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SESQUITERPENE ALCOHOLS AND TRITERPENOIDS FROM *LIATRIS MICROCEPHALA*

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Key Word Index—*Liatris microcephala*; Eupatorieae; Compositae; (+)-T-cadinol; α-cadinol; oplopanol; oplodiol; 30-nor-taraxaster-20-en-3β-yl acetate.

Abstract—*Liatris microcephala* gave the sesquiterpene alcohols (+)-T-cadinol, α-cadinol, oplopanol and oplodiol, the benzofuran euparin and the triterpenes lupeyl acetate, taraxasteryl acetate, and 30-nor-taraxaster-20-en-3β-yl acetate.

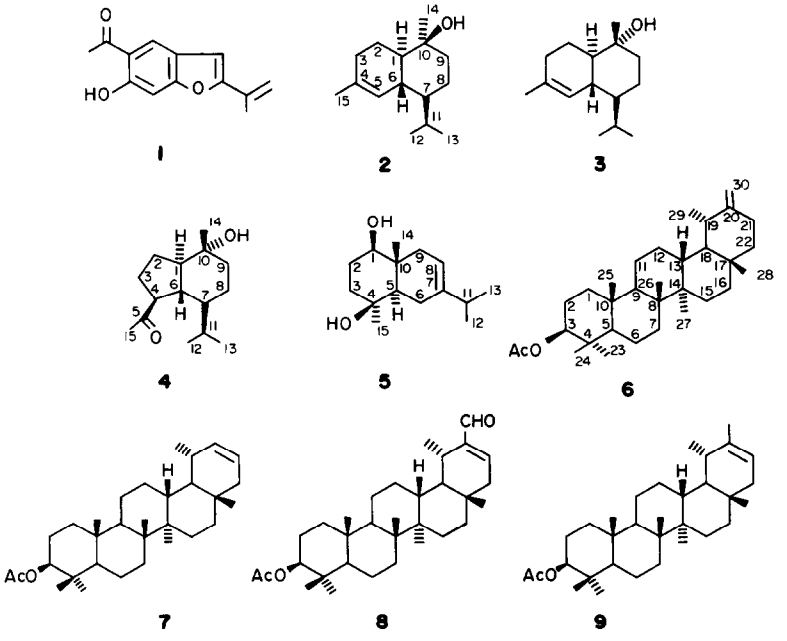
INTRODUCTION

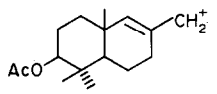
As part of our study of *Liatris* species (Compositae, Eupatorieae), which produce a variety of cytotoxic and antitumor lactones [1, 2], we have examined *Liatris microcephala* (Small) K. Schum. which occurs in the Piedmont plateau and mountain provinces of Georgia and Alabama, the interior plateau and mountain provinces of Tennessee and some adjoining areas [3, 4]. The species appears to elaborate no sesquiterpene lactones, but gave euparin (**1**), the sesquiterpene alcohols (+)-T-cadinol (**2**), α-cadinol (**3**), oplopanone (**4**), oplodiol (**5**), and the triterpenes lupeyl acetate, taraxasteryl acetate (**6**) and the new 30-nor-taraxaster-20-en-3β-yl acetate (**7**).

RESULTS AND DISCUSSION

Physical properties and spectral data of oily **2**, $[\alpha]_D^{27}$ +2.5°, and crystalline **3**, mp 67–68°, $[\alpha]_D^{27}$ −37.5°, were identical with those recently published for (+)-T-cadinol and α-cadinol, respectively [5]. Structures were assigned to **4**, mp 86.5–87°, $[\alpha]_D^{25}$ −21.2°, and **5**, mp 96–97°, $[\alpha]_D^{27}$ −41.7°, on the basis of their IR, NMR and mass spectra. Direct comparison with authentic samples of oplopanone and oplodiol established their identity. These compounds were originally isolated from *Oplopanax japanicus* (Araliaceae) [6, 7]. Oplopanone has since been detected in other plant sources [8, 9] and derivatives have been found in Senecioneae [10–12]. The previously unreported ^{13}C NMR spectra of these sesquiterpenes are listed in the Experimental.

Substance **7**, mp 228–233°, appears to be new. Its empirical formula, $C_{31}H_{50}O_2$ (high resolution mass spectrometry), coupled with the facile loss of the elements of acetic acid on electron impact and the ^1H NMR spectrum, which exhibited signals of an equatorial acetate (methyl singlet at δ 2.04 and one-proton *dd* at 4.49, J = 9, 7 Hz), six other methyl singlets (δ 0.83, 0.84, 0.85, 0.88, 0.95 and 1.05) and one methyl doublet (δ 0.99, J = 7 Hz) as





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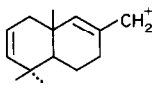

B

Table 1. ^{13}C NMR spectral data for compounds 6–8*

Carbon No.	6	7	8
1	38.52*t*	38.49*t*	38.48*t*
2	23.75*t*	23.73*t*	23.71*t*
3	80.90*d*	81.02*d*	80.96*d*
4	37.84	37.84	37.82
5	55.52*d*	55.44*d*	55.44*d*
6	18.23*t*	18.23*t*	18.20*t*
7	34.08*t*	34.19*t*	34.19*t*
8	40.98	41.08	41.09
9	50.48*d*	50.18*d*	50.36*d*
10	37.10	37.08	37.06
11	21.52*t*	21.57*t*	21.48*t*
12	25.66*t*	27.98*t*	27.28*t*
13	39.42*d*†	39.29*d*	39.06*d*
14	42.09	42.39	42.30
15	26.70*t*	26.91*t*	26.91*t*
16	38.93*t*‡	42.09*t*	43.03*t*
17	34.57	34.38	34.82
18	48.76*d*	47.78*d*	48.28*d*
19	39.23*d*†	32.47*d*	29.43*d*
20	154.60	135.10*d*	148.51
21	26.21*t*	122.23*d*	148.96*d*
22	38.36*t*‡	29.69*t*	36.51*t*
23	27.98*q*	27.98*q*	27.95*q*
24	16.51*q*	16.51*q*	16.50*q*
25	15.94*q*	16.05*q*	16.00*q*
26	16.39*q*	16.34*q*	16.33*q*
27	14.76*q*	14.54*q*	14.70*q*
28	25.52*q*	24.25*q*	23.17*q*
29	19.50*q*	17.84*q*	17.51*q*
30	107.15*t*	—	193.89*d*
1′	170.92	170.92	170.94
2′	21.27*q*	21.28*q*	21.28*q*

*Run at 67.89 MHz in $CDCl_3$ with TMS as internal standard. Unmarked signals are singlets.

†, ‡Assignments with the same sign in each column may be interchanged.

well as a two proton multiplet at δ 5.48, indicated the presence of a monounsaturated pentacyclic 3β-acetoxynortriterpene of the taraxasterane series. The double bond of type –CH=CH– was in ring E because of the presence of strong fragment ions at *m/z* 249 (**A**) and 189 (**B**, base peak) also found in the mass spectrum of **6**, pseudotaraxasterol acetate (**9**) [13] and the aldehyde **8** [1]. More specifically it was located at C-20 because in C_6D_6 the vinylic two proton multiplet was resolved into an AB system (J_{AB} = 10.5 Hz) with H_A coupled to one additional proton (J_{AX} = 5.5 Hz) and H_B to two ($J_{BY} = J_{BZ}$ = 2 Hz). Comparison of the ^{13}C NMR spectra of **6–8** (Table 1) supported this assignment; in particular the correspondence between the frequencies in the spectra of **7** and **8** is striking and demonstrates that **7** is 30-nor-pseudotaraxasteryl acetate (30-nor-taraxaster-20-en-3β-yl acetate).

The recently reported ^{13}C NMR spectrum of **6** [14] requires comment. Signals at δ 25.4, 26.1, 38.3, 30.8, 39.1 and 39.3 were assigned to C-21, C-28, C-19, C-16 and C-22, respectively, without specification as to their multiplicities. We find these signals (under our conditions at δ 25.52, 26.21, 38.25, 38.93, 39.23 and 39.42) to be, in order of their appearance, a quartet, a triplet, a triplet, a triplet, a doublet and a doublet and, hence a change is required in the previous assignments to those given in Table 1.

The chemistry of *L. microcephala* differs significantly from that of *L. acidota* and *L. spicata*, the two other members of section Spicatae according to Gaiser [3] which have been investigated previously [1, 15, 16]. The import of this requires further study.

EXPERIMENTAL

Isolation of Liatris microcephala *constituents.* Above-ground parts of *L. microcephala* (4.6 kg), collected by Dr. S. McDaniel and Mr. C. Duncan on 14 October 1979 in the Little River Canyon area *ca* 8 miles S. of the junction of Alabama highways 275 and 35, DeKalb Co., Alabama (McDaniel and Duncan voucher No. 22988 on deposit in the Herbarium of Mississippi State University) was extracted with $CHCl_3$ and worked-up in the usual fashion [17]. Half of the crude gum (total wt 127 g) was preadsorbed on 100 g Si gel (Merck No. 60) and chromatographed over 1 kg of the same adsorbent packed in *n*-hexane. 600 ml eluent fractions were collected as follows: fractions 1–5, hexane–EtOAc (97:3); 6–13, hexane–EtOAc (19:1); 14–24, hexane–EtOAc (9:1); 25–34, hexane–EtOAc (17:3); 35–44, hexane–EtOAc (3:1); 45–48, hexane–EtOAc (3:2); 49–51, hexane–EtOAc (3:7); 52–58, EtOAc; 59–62, EtOAc–MeOH (19:1); 63 and 64, EtOAc–MeOH (17:3) and 65–70, EtOAc–MeOH (1:1).

Fractions 7 and 8 were combined and purified by TLC (C_6H_6–EtOAc, 19:1), to give 3 g of a 2:1 mixture of lupeyl and taraxasteryl acetates. Recrystallization from *n*-hexane afforded pure **6**, mp 229.5–233°, IR ν_{max}^{KBr} cm^{-1}: 2940, 1725, 1250, 890; ^1H NMR ($CDCl_3$): δ 4.61 (*br t*, *J* = 3 Hz, H-30), 4.49 (*dd*, *J* = 10, 7 Hz, H-3), 1.96 (Ac), 1.02 (*d*, *J* = 7 Hz, H-2a), 1.02, 0.93, 0.88, 0.85, 0.85, 0.84 (Mes); MS *m/z* (rel. int.): 468 $[M]^+$ (14.6), 453 (1.2), 408 (5.6), 249 (14.0), 218 (10.0), 204 (21.7), 189 (100).

Fractions 10–25 contained euparin (**1**) which was separated from the other constituents of fractions 11–15 and 16–19 by CC (Si gel, C_6H_6–EtOAc, 97:3 or 19:1), purified by prep. TLC and recrystallized from *n*-hexane, mp 119–121.5°, total yield 400 mg. The less polar constituent of fractions 11–25 was the nortriterpene, **7**, which was purified by prep. TLC (C_6H_6–EtOAc, 19:1) and recrystallized from $CHCl_3$–EtOAc, mp 228–233°, yield *ca* 50 mg, IR ν_{max}^{KBr} cm^{-1}: 2965, 1735, 1260; ^1H NMR ($CDCl_3$): δ 5.48 (*m*, H-20, H-21), 4.49 (*dd*, *J* = 9, 7 Hz, H-3), 2.04 (Ac), 0.99 (*d*, *J* = 7 Hz, H-29), 1.05, 0.94, 0.88, 0.85, 0.84, 0.83 (Mes); ^1H NMR (C_6D_6): δ 5.62 (*dd*, *J* = 10.5 and 5.5 Hz) and 5.66 (*dt*, *J* = 10.5, 2 Hz, H-20 and H-21), 4.70 (*dd*, *J* = 11.5, 5 Hz, H-3), 1.76 (Ac), 1.06 (*d*, *J* = 7 Hz, H-29), 0.97, 0.95, 0.92, 0.91, 0.89, and 0.79; MS *m/z* (rel. int.): 454 $[M]^+$ (9.6), 394 (10.9), 379 (4.4), 249 (11.3), 243 (3.9), 216 (3.3), 203 (10.3), 189 (100). [Calc. for $C_{31}H_{50}O_2$: MW, 454.3812. Found: MW (MS), 454.3815].

Rechromatography of fractions 17–19 (Si gel, C_6H_6–EtOAc, 49:1) gave, in addition to **1**, 500 mg (+)-T-cadinol (**2**) as an oil after prep. TLC (C_6H_6–EtOAc, 19:1), $[\alpha]_D^{27}$ +2.5° (EtOH; *c* 0.86), IR ν_{max}^{film} cm^{-1}: 3460, 2970, 2950, 2880, 1455, 1375, 775; ^1H NMR ($CDCl_3$): δ 5.56 (*br*, H-5), 2.19 (*m*) 1.67 (*br*, H-15), 1.23 (H-14), 0.93 (*d*) and 0.81 (*d*, *J* = 7 Hz, H-12, H-13); on addition of TAI δ 8.45 (*br*, NH), 5.53 (*br*, H-5), 2.85 (*br d*, *J* = 11 Hz, H-9), 1.66 (*br*), 1.61, 0.91 (*d*) and 0.76 (*d*) (Mes); ^{13}C NMR ($CDCl_3$):

δ 134.09 (C-5), 122.73 (*d*, C-5), 70.56 (C-10), 48.08 (*d*, C-1), 46.75 (*d*, C-7?), 40.40 (*t*, C-9), 37.81 (*d*, C-6?), 30.95 (*t*), 22.66 (*t*) and 19.89 (*t*, C-2, C-3 and C-8), 28.49 (*q*, C-14), 26.23 (*d*, C-11), 23.76 (*q*) and 21.44 (*q*, C-12 and C-13), 15.25 (*q*, C-15); MS *m/z* (rel. int.): 222 $[M]^+$ (0.15), 204 (47.9), 189 (22.0), 161 (100), 134 (20.1), 105 (54.1), 95 (36.2), 81 (52.1).

Combination of fractions 20–23 and prep. TLC (C_6H_6–EtOAc, 19:1) gave euparin and, as major constituent, α-cadinol (**3**) which was purified by sublimation, yield 300 mg, mp 67–68°, $[\alpha]_D^{27}$ – 37.5° (EtOH; *c* 0.66), IR ν_{max}^{KBr} cm^{-1}: 3350, 2970, 2959, 2880, 1380, 1140, 830; ^1H NMR ($CDCl_3$): δ 5.49 (*br*, H-15), 1.66 (*br*, H-15), 1.09 (H-14), 0.91 (*d*) and 0.76 (*d*, J = 7 Hz, H-12, H-13); with added TAI 8.17 (*br*, NH), 5.49 (*br*, H-5), 1.67 (*br*), 1.50, 0.93 (*d*) and 0.77 (*d*) (Mes); ^{13}C NMR ($CDCl_3$): δ 134.90 (C-4), 122.32 (*d*, C-5), 72.88 (C-10), 50.04 (*d*, C-1), 46.75 (*d*, C-7), 42.23 (*t*, C-9), 39.88 (*d*, C-6?), 30.95 (*t*), 22.69 (*t*), 21.99 (*t*, C-2, C-3 and C-8), 26.00 (*d*, C-11), 23.31 (*q*) and 21.52 (*q*, C-12 and C-13), 20.76 (*q*, C-14), 15.15 (*q*, C-15); MS *m/z* (rel. int.): 222 $[M]^+$ (12.7), 204 (67.0), 189 (12.9), 179 (8.7), 164 (55.6), 161 (64.8), 137 (33.1), 121 (100), 109 (51.9), 105 (51.5), 95 (85.9).

Combination of fractions 46–49, prep. TLC (C_6H_6–EtOAc, 4:1) and recrystallization from *n*-hexane gave 1.2 g oplopanone (**4**), mp 86.5–87°, $[\alpha]_D^{25}$ – 21.2° (EtOH; *c* 1.54), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3595, 1710; ^1H NMR ($CDCl_3$): δ 2.65 (*m*, H-3), 2.18 (H-15), 1.20 (H-14), 0.90 (*d*) and 0.69 (*d*, J = 7 Hz, H-12, H-13); ^{13}C NMR ($CDCl_3$): δ 211.33 (C-5), 72.95 (C-10), 57.07 (*d*, C-4), 55.81 (*d*, C-6), 49.50 (*d*), 46.77 (*d*, C-1 and C-7), 42.11 (*t*, C-9), 29.53 (*q*, C-15), 29.45 (*d*, C-11), 28.66 (*t*), 25.31 (*t*), 23.07 (*t*, C-2, C-3 and C-8), 21.94 (*q*), 20.32 (*q*, C-12 and C-13), 15.63 (*q*, C-14); MS *m/z* (rel. int.): 238 $[M]^+$ (12.1), 220 (9.1), 205 (5.3), 177 (30.4), 153 (100), 135 (69.8).

Combination of fractions 50–52, prep. TLC (C_6H_6–EtOAc, 4:1 and $CHCl_3$–EtOAc, 4:1) and recrystallization from *n*-hexane–EtOAc gave 1.5 g oplodiol (**5**), mp 96–97°, $[\alpha]_D^{27}$ – 7° (EtOH; *c* 0.74), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600, 3440, 2960, 1705; ^1H NMR: δ 5.34 (*br d*, J = 4.5 Hz, H-8), 3.31 (*dd*, J = 11, 4 Hz, H-1), 2.21 (*sept.*, J = 7 Hz, H-11), 1.19 (H-15), 1.04 (*d*, J = 7 Hz, H-12, H-13), 0.97 (H-14); ^{13}C NMR ($CDCl_3$): δ 141.94 (C-7), 116.11 (*d*, C-8), 79.93 (*d*, C-1), 70.97 (C-4), 46.34 (*d*, C-5), 40.78 (*t*, C-2 or C-3), 39.53 (*t*, C-3 or C-2), 37.73 (C-10), 35.01 (*d*, C-11), 29.88 (*q*, C-15), 26.83 (*t*, C-6 or C-9), 23.10 (*t*, C-9 or C-6), 21.97 (*q*), 21.25 (*q*, C-12, C-13), 11.72 (*q*, C-14).

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