Absolute Structure of Eremophilenolide from *Solidago dahurica*

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From the aerial parts of *Solidago dahurica* 10β-hydroxy-8β-methoxyeremophilenolide (1) and 8β,10β-dihydroxyeremophilenolide (2) have been isolated. The first X-ray crystal structure analysis of 1 has established the absolute configuration of eremophilenolide.

Key words *Solidago dahurica*; Compositae; eremophilenolide; X-ray crystal structure

Solidago (*S.*) *dahurica* KITAG. (Compositae) occurs in Myangad Somon, Hovd City, Mongolia, and has been used as a Mongolian folk medicine for the treatment of viral infection and female complaints. Isolation of the components of many *Solidago* species has been reported,[1-7] but there is no report about those component of *S. dahurica*. The present paper deals with the isolation and absolute configuration of two eremophilenolides.

Plant material was collected at Mount Altan-Huhii. After drying and pulverization, the aerial parts were extracted with aqueous methanol, and removal of the solvent gave a waxy solid which was successively extracted with hexane and chloroform. From the chloroform extract, two compounds were isolated and identified.

The ^{1}H- and ^{13}C-NMR spectra of compound **1** showed the presence of six quaternary carbon atoms, one methine, five methylenes, three methyl groups and one methoxyl group. The presence of three quaternary carbons at δ 126.8, 158.2 and 173.3 and of a vinylic methyl group at δ_H 1.86 (d, J=2 Hz) and δ_C 8.6 suggested a methyl substituted α,β-unsaturated lactone. The electron impact (EI)-mass spectrum of **1** showed a molecular ion at m/z 280 corresponding to the formula, $C_{16}H_{24}O_4$. These data could be accommodated into the skeletons of several common sesquiterpene lactones, and **1** was shown to be 10-hydroxy-8-methoxyeremophilenolide by the heteronuclear multiple bond connectivity (HMBC) experiment (Fig. 1). Although this compound has four chiral centers, the coupling constant of the ^{1}H-NMR spectra of **1** supply no useful information about the relative configurations of their asymmetric centers. The absolute configuration of the eremophilenolide obtained from the aerial parts of *Hertia cherifolia*, is tentatively assumed to be 10β-hydroxy-8β-methoxyeremophilenolide by comparison of ^{1}H- and ^{13}C-NMR chemical shifts with related compounds.[8,9] In order to confirm the NMR characterization of this type of sesquiterpene lactone[10-12] the molecular structure of **1** has been determined first by single crystal X-ray diffraction, and the absolute configuration has been investigated at the final stage of the X-ray structure refinement. The chiral model of **1** shown in Fig. 2 has been converged at R=4.70% in contrast to the other enantiomer at R=4.71%. The small but distinct difference has proved that the former assignment of absolute configuration[8] is correct.

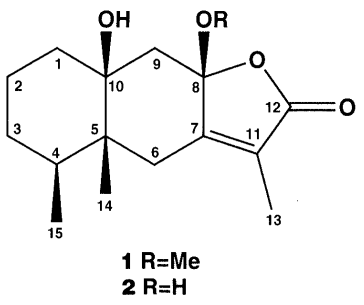
Compound **2** displayed ^{1}H- and ^{13}C-NMR spectra similar to those of **1**, the difference between **1** and **2** was the absence of a methoxyl signal. The mass spectrum of **2** showed a molecular ion at m/z 266 corresponding to a formula of $C_{15}H_{22}O_4$. Similarities between the ^{1}H- and ^{13}C-NMR spectra of **1** and **2** suggested the same relative configurations of their asymmetric centres. **2** is therefore assigned to be 8β,10β-dihydroxyeremophilenolide.

Experimental

General Procedures NMR spectra were recorded on a JEOL JNM-A500 spectrometer in methanol-d_4 with tetramethylsilane (TMS) as internal standard. Electron impact mass spectrum (EI-MS) were recorded on a JEOL JMS-DX300 spectrometer. Optical rotations were measured with a JASCO DIP-4 digital polarimeter.

Plant Material The aerial parts of *Solidago dahurica* were collected in July 1996 from Mount Altan-Huhii in Myangad Somon, Hovd City, Mongolia. The plant was identified by Dr. S. Ligaa in the Herbarium of the Mongolian State University.

Extraction and Isolation Powdered dry material (500 g) was homogenized with 96% methanol (3×5 l). The extract was concentrated to a volume of 100 ml which was successively extracted with hexane, chloroform and ethylacetate. Evaporation of the chloroform extract yielded 20 g of a waxy solid, 15 g of which was chromatographed on silica-gel. Linear elution with hexane and gradient elution with ethylacetate in hexane gave a mixture of **1** and **2**, which was further purified by MPLC. This resulted in **1** (20 mg) and **2** (26 mg).



1 R=Me
2 R=H

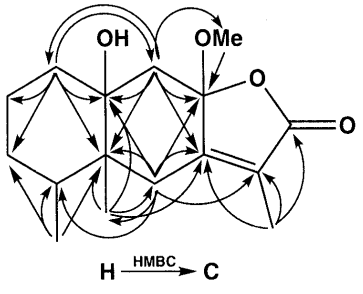


Fig. 1

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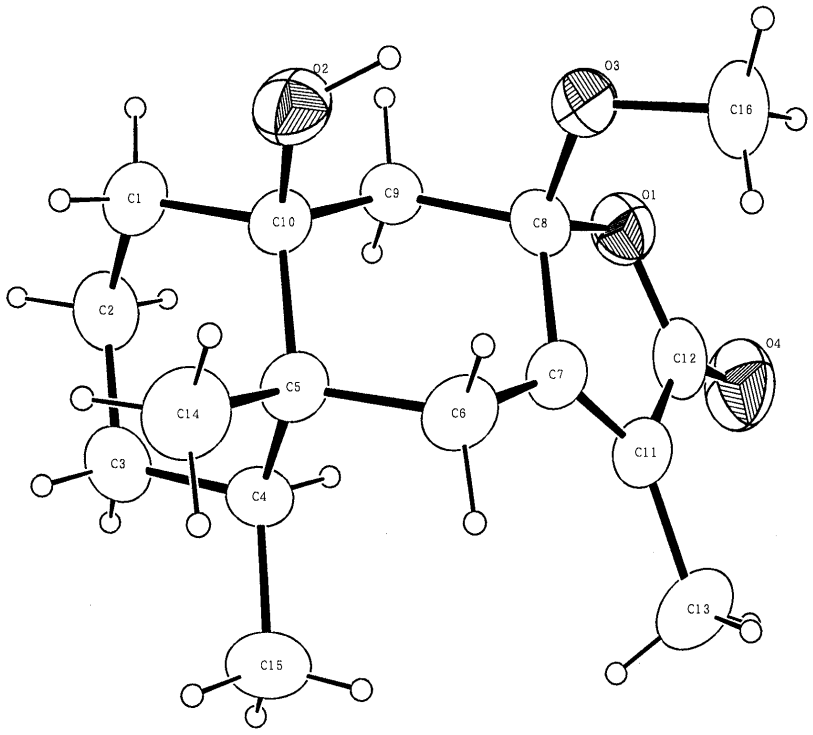

Fig. 2

X-Ray Structure Determination and Refinement X-Ray quality single crystals of **1** were obtained by slow evaporation from methanol and water. The crystal was examined on an Enraf–Nonius CAD4 diffractometer using Mo-$K\alpha$ radiation. The determination of crystal parameters and intensity collection were routine. Intensity data were reduced for standard Lorentz and polarization effects but not for absorption ($\mu = 0.74\,cm^{-1}$). The structure was solved by the direct method and refined by difference Fourier and full-matrix least-squares techniques. The final structure model, using anisotropic thermal parameters for all non-hydrogen and fixed parameters for idealized hydrogen atoms, was carried to convergence. Complete lists of crystal data, atomic coordinates and thermal parameters, and individual bond lengths and angles will be available on request to the authors.

10β-Hydroxy-8β-methoxyeremophilenolide (1) $[\alpha]_D^{23}$: 182° ($c = 0.23$, methanol). MS *m/z*: 280 $[M]^+$. ^{1}H-NMR (methanol-d_4) δ: 3.13 (3H, s, OMe), 2.69 (1H, d, $J = 13$ Hz, H-6a), 2.37 (1H, d, $J = 15$ Hz, H-9a), 2.34 (1H, d, $J = 13$ Hz, H-6b), 2.06 (1H, d, $J = 15$ Hz, H-9b), 1.86 (3H, d, $J = 2$ Hz, H-13), 1.78—1.72 (1H, m, H-1a), 1.59—1.55 (1H, m, H-2a), 1.42—1.26 (5H, m, H-1b, 2b, 3, 4), 1.04 (3H, s, H-14), 0.89 (3H, d, $J = 7$ Hz, H-15). ^{13}C-NMR (methanol-d_4) δ: 35.9, 23.2, 31.0, 34.7, 47.5, 31.7, 158.2, 107.6, 43.9, 74.9, 126.8, 173.3, 8.6, 15.2, 16.8 (C-1—C-15).

8β,10β-Dihydroxyeremophilenolide (2) $[\alpha]_D^{23}$: 126° ($c = 1.30$, methanol). MS *m/z*: 266 $[M]^+$. ^{1}H-NMR (methanol-d_4) δ: 2.68 (1H, d, $J = 14$ Hz, H-6a), 2.46 (1H, dd, $J = 2$, 14 Hz, H-6b), 2.37 (1H, d, $J = 14$ Hz, H-9a), 1.99 (1H, d, $J = 14$ Hz, H-9b), 1.81 (3H, d, $J = 1$ Hz, H-13), 1.78—1.74 (1H, m, H-1a), 1.58—1.56 (1H, m, H-2a), 1.45—1.37 (4H, m, H-1b, 2b, 3a, 4), 1.36—1.28 (1H, m, H-3b), 1.04 (3H, s, H-14), 0.87 (3H, d, $J = 6$ Hz, H-15). ^{13}C-NMR (methanol-d_4) δ: 35.7, 23.0, 30.9, 34.6, 47.4, 31.4, 160.5, 104.7, 43.9, 75.2, 123.5, 174.1, 8.4, 15.2, 16.8 (C-1—C-15).

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