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DIBENZOCYCLO-OCTADIENE LIGNANS FROM *KADSURA HETEROCLITA*

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Key Word Index—*Kadsura heteroclita*; Schizandraceae; stems; heteroclitin; dibenzocyclo-octadiene lignan.

Abstract—From the stems of *Kadsura heteroclita*, new dibenzocyclo-octadiene lignans, named heteroclitins A–E, were isolated together with the known compounds, kadsurin and interiorin. Their structures were determined by spectroscopic means.

INTRODUCTION

The stems of *Kadsura heteroclita* have been used in traditional Chinese medicine. The drug is said to promote vital energy and blood circulation, to expel wind-evil and to remove wetness-evil in terms of the traditional medicine, and has been used for the treatment of gastric and duodenal ulcers, acute and chronic gastroenteritis, dysmenorrhea, postpartum abdominal pain and trauma. As regards the chemical constituents of this plant, a few studies have been conducted and the isolation of some triterpenes has been reported [1–3]. We describe the isolation of five new lignans from stems of *K. heteroclita* together with the two known lignans, kadsurin and interiorin.

RESULTS AND DISCUSSION

An ethanol extract of the stems of *K. heteroclita* was fractionated into hexane- and chloroform-soluble fractions. Repeated column chromatography of these fractions followed by preparative TLC led to the isolation of seven compounds. The structures of these compounds were determined by spectroscopic means.

Compound **1**, $C_{25}H_{30}O_8$, was identified as kadsurin, which has been isolated previously from *K. japonica* [4, 5], by comparisons of the ^1H and ^{13}C NMR, CD spectra and optical rotation with those reported [4–7].

Compound **2** was assigned the molecular formula $C_{28}H_{36}O_8$ by HR mass spectrometry. The UV spectrum showed λ_{max} at 218, 254 and 278 nm, characteristic of a biphenyl chromophore, in which rotation of the phenyl rings is restricted by the condensed acyclic ring [8], and an intense negative CD band at 255 nm ($[\Theta]-45\,000$) was indicative of an *S*-biphenyl configuration [8]. The ^1H NMR spectrum showed the presence of four methoxy, one methylenedioxy and two *sec*-methyl groups and two isolated aromatic protons, as well as two methines (δ1.95–2.15, *m*), one benzylic methylene (δ2.64, *d*, *J* = 4.2 Hz) and one benzylic methine substituted by oxygen (δ 5.66, *br s*), whose protons appeared at positions quite similar to those of **1**. In addition, the presence of a 2-methylbutyryl group was also shown by ^1H and ^{13}C NMR (Table 1), instead of the acetyl group in **1**. In double-resonance experiments, irradiation at δ*ca* 2.0 (H-7, 8) changed the three doublet signals at δ 0.93 (H_3-18), 1.05 (H_3-17) and 2.64 (H_2-6) to three singlet signals, and irradiation at δ 5.66 (H-9) increased the signal intensity at δ *ca* 2.0, suggesting that **2** possesses the same structure as in **1**, except for the acyl group attached to OH-9. On treatment with $LiAlH_4$, **2** gave a deacylated compound, whose R_f on TLC and R_t on HPLC were identical to those of deacetylkadsurin (**1a**) obtained from **1** [5]. These findings led us to conclude that the structure is **2**; the compound is a new natural product named heteroclitin A.

Compound **3** was assigned the molecular formula $C_{28}H_{34}O_8$ by HR mass spectrometry. On treatment with $LiAlH_4$, **3** gave **1a**. The ^1H and ^{13}C NMR spectra (Table 1) of **3** were quite similar to those of **1** except for the characteristic signals due to an angeloyl group, instead of the acetyl group in **1**. The CD spectrum showed an intense negative band at 264 nm ($[\Theta]-21\,100$), indicating an *S*-biphenyl configuration as in **1** and **2** [8]. The structure is **3** which was supported by double-resonance experiments. The compound was named heteroclitin B.

Compound **4** was assigned the molecular formula $C_{28}H_{34}O_8$ by HR mass spectrometry. The ^1H and ^{13}C NMR spectral analysis revealed that **4** is a dibenzocyclo-octadiene lignan similar to **1–3**, but a tigloyl group is attached to OH-9. On treatment with $LiAlH_4$, **4** afforded **1a**. The CD spectrum was indicative of an *S*-biphenyl configuration in **4** [8]. Thus, the structure is **4** and the compound was named heteroclitin C.

Compound **5**, $C_{27}H_{30}O_8$, was identified as interiorin, previously isolated from *K. interior*, by comparing its spectral data with those reported [9].

Compound **6** was assigned the molecular formula $C_{27}H_{30}O_8$ by HR mass spectrometry. Its CD spectral features were quite different from those of **1–5**, and intense bands were observed at 242 (+3400), 320

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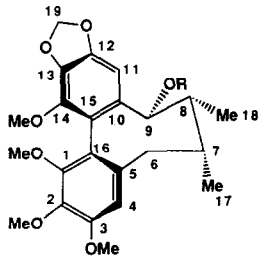

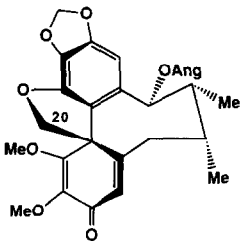

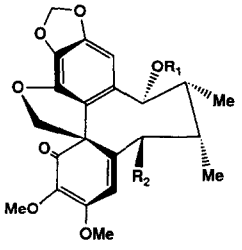

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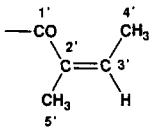
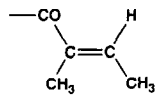
3 R= 

4 R= 

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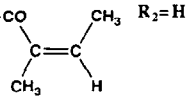
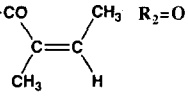
6 R_1=  R_2=H

7 R_1=  R_2=OH

($-11\,800$) and 367 ($+5100$) nm. The presence of a characteristic AB quartet signal centred at $\delta 4.39$ ($J = 8.7$ Hz) in the ^{1}H NMR spectrum and of a quaternary carbon at $\delta 64.6$ (*s*) in the ^{13}C NMR spectrum suggested that **6** is a dibenzocyclo-octadiene lignan having a spirobenzofuranoid skeleton [10]. The ^{1}H NMR spectral patterns were quite similar to that of oxokadsurane derivatives [10]. However, the acyl group was replaced by an angeloyl group in **6**. In the ^{1}H-^{1}H COSY experiment, shift-correlations were observed among the following signals: H-7 ($\delta 1.79$) vs H_3-17 ($\delta 1.00$), Ha-6 ($\delta 2.22$) and Hb-6 ($\delta 2.56$); H-8 ($\delta 1.96$) vs H_3-18 ($\delta 0.86$) and H-9 ($\delta 5.69$); Hb-

Table 1. ^{13}C NMR spectral data for compounds **1**–**7** (in $CDCl_3$)

C	1	2	3	4	5	6	7
1	150.8 *s*	151.0 *s*	151.0 *s*	151.1 *s*	168.3 *s*	195.0 *s*	195.0 *s*
2	139.6 *s*	139.6 *s*	139.7 *s*	140.0 *s*	153.9 *s*	150.3 *s*	150.2 *s*
3	151.4 *s*	151.6 *s*	151.5 *s*	151.5 *s*	184.0 *s*	156.2 *s*	155.1 *s*
4	110.4 *d*	110.3 *d*	110.4 *d*	110.3 *d*	131.6 *d*	120.8 *d*	124.0 *d*
5	133.1 *s*	133.1 *s*	132.8 *s*	132.8 *s*	150.6 *s*	146.8 *s*	145.9 *s*
6	38.7 *t*	38.9 *t*	38.5 *t*	38.7 *t*	37.7 *t*	40.3 *t*	81.7 *d*
7	34.7 *d*	34.7 *d*	34.4 *d*	34.5 *d*	32.0 *d*	31.6 *d*	38.4 *d*
8	41.8 *d*	41.9 *d*	41.6 *d*	41.8 *d*	42.9 *d*	42.6 *d*	42.4 *d*
9	82.1 *d*	82.2 *d*	82.2 *d*	82.0 *d*	79.4 *d*	78.3 *d*	78.1 *d*
10	134.7 *s*	135.1 *s*	134.9 *s*	135.0 *s*	135.4 *s*	132.5 *s*	133.1 *s*
11	102.2 *d*	102.6 *d*	102.6 *d*	102.6 *d*	100.9 *d*	101.2 *d*	100.9 *d*
12	148.6 *s*	148.6 *s*	148.3 *s*	148.5 *s*	144.6 *s*	144.2 *s*	144.5 *s*
13	135.9 *s*	135.9 *s*	135.9 *s*	136.0 *s*	130.2 *s*	130.1 *s*	130.2 *s*
14	141.2 *s*	141.2 *s*	141.1 *s*	141.3 *s*	130.2 *s*	129.1 *s*	128.5 *s*
15	120.5 *s*	120.9 *s*	120.5 *s*	120.5 *s*	120.9 *s*	122.2 *s*	121.6 *s*
16	123.3 *s*	123.1 *s*	123.7 *s*	123.1 *s*	58.0 *s*	64.6 *s*	63.7 *s*
17	19.4 *q*	19.4 *q*	19.3 *q*	19.4 *q*	21.6 *q*	21.6 *q*	20.4 *q*
18	14.6 *q*	15.1 *q*	14.5 *q*	14.7 *q*	10.0 *q*	9.7 *q*	10.0 *q*
19	101.0 *t*	101.1 *t*	100.9 *t*	101.0 *t*	102.1 *t*	102.0 *t*	101.9 *t*
20	—	—	—	—	83.2 *t*	78.1 *t*	79.6 *t*
MeO	59.5 *q*	59.5 *q*	59.3 *q*	59.5 *q*	61.2 *q*	59.1 *q*	58.9 *q*
MeO	60.5 *q*	60.5 *q*	60.1 *q*	60.5 *q*	60.0 *q*	58.4 *q*	58.6 *q*
MeO	55.9 *q*	56.0 *q*	55.8 *q*	56.0 *q*	—	—	—
MeO	59.5 *q*	59.3 *q*	59.5 *q*	59.5 *q*	—	—	—
1′	169.8 *s*	175.9 *s*	166.4 *s*	167.0 *s*	165.7 *s*	168.3 *s*	168.3 *s*
2′	20.5 *q*	40.0 *d*	126.9 *s*	127.5 *s*	127.6 *s*	127.9 *s*	127.9 *s*
3′	—	26.4 *t*	140.2 *d*	135.9 *d*	138.2 *d*	135.4 *d*	135.3 *d*
4′	—	11.1 *q*	15.3 *q*	11.6 *q*	15.7 *q*	15.5 *q*	15.5 *q*
5′	—	15.1 *q*	20.2 *q*	13.9 *q*	20.8 *q*	20.4 *q*	20.4 *q*

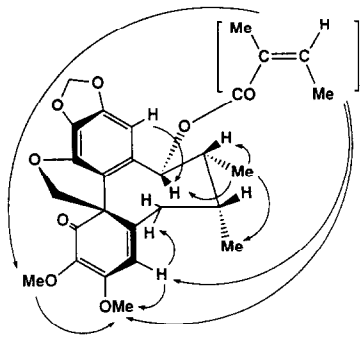


Fig. 1. NOE of compound **6**.

6 vs H-4 (δ6.09); H-3′ (δ5.74)vs H_3-4′ (δ1.66) and H_3-5′ (δ1.73); Ha-6 vs Hb-6; Ha-19 (δ5.97) vs Hb-19 (δ6.02); Ha-20 (δ4.25) vs Hb-20 (δ4.52). Furthermore, in the NOE experiment, appreciable NOE were observed between H-11 (δ6.38) and H-9, H-4 and Ha-6, or H-4 and MeO-3 (δ4.01) (Fig. 1). In addition NOE was also observed between the methyl signals (δ*ca* 1.7; H_3-4′ and H_3-5′) of the angeloyl group and the signals due to MeO-2 (δ3.68), MeO-3, H-9 and H-4. This spectroscopic evidence strongly supported its structure of **6** and it was named heteroclitin D. The ^{13}C NMR spectral data also supported this structure (Table 1), when referred to the reported data of analogous compounds [10].

Compound **7** was assigned the molecular formula $C_{27}H_{30}O_9$. Its UV and CD spectra were quite similar to those of **6**, suggesting that **7** is also a dibenzocyclooctadiene lignan having a spirobenzofuranoid skeleton. The ^{1}H NMR spectrum showed the presence of two *sec*-methyls, two methines, two benzylic methines substituted by oxygen, two methoxyls, one methylenedioxyl, one methylene substituted by oxygen (δ4.56 and 5.04, AB quartet, $J = 8.3$ Hz) and two aromatic protons. In addition, an angeloyl group was shown to be present in the molecule on the basis of the ^{1}H and ^{13}C NMR (Table 1) spectral evidence. In double-resonance experiments, on irradiation at δ1.81 (H-7), the two doublet signal at δ1.04 and 4.12 (H_3-18 and H-6, respectively) were changed to two singlet signals, and the multiplet signals at δ2.10 increased in intensity. On irradiation at δ2.10 (H-8), the doublet signals at δ1.01 and 5.68 (H_3-17 and H-9, respectively) became two singlet signals as well as an appreciable increase of signal intensity at δ1.81, indicating the presence of the partial structure Ph-CH(OAng)-CH(Me)-CH(Me)-CH(OH)-Ph′ (but with Ang = Angeloyl). The coupling constants of $J_{6,7} = 10.3$ Hz and $J_{8,9} = 5.6$ Hz revealed that H-6 and H-9 possessed α- and β-orientations, respectively. These findings led us to conclude that its structure is **7** and we named it heteroclitin E.

EXPERIMENTAL

Mp: uncorr. ^{1}H and ^{13}C NMR: 270 and 22.5 MHz, respectively. EIMS: 70 eV. Optical rotations and CD spectra were measured at 25°.

Chromatography. Wakogel C-200 was used for CC. TLC was performed on Merck Kieselgel 60 F_{254} plates with solvent system A, hexane–Me_2CO–C_6H_6 (14:5:1). Spots were observed under UV light and visualised by spraying with anisaldehyde–H_2SO_4 reagent followed by heating.

Materials. Stems of *K. heteroclita* (Roxo.) crait. were collected in Feng-Qing county, Yunnan Province of China, in August 1989. The plant was identified by Guo-Jun Xu and voucher specimens are deposited at the Herbarium of Materia Medica of China Pharmaceutical University and the Museum of Materia Medica of Toyama Medical and Pharmaceutical University.

Extraction and fractionation. Dried and pulverised stems (4 kg) were extracted × 5 with boiling 95% EtOH (700 ml) for 8 hr. The combined solns were evapd *in vacuo* to give a residue (114 g; 2.8%). The residue was suspended in 90% MeOH (1.5 l) and extracted with hexane to give a hexane-sol. fr. (36.5 g; 0.9%). The 90% MeOH phase was evapd to give a residue (82.5 g), which was suspended in H_2O (1000 ml) and extracted with $CHCl_3$ (2 l × 5) to give another fr. (48.1 g).

The hexane-sol fr. was applied to a silica gel column (3.8 cm i.d × 80 cm), which was successively eluted with hexane containing increasing amounts of $CHCl_3$. Frs eluted with hexane–$CHCl_3$ (4:1) were subjected to repeated CC and prep. TLC to yield compounds **1** (1137 mg), **2** (32 mg), **3** (78 mg) and **4** (144 mg). Similarly, frs eluted with hexane-$CHCl_3$ (2:1) gave **5** (459 mg) and **6** (499 mg).

The $CHCl_3$-sol. fr. was chromatographed on a silica gel column (3.8 cm i.d × 80 cm) with hexane–$CHCl_3$ (1:1) and $CHCl_3$. Frs eluted with $CHCl_3$ were subjected to repeated CC and prep. TLC to give **7** (27 mg).

Kadsurin (**1**). Needles from MeOH, mp 157–158°. $[\alpha]_D$ −23.7° ($CHCl_3$, *c* 1.01). CD (MeOH, *c* 2.0×10^{-4} g ml^{-1}) (nm): −39800 (261), −3700 (shoulder, 290); UV λ_{max}^{MeOH} nm (ε): 219 (27400), 254 (6700), 278 (1800). IR ν_{max}^{KBr} cm^{-1}: 1735 (ester C=O), 1620, 1595, 1460 (aromatic). EIMS *m/z*: 458 $[M]^+$; HRMS: Found, *m/z* 458.1942 $[M]^+$, Calcd for $C_{25}H_{30}O_8$: 458.1941. ^{1}H NMR (270 MHz, $CDCl_3$): δ0.92 (3H, *d*, $J = 7.1$ Hz, H_3-18), 1.07 (3H, *d*, $J = 7.1$ Hz, H_3-17), 1.57 (3H, *s*, AcO-9), 1.95–2.15 (2H, *m*, H-7, 8), 2.65 (2H, *d*, $J = 3.9$ Hz, H_2-6), 3.63 (3H, *s*, MeO), 3.80 (3H, *s*, MeO), 3.87 (3H, *s*, MeO), 3.89 (3H, *s*, MeO), 5.63 (1H, *br*, *s*, H-9), 5.95, 5.98 (each 1H, ABq, $J = 1.5$ Hz, H_2-19), 6.46 (1H, *s*, H-11), 6.57 (1H, *s*, H-4).

Reduction of compound **1** *with* $LiAlH_4$. Compound **1** (25 mg) was treated with $LiAlH_4$ (10 mg) in THF (5 ml) for 12 hr at room temp. The reaction mixt. was filtered and the filtrate neutralised with 5% HCl and extracted with EtOAc. After solvent was evapd *in vacuo*, the residue was chromatographed on a TLC plate with solvent system A to give deacetylkadsurin (**1a**; 4 mg). $[\alpha]_D$ −29.6° ($CHCl_3$; *c* 0.4); ^{1}H NMR (270 MHz, $CDCl_3$): δ0.93 (3H, *d*, $J = 7.3$ Hz, H_3-18), 1.16 (3H, *d*, $J = 7.1$ Hz, H_3-17), 1.91 (1H, *m*, H-7), 2.09 (1H, *m*, H-8), 2.64 (2H, *d*, $J = 4.6$ Hz, H_2-6), 3.66 (3H, *s*, MeO), 3.83 (3H, *s*, MeO), 3.88 (3H, *s*, MeO), 3.90 (3H, *s*, MeO 4.61 (1H, *d*, $J = 9.0$ Hz, H-9), 5.97 (2H, *s*, H_2-19), 6.33 (1H, *s*, H-11), 6.58 (1H, *s*, H-4).

Reduction of compounds **2**–**4** *with* $LiAlH_4$ Compounds **2**–**4** (2 mg each) were treated in a similar manner to that described above. The product had the same R_f value (0.75) on TLC (solvent system A) and R_t (4.7 min) on HPLC (LichroCART 250-4 ODS; solvent, 70% MeOH; flow rate, 0.5 ml min^{-1}; detection, 254 nm) with those of **1a**.

Heteroclitin A (**2**). Amorphous powder. $[\alpha]_D$ +29.2° (MeOH; *c* 0.66). CD (MeOH, *c* 2.0×10^{-4} g ml^{-1}) (nm): −45000 (255), −3000 (shoulder, 290); UV λ_{max}^{MeOH} nm (ε): 218 (30900), 254 (7600), 278 (2600). IR ν_{max}^{KBr} cm^{-1}: 1725 (ester C=O), 1615, 1590, 1455 (aromatic). EIMS *m/z* (rel. int.) 500 $[M]^+$ (100), 398 $[M - C_5H_{10}O_2]^+$ (52); HRMS *m/z* 500.2415 $[M]^+$, Calcd for $C_{28}H_{36}O_8$: 500.2410. ^{1}H NMR (270 MHz, $CDCl_3$): δ0.74 (3H, *dd*, $J = 7.3$, 7.6 Hz, H_3-4′), 0.87 (3H, *d*, $J = 7.1$ Hz, H_3-5′), 1.10–1.44 (3H, *m*, H-2′, H_2-3′), 0.93 (3H, *d*, $J = 7.1$ Hz, H_3-18), 1.05 (3H, *d*, $J = 6.8$ Hz, H_3-17), 1.95–2.15 (2H, *m*, H-7, 8), 2.64 (2H, *d*, $J = 4.2$ Hz, H_2-6), 3.68 (3H, *s*, MeO), 3.78 (3H, *s*, MeO), 3.85 (3H, *s*,

MeO), 3.89 (3H, *s*, MeO), 5.66 (1H, *br s*, H-9), 5.94, 5.97 (each 1H, ABq, $J=1.5$ Hz, H_2-19), 6.48 (1H, *s*, H-11), 6.55 (1H, *s*, H-4).

Heteroclitin B (**3**). Amorphous powder. $[\alpha]_D$ +58.3° (MeOH; *c* 3.92). CD (MeOH; *c* 3.0×10^{-4} g ml^{-1}) (nm): −21 100 (264), −3600 (shoulder, 290). UV λ_{max}^{MeOH} nm (ε): 219 (56 300), 255 (12 000), 280 (3000). IR ν_{max}^{KBr} cm^{-1}: 1715 (conj. ester C=O), 1621, 1600, 1500 (aromatic). EIMS *m/z* (rel. int.): 498 $[M]^+$ (100), 398 $[M-C_5H_8O_2]^+$ (59); HRMS: Found, *m/z* 498.221 $[M]^+$, Calcd for $C_{28}H_{34}O_8$: 498.2253. ^{1}H NMR (270 MHz, $CDCl_3$):δ0.99 (3H, *d*, $J=7.1$ Hz, H_3-18), 1.04 (3H, *d*, $J=6.8$ Hz, H_3-17), 1.27 (3H, *dq*, $J=2.9$, 1.5 Hz, H_3-5′), 1.88 (3H, *dq*, $J=7.2$, 1.5 Hz, H_3-4′), 2.0–2.15 (2H, *m*, H-7, H-8), 2.65 (2H, *d*, $J=3.9$ Hz, H_2-6), 3.48 (3H, *s*, MeO), 3.79 (3H, *s*, MeO), 3.83 (3H, *s*, MeO), 3.87 (3H, *s*, MeO), 5.69 (1H, *br s*, H-9), 5.91 (1H, *m*, H-3′), 5.94, 5.98 (each 1H, ABq, $J=1.5$ Hz, H_2-19), 6.54 (1H, *s*, H-11), 6.57 (1H, *s*, H-4).

Heteroclitin C (**4**). Amorphous powder. $[\alpha]_D$ −12.0° (MeOH; *c* 3.61). CD (MeOH, *c* 2.9×10^{-4} g ml^{-1}) (nm): −52 800 (253), −6500 (290). UV λ_{max}^{MeOH} nm (ε): 218 (39 700), 254 (8200), 278 (2400). IR γ_{max}^{KBr} cm^{-1}: 1710 (conj. ester C=O), 1620, 1600 (aromatic). EIMS *m/z* (rel. int.): 498 $[M]^+$ (100), 398 $[M-C_5H_8O_2]^+$ (55); HRMS: Found, *m/z* 498.2291 $[M]^+$, Calcd for $C_{28}H_{34}O_8$: 498.2253. ^{1}H NMR (270 MHz, $CDCl_3$): δ0.98 (3H, *d*, $J=7.1$ Hz, H_3-18), 1.08 (3H, *d*, $J=6.8$ Hz, H_3-17), 1.48 (3H, *br s*-like, H_3-5′), 1.60 (3H, *br dq*, $J=7.1$, *ca*, 1 Hz, H_3-4′), 2.0–2.15 (*m*, H-7, H-8), 2.68 (2H, *d*, $J=4.1$ Hz, H_2-6), 3.38 (3H, *s*, MeO), 3.80 (3H, *s*, MeO), 3.84 (3H, *s*, MeO), 3.91 (3H, *s*, MeO), 5.80 (1H, *br s*, H-9), 5.94, 5.97 (each 1H, ABq, $J=1.5$ Hz, H_2-19), 5.88 (1H, *qq*, $J=7.1$ Hz, *ca*, 1.0 Hz, H-3′), 6.52 (1H, *s*, H-11), 6.61 (1H, *s*, H-4).

Interiorin (**5**). Pale yellow prisms from EtOAc, mp 163–165°. $[\alpha]_D$ −38.0° ($CHCl_3$; *c* 1.0), −23.7 (MeOH, *c* 0.87). CD (MeOH, *c* 2.0×10^{-4} g ml^{-1}) (nm): +8700 (261), −21 700 (290); UV λ_{max}^{MeOH} nm (ε): 219 (42 800), 245 (16 000), 295 (4200). IR ν_{max}^{KBr} cm^{-1}: 1715 (conj. ester C=O), 1650 (conj. C=O), 1640, 1595. EIMS: *m/z* (rel. int.) 482 $[M]^+$ (100). HRMS: Found, *m/z* 482.1970 $[M]^+$, Calcd for $C_{27}H_{30}O_8$: 482.1941. ^{1}H NMR (270 MHz, $CDCl_3$): δ 0.89 (3H, *d*, $J=6.8$ Hz, H_3-18), 1.03 (3H, *d*, $J=7.3$ Hz, H_3-17), *ca* 1.7 (1H, *m*, H-7), 1.75 (3H, *dq*, $J=1.5$, 1.5 Hz, H_3-5′), 1.83 (3H, *dq*, $J=7.3$, 1.5 Hz, H_3-4′), 1.96 (1H, *dq*, $J=7.1$, 7.3 Hz, H-8), 2.28 (1H, *dd*, $J=15.6$, 12.0 Hz, Ha-6), 2.63 (1H, *dd*, $J=15.6$, 7.8 Hz, Hb-6), 3.79 (3H, *s*, MeO), 3.71 (3H, *s*, MeO), 4.44, 4.57 (each 1H, ABq, $J=8.8$ Hz, H_2-20) 5.56 (1H, *d*, $J=7.1$ Hz, H-9), 5.94 (1H, *qq*, $J=7.3$, 1.5 Hz, H-3′), 6.01, 6.05 (each 1H, ABq, $J=1.5$ Hz, H_2-19), 6.24 (1H, *d*, $J=ca$, 1 Hz, H-4), 6.38 (1H, *s*, H-11).

Heteroclitin D (**6**). Yellowish powder. $[\alpha]_D$−93.9° ($CHCl_3$; *c* 1.02), −29.4° (MeOH; *c* 0.88). CD (MeOH; *c* 2.0 $\times10^{-4}$ g ml^{-1}) (nm): +3400 (242), −11 800 (320), +5100 (367). UV λ_{max}^{MeOH} nm (ε): 221 (32 700), 276 (2200), 332 (4000). IR ν_{max}^{KBr} cm^{-1}: 1720 (conj. ester C=O), 1655 (conj. C=O), 1650. EIMS *m/z* (rel. int.): 482 $[M]^+$ (54), 382 $[M-C_5H_8O_2]^+$(100); HRMS: Found, *m/z* 482.1938 $[M]^+$, Cacld for $C_{27}H_{30}O_8$: 482.1939. ^{1}H NMR (270 MHz, $CDCl_3$): δ 0.86 (3H, *d*, $J=6.8$ Hz, H_3-8), 1.00 (3H, *d*, $J=7.3$ Hz, H_3-17), 1.66 (3H, *br d*-like, H_3-4′), 1.73 (3H, *br s*-like, H_3-5′), 1.79 (1H, *m*, H-7), 1.96 (1H, *m*, H-8), 2.22 (1H, *dd*, $J=15.7$, 12.1 Hz, Ha-6), 2.56 (1H, *dd*, $J=15.7$, 2.8 Hz, Hb-6), 3.68 (2H, *s*, MeO-2), 4.01 (3H, *s*, MeO-3), 4.25, 4.52 (each 1H, ABq, $J=8.7$ Hz, H_2-20), 5.69 (1H, *d*, $J=7.1$ Hz, H-9), 5.74 (1H, *m*, H-3′), 5.97, 6.02 (each, 1H, ABq, $J=1.5$ Hz, H_2-19), 6.09 (1H, *d*, $J=2.2$ Hz, H-4), 6.38 (1H, *s*, H-11).

Heteroclitin E (**7**). Amorphous powder. $[\alpha]_D$ − 38.0° (MeOH; *c* 0.79). CD (MeOH; *c* 2.0×10^{-4} g ml^{-1}) (nm); −5200 (220), −2400 (319), +1300 (367). UV λ_{max}^{MeOH} nm (ε): 219 (42 100), 279 (2600),329 (3400). IR ν_{max}^{KBr} cm^{-1}: 1715 (conj. ester C=O), 1655 (conj. ester C=O), 1625, 1620, 1615 (aromatic). EIMS *m/z* (rel. int.): 498 $[M]^+$ (100), 398 $[M-C_5H_8O_2]^+$ (51). HRMS: Found, *m/z* 498.1920 $[M]^+$, Calcd for $C_{27}H_{30}O_9$: 498.1950. ^{1}H NMR (270 MHz, $CDCl_3$): δ1.01 (3H, $J=8.5$ Hz, H_3-17), 1.04 (3H, $J=6.8$ Hz, H_3-18), 1.68 (3H, *br s*-like, H_3-5′), 1.70 (3H, *br d*-like, H_3-4′), 1.81 (1H, *m*, H-7), 2.10 (1H, *m*, H-8), 3.70 (3H, *s*, MeO), 4.10 (3H,*s*, MeO), 4.12 (1H, *d*, $J=10.3$ Hz, H-6), 4.56, 5.04 (each 1H, ABq, $J=8.3$ Hz, H_2-20), 5.68 (1H, *d*, $J=5.6$ Hz, H-9), 5.73 (1H, *m*, H-3′), 5.97, 6.02 (each 1H, ABq, $J=1.5$ Hz, H_2-19), 6.24 (1H, *s*, H-4), 6.38 (1H, *s*, H-11).

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