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GERMACRADIENOLIDES FROM *BLAINVILLEA LATIFOLIA*

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Key Word Index—*Blainvillea latifolia*; Compositae; sesquiterpene lactones; germacradienolides.

Abstract—Two new germacradienolides have been isolated from the aerial parts of *Blainvillea latifolia* along with a known sesquiterpene lactone. The structures of the new compounds have been established by spectral methods and chemical transformation. © 1997 Elsevier Science Ltd

INTRODUCTION

In our previous publications on *Blainvillea latifolia* D. C. we reported on the isolation of the two new (**1, 2**) and two known (**3, 4**) germacradienolides [1, 2]. Further investigation of *B. latifolia* has led to the isolation of two new (**5, 6**) and a known germacradienolide (**7**) previously isolated from *Podanthus ovatifolius* [3]. The structure and stereochemistry of **5** and **6** have been established as 8β-hydroxy-9β-acetoxy-14-(2-methylbutyryloxy)-6α,7-germacradienolide and 8β-hydroxy-9β-acetoxy-14-isobutyryloxy-6α,7-germacradienolide, respectively.

RESULTS AND DISCUSSION

The inseparable mixture of **5** and **6** was treated with piperidine and the reaction product was chromatographed to isolate the adducts **8** and **9**. Treatment of the adducts with methyl iodide regenerated compounds **5** and **6**. Compound **5**, viscous liquid, showed in its IR spectrum the presence of a hydroxy group (3350 cm^{-1}), an α,β-unsaturated-γ-lactone (1760, 1665 cm^{-1}) and ester carbonyls (1735, 1725 cm^{-1}). Its ^{1}H NMR spectrum revealed the presence of a vinyl and an acetate methyl, a 2-methylbutyryloxy group, along with H-13a (δ 6.35) and H-13b (δ 5.68 *d*), two olefinic protons (δ 4.81 and 5.47) and an AB quartet (2H, δ4.63 and 4.73) assignable to $\underline{CH_2}$OR.

The ^{1}H-^{1}H COSY experiment showed the coupling typical of H-7 (δ 2.97) with H-6 (δ 5.21, *dd*, *J* = 10.5, 10 Hz) confirming the *trans*-lactone junction; the latter further showed coupling with H-5 (δ 4.81, *d*, *J* = 10 Hz). H-7 also coupled with H-8 (δ 4.43, *d*, *J* = 1.5 Hz) which upon room temperature acetylation shifted to δ 5.75 indicating the presence of a secondary hydroxy group at C-8. It also showed the connectivity of the H-8 with H-9 (δ 5.47, *d*, *J* = 1.5 Hz) indicating that H-8 and H-9 were α-oriented. Comparison of the chemical shifts of H-9 and H-14 (AB quartet) in **5** with those of compounds **1–4** and their acetates (**12** and **13**) clearly indicated the positions of acetate and ester groups at C-9 and C-14, respectively.

Compound **6**, viscous liquid, showed in its IR spectrum the presence of a hydroxy group (3335 cm^{-1}), an α,β-unsaturated-γ-lactone (1760, 1660 cm^{-1}) and ester carbonyls (1740, 1730 cm^{-1}). Its ^{1}H NMR spectrum (Table 1) revealed the presence of a vinyl and an acetate methyl, an isobutyryloxy group, along with H-13a (δ 6.32 *d*), and H-13b (δ 5.70, *d*), two olefinic protons (δ 4.63 and 5.45) and an AB quartet (2H, δ 4.60 and 4.75) assignable to CH$_2$OiBu. The presence of a secondary hydroxy group was confirmed by the downfield chemical shift of H-8 (δ 4.40) in the ^{1}H NMR spectrum of **6** to δ 5.67 in the ^{1}H NMR spectrum of the acetylated product **11**. Thus from the almost similar spectral data of **5** and **6** the structure of **6** was elucidated as 8β-hydroxy-9β-acetoxy-14-isobutyryloxy-6α,7-germacranolide.

EXPERIMENTAL

Extraction. The whole plant collected during September 1992 near Pune University Campus was shade dried and powdered. The powder (2 kg) was extracted with Me$_2$CO to give an extract (72 g, 3.6%). A portion (50 g) was fractionated over silica gel (60–120 mesh) with Me$_2$CO–petrol as eluent in increasing proportion of Me$_2$CO to collect 9 broad frs. The fifth frn on

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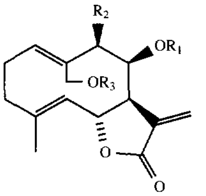
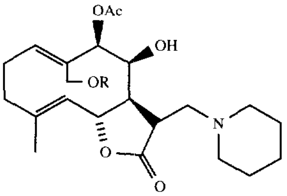


	R$_1$	R$_2$	R$_3$
1	iBu	OH	Ac
2	Mebu	OH	H
3	Mebu	OH	Ac
4	iBu	OH	H
5	H	OAc	Mebu
6	H	OAc	iBu
7	H	H	OAc
10	Ac	OAc	Mebu
11	Ac	OAc	iBu
12	iBu	OAc	Ac
13	Mebu	OAc	Ac



	R
8	Mebu
9	iBu

repeated CC and prep. TLC yielded compound **7** and an inseparable mixt. **A** of compounds **5** and **6**.

Piperidine adduct of the mixture **A**. To the mixture **A** (600 mg) in EtOH (10 ml) piperidine (5 ml) was added dropwise with stirring at room temp. The reaction mixt. was allowed to stand at room temp. overnight. Removal of excess of piperidine and EtOH gave a crude mixt. of piperidine derivatives **8** and **9**. The mixt. was purified by repeated prep. TLC with Me$_2$CO–petrol (1:4) to obtain **8** (50 mg) and **9** (58 mg). EIMS: 70 eV *m/z* (rel. int.): Compound **8**: 491 [M]$^+$ (0.2), 473 (0.1), 431 (0.4), 406 (0.5), 390 (1.5), 389 (4), 330 (25), 98 (100) and 84 (40). Compound **9**: 477 [M]$^+$ (1), 459 (2), 399 (5), 316 (15), 85 (100) and 55 (62).

Regeneration of compound **5**. A soln of 40 mg of **8** in 0.1 ml of MeI was stirred for 30 min. It was then treated with 8 ml of 5% aq. NaHCO$_3$. After being stirred for 24 hr at room temp., it was worked up as usual to afford **5** (25 mg). IR $\nu_{\max}^{\text{neat}}$ cm^{-1}: 3350, 1760, 1735, 1725.

Acetylation of compound **5**. A soln of 10 mg of **5** in 0.1 ml pyridine and 0.1 ml of Ac$_2$O was allowed to stand overnight at room temp. The usual work up gave **8** mg of compound **10** as a viscous liquid. IR $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 1760, 1740, 1735, 1725 and 1660.

Regeneration of compound **6**. 55 mg of piperidine adduct **9** was treated with 0.2 ml of MeI for 30 min. and worked up in a manner analogous to that described above for **5** to afford **6** (30 mg). IR $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 3335, 1760, 1735, 1725.

Acetylation of compound **6**. A soln of 15 mg of **6** in 0.15 ml of pyridine and 0.15 ml of Ac$_2$O was allowed to stand for 24 hr at room temp. The usual work up afforded 10 mg of acetate **11** as a viscous liquid. IR $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 1760, 1745, 1735, 1720 and 1665.

The less polar fr. of the fifth fr. on repeated CC and prep. TLC yielded the known compound **7**, identified by comparing its spectral data with those of ovatofolin [3].

Table 1. ^{1}H NMR (200 MHz, CDCl$_3$, TMS as int. std) spectral data

H	**5**	**8**	**10**	**6**	**9**	**11**
1	5.47 *dd*	5.47 *dd*	5.05 *dd*	5.47 *dd*	5.48 *dd*	5.50 *dd*
5	4.81 *d*	4.75 *d*	4.75 *d*	4.80 *d*	4.75 *d*	4.82 *d*
6	5.21 *dd*	5.09 *dd*	4.92 *dd*	5.21 *dd*	5.10 *dd*	5.0 *dd*
7	2.97 *ddd*	2.90 *m*	3.0 *m*	2.95 *m*	2.90 *m*	2.97 *m*
8	4.43 *d*	4.58 *d*	5.75 *d*	4.45 *d*	4.48 *d*	5.87 *d*
9	5.30 *d*	5.28 *d*	5.45 *d*	5.25 *d*	5.27 *d*	5.45 *d*
11	—	2.5 *m*	—	—	2.5 *m*	—
13a	6.35 *d*	2.7 *m*	6.35 *d*	6.32 *d*	2.7 *m*	6.32 *d*
13b	5.68 *d*	—	5.70 *d*	5.67 *d*	—	5.72 *d*
14a	4.73 *d*	4.76 *d*	4.47 *d*	4.74 *d*	4.76 *d*	4.45 *d*
14b	4.63 *d*	4.60 *d*	4.55 *d*	4.65 *d*	4.60 *d*	4.55 *d*
15	1.69 *d*	1.68 *d*	1.70 *d*	1.69 *d*	1.68 *d*	1.80 *d*
OCOR						
2′	2.51 *m*	2.51 *m*	2.50 *m*	2.60 *m*	2.60 *m*	2.58 *m*
3′	1.5 *m*	1.52 *m*	1.55 *m*	1.14 *d*	1.4 *d*	1.17 *d*
4′	0.90 *t*	0.90 *t*	0.90 *t*	1.15 *d*	1.15 *d*	1.15 *d*
5′	1.17 *d*	1.16 *d*	1.17 *d*	—	—	—
OAc	2.03 *s*	2.02 *s*	2.02 *s* 2.10 *s*	2.03 *s*	2.02 *s*	2.03 *s* 2.15 *s*
Piperidine proton	—	2.1–2.5 *m*	—	—	2.1–2.5 *m*	—

J (Hz): 1, 2a = 4; 1,2b = 12; 5,6 = 10; 6,7 = 10.5; 7,8 = 1.5; 8,9 = 1; 7,13a = 3.5; 7,13b = 3; 14a,14b = 13; 5,15 = 1.5, 2′,3′ = 2′5′ = 3′,4′ = 7.

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