New Furanoid Diterpenes from *Teucrium scordium* L.

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Two new furanoid diterpenes of clerodane type, 6-ketoteuscordin (**1**) and 6 α -hydroxyteuscordin (**2**) have been isolated from *Teucrium scordium* var. *scordium*, Lamiaceae. Their structures and stereochemistry have been determined.

We have recently reported the structure and stereochemistry of a new furanoid diterpene from *T. scordium* L. [1]. In continuation of the above investigation, we have isolated two new furanoid diterpenes, 6-ketoteuscordin and 6 α -hydroxyteuscordin, whose structures and stereochemistry have been accounted for on the basis of the evidence reported below.

6-Ketoteuscordin (**1**), C₂₀H₂₂O₆, m.p. 199–201 °C, $[\alpha]_D^{20}$ 131 (CH₃COCH₃; c 0.224). MS: m/e 358 (M⁺), 178 (base peak), 96, 95, 81. IR (KBr, cm⁻¹): 1780 and 1750 (two γ -lactones), 1710 (ketone), 3140, 1505 and 870 (furan ring). ¹H NMR (CD₃COCD₃, δ): 1.10 (3H, d, J = 7 Hz, s, CH₃), 2.40 (1H, dd, J = 12 Hz, β H-7), 3.29 (1H, t, J = 14 Hz, α H-7), 4.49 and 4.70 (2H, q_{AB}, J = 12 Hz, H₂-19), 5.58 (1H, t, J = 8 Hz, H-12), 6.50 (1H, m, β -furan proton), 7.62 (2H, m, α -furan protons).

The stereochemistry of the C(9)–C(20) bond of **1** was derived from ¹H NMR chemical shift values of the C-7 methylene protons. The considerable paramagnetic shift of the axial H-7 (3.29 ppm) relative to that of the equatorial H-7 (2.40 ppm) may be rationalized, as in the case of methyl teucvinate [2], in terms of the anisotropy effects of the lactone CO group. The proximity of the C-20 carbonyl and H_{ax}-7, necessary for this effect to occur, requires the axial orientation of the C(9)–C(20) bond. Furthermore the observed value of the H₂-7 at the lower field showed unambiguously that the keto group is at C-6 [3].

The stereochemistry at the other chiral centres were deduced by correlation with Teucrin H₂ (**3**), described [3, 4] as a natural clerodane type diterpene

occurring in *Teucrium hyrcanicum* and *T. chamaedrys* L. Treatment of **3** with chromium trioxide in dry pyridine at room temperature for 24 h gave only **1**. Reduction of **1** with sodium borohydride yielded Teucrin E (**4**), isolated from *Teucrium chamaedrys* L. [4, 5]. On the other hand when **4** was treated as **3** with chromium trioxide afforded **1** again. All compounds were identified by comparison of their m.p., TLC, IR, ¹H NMR and mass spectra.

6 α -Hydroxyteuscordin (**2**), C₂₀H₂₂O₆, m.p. 259–261 °C, $[\alpha]_D^{20}$ –59.4 (CH₃COCH₃; c 0.183). Its MS is quite similar to the spectra of **1** and it has the same M⁺ (m/e 358). IR (KBr, cm⁻¹): 3420 (OH), 1750 and 1740 (two γ -lactones), 1660 (double bond), 3135, 1505 and 875 (furan ring). ¹H NMR (C₅D₅N, δ): 0.98 (3H, d, J = 7 Hz, s, CH₃), 2.32 (1H, d, J = 12 Hz, H-11), 3.82 (1H, dd, J = 4 and 13 Hz, H-6), 4.10 and 5.18 (2H, q_{AB}, J = 12 Hz, H₂-19), 5.45 (1H, t, J = 8 Hz, H-12), 6.70 (1H, dd, J = 3 and 7 Hz, H-3), 6.46 (1H, m, β -furan proton), 7.60 (2H, m, α -furan protons).

Acetylation of 6 α -hydroxyteuscordin gave a monoacetate (**5**), C₂₂H₂₄O₇, m.p. 240–242 °C. The spectroscopic properties of **5** revealed the presence of an ester (CD₃COCD₃, δ): 1.86 (3H, s, COOMe) and $\nu_{\max}$ (KBr): 1725 and 1750 cm⁻¹. The secondary nature of the hydroxyl group in **2** is proved by shifting a double doublet from 3.82 to 4.78 (1H, J = 4 and 13 Hz, H-6) after acetylation. According to the ¹H–¹H couplings, the H-6 in **2** and **5** is axial, whereas the orientation of OH and COOMe groups are equatorial. When treated with chromium trioxide as above for 30 h, 6 α -hydroxyteuscordin gave only teuscordinon (**6**) [1], which was characterized by comparison of the m.p., TLC, IR, ¹H NMR and mass spectra. In this way the structure and stereochemistry of **2** was proved.

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- 1: $R_1 = R_2 = O$ 2: $R_1 = H; R_2 = OH$
 3: $R_1 = OH; R_2 = H$ 5: $R_1 = H; R_2 = OAc$
 4: $R_1 = H; R_2 = OH$ 6: $R_1 = R_2 = O$

Experimental

The melting points are uncorrected and have been determined with a Kofler microhostage apparatus. 1H NMR spectra were obtained on a JEOL PS-100 instrument at 100 MHz. Kieselgel 0.05–0.2 mm (Merck) was used for column chromatography. Plates coated with silica gel G nach Stahl (Merck) were used for TLC.

Isolation of 1 and 2

The $CHCl_3$ extract (18 g) was passed over silica gel column. Elution with $CHCl_3$ -MeOH (99.5:0.5) yielded 1 (200 mg). After recrystallization from acetone-ether colourless crystals were obtained. Further elution with $CHCl_3$ -MeOH (99.0:1.0) leads to the isolation of 2 (600 mg) in the form of colourless crystals, which were recrystallized from acetone-dichlormethane.

Sodium borohydride reduction of 1 to 4

To a solution of 1 (70 mg) in methanol (7 ml) was added sodium borohydride (50 mg), and the mixture was stirred for 1 h at room temperature. The mixture was treated with water and extracted with chloroform. The crude crystalline product (60 mg) obtained by the usual treatment of the extract was

recrystallization from acetone-ether to afford pure crystals (55 mg), which were identical with the authentic sample of 4 (mixed m.p., TLC and IR; 1H NMR).

Oxidation of 4 to 1

To a solution of 4 (200 mg) in pyridine (10 ml) was treated with chromium trioxide (300 mg) at room temperature for 24 h. The solution was poured into water and the organic product recovered in chloroform. The extract was washed (aqueous acetic acid, sodium hydrogen carbonate solution, water) and dried. Evaporation of the solvent gave the 6-ketoteuscordin (180 mg), which crystallized from acetone-dichlormethane as colourless prisms, which were identical with the authentic sample of 1 (mixed m.p., TLC and IR, 1H NMR).

Treatment of 3 (200 mg) under identical conditions afforded the same product (1), which was identified by m.p., TLC, IR and 1H NMR.

Acetylation of 2

The usual acetylation of 2 (100 mg) with acetic anhydride (1.5 ml) and pyridine (3–5 drops) yielded crude acetate (85 mg), which was recrystallized from chloroform-ether to give pure acetate (75 mg), ν_{max} 3140, 1600, 1500, 870 (furan ring), 1735, 1250 (ester group), 1765, 1745 (two γ -lactones) and 1660 cm^{-1} (double bond), δ 1.05 (3H, d, $J = 7$ Hz, s, CH_3), 1.86 (3H, s, $COOMe$), 3.88 and 4.68 (each 1H, q_{AB} , $J = 12$ Hz, H_{2-19}), 4.78 (1H, $J = 4$ and 13 Hz, H-6), 5.48 (1H, t, $J = 8$ Hz, H-12), 6.42 (1H, m, β -furan proton), 6.64 (1H, dd, $J = 3$ and 7 Hz, H-3) and 7.60 (2H, m, α -furan protones).

Oxidation of 2 to 6

Treatment of 2 (110 mg) in dry pyridine (6 ml) with chromium trioxide (200 mg) as usual afforded crude crystals (80 mg), which on recrystallization from acetone-ether yielded 6.

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