EXPERIMENTAL

The air-dried aerial parts, voucher RMK 7407, collected in Bolivia, were extracted with Et_2O–petrol (1:2). The resulting extract, on separation by column chromatography and TLC (Si gel), afforded 7 mg **1**, 228 mg **2** and 15 mg **3** (Et_2O–petrol, 1:10), colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1665, 1625, 1605 (C=CCO, C=C); MS m/z (rel. int.): 176.120 (M^+, 100) ($C_{12}H_{16}O$), 161 (M − Me, 41), 147 (M − CHO, 20), 121 (147 − C_2H_2, 68);

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589}{-12.4}\quad\frac{578}{-13.9}\quad\frac{546}{-17.2}\quad\frac{436\,\text{nm}}{-56.3}\quad (c = 1.0,\ CHCl_3).$$

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THE GERMACRADIENOLIDE ISABELIN FROM *ZEXMENIA VALERII*: STEREOCHEMISTRY AND CONFORMATION OF SCANDENOLIDE AND DEOXYMIKANOLIDE*

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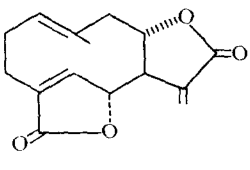
Key Word Index—*Zexmenia valerii*; Compositae; Heliantheae; sesquiterpene lactones; isabelin; germacradienediolide; scandenolide; deoxymikanolide; stereochemistry; conformation.

Abstract—The isolation of the germacradienolide isabelin from *Zexmenia valerii* is reported. In contrast to isabelin, the closely related lactones deoxymikanolide and scandenolide exist in solution in one conformation only, which is similar to that of dihydromikanolide in the solid state. The C-3 stereochemistry of scandenolide is revised.

Several *Zexmenia* species have yielded heliangolides [1–5] or santanolides [6, 7] as well as other terpenoids [6, 7]. We have now isolated the germacradienolide isabelin (**1**) from *Zexmenia valerii* Standl. & Steyerm. Isabelin has been reported previously only from certain small populations of *Ambrosia psilostachya* DC. [8, 9] and *A. artemisiifolia* [10].

In $CDCl_3$ solution, isabelin is a 10:7 mixture of two conformers [8–10] which can be differentiated by NMR spectrometry and give rise to different photochemistry [11, 12]. On the other hand, the ^1H NMR spectra of the very similar dilactones deoxymikanolide (**2a**) and scandenolide (**2b**) in DMSO-d_6 at 90 MHz seemed to indicate only one conformer for each compound [13]. We



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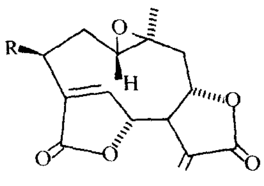

2a R = H
2b R = OAc

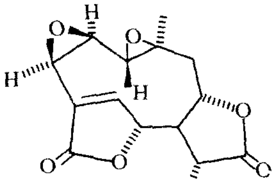

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Table 1. ^{1}H NMR spectral data of sesquiterpene lactones*

	1		2a	2b
	Major	Minor		
H-1	4.97 *dbr* (11)	4.85 *t br* (8)	‡	3.05 *dd* (11.5, 2)
H-2a	†	†	‡	2.58 *ddd* (13, 2, 1.5)
H-2b	†	†	‡	1.88 *ddd* (13, 10.5, 4)
H-3a	†	†	‡	6.02 *dd* (4, 1.5)
H-3b	†	†	‡	—
H-5	6.93 *br*	6.74 *br*	7.74 *br*	7.47 *br*
H-6	5.24 *d* (1.5)	5.09 *dd* (7, 1)	5.27 *br*	5.48 *br*
H-7	3.26 *m*	2.68 *m*	3.41 *dddbr* (9, 3, 3)	3.57 *dddbr* (9, 3, 3)
H-8	4.50 *m*	4.50 *m*	4.50 *ddd* (11, 9, 3.5)	4.60 *ddd* (11, 9, 3.5)
H-9a	3.10 *dd* (15, 5)	2.80 *m*	2.36 *dd* (15, 3.5)	2.38 *dd* (15, 3.5)
H-9b	1.94 *dd* (15, 11.5)	2.25 *m*	2.26 *dd* (15, 11)	2.27 *dd* (15, 11)
H-13a	6.46 *d* (3.5)	6.42 *d* (3.5)	6.51 *d* (3)	6.62 *d* (3)
H-13b	5.92 *d* (3)	6.16 *d* (3)	5.94 *d* (3)	6.06 *d* (3)
H-14	1.63 *br*	1.74 *br*	1.26	1.39 2.32 (Ac)

*Run in $CDCl_3$ at 270 MHz with TMS as internal standard. Shifts are in ppm. Figures in parentheses are coupling constants in hertz.

†Signals superimposed in range 2–2.8 ppm.

‡ One of multiplets which were not identified by spin decoupling at 2.80 *ddbr* (12,3.5), near 2.5.2.3 and 1.61 ppm.

Table 2. ^{13}C NMR spectral data of sesquiterpene lactones*

	1†		2a‡	2b‡
Carbon	Major	Minor		
1	130.5 *d*	129.9 *d*	60.4 *d*	57.6 *d*
2	25.2 *t*§	23.9 *t*§	22.5 *t*§	28.8 *t*
3	23.6 *t*§	22.4 *t*§	21.4 *t*§	66.3 *d*
4	136.9‖	137.3‖	137.2‖	137.0§
5	148.1 *d*	152.2 *d*	149.5 *d*	149.0 *d*
6	81.5 *d*	82.0 *d*	81.6 *d*	82.2 *d*
7	50.5 *d*	55.3 *d*	49.1 *d*	48.9 *d*
8	75.7 *d*	81.4 *d*	77.1 *d*	77.4 *d*
9	41.2 *t*	46.9 *t*	42.6 *t*	42.2 *t*
10	(133.8 or 131.9)	131.5‖	56.2	56.6
11	130.9‖	(131.9 or 133.8)	130.9‖	131.1§
12	171.9	172.7	171.7	169.7
13	122.9 *t*	124.1 *t*	122.1 *t*	122.1 *t*
14	20.7 *q*	17.9 *q*	19.6 *q*	19.7 *q*
15	168.2	168.2	167.6	167.6
1′				169.1
2′				20.6 *q*

*Run at 67.9 MHz with TMS as internal standard. Frequencies in ppm. Unmarked signals are singlets. Assignments are tentative and not established by single off-resonance decoupling.

†In $CDCl_3$ solution. Assignment to major and minor isomer made on basis of relative intensity of signals.

‡In DMSO-d_6 solution.

§, ‖Assignments interchangeable.

have therefore redetermined the spectra in $CDCl_3$ at 270 MHz. These and the previously unreported ^{13}C NMR spectra are compared with those of isabelin in Tables 1 and 2. Again, only one set of signals was observed for **2a** and **2b**. The chemical shifts of the signals correspond reasonably closely to the signals of the major isabelin conformer if allowance is made for the presence of the 1,10-epoxide and, in the case of **2b**, for the acetoxylation of C-3. We deduce that the conformations of **2a**, **2b** in solution are similar to the conformation of the major isabelin isomer which in turn is similar to the conformation of dihydromikanolide (**3**) in the solid state.†

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†The conformation of dihydromikanolide as deduced by X-ray crystallography [14] conforms very closely to Fig. 1 of ref. [13] for mikanolide itself except that the 2,3-epoxide is β-orientated.

The newly determined values of $J_{2,3}$ for scandenolide are, to judge from the model, in better agreement with β-orientation of the C-3 acetoxyl group instead of the α-orientation originally proposed [13]. This possibility has already been suggested earlier [14] as the result of our X-ray analysis of dihydromikanolide which showed that the oxirane function of this compound was β- rather than α-orientated.

EXPERIMENTAL

Above ground *Zexmenia valerii* Standl. & Steyerm., collected by Mr. G. Cruz in the fall of 1974 near Tegucigalpa, Honduras (PR accession number 43728), wt 3 kg, was extracted with $CHCl_3$ and worked up as usual [15]. The crude gum, wt 13 g, was preadsorbed on 25 g of silicic acid (Mallinckrodt 100 mesh) and chromatographed over 330 g of the same adsorbent packed in $CHCl_3$, fractions being collected as follows: 1–8 ($CHCl_3$ 0.5 l. each), 9–15 ($CHCl_3$, 1 l. each), 16–22 ($CHCl_3$–MeOH, 39:1, 1 l. each) and 23, 24 ($CHCl_3$–MeOH 47:3, 1 l. each). Fractions 6–11 were combined and rechromatographed ($CHCl_3$–MeOH, 99:1) to give 0.5 g of isabelin identical with an authentic sample. The other fractions did not yield homogeneous material.

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