Journal of Natural Products
Vol. 49, No. 2, pp. 259-264, Mar-Apr 1986

NEW KAURANE DITERPENOIDS FROM THE ROOTS OF *ELAEOSELINUM TENUIFOLIUM*[1]

MANUEL GRANDE,

Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad de Salamanca, Plaza de los caidos 1, 37008 Salamanca, Spain

MIGUEL SEGURA, and BALBINO MANCHEÑO

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apartado 99, 03080 Alicante, Spain

ABSTRACT.—The C_6H_6 extract from the roots of *Elaeoselinum tenuifolium* afforded two new tetracyclic diterpenes identified as *ent*-15α-angeloyloxykaur-16-en-3β-ol and *ent*-15α-angeloyloxy-16β,17-epoxykauran-3β-ol, as evidenced by spectral data and chemical transformations. 2-Isopropylmethylanisole, thymoquinol dimethyl ether, apiol, and β-sitosterol were also isolated.

In our search for new natural substances from plants endemic to Comunidad Valenciana (East Spain), we have examined the chemical constituents of the roots of *Elaeoselinum tenuifolium* (Lag) Lange (Umbelliferae), also known as *Thapsia tenuifolia* Lag. and *Elaeoselinum lagascae* Boiss.

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 minor components (1). The diterpenes are quite uncommon in these plants; however, some of them have been reported: labdane acids from *Hermes villosa* (2), magydardienediol and other monocyclic derivatives from *Magydaris panacifolia* (3), and also tetracyclic diterpenes from *Elaeoselinum gummiferum* (4-6) and *Elaesoselinum foetidum* (7). We have also found diterpenes with beyerane, kaurane, and atisane skeletons in the roots of *Elaesoselinum asclepium* (8), and in the present study, we report the structural identification of the new kaurane derivatives **1** and **14**.

RESULTS AND DISCUSSION

The C_6H_6 extract from the roots of the plant (3.9%, dry weight) was defatted with MeOH, and the soluble portion was separated into neutral and acidic fractions with 4% aqueous NaOH. The neutral fraction in Et_2O afforded, on standing, a crystalline product from which compounds **1** and **14** were isolated by chromatography on silica gel. The noncrystalline material provided further amounts of the above compounds and sitosterol (9), 2-isopropyl-4-methylanisole (10), thymoquinol dimethyl ether (11), and apiol (12).

Compound **1**, which represents nearly one-third of the C_6H_6 extract, showed in the ms a molecular ion M^+ at *m/z* 386 in agreement with the formula $C_{25}H_{38}O_3$. The ir spectrum showed absorption bands of hydroxyl (3360 cm^{-1}), conjugated ester (1715 cm^{-1}) and methylidene groups (3070, 1650, 880 cm^{-1}). The ^{1}H-nmr spectrum confirmed the presence of an exocyclic methylene group [δ 4.91 (d, J=2.4 Hz, H-17b), 4.87 (m, $W_{1/2}$=5 Hz, H-17a)], one proton geminal to an ester group [δ 5.23 (t, J=2.4 Hz, H-15)], and one proton geminal to a hydroxyl group [δ 3.17, m, X (ABX), J_{AX+BX}=16.3 Hz, H-3].

The ester group was identified as an angelate as deduced from the characteristic ^{1}H-nmr signals [δ 6.07 (qq, J=7.2 and 1.4 Hz, H-3′), 2.00 (dq, J=7.2 and 1.4 Hz, Me-

[1]Dedicated to Professor Joaquín de Pascual Teresa on the occasion of his 70th birthday. Presented at the "XX Reunión Bienal de la R.S.E.Q.," Castellón, Spain, September 1984.

4′) and 1.91 (qnt, J=1.4 Hz, Me-5′)], ^{13}C-nmr signals [δ 168.0 (s, C-1′), 138.1 (d, C-3′), 128.1 (s, C-2′), 20.8 (q, Me-5′), 15.8 (q, Me-4′)] (5,13), as well as from the ms fragments at *m/z* 286, 83, and 55 (14). Furthermore, the alkaline hydrolysis of **1** with 5% KOH/MeOH yielded tiglic acid, isomerization product of angelic acid, and the alcohol **3**.

According to the molecular formula, the ^{1}H- and the ^{13}C-nmr data, it was concluded that **1** was a tetracyclic diterpene with one methylidene group, one equatorial secondary hydroxyl group, and one secondary angeloyloxy group. These functional groups can be accommodated on the common tetracyclic diterpene skeletons beyerane, atisane, kaurane, or phyllocladane. The presence of one exocyclic methylene and three quaternary methyl groups in **1** (δ 1.02, 0.93, 0.74) let us discount a beyerane skeleton. The chemical shift of the methinic allylic proton (H-12 in atisane, H-13 in kaurane and phyllocladane), which resonates at δ 2.66, also allowed us to discard the atisane skeleton. In atisane derivatives, the allylic proton H-12 generally absorbs at ca. δ 2.3 ppm (6).

The ^{13}C-nmr spectrum supported a kaurane skeleton for **1** and allowed us to assign the position of the substituents. According to the available data (5, 6, 15-19), the chemical shift for the quaternary C-10 in kauranes appears at δ>38.8, perhaps because of a γ-*gauche* effect between C-10 and C-12, whereas for phyllocladane derivatives (C-10 and C-12 *anti*), the C-10 signal occurs at higher fields (δ<37.8). As all carbon singlet signals of **1** appear above δ 38.8 (see Experimental section), we tentatively assigned a kaurane skeleton to our diterpene.

The location of the angeloyloxy and hydroxy groups in the 16-kaurene skeleton was deduced as follows. The signal of the geminal proton to the angeloyloxy group [δ 5.23 (t, J=2.4 Hz)] collapses to a singlet by irradiation of the exocyclic methylidene protons, and this fixed the ester group at C-15. The signal of the geminal proton to the free hydroxyl appears as a multiplet at 3.17 (six lines, J_{AX+BX}=16.3 Hz) (20), also observed in other terpenoids when an equatorial hydroxyl group is flanked by a quaternary carbon and a -CH_2- group, and, consequently, the secondary hydroxyl group could be placed either at C-1, at C-3, or at C-7. This hydroxyl group was placed at C-3 according to the ^{13}C-nmr data, fully consistent with the chemical shifts observed for other 3β-hydroxy polycyclic diterpenoids and triterpenoids (19).

The observed deshielding for H-15 in compounds **1-5** suggests the *endo*-(=*ent*-15α) configuration for the angeloyloxy group. Also the ^{13}C-chemical shifts calculated for the *endo*-configuration of the 15-hydroxyl group (16) are nearly the same as observed (Δδ<0.4 ppm), but the calculated shifts for the *exo*-15-hydroxyl are rather different from those observed, particularly for C-8, C-9, C-13, C-14, C-16, and C-17 (Δδ 2-3 ppm). The *endo*-configuration was also supported by chemical transformation of diol **3**. Treatment of this diol with concentrated HCl/MeOH easily gave the rearranged ketone **6**. This rearrangement is difficult in the case of the *exo*-(=*ent*-15β) configuration (21).

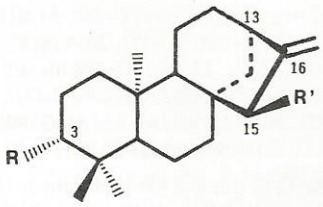
The absolute configuration for **1** was proposed according to the cd spectrum of **4**. The observed Cotton effect [Δε−0.97 (293 nm)] suggests that these kaurane derivatives belong to *enantio*-series.

Lastly, the structure of **1** was confirmed by transformation into the known kaurane derivatives **7** and **9** (22). Kauranol **7** was first isolated in low yield from the Huang-Minlon reduction products from **4**. Further amounts of **7** were obtained as follows. Dehydration of **1** via tosylate **5** gave the alkene **10** which was hydrolyzed to **11**.[2] Catalytic hydrogenation of **11** (PtO_2/HOAc) yielded a mixture of **7** and **9**. Rearrangement of **11**

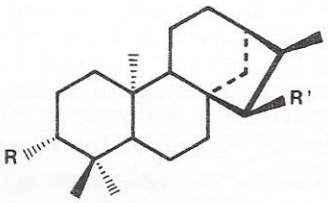
[2]We observed that on standing, **11** was partially oxidized into the ketone **12**.

with concentrated HCl/MeOH to give **13**, followed by catalytic hydrogenation, yielded only the ketone **9**.

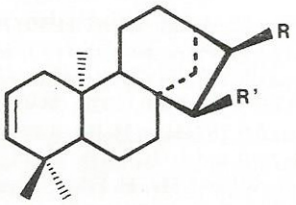
The natural compound **14** showed a molecular ion at *m/z* 402, which corresponds to the molecular formula $C_{25}H_{38}O_4$. The spectra of **1** and **14** are quite similar, but the ^{1}H-nmr and ir traces of **14** revealed the absence of the exocyclic methylidene group signals. On the contrary, the nmr spectrum of **14** showed a broad singlet at δ 2.80 which was assigned to an epoxidic methylene group. The proposed structure for **14** was confirmed by epoxidation of **1** with *m*-CPBA, which results in a compound identical in all aspects to **14**. Assuming that the epoxidation took place by peroxyacid attack from the less hindered *exo*-side, the *ent*-16β configuration was proposed for **14**.



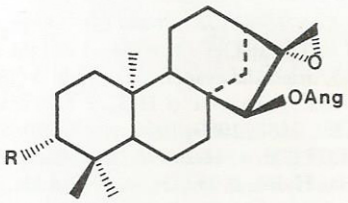
	R	R'
1	OH	OAng
2	OAc	OAng
3	OH	OH
4	=O	OAng
5	OTs	OAng



	R	R'
6	OH	=O
7	H	OH
8	H	OAc
9	H	=O



	R	R'
10	$=CH_2$	OAng
11	$=CH_2$	OH
12	$=CH_2$	=O
13	CH_3	=O



14 R=OH
15 R=OAc

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Spectra were recorded with the following instruments: uv, B & L Spectronic 2000; ir, Pye Unicam SP-200 and SP-2000; nmr, Brucker WP 200 (^{1}H, 200 MHz; ^{13}C, 50.3 MHz) and Varian EM 360L (60 MHz) recorded in $CDCl_3$ with TMS as internal standard (scale δ in ppm); e.i., mass spectra, Hewlett-Packard 5930A with direct inlet probe at 70 eV; Optical Activity AA-100 polarimeter; cd spectra, Jobin Yvon Dichrograph Mark III.

EXTRACTION AND ISOLATION.—The plant was collected at "Cabo las Huertas" Alicante, Spain, and a voucher specimen was deposited in the Department of Biology, University of Alicante. The air-dried roots of *E. tenuifolium* (1.34 kg) were extracted with C_6H_6 in a Dean-Stark apparatus. The C_6H_6 extract (58.8 g, 3.9% weight of dried roots) was treated with MeOH, and the soluble portion (45.5 g) was separated with Et_2O and 4% NaOH into neutral and acidic fractions.

The neutral fraction (35.9 g) in Et_2O afforded a crystalline mixture (15.8 g) containing mainly **1** and **14**, which were isolated by dry column chromatography with hexane-EtOAc (8:2). The mother liquor (18.8 g) was chromatographed on silica gel (Merck ref. 7733, 500 g) in a column packed with hexane, using hexane/EtOAc mixtures as eluent. The concentration of EtOAc was gradually increased, and 88 fractions, each 250 ml, were collected. Fractions 13-14, eluted with hexane-EtOAc (97:3), contained 2-iso-

propyl-4-methylanisole. Thymoquinol dimethyl ether was isolated by rechromatography from fraction 15, and apiol was isolated from fraction 19. Fractions 53-59, eluted with hexane-EtOAc (9:1), afforded a mixture of two substances. Compound **1** crystallized from the mixture (2.3 g), and sitosterol was purified from the mother liquor after chromatography. Fraction 64-83 eluted with hexane-EtOAc (7:3) afforded **14** (0.6 g), which was purified by crystallization.

ent-*15α-Angeloyloxykaur-16-en-3β*-ol (**1**).—Rf 0.4 (hexane-EtOAc, 8:2), needles mp 120-121° (hexane); $[\alpha]_D$ −89° ($CHCl_3$, c 1.1); uv λ max (EtOH) 218 nm (log ε 3.9); ir ν max (KBr) 3360, 3070, 2920, 2860, 1715, 1650, 1450, 1380, 1220, 1150, 1040, 880, 840 cm^{-1}; ^1H nmr (200 MHz) δ 0.74 (3H, s, H-19), 0.93 (3H, s, H-18), 1.02 (3H, s, H-20), 1.91 (3H, qnt, J=1.4 Hz, H-5′), 2.00 (3H, dq, J=7.2 and 1.4 Hz, H-4′), 2.66 (1H, m, H-13), 3.17 (1H, m, X (ABX), J_{AX+BX}=16.3 Hz, H-3),[3] 4.87 (1H, m, W½=5 Hz, H-17a), 4.91 (1H, d, J=2.4 Hz, H-1b), 5.23 (1H, t, J=2.4 Hz, H-15), 6.07 (1H, qq, J=7.2 and 1.4 Hz, H-3′); ^{13}C nmr[4] δ 168.1 (s, C-1′), 153.9 (s, C-16), 138.1 (s, C-2′), 106.3 (t, C-17), 81.2 (d, C-15), 78.9 (d, C-3), 54.9 (d, C-5), 48.2 (d, C-9), 46.0 (s, C-8), 40.8 (d, C-13), 39.0 (s, C-10*), 39.0 (t, C-14**), 38.8 (s, C-4*), 38.8 (t, C-1**), 36.5 (t, C-7), 33.5 (t, C-12), 28.4 (q, C-18), 27.4 (t, C-2), 20.8 (q, C-5′), 19.6 (t, C-6), 17.8 (q, C-20), 15.8 (q, C-4′), 15.6 (q, C-19); ms *m/z* (%) 386 $[M]^+$ (3), 303 $[M\text{-}Ang]^+$ (0.5), 286 $[M\text{-}AngOH]^+$ (20), 271 $[286\text{-}Me]^+$ (10), 268 $[286\text{-}H_2O]^+$ (5), 253 $[271\text{-}H_2O]^+$ (9), 243 $[271\text{-}C_2H_4]^+$ (7), 225(4), 145(5), 119(7), 105(12), 91(19), 83 $[Ang]^+$ (100), 55 $[Ang\text{-}CO]^+$ (62), 41(47). *Anal.* calcd for $C_{25}H_{38}O_3$: C, 77.68; H, 9.91. Found: C, 77.88; H, 10.10.

Acetate **2**.—The alcohol **1** (290 mg) in pyridine (1 ml) and Ac_2O (2 ml) was left overnight at room temperature. After usual work up, acetate **2** (275 mg) was isolated, mp 94-95° (hexane); $[\alpha]_D$ −75° ($CHCl_3$, c 1.2); ir ν max (KBr) 3080, 2940, 2860, 1735, 1715, 1660, 1645, 1480, 1460, 1440, 1380, 1370, 1250, 1150, 885, 760 cm^{-1}; ^1H nmr (60 MHz) δ 0.84 (6H, s, H-18 and H-19), 1.07 (3H, s, H-20), 1.96 (3H, br s, H-5′), 2.03 (3H, br d, J=7 Hz, H-4′), 2.03 (3H, s, H-2″), 2.70 (1H, m, H-13), 4.46 (1H, dd, J=9 and 7 Hz, H-3), 4.92 (2H, br s, H-17), 5.26 (1H, t, J=2.5 Hz, H-15), 6.13 (1H, br q, J=7 Hz, H-3′); ms *m/z* (%) 428 $[M]^+$ (2), 368 $[M\text{-}AcOH]^+$ (4), 345 $[M\text{-}Ang]^+$ (2), 328 $[M\text{-}AngOH]^+$ (5), 313(2), 286(6), 268(6), 253(9), 243(3), 255(3), 145(2), 131(5), 121(6), 105(7), 91(12), 83 $[Ang]^+$ (100), 55 $[Ang\text{-}CO]^+$ (39), 43(52), 29(13).

ent-*Kaur-16-en-15α,3β-diol* (**3**).—Compound **1** (185 mg) was refluxed with 5% KOH/MeOH (20 ml) for 7 h. The MeOH was removed and the residue taken up in H_2O and extracted with Et_2O, washed with H_2O, dried and evaporated to yield **3** (135 mg), which was crystallized from C_6H_6 as white prisms; mp 167-168°; $[\alpha]_D$ −61° ($CHCl_3$, c 1.4); ir ν max (KBr) 3430, 3350, 3060, 2960, 2920, 2830, 1660, 1440, 1280, 1180, 1080, 1060, 1025, 990, 880, 865 cm^{-1}; ^1H nmr δ 0.78 (3H, s, H-19), 0.98 (3H, s, H-18), 1.03 (3H, s, H-20), 2.70 (1H, m, H-13), 3.21 (1H, dd, J=9 and 7 Hz, H-3), 3.75 (1H, t, J=2.4 Hz, H-15), 4.95 (1H, d, J=2.8 Hz, H-17a), 5.09 (1H, m, W½=5 Hz, H-17b); ^{13}C nmr[4] δ 158.6 (s, C-16), 104.8 (t, C-17), 82.4 (d, C-15), 79.0 (d, C-3), 54.6 (d, C-5), 46.5 (d, C-9), 45.7 (s, C-8), 40.2 (d, C-13), 38.9 (s, C-10*), 38.9 (t, C-14**), 38.8 (t, C-1**), 38.8 (s, C-4*), 36.5 (t, C-7), 33.3 (t, C-12), 28.4 (q, C-18), 27.5 (t, C-2), 19.7 (t, C-6), 18.2 (t, C-11), 17.6 (q, C-20), 15.5 (q, C-19); ms *m/z* (%) 304 $[M]^+$ (35), 289 $[M\text{-}Me]^+$ (22), 286 $[M\text{-}H_2O]^+$ (33), 271 $[286\text{-}Me]^+$ (58), 253 $[271\text{-}H_2O]^+$ (20), 246(55), 203(28), 173(18), 164(16), 147(33), 121(45), 107(55), 91(63), 84(70), 83(20), 81(57), 67(50), 55(70), 43(57), 41(100).

ent-*(16S)-3β-Hydroxykauran-15-one* (**6**).—The diol **3** (64 mg) in MeOH (10 ml) and Et_2O (5 ml) was treated with concentrated HCl (2 ml) for 24 h at room temperature. Removal of the solvents and recovery of the product with Et_2O gave **6**; mp 158-159° (hexane); $[\alpha]_D$ −80° ($CHCl_3$, c, 1.0); λ max (EtOH) 204 nm (log ε 4.1); cd (hexane) Δε-1.04 (308 nm); cd (MeOH) Δε-0.53 (308 nm) and +0.09 (276 nm); ir ν max (KBr) 3520, 3300, 2920, 2860, 1725, 1470, 1440, 1380, 1365, 1175, 1090, 1036, 990, 920 cm^{-1}; ^1H nmr (200 MHz) δ 0.77 (3H, s, H-19), 0.98 (3H, s, H-18), 1.06 (3H, s, H-20), 1.09 (3H, d, J=7 Hz, H-17), 2.22 (1H, qnt, J=7 Hz, H-16), 2.42 (1H, m, H-13), 2.43 (1H, br d, J=2 Hz, H-14), 3.19 (1H, m, six lines, X (ABX), J_{AX+BX}=16.3 Hz, H-3); ^{13}C nmr δ 202.3 (s, C-15), 78.8 (d, C-3), 54.5 (d, C-5), 52.5 (s, C-8), 52.4 (d, C-9), 47.8 (d, C-16), 39.4 (s, C-10), 38.9 (s, C-4), 37.9 (t, C-1), 37.5 (t, C-7), 35.0 (d, C-13), 34.3 (t, C-14), 28.2 (q, C-18), 27.1 (t, C-2), 24.8 (t, C-12), 18.7 (t, C-6), 18.1 (t, C-11), 17.8 (q, C-20), 15.4 (q, C-19), 10.1 (q, C-17); ms *m/z* (%) 304 $[M]^+$ (65), 289 $[M\text{-}Me]^+$ (9), 286 $[M\text{-}H_2O]^+$ (10), 271 $[289\text{-}H_2O]^+$ (15), 253(8), 246(100), 228(21), 213(43), 135(51), 107(43), 93(45), 79(41), 69(40), 55(50), 41(62).

ent-*15α-Angeloyloxykaur-16-en-3-one* (**4**).—Pyridinium chlorochromate (PCC, 300 mg) was gradually added to a stirred solution of **1** (250 mg) in $CHCl_3$ (20 ml). After 4 h at room temperature, the mixture was worked up to give **4** (211 mg), gummy; $[\alpha]_D$ −106° ($CHCl_3$, c 2.3); cd (hexane) Δε-0.97 (293 nm); ir

[3]This signal at 60 MHz appeared as a dd, J=9 and 7 Hz.

[4](*, **) Assignments may be reversed.

ν max (film) 3060, 2930, 2860, 1710, 1450, 1380, 1230, 1150, 1040, 960, 940, 890, 845 cm^{-1}; ^1H nmr δ 1.03 (3H, s, H-19), 1.06 (3H, s, H-18), 1.13 (3H, s, H-20), 1.96 (3H, br s, H-5′), 2.03 (3H, br d, J=7 Hz, H-4′), 2.70 (1H, m, H-13), 4.93 (2H, br s, H-17), 5.30 (1H, t, J=2.5 Hz, H-15), 6.13 (1H, br q, J=7 Hz, H-3′); ms *m/z* (%) 384 $[M]^+$ (1), 369 $[M-Me]^+$ (1), 301 $[M-Ang]^+$ (1), 284 $[M-AngOH]^+$ (5), 269 $[284-Me]^+$ (4), 256(1), 227(1), 199(2), 131(3), 93(6), 83 $[Ang]^+$ (100), 67(5), 55 $[Ang-CO]^+$ (61), 41(23).

ent-*(16S)-Kauran-15*α-ol (**7**).—A solution of **4** (140 mg) in diethyleneglycol (4 ml) was refluxed with 80% hydrazine hydrate (1 ml) for 2 h. KOH (300 mg) was added, refluxed for 45 min and then for 1 h to remove the excess of H_2O and hydrazine hydrate; the remaining solution was refluxed for 3 h. The crude product was extracted with Et_2O and purified on a small silica gel column and crystallized from MeOH; mp 133-134°; $[\alpha]_D$ −50° ($CHCl_3$, c 1.8); ir ν max (KBr) 3380, 2980, 2920, 2880, 2850, 1460, 1450, 1365, 1100, 1020, 990 cm^{-1}; ^1H nmr (60 MHz) δ 0.80 (3H, s, H-19), 0.83 (3H, s, H-18), 0.93 (3H, d, J=7 Hz, H-17), 1.01 (3H, s, H-20), 3.60 (1H, d, J=11 Hz, H-15); ms *m/z* (%) 290 $[M]^+$ (58), 275 $[M-Me]^+$ (89), 257 $[275-H_2O]^+$ (12), 231(29), 137(33), 123(28), 107(34), 91(47), 69(50), 55(70), 41(100), 29(44).

Acetate **8**.—The alcohol **7** (34 mg) upon treatment with Ac_2O/Py as above gave **8** (21 mg); mp 111-112° (MeOH); ir ν max (KBr) 2990, 2940, 2920, 2860, 2840, 1720, 1440, 1365, 1230, 1085, 1050, 1015, 915 cm^{-1}; ^1H nmr (200 MHz) δ 0.80 (3H, s, H-19), 0.83 (3H, d, J=7 Hz, H-17), 0.84 (3H, s, H-18), 1.03 (3H, s, H-20), 2.11 (3H, s, H-2′), 2.36 (1H, ddq, $J_{15\text{-}16}$=11, J_d=7.2 and J_q=7 Hz, H-16), 4.76 (1H, d, J=11 Hz, H-15).

Tosylate (**5**).—The alcohol **1** (687 mg) was dissolved in pyridine (10 ml) and treated at 0° with *p*-toluensulphonyl chloride (800 mg) for 1 h. The mixture was left at 0° for 48 h and monitored by tlc. The product was extracted with Et_2O, washed with 2 N HCl, 5% $NaHCO_3$, and H_2O and dried over anhydrous Na_2SO_4. The crude product (503 mg) was crystallized from hexane; mp 130-131°; $[\alpha]_D$ −66° ($CHCl_3$, c 1.9); ir 3080, 2940, 2870, 1700, 1640, 1595, 1440, 1360, 1225, 1175, 1155, 1095, 920, 875, 710, 670 cm^{-1}; ^1H nmr (60 MHz) δ 0.80 (6H, s, H-18 and H-19), 1.03 (3H, s, H-20), 1.96 (3H, br s, H-5′), 2.03 (3H, br d, J=7 Hz, H-4′), 2.42 (3H, s, Me-Ar), 2.67 (1H, m, H-13), 4.26 (1H, dd, J=9 and 7 Hz, H-3), 4.90 (2H, br s, H-17), 5.21 (1H, t, J=2.5 Hz, H-15), 6.13 (1H, br q, J=7 Hz, H-3′), 7.30 (2H, d, J=8.5 Hz, H_m-Ar), 7.80 (2H, d, J=8.5 Hz, H_o-Ar); ms *m/z* (%) 540 $[M]^+$ (5), 497(11), 458(11), 440 $[M-AngOH]^+$ (17), 425 $[440-Me]^+$ (12), 368(56), 325(35), 286(50), 268(59), 253(55), 225(53), 172(26), 107(29), 83 $[Ang]^+$ (100), 55 $[Ang-CO]^+$ (46).

ent-*15*α-*Angeloyloxykaur-2,16-diene* (**10**).—A solution of **5** (803 mg) in quinoline was refluxed at 160° for 1.5 h. H_2O was added, and the product was extracted with Et_2O and washed with 2 N HCl, 5% $NaHCO_3$, and H_2O. Dried over anhydrous Na_2SO_4, the reaction product was purified by column chromatography on silica gel to yield **10** (450 mg), oil; $[\alpha]_D$ −101° ($CHCl_3$, c 1.10); ir ν max (film) 3060, 2920, 2860, 1710, 1645, 1450, 1375, 1360, 1225, 1150, 1045, 990, 965, 940, 885, 845, 750, 735, 720 cm^{-1}; ^1H nmr (60 MHz) δ 0.88 (3H, d, H-19), 0.95 (3H, br d, J=7 Hz, H-4′), 2.73 (1H, m, H-13), 4.93 (2H, br s, H-17), 5.26 (1H, t, J=2.5 Hz, H-15), 5.40 (2H, d, AB(X), H-2 and H-3), 6.10 (1H, br q, J=7 Hz, H-3′).

ent-*Kaur-2,16-diene-15*α-*ol* (**11**).—Compound **10** (350 mg) was hydrolyzed with 5% KOH/MeOH at room temperature for 6 h, affording **11** (219 mg) as an oil; $[\alpha]_D$ −69° ($CHCl_3$, c 2.7); ir ν max (film) 3410, 3060, 2920, 2850, 1655, 1640, 1440, 1370, 1360, 1250, 1120, 1070, 1050, 990, 885, 720 cm^{-1}; ^1H nmr (60 MHz) δ 0.86 (3H, s, H-19), 0.93 (3H, d, H-18), 1.05 (3H, s, H-20), 2.68 (1H, m, H-13), 3.76 (1H, t, J=2.5 Hz, H-15), 4.93 (1H, d, J=3 Hz, H-17a), 5.06 (1H, m, W½=5 Hz, H-17b), 5.38 (2H, m, AB(X), H-2 and H-3).

Catalytic hydrogenation of **11** (60 mg) with H_2/PtO_2-HOAc (see below), afforded a 1:1 mixture of **7** and **9**.

ent-*Kaur-2,16-diene-15-one* (**12**).—The alcohol **11**, on standing in contact with the air at room temperature, was partially oxidized to **12**. After chromatography and crystallization from MeOH showed: mp 100-101°; $[\alpha]_D$ −208° ($CHCl_3$, c 1.0); uv λ max (EtOH) 232 nm (log ε 3.8); ir ν max (KBr) 3060, 2920, 2850, 1710, 1630, 1440, 1250, 1190, 1160, 1045, 1035, 960, 940, 925, 715 cm^{-1}; ^1H nmr (60 MHz) δ 0.92 (3H, s, H-19), 0.98 (3H, s, H-18), 1.15 (3H, s, H-20), 3.06 (1H, m, H-13), 5.23 (1H, br s, H-17a), 5.40 (2H, m, AB(X), H-2 and H-3), 5.97 (1H, br s, H-17b); ms *m/z* (%) 284 $[M]^+$ (100), 269 $[M-Me]^+$ (32), 251(12), 229(35), 144(22), 136(22), 119(30), 105(41), 91(41), 77(26), 67(14), 55(18), 41(26).

ent-*(16S)-Kaur-2-ene-15-one* (**13**).—Treatment of **11** (75 mg) with concentrated HCl in MeOH/Et_2O (see above **6**), afforded **13** (40 mg); mp 107-108° (EtOH); ir ν max (KBr) 3010, 2920, 2860, 1725, 1450, 1370, 725 cm^{-1}; ^1H nmr (60 MHz) δ 0.88 (3H, s, H-19), 0.96 (3H, s, H-18), 1.10 (3H, s, H-20), 1.10 (3H, d, J=7 Hz, H-17), 5.38 (2H, m, AB(X), H-2 and H-3).

ent-*(16S)-Kauran-15-one* (**9**).—A solution of **13** (40 mg) in HOAc (5 ml) and a catalytic amount of PtO_2 (2 mg) was strongly stirred under H_2 for 6 h at room temperature. After usual work up, **9** was isolated; mp 145-147° (Me_2CO); $[\alpha]D$ −92° ($CHCl_3$, c 0.3); ir ν max (KBr) 2920, 2860, 1725, 1480, 1450, 1385, 1370, 970, 920 cm^{-1}; ^1H nmr (60 MHz) δ 0.80 (3H, s, H-19), 0.86 (3H, s, H-18), 1.07 (3H, s, H-20), 1.10 (3H, d, J=7 Hz, H-17); ms *m/z* (%) 288 $[M]^+$ (59), 273 $[M\text{-}Me]^+$ (25), 255(9), 245(13), 230(100), 215(48), 149(12), 137(28), 123(40), 121(15), 107(23), 91(31), 55(36), 41(39).

ent-*15α-Angeloyloxy-16β,17-epoxykaurane-3β-ol* (**14**).—Isolated from fractions 64-83 of the main chromatography. Needles; mp 129-130° (hexane); $[\alpha]D$ −22° ($CHCl_3$, c 1.3); ir ν max (KBr) 3360, 2940, 2870, 1715, 1650, 1460, 1380, 1230, 1150, 1045, 850 cm^{-1}; ^1H nmr (60 MHz) δ 0.78 (3H, s, H-19), 0.96 (3H, s, H-18), 1.07 (3H, s, H-20), 1.93 (3H, br s, H-5′), 2.03 (3H, br d, J=7 Hz, H-4′), 2.80 (2H, s, H-17), 3.20 (1H, dd, J=9 and 7 Hz, H-3), 5.03 (1H, br s, H-15), 6.13 (1H, br q, J=7 Hz, H-3′); ms *m/z* (%) 402$[M]^+$ (0.5), 384 $[M\text{-}H_2O]^+$ (6), 284 $[302\text{-}H_2O]^+$ (7), 269 $[284\text{-}Me]^+$ (7), 251(3), 135(9), 91(10), 83 $[Ang]^+$ (100), 81(10), 79(9), 69(9), 55 $[Ang\text{-}CO]^+$ (48), 43(20), 41(25).

Epoxidation of **1** (70 mg) with *m*-chloroperoxybenzoic acid (40 mg) in CH_2Cl_2 (10 ml) at room temperature for 2 h afforded, after usual work up and purification by chromatography, an epoxide identical in all aspects to natural **14** (42 mg).

Acetate **15**.—Compound **14** (127 mg) in Ac_2O/Py as above gave **15** (131 mg); mp 173-174° (hexane); $[\alpha]D$ −25° ($CHCl_3$, c 1.0); ir ν max (KBr) 2920, 2860, 1730, 1710, 1650, 1450, 1360, 1240, 1160, 1040, 980, 840 cm^{-1}; ^1H nmr (60 MHz) δ 0.86 (6H, s, H-18 and H-19), 1.10 (3H, s, H-20), 1.93 (3H, br s, H-5′), 2.03 (3H, br d, J=7 Hz, H-4′), 2.03 (3H, s, MeCO), 2.79 (2H, s, H-17), 4.46 (1H, dd, J=9 and 7 Hz, H-3), 5.02 (1H, br s, H-15), 6.13 (1H, br q, J=7 Hz, H-3′); ms *m/z* (%) 444 $[M]^+$ (2), 361 $[M\text{-}Ang]^+$ (2), 344 $[M\text{-}AngOH]^+$ (12), 329 $[344\text{-}Me]^+$ (7), 326 $[344\text{-}H_2O]^+$ (5), 301 $[361\text{-}AcOH]^+$ (9), 284 $[344\text{-}AcOH]^+$ (10), 269(12), 251(10), 135(13), 83 $[Ang]^+$ (100), 55 $[Ang\text{-}CO]^+$ (22), 43(10).

ACKNOWLEDGMENTS

The authors are greatly indebted to Professor J. de Pascual Teresa and to Drs. J.M. Hernández and A. Fernández Rodríguez from the Department of Organic Chemistry, University of Salamanca, Spain, for the ms and high field nmr measurements. We also wish to thank Dr. A. Escarré, Department of Biology, University of Alicante, for the identification of plant material and Mr. J. Prieto, CSIC, Madrid, for the microanalysis.

LITERATURE CITED

1. R. Hegnauer, "Chemotaxonomie der Pflanzen," Vol. 6. Birkhauser Verlag, Stutgart, 1973, p. 554.
2. F. Bohlmann and C. Zdero, *Chem. Ber.*, **107**, 1416 (1974).
3. J. de Pascual, C. Grande, J.R. Morán, and M. Grande, *Chem. Lett.*, 247 (1984).
4. M. Pinar, B. Rodríguez, and A. Alemany, *Phytochemistry*, **17**, 1637 (1978).
5. B. Rodríguez and M. Pinar, *Phytochemistry*, **18**, 891 (1979).
6. B. Rodríguez and M. Pinar, *An. Quím.*, **75**, 936 (1979).
7. M. Pinar, *Phytochemistry*, **23**, 2075 (1984).
8. M. Grande, B. Mancheño, and M.J. Sánchez. Presented at the 14th IUPAC International Symposium on Nat. Prod., Poznań, Poland, July 1984, (abstract I, nr. A9, pg 123).
9. J.A. Steele, *J. Org. Chem.*, **28**, 572 (1963).
10. F. Bohlmann, K.H. Knoll, C. Zdero, P.K. Mahanta, M. Grenz, A. Suwita, D. Ehlers, N. Le Van, W.R. Abraham, und A.A. Natu, *Phytochemistry*, **16**, 965 (1977).
11. R.J. Park and M.D. Sutherland, *Aust. J. Chem.*, **22**, 495 (1969).
12. O.B. Von Heinz and K. Thiele, *Helv. Chim. Acta*, **61**, 6 (1978).
13. P. Joseph-Nathan, J.R. Wesener, and H. Guenther, *Org. Magn. Reson.*, **22**, 190 (1984).
14. F. Bohlmann and C. Zdero, *Chem. Ber.*, **109**, 1670 (1976).
15. C. Von Carstenn-Lichterfelde, C. Pascual, R.M. Rabanal, B. Rodríguez, and S. Valverde, *Tetrahedron*, **33**, 1989 (1977).
16. K. Yamasaki, H. Kohda, T. Kobayashi, R. Kasai, and O. Tanaka, *Tetrahedron Lett.*, 1005 (1976).
17. B. Rodríguez, A. Alemany, and M. Pinar, *Tetrahedron Lett.*, 3069 (1978).
18. D.K. Manh Duc, M. Fetizon, S. Lazare, P.K. Grant, M.J. Nicholls, H.T.L. Liau, M.J. Francis, J.M. Bernassau, N.F. Roque, P.M. Wovkulich, and E. Wenkert, *Tetrahedron*, **37**, 2371 (1981).
19. F.W. Wehrli and T. Nishida, *Fortsch. Chem. Org. Naturstoffe*, **36**, 64 (1979).
20. R.M. Carman, *Aust. J. Chem.*, **16**, 1104 (1963).
21. M.F. Barnes and J. MacMillan, *J. Chem. Soc. (C)*, 361 (1967).
22. J. MacMillan and E.R.H. Walker, *J. Chem. Soc. Perkin I*, 986 (1972).

Received 9 August 1985