Constituents from the Root and Stem of *Aristolochia elegans*

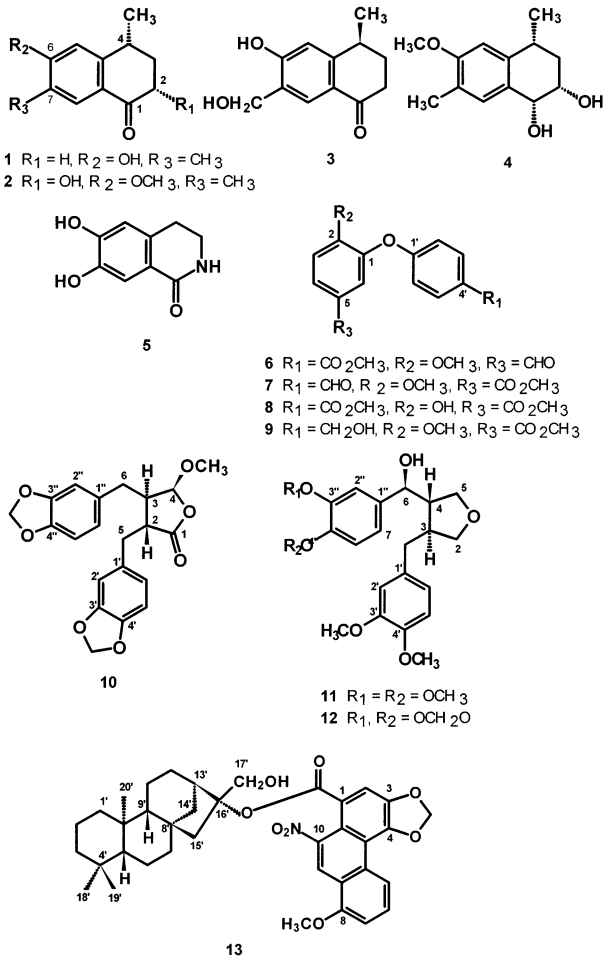
Tian-Shung Wu,* Yao-Lung Tsai, A. G. Damu, Ping-Chung Kuo, and Pei-Lin Wu

Department of Chemistry, National Cheng Kung University, Tainan, Taiwan, Republic of China

Received May 13, 2002

Four new tetralones, aristelegone-A (**1**), aristelegone-B (**2**), aristelegone-C (**3**), and aristelegone-D (**4**); one new isoquinoline, pericampylinone-A (**5**); four new biphenyl ethers, aristogin-A (**6**), aristogin-B (**7**), aristogin-D (**8**), and aristogin-E (**9**); three new lignans, aristelegin-A (**10**), aristelegin-B (**11**), and aristelegin-C (**12**); and a new dimer, aristolin (**13**), have been isolated from the root and stem of *Aristolochia elegans*. The structures were established on the basis of 1D and 2D NMR and mass spectral data. This is the first report of isoquinolones and biphenyl ethers from this plant which may be representative units for the formation of bisbenzylisoquinoline alkaloids that are common metabolites of *Aristolochia* species. Aristolin (**13**) is also the first report of a diterpene linked with an aristolochic acid.

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, sesquiterpenoids, and alkaloids from the leaves, stem, and root of this plant.[2−11] In continuation of our research on *Aristolochia* species, the root and stem of *A. elegans* Mast. was investigated. Thirteen new compounds were isolated from the methanol extract of the root and stem of *A. elegans*: four tetralones, aristelegone-A (**1**), -B (**2**), -C (**3**), and -D (**4**); one isoquinolone, pericampylinone-A (**5**); four biphenyl ethers, aristogin-A (**6**), -B (**7**), -D (**8**), and -E (**9**); three lignans, aristelegin-A (**10**), -B (**11**), and -C (**12**); and one dimer, aristolin (**13**). We report herein the details of structural elucidation of all the new compounds using spectral methods.



Results and Discussion

Aristelegone-A (**1**) was obtained as optically active colorless needles. The high-resolution EIMS determined the molecular formula as $C_{12}H_{14}O_2$. According to the ^{1}H, ^{13}C NMR, ^{1}H−^{1}H COSY, and HMQC spectra, a methyl signal at δ 1.33 (d, J = 7.0 Hz) coupled with a methine proton at δ 2.96 (m) was successively coupled with a methylene at δ 1.84 (m) and 2.18 (m). This diastereotopic methylene was adjacent to another methylene at δ 2.56 (ddd, J = 17.6, 8.4, 4.8 Hz) and 2.75 (ddd, J = 17.6, 8.4, 4.8 Hz). Since the latter methylene protons expressed HMBC correlation with a carbonyl carbon at δ 199.0, a partial structure −CH-(CH_3)−CH_2−CH_2−CO− was established. Two singlets at δ 6.79 and 7.87 were assigned to protons of the *para* position of a benzene ring. The remaining signals in the ^{1}H NMR spectrum indicated two substituents, a hydroxyl (δ 7.78) and a methyl (δ 2.25), on the ring. NOE correlations of the aromatic singlet (δ 6.79) with the doublet methyl (δ 1.33) and the methine (δ 2.96), as well as the other aromatic singlet (δ 7.87) with the singlet methyl (δ 2.25), suggested the complete structure to be 6-hydroxy-4,7-dimethyltetral-1-one. Correlation between 4-CH_3 and 2-H in the NOE spectrum inferred that the methyl was axial. The sign of optical rotation was identical with that reported for 4-methyltetralone,[12] and hence the configuration on C-4 was identified as *R*. On the basis of the above analyses, structure **1** was assigned for aristelegone-A.

Aristelegone-B (**2**), colorless needles, was determined to have molecular formula $C_{13}H_{16}O_3$ by HREIMS. The ^{1}H NMR spectrum of **2** showed signals similar to that of **1** except that a methoxyl group (δ 3.90) was present on C-6. This was supported by an NOE between the methoxyl and H-5 (δ 6.76), and an aliphatic hydroxyl (δ 3.94) located on C-2, which was confirmed by the downfield shift of H-2 (δ 4.32). An NOE between H-2 and H-4 suggested a *cis* configuration between the 2-hydroxyl and 4-methyl, identical with synthetic *cis*-2-hydroxy-6-methoxy-4,7-dimethyltetralone.[13] Moreover, the conformation that the cyclohexenone ring adopted placed the two substituents, hydroxyl and methyl, toward the equatorial direction, which was

* To whom correspondence should be addressed. Tel: 886-6-2747538. Fax: 886-6-2740552. E-mail: tswu@mail.ncku.edu.tw.

10.1021/np020218u CCC: $22.00 © 2002 American Chemical Society and American Society of Pharmacognosy
Published on Web 09/26/2002

different from that in **1**. Thus, **2** was identified as (2*S*,4*R*)-aristelegone-B.

Aristelegone-C (**3**), $C_{12}H_{14}O_3$, also showed spectra very similar to those of **1**. The difference was only a hydroxymethyl signal at δ 4.72, instead of a methyl group. This hydroxymethyl group was placed at C-7 on the basis of the NOESY correlation between hydroxymethyl protons (δ 4.72) and H-8 (δ 7.90). It showed opposite sign in optical rotation of that of **1**, and hence, aristelegone-C was identified as (*S*)-6-hydroxy-7-hydroxymethyl-4-methyltetralone (**3**).

Aristelegone-D (**4**) had the molecular formula $C_{13}H_{18}O_3$ (HRMS). There was no carbonyl absorption in the IR spectrum, and MS indicated that compound **4** was a reduced form of **2**. The NOEs between H-1 (δ 4.63) and H-2 (δ 3.89), H-8 (δ 7.13) suggested that the 1-hydroxyl group oriented toward the axial direction and was *cis* to the 2-hydroxyl and 4-methyl groups. Consequently, **4** is (1*R*,2*S*,4*R*)-aristelegone-D.

Pericampylinone-A (**5**) gave a positive test with Dragendorff reagent, characteristic of an alkaloid. The molecular formula $C_9H_9NO_3$ was established using HREIMS (molecular ion peak at *m*/*z* 179.0584). Carbonyl absorption (1651 cm^{-1}) in the IR spectrum together with ethylene signals (δ 2.81 and 3.44) and two aromatic singlets (δ 6.65 and 7.34) in the ^1H NMR spectrum revealed a 6,7-disubstituted-3,4-dihydro-2*H*-isoquinolin-1-one structure. This structure was further confirmed by the existence of a NOE between H-4 (δ 2.81) and H-5 (δ 3.44). The two hydroxyl groups should be the substituents on C-6 and C-7 of the benzene ring. Thus, structure **5** was assigned to pericampylinone-A.

Aristogin-A (**6**) was isolated as a colorless oil. The ^1H NMR spectrum indicated a 2,5,4′-trisubstituted biphenyl ether skeleton similar to that of aristogin-C (**23**).[11] An NOE between an aldehydic proton (δ 9.80) and H-4 (δ 7.68), H-6 (δ 7.52), and a methoxyl proton (δ 3.85) and H-3 (δ 7.06), suggested the structure to be **6** (as shown). Aristogin-B (**7**) was identified as an isomer of compound **6**, since the molecular formula and ^1H NMR were nearly the same. The placement of substituents was established from NOE correlations between a methoxyl (δ 3.85) and H-3 (δ 7.05), and an aldehydic proton (δ 9.91) and H-3′, -5′ (δ 7.82). Aristogin-D (**8**) was isolated as a colorless oil. The presence of two methoxyl groups (δ 3.84 and 3.92) and the absence of a formyl proton suggested the structure shown. Aristogin-E (**9**) was obtained as colorless oil. The ^1H NMR data of compound **9** was similar to that of aristogin-B except for the presence of a signal at δ 4.67 (s, 2H) instead of a formyl proton. The spectral data of **6**, **7**, and **9** were in good agreement with those of synthetic samples.[14−16] However, it is the first time that they were isolated from a natural source.

Aristelegin-A (**10**) was obtained as optically active colorless needles, and the HREIMS gave the molecular formula $C_{21}H_{20}O_7$. The presence of a γ-butyrolactone ring was supported by a carbonyl absorption at 1770 cm^{-1} in the IR spectrum. The ^1H NMR spectrum together with ^{13}C NMR, $^1H-^1H$ COSY, HMQC, and HMBC spectra exhibited signals similar to (−)-hinokinin[17] assignable to two 3,4-methylenedioxybenzyl groups, as indicated by two sets of ABX aromatic protons at δ 6.38 (d, J = 1.7 Hz), 6.39 (dd, J = 7.3, 1.7 Hz), 6.57 (d, J = 7.3 Hz), and 6.24 (d, J = 1.7 Hz), 6.29 (dd, J = 7.9, 1.7 Hz), 6.55 (d, J = 7.9 Hz,); two dioxygenated protons at δ 5.84 and 5.86; and two sets of benzylic protons at δ 2.25 (dd, J = 16.5, 9.5 Hz), 2.62 (dd, J = 16.5, 10.4 Hz) and 2.63 (dd, J = 13.6, 10.6 Hz), 2.95 (dd, J = 13.6, 4.5 Hz). The benzylic protons coupled with a methine proton, indicating a dibenzyl-butyrolactone lignan derivative. The absence of NOE between H-2 (δ 2.41) and H-3 (δ 2.26) indicated a *trans* dibenzyl lactone. An additional methoxyl group (δ 3.40) was located on C-4 toward the axial direction, due to the very downfield-shifted signal for aliphatic H-4 (δ 5.00) and the small coupling constant, 1.6 Hz, between axial H-3 and equatorial H-4. The NOE between H-3 and H-4 also confirmed this relative stereochemistry. The CD spectrum showed a curve similar to that of (−)-hinokinin. The absolute configuration was established to be 2*R*, 3*R*, 4*S*. Therefore, aristelegin-A was identified as **10**.

Aristelegin-B (**11**), $C_{22}H_{28}O_6$, was shown to be a 3,4-dibenzylfuran lignan by its ^1H NMR, IR, and UV spectra.[11] The presence of four methoxy groups (two at δ 3.87, two at δ 3.90) on the 3 and 4 positions of each benzene ring was supported by the NOEs of these methoxyls with H-2′ (δ 6.38), H-5′ (δ 6.57), H-2″ (δ 6.24), and H-5″ (δ 6.55). The downfield-shifted H-6 (δ 4.86) and the HMBC correlation between H-6 and C-1′ (δ 135.5) indicated a hydroxyl group on a benzylic carbon. The lack of NOE between H-3 (δ 2.75) and H-4 (δ 2.43) led to the *trans* and diaxial configuration between them. The coupling constant of 6.7 Hz between H-6 and H-4 inferred an *S* configuration at C-6.[18] Thus, structure **11** was assigned to aristelegin-B.

Aristelegin-C (**12**) was determined to have molecular formula $C_{21}H_{24}O_6$. The ^1H NMR spectrum of **12** was similar to **11** except in its substituents being two methoxyl (δ 3.85 and 3.86) on one benzene ring and a methylenedioxy group (δ 5.94) on the other ring. The fragment ions at *m*/*z* 149 and 151 showed the hydroxyl group placed on the benzylic carbon which belonged to a ring containing a methylenedioxy group.[19] Consequently, aristelegin-C has structure **12**.

Aristolin (**13**) was isolated as optically active yellow granules. The FABMS exhibited a pseudo molecular ion at *m*/*z* 630 $[M + H]^+$, corresponding to a molecular formula $C_{37}H_{43}NO_8$. The UV bands at 226, 254, 321, and 390 nm for the phenanthrene moiety together with the IR absorptions at 1595 and 1346 cm^{-1} (nitro group) and at 1709 cm^{-1} (carbonyl group) indicated an aristolochic acid type partial structure. In the ^1H NMR spectrum, the aromatic signals were almost identical with those of aristolochic acid I ($C_{17}H_{11}NO_7$), containing two singlets at δ 7.59 and 8.73 typical for H-2 and H-9, respectively; ABC type protons at δ 7.04 (d, J = 8.0 Hz), 7.64 (t, J = 8.0 Hz), and 8.61 (d, J = 8.0 Hz) for H-7, H-6, and H-5, respectively; a methoxyl at δ 3.98 on C-8; and a methylenedioxy at δ 6.30 connected with C-3 and -4. The rest of the 20 carbon and proton signals present in the aliphatic region belonged to a diterpenoid partial structure. Examining these ^1H and ^{13}C signals, we found they were similar to those of *ent*-kauran-16β,17-diol.[20] Slightly downfield-shifted signals corresponding to H-17′ (δ 3.99 and 4.33), H-13′ (δ 2.63), and H-15′ (δ 1.78 and 1.91) meant that an ester linkage occurred between the CO_2H of aristolochic acid I and the 16′-OH of *ent*-kauran-16β,17-diol. The complete assignments of ^1H and ^{13}C NMR signals were further supported by the $^1H-^1H$ COSY, HMQC, HMBC, and NOESY. This is the first report of the isolation of a dimer composed of aristolochic acid and a diterpenoid.

Some bisbenzylisoquinolines, such as (−)-(*R*,*R*)-methylcuspidaline[4] and (−)-temuconine,[7] were found in a Brazilian collection of *A. elegans*. In our study, we did not find any bisbenzylisoquinolines in this plant; instead, we have obtained six isoquinolinones and five biphenyl ethers which

may represent metabolites for the formation of bisbenzylisoquinoline alkaloids.[21]

Experimental Section

General Experimental Procedures. Melting points were recorded on a Yanaco MP-S3 melting point apparatus without correction, UV spectra on a Hitachi UV-3210 spectrophotometer, and IR spectra on a JASCO IR Report-100 spectrophotometer as KBr disks. ^{1}H, ^{13}C, HMQC, HMBC, and NOESY NMR spectra were recorded on Bruker AC-200, AMX-400, and Varian-400 Unity Plus spectrometers, using tetramethylsilane (TMS) as internal standard; all chemical shifts are reported in ppm (δ). Mass spectra (EI or FAB) were obtained on a VG 70-250 S spectrometer. Optical rotations were recorded on a Jasco DIP-370 polarimeter.

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

Extraction and Separation. Fresh roots and stems of *A. elegans* Mast. (3.1 kg) were extracted with hot MeOH (20 L × 9) and concentrated to give a dark brown syrup, which was partitioned between H_2O and $CHCl_3$, and then *n*-BuOH. This resulted in $CHCl_3$, *n*-BuOH, H_2O, and insoluble portions after evaporating the solvent. The $CHCl_3$ solubles were chromatographed over silica gel using a gradient of C_6H_6 and Me_2CO to afford five fractions. Fraction 1 was rechromatographed over silica gel using a mixture of C_6H_6 and Me_2CO as eluents and purified by preparative TLC to yield **1** (23.8 mg), **2** (27.3 mg), **6** (1.8 mg), **7** (1.1 mg), **10** (4.0 mg), and **13** (3.6 mg). Fraction 2 on chromatography yielded **3** (1.7 mg), **4** (1.7 mg), and **11** (7.3 mg). Fraction 5 gave **8** (2.6 mg), **9** (1.7 mg), and **12** (2.0 mg). The *n*-BuOH portion and insoluble portion were chromatographed over cation-exchange resin eluting with H_2O to give a fraction containing nonalkaloids, followed by eluting with 5% NH_3 solution to give a fraction containing alkaloids. The combined alkaloid fraction of the *n*-BuOH and insoluble portions was chromatographed over a C-18 column eluting with a gradient of H_2O and CH_3OH to produce **5** (6.9 mg).

Aristelegone-A (1): colorless needles ($CHCl_3$), mp 150−151 °C; $[\alpha]_D^{25}$ +15.4° (*c* 0.24, $CHCl_3$); UV λ_{max} (log ϵ) 231 (4.17), 279 (4.22), 301 (4.04, sh); IR ν_{max} 3218, 1651, 1585; ^{1}H NMR ($CDCl_3$) δ 1.33 (3H, d, J = 7.0 Hz, 4-Me), 1.84 (1H, m, H-3eq), 2.18 (1H, m, H-3ax), 2.25 (3H, s, 7-Me), 2.56 (1H, ddd, J = 17.6, 8.4, 4.8 Hz, H-2eq), 2.75 (1H, ddd, J = 17.6, 8.4, 4.6 Hz, H-2ax), 2.96 (1H, m, H-4eq), 6.79 (1H, s, H-5), 7.78 (1H, br s, 6-OH), 7.87 (1H, s, H-8); ^{13}C NMR ($CDCl_3$) δ 15.4 (7-Me), 20.4 (4-Me), 30.8 (C-3), 32.6 (C-4), 36.2 (C-2), 122.9 (C-5), 123.4 (C-8a), 124.5 (C-7), 130.7 (C-8), 149.9 (C-4a), 160.3 (C-6), 199.0 (C-1); EIMS *m*/*z* 190 (M^+, 100), 175 (64), 162 (84), 144 (32); HREIMS *m*/*z* 190.0993 (calcd for $C_{12}H_{14}O_2$, 190.0994 $[M]^+$).

Aristelegone-C (3): colorless needles (Me_2CO), mp 108−109 °C; $[\alpha]_D^{25}$ −7.0° (*c* 0.053, $CHCl_3$); UV λ_{max} (log ϵ) 223 (3.75), 274 (3.61), 283 (3.57, sh); IR ν_{max} 3260, 1658, 1604; ^{1}H NMR ($CDCl_3$) δ 1.33 (3H, d, J = 7.0 Hz, 4-Me), 1.83 (1H, m, H-3eq), 2.17 (1H, m, H-3ax), 2.44 (1H, ddd, J = 17.2, 8.6, 4.7 Hz, H-2eq), 2.62 (1H, ddd, J = 17.2, 8.6, 4.5 Hz, H-2ax), 3.00 (1H, m, H-4eq), 4.72 (2H, s, 7-CH_2), 6.78 (1H, s, H-5), 7.90 (1H, s, H-8); EIMS *m*/*z* 206 (M^+, 59), 188 (100), 160 (27), 132 (30), 91 (24); HREIMS *m*/*z* 206.0943 (calcd for $C_{12}H_{14}O_3$, 206.0942 $[M]^+$).

Aristelegone-D (4): colorless needles ($CHCl_3$), mp 126−127 °C; $[\alpha]_D^{25}$ −70.6° (*c* 0.017, $CHCl_3$); UV λ_{max} (log ϵ) 229 (3.11), 274 (3.35); IR ν_{max} 3262, 1558; ^{1}H NMR ($CDCl_3$) δ 1.38 (3H, d, J = 6.9 Hz, 4-Me), 1.72 (1H, m, H-3ax), 1.95 (1H, m, H-3eq), 2.19 (3H, s, 7-Me), 2.89 (1H, m, H-4ax), 3.85 (3H, s, 6-OMe), 3.89 (1H, dt, J = 12.4, 3.8 Hz, H-2ax), 4.63 (1H, d, J = 3.8 Hz, H-1eq), 6.74 (1H, s, H-5), 7.13 (1H, s, H-8); EIMS *m*/*z* 222 (M^+, 68), 204 (13), 189 (27), 178 (100), 161 (46), 151 (28), 91 (27); HREIMS *m*/*z* 222.1255 (calcd for $C_{13}H_{18}O_3$, 222.1256 $[M]^+$).

Pericampylinone-A (5): pale yellow needles ($CHCl_3$), mp 229−230 °C; UV λ_{max} (log ϵ) 220 (4.23), 267 (3.75), 304 (3.69); IR ν_{max} 3456, 3324, 1651, 1561; ^{1}H NMR ($CDCl_3$) δ 2.81 (2H, t, J = 6.7 Hz, H-4), 3.44 (2H, t, J = 6.7 Hz, H-3), 6.65 (1H, s, H-8), 7.34 (1H, s, H-5); EIMS *m*/*z* 179 (M^+, 100), 150 (95), 122 (87); HREIMS *m*/*z* 179.0584 (calcd for $C_9H_9NO_3$, 179.0582 $[M]^+$).

Aristogin-D (8): colorless oil; UV λ_{max} (log ϵ) 255 (4.38), 286 (3.96, sh); IR ν_{max} 3400, 1715,1505; ^{1}H NMR ($CDCl_3$) δ 3.84 (3H, s, OMe), 3.92 (3H, s, OMe), 5.93 (1H, br s, 2-OH), 7.02 (2H, d, J = 8.6 Hz, H-2′ and -6′), 7.10 (1H, d, J = 8.6 Hz, H-3), 7.70 (1H, d, J = 1.9 Hz, H-6), 7.83 (1H, dd, J = 8.6, 1.9 Hz, H-4), 8.05 (2H, d, J = 8.6 Hz, H-3′ and -5′); EIMS *m*/*z* 302 (M^+, 100), 271 (98), 120 (21); HREIMS *m*/*z* 302.0791 (calcd for $C_{16}H_{14}O_6$, 302.0790 $[M]^+$).

Aristelegin-A (10): colorless needles ($CHCl_3$), mp 86−87 °C; $[\alpha]_D^{25}$ −51.5° (*c* 0.04, $CHCl_3$); UV λ_{max} (log ϵ) 234 (3.66), 287 (3.78); IR ν_{max} 1770, 1504; ^{1}H NMR ($CDCl_3$) δ 2.25 (1H, dd, J = 16.5, 9.5 Hz, H-6a), 2.26 (1H, m, H-3), 2.41 (1H, ddd, J = 10.2, 4.5, 3.3 Hz, H-2), 2.62 (1H, dd, J = 16.5, 10.4 Hz, H-6b), 2.63 (1H, dd, J = 13.6, 3.3 Hz, H-5a), 2.95 (1H, dd, J = 13.6, 4.5 Hz, H-5b), 3.40 (3H, s, 4-OMe), 5.00 (1H, d, J = 1.6 Hz, H-4), 5.84 (2H, s, OCH_2O), 5.86 (2H, s, OCH_2O), 6.24 (1H, d, J = 1.7 Hz, H-2″), 6.29 (1H, dd, J = 7.9, 1.7 Hz, H-6″), 6.38 (1H, d, J = 1.7 Hz, H-2′), 6.39 (1H, dd, J = 7.3, 1.7 Hz, H-6′), 6.55 (1H, d, J = 7.9 Hz, H-5″), 6.57 (1H, d, J = 7.3 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ 36.7 (C-5), 37.5 (C-6), 46.4 (C-3), 46.8 (C-2), 57.0 (4-OMe), 100.9 and 110.0 (2 x OCH_2O), 108.0 (C-5′ and −5″), 108.4 (C-4), 108.9 (C-2″), 109.1 (C-2′), 121.8 (C-6″), 122.0 (C-6′), 130.8 (C-1″), 131.6 (C-1′), 146.3 (C-4′ and −4″), 147.7 (C-3′ and- 3″), 177.7 (C-1); EIMS *m*/*z* 384 (M^+, 46), 192 (100), 135 (95), 77 (14); HREIMS *m*/*z* 384.1209 (calcd for $C_{21}H_{20}O_7$, 384.1209 $[M]^+$).

Aristelegin-B (11): colorless oil; $[\alpha]_D^{25}$ −9.9° (*c* 0.073, $CHCl_3$); UV λ_{max} (log ϵ) 231 (4.13), 280 (3.67); IR ν_{max} 3510, 1515; ^{1}H NMR ($CDCl_3$) δ 2.43 (1H, tt, J = 13.6, 6.7 Hz, H-4), 2.58 (1H, dd, J = 13.6, 10.2 Hz, H-7a), 2.75 (1H, m, H-3), 2.93 (1H, dd, J = 13.6, 4.9 Hz, H-7b), 3.76 (1H, dd, J = 8.8, 6.8 Hz, H-2β), 3.78 (1H, dd, J = 13.6, 10.8 Hz, H-5α), 3.87 (6H, s, 2 x OMe), 3.90 (6H, s, 2x OMe), 3.93 (1H, dd, J = 10.8, 6.7 Hz, H-5β), 4.06 (1H, dd, J = 8.8, 6.8 Hz, H-2α), 4.82 (1H, d, J = 6.7 Hz, H-6), 6.71 (1H, d, J = 1.8 Hz, H-2″), 6.74 (1H, dd, J = 8.1, 1.8 Hz, H-6″), 6.80 (1H, d, J = 8.1 Hz, H-5″), 6.82 (1H, d, J = 8.2 Hz, H-5′), 6.85 (1H, dd, J = 8.2, 1.8 Hz, H-6′), 6.89 (1H, d, J = 1.8 Hz, H-2′); ^{13}C NMR ($CDCl_3$) δ 33.3 (C-7), 42.4 (C-3), 52.6 (C-4), 55.9 (4 × OMe), 61.0 (C-5), 73.0 (C-2), 82.8 (C-6), 109.1 (C-2′), 111.1 (C-5′), 111.4 (C-5″), 112.0 (C-2″), 118.0 (C-6′), 120.5 (C-6″), 133.0 (C-1″), 135.5 (C-1′), 147.4 (C-4″), 148.5 (C-4′), 149.0 (C-3′), 152.0 (C-3″); EIMS *m*/*z* 388 (M^+, 100), 208 (23), 194 (21), 165 (34), 151 (70); HREIMS *m*/*z* 388.1887 (calcd for $C_{22}H_{28}O_6$, 388.1886 $[M]^+$).

Aristelegin-C (12): colorless oil; $[\alpha]_D^{25}$ −53.0° (*c* 0.02, $CHCl_3$); UV λ_{max} (log ϵ) 240 (4.52), 270 (3.31); IR ν_{max} 3649, 1508; ^{1}H NMR ($CDCl_3$) δ 2.37 (1H, tt, J = 14.0, 6.4 Hz, H-4), 2.55 (1H, dd, J = 13.2, 10.6 Hz, H-7a), 2.73 (1H, m, H-3), 2.91 (1H, dd, J = 13.2, 4.8 Hz, H-7b), 3.76 (1H, m, H-2β), 3.79 (1H, m, H-5α), 3.85 (3H, s, OMe), 3.86 (3H, s, OMe), 3.91 (1H, dd, J = 10.0, 6.4 Hz, H-5β), 4.04 (1H, dd, J = 8.8, 6.8 Hz, H-2α), 4.78 (1H, d, J = 6.4 Hz, H-6), 5.94 (2H, s, OCH_2O), 6.7−6.9 (6H, m, 6 × Ar−H); EIMS *m*/*z* 372 (M^+, 74), 219 (6), 178 (13), 164 (10), 151 (100), 149 (37); HREIMS *m*/*z* 372.1573 (calcd for $C_{21}H_{24}O_6$, 372.1572 $[M]^+$).

Aristolin (13): yellow granules ($CHCl_3$), mp 119−120 °C; $[\alpha]_D^{25}$ −63.9° (*c* 0.036, $CHCl_3$); UV λ_{max} (log ϵ) 226 (4.19), 254 (4.14), 321 (3.93), 390 (3.80); IR ν_{max} 3649, 1709, 1595, 1346; ^{1}H NMR ($CDCl_3$) δ 0.74 (3H, s, 19′-Me), 0.78 (3H, s, 18′-Me), 0.97 (3H, s, 20′-Me), 1.78 (1H, d, J = 16.0 Hz, H-15′a), 1.91 (1H, d, J = 16.0 Hz, H-15′b), 2.02 (1H, d, J = 12.0 Hz, H-7′a), 2.63 (1H, br s, H-13′), 3.25 (1H, br t, J = 4.0 Hz, 17′-OH), 3.98 (3H, s, 8-OMe), 3.99 (1H, dd, J = 11.5, 4.0 Hz, H-17′a), 4.33 (1H, dd, J = 11.5, 4.0 Hz, H-17′b), 6.30 (2H, s, OCH_2O), 7.04 (1H, d, J = 8.0 Hz, H-7), 7.59 (1H, s, H-2), 7.64 (1H, t, J = 8.0 Hz, H-6), 8.61 (1H, d, J = 8.0 Hz, H-5), 8.73 (1H, s, H-9); ^{13}C NMR ($CDCl_3$) δ 17.1 (C-20′), 18.3 (C-2′), 18.5 (C-11′), 20.4 (C-6′), 21.5 (C-19′), 26.2 (C-12′), 33.2 (C-4′), 33.5 (C-18′), 38.0 (C-7′), 39.4 (C-10′), 40.3 (C-14′), 42.0 (C-1′ and −3′), 43.4 (C-13′), 44.5 (C-8′), 50.9 (C-15′), 55.9 (8-OMe), 56.1 (C-5′), 56.5 (C-9′),

63.5 (C-17′), 98.1 (C-16′), 102.4 (OCH2O), 107.9 (C-7), 112.2 (C-2), 118.2 (C-10a), 118.4 (C-4a), 119.1 (C-5), 120.1 (C-8a), 120.9 (C-9), 125.0 (C-1a), 130.8 (C-5a), 130.9 (C-6), 145.8 (C-10), 146.3 (C-3), 146.8 (C-4), 156.9 (C-8), 167.3 (C═O); FABMS *m*/*z* 630 ([M + H]$^+$, $C_{37}H_{43}NO_8$, 6), 530 (7), 342 (100), 295 (81), 271 (16), 154 (84), 107 (50), 91 (59).

Acknowledgment. We thank the National Science Council, R.O.C. (NSC 86-2113-M-006-008), for support of this research.

References and Notes

(1) Liu, T. S.; Lai, M. J. *Flora of Taiwan*; Epoch: Taiwan, 1976; Vol. 2, p 572.
(2) Hussein, F. T.; El-Sebakhy, N. A. *Planta Med.* **1974**, *25*, 310−314.
(3) Habib, A. A. M.; El-Sebakhy, N. A. *Pharmazie* **1981**, *36*, 291−294.
(4) El-Sebakhy, N. A.; Waterman P. G. *Phytochemistry* **1984**, *23*, 2706−2707.
(5) Urzua, A.; Priestap, H. *Biochem. Syst. Ecol.* **1985**, *13*, 169−170.
(6) Urzua, A. *Contrib. Cient. Tecnol.* **1988**, *18*, 121−123; *Chem. Abstr.* **1998**, *110*, 92349m.
(7) El-Sebakhy, N. A.; Richomme, P.; Taaima, S.; Shamma, M. *J. Nat. Prod.* **1989**, *52*, 1374−1375.
(8) Luiz, V.; Bolzani, V. S.; Trevisan, L. M. V.; Lopes, L. M. X. *Quim. Nova.* **1990**, *13*, 250−251; *Chem. Abstr.* **1990**, *115*, 68484j.
(9) Roser, V.; Marisa, M.; Liliana, M.; Horacio, A. P.; Arnaldo, L. B.; Tomas, A.; Salvador, C. *Phytochemistry* **1997**, *46*, 1127−1129.
(10) Wu, T. S.; Leu, Y. L.; Tsai, Y. L.; Lin, F. W.; Chan, Y. Y.; Chiang, C. Y. *J. Chin. Chem. Soc.* **2001**, *48*, 109−112.
(11) Wu, T. S.; Tsai, Y. L.; Wu, P. L.; Lin, F. W.; Lin, J. K. *J. Nat. Prod.* **2000**, *63*, 692−693.
(12) Yun, J.; Buchwaid, S. L. *J. Org. Chem.* **2000**, *65*, 767−774.
(13) Irie, H.; Matsumoto, R.; Nishimura, M.; Zhang, Y. *Chem. Pharm. Bull.* **1990**, *38*, 1852−1856.
(14) Kodama, M.; Shiobara, Y.; Sumitomo, H.; Matsumura, K.; Tsukamoto, M.; Harada, C. *J. Org. Chem.* **1988**, *53*, 72−77.
(15) Nguyen, T. T. H.; Nogradi, M.; Brlik, J.; Kajtar-Peredy, M.; Wolfner, A. *J. Chem. Res., Synop.* **1991**, 137.
(16) Lopez, G. V.; Pandolfi, E. M.; Seoane, G. A. *Synthesis* **2000**, 1403−1408.
(17) Lopes, L. M. X.; Yoshida, M.; Gottlieb, O. R. *Phytochemistry* **1983**, *22*, 1516−1518.
(18) Kingsbury, C. A.; Thornton, W. B. *J. Org. Chem.* **1966**, *31*, 1000−1004.
(19) Hanuman, J. B.; Mishra, A. K.; Sabata, B. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1181−1185.
(20) Kitagjima, J.; Komori, T.; Kawasaki, T. *Chem. Pharm. Bull.* **1982**, *30*, 3912−3921.
(21) Shamma, M. *The Isoquinoline Alkaloids*; Academic Press: New York, 1972; pp 118, 119, and 235.

NP020218U