Silver-catalyzed cascade radical cyclization of 2-(allyloxy)arylmethanols with cyclopropanols: access to chroman-4-one derivatives

Jie Sheng, a Jidan Liu, *a,b Liuqing Chen, a Lingling Zhang, a Liyao Zheng a and Xingchuan Wei a

a School of Chemistry and Chemical Engineering, Guangzhou University, Guangzhou, 510006, P. R. China. E-mail: jdliu@gzhu.edu.cn
b Key Laboratory of Functional Molecular Engineering of Guangdong Province, South China University of Technology, Guangzhou 510640, P. R. China

Supporting Information

Table of contents

1. General information and starting materials……………………………………...S1
2. Optimization of reaction conditions………………………………………………...S1
3. General procedure for the synthesis of products 3…………………………...S3
4. Control experiments………………………………………………………………...S3
5. Characterization data of products…………………………………………………...S5
1. General information and starting materials

$^1$H NMR and $^{13}$C NMR were recorded in CDCl$_3$ at room temperature on the Bruker spectrometer (500 MHz $^1$H). The chemical-shifts scale is based on internal TMS. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; qui, quintet; sxt, sextet. The coupling constants, $J$ are reported in Hertz (Hz). If not stated otherwise, all melting points are uncorrected. Mass spectroscopy data were collected on an HRMS-ESI instrument. Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Glassware was dried for 4 h at 140 °C. All solvents were purified and dried according to standard methods prior to use. Products were purified by flash column chromatography on 200-300 mesh silica gel, SiO$_2$. 2-(Allyloxy)arylaldehyde derivatives 1 were prepared according to previous reports, spectral properties are consistent with literature values.$^1$ All cyclopropanols 2 were prepared by the addition of Grignard reagent according to the reported procedure.$^2$ Tertiary cyclobutanol 2t and cyclopentanol 2u were prepared by the addition of Grignard reagent to the corresponding cycloketones according to the reported procedure.$^3$

2. Optimization of reaction conditions
Optimization of reaction conditions

\[
\begin{array}{c}
\text{HO} \\
1a \\
\text{H} \\
\end{array} + \begin{array}{c}
\text{HO} \\
2a \\
\text{Ph} \\
\end{array} \xrightarrow{\text{Cat. Oxidant \ Solvent, T(°C)}} \begin{array}{c}
\text{HO} \\
3a \\
\text{Ph} \\
\end{array}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat.</th>
<th>Oxidant</th>
<th>Solvent</th>
<th>Yield* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AgNO₃</td>
<td>K₂S₂O₈</td>
<td>DMSO/H₂O (1:1)</td>
<td>42% &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>2</td>
<td>AgNO₃</td>
<td>(NH₄)₂S₂O₈</td>
<td>DMSO/H₂O (1:1)</td>
<td>54% &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>3</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>76% &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>4</td>
<td>AgNO₃</td>
<td>Oxone</td>
<td>DMSO/H₂O (1:1)</td>
<td>trace &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>5</td>
<td>AgNO₃</td>
<td>Ph(ΟAc)₂</td>
<td>DMSO/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a</td>
</tr>
<tr>
<td>6</td>
<td>AgNO₃</td>
<td>TBHP</td>
<td>DMSO/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>7</td>
<td>AgNO₃</td>
<td>DTBP</td>
<td>DMSO/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>8</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMF/H₂O (1:1)</td>
<td>45% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>9</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>CH₃CN/H₂O (1:1)</td>
<td>8% &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>10</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>THF/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>11</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DCM/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>12</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>Toluene/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>13</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (2:1)</td>
<td>50% &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>14</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:2)</td>
<td>31% &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>15</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO</td>
<td>30% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>16</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>H₂O</td>
<td>5% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>17</td>
<td>AgOAc</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>64% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>18</td>
<td>Ag₂O</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>37% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>19</td>
<td>Cul</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>20</td>
<td>Cu(OAc)₂</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>21</td>
<td>FeCl₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>12% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>22</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>45% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>23</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>74% &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>24</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>56% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>25</td>
<td>AgNO₃</td>
<td>Na₂S₂O₅</td>
<td>DMSO/H₂O (1:1)</td>
<td>70% &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>26</td>
<td>AgNO₃</td>
<td>—</td>
<td>DMSO/H₂O (1:1)</td>
<td>16% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
<tr>
<td>27</td>
<td>AgNO₃</td>
<td>—</td>
<td>DMSO/H₂O (1:1)</td>
<td>0% &amp; recovery of 1a &amp; ring-opening of 2a</td>
</tr>
</tbody>
</table>

* Reaction conditions: 1a (0.2 mmol), 2a (0.3 mmol), catalyst (20 mol%), oxidant (0.6 mmol), solvent (2 mL) at 70 °C for 12 h. † Isolated yield. ‡ Na₂S₂O₅ (0.40 mmol). § Na₂S₂O₅ (0.80 mmol).

At 60 °C. ‡ At 80 °C.

![Chemical structure](image)

2-(Allyloxy)arylaldehyde derivatives 1 (0.2 mmol), cyclopropanols 2 (0.3 mmol), AgNO₃ (20 mol%) and Na₂S₂O₈ (3 equiv.) were added to a 25-mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then 2 ml of DMSO/H₂O (v/v = 1:1) was added under a nitrogen atmosphere. After being stirred at 70 °C for 12 h, 10 mL ethyl acetate and 20 mL water were added to quench the reaction mixture. The organic layer was separated and the aqueous phase was extracted twice with ethyl acetate. The combined organic layer was washed with brine and dried over sodium sulfate. Concentration in vacuo followed by silica gel column purification with petroleum ether/ethyl acetate eluent to afford products 3.

4. Control experiments.

![Chemical structures](image)
Reference


3-(4-oxo-4-phenylbutyl)chroman-4-one (3a)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 76% yield;

**M.p. = 96-97 °C;**

\[ \text{H NMR (500 MHz, CDCl}_3\]: \( \delta \) 7.96-7.92 (m, 2H), 7.88 (dd, \( J \) = 7.9, 1.7 Hz, 1H), 7.55 (dd, \( J \) = 10.5, 4.3 Hz, 1H), 7.47-4.43 (m, 3H), 7.03-6.98 (m, 1H), 6.95 (d, \( J \) = 8.3 Hz, 1H), 4.56 (dd, \( J \) = 11.5, 4.5 Hz, 1H), 4.30 (dd, \( J \) = 11.5, 8.9 Hz, 1H), 3.03 (tt, \( J \) = 7.0 Hz, 2H), 2.74-2.69 (m, 1H), 2.00-1.80 (m, 3H), 1.65-1.59 (m, 1H);

\[ \text{C NMR (125 MHz, CDCl}_3\]: \( \delta \) 199.55, 194.16, 161.45, 136.84, 135.71, 132.99, 128.55, 127.95, 127.34, 121.31, 120.54, 117.66, 70.35, 45.78, 38.22, 25.88, 21.51;


3-(4-oxo-4-(p-tolyl)butyl)chroman-4-one (3b)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 80% yield;

**M.p. = 107-108 °C;**

\[ \text{H NMR (500 MHz, CDCl}_3\]: \( \delta \) 7.87 (dd, \( J \) = 7.9, 1.6 Hz, 1H), 7.84 (d, \( J \) = 8.2 Hz, 2H), 7.48-7.41 (m, 1H), 7.24 (d, \( J \) = 8.0 Hz, 2H), 7.01-6.98 (m, 1H), 6.94 (d, \( J \) = 8.3 Hz, 1H), 4.55 (dd, \( J \) = 11.5, 4.5 Hz, 1H), 4.29 (dd, \( J \) = 11.5, 8.9 Hz, 1H), 2.99 (tt, \( J \) = 7.0 Hz, 2H), 2.74-2.65 (m, 1H), 2.39 (s, 3H), 1.99-1.78 (m, 3H), 1.64-1.57 (m, 1H);

\[ \text{C NMR (125 MHz, CDCl}_3\]: \( \delta \) 199.19, 194.15, 161.42, 143.72, 135.67, 134.35, 129.20, 128.05, 127.31, 121.27, 120.51, 117.63, 70.31, 45.75, 38.08, 25.87, 21.58, 21.53;

3-(4-(4-methoxyphenyl)-4-oxobutyl)chroman-4-one (3c)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 64% yield;

M.p. = 92-93 °C;

$^1$H NMR (500 MHz, CDCl$_3$): δ 7.95-7.91 (m, 2H), 7.88 (dd, $J = 7.9$, 1.7 Hz, 1H), 7.49-7.42 (m, 1H), 7.04-6.98 (m, 1H), 6.94 (dd, $J = 13.6$, 8.6 Hz, 3H), 4.56 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.30 (dd, $J = 11.5$, 8.1 Hz, 1H), 3.86 (s, 3H), 2.98 (t, $J = 7.0$ Hz, 2H), 2.74-2.69 (m, 1H), 1.98-1.79 (m, 3H), 1.65-1.58 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 198.20, 194.26, 163.44, 161.49, 135.73, 130.25, 129.99, 127.37, 121.33, 120.58, 117.69, 113.72, 70.38, 55.43, 45.82, 37.91, 25.97, 21.76;

HRMS (ESI) calcd for C$_{20}$H$_{21}$O$_4$: [M+H]$^+$ 325.1434, found: 325.1432.

3-(4-(3-methoxyphenyl)-4-oxobutyl)chroman-4-one (3d)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 65% yield;

M.p. = 85-86 °C;

$^1$H NMR (500 MHz, CDCl$_3$): δ 7.88 (dd, $J = 7.9$, 1.7 Hz, 1H), 7.52 (d, $J = 7.7$ Hz, 1H), 7.50-7.43 (m, 2H), 7.37-7.34 (m, 1H), 7.10 (dd, $J = 8.1$, 2.4 Hz, 1H), 7.00 (dd, $J = 11.1$, 3.9 Hz, 1H), 6.95 (d, $J = 8.3$ Hz, 1H), 4.56 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.30 (dd, $J = 11.5$, 8.9 Hz, 1H), 3.85 (s, 3H), 3.02 (t, $J = 7.0$ Hz, 2H), 2.74-2.69 (m, 1H), 1.99-1.81 (m, 3H), 1.65-1.58 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 199.42, 194.21, 161.45, 159.80, 138.21, 135.75, 129.56, 127.36, 121.34, 120.62, 120.53, 119.51, 117.68, 112.19, 70.35, 55.40, 45.78, 38.36, 25.89, 21.57;

HRMS (ESI) calcd for C$_{20}$H$_{21}$O$_4$: [M+H]$^+$ 325.1434, found: 325.1437.
3-(4-(2-methoxyphenyl)-4-oxobutyl)chroman-4-one (3e)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a colorless solid in 62% yield;

M.p. = 89-90 °C;

$^{1}$H NMR (500 MHz, CDCl$_{3}$): $\delta$ 7.88 (dd, $J = 7.9$, 1.7 Hz, 1H), 7.66 (dd, $J = 7.7$, 1.8 Hz, 1H), 7.47-7.42 (m, 2H), 7.02-6.97 (m, 2H), 6.95 (d, $J = 8.4$ Hz, 2H), 4.55 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.29 (dd, $J = 11.5$, 8.9 Hz, 1H), 3.89 (s, 3H), 3.05-3.01 (m, 2H), 2.74-2.66 (m, 1H), 1.97-1.76 (m, 3H), 1.62-1.55 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_{3}$): $\delta$ 202.09, 194.34, 161.47, 158.44, 135.68, 133.33, 130.17, 128.30, 127.34, 121.28, 120.62, 120.57, 117.66, 111.48, 70.32, 55.44, 45.81, 43.47, 25.89, 21.66;

HRMS (ESI) calcd for C$_{20}$H$_{21}$O$_{4}$: [M+H]$^+$ 325.1434, found: 325.1435.

3-(4-(4-((tert-butyl)phenyl)-4-oxobutyl)chroman-4-one (3f)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a colorless solid in 60% yield;

M.p. = 85-86 °C;

$^{1}$H NMR (500 MHz, CDCl$_{3}$): $\delta$ 7.83-7.81 (m, 3H), 7.40-7.37 (m, 3H), 6.95-6.92 (m, 1H), 6.88 (d, $J = 8.4$ Hz, 1H), 4.49 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.23 (dd, $J = 11.5$, 9.0 Hz, 1H), 2.94 (t, $J = 7.0$ Hz, 2H), 2.67-2.62 (m, 1H), 1.93-1.86 (m, 2H), 1.84-1.72 (m, 1H), 1.58-1.51 (m, 1H), 1.26 (s, 9H);

$^{13}$C NMR (125 MHz, CDCl$_{3}$): $\delta$ 199.30, 194.25, 161.47, 156.75, 135.74, 134.28, 127.96, 127.37, 127.52, 121.33, 120.55, 117.69, 70.36, 45.81, 38.15, 35.06, 31.05, 25.93, 21.63;


3-(4-(4-fluorophenyl)-4-oxobutyl)chroman-4-one (3g)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 69% yield;

**M.p.** = 104-105 °C;

\[ ^1H \text{ NMR} \ (500 \text{ MHz, CDCl}_3): \delta \ 8.00-7.94 \ (m, \ 2H), \ 7.88 \ (dd, \ J = 7.9, \ 1.7 \text{ Hz}, \ 1H), \ 7.47-7.44 \ (m, \ 1H), \ 7.15-7.08 \ (m, \ 2H), \ 7.03-6.98 \ (m, \ 1H), \ 6.95 \ (dd, \ J = 8.4, \ 0.6 \text{ Hz}, \ 1H), \ 4.56 \ (dd, \ J = 11.5, \ 4.5 \text{ Hz}, \ 1H), \ 4.30 \ (dd, \ J = 11.5, \ 8.9 \text{ Hz}, \ 1H), \ 3.00 \ (t, \ J = 7.0, \ 2H), \ 2.74-2.68 \ (m, \ 1H), \ 1.98-1.81 \ (m, \ 3H), \ 1.66-1.58 \ (m, \ 1H); \]

\[ ^{13}C \text{ NMR} \ (125 \text{ MHz, CDCl}_3): \delta \ 197.93, \ 194.16, \ 165.68 \ (d, \ J_{C-F} = 253.1 \text{ Hz}), \ 161.45, \ 135.76, \ 133.28 \ (d, \ J_{C-F} = 3.0 \text{ Hz}), \ 130.59 \ (d, \ J_{C-F} = 9.3 \text{ Hz}), \ 127.35, \ 121.35, \ 120.53, \ 117.68, \ 115.65 \ (d, \ J_{C-F} = 21.8 \text{ Hz}), \ 70.36, \ 45.76, \ 38.16, \ 25.89, \ 21.51; \]

**HRMS (ESI)** calcd for C_{19}H_{18}FO_{3}: [M+H]^+ 313.1234, found: 313.1236.

3-(4-(4-chlorophenyl)-4-oxobutyl)chroman-4-one (3h)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 73% yield;

**M.p.** = 109-110 °C;

\[ ^1H \text{ NMR} \ (500 \text{ MHz, CDCl}_3): \delta \ 7.84-7.78 \ (m, \ 3H), \ 7.42-7.33 \ (m, \ 3H), \ 6.95-6.92 \ (m, \ 1H), \ 6.88 \ (d, \ J = 8.4 \text{ Hz}, \ 1H), \ 4.49 \ (dd, \ J = 11.5, \ 4.5 \text{ Hz}, \ 1H), \ 4.23 \ (dd, \ J = 11.5, \ 8.9 \text{ Hz}, \ 1H), \ 2.93 \ (t, \ J = 7.0 \text{ Hz}, \ 2H), \ 2.67-2.61 \ (m, \ 1H), \ 1.89-1.74 \ (m, \ 3H), \ 1.58-1.50 \ (m, \ 1H); \]

\[ ^{13}C \text{ NMR} \ (125 \text{ MHz, CDCl}_3): \delta \ 198.30, \ 194.16, \ 161.43, \ 139.45, \ 135.78, \ 135.11, \ 129.38, \ 128.88, \ 127.35, \ 121.36, \ 120.50, \ 117.68, \ 70.34, \ 45.74, \ 38.22, \ 25.85, \ 21.43; \]

**HRMS (ESI)** calcd for C_{19}H_{18}ClO_{3}: [M+H]^+ 329.0939, found: 329.0943.

3-(4-(4-bromophenyl)-4-oxobutyl)chroman-4-one (3i)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 67% yield;

**M.p.** = 102-103 °C;

**$^1$H NMR** (500 MHz, CDCl$_3$): δ 7.88 (d, $J = 7.9$ Hz, 1H), 7.81 (d, $J = 8.5$ Hz, 2H), 7.60 (d, $J = 8.4$ Hz, 2H), 7.48-7.45 (m, 1H), 7.03-7.00 (m, 1H), 6.96 (d, $J = 8.4$ Hz, 1H), 4.56 (dd, $J = 11.5$, 4.4 Hz, 1H), 4.30 (dd, $J = 11.5$, 9.0 Hz, 1H), 3.00 (t, $J = 6.9$ Hz, 2H), 2.74-2.69 (m, 1H), 1.98-1.82 (m, 3H), 1.65-1.58 (m, 1H);

**$^{13}$C NMR** (125 MHz, CDCl$_3$): δ 198.52, 194.19, 161.46, 135.81, 135.53, 131.91, 129.52, 128.21, 127.38, 121.39, 120.52, 117.71, 70.37, 45.77, 38.23, 25.88, 21.44;

**HRMS (ESI)** calcd for C$_{19}$H$_{18}$BrO$_3$: [M+H]$^+$ 373.0434, found: 373.0435.

3-(4-oxo-4-(4-(trifluoromethyl)phenyl)butyl)chroman-4-one (3j)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 48% yield;

**M.p.** = 123-124 °C;

**$^1$H NMR** (500 MHz, CDCl$_3$): δ 8.05 (d, $J = 8.1$ Hz, 2H), 7.88 (d, $J = 7.8$ Hz, 1H), 7.73 (d, $J = 8.1$ Hz, 2H), 7.49-7.45 (m, 1H), 7.03-7.00 (m, 1H), 6.96 (d, $J = 8.3$ Hz, 1H), 4.57 (dd, $J = 11.4$, 4.4 Hz, 1H), 4.31 (dd, $J = 11.4$, 8.9 Hz, 1H), 3.06 (t, $J = 6.6$ Hz, 2H), 2.78-2.68 (m, 1H), 2.01-1.84 (m, 3H), 1.67-1.58 (m, 1H);

**$^{13}$C NMR** (125 MHz, CDCl$_3$): δ 198.55, 194.15, 161.47, 139.49, 135.83, 134.38 (d, $J_{C-F} = 32.6$ Hz), 128.32, 127.39, 125.70 (q, $J_{C-F} = 3.7$ Hz), 123.58 (q, $J_{C-F} = 272.6$ Hz), 121.42, 120.54, 117.72, 70.40, 45.77, 38.59, 25.88, 21.37;

**HRMS (ESI)** calcd for C$_{20}$H$_{18}$F$_3$O$_3$: [M+H]$^+$ 363.1203, found: 363.1206.

3-(4-oxo-6-phenylhexyl)chroman-4-one (3k)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 55% yield;

M.p. = 118-119 °C;

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.81-7.79 (m, 1H), 7.39-7.36 (m, 1H), 7.21-7.17 (m, 2H), 7.11-7.08 (m, 3H), 6.95-6.91 (m, 1H), 6.90-6.84 (m, 1H), 4.43 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.17 (dd, $J = 11.5$, 8.9 Hz, 1H), 2.81 (t, $J = 7.6$ Hz, 2H), 2.65 (t, $J = 7.6$ Hz, 2H), 2.58-2.51 (m, 1H), 2.36 (t, $J = 7.2$ Hz, 2H), 1.78-1.69 (m, 1H), 1.67-1.53 (m, 2H), 1.43-1.35 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 209.37, 194.12, 161.42, 140.94, 135.73, 128.44, 128.26, 127.33, 126.06, 121.33, 120.51, 117.65, 70.30, 45.67, 44.22, 42.62, 29.73, 25.72, 20.99;

HRMS (ESI) calcd for C$_{21}$H$_{23}$O$_3$: [M+H]$^+$ 323.1642, found: 323.1645.

3-(4-oxo-5-phenoxypentyl)chroman-4-one (3l)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless oil in 70% yield;

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.88 (d, $J = 7.9$ Hz, 1H), 7.48-7.44 (m, 1H), 7.31-7.27 (m, 2H), 7.03-6.97 (m, 2H), 6.95 (d, $J = 8.4$ Hz, 1H), 6.87 (d, $J = 8.2$ Hz, 2H), 4.56 -4.50 (m, 3H), 4.26 (dd, $J = 11.2$, 9.1 Hz, 1H), 2.71- 2.61 (m, 3H), 1.93-1.71 (m, 3H), 1.57-1.49 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 207.33, 194.08, 161.43, 157.71, 135.77, 129.68, 127.37, 121.72, 121.37, 120.52, 117.67, 114.47, 72.76, 70.32, 45.67, 38.72, 25.73, 20.43;

HRMS (ESI) calcd for C$_{20}$H$_{21}$O$_4$: [M+H]$^+$ 325.1434, found: 325.1437.

3-(4-oxo-4-(thiophen-3-yl)butyl)chroman-4-one (3m)
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 62% yield;

**M.p.** = 69-70 °C;

**1H NMR** (500 MHz, CDCl₃): δ 8.05 (d, J = 1.4 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 5.0 Hz, 1H), 7.48-7.44 (m, 1H), 7.31 (dd, J = 4.6, 3.1 Hz, 1H), 7.02-6.99 (m, 1H), 6.95 (d, J = 8.4 Hz, 1H), 4.56 (dd, J = 11.5, 4.4 Hz, 1H), 4.30 (dd, J = 10.8, 9.4 Hz, 1H), 2.94 (t, J = 6.9 Hz, 2H), 2.75-2.65 (m, 1H), 1.98-1.80 (m, 3H), 1.65-1.55 (m, 1H);

**13C NMR** (125 MHz, CDCl₃): δ 194.21, 193.97, 161.47, 142.20, 135.76, 131.84, 127.37, 126.87, 126.36, 121.35, 120.54, 117.70, 70.38, 45.76, 39.52, 25.93, 21.57;

**HRMS (ESI)** calcd for C₁₇H₁₇O₃S: [M+H]+ 301.0893, found: 301.0896.

3-(4-cyclohexyl-4-oxobutyl)chroman-4-one (3n)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 66% yield;

**M.p.** = 75-76 °C;

**1H NMR** (500 MHz, CDCl₃): δ 7.85 (d, J = 7.9, 1.6 Hz, 1H), 7.45-7.41 (m, 1H), 7.01-6.95 (m, 1H), 6.92 (dd, J = 8.3, 0.5 Hz, 1H), 4.51 (dd, J = 11.5, 4.5 Hz, 1H), 4.25 (dd, J = 11.5, 8.9 Hz, 1H), 2.67-2.60 (m, 1H), 2.47 (t, J = 7.1 Hz, 2H), 2.33-2.27 (m, 1H), 1.85-1.58 (m, 7H), 1.51-1.43 (m, 1H), 1.33-1.12 (m, 6H);

**13C NMR** (125 MHz, CDCl₃): δ 213.44, 194.15, 161.40, 135.67, 127.28, 121.26, 120.48, 117.62, 70.27, 50.74, 45.73, 40.15, 28.39, 25.75, 25.56, 20.93 (one signal was overlapped by others);

**HRMS (ESI)** calcd for C₁₉H₂₅O₃: [M+H]+ 301.1798, found: 301.1802.

3-(4-cyclopropyl-4-oxobutyl)chroman-4-one (3o)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 66% yield;
Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a colorless oil in 64% yield;

\textbf{H NMR} (500 MHz, CDCl$_3$): $\delta$ 7.84 (d, $J = 7.6$ Hz, 1H), 7.44-7.41 (m, 1H), 6.99-6.967 (m, 1H), 6.91 (d, $J = 8.3$ Hz, 1H), 4.50 (dd, $J = 11.4, 4.4$ Hz, 1H), 4.24 (dd, $J = 11.4, 9.0$ Hz, 1H), 2.67-2.61 (m, 1H), 2.58 (t, $J = 7.2$, 2H), 1.91-1.81 (m, 2H), 1.72-1.64 (m, 2H), 1.54-1.45 (m, 1H), 0.97-0.95 (m, 2H), 0.84-0.81 (m, 2H);

\textbf{13C NMR} (125 MHz, CDCl$_3$): $\delta$ 210.23, 194.12, 161.37, 135.66, 127.25, 121.24, 120.45, 117.60, 70.26, 45.64, 42.99, 25.74, 21.16, 20.32, 10.58, 10.57;

\textbf{HRMS (ESI)} calcd for C$_{16}$H$_{19}$O$_3$: [M+H]$^+$ 259.1329, found: 259.1331.

\textbf{3-(4-oxohexyl)chroman-4-one (3p)}

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 50% yield;

\textbf{M.p.} = 62-63$^\circ$C;

\textbf{H NMR} (500 MHz, CDCl$_3$): $\delta$ 7.89-7.83 (m, 1H), 7.46-7.42 (m, 1H), 7.03-6.96 (m, 1H), 6.96-6.90 (m, 1H), 4.52 (dd, $J = 11.4, 4.5$ Hz, 1H), 4.26 (dd, $J = 11.4, 8.9$ Hz, 1H), 2.70-2.59 (m, 1H), 2.50-2.34 (m, 4H), 1.87-1.80 (m, 1H), 1.76-1.61 (m, 2H), 1.55-1.45 (m, 1H), 1.03 (t, $J = 7.3$ Hz, 3H);

\textbf{13C NMR} (125 MHz, CDCl$_3$): $\delta$ 210.90, 194.15, 161.42, 135.71, 127.32, 121.31, 120.50, 117.65, 70.31, 45.72, 41.94, 35.89, 25.78, 21.13, 7.74;

\textbf{HRMS (ESI)} calcd for C$_{16}$H$_{19}$O$_3$: [M+H]$^+$ 247.1329, found: 247.1326.

\textbf{3-(4-oxononyl)chroman-4-one (3q)}

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow oil in 53% yield;
$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.87 (dd, $J = 7.9, 1.5$ Hz, 1H), 7.48-7.42 (m, 1H), 7.02-6.98 (m, 1H), 6.94 (d, $J = 8.4$ Hz, 1H), 4.53 (dd, $J = 11.5, 4.5$ Hz, 1H), 4.27 (dd, $J = 11.5, 8.9$ Hz, 1H), 2.69-2.62 (m, 1H), 2.45 (t, $J = 7.2$ Hz, 2H), 2.38 (t, $J = 7.5$ Hz, 2H), 1.88-1.81 (m, 1H), 1.78-1.61 (m, 2H), 1.59-1.46 (m, 3H), 1.34-1.21 (m, 4H), 0.88 (t, $J = 7.1$ Hz, 3H);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 210.66, 194.18, 161.46, 135.74, 127.36, 121.34, 120.54, 117.68, 70.35, 45.77, 42.84, 42.36, 31.37, 25.81, 23.50, 22.40, 21.11, 13.86;

HRMS (ESI) calcd for C$_{18}$H$_{25}$O$_3$: [M+H]$^+$ 289.1798, found: 289.1795.

7-methyl-3-(4-oxo-4-phenylbutyl)chroman-4-one (3r)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 65% yield;

M.p. = 95-96 °C;

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.98-7.93 (m, 2H), 7.77 (d, $J = 8.0$ Hz, 1H), 7.58-7.53 (m, 1H), 7.48-7.42 (m, 2H), 6.82 (dd, $J = 8.0, 0.9$ Hz, 1H), 6.76 (s, 1H), 4.53 (dd, $J = 11.4, 4.4$ Hz, 1H), 4.28 (dd, $J = 11.4, 8.7$ Hz, 1H), 3.03 (t, $J = 7.0$ Hz, 2H), 2.70-2.65 (m, 1H), 2.34 (s, 3H), 1.99-1.79 (m, 3H), 1.66-1.56 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 199.63, 193.94, 161.49, 147.24, 136.86, 133.00, 128.56, 127.97, 127.25, 122.74, 118.28, 117.65, 70.37, 45.72, 38.27, 26.00, 21.84, 21.56;


7-methoxy-3-(4-oxo-4-phenylbutyl)chroman-4-one (3s)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 58% yield;

M.p. = 98-99 °C;
$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.99-7.91 (m, 2H), 7.82 (d, $J = 8.8$ Hz, 1H), 7.59-7.52 (m, 1H), 7.45 (dd, $J = 10.6$, 4.7 Hz, 2H), 6.57 (dd, $J = 8.8$, 2.4 Hz, 1H), 6.40 (d, $J = 2.4$ Hz, 1H), 4.55 (dd, $J = 11.4$, 4.4 Hz, 1H), 4.30 (dd, $J = 11.4$, 8.6 Hz, 1H), 3.83 (s, 3H), 3.03 (t, $J = 7.0$ Hz, 2H), 2.68-2.63 (m, 1H), 1.97-1.82 (m, 3H), 1.63-1.58 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 199.68, 192.92, 165.85, 163.43, 136.90, 133.02, 129.10, 128.59, 127.99, 114.46, 109.95, 100.55, 70.73, 55.58, 45.47, 38.30, 26.12, 21.62;

HRMS (ESI) calcld for C$_{20}$H$_{21}$O$_4$: [M+H]$^+$ 325.1434, found: 325.1432.

6-fluoro-3-(4-oxo-4-phenylbutyl)chroman-4-one (3t)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 72% yield;

M.p. = 108-109 °C;

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.95 (d, $J = 7.4$ Hz, 2H), 7.58-7.51 (m, 2H), 7.47-7.44 (m, 2H), 7.20-7.16 (m, 1H), 6.94 (dd, $J = 9.1$, 4.2 Hz, 1H), 4.55 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.29 (dd, $J = 11.5$, 9.0 Hz, 1H), 3.04 (t, $J = 6.9$ Hz, 2H), 2.74-2.69 (m, 1H), 1.98-1.83 (m, 3H), 1.65-1.59 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 199.52, 193.46, 157.74 (d, $J_{C,F} = 1.6$ Hz), 157.24 (d, $J_{C,F} = 240.3$ Hz), 136.84, 133.08, 128.61, 127.97, 123.31 (d, $J_{C,F} = 24.5$ Hz), 120.97 (d, $J_{C,F} = 6.3$ Hz), 119.36 (d, $J_{C,F} = 7.3$ Hz), 112.28 (d, $J_{C,F} = 23.1$ Hz), 70.57, 45.64, 38.20, 25.84, 21.46;

HRMS (ESI) calcld for C$_{19}$H$_{18}$FO$_3$: [M+H]$^+$ 313.1234, found: 313.1231.

6-chloro-3-(4-oxo-4-phenylbutyl)chroman-4-one (3u)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 77% yield;

M.p. = 112-113 °C;
\( ^1H \) NMR (500 MHz, CDCl\(_3\)): \( \delta \) 7.97-7.92 (m, 2H), 7.83 (d, \( J = 2.7 \) Hz, 1H), 7.57-7.54 (m, 1H), 7.47-7.44 (m, 2H), 7.39 (dd, \( J = 8.8, 2.7 \) Hz, 1H), 6.92 (d, \( J = 8.8 \) Hz, 1H), 4.56 (dd, \( J = 11.5, 4.5 \) Hz, 1H), 4.30 (dd, \( J = 11.5, 9.0 \) Hz, 1H), 3.03 (t, \( J = 6.9 \) Hz, 2H), 2.74-2.69 (m, 1H), 1.96-1.81 (m, 3H), 1.63-1.58 (m, 1H);

\( ^{13}C \) NMR (125 MHz, CDCl\(_3\)): \( \delta \) 199.49, 193.07, 159.91, 136.81, 135.59, 133.08, 128.60, 127.96, 126.88, 126.67, 121.32, 119.45, 70.51, 45.57, 38.16, 25.82, 21.42;


6-bromo-3-(4-oxo-4-phenylbutyl)chroman-4-one (3v)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 71% yield;

M.p. = 106-107 °C;

\( ^1H \) NMR (500 MHz, CDCl\(_3\)): \( \delta \) 7.98 (d, \( J = 2.5 \) Hz, 1H), 7.95 (d, \( J = 7.5 \) Hz, 2H), 7.58-7.51 (m, 2H), 7.48-7.45 (m, 2H), 6.87 (d, \( J = 8.8 \) Hz, 1H), 4.57 (dd, \( J = 11.5, 4.5 \) Hz, 1H), 4.30 (dd, \( J = 11.5, 9.0 \) Hz, 1H), 3.04 (t, \( J = 6.9 \) Hz, 2H), 2.75-2.67 (m, 1H), 1.98-1.79 (m, 3H), 1.64-1.58 (m, 1H);

\( ^{13}C \) NMR (125 MHz, CDCl\(_3\)): \( \delta \) 199.50, 192.95, 160.37, 138.38, 136.81, 133.10, 129.81, 128.61, 127.97, 121.81, 119.82, 114.03, 70.48, 45.55, 38.17, 25.82, 21.41;

HRMS (ESI) calcd for C\(_{19}\)H\(_{18}\)BrO\(_3\): [M+H]** 373.0434, found: 373.0436.

7-chloro-3-(4-oxo-4-phenylbutyl)chroman-4-one (3w)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 64% yield;

M.p. = 114-115 °C;
$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.98-7.92 (m, 2H), 7.82 (d, $J = 8.9$ Hz, 1H), 7.59-7.54 (m, 1H), 7.49-7.43 (m, 2H), 7.00-6.98 (m, 2H), 4.58 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.32 (dd, $J = 11.5$, 8.9 Hz, 1H), 3.04 (t, $J = 6.9$ Hz, 2H), 2.76-2.68 (m, 1H), 1.98-1.83 (m, 3H), 1.64-1.58 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 199.52, 193.19, 161.83, 141.63, 136.85, 133.09, 128.65, 128.62, 127.99, 122.20, 119.14, 117.87, 70.74, 45.66, 38.20, 25.86, 21.46;

HRMS (ESI) caled for C$_{19}$H$_{18}$ClO$_3$: [M+H]$^+$ 329.0939, found: 329.0941.

8-bromo-3-(4-oxo-4-phenylbutyl)chroman-4-one (3x)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 60% yield;

M.p. = 116-117 °C;

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.95 (d, $J = 7.7$ Hz, 2H), 7.85 (dd, $J = 7.8$, 0.9 Hz, 1H), 7.74-7.69 (m, 1H), 7.57-7.54 (m, 1H), 7.48-7.44 (m, 2H), 6.93-6.90 (m, 1H), 4.69 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.41 (dd, $J = 11.5$, 9.2 Hz, 1H), 3.04 (t, $J = 6.9$ Hz, 2H), 2.82-2.72 (m, 1H), 2.00-1.84 (m, 3H), 1.67-1.60 (m, 1H);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 199.45, 193.32, 157.80, 139.00, 136.82, 133.07, 128.60, 127.97, 126.79, 122.09, 121.78, 111.38, 71.02, 45.40, 38.17, 25.74, 21.42;

HRMS (ESI) caled for C$_{19}$H$_{18}$BrO$_3$: [M+H]$^+$ 373.0434, found: 373.0436.

8-chloro-3-(4-oxo-4-phenylbutyl)chroman-4-one (3y)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 66% yield;

M.p. = 116-117 °C;
1H NMR (500 MHz, CDCl$_3$): $\delta$ 7.94 (dd, $J = 5.2$, 3.3 Hz, 2H), 7.81 (dd, $J = 7.9$, 1.6 Hz, 1H), 7.58-7.53 (m, 2H), 7.45 (dd, $J = 10.6$, 4.8 Hz, 2H), 6.98-6.95 (m, 1H), 4.69 (dd, $J = 11.5$, 4.5 Hz, 1H), 4.41 (dd, $J = 11.5$, 9.0 Hz, 1H), 3.04 (t, $J = 7.0$ Hz, 2H), 2.81-2.72 (m, 1H), 1.99-1.84 (m, 3H), 1.65-1.60 (m, 1H);

13C NMR (125 MHz, CDCl$_3$): $\delta$ 199.47, 193.32, 156.92, 136.81, 135.84, 133.07, 128.60, 127.96, 125.99, 122.47, 121.82, 121.45, 70.99, 45.49, 38.16, 25.75, 21.42;

HRMS (ESI) calcd for C$_{19}$H$_{18}$ClO$_3$: [M+H]$^+$ 329.0939, found: 329.0941.

2-(4-oxo-4-phenylbutyl)-2,3-dihydro-1H-benzo[f]chromen-1-one (3z)

Following the general procedure the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 52% yield;

M.p. = 82-83 °C;

1H NMR (500 MHz, CDCl$_3$): $\delta$ 9.45 (d, $J = 8.6$ Hz, 1H), 7.97-7.94 (m, 2H), 7.91 (d, $J = 9.0$ Hz, 1H), 7.74 (dd, $J = 8.0$, 0.6 Hz, 1H), 7.64-7.60 (m, 1H), 7.57-7.53 (m, 1H), 7.47-7.41 (m, 3H), 7.09 (d, $J = 9.0$ Hz, 1H), 4.66 (dd, $J = 11.3$, 4.4 Hz, 1H), 4.43 (dd, $J = 11.3$, 8.2 Hz, 1H), 3.05 (t, $J = 7.0$ Hz, 2H), 2.81-2.75 (m, 1H), 2.03-1.84 (m, 3H), 1.74-1.67 (m, 1H);

13C NMR (125 MHz, CDCl$_3$): $\delta$ 199.69, 195.54, 163.30, 137.23, 136.87, 133.01, 131.71, 129.51, 129.21, 128.57, 128.37, 127.99, 125.76, 124.72, 118.60, 111.95, 70.24, 46.53, 38.29, 26.51, 21.64;

HRMS (ESI) calcd for C$_{23}$H$_{21}$O$_3$: [M+H]$^+$ 345.1485, found: 345.1488.