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KAURANE, ISOKAURANE, AND BEYERANE DERIVATIVES FROM *PETERAVENIA* SPECIES

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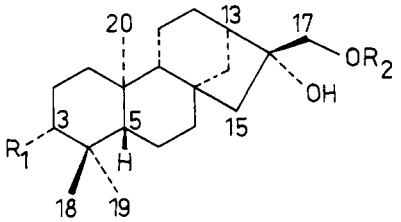
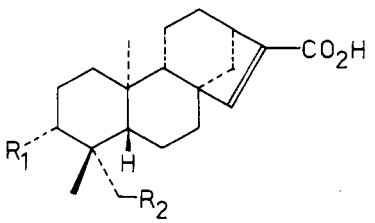
ABSTRACT.—The investigation of two *Peteravenia* species afforded, in addition to known diterpenes, a new beyerene, two kaurane, and three isokaurene derivatives. The structures were elucidated by high-field ^{1}H-nmr spectroscopy. The chemotaxonomy of these species is discussed briefly.

The small genus *Peteravenia* (Compositae, tribe Eupatorieae) (1) is placed in the subtribe Hebecliniinae (2,3), a group of genera that are weakly differentiated from the Critoniinae and that were distinguished on the basis of their generally hirsute receptacles, elongated anther collars of subquadrate cells, and carpodia continuous with the lower parts of the achenes (2,3). These characters, however, are not very prounounced within *Peteravenia*. We have, therefore, studied two species chemically, and the results are discussed in this paper.

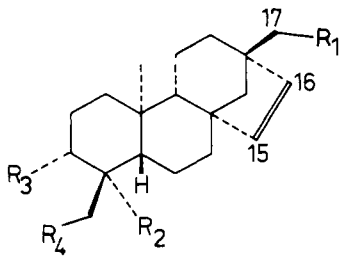
The aerial parts of *Peteravenia malvaefolia* (DC.) K. et R. afforded stigmasterol, β-sitosterol, and the diterpenes *ent*-16β,17-dihydroxykaurane [**1**] (4), *ent*-3β-acetoxy-16β,17-dihydroxykaurane [**2**] (5), *ent*-3β,17-diacetoxy-16β-hydroxykaurane [**3**], *ent*-kaur-15-en-17-oic acid [**4**], *ent*-3β-acetoxy-kaur-15-en-17-oic acid [**5**], *ent*-3β, 19-diacetoxy-kaur-15-en-17-oic acid [**6**], 3α-hydroxybeyer-15-en-19-oic acid [**7**] (6), 18-acetoxybeyer-15-en-19-oic acid [**8**], and 3α,17-dihydroxybeyer-15-ene [**9**] (7). The acids **4-8** were isolated as the corresponding methyl esters **4a-8a**.



1 $R_1=R_2=H$
2 $R_1=OH$, $R_2=Ac$
3 $R_1=OAc$, $R_2=Ac$



4 $R_1=R_2=H$
5 $R_1=OAc$, $R_2=H$
6 $R_1=R_2=OAc$



7 $R=R_4=H$, $R_2=COOH$, $R_3=OH$
8 $R=R_3=H$, $R_2=COOH$, $R_4=OAc$
9 $R=R_3=OH$, $R_2=CH_3$, $R_4=H$

The structures of **2** and **3** followed from their ^{1}H-nmr spectra (see Experimental section), which were close to that of **1** (4); the spectrum of **2** agreed with values reported for this acetate prepared from the corresponding ketone (5). As expected, the H-3 signal was shifted downfield in the diacetate **3** when compared with the chemical shift of H-3 in **2**. The stereochemistry and also the position of the oxygen function of these derivatives were established by nOe difference spectroscopy. Clear nOe's were observed between H-5, H-3 (10%), and H-9 (4%), between H-19 and H-20 (5%), between H-18 and H-3 (12%) as well as between H-20, H-19 (7%), and H-14 (11%) (the first proton listed is always the one irradiated). Because the sign of the optical rotation of **2** was identical with that reported (5), the presence of *ent*-kauranes was established.

The structure of **4a** also followed from its ^{1}H-nmr spectrum (see Experimental section). Most signals were close to those of **1** (4), but the changed situation in the five-membered ring caused a downfield shift of the signal of H-13 and of H-15, which occurred as a singlet at δ 6.49; this can be explained by the presence of an isokaurene with a carbomethoxy group at C-16.

The ^{1}H-nmr spectra of **5a** and **6a** (see Experimental section) were close to that of **4a**; however, an additional lowfield signal in the spectrum of **5a** (δ 4.47 dd) and an acetate methyl singlet indicated the presence of a 3α-acetoxy derivative of **4a**. In the spectrum of **6a**, pairs of doublets at δ 4.33 and 4.13 and a further acetate methyl singlet clearly showed that in **6a** one of the methyl groups was replaced by an acetoxy methylene group. The nOe difference spectroscopy indicated that a 19-acetoxy derivative of **5a** was present. Clear effects were observed between H-18, H-3 (12%), and H-19 (3%), between H-20, H-19 (5%), H-19′ (7%), and H-14 (11%) as well as between H-3 and H-5 (5%). These effects clearly established the position of the acetoxy groups and also the stereochemistry at C-3—C-5 and C-8—C-10.

Compound **7a** had been isolated previously (6). The proposed stereochemistry was established by nOe difference spectroscopy. Clear effects were obtained between H-20, OMe (2%), and H-15 (8%), between H-17, H-16 (6%), and H-14 as well as between H-3, H-5 (5%), and H-18 (6%). This technique also assigned the methyl singlets and the position of the oxygen functions. The ^{1}H-nmr spectrum of **8a** showed some similarities to that of **7a**. However, the chemical shifts of one of the tertiary methyl groups differed clearly, and a second methyl singlet was replaced by a pair of doublets and an acetoxy methyl singlet. Furthermore, the H-3 signal was shifted upfield and was not separated from the upfield multiplets. Accordingly, the 3-hydroxy group was replaced by an 18-acetoxy group as required by the chemical shifts of H-19 and H-20. The spectral data of **9a** agreed with those reported in the literature (7). The ^{1}H-nmr data were in part similar to those of **7a** and **8a**, respectively. The absolute configurations of **4-9** were not determined, but biogenetic considerations favor the ones proposed.

The aerial parts of *Peteravenia schultzii* (Schnitts.) K. et R. gave germacrene D, stigmasterol, β-sitosterol, and the diterpenes **6**, **7**, and **8**. Previously, the investigation of a sample from Guatemala gave dehydronerolidol derivatives, while diterpenes were not observed (8).

The genus *Peteravenia* has been distinguished on the basis of its deciduous pappus setae, discolored phyllaries, and cordate leaves (1). The genus was said to be Critonioid due to its smooth corolla lobes, usually simple style base, and Ageratinoid in the placement of the embryo in the achene (1). The chemistry of the genus *Peteravenia* shows no relationship to *Decachaeta*, where sesquiterpene lactones are reported (9), or to *Hebeclinium* (10) both of which are placed in the Hebecliniinae. In the subtribe Critoniinae several genera contain diterpenes, mostly labdane derivatives (11,12); however, sesquiterpene lactones are also common (13-15). The accumulation of diterpenes of types

1-9 so far has not been reported from genera related to *Peteravenia*. More species from the two subtribes must be investigated to get a clearer picture.

EXPERIMENTAL

The air-dried plant material was extracted with MeOH-Et_2O-petrol (1:1:1) at room temperature and separated following the methods reported previously (16). The extract of *P. malvaefolia* (240 g, collected in Nuevo Leon, Mexico, voucher B.L. Turner and co-workers 15611, stored in the herbarium of The University of Texas), after defatting with MeOH, was separated by cc (SiO_2) into four crude fractions: (a) Et_2O-petrol (1:3), (b) Et_2O-petrol (1:1), (c) Et_2O, and (d) Et_2O-MeOH (9:1) (all contained acids, and therefore, they were treated with CH_2N_2 in Et_2O). Preparative tlc provided the following results: fraction a (SiO_2, PF 254, Et_2O-petrol, 1:9) gave 166 mg of **4a**; fraction b (Et_2O-petrol, 3:7, two developments) gave 79 mg **4a**, 20 mg **8a**, 10 mg stigmasterol, and 10 mg β-sitosterol; fraction c (Et_2O) gave three bands (3/1-3/3). Preparative tlc of the bands gave the following: band 3/1 (Et_2O-petrol, 3:7, two developments) 31 mg **4a**, 14 mg **8a**, and 8 mg **5a**; band 3/2 (Et_2O-petrol, 1:1, two developments) 74 mg **4a** and 47 mg **5a**. Hplc (RP 8, MeOH-H_2O, 4:1, ca. 100 bar) gave 12 mg **2** (R_t 5.0 min), 3.4 mg **9** (R_t 5.5 min), 9.6 mg **3** (R_t 7.4 min), and 2 mg **1** (R_t 16.5 min). Preparative tlc of fraction d (Et_2O-petrol, 7:3) gave 67 mg **4a**, 25 mg **5a**, and two mixtures (4/3 and 4/4). Preparative tlc and hplc (RP 8, MeOH-H_2O, 4:1) of 4/3 gave 12 mg **5a** and 2 mg **7a** (R_t 13.6 min). Hplc of 4/4 (RP 8, MeOH-H_2O, 4:1) gave 5 mg **6a** (R_t 7.8 min). The extract of *P. schultzii* (650 g, collected near Oaxaca, Mexico, voucher R. Scott A-111) gave, after addition of CH_2N_2 by cc and preparative tlc 10 mg **6a**, 18 mg **7a**, and 63 mg **8a**. Known compounds were identified by comparing the 400 MHz ^{1}H-nmr spectra with those of authentic material.

ENT-3β,17-DIACETOXY-16β-HYDROXY-*ENT*-KAURANE [**3**].—Colorless oil; ir ν (CCl_4) cm^{-1} 3600 (OH), 1750 (OAc); ms *m/z* 406.272 (M^+) (0.7) (calcd for $C_{24}H_{38}O_5$: 406.272), 388 (M-H_2O) (2), 333 (M-CH_2OAc) (58), 273 (333-HOAc) (44), 135 (100); ^{1}H nmr ($CDCl_3$) 1.80 (ddd, H-1, *J*=13, 3.5, 3.5 Hz), 0.95 (ddd, H-1β, *J*=13, 13, 5.5 Hz), 1.68 (m, H-2), 4.45 (dd, H-3, *J*=10.5, 6 Hz), 0.84 (dd, H-5, *J*=13, 2 Hz), 1.37 (dq, H-6, *J*=3, 13 Hz), 1.53 (m, H-6β), 1.00 (d, H-9, *J*=6.5 Hz), 2.05 (br s, H-13), 1.93 (d, H-14), 1.64 (m, H-14′), 4.22 (s, H-17), 0.85 (s, H-19), 1.04 (s, H-20); [α] ^{24}D -19° ($CHCl_3$, *c* 0.25).

METHYL-*ENT*-KAUR-15-EN-17-OATE [**4a**].—Colorless crystals, mp 138°; ir ν (CCl_4) cm^{-1} 1705, 1620 (C=CCO_2R); ms *m/z* 316.240 (M^+) (90) (calcd for $C_{21}H_{32}O_2$: 316.240), 301 (M-Me) (100), 285 (M-OMe) (8), 193 (57), 192 (63), 191 (46), 81 (96); ^{1}H nmr ($CDCl_3$) 2.93 (br s, H-13), 2.16 (d, H-14, *J*=10.5 Hz), 6.49 (s, H-15), 0.87 and 0.89 (s, H-18, H-19), 1.06 (s, H-20), 3.72 (s, OMe); [α]^{24}D −29° ($CHCl_3$, *c* 1.6).

METHYL-*ENT*-3β-ACETOXY-KAUR-15-EN-17-OATE [**5a**].—Colorless oil; ir ν (CCl_4) cm^{-1} 3540 (OH), 1730, 1250 (OAc), 1705, 1620 (C=CCO_2R); ms *m/z* 374.246 (M^+) (15) (calcd for $C_{23}H_{34}O_4$: 374.246), 314 (M-HOAc) (70), 299 (314-Me) (16), 61 (100); ^{1}H nmr ($CDCl_3$) 4.47 (dd, H-3, *J*=11, 5.5 Hz), 2.93 (br s, H-13), 2.13 (d, H-14, *J*=10.5 Hz), 6.49 (s, H-15), 0.84 and 0.87 (s, H-18, H-19), 1.08 (s, H-19), 3.73 (s, OMe); [α]^{24}D −43° ($CHCl_3$, *c* 1.0).

METHYL-*ENT*-3β, 19-DIACETOXY-KAUR-15-EN-17-OATE [**6a**].—Colorless oil; ir ν (CCl_4) cm^{-1} 3540 (OH), 1745, 1250 (OAc), 1720, 1630 (C=CCO_2R); ms *m/z* 432.251 (M^+) (5.5) (calcd for $C_{25}H_{36}O_6$: 432.251), 372 (M-HOAc) (10), 312 (372-HOAc) (52), 297 (312-Me) (22), 61 (100); ^{1}H nmr ($CDCl_3$) 4.55 (dd, H-3, *J*=10, 8 Hz), 0.99 (d (br), H-5, *J*=13 Hz), 1.92 (ddd, H-6, *J*=13.5, 4.5, 3.5 Hz), 2.95 (br s, H-13), 2.10 (d, H-14, *J*=10.5 Hz), 6.48 (s, H-15), 1.01 (s, H-17), 4.33 and 4.13 (d, H-19, *J*=12 Hz), 1.10 (s, H-20), 3.73 (s, OMe).

METHYL-18-ACETOXYBEYER-15-EN-19-OATE [**8a**].—Colorless oil; ir ν (CCl_4) cm^{-1} 1750, 1255 (OAc), 1740 (CO_2R); ms *m/z* 374.246 (M^+) (36) (calcd for $C_{23}H_{34}O_4$: 374.246), 342 (M-MeOH) (4), 314 (M-HOAc) (20), 299 (314-Me) (3), 254 (314-HCO_2Me) (10), 55 (100); ^{1}H nmr ($CDCl_3$) 2.29 (d (br), H-3, *J*=13.5 Hz), 0.88 (ddd, H-3β, *J*=13, 13, 5 Hz), 5.68 (d, H-15), 5.45 (d, H-16, *J*=5.5 Hz), 0.99 (s, H-17), 3.92 and 4.39 (d, H-19, *J*=10.5 Hz), 0.59 (s, H-20), 3.67 (s, OMe), 2.02 (s, OAc); [α]^{24}D −9° ($CHCl_3$, c 0.77).

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