LINKIOL, A NEW SESQUITERPENE FROM *FERULA LINKII*

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Abstract—A new sesquiterpene ester, linkiol with a daucane skeleton was isolated from *Ferula linkii*.

Continuing with our work on the chemistry of the Umbelliferae, we have studied *Ferula linkii*, a plant endemic to the Canary Isles [1]. From this species we have isolated a new sesquiterpene ester, linkiol (1).

Linkiol (1), C_{25}H_{34}O_{5}, showed bands characteristic of alcohol and ester groups in its IR spectrum. By hydrolysis it gave a sesquiterpene alcohol 2, C_{15}H_{26}O_{3}, with an IR spectrum in which signals typical of hydroxyls were noted. In the NMR spectrum this product presented a triplet at δ 3.65 (W_{1/2} 12 Hz) characteristic of a proton geminal to an equatorial alcohol, two singlets at 1.02 and 1.25 resulting from tertiary methyls and a triplet at 9.05 (6H) due to the methylene of an isopropyl group. Equilibration with D_{2}O caused three hydroxyl hydrogens to disappear.

Mild acetylation yielded the monoacetate 3. The geminal proton to the acetate seemed, in the NMR spectrum, to be a quartet centred at 4.95. By treatment of 2 with acetone in anhydrous CuSO_{4}, acetone 4 was obtained. Dehydration of this latter with thionyl chloride gave compound 9 with a tetrasubstituted double bond. A mixture of azulenoids was obtained from dehydrogenation with Se.

The above chemical and spectroscopic information suggests that this alcohol had an x,y-dimethyl-isopropyl-bicyclo-5,3,0-decane skeleton with one secondary and two tertiary alcohol groups. It could also be assumed from the NMR data and acetate formation described above that one of the latter was geminal to a methyl group, while the other was sited in such a way that on dehydration it gave a compound with a =C—CH(Me)$_2$ grouping since in the NMR spectrum of 9 the proton of the isopropyl group appeared as a multiplet centred at δ 2.68. Since jaeschkeanadiol (17) [2], a sesquiterpene with a daucane skeleton, and its esters have been isolated from other species of *Ferula* [2], [3], it seemed reasonable to expect our product to have this type of skeleton.

A secondary alcohol group with the attributes described above can be found in a daucane structure at C-3, C-6 or C-10, and a tertiary at C-2 or C-4. As the isopropyl group in the alcohol's NMR spectrum was not in the same position as the equivalent group in jaeschkeanadiol (17), which has a hydroxyl at C-10, we can assign position C-6 to the second tertiary alcohol, while the formation of acetone points to the secondary hydroxyl being located at C-2 or C-4.

In order to distinguish correctly between these two positions and to relate our product to one already known, we treated alcohol 2 with tosyl chloride in pyridine, obtaining the tosylate 6 and miniscule quantities of ketone 5 and a compound identified with daucol (7) [4–6], which was produced by solvolysis of the tosyl-
ate in the reaction medium. When the tosylate was solvolyzed with methanolic KOH, daucol (7) was obtained in pure form. In view of these products and the reaction mechanism, we could then determine the structure and stereochemistry of the carbon skeleton of sesquiterpene 2, the position and stereochemistry of the tertiary hydroxyls and the location of the secondary alcohol at C-2.

Thus, only the stereochemistry of the secondary alcohol group remained to be solved. The NMR spectrum suggested that this hydroxyl was equatorial, but this molecule may adopt two conformations in which the hydroxyl, being equatorial, can be α or β. Alcohols 2 differs from the triol 15, obtained from carotol by treatment with potassium permanganate [4, 7–11], and, hence, must be β. Moreover, when the tosylate obtained from the triol 15 was solvolyzed, ketone 16 and not daucol (7) was obtained. The result of this solvolysis fits in with the trans and cis stereochemistry of the hydroxy group at C-2 and C-3 for both the alcohols 2 and 15.

The solvolysis of the tosylate 6 to give daucol must be achieved through an epoxide, because when the tosylate of diol 11, which does not have a hydroxyl at C-6, was solvolyzed under the same conditions as 6, the epoxide 13 was obtained. Perchloric acid catalysed opening of the epoxide gave a single trans diaxial diol 14.

Diol 11 could be obtained both by hydrolysis of the dehydrated acetone or by treatment of the alcohol 2 with thionyl chloride in pyridine, followed by basic hydrolysis of the sulphite formed.

The acid which esterifies to alcohol 2 forming linkol was identified as angelic acid from its spectroscopic data. Thus, the MS spectrum of linkol (I) showed a M+ at m/e 338 and other prominent peaks at m/e 238 (M+ –100), 83 (base peak) and 55. These fragments are typical of the cleavage of esters of angelic, tiglic, and seconicoic acids. In the NMR spectrum of linkol, a quartet appeared at δ 6.12, a chemical shift typical of the vinyl proton of angelic acid [12].

**EXPERIMENTAL**

Mps are uncorr. Optical activities were taken in CHCl₃, NMR spectra on a 60 MHz instrument in CDCl₃ with TMS as internal reference except where otherwise indicated. Column and dry column chromatography was performed on Si gel 0.2–0.5 and 0.83–0.2 mm respectively.

**Isolation of linkol.** Air-dried roots of the plant *Ferula linkii* Webb (3.1 kg) collected at San Mateo (Gran Canaria, Canary Isles), were finely cut and Soxhlet extracted several times with EtOH. Combined filtered cold extracts were concentrated in vacuo and extracted with C₆H₅O. Chromatography, with C₆H₅O as eluent, gave linkol (11 g).

**Linkol (1).** Mp 123–125° (C₆H₆ [α]D −17 (c 0.28); (found: C 71.02; H 9.99. C₉H₆O₅ requires: C 70.97; H 10.12%); IRνcm⁻¹: 3400, 1700, 1660, 1270, 1170; NMR: δ 0.93 (9H, t, J 6 Hz), 0.95 (6H, δ, δ), 1.03 (3H, s), 1.25 (3H, s), 3.65 (1H, t, W 12 Hz); MS m/e (%): 338 (M+), 230, 305, 302, 277, 269, 265, 254, 238, 212, 209, 194, 193, 167, 154, 150, 151, 140, 136, 83.

**Alcohol (2).** By saponification of linkol with 5% KOH in MeOH, the alcohol 2 was obtained: mp 84–85° [α]D = −33 (c 0.26); IRνcm⁻¹: 3400, 1700, 1500, 1270, 1170; NMR: δ 0.95 (6H, δ, δ), 1.03 (3H, s), 1.25 (3H, s), 3.65 (1H, t, W 12 Hz); MS m/e (%): 256 (M+), 238, 223, 212, 209, 195, 194, 185, 183, 172 (100), 151. Monooacetate (3) obtained in the usual way: mp 111–117°; NMR: δ 0.92 (9H, t, W 12 Hz), 1.20 (3H, s), 2.07 (3H, s), 4.95 (1H, q, J 4 Hz, J 10 Hz).
ate (35 mg) and unchanged triol (30 mg). Ketone 16; NMR: δ 0.99 (6H, t), 1.03 (3H, s), 2.14 (3H, s). Tosylate of 15; NMR: δ 0.85, 0.93, 1.00 and 1.22 (each 3H, s), 2.45 (3H, s), 4.68 (1H, q), 7.33 and 7.80 (each 2H, d, J 9 Hz). The tosylate was solvolyzed by the same process as 6 and also yielded ketone 16.

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REFERENCES