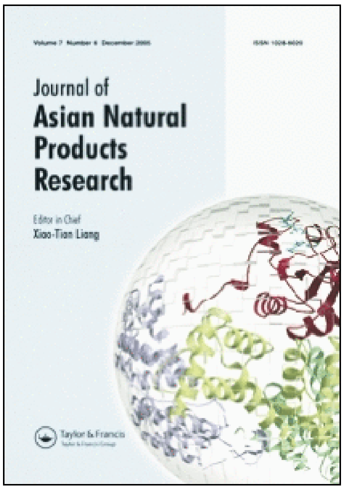

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Note

A new 1,5-seco grayanotoxin from *Rhododendron decorum*

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A new minor 1,5-seco-5-oxo-grayanotoxin named grayanotoxin XXI (**1**), together with three known grayanotoxins, grayanotoxins I, IV and VIII, has been isolated from the leaves of *Rhododendron decorum* (Ericaceae). The structure of the new compound (**1**) was determined on the basis of spectroscopic data.

Keywords: Grayanotoxin XXI; *Rhododendron decorum*; Ericaceae

1. Introduction

Rhododendron decorum Fr. (Ericaceae), an evergreen shrub or tree, is a well-known poisonous plant growing mainly in hilly and valley regions of south and southwest China. Poultry have been reported to fall into a coma after eating leaves of the plant accidentally; grayanotoxins I and IV are its main toxic components [1]. Our investigation into the plant leaves, which were collected in the Dali district of Yunnan province, China, has resulted in the isolation of a new minor 1,5-seco-5-oxo-grayanotoxin named grayanotoxin XXI (**1**), together with the three known grayanotoxins I, IV and VIII. We report here the isolation and structural elucidation of the new compound (**1**).

2. Results and discussion

Grayanotoxin XXI (**1**) was isolated as an amorphous solid and was shown by HR-ESIMS to have the molecular formula $C_{22}H_{34}O_6$ (six unsaturations). The IR absorption bands (3545, 1725, 1685, 1640 cm^{-1}) showed the presence of hydroxyl, carbonyl (ester and keto) and

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carbon–carbon double bond groups. From its ^{1}H and ^{13}C NMR (DEPT) data (table 1), it was evident that three of the elements of unsaturation are one double bond and two CO (one ketone and one ester), indicating that the molecule is tricyclic. The NMR data also show clearly that **1** contains five CH_3 (three tertiary, one olefinic and one acetyl), five CH_2, six CH (one olefinic methine and three oxymethines), six carbons (one carbonyl, one ester, one olefinic and one oxyquaternary) not bonded to hydrogen, and three protons due to OH groups.

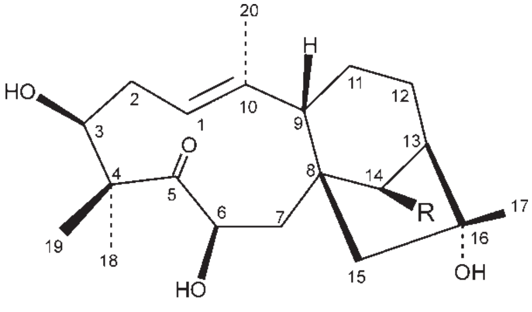
The ^{1}H and ^{13}C NMR spectra of compound **1** are very similar to those of 3(S),6(*R*),14(*R*),16(*R*)-tetrahydroxy-5-oxo-5,10-seco-ent-kaur-1(10)-ene (**2**) [2] (figure 1), a known grayanotoxin isolated from *Leucothoe grayana* Max. (Ericaceae), but had the resonances due to an additional acetyl group. Compound **1** was deduced to be the C-14 monoacetate of **2** by comparison of the chemical shift of H-14 in the ^{1}H NMR spectrum from δ 4.26 (d, $J = \mathbf{6.4\,Hz}$) in **2** to δ 5.89 (s) in (**1**) and by a strong HMBC correlation between H-14 and the ester carbonyl carbon (δ 170.5). This was confirmed by ^{1}H–^{1}H COSY, HMQC and HMBC (figure 2) experiments and the unambiguous assignment of all ^{1}H and ^{13}C NMR signals (table 1); the assignments of C-18, 19, 20 NMR data in **2** should be revised.

The relative stereochemistry was assigned by a NOESY experiment, detailed comparison of NMR data to **2**, and on biogenetic grounds [3]. The conformation of the cyclodecenone ring in C_5D_5N solution was boat-chair but the olefinic methyl (C-20) must be located on the α-side of the ten-membered ring (figure 3) as NOESY correlations (table 1) were observed between H-9 (β) and H-1 (β), between H-14 (α) and H-6 (α), between H-14, H-6, H-2 (α),

Table 1. ^{1}H and ^{13}C NMR data of compound **1***.

No.	δ_H	δ_C	*HMBC (H–C)*	*NOESY (H–H)*
1	5.18 (dd, 11.5, 3.1)	126.3 (d)	C-3, 9	H-9
2α	2.65 (ddd, 15.6, 11.5, 2.9)	33.4 (t)	C-4, 10	H-2β, 3, 20
2β	2.34 (dd, 15.6, 3.1)		C-1, 4, 10	H-2α, 19
3	4.29 (brs)	77.4 (d)	C-1, 5	H-6, 20
4		51.6 (s)		
5		214.8 (s)		
6	4.54 (brs)	69.8 (d)	C-4, 7, 8	H-3, 14, 18, 20
7α	2.38 (d, 15.9)	42.7 (t)	C-6, 8, 9, 15	H-7β, 14
7β	3.01 (dd, 15.9,4.0)		C-5, 6, 8, 14, 15	H-7α, 9, 15α
8		54.6 (s)		
9	2.26 (d, 9.1)	57.8 (d)	C-1, 8, 10, 11, 12, 14, 20	H-1, 7β, 15β
10		141.7 (s)		
11α	1.22 (m)	22.4 (t)	C-9, 10, 12, 13	H-11β, 12α
11β	1.70 (m)		C-9, 10, 12	H-11α, 12β
12α	2.20 (m)	27.4 (t)	C-9, 16	H-11α, 12β, 13
12β	1.67 (m)		C-11, 14, 16	H-11β, 12α, 17
13	2.40 (d, 6.4)	53.5 (d)	C-8, 11	H-11α, 12α, 12β, 17
14	5.89 (s)	80.8 (d)	C-9, 12, 15, 16, OAc	H-6, 7α, 20
15α	2.22 (d, 15.5)	58.0 (t)	C-7, 8, 9, 16	H-7β, 15β
15β	1.90 (d, 15.5)		C-8, 9, 14, 17	H-9, 15α, 17
16		78.7 (s)		
17	1.46 (s)	24.3 (q)	C-13, 15, 16	H-12β, 13, 15β
18	1.65 (s)	24.3 (q)	C-3, 4, 5, 19	H-6, 19
19	1.49 (s)	20.3 (q)	C-3, 4, 5, 18	H-2β, 18
20	2.03 (s)	16.3 (q)	C-1, 9, 10	H-2α, 3α, 6, 14
14-OAc		170.5 (s)		
	2.14 (s)	21.5 (q)	OAc	

* Measured in C_5D_5N at 400 and 150 MHz. δ (ppm) relative to internal TMS. Multiplicities and splittings (Hz) are in brackets.



1 R = OCOCH$_3$
2 R = OH

Figure 1. Structures of compounds **1** and **2**.

H-3 (α) and the olefinic methyl H$_3$-20 [the orientation of the olefinic methyl in **2** should also be revised].

The known grayanotoxins I, IV, VIII were identified by comparison of their spectral data (ESIMS, ^{1}H and ^{13}C NMR) with those in reported the literature [1,4].

3. Experimental

3.1 General experimental procedures

Melting points were determined on a WC-1 micro-melting point apparatus and are uncorrected. IR spectra were taken on a Perkin-Elmer 577 instrument and recorded in KBr pellets. Mass spectra were obtained on a Q-Tof Micro LC/MS/MS mass spectrometer. All NMR spectra were recorded on a Bruker AM-400 or AM-600 NMR spectrometer with TMS as internal standard.

3.2 Plant material

Rhododendron decorum Fr. was collected at Dali (Yunnan), China in September 2001 and was identified by Professor Li Hen of the Kunming Institute of Botany, where a voucher specimen has been deposited.

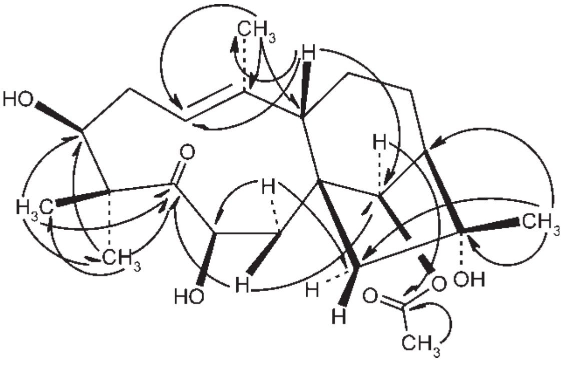


Figure 2. Selected HMBC correlations of **1**.

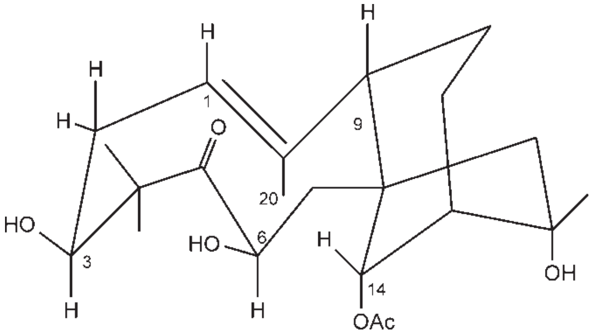


Figure 3. Conformation of **1**.

3.3 Extraction and isolation

The dried and powdered leaves (10 kg) were extracted with 95% EtOH (25 L) three times at room temperature. The combined residue (1.5 kg), after removal of the solvent, was suspended in H_2O (1 L) and extracted successively with light petroleum, $CHCl_3$ and EtOAc. The EtOAc phase was evaporated to give a red mass (500 g), which was applied to a silica gel column, eluting with $CHCl_3$ containing increasing amounts of MeOH. Repeated column chromatography yielded 1 (10 mg, eluting system $CHCl_3$–CH_3COCH_3 5:1), grayanotoxin VIII (30 mg, eluting system $CHCl_3$–EtOAc 5:1), grayanotoxin IV (60 mg, eluting with $CHCl_3$–EtOAc 3:1) and grayanotoxin I (140 mg, eluting with $CHCl_3$–CH_3COCH_3 4:1).

Grayanotoxin XXI (**1**), mp 150–152°C, $[\alpha]_D^{27}$ -11.5 (*c* 0.1, MeOH), IR (KBr); ν_{max} (cm^{-1}): 3545, 1725, 1685, 1640, 1350, 1050, 878. ^1H and ^{13}C NMR data see table 1. ESIMS: *m/z* 417 $[M+Na]^+$, HR-ESIMS: *m/z* 417.2262 $[M+Na]^+$, calcd. for $C_{22}H_{34}O_6Na$ 417.2253.

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