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## NEW CADINENE DERIVATIVES FROM *HETEROOTHECA LATIFOLIA*\*

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

**Abstract**—*Heterotheca latifolia* afforded several new acids all derived from cadinane.

So far five species of the North American genus *Heterotheca* have been investigated chemically [1-3]; however, in only three species have the aerial parts been investigated. The roots of *H. latifolia* Buckl. gave a  $C_{10}$ -acetylenic compound which is widespread in the tribe [2]. We have now studied the aerial parts of *H. latifolia*. In addition to germacrene D, caryophyllene and bicyclogermacrene several cadinene derivatives were present, the already known angelate **1** [3] and the acids **2a-9a**, which could be separated only after esterification with  $CH_2N_2$ . The main compound was the acetate **2b**. Its  $^1H$  NMR spectrum (Table 1) indicated the presence of an  $\alpha,\beta$ -unsaturated ester group with a  $\beta$ -hydrogen ( $\delta$  7.33 d,  $J = 2$  Hz) and an olefinic methyl group ( $\delta$  1.62 s, br). A broadened doublet at  $\delta$  2.72 was coupled with the olefinic proton and with the olefinic methyl indicating a similar situation as in **1**. The position of the acetoxy group followed from the chemical shift of the corresponding signal for the proton under the acetoxy group. As this signal showed small vicinal couplings only, a  $2\beta$ -orientation was assumed, especially as a very similar  $2\alpha$ -alcohol [3] showed larger couplings ( $J_{1,2} = 5.5$  Hz). Though some signals were overlapped,

spin decoupling and Eu(fod)<sub>3</sub> induced shifts clearly supported the proposed structures. The esters **3b-5b** could not be separated. However, the  $^1H$  NMR spectrum showed that they differed from **2b** only by the ester residues at C-2. The typical ester signals indicated the nature of these groups (Table 1). The ester **6b** was isomeric with **2b**. Spin decoupling showed that in this case the acetoxy group had to be placed at C-8. Again, a  $\beta$ -orientation was more likely though an  $\alpha$ -position could not be excluded. The  $^1H$  NMR data of **7b** (Table 1) showed the presence of a hydroxylated isopropyl group. One methyl doublet was replaced by two double doublets at  $\delta$  3.76 and 3.47. These were coupled with a multiplet at  $\delta$  2.15, which was also coupled with the remaining methyl doublet at  $\delta$  1.07. The other signals were close to those of **2b** indicating the same stereochemistry. Two further alcohols, were obviously isomeric at C-10 only. Both compounds, **8b** and **9b** afforded **10** after heating with *p*-toluenesulfonic acid in benzene. The relative configurations were assigned by the observed shift differences for H-10. In the spectrum of **9b** this signal was shifted downfield most probably due to the *cis*-orientated 7-hydroxy group.

The absolute configurations of the natural compounds could not be assigned with certainty, the given ones are the most probable from biogenetic considerations. The newly isolated cadinene derivatives provide further support that these compounds are characteristic for the genus *Heterotheca*.

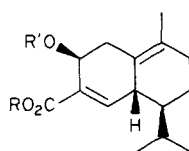
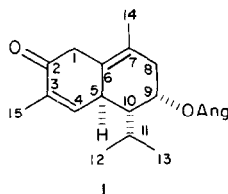
\*Part 347 in the series "Naturally Occurring Terpene Derivatives". For Part 346, see Bohlmann, F., Suwita, A., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 1649.

Table 1.  $^1\text{H}$  NMR spectral data of compounds **2b–9b** and **10** (270 MHz,  $\text{CDCl}_3$ , TMS as int. standard)

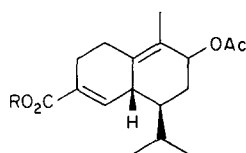
	<b>2b</b> *	+ Eu(fod) <sub>3</sub>	<b>6b</b> †	<b>7b</b> †	<b>8b</b>	<b>9b</b>	<b>10</b>
H-1	3.08 <i>dd</i>	4.18 <i>d(br)</i>	2.79 <i>dddd</i>	2.78 <i>dddd</i>	7.70 <i>d</i>	7.67 <i>d</i>	7.28 <i>d</i>
H-1'	1.99 <i>d(br)</i>	2.44 <i>d(br)</i>	1.95 <i>ddd(br)</i>	1.87 <i>ddd(br)</i>			
H-2	5.79 <i>dd(br)</i>	10.03 <i>rs(br)</i>	2.55 <i>dd(br)</i>	2.51 <i>ddd</i>	7.86 <i>dd(br)</i>	7.87 <i>d(br)</i>	7.87 <i>dd</i>
H-4	7.33 <i>d</i>	8.29 <i>d</i>	2.59 <i>ddd(br)</i>	2.2 <i>m</i>	7.93 <i>s(br)</i>	7.94 <i>s(br)</i>	7.76 <i>d</i>
H-5	2.72 <i>d(br)</i>	3.25 <i>d(br)</i>	6.99 <i>rs(br)</i>	7.32 <i>s(br)</i>	—	—	—
H-8	2.0 <i>m</i>	2.5 <i>m</i>	2.67 <i>d(br)</i>	2.70 <i>d(br)</i>	1.5–1.9 <i>m</i>	1.5–1.9 <i>m</i>	5.87 <i>s(br)</i>
H-8'	2.0 <i>m</i>	2.5 <i>m</i>	5.23 <i>s(br)</i>	2.15 <i>m</i>			
H-9	1.3 <i>m</i>	1.57 <i>dddd</i>	1.43 <i>dddd</i>	1.3 <i>m</i>	2.08 <i>m</i>	2.69 <i>ddd</i>	1.90 <i>m</i>
H-9'	1.74 <i>d(br)</i>	2.00 <i>d(br)</i>	1.83 <i>d(br)</i>	1.75 <i>m</i>			2.08 <i>m</i>
H-10	1.3 <i>m</i>	1.88 <i>dd(br)</i>	1.47 <i>dd(br)</i>	1.3 <i>m</i>	2.45 <i>dqq</i>	2.35 <i>dqq</i>	2.43 <i>m</i>
H-11	2.16 <i>qq(br)</i>	2.5 <i>m</i>	2.18 <i>qq(br)</i>	2.15 <i>m</i>	1.07 <i>d</i>	1.08 <i>d</i>	
H-12	1.03 <i>d</i>	1.24 <i>d</i>	0.95 <i>d</i>	1.07 <i>d</i>	0.70 <i>d</i>	0.78 <i>d</i>	0.82 <i>d</i>
H-13	0.87 <i>d</i>	1.04 <i>d</i>	0.81 <i>d</i>	3.76 3.47 <i>dd</i>	1.53 <i>s</i>	1.55 <i>s</i>	2.05 <i>s(br)</i>
H-14	1.62 <i>s(br)</i>	2.15 <i>s(br)</i>	1.68 <i>s(br)</i>	1.66 <i>s(br)</i>	3.92 <i>s</i>	3.92 <i>s</i>	3.91 <i>s</i>
OMe	3.74 <i>s</i>	4.63 <i>s</i>	3.75 <i>s</i>	3.73 <i>s</i>	—	—	—
OAc	2.01 <i>s</i>	3.29 <i>s</i>	2.05 <i>s</i>	—	—	—	—

\***3b–5b** identical signals, except those of the ester part. †400 MHz.

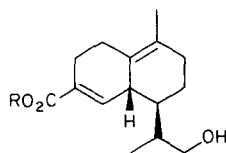
*J* (Hz): compounds **2b–5b**: 1,1' = 15; 1,2 = 2.5; 1',2' = 2; 4,5 = 2; 5,10 = 9; 8,9 = 12,8'9 = 4.5; 9,9' = 12; 9,10 = 12; 10,11 = 2; 11,12 = 11,13 = 7; OCOCH(Me)Et: 2.30 *ddq*, 1.43 *ddq*, 1.30 *m*, 0.88 *t*, 1.12 *d*; OiVal: 2.15 *d(br)*, 1.3 *m*, 0.96 *d*; OiBu: 2.47 *qq*, 1.13 *d*; compound **6b**: 1,1' = 13; 1,2 = 5; 1,2' = 2.5; 1',2' = 5; 1',2' = 12; 2,2' = 15; 5,10 = 9; 8,9 = 3; 8',9' = 2; 9,9' = 13; 9,10 = 13; 9',10 = 10,11 = 2; 11,12 = 11,13 = 7; compound **7b**: 1,1' = 13; 1,2 = 5; 1,2' = 2; 1',2' = 5; 1',2' = 12; 2,2' = 16; 5,10 = 8; 11,12 = 7; 11,13 = 5; 11,13' = 7.5; 13,13' = 11; compounds **8b/9b**: 1,2 = 8; 9,10 = 7; 9',10 = 5; 10,11 = 5; 11,12 = 11,13 = 7; compound **10**: 1,2 = 8; 2,4 = 1.5; 11,12 = 11,13 = 6.5.



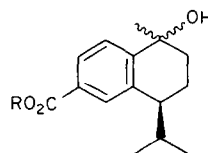
	<b>2a</b>	<b>2b</b>	<b>3a</b>	<b>3b</b>	<b>4a</b>	<b>4b</b>	<b>5a</b>	<b>5b</b>
R	H	Me	H	Me	H	Me	H	Me
R'	Ac		<i>i</i> -Val		Mebu		<i>i</i> -Bu	



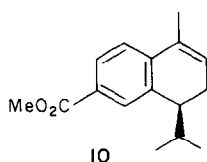
**6a** R = H  
**6b** R = Me



**7a** R = H  
**7b** R = Me



**8a** R = H, 7 $\alpha$ -OH  
**8b** R = Me, 7 $\alpha$ -OH  
**9a** R = H, 7 $\beta$ -OH  
**9b** R = Me, 7 $\beta$ -OH



## EXPERIMENTAL

The air-dried aerial parts (300 g) (voucher RMK-8429) were extracted with Et<sub>2</sub>O–petrol (1:2) and the resulting extract was separated first by CC and further by repeated TLC (Si gel). The less polar fractions afforded 100 mg germacrene D, 30 mg caryophyllene and 20 mg bicyclogermacrene, followed by 20 mg **1**. The polar fractions could be separated only after esterification with CH<sub>2</sub>N<sub>2</sub>. Finally, 15 mg **2b**, 3 mg **3b–5b** (ca 2:3:1), 3 mg **6b**, 3 mg **7b**, 1 mg **8b** and 1 mg **9b** were obtained (sepn with Et<sub>2</sub>O–petrol, 1:3, several times).

**Methyl-2β-acetoxy-δ-cadinene-15-oate (2b).** Colourless oil, IR  $\nu_{\text{max}}^{\text{CCl}_4}$ , cm<sup>-1</sup>: 1730, 1245 (OAc), 1720, 1645 (C=CCO<sub>2</sub>R); MS *m/z* (rel. int.): 306.183 [M]<sup>+</sup> (0.7) (C<sub>18</sub>H<sub>26</sub>O<sub>4</sub>), 246 [M – AcOH]<sup>+</sup> (21), 215 [246 – OMe]<sup>+</sup> (7), 203 [246 – CHMe<sub>2</sub>]<sup>+</sup> (42), 187 [215 – CO]<sup>+</sup> (61), 176 [246 – H<sub>2</sub>C=CHCHMe<sub>2</sub>]<sup>+</sup> (RAD, 100), 145 [176 – OMe]<sup>+</sup> (38);

$$[\alpha]_{24}^{25} = \frac{589}{-16} \frac{578}{-17} \frac{546}{-21} \frac{436}{-36} \text{ nm} \quad (c = 1.4, \text{CHCl}_3).$$

**Methyl-2β-isovaleryloxy-2-methylbutyryloxy and isobutyryloxy-δ-cadinene-15-oate (3b–5b).** Not separated. Oily mixture, IR  $\nu_{\text{max}}^{\text{CCl}_4}$ , cm<sup>-1</sup>: 1730 (CO<sub>2</sub>R), 1645 (C=C); MS *m/z* (rel. int.): 348.230 [M]<sup>+</sup> (0.4) (C<sub>21</sub>H<sub>30</sub>O<sub>4</sub>), 334 [M]<sup>+</sup> (0.1) (C<sub>20</sub>H<sub>30</sub>O<sub>4</sub>), 246–162 [M – RCO<sub>2</sub>H]<sup>+</sup> (24) (C<sub>16</sub>H<sub>22</sub>O<sub>6</sub>), 203 [246 – CHMe<sub>2</sub>]<sup>+</sup> (41), 187 [246 – OMe, CO]<sup>+</sup> (81), 176 [246 – H<sub>2</sub>C=CHCHMe<sub>2</sub>]<sup>+</sup> (100), 85 [RCO]<sup>+</sup> (5), 71 [RCO]<sup>+</sup> (4).

**Methyl-13-hydroxy-δ-cadinene-15-oate (7b).** Colourless oil, IR  $\nu_{\text{max}}^{\text{CCl}_4}$ , cm<sup>-1</sup>: 3620 (OH), 1715, 1640 (C=CCO<sub>2</sub>R); MS *m/z* (rel. int.): 264.173 [M]<sup>+</sup> (37), 246 [M – H<sub>2</sub>O]<sup>+</sup> (28),

232 [M – MeOH]<sup>+</sup> (100), 205 [M – CH(Me)CH<sub>2</sub>OH]<sup>+</sup> (53), 203 [205 – H<sub>2</sub>]<sup>+</sup> (70);

$$[\alpha]_{24}^{25} = \frac{589}{-116} \frac{578}{-122} \frac{546}{-139} \frac{436}{-248} \text{ nm} \quad (c = 0.3, \text{CHCl}_3).$$

**Methyl-7α-hydroxy-calamenene-15-oate (8b).** Colourless oil, IR  $\nu_{\text{max}}^{\text{CCl}_4}$ , cm<sup>-1</sup>: 3620 (OH), 1730 (CO<sub>2</sub>R); MS *m/z* (rel. int.): 262.157 [M]<sup>+</sup> (3) (C<sub>16</sub>H<sub>22</sub>O<sub>3</sub>), 244 [M – H<sub>2</sub>O]<sup>+</sup>, (51), 201 [244 – CHMe<sub>2</sub>]<sup>+</sup> (100), 169 [201 – MeOH]<sup>+</sup>, (28), 142 [201 – CO<sub>2</sub>Me]<sup>+</sup> (44); [α]<sub>D</sub> = +65° (c = 0.1, CHCl<sub>3</sub>).

1 mg **8b** in 2 ml C<sub>6</sub>H<sub>6</sub> was heated with 2 mg *p*-TS acid for 1 hr at 70°. TLC afforded **10**; <sup>1</sup>H NMR see Table 1.

**Methyl-7β-hydroxy-calamenene-15-oate (9b).** Colourless oil, IR  $\nu_{\text{max}}^{\text{CCl}_4}$ , cm<sup>-1</sup>: 3620 (OH), 1730 (CO<sub>2</sub>R); MS identical with that of **8b**. 1 mg **9b** with *p*-TS also afforded **10**, colourless oil, MS *m/z* (rel. int.): 244.146 [M]<sup>+</sup> (C<sub>16</sub>H<sub>20</sub>O<sub>2</sub>), 201 [M – CHMe<sub>2</sub>]<sup>+</sup> (81), 169 [201 – MeOH]<sup>+</sup> (43), 142 [201 – CO<sub>2</sub>Me]<sup>+</sup> (100).

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## TWO SINAPYL ALCOHOL DERIVATIVES FROM BERGAMOT ESSENTIAL OIL

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(Revised received 5 March 1982)

**Key Word Index**—*Citrus bergamia*; Rutaceae; sesquiterpenes; coumarin; sinapyl alcohol.

**Abstract**—Together with T-cadinol, β-eudesmol, farnesol, sitosterol and suberosin, two derivatives of sinapyl alcohol have been identified in the less volatile fraction of Bergamot oil.

## INTRODUCTION

Bergamot oil, widely used in perfumery, is obtained by cold pressing the peel of the Bergamot fruit (*Citrus bergamia* Risso); two comprehensive reviews concerned with the chemical composition of this oil have been published recently [1, 2].

## RESULTS AND DISCUSSION

In the course of our work on the less volatile components of Bergamot oil, we have shown the presence of three sesquiterpene alcohols: T-cadinol, β-eudesmol and farnesol (GC/MS) and have isolated sitosterol, suberosin (**1**), 3-(3, 4, 5-trimethoxy-