New Lignans from *Jatropha curcas* Linn.

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Z. Naturforsch. **2012**, *67b,* 176 – 180; received November 3, 2011

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)

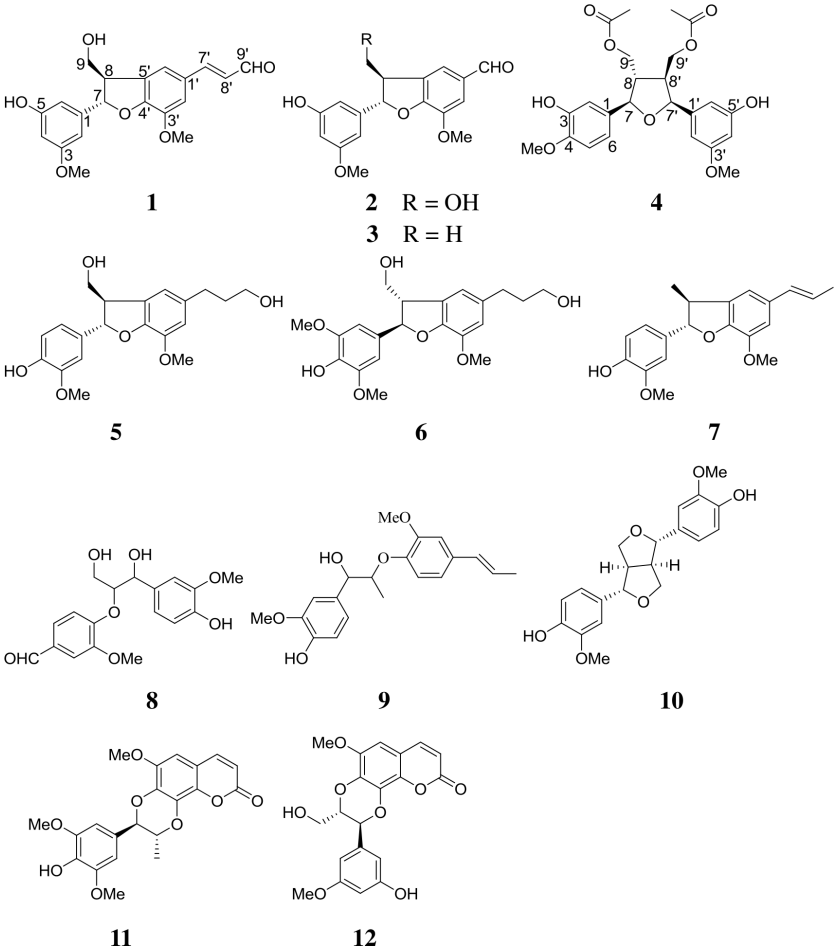

Fig. 1. Structures of compounds **1** – **12**.

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,

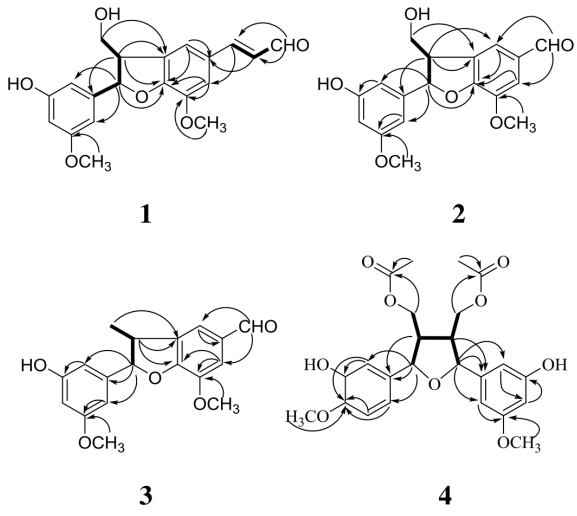

Fig. 2. Key ^{1}H-^{1}H COSY (▬) and HMBC (H → C) correlations of compounds **1** – **4**.

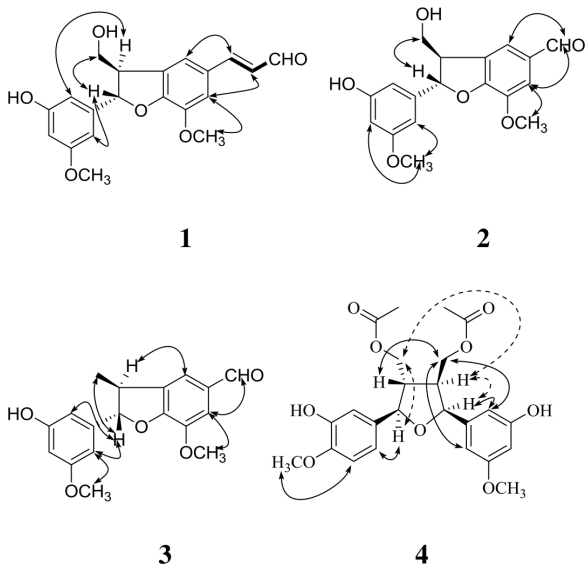

Fig. 3. Key NOESY correlations for compounds **1** – **4**.

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 $C_{24}H_{28}O_9Na$, $[M+Na]^+$).

Acknowledgements

This work was supported by the National Natural Science Foundation of China (30725048, 91013002, 31000159, U1032602), the National Basic Research Program of China (2009CB522300), the Fund of the Chinese Academy of Sciences (KSCX2-YW-R-177), the National New Drug Innovation Major Project of China (2011ZX09307-002-002), and the Fund of the Yunnan Provincial Department of Education (2010Y337). The authors are grateful to the staff of the analytical group at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, for the spectral data.

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