Limonoids and Triterpenoids from the Stem Bark of *Melia toosendan*

Yi Zhang, Chun-Ping Tang, Chang-Qiang Ke, Sheng Yao, and Yang Ye*

State Key Laboratory of Drug Research & Natural Products Chemistry Department, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu-Chong-Zhi Road, Zhangjiang Hi-Tech Park, Shanghai 201203, People's Republic of China

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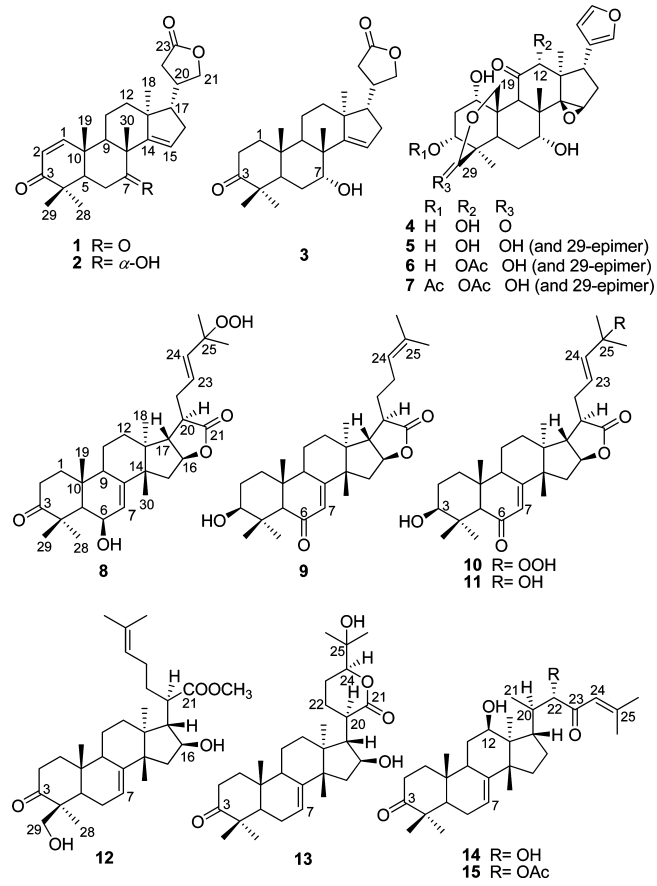
Four new limonoids (**1**, **3**, **4**, **6**), named meliatoosenins A−D, eight new euphane- and tirucallane-type triterpenoids (**8**−**15**), named meliasenins A−H, and 13 known compounds have been isolated from the stem bark of *Melia toosendan*. The structures of new compounds were established on the basis of 1D and 2D NMR experiments (^{1}H−^{1}H COSY, HSQC, HMBC, and ROESY).

Melia toosendan Sieb. et Zucc. (Meliaceae) is distributed mainly in the southwest region of China. The fruits and bark are commonly used in traditional Chinese medicine for acesodyne and desinsection.[1] Its chemical constituents reported in previous investigations included highly functionalized limonoids such as meliacins, trichilinins, C-19/C-29-bridged acetals, ring C-*seco* limonoids, highly oxidized C-*seco* limonoids and spiro limonoids, and euphane- and tirucallane-type triterpenoids.[2–5] Some limonoids were reported to have antifeedant,[2] cytotoxic,[3] antibacterial,[4] antineoplastic,[6] anti-inflammatory,[7] and/or analgesic[7] activities. In this paper, we report results of a detailed investigation of the stem bark of *M. toosendan*. Four new limonoids (**1**, **3**, **4**, **6**), eight new euphane- and tirucallane-type triterpenoids (**8**−**15**), and 13 known compounds were isolated. Their structures were elucidated by analyses of 1D and 2D NMR spectra and comparison with literature data.



Results and Discussion

Compound **1** was obtained as a white solid. Its molecular formula was established by HRESIMS as $C_{26}H_{34}O_4$ with 10 degrees of unsaturation. Inspection of ^{1}H and ^{13}C NMR data of **1** (Tables 1 and 2) showed the presence of five methyl, six methylene (one oxygenated), seven methine (three olefinic), and eight quaternary carbons (one olefinic and three carbonyls). The IR spectrum had absorption bands at 1780, 1711, and 1670 cm^{-1}, assigned to a γ-lactone group (supported by ^{13}C NMR data at δ_C 176.6 and 72.3), a carbonyl (δ_C 209.2), and an α,β-unsaturated carbonyl group (δ_C 203.4, 126.1, and 156.1), respectively.[8] The presence of a γ-lactone ring was further supported by HMBC correlations from the carbonyl to the oxygenated methylene (δ_H 4.46 and 3.95). The *Z*-geometry of the double bond was deduced from the coupling constant (10.2 Hz) between two olefinic protons at δ_H 7.12 and 5.92 in the ^{1}H NMR. The spectroscopic data revealed that compound **1** was a tetranortriterpenoid possessing a structure similar to the known compound **2**, isolated also from this plant.[8] However, the 7-oxygenated carbon in the latter was replaced by a carbonyl (δ_C 209.2). The structure was confirmed by HMBC correlations from this carbonyl carbon to H-5, H-9, and H_3-30, and the relative configuration of **1** was deduced from its ROESY spectrum to be the same as that of **2**. Compound **1** was named meliatoosenin A.

The molecular formula of compound **3** was determined to be $C_{26}H_{38}O_4$, by HRESIMS, with eight degrees of unsaturation. Comparison of NMR data of compounds **2** and **3** (Tables 1 and 2) indicated that they were similar in structure, except that two methylenes (δ_H 1.52, 1.84, H_2-1; δ_H 2.43, 2.53, H_2-2) were observed in **3** rather than two methines of the $\Delta^{1,2}$-double bond in **2**.[8] This observation was confirmed by HMBC correlations from the carbonyl C-3 to H_2-1 and H_2-2. The relative configuration of **3** resembled that of **2**, which was substantiated by the ROESY experiment. Thus, compound **3** was named meliatoosenin B.

The molecular formula of compound **4** ($C_{26}H_{32}O_9$, by HRESIMS) indicated 11 degrees of unsaturation. The IR spectrum showed OH and carbonyl absorptions at 3425 and 1714 cm^{-1}, respectively. The ^{1}H NMR spectrum of **4** (Table 1) displayed signals typical of a β-substituted furan ring (δ_H 7.57, 6.98, 7.56), and three tertiary methyls (δ_H 1.89, 1.54, 1.35). Analyses of 1D and 2D spectra suggested that **4** was a tetranortriterpenoid, similar to the known compound **5** except for replacement of the 29-hemiacetal group in the latter by a carbonyl group.[9] This was consistent with one more degree of unsaturation in **4**, compared with **5**, and was supported by HMBC correlations from the carbonyl C-29 to H_3-28, H-5, and H_2-19. Assignments of the ^{1}H and ^{13}C NMR signals of **4** were inferred by ^{1}H−^{1}H COSY, HSQC, HMBC, and ROESY spectra.

Compound **6**, a white powder, was designated a molecular formula of $C_{28}H_{36}O_{10}$ by HRESIMS. The ^{1}H and ^{13}C NMR spectra of **6** revealed chemical shifts at δ_H 2.05 (3H, s) and at δ_C 27.8 (q)

* To whom correspondence should be addressed. Tel: +86-21-50806726. Fax: +86-50806726. E-mail: yye@mail.shcnc.ac.cn.

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Table 1. ^{1}H NMR Data of Compounds **1**, **3**, **4**, and **6** (δ in ppm, J in Hz)

no.	**1**[a]	**3**[a]	**4**[b]	**6**[c]
1	7.12 (d, 10.2)	1.52 (m), 1.84 (m)	4.64 (s)	4.67 (s)
2a	5.92 (d, 10.2)	2.43 (ddd, 15.8, 7.2, 3.8)	2.18 (d, 15.3)	2.18 (m)
2b		2.53 (dt, 15.9, 8.0)	2.26 (d, 16.0)	2.26 (m)
3			4.14 (s)	3.61 (m)
5	2.10 (dd, 14.6, 2.8)	2.08 (dd, 12.5, 2.5)	3.58 (d, 13.1)	3.49 (dt, 14.8, 3.7)
6a	2.40 (dd, 14.3, 2.3)	1.78 (m)	2.11 (t, 13.4)	2.27 (m)
6b	2.88 (t, 14.5)		1.80 (t, 13.5)	2.05 (m)
7		3.96 (t, 3.4)	3.93 (s)	3.95 (br s)
9	2.13 (d, 5.7)	2.02 (t, 9.6)	5.40 (s)	5.45 (s)
11	1.88 (m), 1.99 (m)	1.60 (m), 1.74 (m)		
12	1.63 (m), 1.70 (m)	1.49 (m), 1.68 (m)	4.51 (s)	6.02 (s)
15	5.97 (dd, 3.4, 1.8)	5.49 (s)	3.99 (s)	4.04 (s)
16a	2.23 (m)	2.21 (m)	2.02 (dd, 14.0, 9.7)	2.18 (m)
16b			2.32 (dd, 13.1, 5.9)	2.35 (m)
17	1.74 (m)	1.74 (m)	3.29 (dd, 10.4, 6.3)	3.28 (dd, 10.7, 6.1)
18	1.00 (s)	1.03 (s)	1.89 (s)	1.93 (s)
19a	1.36 (s)	1.00 (s)	4.89 (d, 13.9)	4.80 (d, 12.3)
19b			5.31 (d, 13.9)	4.93 (d, 10.8)
20	2.74 (m)	2.72 (m)	7.57 (s)	7.60 (s)
21a	4.46 (t, 9.3)	4.47 (t, 9.4)	6.98 (s)	6.35 (s)
21b	3.95 (t, 9.3)	3.93 (t, 9.4)		
22a	2.23 (m)	2.24 (m)	7.56 (s)	7.42 (s)
22b	2.55 (dd, 17.1, 8.0)	2.53 (m)		
28	1.16 (s)	1.05 (s)	1.54 (s)	1.43 (s)
29	1.12 (s)	1.10 (s)		5.45 (s)
30	1.38 (s)	1.10 (s)	1.35 (s)	1.38 (s)
-AcO				2.05 (s)

[a] In $CDCl_3$, 600 MHz. [b] In C_5D_5N, 600 MHz. [c] In C_5D_5N, 300 MHz.

Table 2. ^{13}C NMR Data of Compounds **1**, **3**, **4**, and **6** (100 MHz, δ in ppm)

no.	**1**[a]	**3**[a]	**4**[b]	**6**[b]
1	156.1 d	38.5 t	72.0 d	71.9 d
2	126.1 d	34.0 t	34.3 t	38.3 t
3	203.4 s	217.3 s	74.8 d	75.5 d
4	39.6 s	46.9 s	48.9 s	41.8 s
5	52.5 d	46.4 d	27.7 d	27.8 d
6	36.1 t	24.7 t	29.1 t	26.2 t
7	209.2 s	71.9 d	69.8 d	70.1 d
8	52.4 s	44.0 s	43.7 s	43.2 s
9	44.6 d	40.8 d	49.6 d	50.0 d
10	44.7 s	37.1 s	40.8 s	43.2 s
11	17.2 t	16.1 t	215.4 s	208.7 s
12	34.2 t	33.1 t	79.0 d	78.8 d
13	47.2 s	46.7 s	47.4 s	46.2 s
14	152.1 s	161.2 s	73.5 s	73.2 s
15	126.3 d	119.6 d	58.2 d	59.2 d
16	35.3 t	34.7 t	33.5 t	34.2 t
17	58.2 d	58.1 d	40.6 d	39.2 d
18	21.0 q	19.4 q	15.0 q	15.7 q
19	18.5 q	15.0 q	73.3 t	64.5 t
20	37.4 d	37.3 d	125.3 s	123.7 s
21	72.3 t	72.4 t	141.2 d	141.3 d
22	34.0 t	37.3 d	113.8 d	112.6 d
23	176.6 s	176.6 s	142.5 d	143.0 d
28	26.6 q	26.2 q	21.0 q	21.4 q
29	21.0 q	21.1 q	175.4 s	97.3 d
30	28.0 q	27.2 q	22.2 q	23.0 q
-OAc				170.6 s
				27.8 q

[a] In $CDCl_3$. [b] In C_5D_5N.

and 170.6 (s), indicative of an acetyl group. The remaining resonances of **6** suggested a tetranortriterpenoid skeleton similar to that in **5** and its analogue toosendanin (**7**).[9,10] Compared to **5**, the relatively big NMR differences were observed at positions 11 and 17 of **6**, while at positions 1 and 5 compared to **7**. Therefore, the acetyl group in **6** was deduced to be at C-12. Accordingly, the structure of **6** was established as shown.

The molecular formula of compound **8** was determined to be $C_{30}H_{44}O_6$. The IR spectrum indicated the presence of an OH group (3435 cm^{-1}), a γ-lactone group (1778 cm^{-1}, supported by δ_C 179.6 and 82.3), and a carbonyl (1705 cm^{-1}).[11] Analyses of its NMR data revealed that **8** possessed a euphane-type triterpenoid skeleton. Compared with the reference compounds 6β-hydroxykulactone and meliastatin 3, compound **8** was deduced to share the same tetranuclear moiety as the former and the same side chain as the latter.[11,12] The structure of **8** was supported by the HMBC experiment.

Meliasenin B (**9**) possessed a molecular formula of $C_{30}H_{44}O_4$ by HRESIMS, suggesting nine degrees of unsaturation. The IR spectrum indicated the presence of OH, γ-lactone, and α,β-unsaturated carbonyl groups. NMR data (Tables 3 and 4) indicated a euphane-type triterpenoid similar to 6β-hydroxykulactone. In the HMBC spectrum, correlations from the oxygenated methine carbon to H_2-1, H_3-28, and H_3-29 suggested an OH group at C-3, and the presence of an α,β-unsaturated carbonyl group in the molecule indicated a carbonyl at C-6. The relative configuration of **9** was deduced from its analogues 6β-hydroxykulactone and kulactone (its relative configuration was confirmed by X-ray diffraction technology) and substantiated by its ROESY spectrum.[13] The OH-3 was determined to be β-oriented by the ROESY correlations of H-3/H_3-28α and H-3/H-5α.

The molecular formula of **10** was established to be $C_{30}H_{44}O_5$ by HREIMS. Its NMR data (Tables 3 and 4), compared with those of compound **9** and meliastatin 2, revealed that **10** had the same tetranuclear moiety as the former and the same side chain as the latter.[12] The structure of **10** was further supported by its ^{1}H$-^1$H COSY, HMBC, and ROESY spectra.

Meliasenin D (**11**) exhibited a molecular formula of $C_{30}H_{44}O_6$ by HREIMS, one oxygen atom more than that of **10**. Its NMR data (Tables 3 and 4) resembled those of **10**, except for some slight differences in the side chain. Taking one more oxygen atom into account, a hydroperoxy group instead of a hydroxy group was placed at C-25 in this structure. Such a side chain, the same as that of **8**, was verified by the highly superimposable NMR data of the corresponding moieties in compounds **8** and **10**.

Compound **12** was obtained as a white solid ($C_{31}H_{48}O_5$ by HREIMS). Inspection of the ^{1}H and ^{13}C NMR data of **12** (Tables 3 and 4) revealed that these data were very similar to those of methyl kulonate, another triterpenoid from this plant, except for

Table 3. ^{1}H NMR Data of Compounds **8**−**13** (δ in ppm, J in Hz)

no.	**8**[a]	**9**[b]	**10**[b]	**11**[c]	**12**[b]	**13**[b]
1a	1.48 (m)	1.39 (m)	1.40 (m)	1.40 (m)	1.52 (td, 13.5, 4.3)	1.45 (td, 14.4, 4.2)
1b	1.95 (m)	1.67 (m)	1.68 (m)	1.68 (m)	2.01 (m)	1.98 (m)
2a	2.21 (ddd, 16.6, 9.5, 3.1)	1.56 (m)	1.56 (m)	1.56 (m)	2.37 (br d, 15.7)	2.25 (m)
2b	2.86 (td, 14.3, 5.5)	1.65 (m)	1.65 (m)	1.65 (m)	2.68 (td, 14.4, 5.7)	2.77 (td, 14.6, 5.6)
3		3.19 (dd, 11.7, 3.5)	3.21 (dd, 11.1, 3.3)	3.21 (dd, 11.2, 3.5)		
5	1.48 (m)	2.09 (s)	2.10 (s)	2.11 (s)	1.86 (m)	1.72 (dd, 10.9, 6.6)
6a	4.48 (br s)				2.17 (br d, 17.4)	2.10 (m)
6b					2.00 (m)	
7	5.45 (m)	5.69 (d, 2.7)	5.74 (s)	5.70 (d, 2.5)	5.27 (s)	5.37 (d, 2.8)
9	2.32 (m)	2.89 (m)	2.88 (ddd, 11.6, 8.0, 3.5)	2.89 (m)	2.32 (m)	2.25 (m)
11	1.62 (m), 1.76 (m)	1.64 (m), 1.92 (m)	1.63 (m), 1.91 (m)	1.62 (m), 1.89 (m)	1.59 (m)	1.59 (m)
12	1.76 (m)	1.79 (m)	1.78 (m)	1.78 (m)	1.64 (m)	1.58 (m), 1.91 (t, 11.2)
15a	2.32 (m)	2.32 (dd, 13.7, 10.2)	2.34 (m)	2.33 (dd, 13.8, 10.2)	2.04 (m)	2.06 (m)
15b	1.76 (m)	1.76 (dd, 13.7, 7.7)	1.80 (m)	1.77 (dd, 13.5, 8.1)	1.61 (m)	1.75 (d, 13.4)
16	4.18 (td, 10.3, 7.6)	4.14 (td, 10.2, 7.8)	4.18 (ddd, 10.6, 7.6, 1.1)	4.19 (dt, 10.0, 7.7)	3.97 (dd, 7.6, 6.4)	4.02 (dd, 8.3, 5.1)
17	2.21 (m)	2.12 (dd, 14.5, 9.4)	2.19 (t, 11.4)	2.23 (t, 11.8)	2.07 (dd, 10.4, 5.8)	2.10 (m)
18	0.90 (s)	1.09 (s)	0.98 (s)	0.98 (s)	1.16 (s)	0.91 (s)
19	1.25 (s)	0.85 (s)	0.87 (s)	0.86 (s)	0.98 (s)	1.03 (s)
20	2.55 (m)	2.43 (ddd, 12.5, 7.9, 4.6)	2.54 (m)	2.54 (m)	2.59 (td, 10.5, 3.6)	2.64 (m)
22	2.43 (m), 2.55 (m)	1.45 (m), 1.92 (m)	2.38 (m), 2.60 (m)	2.45 (m), 2.58 (m)	1.96 (m), 1.60 (m)	2.26 (m), 1.55 (m)
23	5.66 (m)	2.02 (dd, 14.9, 7.4)	5.60 (ddd, 15.3, 7.2, 5.4)	5.66 (m)	1.88 (m)	1.96 (m), 1.82 (m)
24	5.66 (m)	5.08 (m)	5.70 (br d, 15.3)	5.67 (br s)	5.05 (t, 6.6)	4.15 (dd, 11.9, 3.3)
26	1.32 (s)	1.67 (s)	1.32 (s)	1.32 (s)	1.67 (s)	1.31 (s)
27	1.34 (s)	1.60 (s)	1.32 (s)	1.34 (s)	1.57 (s)	1.24 (s)
28	1.52 (s)	1.29 (s)	1.32 (s)	1.31 (s)	1.16 (s)	1.05 (s)
29a	1.22 (s)	1.09 (s)	1.11 (s)	1.11 (s)	4.05 (d, 11.0)	1.13 (s)
29b					3.62 (d, 11.0)	
30	1.28 (s)	1.25 (s)	1.26 (s)	1.25 (s)	1.26 (s)	1.34 (s)
-MeO					3.70 (s)	

[a] In $CDCl_3$, 400 MHz. [b] In $CDCl_3$, 600 MHz. [c] In $CDCl_3$, 300 MHz.

Table 4. ^{13}C NMR Data of Compounds **8**−**15** (in $CDCl_3$, 100 MHz, δ in ppm)

no.	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
1	39.9 t	36.7 t	36.7 t	36.7 t	37.3 t	38.5 t	38.4 t	38.4 t
2	34.6 t	26.4 t	26.4 t	26.4 t	35.5 t	34.9 t	34.8 t	34.8 t
3	215.8 s	78.7 d	78.9 t	78.9 d	216.2 s	216.7 t	216.7 s	216.6 s
4	49.0 s	38.0 s	38.0 t	38.0 s	53.2 s	47.9 s	47.8 s	47.8 s
5	56.7 d	65.6 d	65.6 d	65.6 d	53.4 d	52.4 d	52.2 d	52.2 d
6	67.0 d	199.2 s	199.2 s	199.3 s	24.6 t	24.3 t	24.4 t	24.4 t
7	121.9 d	124.6 d	124.7 d	124.6 d	118.5 d	118.7 d	118.8 d	119.0 d
8	145.9 s	167.2 s	167.0 s	167.2 s	144.8 s	144.4 s	144.8 s	144.5 s
9	48.8 d	49.8 d	49.9 d	49.9 d	47.7 d	48.0 d	47.6 d	47.5 d
10	35.4 s	44.3 s	44.4 s	44.4 s	35.0 s	35.0 s	35.0 s	34.9 s
11	16.7 t	16.4 t	16.4 t	16.4 t	18.2 t	18.1 t	29.8 t	30.0 t
12	29.0 t	28.9 t	28.9 t	28.5 t	31.4 t	33.4 t	74.5 d	74.4 d
13	39.3 s	39.2 s	39.2 s	39.2 s	45.4 s	45.8 s	47.9 s	48.0 s
14	55.2 s	55.8 s	55.9 s	55.9 s	49.8 s	49.9 s	51.6 s	51.7 s
15	35.5 t	34.8 t	34.8 t	34.8 t	44.6 t	43.9 t	35.1 t	34.9 t
16	82.3 d	81.5 d	81.7 d	81.8 d	77.2 d	77.3 d	28.2 t	28.0 t
17	56.7 d	57.5 d	56.5 d	56.2 d	58.6 d	57.9 d	40.7 d	40.5 d
18	21.4 q	21.3 q	21.5 q	21.4 q	23.6 q	23.2 q	19.8 q	19.7 q
19	15.0 q	13.8 q	13.9 q	13.9 q	13.5 q	12.8 q	12.7 q	12.7 q
20	45.5 d	45.1 d	45.7 d	45.4 d	47.2 d	41.8 d	39.6 d	37.7 d
21	179.6 s	180.0 s	179.2 s	179.2 s	177.7 s	178.3 s	11.5 q	12.8 q
22	31.6 t	29.1 t	31.4 t	31.5 t	33.0 t	21.2 t	78.5 d	80.1 d
23	127.2 d	25.9 t	123.0 d	127.0 d	25.7 t	22.7 t	200.9 s	196.1 s
24	137.0 d	123.1 d	141.3 d	137.2 d	123.3 d	83.4 d	118.9 d	119.4 d
25	81.8 s	132.8 s	70.6 s	81.7 s	132.5 s	71.0 s	160.0 s	159.3 s
26	24.4 q	25.6 q	29.9 q	24.4 q	25.7 q	26.1 q	28.1 q	28.1 q
27	24.2 q	17.8 q	29.9 q	24.1 q	17.6 q	24.3 q	21.4 q	21.2 q
28	24.7 q	28.2 q	28.2 q	28.2 q	20.6 q	24.5 q	24.5 q	24.5 q
29	23.8 q	14.7 q	14.7 q	14.7 q	65.7 t	21.5 q	21.5 q	21.5 q
30	31.3 q	29.6 q	29.6 q	29.5 q	27.9 q	27.4 q	28.2 q	28.1 q
−OMe					51.3 q			
−OAc								170.7 s
								20.8 q

the chemical shifts of a hydroxymethylene (δ_C 65.7, t; δ_H 4.05, d, J = 11.0 Hz and 3.62, d, J = 11.0 Hz) in **12** taking the place of CH_3-29 in methyl kulonate.[12,14] This suggested that an OH was present at C-29. This was confirmed by HMBC correlations from C-29 to H_3-28 and H-5 and from H_2-29 to C-3 and C-28. The relative configuration of **12** was the same as that of methyl kulonate, as established by the ROESY spectrum. The ROESY correlation of H_2-29/H_3-19 definitely indicated β-orientation for the hydroxymethylene group.

The ^{1}H and ^{13}C NMR data of compound **13**, $C_{30}H_{46}O_5$ by HREIMS (Tables 3 and 4), suggested that **13** had the same carbon skeleton as dubione 7, but it differed in the side chain.[12] Compared with dubione 7, **13** contained two more hydrogen and one more oxygen atom and one less degree of unsaturation. In its ^{13}C NMR

Table 5. ^{1}H NMR Data of Compounds **14** and **15** (in $CDCl_3$, δ in ppm, J in Hz)

no.	**14**[a]	**15**[b]
1a	1.48 (m)	1.48 (m)
1b	2.03 (ddd, 13.2, 5.3, 3.1)	2.03 (m)
2a	2.24 (m)	2.24 (m)
2b	2.77 (td, 14.5, 5.5)	2.77 (td, 14.4, 4.9)
5	1.71 (m)	1.71 (m)
6	2.11 (m)	2.10 (m)
7	5.36 (d, 2.9)	5.37 (s)
9	2.25 (m)	2.25 (m)
11	1.54 (m), 2.20 (m)	1.54 (m), 2.20 (m)
12	3.87 (dd, 8.8, 7.4)	3.90 (t, 8.3)
15	1.59 (m)	1.60 (m)
16	1.49 (m), 2.28 (m)	1.50 (m), 2.28 (m)
17	2.56 (dd, 18.4, 9.8)	2.35 (dd, 19.1, 9.4)
18	0.82 (s)	0.82 (s)
19	1.03 (s)	1.04 (s)
20	1.88 (m)	2.08 (m)
21	0.75 (d, 7.5)	0.96 (d, 6.7)
22	4.20 (s)	5.15 (s)
24	6.09 (s)	6.09 (d, 1.2)
26	1.98 (s)	1.95 (s)
27	2.23 (s)	2.18 (s)
28	1.05 (s)	1.06 (s)
29	1.12 (s)	1.13 (s)
30	1.17 (s)	1.14 (s)
-AcO		2.20 (d, 1.2)

[a] In $CDCl_3$, 600 MHz. [b] In $CDCl_3$, 300 MHz.

spectrum, the typical $\Delta^{7,8}$-double bond [δ_C 118.7 (d) and 144.4 (s)] was present, while the $\Delta^{25,26}$-double bond was replaced by a methyl carbon and an oxygenated quaternary carbon. Therefore, the $\Delta^{25,26}$-double bond of dubione 7 was not present in **13**, whereas an OH group was attached to C-25. The structure was supported by HMBC correlations between C-24 and H_3-26, H_3-27, and the relative configuration of **13** was determined by the ROESY spectrum to be the same as that of dubione 7.

Compound **14** had the molecular formula $C_{30}H_{46}O_4$, and inspection of the ^{1}H and ^{13}C NMR data (Tables 4 and 5) revealed a tirucallane-type triterpenoid skeleton similar to that of 22α-hydroxytirucalla-7,24-dien-3,23-dione.[15,16] The difference was that one oxygenated methine (δ_H 3.87, dd, J = 8.8, 7.4 Hz; δ_C 74.5, d) in **14** replaced a methylene in the known compound. The HMBC spectrum showed correlations from the oxymethine proton to C-11, C-14, C-15, and C-18, suggesting an OH at C-12. The relative configuration of **14** was confirmed to be identical to that of 22α-hydroxytirucalla-7,24-dien-3,23-dione by the ROESY spectrum, and the β-orientation of OH-12 was deduced from the correlations of H-12/H_3-18α and H-12/H-9α.

The NMR data (Tables 4 and 5) of compound **15** ($C_{32}H_{48}O_5$) resembled those of **14** except for signals of an additional acetyl group (δ_H 2.20, d, J = 1.2 Hz; δ_C 170.7, s; 20.8, q). The acetyl group was placed at C-22 due to the NMR differences observed at/around this position ($\Delta\delta_H$ 0.20, H-20; 0.21, H_3-21; 0.95, H-22; $\Delta\delta_C$ 1.9, C-20; 1.6, C-22; −4.8, C-23) compared with **14**. Thus, compound **15** had an acetoxy group at C-22, rather than a hydroxy as in **14**.

Compared with the literature data, the known compounds were identified as carda-1,4-dienolide,7-hydroxy-4,4,8-trimethyl-3-oxo-(5α,7α,13α,17α)-(9Cl) (**2**),[8] 24-norchola-20,22-diene-4-carboraldehyde-14,15:21,23-diepoxy-1,3,7,12,19-pentachydroxy-4,8-dimethyl-11-oxo-cyclic-4,19-hemiacetal[C(S),1α,3α,4β,5α,7α,12α,13α,14β,15β,17α]-(9Cl) (**5**),[9] toosendanin (**7**),[10] 12-deacetyltoosendanin,[2] 12-*O*-acetylazedarachin A,[2] 12-hydroxyamoorastatone,[2,19] iso-chuanliansu,[10] 1-tigloyl-3,20-diacetyl-11-methoxymeliacarpinin,[20] 3-tigloyl-1,20-diacetyl-11-methoxylmeliacarpinin,[20] 1-cinnamoy-3-acetyl-11-methoxymeliacarpinin,[20] meliastatin 2,[12] methyl kulonate,[12,14] and toosendanone A,[5] respectively (structures, see Supporting Information).

Experimental Section

General Experimental Procedures. Melting points were determined on a XT-4 microscopic thermometer without correction. Optical rotations were taken on a Perkin-Elmer 341 polarimeter. IR spectra were recorded on Nicolet Magna FT-IR 750 spectrophotometer using KBr disks. NMR spectra were recorded on Bruker AM-300, AM-400, and INVOR-600 NMR spectrometers. The chemical shift (δ) values are given in ppm with TMS as internal standard, and coupling constants (J) are in Hz. EIMS and HREIMS spectra were recorded on a Finnigan MAT-95 mass spectrometer. ESIMS and HRESIMS spectra were recorded on a Micromass LC-MS-MS mass spectrometer. Column chromatographic separations were carried out using silica gel (200−300 mesh and H60, QingdaoHaiyang Chemical Group Corporation, People's Republic of China), MCI gel CHP20P (75−150 μm, Mitsubishi Chemical Industries, Japan), and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala, Sweden) as packing material. TLC was carried out on precoated silica gel GF_{254} plates (Yantai Chemical Industrials), and the TLC spots were viewed at 254 nm and visualized using 5% sulfuric acid in alcohol containing 10 mg/mL vanillin. Analytical HPLC was performed on a Waters 2690 instrument with a 996 PAD (photodiode array detector) coupled with an Alltech ELSD 2000 detector. Semi-preparative and preparative HPLC was performed on a Varian SD1 instrument with a 320 single-wave detector. Their chromatographic separations were carried out on C-18 columns (250 × 10 mm, 5 μm, Waters; 220 × 25 mm, 10 μm, Merck, respectively), using a gradient solvent system comprised of H_2O and CH_3CN, with a flow rate of 3.0 and 15.0 mL/min, respectively.

Plant Material. Stem bark of *M. toosendan* was collected in Yunnan Province of China and identified by Prof. Jin-Gui Shen of the Shanghai Institute of Materia Medica. A voucher (20080918) was deposited at the herbarium of the Shanghai Institute of Materia Medica, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried stem bark (4.6 kg) of *M. toosendan* was ground into powder and extracted with 95% EtOH. After evaporation of the EtOH, the crude extract was partitioned between water and ethyl ether. The ether-soluble portion (110 g) was chromatographed on a silica gel column eluted with petroleum ether/Me_2CO (from 20:1 to 1:1) to afford fractions 1−10. Fraction 5 (6.575 g) was chromatographed on a MCI gel column eluted with MeOH/H_2O (70% to 95%) to yield seven subfractions, 5A−5G. Subfractions 5D (922 mg) and 5G (886 mg) were separated by repeated column chromatography (CC) over Sephadex LH-20 ($CHCl_3$/MeOH, 1:1, and MeOH), silica gel, and preparative TLC, successively, affording **8** (7 mg), **14** (12 mg), and **15** (18 mg). Fraction 6 (5.718 g) was divided into eight subfractions (6A−6H) by MCI gel CC eluted with MeOH/H_2O (50% to 95%). Subfraction 6C (186 mg) was subjected to Sephadex LH-20 (MeOH) and silica gel ($CHCl_3$/Me_2CO, 50:1 to 20:1) CC to yield **10** (8 mg) and subfraction 6C1 (92 mg). Subfraction 6C1 was further separated by preparative HPLC (MeCN/H_2O, 30% to 55%) to afford **11** (30 mg). Subfraction 6E was chromatographed on a Sephadex LH-20 column ($CHCl_3$/MeOH, 1:1) and then a silica gel column ($CHCl_3$/Me_2CO, 20:1) to give **1** (5 mg) from 6E1 and seven other fractions (6E2−6E8). Subfraction 6E3 (30 mg) was purified by Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) CC and semipreparative HPLC (MeCN/H_2O, 40% to 75%), affording **3** (6 mg). Subfraction 6F (965 mg) was purified by Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) and silica gel ($CHCl_3$/Me_2CO, 50:1 to 10:1) CC to give two fractions. From the first fraction, compound **9** (111 mg) was crystallized from MeOH. Fraction 7 (2.586 g) was subjected to Sephadex LH-20 ($CHCl_3$/MeOH, 1:1, and then MeOH), MCI gel (MeOH/H_2O, 50% to 95%), silica gel ($CHCl_3$/MeOH, 300:1 to 200:1; $CHCl_3$/Me_2CO, 20:1) CC, and then preparative HPLC (MeCN/H_2O 45% to 70%), yielding **12** (18 mg) and **13** (21 mg). Fraction 9 (13.5 g) was subjected to CC over MCI gel (MeOH/H_2O, 30% to 90%) and silica gel ($CHCl_3$/MeOH, 125:1 to 10:1) to produce 10 subfractions (A−J). Subfraction 9H (98 mg) was separated on Sephadex LH-20 (MeOH) CC to afford **4** (10 mg). Subfraction 9J (593 mg) was purified by Sephadex LH-20 ($CHCl_3$/MeOH, 1:1, and then MeOH) and then silica gel ($CHCl_3$/MeOH, 50:1−20:1) CC to give **6** (119 mg).

Meliatoosenin A (1): white solid; mp 75.0−76.0 °C; $[\alpha]^{24}_D$ −86 (*c* 0.07, MeOH); IR (KBr) ν_{max} 3435, 2929, 1780, 1711, 1670, 1460, 1377, 1174, 1028 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m/z* 411.4 $[M + H]^+$, 433.3 $[M + Na]^+$, 843.5 $[2 M + Na]^+$; HRESIMS *m/z* 433.2372 $[M + Na]^+$ (calcd for $C_{26}H_{34}O_4Na$, 433.2355).

Meliatoosenin B (3): white powder; mp 215.0−216.0 °C; $[\alpha]^{24}_D$ −73 (*c* 0.075, MeOH); IR (KBr) ν_{max} 3543, 3448, 2970, 2870, 1782, 1701, 1458, 1385, 1174, 1026, 1001 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m/z* 437.3 $[M + Na]^+$, 851.7 $[2 M + Na]^+$; HRESIMS *m/z* 437.2687 $[M + Na]^+$ (calcd for $C_{26}H_{38}O_4Na$, 437.2668).

Meliatoosenin C (4): white powder; mp 227.5−228.5 °C; $[\alpha]^{24}_D$ −66 (*c* 0.08, MeOH); IR (KBr) ν_{max} 3425, 2945, 1714, 1637, 1383, 1157, 1070, 1028 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m/z* 489.2 $[M + H]^+$, 999.5 $[2 M + Na]^+$, 533.6 $[M + HCOO]^-$, 975.3 $[2 M - H]^-$; HRESIMS *m/z* 511.1953 $[M + Na]^+$ (calcd for $C_{26}H_{32}O_9Na$, 511.1944).

Meliatoosenin D (6): white, amorphous powder; $[\alpha]^{24}_D$ +22 (*c* 0.095, MeOH); IR (KBr) ν_{max} 3546, 3469, 3383, 2970, 1736, 1712, 1375, 1246, 1063, 1036, 982, 791, 600 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS *m/z* 555.3 $[M + Na]^+$, 1087.6 $[2 M + Na]^+$, 532.7 $[M - H]^-$, 578.0 $[M + HCOO]^-$; HRESIMS *m/z* 555.2205 $[M + Na]^+$ (calcd for $C_{28}H_{36}O_{10}Na$, 555.2206).

Meliasenin A (8): colorless oil; $[\alpha]^{24}_D$ −51 (*c* 0.1, MeOH); IR (KBr) ν_{max} 3435, 2970, 2877, 1778, 1705, 1664, 1458, 1385, 1161, 1134, 1061, 953, 754 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 3 and 4; ESIMS *m/z* 523.3 $[M + Na]^+$, 1023.6 $[2 M + Na]^+$, 545.7 $[M + HCOO]^-$; HRESIMS *m/z* 523.3035 $[M + Na]^+$ (calcd for $C_{30}H_{44}O_6Na$, 523.3036).

Meliasenin B (9): white solid; mp 206.5−207.0 °C; $[\alpha]^{24}_D$ −4 (*c* 0.125, MeOH); IR (KBr) ν_{max} 3500, 2931, 2872, 1774, 1658, 1626, 1456, 1388, 1153, 1045, 951, 866, 611 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 3 and 4; ESIMS *m/z* 469.3 $[M + H]^+$, 959.8 $[2 M + Na]^+$, 567.6 $[M - H]^-$; HRESIMS *m/z* 491.3118 $[M + Na]^+$ (calcd for $C_{30}H_{44}O_4Na$, 491.3137).

Meliasenin C (10): white, amorphous solid; $[\alpha]^{24}_D$ −6 (*c* 0.065, MeOH); IR (KBr) ν_{max} 3431, 2929, 2877, 1778, 1658, 1462, 1387, 1161, 1049, 951 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 3 and 4; EIMS *m/z* 484 $[M]^+$(6), 469 $[M - CH_3]^+$ (22), 451 (16), 423 (8), 327 (14), 313 (100), 161 (22), 135 (17), 121 (25), 91(20), 81(25), 55 (15); HREIMS *m/z* 484.3185 $[M]^+$ (calcd for $C_{30}H_{44}O_5$, 484. 3188).

Meliasenin D (11): white solid; mp 124.0−125.0 °C; $[\alpha]^{24}_D$ +10 (*c* 0.07, MeOH); IR (KBr) ν_{max} 3423, 2937, 2877, 1778, 1658, 1458, 1388, 1360, 1242, 1163, 1047, 951, 878, 611 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 3 and 4; EIMS *m/z* 500 $[M]^+$ (6), 484 $[M - O]^+$ (20), 469 (44), 451 (22), 429 (26), 411 (22), 385 (12), 327 (26), 313 (100), 161 (58), 121 (60), 81(36), 55 (25); HREIMS *m/z* 500.3138 $[M]^+$ (calcd for $C_{30}H_{44}O_6$, 500.3138).

Meliasenin E (12): white solid; mp 67.0−68.0 °C; $[\alpha]^{24}_D$ −27 (*c* 0.215, MeOH); IR (KBr) ν_{max} 3446, 2949, 1712, 1439, 1383, 1198, 1171, 1041, 991, 756 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 3 and 4; EIMS *m/z* 500 $[M]^+$ (2), 482 $[M - H_2O]^+$ (6), 467 (28), 437 (20), 418 (100), 388 (64), 370 (32), 355 (22), 329 (16), 299 (24), 257 (24), 211 (22), 154 (34), 145 (26), 119 (30), 69 (34), 55 (20); HREIMS *m/z* 500.3516 $[M]^+$ (calcd for $C_{31}H_{48}O_5$, 500.3502).

Meliasenin F (13): white powder; mp 189.0−190.0 °C; $[\alpha]^{24}_D$ −24 (*c* 0.14, MeOH); IR (KBr) ν_{max} 3446, 2972, 1709, 1448, 1387, 1202, 1047, 1016, 754 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 3 and 4; EIMS *m/z* 486 $[M]^+$ (2), 471 $[M - CH_3]^+$ (10), 453 (46), 435 (20), 407 (8), 314 (20), 370 (32), 329 (4), 313 (100), 295 (58), 267 (5), 239 (4), 211 (6), 158 (60), 141 (16), 112 (18), 85 (24), 71 (28), 57 (30); HREIMS *m/z* 486.3345 $[M]^+$ (calcd for $C_{30}H_{46}O_5$, 486.3345).

Meliasenin G (14): colorless oil; $[\alpha]^{24}_D$ +11 (*c* 0.125, MeOH); IR (KBr) ν_{max} 3450, 2947, 1707, 1678, 1620, 1450, 1385, 1247, 1107, 1026, 756 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 4 and 5; ESIMS *m/z* 963.8 $[2 M + Na]^+$, 469.9 $[M - H]^-$, 515.6 $[M + HCOO^-]^-$; HRESIMS *m/z* 493.3284 $[M + Na]^+$ (calcd for $C_{30}H_{46}O_4Na$, 493.3294).

Meliasenin H (15): colorless oil; $[\alpha]^{24}_D$ +21 (*c* 0.115, MeOH); IR (KBr) ν_{max} 3483, 2968, 1741, 1707, 1622, 1648, 1385, 1244, 1026, 754 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 4 and 5; ESIMS *m/z* 535.4 $[M + Na]^+$, 1047.7 $[2 M + Na]^+$, 557.7 $[M + HCOO]^-$; HRESIMS *m/z* 535.3390 $[M + Na]^+$ (calcd for $C_{32}H_{48}O_5Na$, 535.3399).

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Supporting Information Available: ^1H and ^{13}C NMR spectra for **1**−**15**, HMQC spectra for **1**, **3**, **4**, **6**, **10**, **12**−**14**, $^1H-^1H$ COSY spectra for **4**, **9**, **10**, **12**, **13**, HMBC spectra for **1**, **3**, **4**, **8**−**10**, **12**−**14**, ROESY spectra for **1**, **3**, **4**, **9**, **10**, **12**−**14**, HMBC correlations indicated for **1**, **3**, **4**, **8**−**14**, ROESY correlations indicated for **1**, **3**, **4**, **9**, **10**, **12**−**14**, and chemical structures of the 13 known compounds are available free of charge via the Internet at http://pubs.acs.org.

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