Furanoid Diterpenes in the Bitter Fraction of *Teucrium polium* L.

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*Teucrium polium* L., Labiatae, Clerodane and Norclerodane Diterpenes, Teucrin P1 and H3, Montanin B

Three known furanoid diterpenes Teucrin P1 (2), Teucrin H3 (3) and Montanin B (4) have been isolated for the first time from the bitter fraction of the aerial parts of *Teucrium polium* L. In addition two new diterpenes of this type Teupolin I (5) and Teupolin II (6) have been also found in the plant extract. The structure and stereochemistry were established using spectral methods and chemical evidence.

The major component of the bitter principle of *Teucrium polium* L. is picropolin (1) [1]. Picropolin-monoacetate and a product identical with the compound of the alkaline hydrolysis and reacetylation of 1 have been discovered [1]. Teucrin P1 and Teucrin P2 were isolated from Moldavian *T. polium* [2].

*T. polium* is widely spread in Bulgaria. The plant is a very popular drug in the folk medicine. The present paper contains the results of the isolation and identification of furanoid diterpenes of clerodane and norclerodane type from the bitter fraction of this plant.

Dry aerial parts of *T. polium* has been extracted with acetone and treated by the procedure described in [3]. Passing the extract through a column of Silica-gel and eluting with petroleum or chloroform leads to isolation of five crystalline furanoid diterpenes. Three of them were identified by means of IR, NMR and TLC as Taucrin Pi (2) [4], Teucrin H3 (19-acetylgnaphalin) (3) [5, 6] and Montanin B (4) [7]. These compounds are described for the first time in *T. polium*. The other two diterpenes are new and they are named Teupolin I and Teupolin II. 1 and picropolin-acetate are not discovered in the bitter fraction of the plant.

![Chemical structures](image-url)

1. X = O; R1 + R2 = H + OH; R3 = CH3OAc;
2. X = H; R1 + R2 = O; R3 = CH3OAc;
3. X = H2; R1 + R2 = H; R3 = CH3OAc;
4. X = H; R1 = OAc; R2 = H; R3 = CH3OH;
5. X = H2; R1 = OAc; R2 = H; R3 = CH3OH;
6. X = H; R1 = OAc; R2 = H; R3 = CHO.

Teupolin I (5) was isolated as colourless crystals with m.p. 211–213 °C and [α]D 23 + 60,0°. The molecular formula C28H32O7 is supported by the molecular weight 404 (MS). The furan ring and the γ-lactone are indicated with MS fragments at m/e 81 and 95, the IR bands at 1750, 3130, 1600, 1505 and 870 cm⁻¹ and NMR peaks at 7,98 (m., 2H) for α-furan protons and 6,30 (m., 1H) for β-furan proton. The C-12 proton of γ-lactone appears as a triplet at 5,28 (1H, J = 8 Hz). The other part of molecule contains a methyl group at C-18 which appears as a doublet at 0,98 (3H, J = 7 Hz). The hydroxy group located at C-6 absorbs at 3500 cm⁻¹. Its secondary nature is proved by the shifting of a double doublet from 3,56 and 3,66 to 4,70 and 4,82 (1H, J = 4 and 10 Hz) after treating with trichloroacetyl isocyanate. The one proton singlet from the NH-group appears at 8,38. The acetyl group absorbs at 1710 and 1250 cm⁻¹ in the IR spectrum. The NMR singlet for this group is at 2,04 (3H). The AB type quartet at 4,62 and 4,94 (2H, J = 13 Hz) shows that this group is connected with C-19. C-18 is involved in a 1,2-epoxyde ring, one proton of which can be seen at 3,16 (1H, m.).

The structure of 5 was proved by hydrogenation of 3 with NaBH4. The compound obtained is identical with 5 by means of IR, NMR, MS, TLC and m.p. The hydrogenation of 3 is going stereoselectively due to the chirality of the molecule. C-6 atom has the hydrogen in axial and the hydroxyl...
group in the equatorial position according to the large spin constant.

Teupolin II (6) is a colourless crystalline compound with m.p. 187-189 °C and [α]D +52°. The molecular formula C22H26O7 was calculated from the elemental analysis and supported by the molecular weight 404 (MS). The IR, NMR and MS spectral data of this compound are in good agreement with the clerodane-type diterpene lactone and are very similar to that of 1. The difference seems to be in the position of the acetyl group. In 6 it is at C-6, while C-19 is occupied by hydroxyl group. This group can be oxidized by CrO3-pyridine to 7, a colourless crystalline compound with m.p. 175 to 177 °C. The resonance of the aldehyde proton in the NMR spectrum is at 10, 20 (1H, s). The structure and stereochemistry of 6 were proved by correlation with 5. The acetylation of 5 and 6 with acetic anhydride and trifluoroacetic acid gave the same diacetyl compound. The identity was proved by means of IR, NMR and TLC.

**Experimental**

Melting points taken on a Kofler microhotstage are uncorrected. IR spectra were recorded on KBr pellets or in chloroform solution. NMR spectra were measured on a JEOL PS-100 spectrometer at 100 MHz in CDCl3 with TMS as internal standard. The chemical shift is expressed in δ-units. Kieselgel 0.05-0.2 mm (Merck) were used for column chromatography. Plates coated with silica-gel G (Merck) were used for TLC. Aerial parts of T. polium L. were collected near Plovdiv in July 1975.

**Plant extraction and isolation of the bitter principle**

Dry plant material (6 kg) was extracted 3 times with acetone (20 l). The solvent was evaporated and the residue was treated as [3]. 100 g bitter principle was isolated.

**Isolation of 2**

The bitter fraction was passed over silica gel (2.5 kg). Elution with light petroleum gave plant waxes. Elution with petroleum and chloroform (1:1) afforded 2 (4 g). After recrystallization from Et2O/acetone (9:1) colourless prisms were obtained with m.p. 164-166 °C and [α]D +6.6° (c = 3%, CH2Cl2). The identity was proved by m.p., TLC, IR and NMR comparison with an authentic sample of Teucrin P1.

**Isolation of 3**

Further elution with petroleum-chloroform (4:6) lead to the isolation of 3 as colourless crystals (1 g) with m.p. 222-223 °C (Et2O/CH2Cl2) and [α]D +76° (c = 2.5%, CH2Cl2). The identification with Teucrin H3 was made by m.p., TLC, IR, NMR and MS.

**Isolation of 5**

The elution with petroleum-chloroform (3:7) gave 5 (1 g). Recrystallization from Et2O/CH2Cl2 yielded 5 as colourless crystals with m.p. 211-213 °C and [α]D +60° (c = 2%, CH2Cl2).

Found C 65.77 H 7.12, 
Calcd C 65.41 H 6.98.

**Isolation of 6**

Further elution with petroleum-chloroform (3:7) afforded 6 which crystallized from Et2O/acetone as colourless crystals with m.p. 187-189 °C and [α]D +52° (c = 2%, CH2Cl2).

IR νmax cm⁻¹: 3600, 3130, 1760, 1740, 1600, 1505, 1240, 1050 and 870.

NMR (CDCl3) δ: 0.90 (3H, d, J = 6.5 Hz, C-17), 2.00 (3H, s, CH3COO), 2.88 (1H, m, 1,2-epoxyde ring), 3.92 (1H, t, J = 12 Hz, C-19, OH), 4.69 and 5.30 (each 1H, AB-system, J = 12 Hz, C-19), 6.30 (1H, m, C-14), 7.38 (2H, m, C-15 and C-16).

MS (70 eV) m/z: 404, 95, 81.

**Sodium borohydride reduction of 3**

To a solution of 3 (70 mg) in methanol-dioxane (1:1, 10 ml) 50 mg H3BO3 and 20 mg NaBH4 was added. After stirring 20 min at room temperature the mixture was treated with water and extracted with chloroform. 50 mg from the alcohol was obtained with m.p. 211-214 °C and [α]D +60° (c = 2%, CH2Cl2). The product is identical with 5 by means of m.p., TLC, IR and NMR.

**Oxidation of 6 to 7**

180 mg of 6 in dry pyridine (6 ml) was treated with chromium trioxide (300 mg) at room temperature for 48 h. The solution was poured into water and extracted with chloroform. The extract was dried and evaporated to dryness. 100 mg of 7 was obtained. After recrystallization from Et2O/CH2Cl2 colourless crystals with m.p. 175-177 °C were obtained. IR νmax cm⁻¹: 1760, 1730, 1720, 1600, 1505 and 870.

**Acetylation of 5 and 6**

To 60 mg from 5 or 6 acetic anhydride (1 ml) and 1 drop trifluoroacetic acid was added. After 24 h the mixture was treated with water and extracted with Et2O. Resine-like diacetate was passed through silica gel and eluted with petroleum. Colourless resin.

IR νmax cm⁻¹: 1760, 1730, 1720, 1600, 1505, 1250 and 870.

NMR (CDCl3) δ: 1.00 (3H, d, J = 7 Hz, C-17),
1.96 and 2.06 each 3H, s, \( \text{CH}_3\text{COO} \)), 2.97 (1H, m, 1,2-epoxyde, C-18). 4.38 and 5.30 (each 1H, AB-system, \( J = 13 \text{ Hz} \), C-19), 4.78 (1H, dd, \( J = 4 \) and 16 Hz C-6). 5.34 (1H, t, \( J = 8 \text{ Hz} \), C-12), 6.32 (1H, m, C-14) and 7.31 (2H, m, C-15 and C-16).

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