Supporting Information

De Novo Synthesis of Benzofurans via Trifluoroacetic Acid Catalyzed One-pot Cascade Reaction of 2-Hydroxy-1,4-diones

Qiang Sha\textsuperscript{a*}, Haixuan Liu\textsuperscript{b}

\textsuperscript{a} Jiangsu Key Laboratory of Pesticide Science and Department of Chemistry, College of Sciences, Nanjing Agricultural University, Nanjing 210095, P. R. China. Email: qsha@njau.edu.cn

\textsuperscript{b} Sanhome R&D Centre, Nanjing Sanhome Pharmaceutical Co., Ltd., Nanjing 211135, P. R. China.

Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>S2</td>
</tr>
<tr>
<td>General procedure for the \textit{L}-proline catalyzed aldol reaction</td>
<td>S2-S3</td>
</tr>
<tr>
<td>General procedure for the synthesis of benzofuran derivatives</td>
<td>S3</td>
</tr>
<tr>
<td>Detect the intermediate by \textsuperscript{1}H NMR and HRMS</td>
<td>S4</td>
</tr>
<tr>
<td>Capture possible intermediate by 1,3,5-trimethoxybenzene</td>
<td>S5-S6</td>
</tr>
<tr>
<td>Characterization data of products 2 and 3</td>
<td>S7-S22</td>
</tr>
<tr>
<td>References</td>
<td>S22</td>
</tr>
<tr>
<td>\textsuperscript{1}H and \textsuperscript{13}C spectra of 2 and 3</td>
<td>S23-S73</td>
</tr>
</tbody>
</table>
General. Solvents and reagents (AR grade) were used without purification unless otherwise noted. $^1$H NMR and $^{13}$C NMR spectra were recorded in CDCl$_3$ on an Agilent DD2-500 MHz spectrometer. Chemical shifts are reported in ppm with the solvent signals as reference, and coupling constants ($J$) are given in Hertz (Hz). The peak information is described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) were performed on a microTOF-ESI mass spectrometer using CsOAc as the standard. Melting points were obtained uncorrected from an Electrothermo Mel-Temp DLX 104 device.

General procedure for the $L$-proline catalyzed aldol reaction$^1$

![Diagram](attachment:image.png)

List of the products:

<table>
<thead>
<tr>
<th>R</th>
<th>Product</th>
<th>d.r.</th>
<th>d.r.</th>
<th>d.r.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bn</td>
<td>2a</td>
<td>24 h, 92%</td>
<td>74:26</td>
<td>51:24:13:12</td>
</tr>
<tr>
<td>Me</td>
<td>2b</td>
<td>32 h, 75%</td>
<td>79:21</td>
<td>44:25:16:15</td>
</tr>
<tr>
<td>Et</td>
<td>2c</td>
<td>32 h, 80%</td>
<td>77:23</td>
<td>45:25:16:14</td>
</tr>
<tr>
<td>ph</td>
<td>2d</td>
<td>32 h, 77%</td>
<td>75:25</td>
<td>44:25:16:16</td>
</tr>
<tr>
<td>2e</td>
<td>32 h, 75%</td>
<td>78:22</td>
<td>31:28:25:16</td>
<td></td>
</tr>
<tr>
<td>2f</td>
<td>32 h, 69%</td>
<td>73:27</td>
<td>45:25:16:15</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>Me</td>
<td>2l</td>
<td>32 h, 71%</td>
<td>51:24:13:12</td>
</tr>
<tr>
<td>Et</td>
<td>2m</td>
<td>32 h, 73%</td>
<td>44:25:16:15</td>
<td></td>
</tr>
<tr>
<td>n-Pr</td>
<td>2n</td>
<td>32 h, 94%</td>
<td>45:25:16:14</td>
<td></td>
</tr>
<tr>
<td>t-Bu</td>
<td>2o</td>
<td>32 h, 88%</td>
<td>31:28:25:16</td>
<td></td>
</tr>
<tr>
<td>Ph</td>
<td>2p</td>
<td>32 h, 70%</td>
<td>45:25:16:15</td>
<td></td>
</tr>
<tr>
<td>CO$_2$Me</td>
<td>2q</td>
<td>32 h, 90%</td>
<td>50:20:15:15</td>
<td></td>
</tr>
<tr>
<td>NHCO$_2$H</td>
<td>2r</td>
<td>32 h, 85%</td>
<td>minor</td>
<td>complex mixture unable to calculate d.r. by $^1$H NMR</td>
</tr>
</tbody>
</table>

In a 25 mL one-neck flask containing a magnetic stirring bar, dichloromethane (5.0 mL), 1 (1.0 mmol), 2 (2.0 mmol) and $L$-proline (23.0 mg, 0.2 mmol) were added in sequence, then the reaction mixture was stirred at room temperature for 24-54 h. After reaction was complete, the product mixture was concentrated and its components were purified by flash column chromatography.
(SiO$_2$), eluting with hexane/ethyl acetate, to provide product 2.

Note: Among the products, 2a, 2b, 2j, 2k, 2t, 2w, 2x, 2y, 2z, 2aa are known compounds, the others are new compounds and were fully characterized.

**General procedure for the synthesis of benzofuran derivatives**

**Procedure for the synthesis of 3a-3r**

A Schlenk tube with a magnetic stir bar charged with 2-hydroxy-1,4-diones 2 (0.20 mmol), trifluoroacetic acid (0.04 mmol, 0.2 equiv.), 1,2-dichloroethane (DCE, 2.0 mL) and N-Bromobutanimide (NBS, 0.30 mmol, 1.5 equiv.). The reaction mixture was then heated to 80 ºC and stirred for 6 hours. The reaction mixture was then allowed to cool to ambient temperature and all of the volatiles were removed under vacuum, the crude product was purified on flash chromatography, eluting with petroleum ether/ethyl acetate, to provide substituted benzofuran 3.

**Procedure for the synthesis of 3t-3aa**

A Schlenk tube with a magnetic stir bar charged with 2-hydroxy-1,4-diones 2 (0.20 mmol), trifluoroacetic acid (0.04 mmol, 0.2 equiv.), 1,2-dichloroethane (DCE, 2.0 mL) and N-Bromobutanimide (NBS, 0.30 mmol, 1.5 equiv.). The reaction mixture was then heated to 130 ºC and stirred for 36 hours. The reaction mixture was then allowed to cool to ambient temperature and all of the volatiles were removed under vacuum, the crude product was purified on flash chromatography, eluting with petroleum ether/ethyl acetate, to provide substituted benzofuran 3.
Detect the intermediate by $^1$H NMR and HRMS

In order to detect possible intermediates, we performed the reaction without using NBS. By analyzing the reaction mixture, we were glad to detect the intermediate benzyl 2-methyl-4,5-dihydrobenzofuran-3-carboxylate by both $^1$H NMR and HRMS.

Chemical Formula: C$_{17}$H$_{16}$O$_3$

Exact Mass: 268.1099
Capture possible intermediate by 1,3,5-trimethoxybenzene

A Schlenk tube with a magnetic stir bar charged with 2-hydroxy-1,4-dione 3a (0.20 mmol), trifluoroacetic acid (0.04 mmol, 0.2 equiv.), 1,2-dichloroethane (DCE, 2.0 mL) and 1,3,5-trimethoxybenzene (0.40 mmol, 2.0 equiv.). The reaction mixture was then heated to 80 °C and stirred for 48 hours. The reaction mixture was then allowed to cool to ambient temperature and all of the volatiles were removed under vacuum, the crude product was purified on flash chromatography, eluting with petroleum/ethyl acetate, to provide 4a in 41% yield.

Benzyl 2-methyl-7-(2,4,6-trimethoxyphenyl)-4,5,6,7-tetrahydrobenzofuran-3-carboxylate (4a)

35.8 mg (white solid, 41% yield); R_f = 0.33 (PE/EtOAc = 10:1); ^1H NMR (400 MHz, CDCl_3) δ 7.47-7.35 (m, 5H), 6.16 (s, 2H), 5.31 (s, 2H), 4.45 (brs, 1H), 3.83 (s, 3H), 3.68 (brs, 6H), 2.83-2.78 (m, 1H), 2.62-2.56 (m, 1H), 2.47 (s, 3H), 2.00-1.90 (m, 3H), 1.75-1.67 (m, 1H); ^13C NMR (101 MHz, CDCl_3) δ 165.3, 159.7, 159.3, 157.2, 152.1, 136.6, 128.5, 128.0, 127.9, 115.8, 112.3, 111.0, 91.3, 65.5, 55.9, 55.3, 30.6, 29.5, 23.7, 22.7, 14.2; HRMS (ESI) m/z calculated for [C_{26}H_{28}O_{6}+H]^- [M+H]^+ 437.1959, found: 437.1957.

^1H NMR (400 MHz, CDCl_3)
$^{13}$C NMR (101 MHz, CDCl$_3$)
Characterization data of products 2 and 3

![Chemical Structure](image)

**Ethyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2c, major diastereoisomer)**

149.1 mg (colorless oil); $R_f = 0.19$ (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.26 (s, 1H), 4.18 (q, $J = 7.1$ Hz, 2H), 3.57 (dd, $J = 11.6$ Hz, 6.2 Hz, 1H), 2.35-2.25 (m, 5H), 2.01-1.98 (m, 1H), 1.89-1.86 (m, 1H), 1.79-1.72 (m, 2H), 1.66-1.54 (m, 2H), 1.22 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 209.4, 204.8, 169.7, 84.8, 63.0, 56.5, 41.8, 27.5, 26.6, 24.9, 24.5, 14.0; HRMS (ESI) $m/z$ calculated for [C$_{12}$H$_{18}$O$_5$+Na]$^+$ [M+Na]$^+$ 265.1046, found: 265.1044.

**Ethyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2c, minor diastereoisomer)**

44.5 mg (colorless oil); $R_f = 0.29$ (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.17 (q, $J = 7.1$ Hz, 2H), 4.08 (s, 1H), 3.55 (dd, $J = 11.5$ Hz, 5.6 Hz, 1H), 2.36-2.29 (m, 2H), 2.22 (s, 3H), 2.05-2.04 (m, 1H), 1.86-1.85 (m, 1H), 1.79-1.78 (m, 1H), 1.71-1.60 (m, 3H), 1.20 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 210.2, 206.0, 170.2, 84.6, 62.7, 55.8, 41.9, 27.5, 27.1, 25.8, 24.6, 13.8.

![Chemical Structure](image)

**Pentyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2d, major diastereoisomer)**

164.0 mg (colorless oil); $R_f = 0.19$ (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.16 (s, 1H), 4.09-4.02 (m, 2H), 3.53-3.48 (m, 1H), 2.30-2.13 (m, 5H), 1.95-1.52 (m, 8H), 1.19-1.13 (m, 4H), 0.78-0.75 (m, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 209.4, 204.8, 169.8, 84.9, 67.1, 56.6, 41.9, 28.1, 27.8, 27.6, 26.7, 25.0, 24.6, 22.1, 13.9; HRMS (ESI) $m/z$ calculated for [C$_{15}$H$_{24}$O$_5$+Na]$^+$ [M+Na]$^+$ 307.1520, found: 307.1517.

**Pentyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2d, minor diastereoisomer)**

54.7 mg (colorless oil); $R_f = 0.33$ (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.08 (s, 1H), 4.02 (t, $J = 6.6$ Hz, 2H), 3.51-3.47 (m, 1H), 2.30-2.19 (m, 3H), 2.15 (s, 3H), 1.99-1.96 (m, 1H), 1.78-1.72 (m, 3H), 1.64-1.59 (m, 3H), 1.23-1.15 (m, 4H), 0.78 (t, $J = 6.4$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 210.0, 205.8, 170.2, 84.5, 66.6, 55.7, 41.8, 27.8, 27.7, 27.5, 27.0, 24.9, 24.5, 22.0, 13.8.
Isobutyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2e, major diastereoisomer) 158.0 mg (colorless oil); Rf = 0.27 (PE/EtOAc = 5:1); 1H NMR (400 MHz, CDCl₃) δ 4.25 (s, 1H), 3.86 (d, J = 6.6 Hz, 2H), 3.57-3.53 (m, 1H), 2.28-2.22 (m, 5H), 1.98-1.95 (m, 1H), 1.88-1.83 (m, 2H), 1.75-1.69 (m, 2H), 1.61-1.54 (m, 2H), 0.82 (d, J = 6.7 Hz, 6H); 13C NMR (101 MHz, CDCl₃) δ 209.1, 204.7, 169.7, 84.8, 72.7, 56.5, 41.7, 27.6, 27.5, 26.6, 24.9, 24.5, 18.7; HRMS (ESI) m/z calculated for [C₁₄H₂₄O₅+Na]+ [M+Na]+ 293.1359, found: 293.1355.

Isobutyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2e, minor diastereoisomer) 44.5 mg (colorless oil); Rf = 0.38 (PE/EtOAc = 5:1); 1H NMR (400 MHz, CDCl₃) δ 4.07 (s, 1H), 3.91-3.84 (m, 2H), 3.58-3.53 (m, 1H), 2.33-2.25 (m, 2H), 2.21 (s, 3H), 2.05-2.01 (m, 1H), 1.89-1.79 (m, 4H), 1.70-1.60 (m, 2H), 0.83 (d, J = 6.7 Hz, 6H); 13C NMR (101 MHz, CDCl₃) δ 210.3, 206.0, 170.3, 84.6, 72.6, 55.8, 41.9, 27.6, 27.5, 25.8, 24.6, 18.8.

2-Methoxyethyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2f, major diastereoisomer) 137.0 mg (colorless oil); Rf = 0.10 (PE/EtOAc = 3:1); 1H NMR (400 MHz, CDCl₃) δ 4.33 (s, 1H), 4.30-4.25 (m, 1H), 4.21-4.17 (m, 1H), 3.54 (dd, J = 12.1 Hz, 5.3 Hz, 1H), 3.7 (t, J = 4.7 Hz, 2H), 3.23 (s, 3H), 2.26-2.15 (m, 5H), 1.97-1.93 (m, 1H), 1.84-1.79 (m, 2H), 1.75-1.49 (m, 3H); 13C NMR (101 MHz, CDCl₃) δ 209.3, 204.6, 169.6, 84.8, 69.8, 65.2, 58.7, 56.4, 41.7, 27.4, 26.6, 24.8, 24.4; HRMS (ESI) m/z calculated for [C₁₃H₂₀O₆+Na]+ [M+Na]+ 295.1152, found: 295.1147.

2-Methoxyethyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2f, minor diastereoisomer) 50.7 mg (colorless oil); Rf = 0.19 (PE/EtOAc = 3:1); 1H NMR (400 MHz, CDCl₃) δ 4.31 (t, J = 4.7 Hz, 2H), 4.11 (s, 1H), 3.65-3.53 (m, 3H), 3.33 (s, 3H), 2.43-2.32 (m, 2H), 2.28 (s, 3H), 2.10-2.07
(m, 1H), 1.91-1.78 (m, 2H), 1.75-1.63 (m, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 210.3, 205.6, 170.3, 84.7, 69.9, 65.3, 58.8, 55.9, 41.9, 27.6, 27.1, 25.7, 24.6.

Ethyl ($R$)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)hexanoate (2g, major diastereoisomer)

148.3 mg (colorless oil); $R_f$ = 0.32 (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) δ 4.23-4.18 (m, 3H), 3.63-3.58 (m, 1H), 2.85-2.79 (m, 1H), 2.46-2.26 (m, 3H), 2.03-2.00 (m, 1H), 1.90-1.49 (m, 7H), 1.22 (t, $J$ = 7.0 Hz, 3H), 0.83 (t, $J$ = 7.3 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 209.5, 206.6, 170.4, 84.6, 62.6, 55.9, 42.0, 39.5, 27.6, 27.1, 24.6, 16.6, 13.9; HRMS (ESI) $m/z$ calculated for [C$_{14}$H$_{22}$O$_5$]+Na$^+$ [M+Na]$^+$ 293.1359, found: 293.1355.

Ethyl ($S$)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)hexanoate (2g, minor diastereoisomer)

32.6 mg (colorless oil); $R_f$ = 0.43 (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) δ 4.17 (q, $J$ = 7.1 Hz, 2H), 4.04 (s, 1H), 3.60-3.55 (m, 1H), 2.69-2.50 (m, 2H), 2.39-2.30 (m, 2H), 2.06-2.03 (m, 1H), 1.87-1.49 (m, 7H), 1.20 (t, $J$ = 7.1 Hz, 3H), 0.84 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 210.4, 207.8, 170.4, 84.6, 62.6, 55.9, 42.0, 39.5, 27.6, 27.1, 24.6, 16.6, 13.9, 13.4.

Ethyl ($R$)-2-hydroxy-4-methyl-3-oxo-2-((S)-2-oxocyclohexyl)pentanoate (2h, major diastereoisomer)

129.6 mg (colorless oil); $R_f$ = 0.25 (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) δ 4.17-4.11 (m, 3H), 3.59-3.54 (m, 1H), 3.42 (sep, $J$ = 6.8 Hz, 1H), 2.27-2.17 (m, 2H), 1.96-1.93 (m, 1H), 1.82-1.80 (m, 1H), 1.68-1.47 (m, 4H), 1.16 (t, $J$ = 7.1 Hz, 3H), 0.98 (d, $J$ = 6.7 Hz, 3H), 0.86 (d, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 210.7, 209.2, 170.3, 84.0, 63.0, 57.3, 41.8, 34.9, 27.2, 26.8, 24.5, 18.9, 18.4, 13.9; HRMS (ESI) $m/z$ calculated for [C$_{14}$H$_{22}$O$_5$]+Na$^+$[M+Na]$^+$ 293.1359, found: 293.1355.

Ethyl ($S$)-2-hydroxy-4-methyl-3-oxo-2-((S)-2-oxocyclohexyl)pentanoate (2h, minor diastereoisomer)
32.4 mg (colorless oil); $R_f = 0.38$ (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.15 (q, $J = 7.1$ Hz, 2H), 4.04 (s, 1H), 3.57-3.54 (m, 1H), 3.30 (sep, $J = 6.7$ Hz, 1H), 2.36-2.25 (m, 2H), 2.04-2.01 (m, 1H), 1.84-1.83 (m, 1H), 1.71-1.60 (m, 4H), 1.17 (t, $J = 7.1$ Hz, 3H), 0.99-0.96 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 211.9, 210.7, 170.4, 84.7, 62.6, 40.2, 35.0, 28.0, 27.1, 24.6, 18.8, 18.5, 13.8.

Methyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)-4-phenylbutanoate (2i, major diastereoisomer)

161.3 mg (light yellow oil); $R_f = 0.25$ (PE/EtOAc = 3:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34-7.28 (m, 3H), 7.18-7.16 (m, 2H), 4.18 (brs, 1H), 4.03 (d, $J = 16.6$ Hz, 1H), 3.95 (d, $J = 16.6$ Hz, 1H), 3.72 (s, 3H), 3.63 (dd, $J = 11.2$ Hz, 5.9 Hz, 1H), 2.44-2.34 (m, 2H), 2.10-2.06 (m, 1H), 1.90-1.87 (m, 1H), 1.79-1.76 (m, 2H), 1.69-1.64 (m, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 210.7, 205.2, 170.8, 133.1, 129.8, 128.5, 127.0, 84.8, 56.1, 53.6, 44.3, 42.0, 27.7, 27.1, 24.6; HRMS (ESI) $m/z$ calculated for [C$_{17}$H$_{20}$O$_5$+Na]$^+ [M+Na]^+$ 327.1203, found: 327.1199.

Methyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)-4-phenylbutanoate (2i, minor diastereoisomer)

45.5 mg (light yellow oil); $R_f = 0.40$ (PE/EtOAc = 3:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.28-7.25 (m, 2H), 7.22-7.17 (m, 3H), 4.31 (brs, 1H), 4.18 (d, $J = 16.3$ Hz, 1H), 4.00 (d, $J = 16.3$ Hz, 1H), 3.69-3.63 (m, 4H), 2.40-2.36 (m, 1H), 2.31-2.23 (m, 1H), 2.02-2.01 (m, 1H), 1.90-1.87 (m, 1H), 1.79-1.74 (m, 2H), 1.67-1.56 (m, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 209.3, 204.4, 170.4, 133.7, 129.9, 128.4, 126.9, 84.7, 57.2, 53.8, 44.1, 41.8, 27.3, 26.7, 24.4.

Benzyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)-4-phenylbutanoate (2j, major diastereoisomer)$^1$

222.0 mg; $R_f = 0.35$ (PE/EtOAc = 3:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.35 (m, 4H), 7.32-7.26
(m, 4H), 7.08 (d, $J = 6.8$ Hz, 2H), 5.20 (d, $J = 12.2$ Hz, 1H), 5.12 (d, $J = 12.2$ Hz, 1H), 4.20 (s, 1H), 4.00 (d, $J = 16.9$ Hz, 1H), 3.91 (d, $J = 16.9$ Hz, 1H), 3.67 (dd, $J = 12.0$ Hz, 5.7 Hz, 1H), 2.44-2.28 (m, 2H), 2.10-2.03 (m, 1H), 1.89-1.81 (m, 2H), 1.77-1.66 (m, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 210.8, 204.9, 170.2, 135.0, 133.2, 129.8, 128.6, 128.5, 128.3, 127.0, 85.0, 68.3, 56.1, 44.3, 42.0, 27.8, 27.2, 24.6; HRMS (ESI) $m/z$ calculated for [C$_{23}$H$_{24}$O$_5$+Na]$^+$ [M+Na]$^+$ 403.1516, found: 403.1512.

**Benzyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)-4-phenylbutanoate (2j, minor diastereoisomer)**

82.1 mg; $R_f = 0.48$ (PE/EtOAc = 3:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39-7.37 (m, 2H), 7.33-7.25 (m, 6H), 7.15 (d, $J = 6.8$ Hz, 2H), 5.17 (d, $J = 12.2$ Hz, 1H), 5.11 (d, $J = 12.1$ Hz, 1H), 4.28 (s, 1H), 4.18 (d, $J = 16.4$ Hz, 1H), 4.03 (d, $J = 16.4$ Hz, 1H), 3.73 (dd, $J = 12.5$ Hz, 5.8 Hz, 1H), 2.46-2.42 (m, 1H), 2.36-2.28 (m, 1H), 2.07-2.04 (m, 1H), 1.88-1.87 (m, 1H), 1.80-1.60 (m, 4H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 209.4, 204.3, 169.8, 134.7, 133.7, 129.9, 128.8, 128.7, 128.4, 128.4, 126.9, 84.8, 68.5, 57.2, 44.3, 41.9, 27.3, 26.8, 24.5.

**Benzyl 2-hydroxy-2-(5-methyl-2-oxocyclohexyl)-3-oxobutanoate (2l)**

225.9 mg (71% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can calculate the d.r value (d.r. = 51:24:13:12); HRMS (ESI) $m/z$ calculated for [C$_{18}$H$_{22}$O$_5$+Na]$^+$ [M+Na]$^+$ 341.1359, found: 341.1354.

**Benzyl 2-(5-ethyl-2-oxocyclohexyl)-2-hydroxy-3-oxobutanoate (2m)**

242.5 mg (73% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can calculate the d.r value (d.r. = 44:25:16:15); HRMS (ESI) $m/z$ calculated for [C$_{19}$H$_{24}$O$_5$+Na]$^+$ [M+Na]$^+$ 355.1516, found:
355.1510.

Benzyl 2-hydroxy-3-oxo-2-(2-oxo-5-propylcyclohexyl)butanoate (2n)
325.4 mg (94% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can calculate the d.r value (d.r. = 45:25:16:14); HRMS (ESI) m/z calculated for [C$_{20}$H$_{26}$O$_5$+Na]$^+$ [M+Na]$^+$ 369.1673, found: 369.1668.

Benzyl 2-(5-(tert-butyl)-2-oxocyclohexyl)-2-hydroxy-3-oxobutanoate (2o)
316.9 mg (88% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can calculate the d.r value (d.r. = 31:28:25:16); HRMS (ESI) m/z calculated for [C$_{21}$H$_{28}$O$_5$+Na]$^+$ [M+Na]$^+$ 383.1829, found: 383.1820.

Benzyl 2-hydroxy-3-oxo-2-(2-oxo-5-phenylcyclohexyl)butanoate (2p)
266.1 mg (70% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can calculate the d.r value (d.r. = 45:20:20:15); HRMS (ESI) m/z calculated for [C$_{23}$H$_{24}$O$_5$+Na]$^+$ [M+Na]$^+$ 403.1516, found: 403.1510.
Methyl 3-(1-(benzyloxy)-2-hydroxy-1,3-dioxobutan-2-yl)-4-oxocyclohexane-1-carboxylate (2q)

325.9 mg (90% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can calculate the d.r value (d.r. = 50:20:15:15); HRMS (ESI) m/z calculated for $[\text{C}_{19}\text{H}_{22}\text{O}_7+\text{Na}]^+$ [M+Na]$^+$ 385.1258, found: 385.1250.

Benzyl 2-(5-acetamido-2-oxocyclohexyl)-2-hydroxy-3-oxobutanoate (2r)

306.9 mg (85% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can’t able to calculate the d.r value; HRMS (ESI) m/z calculated for $[\text{C}_{17}\text{H}_{23}\text{NO}_6+\text{Na}]^+$ [M+Na]$^+$ 384.1415, found: 384.1411.

3-Hydroxy-3-(2-oxocyclohexyl)pentane-2,4-dione (2s)

165.4 mg (colorless oil, 78% yield); $R_f$ = 0.29 (PE/EtOAc = 5:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.67 (s, 1H), 3.60-3.56 (m, 1H), 2.31-2.15 (m, 3H), 2.11 (s, 3H), 2.10 (s, 3H), 1.94-1.92 (m, 1H), 1.81-1.78 (m, 1H), 1.61-1.51 (m, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 208.6, 207.1, 205.9, 91.2, 57.1, 41.7, 27.0, 26.3, 25.0, 24.8, 24.3; HRMS (ESI) m/z calculated for $[\text{C}_{11}\text{H}_{16}\text{O}_4-\text{H}]^-$ [M-H]$^-$ 211.0976, found: 211.0972.
Ethyl 2-(5-ethyl-2-oxocyclohexyl)-2-hydroxy-3-oxo-3-phenylpropanoate (2u)
209.4 mg (65% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can’t able to calculate the d.r value; HRMS (ESI) $m/z$ calculated for [C$_{10}$H$_{24}$O$_5$-H$^-$] [M-H$^-$] 331.1551, found: 331.1553.

Ethyl 2-hydroxy-3-oxo-2-(2-oxo-5-phenylcyclohexyl)-3-phenylpropanoate (2v)
228.1 mg (60% yield); The diastereoisomers can’t be separated in pure form by column chromatography. From the $^1$H NMR of the reaction mixture, we can’t able to calculate the d.r value; HRMS (ESI) $m/z$ calculated for [C$_{23}$H$_{24}$O$_5$-H$^-$] [M-H$^-$] 379.1545, found: 379.1547.

2-Hydroxy-2-(2-oxocyclohexyl)-$^{1}H$-indene-1,3($^{2}H$)-dione (2aa)$^{2}$
206.4 mg (light yellow solid, 80% yield); m.p.: 121.3-122.6 °C; $R_f = 0.14$ (PE/EtOAc = 3:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03-8.01 (m, 2H), 7.91-7.89 (m, 2H), 3.52 (brs, 1H), 3.29 (dd, $J = 13.0$ Hz, 5.7 Hz, 1H), 2.35-2.31 (m, 2H), 2.10-2.03 (m, 3H), 1.69-1.63 (m, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 211.5, 199.4, 198.7, 141.4, 140.6, 136.02, 135.97, 123.9, 123.8, 74.1, 55.6, 41.5, 27.1, 26.7, 24.7.

Benzyl 2-methylbenzofuran-3-carboxylate (3a)$^{3}$
45.8 mg (colorless oil, 86% yield); \( R_f = 0.38 \) (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.00-7.98 (m, 1H), 7.52 (d, \( J = 7.2 \) Hz, 2H), 7.48-7.39 (m, 4H), 7.33-7.30 (m, 2H), 5.45 (s, 2H), 2.81 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.3, 164.0, 153.6, 136.2, 128.7, 128.3, 128.2, 126.2, 124.4, 123.9, 121.8, 110.8, 108.8, 66.1, 14.6.

**Methyl 2-methylbenzofuran-3-carboxylate (3b)**

30.4 mg (colorless oil, 80% yield); \( R_f = 0.36 \) (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.97 (d, \( J = 6.5 \) Hz, 1H), 7.45 (d, \( J = 7.8 \) Hz, 1H), 7.32-7.28 (m, 2H), 3.98 (s, 3H), 2.80 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 165.0, 163.7, 153.6, 126.1, 124.3, 123.8, 121.7, 110.8, 108.9, 51.4, 14.5.

**Ethyl 2-methylbenzofuran-3-carboxylate (3c)**

31.8 mg (colorless oil, 78% yield); \( R_f = 0.36 \) (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.98 (d, \( J = 6.6 \) Hz, 1H), 7.45 (d, \( J = 8.3 \) Hz, 1H), 7.32-7.28 (m, 2H), 4.44 (q, \( J = 7.1 \) Hz, 2H), 2.80 (s, 3H), 1.47 (t, \( J = 7.1 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.6, 163.6, 153.6, 126.2, 124.3, 123.7, 121.7, 110.8, 109.0, 60.3, 14.4.

**Pentyl 2-methylbenzofuran-3-carboxylate (3d)**

44.3 mg (colorless oil, 90% yield); \( R_f = 0.46 \) (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.99-7.97 (m, 1H), 7.46-7.44 (m, 1H), 7.33-7.30 (m, 2H), 4.38 (t, \( J = 6.7 \) Hz, 2H), 2.80 (s, 3H), 1.88-1.81 (m, 2H), 1.53-1.41 (m, 4H), 0.97 (t, \( J = 7.1 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.6, 163.6, 153.6, 126.3, 124.3, 123.7, 121.7, 110.8, 109.1, 64.5, 28.5, 28.3, 22.4, 14.5, 14.0; HRMS (ESI) \textit{m/z} calculated for [C\(_{12}\)H\(_{16}\)O\(_3\)H\(^+\)] \([\text{M+H}^+]\) 247.1329, found: 247.1328.
Isobutyl 2-methylbenzofuran-3-carboxylate (3e)
36.7 mg (colorless oil, 79% yield); \( R_f = 0.46 \) (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \)
7.99 (d, \( J = 7.2 \) Hz, 1H), 7.46 (d, \( J = 7.5 \) Hz, 1H), 7.34-7.28 (m, 2H), 4.18 (d, \( J = 6.5 \) Hz, 2H), 2.81 (s, 3H), 2.21-2.11 (m, 1H), 1.09 (d, \( J = 6.7 \) Hz, 6H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \)
164.7, 163.7, 153.6, 126.3, 124.3, 123.8, 121.7, 110.8, 109.1, 70.6, 27.9, 19.4, 14.5; HRMS (ESI) m/z calculated for \([C_{14}H_{16}O_{3}+H]^+\) [M+H]^+ 233.1172, found: 233.1172.

2-Methoxyethyl 2-methylbenzofuran-3-carboxylate (3f)
29.0 mg (colorless oil, 62% yield); \( R_f = 0.38 \) (PE/EtOAc = 10:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \)
8.01-7.99 (m, 1H), 7.46-4.44 (m, 1H), 7.32-7.28 (m, 2H), 4.52 (d, \( J = 4.7 \) Hz, 2H), 3.79 (d, \( J = 4.7 \) Hz, 2H), 3.47 (s, 3H), 2.80 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \)
164.4, 163.9, 153.6, 126.2, 124.3, 123.8, 121.8, 110.7, 108.9, 70.6, 63.1, 59.0, 14.5; HRMS (ESI) m/z calculated for \([C_{13}H_{14}O_{4}+H]^+\) [M+H]^+ 235.0965, found: 235.0963.

Ethyl 2-propylbenzofuran-3-carboxylate (3g)
33.4 mg (colorless oil, 72% yield); \( R_f = 0.44 \) (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \)
8.01-7.99 (m, 1H), 7.47-7.45 (m, 1H), 7.34-7.28 (m, 2H), 4.44 (q, \( J = 7.0 \) Hz, 2H), 3.19 (t, \( J = 7.4 \) Hz, 2H), 1.89-1.80 (m, 2H), 1.47 (t, \( J = 7.0 \) Hz, 3H), 1.04 (t, \( J = 7.4 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \)
167.4, 164.5, 153.6, 126.3, 124.3, 123.7, 121.9, 110.8, 108.7, 60.2, 30.0, 21.4, 14.4, 13.9; HRMS (ESI) m/z calculated for \([C_{14}H_{16}O_{3}+H]^+\) [M+H]^+ 233.1172, found: 233.1171.
Ethyl 2-isopropylbenzofuran-3-carboxylate (3h)
31.2 mg (colorless oil, 68% yield); R_f = 0.44 (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl_3) \(\delta\) 8.02-8.00 (m, 1H), 7.50-7.47 (m, 1H), 7.34-7.30 (m, 2H), 4.45 (q, \(J = 7.1 \text{ Hz}, 2\text{H}\)), 4.07 (sep, \(J = 7.0 \text{ Hz}, 3\text{H}\)), 1.48 (t, \(J = 7.1 \text{ Hz}, 3\text{H}\)); \(^{13}\)C NMR (101 MHz, CDCl_3) \(\delta\) 171.5, 164.5, 153.5, 126.3, 124.2, 123.7, 122.0, 110.9, 107.1, 60.3, 27.5, 20.6, 14.4; HRMS (ESI) m/z calculated for \([C_{14}H_{16}O_3+H]\)\(^+\) [M+H]\(^+\) 233.1172, found: 233.1172.

Methyl 2-benzylbenzofuran-3-carboxylate (3i)
29.3 mg (colorless oil, 55% yield); R_f = 0.35 (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl_3) \(\delta\) 8.02-8.00 (m, 1H), 7.46-7.44 (m, 1H), 7.40-7.38 (m, 2H), 7.35-7.30 (m, 4H), 7.28-7.26 (m, 1H), 4.58 (s, 2H), 4.01 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl_3) \(\delta\) 164.8, 164.6, 153.9, 136.8, 128.9, 128.6, 126.9, 125.9, 124.7, 123.9, 122.1, 111.1, 109.0, 51.6, 34.1; HRMS (ESI) m/z calculated for \([C_{17}H_{14}O_3-H]\) [M-H] 265.0870, found: 265.0866.

Benzyl 2-benzylbenzofuran-3-carboxylate (3j)
34.2 mg (colorless oil, 50% yield); R_f = 0.38 (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl_3) \(\delta\) 8.00-7.98 (m, 1H), 7.50-7.49 (m, 2H), 7.46-7.39 (m, 4H), 7.35-7.28 (m, 6H), 7.26-7.24 (m, 1H), 5.46 (s, 2H); \(^{13}\)C NMR (101 MHz, CDCl_3) \(\delta\) 164.8, 164.1, 153.9, 136.7, 135.9, 128.9, 128.7, 128.6, 128.4, 126.8, 126.0, 124.7, 123.9, 122.1, 111.1, 108.9, 66.4, 34.1; HRMS (ESI) m/z calculated for \([C_{23}H_{18}O_3-H]\) [M-H] 341.1183, found: 341.1179.
Methyl 2-ethylbenzofuran-3-carboxylate (3k)

28.6 mg (colorless oil, 70% yield); \( R_f = 0.40 \) (PE/E\textsubscript{t}OAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.00-7.98 (m, 1H), 7.48-7.46 (m, 1H), 7.33-7.30 (m, 2H), 3.97 (s, 3H), 3.24 (q, \( J = 7.6 \) Hz, 2H), 1.38 (t, \( J = 7.6 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 168.5, 164.9, 153.6, 126.2, 124.3, 123.8, 121.9, 110.9, 107.9, 51.4, 21.7, 12.1.

Benzyl 2,5-dimethylbenzofuran-3-carboxylate (3l)

43.7 mg (colorless oil, 78% yield); \( R_f = 0.40 \) (PE/E\textsubscript{t}OAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.79 (s, 1H), 7.52-7.51 (m, 2H), 7.46-7.38 (m, 3H), 7.33 (d, \( J = 8.4 \) Hz, 1H), 7.11 (d, \( J = 8.4 \) Hz, 1H), 5.44 (s, 2H), 2.78 (s, 3H), 2.46 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.4, 164.0, 136.3, 133.4, 128.7, 128.2, 128.1, 126.2, 125.5, 121.6, 110.3, 66.0, 21.5, 14.7.

Benzyl 5-ethyl-2-methylbenzofuran-3-carboxylate (3m)

41.8 mg (colorless oil, 71% yield); \( R_f = 0.40 \) (PE/E\textsubscript{t}OAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.83 (s, 1H), 7.54-7.52 (m, 2H), 7.46-7.39 (m, 3H), 7.36 (d, \( J = 8.4 \) Hz, 1H), 7.15 (d, \( J = 8.4 \) Hz, 1H), 5.46 (s, 2H), 2.80 (s, 3H), 2.77 (q, \( J = 7.6 \) Hz, 2H), 1.30 (t, \( J = 7.6 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.4, 164.0, 152.2, 140.0, 136.3, 128.7, 128.2, 128.1, 126.3, 124.5, 120.4, 110.4, 108.7, 66.1, 28.9, 16.2, 14.7; HRMS (ESI) \( m/z \) calculated for \([C_{19}H_{18}O_3]^+ [M+H]^+ \) 295.1329, found: 295.1328.

Benzyl 2-methyl-5-propylbenzofuran-3-carboxylate (3n)

47.4 mg (white solid, 77% yield); m.p.: 44.2-45.0 °C; \( R_f = 0.36 \) (PE/E\textsubscript{t}OAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.81 (d, \( J = 1.2 \) Hz, 1H), 7.53 (d, \( J = 7.2 \) Hz, 2H), 7.47-7.35 (m, 4H), 7.12 (dd, \( J = 12.1 \))
8.4 Hz, 1.7 Hz, 1H), 5.45 (s, 2H), 2.79 (s, 3H), 2.70 (t, $J = 8.2$ Hz, 2H), 1.73-1.65 (m, 2H), 0.98 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.4, 164.0, 152.2, 138.4, 136.3, 128.6, 128.2, 128.1, 126.2, 125.0, 121.1, 110.3, 108.7, 66.1, 38.0, 25.0, 14.7, 13.8; HRMS (ESI) m/z calculated for [C$_{20}$H$_{20}$O$_3$-H] $^-$ [M-H] 307.1340, found: 307.1337.

![3o](image)

**Benzyl 5-((tert-butyl)-2-methylbenzofuran-3-carboxylate (3o)**

47.7 mg (white solid, 74% yield); m.p.: 94.6-97.9 °C; $R_f = 0.33$ (PE/EtOAc = 20:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.01 (s, 1H), 7.55 (d, $J = 7.0$ Hz, 2H), 7.48-7.41 (m, 3H), 7.38-7.37 (m, 2H), 5.45 (s, 2H), 2.81 (s, 3H), 1.38 (s, 9H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.5, 164.1, 151.9, 146.9, 136.1, 128.7, 128.3, 128.2, 125.8, 122.2, 118.1, 110.1, 108.8, 66.2, 34.9, 31.8, 14.6; HRMS (ESI) m/z calculated for [C$_{21}$H$_{22}$O$_3$-H] $^-$ [M-H] 321.1496, found: 321.1494.

![3p](image)

**Benzyl 2-methyl-5-phenylbenzofuran-3-carboxylate (3p)**

56.1 mg (white solid, 82% yield); m.p.: 121.2-123.8 °C; $R_f = 0.24$ (PE/EtOAc = 20:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.22 (d, $J = 1.6$ Hz, 1H), 7.65-7.61 (m, 2H), 7.57-7.52 (m, 3H), 7.51-7.45 (m, 4H), 7.44-7.36 (m, 3H), 5.46 (s, 2H), 2.83 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.6, 164.2, 153.2, 141.3, 137.3, 136.1, 128.9, 128.8, 128.7, 128.3, 128.2, 127.4, 127.0, 126.7, 123.8, 120.4, 110.9, 109.0, 66.3, 14.7; HRMS (ESI) m/z calculated for [C$_{23}$H$_{18}$O$_3$-H] $^-$ [M-H] 341.1183, found: 341.1182.

![3q](image)

**3-Benzyl 5-methyl 2-methylbenzofuran-3,5-dicarboxylate (3q)**

42.8 mg (white solid, 66% yield); m.p.: 124.4-125.3 °C; $R_f = 0.27$ (PE/EtOAc = 10:1); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.69 (d, $J = 1.5$ Hz, 1H), 8.03 (dd, $J = 8.6$ Hz, 1.8 Hz, 1H), 7.53 (d, $J = 7.1$
Hz, 2H); 7.47-7.39 (m, 4H), 5.45 (s, 2H), 3.94 (s, 3H), 2.81 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 167.1, 165.2, 163.7, 156.0, 135.9, 128.7, 128.3, 128.2, 126.3, 126.2, 124.1, 110.8, 109.3, 66.4, 52.2, 14.6; HRMS (ESI) m/z calculated for [C\(_{19}\)H\(_{16}\)O\(_5\)-H] [M-H] 323.0925, found: 323.0921.

Benzyl 5-acetamido-2-methylbenzofuran-3-carboxylate (3r)
38.8 mg (white solid, 60% yield); m.p.: 189.0-190.1 °C; R\(_f\) = 0.33 (PE/EtOAc = 1:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.90 (d, \(J = 1.9\) Hz, 1H), 7.59 (dd, \(J = 8.8\) Hz, 2.1 Hz, 1H), 7.51-7.40 (m, 5H), 7.39-7.33 (m, 2H), 5.41 (s, 2H), 2.76 (s, 3H), 2.19 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 168.5, 164.8, 164.1, 150.6, 136.1, 134.1, 128.7, 128.2, 128.1, 126.5, 118.1, 113.4, 110.9, 108.9, 66.1, 24.5, 14.7; HRMS (ESI) m/z calculated for [C\(_{19}\)H\(_{17}\)NO\(_4\)-H] [M-H] 322.1085, found: 322.1081.

1-(2-Methylbenzofuran-3-yl)ethan-1-one (3s)
16.4 mg (colorless oil, 47% yield); R\(_f\) = 0.45 (PE/EtOAc = 10:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.97-7.95 (m, 1H), 7.48-7.46 (m, 1H), 7.36-7.31 (m, 2H), 2.80 (s, 3H), 2.66 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 194.3, 162.8, 153.5, 126.1, 124.4, 124.0, 121.4, 117.6, 110.0, 31.2, 15.4.

Ethyl 2-phenylbenzofuran-3-carboxylate (3t)
30.3 mg (white solid, 57% yield); m.p.: 88.8-90.7 °C; R\(_f\) = 0.31 (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 8.16-8.01 (m, 3H), 7.59-7.48 (m, 4H), 7.44-7.34 (m, 2H), 4.44 (q, \(J = 7.1\) Hz, 2H), 1.44 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 164.0, 160.8, 153.8, 130.3, 129.6, 129.5, 128.1, 127.2, 125.2, 124.0, 122.7, 111.2, 109.0, 60.7, 14.3.
Ethyl 5-ethyl-2-phenylbenzofuran-3-carboxylate (3u)

27.1 mg (colorless oil, 46% yield); \( R_f = 0.33 \) (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \)
8.09-7.99 (m, 2H), 7.92 (d, \( J = 1.1 \) Hz, 1H), 7.56-7.44 (m, 4H), 7.23 (dd, \( J = 8.4 \) Hz, 1.8 Hz, 1H),
4.44 (q, \( J = 7.1 \) Hz, 2H), 2.82 (q, \( J = 7.6 \) Hz, 2H), 1.44 (t, \( J = 7.1 \) Hz, 3H), 1.35 (t, \( J = 7.6 \) Hz, 3H);
\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.2, 160.8, 152.4, 140.2, 130.1, 129.8, 129.5, 128.1, 128.0, 127.2,
125.5, 121.2, 110.8, 108.8, 60.6, 29.1, 16.3, 14.3; HRMS (ESI) \( m/z \) calculated for \([\text{C}_{19}\text{H}_{18}\text{O}_3+\text{H}]^+\)
\([\text{M+H}]^+\) 295.1329, found: 295.1325.

Ethyl 2,5-diphenylbenzofuran-3-carboxylate (3v)

23.9 mg (white solid, 35% yield); m.p.: 108.4-111.3 °C; \( R_f = 0.27 \) (PE/EtOAc = 20:1); \(^1\)H NMR
(400 MHz, CDCl\(_3\)) \( \delta \) 8.33 (s, 1H), 8.08 (dd, \( J = 6.6 \) Hz, 3.2 Hz, 2H), 7.74-7.67 (m, 2H), 7.62 (d, \( J = 0.9 \) Hz, 2H),
7.56-7.48 (m, 5H), 7.43-7.39 (m, 1H), 4.47 (q, \( J = 7.1 \) Hz, 2H), 1.45 (t, \( J = 7.1 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.0, 161.3, 153.4, 141.5, 137.7, 130.4, 129.6, 129.6, 128.8,
128.1, 127.5, 127.1, 124.9, 121.2, 111.3, 109.1, 60.7, 14.3; HRMS (ESI) \( m/z \) calculated for
\([\text{C}_{23}\text{H}_{18}\text{O}_3+\text{H}]^+\) \([\text{M+H}]^+\) 343.1329, found: 243.1324.

Ethyl 2-(naphthalen-2-yl)benzofuran-3-carboxylate (3w)

22.8 mg (colorless oil, 36% yield); \( R_f = 0.31 \) (PE/EtOAc = 20:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \)
8.63 (s, 1H), 8.16-8.09 (m, 2H), 8.00-7.91 (m, 3H), 7.62-7.56 (m, 3H), 7.45-7.38 (m, 2H), 4.47 (q,
\( J = 7.1 \) Hz, 2H), 1.45 (t, \( J = 7.1 \) Hz, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.1, 160.7, 153.9, 134.0,
132.7, 129.9, 128.9, 127.7, 127.6, 127.4, 127.3, 127.0, 126.5, 126.2, 125.3, 124.1, 122.8, 111.2,
109.2, 60.7, 14.4; HRMS (ESI) \( m/z \) calculated for \([\text{C}_{21}\text{H}_{16}\text{O}_3+\text{H}]^+\) \([\text{M+H}]^+\) 317.1172, found:
317.1169.
Ethyl 2-(4-chlorophenyl)benzofuran-3-carboxylate (3y)
27.0 mg (white solid, 45% yield); m.p.: 87.8-89.4 °C; R_f = 0.44 (PE/EtOAc = 20:1); ¹H NMR (400 MHz, CDCl₃) δ 8.13-8.07 (m, 1H), 8.05 (d, J = 8.7 Hz, 2H), 7.57-7.54 (m, 1H), 7.49 (d, J = 8.7 Hz, 2H), 7.44-7.35 (m, 2H), 4.45 (q, J = 7.1 Hz, 2H), 1.46 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 163.9, 159.4, 153.7, 136.4, 130.8, 128.4, 128.0, 127.0, 125.5, 124.2, 122.8, 111.2, 109.3, 60.8, 14.3; HRMS (ESI) m/z calculated for [C₁₇H₁₄O₃Cl⁺][M+H]+ 301.0626, found: 301.0622; calculated for [C₁₇H₁₄O₃Cl³⁷⁺][M+H]+ 303.0597, found: 301.0593.

Ethyl 2-(4-bromophenyl)benzofuran-3-carboxylate (3z)
35.1 mg (white solid, 51% yield); m.p.: 82.5-83.7 °C; R_f = 0.40 (PE/EtOAc = 20:1); ¹H NMR (400 MHz, CDCl₃) δ 8.12-8.06 (m, 1H), 7.98 (d, J = 8.7 Hz, 2H), 7.65 (d, J = 8.6 Hz, 2H), 7.57-7.54 (m, 1H), 7.43-7.35 (m, 2H), 4.45 (q, J = 7.1 Hz, 2H), 1.46 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 163.9, 159.4, 153.8, 131.4, 131.0, 128.5, 127.0, 125.5, 124.8, 124.2, 122.8, 111.2, 109.4, 60.8, 14.3; HRMS (ESI) m/z calculated for [C₁₇H₁₄O₃Br⁷⁹⁺][M+H]+ 345.0121, found: 345.0115; calculated for [C₁₇H₁₄O₃Br³⁷⁺][M+H]+ 347.0101, found: 347.0095.

10H-Indeno[1,2-b]benzofuran-10-one (3aa)
16.7 mg (orange solid, 38% yield); m.p.: 159.0-161.6 °C; R_f = 0.35 (PE/EtOAc = 20:1); ¹H NMR (400 MHz, CDCl₃) δ 7.77-7.75 (m, 1H), 7.56-7.51 (m, 2H), 7.40-7.27 (m, 5H); ¹³C NMR (101 MHz, CDCl₃) δ 185.0, 178.4, 160.8, 138.7, 133.6, 132.9, 130.4, 125.3, 125.1, 123.6, 122.2, 121.0, 118.5, 118.3, 112.6; HRMS (ESI) m/z calculated for [C₁₃H₈O₂⁺][M+H]+ 221.0597, found: 221.0594.
References


\(^1\)H NMR and \(^{13}\)C NMR spectra of products 2 and 3

**Ethyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2c, major diastereoisomer)**

\(^1\)H NMR (400 MHz, CDCl\(_3\)):

\[^{13}\]C NMR (101 MHz, CDCl\(_3\)):

![NMR spectra](image-url)
Ethyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2c, minor diastereoisomer)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Pentyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2d, major diastereoisomer)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Pentyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2d, minor diastereoisomer)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Isobutyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2e, major diastereoisomer)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Isobutyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate (2e, minor diastereoisomer)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)

S28
2-Methoxyethyl \((R)-2\)-hydroxy-3-oxo-2-\((S)-2\text{-oxocyclohexyl})\)butanoate (2f, major diastereoisomer)

\[^1\text{H} \text{NMR (400 MHz, CDCl}_3\text{)}\]

\[
\begin{align*}
4.297 & 4.2927 \\
4.2514 & 4.2532 \\
4.2111 & 4.2119 \\
4.1998 & 4.1998 \\
3.591 & 3.591 \\
3.541 & 3.5415 \\
3.3588 & 3.3588 \\
3.3492 & 3.3492 \\
3.3204 & 3.3204 \\
3.2794 & 3.2794 \\
3.2419 & 3.2419 \\
3.2219 & 3.2219 \\
2.967 & 2.967 \\
2.7062 & 2.7062 \\
1.9468 & 1.9468 \\
1.9619 & 1.9619 \\
1.9938 & 1.9938 \\
1.9973 & 1.9973 \\
1.9995 & 1.9995 \\
1.9968 & 1.9968 \\
1.9983 & 1.9983 \\
1.9988 & 1.9988 \\
1.8466 & 1.8466 \\
1.7651 & 1.7651 \\
1.6985 & 1.6985 \\
1.6784 & 1.6784 \\
1.6244 & 1.6244 \\
1.5530 & 1.5530 \\
1.5877 & 1.5877 \\
1.4941 & 1.4941 
\end{align*}
\]
\[ \text{2-Methoxyethyl} \quad (S)-2\text{-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)butanoate} \quad (2f, \text{ minor diastereoisomer}) \]

\[ ^{13}\text{C NMR (101 MHz, CDCl}_3\text{)} \]

\[ ^{1}\text{H NMR (400 MHz, CDCl}_3\text{)} \]
Ethyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)hexanoate (2g, major diastereoisomer)

\[ \text{\(^1H\) NMR (400 MHz, CDCl}_3\) } \]

\[ \text{\(^{13}C\) NMR (101 MHz, CDCl}_3\) } \]
Ethyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)hexanoate (2g, minor diastereoisomer)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Ethyl (R)-2-hydroxy-4-methyl-3-oxo-2-((S)-2-oxocyclohexyl)pentanoate (2h, major diastereoisomer)

$^1$H NMR (400 MHz, CDCl$_3$)
Ethyl (S)-2-hydroxy-4-methyl-3-oxo-2-((S)-2-oxocyclohexyl)pentanoate (2h, minor diastereoisomer)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Methyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)-4-phenylbutanoate (2i, major diastereoisomer)

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

Methyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)-4-phenylbutanoate (2i, minor diastereoisomer)

$^1$C NMR (101 MHz, CDCl$_3$)
Benzyl (R)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)-4-phenylbutanoate (2j, major diastereoisomer)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$C NMR (101 MHz, CDCl$_3$)

Benzyl (S)-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)-4-phenylbutanoate (2j, minor diastereoisomer)

$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

Benzyl 2-hydroxy-2-(5-methyl-2-oxocyclohexyl)-3-oxobutanoate (2l)

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

Benzyl 2-(5-ethyl-2-oxocyclohexyl)-2-hydroxy-3-oxobutanoate (2m)
\(^1\)H NMR (400 MHz, CDCl\(_3\))

Benzyl 2-hydroxy-3-oxo-2-(2-oxo-5-propylcyclohexyl)butanoate (2n)

\(^1\)H NMR (400 MHz, CDCl\(_3\))

Benzyl 2-(5-(tert-butyl)-2-oxocyclohexyl)-2-hydroxy-3-oxobutanoate (2o)

540
\(^1\text{H NMR (400 MHz, CDCl}_3\text{)}\)

Benzyl 2-hydroxy-3-oxo-2-(2-oxo-5-phenylcyclohexyl)butanoate (2p)

Methyl 3-(1-(benzyloxy)-2-hydroxy-1,3-dioxobutan-2-yl)-4-oxocyclohexane-1-carboxylate (2q)

\(^1\text{H NMR (400 MHz, CDCl}_3\text{)}\)
Benzyl 2-(5-acetamido-2-oxocyclohexyl)-2-hydroxy-3-oxobutanoate (2r)
$^1$H NMR (400 MHz, CDCl$_3$)

3-Hydroxy-3-(2-oxocyclohexyl)pentane-2,4-dione (2s)
Ethyl 2-((5-ethyl-2-oxocyclohexyl)-2-hydroxy-3-oxo-3-phenylpropanoate (2u)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Ethyl 2-hydroxy-3-oxo-2-(2-oxo-5-phenylcyclohexyl)-3-phenylpropanoate (2v)

$^1$H NMR (400 MHz, CDCl$_3$)
Methyl (R)-3-cyclopropyl-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)propanoate (2ab, major diastereoisomer)
$^1$H NMR (400 MHz, CDCl$_3$)

Methyl (S)-3-cyclopropyl-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)propanoate (2ab, minor diastereoisomer)

$^{13}$C NMR (101 MHz, CDCl$_3$)

Methyl (S)-3-cyclopropyl-2-hydroxy-3-oxo-2-((S)-2-oxocyclohexyl)propanoate (2ab, minor diastereoisomer)
**Benzyl 2-methylbenzofuran-3-carboxylate (3a)**

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Methyl 2-methylbenzofuran-3-carboxylate (3b)

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \]
Ethyl 2-methylbenzofuran-3-carboxylate (3c)

$^1$H NMR (400 MHz, CDCl$_3$)
Pentyl 2-methylbenzofuran-3-carboxylate (3d)

$^1$H NMR (400 MHz, CDCl$_3$)
Isobutyl 2-methylbenzofuran-3-carboxylate (3e)

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

$^1$C NMR (101 MHz, CDCl$_3$)
2-Methoxyethyl 2-methylbenzofuran-3-carboxylate (3f)

\(^1\)H NMR (400 MHz, CDCl\(_3\))

\(^{13}\)C NMR (101 MHz, CDCl\(_3\))
$^1$H NMR (400 MHz, CDCl$_3$)

$^1$C NMR (101 MHz, CDCl$_3$)

**Ethyl 2-propylbenzofuran-3-carboxylate (3g)**
Ethyl 2-isopropylbenzofuran-3-carboxylate (3h)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Methyl 2-benzylbenzofuran-3-carboxylate (3i)

$^1$H NMR (400 MHz, CDCl$_3$)
Methyl 2-benzylbenzofuran-3-carboxylate (3j)
Methyl 2-ethylbenzofuran-3-carboxylate (3k)
1H NMR (400 MHz, CDCl₃)

13C NMR (101 MHz, CDCl₃)

Benzyl 2,5-dimethylbenzofuran-3-carboxylate (3l)
Benzyl 5-ethyl-2-methylbenzofuran-3-carboxylate (3m)
Benzyl 2-methyl-5-propylbenzofuran-3-carboxylate (3n)

1H NMR (400 MHz, CDCl$_3$)

13C NMR (101 MHz, CDCl$_3$)
Benzyl 5-(tert-butyl)-2-methylbenzofuran-3-carboxylate (3o)
$^1$H NMR (400 MHz, CDCl$_3$)

Benzyl 2-methyl-5-phenylbenzofuran-3-carboxylate (3p)

$^{13}$C NMR (101 MHz, CDCl$_3$)

Benzyl 2-methyl-5-phenylbenzofuran-3-carboxylate (3p)
3-Benzyl 5-methyl 2-methylbenzofuran-3,5-dicarboxylate (3q)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Benzyl 5-acetamido-2-methylbenzofuran-3-carboxylate (3r)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
1-(2-Methylbenzofuran-3-yl)ethan-1-one (3s)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Ethyl 2-phenylbenzofuran-3-carboxylate (3t)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Ethyl 5-ethyl-2-phenylbenzofuran-3-carboxylate (3u)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Ethyl 2,5-diphenylbenzofuran-3-carboxylate (3v)

$^1$H NMR (400 MHz, CDCl₃)

$^{13}$C NMR (101 MHz, CDCl₃)

S69
Ethyl 2-(naphthalen-2-yl)benzofuran-3-carboxylate (3w)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Ethyl 2-(4-chlorophenyl)benzofuran-3-carboxylate (3y)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
Ethyl 2-((4-bromophenyl)benzofuran-3-carboxylate (3z)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)
$10H$-Indeno[1,2-$b$]benzofuran-10-one (3aa)

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

$^{13}$C NMR (101 MHz, CDCl$_3$)