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New terpenoids from the roots of *Jatropha curcas*

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Two new sesquiterpenoids, (1*S*,2*R*)-dihydroxycycloax-4(15)-ene (**1**), 14-dehydroxyl daucucarotol (**2**), and one new rhamnofalane diterpenoid, 2-hydroxy-3-dehydroxycaniojane (**3**), together with two known compounds, curcusone D (**4**) and curcusone C (**5**), were isolated from the roots of *Jatropha curcas*. The chemical structures of these compounds were established by chemical methods and extensive 1D- and 2D-NMR spectroscopic data analyses.

***Jatropha curcas*, sesquiterpenoids, diterpenoid**

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Jatropha curcas (Euphorbiaceae) is indigenous to southwest and southeast China. The plant has been used as folk medicine for the treatment of injuries and swelling, fracture, skin itching, eczema, and acute gastroenteritis embolism [1]. Besides, the seeds containing 30% oil can be processed to produce a high-quality biodiesel fuel, usable in a standard diesel engine. And that is why *Jatropha curcas* was greatly focused as biodiesel source all over the world. The plants of genus *Jatropha*, mainly distributed in tropical and subtropical America [2]. The chemical constituents from this genus were plentiful, covered of diterpenoids, sesquiterpenoids, lignans and coumarins, flavonoids, and some others [3], and some of the diterpenoids have been proved to be effective as anti-inflammatory [4], antiproliferation [5,6], antiplasmodial [7], antituberculosis [8], antitumor [8,9], and cytotoxic activities [10].

Lately, several structurally interesting diterpenoids were isolated from this plant [9,11,12]. Its potential medicinal value and the diverse constituents prompted us to initiate the chemical investigation of *J. curcas*.

Our phytochemical study from the methanol extracts of roots of *J. curcas* led to the isolation of five compounds (**1–5**) (Figure 1), including two new sesquiterpenes, (1*S*, 2*R*)-dihydroxycycloax-4(15)-ene (**1**) and 14-dehydroxyl daucucarotol (**2**), one new rhamnofalane endoperoxide, 2-hydroxy-3-dehydroxy caniojane (**3**), and two known

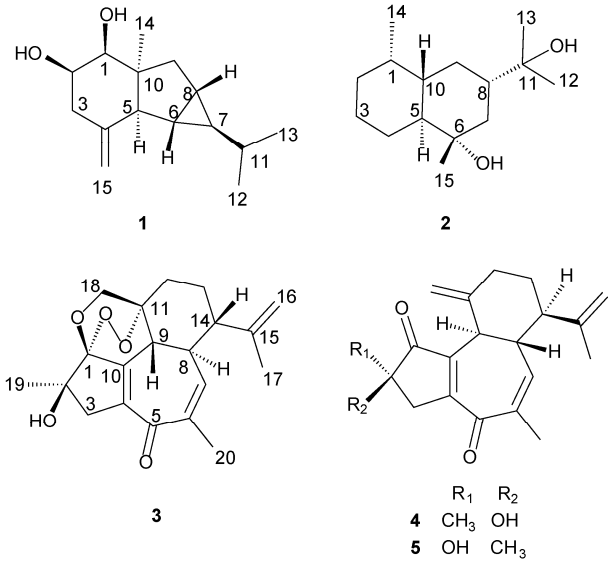

Figure 1 Structures of compounds **1–5**.

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compounds, curcusone D (**4**) [13] and curcusone C (**5**) [13]. This paper deals with the isolation and structure elucidation of new compounds **1**–**3**.

1 Experimental

1.1 General experimental procedures

UV spectra were obtained in MeOH with a Shimadzu double-beam 22210A spectrophotometer; Optical rotations were measured on a SEPA-300 polarimeter; IR spectra were obtained using a Bio-Rad FTS-135 infrared spectrometer with KBr pellets; NMR spectra were recorded on Bruker DRX-600 (600/150 MHz) spectrometers with TMS as internal standard; high resolution electrospray ionization mass spectroscopy (HRESIMS) and low resolution ESIMS were recorded on an APIQSTAR time-of-flight mass spectrometer while high resolution electron impact mass spectroscopy (HREIMS) were measured on a VG Auto Spec-3000 mass spectrometer; Semipreparative HPLC was performed on an Agilent 1100 apparatus equipped with a diode-array detector and a YMC-PackProC_{18}RS (YMC, 250 mm × 10 mm, 5 μm) column; column chromatography was performed on silica gel (200–300 mesh, Qingdao Marine Chemical Factory, Qingdao, China), Lichroprep RP-18 gel (40–63 μm, Merck, Darmstadt, Germany), Sephadex LH-20 (General Electric Company, Fairfield, CT); Fractions were monitored by TLC, and spots were visualized by heating silica gel plates sprayed with 10% H_2SO_4.

1.2 Plant material

The roots of *Jatropha curcas* were collected from E-Shan county, Yunnan Province, China, in July 2010, and identified by Prof. Hua Peng. A voucher specimen (No. KIB 20100701) was deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

1.3 Extraction and isolation

The dried and powdered roots of *J. curcas* (5 kg) were refluxed three times with 95% aqueous MeOH at room temperature. The combined MeOH extracts were concentrated under reduced pressure, and then partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer (130 g) was subjected to a macroporous resin gel column chromatography eluted with a gradient solvent system of MeOH-H_2O to yield 80% MeOH-H_2O extract, The 80% MeOH-H_2O extract (70 g) was chromatographed on silica gel CC with Me_2CO-PE mixtures (1:15, 1:10, 1:5, and 1:1) to get four fractions (Fr.1, Fr.2, Fr.3, and Fr.4). Fr.3 (10 g) was separated on an ODS column eluting with MeOH-H_2O (45%, 60%, and 70%) to give subfractions Fr.3.1–Fr.3.3. Subfraction Fr.3.1 (3 g) was further isolated and purified by silica gel column (PE-Me_2CO, 10:1), Sephadex LH-20 (MeOH), Preparative TLC (CH_3Cl-Me_2CO) to yield **1** (10 mg) and **2** (7 mg). Fr.1 (20 g) was further fractionized on an ODS column eluting with MeOH-H_2O (55%, 65%, and 80%) to afford subfractions Fr.1.1–Fr.1.3. Subfraction Fr.1.3 (5 g) was further isolated and purified by silica gel column (PE-Me_2CO), semipreparative HPLC (CH_3CN-H_2O) to afford **3** (1.3 mg). Fr.2 (20 g) was further fractionized on an ODS column eluting with MeOH-H_2O (50%, 62%, and 75%) to afford subfractions Fr.2.1–Fr.2.3. Subfraction Fr.2.2 (8 g) was further isolated and purified by silica gel column (PE-Me_2CO) to afford **4** (40 mg) and **5** (30 mg).

(i) (1*S*,2*R*)-Dihydroxycycloax-4(15)-ene (**1**). Yellow, oil; $[\alpha]_D^{25}$ = −33.2 (*c* 1.0, $CHCl_3$); IR (KBr) ν_{max}: 3350, 2958, 2953, 2870, 1047 cm^{-1}; ^1H and ^{13}C NMR data see Table 1; positive ESIMS (pos.): *m/z* 259 $[M + Na]^+$; positive HRESIMS (pos.): *m/z* 259.1668 $[M + Na]^+$ (calcd for $C_{15}H_{24}O_2$ $[M + Na]^+$, *m/z* 259.1673).

(ii) 14-Dehydroxyl daucucarotol (**2**). White, amorphous powder; $[\alpha]_D^{25}$ = +2.8 (*c* 1.0, $CHCl_3$); IR (KBr) ν_{max}: 3340, 2950, 2933, 2865, 1056 cm^{-1}; ^1H and ^{13}C NMR data see Table 1; positive ESIMS (pos.): *m/z* 263 $[M + Na]^+$; positive HRESIMS (pos.): *m/z* 263.1985 $[M + Na]^+$ (calcd for $C_{15}H_{28}O_2$ $[M + Na]^+$, *m/z* 263.1987).

(iii) 2-Hydroxy-3-dehydroxycaniojane (**3**). White, crystalline solid; $[\alpha]_D^{25}$ = −63.2 (*c* 0.03, MeOH); UV (MeOH) λ_{max} (log ε): 254 (3.00), 202 (5.19) nm; IR (KBr) ν_{max}: 3440, 1711, 1628, 1452 cm^{-1}; ^1H and ^{13}C NMR data see Table 1; positive TOF MS *m/z* 345 $[M + H]^+$; positive HREIMS *m/z* 367.1742 $[M + Na]^+$ (calcd for $C_{20}H_{24}O_5$ $[M + Na]^+$, *m/z* 367.1521).

2 Results and discussion

Compound **1** was obtained as yellowish oil. Its molecular formula was determined as $C_{15}H_{24}O_2$ by positive HRESIMS *m/z* 259.1668 $[M + Na]^+$ (calcd for $C_{15}H_{24}O_2$ $[M + Na]^+$, *m/z* 259.1673). The IR spectrum exhibited absorption bands for OH group (3350 cm^{-1}) and an olefinic function (1047 cm^{-1}). The ^1H, ^{13}C NMR, and DEPT (Distortionless enhancement by polarization transfer) data of **1** (Table 1) showed the presence of three methyls (two geminal methyls), three methylenes (one olefinic), seven methines (two oxygenated), and two quaternary carbons (one olefinic). The above-mentioned data, together with the evidence of four degrees of unsaturation suggested that **1** was quite similar to (1*R*,2*R*)-dihydroxycycloax-4(15)-ene [14].

Comprehensive analysis of HSQC (heteronuclear single quantum correlation) and ^1H-^1H COSY (correlation spectrometry) spectra of **1** allowed the establishment of one structural fragment as drawn in blue bold lines in Figure 2(a). One exocyclic double bond was evident from ^1H NMR signal at δ_H 4.98 and ^{13}C NMR signals at δ_C 106.5 (t). In the

Table 1 ^{1}H and ^{13}C NMR data of **1–3** in $CDCl_3$ (600 and 150 MHz, respectively)

	1		**2**		**3**	
	δ_C	δ_H (mult, *J* in Hz)	δ_C	δ_H (mult, *J* in Hz)	δ_C	δ_H (mult, *J* in Hz)
1	82.4 (d)	3.72 (d, 8.5)	39.5 (d)	2.02–2.05 (m)	103.8 (s)	
2	72.7 (d)	4.12 (ddd, 10.6, 8.8, 6.5)	34.6 (t)	1.60–1.64 (m) 1.29–1.32 (m)	77.6 (s)	
3	44.4 (t)	2.88 (dd, 13.2, 7.5) 2.43 (brdd, 13.2, 5.9)	27.3 (t)	1.96–1.99 (m)	43.9 (t)	2.80–2.84 (m) 2.63 (dd, 16.1, 4.1)
4	145.8 (s)		24.1 (t)	2.22 (ddd, 22.6, 15.1, 7.6) 1.27–1.30 (m)	138.9 (s)	
5	58.6 (d)	1.88 (d, 3.5)	53.0 (d)	2.20 (m)	193.6 (s)	
6	32.7 (d)	0.85–0.94 (m)	74.3 (s)		137.1 (s)	
7	48.4 (d)	0.50–0.55 (m)	48.9 (t)	1.88 (m) 2.24 (m)	138.6 (d)	5.94 (dd, 4.0, 1.5)
8	25.5 (d)	1.18–1.24 (m)	51.1 (d)	1.93 (m)	35.3 (d)	2.87 (d, 10.8)
9	43.5 (t)	2.24 (dd, 12.1, 6.6) 1.25–1.27 (m)	30.2 (t)	1.70–1.73 (m) 1.54–1.58 (m)	47.2 (d)	2.45–2.49 (m)
10	59.5 (s)		41.0 (d)	1.81–1.84 (m)	147.3 (s)	
11	24.2 (d)	1.32–1.37 (m)	73.4 (q)		69.8 (s)	
12	22.2 (q)	0.90 (d, 4.5)	28.7(q)	1.37 (s)	32.2 (t)	1.53–1.55 (overlapped) 1.36 (m)
13	22.0 (q)	0.93 (d, 4.5)	26.4(q)	1.32 (s)	25.7 (t)	1.88 (ddd, 9.1, 4.5, 2.5) 1.53–1.55 (overlapped)
14	15.9 (q)	1.18 (s)	15.9 (q)	0.85 (d, 7.0)	51.3 (d)	2.01–2.05 (m)
15	106.5 (t)	4.98 (dd, 3.7, 1.4)	22.4 (q)	1.34 (s)	146.5 (s)	
16					113.3 (t)	4.80, 4.77 (s)
17					18.9 (q)	1.60 (s)
18					70.0 (t)	4.01–4.04 (m) 3.41–3.43 (m)
19					23.6 (q)	1.39 (s)
20					20.5 (q)	1.76 (s)

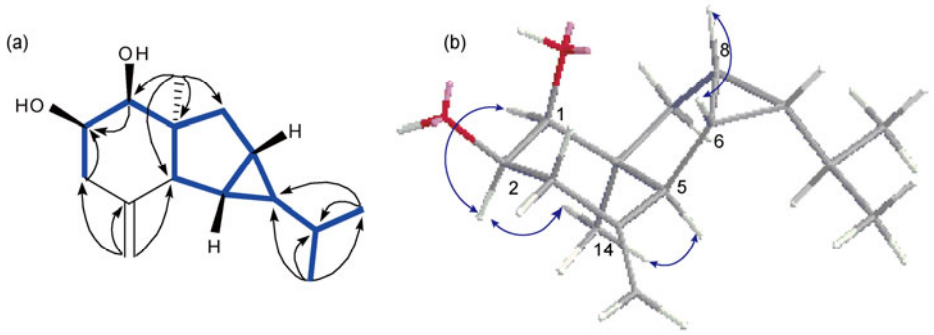

Figure 2 The ^{1}H-^{1}H COSY (—), key HMBC correlations (H→C) (a), and key ROESY correlations (⌒) (b) of **1**.

HMBC spectrum of **1**, the correlations from the olefinic proton signal δ_H 4.98 to C-3, C-4, and C-5 indicated the assignment of the exocyclic double bond between C-4 and C-15. The HMBC (heteronuclear multiple bond correlation) correlations from the quaternary methyl signal at δ_H 1.18 to C-1, C-5, C-9, and C-10, and from one of the methylene proton signals at δ_H 2.88 (dd, 13.2, 5.9) to C-1 and C-2 suggested the presence of hydroxyl groups at C-1 and C-2, respectively. Moreover, the existence of strong NOE correlations between H-1/H-2, H-2/H_3-14, H_3-14/H-5, and H-6/H-8 in the ROESY (rotating frame overhauser effect spectroscopy) spectrum of **1** (Figure 2(b)) suggested that OH-1 was β-oriented, which was the only difference between **1** and (1*R*,2*R*)-dihydroxycycloax-4(15)-ene. Consequently, the structure of **1** was deduced as (1*S*,2*R*)-dihydroxycycloax-4(15)-ene.

Compound **2** obtained as white powder, possessed a molecular formula of $C_{15}H_{28}O_2$, as evidenced by HRESIMS at *m/z* 263.1985 $[M + Na]^+$ (calcd for $C_{15}H_{28}O_2$ $[M + Na]^+$, *m/z* 263.1987), in accordance with two degrees of unsaturation. Importantly, the absence of any olefinic moieties in the ^{13}C NMR spectrum required the presence of two rings to satisfy the degrees of unsaturation.

The ^{13}C NMR and DEPT (Table 1) data of **2** exhibited four methyls, five methylenes, four methines, and two oxygenated quaternary carbons. These spectral features were closely related to those of daucucarotol [15], except for a tertiary methyl signal in **2** instead of an oxygenated methylene signal in daucucarotol. The HMBC spectrum of **2** displayed cross-peaks from the doublet methyl signal at δ_H 0.85 to C-1, C-2, and C-10, which suggested that the doublet methyl group located at C-1. The planar structure of **2** was further established from the ^1H-^1H COSY and HMBC spectra (Figure 3(a)).

The ROESY (Figure 3(b)) correlations of Me-14/H-5, H-10/H-8, and H-10/Me-15 suggested that the H-1, H-8, Me-15, and H-11 were of β-orientation. Ultimately, the structure of **2** was determined and named 14-dehydroxyl daucucarotol.

Compound **3** was obtained as crystalline solid. The HREIMS spectrum gave an $[M + Na]^+$ ion at *m/z* 367.1742, corresponding to the molecular formula $C_{20}H_{24}O_5$. The IR spectrum displayed absorption bands for unsaturated carbonyl (1658 cm^{-1}) and olefinic (1628 cm^{-1}) groups. The ^1H, ^{13}C, and DEPT (Table 1) NMR data of **3** showed the presence of three methyls, one oxymethylene (δ_C 70.0), one dioxygenated carbon (δ_C 103.8), two oxygenated carbon, a terminal double-bond, two double-bonds, and a keto carbonyl carbon (δ_C 193.6). These data showed that **3** was similar with caniojane [16]. The key difference was that one oxygenated quaternary carbon signal in **3** instead of an oxygenated methine in caniojane. Meanwhile, there was no doublet methyl signal in ^1H NMR spectrum. Above data indicated that a hydroxyl group would attach to C-2, which was confirmed by the HMBC correlations from H_3-19 to C-1, C-2 (δ_C 77.6, s), and C-3.

The planar structure of **3** was further determined by the correlations in the HMBC and ^1H-^1H COSY spectra (Figure 4(a)). The relative configuration of Me-19 was determined as α-oriented on the basis of the chemical shift of C-19 at δ_C 23.6 and were consistent with those reported for curcusone C [13]. The relative configuration of the peroxy bond between C-1 and C-11 was assigned as β by the correlations between H_2-18 and H-9 in the ROESY (Figure 4(b)) spectrum. Finally the structure of **3** was proposed to be 2-hydroxy-3-dehydroxycaniojane.

Caniojane and 1,11-bisepicaniojane [16,17], having peroxide bridge, performed certain antimalarial activity [18]. Well-known to all, artemisinin (Figure 5) is the antimalarial drug containing peroxide bridge, and the peroxy bond is necessary for the activity based on the structure-activity relationships. So, whether compound **3** with peroxide bridge playing a similar role in the resistance of plasmodium activity needs further study.

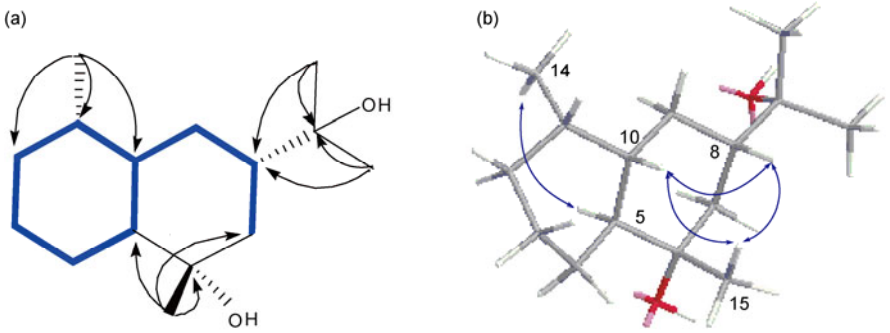

Figure 3 The ^1H-^1H COSY (—), key HMBC correlations (H→C) (a), and key ROESY correlations (⌒) (b) of **2**.

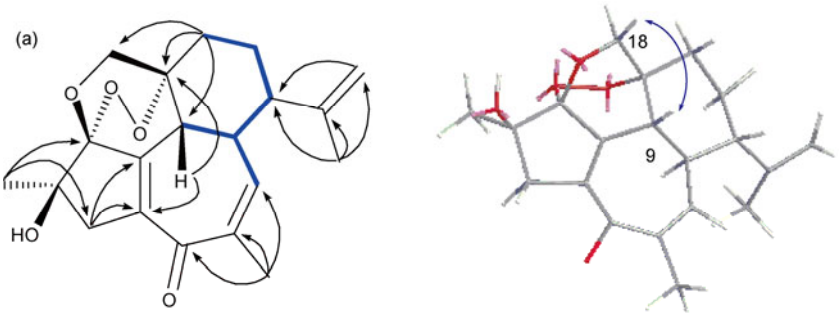

Figure 4 The ^1H-^1H COSY (—), key HMBC correlations (H→C) (a), and key ROESY correlations (⌒) (b) of **3**.

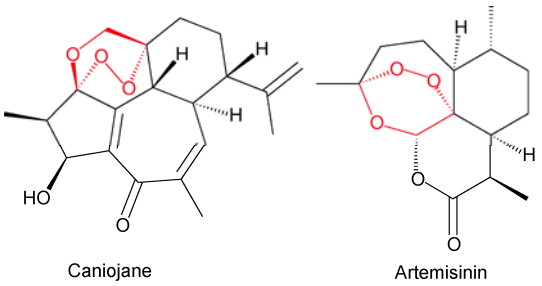

Figure 5 Structures of caniojane and artemisinin.

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