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Rocaglamides, Glycosides, and Putrescine Bisamides from *Aglaia dasyclada*

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A phytochemical analysis of the leaves of *Aglaia dasyclada* collected in Yunnan Province (People's Republic of China) yielded five cyclopentabenzofurans (**1–5**) of the rocaglamide family that are common secondary metabolites of *Aglaia* species as well as four biogenetically related compounds of the aglain (**7**), aglaforbesin (**8**) and forbaglin (**9**, **10**) types. In addition, the cinnamic acid amide dasyclamide (**6**), which is a putative biogenetic precursor of these compounds (**7–10**), was isolated. The structures of the new compounds (**6–10**) were assigned unambiguously from the combined use of 1D and 2D NMR spectroscopy and mass spectrometry.

Members of the genus *Aglaia* have recently received considerable attention due to the presence of a structurally unique group of cyclopentabenzofurans, the so-called rocaglamide derivatives, which occur exclusively in this genus.^{1–13} The parent compound rocaglamide and many of its congeners are potent natural insecticides comparable in activity to azadirachtin.^{7–9} In addition to their insecticidal activity, the rocaglamides exhibit pronounced antiproliferative activity against human cancer cells in vitro, comparable to that of vinblastine sulfate,^{3,14,15} thus making these compounds an even more fascinating group of potentially bioactive plant metabolites. In contrast, natural products exhibiting an aglain, aglaforbesin, or forbaglin skeleton appear to be devoid of any insecticidal or antiproliferative activity even though they are structurally related to rocaglamide and its numerous congeners and are probably derived through the same biosynthetic pathway.

In continuation of our phytochemical screening of *Aglaia* species, we report here the isolation and structure elucidation of rocaglamide derivatives and related compounds from *A. dasyclada* Miq. (Meliaceae) from Yunnan Province (People's Republic of China), which include the new natural products **6–10**.

Results and Discussion

Leaves of *A. dasyclada* were pulverized and extracted with MeOH, followed by solvent–solvent partitioning yielding hexane, EtOAc, and H₂O fractions. When incorporated into artificial diet and offered to neonate larvae of the polyphagous insect *Spodoptera littoralis* in a nonchoice bioassay, only the EtOAc fraction caused significant larval mortality (>90% compared to controls). Subsequent phytochemical analysis was therefore focused on the EtOAc fraction. Chromatographic separation of the latter fraction yielded five rocaglamide derivatives (**1–5**), a new aglain (**7**), and an aglaforbesin (**8**) derivative, as well as two new

forbaglin congeners (**9**, **10**). In addition, the new putrescine bisamide **6**, which is probably a biosynthetic precursor of **7–10**, was also isolated. The structures of the new natural products were determined unambiguously by NMR spectroscopy including 2D experiments as well as by mass spectrometry.

Careful examination of the EIMS and ¹H and ¹³C NMR data revealed that compounds **1–5** are rocaglamide-type compounds possessing the cyclopentatetrahydrobenzofuran skeleton. Previously published data show compounds **1–5** to be the known derivatives rocaglaol (**1**), methylrocaglate (**2**), 1-*O*-formylmethyl rocaglate (**3**), and 4'-demethoxy-3',4'-methylenedioxy-methyl rocaglate (**4**) and rocagloic acid (**5**), which were previously isolated from *A. odorata*,¹ *A. elliptica*,³ *A. spectabilis*,¹¹ and *A. elliptifolia*.¹³

Dasyclamide (**6**) was isolated as white crystalline needles. The molecular formula C₁₈H₂₄N₂O₃ was established by HRQTOFMS (*m/z* found 339.1681, calcd for C₁₈H₂₄N₂O₃Na, 339.1685). The spectroscopic data of **6** were quite similar to those of grandiamide B, previously isolated from *A. grandis*,¹² indicating that both compounds possess a putrescine group, with amide linkages to two carboxylic acids. The only difference in the ¹H NMR spectrum of **6** from that of grandiamide B was the absence of the methyl signal for the tiglic acid moiety. The molecular ion peak of **6** (*m/z* 317 [M + H]⁺) was 16 mass units larger than that of grandiamide B, and the presence of a methylene signal at δ 4.23 ppm indicated that C-4 of the tiglic acid moiety was substituted by a hydroxyl group in **6**. The cinnamic acid and hydroxytiglic acid moieties are linked to putrescine by amide bonds, as was evident from the 2D correlations (COSY and HMBC) and their respective configurations as deduced from coupling constant and NOE data. The relative configurations at C-2 and C-3 were established from a NOESY spectrum. A cross-peak was observed between methylene H-4 and methyl H-5, indicating that they are *cis* to each other. In turn, the stereochemistry of protons H-2'' and H-3'' was identified from the coupling constant (*J*_{H-2''/H-3''} = 15.8 Hz) typical of a *trans* configuration. Therefore, dasyclamide (**6**) was assigned as shown in Figure 2.

The molecular formula of **7** was established as C₄₂H₅₂N₂O₁₄ by HRQTOFMS (*m/z* found 810.3572, calcd for C₄₂H₅₂DN₂O₁₄, 810.3559, after partial H/D exchange),

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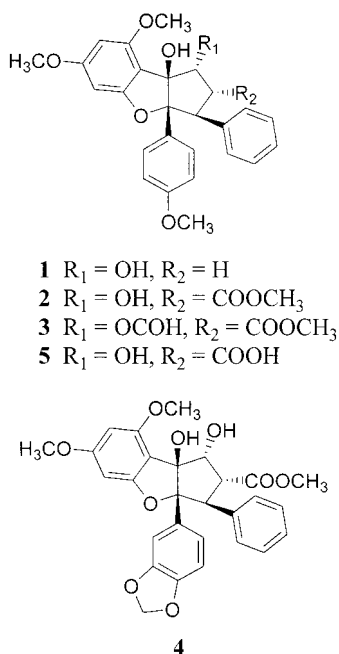


Figure 1. Structures of rocaglamide derivatives (**1–5**), isolated from leaves of *Aglaia dasyclada*.

while the negative-ion FABMS showed a molecular ion peak at m/z 807 $[\text{M} - \text{H}]^-$. The ^1H NMR spectrum of **7** showed spin systems for three benzyl and three methoxyl groups similar to those of the rocaglamides except for having only two methine protons, H-3 and H-4 (δ 4.10 d, $J = 9.7$ Hz and δ 3.38 d, $J = 9.7$ Hz, respectively) and a

Table 1. ^1H (400 MHz) and ^{13}C (125 MHz) NMR Data of Compound **6**^a

position	^{13}C δ_{C} mult.	^1H δ_{H} mult. (J in Hz)	HMBC	ROESY ^b
1	172.5 s			
2	133.5 s			
3	136.2 d	6.34 qt (1.6, 6.0)	1, 5	5 ^b
4	60.0 t	4.23 qd (0.9, 6.0)	2, 3	5
5	13.5 q	1.83 dt (1.6, 0.9)	1, 3, 2	4, 3 ^b
1'	40.8 t	3.30 m	1, 2'3'	
2'	28.4 t	1.60 m	3', 1'4'	
3'	28.4 t	1.60 m	1', 4', 2'	
4'	38.8 t	3.30 m	1'', 2'3'	
1''	169.1 s			
2''	122.4 d	6.60 d (15.8)	4'', 1'', 3''	
3''	142.1 d	7.52 d (15.8)	1'', 5''9'', 2'', 4''	
4''	136.8 s			
5''/9''	129.3 d	7.55 m	3'', 7''	
6''/8''	130.4 d	7.38 m	4''	
7''	131.3 d	7.38 m	5''9''	

^a Spectra were recorded in CD_3OD . ^b Correlation between H-3 and H-5 was weaker than that between H-4 and H-5.

proton singlet at 5.05 ppm, which is typical of H-10 of the aglain system, previously isolated from *A. argentea*.² A close inspection of ^1H and ^{13}C NMR data as well as COSY and HMBC correlations, and comparison with the spectral data of **6**, also indicated the presence of the 4-hydroxytiglic acidic putrescine moiety (Table 2), which formed an amide linkage with carbonyl C-11 from the long-range correlation with H-4 in the HMBC spectrum. The presence of a glucose moiety was confirmed in the ^{13}C NMR spectrum by signals at δ 103.3 (C-1''), 74.7 (C-2''), 78.0 (C-3''), 71.6 (C-4''), 77.9 (C-5''), and 63.0 (C-6'') together with signals in the

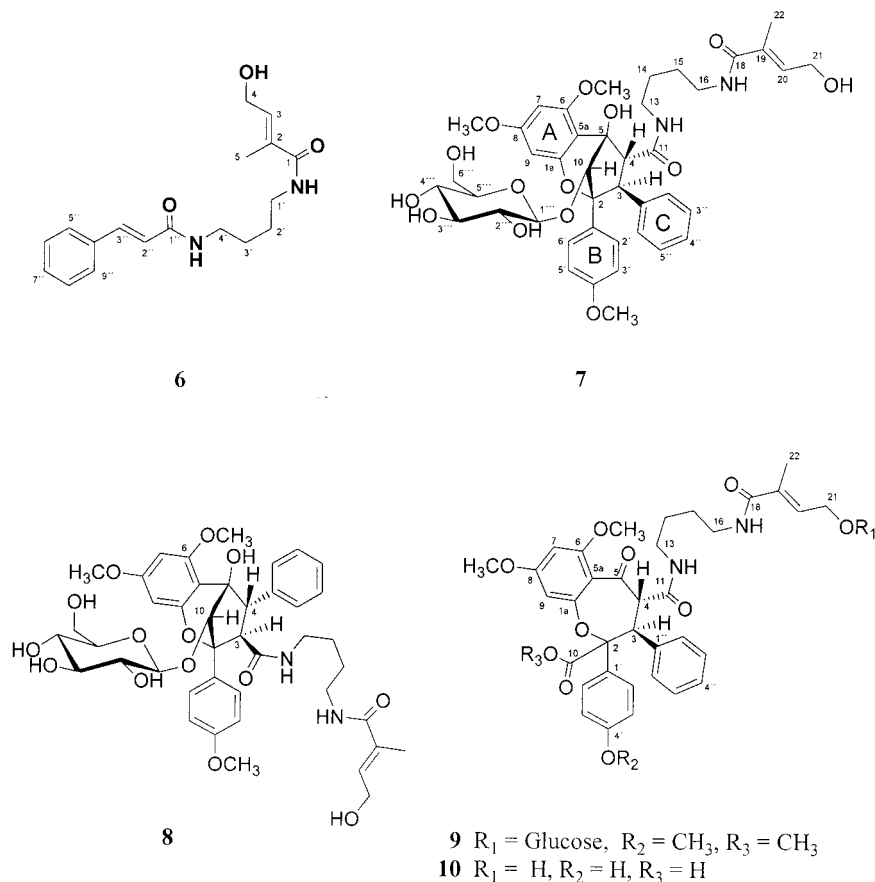


Figure 2. Structures of dasyclamide (**6**) and new derivatives of aglain (**7**), aglaforbesin (**8**), and forbaglin (**9, 10**) isolated from leaves of *Aglaia dasyclada*.

Table 2. ^1H (500 MHz) and ^{13}C (150 MHz) NMR Data of Compound **7**^a

position	^{13}C δ_{C} mult.	^1H δ_{H} mult. (J in Hz)	HMBC	ROESY ^b
1a	155.6 s			
2	88.5 s			
3	55.5 d	4.10 d (9.7)	10, 2''6'', 11, 4, 2, 1''	2'6', 2''6''
4	61.8 d	3.38 d (9.7)	10, 5a, 1'', 3, 5, 11	10, 2''6'', NH-12
5	80.7 s			
5a	105.4 s			
6	161.1 s			
7	93.5 d	6.21 d (2.4)	5a, 9, 6, 8	OCH ₃ -6, OCH ₃ -8
8	162.3 s			
9	95.2 d	6.22 d (2.4)	5a, 1a, 7, 8	OCH ₃ -8
10	81.7 d	5.05 s	1''', 5a, 5	4, 2''6'', 1'''
11	171.9 s			
13	40.0 t	A: 3.17 m B: 3.07 m	14, 15	
14	27.8 t	1.50 m	16, 13	
15	27.8 t	1.50 m	13, 16	
16	40.4 t	3.22 m	14, 18, 15	
18	171.6 s			
19	133.0 s			
20	135.7 d	6.34 qt (0.8, 6.1)	18	NH-17
21	59.5 t	4.27 dd (0.8, 6.1)		22
22	13.0 q	1.85 d (0.8)	18, 20, 19	21
1'	131.2 s			
2'/6'	129.4 d	7.37 d (8.9) ^c	2, 4', 3'5'	3
3'/5'	113.7 d	6.67 d (8.9) ^c	1', 2'6', 4'	OCH ₃ -4'
4'	160.0 s			
1''	141.2 s			
2''/6''	130.6 d	7.00 m	3, 1''	3, 4, 10
3''/5''	128.8 d	7.00 m		
4''	127.3 d	7.00 m		
1'''	103.3 d	4.54 d (7.9)	10, 3'''5'''	10, 3''', 5'''
2'''	74.7 d	3.11 dd (7.9, 8.9)		
3'''	78.0 d ^d	3.22 m		1'''
4'''	71.6 d	3.22 m		
5'''	77.9 d ^d	3.22 m		1'''
6'''	63.0 t	A: 3.92 dd (1.3, 11.6) B: 3.62 dd (6.1, 11.6)		
OCH ₃ -6	56.5 q	3.86 s	6	7
OCH ₃ -8	55.8 q	3.81 s	8	7, 9
OCH ₃ -4'	55.5 q	3.68 s	4'	3'5'
NH-12		7.31 t ^b		4
NH-17		7.74 t ^b		20

^a Spectra were recorded in CD_3OD . ^b Spectra were recorded in $\text{DMSO}-d_6$. ^c Signals appeared as an AA'BB' spin system. ^d Interchangeable signals.

^1H NMR spectrum in the range 3.11–4.54 ppm, and from the MS fragment at m/z 181. The glucose possessed a β anomeric configuration (δ 4.54, d, $J = 7.9$ Hz) and had an *O*-glycosidic bond to the aglycon from the HMBC correlation of the anomeric proton H-1''' to C-10. Hence, **7** is the *O*-glycoside derivative of an aglain system and is the first glycoside of this type to be isolated from the genus *Aglaia* bearing a putrescine group and hydroxytiglic acid instead of an odorine moiety previously found as the amine substituent in the aglain, aglaforbesin, and forbaglin systems.² The relative configuration of **7** was deduced from a detailed analysis of its ROESY spectrum. A correlation between H-10 and H-4 supported the relative configuration of H-3, H-4, and H-10, as shown in Figure 2.

The FABMS and ^1H and ^{13}C NMR spectra of **8** were comparable to those of **7** except that the signal for the

methoxyl group at C-6 was shifted to a higher field at δ 3.16. This change suggested that the phenyl ring is in the vicinity of this methoxyl group. Compound **8** therefore has a framework similar to that of aglaforbesin previously isolated from *A. forbesii*.² Moreover, detailed analysis of ^1H and ^{13}C NMR data in combination with 2D NMR data (COSY, HMBC, and HMQC) showed signals corresponding to the putrescine group and a hydroxytiglic acid moiety similar to those of **7** and indicated an interchange of the phenyl and putrescine systems. The peak at m/z 181 also indicated the presence of a hexose sugar which was similar to that of **7** from the ^1H and ^{13}C NMR data. Thus, **8** is a glycoside of an aglaforbesin system with a putrescine group and hydroxytiglic acid moiety at C-3. The relative configurations of H-3, H-4, and H-10 of **8** were deduced with the aid of a ROESY spectrum and were assigned as shown in Figure 2.

The ^1H NMR spectrum of **9** showed signals typical of an aglain system. The downfield shifts of H-3 and H-4 at δ 5.10 (d, $J = 10.5$ Hz) and δ 4.37 (d, $J = 10.5$ Hz), respectively, together with the absence of H-10, C-10, and C-5 suggested the C-10 bridge had been disrupted to form a forbaglin-type skeleton,² which was supported by analyses of data from the 2D NMR spectra (COSY, HMBC, and HMQC). Compound **9** showed a molecular peak at m/z 837 $[\text{M} + \text{H}]^+$ and a fragment peak at m/z 181 typical for a hexose sugar moiety in the positive FABMS. The proton signals corresponding to glucose were similar to those of compounds **7** and **8**. The HMQC and HMBC correlations indicated a 21-hydroxytiglic amidic putrescine moiety bound to the carbonyl C-11. The β -anomeric proton of the sugar moiety showed a correlation with C-21 of the hydroxytiglic acid moiety, indicating the sugar is attached to C-21. The relative stereochemical assignment at positions 3 and 4 of **9** was established as H-3 α , H-4 β from a comparison of the proton and carbon signals, which were almost identical to those of forbaglin A,² whose relative configurations for these positions were derived from X-ray crystallography. Hence the structure of **9** is as shown in Figure 2.

Compound **10** had a molecular formula of $\text{C}_{35}\text{H}_{38}\text{N}_2\text{O}_{10}$ from the HRESIMS. Its ^1H and ^{13}C NMR data resembled those of **9**, indicative of a forbaglin unit, with the absence of a glucose moiety at C-21 and the two methoxyl groups at C-4' and C-10, deduced from the absence of long-range correlations to C-4' and C-10 as well as the appearance of a carboxylic acid carbon at δ 177.0 (s) for C-10. Thus, **10** is the 4'-hydroxy-10-acidic-21-deglycosyloxy derivative of **9**, as shown in Figure 2.

All new compounds (**6**–**10**) were subjected to a long-term antifeedant insect bioassay (duration of 8 days) against the polyphagous pest insect *Spodoptera littoralis*,⁹ with rocaglamide and azadirachtin as positive controls, but as expected⁷ no insecticidal activity (up to a concentration of 50 ppm) was detected for any of the new natural products.

Experimental Section

General Experimental Procedures. Optical rotations were determined on a Perkin-Elmer 241 MC polarimeter. CD spectra were measured in MeOH on an Yvon Dichrograph CD 6 spectrophotometer. ^1H NMR and ^{13}C NMR were recorded in CD_3OD and $\text{DMSO}-d_6$ on Bruker ARX 400 or DRX 500 NMR spectrometers in the 1D (^1H and ^{13}C , including DEPT) and 2D (COSY, HMQC, HMBC, NOESY, ROESY) modes. EI- (70 eV, direct inlet), CI-, ESI-, and FABMS were recorded on a Finnigan MAT 8430, Finnigan MAT INCOS 50, Finnigan TSQ 7000, and Finnigan 8400 mass spectrometers, respectively.

Table 3. ^1H (400 MHz) and ^{13}C (100 MHz) NMR Data of Compound **8**^a

position	^{13}C δ_{C} mult.	^1H δ_{H} mult. (J in Hz)	HMBC	ROESY
1a	154.7 s			
2	86.4 s			
3	59.9 d	3.49 d (9.8)	10, 1'', 11, 2, 4	2'6', 2''6''
4	57.7 d	3.97 d (9.8)	5a, 11, 2''6'', 3, 5, 1''	10, 2''6''
5	82.3 s			
5a	106.5 s			
6	162.0 s			
7	93.6 d	6.00 d (2.2)	5a, 9, 6, 8	OCH ₃ -6, OCH ₃ -8
8	162.3 s			
9	95.6 d	6.34 d (2.2)	5a, 7, 1a, 8	OCH ₃ -8
10	78.7 d	5.19 s	4, 5a, 1', 1''', 5	4, 1'''
11	172.0 s			
13	39.9 t	A: 2.78 dd (7.0, 14.0) B: 2.57 dd (7.0, 14.0)	11 11	
14	27.1 t	1.14 m	13, 15	
15	27.5 t	0.99 m	14, 16	
16	40.1 t	3.05 m	18	
18	172.0 s			
19	133.0 s			
20	135.7 d	6.34 qt (1.0, 6.0)	18	
21	59.5 t	4.27 d (6.0)	19, 20	22
22	13.0 q	1.86 d (1.0)	18, 20, 19	21
1'	130.7 s			
2'/6'	129.1 d	7.75 d (8.8) ^b	2, 4'	3, 1'''
3'/5'	114.1 d	6.98 d (8.8) ^b	1', 4'	OCH ₃ -4'
4'	160.9 s			
1''	138.0 s			
2''/6''	129.9 d	6.98 m	4''	3, 4
3''/5''	128.8 d	7.22 m	1'', 2''6''	
4''	128.2 d	7.22 m	2''6''	
1'''	101.9 d	4.37 d (7.8)	10	10, 2'6', 3'', 5'''
2'''	74.8 d	3.15 m	4'''	
3'''	77.8 d	3.15 m	4'''	1'''
4'''	71.4 d	3.27 t (9.0)		6'''A, 6'''B
5'''	77.8 d	3.05 m	4'''	1'''
6'''	62.9 t	A: 3.89 dd (2.3, 12.0) B: 3.69 dd (5.8, 12.0)	5'''	4'''
OCH ₃ -6	56.2 q	3.16 s	6	7
OCH ₃ -8	55.8 q	3.82 s	8	7, 9
OCH ₃ -4'	55.8 q	3.85 s	4'	3'5'

^a Spectra were recorded in CD₃OD. ^b Signals appeared as an AA'BB' spin system.

Solvents were distilled prior to use, and spectral grade solvents were used for spectroscopic measurements. HRMS data were determined on a Micromass QTOF mass spectrometer by peak matching against a suitable reference compound (the sugar stachyose) as internal standard.

Plant Material. Plant material of *Aglaia dasyclada* Miq. was collected in Yunnan, People's Republic of China, in August 1999 and identified by Prof. H. B. Cheng, Department of Botany, Peking University. A voucher specimen is on file at the National Research Laboratories of Natural and Biomimetic Drugs, Peking University, Beijing, People's Republic of China, and at the Institut für Pharmazeutische Biologie, Universität Düsseldorf.

Extraction and Isolation. Air-dried leaves of *A. dasyclada* (1.0 kg dry weight) were ground and extracted exhaustively with MeOH. Following evaporation of the solvent, the extract was partitioned between aqueous MeOH-hexane and H₂O-EtOAc. Each fraction obtained was subjected to a bioassay with neonate *Spodoptera littoralis* larvae. From this bioassay, the insecticidal activity was found to reside in the EtOAc fraction. Fractionation of the EtOAc extract was carried out

Table 4. ^1H (400 MHz) and ^{13}C (150 MHz) NMR Data of Compound **9**^a

position	^{13}C δ_{C} mult.	^1H δ_{H} mult. (J in Hz)	HMBC
1a	161.3 s		
2	92.0 s		
3	52.0 d	5.10 d (10.5)	1', 2''6'', 11, 2, 4, 1''
4	67.5 d	4.37 d (10.5)	1'', 3, 5, 11
5	194.0 s		
5a	115.0 s		
6	161.4 s		
7	94.9 d	6.20 d (2.4)	5a, 9, 6, 8
8	165.8 s		
9	100.2 d	6.68 d (2.4)	5a, 7, 1a, 8
10	172.5 s		
11	169.3 s		
13	39.9 t	A: 3.13 m B: 3.07 m	11, 14 11, 14
14	27.2 t ^b	1.33 m	15
15	27.3 t ^b	1.27 m	14, 16
16	40.2 t	3.13 m	18, 15
18	172.3 s		
19	134.7 s		
20	132.5 d	6.38 qdd (1.1, 5.6, 6.8)	18
21	66.6 t	A: 4.56 qdd (1.1, 5.6, 13.7) B: 4.43 qdd (1.1, 6.8, 13.7)	19, 1''', 20 19, 1''', 20
22	13.2 q	1.88 m	18, 20, 19
1'	128.5 s		
2'/6'	130.4 d	7.42 d (9.0) ^c	2, 4', 1'
3'/5'	114.8 d	6.79 d (9.0) ^c	1', 4'
4'	161.4 s		
1''	141.1 s		
2''/6''	130.7 d	7.61 m	3, 4''
3''/5''	129.3 d	7.35 m	1''
4''	128.8 d	7.32 m	3''5''
1'''	103.8 d	4.35 d (7.8)	21
2'''	75.1 d	3.24 dd (7.8, 9.2)	4''', 1''', 3'''
3'''	78.1 d	3.39 m	4'''
4'''	71.7 d	3.31 m	
5'''	78.1 d	3.31 m	
6'''	62.8 t	A: 3.91 dd (1.6, 11.9) B: 3.69 dd (5.9, 11.9)	5'''
OCH ₃ -6	56.5 q	3.66 s	6
OCH ₃ -8	56.2 q	3.91 s	8
OCH ₃ -4'	55.7 q	3.76 s	4'
OCH ₃ -10	52.6 q	3.16 s	10

^a Spectra were recorded in CD₃OD. ^b Interchangeable signals. ^c Signals appeared as an AA'BB' spin system.

through vacuum-liquid chromatography (silica gel [Merck, Darmstadt, FRG], mobile phase: CH₂Cl₂-*i*-PrOH) and by repeated normal-phase column chromatography employing silica gel (mobile phase: 90:10 and 95:5 CH₂Cl₂-*i*-PrOH or 70:30 hexanes-EtOAc). Final purification was performed using RP-18 Lobar columns (Merck, Darmstadt, FRG) (mobile phase: mixtures of MeOH-H₂O) and by preparative HPLC (Merck Hitachi). The separation column (7 or 10 μm , 300 \times 8 mm, i.d.) was pre-filled with Eurospher RP-18 (Knauer, Berlin, FRG). Solvents were distilled prior to use, and spectral grade solvents were used for spectroscopic measurements. Fractions were monitored by TLC on precoated TLC plates with silica gel 60 F₂₅₄ (Merck, Darmstadt, FRG) (mobile phase: 95:5 CH₂Cl₂-MeOH or 8:2 hexanes-EtOAc). Rocaglamide derivatives were detected by their gray color after spraying the TLC plates with anisaldehyde reagent or their typical UV spectrum on HPLC. Yields of compounds were (1) 0.5 mg; (2) 1 mg; (3) 2.2 mg; (4) 0.5 mg; (5) 1 mg; (6) 37 mg; (7) 10 mg; (8) 2.1 mg; (9) 2 mg; and (10) 1.2 mg. The known compounds (1-5) were identified by their HPLC retention times (co-chromatography

with reference substances) as well as EIMS and 1D ^1H NMR data and by comparison with literature data.^{1,3,11,13}

Compound 6: white crystalline needles; ^1H and ^{13}C NMR, see Table 1; CIMS m/z 334 $[\text{M} + \text{NH}_4]^+$, 317 $[\text{M} + \text{H}]^+$; HRQTOFMS m/z 339.1681 (calcd for $\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}_3\text{Na}$, 339.1685).

Compound 7: white amorphous residue; $[\alpha]^{20}_{\text{D}} -22.4^\circ$ (c 1.0, MeOH); CD 203 nm ($\Delta\epsilon -10.1$), 216 ($\Delta\epsilon +4.1$), 242 ($\Delta\epsilon -2.3$); ^1H and ^{13}C NMR, see Table 2; FABMS negative m/z 807 $[\text{M} - \text{H}]^-$; HRQTOFMS m/z 810.3572 (calcd for $\text{C}_{42}\text{H}_{52}\text{DN}_2\text{O}_{14}$, 810.3559).

Compound 8: white amorphous residue; $[\alpha]^{20}_{\text{D}} -28.2^\circ$ (c 0.04, MeOH); CD 192 nm ($\Delta\epsilon -3.4$), 214 ($\Delta\epsilon +17$), 244 ($\Delta\epsilon -2.3$); ^1H and ^{13}C NMR, see Table 3; CIMS m/z 826 $[\text{M} + \text{NH}_4]^+$, 809 $[\text{M} + \text{H}]^+$; HRQTOFMS m/z 809.3499 $[\text{M} + \text{H}]^+$ (calcd for $\text{C}_{42}\text{H}_{53}\text{N}_2\text{O}_{14}$, 809.3497).

Compound 9: white amorphous residue; $[\alpha]^{20}_{\text{D}} -38.5^\circ$ (c 0.2, MeOH); CD 207 nm ($\Delta\epsilon -3.2$), 227 ($\Delta\epsilon +1.1$), 241 ($\Delta\epsilon -0.01$) 256 ($\Delta\epsilon +1.9$) 292 ($\Delta\epsilon -1.8$); ^1H and ^{13}C NMR, see Table 4; FABMS positive m/z 837 $[\text{M} + \text{H}]^+$; HRQTOFMS m/z 837.3465 $[\text{M} + \text{H}]^+$ (calcd for $\text{C}_{43}\text{H}_{53}\text{N}_2\text{O}_{15}$, 837.3446).

Compound 10: white amorphous residue; $[\alpha]^{20}_{\text{D}} -11^\circ$ (c 0.1, MeOH); ^1H NMR (CD_3OD , 300 MHz) δ 7.52 (2H, d, $J = 8.9$ Hz, H-2', H-6'), 7.36 (2H, m, H-2'', H-6''), 7.26 (3H, m, H-3'', H-4'', H-5''), 6.61 (2H, d, $J = 8.9$ Hz, H-3', H-5'), 6.37 (1H, qt, $J = 1.2, 6.2$ Hz, H-20), 5.89 (1H, d, $J = 2.4$ Hz, H-9), 5.52 (1H, d, $J = 2.4$ Hz, H-7), 4.62 (1H, d, $J = 11.7$ Hz, H-3), 4.27 (2H, dq, $J = 1.1, 6.2$ Hz, H-21), 4.26 (1H, d, $J = 11.7$ Hz, H-4), 3.81 (3H, s, OCH_3 -6), 3.54 (2H, m, H-16), 3.49 (3H, s, OCH_3 -8), 3.34 (2H, m, H-13), 1.87 (3H, dt, $J = 1.2, 1.1$ Hz, H-22), 1.63 (4H, m, H-14, H-15); ^{13}C NMR (CD_3OD , 75 MHz) δ 193.0 (s, C-5), 177.0 (s, C-10), 172.0 (s, C-18), 171.0 (s, C-11), 163.2 (s, C-8), 163.1 (s, C-4'), 158.0 (s, C-6), 138.0 (s, C-1''), 135.8 (s, C-19), 133.0 (d, C-20), 131.9 (d, C-2'', C-6''), 130.3 (d, C-2', C-6'), 129.5 (d, C-3'', C-5''), 128.3 (s, C-4''), 128.1 (s, C-1'), 115.4 (d, C-3', C-5'), 112.0 (s, C-5a), 96.7 (d, C-9), 92.1 (d, C-7), 59.5 (t, C-21), 58.7 (d, C-4), 52.3 (d, C-3), 40.1 (t, C-16), 39.4 (t, C-13), 56.3 (q, OCH_3 -6), 55.4 (q, OCH_3 -8), 27.9 (t, C-15), 26.3 (t, C-14), 13.0 (q, C-22), undetectable quaternary carbons (C-1a, C-2); CIMS m/z 664 $[\text{M} + \text{NH}_4]^+$, 647 $[\text{M} + \text{H}]^+$; HRESIMS m/z 669.2414 $[\text{M} + \text{Na}]^+$ (calcd for $\text{C}_{35}\text{H}_{38}\text{N}_2\text{O}_{10}\text{Na}$, 669.2424).

Antifeedant Insect Bioassay. See ref 9.

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