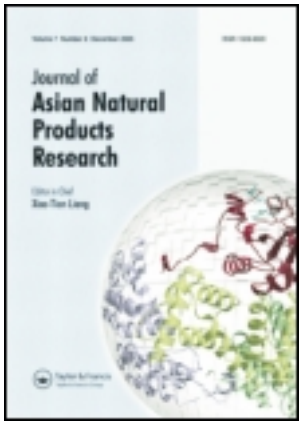
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A new cembrane glycoside in Asterothamnus centrali-asiaticus from Gobi desert

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A new cembrane glycoside in *Asterothamnus centrali-asiaticus* from Gobi desert

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A new cembrane glycoside, nephthenol 15-*O*-β-D-quinovoside, was isolated from the aerial parts of *Asterothamnus centrali-asiaticus*. Its structure was elucidated by 1D and 2D NMR spectroscopic analysis, as well as by mass spectrometry. This is the first report of the occurrence of a cembrane glycoside in vascular plants.

Keywords: *Asterothamnus centrali-asiaticus*; Asteraceae; cembrane glycoside

1. Introduction

Asterothamnus centrali-asiaticus Novopokr. (syn. *Aster alyssoides* var. achnolepis Hand.-Mazz., *Aster centraliasiaticus* Novopokr.) (Asteraceae) is a plant species widespread in Mongolia and northwest inner Mongolia, China [1]. The literature survey revealed only two reports on the essential oil composition from the leaves [2] and on the content of fatty acids in the seeds of this species [3]. No phytochemical data have been found for any other *Asterothamnus* species. Studies on secondary metabolites isolated from different *Aster* species revealed that while some of them are rich in sesquiterpene lactones [4–8], others are rich in diterpenes [9–12]. Obviously, both types of natural compounds could be used as chemotaxonomic markers in genus *Asterothamnus*. On the other hand, many representatives of these types of secondary metabolites were shown to exhibit a wide range of biological activities [13,14]. Thus, we were provoked to study *A. centrali-asiaticus*.

In this study, we describe the structure of one new diterpene with cembrane carbon skeleton.

2. Results and discussion

Compound **1** was isolated from the chloroform extract of *A. centrali-asiaticus.* The NMR spectra indicated that **1** was a diterpene incorporating a sugar moiety. Thus, the ^{1}H NMR spectrum (Table 1) contained signals at δ 3.25 (t), 3.30 (dd), 3.35 (dd), and 3.50 (t) for four oxymethine protons, a three-proton doublet at δ 1.30 for a methyl group, and a doublet at δ 4.43, corresponding to a 6-deoxyhexose. The sugar moiety was assigned as quinovose (6-deoxy-glucopyranose), on the basis of ^{1}H–^{1}H COSY correlations, interpretation of the coupling constants between the protons, and comparison with reported data [15,16]. Thus, the observed $J_{2',3} = J_{3',4'} = J_{4',5'} = 9.0$ Hz revealed an axial disposition of H-2′-H-5′ protons, while the large coupling constant $J_{1',2'} = 7.6$ Hz indicated β-configuration of the glycosyl linkage. The ^{13}C NMR

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Table 1. ^{1}H and ^{13}C NMR spectral data for **1**.

Position	δ_H mult. (*J* in Hz)	COSY	δ_C[a]
1	1.50 m, 1H	H-2α, H-2β, H-14α, H-14β	47.6 (CH)
2α	2.10 m, 1H	H-1, H-2β, H-3	27.9[b] (CH_2)
2β	1.90 m, 1H	H-1, H-2α, H-3	
3	5.07 br t, 1H (5.7)	H-2α, H-2β, H-18	126.7 (CH)
4	–		133.8 (C)
5	2.00–2.20 m, 2H		38.3 (CH_2)
6	2.00–2.20 m, 2H	H-7	24.6[b] (CH_2)
7	4.90 br t, 1H (6.4)	H-6, H-6a, H-19	125.8 (CH)
8	–		133.4 (C)
9	2.00–2.20 m, 2H		39.2 (CH_2)
10	2.05–2.15 m, 2H	H-11	24.0[b] (CH_2)
11	4.97 br t, 1H (6.0)	H-10, H-20	125.4 (CH)
12	–		133.2 (C)
13	2.00, 2.10 m (2H)	H-14α, H-14β	37.5 (CH_2)
14α	1.25 m, 1H	H-1, H-13, H-14β	27.7[b] (CH_2)
14β	1.60 m, 1H	H-1, H-13, H-14α	
15	–		81.5 (C)
16	1.18 s, 3H		22.1 (CH_3)
17	1.28 s, 3H		26.2 (CH_3)
18	1.55 s, 3H	H-3	15.5 (CH_3)
19	1.56 s, 3H	H-7	15.9 (CH_3)
20	1.54 s, 3H	H-11	15.4 (CH_3)
1′	4.43 d, 1H (7.6)	H-2′	96.6 (CH)
2′	3.30 dd, 1H (7.6, 9.0)	H-1′, H-3′	74.3 (CH)
3′	3.50 t, 1H (9.0)	H-2′, H-4′	76.4 (CH)
4′	3.25 t, 1H (9.0)	H-4′, H-5′	75.3 (CH)
5′	3.35 dd, 1H (6.1, 9.0)	H-4′, H-6′	71.3 (CH)
6′	1.30 d, 3H (6.1)	H-5′	17.8 (CH_3)

[a] Deduced by HSQC and HMBC experiments.
[b] Interchangeable.

spectrum (Table 1) exhibited 26 signals, among which 6 were unambiguously assigned to the quinovosyl moiety based on HSQC and HMBC correlations (Figure 1). In addition, the ^{13}C NMR and HSQC spectra showed signals for five methyls (three olefinic at δ 15.4, 15.5, and 15.9), seven methylenes, three olefinic methines (δ 125.4, 125.8, and 126.7), one methine at δ 47.6, and four quaternary carbons (three olefinic at δ 133.2, 133.4, and 133.8 and one at δ 81.5, attached to an oxygen atom). Singlets for three vinylic methyl groups (δ 1.54, 1.55, and 1.56) and three olefinic protons (δ 5.07 br t, 4.90 br t, and 4.97 br t) in the ^{1}H NMR spectrum confirmed the presence of three 3-substituted double bonds. The long-range

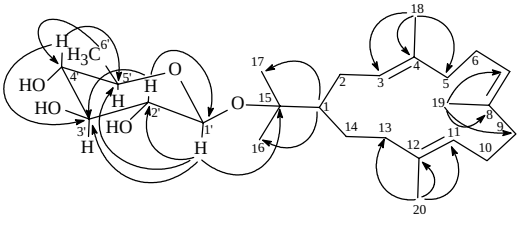


Figure 1. Structure of compound **1** and its key HMBC correlations (H → C).

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$^{1}H-^{13}C$ correlations, observed between H-18/C-3, C-4, and C-5, between H-19/C-7, C-8, and C-9, and between H-20/C-11, C-12, and C-13, exhibited three identical isobutenyl moieties (a ring of 14 carbons for the analyzed compound). An additional C-2/C-1/C-14 chain was confirmed by $^{1}H-^{1}H$ COSY cross-peaks between the respective protons H-1 (δ 1.50) and two CH_2 groups (δ 1.25; 1.60 and 1.90; 2.10) as well as two methylene groups (δ_c 24.6 and 24.0) appeared to be connecting units of the isobutenyl functions. An oxygenated isopropyl group was assigned on the basis of two 3-proton singlets at δ 1.18 and 1.28 for two geminal methyl groups linked to a carbon at δ 81.5. Its chemical shift showed that an oxygen function was attached to this position. The HMBC correlations between C-16 (δ 22.1) and C-17 (δ 26.2) and H-1 (δ 1.50) revealed the attachment of the isopropyl group to C-1, the signal of which appeared at δ 47.6. All these data allowed determination of a cembrane diterpene structure of the aglycone part of **1**. Furthermore, the chemical shift of C-15 (δ 81.5) and strong HMBC correlation between C-15 and the anomeric proton H-1′ (δ 4.43) from the quinovosyl moiety clearly indicated the position of the glycosyl function at this carbon atom. Comparison of the ^{1}H and ^{13}C NMR data of the aglycone part of **1** with those of known cembrane diterpenoids showed that the described compound was a nephthenol derivative. Thus, **1** was named nephthenol 15-*O*-β-D-quinovoside.

It is known that nephthenol exists in two enantiomeric forms: (−)-nephthenol and its (+)-nephthenol [17]. The experiment to obtain nephthenol by acidic hydrolysis of **1**, in order to determine its enantiomeric form, was unsuccessful probably because of insufficient amount or decomposition of **1** under reaction conditions. However, by comparison of the measured optical rotation of the studied sample ($[\alpha]$ −32) with the published data for methyl 6-deoxy-D-glucopyranoside ($[\alpha]$ −39.7) [18], (−)-nephthenol ($[\alpha]$ −30) [19], (+)-nephthenol ($[\alpha]$ + 22.8), and known (+)-nephthenol glycosides ($[\alpha]$ + 10, + 11.5) [17], as well as according to the Klyne's rule [20], it was supposed that **1** is a (−)-nephthenol 15-*O*-β-D-quinovoside, which correlated with 1*R* configuration. To the best of our knowledge, there is only one report on the occurrence of (−)-nephthenol in a plant taxon (*Guarea kunthiana,* Meliaceae family) [19], while both forms of this compound have been described as constituents of marine invertebrates (e.g., soft corals). Furthermore, glycosyl derivatives of (+)-nephthenol have been found only in the Caribbean gorgonian octocoral *Eunicea* sp. so far [17]. Thus, compound **1** is the first C-15 analog of (−)-nephthenol isolated up to now.

3. Experimental

3.1 General experimental procedures

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance II + 600 NMR spectrometer (Bruker, Karlsruhe, Germany) with operating frequency 600 MHz (^{1}H) and 150 MHz (^{13}C), using tetramethylsilane as an internal standard and $CDCl_3$ as a solvent. The chemical shifts (δ) are expressed in ppm and coupling constants (J) in Hz. 1D and 2D NMR (^{1}H and ^{13}C NMR, COSY, HSQC, and HMBC) spectra were recorded using the standard Bruker pulse sequence. HR-ESI-TOF-MS was measured using a 6210 Time-of-flight LC/MS system (Agilent Technologies, Santa Clara, CA, USA) coupled with high performance liquid chromatography instrument 1200 Series (Agilent Technologies). For optical rotation, a Rudolph Research Analytical AUTOPOL IV automatic polarimeter (Hackettstown, NJ, USA) was used. The IR spectrum was recorded on FTIR spectrometer Tensor 27 (Bruker). Column chromatography (CC) was carried out on silica gel 60 (230–400 mesh, Merck, Darmstadt, Germany).

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Thin-layer chromatography (TLC) on Silica gel 60 F_{254} plates (Merck) was used for preparative TLC and for checking the purity of the compound. Spots were visualized by spraying with concentrated H_2SO_4 followed by heating.

3.2 Plant material

Aerial parts from the native plants of *A. centrali-asiaticus* were collected from Caagaan cav of Dund Gobi Olzit, Middle Gobi Province in July 2011. The plant species was identified by Prof. S. Shatar, and the voucher specimen (Shatar 7528) has been deposited at the Herbarium of the Mongolian Academy of Sciences, Ulaanbaatar.

3.3 Extraction and isolation

The air-dried aerial parts (10 g) were extracted with $CHCl_3$. The resulting extract (100 mg) was subjected to silica gel CC with $CHCl_3$:acetone (1:1), and eight fractions were collected (F1–F8). Further purification of F4 (10 mg) using preparative TLC (Silica gel) and $CHCl_3$:acetone (1:1) afforded **1** (2 mg).

3.3.1 Nephthenol 15-O-β-D-quinovoside (*1*)

A colorless oil. $[\alpha]_{20}$ −32 ($c = 0.1$, CH_3OH). IR ($CHCl_3$) ν_{max} cm^{-1}: 3400, 1360, 1050, 890, 753. For ^1H and ^{13}C NMR spectral data, see Table 1. HR-ESI-TOF-MS (negative mode): *m/z* 471.2883 $[M + Cl]^-$ (calcd for $C_{26}H_{44}O_5Cl$, 471.2888).

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