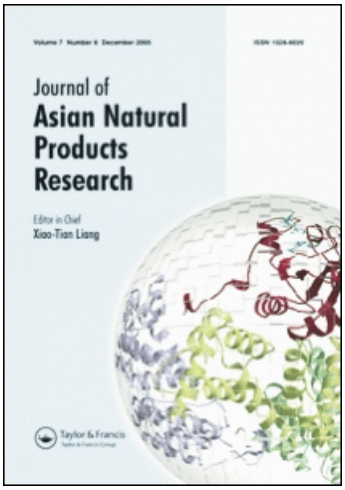

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A NEW ALKALOID FROM *DYSOXYLUM BINECTARIFERUM*

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A NEW ALKALOID FROM *DYSOXYLUM BINECTARIFERUM*

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Two compounds (**1** and **2**) have been isolated from the stem bark of *Dysoxylum binectariferum* (Roxb.) Hook. f. ex Bedd. Compound **1** is rohitukine {5,7-dihydroxy-2-methyl-8-[4-(3-hydroxy-1-methyl)-piperidinyl]-4*H*-1-benzopyran-4-one}, a known compound that has anti-inflammatory and immunomodulatory activities. Compound **2** is a new alkaloid, named rohitukine *N*-oxide, the structure of which was elucidated on the basis of spectral evidences and comparison with the ^{1}H NMR data of rohitukine.

Keywords: *Dysoxylum binectariferum*; Alkaloid; Rohitukine *N*-oxide; Rohitukine

INTRODUCTION

The plant *Dysoxylum binectariferum* (Roxb.) Hook. f. ex Bedd. (Meliaceae) is distributed in Southern China. Phytochemical studies of this plant have been reported [1,2]. A continuation of our research on the bioactive compounds of *D. binectariferum* has led to the isolation of two alkaloids (**1** and **2**, Fig. 1). **1** is rohitukine, a known compound: 5,7-dihydroxy-2-methyl-8-[4-(3-hydroxy-1-methyl)piperidinyl]-4*H*-1-benzopyran-4-one, which has anti-inflammatory and immunomodulatory activities. The absolute configuration of **1** has been determined as 5,7-dihydroxy-2-methyl-8-[4-(3*S*,4*R*-3-hydroxy-1-methyl)piperidinyl]-4*H*-1-benzopyran-4-one by X-ray crystallographic analysis of the 4-bromobenzoyl derivative [3]. Compound **2** is rohitukine *N*-oxide, as a new compound, the structure of which was determined on the basis of spectral evidence and comparison with the ^{1}H NMR data of rohitukine.

RESULTS AND DISCUSSION

Compound **2** is positive to Dragendorff reagent. HRMS (−) showed a molecular ion peak at *m/z* 320.1124, which is consistent with the formula $C_{16}H_{19}O_6N$. The UV spectrum exhibited absorptions at λ_{max} (nm): 227, 252, 257, 297 and 320 (sh), similar to those of rohitukine.

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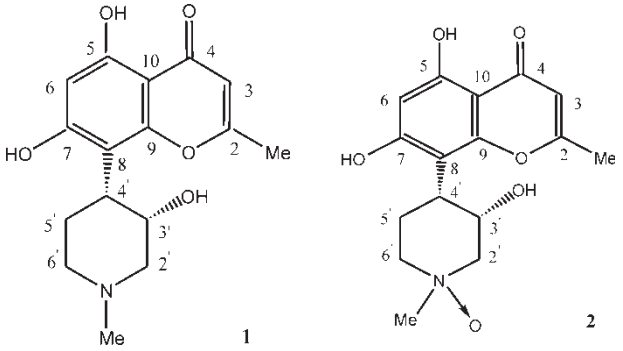

FIGURE 1 Structure of compounds **1** and **2**.

Sixteen carbon and sixteen proton signals were observed in the ^{13}C and ^{1}H NMR spectra, respectively, of **2**. The ^{13}C NMR spectrum showed nine signals of unsaturated carbon at δ 182.0 (C-4), 166.2 (C-2), 165.8 (C-7), 160.0 (C-5), 154.8 (C-9), 107.8 (C-3), 106.5 (C-8), 102.4 (C-10), and 100.4 (C-6), which indicated that **2** is an aromatic compound, and based on the lowfield signals, five carbons (C-4, 2, 7, 5 and 9) were deduced to be connected with oxygen or nitrogen atoms. The ^{1}H NMR spectrum showed two methyl signals at δ 3.18 (3H, s) and 2.38 (3H, s), and two unsaturated proton signals at δ 6.13 (1H, s) and 6.03 (1H, s). Comparison of the ^{1}H NMR spectrum of **2** with that of rohitukine (**1**) revealed similar chemical shifts (Table I). The signals of the piperidinyl proton for C-6′, C-2′ and N-Me shift to lower field, suggesting that **2** is rohitukine *N*-oxide. The poor solubility of **2** in all organic solvents also suggested that this compound is an *N*-oxide. Combining the HMQC, HMBC, COSY and NOESY correlations (Fig. 2), the structure of **2** was elucidated as rohitukine *N*-oxide, which is a new alkaloid. The configuration of the chiral carbons (C-3′, 4′) can be deduced from the coupling constants of 3′-H and 4′-H and NOE experiments. H-3′ (br, s) has an NOE with H-4′ and H-2′, implying that H-3′ is equatorial. H-4′ (dd, $J = 13.3, 2.4$) has an NOE with H-3′ and H-5′, which implies that H-4′ is axial. Therefore, the configuration of C-3′ and C-4′ were determined as C-3′*S*, C-4′*R*, identical to that of rohitukine [3].

EXPERIMENTAL

General Experimental Procedures

HPLC/UV spectra were obtained on a MX-8070 pump and MCPD-3600 spectro multichannel photodetector. A J′sphere ODS-M 80 column was used (250 × 20 mm, 4 μm). ^{1}H and ^{13}C NMR spectra were measured on an AL500 FT NMR (JEOL) using TMS as internal standard. MS spectra were recorded on JMS-SX102AQQ and MDS SCIEX QSTAR spectrometers. For column chromatography and TLC, silica gel was used. The samples were visualized by spraying with Dragendorff reagent to produce an orange spot.

Plant Material

Dysoxylum binectariferum was collected from Ledong County, Hainan Province, China and identified by Professor Hu-biao Chen (School of Pharmaceutical Sciences, Peking University Health Science Center, China). A voucher specimen has been deposited at the Herbarium of Pharmacognosy, School of Pharmaceutical Sciences, Peking University Health Science Center, China.

TABLE I ^{1}H NMR data of **1** and **2** (δ ppm and J in Hz)

No.	*δ (1)*	*δ (2)*	*Δ (2 − 1)*
3	5.99 (1H, s)	6.13 (1H, s)	0.14
6	6.14 (1H, s)	6.03 (1H, s)	− 0.11
2′a	3.44 (1H, d, J = 12.2)	3.78 (1H, d, J = 11.2, H-2′a)	0.34
2′b	3.32 (1H, d, J = 11.2)	3.51 (1H, dt, J = 12.2, 2.4, H-2′b)	0.19
3′	4.21 (1H, br)	4.31 (1H, br)	0.10
4′	3.63 (1H, d, J = 9.5)	3.60 (1H, dd, J = 13.3, 2.4)	− 0.27
5′a	3.16 (1H, m)	2.83 (1H, dq, J = 13.2, 4.4, H-5′a)	− 0.33
5′b	1.71 (1H, d, J = 10.3)	1.60 (1H, d, J = 14.2, H-5′b)	− 0.11
6′a	3.52 (1H, d, J = 8.3)	3.71 (1H, dt, J = 12.2, 3.4, H-6′a)	0.19
6′b	3.14 (1H, m)	3.41 (1H, d, J = 12.2, H-6′b)	0.27
N-Me	2.86 (3H, s)	3.18 (3H, s)	0.32
2-Me	2.37 (3H, s)	2.38 (3H, s)	0.01

Extraction and Isolation

The dried and powdered stem barks of *Dysoxylum binectariferum* (2 kg) were extracted with MeOH. After the solvent was removed, the extract was suspended in water and extracted with EtOAc and *n*-BuOH successively. The *n*-BuOH extract (12 g) was chromatographed on silica gel column using the solvent system EtOAc–MeOH–NH_3·H_2O (5:5:0.1). The fractions were monitored by TLC, and those containing **1** and **2** were purified by

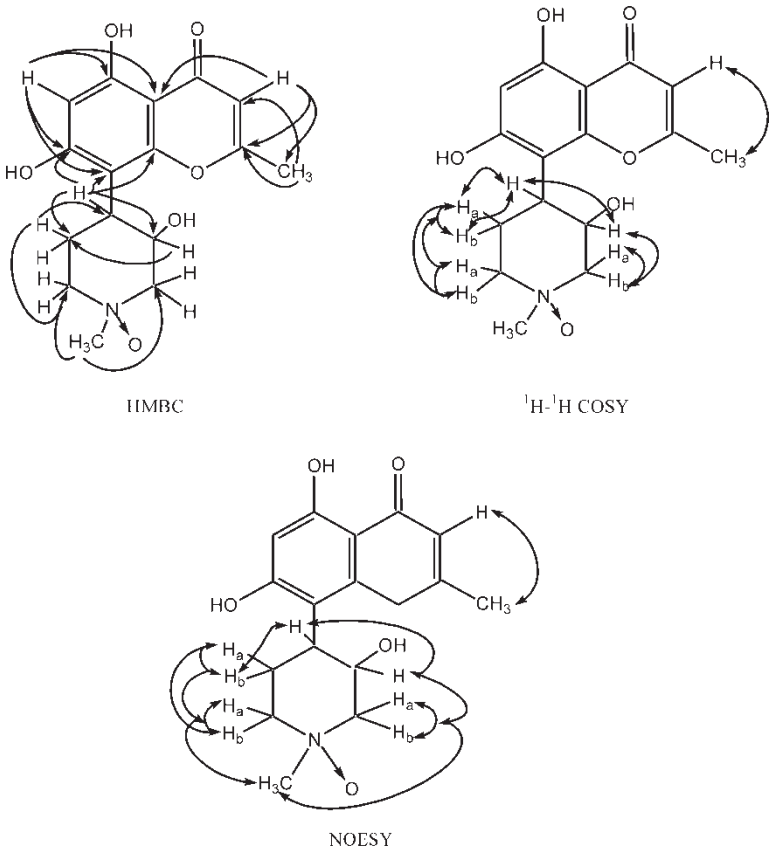

FIGURE 2 HMBC, ^{1}H–^{1}H COSY and NOESY correlations of **2**.

preparative HPLC [HPLC column: J′sphere ODS-M 80 (250×20 mm, 4 μm); solvent: CH_3CN–0.15%KH_2PO_4 buffer solution (20% : 80% → 80% : 20%, 50 min); flow rate: 10 ml min^{-1}] to obtain the two alkaloid compounds **1** (rohitukine) and **2** (rohitukine *N*-oxide).

Rohitukine *N*-oxide (**2**) was obtained as an amorphous powder from MeOH; HRMS: *m/z* 320.1124 $[M - H]^-$, calcd. for $C_{16}H_{18}O_6N$, 320.1134; UV λ_{max} (nm): 227, 252, 257, 297 and 320 (sh); ^1H NMR data (DMSO, see Table I); ^{13}C NMR (DMSO) δ 166.2 (C-2), 107.8 (C-3), 182.0 (C-4), 160.0 (C-5), 100.4 (C-6), 165.8 (C-7), 106.5 (C-8), 154.8 (C-9), 102.4 (C-10), 65.0 (C-2′), 69.0 (C-3′), 36.0 (C-4′), 21.0 (C-5′), 66.0 (C-6′), 58.0 (N-Me), 20.0 (2-Me).

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