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A new compound from *Hypericum reptans*

Yun Niu^{ab}, Ling Zhang^{ab}, Zhong-Yu Zhou^{ab}, Ying-Cheng Zhu^c, Ji-Kai Liu^a

^a State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, China ^b Graduate University of the Chinese Academy of Sciences, Beijing, China ^c Anhui Key Laboratory of Modernized Chinese Materia Medica, Anhui College of Traditional Chinese Medicine, Hefei, China

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NOTE

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Yun Niu^{ab}, Ling Zhang^{ab}, Zhong-Yu Zhou^{ab}, Ying-Cheng Zhu^c and Ji-Kai Liu^{a*}

^aState Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, China; ^bGraduate University of the Chinese Academy of Sciences, Beijing 100049, China; ^cAnhui Key Laboratory of Modernized Chinese Materia Medica, Anhui College of Traditional Chinese Medicine, Hefei 230031, China

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A new compound, 2,7,4a-trimethoxy-1,4,4a,8b-tetrahydrodibenzo-*p*-dioxin-4-one (**1**), was isolated from the aerial parts of the *Hypericum reptans*. The structure of the new compound was elucidated on the basis of extensive analysis of 1D and 2D NMR spectroscopic data and further confirmed by single-crystal X-ray diffraction.

Keywords: 2,7,4a-trimethoxy-1,4,4a,8b-tetrahydrodibenzo-*p*-dioxin-4-one; *Hypericum reptans*; crystal X-ray diffraction; structure elucidation

1. Introduction

The genus *Hypericum* comprises about 400 species that occur commonly in temperate regions throughout the world. Some of them have been used as traditional medicinal herbs for a long time [1–3]. Many natural products such as flavonoids, xanthenes, and phloroglucinols have been isolated from the genus *Hypericum* [4–6]. Particularly, the prenylated phloroglucinol isolated from *Hypericum perforatum* exhibits antibiotic and antidepressant activities [7], which have been used for several disorders of the central nervous system such as insomnia and mental illness [8]. Several other *Hypericum* species have been studied, resulting in the isolation of a variety of bioactive compounds possessing anti-HIV, antitumor, antibacterial, and antioxidant properties [9–11]. *Hypericum reptans* is widely distributed in the grassy slopes, rocky places, streamside at forest edges of southeast of Tibet and northwest

of Yunnan in China [12]. However, there is no report on the chemical constituents of this plant in the literature. In this paper, we report the isolation and structural elucidation of the new compound (**1**) by detailed 1D and 2D NMR spectroscopic analyses.

2. Results and discussion

Compound **1** was obtained as a white amorphous powder. Its molecular formula was assigned as C₁₅H₁₆O₆ by HR-ESI-MS at *m/z* 315.0837 [M + Na]⁺, in combination with ¹³C NMR and DEPT analyses, indicating eight degrees of unsaturation. Taking ¹³C NMR and DEPT spectra into consideration, it suggested the presence of one carbonyl carbon, one double bond, and one aromatic ring, and thus compound **1** must be tricyclic in order to satisfy the molecular formula. The IR spectrum showed the presence of both carbonyl group (1675 cm⁻¹) and benzene ring

*Corresponding author. Email: jkliu@mail.kib.ac.cn

Table 1. ^1H and ^{13}C NMR spectral data (CDCl_3) for compound **1**.

No.	δ_{H}	δ_{C}
1 α	2.86 (dd, 16.5, 6.0)	32.7 (t)
1 β	2.86 (dd, 16.5, 10.5)	
2		175.0 (s)
3	5.44 (s)	100.7 (d)
4		188.4 (s)
4a		91.9 (s)
4b		134.1 (s)
5	7.04 (d, 8.5)	118.6 (d)
6	6.48 (d, 8.5, 2.5)	108.3 (d)
7		155.0 (s)
8	6.49 (d, 2.5)	102.2 (d)
8a		142.7 (s)
8b	4.28 (dd, 10.5, 6.0)	71.6 (d)
2-OCH ₃	3.76 (s)	56.5 (s)
7-OCH ₃	3.72 (s)	55.5 (s)
4a-OCH ₃	3.29 (s)	51.5 (s)

Notes: Chemical shift values δ in ppm, coupling constants J in Hz (in parentheses).

(1605 and 1507 cm^{-1}). The signals of aromatic protons at δ 6.48 (dd, $J = 8.5, 2.5$ Hz), 7.04 (d, $J = 8.5$ Hz), and 6.49 (d, $J = 2.5$ Hz) in the ^1H NMR spectrum of **1** (Table 1) indicated that the benzene ring was 1,2,4-trisubstituted. The ^1H and ^{13}C NMR spectra showed the presence of an α, β -unsaturated carbonyl system [δ_{H} 5.44 (1H, s, H-3); δ_{C} 175.0 (s, C-2), 100.7 (d, C-3), and 188.4 (s, C-4)].

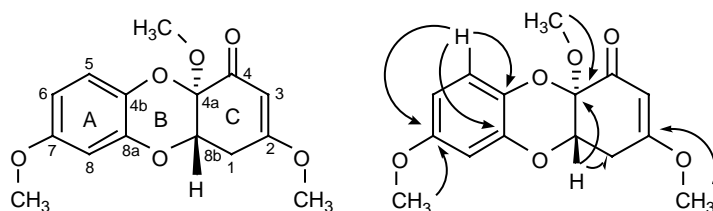
In the HMBC spectrum, the linkage of three methoxyl groups was deduced from the following correlations of 7-OCH₃ at δ_{H} 3.72 to C-7 at δ_{C} 155.0, from 2-OCH₃ at δ_{H} 3.76 to C-2 at δ_{C} 175.0, and from 4a-OCH₃ at δ_{H} 3.29 to C-4a at δ_{C} 91.9. The significant HMBC correlations from H-3 to C-2, C-4a, and C-4, from H-5

to C-4b, C-6, C-7, and C-8a, from H-6 to C-4b and C-8, and from H-8 to C-4b and C-6, from H-8b to C-1, C-2, C-4, and C-4a, from H-1 to C-2 and C-3, were observed (Figure 1), respectively. From these observations, the basic structure for compound **1** was established as 2,7,4a-trimethoxy-1,4,4a,8b-tetrahydrodibenzo-*p*-dioxin-4-one, which was further confirmed by X-ray diffraction. The α -orientation of 4a-OCH₃ and the β -orientation of H-8b were unambiguously determined from the X-ray crystal structure of **1** (Figure 2).

3. Experimental

3.1 General experimental procedures

Optical rotation was obtained on a Horiba SEPA-300 polarimeter. UV spectrum was measured on a Shimadzu UV-2401PC spectrophotometer. IR spectrum was taken on a Bruker Tensor 27 FT-IR spectrometer with KBr pellets. NMR spectra were recorded with a Bruker AM-400 or DRX-500 instruments with tetramethylsilane as the internal standard. The EI-MS was measured on a VG Autospec-3000 spectrometer. The HR-ESI-MS were recorded with an API QSTAR Pulsar 1 spectrometer. X-ray crystallographic data were collected on a Bruker Smart APEX II CCD diffractometer with graphite-monochromated Mo KR radiation. Silica gel (200–300 mesh, Qingdao Marine Chemical Inc., Qingdao, China), RP-18 gel (40–75 μm , Fuji Silysia Chemical Ltd, Aichi, Japan), and Sephadex LH-20 (Amersham Biosciences,

Figure 1. Structure and selected HMBC correlations of **1**.

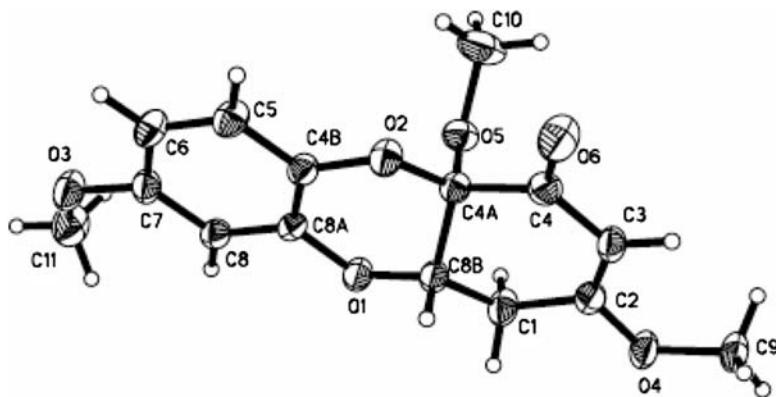


Figure 2. X-ray structure of **1** showing the relative configuration.

Uppsala, Sweden) were used for column chromatography (CC). TLC analysis was carried out on silica gel GF₂₅₄ pre-coated plates (0.20–0.25 mm; Qingdao Marine Chemical Inc.) with detection by heating silica gel plates sprayed with 10% H₂SO₄ in ethanol.

3.2 Plant material

The aerial parts of *H. reptans* were collected in Yimen, Yunnan Province, China, in June 2008. The sample was identified by Prof. Peng Hua, and a voucher specimen (KIB0689075) has been deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

3.3 Extraction and isolation

The air-dried aerial parts of the plant (18.0 kg) were pulverized using a laboratory mill, and successively extracted three times with MeOH at room temperature. The methanol extract was concentrated *in vacuo* to give a crude extract, which was partitioned between petroleum ether, EtOAc, n-BuOH, and water, respectively. The EtOAc extract (500 g) was subjected to silica gel CC eluted with a solvent system of petroleum ether–acetone (from 100:0 to 0:100, v/v) to produce fractions 1–6. Fraction 2 (10.7 g) eluted with petroleum ether–acetone (90:10) was

separated by MPLC with a reversed-phase C₁₈ column (methanol–water, 0:100 to 100:0, v/v), followed by Sephadex LH-20 (CHCl₃/MeOH, 1:1, v/v), and silica gel CC (petroleum ether–acetone, 15:1, v/v) to give compound **1** (60.0 mg).

Compound **1**, white amorphous powder; $[\alpha]_D^{16} = -120.3$ ($c = 0.13$, CHCl₃). IR (KBr) cm⁻¹: 3432, 2922, 2938, 2852, 1675, 1605, 1383, 1206, 1059. UV (CHCl₃) λ_{\max} (log ϵ): 253 (3.93), 288 (3.36) nm. ¹H and ¹³C NMR spectral data (CDCl₃): see Table 1. EI-MS: m/z 292 [M]⁺ (100), 277 (19), 259 (44), 231 (56), 194 (30), 151 (26), 139 (24), 69 (14). HR-ESI-MS (pos.): m/z 315.0837 [M + Na]⁺ (calcd for C₁₅H₁₆O₆Na, 315.0844).

3.4 X-ray crystallographic analysis of **1**

C₁₅H₁₆O₆ MW = 292.28, orthorhombic, space group P2(1)2(1)2(1), $a = 9.0063(13)$ Å, $b = 11.2861(17)$ Å, $c = 13.832(2)$ Å, $V = 1406.0(4)$ Å³, $Z = 4$, $D_{\text{calcd}} = 1.381$ g/cm³, $\lambda = 0.71073$ Å, $\mu(\text{Mo KR}) = 0.107$ mm⁻¹, $F(000) = 616$, and $T = 298(2)$ K. A colorless crystal of dimensions 0.18 × 0.14 × 0.10 mm was selected for X-ray analysis. A total of 9121 reflections, collected in the range $2.33^\circ \leq \theta \leq 28.32^\circ$, yielded 3324 unique reflections. The structure was solved using direct methods and was refined by full-matrix least-squares on F^2 values for 3324 $I > 2\sigma(I)$. Hydrogen atoms

were fixed at calculated positions. The final indices were $R_1 = 0.0493$, $wR_2 = 0.0827$ with goodness-of-fit = 0.981. Crystallographic data for structure **1** have been deposited at the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication No. CCDC 759971. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1223 336033; Email: deposit@ccdc.cam.ac.uk).

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