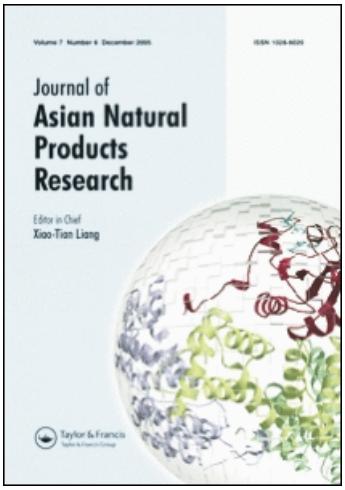

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Two new compounds from the dried tender stems of *Cinnamomum cassia*

Chao Liu[a]; Shao-Min Zhong[b]; Ruo-Yun Chen[a]; Yan Wu[b]; Xue-Jun Zhu[b]
[a] Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Ministry of Education, Beijing, China [b] Department of Dermatology, Peking University First Hospital, Beijing, China

To cite this Article Liu, Chao , Zhong, Shao-Min , Chen, Ruo-Yun , Wu, Yan and Zhu, Xue-Jun(2009) 'Two new compounds from the dried tender stems of *Cinnamomum cassia*', Journal of Asian Natural Products Research, 11: 9, 845 — 849
To link to this Article: DOI: 10.1080/10286020903185942
URL: http://dx.doi.org/10.1080/10286020903185942

Journal of Asian Natural Products Research
Vol. 11, No. 9, September 2009, 845–849

Two new compounds from the dried tender stems of *Cinnamomum cassia*

Chao Liu[a], Shao-Min Zhong[b], Ruo-Yun Chen[a]*, Yan Wu[b] and Xue-Jun Zhu[b]

[a]*Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Ministry of Education, Beijing 100050, China;* [b]*Department of Dermatology, Peking University First Hospital, Beijing 100034, China*

(*Received 15 July 2009; final version received 15 July 2009*)

Two new compounds, cinnamic aldehyde cyclic D-galactitol 3′*R*,4′*S*-acetal (**1**) and cinnamomumolide (**2**), along with six known compounds, syringaresinol (**3**), lyoniresinol (**4**), 5,7,3′-trimethoxyl-(−)-epicatechin (**5**), 5,7-dimethoxyl-3′,4′-di-*O*-methylene-(±)-epicatechin (**6**), 2-methoxyl-4-hydroxy cinnamyl aldehyde (**7**), and glucosyringic acid (**8**), have been isolated from the dried tender stems of *Cinnamomum cassia*. Their structures were elucidated based on spectroscopic data. Compound **2** was elucidated as 8-methoxyl-9-hydroxy-3′,4′-methylenedioxy-3*S*,4*R*-diphenyl butyrolactone, named cinnamomumolide, which exhibited activity in protecting against the injury caused by hydrogen peroxide oxidation on human umbilical vein endothelial cells, with an EC_{50} value of 10.7 μM. Compounds **3**–**8** were isolated from the title plant for the first time.

Keywords: dried tender stems; *Cinnamomum cassia*; cinnamic aldehyde cyclic D-galactitol 3′*R*,4′*S*-acetal; cinnamomumolide

1. Introduction

The dried tender stems of *Cinnamomum cassia*, a Chinese traditional medicine, are widely used in Chinese prescriptions, which can treat influenza and arthritis. Previous chemical investigations of this plant have identified various compounds, including cinnamic acid, coumarin, and protocatechuric acid [1]. During activity screening, the EtOH extract of the dried tender stems of *C. cassia* was found to exhibit anti-oxidative, antibiotic, and anti-allergic activities. In order to search for active constituents from the title plant, chemical investigation on the EtOH extract of the dried tender stems of *C. cassia* led to the isolation of two novel compounds (Figure 1) and six known compounds. This paper deals with the isolation and structural elucidation of the new compounds.

2. Results and discussion

Compound **1**, which was obtained as white needles from acetone with mp 169.5–170.4°C and $[\alpha]_D^{20}$ 0 ($c = 0.2$, MeOH), showed IR absorption bands at 3304 cm^{-1} for hydroxyl groups, 1657 cm^{-1} for an ethylenic linkage, and 1577, 1494, and 1451 cm^{-1} for an aromatic ring. Its UV absorption maxima at 250 and 291 nm (MeOH) were also due to the ethylenic linkage and the aromatic ring. The molecular formula was confirmed as $C_{15}H_{20}O_6$ by the HR-FAB-MS analysis at *m/z* 297.1333 $[M+H]^+$, together with

*Corresponding author. Email: rych@imm.ac.cn

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020903185942
http://www.informaworld.com

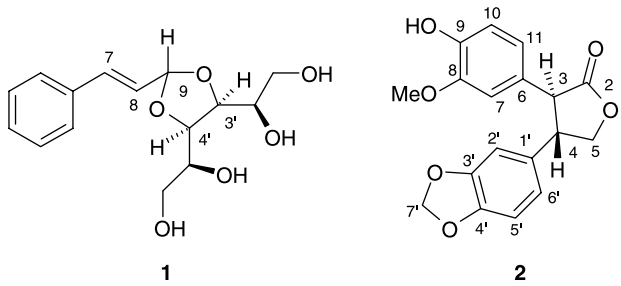

Figure 1. The structures of compounds **1** and **2**.

^{1}H and ^{13}C NMR spectra. The ^{1}H NMR spectrum of **1** (500 MHz, DMSO-d_6) exhibited signals at δ 7.49–7.28 (5H, m, H-2–6), 6.74 (1H, d, $J = 16.0$ Hz, H-7), 6.17 (1H, dd, $J = 16.0$, 6.5 Hz, H-8), and 5.49 (1H, d, $J = 6.5$ Hz, H-9), and showed the presence of a cinnamyl moiety. The remaining eight signals at δ 4.06–4.01 (2H, m), 3.63–3.61 (1H, m), 3.53–3.47 (3H, m), and 3.40–3.34 (2H, m) and four active hydrogen signals at δ 5.01 (1H, d, $J = 5.0$ Hz), 4.93 (1H, d, $J = 4.5$ Hz), 4.51 (1H, t, $J = 5.5$ Hz), and 4.48 (1H, t, $J = 5.5$ Hz) led **1** to have a ramification of hexahydric alcohol. Correspondingly, the ^{13}C NMR spectrum showed 15 carbon signals, including nine signals of the cinnamyl moiety at δ 135.5 (C-1), 134.2 (C-8), 128.7 (C-3, 5), 128.4 (C-4), 126.8 (C-2, 6), 126.5 (C-7), 103.5 (C-9) and other six signals at δ 78.1, 78.1, 72.6, 72.1, 62.8 (C × 2), which belong to the hexahydric alcohol, such as galactitol, sorbitol, or mannitol. Moreover, based on the literatures [2,3], $[\alpha]_D^{20}$ 0, and the long-range HMBC correlations from H-3′ and H-4′ (δ 4.06–4.01) to C-9 (δ 103.5), the hexahydric alcohol must be root in D-galactitol. Therefore, the structure of compound **1** was elucidated as cinnamic aldehyde cyclic D-galactitol 3′*R*,4′*S*-acetal, which was a product from the aldolization of cinnamic aldehyde and D-galactitol, and the configurations of C-2′ and 5′ were *S* and *R* according to the literature [4].

Compound **2**, which was obtained as pale white needles from EtOAc with mp 138.8–139.9°C, showed IR absorption bands at 3414 cm^{-1} for the hydroxyl group, 1773 cm^{-1} for the carbonyl group, and 1611 and 1503 cm^{-1} for aromatic rings. Its UV absorption maxima at 234 and 284 nm (MeOH) were also due to the aromatic ring. The molecular formula was confirmed as $C_{18}H_{16}O_6$ by HR-EI-MS at *m/z* 328.0942 $[M]^+$, together with ^{1}H and ^{13}C NMR spectra. The ^{1}H NMR spectrum of **2** (Table 1) exhibited two groups of ABX-type signals, one at δ 6.84 (d, $J = 8.4$ Hz), 6.64 (dd, $J = 8.4$, 1.8 Hz), and 6.67 (d, $J = 1.8$ Hz) and the other at δ 6.75 (d, $J = 7.8$ Hz), 6.64 (dd, $J = 7.8$, 1.8 Hz), and 6.70 (d, $J = 1.8$ Hz), indicating the presence of two tri-substituted benzene rings. In addition, the signals of a methoxyl at δ 3.85 (s), a methylenedioxy group at δ 5.96 (2H, s), two proton signals on the oxygen-bearing carbon at δ 4.65 (1H, dd, $J = 9.0$, 7.8 Hz) and 4.43 (t, $J = 9.0$, 7.8 Hz), and two high-field signals at δ 3.78 (d, $J = 11.4$ Hz) and 3.75–3.70 (dt, $J = 11.4$, 7.8 Hz) were also obtained. The ^{13}C NMR spectrum showed 18 carbon signals, including two benzene rings (δ 146.8, 145.3, 126.8, 121.3, 114.6, 110.7 and δ 148.3, 147.3, 130.7, 120.7, 108.7, 107.2), a methoxyl (δ 55.9) and a methylenedioxy group (δ 101.3), an ester-carbonyl group (δ 176.5), an oxygen-bearing carbon (δ 71.7), and other two high-field signals (δ 53.0 and 51.3). In consideration of the ^{1}H–^{1}H COSY and HSQC experiments, **2** should have a

Table 1. ^{1}H and ^{13}C NMR spectral data of compound **2** in $CDCl_3$ (400 MHz for ^{1}H, 100 MHz for ^{13}C).

No.	HSQC δ_C	HSQC δ_H	COSY	HMBC
2	176.5			
3	53.0	3.78 (d, $J = 11.4$ Hz)	H-3/H-4	H-3/C-2, 4, 5, 6, 7, 11, 1′
4	51.3	3.75–3.70 (dt, $J = 11.4$, 7.8 Hz)	H-4/H-3, 5α, 5β	H-4/C-3, 6, 1′, 2′, 6′
5	71.7	α 4.65 (dd, $J = 9.0$, 7.8 Hz)	H-5α/H-4, 5β	H-5α/C-2, 3, 4
		β 4.43 (t, $J = 9.0$, 7.8 Hz)	H-5β/H-4, 5α	H-5β/4, 1′
6	126.8			
7	110.7	6.67 (d, $J = 1.8$ Hz)	H-7/H-11	H-7/C-3, 6, 9, 11
8	145.3			
9	146.8			
10	114.6	6.84 (d, $J = 8.4$ Hz)	H-10/H-11	H-10/C-6, 8, 9, 11
11	121.3	6.64 (dd, $J = 8.4$, 1.8 Hz)	H-11/H-7, 10	H-11/C-3, 7, 9
1′	130.7			
2′	107.2	6.70 (d, $J = 1.8$ Hz)	H-2′/H-6′	H-2′/C-4, 3′, 6′
3′	147.3			
4′	148.3			
5′	108.7	6.75 (d, $J = 7.8$ Hz)	H-5′/H-6′	H-5′/C-1′, 4′
6′	120.7	6.64 (dd, $J = 7.8$, 1.8 Hz)	H-6′/H-2′, 5′	H-6′/C-4, 2′, 3′, 5′
7′	101.3	5.96 (2H, s)		H-7′/C-3′, 4′
OMe	55.9	3.85 (3H, s)		OMe/C-8

butyrolactone ring. The final structure was established by the 2D NMR experiments HSQC and HMBC.

In the HMBC spectrum, the long-range correlations from H-7′ (δ 5.96) to C-3′ and 4′ (δ 147.3, 148.3) revealed that the methylenedioxy group was attached to C-3′ and 4′. Meanwhile, the long-range correlations from OMe (δ 3.85) to C-8 (δ 145.3) demonstrated that the methoxyl was attached to C-8. The HMBC correlations from H-7 (δ 6.67) and H-11 (δ 6.64) to C-3 (δ 53.0), H-2′ (δ 6.70) and H-6′ (δ 6.64) to C-4 (δ 51.3) indicated the connection positions of the two benzene rings. Furthermore, the long-range correlations from H-5 (δ 4.65) to C-2, 3, and 4 (δ 176.5, 53.0, 51.3), H-3 (δ 3.78) to C-2 and 5 (δ 176.5, 71.7), H-4 (δ 3.75–3.70) to C-3 (δ 56.3) confirmed the presence of the butyrolactone ring. The configurations of C-3 and 4 were confirmed as *R* and *S* according to the Cotton effect at around 234 nm in the CD curve, corresponding to the similar compounds in the literatures [5,6]. Therefore, the structure of compound **2** was elucidated as 8-methoxyl-9-hydroxy-3′,4′-methylenedioxy-3*S*,4*R*-diphenyl butyrolactone, and named cinnamomumolide.

Compounds **3**–**8** were identified as syringaresinol [2,5,7], lyoniresinol [8], 5,7,3′-trimethoxyl-(−)-epicatechin [2], 5,7-dimethoxyl-3′,4′-di-*O*-methylene-(±)-epicatechin [2], 2-methoxyl-4-hydroxy cinnamyl aldehyde [5], and glucosyringic acid [9], respectively.

It was found that compound **2** possessed activity in protecting against the injury induced by hydrogen peroxide oxidation on human umbilical vein endothelial cells, with a protective rate of 57.93% and an EC_{50} value of 10.7 μM.

3. Experimental

3.1 General experimental procedures

Melting points were measured on an XT4-100 micromelting apparatus and are uncorrected. The IR spectra were obtained

on a Nicolet infrared spectrometer with KBr pellets. The UV spectra were measured on a Labtech UV 2000 spectrophotometer. The MS spectra were taken on an Autospec Ultima ETOF spectrometer. The ^{1}H, ^{13}C, and 2D NMR were recorded on Mercury 400 and Inova 500 spectrometers with TMS as the internal standard. The CD spectra were measured on a JASCO J-815 CD spectrometer. Silica gel for TLC and column chromatography was obtained from Qingdao Marine Chemical, Inc. (Qingdao, China).

3.2 Plant material

The dried tender stems of *C. cassia* were purchased from Beijing Pushenglin Medicine Corp. (Beijing, China, Lot No. 06050101), and identified by Prof. Lin Ma.

3.3 Extraction and isolation

The dried tender stems of *C. cassia* (30 kg) were extracted with 95% ethanol and filtered. The filtrate was concentrated *in vacuo* and partitioned with petroleum ether, chloroform, and ethyl acetate. The $CHCl_3$ and EtOAc extracts were evaporated to afford 360 and 223 g of residues, respectively. The $CHCl_3$ residue was subsequently subjected to column chromatography on silica gel, eluted with chloroform–methanol (from 15:1 to 1:1). The fractions were combined by monitoring with TLC to obtain fractions 1–7. Fraction 2 (30.5 g) was chromatographed repeatedly on silica gel eluted with chloroform–methanol and chloroform–acetone to give **3** (200 mg), **5** (12 mg), and **7** (100 mg). In the same way, compound **4** (100 mg) was isolated from fraction 3 (23.7 g). The EtOAc residue was subjected to column chromatography on silica gel, eluted with chloroform–methanol (from chloroform to chloroform–methanol 1:1). The fractions were combined by monitoring with TLC to obtain fractions 1–10. Fraction 3 (15.2 g) was chromatographed repeatedly on silica gel eluted with chloroform–methanol (10:1) and chloroform–acetone (3:1) to give **4** (18 mg). Fraction 4 (41.9 g) afforded **1** (151 mg) and **6** (15 mg). Fraction 5 (12.6 g) afforded **2** (18 mg) and **8** (4 mg).

3.3.1 Compound *1*

White needles (acetone), mp 169.5–170.4°C, $[\alpha]_D^{20}$ 0 ($c = 0.2$, MeOH). IR (KBr) ν_{max} (cm^{-1}): 3304, 2944, 2886, 1657, 1577, 1494, 1451, 1161, 1015, 954, 882, 749. UV (MeOH) λ_{max}: 204, 250, 291 nm. ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 7.49–7.28 (5H, m, H-2–6), 6.74 (1H, d, $J = 16.0$ Hz, H-7), 6.17 (1H, dd, $J = 16.0$, 6.5 Hz, H-8), 5.49 (1H, d, $J = 6.5$ Hz, H-9), 5.01 (1H, d, $J = 5.0$ Hz, OH), 4.93 (1H, d, $J = 4.5$ Hz, OH), 4.51 (1H, t, $J = 5.5$ Hz, OH), 4.48 (1H, t, $J = 5.5$ Hz, OH), 4.06–4.01 (2H, m, H-3′, 4′), 3.63–3.61 (1H, m, H-2′ or 5′), 3.53–3.47 (3H, m, H-2′ or 5′, H-1′α, H-6′α), 3.40–3.34 (2H, m, H-1′β, H-6′β). ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 135.5 (C-1), 134.2 (C-8), 128.7 (C-3, 5), 128.4 (C-4), 126.8 (C-2, 6), 126.5 (C-7), 103.5 (C-9), 78.1 (C-2′), 78.1 (C-5′), 72.6, 72.1 (C-3′, 4′), 62.8 (C-1′, 6′). FAB-MS *m/z* (%): 297 (12), 219 (5), 185 (6), 133 (32), 77 (17). HR-FAB-MS: *m/z* 297.1333 $[M+H]^+$ (calcd for $C_{15}H_{21}O_6$, 297.1338).

3.3.2 Compound *2*

Pale white needles (EtOAc), mp 138.8–139.9°C. IR (KBr) ν_{max} (cm^{-1}): 3414, 1773, 1611, 1518, 1503, 1488, 1237, 1021, 931, 861, 810. UV (MeOH) λ_{max}: 206, 234, 284 nm. ^{1}H, ^{13}C NMR, HSQC, and HMBC spectral data, see Table 1. EI-MS *m/z* (%): 328 (38), 270 (5), 164 (18), 148 (100), 147 (19), 115 (10), 77 (15). HR-EI-MS: *m/z* 328.0942 $[M]^+$ (calcd for $C_{18}H_{16}O_6$, 328.0947).

Acknowledgements

This research project was sponsored by Amore Pacific Corporation, Korea.

References

[1] J.Y. Liu, X.D. Yang, and L.Z. Xu, *Chin. Tradit. Herb Drugs* **33**, 681 (2002).

[2] M. Miyamura, T. Nohara, T. Tomimatsu, and I. Nishioka, *Phytochemistry* **22**, 215 (1983).

[3] Y.H. Gong and L.S. Ding, *^{13}C NMR Analysis of Nature Products* (Yunnan Science and Technology Press, Yunnan, 2006), p. 884.

[4] Q.Y. Xing, R.Q. Xu, Z. Zhou, and W.W. Pei, *Basic Organic Chemistry*, 2nd ed. (Advanced Education Press, Beijing, 2001), p. 100.

[5] F. Abe and T. Yamauchi, *Phytochemistry* **27**, 575 (1988).

[6] S. Nishibe, M. Chiba, A. Sakushima, S. Hisada, S. Yamanouchi, M. Takido, U. Sankawa, and A. Sakakibara, *Chem. Pharm. Bull.* **28**, 850 (1980).

[7] P.J. Cong and S.Y. Li, *Natural Organic* (Chinese Medical Technology Press, Beijing, 2003), p. 1220.

[8] D.Q. Yu and J.S. Yang, *Analytical Chemistry Manual*, 7th ed. (Chemical Industry Press, Beijing, 1999), p. 898.

[9] K. Shima, S. Hisada, and I. Inagaki, *Phytochemistry* **10**, 894 (1971).