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ISOMERIC 2,3-SECO-HOPENE LACTONES FROM *SWERTIA PETIOLATA*

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Key Word Index—*Swertia petiolata*; Gentianaceae; seco-triterpene lactone; Swertialactone C; Swertialactone D.

Abstract—Two novel isomeric hopene triterpenes, Swertialactone C and Swertialactone D have been isolated from *Swertia petiolata*. Their structures were established as 2,3-seco-2 → 3 lactone, 1β,3β-epoxy-hop-17(21)-ene and 2,3-seco-2 → 3 lactone, 1β,3β-epoxy-hop-16-ene, respectively.

Swertia petiolata Royle is a perennial medicinal herb growing at high altitude on grassy and moist meadows of Kashmir (2800–3700 m). The plant has not been chemically investigated previously, although some members of the genus are reported to contain xanthones [1, 2], secoiridoid glycosides [3, 4], triterpenoids [5, 6], flavonoids [7], and an alkaloid [8]. The present communication deals with the isolation and characterisation of 2,3-seco-2 → 3 lactone, 1β,3β-epoxy-hop-17(21)-ene (**1**) and 2,3-seco-2 → 3 lactone, 1β,3β-epoxy-hop-16-ene (**2**). These triterpenes are being reported for the first time from the genus *Swertia* and to our knowledge **1** and **2** have not been reported previously from any other source.

The petrol extract of the whole plant was subjected to repeated column chromatography over silica gel to yield a white amorphous solid which on further column chromatography on silver nitrate-impregnated silica gel furnished compounds **1** and **2**. Both gave a positive Liebermann–Burchard test for triterpenes and did not show any absorption above 220 nm in the UV spectrum. Compound **1**, mp 308° and compound **2**, mp 304.5° displayed $[M]^+$ at *m/z* 454 and both analysed for $C_{30}H_{46}O_3$. Compound **2** in its IR spectrum exhibited an intense band at 1792 cm^{-1} which was ascribed to the carbonyl group of a γ-lactone, with an ether linkage α to oxygen as no other carbonyl or hydroxyl group was detected in the IR spectrum. This seco-lactone moiety was supported by singlets at δ5.34 and 4.08 in the ^1H NMR spectrum, assignable to the hydrogens on the oxygen bearing C-atoms in the molecule. The above substitution pattern could only be placed in the ring A part of a triterpene skeleton. A base peak at *m/z* 189, supported by strong $[M-Me]^+$ and $[M-isopropyl]^+$ fragments was suggestive of a hopane or lupane carbon skeleton for **2** [9, 10], with unsaturation in ring D or E, as ^1H NMR also did not indicate the presence of an isopropenyl side chain. In the IR spectrum weak absorptions at 1639 and 824 cm^{-1} were indicative of a trisubstituted double bond. In addition a doublet at 1389 and 1354 cm^{-1} was observed for *gem* dimethyl and/or isopropyl groups. An olefinic proton was observed as a broad doublet with a coupling constant of 8 Hz in the ^1H NMR spectrum. The presence of unsaturation at C-12 was ruled out due to lack of an ion at *m/z* 218 in the mass spectrum. However, the double bond could conveniently be placed at C-19 (21) in the lupane or at C-20 in the hopane skeleton, but these positions were ruled out on the basis of a large *J* value. Therefore, the unsaturated linkage was most favourably placed at C-16 in the hopane skeleton. This was supported by a strong retro-Diels–Alder fragment at *m/z* 150 in mass spectrum of **2**. The ^{13}C NMR spectrum also supported this linkage with resonance signals at δ121 and 140 for C-16 and C-17. The above data suggested the depicted structure for compound **2**. Though the ring A part of **2** can have four possible regio and stereochemical arrangements, the proposed arrangement was prefered on the basis of a comparison of physico-chemical data with the only structurally related hopene triterpene, thysanolactone [11], which has its stereochemistry firmly established by X-ray analysis. The final proof for the proposed structure was provided by catalytic hydrogenation of **2**. The hydrogenated product **3**, mp 278.5°, displayed M^+ at *m/z* 456 and a base peak at *m/z* 191 which indicated a gain of two mass units. The spectral data and mp of **3** were identical with those of the dihydro product of thysanolactone [11] which confirmed the structure for **2**.

The ^1H NMR pattern and other spectral data of compound **1** were identical to those of **2**, but lacked the olefinic proton signal in the ^1H NMR spectrum and showed an additional multiplet due to a methine proton of the isopropyl group. The ^1H NMR spectrum also did not support an olefinic methyl or terminal methylene signal. The unsaturation was in ring D or E as proved by the base peak at *m/z* 189 in the mass spectrum. The compound resisted prolonged hydrogenation with Pd-C–ethyl acetate in the presence of glacial acetic acid, thereby suggesting the tetrasubstituted nature of the double bond, which can only be placed at C-17 (21) in a hopane skeleton, leading to the proposed structure for **1**.

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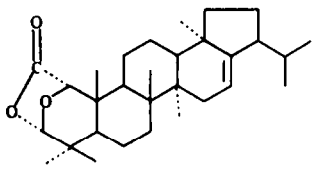

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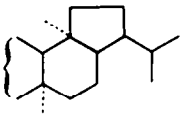

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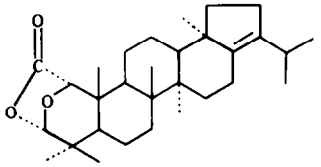

1

EXPERIMENTAL

Mps: uncorr. The air-dried whole plant material (1.2 kg) of *S. petiolata* Royle (voucher No. 4536 U.D., deposited with the Herbarium of Botany Department, University of Kashmir), collected in July–August from Gulmarg (Kashmir) was extracted with petrol. The extract after filtration was chromatographed over silica gel (125 g, 60–120 mesh) and eluted with petrol, petrol–EtOAc and EtOAc successively. The fraction eluted with petrol–EtOAc (96:4) was re-chromatographed on silica gel and the middle collections from petrol–EtOAc (99:1) elute upon evapn yielded a white amorphous solid, which repeatedly failed to crystallize and appeared as a single spot on TLC plates in different solvent systems. However, it could be resolved on 5% $AgNO_3$ impregnated silica gel G plates in to two distinct spots, **1** (R_f 0.60) and **2** (R_f 0.45) [petrol–$CHCl_3$, 2 ml:1 drop]. Therefore, the whole solid was chromatographed (20 g silica gel + 1 g $AgNO_3$ in 40 ml H_2O, activated at 105°) in the dark and eluted only with petrol (100 × 100 ml). Pooled fractions 19–28 and 73–85 were concd separately and upon recrystallization from MeOH yielded 82 mg **1** and 147 mg **2**, respectively as white micro-crystalline needles.

Compound **1**. Mp 308°, $C_{30}H_{46}O_3$, IR ν_{max}^{KBr} cm^{-1}: 2959, 1792, 1454, 1394, 1358, 1190, 1082, 998, 929 and 701. ^1H NMR (100 MHz, $CDCl_3$): δ5.35 (1H, *s*, H-3), 4.06 (1H, *s*, H-1), 2.76 (1H, *m*, H-22), 1.23 (3H, *s*), 1.20 (3H, *s*), 1.02 (3H, *s*), 1.0 (3H, *s*), 0.95 (3H, *s*), 0.94 (3H, *s*), 0.91 (3H, *s*), 0.70 (3H, *s*) [Me 23–30]. EIMS (probe) 70 eV, *m/z* (rel. int.): 454 $[M]^+$ (75), 439 (45), 411 (12), 393, 217, 205, 203, 189 (100), 175, 161, 159, 135, 95. (Found: C, 79.01; H, 10.32; calcd for $C_{30}H_{46}O_3$ C, 79.24; H, 10.20%).

Compound **2**, mp 304.5°, $C_{30}H_{46}O_3$, IR ν_{max}^{KBr} cm^{-1}: 2957, 1792, 1639, 1458, 1389, 1354, 1176, 1087, 1010, 998, 963, 954, 922, 882, 824, 704. ^1H NMR (100 MHz, $CDCl_3$): δ5.34 (1H, *s*, H-3), 5.22 (1H, *br d*, J = 8 Hz, H-16), 4.08 (1H, *s*, H-1), 1.23 (6H, *s*), 1.02 (6H, *s*), 0.97 (3H, *s*), 0.94 (6H, *s*), 0.77 (3H, *s*) [Me 23–30]. EIMS (probe) 70 eV, *m/z* (rel. int.): 454 $[M]^+$ (50), 439 (30), 411 (21), 393, 275, 217, 205, 203, 189 (100), 175, 161, 150 (45), 149, 137, 135, 95. (Found: C, 78.96; H, 10.03; calcd for $C_{30}H_{46}O_3$ C, 79.24; H, 10.20%). ^{13}C NMR (25.2 MHz, CCl_4–C_6D_6): δ79.0 (C-1), 173.1 (C-2), 111.0 (C-3), 40.1 (C-4), 49.8[a] (C-5), 18.0 (C-6), 34.2 (C-7), 42.6 (C-8), 50.5[a] (C-9), 37.0 (C-10), 21.0 (C-11), 24.1 (C-12), 39.0 (C-13), 42.8 (C-14), 34.6 (C-15), 121.0 (C-16), 140.0 (C-17), 47.0[b] (C-18), 29.4 (C-19), 30.1 (C-20), 48.2[b] (C-21), 31.0 (C-22), 27.5 (C-23), 19.3[c] (C-24), 26.0 (C-25), 16.9 (C-26), 16.4 (C-27), 19.1[c] (C-28), 20.0[d] (C-29), 21.0[d] (C-30). (a, b, c, d assignments bearing same superscript may be reversed.)

Catalytic reduction of **2**. Compound 2 (40 mg) was dissolved in EtOAc (15 ml) and glacial AcOH (0.3 ml) and reduced catalytically with 10% Pd-C (12 mg). The reaction was worked-up as usual and the product recrystallized from petrol–EtOAc (1:1) to afford white needles of **3** (30 mg), mp 278.5°. IR ν_{max}^{KBr} cm^{-1}: 1793 (γ-lactone C=O). ^1H NMR (100 MHz, $CDCl_3$): δ5.30 (1H, *s*, H-3), 4.08 (1H, *s*, H-1), 1.16 (6H, *s*), 0.99 (6H, *s*), 0.96 (3H, *s*), 0.91 (6H, *s*), 0.78 (3H, *s*) [Me 23–30]. EIMS (probe) 70 eV *m/z* (rel. int.): 456 $[M]^+$ (68), 441 (48), 413 (18), 395, 207, 205, 191 (100), 177, 152, 139, 125, 121, 110. (Found: C, 78.81; H, 10.31; calcd for $C_{30}H_{48}O_3$ C, 78.89; H, 10.53%).

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