

SHIKIMIC ACID DERIVATIVE FROM *SENECIO HIERACIOIDES*

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In continuation of our investigations of *Senecio* species, we have now studied the constituents of *Senecio hieracioides* DC, collected in the Transvaal. The main constituent was 9,10-dehydrofuranoeremophilane (1). Furthermore, ligularenolide (2), eremophil-7(11)-en-8,12-olide (3), and its 8,8'-epimeric dimers (2), so far isolated only from a *Bedfordia* species, were present as well as the lactones **1** and **2**.

The structure of **1** could be deduced from the pmr spectrum (Table 1), which was close to that of the corresponding  $\Delta^{1(10)}$  isomer and ligularenolide. Spin decoupling allowed the assignment of most signals. The broadened singlet at  $\delta = 5.14$  was coupled with a second low field, broadened singlet at 5.52, with an olefinic methyl (1.84 t), with a broadened doublet at 2.18, and with a multiplet at 2.11. The chemical shifts required that the signals at 2.11, 2.18, and 2.81 be those of allylic protons. Accordingly, the position of the double bonds was settled. The couplings were observed, and the chemical shifts of the methyl signals agreed with the proposed

configuration at C-8 if compared with the data of similar compounds.

The structure of **2** followed from the presence of an additional oxygen, which could be deduced from the molecular ion and from the pmr spectrum (Table 1). The downfield shift of the methyl singlet obviously required a  $\beta$ -orientated hydroxyl at C-8. The remaining signals were close to those of **1**; that of H-9, however, was less broadened due to the missing coupling  $J_{8,9}$ .

Furthermore, an acid fraction was obtained, which, after esterification with  $\text{CH}_2\text{N}_2$ , gave a complex mixture of esters that could be separated by hplc. Three compounds were obtained, which differed in the molecular formulae by only one methylene group ( $\text{C}_{24}\text{H}_{32}\text{O}_8$ ,  $\text{C}_{25}\text{H}_{34}\text{O}_8$  and  $\text{C}_{26}\text{H}_{36}\text{O}_8$ ). The pmr spectra (Table 2) both in  $\text{CDCl}_3$  and  $\text{C}_6\text{D}_6$  showed that obviously the methyl ester of shikimic acid was esterified with senecio or methylsenecio acid. We have isolated similar triesters of shikimic acid from *Senecio subrubrioflorus* (5). Accordingly, the pmr data were in part close to those of the corresponding triphenyl acetate which was isolated previously (5).

From the mass and pmr spectra, one methyl ester was a *tris* methylsenecioate; the second, a *bis* methylsenecioate senecioate, and the third, a methylsenecioate *bis* senecioate. Due to the very small differences in the ester residues, it was not possible to assign the relative position of the different ester groups, the general structures of the acids were **3-5**. As the couplings of H-2-H-6 were identical with those of the phenyl acetate (5), the stereochemistry at C-3-C-5 was the same. Further investigations of *Senecio* species may show whether these esters are of chemotaxonomic importance.

TABLE 1. Pmr Spectral Data of Compounds **1** and **2** (400 MHz,  $\text{CDCl}_3$ , TMS as Internal Standard)<sup>a</sup>

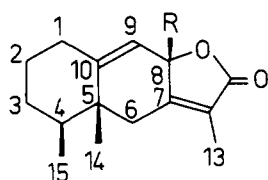
	<b>1</b>	<b>2</b>
H-1 . . . .	2.11 brd	2.38 m
H-6 . . . .	2.81 d	2.65 d
H-6' . . . .	2.18 br d	2.59 dd
H-8 . . . .	5.14 brs	—
H-9 . . . .	5.52 brs	5.47 brs
H-13 . . . .	1.84 t	1.90 brs
H-14 . . . .	0.85	1.06 s
H-15 . . . .	0.93 d	0.80 d

<sup>a</sup>J (Hz): Compound **1**: 9~1.5; 1,8~1; 4,15=7; 6,6'=13; 6',8=8,13~1.5; 8,9=3; compound **2**: 1,9~1; 4,15=7; 6,6'=16; 6',13=1.5.

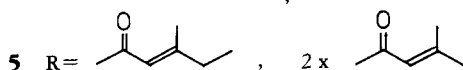
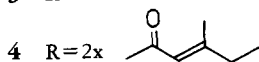
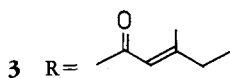
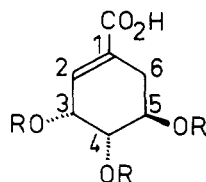
TABLE 2. Pmr Spectral Data of the Methyl (Esters of 3-5 (400 MHz, CDCl<sub>3</sub>, TMS as Internal Standard)<sup>a</sup>

	3	C <sub>6</sub> D <sub>6</sub>	4	C <sub>6</sub> D <sub>6</sub>	5
H-2 . . . . .	6.83 ddd	7.01 ddd	6.83 ddd	6.99 ddd	6.78 ddd
H-3 . . . . .	5.82 br dd	6.25 br dd	5.82 br dd	6.22 br dd	5.75 br dd
H-4 . . . . .	5.36 dd	5.85 dd	5.38 dd	5.83 dd	5.08 dd
H-5 . . . . .	5.63 ddd	5.87 ddd	5.67 ddd	5.85 ddd	5.53 ddd
H-6 $\alpha$ . . . . .	2.47 dddd	2.61 dddd	2.47 dddd	2.61 dddd	2.46 dddd
H-6 $\beta$ . . . . .	2.90 dddd	3.15 dddd	2.90 dddd	3.14 dddd	2.89 dddd
OMe . . . . .	3.76 s	3.30 s	3.76 s	3.30 s	3.76 s
OSen . . . . .	—	—	5.67 br s 2.15 d 1.90 d	5.80 br s 2.12 d 1.42 d	5.66, 5.64 qq 2.15, 2.12 d 1.89, 1.87 d
OMesen . . . . .	5.63 tq 5.64 tq 2.16 br q  2.15 d 2.13 d  1.08 t 1.07 t	5.80 tq 5.73 tq 1.73 br q 1.71 br q 2.15 d 2.16 d 2.17 d 0.75 t 0.71 t	5.62 tq 5.63 tq 2.16 br q  2.15 d 2.13 d  1.07 t 1.06 t	5.76 tq 5.74 tq 1.73 br q 1.71 br q 2.17 d 2.16 d  0.75 t 0.72 t	5.60 tq  2.15 br q  2.15 d   1.03 t

<sup>a</sup>J (Hz): 2,3=4; 2,6 $\alpha$ =2,6 $\beta$ =1.5; 3,4=4; 3,6 $\alpha$ =3,6 $\beta$ =1.5; 4,5=8.5; 5,6 $\alpha$ =6.5; 5,6 $\beta$ =5; 6 $\alpha$ ,6 $\beta$ =18.5; OSen: 2'4'=2'5'~1; OMesen: 2',4'=2',6~1; 4',5'=7.



- 1 R=H  
2 R=OH



## EXPERIMENTAL

**MATERIAL AND METHODS.**—Plant material was collected in February 1981, in Transvaal, South Africa, voucher 81/120 (deposited in the Herbarium of the Botanic Research Institute, Pretoria). Nmr spectra were recorded on a Bruker WM 400, ir spectra on a Beckmann IR 9, mass spectra on a Varian MAT 711, 70 eV, direct inlet and optical rotations on a Perkin-Elmer polarimeter.

**ISOLATION.**—The air-dried aerial parts (290 g) were extracted with Et<sub>2</sub>O-petroleum, 1:1, and the resulting extract was separated by cc (SiO<sub>2</sub>). The cc fractions (200 ml) were as follows: 1 (petroleum), 2 (Et<sub>2</sub>O-petroleum, 1:10), 3 (Et<sub>2</sub>O-petroleum, 1:3), 4 (Et<sub>2</sub>O-petroleum, 1:1), 5 (Et<sub>2</sub>O-MeOH, 10:1). Tlc (SiO<sub>2</sub>, PF 254, detection by uv light and KMnO<sub>4</sub> spraying) of 10 percent of fraction 1 gave 98 mg of 9,10-dehydrofuroeremophilane and 12 mg of 1,10-epoxycaryophyllene. Tlc of 10 percent of the combined fractions 4-6 (Et<sub>2</sub>O-petroleum, 3:1, several times) gave 20 mg of eremophil-7(11)-en-8,12-olide, 9 mg of ligularenolide, 25 mg of **1**, 65 mg of the epimeric 8,8'-dimeric eremophil-7(11)-en-8,12-olides (1:1), 3 mg of **2**, and a mixture of 15 mg of **3-5**. After addition of CH<sub>2</sub>N<sub>2</sub>, the methyl esters of **3-5** were purified by tlc (Et<sub>2</sub>O-petroleum, 1:3) and separated by repeated hplc (RP 8, MeOH-H<sub>2</sub>O, 3:1). Finally, the methyl esters of **3** (4 mg, R<sub>t</sub>=6.2 min), **4** (5 mg, R<sub>t</sub>=5.6 min), and **5** (6 mg, R<sub>t</sub>=5.1 min) were obtained.

*Eremophila-7(11),9-dien-8,12-olide (1):* Colorless oil, ir (CCl<sub>4</sub>) 1770 cm<sup>-1</sup> (γ-lactone), (Found: M<sup>+</sup> 232.146 C<sub>15</sub>H<sub>20</sub>O<sub>2</sub> requires 232.146), ms *m/z* (rel. int., %) 232 (M<sup>+</sup>, 42), 217 (M-Me, 10), 203 (M-CHO, 100), 109 (79).

$$[\alpha]_{D}^{25} = \frac{589}{-10} \quad \frac{578}{-12} \quad \frac{546}{-13} \quad \frac{436 \text{ nm}}{-15} \quad \text{CHCl}_3, c=0.92$$

*8β-Hydroxyeremophil-7(11),9-dien-9,12-olide (2):* Colorless oil, ir (CCl<sub>4</sub>) 1780 cm<sup>-1</sup> (γ-lactone), (Found: M<sup>+</sup> 248.141 C<sub>15</sub>H<sub>20</sub>O<sub>3</sub> requires 248.141), ms *m/z* (rel. int., %) 248 (M<sup>+</sup>, 17),

230 (M-H<sub>2</sub>O, 37), 215 (230-Me, 16), 69 (83), 55 (100).

*Methyl ester of 3:* Colorless oil, ir (CCl<sub>4</sub>) 1725, 1650 cm<sup>-1</sup> (C=CCO<sub>2</sub>R), (Found: M<sup>+</sup> 476.241 C<sub>26</sub>H<sub>36</sub>O<sub>8</sub> requires 476.241), ms *m/z* (rel. int., %) 476 (M<sup>+</sup>, 1), 362 (M-C<sub>5</sub>H<sub>9</sub>CO<sub>2</sub>H, 3), 248 (362-C<sub>5</sub>H<sub>9</sub>CO<sub>2</sub>H<sub>2</sub>, 0.5), 97 (C<sub>5</sub>H<sub>9</sub>CO<sup>+</sup>, 100), 69 (97-CO, 7).

$$[\alpha]_{D}^{25} = \frac{589}{-45} \quad \frac{578}{-45} \quad \frac{546}{-53} \quad \frac{436 \text{ nm}}{-100} \quad \text{CHCl}_3, c=0.75$$

*Methyl ester of 4:* Colorless oil, ir (CCl<sub>4</sub>) 1725, 1640 cm<sup>-1</sup> (C=CCO<sub>2</sub>R), (Found: M<sup>+</sup> 462.225 C<sub>25</sub>H<sub>34</sub>O<sub>8</sub> requires 462.225), ms *m/z* 462 (M<sup>+</sup>, 1), 362 (M-C<sub>5</sub>H<sub>9</sub>CO<sub>2</sub>H, 1), 348 (M-C<sub>5</sub>H<sub>9</sub>CO<sub>2</sub>H, 3), 248 (348-C<sub>4</sub>H<sub>7</sub>CO<sub>2</sub>H, 0.5), 97 (C<sub>5</sub>H<sub>9</sub>CO<sup>+</sup>, 100), 83 (C<sub>4</sub>H<sub>7</sub>CO, 51), 69 (97-CO, 11), 55 (83-CO, 9).

*Methyl ester of 5:* Colorless oil, ir (CCl<sub>4</sub>) 1725, 1650 cm<sup>-1</sup> (C=CCO<sub>2</sub>R), (Found: M<sup>+</sup> 448.210 C<sub>24</sub>H<sub>32</sub>O<sub>8</sub> requires 448.210), ms *m/z* (rel. int., %) 448 (M<sup>+</sup>, 3), 348 (M-C<sub>4</sub>H<sub>7</sub>CO<sub>2</sub>H, 6), 334 (M-C<sub>5</sub>H<sub>9</sub>CO<sub>2</sub>H, 2), 234 (334-C<sub>4</sub>H<sub>7</sub>CO<sub>2</sub>H, 0.5), 97 (C<sub>5</sub>H<sub>9</sub>CO, 58), 83 (C<sub>4</sub>H<sub>7</sub>CO, 100), 69 (97-CO, 12), 55 (83-CO, 20).

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