New Lignans from *Jatropha curcas* Linn.

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Four new lignans, curcasinlignan A (**1**), curcasinlignan B (**2**), curcasinlignan C (**3**), and curcasinlignan D (**4**), together with eight known compounds, (±)-*rel*-(2α,3β)-7-*O*-methylcedrusin (**5**), (±)-7*R*∗,8*S*∗-5-methoxydihydrodehydroconiferyl alcohol (**6**), dehydrodiisoeugeno1 (**7**), (*threo*)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-formyl-2-methoxy-phenoxy)-propane-1,3-diol (**8**), (±)-machilin D (**9**), (+)-pinoresinol (**10**), 5′-methoxypropacin (**11**), and hemidesmin-2 (**12**), were isolated from the aerial parts of *Jatropha curcas*. Their structures were established on the basis of extensive spectroscopic analysis.

Key words: Euphorbiaceae, *Jatropha curcas*, Lignans, Curcasinlignans A – D

Introduction

The plant of *Jatropha curcas* Linn., growing naturally in tropical and subtropical areas in many countries, including southern regions of China, belongs to the family of Euphorbiaceae, which is widely used as a traditional medicine to treat malarial fever, arthritis, gout, jaundice, wounds, ulcers *etc.* [1 – 4]. Previous chemical investigations on the constituents of this plant have revealed the presence of diterpenes, phorbol esters, cyclopeptides, and courmarino lignans [3 – 13]. In continuation of our search for metablites from aerial parts of this plant, four new lignans, curcasinlignan A (**1**), curcasinlignan B (**2**), curcasinlignan C (**3**), and curcasinlignan D (**4**), together with eight known compounds, (±)-*rel*-(2α,3β)-7-*O*-methylcedrusin (**5**) [14, 15], (±)-7*R*∗, 8*S*∗-5-methoxydihydrodehydroconiferyl alcohol (**6**) [16], dehydrodiisoeugeno1 (**7**) [17, 18], (*threo*)-1-(4-hydroxy-3-methoxyphenyl)-2-(4-formyl-2-methoxy-phenoxy)-propane-1,3-diol (**8**) [19], (±)-machilin D (**9**) [20], (+)-pinoresinol (**10**) [21], 5′-methoxypropacin (**11**) [22, 23], and hemidesmin-2 (**12**) [24], were obtained (Fig. 1). The isolation and structure elucidation of the new compounds are reported in this paper.

Results and Discussion

Compound **1** has the molecular formula $C_{20}H_{20}O_6$ as inferred from HR-ESI-MS data at m/z = 357.1335 $[M+H]^+$ (calcd. 357.1338). The ^{13}C NMR spectrum (Table 1) revealed the signals of a conjugated aldehyde carbon atom [δ_C = 193.7 (d, C-9′)], fourteen olefinic carbons including seven quaternary ones, a hydroxymethyl group [δ_C = 63.9 (t, C-9)], two oxygenated methyls [δ_C = 56.0 (q, 3-OCH_3), 56.1 (q, 3′-OCH_3)], two methines [δ_C = 89.0 (d, C-7), 53.0 (d, C-8)] indica-

Table 1. ^{13}C NMR data of compounds **1** – **4** (100 MHz, in $CDCl_3$; multiplicities in parentheses).

C	**1**	**2**	**3**	**4**
1	132.2 (s)	131.9 (s)	131.4 (s)	132.1 (s)
2	119.4 (d)	119.5 (d)	120.0 (d)	109.1 (d)
3	146.7 (s)	146.6 (s)	146.7 (s)	145.5 (s)
4	114.4 (d)	114.4 (d)	114.3 (d)	146.4 (s)
5	145.9 (s)	146.0 (s)	146.1 (s)	114.4 (d)
6	108.7 (d)	108.7 (d)	108.8 (d)	119.6 (d)
7	89.0 (d)	89.5 (s)	95.0 (s)	83.0 (d)
8	53.0 (d)	52.7 (d)	44.8 (d)	50.1 (d)
9	63.9 (t)	63.8 (t)	17.7 (q)	64.3 (t)
1′	128.1 (s)	131.4 (s)	131.0 (s)	129.5 (s)
2′	112.1 (d)	112.0 (d)	111.6 (d)	119.1 (d)
3′	144.8 (s)	145.3 (s)	144.9 (s)	146.6 (s)
4′	151.5 (s)	153.7 (s)	153.2 (s)	114.2 (d)
5′	129.0 (s)	128.6 (s)	133.6 (s)	145.0 (s)
6′	118.1 (d)	120.9 (d)	120.1 (d)	108.6 (d)
7′	153.1 (d)	190.6 (d)	190.7 (d)	81.0 (d)
8′	126.4 (d)			45.4 (d)
9′	193.7 (d)			64.6 (t)
3-OCH_3	56.0 (q)	56.0 (q)	56.0 (q)	
3′-OCH_3	56.1 (q)	56.1 (q)	56.1 (q)	55.9 (q)
4-OCH_3				55.9 (q)
9-$OCOCH_3$				170.9 (s)
9′-$OCOCH_3$				170.7 (s)
9-$OCOCH_3$				20.9 (q)
9′-$OCOCH_3$				20.7 (q)

Table 2. ^{1}H NMR data of compounds **1** – **4** (400 MHz, in $CDCl_3$; multiplicities and *J* values in Hz in parentheses).

H	1	2	3	4
2	6.89 (s)	6.91 (s)	6.90 (s)	7.00 (d, 1.7)
4	6.89 (s)	6.91 (s)	7.34 (s)	
5				6.93 (d, 8.1)
6	6.89 (s)	6.91 (s)	6.93 (s)	6.97 (dd, 1.7, 8.1)
7	5.64 (d, 7.1)	5.70 (d, 7.2)	5.24 (d, 9.2)	4.62 (d, 8.3)
8	3.68 (m)	3.73 (m)	3.55 (m)	2.39 (m)
9	3.97 (m)	4.03 (m)	1.44 (d, 6.9)	4.26 (m)
2′	7.04 (s)	7.41 (s)	7.37 (s)	6.89 (s)
4′				6.91 (s)
6′	7.14 (s)	7.44 (s)	6.90 (s)	6.90 (s)
7′	7.42 (d, 15.8)	9.85 (s)	9.84 (s)	5.10 (d, 7.2)
8′	6.60 (dd, 7.8, 15.8)			2.69 (m)
9′	9.64 (d, 7.8)			3.84 (m), 3.77 (m)
3-OCH_3	3.87 (s)	3.89 (s)	3.88 (s)	
3′-OCH_3	3.93 (s)	3.96 (s)	3.94 (s)	3.94 (s)
4-OCH_3				3.89 (s)
9-$OCOCH_3$				2.02 (s)
9′-$OCOCH_3$				1.89 (s)

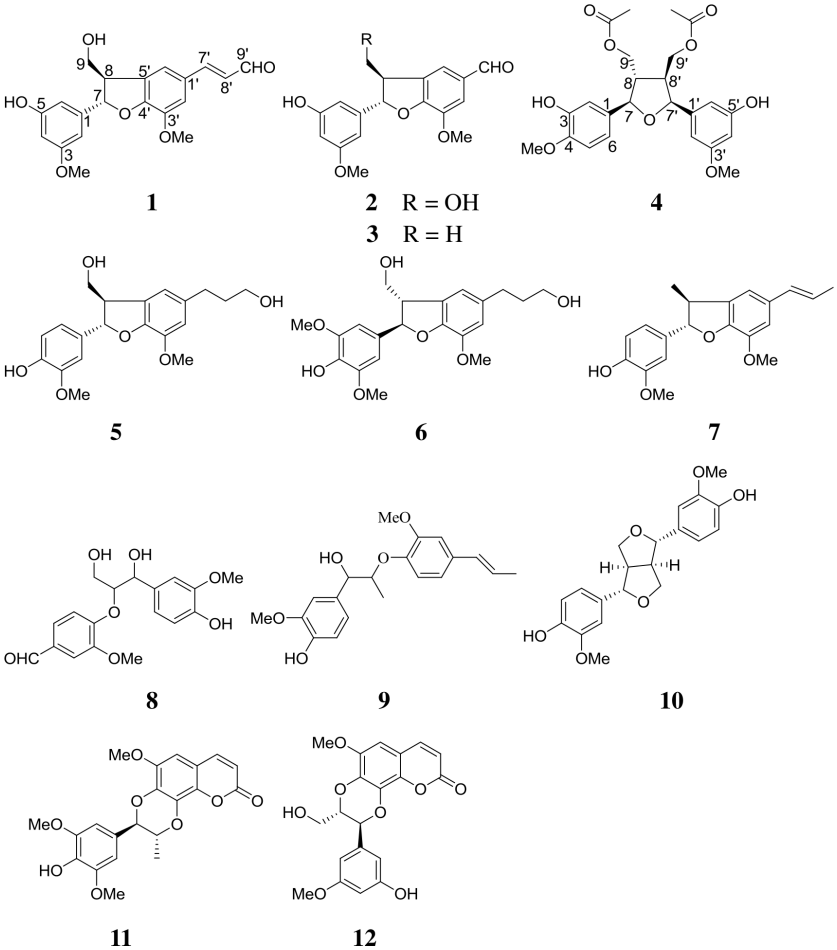

Fig. 1. Structures of compounds **1** – **12**.

tive of a dihydrobenzofuran lignan [25]. The ^{1}H NMR data (Table 2) showed two sets of isolated aromatic protons [δ_H = 6.89 (1H, s, H-2), 6.89 (1H, s, H-4), 6.89 (1H, s, H-6)] and [δ_H = 7.04 (1H, s, H-2′), 7.14 (1H,

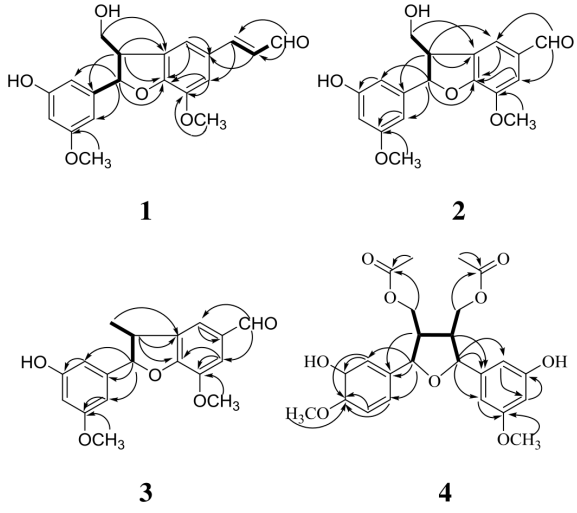

Fig. 2. Key ^{1}H-^{1}H COSY (▬) and HMBC (H → C) correlations of compounds **1** – **4**.

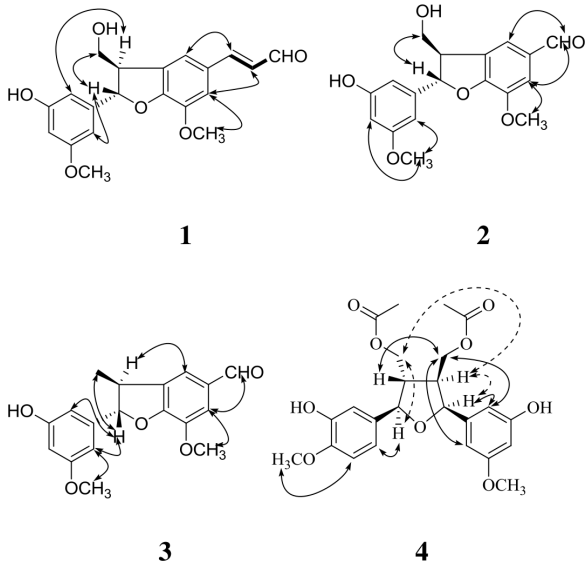

Fig. 3. Key NOESY correlations for compounds **1** – **4**.

s, H-6′)] arising from 1,3,5-trisubstituted and 1,3,4,5-tetrasubstituted aromatic ring systems, respectively, an aldehyde proton at δ_H = 9.64 (1H, d, J = 7.8 Hz, H-9′), a pair of olefinic protons [δ_H = 7.42 (1H, d, J = 15.8 Hz, H-7′), 6.60 (1H, dd, J = 7.8, 15.8 Hz, H-8′)] suggesting the presence of an (*E*)-double bond. In the COSY spectrum, two spin systems corresponding to CH(7)/CH(8)/CH_2(9) and CH(7′)/CH(8′)/CH(9′) were observed (Fig. 2). The methoxy groups were positioned at the aromatic rings as shown *via* HMBC correlations between the methoxyl protons at δ_H = 3.87 (3H, s, 3-OCH_3) and 3.93 (3H, s, 3′-OCH_3) with aromatic carbons at δ_C = 146.7 (s, C-3) and 144.8 (s, C-3′), respectively (Fig. 2). A coupling constant of 7.1 Hz between H-7 with H-8, along with the observed NOE correlation between H-9 with H-7, suggested a *trans* configuration of H-7 and H-8 (Fig. 3). Therefore, the structure of **1** was determined as shown in Fig. 1.

Compound **2** was obtained as a pale-yellow oil, and the NMR data were similar to those of **1**. The most prominent differences in ^{1}H and ^{13}C NMR spectra were the absence of the double bond signals in **2**. The NOE correlations between H-7′ with H-2′ and H-6′ (Fig. 3) suggested that C-1′ was linked to an aldehyde group.

A detailed comparison of the NMR spectroscopic data of **3** to those of **2** indicated that they were analogs. The main difference between them was that the hydroxymethyl was replaced by a methyl group in **3**, which led to upfield shifts of H-9 [δ_H = 1.44 (3H, d, J = 6.9 Hz)], H-8 [δ_H = 3.55 (1H, m)] and H-7 [δ_H = 5.24 (1H, d, J = 9.2 Hz)] in **3**. Thus, compound **2** and **3** were also dihydrobenzofuran lignans with the same *trans* configuration between C-7 and C-8, as confirmed by HSQC, ^{1}H-^{1}H COSY, HMBC, ROESY experiments (Figs. 2 and 3) and the coupling constant of H-7/H-8.

Compound **4** has the molecular formula $C_{24}H_{28}O_9$ (HR-ESI-MS). The ^{1}H and ^{13}C NMR data of **4** revealed a tetrahydrofuran lignan derivative [26]. The ^{1}H NMR data showed two sets of aromatic proton signals [δ_H = 7.00 (1H, d, J = 1.7 Hz, H-2), 6.93 (1H, d, J = 8.1 Hz, H-5), 6.97 (1H, dd, J = 1.7, 8.1 Hz, H-6)] and [δ_H = 6.89 (1H, s, H-2′), 6.91 (1H, s, H-4′), 6.90 (1H, s, H-6′)], attributing to 1,3,4-trisubstituted and 1,3,5-trisubstituted aromatic rings. From the ^{1}H-^{1}H COSY spectrum, the protons resonating at δ_H = 4.62 (1H, d, J = 8.3 Hz, H-7), 2.39 (1H, m, H-8), 4.26 (2H, m, H-9), 5.10 (1H, d, J = 7.2 Hz, H-7′), 2.69 (1H, m, H-8′), 3.84 (1H, m, H-9′a), and 3.77 (1H, m, H-9′b) were assigned to moieties CH(7)/CH(8)/CH_2(9), CH(7′)/CH(8′)/CH_2(9′) and CH(8)/CH(8). The location of two acetoxy groups on C-9 and C-9′ was confirmed by HMBC correlations between H-9 and H-9′ with the carbonyl carbons at δ_C = 170.9 and 170.7, respectively. In addition, the methoxy groups were positioned on C-4 and C-3′ based on NOE correlations between H-5 with the methoxy proton at δ_H = 3.89 (3H, s, 4-OCH_3) and H-4′ with the methoxy proton at δ_H = 3.94 (3H, s, 3′-OCH_3). Moreover, the NOE cross peaks between H-7

with H-7′ and H-9, H-9′ with H-8 suggested a relative 7,8-*trans*-8,8′-*trans*-7′,8′-*cis* configuration. Thus, compound **4** was established as shown in Fig. 1.

Experimental Section

General

Column chromatography (CC) was performed on silica gel (SiO_2, 100 – 200 or 200 – 300 mesh, Qingdao Marine Chemical Ltd. Co., China), Lichroprep RP-18 gel (40 – 63 μM, Merck, Germany) and MCI gel CHP20P (75 – 150 μm, Mitsubishi Chemical Co. Japan). TLC was performed on silica gel GF254 (Qingdao Marine Chemical Ltd. Co., China). Semiprep. reverse-phase (RP) HPLC was performed on an Agilent 1100 liquid chromatograph with a Zorbax SB-C_{18} column. NMR spectra were taken on a Bruker AM-400 instrument with TMS as internal standard. IR Spectra were recorded on a Bio-Rad FTS-135 spectrometer from KBr pellets. UV spectra were measured on a Shimadzu 210A double-beam spectrophotometer. Optical rotations were recorded on a Jasco DIP-370 digital polarimeter. ESI and HR-ESI-MS were carried out on an API Qstar Pulsar instrument.

Plant material

The aerial parts of *Jatropha curcas* were collected from Luquan county of Kunming, Yunnan province, People's Republic of China, in November 2008, and identified by Prof. Chun-Lin Long of Kunming Institute of Botany, Chinese Academy of Sciences, where a voucher specimen (number 593204) was deposited.

Extraction and isolation

The dried and powdered plant material (35 kg) was extracted with methanol under reflux for 8 h (3 × 30 L). The resulting residue was partitioned between AcOEt and H_2O, and then between BuOH and H_2O. The AcOEt extract (220 g) was subjected to CC (silica gel, $CHCl_3$-Me_2CO 9 : 1 – 1 : 1, and MCI, MeOH-H_2O 85 : 15) to yield 7 fractions (Fr. 1 – 7). Fr. 1 (25 g) was subjected to CC (RP-18, MeOH-H_2O 2 : 8 – 1 : 0) to afford 5 subfractions (Fr. 1.1 – 1.5). Fr. 1.4 was further purified by CC (silica gel, petroleum ether-acetone 4 : 1) to yield **7** (3 mg). Fr. 3 (15 g) was subjected to CC (RP-18, MeOH-H_2O 15 : 85 – 1 : 0) to afford 4 subfractions (Fr. 3.1 – 3.4). Fr. 3.1 was further purified by CC (silica gel, petroleum ether-acetone 4 : 1) and HPLC (CH_3CN-H_2O 38 : 62) to yield **3** (50 mg). Fr. 4 (23 g) was subjected to CC (RP-18, MeOH-H_2O 2 : 8 – 1 : 0) to afford 6 subfractions (Fr. 4.1 – 4.6). Fr. 4.1 was further purified by CC (silica gel, petroleum ether-AcOEt 1 : 1) and HPLC (MeOH-H_2O 4 : 6) to yield **10** (7 mg). Fr. 5 (9 g) was subjected to CC (RP-18, MeOH-H_2O 2 : 8 – 1 : 0) to afford 5 subfractions (Fr. 5.1 – 5.5). Fr. 5.1 was further purified by CC (silica gel, petroleum ether-Me_2CO 2 : 1) and HPLC (CH_3CN-H_2O 2 : 8) to yield **1** (3 mg). Fr. 5.3 was subjected to CC (silica gel, CH_3Cl-AcOEt 2 : 1) and then purified by HPLC (MeOH-H_2O 35 : 65 and CH_3CN-H_2O 2 : 8) to yield **2** (3 mg), **9** (7 mg), and **12** (4 mg). Fr. 6 (30 g) was subjected to CC (RP-18, MeOH-H_2O 2 : 8 – 1 : 0) to afford 6 subfractions (Fr. 6.1 – 6.6). Fr. 6.1 was purified by CC (silica gel, petroleum ether-Me_2CO 1 : 1) and HPLC (CH_3CN-H_2O 25 : 75) to yield **11** (4 mg), **6** (4 mg). Fr. 6.2 was subjected to CC (silica gel, CH_3Cl-AcOEt 1 : 1) and further purified by HPLC (MeOH-H_2O 3 : 7) to yield **4** (3 mg), **5** (3 mg), and **8** (5 mg).

*Curcasinlignan A (**1**)*. Colorless oil. – $[\alpha]_D^{25.0}$ = −4.30 (c = 0.38, MeOH). – UV (MeOH): $\lambda(\varepsilon)$ = 340.2 (4.21), 289.4 (3.89), 226.6 (4.26), 203.6 (4.59), 193.2 nm (4.28). – IR (KBr): ν = 3423, 1661, 1596, 1135 cm^{-1}. – ^1H and ^{13}C NMR spectral data: see Tables 1 and 2. – HRMS ((+)-ESI):m/z = 357.1335 (calcd. 357.1338 for $C_{20}H_{21}O_6$, $[M+H]^+$).

*Curcasinlignan B (**2**)*. Pale-yellow oil. – $[\alpha]_D^{24.6}$ = −13.13 (c = 0.16, MeOH). – UV (MeOH): $\lambda(\varepsilon)$ = 303.4 (3.83), 288.4 (3.85), 231.4 (4.04), 203.8 (4.36), 193.8 nm (4.08). – IR (KBr): ν = 3430, 1675, 1615, 1138 cm^{-1}. – ^1H and ^{13}C NMR spectral data: see Tables 1 and 2. – HRMS ((+)-ESI):m/z = 353.0986 (calcd. 353.1001 for $C_{18}H_{18}O_6Na$, $[M+Na]^+$).

*Curcasinlignan C (**3**)*. Pale-yellow oil. – $[\alpha]_D^{18.5}$ = −4.69 (c = 0.20, $CHCl_3$). – UV (MeOH): $\lambda(\varepsilon)$ = 300.6 (3.90), 289.4 (3.93), 234.2 (4.13), 207.0 (4.33), 196.6 nm (4.12). – IR (KBr): ν = 3423, 2932, 1678, 1592, 1325, 1137 cm^{-1}. – ^1H and ^{13}C NMR spectral data see Tables 1 and 2. – HRMS ((+)-ESI):m/z = 315.1234 (calcd. 315.1232 for $C_{18}H_{19}O_5$, $[M+H]^+$).

*Curcasinlignan D (**4**)*. Yellow gum. – $[\alpha]_D^{18.5}$ = −4.47 (c = 0.20, $CHCl_3$). – UV (MeOH): $\lambda(\varepsilon)$ = 281.0 (3.87), 231.0 (4.19), 204.0 nm (4.76). – IR (KBr): ν = 3431, 1737, 1611, 1517, 1270, 1240 cm^{-1}. – ^1H and ^{13}C NMR spectral data: see Tables 1 and 2. – HRMS ((+)-ESI):m/z = 483.1638 (calcd. 483.1631 for $C_{24}H_{28}O_9Na$, $[M+Na]^+$).

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