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# MELAMPOLIDES FROM *TETRAGONOTHECA* SPECIES

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**Key Word Index**—*Tetragonotheca ludoviciana*; *T. repanda*; Compositae; sesquiterpene lactones; melampolides.

**Abstract**—The investigation of the extracts from two *Tetragonotheca* species collected in Mexico afforded, in addition to the sesquiterpene lactones repandin A–D, 12 new compounds, two of them being chloro-compounds with an ether ring which were present in two conformations at room temperature. The structures of these new sesquiterpenes were elucidated by high field NMR spectroscopic methods.

## INTRODUCTION

The small genus *Tetragonotheca* (Compositae, tribe Helianteae) with four species growing in southern U.S.A. and in Mexico has been placed traditionally in the subtribe Verbesininae [1]. It was then transferred to Helianthinae [2] and later to the Galinsoginae [3]. So far the chemistry does not agree with the latter placement as in addition to $C_{17}$-acetylenic compounds [4] several melampolides have been reported [5–7] which are typical for representative of the subtribes Melampodinae, Clibadiinae, Enhydrinae and Millerinae. We have reinvestigated two species collected in northern Mexico and the results are discussed in this paper.

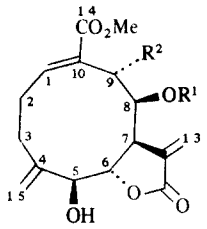
## RESULTS AND DISCUSSION

The polar fractions from the aerial parts of *T. repanda* Buckl.) Small. afforded, as reported previously, repandin A–D (**1a–1d**) [6] and some widespread compounds (see Experimental). Furthermore, the melampolides **1e–1g**, **2a**, **3b** and the cyclic ether **4a** were isolated. The polar parts of the extract of the aerial parts of *T. ludoviciana* (T. et G.) Gray also afforded the same lactones except **1g** but also **1h**, **1i**, **2b**, **2c**, **3a** and **4c** as well as the eudesmane derivative **5**.

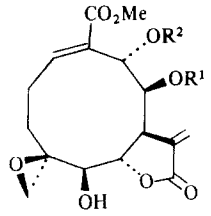
The structures of **1e–1h** was deduced from the $^1$H NMR spectra (Table 1) which were close to those of compounds **1a–1d**. The changed nature of the oxygen functions followed from the typical $^1$H NMR signals. The chemical shifts of H-8 and H-9 indicated that the unsaturated ester group was always at C-8. This was established in the case of **1b** by selective INEPT which connected H-8 and H-9 with the corresponding ester carbonyl. In the spectrum of **1g** the presence of a free hydroxy group at C-9 caused, as expected, a considerable up field shift both of H-9 and H-8. The $^1$H NMR spectrum of **1i** (Table 1) showed the absence of an ester group at C-9. The low field signal around $\delta$6.0 therefore was replaced by multiplets at $\delta$2.96 and 2.61. For the 8-desacyl-9-desacyloxy derivative of **1a–1i** we propose the name repandanolide.

The $^1$H NMR spectra of **2a–2c** (Table 1) differed significantly from those of the repandins. The nature of the oxygen functions at C-8 to C-10 followed from the characteristic signals. A pair of doublets at $\delta$2.51 and 2.45 with a 5 Hz coupling constant indicated the presence of 4,15-epoxides of **1a**, **1b** and **1e**. If biogenetic consideration were valid the stereochemistry at C-4 was supported by the conformation of **1b** which followed from the observed NOE's. Especially strong effects between H-15′, H-5 and H-7, between H-15, H-1 and H-3$\alpha$, between H-9, H-2$\beta$ and H-6, between H-6, H-2$\beta$, and H-9, as well as between H-2$\beta$, H-6 and H-9, showed that both C-14 and C-15 were below the plane. In agreement with this a $\beta$-configuration was deduced from the observed NOE's for the epoxides. Thus clear effects were visible between H-15 and H-5, between H-2$\beta$ and H-6, as well as between H-9$\beta$, H-6 and H-2$\beta$. The $^{13}$C NMR spectrum of **2a** (Table 2) supported the structure.

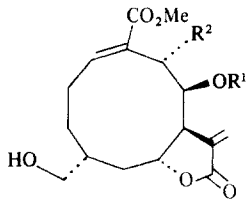
The $^1$H NMR spectrum of **3a** (Table 3) was in part again similar to that of **1c**. However, the exomethylene signals were replaced by a pair of partly overlapped double doublets around $\delta$3.50 indicating the presence of a hydroxymethylene group. Spin decoupling led to the complete sequence. The NOE's required an $\alpha$-orientation of this hydroxymethylene group and a conformation very close to that deduced for **1a** and **2a**, however, with C-15 being more quasi-equatorially orientated. Thus clear NOE's were observed between H-4 and H-6, between H-7, H-5$\alpha$, H-8 and H-13′, between H-6, H-4 and H-9, as well as between H-9, H-6 and H-2$\beta$. The chemical shifts of H-8 and H-9 agreed with the proposed relative position of the ester groups. The spectrum of **3b** differed from that of **3a** by the absence of a second ester group, the replacement of epoxy angelate by angelate and in several shifts and couplings. Spin decoupling showed that the substitution pattern was identical in both melampolides. Several different couplings indicated a changed stereochemistry which could be determined by the NOE's. Clear effects were observed between H-4, H-7 and H-1 indicating a $\beta$-orientation of the hydroxymethylene group. Further NOE's between H-7, H-8, H-4 and H-13′, between H-6, H-2, H-9$\beta$ and H-5, as well as between H-8,



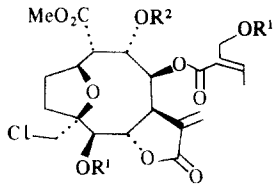
| | 1a | 1b | 1c | 1d | 1e | 1f | 1g | 1h | 1i |
|---|---|---|---|---|---|---|---|---|---|
| $R^1$ | 5AcAng | | Epang | | Ang | | Ang | 5AcAng | Ang |
| $R^2$ | *O*iBu | OMeBu | *O*iBu | OMeBu | *O*iBu | OMeBu | OH | OMeBu | H |



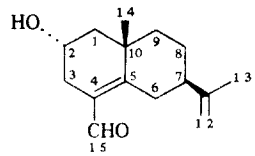
| | 2a | 2b | 2c |
|---|---|---|---|
| $R^1$ | 5OHAng | | Ang |
| $R^2$ | *i*Bu | MeBu | *i*Bu |



| | 3a | 3b |
|---|---|---|
| $R^1$ | Epang | Ang |
| $R^2$ | O*i*Bu | H |
| | | 4*epi* |



| | 4a | 4b | 4c |
|---|---|---|---|
| $R^1$ | H | Ac | H |
| $R^2$ | *i*Bu | *i*Bu | MeBu |



**5**

H-7, H-9 and H-13′, required the same configuration of the other chiral centers as in **3a** and a conformation with both C-14 and C-15 below the plane. The $^{13}$C NMR data also agreed with the structure (Table 2). For comparison the data of **1b** and **1d** were measured. The $^1$H NMR spectrum of **3b** was close to that of the melnerins [8, 9] where the same stereochemistry was determined.

The $^1$H NMR spectra of **4a** and **4c** (Table 4) only differed in the signals of the ester residues. Furthermore in both spectra nearly all signals were doubled. As irradiation of signals belonging to one set of signals also saturated the corresponding ones of the second set, two conformers were present. At 60° these two sets of signals collapsed to highly broadened signals as usually observed at room temperature for many cyclodecane derivatives. At −30° a clear set of signals for two conformers were recognized and saturation of a single signal did not lead to saturation of the corresponding one in the second conformer. Sequences obtained by spin decoupling were in part identical with those of **2a**. However, one olefinic proton signal (H-1) was replaced by pairs of double doublets and the epoxy signal (H-15) by pairs of doublets. The chemical shifts of the latter indicated that a 15-hydroxy or chloro-derivative was present.The molecular formula of **4a** could be deduced from the mass spectrum where *m/z* 429 corresponds to $C_{20}H_{26}O_8Cl$. As followed from the $^{13}$C NMR spectrum (Table 2) the lactone **4a** had 24 carbons. Accordingly, *m/z* 429 was a fragment, obviously formed by loss of an acyloxy group. The resulting molecular formula required an ether ring and a chloro-group most probably at C-15. This was supported by elimination of $CH_2Cl$ from the *m/z* 429 ion and by acetylation of **4a** which afforded the diacetate **4b** where only one primary acetate (C-20) was formed. Again, two conformers were present, but in very different concentrations. The configuration at C-1, C-4 and C-10 followed from the observed couplings if models were inspected. The two conformers differed mainly in the orientation of the oxygen functions at C-8 and C-9. As could be shown by the observed couplings in the case of $\mathbf{4a}_1$ these groups were *trans*-diaxial and in $\mathbf{4a}_2$ they were diequatorially orientated. Furthermore, clear NOE's between H-6, H-10

Table 1. $^1$H NMR spectral data of components of **1e–1i** and **2a–2c** (400 MHz, $CDCl_3$, $\delta$-values)

| H | 1e | 1f* | 1g* | 1h* | 1i | 2a | 2b† | 2c† |
|---|---|---|---|---|---|---|---|---|
| 1 | 6.74 *dd* | 6.74 | 6.84 | 6.73 | 6.85 *dd* | 6.93 *dd* | 6.93 | 6.93 |
| 2 | 2.79 *dddd* | 2.82 | 2.66 | 2.78 | 2.65 *m* | 2.98 *dddd* | 2.97 | 2.98 |
| 2′ | 2.52 *m* | 2.51 | 2.58 | 2.51 | 2.32 *m* | 2.49 *m* | 2.49 | 2.50 |
| 3 | 3.04 *m* | 3.05 | 3.01 | 3.04 | 2.95 *m* | 2.89 *ddd* | 2.88 | 2.87 |
| 3′ | 2.34 *ddd* | 2.33 | 2.34 | 2.32 | 2.30 *m* | 1.40 *ddd* | 1.42 | 1.41 |
| 5 | 3.92 *br d* | 3.92 | 3.92 | 3.91 | 3.94 *br d* | 2.81 *d* | 2.81 | 2.80 |
| 6 | 4.85 *br d* | 4.85 | 4.78 | 4.82 | 4.86 *br d* | 5.11 *br d* | 5.11 | 5.07 |
| 7 | 3.03 *br s* | 3.06 | 2.96 | 3.04 | 2.94 *br s* | 3.66 *br s* | 3.65 | 3.62 |
| 8 | 6.24 *dd* | 6.26 | 5.77 | 6.27 | 5.47 *ddd* | 6.32 *dd* | 6.32 | 6.27 |
| 9 | 6.02 *d* | 6.00 | 4.71 *dd* | 5.95 | 2.96 *m*<br>2.61 m | 6.21 *d* | 6.24 | 6.16 |
| 13 | 6.39 *d* | 6.40 | 6.35 | 6.39 | 6.31 *d* | 6.36 *d* | 6.37 | 6.35 |
| 13′ | 5.89 *d* | 5.90 | 5.81 | 5.88 | 5.72 *d* | 5.90 *d* | 5.90 | 5.88 |
| 15 | 5.02 *br s* | 5.02 | 5.05 | 5.01 | 5.05 *br s* | 2.51 *d* | 2.51 | 2.51 |
| 15′ | 4.99 *br s* | 5.00 | 4.97 | 4.99 | 4.95 *br s* | 2.45 *d* | 2.45 | 2.45 |
| OMe | 3.84 *s* | 3.83 | 3.85 | 3.82 | 3.82 *s* | 3.85 *s* | 3.85 | 3.85 |
| OR | 6.10 *qq* | 6.11 *qq* | 6.12 *qq* | 6.53 *q* | 6.08 *qq* | 6.41 *q* | 6.39 *q* | 6.07 *qq* |
| | 1.93 *dq* | 1.94 *dq* | 1.98 *dq* | 4.70 *br d* | 1.98 *dq* | 4.19 *br d* | 4.21 *br d* | 1.93 *dq* |
| | 1.81 *dq* | 1.80 *dq* | 1.87 *dq* | 4.58 *br d* | 1.82 *dq* | 4.12 *br d* | 4.12 *br d* | 1.80 *dq* |
| | | | | 2.08 *d* | | 2.03 *br d* | 2.02 *br d* | |
| | | | | 2.08 *s* | | | | |
| OR′ | 2.45 *qq* | 2.29 *ddq* | 3.41 *d* | 2.26 *ddq* | | 2.30 *ddq* | 2.48 *qq* | 2.47 *qq* |
| | 1.07 *d* | 1.56 *m* | | 1.55 *m* | | 1.56 *ddq* | 1.08 *d* | 1.06 *d* |
| | 1.05 *d* | 1.35 *m* | | 1.33 *m* | | 1.34 *ddq* | 1.06 *d* | 1.04 *d* |
| | | 1.03 *d* | | 1.00 *d* | | 1.02 *d* | | |
| | | 0.79 *t* | | 0.76 *t* | | 0.78 *t* | | |

*Multiplicity as in **1e**; †multiplicity as in **2a**;
*J*[Hz]: 1,2 = 13; 1,2′ = 2,3 = 4.5; 2,2′ = 2,3′ = 3,3′ = 14; 2′,3 = 3; 2′,3′ = 5.5; 5,6 = 9; 7,8 = 2; 7,13 = 7,13′ = 1.5; 8,9 = 9.5; compound **1g**: 9, OH = 9; compound **1i**: 8,9′ = 5; compounds **2a–2c**: 15,15′ = 5.

Table 2. $^{13}$C NMR spectral data of compounds **1b**, **1d**, **2a**, **3b** and **4a** ($CDCl_3$, $\delta$-values)

| C | 1b | 1d | 2a($C_6D_6$) | 3b | $4a_{1/2}$ | | multiplicity |
|---|---|---|---|---|---|---|---|
| 1 | 147.6 | 147.5 | 147.8 | 145.0 | 75.9 | 74.4 | *d* |
| 2 | 29.2 | 29.0 | 28.8 | 29.2 | 29.6 | 29.4 | *t* |
| 3 | 26.8 | 26.8 | 26.5 | 27.3 | 29.2 | 28.9 | *t* |
| 4 | 143.6 | 143.3 | 57.3 | 35.7 *d* | 88.5 | 86.2 | *s* |
| 5 | 80.2 | 80.3 | 78.4 | 38.6 *t* | 77.9 | 77.2 | *d* |
| 6 | 80.6 | 80.4 | 80.7 | 76.4 | 80.3 | 79.2 | *d* |
| 7 | 41.1 | 40.9 | 40.9 | 43.2 | 42.6 | 41.7 | *d* |
| 8 | 74.6 | 76.2 | 75.6 | 73.7 | 74.2 | 72.9 | *d* |
| 9 | 69.1 | 69.1 | 69.9 | 30.2 | 70.6 | 70.2 | *d* |
| 10 | 127.8 | 127.7 | 127.2 | 127.8 | 54.7 *d* | 50.3 *d* | *s* |
| 11 | 133.9 | 134.1 | 135.0 | 136.0 | 136.4 | 134.2 | *s* |
| 12 | 168.9 | 168.5 | 169.5 | 169.5 | 169.1 | 169.1 | *s* |
| 13 | 126.6 | 126.3 | 125.8 | 124.5 | 126.4 | 125.8 | *t* |
| 14 | 166.0 | 165.9 | 166.0 | 166.3 | 171.8 | 170.6 | *s* |
| 15 | 121.3 | 121.5 | 53.7 | 68.1 | 52.0 | 50.3 | *t* |
| OMe | 52.2 | 52.2 | 51.4 | 52.2 | 52.5 | 52.4 | *q* |
| OR | 164.9 | 168.0 | 164.8 | 167.2 | 165.2 | 164.7 | *s* |
| | 130.6 | 59.1 | 131.3 | 127.5 | 131.0 | 130.9 | *s* |
| | 143.2 | 60.3 | 141.9 | 139.8 | 142.4 | 142.4 | *d* |
| | 15.7 | 12.7 | 15.3 | 15.8 | 15.6 | 15.5 | *q* |
| | 64.1 | 18.9 *q* | 63.7 | 20.3 *q* | 64.5 | 64.3 | *t* |
| OR′ | 176.0 | 175.6 | 176.5 | — | 176.7 | 175.7 | *s* |
| | 41.1 | 41.1 | 34.0 | | 33.9 | 33.9 | *d* |
| | 26.2 *t* | 26.0 *t* | 18.5 | | 19.0 | 18.6 | *q* |
| | 16.2 | 16.6 | 18.4 | | 18.9 | 18.5 | *q* |
| | 11.3 | 11.5 | | | | | *q* |

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

| H | 3a | 3b |
|---|---|---|
| 1 | 7.01 *dd* | 6.89 *dd* |
| 2 | 2.89 *br ddd* | 2.63 *dddd* |
| 2′ | 2.63 *br ddd* | 2.40 *br d* |
| 3 | 2.18 *br ddd* | 1.96 *ddd* |
| 3′ | 1.41 *br ddd* | 1.60 *m* |
| 4 | 1.98 *m* | 1.52 *m* |
| 5 | 1.90 *ddd* | 1.80 *ddd* |
| 5′ | 1.53 *ddd* | 1.60 *m* |
| 6 | 4.68 *ddd* | 5.11 *ddd* |
| 7 | 2.95 *dddd* | 2.88 *br s* |
| 8 | 6.40 *dd* | 5.56 *ddd* |
| 9 | 6.03 | 3.01 *br dd*<br>2.65 *m* |
| 13 | 6.31 *d* | 6.30 *d* |
| 13′ | 5.80 *d* | 5.71 *d* |
| 15 | 3.53 dd*<br>3.48 dd* | 3.48 dd*<br>3.44 dd* |
| OMe | 3.83 *s* | 3.84 *s* |
| OR | 2.98 *q* | 6.08 *qq* |
| | 1.45 *s* | 1.98 *dq* |
| | 1.17 *d* | 1.82 *dq* |
| OR′ | 2.50 *qq* | |
| | 1.10 *d* | |
| | 1.09 *d* | |

*partly overlapped.

*J*[Hz]: Compound **3a**: 1,2 = 2,2′ = 2,3′ = 3,3′ = 3′,4 ≈ 12.5; 1,2′ = 5; 2′,3 = 8; 3,4 = 4; 4,5 = 2; 4,5′ = 8; 5,5′ = 16; 5,6 = 6.5; 5′,6 = 6; 6,7 = 4; 7,8 = 3; 7,13 = 2.5; 7,13′ = 2; 8,9 = 8.5; compound **3b**: 1,2 = 2,2′ = 2,3 = 3,3′ ≈ 12.5; 1,2′ = 2,3′ = 4.5; 2′,3 = 6; 4,5 = 10.5; 5,5′ = 14; 5,6 = 4.5; 5′,6 = 11; 6,7 = 1.5; 7,8 = 2.5; 7,13 = 1.8; 7,13′ = 1.5; 8,9 = 5.5; 8,9′ = 10.5; 9,9′ = 13.5.

and H-3 required the proposed configuration at C-1 and C-4. Similar assignments followed from the couplings $J_{1,10}$ and $J_{9,10}$. This agrees with the assumption that **4a** is formed by transformation of **2a** to the corresponding 4α,15-diol followed by addition of the 4α-hydroxy group at the 1(10)-double bond and substitution at C-15 by chloride. For lactone **4a** with the free 9-hydroxy group we propose the name tetragonolide.

## EXPERIMENTAL

The air-dried aerial parts, collected in northern Mexico, were extracted and worked-up as reported previously [10]. The extract of *Tetragonotheca repanda* (300 g, voucher Dominguez 8252) gave by CC, TLC and HPLC (always RP 8, *ca* 100 bar) 30 mg heptadeca-1,7*E*,9*E*,15*E*-tetraene-11,13-diyn-17-ol, 25 mg of the 15*Z*-isomer, 15 mg methyl-3,4-dihydroxybenzoate, 10 mg methyl-4-hydroxy-3-methoxybenzoate, 25 mg phytol, 50 mg **1a** (HC 1, $R_t$ 5.5 min), 70 mg **1b** (HC 1, $R_t$ 7.0 min), 50 mg **1c** (HC 1, $R_t$ 6.0 min), 40 mg **1d** (HC 1, $R_t$ 7.5 min), 15 mg **1e** (HC 2, $R_t$ 9.5 min), 12 mg **1f** (HC 2, $R_t$ 12.0 min), 2 mg **1g** (HC 2, $R_t$ 5.3 min), 3 mg **2a** (HC 2, $R_t$ 7.5 min), 4 mg **3b** (HC 3, $R_t$ 9.5 min) and 5 mg **4a** (HC 3, $R_t$ 11.0 min).

The extract of *T. ludoviciana* (300 g, voucher Dominguez 8263) was separated as above. Finally 8 mg vomifoliol (HC 1, $R_t$ 5.0 min), 60 mg **1a**, 50 mg **1b**, 20 mg **1c**, 15 mg **1d**, 18 mg **1e**, 15 mg **1f**, 6 mg **1h** (HC 3, $R_t$ 16 min), 2 mg **1i** (HC 1, $R_t$ 5.5 min), 20 mg **2a**, 20 mg **2b** (HC 1, $R_t$ 10.5 min), 5 mg **2c** (HC 3, $R_t$ 13.0 min), 5 mg **3a** (HC 2, $R_t$ 9.0 min and TLC ($Et_2O$) $R_f$ 0.45), 10 mg **3b**, 16 mg **4a**, 5 mg **4c** (HC 3, $R_t$ 17.0 min) and 8 mg **5** (HC 1, $R_t$ 8.5 min). HPLC solvents were MeOH-$H_2O$ (HC 1=7:3; HC 2=3:2 and HC 3=13:7). Known compounds were identified by comparing their 400 MHz $^1$H NMR spectra with those of authentic material and with the lit. data.

9α-*Isobutyryloxyrepandanolide*-8-O-*angelate* (**1e**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1780 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 476 [M]$^+$ (19 (calc. for $C_{25}H_{32}O_9$: 476), 388 [M − $C_3H_7CO_2H$]$^+$ (6), 377 [M − OAng]$^+$ (6), 376 [M − AngOH]$^+$ (2), 288 [388 − AngOH]$^+$ (2.5), 83 [$C_4H_7CO$]$^+$ (100), 71 [$C_3H_7CO$]$^+$ (25).

9α-[2-*Methylbutyryloxy*]-*repandanolide*-8-O-*angelate* (**1f**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1780 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 490.220 [M]$^+$ (1) (calc. for $C_{26}H_{34}O_9$: 490.220), 391 [M − AngO]$^+$ (7), 388 [M − $C_4H_9CO_2H$]$^+$ (8), 288 [388 − AngOH]$^+$ (3), 85 [RCO]$^+$ (12), 83 [RCO]$^+$ (100).

9α-*Hydroxyrepandanolide*-8-O-*angelate* (**1g**) Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3590 (OH), 1770 (γ-lactone), 1720 (C=C$CO_2$R); MS *m/z* (rel. int.): 406 [M]$^+$ (2) ($C_{21}H_{26}O_8$), 388 [M − $H_2O$]$^+$ (1.5), 307 [M − AngO]$^+$ (6), 83 [RCO]$^+$ (100).

9α-[2-*Methylbutyryloxy*]-*repandanolide*-8-O-[5-*acetoxyangelate*] (**1h**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1780 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 488 [M − HOAc]$^+$ (0.5) ($C_{26}H_{32}O_9$), 446 [M − $C_4H_9CO_2H$]$^+$ (1.5), 391 [M − AcOAngO]$^+$ (7), 141 [RCO]$^+$ (65), 81 [141 − HOAc]$^+$ (100); $[\alpha]_D^{24}$ −98° ($CHCl_3$; *c* 0.5).

*Repandanolide*-8-O-*angelate* (**1i**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1775 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel.int.): 291 [M − OAng]$^+$ (4), 290 [M − HOAng]$^+$ (1.5), 258 [290 − MeOH]$^+$ (2), 83 [RCO]$^+$ (100); $[\alpha]_D^{24}$ −74° ($CHCl_3$; *c* 0.2).

9-*Isobutyryloxy*-4β,15-*epoxyrepandanolide*-8-O-[5-*hydroxyangelate*] (**2a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3850 (OH), 1770 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 393 [M − OCOR]$^+$ (5), 99 [RCO]$^+$ (100), 71 [$C_3H_7CO$]$^+$ (52); CIMS *m/z* (rel. int.): 509 [M + 1]$^+$ (1) ($C_{25}H_{32}O_{11}$ + 1]$^+$.

9-[2-*Methylbutyryloxy*-4β,15-*epoxy*-*repandanolide*-8-O-[5-*hydroxyangelate*] (**2b**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1775 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 504.200 [M − $H_2O$]$^+$ (0.2) ($C_{26}H_{32}O_{10}$), 99 [RCO]$^+$ (100), 85 [RCO]$^+$ (67); $[\alpha]_D^{24}$ −88° ($CHCl_3$; *c* 1.0).

9α-*Isobutyryloxy*-4β,15-*epoxyrepandanolide*-8-O-*angelate* (**2c**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1775 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 492 [M]$^+$ (0.1) ($C_{25}H_{32}O_{10}$), 404 [M − $RCO_2H$]$^+$ (6.5), 393 [M − OAng]$^+$ (4), 83 [RCO]$^+$ (100), 71 [RCO]$^+$ (34); $[\alpha]_D^{24}$ −110° ($CHCl_3$; *c* 0.5).

9-*Isobutyryloxy*-15-*hydroxy*-4β,15-*dihydrorepandanolide*-8-O-*epoxyangelate* (**3a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1775 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 379 [M − OCOR]$^+$ (8), 71 [RCO]$^+$ (100); CIMS *m/z* (rel. int.): 495 [M + 1]$^+$ (7) ($C_{25}H_{34}O_{10}$ + 1), 379 [M − $RCO_2H$]$^+$ (100); $[\alpha]_D^{24}$ −16° ($CHCl_3$; *c* 0.5).

15-*Hydroxy*-4α,15-*dihydrorepandanolide*-8-O-*angelate* (**3b**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1770 (γ-lactone), 1725 ($CO_2R$); MS *m/z* (rel. int.): 392.184 [M]$^+$ (2) ($C_{21}H_{28}O_7$), 293 [M − OAng]$^+$ (5), 261 [293 − MeOH]$^+$ (3), 83 [RCO]$^+$ (100).

*Tetragonolide isobutyrate* (**4a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1770 (γ-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 429.132 [M − OCOR]$^+$ (34) ($C_{20}H_{26}O_8Cl$), 428 [M − $RCO_2H$]$^+$ (16), 393 [429 − HCl]$^+$ (6), 379 [428 − $CH_2Cl$]$^+$ (9), 99 [RCO]$^+$ (82), 71 [99 − CO]$^+$ (100); CIMS *m/z* (rel. int.):

Table 4. $^1$H NMR spectral data of compounds **4a–4c** (400 MHz, $CDCl_3$, $\delta$-values)

| H | $4a_1$ | $4a_2$ | $4b_1$* | $4b_2$† | $4c_1$ | $4c_2$ |
|---|---|---|---|---|---|---|
| 1 | 4.52 *dd* | 4.91 *br ddd* | 4.57 *dd* | 4.92 *br ddd* | 4.54 *dd* | 4.89 *br ddd* |
| 5 | 4.04 *br d* | 3.82 *d* | 5.35 *br d* | 5.14 *br d* | 4.02 *d* | 3.82 *d* |
| 6 | 4.78 *dd* | 4.74 *dd* | 4.79 *dd* | 4.80 *dd* | 4.73 *dd* | 4.75 *dd* |
| 7 | 3.77 *br s* | 4.33 *dddd* | 3.77 *br s* | 4.35 *dddd* | 3.75 *br s* | 4.34 *dddd* |
| 8 | 5.21 *br d* | 6.37 *dd* | 5.21 *br d* | 6.32 *dd* | 5.20 *br d* | 6.36 *dd* |
| 9 | 5.45 *br d* | 5.23 *br d* | 5.41 *br d* | 5.17 *br d* | 5.44 *br d* | 5.19 *br d* |
| 10 | 2.81 *br d* | 2.73 *br s* | 2.89 *br d* | 2.76 *br s* | 2.82 *br d* | 2.73 *br s* |
| 13 | 6.45 *d* | 6.42 *d* | 6.42 *d* | 6.40 *d* | 6.43 *d* | 6.41 *d* |
| 13′ | 5.83 *d* | 5.97 *d* | 5.81 *d* | 5.96 *d* | 5.80 *d* | 5.96 *d* |
| 15 | 3.74 *d* | 3.75 *d* | 3.47 *d* | 3.52 *d* | 3.73 *d* | 3.74 *d* |
| 15′ | 3.53 *d* | 3.68 *d* | 3.42 *d* | 3.48 *d* | 3.52 *d* | 3.68 *d* |
| OMe | 3.69 *s* | 3.81 *s* | 3.69 *s* | 3.81 *s* | 3.68 *s* | 3.80 *s* |
| OR | 6.40 *q* | 6.37 *q* | 6.60 *q* | 6.51 *q* | 6.40 *q* | 6.38 *q* |
| | 4.27 AB syst. | 4.14 AB syst. | 4.86 *br d* | 4.70 *br d* | 4.25 AB syst. | 4.12 *br s* |
| | 2.04 *br d* | 1.99 *br d* | 4.68 *br d* | 4.53 *br d* | 2.03 *br d* | 1.99 *br d* |
| | | | 2.14 *br d* | 2.08 *br d* | | |
| OR′ | 2.70 *qq* | 2.48 *qq* | 2.70 *qq* | 2.48 *qq* | 2.51 *ddq* | 2.29 *ddq* |
| | 1.29 *d* | 1.11 *d* | 1.29 *d* | 1.10 *d* | 1.75 *m* | 1.56 *m* |
| | 1.25 *d* | 1.07 *d* | 1.25 *d* | 1.06 *d* | 1.55 *m* | 1.32 *m* |
| | | | | | 1.23 *d* | 1.04 *d* |
| | | | | | 0.96 *t* | 0.79 *t* |

*OAc 2.13 *s*, 2.08 *s*.

† OAc 2.14 *s*, 2.07 *s*.

*J*[Hz]: Compounds $4a_1$, $4b_1$ and $4c_1$: 1,2 = 7; 1,10 = 11; 5,6 = 10; 6,7 = 7,13 = 2.5; 7,13′ = 2; 8,9 = 5; 15,15′ = 11.5; Compounds $4a_2$, $4b_2$ and $4c_2$: 1,2 = 1,10 = 2; 1,2′ = 9; 5,6 = 10; 6,7 = 3; 7,8 = 2; 7,13 = 2.5; 7,13′ = 2; 8,9 = 10; 15,15′ = 11.5.

431, 429 $[M-RCO_2H]^+$ (42, 100). Acetylation ($Ac_2O$, DMAP, $CH_2Cl_2$) afforded the diacetate **4b**.

*Tetragonolide-[2-methylbutyrate]* (**4c**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1780 ($\gamma$-lactone), 1730 ($CO_2R$); MS *m/z* (rel. int.): 443.147 $[M-OCOR]^+$ (7) ($C_{21}H_{28}O_8Cl$), 442 $[M-RCO_2H]^+$ (14), 407 (443 − HCl)$^+$ (4), 393 [442 − $CH_2Cl]^+$ (3), 99 $[RCO]^+$ (57), 85 $[RCO]^+$ (50), 57 [85 − CO]$^+$ (100); $[\alpha]_D^{24°}$ −67° ($CHCl_3$; *c* 0.5).

*2α-Hydroxy-15-oxo-eudesma-4,11(13)-diene* (**5**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm$^{-1}$: 3600 (OH), 1670, 1615 (C=CCHO); MS *m/z* (rel. int.): 234 $[M]^+$ (44) ($C_{15}H_{22}O_2$), 216 $[M-H_2O]^+$ (100), 201 [216 − Me]$^+$ (97), 187 [216 − CHO]$^+$ (62), 131 (53), 107 (60), 105 (53), 91 (68); $[\alpha]_D^{24°}$ + 51° ($CHCl_3$; *c* 0.7); $^1$H NMR ($CDCl_3$): $\delta$ 1.37 (*br dd*, H-1α), 1.85 (*ddd*, H-1β), 3.96 (*dddd*, H-2), 1.93 (*ddd*, H-3α), 2.88 (*dddd*, H-3β), 3.37 (*m*, H-6α), 2.09 (*m*, H-6β, H-7), 1.68 (*m*, H-8), 1.51 (*br dd*, H-9α), 1.80 (*ddd*, H-9β), 4.78 (*br s*, H-12), 4.77 (*br s*, H-12′), 1.77 (*br s*, H-13), 1.24 (*s*, H-14), 10.18 (*s*, H-15); *J* [Hz]: 1α,1β = 1α,2 = 12.5; 1β,2 = 3.5; 1β,3β = 2.5; 2,3α = 10; 2,3β = 5.5; 3α,3β = 17; 8α,9β = 8β,9β = 3; 8β,9α = 9α,9β = 13.

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