Kadsutherins A–C: Three New Dibenzocyclooctane Lignans from the Stems of *Kadsura* Species

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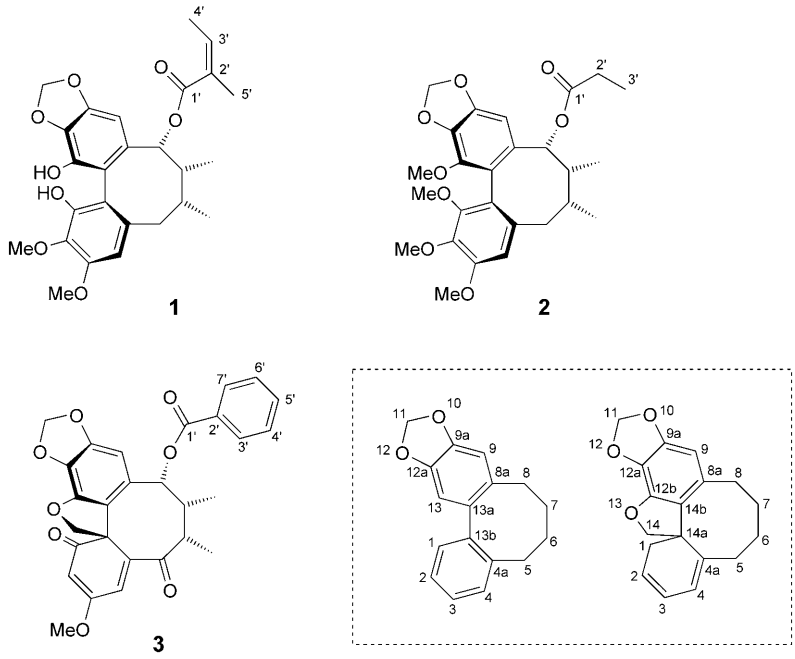
Three new dibenzocyclooctane-type lignans, kadsutherins A–C (**1**–**3**), were isolated from the stems of two *Kadsura* species. Their structures and configurations were elucidated by spectroscopic methods including 2D-NMR and HR-MS techniques. Kadsutherin C (**3**) is the first dibenzocyclooctane lignan without an oxygen-containing substituent at C(2).

Introduction. – The stems of *Kadsura interior* A. C. SMITH and *K. heteroclita* (ROXB.) CRAIB. are used as '*Dian-Jixueteng*', a herbal Chinese medicine, to produce a compound preparation called '*Fufang Jixueteng Gao*' for the treatment of blood deficiency, numb hands and feet, painful aching of joints, and irregular menstruation [1][2]. Previous studies have indicated that lignans, especially those of the dibenzocyclooctane-type, are principal bioactive constituents of *K. interior* and *K. heteroclita*, with various biological activities such as antitumor-promoting effects, calcium antagonism, anti-lipid peroxidation, and anti-HIV effects [3–10]. No chemical study of '*Dian-Jixueteng*' has been reported yet. Our investigation on the chemical constituents of this medicine now led to the isolation and characterization of three new dibenzocyclooctane-type lignans, kadsutherins A–C (**1**–**3**), which were obtained by repeated column-chromatographic purification of the AcOEt extract of '*Dian-Jixueteng*'.

Results and Discussion. – Kadsutherin A (**1**), obtained as a yellow powder, was shown to have the molecular formula $C_{26}H_{30}O_8$ based on HR-ESI-MS (*m*/*z* 493.1841 ($[M+Na]^+$)). The UV and NMR spectra of **1** indicated a dibenzocyclooctane-type lignan [4].

The ^{1}H-NMR spectrum of **1** (*Table 1*) showed signals due to two Me groups at δ(H) 0.96 (*d*, *J* = 7.1) and 1.11 (*d*, *J* = 6.7 Hz), assignable to 6-Me and 7-Me [4], respectively, as well as two MeO groups at δ(H) 3.89 (*s*, 3 H) and 3.90 (*s*, 3 H), and a methylenedioxy (O–CH_2–O) moiety at δ(H) 6.00 (*s*, 1 H) and 6.01 (*s*, 1 H) on two aromatic rings. The signal at δ(H) 2.13–2.15 (*m*, 2 H), which exhibited HMBC correlations (*Fig. 1*) with 6-Me at δ(C) 14.8 and 7-Me at δ(C) 19.7, was assigned to both H–C(6) and H–C(7). HMBC correlations observed between the signals at δ(H) 2.62–2.63 (*m*, 2 H) and δ(C) 34.4 (C(6)), 41.6 (C(7)), and 14.8 (6-Me) suggested a CH_2 group in position 5, as further confirmed by the HMBC cross-peak from H–C(4) at δ(H) 6.47 (*s*) to C(5) at δ(C) 38.5, and by a ROESY correlation between H–C(4) and H–C(5). The H-atom at δ(H) 5.61 (*s*, 1 H), correlating with C(6), C(7), and 7-Me in the HMBC spectrum, was in benzylic position, carrying an acyloxy group at C(8) (δ(C) 82.7)) [4].



The two signals at δ(H) 5.74 (*s*, 1 H) and 5.03 (*s*, 1 H), lacking any HSQC correlations, suggested the presence of two additional OH groups on the aromatic rings, as confirmed by an IR band at 3442 cm^{-1}. The methylenedioxy moiety was attached to C(9a) (δ(C) 148.6) and C(12a) (δ(C) 133.9) on the basis of the HMBC correlations of H–C(9) with C(9a) and C(12a), and between the methylenedioxy resonances (δ(H) 6.00, 6.01) with C(9a) and C(12a). Similarly, the 2- and 3-MeO groups at δ(H) 3.89 and 3.90, respectively, were established by the HMBC correlations of 2-MeO with C(2) (δ(C) 133.5), of 3-MeO with C(3) (δ(C) 150.8), and of H–C(4) with C(2) and C(3). Based on the above considerations, the two OH groups could only be located at C(1) (δ(C) 145.6) and C(13) (δ(C) 137.0). HMBC cross-peaks observed between δ(H) 5.74 (1-OH) and δ(C) 145.6 (C(1)), 133.5 (C(2)), and 114.2 (C(13b)), and between δ(H) 5.03 (13-OH) and δ(C) 137.0 (C(13)), 133.9 (C(12a)), and 115.4 (C(13a)), respectively, further supported the above assignment.

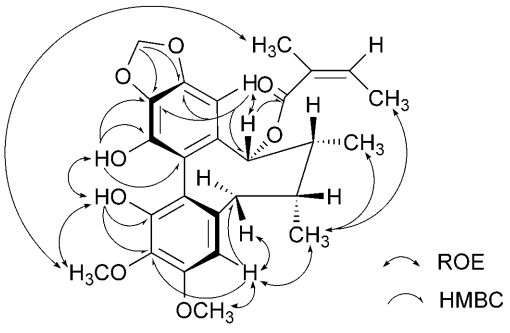


Fig. 1. *Key HMBC and ROESY correlations in* **1**

Table 1. *^{1}H-NMR Data of* **1**–**3**. At 400 MHz in $CDCl_3$, $T = 27°$; δ in ppm, J in Hz.

Position	**1**	**2**	**3**
H–C(2)	–	–	5.96 (*s*)
H–C(4)	6.47 (*s*)	6.56 (*s*)	6.72 (*s*)
H_α–C(5)	2.62–2.63 (*m*)	2.64 (*s*)	–
H_β–C(5)		2.65 (*d*, *J* = 1.5)	–
H–C(6)	2.13–2.15 (*m*)	1.99–2.10 (*m*)	3.06–3.15 (*m*)
H–C(7)	2.13–2.15 (*m*)	1.99–2.10 (*m*)	1.96–1.99 (*m*)
H–C(8)	5.61 (*s*)	5.65 (*s*)	5.98 (*d*, *J* = 4.9)
H–C(9)	6.49 (*s*)	6.47 (*s*)	6.58 (*s*)
CH_2(11)	6.00, 6.01 (2*s*)	5.95, 5.98 (*AB*, *J* = 1.6)	6.00, 6.04 (*AB*, *J* = 1.6)
CH_2(14)	–	–	4.81, 4.39 (*AB*, *J* = 9.4)
6-Me	0.96 (*d*, *J* = 7.1)	0.92 (*d*, *J* = 7.0)	1.08 (*d*, *J* = 6.7)
7-Me	1.11 (*d*, *J* = 6.7)	1.06 (*d*, *J* = 7.0)	1.12 (*d*, *J* = 7.0)
1-MeO	–	3.62 (*s*)	–
2-MeO	3.89 (*s*)	3.86 (*s*)	–
3-MeO	3.90 (*s*)	3.89 (*s*)	3.83 (*s*)
13-MeO	–	3.79 (*s*)	–
1-OH	5.74 (*s*)	–	–
13-OH	5.03 (*s*)	–	–
Angeloyl[1]):			
2′-Me	1.30 (*s*)	–	–
H–C(3′)	5.85–5.89 (*m*)	–	–
3′-Me	1.89 (*dd*, *J* = 7.4, 1.6)	–	–
Propanoyl:			
CH_2(2′)	–	1.73–1.88 (*m*)	–
Me(3′)	–	0.85 (*t*, *J* = 7.4)	–
Benzoyl:			
H–C(3′,7′)	–	–	7.73 (*d*, *J* = 7.4)
H–C(4′,6′)	–	–	7.22 (*t*, *J* = 7.4)
H–C(5′)	–	–	7.45 (*t*, *J* = 7.4)

In the EI mass spectrum of **1**, the signals at m/z 370 ($[M - C_4H_7COOH]^+$), 83 ($C_4H_7CO^+$), and 55 ($C_4H_7^+$) suggested the presence of an angeloyl[1]) group, as confirmed by the ^{1}H-NMR signals at δ(H) 1.30 (*s*, 3 H), 1.89 (*dd*, *J* = 7.4, 1.6 Hz, 3 H), and 5.85–5.89 (*m*, 1 H), along with the corresponding ^{13}C-NMR signals (*Table 2*) at δ(C) 166.6 (C=O), 140.0, 127.0, 20.5, and 15.7. The HMBC correlations of H–C(8) at δ(H) 5.61 with the C=O group at δ(C) 166.6, and the ROESY cross-peak for H–C(8) and H–C(9) revealed that the angeloyl group was α-oriented and located at C(8).

The circular dichroism (CD) spectrum of **1** showed a negative *Cotton* effect at 243 nm, and a positive one at 213 nm, indicating that **1** contained an axially chiral (a*S*)-1,1′-biphenyl unit ((*P*)-helicity) [11]. The ROESY cross-peaks (*Fig. 1*) between 6-Me and H–C(4), 6-Me and H–C(5), 7-Me and H–C(8), 6-Me and 7-Me, and between 2-MeO and 2′-Me indicated a twist–boat–chair (TBC) conformation for the cyclooctane ring [12]. Thus, from the above data, the structure of **1** was elucidated as (a*S*,6*R*,7*R*,8*R*)-5,6,7,8-tetrahydro-1,13-dihydroxy-2,3-dimethoxy-6,7-dimethylbenzo[3′,4′]cycloocta-[1′,2′:4,5]benzo[1,2-*d*][1,3]dioxol-8-yl (2*Z*)-2-methylbut-2-enoate.

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[1]) Angeloyl = 2-methylbut-2-enoyl.

Table 2. *^{13}C-NMR Data of* **1**–**3**. At 100 MHz in $CDCl_3$, $T=27°$; δ in ppm.

Position	**1**	**2**	**3**	Position	**1**	**2**	**3**
C(1)	145.6 (*s*)	150.9 (*s*)	189.3 (*s*)	CH_2(14)	–	–	79.7 (*t*)
C(2)	133.5 (*s*)	139.4 (*s*)	140.5 (*s*)	1-MeO	–	60.3 (*q*)	–
C(3)	150.8 (*s*)	151.5 (*s*)	151.0 (*s*)	2-MeO	60.6 (*q*)	60.6 (*q*)	–
C(4)	108.5 (*d*)	110.2 (*d*)	125.6 (*d*)	3-MeO	56.0 (*q*)	55.9 (*q*)	55.6 (*q*)
C(4a)	135.4 (*s*)	123.1 (*s*)	150.6 (*s*)	13-MeO	–	60.0 (*q*)	–
C(5)	38.5 (*t*)	38.7 (*t*)	175.4 (*s*)	Angeloyl:			
C(6)	34.5 (*d*)	34.8 (*d*)	30.6 (*d*)	C(1′)	166.6 (*s*)	–	–
C(7)	41.6 (*d*)	41.8 (*d*)	44.1 (*d*)	C(2′)	127.0 (*s*)	–	–
C(8)	82.7 (*d*)	82.3 (*d*)	79.7 (*d*)	C(3′)	140.0 (*d*)	–	–
C(8a)	136.0 (*s*)	120.5 (*s*)	129.8 (*s*)	2′-Me	20.5 (*q*)	–	–
C(9)	101.5 (*d*)	102.5 (*d*)	102.0 (*d*)	3′-Me	15.7 (*q*)	–	–
C(9a)	148.6 (*s*)	148.6 (*s*)	130.8 (*s*)	Propanoyl:			
C(12a)	133.9 (*s*)	135.9 (*s*)	118.6 (*s*)	C(1′)	–	173.6 (*s*)	–
C(12b)	–	–	142.8 (*s*)	CH_2(2′)	–	27.1 (*t*)	–
C(13)	137.0 (*s*)	141.2 (*s*)	–	Me(3′)	–	8.6 (*q*)	–
C(13a)	115.4 (*s*)	135.0 (*s*)	–	Benzoyl:			
C(13b)	114.2 (*s*)	133.2 (*s*)	–	C(1′)	–	–	165.7 (*s*)
C(14a)	–	–	67.1 (*s*)	C(2′)	–	–	132.8 (*s*)
C(14b)	–	–	129.4 (*s*)	C(3′, 7′)	–	–	129.1 (*d*)
6-Me	14.8 (*q*)	14.8 (*q*)	19.6 (*q*)	C(4′,6′)	–	–	128.2 (*d*)
7-Me	19.7 (*q*)	19.6 (*q*)	10.8 (*q*)	C(5′)	–	–	133.2 (*d*)
CH_2(11)	101.8 (*t*)	101.1 (*t*)	102.3 (*t*)				

Kadsutherin B (**2**), obtained as a colorless powder, had the molecular formula $C_{26}H_{32}O_8$ according to HR-ESI-MS (*m/z* 495.1992 ($[M+Na]^+$)). The corresponding UV and NMR spectra indicated that **2** was also a dibenzocyclooctane-type lignan.

The ^{1}H-NMR data of **2** (*Table 1*) were quite similar to those of kadsurin [5], with signals at δ(H) 0.92 and 1.06 (*d*, $J=7.0$ Hz each, 3 H each), assignable to the *cis*-oriented 6- and 7-Me groups, respectively [4]. Also observed were one methylenedioxy moiety at δ(H) 5.95, 5.98 (*AB*, $J=1.6$ Hz, 1 H each) and MeO groups at δ(H) 3.62, 3.79, 3.86, and 3.89 (4*s*, 3 H each) on two aromatic rings. Two aromatic resonances at δ(H) 6.56 and 6.47 (2*s*, 1 H each), which correlated with δ(C) 38.7 (C(5)) and 82.3 (C(8)) in the HMBC spectrum, respectively, were assigned to H–C(4) at δ(H) 6.56 and H–C(9) at δ(H) 6.47. Based on the HMBC correlations of the two H-atoms at δ(H) 5.95 and 5.98 with δ(C) 148.6 (C(9a)) and 135.9 (C(12a)), and of H–C(9) with C(9a) and C(12a), the O–CH_2–O moiety was attached at C(9a) and C(12a).

EI-MS signals for **2** at *m/z* 398 ($[M-C_2H_5COOH]^+$), 74 ($C_2H_5COOH^+$), and 57 ($C_2H_5CO^+$) suggested the presence of a propanoyl group, which was supported by the signals at δ(H) 0.85 (*t*, $J=7.4$ Hz, 3 H) and 1.73–1.88 (*m*, 2 H), and those at δ(C) 173.6 (C=O), 27.1, and 8.6. The propanoyl group was located at C(8), as deduced from the HMBC correlations of δ(H) 5.65 (*s*, H–C(8)) with the propanoyl C=O group, as well as with δ(C) 135.0 (C(13a)), 120.5 (C(8a)), 102.5 (C(9)), 41.8 (C(7)), 34.8 (C(6)), and 19.6 (7-Me).

The CD spectrum showed negative and positive *Cotton* effects at 253 and 223 nm, respectively. Correlations of 6-Me with both H–C(4) and H_α–C(5) at δ(H) 2.64 (*s*), of H–C(8) at δ(H) 5.65 (*s*) with H–C(9), and of 7-Me with H–C(8) were observed in the ROESY spectrum. These data indicated that **2** was in the same conformation as **1**. Thus,

the structure of **2** was elucidated as (a*S*,6*R*,7*R*,8*R*)-5,6,7,8-tetrahydro-1,2,3,13-tetramethoxy-6,7-dimethylbenzo[3′,4′]cycloocta[1′,2′:4,5]benzo[1,2-*d*][1,3]dioxol-8-yl propanoate.

Kadsutherin C (**3**) was assigned the molecular formula $C_{28}H_{24}O_8$ by HR-ESI-MS (*m*/*z* 511.1368 ([*M*+Na]$^+$)). The presence of characteristic *AB* signals at δ(H) 4.81 and 4.39 in the ^{1}H-NMR spectrum (*Table 1*), and a quaternary C-atom at δ(C) 67.1 in the ^{13}C-NMR spectrum (*Table 2*), indicated that **3** was a dibenzocyclooctane-type lignan with a spirobenzofuranoid skeleton [13].

The ^{1}H-NMR spectrum of **3** showed the presence of two Me groups at δ(H) 1.08 (*d*, *J*=6.7, 3 H) and 1.12 (*d*, *J*=7.0 Hz, 3 H), assignable to 6-Me and 7-Me, respectively, one methylenedioxy moiety at δ(H) 6.00 and 6.04 (*AB*, *J*=1.6 Hz, 1 H each), and one MeO group at δ(H) 3.83 (*s*, 3 H). Signals at δ(H) 3.06–3.15 (*m*, 1 H) and 1.96–1.99 (*m*, 1 H), which exhibited ^{1}H,^{1}H correlations with the two Me groups at δ(H) 1.08 and 1.12, were assigned to H–C(6) and H–C(7), respectively. The H-atom at δ(H) 5.98 (*d*, *J*=4.9 Hz), which correlated with δ(C) 44.1 (C(7)), 10.8 (7-Me), and 102.0 (C(9)) in the HMBC spectrum (*Fig. 2*), was in benzylic position carrying an acyloxy group at C(8) (δ(C) 79.7). The HMBC correlations of the methylenedioxy signals with δ(C) 130.8 (C(9a)) and 118.6 (C(12a)), and of H–C(9) at δ(H) 6.58 (*s*) with C(8), C(9a), and C(12a) indicated that the O–CH_2–O moiety was attached to C(9a) and C(12a).

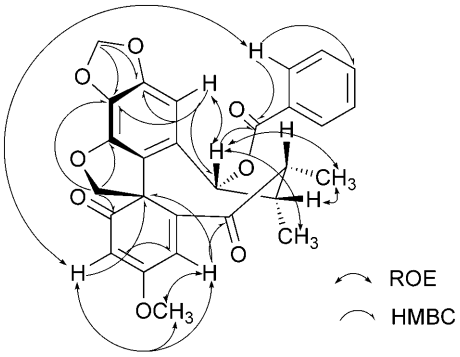

Fig. 2. *Key HMBC and ROESY correlations in* **3**

The IR absorptions at 1721, 1681, and 1650 cm^{-1} revealed the presence of three C=O groups, as confirmed by the ^{13}C-NMR signals at δ(C) 189.3, 175.4, and 165.7. EI-MS Signals at *m*/*z* 366 ([*M* – C_6H_5COOH]$^+$), 383 ([*M* – C_6H_5CO]$^+$), 105 ([C_6H_5CO]$^+$), and 77 ([C_6H_5]$^+$) suggested the presence of a benzoyl (Bz) group, as support by the ^{1}H-NMR signals at δ(H) 7.22 (*t*, *J*=7.4, 2 H), 7.45 (*t*, *J*=7.4, 1 H), and 7.73 (*d*, *J*=7.4 Hz, 2 H), and by the ^{13}C-NMR signals at δ(C) 165.7 (C=O), 132.8, 129.1, 128.2, and 133.2, which were quite similar to those of schiarisanrin C [14]. The C(1′)=O function of the Bz group at δ(C) 165.7 was deduced from the HMBC correlations of δ(H) 7.73 (H–C(3′,7′)) with δ(C) 165.7 (C=O). The HMBC correlation of δ(H) 4.39 and 4.81 (CH_2(14)) with δ(C) 189.3 (C=O) revealed the presence of a 2,4-dien-1-one, the C=O moiety resonating at δ(C) 189.3 [13]. The HMBC correlations of δ(H) 6.72 (*s*, 1 H) with δ(C) 175.4 (C=O), 140.5, 151.0, 150.6 (C(4a)), and 67.1 (C(14a)) revealed that the third C=O group at δ(C) 175.4 had to be assigned to C(5).

Commonly, dibenzocyclooctane lignans with $\alpha,\beta,\gamma,\delta$-unsaturated keto functions have MeO groups at C(2) and C(3), *e.g.*, heteroclitin D and E [5]. However, the ^{1}H-NMR spectrum of **3** showed only *one* MeO signal at δ(H) 3.83, and a *singlet* at δ(H) 5.96 (1 H), suggesting the presence of another H-proton on the dienone ring, besides H–C(4). Based on the above considerations – in combination with HMBC correlations of δ(H) 5.96 (*s*, 1 H) with δ(C) 67.1 (C(14a)) and 125.6 (C(4)), of δ(H) 3.83 (MeO) with δ(C)

151.0, and of δ(H) 6.72 (H–C(4)) with δ(C) 140.5, 151.0, 150.6 (C(4a)), and 67.1 (C(14a)) – the signal at δ(H) 5.96 was assigned to H–C(2), and the MeO group was located at C(3) (δ(C) 151.0), as supported by ROESY cross-peaks for the MeO group and both H–C(2) and H–C(4).

The CD spectrum of **3** was similar to that of benzoyl oxokadsurane [13], with negative *Cotton* effects at 213 and 245 nm, and positive ones at 229 and 264 nm. This, again, indicated an axially chiral (a*S*)-1,1′-biphenyl unit. The cyclooctane ring was deduced to be in a boat-like conformation, with (6*S*,7*R*,8*R*,14a*R*)-configuration, in accord with a coupling constant *J*(8,9) of 4.9 Hz, and ROESY correlations of H–C(8) with H–C(9), H–C(8) with both 7- and 6-Me, H–C(7) with 6-Me, and H–C(2) with H–C(3′,7′) (*Fig. 2*).

From the above data, the structure of **3** was elucidated as (6*S*,7*R*,8*R*,14a*R*)-5,6,7,8-tetrahydro-3-methoxy-6,7-dimethyl-1,5-dioxo-1*H*-10,12,13-trioxabenzo[1,8]cycloocta-[1,2,3-*cd*]-*as*-indacen-8-yl benzoate. Note that compound **3** is the first example of a dibenzocyclooctane-type lignan lacking an oxygen-containing substituent at C(2).

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Experimental Part

General. Anal. and prep. TLC: silica-gel plates GF_{254} (*Yan-tai Institute of Chemical Technology*). Column chromatography (CC): silica gel (200–300, or 300–400 mesh; *Qingdao Marine Chemical Factory*). Prep. HPLC: *Waters* system, with RP-C_{18} column (250×10 mm). UV Spectra: *Shimadzu UV-260* spectrophotometer, in anh. MeOH; λ_{max} in nm (log ε). CD Spectra: *JASCO J-715* spectropolarimeter; λ in nm ($\Delta\varepsilon$ in mdeg). Optical rotation (ORD): *JASCO P-1020* spectropolarimeter. IR Spectra: *Avatar 360-ESP* spectrophotometer (*Thermo Nicolet*), as KBr pellets; in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker AV-500* or *DRX-400* spectrometers, in $CDCl_3$ soln.; δ in ppm rel. to Me_4Si, *J* in Hz. EI-MS: *HP-5989A* mass spectrophotometers. HR-ESI-MS: *Micromass Q-Tof* mass spectrometer; in *m*/*z*.

Plant Material. The crude drug of '*Dian-Jixueteng*' was provided by *Guangfu Pharmaceutical Co., Ltd*. (Yunnan Province, P. R. China) in July 2004, and identified by Dr. *Daofeng Chen* (*D. S.*) as the stems of *K. interior* and *K. heteroclita*. A voucher specimen (JXT-GF-0401) was deposited at the Herbarium of Materia Medica, Department of Pharmacognosy, School of Pharmacy, Fudan University, Shanghai, P. R. China.

Extraction and Isolation. The air-dried stems (10 kg) of '*Dian-Jixueteng*' were ground and extracted exhaustively with 95% aq. EtOH at r.t. The EtOH extract was evaporated *in vacuo* to yield a semi-solid (620 g), which was suspended in H_2O (2 l), and extracted with AcOEt (10×2 l). The resulting AcOEt soln. was concentrated to yield a residue (260 g), which was subjected to CC (SiO_2 (2 kg), petroleum ether (PE)/ acetone gradient). *Fr. 16* (eluted with PE/acetone 8:2) was subjected to repeated CC (SiO_2; PE/acetone 10:1) and prep. TLC (SiO_2; PE/$CHCl_3$/acetone 15:1:1) to yield **2** (13 mg). *Fr. 19* (eluted with PE/Me_2CO 7:3) was subjected to repeated CC (SiO_2; PE/$CHCl_3$/acetone 5:5:1) and prep. TLC (SiO_2; PE/$CHCl_3$/acetone 5:5:1) to afford **1** (15 mg). *Fr. 20* (eluted with PE/acetone 6:4) was subjected to repeated CC (SiO_2; PE/$CHCl_3$/acetone 15:2:2) and prep. RP-HPLC (MeOH/H_2O 7:3) to give **3** (4 mg).

Kadsutherin A (=*(a*S,*6*R,*7*R,*8*R*)-5,6,7,8-Tetrahydro-1,13-dihydroxy-2,3-dimethoxy-6,7-dimethylbenzo[3′,4′]cycloocta[1′,2′:4,5]benzo[1,2-*d*][1,3]dioxol-8-yl (2*Z*)-2-Methylbut-2-enoate*; **1**). Yellow powder. UV (MeOH): 220 (4.67), 280 (sh, 3.50). CD (*c*=0.02, MeOH): 213 (+85), 243 (−37). $[\alpha]_D^{25}$ = +236.7 (*c*=0.02, MeOH). IR (KBr): 3442, 2966, 1709, 1615, 1507, 1425, 907, 732. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. EI-MS: 470 (88, M^+), 370 (12), 83 (10), 55 (23). HR-ESI-MS: 493.1841 ($[M+Na]^+$, $C_{26}H_{30}NaO_8^+$; calc. 493.1838).

Kadsutherin B (= *(a*S,*6*R,*7*R,*8*R*)-5,6,7,8-Tetrahydro-1,2,3,13-tetramethoxy-6,7-dimethylbenzo[3′,4′]-cycloocta[1′,2′:4,5]benzo[1,2-*d*][1,3]dioxol-8-yl Propanoate*; **2**). Colorless powder. UV (MeOH): 218 (4.46), 253 (sh, 3.88), 281 (sh, 3.30). CD ($c = 0.01$, MeOH): 223 (+19), 253 (−17). $[\alpha]_D^{25} = 239$ ($c = 0.01$, MeOH). IR (KBr): 2924, 1734, 1621, 1596, 1407, 1107, 928, 732. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. EI-MS: 472 (81, M^+), 398 (72), 74 (6), 57 (100). HR-ESI-MS: 495.1992 ($[M+Na]^+$, $C_{26}H_{32}NaO_8^+$; calc. 495.1995).

Kadsutherin C (= *(6*S,*7*R,*8*R,*14a*R*)-5,6,7,8-Tetrahydro-3-methoxy-6,7-dimethyl-1,5-dioxo-1*H*-10,12,13-trioxabenzo[1,8]cycloocta[1,2,3-*cd*]-as-indacen-8-yl Benzoate*; **3**). Yellow powder. UV (MeOH): 216 (4.28), 374 (2.88). CD ($c = 0.04$, MeOH): 213 (−21), 229 (+5), 245 (−5), 264 (+4). $[\alpha]_D^{25} = -50.3$ ($c = 0.04$, MeOH). IR (KBr): 1721, 1681, 1650, 1585, 1505, 1386, 1274, 1097, 912, 724. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. EI-MS: 488 (11, M^+), 460 (36), 383 (1), 366 (3), 122 (9), 105 (100), 77 (11). HR-ESI-MS: 511.1368 ($[M+Na]^+$, $C_{28}H_{24}NaO_8^+$; calc. 511.1369).

REFERENCES

[1] D.-F. Chen, G.-J. Xu, L.-S. Xu, R.-L. Jin, *Chin. Tradit. Herb. Drugs* **1993**, *24*, 34.
[2] 'Pharmacopoeia of the People's Republic of China', Chemical Industry Press, Beijing, 2005, Vol. 1, p. 531.
[3] Z.-H. Ding, S.-D. Luo, *Acta Chim. Sin.* **1990**, *48*, 1075.
[4] D.-F. Chen, S.-X. Zhang, K. Chen, B.-N. Zhou, P. Wang, L. M. Cosentino, K.-H. Lee, *J. Nat. Prod.* **1996**, *59*, 1066.
[5] D.-F. Chen, G.-J. Xu, X.-W. Yang, M. Hattori, Y. Tezuka, T. Kikuchi, T. Namba, *Phytochemistry* **1992**, *31*, 629.
[6] D.-F. Chen, S.-X. Zhang, M. Kozuka, Q.-Z. Sun, J. Feng, Q. Wang, T. Mukainaka, Y. Nobukuni, H. Tokuda, H. Nishino, H.-K. Wang, S. L. Morris-Natschke, K.-H. Lee, *J. Nat. Prod.* **2002**, *65*, 1242.
[7] D.-F. Chen, S.-X. Zhang, L. Xie, J.-X. Xie, K. Chen, Y. Kashiwada, B.-N. Zhou, P. Wang, L. M. Cosentino, K.-H. Lee, *Bioorg. Med. Chem.* **1997**, *5*, 1715.
[8] X.-M. Zhang, D.-F. Chen, X.-J. He, S. Yang, P. Zheng, M.-H. Jiang, *Acta Pharmacol. Sin.* **2000**, *21*, 373.
[9] H. L. Peng, D.-F. Chen, H.-X. Lan, X.-M. Zhang, Z. Gu, M. H. Jiang, *Acta Pharmacol. Sin.* **1996**, *17*, 538.
[10] X.-W. Yang, H. Miyashiro, M. Hattori, T. Namba, Y. Tezuka, T. Kikuchi, D.-F. Chen, G.-J. Xu, T. Hori, M. Extine, H. Mizuno, *Chem. Pharm. Bull.* **1992**, *40*, 1510.
[11] Y. Ikeya, H. Taguchi, I. Yosioka, H. Kobayashi, *Chem. Pharm. Bull.* **1979**, *27*, 1383.
[12] Y. Ikeya, H. Taguchi, I. Yosioka, H. Kobayashi, *Chem. Pharm. Bull.* **1980**, *28*, 3357.
[13] L. Li, H. Xue, *Phytochemistry* **1990**, *29*, 2730.
[14] Y.-H. Kuo, L.-M. Yang, C.-F. Chen, *J. Org. Chem.* **1997**, *62*, 3242.

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