Supporting Online Material for
Catalytic asymmetric conjugate addition of Grignard reagents to chromones
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General Methods:

Column chromatography was performed on silica gel (Silica-P flash silica gel from Silicycle, size 40-63 μm). TLC was performed on silica gel 60/Kieselguhr F254. Components were visualized by UV and staining with a solution of a mixture of KMnO₄ (10 g) and K₂CO₃ (10 g) in H₂O (500 mL). Mass spectra were recorded on a AEI-MS-902 mass spectrometer (EI+) or a LTQ Orbitrap XL (ESI+). ¹H- and ¹³C-NMR were recorded on a Varian AMX400 (400 and 101 MHz, respectively) using CDCl₃ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl₃: d 7.26 for ¹H, d 77.0 for ¹³C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q =quartet, p =pentet, br = broad, m = multiplet), coupling constants (Hz), and integration. Optical rotations were measured in CHCl₃ on a Schmidt + Haensch polarimeter (Polartronic MH8) with a 10 cm cell (c given in g/100 mL). Conversion of the reaction was determined by GC (GC, HP6890: MS HP5973) with an HP5 column (Agilent Technologies, Palo Alto, CA). Enantiomeric excess values were determined by HPLC analysis using a Shimadzu LC-10ADVP HPLC equipped with a Shimadzu SPD-M10AVP diode array detector. All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. All solvents were reagent grade and were dried and distilled prior to use, if necessary. Tetrahydrofuran (THF), tert-butyl methyl ether (t-BuOMe) and diethylether (Et₂O) were distilled over Na/benzophenone. Toluene and dichloromethane (CH₂Cl₂) were distilled over calcium hydride. All the ligands, copper salts and chromanones were purchased from Aldrich, ABCR and Acros and used as received. Grignard reagents RMgBr (R = Et, n-pentyl, n-hexyl, i-Bu, 3-pentyl, dodecyl, cyclopentyl) were purchased from Aldrich. Phenethylmagnesium bromide and but-3-en-1-ylmagnesium bromide were prepared from the corresponding alkyl bromides and magnesium turnings in Et₂O following standard procedures. Grignard reagents were titrated using sec-BuOH and catalytic amounts of 1,10-phenanthroline.
General procedure for the synthesis of the racemic product of the copper catalyzed 1,4-addition of Grignard reagents to chromones

CuBr·SMe$_2$ (0.01 mmol, 2.02 mg) and PPh$_3$ (0.012 mmol, 6.3 mg) were dissolved in dry DCM (2.0 mL) and the mixture was stirred at room temperature for 10 min. The mixture was cooled to -80 °C and subsequently the corresponding Grignard reagent solution (1.25 equiv.) were added dropwise. The reaction mixture was stirred at -80 °C for another 10 min. Then a solution of chromonone (0.2 mmol) in DCM (1.0 mL) was added dropwise. The reaction mixture was stirred until TLC ($n$-pentane:EtOAc 9:1) showed full conversion and quenched with saturated aqueous NH$_4$Cl solution (2 mL). The mixture was separated and the water layer was extracted with DCM (3x5 mL). The combined organic layers were dried over MgSO$_4$, filtered and the solvent was evaporated under vacuo. Purification by flash chromatography over silica gel, using $n$-pentane:Et$_2$O 9:1 afforded the desired compounds. (The reaction in some cases shown 1,2 and 1,4 addition products)

General procedure for the asymmetric 1,4-addition of Grignard reagents to chromones:

CuBr·SMe$_2$ (0.01 mmol, 2.02 mg) and L4 (R,S)-Rev-Josiphos (0.012 mmol, 7.2 mg) were dissolved in dry DCM (2.0 mL) and the mixture was stirred at room temperature for 10 min. The mixture was cooled to -80 °C and subsequently the corresponding Grignard reagent solution (1.25 equiv.) was added dropwise. The reaction mixture was stirred at -80 °C for another 10 min. Then a solution of chromonone (0.4 mmol) in DCM (1.0 mL) was added slowly over 1h using a syringe pump. The reaction was stirred until TLC ($n$-pentane:EtOAc 9:1) showed full conversion and quenched with saturated aqueous NH$_4$Cl solution (2 mL). The mixture was separated and the water layer was extracted with DCM (3x5 mL). The combined organic layers were dried over MgSO$_4$, filtered and the solvent was evaporated under vacuo. Purification by flash chromatography over silica gel, using $n$-pentane:Et$_2$O 9:1 afforded the desired compounds.

Characterization of products 2, 3, 4, 5, 6, 7

(R)-2-ethylchroman-4-one (2a)

Synthesized according the general procedure, obtained in 98% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer $t_r = 14.2$ min, minor enantiomer $t_r = 16.0$ min, ee= 95%; $[\alpha]^{25}_D$ = +51.5 (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.85 (dd, $J = 7.8$, 1.3 Hz, 1H), 7.44 (td, $J = 7.8$, 1.6 Hz, 1H), 7.03-6.88 (m, 2H), 4.45-4.29 (m, 1H), 2.66 (d, $J = 7.8$ Hz, 2H), 1.88 (dp, $J = 14.7, 7.4$ Hz,
(R)-2-pentylchroman-4-one (2b)

Synthesized according the general procedure, obtained in 80% yield; oil; enantiomeric excess was determined by HPLC (Chiracel OBH), hexane:i-PrOH 99:1, 0.5 mL/min, minor enantiomer t_r = 12.3 min, major enantiomer t_r = 12.9 min, ee = 96%; [α]^{25}_D = +48.9 (c 1.05, CHCl_3); \(^1^H\) NMR (400 MHz, CDCl_3): δ 7.87 (dd, J = 7.8, 1.7 Hz, 1H), 7.46 (td, J = 8.0, 1.6 Hz, 1H), 7.02-6.94 (m, 2H), 4.43 (qd, J = 7.6, 5.2 Hz, 1H), 2.68 (d, J = 7.5 Hz, 2H), 1.88 (dddd, J = 12.8, 10.1, 7.4, 5.3 Hz, 1H), 1.75-1.64 (m, 1H), 1.61-1.41 (m, 2H), 1.39-1.29 (m, 4H), 0.91 (t, J = 7.5 Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl_3) δ 192.5, 161.6, 135.8, 126.8, 121.0, 120.9, 117.8, 78.9, 42.4, 27.9, 9.2 ppm; HRMS (ESI) calculated for C_{11}H_{13}O_2 [M + H] 177.0910 found 177.0910.

(R)-2-hexylchroman-4-one (2c)

Synthesized according the general procedure, obtained in 87% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer t_r = 12.1 min, minor enantiomer t_r = 12.8 min, ee = 96%; [α]^{25}_D = +51.3 (c 1.09, CHCl_3); \(^1^H\) NMR (400 MHz, CDCl_3): δ 7.86 (dd, J = 7.8, 1.7 Hz, 1H), 7.44 (td, J = 7.8, 1.5 Hz, 1H), 7.00-6.94 (m, 2H), 4.42 (qd, J = 7.6, 5.4 Hz, 1H), 2.67 (d, J = 7.9 Hz, 2H), 1.93-1.81 (m, 1H), 1.69 (ddd, J = 13.9, 10.4, 5.4 Hz, 1H), 1.60-1.40 (m, 2H), 1.39-1.21 (m, 6H), 0.89 (t, J = 6.7 Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl_3) δ 192.5, 161.7, 135.9, 126.9, 121.1, 121.0, 117.8, 77.9, 43.0, 34.9, 31.5, 24.5, 22.5, 14.0 ppm; HRMS (ESI) calculated for C_{14}H_{19}O_2 [M + H] 219.1380 found 219.1379.

(R)-2-dodecylchroman-4-one (2d)
Synthesized according the general procedure, obtained in 53% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer \( t_r = 10.6 \) min, minor enantiomer \( t_r = 11.5 \) min, ee= 86%; \([\alpha]^{25}_D = +24.5\) (c 0.85, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.82\) (dd, \( J = 7.8, 1.6\) Hz, 1H), 7.41 (td, \( J = 7.8, 2.0\) Hz, 1H), 6.96-6.91 (m, 2H), 4.41-4.35 (m, 1H), 2.63 (d, \( J = 7.9\) Hz, 2H), 1.89-1.77 (m, 1H), 1.71-1.60 (m, 1H), 1.55-1.35 (m, 2H), 1.33-1.10 (m, 18H), 0.83 (t, \( J = 6.8\) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 192.6, 161.6, 135.8, 126.9, 121.0, 120.9, 117.8, 77.9, 42.9, 34.9, 31.9, 29.63, 29.59, 29.57, 29.49, 29.43, 29.32, 29.29, 24.8, 22.6, 14.0\) ppm; HRMS (ESI) calculated for C\(_{21}\)H\(_{33}\)O\(_2\) \([\text{M} + \text{H}]^+\) 317.2475 found 317.2477.

(R)-2-isobutylchroman-4-one (2e)

Synthesized according the general procedure, obtained in 82% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer \( t_r = 12.4 \) min, minor enantiomer \( t_r = 13.2 \) min, ee= 98%; \([\alpha]^{25}_D = +57.2\) (c 0.97, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.76\) (dd, \( J = 7.8, 1.5\) Hz, 1H), 7.34 (td, \( J = 7.8, 1.6\) Hz, 1H), 6.90-6.83 (m, 2H), 5.79 (dt, \( J = 16.9, 10.1, 6.6\) Hz, 1H), 5.03 (d, \( J = 17.1\) Hz, 1H), 4.97 (d, \( J = 10.2\) Hz, 1H), 4.45-4.37 (m, 1H), 2.64 (d, \( J = 7.7\) Hz, 2H), 2.33-2.16 (m, 2H), 1.95 (td, \( J = 14.2, 8.0\) Hz, 1H), 1.74 (dddd, \( J = 13.9, 8.9, 6.7\) Hz, 1H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 192.6, 161.6, 135.9, 126.9, 121.1, 121.0, 117.9, 76.3, 43.9, 43.4, 24.2, 23.0, 22.2\) ppm; HRMS (ESI) calculated for C\(_{13}\)H\(_{17}\)O\(_2\) \([\text{M} + \text{H}]^+\) 205.1223 found 205.1223.

(R)-2-(but-3-en-1-yl)chroman-4-one (2f)

Synthesized according the general procedure, obtained in 79% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH),hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer \( t_r = 15.3 \) min, minor enantiomer \( t_r = 17.1 \) min, ee= 87%; \([\alpha]^{25}_D = +44.4\) (c 0.9, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.82\) (d, \( J = 7.3\) Hz, 1H), 7.41 (t, \( J = 7.3\) Hz, 1H), 6.98-6.90 (m, 2H), 5.79 (ddt, \( J = 16.9, 10.1, 6.6\) Hz, 1H), 5.03 (d, \( J = 17.1\) Hz, 1H), 4.97 (d, \( J = 10.2\) Hz, 1H), 4.45-4.37 (m, 1H), 2.64 (d, \( J = 7.7\) Hz, 2H), 2.33-2.16 (m, 2H), 1.95 (td, \( J = 14.2, 8.0\) Hz, 1H), 1.74 (dddd, \( J = 13.9, 8.9, 6.7\) Hz, 1H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 192.3, 161.5, 137.2, 135.9, 126.9, 121.2, 121.0, 117.8, 117.5, 77.0, 42.9, 34.0, 29.0\) ppm; HRMS (ESI) calculated for C\(_{13}\)H\(_{15}\)O\(_2\) \([\text{M} + \text{H}]^+\) 203.1067 found 203.1066.
(R)-2-phenethylchroman-4-one (2g)

Synthesized according the general procedure, obtained in 77% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 95:5, 0.5 mL/min, major enantiomer \( t_r = 29.2 \text{ min} \), minor enantiomer \( t_r = 12.5 \text{ min} \), ee = 75%; \([\alpha]^D_{25} = +56.7 \) (c 0.8, CHCl\(_3\)). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.89 (dd, \( J = 8.1, 1.7 \) Hz, 1H), 7.49 (td, \( J = 7.8, 1.6 \) Hz, 1H), 7.32-7.29 (m, 2H), 7.26-7.19 (m, 3H), 7.03-7.00 (m, 2H), 4.44 (dt, \( dt = 11.0, 8.6, 4.5 \) Hz, 1H), 2.96-2.81 (m, 2H), 2.77-2.65 (m, 2H), 2.23 (dtd, \( J = 14.2, 8.6, 4.4 \) Hz, 1H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 192.3, 161.5, 140.9, 136.0, 128.5, 128.4, 127.0, 126.2, 121.3, 117.9, 76.8, 43.0, 36.5, 31.1 ppm; HRMS (ESI) calculated for C\(_{17}\)H\(_{17}\)O\(_2\) [M + H] 253.1223 found 253.1224.

(S)-2-(pentan-3-yl)chroman-4-one (2h)

Synthesized according the general procedure, obtained in 68% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer \( t_r = 11.4 \text{ min} \), minor enantiomer \( t_r = 12.3 \text{ min} \), ee = 84%; \([\alpha]^D_{25} = +53.5 \) (c 0.92, CHCl\(_3\)). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.87 (dd, \( J = 7.9, 1.5 \) Hz, 1H), 7.44 (dd, \( J = 8.4, 7.3, 1.8 \) Hz, 1H), 7.01-6.94 (m, 2H), 4.43 (ddd, \( J = 13.5, 4.9, 2.7 \) Hz, 1H), 2.75 (dd, \( J = 16.6, 13.5 \) Hz, 1H), 2.60 (dd, \( J = 16.6, 2.7 \) Hz, 1H), 1.69-1.59 (m, 2H), 1.58-1.49 (m, 2H), 1.36 (dt, \( J = 15.7, 7.9 \) Hz, 1H), 0.96 (t, \( J = 7.3 \) Hz, 3H), 0.95 (t, \( J = 7.4 \) Hz, 3H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 193.2, 162.1, 135.8, 126.9, 121.0, 117.9, 79.5, 44.8, 40.0, 21.5, 21.3, 11.4 ppm; HRMS (ESI) calculated for C\(_{14}\)H\(_{19}\)O\(_2\) [M + H] 219.1380 found 219.1380.

(S)-2-cyclopentylchroman-4-one (2i)

Synthesized according the general procedure, obtained in 79% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer \( t_r = 13.8 \text{ min} \), minor enantiomer \( t_r = 14.5 \text{ min} \), ee = 97%; \([\alpha]^D_{25} = +72.1 \) (c 0.9,
CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.86 (dd, J = 7.8, 1.3 Hz, 1H), 7.45 (td, J = 7.8, 1.7 Hz, 1H), 7.00-6.93 (m, 2H), 4.22 (ddd, J = 9.6, 7.8, 5.7 Hz, 1H), 2.74-2.64 (m, 2H), 2.28-2.20 (m, 1H), 1.97-1.89 (m, 1H), 1.79-1.74 (m, 1H), 1.72-1.50 (m, 5H), 1.37-1.25 (m, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 192.8, 161.8, 135.9, 126.9, 121.4, 121.0, 117.5, 81.7, 44.1, 42.2, 28.8, 28.4, 25.5, 25.4 ppm; HRMS (ESI) calculated for C₁₄H₁₇O₂ [M + H] 217.1223 found 217.1223.

(R)-2-ethyl-6-methylchroman-4-one (3)

Synthesized according the general procedure, obtained in 93% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer tᵣ = 13.8 min, minor enantiomer tᵣ = 15.2 min, ee= 92%; [α]²⁵D = +69.6 (c 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.64 (d, J = 1.3 Hz, 1H), 7.25 (dd, J = 8.4, 2.1 Hz, 1H), 6.86 (d, J = 8.4, 1H), 4.32 (qd, J = 7.6, 5.6 Hz, 1H), 4.29 (m, 1H), 2.64 (d, J = 8.0 Hz, 2H), 2.28 (s, 3H), 1.87 (dp, J = 14.4, 7.3 Hz, 1H), 1.80-1.68 (m, 1H), 1.05 (t, J = 7.5 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 192.8, 159.7, 137.0, 130.5, 130.5, 126.4, 120.6, 117.6, 79.0, 42.6, 28.0, 20.4, 9.3 ppm; HRMS (ESI) calculated for C₁₂H₁₅O₂ [M + H] 191.1067 found 191.1065.

(R)-2-ethyl-6-fluorochroman-4-one (4)

Synthesized according the general procedure, obtained in 75% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer tᵣ = 12.9 min, minor enantiomer tᵣ = 14.3 min, ee= 92%; [α]²⁵D = +72.3 (c 1.11, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.45 (dd, J = 8.3, 3.1 Hz, 1H), 7.12 (td, J = 8.6, 3.2 Hz, 1H), 6.89 (dd, J = 9.0, 4.2, 1H), 4.29 (m, 1H), 2.66-2.62 (m, 2H), 1.83 (dp, J = 14.7, 7.4 Hz, 1H), 1.77-1.65 (m, 1H), 1.01 (t, J = 7.5 Hz, 3H) ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -121.9 (td, JₙF = 8.0, 4.3) ¹³C NMR (100 MHz, CDCl₃) δ 191.8 (d, Jₖ-F = 1.8), 158.0 (d, Jₖ-F = 31.6), 156.9 (d, Jₖ-F = 208.6), 123.4 (d, Jₖ-F = 24.6), 121.4 (d, Jₖ-F = 6.5), 119.5 (d, Jₖ-F = 7.3), 111.8 (d, Jₖ-F = 23.2), 79.3, 42.2, 27.8, 9.2 ppm; HRMS (ESI) calculated for C₁₁H₁₂FO₂ [M + H] 195.0816 found 195.0815.
(R)-6-chloro-2-ethylchroman-4-one (5)

Synthesized according the general procedure, obtained in 85% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer $t_r = 13.6$ min, minor enantiomer $t_r = 15.2$ min, ee $= 90\%$; $[\alpha]^{25}_D = +78.2$ (c 1.01, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.82 (d, $J = 2.7$ Hz, 1H), 7.40 (dd, $J = 8.8$, 2.7 Hz, 1H), 6.93 (d, $J = 8.8$ Hz, 1H), 4.36 (dt, $J = 11.0$, 6.9, 5.5 Hz, 1H), 2.72-2.61 (m, 2H), 1.89 (dp, $J = 14.7$, 7.4 Hz, 1H), 1.83-1.71 (m, 1H), 1.07 (t, $J = 7.5$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 191.4, 160.1, 135.7, 126.6, 126.2, 121.7, 119.6, 79.3, 42.2, 27.9, 9.2 ppm; HRMS (ESI) calculated for C$_{11}$H$_{12}$ClO$_2$ [M + H] $211.0520$ found 211.0519.

(R)-6-bromo-2-ethylchroman-4-one (6)

Synthesized according the general procedure, obtained in 81% yield; oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer $t_r = 14.4$ min, minor enantiomer $t_r = 15.9$ min, ee $= 89\%$; $[\alpha]^{25}_D = +64.3$ (c 1.15, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.88 (d, $J = 2.2$ Hz, 1H), 7.45 (dd, $J = 8.8$, 2.1 Hz, 1H), 6.80 (d, $J = 8.8$ Hz, 1H), 4.32-4.24 (m, 1H), 2.65-2.52 (m, 2H), 1.81 (dp, $J = 14.7$, 7.4 Hz, 1H), 1.75-1.54 (m, 1H), 0.99 (t, $J = 7.5$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 191.3, 160.5, 138.5, 129.3, 122.2, 120.0, 113.7, 79.3, 42.1, 27.8, 9.2 ppm; HRMS (ESI) calculated for C$_{11}$H$_{12}$BrO$_2$ [M + H] $255.0015$ found 255.0016.

(R)-2-ethyl-7-methoxycroman-4-one (7)

Synthesized according the general procedure, obtained in 81% yield; oil; enantiomeric excess was determined by HPLC (Chiracel OJH), hexane:i-PrOH 99:1, 0.5 mL/min, minor enantiomer $t_r = 28.9$ min, minor enantiomer $t_r = 30.3$ min, ee $= 92\%$; $[\alpha]^{25}_D = +50.9$ (c 0.82, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78 (d, $J = 8.8$ Hz, 1H), 6.53 (dd, $J = 8.8$, 2.4 Hz, 1H), 6.40 (d, $J = 2.3$ Hz, 1H), 4.38-4.29 (m, 1H), 3.81 (s, 3H), 2.66-2.54 (m, 2H), 1.86 (dp, $J = 14.7$, 7.3 Hz, 1H), 1.80-1.68 (m, 1H), 1.05 (t, $J = 7.5$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$
191.2, 166.0, 163.6, 128.6, 114.9, 109.7, 100.6, 79.4, 55.6, 42.2, 28.0, 9.3 ppm; HRMS (ESI) calculated for C_{12}H_{15}O_{3} [M + H] 207.1016 found 207.1016.

\((2R,3R)-2\text{-ethyl-3-(hydroxy(phenyl)methyl)}\text{chroman-4-one (9)}\)

\[\text{CuBr·SMe}_2\ (0.01 \text{ mmol, 2.02 mg}) \text{ and } \text{L4 (R,S)-Rev-Josiphos (0.012 mmol, 7.2 mg)}\]

were dissolved in dry DCM (2.0 mL) and the mixture was stirred at room temperature for 10 min. The mixture was cooled to -80 °C and subsequently the corresponding Grignard reagent solution (1.25 equiv.) was added dropwise. The reaction mixture was stirred at -80 °C for another 10 min. Then a solution of chromonone 2a (0.4 mmol, 58.4 mg) in DCM (1.0 mL) was added slowly over 1h using a syringe pump. The reaction was stirred until TLC (n-pentane:EtOAc 9:1) showed full conversion. PhCHO (1.6 mmol, 150 μL) was added and the mixture was stirred at room temperature for 3 h. After that the reaction mixture was quenched with saturated aqueous NH₄Cl solution (2 mL). The mixture was separated and the water layer was extracted with DCM (3×5 mL). The combined organic layers were dried over MgSO₄, filtered and the solvent was evaporated under vacuo. Purification by flash chromatography over silica gel, using n-pentane:Et₂O 9:1 afforded the desired compound 9 was obtained as an oil (101.5 mg, 0.36 mmol, 90% yield, dr: 1:1.1); \(^1\)H NMR (400 MHz, CDCl₃): \(\delta\) 7.90 (dd, \(J = 7.8, 1.5 \text{ Hz}, 1\text{H}), 7.75 (d, \(J = 7.8 \text{ Hz}, 1\text{H}), 7.54-7.20 (m, 12\text{H}), 7.01 (t, \(J = 7.5 \text{ Hz}, 1\text{H}), 6.99-6.92 (m, 3\text{H}), 5.15 (d, \(J = 6.7 \text{ Hz}, 1\text{H}), 4.98^* (d, \(J = 9.1 \text{ Hz}, 1\text{H}), 4.72-4.63 (m, 1\text{H}), 4.04^* (ddd, \(J = 9.4, 5.0, 2.3 \text{ Hz}, 1\text{H}), 2.90 (dd, \(J = 6.6, 4.8 \text{ Hz}, 1\text{H}), 2.73^* (dd, \(J = 9.1, 2.3 \text{ Hz}, 1\text{H}), 1.87-1.67 (m, 2\text{H}), 1.63-1.51 (m, 1\text{H}), 1.50-1.39^* (m, 1\text{H}), 0.95 (t, \(J = 7.3 \text{ Hz}, 3\text{H}), 0.84^* (t, \(J = 7.3 \text{ Hz}, 3\text{H}) \text{ ppm}; \(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta\) 193.8, 193.4, 159.6, 158.9, 141.4, 141.1, 136.6, 136.4, 128.7, 128.5, 128.43, 128.39, 128.0, 127.22, 127.0, 126.8, 126.8, 126.3, 121.3, 121.1, 118.20, 118.17, 79.7, 79.3, 72.9, 72.6, 57.9, 57.0, 25.1, 24.7, 9.84, 9.75 ppm; HRMS (ESI) calculated for C_{18}H_{19}O_{3} [M + H] 283.1329 found 283.1328.

\((R)-4\text{-ethyl-3,4-dihydro-2H-benzo[b][1,4]dioxepin-2-one (10)}\)

\((R)-2\text{-ethylchroman-4-one (2a) (0.25 mmol, 44.1 mg) and MCPBA (0.625 mmol, 107.9 mg)}\)

were dissolved in 5 mL of ClCH₂CH₂Cl, and the mixture was heated to 60 °C. The reaction mixture was stirred until TLC (n-pentane:EtOAc 9:1) showed full conversion and quenched with
saturated aqueous NaHCO₃ solution (10 mL) and 15 mL of DCM. The mixture was separated and the organic layer was washed with aq. NaHCO₃ (2×7 mL). The combined organic layers were dried over MgSO₄, filtered and the solvent was evaporated under vacuo. Purification by flash chromatography over silica gel, using n-pentane:Et₂O 9:1 afforded the desired compound 10 as an oil (33.7 mg, 0.178 mmol, 71% yield); oil; enantiomeric excess was determined by HPLC (Chiracel ODH), hexane:i-PrOH 99:1, 0.5 mL/min, major enantiomer tᵣ = 30.9 min, minor enantiomer tᵣ = 23.7 min, ee = 93%; [α]²⁵⁺D = +67.1 (c 0.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.19-7.08 (m, 4H), 4.62-4.53 (m, 1H), 2.83 (dd, J = 13.2, 5.5 Hz, 1H), 2.65 (dd, J = 13.2, 7.5 Hz, 1H), 1.93-1.80 (m, 1H), 1.67-1.55 (m, 1H), 1.08 (t, J = 7.4 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 168.2, 145.9, 144.8 126.7, 125.5, 124.1, 120.2, 84.0, 37.5, 27.5, 10.0 ppm; HRMS (ESI) calculated for C₁₁H₁₃O₃ [M + H] 193.0859 found 193.0858.

References:


NMR Spectra of Characterized Compounds

(R)-2-ethylchroman-4-one
(R)-2-pentylchroman-4-one
(R)-2-hexylchroman-4-one
(R)-2-dodecylchroman-4-one
(R)-2-isobutylchroman-4-one
(R)-2-(but-3-en-1-yl)chroman-4-one
(R)-2-phenethylchroman-4-one
(S)-2-(pentan-3-yl)chroman-4-one
(S)-2-cyclopentylchroman-4-one
(R)-2-ethyl-6-methylchroman-4-one
(R)-2-ethyl-6-fluorochroman-4-one

Electronic Supplementary Material (ESI) for Chemical Communications
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(R)-6-chloro-2-ethylchroman-4-one
(R)-6-bromo-2-ethylchroman-4-one

Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013
(R)-2-ethyl-7-methoxychroman-4-one
(2R,3R)-2-ethyl-3-(hydroxy(phenyl)methyl)chroman-4-one
(R)-4-ethyl-3,4-dihydro-2H-benzo[b][1,4]dioxepin-2-one
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