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Moluccensins R–Y, Limonoids from the Seeds of a Mangrove, *Xylocarpus moluccensis*

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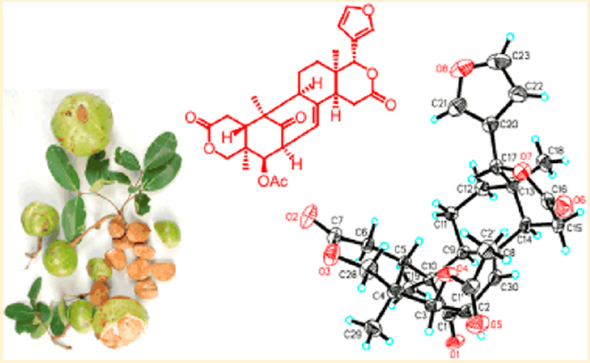
Supporting Information

ABSTRACT: Eight limonoids, named moluccensins R–Y (**1**, **2**, **5**–**10**), and six known compounds, including 6-hydroxymexicanolide (**3**), were isolated from the seeds of an Indian mangrove, *Xylocarpus moluccensis*, collected in the estuaries of Andhra Pradesh. The absolute configuration of moluccensin V (**7**) was confirmed by means of single-crystal X-ray diffraction analysis. The ^{1}H and ^{13}C NMR data for 6-hydroxymexicanolide (**3**) was assigned for the first time, and the 6*R* absolute configuration established by single-crystal X-ray diffraction analysis. Moluccensin R (**1**), 6*R*-hydroxymexicanolide (**3**), and 2-hydroxyfissinolide (**4**) exhibited marked antifeedant activity against the third-instar larvae of *Brontispa longissima* at a concentration of 1 mg/mL. The most potent compound tested was 2-hydroxyfissinolide (**4**), with an AFC_{50} (concentration for 50% antifeedant activity) value of 94 μg/mL at 24 h.



Limonoids, modified triterpene derivatives from a precursor with a 4,4,8-trimethyl-17-furanylsteroid skeleton, have been found mainly in the plants of the families Meliaceae, Rutaceae, and Simaroubaceae. They are classified by the type of four—usually highly oxidized—rings in the intact triterpene. Two meliaceous mangroves, *Xylocarpus granatum* and *X. moluccensis*, are known for producing antifeedant limonoids, especially mexicanolides and phragmalins.[1−11] Previous investigations on the seeds of these two species yielded an andirobin, an obacunol, two phragmalins, three gedunins, and 14 mexicanolides, including xyloccensins A–K.[12−15] Previously we reported the isolation and identification of eight 8,9,30-phragmalin *ortho* esters and 13 limonoids from the bark and seeds of a Chinese mangrove, *X. granatum*,[16−18] and two andirobins, 19 mexicanolides, and 16 phragmalins from the seeds of Indian mangroves, *X. granatum* and *X. moluccensis*.[19−25] Further investigation on limonoids from the seeds of an Indian mangrove, *X. moluccensis* (Lam.) M. Roem. (Meliaceae), collected in the estuaries of Andhra Pradesh, afforded eight new limonoids, named moluccensins R–Y (**1**, **2**, **5**–**10**), together with six known ones, viz., 6-hydroxymexicanolide (**3**),[26−28] 2-hydroxyfissinolide (**4**),[29−31] swietmanins G and H,[32] and xyloccensins E[33] and Q.[17,34] Herein, we describe the isolation and structural elucidation of those new limonoids and 6-hydroxymexicanolide. Antifeedant and insecticidal activities of four limonoids with a $\Delta^{8,14}$ double bond against the third-instar larvae of *Brontispa longissima* are also reported.

RESULTS AND DISCUSSION

Moluccensin R (**1**), a white, amorphous powder, had the molecular formula $C_{31}H_{40}O_{10}$, as established by HR-TOFMS (*m*/*z* 573.2683, calcd for $[M + H]^+$ 573.2694). The NMR spectroscopic data of **1** (Tables 1 and 2) were similar to those of 2,6-dihydroxyfissinolide,[35] except for the presence of an isobutyryl group [δ_H 1.22 (d, *J* = 7.0 Hz), 1.23 (d, *J* = 7.0 Hz), 2.64 m; δ_C 19.9 CH_3, 18.4 CH_3, 34.4 CH, 175.8 qC] and the absence of an acetyl group. The existence of the isobutyryl group was corroborated by ^{1}H–^{1}H COSY cross-peaks between H-2′/H-3′ and H-2′/H-4′ and HMBC correlations between H-2′/C-1′, H-3′/C-1′, H-4′/C-1′, H-3′/C-2′, and H-4′/C-2′. The presence of a strong HMBC correlation from H-3 (δ 4.92, s) to C-1′ (δ 175.8 qC) of the isobutyryl group placed it at C-3. Moreover, the significant NOE interaction observed in **1** from

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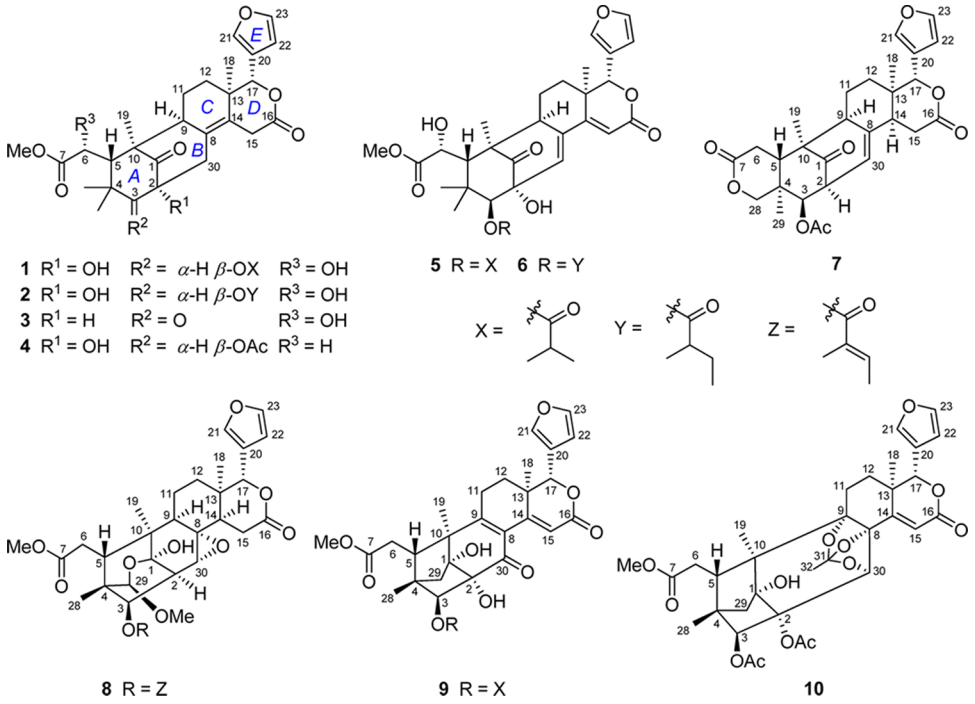
Chart 1



H-3 to H_3-29, but not from H-3 to H-5, helped to establish this 3α-H and the corresponding 3β-*O*-isobutyryl group. On the basis of the above results, the structure of **1**, named moluccensin R, was elucidated as shown.

Moluccensin S (**2**) was obtained as a white, amorphous powder. In the HR-TOFMS spectrum, it exhibited a quasi-molecular ion at *m*/*z* 587.2857 ($[M + H]^+$, calcd for 587.2851), consistent with the molecular formula $C_{32}H_{42}O_{10}$. The NMR spectroscopic data of **2** (Tables 1 and 2) were similar to those of moluccensin R (**1**), except for the replacement of the 3-*O*-isobutyryl group in **1** by a 3-*O*-2-methylbutyryl group [δ_H 1.00 (t, *J* = 7.2 Hz), 1.19 (d, *J* = 7.2 Hz), 1.50 overlapped, 1.82 overlapped, 2.44 m; δ_C 11.6 CH_3, 17.5 CH_3, 26.1 CH_2, 41.3 CH, 175.6 qC]. The existence of the 2-methylbutyryl group was confirmed by $^1H-^1H$ COSY cross-peaks between H_3-4′/H_2-3′, H_2-3′/H-2′, and H-2′/H_3-5′ and HMBC correlations between H_3-4′/C-3′, H_3-4′/C-2′, H_3-5′/C-2′, H_3-5′/C-1′, and H-2′/C-1′. The HMBC correlation from H-3 (δ 4.92, s) to the carbonyl carbon (δ 175.6) of this 2-methylbutyryl group clearly indicated its attachment to C-3. Moreover, the significant NOE interaction from H-3 to H_3-29, but not from H-3 to H-5, helped to establish 3α-H and the corresponding 3β-*O*-2-methylbutyryl group. Thus, compound **2**, named moluccensin S, was identified as 3-*O*-(2-methylbutyryl)-3-deisobutyrylmoluccensin R.

6-Hydroxymexicanolide (**3**) was obtained as colorless crystals ($CHCl_3$–MeOH, 1:1). The molecular formula $C_{27}H_{32}O_8$ was established by HR-TOFMS (*m*/*z* 485.2173, calcd for $[M + H]^+$ 485.2170). Compound **3** was first reported in 1968 as the oxidation of swietenolide with the Jones reagent.[26] In the same year, it was again reported as a new natural product obtained from the seeds of *Cedrela odorata*.[27] The relative configuration of **3** was established by single-crystal X-ray diffraction analysis using Mo Kα radiation.[28] In the current paper, the unambiguous assignment of ^1H and ^{13}C NMR data for 6-hydroxymexicanolide was achieved for the first time. The 6*R*-configuration and the complete absolute configuration of **3** (Figure 1) were established by single-crystal X-ray diffraction analysis using Cu Kα radiation [Flack parameter 0.0(2)]. In the crystal, molecules of **3** were found to be stabilized by intermolecular C···H–O hydrogen bonds between H-23/O-2′, H-15′/O-8, H-29′/O-1, and H-11′/O-1. Therefore, the structure of **3** was defined as 6*R*-hydroxymexicanolide.

Moluccensin T (**5**), a white, amorphous powder, gave the molecular formula $C_{31}H_{38}O_{10}$, as established by HR-TOFMS (*m*/*z* 571.2512, calcd for $[M + H]^+$ 571.2538), i.e., two hydrogen atoms less than **1**. The NMR data of **5** (Tables 1 and 2) were similar to those of **1**, except for the presence of two conjugated double bonds, viz., $\Delta^{8,9}$ and $\Delta^{14,15}$ in **5**. This finding was corroborated by the higher frequency shifted H-15 (δ 6.29 br s) and H-30 [δ 6.28 (d, *J* = 3.0 Hz)]. Further evidence could be found from HMBC correlations between H-15/C-13, H-15/C-14, H-15/C-30, H-30/C-8, H-30/C-9, H_3-19/C-9, and H_3-18/C-14. The relative configuration of **5** was established to be the same as that of **1** by the NOESY spectrum. Therefore, the structure of **5**, named moluccensin T, was assigned as $\Delta^{8,9}$,$\Delta^{14,15}$-didehydromoluccensin R.

Moluccensin U (**6**) was obtained as a white, amorphous powder. Its molecular formula was determined to be $C_{32}H_{40}O_{10}$ by HR-TOFMS (*m*/*z* 585.2686, calcd for $[M + H]^+$ 585.2694). Comparison of the ^1H and ^{13}C NMR spectroscopic data of **6** (Tables 1 and 2) with those of **5** suggested that two compounds were structural analogues. The only difference was the replacement of the 3-*O*-isobutyryl group in **5** by a 3-*O*-2-methylbutyryl group [δ_H 1.03 (t, *J* = 7.2 Hz), 1.25 (d, *J* = 7.2 Hz), 1.58 m, 1.80 m, 2.54 m; δ_C 11.9 CH_3, 17.0 CH_3, 26.7 CH_2, 41.5 CH, 175.5 qC] in **6**. This finding was verified by $^1H-^1H$ COSY cross-peaks between H_3-4′/H_2-3′, H_2-3′/H-2′, and H-2′/H_3-5′ and HMBC correlations between H_3-4′/C-3′, H_3-4′/C-2′, H_3-5′/C-2′, H_3-5′/C-1′, H-2′/C-1′, and H-3/C-1′. Furthermore, the strong NOE interaction from H-3 to H_3-29, but not from H-3 to H-5, helped to establish 3α-H and the corresponding

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Table 1. ^{1}H (400 MHz for 2, 3, and 6, 500 MHz for 1 and 5) NMR Data (δ) for Compounds 1−3, 5, and 6 in $CDCl_3$ (J in Hz)

position	1	2	3	5	6
2			3.24 dd (5.6, 2.8)		
3	4.92 s	4.92 s		4.82 s	4.82 s
5	3.14 s	3.14 s	2.69 s	3.16 s	3.16 s
6	4.52 s	4.53 s	4.64 s	4.37 s	4.39 s
9	2.15 m	2.14 m	2.19 m	2.30 m	2.30 m
11α	1.86 m	1.84[a]	1.86[a]	1.87 m	1.87 m
11β	1.86 m	1.84[a]	1.86[a]	1.40 m	1.40 m
12α	1.22[a]	1.20[a]	1.16[a]	1.27 m	1.26[a]
12β	1.73 m	1.74[a]	1.78 m	1.99 m	1.99 m
15α	3.47 dt (21.0, 3.0)	3.46 dt (20.8, 3.2)	3.44 dt (21.2, 2.4)	6.29 br s	6.30 br s
15β	3.79 d (21.0)	3.82 d (20.8)	3.55 dt (21.2, 1.6)		
17	5.51 s	5.52 s	5.26 s	5.12 s	5.12 s
18	1.03 s	1.04 s	0.98 s	1.06 s	1.06 s
19	1.52 s	1.52 s	1.55 s	1.55 s	1.54 s
21	7.47 br s	7.48 br s	7.49 br s	7.52 br s	7.53 br s
22	6.40 br d (1.5)	6.41 br d (1.6)	6.40 br d (1.6)	6.49 br d (2.0)	6.50 br d 1.6)
23	7.43 t (1.5)	7.44 t (1.6)	7.41 t (1.6)	7.45 t (2.0)	7.45 t (1.6)
28	0.79 s	0.79 s	1.03 s	0.81 s	0.82 s
29	1.05 s	1.05 s	1.15 s	1.10 s	1.10 s
30α	1.79 d (15.0)	1.80[a]	2.37 dd (14.0, 5.6)	6.28 d (3.0)	6.28 d (3.2)
30β	3.24 d (15.0)	3.23 d (14.8)	3.20 dd (14.0, 2.8)		
7-OMe	3.82 s	3.82 s	3.85 s	3.82 s	3.82 s
6-OH			2.88 br s		
3-*O*Acyl					
2′	2.64 m	2.44 m		2.73 m	2.54 m
3′	1.23 d (7.0)	1.82[a]		1.29 d (6.5)	1.80 m
		1.50[a]			1.58 m
4′	1.22 d (7.0)	1.00 t (7.2)		1.28 d (6.5)	1.03 t (7.2)
5′		1.19 d (7.2)			1.25 d (7.2)

[a]Overlapped signals assigned by ^{1}H−^{1}H COSY, HSQC, and HMBC spectra without designating multiplicity.

Table 2. ^{13}C (100 MHz for 2, 3, and 6, 125 MHz for 1 and 5) NMR Data (δ) for Compounds 1−3, 5, and 6 in $CDCl_3$

position	1	2	3	5	6
1	217.3	217.3	213.2	212.0	212.1
2	77.9	77.9	57.8	77.6	77.6
3	86.4	86.5	209.9	86.8	86.8
4	39.6	39.6	49.4	40.2	40.1
5	45.1	45.1	44.4	44.7	44.7
6	73.0	73.0	73.2	72.0	72.0
7	175.4	175.4	174.9	175.6	175.6
8	126.7	126.6	126.0	134.4	134.5
9	53.4	53.2	52.1	55.2	55.1
10	52.3	52.4	54.4	53.1	53.2
11	18.9	18.9	18.7	22.5	22.5
12	29.7	29.6	28.8	33.2	33.2
13	38.2	38.2	38.2	37.6	37.6
14	132.6	132.6	134.1	160.6	160.6
15	33.5	33.6	33.1	113.2	113.2
16	169.1	169.2	169.4	164.6	164.6
17	80.9	80.9	80.6	79.8	79.7
18	18.3	18.2	17.7	22.6	22.4
19	17.6	17.6	17.6	16.2	16.2
20	120.6	120.6	120.5	120.0	120.0
21	141.1	141.1	141.2	141.4	141.4
22	109.7	109.7	109.8	110.2	110.1
23	143.2	143.2	143.0	143.3	143.3
28	22.6	22.6	21.0	21.5	21.5
29	22.6	22.7	20.5	23.0	23.0
30	44.6	44.6	36.4	133.6	133.6
7-OMe	53.3	53.2	53.5	53.3	53.2
3-*O*Acyl					
1′	175.8	175.6		175.6	175.5
2′	34.4	41.3		34.4	41.5
3′	18.4	26.1		18.9	26.7
4′	19.9	11.6		19.3	11.9
5′		17.5			17.0

3β-*O*-2-methylbutyryl group. On the basis of the above results, the structure of moluccensin U was concluded to be 3-*O*-(2-methylbutyryl)-3-deisobutyrylmoluccensin T.

Moluccensin V (7), colorless crystals ($CHCl_3$−MeOH, 1:1), had the molecular formula $C_{28}H_{32}O_8$, as established by HR-TOFMS (m/z 519.1929, calcd for $[M + Na]^+$ 519.1989). The NMR spectroscopic data of 7 (Table 3) were similar to those of godavarin A,[23] except for the replacement of the 3-*O*-tigloyl group in godavarin A by a 3-*O*-acetyl group (δ_H 2.11 s; δ_C 170.2 qC, 20.3 CH_3). This deduction was further confirmed by the strong HMBC correlation between H-3 [δ 4.97 (d, J = 9.2 Hz)] and C-1′ of the acetyl group (Figure S2 in the Supporting Information). The relative configuration of 7 was established on the basis of the NOE spectrum. Significant NOE interactions from H-3 to H_3-29 and H-28α served to establish the 3α-H and the corresponding 3β-acetyl group (Figure S3). Moreover, those between H-5/H-6β, H-5/H-28β, H-5/H-11β, and H-5/H-17 established the β-orientation of H-5 and H-17.

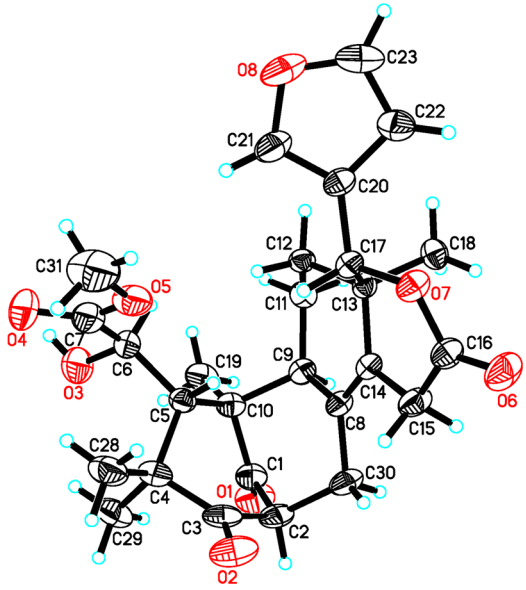

Figure 1. Perspective drawing of the X-ray structure of 6*R*-hydroxymexicanolide (3).

Similarly, those between H-9/H_3-19 and H-14/H_3-18 indicated their mutual *cis* relationship and the α-orientation. The absolute

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Table 3. ^{1}H (400 MHz for 7, 500 MHz for 8) and ^{13}C (100 MHz for 7, 125 MHz for 8) NMR Data for Compounds 7 and 8 in $CDCl_3$

	7		8	
position	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C
1		214.6		98.2
2	3.59 dd (9.2, 7.2)	47.8	3.05 dd (10.0, 3.0)	41.1
3	4.97 d (9.2)	75.5	5.43 d (10.0)	71.2
4		35.7		42.5
5	3.11 dd (12.0, 7.2)	38.7	2.88 br d (11.0)	35.4
6a	2.68 dd (18.4, 12.0)	31.6	2.27 d (17.0)	32.2
6b	2.60 dd (18.4, 7.2)		2.41 dd (17.0, 11.0)	
7		169.6		173.8
8		139.0		61.3
9	2.33[a]	55.8	2.05[a]	46.0
10		48.8		41.0
11α	1.78 m	21.3	1.84[a]	18.9
11β	1.72 m		1.72 m	
12α	1.51 m	33.9	1.39 m	33.2
12β	1.81 m		2.00[a]	
13		36.6		35.7
14	2.30[a]	45.0	1.67[a]	44.7
15α	2.82 br d (18.4)	29.9	2.62 dd (17.5, 6.0)	31.6
15β	2.92 dd (18.4, 6.0)		2.90 dd (17.5, 11.0)	
16		169.0		170.5
17	5.42 s	77.5	5.18 s	79.5
18	1.03 s	21.8	1.04 s	25.9
19	1.16 s	15.9	1.06 s	15.8
20		120.7		120.7
21	7.45 br s	140.4	7.52 br s	140.9
22	6.35 br s	109.2	6.40 dd (2.0, 1.0)	109.9
23	7.46 br s	143.5	7.43 t (2.0)	143.2
28α	3.93 d (12.0)	74.4	0.78 s	14.0
28β	4.38 d (12.0)			
29	1.03 s	16.8	4.70 s	99.3
30	5.35 d (7.2)	122.2	3.08 d (3.0)	60.5
7-OMe			3.74 s	52.3
29-OMe			3.46 s	56.3
3-OAcyl				
1′		170.2		167.6
2′	2.11 s	20.3		127.6
3′			7.02 q (7.0)	140.3
4′			1.84 d (7.0)	14.7
5′			1.91 s	12.2

[a]Overlapped signals assigned by ^{1}H–^{1}H COSY, HSQC, and HMBC spectra without designating multiplicity.

configuration of **7** (Figure 2) was established by single-crystal X-ray diffraction analysis using Cu Kα radiation [Flack parameter 0.00(19)]. In the crystal, **7** was stabilized by intermolecular C···H–O hydrogen bonds between H-5/O-5′ and H-28/O-5′. Thus, the absolute configuration of **7**, named moluccensin V, was identified as 3-*O*-(acetyl)-3-detigloylgodavarin A.

Moluccensin W (**8**), a white, amorphous powder, was determined to have the molecular formula $C_{33}H_{42}O_{11}$, as established by HR-TOFMS (m/z 615.2752, calcd for $[M + H]^+$ 615.2800). The NMR spectroscopic data of **8** (Table 3) were similar to those of godavarin G,[23] except for the presence of a tigloyl group [δ_H 7.02 (q, J = 7.0 Hz), 1.84 (d, J = 7.0 Hz), 1.91 s; δ_C 167.6 qC, 127.6 qC, 140.3 CH, 14.7 CH_3, 12.2 CH_3] and the absence of an isobutyryl group. The existence of the tigloyl

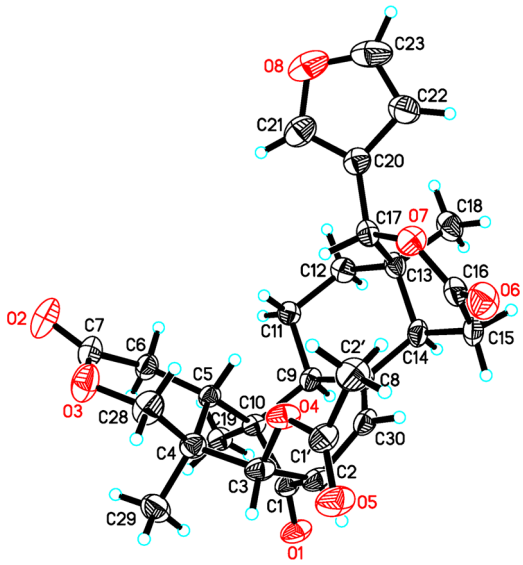

Figure 2. Perspective drawing of the X-ray structure of moluccensin V (**7**).

group was corroborated by ^{1}H–^{1}H COSY cross-peaks and HMBC correlations within this group, and its location at C-3 was confirmed by the HMBC correlation from H-3 [δ 5.43 (d, J = 10.0 Hz)] to C-1′ of this group (Figure 3). Moreover, NOE

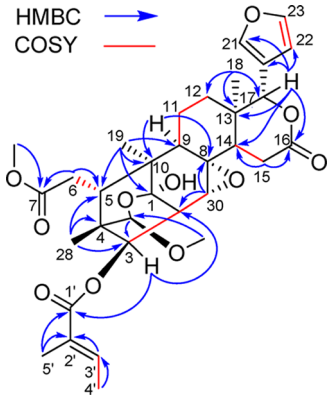

Figure 3. Selected ^{1}H–^{1}H COSY cross-peaks and HMBC correlations for moluccensin W (**8**).

interactions between H-5/H-11β, H-5/H-17, H-17/H-11β, H-17/H-12β, and H-17/H-15β established the β-orientation of H-5 and H-17 (Figure 4). However, contrary to godavarin G, significant NOE interactions from H-29 to H_3-28 and H_3-19, but not from H-29 to H-3, served to establish the α-orientation of H-29 in **8**. Therefore, the structure of **8**, named moluccensin W, was elucidated as shown.

Moluccensin X (**9**) was obtained as a white, amorphous powder. The molecular formula $C_{31}H_{36}O_{10}$ was established by HR-TOFMS (m/z 569.2364, calcd for $[M + H]^+$ 569.2381). The NMR spectroscopic data of **9** (Table 4) were similar to those of moluccensin G,[19] except for the absence of the 1-*O*-isobutyryl group, which is one of the two isobutyryl groups in moluccensin G. The presence of the only isobutyryl group [δ_H 1.12 (d, J = 7.0 Hz), 1.14 (d, J = 7.0 Hz), 2.49 overlapped; δ_C 18.9 CH_3, 19.0 CH_3, 34.1 CH, 175.2 qC] in **9** was confirmed by ^{1}H–^{1}H COSY cross-peaks between H-2′/H-3′ and H-2′/H-4′ and HMBC correlations between H-2′/C-1′, H-2′/C-3′, H-2′/

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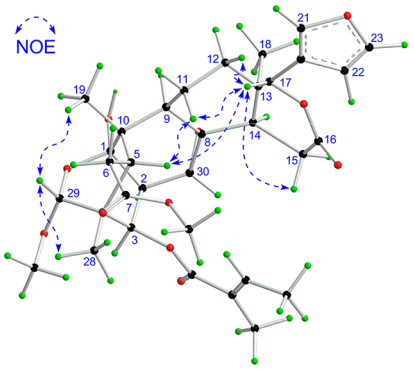

Figure 4. Diagnostic NOE interactions for moluccensin W (**8**).

C-4′, H-3′/C-1′, H-3′/C-2′, H-4′/C-1′, and H-4′/C-2′. The HMBC correlation from H-3 (δ 4.97 s) to C-1′ of the isobutyryl group placed it at C-3. Moreover, the significant NOE interaction from H-3 to $H_{pro\text{-}R}$-29 helped to establish the 3α-H and the corresponding 3β-isobutyryl group. Similarly, those between H-5/H-28, H-17/H-12β, and H-12α/H_3-18 helped to establish the β-orientation of H-5 and H-17 and the α-orientation of H_3-18. Thus, the structure of **9**, named moluccensin X, was identified as 1-*O*-deisobutyrylmoluccensin G.

Moluccensin Y (**10**), obtained as a white, amorphous powder, had the molecular formula $C_{33}H_{38}O_{13}$, as established by HR-TOFMS (*m*/*z* 643.2380, calcd for $[M + H]^+$ 643.2385). Its NMR spectroscopic data (Table 4) indicated that **10** was a phragmalin *ortho* ester, characterized by an orthoacetate group [δ_H 1.70 s; δ_C 119.6 qC, 16.6 CH_3]. Three oxygenated quaternary carbons, at δ 84.0, 86.3, and 74.2, were assigned to C-8, C-9, and C-30, respectively, by HMBC correlations between H-15/C-8, H_2-11/C-9, H_3-19/C-9, H-30/C-9, and H-3/C-30. The above observations revealed that **10** was an 8,9,30-phragmalin *ortho* ester. This finding was further supported by the HMBC correlation from H-30 (δ 5.36 s) to C-31 (δ 119.6 qC) (Figure 5). Moreover, the presence of the functional groups, including a methoxy (δ_H 3.68 s; δ_C 52.2 CH_3), two *O*-acetyl groups, and a β-furanyl ring [δ_H 6.44 (br d, *J* = 2.0), 7.42 (br t, *J* = 2.0), 7.45 br s; δ_C 110.0 CH, 143.1 CH, 141.9 CH, 119.8 qC], were corroborated by the 2D NMR studies ($^1H-^1H$ COSY, HSQC, and HMBC). The location of one *O*-acetyl group (δ_H 2.10 s; δ_C 169.3 qC, 21.7 CH_3) at C-3 was confirmed by the HMBC correlation from H-3 (δ 5.25 s) to its carbonyl carbon, and the attachment of another *O*-acetyl group (δ_H 2.17 s; δ_C 170.5 qC, 21.9 CH_3) to C-2 was suggested by the higher frequency shifted C-2 (δ 83.9 qC). The existence of a $\Delta^{14,15}$ double bond was further confirmed by HMBC correlations between H-15/C-14, H-17/C-14, H_3-18/C-14, H-15/C-13, and H-15/C-16. Furthermore, the strong NOE interaction from H-3 to $H_{pro\text{-}R}$-29 served to establish the 3α-H and the corresponding 3β-*O*-acetyl group (Figure 6). Similarly, that from H-12α to H_3-18 suggested the α-orientation of H_3-18. NOE interactions between H-5/H-11β, H-12β/H-17, H-15/H-17, H-15/H-30, and H-17/H-5 established the β-orientation of H-5 and H-17. Therefore, the structure of compound **10**, named moluccensin Y, was established as shown.

Antifeedant and Insecticidal Activities of Compounds 1−4. Mexicanolides with a $\Delta^{8,14}$ double bond usually exhibit potent antifeedant and insecticidal activities against the instar larvae of *Brontispa longissima* (Gestro).[36] Accordingly, compounds **1**−**4** were tested for their antifeedant and insecticidal activities against the third-instar larvae of *B. longissima* by using a previously reported conventional leaf disk method.[34] Moluccensin R (**1**), 6*R*-hydroxymexicanolide (**3**),[26−28] and 2-hydroxyfissinolide (**4**)[29−31] were found to exhibit marked antifeedant activity against the third-instar larvae of *B. longissima* at a concentration of 1 mg/mL (Table 5). The antifeedant rates of these compounds at exposure times of 24 and 48 h were over 60%. The most potent compound tested was **4**.[29−31] Its antifeedant rates at exposure times of 24 and 48 h were over 90%. The AFC_{50} (concentration for 50% antifeedant activity) value of **4**[29−31] at the exposure time of 24 h was 94 μg/mL. However, all the tested compounds showed weak insecticidal activities (Table 5).

Table 4. ^1H (400 MHz for 9, 500 MHz for 10) and ^{13}C (100 MHz for 9, 125 MHz for 10) NMR Data for Compounds 9 and 10 in $CDCl_3$

	9		10	
position	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C
1		86.2		84.3
2		80.5		83.9
3	4.97 s	86.2	5.25 s	85.0
4		45.7		44.7
5	2.84 dd (9.6, 4.8)	43.3	2.32[a]	39.5
6a	2.44[a]	33.1	2.36[a]	33.7
6b	2.55[a]		2.36[a]	
7		173.3		173.4
8		121.4		84.0
9		169.6		86.3
10		48.2		48.0
11α	2.44[a]	25.4	2.14 m	26.5
11β	2.44[a]		1.93[a]	
12α	1.69 m	30.1	1.17 m	29.2
12β	1.47 m		1.50 m	
13		36.5		38.0
14		152.2		154.4
15	7.16 s	115.6	6.58 s	122.5
16		165.5		164.0
17	5.01 s	80.4	5.77 s	80.4
18	1.01 s	15.8	1.40 s	19.7
19	1.26 s	16.1	1.28 s	15.5
20		119.9		119.8
21	7.50 br s	141.3	7.45 br s	141.9
22	6.46 br d (1.6)	110.0	6.44 br d (2.0)	110.0
23	7.45 t (1.6)	143.2	7.42 t (2.0)	143.1
28	0.96 s	16.6	0.74 s	14.5
$29_{pro\text{-}R}$	1.89 dd (11.2, 2.0)	41.8	1.72[a]	39.5
$29_{pro\text{-}S}$	1.97 br d (11.2)		1.94[a]	
30		194.6	5.36 s	74.2
31				119.6
32			1.70 s	16.6
7-OMe	3.71 s	52.2	3.68 s	52.2
2-OAc				
1′				170.5
2′			2.17 s	21.9
3-OAcyl				
1″		175.2		169.3
2″	2.49[a]	34.1	2.10 s	21.7
3″	1.12 d (7.0)	18.9		
4″	1.14 d (7.0)	19.0		

[a]Overlapped signals assigned by $^1H-^1H$ COSY, HSQC, and HMBC spectra without designating multiplicity.

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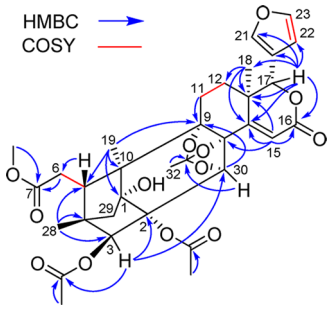

Figure 5. Selected ^{1}H−^{1}H COSY cross-peaks and HMBC correlations for moluccensin Y (**10**).

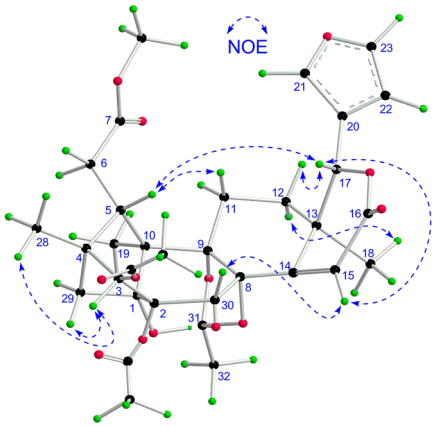

Figure 6. Diagnostic NOE interactions for moluccensin Y (**10**).

Table 5. Antifeedant and Insecticidal Activities of Compounds 1−4 against the Third-Instar Larvae of *Brontispa longissima*

		antifeedant rates (mean ± SD%)		corrected mortality (mean ± SD%)
compound	concentration (mg/mL)	24 h	48 h	9 d
1	1.0	69.6 ± 4.1	62.1 ± 4.3	17.0 ± 5.1
2	1.0	42.3 ± 2.8	44.1 ± 3.9	48.2 ± 3.2
3	1.0	76.6 ± 4.6	69.3 ± 2.6	20.7 ± 1.3
4	1.0	93.7 ± 5.5	91.5 ± 3.5	34.4 ± 5.1

EXPERIMENTAL SECTION

General Experimental Procedures. Melting points were measured on an X_4 micromelting point detector (Beijing Tech. Instrument Co. Ltd., China). Optical rotations were recorded on a Polaptronic HNQW5 automatic high-resolution polarimeter (Schmidt & Haensch Co. Ltd.). UV spectra were obtained on a Beckman DU-640 UV spectrophotometer, and NMR spectra were recorded in $CDCl_3$ using Bruker Avance AV-500 or AV-400 NMR spectrometers (Bruker BioSpin, Fällanden, Switzerland) with TMS as the internal standard. HR-TOF mass spectra were measured by an LC-DAD-ESI-TOF-MS system. Reversed-phase HPLC analysis was performed on an Agilent HPLC 1200 series equipped with a diode array detector (Agilent Technologies, Waldbronn, Germany), and mass spectra were recorded on a micrOTOF-Q ESI-mass spectrometer (Bruker Daltonics, Bremen, Germany). Single-crystal X-ray diffraction analysis was performed on an Oxford Gemini S Ultra detector employing graphite-monochromated Cu Kα radiation (λ = 1.54184 Å) at 298 K. Preparative HPLC was carried out on ODS columns (250 × 10 mm i.d. and 250 × 4.6 mm i.d., YMC) with a Waters 2998 photodiode array detector. For CC, silica gel (200−300 mesh) (Qingdao Marine Chemical Industrial Co. Ltd.) and RP C_{18} gel (Cosmosil C_{18}-PREP 140 μm, Nacalai Tesque, Kyoto, Japan) were used.

Plant Material. The seeds of *X. moluccensis* were collected in September 2007 at the mangrove wetlands of the Godavari estuary and in October 2007 at the mangrove wetlands in the Krishna estuary, Andhra Pradesh, India, respectively. The identification of the plants was performed by one of the authors (T.S.). Voucher samples (No. IndianXM-03 and No. IndianXM-01) are maintained in the herbarium of the South China Sea Institute of Oceanology, Chinese Academy of Sciences.

Extraction and Isolation. Dried seeds (8.7 kg) of *X. moluccensis*, collected at the Godavari estuary, were extracted three times with 95% aqueous EtOH at room temperature. The extract was concentrated under reduced pressure, followed by suspension in H_2O and extraction with EtOAc. The resulting EtOAc extract (198.0 g) was chromatographed on silica gel eluted using a $CHCl_3$−MeOH system (100:0 to 5:1) to yield 127 fractions. Fractions 47 to 62 (66.2 g) were combined and further separated using RP C_{18} CC (MeCN−H_2O, 50:50 to 100:0) to afford 132 subfractions. Subfractions 33 to 39 were combined and subjected to preparative HPLC (YMC-Pack ODS-5-A, 250 × 20 mm i.d. and 250 × 10 mm i.d., MeCN−H_2O, 53:47) to yield compounds **7** (35.5 mg) and **8** (4.4 mg).

Dried seeds (7.0 kg) of *X. moluccensis*, collected at the Krishna estuary, were extracted three times with 95% aqueous EtOH at room temperature. The extract was concentrated under reduced pressure, followed by suspension in H_2O and extraction with EtOAc. The resulting EtOAc extract (320 g) was chromatographed on Si gel CC and eluted using a $CHCl_3$−MeOH system (100:0 to 5:1) to yield 230 fractions. Fractions 81 to 87 (33.9 g) were combined and further purified with RP C_{18} CC (MeCN−H_2O, 50:50 to 100:0) to afford 68 subfractions. Subfractions 5 to 8 were combined and further separated using RP C_{18} CC (MeCN−H_2O, 50:50 to 100:0) to afford 71 subfractions. Subfractions 21 to 39 were combined and further purified with preparative HPLC (YMC-Pack ODS-5-A, 250 × 20 mm i.d. and 250 × 4.6 mm i.d., MeOH−H_2O, 50:50 to 55: 45) to yield compounds **1** (27.0 mg), **2** (51.2 mg), **3** (10.6 mg), **4** (16.2 mg), **5** (4.9 mg), **6** (22.2 mg), **9** (21.2 mg), **10** (30.1 mg), swietmanin G (9.5 mg), swietmanin H (6.0 mg), xyloccensin E (20.0 mg), and xyloccensin Q (1.8 mg).

X-ray Crystallographic Analysis of 6*R*-Hydroxymexicanolide (3). Colorless blocks, $C_{27}H_{32}O_8$, M_r = 484.53, orthorhombic, space group $P2_12_12_1$, a = 10.6167(3) Å, b = 10.7288(2) Å, c = 21.4881(1) Å, V = 2446.79(8) Å^3, Z = 4, d_x = 1.264 Mg/m^3, $F(000)$ = 1032, μ(Cu Kα) = 0.792 mm^{-1}. Data collection was performed on a Gemini S Ultra using graphite-monochromated radiation (λ = 1.54184 Å); 2460 unique reflections were collected to θ_{max} = 62.58°, where 3273 reflections were observed [$F^2 > 4\sigma(F^2)$]. The structures were solved by direct methods (SHELXTL version 5.1) and refined by full-matrix least-squares on F^2. The final R = 0.0405, R_w = 0.0427, and S = 1.068.

X-ray Crystallographic Analysis of Moluccensin V (7). Colorless blocks, monoclinic, space group $P2_1$, a = 11.2839(2) Å, b = 10.5826(2) Å, c = 22.4195(4) Å, V = 2666.87(8) Å^3, Z = 2, d_x = 1.329 Mg/m^3, $F(000)$ = 1136, μ(Cu Kα) = 0.812 mm^{-1}. Data collection was performed on a Gemini S Ultra using graphite-monochromated radiation (λ = 1.54184 Å); 5882 unique reflections were collected to θ_{max} = 62.76°, where 5565 reflections were observed [$F^2 > 4\sigma(F^2)$]. The structures were solved by direct methods (SHELXTL version 5.1) and refined by full-matrix least-squares on F^2. The final R = 0.0398, R_w = 0.0421, and S = 1.040.

Moluccensin R (1): white, amorphous powder; $[\alpha]^{25}_D$ −77 (*c* 2.7, Me_2CO); UV (MeCN) λ_{max} 197.6 nm; ^{1}H and ^{13}C NMR spectroscopic data (see Tables 1 and 2); HR-TOFMS *m/z* 573.2683 [calcd for $C_{31}H_{41}O_{10}$ [M + H]$^+$, 573.2694].

Moluccensin S (2): white, amorphous powder; $[\alpha]^{25}_D$ −65 (*c* 0.28, Me_2CO); UV (MeCN) λ_{max} 197.6 nm; ^{1}H and ^{13}C NMR spectroscopic data (see Tables 1 and 2); HR-TOFMS *m/z* 587.2857 [calcd for $C_{32}H_{43}O_{10}$ [M + H]$^+$, 587.2851].

6*R*-Hydroxymexicanolide (3): colorless crystals ($CHCl_3$−MeOH); mp 248−250 °C; $[\alpha]^{25}_D$ −72 (*c* 0.27, Me_2CO); UV (MeCN) λ_{max} 198.8 nm; ^{1}H and ^{13}C NMR spectroscopic data (see

Tables 1 and 2); HR-TOFMS *m/z* 485.2173 [calcd for $C_{27}H_{33}O_8$ [M + H]$^+$, 485.2170].

Moluccensin T (5): white, amorphous powder; $[\alpha]^{25}_D$ +133 (*c* 0.49, Me_2CO); UV (MeCN) λ_{max} 196.4, 281.5 nm; ^1H and ^{13}C NMR spectroscopic data (see Tables 1 and 2); HR-TOFMS *m/z* 571.2512 [calcd for $C_{31}H_{39}O_{10}$ [M + H]$^+$, 571.2538].

Moluccensin U (6): white, amorphous powder; $[\alpha]^{25}_D$ +148 (*c* 0.24, Me_2CO); UV (MeCN) λ_{max} 198.8, 281.5 nm; ^1H and ^{13}C NMR spectroscopic data (see Tables 1 and 2); HR-TOFMS *m/z* 585.2686 [calcd for $C_{32}H_{41}O_{10}$ [M + H]$^+$, 585.2694].

Moluccensin V (7): colorless crystals ($CHCl_3$–MeOH); mp 224–226 °C; $[\alpha]^{25}_D$ −51 (*c* 0.34, Me_2CO); UV (MeCN) λ_{max} 192.1 nm; ^1H and ^{13}C NMR spectroscopic data (see Table 3); HR-TOFMS *m/z* 519.1929 [calcd for $C_{28}H_{32}O_8Na$ [M + Na]$^+$, 519.1989].

Moluccensin W (8): white, amorphous powder; $[\alpha]^{25}_D$ −24 (*c* 0.44, Me_2CO); UV (MeCN) λ_{max} 215.7 nm; ^1H and ^{13}C NMR spectroscopic data (see Table 3); HR-TOFMS *m/z* 615.2752 [calcd for $C_{33}H_{43}O_{11}$ [M + H]$^+$, 615.2800]; *m/z* 632.3014 [calcd for $C_{33}H_{46}O_{11}N$ [M + NH_4]$^+$, 632.3071].

Moluccensin X (9): white, amorphous powder; $[\alpha]^{25}_D$ +133 (*c* 2.12, Me_2CO); UV (MeCN) λ_{max} 198.8, 285.1 nm; ^1H and ^{13}C NMR spectroscopic data (see Table 4); HR-TOFMS *m/z* 569.2364 [calcd for $C_{31}H_{37}O_{10}$ [M + H]$^+$, 569.2381].

Moluccensin Y (10): white, amorphous powder; $[\alpha]^{25}_D$ +48 (*c* 3.01, Me_2CO); UV (MeCN) λ_{max} 214.1 nm; ^1H and ^{13}C NMR spectroscopic data (see Table 4); HR-TOFMS *m/z* 643.2380 [calcd for $C_{33}H_{39}O_{13}$ [M + H]$^+$, 643.2385].

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

HR-TOFMS, ^1H NMR, ^{13}C NMR, ^1H–^1H COSY, HSQC, and HMBC spectra of compounds **1**–**3** and **5**–**10** and NOESY spectra of compounds **3**, **7**, **8**, and **10**. X-ray crystal data for **3** and **7**. These materials are available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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