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ISOERIOCEPHALIN AND 20-DEACETYLERIOCEPHALIN, NEO-CLERODANE DITERPENOIDS FROM *TEUCRIUM LANIGERUM*

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Key Word Index—*Teucrium lanigerum*; Labiatae; diterpenoids; new neo-clerodane derivatives; isoeriocephalin; 20-deacetyleriocephalin; eriocephalin.

Abstract—From the aerial part of *Teucrium lanigerum* two new neo-clerodane diterpenoids, 20-deacetyleriocephalin and isoeriocephalin, have been isolated, together with the previously known diterpene eriocephalin. The structures of 20-deacetyleriocephalin [19-acetoxy-4α,18:15,16-diepoxy-7α-hydroxy-6-keto-neo-cleroda-13(16),14-diene-20*S*,12*S*-hemiacetal] and isoeriocephalin [19-acetoxy-4α,18:15,16-diepoxy-6α-hydroxy-7-keto-neo-cleroda-13(16),14-diene-(20-acetyl)-20*S*,12*S*-hemiacetal] were established by chemical and spectroscopic means and by correlation with known compounds.

INTRODUCTION

In continuation of our studies on diterpenoid compounds from *Teucrium* species (family Labiatae) [1–4], we have now investigated *Teucrium lanigerum* Lag. (synonymous *T. eriocephalum* Wk. var. *rubrifolium* Coincy.), a species which grows only in restricted areas of south-east Spain. From the aerial part of this plant we have isolated large amounts of the previously known neo-clerodane diterpenoid eriocephalin (**1**, 1.11% from dry plant material) [5] besides two new neo-clerodane derivatives, 20-deacetyleriocephalin (**2**) and isoeriocephalin (**7**), whose structures and absolute configurations were established on the basis of spectroscopic evidence, chemical transformations and correlation with previously described compounds.

RESULTS AND DISCUSSION

The first of the new diterpenoids isolated from *Teucrium lanigerum*, 20-deacetyleriocephalin (**2**), had a $C_{22}H_{28}O_8$ molecular formula and its ^{1}H NMR spectrum (Table 1) showed signals almost identical with those found in the ^{1}H NMR spectrum of eriocephalin (**1**) [5]. In fact, the only differences between the ^{1}H NMR spectra of the new diterpenoid and eriocephalin (**1**) were the absence in the former of an acetyl group and also the higher field resonance of the C-20 hemiacetalic proton (δ 5.47, *s*). Thus, structure **2** can be attributed to this new compound. In agreement with this conclusion, acetic anhydride–pyridine treatment of **2** yielded a substance (**3**) identical in all respects with the acetyl derivative of eriocephalin (**1**), a diterpenoid previously isolated from *Teucrium eriocephalum*, the structure and absolute configuration of which have been firmly established by X-ray diffraction analysis [5].

It is important to note that chromium trioxide–pyridine oxidation of 20-deacetyleriocephalin (**2**) yielded a complex mixture of substances, the main constituent of which was the derivative **4**. The structure of this substance was supported by its UV absorption at λ_{max} 256 nm (log ε 3.60), which is typical of a furan ring with a conjugated ketone [3], and by its ^{1}H NMR and ^{13}C NMR spectra (Tables 1 and 2, respectively) which showed signals of the substituted decaline moiety identical with those found for the same part of compound **5**, a derivative of the neo-clerodane diterpenoid auropolin (**6**), previously isolated from *T. polium* subsp. *aureum* and whose structure has been established by X-ray diffraction analysis [6]. The presence of compounds such as **4** among the oxidation products of **2** may be rationalized by considering that, in the reaction conditions, an equilibrium exists between the C-20 → C-12 and C-20 → C-7 hemiacetalic forms. Moreover, we have now observed that oxidation of eriocephalin (**1**) [5] with Jones reagent also yielded **4** (see Experimental), thus confirming this hemiacetalic equilibrium, which in eriocephalin (**1**) must be subsequent to a C-20 deacetylation reaction.

The other of the new diterpenoids isolated from *T. lanigerum*, isoeriocephalin (**7**), had a $C_{24}H_{30}O_9$ molecular formula and its IR spectrum showed characteristic absorptions for a furan ring (3140, 3120, 1505, 875 cm^{-1}), a ketone (1715 cm^{-1}), two ester groups (1760, 1740 cm^{-1}) and a hydroxyl group (3460 cm^{-1}). The ^{1}H NMR spectrum of isoeriocephalin (**7**, Table 1) was very similar to that of eriocephalin (**1**) [5], showing identical signals of a β-substituted furan ring, a C-20, C-12 acetylated hemiacetalic function and an α,α-disubstituted oxirane ring (see Table 1), whereas the differences being the lower field resonance of the secondary methyl group of isoeriocephalin (at δ 1.45, *d*, *J* = 6.8 Hz in **7** and at δ 0.89, *d*, *J* = 7 Hz in **1**), the chemical shift and coupling value of the geminal proton of the secondary hydroxyl group (at δ 4.07, *d*, *J* = 1.2 Hz in **7** and at δ 4.77, *d*, *J* = 6 Hz in **1**) and the signal due to the acetoxymethylene grouping, which appeared at δ 4.69 as a singlet in eriocephalin (**1**)

Table 1. ^{1}H NMR data of compounds **2**, **4**, **7**–**14** (90 MHz, in $CDCl_3$ solution, TMS as internal standard)*

	2	**4**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
H-6α	—	—	—	—	—	—	—	—	—	3.70‡
H-6β	—	—	4.07 *d*	5.05 *br s*	5.40 *q*	4.60 *br d*	3.66 *br d*	4.75 *dd*	3.41 *br d*	—
H-7β	4.83 *d*	4.38 *s*	—	—	—	3.80 *dd*	5.47 *dd*	5.26 *dd*	3.92 *dd*	3.60‡
H-8	†	2.95 *q*	†	2.67 *q*	—	†	†	†	†	†
H_A-11	†	2.92 *d*	2.38 *d*	2.43 *d*	2.20 *dd*	†	†	†	†	†
H_B-11	†	3.50 *d*	2.38 *d*	2.43 *d*	2.50 *dd*	†	2.45 *dd*	2.53 *dd*	2.52 *dd*	†
H-12	5.27 *dd*	—	4.93 *t*	5.05 *t*	5.08 *t*	5.12 *dd*	5.15 *dd*	5.19 *dd*	5.11 *dd*	5.10 *t*
H-14	6.30 *m*	6.77 *d*	6.42 *m*	6.40 *m*	6.40 *m*	6.41 *m*	6.45 *m*	6.42 *m*	6.46 *m*	6.48 *m*
H-15	7.35 *m*	7.48 *t*	7.40 *m*	7.37 *m*	7.36 *m*	7.33 *m*	7.42 *m*	7.35 *m*	7.35 *m*	7.40 *m*
H-16	7.35 *m*	8.17 *d*	7.40 *m*	7.37 *m*	7.36 *m*	7.33 *m*	7.42 *m*	7.35 *m*	7.35 *m*	7.40 *m*
Me-17	0.88 *d*	1.10 *d*	1.45 *d*	1.42 *d*	1.69 *d*	1.34 *d*	1.20 *d*	1.25 *d*	1.40 *d*	1.35 *d*
H_A-18‖	†	2.40 *d*	2.58 *d*	2.42 *d*	2.32 *d*	2.20 *d*	2.40 *d*	2.21 *d*	2.42 *d*	2.40 *d*
H_B-18§	†	3.27 *dd*	3.27 *dd*	3.03 *dd*	3.08 *dd*	2.92 *dd*	3.20 *dd*	2.95 *dd*	3.18 *dd*	3.80‡
H_A-19	4.65 *s*	4.55 *d*	4.23 *dd*	4.41 *br d*	4.39 *d*	4.63 *br d*	4.71 *br d*	4.53 *dd*	4.95 *br d*	4.85 *s*
H_B-19	4.65 *s*	5.03 *d*	4.32 *d*	4.57 *d*	4.57 *d*	5.80 *d*	5.54 *d*	5.72 *d*	5.45 *d*	4.85 *s*
H-20	5.47 *s*	—	6.10 *s*	6.24 *s*	6.38 *s*	6.35 *s*	6.48 *s*	6.40 *s*	6.38 *s*	6.40 *s*
–OAc	2.05 *s*	2.05 *s*	2.06 *s*	2.08 *s*	2.05 *s*	2.08 *s*	2.10 *s*	2.13 *s*	2.09 *s*	2.11 *s*
	—	—	1.99 *s*	2.00 *s*	2.03 *s*	2.00 *s*	2.03 *s*	2.10 *s*	1.99 *s*	2.01 *s*
	—	—	—	1.92 *s*	2.02 *s*	1.95 *s*	1.90 *s*	1.92 *s*	—	—
	—	—	—	—	2.00 *s*	—	—	1.90 *s*	—	—
J (Hz)										
6β, 7β	—	—	—	—	—	3	4	4	3.5	—
6β, 17	—	—	0	0	1.8	0	0	0	0	—
7β, 8β	6	0	—	—	—	2	2.1	2.1	2.1	‡
8, 17	7	7	6.8	7	—	7	7	7	7	7
11A, 11B	‡	20	0	0	14	‡	13.5	13.5	13.5	‡
11A, 12	9	—	8.4	8	8.1	9	9	9	9	8
11B, 12	4	—	8.4	8	8.1	6	7	6.6	7	8
14, 15	1.6	1.6	¶	¶	¶	¶	¶	¶	¶	¶
15, 16	1.6	1.6	¶	¶	¶	¶	¶	¶	¶	¶
18A, 18B	‡	5	3.6	4.5	3.6	4.5	3.6	3.6	3.4	4.5
18B, 3α	‡	2	2.1	3	2.1	3	2.1	2.4	2.4	‡
19A, 19B	0	12	12.6	11	12	12	11.5	12	12	0
19A, 6β	—	—	1.2	<0.5	0	<0.5	<0.5	1	<0.5	—

*Spectral parameters were obtained by first order approximation. All these assignments have been confirmed by double resonance experiments.
†Could not be identified.
‡Overlapped signal.
§*Endo* hydrogen respect ring B.
‖*Exo* hydrogen respect ring B.
¶ $W_{1/2}$ = 4–5 Hz.

Table 2. ^{13}C NMR chemical shifts (in δ values from TMS) of compounds **4**, **5**, **7**, **8**, **13** and **14**

	4*	5*†	7‡	8*	13‡	14‡
C-1	21.7 *t*§	21.5 *t*	23.2 *t*	23.0 *t*	22.6 *t*	22.7 *t*
C-2	24.1 *t*	24.2 *t*	25.2 *t*	24.8 *t*	25.4 *t*	24.1 *t*
C-3	31.7 *t*	31.6 *t*	33.0 *t*	32.0 *t*	31.3 *t*	33.4 *t*
C-4	62.0 *s*	62.1 *s*	65.3 *s*	64.4 *s*	66.8 *s*	62.9 *s*
C-5	52.7 *s*	52.8 *s*	50.0 *s*	49.2 *s*	53.8 *s*	54.0 *s*
C-6	199.5 *s*	199.4 *s*	79.1 *d*	76.5 *d*	73.8 *d*‖	69.3 *d*
C-7	87.9 *d*	87.3 *d*	206.8 *s*	200.8 *s*	75.0 *d*	76.8 *d*
C-8	47.9 *d*‖	47.4 *d*	51.3 *d*‖	52.8 *d*‖	42.0 *d*	37.3 *d*
C-9	49.7 *s*	50.4 *s*	56.8 *s*	56.7 *s*	46.2 *s*	45.9 *s*
C-10	48.9 *d*‖	50.4 *d*	50.6 *d*‖	50.6 *d*‖	54.5 *d*	47.9 *d*
C-11	37.1 *t*	32.1 *t*	46.0 *t*	45.3 *t*	43.1 *t*	45.1 *t*
C-12	191.3 *s*	64.9 *d*	71.3 *d*	72.0 *d*	73.3 *d*‖	73.0 *d*
C-13	127.2 *s*	124.7 *s*	127.1 *s*	126.7 *s*	129.6 *s*	129.4 *s*
C-14	108.3 *d*	108.4 *d*	109.5 *d*	108.6 *d*	109.5 *d*	109.4 *d*
C-15	144.9 *d*	143.8 *d*	144.3 *d*	143.7 *d*	143.6 *d*	143.5 *d*
C-16	148.1 *d*	140.1 *d*	140.3 *d*	139.5 *d*	139.7 *d*	139.6 *d*
C-17	14.1 *q*	14.6 *q*	11.0 *q*	10.7 *q*	16.4 *q*	15.9 *q*
C-18	49.6 *t*	49.5 *t*	51.6 *t*	51.1 *t*	49.4 *t*	53.6 *t*
C-19	61.1 *t*	61.1 *t*	63.1 *t*	61.7 *t*	63.8 *t*	63.8 *t*
C-20	177.3 *s*	176.4 *s*	97.8 *d*	97.6 *d*	99.2 *d*	99.6 *d*
OAc	170.2 *s*	170.0 *s*	170.1 *s*	169.8 *s*	170.1 *s*	170.5 *s*
	20.7 *q*	169.7 *s*	169.6 *s*	169.6 *s*	168.8 *s*	169.2 *s*
		21.5 *q*	20.9 *q*	169.4 *s*	21.4 *q*	21.4 *q*
		20.9 *q*	20.7 *q*	21.0 *q*	21.0 *q*	21.2 *q*
				20.5 *q*		
				20.5 *q*		

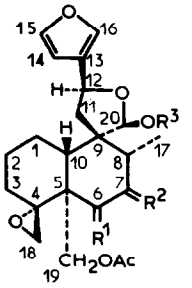
*In deuteriochloroform solution.
†Taken from ref. [6].
‡In pyridine-d_5 solution.
§SFORD multiplicity.
‖These assignments may be reversed, but those given here are considered to be the most likely.

whereas it showed an AB system (δ 4.23 and 4.32, J = 12.6 Hz) with additional long-range coupling (J = 1.2 Hz) in its A part in the ^1H NMR spectrum of isoeriocephalin (**7**). All these data pointed towards a structural assignment such as **7** for this new diterpenoid [7], which was also in agreement with the ^{13}C NMR spectrum of isoeriocephalin (Table 2 and ref. [5]).

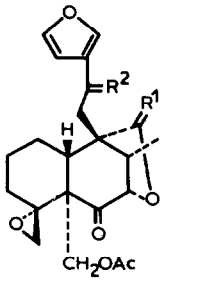
On the other hand, acetic anhydride–pyridine treatment of isoeriocephalin (**7**) yielded a monoacetyl derivative (**8**, $C_{26}H_{32}O_{10}$) besides minor quantities of a diacetyl derivative ($C_{28}H_{34}O_{11}$) to which structure **9** was attributed because its IR spectrum was devoid of ketone absorption and its ^1H NMR spectrum (Table 1) showed the signal of the secondary methyl group as a doublet at δ 1.69, with homoallylic coupling (J = 1.8 Hz) with the C-6 proton (δ 5.40, *q*, $J_{6,17}$ = 1.8 Hz). An identical behaviour on acetylation has been previously found [7] in picropolin [19-acetoxy-4α,18:15,16-diepoxy-6α-hydroxy-7-keto-cleroda-13(16),14-dien-20,12-olide], a clerodane diterpenoid isolated from *Teucrium polium* [7, 8]. Thus, it was evident that isoeriocephalin (**7**) possessed a 6α-hydroxyl and 7-keto functions. In complete agreement with this conclusion sodium borohydride reduction of **8** yielded the derivative **10** ($J_{7\beta,6\beta}$ = 3 Hz, $J_{7\beta,8\beta}$ = 2 Hz, Table 1) in which the C-7α axial configuration of the hydroxyl group was supported by the fact that no acetylation of it was achieved even under drastic conditions [9, 10] (see Experimental). Moreover, a 6β-H, 7β-H and 8β-H arrangement in compound **10** was also supported by comparing the $J_{6,7}$ and $J_{7,8}$ values of this substance with those of compounds **11** and **12**, both obtained from eriocephalin (**1**) *via* its acetate **3**. Effectively, all these compounds (**10**–**12**) showed almost identical coupling values between these protons ($J_{6\beta,7\beta}$ = 3–4 Hz, $J_{7\beta,8\beta}$ = 2–2.1 Hz, see Table 1).

It is interesting to note that in contrast to compound **10**, eriocephalin (**1**) possesses its ring B in a distorted boat conformation, in which the 7α-hydroxyl group is pseudoequatorial and, consequently, easily acetylated yielding the derivative **3** [5]. However, when the 6-keto function is transformed into a 6α-hydroxyl group (compound **11**) a ring B conformational change from a distorted boat to a chair takes place and, in this last conformation, a C-7α axial hydroxyl group is not acetylated because of the C-7α–C-20 interactions [9], as can be shown in the case of compound **10**.

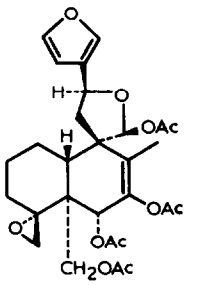
Finally, the structure and absolute configuration depicted in **7** for isoeriocephalin were firmly established by chemical correlation with a derivative obtained from eriocephalin (**1**). Effectively, sodium borohydride reduction of isoeriocephalin (**7**) yielded only a product (**13**) which was identical in all respects with the major epimer



	R^1	R^2	R^3
1	O	αOH, βH	Ac
2	O	αOH, βH	H
3	O	αOAc, βH	Ac
7	αOH, βH	O	Ac
8	αOAc, βH	O	Ac
10	αOAc, βH	αOH, βH	Ac
11	αOH, βH	αOAc, βH	Ac
12	αOAc, βH	αOAc, βH	Ac
13	αOH, βH	αOH, βH	Ac
14	αH, βOH	αOH, βH	Ac



	R^1	R^2
4	O	O
5	O	H, OAc (S)
6	H, OH	H, OAc (S)



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obtained by the same treatment of eriocephalin (**1**). The α-configuration of the C-6 hydroxyl group of compound **13**, and consequently of isoeriocephalin (**7**), was evident on the basis of the following considerations. (a) Reduction of a C-6 ketone in a neo-clerodane hydrocarbon skeleton yields predominantly the C-6α equatorial alcohol [11]. (b) Comparison of the ^{13}C NMR spectra of the epimers **13** and **14** (Table 2) clearly showed that compound **13** was the C-6α equatorial alcohol, because the C-8 and C-10 carbon atom resonances appeared at higher field in the C-6β axial epimer (**14**, δ 37.3 and 47.9, respectively, γ-gauche effect) than in **13** (C-6α equatorial epimer, δ 42.0 and 54.5, respectively, γ-*trans* effect) [12]. The difference between the C-18 carbon atom resonance in **13** (δ 49.4) and **14** (δ 53.6) was also in agreement with this conclusion [2, 12]. (c) The lower field resonance of the H_B-18 oxiranic proton in **14** (δ 3.80, Table 1) with respect to **13** (δ 3.18) also confirmed [2, 13] this point.

Therefore, in accordance with the terminology suggested by Rogers *et al.* [14], isoeriocephalin is 19-acetoxy-4α,18:15,16-diepoxy-6α-hydroxy-7-keto-neo-cleroda-13(16),14-diene-(20-acetyl)-20*S*,12*S*-hemiacetal (**7**).

EXPERIMENTAL

Mps are uncorr. For general details on methods see refs [5, 6, 11]. Assignments of ^{13}C NMR chemical shifts were made with the aid of off-resonance and noise-decoupled ^{13}C NMR spectra. Plant materials were collected in June 1982, at Isla de Mazarrón, Murcia, Spain, and voucher specimens were deposited in the Herbarium of the Royal Botanical Garden of Madrid.

Extraction and isolation of the diterpenoids. Dried and finely powdered *Teucrium lanigerum* Lag. aerial parts (2.5 kg) were extracted with Me_2CO (20 l.) at room temp. for a week. The extract (160 g) was chromatographed on a silica gel column (Merck, No. 7734, deactivated with 15% H_2O, 2.8 kg). Elution with EtOAc–*n*-hexane (3:1) yielded, in order of elution, 20-deacetyleriocephalin (**3**, 6.2 g), eriocephalin (**1**, 27.8 g) and isoeriocephalin (**7**, 4.8 g) as the main diterpenoid constituents.

The previously known diterpenoid, eriocephalin (**1**), was identified by its physical (mp, $[\alpha]_D$) and spectroscopic (IR, ^{1}H and ^{13}C NMR, mass spectra) data and by comparison (TLC, mmp) with an authentic sample.

20-Deacetyleriocephalin (**2**). An amorphous solid, mp 104–111°; $[\alpha]_D^{26}$ + 118.9° ($CHCl_3$; *c* 0.582); IR ν_{max}^{KBr} cm^{-1}: 3460, 3150, 2950, 2880, 1740, 1720, 1505, 1450, 1370, 1255, 1240, 1160, 1130, 1050, 1025, 880, 860, 790; ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 420 $[M]^+$ (1.5), 402 (2.5), 374 (2.5), 360 (4), 347 (2), 342 (2), 320 (7), 319 (5), 312 (4), 311 (8), 283 (8), 269 (4), 255 (7), 239 (4), 227 (4), 219 (7), 203 (9), 189 (11), 175 (12), 163 (30), 145 (15), 135 (15), 121 (15), 105 (15), 95 (35), 94 (50), 91 (24), 81 (34), 79 (20), 69 (15), 67 (15), 55 (17), 43 (100), 41 (29). (Found: C, 62.63; H, 6.57. $C_{22}H_{28}O_8$ requires: C, 62.84; H, 6.71%.)

Eriocephalin acetate (**3**) *from compound* **2**. Ac_2O–pyridine treatment of **2** (300 mg) at room temp. for 24 hr yielded a compound (300 mg) which after preparative TLC purification was identical in all respects ($[\alpha]_D$, IR, ^{1}H NMR, MS, TLC) with 7-acetyleriocephalin [**3**, an amorphous solid, mp 94–99°, $[\alpha]_D^{27}$ + 29.0° ($CHCl_3$; *c* 0.704)] [5].

Chromium trioxide–pyridine treatment of **2** *to yield compound* **4**. CrO_3–pyridine treatment of **2** (1 g) in the usual manner yielded a complex mixture of compounds (TLC). The main constituent of this mixture was isolated after chromatography on a silica gel column eluted with *n*-hexane–EtOAc (9:1). Compound **4** (400 mg, less polar constituent) was an amorphous solid, mp

83–88°; $[\alpha]_D^{27}$ +47.3° ($CHCl_3$; *c* 0.677); IR ν_{max}^{KBr} cm^{-1}: 3140, 3060, 2980, 2880, 1790, 1745 (br), 1680, 1565, 1510, 1450, 1425, 1385, 1340, 1245, 1230, 1170, 1155, 1095, 1055, 1045, 990, 950, 940, 875; UV λ_{max}^{EtOH} nm (log ε): 216 (3.79), 256 (3.60); ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, $CDCl_3$): see Table 2; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 416 $[M]^+$ (0.5), 374 (0.5), 356 (0.2), 344 (12), 343 (45), 326 (5), 298 (8), 276 (5), 233 (17), 216 (17), 205 (7), 187 (13), 173 (14), 123 (6), 110 (6), 95 (100), 93 (4), 91 (6), 81 (5), 79 (5), 77 (5), 69 (5), 55 (5), 43 (55). (Found: C, 63.25; H, 5.55. $C_{22}H_{24}O_8$ requires: C, 63.45; H, 5.81%.)

Compound **4** *from eriocephalin* (**1**). A soln of **1** (200 mg) in Me_2CO (30 ml) was treated with Jones reagent (0.3 ml) at room temp. during 15 min. Work-up in the usual manner yielded a mixture of products from which 58 mg of pure **4** were isolated. This compound was identical in all respects (mp, $[\alpha]_D$, IR, UV, ^{1}H NMR, MS, TLC) with the substance obtained from **2** by CrO_3–pyridine treatment.

Isoeriocephalin (**7**). Mp 232–234° (from Me_2CO–Et_2O); $[\alpha]_D^{20}$ −33.1° ($CHCl_3$; *c* 0.738); IR ν_{max}^{KBr} cm^{-1}: 3460, 3140, 3120, 3070, 2985, 2950, 2870, 1760, 1740, 1715, 1505, 1465, 1450, 1380, 1360, 1285, 1250, 1205, 1155, 1135, 1090, 1065, 1045, 1020, 1005, 915, 895, 875, 800, 735, 645; UV λ_{max}^{EtOH} nm (log ε): 212 (3.81); ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, pyridine-d_5): see Table 2; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 462 $[M]^+$ (1.5), 444 (0.5), 433 (1), 420 (1.5), 403 (10), 402 (20), 373 (15), 360 (30), 344 (15), 332 (18), 329 (20), 314 (20), 302 (10), 296 (10), 285 (11), 283 (15), 273 (10), 255 (15), 245 (11), 238 (11), 232 (11), 219 (15), 203 (15), 181 (18), 179 (19), 175 (21), 173 (20), 163 (38), 161 (28), 153 (35), 147 (27), 145 (30), 135 (28), 133 (22), 121 (27), 111 (35), 105 (25), 97 (20), 95 (40), 94 (50), 93 (21), 91 (30), 81 (40), 79 (30), 77 (22), 69 (19), 67 (22), 65 (15), 57 (15), 55 (24), 53 (19), 43 (100). (Found: C, 61.98; H, 6.60. $C_{24}H_{30}O_9$ requires: C, 62.32; H, 6.54%.)

Acetylation of **7** *to produce compounds* **8** *and* **9**. Ac_2O–pyridine (20 ml, 1:1) treatment of **7** (230 mg) during 5 days at room temp. yielded a mixture of two compounds which were easily separated by column (silica gel) chromatography eluted with *n*-hexane–EtOAc (3:1) to give pure **9** (less polar constituent, 66 mg) and **8** (153 mg).

Compound **8**. Mp 196–198° (from EtOAc–*n*-hexane), $[\alpha]_D^{26}$ −14.8° ($CHCl_3$; *c* 0.405); IR ν_{max}^{KBr} cm^{-1}: 3140, 3115, 3070, 3050, 3020, 3000, 2940, 2900, 2860, 1750, 1735, 1725, 1500, 1450, 1380, 1365, 1300, 1250, 1225, 1150, 1080, 1025, 990, 955, 910, 880, 865, 815, 670; ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, $CDCl_3$): see Table 2; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 504 $[M]^+$ (0.5), 461 (0.5), 445 (4), 444 (3), 416 (1.5), 402 (11), 389 (4), 385 (2), 374 (2), 360 (2), 356 (2.5), 342 (8), 329 (9), 314 (10), 296 (8), 283 (7), 268 (5), 255 (6), 239 (5), 214 (5), 202 (8), 189 (9), 175 (9), 173 (10), 163 (17), 153 (38), 145 (14), 135 (13), 121 (16), 111 (38), 105 (14), 97 (9), 95 (25), 94 (56), 93 (11), 91 (18), 81 (31), 67 (10), 55 (18), 43 (100). (Found: C, 61.63; H, 6.45. $C_{26}H_{32}O_{10}$ requires: C, 61.89; H, 6.39%.)

Compound **9**. Mp 173–174° (from MeOH); $[\alpha]_D^{26}$ +17.2° ($CHCl_3$; *c* 0.541); IR ν_{max}^{KBr} cm^{-1}: 3150, 3140, 3090, 3040, 2995, 2970, 2950, 2880, 1760 (br), 1735, 1505, 1490, 1450, 1400, 1375, 1265, 1240, 1220, 1195, 1150, 1130, 1090, 1070, 1050, 1020, 920, 890, 870, 820, 755, 740, 685; ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV *m/z* (rel. int.): $[M]^+$ absent, 487 $[M-59]^+$ (0.2), 486 $[M-60]^+$ (0.1), 458 (2), 444 (0.5), 427 (0.3), 416 (8), 398 (4), 374 (4), 356 (4), 325 (9), 314 (7), 296 (10), 283 (18), 265 (15), 255 (15), 253 (4), 233 (7), 215 (7), 201 (7), 189 (7), 173 (6), 161 (7), 159 (6), 145 (7), 123 (5), 121 (5), 111 (5), 105 (8), 97 (5), 95 (19), 94 (70), 91 (17), 81 (18), 69 (6), 55 (5), 43(100). (Found: C, 61.43; H, 6.12. $C_{28}H_{34}O_{11}$ requires: C, 61.55; H, 6.22%.)

Sodium borohydride reduction of **8** *to yield compound* **10**. Compound **8** (130 mg) in MeOH soln (20 ml) was treated with excess of $NaBH_4$ in the usual manner yielding pure **10** (120 mg after crystallization from $CHCl_3$–*n*-hexane), mp 210–212°; $[\alpha]_D^{26}$ −46.3° ($CHCl_3$; *c* 0.564); IR ν_{max}^{KBr} cm^{-1}: 3400, 3120, 3040, 2970, 2950, 2920, 2880, 2860, 1730, 1705, 1500, 1380, 1360, 1270, 1235, 1080, 1065, 1035, 1015, 1000, 970, 950, 880, 870, 810, 735, 700; ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 506 $[M]^+$ (0.3), 488 (0.2), 476 (0.3), 447 (4), 446 (3), 429 (2), 418 (3), 404 (4), 403 (4), 386 (41), 373 (9), 357 (15), 331 (20), 327 (30), 326 (20), 313 (18), 298 (20), 285 (25), 267 (31), 251 (21), 239 (20), 217 (40), 216 (25), 201 (30), 191 (34), 187 (33), 175 (39), 173 (35), 171 (27), 163 (70), 161 (45), 159 (35), 157 (29), 147 (40), 145 (50), 135 (45), 123 (55), 121 (39), 111 (60), 109 (47), 107 (48), 105 (45), 95 (75), 94 (75), 93 (40), 91 (55), 81 (70), 79 (41), 77 (27), 69 (30), 67 (40), 55 (35), 45 (35), 43 (100). (Found: C, 61.73; H, 6.54. $C_{26}H_{34}O_{10}$ requires: C, 61.65; H, 6.77%.)

Attempts to obtain the 7-acetyl derivative of **10** by reaction with Ac_2O–pyridine (7 days at room temp. or 6 hr at 100°) or with acetyl chloride–*N*,*N*-dimethyl-aniline (5 hr at 100°) were unsuccessful.

Sodium borohydride reduction of acetyleriocephalin (**3**) *to give compound* **11**. Reduction of **3** (300 mg) [5] with $NaBH_4$ in the usual manner quantitatively yielded **11**, mp 241–243° (from MeOH); $[\alpha]_D^{27}$ −49.9° ($CHCl_3$; *c* 0.841); IR ν_{max}^{KBr} cm^{-1}: 3500, 3140, 3120, 3070, 3000, 2980, 2940, 2910, 2870, 1745, 1730, 1505, 1460, 1410, 1380, 1365, 1310, 1295, 1240, 1145, 1120, 1110, 1080, 1030, 1005, 945, 875, 860, 810, 780, 755, 730, 650; ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 506 $[M]^+$ (0.5), 447 (0.5), 446 (2), 418 (1), 404 (1), 387 (3), 357 (2), 345 (3), 344 (3), 327 (4), 326 (4), 310 (4), 298 (8), 297 (6), 285 (4), 280 (4), 279 (3), 269 (4), 267 (6), 232 (5), 217 (5), 204 (5), 191 (5), 187 (7), 174 (9), 163 (10), 153 (8), 147 (8), 145 (9), 135 (7), 121 (8), 111 (15), 107 (6), 105 (7), 95 (16), 94 (15), 93 (7), 91 (10), 81 (17), 79 (19), 77 (5), 69 (7), 67 (7), 57 (3), 55 (6), 53 (4), 43 (100). (Found: C, 61.42; H, 6.48. $C_{26}H_{34}O_{10}$ requires: C, 61.65; H, 6.77%.)

Compound **12**. Ac_2O–pyridine treatment of **11** (100 mg) during 24 hr at room temp. quantitatively yielded the acetyl derivative **12**, mp 223–224° (from EtOAc–*n*-hexane); $[\alpha]_D^{26}$ −41.7° ($CHCl_3$; *c* 0.544); IR ν_{max}^{KBr} cm^{-1}: 3130, 3050, 3000, 2980, 2960, 2930, 2880, 1745 (br), 1505, 1480, 1465, 1370, 1245, 1155, 1090, 1070, 1020, 945, 875, 870, 795, 740, 685, 650, 625; ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 548 $[M]^+$ (1.8), 518 (0.5), 489 (4), 488 (10), 445 (5), 428 (10), 385 (4), 373 (15), 355 (10), 326 (12), 325 (8), 296 (10), 279 (10), 266 (11), 232 (12), 217 (9), 201 (6), 187 (7), 174 (6), 163 (8), 153 (8), 145 (7), 135 (6), 121 (7), 111 (15), 95 (12), 94 (12), 91 (7), 81 (15), 55 (7), 43 (100). (Found: C, 60.99; H, 6.31. $C_{28}H_{36}O_{11}$ requires: C, 61.33; H, 6.56%.)

Sodium borohydride reduction of isoeriocephalin (**7**) *to yield compound* **13**. Compound **7** (100 mg) in MeOH soln (15 ml) was treated with excess of $NaBH_4$ in the usual manner yielding **13** (85 mg after crystallization from MeOH), mp 148–150°; $[\alpha]_D^{27}$ −48.1° ($CHCl_3$; *c* 0.595); IR ν_{max}^{KBr} cm^{-1}: 3570, 3510, 3470, 3390, 3140, 3120, 3110, 3070, 3010, 2960, 2950, 2890, 1750, 1720, 1640, 1505, 1460, 1375, 1315, 1300, 1270, 1250, 1220, 1150, 1125, 1085, 1020, 1000, 970, 940, 875, 870, 800, 735; ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, pyridine-d_5): see Table 2; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 464 $[M]^+$ (0.5), 446 (1), 433 (0.5), 404 (3), 386 (2), 344 (3), 331 (3), 327 (2), 269 (5), 267 (5), 265 (5), 251 (6), 234 (6), 217 (6), 203 (7), 191 (11), 175 (10), 173 (10), 163 (25), 145 (15), 135 (15), 121 (14), 105 (15), 95 (35), 94 (30), 93 (14), 91 (20), 81 (35), 79 (19), 77 (13), 67 (13), 55 (15), 43 (100). (Found: C, 62.12; H, 6.86. $C_{24}H_{32}O_9$ requires: C, 62.05; H, 6.94%.)

Sodium borohydride reduction of eriocephalin (**1**) *to produce compounds* **13** *and* **14**. Reduction of **1** (400 mg) with $NaBH_4$ as previously described for **7** yielded a 2:1 mixture of compounds

13 and **14**, respectively. This mixture was separated into its constituents by column chromatography (silica gel, eluent EtOAc–*n*-hexane, 1:1) to give **13** (240 mg, less polar constituent, identical in all respects with the compound described above) and **14** (120 mg), an amorphous solid which melted at 95–101°, $[\alpha]_D^{26}$ −70.1° (CHCl; *c* 0.582); IR ν_{max}^{KBr} cm^{-1}: 3470 (br), 3140, 3130, 2940, 2880, 1745, 1720, 1505, 1450, 1365, 1250, 1155, 1090, 1010, 950, 920, 870, 790, 730; ^1H NMR (90 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (20.15 MHz, pyridine-d_5): see Table 2; EIMS (direct inlet) 75 eV *m/z* (rel. int.): 464 $[M]^+$ (0.3), 446 (0.5), 404 (2), 386 (1.5), 376 (2), 362 (2), 361 (2), 358 (1), 345 (2.5), 344 (3), 297 (5), 285 (5), 267 (8), 251 (6), 234 (6), 215 (8), 203 (10), 191 (11), 175 (20), 173 (22), 163 (25), 161 (20), 147 (22), 145 (25), 135 (22), 121 (22), 107 (22), 105 (25), 97 (25), 95 (30), 94 (30), 93 (25), 91 (30), 81 (30), 79 (15), 77 (20), 69 (15), 67 (22), 65 (10), 57 (10), 55 (24), 43 (100). (Found: C, 61.83; H, 6.70. $C_{24}H_{32}O_9$ requires: C, 62.05; H, 6.94%.)

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