

NEW SESQUITERPENE LACTONE TYPE FROM  
*DUGALDIA HOOPESII*

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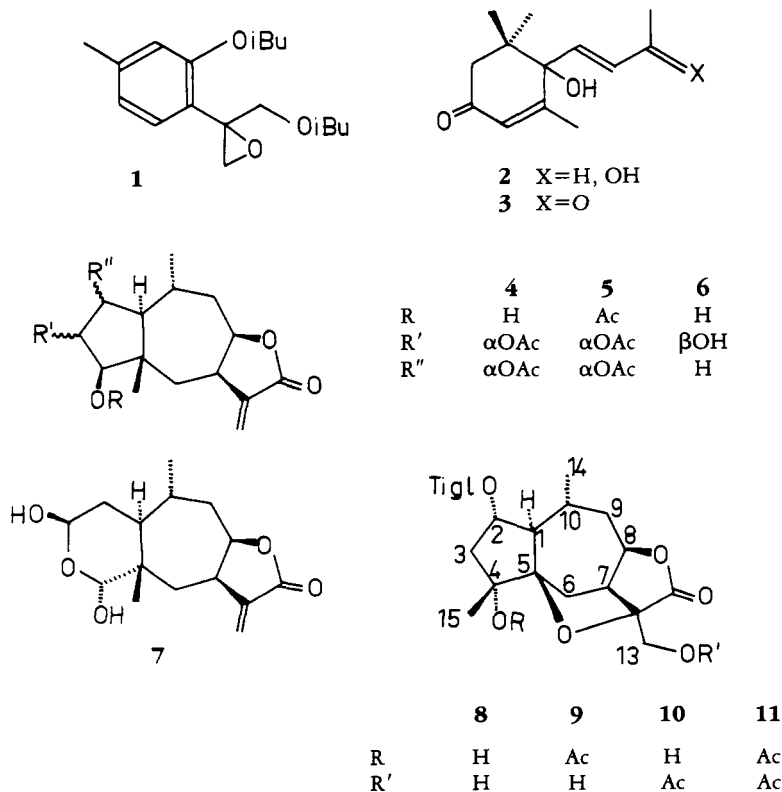
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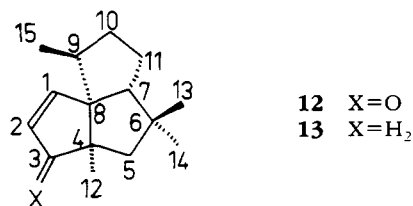
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ABSTRACT.—The aerial parts of *Dugaldia hoopesii* afforded, in addition to the sesquiterpene lactones hymenoratin, hymenograndin, its 4-O-acetyl derivative, and hymenoxon, a new type of guaianolide. Furthermore, several more widespread compounds, vomifoliol and the corresponding ketone, as well as a derivative of silphinene were present. The structures were elucidated by spectroscopic methods and a few chemical transformations.

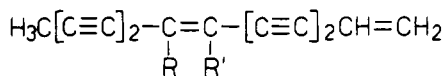
In addition to several flavones (1) and a tetrayne sulfoxide (2), only one sesquiterpene lactone, hymenovin (3), has been isolated from *Dugaldia hoopesii* (A. Gray) Rydb. *Dugaldia* has been separated from the genus *Helenium* as clear morphological differences are visible (4). Because hymenovin and related seco-pseudoguaianolides have not been reported from *Helenium* species, we have again studied *D. hoopesii*. The results will be discussed in this paper.

The separation of the extract of the aerial parts afforded vomifoliol (2) (5) and the corresponding ketone 3, which already has been prepared from  $\beta$ -ionone (5); hymenograndin (4) (6); the corresponding acetate 5 (6); hymenoratin (6) (7); hymenoxon (7) (8), the guaianolide derivative 8, and the ketone 12. The structure of the latter could be de-

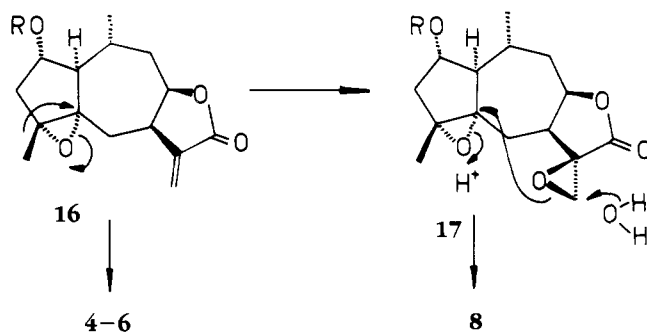




**12** X=O  
**13** X=H<sub>2</sub>



**14** R=H, R'=SOCH<sub>3</sub>  
**15** R=SOCH<sub>3</sub>, R'=H



duced from the molecular formula (C<sub>15</sub>H<sub>22</sub>O) and from the pmr and cmr spectra (Table 1). The pmr doublets at  $\delta=7.62$  and  $6.04$  clearly indicated the presence of a conjugated five-membered ring ketone. In agreement with this, the ir spectrum displayed a strong band at  $1715\text{ cm}^{-1}$ . The pmr signals at  $0.77\text{ s}$ ,  $0.89\text{ s}$ ,  $1.04\text{ s}$ , and  $0.93\text{ d}$  showed that a sesquiterpene was present bearing four methyls, only one of them being secondary. The signal of the proton coupled to this methyl group ( $\delta=2.14\text{ ddq}$ ) and a pair of doublets

TABLE 1. Spectral Data of **12** (400 MHz, CDCl<sub>3</sub>, TMS as Internal Standard)<sup>a</sup>

|                          | Pmr       |                | Cmr       |           |
|--------------------------|-----------|----------------|-----------|-----------|
|                          | <b>12</b> |                | <b>12</b> | <b>13</b> |
| 1-H . . . . .            | 7.62 d    | C-1 . . . . .  | 169.6 d   | 138.5 d   |
| 2-H . . . . .            | 6.04 d    | C-2 . . . . .  | 129.8 d   | 125.4 d   |
| 3-H . . . . .            | —         | C-3 . . . . .  | 216.8 s   | 51.4 t    |
| 5 $\alpha$ -H . . . . .  | 1.56 d br | C-4 . . . . .  | 57.1 s    | 49.4 s    |
| 5 $\beta$ -H . . . . .   | 1.99 d    | C-5 . . . . .  | 51.2 t    | 58.7 t    |
| 7-H . . . . .            | 1.97 m    | C-6 . . . . .  | 40.1 s    | 39.4 s    |
| 9-H . . . . .            | 2.14 ddq  | C-7 . . . . .  | 61.0 d    | 64.0 d    |
| 10 $\alpha$ -H . . . . . | 1.91 m    | C-8 . . . . .  | 68.5 s    | 72.6 s    |
| 10 $\beta$ -H . . . . .  | 1.32 m    | C-9 . . . . .  | 38.8 d    | 38.7 d    |
| 11 $\alpha$ -H . . . . . | 1.71 m    | C-10 . . . . . | 36.4 t    | 37.6 t    |
| 11 $\beta$ -H . . . . .  | 1.32 m    | C-11 . . . . . | 28.9 t    | 27.7 t    |
| 12-H . . . . .           | 1.04 s    | C-12 . . . . . | 20.8 q    | 26.7 q    |
| 13-H . . . . .           | 0.77 s br | C-13 . . . . . | 30.2 q    | 31.1 q    |
| 14-H . . . . .           | 0.89 s br | C-14 . . . . . | 27.0 q    | 27.4 q    |
| 15-H . . . . .           | 0.93 d    | C-15 . . . . . | 16.1 q    | 16.4 q    |

<sup>a</sup>J[Hz]: 1,2=5.5; 5 $\alpha$ ,5 $\beta$ =14; 5 $\beta$ ,12~1; 9,10 $\alpha$ =5; 9,10 $\beta$ =11; 9,15=7.

( $\delta=1.99$  and  $1.56$ ) indicated some similarities to silphinene (9). Spin decoupling allowed the assignment of all signals, though several were multiplets. One of the methyl groups (13-H) showed a W-coupling with  $5\alpha$ -H and 13-H with 14-H, which allowed the assignment of the methyl signals. Obviously, 13-H was shielded by the keto group, while  $5\beta$ -H was deshielded by the latter. Thus, the data agreed with the presence of silphinene-3-one. This was further supported by nOe difference spectra. Irradiation of 12-H caused a clear effect of H-5 $\alpha$  and H-9, while saturation of 15-H showed a strong nOe of 1-H. The cmr spectrum of **12** also agreed nicely with the proposed structure, especially when compared with that of the corresponding hydrocarbon **13** (8) (Table 1). Some of the signals were shifted in the expected way by the influence of the carbonyl group. Accordingly, the relative position of the keto group could be assigned. The absolute configuration was deduced from the cd spectrum, assuming that the octant rule applies to this compound.

Compound **8** showed ir bands typical for a  $\gamma$ -lactone, a hydroxy, and an unsaturated ester group ( $3580$ ,  $1770$ , and  $1725$   $\text{cm}^{-1}$ ). The mass spectrum showed no molecular ion. However, an ion at  $m/z$  280 formed by loss of  $\text{C}_5\text{H}_8\text{O}_2$  from the parent compound and the base peak at  $m/z$  83 ( $\text{C}_5\text{H}_7\text{O}$ ) were characteristic for a conjugated  $\text{C}_5$ -ester. Furthermore, the pmr spectrum (Table 2) showed that 28 protons were present. All signals could be assigned by spin decoupling leading to sequence A, R, or R' being a tiglate re-

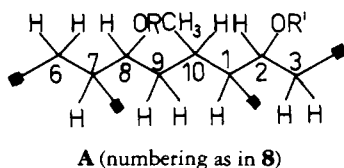


TABLE 2. Pmr Spectral Data of **8-11** (400 MHz,  $\text{CDCl}_3$ , TMS as Internal Standard)<sup>a</sup>

|                         | <b>8</b>   | <b>10</b>  | <b>9</b>  | <b>11</b> |
|-------------------------|------------|------------|-----------|-----------|
| 1-H . . . . .           | 2.28 dd    | 2.30 dd    | 2.08 dd   | 2.08 dd   |
| 2-H . . . . .           | 4.79 ddd   | 4.78 ddd   | 4.93 m    | 4.93 ddd  |
| 3 $\alpha$ -H . . . . . | 1.74 dd    | 1.75 dd    | 2.62 d br | 2.63 d br |
| 3 $\beta$ -H . . . . .  | 2.48 dd    | 2.49 dd    | 2.33 dd   | 2.33 dd   |
| 6 $\alpha$ -H . . . . . | 2.10 d     | 2.11 d     | 2.12 d    | 2.12 d    |
| 6 $\beta$ -H . . . . .  | 2.32 dd    | 2.35 dd    | 2.35 dd   | 2.38 dd   |
| 7-H . . . . .           | 3.28 dd    | 3.16 dd    | 3.31 dd   | 3.17 dd   |
| 8-H . . . . .           | 4.91 ddd   | 4.91 ddd   | 4.93 m    | 4.92 ddd  |
| 9 $\alpha$ -H . . . . . | 1.65 ddd   | 1.65 ddd   | 1.65 ddd  | 1.65 ddd  |
| 9 $\beta$ -H . . . . .  | 2.04 dd br | 2.05 dd br | 2.07 dd   | 2.08 dd   |
| 10-H . . . . .          | 1.74 m     | 1.74 m     | 1.76 m    | 1.77 m    |
| 13-H . . . . .          | 3.91 d br  | 4.27 d     | 3.93 d br | 4.27 d    |
| 13'-H . . . . .         | 3.53 d br  | 4.13 d     | 3.54 d br | 4.17 d    |
| 14-H . . . . .          | 0.99 d     | 0.99 d     | 0.98 d    | 0.97 d    |
| 15-H . . . . .          | 1.21 s     | 1.25 s     | 1.49 s    | 1.51 s    |
| OH . . . . .            | 2.34 s br  | 2.38 s br  |           |           |
|                         | 2.00 s br  |            |           |           |
| OCOR . . . . .          | 6.82 qq    | 6.82 qq    | 6.76 qq   | 6.74 qq   |
|                         | 1.80 s br  | 1.80 s br  | 1.78 s br | 1.77 s br |
|                         | 1.78 d br  | 1.78 d br  | 1.77 d br | 1.76 s br |
| OAc . . . . .           | —          | 2.07 s     | 2.01 s    | 2.07 s    |
|                         | —          | —          | —         | 1.99 s    |

<sup>a</sup>J[Hz]: 1,2=7; 1,10=11; 2,3 $\alpha$ =2; 2,3 $\beta$ =9; 3 $\alpha$ ,3 $\beta$ =15.5; 6 $\alpha$ ,6 $\beta$ =14; 6 $\beta$ ,7=7; 7,8=9.5; 8,9 $\alpha$ =2; 8,9 $\beta$ =5; 9 $\alpha$ ,9 $\beta$ =15.5; 9 $\alpha$ ,10=11.5; 10,14=6.5; 13,13'=12. OTig: 3',4'=7; 3',5'=4',5'=1.5.

sidue. Furthermore, signals of two hydroxyls, a hydroxy-methylene group, and a tertiary methyl were present. The nature of the hydroxyls was established by transforming the natural compound to a monoacetate and a diacetate (**10** and **11**). Partial hydrolysis of **11** gave the isomeric monoacetate **9**. The observed shift differences in the spectra of **8-11** (Table 2) clearly showed that **8** has a tertiary and a primary hydroxyl. The nOe difference spectra of **8** gave further information. Irradiation of the methyl doublet left signals at  $\delta=4.79$ , 2.28, and 2.04 unchanged. The threefold doublet at  $\delta=4.79$  was the signal of 2-H, assuming the lactone had a normal carbon skeleton. Accordingly, the threefold doublet at  $\delta=4.91$  was due to 8-H, just as the double doublet at  $\delta=3.28$  should be the signal of 7-H. This, however, required that some kind of addition had transformed the usual methylene lactone to a lactone with oxygen functions at C-11 and C-13. The latter obviously bears a hydroxy group. Irradiation at  $\delta=1.21$  (15-H) caused an nOe at  $\delta=2.48$  (3 $\beta$ -H), 2.23 (6 $\beta$ -H), and 3.53 (13'-H). A nOe of the tiglate methyl singlet with the signal of 2-H supported the proposed position of the ester group. Inspection of a model showed that only the proposed structure and stereochemistry agreed with these data. Thus, the new lactone, which we have named 2 $\alpha$ -tigloyloxydugaldiolide, obviously was formed via the diepoxide (**17**), which itself would be an oxidation product of **16**. Compound **16** is also the most likely precursor of the pseudoguaianolide like **4-6**.

The roots afforded several common compounds (see Experimental), **5**, **12**, the hydrocarbon **13** (**9**), as well as **14** and **15** (**2**).

The chemistry of this species supports the separation of *Dugaldia* from *Helenium*, where mostly helenalin-like pseudoguaianolides are common (**10**), whereas lactones like **4-7** have not been reported from *Helenium* (**10**) but from some *Hymenoxys* species (**7**) and also from *Dugaldia integrifolia* (H. B. K.) Cass. (**11**), which also had been placed previously in *Helenium*. However, lactones like **8** and the ketone **12** never have been found in related genera.

## EXPERIMENTAL

**MATERIAL AND METHODS.**—The plant material was collected in Colorado (voucher RMK 9085, deposited in the US National Herbarium, Washington, D.C.). Pmr spectra were recorded on a Bruker WM 400 and mass spectra on a Varian MAT 711, 70 eV, direct inlet. Known compounds were identified by comparing the 400 MHz pmr spectra with those of authentic material and by tlc in different solvent mixtures.

**ISOLATION.**—Column chromatography (Si gel) of the extract obtained from 220 g air-dried aerial parts (MeOH-Et<sub>2</sub>O, 1:1, 12 h room temperature) gave several fractions which after tlc comparison were combined to three: 1 (Et<sub>2</sub>O-petrol, 1:4), 2 (Et<sub>2</sub>O) and 3 (Et<sub>2</sub>O-MeOH, 9:1). Tlc (SiO<sub>2</sub> PF 254) of fraction 1 (Et<sub>2</sub>O-petrol, 1:3) gave 25 mg **12** (R<sub>f</sub> 0.71). Hplc (RP 8, MeOH-H<sub>2</sub>O, 1:1) of fraction 2 gave 2 mg **3** (R<sub>f</sub> 4.0) (pmr: 2.31 s (3 H), 6.83 and 6.46 d (J=15 Hz), 5.96 s br, 2.50 and 2.34 d (J=18 Hz), 1.11 and 1.02 s (each 3 H) and 1.89 s br (3 H)) and 4 mg **4** [mp. 152°, lit. 153-154° [6]], hplc (RP 8, MeOH-H<sub>2</sub>O, 1:1) of fraction 3 gave 5 mg **2**, 8 mg **5**, 10 mg **7** [mp. 135°, lit. 136° (8)], 3 mg **6** and a mixture of **6** and **8**. Tlc (aluminium sheets, silicagel PF<sub>254</sub> 20 x 20 cm, Et<sub>2</sub>O-MeOH, 20:1) gave 3 mg **6** [mp. 164°, lit. 165-167° (7)] and 4 mg **8** (R<sub>f</sub> 0.42). Column chromatography of the extract of 180 g roots gave three fractions: fraction 1 (petrol) gave 80 mg of hydrocarbons which were identified by comparing with authentic samples. The mixture contained ca. 6 mg isocomene, 9 mg  $\alpha$ -isocomene, 6 mg  $\alpha$ - and 20 mg  $\gamma$ -humulene, 6 mg caryophyllene and 10 mg **13**. Fraction 2 (Et<sub>2</sub>O-petrol, 1:4) afforded by tlc (SiO<sub>2</sub> PF 254, Et<sub>2</sub>O-petrol, 1:3) 200 mg **12** (purified by distillation), 20 mg **1**, 10 mg stigmaterol, 1 mg **14**, and 1 mg **15**. Tlc (Et<sub>2</sub>O) of fraction 3 (Et<sub>2</sub>O-MeOH, 9:1) gave 2 mg **5**.

**2 $\alpha$ -Tigloyloxydugaldiolide (8):** Colorless oil, which could not be induced to crystallize though it was homogeneous by pmr and by tlc; ir (CHCl<sub>3</sub>) 3580, 3380 (OH), 1770 ( $\gamma$ -lactone), 1725 cm<sup>-1</sup> (C=CCO<sub>2</sub>R); (Found: M<sup>+</sup>-RCO<sub>2</sub>H 280.131, C<sub>15</sub>H<sub>20</sub>O<sub>5</sub> requires 280.131) ms/mz (relative intensity, %) 297 (M-COR, 3), 280 (M-RCO<sub>2</sub>H, 4), 262 (280-H<sub>2</sub>O, 19), 83 (C<sub>4</sub>H<sub>7</sub>CO<sup>+</sup>, 100), 55 (83-CO, 92);

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436 \text{ nm}}{+25 \quad +27 \quad +31 \quad +54} \quad (c=0.3, \text{CHCl}_3)$$

To 4 mg **8** in 0.1 ml  $\text{CHCl}_3$ , 0.05 ml dimethylaniline and 0.05 ml acetylchloride were added. After standing at room temperature for 12 h, hplc (RP 8, MeOH- $\text{H}_2\text{O}$ , 13:7) gave 1.5 mg **10** and 2 mg **11**. Compound **10**: Colorless oil; (Found:  $\text{M}^+$ - $\text{RCO}_2\text{H}$  322.142,  $\text{C}_{17}\text{H}_{22}\text{O}_6$  requires 322.142) ms  $m/z$  (relative intensity, %) 322 ( $\text{M}^+$ - $\text{RCO}_2\text{H}$ , 12), 280 (322-ketene, 3), 263 (322- $\text{H}_3\text{CCO}_2$ , 12), 262 (322-AcOH, 8), 83 ( $\text{C}_4\text{H}_7\text{CO}^+$ , 100), 55 (83-CO, 52). Compound **11**: Colorless oil, pmr, see Table 2. Saponification at room temperature with a trace of NaOH in MeOH gave **9**, colorless oil, pmr, see Table 2.

*3-Oxosilphinene* (**12**): Colorless oil,  $\text{bp}_{0.1\text{ Torr}}$   $85^\circ$  (bathtemp.); ir ( $\text{CCl}_4$ ) 1715, 1595, 1460, 1380, 1370, 1137, 1105  $\text{cm}^{-1}$ ; (Found:  $\text{M}^+$ , 218.167  $\text{C}_{15}\text{H}_{22}\text{O}$  requires 218.167) ms  $m/z$  (relative intensity, %) 218 ( $\text{M}^+$ , 100), 203 (M-Me, 51), 190 (M-CO, 8), 175 (190-Me, 34), 162 (38), 161 (35), 147 (24), 133 (18), 119 (26), 91 (37); cd (MeCN):  $\Delta\epsilon_{335}$ -0.28;  $\Delta\epsilon_{315}$ -0.55;  $\Delta\epsilon_{299}$ -0.58;  $\Delta\epsilon_{285}$ -0.53;  $[\alpha]_D = +7.1$  ( $c=0.4$ ,  $\text{CHCl}_3$ ).

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