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ENT-KAURANES AND TRACHYLOBANES FROM *HELIANTHUS RADULA*

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Key Word Index—*Helianthus radula*; Compositae; Heliantheae; *ent*-kauranes; trachylobanes; 11-oxotrachyloban-19-oic acid; ester of (−)-16α-hydroxykauranoic acid and 11α-hydroxytrachyloban-19-oic acid.

Abstract—The aerial parts of *Helianthus radula* afforded a variety of known *ent*-kauranoic acids as well as two new substances, 11-oxotrachyloban-19-oic acid and an ester involving the carboxyl group of (−)-16α-hydroxykauranoic acid and the hydroxyl group of 11α-hydroxytrachyloban-19-oic acid.

INTRODUCTION

In continuation of our earlier work on *Helianthus* species [1–6] we have examined *Helianthus radula* (Pursh) T. & G. which is a species found in the pine barrens of the deep South [7]. This contained various *ent*-kauranoic acids as do many other previously studied *Helianthus* species [3, 5, 6, 8–13], but gave none of the sesquiterpene lactones which have been found in various other representatives of the genus [1–4, 6, 8, 9, 11, 13–22]. Two new trachylobanes were also isolated.

RESULTS AND DISCUSSION

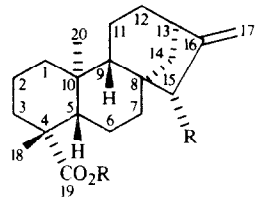
The main diterpenoid constituent of the chloroform extract of *H. radula* was **1a**; other *ent*-kauranes isolated in smaller amounts were **1b**, **2**, **3a**, **3c**, **4a** [8], the last three in the form of methyl esters **3b**, **3d** and **4b**, and **5a**. The nor-*ent*-kauranone **6a**, isolated in the form of its methyl ester **6b**, was identified through its ^{1}H NMR (see Experimental) and ^{13}C NMR spectra (Table 2). Compound **6a** has been obtained previously by degradation of **1a** [23], but never to our knowledge as a natural product.

11-Oxotrachyloban-19-oic acid (**7a**) was isolated in the form of its methyl ester **7b**, which could not be induced to crystallize. The empirical formula $C_{21}H_{30}O_3$ (high resolution MS), IR spectrum (C=O frequencies at 1725 and 1675 cm^{-1}) and ^{1}H NMR and ^{13}C NMR spectra (Tables 1 and 2) characterized it as the methyl ester of a ketonic trachyloban-19-oic acid.* In the ^{1}H NMR spectrum the unusual chemical shift of a signal at δ2.83, which was assigned to H-1β by decoupling experiments, could be explained only by placing the carbonyl group at C-11 (model). In the ^{13}C NMR spectrum the significant downfield shifts of the signals associated with C-9 and the cyclopropyl carbons C-12, C-13 and C-16, compared with the spectra of trachyloban-19-oic acid [29], ciliaric acid [13] and related compounds [30, 31], were also in accord with this formulation, as was the IR band at 1675 cm^{-1} which indicated conjugation and inclusion of the carbonyl in a 6-membered ring or larger. The location of the keto group at C-11 was further proved by $LiAlH_4$ reduction ($NaBH_4$ was ineffective) of **7b** to a 3:2 mixture of diols **8a** and **8b**. The multiplicities and coupling constants of the protons under the new secondary hydroxyl group (δ4.53 *dd*, J = 9, 4 Hz for **8a**, δ4.11 *tbr*, J *s* = 3, 3 Hz for **8b**) were as expected for 11β- and 11α-hydroxylated derivatives (models). The CD curve of **7b**, which exhibited a positive Cotton effect ($[\theta]_{298}$ +4360), indicated that the absolute configuration was as depicted in the formula.

A very minor constituent was the acid **9a**, again isolated as a methyl ester, mp 233–234°, which exhibited IR bands at 3450, 1730 and 1700 cm^{-1}. The molecular formula $C_{41}H_{60}O_5$ was established by high resolution mass spectrometry; detailed analysis of the ^{1}H NMR (see Experimental) and ^{13}C NMR spectra (Table 2) led to formula **9b**. The presence of the *ent*-16β-hydroxykaur-11-en-19-oate fragment (A half) could be inferred from the IR and ^{1}H NMR spectra, with the latter displaying the characteristic low field C-17 methyl and mutually coupled vinylic proton signals at δ5.91 and 5.55 of this moiety [5], and was verified by comparing the ^{13}C NMR spectra of **5b** and **9b** (Table 2). The ^{1}H NMR spectrum of **9b** also exhibited a low field signal at δ5.28, apparently due to hydrogen under an ester function in the second (B) half of the molecule, as a second double bond was lacking and as the δ65–90 region of the ^{13}C NMR spectrum exhibited only one signal, a doublet at δ71.11, in addition to the C-16 singlet of the A half. The appearance (*tbr*) and coupling constants (J = 3, 3 Hz) of this signal were strictly comparable to H-11β of **8b**; this and the appropriate shifts in the ^{1}H NMR and ^{13}C NMR spectra identified this portion of the molecule as methyl 11α-hydroxytrachyloban-19-oate. Paucity of material prevented verification of the structure by chemical methods. However, the alternative formula, in which the ether linkage between the two halves involves the carboxyl group of the trachylobane and the tertiary hydroxyl of the kaurene portion, is clearly ruled out by the chemical shifts in rings C and D of both halves and that of H-11 in the B half.

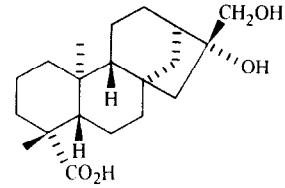
In a recent revision [32] of Heiser's infrageneric

* Trachyloban-19-oic acids have been encountered in several other *Helianthus* species [3, 5, 10, 11, 13, 24–27] as well as in members of the related genus *Viquiera* [28].

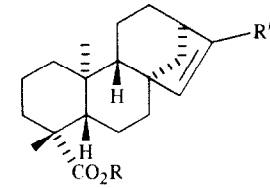


1a R = H

1b R = OAng



2

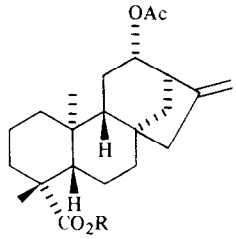


3a R = H, R′ = CHO

3b R = Me, R′ = CHO

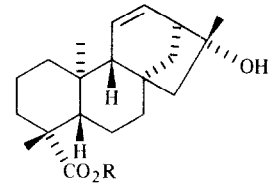
3c R = H, R′ = CH_2OH

3d R = Me, R′ = CH_2OH



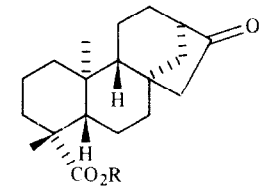
4a R = H

4b R = Me



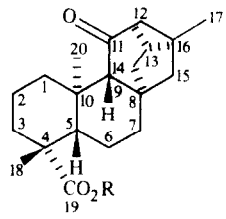
5a R = H

5b R = Me



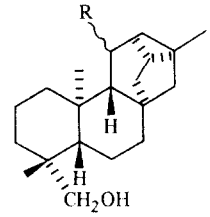
6a R = H

6b R = Me



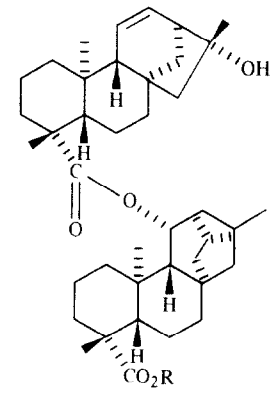
7a R = H

7b R = Me



8a R = β — OH

8b R = α — OH



9a R = H

9b R = Me

classification of *Helianthus* [7], *H. radula* was placed in series Angustifolii of section Divaricati. Chemically it more closely resembles *H. rigidus* [5] and *H. occidentalis* [6] of series Atrorubentes in producing *ent*-kaurenic acids and trachylobanic acids but no lactones. It shows less resemblance to *H. angustifolius* [8, 9] and *H. simulans* [6], the only other previously studied members of series Angustifolii, which yielded *ent*-kaurenic acids, very similar lactones and the flavone hymenoxin.

EXPERIMENTAL

Above-ground parts of *Helianthus radula* (Pursh) T. & G. (1.1 kg) collected by Mr. D. Gage in the vicinity of Tallahassee in September 1979 (voucher not available) was extracted with $CHCl_3$ and worked up in the usual manner. The crude gum on agitation with $CHCl_3$ gave a residue (0.8 g) identified as the usual mixture of sitosterol and stigmasterol β-D-glucosides. The mother liquor was evapd, the crude gum (28 g) was adsorbed on

Table 1. ^{1}H NMR spectral data of compound **7b***

Proton No.	**7b**	**7b** + Eu (fod)$_3$
H-1a	2.83 *tdbr* (3, 13)	3.04
1b	1.10 *m*	1.18
3a	2.15 *tdbr* (3, 13)	2.18
3b	1.03 *dt* (4, 13)	1.06
5	1.10 *m*	1.13 *dd* (12, 3)
6a	1.87 *qd* (3, 13)	obsc.
9	1.41 *s*	1.78 *s*
14a	2.27 *dbr* (12)	2.38
14b	1.49 *dbr*	obsc.
15a	1.67 *d* (12)	obsc.
15b	1.37 *d* (12)	obsc.
17†	1.26	1.28
18†	1.17	1.19
20†	0.78	0.88
OMe†	3.63	3.65

*Run at 270 MHz in $CDCl_3$ with TMS as internal standard. Chemical shifts in δ. Coupling constants in parentheses in hertz. Signals of unlisted protons were obscured (obsc.).

†Intensity of three protons.

40 g silica gel (Mallinckrodt 100 mesh) and chromatographed over 0.3 kg of the same adsorbent in hexane, 500 ml fractions being collected as follows: 1–4 (hexane), 5–10 (hexane–EtOAc, 19:1), 11–16 (hexane–EtOAc, 9:1), 17–22 (hexane–EtOAc, 4:1), 23–26 (hexane–EtOAc, 3:2), 27–30 (hexane–EtOAc, 2:3), 31–34 (hexane–EtOAc, 1:4) 35–38 (EtOAc), 39–40 (EtOAc–MeOH, 99:1), 41–42 (EtOAc–MeOH, 49:1), 43–44 (EtOAc–MeOH, 19:1) and 45–46 (EtOAc–MeOH, 9:1).

Fraction 6 (0.605 g) on purification by TLC (hexane–EtOAc, 19:1) furnished 32 mg of **1a**. Fraction 7 (6.3 g) was mainly **1a**. Purification of fractions 9, 11 and 12 by TLC (C_6H_6–EtOAc, 39:1) gave 0.22 g of a mixture of α-amyrin, β-amyrin and lupeol, 66 mg of **1b**, mp 198–200°, and 72 mg of a mixture of sitosterol and stigmasterol. Fraction 17 (0.645 g) on initial purification gave a mixture of **3a** and **4a**. Methylation with CH_2N_2 and subsequent purification by TLC (C_6H_6–EtOAc, 39:1) yielded 19 mg of **3b**, 53 mg of **4b** and 43 mg of a mixture of **3b** and **4b**. Methylation of fractions 18 and 19 (combined wt 0.54 g) and purification by TLC (C_6H_6–EtOAc, 39:1, developed × 3) gave **3b** and **4b** in 5 mg amounts and **7b** in 67 mg yield.

Trituration of fractions 23 and 24 with hexane–EtOAc gave 441 mg of **5a**, mp 241–247° (EtOAc–MeOH). Trituration of fraction 30 with Et_2O gave 42 mg of **2**, mp 268–270°, fractions 21 and 22 and the mother liquors of fractions 23 and 24 were combined (wt 2.6 g), esterified with CH_2N_2 and purified by a combination of CC (silica gel) and TLC (C_6H_6–EtOAc, 39:1, multiple developments) to yield 37 mg of **6b**, 9 mg of **9b**, 84 mg of **3d**, mp 130–132°, and 170 mg of **5b**. Compound **6b** had mp 143–145°, lit. mp. 142–143° [23], IR bands (KBr) 1742 and 1725 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ2.40 (*m*, H-13), 2.20 (*dbr*, J = 13 Hz, H-3a), 1.21 (H-18) and 0.91 (H-20). The ^{13}C NMR spectrum is listed in Table 2.

Methyl 11-*oxotrachyloban*-19-*oate* (**7b**). Compound **7b** which could not be induced to crystallize had IR bands (neat) at 1725 and 1675 cm^{-1}; CD curve (MeOH) $[\theta]_{298}$ +4360 (maximum); ^{1}H NMR and ^{13}C NMR spectra are listed in Tables 1 and 2. (Calc. for $C_{21}H_{30}O_3$: MW, 330.2195. Found: MW (MS), 330.2167.) Other significant ions in the high resolution MS were at *m/z* (rel. int.): 315 ($C_{20}H_{27}O_3$, 2.1), 271 ($C_{19}H_{27}O$, 9.5), 270

Table 2. ^{13}C NMR spectral data for compounds **5b**, **6a**, **7b** and **9b***

Carbon No.	**5b**	**6a**	**7b**	**9b** A half	**9b** B half
C-1	41.30 *t*‡	41.09 *t*‡	41.36 *t*	41.48 *t*	39.88 *t*
2	19.00 *t*	18.76 *t*	18.77 *t*	18.89 *t*, 18.55 *t*	
3	38.01 *t*	37.97 *t*	37.85 *t*†	38.29 *t*, 37.92 *t*	
4	43.24§	43.82	43.94	43.65‡	43.65
5	55.83 *d*	56.84 *d*	56.82 *d*	55.64 *d*	56.53 *d*
6	21.86 *t*	20.82 *t*	21.32 *t*	22.19 *t*, 21.98 *t*	
7	39.87 *t*‡	40.71 *t*‡	38.31 *t*	39.50 *t*	38.48 *t*
8	43.85§	42.46	39.82§	43.25‡	40.12
9	50.06 *d*	54.03 *d*	65.55 *d*†	50.12 *d*	59.31 *d*
10	38.68	39.56	39.74	38.89, 38.11	
11	130.50 d	19.08 t	211.56	132.86 d†	71.11 *d*
12	126.93 *d*	29.49 *t*	40.23 *d*	126.91 *d*†	24.59 *d*
13	61.16 *d*	47.77 *d*	31.12 *d*	61.20 *d*	23.74 *d*
14	34.39 *t*	37.32 *t*	34.20 *t*	34.51 *t*	32.38 *t*
15	58.59 *t*	54.98 *t*	48.55 *t*	58.60 *t*	48.71 *t*
16	83.75	222.37	31.24	83.71	21.98
17	25.81 *q*	—	19.38 *q*	25.77 *q*	20.15 *q*
18	28.53 *q*	28.76 *q*	29.87 *q*	28.73 *q*, 28.63 *q*	
19	177.83	177.83	177.57	176.38	177.42
20	15.31 *q*	15.92 *q*	14.90 *q*	15.94 *q*	13.68 *q*
OMe	51.18 q	51.21 *q*	51.18 *q*	—	51.11 *q*

*Run in $CDCl_3$ at 67.98 MHz with TMS as internal standard. Unmarked signals are singlets.

†Assignments made by selective irradiation.

‡, §Assignments may be interchanged.

($C_{19}H_{26}O$, 5.4) and 255 ($C_{18}H_{23}O$, 5.8).

Reduction with $NaBH_4$ in MeOH resulted in the recovery of **7b**. Reduction of 20 mg of **7b** in 1 ml THF with 20 mg $LiAlH_4$ for 30 min at 45° followed by the usual work-up gave 12 mg of a 3:2 mixture of diols **8a** and **8b**. (Calc. for $C_{20}H_{32}O_2$: MW, 304.2402. Found: MW (MS), 304.2388.) Other significant ions were at *m/z* (rel. int.): 286 ($C_{20}H_{30}O$, 32.4), 273 ($C_{19}H_{29}O$, 44.5), 255 ($C_{19}H_{27}$, 100). The major diol **8a** exhibited ^1H NMR signals (270 MHz, $CDCl_3$) at δ4.53 (*dd*, J = 9, 4 Hz, H-11α), 3.69 (*d*, J = 11 Hz, H-19α) and 3.45 (*dbr*, J = 11 Hz, H-19b). The isomeric diol **8b** had signals at δ4.11 (*tbr*, J = 3 Hz, H-11β), 3.69 (*d*, J = 11 Hz, H-19a) and 3.43 (*dbr*, J = 11 Hz, H-19b).

Ester **9b**. Compound **9b**, mp 233–234° (EtOAc), IR ν_{max}^{KBr} cm^{-1}: 3450, 1730 and 1700; ^1H NMR (270 MHz, $CDCl_3$): δ5.91 (*ddbr*, J = 10, 8 Hz) and 5.55 (*dd*, J = 10, 4 Hz, H-12 and H-11 of kaurene half), 5.28 (*tbr*, J = 3 Hz, H-11β of trachylobane half) 2.20 (*m*, H-13 of kaurene half), 1.56 (H-17 of kaurene half), 1.16 (H-18 of kaurene, H-17 and H-18 of trachylobane), 0.85 (H-20 of trachylobane) and 0.76 (H-20 of kaurene). The ^{13}C NMR spectrum is listed in Table 2. (Calc. for $C_{41}H_{60}O_5$: MW, 632.4437. Found: MW (MS), 632.4447.) The low resolution MS also exhibited significant ions at *m/z* (rel. int.): 6.14 (0.2), 331 (0.4), 317 (2.6), 315 (100), 299 (11.9), 273 (5.4) and 255 (91.9).

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