Flavonol−Cinnamate Cycloadducts and Diamide Derivatives from *Aglaia laxiflora*

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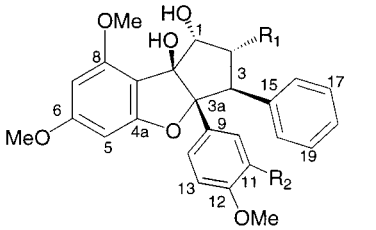
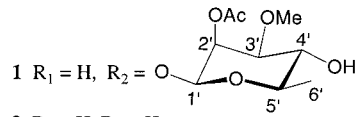
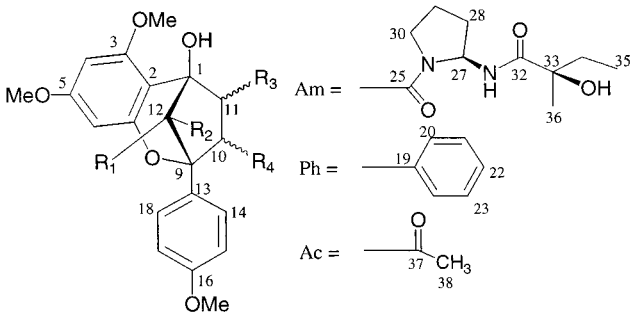
Leaf extracts of the Malaysian plant *Aglaia laxiflora* provided two cytotoxic compounds, a new rocaglaol rhamnoside (**1**), a known rocaglaol (**2**), new (but inactive) flavonol−cinnamaminopyrrolidine adducts (**3**−**6**), and their probable biosynthetic precursors (**7** and trimethoxyflavonol). All structures were elucidated primarily by 2D NMR spectroscopy. The structure and stereochemistry of aglaxiflorin A (**3**) were confirmed by single-crystal X-ray crystallography.

Aglaia species of the family Meliaceae are of ethnomedicinal value[1,2] and have insecticidal[3] and cytotoxic[4] properties. Study of the Malaysian plant *A. laxiflora* has led to the isolation of a cytotoxic cyclopentatetrahydrobenzofuran-rhamnoside (**1**), a derivative of rocaglaol (**2**), and several new bicyclic diamides (**3**−**6**), which appear to be cycloadducts of likely biosynthetic precursors such as (+)-odorinol (**7**) and trimethoxylflavonol.

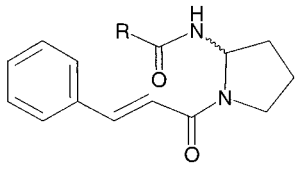




2 $R_1 = H, R_2 = H$



3 $R_1 = OAc$, $R_2 = H$, H - 10β, H - 11α, $R_3 = Am$, $R_4 = Ph$
4 $R_1 = OAc$, $R_2 = H$, H - 10α, H - 11β, $R_3 = Am$, $R_4 = Ph$
5 $R_1 = H$, $R_2 = OAc$, H - 10α, H - 11β, $R_3 = Ph$, $R_4 = Am$
6 $R_1 = H$, $R_2 = OH$, H - 10α, H - 11β, $R_3 = Am$, $R_4 = Ph$



7 R = 2-hydroxy-2-butyl
8 R = (2*E*)-2-but-2-enyl
9 R = 2-butyl

Results and Discussion

Compound **1** exhibited a peak at *m*/*z* 651[M − H]$^-$ ($C_{35}H_{39}O_{12}$, FABMS negative ion mode). The IR spectrum showed a strong band at 1744 cm^{-1}, corresponding to an ester, and strong bands at 1148 and 1124 cm^{-1}, typical of sugars, indicating that **1** was a glycoside. The ^{1}H NMR spectrum showed four methoxyl groups, one phenyl group, one disubstituted phenyl group, and one oxygenated benzene group with two meta protons. Other peaks of the ^{1}H NMR spectrum reflected the presence of a modified rhamnose unit. The ^{13}C NMR data were similar to a known rocaglamide glycoside,[6] except that **1** contained an additional acetyl group on the glycoside moiety. The acetyl group was determined to be at 2′ of the rhamnose, inasmuch as the 2′ proton was significantly shielded (δ 5.52). This conclusion was confirmed by a HMBC cross-peak H-2′/C=O. The 3′-methoxyl group was determined by a NOE-difference experiment; irradiation of the three-proton signal at δ 3.45 caused enhancements of the one-proton signals at δ 5.52 (H-2′) and 3.70 (H-3′). The modified rhamnose was placed at the 11-position because of the observed HMBC cross-peak H-1′/C-11 and the H-1′/H-11 NOE correlation. The glycosidic bond is α, because H-1′ has a small coupling constant (1.6 Hz) with H-2′. The absolute configuration of rocaglaol (**2**) is known from enantioselective synthesis,[7] and the rhamnoside residue has been found to have no significant influence on the rotation of this class of compounds.[4] It is therefore likely the absolute sterochemistry of **1** is as depicted, based on similarity of the sign and magnitude of the rotation of **1** to the parent compound **2** and its derivatives.[4] Thus, **1** was assigned as 11-α-(2′-acetoxy-3′-methoxyrhamnosyl)-rocaglaol, the second rocaglaol glycoside isolated from nature.[6]

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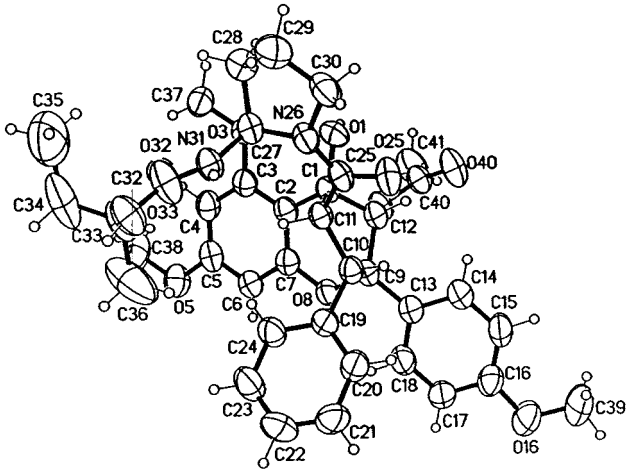

Figure 1. X-ray structure of aglaxiflorin A (**3**).

Aglaxiflorin A (**3**) was isolated as colorless needles, $[\alpha]^{25}_D$ +8.1°, and its molecular formula was determined as $C_{38}H_{44}N_2O_{10}$ by HRFABMS. The IR spectrum showed absorption bands at 3467 (OH), 3400 (NH), 1742 (an unconjugated ester C=O), 1647, and 1615 cm^{-1} (amide carbonyl). Being amides, rotamers were detectable in both the ^1H and ^{13}C NMR as two sets of signals of unequal intensity when $CDCl_3$ was used as solvent, but in methanol-d_4 only one major set of peaks was prominent. The ^1H NMR spectrum disclosed three methoxyl groups. In addition, three aromatic rings related to those observed for rocaglaol[2−4] (**2**) were deduced to be one phenyl group, one para-substituted phenyl, and one aromatic ring with meta positions unsubstituted. Analysis of the ^1H and ^{13}C NMR spectra of **3** indicated a skeleton similar to those found in aglains.[5] However, the low-field signal (δ_C 76.0) indicated that **3** had a new 2-hydroxy-2-methylbutyryl group. The HMBC and NOESY spectra confirmed the structure of **3** as depicted. Notable HMBC correlations were H-10/C-1, -9, -11, -19, -20, -24 and H-12/C-1, -2, -13, CH_3CO. Relative stereochemical assignments were from NOE difference and NOESY correlations, e.g. H-10/H-12, -20, -24; H-11/H-20, -24, -27; and H-12/H-10, -14, -18.

A single-crystal X-ray diffraction experiment established the definitive structure and relative stereochemistry of aglaxiflorin A (**3**) (Figure 1). The trans H-10/H-11 stereochemistry and the relative proximity of H-11 and H-27 were also revealed. Assuming that **3** is derived from the isolated (+)-odorinol **7**, which has known absolute stereochemistry, the absolute configuration for **3** was assigned as depicted. The 27*S* configuration has also been postulated for some aglains from *A. argentea*.[5]

Aglaxiflorin B (**4**), $[\alpha]^{25}_D$ −105.5°, an isomer of aglaxiflorin A (**3**), gave M^+ at *m/z* 688.2979 (HREIMS), which is consistent with $C_{38}H_{44}N_2O_{10}$ (688.2996). The IR spectrum showed an ester band at 1732 cm^{-1} and two amide bands at 1651 and 1617 cm^{-1}. The NMR and HMBC data were similar to those of **3**, indicating that its structure differed in the configurations of C-10 and C-11. NOESY correlations H-12/H-11 and H-11/H-12, -20, -24 support the relative stereochemical assignments shown for **4**.

Aglaxiflorin C (**5**), $[\alpha]^{25}_D$ +34.9°, another isomer of **3** and **4**, had molecular formula $C_{38}H_{44}N_2O_{10}$ (HREIMS). The IR spectrum of **5** exhibited absorption bands at 3507 (OH), 3405 (NH), 1749 (an unconjugated ester carbonyl), 1648, and 1620 cm^{-1} (amide carbonyls). The 1D NMR and HMBC data showed significant differences, compared to those of **3** and **4**. With NOESY correlations for H-11/H-10, -20, -24,CH_3CO but not for H-12/H-10, -11, the stereochemical assignments for C-12, H-10β, H-11α were made for **5** as shown. The chemical shifts for H-10 and H-11 and the corresponding carbon resonances indicated that the pyrrolidamide and phenyl groups are attached at carbons 10 and 11, respectively. This was confirmed from the HMBC correlations H-11/C-1, -2, -19, -20 and NOESY correlations H-12/OH-1,H-14. Protons in the shielding cones of the aromatic rings were significantly shifted upfield, e.g. OCH_3-3 and H-27 at δ 3.06 and δ 5.38, respectively.

Accurate mass measurement confirmed the molecular formula of **6** as $C_{36}H_{42}N_2O_9$ corresponding to a deacetylated **3**. The IR spectrum showed OH and NH absorption bands at 3482 and 3399 cm^{-1}, respectively, and amide carbonyl bands at 1621 and 1610 cm^{-1}; the ester band found in **3** was absent. ^{13}C NMR data showed some similarities to those of **3**, but marked differences were found for C-11, C-12, H-11, and H-12. The structure of **6** was determined from the NOESY correlations H-12/H-14 and HMBC correlations H-11/C-1, -2, -19, -20.

Diamides of aminopyrrolidine with cinnamic and 2-methylbutanoic (or derivatives) acids (**7**−**9**) have previously been isolated from *Aglaia* species.[1,3] Odorinol, in particular, has been isolated in two enantiomeric form from the same species.[1,3] (+)-Odorinol (**7**), presently isolated from *A. laxiflora*, had a rotation similar in magnitude but opposite to that of (−)-odorinol for which the absolute stereochemistry is known. Thus, the enantiomeric structure is likely to be as shown, and this is corroborated by the X-ray structure as for **3** (Figure 1).

It is likely that the cycloadducts (**3**−**6**) from *Aglaia* are cycloaddition products of cinnamamidopyrrolidine derivatives with trimethoxyflavonol. An acid-catalyzed cycloaddition of flavonol to a cinnamyl derivative could lead to aglaxiflorin intermediates, which could subsequently undergo a Wagner−Meerwein rearrangement to rocaglaol-type compounds.

Rocaglaol (**2**) and its rhamnoside derivative (**1**) were determined to be the main cytotoxic compounds, while the diamide **7** had previously been found to have antileukemic activity.[4] Aglaxiflorins A−D (**3**−**6**) were, however, inactive to P-388 and MOLT4 cell lines.

Experimental Section

General Experimental Procedures. Optical rotations at 25° were taken on a Perkin-Elmer 241 polarimeter. EIMS was run on a Micromass VG 7035 mass spectrometer at 70 ev. NMR spectra were recorded by Bruker ACF 300 [300 MHz (^1H) and 75 MHz (^{13}C)] and AMX [500/400 MHz (^1H) and 125/100 MHz (^{13}C)] instruments using $CDCl_3$, with TMS as an internal standard unless otherwise stated. IR spectra were recorded on a Bio-Rad FT-IR spectrometer, and UV spectra were recorded on a Hewlett-Packard 8452A diode array spectrometer. X-ray data collection was carried out on a Siemens CCD SMART system. Liquid chromatography was performed on Si gel (Kieselgel 60, particle size 0.040−0.063 mm) and Sephadex LH-20. TLC was run on Si gel precoated glass plates (Merck Si gel 60 F_{254}).

Plant Material. The leaves of *A. laxiflora* (Meliaceae) were collected from Mt. Tawai, Kinabatangan, Sabah, Malaysia, in 1996, and identified by L. Madani. A voucher specimen (SAN135189) was deposited at the herbarium of the Forest Research Centre, Sepilok, Sandakan, Sabah, Malaysia.

Cytotoxicity. Cytotoxic activity was determined as described previously:[8] rocaglaol (**2**) (IC_{50} = 0.023, 0.034, <0.01 μg/mL on WEHI 164, LL/2, P-388 cell lines, respectively) and its rhamnoside derivative **1** (IC_{50} = 0.0022, 0.0042, 0.036 μg/mL on JURKAT, LL/2, P-388 cell lines, respectively). Cell lines were: WEHI 164 = mouse fibrosarcoma, LL/2 = mouse Lewis

lung carcinona, P-388 = mouse leukemia, MOLT4 = human acute lymphoblastic leukemia, and JURKAT = human leukemia.

Extraction and Isolation. Dried and powdered leaves (1000 g) of *A. laxiflora* were exhaustively extracted with MeOH (10 L × 3). Evaporation in vacuo reduced the extract to a residue of 100 g. The residue was suspended in MeOH/H_2O (1:9), then re-extracted with *n*-hexane, $CHCl_3$, and *n*-butanol. The *n*-hexane fraction gave 44 g of residue after concentration in vacuo, and this was fractionated on a Si gel (Merck 9385) column eluting with hexane, with a gradient of ethyl acetate to 100%, followed by hexane/acetone (10:1 to 1:1 gradient). The compounds were eluted in the following order: **7** (15 mg, 0.034%), **8** (23 mg, 0.0052%), **9** (30 mg, 0.0068%), and **2** (5.2 mg, 0.012%). From the $CHCl_3$-soluble residue (19 g) compounds **1** (4.2 mg, 0.022%), **3** (10 mg, 0.053%), **4** (3.2 mg, 0.017%), **5** (3.0 mg, 0.016%), and **6** (2.8 mg, 0.015%) were isolated using Si gel chromatography, eluted with $CHCl_3$/MeOH (10:1) followed by hexane/acetone (1.5:1).

Compound 1: colorless crystals ($CDCl_3$); mp 107−109°; $[\alpha]^{25}_D$ −92.7° (*c* 0.03, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 214 (5.59), 268 (4.73) nm; IR (KBr) ν_{max} 3476, 2936, 1744, 1623, 1597, 1516, 1457, 1148, 1124 cm^{-1}; ^1H NMR ($CDCl_3$ 300 MHz) δ 7.10 (1H, m, H-18), 7.08 (2H, m, H-17, H-19), 7.00 (1H, d, J = 2.2 Hz, H-10), 6.95 (2H, dd, J = 7.7, 1.7 Hz, H-16, H-20), 6.88 (1H, dd, J = 8.7, 2.2 Hz, H-14), 6.66 (1H, d, J = 8.7 Hz, H-13), 6.29 (1H, d, J = 1.9 Hz, H-5), 6.15 (1H, d, J = 1.9 Hz, H-7), 5.52 (1H, dd, J = 1.6, 3.3 Hz, H-2′), 5.13 (1H, d, J = 1.6 Hz, H-1′), 4.84 (1H, d, J = 6.2 Hz, H-1), 3.96 (1H, m, H-3), 3.95 (1H, m, H-5′), 3.91 (3H, s, OCH_3-8), 3.84 (3H, s, OCH_3-6), 3.74 (3H, s, OCH_3-12), 3.70 (1H, dd, J = 9.5, 3.3 Hz, H-3′), 3.55 (1H, t, J = 9.5 Hz, H-4′), 3.45 (3H, s, OCH_3-3′), 2.72 [1H, dt, J = 6.5, 13.9 Hz, H-2 (*pro*-R)], 2.15 [1H, m, H-2 (*pro*-S)], 2.16 (3H, s, CH_3CO), 1.31 (3H, d, J = 6.2 Hz, H-6′); ^{13}C NMR ($CDCl_3$ 300 MHz) δ 170.0 (CH_3CO), 163.9 (C-6), 160.7 (C-4a), 156.9 (C-8), 149.5 (C-12), 143.3 (C-11), 138.4 (C-15), 128.0 (C-16, C-20), 127.6 (C-17, C-19), 127.4 (C-9), 126.3 (C-18), 123.2 (C-14), 118.8 (C-10), 110.9 (C-13), 107.5 (C-8a), 103.1 (C-3a), 97.9 (C-1′), 92.5 (C-7), 89.4 (C-5), 79.2 (C-1), 79.1 (C-3′), 71.7 (C-4′), 68.9 (C-5′), 67.2 (C-2′), 57.3 (OCH_3-3′), 55.7 (OCH_3-8), 55.6 (OCH_3-6 and OCH_3-12), 53.4 (C-3), 36.3 (C-2), 20.9 (CH_3CO), 17.6 (C-6′); HRFABMS (negative mode) *m*/*z* [M − H]$^-$ 651.2470 (calcd for $C_{35}H_{39}O_{12}$, 651.2499).

Aglaxiflorin A (**3**): colorless crystals ($CDCl_3$); mp 217−219°; $[\alpha]^{25}_D$ +8.1° (*c* 0.12, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 214 (4.64), 268 (3.73) nm; IR (KBr) ν_{max} 3467, 3400, 2980, 2930, 1742, 1647, 1615, 1518, 1427, 1229, 1146, 1094 cm^{-1}; ^1H NMR (CD_3OD 300 MHz) δ 7.47 (2H, d, J = 8.7 Hz, H-14, H-18), 7.04 (1H, d, J = 7.4 Hz, H-22), 6.98 (2H, t, J = 7.4 Hz, H-21, H-23), 6.88 (2H, d, J = 8.7 Hz, H-15, H-17), 6.50 (2H, d, J = 7.4 Hz, H-20, H-24), 6.45 (1H, s, H-12), 6.33 (1H, d, J = 1.7 Hz, H-4), 6.32 (1H, d, J = 5.8 Hz, H-27), 6.03 (1H, d, J = 1.7 Hz, H-6), 4.40 (1H, d, J = 4.7 Hz, H-10), 4.04 (3H, s, OCH_3-5), 4.03 (1H, d, J = 4.7 Hz, H-11), 3.71 (3H, s, OCH_3-16), 3.70 (3H, s, OCH_3-3), 3.56−3.64 (2H, m, H-30), 2.24 (1H, m, H-28a), 1.96−2.06 (2H, m, H-29), 1.93 (1H, m, H-28b), 1.78 (3H, s, CH_3CO), 1.66 (1H, m, H-34a), 1.39 (1H, m, H-34b), 0.93 (3H, s, H-36), 0.75 (3H, t, J = 7.4 Hz, H-35); ^{13}C NMR (CD_3OD 75 MHz) δ 177.3 (C-32), 172.5 (C-25), 171.6 (CH_3CO), 162.5 (C-5), 159.4 (C-3, C-16), 155.5 (C-7), 137.5 (C-19), 131.8 (C-13), 130.4 (C-21, C-23), 128.7 (C-20, C-24), 128.3 (C-14, C-18), 127.8 (C-22), 114.3 (C-15, C-17), 108.3 (C-2), 94.6 (C-6), 93.5 (C-4), 86.7 (C-9), 80.1 (C-1), 76.0 (C-33), 74.7 (C-12), 64.8 (C-27), 57.6 (C-11), 56.7 (OCH_3-5), 56.4 (C-10), 55.9 (OCH_3-3), 55.6 (OCH_3-16), 47.0 (C-30), 34.0 (C-34), 35.0 (C-28), 26.4 (C-36), 22.2 (C-29), 20.6 (CH_3CO), 8.1 (C-35); FABMS *m*/*z* 710 [M + Na]$^+$ (15), 689 [M+H]$^+$ (15), 572 (35), 503 (30), 313 (100); HRFABMS *m*/*z* 689.3091 (calcd for $C_{38}H_{44}N_2O_{10}$, 689.3074).

Crystal Data for 3: $C_{38}H_{44}N_2O_{10}$, M = 688.75, orthorhombic, $P2_12_12_1$, a = 11.6837(1) Å, b = 16.9642(3) Å, c = 18.5027-(3) Å, V = 3667.32(9) Å^3, Z = 4, D_{calc} = 1.247 g/cm^3, $F(000)$ = 1464. Data were collected at 293(2) K in the θ range of 2.06−29.38° (−12 ≤ h ≤ 15, −20 ≤ k ≤ 22, −20 ≤ l ≤ 25). Following application of an empirical absorption correction, SADABS, the structure was solved by direct methods; O-32 oxygen atom was disordered. Three orientations of O-32 were resolved with occupancies 0.4, 0.3, and 0.3. Isotropic thermal parameters were refined for these disordered atoms. Refinement by full-matrix least-squares was performed with hydrogen atoms placed in calculated positions and allowed to ride on the atoms to which they are attached. Anisotropic thermal parameters were refined for all the ordered non-hydrogen atoms. The model converged at R_1 = 0.0611, wR_2 = 0.1162, GOF = 1.052 for 5832 reflections, with $F_o \geq 4\sigma(F_o)$; R_1 = 0.1023, wR_2 = 0.1325 for all 22 164 reflections. In the final difference, the residual electron density fluctuates between 0.178 and −0.205 e Å^{-3}. Crystallographic data for **3** have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Aglaxiflorin B (**4**): colorless crystals ($CDCl_3$); mp 158−160°; $[\alpha]^{25}_D$ −105.5° (*c* 0.13, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 222 (4.47), 274 (3.66) nm; IR (KBr) ν_{max} 3480, 3400, 2963, 2928, 1732, 1651, 1617, 1512, 1426, 1252, 1151 cm^{-1}; ^1H −NMR ($CDCl_3$ 500 MHz) δ 7.04−7.14 (4H, m, H-20, -21, -23, and -24), 7.02 (2H, d, J = 8.9 Hz, H-14, H-18), 7.00 (1H, m, H-22), 6.64 (2H, d, J = 8.9 Hz, H-15, H-17), 6.43 [1H, d (br), 31-NH], 6.41 (1H, m, H-27), 6.19 (1H, s, H-12), 6.06 (1H, d, J = 0.8 Hz, H-6), 6.05 (1H, d, J = 0.8 Hz, H-4), 5.69 (1H, s, 1-OH), 4.64 (1H, d, J = 9.3 Hz, H-10), 4.00 (1H, d, J = 9.3 Hz, H-11), 3.76 (3H, s, OCH_3-5), 3.70 (6H, s, OCH_3-3 and OCH_3-16), 3.59−3.66 (1H, m, H-30a), 3.17−3.22 (1H, m, H-30b), 2.36 (3H, s, CH_3CO), 1.92−2.10 (2H, m, H-28), 1.67−1.92 (2H, m, H-29), 1.35−1.67 (2H, m, H-34), 1.24 (3H, s, H-36), 0.74 (3H, s, H-35); ^{13}C NMR ($CDCl_3$ 75 MHz) δ 174.2 (C-32), 170.4 (CH_3CO), 169.0 (C-25), 161.7 (C-5), 159.9 (C-16), 157.8 (C-3), 153.3 (C-7), 142.5 (C-19), 130.0 (C-14, -18, -21, and -23), 128.8 (C-13), 128.3 (C-20, C-24), 125.7 (C-22), 113.3 (C-15, C-17), 105.2 (C-2), 94.3 (C-6), 92.4 (C-4), 88.1 (C-9), 81.5 (C-1), 79.4 (C-12), 75.8 (C-33), 63.9 (C-27), 63.8 (C-11), 56.3 (C-10), 55.9 (OCH_3-16), 55.2 (OCH_3-5), 55.1 (OCH_3-3), 46.0 (C-30), 34.4 (C-28), 33.2 (C-34), 25.4 (C-36), 21.3 (C-29), 21.2 (CH_3CO), 7.7 (C-35); FABMS *m*/*z* 689 [M + H]$^+$ (40), 418 (30), 313 (70); HREIMS *m*/*z* [M]$^+$ 689.2979 (calcd for $C_{38}H_{44}N_2O_{10}$, 688.2996).

Aglaxiflorin C (**5**): colorless crystals ($CDCl_3$); mp 147−149°; $[\alpha]^{25}_D$ +34.9° (*c* 0.05, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 222 (4.42), 272 (3.29) nm; IR (KBr) ν_{max} 3507, 3405, 2974, 2936, 1749, 1648, 1620, 1516, 1427, 1223, 1148 cm^{-1}; ^1H NMR ($CDCl_3$ 300 MHz) δ 7.73 (2H, d, J = 8.9 Hz, H-14, -18), 7.15 (2H, m, H-21, -23), 7.12 (1H, m, H-22), 6.97 (2H, dd, J = 7.5, 1.8 Hz, H-20, H-24), 6.68 (2H, d, J = 8.9 Hz, H-15, H-17), 6.66 (1H, d, J = 7.4 Hz, 31-NH), 6.43 (1H, d, J = 2.2 Hz, H-6), 5.84 (1H, d, J = 2.2 Hz, H-4), 5.57 (1H, s, H-12), 5.38 (1H, t, J = 6.4 Hz, H-27), 5.15 (1H, s, 1-OH), 4.74 (1H, d, J = 11.0 Hz, H-11), 3.94 (1H, d, J = 11.0 Hz, H-10), 3.82 (3H, s, OCH_3-16), 3.80 (3H, s, OCH_3-5), 3.33−3.39 (1H, m, H-30a), 3.06 (3H, s, OCH_3-3), 2.76−2.85 (1H, m, H-30b), 2.20 (3H, s, H-38), 1.76−1.83 (2H, m, H-28), 1.47−1.50 (2H, m, H-29), 1.41−1.48 (2H, m, H-34), 1.26 (3H, s, H-36), 0.79 (3H, t, J = 7.6 Hz, H-35); ^{13}C NMR ($CDCl_3$ 75 MHz) δ 173.6 (C-32), 169.4 (CH_3CO), 168.4 (C-25), 160.8 (C-5), 159.1 (C-16), 158.6 (C-3), 152.1 (C-7), 136.6 (C-19), 128.5 (C-20, C-24), 127.5 (C-21, C-23), 127.7 (C-14, C-18), 127.0 (C-22), 112.8 (C-15, C-17), 106.7 (C-2), 95.1 (C-6), 93.0 (C-4), 85.3 (C-9), 81.2 (C-1), 80.3 (C-12), 75.8 (C-33), 63.6 (C-27), 57.1 (C-11), 55.7 (C-10), 55.6 (OCH_3-5 and OCH_3-16), 55.2 (OCH_3-3), 38.5 (C-28), 33.6 (C-30), 33.2 (C-34), 26.0 (C-36), 21.1 (CH_3CO), 20.6 (C-29), 7.6 (C-35); FABMS *m*/*z* 689 [M + H]$^+$ (55), 645 (20), 503 (30), 443 (25), 415 (20), 313 (100); HREIMS *m*/*z* [M]$^+$ 689.2996 (calcd for $C_{38}H_{44}N_2O_{10}$, 689.2996).

Aglaxiflorin D (**6**): colorless crystals ($CDCl_3$); mp 131−133°; $[\alpha]^{25}_D$ −102.1° (*c* 0.04, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 210 (5.62), 214 (5.66), 268 (4.66) nm; IR (KBr) ν_{max} 3482, 3399, 2981, 2930, 1621, 1610, 1512, 1422, 1223, 1140 cm^{-1}; ^1H NMR ($CDCl_3$ 300 MHz) δ 7.38 (2H, d, J = 8.4 Hz, H-14, H-18), 7.19 (2H, d, J = 7.4 Hz, H-20, H-24), 7.0 (3H, m, H-21, -22, and -23), 6.65 (2H, d, J = 8.4 Hz, H-15, H-17), 6.53 (1H, d, J = 6.2 Hz, NH-31), 6.38 (1H, m, H-27), 6.08 (1H, d, J = 0.8 Hz, H-6), 6.05 (1H, d, J = 0.8 Hz, H-4), 5.83 (1H, s, OH-1), 4.83 (1H, s,

H-12), 4.56 (1H, d, $J = 9.0$ Hz, H-10), 4.04 (1H, d, $J = 9.0$ Hz, H-11), 3.78 (3H, s, OCH_3-3), 3.71 (3H, s, OCH_3-5), 3.69 (3H, s, OCH_3-16), 3.61 (1H, m, H-30a), 3.20 (1H, m, H-30b), 2.05 (1H, m, H-28a), 1.96 (1H, m, H-28b), 1.91 (1H, m, H-29a), 1.74 (1H, m, H-29b), 1.62 (1H, m, H-34a), 1.42 (1H, m, H-34b), 1.24 (3H, s, H-36), 0.74 (3H, t, $J = 7.3$ Hz, H-35); ^{13}C NMR ($CDCl_3$ 75 MHz) δ 174.9 (C-32), 169.5 (C-25), 161.1 (C-5), 158.7 (C-16), 157.8 (C-3), 153.7 (C-7), 142.8 (C-19), 130.5 (C-20, C-24 or C-14, C-18), 130.4 (C-14, C-18 or C-20, C-24), 130.1 (C-13), 128.0 (C-21, C-23), 125.7 (C-22), 112.9 (C-15, C-17), 105.0 (C-2), 94.4 (C-6), 92.1 (C-4), 89.0 (C-9), 81.9 (C-1), 79.7 (C-12), 75.9 (C-33), 63.8 (C-27), 63.4 (C-11), 57.0 (C-10), 55.8 (OCH_3-3), 55.1 (OCH_3-5), 54.9 (OCH_3-16), 46.1 (C-30), 34.4 (C-28), 33.1 (C-34), 25.5 (C-36), 21.2 (C-29), 7.7 (C-35); FABMS *m*/*z* 647 $[M + H]^+$ (55), 645 (20), 461 (35), 376 (65), 313 (100); HRFABMS *m*/*z* 647.2994 (calcd for $C_{36}H_{43}N_2O_9$, 647.2968).

(+)-Odorinol (7): colorless needles ($CDCl_3$); mp 162−164°; $[\alpha]^{25}_D$ +38.5° (*c* 0.02, $CHCl_3$); ^{1}H and ^{13}C NMR, EIMS, and IR data of **7** were identical to those reported.[4]

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Supporting Information Available: 2D NMR data of **1**, **3**−**6**, and postulated pathways for the biosynthesis of **2**−**6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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