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ELASCLEPIOL AND ELASCLEPIC ACID, BEYERANE DITERPENOIDS FROM *ELAEOSELINUM ASCLEPIUM*

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Key Word Index—*Elaeoselinum asclepium*; Umbelliferae; beyerane diterpenoids; elasclepiol; elasclepic acid.

Abstract—Two new beyerane diterpenoids were isolated from the roots of *Elaeoselinum asclepium* as the main components of the benzene extract. The structures of these substances were established as *ent*-14β-tigloyloxybeyer-15-en-19-ol (elasclepiol) and *ent*-14β-tigloyloxybeyer-15-en-19-oic acid (elasclepic acid), as evidenced by spectral data and chemical transformations.

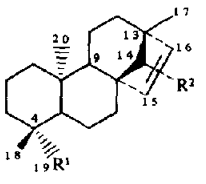
INTRODUCTION

As a part of our studies on new natural substances from plants native to the 'Comunidad Valenciana' (East Spain), we have examined the chemical constituents of the roots of *Elaeoselinum asclepium* (L), subsp. *meoides* (Desf.) Fiori, also known as *E. meoides* (Desf.) Koch ex D.C. and *E. millefolium* Boiss [1].

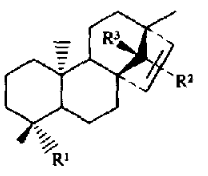
The most characteristic components found in the Umbelliferae are coumarins, terpenoids and aromatic derivatives from the essential oils, as well as phenylpropanoids and flavonoids, usually present as minor components [2]. Diterpenoids are quite uncommon in these plants; however some tetracyclic diterpenes have been reported in *Elaeoselinum* species, such as *E. gummiferum* [3–5] and *E. foetidum* [6]. We also found two new kaurane derivatives from *E. tenuifolium* [7] and in a previous communication [8] we reported the isolation of some new diterpenes with beyerane, kaurane and atisane skeletons from the roots of *E. asclepium*. We now report on the structural identification of the main components of this plant as the alcohol **1** and the carboxylic acid **4**, two new beyerane derivatives for which the names elasclepiol and elasclepic acid are proposed.

RESULTS AND DISCUSSION

The benzene extract from the roots of the plant (4.8%, dry wt) was separated into neutral and acid fractions with 4% aqueous sodium hydroxide. The main components of the neutral fraction were identified as beyerane derivatives [8], from which elasclepiol (**1**) was isolated by chromatography on silica gel and crystallization in hexane.



	R¹	R²
1	CH_2OH	OTgl
2	CH_2OAc	OTgl
3	CH_2OH	OH
4	COOH	OTgl
5	COOMe	OTgl



	R¹	R²	R³
6	COOMe	ODHTgl	H
7	COOMe	OH	H
8	COOMe	=O	
9	CH_2OH	H	OH
10	CH_2OAc	ODHTgl	H
11	CH_2OH	OH	H

$\mathrm{Tgl} = \mathrm{COCMe}\overset{E}{=\!=}\mathrm{CHMe}$
$\mathrm{DHTgl} = \mathrm{COCHMe}\text{—}\mathrm{CH_2Me}$

The MS of compound **1** showed a molecular ion at m/z 386, in agreement with the formula $C_{25}H_{38}O_3$. The UV spectrum had an absorption maximum at 213.5 nm characteristic of a conjugated ester. The IR spectrum showed absorption bands of a hydroxyl (3560, 3480 *br* cm^{-1}), a conjugated ester (1690 cm^{-1}) and a 1,2-disubstituted *cis*-alkene (3050, 1640, 735 cm^{-1}). The ^1H NMR spectrum confirmed the presence of two vinylic protons of a 1,2-disubstituted *cis*-olefin attached to quaternary carbon atoms [δ5.63 (1H, *dd*, $J = 6$ Hz, 0.9 Hz, H-16), 5.43 (1H, *dd*, $J = 6$ Hz, 1.3 Hz, H-15)], one proton geminal to an ester group [δ4.54 (1H, *dd*, $J = 0.9$ Hz, 1.3 Hz, H-14)] and a hydroxymethylene group [δ3.75 (1H, *d*, $J = 10.5$ Hz, H-19a), 3.41 (1H, *d*, $J = 10.5$ Hz, H-19b)].

The ester group was identified as a tiglate from the characteristic ^1H NMR signals [δ6.82 (1H, *br q*, $J = 6$ Hz, H-3′), 1.79 (3H, *br s*, H-5′), 1.78 (3H, *br d*, $J = 6$ Hz, H-4′)], ^{13}C NMR signals [δ168.2 (C-1′, *s*), 136.4 (C-3′, *d*), 128.9 (C-2′, s), 14.2 (C-4′, *q*), 12.0 (C-5′, *q*)] [9], and MS fragments at m/z 286 $[M-100]^+$, 83 and 55 [10]. Alkaline hydrolysis of **1** with 5% methanolic potassium hydroxide yielded tiglic acid and the diol **3**.

Besides the tiglic ester signals, the ^{13}C NMR spectrum revealed the presence of two olefinic carbon atoms (133.5, *d* and 132.4, *d*), one primary and one secondary hydroxylated carbon atom (65.4 *t* and 94.4 *d*) and four quaternary, three CH, eight CH_2, and three CH_3 signals.

Based on the molecular formula and the ^{1}H and the ^{13}C NMR data, it was concluded that **1** was a tetracyclic diterpene with a *cis* 1,2-disubstituted double bond, one primary hydroxyl group and one secondary tigloyloxy group. These functional groups can be accommodated on the common tetracyclic diterpene skeletons of beyerane, atisane, kaurane and phyllocladane. However, the presence of three quaternary methyl groups [δ0.93 (6H, *s*, H-17, H-18), 0.75 (3H, *s*, H-20)] and a *cis*-disubstituted double bond attached to quaternary carbon atoms is only compatible with a beyer-15-ene skeleton for **1**. The beyerane skeleton assigned to **1** was also supported by the ^{13}C NMR data as compared with those described for other beyerane derivatives [11–13].

The location of the tigloyloxy and hydroxy groups on the beyer-15-ene skeleton were deduced as follows: The signal displayed by the –CH$_2$OH appeared as an AB system of two diastereotopic protons. The splitting between AB doublets (δ_A–δ_B *ca* 19 Hz) and their chemical shifts are characteristic of a primary axial alcohol [14]. The same conclusion was deduced from the –CH$_2$OAc signal of the acetyl derivative **2**. In a beyerene skeleton there are only two axial methyl groups, namely C-19 and C-20, the latter shielded by the double bond. The presence of one methyl singlet deshielded at δ0.74 led us to assign this signal to the C-20 methyl group and consequently the primary hydroxyl must be located at C-19.

The axial configuration of the primary hydroxymethylene group was also confirmed by comparison with the ^{13}C chemical shifts of other diterpenoids with axial and equatorial –CH$_2$OH groups attached to C-4: there are important differences, mainly in the C-5, C-18 and C-19 shifts (*ca* δ7), that depend on the configuration of the hydroxymethyl group [15].

The signal of the proton geminal to the tigloyloxy group appeared as an ABX system ($J_{AX} = 0.9$ Hz, and $J_{BX} = 1.3$ Hz) coupled with the vinylic protons of Δ^{15}. Accordingly this ester must be situated at C-14. The observed coupling constants between H-14 and the vinylic protons are relatively strong, probably due to a 'W' pathway connecting H-14 with the vinylic protons [16]. This hypothesis was supported by the data described for some 7-monosubstituted norbornene derivatives [17]: the proton H-7 *anti* to the double bond showed a coupling constant $J_{2,7} = 0.8$ Hz, while no coupling was observed with H-7 *syn*. This effect was ascribed to the overlapping between the π orbital and the back lobe of the sp^3 orbital of H-7 *anti* [18]. From these data, we concluded that the tigloyloxy group and the double bond Δ^{15} must be *syn*.

The absolute configuration shown for **1** (i.e. that expected according to the biogenesis of these substances) was established by circular dichroism. The CD spectrum of the ketone **8** (see below) displayed a positive Cotton effect [$\Delta\varepsilon$ +1.08 (300 nm)], which according to the ketone octant rule implies that this beyerane derivative belongs to the *enantio*-series.

The main component of the acid fraction of the extract studied was elasclepic acid (**4**), a substance whose ^{1}H NMR spectrum was quite similar to that of elasclepiol. The spectra of this substance also revealed the presence of a tiglate ester, a *cis*-disubstituted double bond, a carboxylic acid and three quarternary methyl groups. Elasclepic acid was readily transformed into a diol by esterification with diazomethane and reduction with lithium aluminium hydride. The reduction product was identical to **3**, which corroborates the assignment of structure **4** for the natural carboxylic acid.

To our knowledge structures **1** and **4** have not been reported previously. However, in 1968 Edwards and Rosich [19] described the synthesis of the related diterpenoid hiban-14α,19-diol, the enantiomer of **11**, starting from agatadiol. These authors assigned the 14α configuration for the agatadiol cyclization product on the basis of the chemical behaviour of the corresponding 14-ketone. Although they attempted to obtain the C-14 epimeric alcohols by reduction of the ketone under different conditions, the only material isolated was the starting alcohol and they therefore concluded that this alcohol, arising from 'product development control', is the less hindered of the two C-14 epimers and hence proposed the 14α configuration (*anti* respect to the C-15 C-16 bridge) for the hydroxyl group of the hibandiol.

In order to confirm the proposed structure for **1** and **4**, we performed the synthesis of the epimeric alcohols **9** and **11**. The synthesis of **9** was accomplished starting from the ester **5**, which is easier to purify and to handle than the elasclepiol derivatives. Catalytic hydrogenation of **5** (Raney-Ni/EtOH) yielded **6** which was hydrolysed to the hydroxyester **7** (3520, 1690 cm^{-1}; axial –COOMe). Oxidation of **7** with PCC afforded the ketone **8** (1715 cm^{-1}) and further reduction with lithium aluminium hydride yielded the diol **9**, identical to the synthetic hiban-14α,19-diol except in its specific rotation.

The epimeric alcohol **11** was prepared from the acetyl derivative **2** by catalytic hydrogenation to **10** and reduction with lithium aluminium hydride. As compared with **9** this epimeric alcohol, **11**, showed the carbon signals of C-7, C-17 and C-15 more shielded and those of C-9 and C-12 more deshielded, as expected for a change in the γ-*gauche* effect of the hydroxyl group on the neighbouring carbon atoms.

EXPERIMENTAL

Mps: uncorr; NMR: ^{1}H, 200 MHz; ^{13}C, 50.3 MHz and 60 MHz in CDCl$_3$ with TMS as int. standard; EIMS: direct inlet probe at 70 eV.

Extraction and isolation. The plant was collected at Puerto de Albaida, Alicante, Spain, and a voucher specimen is registered in the Department of Biology, University of Alicante. The air-dried roots of *E. asclepium* (1.56 kg) were extracted with C$_6$H$_6$ in a Dean–Stark apparatus. The C$_6$H$_6$ extract (75 g, 4.8% wt of dried roots) was separated with Et$_2$O and 4% NaOH into neutral (28.3 g) and acid (34.8 g) fractions.

The neutral fraction (25.9 g) was chromatographed on silica gel (Merck ref. 7733, 100 g) in a column packed with hexane using hexane–EtOAc mixtures as eluent. The amount of EtOAc was gradually increased, and 41 fractions of 250 ml each were collected. Fractions 25–36, eluted with hexane–EtOAc (19:1) contained compound **1** (2 g) which was purified by crystallization in hexane. Chromatography of the acid fraction (15 g) on silica gel (Merck ref. 7733) with hexane–EtOAc followed by CC on 8% AgNO$_3$ with silica gel (Merck 60 PF$_{254}$) under N$_2$ pressure (1.5 atm), allowed us to isolate pure **4** (150 mg).

ent-*14β-Tigloyloxybeyer-15-en-19-ol* (**1**). R_f 0.37 (hexane–EtOAc, 4:1), needles mp 142–143° (hexane); $[\alpha]_D$ +45.4° (CHCl$_3$; *c* 1); UV λ_{max}^{EtOH} nm (log ε): 213.5 (4.2); IR ν_{max}^{KBr} cm^{-1}: 3560, 3480, 3050, 2960, 2930, 2845, 1690, 1640, 1440, 1385, 1260, 1150, 1070, 1030, 780, 735; ^{1}H NMR (200 MHz): δ6.82 (1H, *br q*, $J = 6$ Hz, H-3′), 5.63 (1H, *dd*, $J = 6$, 0.9 Hz, H-16), 5.43 (1H, *dd*, $J = 6$, 1.3 Hz, H-15), 4.54 (1H, *dd*, $J = 0.9$, 1.3 Hz, H-14), 3.75 (1H, *d*, J

= 10.5 Hz, H-19a), 3.41 (1H, *d*, $J = 10.5$ Hz, H-19b), 1.79 (3H, *br s*, H-5′), 1.78 (3H, *br d*, $J = 6$ Hz, H-4′), 0.94 (3H, *s*, H-18), 0.93 (3H, *s*, H-17), 0.75 (3H, *s*, H-20); ^{13}C NMR: δ168.2 (*s*, C-1′), 136.4 (*d*, C-3′), 133.5 (*d*, C-16), 132.4 (*d*, C-15), 128.9 (*s*, C-2′), 94.4 (*d*, C-14), 65.4 (*t*, C-19), 56.1 (*d*, C-5), 53.2 (*s*, C-8), 52.9 (*d*, C-9), 48.3 (*s*, C-13), 39.4 (*t*, C-1), 38.4 (*s*, C-4), 37.3 (*s*, C-10), 35.6 (*t*, C-3), 32.6* (*t*, C-7), 31.6* (*t*, C-12), 27.0 (*q*, C-18), 19.7** (*t*, C-6), 19.4** (*t*, C-11), 19.2 (*q*, C-17), 18.3 (*t*, C-2), 16.0 (*q*, C-20), 14.2 (*q*, C-4′), 12.0 (*q*, C-5′); MS *m/z* (rel. int.): 386 $[M]^+$ (3), 371 $[M-Me]^+$ (2), 356 $[M-CH_2O]^+$ (1), 355 $[M-CH_2OH]^+$ (1), 303 $[M-Tgl]^+$ (1), 286 $[M-TglOH]^+$ (15), 273 (2), 271 (3), 258 (3), 255 (10), 243 (4), 227 (2), 147 (6), 146 (6), 109 (2), 83 $[Tgl]^+$ (100), 55 $[Tgl-CO]^+$ (44).

Acetate (**2**). The alcohol **1** (400 mg) in pyridine (1 ml) and Ac_2O (2 ml) was left overnight at room temp. After the usual work-up and purification by chromatography, the acetate **2** (350 mg) was isolated: mp 86–87° (MeOH); $[\alpha]_D + 17.9°$ ($CHCl_3$; *c* 1); IR ν_{max}^{KBr} cm^{-1}: 3040, 2960, 2920, 2840, 1730, 1690, 1640, 1445, 1380, 1360, 1260, 1240, 1135, 1050, 1025, 855, 785, 745, 735; ^{1}H NMR (60 MHz): δ6.83 (1H, *br q*, $J = 6$ Hz, H-3′), 5.66 (1H, *br d*, $J = 6$ Hz, H-16), 5.43 (1H, *br d*, $J = 6$ Hz, H-15), 4.56 (1H, *br s*, H-14), 4.28 (1H, *d*, $J = 10.5$ Hz, H-19a), 3.88 (1H, *d*, $J = 10.5$ Hz, H-19b), 2.01 (3H, *s*, H-2″), 1.81 (3H, *br s*, H-5′), 1.76 (3H, *br d*, $J = 6$ Hz, H-4′), 0.94 (6H, *s*, H-17, H-18), 0.78 (3H, *s*, H-20); MS *m/z* (rel. int.): 428 $[M]^+$ (17), 328 $[M-TglOH]^+$ (13), 313 $[328-Me]^+$ (3), 300 (3), 285 (4), 268 $[328-AcOH]^+$ (4), 255 (6), 146 (11), 132 (11), 83 $[Tgl]^+$ (100), 55 $[Tgl-CO]^+$ (47), 44 (22).

ent-*Beyer-15-en-14β,19-diol* (**3**). Acetate **2** (154 mg) was refluxed with 5% KOH–MeOH (20 ml) for 48 hr. The MeOH was removed and the residue extracted with Et_2O, washed with H_2O, dried and evapd to yield **3** (91 mg) which was crystallized from C_6H_6. Compound **3** (68 mg) was obtained from **1** (157 mg) by hydrolysis with 5% KOH–MeOH under reflux for 2 hr; Mp 187–189° (C_6H_6); $[\alpha]_D + 51.4°$ ($CHCl_3$, *c* 1); IR ν_{max}^{KBr} cm^{-1}: 3480, 3380, 2960, 2840, 2760, 1400, 1390, 1340, 1050, 1020, 990, 965, 930, 720, 715; IR ν_{max}^{KBr} cm^{-1}: (5×10^{-3} M): 3635 (–CH_2OH), 3580 (CH–OH . . . H–C=C), 3050 (=C–H); ^{1}H NMR (60 MHz): δ5.63 (1H, *br d*, $J = 6$ Hz, H-16), 5.41 (1H, *br d*, $J = 6$ Hz, H-15), 3.76 (1H, *d*, $J = 10.5$ Hz, H-19a), 3.42 (1H, *d*, $J = 10.5$ Hz, H-19b), 2.94 (1H, *br s*, H-14), 1.03 (3H, *s*, H-17), 0.96 (3H, *s*, H-18), 0.73 (3H, *s*, H-20); MS *m/z* (rel. int.): 304 $[M]^+$ (55), 289 $[M-Me]^+$ (11), 286 $[M-H_2O]^+$ (11), 274 $[286-Me]^+$ (68), 273 $[M-CH_2OH]^+$ (61), 255 (44), 149 (47), 147 (48), 135 (61), 133 (50), 131 (44), 123 (52), 121 (77), 119 (58), 109 (58), 107 (77), 105 (68), 95 (71), 93 (71), 91 (77), 81 (100), 79 (65), 55 (58), 44 (61), 42 (52).

ent-*14β-Tigloyloxybeyer-15-en-19-oic acid* (**4**). Oil; $[\alpha]_D - 8.4°$ (EtOH, *c* 1.6); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: (4%): 3400–2400, 2945, 2920, 2840, 1685, 1640, 1445, 1370, 1260, 1140, 1075, 1040, 970; ^{1}H NMR (60 MHz): δ6.84 (1H, *br q*, $J = 6$ Hz, H-3′), 5.73 (1H, *br d*, $J = 6$ Hz, H-16), 5.43 (1H, *br d*, $J = 6$ Hz, H-15), 4.54 (1H, *br s*, H-14), 1.83 (3H, *br d*, H-5′), 1.77 (3H, *br d*, $J = 6$ Hz, H-4′), 1.22 (3H, s, H-18), 0.95 (3H, *s*, H-17), 0.72 (3H, *s*, H-20); ^{1}H NMR (200 MHz, C_3D_6O): δ6.77 (1H, *br q*, $J = 6$ Hz, H-3′), 5.72 (1H, *br d*, $J = 6$ Hz, H-16), 5.43 (1H, *br d*, $J = 6$ Hz, H-15), 4.49 (1H, *br s*, H-14), 1.77 (3H, *br s*, H-5′), 1.76 (3H, *br d*, $J = 6$ Hz, H-4′), 1.19 (3H, *s*, H-18), 0.90 (3H, *s*, H-17), 0.72 (3H, *s*, H-20); ^{13}C NMR (50.3 MHz, C_3D_6O): δ179.1 (*s*, C-19), 168.1 (*s*, C-1′), 136.9 (*d*, C-3′), 134.1 (*d*, C-16), 132.9 (*d*, C-15), 129.6 (*s*, C-2′), 94.9 (*d*, C-14), 56.9 (*d*, C-5), 54.0 (*s*, C-8), 53.0 (*d*, C-9), 48.9 (*s*, C-13), 44.0 (*s*, C-4), 40.4 (*t*, C-1), 38.8 (*s*, C-10), 38.6 (*t*, C-3), 33.1 (*t*, C-12), 32.3 (*t*, C-7), 29.4 (*q*, C-18), 21.5 (*t*, C-6), 20.5 (*t*, C-11), 20.0 (*t*, C-2), 19.6 (*q*, C-17), 14.6 (*q*, C-20), 14.2 (*q*, C-4′), 12.2 (*q*, C-5′).

Methyl ent-*14β-tigloyloxybeyer-15-en-19-oate* (**5**). Acid **4** was esterified with CH_2N_2, affording methyl ester **5** (69 mg): oil; $[\alpha]_D - 0.8°$ ($CHCl_3$, *c* 2.3); IR ν_{max}^{film} cm^{-1};2940, 2850, 1720, 1700, 1645, 1450, 1375, 1265, 1230, 1190, 1150, 1075, 1050, 970, 790, 735; ^{1}H NMR (200 MHz): δ6.78 (1H, *br q*, $J = 6$ Hz, H-3′), 5.65 (1H, *br d*, $J = 6$ Hz, H-16), 5.40 (1H, *br d*, $J = 6$ Hz, H-15), 4.49 (1H, *br s*, H-14), 3.58 (3H, *s*, COOMe), 1.76 (3H, *br s*, H-5′), 1.73 (3H, *br d*, $J = 6$ Hz, H-4′), 1.11 (3H, *s*, H-18), 0.89 (3H, *s*, H-17), 0.55 (3H, *s*, H-20); ^{13}C NMR: δ177.9 (*s*, C-19), 168.3 (*s*, C-1′), 136.6 (*d*, C-3′), 133.5 (*d*, C-16), 132.0 (*d*, C-15), 128.8 (*s*, C-2′), 94.3 (*d*, C-14), 56.3 (*d*, C-5), 53.3 (*s*, C-8), 52.1 (*d*, C-9), 51.1 (*q*, COOMe), 48.2 (*s*, C-13), 43.8 (*s*, C-4), 39.6 (*t*, C-1), 38.0 (*t*, C-3), 37.7 (*s*, C-10), 32.4 (*t*, C-12), 31.4 (*t*, C-7), 28.8 (*q*, C-18), 20.7 (*t*, C-6), 19.7 (*t*, C-11), 19.2 (*t*, C-2), 19.2 (*q*, C-17), 14.2 (*q*, C-4′), 13.9 (*q*, C-20), 12.0 (*q*, C-5′); MS *m/z* (rel. int.): 414 $[M]^+$ (7), 314 $[M-TglOH]^+$ (50), 299 $[314-Me]^+$ (19), 271 (19), 255 $[M-COOMe]^+$ (20), 254 (25), 239 (16), 185 (19), 159 (19), 147 (20), 131 (26), 121 (40), 119 (22), 117 (20), 105 (38), 91 (44), 83 $[Tgl]^+$ (100), 82 (74), 55 $[Tgl-CO]^+$ (94), 41 (21).

ent-*19-Acetoxy-14β-(2-methylbutyryloxy)-beyerane* (**10**). A soln of **2** (119 mg) in EtOH (10 ml) and Raney Ni (2 g) was stirred vigorously under H_2 for 1 hr at room temp. The liquid was decanted and the residue washed with MeOH. After filtration through silica gel, oily **10** (82 mg) was isolated: $[\alpha]_D - 15.4°$ ($CHCl_3$, *c* 2.3); IR ν_{max}^{film} cm^{-1}: 2920, 2840, 1725, 1450, 1380, 1360, 1230, 1175, 1140, 1070, 1020, 965, 980, 780; ^{1}H NMR (60 MHz): δ4.45 (1H, s, H-14), 4.23 (1H, *d*, $J = 10.5$ Hz, H-19a), 3.82 (1H, *d*, $J = 10.5$ Hz, H-19b), 2.03 (3H, *s*, H-2″), 1.16 (3H, *d*, $J = 7$ Hz, H-5′), 0.92 (6H, *s*, H-17, H-18), 0.90 (3H, *t*, $J = 7$ Hz, H-4′), 0.85 (3H, *s*, H-20); MS *m/z* (rel. int.): 432 $[M]^+$ (10), 360 $[M-CHOAc]^+$ (24), 331 (13), 330 $[M-C_5H_{10}O_2]^+$ (51), 315 $[330-Me]^+$ (10), 271 (15), 270 (51), 257 (23), 255 (14), 135 (2), 107 (36), 105 (35), 95 (37), 93 (40), 91 (44), 85 (54), 83 (100), 82 (62), 79 (45), 55 (42), 43 (94), 41 (50).

ent-*Beyeran-14β,19-diol* (**11**). A soln of **10** (50 mg) in dry Et_2O (5 ml) was gradually added to a stirred suspension of $LiAlH_4$ in dry Et_2O. The mixture was refluxed for 1.5 hr and after the usual work-up, alcohol **11** was obtained; Mp 216–217° (hexane–Me_2CO); $[\alpha]_D + 13.5°$ (EtOH, *c* 0.8); IR ν_{max}^{KBr} cm^{-1}: 3450, 2960, 2840, 1430, 1370, 1360, 1130, 1070, 1000, 960, 925; IR $\nu_{max}^{CCl_4}$ cm^{-1}: (5×10^{-3} M): 3635 (–CH_2OH, >CHOH, free); ^{1}H NMR (200 MHz, C_5D_5N): δ4.03 (1H, *d*, $J = 10.6$ Hz, H-19a), 3.63 (1H, *d*, $J = 10.6$ Hz, H-19b), 3.17 (1H, s, H-14), 1.23 (3H, *s*, H-17), 1.19 (3H, *s*, H-18), 0.99 (3H, s, H-20); ^{13}C NMR (50.3 MHz, C_5D_5N): δ91.4 (*d*, C-14), 64.4 (*t*, C-19), 57.1* (*d*, C-5), 56.7* (*d*, C-9), 49.5 (*s*, C-8), 44.1 (*s*, C-13), 40.4 (*t*, C-1), 39.2 (*s*, C-4), 39.2 (*t*, C-12), 38.2 (*s*, C-10), 37.2 (*t*, C-7), 36.1 (*t*, C-3), 31.7 (*d*, C-15), 30.0 (*d*, C-16), 28.1 (*q*, C-18), 22.6 (*q*, C-17), 20.4** (*t*, C-11), 20.3** (*t*, C-6), 18.7 (*t*, C-2), 16.3 (*q*, C-20); MS *m/z* (rel. int.): 306 $[M]^+$ (5), 276 $[M-CH_2O]^+$ (15), 275 $[M-CH_2OH]^+$ (34), 258 $[276-H_2O]^+$ (20), 257 $[275-H_2O]^+$ (36), 244 (6), 175 (20), 161 (26), 149 (22), 135 (29), 133 (28), 123 (54), 121 (55), 109 (61), 107 (55), 105 (44), 95 (75), 93 (78), 91 (64), 81 (100), 79 (73), 77 (34), 67 (77), 55 (86), 45 (99), 43 (88), 41 (78).

Methyl ent-14β-(2-methylbutyryloxy)-beyeran-19-oate (**6**). Compound **5** (120 mg) was hydrogenated over Raney Ni in EtOH at room temp. for 1 hr to yield **6** (79 mg); oil; IR ν_{max}^{film} cm^{-1}: 2940, 2865, 2845, 1725, 1460, 1375, 1335, 1260, 1235, 1190, 1155, 1075, 1025, 970, 810; ^{1}H NMR (60 MHz): δ4.45 (1H, s, H-14), 3.63 (3H, *s*, COOMe), 1.20 (3H, *d*, $J = 7$ Hz, H-5′), 1.16 (3H, s, H-18), 0.93 (3H, *t*, $J = 7$ Hz, H-4′), 0.87 (3H, s, H-17), 0.76 (3H, *s*, H-20).

Methyl ent-*14-β-hydroxy-beyeran-19-oate* (**7**). Compound **6** (57 mg) was hydrolysed with 10% KOH–MeOH, stirred at room temp. for 24 hr, affording **7** (41 mg); Mp 179–180° (hexane);

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IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3520, 2975, 2940, 2860, 1690, 1440, 1365, 1240, 1185, 1165, 1145, 1080, 1010, 965, 830, 770; ^{1}H NMR (60 MHz): δ3.63 (3H, *s*, COOMe), 2.93 (1H, *s*, H-14), 1.16 (3H, *s*, H-18), 0.98 (3H, *s*, H-17), 0.73 (3H, *s*, H-20).

Methyl ent-*beyeran*-14-*one*-19-*oate* (**8**). Pyridinium chlorochromate (PCC 40 mg) was gradually added to a stirred soln of **7** (38 mg) in CH_2Cl_2 (20 ml). After 2 hr at room temp. the mixture was worked-up to give **8** (35 mg); mp 119–120° (hexane); CD: $\Delta\varepsilon_{300}+1.08$ (hexane); IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 2940, 2860, 1715, 1440, 1370, 1225, 1190, 1145, 970, 910, 855, 805, 770; ^{1}H NMR (200 MHz): δ3.64 (3H, *s*, COOMe), 2.51 (1H, *m*, H-11), 2.16 (1H, *dddd*, $J = 13.17$, 3.50, 3.50, 1.61 Hz, H-11), 1.18 (3H, *s*, H-18), 0.99 (3H, *s*, H-17), 0.84 (3H, *s*, H-20); ^{13}C NMR: δ222.7 (*s*, C-14), 177.8 (*s*, C-19), 59.3 (*d*, C-9), 56.0 (*d*, C-5), 51.1 (*s*, C-8), 51.1 (*q*, COOMe), 46.8 (*s*, C-13), 43.8 (*s*, C-4), 42.1 (*t*, C-12), 40.3 (*t*, C-1), 39.1 (*s*, C-10), 37.9 (*t*, C-3), 32.6 (*t*, C-7), 30.3 (*t*, C-15), 28.9 (*q*, C-18), 27.4 (*t*, C-16), 20.2 (*t*, C-6), 19.5 (*t*, C-11), 19.5 (*q*, C-17), 19.0 (*t*, C-2), 13.7 (*q*, C-20); MS *m/z* (rel. int.): 332 $[M]^+$ (33), 304 $[M-CO]^+$ (9), 273 $[M-COOMe]^+$ (30), 272 $[M-COHOMe]^+$ (49), 257 $[272-Me]^+$ (10), 255 (14), 245 (10), 230 (20), 189 (8), 175 (14), 166 (20), 149 (22), 135 (33), 123 (100), 107 (67), 93 (70), 81 (67), 67 (50), 55 (70), 41 (86), 18 (31).

ent-*Beyeran*-14α,19-*diol* (**9**). Compound **8** (30 mg) was reduced with $LiAlH_4$ in Et_2O as above, affording diol **9** (25 mg); mp 203–204° (hexane–EtOAc); $[\alpha]_D+1.54°$ (EtOH; *c* 1.6) [Lit. [19], enantiomer $-10°$ (*c*, 0.18)]; IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3390, 2930, 2850, 1440, 1365, 1245, 1100, 1025, 970, 850; ^{1}H NMR (200 MHz, C_5D_5N): δ4.07 (1H, *d*, $J = 10.8$ Hz, H-19a), 3.66 (1H, *d*, $J = 10.8$ Hz, H-19b), 3.14 (1H, *s*, H-14), 1.18 (3H, *s*, H-18), 1.12 (3H, *s*, H-17), 1.00 (3H, *s*, H-20); ^{13}C NMR (50.3 MHz, C_5D_5N); δ83.3 (*d*, C-14), 64.4 (*t*, C-19), 57.0 (*d*, C-5), 47.1 (*d*, C-9), 45.9 (*s*, C-8), 40.6 (*s*, C-13), 40.3 (*t*, C-1), 39.5 (*t*, C-7), 39.2 (*s*, *C*-4), 37.6 (*s*, C-10), 36.2 (*t*, C-3), 32.9 (*t*, C-12), 32.6 (*t*, C-15), 30.0 (*t*, C-16), 28.0 (*q*, C-18), 25.7 (*q*, C-17), 20.6* (*t*, C-11), 20.2* (*t*, C-6), 18.7 (*t*, C-2), 16.3 (*q*, C-20); MS *m/z* (rel. int.): 306 $[M]^+$ (8), 288 $[M-H_2O]^+$ (4), 276 $[M-CH_2O]^+$ (47), 275 $[M-CH_2OH]^+$ (100), 257 (71), 245 (4), 229 (3), 201 (6), 187 (18), 175 (34), 161 (16), 149 (14), 135 (15), 123 (28), 109 (29), 95 (34), 81 (49), 67 (34), 55 (53), 41 (51), 29 (24), 18 (29).

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*Assignments may be reversed.