*1α,3β-Dihydroxy-9β,10β-epoxy-7α,11β*H*-germacra-4Z-en*-12,6α-*olide* (**4**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3600 (OH), 1770 (γ-lactone); MS *m/z* (rel. int.): 266.152 $[M-H_2O]^+$ (1.5) (calc. for $C_{15}H_{22}O_4$; 266.152), 251 $[266-Me]^+$ (6), 109 (70), 95 (97), 55 (100); $[\alpha]_D^{24°}$ +34° ($CHCl_3$; *c* 0.21).

*1α,3β,4β-Trihydroxy*-(5α,7α,11βH-10α *methyl*)-*eudesman*-12,6α-*olide* (**5**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3600 (OH), 1770 (γ-lactone); MS *m/z* (rel. int.): 266.152 $[M-H_2O]^+$ (6) (calc. for $C_{15}H_{22}O_4$: 266.152), 251 $[266-Me]^+$ (11), 248 $[266-H_2O]^+$ (7), 233 $[251-H_2O]^+$ (5), 192 (100); $[\alpha]_D^{24°}$ + 10° ($CHCl_3$; *c* 0.33).

## REFERENCES

1. El-Sebakhy, N. A., El-Ghazouly, M. G., Seif El-Din, A. A. and Zdero, C. (1986) *Pharmazie* **41**, 525.
2. Jakupovic, J., Eid, F., Bohlmann, F. and El-Dahmy, S. (1987) *Phytochemistry* **26**, 1536.
3. Herz, W., de Groote, R. and Murari, R. (1978) *J. Org. Chem.* **43**, 3559.
4. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.

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# ONOSERIOLIDE DERIVATIVES FROM *LEUCERIA* SPECIES

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**Key Word Index**—*Leuceria leontopodioides*, *L. purpurea*, *L. thermarum*, *L. hahnii*; Compositae; sesquiterpene lactones; onoseriolides; acetylenic compounds.

**Abstract**—From *Leuceria* species in addition to known, widespread compounds, four new onoseriolide derivatives and a known tetraynene together with an isomeric derivative, were isolated. The structures were elucidated by high field NMR techniques. The chemotaxonomy is discussed briefly.

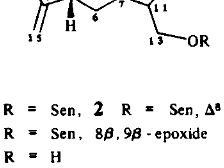
## INTRODUCTION

The genus *Leuceria* has 46 species distributed from south Peru to Patagonia [1] but so far only one species has been studied chemically. In addition to the tetrayne derivative **6** the rare sesquiterpene lactone onoseriolide (**4**) and its Δ⁸-derivative were isolated [2]. We have studied four further species and the resuls are discussed in this paper.

## RESULTS AND DISCUSSION

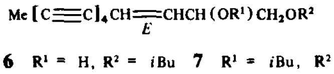
The aerial parts of *L. leontopodioides* (O. K.) Schum. afforded in addition to curcumene and tridecapentaynene, the onoseriolide derivatives **1–3** and **5**, and the tetraynenes **6** [3] and **7**. From the extract of *L. purpurea* (Vahl.) H. et A. also tridecapentaynene and the lactone **3** were isolated while the aerial parts of *L. thermarum* (Phil.) Phil. only gave triterpenes (see Experimental) and those of *L. hahnii* Franchet gave lupenone, tridecapentaynene and tetradeca-4,6-dien-8,10,12-triyn-1-ol.

The structures of **1** and **2** were deduced from the $^1H$ NMR spectra (Table 1) as they were similar to those of onoseriolide (**4**) and its 8,9-dihydro derivative [4, 5] respectively. However, the typical signals of senecioates and the down field shift of the H-13 signals indicated that the corresponding ester were present. The $^1H$ NMR spectrum of **3** (Table 1) was similar to that of **2**. However, the low field singlet at δ 6.43 was replaced by a singlet at δ 4.21. As followed from the molecular formula ($C_{20}H_{22}O_5$) lactone **3** had one more oxygen. Accordingly, all data agreed with the presence of the epoxide of compound **2**. This was supported by the $^{13}C$ NMR data (Table 2) especially if compared with those of **1** and **2** (Table 2). The configuration at C-8 and C-9 could not be determined. However, biogenetic considerations strongly favour a β-epoxidation of the Δ⁸-bond. The $^1H$ NMR spectrum of **5** (Table 1) was in part similar to that of compound **2**. As already followed from the molecular



**1** R = Sen, **2** R = Sen, Δ⁸
**3** R = Sen, 8β, 9β - epoxide
**4** R = H

**5**



$$\mathrm{Me}[C{\equiv}C]_4CH\underset{E}{=}CHCH(OR^1)CH_2OR^2$$

**6** $R^1$ = H, $R^2$ = *i*Bu **7** $R^1$ = *i*Bu, $R^2$ = H

Table 1. $^1$H NMR spectral data of compounds **1**–**3** and **5** ($CDCl_3$, 400 MHz, $\delta$-values)

| H | **1*** | **2** | **3** | **5** |
|---|---|---|---|---|
| 1 | 1.38 *ddd* | 1.68 *ddd* | 1.72 *ddd* | 1.68 *m* |
| 2 | 0.92 *ddd* | 0.94 *ddd* | 0.86 *m* | 0.39 *ddd* |
| 2′ | 0.85 *ddd* | 0.88 *ddd* | 0.91 *m* | 0.88 *m* |
| 3 | 1.97 *br ddd* | 1.99 *br ddd* | 2.00 *br ddd* | 1.93 *m* |
| 5 | 2.51 *br dddd* | 3.00 *br dddd* | 3.39 *br dddd* | — |
| 6 | 2.97 *br dd* | 2.95 *br dd* | 2.73 *br dd* | 4.00 *d* |
| 6′ | 2.12 *br dd* | 2.38 *br dd* | 2.33 *br dd* | 3.01 *d* |
| 9 | 1.66 *dd*<br>1.57 *br dd* | 6.43 *s* | 4.21 *s* | 6.09 *s* |
| 13 | 4.86 *br d*<br>4.79 *br d* | 4.89 *br s* | 4.90 *br d*<br>4.86 *br d* | 4.95 *d*<br>4.79 *br d* |
| 14 | 0.78 *s* | 0.81 *s* | 0.66 *s* | 1.30 *s* |
| 15 | 5.02 *br s*<br>4.77 *br s* | 5.07 *br s*<br>4.80 *br s* | 5.04 *br s*<br>4.70 *br s* | 4.31 *s*<br>4.23 *d* |
| OR | 5.68 *qq*<br>2.17 *d*<br>1.89 *d* | | 5.69 *qq*<br>2.17 *d*<br>1.92 *d* | 5.69 *qq*<br>2.17 *d*<br>2.91 *d* |

* H-8 5.09 *br dd*.

*J*[Hz]: Compounds **1**–**3**: 1,2 = 3.5; 1,2′ = 1,3 = 8; 2,2′ = 5; 2,3 = 4; 2′,3 = 9; 5,6 = 3; 5,6′ = 13; 5,15 = 5,15′ = 2; 6,6′ = 13.5; 13,13′ = 13; (compound **1**: 8,9 = 6.5; 8,9′ = 10; 9,9′ = 12); compound **5**: 1,2 = 2,2′ = 2,3 ~ 4; 6,6′ = 16; 13,13′ = 13; 15,15′ = 13.

Table 2. $^{13}$C NMR spectral data of compounds **2**–**4** ($CDCl_3$, 100.6 MHz, $\delta$-values)

| C | **2** | **3** | **4** |
|---|---|---|---|
| 1 | 23.0 *d* | 26.4 *d* | 23.0 *d* |
| 2 | 16.8 *t* | 17.1 *t* | 16.8 *t* |
| 3 | 23.3 *d* | 22.7 *d* | 23.4 *d* |
| 4 | 149.7 *s* | 149.7 *s* | 149.7 *s* |
| 5 | 50.4 *d* | 61.8 *d* | 50.4 *d* |
| 6 | 22.9 *t* | 22.1 *t* | 21.8 *t* |
| 7 | 157.5 *s* | 152.6 *s* | 157.6 *s* |
| 8 | 64.8 *d* | 149.3 *s* | 88.0 *s* |
| 9 | 29.7 *t* | 115.2 *d* | 64.8 *d* |
| 10 | 41.0 *s* | 40.1 *s* | 41.0 *s* |
| 11 | 127.8 *s* | 120.9 *s* | 127.9 *s* |
| 12 | 168.2 *s* | 169.1 *s* | 168.2 *s* |
| 13 | 54.9 *t* | 54.7 *t* | 54.9 *t* |
| 14 | 17.0 *q* | 22.1 *q* | 17.0 *q* |
| 15 | 106.9 *t* | 106.9 *q* | 107.0 *t* |

OSen: 165.7 *s*, 114.8 *d*, 158.9 *s*, 21.7 *q*, 27.5 *q*.

formula ($C_{20}H_{22}O_5$) again an additional oxygen was present. As the $^1$H NMR signal of the exomethylene proton (H-15) was replaced by a pair of doublets at $\delta$ 4.31 and 4.23 it is most likely that a 15-hydroxy derivative of an isomer of **2** was present.

The structure of compound **7** was deduced from the UV and $^1$H NMR data (see Experimental). As expected in the $^1$H NMR spectrum the signal of H-2 was shifted downfield and that of H-1 upfield if compared with the data of **6** which was isolated from another *Leuceria* species [2].

The presence of onoseriolides seems to be characteristic for the genus *Leuceria* which is placed in the subtribe Nassauviinae though no close relationships to other groups in this subtribe are apparent [1]. The rare onoseriolides so far have been reported from *Wunderlichia* [5] and *Onoseris* [4], both members of the subtribe Gochnatiinae [1], but also from one *Trixis* species [6], where usually isocedrenes are present. Further investigations may show whether the taxonomy of this taxonomically difficult tribe needs some changes.

## EXPERIMENTAL

The air-dried aerial parts of the plants were extracted and worked-up as reported previously [7]. The extract of the aerial parts (570 g) of *L. leontopodioides* (collected 31. 12. 1986 in the province Ultima Esperanza, Sierra de los Baguales, voucher A. Landeros 710, deposited, as all others, in the Herbarium of the University of Conception, Chile) gave by CC (silica gel) three combined fractions: Fr. 1: petrol: Fr. 2: $Et_2O$–petrol (1:1); Fr. 3: $Et_2O$. TLC of fraction 1 (petrol) gave 4 mg tridecapentaynene and 8 mg curcumene. HPLC of fraction 2 (RP 8, MeOH–$H_2O$, 3:1, *ca* 100 bar) gave two fractions (Fr. 2/1 and Fr. 2/2) which were further purified by TLC. Fraction 2/1 ($Et_2O$–petrol, 1:3, three developments) gave 25 mg **2** ($R_f$ 0.85) and fraction 2/2 ($Et_2O$–petrol, 1:1, two developments) gave three fractions (Fr. 3/1–Fr. 3/3). TLC of fraction 3/1 ($Et_2O$–petrol, 1:2, two developments) gave 10 mg **3** ($R_f$ 0.67) and TLC of fraction 3/2 ($Et_2O$–petrol, 2:3, four developments) afforded 6 mg **5** ($R_f$ 0.3). TLC of fraction 3/3 ($Et_2O$–petrol, 1:1, two developments) yielded 26 mg **6** and 5 mg **7** purified by HPLC (RP 18, MeOH–$H_2O$, 3:1, $R_t$ 32.2 min).

The extract of 130 g aerial parts of *L. thermarum* (collected 16. 1. 1987, Parque Nacional Nahauelbuta, voucher R. Rodriguez et P. Pacheo 1982) gave by CC and TLC 20 mg lupenone, 5 mg lupeyl acetate and 5 mg taraxasteryl acetate.

The extract of 240 g aerial parts of *L. purpurea* (collected 18. 12. 1986, province Ultima Esperanza, Sierra de los Baguales, voucher A. Landeros 704) gave by CC and TLC 2 mg tridecapentaynene and 400 mg **2**.

The extract of 480 g aerial parts of *L. hahnii* (collected 19. 1. 1987, province Ultima Esperanza, Sierra de los Baguales, voucher A. Landeros 769) gave by CC and TLC 2 mg tridecapentaynene, 5 mg lupenone and 3 mg tetradeca-4,6-dien-8,10,12-triyne-1-ol.

*8α,9-Dihydroonoseriolide senecioate* (**1**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 1765 ($\gamma$-lactone), 1715 (C=$CCO_2R$); MS *m/z* (rel. int.). 328.167 $[M]^+$ (1) (calc. for $C_{20}H_{24}O_4$: 328.167), 228 $[M-RCO_2H]^+$ (31), 213 $[228-Me]^+$ (7), 83 $[RCO]^+$ (100); $[\alpha]_D^{24}$ −45° ($CHCl_3$; *c* 0.2).

*Onoseriolide senecioate* (**2**). Colourless oil; IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1775 ($\gamma$-lactone), 1720, 1640 (C=$CCO_2R$); MS *m/z* (rel. int.). 326.152 $[M]^+$ (3.5) (calc. for $C_{20}H_{22}O_4$: 326.152), 226 $[M-RCO_2H]^+$ (31), 211 $[226-Me]^+$ (30), 83 $[RCO]^+$ (100).

*8β,9β-Epoxyonoseriolide senecioate* (**3**). Colourless oil; IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1788 ($\gamma$-lactone), 1718 (C=$CCO_2R$); CIMS *m/z* (rel. int.): 343 $[M+1]^+$ (17), 243 $[343-RCO_2H]^+$ (7), 101 $[RCO_2H+1]^+$ (42), 83 $[101-H_2O]^+$ (100).

*15-Hydroxyisoonoseriolide senecioate* **5**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3600 (OH), 1770 ($\gamma$-lactone), 1710 (C=$CCO_2R$); MS *m/z* (rel. int.). 242.102 $[M-RCO_2H]^+$ (8) (calc. for $C_{15}H_{14}O_3$: 242.102), 89 $[RCO]^+$ (100); CIMS *m/z* (rel. int.): 343 $[M+1]^+$ (40), 101 $[RCO_2H+1]^+$ (69), 83 $[101-H_2O]^+$ (100).

*2-Isobutyryloxy-tridec-*3E*-ene-*5,7,9,11*-tetrayn-*1*-ol* (**7**). Colourless oil, rapidly polymerizing; IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3600 (OH), 2230 (C=C), 1740 ($CO_2R$); MS *m/z* (rel. int.): 180.058 [M

$-RCO_2H]^+$ (88) (calc. for $C_{13}H_8O$: 180.058), 152 [180 $-C_2H_4]^+$ (26), 71 $[RCO]^+$ (100); UV $\lambda_{max}^{Et_2O}$ nm: 373, 347, 324, 304, 285, 272, 258, 239; $^1H$ NMR ($CDCl_3$): $\delta$ 3.74 and 3.71 (*dd*, H-1), 5.39 (*ddd*, H-2), 6.35 (*dd*, H-3), 5.83 (*dd*, H-4), 2.01 (*s*, H-13), OCOR: 2.61 (*qq*, H-2′), 1.20 (*d*, H-3′, H-4′); (*J* [Hz]: 1,2 = 3.5; 1′,2 = 2,3 = 6; 2,4 = 1; 2′,3′ = 2′,4′ = 7].

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## REFERENCES

1. Cabrera, A. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds), p. 1044. Academic Press, London.
2. Zdero, C., Bohlmann, F., King, R. M. and Robinson, H. (1986) *Phytochemistry* **25**, 2873.
3. Bohlmann, F., Banerjee, S., Jakupovic, J., King, R. M. and Robinson, H. (1985) *Phytochemistry* **24**, 1295.
4. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1980) *Phytochemistry* **19**, 689.
5. Bohlmann, F., Ludwig, G. W., Jakupovic, J., King, R. M. and Robinson, H. (1984) *Lieb. Ann. Chem.* 228.
6. Bohlmann, F., Suwita, A., Jakupovic, J., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1649.
7. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.

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# TINOSPORASIDE, AN 18-NORCLERODANE GLUCOSIDE FROM *TINOSPORA CORDIFOLIA*

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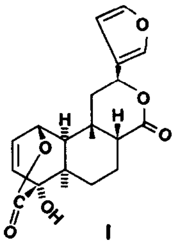
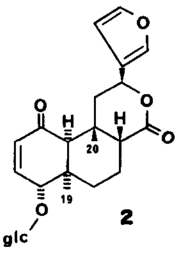
**Key Word Index**—*Tinospora cordifolia*; Menispermaceae; diterpene; 18-norclerodane glucoside; tinosporaside.

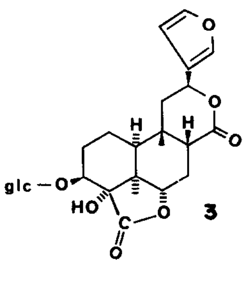
**Abstract**—The stem wood of *Tinospora cordifolia* has yielded a novel 18-norclerodane diterpene *O*-glucoside which has been assigned the trivial name tinosporaside. On the basis of extensive NMR studies this has been assigned the structure (relative stereochemistry) 1,17-dioxo-8*β*,10*α*,12*α*,19*α*,20*β*-18-norclerod-2,13(16),14-trien-4*α*-*β*-D-glucopyranoside-12,17;15,16-dioxide.

## INTRODUCTION

*Tinospora cordifolia* Miers has long been used in Ayurvedic medicine for the treatment of jaundice, rheumatism and urinary diseases [1]. Previous studies on this and other species of *Tinospora* [1–4] have revealed the presence of a range of clerodane-derived sesquiterpenes related to columbin (**1**) [5]. In this paper we report the isolation of an 18-norclerodane glucoside from the stem bark of *T. cordifolia*.







## RESULTS AND DISCUSSION

Column chromatography of the ethyl acetate soluble part of an ethanolic extract of the stem bark gave, on repeated recrystallization from methanol, tinosporaside (**2**). High resolution EIMS indicated an empirical formula $C_{25}H_{32}O_{10}$ with major fragments at *m/z* 330 $[C_{19}H_{22}O_5]^+$ and 314 $[C_{19}H_{22}O_4]^+$ for loss of a hexose sugar moiety (as an *O*-glycoside) with, respectively, retention and loss of the ether oxygen. The IR spectrum revealed the presence of two carbonyl bands at 1708 $cm^{-1}$ (*γ*-lactone) and 1670 $cm^{-1}$ (*α*,*β*-unsaturated carbonyl).