Meliarachins A – K: Eleven Limonoids from the Twigs and Leaves of *Melia azedarach*

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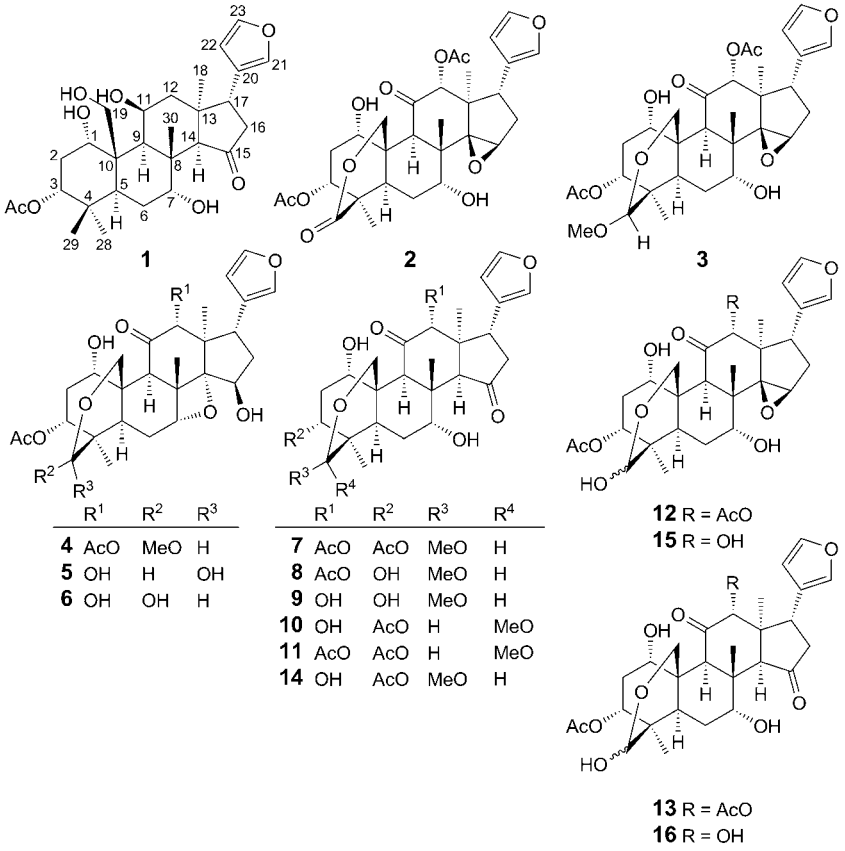
Eleven new limonoids, meliarachins A – K (**1** – **11**, resp.), together with five known ones, were isolated from the twigs and leaves of *Melia azedarach*. The structures of the new compounds were elucidated on the basis of spectroscopic analysis. Compounds **4** and **8** exhibited moderate antibacterial activities against *Gram*-positive bacteria.

Introduction. – Plants of the Meliaceae family are recognized for producing structurally diverse and biologically significant limonoids [1]. The tree *Melia azedarach* LINN. growing mainly in the tropical and subtropical area, such as India, Australia, and southern China, has been attracting considerable interests due largely to its insect antifeedant property and the traditional applications for medical purposes [2][3]. Previous studies on this plant have afforded a series of limonoids [4], triterpenoids [5], steriods [6], flavonoid glycosides [7], and simple phenolics [8]. As a part of our ongoing investigation on the chemical components of Meliaceae family, eleven new limonoids, meliarachins A – K (**1** – **11**, resp.), along with five known ones, toosendanin (**12**) [4a], isochuanliansu (**13**) [4a], neoazedarachin D (**14**) [4b], 12α-hydroxyamoorastatin (**15**) [4c], and 12α-hydroxyamoorastatone (**16**) [4c], were isolated from an EtOH extract of the twigs and leaves of *M. azedarach*. Among them, compounds **4** – **6** possessed a rare oxetane ring. Here, we present the details of the isolation, structure elucidation, and the antimicrobial evaluation of compounds **1** – **11**.

Results and Discussion. – Compound **1** has the molecular formula of $C_{28}H_{40}O_8$, as determined by the sodiated ion at *m/z* 527.2619 ($[M + Na]^+$, $C_{28}H_{40}NaO_8^+$; calc. 527.2621) in HR-ESI-MS. The IR spectrum indicated the presence of OH groups (3365 cm^{-1}) and of a CO group (1728 cm^{-1}). The ^{13}C-NMR spectrum exhibited 28 C-atom resonances consistent with the molecular composition. Four tertiary Me groups (δ(H) 0.81 (*s*), 0.93 (*s*), 1.06 (*s*), and 1.83 (*s*)), one O-bearing CH_2 group (δ(H) 4.32 (*d*, $J = 12.2$) and 4.51 ($J = 12.2$); δ(C) 61.2), an AcO group (δ(H) 1.92; δ(C) 21.1, 170.3), a keto CO group (δ(C) 221.8), and a β-substituted furanyl ring were readily distinguished by analysis of its NMR data (*Tables 1* and *2*) in combination with the HSQC spectrum. The identified functional groups accounted for five out of nine degrees of unsaturation



	R^1	R^2	R^3
4	AcO	MeO	H
5	OH	H	OH
6	OH	OH	H

	R^1	R^2	R^3	R^4
7	AcO	AcO	MeO	H
8	AcO	OH	MeO	H
9	OH	OH	MeO	H
10	OH	AcO	H	MeO
11	AcO	AcO	H	MeO
14	OH	AcO	MeO	H

12 R = AcO
15 R = OH

13 R = AcO
16 R = OH

in the molecule of **1**, the remaining four degrees of unsaturation required **1** being tetracyclic. The aforementioned data implied that compound **1** was a limonoid.

Detailed analyses of 1D- and 2D-NMR spectra revealed that the structure of **1** was highly related with that of neohavanensin [4d], with the differences being the presence of an O-bearing CH_2 group (δ(H) 4.32 (d, J = 12.2), 4.51 (d, J = 12.2); δ(C) 61.2) and an O-bearing CH group (δ(H) 4.94 – 4.97 (m); δ(C) 66.1) in **1** replacing one tertiary Me group and one CH_2 group of neohavanensin, respectively. The HMBCs (*Fig. 1*) from the O-bearing CH_2 groups H–C(19) to C(1), C(5), C(9), and C(10), and from the O-bearing CH group H–C(11) to C(12) and C(13), combined with their shifts, located two OH groups at C(11) and C(19), respectively. The AcO group was confirmed to be at C(3) on the basis of the HMBC between H–C(3) and CO of the AcO group.

The relative configuration of **1** was mainly deduced by the ROESY spectrum (*Fig. 1*), and comparing the NMR data with those of neohavanensin. The ROESY correlations H_a–C(19)/H–C(1) and Me(29), and H_b–C(19)/H_β–C(6) and Me(30) indicated that the HO–CH_2 group was β-oriented. The OH–C(11) was assigned β-configuration by the ROESY correlation between H–C(11) and H–C(9). Hence, the structure of **1** was assigned as depicted.

Table 1. *^{1}H-NMR Data of Compounds* **1**–**4**. At 400 MHz, δ in ppm, J in Hz.

Position	**1**[a])	**2**[b])	**3**[c])	**4**[c])
1	4.94 (d, J = 2.6)	4.11–4.12 (m)	4.33 (s)	4.76 (d, J = 4.8)
2	2.28 (t, J = 2.6), 2.50–2.53 (m)	2.05–2.11 (m), 2.05–2.11 (m)	1.78 (d, J = 16.2), 2.85–2.92 (m)	1.77 (d, J = 16.4), 2.81–2.88 (m)
3	5.01–5.05 (m)	4.85 (s)	4.89 (d, J = 4.2)	4.86 (d, J = 4.0)
5	3.14 (d, J = 11.9)	1.82–1.89 (m)	2.46 (d, J = 2.0)	2.42 (s)
6	1.81–1.88 (m), 2.02–2.09 (m)	1.51–1.59 (m), 3.06 (m)	1.63–1.67 (m), 2.48 (s)	1.96–2.01 (m), 2.41–2.44 (m)
7	4.28–4.33 (m)	3.69 (s)	3.57 (d, J = 2.6)	4.92 (d, J = 2.0)
9	2.88 (s)	4.77 (s)	4.57 (s)	4.50 (s)
11	4.94–4.97 (m)			
12	2.44 (dd, J = 14.2, 2.2), 1.61 (dd, J = 14.2, 3.3)	5.36 (s)	5.31 (s)	5.26 (s)
14	3.79 (s)			
15		3.89 (s)	3.75 (s)	4.92 (s)
16	2.79 (dd, J = 19.0, 12.2), 2.63 (dd, J = 19.0, 8.9)	1.51–1.59 (m), 2.0–2.06 (m)	2.22 (dd, J = 13.2, 6.4), 1.91 (dd, J = 13.2, 11.2)	1.85–1.95(m), 1.85–1.95(m)
17	4.91–4.94 (m)	2.87 (dd, J = 10.9, 6.7)	2.96 (dd, J = 13.2, 4.9)	3.37 (dd, J = 11.7, 5.8)
18	0.81 (s)	1.38 (s)	1.16 (s)	1.11 (s)
19	4.32 (d, J = 12.2), 4.51 (d, J = 12.2)	4.42 (d, J = 14.2), 4.86 (d, J = 14.2)	4.15 (d, J = 12.4), 4.24 (d, J = 12.4)	3.63 (d, J = 11.5), 4.02 (d, J = 11.5)
21	7.72 (s)	7.27 (d, J = 1.1)	7.12 (br. s)	7.11 (s)
22	6.68 (d, J = 1.1)	6.19 (d, J = 0.9)	6.12 (d, J = 0.9)	6.15 (d, J = 1.0)
23	7.61 (d, J = 1.6)	7.46 (t, J = 1.5)	7.32 (t, J = 1.6)	7.34 (t, J = 1.6)
28	1.06 (s)	1.07 (s)	0.84 (s)	0.83 (s)
29	0.93 (s)		4.19 (s)	4.17 (s)
30	1.83 (s)	1.15 (s)	1.31 (s)	1.38 (s)
AcO–C(3)	1.92 (s)	1.94 (s)	2.10 (s)	2.07 (s)
AcO–C(12)		2.03 (s)	1.91 (s)	2.18 (s)
MeO			3.33 (s)	3.31 (s)

[a]) Recorded in (D_5)pyridine. [b]) Recorded in (D_6)acetone. [c]) Recorded in $CDCl_3$.

Table 2. *^{13}C-NMR Data* (at 100 MHz) *of Compounds* **1**–**11**

Position	**1**[a])	**2**[b])	**3**[c])	**4**[c])	**5** [**6**][a])	**7**[c])	**8**[c])	**9**[c])	**10**[a])	**11**[c])
1	66.8	69.9	70.6	69.5	69.0	70.9	71.9	71.6	69.8	71.0
2	29.6	32.0	36.4	36.4	37.5 [37.6][d])	36.2	37.5	37.8	36.6	35.4
3	78.0	74.1	76.3	76.2	74.0 [77.2][d])	76.3	75.6	75.1	73.8	74.1
4	36.3	46.8	40.2	40.9	41.1 [41.3][d])	40.2	41.3	41.4	39.9	39.8
5	36.1	28.0	25.7	29.4	32.4 [30.0][d])	25.6	24.5	24.5	28.3	28.0
6	25.6	28.4	27.3	24.0	23.4 [25.0][d])	25.1	25.2	25.0	23.9	23.3
7	71.4	69.2	70.6	82.7	82.5 [83.0][d])	69.3	69.6	69.8	69.3	69.4
8	42.0	43.3	41.7	43.8	43.9 [44.1][d])	42.2	42.8	43.6	42.5	43.9
9	45.2	49.5	48.5	52.6	52.3 [53.0][d])	47.9	48.3	48.5	47.9	47.8
10	49.0	39.9	42.5	39.3	39.9 [39.7][d])	44.4	44.3	41.5	42.9	44.5
11	66.1	208.2	206.7	203.5	211.0 [211.3][d])	207.1	207.3	212.9	213.8	206.9
12	40.6	78.2	78.6	80.0	80.9 [81.0][d])	79.5	79.7	78.9	77.8	79.3
13	41.5	46.2	45.7	49.5	51.3 [51.2][d])	46.7	46.6	45.7	46.9	46.9
14	61.7	72.4	72.2	96.5	97.7 [97.6][d])	60.0	60.2	60.1	58.3	60.2
15	221.8	58.7	58.6	75.7	76.1 [75.9][d])	218.0	217.8	218.6	218.5	218.1
16	43.7	33.9	33.6	38.8	38.4	43.9	44.0	44.6	45.4	42.3
17	38.4	39.1	38.2	42.8	43.9 [44.1][d])	39.1	39.5	40.8	38.5	39.1
18	27.6	15.3	22.8	15.8	15.6	21.4	21.0	21.0	22.0	21.5
19	61.2	73.3	58.6	58.5	64.8 [59.4][d])	58.2	58.4	57.9	64.2	63.5
20	124.6	123.4	122.6	124.3	127.2	122.2	122.4	123.9	125.6	122.1
21	141.0	141.3	140.6	140.0	140.6	140.3	140.4	140.1	140.4	140.4
22	112.1	112.4	111.9	111.4	113.5	110.3	110.4	111.0	111.2	110.4
23	142.8	143.1	142.4	142.7	142.6	143.2	143.2	143.0	143.1	143.3
28	28.7	20.0	18.2	17.5	18.9 [18.8][d])	18.0	18.6	18.7	19.4	19.3
29	22.9	173.8	102.7	102.9	96.2 [96.7][d])	102.5	102.9	103.1	103.6	102.9
30	20.6	21.8	15.7	18.2	18.3 [18.5][d])	20.6	21.5	22.3	21.4	21.5
AcO–C(3)	21.1, 170.3	20.5, 170.4	20.8, 170.0	20.9, 170.0	21.2 [21.1][d]), 170.8 [170.7][d])	20.8, 169.9			21.0, 170.4	20.8, 169.7
AcO–C(12)		20.8, 170.4	21.4, 170.4	21.4, 170.5		21.3, 170.6	20.7, 170.7			21.3, 170.6
MeO			55.4	55.8		55.4	55.4	55.5	56.4	56.9

[a]) Recorded in (D_5)pyridine. [b]) Recorded in (D_6)acetone. [c]) Recorded in $CDCl_3$. [d]) Chemical shifts of some C-atoms of **6** were resolved from those of compound **5**.

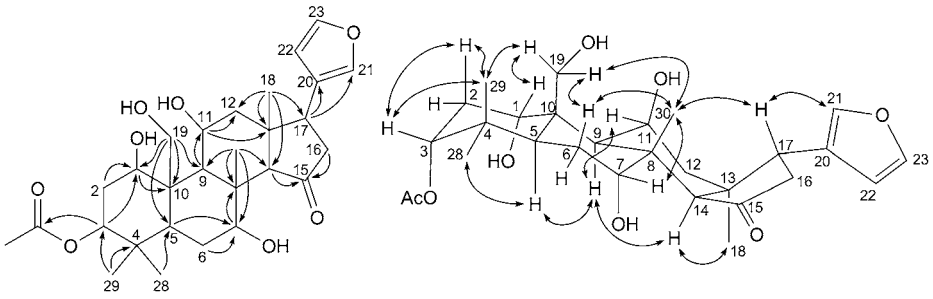


Fig. 1. *Key HMBC* (H → C) *and ROESY* (H ↔ H) *correlations of* **1**

Compound **2**, obtained as a white powder, showed a molecular formula $C_{30}H_{36}O_{11}$ as established by HR-EI-MS. The IR spectrum indicated the presence of OH groups (3467 cm^{-1}) and of a CO group (1751 cm^{-1}). The ^{1}H-NMR resonances at δ(H) 7.27 (*d*, $J = 1.1$), 6.19 (*d*, $J = 0.9$), and 7.46 (*t*, $J = 1.5$) featured a β-substituted furyl ring. The resonances at δ(H) 1.38 (*s*), 1.07 (*s*), and 1.15 (*s*) indicated the presence of three angular Me groups. The ^{13}C-NMR spectrum (*Table 2*) exhibited 30 C-atom resonances comprising those of five Me groups, four CH_2 groups (one O-bearing), eleven CH groups (three sp^2 and four O-bearing), and ten quaternary C-atoms (five sp^2, and one O-bearing) as attributed by DEPT experiments. Analyses of 1D and 2D spectra indicated that the structure of **2** was highly related to that of toosendanin [4a], except that the hemiacetal unit at C(29) in toosendanin was replaced by a lactone unit (δ(C) 173.8) in **2**. This was verified by the key HMBCs for both Me(19) and Me(28) to C(29). The relative configuration of **2** was deduced from its ROESY spectroscopic data to be the same as that of toosendanin.

Compound **3** was obtained as a white powder. The HR-ESI-MS displayed a sodiated molecular-ion peak at *m/z* 611.2463 ($[M+Na]^+$) consistent with the molecular formula of $C_{31}H_{40}O_{11}$ ($C_{31}H_{40}NaO_{11}^+$; calc. 611.2468). The IR spectrum exhibited absorption bands at 3448 and 1716 cm^{-1} evidencing the presence of OH and ester functions, respectively. The ^{13}C-NMR spectrum (*Table 2*) with DEPT experiments indicated the presence of five Me, four CH_2 (one O-bearing), and twelve CH groups (three sp^2 and five O-bearing), nine quaternary C-atoms (four sp^2, and one O-bearing), and a MeO group. Detailed analysis of its ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*) revealed that **3** was the methylated derivative of toosendanin [4a], which was confirmed by the key HMBC between the MeO groups to C(29), indicating the ketal formation at C(29) instead of the hemiketal of toosendanin. The relative configuration of **3** was mainly assigned by the ROESY spectrum. The 29-*endo*-configuration of **3** was assigned from the chemical shift of H–C(3) (δ(H) 4.89), since H–C(3) resonated at δ(H) 4.9–5.1 and 5.3–5.6 for 29-*endo*- and 29-*exo*-configurations, respectively [4e].

Compound **4**, a white powder, has a molecular formula $C_{31}H_{40}O_{11}$. The IR absorptions revealed the presence of OH (3448 cm^{-1}) and CO (1732 cm^{-1}) functions. The presence of three tertiary Me groups (δ(H) 0.83 (*s*), 1.11 (*s*), 1.38 (*s*)), two AcO groups (δ(H) 2.07 (*s*), and 2.18 (*s*)), a MeO group (δ(H) 3.31 (*s*)), and a β-substituted furan ring (δ(H) 7.11 (*s*), 6.15 (*d*, $J = 1.0$), 7.34 (*t*, $J = 1.6$)) was readily revealed by the ^{1}H-NMR spectrum (*Table 1*). The ^{13}C-NMR spectrum with the DEPT experiments displayed 31 C-atom resonances comprising those of five Me, nine sp^3 CH, three sp^2 CH, four sp^3 CH_2 groups, nine quaternary C-atoms, and a MeO group. The NMR spectra of **4** were very similar to those of mesendanin H [4f], except for the presence of an additional MeO group. The MeO group was determined to be at C(29) by the key HMBC between the MeO group and C(29) (*Fig. 2*). The relative configuration of **4** was mainly deduced from the ROESY spectrum (*Fig. 2*), and also by comparing the NMR data with those of toosendanin [4a]. The 29-*endo*-configuration of **4** was assigned from the chemical shift of H–C(3) (δ(H) 4.86) [4e].

Compounds **5** and **6** were isolated as a mixture of epimers in a ratio of 3:2 as estimated by ^{1}H-NMR. The ^{1}H- and ^{13}C-NMR spectral features of the mixture (*Tables 2* and *3*), showing two sets of H-atom and C-atom resonances (partially overlapped), were similar to those of **4**, except for the absence of resonances of the

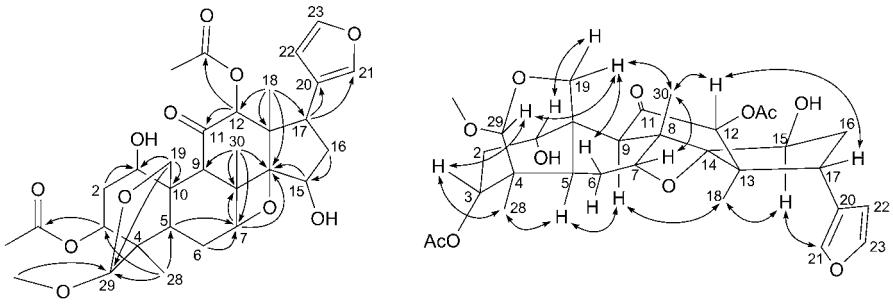


Fig. 2. *Key HMBC* (H → C) *and ROESY* (H ↔ H) *correlations of* **4**

AcO and MeO groups at C(11) and C(29) in **4**. In addition, C(19) and C(29) resonated at δ(C) 64.8, and 96.2, respectively, for **5** and at δ(C) 59.4 and 96.7 for **6** (*Table 2*). This suggested that **5** and **6** were hemiacetal 29-epimers of 11-deacetyl-29-demethyl analogue of **4**, which was supported by HR-ESI-MS data of the mixture at *m*/*z* 555.2201 ($C_{28}H_{36}NaO_{10}^{+}$; calc. 555.2206). One the basis of the chemical shifts of H–C(3) (δ(H) 6.00 (*s*) for **5** and 4.89 (*d*, $J = 4.7$) for **6**) [4e], compounds **5** and **6** were assigned as 29-*exo*- and 29-*endo*-epimers, respectively. This assignment was confirmed by 2D-NMR data analysis including the ROESY experiment of the mixture.

Compound **7** was obtained as a white powder with a molecular formula $C_{31}H_{40}O_{11}$ as established by the HR-ESI-MS. The NMR data of **7** (*Tables 2* and *3*) resembled those of neoazedarachin D [4b], a limonoid isolated from *M. toosendan*, except for the presence of an additional AcO group. The AcO group was located at C(12) of **7** by the HMBC for H–C(12) (δ(H) 5.09 (*s*)) and the AcO CO group (δ(C) 170.6). The relative configuration of **7** was determined to be identical to that of neoazedarachin D on the basis of ^{1}H- and ^{13}C-NMR and ROESY data analyses.

Compound **8**, a white powder, gave a molecular formula of $C_{29}H_{38}O_{10}$, as established by HR-ESI-MS ($[M + Na]^{+}$ at *m*/*z* 569.2357; calc. 569.2363). The NMR data (*Tables 2* and *3*) of **8** were similar to those of **7**, with the only exception being the absence of the resonances for the AcO group and a significant upfield shift of the resonance for H–C(3) ($\Delta\delta$(H) 1.3) in **8**. This suggested that **8** was a 3-deacetyl analog of **7**. The planar structure of **8** was further confirmed by 2D-NMR spectra. The relative configuration of **8** was assigned to be the same as that of **7** on the basis of their similar 1D-NMR data and ROESY spectrum.

Compound **9** was obtained as a white powder with a molecular formula $C_{27}H_{36}O_{9}$, as established by the HR-EI-MS. The NMR data (*Tables 2* and *4*) of **9** were very similar to those of **8**, with the differences being the absence of the resonances for the 12-AcO group and a significant shielding of H–C(12) ($\Delta\delta$(H) 0.76) in **9**. This data indicated that **9** was a 12-deacetyl derivative of **8**. The ROESY spectrum revealed that **9** displayed the same relative configuration as **8**.

Compound **10**, a white powder, was assigned the molecular formula of $C_{29}H_{38}O_{10}$ by the HR-ESI-MS ($[M + Na]^{+}$ at *m*/*z* 569.2357; calc. 569.2363). The NMR data (*Tables 2* and *4*) of **10** were similar to those of neoazedarachin D [4b]. However, H–C(3) (δ(H) 5.68; $\Delta\delta$(H) 0.78) and C(19) (δ(C) 64.2; $\Delta\delta$(C) 6.4) of **10** were deshielded significantly

Table 3. *^{1}H-NMR Data of Compounds* **5**–**8**. At 400 MHz δ in ppm, J in Hz.

Position	**5** [**6**][a])	**7**[a])	**8**[a])
1	5.28–5.35 (*m*)	4.14 (*s*)	4.23 (*s*)
2	2.41 (*d*, *J* = 14.9), 3.35–3.37 (*m*) [3.11–3.19 (*m*)][b])	1.76 (*d*, *J* = 16.2), 2.78–2.84 (*m*)	1.91 (*d*, *J* = 15.3), 2.75–2.81 (*m*)
3	6.00 (*s*) [4.89 (*d*, *J* = 4.7)][b])	4.86 (*d*, *J* = 3.9)	3.56 (*s*)
5	3.36–3.40 (*m*) [3.25–3.29 (*m*)][b]), [3.29 (*m*)][b])	2.46 (*s*)	2.54 (*s*)
6	2.24–2.31 (*m*) [1.93–1.96 (*m*)][b]) [1.94 (*m*)][b]), 2.25–2.31 (*m*), [2.21–2.241 (*m*)][b]) [2.23 (*m*)][b])	1.67 (*d*, *J* = 3.5), 2.46 (*s*)	1.61–1.71 (*m*), 2.51–2.57 (*m*)
7	5.27 (*s*)	3.97 (*s*)	4.02 (*s*)
9	5.26 (*s*)	3.68 (*s*)	3.66 (*s*)
12	4.52 (*s*) [5.27 (*s*)][b])	5.09 (*s*)	5.15 (*s*)
14		3.19 (*s*)	3.23 (*s*)
15	5.31–5.38 (*m*)		
16	2.32–2.38 (*m*), 2.32–2.38 (*m*)	2.56 (*dd*, *J* = 8.6, 2.0), 2.56 (*dd*, *J* = 8.6, 2.0)	2.58–2.61 (*m*), 2.58–2.61 (*m*)
17	4.09–4.18 (*m*)	3.33 (*d*, *J* = 9.7)	3.36 (*d*, *J* = 10.0)
18	1.66 (*s*)	0.98 (*s*)	1.19 (*s*)
19	4.29 (*d*, *J* = 14.5) [4.11 (*d*, *J* = 12.8)][d]), 4.39 (*d*, *J* = 14.5) [4.13 (*d*, *J* = 12.8][d])	3.92 (*d*, *J* = 12.2), 4.11 (*d*, *J* = 12.2)	3.89 (*d*, *J* = 12.2), 4.12 (*d*, *J* = 12.2)
21	6.91 (*s*) [6.77 (*s*)][b])	7.27 (*s*)	7.29 (*s*)
22	6.12 (br. *s*) [6.0 (br. *s*)][b])	6.25 (*s*)	6.26 (*s*)
23	7.51 (*t*, *J* = 1.6)	7.36 (*s*)	7.38 (*s*)
28	1.14 (*s*) [1.19 (*s*)][b])	0.82 (*s*)	0.98 (*s*)
29	5.34 (*s*) [4.19 (*s*)][b])	4.14 (*s*)	4.07 (*s*)
30	1.66 (*s*)	1.16 (*s*)	1.00 (*s*)
AcO–C(3)	1.83 (*s*) [1.82 (*s*)][b])	2.07 (*s*)	
AcO–C(12)		2.07 (*s*)	2.09 (*s*)
MeO		3.29 (*s*)	3.32 (*s*)

[a]) Recorded in $CDCl_3$. [b]) Chemical shifts of some H-atoms of **6** were resolved from those of compound **5**.

Table 4. *^{1}H-NMR Data of Compounds* **9**–**11**. At 400 MHz, δ in ppm, J in Hz.

Position	**9**[a])	**10**[b])	**11**[a])
1	4.74 (*s*)	5.09 (*s*)	4.09–4.10 (*m*)
2	1.95 (*d*, $J = 15.4$), 2.71–2.82 (*m*)	2.34 (*d*, $J = 15.2$), 3.07–3.13 (*m*)	1.73–1.76 (*m*), 2.76–2.82 (*m*)
3	3.80 (*s*)	5.68 (*s*)	5.31 (*d*, $J = 3.1$)
5	2.65 (*d*, $J = 8.6$)	3.63 (*s*)	2.54 (*s*)
6	1.68–1.72 (*m*), 1.69–1.73 (*m*)	1.98–2.02 (*m*), 2.24–2.37 (*m*)	1.76–1.82 (*m*), 2.16 (*s*)
7	4.13 (*s*)	4.61–4.69 (*m*)	4.05 (*s*)
9	3.41 (*s*)	3.66 (*s*)	3.74 (*s*)
12	4.39 (*s*)	4.66 (*s*)	5.09 (*s*)
14	3.06 (*s*)	4.09 (*s*)	3.23 (*s*)
16	2.53–2.58 (*m*), 2.67 (*d*, $J = 8.5$)	2.65 (*dd*, $J = 17.1$, 5.7), 2.89 (*dd*, $J = 17.1$, 8.5)	2.58 (*dd*, $J = 8.9$, 2.1), 2.58 (*dd*, $J = 8.9$, 2.1)
17	3.56 (*s*)	3.78 (*d*, $J = 7.6$)	3.34 (*d*, $J = 9.4$)
18	0.81 (*s*)	1.26 (*s*)	1.01 (*s*)
19	3.63 (*d*, $J = 12.0$), 4.06 (*d*, $J = 12.0$)	4.46 (*d*, $J = 11.6$), 4.68 (*d*, $J = 11.6$)	4.15 (*d*, $J = 13.2$), 4.15 (*d*, $J = 13.2$)
21	7.29 (*s*)	7.48 (*s*)	7.30 (*s*)
22	6.39 (*d*, $J = 0.9$)	6.42 (*s*)	6.27 (*d*, $J = 0.5$)
23	7.36 (*t*, $J = 1.6$)	7.50 (*s*)	7.38 (*t*, $J = 1.6$)
28	0.97 (*s*)	1.01 (*s*)	0.84 (*s*)
29	4.09 (*s*)	4.67 (*s*)	4.37 (*s*)
30	1.19 (*s*)	1.36 (*s*)	1.17 (*s*)
AcO–C(3)		1.91 (*s*)	2.08 (*s*)
AcO–C(12)			2.09 (*s*)
MeO	3.32 (*s*)	3.46 (*s*)	3.39 (*s*)

[a]) Recorded in $CDCl_3$. [b]) Recorded in (D_5)pyridine.

as compared with those of neoazedarachin D [4b]. On the basis of the chemical shift of H–C(3) (δ(H) 5.68), compound **10** was assigned as 29-*exo*-configuration [4e]. This indicated that **10** was the 29-epimer of neoazedarachin D, which was confirmed by the 2D-NMR spectra.

Compound **11** was obtained as a white powder. The HR-ESI-MS at *m*/*z* 611.2463 ($[M + Na]^+$) gave a molecular formula $C_{31}H_{40}O_{11}$ ($C_{31}H_{40}NaO_{11}^+$; calc. 611.2468) with 42 mass units more than **10**. Comparison of the NMR data of **11** with those of **10** (*Tables 2* and *4*) revealed that the resonance for H–C(12) (δ(H) 5.09) of **11** was deshielded significantly. These data indicated the presence of an AcO group at C(12) in **11**, which was confirmed by the HMBC from H–C(12) to the AcO CO group (δ(C) 170.6). Thus, the structure of **11** was determined.

Besides these eleven new compounds, five known compounds were identified to be toosendanin (**12**) [4a], isochuanliansu (**13**) [4a], neoazedarachin D (**14**) [4b], 12α-hydroxyamoorastatin (**15**) [4c], 12α-hydroxyamoorastatone (**16**) [4c] on the basis of the ^{1}H- and ^{13}C- NMR, and EI-MS data. Among them, compound **14** was isolated from this plant for the first time.

Compounds **1**–**11** were evaluated for their antimicrobial activities against *Staphylococcus aureus* (ATCC 25923), *Staphylococcus epidermidis* (ATCC 12228), *Micrococcus luteus* (ATCC 9341), *Bacillus subtilis* (CMCC 63501), *Escherichia coli* (ATCC 25922), *Shigella flexneri* (ATCC 120222), and *Pseudomonas aeruginosa* (ATCC 14502) by microdilution assay [9]. Compound **4** showed weak activities against *S. aureus* (*MIC* 50 μg/ml) and *B. subtilis* (*MIC* 50 μg/ml), and compound **8** exhibited moderate activity against *B. subtilis* (*MIC* 25 μg/ml). Other compounds were inactive.

Financial support from the *National Natural Science Foundation* (grant No. 30701044), the *Key Project of Chinese Academy of Sciences* (grant No. KSCX2-YW-R-117, KSCX2-YW-R-184), the *National Science & Technology Major Project 'Key New Drug Creation and Manufacturing Program'* (grant No. 2009ZX09301-001), and the *Shanghai Municipal Scientific Foundation of P. R. China* (grant No. 08JC1422300) is gratefully acknowledged. We thank Prof. *S. M. Huang*, Department of Biology, Hainan University, for the collection and identification of the plant material.

Experimental Part

General. All the solvents used were of anal. grade (*Shanghai Chemical Plant*, Shanghai, P. R. China). Column chromatography (CC): silica gel (SiO_2; 200–300 mesh; *Qingdao Haiyang Chemical Co. Ltd.*, Qingdao, P. R. China), C_{18} reversed-phase (RP) silica gel (150–200 mesh; *Merck*, D-Darmstadt), *MCI* gel (*CHP20P*, 75–150 μm, *Mitsubishi Chemical Industries Ltd.*, Tokyo, Japan), and *Sephadex LH-20* gel (*Amersham Biosciences*, Little Chanfolt, UK). TLC: Precoated silica gel GF_{254} plates (*Qingdao Haiyang Chemical Co. Ltd.*, Qingdao, P. R. China). Semi-prep. HPLC: *Waters 515* pump equipped with a *Waters 2487* detector and a *YMC-Pack ODS-A* column (250 × 10 mm, S-5 μm, 12 nm). Optical rotations: *Perkin-Elmer 341* polarimeter, at r.t. IR Spectra: *Perkin-Elmer 577* spectrometer; KBr disc. NMR Spectra: *Bruker AM-400* spectrometer with TMS as internal standard. EI-MS and HR-EI-MS (70 eV) spectra: *Finnigan MAT 95* mass spectrometer. ESI-MS Spectra: *Esquire 3000plus* LC-MS instrument. HR-ESI-MS: *Bruker Daltonics micro TOF* mass spectrometer.

Plant Material. The aerial parts of *M. azedarach* were collected in August of 2005 from Sanya of Hainan Province and were authenticated by Prof. *S. M. Huang*, Department of Biology, Hainan University of China. A voucher specimen (No. Meaz-2005–1Y) has been deposited with the Shanghai Institute of Materia Medica.

Extraction and Isolation. The dried, powdered twigs and leaves of *M. azedarach* (5 kg) were percolated three times with 95% EtOH (3 × 8.0 l). After removal of the solvent under reduced pressure, the EtOH extract (240g) was partitioned between H_2O (1.0 l) and AcOEt (3 × 1.0 l). The AcOEt-soluble fraction (110 g) was subjected to CC (*MCI* gel; MeOH/H_2O 5 :5 to 9 :1) to give five fractions, *Frs. A1 – A5*. *Fr. A2* (19 g) was separated on a SiO_2 column eluted with a gradient of petroleum ether (PE)/acetone (20 :1 to 2 :1) to afford four subfractions, *Fr. A2a – A2d*). *Fr. A2b* (6.8 g) was chromatographed on a *Sephadex LH-20* eluted with MeOH to obtain three fractions, *Fr. A2b1 – A2b3*, and each of them were then purified by a semi-prep. HPLC with 60% MeOH in H_2O as the mobile phase to yield compounds **2** (12 mg, t_R 16.5 min), **15** (16 mg, t_R 9.0 min), and **12** (23 mg, t_R 8.3 min). *Fr. A2c* (3.5g) was chromatographed on a SiO_2 column, eluted with PE/AcOEt (3 :1 to 1 :1), to give five subfractions, *Frs. A2c1 – A2c5*. *Fr. A2c2* (0.8g) was purified on a column of *Sephadex LH-20* gel and then purified by semi-prep. HPLC with 73% MeOH in H_2O as the mobile phase, to yield **4** (8 mg, t_R 8.9 min), **7** (11 mg; t_R 11.3 min), and **14** (10 mg; t_R 9.6 min). *Fr. A2c3* (0.65g) was chromatographed on a SiO_2 column eluted with PE/acetone (8 :1 to 3 :1) to give the major fractions, which were further purified by semi-prep. HPLC (70% MeOH in H_2O) to yield **10** (8 mg; t_R 8.9 min), **11** (15 mg; t_R 10.7 min), and **16** (7 mg; t_R 9.6 min). *Fr. A2c4* (0.3g) was separated by semi-prep. HPLC with 75% MeOH in H_2O as the mobile phase to yield compounds **8** (7 mg; t_R 7.4 min), **9** (8 mg; t_R 7.8 min), and **13** (13 mg; t_R 8.5 min). *Fr. A3* (17 g) was subjected to CC (RP-C_{18} SiO_2; MeOH/H_2O from 5 :5 to 8 :2) to give three major fractions, *Frs. A3a – A3c*. *Fr. A3a* (3.1g) was separated by CC (SiO_2; PE/AcOEt 3 :1 to 1 :1) to yield compounds **1** (25 mg) and **3** (14 mg). *Fr. A3b* (4.5g) was subjected to CC (SiO_2; PE/AcOEt 1 :1) to obtain a major component, which was then purified by a semi-prep. HPLC with 50% MeOH in H_2O as the mobile phase to yield a mixture **5**/**6** (9 mg; t_R 10.4 min).

Meliarachin A (= *(1α,3α,5α,7α,11β,13α,17α)-17-(Furan-3-yl)-1,7,11,19-tetrahydroxy-4,4,8-trimethyl-15-oxoandrostan-3-yl Acetate*; **1**). Colorless amorphous powder. $[\alpha]_D^{20} = -19.0$ ($c = 0.1$, MeOH). UV (MeOH): 207 (4.26). IR (KBr): 3365, 2964, 1728, 1639, 1466, 1381, 1257, 1072, 876. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*, resp. EI-MS: 504 (9, M^+), 486 (6), 408 (12), 378 (29), 360 (22), 247 (32), 162 (100), 95 (36). HR-ESI-MS: 527.2619 ($[M+Na]^+$, $C_{28}H_{40}NaO_8^+$; calc. 527.2621).

Meliarachin B (= rel-*(1S,3R,4R,4aR,6R,6aS,6bS,7aR,9R,9aR,10R,11aR,11bS)-9-(Furan-3-yl)-decahydro-1,6-dihydroxy-4,6a,9a-trimethyl-11,14-dioxotetra-1*H*-4,11b-(methanooxymethano)naphtho[1′,2′:6,7]indeno[1,7a-*b*]oxirene-3,10-diyl Diacetate*; **2**). Colorless amorphous powder. $[\alpha]_D^{20} = -44.0$ ($c = 0.165$, MeOH). UV (MeOH): 207 (4.72). IR (KBr): 3467, 2924, 1751, 1724, 1701, 1375, 1215, 1176, 1024, 797. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*. EI-MS: 570 (16, $[M-H_2O]^+$), 552 (6), 512 (61), 494 (23), 452 (57), 419 (47), 175 (67), 162 (77), 94 (100). HR-EI-MS: 572.2258 (M^+, $C_{30}H_{36}O_{11}^+$; calc. 572.2258).

Meliarachin C (= rel-*(1S,3R,4R,4aR,6R,6aS,6bS,7aR,9R,9aR,10R,11aR,11bS)-9-(Furan-3-yl)-tetradecahydro-1,6-dihydroxy-14-methoxy-4,6a,9a-trimethyl-11-oxo-1*H*-4,11b-(methanooxymethano)naphtho-[1′,2′:6,7]indeno[1,7a-*b*]oxirene-3,10-diyl Diacetate*; **3**). Colorless amorphous powder. $[\alpha]_D^{20} = +44.0$ ($c = 0.07$, MeOH). UV (MeOH): 205 (3.61). IR (KBr): 3448, 2931, 1716, 1618, 1458, 1375, 1246, 1115, 1047, 731. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*. EI-MS: 588 (12, M^+), 570 (6), 557 (28), 528 (24), 510 (58), 468 (97), 450 (45), 390 (46), 175 (65), 107 (100), 95 (55). ESI-MS: 611 ($[M+Na]^+$). HR-ESI-MS: 611.2463 ($[M+Na]^+$, $C_{31}H_{40}NaO_{11}^+$; calc. 611.2468).

Meliarachin D (= rel-*(1R,3R,3aR,4aR,5aR,6R,7R,9S,9aS,9bR,9cS,11R,11aR)-1-(Furan-3-yl)-tetradecahydro-3,9-dihydroxy-14-methoxy-6,9c,11a-trimethyl-10-oxo-1*H*-6,9a-(methanooxymethano)cyclopenta[1,2]phenanthro[1,10-*bc*]oxete-7,11-diyl Diacetate*; **4**). Colorless amorphous powder. $[\alpha]_D^{20} = +28.0$ ($c = 0.095$, MeOH). UV (MeOH): 203 (4.09). IR (KBr): 3448, 2933, 1732, 1375, 1240, 1047. ^{1}H- and ^{13}C-NMR: see *Tables 1* and *2*. EI-MS: 570 (76, $[M-H_2O]^+$), 528 (100), 510 (68), 495 (22), 468 (38), 378 (73), 336 (28), 171 (53), 95 (45). ESI-MS: 611 ($[M+Na]^+$). HR-ESI-MS: 611.2463 ($[M+Na]^+$, $C_{31}H_{40}NaO_{11}^+$; calc. 611.2468).

Meliarachins E and F (= rel-*(1R,3R,3aS,4aR,5aR,6R,7R,9S,9aS,9bR,9cS,11R,11aR)-1-(Furan-3-yl)-tetradecahydro-3,9,11,14-tetrahydroxy-6,9c,11a-trimethyl-10-oxo-1*H*-6,9a-(methanooxymethano)cyclopenta[1,2]phenanthro[1,10-*bc*]oxet-7-yl Acetate*; **5** and **6**). Colorless amorphous powder. $[\alpha]_D^{20} = -23.0$ ($c = 0.22$, MeOH). UV (MeOH): 210 (4.10). IR (KBr): 3408, 2922, 1724, 1375, 1261, 1022, 966, 825. ^{1}H- and ^{13}C-NMR: see *Tables 3* and *2*, resp. EI-MS: 532 (3, M^+), 514 (100), 472 (9), 454 (25), 336 (16), 275

(17), 201 (24), 171 (49), 157 (54), 105 (44), 95 (34). ESI-MS: 555 ($[M+Na]^+$). HR-ESI-MS: 555.2201 ($[M+Na]^+$, $C_{28}H_{36}NaO_{10}^+$; calc. 555.2206).

Meliarachin G (= rel-*(1S,3R,4R,5R,7R,8S,9S,10S,12R,13S,14S,17R)-17-(Furan-3-yl)-hexadecahydro-1,7-dihydroxy-20-methoxy-4,8,13-trimethyl-11,15-dioxo-4,10-(methanooxymethano)cyclopenta[a]phenanthrene-3,12-diyl Diacetate*; **7**). Colorless amorphous powder. $[\alpha]_D^{20} = +38.0$ ($c = 0.29$, MeOH). UV (MeOH): 205 (4.76). IR (KBr): 3448, 2935, 1736, 1373, 1244, 1047, 874. ^{1}H- and ^{13}C-NMR: see *Tables 3* and *2*, resp. EI-MS: 588 (2, M^+) (2), 557 (10), 528 (12), 510 (28), 468 (100), 436 (18), 408 (16), 365 (14), 121 (30), 95 (21). ESI-MS: 611 ($[M+Na]^+$). HR-ESI-MS: 611.2463 ($[M+Na]^+$, $C_{31}H_{40}NaO_{11}^+$; calc. 611.2468).

Meliarachin H (= *(1S,3R,4R,5R,7R,8S,9S,10S,12R,13S,14S,17R)-17-(Furan-3-yl)-hexadecahydro-1,3,7-trihydroxy-20-methoxy-4,8,13-trimethyl-11,15-dioxo-4,10-(methanooxymethano)cyclopenta[a]phenanthren-12-yl Acetate*; **8**). Colorless amorphous powder. $[\alpha]_D^{20} = +43.0$ ($c = 0.065$, MeOH). UV (MeOH): 204 (4.22). IR (KBr): 3437, 2928, 1734, 1637, 1373, 1234, 1115, 1051, 602. ^{1}H- and ^{13}C-NMR: *Tables 3* and *2*, resp. EI-MS: 528 (3, $[M-H_2O]^+$), 496 (11), 486 (100), 468 (23), 453 (73), 393 (38), 251 (37), 163 (46), 121 (59), 95 (54). ESI-MS: 569 ($[M+Na]^+$). HR-ESI-MS: 569.2357 ($[M+Na]^+$, $C_{29}H_{38}NaO_{10}^+$; calc. 569.2363).

Meliarachin I (= *(1S,3R,4R,5R,7R,8S,9S,10S,12R,13S,14S,17R)-17-(Furan-3-yl)-dodecahydro-1,3,7,12-tetrahydroxy-20-methoxy-4,8,13-trimethyl-4,10-(methanooxymethano)cyclopenta[a]phenanthrene-11,15(1H,9H)-dione*; **9**). Colorless amorphous powder. $[\alpha]_D^{20} = +40.0$ ($c = 0.12$, MeOH). UV (MeOH): 200 (4.46). IR (KBr): 3435, 2926, 1730, 1707, 1389, 1051, 874. ^{1}H- and ^{13}C-NMR: *Tables 4* and *2*, resp. EI-MS: 504 (12, M^+), 486 (47), 453 (36), 310 (82), 251 (56), 163 (100), 121 (50), 95 (50). ESI-MS: 527 ($[M+Na]^+$). HR-EI-MS: 504.2374 (M^+, $C_{27}H_{36}O_9^+$; calc. 504.2359).

Meliarachin J (= *(1S,3R,4R,5R,7R,8S,9S,10S,12R,13S,14S,17R)-17-(Furan-3-yl)-hexadecahydro-1,7,12-trihydroxy-20-methoxy-4,8,13-trimethyl-11,15-dioxo-4,10-(methanooxymethano)cyclopenta[a]phenanthren-3-yl Acetate*; **10**). Colorless amorphous powder. $[\alpha]_D^{20} = -14.0$ ($c = 0.105$, MeOH). UV (MeOH): 202 (4.06). IR (KBr): 3475, 2941, 1709, 1383, 1279, 1043, 970, 874, 604. ^{1}H- and ^{13}C-NMR: see *Tables 4* and *2*, resp. EI-MS: 546 (2, M^+), 528 (4), 486 (34), 454 (100), 436 (64), 408 (21), 163 (58), 121 (34), 95 (36). ESI-MS: 569 ($[M+Na]^+$) HR-ESI-MS: 569.2357 ($[M+Na]^+$, $C_{29}H_{38}NaO_{10}^+$; calc. 569.2363).

Meliarachin K (= *(1S,3R,4R,5R,7R,8S,9S,10S,12R,13S,14S,17R)-17-(Furan-3-yl)-hexadecahydro-1,7-dihydroxy-20-methoxy-4,8,13-trimethyl-11,15-dioxo-4,10-(methanooxymethano)cyclopenta[a]phenanthrene-3,12-diyl Diacetate*; **11**). Colorless amorphous powder. $[\alpha]_D^{20} = -25.0$ ($c = 0.095$, MeOH). UV (MeOH): 205 (4.25). IR (KBr): 3435, 2928, 1726, 1637, 1375, 1246, 1072, 604. ^{1}H- and ^{13}C-NMR: see *Tables 4* and *2*, resp. EI-MS: 570 (2, $[M-H_2O]^+$), 528 (29), 496 (67), 468 (86), 436 (100), 408 (33), 162 (47), 121 (51). ESI-MS: 611 ($[M+Na]^+$). HR-ESI-MS: 611.2463 ($[M+Na]^+$, $C_{31}H_{40}NaO_{11}^+$; calc. 611.2468).

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Received December 3, 2010