Electronic Supporting Information

Bi(OTf)$_3$-catalysed prenylation of electron-rich aryl ethers and phenols with isoprene: a direct route to prenylated derivatives

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General

Chemicals, solvents and reagents used are commercially available and were used without further purification. PE refers to petroleum ether, bp 40-60 °C. Anhydrous solvents were used where indicated. Glassware for dry reactions was dried either by heating in an oven at 120 °C for at least 1 h, or heating with a hot air gun for 5 min. The glassware was then allowed to cool under a stream of N₂.

TLCs were carried out on Merck Aluminium backed TLC plates Silica Gel 60 F254 and viewed using UV light of wavelength 254 nm and then stained with potassium permanganate. Merck Silica Gel (0.040-0.063 mm) was used for column chromatography. Compounds were loaded as an oil, CH₂Cl₂ solution or dry loaded by adsorption onto silica.

Melting points were obtained using a Reichert-Jung heated-stage microscope. Infrared spectra were recorded on a Perkin-Elmer Spectrum RXI FT-IR system and all values are recorded in cm⁻¹.

NMR spectra were obtained on Varian Mercury VX (400 MHz) or Bruker Avance III (400 MHz) spectrometers. The chemical shifts are recorded in parts per million (ppm) with reference to tetramethylsilane. The coupling constants J are quoted to the nearest 0.5 Hz and are not corrected. The multiplicities are assigned as a singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet of doublets (td) and multiplet (m). Mass spectra and high resolution mass spectra were obtained on a microTOF™ from Bruker Daltonics (Bremen, Germany) coupled with an electrospray source (ESI-TOF) using an autosampler in an Agilent 1100 LC system. Data was processed using external calibration with the Bruker Daltonics software, DataAnalysis™ as part of the overall hardware control software, Compass 1.1™.

Methyl 3,4,5-trimethoxybenzoate 9, methyl E-3-(3,4,5-trimethoxyphenyl)propenoate 11, methyl 3-(3,4,5-trimethoxyphenyl)propanoate 13, methyl E-3-(3,4-dimethoxyphenyl)-propenoate 15 and methyl 4-hydroxybenzoate 23 were all synthesised from their corresponding carboxylic acids following the procedure reported by Parrain¹ and gave samples that were consistent with the spectroscopic data reported for 9,² 11,¹ 13,³ 15⁴ and 23.⁵
Methyl 3-(3,4-dimethoxyphenyl)propanoate (17)

10% Palladium on carbon (50 mg, 0.05 mmol) was added to a vigorously stirred solution of methyl 3,4-dimethoxycinnamate (819 mg, 3.69 mmol) in EtOH (20 mL). After 3 cycles of purging the flask with N₂ then a vacuum, the flask was put under an atmosphere of H₂. After 2 h, the mixture was filtered through Celite®, washing thoroughly with EtOH, then the solvent removed under reduced pressure to afford the methyl propionate 17 (821 mg, 99%) as a colourless oil without need for further purification.

**¹H NMR** δ (400 MHz, CDCl₃) 6.84 (1H, d, J 8.5 Hz, C5-ArH), 6.77 (1H, dd, J 8.5 and 2.0 Hz, C6-ArH), 6.76 (1H, d, J 2.0 Hz, C2-ArH), 3.90 (3H, s, ArOMe), 3.88 (3H, s, ArOMe), 3.70 (3H, s, CO₂Me), 2.93 (2H, t, J 7.5 Hz, ArCH₂) and 2.64 (2H, t, J 7.5 Hz, CH₂CO₂Me); **¹³C NMR** δ (100 MHz, CDCl₃) 173.4, 149.0, 147.6, 133.2, 120.1, 111.8, 111.4, 56.0, 55.9, 51.6, 36.0 and 30.6.

Consistent with the spectroscopic data previously reported.⁶

**General procedure: Formation of prenylated and chroman compounds**

Bi(OTf)₃ (136 mg, 0.2 mmol) was added to a vigorously stirred solution of the arene (2 mmol) and isoprene (400 µl, 4 mmol) in anhydrous toluene (10 mL) in a thick-walled pressure tube at room temperature under Ar. The tube was sealed and the reaction heated at 40 °C for between 75 min and 24 h and the crude reaction mixture (often dark purple/black in colour) was applied directly to a silica gel chromatography column to afford the purified product(s). Representative reactions have also been performed in a conventional round-bottomed flask with a tightly fitted stopper to afford similar results.
1,2,3-Trimethoxy-4-(3-methylbut-2-en-1-yl)benzene (6a) and 2,3,4-trimethoxy-1,5-bis(3-methylbut-2-en-1-yl)benzene (6b)

Following the general procedure, 1,2,3-trimethoxybenzene 5 (336 mg, 2 mmol) gave, after 75 min and subsequent column chromatography [silica, PE-Et₂O gradient from 100:0 to 90:10], the mono-product 6a (292 mg, 62%) and the bis-product 6b (122 mg, 20%) as colourless oils.

Mono-product (6a)

IR ν_max (thin film) 2936, 1599, 1464, 1294, 1256, 1096 and 1017; ^1H NMR δ_H (400 MHz, CDCl₃) 6.86 (1H, d, J 8.5 Hz, ArH), 6.64 (1H, d, J 8.5 Hz, ArH), 5.28 (1H, triplet of septets, J 7.5 and 1.5 Hz, CH=CMe₂), 3.91 (3H, s, OMe), 3.90 (3H, s, OMe), 3.87 (3H, s, OMe), 3.31 (2H, d, J 7.5 Hz, ArCH₂), 1.77 (3H, br s, CH=CMe₆Me₆) and 1.77 (3H, br s, CH=CMe₆Me₆); ^13C NMR δ_C (100 MHz, CDCl₃) 152.0, 151.8, 132.0, 127.9, 123.5, 123.3, 107.4, 60.7, 56.0, 28.2, 25.7 and 17.7. Consistent with the spectroscopic data previously reported.²

Bis-product (6b)

IR ν_max (thin film) 2965, 2931, 1479, 1460, 1411, 1325, 1235, 1092, 1065 and 1015; ^1H NMR δ_H (400 MHz, CDCl₃) 6.67 (1H, s, ArH), 5.25 (2H, triplet of septets, J 7.0 and 1.5 Hz, CH=CMe₂), 3.91 (3H, s, OMe), 3.83 (6H, s, OMe), 3.27 (4H, d, J 7.0 Hz, ArCH₂) and 1.74 (12H, d, J 1.5 Hz, CH=CMe₆); ^13C NMR δ_C (100 MHz, CDCl₃) 149.8, 146.3, 132.0, 130.3, 124.2, 123.3, 60.8, 60.6, 28.4, 25.7 and 17.8; MS (+ESI) m/z 305 (MH⁺, 9%); HRMS (+ESI) Found MH⁺, 305.2103; C₁₀H₂₀O₃ requires MH⁺ 305.2117.
1-Bromo-3,4,5-trimethoxy-2-(3-methylbut-2-en-1-yl)benzene (8)

Following the general procedure, the aryl bromide 7 (494 mg, 2 mmol) gave, after 7 h and subsequent column chromatography [silica, PE-Et₂O gradient from 100:0 to 95:5], the product 8 (275 mg, 44%) as a colourless oil in addition to recovered starting material 7 (246 mg, 50%).

**Rf** [PE-Et₂O 70:30] 0.63; **IR** νₘₐₓ (thin film) 2935, 1590, 1482, 1452, 1430, 1396, 1313, 1270, 1237, 1195, 1156, 1113, 1045 and 1019; **¹H NMR** δₜ (400 MHz, CDCl₃) 6.87 (1H, s, ArH), 5.12 (1H, triplet of septets, J 7.0 and 1.5 Hz, CH=CMₑ₂), 3.84, (6H, s, OMe), 3.82 (3H, s, OMe), 3.42, (2H, d, J 7.0 Hz, ArCH₂), 1.79 (3H, br s, CH=CMₑ₂Me₈) and 1.68 (3H, d, J 1.0 Hz, CH=CMₑ₂Me₈); **¹³C NMR** δₜ (100 MHz, CDCl₃) 152.6, 152.1, 142.0, 131.8, 128.1, 122.1, 117.9, 112.0, 61.1, 60.7, 56.2, 29.3, 25.7 and 18.1; **MS (+ESI) m/z** 315 (MH⁺, 97%), 317 (MH⁺, 100) and 337 (MNa⁺, 23); **HRMS (+ESI)** Found MNa⁺, 337.0400; C₁₄H₁₉BrNaO₃ requires MNa⁺ 337.0415.

Methyl 3,4,5-trimethoxy-2-(3-methylbut-2-en-1-yl)benzoate (10)

Following the general procedure, ester 9 (452 mg, 2 mmol) gave, after 5 h and subsequent column chromatography [silica, PE-Et₂O gradient from 100:0 to 95:5], the product 10 (87 mg, 15%) as a colourless oil in addition to ester 9 (384 mg, 85%).

**IR** νₘₐₓ (thin film) 2939, 1723 (C=O), 1594, 1491, 1455, 1431, 1401, 1337, 1222, 1154, 1115 and 1055; **¹H NMR** δₜ (400 MHz, CDCl₃) 7.17 (1H, s, ArH), 5.12 (1H, triplet of septets, J 6.5 and 1.5 Hz, CH=CMₑ₂), 3.91 (3H, s, OMe), 3.86 (3H, s, OMe), 3.86 (3H, s, OMe), 3.82 (3H, s, OMe), 3.62 (2H, d, J 6.5 Hz, ArCH₂), 1.75 (3H, d, J 0.5 Hz, CH=CMₑ₂Me₈) and 1.66 (3H, d, J 1.0 Hz, CH=CMₑ₂Me₈); **¹³C NMR** δₜ (100 MHz, CDCl₃) 168.0, 152.3, 151.0, 145.7, 131.1, 130.7, 125.2, 123.8, 109.7, 61.0, 60.7, 56.1, 52.0, 25.9, 25.7 and 17.9; **MS (+ESI) m/z** 295 (MH⁺, 29%) and 317 (MNa⁺, 12); **HRMS (+ESI)** Found MH⁺, 295.1551; C₁₆H₂₃O₄ requires MH⁺ 295.1546.
Methyl E-3-(3,4,5-trimethoxy-2-(3-methylbut-2-en-1-yl)phenyl)propenoate (12)

Following the general procedure, ester 11 (504 mg, 2 mmol) gave, after 4 h and subsequent column chromatography [silica, PE-Et₂O gradient from 100:0 to 90:10], the mono-product 12 (302 mg, 47%) as a colourless oil in addition to ester 11 (90 mg, 18%).

**IR** $\nu_{\text{max}}$ (thin film) 2937, 1719 (C=O), 1631, 1592, 1566, 1487, 1409, 1347, 1289, 1254, 1168, 1124; **$^1$H NMR** $\delta_H$ (400 MHz, CDCl₃) 7.92 (1H, d, $J$ 15.5 Hz, $CH=CH$CO₂Me), 6.87 (1H, s, ArH), 6.26 (1H, d, $J$ 15.5 Hz, CH=CHCO₂Me), 5.02 (1H, t, $J$ 6.5 Hz, CH=CH₂), 3.89 (3H, s, OMe), 3.86 (3H, s, OMe), 3.83 (3H, s, OMe), 3.79 (3H, s, OMe), 3.42 (2H, d, $J$ 6.5 Hz, ArCH₂), 1.81 (3H, s, CH=CMe₃Me₃) and 1.67 (3H, s, CH=CMe₃Me₃); **$^{13}$C NMR** $\delta_C$ (100 MHz, CDCl₃) 167.4, 151.9, 151.7, 144.2, 142.6, 131.6, 129.0, 128.6, 123.1, 118.0, 105.3, 61.0, 60.8, 55.9, 51.6, 25.7, 25.0 and 17.9; **MS** (+ESI) $m/z$ 343 (MNa⁺, 11%); **HRMS** (+ESI) Found MNa⁺, 343.1508; C₁₈H₂₄NaO₅ requires MNa⁺ 343.1521.
Methyl 3-(3,4,5-trimethoxy-2-(3-methylbut-2-en-1-yl)phenyl)propanoate (14a) and methyl 3-(3,4,5-trimethoxy-2,6-bis(3-methylbut-2-en-1-yl)phenyl)propanoate (14b)

Following the general procedure, ester 13 (508 mg, 2 mmol) gave, after 90 min and subsequent column chromatography [silica, PE-Et₂O gradient from 100:0 to 80:20], the mono-product 14a (376 mg, 58%) and the bis-product 14b (233 mg, 30%) as colourless oils.

Mono-product (14a)

\[ R_f\] [PE-Et₂O 80:20] 0.27; \textbf{IR} \( \nu_{\text{max}} \) (thin film) 2935, 1739 (C=O), 1599, 1578, 1494, 1453, 1406, 1338, 1283, 1239, 1196, 1121, 1073 and 1042; \textbf{¹H NMR} \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 6.53 (1H, s, ArH), 5.08-5.04 (1H, m, CH=CMe₂), 3.87 (3H, s, OMe), 3.86 (3H, s, OMe), 3.84 (3H, s, OMe), 3.71 (3H, s, OMe), 3.33 (2H, d, J 6.5 Hz, ArCH₂CH=CMe₂), 2.93-2.89 (2H, m, ArCH₂CH₂CO₂Me) 2.60-2.56 (2H, m, CH₂CO₂Me), 1.79 (3H, br s, CH=CMe₃Me₃) and 1.71 (3H, d, J 1.0 Hz, CH=CMe₃Me₃); \textbf{¹³C NMR} \( \delta_{\text{C}} \) (100 MHz, CDCl₃) 173.4, 152.1, 151.5, 140.9, 134.2, 131.1, 126.2, 123.8, 108.4, 60.9, 60.7, 56.0, 51.6, 35.5, 28.3, 25.6, 25.2 and 17.8; \textbf{MS} (+ESI) \( m/z \) 345 (MNa⁺, 24%); \textbf{HRMS} (+ESI) Found MNa⁺, 345.1661; C₁₈H₂₆NaO₅ requires MNa⁺ 345.1678.

Bis-product (14b)

\[ R_f\] [PE-Et₂O 80:20] 0.51; \textbf{IR} \( \nu_{\text{max}} \) (thin film) 2948, 2933, 1740 (C=O), 1463, 1416, 1334, 1195, 1170, 1096, 1048 and 982; \textbf{¹H NMR} \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 5.10-5.06 (2H, m, CH=CMe₃Me₃), 3.91 (3H, s, OMe), 3.85 (6H, s, OMe), 3.72 (3H, s, OMe), 3.36 (4H, d, J 6.5 Hz, ArCH₂CH=CH₂), 2.93-2.89 (2H, m, ArCH₂CH₂CO₂Me), 2.50-2.46 (2H, m, CH₂CO₂Me), 1.79 (6H, d, J 1.0 Hz, CH=CMe₃Me₃) and 1.71 (6H, d, J 1.0 Hz, CH=CMe₃Me₃); \textbf{¹³C NMR} \( \delta_{\text{C}} \) (100 MHz, CDCl₃) 173.4, 150.3, 144.8, 133.0, 131.1, 129.5, 124.0, 60.8, 60.4, 51.5, 34.9, 25.7, 25.6, 24.8 and 17.8; \textbf{MS} (+ESI) \( m/z \) 391 (MH⁺, 20%); \textbf{HRMS} (+ESI) Found MH⁺, 391.2652; C₂₂H₃₅O₅ requires MH⁺ 391.2485.
Methyl E-3-(4,5-dimethoxy-2-(3-methylbut-2-en-1-yl)phenyl)propenoate (16)

Following the general procedure, ester 15 (446 mg, 2 mmol) gave, after 6 h and subsequent column chromatography [silica, PE-Et2O gradient from 100:0 to 90:10], the mono-product 16 (100 mg, 17%) as a colourless oil.

**IR** $\nu_{\text{max}}$ (thin film) 2934, 1715 (C=O), 1602, 1514, 1458, 1268, 1167 and 1102; $^1$H NMR $\delta_H$ (400 MHz, CDCl$_3$) 7.95 (1H, d, $J=16.0$ Hz, $CH=CHCO_2$Me), 7.05 (1H, s, ArH), 6.68 (1H, s, ArH), 6.24 (1H, d, $J=16.0$ Hz, CH=CHCO$_2$Me), 5.16 (1H, triplet of septets, $J=7.0$ and 1.5 Hz, $CH=CMe_2$), 3.87 (3H, s, OMe), 3.78 (3H, s, OMe), 3.40 (2H, d, $J=7.0$ Hz, ArCH$_2$), 1.76 (3H, br s, CH=CMe$_2$Me$_A$) and 1.71 (3H, d, $J=1.0$ Hz, CH=CMe$_A$Me$_B$); $^{13}$C NMR $\delta_C$ (100 MHz, CDCl$_3$) 167.7, 151.0, 147.6, 142.1, 135.5, 132.6, 125.0, 122.9, 116.3, 112.6, 109.0, 56.0, 55.9, 51.5, 31.8, 25.7 and 17.9; MS (+ESI) $m/z$ 313 (M$^{\text{Na}^+}$, 9%); HRMS (+ESI) Found M$^{\text{Na}^+}$, 313.1424; C$_{17}$H$_{22}$NaO$_4$ requires M$^{\text{Na}^+}$ 313.1416.

Methyl 3-(4,5-dimethoxy-2-(3-methylbut-2-en-1-yl)phenyl)propanoate (18)

Following the general procedure, ester 17 (448 mg, 2 mmol) gave, after 6 h and subsequent column chromatography [silica, PE-Et$_2$O gradient from 100:0 to 90:10], the mono-product 18 (376 mg, 64%) as a colourless oil.

**IR** $\nu_{\text{max}}$ (thin film) 2934, 1737 (C=O), 1516, 1458, 1361, 1271, 1209 and 1093; $^1$H NMR $\delta_H$ (400 MHz, CDCl$_3$) 6.69 (1H, s, ArH), 6.69 (1H, s, ArH), 5.21 (1H, triplet of septets, $J=7.0$ and 1.5 Hz, CH=CMe$_2$), 3.85 (3H, s, OMe), 3.85 (3H, s, OMe), 3.69 (3H, s, OMe), 3.29 (2H, d, $J=7.0$ Hz, ArCH$_2$CH=CM$_2$), 2.92-2.88 (2H, m, ArCH$_2$CH$_2$CO$_2$Me), 2.59-2.55 (2H, m, CH$_3$CO$_2$Me), 1.75 (3H, br s, CH=CMe$_A$Me$_B$) and 1.74 (3H, br s, CH=CMe$_A$Me$_B$); $^{13}$C NMR $\delta_C$ (100 MHz, CDCl$_3$) 173.4, 147.5, 147.2, 132.1, 131.7, 130.4, 123.4, 113.0, 112.7, 56.0, 55.9, 51.5, 35.5, 31.3, 27.8, 25.7 and 17.9; MS (+ESI) $m/z$ 293 (MH$^+$, 15%) and 315 (M$^{\text{Na}^+}$, 27); HRMS (+ESI) Found MH$^+$, 293.1723; C$_{17}$H$_{22}$O$_4$ requires MH$^+$ 293.1753.
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1-(2,2-Dimethylchroman-6-yl)ethanone (20)

Following the general procedure, phenol 19 (272 mg, 2 mmol) gave, after 18 h and subsequent column chromatography [silica, PE-Et₂O-EtOAc gradient from 100:0 to 85:15:0 then 50:0:50], the chroman 20 (235 mg, 58%) as a white solid in addition to phenol 19 (62 mg, 23%).

**Rf** [PE-Et₂O 70:30] 0.63; **Mp** 89-93 °C (from CH₂Cl₂); **IR** ν<sub>max</sub> (thin film) 2976, 1670 (C=O), 1537, 1498, 1419, 1358, 1289, 1265, 1156 and 1117; **¹H NMR** δ<sub>H</sub> (400 MHz, CDCl₃) 7.75 (1H, d, J 2.5 Hz, C5-ArH), 7.73 (1H, dd, J 8.5 and 2.5 Hz, C7-ArH), 6.81 (1H, d, J 8.5 Hz, C8-ArH), 2.83 (2H, t, J 6.5 Hz, C4-CH₂), 2.54 (3H, s, COMe), 1.84 (2H, t, J 6.5 Hz, C3-CH₂) and 1.37 (6H, s, CMe₂); **¹³C NMR** δ<sub>C</sub> (100 MHz, CDCl₃) 196.9, 158.6, 130.5, 129.4, 128.3, 120.7, 117.2, 75.5, 32.5, 26.9, 26.2 and 22.4.

Consistent with the spectroscopic data previously reported. ⁸

2,2-Dimethylchroman-6-carboxylic acid (22)

Following the general procedure, phenol 21 (276 mg, 2 mmol) gave, after 24 h and subsequent column chromatography [silica, PE-EtOAc gradient from 100:0 to 40:60], the chroman 22 (14 mg, 3%) as a white solid in addition to phenol 21 (254 mg, 92%).

**IR** ν<sub>max</sub> (thin film) 2975, 1681 (C=O), 1608, 1578, 1443, 1411, 1324, 1296, 1265, 1156 and 1120; **¹H NMR** δ<sub>H</sub> (400 MHz, CDCl₃) 7.86 (1H, d, J 2.0 Hz, C5-ArH), 7.84 (1H, dd, J 8.5 and 2.0 Hz, C7-ArH), 6.82 (1H, d, J 8.5 Hz, C8-ArH), 2.84 (2H, t, J 7.0 Hz, C4-CH₂), 1.84 (2H, t, J 7.0 Hz, C3-CH₂) and 1.36 (6H, s, CMe₂); **¹³C NMR** δ<sub>C</sub> (100 MHz, CDCl₃) 172.1, 159.1, 132.4, 129.9, 120.8, 120.7, 117.4, 75.6, 32.5, 26.9 and 22.3; **MS** (+ESI) m/z 207 (MH<sup>+</sup>, 100%) and 229 (MNa<sup>+</sup>, 45); **HRMS** (+ESI) Found MH<sup>+</sup>, 207.1033; C₁₂H₁₅O₃ requires MH<sup>+</sup> 207.1021.

Consistent with the spectroscopic data previously reported. ⁹
Methyl 2,2-dimethylchroman-6-carboxylate (24)

Following the general procedure, phenol 23 (304 mg, 2 mmol) gave, after 5 h and subsequent column chromatography [silica, PE-Et$_2$O gradient from 100:0 to 85:15] the chroman 24 (285 mg, 65%) as a white solid in addition to phenol 23 (32 mg, 11%).

R$_f$ [PE-Et$_2$O 70:30] 0.61; IR $\nu_{\text{max}}$ (thin film) 2975, 2948, 1716 (C=O), 1613, 1581, 1493, 1437, 1290, 1263, 1155 and 1118; $^1$H NMR $\delta$H (400 MHz, CDCl$_3$) 7.78 (1H, d, $J$ 2.0 Hz, C$_5$-ArH), 7.76 (1H, dd, $J$ 8.5 and 2.0 Hz, C$_7$-ArH), 6.77 (1H, d, $J$ 8.5 Hz, C$_8$-ArH), 3.86 (3H, s, OMe), 2.80 (2H, t, $J$ 7.0 Hz, C$_4$-CH$_2$), 1.82 (2H, t, $J$ 7.0 Hz, C$_3$-CH$_2$) and 1.34 (6H, s, CMe$_2$); $^{13}$C NMR $\delta$C (100 MHz, CDCl$_3$) 167.1, 158.3, 131.6, 129.1, 121.5, 120.6, 117.2, 75.3, 51.7, 32.6, 26.9 and 22.3.

Consistent with the spectroscopic data previously reported.$^{10}$
1-(7-Hydroxy-2,2-dimethylchroman-6-yl)ethanone (26), 1-(5-hydroxy-2,2-dimethylchroman-8-yl)ethanone (27) and 1-(2,2,8,8-tetramethyl-2,3,4,8,9,10-hexahydropyrano[2,3-f]chromen-6-yl)ethanone (28)

Following general procedure, phenol 25 (304 mg, 2 mmol) gave, after 8 h and subsequent column chromatography [silica, PE-EtOAc gradient from 100:0 to 70:30], the chroman products 26 (105 mg, 24%) as a white solid, 27 (46 mg, 10%) as a white solid and 28 (77 mg, 13%) as a colourless oil.

Chroman (26)

\[ \text{Mp} \text{ 115-118 °C (from EtOAc); } \text{IR } \nu_{\text{max}} \text{ (thin film) 2937, 2957, 1867, 1647 (C=O), 1612, 1495, 1369, 1288, 1280, 1161, 1118, 1058 1020 and 885;} \]

\[ ^{\text{1H NMR}} \delta_{\text{H}} \text{ } (400 \text{ MHz, CDCl}_3) \text{ 12.30 (1H, s, OH), 7.41 (1H, s, C5-ArH), 6.28 (1H, s, C8-ArH), 2.71 (2H, t, } J = 7.0 \text{ Hz, C4-CH}_2, \text{ 2.70 (3H, s, COMe), 1.80 (2H, t, } J = 7.0 \text{ Hz, C3-CH}_2 \text{ and 1.33 (6H, s, CMe}_2) ;} \]

\[ ^{\text{13C NMR}} \delta_{\text{C}} \text{ (100 MHz, CDCl}_3) \text{ 202.3, 162.8, 161.4, 132.2, 113.9, 112.7, 104.6, 75.9, 32.7, 26.4, 26.1 and 21.7.} \]

Consistent with the spectroscopic data previously reported. 11,12

Chroman (27)

\[ \text{Mp} \text{ 165-170 °C (from EtOAc); IR } \nu_{\text{max}} \text{ (thin film) 3172, 2974, 2921, 1638 (C=O), 1583, 1433, 1362, 1277, 1217, 1157, 1119 and 1051;} \]

\[ ^{\text{1H NMR}} \delta_{\text{H}} \text{ (400 MHz, CDCl}_3) \text{ 7.68 (1H, d, } J = 8.5 \text{ Hz, C7-ArH), 7.20 (1H, broad s, OH), 6.47 (1H, d, } J = 8.5 \text{ Hz, C6-ArH), 2.74 (2H, t, } J = 7.0 \text{ Hz, C4-CH}_2, \text{ 2.64 (3H, s, COMe), 1.87 (2H, t, } J = 7.0 \text{ Hz, C3-CH}_2 \text{ and 1.43 (6H, s, CMe}_2) ;} \]

\[ ^{\text{13C NMR}} \delta_{\text{C}} \text{ (100 MHz, CDCl}_3) \text{ 199.7, 159.2, 156.4, 129.9, 120.3, 108.5, 107.0, 75.3, 32.2, 31.6, 26.9 and 17.0.} \]

Chroman (28)

\[ \text{IR } \nu_{\text{max}} \text{ (thin film) 2974, 2933, 1662 (C=O), 1603, 1579, 1457, 1357, 1298, 1258, 1178, 1154, 1120 and 1096;} \]

\[ ^{\text{1H NMR}} \delta_{\text{H}} \text{ (400 MHz, CDCl}_3) \text{ 7.48 (1H, s, C5-ArH), 2.70 (2H, t, } J = 7.0 \text{ Hz, C4-CH}_2, \text{ 2.60 (2H, t, } J = 7.0 \text{ Hz, C10-CH}_2, \text{ 2.56 (3H, s, COMe), 1.76 (2H, t, } J = 7.0 \text{ Hz, C9-CH}_2, \text{ 1.76 (2H, t, } J = 7.0 \text{ Hz, C3-CH}_2, \text{ 1.35 (6H, s, C8-CMe}_2 \text{ and 1.32 (6H, s, C2-CMe}_2) ;} \]

\[ ^{\text{13C NMR}} \delta_{\text{C}} \text{ (100 MHz, CDCl}_3) \text{ 198.6, 156.2, 153.8, 129.2, 120.0, 111.9, 109.4, 75.3, 74.7, 32.8, 32.3, 31.8, 27.1, 26.8, 21.7 and 17.2.} \]

Consistent with the spectroscopic data previously reported. 12
Following the general procedure, phenol 30 (368 mg, 2 mmol) gave, after 18 h and subsequent column chromatography [silica, PE-Et₂O gradient from 100:0 to 85:15 then PE-EtOAc gradient from 50:50 to 30:70], the chroman product 32 (279 mg, 55%) as a colourless oil and the dienone 33 (132 mg, 26%) as a white solid.

**Chroman (32)**

\[
R_f [\text{PE-Et}_2\text{O 80:20}] \ 0.52; \ \text{IR} \ \nu_{\text{max}} \ (\text{thin film}) \ 2973, 2937, 1611, 1489, 1460, 1413, 1324, 1203, 1158, 1131, 1098, 1045 \text{ and } 1013; \ \text{¹H NMR} \ \delta_H (400 MHz, \text{CDCl}_3) \ 6.15 \ (1\text{H}, \text{s}, \text{C}8-\text{ArH}), \ 3.87 \ (3\text{H}, \text{s}, \text{C}6-\text{OMe}), \ 3.79 \ (3\text{H}, \text{s}, \text{C}5-\text{OMe}), \ 3.78 \ (3\text{H}, \text{s}, \text{C}7-\text{OMe}), \ 2.63 \ (2\text{H}, \text{t}, J \ 7.0 \text{ Hz}, \text{C}4-\text{CH}_2), \ 1.73 \ (2\text{H}, \text{t}, J \ 7.0 \text{ Hz}, \text{C}3-\text{CH}_2), \ 1.30 \ (3\text{H}, \text{s}, \text{C}2-\text{CMe}_\text{A}\text{Me}_\text{B}) \text{ and } 1.28 \ (3\text{H}, \text{s}, \text{C}2-\text{CMe}_\text{A}\text{Me}_\text{B}); \ \text{¹³C NMR} \ \delta_C (100 MHz, \text{CDCl}_3) \ 152.4, \ 151.4, \ 150.0, \ 135.4, \ 106.7, \ 96.6, \ 74.0, \ 61.0, \ 60.5, \ 55.8, \ 32.4, \ 26.7, \ 26.7 \text{ and } 17.0. \ \text{Consistent with the spectroscopic data previously reported}^{13}
\]

**Dienone (33)**

\[
R_f [\text{PE-EtOAc 40:60}] \ 0.50; \ \text{Mp} \ 106-109 \text{ °C (from CH}_2\text{Cl}_2); \ \text{IR} \ \nu_{\text{max}} \ (\text{thin film}) \ 2934, \ 2852, \ 1659 \ (\text{C}=\text{O}), \ 1625, \ 1597, \ 1459, \ 1374, \ 1240, \ 1215, \ 1163, \ 1078 \text{ and } 888; \ \text{¹H NMR} \ \delta_H (400 MHz, \text{CDCl}_3) \ 5.56 \ (2\text{H}, \text{s}, \text{C}2/\text{C}6-\text{CH}), \ 4.66 \ (1\text{H}, \text{triplet of septets}, J \ 7.5 \text{ and } 1.5 \text{ Hz}, \text{CH}=\text{CMe}_2), \ 3.73 \ (6\text{H}, \text{s}, \text{C}3/\text{C}5-\text{OMe}), \ 3.08 \ (3\text{H}, \text{s}, \text{C}4-\text{OMe}), \ 2.67 \ (2\text{H}, \text{d}, J \ 7.5 \text{ Hz}, \text{CH}_2\text{CH}=\text{CMe}_2), \ 1.56 \ (3\text{H}, \text{br s}, \text{CH}=\text{CMe}_\text{A}\text{Me}_\text{B}) \text{ and } 1.52 \ (3\text{H}, \text{br s}, \text{CH}=\text{CMe}_\text{A}\text{Me}_\text{B}); \ \text{¹³C NMR} \ \delta_C (100 MHz, \text{CDCl}_3) \ 187.3, \ 169.4, \ 136.3, \ 115.7, \ 104.3, \ 79.4, \ 56.0, \ 52.5, \ 35.6, \ 25.7 \text{ and } 17.6; \ \text{MS} \ (+\text{ESI}) \ m/z \ 253 \text{ (MH}^+)\); \ \text{HRMS} \ (+\text{ESI}) \text{ Found MH}^+, \ 253.1427; \ \text{C}_{14}\text{H}_{21}\text{O}_4 \text{ requires MH}^+ \ 253.1440.
3,4,5-Trimethoxy-2-(3-methylbut-2-en-1-yl)-phenyl acetate (35a) and 3,4,5-trimethoxy-2,6-bis(3-methylbut-2-en-1-yl)phenyl acetate (35b)

Incorporating the procedure reported by Mohammadpoor-Baltork,\textsuperscript{14} Ac\textsubscript{2}O (283 \textmu l, 3 mmol) was added to a rapidly stirred suspension of Bi(OTf\textsubscript{3}) (136 mg, 0.2 mmol) and phenol 30 (368 mg, 2 mmol) in anhydrous toluene (10 mL) in a thick-walled pressure tube at room temperature under Ar. After 5 min, isoprene (400 \textmu l, 4 mmol) was added to the solution and the tube was sealed and the reaction heated at 40 °C for 1 h. Column chromatography [silica, PE-Et\textsubscript{2}O gradient from 100:0 to 90:10] gave the mono-prenylated product 35a (414 mg, 70\%) and the bis-prenylated product 35b (108 mg, 15\%) as colourless oils.

**Mono-product (35a)**

R\textsubscript{f}[PE-Et\textsubscript{2}O 80:20] 0.37; \textbf{IR} v\textsubscript{max} (thin film) 2937, 1767 (C=O), 1658, 1490, 1456, 1408, 1368, 1339, 1206, 1122, 1075 and 1042; \textbf{\textsuperscript{1}H NMR} \textit{\delta} (400 MHz, CDCl\textsubscript{3}) 6.38 (1H, s, C6-ArH), 5.06 (1H, triplet of septets, J\textsubscript{7.0} and 1.5 Hz, CH=CH\textsubscript{2}Me), 3.85 (3H, s, OMe), 3.84 (3H, s, OMe), 3.80 (3H, s, OMe), 3.17 (2H, d, J 7.0 Hz, ArCH\textsubscript{2}), 2.27 (3H, s, Ac), 1.73 (3H, br s, CH=CMe\textsubscript{2}Me\textsubscript{2}) and 1.66 (3H, d, J 1.0 Hz, CH=CMe\textsubscript{2}Me\textsubscript{2}); \textbf{\textsuperscript{13}C NMR} \textit{\delta} (100 MHz, CDCl\textsubscript{3}) 169.5, 152.3, 151.7, 144.5, 140.5, 131.3, 122.7, 102.4, 61.0, 60.8, 56.0, 25.6, 23.5, 20.8 and 17.7; \textbf{MS} (+ESI) m/z 295 (MH\textsuperscript{+}, 24\%), 317 (MNa\textsuperscript{+}, 20\%); \textbf{HRMS} (+ESI) Found MH\textsuperscript{+}, 295.1533; C\textsubscript{16}H\textsubscript{23}O\textsubscript{5} requires MH\textsuperscript{+} 295.1546.

**Bis-product (35b)**

R\textsubscript{f}[PE-Et\textsubscript{2}O 80:20] 0.61; \textbf{IR} v\textsubscript{max} (thin film) 2935, 1765 (C=O), 1600, 1463, 1416, 1367, 1346, 1204, 1097., 1048 and 982; \textbf{\textsuperscript{1}H NMR} \textit{\delta} (400 MHz, CDCl\textsubscript{3}) 5.08 (2H, triplet of septets, J\textsubscript{7.0} and 1.5 Hz, CH=CH\textsubscript{2}Me), 3.87 (3H, s, C4-OMe), 3.82 (6H, s, C3/5-OMe), 3.16 (4H, broad s, ArCH\textsubscript{2}), 2.52 (3H, s, Ac), 1.73 (6H, d, J 1.0 Hz, CH=CMe\textsubscript{2}Me\textsubscript{2}) and 1.73 (6H, d, J 1.0 Hz, CH=CMe\textsubscript{2}Me\textsubscript{2}); \textbf{\textsuperscript{13}C NMR} \textit{\delta} (100 MHz, CDCl\textsubscript{3}) 169.3, 150.3, 144.8, 143.2, 131.3, 123.7, 122.7, 61.0, 60.6, 25.6, 24.1, 20.6 and 17.8; \textbf{MS} (+ESI) m/z 363 (MH\textsuperscript{+}, 5\%) and 385 (MNa\textsuperscript{+}, 14\%); \textbf{HRMS} (+ESI) Found MNa\textsuperscript{+}, 385.1975 C\textsubscript{21}H\textsubscript{30}NaO\textsubscript{5} requires MNa\textsuperscript{+} 385.1991.
General Procedure: Deacetylation of aromatic acetates

**Method A:** Following a procedure reported by Bates *et al.* but at a different concentration, K$_2$CO$_3$ (2 equiv.) was added to a solution of the acetate (1 equiv.) in MeOH (5 mL/mmol) at room temperature and the reaction was stirred for 2 h. The suspension was quenched with saturated aqueous NH$_4$Cl (30 mL) and extracted with EtOAc (3 × 15 mL). The combined organic fractions were washed with saturated brine (15 mL), dried over anhydrous Na$_2$SO$_4$, filtered and the solvent removed under reduced pressure. Column chromatography [silica, PE-EtOAc gradient from 100:1 to 75:25] afforded the phenol product.

**Method B:** Following a procedure reported by Narender *et al.*, NaOAc (10 equiv.) was added to a solution of the acetate (1 equiv.) in EtOH/H$_2$O (10:1, 5.5 mL/mmol) and the reaction heated at reflux for 5 h. After cooling, the reaction was diluted with H$_2$O (15 mL) and extracted with EtOAc (3 × 15 mL). The organic fractions were combined, washed with saturated brine (15 mL), dried over anhydrous Na$_2$SO$_4$, filtered and the solvent removed under reduced pressure. Column chromatography [silica, PE-EtOAc gradient from 100:1 to 75:25] afforded the phenol product.
3,4,5-Trimethoxy-2-(3-methylbut-2-en-1-yl)phenol (31a)

Following Method A, acetate 35a (411 mg, 1.4 mmol) gave the phenol 31a (173 mg, 49%) as a yellow amorphous solid. Following Method B, acetate 35a (132 mg, 0.45 mmol) gave the phenol 31a (41 mg, 36%) as a yellow amorphous solid, in addition to acetate 35a (53 mg, 40%).

$\text{Rf}_{\text{PE-EtOAc 75:25}}$ 0.25; $\text{IR}$ $\nu_{\text{max}}$ (thin film) 3392, 2963, 1935, 1607, 1505, 1463, 1415, 1357, 1237, 1197, 1164, 1126, 1082, 1040 and 993; $^1\text{H NMR}$ $\delta_H$ (400 MHz, CDCl$_3$) 6.20 (1H, s, C6-ArH), 5.70 (1H, s, OH), 5.19 (1H, triplet of septets, $J$ 7.0 and 1.5 Hz, $CH=CMe_2$), 3.83 (3H, s, OMe), 3.79 (3H, s, OMe), 3.72 (3H, s, OMe), 3.31 (2H, d, $J$ 7.0 Hz, ArCH$_2$), 1.78 (3H, d, $J$ 1.0 Hz, CH=CMe$_{\alpha}$Me$_{\beta}$) and 1.70 (3H, d, $J$ 1.0 Hz, CH=CMe$_{\alpha}$Me$_{\beta}$); $^{13}\text{C NMR}$ $\delta_C$ (100 MHz, CDCl$_3$) 151.9, 151.9, 150.9, 136.1, 133.6, 122.6, 113.0, 96.6, 61.2, 61.0, 55.9, 25.7, 22.8 and 17.8; $\text{MS}$ (+ESI) $m/z$ 253 (MH$^+$ 100%) and 275 (MNa$^+$, 92); $\text{HRMS}$ (+ESI) Found MNa$^+$, 275.1272 C$_{14}$H$_{20}$NaO$_4$ requires MNa$^+$ 275.1259.

Consistent with the spectroscopic data previously reported.$^{17}$

3,4,5-Trimethoxy-2,6-bis(3-methylbut-2-en-1-yl)phenol (31b)

Following Method A, acetate 35b (100 mg, 0.27 mmol) gave the phenol 31b (28 mg, 32%) as a colourless oil.

$\text{IR}$ $\nu_{\text{max}}$ (thin film) 3461, 2964, 2933, 1605, 1462, 1418, 1357, 1256, 1171, 1097, 1051 and 987; $^1\text{H NMR}$ $\delta_H$ (400 MHz, CDCl$_3$) 5.59 (1H, s, OH), 5.21 (2H, triplet of septets, $J$ 7.0 and 1.5 Hz, $CH=CMe_2$), 3.85 (3H, s, C4-OMe), 3.84 (6H, s, C3/5-OMe), 3.34 (4H, d, $J$ 7.0 Hz, ArCH$_2$), 1.80 (6H, d, $J$ 1.0 Hz, CH=CMe$_{\alpha}$Me$_{\beta}$) and 1.72 (6H, d, $J$ 1.0 Hz, CH=CMe$_{\alpha}$Me$_{\beta}$); $^{13}\text{C NMR}$ $\delta_C$ (100 MHz, CDCl$_3$) 150.1, 149.2, 140.3, 134.9, 133.6, 122.6, 116.8, 61.1, 60.9, 25.8, 23.1 and 17.8; $\text{MS}$ (+ESI) $m/z$ 321 (MH$^+$, 50%); $\text{HRMS}$ (+ESI) Found MH$^+$, 321.2066; C$_{19}$H$_{29}$O$_4$ requires MH$^+$ 321.2066.
S16

3,4,5-Trimethoxy-2-(3-methylbut-2-en-1-yl)phenol (31a) and 1-(6-hydroxy-2,3,4-trimethoxyphenyl)ethanone (36)

Incorporating the procedure reported by Mohammadpoor-Baltork,\textsuperscript{14} Ac$_2$O (283 µl, 3 mmol) was added to a rapidly stirred suspension of Bi(OTf)$_3$ (136 mg, 0.2 mmol) and phenol 30 (368 mg, 2 mmol) in anhydrous toluene (10 mL) in a thick-walled pressure tube at room temperature under Ar. After 5 min, isoprene (400 µl, 4 mmol) was added to the solution and the tube was sealed and the reaction heated at 40 °C for 4 h. The solvent was removed and following the procedure reported by Bates \textit{et al.},\textsuperscript{15} the residue was dissolved in MeOH (10 mL) and K$_2$CO$_3$ (552 mg, 4 mmol) was added. The reaction was stirred for 50 min at room temperature and then quenched with saturated aqueous NH$_4$Cl (30 mL) and extracted with CH$_2$Cl$_2$ (3 × 30 mL). The combined organic fractions were washed with saturated brine (30 mL), dried over anhydrous Na$_2$SO$_4$, filtered and the solvent removed under reduced pressure. Column chromatography [silica, PE-EtOAc gradient from 100:0 to 70:30] gave the mono-prenylated product 31a (223 mg, 44%), consistent with the spectroscopic data reported, in addition to the acetophenone product 36 (39 mg, 9%) as colourless oils.

\textbf{Acetophenone product (36)}

$^1$H NMR $\delta$ (400 MHz, CDCl$_3$) 13.39 (1H, s, OH), 6.22 (1H, s, C5-ArH), 3.97 (3H, s, OMe), 3.87 (3H, s, OMe), 3.76 (3H, s, OMe) and 2.63 (3H, s, COMe); $^{13}$C NMR $\delta$ (100 MHz, CDCl$_3$) 203.3, 161.9, 160.1, 155.2, 134.8, 108.5, 96.1, 61.0, 60.9, 56.0 and 31.8. Consistent with the spectroscopic data previously reported.$^{18}$
References


![Chemical Structure](image)

![NMR Spectrum](image)

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**NMR**

**Model:**
- F1

**F1**
- 12.00 ppm

**PLINE:**
- 1.00 pH

**SPOW:**
- 400.0012 MHz

**SFL:**
- 400.00018 MHz

**LW:**
- 0.20 Hz

**PB:**
- 0.20 Hz

**PC:**
- 1.00