Heteroclitins N – Q, New Compounds from Stems of *Kadsura heteroclita* (ROXB.) CRAIB

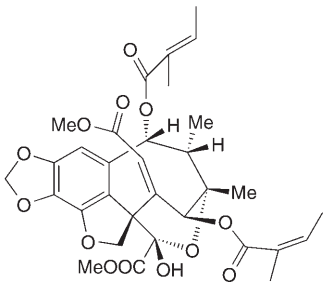
by **Li-Jia Xu**[a])[b]), **Hai-Tao Liu**[a]), **Yong Peng**[a])[b]), **Si-Bao Chen**[a]), **Shi-Lin Chen**[a])[b]), and **Pei-Gen Xiao***[a])[b])

[a]) Institute of Medicinal Plant Development, Peking Union Medical College & Chinese Academy of Medical Sciences, No. 151 Malianwa North Road, Haidian District, Beijing 100094, P. R. China (phone: +86-10-62894462; fax: +86-10-62899714; e-mail: xiaopg@public.bta.net.cn)

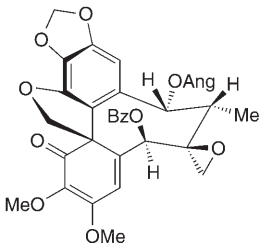
[b]) Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine, Ministry of Education Beijing 100094, P. R. China

From the stems of *Kadsura heteroclita* (ROXB.) CRAIB, a new novel C_{19} homolignan, heteroclitin N (**1**), as well as three new lignans, heteroclitins O–Q (**2**–**4**), were isolated. Their structures were elucidated based on spectral analysis, including 1D and 2D NMR experiments. There is an additional spirocyclic oxirane system in heteroclitin O (**2**), which is the first example of a lignan with an oxirane ring in a spirobenzofuranoid dibenzocyclooctene structure in the genus *Kadsura*.

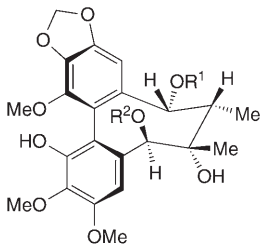
Introduction. – Plants of the genus *Kadsura* have attracted increasing interest as a promising source of bioactive compounds. Dibenzocyclooctene lignans, lanostane, and triterpenoids [1–5] isolated from this genus proved to have pharmacological activities, especially anti-HIV and antitumor properties. *Kadsura heteroclita* (ROXB.) CRAIB, a climbing species mainly distributed in the south-western part of China, has been used for the treatment of rheumatism and traumatic injuries for a long time [6][7]. Recently, the chemical investigations conducted in our laboratory have led to the isolation of four lignans [8] with spirodienone structures from the ether-soluble fraction of the EtOH extract. In continuation of our search for structurally interesting compounds, a new C_{19} homolignan, heteroclitin N (**1**), as well as three new lignans, heteroclitins O–Q (**2**–**4**), were isolated from the petroleum ether soluble fraction of the EtOH extract from the



1



2



3 R^1 = Bz, R^2 = Ang
4 R^1 = Ac, R^2 = Bz

stems of this plant. This report describes the isolation and structural elucidation of these novel lignans.

Results and Discussion. – Heteroclitin N (**1**) was obtained as colorless needles and possesses the molecular formula $C_{36}H_{36}O_{10}$, as derived from its HR-EI-MS (M^+ at m/z 628.2299). The NMR data of **1** (*Table 1*) were similar to those of the known compound taiwankadsurin B [9]. The relative configuration of **1** was established by a NOESY experiment (*Fig. 1*). Further spectroscopic data established the structure of heteroclitin N unambiguously as **1**.

Table 1. *^1H- (400 MHz) and ^{13}C-NMR (100 MHz) Data of Heteroclitin N* (**1**) *in $CDCl_3$.* Ang = angeloyl = (2*Z*)-2-methyl-1-oxobut-2-en-1-yl. For atom numbering[1]), see *Fig. 1*.

	δ(H)	δ(C)		δ(H)	δ(C)
C(1)		97.51	Me(18)	1.32 (*s*)	28.52
C(2)		171.00	CH_2(19)	6.00, 5.97 (2 br. *s*)	101.84
C(3)		165.50	CH_2(20)	5.00, 4.53 (2 *d*, each $J = 10.4$)	80.43
H–C(4)	6.02 (*d*, $J = 2.8$)	117.27	MeO–C(2)	3.94 (*s*)	53.65
C(5)		150.33	MeO–C(3)	3.61 (*s*)	51.79
H–C(6)	6.30 (*d*, $J = 2.8$)	72.53	Ang_1[a]):		
C(7)		79.21	C(1′)		166.09
H–C(8)	2.23–2.25 (*m*)	45.63	C(2′)		127.45
H–C(9)	6.66 (*d*, $J = 3.2$)	69.91	H–C(3′)	6.27 (*dd*, $J = 6.8, 1.2$)	142.32
C(10)		128.16	Me(4′)	2.06 (*d*, $J = 7.2$)	20.80
H–C(11)	6.45 (*s*)	98.97	Me(5′)	2.00 (*s*)	16.05
C(12)		150.33	Ang_2[a]):		
C(13)		129.27	C(1″)		165.43
C(14)		144.10	C(2″)		126.38
C(15)		118.30	H–C(3″)	6.13 (*dd*, $J = 6.8, 1.2$)	139.09
C(16)		56.99	Me(4″)	1.99 (overlapped)	20.43
Me(17)	1.07 (*d*, $J = 6.8$)	9.19	Me(5″)	2.00 (overlapped)	15.83

[a]) Ang_1 located at C(6) and Ang_2 located at C(9).

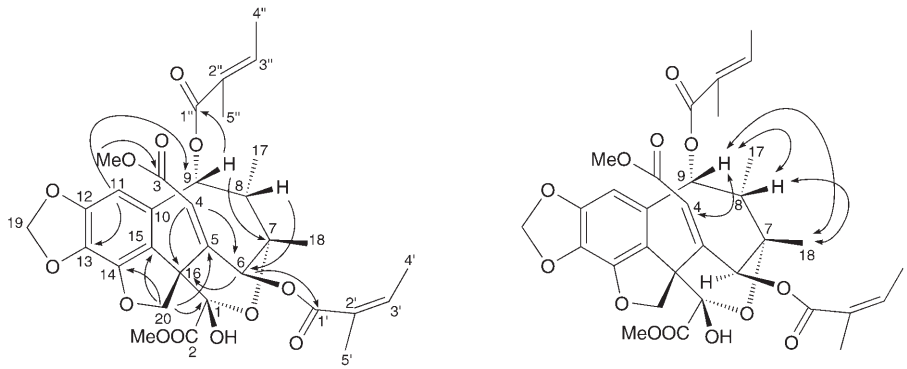


Fig. 1. *Key HMBC* (→) *and key NOESY* (↔) *correlations of* **1**[1])

[1]) Arbitrary atom numbering; for systematic names, see *Exper. Part.*

The ^{1}H-NMR spectra of **1** revealed the presence of a Me group at a tertiary C-atom (δ(H) 1.32 (*s*)), a Me group at a secondary C-atom (δ(H) 1.07 (*d*, *J* = 6.8 Hz)), an OCH_2 moiety (δ(H) 6.00 and 5.97 (2 br. *s*, 1 H each), and two MeO groups (δ(H) 3.61 and 3.94 (2 *s*)). Two OCH groups observed at δ(H) 6.30 (*d*, *J* = 2.8 Hz) and 6.66 (*d*, *J* = 3.2 Hz) were assigned to H–C(6) and H–C(9)[1]), respectively. The *s* at δ(H) 6.45 arose from H–C(11) of the benzo moiety, and the *d* at δ(H) 6.02 (*d*, *J* = 2.8 Hz) arose from H–C(4) of an allyl moiety. Moreover, the signals of two angelate (=(2*Z*)-2-methylbut-2-enoate) groups (δ(H) 2.00 (*s*, Me), 2.06 (*d*, *J* = 7.2 Hz, Me), and 6.27 (*dd*, *J* = 6.8 Hz, 1 H), and δ(H) 2.00 (overlapped, Me), 1.99 (overlapped, Me), and 6.13 (*dd*, *J* = 6.8 Hz, 1 H)) were also observed. The ^{13}C-NMR and DEPT spectra revealed signals for four esters carbonyl groups (δ(C) 171.0, 166.1, 165.5, and 165.4), an aromatic ring (δ(C)128.16, 98.97, 150.33, 129.27, 144.10, and 118.30), six olefinic C-atoms (δ(C) 117.27, 150.33, 142.32, 127.45, 139.09, and 126.38), an OCH_2O group (δ(C) 101.8), an OCH_2 group (δ(C) 80.4), two OCH groups (δ(C) 72.5 and 69.9), two oxygenated tertiary C-atoms (δ(C) 98.9 and 79.2), two MeO groups (δ(C) 53.6 and 51.8) and six Me groups (δ(C) 28.2, 9.2, 20.8, 16.1, 20.4, and 15.8). The HMBC (*Fig. 1*) experiment of **1** revealed the correlations H–C(9)/C(10), C(11), and C(15), Me(18)/C(7), C(8), and C(9), Me(17)/C(6), C(7), and C(8), and CH_2(20)/C(5), indicating the partial structure of the ethylidene-cyclooctane moiety. The correlation CH_2(20)/C(1) revealed the connection of C(1) and C(16). Furthermore, the MeO at δ(H) 3.94 was correlated with C(2) (δ(C) 171.0), and the MeO at δ(H) 3.61 with C(3) (δ(C) 165.5). Detailed comparison of the NMR data of **1** with those of taiwankadsurin B revealed that the difference between them concerned the ester moieties at C(6) and C(9). Two intense peaks at *m*/*z* 528 ($[M - C_4H_7COOH]^+$) and 428 ($[M - C_4H_7COOH - C_4H_7COOH]^+$) were assigned to two fragments produced by the 1,2-elimination of one and two angelic acids *via* a *McLafferty* ester rearrangement [10]. The HMBC cross-peaks H–C(6) (δ(H) 6.30)/C(1′) (δ(C) 166.1) and H–C(9) (δ(H) 6.66)/C(1″) (δ(C) 165.4) indicated that the two angeloyloxy groups were located at C(6) and C(9). The NOESY cross-peaks H–C(4)/H–C(9), H–C(9)/H–C(8), and H–C(8)/Me(18), indicated that H–C(9), H–C(8), and Me(18) were β-oriented, while H–C(6) was α-oriented (*Fig. 1*).

Heteroclitin O (**2**), obtained as pale yellow needles, showed a HR-EI-MS molecular ion at *m*/*z* 616.1945, corresponding to a molecular formula $C_{34}H_{32}O_{11}$. The CD spectra and ^{1}H- and ^{13}C-NMR data (*Tables 2* and *3*) revealed that **2** was a dibenzocyclooctene lignan with a spirobenzofuranoid skeleton. The HMBC and NOESY data (*Fig. 2*) and comparison of the NMR data with those of kadsulignan D [11] and renchangianin D [12] established the structure of heteroclitin O as **2**. It is the first example of a lignan with an oxirane ring in a spirobenzofuranoid dibenzocyclooctene structure within the genus *Kadsura*.

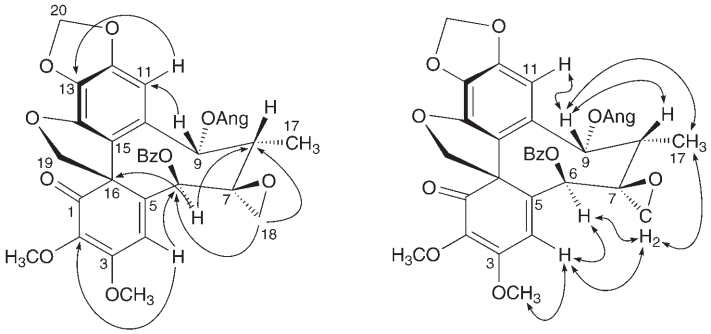


Fig. 2. *Key HMBC* (→) *and key NOESY* (↔) *correlations of* **2**[1])

Table 2. *^{1}H-NMR Data* (400 MHz, $CDCl_3$) *of Heteroclitins O–Q* (**2**–**4**). Ang = angeloyl, Bz = benzoyl. For atom numbering[1]), see *Fig. 2*.

	2	**3**	**4**
H–C(4)	6.38 (*s*)	6.68 (*s*)	6.70 (*s*)
H–C(6)	5.74 (*s*)	5.86 (*s*)	5.85 (*s*)
OH–C(7)	–	2.34	2.11
H–C(8)	2.64 (*q*, *J* = 7.2)	2.37–2.39 (*m*)	2.32–2.35 (*m*)
H–C(9)	5.73 (*s*)	5.68 (*s*)	5.68 (*s*)
H–C(11)	6.60 (*s*)	6.60 (*s*)	6.56 (*s*)
Me(17)	1.09 (*d*, *J* = 7.2)	1.37 (*d*, *J* = 7.2)	1.33 (*d*, *J* = 7.2)
CH_2(18) or Me(18)	2.83, 2.81 (*d*, each *J* = 4)	1.43 (*s*)	1.41 (*s*)
CH_2(19)	4.58, 4.20 (2 *d*, each *J* = 8.8)	–	–
CH_2(20)	6.03, 5.97 (2 br. *s*)	5.77, 5.61 (2 br. *s*)	5.78, 5.62 (2 br. *s*)
MeO–C(2)	3.70 (*s*)	3.85 (*s*)	3.93 (*s*)
MeO–C(3)	4.05 (*s*)	3.96 (*s*)	3.96 (*s*)
MeO–C(14)	–	3.38 (*s*)	3.39 (*s*)
Bz:			
H–C(3′), H–C(7′)	7.54 (*d*, *J* = 7.2)	7.49 (*d*, *J* = 7.2)	7.49 (*d*, *J* = 7.2)
H–C(4′), H–C(6′)	7.35 (*t*, *J* = 8)	7.33 (*t*, *J* = 8)	7.33 (*t*, *J* = 8)
H–C(5′)	7.55 (*t*, *J* = 7.2)	7.51 (*t*, *J* = 7.2)	7.52 (*t*, *J* = 7.2)
Ang:			
H–C(3″)	5.89 (*dd*, *J* = 7.2, 1.2)	5.96 (*dd*, *J* = 7.2, 1.6)	–
Me(4″)	1.81 (*d*, *J* = 7.2)	1.89 (*d*, *J* = 7.2)	–
Me(5″)	1.73 (*s*)	1.32 (*s*)	–
Ac:			
Me(1″)			1.56 (*s*)

Table 3. *^{13}C-NMR, Data* (100 MHz, $CDCl_3$) *of Heteroclitins O–Q* (**2**–**4**). Ang = angeloyl, Bz = benzoyl. For atom numbering[1]), see *Fig. 2*.

	2	**3**	**4**		**2**	**3**	**4**
C(1)	194.44	147.26	147.05	C(20)	102.07	100.97	101.00
C(2)	132.94	135.07	134.74	*Me*O–C(2)	59.11	60.33	60.77
C(3)	154.58	150.67	150.53	*Me*O–C(3)	58.89	55.93	55.89
C(4)	124.11	107.37	107.20	*Me*O–C(14)	–	59.05	59.09
C(5)	141.46	129.96	130.11	Bz:			
C(6)	79.31	85.49	85.35	C(1′)	164.79	165.25	164.75
C(7)	61.56	74.02	74.00	C(2′)	128.20	129.34	129.29
C(8)	41.16	43.32	43.13	C(3′,7′)	129.80	129.44	129.42
C(9)	78.10	83.75	83.57	C(4′,6′)	128.42	127.87	127.87
C(10)	128.55	133.75	132.93	C(5′)	133.78	132.90	133.40
C(11)	101.22	102.07	102.21	Ang:			
C(12)	150.27	149.14	149.08	C(1″)	167.01	164.77	–
C(13)	130.53	135.86	135.90	C(2″)	138.29	125.68	–
C(14)	143.94	140.38	140.43	H–C(3″)	126.67	141.53	–
C(15)	119.57	118.68	118.71	Me(4″)	20.45	19.90	–
C(16)	63.76	115.58	115.61	Me(5″)	15.75	15.79	–
C(17)	15.23	17.39	17.22	Ac:			
C(18)	47.94	28.90	28.91	C(1′)	–	–	168.79
C(19)	78.88	–	–	C(2′)	–	–	20.12

The characteristic two *d* at δ(H) 4.58 and 4.20 in the ^{1}H-NMR spectra and a CH_2 group at δ(C) 78.9 in the ^{13}C-NMR spectrum, together with the CD spectra established that **2** was a dibenzocyclooctene lignan with a spirobenzofuranoid skeleton. The ^{1}H-NMR spectrum revealed the presence of a Me group at a secondary C-atom (δ(H) 1.09 (*d*)), as well as of two aromatic protons (δ(H) 6.38 and 6.60 (2 *s*)), an OCH_2O moiety (δ(H) 6.03 and 5.97 (2 br. *s*)), and two MeO groups (δ(H) 3.70 and 4.05 (2 *s*)), located at the benzo moieties. Moreover, the signals of a benzoate group (δ(H) 7.54 (*d*, *J* = 7.2 Hz, 2 H), 7.35 (*t*, *J* = 8 Hz, 2 H), and 7.55 (*t*, *J* = 7.2 Hz, 1 H)) and of an angelate group (δ(H) 1.73 (*s*, Me), 1.81 (*dd*, *J* = 7.2 Hz, Me), and 5.89 (*q*, *J* = 7.2 Hz, 1 H)) were observed in the NMR spectra. In the MS, the two intense peaks at *m*/*z* 516 ([$M - C_4H_7COOH$]$^+$) and 394 ([$M - C_4H_7COOH - C_5H_6COOH$]$^+$) were assigned to fragments produced by the 1,2-elimination of benzoic and angelic acid *via McLafferty* ester rearrangement [10]. The HMBC plots of **2** (*Fig. 2*) displayed the correlations H–C(6) (δ(H) 5.74)/C(1′) (δ(C) 164.8) of the benzoyloxy group, and H–C(9) (δ(H) 5.73)/C(1″) (δ(C) 167.0) of the angeloyloxy group, suggesting that these two residues were located at C(6) and C(9), respectively[1]). According to the NOESY plots of **2**, the correlations H–C(4)/H_α–C(6) and H–C(11)/H_β–C(9) indicated that the benzoyloxy group was β-positioned at C(6) and the angeloyloxy group α-positioned at C(9). By comparing the NMR spectra of **2** to the known kadsulignan D [11], it was noticed that the Me (Me(18)) resonance of kadsulignan D was replaced by a CH_2 signal at δ(H) 2.83 and 2.81 (*AB*, *J* = 4.0 Hz) in **2**. Meanwhile, the ^{13}C-NMR signal of C(18) of **2** was observed at δ(C) 47.94, as assigned by the HMQC experiment. These data were in accordance with those of the corresponding oxirane system of renchangianin D [12]. The HMBC cross-peaks CH_2(18)/C(7), C(8), and C(6) confirmed that the oxirane CH_2 group was connected to C(7). The NOESY correlations (*Fig. 2*) CH_2(18)/H–C(4), H–C(6), and Me(17) indicated that CH_2(18) was α-oriented with respect to the fused cyclooctene moiety, and the cross-peaks H_α–C(4) /H–C(6), H_β–C(9)/H–C(11), and H_β–C(9)/Me(17) further revealed a twist-boat-chair conformation.

Heteroclitin P (**3**) had a molecular formula $C_{34}H_{46}O_{11}$, as established by the molecular-ion peak at *m*/*z* 620.2168. According to the spectral data (*Tables 2* and *3*), the structure of **3** was similar to that of schisantherin G [13], except for a benzoyloxy group instead of an acetyloxy group at C(9) in schisantherin G.

The NMR spectra of **3** indicated a C_{18} lignan skeleton. The ^{1}H-NMR spectra showed signals of two aromatic protons (δ(H)6.68 (H–C(4)) and 6.60 (H–C(1)[1])) and three MeO groups (δ(H) 3.96, 3.85, and 3.38 (3 *s*)) located at the benzo moieties. The *d* at δ(H) 1.37 (*d*, *J* = 7.2 Hz) and the *s* at δ(H) 1.43 were assigned to Me(17) and Me(18), respectively. The signals of the angeloyl group (δ(H) 1.32 (br. *s*, Me), 1.89 (*d*, *J* = 7.2 Hz, Me), and 5.96 (*dd*, *J* = 7.2, 1.6 Hz, 1 H) and of the benzoyl group (δ(H) 7.49 (*d*, *J* = 7.2 Hz, 2 H), 7.33 (*t*, *J* = 8 Hz, 2 H), and 7.51 (*t*, *J* = 7.2 Hz, 1 H)) were also observed in the ^{1}H-NMR spectra. This was confirmed by two intense peaks at *m*/*z* 498 ([$M - CH_3C_4H_8COOH$]$^+$) and 398 ([$M - CH_3C_4H_8COOH - C_4H_7COOH$]$^+$) in the MS of **3**. The angeloyloxy and benzoyloxy groups were positioned at C(6) and C(9), respectively, based on the HMBC cross-peaks H–C(6) (δ(H) 5.86)/C(1″) (δ(C) 164.27) of the angeloyloxy group, and H–C(9) (δ(H) 5.68)/C(1′) (δ(C) 165.25) of the benzoyloxy group. The NOESY cross-peaks H–C(4)/H_α–C(6), and H–C(11)/H_β–C(9) indicated the β-position of the angeloyloxy group at C(6) and the α-position of the benzoyloxy group at C(9).

Heteroclitin Q (**4**) had the molecular formula $C_{31}H_{32}O_{11}$, as deduced from the molecular-ion peak at *m*/*z* 580.2094 in the HR-EI-MS. The UV, CD, and NMR spectra were very close to those of **3**. The structure of heteroclitin Q was established as **4**.

The ^{1}H- and ^{13}C-NMR spectra of **4** (*Tables 2* and *3*) showed signals for an acetyl group (δ(H) 1.56 (*s*)) and a benzoyl group (δ(H) 7.49 (*d*, *J* = 7.2 Hz, 2 H), 7.33 (*t*, *J* = 8 Hz, 2 H), and 7.52 (*t*, *J* = 7.2 Hz, 1 H)). Based on the HMBC cross-peaks C(1′) (δ(C) 164.75)/H–C(6) (δ(H) 5.85), and C(1″) (δ(C) 168.79)/H–C(9) (δ(H) 5.68), the benzoyloxy and the acetyloxy groups were positioned at C(6) and C(9), respectively[1]).

The relative and absolute configurations of **3** and **4** were determined based on their NOESY data and characteristic circular-dichroism (CD) spectra, respectively. Both of them adopted a twist-boat-chair conformation as established by the NOESY correlations Me(18)/Me(17), H_β–C(9)/Me(17), and Me(18)/H_α–C(6). The CD spectra of **3** and **4** showed a positive *Cotton* effect at 220 and 219 nm, respectively, and a negative *Cotton* effect at 254 and 257 nm, respectively, which suggested that they all possessed the same configuration (*S*) of the stereogenic biphenyl axis as gomisin B [14][15].

The authors thank the *National Natural Science Foundation of People's Republic of China* for financial support (No. 30530860)

Experimental Part

General. Column chromatography (CC): silica gel *60H* (400–500 mesh) from *Qingdao Haiyang Chemical Group Co.*, Shandong Province, People's Republic of China. TLC: silica gel GF_{254} sheets (0.20–0.25 mm) from *Qingdao Haiyang Chemical Group Co.* Melting points: *Fisher–Johns* apparatus; uncorrected. CD Spectra: *Jasco J-715* spectropolarimeter; λ ($\Delta\varepsilon$) in nm. Optical rotations: *Perkin-Elmer* digital polarimeter. UV Spectra: *Perkin-Elmer Lambda-35* UV/VIS spectrometer; λ_{max} (log ε) in nm. IR Spectra: *Shimadzu FTIR-8400* infrared spectrometer; KBr pellets; $\tilde{\nu}_{max}$ in cm^{-1}. NMR Spectra: *Bruker AV-400* spectrometer; δ in ppm rel. to $SiMe_4$ as an internal standard, *J* in Hz. EI-MS: *Micromass ZabSpec* high-resolution mass spectrometer; in *m*/*z* (rel. %).

Plant Material. Kadsura heteroclita (ROXB.) CRAIB. (Schisandraceae) was collected at Sangzhi, Hunan Province, People's Republic of China, in November 2004, and identified by Prof. *Si-bao Chen*, Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College. A voucher specimen (2004KH09) has been deposited in the herbarium of this institute.

Extraction and Isolation. The dried stems of *Kadsura heteroclita* (ROXB.) CRAIB. (15 kg) were ground and extracted in four portions with 95% EtOH (30 l each) under reflux (3 × 2 h each). The combined EtOH extract was concentrated, and the concentrated extract (800 ml) was mixed with SiO_2 (1 kg). After evaporation of the solvent, the residue was extracted with petroleum ether in a *Soxhlet* apparatus for 5 h. The petroleum ether part (120 g) was subjected to CC (silica gel, hexane/acetone 95:5, 85:15, and 70:30): *Fractions A* (19 g), *B* (15 g), and *C* (9 g). *Fr. A* was subjected to repeated CC (petroleum ether/acetone 92:8): heteroclitin P (**3**; 31 mg) and heteroclitin Q (**4**; 7 mg). *Fr. B* was subjected to repeated CC (hexane containing increasing amounts of acetone). The fraction eluted with hexane/acetone 85:15 was purified by CC (*Sephadex LH-20*, MeOH): heteroclitin N (**1**; 23 mg) and heteroclitin O (**2**; 17 mg).

Heteroclitin N (= rel-*(2a*R,*3*R,*5*R,*6*R,*7*S,*12*R,*13*E*)-6,7-Dihydro-3-hydroxy-13-(2-methoxy-2-oxoethylene)-5,6-dimethyl-7,12-bis[[(2*Z*)-2-methyl-1-oxobut-2-en-1-yl]oxy}-5*H-*2a,5-ethano-2*H,*3*H-*[1,3]dioxolo[*i*]furo[2,3,4-kl*]*[3]benzoxocin-3-carboxylic Acid Methyl Ester*; **1**): Colorless needles. M.p. 195–196°. $[\alpha]_D^{20} = +29$ (*c* = 0.51, MeOH). UV (MeOH): 220 (4.80), 275 (3.02). IR (KBr): 3457, 2938, 1735, 1721, 1632, 1458. ^{1}H- and ^{13}C-NMR ($CDCl_3$): *Table 1*. EI-MS: 628 (5, M^+), 568 (4), 528 (11), 424 (7), 341 (19), 324 (16), 281 (23), 83 (100). HR-EI-MS: 628.2299 (M^+, $C_{36}H_{36}O_{10}^+$; calc. 628.2308).

Heteroclitin O (=*(2*Z*)-2-Methylbut-2-enoic Acid (2′*R,*5*R,*7*R,*8*S,*14a*S*)-5-(Benzoyloxy)-5,6,7,8-tetrahydro-2,3-dimethoxy-7-methyl-1-oxospiro[1*H,*14*H-benzo[1,8]cycloocta[1,2,3-cd*]*[1,3]dioxolo[4,5-g]benzofuran-6,2′-oxiran]-8-yl Ester*; **2**): Yellow needles. M.p. 190–191°. $[\alpha]_D^{20} = -134$ (*c* = 0.68, MeOH). CD (MeOH): 219 (+23.61), 320 (−58.56), 373 (+52.27). UV (MeOH): 221 (3.77), 278 (2.89), 328 (3.13). IR (KBr): 3433, 2930, 1717, 1580, 1490. ^{1}H- and ^{13}C-NMR ($CDCl_3$): *Tables 2* and *3*. EI-MS: 616 (20, M^+), 516 (10), 476 (6), 447 (5), 394 (17), 353 (11), 329 (9), 313 (12), 105 (100), 83 (68). HR-EI-MS: 616.1930 (M^+, $C_{34}H_{32}O_{11}^+$; calc. 616.1945).

Heteroclitin P (=*(2*Z*)-2-Methylbut-2-enoic Acid (5*S,*6*S,*7*S,*8*R,*13a*S*)-8-(Benzoyloxy)-5,6,7,8-tetrahydro-1,6-dihydroxy-2,3,13-trimethoxy-6,7-dimethylbenzo[3,4]cycloocta[1,2-f*]*[1,3]benzodioxol-5-yl Ester*; **3**): White needles. M.p. 195–197°. $[\alpha]_D^{20} = -110$ (*c* = 0.095, $CHCl_3$). CD (MeOH): 220 (+14.70), 254

(– 30.32). UV (MeOH): 220 (3.87), 253 (2.98), 278 (3.01). IR (KBr): 3565, 2945, 1728, 1597, 1450. ^{1}H- and ^{13}C-NMR ($CDCl_3$): *Tables 2* and *3*. EI-MS: 620 (10, M^+), 498 (23), 398 (9), 321 (11), 83 (100). HR-EI-MS: 620.2168 (M^+, $C_{34}H_{36}O_{11}^+$; calc.620.2258).

Heteroclitin Q (=*(5*S*,6*S*,7*S*,8*R*,13a*S*)-5,6,7,8-Tetrahydro-2,3,13-trimethoxy-6,7-dimethylbenzo[3,4]-cycloocta[1,2-f][1,3]benzodioxol-1,5,6,8-tetrol 8-Acetate 5-Benzoate*; **4**): Yellow gum. $[\alpha]_D^{20} = +80.4$ ($c =$ 1.48, $CHCl_3$). CD (MeOH): 222 (+20.19), 257 (– 39.43). UV (MeOH): 221 (4.45), 257 (3.57), 280 (3.80). ^{1}H- and ^{13}C-NMR ($CDCl_3$): *Tables 2* and *3*. EI-MS: 580 (9, M^+), 480 (14), 420 (17), 105 (100), 83 (26). HR-EI-MS: 580.2094 (M^+, $C_{31}H_{32}O_{11}^+$; calc. 580.1945).

REFERENCES

[1] G.-Q. Han, P. Dai, R. Xue, B. H. Arison, D. C. Lankin, S.-B. Hwang, *J. Chin. Pharm. Sci*. **1992**, *1*, 20.
[2] 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.
[3] D.-F. Chen, S.-X. Zhang, H.-K. Wang, S.-Y. Zhang, Q.-Z. Sun, L. M. Cosentino, K.-H. Lee, *J. Nat. Prod.* **1999**, *62*, 94.
[4] R.-T. Li, Q.-B. Han, Y.-T. Zheng, R.-R. Wang, L.-M. Yang, Y. Lu, S.-Q. Sang, Q.-T. Zheng, Q.-S. Zhao, H.-D. Sun, *Chem. Commun.* **2005**, *23*, 2936.
[5] J.-X. Pu, W.-L. Xiao, Y. Lu, R.-T. Li, H.-M. Li, L. Zhang, S.-X. Huang, X. Li, Q.-S. Zhao, Q.-T. Zheng, H.-D. Sun, *Org. Lett*. **2005**, *7*, 5079.
[6] D.-F. Chen, G.-J. Xu, X.-W. Yang, M. Hattori, Y. Tezuka, T. Kikuchi, T. Namba, *Phytochemistry* **1992**, *31*, 629.
[7] X.-W. Yang, M. Hattori, T. Namba, D.-F. Chen, G.-J. Xu, *Chem. Pharm. Bull*. **1992**, *40*, 406.
[8] L.-J. Xu, P. Yong, S.-B. Chen, S.-L. Chen, P.-G. Xiao, *Heterocycles* **2007**, *71*, 941.
[9] Y.-C. Shen, Y.-C. Lin, Y.-B. Cheng, Y.-H. Kuo, Ch.-C. Liaw, *Org. Lett*. **2005**, *7*, 5297.
[10] M.-D. Wu, R.-L. Huang, L.-M. Y. Kuo, C.-C. Hung, C.-W. Ong, Y.-H. Kuo, *Chem. Pharm. Bull*. **2003**, *51*, 1233.
[11] J.-S. Liu, M.-F. Huang, H.-X. Zhou, *Can. J. Chem.* **1991**, *69*, 1403.
[12] M. Chen, Z. Liao, D. Chen, *Helv. Chim. Acta* **2004**, *87*, 1368.
[13] J.-S. Liu, Y.-T. Ma, *Huaxue Xuebao* **1988**, *46*, 465.
[14] Y.-H. Kuo, M.-D. Wu, R.-L. Huang, S.-Y. Li, H.-C. Huang, K.-H. Lee, *J. Nat. Prod.* **2001**, *64*, 487.
[15] Y. Ikeya, H. Taguchi, H. Yosioka, *Chem. Pharm. Bull.* **1979**, *27*, 1383.

Received June 26, 2007