Constituents from the Leaves of *Aristolochia elegans*

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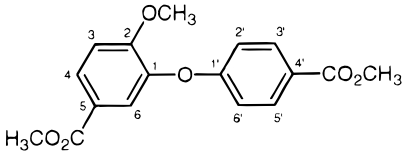
One new biphenyl ether, aristogin C (**1**), and two new porphyrins, aristophylls A (**2**) and B (**3**), as well as 11 known compounds, were isolated from the leaves of *Aristolochia elegans*. Their structures were elucidated according to the spectroscopic (NMR and MS) analyses or by comparison with literature values.

Aristolochia elegans Mast. (Aristolochiaceae) is a perennial shrub cultivated as an ornamental plant in Taiwan.[1] Several reports have been found on the isolation of lignans, diterpenoids, and alkaloids from the leaves, stems, and roots of this plant.[2−8] In a continuing search for novel bioactive compounds from the genus *Aristolochia*,[9] the leaves of *A. elegans* were investigated. Three new compounds—one biphenyl ether, aristogin C (**1**), and two porphyrins, aristophylls A (**2**) and B (**3**)—and 11 known compounds were isolated from the hot methanolic extract. Here we report the structure elucidation of **1**−**3** by spectroscopic (NMR and MS) analyses.

Aristogin C (**1**), $C_{17}H_{16}O_6$, was obtained as a colorless oil. There were two sets of mutually coupled protons in the aromatic region of the ^{1}H NMR spectrum of **1**: one at δ 7.04 (d, J = 8.7 Hz, H-3), 7.74 (d, J = 1.7 Hz, H-6), and 7.93 (dd, J = 8.7, 1.7 Hz, H-4) indicated a 1,2,5-trisubstituted benzene; the other at δ 6.90 (2H, d, J = 8.8 Hz, H-2′ and H-6′) and 7.98 (2H, d, J = 8.8 Hz, H-3′ and H-5′) indicated a 1′,4′-disubstituted benzene. A strong carbonyl band in the IR spectrum and two ester carbonyl signals at δ 166.1 and 166.6 in the ^{13}C NMR spectrum indicated that two of the three methoxyl singlets were carbomethoxy groups. Consequently, the two benzene rings are linked by an oxygen, typical of a diphenyl ether. The regiochemistry of the substituents, two carbomethoxyls and one methoxyl, was confirmed by NOEs between δ 7.04 (H-3) and 3.88 (OMe) and 7.93 (H-4) in a 2D NOESY experiment, which led us to place a carbomethoxyl group on C-5 and to assign structure **1** to aristogin C.

Aristophyll A (**2**) was isolated as violet granules that exhibited NMR data similar to those of methyl pheophorbide-a.[10] UV absorption bands at 221, 282, 305, 369 (sh), 398, 498, 527, 607, and 664 nm suggested that **2** was a chlorophyll derivative.[11] The FABMS quasi molecular ion at m/z 567 $[M + H]^+$ indicated the molecular formula $C_{34}H_{38}N_4O_4$. Broad IR absorption at 3327 cm^{-1} and the broad ^{1}H NMR signal at δ 1.64 (2H, D_2O exchangeable) showed the presence of two typical upfield NH protons in the porphyrin ring. The IR spectrum also showed carbonyl absorptions at 1740 and 1699 cm^{-1}. As in the aliphatic region of the ^{1}H NMR spectrum of **2**, a doublet methyl at δ 1.88 (J = 7.2 Hz, 4-Me) coupled with a downfield methine proton at δ 4.51 (m, H-4) were typical of a partially reduced dihydroporphyrin. In addition, an ethylene group at δ 2.38 and 2.55 (m, each 1H, H-3^2), as well as 2.47 and 2.59 (m, each 1H, H-3^1), along with a carbomethoxyl, constructed a methyl propanoate side chain attached to C-3. The characteristic ethyl group at δ 1.72 and 3.78, together with a vinyl substituent at δ 6.14, 6.33, and 8.07, were placed on C-14 and C-9, respectively. Three methyl singlets at δ 3.30 (13-Me), 3.46 (8-Me), and 3.79 (18-Me) and four aromatic singlets at δ 8.73 (H-6), 9.61 (H-11), 9.75 (H-16), and 9.80 (H-1) represent the protons outside the dihydroporphyrin ring that caused these downfield shifted signals. Therefore, the last carbomethoxyl group was placed on C-19. All of the ^{1}H and ^{13}C NMR assignments were confirmed by COSY, HMQC, NOESY, and HMBC experiments. Thus, structure **2** was assigned to aristophyll A.



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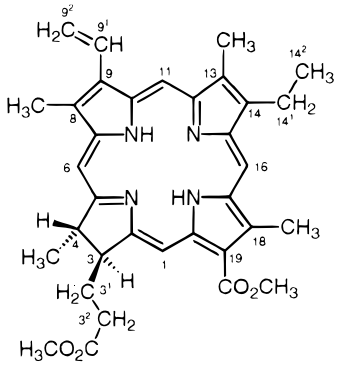

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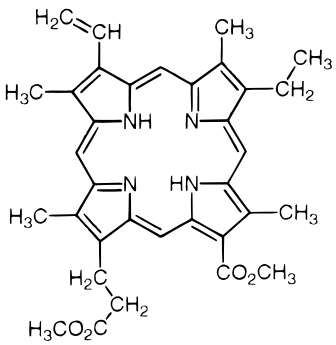

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Aristophyll B (**3**), $C_{34}H_{36}N_4O_4$, had two fewer hydrogens than **2**. The spectral data of **3** were almost the same as those of **2**. Four downfield methyl groups in **3**, instead of three, suggested that it consisted of a porphyrin ring. The NOE experiment confirmed the locations of substituents as shown. Consequently, aristophyll B was established as **3**, a compound previously synthesized by Conant and Bailey.[12]

The known compounds phytol,[13] β-sitosterol,[13] (−)-pinoresinol,[14] methylparaben,[15] *p*-methylvanillate,[16] *p*-hydroxybenzoic acid,[15] corydaldine,[17] thalifoline,[18] northalifoline,[19] *N*-methylcorydaldine,[20] and *N*-methyl-6,7-dimethylisoquinolone[21] were also isolated and characterized by comparison of their spectroscopic data (UV, IR, NMR, and MS) with literature values. In this study, we have isolated five 1-quinolones and a biphenyl ether, which may represent metabolites of bisbenzylisoquinoline alkaloids in the plant.[22]

Experimental Section

General Experimental Methods. Melting points were not corrected. UV spectra were recorded in MeOH. IR spectra were recorded as KBr disks. NMR spectra were recorded at 200 or 400 MHz for ^{1}H and 50 or 100 MHz for ^{13}C; all chemical shifts are reported in parts per million (δ) from TMS as an internal standard. Mass spectra were performed in the EI or FAB (matrix: glycerol) mode.

Plant Material. *A. elegans* Mast. was collected in May 1992, from Tainan Hsien, Taiwan, and verified by Prof. C. S. Kuoh. A specimen of the plant (NCKU Wu 92008) has been deposited at the herbarium of National Cheng Kung University, Tainan, Taiwan.

Extraction and Separation. Fresh leaves of *A. elegans* (1.1 kg) were extracted with hot MeOH (× 5) and concentrated to give a dark brown syrup that was partitioned between H_2O and $CHCl_3$, and then *n*-butanol. This resulted in $CHCl_3$, *n*-butanol, H_2O, and insoluble portions after evaporation of the solvent. The $CHCl_3$ portion was chromatographed over Si gel using a gradient of *n*-hexane and Me_2CO to afford 11 fractions. Fraction 7 was chromatographed over silica gel using $CHCl_3$−Me_2CO and rechromatographed by preparative TLC to yield phytol (68.2 mg), **1** (3.4 mg), and β-sitosterol (648.2 mg). Using the same procedure, fraction 8 yielded methylparaben (1.8 mg), *p*-methylvanillate (1.0 mg), *p*-hydroxybenzoic acid (1.0 mg), **2** (6.2 mg), and **3** (5.3 mg). Fraction 10 gave corydaldine (2.3 mg), *N*-methyl-6,7-dimethylisoquinolone (3.7 mg), (−)-pinoresinol (1.6 mg), and thalifoline (2.1 mg). The combined *n*-butanol and insoluble portions were chromatographed on a cation exchange column eluted with 5% NH_4OH to give an alkaloid fraction. Repeated chromatography on a C_{18} column produced thalifoline (2.2 mg), *N*-methylcorydaldine (1.2 mg), and northalifoline (1.9 mg).

Aristogin C (1): colorless oil; UV λ_{max} (log ϵ) 255 (4.82), 286 (4.09, sh) nm; IR ν_{max} 1645, 1610, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.85 (3H, s, OMe), 3.88 (3H, s, OMe), 3.89 (3H, s, OMe), 6.90 (2H, d, J = 8.8 Hz, H-2′ and H-6′), 7.04 (1H, d, J = 8.7 Hz, H-3), 7.74 (1H, d, J = 1.7 Hz, H-6), 7.93 (1H, dd, J = 8.7, 1.7 Hz, H-4), 7.98 (2H, d, J = 8.8 Hz, H-3′ and H-5′); ^{13}C NMR ($CDCl_3$) δ 52.0, 52.1, 56.1, 112.1, 115.9, 123.3, 123.4, 124.3, 128.1, 131.6, 143.1, 155.5, 161.7, 166.1, 166.6; EIMS *m*/*z* 316 (M^+, 100), 285 (85), 183 (10), 127 (24), 104 (7), 77 (12); HREIMS *m*/*z* 316.0946 (calcd for $C_{17}H_{16}O_6$, 316.0948).

Aristophyll A (2): violet granules (Et_2O), mp 261−262 °C; $[\alpha]_D$ −238.3° (c 0.06, $CHCl_3$); UV λ_{max} 221, 282, 305, 369 (sh), 398, 498, 527, 607, 664 nm; IR ν_{max} 3327, 1740, 1699, 1616, 1506 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.64 (2H, br s, D_2O exchangeable, 2 × NH), 1.72 (3H, t, J = 7.2 Hz, H-14^2), 1.88 (3H, d, J = 7.2 Hz, 4-Me), 2.38 and 2.55 (each 1H, m, H-3^2), 2.47 and 2.59 (each 1H, m, H-3^1), 3.30 (3H, s, 13-Me), 3.46 (3H, s, 8-Me), 3.61 (3H, s, OMe), 3.78 (2H, q, J = 7.2 Hz, H-14^1), 3.79 (3H, s, 18-Me), 4.35 (3H, s, OMe), 4.48 (1H, m, H-3), 4.51 (1H, m, H-4), 6.14 (1H, d, J = 10.0 Hz, H-9^2), 6.33 (1H, d, J = 16.4 Hz, H-9^2), 8.07 (1H, dd, J = 16.4, 10.0 Hz, H-9^1), 8.73 (1H, s, H-6), 9.61 (1H, s, H-11), 9.75 (1H, s, H-16), 9.80 (1H, s, H-1); ^{13}C NMR ($CDCl_3$) δ 11.4 (3-Me), 12.1 (8-Me), 13.7 (8-Me), 17.6 (C-14^2), 19.7 (C-14^1), 23.4 (4-Me), 31.1 (C-3^2), 32.4 (C-3^1), 48.6 (C-4), 51.6 (OMe), 51.9 (OMe), 54.7 (C-3), 93.0 (C-6), 96.3 (C-1), 98.9 (C-11), 102.1 (C-16), 119.0 (C-19), 121.9 (C-9^2), 129.4 (C-9^1), 130.2 (C-8), 130.5 (C-17), 134.7 (C-9), 135.1 (C-10), 136.1 (C-13), 137.2 (C-2), 140.0 (C-18), 140.3 (C-7), 144.9 (C-14), 149.4 (C-15), 154.1 (C-12), 166.7 (C-20), 167.1 (C═O), 171.3 (C-5), 173.9 (C═O); FABMS *m*/*z* 567 $[M + H]^+$ for $C_{34}H_{38}N_4O_4$ (100), 537 (11), 493 (10), 307 (12), 176 (28), 154 (83), 136 (71), 107 (32).

Aristophyll B (3): violet granules (Et_2O), mp 269−271 °C; UV λ_{max} 264, 389, 404, 512, 553, 633 nm; IR ν_{max} 3300, 1715, 1695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.31 (2H, br s, D_2O exchangeable, 2 x NH), 1.81 (3H, t, J = 7.6 Hz, H-14^2), 3.26 (2H, t, J = 7.6 Hz, H-3^2), 3.51 (3H, s, 4-Me), 3.52 (3H, s, 13-Me), 3.53 (3H, s, 8-Me), 3.68 (3H, s, OMe), 3.86 (3H, s, 18-Me), 3.97 (2H, q, J = 7.6 Hz, H-14^1), 4.33 (2H, t, J = 7.6 Hz, H-3^1), 4.44 (3H, s, OMe), 6.13 (1H, d, J = 11.2 Hz, H-9^2), 6.26 (1H, d, J = 16.0 Hz, H-9^2), 8.11 (1H, dd, J = 16.0, 11.2 Hz, H-9^1), 9.69 (1H, s, H-6), 9.85 (1H, s, H-11), 9.89 (1H, s, H-16), 10.82 (1H, s, H-1); FABMS *m*/*z* 565 $[M + H]^+$ for $C_{34}H_{38}N_4O_4$ (67), 491 (6), 307 (11), 176 (15), 154 (100), 136 (78), 107 (37).

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