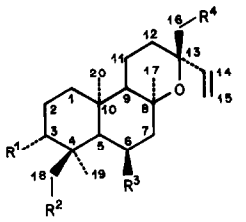
*Part 20 in the series "Terpenic Components of Spanish Labiatae".

Table 1. ^{13}C NMR chemical shifts of compounds **1**, **7**, **8**, **12**, **17** and the reference compound

Carbon No.	1	7	8	12	17	23*
1	39.28	39.38	39.84	38.87	39.46	39.76
2	17.80	18.36	18.24	17.51	17.87	18.50
3	35.29	43.68	43.52	35.69	35.85	42.03
4	37.61	34.77	34.88	36.41	37.74	33.29
5	49.19	61.51	58.67	50.00	49.37	56.19
6	20.28	69.14	71.02	20.33	20.41	20.60
7	44.25	54.36	50.52	44.10	44.64	44.62
8	74.12	73.75	75.52	73.69	74.16	74.28
9	61.81	61.23	60.93	61.62	61.59	61.28
10	39.01	40.07	39.64	39.09	39.22	39.17
11	24.59	24.52	24.56	24.52	24.05	24.75
12	35.10	33.85	34.88	34.95	35.36	35.13
13	147.49	147.24	147.04	147.37	149.27	147.47
14	138.85	138.88	138.93	138.76	117.22	138.82
15	115.43	115.69	115.77	115.22	72.65	115.60
16	113.42	113 54	113.63	113.25	70.12	113.51
17	23.94	25.69	25.44	23.94	23.49	24.05
18	71.83	36.28	36.04	72.71	72.15	33.43
19	17.38	22.09	21.97	17.17	17.47	21.52
20	15 81	16.60	16.55	15.66	15.91	15.50
$\underline{C}H_3COO$			21.97	20.74		
Me$\underline{C}$OO			171.08	170.91		

The ^{13}C chemical shifts are given in δ-values (ppm) relative to TMS. Assignments were made with the aid of DEPT experiments.

*See ref. [12].



	R^1	R^2	R^3	R^4
5	OH	H	H	H
9	H	OH	H	OH
11	H	H	H	H
13	H	OAc	H	OH
14	H	OAc	H	OAc
18	H	OH	OH	OH
19	H	OAc	OAc	OAc
20	H	-O-CMe_2-O-		OH
22	H	OAc	OAc	OH

2.95 and 3.32) must be situated at C-16, C-17, C-19 or C-20. Nevertheless, the presence of two methyl singlets at δ0.75 and 0.725 indicated that this hydroxymethylene group was not situated at C-19 or C-20. Thus, the most probable location of the hydroxymethylene group must be C-16 or C-17. The ^{13}C NMR chemical shifts of product **9** and reference compounds manoyl oxide (**10**) and 13-epi-manoyl oxide (**11**) [8] are shown in Table 2. Similar chemical shifts of C-8 for products **9**, **10** and **11** (δ75.97 or 76.40) suggested that the primary hydroxyl group was not situated at C-17. On the other hand, the chemical shift attributed to C-13 (δ75.97 or 76.40) seemed to indicate that the hydroxyl group was situated at C-16. These considerations have nothing to do with the configuration at C-13, which can be deduced from a comparison of the chemical shifts of C-9 of products **9** (δ58.20), **10** (δ55.7) and **11** (δ58.5).

From the biogenetic and other considerations, the structure of *ent*-16,18-dihydroxy-13-epi-manoyl oxide and the trivial name of 13-epi-jabugodiol were proposed for product **9**.

In order to confirm the structure of **9**, we carried out a biomimetic-type reaction. Probably 6-deoxyandalusol (**1**) is the biogenetic precursor of product **9**. Acetylation of 6-deoxyandalusol (**1**) gave an 18-acetoxy derivative (**12**), which was epoxidized by metachlorperbenzoic acid (MCPBA). No epoxides were isolated from this reaction, which resulted in one main product (**13**). Saponification of product **13** gave 13-epi-jabugodiol (**9**). Acetylation of natural product **9** and product **13** produced the same diacetate (**14**). Thus an *ent*-configuration was demonstrated for the new natural product **9**.

Another natural product (**15**) isolated from this plant appeared to be similar to the one previously described as

Table 2. ^{13}C NMR chemical shifts of compounds **9**, **13**, **14**, **15** and the reference compounds

Carbon No.	9	10*	11†	13	14	15
1	38.70	39.0	39.4	38.76	38.83	38.53
2	17.80	18.6	18.7	17.80	17.83	17.88
3	35.20	42.1	42.2	35.90	35.97	35.37
4	37.50	33.2	33.4	36.83	36.89	37.25
5	49.41	56.4	56.5	50.47	50.68	49.77
6	19.41	19.9	19.9	19.70	19.82	20.00
7	42.50	43.2	43.1	42.60	42.61	43.42
8	75.97	74.8	76.1	76.31	76.11	75.50
9	58.20	55.7	58.5	58.42	58.29	52.86
10	36.60	36.9	36.9	36.50	36.60	37.66
11	15.12	15.4	15.9	15.28	15 26	14.65
12	28.30	35.8	34.9	28.49	30.09	27.23
13	76.40	73.0	73.3	76.10	74.34	76.33
14	144.02	147.8	147.8	144.14	143.54	144.03
15	113.10	110.1	109.5	113.38	113.58	113.64
16	69.60	28.5	32.7	69.75	71.40	68.71
17	23.80	25.5	24.0	23.91	24.00	25.83
18	71.50	33.4	33.3	72.73	72.92	72.14
19	16.97	21.3	21.3	17.10	17.11	17.38
20	16.02	15.3	15.9	16.22	16.19	15.58
$\underline{C}H_3COO$				20.90	20.97	
					20.97	
Me$\underline{C}$OO				171.12	170.78	
					171.17	

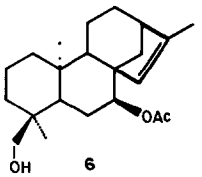
See footnote of Table 1.

*See refs. [8, 9].

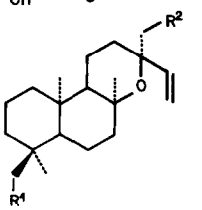
†See ref. [10].

epi-jabugodiol (**9**). Thus, **15** has the same molecular formula, $C_{20}H_{34}O_3$, and IR spectrum with bands indicative of hydroxyl and double-bond functions. Its ^{1}H NMR spectrum (see Experimental) showed a vinylic ABX system (part X at δ5.85, 1H, *dd*, $J_{AX}+J_{BX}=29$ Hz; part AB between δ5.0 and 5.4), an AB system (2H, *dd*, signals centred at δ3.45 and 3.10, $J=12$ Hz), an A_2 system at δ3.30 (2H, *s*) and methyl singlet signals at δ1.29 (3H), 0.85 (3H) and 0.76 (3H). Cold acetylation of product **15** gave a diacetate (**16**). Product **15** must be an epimer at C-13 of product **9**. This supposition was confirmed by analysis of the ^{13}C NMR spectrum of product **15**. Thus, the chemical shift assigned to C-9 of product **15** (δ52.86, see Table 2) is in better agreement with a C-9 chemical shift for manoyl oxide (δ55.7) than with a shift of C-9 of 13-epi-manoyl oxide (δ58.5, see Table 2). As indicated for product **9**, biogenetic considerations led us to propose an *ent*-16,18-dihydroxymanoyl oxide structure for product **15**, and the trivial name of jabugodiol for this new natural product. No products with this type of configuration at C-13 were isolated from the previously described chemical syntheses of product **9**.

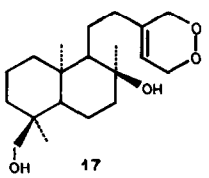
The natural product **17**, isolated from this plant, showed a molecular formula $C_{20}H_{34}O_4$ and IR bands of hydroxyl and double-bond groups. Its ^{1}H NMR spectrum exhibited a signal attributable to a vinylic methyne group at δ5.70 (1H, *m*, $W_{1/2}=7.5$ Hz), hydroxymethylenic AB system (2H, *dd*, $J=12$ Hz, with signals centred at 3.45 and 3.10) and methyl singlet signals at 1.16 (3H), 0.85 (3H) and 0.75 (3H). Furthermore, a broad signal at δ4.52 (4H, *m*, $W_{1/2}=10$ Hz) was also detected. The ^{13}C NMR spectrum of **17** (see Table 1) showed signals attributable to a quaternary unsaturated carbon (δ149.27) and a vinylic methynic carbon (δ117.22), as well as four oxygenated carbons (δ74.16, 72.65, 72.15 and 70.12). As the chemical shifts of the other carbons are similar to those of 6-deoxyandalusol (**1**), we believe that product **17** must be a 15,16-peroxy derivative of 6-deoxyandalusol (**1**). In order to verify this hypothesis, product **17** was obtained by photo-oxidation of 6-deoxyandalusol (**1**). We do not know if product **17** is a genuine natural product or an artefact produced by aerial photo-oxidation which may have taken place during the extraction procedure.



6



	R¹	R²
10	H	H
15	OH	OH
16	OAc	OAc



17

The most polar product (**18**) isolated from this subspecies of *S. arborescens* had the molecular formula $C_{20}H_{34}O_4$ and IR bands of hydroxyl and double-bond groups. Its ^{1}H NMR spectrum indicated that product **18** was presumably a manoyl oxide (see Experimental) with a signal similar to that attributed to the proton geminal to the hydroxyl group at C-6 of product **7** (1H, *ddd*, $J_1=10$, $J_2=10$, $J_3=4$ Hz) and two AB systems, each attributable to one hydroxymethylene group, similar to those described for 13-epi-jabugodiol (**9**). The presence of three hydroxyl groups was confirmed by acetylation of product **18** to give a triacetate (**19**). The ^{1}H NMR spectrum of product **19** showed both the AB systems similar to those described for the diacetate of 13-epi-jabugodiol (**14**) (see Experimental). Presumably, product **18** must be *ent*-6α,16,18-trihydroxy-13-epi-manoyl oxide. Hydroxylation at C-6 and C-18 was confirmed by conversion of product **18** into an isopropylidenedioxy derivative (**20**). Other chemical evidence supporting the structure proposed for product **18** was its chemical correlation with andalusol (**4**). Acetylation of andalusol (**4**) gave a diacetate (**21**), which was epoxidized as described for product **12**. Similarly, a product (**21**) of cyclization (**22**) was obtained. Acetylation of products **18** and **22** gave the same triacetate (**19**). Saponification of product **22** led to a product identical to **18**. Thus we conclude that product **18** has an *ent*-configuration. On the other hand, if the reaction of cyclization is similar to that described for product **12**, product **18** must be an *ent*-13-epi-manoyl oxide. To confirm this point we carried out ^{13}C NMR experiments for **18** and **19**. In order to compare results, these experiments were performed with $CDCl_3$ as the solvent. The ^{13}C NMR spectrum of **18** is mostly, but not completely, assigned because this product is poorly soluble in $CDCl_3$. In any case, C-9 assignments for products **18** and **19** indicated clearly that these products both have a 13-epi configuration (see Table 3). Thus, the C-9 chemical shifts for products **18** (δ57.81), **19** (δ57.80) and the 18-acetate of *ent*-13-epi-jabugodiol were all similar (**13**, δ58.42). As an acetoxy group at C-6 has a weak influence on the chemical shift at C-9 (see the C-9 chemical shifts for **12** at δ61.62 and **21** at δ60.80 [9]), we conclude that **18** is *ent*-6α,16,18-trihydroxy-13-epi-manoyl oxide, a new natural product for which we propose the trivial name of 13-epi-jabugotriol.

EXPERIMENTAL

Mps were determined in a Kofler apparatus and are uncorr. ^{1}H NMR spectra were measured at 80 MHz ($CDCl_3$ soln with TMS as internal standard). ^{13}C NMR spectra were determined at 20.13 MHz, also in $CDCl_3$ soln, in a Bruker WP80SY spectrometer equipped with a three-clock multi-pulser. Assignments of the ^{13}C NMR chemical shifts were made with the aid of broad-band proton decoupling and experiments of distortionless enhancement by polarization transfer (DEPT), using a 'flip angle' of 135°. Silica gel Merck 7729 (< 0.08 mm) was used for CC. Plant

Table 3. ^{13}C NMR chemical shifts of compounds **18**, **19** and the reference compound

Carbon No.	18	19	21*
1	38.62	38.68	39.1
2	17.54	17.53	17.3
3	39.20	36.95	37.0
4	—	37.68	36.3
5	53.58	52.54	51.8
6	67.78	70.45	70.5
7	—	49.24	50.1
8	—	74.60	73.1
9	57.81	57.80	60.8
10	—	36.58	39.3
11	15.63	15.53	24.5
12	28.50	29.87	34.7
13	76.38	75.20	146.9
14	143.90	143.18	138.5
15	113.77	113.89	115.6
16	69.86	71.36	113.5
17	25.33	25.22	25.2
18	74.97	74.28	74.1
19	17.75	17.82	17.9
20	18.10	17.41	16.7
$\underline{C}H_3COO$		21.72	21.7
		21.07	21.0
		21.07	
$Me\underline{C}OO$		170.18	170.0
		171.19	170.8
		171.62	

See footnote of Table 1.
*See ref. [11].

material was collected in July 1983, near Aracena and Jabuguillo (Huelva, Spain); voucher specimens have been deposited at the Herbarium of the Faculty of Pharmacy (University of Granada).

Extraction and isolation of the diterpenouds. Dried and finely powdered plants of *Sideritis arborescens* subsp. *pauli* (2 kg) were extracted with hexane (4 l.) in a Soxhlet and processed as indicated in ref. [3] to give 26 g of a terpenoid fraction, which was chromatographed on a silica gel column and eluted with CH_2Cl_2–Me_2CO mixtures of increasing polarity. The homogeneous fractions were chromatographed repeatedly on 10% $AgNO_3$–silica gel columns and eluted with CH_2Cl_2–Me_2CO mixtures of increasing polarity, yielding the following compounds in order of elution: 80 mg 6-deoxyandalusal (**2**), 150 mg ribenol (**5**), 120 mg siderol (**6**), 300 mg 6-deoxyandalusoic acid (**3**), 5 g 6-deoxyandalusol (**1**), 40 mg 18-deoxyandalusol (**7**), 25 mg jabugodiol (**15**), 50 mg epi-jabugodiol (**9**), 20 mg peroxy compound (**17**), 3 g andalusol (**4**) and 40 mg epi-jabugotriol (**18**).

ent-6α,8α-*Dihydroxylabda*-13(16),14-*diene* (18-*deoxyandalusol*, **7**). Colourless gum, $[\alpha]_D^{20}$ −32.7° (*c* 1; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3500, 3080, 1630, 1600, 1040, 995, 930 and 900. UV λ_{max}^{hexane} nm (ε): 226 (10 500). ^1H NMR: δ6.37 (1H, *dd*, part X of an A_2B_2X system, $J_{AX}+J_{BX}$ = 28 Hz, H-14), 4.85–5.45 (4H, part A_2B_2 of an A_2B_2X system, 2H-15 and 2H-16), 3.86 (1H, *ddd*, J_1 = 10, J_2 = 10, J_3 = 4 Hz, H-6), 1.21 (3H), 1.15 (3H), 0.99 (3H) and 0.825 (3H) (singlet signals of Me groups at C-17, C-18, C-19 and C-20). ^{13}C NMR: See Table 1). (Found: C, 78.02; H, 11.23. $C_{20}H_{34}O_2$ requires: C, 78.38; H, 11.18%.)

ent-6α-*Acetoxy*-8α-*hydroxylabda*-13(16),14-*diene* (**8**). Product **7** (15 mg) was acetylated at room temp. for 12 hr with pyridine (1 ml) and Ac_2O (0.5 ml). After CC, 13 mg of product **8** was obtained. Colourless oil, $[\alpha]_D^{20}$ −47° (*c* 0.25; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3450, 3080, 1740, 1630, 1595, 1260, 1035, 990, 960, 925, 900 and 890. UV λ_{max}^{hexane} nm (ε): 226 (11 000). ^1H NMR: δ6.37 (1H, *dd*, part X of an A_2B_2X system, $J_{AX}+J_{BX}$ = 28 Hz, H-14), 4.85–5.45 (4H, part A_2B_2 of an A_2B_2X system, 2H-15 and 2H-16), 5.07 (1H, *ddd*, J_1 = 10, J_2 = 10, J_3 = 4 Hz, H-6), 2.05 (3H, acetoxy group), 1.26 (3H), 1.02 (3H), 0.90 (3H) and 0.875 (3H) (singlet signals of Me groups at C-17, C-18, C-19 and C-20). ^{13}C NMR: See Table 1. (Found: C, 75.57; H, 10.73. $C_{22}H_{36}O_3$ requires: C, 75.82; H, 10.41%.)

ent-16,18-*Dihydroxy*-13-*epi-manoyl oxide* (*epi-jabugodiol*, **9**). Mp 194–196°, $[\alpha]_D^{20}$ −44.05° (*c* 1; EtOH). IR ν_{max}^{KBr} cm^{-1}: 3500, 3080, 1640, 1450, 1095, 1075, 1040, 1020, 990, 955, 930 and 915. ^1H NMR: δ5.94 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 4.90–5.30 (2H, part AB of an ABX system, 2H-15), centred at 3.44, 3.32, 3.09 and 2.95 (4H, *d*, *J* = 12 Hz, two AB systems, 2H-16 and 2H-18), 1.25 (3H), 0.75 (3H) and 0.725 (3H) (methyl singlet signals of C-17, C-19, C-20). ^{13}C NMR: See Table 2. (Found: C, 74.35; H, 10.72. $C_{20}H_{34}O_3$ requires: C, 74.49; H, 10.63%.)

ent-16-*Hydroxy*-18-*acetoxy*-13-*epi-manoyl oxide* (**13**). 6-Deoxyandalusol (**1**, 1.5 g) was acetylated at room temp. for 12 hr with pyridine (25 ml) and Ac_2O (20 ml). After CC, 1 g of product **12** was isolated [2]. This product was epoxidized with 2.5 g of m-chlorperbenzoic acid (MCPBA) in $CHCl_3$ (30 ml) for 48 hr at 4°, after which the soln was diluted with $CHCl_3$, washed with aq. $FeSO_4$, aq. $NaHCO_3$ and H_2O, dried ($MgSO_4$) and concd *in vacuo*. After CC, 150 mg of product **13** was isolated. Colourless gum, $[\alpha]_D^{20}$ −34.16° (*c* 2; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3450, 3090, 1740, 1650, 1450, 1380, 1250, 1095, 1075, 1040, 1020, 990, 940 and 915. ^1H NMR: δ5.95 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 4.90–5.25 (2H, part AB of an ABX system, 2H-15), 3.87 and 3.62 (2H, AB system, *J* = 12 Hz, 2H-18), 3.32 and 2.92 (2H, AB system, *J* = 12 Hz, 2H-16), 2.07 (3H, *s*, AcO group), 1.25 (3H), 0.80 (3H) and 0.77 (3H) (singlet signals of methyl groups at C-17, C-19 and C-20). ^{13}C NMR: See Table 1. (Found: C, 72.17; H, 9.99. $C_{22}H_{36}O_4$ requires: C, 72.49; H, 9.95%.)

ent-16,18-*Diacetoxy*-13-*epi-manoyl oxide* (**14**). Epi-jabugodiol (**9**, 25 mg) was acetylated at room temp. for 12 hr with pyridine (2 ml) and Ac_2O (1 ml). After CC, 24 mg of diacetate (**14**) was obtained. Product **13** (10 mg) was acetylated with pyridine (1 ml) and Ac_2O (0.5 ml) to yield 10 mg of product **14**. Colourless gum, $[\alpha]_D^{20}$ −48.4° (*c* 1; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3100, 1740, 1650, 1380, 1250, 1080, 1050, 1020, 995, 970, 950, 910 and 850. ^1H NMR: δ5.95 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 4.90–5.25 (2H, part AB of an ABX system, 2H-15), 3.87 and 3.62 (2H, AB system, *J* = 12 Hz, 2H-18), 3.82 (2H, *s*, 2H-16), 2.08 (3H) and 2.06 (3H) (methyl singlet signals of AcO groups), 1.25 (3H), 0.82 (3H) and 0.78 (3H) (singlet signals of methyl groups at C-17, C-19 and C-20). ^{13}C NMR: See Table 2. (Found: C, 70.73; H, 9.71. $C_{24}H_{38}O_5$ requires: C, 70.90; H, 9.42%.)

ent-16,18-*Dihydroxymanoyl oxide* (*jabugodiol*, **15**). Colourless gum, $[\alpha]_D^{20}$ −25.3° (*c* 1; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3450, 3080, 1640, 1450, 1380, 1095, 1075, 1040, 1020, 990, 955, 930 and 915. ^1H NMR: δ5.85 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 5.0–5.40 (2H, part AB of an ABX system, 2H-15), 3.45 and 3.10 (2H, AB system, *J* = 12 Hz, 2H-18), 3.30 (2H, *s*, 2H-16), 1.29 (3H), 0.85 (3H) and 0.76 (3H) (singlet signals of methyl groups at C-17, C-19 and C-20). ^{13}C NMR: See Table 2. (Found: C, 74.20; H, 10.83. $C_{20}H_{34}O_3$ requires: C, 74.49; H, 10.63%).

ent-16,18-*Diacetoxymanoyl oxide* (**16**). Jabugodiol (**15**, 7 mg) was acetylated with 0.5 ml of Ac_2O in pyridine (1 ml) at room

temp. for 12 hr. After CC, 5 mg of diacetyl derivative (**16**) was isolated. Colourless oil, $[\alpha]_D^{20}$ −34.66° (*c* 0.33; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3080, 1745, 1350, 1250, 1080, 1050, 1020, 995, 970, 950, 920 and 850. ^1H NMR: δ5.85 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 5.0–5.45 (2H, part AB of an ABX system, 2H-15), 3.93 and 3.65 (2H, AB system, J = 12 Hz, 2H-18), 3.95 (2H, *s*, 2H-16), 2.06 (6H, *s*, 2 AcO groups), 1.27 (3H), 0.83 (6H) (singlet signals of methyl groups at C-17, C-19 and C-20). (Found: C, 70.57; H, 9.8. $C_{24}H_{38}O_5$ requires: C, 70.90; H, 9.42%.)

ent-8α,18-*Dihydroxy*-15,16-*peroxylabda*-13-*ene* (**17**). Colourless oil, $[\alpha]_D^{20}$ −13.70° (*c* 0.33; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3450, 3070, 1660, 1450, 1150, 1090, 1070, 1040, 1020, 990, 970, 945, 910 and 850. ^1H NMR: δ5.70 (1H, *m*, $W_{1/2}$ = 7.5 Hz, H-14), 4.52 (4H, *m*, $W_{1/2}$ = 10 Hz, 2H-15 and 2H-16), 3.45 and 3.10 (2H, AB system, J = 12 Hz, 2H-18), 1.16 (3H), 0.85 (3H) and 0.75 (3H) (singlet signals of methyl groups at C-17, C-19 and C-20). ^{13}C NMR: See Table 1. (Found: C, 70.82; H, 10.45. $C_{20}H_{34}O_4$ requires: C, 70.97; H, 10.12%.) Product **17** was easily obtained by photo-oxidation of 6-deoxyandalusol (**1**) in CH_2Cl_2 with methylene blue and an O_2 stream for 5 min under solar illumination.

ent-6α,16,18-*Trihydroxy*-13-*epi-manoyl oxide* (*epi-jabugotriol*, **18**). Mp 227–228°, $[\alpha]_D^{20}$ −51.34° (*c* 0.5; EtOH). IR ν_{max}^{KBr} cm^{-1}: 3500, 3080, 1640, 1450, 1380, 1095, 1075, 1040, 1020, 990, 955, 930 and 910. ^1H NMR: δ5.92 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 4.90–5.25 (2H, part AB of an ABX system, 2H-15), 3.83 (1H, *ddd*, J_1 = 10, J_2 = 10, J_3 = 4 Hz, H-6), 3.56 and 2.94 (2H, AB system, J = 12 Hz, 2H-16), 3.27 and 3.08 (2H, AB system, J = 12 Hz, 2H-18), 1.30 (3H), 0.90 (3H) and 0.79 (3H) (singlet signals of methyl groups at C-17, C-19 and C-20). ^{13}C NMR: See Table 3. (Found: C, 70.85; H, 10.10. $C_{20}H_{34}O_4$ requires: C, 70.97; H, 10.12%.)

ent-6α,16,18-*Triacetoxy*-13-*epi-manoyl oxide* (**19**). Epi-jabugotriol (**18**, 10 mg) was acetylated with 1 ml Ac_2O in pyridine (2 ml) at room temp. for 12 hr. After CC, 8 mg of triacetate (**19**) was isolated. Colourless gum, $[\alpha]_D^{20}$ −72.6° (*c* 1; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3090, 1745, 1640, 1380, 1250, 1080, 1050, 1020, 995, 965, 950, 915 and 850. ^1H NMR: δ5.93 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 4.90–5.24 (2H, part AB of an ABX system, 2H-15), 5.05 (1H, *ddd*, J_1 = 10, J_2 = 10, J_3 = 4 Hz, H-6), 4.05 and 3.62 (2H, AB system, J = 12 Hz, 2H-18), 3.83 (2H, *s*, 2H-16), 2.06 (3H), 2.02 (3H), 1.97 (3H) (singlet signals of AcO groups at C-6, C-16 and C-18), 1.32 (3H), 0.84 (6H) (singlet signals of methyl groups at C-17, C-19 and C-20). ^{13}C NMR: See Table 3. (Found: C, 66.81; H, 9.01. $C_{26}H_{40}O_7$ requires: C, 67.22; H, 8.68%.)

ent-6α,18-*Isopropylidenedioxy*-16-*hydroxy*-13-*epi-manoyl oxide* (**20**). Epi-jabugotriol (**18**, 15 mg) was treated with 10 ml 2,2-dimethoxypropane and 5 mg pyridinium *p*-toluenesulfonate with refluxing for 5 hr, after which the conc. mixture was washed with H_2O and extracted with CH_2Cl_2. After CC, 14 mg acetonide (**20**) was isolated. Mp 128–130°, $[\alpha]_D^{20}$ −10.32° (*c* 1; $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3450, 3080, 1640, 1450, 1150, 1050, 1020, 990, 960, 950, 910 and 850. ^1H NMR: δ5.92 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 4.95–5.20 (2H, part AB of an ABX system, 2H-15), 3.82 (1H, *ddd*, J_1 = 10, J_2 = 10, J_3 = 4 Hz, H-6), 3.60 and 2.81 (2H, AB system, J = 12 Hz, 2H-16), 3.32 and 2.95 (2H, AB system, J = 12 Hz, 2H-18), 1.35 (3H), 1.27 (3H), 1.25 (3H), 1.025 (3H) and 0.75 (3H) (singlet signals of isopropylidenedioxy and methyl groups at C-17, C-19 and C-20). (Found: C, 72.95; H, 10.23. $C_{23}H_{38}O_4$ requires: C, 72.98; H, 10.12%.)

ent-6α,18-*Diacetoxy*-16-*hydroxy*-13-*epi-manoyl oxide* (**22**). Andalusol (**4**, 1.5 g) was acetylated with 20 ml Ac_2O in 25 ml pyridine at room temp. for 12 hr. After CC, 1.3 g of diacetate **21** was isolated [5]. This product was epoxidized with MCPBA in $CHCl_3$ (30 ml) as described for product **13**. After CC, 180 mg of product **22** was isolated. Colourless gum, $[\alpha]_D^{20}$ −59.54° (*c* 2; $CHCl_3$). IR ν_{max}^{neat} cm^{-1}: 3450, 3090, 1745, 1640, 1380, 1260, 1080, 1050, 1020, 990, 960, 950, 910 and 850. ^1H NMR: δ5.93 (1H, *dd*, part X of an ABX system, $J_{AX}+J_{BX}$ = 29 Hz, H-14), 4.90–5.25 (2H, part AB of an ABX system, 2H-15), 5.05 (1H, *ddd*, J_1 = 10, J_2 = 10, J_3 = 4 Hz, H-6), 4.05 and 3.62 (2H, AB system, J = 12 Hz, 2H-18), 3.32 and 2.98 (2H, AB system, J = 12 Hz, 2H-16), 2.08 (3H) and 2.02 (3H) (singlet signals of AcO groups at C-6 and C-18), 1.35 (3H) and 0.85 (6H) (singlet signals of methyl groups at C-17, C-19 and C-20). (Found: C, 67.85; H, 8.78. $C_{24}H_{38}O_6$ requires: C, 68.22; H, 9.06%.)

Acknowledgements—We thank Dr. O. Socorro, Botany Department, University of Granada for identification of the plant material. This work was supported by a grant from the Comisión Asesora de Investigación Científica y Técnica.

REFERENCES

1. Rodríguez, B. and Valverde, S. (1976) *An. Quím.* **72**, 189.
2. Rodríguez, B. and von Carstenn, C. (1979) *An. Quím* **75**, 110.
3. Algarra, J., Garcia-Granados, A., Sáenz de Buruaga, A. and Sáenz de Buruaga, J. M. (1983) *Phytochemistry* **22**, 1779.
4. García-Granados, A., Martínez, A., Molina, A., Onorato, M. E., Rico, M., Sáenz de Buruaga, A. and Sáenz de Buruaga, J. M., *Phytochemistry* (submitted).
5. López, A., von Carstenn, C., Rodriguez, B., Fayos, J. and Ripoll, M. M. (1977) *J. Org. Chem.* **42**, 2517.
6. González, A., Fraga, B. M., Hernández, M. G. and Luis, J. G. (1973) *Phytochemistry* **12**, 1113.
7. Piozzi, F., Venturella, P., Bellino, A. and Mondelli, R. (1968) *Tetrahedron* **24**, 4073.
8. Buckwalter, B. L., Burfitt, I. R., Nagel, A. A., Wenkert, E. and Näf, F. (1975) *Helv Chim. Acta* **58**, 1567.
9. Wenkert, E., Baddeley, G. V., Burfitt, I. R. and Moreno, L. N. (1978) *Org. Magn. Reson.* **11**, 337.
10. Wehrli, F. W. and Nishida, T (1979) in *Progress in the Chemistry of Organic Natural Products* (Herz, N., Grisebach, H. and Kirby, G. W., eds.), Vol. 36, p. 56. Springer, Wien.
11. García-Alvarez, M. C. and Rodriguez, B. (1980) *Phytochemistry* **19**, 2405.
12. Cabrera, E., García-Granados, A., Sáenz de Buruaga, A. and Sáenz de Buruaga, J. M. (1983) *Phytochemistry* **22**, 2779.