An asymmetric organocatalytic approach towards allylic amines and \(\beta\)-keto amino compounds

Christian Borch Jacobsen, Lennart Lykke, David Monge, Martin Nielsen, Lars Krogager Ransborg
and Karl Anker Jørgensen*

Center for Catalysis
Department of Chemistry, Aarhus University
DK-8000 Aarhus C, Denmark
Fax (45) 8919 6199, e-mail: kaj@chem.au.dk

Contents

1. General Methods ........................................................................................................................................ 2
2. General procedure for the synthesis of nucleophiles 2a-e ........................................................................ 3
3. Initial screening results .............................................................................................................................. 5
4. General procedure for the formation of allylic amines 4a-h .................................................................. 7
5. General procedure for the formation of \(\beta\)-keto amino compounds 5a-c ........................................... 11
6. General procedure for the formation of \(\beta\)-keto amino compounds 5d-f .......................................... 13
1. General Methods
NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 and 100 MHz for $^1$H and $^{13}$C acquisition, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals (CDCl$_3$, 7.26 ppm for $^1$H NMR; CDCl$_3$, 77.0 ppm for $^{13}$C NMR). The following abbreviations are used to indicate the multiplicity in $^1$H NMR spectra: s, singlet; d, doublet; t, triplet; dd, double doublet; m, multiplet; bs, broad signal. $^{13}$C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES$^+$) ionization techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation, KMnO$_4$ or vanillin dip. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary-phase HPLC (Daicel Chiralpak AD and Daicel Chiralcel OD/OJ columns). Analytical grade solvents and commercially available reagents were used without further purification. Propionitrile was dried over activated molecular sieves (4Å) prior to use. Racemates were prepared using Et$_3$N as catalyst. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka) or Iatrobeads (Iatrobeads 6RS-8060) were used. Imines 1a-c$^1$ and sulfones 2a-e$^2$ were prepared according to literature.
2. General procedure for the synthesis of nucleophiles 2a-e

![Chemical structure]

The nucleophiles 2a-e was prepared according to literature procedure. Hereafter the crude products was recrystallised in MeOH yielding the pure nucleophiles.

2-(Benzothiazole-2-sulfonyl)-1-phenyl-ethanone (2a)

Following the general procedure 2a was obtained as a white solid. 

$^1$H NMR (CDCl$_3$) δ ppm 8.19 (d, $J = 8.0$ Hz, 1H), 8.00 (d, $J = 7.7$ Hz, 1H), 7.93 (d, $J = 7.3$ Hz, 2H), 7.65-7.56 (m, 3H), 7.46 (t, $J = 7.9$ Hz, 2H), 5.21 (s, 2H). $^{13}$C NMR (CDCl$_3$) δ ppm 187.1, 165.2, 152.3, 137.0, 135.3, 134.6, 129.0 (2 C), 128.9 (2 C), 128.1, 127.6, 125.4, 122.3, 61.1. HRMS calc. for C$_{15}$H$_{11}$NNaO$_3$S$_2$: 340.0078; found: 340.0079.

2-(Benzothiazole-2-sulfonyl)-1-m-tolyl-ethanone (2b)

Following the general procedure 2b was obtained as a white solid.

$^1$H NMR (CDCl$_3$) δ ppm 8.19 (d, $J = 7.4$ Hz, 1H), 7.99 (d, $J = 7.5$ Hz, 1H), 7.74-7.69 (m, 2H), 7.65-7.56 (m, 2H), 7.40 (d, $J = 7.6$ Hz, 1H), 7.34 (t, $J = 7.6$ Hz, 1H), 5.19 (s, 2H), 2.35 (s, 3H). $^{13}$C NMR (CDCl$_3$) δ ppm 187.2, 165.3, 152.4, 139.8, 137.0, 135.4, 135.4, 129.3, 128.8, 128.1, 127.6, 126.2, 125.5, 122.3, 61.2, 21.2. HRMS calc. for C$_{16}$H$_{13}$NNaO$_3$S$_2$: 354.0235; found: 354.0234.

2-(Benzothiazol-2-ylsulfonyl)-1-p-tolylethanone (2c)

Following the general procedure 2c was obtained as a white solid.

$^1$H NMR (CDCl$_3$) δ ppm 8.19 (d, $J = 7.9$ Hz, 1H), 8.00 (d, $J = 7.9$ Hz, 1H), 7.82 (d, $J = 8.3$ Hz, 2H), 7.65-7.56 (m, 2H), 7.25 (d, $J = 8.3$ Hz, 2H), 5.17 (s, 2H), 2.40 (s,
3H). $^{13}$C NMR (CDCl$_3$) $\delta$ ppm 186.6, 165.3, 152.4, 145.9, 137.0, 132.9, 129.6 (2 C), 129.1 (2 C), 128.1, 127.6, 125.5, 122.3, 61.1, 21.8. HRMS calc. for C$_{16}$H$_{13}$NNaO$_3$S$_2$: 354.0235; found: 354.0238.

2-(Benzothiazol-2-ylsulfonyl)-1-(naphthalen-2-yl)ethanone (2d)

Following the general procedure 2d was obtained as a white solid.
$^1$H NMR (CDCl$_3$) $\delta$ ppm 8.44 (s, 1H), 8.20 (d, $J$ = 8.0 Hz, 1H), 8.03-7.82 (m, 5H), 7.69-7.52 (m, 4H), 5.33 (s, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ ppm 187.2, 165.5, 152.7, 137.3, 136.3, 133.0, 132.4, 132.0, 130.1, 129.7, 129.2, 128.4, 128.0, 127.9, 127.5, 125.7, 123.8, 122.6, 61.6. HRMS calc. for C$_{19}$H$_{13}$NNaO$_3$S$_2$: 390.0235; found: 390.0238.

2-(Benzothiazol-2-ylsulfonyl)-1-(3-chlorophenyl)ethanone (2e)

Following the general procedure 2e was obtained as a white solid.
$^1$H NMR (CDCl$_3$) $\delta$ ppm 8.21-8.16 (m, 1H), 8.02-7.97 (m, 1H), 7.88 (t, $J$ = 1.6 Hz, 1H), 7.85-7.79 (m, 1H), 7.67-7.52 (m, 3H), 7.41 (t, $J$ = 8.0 Hz, 1 H), 5.18 (s, 2 H). $^{13}$C NMR (CDCl$_3$) $\delta$ ppm 186.0, 164.9, 152.3, 137.0, 136.8, 135.3, 134.5, 130.2, 128.9, 128.3, 127.7, 127.2, 125.5 122.3, 61.2. HRMS calc. for C$_{15}$H$_{10}$ClNNaO$_3$S$_2$: 373.9688; found: 373.9694.
3. Initial screening results

\[
\begin{align*}
\text{1} & \quad \text{Boc} + \text{BTSO}_2 \text{C} \rightarrow \text{Boc} \text{NH} \\
\text{2} & \quad \text{1. 6 (10 mol\%)} \\
\text{3} & \quad \text{solvent, temp} \\
\text{4} & \quad \text{2. NaBH}_4 \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Catalyst ((10 \text{ mol%}))</th>
<th>Time (h)</th>
<th>Temp (°C)</th>
<th>Conv. ((1^{\text{st}} \text{ step})) (b) (%)</th>
<th>Ee (c) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene</td>
<td>6a</td>
<td>48</td>
<td>rt</td>
<td>90</td>
<td>Rac</td>
</tr>
<tr>
<td>2</td>
<td>Toluene</td>
<td>6b</td>
<td>48</td>
<td>rt</td>
<td>95</td>
<td>Rac</td>
</tr>
<tr>
<td>3</td>
<td>Toluene</td>
<td>6c</td>
<td>48</td>
<td>rt</td>
<td>90</td>
<td>Rac</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>6d</td>
<td>48</td>
<td>rt</td>
<td>90</td>
<td>Rac</td>
</tr>
<tr>
<td>5</td>
<td>Toluene</td>
<td>6e</td>
<td>48</td>
<td>rt</td>
<td>90</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>Toluene</td>
<td>6f</td>
<td>48</td>
<td>rt</td>
<td>95</td>
<td>35</td>
</tr>
<tr>
<td>7</td>
<td>Toluene</td>
<td>(DHQD)$_2$PYR</td>
<td>20</td>
<td>0</td>
<td>95</td>
<td>Rac</td>
</tr>
<tr>
<td>8</td>
<td>CH$_2$Cl$_2$</td>
<td>6g</td>
<td>48</td>
<td>-30</td>
<td>n.d.</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>CH$_2$Cl$_2$</td>
<td>6h</td>
<td>48</td>
<td>-30</td>
<td>n.d.</td>
<td>6</td>
</tr>
<tr>
<td>10</td>
<td>CH$_2$Cl$_2$</td>
<td>6i</td>
<td>48</td>
<td>-30</td>
<td>n.d.</td>
<td>Rac</td>
</tr>
<tr>
<td>11</td>
<td>CH$_2$Cl$_2$</td>
<td>6e</td>
<td>48</td>
<td>-30</td>
<td>n.d.</td>
<td>8</td>
</tr>
<tr>
<td>12</td>
<td>CH$_2$Cl$_2$</td>
<td>6f</td>
<td>18</td>
<td>-30</td>
<td>n.d.</td>
<td>70</td>
</tr>
<tr>
<td>13</td>
<td>Toluene</td>
<td>6f</td>
<td>24</td>
<td>-30</td>
<td>0</td>
<td>n.d.</td>
</tr>
<tr>
<td>14</td>
<td>CHCl$_3$</td>
<td>6f</td>
<td>24</td>
<td>-30</td>
<td>Full</td>
<td>37</td>
</tr>
<tr>
<td>15</td>
<td>Et$_2$O</td>
<td>6f</td>
<td>24</td>
<td>-30</td>
<td>Full</td>
<td>30</td>
</tr>
<tr>
<td>16</td>
<td>THF</td>
<td>6f</td>
<td>24</td>
<td>-30</td>
<td>Full</td>
<td>57</td>
</tr>
<tr>
<td>17</td>
<td>Acetone</td>
<td>6f</td>
<td>48</td>
<td>-30</td>
<td>Full</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>MeCN</td>
<td>6f</td>
<td>42</td>
<td>-30</td>
<td>Full</td>
<td>67</td>
</tr>
<tr>
<td>19</td>
<td>Propionitrile</td>
<td>6f</td>
<td>48</td>
<td>-30</td>
<td>Full</td>
<td>84</td>
</tr>
<tr>
<td>20</td>
<td>Propionitrile</td>
<td>6f</td>
<td>72</td>
<td>-40</td>
<td>Full</td>
<td>89</td>
</tr>
<tr>
<td>21</td>
<td>Propionitrile</td>
<td>6f</td>
<td>72</td>
<td>-40</td>
<td>Full</td>
<td>n.d.</td>
</tr>
<tr>
<td>22</td>
<td>Propionitrile</td>
<td>6f</td>
<td>72</td>
<td>-40</td>
<td>Full</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

^a All reactions performed on a 0.10 mmol scale (0.20 M) using 1a (0.25 mmol), 2a (0.10 mmol) and 6 (0.01 mmol).  
^b Determined by \(^1\)H NMR.  
^c Determined by chiral stationary-phase HPLC after reduction with NaBH₄.  
^d Reduction performed in CH₂Cl₂ giving an E:Z ratio of 9:1 (determined by \(^1\)H-NMR).  
^e Reduction performed in propionitrile giving an E:Z ratio of 3:1 (determined by \(^1\)H-NMR).  
^f Reduction performed in CH₂Cl₂ with LiBH₄ giving an E:Z ratio of 2:1 (determined by \(^1\)H-NMR).
4. General procedure for the formation of allylic amines 4a-h

An ordinary vial equipped with a magnetic stirring bar was charged with β-keto benzothiazole (BT) sulfone nucleophile 2 (0.10 mmol, 1.0 equiv.) and catalyst 6f (0.01 mmol, 0.1 equiv.), which were dissolved in 0.5 mL propionitrile and cooled to the desired temperature (see below). Upon cooling the imine 1 (0.25 mmol, 2.5 equiv.) was added. The reaction was run until judged complete by $^1$H NMR spectroscopy. The solvent was evaporated (0.5 mL of toluene was added to ensure complete evaporation of propionitrile) and 1.0 mL of CH$_2$Cl$_2$ and 0.1 mL of MeOH was added. The reaction mixture was cooled to -30 ºC and treated with NaBH$_4$ (0.50 mmol, 5.0 equiv.). After 1 h the reaction was allowed to warm up to room temperature and was left until judged complete by TLC (aprox. 30 min – 1 h). The reaction was then quenched with NH$_4$Cl, extracted with CH$_2$Cl$_2$ and purified by FC.

(R)-tert-Butyl 1,3-diphenylallylcarbamate (4a)

Following the general procedure (-40 ºC) 4a was isolated by FC (CH$_2$Cl$_2$/pentane) in 63% yield (E:Z 9:1) as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.42-7.20 (m, 10H), 6.55 (d, $J = 16.0$ Hz, 1H), 6.32 (dd, $J = 6.0$, 15.6 Hz, 1H), 5.47 (bs, 1H), 4.98 (bs, 1H), 1.46 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 154.9, 139.2, 136.6, 130.8, 129.4, 128.5 (2C), 127.6 (2C), 127.5 (2C), 126.5 (2C), 126.3, 126.2, 79.7, 52.8, 28.4 (3C). HRMS: Calculated for [C$_{20}$H$_{23}$NNaO$_2$]: 332.1626; found: 332.1631. The enantiomeric excess was determined by HPLC using a Chiralcel OD column [hexane/i-PrOH (95:5)]; flow rate 1.0 mL/min; $\tau_{\text{minor}} = 10.11$ min, $\tau_{\text{major}} = 8.96$ min (89% ee); [$\alpha$]$_D^{20}$ -4.4 (c = 0.73, CH$_2$Cl$_2$).

(R)-tert-Butyl 1-phenyl-3-m-tolylallylcarbamate (4b)

Following the general procedure (-40 ºC) 4b was isolated by FC (CH$_2$Cl$_2$) in 65% yield (E:Z 12:1) as a clear oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm
7.27-6.97 (m, 9H), 6.43 (d, J = 16.0 Hz, 1H), 6.23 (dd, J = 4.0, 15.9 Hz, 1H), 5.39 (bs, 1H), 4.90 (bs, 1H), 2.26 (s, 3H), 1.38 (s, 9H). 13C NMR (100 MHz, CDCl3) δ ppm 155.1, 141.5, 138.2, 136.6, 131.1, 129.5, 128.8, 128.6 (2C), 127.7, 127.4, 127.1, 123.8, 79.9, 56.4, 28.5 (3C), 21.5. HRMS: Calculated for [C21H25NO2Na]: 346.1783; found: 343.1779. The enantiomeric excess was determined by HPLC using two Chiralcel OD column [hexane/i-PrOH (97:3)]; flow rate 0.5 mL/min; τ_minor = 33.80 min, τ_major = 31.24 min (90% ee); [α]20D −10.5 (c = 0.47, CH2Cl2).

(R)-tert-Butyl 1-phenyl-3-p-tolyllallylcarbamate (4c)

Following the general procedure (-30 ºC) 4c was isolated by FC (CH2Cl2/pentane) in 61% yield (E:Z 13:1) as a white solid. 1H NMR (400 MHz, CDCl3) δ ppm 7.40-7.08 (m, 9H), 6.51 (dd, J = 1.6, 15.6 Hz, 1H), 6.27 (dd, J = 6.0, 16.0 Hz, 1H), 5.45 (bs, 1H), 4.97 (bs, 1H), 2.33 (s, 3H), 1.46 (s, 9H). 13C NMR (100 MHz, CDCl3) δ ppm 155.0, 141.5, 137.5, 133.7, 130.8, 129.2 (2C), 128.7 (2C), 128.5, 127.5, 127.0 (2C), 126.4 (2C), 79.8, 56.3, 28.4 (3C), 21.2. HRMS: Calculated for [C21H25NO2Na]: 346.1783; found: 346.1782. The enantiomeric excess was determined by HPLC using a Chiralpak AD column [hexane/i-PrOH (95:5)]; flow rate 1.0 mL/min; τ_minor = 13.01 min, τ_major = 15.29 min (84% ee); [α]20D −6.4 (c = 0.53, CH2Cl2).

(R)-tert-Butyl 3-(naphthalen-2-yl)-1-phenyllallylcarbamate (4d)

Following the general procedure (-30 ºC) 4d was isolated by FC (CH2Cl2/pentane) in 65% yield (E:Z 9:1) as a white solid. 1H NMR (400 MHz, CDCl3) δ ppm 7.84-7.74 (m, 3H), 7.73 (s, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.49-7.29 (m, 7H), 6.70 (d, J = 16.0 Hz, 1H), 6.46 (dd, J = 6.0, 16.0 Hz, 1H), 5.53 (bs, 1H), 5.01 (bs, 1H), 1.47 (s, 9H). 13C NMR (100 MHz, CDCl3) δ ppm 155.0, 141.3, 134.0, 133.5, 133.0, 131.0, 130.0, 128.8 (2C), 128.2, 128.0, 127.6 (2C), 127.0 (2C), 126.6, 126.3, 125.9, 123.4, 79.8, 56.4, 28.4 (3C). HRMS: Calculated for [C24H22NNaO2]: 382.1783; found: 382.1776. The enantiomeric excess was determined by HPLC using a Chiralcel OD column [hexane/i-PrOH (85:15)]; flow rate 1.0 mL/min; τ_minor = 11.04 min, τ_major = 8.32 min (85% ee); [α]20D −14.3 (c = 0.39, CH2Cl2).
(R)-tert-Butyl 3-(3-chlorophenyl)-1-phenylallylcarbamate (4e)

Following the general procedure (-40 °C) 4e was isolated by FC (CH₂Cl₂/pentane) in 54% yield (E:Z 10:1) as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.41-7.18 (m, 9H), 6.48 (dd, J = 1.2, 15.6 Hz, 1H), 6.34 (dd, J = 6.0, 16.0 Hz, 1H), 5.45 (bs, 1H), 4.95 (bs, 1H), 1.46 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 154.9, 140.9, 138.4, 134.5, 131.2, 129.7, 129.5, 128.8 (2C), 127.7, 127.6, 127.0 (2C), 126.4, 124.8, 79.9, 56.2, 28.4 (3C). HRMS: Calculated for [C₂₀H₂₂ClNNaO₂]: 366.1237; found: 366.1237. The enantiomeric excess was determined by HPLC using a Chiralcel OJ column [hexane/i-PrOH (98:2)]; flow rate 1.0 mL/min; τₘᵲᵣₐᵢᵦ = 14.44 min, τₙᵲᵢᵦᵢᵦ = 10.77 min (82% ee); [α]ᵋD₂₀ = -3.4 (c = 0.50, CH₂Cl₂).

(R)-tert-Butyl 3-phenyl-1-o-tolylallylcarbamate (4f)

Following the general procedure (-40 °C) 4f was isolated by FC (CH₂Cl₂/pentane) in 61% yield (E:Z 10:1) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.40-7.16 (m, 9H), 6.46 (d, J = 16.4 Hz, 1H), 6.35 (dd, J = 5.2, 16.0 Hz, 1H), 5.66 (bs, 1H), 4.93 (bs, 1H), 2.42 (s, 3H), 1.46 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 154.9, 139.3, 136.6, 130.8, 130.6, 129.4, 128.6, 128.5 (2C), 127.6, 127.5, 126.5 (2C), 126.3, 126.2, 79.7, 52.8, 28.4 (3C), 19.3. HRMS: Calculated for [C₂₁H₂₅NNaO₂]: 346.1783; found: 346.1772. The enantiomeric excess was determined by HPLC using a Chiralcel OD column [hexane/i-PrOH (95:5)]; flow rate 1.0 mL/min; τₘᵲᵦᵢᵦ = 25.20 min, τₙᵲᵢᵦᵦᵦ = 18.61 min (96% ee); [α]ᵋD₂₀ = +27.5 (c = 0.80, CH₂Cl₂).

(R)-tert-Butyl 1-(2-bromophenyl)-3-phenylallylcarbamate (4g)

Following the general procedure (0 °C) 4g was isolated by FC (CH₂Cl₂/pentane) in 42% yield (E:Z >20:1) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.59 (dd, J = 0.8, 8.0 Hz, 1H), 7.43-7.11 (m, 8H), 6.48 (d, J = 16.0 Hz, 1H), 6.31 (bs, 1H), 5.79 (bs, 1H), 5.11 (bs, 1H), 1.44 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 154.7, 140.4, 136.4, 133.4, 131.5, 129.0, 128.5 (2C), 127.8, 127.7, 126.5 (2C), 123.5, 79.9, 55.9, 28.3 (3C). HRMS: Calculated for [C₂₀H₂₂BrNNaO₂]: 410.0732; found: 410.0728. The enantiomeric
excess was determined by HPLC using a Chiralpak AD column [hexane/i-PrOH (95:5)]; flow rate 1.0 mL/min; \( \tau_{\text{minor}} = 10.52 \) min, \( \tau_{\text{major}} = 11.40 \) min (87% ee); \([\alpha]_D^{20} +2.2\) (c = 0.50, CH\(_2\)Cl\(_2\)).

\((R)-\text{tert-Butyl 3-phenyl-1-(thiophen-2-yl)allylcarbamate (4h)}\)

Following the general procedure (-30 °C) \(4h\) was isolated by FC (CH\(_2\)Cl\(_2\)) in 83% yield as a white solid. The \(E:Z\) ratio could not be determined accurately by neither NMR or GC. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.32 (d, \(J = 6.0\) Hz, 1H), 7.28-7.25 (m, 4H), 7.00-6.98 (m, 2H), 6.65 (d, \(J = 12.0\) Hz, 1H), 6.37 (dd, \(J = 4.0, 16.0\) Hz, 1H), 5.71 (bs, 1H), 5.03 (bs, 1H), 1.48 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 154.9, 145.6, 136.5, 131.4, 128.8, 128.7, 128.0, 127.1, 126.8, 124.9, 124.7, 80.2, 52.3, 28.5 (3C). HRMS: Calculated for [C\(_{18}\)H\(_{21}\)NO\(_2\)S\(_2\)Na]: 338.1191; found: 338.1190. The enantiomeric excess was determined by HPLC using a Chiralcel OD column [hexane/i-PrOH (95:5)]; flow rate 1.0 mL/min; \(\tau_{\text{minor}} = 10.33\) min, \(\tau_{\text{major}} = 8.24\) min (58% ee); \([\alpha]_D^{20} -8.8\) (c = 0.84, CH\(_2\)Cl\(_2\)).
5. General procedure for the formation of β-keto amino compounds 5a-c

An ordinary vial equipped with a magnetic stirring bar was charged with β-keto benzothiazole (BT) sulfone nucleophile 2 (0.10 mmol, 1.0 equiv.) and catalyst 6f (0.01 mmol, 0.1 equiv.), which were dissolved in 0.5 mL propionitrile and cooled to the desired temperature (see below). Upon cooling the imine 1 (0.25 mmol, 2.5 equiv.) was added. The reaction was run until judged complete by ¹H NMR spectroscopy. The adduct was plugged through a pad of silica (1% Et₂O in CH₂Cl₂), and dissolved in 1 mL CH₂Cl₂. EtSNa (0.30 mmol, 3.0 equiv.) was added and the reaction was allowed to stir at ambient temperature until judged complete by TLC (approx. 2–4 h). The reaction was washed with water and purified by FC on silica.

(R)-tert-Butyl 3-oxo-3-phenyl-1-o-tolylpropylcarbamate (5a)

Following the general procedure (-40 ºC) 5a was isolated by FC (CH₂Cl₂) in 80% yield as a white solid. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.93-7.87 (m, 2H), 7.59-7.51 (m, 1H), 7.48-7.40 (m, 2H), 7.34-7.28 (m, 1H), 7.19-7.13 (m, 3H), 5.46 (dd, J = 6.0, 13.2 Hz, 1H), 5.29 (bs, 1H), 3.65-3.37 (m, 2H), 2.44 (s, 3H), 1.40 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 197.9, 154.9, 139.7, 136.8, 135.5, 133.2, 130.7, 128.6 (2C), 128.1 (2C), 127.3, 126.6, 125.3, 79.5, 48.0, 43.7, 28.3, 19.3. HRMS: Calculated for [C₂₁H₂₅NNaO₃]: 362.1732; found: 362.1733. The enantiomeric excess was determined by HPLC using a Chiralpak AD column [hexane/i-PrOH (85:15)]; flow rate 0.5 mL/min; τₘ𝑖𝑛𝑜𝑟 = 12.79 min, τₘ𝑎𝑗𝑜𝑟 = 11.43 min (86% ee); [α]D⁺20°+24.0 (c = 0.73, CH₂Cl₂, measured on sample with 82% ee).

(R)-tert-Butyl 3-oxo-1-phenyl-3-p-tolylpropylcarbamate (5b)

Following the general procedure (-24 ºC) 5b was isolated by FC (CH₂Cl₂) in 85% yield as a white solid. ¹H NMR (400 MHz, CDCl₃) δ
ppm 7.79 (d, J = 8.0 Hz, 2H), 7.39-7.14 (m, 7H), 5.62 (bs, 1H), 5.24 (bs, 1H), 3.61 (bs, 1H), 3.41 (dd, J = 6.0, 16.4 Hz, 1H), 2.39 (s, 3H), 1.41 (s, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 197.7, 155.2, 144.2, 141.8, 134.3, 129.3 (2C), 128.5 (2C), 128.2 (2C), 127.2, 126.3 (2C), 79.6, 51.4, 44.2, 28.3 (3C), 21.6. HRMS: Calculated for [C$_{21}$H$_{25}$NNaO$_3$]: 362.1732; found: 362.1737. The enantiomeric excess was determined by HPLC using a Chiralcel AD column [hexane/i-PrOH (85:15)]; flow rate 1.0 mL/min; τ$_{\text{minor}}$ = 25.10 min, τ$_{\text{major}}$ = 26.60 min (76% ee); $[\alpha]_D^{20}$-5.4 (c = 0.70, CHCl$_3$).

The absolute configurations of the products 4 and 5 were correlated to the absolute configuration of 5b, which was determined to be $R$ by comparison of the specific rotation to the literature.$^3$

Following the general procedure (-40 ºC) 5c was isolated by FC (CH$_2$Cl$_2$) in 88% yield as a white solid. $^1$H NMR (400 MHz, CDCl$_3$) δ ppm 7.78 (t, J = 1.6 Hz, 1H), 7.73-7.68 (m, 1H), 7.49-7.42 (m, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.30-7.13 (m, 5H), 5.40 (bs, 1H), 5.18 (m, 1H), 3.57 (bs, 1H), 3.35 (dd, J = 6.4, 16.4 Hz, 1H), 1.35 (9H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 196.7, 155.1, 141.4, 138.2, 135.0, 133.2, 130.0, 128.6 (2C), 128.2, 127.5, 126.3 (2C), 126.2, 79.7, 51.3, 44.6, 28.3 (3C). HRMS: Calculated for [C$_{20}$H$_{22}$ClNNaO$_3$]: 382.1186; found: 382.1183. The enantiomeric excess was determined by HPLC using a Chiralcel OD column [hexane/i-PrOH (70:30)]; flow rate 0.5 mL/min; τ$_{\text{minor}}$ = 11.24 min, τ$_{\text{major}}$ = 14.73 min (73% ee); $[\alpha]_D^{20}$-0.8 (c = 0.50, CH$_2$Cl$_2$).
6. General procedure for the formation of β-keto amino compounds 5d-f

An ordinary vial equipped with a magnetic stirring bar was charged with β-keto benzothiazole (BT) sulfone nucleophile 2 (0.10 mmol, 1.0 equiv.) and catalyst 6f (0.01 mmol, 0.1 equiv.), which were dissolved in 0.5 mL propionitrile and cooled to the desired temperature (see below). Upon cooling the imine 1 (0.25 mmol, 2.5 equiv.) was added. The reaction was run until judged complete by \(^1\)H NMR spectroscopy. The adduct was plugged through a pad of silica (1% Et\(_2\)O in CH\(_2\)Cl\(_2\)), and dissolved in 3 mL CH\(_2\)Cl\(_2\)/TFA (5:1). The reaction was allowed to stir at ambient temperature until judged complete by \(^1\)H NMR (approx. 1–2 h), after which the solvent was evaporated. 1 mL of toluene was added and evaporated to remove TFA as an azeotrope, after which the product was purified by FC on silica.

(R)-3-(Benzothiazol-2-ylamino)-1-phenyl-3-o-tolylpropan-1-one (5d)

Following the general procedure (−40 °C) 5d was isolated by FC (Et\(_2\)O/CH\(_2\)Cl\(_2\)) in 87% yield as a white foam. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) ppm 7.82 (d, \(J = 7.6\) Hz, 2H), 7.56-7.44 (m, 4H), 7.38 (t, \(J = 8.0\) Hz, 2H), 7.25-7.14 (m, 4H), 7.08 (bs, 1H), 7.05 (t, \(J = 7.2\) Hz, 1H), 5.57 (bs, 1H), 3.70 (dd, \(J = 6.8, 16.8\) Hz, 1H), 3.43 (dd, \(J = 5.6, 16.8\) Hz, 1H), 2.53 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 197.3, 167.0, 152.0, 138.9, 136.4, 135.8, 133.3, 130.9, 130.7, 128.6 (2C), 128.0 (2C), 127.8, 126.6, 125.8, 125.6, 121.4, 120.8, 118.9, 52.8, 43.9, 19.4. HRMS: Calculated for [C\(_{23}\)H\(_{20}\)N\(_2\)NaOS]: 395.1194; found: 395.1200. The enantiomeric excess was determined by HPLC using a Chiralcel OD column [hexane/i-PrOH (70:30)]; flow rate 0.5 mL/min; \(\tau_{\text{minor}} = 14.73\) min, \(\tau_{\text{major}} = 18.88\) min (92% ee); \([\alpha]_D^{20} +29.4\) (c = 0.50, CH\(_2\)Cl\(_2\)).
(R)-3-(Benzothiazol-2-ylamino)-3-phenyl-1-p-tolylpropan-1-one (5e)

Following the general procedure (-24 ºC) 5e was isolated by FC (Et₂O/CH₂Cl₂) in 92% yield as a white foam. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.81-7.74 (m, 2H), 7.57-7.46 (m, 4H), 7.40-7.25 (m, 4H), 7.24-7.18 (m, 2H), 7.15-7.08 (m, 1H), 5.36-5.31 (m, 1H), 3.80 (dd, J = 6.8, 17.2 Hz, 1H), 3.47 (dd, J = 5.2, 17.2 Hz, 1H), 2.39 (3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 196.6, 167.8, 148.0, 144.5, 140.3, 133.9, 129.3 (2C), 128.9 (2C), 128.3, 128.2 (2C), 128.0, 126.7 (2C), 126.4, 122.3, 121.3, 117.6, 56.7, 44.8, 21.6. HRMS: Calculated for [C₂₃H₂₀N₂ONaS]: 395.1194; found: 395.1195. The enantiomeric excess was determined by HPLC using a Chiralpak AD column [hexane/i-PrOH (80:20)]; flow rate 1.0 mL/min; τ_minor = 23.50 min, τ_major = 19.70 min (74% ee); [α]²⁰D -16.2 (c = 1.30, CH₂Cl₂).

(R)-3-(Benzothiazol-2-ylamino)-1-(3-chlorophenyl)-3-phenylpropan-1-one (5f)

Following the general procedure (-40 ºC) 5f was isolated by FC (Et₂O/CH₂Cl₂) in 90% yield as a white foam. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.83 (t, J = 1.6 hz, 1H), 7.72-7.66 (m, 1H), 7.56-7.42 (m, 5H), 7.41-7.23 (m, 5H), 7.12-7.03 (m, 1H), 5.41 (t, J = 6.0 Hz, 1H), 3.79 (dd, J = 6.4, 17.2 Hz, 1H), 3.46 (dd, J = 6.0, 17.2 Hz, 1H), 1.71 (bs, 1H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 196.0, 167.1, 151.8, 140.6, 137.9, 134.9, 133.3, 130.6, 129.9, 128.9 (2C), 128.2, 128.0, 126.7 (2C), 126.1, 125.9, 121.7, 120.9, 118.8, 55.8, 45.0. HRMS: Calculated for [C₂₂H₁₉ClN₂OS]: 393.0828; found: 393.0829. The enantiomeric excess was determined by HPLC using a Chiralpak AD column [hexane/i-PrOH (85:15)]; flow rate 1.0 mL/min; τ_minor = 19.70 min, τ_major = 27.50 min (70% ee); [α]²⁰D +14.0 (c = 0.89, CH₂Cl₂).