A Facile Synthetic Approach to Prenylated Flavanones: First Total Syntheses of (±)-Bonannione A and (±)-Sophoraflavanone A

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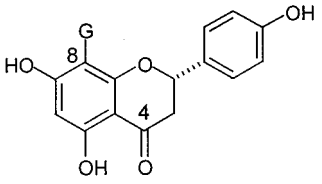
A facile and efficient approach for the syntheses of both C-8 and C-6 prenylated flavonoids has been developed that features a highly regioselective prenylation of 2,4,6-trihydroxyacetophenone and regioselective cyclization of prenylated polyhydroxy chalcones. Thus, the first efficient total syntheses of (±)-sophoraflavanone A (**1**) and (±)-bonannione A (**2**), two naturally occurring geranylated flavanones with antibacterial activities, have been achieved starting from the key intermediate **3** via regioselective cyclization of geranylated tetrahydroxychalcone **4**.

Prenylated flavanones are a unique class of naturally occurring flavonoids characterized by the presence of a prenylated side chain (i.e., prenyl, geranyl) in the flavonoid skeleton. Existing in various traditional medicinal plants, prenylated flavanones exhibit a wide range of interesting physiological properties (i.e., hypotensive, antifungal, antibacterial, and antitumor).[1,2] It was reported that the presence of a prenyl or geranyl group led to a remarkable increase of corresponding bioactivities.[3] We have been interested in the development of a facile and general synthetic approach to the prenylated flavanones in connection with ongoing studies of flavonoids.

The lack of a general, efficient, and regioselective method for the introduction of a prenylated side chain and the appropriate use of protective groups for the phenoxy functions presents a major challenge for the total synthesis of this class of natural products. For example, Trost's synthesis[4,5] of the trimethyl ether of (±)-sophoraflavanone A (**1**) involved a direct geranylation of a metalated phenoxy ether derivative. The geranylation method employed by Fukai et al.[6,7] in the syntheses of albanins D and E, two C-6-geranylated natural flavones, suffered from both low yields and poor selectivity. A facile and efficient geranylation approach was developed in our laboratory and used in the total synthesis[8] of the C-8 geranylated flavanone, (±)-sophoraflavanone C, via the key geranylated intermediate **3**.

In continuation of our studies on the synthesis of prenylated flavanones, herein we report the development of a facile and selective approach for the synthesis of both C-8 and C-6 prenylated flavanoids exemplified by the first total syntheses of (±)-sophoraflavanone A (**1**)[9,10] and (±)-bonannione A (**2**),[11] two antibacterial geranylated flavanones isolated from *Sophora tomentosa* L. and *Bonannia greasa*, respectively. The synthesis of the C-6 geranylated flavanone (±)-bonannione A (**2**) (Scheme 1) commenced from C-3 geranylated acetophenone (**3**), which is readily prepared from 2,4,6-trihydroxyacetophenone by the geranylation method previously reported by us.[8] Selective bismethoxymethylation of **3** was followed by methylation of the resulting **4a** to give geranylated acetophenone **4b**, which was condensed with *p*-[(methoxy)methoxy]benzaldehyde to afford chalcone **5**. Deprotection of methoxymethyl group by treatment with 3 M HCl led to chalcone **6**, which



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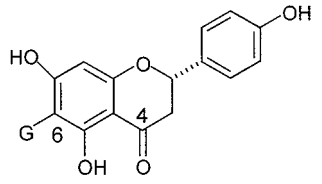
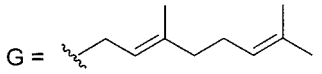


2



was cyclized under the usual conditions to give methylated flavanone **7** (mp 116−118 °C). (±)-Boninnione A (**2**) was obtained (see Experimental Section) by demethylation of **7** with BBr_3 in CH_2Cl_2 in 92% yield. The synthetic (±)-**2** showed spectral data as well as melting point and chromatographic behavior identical with those previously reported for (±)-boninnione A.[11] Using the same approach, the geranylated hydroxyacetophenone **4a** was condensed with *p*-[(methoxy)methoxy]benzaldehyde to yield the corresponding chalcone **8b**, which was deprotected to give tetrahydroxychalcone **9b** (mp 70−71 °C).[12] The subsequent regioselective cyclization afforded the C-6 geranylated flavanone (±)-boninnione A (**2**) and the C-8 geranylated flavanone (±)-sophoraflavanone A (**1**) (mp 144−145 °C, lit.[9,10] mp 144−145 °C) in a ratio of 4:1 with a combined yield of 100%. The cyclization of analogous chalcone **9a** (derived from benzaldehyde and **4a**)[13] quantitatively produced a single product that was identified as the C-6 geranylated flavanone (±)-**10**, a natural product isolated from the seeds of *Amorpha fruticosa*.[14] The remarkable regioselectivity for the cyclization of the geranylated polyhydroxychalcones **9a** and **9b** may result from the presence of the geranyl group, which would lead to a greater tendency for the formation of intramolecular hydrogen bonding of C-2′ phenoxy over C-6′ phenoxy with the carbonyl group (Scheme 2). The result, to some extent, is analogous to the well-known Wessely−Moser rearrange-

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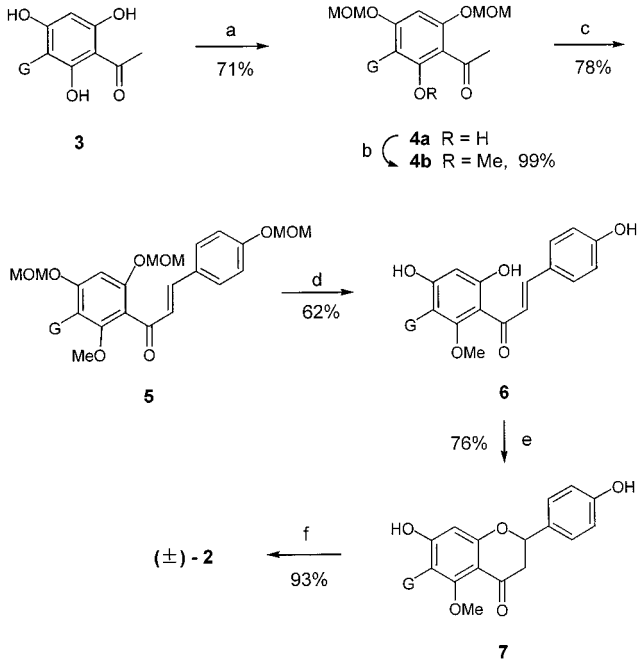
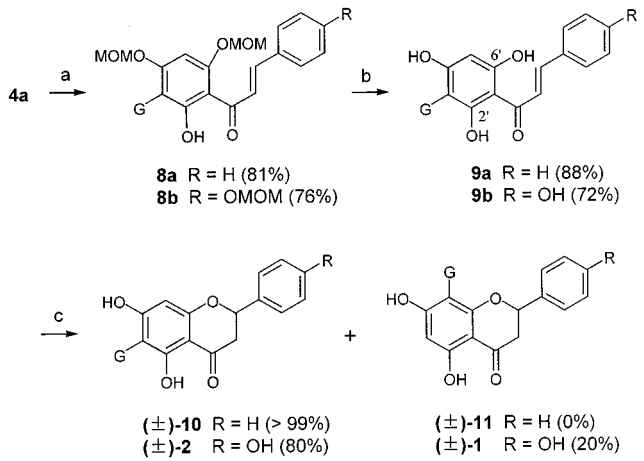
Scheme 1[a]



[a] Reagents and conditions: (a) MOMCl, K_2CO_3, Me_2CO, reflux; (b) $(CH_3)_2SO_4$, *n*-$Bu_4N^+I^-$, NaOH, $CH_2Cl_2-H_2O$ (v/v 3:2), 23 °C; (c) (*p*-MOMO)C_6H_4CHO, KOH, H_2O−EtOH (v/v 1:1), 0−23 °C; (d) 3 M HCl, MeOH, reflux; (e) NaOAc, EtOH, reflux; (f) BBr_3, $CHCl_2$, −78 to 23 °C.

Scheme 2[a]

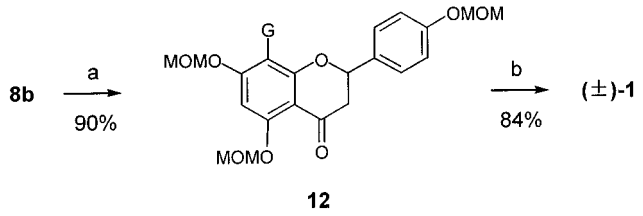


[a] Reagents and conditions: (a) PhCHO or (*p*-MOMO)C_6H_4CHO, KOH, H_2O-EtOH (v/v 1: 1), 0−23 °C; (b) 3 M HCl, MeOH, reflux; (c) NaOAc, EtOH, reflux.

ment[15,16] of corresponding flavones under acidic conditions. In this case, the predominant production of the C-6 geranylated flavanones over C-8 ones is a result of a thermodynamically controlled process. The present synthetic method provides a selective and efficient route for the synthesis of C-6 prenylated natural flavanoids.

Furthermore, we envisioned that the chalcone **8b** might serve as a precursor for the synthesis of C-8 geranylated flavanones. Thus, cyclization of **8b** (performed as usual by treatment with NaOAc in EtOH) was followed by demethoxymethylation to give (±)-sophoraflavanone A (**1**) in 84% yield. The synthetic product has identical spectral data with those of the natural product.[15,16] In conclusion, this facile and efficient approach for the syntheses of C-6 and C-8 prenylated flavanones features a prenylation of phenoxy acetophenone and regioselective cyclization of prenylated hydroxychalcones, which has been exemplified by the first efficient total syntheses of geranylated natural

Scheme 3[a]



[a] Reagents and conditions: (a) NaOAc, EtOH, reflux; (b) 3 M HCl, MeOH, reflux.

flavanoids (±)-**1** and (±)-**2**. The new method will greatly facilitate the synthesis of prenylated flavanoids and their analogues for further physiological evaluations.

Experimental Section

General Experimental Procedures. Melting points were measured on a Kofler hot stage and are uncorrected. For column chromatography, 200−300 mesh silica gel was used. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-400 or AC-80 instrument in $CDCl_3$ unless otherwise noted. Chemical shifts were reported in ppm units with TMS as the internal standard. IR spectra were obtained on a FT-170-SX spectrometer. LRMS were measured on a ZAB-HS spectrometer by direct inlet at 70 eV. HRMS were determined on a Bruker Daltonics APEXII 47e Fourier transform spectrometer with either EI, CI, FAB, or SIMS ionization methods. 3-Geranyl-2,4,6-trihydroxyacetophenone (**3**) was prepared according to our previously described procedure.[8]

4,6-Bis[(methoxy)methoxy]-2-hydroxy-3-(1′-geranyl)acetophenone (4a). To a stirred mixture of **3** (304 mg, 1 mmol) and anhydrous K_2CO_3 (966 mg, 7 mmol) in dry acetone (20 mL) was added dropwise MOMCl (200 mg, 25 mmol). The mixture was heated at reflux for 45 min, then cooled to room temperature, filtered, and evaporated under reduced pressure. The resulting residue was purified by silica gel column chromatography eluting with petroleum ether−EtOAc (6:1) to afford **4a** (279 mg, 71% yield) as a deep red gum: UV (CH_3OH) λ_{max} (log ϵ) 225 (4.16), 285 (4.18), 328 (3.48) nm; IR (KBr) ν 2967, 2918, 1617, 1486, 1428, 1406, 1373, 1273, 1231, 1152, 1107, 1070, 1044, 962 cm^{-1}; ^1H NMR (80 MHz) δ 1.57, 1.64, 1.78 (3H each s, 8′-CH_3, 9′-CH_3, and 10′-CH_3), 1.90−2.30 (4H, m, 4′-2*H* and 5′-2*H*), 2.65 (3H, s, COCH_3), 3.31 (2H, d, J = 6.9 Hz, 1′-2*H*), 3.47, 3.51 (3H each s, 2 OCH_3), 4.90−5.48 (6H, m, 2 OCH_2O, 2′-*H* and 6′-*H*), 6.40 (1H, s, Ar*H*), 13.84 (1H, s, O*H*); EIMS *m*/*z* [M^+] 392 (4), 347 (10), 273 (7), 269 (3), 225 (3), 69 (10), 45 (100).

4,6-Bis[(methoxy)methoxy]-2-methoxy-3-(1′-geranyl)acetophenone (4b). To a well-stirred mixture of **4a** (392 mg, 1 mmol), NaOH (60 mg, 1.5 mmol), and (*n*-$C_4H_9)_4N^+I^-$ (47 mg, 0.1 mmol) in $CH_2Cl_2-H_2O$ (15 mL, v/v = 3:2) was added dropwise $(CH_3)_2SO_4$ (151 mg, 1.2 mmol). After the mixture was stirred for 3 h at ambient temperture, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined CH_2Cl_2 layers were washed with H_2O and brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography eluting with petroleum ether−EtOAc (4:1) to give **4b** (403 mg, 99% yield) as a deep red gum: UV (CH_3OH) λ_{max} (log ϵ) 231 (3.81), 262 (3.52) nm; IR (KBr) ν 2932, 1625, 1470, 1432, 1352, 1223, 1109, 1017, 1038 cm^{-1}; ^1H NMR (80 MHz) δ 1.58, 1.65, 1.77 (3H each s, 8′-CH_3, 9′-CH_3, and 10′-CH_3), 1.90−2.15 (4H, m, 4′-2*H* and 5′-2*H*), 2.53 (3H, s, COCH_3), 3.31 (2H, d, J = 6.8 Hz, 1′-2*H*), 3.48, 3.72, 3.97 (3H each s, 3 OCH_3), 4.80−5.30 (6H, m, 2 OCH_2O, 2′-*H* and 6′-*H*), 5.30 (1H, br, J = 6.5 Hz, 2′-*H*), 6.72 (1H, s, Ar*H*); EIMS *m*/*z* [M^+] 406 (3), 36 (10), 287 (2), 283 (2), 239 (5), 91 (30), 69 (45), 45 (100).

4,4′,6′-Tris[(methoxy)methoxy]-2′-methoxy-3′-(1″-geranyl)chalcone (5). To a stirred mixture of potassium hydroxide (1.0 g, 17.8 mmol) in H_2O−EtOH (2 mL, v/v = 2:3) cooled to 0 °C in an ice bath was added dropwise a solution of **4b** (406

mg, 1 mmol) and *p*-methoxymethoxybenzaldehyde (166 mg, 1 mmol, prepared from *p*-hydroxybenzaldehyde) in EtOH (2 mL) cooled to 0 °C under argon. The reaction mixture was kept in the ice bath for 3 h, then at ambient temperature for 40 h. The resulting mixture was poured into ice water (5 mL), and the solution was adjusted to pH 3−4 with 2 M HCl, then extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with H_2O and saturated brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography eluting with petroleum ether−EtOAc (10:1) to give chalcone **5** (435 mg, 78% yield) as a red liquid: UV (CH_3OH) λ_{max} (log ϵ) 219 (4.31), 327 (4.33) nm; IR (KBr) ν 2923, 1645, 1599, 1511, 1425, 1316, 1297, 1151, 1072, 995 cm^{-1}; ^1H NMR (80 MHz) δ 1.59, 1.66, 1.78 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 1.90−2.40 (4H, m, 4″-2H and 5″-2H), 3.34 (2H, d, J = 6.5 Hz, 1″-2H), 3.41, 3.49, 3.51, 3.71 (3H each s, 4 OCH_3), 4.90−5.20 (8H, m, 3 OCH_2O, 2″-H and 6″-H), 6.41(1H, s, 5′-H), 6.77 (1H, s, H_β), 6.90−7.20 (2H, m, 3-H, 5-H), 7.40−7.70 (2H, m, 2-H, 6-H), 7.81 (1H, s, H_α); EIMS m/z [M^+] 554 (0.3), 509 (0.4), 495 (0.7), 431 (0.7), 399 (1), 387 (1), 341 (2), 313 (1), 269 (2), 223 (3), 191 (15), 161 (4), 69 (11), 45 (100); HRMS (EI) m/z calcd for $C_{32}H_{42}O_8$ 554.2864, found for [M^+] 554.2854.

4,4′,6′-Trihydroxy-2′-methoxy-3′-(1″-geranyl)chalcone (6). To a stirred solution of **5** (277 mg, 0.5 mmol) in MeOH (10 mL) was added dropwise 3 M HCl (2 mL). The solution was heated at reflux for 45 min, then H_2O (10 mL) was added, and the solution was extracted with EtOAc. The combined organic layers were washed with H_2O and brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography eluting with petoleum ether−EtOAc (10:1) to give chalcone **6** (131 mg, 62% yield) as a yellow gum: UV (CH_3OH) λ_{max} (log ϵ) 218 (4.13), 369 (3.96) nm; IR (KBr) ν 3368, 2930, 1623, 1604, 1547, 1512, 1442, 1352, 1228, 1170, 1075, 1031 cm^{-1}; ^1H NMR (400 MHz) δ 1.59, 1.67, 1.82 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 1.95−2.16 (4H, m, 4″-2H and 5″-2H), 3.39 (2H, d, J = 6.7 Hz, 1″-2H), 3.67 (3H, s, OCH_3), 5.05 (1H, br, 6″-H), 5.23 (1H, m, 2″-H), 6.04 (1H, s, 5′-H), 6.27 (1H, s, OH), 6.88 (2H, d, J = 8.5 Hz, 3-H, 5-H), 7.55 (2H, d, J = 8.5 Hz, 2-H, 6-H), 7.83 (2H, s, H_α, H_β), 12.01 (1H, s, OH), 13.36 (1H, s, OH); EIMS m/z [M^+] 422 (7), 391 (1), 353 (7), 299 (34), 285 (19), 233 (35), 219 (26), 179 (88), 165 (26), 69 (96), 41(100); HRMS (EI, negative SIMS, NBA) m/z calcd for $C_{26}H_{29}O_5$ 421.2005, found for [$M - H]^-$ 421.2028.

4′,7-Dihydroxy-5-methoxy-6-(1″-geranyl)flavanone (7). To a solution of **6** (55 mg, 0.13 mmol) in EtOH (1 mL) were added NaOAc (41 mg, 0.5 mmol) and H_2O (one drop). The mixture was heated at reflux for 24 h. After the mixture was cooled to ambient temperature, H_2O (5 mL) was added and the mixture was extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with H_2O and brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography eluting with petroleum ether−EtOAc (15:1) to give flavanone **7** (42 mg, 76% yield) as colorless needles (10% EtOAc in petroleum ether), mp 116−118 °C; UV (CH_3OH) λ_{max} (log ϵ) 229 (4.35), 282 (4.18) nm; IR (KBr) ν 3337, 2926, 1652, 1595, 1517, 1454, 1435, 1334, 1274, 1168, 1082 cm^{-1}; ^1H NMR (400 MHz) δ 1.59, 1.66, 1.80 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 1.97−2.13 (4H, m, 4″-2H and 5″-2H), 2.76 (1H, dd, J = 2.6, 16.8 Hz, $H_{3\beta}$), 3.01 (1H, dd, J = 13.2, 16.8 Hz, $H_{3\alpha}$), 3.39 (2H, d, J = 6.9 Hz, 1″-2H), 3.84 (3H, s, OCH_3), 5.04 (1H, t, J = 5.7 Hz, 6″-H), 5.20 (1H, t, J = 6.9 Hz, 2″-H), 5.31 (1H, dd, J = 2.6, 13.2 Hz, 2-H), 6.31 (1H, s, 8-H), 6.78 (1H, br, OH), 6.88 (2H, d, J = 8.3 Hz, 3′-H, 5′-H), 7.28 (2H, d, J = 8.3 Hz, 2′-H, 6′-H); EIMS m/z [M^+] 422 (9), 353 (10), 299 (46), 233 (35), 203 (14), 179 (100), 123 (17), 91 (30), 69 (94), 41 (91); EIHRMS (negative SIMS, NBA) m/z calcd for $C_{26}H_{29}O_5$ 421.2005, found for [$M - H]^-$ 421.2014.

4′,6′-Bis[(methoxy)methoxy]-2′-hydroxy-3′-(1″-geranyl-)chalcone (8a). Following the same procedure as the preparation of **5**, **4a** was condensed with benzaldehyde to afford chalcone **8a** in 81% yield as an oil: UV (CH_3OH) λ_{max} (log ϵ) 219 (4.23), 356 (4.34) nm; IR (KBr) ν 2920, 1694, 1616, 1583, 1448, 1420, 1317, 1282, 1230, 1156, 1069, 961 cm^{-1}; ^1H NMR (80 MHz) δ 1.61, 1.68, 1.82 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 1.90−2.30 (4H, br, 4″-2H and 5″-2H), 3.38 (2H, d, J = 7.0 Hz, 1″-2H), 3.52, 3.55 (3H each s, 2 OCH_3), 4.90−5.50 (6H, m, 2 OCH_2O, 2″-H and 6″-H), 6.43 (1H, s, 5′-H), 7.20−7.75 (5H, m, Ph), 7.86 (1H, s, H_β), 7.90 (1H, s, H_α), 13.83 (1H, s, OH); EIMS m/z [M^+] 480 (1), 435 (6), 403 (1), 347 (2), 325 (4), 273 (4), 131 (48), 69 (16), 45 (100).

4,4′,6′-Tris[(methoxy)methoxy]-2′-hydroxy-3′-(1″-geranyl)chalcone (8b). Following the same procedure as the preparation of **5**, **4a** was condensed with *p*-methoxymethoxybenzaldehyde to afford chalcone **8b** as a red oil in 76% yield: UV (CH_3OH) λ_{max} (log ϵ) 219 (4.56), 336 (4.57) nm; IR (KBr) ν 2925, 1643, 1599, 1511, 1447, 1421, 1379, 1314, 1237, 1153, 1072, 996 cm^{-1}; ^1H NMR (80 MHz) δ 1.59, 1.66, 1.78 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 1.90−2.30 (4H, m, 4″-2H and 5″-2H), 3.10−3.85 (11H, m, 1″-2H and 3 OCH_3), 4.90−5.40 (8H, m, 3 OCH_2O, 2″-H and 6″-H), 6.41 (1H, s, 5′-H), 6.70−7.90 (6H, m, H_α , H_β, 2-H, 3-H, 5-H, 6-H), 13.86 (1H, s, OH); EIMS m/z [M^+] 540 (0.4), 395 (3), 417 (2), 385 (4), 331 (3), 263 (2), 231 (3), 191 (18), 161 (5), 69 (11), 45 (100); HRMS (ESI) m/z calcd for $C_{31}H_{40}O_8Na$ 563.2605, found for [$M + Na]^+$ 563.2617.

2′,4′,6′-Trihydroxy-3′-(1″-geranyl)chalcone (9a). Following the same procedure as the preparation of **6**, **9a** was obtained as amorphous reddish solids (10% EtOAc in petroleum ether) in 88% yield: mp 122−124 °C; UV (CH_3OH) λ_{max} (log ϵ) 219 (4.24), 302 (4.05), 343 (4.12) nm; IR (KBr) ν 3306, 2917, 1626, 1499, 1451, 1345, 1288, 1232, 1138, 1080 cm^{-1}; ^1H NMR (80 MHz) δ 1.62, 1.69, 1.84 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 1.95−2.40 (4H, br, 4″-2H and 5″-2H), 3.41 (2H, d, J = 7.1 Hz, 1″-2H), 4.90−5.50 (2H, m, 2″-H, 6″-H), 5.98 (1H, s, 5′-H), 6.73 (1H, br, OH), 7.15−7.70 (5H, m, Ph), 7.88 (1H, s, H_β), 8.01 (1H, s, H_α), 9.46 (1H, br, OH), 11.79 (1H, br, OH); EIMS m/z [M^+] 392 (12), 349 (3), 323 (6), 307 (12), 269 (86), 219 (100), 165 (69), 69 (58), 41 (53).

4,2′,4′,6′-Tetrahydroxy-3′-(1″-geranyl) chalcone (9b). Following the same procedure as the preparation of **6**, **9b** was obtained as amorphous reddish solids (10% EtOAc in petroleum ether) in 72% yield: mp 70−71 °C; UV (CH_3OH) λ_{max} (log ϵ) 219 (4.22), 355 (4.25) nm; IR (KBr) ν 3275, 2923, 1700, 1623, 1604, 1514, 1440, 1344, 1230, 1169, 1082 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.51, 1.58, 1.68 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 1.70−2.05 (4H, m, 4″-2H and 5″-2H), 3.09 (2H, d, J = 7.1 Hz, 1″-2H), 5.02 (1H, t, J = 6.8 Hz, 6″-H), 5.12 (1H, t, J = 7.1 Hz, 2″-H), 6.04 (1H, s, 5′-H), 6.82 (2H, d, J = 8.4 Hz, 3-H, 5-H), 7.50 (2H, d, J = 8.4 Hz, 2-H, 6-H), 7.64 (1H, d, J = 15.6 Hz, H_β), 7.98 (1H, d, J = 15.6 Hz, H_α), 10.07 (1H, s, 4-OH),10.36 (1H, s, 4′-OH), 10.66 (1H, s, 6′-OH), 14.53 (1H, s, 2′-OH); EIMS m/z [M^+] 408 (19), 365 (3), 339 (6), 323 (11), 285 (89), 245 (6), 219 (100), 165 (92), 91 (28), 69 (67), 41 (68).

(±)-5,7-Dihydroxy-6-(1″-geranyl)flavanone (10). Following the same procedure as the preparation of **7**, **9a** was cyclized to afford **10** in 99% yield as amorphous solids (15% EtOAc in petroleum ether): mp 144−145 °C; UV (CH_3OH) λ_{max} (log ϵ) 227 (4.31), 293 (4.33), 334 (3.62) nm; IR (KBr) ν 3150, 2912, 1631, 1584, 1445, 1298, 1225, 1177, 1083 cm^{-1}; ^1H NMR (400 MHz) δ 1.61, 1.69, 1.82 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 2.00−2.17 (4H, m, 4″-2H and 5″-2H), 2.82 (1H, dd, J = 2.9, 17.1 Hz, $H_{3\beta}$), 3.09 (1H, dd, J = 13.0, 17.1 Hz, $H_{3\alpha}$), 3.38 (2H, d, J = 7.1 Hz, 1″-2H), 5.06 (1H, t, J = 5.8 Hz, 6″-H), 5.24 (1H, t, J = 7.1 Hz, 2″-H), 5.40 (1H, dd, J = 2.9, 13.0 Hz, 2-H), 6.04 (1H, s, 8-H), 6.74 (1H, s, 7-OH), 7.39−7.47 (5H, m, 2′, 3′, 4′, 5′, 6′-5H), 12.38 (1H, s, 5-OH); ^{13}C NMR ($CDCl_3$) 195.9 (C_4), 164.1 (C_7), 161.2 (C_5), 161.0 (C_9), 139.0 ($C_{3''}$), 138.5 ($C_{8''}$), 132.0 ($C_{1'}$), 128.8 ($C_{3',4',5'}$), 126.1 ($C_{2',6'}$), 123.7 ($C_{7''}$), 121.3 ($C_{2''}$), 107.1 (C_6), 102.9 (C_{10}), 95.6 (C_8), 78.9 (C_2), 43.4 (C_3), 39.7 ($C_{5''}$), 26.3 ($C_{6''}$), 25.6 ($C_{10''}$), 21.0 ($C_{1''}$), 17.7 ($C_{9''}$), 16.1 ($C_{4''}$); EIMS m/z [M^+] 392 (7), 307 (7), 269 (60), 219 (54), 165 (56), 123 (20), 121 (12), 84 (100), 69 (57), 41 (39).

5,7,4′-Tris[(methoxy)methoxy]-8-(1″-geranyl)flavanone (12). Following the same procedure as the preparation of **7**, **8b** was cyclized to afford **12** in 90% yield (based on recovered starting material), as amorphous yellowish solids (15% EtOAc in petroleum ether): mp 40−41 °C; UV (CH_3OH)

λ_{max} (log ϵ) 227 (4.30), 281 (4.10), 320 (3.56) nm; IR (KBr) ν 2914, 1682, 1599, 1515, 1445, 1336, 1270, 1233, 1154, 1073, 1000 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.57 (3H, s, 8″-CH_3), 1.64 (6H, s, 9″-CH_3 and 10″-CH_3), 1.90−2.07 (4H, m, 4″-2*H* and 5″-2*H*), 2.80 (1H, dd, J = 2.9, 16.5 Hz, $H_{3\beta}$), 2.99 (1H, dd, J = 12.8, 16.5 Hz, $H_{3\alpha}$), 3.32 (2H, d, J = 7.0 Hz, 1″-2*H*), 3.48, 3.50, 3.54 (3H each s, 3 OCH_3), 5.06 (1H, t, J = 7.0 Hz, 2″-*H*), 5.21, 5.24, 5.27 (2H, each s, 3 OCH_2O), 5.36 (1H, dd, J = 2.9, 12.8 Hz, 2-*H*), 6.58 (1H, s, 6-*H*), 7.08 (1H, d, J = 8.5 Hz, 3′-*H*, 5′-*H*), 7.38 (2H, d, J = 8.5 Hz, 2′-*H*, 6′-*H*); EIMS m/z [M$^+$] 540 (1), 495 (2), 417 (8), 395 (1), 385 (11), 373 (5), 331 (11), 307 (11), 209 (8), 191 (26), 165 (7), 69 (19), 45 (100); HRMS (EI) m/z calcd for $C_{31}H_{40}O_8$ 540.2707, found for [M$^+$] 540.2711.

(±)-Sophoraflavanone A (1). Following the same procedure as the preparation of **6**, **12** was deprotected to afford **1** as amorphous solids (20% EtOAc in petroleum ether) in 84% yield: mp 144−145 °C; UV (CH$_3$OH) λ_{max} (log ϵ) 226 (4.28), 294 (4.25), 337 (3.62) nm; IR (KBr) ν 3451, 3313, 2937, 1634, 1588, 1510, 1435, 1373, 1341, 1212, 1155, 1059 cm^{-1}; ^{1}H NMR (80 MHz) δ 1.60, 1.69, 1.72 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 1.90−2.40 (4H, m, 4″-2*H* and 5″-2*H*), 2.85−3.15 (2H, m, $H_{3\alpha}$ $H_{3\beta}$), 3.33 (2H, d, J = 7.3 Hz, 1″-2*H*), 4.85−5.50 (3H, t, 2-*H*, 6″-*H*, 2″-*H*), 6.05 (1H, s, 6-*H*), 6.89 (2H, d, J = 8.6 Hz, 3′-*H*, 5′-*H*), 7.34 (2H, d, J = 8.6, 2′-*H*, 6′-*H*), 12.00 (1H, s, 5-O*H*); ^{13}C NMR (CDCl$_3$) 196.5 (C$_4$), 164.0 (C$_7$), 162.2 (C$_5$), 159.7 (C$_{4'}$), 156.0 (C$_9$), 138.8 (C$_{3''}$), 132.0 (C$_{8''}$), 130.8 (C$_{1'}$), 127.7 (C$_{2',6'}$), 123.7 (C$_{7''}$), 121.4 (C$_{2''}$), 115.6 (C$_{3',5'}$), 106.2 (C$_6$), 103.1 (C$_{10}$), 97.0 (C$_8$), 78.7 (C$_2$), 43.1 (C$_3$), 39.7 (C$_{5''}$),26.3 (C$_{6''}$), 25.7 (C$_{10''}$), 21.7 (C$_{1''}$), 17.7 (C$_{9''}$), 16.1 (C$_{4''}$); EIMS m/z [M$^+$] 408 (9), 285 (96), 219 (100), 205 (13), 203 (11), 165 (84), 120 (23), 107 (13), 69 (64), 41 (62).

(±)-Bonannione A (2). To a well-stirred solution of **7** (21 mg, 0.05 mmol) in CH_2Cl_2 (3 mL) at −78 °C was added dropwise BBr_3 (4.7 μL, 13 mg, 0.05 mmol). The mixture was stirred at −78 °C for 1 h, then slowly warmed to ambient temperature and stirred for an additional 2 h. The reaction was quenched by the addition of H_2O (5 mL). The layers were separated, and the aqueous layer was extracted wih CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with H_2O and brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The resulting residue was purified by silica gel column chromatography eluting with petroleum ether−EtOAc (4:1) to give flavanone **2** (19 mg, 93% yield) as amorphous solids (20% EtOAc in petroleum ether): mp 119−120 °C; UV (CH$_3$OH) λ_{max} (log ϵ) 227 (4.44), 294 (4.32), 332 (3.65) nm; IR (KBr) ν 3387, 2923, 1638, 1598, 1517, 1492, 1451, 1340, 1309, 1221, 1152, 1087 cm^{-1}; ^{1}H NMR δ 1.60, 1.69, 1.82 (3H each s, 8″-CH_3, 9″-CH_3, and 10″-CH_3), 2.00−2.15 (4H, m, 4″-2*H* and 5″-2*H*), 2.79 (1H, dd, J = 2.9, 17.1 Hz, $H_{3\beta}$), 3.09 (1H, dd, J = 12.8, 17.1 Hz, $H_{3\alpha}$), 3.43 (2H, d, J = 7.1 Hz, 1″-2*H*), 5.06 (1H, t, J = 5.8 Hz, 6″-*H*), 5.27 (1H, t, J = 7.1 Hz, 2″-*H*), 5.34 (1H, dd, J = 2.9, 12.8 Hz, 2-*H*), 6.00 (1H, s, 8-*H*), 6.35 (1H, br, O*H*), 6.89 (2H, d, J = 8.4 Hz, 3′-*H*, 5′-*H*), 7.33 (2H, d, J = 8.4 Hz, 2′-*H*, 6′-*H*), 12.42 (1H, s, O*H*); ^{13}C NMR (CDCl$_3$) 196.2 (C$_4$), 164.1 (C$_7$), 161.2 (C$_5$), 161.1 (C$_{4'}$), 156.1 (C$_9$), 139.5 (C$_{3''}$), 132.1 (C$_{8''}$), 130.7 (C$_{1'}$), 127.9 (C$_{2',6'}$), 123.7 (C$_{7''}$), 121.3 (C$_{2''}$), 115.6 (C$_{3',5'}$), 106.8 (C$_6$), 102.9 (C$_{10}$), 95.7 (C$_8$), 78.8 (C$_2$), 43.2 (C$_3$), 39.7 (C$_{5''}$), 26.3 (C$_{6''}$), 25.7 (C$_{10''}$), 21.1 (C$_{1''}$), 17.7 (C$_{9''}$), 16.2 (C$_{4''}$); EIMS m/z [M$^+$] 408 (19), 285 (68), 219 (100), 203 (21), 165 (94), 121 (22), 107 (18), 69 (85), 41 (40).

Following a procedure similar to that for the preparation of **7**, **9b** was cyclized to afford (±)-**1** in 20% yield and (±)-**2** in 80% yield. The spectral data (MS, NMR, IR) of synthetic (±)-**1** and (±)-**2** were identical with those of the natural products, respectively.[17]

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