Supporting Information

Bifunctional Squaramide-catalyzed Synthesis of Chiral Dihydrocoumarins via the ortho-Quinone Methides Generated from 2-(1-Tosylalkyl)phenols

Ji Zhou, Mao-Lin Wang, Xiang Gao, Guo-Fang Jiang* and Yong-Gui Zhou*
Email: gfjiang@hnu.edu.cn; ygzhou@dicp.ac.cn

Table of Contents

1. General..........................................................................................................................S1
2. General Procedure for Synthesis of 2-(1-Tosylalkyl)phenols 1.........................S1
3. General Procedure for Synthesis of Azlactones 2.............................................S2
4. General Procedure for Synthesis of Chiral 3,4-Dihydrocoumarins ........S3-S10
5. Determination of Absolute Configuration of the Product..............................S11
6. References....................................................................................................................S11
7. Copy of NMR and HPLC for the Compounds.................................................S12-S105
1. General

All reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques, unless otherwise noted. Commercially available reagents were used without further purification. Solvents were treated prior to use according to the standard methods. $^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were recorded at room temperature in CDCl$_3$ on 400 MHz instrument with tetramethylsilane (TMS) as internal standard. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC analysis. The chiral thiourea and squaramide organocatalysts were prepared according to the known methods.[1]

2. General Procedure for Synthesis of 2-(1-Tosylalkyl)phenols 1

2-(1-Tosylalkyl)phenols 1 were prepared according to the known methods, among them, 1a-1b, 1d-1f, 1i-1m are the known compounds.[2]

Under an atmosphere of nitrogen, a solution of 2-hydroxybenzaldehyde 5 (4.0 mmol) in tetrahydrofuran (10 mL) was added to a solution of Grignard reagent 6 (10.0 mmol), the mixture was stirred at room temperature for 4 hours. The reaction mixture was quenched by saturated ammonium chloride (20 mL) and extracted with dichloromethane (50 mL×3). Then the combined organic layer was dried over anhydrous sodium sulfate, concentrated in vacuo. A short silica gel column filtration of the crude mixture afforded 2-hydroxyalkylphenols 7.

A reaction mixture of sodium p-toluenesulfinate tetrahydrate (1.001 g, 4.0 mmol) and p-toluenesulfonic acid monohydrate (1.141 g, 6.0 mmol) in dichloromethane (20 mL) was stirred at room temperature for 20 min. Then, a solution of 2-hydroxyalkylphenol 7 in dichloromethane (10 mL) was added to the resulting slurry, the suspension was stirred at room temperature for 24 hours. The reaction mixture was quenched and adjusted to pH = 8 by saturated sodium bicarbonate. After being extracted with dichloromethane (50 mL×3), the combined organic layer was dried over anhydrous sodium sulfate, concentrated in vacuo. The crude mixture was recrystallized from dichloromethane and hexanes, giving the product 2-(1-tosylalkyl)phenols 1.

2-(Tosyl(4-(trifluoromethyl)phenyl)methyl)naphthalen-1-ol (1c): 604 mg, 44% yield, new compound, orange solid, mp = 65-66 °C, Rf = 0.35 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.35-8.19 (m, 1H), 7.93 (s, 1H), 7.74 (d, $J = 7.7$ Hz, 3H), 7.67-7.46 (m, 6H), 7.34 (d, $J = 8.7$ Hz, 1H), 7.24-7.06 (m, 3H), 6.00 (s, 1H), 2.34 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.5, 145.6, 136.1, 134.4, 130.8, 129.9, 129.0, 127.8, 127.6, 127.4, 126.4, 126.2, 125.9 (q, $J = 3.6$ Hz), 122.6, 121.6, 113.3, 72.8, 21.8; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -62.81. HRMS Calculated for C$_{25}$H$_{23}$F$_3$NO$_3$S [M+NH$_4$]$^+$ 474.1345, found 474.1346.

2-((3,5-Dimethylphenyl)(tosyl)methyl)naphthalen-1-ol (1g): 672 mg, 54% yield, new compound, white solid, mp = 164-165 °C, Rf = 0.35 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.39-8.28 (m, 1H), 8.18 (s, 1H), 7.74 (d, $J = 7.7$ Hz, 3H), 7.67-7.46 (m, 6H), 7.34 (d, $J = 8.7$ Hz, 1H), 7.24-7.06 (m, 3H), 6.00 (s, 1H), 2.34 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 151.5, 145.6, 136.1, 134.9, 134.4, 130.8, 129.9, 129.0, 127.8, 127.6, 127.4, 126.4, 126.2, 125.9 (q, $J = 3.6$ Hz), 122.6, 121.6, 113.3, 72.8, 21.8; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -62.81. HRMS Calculated for C$_{25}$H$_{23}$F$_3$NO$_3$S [M+NH$_4$]$^+$ 474.1345, found 474.1346.
134.8, 131.8, 130.7, 129.6, 128.1, 127.9, 127.6, 127.3, 126.6, 125.9, 122.9, 121.2, 114.1, 73.4, 21.8, 21.5. HRMS Calculated for C_{26}H_{28}NO_{3}S [M+NH\textsubscript{4}]\textsuperscript{+} 434.1784, found 434.1784.

2-((3,5-Dimethoxylphenyl)(tosyl)methyl)naphthalen-1-ol (1h): 1.598 g, 94% yield, new compound, yellow solid, mp = 188-189 °C, R\textsubscript{f} = 0.40 (hexanes/ethyl acetate 5/1). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \textdelta 8.37-8.30 (m, 1H), 8.16 (s, 1H), 7.73 (dt, J = 6.4, 2.7 Hz, 1H), 7.65 (d, J = 8.3 Hz, 2H), 7.54-7.46 (m, 2H), 7.33 (q, J = 8.7 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 6.74 (d, J = 2.2 Hz, 2H), 6.39 (t, J = 2.2 Hz, 1H), 5.91 (s, 1H), 3.73 (s, 6H), 2.34 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \textdelta 161.0, 151.6, 145.3, 134.8, 134.7, 134.1, 129.7, 129.2, 127.6, 127.4, 126.7, 126.0, 123.0, 121.4, 113.9, 108.6, 101.0, 73.1, 55.6, 21.8. HRMS Calculated for C_{26}H_{24}NaO_{5}S [M+Na]\textsuperscript{+} 471.1237, found 471.1231.

3. General Procedure for Synthesis of azlactones 2

Azlactones 2 were prepared according to the known procedure with minor modification, among them, 2a-2g, 2i-2l are the known compounds.\textsuperscript{[3]}

\[
\begin{array}{c}
\text{R}^1\text{COOH} + \text{R}^2\text{Cl} & \xrightarrow{\text{NaOH aq., 75 °C}} & \text{R}^1\text{N}=\text{R}^2\text{COOH} \\
8 & & 9 \\
\text{Ac}_2\text{O, CH}_2\text{Cl}_2 & \xrightarrow{\text{rt}} & \text{N}=\text{R}^2\text{COO} \\
10 & & 2
\end{array}
\]

To a vigorously stirred solution containing amino acid 8 (10.0 mmol, 1 equiv.) and NaOH (20.0 mmol, 2 equiv.) in 40 mL of water at 75 °C was added acyl chloride 9 (11.0 mmol, 1.1 equiv.) in small portions during 10 min, the mixture was stirred an additional 12 hours, then cooled to 0 °C and acidified to pH = 1-2 with 2 N HCl. The residue was extracted into ethyl acetate (50 mL×3) and dried with anhydrous sodium sulfate. Then, the solvent was removed in \textit{vacuo}. The crude products was purified through a short column of silica gel using hexane/EtOAc = 1:1 (and then with 10% CH\textsubscript{3}OH/CH\textsubscript{2}Cl\textsubscript{2}) as an eluent to give N-acylalanine 10.

The anhydrous acetic anhydride (21.0 mmol, 3 equiv.) was added dropwise to the solution of N-acylalanine 10 (7.0 mmol, 1 equiv.) in dichloromethane (20 mL) at room temperature, the reaction was stirred for 16 hours at which point TLC analysis indicated total consumption of the starting material. The mixture was washed with saturated sodium bicarbonate solution (20 mL×3) and extracted into dichloromethane (50 mL×3), the combined organic layer was dried over anhydrous sodium sulfate, concentrated in \textit{vacuo}. The crude mixture was recrystallized from dichloromethane and hexanes, giving the corresponding product 2.

4-benzyl-2-(m-tolyloxazol-5(4H)-one (2h): 1.791 g, 79% yield, new compound, colorless oil, R\textsubscript{f} = 0.90 (hexanes/ethyl acetate 5/1). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \textdelta 7.80-7.66 (m, 2H), 7.39-7.31 (m, 2H), 7.31-7.18 (m, 5H), 4.81-4.56 (m, 1H), 3.38 (dd, J = 14.0, 6.7 Hz, 1H), 2.40 (s, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \textdelta 177.8, 162.0, 138.8, 135.5, 133.7, 129.8, 128.8, 128.6, 128.5, 127.4, 125.3, 66.7, 37.5, 21.4. HRMS Calculated for C\textsubscript{17}H\textsubscript{16}NO\textsubscript{2} [M+H]\textsuperscript{+} 266.1176, found 266.1182.
4. General Procedure for Synthesis of Chiral 3,4-Dihydrocoumarins 3

A reaction mixture of 1 (0.20 mmol), 2 (0.20 mmol), sodium carbonate (0.24 mmol, 25.4 mg) and bifunctional squaramide organocatalyst 4b (0.02 mmol, 12.6 mg) in chloroform (3.0 mL) was stirred at 30 °C for 72-96 hours. Then the crude product was purified by flash chromatography on silica gel using hexanes and ethyl acetate to give the corresponding product dihydrocoumarins 3.

(+)-N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamide (3aa): new compound, 91% yield, 96% ee, 88 mg, [α]D20 = +276.36 (c 1.0, CHCl3), pale yellow solid, mp = 227-228 °C, Rf = 0.65 (hexanes/ethyl acetate 5/1). 1H NMR (400 MHz, CDCl3) δ 8.49 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.73 (t, J = 7.0 Hz, 2H), 7.65 (t, J = 7.5 Hz, 1H), 7.52-7.42 (m, 3H), 7.42-7.31 (m, 3H), 7.26-7.13 (m, 8H), 7.11 (dd, J = 6.5, 2.5 Hz, 2H), 6.84 (s, 1H), 5.61 (s, 1H), 4.27 (d, J = 14.0 Hz, 1H), 3.21 (d, J = 13.9 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 168.6, 168.3, 145.0, 138.1, 135.4, 135.0, 134.1, 131.8, 130.1, 129.0, 128.8, 128.6, 128.3, 128.1, 127.6, 127.4, 126.9, 126.7, 125.7, 123.3, 121.2, 120.3, 66.1, 50.8, 38.7. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 6.5 min and 8.1 min (maj). HRMS Calculated for C33H26NO3 [M+H]+ 484.1907, found 484.1901.

(+)-N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-4-chlorobenzamide (3ab): new compound, 85% yield, 94% ee, 88 mg, [α]D20 = +263.58 (c 1.0, CHCl3), pale yellow solid, mp = 242-243 °C, Rf = 0.95 (hexanes/ethyl acetate 5/1). 1H NMR (400 MHz, CDCl3) δ 8.45 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.71 (d, J = 8.2 Hz, 1H), 7.52-7.42 (m, 3H), 7.42-7.31 (m, 3H), 7.26-7.13 (m, 8H), 7.11 (dd, J = 6.5, 2.5 Hz, 2H), 6.84 (s, 1H), 5.61 (s, 1H), 4.27 (d, J = 14.0 Hz, 1H), 3.21 (d, J = 13.9 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 168.6, 168.3, 145.0, 138.1, 135.4, 135.0, 134.1, 131.8, 130.1, 129.0, 128.8, 128.6, 128.3, 128.1, 127.6, 127.4, 126.9, 126.7, 125.7, 123.3, 121.2, 120.3, 66.1, 50.8, 38.7. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 6.5 min and 8.1 min (maj). HRMS Calculated for C33H25ClNO3 [M+H]+ 518.1517, found 518.1518; HRMS Calculated for C33H25ClNO3 [M+H]+ 520.1517, found 520.1502.

(+)-N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-4-fluorobenzamide (3ac): new compound, 90% yield, 95% ee, 90 mg, [α]D20 = +289.18 (c 1.0, CHCl3), yellow solid, mp = 245-246 °C, Rf = 0.95 (hexanes/ethyl acetate 5/1). 1H NMR (400 MHz, CDCl3) δ 8.45 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.71 (d, J = 8.2 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 168, 167.1, 145.0, 138.1, 138.0, 134.9, 134.1, 133.6, 130.1, 129.1, 128.6, 128.3, 128.1, 128.1, 127.7, 127.4, 126.7, 126.7, 125.8, 123.4, 121.2, 120.1, 66.2, 50.9, 38.7. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 6.5 min and 7.6 min (maj). HRMS Calculated for C33H25ClFNO3 [M+H]+ 520.1517, found 520.1502.
145.0, 138.1, 135.0, 134.1, 131.5 (d, $J_{CF} = 3.1$ Hz), 130.1, 129.2 (d, $J_{CF} = 9.0$ Hz), 129.0, 128.6, 128.3, 128.1, 127.6, 127.4, 127.4, 126.7, 125.7, 123.4, 121.2, 120.2, 115.9 (d, $J_{CF} = 21.8$ Hz), 66.2, 50.9, 38.7; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -107.78. HPLC: Chiralcel OD-H column, 254 nm, 30 $^\circ$C, $n$-hexane/$i$-propanol = 90/10, flow = 0.8 mL/min, retention time 6.5 min and 7.6 min (maj). HRMS Calculated for C$_{33}$H$_{25}$FNO$_3$ [M+H]$^+$ 502.1813, found 502.1818.

(+) – N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-4-bromobenamide (3ad): new compound, 91% yield, 92% ee, 102 mg, $[\alpha]_{D}^{20} = +297.48$ (c 1.0, CHCl$_3$), yellow solid, mp = 250-251 $^\circ$C, $R_f = 0.85$ (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.45 (d, $J = 8.3$ Hz, 1H), 7.90 (d, $J = 8.1$ Hz, 1H), 7.78-7.66 (m, 2H), 7.62 (t, $J = 7.4$ Hz, 1H), 7.47 (d, $J = 8.4$ Hz, 2H), 7.35 (d, $J = 8.4$ Hz, 1H), 7.30 (d, $J = 8.4$ Hz, 2H), 7.18 (dt, $J = 7.9, 4.4$ Hz, 8H), 7.10-7.00 (m, 2H), 6.76 (s, 1H), 5.54 (s, 1H), 4.19 (d, $J = 14.0$ Hz, 1H), 3.18 (d, $J = 14.0$ Hz, 1H), $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.6, 167.2, 145.0, 138.0, 134.9, 134.2, 134.1, 132.1, 130.1, 129.1, 128.6, 128.5, 128.2, 128.1, 128.1, 127.7, 127.4, 127.4, 126.7, 125.8, 123.4, 121.2, 120.1, 66.2, 50.9, 38.7. HPLC: Chiralcel OD-H column, 254 nm, 30 $^\circ$C, $n$-hexane/$i$-propanol = 90/10, flow = 0.8 mL/min, retention time 6.7 min and 7.6 min (maj). HRMS Calculated for C$_{33}$H$_{25}$FNO$_3$ [M+H]$^+$ 562.1012, found 562.1003; HRMS Calculated for C$_{33}$H$_{25}$BrNO$_3$ [M+H]$^+$ 564.1012, found 564.0982.

(+) – N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-4-(trifluoromethyl)benzamidine (3ae): new compound, 91% yield, 92% ee, 100 mg, $[\alpha]_{D}^{20} = +291.66$ (c 1.0, CHCl$_3$), pale yellow solid, mp = 243-244 $^\circ$C, $R_f = 0.75$ (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.46 (d, $J = 8.3$ Hz, 1H), 7.91 (d, $J = 8.1$ Hz, 1H), 7.79-7.67 (m, 2H), 7.63 (dd, $J = 13.6, 7.9$ Hz, 3H), 7.51 (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 8.4$ Hz, 1H), 7.25-7.12 (m, 8H), 7.11-7.00 (m, 2H), 6.82 (s, 1H), 5.54 (s, 1H), 4.19 (d, $J = 14.0$ Hz, 1H), 3.21 (d, $J = 14.1$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.6, 167.0, 145.0, 144.7, 138.5, 138.0, 134.8, 134.2, 133.7, 133.4, 130.1, 129.1, 128.7, 128.2, 128.2, 127.8, 127.5, 127.4, 126.7, 125.9 (q, $J = 3.6$ Hz), 125.8, 125.1, 123.4, 121.2, 120.0, 66.2, 50.9, 38.8; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -63.01. HPLC: Chiralcel OD-H column, 254 nm, 30 $^\circ$C, $n$-hexane/$i$-propanol = 90/10, flow = 0.8 mL/min, retention time 5.8 min and 6.4 min (maj). HRMS Calculated for C$_{33}$H$_{25}$F$_3$NO$_3$ [M+H]$^+$ 552.1781, found 552.1787.

(+) – N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-3,5-dimethylbenzamidine (3af): new compound, 95% yield, 97% ee, 97 mg, $[\alpha]_{D}^{20} = +302.18$ (c 1.0, CHCl$_3$), yellow solid, mp = 239-240 $^\circ$C, $R_f = 0.90$ (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.46 (d, $J = 8.4$ Hz, 1H), 7.90 (d, $J = 8.1$ Hz, 1H), 7.70 (dd, $J = 10.4, 4.6$ Hz, 2H), 7.65-7.57 (m, 1H), 7.36 (d, $J = 8.4$ Hz, 1H), 7.19 (d, $J = 17.0, 6.1, 2.0$ Hz, 8H), 7.07 (dd, $J = 6.1, 3.2$ Hz, 3H), 7.02 (s, 2H), 6.77 (s, 1H), 5.57 (s, 1H), 4.23 (d, $J = 14.0$ Hz, 1H), 3.16 (d, $J = 13.9$ Hz, 1H), 2.28 (s, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.7, 168.6, 145.1, 138.5, 138.2, 135.4, 135.1, 133.4, 130.2, 129.0, 128.6, 128.3, 128.1, 127.9, 127.6, 127.3, 127.3, 126.8, 125.6, 124.7, 123.4, 121.2, 120.4, 66.1, 50.9, 38.7, 21.4. HPLC: Chiralcel OD-H column, 254 nm, 30 $^\circ$C, $n$-hexane/$i$-propanol = 90/10, flow = 0.8 mL/min, retention time 5.8 min and 7.4 min (maj). HRMS Calculated for C$_{33}$H$_{30}$NO$_3$ [M+H]$^+$ 512.2220, found 512.2228.
(+)-N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-4-methylbenzamide (3ag): new compound, 95% yield, 88% ee, 95 mg, $\alpha^D = +227.68$ (c 1.0, CHCl$_3$), yellow solid, mp = 209-210 °C, R$_f$ = 0.85 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.46 (d, $J = 8.4$ Hz, 1H), 7.90 (d, $J = 8.1$ Hz, 1H), 7.74-7.65 (m, 2H), 7.61 (t, $J = 7.5$ Hz, 1H), 7.35 (d, $J = 8.0$ Hz, 3H), 7.17 (dd, $J = 21.4$, 6.0 Hz, 10H), 7.10-7.02 (m, 2H), 6.78 (s, 1H), 5.58 (s, 1H), 4.24 (d, $J = 14.0$ Hz, 1H), 3.16 (d, $J = 13.9$ Hz, 1H), 2.35 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.7, 168.2, 145.1, 142.2, 138.1, 135.1, 134.1, 132.5, 130.2, 129.4, 129.0, 128.6, 128.3, 128.1, 128.0, 127.5, 127.3, 127.3, 126.9, 126.8, 125.6, 123.4, 121.2, 120.4, 66.1, 50.9, 38.7, 21.6. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 6.5 min and 8.1 min (maj). HRMS Calculated for C$_{34}$H$_{26}$N$_{30}$O$_{5}$ [M+H]$^+$ 498.2064, found 498.2069.

(+)-N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-3-methylbenzamide (3ah): new compound, 95% yield, 82% ee, 95 mg, $\alpha^D = +260.82$ (c 0.6, CHCl$_3$), yellow solid, mp = 110-111 °C, R$_f$ = 0.70 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.49 (d, $J = 8.4$ Hz, 1H), 7.93 (d, $J = 8.1$ Hz, 1H), 7.73 (t, $J = 7.0$ Hz, 2H), 7.64 (t, $J = 7.4$ Hz, 1H), 7.39 (d, $J = 8.4$ Hz, 1H), 7.30-7.14 (m, 12H), 7.10 (dd, $J = 6.5$, 2.7 Hz, 2H), 6.82 (s, 1H), 5.60 (s, 1H), 4.26 (d, $J = 14.0$ Hz, 1H), 3.19 (d, $J = 14.0$ Hz, 1H), 2.36 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.7, 168.5, 145.0, 138.7, 138.1, 135.4, 135.1, 134.1, 132.5, 130.2, 129.0, 128.7, 128.6, 128.3, 128.1, 128.0, 127.6, 127.6, 127.4, 127.3, 126.8, 125.7, 123.9, 123.4, 121.2, 120.3, 66.1, 50.9, 38.7, 21.5. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 6.1 min and 7.3 min (maj). HRMS Calculated for C$_{33}$H$_{28}$N$_{3}$O$_{5}$ [M+H]$^+$ 498.2064, found 498.2067.

(+)-N-((3S,4S)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-4-methoxybenzamide (3ai): new compound, 94% yield, 95% ee, 97 mg, $\alpha^D = +278.31$ (c 0.60, CHCl$_3$), yellow solid, mp = 219-220 °C, R$_f$ = 0.50 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.45 (d, $J = 8.4$ Hz, 1H), 7.90 (d, $J = 8.1$ Hz, 1H), 7.73-7.65 (m, 2H), 7.62 (t, $J = 7.3$ Hz, 1H), 7.44 (d, $J = 8.7$ Hz, 2H), 7.35 (d, $J = 8.4$ Hz, 1H), 7.17 (dd, $J = 12.1$, 6.6, 2.5 Hz, 8H), 7.05 (dd, $J = 6.4$, 2.7 Hz, 2H), 6.83 (d, $J = 8.7$ Hz, 2H), 6.73 (s, 1H), 5.57 (s, 1H), 4.23 (d, $J = 14.0$ Hz, 1H), 3.81 (s, 3H), 3.15 (d, $J = 13.9$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.8, 167.7, 162.5, 145.1, 138.1, 135.1, 134.1, 130.2, 129.0, 128.8, 128.6, 128.3, 128.1, 127.9, 127.6, 127.5, 127.3, 126.8, 125.6, 123.3, 121.2, 120.4, 114.0, 66.1, 55.6, 50.8, 38.7. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 9.2 min and 11.5 min (maj). HRMS Calculated for C$_{33}$H$_{28}$N$_{3}$O$_{5}$ [M+H]$^+$ 514.2013, found 514.2014.

(+)-N-((3S,4S)-3-(4-chlorobenzyl)-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-benzamide (3aj): new compound, 98% yield, 93% ee, 101 mg, $\alpha^D = +335.14$ (c 0.60, CHCl$_3$), yellow solid, mp = 231-232 °C, R$_f$ = 0.70 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.44 (d, $J = 8.3$ Hz, 1H), 7.91 (d, $J = 8.1$ Hz, 1H), 7.76-7.66 (m, 2H), 7.63 (dd, $J = 11.1$, 3.9 Hz, 1H), 7.46 (dd, $J = 14.3$, 7.2 Hz, 3H), 7.40-7.29 (m, 3H), 7.24-7.06 (m, 7H), 7.00 (d, $J = 8.3$ Hz, 2H), 6.79 (s, 1H), 5.55 (s, 1H), 4.22 (d, $J = 14.1$ Hz, 1H), 3.15 (d, $J = 14.0$ Hz, 1H); $^{13}$C NMR
(+)-N-((3S,4S)-3-cyclohexyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamid e (3ak): new compound, 89% yield, 90% ee, 85 mg, $[\alpha]_D^{20} = +361.47 \ (c \ 0.80, CHCl_3)$, colorless oil, Rf = 0.60 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.36 (d, $J = 8.3$ Hz, 1H), 7.86 (d, $J = 8.1$ Hz, 1H), 7.65 (dd, $J = 9.8, 5.5$ Hz, 2H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.52-7.42 (m, 3H), 7.40-7.26 (m, 5H), 7.19 (s, 1H), 7.17-7.08 (m, 3H), 5.64 (s, 1H), 2.24 (t, $J = 9.0$ Hz, 1H), 2.07 (d, $J = 12.6$ Hz, 1H), 1.68 (dd, $J = 19.5, 6.8$ Hz, 3H), 1.52 (d, $J = 9.9$ Hz, 1H), 1.17-0.83 (m, 5H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.1, 167.4, 145.0, 139.2, 135.5, 133.9, 131.6, 129.8, 128.7, 128.3, 128.0, 127.7, 127.1, 127.1, 126.8, 126.4, 125.7, 123.2, 121.3, 120.7, 66.9, 47.5, 44.8, 29.1, 29.0, 27.0, 26.7, 26.0. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 13.3 min and 14.9 min (maj). HRMS Calculated for C$_{32}$H$_{30}$NO$_3$ [M+H]$^+$ 476.2220, found 476.2226.

(+)-N-((3S,4S)-3-ethyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamide (3al): new compound, 95% yield, 90% ee, 80 mg, $[\alpha]_D^{20} = +677.79 \ (c \ 0.60, CHCl_3)$, pale yellow solid, mp = 79-80 °C, Rf = 0.65 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.47 (d, $J = 8.4$ Hz, 1H), 7.93 (d, $J = 8.1$ Hz, 1H), 7.72 (dd, $J = 7.9, 5.6$ Hz, 2H), 7.65 (t, $J = 7.4$ Hz, 1H), 7.49 (dd, $J = 7.3, 4.9$ Hz, 3H), 7.38 (dd, $J = 15.8, 7.9$ Hz, 2H), 7.20 (ddd, $J = 11.9, 5.9, 3.0$ Hz, 5H), 7.08 (dd, $J = 6.4, 2.7$ Hz, 2H), 6.96-6.74 (m, 3H), 5.61 (s, 1H), 4.21 (d, $J = 14.0$ Hz, 1H), 3.18 (d, $J = 13.9$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.5, 168.2, 162.4 (d, $J_{C,F} = 245.4$ Hz), 145.0, 135.1, 134.9, 134.2, 133.9 (d, $J_{C,F} = 3.2$ Hz), 131.9, 130.1, 130.0 (d, $J_{C,F} = 8.1$ Hz), 128.9, 128.6, 128.2, 127.7, 127.5, 126.9, 126.8, 126.6, 125.8, 123.3, 121.2, 120.1, 115.9 (d, $J_{C,F} = 21.3$ Hz), 66.2, 50.0, 38.6; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -114.11. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 10.9 min and 14.4 min (maj). HRMS Calculated for C$_{33}$H$_{25}$FNO$_3$ [M+H]$^+$ 502.1813, found 502.1818.
(+)–N–((3S,4S)-3-benzyl-2-oxo-4-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-benzo[\text{h}]chromen-3-yl)benzamide (3ca): new compound, 95% yield, 95% ee, 105 mg, $\alpha^2$D = +312.78 (c 1.0, CHCl$_3$), yellow solid, mp = 160-161 °C, R$_f$ = 0.65 (hexanes/ethyl acetate 5/1). 1H NMR (400 MHz, CDCl$_3$) $\delta$ 8.47 (d, $J$ = 8.3 Hz, 1H), 7.92 (d, $J$ = 8.1 Hz, 1H), 7.79-7.68 (m, 2H), 7.65 (dd, $J$ = 11.0, 1.3 Hz), 7.59-7.32 (m, 10H), 7.24-7.15 (m, 3H), 7.06 (dd, $J$ = 6.4, 2.9 Hz, 2H), 6.85 (s, 1H), 4.21 (d, $J$ = 14.0 Hz, 1H), 3.18 (d, $J$ = 14.0 Hz, 1H); 13C NMR (100 MHz, CDCl$_3$) $\delta$ 168.3, 168.3, 145.1, 142.2, 134.9, 134.6, 135.3, 131.2, 130.1, 130.1, 129.4, 129.3, 127.7, 127.6, 126.9, 126.4, 126.0 (q, $J$ = 7.6 Hz), 125.4, 123.3, 122.7, 121.2, 119.4, 65.9, 50.5, 38.7; 19F NMR (376 MHz, CDCl$_3$) $\delta$ -62.69. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 8.1 min and 10.5 min (maj). HRMS Calculated for C$_{34}$H$_{25}$F$_3$NO$_3$ [M+H]$^+$ 552.1781, found 552.1769.

(+)–N–((3S,4S)-3-benzyl-2-oxo-4-(p-tolyl)-3,4-dihydro-2H-benzo[\text{h}]chromen-3-yl)benzamide (3da): new compound, 94% yield, 95% ee, 94 mg, $\alpha^2$D = +234.38 (c 0.50, CHCl$_3$), white solid, mp = 210-211 °C, R$_f$ = 0.70 (hexanes/ethyl acetate 10/1). 1H NMR (400 MHz, CDCl$_3$) $\delta$ 8.45 (d, $J$ = 8.3 Hz, 1H), 7.90 (d, $J$ = 8.1 Hz, 1H), 7.70 (t, $J$ = 7.4 Hz, 2H), 7.62 (t, $J$ = 7.5 Hz, 1H), 7.46 (dd, $J$ = 8.2, 6.9 Hz, 3H), 7.35 (dd, $J$ = 7.7, 6.0 Hz, 3H), 7.20 (dd, $J$ = 4.8, 1.5 Hz, 3H), 7.12-7.03 (m, 4H), 6.96 (d, $J$ = 8.0 Hz, 2H), 6.81 (s, 1H), 5.55 (s, 1H), 4.21 (d, $J$ = 14.0 Hz, 1H), 3.16 (d, $J$ = 14.0 Hz, 1H), 2.19 (s, 3H); 13C NMR (100 MHz, CDCl$_3$) $\delta$ 168.7, 168.2, 145.0, 137.7, 135.5, 135.1, 135.0, 134.1, 131.7, 130.2, 129.7, 128.8, 128.6, 128.2, 128.1, 127.6, 127.3, 127.0, 126.7, 125.7, 123.4, 121.2, 120.6, 66.2, 50.4, 38.6, 21.2. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 14.7 min and 16.6 min (maj). HRMS Calculated for C$_{34}$H$_{28}$NO$_3$ [M+H]$^+$ 498.2064, found 498.2069.

(+)–N–((3S,4S)-3-benzyl-2-oxo-4-(m-tolyl)-3,4-dihydro-2H-benzo[\text{h}]chromen-3-yl)benzamide (3ea): new compound, 89% yield, 96% ee, 88 mg, $\alpha^2$D = +337.98 (c 1.0, CHCl$_3$), white solid, mp = 206-207 °C, R$_f$ = 0.65 (hexanes/ethyl acetate 10/1). 1H NMR (400 MHz, CDCl$_3$) $\delta$ 8.46 (d, $J$ = 8.3 Hz, 1H), 7.91 (d, $J$ = 8.1 Hz, 1H), 7.70 (t, $J$ = 7.4 Hz, 2H), 7.62 (t, $J$ = 7.5 Hz, 1H), 7.46 (dd, $J$ = 8.2, 6.9 Hz, 3H), 7.35 (dd, $J$ = 7.7, 6.0 Hz, 3H), 7.20 (dd, $J$ = 4.8, 1.5 Hz, 3H), 7.12-7.03 (m, 4H), 6.96 (d, $J$ = 8.0 Hz, 2H), 6.81 (s, 1H), 5.55 (s, 1H), 4.21 (d, $J$ = 14.0 Hz, 1H), 3.16 (d, $J$ = 14.0 Hz, 1H), 2.19 (s, 3H); 13C NMR (100 MHz, CDCl$_3$) $\delta$ 168.7, 168.2, 145.0, 137.7, 135.5, 135.1, 135.0, 134.1, 131.7, 130.2, 129.7, 128.8, 128.6, 128.2, 128.1, 127.6, 127.3, 127.0, 126.7, 125.7, 123.4, 121.2, 120.6, 66.2, 50.4, 38.6, 21.2. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 14.1 min and 16.4 min (maj). HRMS Calculated for C$_{34}$H$_{28}$NO$_3$ [M+H]$^+$ 498.2064, found 498.2072.

(+)–N–((3S,4S)-3-benzyl-2-oxo-4-(o-tolyl)-3,4-dihydro-2H-benzo[\text{h}]chromen-3-yl)benzamide (3fa): new compound, 95% yield, 91% ee, 95 mg, $\alpha^2$D = +327.38 (c 1.0, CHCl$_3$), white solid, mp = 160-161 °C, R$_f$ = 0.65 (hexanes/ethyl acetate 10/1). 1H NMR (400 MHz, CDCl$_3$) $\delta$ 8.45 (d, $J$ = 8.4 Hz, 1H), 7.86 (d, $J$ = 8.1 Hz, 1H), 7.63 (t, $J$ = 14.5, 7.2 Hz, 3H), 7.44-7.27 (m, 6H), 7.22 (dd, $J$ =

S7
5.1, 1.6 Hz, 3H), 7.10 (dd, J = 6.8, 2.6 Hz, 3H), 7.00 (dd, J = 5.8, 3.5 Hz, 3H), 6.80 (s, 1H), 5.79 (s, 1H), 4.38 (d, J = 13.9 Hz, 1H), 3.25 (d, J = 13.9 Hz, 1H), 2.72 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ 169.3, 168.0, 144.1, 137.9, 136.9, 135.4, 134.9, 133.9, 131.7, 131.6, 130.2, 128.7, 128.6, 128.0, 127.6, 127.5, 127.3, 127.2, 127.1, 127.0, 126.8, 126.2, 125.6, 123.6, 121.4, 121.2, 65.3, 47.3, 38.9, 20.4. HPLC: Chiralcel IA column, 254 nm, 30 °C, n-hexane/i-propanol = 80/20, flow = 0.7 mL/min, retention time 10.9 min and 17.3 min (maj). HRMS Calculated for C₁₃H₁₂NO₃ [M+H]^+ 498.2064, found 498.2069.

(+)-N-((3S,4S)-3-benzyl-4-(3,5-dimethylphenyl)-2-oxo-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamide (3ga): new compound, 97% yield, 97% ee, 99 mg, [α]₂⁰_D = +171.79 (c 1.0, CHCl₃), white solid, mp = 181-182 °C, Rₚ = 0.55 (hexanes/ethyl acetate 10/1). ¹H NMR (400 MHz, CDCl₃) δ 8.46 (d, J = 8.3 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.71 (t, J = 7.1 Hz, 2H), 7.63 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 6.5 Hz, 3H), 7.40-7.29 (m, 3H), 7.22 (dd, J = 5.0, 1.6 Hz, 3H), 7.08 (dd, J = 6.6, 2.5 Hz, 2H), 6.88-6.57 (m, 4H), 5.48 (s, 1H), 4.24 (d, J = 14.0 Hz, 1H), 3.14 (d, J = 14.0 Hz, 1H), 2.10 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 168.7, 168.5, 145.2, 138.5, 138.5, 137.7, 135.7, 135.2, 134.1, 131.7, 130.2, 129.8, 128.6, 128.1, 127.6, 127.3, 126.9, 126.1, 125.6, 123.4, 121.3, 120.4, 66.3, 50.6, 38.6, 21.4. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 12.3 min (maj) and 15.3 min. HRMS Calculated for C₃₅H₃₀NO₃ [M+H]^+ 512.2220, found 512.2222.

(+)-N-((3S,4S)-3-benzyl-4-(3,5-dimethoxyphenyl)-2-oxo-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamide (3ha): new compound, 94% yield, 96% ee, 102 mg, [α]₂⁰_D = +230.82 (c 0.60, CHCl₃), pale yellow solid, mp = 178-179 °C, Rₚ = 0.50 (hexanes/ethyl acetate 5/1). ¹H NMR (400 MHz, CDCl₃) δ 8.44 (d, J = 8.3 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.69 (dd, J = 11.7, 4.6 Hz, 2H), 7.65-7.57 (m, 1H), 7.54-7.44 (m, 3H), 7.37 (t, J = 7.7 Hz, 3H), 7.23-7.16 (m, 3H), 7.06 (dd, J = 6.5, 2.9 Hz, 2H), 6.88 (s, 1H), 6.36 (d, J = 2.2 Hz, 2H), 6.23 (s, 1H), 5.50 (s, 1H), 4.22 (d, J = 14.0 Hz, 1H), 3.57 (s, 6H), 3.14 (d, J = 13.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 168.5, 168.2, 161.0, 145.1, 140.2, 135.2, 135.0, 134.2, 131.9, 130.2, 128.8, 128.6, 128.1, 127.6, 127.4, 127.3, 127.0, 126.6, 125.7, 123.4, 121.3, 120.1, 106.4, 100.0, 66.1, 55.4, 50.8, 38.6. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 26.0 min (maj) and 48.8 min. HRMS Calculated for C₃₅H₃₀NO₅ [M+H]^+ 544.2118, found 544.2111.

(+)-N-((3S,4S)-3-benzyl-4-ethyl-2-oxo-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamide (3ia): new compound, 91% yield, 85% ee, 79 mg, [α]₂⁰_D = +2.08 (c 0.60, CHCl₃), white solid, mp = 142-143 °C, Rₚ = 0.60 (hexanes/ethyl acetate 10/1). ¹H NMR (400 MHz, CDCl₃) δ 8.35 (d, J = 8.3 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.69-7.51 (m, 3H), 7.47 (t, J = 7.5 Hz, 2H), 7.40 (d, J = 8.3 Hz, 1H), 7.23 (s, 1H), 7.19 (dd, J = 4.9, 1.7 Hz, 3H), 6.97 (dd, J = 6.5, 2.9 Hz, 2H), 4.33 (dd, J = 10.1, 3.9 Hz, 1H), 3.85 (d, J = 14.0 Hz, 1H), 2.97 (d, J = 14.0 Hz, 1H), 1.95 (dd, J = 13.5, 7.5, 3.9 Hz, 1H), 1.43 (ddd, J = 13.6, 10.1, 7.2 Hz, 1H), 0.88 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 169.7, 167.2, 142.4, 135.1, 134.7, 134.0, 132.1, 130.1, 129.0, 128.8, 128.6, 128.1, 127.6, 127.4, 127.3, 127.0, 126.6, 125.7, 123.4, 121.3, 120.1, 106.4, 100.0, 66.1, 55.4, 50.8, 38.6. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 26.0 min (maj) and 48.8 min. HRMS Calculated for C₃₅H₃₀NO₅ [M+H]^+ 544.2118, found 544.2111.
128.5, 128.0, 127.5, 127.2, 127.0, 124.8, 123.3, 121.0, 120.6, 65.0, 45.5, 38.4, 24.4, 11.2. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 11.5 min and 14.6 min (maj). HRMS Calculated for C$_{29}$H$_{28}$NO$_3$ [M+H]$^+$ 436.1907, found 436.1909.

(+)-N-(3S,4S)-3-benzyl-7-methoxy-2-oxo-4-phenylchroman-3-yl)benzamide (3ja): new compound, 97% yield, 90% ee, 90 mg, [$\alpha$]$^D_{20}$ = +52.50 (c 0.6, CHCl$_3$), white solid, mp = 137-138 °C, R$_f$ = 0.75 (hexanes/ethyl acetate 4/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.42 (dd, J = 15.8, 7.3 Hz, 3H), 7.32 (t, J = 7.6 Hz, 2H), 7.24-7.11 (m, 9H), 7.07 (dd, J = 6.6, 2.8 Hz, 2H), 6.85 (d, J = 2.4 Hz, 1H), 6.76 (dd, J = 8.4, 2.5 Hz, 1H), 6.71 (s, 1H), 5.40 (s, 1H), 4.17 (d, J = 14.0 Hz, 1H), 3.87 (s, 3H), 3.13 (d, J = 14.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.6, 168.2, 160.6, 151.0, 138.9, 135.5, 135.1, 131.7, 130.8, 130.1, 129.0, 128.8, 128.6, 128.0, 127.8, 127.6, 126.9, 117.3, 112.0, 102.3, 66.3, 55.9, 49.7, 38.6. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 7.4 min and 9.3 min (maj). HRMS Calculated for C$_{29}$H$_{28}$NO$_4$ [M+H]$^+$ 464.1856, found 464.1867.

(+)-N-(3S,4S)-3-benzyl-6-methoxy-2-oxo-4-phenylchroman-3-yl)benzamide (3ka): new compound, 97% yield, 93% ee, 90 mg, [$\alpha$]$^D_{20}$ = +54.68 (c 0.64, CHCl$_3$), white solid, mp = 122-123 °C, R$_f$ = 0.50 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.42 (dt, J = 8.5, 4.4 Hz, 3H), 7.33 (t, J = 7.6 Hz, 2H), 7.26-7.11 (m, 9H), 7.07 (dd, J = 6.6, 2.9 Hz, 2H), 6.93 (dd, J = 8.9, 3.0 Hz, 1H), 6.81 (d, J = 2.9 Hz, 1H), 6.74 (s, 1H), 5.42 (s, 1H), 4.16 (d, J = 14.0 Hz, 1H), 3.79 (s, 3H), 3.13 (d, J = 13.9 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.6, 168.3, 157.3, 157.3, 144.1, 138.3, 135.4, 135.1, 131.2, 130.1, 129.0, 128.8, 128.6, 128.1, 128.0, 127.6, 126.9, 126.3, 117.6, 115.2, 114.5, 66.1, 55.9, 50.5, 38.4. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 7.5 min and 9.2 min (maj). HRMS Calculated for C$_{29}$H$_{28}$NO$_4$ [M+H]$^+$ 464.1856, found 464.1867.

(+)-N-((7S,8S)-7-benzyl-8-(4-methoxyphenyl)-6-oxo-7,8-dihydro-6H-[1,3]dioxololo[4,5-g]chromen-7-yl)benzamide (3la): known compound, 88% yield, 92% ee, 101 mg, [$\alpha$]$^D_{20}$ = +104.73 (c 0.19, CH$_2$Cl$_2$) [lit.$^4$: (+)-(7R,8R) [$\alpha$]$^D_{20}$ = -203.2 (c 0.19, CH$_2$Cl$_2$) for 91% ee], pale yellow solid, R$_f$ = 0.50 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.52-7.41 (m, 3H), 7.39-7.30 (m, 2H), 7.25-7.15 (m, 3H), 7.06 (d, J = 8.5 Hz, 4H), 6.82 (s, 1H), 6.76-6.64 (m, 4H), 6.01 (d, J = 15.2 Hz, 2H), 5.29 (s, 1H), 4.14 (d, J = 14.0 Hz, 1H), 3.69 (s, 3H), 3.17 (d, J = 14.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.6, 168.2, 159.2, 148.2, 145.5, 144.5, 135.3, 135.2, 131.8, 130.3, 129.1, 128.8, 128.6, 127.6, 126.9, 117.9, 114.3, 108.2, 102.2, 98.7, 66.1, 55.4, 49.3, 38.3. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 80/20, flow = 0.7 mL/min, retention time 9.7 min and 11.2 min (maj).

(+)-N-((3S,4S)-3-benzyl-2-oxo-4-phenylchroman-3-yl)benzamide (3ma): new compound, 95% yield, 84% ee, 82 mg, [$\alpha$]$^D_{20}$ = +148.32 (c 0.30, CHCl$_3$), white solid, mp = 69-70 °C, R$_f$ = 0.65 (hexanes/ethyl acetate 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.49-7.37 (m, 4H), 7.37-7.28 (m, 4H), 7.24-7.11 (m, 9H), 7.07 (dd, J = 6.6, 2.9 Hz, 2H), 6.73 (s, 1H), 5.48 (s, 1H), 4.18 (d, J = 14.0 Hz, 1H), 3.11 (d, J = 14.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.6, 168.2, 150.3, 138.4, 135.4, 131.8, 130.3, 129.1, 128.8, 128.6, 127.6, 126.9, 117.9, 114.3, 108.2, 102.2, 98.7, 66.1, 55.4, 49.3, 38.3. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 7.4 min and 9.3 min (maj).
135.0, 131.8, 130.3, 129.5, 129.0, 128.8, 128.1, 127.9, 127.6, 126.9, 126.0, 125.4, 116.7, 66.1, 50.3, 38.5. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, n-hexane/i-propanol = 90/10, flow = 0.8 mL/min, retention time 6.5 min and 7.4 min (maj). HRMS Calculated for C_{29}H_{24}NO_{3} \[M+H]\^+ 434.1751, found 434.1750.

(+)-N-((3S,4S)-3-ethyl-2-oxo-4-(p-tolyl)-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamide (3dl): new compound, 90% yield, 84% ee, 78 mg, [\(\alpha\)]{\(^{20}\)}D = +358.14 (c 0.60, CHCl\(_3\)), yellow solid, mp = 240-241 °C, Rf = 0.65 (hexanes/ethyl acetate 5/1). 1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.34 (d, \(J\) = 8.3 Hz, 1H), 7.85 (d, \(J\) = 8.0 Hz, 1H), 7.68-7.53 (m, 5H), 7.48 (t, \(J\) = 7.4 Hz, 1H), 7.39 (t, \(J\) = 7.5 Hz, 2H), 7.27 (d, \(J\) = 8.4 Hz, 1H), 7.04 (d, \(J\) = 8.0 Hz, 3H), 6.95 (d, \(J\) = 8.0 Hz, 2H), 5.35 (s, 1H), 2.94 (dq, \(J\) = 15.1, 7.6 Hz, 1H), 2.20 (s, 3H), 1.94 (dq, \(J\) = 14.5, 7.3 Hz, 1H), 0.92 (t, \(J\) = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 169.8, 167.5, 145.1, 137.6, 135.4, 135.1, 134.0, 131.8, 129.7, 128.8, 128.0, 127.1, 127.0, 126.8, 125.5, 123.2, 121.3, 120.5, 65.5, 50.5, 26.4, 21.2, 9.0. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 12.6 min and 14.2 min (maj). HRMS Calculated for C_{30}H_{28}NO_{5} \[M+H]\^+ 482.1962, found 482.1961.

(+)-N-((3S,4S)-4-(3,5-dimethoxyphenyl)-3-ethyl-2-oxo-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamide (3hl): new compound, 95% yield, 88% ee, 91 mg, [\(\alpha\)]{\(^{20}\)}D = +312.88 (c 1.0, CHCl\(_3\)), yellow oil, Rf = 0.50 (hexanes/ethyl acetate 5/1). 1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.34 (d, \(J\) = 8.2 Hz, 1H), 7.87 (d, \(J\) = 8.0 Hz, 1H), 7.70-7.58 (m, 5H), 7.51 (t, \(J\) = 7.2 Hz, 1H), 7.42 (t, \(J\) = 7.4 Hz, 2H), 7.31 (d, \(J\) = 8.4 Hz, 1H), 7.11 (s, 1H), 6.34 (d, \(J\) = 1.6 Hz, 2H), 6.26 (s, 1H), 5.32 (s, 1H), 3.57 (s, 6H), 2.97 (dq, \(J\) = 14.9, 7.5 Hz, 1H), 1.95 (dt, \(J\) = 14.5, 7.2 Hz, 1H), 0.94 (t, \(J\) = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 169.5, 167.4, 161.0, 145.2, 140.7, 140.0, 134.9, 134.0, 131.9, 128.9, 128.0, 127.2, 127.1, 127.0, 126.6, 125.5, 123.2, 121.3, 120.0, 106.2, 100.0, 65.4, 55.3, 50.9, 26.5, 9.0. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 22.6 min (maj) and 30.9 min. HRMS Calculated for C_{33}H_{28}NO_{5} \[M+H]\^+ 492.1962, found 482.1961.

(+)-N-((3S,4S)-3-cyclohexyl-2-oxo-4-(p-tolyl)-3,4-dihydro-2H-benzo[h]chromen-3-yl)benzamide (3dk): new compound, 92% yield, 85% ee, 90 mg, [\(\alpha\)]{\(^{20}\)}D = +314.28 (c 1.0, CHCl\(_3\)), yellow oil, Rf = 0.65 (hexanes/ethyl acetate 5/1). 1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.36 (d, \(J\) = 8.3 Hz, 1H), 7.87 (d, \(J\) = 8.0 Hz, 1H), 7.70-7.58 (m, 5H), 7.51 (t, \(J\) = 7.2 Hz, 1H), 7.42 (t, \(J\) = 7.4 Hz, 2H), 7.31 (d, \(J\) = 8.4 Hz, 1H), 7.11 (s, 1H), 6.34 (d, \(J\) = 1.6 Hz, 2H), 6.26 (s, 1H), 5.32 (s, 1H), 3.57 (s, 6H), 2.97 (dq, \(J\) = 14.9, 7.5 Hz, 1H), 1.95 (dt, \(J\) = 14.5, 7.2 Hz, 1H), 0.94 (t, \(J\) = 7.4 Hz, 3H); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.2, 167.4, 145.0, 137.4, 136.1, 135.6, 133.8, 131.5, 129.5, 128.7, 128.2, 128.0, 127.0, 127.0, 126.9, 126.4, 125.7, 123.2, 121.3, 120.9, 67.0, 47.0, 44.8, 29.2, 29.0, 27.0, 26.7, 26.0, 21.1. HPLC: Chiralcel IC column, 254 nm, 30 °C, n-hexane/i-propanol = 98/2, flow = 0.7 mL/min, retention time 8.0 min (maj) and 8.9 min. HRMS Calculated for C_{33}H_{32}NO_{3} \[M+H]\^+ 490.2377, found 490.2376.
4. The determination of Absolute Configuration of (+)-3af

The n-hexane (5 mL) and toluene (0.5 mL) was slowly added into solution of (+)-N-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-benzo[h]chromen-3-yl)-3,5-dimethylbenzamide (3af) in dichloromethane (0.5 mL), then the solvent was slowly evaporated and single crystal of 3af was obtained after 4 days. The structure showed the absolute configuration of (+)-3af is (3S,4S). The CCDC number is 1516157. These details can be obtained free of charge via www.ccdc.com.ac.uk/data_request/cif from the Cambridge Crystallographic Data Centre.

X-ray Single Crystal Structure of 3,4-dihydrocoumarin (+)-3af

5. References


6. Copy of NMR and HPLC for the Compounds

1H NMR 8.9-2.9 in CDCl3

1c 1H NMR (400 MHz, CDCl3)
$^{13}$C NMR (100 MHz, CDCl$_3$)

**1c** $^{13}$C NMR (100 MHz, CDCl$_3$)
$^{19}$F NMR BW-8-29 in CDCl$_3$

$^{19}$F NMR (376 MHz, CDCl$_3$)

[Chemical structure image]
1H NMR (400 MHz, CDCl3)
13C NMR BW-9-26 in CDCl3

1g $^{13}$C NMR (100 MHz, CDCl3)
1H NMR (400 MHz, CDCl₃)
$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (100 MHz, CDCl$_3$)

S20
$^{13}$C NMR JZ-4-91A in CDCl$_3$

3aa $^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR JZ-4-91B in CHCl$_3$
$^{13}$C NMR JZ-4-918 in CDCl$_3$
$^{1}H$ NMR 49°C in CDCl₃

3ac $^{1}H$ NMR (400 MHz, CDCl₃)
$^{19}$F NMR 3Z-4-91C in CDCl$_3$

$^{3}$ac $^{19}$F NMR (378 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR JZ-4-99A in CDCl₃
$^1$H NMR JZ-4-99B in CDCl$_3$
$^{13}$C NMR JZ-4-99C in CDCl$_3$

$^{13}$C NMR (100 MHz, CDCl$_3$)
19F NMR JZ-4-99B in CDC13

3ae $^{19}$F NMR (376 MHz, CDC13)
$^1$H NMR JZ-4-99C in CDCl$_3$

$3af$ $^1$H NMR (400 MHz, CDCl$_3$)
$^1$H NMR, J2-5-4A in CDCl$_3$

3ag $^1$H NMR (400 MHz, CDCl$_3$)

S35
$^{13}$C NMR JZ-S-4A in CDCl$_3$

$3ag$ $^{13}$C NMR (100 MHz, CDCl$_3$)
$3_{7}$

$1H$ NMR JZ-5-21A in CDCl$_3$

$3_{ah}^1H$ NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR JZ-5-21A in CDCl$_3$
1H NMR (400 MHz, CDCl3)

3ai 1H NMR (400 MHz, CDCl3)
$^{13}$C NMR JZ-5-4B in CDCl$_3$
1H NMR (400 MHz, CDCl₃)
$^{13}$C NMR JZ-5-11B in CDCl$_3$
$^{1}H$ NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR JZ-6-49B in CDC$_3$

3a$k^{13}$C NMR (100 MHz, CDC$_3$)
$^1$H NMR J2-6-548 in CDCl$_3$
$^{13}$C NMR $^{13}$C NMR (100 MHz, CDCl$_3$)
1H NMR J2-5 41A in CDCl3

3ba 1H NMR (400 MHz, CDCl3)
$^{19}$F NMR JZ-5-41A in CDCl$_3$
$^{1}H$ NMR of 3ca in CDCl$_3$

![NMR spectrum of 3ca](image-url)
13C NMR JZ-5-32A in CDC13

3ca $^1$C NMR (100 MHz, CDC13)
$^{19}$F NMR JZ-5-32A in CDCl$_3$

3ca $^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR JZ-5-34A in CDCl$_3$

3da $^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR JZ-S-34A in CDCl$_3$
$^{1}$H NMR (400 MHz, CDCl$_3$)
$\text{1H NMR JZ-5-34C in CDCl}_3$

$\text{3fa }^1\text{H NMR (400 MHz, CDCl}_3)$
$^{13}$C NMR JZ-5-34C in CDCl$_3$
$\text{H NMR JZ-S-34D in CDCl}_3$
1H NMR of 3ha in CDCl₃
$^{13}$C NMR JZ-5-418 in CDCl$_3$

3ha

$^{13}$C NMR (100 MHz, CDCl$_3$)
1H NMR JZ-5-48A in CDCl₃

3ia ¹H NMR (400 MHz, CDCl₃)
$^{13}$C NMR JZ-S-48A in CDCl$_3$
$^{1}H$ NMR J2=5-89A in CDCl$_3$

3ja $^1H$ NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR JZ-5-89A in CDCl$_3$
$^{1}H$ NMR of 3ka in CDCl$_3$
1H NMR JZ-S-568 in CDCl3

$3\text{la}^1\text{H NMR (400 MHz, CDCl}_{3}\text{)}$
$^{1}$H NMR JZ-5-78 in CDCl$_3$

3ma $^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR J2-S-78 in CDCl$_3$

$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR [2-H-92C] in CDCl$_3$
$^{13}$C NMR J2-6-92C in CDCl$_3$
$^1$H NMR JZ-7-4A in CDCl$_3$
$^{13}$C NMR JZ-7-4A in CDCl$_3$
$^1$H NMR: JZ-7-48 in CDCl$_3$

$3d$ $^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR JZ-7-48 in CDCl$_3$

3dk $^{13}$C NMR (100 MHz, CDCl$_3$)
Sorted By: Signal
Multiplier: 1.0000
Division: 1.0000
Use Multiplier x Division Factor with ID/ID

Signal 1: WDI A, Wavelength=234 nm

Peak RetTime Type Width Area Height Area
1 3.007 TN 0.2024 4033.2 296.2 3870.5 30.0
2 12.115 BT 0.3299 4544.7061 154.82287 40.9362

Totals: 9380.10252 4313.2434

S87
Data File (1\(\text{CHEM}\).321\(\text{DATA}\)A1B00-16\(\text{V1M002555.D}

Sample Name: 2D-0-8M(+-)

---

Acq. Operator: 
Acq. Instrument: Instrument 1 
Location: Vial 1 
Injection Date: 9/7/2016 9:00:14 AM 
Acq. Method: C1\(\text{CHEM}\).321\(\text{METHOD}\)_LC.M 
Last changed: 9/7/2016 12:00:22 AM 
(modified after loading)

Analysis Method: C1\(\text{CHEM}\).321\(\text{METHOD}\)_LC.M 
Last changed: 10/27/2016 9:00:20 PM by 0 
(modified after loading)

Sample Info: 
2C, Hexane/1-TFAH \(\times \) 900, 0.7 mL/min, 300C, 254 nm

---

Sorted By: Signal 
Multiplier: 1.0000 
Dilution: 1.0000 
Use Multiplier \& Dilution Factor with Isotopes

Signal 1: VWD A, Wavelength=254 nm 

Peak RetTime Type Width Area Height Area 
# (min) (min) % tot % fa % fa % fa % fa % fa % fa % fa
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
1 35.77E-05 0.7055 3365.25147 35.14433 50.3661
2 47.49E-05 1.3661 3316.79391 37.88858 40.6359

Totals: 6691.6069 102.7078

---

*** End of Report ***

---

Data File (1\(\text{CHEM}\).321\(\text{DATA}\)A1B00-16\(\text{V1M002555.D}

Sample Name: 2D-0-8M(+-)

---

Acq. Operator: 
Acq. Instrument: Instrument 1 
Location: Vial 1 
Injection Date: 9/9/2016 8:41:00 AM 
Acq. Method: C1\(\text{CHEM}\).321\(\text{METHOD}\)_LC.M 
Last changed: 9/9/2016 9:31:29 AM 
(modified after loading)

Analysis Method: C1\(\text{CHEM}\).321\(\text{METHOD}\)_LC.M 
Last changed: 10/27/2016 9:18:10 PM by 0 
(modified after loading)

Sample Info: 
2C, Hexane/1-TFAH \(\times \) 900, 0.7 mL/min, 300C, 254 nm

---

Sorted By: Signal 
Multiplier: 1.0000 
Dilution: 1.0000 
Use Multiplier \& Dilution Factor with Isotopes

Signal 1: VWD A, Wavelength=254 nm 

Peak RetTime Type Width Area Height Area 
# (min) (min) % tot % fa % fa % fa % fa % fa % fa % fa % fa % fa
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
1 26.02E-05 0.9223 3289.94946 65.79586 35.9127
2 48.06E-05 1.4037 67.26708 7.294081-1 1.9425

Totals: 3466.73628 63.91469

---

*** End of Report ***

---

Instrument 1 10/27/2016 9:00:46 PM 0

Page 1 of 4

---

Instrument 1 10/27/2016 9:15:05 PM 0

Page 1 of 1

S97