Phytochemistry, Vol. 22, No. 3, pp. 727–731, 1983.
Printed in Great Britain.

0031-9422/83/030727-05$03.00/0

TEUSCORODIN, TEUSCORODONIN AND 2-HYDROXYTEUSCOROLIDE, NEO-CLERODANE DITERPENOIDS FROM *TEUCRIUM SCORODONIA*

JOSÉ L. MARCO, BENJAMÍN RODRÍGUEZ*, CONRAD PASCUAL, GIUSEPPE SAVONA† and FRANCO PIOZZI†

Instituto de Química Orgánica, CSIC, Juan de la Cierva 3, Madrid-6, Spain; †Istituto di Chimica Organica dell'Università, Archirafi 20, 90123 Palermo, Italy

(*Received* 6 *July* 1982)

Key Word Index—*Teucrium scorodonia*; Labiatae; diterpenoids; neo-clerodanes; teuscorolide; 2-hydroxyteuscorolide; teuscorodin; teuscorodonin.

Abstract—From the aerial part of *Teucrium scorodonia* (Labiatae) three new neo-clerodane diterpenoids have been isolated. Their structures, (12*S*)-15,16-epoxy-2α-hydroxy-19-nor-neo-clerodane-4,6,13(16),14-tetraene-18,6:20,12-diolide (2-hydroxyteuscorolide), (12*S*,18*R*)-15,16-epoxy-6-keto-neo-clerodane-13(16),14-dien-20,12-olide-18,19-hemiacetal (teuscorodin) and (12*S*)-15,16-epoxy-19-hydroxy-neo-clerodane-3,13(16),14-triene-18,6β:20,12-diolide (teuscorodonin), have been established by chemical and spectroscopic means and by correlation with known products.

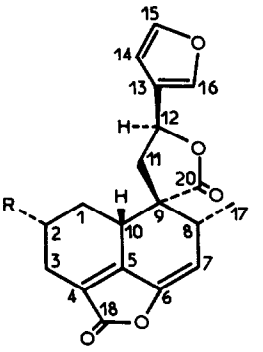
INTRODUCTION

In a previous communication [1] we reported the isolation of three new diterpenoids [teuscorolide (**1**), teuscorodal and teuscorodol] and a known substance (teupolin I [2, 3]) from the aerial part of *Teucrium scorodonia* L. (Labiatae). In this communication we report the structure determination of three new diterpenoids [2-hydroxyteuscorolide (**2**), teuscorodin (**3**) and teuscorodonin (**6**)], which have been isolated from the same plant.

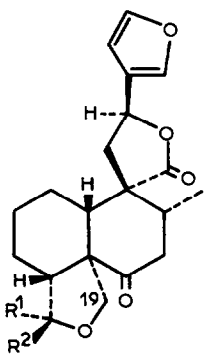
RESULTS AND DISCUSSION

The first of the new diterpenoids (2-hydroxyteuscorolide, **2**), $C_{19}H_{18}O_6$, had an IR spectrum which showed hydroxyl (3520 cm^{-1}), furanic (3165, 3140, 3130, 1510, 880 cm^{-1}), γ-lactone (1775 cm^{-1}) and α,β-unsaturated enol-γ-lactone (3060, 1755, 1670, 1605 cm^{-1}) absorptions. The presence in compound **2** of an α,β-unsaturated enol-γ-lactone group was confirmed by its UV absorption at λ_{max} 281 nm (log ε 4.18), identical with that found in teuscorolide (**1**) [1, 4–6]. The ^1H NMR spectrum of compound **2** was very similar to that of teuscorolide (**1**) with characteristic signals for a β-substituted furan ring, a γ-lactone group, a secondary methyl group and an α,β-unsaturated enol-γ-lactone moiety (see Table 1).

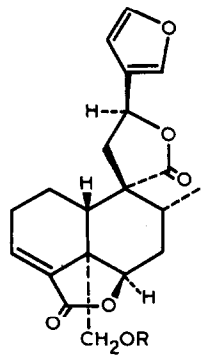
In addition, the ^1H NMR spectrum of 2-hydroxyteuscorolide (**2**) showed a one-proton multiplet at δ 4.33 which was assigned to the geminal proton of a secondary hydroxyl group. This alcohol function must be placed between two methylene groups, because its geminal proton appeared as a broad multiplet ($W_{\frac{1}{2}}$ = 24 Hz). Thus, only the C-2 position of the clerodane skeleton of teuscorolide (**1**) is likely for the secondary hydroxyl group of the new diterpenoid **2**. The α-configuration (equatorial) of this alcohol was revealed by the fact that the ^1H NMR spectrum of compound **2** (Table 1) showed a four-line signal for the C-1α axial proton ($J_{1\alpha,10\beta} = J_{1\alpha,2\beta}$ = $J_{1\alpha,1\beta}$ = 10 Hz), which collapsed into a triplet (J = 10 Hz) on irradiation at δ 4.33 (2β-axial proton). On the other hand, comparison of the ^{13}C NMR spectra of



1 R = H
2 R = OH



3 R^1 = H, R^2 = OH
4 R^1 = H, R^2 = OAc
5 R^1, R^2 = O



6 R = H
7 R = Ac

*Author to whom correspondence should be addressed.

Table 1. ^{1}H NMR spectral data of compounds 1–5*

	1†‡	2§	3§	4‡	5‡
H-1α	‖	1.77 *ddd*	‖	‖	‖
H-2β	‖	4.33 *m*	‖	‖	‖
H-4β	—	—	2.67 *br dd*	2.77 *ddd*	2.83 *dd*
H-7α	5.28 *d*	5.40 *d*	3.45 *t*	3.38 *t*	3.40 *t*
H_A-11	2.50 *dd*	2.70 *dd*	2.42 *d*	2.38 *d*	2.47 *d*
H_B-11	2.43 *dd*	2.50 *dd*	2.42 *d*	2.38 *d*	2.47 *d*
H-12	5.40 *t*	5.53 *t*	5.50 *t*	5.35 *t*	5.43 *t*
H-14	6.38 *m*	6.55 *m*	6.58 *m*	6.35 *m*	6.40 *m*
H-15	7.47 *m*	7.63 *t*	7.63 *m*	7.42 *m*	7.47 *m*
H-16	7.47 *m*	7.73 *m*	7.78 *m*	7.42 *m*	7.47 *m*
Me-17	1.23 *d*	1.23 *d*	1.02 *d*	1.07 *d*	1.13 *d*
H-18	—	—	5.07 *br s*	6.13 *d*	—
H_A-19	—	—	4.70 *d*	4.53 *d*	4.75 *d*
H_B-19	—	—	4.25 *d*	4.19 *d*	4.49 *d*
OAc	—	—	—	2.03 *s*	—

J: **1** and **2**: 7, 8 = 1.5; 8, 17 = 7.5; 11A, 11B = 13.5; 11A, 12 = 11B, 12 = 8.5; 14, 15 = 15, 16 = 1.5; 14, 16 + 14, 15 = 3.5. **2**: 1α, 1β = 1α, 2β = 1α, 10β = 10; 2β, 1α + 2β, 1β + 2β, 3α + 2β, 3β = 24. **3–5**: 4β, 3 = 9; 4β, 3′ = 6; 7α, 7β = 7α, 8β = 13; 8, 17 = 7; 11A, 12 = 11B, 12 = 9; 11A, 11B, not observed; 14, 15 + 14, 16 = 4; 14, 16 + 15, 16 = 4; 19A, 19B = 10.5. **3**: 4β, 18 ≃ 0. **4**: 4β, 18 = 5.

*At 90 MHz. Chemical shifts are in δ-values from TMS, *J* in Hz.

†Taken from ref. [1].

‡In $CDCl_3$ solution.

§In pyridine-d_5 solution.

‖Could not be identified. All these assignments have been confirmed by double resonance experiments.

compounds **1** and **2** (Table 2), clearly confirmed all the above assignments and established the structure and relative stereochemistry depicted in **2** for this new diterpenoid. In particular, the β-effects on C-1 (Δδ + 12.2) and C-3 (Δδ + 10.8) and the γ-effects on C-4 (Δδ − 0.7) and C-10 (Δδ − 0.5) clearly established the existence in compound **2** of an equatorial hydroxyl group attached to the C-2 position. Finally, a neo-clerodane [7] absolute configuration was established for 2-hydroxyteuscorolide (**2**), because the variation of the optical rotations of this compound and teuscorolide (**1**) (see Experimental) is similar, and the neo-clerodane absolute configuration of this last compound (**1**) is well-known [1, 4–6].

Another of the diterpenoids, teuscorodin (**3**), had a molecular formula $C_{20}H_{24}O_6$ and possessed a β-substituted furan ring, a γ-lactone and a secondary methyl group identical with those found in **2** (see Tables 1 and 2). In addition, the IR spectrum of teuscorodin (**3**) revealed the existence of a hydroxyl (3450 cm^{-1}) and a ketone (1695 cm^{-1}) group, which were confirmed by ^{1}H and ^{13}C NMR spectroscopy. The geminal proton of the secondary hydroxyl group showed a one-proton broad singlet at δ 5.07 (Table 1) and the ketone group showed a singlet at δ 214.9 (Table 2). In agreement with these conclusions, teuscorodin (**3**) was easily acetylated to give the derivative **4**, and treatment with chromium trioxide–pyridine yielded a compound (**5**) identical in all respects (mp, mmp, $[\alpha]_D$, CD, IR, ^{1}H NMR, mass spectrum) with 6-ketoteuscordin, previously isolated from *Teucrium scordium* [8] and known as a synthetic derivative of teucrin E [9] and teuchamaedryn B [10]. Thus, it was clear that teuscorodin (**3**) possessed a hemiacetalic function, which was placed at

Table 2. ^{13}C NMR chemical shifts of compounds 1–4 and 6*

	1	2	3	4	6
C-1	22.5 *t*†‡	34.7 *t*‡	23.0 *t*	21.4 *t*	17.6 *t*
C-2	24.3 *t*	67.7 *d*	23.9 *t*	23.3 *t*	24.6 *t*
C-3	19.5 *t*‡	30.3 *t*‡	26.4 *t*	24.8 *t*	134.9 *d*
C-4	123.7 *s*	123.0 *s*	47.2 *d*	41.9 *d*‡	139.7 *s*
C-5	151.1 *s*	151.4 *s*	59.4 *s*	59.9 *s*	45.6 *s*
C-6	147.4 *s*	147.3 *s*	214.9 *s*	210.1 *s*	77.4 *d*
C-7	108.8 *d*	109.2 *d*	41.2 *t*	41.6 *t*	31.2 *t*
C-8	37.5 *d*	37.9 *d*	40.7 *d*	41.4 *d*‡	37.0 *d*
C-9	53.8 *s*	53.9 *s*	51.3 *s*	51.3 *s*	48.2 *s*
C-10	40.8 *d*	40.3 *d*	50.4 *d*	51.6 *d*	45.5 *d*
C-11	39.4 *t*	39.2 *t*	43.1 *t*	42.2 *t*	44.3 *t*
C-12	71.8 *d*	72.0 *d*	72.1 *d*	71.9 *d*	71.9 *d*
C-13	125.7 *s*	125.7 *s*	125.8 *s*	124.9 *s*	127.0 *s*
C-14	108.8 *d*	108.9 *d*	108.8 *d*	108.0 *d*	108.7 *d*
C-15	144.8 *d*	144.8 *d*	144.8 *d*	144.4 *d*	144.7 *d*
C-16	140.7 *d*	140.7 *d*	140.7 *d*	139.8 *d*	139.7 *d*
C-17	16.9 *q*	16.9 *q*	17.1 *q*	17.2 *q*	17.6 *q*
C-18	169.5 *s*	169.1 *s*	103.9 *d*	98.5 *d*	169.3 *s*
C-19	—	—	70.5 *t*	69.0 *t*	63.4 *t*
C-20	175.2 *s*	175.2 *s*	176.9 *s*	176.5 *s*	177.3 *s*
OAc	—	—	—	170.0 *s*	—
	—	—	—	21.1 *q*	—

*In δ-values from TMS, at 20.15 MHz, all in pyridine-d_5 solution, except **4** ($CDCl_3$ solution).

†SFORD multiplicity.

‡Values in any vertical column may be interchanged, but those given here are considered to be most likely.

the C-18 position because, although its ^{1}H NMR spectrum showed a broad singlet for the hemiacetalic proton, that of the acetyl derivative **4** showed this proton as a clear doublet ($J_{18,4\beta} = 5$ Hz) at δ 6.13 (Table 1). The ^{13}C NMR spectra of compounds **3** and **4** (Table 2) confirmed these conclusions and established that the hemiacetalic hydroxyl group is involved in a hydrogen bond with the C-6 ketone group, because the C-6 carbon atom appeared at δ 214.9 in **3** and at δ 210.1 in its acetyl derivative (**4**). The difference of the ketone absorptions in the IR spectra of compounds **3** and **4** (1695 and 1710 cm^{-1}, respectively) also confirmed this point. This was also in agreement with the observed $J_{18,4\beta}$ values in teuscorodin (**3**, $J \simeq 0$ Hz) and its acetate **4** ($J = 5$ Hz), since the C-18 acetate–C-6 ketone steric interactions force the C-18–C-19 hemiacetalic ring to adopt a conformation in which the H-18–H-4 dihedral angle is larger than 90°, whereas in compound **3** it is close to 90°.

The neo-clerodane [7] absolute stereochemistry of teuscorodin (**3**) was established by correlation with 6-ketoteuscordin (**5**) [8–10] and by its CD curve, which showed a negative Cotton effect ($\Delta\varepsilon_{298} - 0.54$, $\Delta\varepsilon_{292} - 0.55$) for the C-6 ketone, in complete agreement with a neo-clerodane absolute configuration [3]. Teuscorodin (**3**) is the first diterpenoid isolated from *Teucrium* species which possesses a C-18–C-19 hemiacetalic function [1–6, 8–11].

The last diterpenoid isolated from *T. scorodonia* has been named teuscorodonin (**6**) and its molecular formula was $C_{20}H_{22}O_6$. The IR spectrum of this substance showed hydroxyl (3480 cm^{-1}), furanic (3150, 1508, 880 cm^{-1}), γ-lactone (1760 cm^{-1}) and α,β-unsaturated-γ-lactone (1740, 1670 cm^{-1}) absorptions. The ^{1}H NMR spectrum of teuscorodonin (**6**) showed typical absorptions for a β-substituted furan ring, a C-20, C-12-γ-lactone and a C-17 secondary methyl group (Table 3), identical with those found in the previously described diterpenoids. In addition, **6** possessed an exocyclic, α,β-unsaturated-γ-lactone group [λ_{max} 220 nm (log ε 4.00); a β-olefinic proton at δ 6.74, *dd*, and a one-proton double doublet at δ 5.39] and a primary hydroxyl group attached to a fully substituted sp^3 carbon atom (an AB system at δ 4.64 and 4.14, $J = 10.9$ Hz, Table 3). Acetic anhydride–pyridine treatment of teuscorodonin (**6**) yielded the acetyl derivative **7**, the ^{1}H NMR spectrum of which (Table 3) showed the paramagnetically shifted AB system (δ 4.58 and 4.47), thus confirming that the free alcohol of teuscorodonin is a primary one.

All these data pointed toward the structure **6** for teuscorodonin, which was confirmed on the basis of the following considerations. The chemical shift and coupling values of the C-6α-lactonic proton of **7** (Table 3) are identical with those found in some neo-clerodan-3-en-18,6β-olides, such as plaunols A, B and C [12, 13]. Furthermore, in **6** H-6 must be *trans*-oriented with respect to one of the C-7 protons ($J_{6,7'} = 10.7$ Hz, $J_{6,7} = 6.2$ Hz), and since H-8 showed an identical coupling value with the C-7 methylene protons ($J = 4.3$ Hz), only a H-6α-axial, H-7β-axial, H-7α-equatorial and H-8β-pseudoaxial arrangement with ring B in a boat conformation is compatible with these results (see the molecular model of **6**). The 6β-closure of the α,β-unsaturated-γ-

Table 3. ^{1}H NMR spectral data of compounds **6** and **7***

	6†	7‡
H-3	6.74 *dd*, $J_{3,2} = 5.9$ $J_{3,2'} = 2.7$	6.75 *dd*, $J_{3,2} = 5$; $J_{3,2'} = 3.5$
H-6	5.39 *dd*, $J_{6\alpha,7\beta} = 10.7$ $J_{6\alpha,7\alpha} = 6.2$	4.82 *dd*, $J_{6\alpha,7\beta} = 10$ $J_{6\alpha,7\alpha} = 5.5$
H-7α	~ 2.06, complex and overlapped signal	§
H-7β	~ 1.88, complex and overlapped signal	§
H-8	2.13 *tq*, $J_{8\beta,7\alpha} = J_{8\beta,7\beta} = 4.3$ $J_{8,17} = 7.4$	§
H_A-11	2.69 *dd*, $J_{11A,12} = 8.6$ $J_{11A,11B} = 13.2$	2.60 *dd*, $J_{11A,12} = 8$ $J_{11A,11B} = 13$
H_B-11	2.41 *dd*, $J_{11B,12} = 4.3$	2.27 *dd*, $J_{11B,12} = 4$
H-12	5.66 *ddd*, $J_{12,11A} = 8.6$ $J_{12,11B} = 4.3$; $J_{12,16} = 1.1$	5.48 *ddd*, $J_{12,11A} = 8$ $J_{12,11B} = 4$; $J_{12,16} = 1$
H-14	6.56 *dd*, $J_{14,15} = 1.9$ $J_{14,16} = 1.0$	6.38 *m*, $W_{1/2} = 3.5$
H-15	7.68 *dd*, $J_{15,14} = 1.9$ $J_{15,16} = 1.6$	7.42 *m*, $W_{1/2} = 4$
H-16	7.79 *ddd*, $J_{16,12} = 1.1$ $J_{16,14} = 1.0$; $J_{16,15} = 1.6$	7.42 *m*, $W_{1/2} = 4$
Me-17	1.10 *d*, $J_{17,8} = 7.4$	1.08 *d*, $J_{17,8} = 7.5$
H_A-19	4.64 *d*, $J_{19A,19B} = 10.9$	4.58 *d*, $J_{19A,19B} = 10.5$
H_B-19	4.14 *d* $J_{19B,19A} = 10.9$	4.47 *d*, $J_{19B,19A} = 10.5$
OAc		2.00 *s*

* Chemical shifts are in δ-values from TMS, J in Hz.
†At 270 MHz, pyridine-d_5 solution.
‡At 90 MHz, $CDCl_3$ solution.
§Could not be identified.
All these assignments have been confirmed by double resonance experiments.

lactone was also supported by the fact that neither of the two protons at C-19 in **6** and **7** showed any long-range coupling in their ^{1}H NMR spectra. The requirement for the existence of such a long-range coupling [14, 15], which has been observed (J = 1–2.5 Hz) in some neo-clerodanes lacking a substituent at C-6 [16–19], is the existence of a β-proton at C-6. All these assignments were also supported by the ^{13}C NMR spectrum of teuscorodonin (Table 2), which showed carbon atom resonances in complete agreement with structure **6** [20, 21].

On the other hand, the ^{1}H NMR spectra of **6** and **7** (Table 3) showed for the C-11 methylene and the C-12 lactonic protons an ABX system (δ_A 2.69, δ_B 2.41, δ_X 5.66; J_{AB} = 13.2 Hz, J_{AX} = 8.6 Hz, J_{BX} = 4.3 Hz), the X part of which has allylic coupling with the C-16 α-furanic proton ($J_{12,16}$ = 1.1 Hz). An identical behaviour has been previously observed in chamaedroxide [22], a neo-clerodane diterpenoid whose 12*S*-configuration was firmly established by *X*-ray diffraction analysis. Thus, a 12*S*-configuration may be attributed to teuscorodonin (**6**). However, these coupling values of the C-11 and C-12 protons in **6** and chamaedroxide [22] are unusual for *Teucrium* diterpenoids ($J_{11A,12} = J_{11B,12}$ = 8–9 Hz, no detectable coupling between C-12 and C-16 protons [1–6, 8–11, 16–19]). Thus, the 12*S*-configuration of teuscorodonin (**6**) required further confirmation and this was obtained by nuclear Overhauser effect experiments. Effectively, on irradiation at δ 2.13 (H-8β proton) a small (*ca* 5%) NOE on the C-14 and C-16 protons was observed, thus establishing a *cis*-relationship between the C-8 proton and the furan ring. Consequently, teuscorodonin (**6**) has the 12*S*-configuration and this is identical with that found in all the neo-clerodane diterpenoids isolated from *Teucrium* species [1–11, 19, 20, 22–25].

Finally, the CD curve of teuscorodonin (**6**) showed two Cotton effects at 250 nm ($\Delta\varepsilon$ +2.16) and 225 nm ($\Delta\varepsilon$ −4.04), in complete agreement with a neo-clerodane absolute configuration [7, 13, 23–25] and with a H-10β–18, 6β-lactone groups arrangement [23–25].

EXPERIMENTAL

Mps are uncorr. For general details on exptal see refs. [1, 3, 19, 22]. Assignments of ^{13}C NMR chemical shifts were made with the aid of off-resonance and noise-decoupled ^{13}C NMR spectra. NOE expts were performed with the technique of differential spectra. Plant material was the same as that used in ref. [1].

Isolation of the diterpenoids. Dried and finely powdered *T. scorodonia* aerial parts (1.5 kg) were extracted with Me_2CO as previously described [1]. Careful chromatography on Si gel columns eluted with *n*-hexane–EtOAc (4:1) of the fractions containing teuscorolide (**1**) allowed the isolation of teuscorodin (**3**, 380 mg), and chromatography of the more polar chromatographic fractions of the total extract over Si gel columns eluted with *n*-hexane–EtOAc (1:1) yielded teuscorodonin (**6**, 240 mg, less polar compound) and 2-hydroxyteuscorolide (**2**, 104 mg).

2-Hydroxyteuscorolide (**2**). Mp 243–246° (from EtOAc–*n*-hexane); IR ν_{max}^{KBr} cm^{-1}: 3520 (hydroxyl), 3165, 3140, 3130, 1510, 880 (furan ring), 1775 (γ-lactone), 3060, 1755, 1670, 1605 (α,β-unsatd enol-γ-lactone), 2990, 2980, 2945, 2930, 2910, 2860, 1460, 1355, 1330, 1300, 1220, 1190, 1160, 1100, 1035, 1030, 1020, 995, 975, 965, 935, 860, 815, 805, 780, 745, 725, 695. UV λ_{max}^{EtOH} nm (log ε): 211 (3.86) (furan ring), 281 (4.16) (α,β-unsatd enol-γ-lactone). ^{1}H NMR (90 MHz, C_5D_5N): see Table 1. ^{13}C NMR (20.15 MHz, C_5D_5N): see Table 2. EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 342 $[M]^+$ (18), 324 (2), 314 (5), 312 (3), 248 (9), 230 (9), 218 (7), 203 (8), 199 (7), 186 (100), 175 (45), 158 (12), 131 (13), 128 (14), 115 (19), 95 (80), 94 (68), 91 (40), 81 (43), 77 (43), 69 (82). (Found: C, 66.54; H, 5.26. $C_{19}H_{18}O_6$ requires: C, 66.66; H, 5.30%.)

Optical rotations of **1** *and* **2**. [α] values in degrees

	589	578	546	436	365 nm	
2	+20.8	+21.5	+22.7	+31.5	−7.7	($CHCl_3$–C_5H_5N, 9:1; *c* 0.260);
1	+13.5	+14.2	+15.5	+14.2	−44.2	($CHCl_3$; *c* 0.312).

Teuscorodin (**3**). Mp 152–153° (Me_2CO–*n*-hexane); $[\alpha]_D^{22}$ +2.9°, $[\alpha]_{365}^{22}$ −14.2° ($CHCl_3$; *c* 0.240); IR ν_{max}^{KBr} cm^{-1}: 3450 (hydroxyl) 3160, 3135, 1508, 880 (furan ring), 1765 (γ-lactone), 1695 (ketone), 2980, 2950, 2880, 1455, 1335, 1230, 1185, 1160, 1140, 1025, 975, 905, 810, 745, 730. UV λ_{max}^{EtOH} nm (log ε): 214 (3.84) (furan ring), 292 (2.20) (ketone). CD nm ($\Delta\varepsilon$): 325 (0), 310 (−0.32), 298 (−0.54), 292 (−0.55), 255 (0) (MeOH; *c* 0.596). ^{1}H NMR (90 MHz, C_5D_5N): see Table 1. ^{13}C NMR (20.15 MHz, C_5D_5N): see Table 2. EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 360 $[M]^+$ (4), 342 (10), 314 (20), 301 (44), 220 (24), 208 (22), 178 (32), 161 (34), 136 (56), 121 (36), 105 (40), 95 (100), 94 (72), 91 (68), 81 (84), 77 (64), 69 (60), 53 (68). (Found: C, 66.52; H, 6.63. $C_{20}H_{24}O_6$ requires: C, 66.65; H, 6.71%.)

Acetyl teuscorodin (**4**). Ac_2O–pyridine treatment of **3** (200 mg) in the usual manner yielded **4** (200 mg, after crystallization from EtOAc–*n*-hexane): mp 222–225°; $[\alpha]_D^{24}$ +31.7° ($CHCl_3$; *c* 0.366); IR ν_{max}^{KBr} cm^{-1}: 3150, 1508, 880 (furan ring), 1760 (γ-lactone), 1735, 1250 (acetate), 1710 (ketone), 2995, 2960, 2870, 1430, 1385, 1225, 1190, 1145, 1025, 1015, 985, 905, 830, 735. ^{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.): 402 $[M]^+$ (1), 366 (2), 359 (21), 343 (22), 342 (17), 314 (24), 301 (7), 271 (6), 255 (6), 220 (16), 178 (14), 161 (17), 136 (30), 121 (20), 105 (23), 95 (42), 94 (37), 91 (41), 81 (44), 69 (36), 55 (35), 43 (100). (Found: C, 65.38; H, 6.67. $C_{22}H_{26}O_7$ requires: C, 65.66; H, 6.51%.)

6-Ketoteuscordin (**5**) *from teuscorodin* (**3**). CrO_3–pyridine oxidation of **3** (80 mg) in the usual manner yielded **5** (63 mg after crystallization from EtOAc–*n*-hexane): mp 203–205°; $[\alpha]_D^{24}$ +38.4° ($CHCl_3$; *c* 0.375), $[\alpha]_D^{24}$ +42.6° (Me_2CO; *c* 0.230); IR ν_{max}^{KBr} cm^{-1}: 3160, 3135, 1508, 880 (furan ring), 1785, 1760 (γ-lactones), 1705 (ketone), 2995, 2950, 2880, 1480, 1370, 1345, 1215, 1185, 1025, 1015, 945, 905, 795, 740. ^{1}H NMR (90 MHz, $CDCl_3$): see Table 1. CD nm ($\Delta\varepsilon$): 330 (0), 309 (−0.64), 300 (−1.17), 292 (−1.20), 255 (0) (MeOH; *c* 0.334). EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 358 $[M]^+$ (56), 344 (4), 340 (2), 330 (2), 326 (6), 264 (15), 232 (10), 220 (21), 178 (30), 161 (18), 150 (12), 147 (16), 121 (22), 109 (13), 105 (25), 95 (100), 94 (93), 91 (38), 81 (36), 79 (37), 69 (36), 53 (28). (Found: C, 66.78; H, 6.18. Calc. for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19%.) Identical in all respects with the previously described compound [8–10] and with an authentic sample (mmp, TLC).

Teuscorodonin (**6**). Mp 189–191° (EtOAc–*n*-hexane); $[\alpha]_D^{22}$ +110.8° ($CHCl_3$; *c* 0.204); IR ν_{max}^{KBr} cm^{-1}: 3480 (hydroxyl), 3150, 1508, 880 (furan ring), 1760 (γ-lactone), 1740, 1670 (α,β-unsatd-γ-lactone), 2980, 2920, 2900, 1420, 1350, 1240, 1220, 1200, 1165, 1050, 1015, 980, 775, 745. UV λ_{max}^{EtOH} nm (log ε): 216 sh (3.95) (furan ring), 220 (4.00) (α,β-unsatd-γ-lactone). CD nm ($\Delta\varepsilon$): 260 (0), 250 (+2.16), 239 (0), 225 (−4.04), 210 (0) (MeOH; *c* 0.124). ^{1}H NMR (270 MHz, C_5D_5N): see Table 3. ^{13}C NMR (20.15 MHz, C_5D_5N): see Table 2. EIMS (direct inlet) 10 eV, *m/z* (rel. int.): 358 $[M]^+$ (6), 340 (5), 328 (9), 310 (10), 283 (4), 234 (16), 215 (9), 201 (8), 148 (15), 131 (10), 117 (10), 105 (14), 95 (100), 94 (38), 91 (22), 81 (34), 69 (24). (Found: C, 66.89; H. 6.09. $C_{20}H_{22}O_6$ requires: C, 67.02; H, 6.19%.)

19-*Acetyl teuscorodonin* (7). Obtained from **6** (45 mg) in the usual manner. Compound **7** was an amorphous solid, mp 74–80°; $[\alpha]_D^{24}$ +53.6° ($CHCl_3$; *c* 0.80); IR ν_{max}^{KBr} cm^{-1}: 3165, 3130, 1505, 880 (furan ring), 1770 (γ-lactone), 1760, 1670 (α,β-unsatd-γ-lactone), 1735, 1235 (acetate), 2980, 2895, 1475, 1390, 1375, 1165, 1105, 1040, 1010, 995, 810, 745. ^1H NMR (90 MHz, $CDCl_3$): see Table 3. (Found: C, 65.81; H, 5.92. $C_{22}H_{24}O_7$ requires: C, 65.99; H, 6.04%.)

Acknowledgements—J. L. M. thanks the Spanish CSIC for a fellowship. This work was supported in part by the 'Comisión Asesora de Investigación Científica y Técnica' (Madrid, grant No. 11/1981) and by the National Research Council (CNR, Rome). The financial support of the Spanish Foreign Ministry for travel facilities between Spain and Italy is gratefully acknowledged.

REFERENCES

1. Marco, J. L., Rodríguez, B., Savona, G. and Piozzi, F. (1982) *Phytochemistry* **21**, 2567.
2. Malakov, P. Y., Papanov, G. Y. and Mollov, N. M. (1979) *Z. Naturforsch. Teil B* **34**, 1570.
3. Martínez-Ripoll, M., Fayos, J., Rodríguez, B., García-Alvarez, M. C., Savona, G., Piozzi, F., Paternostro, M. and Hanson, J. R. (1981) *J. Chem. Soc. Perkin Trans.* 1, 1186.
4. Popa, D. P. and Reinbol'd, A. M. (1973) *Khim. Prir. Soedin.* **9**, 31.
5. Popa, D. P., Reinbol'd, A. M. and Rezvukhin, A. I. (1973) *Khim. Prir. Soedin.* **9**, 169.
6. Popa, D. P. and Reinbol'd, A. M. (1974) *Khim. Prir. Soedin.* **10**, 321.
7. Rogers, D., Unal, G. G., Williams, D. J., Ley, S. V., Sim, G. A., Joshi, B. S. and Ravindranath, K. R. (1979) *J. Chem. Soc. Chem. Commun.* 97.
8. Papanov, G. Y. and Malakov, P. Y. (1981) *Z. Naturforsch. Teil B* **36**, 112.
9. Reinbol'd, A. M. and Popa, D. P. (1974) *Khim. Prir. Soedin.* **10**, 589.
10. Papanov, G. Y. and Malakov, P. Y. (1980) *Z. Naturforsch. Teil B* **35**, 764.
11. Piozzi, F. (1981) *Heterocycles* **15**, 1489.
12. Kitazawa, E., Ogiso, A., Takahashi, S., Sato, A., Kurabayashi, M., Kuwano, H., Hata, T. and Tamura, C. (1979) *Tetrahedron Letters* 1117.
13. Kitazawa, E., Sato, A., Takahashi, S., Kuwano, H. and Ogiso, A. (1980) *Chem. Pharm. Bull.* **28**, 227.
14. Meinwald, J. and Lewis, A. (1961) *J. Am. Chem. Soc.* **83**, 2769.
15. Aranda, G., Bernassau, J. M. and Fétizon, M. (1977) *J. Org. Chem.* **42**, 4256.
16. Stapel, G., Menssen, H. G. and Snatzke, G. (1980) *Planta Med.* **38**, 366.
17. Herz, W., Pilotti, A., Söderholm, A., Shuhama, I. K. and Vichnewski, W. (1977) *J. Org. Chem.* **42**, 3913.
18. Wagner, H., Seitz, R., Lotter, H. and Herz, W. (1978) *J. Org. Chem.* **43**, 3339.
19. Bruno, M., Savona, G., Pascual, C. and Rodríguez, B. (1981) *Phytochemistry* **20**, 2259.
20. Savona, G., Paternostro, M., Piozzi, F. and Rodríguez, B. (1980) *Heterocycles* **14**, 193.
21. Luteijn, J. M., van Veldhuizen, A. and de Groot, A. (1982) *Org. Magn. Reson.* **19**, 95.
22. Eguren, L., Perales, A., Fayos, J., Rodríguez, B., Savona, G. and Piozzi, F. (1982) *J. Org. Chem.* **47**, 4157.
23. Gács-Baitz, E., Radics, L., Oganessian, G. B. and Mnatsakanian, V. A. (1978) *Phytochemistry* **17**, 1967.
24. Savona, G., Paternostro, M., Piozzi, F., Hanson, J. R., Hitchcock, P. B. and Thomas, S. A. (1979) *J. Chem. Soc. Perkin Trans.* 1, 1915.
25. Node, M., Sai, M. and Fujita, E. (1981) *Phytochemistry* **20**, 757.