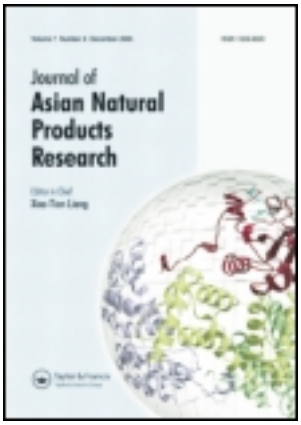

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Brachystemols A–C, three new furan derivatives from *Brachystemma calycinum*

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Three new furan derivatives, brachystemols A–C (**1**–**3**), and 13 known compounds (**4**–**15**) were isolated from the EtOH extract of *Brachystemma calycinum*. Their structures were identified by means of spectroscopic methods. Compounds **4**–**13** were isolated from this plant for the first time.

Keywords: *Brachystemma calycinum*; Caryophyllaceae; furans

1. Introduction

Brachystemma calycinum (Caryophyllaceae) is a Chinese folk herb used for the treatment of rheumatism, limb numbness, impotence, and foot edema [1]. Our previous work on the roots of *B. calycinum* led to the isolation of cyclic peptides and immunosuppressive alkaloids [2–4]. Continuous efforts on the aerial parts of this plant resulted in three new furan derivatives and 12 known compounds (Figure 1). Compounds **4**–**13** were isolated from this plant for the first time.

2. Results and discussion

Compound **1** had the molecular formula $C_9H_{18}O_4$ derived from its HR-ESI-MS, ^{13}C NMR, and DEPT spectra, indicating one degree of unsaturation. The IR absorption at 3423 cm^{-1} suggested the presence of a hydroxy group. The ^{13}C NMR and DEPT spectra showed nine carbon signals assigned to two methyls, four methylenes, and three methines. The COSY spectrum showed the spin systems of H-2/H-3/H-4/H-5, H-3/H-6, H-7/H-8, and H-9/H-10, indicating two ethyl moieties and the furan structure, which accounts for one degree of unsaturation. The HMBC correlations of H-6/C-2, C-3, and C-4, H-7/C-2, and H-9/C-4 assigned the positions of hydroxymethyl and two ethyloxy moieties (Figure 2). The split pattern of H-2 (dd, 12.2, 4.7 Hz) indicated the presence of a 'W' coupling [2], and the dihedral angle of H-C(2)–C(3)-H is *ca.* 0° [5], implying the *cis* relationship of H-2 and H-3. The *J* values of H-4, H-5a, and H-5b indicated that the triplet of H-4 (d, 3.8 Hz) is derived from H-3, which means that the dihedral angle of H-C(3)–C(4)-H is *ca.* 130° [6], and H-3 and H-4 are *trans*. The above conclusion was in accordance with the observed ROESY correlations of H-2/H-3/H-5. Accordingly, the structure

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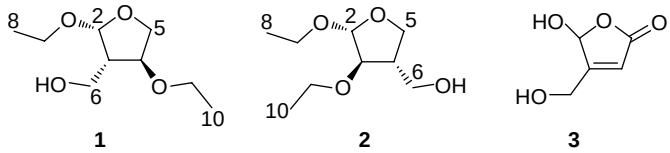

Figure 1. The structures of compounds **1**–**3**.

of **1** was assigned as (2,4-diethoxytetrahydrofuran-3-yl)methanol, named brachystemol A.

The molecular formula of compound **2** was established as $C_9H_{18}O_4$ from its HR-ESI-MS, ^{13}C NMR, and DEPT spectra. The ^1H and ^{13}C NMR spectral data (Table 1) were very similar to those of **1**. Analysis of $^1H-^1H$ COSY, HMQC, and HMBC spectra demonstrated that **2** was isomeric with compound **1** (Figure 2). $^1H-^1H$ COSY correlations of H-2/H-3/H-4/H-5 and H-4/H-6, and HMBC correlations of H-7/C-2, H-2/C-5, H-9/C-3, and H-6/C-3, C-4 confirmed the positions of hydroxymethyl and two ethyloxy moieties. H-2 behaving as a singlet (δ 5.17, s) indicated that the dihedral angle of H-C(2)–C(3)-H approaches 90° and there was no 'W' coupling for H-2 via oxygen bridge [6], which could occur when H-2 and H-3 have *trans* relationship. H-3 behaving as a d-like peak with small *J* value indicated that H-3 and H-4 have *trans* relationship from a molecular model study. Unfortunately, no effective ROESY correlations were observed in the ROESY spectrum. Therefore, the structure of **2** was assigned as (4,5-diethoxytetrahydrofuran-3-yl)methanol, named brachystemol B.

The molecular formula of compound **3** was deduced as $C_5H_6O_4$ by its positive HR-ESI-MS, ^{13}C NMR, and DEPT spectra. The IR spectrum showed the presence of hydroxy (3384 cm^{-1}) and carbonyl groups (1757 cm^{-1}). The ^{13}C NMR and DEPT spectra showed five carbons attributed to an ester carbonyl group, two olefinic carbons, and two oxygen-bearing carbons. The HMBC correlations of H-5/C-2, C-3, C-4, and C-6; H-3/C-2, C-4, C-5, and C-6; and H-6/C-3, C-4, and C-5 were observed, which suggested the structure of **3** as shown in Figure 1, and named brachystemol C. The absolute configuration at C-5 is yet to be determined.

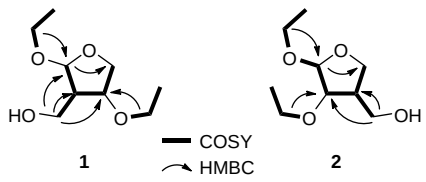

Figure 2. Key COSY and HMBC correlations of **1** and **2**.

The known compounds were identified as 3-furancarboxylic acid (**4**), 4-hydroxy-3-methoxybenzoic acid (**5**) [7], ω-hydroxypropioquaiacone (**6**) [8], methyl α-D-fructofuranoside (**7**) [9], methyl β-D-fructofuranoside (**8**) [10], ethyl β-D-fructofuranoside (**9**) [10], *n*-pentyl *α*-D-fructofuranoside (**10**) [10], *n*-pentyl β-D-fructofuranoside (**11**) (10), bergenin (**12**) [11], (6*S*,9*R*)-roseoside (**13**) [12], 2-pyrrolecarboxylic acid (**14**) [13], and adenosine (**15**), respectively, by comparing their spectroscopic data with literature data or directly identified by spectroscopic data.

3. Experimental

3.1 General experimental procedures

Optical rotation was recorded on a Horiba SEPA-300 polarimeter. UV spectra were measured on a Shimadzu UV-2401PC spectrophotometer. IR spectra were obtained on a Tensor 27 spectrometer, with KBr pellets. NMR spectra were recorded on a Bruker AV-400 or DRX-500 spectrometer. EI-MS were recorded on a VG Auto Spec-3000 spectrometer, and HR-ESI-MS were determined on an API QSTAR

Table 1. ^{1}H (500 MHz) and ^{13}C (100 MHz) NMR spectral data of **1**–**3**, δ in ppm, J in Hz.

	1[a]		**2**[a]		**3**[b]	
No.	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
2	5.26 (dd, 12.2, 4.7)	98.8 (CH)	5.17 (s)	100.7 (CH)		171.4 (qC)
3	2.28 (m)	48.7 (CH)	3.94 (d-like)	80.4 (CH)	5.97 (s)	116.7 (CH)
4	4.07 (t, 3.8)	78.5 (CH)	2.53 (t-like)	52.3 (CH)		171.2 (qC)
5a	3.79 (dd, 9.9, 4.7)	72.1 (CH_2)	3.99 (dd, 10.0, 4.9)	71.5 (CH_2)	6.12 (s)	98.3 (CH)
5b	4.21 (d, 9.9)		4.12 (dd, 10.0, 1.8)			
6	3.68 (overlap)	64.9 (CH_2)	3.51 (d, 7.0)	64.9 (CH_2)	4.46 (s)	58.4 (CH_2)
7a	3.43 (dd, 9.2, 7.0)	65.7 (CH_2)	3.47 (q, 7.0)	66.4 (CH_2)		
7b	3.68 (overlap)					
8	1.19 (overlap)	15.3 (CH_3)	1.18 (overlap)	15.2 (CH_3)		
9a	3.52 (m)	66.7 (CH_2)	3.22 (dd, 9.5, 8.2)	68.3 (CH_2)		
9b			3.34 (m)			
10	1.19 (overlap)	15.2 (CH_3)	1.18 (overlap)	14.9 (CH_3)		

[a] CD_3Cl.
[b] CD_3OCD_3.

Pulsar 1 spectrometer. Column chromatography (CC) was carried out on silica gel (200–300 mesh; Qingdao Marine Chemical, Inc., Qingdao, China), MCI gel CHP 20P (75–150 μm; Mitsubishi Chem. Co. Tokyo, Japan), RP-18 (40–60 μm; Daiso Co. Osaka, Japan), and Sephadex LH-20 (Amersham Pharmacia, Uppsala, Sweden).

3.2 Plant material

The aerial parts of *B. calycinum* were collected in Xishuangbanna, Yunnan Province, China, at the end of March 2008, and identified by Prof. H. Peng at the Kunming Institute of Botany. A voucher specimen (CHYX0572) is deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China of our institute.

3.3 Extraction and isolation

The dried and powdered aerial parts of *B. calycinum* (12 kg) were extracted with 80% EtOH (3 × 60 l) to give an extract, which was suspended in H_2O and partitioned by petroleum ether, EtOAc, and *n*-BuOH (each 4 × 6 l), respectively. The EtOAc portion (42 g) was subjected to CC over silica gel (80–100 mesh) using increasing amounts (2%–50%) of MeOH in $CHCl_3$ and finally MeOH as eluents to produce fractions A–G. Fr. A (3 g) was separated by silica gel CC to yield three parts (A.1–A.3). Fr. A.2 (600 mg) was purified by vacuum liquid chromatograph to give compound **4** (23 mg). Fr. A.3 (200 mg) was purified by Sephadex LH-20 to yield compounds **5** (10 mg) and **6** (15 mg). Fr. B (2 g) was subjected to RP-18 CC eluted with gradient aqueous MeOH (10–95%) to obtain fractions B_1–B_5. Fr. B_3 (350 mg) was passed through a Sephadex LH-20 column ($CHCl_3$–MeOH, 6:4), followed by silica gel CC (petroleum ether–*i*-PrOH, 15:1 and 10:1) to obtain compounds **1** (11.5 mg) and **2** (11.5 mg). Fr. F (2.5 g) was fractionated over RP-18 CC eluted with aqueous MeOH (50%–80%) to yield fractions F_1 and F_2. Fr. F_1 (1.2 g) was separated on a Sephadex LH-20 column (MeOH), followed by silica gel CC ($CHCl_3$–MeOH, 10:1–5:1) to obtain **3** (62 mg). The *n*-BuOH-soluble extract (107 g) was fractionated by silica gel CC eluted with $CHCl_3$ with increasing amounts of MeOH (10%–100%) to afford 10 fractions (Frs 1–10). Fr. 4 (2.2 g) was divided into five portions (Frs 4.1–4.5) by MCI gel CHP 20P eluted with gradient aqueous MeOH (20%–90%). Fr. 4.2 (200 mg) was subjected to RP-18 (MeOH–H_2O, 20%–80%) and purified

by Sephadex LH-20 (MeOH) to give compounds **11** (2 mg) and **14** (66 mg). Fr. 5 (15 g) was divided into five parts (Frs 5.1–5.5) by gel filtration on Sephadex LH-20 (MeOH). Fr. 5.1 (310 mg) was subjected to vacuum liquid chromatography over silica gel ($CHCl_3$–MeOH, 20:1), followed by RP-18 CC (aqueous MeOH, 10%–50%) to give compound **7** (35 mg). Fr. 5.3 (1.4 g) was subjected to RP-18 (MeOH–H_2O, 10%–50%) to afford two portions. One was chromatographed on silica gel CC (Me_2CO–MeOH, 90:1) and followed by purification on Sephadex LH-20 (MeOH) to yield compounds **10** (26 mg) and **15** (213 mg), and the other was recrystallized in MeOH to yield **12** (25 mg). Fr. 6 (1.5 g) was subjected to Sephadex LH-20 (MeOH), followed by RP-18 CC (MeOH–H_2O, 10%–80%) to yield compounds **8** (130 mg), **9** (26 mg), and **13** (29 mg).

*3.3.1 1,3-Diethoxy-2-hydroxymethyl-furan (**1**)*

Colorless gums: $[\alpha]_D^{24}$ −19.7 (*c* 0.10, MeOH). IR (KBr) ν_{max}: 3423, 2973, 2929, 2870, 1727, 1640, 1629, 1449, 1379, 1125, 1042 cm^{-1}. ^1H (500 MHz) and ^{13}C NMR (100 MHz) spectral data, see Table 1. EI-MS (70 eV): *m/z* 191 $[M + H]^+$ (25), 177 (15), 149 (40), 123 (40), 85 (60), 71 (100). HR-ESI-MS (positive): *m/z* 213.1099 $[M + Na]^+$ (calculated for $C_9H_{18}O_4Na$, 213.1102).

*3.3.2 1,2-Diethoxy-3-hydroxymethyl-furan (**2**)*

Colorless gums: $[\alpha]_D^{24}$ −12.1 (*c* 0.10, MeOH). IR (KBr) ν_{max}: 3424, 2975, 2931, 2870, 1379, 1123, 1044, 982 cm^{-1}. ^1H (500 MHz) and ^{13}C NMR (100 MHz) spectral data, see Table 1. EI-MS (70 eV): *m/z* 173 (70), 129 (60), 101 (86), 85 (100). HR-ESI-MS (positive): *m/z* 213.1101 $[M + Na]^+$ (calculated for $C_9H_{18}O_4Na$, 213.1102).

*3.3.3 5-Hydroxy-4-(hydroxmethyl)-furan-2(5H)-one (**3**)*

Colorless gums: $[\alpha]_D^{24}$ −7.9 (*c* 0.32, MeOH). IR (KBr) ν_{max}: 3384, 2921, 1757, 1656, 1439, 1339, 1149, 1129, 1054, 947, 890, 668 cm^{-1}. ^1H (500 MHz) and ^{13}C NMR (100 MHz) spectral data, see Table 1. FAB-MS (negative): *m/z* 129 $[M - H]^-$; HR-ESI-MS (positive): *m/z* 129.0185 $[M - H]^-$ (calculated for $C_5H_5O_4$, 129.0187).

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Note

1. These authors contributed equally to this work.

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