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TEULAMIFIN B, A NEO-CLERODANE DITERPENOID FROM *TEUCRIUM LAMIIFOLIUM* AND *T. POLIUM*

PETER Y. MALAKOV, IVA M BONEVA,* GEORGI Y PAPANOV and STEFAN L. SPASSOV†

Department of Organic Chemistry, Plovdiv University, 4000 Plovdiv, *Department of Chemistry, Higher Institute of Agriculture 'V Kolarov', 4000 Plovdiv, Bulgaria, †Institute of Organic Chemistry Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria

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Key Word Index—*Teucrium lamiifolium*, *Teucrium polium*, Labiatae, neo-clerodane derivatives, teulamifin B, 19-deacetylteuscorodol, teucroxide

Abstract—From the aerial parts of *Teucrium lamiifolium and T polium*, a neo-clerodane diterpenoid, teulamifin B has been isolated, besides the previously known diterpenoids 19-deacetylteuscorodol and teucroxide The structure of teulamifin B[15,16-epoxy-6β,12*S*,18-trihydroxy-neo-cleroda-3,13(16),14-trien20,19-olide] was established by chemical and spectroscopic means and by correlation with 19-deacetylteuscorodol

INTRODUCTION

In previous communications, we reported the isolation of teuscordin, teuflin, montanin C, 19-acetylgnaphalin, isoteuflidin [1] and 12-epiteupolin II [2] as diterpenoid constituents of *T lamiifolium*. In this communication, we report the isolation and structural determination of a new diterpenoid, teulamifin B(**1**) which has been isolated from the same plant as well as from *T polium* (var *polium*), besides the previously described diterpenoids 19-deacetylteuscorodol [3] and teucroxide [4]

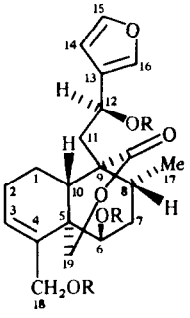
RESULTS AND DISCUSSION

Teulamifin B(**1**) had a molecular formula of $C_{20}H_{26}O_6$, from the elemental analysis and mass spectroscopy. Its IR spectrum was consistent with the presence of a furan ring (3140, 1500, 875 cm^{-1}), a δ-lactone ring (1700 cm^{-1}) and hydroxyl groups (3430, 3300 cm^{-1}) Its ^1H NMR and ^{13}C NMR spectra (Tables 1 and 2) supported the structure **1** However its mp (207–209°) as well as some of the ^{13}C NMR parameters were markedly different from these recently reported [3] for teubotrin(mp 110–114°), a diterpenoid isolated from *T botrys* and possessing the same structure, with C-12 stereochemistry unknown

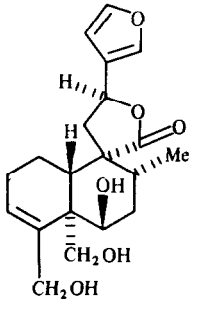
As expected, the IR, ^1H NMR and mass spectral parameters of teulamifin B(**1**) and teubotrin [3] were very similar Significant differences in the ^{13}C NMR chemical shifts (1.5–3 ppm) were observed for the carbon adjacent to the C-12 chiral centre as well as for the olefinic C-3 and C-4.

A final proof that teulamifin B(**1**) has the structure and absolute configuration depicted in formula **1** was obtained by sodium hydroxide treatment [5] of 19-deacetylteuscorodol (**3**) [3] which yielded a compound identical in all respects (mp, mmp $[\alpha]_D$, IR, ^1H NMR and MS) with natural teulamifin B.

Acetylation of teulamifin B(**1**) yielded the triacetate (**2**) which showed very similar spectral parameters to those of teubotrin triacetate [3]



1 R = H
2 R = Ac



3

EXPERIMENTAL

Mps uncorr., ^1H NMR and ^{13}C NMR at 250.1 MHz and 50 MHz, respectively with TMS as int standard Plant materials of *T lamiifolium* were collected in July 1984 near Malko Tirnovo, while those of *T polium* were collected in July 1982 near Plovdiv

Extraction and isolation of the diterpenoids from T lamiifolium Dried and finely powdered *T lamiifolium* aerial parts (1.28 kg) were extracted as described in previous papers [1, 2] The $CHCl_3$ extract (6 g) was chromatographed over silica gel column (110 g, Merck N 7734, deactivated with 10% H_2O) Elution with CH_2Cl_2, CH_2Cl_2–MeOH mixture and CH_2Cl_2–MeOH (99:1) gave teulamifin B(**1**), (100 mg) and 19-deacetylteuscorodol (**3**) (210 mg) [3] Further elution with CH_2Cl_2–MeOH (97:3) yielded teocroxide (240 mg) [4] Teulamifin B(**1**) on recrystallization from Me_2CO–petrol showed mp 207–209°, $[\alpha]_D^{20}$ −49.3° (Me_2CO, *c* 0.23), IR ν_{max}^{KBr} cm^{-1} 3430, 3300, 2980, 2940, 1700, 1480, 1180, 1120, 1040, 875 EIMS (direct inlet 70 eV, *m/z* (rel. int.). 362 $[M]^+$ (60), 344 $[M-H_2O]^+$ (15), 326 $[M-2H_2O]^+$ (10), 314 (8), 296, (6), 95, (80), 91, (70), 41,

(100). Found: C, 66.00; H, 7.38. $C_{26}H_{26}O_6$ requires: C, 66.28; H, 7.23%. ^{1}H NMR and ^{13}C NMR: see Table 1 and 2.

Isolation of teulamifin B(**1**) *from* T. polium. The chromatographic fractions obtained before elution of montanin E[6] were evaporated to dryness and the residue (320 mg) was chromatographed on a silica gel column (Merck No. 7734, deactivated with 10% H_2O, 160 g), eluted with $CHCl_3$–MeOH (98:2) to give teulamifin B(90 mg) and 19-deacetylteuscorodol (38 mg) [3].

Acetylation of teulamifin B(**1**). Ac_2O–pyridine treatment of **1** (38 mg) in the usual manner gave the triacetate (**2**) (38 mg), as a colourless resin. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2940, 1735 (*br*), 1450, 1380, 1250 (*br*), 1020, 880. ^{1}H NMR: see Table 1. EIMS (70 eV), *m/z* (rel. int.) (direct inlet): 488 $[M]^+$ (3), 446 $[M-C_2H_2O]^+$ (20), 428 (30), 326 (15), 43 $[MeCOO]^+$ (100).

Preparation of teulamifin B(**1**) *from 19-deacetylteuscorodol* (**3**). 19-Deacetylteuscorodol (**3**), (70 mg) dissolved in MeOH (4 ml) was added to a 2% soln of NaOH and the mixture was refluxed for 2 hr and then extracted with CH_2Cl_2. The extract was

Table 1. ^{1}H NMR spectral data of compounds **1**, **2** and **3** (TMS as int. standard)*

H	**1** (Pyridine-d_5)†	**1** ($CDCl_3$)†	**2** ($CDCl_3$)	**3** (Pyridine-d_5)
1α	1.56 *m*		1.48 *m*	2.15 *m*
1β	2.84 *m*		2.40 *m*‡	1.93 *m*‡
2α	2.12 *m*‡		2.05 *m*‡	2.26 *m*
2β	2.32 *m*		2.20 *m*	2.26 *m*
3	5.93 *m*	6.01 *t*	5.96 *m*	6.02 *t*
6α	4.75 *m*	4.29 *m*	5.17 *t*	5.09 *m*‡
7α	1.97 *m*		1.70 *m*	2.60 *m*‡
7β	2.12 *m*		1.70 *m*	1.93 *m*‡
8β	3.07 *m*		2.22 *dd*	2.60 *m*‡
10β	3.55 *dd*	2.79 *dd*	2.40 *m*‡	2.76 *dd*
11A	2.70 *dd*	2.24 *dd*	2.40 *m*‡	2.50 *d*
11B	2.96 *dd*		2.62 *dd*	2.50 *d*
12	5.32 *dd*	4.92 *dd*	6.06 *dd*	5.59 *t*
14	6.75 *m*	6.45 *m*	6.44 *t*	6.62 *m*
15	7.63 *t*	7.39 *m*	7.40 *t*	7.69 *t*
16	7.78 *m*	7.42 *m*	7.46 *m*	7.84 *m*
Me-17	1.04 *d*	0.87 *d*	0.87 *d*	1.13 *d*
18A	4.76 *s*	4.11 *br s*	4.24 *d*	4.78 *d*
18B	4.76 *s*	4.11 *br s*	4.52 *d*	4.96 *d*
19A	4.41 *d*	4.21 *d*	4.30 *d*	4.42 *d*
19B	4.71 *d*	4.39 *d*	4.45 *d*	5.04 *d*
OAc			2.05 *s*(6H) 2.08 (3H)	
1α, 10β	13.0	13.4		12.6
1β, 10β	2.2	2.7		2.5
2α,3	3.8	3.6		3.3
2β, 3	<1	3.6		3.3
6α, 7α			2.6	
6α, 7β	-		2.6	
7α, 8β	12.8	- -	13.0	- -
7β, 8β	4.2		4.2	-
8β, 17	6.7		6.7	6.2
11A, 11B	15.8	15.5	16.2	- -
11A, 12	9.7	9.4	9.8	8.8
11B, 12	2.3	2.3	3.5	8.8
14, 15	1.4		1.6	1.5
15, 16	1.4		1.6	1.5
18A, 18B			12.6	11.3
19A, 19B	12.0	12.2	12.8	11.1

*Spectral parameters were obtained by first order approximation. All asssignments were confirmed by double resonance experiments.

†The spectrum of **1** in pyridine-d_5 is better resolved, some parameters in $CDCl_3$ are reported for comparison purposes with teubotrin [4].

After treatment of **1** with trichloroacetylisocianate in $CDCl_3$ the >NH signlets of the resulting tricarbamate were observed at δ 8.47, 8.59 and 8.96 ppm. The corresponding signals for the tricarbamate of 3(in $CDCl_3$) were at 8.53, 8.57 and 8.81 ppm.

‡Overlapped signal.

Table 2 ^{13}C NMR chemical shifts of compound (in pyridine-d_5)

C	δ	C	δ
1	20 9(2)*	11	37.9(2)
2	25 6(2)	12	62 1(1)
3	129 4(1)	13	132 6(0)
4	140 8(0)	14	109 4(1)
5	42 0(0)	15	143 4(1)
6	70 0(1)	16	138 6(1)
7	37 0(2)	17	16 8(3)
8	30 9(1)	18	64 5(2)
9	50 4(0)	19	75 5(2)
10	36 9(1)	20	173 5(0)

*Number of attached protons determined by the DEPT method

washed with H_2O, dried over Na_2SO_4, recrystallized from Me_2CO–petrol to yield pure **1**

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