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Total Synthesis of Chiricanine A, Arahypin-1, *trans*-Arachidin-2, *trans*-Arachidin-3, and Arahypin-5 from Peanut Seeds

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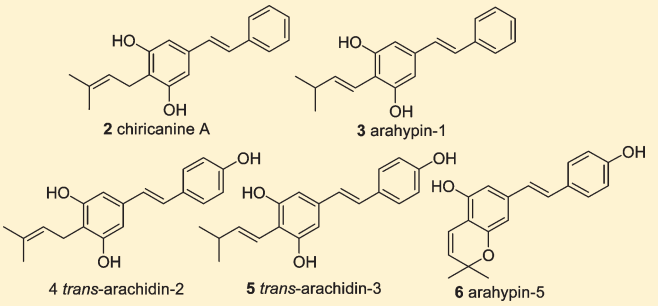
Supporting Information

ABSTRACT: The first and efficient syntheses of the naturally occurring prenylated stilbenes chiricanine A (**2**), arahypin-1 (**3**), *trans*-arachidin-2 (**4**), *trans*-arachidin-3 (**5**), and arahypin-5 (**6**) are described. Syntheses of **2** and **3** were accomplished by either a convergent sequence or a one-step reaction starting from pinosylvin. Syntheses of **4**, **5**, and **6** were achieved from (*E*)-3,5-bis-methoxymethyl-4′-triisopropylsilyloxystilbene obtained by a Horner−Wadsworth−Emmons reaction between a benzaldehyde possessing bis-methoxymethyl ether groups and a benzyl phosphonate with a triisopropylsilyloxy group.



The peanut (*Arachis hypogaea*), which is a species in the legume family (Leguminosae), has been cultivated around the world and has become an economically and nutritionally important crop.[1] Approximately 50 different genera of fungi are parasitic on the peanut,[2] of which *Aspergillus flavus* and *Aspergillus parasiticus* are very dangerous and important because of their ability to produce carcinogenic aflatoxins.[3] However, the peanut plant can resist fungal attacks by promptly producing stilbene-derived phytoalexins.[4] A study of a natural phytoalexin-based peanut resistance has attracted the attention of researchers because the knowledge and understanding of this mechanism of resistance can be crucial for breeding new fungi-resistant peanut cultivars.[5] Recently, several types of stilbene derivatives (**1**−**6**) as fungi-resistant materials were isolated from peanut seeds challenged by an *Aspergillus caelatus* strain[6] and have been shown to play a defensive role against invasive fungi.[7] Resveratrol (**1**) is known to exert a variety of promising biological activities and is beneficial to human health.[8] Chiricanine A (**2**) was also isolated from *Lonchocarpus chiricanus*[9] and has shown antifungal activity against *Cladosporium cucumerinum*.[9] Importantly, polyphenols bearing the stilbene moiety occur widely in nature[10] and have a variety of interesting biological properties, including antimicrobial,[11] antimalarial,[12] antioxidant,[13] antileukemic,[14] antiplatelet aggregative,[15] anticarcinogenic,[16] anti-HIV,[17] protein tyrosine kinase inhibitory,[18] anti-inflammatory,[19] antimutagenic,[20] antifungal,[21] and hepatoprotective[22] activities. In particular, the presence of a prenyl group on the aromatic ring of stilbenoids can lead to a remarkable increase in corresponding bioactivities.[23] This range of important biological activities and properties has stimulated research into the synthesis of naturally occurring stilbenoids. The structures of natural products **2**−**6** have been established by spectroscopic analyses, but no total syntheses of chiricanine A (**2**), arahypin-1 (**3**), *trans*-arachidin-2 (**4**), *trans*-arachidin-3 (**5**), and arahypin-5 (**6**) have been reported.

RESULTS AND DISCUSSION

Recently we developed new methodology for the formation of pinosylvin (**10**), bearing a stilbene skeleton, starting from 3,5-dimethoxybenzaldehyde (**7**) and benzyl phosphonate (**8**) through a Horner−Wadsworth−Emmons reaction followed by demethylation as shown in Scheme 1.[24] As an application of this methodology, we describe herein an efficient synthesis of chiricanine A (**2**), arahypin-1 (**3**), *trans*-arachidin-2 (**4**), *trans*-arachidin-3 (**5**), and arahypin-5 (**6**), each with a prenyl group on the stilbene skeleton.

An initial attempt toward the syntheses of chiricanine A (**2**) and arahypin-1 (**3**) was made using pinosylvin (**10**) as the starting material (Scheme 2). Reaction of **10** with 2.2 equiv of methoxymethyl chloride in the presence of NaH afforded **11** in 82% yield. Treatment of **11** with *n*-butyllithium followed by addition of prenyl bromide to trap the intermediate anion afforded the expected compound **12** (61%), which was deprotected with concentrated HCl in methanol to give **2** in 67% yield. The spectroscopic data of synthetic **2** were identical to those of the natural product reported in the literature.[9] In addition, when **11** was treated with *n*-BuLi in THF, followed by addition of isovaleraldehyde, **13** was obtained in 71% yield. Elimination of the OH group in **13** with $POCl_3$ in pyridine afforded **14** in 61% yield. To complete the synthesis of **3**, deprotection of **14** with concentrated HCl in methanol gave desired product **3** in low yield (25%) due to instability of the compound. The *trans*-configuration was confirmed by observation of the expected chemical shifts and coupling constants of two olefinic H-atoms at δ 6.31 (d, J = 16.5 Hz) and 6.15 (dd, J = 16.5, 6.6 Hz). When other Brønsted acids such as *p*-TsOH, TFA, and CSA were used,

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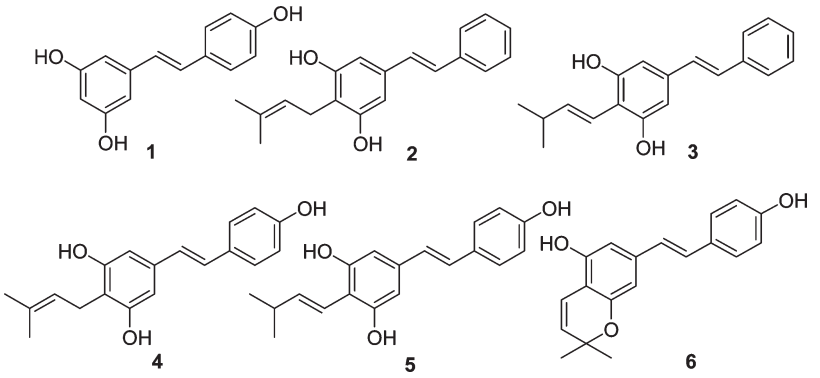
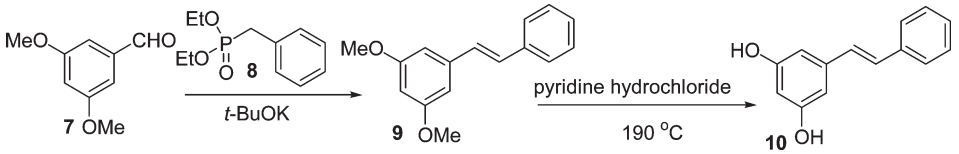
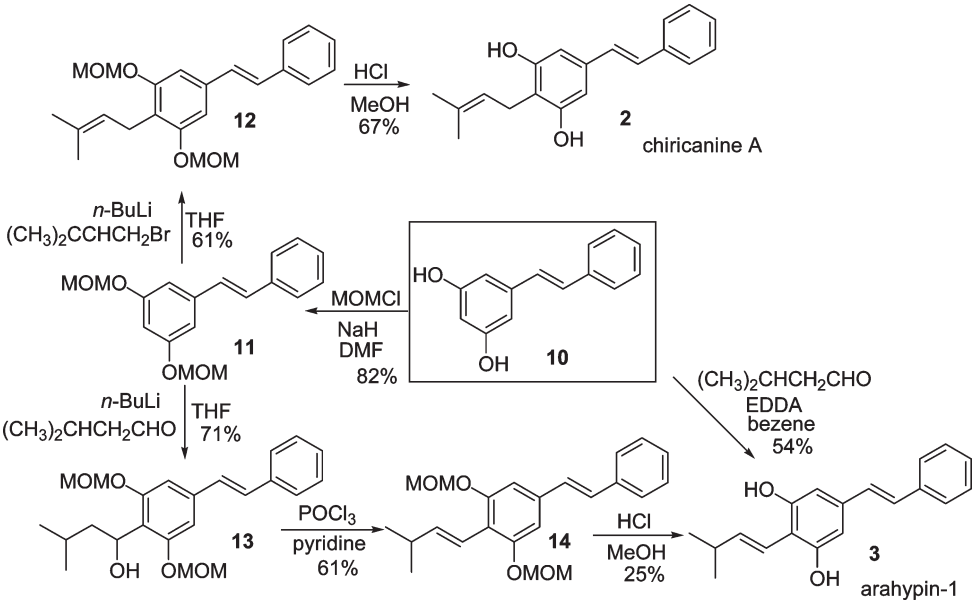
Chart 1



Scheme 1



Scheme 2



the yield did not increase. Thus, another new approach to the synthesis of **3** was attempted from pinosylvin (**10**), as a one-step reaction. Interestingly, treatment of **10** with isovaleraldehyde in the presence of 20 mol % ethylenediamine diacetate in refluxing benzene for 24 h gave **3** in 54% yield. The spectral data of synthetic **3** were in agreement with those previously reported.[6]

Next, the synthesis of naturally occurring *trans*-arachidin-2 (**4**) was attempted (Scheme 3). The Horner−Wadsworth−Emmons reaction between benzaldehyde (**15**), having MOM ether groups, and benzyl phosphonate (**16**), with a triisopropylsilyloxy group, in the presence of potassium *tert*-butoxide in THF gave desired compound **17** in 82% yield. Deprotonation at the 2-position of the bis-MOM ether of **17** with *n*-BuLi in THF followed by addition of prenyl bromide provided **18** in 80% yield. Deprotection of **18** with concentrated HCl in methanol provided **19** in 80% yield, which was treated with TBAF to give **4** in 75% yield.

Finally, the syntheses of naturally occurring *trans*-arachidin-3 (**5**) and arahypin-5 (**6**) were carried out starting from **17** as outlined in Scheme 4. Deprotection of the two MOM ether groups with concentrated HCl solution in methanol gave **20** in 80% yield. Treatment of **20** with isovaleraldehyde in the presence

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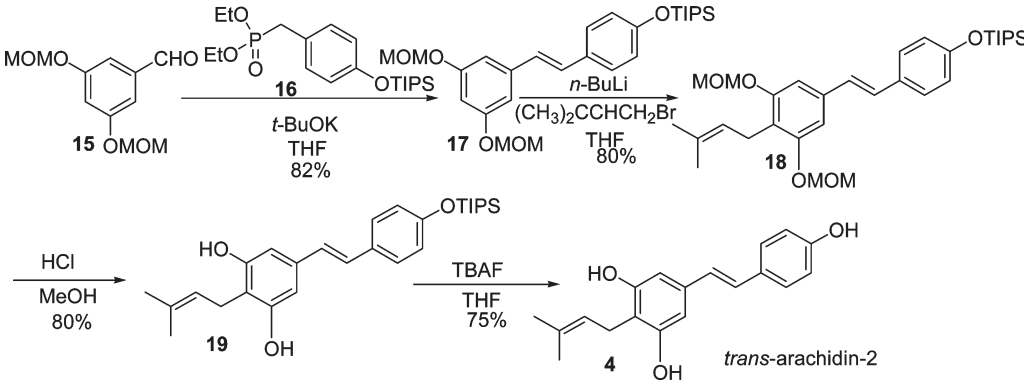
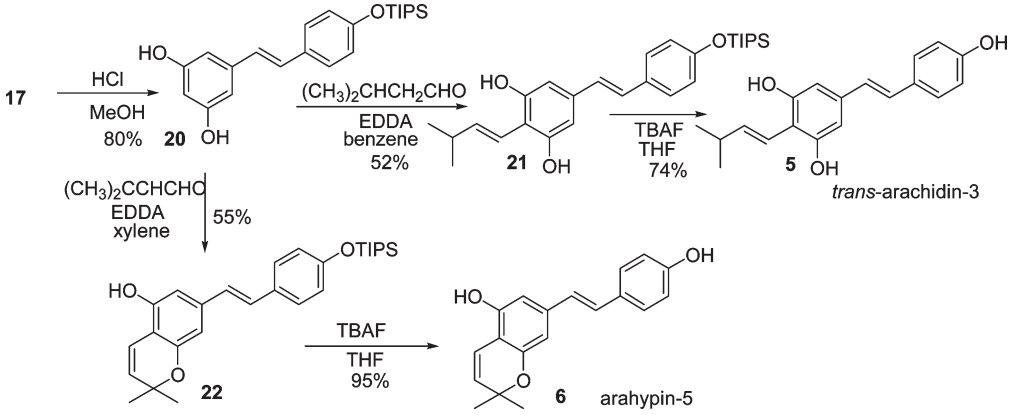
Scheme 3



Scheme 4



of 20 mol % ethylenediamine diacetate afforded **21** in 52% yield. Cleavage of the TIPS group with TBAF gave **5** in 74% yield. To complete the synthesis of arahypin-5 (**6**), a benzopyran formation reaction was next attempted. Reaction of **20** with 3-methyl-2-butenal in the presence of 20 mol % EDDA in refluxing xylene for 5 h gave cycloadduct **22** in 55% yield. Deprotection of **22** with TBAF in THF gave **6** in 95% yield.

In conclusion, total synthesis of naturally occurring and biologically interesting chiricanine A (**2**), arahypin-1 (**3**), *trans*-arachidin-2 (**4**), *trans*-arachidin-3 (**5**), and arahypin-5 (**6**) is described. The synthesis of **2** and **3** was accomplished by either a convergent sequence or a one-step reaction starting from pinosylvin (**10**). The syntheses of **4**, **5**, and **6** were achieved from stilbene **17** obtained by a Horner−Wadsworth−Emmons reaction of benzaldehyde **15**, having MOM ether groups, with benzyl phosphonate **16**, with a triisopropylsilyloxy group, in a straightforward fashion.

EXPERIMENTAL SECTION

General Experimental Procedures. Merck precoated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical TLC. Flash column chromatography (CC) was performed using silica gel 9385 (Merck). All experiments were carried out in a nitrogen atmosphere. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker model ARX (300 and 75 MHz, respectively) spectrometer in $CDCl_3$, CD_3OD, or acetone-d_6 as the solvent. IR spectra were recorded on a Jasco FTIR 5300 spectrophotometer. HRMS were carried out at the Korea Basic Science Institute. Abbreviations: MOM = methoxymethyl, TIPS = triisopropylsilyl, TBAF = tetrabutylammonium fluoride, EDDA = ethylenediamine diacetate.

(*E*)-3,5-Bis-methoxymethoxystilbene (11). Methoxymethyl chloride (0.51 g, 6.3 mmol) was added to a solution of **10** (0.509 g, 2.4 mmol) and NaH (0.288 g, 12.0 mmol) in DMF (20 mL) at 0 °C. The reaction mixture was stirred at room temperature for 12 h, and then H_2O (40 mL) was added at 0 °C. The reaction mixture was extracted with EtOAc (3 × 30 mL), and the extract was washed with saturated NH_4Cl solution (30 mL) and H_2O (30 mL), dried ($MgSO_4$), and evaporated under reduced pressure. Flash chromatography on silica gel using hexane/ethyl acetate (20:1) afforded **11** (0.591 g, 82%) as an oil.: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (2H, d, J = 7.2 Hz), 7.26 (2H, dd, J = 7.5, 7.2 Hz), 7.17 (1H, t, J = 7.5 Hz), 7.01 (1H, d, J = 16.0 Hz), 6.93 (1H, d, J = 16.0 Hz), 6.79 (2H, s), 6.57 (1H, s), 5.01 (4H, s), 3.41 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 158.5, 139.5, 137.0, 129.3, 128.6, 128.6, 128.3, 127.7, 126.5, 126.5, 107.8, 107.8, 104.2, 94.4, 94.4, 56.0, 56.0; IR (neat) 2953 (C−H), 2825 (C−H), 1591, 1454, 1400, 1282, 1213, 1147, 1084, 1035, 962, 923, 841, 752 cm^{-1}; HREIMS, 70 eV, m/z 300.1364 (calcd for $C_{18}H_{20}O_4$ 300.1362).

(*E*)-3,5-Bis-methoxymethoxy-2-(3-methylbut-2-enyl)stilbene (12). *n*-BuLi (0.72 mL, 2.5 M in hexane, 1.8 mmol) was added at 0 °C to a solution of **11** (0.451 g, 1.5 mmol) in THF (20 mL), and the resulting solution was stirred at 0 °C for 2 h. Prenyl bromide (0.238 g, 1.6 mmol) was added dropwise to the reaction mixture at 0 °C, which was stirred at room temperature for 10 h. The reaction mixture was quenched with saturated NH_4Cl solution (20 mL) and extracted with

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EtOAc (3 × 30 mL). The combined extracts were washed with water (30 mL), dried ($MgSO_4$), and evaporated under reduced pressure. Flash chromatography on silica gel using hexane/EtOAc (20:1) afforded **12** (0.337 g, 61%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (2H, d, J = 7.2 Hz), 7.34 (2H, dd, J = 7.5, 7.2 Hz), 7.23 (1H, t, J = 7.5 Hz), 7.03 (2H, s), 6.94 (2H, s), 5.24 (4H, s), 5.21(1H, t, J = 7.2 Hz), 3.50 (6H, s), 3.39 (2H, d, J = 7.2 Hz), 1.79 (3H, s), 1.67 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8, 155.8, 137.3, 136.3, 131.1, 128.8, 128.6, 128.6, 128.3, 127.5, 126.5, 126.5, 122.7, 119.9, 106.2, 106.2, 94.5, 94.5, 56.0, 56.0, 25.8, 22.8, 17.5; IR (neat) 2912 (C−H), 1600, 1576, 1438, 1394, 1316, 1211, 1153, 1102, 1048, 944, 750 cm^{-1}; HREIMS, 70 eV, m/z 368.1990 (calcd for $C_{23}H_{28}O_4$ 368.1988).

Chiricanine A (2). To a solution of **12** (0.184 g, 0.5 mmol) in MeOH (5 mL) was added concentrated HCl (0.2 mL), and the reaction mixture was stirred at room temperature for 10 h. The reaction mixture was diluted with saturated $NaHCO_3$ solution (30 mL) and extracted with EtOAc (3 × 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by CC on silica gel with hexane/EtOAc (4:1) to give **2** (0.094 g, 67%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (2H, d, J = 7.2 Hz), 7.34 (2H, t, J = 7.2 Hz), 7.24 (1H, t, J = 7.2 Hz), 6.99 (1H, d, J = 16.5 Hz), 6.91 (1H, d, J = 16.5 Hz), 6.57 (2H, s), 5.27 (1H, t, J = 6.9 Hz), 3.42 (2H, d, J = 6.9 Hz), 1.82 (3H, s), 1.76 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.0, 155.0, 137.2, 136.8, 135.6, 128.7, 128.7, 128.6, 128.0, 127.6, 126.5, 126.5, 121.3, 113,2, 106.5, 106.5, 25.8, 22.5, 17.9; IR (neat) 3412 (O−H), 2973 (C−H), 2925 (C−H), 1611, 1584, 1445, 1352, 1264, 1158, 1051, 963, 826, 743 cm^{-1}; HREIMS, 70 eV, m/z 280.1466 (calcd for $C_{19}H_{20}O_2$: 280.1463).

(*E*)-3,5-Bis-methoxymethoxy-2-(1-hydroxy-3-methylbutyl)-stilbene (13). *n*-BuLi (0.8 mL, 2.5 M in hexane, 2.0 mmol) was added at 0 °C to a solution of **11** (0.541 g, 1.8 mmol) in THF (20 mL), and the resulting solution was stirred at 0 °C for 2 h. Isovaleraldehyde (0.164 g, 1.9 mmol) was added dropwise to the reaction mixture at 0 °C, which was stirred at room temperature for 10 h. The reaction mixture was quenched with saturated NH_4Cl solution (20 mL) and extracted with EtOAc (3 × 30 mL). The extract was washed with H_2O (30 mL), dried ($MgSO_4$), and evaporated under reduced pressure. Flash chromatography on silica gel using hexane/EtOAc (4:1) afforded **13** (0.494 g, 71%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (2H, d, J = 7.2 Hz), 7.34 (2H, t, J = 7.2 Hz), 7.24 (1H, t, J = 7.2 Hz), 7.01 (1H, d, J = 16.2 Hz), 7.07 (1H, d, J = 16.2 Hz), 6.97 (2H, s), 5.28−5.25 (1H, m), 5.26 (4H, s), 3.50 (6H, s), 1.93−1.84 (1H, m), 1.80−1.71 (1H, m), 1.67−1.58 (1H, m), 0.99 (3H, d, J = 6.6 Hz), 0.95 (3H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5, 155.5, 137.7, 137.0, 129.0, 128.6, 128.6, 128.2, 127.6, 126.5, 126.5, 121.3, 106.3, 106.3, 94.5, 94.5, 66.3, 56.2, 56.2, 47.0, 25.0, 23.2, 22.4; IR (neat) 3600 (O−H), 2953 (C−H), 1603 (C−H), 1576, 1448, 1215, 1152, 1100, 1042, 921, 751 cm^{-1}; HREIMS, 70 eV, m/z 386.2097 (calcd for $C_{23}H_{30}O_5$ 386.2093).

(*E*)-3,5-Bis-methoxymethoxy-2-{(*E*)-3-methylbut-1-enyl}-stilbene (14). Compound **13** (0.425 g, 1.1 mmol) was dissolved in pyridine (10 mL), and the reaction mixture was cooled to 0 °C. $POCl_3$ (0.506 g, 3.3 mmol) was added dropwise. The reaction was stirred at room temperature for 1 h, then heated at 100 °C for 1 h. After cooling to room temperature, the reaction mixture was diluted with EtOAc (50 mL) and poured into 2 N HCl (50 mL), and the phases were separated. The aqueous phase was extracted with EtOAc (3 × 30 mL). The extract was washed with 2 N HCl (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography on silica gel using hexane/EtOAc (4:1) afforded **14** (0.259 g, 64%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (2H, d, J = 7.2 Hz), 7.34 (2H, t, J = 7.2 Hz), 7.25 (1H, t, J = 7.2 Hz), 7.01 (1H, d, J = 16.2 Hz), 7.07 (1H, d, J = 16.0 Hz), 6.95 (2H, s), 6.60−6.58 (2H, m), 5.24 (4H, s), 3.52 (6H, s), 2.53−2.43 (1H, m), 1.10 (6H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9, 155.9, 143.1, 137.2, 136.5, 128.7, 128.6, 128.6, 128.5, 128.5, 127.6, 126.5, 126.5, 117.2, 107.2, 107.2, 94.9, 94.9, 56.2, 56.2, 33.1, 22.7, 22.7; IR (neat) 2955 (C−H), 1600, 1447, 1393, 1152, 1044, 965, 824, 739 cm^{-1}; HREIMS, 70 eV, m/z 368.1985 (calcd for $C_{23}H_{28}O_4$ 368.1988).

Arahypin-1 (3) from Compound 14. To a solution of **14** (0.184 g, 0.5 mmol) in MeOH (5 mL) was added concentrated HCl (0.5 mL), and the reaction mixture was stirred at room temperature for 10 h. The reaction was diluted with saturated $NaHCO_3$ solution (30 mL) and extracted with EtOAc (3 × 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by CC on silica gel with hexane/EtOAc (4:1) to give **3** (0.035 g, 25%) as an oil: IR (neat) 3409 (OH), 2949 (C−H), 1624, 1574, 1433, 1360, 1301, 1028, 975, 828 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (2H, d, J = 7.6 Hz), 7.33 (2H, t, J = 7.6 Hz), 7.24 (1H, t, J = 7.6 Hz), 7.03 (1H, d, J = 16.2 Hz), 6.93 (1H, d, J = 16.2 Hz), 6.63 (2H, s), 6.31 (1H, d, J = 16.5 Hz), 6.15 (1H, dd, J = 16.5, 6.6 Hz), 5.34 (1H, br s), 2.60−2.49 (1H, m), 1.13 (6H, d, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 153.8, 145.7, 137.6, 137.0, 129.1, 128.6, 128.6, 127.9, 127.6, 126.5, 126.5, 117.3, 111.8, 105.8, 105.8, 32.2, 22.3, 22.3; HREIMS, 70 eV, m/z 280.1466 (calcd for $C_{19}H_{20}O_2$ 280.1463).

Arahypin-1 (3) from Compound 10. To a solution of **10** (0.212 g, 1.0 mmol) and isovaleraldehyde (0.129 g, 1.5 mmol) in benzene (20 mL) was added ethylenediamine diacetate (36 mg, 0.2 mmol) at room temperature. The reaction mixture was refluxed for 10 h and then cooled to room temperature. Evaporation of solvent and purification by CC on silica gel using hexane/EtOAc (4:1) gave **3** (0.151 g, 54%) as an oil. The spectral data were the same as described above.

(*E*)-3,5-Bis-methoxymethoxy-4′-triisopropylsilyloxystilbene (17). To a solution of aldehyde **15** (0.679 g, 3.0 mmol) and benzyl phosphonate **16** (1.202 g, 3.0 mmol) in THF (30 mL) was added *t*-BuOK (0.717 g, 6.4 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 5 h. The reaction was quenched by addition of H_2O (30 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layer was washed with NH_4Cl solution (30 mL), H_2O (30 mL), and brine (30 mL), dried over $MgSO_4$, and concentrated at reduced pressure. The removal of the solvent under reduced pressure left an oily residue, which was then purified by CC on silica gel using hexane/EtOAc (4:1) to give **17** (1.163 g, 82%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (2H, d, J = 9.0 Hz), 7.01 (1H, d, J = 16.2 Hz), 6.88−6.81 (5H, m), 6.60 (1H, t, J = 2.0 Hz), 5.17 (4H, s), 3.48 (6H, s), 1.41−1.20 (3H, m), 1.09 (18H, d, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 158.2, 155.7, 139.7, 129.8, 128.8, 127.5, 127.5, 126.0, 119.8, 119.8, 107.4, 107.4, 103.6, 94.2, 94.2, 55.7, 55.7, 17.6 (6 carbons), 12.4 (3 carbons); IR (neat) 2952 (C−H), 2868 (C−H), 1597, 1509, 1463, 1396, 1275, 1151, 1037, 918, 841 cm^{-1}; HREIMS, 70 eV, m/z 472.2646 (calcd for $C_{27}H_{40}O_5Si$ 472.2645).

(*E*)-3,5-Bis-methoxymethoxy-2-(3-methylbut-2-enyl)-4′-triisopropylsilyloxystilbene (18). *n*-BuLi (0.44 mL, 2.5 M in hexane, 1.1 mmol) was added at 0 °C to a solution of **17** (0.473 g, 1.0 mmol) in THF (20 mL), and the resulting solution was stirred at 0 °C for 2 h. Prenyl bromide (0.164 g, 1.1 mmol) was added dropwise to the reaction mixture at 0 °C, which was stirred at room temperature for 10 h. The reaction was quenched with saturated NH_4Cl solution (20 mL) and extracted with EtOAc (3 × 30 mL). The combined extracts were washed with H_2O (30 mL), dried ($MgSO_4$), and evaporated under reduced pressure. Flash chromatography on silica gel using hexane/EtOAc (5:1) afforded **18** (0.433 g, 80%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (2H, d, J = 7.8 Hz), 7.01−6.84 (6H, m), 5.23 (4H, s), 5.22 (1H, t, J = 6.5 Hz), 3.50 (6H, s), 3.39 (2H, d, J = 6.5 Hz), 1.78 (3H, s), 1.67 (3H, s), 1.38−1.19 (3H, m), 1.11 (18H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8, 155.8, 155.7, 136.8, 131.0, 130.4, 128.0, 127.6, 127.6, 126.7, 122.8, 120.1, 120.1, 119.5, 106.0, 106.0, 94.5, 94.5, 56.0, 56.0, 25.8, 22.8, 17.9 (6 carbons), 17.8, 12.7 (3 carbons); IR (neat) 2947 (C−H), 1599, 1511, 1452, 1271, 1156, 1053, 916 cm^{-1}; HREIMS, 70 eV, m/z 540.3268 (calcd for $C_{32}H_{48}O_5Si$ 540.3271).

(*E*)-3,5-Dihydroxy-2-(3-methylbut-2-enyl)-4′-triisopropylsilyloxystilbene (19). To a solution of **18** (0.27 g, 0.5 mmol) in MeOH (5 mL) was added concentrated HCl (0.5 mL), and the reaction mixture was stirred at room temperature for 10 h. The mixture was diluted with saturated $NaHCO_3$ solution (30 mL) and extracted with EtOAc (3 × 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by CC on silica gel with hexane/EtOAc (4:1) to give **19** (0.181 g, 80%) as an oil: IR (neat) 2946 (C−H), 2865 (C−H), 1598, 1509, 1456, 1391, 1269, 1155, 1103, 1051, 916, 838 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (2H, d, J = 8.7 Hz), 7.01 (1H, d, J = 16.2 Hz), 6.85 (2H, d, J = 8.7 Hz), 6.76 (1H, d, J = 16.8 Hz), 6.53 (2H, s), 5.40 (1H, br s), 5.27 (1H, t, J = 6.6 Hz), 3.41 (2H, d, J = 6.6 Hz), 1.82 (3H, s), 1.75 (3H, s), 1.34−1.20 (3H, m), 1.11 (18H, d, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8, 155.0, 155.0, 137.2, 135.3, 130.2, 128.3, 127.6, 127.6, 125.9, 121.5, 120.1, 120.1, 112.8, 106.2, 106.2, 25.7, 22.5, 17.8 (7 carbons), 12.6 (3 carbons); HREIMS, 70 eV, m/z 452.2745 (calcd for $C_{28}H_{40}O_3Si$ 452.2747).

***trans*-Arachidin-2 (4).** To the solution of **19** (0.136 g, 0.3 mmol) in THF (10 mL) was added TBAF (0.6 mL, 0.6 mmol, 1.0 M in THF) at 0 °C, and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was quenched by addition of saturated NH_4Cl solution (30 mL) and extracted with EtOAc (3 × 30 mL). The organic layer was washed with water (30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by CC with hexane/EtOAc (4:1) to afford **4** (0.067 g, 75%) as an oil: ^1H NMR (300 MHz, acetone-d_6) δ 8.41 (1H, s), 8.07 (1H, s), 7.38 (2H, d, J = 8.7 Hz), 6.93 (1H, d, J = 16.2 Hz), 6.84−6.79 (3H, m), 6.59 (2H, s), 5.30 (1H, t, J = 7.2 Hz), 3.35 (2H, d, J = 7.2 Hz), 1.76 (3H, s), 1.64 (3H, s); ^{13}C NMR (75 MHz, acetone-d_6) δ 158.0, 157.0, 157.0, 137.3, 130.8, 130.1, 128.6, 128.6, 128.2, 127.0, 124.4, 116.5, 116.5, 115.3, 105.8, 105.8, 26.0, 23.2, 18.0; IR (neat) 3389 (O−H), 2926 (C−H), 1599, 1513, 1437, 1358, 1250, 1166, 1047, 819 cm^{-1}; HREIMS, 70 eV, m/z 296.1414 (calcd for $C_{19}H_{20}O_3$ 296.1412).

(*E*)-3,5-Dihydroxy-4′-triisopropylsilyloxystilbene (20). To a solution of **17** (0.473 g, 1.0 mmol) in MeOH (5 mL) was added concentrated HCl (1.0 mL), and the reaction mixture was stirred at room temperature for 10 h. The reaction was diluted with saturated $NaHCO_3$ solution (30 mL) and extracted with EtOAc (3 × 30 mL). Removal of solvent at reduced pressure left an oily residue, which was then purified by CC on silica gel with hexane/EtOAc (4:1) to give **20** (0.308 g, 80%) as an oil: IR (neat) 3389 (O−H), 2946 (C−H), 1602, 1510, 1270, 1156, 1007, 911 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (2H, d, J = 8.7 Hz), 6.97 (1H, d, J = 16.2 Hz), 6.84 (2H, d, J = 8.7 Hz), 6.79 (1H, d, J = 16.2 Hz), 6.52 (2H, d, J = 2.1 Hz), 6.23 (1H, t, J = 2.1 Hz), 1.30−1.22 (3H, m), 1.09 (18H, d, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 156.7, 156.0, 140.4, 130.0, 129.2, 127.8, 127.8, 125.8, 120.1, 120.1, 106.0, 106.0, 101.9, 17.9 (6 carbons), 12.6 (3 carbons); HREIMS, 70 eV, m/z 384.2118 (calcd for $C_{23}H_{32}O_3Si$ 384.2121).

(*E*)-3,5-Dihydroxy-2-{(*E*)-3-methylbut-1-enyl}-4′-triisopropylsilyloxystilbene (21). To a solution of **20** (0.154 g, 0.4 mmol) and isovaleraldehyde (0.043 g, 0.5 mmol) in benzene (20 mL) was added ethylenediamine diacetate (14 mg, 0.08 mmol) at room temperature. The reaction mixture was refluxed for 10 h and then cooled to room temperature. Evaporation of solvent and CC on silica gel using hexane/ethylacetate (5:1) gave **21** (0.094 g, 52%) as an oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (2H, d, J = 8.7 Hz), 7.32 (1H, br s), 6.97 (1H, d, J = 16.2 Hz), 6.86 (2H, d, J = 8.7 Hz), 6.78 (1H, d, J = 16.2 Hz), 6.60 (2H, s), 6.31 (1H, d, J = 16.5 Hz), 6.13 (1H, dd, J = 16.5, 6.6 Hz), 5.30 (1H, br s), 2.60−2.48 (1H, m), 1.30−1.22 (3H, m), 1.14−1.09 (24H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 153.8, 153.8, 145,5, 130.1, 128.8, 128.3, 127.7, 127.7, 125.8, 120.1, 120.1, 117.4, 111.3, 105.5, 105.5, 32.3, 22.4, 22.4, 17.9 (6 carbons), 12.6 (3 carbons); IR (neat) 3422 (O−H), 2945 (C−H), 2871 (C−H), 1601, 1510, 1447, 1268, 1168, 1036, 909 cm^{-1}; HREIMS, 70 eV, m/z 452.2743 (calcd for $C_{28}H_{40}O_3Si$ 452.2747).

***trans*-Arachidin-3 (5).** To the solution of **21** (0.045 g, 0.1 mmol) in THF (10 mL) was added TBAF (0.2 mL, 0.2 mmol, 1.0 M in THF) at 0 °C, and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was quenched by the addition of saturated NH_4Cl solution (30 mL) and extracted with EtOAc (3 × 30 mL). The organic layer was washed with water (30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by CC with hexane/EtOAc (4:1) and afforded **5** (0.022 g, 74%) as an oil: IR (neat) 3393 (O−H), 2931 (C−H), 1598, 1512, 1435, 1246, 1034, 821 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (2H, d, J = 8.7 Hz), 6.97 (1H, d, J = 16.2 Hz), 6.80 (2H, d, J = 8.7 Hz), 6.77 (1H, d, J = 16.2 Hz), 6.60 (2H, s), 6.29 (1H, d, J = 16.5 Hz), 6.12 (1H, dd, J = 16.5, 6.6 Hz), 5.09 (1H, s), 2.60−2.49 (1H, m), 1.13 (6H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, acetone-d_6) δ 158.2, 157.1, 157.1, 141.3, 137.7, 130.0, 128.7, 128.7, 128.6, 126.6, 119.3, 116.5, 116.5, 112.7, 106.1, 106.1, 34.0, 23.3, 23.3; HREIMS, 70 eV, m/z 296.1409 (calcd for $C_{19}H_{20}O_3$ 296.1412).

(*E*)-2,2-Dimethyl-7-[2-(4-triisopropylsilanyloxyphenyl)-vinyl]-2*H*-chromen-5-ol (22). To a solution of **20** (0.115 g, 0.3 mmol) and 3-methyl-2-butenal (0.034 g, 0.4 mmol) in benzene (20 mL) was added ethylenediamine diacetate (11 mg, 0.06 mmol) at room temperature. The reaction mixture was refluxed for 10 h and then cooled to room temperature. Evaporation of solvent and CC on silica gel using hexane/EtOAc (5:1) gave **22** (0.074 g, 55%) as an oil: IR (neat) 3396 (O−H), 3028 (=C−H), 2943 (C−H), 2865 (C−H), 1600, 1565, 1509, 1462, 1271, 1168, 1139, 1115, 1060, 912, 884 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (2H, d, J = 8.4 Hz), 6.95 (1H, d, J = 16.2 Hz), 6.83 (2H, d, J = 8.4 Hz), 6.74 (1H, d, J = 16.2 Hz), 6.63 (1H, d, J = 9.9 Hz), 6.57 (1H, s), 6.46 (1H, s), 5.56 (1H, d, J = 9.9 Hz), 1.34 (6H, s), 1.26−1.11 (3H, m), 1.01 (18H, d, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9, 154.0, 151.6, 138.8, 130.2, 128.9, 128.6, 127.7, 127.7, 126.1, 120.1, 120.1, 116.6, 109.0, 106.9, 106.1, 76.0, 27.8, 27.8, 17.9 (6 carbons), 12.7 (3 carbons); HREIMS, 70 eV, m/z 450.2593 (calcd for $C_{28}H_{38}O_3Si$ 450.2590).

Arahypin-5 (6). To the solution of **22** (0.045 g, 0.1 mmol) in THF (10 mL) was added TBAF (0.2 mL, 0.2 mmol, 1.0 M in THF) at 0 °C, and the mixture was stirred at room temperature for 3 h. The reaction mixture was quenched by the addition of saturated NH_4Cl solution (30 mL) and extracted with EtOAc (3 × 30 mL). The organic layer was washed with H_2O (30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by CC with hexane/EtOAc (5:1), yielding **6** (0.028 g, 95%) as an oil: IR (neat) 3412 (O−H), 1600, 1512, 1441, 1252, 1010, 819, 761 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 7.35 (2H, d, J = 8.7 Hz), 6.96 (1H, d, J = 16.2 Hz), 6.80 (1H, s), 6.78 (2H, d, J = 8.7 Hz), 6.64 (1H, d, J = 9.9 Hz), 6.51 (1H, s), 6.46 (1H, s), 5.57 (1H, d, J = 9.9 Hz), 1.40 (6H, s); ^{13}C NMR (75 MHz, CD_3OD) δ 158.4, 155.4, 154.5, 140.4, 130.5, 129.5, 129.3, 129.0, 129.0, 126.9, 118.3, 116.6, 116.6, 110.4, 106.9, 106.7, 76.9, 28.2, 28.2; HREIMS, 70 eV, m/z 294.1256 (calcd for $C_{19}H_{18}O_3$ 294.1256).

■ ASSOCIATED CONTENT

Supporting Information. Copies of ^1H and ^{13}C NMR spectra for compounds **2**−**6**, **11**−**14**, and **17**−**22**. This information can be accessed free of charge via the Internet at http://pubs.acs.org.

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