Montanin-C, A New Furanoid Diterpene from *Teucrium montanum* L

Peter Y. Malakov, Georgi Y. Papanov, and Nikola M. Mollov

University of Plovdiv, 4000 Plovdiv, Bulgaria

Stefan L. Spassov

Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria

Z. Naturforsch. 33b, 789–791 (1978); received February 16, 1978

*Teucrium montanum* L., Labiatae, Clerodane Type, Furanoid Diterpene, Montanin-C

A new furanoid diterpene of clerodane type, Montanin-C (1) is isolated from the bitter fraction of the aerial parts of *Teucrium montanum* L., spread in Bulgaria. Its structure is established on the basis of spectral evidence and chemical transformations.

Furanoid diterpenes of clerodane and norclerodane type are common in *Teucrium* species. Pikropolin and Teucrin P, were reported for *T. polium* [1, 2]. In *T. chamaedrys* were found Teucrins A, B, C, E, F and G [3]. Teucrin was obtained from *T. viscidum* and *T. cubense* [4, 5]. Recently Teucvidin was described for the former plant [6].

In this paper we report the isolation and structure elucidation of a new furanoid diterpene of clerodane type, Montanin-C. Montanin-C (1) was isolated as colourless prisms with m.p. 181–183 °C and [α]D + 8.4° from the bitter fraction of the aerial parts of *Teucrium montanum* L., spread in Bulgaria. The molecular formula C24H30O8 was calculated from the elemental analysis and supported by the molecular weight 446 (MS). Its IR absorption at 3130, 1600, 1505 and 875 cm⁻¹ and positive Ehrlich test [7] indicated the presence of a furan ring. The NMR spectrum showed multiplets at δ 7.50 (2 H) and 6.40 (1 H), which were assigned to the α- and β-protons on the furan ring in 1. The γ-lactone carbonyl appear as a strong IR band at 1760 cm⁻¹. The secondary methyl group could be observed in NMR as a doublet at 1.13 (3 H, J = 7 Hz) while the proton at C-12 appeared as a triplet at 5.42 (1 H, J = 11.2, 4.1 Hz). The latter is connected to a tertiary carbon atom, most probable at C-5. The second acetylated hydroxyl is attached to a methine group appearing at 4.83 (1 H, dd, J = 11.2, 4.1 Hz). By analogy to 6 and the similarity of NMR spectral data with ajugarin – I [8] the C-6 position seems very probable for it. The coupling constants indicated that the C-6 proton is axial and the acetoxy group is equatorial. It has an axial and an equatorial protons as neighbours.

The presence of the furan ring and γ-lactone in 1 were supported and by the results of the Pd/C hydrogenation. Two products 4 and 5 were isolated. Their spectra showed that in both compounds the ester groups are preserved (NMR three protons singlets at 1.97 and 2.08; IR bands at 1720 and 1725 cm⁻¹) whereas the furan ring is hydrogenated. The γ-lactone ring is presented in 4 (IR band at 1760 cm⁻¹). Compound 5 is analogous to the product obtained in similar condition from 6 [1]. In its IR spectrum the lactone band is replaced by a carboxyl group (IR bands at 1700 and 2500–3500 cm⁻¹, NMR broad one proton singlet at 7.30).

The other part of the molecule of 1 was resolved on the basis of following spectral data and chemical experiments. The two acetate residues absorbed in the IR spectrum of 1 at 1720 and 1725 cm⁻¹. In the NMR they appeared as proton singlets at 2.00 (3 H) and 2.12 (3 H). One of the acetylated hydroxyl is primary (MS, m/e 373, M-CH₂OOC-CH₃). Its methylene group is resonated at 4.50 and 5.37 (1 H each AB quartet, J = 13.0 Hz). The latter is connected to a tertiary carbon atom, most probable at C-5. The second acetylated hydroxyl is attached to a methine group appearing at 4.83 (1 H, dd, J = 11.2, 4.1 Hz). By analogy to 6 and the similarity of NMR spectral data with ajugarin – I [8] the C-6 position seems very probable for it. The coupling constants indicated that the C-6 proton is axial and the acetoxy group is equatorial. It has an axial and an equatorial protons as neighbours.

Montanin-C (1) was isolated and obtained in similar condition from 6 [1]. In its NMR they appeared as proton singlets at 2.00 (3 H) and 2.12 (3 H). One of the acetylated hydroxyl is primary (MS, m/e 373, M-CH₂OOC-CH₃). Its methylene group is resonated at 4.50 and 5.37 (1 H each AB quartet, J = 13.0 Hz). The latter is connected to a tertiary carbon atom, most probable at C-5. The second acetylated hydroxyl is attached to a methine group appearing at 4.83 (1 H, dd, J = 11.2, 4.1 Hz). By analogy to 6 and the similarity of NMR spectral data with ajugarin – I [8] the C-6 position seems very probable for it. The coupling constants indicated that the C-6 proton is axial and the acetoxy group is equatorial. It has an axial and an equatorial protons as neighbours.

Requests for reprints should be sent to Prof. Dr. N. Mollov, University of Plovdiv, 4000 Plovdiv, Bulgaria.
The last oxygen atom to be accounted for in 1 is included in a 1,2-epoxide grouping of the type 
\[
\overset{\circ}{\text{O}} \quad \text{CH}_3
\]
\[\text{C} \quad \text{CH}_2.\]
The evidence for it was found in the experiments with LiAlH\(_4\) and POCI\(_3\). When 1 was treated with LiAlH\(_4\) in THF under conditions similar to that for 6 [1], the compound 7 was isolated. Its molecular formula \(\text{C}_{20}\text{H}_{28}\text{O}_6\) m.p. 169-170 °C and \([\alpha]^0 + 9.3°\). The IR, NMR and MS showed that the furan and lactone rings remained intact. Besides the original secondary methyl one new methyl group appeared, which absorbed at 1.42 as a three protons singlet. The strong hydroxyl band in IR (3250-3650 cm\(^{-1}\)) corresponded to three separate hydroxyl signals in the NMR at 3.72 (1 H, t, \(J = 6.5 \text{ Hz}\), primary OH), 4.42 (1 H, d, \(J = 6.5 \text{ Hz}\), secondary OH) and 4.68 (1 H, s, tertiary OH). All hydroxyl signals vanished after D\(_2\)O exchange, as well as upon treatment with trichloroacetylisocyanate. In the latter case the corresponding -NH-singlets of the resulting carbamates were observed at 8.77, 8.88 and 9.09. The presence of one tertiary hydroxyl group was also demonstrated through acetilation of 7 with acetic anhydride in pyridine at room temperature. A crystalline compound with m. p. 146-147 °C was isolated, in which the hydroxyl absorption was still present.

The reaction of 1 with phosphorus oxychloride led to the product 8. Its NMR contained a singlet at 5.60 (1 H, olefinic), whereas the IR showed that the lactone and both acetate groups were preserved. This result shows that the bond C-4-oxigen is in equatorial position [9].

The structure 1 of Montanin-C is supported also by \(^{13}\text{C}\) NMR data, which are similar to that of ajugarin [8] and are presented in the following Table:

<table>
<thead>
<tr>
<th>C ppm</th>
<th>C ppm</th>
<th>C ppm</th>
<th>C ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 22.2</td>
<td>6 64.7</td>
<td>11 40.9</td>
<td>16 139.4</td>
</tr>
<tr>
<td>2 21.2</td>
<td>7 32.2</td>
<td>12 71.6</td>
<td>17 16.9</td>
</tr>
<tr>
<td>3 24.7</td>
<td>8 33.0</td>
<td>13 125.5</td>
<td>18 50.3</td>
</tr>
<tr>
<td>4 62.0</td>
<td>9 43.0</td>
<td>14 108.2</td>
<td>19 61.7</td>
</tr>
<tr>
<td>5 45.4</td>
<td>10 51.3</td>
<td>15 144.2</td>
<td>20 176.2</td>
</tr>
</tbody>
</table>

**Isolation of 1**

The bitter fraction of *T. montanum L.* was chromatographed on Si gel column. The elution with petrol-chloroform (3 : 7) yielded a single compound. Eto\(_2\)O-Ac (9 : 1) crystallization gave 1 as colourless prisms, m. p. 182-183 °C, \([\alpha]^0 + 9.3°\). The IR, NMR and MS showed that the furan and lactone rings remained intact. Besides the original secondary methyl one new methyl group appeared, which absorbed at 1.42 as a three protons singlet. The strong hydroxyl band in IR (3250-3650 cm\(^{-1}\)) corresponded to three separate hydroxyl signals in the NMR at 3.72 (1 H, t, \(J = 6.5 \text{ Hz}\), primary OH), 4.42 (1 H, d, \(J = 6.5 \text{ Hz}\), secondary OH) and 4.68 (1 H, s, tertiary OH). All hydroxyl signals vanished after D\(_2\)O exchange, as well as upon treatment with trichloroacetylisocyanate. In the latter case the corresponding -NH-singlets of the resulting carbamates were observed at 8.77, 8.88 and 9.09. The presence of one tertiary hydroxyl group was also demonstrated through acetilation of 7 with acetic anhydride in pyridine at room temperature. A crystalline compound with m. p. 146-147 °C was isolated, in which the hydroxyl absorption was still present.

**Hydrogenation of 1**

A solution of 200 mg of 1 in 20 ml MeOH was hydrogenated over 10% Pd/C (20 mg). 2.7 mol. equiv. of hydrogen was consumed. Evaporation of the solvent after filtration left a gum (192 mg), which was dissolved in Eto\(_2\)O and kept at 4 °C for 1 day. Colourless crystals of 4 (28 mg) were separated with m. p. 218-219 °C.

**Acetylation of 7**

To the solution of 7 (57 mg) in (Ac)\(_2\)O (1.5 ml) 3 drops of Py were added. The solution was allowed to stay at room temperature for 30 h. Than was treated with water and extracted with CHCl\(_3\). The extract was washed with 1% NaHCO\(_3\) solution (650 ml) and evaporated. Crystallization of the residue from Eto\(_2\)O-CHCl\(_3\) (1 : 1) gave 53 mg colourless crystals of diacetate of 7, m. p. 146-147 °C.
To a solution of 1 (150 mg) in Py (15 ml) was added POCI₃ (4.5 ml). The mixture was stirred at 110°C for 6 h, cooled to ca. 10°C and destroyed with ice. After extraction and evaporation of the solvent was obtained from Et₂O–CHCl₃ (1:1) a colourless crystals (130 mg) of 8, m.p. 212–213°C. IR νₘₐₓ cm⁻¹: 1760 (γ-lactone), 1725, 1720 (ester groups), 1630 (double bond), 3130, 1600, 1505 and 875 (furan). NMR, 1.08 (3 H, d, 17-Me), 1.87 and 1.91 (each 3 H, s, 2 × CH₃COO), 2.32 (2 H, m, AB-part of ABX-system, C-11), 4.85 and 5.52 (each 1 H, AB-system, \( J = 5.0, 4.8 \text{ Hz, C-10} \)), 5.28 (1 H, t, C-12), 6.24 (1 H, m, C-14) and 7.31 (2 H, m, C-15 and 16).

**POCl₃ treatment of 1**

To a solution of 1 (150 mg) in Py (15 ml) was added POCI₃ (4.5 ml). The mixture was stirred at 110°C for 6 h, cooled to ca. 10°C and destroyed with ice. After extraction and evaporation of the solvent was obtained from Et₂O–CHCl₃ (1:1) a colourless crystals (130 mg) of 8, m.p. 212–213°C. IR νₘₐₓ cm⁻¹: 1760 (γ-lactone), 1725, 1720 (ester groups), 1630 (double bond), 3130, 1600, 1505 and 875 (furan). NMR, 1.08 (3 H, d, 17-Me), 1.87 and 1.91 (each 3 H, s, 2 × CH₃COO), 2.32 (2 H, m, AB-part of ABX-system, C-11), 4.85 and 5.52 (each 1 H, AB-system, \( J = 5.0, 4.8 \text{ Hz, C-10} \)), 5.28 (1 H, t, C-12), 6.24 (1 H, m, C-14) and 7.31 (2 H, m, C-15 and 16).