Constituents from the Leaves of *Phellodendron amurense* var. *wilsonii* and Their Bioactivity

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Two new dihydroflavonols, phellodensin-A (**1**) and phellodensin-C (**2**); three new coumarins, phellodenol-A (**3**), phellodenol-B (**4**), and phellodenol-C (**5**); one new chlorophyll, phellophyll-a (**6**); and one new phenyllactate, (2*R*)-sodium 3-phenyllactate (**7**), in addition to 35 known compounds have been isolated from the leaves of *Phellodendron amurense* var. *wilsonii*. The structures of the new compounds were established based on 1D, 2D NMR and mass spectral analyses. The stereochemistry at the C-2, C-3, and C-2″ positions of new dihydroflavonol **1** was determined by CD spectroscopy. The known compounds were identified by comparison with authentic samples. The antioxidant and antityrosinase activities were also described.

During the course of our investigation on the bioactive chemical components of the plants belonging to the family Rutaceae, we have focused on *Phellodendron amurense* var. *wilsonii*, which is a deciduous tree found widely in the northern and central parts of Taiwan.[1] It has been used as a Chinese traditional medicine for the treatment of meningitis, bacillary dysentery, pneumonia, tuberculosis, and liver cirrhosis.[2,3] Several reports have been encountered on the isolation of berberine alkaloids, aporphine alkaloids, and flavonoids from this plant.[4−7] Reinvestigation on the leaves of *P. amurense* has resulted in the isolation of seven new compounds: two dihydroflavonols, phellodensin-A (**1**) and phellodensin-C (**2**); three coumarins, phellodenol-A (**3**), phellodenol-B (**4**), and phellodenol-C (**5**); a chlorophyll, phellophyll-a (**6**); and a phenyllactate, (2*R*)-sodium 3-phenyllactate (**7**), in addition to 35 known compounds. We report herein the details of structural elucidation of all the new compounds using spectral methods.

Results and Discussion

Phellodensin-A (**1**) was obtained with HPLC as a colorless powder. The HREIMS showed a molecular ion peak at *m*/*z* 354.1100 corresponding to the molecular formula $C_{20}H_{18}O_6$. The IR absorption bands at 3433 and 1624 cm^{-1} were consistent with the presence of a hydroxyl group and a hydrogen-bonded carbonyl group. The UV absorptions at 221, 296, and 333 nm were characteristic of a dihydroflavonol skeleton.[8] The bathochromic shift in the UV absorption maximum observed after addition of $AlCl_3$ was in agreement with the presence of the hydrogen-bonded hydroxyl group of dihydroflavonol at C-5.[8] Accordingly, the ^{1}H NMR spectrum displayed a hydrogen-bonded hydroxyl singlet at δ 11.65, and it showed ^2J, ^3J-HMBC correlations with the carbons at δ 162.5 (C-5), 96.9 (C-6), and 100.9 (C-10). A singlet at δ 6.02 was assumed to be H-6, as it showed a correlation with carbon at δ 96.9 in the HMQC spectrum. One set of A_2B_2 signals at δ 7.42 (2H, d, J = 8.4 Hz) and 6.88 (2H, d, J = 8.4 Hz) were attributed to H-2′, -6′ and H-3′, -5′ of the *para*-substituted B-ring, which was further supported by a D_2O exchangeable downfield proton signal at δ 8.76 for 4′-OH in the ^{1}H NMR spectrum. The ^{1}H and ^{13}C NMR spectra of **1** showed mutually coupled proton signals due to H-2 at δ 5.00 (1H, d, J = 12.0 Hz), H-3 at δ 4.45 (1H, dd, J = 12.0, 4.0 Hz), and 3-OH at δ 4.76 (1H, d, J = 4.0 Hz, D_2O exchangeable); C-2 at δ 83.7; and C-3 at δ 72.6 of a dihydroflavonol, indicating that **1** was a 2,3-*trans*-dihydroflavonol derivative.[9] Two broad singlets at δ 4.71 and 4.65 correlated with the same carbon at δ 109.5 in the HMQC spectrum for the terminal methylene of the carbon−carbon double bond in addition to three mutually coupled protons at δ 4.28 (1H, br t, J = 5.8 Hz, H-2″), 2.82 (1H, dd, J = 14.0, 5.8 Hz, H-1″), and 2.75 (1H, dd, J = 14.0, 5.8 Hz, H-1″), and one methyl at δ 1.60 (3H, s, CH_3-5″) suggested that **1** contained an isopropenyl dihydrofuran group.[10] The presence of this partial structure was also supported by the correlations H-4b″/C-2″, H-5″/C-2″, -3″, -4″, H-4a″/C-5″ in the HMBC spectrum. The location of the fusion of the isopropenyl dihydrofuran ring was confirmed as C-7, -8 of the A-ring and excluded the possible linear fusion at C-6, -7, since HMBC correlations of both H-1″ and H-6 were observed with C-7 and -8, whereas H-1″ only with C-9. The CD spectrum of **1** showed a positive Cotton effect in the region of 305 nm and a negative effect at 284 nm, establishing the *R*-configuration at the C-2 position,[11] whereas the coupling constant between H-2 and H-3 also indicated the stereochemistry of C-3 to be *R*. Finally, the CD measurement for the osmate ester of **1** gave a negative [θ] value at 474 nm, indicative of an *R* side chain stereochemistry at C-2″, as in the model compound (2′*R*)-rotenone.[11] From the foregoing spectral analysis, the structure of phellodensin-A can be represented by **1**.

Phellodensin-C (**2**) was isolated as a colorless powder with elemental composition $C_{20}H_{20}O_7$ from its HREIMS (*m*/*z* 372.1209). The IR absorption bands at 3400 and 1647 cm^{-1} indicated the presence of hydroxyl and hydrogen-bonded carbonyl groups, respectively. The UV absorptions at 296 and 333 nm were typical of a dihydroflavonol skeleton.[8] The ^{1}H NMR of **2** revealed an A_2B_2 system of proton signals at δ 7.43 (2H, d, J = 8.2 Hz, H-2′, 6′) and 6.89 (2H, d, J = 8.2 Hz, H-3′, 5′), a D_2O exchangeable

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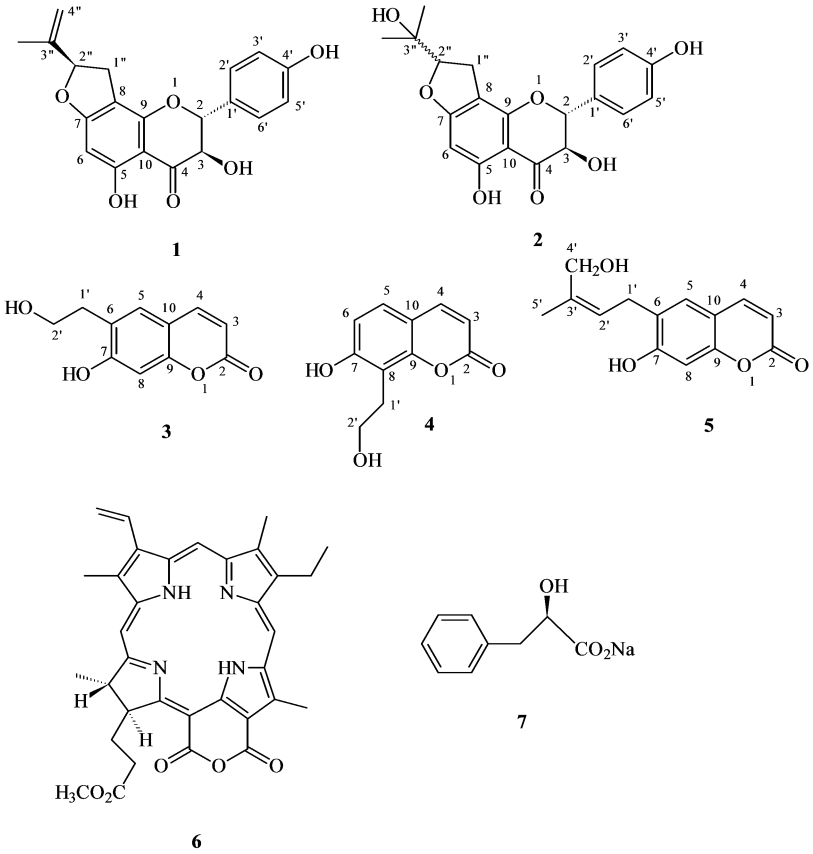

Figure 1. Structures of new compounds **1**−**7**.

proton at δ 8.57 (1H, s, 4′-OH), and a hydrogen-bonded hydroxyl signal at δ 11.60 (1H, s, 5-OH). Additionally, three proton signals at δ 5.12 (1H, d, J = 11.4 Hz, H-2), 4.66 (1H, dd, J = 11.4, 3.8 Hz, H-3), and 4.72 (1H, d, J = 3.8 Hz, 3-OH) and four proton signals at δ 2.80 (2H, m, H-1″), 4.75 (1H, dd, J = 9.2, 8.2 Hz, H-2″), 1.22 (3H, s, 3″-CH_3), and 1.11 (3H, s, 3"-CH_3) indicated that **2** was based on a 2,3-*trans*-dihydroflavonol skeleton with a 1-hydroxy-1-methylethyldihydrofuran group. The carbon signals at δ 165.6 and 91.7 were assigned to C-5 and C-6, respectively, on the basis of their ^2J- and ^3J-HMBC correlations with the hydrogen-bonded hydroxyl proton. A singlet at δ 5.92 was attributed to H-6, as it showed connectivity with the carbon at δ 91.7 in the HMQC spectrum. From these 2D analyses, the site of fusion of the 1-hydroxy-1-methylethyldihydrofuran group could be determined at C-7, -8 as in **1**. The CD measurements involving the underivatized dihydroflavonol gave a positive Cotton effect in the 320 nm region and a negative Cotton effect at 294 nm, which are characteristic of the 2*R*, 3*R* absolute stereochemistry of dihydroflavonol.[11] However, the stereochemistry of C-2″ was not determined. Thus, the structure of phellodensin-C was elucidated as shown in **2**.

Phellodenol-A (**3**), obtained as colorless amorphous powder, was determined to have molecular formula $C_{11}H_{10}O_4$ from its HREIMS. The IR bands at 3368 and 1688 cm^{-1} revealed the presence of hydroxyl and conjugated ester carbonyl groups. The UV spectrum exhibited absorption maxima at 298 (sh) and 332 nm similar to those for a 7-oxygenated coumarin.[12] Accordingly, a bathochromic shift of 46 nm in the UV absorption maxima was also observed after addition of NaOAc.[12] In the aromatic region of ^{1}H NMR spectrum, vicinal doublets at δ 7.81 and 6.13 (each 1H, J = 9.6 Hz) for H-4 and H-3 and two singlets at δ 7.40 and 6.74 were consistent with the 6,7-disubstituted coumarin. From the HMBC spectrum, the signal at δ 7.40 was assigned to H-5, as it exhibited correlation with C-4. In the high-field region, two mutually coupled triplets at δ 2.89 (2H, t, J = 6.1 Hz) and 3.83 (2H, t, J = 6.1 Hz) were indicative of a 2-hydroxyethyl group in **3**. The ^2J, ^3J-correlations of H-1′ with C-6, C-5, and C-7 and ^3J-correlation of H-2′ with C-6 in the HMBC spectrum inferred that the 2-hydroxyethyl group was connected to C-6. Thus the structure of phellodenol A was established as **3**.

Phellodenol B (**4**) was obtained as colorless needles. The molecular formula was derived from the HREIMS as $C_{11}H_{10}O_4$. The UV and IR spectral data of **4** revealed the presence of a 7-oxygenated coumarin basic skeleton.[12] The ^{1}H NMR exhibited the typical signals in the aromatic region associated with H-3 at δ 6.14 (d, J = 9.5 Hz), H-4 at δ 7.83 (d, J = 9.5 Hz), H-5 at δ 7.37 (d, J = 8.5 Hz), and H-6 at δ 6.86 (d, J = 8.5 Hz) of a 7,8-disubstituted coumarin. Two mutually coupled triplets at δ 3.83 (2H, t, J = 6.5 Hz) and 3.08 (2H, t, J = 6.5 Hz) evidenced of presence of a 2-hydroxyethyl side chain. The location of this side chain at C-8 was determined on the basis of cross-peaks from H-1′ to C-7, -8, and -9 and from H-2′ to C-8 in the HMBC spectrum. From this spectral evidence, the structure of phellodenol B was derived as **4**.

Phellodenol C (**5**) was isolated as colorless needles and exhibited a molecular ion peak in its HREIMS at m/z 246.0890 associated with the molecular formula $C_{14}H_{14}O_4$. The UV and IR spectral data and the ^{1}H NMR signals corresponding to the coumarin skeleton of **5** were similar to those of **3**, indicating the presence of a 6,7-disubstituted coumarin basic skeleton. Additionally, characteristic signals for a 4-hydroxy-3-methyl-2-butenyl group at δ 3.43 (2H, br d, J = 7.4 Hz, H-1′), 5.39 (1H, t, J = 7.4 Hz, H-2′), 4.21 (2H, s, H-4′), 3.98 (1H, br s, 4′-OH), and 1.73 (3H, s, 5′-CH_3) were also observed. The *Z* geometry at C-2′ was

inferred by the NOE cross-peaks between H-1′ and H-4′. Unambiguous location of the phenolic hydroxyl group at C-7 and hence of the 4-hydroxy-3-methyl-2-butenyl side chain at C-6 was carried out using multidimensional NOESY, HMQC, and HMBC experiments. Indeed, the NOESY spectrum showed a strong cross-peak between H-1′ and H-5, whereas the typical ^2J, ^3J-HMBC connectivities of H-1′/C-5, -6, and -7 and H-5/C-1′ were observed. These spectral elucidations defined the structure of phellodenol C as **5**.

Phellophyll-a (**6**) was obtained as a deep green powder. The UV maxima at 212, 279, 360, 407, 508, 546, and 697 nm were characteristic for chlorophyll derivatives.[13] The IR spectrum showed bands at 3450 and 1744 cm^{-1} typical of the N−H and carbonyl groups, respectively. The ^{1}H NMR spectrum showed signals for two NH groups [δ −0.12 (1H, br s) and 0.15 (1H, br s) (D_2O exchangeable)], a vinyl group [δ 7.87 (1H, dd, J = 17.8, 15.6 Hz, H-9a), 6.30 (1H, d, J = 17.8 Hz, H-9b), and 6.19 (1H, d, J = 15.6 Hz, H-9b)], an ethyl group [δ 3.56−3.65 (2H, m, H-14a) and 1.64 (3H, t, J = 7.6 Hz, H-14b)], three downfield-shifted methyl groups [δ 3.72 (s), 3.34 (s), and 3.13 (s)], a methyl group [δ 1.76 (d, J = 7.2 Hz, 4-CH_3)], and a methyl propionate group [δ 1.90−2.10 (1H, m, H-3a), 2.35−2.50 (2H, m, H-3a, -3b), 2.65−2.80 (1H, m, H-3b), and 3.58 (3H, s, OCH_3)]. In addition, signals of H-3, H-4, H-6, H-11, and H-16 at δ 5.20 (1H, br d, J = 7.6 Hz), 4.30−4.50 (1H, m), 8.58 (1H, s), 9.34 (1H, s), and 9.52 (1H, s), respectively, were also observed. These data are very close to that of methyl pheophorbide-a.[14] Lack of signals corresponding to H-21 and the $COOCH_3$ group suggested that **6** was different from methyl pheophorbide-a at C-21. The carbon signals at δ 93.0 (C-1), 112.0 (C-19), and 178.0 (C-20) in the ^{13}C NMR spectrum and a protonated molecular ion at m/z 579 in the FABMS spectrum indicated that C-1 and C-19 were involved in a six-membered anhydride ring. Thus, phellophyll-a was best represented by structure **6**, the gross structure of which was substantiated by extensive 2D NMR experiments involving the determination of its COSY, HMQC, and HMBC spectra. The spectral data of **6** were in good agreement with that of a synthetic sample.[15] However, it is the first report of isolation from a natural source.

(2*R*)-Sodium 3-phenyllactate (**7**) was obtained as a colorless crystalline solid. The UV spectrum showed maxima at 208 and 258 nm, suggesting that **7** is a benzenoid derivative.[16] In the IR spectrum, absorptions at 746 and 700 cm^{-1} revealed the presence of a monosubstituted phenyl ring. Proton signals at δ 7.29 integrating for five protons confirmed this. The remaining ^{1}H NMR signals of **7** appeared as a mutually coupled doublet of doublets at δ 4.25 (1H, J = 8.0, 4.0 Hz, H-2), 3.07 (1H, J = 14.0, 4.0 Hz, H-3), and 2.85 (1H, J = 14.0, 8.0 Hz, H-3), which could be associated with the lactate moiety. The IR spectrum also exhibited the hydroxyl band at 3300 cm^{-1} and the carbonyl band of the carboxylate salt at 1595 cm^{-1}. To identify the counterion of this compound, **7** was acidified with 5% HCl and column chromatographed over Sephadex LH-20, and the water elution was determined to contain sodium using atomic absorption spectroscopy. The stereochemistry at C-2 was assigned as *R* by the comparison of the optical rotation value $[\alpha]^{25}_D$ −26.8° with the reported value of (2*R*)-sodium 3-(*p*-hydroxyphenyl)lactate. All these data coincided well with those of a synthetic sample.[17] However, it is the first report from a natural source.

In addition, 34 compounds, amurensin (**8**),[18] quercetin 3-*O*-β-D-glucoside (**9**), [19] quercetin (**10**),[20] kaempferol (**11**),[19] kaempferol-3-*O*-β-D-glucoside (**12**),[19] kaempferol-3-*O*-β-D-galactoside (**13**),[21] phellodensin-B (**14**),[22] phellamuretin (**15**),[22] 4-oxoobovatachromene (**16**),[20] neophellamuretin (**17**),[20] phellamurin (**18**),[18] aromadendrin (**19**),[23] seselin (**20**),[24] osthenol (**21**),[24] umbelliferone (**22**),[25] scopoletin (**23**),[25] (*S*)-(−)-7-hydroxy-8-(2-hydroxy-3-methyl-3-butenyl)-2*H*-1-benzopyran-2-one (**24**),[26] (*R*)-(+)-7-hydroxy-8-(2-hydroxy-3-methyl-3-butenyl)-2*H*-1-benzopyran-2-one (**25**),[26] methyl pheophorbide-a (**26**),[14] methyl 21-hydroxy-(21*S*)-pheophorbide-a (**27**),[14] methyl 21-hydroxy-(21*S*)-pheophorbide-b (**28**),[14] *p*-hydroxybenzaldehyde (**29**),[27] methylparaben (**30**),[28] vanillic acid (**31**),[27] *p*-hydroxybenzoic acid (**32**),[27] methyl *p*-hydroxycinnamate (**33**),[27] methyl caffeate (**34**),[18] methyl ferulate (**35**),[28] lupenone (**36**),[29] 3,4-*seco*-20(29)-lupen-3-oic acid (**37**),[30] β-sitosterol (**38**),[18] 3-formylindole (**39**),[31] limonin (**40**),[32] and glyceryl-1-butcosanate (**41**),[33] were also isolated from the leaves of *P. amurense* var. *wilsonii*. All the known compounds were identified by comparison of their spectroscopic data (UV, IR, NMR, MS spectrometry) with the authentic samples.

The isolated compounds **8**, **9**, **12**, **13**, **16**, **17**, and **18** were examined for their antioxidant properties using the scavenging of the α,α-diphenyl-β-picrylhydrazyl free radical (DPPH) assay. Compounds **12**, **13**, **16**, **17**, and **18** were found to have weak activity at 250 μM with inhibition percentages 5.7%, 4.5%, −1.8%, 20.9%, and 34.6%, respectively. Compounds **8** and **9** exhibited moderate scavenging activity with the IC_{50} values 88.3 and 32.2 μM, compared to the reference compound vitamin E (IC_{50}, 8.3 μM). The antityrosinase activities of compounds **8**, **9**, **12**, **13**, **17**, **18**, **36**, **38**, and **40** were also evaluated. Among these compounds, **8**, **36**, **38**, and **40** inhibited tyrosinase at 333 μM with 15.4%, −2.4%, 14.3%, and 3.6% inhibition percentages, respectively, compared to the reference compound kojic acid (IC_{50} values of 125 μM).

Experimental Section

General Experimental Procedures. Melting points were recorded on a Yanaco MP-S3 melting point apparatus without correction. UV spectra were measured on a Hitachi UV-3210 spectrophotometer; 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 parts per million (ppm, δ). Mass spectra (EI or FAB) were recorded on a VG 70-250 S spectrometer. Optical rotations were recorded on a Jasco DIP-370 polarimeter. CD spectra were recorded with a Jasco J-720 spectropolarimeter.

Plant Material. The leaves of *P. amurense* var. *wilsonii* were collected in August 1996 from Taipei, Taiwan, and authenticated by Prof. C. S. Kuoh. A voucher specimen of the plant (NCKU Wu 19960009) has been deposited at the herbarium of National Cheng Kung University, Tainan, Taiwan.

Extraction and Separation. The air-dried and powdered leaves of *P. amurense* var. *wilsonii* (1.0 kg) were extracted with hot methanol (5 L × 6) and concentrated to give a dark brown syrup and colorless crystals **8** (24.2 g). The syrup was partitioned between water and chloroform, and the resulting chloroform solubles (27 g) were chromatographed over silica gel using a gradient of chloroform and methanol to afford seven fractions. Fraction 1 was rechromatographed over silica gel using a mixture of *n*-hexane and ethyl acetate as eluents and purified by preparative TLC to yield **36** (552.3 mg). Fraction 2 on column chromatography with *n*-hexane and acetone (3:1) yielded **20** (1.2 mg). Fraction 3 was chromatographed over silica gel using a gradient of chloroform and isopropyl ether to afford **21** (1.3 mg), **25** (1.5 mg), **27** (110.0 mg), **30** (1.7 mg), **37** (9.4 mg), and **38** (15.9 mg). Fraction 4 was subjected to

column chromatography over silica gel with *n*-hexane−acetone (3:1) to give **23** (1.6 mg), **27** (5.0 mg), and **28** (4.2 mg). Similarly, fraction 5 was also chromatographed over silica gel with *n*-hexane−acetone (3:1) and further purified by HPLC [Cosmosil 5C-18-AR-II waters (5 μm)] with methanol−water (46:54) to give **22** (2.1 mg), **24** (1.6 mg), and **39** (1.3 mg). Silica gel column chromatography of fraction 6, followed by HPLC purification [Cosmosil 5C-18-AR-II waters (5 μm)] with methanol−water (50:50), resulted in **1** (1.8 mg), **2** (0.9 mg), **4** (2.2 mg), **14** (1.2 mg), **16** (5.3 mg), **17** (251.6 mg), **29** (0.8 mg), **40** (3.9 mg), and **41** (2.0 mg). The last fraction of the chloroform layer was separated with silica gel column chromatography by chloroform and methanol in 19:1 ratio and then purified by recrystallization with methanol to afford **6** (3.1 mg). The water-soluble fraction (110 g) was chromatographed over Diaion HP-20 using water−methanol gradients, which yielded six fractions. Fraction 1 was column chromatographed with C-18 gel using gradients of water and methanol, affording **7** (5.1 mg) and **32** (3.7 mg). Fraction 2 on column chromatography over silica gel with chloroform−acetone−methanol (6:0.5:1) yielded **3** (0.8 mg), **4** (5.0 mg), **9** (0.6 g), **29** (0.7 mg), **31** (1.2 mg), and **34** (5.1 mg). Column chromatography of fraction 3 over silica gel with diisopropyl ether−acetone−methanol (8:1:1) afforded **3** (0.8 mg), **8** (5.1 mg), **9** (0.7 mg), **10** (1.0 mg), **12** (185.0 mg), **13** (4.0 mg), **18** (5.2 mg), **22** (1.8 mg), and **31** (2.0 mg). Fraction 4 was chromatographed over silica gel using a mixture of chloroform, methanol, and water as eluents (8:1:0.01), resulting in **10** (0.7 mg), **11** (1.4 mg), **12** (400.2 mg), **13** (3.2 mg), **15** (4.4 mg), **18** (26.1 g), **19** (3.3 mg), **22** (2.2 mg), and **33** (1.7 mg). Fraction 5 was subjected to column chromatography over silica gel using mixtures of diisopropyl ether−methanol (10:1) and successively purified by HPLC [Cosmosil 5C-18-AR-II waters (5 μm)] with methanol−water (50:50) to afford **1** (3.5 mg), **14** (2.0 mg), **17** (201.3 mg), and **18** (0.8 mg). Silica gel column chromatography of fraction 6 and followed by recrystallization with methanol yielded **8** (1.5 g), **17** (50.3 mg), and **35** (1.0 mg).

Preparation and CD Determination of the Osmate Ester of 1. Stock solutions of CH_2Cl_2 + pyridine (3.05 mL + 0.1 mL; A) and osmic acid + CH_2Cl_2 (4.7 mg in 125 μL; B) were first prepared. A dry sample of **1** (0.68 mg) was dissolved in A (63 μL), and B (10 μL) was then added. After incubation for 30 min at 25 °C, the mixture was diluted to 2.8 mL with CH_2Cl_2. The CD curve of the resulting osmate ester was immediately measured over the range 470−480 nm on a Jasco J-720 spectropolarimeter zeroed with a blank consisting of A + B. Like 2′*R*-rotenone ($[\theta]_{474}$ −5800) and shuterol ($[\theta]_{474}$ −3100),[11] phellodensin A ($[\theta]_{474}$ −1062) was found to possess the *R* side-chain stereochemistry at C-2″.

Antioxidant Assays. The antioxidant assays were based on methods reported by Ko *et al.*[34] and Mellors *et al.*[35] The percentage values of inhibition were recorded after incubating for 30 min.

Antityrosinase Assays. The antityrosinase assays were based on the method of Bernard *et al.*[36]

Phellodensin-A (1): $C_{20}H_{18}O_6$, white powder, mp 150−151 °C (MeOH); $[\alpha]_D^{25}$ −18.8° (*c* 0.06, MeOH); UV λ_{max}^{MeOH} nm (log ϵ) 221 (3.30), 296 (3.07), 331 (2.57); UV $\lambda_{max}^{MeOH+NaOAc}$ nm (log ϵ) 247 (2.97), 331 (3.26); IR ν_{max} cm^{-1} 3433 (OH), 3086, 1624 (C═O), 1445, 1283; ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.60 (3H, s, CH_3-5″), 2.75 (1H, dd, J = 14.0, 5.8 Hz, H-1″), 2.82 (1H, dd, J = 14.0, 5.8 Hz, H-1″), 4.28 (1H, br t, J = 5.8 Hz, H-2″), 4.57 (1H, dd, J = 12.0, 4.0 Hz, H-3), 4.65 (1H, br s, H-4″a), 4.71 (1H, br s, H-4″b), 4.76 (1H, d, J = 4.0 Hz, D_2O exchangeable, 3-OH), 5.00 (1H, d, J = 12.0 Hz, H-2), 6.02 (1H, s, H-6), 6.88 (2H, d, J = 8.4 Hz, H-3′, -5′), 7.42 (2H, d, J = 8.4 Hz, H-2′, -6′), 8.76 (1H, br s, D_2O exchangeable, 4′-OH), 11.64 (1H, br s, D_2O exchangeable, 5-OH); ^{13}C NMR (acetone-d_6, 100 MHz) δ 17.6 (CH_3), 29.1 (C-1″), 72.6 (C-3), 75.5 (C-2″), 83.7 (C-2), 96.9 (C-6), 100.9 (C-10), 105.6 (C-8), 109.5 (C-4″), 115.2 (C-3′, 5′), 128.6 (C-1′), 129.5 (C-2′, 6′), 147.4 (C-3″), 158.1 (C-4′), 160.8 (C-9), 162.5 (C-5), 166.1 (C-7), 198.0 (C-4); CD (underivatized **1**) (MeOH: *c* 0.0002): $[\theta]_{305}$ +118.6, $[\theta]_{293}$ 0, $[\theta]_{284}$ −126.5, $[\theta]_{258}$ 0, $[\theta]_{244}$ −84.0; EIMS *m*/*z* 354 (M$^+$, 11), 320 (30), 301 (87), 219 (27), 165 (100), 117 (24); HREIMS *m*/*z* 354.1100 (calcd for $C_{20}H_{18}O_6$, 354.1103).

Phellodensin-C (2): $C_{20}H_{20}O_6$, white powder, mp 108−109 °C (MeOH); $[\alpha]_D^{25}$ −28.0° (*c* 0.046, MeOH); UV λ_{max}^{MeOH} nm (log ϵ) 293 (4.45), 332 (2.95); IR ν_{max} cm^{-1} 3400 (OH), 2926, 1647 (C═O), 1458, 1383; ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.11 (3H, s, CH_3), 1.22 (3H, s, CH_3), 2.80−3.10 (1H, m, H-1″), 3.76 (1H, br s, D_2O exchangeable, 3″-OH), 4.66 (1H, dd, J = 11.4, 3.8 Hz, H-3), 4.72 (1H, d, J = 3.8 Hz, 3-OH), 4.75 (1H, dd, J = 9.2, 8.2 Hz, H-2″), 5.12 (1H, d, J = 11.4 Hz, H-2), 5.92 (1H, s, H-6), 6.89 (2H, d, J = 8.2 Hz, H-3′, -5′), 7.43 (2H, d, J = 8.2 Hz, H-2′, -6′), 8.57 (1H, br s, D_2O exchangeable, 4′-OH), 11.96 (1H, br s, D_2O exchangeable, 5-OH); ^{13}C NMR (acetone-d_6, 100 MHz) δ 25.6 (CH_3), 25.7 (CH_3), 26.9 (C-1″), 71.3 (C-3″), 73.0 (C-3), 84.0 (C-2), 91.7 (C-6), 92.8 (C-2″), 106.8 (C-8), 109.4 (C-10), 115.9 (C-3′, -5′), 129.0 (C-1′), 130.2 (C-2′, -6′), 158.0 (C-9), 158.9 (C-4′), 165.6 (C-5), 170.3 (C-7), 197.8 (C-4); CD (MeOH: *c* 0.0001) $[\theta]_{320}$ +817, $[\theta]_{312}$ 0, $[\theta]_{294}$ −5396, $[\theta]_{275}$ 0, $[\theta]_{243}$ +266, $[\theta]_{220}$ +6562; EIMS *m*/*z* 372 (M$^+$, 15), 284 (13), 231 (23), 117 (100); HREIMS *m*/*z* 372.1209 (calcd for $C_{20}H_{20}O_6$, 372.1209).

Phellodenol-A (3): $C_{11}H_{10}O_4$, white powder, mp 179−180 °C (MeOH); UV λ_{max}^{MeOH} nm (log ϵ) 205 (4.38), 221 (3.93), 298 (3.51, sh), 332 (3.82); UV $\lambda_{max}^{MeOH+NaOAc}$ nm (log ϵ) 341 (3.66, sh), 378 (3.79); IR ν_{max} cm^{-1} 3368 (OH), 1688 (C═O), 1611, 1398, 1146; ^{1}H NMR (acetone-d_6, 400 MHz) δ 2.89 (2H, t, J = 6.1 Hz, H-1′), 3.83 (2H, t, J = 6.1 Hz, H-2′), 6.13 (1H, d, J = 9.6 Hz, H-3), 6.74 (1H, s, H-8), 7.40 (1H, s, H-5), 7.81 (1H, d, J = 9.6 Hz, H-4); ^{13}C NMR (acetone-d_6, 100 MHz) δ 34.5 (C-1′), 62.7 (C-2′), 103.4 (C-8), 112.5 (C-10), 112.8 (C-3), 125.9 (C-6), 131.0 (C-5), 144.7 (C-4), 155.5 (C-9), 160.5 (C-7), 161.2 (C-2); EIMS *m*/*z* 206 (M$^+$, 18), 188 (36), 176 (54), 107 (100); HREIMS *m*/*z* 206.0578 (calcd for $C_{11}H_{10}O_4$, 206.0579).

Phellodenol-B (4): $C_{11}H_{10}O_4$, white needles, mp 159−160 °C (MeOH); UV λ_{max}^{MeOH} nm (log ϵ) 259 (3.40), 327 (4.00); UV $\lambda_{max}^{MeOH+NaOAc}$ nm (log ϵ) 252 (3.66), 276 (3.39), 375 (4.06); IR ν_{max} cm^{-1} 1688 (C═O), 1605, 1576, 1317, 1246; ^{1}H NMR (acetone-d_6, 400 MHz) δ 3.09 (2H, t, J = 6.5 Hz, H-1′), 3.83 (2H, t, J = 6.5 Hz, H-2′), 6.14 (1H, d, J = 9.5 Hz, H-3), 6.86 (1H, J = 8.5 Hz, H-6), 7.37 (1H, J = 8.5 Hz, H-5), 7.83 (1H, d, J = 9.5 Hz, H-4); ^{13}C NMR (acetone-d_6, 100 MHz) δ 27.0 (C-1′), 62.3 (C-2′), 112.5 (C-3), 113.0 (C-10), 113.8 (C-6), 114.4 (C-8), 128.1 (C-5), 145.2 (C-4), 154.8 (C-7), 160.6 (C-9), 161.2 (C-2); EIMS *m*/*z* 206 (M$^+$, 70), 188 (44), 175 (100), 160 (60), 147 (27); HREIMS *m*/*z* 206.0578 (calcd for $C_{11}H_{10}O_4$, 206.0579).

Phellodenol-C (5): $C_{14}H_{14}O_4$, white needles, mp 177−178 °C (MeOH); UV λ_{max}^{MeOH} nm (log ϵ) 223 (4.19), 257 (2.50), 332 (4.07); UV $\lambda_{max}^{MeOH+NaOAc}$ nm (log ϵ) 254 (3.70), 338 (3.92), 384 (4.02); IR ν_{max} cm^{-1} 3398 (OH), 1687 (C═O), 1604, 1398, 1265; ^{1}H NMR (acetone-d_6, 400 MHz) δ 1.73 (3H, s, CH_3), 3.43 (2H, br d, J = 7.4 Hz, H-1′), 4.21 (2H, br s, H-4′), 5.39 (1H, t, J = 7.4 Hz, H-2′), 6.13 (1H, d, J = 9.4 Hz, H-3), 6.74 (1H, s, H-8), 7.37 (1H, s, H-5), 7.82 (1H, d, J = 9.4 Hz, H-4), 9.61 (1H, br s, D_2O exchangeable, 7-OH); ^{13}C NMR (acetone-d_6, 100 MHz) δ 18.4 (CH_3), 27.8 (C-1′), 61.4 (C-4′), 103.0 (C-8), 112.7 & 112.8 (C-3, 10), 124.9 (C-2′), 126.1 (C-6), 129.7 (C-5), 137.3 (C-3′), 144.7 (C-4), 155.3 (C-9), 159.7 (C-7), 161.1 (C-2); EIMS *m*/*z* 246 (M$^+$, 21), 228 (13), 194 (12), 176 (17), 154 (100); HREIMS *m*/*z* 246.0890 (calcd for $C_{14}H_{14}O_4$, 246.0892).

Phellophyll-a (6): $C_{34}H_{34}N_4O_5$, deep green powder, mp 141−142 °C (MeOH); $[\alpha]_D^{25}$ +298.0° (*c* 0.007, MeOH); UV λ_{max}^{MeOH} nm (log ϵ) 212 (2.99), 279 (2.82), 360 (3.25), 407 (3.60), 508 (2.53), 546 (2.90), 697 (3.14); IR ν_{max} cm^{-1} 3450 (OH), 2920, 1744 (C═O), 1602, 1528, 1402, 1308; ^{1}H NMR ($CDCl_3$, 400 MHz) δ −0.12 (1H, br s, NH), 0.15 (1H, br s, NH), 1.64 (2H, t, J = 7.6 Hz, H-14b), 1.76 (3H, d, J = 7.2 Hz, 4-CH_3), 1.90−2.10 (1H, m, H-3a), 2.35−2.50 (2H, m, H-3a, -3b), 2.65−2.80 (1H, m, H-3b), 3.13 (3H, s, 13-CH_3), 3.34 (3H, s, 8-CH_3), 3.56−3.65 (2H, m, H-14a), 3.58 (3H, s, OCH_3), 3.72 (3H, s, 18-CH_3), 4.30−4.50 (1H, m, H-4), 5.20 (1H, br d, J = 7.6 Hz, H-3), 6.19 (1H, d, J = 15.6 Hz, H-9b), 6.30 (1H, d, J = 17.8 Hz, H-9b), 7.87 (1H, dd, J = 17.8, 15.6 Hz, H-9a), 8.58 (1H, s, H-6), 9.34 (1H, s, H-11), 9.52 (1H, s, H-16); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.1 (13-CH_3), 11.9 (8-CH_3), 12.4 (18-CH_3), 17.4 (C-14b), 19.4 (C-14a), 23.9 (4-CH_3), 31.3 (C-3a), 32.6 (C-3b), 49.3 (C-4), 51.6

(OCH_3), 55.1 (C-3), 93.0 (C-1), 95.2 (C-6), 103.0 (C-11), 107.6 (C-16), 111.7 (C-19), 123.4 (C-9b), 128.4 (C-9a), 131.7 (C-18), 131.9 (C-8), 136.6 (C-13), 138.0 (C-9), 139.3 (C-10), 140.4 (C-17), 144.3 (C-7), 146.0 (C-14), 149.4 (C-15), 155.6 (C-12), 159.3 (C-2), 164.1 (C-20), 173.6 (CO_2CH_3), 176.8 (C-5), 177.7 (C═O); FABMS *m*/*z* 579 ($[M + 1]^+$, 8), 219 (8), 154 (81), 136 (100).

(2*R*)-Sodium 3-phenyllactate (7): $C_9H_9O_3Na$, colorless needles, mp > 280 °C (MeOH); $[\alpha]_D^{25}$ −26.8° (*c* 0.0025, MeOH); UV λ_{max}^{MeOH} nm (log ϵ) 205 (2.64), 258 (1.91); IR ν_{max} cm^{-1} 3300 (OH), 1595 (C═O), 1085, 746; ^1H NMR (D_2O, 200 MHz) δ 2.85 (1H, dd, J = 14.0, 8.0 Hz, H-3), 3.07 (1H, dd, J = 14.0, 4.0 Hz, H-3), 4.25 (1H, dd, J = 8.0, 4.0 Hz, H-2), 7.29 (5H, m, H-5−9).

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