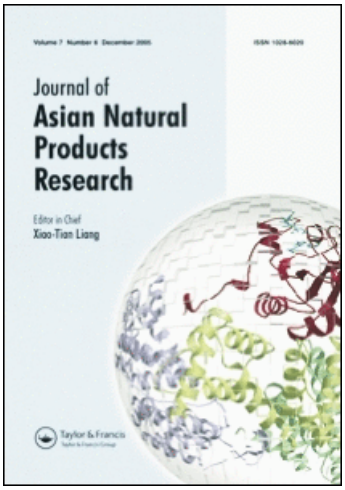

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

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To cite this Article Sun, Sheng-Guo , Chen, Ruo-Yun and Yu, De-Quan(2001) 'Structures of Two New Benzofuran Derivatives from the Bark of Mulberry Tree (*Morus Macroura* Miq.)', Journal of Asian Natural Products Research, 3: 4, 253 — 259
To link to this Article: DOI: 10.1080/10286020108040364
URL: http://dx.doi.org/10.1080/10286020108040364

JANPR, Vol. 3, pp. 253–259
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STRUCTURES OF TWO NEW BENZOFURAN DERIVATIVES FROM THE BARK OF MULBERRY TREE (*MORUS MACROURA* MIQ.)

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(Received 24 March 2000; In final form 3 April 2000)

Two new benzofuran derivatives, macrourins **A** (**1**) and **B** (**2**), together with two known stilbene derivatives, were isolated from the barks of *Morus macroura* Miq. Their structures were elucidated by means of spectroscopic evidence.

Keywords: *Morus macroura* Miq.; Macrourin **A**; Macrourin **B**; Benzofuran

INTRODUCTION

"Sang Bai Pi", the bark of mulberry, has been used as herbal medicine to treat diseases, such as diabetes, arthritis, rheumatism, for thousands of years. Phytochemical studies on some *Morus* species revealed that they contained flavone, stilbene and benezofuran derivatives [1–3], but there are no reports about those compounds from *Morus macroura* Miq. As part of our research work, we investigated the chemical constituents of *Morus macroura* Miq. which grows in the south part of China, especially in Xishuangbanna, Yunnan province. Macrourin **A** (**1**) and **B** (**2**), two new benzofuran derivatives, have been isolated along with two known compounds, moracin **M** and oxyreseratrol.

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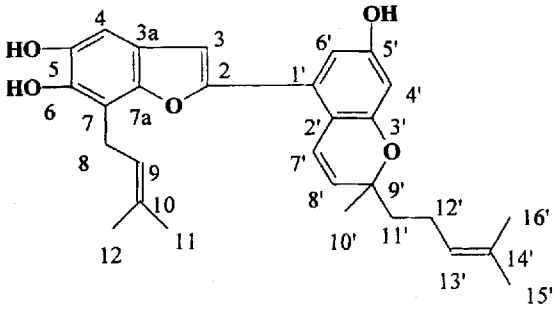
RESULTS AND DISCUSSION

Macrourin **A** (**1**) was obtained as an oily substance exhibiting dark fluorescence under UV light at 254 nm. The molecular formula of **1** was deduced to be $C_{29}H_{32}O_5$ based on HRFAB-MS at *m/z* 460.2232 (for $C_{29}H_{32}O_5$, calcd 460.2249). The IR spectrum showed the presence of hydroxyls (3365 cm^{-1} broad), aromatic group (1604 cm^{-1}) and the absence of carbonyl function. The UV spectrum of **1** (λmax: 210, 300 nm) suggested the presence of a 2-phenylbenzofuran skeleton [1], which was supported by the ^{1}H-NMR spectrum (CD_3COCD_3) of **1**: δ 6.82 (1 H, *s*, 3-H), 6.38 (1H, *s*, 4′-H) and 6.89 (2 H, *s*, 4 and 6′-H). The ^{1}H-NMR spectrum also revealed the presence of a 2-methyl-2-(4-methylpent-3-enyl) chromene system with a hydroxyl group at *peri* position (C-2′) to C-5′, similar to that of australone **A** [4]. Furthermore, the spectrum of ^{1}H-^{1}H-COSY of **1** suggested that H-4′ and H-6′ were at *meta* position. In the HMBC spectra of **1** (Fig. 2), the CH long-range correlation between H-3 and C-1′ indicated that it was a 2-methyl-2-(4-methylpent-3-enyl) chromene moiety on C-2. On the other hand, the ^{1}H-NMR spectrum indicated the presence of a 3-methyl-2-butenyl (prenyl) which was similar to that of moracin **C** [3]. The prenyl must be substituted on C-7 because of the absence of 7-H which would have given rise to long-range coupling between 3-H and 7-H [5]. Also C-5 (δ 137.7) and C-6 (δ 137.8) were in the upfield compared to that at an ordinary hydroxyl-bearing carbon [C-3′ (δ 157.1)], so the hydroxyls were at *ortho* positions and the geranyl was at C-7. In the HMBC spectra of **1** (Fig. 2), the CH long-range correlation between H-8 and C-(6, 7, 9, 10), confirmed the conclusion. Based on the above evidence, the structure of **1** was established and named as macrourin **A**.

Macrourin **B** (**2**) was obtained as brown powder exhibiting blue fluorescence under UV light at 254 nm. HRFAB-MS of **2** gave a $[M+H]^-$ ion peak at *m/z* 501.1182 corresponding to the molecular formula $C_{28}H_{20}O_9$ (for $C_{28}H_{20}O_9$, calcd 501.1185). The IR spectrum of **2** showed the presence of hydroxyls (3419 cm^{-1} broad), aromatic groups (1621 cm^{-1}) and the absence of carbonyl function. The UV spectrum (λmax: 205, 325 nm) of **2** was very similar to that of **1**, so it was also a 2-phenylbenzofuran derivative. The ^{1}H-NMR spectrum of **2** showed two sets of signals for 3, 5 dihydroxybenzene moieties at δ 6.74 (2 H, *d*, $J=2.0$) and δ 6.46 (1 H, *t*, $J=2.0$), δ 6.33 (2 H, *d*, $J=2.0$) and δ 6.30 (1 H, *t*, $J=2.0$); one set of signals for 2, 4 dihydroxybenzene moiety at δ 6.22 (1 H, *d*, $J=2.0$), δ 6.29 (1 H, *dd*, $J=2.0$, 8.5) and δ 7.14 (1 H, *d*, $J=8.5$); one aromatic proton singlet at δ 6.96 and a proton of furan ring at δ 6.56 (3-H) as well as two coupled doublets at δ 5.81 (1 H, *d*, $J=7.0$) and 4.78 (1 H, *d*, $J=7.0$). Besides, in the HMBC



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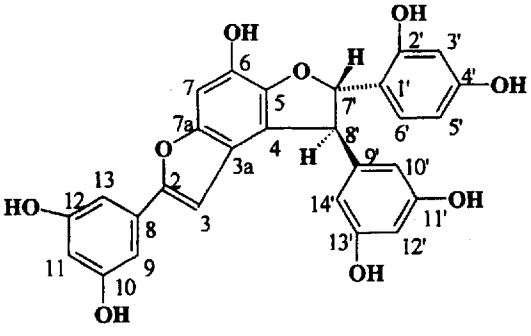

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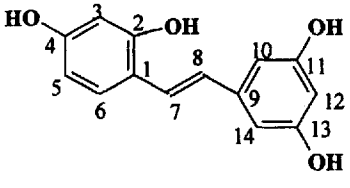

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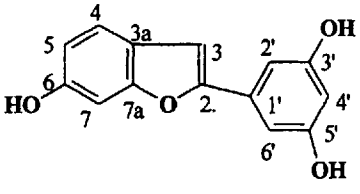
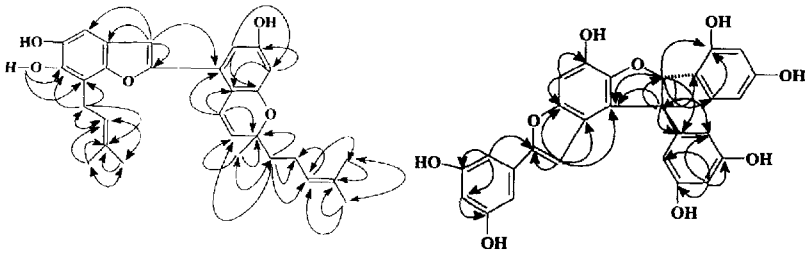


4

FIGURE 1 Structures **1**–**4**.

spectrum of **2** (Fig. 2), the CH long-range correlation between H-7′/C-(2′, 6′, 7′, 4), H-8′/C [1′, 7′, 9′, 10′ (or 14′), 4], and H-9 (or 13)/C-2 allowed the connection of **2** as indicated. A pair of *trans* protons at δ 5.81 (1 H, *d*, $J = 7.0$) and 4.78 (1 H, *d*, $J = 7.0$) were similar to those of gnetuhainin **A** [6].



1 2

FIGURE 2 Key long-range (HMBC) correlations for **1** and **2**.

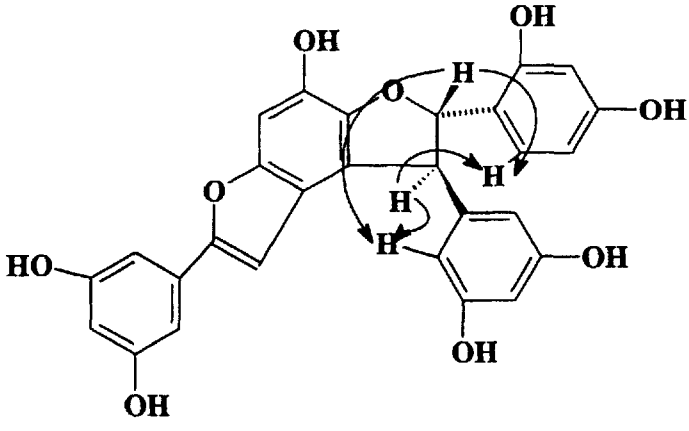


FIGURE 3 Key NOE correlations of **2**.

In the selected NOE spectrum of **2** (Fig. 3), the strong NOEs between H-7′ and H-10′ (or 14′), as well as between H-8′ and H-6′ suggested a *trans* orientation of H-7′ and H-8′. If it was a *cis* orientation, the NOEs between H-7′ and H-8′ would be strong, furthermore, the chemical shifts of 10′-H and 14′-H would be further upfield due to the shielding of 7′-phenyl [7]. Thus the structure of **2** was determined as shown and named as macrourin **B**.

EXPERIMENTAL SECTION

General Experimental Procedures

Melting points were measured on a micromelting apparatus and are uncorrected. UV spectra were taken on a Shimadzu UV-300 spectrophotometer.

IR spectra were run a Perkin Elmer 683 infrared spectrometer with KBr plates. Optical rotation was measured on Perkin Elmer 241 spectrometer. NMR spectra were carried out on Bruker AM 500. FAB-MS spectra were taken on an Autospec-Tof mass spectrometer and HPLC on TSP 3200.

Plant Material

The barks of *Morus macroura* Miq. were collected from Xishuangbanna, Yunnan province, in July, 1997, identified as *Morus macroura* Miq. by Prof. Song. A voucher specimen (EX 97038) was deposited in the herbarium of the Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College.

Extraction and Isolation

Dried and powdered barks of *Morus macroura* Miq. (10 kg) were refluxed with 95% EtOH. The extract was concentrated *in vacuo* to yield 425 g residue, which was mixed with silica gel (160–200 mesh), then eluted successively with petroleum ether, $CHCl_3$, EtOAc, MeOH to give four fractions. The EtOAc fraction (114 g) was subjected to silica gel column chromatography and eluted with petroleum–Me_2CO (100:2–100:100) and MeOH, to give ten fractions. We obtained **1** (100 mg), **2** (20 mg), **3** (50 mg), **4** (30 mg) from the fifth fraction by repeated column chromatography (silica gel, 160–200 mesh, petroleum–Et_2O). Macrourin **A** was purified by MPLC through ODS RP_{18} eluted with 70% MeOH and macrourin **B** was purified by PTLC ($CHCl_3$: EtOAc = 1 : 1).

Macrourin **A** (**1**) was obtained as oily substance. EI-MS *m/z* 460 [M^+], 391, 377, 349, 321, 293, 255, 137, 109, 69, HRFAB-MS *m/z* 460.2232 [M^+]; UV (MeOH) λmax (log ε): 210 (4.58) nm, 300 (4.44) nm; IR (KBr) ν_{max}: 3365, 1604, 1423, 1371, 1155, 1120, 1001, 839 cm^{-1}; ^{1}H-NMR and ^{13}C-NMR spectra see Table I.

Macrourin **B** (**2**) was obtained as brown amorphous powder. mp 170°C (dec.). $[\alpha]_D^{23} = +0.006$(c 0.070, MeOH); FAB-MS*m/z*501[M+H]$^+$, HRFAB-MS *m/z* 501.1182 [M+H]$^+$; UV (MeOH) λmax (log ε): 205 (4.80), 325 (4.32) nm; IR (KBr) ν_{max}: 3419, 1621, 1456, 1157, 1001, 978, 953, and 833 cm^{-1}; ^{1}H-NMR and ^{13}C-NMR spectra see Table I.

Oxyreseratrol (**3**) was obtained as colorless needles, mp 197–199°C. EI-MS *m/z* 244 [M^+], 110; IR (KBr) ν_{max}: 3400, 3242, 1616, 1593, 1518, 1313, 1157 and 825 cm^{-1}; ^{1}H-NMR (500 MHz, in CD_3COCD_3) δ 7.33 (1 H, *d*, *J* = 9.5 Hz, 6-H), 6.34 (1 H, *dd*, *J* = 9.5, 2.5 Hz, 5-H), 6.39 (1 H, *d*, *J* = 2.5 Hz, 3-H),

TABLE I ^{1}H-NMR and ^{13}C-NMR chemical shift for macrourin **A** (**1**) and macrourin **B** (**2**)

	1		**2**	
Position	H^a	C^b	H^a	C^b
2		153.8		155.7
3	6.82 *s*	101.2	6.56 *s*	100.5
3a		121.4		119.0
4	6.89 *s*	104.1		118.8
5		137.7		133.2
6		138.6		141.0
7		118.2	6.96 *s*	98.4
7a		133.1		151.8
8	3.48 *d* (6.5)	26.1		145.6
9	5.30 *t* (6.5)	122.2	6.74 *d* (2.0)	103.5
10		132.0		159.7
11	1.67 *s*	25.5	6.46 *t* (2.0)	103.3
12	1.79 *s*	17.8		159.7
13			6.74 *d* (2.0)	103.5
1′		144.4		121.4
2′		103.7		156.8
3′		157.1	6.22 *d* (2.5)	102.0
4′	6.38 *s*	102.6		159.2
5′		157.1	6.29 *dd* (8.5, 2.5)	107.3
6′	6.89 *s*	104.1	7.14 *d* (8.5)	129.0
7′	6.74 *d* (10.0)	116.6	5.81 *d* (7.0)	89.6
8′	5.53 *d* (10.0)	128.2	4.78 *d* (7.0)	56.3
9′		80.0		145.6
10′	1.40 *s*	26.1	6.33 *d* (2.0)	107.1
11′	1.75 *m*	40.7		159.4
12′	2.09 *m* (7.0)	22.7	6.30 *t* (2.0)	103.5
13′	5.07 *t* (7.0)	123.8		159.4
14′		131.8	6.33 *d* (2.0)	107.1
15′	1.65 *s*	25.6		
16′	1.55 *s*	17.5		

[a] Recorded at 500 MHz in CD_3COCD_3.
[b] Recorded at 125 MHz in CD_3COCD_3. Coupling constants (J) are in parentheses.

6.83 (1 H, *d*, $J = 16.5$ Hz, 7-H), 7.28 (1 H, *d*, $J = 16.5$ Hz, 8-H), 6.47 (2 H, *d*, $J = 2.5$ Hz, 10, 14-H), 6.18 (1 H, *d*, $J = 2.5$ Hz, 12-H).

Moracin **M** (**4**) was obtained as crystals, mp 204–206°C, EI-MS *m/z* 242 [M^+], 213, 187, 185; IR (KBr) ν_{max}: 3519, 1614, 1437, 1142, 1120 and 818 cm^{-1}; ^{1}H-NMR (500 MHz, in CD_3COCD_3) δ 7.38 (1 H, *d*, $J = 8.5$ Hz, 4-H), 6.78 (1 H, *dd*, $J = 8.5, 2.3$ Hz, 5-H), 6.96 (1 H, *d*, $J = 2.3$ Hz, 7-H), 6.98 (1 H, *s*, br., 3-H), 6.82 (2 H, *d*, $J = 2.1$ Hz, 2′, 6′-H), 6.33 (1 H, *t*, $J = 2.1$ Hz, 4′-H).

Acknowledgments

This research program was supported by Taisho Pharmaceutical Company. We thank the Department of Instrumental Analysis, Institute of Materia

Medica, Chinese Academy of Medical Science and Peking Union Medical College for the measurements of UV, IR, NMR and MS spectra.

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