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Novel antifeeding limonoids from *Dysoxylum hainanense*

Xiao-Dong Luo,* Shao-Hua Wu, Da-Gang Wu, Yun-Bao Ma and Shu-Hua Qi

State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, The Chinese Academy of Sciences, Kunming 650204, Yunnan, People's Republic of China

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Abstract—Seven novel limonoids were isolated from the bark of *Dysoxylum hainanense* Merr, of which four were limonoid acids {dysoxylumic acids A (**1**), B (**2**), C (**3**), D (**5**)}, and three others {dysoxylumolides A (**4**), B (**6**), C (**7**)}. Their structures were established by extensive NMR experiments. In compounds (**1**)–(**6**), C-16 was an oxymethine group, which is rare in limonoids. Dysoxylumic acids A–C as well as known compounds dysoxylumins A–C exhibited significant antifeeding activity against *Pieris rapae* L, while dysoxylumolides A–C and dysoxylumic acid D showed moderate activity. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

The genus *Dysoxylum*, with about 200 species, is distributed naturally in India and Southeast Asia. Fourteen species are distributed in China. About 10 species of this genus have been found in Yunnan province.[1] Many plants in this genus have been used as traditional medicine by the indigenous people. *D. richii* is such an example which has been used by the indigenous Fijians as a traditional medicine plant to treat many diseases.[2] According to the literature, many types of compounds have been isolated from this genus, such as triterpenes,[2–4] triterpene glycosides,[5] tetranortriterpenoids,[6,7] diterpenes,[8,9] a steroid,[10] and alkaloids.[11] *Dysoxylum hainanense* Merr is distributed in Guangxi Zhuang Autonomous Region, Hainan province, and Xishuangbanna, Yunnan province.[2] As part of a program of seeking novel antifeedant limonoids from Meliaceae plants,[12–15] we reported three new tetranortriterpenoids structurally related to prieurianin, dysoxylumins A–C from the EtOH extracts of *D. hainanense* previously.[16] In our continued search for new limonoids from more polar fractions of the same species, seven novel *seco*-limonoids were isolated, in which four were limonoid acids {dysoxylumic acids A (**1**), B (**2**), C (**3**), D (**5**)}, and three others {dysoxylumolides A (**4**), B (**6**), C (**7**)}. Their structures were elucidated on the basis of extensive 1D and 2D NMR experiments, including COSY, HMQC, HMBC, and ROESY experiments. All the liminoids from *D. hainanense* were subjected to an antifeedant assay toward *Pieris rapae* L.

2. Results and discussion

Compound **1** was assigned the molecular formula of $C_{31}H_{40}O_{12}$ by negative-ion HRFABMS. Its IR spectrum showed absorption bands for hydroxyls (3447 cm^{-1}), carbonyl groups (1736 cm^{-1}) and double bonds (1649 cm^{-1}). The negative-ion FABMS exhibited strong ion peak at *m/z* 603 $[M-H]^-$, fragment ion peak at *m/z* 485 $[M-H-C_5H_{10}O_3]^-$ and base peaks at *m/z* 117 $[C_5H_9O_3]^-$. The ^1H and ^{13}C NMR spectra of **1** exhibited signals of an ester substituent [δ_C 175.3 (s, C-1′), 75.9 (d, C-2′), 32.2 (d, C-3′), 16.5 (q, C-4′), 19.7 (q, C-5′); δ_H 4.02 (d, J=3.3 Hz), 2.17 (m), 0.90 (d, J=6.8 Hz), 0.86 (d, J=6.8 Hz)], which were assigned to be 2-hydroxy-3-methyl-butyrate on the basis of HMBC spectral data. Besides the ester substituent, compound **1** contained 26 carbons; three tertiary methyls, two methylenes, one of which was oxymethylene, three skeleton methines at δ_C 55.3 (C-9), 46.6 (C-17), 43.3 (C-5), six oxymethines, four quaternary carbons (δ_C 82.6, 70.3, 45.6, 43.3), a typical β-substituted furan ring [δ_C 143.0 (d), 142.1 (d), 123.4 (s), 112.6 (d)], two olefinic carbons [139.2 (s), 121.6 (t)], and three carbonyl carbons (δ_C 177.7, 175.3, 174.8). These data suggested that **1** was a ring A, B-*seco*-limonoid having a double bond between C-8 and C-30.[17–19]

The peak at δ_H 4.67 (d, J=8.5 Hz) was attributed to the proton attached to the carbon (C-16) bearing a hydroxyl by the $^1H-^1H$ COSY spectrum, with correlation between δ_H 4.67 (d, J=8.5 Hz) and 3.50 (d, J=8.5 Hz, H-17). In the HMBC spectrum, δ_H 4.67 showing cross peaks to δ_C 46.6 (d, C-17) and 62.8 (d, C-15), respectively, further supported the assignment and indicated an oxirane between C-14 and C-15. ROE interactions between δ_H 4.67 with 1.18 (3H, s, H-18), and with 4.28 (1H, s, H-15) in the ROESY spectrum indicated 15β and 16β substituents. A hydroxyl was placed at C-11 by the observation of cross peaks between δ_H 4.75

Keywords: *Dysoxylum hainanensis*; limonoids; dysoxylumic acids; dysoxylumolides; antifeedent.

* Corresponding author. Tel.: +86-871-5223421; fax: +86-871-5150227; e-mail: x_dluo@hotmail.com

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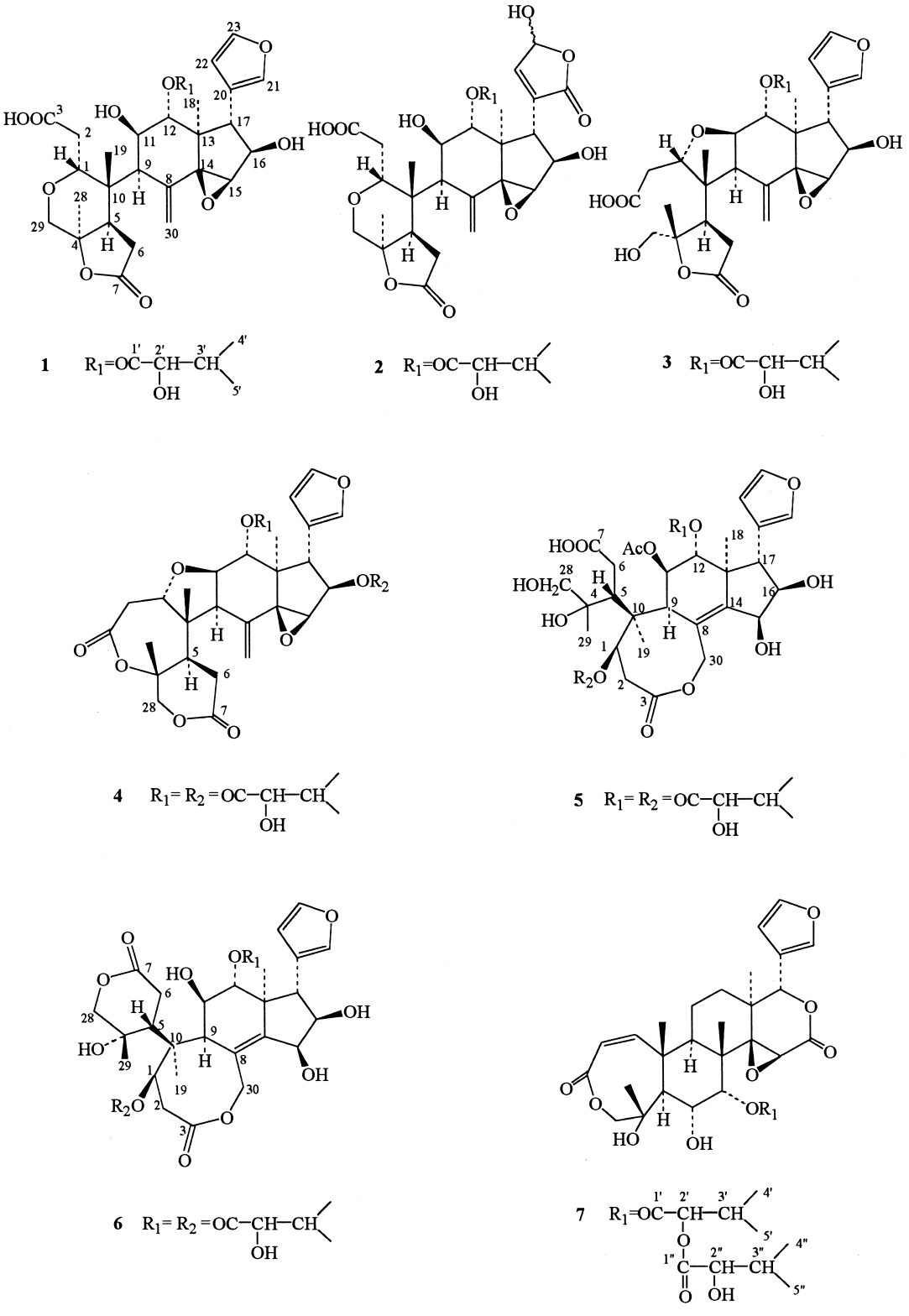

(dd, J=10.7, 8.4 Hz, H-11) to δ_C 44.2 (s, C-10), and the former to 55.3 (d, C-9) in the HMBC spectrum. In the $^1H-^1H$ COSY spectrum, H-11 showed correlations to δ_H 3.28 (d, J=8.4 Hz) and 6.44 (d, J=10.7 Hz), respectively, assigned H-9 and H-12. δ_H 6.44 (d, J=10.7 Hz, H-12) exhibited a cross peak to δ_C 175.3 (s) attributed to the ester carbonyl group in 2-hydroxy-3-methyl-butyrate, in the HMBC spectrum, which placed 2-hydroxy-3-methyl-butyrate at the C-12 position. In the ROESY spectrum, ROE interactions between H-12 with H-17, and H-12 with H-19 indicated a 12α substituent, while ROE interactions between H-11 with H-18, and H-11 with H-9 suggested a 11β substituent. The olefinic carbons δ_C 121.6 (t), 139.2 (s) and corresponding protons δ_H 5.38 (s), 5.46 (s) suggested an olefinic linkage between C-8 and C-30, which was confirmed by the HMBC spectrum, with

cross peaks between H-30 to δ_C 55.3 (d, C-9), and to 70.3 (s, C-14).

The B ring has been cleaved to form a γ-lactone between C-7 and C-4 on the basis of the observation of a weak cross signal between δ_H 4.12 (1H, d, J=14.0 Hz, H-29a) to δ_C 177.7 (s, C-7) in the HMBC spectrum. A ROE correlation between H-5 with H-28 indicated their *cis*-relationship. The peak at δ_H 6.09 (dd, J=12.0, 3.6 Hz) was assigned to the proton adjacent to the carbon (C-1) bearing an oxygen atom by the HMBC spectrum. This proton shows a cross signal to δ_C 64.2 (t, C-29), indicating that there was an ether bridge across the C-1 and oxymethylene (C-29). H-1 occupying the β position was determined by the ROESY spectrum, with a ROE correlation between H-1 and H-19. Based on the above evidence, we proposed structure **1** for this limonoid, named dysoxylumic acid A.

The high resolution negative-ion FABMS spectrum of **2** indicated a molecular formula of $C_{31}H_{40}O_{14}$, which revealed that **2** possessed two oxygen atoms more than **1**. The ^{1}H and ^{13}C NMR spectra of **2** were very similar to those of **1**, with the exception of the side chain. The presence of a γ-hydroxybutyrolactone as side chain was revealed by the signals δ_H 7.64 (H-22) and 6.69 (H-23) in the ^{1}H NMR spectrum. This was corroborated by the ^{13}C NMR spectrum which showed a hemiacetal carbon at 98.2 (C-23) and an α,β-unsaturated-γ-lactone [δ 134.1 (s, C-20), 171.3 (s, C-21), and 151.9 (d, C-22)]. These signals required the presence of a 23-hydroxy-20(22)-en-21,23-γ-lactone in **2**.[19,20] In an HMBC experiment, δ_H 7.64 (7.42) (1H, s, H-22) showed cross peaks to δ_C 171.3 (s, C-20), 134.1 (134.3) (s, C-21), and 98.2 (97.3) (d, C-23), respectively, which further supported this suggestion. The presence of double signals at some protons and carbons was caused by the equilibrium between two epimeric forms at the hemiacetal carbon (C-23). The rings A–D of **2** were identical to those of **1** by detailed analysis the ^{13}C, ^{1}H, HMBC, HMQC, and ^{1}H–^{1}H COSY spectra of **2**.

Compound **3** also possessed the molecular formula $C_{31}H_{40}O_{12}$ by negative-ion HRFABMS, which was identical to that of **1**. The ^{1}H and ^{13}C NMR of **3** were very similar to those of **1**. In the HMBC spectrum, cross signals between δ_H 4.92 (brd, J=10.2 Hz, H-1) to δ_C 79.4 (C-11), and the former to δ_C 173.8 (C-3), indicated an ether bridge across the C-1 and C-11. H-1 was the β substituent while H-11 was α as determined from the presence of ROE correlations between H-1 with δ_H 1.55 (H-19), and δ_H 4.62 (dd, H-11) with δ_H 1.02 (3H, s, H-18), in the ROESY spectrum. The chemical shifts of oxymethylene at δ_H 3.81 and 3.96 in the ^{1}H NMR spectrum, and a long range cross signal between δ_H 3.81 (1H, d, J=11.8 Hz, H-28a) to δ_C 176.4 (s, C-7) in the HMBC spectrum, indicated a γ-lactone between C-7 and C-4. Unlike compounds **1** and **2**, the methyl attached to C-4 was β in compound **3**, which was supported by the ROESY spectrum, with a ROE correlation between H-1 with δ_H 1.70 (H-29). The stereochemistry at the other chiral centers in **3** was identical to that of compound **1**, as supported by its ^{1}H, ^{13}C NMR, HMBC, HMQC, ^{1}H–^{1}H COSY and ROESY spectra.

The molecular formula of **4** was established as $C_{36}H_{46}O_{13}$ on the basis of negative-ion HRFABMS. Its ^{1}H and ^{13}C NMR spectra exhibited similarities to those of **3**. Inspection of the ^{1}H, ^{13}C and 2D NMR spectrum of **4**, indicated that there were four doublet methyls attributed to two substituents. These groups were determined as 2-hydroxy-3-methyl-butyrates by the HMBC spectrum, in which one was attached to C-12, as in compounds **1**–**3**. Another was placed at C-16 in **4** instead of a hydroxyl in **3**, on the basis of signals between δ_H 5.30 (d, J=9.2 Hz, H-16) to δ_C 175.0. In the HMBC spectrum, δ_H 4.00 (d, J=12.8 Hz, H-28a) showing an obvious cross peak to δ_C 170.9 (C-7), and a weak cross peak to 167.3 (s, C-3), respectively, indicated a six-membered ring lactone between C-7 and C-28, and a seven-membered ring lactone between C-3 and C-4 for compound **4**. According to the above spectral data, structure **4** was established for dysoxylumolide A.

Dysoxylumic acid **5** had a molecular formula $C_{38}H_{54}O_{17}$, as suggested from its negative-ion HRFABMS, which was also supported from its ^{13}C NMR (including DEPT) spectrum. Its IR spectrum showed hydroxyl (3448 cm^{-1}), carbonyl (1735 cm^{-1}) and double bond (1650 cm^{-1}) absorption bands. The ^{1}H and ^{13}C NMR spectra exhibited the presence of three tertiary methyls, four doublet peak methyls attributed to two ester groups, four methylenes, two of which were oxygenated, 12 methines, of which seven were oxymethines, a typical β-substituted furan ring, two substituted olefinic carbons, five carbonyl groups including an acetyl [δ_C 170.7 (s), 21.8 (q), δ_H 2.21 (3H, s)]. These data suggested that **5** was an A, B-*seco*-limonoid with three ester substituents. The three substituents were determined as two 2-hydroxy-3-methyl-butyrates and an acetate, on the basis of HMBC spectral data. Detailed analysis of the HMBC spectrum placed the acetate at C-11, and two 2-hydroxy-3-methyl-butyrates at the C-1 and C-12 positions, respectively. In the ROESY spectrum, ROE correlations between δ_H 6.03 (H-11) with 1.23 (H-18), and with 3.71 (H-9) suggested that the acetate adopted the 11β position, whereas a ROE correlation between δ_H 6.33 (H-12) with 3.85 (H-17) indicated a 12α substituent.

The peak at δ_H 3.85 (d, J=9.3 Hz) was assigned to H-17, since it showed cross peaks to the signals of the β-substituted furan ring, in the HMBC spectrum. The correlation between H-17 with δ_H 4.83 (dd, J=9.3, 8.2 Hz, H-16), and the latter with 5.42 (d, J=8.2 Hz, H-15) in the ^{1}H–^{1}H COSY spectrum revealed that there were two hydroxyl groups attached to C-16 and C-15. In the ROESY spectrum, ROE interactions among H-18 (δ_H 1.23), H-16, and H-15, indicated that both hydroxyls (15-OH, 16-OH) was in the β orientation. An olefinic linkage was established between C-8 and C-14 by the observation of cross peaks between δ_H 5.42 (H-15) to δ_C 128.9 (s, C-8), H-15 to 154.1 (s, C-14), δ_H 3.71 (d, 6.2, H-9) to δ_C 128.9 (C-8), and H-9 to 154.1 (C-14) in the HMBC spectrum. The protons δ_H 6.28 (d, J=12.6 Hz) and 5.24 (d, J=12.6 Hz) were attributed to the oxymethylene adjacent to the olefinic linkage (C-30). In the HMBC spectrum, δ_H 6.28 (d, J=12.6 Hz) and 5.24 (d, J=12.6 Hz) showing cross signals to the olefinic carbons, and to δ_C 174.8 (s, C-3), indicated an eight-membered ring lactone between C-3 and C-30 in **5**. ROE interactions between δ_H 5.25 (H-1), 3.71 (H-9), and 1.29 (H-19) in the ROESY spectrum, revealed three protons on the same side

Table 1. ^{13}C NMR spectral data of compounds **1**–**7**

C	1	2	3	4	5	6	7
1	78.4d	78.4d	85.1d	79.8d	78.6d	80.1d	148.8d
2	34.4t	34.4t	36.6t	37.5t	37.2t	36.7t	120.0d
3	174.8s	174.9s	173.8s	167.3s	174.8s	174.9s	165.3s
4	82.6s	82.7s	90.3s	79.1s	83.9s	78.5s	84.3s
5	43.3d	43.2d	44.4d	44.5d	44.9d	48.2d	53.8d
6	34.5t	34.5t	33.8t	31.0t	32.0t	31.2t	75.6d
7	177.7s	177.7s	176.4s	170.9s	176.7s	175.1s	72.7d
8	139.2s	138.6s	138.5s	135.5s	128.9s	129.4s	44.3s
9	55.3d	55.2d	52.8d	54.9d	48.0d	53.5d	41.8d
10	44.2s	44.1s	50.3s	51.1s	52.6s	52.6s	43.5s
11	71.2d	71.2d	79.4d	78.9d	72.3d	74.2d	15.6t
12	77.7d	77.5d	80.1d	74.1d	73.8d	76.8d	25.8t
13	45.6s	46.7s	45.2s	43.8s	48.7s	48.7s	38.8s
14	70.3s	70.3s	70.8s	69.8s	154.1s	154.4s	69.2s
15	62.8d	62.9d	63.3d	58.6d	69.2d	68.9d	56.8d
16	76.6d	76.5d	76.7d	78.2d	74.2d	74.2d	166.2s
17	46.6d	48.4d	46.6d	42.2d	52.0d	54.1d	77.8d
18	15.3q	15.0q	15.9q	14.9q	19.6q	19.6q	17.5q
19	18.1q	18.1q	18.8q	18.6q	18.6q	19.7q	17.4q
20	122.8s	134.1, 134.3s	123.2s	119.4s	123.4s	123.3s	120.3s
21	143.0d	171.3s	143.1d	143.3d	142.9d	143.0d	143.1d
22	112.6d	151.9, 152.7d	112.5d	110.9d	111.9d	112.0d	109.9d
23	142.1d	98.2, 97.3d	141.9d	140.9d	142.0d	141.5d	141.3d
28	24.5q	24.5q	69.1t	72.1t	69.1t	73.1t	81.2t
29	64.2t	64.2t	20.1q	26.6q	21.5q	23.3q	23.4q
30	121.6t	122.1t	122.1t	121.9t	67.4t	66.7t	19.5q
R_1							
1′	175.3s	174.9s	175.1s	175.1s	175.3s	173.7s	168.7s
2′	75.9d	76.5d	75.9d	75.0d	76.3d	76.4d	76.7d
3′	32.2d	32.4d	33.1d	32.2d	33.3d	32.5d	30.1d
4′	16.5q	17.1q	17.1q	15.7q	17.3q	17.0q	16.5q
5′	19.7q	19.6q	19.3q	18.6q	19.6q	19.4q	19.1q
R_2							
1″				175.0s	174.2s	174.6s	173.4s
2″				74.8d	76.2d	76.1d	76.1d
3″				32.2d	32.8d	32.8d	32.4d
4″				15.5q	17.5q	17.4q	16.3q
5″				17.3q	19.6q	19.1q	18.7q
OAc					170.7s		
					21.8q		

Compounds **1**, **2**, **4** and **5** were determined at 125 MHz, and **3**, **6** and **7** at 100 MHz with TMS as internal standard; compounds **1**, **2**, **3**, **5** and **6** were measured in pyridine-d_5, while **4** and **7** in $CDCl_3$; chemical shifts are in ppm.

Table 2. ^1H NMR spectral data of compounds **1**–**3** (pyridine-d_5)

H	1	2	3
1	6.09 (dd, 12.0, 3.6)	6.09 (brd, 11.9)	4.92 (brd, 10.2)
2	3.25 (m)	3.25 (m)	2.95 (dd, 14.6, 10.8)
	3.50 (m)	3.50 (m)	3.18 (dd, 14.6, 4.0)
5	2.55 (d, 8.1)	2.54 (d, 7.7)	3.39 (t, 8.0)
6	2.82 (dd, 10.1, 18.1)	2.82 (m)	3.25 (m)
	3.61 (d, 18.1)	3.56 (m)	
9	3.28 (d, 8.4)	3.27 (d, 8.2)	3.89 (d, 9.7)
11	4.75 (dd, 10.7, 8.4)	4.73 (t, 8.2)	4.62 (dd, 8.0, 9.7)
12	6.44 (d, 10.7)	6.40, 6.43 (1H, d, 8.2)	6.28 (d, 8.0)
15	4.28 (s)	4.25, 4.24 (1H, s)	4.29 (s)
16	4.67 (d, 8.5)	5.54, 5.48 (1H, d, 8.6)	4.69 (d, 8.8)
17	3.51 (d, 8.5)	3.53 (d, 8.6)	3.57 (d, 8.8)
18	1.18 (s)	1.37 (s)	1.02 (s)
19	2.31 (s)	2.23, 2.35 (3H, s)	1.55 (s)
21	7.67 (s)		7.59 (s)
22	6.64 (s)	7.64, 7.42 (1H, s)	6.56 (s)
23	7.58 (s)	6.69, 6.27 (1H, s)	7.49 (d, 0.7)
28	1.28 (s)	1.28 (s)	3.96 (d, 11.8)
			3.81 (d, 11.8)
29	4.35 (d, 14.0)	4.35 (d, 14.0)	1.70 (s)
	4.12 (d, 14.0)	4.12 (d, 14.0)	
30	5.46 (s)	5.49 (s)	5.51 (s)
	5.38 (s)	5.36 (s)	5.46 (s)
R_1			
2′	4.02 (d, 3.3)	4.48, 4.25 (1H, d, 3.8)	4.10 (d, 4.0)
3′	2.17 (m)	2.21 (m)	2.24 (m)
4′	0.90 (d, 6.8)	0.96 (d, 6.8)	1.10 (d, 6.8)
5′	0.86 (d, 6.8)	0.93 (d, 6.8)	1.06 (d, 6.8)

Compounds **1** and **2** were determined at 500 MHz, while **3** at 400 MHz; chemical shift values δ are in ppm, and coupling constant values J in Hz.

of the eight-membered ring lactone. Another oxymethylene was assigned as C-28 also from the HMBC spectrum, with cross signals between δ_H 4.39 (d, J=11.2 Hz) and 4.10 (d, J=11.2 Hz) to δ_C 83.9 (s, C-4).

Negative-ion HRFABMS spectrum of dysoxylumolide B (**6**) indicated its molecular formula as $C_{36}H_{50}O_{15}$. Compound **6** was very closely related to **5**. Comparison of ^1H and ^{13}C NMR spectra of two compounds, indicated that the acetate adjunct to C-11 was absent in **6**. Instead of it, a hydroxyl was attached to C-11 by the observation of correlation between δ_H 4.80 (dd, J=11.0, 6.0 Hz, H-11) and 6.16 (d, J=11.0 Hz, H-12) in the ^1H–^1H COSY spectrum. The HMBC spectrum displayed the presence of cross peaks between δ_H 4.39 (d, J=12.1 Hz, H-28b), 4.15 (d, J=12.1 Hz, H-28a) to δ_C 175.1 (s, C-7) and 78.5 (s, C-4), which suggested the formation of a six-membered ring lactone between C-7 and C-28. ROE interactions between δ_H 1.69 (3H, s, H-29) with 3.56 (H-5), and with 3.67 (H-6β) suggested their *cis*-relationship. The stereochemistry at the other chiral centers in **6** was identical to that of compound **5** by detailed analysis of HMBC, HMQC, ^1H–^1H COSY and ROESY spectra of **6**.

The molecular formula of dysoxylumolide C (**7**) was determined as $C_{36}H_{48}O_{13}$ by negative-ion HRFABMS. The ^1H and ^{13}C NMR of **7** exhibited signals for four tertiary methyls [δ_H 1.12 (H-18), 1.16 (H-30), 1.28 (H-19), 1.56 (H-29)], three methylenes, one of which was oxymethylene, 10 methines, of which five were oxymethines, three upfield (δ_C 38.8, 43.5, 44.3) and two downfield quaternary carbons (δ_C 84.3, 69.2), a β-substituted furan ring, and four ester carbonyl groups. In addition, The HMBC spectrum indicated a substituent containing 10 carbons. The data suggested that **7** was a limonoid.

The signals at δ_C 148.8 (d), 120.0 (d), and 165.3 (s) in the ^{13}C NMR spectrum, and corresponding protons at δ_H 6.28 (d, J=12.5 Hz, H-1) and 5.90 (d, J=12.5 Hz, H-2) in the ^1H NMR spectrum were typical signals for an α,β-unsaturated ester group moiety in the A ring.[17,19] This inference was supported by the HMBC spectrum, with cross peaks between olefinic protons δ_H 6.28 (H-1) and 5.90 (H-2) to 165.3 (s, C-3). A cross peak between δ_H 3.73 (1H, d, J=10.0 Hz, H-28a) to 165.3 (s, C-3), indicated an eight-membered lactone between C-3 and 28. The methyl adjunct to C-4 was β as supported by the ROESY spectrum, with ROE correlations between δ_H 1.56 (H-29) with 1.28 (H-19), and H-29 with 4.07 (H-6). The ^1H and ^{13}C NMR of **7** also showed signals characteristic of a normal limonoid D-ring, i.e. a six-membered lactone and 14β,15β-epoxide.[21–23] The assignment also supported by the ROESY and HMBC spectra. It could be inferred that C-6 and C-7 were oxygenated, based on the HMBC and ^1H–^1H COSY

Table 3. ^{1}H NMR spectral data of compounds **4**–**7**

H	4	5	6	7
1	4.12 (dd, 7.4, 5.6)	5.25 (d, 7.6)	5.23 (d, 9.8)	6.28 (d, 12.5)
2	3.04 (dd, 13.2, 5.6)	2.80 (dd, 15.5, 7.6)	2.87 (dd, 15.8, 9.8)	5.90 (d, 12.5)
	2.80 (dd, 13.2, 7.4)	3.26 (d, 15.5)	3.40 (d, 15.8)	
5	2.42 (t, 7.2)	3.50 (brd, 11.2)	3.56 (dd, 11.6, 3.0)	2.90 (brd, 12.4)
6	2.72, 2.80 (m)	3.00 (dd, 15.0, 11.2)	3.17 (dd, 14.2, 11.6)	4.07 (dd, 12.4, 2.7)
		3.60 (d, 15.0)	3.67 (d, 14.2)	5.03 (d, 2.7, H-7)
9	3.24 (d, 8.9)	3.71 (d, 6.2)	3.56 (d, 6.0)	2.43 (t, 10.0)
11	4.22 (dd, 9.2, 8.9)	6.03 (dd, 11.7, 6.2)	4.80 (dd, 11.0, 6.0)	1.90 (m)
12	5.62 (d, 9.2)	6.33 (d, 11.7)	6.16 (d, 11.0)	1.75, 1.52 (m)
15	4.12 (s)	5.42 (d, 8.2)	5.41 (d, 7.8)	3.69 (s)
16	5.30 (d, 9.2)	4.83 (dd, 9.3, 8.2)	4.86 (dd, 8.6, 7.8)	
17	3.12 (d, 9.2)	3.85 (d, 9.3)	3.55 (d, 8.6)	5.51 (s)
18	0.94 (s)	1.23 (s)	1.25 (s)	1.12 (s)
19	1.25 (s)	1.29 (s)	1.51 (s)	1.28 (s)
21	7.36 (s)	7.58 (s)	7.57 (s)	7.38 (s)
22	6.14 (s)	6.67 (s)	6.65 (s)	6.31 (s)
23	7.15 (s)	7.26 (s)	7.50 (s)	7.38 (s)
28	4.00 (d, 12.8)	4.10 (d, 11.2)	4.15 (d, 12.0)	4.34 (d, 10.0)
	4.25 (d, 12.8)	4.39 (d, 11.2)	4.39 (d, 12.0)	3.73 (d, 10.0)
29	1.65 (s)	1.63 (s)	1.69 (s)	1.56 (s)
30	5.34 (s)	6.28 (d, 12.6)	6.26 (d, 12.6)	1.16 (s)
	5.48 (s)	5.24 (d, 12.6)	5.24 (d, 12.6)	
R_1				
2′	3.98 (brs)	3.75 (d, 4.1)	4.00 (d, 3.6)	5.14 (d, 2.8)
3′	2.08 (m)	2.00 (m)	2.3 (m)	2.25 (m)
4′	0.97 (d, 7.0)	0.99 (d, 6.8)	1.07 (d, 7.8)	1.02 (d, 6.8)
5′	0.87 (d, 7.0)	0.97 (d, 6.8)	1.07 (d, 7.8)	1.02 (d, 6.8)
R_2				
2′	3.70 (brs)	4.40 (d, 4.7)	4.40 (d, 4.8)	4.04 (d, 2.4)
3′	1.95 (m)	2.37 (m)	2.30 (m)	2.15 (m)
4′	0.96 (d, 6.9)	1.15 (d, 6.8)	1.07 (d, 7.8)	1.02 (d, 6.8,)
5′	0.84 (d, 6.9)	1.15 (d, 6.8)	1.07 (d, 7.8)	0.94 (d, 6.8)
Oac		2.21 (s)		

Compounds **4** and **5** were determined at 500 MHz, while **6** and **7** at 400 MHz; compounds **5** and **6** were measured in pyridine-d_5, while **4** and **7** in $CDCl_3$; chemical shift values δ are in ppm, and coupling constant values J in Hz.

spectral data. A large coupling constant between H-5 and H-6 (J=12.4 Hz), and a small one between H-6 and H-7 (J=2.7 Hz) assumed that both substituents took the α orientation. The inference was supported by the ROESY spectrum, in which ROE interactions among δ_H 1.16 (H-30), 1.28 (H-19), 4.07 (H-6), and 5.03 (H-7) were observed. Unusually, instead of two 2-hydroxy-3-methyl-butyrates, a 2-(2-hydroxy-3-methyl-butyratoxyl)-3-methyl-butyrate and a hydroxyl group were adjacent to C-7 and C-6, respectively, which was unambiguously determined by the observation of cross signals between δ_H 5.14 (d, J=2.8 Hz, H-2′) to δ_C 173.4 (s, C-1″), H-2′ to 168.7 (s, C-1′), H-2′ to 30.1 (d, C-3′), and δ_H 5.03 (H-7) to 168.7 (s, C-1′). Furthermore, the substituent 2-(2-hydroxy-3-methyl-butyratoxyl)-3-methyl-butyrate was also found in the negative-ion FABMS spectrum of **7**, with fragment ion peak at m/z 217 $[RO]^-$.

Table 4. Antifeedant activity of limonoids and EtOH extract of *D. hainanense* bioassayed with *P. rapae* L

Compounds or extracts	AR[a]
EtOH extract	61.2
Dysoxylumic acid A (**1**)	78.7
Dysoxylumic acid B (**2**)	64.1
Dysoxylumic acid C (**3**)	59.4
Dysoxylumic acid D (**5**)	29.5
Dysoxylumolide A (**4**)	27.9
Dysoxylumolide B (**6**)	28.3
Dysoxylumolide C (**7**)	22.4
Dysoxylumins A	73.8
Dysoxylumins B	77.4
Dysoxylumins C	74.9
Azadirachtin	100

[a] AR represents the antifeeding rate calculated from AR=[($C-T$)/C]100. C and T represent the areas eaten by the larvae of the control and treatment disks, respectively.

All signals for compounds **1**–**7** are assigned in Tables 1–3 on the basis of the HMBC, HMQC and ^{1}H–^{1}H COSY spectral evidence.

The antifeedant activities of EtOH extract and the limonoids included new compounds **1**–**7** and reported dysoxylumins A–C, were tested by the conventional leaf disk method against the larvae of *P. rapae* L. Limonoids were at concentrations of 500 ppm, and EtOH extract at 1000 ppm. The results (Table 4) indicated that dysoxylumic acids **1**–**3** and dysoxylumins A–C were most potent but less active than the model compound azadirachtin.

3. Experimental

3.1. General experimental procedures

All the mps were obtained on an XRC-1 micromelting apparatus and were uncorrected. Optical rotations were

Table 5. HMBC correlation data of compounds **1**–**7**

C	1	2	3	4	5	6	7
1	H-2, 19, 28	H-2, 19, 28	H-2, 11, 19	H-2, 11, 19	H-2, 19	H-2, 19	H-2, 5, 19
2	H-1	H-1	H-1	H-1		H-1	H-1, 19
3	H-1, 2	H-2	H-1, 2	H-2, 28	H-2, 30	H-2, 30	H-1, 2
4	H-6, 28, 29	H-6, 28, 29	H-6, 28, 29	H-6, 28, 29	H-6, 28, 29	H-28, 29	H-5, 28, 29
5	H-1, 6, 19, 28, 29	H-1, 6, 19, 28, 29	H-1, 6, 19, 28, 29	H-1, 6, 19, 28, 29	H-6, 19, 28, 29	H-6, 19, 28, 29	H-1, 6, 7, 19, 28, 29
6	H-5	H-5	H-5	H-5	H-5	H-5	H-5, 7
7	H-6, 29	H-6, 28	H-6, 29	H-6, 28	H-5, 6	H-5, 6, 28	H-5, 6, 30
8	H-9, 30	H-9, 30	H-9, 30	H-9, 30	H-9, 15, 30	H-9, 15, 30	H-9, 30
9	H-11, 19, 30	H-5, 19, 30	H-1, 19, 30	H-19, 30	H-11, 19, 30	H-11, 19, 30	H-1, 19, 30
10	H-1, 9, 19	H-1, 5, 9, 11, 19	H-9, 11, 19	H-9, 11, 19	H-9, 11, 19	H-9, 11, 19	H-5, 9, 11, 19
11	H-9, 12, 18, 30	H-9, 12, 18, 30	H-1, 9, 12, 18	H-1, 9, 12, 19	H-9, 12, 19	H-9, 12, 19	H-1, 9, 12
12	H-9, 11, 18	H-9, 11, 18	H-11, 18	H-11, 18	H-11, 18	H-11, 18	H-11, 17, 18
13	H-9, 11, 12, 15, 18	H-9, 11, 12, 18	H-12, 15, 18	H-12, 15, 18	H-12, 15, 18	H-12, 18	H-15, 17, 18
14	H-9, 12, 15, 18, 30	H-12, 15, 18, 30	H-9, 15, 18, 30	H-9, 15, 18, 30	H-9, 15, 16, 18, 30	H-15, 16, 18, 30	H-7, 9, 15, 18, 30
15	H-16, 18	H-18	H-16	H-16		H-16	H-18
16	H-15, 17	H-15, 17	H-15, 17	H-15, 17	H-17	H-17	H-15, 17
17	H-15, 16, 18	H-16, 18	H-15, 16, 18	H-15, 16, 18	H-15, 18	H-15, 18	H-15, 18
18	H-12, 17	H-12, 17	H-12, 17	H-12, 17	H-12, 17	H-12, 17	H-12, 17
19	H-1, 5, 9	H-1, 5, 9	H-1, 5, 9	H-1, 5	H-5	H-5	H-1, 2, 5
20	H-16, 17, 21, 22, 23	H-16, 17, 22	H-16, 17, 21, 22	H-16, 17, 21, 22	H-16, 17, 21, 22, 23	H-16, 17, 21, 22, 23	H-17, 21, 22, 23
21	H-22	H-22	H-22	H-22	H-20, 22	H-20, 22	H-17, 22, 23
22	H-17, 23	H-17	H-17, 21, 23	H-17, 21, 23	H-17, 21, 23	H-17, 21, 23	H-17, 21, 23
23	H-22	H-22	H-22	H-21, 22	H-21, 22	H-21, 22	H-20, 21, 22
28	H-5, 29	H-5, 29	H-5, 29	H-5, 29	H-5, 29	H-5, 29	H-29
29	H-1, 28	H-1, 28	H-1, 28	H-28	H-28	H-28	H-5, 28
30	H-9	H-9	H-9	H-9	H-9	H-9	H-9
R_1							
1′	H-12, 2′	H-12, 2′	H-12, 2′	H-12, 2′	H-12, 2′	H-12, 2′	H-7, 2′
2′	H-4′, 5′	H-4′, 5′	H-4′, 5′	H-4′, 5′	H-4′, 5′	H-4′, 5′	H-4′, 5′
3′	H-2′, 4′, 5′	H-2′, 4′, 5′	H-2′, 4′, 5′	H-2′, 4′, 5′	H-2′, 4′, 5′	H-2′, 4′, 5′	H-2′, 4′, 5′
4′	H-3′, 5′	H-3′, 5′	H-3′, 5′	H-5′	H-3′, 5′	H-3′, 5′	H-3′, 5′
5′	H-3′, 4′	H-3′, 4′	H-3′, 4′	H-4′	H-3′, 4′	H-3′, 4′	H-3′, 4′
R_2							
1″				H-16, 2″	H-1, 2″	H-1, 2″	H-2′, 2″, 3″
2″				H-4″, 5″	H-3″, 4″, 5″	H-3″, 4″, 5″	H-4″, 5″
3″				H-4″, 5″	H-4″, 5″	H-4″, 5″	H-4″, 5″
4″				H-5″	H-3″, 5″	H-5″	H-3″, 5″
5″				H-4″	H-3″, 4″	H-4″	H-3″, 4″
CH_3COO					H-11, CH_3COO		

measured with a Horiba SEAP-300 spectropolarimeter. UV spectra were measured with a Shimadzu double-beam 210A spectrophotometer in MeOH solution. IR (KBr) spectra were obtained on a Bio-Rad FTS-135 infrared spectrophotometer. ^1H, ^{13}C NMR and 2D NMR spectra were recorded on a Bruker AM-400 and a DRX-500 MHz NMR spectrometer with TMS as internal standard. MS spectral data were obtained on a VG Autospec-3000 spectrometer, 70 eV for EI. Si gel (200–300 mesh) for column chromatography and GF_{254} for TLC were obtained from the Qindao Marine Chemical Factory, Qindao, People's Republic of China.

3.2. Plant material

The bark of *D. hainanense* was collected from Xishuangbanna, Yunnan province, People's Republic of China, in December 1996. It was identified by Professor Tao, G. D., Xishuangbanna Botany Garden, *Academia Sinica*. A Voucher specimen (No. 7188) was deposited in the herbarium of the Department of Taxonomy, Kunming Institute of Botany, *Academia Sinica*, Kunming, People's Republic of China.

3.3. Extraction and isolation

The dried and powdered bark (4.2 kg) of *D. hainanense* was extracted with EtOH three times under reflux, and the solvent was evaporated *in vacuo*. The residue was partitioned in H_2O and extracted with EtOAc three times. The EtOAc extracts were concentrated *in vacuo* to afford 72 g of residue, which was subjected to column chromatography on a silica gel, using $CHCl_3$–Me_2CO (from $CHCl_3$ to $CHCl_3$–Me_2CO 1:1) as eluent. Combining the fractions with TLC (GF_{254}) monitoring, 12 fractions were obtained. Then, the third fraction (3.6 g) was further purified using CC on silica gel with petroleum ether–acetone (2:1) to yield **4** (28 mg). Fraction five (1.7 g) was subjected to CC on silica gel, eluted with $CHCl_3$–EtOAc (2:1), as well as recrystallized in acetone to afford **7** (28 mg). Fractions eleven and twelve were subjected to CC on silica gel, repeatedly eluted with $CHCl_3$–acetone (1:1), respectively,

to give three subfractions (A–C). Sediment from fraction C was washed intensively with $CHCl_3$–acetone (1:1) to afford **2** (16 mg). Fractions A and B were subjected to CC on reversed-phase C_{18} silica gel using CH_3OH–H_2O (from 3:2 to 1:1) as eluent, finally yielding **1** (18 mg), **3** (33 mg) **5** (36 mg) and **6** (30 mg) (Table 5).

3.3.1. Dysoxylumic acid A (1). White powder: mp 168–170°C; $[\alpha]_D^{26}$=+11.1 (*c* 0.45, CH_3OH); IR (KBr) ν_{max} 3447, 2970, 2921, 2853, 1736, 1649, 1469, 1387, 1312, 1272, 1220, 1095, 1079, 1004, 945, 874 cm^{-1}; ^1H NMR spectral data, see Table 2; ^{13}C NMR spectral data, see Table 1; EIMS *m/z* 604 $[M]^+$ (0.4), 568 (4), 450 (2), 359 (3), 242 (14), 224 (12), 211 (14), 197 (12), 185 (14), 167 (41), 155 (23), 137 (22), 111 (38), 91 (36), 73 (93), 55 (100); HRFABMS *m/z* 603.2458 $[M-H]^-$ (calcd for $C_{31}H_{39}O_{12}$ 603.2442, error: 2.8 ppm).

3.3.2. Dysoxylumic acid B (2). The title compound was obtained as white powder: mp 208–210°C; $[\alpha]_D^{25}$=+21.6 (*c* 0.15, CH_3OH); IR (KBr) ν_{max} 3437, 2973, 2934, 1739, 1642, 1583, 1463, 1387, 1273, 1206, 1139, 1095, 1020, 933, 908, 856 cm^{-1}; ^1H NMR spectral data, see Table 2; ^{13}C NMR spectral data, see Table 1; FABMS *m/z* 635 $[M-H]^-$ (45), 620 (20), 571 (12), 537 (15), 507 (20), 491 (50), 463 (40), 417 (15), 375 (30), 311 (35), 283 (43), 265 (62), 235 (98), 189 (25), 117 (100); HRFABMS *m/z* 635.2324 $[M-H]^-$ (calcd for $C_{31}H_{39}O_{14}$ 635.2340, error: 2.5 ppm).

3.3.3. Dysoxylumic acid C (3). The title compound was obtained as white powder: mp 173–175°C; $[\alpha]_D^{19}$=+11.2 (*c* 0.67, CH_3OH); IR (KBr) ν_{max} 3422, 2972, 2939, 2881, 1745, 1640, 1507, 1461, 1391, 1267, 1138, 1068, 1031, 1000, 957, 909, 874, 792, 633 cm^{-1}; ^1H NMR spectral data, see Table 2; ^{13}C NMR spectral data, see Table 1; EIMS *m/z* 486 $[M-ROH]^+$ (2), 468 (4), 450 (7), 406 (5), 339 (4), 263 (6), 241 (13), 224 (15), 197 (13), 169 (13), 152 (16), 141 (14), 128 (18), 109 (30), 95 (25), 76 (100); HRFABMS *m/z* 603.2464 $[M-H]^-$ (calcd for $C_{31}H_{39}O_{12}$ 603.2442, error: 3.7 ppm).

3.3.4. Dysoxylumolide A (4). The title compound was obtained as white powder: mp 171–174°C; $[\alpha]_D^{19}$=+55.6 (*c* 0.45, CH_3OH); IR (KBr) ν_{max} 3480, 2967, 2930, 2878, 1743, 1642, 1465, 1393, 1271, 1181, 1173, 1075, 1032, 913, 873, 774 cm^{-1}; ^1H NMR spectral data, see Table 3; ^{13}C NMR spectral data, see Table 1; EIMS *m/z* 686 $[M]^+$ (0.4) 568 $[M-ROH]^+$ (25) 553 $[M-ROH-CH_3]^+$ (10) 451 (6) 435 (7) 421 (10), 379 (5), 357 (6), 343 (8), 3.9 (5), 293 (6), 265 (7), 241 (20), 225 (32), 211 (35), 197 (21), 143 (20), 115 (43), 91 (33), 73 (93), 55 (100); HRFABMS *m/z* 685.2862 $[M-H]^-$ (calcd for $C_{36}H_{45}O_{13}$ 685.2860, error: 0.3 ppm).

3.3.5. Dysoxylumic acid D (5). The title compound was obtained as white powder: mp 128–130°C; $[\alpha]_D^{19}$=−20.3 (*c* 0.61, CH_3OH); IR (KBr) ν_{max} 3448, 2970, 2938, 2881, 1735, 1650, 1506, 1468, 1389, 1228, 1137, 1036, 943, 874, 794, 603 cm^{-1}; ^1H NMR spectral data, see Table 3; ^{13}C NMR spectral data, see Table 1; FABMS *m/z* 781 $[M-H]^-$ (60), 663 $[M-H-ROH]^+$ (5), 603 (25), 485 (4), 199 (22), 117 $[RO]^+$ (100); HRFABMS *m/z* 781.3319 $[M-H]^-$ (calcd for $C_{38}H_{53}O_{17}$ 781.3283, error: 4.6 ppm).

3.3.6. Dysoxylumolide B (6). The title compound was obtained as white powder: mp 134–136°C; $[\alpha]_D^{19}$=−23.7 (*c* 0.70, CH_3OH); IR (KBr) ν_{max} 3424, 2969, 2937, 2880, 1737, 1648, 1466, 1388, 1202, 1137, 1063, 1032, 999, 875, 791, 646 cm^{-1}; ^1H NMR spectral data, see Table 3; ^{13}C NMR spectral data, see Table 1; EIMS *m/z* 604 $[M-ROH]^+$ (5), 568 (6), 552 (2), 468 (5), 450 (10), 422 (5), 388 (5), 241 (22), 226 (42), 197 (17), 181 (34), 167 (41), 137 (25), 123 (46), 109 (54), 91 (27), 70 (100); HRFABMS *m/z* 721.3039 $[M-H]^-$ (calcd for $C_{36}H_{49}O_{15}$ 721.3071, error: 4.5 ppm).

3.3.7. Dysoxylumolide C (7). The title compound was obtained as colorless crystals: mp 129–132°C; $[\alpha]_D^{27}$=+31.8 (*c* 0.21, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 209.5 (4.28) nm; IR (KBr) ν_{max} 3510, 2970, 2881, 1743, 1692, 1636, 1469, 1398, 1373, 1324, 1265, 1217, 1074, 1058, 1029, 994, 929, 804, 766 cm^{-1}; ^1H NMR spectral data, see Table 3; ^{13}C NMR spectral data, see Table 1; EIMS *m/z* 670 $[M-H_2O]^+$ (2), 554 (5), 453 (8), 329 (47), 313 (5), 145 (30), 95 (50), 73 (100); HRFABMS *m/z* 687.3071 $[M-H]^-$ (calcd for $C_{36}H_{47}O_{13}$ 687.3017, error: 8.0 ppm).

3.4. Feeding inhibition assay on the fifth instar larvae of *P. rapae* L

The test compounds and EtOH extract were dissolved in acetone at concentrations of 500 and 1000 ppm, respectively. Leaf disks of *Brassica oleracea* L (2.0 cm diameter) were dipped in the test solutions and the control discs were in acetone for 1 s. All the leaf disks were dried before being presented to the insect. The test insects were fifth instar larvae of *P. rapae* L, which had been deprived of food for 6 h prior to being individually placed in the Petri dish. Ten Petri dishes, each containing one larva and five leaf discs were used for each sample. After 24 h, the areas eaten were measured by a LI-3000 area-measurement apparatus. The antifeedant rate (AR) was calculated from $[(C-T)/C]100$, where *C* and *T* are control discs areas eaten and treated discs areas eaten, respectively.

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