Supporting Information

Enantioselective Organocatalytic Michael Additions to Acrylic Acid Derivatives: Generation of All-Carbon Quaternary Stereocentres

Caroline L. Rigby and Darren J. Dixon*

School of Chemistry, The University of Manchester, Oxford Road, Manchester, M13 9PL, United Kingdom

Darren.Dixon@manchester.ac.uk
## Contents

**General Experimental** 5

**Starting Materials** 7

**Synthesis of Michael Acceptors 3c, 3d, 3f, 3g and pro-nucleophile 11** 7
  - Synthesis and characterisation of Michael acceptor 3c 7
  - Synthesis and characterisation of Michael acceptor 3d 8
  - Synthesis and characterisation of Michael acceptor 3f 9
  - Synthesis and characterisation of Michael acceptor 3g 9
  - Synthesis and characterisation of pro-nucleophile 11 10

**Structure of the Catalysts** 11

**Optimisation** 11

**Optimised General Procedure** 12
  - Synthesis and characterisation of compound 4c 12
  - Synthesis and characterisation of compound 4d 13
  - Synthesis and characterisation of compound 4e 14
  - Synthesis and characterisation of compound 4f 15
  - Synthesis and characterisation of compound 4g 16
  - Synthesis and characterisation of compound 4h 17
  - Synthesis and characterisation of compound 4i 18
  - Synthesis and characterisation of compound 12c 19
  - Synthesis and characterisation of compound 13c 20
  - Synthesis and characterisation of compound 14c 21
  - Synthesis and characterisation of compound 15c 22
  - Synthesis and characterisation of compound 16c 23
  - Synthesis and characterisation of compound 17c 24
  - Synthesis and characterisation of compound 18c 25
  - Synthesis and characterisation of compound 20 26

---

**Supplementary Material (ESI) for Chemical Communications**

This journal is (c) The Royal Society of Chemistry 2008
Synthesis and characterisation of compound 21

Determination of Relative Configuration of 20 and 21

References

NMR Spectra
Spectra for compound 3c
Spectra for compound 3d
Spectra for compound 3f
Spectra for compound 3g
Spectra for compound 11
Spectra for compound 4c
Spectra for compound 4d
Spectra for compound 4e
Spectra for compound 4f
Spectra for compound 4g
Spectra for compound 4h
Spectra for compound 4i
Spectra for compound 12c
Spectra for compound 13c
Spectra for compound 14c
Spectra for compound 15c
Spectra for compound 16c
Spectra for compound 17c
Spectra for compound 18c
Spectra for compound 20
Spectra for compound 21

HPLC Traces
HPLC trace for compound 4c
HPLC trace for compound 4d
HPLC trace for compound 4e
HPLC trace for compound 4f  75
HPLC trace for compound 4g  76
HPLC trace for compound 4h  77
HPLC trace for compound 4i  78
HPLC trace for compound 12c  79
HPLC trace for compound 13c  81
HPLC trace for compound 14c  82
HPLC trace for compound 15c  83
HPLC trace for compound 16c  84
HPLC trace for compound 17c  85
HPLC trace for compound 18c  86
**General Experimental**

For all reactions conducted under anhydrous conditions glassware was dried in an oven at 100°C and carried out under a nitrogen atmosphere, unless otherwise stated.

**Solvents and Reagents**

Bulk solutions were evaporated under reduced pressure using a Büchi rotary evaporator. Reagents used were obtained from commercial suppliers or purified according to standard procedures. Petrol refers to distilled light petroleum of fraction (40 – 65 °C). Anhydrous tetrahydrofuran and diethyl ether were freshly distilled from sodium-benzophenone.

**Chromatography**

Flash column chromatography was performed with commercial solvents using Merck Kieselgel 60 silica gel (200-400 mesh). Thin layer chromatography (TLC) was performed on aluminium or glass plates pre-coated with Merck Kieselgel 60 F254 and visualised by ultra-violet radiation or by staining with either aqueous basic potassium permanganate or vanillin. Enantiomeric excesses were determined using high performance liquid chromatography (HPLC) performed on a Hewlett-Packard Series 1050 series system (column conditions are given with the compound).

**Melting Points**

Melting points were recorded on a Gallenkamp melting point apparatus with the sample contained in a thin glass tube at ambient pressure and are uncorrected.

**Polarimetry**

Optical rotations were recorded using an Optical Activity AA-1000 polarimeter; specific rotations ([α]_D) are reported in 10^−1 deg•cm^2•g⁻¹; concentrations (c) are quoted in g•(100 mL)^⁻¹; D refers to the D-line of sodium (589 nm); temperatures (T) are given in degrees Celsius (°C).
**Infra-Red Spectroscopy**

Infrared spectra were recorded on a Perkin Elmer Spectrum RX1 FTIR spectrometer (thin film deposited onto a sodium chloride plate). Only selected absorbencies (ν<sub>max</sub>) are reported.

**NMR Spectroscopy**

<sup>1</sup>H, <sup>13</sup>C, DEPT, COSY and HMQC NMR spectra were recorded on Brucker 500 MHz and Varian 300 MHz spectrometers. Chemical shifts (δ<sub>H</sub>) are quoted in parts per million (ppm ± 0.01 ppm) downfield of tetramethylsilane, relative to the residual protiosolvent (δ<sub>H</sub> (CHCl<sub>3</sub>) = 7.26 ppm) against an internal deuterium lock. Coupling constants (J) are given in Hertz (Hz ± 0.1 Hz). The <sup>1</sup>H NMR spectra are reported as follows: δ / ppm (multiplicity, coupling constants J / Hz, number of protons, assignment). DEPT and two-dimensional NMR spectroscopy (COSY and HMQC) were used where appropriate to assist the assignment of the signals in the <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra.

**Mass Spectrometry**

Low resolution mass spectrometry (electron impact / chemical ionisation) was recorded on a Micromass Trio 2000 quadropole mass spectrometer and (electrospray) on a Micromass Platform II spectrometer. High resolution mass spectra (accurate mass) were recorded on a Thermo Finnigan Mat95XP mass spectrometer.
Starting Materials

Michael acceptor 3b was prepared by the treatment of 1,2-dibromopropionyl chloride with ethanethiol followed by the elimination of bromine.\textsuperscript{S1} Michael acceptors 3e and 3h were prepared by the treatment of acryloyl chloride with thiophenol or phenol.\textsuperscript{S2,S3} Michael acceptor 3i was prepared by the treatment of carbonyl dipyrrole with vinyl magnesium bromide.\textsuperscript{S4} β-Keto esters 2, 5, 6 and 7 were prepared by acylation of the parent indanone followed by Sn-catalysed transesterification.\textsuperscript{S5} β-Keto esters 8, 9 and 10 were prepared by Dieckmann cyclisation of the corresponding open chain diester.\textsuperscript{S6}

Michael Acceptors 3c, 3d, 3f, 3g

Michael acceptors 3c, 3d, 3f and 3g were prepared using a modified literature procedure as described here.\textsuperscript{S2}

1-Naphthyl Thioacrylate 3c:

\begin{center}
\includegraphics[width=0.2\textwidth]{chemical_structure}
\end{center}

Acryloyl chloride (1.14 mL, 14 mmol) was added to a suspension of 1-thionaphthol (1 mL, 7 mmol) in 5 % aqueous NaOH solution (20 mL) at 0 °C. The mixture was stirred at 0°C for 2 minutes. It was then extracted into CH\textsubscript{2}Cl\textsubscript{2} (20 mL x 2), washed with NaHCO\textsubscript{3} (20 mL) and brine (20 mL) and dried over Na\textsubscript{2}SO\textsubscript{4}. The solvent was removed \textit{in vacuo} and the crude reaction mixture was subjected to flash column chromatography (eluting with 95:5 petrol:Et\textsubscript{2}O) to furnish the title compound as a pale yellow oil (1.04 g, 69 %).

**IR** ν\textsubscript{max} (film): 3056 (CH), 1685 (C=O); **\textsuperscript{1}H NMR** (500 MHz, CDCl\textsubscript{3}) δ\textsubscript{H} ppm: 8.19 (d, J = 8.2, 1H, Ar-H), 7.99 (d, J = 8.3, 1H, Ar-H), 7.92 (d, J = 7.6, 1H, Ar-H), 7.76 (dd, J = 7.1, 1.1, 1H, Ar-H), 7.63-7.48 (m, 3H, Ar-H), 6.56 (dd, J = 17.2, 10.2, 1H, CH\textsubscript{2}=CH), 6.46 (dd, J = 17.2, 0.9, 1H, CH\textsubscript{2}=CH), 5.83 (dd, J = 10.2, 0.9, 1H, CH\textsubscript{2}=CH); **\textsuperscript{13}C NMR** (126 MHz, CDCl\textsubscript{3}) δ\textsubscript{C} ppm: 188.3 (C=O), 135.2 (CH\textsubscript{2}=CH), 134.3 (CH\textsubscript{2}=CH), 134.2, 131.1, 128.7,
127.7, 127.3, 126.5, 125.6, 125.3, 124.6 (Ar-C); **MS**: $m/z$ (Cl) 232 (M + NH$_4^+$); **HRMS**: (ES$^+$) Found 232.0790. C$_{13}$H$_{14}$ONS requires $M$ 232.0791.

**2-Naphthyl Thioacrylate 3d:**

Acryloyl chloride (2.44 mL, 30 mmol) was added to a suspension of 2-thionaphthol (500 mg, 3 mmol) in 5\% aqueous NaOH solution (25 mL) at 0 °C. The mixture was stirred at 0 °C for 5 minutes. It was then extracted into CH$_2$Cl$_2$ (20 mL x 2), washed with NaHCO$_3$ (20 mL) and brine (20 mL) and dried over Na$_2$SO$_4$ before being filtered. The solvent was removed *in vacuo* and the crude reaction mixture was subjected to flash column chromatography (eluting with 95:5 petrol:Et$_2$O) to furnish the title compound as a colourless solid (230 mg, 33 \%).

m.p. 75-77°C; **IR** $\nu_{\text{max}}$ (film): 3028, 3016 (CH), 1677 (C=O); **$^1$H NMR** (500 MHz, CDCl$_3$) $\delta$H ppm: 8.00 (s, 1H, Ar-H), 7.93-7.80 (m, 3H, Ar-H), 7.62-7.42 (m, 3H, Ar-H), 6.51 (dd, $J$ = 17.2, 9.9, 1H, CH$_2$=CH), 6.44 (dd, $J$ = 17.2, 1.1, 1H, CH$_2$=CH), 5.81 (dd, $J$ = 9.9, 1.1, 1H, CH$_2$=CH); **$^{13}$C NMR** (126 MHz, CDCl$_3$) $\delta$C ppm: 188.8 (C=O), 134.5 (CH$_2$=CH), 134.4 (CH$_2$=CH), 133.6, 133.4, 130.9, 128.9, 128.0, 127.8, 127.6, 127.2, 126.6, 124.5 (Ar-C); **MS**: $m/z$ (Cl) 232 (M + NH$_4^+$); **HRMS**: (ES$^+$) Found 232.0792. C$_{13}$H$_{14}$ONS requires $M$ 232.0791.
1-Naphthyl Acrylate 3f:

Acryloyl chloride (1.14 mL, 14 mmol) was dissolved in CH₂Cl₂ (5 mL) and added dropwise to a solution of 1-naphthol (2 g, 14 mmol) and Et₃N (2.5 mL, 18 mmol) in CH₂Cl₂ (10 mL) under an atmosphere of N₂. The mixture was stirred at room temperature for 30 minutes. The reaction mixture was extracted into CH₂Cl₂ (20 mL x 2) and washed with brine (20 mL); it was then dried over Na₂SO₄, filtered and the solvent was removed in vacuo. The crude reaction mixture was subjected to flash column chromatography on silica gel (eluting with 9:1 petrol:EtOAc) to afford the title compound as a yellow oil (2.445 g, 88 %).

IR ν max (film): 3062 (CH), 1742 (C=O); ¹H NMR (500 MHz, CDCl₃) δ ppm: 7.92-7.84 (m, 2H, Ar-H), 7.77 (d, J = 8.29, 1H, Ar-H), 7.55-7.45 (m, 3H, Ar-H), 7.30 (dd, J = 7.45, 0.86, 1H, Ar-H), 6.75 (dd, J = 17.3, 1.1, 1H, CH₂=CH), 6.50 (dd, J = 17.3, 10.5, 1H, CH₂=CH), 6.12 (dd, J = 10.5, 1.1, 1H, CH₂=CH); ¹³C NMR (126 MHz, CDCl₃) δ ppm: 164.6 (C=O), 146.5 (CH₂=CH), 134.7 (CH₂=CH), 133.0, 128.1, 127.8, 126.8, 126.5, 126.5, 126.1, 125.4, 121.2, 118.1 (Ar-C); MS: m/z (Cl) 216 (M + NH₄⁺); HRMS: (ES⁺) Found 216.1022. C₁₃H₁₄O₂N requires M 216.1019.

2-Naphthyl Acrylate 3g:

Acryloyl chloride (1.14 mL, 14 mmol) was dissolved in CH₂Cl₂ (5 mL) and added dropwise to a solution of 2-naphthol (2 g, 14 mmol) and Et₃N (2.5 mL, 18 mmol) in CH₂Cl₂ (10 mL) under an atmosphere of N₂. The mixture was stirred at room temperature for 30 minutes. The reaction mixture was extracted into CH₂Cl₂ (20 mL x 2) and washed with brine (20 mL); it was then dried over Na₂SO₄, filtered and the solvent was removed in vacuo. The crude reaction mixture was...
subjected to flash column chromatography on silica gel (eluting with 9:1 petrol:EtOAc) to afford the title compound as a colourless solid (2.285 g, 82 %).

m.p. 43-45°C; IR \( \nu_{\text{max}} \) (film): 3058, 3034 (CH), 1742 (C=O); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta_H \) ppm: 7.90-7.79 (m, 3H, Ar-H), 7.62 (d, J = 2.3, 1H, Ar-H), 7.52-7.45 (m, 2H, Ar-H), 7.28 (dd, J = 8.8, 2.3, 1H, Ar-H), 6.66 (dd, J = 17.3, 1.2, 1H, CH\(_2\)=CH), 6.39 (dd, J = 17.3, 10.4, 1H, CH\(_2\)=CH), 6.06 (dd, J = 10.4, 1.2, 1H, CH\(_2\)=CH); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta_C \) ppm: 164.8 (C=O), 148.2 (CH\(_2\)=CH), 133.8 (CH\(_2\)=CH), 132.7, 131.5, 129.5, 128.0, 127.8, 127.7, 126.6, 125.8, 121.1, 118.5 (Ar-C); MS: m/z (CI) 216 (M + NH\(_4^+\)); HRMS: (ES\(^+\)) Found 216.1028. C\(_{13}\)H\(_{14}\)O\(_2\)N requires M \( 216.1019 \).

\[ \text{1,1,1,3,3,3-hexafluoropropan-2-yl 2-methyl-3-oxobutanoate 11:} \]

\[ \begin{array}{c}
\text{O} \\
\text{O} \\
\text{CF}_3 \\
\text{CF}_3
\end{array} \]

2-Methyl-3-oxobutanoic acid (1.99 g, 17 mmol), was dissolved in CH\(_2\)Cl\(_2\) (50 ml) and cooled to 0°C. DMAP (1.04 g, 8.5 mmol) and 1,1,1,3,3,3-hexafluoro-2-propanol (1.99 ml, 19 mmol) were added followed by EDC.HCl (3.58 g, 18.7 mmol) and the mixture was stirred for two hours. It was then warmed to room temperature, extracted into EtOAc (50 ml x 2) and washed with 1M HCl (30 ml), 1M NaHCO\(_3\) (30 ml) and brine (30 ml). The combined organic were dried over Na\(_2\)SO\(_4\), the solvent removed in vacuo, and the crude reaction mixture subjected to flash column chromatography on silica gel (eluting with 9:1 petrol:EtOAc) to afford the title compound as a pale yellow liquid (859 mg, 19 %).

IR \( \nu_{\text{max}} \) (film): 3439 (OH), 2950, 2973, 2888 (CH), 1790, 1726 (C=O); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta_H \) ppm: 11.81 (s, 0.1H, enol O\(H\)), 5.80 (sept., J = 6.2, 0.1H, CH(CF\(_3\))\(_2\)), 5.73 (sept., J = 6.0, 0.9H, CH(CF\(_3\))\(_2\)), 3.66 (q, J = 7.2, 0.9H, CH\(_2\)CH\(_3\)), 2.21 (s, 2.7H, COCH\(_3\)), 2.02 (s, 0.3H, COCH\(_3\)), 1.76 (s, 0.3H, CCH\(_3\)), 1.38 (d, J = 7.2, 2.7H, CHCH\(_3\)); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta_C \) ppm: 201.1 (C=O), 167.5 (C=O), 120.2 (q, J = 282.2, CH(CF\(_3\))\(_2\)), 66.9 (sept., J = 34.9, (CH(CF\(_3\))\(_2\)), 52.7 (CHCH\(_3\)), 28.2 (C=OCH\(_3\)), 12.6 (CHCH\(_3\)); MS: m/z (ES\(^+\)) 265 (M − H\(^+\)); HRMS: (ES\(^+\)) Found 265.0299. C\(_{13}\)H\(_{14}\)O\(_2\)F\(_6\) requires M 265.0305.
**Structure of the Catalysts**

Cinchona alkaloid based catalysts 1b, 1c and 1d were prepared according to literature procedures.\(^{S7,S8}\)

![Catalyst Structures](image)

**Optimisation**

Michael acceptor 3c (3 equivalents) was added to a solution of β-keto ester 2 (1 equivalent) followed by catalyst (10 mol%); the mixture was stirred until TLC analysis showed that all 2 had been consumed. The solvent was then removed *in vacuo* and the crude product subjected to flash column chromatography on silica gel (eluting with 95:5 petrol:Et\(_2\)O followed by 9:1 petrol:EtOAc) to afford the desired product 4c.

Details of optimisation of Michael addition of 2 to 3c are shown below:

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Conc. (M)</th>
<th>Reaction Time</th>
<th>Temp (°C)</th>
<th>Conv. (%)</th>
<th>e.e. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1b</td>
<td>CH(_2)Cl(_2)</td>
<td>1</td>
<td>30 mins</td>
<td>r.t.</td>
<td>&gt;95</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>1c</td>
<td>CH(_2)Cl(_2)</td>
<td>1</td>
<td>30 mins</td>
<td>r.t.</td>
<td>&gt;95</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>1c</td>
<td>CH(_2)Cl(_2)</td>
<td>1</td>
<td>30 mins</td>
<td>0</td>
<td>&gt;95</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>1c</td>
<td>CH(_2)Cl(_2)</td>
<td>1</td>
<td>30 mins</td>
<td>-20</td>
<td>&gt;95</td>
<td>88</td>
</tr>
<tr>
<td>5</td>
<td>1c</td>
<td>CH(_2)Cl(_2)</td>
<td>(\frac{1}{3})</td>
<td>90 mins</td>
<td>-20</td>
<td>&gt;95</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>1c</td>
<td>Solvent</td>
<td>Vol %</td>
<td>Time</td>
<td>Temp</td>
<td>Yield</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>----</td>
<td>---------</td>
<td>-------</td>
<td>--------</td>
<td>------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Toluene</td>
<td>⅓</td>
<td>2 hours</td>
<td>-20</td>
<td>&gt;95</td>
<td>82</td>
</tr>
<tr>
<td>7</td>
<td>1c</td>
<td>THF</td>
<td>⅓</td>
<td>90 mins</td>
<td>-20</td>
<td>&gt;95</td>
<td>74</td>
</tr>
<tr>
<td>8</td>
<td>1c</td>
<td>TBME</td>
<td>⅓</td>
<td>2 hours</td>
<td>-20</td>
<td>80</td>
<td>85</td>
</tr>
<tr>
<td>9</td>
<td>1c</td>
<td>EtOAc</td>
<td>⅓</td>
<td>90 mins</td>
<td>-20</td>
<td>&gt;95</td>
<td>79</td>
</tr>
<tr>
<td>10</td>
<td>1c</td>
<td>CHCl₃</td>
<td>⅓</td>
<td>90 mins</td>
<td>-20</td>
<td>&gt;95</td>
<td>90</td>
</tr>
<tr>
<td>11</td>
<td>1c</td>
<td>Me₂CO</td>
<td>⅓</td>
<td>2 hours</td>
<td>-20</td>
<td>&gt;95</td>
<td>70</td>
</tr>
<tr>
<td>12</td>
<td>1c</td>
<td>Et₂O</td>
<td>⅓</td>
<td>2 hours</td>
<td>-20</td>
<td>&gt;95</td>
<td>84</td>
</tr>
<tr>
<td>13</td>
<td>1c</td>
<td>MeCN</td>
<td>⅓</td>
<td>2 hours</td>
<td>-20</td>
<td>&gt;95</td>
<td>76</td>
</tr>
<tr>
<td>14</td>
<td>1d</td>
<td>CH₂Cl₂</td>
<td>⅓</td>
<td>2 hours</td>
<td>-20</td>
<td>&gt;95</td>
<td>96</td>
</tr>
</tbody>
</table>

**Optimised General procedure for Michael addition**

A ½M solution of β-keto ester (1 equivalent) in CH₂Cl₂ was cooled to -20°C. Michael acceptor (3 equivalents) was added followed by catalyst 1d (10 mol %) and the mixture was stirred at -20 °C until TLC analysis showed that all β-keto ester had been consumed. The solvent was then removed *in vacuo* and the crude product subjected to flash column chromatography on silica gel (eluting with 95:5 petrol:Et₂O followed by 9:1 petrol:EtOAc) to afford the desired product.

*(S)-tert-butyl 2-(3-(naphthalen-1-ylthio)-3-oxopropyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 4c:*

![Chemical structure](image)

The product was isolated as a colourless solid (38 mg, 83 %).
e.e.: 96 % (Chiralcel OD, 96:4 hexanes:IPA, 1mL/min, tᵣ = 34.6 min (minor), 40.2 min (major)).
m.p. 104-108°C; IR νₘₐₓ (film): 3054, 2975, 2930 (CH), 1734, 1708 (C=O); ¹H NMR (500 MHz, CDCl₃) δH ppm: 8.14 (d, J = 8.3, 1H, Ar-H), 7.93 (d, J = 8.2, 1H, Ar-H), 7.87 (d, J = 7.7, 1H, Ar-H), 7.78 (d, J = 7.7, 1H, Ar-H), 7.68-7.60 (m, 2H, Ar-H), 7.58-7.45 (m, 4H, Ar-...
H), 7.41 (t, J = 7.5, 1H, Ar-H), 3.65 (d, J = 17.2, 1H, indanone CH$_A$H$_B$), 3.04 (d, J = 17.2, 1H, indanone CH$_A$H$_B$), 2.92 (ddd, J = 14.2, 9.4, 3.8, 1H, CH$_2$CH$_A$H$_B$COSAr), 2.83 (ddd, J = 16.1, 11.0, 5.2, 1H, CH$_2$CH$_A$H$_B$COSAr), 2.43 (ddd, J = 14.0, 11.0, 5.1, 1H, CH$_A$H$_B$CH$_2$COSAr), 2.28 (ddd, J = 14.0, 11.1, 5.2, 1H, CH$_A$H$_B$CH$_2$COSAr), 1.41 (s, 9H, C(CH$_3$)$_3$); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$$_C$ ppm: 202.3 (C=O), 196.5 (C=O), 169.7 (C=O), 152.7, 135.4, 135.2, 134.4, 133.5, 133.3, 130.9, 128.6, 127.9, 127.2, 126.4, 126.4, 125.6, 125.3, 125.0, 124.8 (Ar-C), 82.3 (quaternary C), 60.2 (C(CH$_3$)$_3$), 39.3 (indanone CH$_A$), 27.9 (C(CH$_3$)$_3$); MS: $m/z$ (ES$^+$) 464 (M + NH$_4^+$); HRMS: (ES$^+$) Found 464.1887. C$_{27}$H$_{30}$O$_4$NS requires M 464.1890; [$\alpha$]$_D$ $^{23}$: -28.4 (c 1, CHCl$_3$).

(S)-**tert**-butyl 2-(3-(naphthalen-2-ylthio)-3-oxopropyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 4d:

![Chemical Structure](image)

The product was isolated as a colourless solid (33 mg, 75%).

e.e.: 95% (Chiralcel OD, 96:4 hexanes:IPA, 1mL/min, $t_R$ = 23.3 min (minor), 29.9 min (major)).
m.p. 92-95°C; IR $\nu_{max}$ (film): 3054, 2977, 2930 (CH), 1732, 1710 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$$_H$ ppm: 7.92 (s, 1H, Ar-H), 7.88-7.74 (m, 4H, Ar-H), 7.63 (dt, J = 7.6, 1.1, 1H, Ar-H), 7.55-7.45 (m, 3H, Ar-H), 7.44-7.38 (m, 2H, Ar-H), 3.65 (d, J = 17.2, 1H, indanone CH$_A$H$_B$), 3.05 (d, J = 17.2, 1H, indanone CH$_A$H$_B$), 2.87 (ddd, J = 15.9, 11.1, 5.1, 1H, CH$_2$CH$_A$H$_B$COSAr), 2.76 (ddd, J = 16.0, 11.0, 5.1, 1H, CH$_2$CH$_A$H$_B$COSAr), 2.43 (ddd, J = 14.0, 11.0, 5.1, 1H, CH$_A$H$_B$CH$_2$COSAr), 2.27 (ddd, J = 14.0, 11.1, 5.2, 1H, CH$_A$H$_B$CH$_2$COSAr), 1.41 (s, 9H, C(CH$_3$)$_3$); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$$_C$ ppm: 202.2 (C=O), 196.9 (C=O), 169.7 (C=O), 152.7, 135.4, 135.2, 134.4, 133.5, 133.3, 130.9, 128.8, 128.0, 127.9, 127.8, 127.2, 126.6, 126.4, 124.9, 124.8 (Ar-C), 82.3 (quaternary C), 60.2 (C(CH$_3$)$_3$), 39.3 (indanone CH$_A$), 37.5 (CH$_2$CH$_2$COSAr), 30.0 (CH$_2$CH$_2$COSAr), 27.8
(C(CH₃)₃); **MS:** m/z (ES⁺) 464 (M + NH₄⁺); **HRMS:** (ES⁺) Found 464.1884. C₂₇H₃₀O₄NS requires M 464.1890; [α]D²³: -16.8 (c 0.5, CHCl₃).

(S)-*tert*-butyl 1-oxo-2-(3-oxo-3-(phenylthio)propyl)-2,3-dihydro-1H-indene-2-carboxylate 4e:

![Chemical structure](image)

The product was isolated as a yellow oil (314 mg, 83 %).
ed.e.: 95% (Chiralpak AS, 98:2 hexanes:IPA, 1mL/min, tᵣ = 16.3 min (major), 19.0 min (minor)).

**IR** ν_max (film): 2976, 2928 (CH), 1734, 1709 (C=O); **¹H NMR** (500 MHz, CDCl₃) δ_H ppm: 7.77 (d, J = 7.7, 1H, Ar-H), 7.63 (dt, J = 7.5, 1.2, 1H, Ar-H), 7.48 (d, J = 7.7, 1H, Ar-H), 7.43-7.35 (m, 6H, Ar-H), 3.64 (d, J = 17.2, 1H, indanone CH), 3.03 (d, J = 17.2, 1H, indanone CH), 2.83 (ddd, J = 16.0, 11.1, 5.1, 1H, CH₂CH₃H₃COSAr), 2.72 (ddd, J = 16.2, 11.0, 5.2, 1H, CH₂CH₃H₃COSAr), 2.40 (ddd, J = 14.0, 11.0, 5.1, 1H, CH₃H₃CH₂COSAr), 2.24 (ddd, J = 14.0, 11.1, 5.2, 1H, CH₃H₃CH₂COSAr), 1.41 (s, 9H, C(CH₃)₃); **¹³C NMR** (126 MHz, CDCl₃) δ_C ppm: 202.2 (C=O), 196.7 (C=O), 169.7 (C=O), 152.7, 135.4, 135.1, 134.5, 129.4, 129.2, 127.9, 127.5, 126.4, 124.8 (Ar-C), 82.3 (quaternary C), 60.2 (C(CH₃)₃), 39.2 (indanone CH₂), 37.5 (CH₂CH₂COSAr), 30.0 (CH₂CH₂COSAr), 27.8 (C(CH₃)₃); **MS:** m/z (ES⁺) 414 (M + NH₄⁺); **HRMS:** (ES⁺) Found 414.1736. C₂₇H₃₀O₄NS requires M 414.1734; [α]D²²: -29.6 (c 1, CHCl₃).
(S)-tert-butyl 2-(3-(naphthalen-1-yloxy)-3-oxopropyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 4f:

The product was isolated as a pale yellow oil (34 mg, 83 %).
e.e. 94% (Chiralcel OD, 96:4 hexanes:IPA, 1mL/min, t_R = 27.7 min (minor), 37.9 min (major)).

**IR** ν_{max} (film): 3063, 2977, 2932 (CH), 1760, 1735, 1711 (C=O);

**^1H NMR** (500 MHz, CDCl_3) δ ppm: 7.88-7.80 (m, 3H, Ar-H), 7.73 (d, J = 8.3, 1H, Ar-H), 7.65 (dt, J = 7.6, 0.9, 1H, Ar-H), 7.54-7.39 (m, 5H, Ar-H), 7.23 (dd, J = 7.5, 0.4, 1H, Ar-H), 3.71 (d, J = 17.2, 1H, indanone CH_AH_B), 3.15 (d, J = 17.2, 1H, indanone CH_AH_B), 2.96 (ddd, J = 16.4, 10.3, 5.3, 1H, CH_2CH_AH_BCO_2Ar), 2.83 (ddd, J = 16.4, 10.9, 5.4, 1H, CH_2CH_AH_BCO_2Ar), 2.53 (ddd, J = 14.1, 10.9, 5.3, 1H, CH_AH_BCH_2CO_2Ar), 2.45 (ddd, J = 14.1, 11.0, 5.4, 1H, CH_AH_BCH_2CO_2Ar), 1.44 (s, 1H, C(CH_3)_3);

**^13C NMR** (126 MHz, CDCl_3) δ ppm: 202.5 (C=O), 171.5 (C=O), 170.0 (C=O), 152.7, 146.5, 135.4, 135.3, 134.6, 128.0, 127.9, 126.7, 126.5, 126.4, 126.0, 125.4, 124.9, 121.2, 118.0 (Ar-C), 82.3 (quaternary C), 60.1 (C(CH_3)_3), 37.8 (indanone CH_2), 30.0 (CH_2CH_2CO_2Ar), 29.7 (CH_2CH_2CO_2Ar), 27.9 (C(CH_3)_3);

**MS** m/z (ES^+) 453 (M + Na^+), **HRMS** (ES^+) Found 453.1681. C_{27}H_{26}O_5Na requires M 453.1672; [α]_D^{22}: -24 (c 1, CHCl_3).
(S)-tert-butyl 2-(3-(naphthalen-2-yloxy)-3-oxopropyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 4g:

The product was isolated as a colourless solid (31 mg, 76 %).
e.e.: 94% (Chiralcel OD, 96:4 hexanes:IPA, 1mL/min, t_R = 30.3 min (minor), 47.6 (major)).
m.p. 92-94°C; IR ν_max (film): 3058, 2976, 2930 (CH), 1756, 1736, 1710 (C=O); 1H NMR (500 MHz, CDCl_3) δ_H ppm: 7.86-7.76 (m, 4H, Ar-H), 7.64 (dt, J = 7.5, 1.1, 1H, Ar-H), 7.55-7.39 (m, 5H, Ar-H), 7.21 (dd, J = 8.9, 2.3, 1H, Ar-H), 3.69 (d, J = 17.2, 1H, indanone CH_A), 3.12 (d, J = 17.2, 1H, indanone CH_B), 2.82 (ddd, J = 16.3, 10.9, 5.4, 1H, CH_2CH_AH_BCO_2Ar), 2.69 (ddd, J = 16.3, 10.8, 5.4, 1H, CH_2CH_AH_BCO_2Ar), 2.47 (ddd, J = 14.1, 10.8, 5.4, 1H, CH_AH_BCH_2CO_2Ar), 2.38 (ddd, J = 14.1, 10.9, 5.4, 1H, CH_AH_BCH_2CO_2Ar), 1.43 (s, 1H, C(CH_3)_3); 13C NMR (126 MHz, CDCl_3) δ_C ppm: 202.5 (C=O), 171.7 (C=O), 169.9 (C=O), 152.7, 148.3, 135.4, 135.3, 133.7, 131.4, 129.4, 127.9, 127.8, 127.7, 126.5, 126.4, 125.7, 124.8, 121.1, 118.5 (Ar-C), 82.3 (quaternary C), 60.1 (C(CH_3)_3), 37.7 (indanone CH_2), 30.1 (CH_2CH_2CO_2Ar), 29.6 (CH_2CH_2CO_2Ar), 27.9 (C(CH_3)_3); MS m/z (ES^+) 453 (M + Na^+); HRMS (ES^+) Found 453.1675. C_{27}H_{26}O_5Na requires M 453.1672; [α]_D^{22} -20 (c 1, CHCl_3).
(S)-tert-butyl 1-oxo-2-(3-oxo-3-phenoxypropyl)-2,3-dihydro-1H-indene-2-carboxylate 4h:

The product was isolated as a colourless solid (28 mg, 78%).

e.e. 94% (Chiralpak IA, 97:3 hexanes:IPA, 1mL/min, t_R = 21.1 min (minor), 22.4 min (major)).

m.p. 102-104°C; IR v_max (film): 3039, 2977, 2932 (CH), 1756, 1736, 1711 (C=O); 1H NMR (500 MHz, CDCl3) δ_H ppm: 7.79 (d, J = 7.7, 1H, Ar-H), 7.63 (dt, J = 7.5, 1.1, 1H, Ar-H), 7.49 (d, J = 7.7, 1H, Ar-H), 7.41 (t, J = 7.4, 1H, Ar-H), 7.38-7.33 (m, 2H, Ar-H), 7.21 (t, J = 7.4, 1H, Ar-H), 7.08-7.02 (m, 2H, Ar-H), 3.67 (d, J = 17.2, 1H, indanone CHB), 3.10 (d, J = 17.2, 1H, indanone C_AH_B), 2.76 (ddd, J = 16.3, 10.9, 5.3, 1H, CH2CH_AH_BCO2Ar), 2.62 (ddd, J = 16.3, 10.8, 5.4, 1H, CH2CH_AH_BCO2Ar), 2.43 (ddd, J = 14.1, 10.8, 5.3, 1H, CH_AH_BCH2CO2Ar), 2.33 (ddd, J = 14.1, 11.0, 5.4, 1H, CH_AH_BCH2CO2Ar), 1.41 (s, 1H, C(CH3)_3); 13C NMR (126 MHz, CDCl3) δ_C ppm: 202.4 (C=O), 171.5 (C=O), 169.9 (C=O), 152.7, 150.6, 135.4, 135.3, 129.4, 127.9, 126.4, 125.8, 124.8, 121.5 (Ar-C), 82.3 (quaternary C), 60.1 (C(CH3)_3), 37.6 (indanone CH2), 30.0 (CH2CH2CO2Ar), 29.5 (CH2CH2CO2Ar), 27.8 (C(CH3)_3); MS m/z (ES+) 403 (M + Na+); HRMS (ES+) Found 403.1520. C23H24O5Na requires M 403.1516; [α]D^22: -32 (c 1, CHCl3).
(S)-tert-butyl 1-oxo-2-(3-oxo-3-(1H-pyrrol-1-yl)propyl)-2,3-dihydro-1H-indene-2-carboxylate 4i:

The product was isolated as a colourless solid (32 mg, 96%).

e.e. 95% (Chiralpak AS-H, 98:2 hexanes:IPA, 1mL/min, tR = 22.4 min (major), 29.2 min (minor)).

m.p. 86-90°C; IR νmax (film): 3147, 2978, 2932 (CH), 1717 (C=O); 1H NMR (500 MHz, CDCl3) δH ppm: 7.78 (d, J = 7.7, 1H, Ar-H), 7.63 (t, J = 7.4, 1H, Ar-H), 7.48 (d, J = 7.7, 1H, Ar-H), 7.41 (t, J = 7.4, 1H, Ar-H), 7.35-7.27 (m, 2H, pyrrole-H), 6.28 (t, J = 2.2, 2H, pyrrole-H), 3.65 (d, J = 17.2, 1H, indanone-CH2B), 3.13-3.04 (m, 2H, indanone CHA and CH2CON), 3.01-2.91 (m, 1H, CH2CH3H8CON), 2.37 (t, J = 8.0, 2H, CH2CH2CON), 1.38 (s, 9H, C(CH3)3); 13C NMR (126 MHz, CDCl3) δC ppm: 202.5 (C=O), 170.1 (C=O), 152.5 (C=O), 135.4, 135.6, 127.9, 126.4, 124.8 (Ar-C), 119.1, 113.2 (pyrrole-C), 82.3 (quaternary C), 59.9 (C(CH3)3), 38.2 (indanone CH2), 30.3 (CH2CH2CON), 29.5 (CH2CH2CON), 27.8 (C(CH3)3); MS m/z (ES+): 376 (M + Na+), 412 (M + MeCN + NH4+); HRMS (ES+): Found 376.1510. C21H23O4NNa requires M 376.1519; [α]D22: -37.6 (c 1, CHCl3).
(S)-tert-butyl 5-bromo-2-(3-(naphthalen-1-ylthio)-3-oxopropyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 12c:

The product was isolated as a colourless solid (411 mg, 78%).
e.e. 93% (Chiralcel OD, 95:5 hexanes:IPA, 1mL/min, t<sub>R</sub> = 50.3 min (minor), 76.4 min (major)).
m.p. 103-105°C; IR ν<sub>max</sub> (film): 3057, 2977, 2931 (CH), 1735, 1711 (C=O); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> ppm: 8.14 (d, J = 8.2, 1H, Ar-H), 7.94 (d, J = 8.2, 1H, Ar-H), 7.88 (d, J = 7.6, 1H, Ar-H), 7.70-7.63 (m, 3H, Ar-H), 7.60-7.48 (m, 4H, Ar-H), 3.61 (d, J = 17.5, 1H, indanone CH<sub>A</sub>H<sub>B</sub>), 2.99 (d, J = 17.4, 1H, indanone CH<sub>A</sub>H<sub>B</sub>), 2.90 (ddd, J = 15.9, 10.8, 5.1, 1H, CH<sub>2</sub>CH<sub>2</sub>H<sub>B</sub>COSAr), 2.78 (ddd, J = 15.9, 10.8, 5.3, 1H, CH<sub>2</sub>CH<sub>2</sub>H<sub>B</sub>COSAr), 2.41 (ddd, J = 14.2, 10.8, 5.1, 1H, CH<sub>2</sub>CH<sub>2</sub>H<sub>B</sub>COSAr), 2.26 (ddd, J = 14.1, 10.9, 5.3, 1H, CH<sub>A</sub>H<sub>B</sub>CH<sub>2</sub>COSAr), 1.41 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>); <sup>1</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> ppm: 201.0 (C=O), 196.4 (C=O), 169.3 (C=O), 154.2, 135.0, 134.2, 134.0, 131.6, 131.0, 130.9, 129.7, 128.7, 127.3, 126.5, 126.0, 125.6, 125.2, 124.9 (Ar-C), 82.6 (quaternary C), 60.3 (C(CH<sub>3</sub>)<sub>3</sub>), 39.1 (indanone CH<sub>2</sub>), 37.1 (CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Ar), 29.8 (CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Ar), 27.8 (C(CH<sub>3</sub>)<sub>3</sub>); MS m/z (ES<sup>+</sup>) 547 (M + Na<sup>+</sup>); HRMS (ES<sup>+</sup>) Found 547.0552. C<sub>27</sub>H<sub>25</sub>O<sub>4</sub>BrNaS requires M 547.0549; [α]<sub>D</sub><sup>22</sup>: -10 (c 1, CHCl<sub>3</sub>).
(S)-tert-butyl 6-methoxy-2-(3-(naphthalen-1-ylthio)-3-oxopropyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate 13c:

The product was isolated as a colourless solid (447 mg, 90 %).

e.e. 94% (Chiralcel OD, 96:4 hexanes:IPA, 1mL/ min, \( t_R = 35.6 \) min (minor), 47.9 min (major)).
m.p. 84-86°C; IR \( \nu_{\max} \) (film): 3056, 2975, 2932, 2837 (CH), 1734, 1707 (C=O); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) ppm: 8.15 (d, \( J = 8.3 \), 1H, Ar-\( H \)), 7.93 (d, \( J = 8.2 \), 1H, Ar-\( H \)), 7.87 (d, \( J = 7.6 \), 1H, Ar-\( H \)), 7.67 (dd, \( J = 1.1 \), 7.1, 1H, Ar-\( H \)), 7.58-7.46 (m, 3H, Ar-\( H \)), 7.35 (d, \( J = 8.3 \), 1H, Ar-\( H \)), 7.24-7.17 (m, 2H, Ar-\( H \)), 3.84 (s, 1H, OCH\(_3\)), 3.55 (d, \( J = 17.0 \), 1H, indanone CH\(_A\)H\(_B\)), 2.99-2.86 (m, 2H, indanone CH\(_A\)H\(_B\) and CH\(_2\)CH\(_A\)H\(_B\)COSAr), 2.78 (ddd, \( J = 15.8 \), 11.0, 5.2, 1H, CH\(_2\)CH\(_A\)H\(_B\)COSAr), 2.41 (ddd, \( J = 14.0 \), 11.0, 5.1, 1H, CH\(_A\)H\(_B\)CH\(_2\)COSAr), 2.29 (ddd, \( J = 14.0 \), 11.1, 5.2, 1H, CH\(_A\)H\(_B\)CH\(_2\)COSAr), 1.38 (m, 9H, C(C\(_H\)\(_3\))\(_3\)); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \( \delta \) ppm: 202.3 (C=O), 196.5 (C=O), 169.8 (C=O), 159.7, 145.6, 136.4, 135.0, 134.2, 134.1, 131.0, 128.6, 127.2, 127.1, 126.4, 125.6, 125.3, 125.0, 124.9, 105.7 (Ar-\( C \)), 82.3 (quaternary C), 60.9 (C(CH\(_3\))\(_3\)), 55.6 (OCH\(_3\)), 39.3 (indanone CH\(_2\)), 36.9 (CH\(_2\)CH\(_2\)CO\(_2\)Ar), 30.0 (CH\(_2\)CH\(_2\)CO\(_2\)Ar), 27.9 (C(CH\(_3\))\(_3\)); MS \( m/z \) (ES\(^+\)) 499 (M + Na\(^+\)); HRMS (ES\(^+\)) Found 499.1547. C\(_{28}\)H\(_{28}\)O\(_5\)NaS requires \( M \) 499.1550; [\( \alpha \)]\(_D\)\(^{23}\): -33.6 (c 1, CHCl\(_3\)).
(S)-tert-butyl 1-(3-(naphthalen-1-ylthio)-3-oxopropyl)-2-oxo-2,3-dihydro-1H-indene-1-carboxylate 14c:

The product was isolated as a pale yellow oil (42 mg, 95 %).
e.e. 88% (Chiralcel OD, 96:4 hexanes:IPA, 1mL/ min, t<sub>R</sub> = 15.3 min (major), 35.4 min (minor)).

**IR** ν<sub>max</sub> (film): 2977 (CH), 1757, 1728 (C=O); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> ppm: 8.09 (d, J = 8.0, 1H, Ar-H), 7.92 (d, J = 8.2, 1H, Ar-H), 7.87 (d, J = 7.4, 1H, Ar-H), 7.62 (dd, J = 7.1, 1.0, 1H, Ar-H), 7.57-7.44 (m, 3H, Ar-H), 7.38-7.26 (m, 4H, Ar-H), 3.79 (d, J = 22.5, 1H, indanone CH<sub>2</sub>H<sub>3</sub>), 3.51 (d, J = 22.5, 1H, indanone CH<sub>2</sub>H<sub>3</sub>); **<sup>13</sup>C NMR** (126 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> ppm: 212.0 (C=O), 196.1 (C=O), 168.7 (C=O), 140.3, 137.3, 135.0, 134.2, 134.1, 130.9, 128.7, 128.1, 127.2, 126.4, 125.5, 125.3, 125.2, 125.0, 123.9 (Ar-C), 82.7 (quaternary C), 64.9 (C(CH<sub>3</sub>)<sub>2</sub>), 43.4 (indanone CH<sub>2</sub>), 38.8 (CH<sub>2</sub>CH<sub>2</sub>COSAr), 28.7 (CH<sub>2</sub>CH<sub>2</sub>COSAr), 27.7 (C(CH<sub>3</sub>)<sub>3</sub>); **MS** m/z (ES<sup>+</sup>) 469 (M + Na<sup>+</sup>); **HRMS** (ES<sup>+</sup>) Found 469.1447. C<sub>27</sub>H<sub>26</sub>O<sub>4</sub>NaS requires M 469.1444; [α]<sub>D</sub><sup>23</sup> = +19.2 (c 2, CHCl<sub>3</sub>).
(R)-1,1,1,3,3,3-hexafluoropropan-2-yl 1-(3-(naphthalen-1-ylthio)-3-oxopropyl)-2-oxocyclopentanecarboxylate 15c:

The product was isolated as a colourless oil (38 mg, 75%).

e.e. 95% (Chiralpak AD, 98:2 hexanes:IPA, 1mL/min, t_R = 13.7 min (minor), 19.8 min (major)).

**IR** \( \nu_{\text{max}} \) (film): 3059, 2971 (CH), 1780, 1745, 1708 (C=O); **\(^1\)H NMR** (500 MHz, CDCl\(_3\)) \( \delta_H \) ppm: 8.16 (d, \( J = 8.3, 1\text{H, Ar-}H \)), 7.96 (d, \( J = 8.2, 1\text{H, Ar-}H \)), 7.89 (d, \( J = 7.7, 1\text{H, Ar-}H \)), 7.69 (d, \( J = 7.2, 1\text{H, Ar-}H \)), 7.54 (m, 3H, Ar-\( H \)), 5.78 (sept., 1H, \( J = 5.9, \text{CH(CF}_3)_2 \)) 3.00 (ddd, 1H, \( J = 15.9, 9.9, 5.7, \text{CH}_2\text{CH}_3\text{H}_8\text{COSAr} \)) 2.80 (m, 1H, \( \text{CH}_2\text{CH}_3\text{H}_8\text{COSAr} \)) 2.43 (m, 4H, \( \text{CH}_2\text{CH}_2\text{COSAr} \) and 2 x cyclopentanone \( \text{CH}_2 \)) 2.07 (m, 4H, cyclopentanone \( \text{CH}_2 \)); **\(^{13}\)C NMR** (126 MHz, CDCl\(_3\)) \( \delta_C \) ppm: 211.6 (C=O), 196.3 (C=O), 168.2 (C=O), 135.1, 134.2, 131.1, 128.7, 127.3, 126.5, 125.6, 125.2, 124.7 (Ar-C), 120.2 (q, \( J = 275.9, \text{CH(CF}_3)_2 \)), 66.9 (sept., \( J = 35.0, \text{CH(CF}_3)_2 \)), 58.9 (quaternary C), 38.6 (\( \text{CH}_2\text{CH}_2\text{COSAr} \)), 37.6 (\( \text{CH}_2\text{CH}_2\text{COSAr} \)), 33.7 (cyclopentanone \( \text{CH}_2 \)), 28.2 (cyclopentanone \( \text{CH}_2 \)), 19.6 (cyclopentanone \( \text{CH}_2 \)); **MS** \( m/z \) (ES\(^+\)) 515 (M + Na\(^+\)), 551 (M + MeCN + NH\(_4\)^+); **HRMS** (EI) Found 492.0822. \( \text{C}_{22}\text{H}_{18}\text{O}_4\text{F}_6\text{S} \) requires \( M 492.0825; [\alpha]_D^{22} : -2.4 \) (c 1, CHCl\(_3\)).
(R)-1,1,1,3,3,3-hexafluoropropan-2-yl 1-(3-(naphthalen-1-ylthio)-3-oxopropyl)-2-oxocyclohexanecarboxylate 16c:

![Chemical structure](image)

The product was isolated as a colourless oil (26 mg, 52%).
e.e. 98% (Chiralcel OD, 96:4 hexanes:IPA, 1mL/min, t_R = 20.9 min (minor), 41.4 min (major)).

**IR** ν_max (film): 3058, 2950, 2870 (CH), 1769, 1728 (C=O); **^1H NMR** (500 MHz, CDCl_3) δ_H ppm: 8.14 (d, J = 8.3, 1H, Ar-H), 7.95 (d, J = 8.2, 1H, Ar-H), 7.89 (d, J = 7.6, 1H, Ar-H), 7.69 (dd, J = 7.1, 0.8, 1H, Ar-H), 7.53 (m, 3H, Ar-H), 5.83 (sept., J = 6.0, 1H, CH(CF_3)_2), 2.85 (ddd, J = 16.1, 10.9, 5.2, 1H, CH_2CH_2H_8COSAr), 2.68 (ddd, 1H, J = 16.1, 10.9, 5.3, 1H, CH_2CH_2H_8COSAr), 2.49 (m, 3H, cyclohexanone CH_2), 2.35 (ddd, 1H, J = 14.4, 10.9, 5.2, CH_4H_8CH_2COSAr), 2.14 (ddd, 1H, J = 14.4, 10.9, 5.3, CH_4H_8CH_2COSAr), 2.04 (m, 1H, cyclohexanone CH_2), 1.84 (m, 1H, cyclohexanone CH_2), 1.71 (m, 3H, cyclohexanone CH_2); **^13C NMR** (126 MHz, CDCl_3) δ_C ppm: 205.3 (C=O), 196.1 (C=O), 169.1 (C=O), 135.1, 134.2, 131.0, 128.6, 127.2, 126.5, 125.6, 125.1, 124.8 (Ar-C), 120.2 (q, J = 284.9, CH(CF_3)_2), 66.8 (sept., J = 34.8, (CH(CF_3)_2), 58.4 (quaternary C), 40.5 (CH_2CH_2COSAr), 38.4 (CH_2CH_2COSAr), 36.0 (cyclohexanone CH_2), 29.7 (cyclohexanone CH_2), 27.2 (cyclohexanone CH_2), 21.9 (cyclohexanone CH_2); **MS** m/z (ES^+) 529 (M + Na^+), 565 (M + MeCN + NH_4^+); **HRMS** (ES^+) Found 529.0876. C_{23}H_{20}O_4F_6NaS requires M 529.0879; [α]_D {^22} +7.85 (c 2, CHCl_3).
(R)-tert-butyl 1-(3-(naphthalen-1-ylthio)-3-oxopropyl)-2-oxocyclopentanecarboxylate
17c:

The product was isolated as a colourless oil (25 mg, 64%).
e.e. 67% (Chiralcel AD, 95:5 hexanes:IPA, 1mL/ min, \( t_R = 10.8 \) min (minor), 12.2 min (major)).

**IR** \( \nu_{\text{max}} \) (film): 2975 (CH), 1746, 1716 (C=O); **\(^1\)H NMR** (500 MHz, CDCl\(_3\)) \( \delta_H \) ppm: 8.18 (d, \( J = 8.4 \), 1H, Ar-H), 7.94 (d, \( J = 8.2 \), 1H, Ar-H), 7.88 (d, \( J = 8.5 \), 1H, Ar-H), 7.69 (dd, \( J = 7.1 \), 1.0, 1H, Ar-H), 7.60-7.45 (m, 3H, Ar-H), 3.02 (ddd, \( J = 15.8 \), 10.5, 5.3, 1H, CH\(_2\)CH\(_3\)H\(_2\)COSAr), 2.77 (ddd, 1H, \( J = 15.9 \), 10.6, 5.3, CH\(_2\)CH\(_3\)H\(_2\)COSAr), 2.50-2.35 (m, 2H, CH\(_3\)H\(_2\)CH\(_2\)COSAr and cyclopentanone CH\(_2\)), 2.31-2.15 (m, 2H, CH\(_3\)H\(_2\)CH\(_2\)COSAr and cyclopentanone CH\(_2\)), 2.08-1.81 (m, 4H, cyclopentanone CH\(_2\)), 1.44 (m, 9H, C(CH\(_3\))\(_3\));

**\(^{13}\)C NMR** (126 MHz, CDCl\(_3\)) \( \delta_C \) ppm: 214.6 (C=O), 196.7 (C=O), 170.2 (C=O), 135.0, 134.2, 134.2, 130.9, 128.6, 127.2, 126.4, 125.6, 125.3, 125.2 (Ar-C), 82.3 (C(CH\(_3\))\(_3\)), 59.7 (quaternary C), 39.2 (CH\(_2\)CH\(_2\)COSAr), 37.9 (CH\(_2\)CH\(_2\)COSAr), 34.1 (cyclopentanone CH\(_2\)), 28.7 (cyclopentanone CH\(_2\)), 27.9 (C(CH\(_3\))\(_3\)), 19.6 (cyclopentanone CH\(_2\)); **MS** \( m/z \) (ES\(^+\)) 421 (M + Na\(^+\)); **HRMS** (ES\(^+\)) Found 421.1445. \( \text{C}_{23}\text{H}_{26}\text{O}_{4}\text{NaS} \) requires \( M = 421.1444 \); [\( \alpha \)]\(_D\)\(^{23}\): +5.6 (c 1, CHCl\(_3\)).
(R)-1,1,1,3,3,3-hexafluoropropan-2-yl 2-acetyl-2-methyl-5-(naphthalen-1-ylthio)-5-oxopentanoate 18c:

The product was isolated as a colourless oil (56 mg, 58%).

e.e. 71% (Chiralcel IA, 95:5 hexanes:IPA, 1mL/ min, t_R = 13.4 min (minor), 19.1 min (major)).

M.p. 59-62˚; IR ν_max (film): 3058, 2972 (CH), 1778, 1716 (C=O); ^1H NMR (500 MHz, CDCl_3) δ_H ppm: 8.15 (d, J = 8.2, 1H, Ar-H), 7.96 (d, J = 8.2, 1H, Ar-H), 7.90 (d, J = 7.6, 1H, Ar-H), 7.69 (dd, J = 7.2, 0.9, 1H, Ar-H), 7.60-7.48 (m, 1H, 3H), 5.82 (sept., J = 6.0, 1H, CH(CF_3)_2), 2.74 (t, J = 8.0, 2H, CH_2CH_2COSAr), 2.40-2.25 (m, 1H, CH_2CH_2COSAr), 2.20 (s, 1H, C=OCH_3), 1.46 (s, 1H, CCH_3); ^13C NMR (126 MHz, CDCl_3) δ_C ppm: 202.6 (C=O), 195.9 (C=O), 169.6 (C=O), 135.1, 134.2, 134.1, 131.1, 128.7, 127.3, 126.5, 125.6, 125.1, 124.6 (Ar-C), 120.0 (q, J = 281.2, CH(CF_3)_2), 67.0 (sept., J = 34.9, CH(CF_3)_2), 59.1 (quaternary C), 38.2 (CH_2CH_2COSAr), 29.7 (CH_2CH_2COSAr), 25.9 (C=OCH_3), 18.9 (CH_3); MS m/z (ES^+) 505 (M + Na^+); HRMS (ES^+) Found 498.1159 (M + Na^+). C_{21}H_{22}O_4NF_6S requires M 498.1168; [α]_D^{23}: -1.2 (c 1, CHCl_3).
(S, S, S)-2-Ethoxycarbonylmethyl-3,4,5,9b-tetrahydro-2H-indeno[1,2-b]pyran-4a-carboxylic acid tert-butyl ester 20:

Adduct 4i (100 mg, 0.3 mmol) was dissolved in dry Et₂O (10 mL) and cooled to 0 °C under N₂. Super-Hydride® (600 µl of a 1M solution in THF) was added dropwise and the mixture was stirred for 30 minutes until TLC analysis showed that all starting material had been consumed. The reaction mixture was quenched with saturated aqueous NH₄Cl (2 mL) and cooled to room temperature; it was then extracted into EtOAc (2 x 10 mL), washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated in vacuo.

The crude reaction mixture was dissolved in THF (10 mL) and NaOMe (0.8 mg, 0.015 mmol) was added. It was stirred for 2 hours before being extracted into EtOAc (2 x 10 mL), washed with brine (10 mL), dried over Na₂SO₄ and concentrated in vacuo. Triethyl phosphonoacetate (118 µl, 0.59 mmol) was added to a suspension of NaH (24 mg, 0.6 mmol (60 % dispersion in mineral oil)) in dry THF (5 mL) at 0 °C under N₂. The mixture was warmed to room temperature over 30 minutes, cooled back to 0 °C and the crude reaction mixture in THF (5 mL) was added dropwise. The mixture was warmed to room temperature over 4 hours, quenched with NH₄Cl, extracted into EtOAc (2 x 10 mL), washed with brine and dried over Na₂SO₄. It was then filtered, concentrated in vacuo, and filtered through a pad of silica (eluting with 4:1 petrol EtOAc) to yield 20 as a colourless oil (81 mg, 75 % over three steps, 5:1 mixture of diastereoisomers).

IR ν_{max} (film): 2927, 2854 (CH), 1725 (C=O); \(^1\)H NMR (500 MHz, CDCl₃, major diastereoisomer) δ_{H} ppm: 7.34 (d, J = 7.3, 1H, Ar-H), 7.20 (m, 2H, Ar-H), 7.11 (d, J = 7.2, 1H, Ar-H), 5.68 (s, 1H, CCHO), 4.13 (q, J = 7.1, 2H, CH₂CH₃), 3.84 (m, 1H, CHCH₂), 3.09 (d, J = 15.2, 1H, indanone CH₃H₈), 2.63 (d, J = 15.3, 1H, indanone CH₃H₈), 2.52 (dd, J = 8.6, 1H, 15.5, CHCH₃H₈CO), 2.32 (dd, J = 15.5, 4.3, 1H CHCH₃H₈CO), 2.20 (dd, J = 10.1, 2.8, 1H, CH₄H₈CH₂), 1.43 (s, 1H, C(CH₃)₃), 1.36 (m, 3H, CH₂CH₂), 1.24 (t, J = 7.1, 1H, CH₂CH₂); \(^1\)C NMR (126 MHz, CDCl₃ major diastereoisomer) δ_{C} ppm: 173.3 (C=O),
170.3 (C=O), 139.4, 137.9, 126.9, 126.0, 124.4, 123.2, (Ar-C), 82.1 (CCHO), 79.9 (quaternary C), 66.3 (CHCH$_2$), 59.5 (CH$_2$CH$_3$), 50.4 (C(CH$_3$)$_3$), 40.6 (indanone C), 40.1 (CH$_2$CO), 27.1 (C(CH$_3$)$_3$), 26.9 (CH$_2$CH$_2$), 26.7 (CH$_2$CH$_2$), 14.3 (CH$_2$CH$_3$); MS m/z (ES$^+$) 378 (M + NH$_4^+$), 383 (M + Na$^+$); HRMS (ES$^+$) Found 378.2266. C$_{21}$H$_{32}$O$_5$N requires M 378.2275; [$\alpha$]$_D^{22}$: +72 (c 1, CHCl$_3$).

(S, S)-1-Hydroxy-2-(3-oxo-3-pyrrol-1-yl-propyl)-indan-2-carboxylic acid tert-butyl ester 21:

Adduct 4i (100 mg, 0.3 mmol) was dissolved in dry THF (10 mL) and cooled to –78°C. Super-Hydride$^\circledR$ (300 µl of a 1M solution in THF) was added dropwise and the mixture was stirred at –78°C for 5 hours. It was then quenched with saturated aqueous NH$_4$Cl (2 mL), warmed to room temperature and extracted into EtOAc (2 x 10 mL). The combined organics were washed with brine, dried over Na$_2$SO$_4$ and concentrated in vacuo; the crude product was then subjected to flash column chromatography on silica gel (eluting with 9:1 petrol:EtOAc) to yield 21 as a colourless oil (68 mg, 68 % (+ 9 % recovered starting material), 5:1 mixture of diastereoisomers).

IR $\nu_{\text{max}}$ (film): 3488 (broad OH), 3248, 3074, 2977, 2933 (CH), 1718 (C=O); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$H ppm: 7.20 (m, 6H, Ar-$H$), 6.21 (t, $J = 2.1$, 2H, pyrrole-$H$ (minor diastereoisomer)), 6.17 (t, $J = 2.1$, 2H, pyrrole-$H$ (major diastereoisomer)), 5.37 (d, $J = 4.5$, 1H, CHO (major diastereoisomer)), 4.93 (d, $J = 8.1$, 1H, CHO (minor diastereoisomer)), 3.42 (d, $J = 16.3$, 1H, indanone CH$_A$H$_B$ (minor diastereoisomer)), 3.25 (d, $J = 16.2$, 1H, indanone CH$_A$H$_B$ (major diastereoisomer)), 2.87 (d, $J = 16.2$, 1H, indanone CH$_A$H$_B$, 2.68 (ddd, 2H, $J = 9.6$, 6.0, 4.3, CH$_2$CH$_2$CON), 2.43 (d, $J = 5.5$, 1H, O$H$), 2.25 (ddd, $J = 14.2$, 10.3, 5.9, 1H, CH$_A$H$_B$CH$_2$CON), 2.05 (m, 1H, CH$_A$H$_B$CH$_2$CON), 1.36 (m, 9H, C(CH$_3$)$_3$); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$C ppm: major diastereoisomer: 173.9 (C=O), 169.4 (C=O), 141.6, 138.4, 127.5, 126.2, 123.5, 123.1, 118.0, 112.1 (Ar-C), 80.6 (quaternary C), 77.9
(CHOH), 57.8 (C(CH$_3$)$_3$), 37.6 (indanone C), 30.0 (CH$_2$CH$_2$CON), 27.0 (C(CH$_3$)$_3$), 26.2 (CH$_2$CH$_2$CON); minor diastereoisomer: 173.2 (C=O), 168.9 (C=O), 141.9, 139.0, 127.6, 126.2, 123.4, 123.2, 117.9, 112.2 (Ar-C), 81.2 (quaternary C), 80.6 (CHOH), 58.2 (C(CH$_3$)$_3$), 38.3 (indanone C), 30.2 (CH$_2$CH$_2$CON), 26.9 (C(CH$_3$)$_3$), 26.2 (CH$_2$CH$_2$CON); MS m/z (ES$^-$) 354 (M – H$^+$); HRMS (ES$^+$) Found 356.1852. C$_{21}$H$_{26}$O$_4$N requires M 356.1856; [$\alpha$]$_D^{22}$: +0.8 (c 0.5, CHCl$_3$).

**Determination of Relative Configuration of 20 and 21**

The relative configuration of compounds 20 and 21 was determined by nOe experiments.

**nOe of compound 20:**

**nOe of compound 21:**

**References**


Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

ppm (t1)
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

3d

ppm (t1)
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

ppm (t1)
3g ppm (t1)
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

ppm (t1)

3g
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

4c

ppm (t1)
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

ppm (t1)
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

ppm (t1)
ppm (t1)
ppm (t1)
ppm (t1)
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

ppm (t1)
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

ppm (t1)
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

Chemical structure

ppm (t1)

4g
ppm (t1)
15c
Supplementary Material (ESI) for Chemical Communications

This journal is (c) The Royal Society of Chemistry 2008
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

17c

ppm (t1)
ppm (t1)
21
4d

![Chemical structure image](image)

4d

![Graph image](image)
4h

4h
Recrystallised:

12c
Supplementary Material (ESI) for Chemical Communications
This journal is (c) The Royal Society of Chemistry 2008

16c

[Chemical structure image]

16c

[Chemical structure image]
17c