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# NEO-CLERODANE DITERPENOIDS FROM *TEUCRIUM LANIGERUM*

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**Key Word Index** *Teucrium lanigerum*; Labiatae; neo-clerodane derivatives; 7,8-dehydroeriocephalin; teulanigeral; teulanigin; 20-epi-teulanigin; teulanigerin; teulanigeridin.

**Abstract**—From the aerial part of *Teucrium lanigerum*, six new neo-clerodane diterpenoids, 7,8-dehydroeriocephalin, teulanigeral, teulanigin, 20-epi-teulanigin, teulanigerin and teulanigeridin, have been isolated. The first of these, 7,8-dehydroeriocephalin, is a natural substance, whereas the other compounds were isolated as their acetyl derivatives after acetylation of an inseparable mixture of natural diterpenoids. The structures of these substances were established mainly by spectroscopic means and, in the case of 7,8-dehydroeriocephalin, by partial synthesis from eriocephalin.

## INTRODUCTION

In previous communications [1, 2], we reported the structure elucidation of some neo-clerodane diterpenoids isolated as the main diterpenoid constituents from the acetone extract of the aerial part of *Teucrium lanigerum* Lag. (syn *T. eriocephalum* Wk. var. *rubrifolium* Coincy.). In this communication, we report the isolation of six new diterpenoids which were obtained as minor constituents from the chromatographic fractions collected after the elution of isoeriocephalin [1]. These fractions contained a natural diterpenoid, 7,8-dehydroeriocephalin (**1**), and an inseparable mixture of several diterpenoids which did not show any acetoxyl signal in its $^1$H NMR spectrum. Acetic anhydride–pyridine treatment of this mixture followed by careful chromatographic separation yielded five minor diterpenoid constituents: teulanigeral (**3**), teulanigin (**4**), 20-epi-teulanigin (**5**), teulanigerin (**6**) and teulanigeridin (**7**), which had not previously been described as natural or synthetic substances.

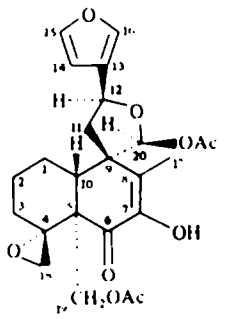
The structures of all these new compounds were established mainly on the basis of spectroscopic evidence and, in the case of 7,8-dehydroeriocephalin (**1**), by partial synthesis from eriocephalin (**2**).

## RESULTS AND DISCUSSION

The first of the new diterpenoids isolated from *T. lanigerum*, 7,8-dehydroeriocephalin (**1**), had a molecular formula of $C_{24}H_{28}O_9$ and its $^1$H NMR spectrum (Table 1) showed characteristic signals for a $\beta$-substituted furan ring, a 4$\alpha$,18-oxirane ring, a C-19 acetoxymethyl group and an acetylated C-20–C-12 hemiacetal function identical with those found in eriocephalin (**2**), a neo-clerodane diterpenoid previously isolated from *T. eriocephalum*, the structure and absolute configuration of which have been clearly established by X-ray diffraction analysis [3]. In addition, the IR, UV and $^1$H NMR spectra of compound **1** revealed the presence of a (C)–CO–C(OH)=C(Me)–(C) structural moiety ($\nu$1680 and 1645 cm$^{-1}$; $\lambda$ 283 nm, log $\varepsilon$ 3.94; $\delta$ 1.92, 3H, *s*, Me-17) [4]. Since chromium trioxide–pyridine oxidation of eriocephalin (**2**) [3] yielded a compound identical in all respects with 7,8-dehydroeriocephalin, the structure and absolute configuration depicted in formula **1** were firmly established for this new diterpenoid.

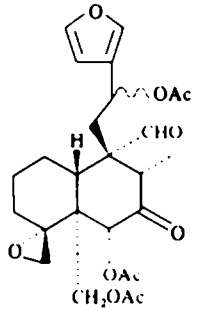
Another of the new diterpenoids, teulanigeral (**3**), had a molecular formula of $C_{26}H_{32}O_{10}$. Its IR (see Experimental) and $^1$H NMR (Table 1) spectra showed a $\beta$-substituted furan ring, a 4$\alpha$,18-oxirane ring and a C-19 methylenacetoxy group identical with those found in **1**. Teulanigeral (**3**) also possessed the characteristic features of a C-12 acetoxyl group in a furoclerodane hydrocarbon skeleton ($\delta_{H\text{-}12}$ 6.05 *dd*, $\delta_{H_A\text{-}11}$ 2.70 *dd*, $\delta_{H_B\text{-}11}$ 2.77 *dd*, Table 1) [5], an axial aldehyde group at the C-20 position ($\delta_{H\text{-}20}$ 9.67 *d*, $J_{long\text{-}range}$ = 0.6 Hz; $\nu_{CHO}$ 2760 and 1720 cm$^{-1}$; [M − 1]$^+$ ion fragment at *m/z* 503) and a (C)–CH(OAc)–CO·CH(Me)–(C) structural moiety ($\delta_{H\text{-}6\beta}$ 5.09 *d*, $J$ = 0.9 Hz; $\delta_{Me\text{-}17}$ 1.15 *d*, $J_{8,17}$ = 7.2 Hz). This moiety was identical with that previously found in the acetyl derivative of isoeriocephalin [1], a substance possessing an equatorial C-17 methyl group, a C-6$\alpha$ acetoxyl group and a C-7 ketone function and very different from that of a C-6 keto, C-7$\alpha$ acetoxyl isomeric structure, such as eriocephalin acetate ($\delta_{H\text{-}7\beta}$ 5.60 *d*, $J$ = 5 Hz; $\delta_{Me\text{-}17}$ 1.03 *d*, $J$ = 7 Hz) [3]. Thus, structure **3** could be established for teulanigeral, although the configuration at C-12 and the absolute stereochemistry were not ascertained. However, on biogenetic grounds it may be supposed that teulanigeral (**3**) possesses a neo-clerodane absolute configuration [6] as do the other diterpenoids occurring in the same species ([1, 2] and this work).

Teulanigin (**4**) and 20-epi-teulanigin (**5**) possessed the same molecular formula ($C_{26}H_{32}O_{10}$) and their $^1$H NMR spectra (Table 2) revealed the presence in both compounds of a $\beta$-substituted furan ring, a 4$\alpha$,18-oxirane ring, a secondary C-17 methyl group, a C-19 acetoxymethyl group and an acetylated C-20–C-12



1

2 7β, 8β-Dihydro



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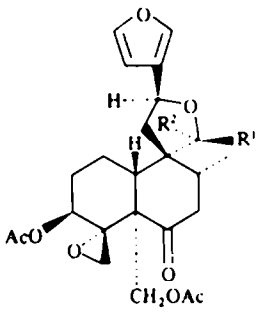
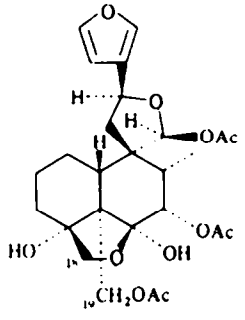


4 R¹ = H, R² = OAc

5 R¹ = OAc, R² = H



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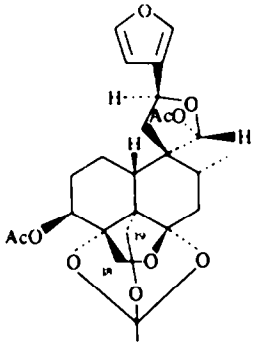

7

hemiacetal function identical with those found in several neo-clerodane derivatives isolated from other *Teucria* species, such as eriocephalin (**2**) [3]. In addition, compounds **4** and **5** possessed a C-6 ketone group ($\nu_{CO}$ 1715 $cm^{-1}$ in **4** and 1720 $cm^{-1}$ in **5**; $\delta_{CO}$ 204.4 *s* in **4** and 204.7 *s* in **5**, see Table 3) and an equatorial acetoxyl group at the C-3β position (**4**: $\delta_{H\text{-}3\alpha}$ 5.00 *dd*, $J_{a,a'}$ = 8.8 Hz, $J_{a,e}$ = 5.6 Hz; **5**: $\delta_{H\text{-}3\alpha}$ 5.31 *dd*, $J_{a,a'}$ = 11.4 Hz, $J_{a,e}$ = 5.0 Hz). The presence of the latter function in compounds **4** and **5** was confirmed [7] by the fact that the signal of the $H_B$-18 proton (see Table 2) appeared as a doublet, without the long-range $H_B$-18, H-3β coupling characteristic of 4α,18-epoxyclerodanes possessing a 3β equatorial proton [1–5].

The $^{13}C$ NMR spectrum of 20-epi-teulanigin (**5**) provided further support for the proposed structure. The chemical shift values for the C-4–C-9, C-11–C-17, C-19 and C-20 atoms were identical with those reported for the corresponding carbon atoms of gnaphalidin [3], a neo-clerodane diterpenoid possessing the same structure as that depicted in formula **5**, but lacking the C-3β acetoxyl function. Moreover, the shift values for the C-1–C-3, C-10 and C-18 atoms of 20-epi-teulanigin (**5**) were the same as in 4α,18-epoxy *trans* neo-clerodanes with a 3β-acetoxyl group, such as teupyreinin [7].

All the above data established structure **5** for 20-epi-teulanigin, the configurations of the C-12 and C-20 centres being confirmed by NOE experiments. Irradiation of the Me-17 protons (δ1.32, Table 4) produced a 6% NOE enhancement of the H-14 signal, whereas no effect was observed on the signals of the H-12 and H-20 protons. This indicated an *exo* relationship between the Me-17 group and the H-12 and H-20 protons [2]. Furthermore, irradiation of the H-20 proton caused a 5% NOE enhancement (Table 4) of the signal of the H-12 proton, which was in agreement with all the above conclusions.

The neo-clerodane [6] absolute configuration depicted in formula **5** for 20-epi-teulanigin was inferred from its CD curve, which showed a negative Cotton effect ($\Delta\varepsilon_{305}$ – 1.04), as does gnaphalidin ($\Delta\varepsilon_{305}$ – 0.72) [3, 8]. Thus, 20-epi-teulanigin is 3β-acetoxy-20-*O*-acetyl-4α,18; 15,16-diepoxy-6-keto-neo-clerodane-13(16),14-diene-20*S*, 12*S*-hemiacetal (**5**).

Teulanigin (**4**) is the 20*R* epimer of compound **5**. This was established from the following facts: (i) a comparison of the $^{13}C$ NMR spectra of compounds **4** and **5** revealed significant differences in the chemical shifts of the C-8–C-11, C-13, C-17 and C-19 atoms (see Table 3), which can be attributed to configurational differences in the C-12 or/and C-20 centres [2]; (ii) irradiation of the Me-17 protons of compound **4** produced an NOE enhancement in the signals of the H-14 and H-20 protons (7% and 13%, respectively), whereas no effect was observed in the H-12 signal (see Table 4). Furthermore, irradiation of the H-20 proton caused NOE enhancements in the signals of the H-7α (7%) and Me-17 (2%) protons but not in the H-12 signal (Table 4). All these facts established a *trans*

Table 1. $^1$H NMR data of compounds 1 and 3 (90 MHz, $CDCl_3$, TMS as internal standard, $J$ values in Hz)*

| | 1 | 3 |
|---|---|---|
| H-6$\beta$ | | 5.09 *d*<br>$J_{6\beta,8\beta}$ = 0.9 |
| $H_A$-11 | 2.30 *dd*<br>$J_{11A,11B}$ = 13.5, $J_{11A,12}$ = 9.0 | 2.70 *dd*<br>$J_{11A,11B}$ = 12, $J_{11A,12}$ = 8.4 |
| $H_B$-11 | 2.70 *dd*<br>$J_{11B,12}$ = 7.2 | 2.77 *dd*<br>$J_{11B,12}$ = 3.6 |
| H-12 | 5.29 *dd* | 6.05 *dd* |
| H-14 | 6.43 *dd*<br>$J_{14,15}$ = 1.7, $J_{14,16}$ = 0.8 | 6.43 *dd*<br>$J_{14,15}$ = 1.8, $J_{14,16}$ = 0.8 |
| H-15 | 7.39§ | 7.41 *t*<br>$J_{15,16}$ = 1.8 |
| H-16 | 7.39§ | 7.49 *dd* |
| Me-17 | 1.92 *s* | 1.15 *d*<br>$J_{17,8\beta}$ = 7.2 |
| $H_A$-18† | 2.41 *d*<br>$J_{18A,18B}$ = 4.8 | 2.43 *d*<br>$J_{18A,18B}$ = 3.6 |
| $H_B$-18‡ | 2.65 *dd*<br>$J_{18B,3\beta}$ = 2.8 | 3.05 *dd*<br>$J_{18B,3\beta}$ = 1.8 |
| $H_A$-19 | 4.50 *d*<br>$J_{19A,19B}$ = 11.5 | 4.17 *d*<br>$J_{19A,19B}$ = 12 |
| $H_B$-19 | 4.67 *d* | 4.75 *d* |
| H-20 | 6.43 *s* | 9.67 *d*<br>$J_{long\text{-}range}$ = 0.6 |
| OAc | 2.05 *s*<br>1.95 *s*<br>— | 2.10 *s*<br>2.07 *s*<br>1.92 *s* |

*Spectral parameters were obtained by first order approximation. All these assignments have been confirmed by double resonance experiments.

†*Exo* hydrogen with respect to ring B.

‡*Endo* hydrogen with respect to ring B.

§Overlapped signal.

relationship between the H-12 and H-20 protons and indicated that the Me-17 group, as well as the H-14 and H-20 protons, were on the same side of the plane defined by the hemiacetal ring [2]. Finally, teulanigin (4) showed a negative Cotton effect ($\Delta\varepsilon_{306}$ − 0.60), which confirmed a neo-clerodane absolute configuration for this compound. The smaller $\Delta\varepsilon$ negative value of 4 with respect to compound 5 ($\Delta\varepsilon$ − 0.60 and − 1.04, respectively) is in accordance with the structural difference between these two compounds and in complete agreement with the predictions based on the octant rule. The C-20 acetoxyl group of compound 4 is placed in an octant of positive contribution, whereas that of 20-epi-teulanigin (5) is in a negative one.

Another of the neo-clerodane diterpenoids isolated from *T. lanigerum*, teulanigerin ($C_{26}H_{34}O_{11}$), possesses the structure depicted in formula 6. The IR, $^1$H NMR (Table 2) and $^{13}$C NMR (Table 3) spectra of this compound clearly indicated the presence of two tertiary hydroxyl groups at the C-4$\alpha$ and C-6$\alpha$ positions ($\nu_{OH}$ 3450 cm$^{-1}$, br; $\delta_{OH}$ 4.21, 1H, and 4.09, 1H, disappearing after the addition of $D_2O$; $\delta_{C\text{-}4}$ 82.5 *s*, and $\delta_{C\text{-}6}$ 106.4 *s*) and a C-6$\beta$–C-18 hemiacetal grouping (C-18 protons as an AB system at $\delta$4.04 and 4.23, $J_{gem}$ = 10.2 Hz; $\delta_{C\text{-}18}$ 76.3 *t*) identical with those of teupolin V [9]. The presence in teulanigerin (6) of a (C)–CH(OAc)–CH(Me)–(C) structural moiety with a C-7$\alpha$ axial configuration of the acetoxyl group was clearly established because the H-7$\beta$, H-8$\beta$ and Me-17 protons showed a $^1$H NMR pattern ($\delta_{H\text{-}7\beta}$ 5.12 *d*, $J_{7\beta,8\beta}$ = 2.9 Hz; $\delta_{H\text{-}8\beta}$ 2.38 *dq*, $J_{8\beta,17}$ = 7.3 Hz; $\delta_{Me\text{-}17}$ 1.21 *d*, see Table 2) almost identical with that for the acetyl derivative of eriocephalin (2) [3]. Finally, the 12*S* and 20*S* configurations of teulanigerin (6) were inferred from NOE experiments (Table 4) [2]. Irradiation at $\delta$1.21 (Me-17 signal) caused a 5% NOE enhancement in the signal of the H-14 proton, but the signals of the H-12 and H-20 protons were not affected. All the above data are only compatible with structure 6.

The last diterpenoid isolated from *T. lanigerum*, teulanigeridin (7), had a molecular formula of $C_{26}H_{32}O_{10}$ and its IR spectrum showed no hydroxyl absorption. It possessed two acetoxyl groups ($\delta$2.14 and 2.10, 3H each, both *s*; $^{13}$C NMR signals at $\delta$170.5 *s*, 169.2 *s*, 21.7 *q* and 21.2 *q*, see Tables 2 and 3) and an orthoacetate function ($\delta$1.47, 3H, *s*; $^{13}$C NMR signals at $\delta$106.1 *s* and 23.3 *q*) [10], besides a $\beta$-substituted furan ring, a C-17 secondary methyl group, an acetylated C-20–C-12 hemiacetal grouping and an equatorial 3$\beta$ acetoxyl group identical with those found in teulanigin (4). In addition, like teulanigerin (6), teulanigeridin (7) had a C-18–C-6$\beta$ hemiacetal ring (see signals of the C-18 protons and the carbon atom resonances of C-4, C-6 and C-18 in Tables 2 and 3, respectively) instead of the 4$\alpha$,18-epoxide and the C-6 ketone of compound 4. All the above data can be

Table 2. $^1$H NMR data of compounds 4–7 (300 MHz, $CDCl_3$, TMS as internal standard)*

| | 4 | 5 | 6 | 7 |
|---|---|---|---|---|
| H-3α | 5.00 *dd* | 5.31 *dd* | § | 5.32 *dd* |
| H-7α | 2.59 *dd* | 3.01 *t* | § | § |
| H-7β | § | § | 5.12 *d* | § |
| H-8β | 1.92 *ddq* | § | 2.38 *dq* | § |
| $H_A$-11 | 2.40 *dd* | 2.14 *dd* | 2.06 *dd* | 1.82 *dd* |
| $H_B$-11 | 2.48 *dd* | 2.41 *dd* | 2.57 *dd* | 2.41 *dd* |
| H-12 | 5.14 *dd* | 5.00 *t* | 5.16 *t* | 5.02 *dd* |
| H-14 | 6.40 *dd* | 6.44 *dd* | 6.43 *dd* | 6.36 *dd* |
| H-15 | 7.40 *t* | 7.40‖ | 7.38 *t* | 7.38 *t* |
| H-16 | 7.43 *dd* | 7.40‖ | 7.35 *dd* | 7.39 *dd* |
| Me-17 | 1.10 *d* | 1.32 *d* | 1.21 *d* | 1.02 *d* |
| $H_A$-18 | 2.81 *d*† | 2.69 *d*† | 4.04 *d* | 3.54 *d* |
| $H_B$-18 | 2.93 *d*‡ | 3.16 *d*‡ | 4.23 *d* | 4.06 *d* |
| $H_A$-19 | 4.15 *d* | 4.60 *d* | 4.72 *d* | 3.99 *d* |
| $H_B$-19 | 4.68 *d* | 4.82 *d* | 5.06 *d* | 4.36 *d* |
| H-20 | 6.34 *s* | 6.32 *s* | 6.75 *s* | 6.12 *s* |
| OAc | 2.22 *s* | 2.16 *s* | 2.15 *s* | 2.14 *s* |
| | 2.02 *s* | 2.07 *s* | 2.05 *s* | 2.10 *s* |
| | 2.01 *s* | 2.01 *s* | 1.97 *s* | — |
| Orthoacetate | — | | — | 1.47 *s* |
| *J* (Hz) | | | | |
| 3α, 2α | 5.6 | 5.0 | § | 5.9 |
| 3α, 2β | 8.8 | 11.4 | § | 11.3 |
| 7α, 7β | 15.3 | 14.6 | — | § |
| 7α, 8β | 13.5 | 14.6 | — | § |
| 7β, 8β | 4.0 | § | 2.9 | § |
| 8β, 17 | 6.9 | 6.8 | 7.3 | 6.5 |
| 11A, 11B | 13.4 | 13.9 | 13.7 | 13.2 |
| 11A, 12 | 10.0 | 8.3 | 7.6 | 9.6 |
| 11B, 12 | 7.3 | 8.8 | 7.2 | 7.7 |
| 14, 15 | 1.7 | 1.4 | 1.6 | 1.6 |
| 15, 16 | 1.7 | § | 1.6 | 1.6 |
| 16, 14 | 0.9 | 1.0 | 0.9 | 1.0 |
| 18A, 18B | 5.3 | 5.7 | 10.2 | 9.9 |
| 19A, 19B | 11.7 | 12.0 | 13.8 | 10.1 |

*Spectral parameters were obtained by first order approximation. All these assignments have been confirmed by double resonance experiments.

†*Exo* hydrogen with respect to ring B.

‡*Endo* hydrogen with respect to ring B.

§Could not be identified.

‖Overlapped signal.

accommodated only in a structure such as 7, in which the orthoacetate function must be attached to the 4α,6α and 19 positions. The 12*S* and 20*R* configurations were established from a NOE experiment (Table 4), since irradiation at δ1.02 (Me-17 signal) caused a NOE enhancement in the H-14 (5%) and H-20 (15%) proton signals but no effect was observed on the signal of the H-12 proton [2].

The absolute configuration of the latter two diterpenoids (6 and 7) was not ascertained; however, it is reasonable to assume that compounds 6 and 7 belong to the neo-clerodane [6] series, like all the diterpenoids isolated from *Teucria* hitherto ([1–5, 7–9] and references therein).

Since compounds 3–7 were isolated as their acetyl derivatives and, before acetylation, the $^1$H NMR spectrum of the mixture of diterpenoids was devoid of acetoxyl signals, it is clear that the natural products isolated from *T. lanigerum* were the corresponding deacetylated compounds. Finally, it is important to note that the $^1$H NMR spectrum of the natural mixture of diterpenoids showed a singlet signal at δ1.47, thus confirming that the orthoacetate grouping of teulanigeridin (7) is not an artefact.

## EXPERIMENTAL

Mps are uncorr. For general details of the collection of plant materials and the extraction of the diterpenoids see ref. [1].

*Isolation of* 7,8-*dehydroeriocephalin* (1). The chromatographic

Table 3. $^{13}C$ NMR data of compounds 4–7 ($CDCl_3$, $\delta$ values from TMS)

| C | 4 | 5 | 6 | 7 |
|---|---|---|---|---|
| 1 | 21.8 *t** | 21.3 *t* | 22.2 *t* | 22.1 *t* |
| 2 | 31.0 *t* | 30.7 *t* | 25.0 *t* | 30.6 *t* |
| 3 | 68.5 *d* | 66.6 *d* | 30.5 *t* | 73.5 *d* |
| 4 | 60.2 *s* | 61.2 *s* | 82.5 *s* | 83.1 *s* |
| 5 | 53.9 *s* | 54.3 *s* | 53.4 *s*† | 42.8 *s* |
| 6 | 204.4 *s* | 204.7 *s* | 106.4 *s* | 106.6 *s*† |
| 7 | 46.2 *t*† | 45.5 *t*† | 74.7 *d* | 35.0 *t* |
| 8 | 43.1 *d* | 41.4 *d* | 39.4 *d* | 40.3 *d* |
| 9 | 52.7 *s* | 51.8 *s* | 53.1 *s*† | 52.0 *s* |
| 10 | 50.9 *d* | 54.2 *d* | 51.3 *d* | 43.6 *d* |
| 11 | 46.5 *t*† | 43.6 *t*† | 42.0 *t* | 42.7 *t* |
| 12 | 72.2 *d* | 71.2 *d* | 72.5 *d* | 71.9 *d* |
| 13 | 124.1 *s* | 125.7 *s* | 128.5 *s* | 124.3 *s* |
| 14 | 108.5 *d* | 108.4 *d* | 108.9 *d* | 108.7 *d* |
| 15 | 143.3 *d* | 143.5 *d* | 143.5 *d* | 143.5 *d* |
| 16 | 139.2 *d* | 139.5 *d* | 139.6 *d* | 139.4 *d* |
| 17 | 17.3 *q* | 18.0 *q* | 15.0 *q* | 16.9 *q* |
| 18 | 44.2 *t* | 44.5 *t* | 76.3 *t* | 73.7 *t* |
| 19 | 63.3 *t* | 61.7 *t* | 61.3 *t* | 59.4 *t* |
| 20 | 98.0 *d* | 97.6 *d* | 98.4 *d* | 98.2 *d* |
| OAc | 170.1 *s* | 170.4 *s* | 171.4 *s* | 170.5 *s* |
| | 169.3 *s* | 169.3 *s* | 171.3 *s* | 169.2 *s* |
| | 169.3 *s* | 169.2 *s* | 169.0 *s* | — |
| | 21.6 *q* | 21.5 *q* | 21.5 *q* | 21.7 *q* |
| | 20.9 *q* | 20.9 *q* | 21.3 *q* | 21.2 *q* |
| | 20.6 *q* | 20.6 *q* | 20.7 *q* | – |
| Orthoacetate | · | | | 106.1 *s*† |
| | | -- | — | 23.3 *q* |

*SFORD multiplicity.

†These assignments may be reversed, but those given here are considered to be the most likely.

fractions obtained after elution of isoeriocephalin [1] were evaporated to dryness and the residue (2.3 g) was chromatographed on a silica gel column (Merck No. 7734, deactivated with 10% $H_2O$, 300 g) eluted with EtOAc–*n*-hexane (4:1), yielding pure 7,8-dehydroeriocephalin (**1**, 100 mg) followed by a complex mixture of diterpenoids (2 g). 7,8-Dehydroeriocephalin (**1**) had mp 191–192° (EtOAc–*n*-hexane); $[\alpha]_D^{20}$ – 43.6° ($CHCl_3$; *c* 0.112); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3430, 3150, 3130, 2960, 2880, 1740, 1680, 1645, 1505, 1445, 1380, 1235, 1095, 1045, 960, 950, 880, 810, 740; UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 283 (3.94); $^1H$ NMR (90 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 460 $[M]^+$ (0.5), 372 (3), 341 (4), 312 (3.2), 300 (15), 281 (14), 253 (11), 219 (11), 177 (13), 161 (12), 115 (12), 105 (15), 95 (15), 94 (22), 91 (19), 81 (29), 77 (20), 69 (13), 53 (17), 43 (100). (Found: C, 62.48; H, 6.23. $C_{26}H_{28}O_9$ requires: C, 62.60; H, 6.13%.)

*7,8-Dehydroeriocephalin* (**1**) *from eriocephalin* (**2**). $CrO_3$–$C_5H_5N$ treatment of compound **2** (200 mg) [3] in the usual manner gave a compound (70 mg, after chromatographic purification) identical in all respects (mp, mmp, $[\alpha]_D$, IR, UV, $^1H$ NMR, MS, TLC) with natural 7,8-dehydroeriocephalin (**1**).

*Acetylation of the mixture of diterpenoids to produce compounds* **3–7**. $Ac_2O$ $C_5H_5N$ (20 ml, 1:1) treatment of the complex mixture of diterpenoids (2 g, see above) during 24 hr at room temp. yielded a mixture of several compounds which was subjected to column (silica gel) chromatography. Elution with *n*-hexane–EtOAc (3:1) gave the following pure compounds in order of elution: teulanigeridin (**7**, 20 mg), teulanigeral (**3**, 8 mg), teulanigin (**4**, 60 mg), 20-epi-teulanigin (**5**, 20 mg) and teulanigerin (**6**, 110 mg), besides several fractions containing mixtures of the above substances and other unidentified compounds. Before acetylation the mixture of diterpenoids showed a $^1H$ NMR spectrum without acetoxyl signals, but with a singlet signal at $\delta$ 1.47 due to the orthoacetate function of teulanigeridin (**7**).

*Teulanigeral* (**3**). Mp 171–172° (EtOAc *n*-hexane); $[\alpha]_D^{18}$ – 2.5° ($CHCl_3$; *c* 0.244); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3170, 3150, 3120, 3080, 2970, 2880, 2760, 1745 (br), 1720, 1505, 1440, 1370, 1250, 1230, 1165, 1055, 1035, 1025, 980, 920, 880, 810, 790, 770; $^1H$ NMR (90 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 504 $[M]^+$ (1), 503 (0.8), 474 (2), 462 (1), 445 (1.5), 402 (5), 314 (5), 296 (7), 283 (5), 189 (5), 153 (8), 111 (8), 105 (7), 97 (11), 95 (12), 94 (23), 91 (9), 81 (13), 67 (5), 55 (6), 43 (100). (Found: C, 62.01; H, 6.28. $C_{26}H_{32}O_{10}$ requires: C, 61.89; H, 6.39%.)

*Teulanigin* (**4**). Mp 168–170° (EtOAc–*n*-hexane); $[\alpha]_D^{18}$ + 23.8° ($CHCl_3$; *c* 0.412); CD nm ($\Delta\varepsilon$): 358 (0), 306 (– 0.60), 250 (0), (MeOH; *c* 0.048); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3150, 3125, 3080, 2980, 2890, 1745 (br), 1715, 1502, 1450, 1380, 1240, 1220, 1160, 1070, 1050, 1030, 960, 885, 875, 780; $^1H$ NMR (300 MHz, $CDCl_3$): see Table 2; $^{13}C$ NMR (25.2 MHz, $CDCl_3$): see Table 3; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 504 $[M]^+$ (0.5), 445 (1.5), 402 (3.5), 308 (3), 283 (5), 266 (4), 248 (5), 217 (5), 203 (6), 201 (6), 189 (5), 187 (6), 175 (7), 145 (9), 105 (7), 95 (11), 94 (20), 91 (11), 81 (12), 69 (11), 55 (6), 43 (100). (Found: C, 61.75; H, 6.31. $C_{26}H_{32}O_{10}$ requires: C, 61.89; H, 6.39%.)

*20-Epi-teulanigin* (**5**). Mp 182–183° (EtOAc–*n*-hexane); $[\alpha]_D^{18}$ – 52.10 ($CHCl_3$; *c* 0.330); CD nm ($\Delta\varepsilon$): 335 (0), 305 (– 1.04), 245 (0) (MeOH; *c* 0.046); IR $\nu_{max}^{KBr}$ cm $^{-1}$: 3160, 3140, 3080, 2950, 2880, 1755, 1735 (br), 1720, 1505, 1430, 1390, 1250, 1230, 1065, 1040, 905, 875, 810; $^1H$ NMR (300 MHz, $CDCl_3$): see Table 2; $^{13}C$ NMR (25.2 MHz, $CDCl_3$): see Table 3; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 504 $[M]^+$ (0.2), 445 (0.8), 402 (2.5), 308 (2), 283 (3), 266 (3), 248 (4), 217 (4), 201 (4), 189 (5), 187 (4), 175 (4), 145

Table 4. NOE experiments on compounds 4–7

| | Irradiation ($\delta$) | Observed NOE enhancement (%) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | H-7α | H-7β | H-12 | H-14 | $H_A$-19 | $H_B$-19 | H-20 | Me-17 |
| 4 | 1.10 (Me-17) | • | • | 0 | 7 | 0 | 0 | 13 | — |
| | 6.34 (H-20) | 7 | 0 | 0 | • | 4 | 0 | – | 2 |
| 5 | 1.32 (Me-17) | • | • | 0 | 6 | 0 | 0 | 0 | — |
| | 6.32 (H-20) | 0 | 0 | 5 | 0 | 2 | 6 | | 0 |
| 6 | 1.21 (Me-17) | — | 8 | 0 | 5 | 0 | 0 | 0 | — |
| 7 | 1.02 (Me-17) | • | • | 0 | 5 | 0 | 0 | 15 | · |

*Not determined.

(6), 105 (7), 95 (13), 94 (21), 91 (12), 81 (16), 69 (11), 55 (6), 43 (100). (Found: C, 61.80; H, 6.24. $C_{26}H_{32}O_{10}$ requires: C, 61.89; H, 6.39%.)

*Teulanigerin* (6). An amorphous solid which melted at 90–95°; $[\alpha]_D^{20} - 69.8°$ ($CHCl_3$; *c* 1.037); IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3450 (br), 3160, 2970, 2940, 2870, 1750 (br), 1505, 1450, 1375, 1250, 1090, 1030, 960, 875, 800; $^1$H NMR (300 MHz, $CDCl_3$): see Table 2; $^{13}$C NMR (75.4 MHz, $CDCl_3$): see Table 3; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 522 $[M]^+$ (0.5), 504 (5), 476 (2), 462 (5), 445 (11), 416 (11), 403 (20), 402 (24), 342 (9), 266 (11), 163 (17), 153 (13), 145 (12), 121 (11), 111 (16), 105 (12), 95 (22), 94 (23), 91 (11), 81 (25), 69 (15), 55 (11), 43 (100). (Found: C, 59.40; H, 6.41. $C_{26}H_{34}O_{11}$ requires: C, 59.76; H, 6.56%.)

*Teulanigeridin* (7). An amorphous solid which melted at 100–110°; $[\alpha]_D^{19} + 44.4°$ ($CHCl_3$; *c* 0.251); IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3150, 2930, 2860, 1745, 1505, 1455, 1405, 1375, 1290, 1250, 1230, 1090, 1030, 980, 875, 818; $^1$H NMR (300 MHz, $CDCl_3$): see Table 2; $^{13}$C NMR (75.4 MHz, $CDCl_3$): see Table 3; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 504 $[M]^+$ (1), 460 (0.4), 445 (6), 444 (3), 400 (4), 359 (4), 329 (4), 311 (4), 283 (6), 187 (8), 163 (13), 145 (10), 137 (11), 105 (10), 95 (16), 94 (18), 91 (14), 81 (18), 69 (12), 55 (11), 43 (100). (Found: C, 61.60; H, 6.22. $C_{26}H_{32}O_{10}$ requires: C, 61.89; H, 6.39%.)

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