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Epoxysesquithujene, a novel sesquiterpenoid from *Valeriana hardwickii* var. *hardwickii*

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Abstract

Epoxysesquithujene, a new sesquiterpene epoxide has been characterized in the essential oil of *Valeriana hardwickii* var. *hardwickii* on the basis of chemical reactions and extensive NMR data. Fourteen other terpenoids have also been identified on the basis of GC-MS.

Keywords: *Valeriana hardwickii* var. *hardwickii*; Essential oil; Epoxysesquithujene

1. Introduction

Valeriana, a major genus in the Valerianaceae, is known for its use in traditional herbal medicines in treatment of epilepsy and insanity [1,2]. Recently Himalayan *Valeriana* have been analysed for their terpenoid diversity [3,4]. We report here the isolation of a new compound (**1**) and the composition of Himalayan *Valeriana hardwickii* var. *hardwickii,* a rare aromatic herb growing at an altitude of 2200m.

2. Experimental

2.1. General

HPLC: Waters 440 with RI detector and μ-porasil column (250 mm × 7.8 mm size) using varying concentrations of Et_2O in hexane at a flow rate of 2.0 ml/min. The sample was dissolved in the mobile phase and injected using a 25 ml loop.

GC: Nucon 5765 Gas Chromatograph using a RTX-5 MS capillary column (30 m × 0.32 mm, 0.25 μm film coating).

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Table 1
NMR data of compound **1**, **2** and **3** ($CDCl_3$, *J* in Hertz)

Carbon	^1H		^{13}C		Direct correlation of ^1H to ^{13}C in 1	Long-range correlations of ^1H to ^{13}C in 1
	1	3 [a]	1	2 [b]		
1	1.26 (3H, *s*)	1.61(3H, *s*)	18.6	29.6	1 (126.6)	14, 2, 3
2	–	–	58.0	71.4		–
3	2.71 (1H, *t*)	5.12 (1H, *t*)	64.6	44.7	3 (165.9)	14, 4, 5, 2
4	1.59 (1H, *m*)	2.04 (2H, *dt*)	27.0	32.0		13, 5, 8
5	1.59 (1H, *m*)	1.1 (1H, *m*)	31.8	36.1		
6	1.17 (1H, *m*)	1.4 (1H, *m*)	38.3	38.8		
7	–	–	33.0	33.4		
8	α 2.39 (1H, *dt*) β 2.10 (1H, *dm*)	α 2.38 (1H, *dt*) β 2.11 (1H, *dm*)	35.3	35.9		α 12, 7, 6, 9, 10 β 9,10
9	4.90 (1H, *br s*)	4.95 (1H, *br s*)	120.8	121.3		15, 11, 7, 8, 10
10	–	–	145.0	145.5		
11	1.32 (1H, *m*)	1.31 (1H, *m*)	30.9	31.3		13, 5, 8
12	α 0.11 (1H, *m*) β 0.76 (1H, *m*)	α 0.10 (1H, *dd*) β 0.76 (1H, *dd*)	23.6	24.1	12 β (158.7)	
13	0.95 (3H, *d*)	0.93 (3H, *d*)	17.8	18.3	13 (131.7)	5, 7, 6
14	1.31 (3H, *s*)	1.68 (3H, *s*)	24.9	24.6	14 (128.0)	1, 2, 3
15	1.75 (3H, *bs*)	1.76 (3H, *dt*)	16.2	16.7	15 (127.8)	11, 9, 10

[a] Data taken from Ref. [8].
[b] The ^{13}C signals of C-1, C-2, C-3 and C-4 were assigned from a comparison with the shifts of 2-methylhexan-2-ol [9].

GC-MS: Thermo Quest Trace GC 2000 interfaced with Finnigan MAT Polaris Q ion trap MS using a RTX-5 MS non-polar capillary column (30 m × 0.25 mm, 0.25 μm film coating), the oven temp from 60 °C at 3 °C/ min ramp to 210 °C with a final hold time of 10 min. The EI-MS were recorded at 30 and 70 eV.

^1H NMR (300 MHz) and ^{13}C NMR (75 MHz): Bruker DRX-300 in $CDCl_3$.

IR: Perkin Elmer 881 IR spectrometer.

Optical rotations: Autopol III in $CHCl_3$.

2.2. Plant

V. hardwickii var. *hardwickii* roots/rhizomes, collected from the Khati village located in Kumaon Himalaya (2200 m) in September 2003 was identified by the Botanical Survey of India, Dehradun. A voucher specimen has been deposited in the Phytochemistry Laboratory, Chemistry Department, Kumaun University.

2.3. Extraction and isolation

The fresh roots/rhizomes (200 g) steam distilled with a copper still fitted with spiral glass condensers for 2 h yielded 5 l water distillate. Water distillate was saturated with NaCl and extracted with hexane/CH_2Cl_2. The organic phase was dried over anhydrous Na_2SO_4 and evaporated on thin-film rotary evaporator giving 0.5 ml of oil. The oil fractionated on Si-gel CC with gradient elution from *n*-hexane to 30% Et_2O in *n*-hexane. Et_2O in *n*-hexane (5%) gave four fractions (I–IV). Fraction III (100 mg) was purified by using μ-porasil column 2.0 ml/min flow rate and RI detector using 5.0% Et_2O in *n*-hexane to give compound **1** (65 mg). Fractions V–VIII gave bornyl acetate [5].

Epoxysesquithujene (**1**). $C_{15}H_{24}O$, colourless liquid; $[\alpha]^{20}_D - 38.04$ ($CHCl_3$; c 0.34); EI-MS *m/z*: 220 [M^+]; ^1H NMR and ^{13}C NMR: reported in Table 1.

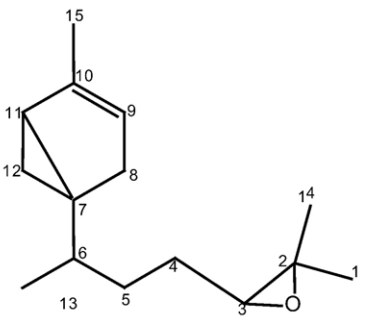
Compound 1 with $LiAlH_4$/ THF at 20 °C for 1 h gave a mixture with sesquithujenol (**2**) as the major product. ^{13}C NMR data: see Table 1.

3. Results and discussion

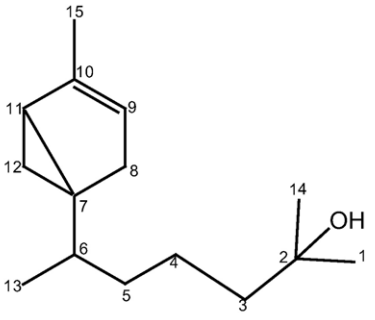
Organic solvent extraction of the steam distillate of the root/rhizomes of *V. hardwickii* var. *hardwickii* afforded the essential oil that after CC and HPLC yielded a novel compound epoxysesquithujene **1** along with bornyl acetate.

The essential oil analysis showed the presence of more than 20 compounds, 15 of which were identified by GC-MS using the NIST and WILEY MS library search [6]. α-Pinene (0.12%), β-pinene (0.16%), camphene (1.42%), p-cymene (0.10%), limonene (0.12%), γ-terpinene (0.26%), borneol (0.30%), thymol methyl ether (1.81%), carvacrol methyl ether (0.58%), bornyl acetate (20.45%), *cis*-caryophyllene (3.22%), methyl thymohydroquinone (0.51%), *trans*-caryophyllene (0.36%) and ar-curcumene (1.17%) are among the major compounds identified. On the contrary, *Valeriana javanica*, a morphologically indistinguishable species, has been reported to possess kessyl acetate (36.2%), patchouli alcohol (10.3%), kessane (6.8%) and valeranone (3.2%) [7]. Thus, the results conclude that the *V. hardwickii* and *V. javanica* have no similarity in their flavor compositions and this will consequently affect their use as medicine and flavour materials. Significantly epoxysesquithujene is ca. 50% of *V. hardwickii* var. *hardwickii* essential oil and has not been found in any other *Valeriana* sp.

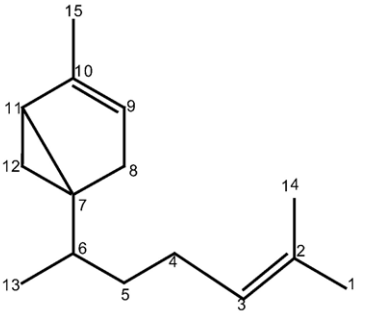
Compound **1** was obtained as a colourless oil whose EI-MS: *m*/*z* 220 [M^+] was compatible with a molecular formula $C_{15}H_{24}O$. Comparison of the NMR data reported in Table 1 with those of compound sesquithujene (**3**) [8] and the reduction product sesquithujenol (**2**) [9] revealed it to be the novel compound epoxysesquithujene.



Epoxysesquithujene **1**



Sesquithujenol **2**



Sesquithujene **3**

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