

Two New Polyoxygenated Cyclohexenes from *Uvaria kweichowensis*

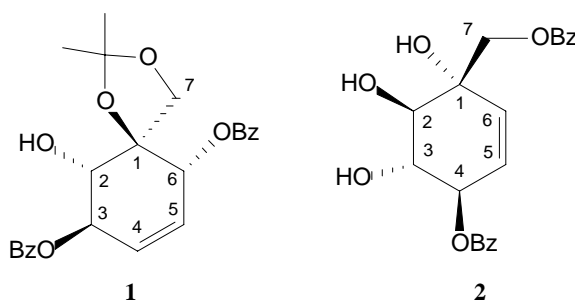
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Abstract: Two new polyoxygenated cyclohexenes, kweichowenol A and B were isolated from the leaves of *Uvaria kweichowensis* and their structures were established on the basis of their spectral data.

Keywords: Annonaceae, *Uvaria kweichowensis*, leaves, cyclohexenes, kweichowenol A, kweichowenol B.

Over the past two decades, the *Uvaria* genus has been found to be an important source of natural products with various structures and some of them have shown antitumour, antileukemic or antibiotic activities^{1, 2}. Our previous studies have resulted in the isolation of a series of polyoxygenated cyclohexenes from *U. grandiflora*, *U. tonkinensis* var. *Subglabra*^{3, 4}. To further search for active compounds from this genus, *Uvaria kweichowensis*, distributed in the southwest of China, was subjected to phytochemical investigation. From the chloroform extract of the leaves of *Uvaria kweichowensis*, two new polyoxygenated cyclohexenes, kweichowenol A (**1**) and B (**2**) were isolated. We now report the structural elucidation of two new compounds **1** and **2**.



Kweichowenol A (**1**) white needles, mp 51-53, $[\alpha]_D^{20}$ -95.8 (c 0.0011, CHCl_3). The molecular formula was established as $\text{C}_{24}\text{H}_{24}\text{O}_7$ by HR-ESI-MS showing the quasi-molecular ion at m/z 425.1598($[\text{M}+\text{H}]^+$, calcd. 425.1600). The IR spectrum of compound **1** suggested the presence of hydroxyl group(s) (3587, 3454, 1115 and 1090

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cm^{-1}), ester group(s) (strong absorption at 1722 cm^{-1}), and monosubstituted phenyl ring(s) ($1601, 1454$ and 710 cm^{-1}). The UV spectrum gave absorption maxima at λ 230, 274, and 280 nm, indicating the presence of one or two benzoyl group(s).

The proton signals between δ 7.3-8.1 (m, 10H) in the $^1\text{H-NMR}$ spectrum of **1** (**Table 1**) were attributed to the aromatic protons of two benzoyl groups. Its $^1\text{H-NMR}$ spectrum also showed two olefinic proton signals at δ 5.82 (m, 2H), two oxygenated methylene proton signals at δ 4.37, 4.32, and three oxygenated methine proton signals at δ 4.28, 5.60 and 5.79. The two methyl signals at δ 1.31 (s, 3H) and 1.46 (s, 3H) and its correlation with the quaternary carbon signal at δ 110 in the HMBC spectrum indicated the presence of the isopropylidene moiety in the structure. The signals of two benzoxy groups located at C-3 and C-6 based upon the downfield shifts of H-3 at δ 5.60 and H-6 at δ 5.79, whilst the isopropylidene group was established at C-1 and C-7, deduced from the downfield shifts of H-7 at δ 4.37 and 4.32.

Table 1 ^1H (600MHz) and ^{13}C (150MHz) NMR data of compounds **1** and **2** (CDCl_3 , δ ppm)

	1		2	
	δ_{C}	δ_{H}	δ_{C}	δ_{H}
1	85.4		74.5	
2	72.1	4.28 d (8.4)*	77.2	3.88 d (10.2)
3	73.7	5.60 dd (8.4, 2.4)	72.3	4.29 dd (10.2, 7.8)
4	129.1	5.82 m	76.0	5.63 dd (7.8, 2.4)
5	127.4	5.82 m	126.8	5.78 dd (10.2, 2.4)
6	74.1	5.79 m	133.6	5.83 dd (10.2, 1.8)
7	64.3	4.37 d, 4.32 d (8.4)	66.2	4.58 d, 4.50 d (10.8)

* Data in parentheses are J values (in Hz).

The above conclusion was supported by the existence of the fragment ion peaks (m/z 294 and 130) resulted from the typical RDA cleavage of the molecule of compound **1** in the EI-MS spectrum.

In comparison with the $^1\text{H-NMR}$ spectral data of uvarigranol F⁵, the coupling constant of the H-2 and H-3 ($J_{2,3} = 8.4$ Hz) suggested the *trans* diaxial relationship between H-2 and H-3 in the preferred half-chair conformation⁶. In addition, the coupling constant of the H-5 and H-6 ($J_{5,6} = 2.4$ Hz) revealed that the benzoxy group at C-6 was likely in the *pseudo-equatorial* position⁷.

The relative stereochemistry of compound **1** was further confirmed by its NOESY spectrum. Interactions between H-3 (δ 5.64) and H-7 (δ 4.37 and 4.32) indicated that they were at the same side of the molecule, while those between H-2 (δ 4.28) and H-6 (δ 5.79) suggested that H-2 and H-6 were at the other side.

The CD spectrum of compound **1** exhibited a split curve centered at λ 227 nm with a positive cotton effect at λ 235 (+3.42), and a negative cotton effect at λ 219 (-8.20), indicating the clockwise manner⁸ for the orientation of the two benzoxy groups at C-3 and C-6. The relative configuration of compound **1** was confirmed through the analysis of the coupling constants and its NOESY spectrum, thus the absolute configuration was established as 1R, 2S, 3R, 6R.

In order to determine whether compound **1** was naturally occurring in the leaves of *Uvaria kweichowensis*, the leaves were extracted with CHCl_3 , and the resultant extract was subjected to HR-TLC analysis. Same spot as kweichowenol A was detected in the CHCl_3 extract of the leaves of *Uvaria kweichowensis*, indicating that compound **1** occurred naturally, rather than formed during the separation procedure.

Kweichowenol B (**2**) white needles, mp 166-167, $[\alpha]_{\text{D}}^{20}$ -5.78 (c 0.0019, CHCl_3). The molecular formula was established as $\text{C}_{21}\text{H}_{20}\text{O}_7$ by HR-ESI-MS showing the quasi-molecular ion at m/z 385.1284 ($[\text{M}+\text{H}]^+$, calcd. 385.1287). Compound **2** had similar IR and UV spectra to those of compound **1**. Its $^1\text{H-NMR}$ spectrum displayed two olefinic protons (δ 5.78, 5.63), two oxygenated methylene protons (δ 4.50, 4.58) and three methane protons (δ 3.88, 4.29, 5.63) (Table 1). Among them, an AB quartet at δ 4.50 and 4.58 (10.8 Hz) was attributed to the two methylene protons at C-7, similar to those of the known polyoxygenated cyclohexenes⁷. The correlation between H-7 and the olefinic carbon at δ 133.6 in the HMBC spectrum of compound **2** suggested that the double bond located at C-5/C-6 instead of the usual C-4/C-5 position in the known compounds. Further correlation of H-7 with the ester carbonyl at δ 167.2 in the HMBC spectrum indicated that one of two benzoxy groups was located at C-7, while H-4 (δ 5.63) correlated with the ester carbonyl at δ 167.0 evidenced the other benzoxy group located at C-4. These assignments were further confirmed by the presence of the fragment ion at m/z 249 due to the loss of benzoxyloxymethyl segment from the $[\text{M}]^+$ and the diene ion at m/z 324 due to RDA cleavage in the EI-MS spectrum.

Base upon analysis of the coupling constants and the correlations shown in the NOESY spectrum, the relative stereochemistry of compound **2** was established. The $J_{2,3}$ value of 10.2 Hz revealed that *trans* diaxial relationship between H-2 and H-3, whilst the $J_{3,4}$ value of 7.8 Hz indicated the *pseudo*-axial orientation of H-4. In the NOESY spectrum of uvarigranol I⁵, H-2 correlated with H-7, however correlation between H-3 and H-7 was observed in the NOESY spectrum of compound **2**, so the benzoxyloxymethyl group of compound **2** was deduced to locate at *pseudo*-axial position.

The CD spectrum of compound **2** exhibited a positive cotton effect at λ 235.5 (+5.08), and a negative cotton effect at λ 218.5 (-4.09), indicating the two benzoxy groups were oriented in a clockwise manner⁸. Since the overall relative configuration was known, the absolute configuration of compound **2** was established as 1R, 2S, 3S, 4S.

Compound **2** is a stereoisomer of piperenol B⁹, the absolute configuration of which was reported as 1S, 2S, 3S, 4R, and the differences between them were in its configuration at C-1 and C-4.

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