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ent-Kauranoid derivatives from *Sideritis moorei*

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Abstract

Seven new *ent*-kauranoid derivatives *ent*-7α,18-dihydroxykaur-16-en-3-one, *ent*-18-acetoxy-3β,7α-dihydroxykaur-15-en-17-al, *ent*-3β-acetoxy-7α,18-dihydroxykaur-15-en-17-al, *ent*-18-acetoxy-3β,7α,17-trihydroxykaur-15-ene, *ent*-3β-acetoxy-7α,17,18-trihydroxykaur-15-ene, *ent*-18-acetoxy-3β,7α,17-trihydroxy-15β,16β-epoxykaurane and *ent*-3β-acetoxy-7α,17,18-trihydroxy-15β,16β-epoxykaurane have been isolated from *Sideritis moorei*. The structures of these compounds have been established by spectroscopic means and chemical correlations.

Keywords: *Sideritis moorei*; Labiatae; Diterpenoids; *ent*-Kaur-16-enes; *ent*-Kaur-15-enes; *ent*-Kaur-15β,16β-epoxykauranes

1. Introduction

The genus *Sideritis* is comprised of around 25 species in Morocco, of which 16 are endemic. These plants have been taxonomically studied (Obon de Castro and Rivera-Nuñez, 1994; Barber et al., 2002) but only two phytochemical studies have been conducted. The first investigated the flavonoid composition from several endemic species growing in North Africa, which were very similar to those found in Spanish species (Tomás-Barberán et al., 1988). And the second studied a Moroccan Atlas plant, *Sideritis ochroleuca* de Noé, in which the terpene composition was found to be very poor (López et al., 1976). Just the opposite is true of *Sideritis* of the Iberian Peninsula or Canary Islands, where it is difficult to find a taxon for which the chemical composition has not been studied (González et al., 1990). In the present work, we investigate the terpene composition of *Sideritis moorei* Peris, Stübing, Jury & Rejdali, an endemic plant of the Moroccan High Atlas (Peris et al., 1993) analysing diterpene composition of this Moroccan *Sideritis* and making comparisons with other *Sideritis* distributed throughout the Mediterranean region and the Canary Islands. These *Sideritis* have been used in traditional medicine and as infusions due to their biological properties. Many of the compounds isolated from *Sideritis* and some derivatives have been shown to possess different types of biological properties, including activities that are anti-inflammatory (Barberan et al., 1987; Alcaraz et al., 1989; Hernández-Pérez and Rabanal, 2002, 2004), anti-HIV (Bruno et al., 2002), cytostatic, antibacterial (Darias et al., 1990), antimicrobial (Rodriguez-Linde et al., 1994; Aligiannis et al., 2001), antifeedant (Bondi et al., 2000; Bruno et al., 2001) and antioxidant (Tunalier et al., 2004; Gabriela et al., 2005).

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2. Results and discussion

The phytochemical study of *S. moorei* revealed the known diterpenoids *ent*-18-acetoxy-3β,7α-dihydroxykaur-16-ene (linearol, **1**), *ent*-3β-acetoxy-7α,18-dihydroxykaur-16-ene (sidol, **2**), *ent*-7α,18-dihydroxykaur-16-ene (epicandicandiol, **3**), and *ent*-3β,7α,18-trihydroxykaur-16-ene (foliol, **4**), together with seven new minor *ent*-kaurane derivatives (**5**–**11**).

Diterpenoid (**5**) had a molecular formula of $C_{20}H_{30}O_3$, and its IR spectrum showed absorption bands for hydroxyl, carbonyl and double-bond groups. Its ^{1}H NMR spectrum included two singlet signals at δ 4.83 and 4.80, corresponding to an exo-methylene group, besides an AB system (doublets centred at δ 3.64 and 3.34) due to the geminal protons of the hydroxymethylene group at C-18, and a signal of the geminal proton to the axial hydroxyl group at C-7 (δ, 3.63, *t*, *J* 3.0 Hz). The ^{13}C NMR spectrum of **5** (Table 1) revealed the presence of a signal at δ 218.1 due to a carbonyl group, the position of which was determined by a HMBC experiment. The cross-peak signals between the protons at C-2, C-5, C-18 and C-19, and the carbonyl carbon indicated that this group was situated at C-3. In addition, we have chemically correlated this compound (**5**), by acetylation, with diacetate **12** (*ent*-7α,18-diacetoxykaur-16-en-3-one), previously isolated from the biotransformation of *ent*-18-acetoxykaur-16-en-3,7-dione (**13**) by *Curvularia lunata* (García-Granados et al., 1990). Thus, the new natural ketodiol **5** has a structure of *ent*-7α,18-dihydroxykaur-16-en-3-one.

Compounds (**6** and **7**) had a molecular formula of $C_{22}H_{32}O_5$ and very similar spectroscopic data. In their ^{1}H NMR spectra, the signals of an aldehyde proton (δ 9.73 for **6** and δ 9.74 for **7**) and a hydrogen of a double bond conjugated with the aldehyde group (δ 7.08 for **6** and δ 7.10 for **7**) were detected, together with a signal of a geminal proton to an axial hydroxyl group (δ 3.73 for **6** and δ 3.74 for **7**). The main differences in the ^{1}H NMR spectra resided in the chemical shifts of the AB systems, caused by: an acetoxymethylene group in **6** (δ 4.08 and 4.00), and a hydroxymethylene group in **7** (δ 3.30 and 2.97); and the signals due to a geminal proton, to an equatorial hydroxyl group for **6** (δ 3.54), and to an equatorial acetoxyl group for **7** (δ 4.88). Comparing the spectroscopic data of linearol (**1**) and sidol (**2**) with those of **6** and **7**, an *ent*-isokaurene skeleton can be assumed for these compounds, with an aldehyde at C-17, a double bond at C-15 and C-16, and an axial hydroxyl group at C-7. The position of an aldehyde group at C-17 and a double bond between C-15 and C-16 was confirmed by a NOE effect observed between the protons of C-15 and C-17. In addition, HMBC experiments showed correlations of C-17 and H-15, and C-15 and H-17. ^{13}C

Table 1
^{13}C NMR chemical shifts

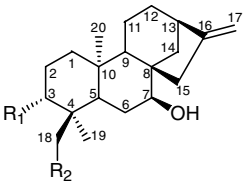
Carbon	5	6	7	8	9	10	11	15
1	38.6	38.3	38.4	38.4	38.3	38.4	38.3	37.9
2	35.7	26.5	23.5	26.4	23.4	26.4	23.3	23.3
3	218.1	72.0	74.5	72.2	74.8*	72.2	74.5	73.7
4	52.0	42.1	41.9	41.9	41.8	42.0	41.8	40.4
5	38.6	37.7	37.1	37.8	37.1	37.9	37.1	39.3
6	28.1	26.8	26.1	26.8	26.1	26.8	26.1	22.9
7	76.7	73.1	73.0	74.4	74.7*	71.4	71.5	74.7
8	48.2	54.8	54.9	52.8	53.1	47.3	47.4	46.2
9	48.7	42.3	42.1	43.4	43.5	45.4	45.2	45.8
10	38.1	39.5	39.2	39.1	39.0	38.8	38.6	38.6
11	18.3	18.2	18.3	18.4	18.6	17.8	17.9	17.8
12	33.9	25.2	25.3	25.4	25.6	27.0	27.1	26.6
13	43.7	37.9	37.9	40.9	41.3	35.7	35.8	35.6
14	38.5	41.4	41.2	42.1	42.1	30.9	30.9	30.6
15	45.1	157.8	158.0	130.6	130.0	61.3	61.2	60.8
16	154.5	149.1	149.0	147.3	147.7	65.7	65.9	62.2
17	104.0	189.6	189.7	61.3	61.3	59.1	58.9	62.0
18	67.0	65.8	64.0	66.0	64.0	66.1	64.0	64.9
19	17.6	11.8	12.7	11.8	12.8	11.9	12.8	12.9
20	16.9	18.1	18.1	18.0	18.1	17.9	17.9	17.9
*C*H$_3$COO		21.2	21.2	21.2	21.3	21.2	21.3	21.4
*C*H$_3$COO								21.2
*C*H$_3$COO								21.0
*C*H$_3$COO								20.8
CH$_3$*C*OO		172.0	172.3	172.0	171.8	172.0	171.9	170.9
CH$_3$*C*OO								170.6
CH$_3$*C*OO								170.5
CH$_3$*C*OO								169.6

* Values bearing an asterisk may be interchanged.

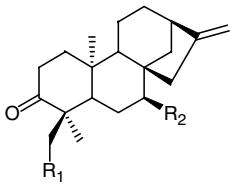
NMR data (Table 1) confirmed that **6** and **7** were new natural compounds with a structure of *ent*-18-acetoxy-3β,7α-dihydroxykaur-15-en-17-al for **6**, with an acetoxyl group at C-18 and an equatorial hydroxyl group at C-3 as linearol (**1**); and a structure of *ent*-3β-acetoxy-7α,18-dihydroxykaur-15-en-17-al for product **7**, with a hydroxyl group at C-18 and an equatorial acetoxyl group at C-3 as sidol (**2**).

Compounds **8** and **9** had identical spectroscopic data that *ent*-18-acetoxy-3β,7α,17-trihydroxykaur-15-ene and *ent*-3β-acetoxy-7α,17,18-trihydroxykaur-15-ene, respectively, previously obtained from the epoxidation of linearol (**1**) (Topçu et al., 2002). These compounds (**8** and **9**) were also derived from aldehydes **6** and **7**, by their respective reduction with $NaBH_4$. Although the ^{13}C NMR data confirmed the structures of **8** and **9**, a chemical correlation of these compounds, by direct acetylation, has been established with *ent*-3β,7α,17,18-tetracetoxykaur-15-ene (**14**), previously characterized (García de Quesada et al., 1973).

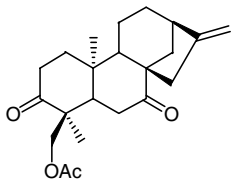
The last compounds isolated from *S. moorei* (**10** and **11**) had a molecular formula of $C_{22}H_{34}O_6$ and very similar spectroscopic data. In their ^1H NMR spectra, a singlet signal of a geminal proton to an oxygenated group (δ 3.40 for **10** and δ 3.43 for **11**), and an AB system of a hydroxymethylene group (δ 4.04 and 3.78 for **10** and δ 4.01 and 3.81 for **11**) were observed. In addition, the ^1H NMR data of **10** also showed signals similar to those described for **1** and **6**, originated by the acetoxymethylene group at C-18 and the hydroxyl groups at C-3 and C-7, and, in those of **11,** signals similar to those described for **2** and **7**, due to the acetoxyl group at C-3 and the hydroxyl groups at C-7 and C-18. The ^{13}C NMR spectra of **10** and **11** pointed to the presence of a 15,16-epoxyde group (δ 61.3 and 65.7 for **10** and δ 61.2 and 65.9 for **11**) and a hydroxylation at C-17 (δ 59.1 for **10** and 58.9 for **11**) (Table 1). Thus, **10** and **11** were the 15,16-epoxyderivatives of **8** and **9**, respectively. Acetylation of both compounds (**10** and **11**) gave the same product, *ent*-3β,7α,17,18-tetracetoxy-15β,16β-epoxykaurane (**15**). Its chemical correlation with the tetracetate **14**, carried out by means of the epoxidation with *m*-CPBA, afforded only the epoxide **15**, since it is known that epoxidation of an *ent*-kaur-15-ene double bond takes place from the attack of the reagent on the less hindered *ent*-β-side (Venturella et al., 1978). Thus,



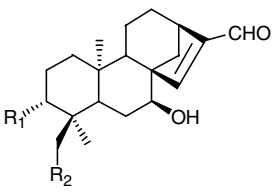
1: R_1=OH, R_2=OAc
2: R_1=OAc, R_2=OH
3: R_1=H, R_2=OH
4: R_1=R_2=OH



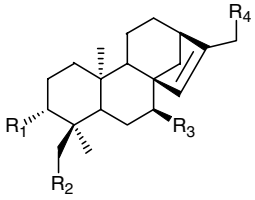
5: R_1=R_2=OH
12: R_1=R_2=OAc



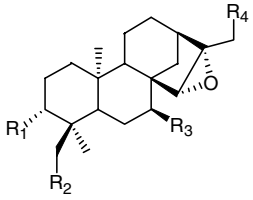
13



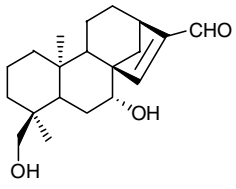
6: R_1=OH, R_2=OAc
7: R_1=OAc, R_2=OH
17: R_1=H, R_2=OH



8: R_1=R_3=R_4=OH, R_2=OAc
9: R_1=OAc, R_2=R_3=R_4=OH
14: R_1=R_2=R_3=R_4=OAc
16: R_1=R_2=R_3=R_4=OH



10: R_1=R_3=R_4=OH, R_2=OAc
11: R_1=OAc, R_2=R_3=R_4=OH
15: R_1=R_2=R_3=R_4=OAc
19: R_1=R_4=H, R_2=OH, R_3=OAc
20: R_1=R_4=H, R_2=R_3=OH
21: R_1=R_3=OH, R_2=OAc, R_4=H
22: R_1=OAc, R_2=R_3=OH, R_4=H
23: R_1=R_2=R_3= OH, R_4=H
24: R_1=H, R_2=R_3=R_4=OH



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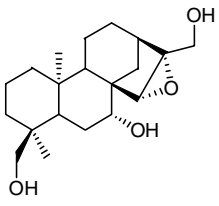

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we conclude that the new natural compounds **10** and **11** were *ent*-18-acetoxy-3β,7α,17-trihydroxy-15β,16β-epoxykaurane and *ent*-3β-acetoxy-7α,17,18-trihydroxy-15β,-16β-epoxykaurane, respectively.

The major compounds isolated from *S. moorei* (**1** and **2**) are diterpenoids broadly distributed in plants of the genus *Sideritis* which grow in extensive areas of the Mediterranean region and the Canary Islands (Table 2). Epicandicandiol (**3**), a minor compound isolated from *S. moorei*, was present in endemic *Sideritis* of the Canary Islands, and in some *Sideritis* of Turkey. The new natural compounds with an *ent*-isokaurene skeleton (**6**–**11**), are structurally related with isoleucanthol (**16**). Compounds **6** and **7**, with an α,β-unsaturated system on the D ring and an aldehyde at C-17, have related structures as episinfernal (**17**) and sinfernal (**18**) – isolated from endemic plants of the Canary Islands – the main difference being the existence of an equatorial hydroxyl group at C-3 in **6** and **7**. Difunctionalized epoxyisokaurenes such as epoxysiderol (**19**) and sideroxol (**20**), or trifunctionalized such as epoxyisolinearol (**21**), epoxyisosidol (**22**), epoxyisofoliol (**23**), epoxysideritriol (**24**) or epoxysinfernol (**25**) were isolated from numerous *Sideritis* species; however, compounds **10** and **11** are the first new natural tetrafunctionalized epoxyisokauranes found in this genus.

3. Experimental

3.1. General

Measurements of NMR spectra (300.13 MHz ^{1}H and 75.47 MHz ^{13}C) were made in $CDCl_3$ (which also

Table 2
Natural compounds isolated from *Sideritis* species distributed throughout the Mediterranean region and the Canary Islands (*), which are structurally related with those derived from *S. moorei*

Compounds	Localization	*Sideritis* species	Reference
3	Spain*	*candicans*	Piozzi et al. (1971)
1, **2**, **4**, **16**	Spain	*leucantha*	García de Quesada et al. (1973)
1, **2**, **4**	Spain	*linearifolia*	García de Quesada et al. (1973)
1, **2**, **4**, **16**	Spain	*lagascana*	García de Quesada et al. (1974)
19	Spain	*glacialis*	González et al. (1974)
1, **2**, **4**	Spain	*luteola*	Rodríguez et al. (1975)
20, **21**	Greece	*theezans*	Venturella et al. (1975)
4	Morocco	*ochreleuca*	López et al. (1976)
23	Spain	*paulii*	Rodríguez and Valverde (1976)
1, **2**, **4**, **16**, **21**–**23**	Spain	*biflora*	García-Alvarez and Rodriguez (1976)
19, **20**, **21**	Greece	*roeseri*	Venturella and Bellino (1977)
19, **20**	Greece	*euboea; distans; syriaca*	Venturella and Bellino (1977)
19, **20**, **24**	Italy	*sicula*	Venturella et al. (1978)
1, **2**, **3**, **16**	Spain	*hirsuta*	López Gómez et al. (1979)
1, **2**, **4**	Spain	*funkiana*	García-Granados et al. (1979)
1, **2**	Spain	*flavovirens*	Escamilla and Rodriguez (1980)
1, **2**, **4**	Spain	*arborescens*	García-Granados et al. (1980)
1	Spain	*leucantha var. meridionalis*	García-Granados et al. (1982)
1, **2**	Spain	*varoi*	Algarra et al. (1983)
1, **2**, **4**	Spain	*hirsuta subsp nivalis*	Cabrera et al. (1983)
1, **2**, **4**	Spain	*almeriensis*	García-Granados et al. (1983)
1, **2**, **4**	Spain	*granatensis*	García-Granados et al. (1983)
1, **2**	Spain	*zafrae*	García-Granados et al. (1983)
1, **2**, **4**	Spain	*leucantha var. incana*	García-Granados et al. (1983)
17, **18**	Spain*	*infernalis*	Fernández et al. (1986)
3, **17**	Spain*	*cystosiphon*	Fraga et al., 1987
3, **17**	Spain*	*sventenii*	Fraga et al. (1990)
3, **17**	Spain*	*ferrensis*	Fraga et al. (1991a)
3, **17**	Spain*	*canariensis var. pannosa*	Fraga et al. (1991b)
1, **2**, **3**	Turkey	*brevidens*	Bondi et al. (2000)
1, **2**, **3**, **20**	Turkey	*rubriflora*	Bondi et al. (2000)
1, **4**, **20**	Turkey	*akmanii*	Bondi et al. (2000)
1, **3**, **4**	Turkey	*niveotomentosa*	Bondi et al. (2000)
1, **3**	Turkey	*gulendamii*	Bondi et al. (2000)
1, **2**, **3**, **4**	Turkey	*argyrea*	Topçu et al. (2001)
1, **3**, **21**	Turkey	*sipylea*	Topçu et al. (2002)
20	Turkey	*dichotoma*	Topçu et al. (2002)
1, **2**, **3**, **4**	Turkey	*athoa; argyrea*	Kiliç et al. (2003)
3	Turkey	*trojana*	Kiliç et al. (2003)
1, **2**, **20**, **21**	Turkey	*ozturkii*	Pinar et al. (2004)

provided the lock signal) in a Bruker AM-300 spectrometer. Assignments of ^{13}C chemical shifts (Table 1) were made with the aid of distortionless enhancement by polarization transfer (DEPT) using a flip angle of 135°. Several programs were used for HMQC, HMBC and NOE experiments. IR spectra were recorder on a MATTSON SATELLITE FT-IR spectrometer. High-resolution mass spectra were made by LSIMS (FAB) ionization mode in a MICROMASS AUTOSPEC-Q spectrometer (EBE geometry). Mps were determined using a Kofler (Reichert) apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 431 polarimeter at 25°. Silica-gel (40–60 μm) was used for flash chromatography. CH_2Cl_2 with increasing amounts of Me_2CO was used as eluent. Analytical plates were rendered visible by spraying with H_2SO_4–HOAc–H_2O, followed by heating to 120 °C.

3.2. Plant material

Aerial parts of *S. moorei* was collected to the south of Azrou on the road from Midelt (Morocco), 33°14′N, 5°17′W at an altitude of 1890 m. A voucher specimen (GDA-49857) is deposited in the Herbarium of the University of Granada (Spain).

3.3. Extraction and isolation of the terpenoids

Dried and finely powdered aerial parts of *S. moorei* (850 g) were distributed into eight cartridge cases of around 100 g each one, and extracted with *n*-hexane in a Soxhlet (0.5 l) for 48 h. After each extraction, *n*-hexane was removed at reduced pressure. The eight extracts were joined, resulting a syrupy residue, which was chromatographed through a silica-gel column to give the following compounds: linearol (**1**, 5.4 g), sidol (**2**, 1.2 g) (García de Quesada et al., 1973), epicandicandiol (**3**, 50 mg) (Rodriguez et al., 1970; Piozzi et al., 1971), foliol (**4**, 30 mg) (García de Quesada et al., 1973), *ent*-7α,18-dihydroxykaur-16-en-3-one (**5**, 18 mg), *ent*-18-acetoxy-3β,7α-dihydroxykaur-15-en-17-al (**6**, 75 mg), *ent*-3β-acetoxy-7α,18-dihydroxykaur-15-en-17-al (**7**, 15 mg), *ent*-18-acetoxy-3β,7α,17-trihydroxykaur-15-ene (**8**, 32 mg), *ent*-3β-acetoxy-7α,17,18-trihydroxykaur-15-ene (**9**, 17 mg), *ent*-18-acetoxy-3β,7α,17-trihydroxy-15β,16β-epoxykaurane (**10**, 28 mg), and *ent*-3β-acetoxy-7α,17,18-dihydroxy-15β,16β-epoxykaurane (**11**, 23 mg).

3.4. ent-7α,18-Dihydroxykaur-16-en-3-one (*5*)

Syrup; $[\alpha]_D$ −45.8° ($CHCl_3$; *c* 0.5); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3390, 3063, 1699, 1042, 875, 736; ^1H NMR ($CDCl_3$): δ 4.83 and 4.80 (1H each, *s*, 2H-17), 3.64 and 3.34 (2H, AB system, J = 11.2, 2H-18), 3.63 (1H, *t*, J = 3.0 Hz, H-7), 2.70 (1H, *m*, $W_{1/2}$ = 12 Hz, H-13), 2.56 (1H, *ddd*, J_1 = 16.8, J_2 = 11.2, J_3 = 7.5 Hz) and 2.41 (1H, *ddd*, J_1 = 16.8, J_2 = 7.1, J_3 = 3.2 Hz) (2H-2), 2.45 (1H, *dd*, J_1 = 12.6, J_2 = 2.5 Hz, H-5), 2.26 (2H, *br s*, 2H-15), 1.15 (3H, *s*, 3H-20) and 0.94 (3H, *s*, 3H-19); HRLSIMS *m/z*: 341.2090 $[M + Na]^+$ (calcd. for $C_{20}H_{30}O_3Na$, 341.2093).

3.5. ent-18-Acetoxy-3β,7α-dihydroxykaur-15-en-17-al (*6*)

Syrup; $[\alpha]_D$ −13.6° ($CHCl_3$; *c* 1); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3441, 3055, 2722, 1719, 1671, 1251, 1045, 736; ^1H NMR ($CDCl_3$): δ 9.73 (1H, *s*, H-17), 7.08 (1H, *s*, H-15), 4.08 and 4.00 (2H, AB system, J = 11.6, 2H-18), 3.73 (1H, *br s*, H-7), 3.54 (1H, *t*, J = 8.2 Hz, H-3), 3.07 (1H, *m*, $W_{1/2}$ = 11.5 Hz H-13), 2.10 (3 H, *s*, OAc), 1.08 (3H, *s*, 3H-20) and 0.75 (3H, *s*, 3H-19); HRLSIMS *m/z*: 399.2148 $[M + Na]^+$ (calcd. for $C_{22}H_{32}O_5Na$, 399.2147).

3.6. ent-3β-Acetoxy-7α,18-dihydroxykaur-15-en-17-al (*7*)

Syrup; $[\alpha]_D$ −8.2° ($CHCl_3$; *c* 0.5); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3406, 3057, 2718, 1720, 1673, 1260, 1047; ^1H NMR ($CDCl_3$): δ 9.74 (1H, *s*, H-17), 7.10 (1H, *s*, H-15), 4.88 (1H, *dd*, J_1 = 11.7, J_2 = 4.7 Hz, H-3), 3.74 (1H, *t*, J = 3 Hz, H-7), 3.30 and 2.97 (2H, AB system, J = 12.5, 2H-18), 3.07 (1H, m, $W_{1/2}$ = 11.5 Hz H-13), 2.07 (3H, *s*, OAc), 1.10 (3H, *s*, 3H-20) and 0.67 (3H, *s*, 3H-19); HRLSIMS *m/z*: 399.2146 $[M + Na]^+$ (calcd. for $C_{22}H_{32}O_5Na$, 399.2147).

3.7. ent-18-Acetoxy-3β,7α,17-trihydroxykaur-15-ene (*8*)

Syrup; $[\alpha]_D$ +8.6° ($CHCl_3$; *c* 0.63); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3437, 1718, 1252, 1047, 757 cm^{-1}; ^1H NMR ($CDCl_3$), δ 5.82 (1H, *s*, H-15), 4.19 (2H, *s*, 2H-17), 4.05 and 3.98 (2H, AB system, J = 11.6 Hz, 2H-18), 3.65 (1H, *br s*, H-7), 3.52 (1H, *t*, J = 8.2 Hz, H-3), 2.60 (1H, *m*, $W_{1/2}$ = 11 Hz, H-13), 2.09 (3H, *s*, OAc), 1.06 and 0.74 (3H each, *s*, 3H-19 and 3H-20); HRLSIMS *m/z*: 401.2307 $[M + Na]^+$ (calcd. for $C_{22}H_{34}O_5Na$, 401.2304).

3.8. ent-3β-Acetoxy-7α,17,18-trihydroxykaur-15-ene (*9*)

White solid, m.p. 147–149°C; $[\alpha]_D$ +13.2° ($CHCl_3$; *c* 0.5); IR ν_{max}^{KBr} cm^{-1}: 3287, 1729, 1249, 1049; ^1H NMR ($CDCl_3$), δ 5.83 (1H, *s*, H-15), 4.87 (1H, *dd*, J_1 = 10.7, J_2 = 6.0 Hz, H-3), 4.18 (2H, *s*, 2H-17), 3.65 (1H, *t*, J = 2.6 Hz, H-7), 3.32 and 3.02 (2H, AB system, J = 12.4 Hz, 2H-18), 2.54 (1H, *m*, $W_{1/2}$ = 12 Hz, H-13), 2.04 (3H, *s*, OAc), 1.07 and 0.66 (3H each, *s*, 3H-19 and 3H-20); HRLSIMS *m/z*: 401.2297 $[M + Na]^+$ (calcd. for $C_{22}H_{34}O_5Na$, 401.2304).

3.9. *ent*-18-Acetoxy-3β,7α,17-trihydroxy-15β,16β-epoxykaurane (**10**)

White solid, m.p. 134–136 °C; $[\alpha]_D$ +12.8° ($CHCl_3$; *c* 0.5); IR ν_{max}^{KBr} cm^{-1}: 3431, 1715, 1251, 1052; ^1H NMR ($CDCl_3$): δ 4.04 and 3.99 (2H, AB system, $J = 11.7$, 2H-18), 4.04 and 3.78 (2H, AB system, $J = 12.6$, 2H-17), 3.80 (1H, *br s*, H-7), 3.53 (1H, *dd*, $J_1 = 9.6$, $J_2 = 6.9$ Hz, H-3), 3.40 (1H, *s*, H-15), 2.34 (1H, *m*, $W_{1/2} = 11$ Hz, H-13), 2.09 (3H, *s*, OAc), 1.02 and 0.73 (3H each, *s*, 3H-19 and 3H-20); HRLSIMS *m*/*z*: 417.2249 $[M + Na]^+$ (calcd. for $C_{22}H_{34}O_6Na$, 417.2253).

3.10. *ent*-3β-Acetoxy-7α,17,18-dihydroxy-15β,16β-epoxykaurane (**11**)

Syrup; $[\alpha]_D$ +13.5° ($CHCl_3$; *c* 1); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3431, 1727, 1671, 1249, 1051; ^1H NMR ($CDCl_3$): δ 4.90 (1H, *dd*, $J_1 = 11.3$, $J_2 = 5.4$ Hz, H-3), 4.01 and 3.81 (2H, AB system, $J = 12.8$, 2H-17), 3.81 (1H, *br s*, H-7), 3.43 (1H, *s*, H-15), 3.32 and 3.00 (2H, AB system, $J = 12.5$, 2H-18), 2.31 (1H, *m*, $W_{1/2} = 11$ Hz, H-13), 2.04 (3H, *s*, OAc), 1.03 and 0.66 (3H each, *s*, 3H-19 and 3H-20); HRLSIMS *m*/*z*: 417.2256 $[M + Na]^+$ (calcd. for $C_{22}H_{34}O_6Na$, 417.2253).

3.11. Acetylations of **5**, **8**, **9**, **10** and **11**

Compounds **5**, **8**, **9** **10** and **11** were acetylated separately. In each case, 10 mg of compound were dissolved in pyridine (1 ml) and Ac_2O (0.5 ml). All the mixtures were stirred for 24 h at room temp. and extracted in the usual way. Purifications by column chromatography on silica gel yielded *ent*-7α,18-diacetoxykaur-16-en-3-one (**12**) (García-Granados et al., 1990) from **5**, tetracetate **14** (García de Quesada et al., 1973) from **8** and **9**, and the same tetracetate (**15**) from **10** and **11**. In all acetylations, the yields were between the 85% and 90%.

3.12. *ent*-18,3β,7α,17-Tetracetoxy-15β,16β-epoxykaurane (**15**)

Syrup; $[\alpha]_D$ +24.6° ($CHCl_3$; *c* 1); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1736, 1245, 1041; ^1H NMR ($CDCl_3$): δ 4.83 (1H, *t*, $J = 2.8$ Hz, H-7), 4.71 (1H, *dd*, $J_1 = 11.6$, $J_2 = 4.9$ Hz, H-3), 4.65 and 4.08 (2H, AB system, $J = 12.6$, 2H-17), 3.95 and 3.50 (2H, AB system, $J = 11.9$, 2H-18), 3.15 (1H, *s*, H-15), 2.43 (1H, *m*, $W_{1/2} = 12$ Hz, H-13), 2.09, 2.07, 2.03, 2.01 (3H each, *s*, OAc), 1.07 and 0.79 (3H each, *s*, 3H-19 and 3H-20); HRLSIMS *m*/*z* : 543.2569 $[M + Na]^+$ (calcd. for $C_{28}H_{40}O_9Na$, 543.2570).

3.13. Reduction of aldehydes **6** and **7**

Aldehyde **6** (15 mg) was dissolved in EtOH (5 ml), and $NaBH_4$ (5 mg) was added. The mixture was stirred for 1 h at room temp., after which the reaction mixture was diluted with H_2O (20 ml) and extracted with CH_2Cl_2. The organic layer was dried with dry Na_2SO_4 and concentrated at reduced pressure to give 10 mg of monoacetate **8**. The reduction of aldehyde **7** (10 mg) under the same conditions described above for **6**, gave 6 mg of monoacetate **9**.

3.14. Epoxidation of tetracetate **14**

Compound **14** (12 mg) was dissolved in $CHCl_3$ (5 ml), and *m*-CPBA (10 mg) were added. After 3 h at room temp., the mixture was diluted with $CHCl_3$ (20 ml) and washed with aq. $FeSO_4$, $NaHCO_3$ and H_2O. The organic layer was dried with dry $MgSO_4$, conc. at reduced pressure and chromatographed on a silica-gel column to give 7 mg of epoxide **15**.

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