Supporting Information

Divergent Total Syntheses of Flavonoid Natural Products Isolated From Rosa rugosa and Citrus unshiu

Tze Jing Sum, Tze Han Sum, Warren R. J. D. Galloway, David R. Spring*

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, CB2 1EW, UK
spring@ch.cam.ac.uk

General experimental information

All non-aqueous reactions were performed under a constant stream of dry nitrogen using oven-dried glassware. Standard practices were employed when handling moisture and air-sensitive materials. All reagents and solvents were purchased from commercial sources and used without further purification unless otherwise stated. Room temperature refers to ambient temperature. Temperatures of 0 °C were maintained using an ice-water bath. Petroleum ether was distilled before use. Ethyl acetate (EtOAc) and methanol (MeOH) were distilled from calcium hydride. Melting points were measured using a Büchi B545 melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was performed on pre-coated Merck silica gel GF254 plates. Infrared (IR) spectra were recorded on a Perkin-Elmer Spectrum One (FT-IR) spectrophotometer with internal referencing. Absorption maxima ($\nu_{\text{max}}$) are reported in wavenumbers (cm$^{-1}$). Abbreviations used: br = broad; m = medium; s = strong; str = stretch; w = weak. Flash column chromatography was performed on silica gel (230-400 mesh). $^1$H NMR and $^{13}$C NMR were recorded on a Bruker Avance 500 MHz instrument in CDCl$_3$ or (CD$_3$)$_2$CO. Chemical shifts (δ) are quoted in ppm, to the nearest 0.01 ppm ($^1$H NMR) or 0.1 ppm ($^{13}$C NMR) and are referenced to the residual non-deuterated solvent peak. High resolution mass spectrometry (HRMS) measurements were recorded on a Micromass Q-TOF mass spectrometer or a Waters LCT Premier Time of Flight mass spectrometer. Mass...
values are quoted within the error limits of ± 5 ppm mass units. ESI+ refers to the mass ionisation technique.

**General procedure A: Synthesis of chalcones.**
To a stirred solution of KOH (12.0 equiv) in absolute ethanol (50 mL) cooled to 0 °C in an ice-bath was added dropwise a solution of the corresponding acetophenone (1.0 equiv) and aldehyde (1.0 equiv) in EtOH (20 mL). The reaction mixture was stirred at 0 °C for 1 h and then at 70 °C for 72 h under nitrogen. The resulting mixture was allowed to cool to room temperature and then poured into ice-water (100 mL) and acidified to pH 3-4 with 3 M HCl. The aqueous solution was extracted with CHCl₃ (3 × 100 mL) and the combined organic layer was washed with satd NaHCO₃ (2 × 100 mL), brine (2 × 100 mL), dried over anhydrous MgSO₄, filtered and the solvent removed under reduced pressure. The crude residue was purified by flash column chromatography over silica and recrystallized from MeOH to afford the pure corresponding chalcones.

**General procedure B: Synthesis of chalcones.**
To a stirred solution of KOH (12.0 equiv) in absolute ethanol (50 mL) cooled to 0 °C in an ice-bath was added dropwise a solution of the corresponding acetophenone (1.0 equiv) and aldehyde (1.0 equiv) in EtOH (20 mL). The reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 72 h under nitrogen. The resulting mixture was then poured into ice-water (100 mL) and acidified to pH 3-4 with 3 M HCl. The aqueous solution was extracted with CHCl₃ (3 × 100 mL) and the combined organic layer was washed with satd NaHCO₃ (2 × 100 mL), brine (2 × 100 mL), dried over anhydrous MgSO₄, filtered and the solvent removed under reduced pressure. The crude residue was purified by flash column chromatography over silica to afford the pure corresponding chalcones.

**General procedure C: Synthesis of aurones.**
To a stirred solution of the corresponding chalcone (1.0 equiv) in pyridine (10 mL) was added mercury(II) acetate (1.0 equiv). The reaction mixture was stirred at 110 °C for 1 h under a nitrogen atmosphere. The resulting mixture was then poured into ice-water (50 mL) and acidified to pH 3-4 with 3 M HCl. The aqueous solution was
extracted with CHCl₃ (3 × 50 mL) and the combined organic layer was washed with water (2 × 50 mL), brine (2 × 50 mL), dried over anhydrous MgSO₄, filtered and the solvent removed under reduced pressure. The crude residue was purified by flash column chromatography over silica to afford the corresponding aurones.

**General procedure D: Synthesis of hydroxyaurones.**
To a stirred solution of the corresponding aurone (1.0 equiv) in MeOH (10 mL) was added 3 M HCl and the reaction mixture was heated at 50 °C under a nitrogen atmosphere until TLC analysis indicated complete consumption of starting material. The resulting mixture was allowed to cool to room temperature and the solvent removed under reduced pressure. The crude residue was resuspended in EtOAC (50 mL), washed with H₂O (2 × 50 mL), brine (2 × 50 mL), dried over anhydrous MgSO₄, filtered and the solvent removed under reduced pressure. The crude residue was purified by recrystallization from MeOH to afford the corresponding hydroxyaurones.
**Experimental procedures**

1-(2-Hydroxy-4,5-dimethoxyphenyl)-3-(4-methoxymethoxyphenyl)propenone (14)

Prepared according to General Procedure A using 4-methoxymethoxybenzaldehyde (1.00 g, 6.02 mmol), 2-hydroxy-4,5-dimethoxyacetophenone (1.18 g, 6.01 mmol) and KOH (4.37 g, 77.8 mmol) in absolute EtOH (50 mL). The crude residue was purified by flash column chromatography (SiO$_2$, Petroleum Ether/EtOAc; 5:1) and recrystallized from MeOH to afford 14 (360 mg, 17%) as a bright red-brown powdery solid. Mp 110-112 °C. TLC $R_f$ = 0.38 (Petroleum Ether/EtOAc; 2:1). IR $\nu_{\max}$ (neat)/cm$^{-1}$: 2945w (C-H str), 2821w (C-H str), 1737m (C=O str), 1630s (C=C str), 1558s (C=C str), 1510s (C=C str), 1439m, 1395s, 1277m, 1234s, 1206s, 1177m, 1147s, 1080m, 1037w. $^1$H NMR (500 MHz, CDCl$_3$): δ 3.51 (3H, s, -OCH$_2$OC$_3$H$_3$), 3.93 (3H, s, -OCH$_3$), 3.95 (3H, s, -OCH$_3$), 5.24 (2H, s, -OCH$_2$O-), 6.52 (1H, s, ArH), 7.10 (2H, d, $J$ 8.5 Hz, ArH), 7.27 (1H, s, ArH, overlain by CDCl$_3$), 7.42 (1H, d, $J$ 15.5 Hz, -CH=CHCO-), 7.63 (2H, d, $J$ 8.5 Hz, ArH), 7.89 (1H, d, $J$ 15.0 Hz, -CH=CHCO-), 13.45 (1H, s, OH). $^{13}$C NMR (500 MHz, CDCl$_3$): δ 56.2, 56.9, 94.2, 100.8, 111.0, 112.0, 116.6, 118.4, 128.3, 130.3, 141.9, 144.2, 156.9, 159.4, 161.7, 191.5.

5,6-Dimethoxy-4’-methoxymethoxy-aurone (15)

Prepared according to General Procedure C using chalcone 14 (152 mg, 0.440 mmol) and Hg(OAc)$_2$ (148 mg, 0.464 mmol) in pyridine (10 mL). The crude residue was purified by flash column chromatography (SiO$_2$, Petroleum Ether/EtOAc; 5:1) to afford 15 (127 mg, 84%) as a bright yellow-orange powdery solid. Mp 182-184 °C. TLC $R_f$ = 0.43 (Petroleum Ether/EtOAc; 1:1). IR $\nu_{\max}$ (neat)/cm$^{-1}$: 2936w (C-H str), 2826w (C-H str), 1686m (C=O str), 1645m (C=C str), 1599s (C=C str), 1508w (C=C str), 1496s, 1477s, 1436m, 1342m, 1315m, 1277s, 1241s, 1217m, 1195m, 1181m, 1135s, 1111m, 1075m, 1036w. $^1$H NMR (500 MHz, CDCl$_3$): δ 3.50 (3H, s, -OCH$_2$OCH$_3$), 3.91 (3H, s, -OCH$_3$), 4.02 (3H, s, -OCH$_3$), 5.24 (2H, s, -OCH$_2$O-), 6.81 (1H, s, ArH), 6.82 (1H, s, ArH), 7.11 (2H, d, $J$ 8.5 Hz, ArH), 7.18 (1H, s, C=CH), 7.85 (2H, d, $J$ 9.0 Hz, ArH). $^{13}$C NMR (500 MHz, CDCl$_3$): δ 56.2, 56.4, 56.6, 94.2, 95.5, 104.0, 112.1, 113.2, 116.5,
126.2, 133.1, 146.5, 147.1, 157.4, 158.4, 163.2, 183.3. HRMS (ESI+) m/z = 343.1167 [M+H]+ found, C_{19}H_{15}O_{6}+ required 343.1176.

**5,6-Dimethoxy-4'-hydroxy-aurone – Rugaurone A (1)**

Prepared according to General Procedure D using aurone 15 (60 mg, 0.175 mmol) and 3 M HCl (2 mL) in MeOH (10 mL). The crude product was purified by recrystallization from MeOH to afford 1 (25.6 mg, 49%) as a bright orange powdery solid. Mp 286-288 °C. TLC R_f = 0.43 (Petroleum Ether/EtOAc; 1:2). IR ν_{max} (neat)/cm\(^{-1}\): 3219 m(br) (O-H str), 2959 w (C-H str), 2835 w (C-H str), 1678 m (C=O str), 1638 m (C=C str), 1594 s (C=C str), 1572 s (C=C str), 1514 m, 1486 s, 1381 m, 1346 s, 1281 s, 1238 m, 1223 m, 1189 m, 1169 m, 1143 s, 1117 m, 1098 m, 1030 w, 1003 s. \(^{1}\)H NMR (500 MHz, (CD\(_2\))\(_2\)CO): \(\delta\) 3.89 (3H, s, -OCH\(_3\)), 4.02 (3H, s, -OCH\(_3\)), 6.70 (1H, s, C=CH), 6.96 (2H, d, \(J\) 8.8 Hz, ArH), 7.09 (1H, s, ArH), 7.13 (1H, s, ArH), 7.87 (2H, d, \(J\) 8.4 Hz, ArH). \(^{13}\)C NMR (500 MHz, (CD\(_2\))\(_2\)CO): \(\delta\) 55.9, 56.3, 96.2, 104.1, 111.3, 113.0, 116.2, 124.4, 133.5, 146.8, 147.3, 158.2, 159.3, 163.2, 182.2. HRMS (ESI+) m/z = 299.0928 [M+H]+ found, C\(_{17}\)H\(_{15}\)O\(_{5}\)+ required 299.0919.

**1-(2-Hydroxy-4-methoxy-5-methoxymethoxyphenyl)-3-(4-methoxymethoxyphenyl)proponone (21)**

Prepared according to General Procedure A using 4-methoxymethoxybenzaldehyde (677 mg, 4.07 mmol), 2-hydroxy-4-methoxy-5-methoxymethoxyacetophenone (903 mg, 3.99 mmol) and KOH (3.17 g, 56.5 mmol) in absolute EtOH (50 mL). The crude product was purified by flash column chromatography (SiO\(_2\), Petroleum Ether/EtOAc; 5:1) and recrystallized from MeOH to afford 21 (497 mg, 33%) as a bright yellow fluffy solid. mp 154-156 °C. TLC R_f = 0.31 (Petroleum Ether/EtOAc; 2:1). IR ν_{max} (neat)/cm\(^{-1}\): 2938 w (C-H str), 2903 w (C-H str), 2829 w (C-H str), 1640 m (C=O str), 1585 s (C=C str), 1570 s (C=C str), 1507 s (C=C str), 1446 m, 1393 s, 1279 s, 1238 s, 1219 m, 1206 s, 1147 s, 1076 s, 1003 s. \(^{1}\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 3.51 (3H, s, -OCH\(_2\)OCH\(_3\)), 3.59 (3H, s, -OCH\(_2\)OCH\(_3\)), 3.94 (3H, s, -OCH\(_3\)), 5.20 (2H, s, -OCH\(_2\)O-), 5.24 (2H, s, -OCH\(_2\)O-), 6.52 (1H, s, ArH), 7.10 (2H, d, \(J\) 9.0 Hz, ArH), 7.41 (1H, d, \(J\) 15.5 Hz, -CH=CHCO-), 7.61-7.63 (3H, m, ArH), 7.88 (1H, d, \(J\) 15.5 Hz, -CH=CHCO-). \(^{13}\)C NMR (500 MHz, CDCl\(_3\)): \(\delta\) 56.2, 56.2, 56.4, 94.2, 96.8, 100.8, 112.4, 116.6,
117.2, 118.3, 128.5, 130.3, 139.0, 144.3, 157.6, 159.4, 162.3, 191.6. HRMS (ESI+) m/z = 395.1087 [M+Na]+ found, C_{20}H_{20}O_{7}Na+ required 395.1101.

1-(2-Hydroxy-4-methoxy-5-methoxymethoxyphenyl)-3-(4-methoxymethoxyphenyl)propenone (22)
Prepared according to General Procedure A using 4-methoxybenzaldehyde (0.42 mL, 3.45 mmol), 2-hydroxy-4-methoxy-5-methoxymethoxyacetophenone (770 mg, 3.40 mmol) and KOH (2.92 g, 56.5 mmol) in absolute EtOH (50 mL). The crude product was purified by flash column chromatography (SiO₂, Petroleum Ether/EtOAc; 5:1) and recrystallized from MeOH to afford 22 (267 mg, 23%) as a bright yellow-orange powdery solid. Mp 178-180 °C. TLC Rₐ = 0.28 (Petroleum Ether/EtOAc; 2:1). IR ν_{max} (neat)/cm⁻¹: 2957w (C-H str), 2903w (C-H str), 2835w (C-H str), 1637m (C=O str), 1607m (C=C str), 1568s (C=C str), 1446m, 1426m, 1391m, 1368m, (neat)/cm⁻¹: 2957w (C-H str), 2903w (C-H str), 2835w (C-H str), 1637m (C=O str), 1607m (C=C str), 1568s (C=C str), 1446m, 1426m, 1391m, 1368m, 1279s, 1241s, 1211s, 1178s, 1148s, 1078s, 1031m, 1003m. ¹H NMR (500 MHz, CDCl₃): δ 3.59 (3H, s, -OCH₂OCH₃), 3.88 (3H, s, -OCH₃), 3.94 (3H, s, -OCH₃), 5.20 (2H, s, -OCH₂O-), 6.52 (1H, s, ArH), 6.97 (2H, d, J 8.5 Hz, ArH), 7.40 (1H, d, J 15.0 Hz, -CH=CHCO-), 7.62-7.64 (3H, m, ArH), 7.88 (1H, d, J 15.0 Hz, -CH=CHCO-), 13.47 (1H, s, OH). ¹³C NMR (500 MHz, CDCl₃): δ 55.4, 56.1, 56.4, 96.8, 100.8, 112.4, 114.5, 117.1, 117.8, 127.5, 130.4, 139.0, 144.5, 157.5, 161.8, 162.3, 191.7. HRMS (ESI+) m/z = 345.1328 [M+H]+ found, C₁₉H₂₁O₆+ required 345.1333.

5-methoxy-6-methoxymethoxy-4'-methoxymethoxy-aureone (23)
Prepared according to General Procedure C using chalcone 21 (95.0 mg, 0.254 mmol), Hg(OAC)₂ (97.1 mg, 0.291 mmol) in pyridine (10 mL). The crude residue was purified by flash column chromatography (SiO₂, Petroleum Ether/EtOAc; 3:1) to afford 23 (74.0 mg, 78%) as a bright yellow powdery solid. Mp 160-162 °C. TLC Rₐ = 0.43 (Petroleum Ether/EtOAc; 1:1). IR ν_{max} (neat)/cm⁻¹: 2904w (C-H str), 2831w (C-H str), 1687s (C=0 str), 1650m (C=C str), 1602s (C=C str), 1513w (C=C str), 1497m, 1474m, 1457m, 1340m, 1277s, 1195m, 1161s, 1135s, 1100m, 1075s, 1015w. ¹H NMR (500 MHz, CDCl₃): δ 3.51 (3H, s, -OCH₂OCH₃), 3.54 (3H, s, -OCH₂OCH₃), 4.02 (3H, s, -OCH₃), 5.22 (2H, s, -OCH₂O-), 5.24 (2H, s, -OCH₂O-), 6.82 (1H, s, ArH), 6.83 (1H, s, ArH), 7.11 (2H, d, J 9.0 Hz, ArH), 7.52 (1H, s, C=CH), 7.86 (2H, d, J 9.0 Hz, ArH). ¹³C NMR (500 MHz, CDCl₃): δ 56.2, 56.3, 56.6, 94.2, 95.7, 96.0, 110.6, 112.0, 113.5,
5-methoxy-6-methoxymethoxy-4′-methoxy-aurone (24)

Prepared according to General Procedure C using chalcone 22 (202 mg, 0.586 mmol), Hg(OAc)$_2$ (192 mg, 0.601 mmol) in pyridine (10 mL). The crude residue was purified by flash column chromatography (SiO$_2$, Petroleum Ether/EtOAC; 3:1) to afford 24 (140 mg, 70%) as a bright yellow-orange powdery solid. Mp 150-152 °C. TLC $R_f =$ 0.38 (PE/EtOAc; 1:1). IR $\nu_{max}$ (neat)/cm$^{-1}$: 2991w (C-H str), 2904w (C-H str), 2840w (C-H str), 1685m (C=O str), 1647m (C=C str), 1598s (C=C str), 1512w (C=C str), 1497m, 1475m, 1456s, 1444m, 1340s, 1316m, 1277s, 1255s, 1196m, 1133s, 1100m, 1071s, 1019m. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.53 (3H, s, -OCH$_2$OC$_3$H$_3$), 3.87 (3H, s, -OCH$_3$), 4.01 (3H, s, -OCH$_3$), 5.21 (2H, s, -OCH$_2$O-), 6.81 (1H, s, ArH), 6.82 (1H, s, ArH), 6.96 (2H, d, J 11.5 Hz, ArH), 7.51 (1H, s, C=CH), 7.85 (2H, d, J 11.0 Hz, ArH). $^{13}$C NMR (500 MHz, CDCl$_3$): $\delta$ 55.3, 56.3, 56.5, 95.7, 96.0, 110.5, 112.2, 113.5, 114.4, 125.1, 133.1, 143.6, 146.8, 158.1, 160.8, 163.6, 183.2. HRMS (ESI$^+$) m/z = 343.1165 [M+H]$^+$ found, C$_{19}$H$_{19}$O$_7$$^+$ required 343.1176.

5-Methoxy-6-hydroxy-4′-hydroxy-aurone – Rugaurone B (2)

Prepared according to General Procedure D using aurone 23 (60 mg, 0.161 mmol) and 3 M HCl (2 mL) in MeOH (10 mL). The crude product was purified by recrystallization from CHCl$_3$ to afford 2 (42.7 mg, 93%) as a bright orange powdery solid. Mp 298-300 °C. TLC $R_f =$ 0.29 (Petroleum Ether/EtOAc; 1:2). IR $\nu_{max}$ (neat)/cm$^{-1}$: 3489w(br) (O-H str), 3137 (O-H str), 2823w (C-H str), 1673m (C=O str), 1591m (C=C str), 1572s (C=C str), 1514m (C=C str), 1492s, 1479s, 1344s, 1314s, 1280s, 1254s, 1168s, 1131s, 1097s, 1011m. $^1$H NMR (500 MHz, (CD$_3$)$_2$CO): $\delta$ 4.06 (3H, s, -OCH$_3$), 6.68 (1H, s, C=CH), 6.96 (2H, d, J 8.8 Hz, ArH), 7.06 (1H, s, ArH), 7.09 (1H, s, ArH), 7.87 (2H, d, J 8.8 Hz, ArH), 7.95 (1H, br s, OH), 8.96 (1H, br s, OH). $^{13}$C NMR (500 MHz, (CD$_3$)$_2$CO): $\delta$ 56.4, 96.0, 107.1, 111.1, 113.7, 116.2, 124.5, 133.5, 144.1, 146.7, 156.3, 159.3, 162.3, 182.5. HRMS (ESI$^+$) m/z = 285.0745 [M+H]$^+$ found, C$_{16}$H$_{13}$O$_5$$^+$ required 285.0758.
5-Methoxy-6-hydroxy-4’-methoxy-aurone – Rugaurone C (3)

Prepared according to General Procedure D using aurone 24 (100 mg, 0.292 mmol) and 3 M HCl (2 mL) in MeOH (10 mL). The crude product was purified by recrystallization from MeOH to afford 3 (43.3 mg, 50%) as a bright orange powdery solid. Mp 278-280 °C. TLC \( R_f = 0.40 \) (Petroleum Ether/EtOAc; 1:2). IR \( \nu_{\text{max}} \) (neat)/cm\(^{-1} \): 3175s(br) (O-H str), 2992w (C-H str), 2843w (C-H str), 1676m (C=O str), 1646m (C=C str), 1607m (C=C str), 1585s (C=C str), 1511s (C=C str), 1474s, 1448m, 1342s, 1284s, 1260m, 1196s, 1099s, 1017s. \(^1\)H NMR (500 MHz, (CD\(_3\))\(_2\)CO): \( \delta \) 3.88 (3H, s, -OCH\(_3\)), 4.06 (3H, s, -OCH\(_3\)), 6.70 (1H, s, C=CH), 7.05 (2H, d, \( J = 9.0 \) Hz, ArH), 7.07 (1H, s, ArH), 7.09 (1H, s, ArH), 7.94 (2H, d, \( J = 8.5 \) Hz, ArH), 8.00 (1H, br, OH). \(^13\)C NMR (500 MHz, (CD\(_3\))\(_2\)CO): \( \delta \) 55.1, 56.4, 96.0, 107.1, 110.7, 113.6, 114.7, 125.5, 133.2, 144.2, 147.0, 156.4, 161.2, 162.4, 182.5. HRMS (ESI\(^+\)) \( m/z = 299.0912 \) [M+H\(^+\)]\(^+\) found, \( C_{17}H_{15}O_5^+ \) required 299.0919.

1-(2-Hydroxy-3,4,5-trimethoxyphenyl)-3-(2,5-dimethoxyphenyl)propenone (29)

Prepared according to General Procedure B using 2-hydroxy-3,4,5-trimethoxyacetophenone (2.15 g, 9.50 mmol), 2,5-dimethoxybenzaldehyde (1.57 g, 9.45 mmol) and KOH (6.60 g, 118 mmol) in absolute EtOH (50 mL). The crude product was purified by flash column chromatography (SiO\(_2\), Petroleum Ether/EtOAc; 5:1) to afford 29 (2.07 g, 59%) as a bright orange powdery solid. Mp 148-150 °C. TLC \( R_f = 0.24 \) (Petroleum Ether/EtOAc; 2:1). IR \( \nu_{\text{max}} \) (neat)/cm\(^{-1} \): 2999w (C-H str), 2935w (C-H str), 2839w (C-H str), 1737w, 1634s (C=O str), 1562s (C=C str), 1503s (C=C str), 1494s, 1447m, 1410m, 1355s, 1286s, 1263m, 1234m, 1207m, 1160m, 1114s, 1044s, 1021m. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 3.84 (3H, s, -OCH\(_3\)), 3.90 (6H, s, -OCH\(_3\)), 3.96 (3H, s, -OCH\(_3\)), 4.07 (3H, s, -OCH\(_3\)), 6.90 (1H, d, \( J = 8.8 \) Hz, ArH), 6.97 (1H, dd, \( J = 3.2, 9.2 \) Hz, ArH), 7.13 (1H, s, ArH), 7.17 (1H, d, \( J = 2.8 \) Hz, ArH), 7.61 (1H, d, \( J = 15.6 \) Hz, ArH), 8.17 (1H, d, \( J = 15.6 \) Hz, ArH), 13.15 (1H, s, OH). \(^13\)C NMR (500 MHz, CDCl\(_3\)): \( \delta \) 55.9, 56.1, 56.9, 61.1, 61.3, 107.0, 112.4, 114.5, 114.7, 117.1, 121.3, 124.3, 140.5, 141.5, 144.9, 149.9, 153.5, 154.5, 193.0. HRMS (ESI\(^+\)) \( m/z = 375.1425 \) [M+H\(^+\)]\(^+\) found, \( C_{20}H_{23}O_7^+ \) required 375.1438.
3-Hydroxy-6,7,8,2',5'-pentamethoxyflavone (30)
To a stirred solution of the chalcone 29 (302 mg, 0.807 mmol) in MeOH (10 mL) were added 16% NaOH (aq) (1.60 mL) and 15% H$_2$O$_2$ (0.80 mL). The reaction mixture was stirred at room temperature for 24 h under a nitrogen atmosphere. The resulting mixture was then poured into ice-water (50 mL) and acidified to pH 3-4 with 3 M HCl. The aqueous solution was extracted with CHCl$_3$ (3 × 50 ml) and the combined organic layer was washed with satd NaHCO$_3$ (2 × 50 mL), brine (2 × 50 mL), dried over anhydrous MgSO$_4$, filtered, and the solvent removed under reduced pressure. The crude residue was purified by flash column chromatography (SiO$_2$, 1% MeOH/CH$_2$Cl$_2$) to afford 30 (172 mg, 55%) as a pale yellow-white powdery solid. Mp 202-204 °C. TLC $R_f = 0.29$ (1% MeOH/CH$_2$Cl$_2$). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 3309m (br) (O-H str), 2941w (C-H str), 2835w (C-H str), 1737w, 1606s (C=O str), 1571s (C=C str), 1498s, 1470s, 1426s, 1384m, 1293s, 1275s, 1208s, 1185s, 1164s, 1106s, 1081s, 1059m, 1044s, 1016s. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.83 (3H, s, -OCH$_3$), 3.85 (3H, s, -OCH$_3$), 3.98 (3H, s, -OCH$_3$), 4.03 (3H, s, -OCH$_3$), 4.05 (3H, s, -OCH$_3$), 6.52 (1H, br s, OH), 7.00-7.06 (2H, m, ArH), 7.18 (1H, d, $J$ 2.8 Hz, ArH), 7.39 (1H, s, ArH). $^{13}$C NMR (500 MHz, CDCl$_3$): $\delta$ 55.9, 56.3, 56.6, 61.5, 61.9, 99.1, 113.4, 116.1, 117.2, 117.3, 120.3, 138.2, 141.9, 145.1, 146.0, 147.3, 150.9, 151.6, 153.4, 172.5. HRMS (ESI$^+$) $m/z$ = 389.1220 [M+H]$^+$ found, C$_{20}$H$_{21}$O$_8$+ required 389.1231.

3,6,7,8,2',5'-Hexamethoxyflavone (4)
To a stirred solution of flavone 30 (104 mg, 0.266 mmol) in dry acetone (10 mL) were added anhydrous K$_2$CO$_3$ (134mg, 0.970 mmol) and methyl iodide (0.057 mL, 0.927 mmol). The reaction mixture was heated at reflux with stirring for 3 h under a nitrogen atmosphere. The resulting mixture was allowed to cool to room temperature, filtered under suction, washed with additional acetone (3 × 10 mL) and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography (SiO$_2$, 1% MeOH/CH$_2$Cl$_2$) to afford 4 (100 mg, 94%) as a pale yellow-white powdery solid. Mp 183-185 °C. $R_f = 0.33$ (1% MeOH/CH$_2$Cl$_2$). IR $\nu_{\text{max}}$ (neat)/cm$^{-1}$: 2922m (C-H str), 2853w (C-H str), 1736w, 1635s (C=O str), 1620m, 1569w (C=C str), 1497s, 1466s, 1418s, 1382m, 1289m, 1269m, 1205s, 1164s, 1111m, 1091m, 1042s, 1012s. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 3.80 (3H, s, -OCH$_3$), 3.80 (3H, s, -OCH$_3$), 3.82 (3H, s, -OCH$_3$), 3.96 (3H, s, -OCH$_3$), 3.98 (3H, s, -OCH$_3$), 4.01 (3H,
s, -OCH₃), 6.96-6.98 (1H, ArH), 7.01-7.03 (2H, ArH), 7.42 (1H, ArH). ¹³C NMR (500 MHz, CDCl₃): δ 55.8, 56.2, 60.4, 61.4, 61.9, 99.6, 112.7, 116.2, 117.0, 120.5, 120.7, 141.3, 141.8, 145.5, 147.0, 150.8, 151.6, 153.2, 155.2, 174.1. HRMS (ESI⁺) m/z = 403.1377 [M+H]+ found, C₂₁H₂₃O₈⁺ required 403.1387.