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FURTHER CADINENE DERIVATIVES FROM *HETEROTHECA GRANDIFLORA*

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Key Word Index—*Heterotheca grandiflora*; Compositae; sesquiterpenes; cadinene derivatives.

Abstract—The reinvestigation of *Heterotheca grandiflora* from Hawaii gave in addition to compounds isolated previously five new cadinene derivatives.

INTRODUCTION

The chemical investigation of five species of the genus *Heterotheca* (tribe Astereae) gave mainly cadinene derivatives [1–5]. We now have studied the constituents of *H. grandiflora* Nutt. collected in Hawaii, and compared them to these isolated from *H. grandifola* collected in Arizona [3]. In addition to the compounds isolated previously some further cadinene derivatives were obtained. These were the 2,14-dihydroxycalamene esters **3**–**5**, δ-cadinen-2-one (**6**) and δ-cadinen-14-oic acid (**7**).

RESULTS AND DISCUSSION

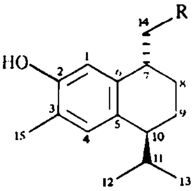
The esters **3**–**5** could be separated in part by HPLC which gave a mixture of the angelate **3** and the 2-methylbutyrate **4** and the isobutyrate **5**. The structures were deduced from the ^1H NMR spectra (Table 1) which were close to that of **2** [3]. The nature of the ester groups followed from the typical ^1H NMR signals. As usual the chemical shifts, especially that of H-14, differed in the spectra of the unsaturated and saturated esters.

The structure of **6** followed from the ^1H NMR spectrum (Table 1) which was close to that of the corresponding 9-angeloyloxy derivative [3]. The structure of **7**, which was transformed by addition of diazomethane to the corresponding methyl ester **8**, was deduced from the molecular formula and the ^1H NMR spectral data of **7** and **8** (Table 1). The presence of a carbonyl group at C-7 caused a considerable downfield shift of H-1β. Spin decoupling allowed the assignment of all signals though some were overlapped multiplets. Furthermore the ^{13}C NMR data of **8** (see Experimental) agreed well with the proposed structure.

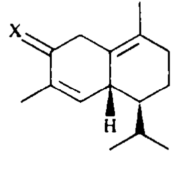
Though the Hawaiian collection mainly gave the same cadinene derivatives as the Arizona collection [3], some clear differences are obvious. In particular the absence of cadalene derivatives in the former collection is remarkable.

EXPERIMENTAL

The air dried aerial parts collected in Hawaii, July 1984 (500 g, voucher RMK 9314 deposited in the US National Herbarium) were extracted with MeOH–Et_2O–petrol (1:1:1) and the extract obtained after removal of MeOH insoluble material was submitted to CC (silica gel) (conditions as in ref. [6]). Six fractions were obtained: 1 (petrol), 2 (Et_2O–petrol, 9:1), 3 (Et_2O–petrol, 1:3), 4 (Et_2O–petrol, 1:1), 5 (Et_2O) and 6 (Et_2O–MeOH, 9:1). TLC of fraction 1 (silica gel PF 254, petrol) gave 50 mg δ-cadinene and repeated TLC of fraction 2 (Et_2O–petrol, 20:1) gave 10 mg **6** (R_f 0.4) and 80 mg **7** (R_f 0.13). Fraction 3 was treated with CH_2N_2 and separated by TLC (Et_2O–petrol, 1:1) affording 40 mg **8** (R_f 0.81), 55 mg 7-desmethyl-2-hydroxycalamene and 2-hydroxycalamene [3] (R_f 0.60) as well as 50 mg of a mixture of **3**–**5** (R_f 0.67). HPLC (RP 8, MeOH–H_2O, 4:1, flow rate, 3 ml/min, 100 bar) gave 30 mg **3** and **4** (*ca* 1:1, R_t 11 min) and 10 mg **5** (R_t 7.5 min). TLC of fraction 4 (Et_2O–petrol, 1:1, two developments) gave 23 mg 2-hydroxy-7-oxo-7-desmethyl calamene [3] and 15 mg cubenol. TLC of fraction 5 (Et_2O) gave 33 mg 2,14-dihydroxycalamene [3] and TLC of fraction 6 (Et_2O–MeOH, 9:1) afforded 20 mg 2-hydroxycalamen-14-oic acid [3]. Known compounds



	1	2	3	4	5
R	H	OH	OAng	OMebu	OiBu



	6	7	8
R	Me	CO_2H	CO_2Me
X	O	H_2	H_2

Table 1. ^{1}H NMR spectral data of **3**–**8** (400 MHz, $CDCl_3$, TMS as int. standard)

H	**3**	**4**	**5**	**6**	**7**	**8**
1	6.64 *s*	6.61 *s*	6.60 *s*	3.52 *d*	3.55 *br dd*	3.30 *br dd*
1′				2.82 *br d*	2.15 *m*	2.15 *m*
2	—	—	—	—		
2′	—	—	—	—		
4	6.99 *s*	6.98 *s*	6.98 *s*	6.74 *br s*	5.36 *br s*	5.77 *br s*
5	—	—	—	2.82 *m*	2.69 *br d*	2.64 *br d*
7	3.06 *dddd*	3.02 *dddd*	3.01 *dddd*	2.82 *m*	2.69 *br d*	2.64 *br d*
8	2.24 *m*	2.24 *m*	2.24 *m*	2.10 *m*	2.10 *br d*	2.07 *br d*
8′	1.65 *m*	1.65 *m*	1.65 *m*		2.54 *br d*	2.46 *br d*
9				1.60 *m*	1.68 *ddd*	1.66 *ddd*
9′					1.15 *ddd*	1.15 *ddd*
10	2.58 *m*	2.58 *m*	2.57 *m*	*	1.06 *dddd*	1.07 *dddd*
11	2.24 *m*	2.24 *m*	2.24 *m*	2.1 *m*	2.0 *m*	2.0 *m*
12	0.99 *d*	0.99 *d*	1.00 *d*	1.02 *d*	0.96 *d*	0.96 *d*
13	0.70 *d*	0.70 *d*	0.70 *d*	0.86 *d*	0.77 *d*	0.77 *d*
14	4.33 *dd*	4.24 *dd*	4.23 *dd*	1.65 *br s*	—	—
14′	4.15 *dd*	4.11 *dd*	4.11 *dd*		—	—
15	2.19 *br s*	2.19 *br s*	2.19 *br s*	1.78 *dd*	1.68 *br s*	1.65 *br s*
OR	6.07 *qq*	2.39 *tq*	2.57 *qq*	—	—	3.70 *s*
	1.99 *dq*	1.75 *ddq*	1.17 *d*			
	1.91 *dq*	1.49 *ddq*	1.18 *d*			
		0.90 *t*				
		1.15 *d*				

*Obscured multiplet.

J (Hz): Compounds **3**–**5**: 7, 8 = 7, 8′ ~ 6; 7, 14 = 5; 7, 14′ = 11; 11, 12 = 11, 13 = 7; 14, 14′ = 12; compound **6**: 1, 1′ = 17; 4, 15 = 5, 15 ~ 2; 11, 12 = 11, 13 = 7; compounds **7** and **8**: 1, 1′ = 8, 9′ = 9, 9′ = 9′, 10 = 12; 1′, 2 = 5; 1′, 2′ ~ 2; 1, 2 = 1, 2′ = 5, 10 ~ 10; 9, 10 = 3.5; 8, 9 = 8′, 9 ~ 5; 11, 12 = 11, 13 = 7.

were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material. All compounds showed no impurities by ^{1}H NMR spectra and TLC.

2,14-*Dihydroxycalamen*-14-O-*angelate and* [2-*methylbutyrate*] (**3** *and* **4**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1740 (CO_2R), 1710 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 318.219 (1.5) and 316.203 (1.0) $[M]^+$, (calc. for $C_{20}H_{30}O_3$: 318.219 and for $C_{20}H_{28}O_3$: 316.203), 216 $[M-RCO_2H]^+$ (28), 173 $[216-C_3H_7]^+$ (100), 158 $[173-Me]^+$ (12), 145 $[173-CO]^+$ (10), 85 $[C_4H_9CO]^+$ (6), 83 $[C_4H_7CO]^+$ (14), 57 $[85-CO]^+$ (20), 55 $[83-CO]^+$ (18); $[\alpha]_D = +6$ ($CHCl_3$; *c* = 0.7).

2,14-*Dihydroxycalamen*-14-O-*isobutyrate* (**5**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1740 (CO_2R); MS *m/z* (rel. int.): 304 $[M]^+$ (0.5) (calc. for $C_{19}H_{28}O_3$: 304), 216 $[M-RCO_2H]^+$ (10), 173 $[216-C_3H_7]^+$ (100), 71 $[C_3H_7CO]^+$ (8).

Cadinen-2-one (**6**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1680 ($C{=}CC{=}O$); MS *m/z* (rel. int.): 218.167 $[M]^+$ (26) (calc. for $C_{15}H_{22}O$: 218.167), 203 $[M-Me]^+$ (5), 175 $[M-C_3H_7]^+$ (100), 148 $[M-CH_2{=}CHCHMe_2, RDA]^+$ (28), 133 $[148-Me]^+$ (15), 105 (31), 91 (24).

Cadinen-14-*oic acid* (**7**). Colourless crystals, mp 104°. Addition of CH_2N_2 gave the methyl ester **8**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1640 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 248.178 $[M]^+$ (46) (calc. for $C_{16}H_{24}O_2$: 248.178), 233 $[M-Me]^+$ (4), 205 $[M-C_3H_7]^+$ (26), 189 $[M-CO_2Me]^+$ (58), 174 $[205-OMe]^+$ (30), 145 $[174-CHO]^+$ (100); ^{13}C NMR ($CDCl_3$) (C-1–C-15): 26.9, 28.0, 134.9, 123.2, 40.9, 148.8, 123.1, 32.7, 20.8, 44.7, 26.8, 23.0, 21.6, 169.7, 15.6 and 51.1 (OMe).

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