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SESQUITERPENES FROM TWO SUBSPECIES OF *SIDERITIS VAROI**

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Key Word Index—*Sideritis varoi*; Labiatae; sesquiterpenes; eudesmenes; ^{13}C NMR.

Abstract—Two subspecies of *Sideritis varoi* afforded, in addition to previously reported diterpenes, the following series of new eudesmane and eudesmene acetates: 1β-hydroxy-6β-acetoxy-eudesm-4(15)-ene; 1β,4β-dihydroxy-6β-acetoxy-eudesmane; 1β-hydroxy-6β-acetoxy-eudesm-3-ene; 1β-hydroxy-6β-acetoxy-eudesm-4-ene. The structures of these compounds were elucidated by chemical and spectroscopic means.

INTRODUCTION

The *Sideritis* genus has proved to be a good source of diterpenoids [1–3], but there have been no reports of the isolation of sesquiterpenoids from these plants. In a previous study, a series of known *ent*-kaur-15-enic and *ent*-kaur-16-enic compounds, and, as main products, several new *ent*-13-epimanoyl oxides were isolated from *S. varoi* subsp. *varoi* [3]. In addition, a series of sesquiterpenoid compounds were detected.

The present paper describes the results obtained in a study of a series of sesquiterpenoids found in high quantities mainly in *Sideritis varoi* subsp. *cuatrecasasii*.

RESULTS AND DISCUSSION

The first sesquiterpenoid compound (**1**) isolated from the aerial parts of both subspecies (*varoi* and *cuatrecasasii*) of *S. varoi* had a MW of 280 (in agreement with the formula $C_{17}H_{28}O_3$), and, as shown by IR spectroscopy, contained hydroxyl, acetoxy and exomethylene groups. The presence of a secondary acetoxyl group was deduced from the high-resolution ^1H NMR spectrum (360 MHz), as the signal of the geminal proton was a singlet at δ5.57 (1H). A 1H signal (*dd*, $J_1 = 11.64$, $J_2 = 4.25$ Hz) attributable to an axial proton (geminal to a hydroxyl group) was observed at δ3.31. Two singlet signals (δ4.74 and 4.59, 1H each) confirmed the presence of an exomethylene group. The spectrum also showed a methyl singlet signal (δ0.88, 3H) and two methyl doublet signals (δ0.96 and 0.84, J = 6.60 Hz, 3H each). The presence of the hydroxyl group was confirmed by its oxidation to a non-conjugated ketone group situated in a six-membered ring (**2**). The benzoylation of **1** gave a benzoyloxy compound (**3**) and the signal at δ3.31 in **1** was shifted downfield (see Experimental). Cleavage of the acetoxy group of **1** was unsuccessful in basic media but was eventually achieved by lithium aluminium hydride reduction. This suggested considerable steric hinderance at the acetoxy group. Thus, the new hydroxyl group of **4** could not be oxidized by Jones' reagent or by reaction with pyridinium dicromate, while the initially free hydroxyl group was oxidized easily to give **5**.

Analysis of the chemical behaviour and spectroscopic data of **1**–**5** suggested a 6β-acetoxy-eudesm-4(15)-ene structure for **1** with an equatorial hydroxyl group situated at either C-1 or C-9. Application of Horeau's method [4] to **1** gave a positive value, which was compatible with either C-1 hydroxylation in a normal series or C-9 hydroxylation in an *ent*-series.

Epoxidation of **1** gave a mixture of epoxide **6** and a product of hydrolysis (**7**). Saponification of **7** and sodium periodate oxidation of the resulting product led to ketone **8**, which exhibited a remarkable negative Cotton effect. These observations indicated a normal skeletal configuration for **1**. Therefore, the free hydroxyl group of **1** must be situated at C-1. The ^{13}C NMR spectrum of **1** was also in agreement with the 1β-hydroxy-6β-acetoxy-eudesm-4(15)-ene structure proposed. This product is closely related structurally to a cinnamoyl derivative isolated from *Verbesina* species [5], whose structure was determined mainly by spectroscopic methods. Correlation of the properties of this 6β-cinnamoyl derivative with those of **1** is difficult due to the considerable steric hinderance at C-6.

Another natural product (**9**), isolated from both species of *Sideritis*, was a new sesquiterpene which also contained a hydroxyl and an acetate group (IR). The estimated MW of this compound was 298, since the highest m/z value observed in its mass spectrum was 281 $[M-17]^+$ it appeared to contain a tertiary hydroxyl group. The ^1H NMR spectrum of **9** confirmed the presence of an acetoxy group, presumably situated axially at C-6, by comparison with the ^1H NMR spectrum of **1**. In addition, a signal at δ3.18 (1H, *dd*, $J_1 = 11$, $J_2 = 4$ Hz) suggested the presence of an equatorial hydroxyl group situated at C-1 of a eudesmane skeleton. **9** was not oxidized by sodium periodate and lead tetraacetate treatment. Application of Horeau's method to **9** gave a positive value. This observation, together with the ^1H NMR spectral data, led us to

*Part 17 in the series "Terpene Components of Spanish Labiatae". For Part 16 see Cabrera, E., García-Granados, A., Sáenz de Buruaga, A. and Sáenz de Buruaga, J. M. (1983) *Phytochemistry* **22**, 2779.

propose that the secondary hydroxyl group present in **9** was located at C-1, which is compatible with the observed positive Cotton effect shown by ketone **10** (obtained from **9**). In addition, acetylation of **9** yielded a diacetate (**11**), which exhibited hydroxyl band in its IR spectrum, confirming the presence of a tertiary alcohol group.

To establish the stereochemistry at C-4 of **9**, we saponified the acetoxy group at C-6. On this occasion, hydrolysis in basic medium was successful and gave **12**, presumably due to the assistance of the possible axial hydroxyl group at C-4. **12** was also obtained from **1** by epoxidation with MCPBA (giving product **6**) and further reduction with lithium aluminium hydride.

12 gave only one acetonide (**13**), formed by the two hydroxyl groups at C-4 and C-6. As there was no doubt about the configuration at C-6 (6β-hydroxy), the easy formation of the acetonide demonstrated that the hydroxyl group at C-4 was in the β-configuration (axial). To eliminate the possibility that the acetonide was formed between the hydroxyl groups at C-1 and C-4, **12** was carefully acetylated to give **14** which contained only one acetyl group at C-1. A new acetonide (**15**) was obtained from this product and correlated with **13** by acetylation of **13**. No isopropylidenedioxy derivatives were obtained after acetonation of **9**, while the acidic and dehydrating conditions of the reaction gave a series of products with the following structures. The less polar (TLC) of these products (**16**) had a MW of 220 corresponding to the molecular formula $C_{15}H_{24}O$. Its UV spectrum showed conjugation, λ_{max} 239 (ε11 200). The IR spectrum of **16** showed that this product had at least one hydroxyl group but no acetate groups. The ^{1}H NMR spectrum showed the presence of two vinylic protons. One of them (δ5.52) was due to a proton at C-6. The other (δ5.40) was coupled with several protons. Irradiation of the allylic methyl group (δ1.75) converted the signal at δ5.40 into a double-doublet ($J_1 = 5$, $J_2 = 2$ Hz). This vinylic proton was situated at C-3. Signals due to protons at C-1 (geminal to hydroxyl group) (δ3.5) and complex signals due to methyl groups (9H, δ0.92) were also observed. Compound **16** was formed by the elimination of water and acetic acid, and provided additional proof of the axial character of both groups in **9**.

Another product isolated from this reaction was **17**. Its structure was correlated with a previously described product (**18**) [6].

The last product isolated from the reaction of **9** was **19**, which was identical to a natural product isolated from these plants. **19** had a MW of 280, and contained hydroxyl, acetoxy and C=C groups (IR). Its ^{1}H NMR spectrum contained two signals (δ5.60, 1H, *s (br)* and δ3.42, 1H, *dd*, $J_1 = 11$, $J_2 = 4$ Hz) similar to those observed for protons at C-1 and C-6 of **1**. In a similar way, a methyl singlet signal and two methyl doublet signals were also observed. In the case of **19**, no signals due to a vinylidene group were detected, although a vinyl group (δ5.35, 1H, *m*, $W_{1/2} = 8$ Hz) and an allylic methyl group (δ1.60, 3H, *s*) were observed. The structure of **19** was, therefore, 1β-hydroxy-6β-acetoxy-eudesm-3-ene. This was confirmed by oxidation to ketone **20**, which exhibited a positive Cotton effect. Treatment of **19** with MCPBA gave a 3β,4β-epoxide (**21**). The configuration at C-3 of **21** was deduced from the signal (δ2.97, 1H, *d(br)*, $J = 3$ Hz) observed in its ^{1}H NMR spectrum similar to that described for 3β-epoxy-eudesmanes [5]. This product is closely related structurally to a cinnamoyl derivative also isolated from *Verbesina* species [5].

Table 1. ^{13}C NMR spectral data for compounds **1** and **9**

C	1	9
1	79 96	80.34
2	30 63	28 82
3	34 49	40 78
4	145 15	71 7
5	51 66	52 98
6	71 14	70 43
7	50.12	49 57
8	21 82	21 19
9	37.35	39.55
10	40.32	39.42
11	28.10	29.65
12	20.39	21.63
13	20.39	20.85
14	12.79	13.51
15	108.48	20.51
$\underline{C}H_3CO$	21.83	21 79
Me$\underline{C}$O	170.69	171.34

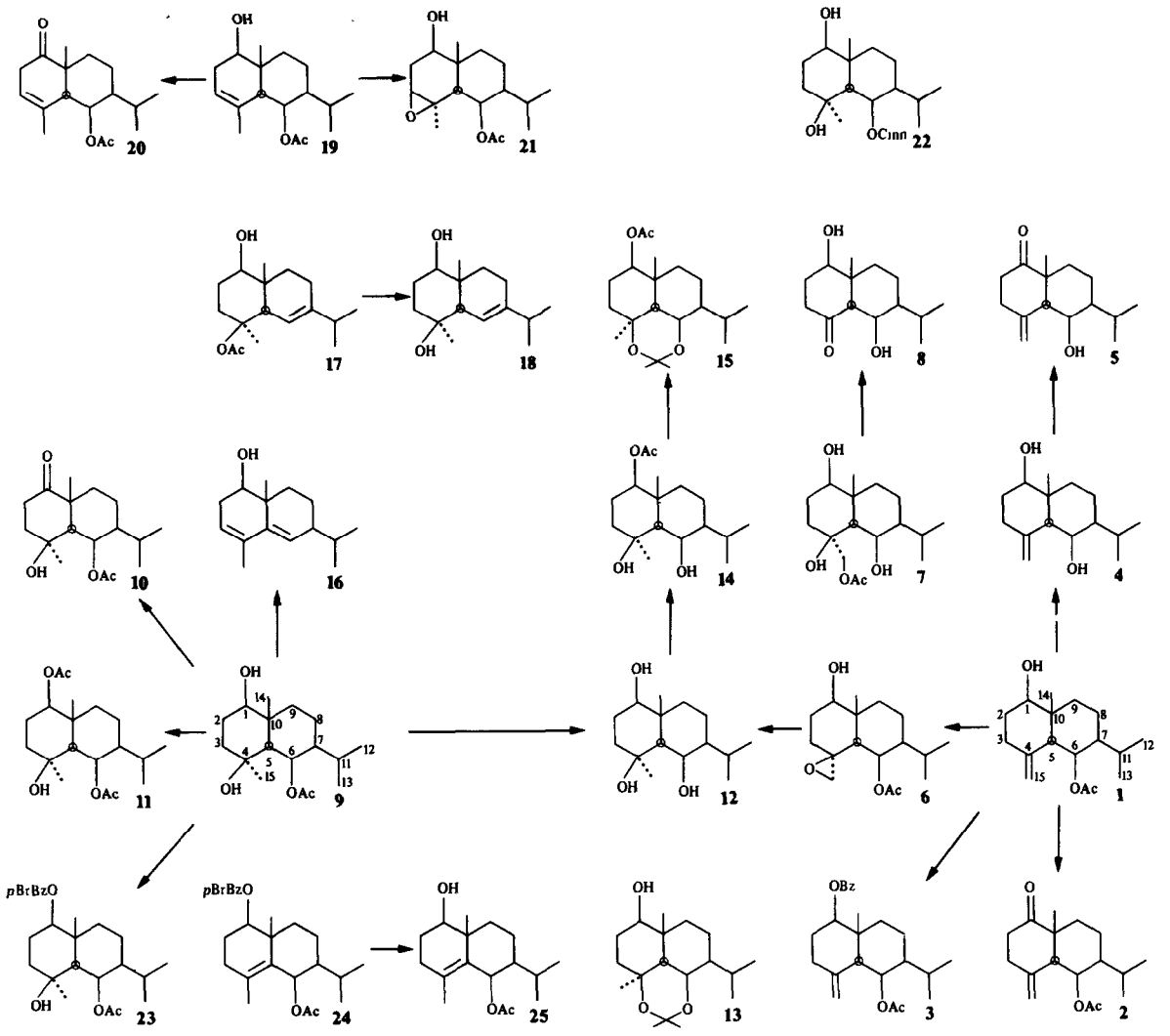
Experiments using ^{13}C NMR were performed in order to confirm the structure of **9** and the related product (Table 1). **9** was close to **22** previously reported [5] and is still under discussion [7].

To confirm the structures previously proposed, the *p*-bromobenzoate derivative was formed by treatment of **9** with an excess of *p*-bromobenzoyl chloride in pyridine to give **23** and **24**. **23** was characterized as the 1-*p*-bromobenzoate of **9**. In addition, a minor product (**24**) was isolated. The ^{1}H NMR spectrum of this product showed signals of protons geminal to a *p*-bromobenzoyloxy group at C-1 (δ4.75) and an acetoxy group at C-6 (δ6.0). No signals of vinylic protons were observed. Moreover, a signal attributable to an allylic methyl group (δ1.87) was detected. Saponification of **24** gave a monoacetate (**25**) identical to another natural product isolated from *Sideritis varoi* subsp. *cuatrecasasii*. The ^{1}H NMR spectrum of **25** contained a signal (δ5.97, 1H, *s, br*) attributable to an equatorial proton geminal to an acetoxy group at C-6, as well as another 1H signal (δ3.32, 1H, *dd*, $J_1 = 9$, $J_2 = 7$ Hz) assignable to an axial proton geminal to a hydroxyl group at C-1. No signals of vinylic protons were observed. On the other hand, signals due to an allylic methyl group (δ1.82, 3H, *s*) and other methyl doublets (δ1.04, 6H, *d*, $J = 6$ Hz) were present. The observed deshielding of proton at C-6 was consistent with its allylic character.

We therefore conclude that **25** is a 1β-hydroxy-6β-acetoxy-eudesm-4-ene, a new natural eudesm-4-ene.

EXPERIMENTAL

Mps (Kofler apparatus) are uncorr; ^{1}H NMR: 60 MHz, 80 MHz, or 360 MHz, $CDCl_3$, TMS as internal standard ^{13}C NMR: 22.5 MHz, $CDCl_3$ (which also provided the lock signal), TMS as internal reference. Assignments of ^{13}C chemical shifts were made with the aid of broad-band proton decoupling and SFORD experiments, setting the decoupler frequency in the middle of the proton range in the former and 2 ppm to the right



Scheme 1.

of TMS in the latter. CC: silica gel Merck 7729 (less than 0.08 mm). Voucher specimens have been deposited at the Herbarium of the Faculty of Pharmacy (University of Granada).

Isolation of sesquiterpenes. (a) *Sideritis varoi* subsp. *varoi.* Aerial parts (4.4 kg) were processed as described in ref. [3]. The sesquiterpenes isolated were 1β-hydroxy-6β-acetoxy-eudesm-4(15)-ene (**1**) (650 mg), 1β-hydroxy-6β-acetoxy-eudesm-3-ene (**19**) (150 mg) and 1β,4β-dihydroxy-6β-acetoxy-eudesmane (**9**) (1 2 g).

(b) *Sideritis varoi* subsp. *cuatrecasasii.* Dried plants (2.80 kg), collected at Carboneras (Almería) in April 1981, were processed to give 84 g of terpenic fraction. 60 g of this fraction was processed as described above to give, in order of elution, 1β-hydroxy-6β-acetoxy-eudesm-4(15)-ene (**1**) (1.2 g), 1β-hydroxy-6β-acetoxy-eudesm-3-ene (**19**) (2.4 g), 1β-hydroxy-6β-acetoxy-eudesm-4-ene (**25**) (50 mg) and 1β,4β-dihydroxy-6β-acetoxy-eudesmane (**9**) (3.1 g).

1β-Hydroxy-6β-acetoxy-eudesm-4(15)-ene (**1**). Colourless gum; $[\alpha]_D^{20}$ +62.6° ($CHCl_3$; *c* 1); IR ν_{max}^{neat} cm^{-1}: 3450, 3080, 1740, 1650, 1250, 1240, 895; ^1H NMR (360 MHz): δ5.57 (1H, *s*, H-6), 4.74 and 4.59 (1H each, *s*, 2H-15), 3.31 (1H, *dd*, J_1 = 11.64, J_2 = 4.25 Hz, H-1), 2.27 (1H, *ddd*, J_1 = 14.04, J_2 = 4.82, J_3 = 2.25 Hz, H-3β), 2.09 (1H, *t* (*br*), *J* = 14.04 Hz, H-3α), 2.01 (3H, *s*, AcO group), 1.96 (1H, *dt*, J_d = 12.94, J_t = 3.35 Hz, H-9β), 1.80 (1H, *s* (*br*), H-5), 1.16 (1H, *dt*, J_t = 12.68, J_d = 4.1 Hz, H-9α), 0.96 (3H, *d*, *J* = 6.60 Hz, H-12), 0.88 (3H, *s*, H-14), 0.84 (3H, *d*, *J* = 6.60 Hz, H-13); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.). 280 $[M]^+$ (4), 262 (1), 252 (1), 251 (1), 238 (2), 236 (2), 234 (2), 220 (63), 205 (19), 202 (78), 192 (20), 187 (38), 177 (7), 159 (100). (Calc for $C_{17}H_{28}O_3$: C, 72.82; H, 10 05. Found: C, 72.95; H, 10.16%.) Determination of absolute configuration at C-1 of product **1**: 33 mg product **1** and 100 mg (±)-α-phenylbutyric anhydride [4], $[\alpha]_D$ 0.604° (C_6H_6; *c* 6.4).

Oxidation of **1**. 77 mg **1** was oxidized with 110 mg pyridinium dichromate [8]. CC of the resulting products gave 72 mg ketone **2**. Mp 115–117°; IR ν_{max}^{KBr} cm^{-1}: 3070, 1740, 1715, 1250, 900; ^1H NMR (60 MHz): δ5.65 (1H, *m*, $W_{1/2}$ = 7 Hz, H-6), 4.95 and 4.85 (1H each, *s* (*br*), 2H-15), 2.0 (3H, AcO group), 1.20 (3H, *s*, C-14 Me group), 0.97 (6H, *d*, *J* = 6.5 Hz, C-12 and C-13 Me groups);

$$[\alpha]_{20}^{\lambda} = \frac{\begin{matrix}589 & 578 & 546 & 436 & 365\ nm\end{matrix}}{\begin{matrix}+31 & +32 & +36.5 & +58 & 0°\end{matrix}} (CHCl_3;\ c\ 1)$$

1β-Benzoyloxy-6β-acetoxy-eudesm-4(15)-ene (**3**). 143 mg **1** was benzoylated as usual, yielding after CC, 140 mg benzoate

Colourless gum; $[\alpha]_D^{20}$ +3.5° ($CHCl_3$; *c* 1); IR ν_{max}^{neat} cm^{-1}: 3060, 1745, 1730, 1650, 1603, 1590, 1280, 1250; ^1H NMR (60 MHz): δ8.20–7.20 (5H, benzoate signals), 5.6 (1H, *s (br)*, H-6), 5.0–4.5 (3H, *m*, H-1 and 2H-15), 2.0 (3H, *s*, AcO group), 1.18 (3H, *s*, C-14 Me group), 1.0 and 0.82 (3H each, *d*, *J* = 6 Hz, C-12 and C-13 Me groups).

1β,6β-Dihydroxy-eudesm-4(15)-ene (**4**). 160 mg **1** in Et_2O was treated with $LiAlH_4$ (50 mg) and refluxed for 48 hr. The products on CC gave 90 mg **4**, mp 79–81°, $[\alpha]_D^{20}$ +5° ($CHCl_3$; *c* 1); IR ν_{max}^{KBr} cm^{-1}: 3450, 3060, 1645, 900; ^1H NMR (60 MHz): δ5.0 and 4.86 (1H each, *s (br)*, 2H-15), 4.25 (1H, *m*, $W_{1/2}$ = 7 Hz, H-6), 3.25 (1H, *dd*, J_1 = 11, J_2 = 5 Hz, H-1), 0.95 (6H, *d*, *J* = 6 Hz, C-12 and C-13 Me groups), 0.90 (3H, *s*, C-14 Me group); MS *m/z* (rel int.): 238 $[M]^+$ (10), 220 (100), 205 (24), 202 (29), 191 (20), 178 (33), 159 (28).

Oxidation of **4**. 90 mg **4** was oxidized with 300 mg pyridinium dichromate. After CC, 82 mg pure ketone **5** was obtained. Mp 98–100°; optically inactive; IR ν_{max}^{KBr} cm^{-1}: 3550, 3060, 1715, 1655, 900; ^1H NMR (60 MHz): δ5.30 and 5.18 (1H each, *s (br)*, 2H-15), 4.40 (1H, *m*, $W_{1/2}$ = 8 Hz, H-6), 1.20 (3H, *s*, C-14 Me group), 0.95 (6H, *d*, *J* = 6 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.): 236 $[M]^+$ (100), 218 (53), 208 (17), 203 (23), 193 (20), 177 (4).

Epoxidation of **1**. **1** (223 mg) was treated with MCPBA (966 mg). On work-up, 1β-hydroxy-6β-acetoxy-4β(15)-epoxy-eudesmane (**6**, 81 mg) and 1β, 4β, 6β-trihydroxy-15-acetoxy-eudesmane (**7**, 57 mg) were obtained. **6**: sublime; $[\alpha]_D^{20}$ +26.4° ($CHCl_3$, *c* 1), IR ν_{max}^{KBr} cm^{-1}: 3500, 1740, 1270, 1250, 1100, 1050; ^1H NMR (60 MHz): δ5.30 (1H, *m*, $W_{1/2}$ = 6 Hz, H-6), 3.25 (1H, *m*, $W_{1/2}$ = 18 Hz, H-1), 3.07 and 2.12 (ABq, *J* = 4.5 Hz, 2H-15), 2.0 (3H, *s*, AcO group), 1.18 (3H, *s*, C-14 Me group), 0.91 and 0.86 (3H each, *d*, *J* = 6 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.) 296 $[M]^+$ (2), 266 (8), 253 (100), 248 (15), 237 (63), 236 (73), 224 (77), 206 (100), **7**: Mp 143–145°; $[\alpha]_D^{20}$ +3.2° (Me_2CO; *c* 1); IR ν_{max}^{KBr} cm^{-1}: 3500, 1760, 1740, 1280, 1250, 1050, 1020; ^1H NMR (60 MHz): δ4.30 (1H, *m*, $W_{1/2}$ = 6 Hz, H-6), 3.95 (ABq, *J* = 12 Hz, 2H-15), 3.10 (1H, *m*, $W_{1/2}$ = 18 Hz, H-1), 2.05 (3H, *s*, AcO group), 1.31 (3H, *s*, C-14 Me group), 0.90 (6H, *d*, *J* = 6 Hz, C-12 and C-13 Me groups).

1β,6β-Dihydroxy-eudesman-4-one (**8**). **7** (57 mg) was saponified with NaOH–MeOH and treated with $NaIO_4$ (20 mg), affording, after CC, 23 mg dihydroxyketone **8**. Mp 108–110°; IR ν_{max}^{KBr} cm^{-1}: 3550, 1705; ^1H NMR (60 MHz): δ4.35 (1H, *m*, $W_{1/2}$ = 7 Hz, H-6), 3.30 (1H, *dd*, J_1 = 11, J_2 = 6 Hz, H-1), 1.02 (3H, *s*, C-14 Me singlet) partly superimposed on a 6H doublet (*J* = 6 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.): 240 $[M]^+$ (8), 223 (5), 222 (20), 207 (6), 204 (6), 189 (5), 179 (13), 155 (100);

$$[\alpha]_{20}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\,nm}{-66.7 \quad -70.4 \quad -83.6 \quad -178.5 \quad -406^\circ} (CHCl_3; c\ 1).$$

$LiAlH_4$ *reduction of epoxide* **6**. **6** (48 mg) was reduced with $LiAlH_4$ (40 mg). Usual work-up followed by CC gave 33 mg **12**. Sublime; $[\alpha]_D^{20}$ 9.8° ($CHCl_3$; *c* 1); IR ν_{max}^{KBr} cm^{-1}: 3450; ^1H NMR (60 MHz): δ4.5 (1H, *m*, $W_{1/2}$ = 6 Hz, H-6), 3.15 (1H, *d (br)*, *J* = 11 Hz, H-1), 1.30 (6H, *s*, C-14 and C-15 Me groups), 0.98 and 0.95 (3H, each, *d*, *J* = 6 Hz, C-12 and C-13 Me groups); MS *m/z* (rel int.): 256 $[M]^+$ (2), 241 (100), 239 (8), 238 (8), 223 (100), 220 (8), 205 (55), 195 (17), 187 (28), 178 (40).

1β,4β-Dihydroxy-6β-acetoxy-eudesmane (**9**). Colourless gum; $[\alpha]_D^{20}$ +27.1° ($CHCl_3$; *c* 1); IR ν_{max}^{neat} cm^{-1}: 3450, 1730, 1250; ^1H NMR (60 MHz): δ5.70 (1H, *s (br)*, H-6), 3.18 (1H, *dd*, J_1 = 11, J_2 = 4 Hz, H-1), 2.08 (3H, *s*, AcO group), 1.38 and 1.28 (3H each, C-14 and C-15 Me groups), 0.92 (6H, *d*, *J* = 6 Hz, C-12 and C-13 Me groups); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 281 $[M-17]^+$ (0.1), 239 (0.1), 221 (1), 205 (1), 203 (0.5), 187 (0.5), 177 (1), 161 (2), 149 (2), 147 (2), 145 (2), 138 (9), 122 (4), 107 (5), 101 (100). (Calc. for $C_{17}H_{30}O_4$: C, 68.43; H, 10.12. Found: C, 68.54; H, 10.25%) Application of Horeau's method to **9**: **9** (30 mg) was treated with (±)-α-phenylbutyric anhydride (100 mg) in pyridine (1 ml); $[\alpha]_D$ 0.476° (C_6H_6; *c* 6).

Oxidation of **9**. **9** (70 mg) was oxidized with pyridinium dichromate (100 mg). CC gave ketone **10** (60 mg). Mp 115–117°; IR ν_{max}^{KBr} cm^{-1}: 3400, 1730, 1680, 1260; $\nu_{max}^{CHCl_3}$ cm^{-1}: 1734 and 1705 carbonyl bands; ^1H NMR (60 MHz): δ5.60 (1H, *s (br)*, H-6), 3.05 (1H, *ddd*, J_1 = 12, J_2 = 12, J_3 = 7 Hz, H-2 axial), 2.02 (3H, *s*, AcO group), 1.50 and 1.45 (3H each, C-14 and C-15 Me groups), 1.0 (6H, *d*, *J* = 6 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.): 296 $[M]^+$ (1), 278 (1), 236 (49), 222 (9), 203 (10), 193 (23), 175 (31), 159 (100);

$$[\alpha]_{20}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\,nm}{+72.5 \quad +76.4 \quad +87.7 \quad +158.2 \quad +286.8^\circ} (CHCl_3; c\ 1).$$

1β,6β-Diacetoxy-4β-hydroxy-eudesmane (**11**). **9** (65 mg) was treated with 2.5 ml Ac_2O and 4 ml pyridine overnight at room temp. **11** was isolated after CC (72 mg). Mp 94–96°; $[\alpha]_D^{20}$ +42.3° ($CHCl_3$; *c* 1); IR ν_{max}^{KBr} cm^{-1}: 3550, 1740, 1250; ^1H NMR (60 MHz): δ5.70 (1H, *s (br)*, H-6), 4.45 (1H, *dd*, J_1 = 11, J_2 = 4 Hz, H-1), 2.05 (6H, *s*, 2 × AcO groups), 1.35 (6H, *s*, C-14 and C-15 Me groups), 0.90 and 0.85 (3H each, *d*, *J* = 6 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.): 340 $[M]^+$ (1), 322 (1), 280 (1), 265 (2), 263 (3), 239 (2), 220 (100)

Saponification of **9**. 74 mg **9** was refluxed for 1.5 hr with aq. MeOH–NaOH After CC, 60 mg **12** was obtained.

1β-Hydroxy-4β,6β-diisopropylidenedioxy-eudesmane (**13**). **12** (30 mg) was dissolved in 2,2-dimethoxypropane (3 ml), refluxed for 4 hr with TsOH (1 mg), washed with aq. $NaHCO_3$, and extracted with CH_2Cl_2 to give 32 mg **13**. Colourless gum; $[\alpha]_D^{20}$ +35.4° ($CHCl_3$; *c* 1); IR ν_{max}^{neat} cm^{-1}: 3450, 1390, 1380, 1200, 1040; ^1H NMR (60 MHz): δ4.30 (1H, *m*, $W_{1/2}$ = 6 Hz, H-6), 3.20 (1H, *d (br)*, *J* = 11 Hz, H-1), 1.37 and 1.28 (3H each, *s*, C-14 and C-15 Me groups), 1.35 (6H, *s*, isopropylidenedioxy group), 0.93 (6H, *d*, *J* = 6 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.): 281 $[M-15]^+$ (31), 221 (100), 203 (58), 187 (4), 177 (6), 161 (12), 149 (28).

1β-Acetoxy-4β,6β-dihydroxy-eudesmane (**14**). **12** (29 mg) was treated with Ac_2O (1.5 ml) and pyridine (3 ml) for 4 hr at room temp. After CC, **14** (33 mg) was isolated. Colourless gum; $[\alpha]_D^{20}$ +19.3° ($CHCl_3$, *c* 1); IR ν_{max}^{neat} cm^{-1}: 3450, 1730, 1250; ^1H NMR (60 MHz): δ4.5 (2H, superimposed signals of H-1 and H-6), 2.05 (3H, *s*, AcO group), 1.40 (3H, *s*, C-15 Me), 1.30 (3H, *s*, C-14 Me), 1.0 and 0.95 (3H each, *d*, *J* = 6.5 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.): 298 $[M]^+$ (2), 283 (77), 265 (29), 247 (6), 238 (5), 220 (25), 205 (100), 187 (51), 177 (34), 159 (51).

1β-Acetoxy-4β,6β-diisopropylidenedioxy-eudesmane (**15**). **13** (30 mg) was dissolved in Me_2CO (8 ml) and 2,2-dimethoxypropane (3 ml) TsOH (1 mg) was added, and the mixture refluxed for 24 hr. The mixture was then concd under vacuum, washed with aq. $NaHCO_3$, extracted with CH_2Cl_2 and dried with $MgSO_4$, yielding 25 mg **15** Colourless gum; $[\alpha]_D^{20}$ +37° ($CHCl_3$, *c* 1); IR ν_{max}^{neat} cm^{-1}. 1745, 1250, 1050; ^1H NMR (60 MHz): δ4.45 (2H, superimposed signals of H-1 and H-6), 2.0 (3H, *s*, AcO group), 1.41 (3H, *s*, C-15 Me), 1.32 (9H, *s*, C-14 Me and isopropylidenedioxy groups), 0.9 (6H, *d*, *J* = 6.5 Hz, C-12 and C-13 Me groups).

Treatment of **9** *with 2,2-dimethoxypropane*. **9** (55 mg) was dissolved in Me_2CO (15 ml) and 2,2-dimethoxypropane (5 ml) and refluxed for 24 hr with TsOH (1 mg). The usual work-up followed by CC gave 17 mg **16**, 10 mg **17**, 2.5 mg **19** and 15 mg **9**. **16**: Mp 48–50°; $[\alpha]_D^{20}$ −7° ($CHCl_3$; *c* 1); IR ν_{max}^{KBr} cm^{-1}: 3400, 1600, 1060, 1050, 860; ^1H NMR (80 MHz): δ5.52 (1H, *d*, *J* = 2 Hz, H-6), 5.40 (1H, *m*, $W_{1/2}$ = 9 Hz, H-3), 3.5 (1H, *dd*, J_1 = 10, J_2 = 7 Hz, H-1), 1.75 (3H, *d*, *J* = 2 Hz, C-15 Me), 0.92 (9H,

complex signals, C-12, C-13 and C-14 Me group); MS *m/z* (rel. int.): 220 $[M]^+$ (33), 202 (8), 187 (7), 177 (100), 159 (88), 149 (31). **17**: Colourless gum; $[\alpha]_D^{20}$ −22.4° ($CHCl_3$; *c* 1); IR ν_{max}^{neat} cm^{-1}: 3480, 1745, 1665, 1250, 1050; ^1H NMR (80 MHz): δ5.48 (1H, *m*, $W_{1/2}$ = 6 Hz, H-6), 3.35 (1H, *dd*, J_1 = 9, J_2 = 8 Hz, H-1), 1.95 (3H, *s*, AcO group), 1.53 (3H, *s*, C-15 Me), 1.02 (3H, *s*, C-14 Me), 0.96 (6H, *d*, *J* = 6 Hz, C-12 and C-15 Me groups); MS *m/z* (rel. int.): 280 $[M]^+$ (13), 279 (21), 269 (6), 252 (15), 220 (88), 210 (31), 202 (39), 192 (16), 187 (40), 177 (50), 159 (100). **19** (1β-hydroxy-6β-acetoxy-eudesm-3-ene): colourless gum; $[\alpha]_D^{20}$ +36.8° ($CHCl_3$; *c* 1); IR ν_{max}^{neat} cm^{-1}: 3450, 3050, 1745, 1250; ^1H NMR (80 MHz): δ5.60 (1H, *s* (*br*), H-6), 5.36 (1H, *m*, $W_{1/2}$ = 8 Hz, H-3), 3.42 (1H, *dd*, J_1 = 11, J_2 = 4 Hz, H-1), 1.98 (3H, *s*, AcO group), 1.60 (3H, *s*, C-15 Me), 0.98 (3H, *s*, C-14 Me), 1 0 and 0.85 (3H each, *d*, *J* = 7 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.): 280 $[M]^+$ (5), 237 (4), 220 (32), 205 (14), 202 (57), 191 (11), 187 (25), 177 (34), 159 (100), 145 (32). (Calc. for $C_{17}H_{28}O_3$: C, 72.82; H, 10.05. Found: C, 72 98; H, 10.14%.)

Saponification of **17** Saponification of **17** (9 mg) with aq. MeOH–NaOH gave **18** (7.5 mg). Colourless gum; $[\alpha]_D^{20}$ −12.6° ($CHCl_3$; *c* 0.8), IR ν_{max}^{neat} cm^{-1}· 3490, 3080, 847; ^1H NMR (80 MHz): δ5.45 (1H, *m*, $W_{1/2}$ = 6 Hz), 3.32 (1H, *dd*, J_1 = 10, J_2 = 6 Hz, H-1), 1 21 (3H, *s*, C-15 Me), 1.01 (6H, *d*, *J* = 7 Hz, C-12 and C-13 Me groups), 0.96 (3H, *s*, C-14 Me)

Oxidation of **19** 60 mg **19** was oxidized with pyridinium dichromate (90 mg). After CC, 35 mg 6β-acetoxy-eudesm-3-en-1-one (**20**) was isolated Mp 95–97°; IR ν_{max}^{KBr} cm^{-1}· 1750, 1730, 1260; ^1H NMR (60 MHz): δ5.65 (1H, *m*, $W_{1/2}$ = 7 Hz, H-6), 5.50 (1H, *m*, $W_{1/2}$ = 18 Hz, H-3), 2.05 (3H, *s*, AcO group), 1.75 (3H, *s* (*br*), C-15 Me), 1.25 (3H, *s*, C-14 Me), 0 97 and 0 87 (3H each, *d*, *J* = 6 Hz, C-12 and C-13 Me groups),

$$[\alpha]_{20}^{\lambda} = \frac{\begin{matrix}589 & 578 & 546 & 436 & 365\ nm\end{matrix}}{\begin{matrix}+38.4 & +40.0 & +45\,0 & +68.7 & +72.8°\end{matrix}}(CHCl_3; c\ 1).$$

Epoxidation of **19**. 132 mg **19** was dissolved in $CHCl_3$ (15 ml) and epoxidized with MCPBA (564 mg) for 24 hr at 0°. The usual work-up followed by CC gave 1β-hydroxy-3β,4β-epoxy-6β-acetoxy-eudesmane (**21**) (80 mg). Colourless gum; $[\alpha]_D^{20}$ +34.5° ($CHCl_3$: *c* 1); IR ν_{max}^{neat} cm^{-1}: 3460, 1745, 1270, 1250; ^1H NMR (60 MHz): δ5.65 (1H, *s* (*br*), H-6), 3 28 (1H, *dd*, J_1 = 11, J_2 = 6 Hz, H-1), 2.97 (1H, *d* (*br*), *J* = 3 Hz, H-3), 2.07 (3H, *s*, AcO group), 1.25 (3H, *s*, C-15 Me), 0.99 (3H, *s*, C-14 Me), 1.0 and 0.85 (3H each, *d*, *J* = 6 Hz, C-12 and C-13 Me groups).

Treatment of **9** *with 4-bromobenzoyl chloride*. 95 mg **9** was treated with 4-bromobenzoyl chloride (800 mg) in pyridine (2.5 ml) and refluxed for 14 hr. The usual work-up followed by CC gave 80 mg 1β-(*p*-bromobenzoyloxy)-6β-acetoxy-eudesmane (**23**) and 20 mg 1β-(*p*-bromobenzoyloxy)-6β-acetoxy-eudesm-4-ene (**24**). **23**: Mp 53–54°; $[\alpha]_D^{20}$ +10.8° ($CHCl_3$; *c* 1); IR ν_{max}^{KBr} cm^{-1}: 3500, 1735, 1718, 1275, 1245; ^1H NMR (60 MHz)· δ7.83 and 7.50 (A_2B_2, *J* = 9 Hz, *p*-bromobenzoyloxy group), 5 62 (1H, *s* (*br*), H-6), 4.60 (1H, *dd*, J_1 = 11, J_2 = 5 Hz, H-1), 2.0 (3H, *s*, AcO group), 1 43 and 1.40 (3H each, *s*, C-14 and C-15 Me groups), 0.85 (6H, *m*, $W_{1/2}$ = 9 Hz, C-12 and C-13 Me groups) Saponification of **24** led to a product identical to natural product **25**.

1β-Hydroxy-6β-acetoxy-eudesm-4-ene (**25**). Colourless gum; $[\alpha]_D^{20}$ +75.2° ($CHCl_3$; *c* 1); IR ν_{max}^{neat} cm^{-1}: 3430, 1740, 1240; ^1H NMR (60 MHz): δ5.97 (1H, *s* (*br*), H-6), 3 32 (1H, *dd*, J_1 = 9, J_2 = 7 Hz, H-1), 1.98 (3H, *s*, AcO group), 1.82 (3H, *s*, C-15 Me), 1.05 (3H, *s*, C-14 Me), 0.88 (6H, *d*, *J* = 6 Hz, C-12 and C-13 Me groups); MS *m/z* (rel. int.): 280 $[M]^+$ (0.8), 255 (0.8), 238 (5), 220 (100), 202 (34), 192 (6), 187 (25), 177 (61), 159 (80), 145 (32), 133 (54), 129 (38), 105 (45). (Calc. for $C_{17}H_{28}O_3$: C, 72.82, H, 10.05. Found: C, 72.91; H, 10.12%.)

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