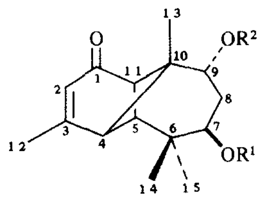
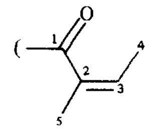


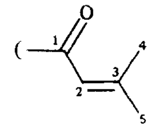
1 R¹ = R² = H
2 R¹ = R² = Ang
3 R¹ = pNO$_2$Bz, R² = OH
4 R¹ = R² = pNO$_2$Bz
5 R¹ = pNO$_2$Bz, R² = Sen
6 R¹ = OH, R² = Sen
7 R¹ = Ang, R² = Sen

Ang =



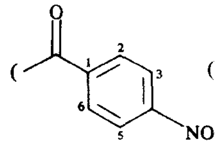
(angeloyl)

Sen =



(senecioyl)

pNO$_2$Bz =



(p-nitrobenzoyl)

(4.40), 248 (3.87); IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1711 and 1653 (C=C–C=O, esters), 1672 and 1617 (C=C–C=O, ketone); ^{1}H NMR (300 MHz) and ^{13}C NMR (75.4 MHz): Tables 1 and 2 respectively.

Acknowledgements—We are grateful to Dr Jerzy Rzedowski for identifying the plant material, and to CoNaCyT and SEP-México for the financial support.

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SESQUITERPENE LACTONES FROM *PYRETHRUM SANTOLINOIDES*

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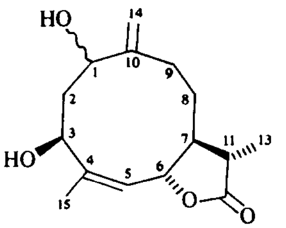
(*Received in revised form* 29 *June* 1988)

Key Word Index—*Pyrethrum santolinoides*; Compositae; sesquiterpene lactones; germacranolides; heliangolides; eudesmanolide.

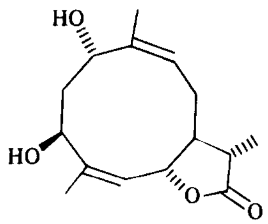
Abstract—A reinvestigation of the aerial parts of *Pyrethrum santolinoides* afforded, in addition to known compounds, four new sesquiterpene lactones, three germacranolides and an eudesmanolide. The structures were elucidated by high field ^{1}H NMR techniques.

INTRODUCTION

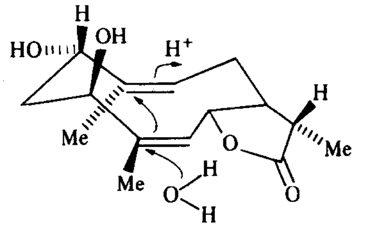
Pyrethrum santolinoides DC (= *Tanacetum sinaicum* Del. ex DC) has been studied previously. From the aerial parts some sesquiterpene lactones were reported [1] and from the roots various compounds, including unusual triterpenes, were isolated [2]. We have studied a sample of the aerial parts collected at Wadi Elarbaeen, Sanct Kathe-



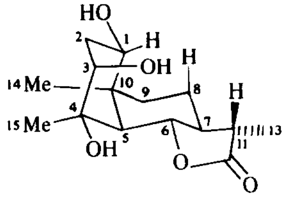
1 1αOH
2 1βOH



3
4 9β,10β epoxide



3



5

rine, Sinai peninsula and the results are discussed in this paper.

RESULTS AND DISCUSSION

The extract of the aerial parts afforded, in addition to some widespread compounds (see Experimental), the germacranolide **1**, which has been isolated previously from the species [1], and three further ones, the epimeric diol **2**, the Δ^9-isomer **3** and the corresponding epoxide **4**. Furthermore the eudesmanolide **5** was present.

The structure of compound **2** followed from its ^{1}H NMR spectrum (Table 1) which was in part similar to that of **1**. However, several signals were shifted and also

Table 1. ^{1}H NMR spectral data of compounds **2–5** (400 MHz, $CDCl_3$, δ-values)

H	**2**	**3**	**4**	**5**
1	4.10 *br ddd*	5.03 *dd*	3.92 *dd*	3.73 *br dd*
2α	2.34 *ddd*	1.92 *ddd*	2.16 *m*	1.82 *ddd*
2β	2.28 *ddd*	2.16 *ddd*	2.25 *m*	2.44 *ddd*
3	4.46 *br dd*	4.48 *dd*	4.48 *br s*	3.15 *br dd*
5	5.24 *dq*	5.09 *br d*	5.18 *br d*	1.83 *d*
6	5.88 *dd*	5.94 *dd*	5.94 *dd*	3.98 *dd*
7	1.81 *m*	1.47 *dddd*	1.75 *br ddd*	1.60 *m*
8α	1.76 *m*	2.22 *m*	2.36 *br d*	1.75 *m*
8β	2.08 *m*	2.45 *ddd*	1.50 *ddd*	1.27 *m*
9α	2.23 *br dd*	5.23 *ddq*	2.83 *dd*	1.08 *ddd*
9β	2.62 *br dd*			2.26 *m*
11	2.35 *m*	2.24 *m*	2.31 *dq*	2.26 *m*
13	1.24 *d*	1.22 *d*	1.26 *d*	1.23 *d*
14	5.32 *br s* 5.13 *br s*	1.68 *dd*	1.24 *s*	0.97 *s*
15	1.78 *d*	1.67 *d*	1.80 *br s*	1.43 *s*

J[Hz]: compound **2**: 1,2α = 4; 1,2β = 10; 2α,2β = 16; 2α,3 = 5; 2β,3 = 4; 3, OH = 6; 5,6 = 6,7 = 10; 5,15 = 1.5; 8β,9 = 10; 8α,9α = 8; 9α,9β = 15; 11,13 = 7; compound **3**: 1,2β = 11.5; 1,2α = 2; 2α,2β = 14.5; 2β,3 = 2.5; 2α,3 = 5; 5,6 = 6,7 = 10; 5,15 = 1.5; 7,8β = 8β,9 = 11; 7,8α = 2; 7,11 = 12; 8α,8β = 13.5; 8α,9 = 6; 8β,14 = 9,14 = 1; 11,13 = 7; compound **4**: 1,2β = 10.5; 1,2α = 2.5; 5,6 = 6,7 = 10; 7,8β = 8β,9 = 11; 7,11 = 12; 8α,8β = 14.5; 8α,9 = 3; 11,13 = 7; compound **5**: 1,2β = 6; 1,2α = 10; 2α,2β = 15; 2β,3 = 1.5; 2α,3 = 2; 5,6 = 6,7 = 10; 8α,9β = 4; 8β,9β = 9α,9β = 13.5; 11,13 = 7.

some of the couplings differed. Spin decoupling indicated that only the configuration at C-1 was changed in the lactone. In agreement with the down field shift of H-14 the lactone **2** had a 1β-hydroxy group.

The molecular formula of compound **3** ($C_{15}H_{22}O_4$) showed that we were dealing with an isomer of compounds **1** and **2**. The ^{1}H NMR spectrum (Table 1) indicated that the exomethylene group was replaced by an olefinic methyl group. Accordingly, two signals (δ1.68 *dd* and 1.67 *d*) for olefinic methyls were visible and in addition to a broadened doublet at δ5.09 (5-H) a further low field signal (δ5.23 *ddq*) was present. Spin decoupling allowed the assignment of all signals, only those of H-8α and H-11 being overlapped. The configuration at C-11 could not be deduced directly from the ^{1}H NMR spectrum and the preferred conformation had to be determined for a clear assignment of the configurations. This was achieved by NOE difference spectroscopy. The observed effects required the proposed configurations and a conformation with both methyls below the plane but not perpendicular (Table 2). The NOE's between H-15 and H-5 as well as between H-9 and H-14 established the presence of a heliangolide with a Δ^9-*Z*-configuration for the double bond. This germacranolide type is relatively rare, for example some exomethylene lactones with 8β-acyloxy groups of this type have been reported from *Eupatorium* species [3].

In the ^{1}H NMR spectrum of **4** (Table 1) one of the olefinic proton signals was replaced by a double doublet at δ2.83. As followed from spin decoupling this signal was due to H-9. The chemical shift required the presence of a proton at an epoxide carbon. Thus, this lactone was the epoxide of **3**. This was established by determining the stereochemistry by the NOE which requires a conformation as in the case of **3** with a β-epoxide moiety. Inspection of models clearly showed that an α-epoxide can not have a conformation which would agree with the observed NOE's and couplings. Compounds **1**–**4** are probably all derived from a 3β-hydroxyheliangolide with a 1(10)-double bond by attack of oxygen accompanied by allylic rearrangement and epoxidation in the case of **4**.

The ^{1}H NMR spectral data of **5** (Table 1) indicated that an eudesmanolide was present. The signals were in part similar to those of reynosin. However, the exomethylene proton signals were replaced by a sharp singlet at δ1.43. Accordingly, a tertiary methyl carbinol was very likely. A double doublet at δ3.15 indicated a further hydroxy group and a methyl doublet at δ1.23 agreed with the presence of a 11,13-dihydro lactone. Spin decoupling showed that the signal of the corresponding vicinal proton (H-11) was overlapped by a multiplet. Therefore, no clear coupling with H-7 could be recognized. However, NOE difference spectroscopy allowed the assignment of the stereochemistry at C-11 and also at all other chiral centres. A clear effect between H-1, H-6 and H-8β as well as a NOE of H-14 with H-5 required the presence of a *cis*-decalin system (Table 2). Most likely the lactone **5** is formed by cyclization of **3** as shown in Scheme 1. Inspection of a model of **3** shows that in the preferred conformation it would lead to a *cis*-decalin system with a stereochemistry as observed for lactone **5**.

EXPERIMENTAL

The air-dried plant material (640 g) was extracted with Et_2O–MeOH–petrol (1:1:1) for 24 hr at room temp. After defatting with MeOH the extract was separated first by CC (silica gel) as reported previously [4] into three fractions (Fr. 1: Et_2O–petrol, 1:9 and 1:3; Fr. 2: Et_2O–petrol, 1:1 and Fr. 3: Et_2O and Et_2O–MeOH, 9:1). TLC of fraction 1 gave 50 mg thymol, of fraction 2 gave 5 mg thymol, 15 mg *p*-methoxyacetophenone and 23 mg stigmasterol. TLC of one-sixth of fraction 3 (Et_2O–MeOH, 99:1) gave two bands (Fr. 3/1 and Fr. 3/2). TLC and HPLC of Fr. 3/1 (MeOH–H_2O, 7:3, always RP 18, flow rate 3 ml/min) gave 3 mg **5** (R_t 4.8 min). HPLC of Fr. 3/2 (MeOH–H_2O, 3:1) gave 3 mg **4** (R_t 1.0 min), 2.5 mg **2** (R_t 1.4 min), 3 mg **1** (R_t 2.1 min) and 7 mg **3** (R_t 2.9 min). Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material.

1α,3β-Dihydroxy-7α,11βH-germacra-4Z,10(14)-dien-12,6α-olide (**2**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone); CIMS *m/z* (rel. int.): 267 $[M+1]^+$ (92) ($C_{15}H_{22}O_4+1$), 249 $[267-H_2O]^+$ (100), 231 $[249-H_2O]^+$ (48); $[\alpha]_D^{24°}$ +46° ($CHCl_3$; *c* 0.18).

1α,3β-Dihydroxy-7α,11βH-germacra-4Z,9Z-dien-12,6α-olide (**3**). Colourless crystals, mp. 163°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone); MS *m/z* (rel. int.): 266.152 $[M]^+$ (14) (calc. for $C_{15}H_{22}O_4$: 266.152), 248 $[M-H_2O]^+$ (14), 233 $[248-Me]^+$ (9), 222 $[M-CO_2]^+$ (12), 100 (100); $[\alpha]_D^{24°}$ +154° ($CHCl_3$; *c* 0.13).

Table 2. NOE's of the lactones **3**–**5** (in parenthesis % NOE)

Irradiated	**3**	**4**	**5**
H-1	H-6 H-8β (3) (4)	H-6 H-8β (3) (3)	H-6 H-8β (10) (5)
H-3	H-2α H-2β H-15 (5) (3) (5)	H-2α H-2β H-15 (6) (6) (5)	H-2α H-2β H-15 (3) (6) (14)
H-5	H-15 H-7 (5) (3)	H-7 H-15 (3) (4)	H-14 H-15
H-6	H-1 H-8β H-11 (4) (2) (3)	H-1 H-8β H-11 (3) (2) (5)	H-1 H-11 H-8β (8) (7) (3)
H-9 (9′)	H-14 H-7 (5) (3)	H-7 H-14 (3) (2)	H-14 (4)
H-14	H-9α (10)	H-9α H-15 (10) (6)	H-2α H-5 H-9α H-15 (5) (10) (5) (2)
H-15	H-3 H-5 (7) (9)	H-3 H-5 H-14 (5) (8) (4)	H-3 H-5 H-14 (7) (5) (2)

1α,3β-Dihydroxy-9β,10β-epoxy-7α,11βH-germacra-4Z-en-12,6α-olide (**4**). Colourless gum; IR $\nu_{\max}^{\mathrm{CHCl_3}}$ 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 $\nu_{\max}^{\mathrm{CHCl_3}}$ 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).

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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.

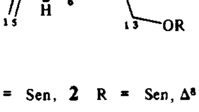
INTRODUCTION

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 Δ^8-derivative were isolated [2]. We have studied four further species and the resuls are discussed in this paper.

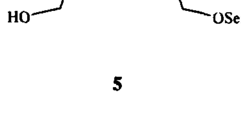
RESULTS AND DISCUSSION

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 ^{1}H 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 ^{1}H 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 Δ^8-bond. The ^{1}H 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, Δ^8
3 R = Sen, 8β, 9β - epoxide
4 R = H



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

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