Phytochemistry, Vol 28, No 10, pp 2763–2768, 1989
Printed in Great Britain

0031-9422/89 $3.00+0.00

NEO-CLERODANE DITERPENOIDS FROM *TEUCRIUM KOTSCHYANUM*

FÁTIMA SIMOES, BENJAMÍN RODRÍGUEZ, MAURIZIO BRUNO,* FRANCO PIOZZI,* GIUSEPPE SAVONA* and NELLY APOSTOLIDES ARNOLD†

Instituto de Química Orgánica, CSIC, Juan de la Cierva 3, 28006 Madrid, Spain, *Department of Organic Chemistry, University of Palermo, Archirafi 20, 90123 Palermo, Italy, †Istituto di Botanica Farmaceutica, Università di Camerino, 62032 Camerino, Italy

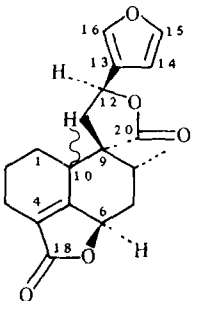
(*Received* 19 *January* 1989)

Key Word Index—*Teucrium kotschyanum*; Labiatae, *neo*-clerodane diterpenoids; 12-epiteucvidin, 12-epiteuflin; teukotschyn

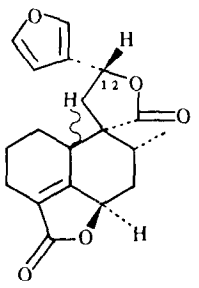
Abstract—From the aerial parts of *Teucrium kotschyanum* three new *neo*-clerodane diterpenoids have been isolated. Their structures, (12*R*)-15,16-epoxy-19-*nor*-10α-*neo*-cleroda-4,13(16),14-triene-18,6β; 20,12-diolide (12-epiteucvidin), (12*R*)-15,16-epoxy-19-*nor*-*neo*-cleroda-4,13(16),14-triene-18,6β; 20,12-diolide (12-epiteuflin) and (12*S*,18*R*)-15,16-epoxy-6β-hydroxy-*neo*-cleroda-13(16),14-dien-20,12-olide-18,19-hemiacetal (teukotschyn), have been established by chemical and spectroscopic means. In addition, ursolic acid, the flavones cirsimaritin and cirsiliol, and six previously known *neo*-clerodane diterpenoids (teucvidin, teuflin, teuscorodin, teucrin H2, teuscorodonin and montanin D) were also found in the same plant.

INTRODUCTION

In a previous communication [1] we reported the isolation of a new diterpenoid, isoteucrin H4, and a known substance, teucrin H4 [2, 3], from the acetone extract of the aerial parts of *Teucrium kotschyanum* Poech (synonym *T. smyrnaeum* Boiss). Further studies on the same extract allowed the isolation of ursolic acid, cirsimaritin (5,4′-dihydroxy-6,7-dimethoxyflavone) [4], cirsiliol (5,3′,4′-trihydroxy-6,7-dimethoxyflavone) [4], the already known *neo*-clerodane derivatives teucvidin (**1**) [2, 5], teuflin (**2**) [2, 6], teuscorodin (**3**) [2, 7], teucrin H2 [2, 3], teuscorodonin [2, 7] and montanin D [2, 8], and three new diterpenoids, 12-epiteucvidin (**4**), 12-epiteuflin (**5**) and teukotschyn (**6**), whose structures have now been established.



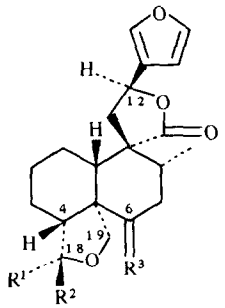
1 H-10α
2 H-10β



4 H-10α
5 H-10β

RESULTS AND DISCUSSION

The first of the new diterpenoids (12-epiteucvidin, **4**), $C_{19}H_{20}O_5$, had an IR spectrum which showed furanic (3150, 1510, 880 cm^{-1}), γ-lactone (1770 cm^{-1}) and α,β-unsaturated γ-lactone (1750, 1600 cm^{-1}) absorptions. The presence in compound **4** of an α,β-unsaturated γ-lactone group was confirmed by its UV absorption at λ_{max} 221 nm (log ε 4.05) [1, 5]. The ^1H NMR spectrum of compound **4** was almost identical with that of teucvidin (**1**, Table 1), a 19-*nor*-*neo*-clerodane diterpenoid whose structure is well known [5], even by an X-ray diffraction analysis [9] In fact, the ^1H NMR spectra of compounds **1** and **4** showed only small differences in the chemical shifts corresponding to the H-10α, H-12, C-11 methylene and C-17 methyl protons (Table 1) which, in principle, could be attributed to an opposite stereochemistry at the C-12 centre in both diterpenoids [10, 11]. The above presumption was also in agreement with the ^{13}C NMR spectra of these compounds (**1** and **4**, Table 2), as marked differences in the chemical shift of the C-8, C-9, C-10, C-11 and C-13



	R^1	R^2	R^3
3	H	OH	O
6	H	OH	αH,βOH
7	H	OAc	αH,βOAc
8	H	OAc	O
9	O		O

Table 1 ^{1}H NMR data of compounds **1**, **2**, **4** and **5** (300 MHz, $CDCl_3$, TMS as internal standard)

	1*	2	4	5
H-6α	5 00 *br t*†	5 74 *br dd*†	5 02 *br dd*†	5 51 *br dd*†
H-10α	3 27 *br t*†	—	3 37 *br t*†	-
H-10β	—	~2 75‡	—	§
H_A-11	1 92 *dd*	§	2 20 *dd*	§
H_B-11	2 59 *dd*	§	2 26 *dd*	§
H-12	5 36 *t*	5 38 *dd*	5 41 *dd*	5 50 *t*
H-14	6 36 *dd*	6 42 *dd*	6 38 *dd*	6 39 *dd*
H-15	7 44‡	7 47‡	7 46 *t*	7 47‡
H-16			7 48 *m*	
Me-17	1 36 *d*	1 23 *d*	1 28 *d*	1 31 *d*
J (Hz)				
6α,7α	7 0	5 4	8 5	5 6
6α,7β	10.0	12 7	10 9	12 6
8β,17	7 3	7 3	7 4	7 3
10α or β,1α	$W_{1/2}$ = 14 5 Hz	‡	6 4	§
10α or β,1β		‡	6 4	§
11A,11B	13 9	§	13 3	§
11A,12	7 5	7 6	6 8	8 5
11B,12	8 2	10 0	9 3	8 5
14,15	1 9	1 8	1 8	1 8
14,16	0 8	0 9	0 9	0 9
15,16	‡	‡	1 8	‡

*These data have been specially obtained by us for this work and are in complete agreement with the previously reported values [5]

†Broadened signals due to homoallylic couplings

‡Overlapped signal

§These signals were not identified in the spectrum of the mixture of **2** and **5**

carbons were observed, whereas the other carbons appeared at almost identical field in both compounds. A similar behaviour has been pointed out previously [11] for some pairs of C-12 epimers of *neo*-clerodane derivatives belonging to the H-10β series

Final proof on the relative stereochemistry depicted in **4** for the new diterpenoid was achieved by NOE experiments Irradiation of the C-17 methyl protons of compound **4** (δ 1.28) produced a 2% NOE enhancement of the H-12 signal (δ 5 41), thus establishing that the C-12 methine proton and the C-17 methyl protons are on the same side of the plane defined by the C-20–C-12 lactone ring [11–13] On the contrary, when the C-17 methyl protons of teucvidin (**1**) [5, 9] were irradiated, no NOE was observed in the signal of its H-12 proton In both cases, strong and almost identical NOE enhancements were also produced in the signals of the H-6α and H-10α protons (Table 3). These results clearly established that teucvidin (**1**) and the new diterpenoid (**4**) possessed an identical substituted decalin moiety, with ring B in a distorted boat conformation in which the C-17 methyl group is pseudoaxially oriented [5] Thus, the structural difference between these two compounds was the stereochemistry at the C-12 centre Since the C-12 (*S*) configuration of teucvidin (**1**) is well known [5, 9], it was clear that compound **4** was the C-12 (*R*) epimer of this diterpenoid and so, it was named 12-epiteucvidin

The *neo*-clerodane [14] absolute configuration of 12-epiteucvidin (**4**) was supported by its specific rotation values ($[\alpha]_D^{22}$ − 155 7°, $[\alpha]_{578}^{22}$ − 163.3°, $[\alpha]_{546}^{22}$ − 187 3°, $[\alpha]_{436}^{22}$ − 338 6°, $[\alpha]_{365}^{22}$ − 577 8°), which showed a similar variation that those of teucvidin (**1**, $[\alpha]_D^{22}$ − 66 3°, $[\alpha]_{578}^{22}$ − 70.2°, $[\alpha]_{546}^{22}$ − 81 8°, $[\alpha]_{436}^{22}$ − 159 1°, $[\alpha]_{365}^{22}$ − 301 7°) Moreover, biogenetic grounds were also in agreement with this conclusion, as all the diterpenoids until now isolated from *Teucrium* species belong to the *neo*-clerodane series [2]

An inseparable mixture of teuflin (**2**) [2, 6] and its C-12 epimer (**5**, 12-epiteuflin), in a 2.3 ratio respectively, was also isolated from *T kotschyanum* This mixture showed only one spot on TLC with several solvents and we could not separate it into its constituents even by crystallization promoted with pure teuflin and by slow sublimation.

Combustion analysis and mass spectrometry established that both constituents of the mixture possessed the same molecular formula ($C_{19}H_{20}O_5$).

The ^{1}H and ^{13}C NMR spectra of this mixture showed a series of signals corresponding to the minor constituent which were rigorously identical with those reported for teuflin (**2**) [6], whereas the remaining signals of the major constituent were only compatible with a structure such as **5** (Tables 1 and 2) Effectively, the C-17 methyl protons resonance of compound **5** appeared at slightly lower field than in teuflin (**2**, Δδ + 0 08), which was in agreement with a C-12 (*R*) configuration for the former (**5**) [10, 11] as the C-12 (*S*) stereochemistry of the latter (**2**) is well known [6] Moreover, the ^{13}C NMR spectrum of the mixture (Table 2, compounds **2** and **5**) showed that the C-8 carbon atom

Table 2 ^{13}C NMR chemical shifts of compounds **1**, **2**, **4**, **5** and **7***

C	1†	2‡	4	5	7
1	20.02 *t*§	18 76 *t*	19.62 *t*	19.38 *t*	23 16 *t*
2	23 36 *t*	23.77 *t*‖	22.96 *t*	23 39 *t*‖	25 15 *t*
3	21 38 *t*	23 39 *t*‖	21 38 *t*	22 95 *t*‖	26 90 *t*
4	127 75 *s*	123.67 *s*	126 70 *s*	123 99 *s*	44.50 *d*
5	162.24 *s*	166.25 *s*	162 95 *s*	167 13 *s*	48.15 *s*
6	76.10 *d*	76.74 *d*	75 86 *d*	76 60 *d*	70 32 *d*
7	35.69 *t*	31.83 *t*	35 76 *t*	32 79 *t*	31 45 *t*
8	38 72 *d*	35.95 *d*	33.02 *d*‖	39 22 *d*¶	33.23 *d*
9	52.09 *s*	51 06 *s*	54 15 *s*	50 77 *s*	51 20 *s*
10	35.81 *d*	43 23 *d*	33 21 *d*‖	40.90 *d*¶	47 84 *d*
11	39 00 *t*	42 80 *t*	36.49 *t*	42 94 *t*	42.63 *t*
12	71 94 *d*	71 60 *d*	71.32 *d*	71 71 *d*	73 31 *d*
13	125.22 *s*	124.32 *s*	123 65 *s*	124 74 *s*	125.24 *s*
14	107 91 *d*	107.89 *d*	107.98 *d*	107.83 *d*	108.06 *d*
15	144 39 *d*	144 38 *d*	144.32 *d*	144 38 *d*	144 18 *d*
16	139 46 *d*	139 92 *d*	139 98 *d*	139 74 *d*	139 54 *d*
17	14 30 *q*	17.65 *q*	14 84 *q*	18 93 *q*	16 52 *q*
18	172 59 *s*	173 78 *s*	172 66 *s*	173.84 *s*	102 61 *d*
19	—	—	—	—	71 78 *t*
20	177.64 *s*	175 96 *s*	176.80 *s*	176.51 *s*	176 91 *s*
OAc	—	—	—	—	171 05 *s*
	—	—	—	—	169 87 *s*
	—	—	—	—	21 44 *q*
	—	—	—	—	21.35 *q*

*In δ values from TMS, at 75.4 MHz, in $CDCl_3$ solution.

†These data have been specially obtained by us for this work and are in complete agreement with the previously reported values [20, 21].

‡These values are identical with those previously reported [6].

§SFORD multiplicity

‖These assignments may be interchanged.

¶These assignments may also be interchanged, but those given here are considered to be the most likely

Table 3. NOE enhancement (%) by irradiating the Me-17 protons of compounds **1**, **4** and **6**

Compound	δMe-17	H-6α	H-10α	H-12	H-14	H-16
1	1.36	7	9	0	2	1.5
4	1 28	7 5	9	2	0	0
6	0 98	0*	—	0	2 8	0.8

*In compound **6** the H-6α proton and the Me-17 group are in a 1,3-diequatorial relationship and, consequently, widely separated for causing an NOE

resonance of the major constituent (**5**) was downfield shifted ($\Delta\delta + 3$ 27) and that the C-10 carbon atom resonance was upfield shifted ($\Delta\delta - 2.33$) with respect to those of teuflin (**2**), whereas the remaining signals appeared at almost identical field in both compounds (Table 2) and the small differences in their chemical shifts were in complete agreement with those reported for teucvin and its C-12 epimer [11], two 19-*nor*-*neo*-clerodanes belonging to the H-10β series.

From the above data, it was evident that the mixture consisted of teuflin (**2**) [6] and a new diterpenoid, 12-epiteuflin (**5**), which differs from teuflin only in its stereochemistry at C-12. The possibility that compound **5** could be a C-6 and/or a C-10 epimer of **2** was also considered but was discarded because two of these epimers, teucvidin (**1**) [5] and teucvin (H-6β teuflin) [2, 5, 11], are known and they show large ^1H and ^{13}C NMR spectroscopic differences from teuflin (**2**) and 12-epiteuflin (**5**).

Although the absolute stereochemistry of the constituents of this mixture was not ascertained, it is reasonable to assume that both compounds possess a *neo*-clerodane absolute configuration [14], as all the diterpen-

Table 4 ^{1}H NMR data of compounds **6** and **7** (300 MHz, $CDCl_3$, TMS as internal standard)

	6	**7**
H-4β	*	2 27 *dd*†‡
H-6α	4 42 *t*	5 39 *t*
H-10β	*	2.18 *dd*
H_A-11	2 36 *dd*	2.38 *dd*
H_B-11	2 46 *dd*	2 48 *dd*
H-12	5 32 *t*	5 34 *t*
H-14	6 39 *dd*	6 39 *dd*
H-15	7 44†	7 45†
H-16		
Me-17	0 98 *d*	0 97 *d*
H-18α	5 02 *s*	5 71 *s*
H_A-19	3 91 *d*	4 00 *d*
H_B-19	4 20 *d*	4 28 *d*
OAc	—	2 10 *s*
	—	2 00 *s*
J (Hz)		
4β,3α	†	9 6‡
4β,3β	†	5 7‡
6α,7α	2 3	3 2
6α,7β	2 3	3 2
8β,17	6 6	6 6
10β,1α	†	11 1
10β,1β	†	2 0
11A,11B	14 0	14 0
11A,12	8.9	8 9
11B,12	8.4	8 4
14,15	1 6	1 6
14,16	1 1	1 1
15,16	†	†
18α,4β	0	0
19A,19B	10 2	10 8

*These signals were not identified

†Overlapped signal

‡This signal and its coupling constants were observed in the NOE differential spectrum of compound **7** (see discussion of results)

oids isolated from *Teucrium* species [1, 2], including teuflin (**2**) itself.

The last of the new diterpenoids isolated from *T kotschyanum* has been named teukotschyn (**6**) and its molecular formula was $C_{20}H_{26}O_6$. The IR spectrum of this substance showed hydroxyl (3430 cm^{-1}), furanic (3150, 3120, 1510, 878 cm^{-1}) and γ-lactone (1765 cm^{-1}) absorptions. The ^{1}H NMR spectrum of teukotschyn (**6**, Table 4) was very similar to that of teuscorodin (**3**) [7] with characteristic signals for a β-substituted furan ring, a γ-lactone group between the C-20 and C-12 positions, a secondary methyl group (Me-17) and a C-18–C-19 hemiacetalic ring. In addition, the ^{1}H NMR spectrum of teukotschyn (**6**) showed a one-proton triplet at δ4 42 (J = 2.3 Hz) which must be attributed to the equatorial proton geminal to a C-6β hydroxyl group [2, 15]. This suggested that the new diterpenoid was identical with teuscorodin (**3**) except in the functionality at the C-6 position.

Acetic anhydride–pyridine treatment of teukotschyn (**6**) yielded the diacetyl derivative **7**, the ^{1}H NMR spectrum of which (Table 4) showed paramagnetically shifted the signals of the H-6α and H-18α protons (at δ5 39 and 5 71, respectively). Comparison between the ^{13}C NMR spectra of the derivative **7** (Table 2) and acetylteuscorodin (**8**) [7] clearly revealed that compound **7** possessed a C-6β acetoxyl group instead of the C-6 ketone function of **8**, since the C-8 and C-10 γ-carbons and the C-5 and C-7 β-carbons appeared at higher field in compound **7** than in **8** ($\Delta\delta$ −8.17, −3 76, −11 75 and −10 15, respectively).

The signal of the hemiacetalic proton of teukotschyn (**6**, δ5 02) and its diacetate (**7**, δ5 71) appeared as singlets, without coupling with the H-4β proton, as in the case of teuscorodin (**3**) [7]. However, it is reported [7] that acetylteuscorodin (**8**) shows a doublet ($J_{18,4\beta}$ = 5 Hz) for its H-18α hemiacetalic proton. This different behaviour of compounds **3** and **8** has been explained [7] considering that in the derivative **8** the C-18β acetate–C-6 ketone steric interactions force the C-18–C-19 hemiacetalic ring to adopt a conformation in which the H-18α–H-4β dihedral angle is larger than 90°, whereas in compound **3** it is close to 90°. Although these reasons were applicable to teukotschyn (**6**) and its diacetate **7**, since in the latter compound the steric interactions between the C-18β and C-6β acetates are not of importance, we considered that the location and the stereochemistry of the hemiacetalic ring of teukotschyn required further support, and this was achieved as follows.

When the H-18 proton of compound **7** (δ5 71) was irradiated under the conditions of the NOE experiment, a noticeable NOE enhancement (11%) was observed in an overlapped signal at δ2 27, besides a minor NOE enhancement in the H_A-19 proton (at δ4 00, 1%). The NOE differential spectrum of compound **7** clearly showed that the signal at δ2 27 was a double doublet (J_1 = 9.6 Hz, J_2 = 5.7 Hz) identical with that of the H-4β proton of teuscorodin (**3**, δ2 67 *dd*, J_1 = 9 Hz, J_2 = 6 Hz) [7]. This result firmly established that the hemiacetal group of teukotschyn was at C-18 and not at the C-20 position, and also that its configuration was the same as that in compound **3**.

The above conclusion was also in agreement with the chemical shift of the H-12 and C-19 methylene protons of teukotschyn (**6**, at δ5 32 and an AB system centred at δ4 05, respectively, Table 4), since in compounds having a C-20–C-12 hemiacetalic ring or a C-18–C-19 γ-lactone group these protons appear at δ4.95–5 20 [2, 16] and δ4 50–4 65 [2, 7], respectively.

Nuclear Overhauser effect experiments established a *cis*-relationship between the Me-17 and the furan ring of teukotschyn (**6**). Irradiation at its C-17 methyl protons signal (δ0 98) caused NOE enhancements in the signals of the H-14 (δ6 39, 2 8%) and H-16 (δ7 44, 0.8%) protons, whereas no effect was observed in the signal of the H-12 proton (δ5 32, Table 3). Thus, teukotschyn (**6**) had a C-12 (*S*) configuration [12], if its absolute configuration was of *neo*-clerodane [14].

Finally, treatment of teukotschyn with chromium trioxide–pyridine yielded a compound (**9**) identical in all respects (mp, mmp, $[\alpha]_D$, IR, ^{1}H NMR, mass spectrum) with 6-ketoteuscordin, previously isolated from *Teucrium scordium* [2, 17] and known as synthetic derivative of teucrin E [18], teucrin H2 (teuchamaedryn B) [19] and teuscorodin (**3**) [7]. This result established a *neo*-clerodane absolute stereochemistry [14] for teukotschyn and

confirmed all the above conclusions on the structure (**6**) of this new diterpenoid.

From a biogenetic point of view it is of interest to note that *Teucrium kotschyanum* is one of the few species belonging to the *Teucrium* genus in which *neo*-clerodane diterpenoids of the C-12 (*R*) series have been found [2].

EXPERIMENTAL

Mps uncorr Plant materials were collected in July 1987, at Cedars Valley, Cyprus, 10 km east of Stavros, and voucher specimens were deposited in the Herbarium of the Botanic Gardens of Camerino and Catania, Italy

Extraction and isolation of the constituents Dried and finely powdered *T kotschyanum* aerial parts (500 g) were extracted × 3 with Me_2CO (5 l) at room temp for 1 week After filtration the solvent was evapd yielding a gum (36 g) which was repeatedly chromatographed over silica gel (Merck, No 7734, deactivated with 15% H_2O) dry columns with *n*-hexane–EtOAc mixtures as eluents, yielding the following compounds in order of increasing chromatographic polarity teucvidin (**1**, 28 mg) [5], 12-epiteucvidin (**4**, 16 mg), a mixture (30 mg) of teuflin (**2**) [6] and 12-epiteuflin (**5**), teuscorodin (**3**, 50 mg) [7], ursolic acid (3 mg), teucrin H2 (20 mg) [3, 19], the flavone cirsimaritin (15 mg) [4], teuscorodonin (500 mg) [7], isoteucrin H4 (22 mg) [1], montanin D (130 mg) [8], teukotschyn (**6**, 43 mg), teucrin H4 (110 mg) [1, 3] and the flavone cirsiliol (12 mg) [4] The previously known compounds were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (IR, UV, ^{1}H NMR, MS) data and by comparison (mmp, TLC) with authentic samples

12-*Epiteucvidin* (**4**) Mp 190–194° (EtOAc–*n*-hexane), $[\alpha]_D^{22}$ −155 7° ($CHCl_3$, *c* 0 158), IR ν_{max}^{KBr} cm^{-1}· 3150, 1510, 880 (furan ring), 1770 (γ-lactone), 1750, 1600 (α,β-unsaturated γ-lactone), 2950, 2880, 2860, 1455, 1390, 1350, 1320, 1240, 1210, 1185, 1175, 1160, 1085, 1070, 1040, 1030, 1005, 995, 970, 940, 810, 740, 690; UV λ_{max}^{MeOH} nm (log ε). 221 (4 05), 230 (3 93), 240 (3 56); ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1, ^{13}C NMR (75 4 MHz, $CDCl_3$) see Table 2, EIMS (direct inlet) 70 eV, *m/z* (rel int.) 328 $[M]^+$ (9), 313 (2), 300 (0 5), 285 (0.5), 283 (0 7), 234 (9), 205 (7), 161 (5), 105 (6), 95 (23), 94 (100), 91 (9), 81 (7), 79 (10), 77 (10), 41 (6). (Found· C, 69 36; H, 6 23 $C_{19}H_{20}O_5$ requires C, 69 50, H, 6 14%.)

Mixture of teuflin (**2**) [6] *and 12-epiteuflin* (**5**). An amorphous solid, IR ν_{max}^{KBr} cm^{-1} 3150, 1510, 878 (furan rings), 1760 *br* (γ-lactones and α,β-unsaturated γ-lactones), 2950, 2880, 1460, 1390, 1325, 1210, 1180, 1155, 1025, 968, 730 ^{1}H NMR (300 MHz, $CDCl_3$) see Table 1, ^{13}C NMR (75 4 MHz, $CDCl_3$): see Table 2 EIMS (direct inlet) 70 eV, *m/z* (rel int.) 328 $[M]^+$ (35), 313 (7), 300 (6), 283 (19), 233 (67), 201 (38), 189 (19), 161 (23), 105 (22), 95 (100), 94 (30), 91 (37), 81 (45), 79 (33), 77 (38), 55 (16), 41 (77). (Found C, 69 63; H, 6 09 Calc for $C_{19}H_{20}O_5$ C, 69 50; H, 6.14%)

Teukotschyn (**6**) An amorphous solid which melted at 95–105°; $[\alpha]_D^{22}$ −5 7° ($CHCl_3$; *c* 0.317), IR ν_{max}^{KBr} cm^{-1}. 3430 (hydroxyl groups), 3150, 3120, 1510, 878 (furan ring), 1765 (γ-lactone), 2940, 2870, 1480, 1460, 1450, 1390, 1320, 1212, 1185, 1160, 1150, 1075, 1060, 1025, 1000, 960, 930, 800; ^{1}H NMR (300 MHz, $CDCl_3$). see Table 4, EIMS (direct inlet) 70 eV, *m/z* (rel int)· 362 $[M]^+$ (4), 344 (71), 326 (9), 314 (9), 271 (13), 250 (33), 222 (23), 179 (24), 161 (32), 159 (21), 147 (22), 136 (22), 133 (21), 123 (25), 107 (21), 105 (35), 95 (100), 94 (52), 91 (51), 81 (62), 77 (29), 55 (27), 41 (42) (Found C, 66.41, H, 7 17 $C_{20}H_{26}O_6$ requires C, 66 28; H, 7 23%)

Diacetylteukotschyn (**7**). Ac_2O–pyridine treatment of **6** (15 mg) 48 hr at room temp yielded the derivative **7** (12 mg after crystallization from EtOAc–*n*-hexane): mp 136–138°; $[\alpha]_D^{22}$ −58.3° ($CHCl_3$, *c* 0.024), IR ν_{max}^{KBr} cm^{-1}: 3140, 1507, 875 (furan ring), 1765 (γ-lactone), 1745, 1735, 1250 (acetates), 2960, 2860, 1445, 1380, 1210, 1185, 1160, 1145, 1025, 995, 930; ^{1}H NMR (300 MHz, $CDCl_3$): see Table 4; ^{13}C NMR (75 4 MHz, $CDCl_3$). see Table 2, EIMS (direct inlet) 70 eV, *m/z* (rel int.): 446 $[M]^+$ (2), 387 (14), 386 (28), 326 (19), 271 (28), 232 (24), 231 (29), 122 (20), 121 (26), 105 (21), 96 (76), 95 (66), 94 (26), 91 (44), 81 (66), 79 (27), 77 (26), 55 (21), 43 (100). (Found C, 64 63; H, 6.68. $C_{24}H_{30}O_8$ requires C, 64 56, H, 6.77%)

6-*Ketoteuscordin* (**9**) *from teukotschyn* (**6**). CrO_3–pyridine oxidation of **6** (20 mg) in the usual manner yielded a compound [13 mg after crystallization from EtOAc–*n*-hexane, mp 204–206°, $[\alpha]_D^{22}$ +38.8° ($CHCl_3$; *c* 0.231)] identical in all respects (IR, ^{1}H NMR, MS) with 6-ketoteuscordin [**9**· lit. [7] mp 203–205°, $[\alpha]_D^{24}$ +38.4° ($CHCl_3$, *c* 0.375)]. Comparison (mmp, TLC) with an authentic sample also confirmed this identity.

Acknowledgements—This work was subsidized by the Spanish "Dirección General de Investigación Científica y Técnica" (Grant No PB87-0418), 'Scientific Research Funds' of the Italian Ministry of Education and by the "Programa conjunto No. 7" CSIC (Spain)-CNR (Italy). One of us (F S.) thanks the Portuguese Ministry of Education for a fellowship.

REFERENCES

1. Simoes, F., Rodríguez, B., Piozzi, F., Savona, G , Bruno, M. and Arnold, N. A. (1989) *Heterocycles* **28**, 111.
2 Piozzi, F., Rodríguez, B. and Savona, G. (1987) *Heterocycles* **25**, 807
3. Gács-Baitz, E., Radics, L , Oganessian, G. B. and Mnatsakanian, V. A. (1978) *Phytochemistry* **17**, 1967.
4 Wollenweber, E. and Dietz, V. H (1981) *Phytochemistry* **20**, 869
5. Uchida, I., Fujita, T and Fujita, E. (1975) *Tetrahedron* **31**, 841.
6 Savona, G., Paternostro, M., Piozzi, F., Hanson, J. R , Hitchcock, P. B. and Thomas, S. A. (1979) *J. Chem. Soc. Perkin Trans I* 1915.
7. Marco, J. L , Rodríguez, B., Pascual, C., Savona, G. and Piozzi, F. (1983) *Phytochemistry* **22**, 727.
8. Malakov, P. Y , Papanov, G Y., Mollov, N. M. and Spassov, S L (1978) *Z. Naturforsch. B* **33**, 1142.
9 Uchida, I., Fujita, E., Taira, Z and Osaki, K. (1974) *Cryst. Struct Commun.* **3**, 569.
10 Takahashi, S., Kurabayashi, M , Kitazawa, E., Haruyama, H. and Ogiso, A. (1983) *Phytochemistry* **22**, 302
11. Fayos, J , Fernández-Gadea, F., Pascual, C., Perales, A., Piozzi, F., Rico, M., Rodríguez, B and Savona, G. (1984) *J. Org. Chem.* **49**, 1789
12. Pascual, C , Fernández, P , García-Alvarez, M. C., Marco, J L., Fernández-Gadea, F., de la Torre, M. C., Hueso-Rodríguez, J. A., Rodríguez, B., Bruno, M., Paternostro, M., Piozzi, F and Savona, G. (1986) *Phytochemistry* **25**, 715
13 Gács-Baitz, E., Papanov, G. Y., Malakov, P. Y. and Szilagyi, L (1987) *Phytochemistry* **26**, 2110.
14 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.
15. Marco, J L., Rodríguez, B , Savona, G. and Piozzi, F. (1982) *Phytochemistry* **21**, 2567.
16. Jakupovic, J , Baruah, R. N , Bohlmann, F. and Quack, W. (1985) *Planta Med.* 341.

17 Papanov, G Y and Malakov, P Y (1981) *Z Naturforsch. B* **36**, 112
18 Reinbol'd, A M and Popa, D P (1974) *Khim Prir Soedin* **10**, 589
19 Papanov, G Y and Malakov, P. Y (1980) *Z Naturforsch B* **35**, 764
20 Savona, G, Paternostro, M, Piozzi, F, Hanson, J R, Hitchcock, P B and Thomas, S A (1978) *J Chem Soc Perkin Trans 1* 1080
21. Savona, G, Piozzi, F, Rodríguez, B, Pascual, C and Servettaz, O (1986) *Phytochemistry* **25**, 2857