Supporting Information
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Synthesis of 2-Substituted Aziridine-2-Carboxylic Esters via Michael Induced Ring Closure Strategy

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Supporting Information

Table of Contents
1. General Information ........................................................................................................................................ S2
2. General Procedures ........................................................................................................................................ S3
3. Characterization: \(^1\)H, \(^{13}\)C and HRMS ........................................................................................................... S5
4. \(^1\)H and \(^{13}\)C NMR spectra .......................................................................................................................... S25
5. HPLC Analysis (Tables 2. and 3.) ................................................................................................................ S149
   5.1. Methods ........................................................................................................................................ S149
   5.2. Traces for Table 2 .............................................................................................................................. S150
   5.3. Traces for Table 3 .............................................................................................................................. S153
6. X-ray Structure of \(13a\) ............................................................................................................................ S154
7. Computational Methods and Figure S1 ..................................................................................................... S156
1. General Information

All chemicals and solvents were purchased from common suppliers and used as received. Chromatographic
purifications were done on Rf-machine CombiFlash Rf 200i Teledyne ISCO equipped with standard silica
columns.

NMR

$^1$H and $^{13}$C NMR spectra were recorder on Brucker spectrometer operating at 400 MHz and 100 MHz
respectively unless otherwise stated. Chemical shifts are given in ppm. Tetramethyl silane was used as external
reference. Following abbreviations describe the multiplets: s - singlet, d - doublet, t- triplet, q -quadruplet, ap -
apparent.

HRMS

Mass spectra were recorded on a High Resolution Mass Spectrometer (Q-Exactive, Orbitrap analyzer) from
Thermofischer equipped with an electrospray source, (Polarity: positive mode, Capillary: 3.8 kV, Capillary
temperature: 320°C, S-lens RF level: 55, Sheath gas flow rate: 40, Mass range: 100 to 1000 m/z) coupled to a
1200 Infinity series UPLC from Agilent: Solvent degasser, binary pump, heated column compartment and diode-
array detector (DAD). DAD Wavelength range (nm): 190 to 400. Column: Waters Acquity UPLC BEH C18, 1.7
µm, 50 x 2.1 mm, Temp: 60 °C. Solvent Gradient: A = water + 5% MeOH + 0.05 % HCOOH, B= Acetonitrile +
0.05 % HCOOH, see Table 1. for further details.

Table S1. Conditions for HRMS.

<table>
<thead>
<tr>
<th>gradient B</th>
<th>flow rate</th>
<th>used for molecules</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% - 100% B in 10 minutes</td>
<td>0.70 ml/min</td>
<td>15</td>
</tr>
<tr>
<td>10% - 100% B in 1.45 minutes</td>
<td>0.85 ml/min</td>
<td>2, 4b, 4d, 4i, 4o, 7a, 7b, 9, 12 (intermediate from step 1), 14</td>
</tr>
<tr>
<td>60% - 90% B in 1.45 minutes</td>
<td>0.85 ml/min</td>
<td>3, 4a, 4c, 4e, 4f, 4g, 4i, 4j, 4k, 4m, 4n, 8, 10, 12, 13</td>
</tr>
</tbody>
</table>

LCMS

Standard method (used for all molecules except 13):

Spectra were recorded on a Mass Spectrometer from Waters (SQD, SQDII Single quadrupole mass
spectrometer) equipped with an electrospray source (Polarity: positive and negative ions), Capillary: 3.00 kV,
Cone range: 30 V, Extractor: 2.00 V, Source Temperature: 150°C, Desolvation Temperature: 350°C, Cone Gas
Flow: 50 l/h, Desolvation Gas Flow: 650 l/h, Mass range: 100 to 900 Da) and an Acquity UPLC from Waters:
Binary pump, heated column compartment, diode-array detector and ELSD detector. Column: Waters UPLC
HSS T3 , 1.8 mm, 30 x 2.1 mm, Temp: 60 °C, DAD Wavelength range (nm): 210 to 500, Solvent Gradient: A =
water + 5% MeOH + 0.05 % HCOOH, B= Acetonitrile + 0.05 % HCOOH, gradient: 10-100% B in 1.2 min;
Flow (ml/min) 0.85

Long method (used for molecule 13):

Spectra were recorded on a Mass Spectrometer from Waters (SQD, SQDII Single quadrupole mass
spectrometer) equipped with an electrospray source (Polarity: positive and negative ions), Capillary: 3.00 kV,
Cone range: 30V, Extractor: 2.00 V, Source Temperature: 150°C, Desolvation Temperature: 350°C, Cone Gas
Flow: 50 l/h, Desolvation Gas Flow: 650 l/h, Mass range: 100 to 900 Da) and an Acquity UPLC from Waters:
2. General Procedures

General procedure I (GPI):

A 2-necked flask (10 mL) equipped with a magnetic stirring bar (ellipsoidal), an Ar-inlet and a rubber septum was charged with DMF (2 mL) and solid NaH in oil (23 mg, 0.52 mmol, 1.10 eq). The mixture was cooled in ice bath and selected nucleophile (0.49 mmol, 1.05 eq) was added. The reaction mixture was stirred for 30 min at low temperature, then 10 min at room temperature. After this time, the reaction mixture was cooled in ice bath and a solution of starting material (150 mg, 0.47 mmol, 1.0 eq) in DMF (2 mL) was added dropwise by means of a syringe. The ice bath was removed and stirring was continued overnight at room temperature.

Work-up: The reaction mixture was cooled in ice bath. Saturated NH₄Cl(aq.) (10 mL) was added first dropwise, then in one portion (pH after quenching 8-9). The resulting mixture was extracted with diethyl ether (3 x 25 mL). Combined organic extracts were washed with water (2 x 30 mL), saturated NaHCO₃(aq.) (10 mL), dried over Na₂SO₄(anhdr.), filtered and evaporated to dryness (bath temperature 35 °C). The crude product was purified by chromatographic separation on Rf-machine yielding the corresponding product as a colourless to yellow oil.

General procedure II (GPII):

A 2-necked flask (10 mL) equipped with a magnetic stirring bar (ellipsoidal), an Ar-inlet and a rubber septum was charged with solid NaH in oil (25 mg, 0.56 mmol, 1.20 eq) and hexane (2 mL). The mixture was stirred for several minutes at room temperature, then the precipitate was allowed to settle down and hexane was removed with a syringe (note 1). DMF (2 mL) was added by means of a syringe and the mixture was cooled in ice bath. The selected nucleophile (0.49 mmol, 1.05 eq) was added in one portion. The reaction mixture was stirred for 30 min at low temperature, then 10 min at room temperature. After this time, the reaction mixture was cooled in ice bath and a solution of starting material (150 mg, 0.47 mmol, 1.0 eq) in DMF (2 mL) was added dropwise by means of a syringe. The ice bath was removed and stirring was continued overnight at room temperature.

Note 1: This portion of hexane has to be quenched with ethanol or isopropanol due to presence of some NaH.

Work-up: The reaction mixture was cooled in ice bath. Saturated NH₄Cl(aq.) (10 mL) was added first dropwise, then in one portion (pH after quenching 8-9). The resulting mixture was extracted with diethyl ether (3 x 25 mL). Combined organic extracts were washed with saturated NaHCO₃(aq.) (20 mL), dried over Na₂SO₄(anhdr.), filtered and evaporated to dryness (bath temperature 35 °C). Chloroform (0.7 mL) and toluene (20 drops) were added and the resulting solution was further evaporated (1 h, 20 mbar, bath temperature 38 °C). The target compound was obtained as a yellow oil.

General procedure III (GPIII):

A dry two-necked flask (10 mL) equipped with a magnetic stirring bar (ellipsoidal), a rubber septum and an Ar-inlet was charged with THF (3.2 mL/mmol) by means of a syringe. The solution was cooled in dry ice/acetone bath (-78 °C) and 1 M solution of LiHMDS in hexanes (1.65 eq.) was injected slowly along precooled wall.
While stirring, a solution of SM (1.0 eq.) in THF (1.6 mL/mmol) was added slowly along precooled wall by means of a syringe. Stirring was continued overnight allowing the reaction mixture to reach room temperature.

Work-up: The reaction mixture was cooled in ice bath. Saturated NH₄Cl(aq.) (10 mL) was added first dropwise, then in one portion (pH after quenching 8-9). The resulting mixture was extracted with diethyl ether (3 x 25 mL). Combined organic extracts were washed with brine (20 mL), dried over Na₂SO₄(anhydr.), filtered and evaporated to dryness (bath temperature 35 °C).

General procedure IV (GPIV):

A 2-necked flask (10 mL) equipped with a magnetic stirring bar (ellipsoidal), an Ar-inlet and a rubber septum was charged with THF (1 mL) and cooled in ethanol bath kept constantly at 0 °C by a thermostat. While stirring, 1 M LiHMDS solution in hexanes (0.495 mL, 0.495 mmol, 1.1 eq.) was injected slowly along precooled wall. Then, a solution of nucleophile (0.472 mmol, 1.05 eq.) in THF (0.8 mL) was added dropwise. The reaction mixture was stirred for 30 min at low temperature, then 10 min at room temperature. After this time, the reaction mixture was cooled again and a solution of starting material (150 mg, 0.450 mmol, 1.0 eq.) in THF (2 mL) was added dropwise by means of a syringe. Stirring was continued at 0 °C for 18 h.

Work-up: The reaction mixture was directly in the cooling bath by adding saturated NH₄Cl(aq.) (10 mL) was added first dropwise. The resulting mixture was extracted with diethyl ether (3 x 25 mL). Combined organic extracts were washed with water (30 mL), saturated NaHCO₃(aq.) (20 mL), dried over Na₂SO₄(anhydr.), filtered and evaporated to dryness (bath temperature 35 °C). The crude product was purified by chromatographic separation on Rf-machine yielding the corresponding product as a colourless to yellow oil.
3. Characterization: $^1$H, $^{13}$C and HRMS

### ethyl 2-((benzyl(hydroxy)amino)methyl)acrylate (2)

**Synthesis:** A 2-necked round-bottom flask (500 mL) was charged with solid N-benzylhydroxylamine hydrochloride (4.52 g, 28.3 mmol, 1.0 eq.). The vessel was then equipped with a magnetic stirring bar (ellipsoidal) and a low temperature thermometer. DCM (250 mL) was added, followed by a solution of ethyl 2-(bromomethyl)prop-2-enoate (5.47 g, 28.3 mmol, 1.0 eq.) in DCM (50 mL). The resulting suspension was cooled in ice/salt bath to -3 °C and triethylamine (7.88 mL, 56.6 mmol, 2.0 eq.) was injected dropwise while stirring. A clear solution formed and the temperature increased to 0 °C upon addition. The reaction vessel was equipped with a bubble counter and the reaction mixture was stirred for 30 min at low temperature.

**Work-up:** The reaction mixture was quenched with water (100 mL). Phases were separated and the aqueous phase was extracted with DCM (2 x 70 mL). Combined organic extracts were washed with saturated NH$_4$Cl(aq.) (100 mL), brine (100 mL), dried over Na$_2$SO$_4$(anhydr.), filtered and evaporated to dryness (bath temperature 35 °C).

**Yield:** quantitative, $R_f$ (TLC plate): 0.37 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.01 min.

- **$^1$H NMR** (400 MHz, CHLOROFORM-d) $\delta =$ 7.30 - 7.19 (m, 5 H, C(Ar)H), 6.25 (d, $J = 4$ Hz, 1 H, C(g)H'), 5.77 (d, $J = 4$ Hz, 1 H, C(g)H'), 4.14 (q, $J = 8$ Hz, 2 H, C(b)H$_2$), 3.81 (s, 2 H, C(f)H$_2$), 3.52 (s, 2 H, C(e)H$_2$), 1.21 (t, $J = 8$ Hz, 3 H, C(a)H$_3$)

- **$^{13}$C NMR** (100 MHz, CHLOROFORM-d) $\delta =$ 166.7 (C(c)), 137.3 (C(d) or C(Ar)ipso), 136.9 (C(d) or C(Ar)ipso), 129.5 (C(Ar)H), 128.4 (C(Ar)H), 128.3 (C(g)H'), 127.5 (C(Ar)H), 64.7 (C(f)H$_2$), 60.8 (C(b)H$_2$), 59.9 (C(e)H$_2$), 14.2 (C(a)H$_3$)

- **HRMS** (ESI/ESI/FT - Orbitrap) $m/z$ calc’d for: C$_{13}$H$_{18}$NO$_3$; found: 236.128; deviation = 0.330 mmu.

### ethyl 2-((benzyl(pivaloyloxy)amino)methyl)acrylate (3)

**Synthesis:** A 2-necked round-bottom flask (250 mL) equipped with a magnetic stirring bar (ellipsoidal) and a low temperature thermometer was charged with a solution of starting material (6.95 g, 29.5 mmol, 1.0 eq.) in DCM (100 mL). While stirring, the reaction mixture was cooled in ice/salt bath to -3 °C and triethylamine (4.11 mL, 29.5 mmol, 1.0 eq.) was injected dropwise. The ice bath was removed and stirring was continued for 10 min
at room temperature allowing the reaction mixture to reach 0 °C. Then, the reaction mixture was cooled again and pivaloyl chloride (3.6 mL, 29.5 mmol, 1 eq.) was added dropwise. Precipitation of a white solid (triethylamine hydrochloride) was observed. The ice bath was removed and stirring was continued at room temperature for 2 h.

Work-up: The reaction mixture was washed with water (2 x 50 mL) and brine (50 mL). The organic phase was dried over Na₂SO₄ (anhyd.), filtered and evaporated to dryness (bath temperature 35 °C). Purified by chromatographic separation on RF-machine.

Yield: 37%, R;: 0.43 (19/1 dichloromethane/ethyl acetate), retention time (LCMS): 1.16 min.

¹H NMR (400 MHz, CHLOROFORM-d) δ = 7.34 - 7.18 (m, 5 H, C(Ar)H), 6.23 (d, J = 4 Hz, 1 H, C(g)H'), 5.85 (d, J = 4 Hz, 1 H, C(g)H'H'), 4.15 (q, J = 8 Hz, 2 H, C(b)H₂), 4.00 (s, 2 H, C(e)H₂), 3.69 (s, 2 H, C(e)H₂), 1.22 (t, J = 8 Hz, 3 H, C(a)H₃), 0.96 (s, 9 H, C(j)H₃).

¹³C NMR (100 MHz, CHLOROFORM-d) δ = 176.1 (C(h)), 166.3 (C(c)), 135.8 (C(d) and C(Ar)ipso), 129.4 (C(Ar)H), 128.2 (C(Ar)H), 127.9 (C(g)HH'), 127.7 (C(Ar)H), 63.0 (C(f)H₂), 60.8 (C(b)H₂), 57.6 (C(e)H₂), 38.4 (C(i)), 27.1 (C(j)H₃), 14.2 (C(a)H₃).

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C₁₈H₂₆NO₄; found: 320.189; deviation = -0.060 mmu.

dimethyl 2-((1-benzyl-2-(ethoxycarbonyl)aziridin-2-yl)methyl)malonate (4a)

Synthesis: According to GPI, 1/1 dr

Yield: 59%, R;: 0.53 (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.07 min

Diastereomer A:

¹H NMR (600 MHz, CHLOROFORM-d) δ = 7.89 or 7.85 (d, J = 6 Hz, 2 H, C(Ar)H), 7.68 (m, 1 H, C(Ar)H), 7.56 (m, 2 H, C(Ar)H), 7.27 or 7.23 (m, 5 H, C(Ar)H), 4.33 or 3.91 (dd, J = 11 Hz, J = 3 Hz, 1 H, C(h)H), 4.21 - 4.06 (m, 2 H, C(b)H'H'), 3.78 (d, J = 14 Hz, 1 H, C(f)H'H'), 3.69 (d, J = 14 Hz, 1 H, C(f)H'H'), 3.57 or 3.53 (s, 3 H, C(k)H₂), 2.73 or 2.66 (dd, J = 14 Hz, J = 3 Hz, 1 H, C(g)H'H'), 2.51 or 2.23 (dd, J = 14 Hz, J = 11 Hz, 1 H, C(g)H'H'), 2.26 or 2.24 (s, 1 H, C(e)HH'), 2.00 or 1.97 (s, 1 H, C(e)HH'), 1.19 (ap t, J = 7 Hz, 3 H, C(a)H₃).

¹³C NMR (100 MHz, CHLOROFORM-d) δ = 168.7 or 168.4 (C(c)), 166.4 or 166.0 (C(j)), 138.7 or 138.6 (C(Ar)ipso), 137.2 or 136.9 (C(i)), 134.2 or 124.1 (C(Ar)H), 129.3 - 127.0 (C(Ar)H), 68.4 or 67.6 (C(b)H), 61.7 (C(b)H'H'), 55.8 or 55.5 (C(f)H'H'), 52.8 or 52.6 (C(k)H₃), 41.6 or 41.4 (C(d)), 39.0 (C(e)HH'), 31.1 or 30.0 (C(g)H'H'), 14.0 (C(a)H₃).
Diastereomer B:

**1H NMR** (600 MHz, CHLOROFORM-d) δ = 7.89 or 7.85 (d, \( J = 6 \text{ Hz} \), 2 H, C(Ar)H), 7.68 (m, 1 H, C(Ar)H), 7.56 (m, 2 H, C(Ar)H), 7.27 or 7.23 (m, 5 H, C(Ar)H), 4.33 or 3.91 (dd, 1 H, \( J = 11 \text{ Hz} \), \( J = 3 \text{ Hz} \), C(b)H), 4.21 - 4.06 (m, 2 H, C(b)HH’), 3.72 (d, \( J = 13 \text{ Hz} \), 1 H, C(f)HH’), 3.65 (d, \( J = 13 \text{ Hz} \), 1 H, C(f)HH’), 3.57 or 3.53 (s, 3 H, C(k)H3), 2.73 or 2.66 (dd, \( J = 14 \text{ Hz} \), \( J = 3 \text{ Hz} \), 1 H, C(g)HH’), 2.51 or 2.23 (dd, \( J = 14 \text{ Hz} \), \( J = 11 \text{ Hz} \), 1 H, C(g)HH’), 2.26 or 2.24 (s, 1 H, C(e)HH’), 2.00 or 1.97 (s, 1 H, C(e)HH’), 1.19 (ap t, \( J = 7 \text{ Hz} \), 3 H, C(a)H3)

**13C NMR** (100 MHz, CHLOROFORM-d) δ = 168.7 or 168.4 (C(c)), 166.4 or 166.0 (C(j)), 138.7 or 138.6 (C(Ar)ipso), 137.2 or 136.9 (C(i)), 134.2 or 124.1 (C(Ar)H), 129.3 - 127.0 (C(Ar)H), 68.4 or 67.6 (C(h)H), 61.7 (C(b)HH’), 55.8 or 55.5 (C(f)HH’), 52.8 or 52.6 (C(k)H3), 41.6 or 41.4 (C(d)), 39.0 (C(e)HH’), 31.1 or 30.0 (C(g)HH’), 14.0 (C(a)H3)

**HRMS** (ESI/FT - Orbitrap) m/z calc’d for: C22H26NO6S; found: 432.148; deviation = 0.640 mmu.

dimethyl 2-((1-benzyl-2-(ethoxycarbonyl)aziridin-2-yl)methyl)malonate (4b)

Synthesis: According to GPI

Yield: 71%, \( R_f \): 0.54 (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.04 min.

**1H NMR** (400 MHz, CHLOROFORM-d) δ = 7.31 - 7.20 (m, 5 H, C(Ar)H), 4.17 (m, 2 H, C(b)HH’), 3.77 (ap s, 2 H, C(f)HH’), 3.69 (ap s, 6 H, C(j)H3 and C’(j)H3), 3.58 (ap t, \( J = 8 \text{ Hz} \), 1 H, C(h)H), 2.45 (ap d, \( J = 4 \text{ Hz} \), 2 H, C(g)HH’), 2.26 (s, 1 H, C(e)HH’), 2.02 (s, 1 H, C(e)HH’), 1.23 (ap t, \( J = 6 \text{ Hz} \), 3 H, C(a)H3)

**13C NMR** (100 MHz, CHLOROFORM-d) δ = 169.7 (C(c) or C(i)), 169.6 (C(c) or C(i)), 139.2 (C(Ar)ipso), 128.3 (C(Ar)H), 128.0 (C(Ar)H), 127.0 (C(Ar)H), 61.6 (C(b)HH’), 56.0 (C(f)HH’), 52.6 (C(j)H3), 52.6 (C’(j)H3), 48.9 (C(h)H), 42.2 (C(d)), 40.1 (C(e)HH’), 32.7 (C(g)HH’), 14.2 (C(a)H3)

**HRMS** (ESI/FT - Orbitrap) m/z calc’d for: C18H24NO6; found: 350.160; deviation = 0.800 mmu.
dimethyl 2-((1-benzyl-2-(ethoxycarbonyl)aziridin-2-yl)methyl)malonate (4c)

Synthesis: According to GPI, 1/1 dr

Yield: 53% overall, Rf: 0.30 (A); 0.25 (B) (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.05 min

Diastereomer A:

$^1$H NMR (400 MHz, CHLOROFORM-d) $\delta = 7.39 - 7.23$ (m, 5 H, C(Ar)H), 4.73 (m, 1 H, C(h)H), 4.18 (m, 2 H, C(b)HH$'$), 3.85 (d, $J = 14$ Hz, 1 H, C(f)HH$'$), 3.76 (d, $J = 14$ Hz, 1 H, C(f)HH$'$), 2.31 (s, 1 H, C(e)HH$'$), 2.29 (m, 2 H, C(g)HH$'$), 2.01 (s, 1 H, C(e)HH$'$), 1.51 (d, $J = 7$ Hz, 3 H, C(i)H$_3$), 1.23 (ap t, $J = 7$ Hz, 3 H, C(i)H$_3$)

$^{13}$C NMR (100 MHz, CHLOROFORM-d) $\delta = 168.9$ (C(c)), 138.9 (C(Ar)ipso), 128.4 (C(Ar)H), 128.2 (C(Ar)H), 127.2 (C(Ar)H), 81.0 (C(h)H), 61.7 (C(b)HH$'$), 56.0 (C(f)HH$'$), 41.5 (C(d)), 40.1 (C(e)HH$'$), 39.4 (C(g)HH$'$), 20.1 (C(i)H$_3$), 14.1 (C(i)H$_3$)

HRMS (ESI/FT - Orbitrap) m/z calc'd for: C$^{15}$H$^{21}$N$_2$O$_4$; found: 293.149; deviation = -0.320 mmu.

Diastereomer B:

$^1$H NMR (400 MHz, CHLOROFORM-d) $\delta = 7.33 - 7.23$, (m, 5 H, C(Ar)H), 4.79 (m, 1 H, C(h)H), 4.18 (m, 2 H, C(b)HH$'$), 3.78 (ap d, $J = 4$ Hz, 2 H, C(f)HH$'$), 2.52 (dd, $J = 14$ Hz, 8 Hz, 1 H, C(g)HH$'$), 2.34 (s, 1 H, C(e)HH$'$), 2.13 (dd, $J = 14$ Hz, 8 Hz, 1 H, C(g)HH$'$), 2.02 (s, 1 H, C(e)HH$'$), 1.48 (d, $J = 7$ Hz, 3 H C(i)H$_3$), 1.25 (ap t, $J = 7$ Hz, 3 H, C(i)H$_3$)

$^{13}$C NMR (100 MHz, CHLOROFORM-d) $\delta = 169.1$ (C(c)), 138.9 (C(Ar)ipso), 128.4 (C(Ar)H), 128.3 (C(Ar)H), 127.2 (C(Ar)H), 81.0 (C(h)H), 61.7 (C(b)HH$'$), 56.4 (C(f)HH$'$), 41.5 (C(d)), 40.7 (C(e)HH$'$), 39.2 (C(g)HH$'$), 19.8 (C(i)H$_3$), 14.1 (C(i)H$_3$)

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C$^{15}$H$^{21}$N$_2$O$_4$; found: 293.149; deviation = -0.320 mmu.
ethyl 1-benzyl-2-(2-(ethoxycarbonyl)-2-methyl-3-oxobutyl)aziridine-2-carboxylate (4d)

Synthesis: According to GPI; 1/1 dr

Yield: 59%, Rf: 0.20 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.12 min

Diastereomer A:

\[ ^1H \text{ NMR} \ (400 \text{ MHz}, \text{CHLOROFORM-d}) \delta = 7.26 - 7.17 \ (m, 5 \text{ H, C(Ar)H}) , 4.15 - 4.00 \ (m, 4 \text{ H, C(b)H'H' and C(j)H'H'}) , 3.75 \ (d, 1 \text{ H, } J = 16 \text{ Hz, C(f)H'H'}) , 3.56 \ (d, 1 \text{ H, } J = 14 \text{ Hz, C(f)H'H'}) , 2.67 \ (d, 1 \text{ H, } J = 16 \text{ Hz, C(g)H'H'}) , 2.30 \ (d, 1 \text{ H, } J = 16 \text{ Hz, C(g)H'H'}) , 2.17 \ (s, 1 \text{ H, C(e)H'H'}) , 2.07 \ (s, 3 \text{ H, C(m)H}_3) 1.97 \ 1.93 \ (s, 1 \text{ H, C(e)H'H'}) , 1.34 \ (s, 3 \text{ H, C(n)H}_3) , 1.20 - 1.10 \ (m, 6 \text{ H, C(a)H}_3 \text{ and C(k)H}_3) \]

\[ ^{13}C \text{ NMR} \ (150 \text{ MHz, CHLOROFORM-d}) \delta = 205.1 \ or \ 204.5 \ (C(l)), 172.7 \ or \ 172.6 \ (C(i)), 169.9 \ or \ 169.6 \ (C(c)), 139.1 \ or \ 138.9 \ (C(Ar)ipso), 128.8 - 126.3 \ (C(Ar)H), 61.5 - 61.3 \ (C(b)H'H' \text{ and C(j)H'H'}) , 59.0 \ or \ 58.9 \ (C(h)), 56.4 \ or \ 56.3 \ (C(f)), 42.2 \ or \ 41.9 \ (C(d)H'H') , 41.4 \ or \ 40.4 \ (C(e)H'H') , 38.3 \ or \ 37.6 \ (C(g)H'H') , 26.1 \ or \ 25.9 \ (C(m)H)_3) \]

Diastereomer B:

\[ ^1H \text{ NMR} \ (400 \text{ MHz, CHLOROFORM-d}) \delta = 7.26 - 7.17 \ (m, 5 \text{ H, C(Ar)H}) , 4.15 - 4.00 \ (m, 4 \text{ H, C(b)H'H' and C(j)H'H'}) , 3.67 \ (d, 1 \text{ H, } J = 12 \text{ Hz, C(f)H'H'}) , 3.59 \ (d, 1 \text{ H, } J = 12 \text{ Hz, C(f)H'H'}) , 2.56 \ (d, 1 \text{ H, } J = 12 \text{ Hz, C(g)H'H'}) , 2.37 \ (d, 1 \text{ H, } J = 12 \text{ Hz, C(g)H'H'}) , 2.17 \ (s, 1 \text{ H, C(e)H'H'}) , 2.07 \ (s, 3 \text{ H, C(m)H}_3) 1.97 \ 1.93 \ (s, 1 \text{ H, C(e)H'H'}) , 1.34 \ (s, 3 \text{ H, C(n)H}_3) , 1.20 - 1.10 \ (m, 6 \text{ H, C(a)H}_3 \text{ and C(k)H}_3) \]

\[ ^{13}C \text{ NMR} \ (150 \text{ MHz, CHLOROFORM-d}) \delta = 205.1 \ or \ 204.5 \ (C(l)), 172.7 \ or \ 172.6 \ (C(i)), 169.9 \ or \ 169.6 \ (C(c)), 139.1 \ or \ 138.9 \ (C(Ar)ipso), 128.8 - 126.3 \ (C(Ar)H), 61.5 - 61.3 \ (C(b)H'H' \text{ and C(j)H'H'}) , 59.0 \ or \ 58.9 \ (C(h)), 56.4 \ or \ 56.3 \ (C(f)), 42.2 \ or \ 41.9 \ (C(d)H'H') , 41.4 \ or \ 40.4 \ (C(e)H'H') , 38.3 \ or \ 37.6 \ (C(g)H'H') , 26.1 \ or \ 25.9 \ (C(m)H)_3) \]

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C_{20}H_{28}NO_5; found: 362.198; deviation = 1.700 mmu.
ethyl 1-benzyl-2-(2-(ethoxycarbonyl)-2-fluoro-3-oxobutyl)aziridine-2-carboxylate (4e)

Synthesis: According to GPI; 1/1 dr

Yield: 37%, Rf: 0.22 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.11 min

Diastereomer A:

$^1$H NMR (600 MHz, CHLOROFORM-d) $\delta = 7.33 - 7.28$ (m, 5 H, C(Ar)H), 4.25 - 4.10 (m, 4 H, C(b)HH' and C(j)HH'), 3.87 (d, 1 H, $J = 12$ Hz, C(f)HH'), 3.72 (d, 1 H, $J = 12$ Hz, C(f)HH'), about 2.9 or 2.7 (m, 2 H, C(g)HH'), 2.30 (s, 1 H, C(e)H'), 2.28 or 2.26 (s, 3 H, C(m)H$_3$), 2.16 (s, 1 H, C(e)HH'), 1.32 - 1.22 (m, 6 H, C(a)H$_3$ and C(k)H$_3$)

$^{13}$C NMR (150 MHz, CHLOROFORM-d) $\delta = 202.0$ or 201.0 (d, $J = 28$ Hz, C(l)), 169.2 or 169.1 (C(c)), 166.1 or 166.0 (d, $J = 15$ Hz, C(i)), 138.8 or 138.7 (C(Ar)ipso), 128.4 - 127.0 (C(Ar)H), 99.1 or 98.9 (d, $J = 200$ Hz, C(h)), 62.6 (C(b)HH'), 61.7 or 61.6 (d, $J = 3$ Hz, C(j)HH'), 40.5 (C(d)), 55.7 or 55.6 (C(f)HH'), 40.3 (C(e)HH'), 36.8 or 36.7 (d, $J = 5$ Hz, C(g)HH'), 25.8 or 25.2 (C(m)H$_3$), 14.1 (C(a)H$_3$ and C(k)H$_3$)

$^{19}$F NMR (372 MHz, CHLOROFORM-d) $\delta = -165.9$ or -166.5

Diastereomer B:

$^1$H NMR (600 MHz, CHLOROFORM-d) $\delta = 7.33 - 7.28$ (m, 5 H, C(Ar)H), 4.25 - 4.10 (m, 4 H, C(b)HH' and C(j)HH'), 3.80 (d, 1 H, $J = 12$ Hz, C(f)HH'), 3.66 (d, 1 H, $J = 12$ Hz, C(f)HH'), about 2.9 or 2.7 (m, 2 H, C(g)HH'), 2.28 (s, 1 H, C(e)H'), 2.28 or 2.26 (s, 3 H, C(m)H$_3$), 2.16 (s, 1 H, C(e)HH'), 1.32 - 1.22 (m, 6 H, C(a)H$_3$ and C(k)H$_3$)

$^{13}$C NMR (150 MHz, CHLOROFORM-d) $\delta = 202.0$ or 201.0 (d, $J = 28$ Hz, C(l)), 169.2 or 169.1 (C(c)), 166.1 or 166.0 (d, $J = 15$ Hz, C(i)), 138.8 or 138.7 (C(Ar)ipso), 128.4 - 127.0 (C(Ar)H), 99.1 or 98.9 (d, $J = 200$ Hz, C(h)), 62.6 (C(b)HH'), 61.7 or 61.6 (d, $J = 3$ Hz, C(j)HH'), 40.3 (C(d)), 55.7 or 55.6 (C(f)HH'), 39.8 (C(e)HH'), 36.8 or 36.7 (d, $J = 5$ Hz, C(g)HH'), 25.8 or 25.2 (C(m)H$_3$), 14.1 (C(a)H$_3$ and C(k)H$_3$)

$^{19}$F NMR (372 MHz, CHLOROFORM-d) $\delta = -165.9$ or -166.5

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C$_{19}$H$_{25}$FNO$_5$; found: 366.171; deviation = -0.360 mmu.
ethyl 2-((3-acetyl-2-oxotetrahydrofuran-3-yl)methyl)-1-benzylaziridine-2-carboxylate (4f)

Synthesis: According to GPI; 1/1 dr

Yield: 57%, Rf: 0.44 (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.01 min

Diastereomer A:

\[\text{1H NMR} \quad (600 \text{ MHz, CHLOROFORM-d}) \delta = 7.36 - 7.27 \text{ (m, 5 H, C(Ar)H)}, 4.25 \text{ (m, 2 H, C(b)HH')}, 4.18 \text{ (m, 1 H, C(j)HH')}, 4.14 \text{ (m, 1 H, C(j)HH')}, 3.78 \text{ (d, 1 H, } J = 12 \text{ Hz, C(f)HH')}, 3.72 \text{ (d, 1 H, } J = 12 \text{ Hz, C(f)HH')}, 2.77 \text{ (m, 1 H, C(k)HH')}, 2.60 \text{ (d, 2 H, } J = 18 \text{ Hz, C(g)HH')}, 2.56 \text{ (d, 1 H, } J = 18 \text{ Hz, C(g)HH')}, 2.31 \text{ (s, 3 H, C(m)H)}, 2.27 \text{ (s, 1 H, C(e)HH')}, 2.15 \text{ (m, 1 H, C(k)HH')}, 2.06 \text{ (s, 1 H, C(e)HH')}, 1.32 \text{ (ap t, 3 H, } J = 6 \text{ Hz, 3 H, C(a)H)}

\[\text{13C NMR} \quad (150 \text{ MHz, CHLOROFORM-d}) \delta = 201.9 \text{ (C(l))}, 175.6 \text{ (C(i))}, 169.4 \text{ (C(c))}, 138.6 \text{ (C(Ar)ipso)}, 128.5 - 127.2 \text{ (C(Ar)H)}, 66.4 \text{ (C(j)HH')}, 61.8 \text{ (C(b)HH')}, 60.3 \text{ (C(h)HH')}, 56.0 \text{ (C(f)HH')}, 41.7 \text{ (C(d))}, 40.8 \text{ (C(e)HH')}, 38.2 \text{ (C(g)HH')}, 29.6 \text{ (C(k)HH')}, 25.8 \text{ (C(m)H)}, 14.2 \text{ (C(a)H)}

Diastereomer B:

\[\text{1H NMR} \quad (600 \text{ MHz, CHLOROFORM-d}) \delta = 7.36 - 7.27 \text{ (m, 5 H, C(Ar)H)}, 4.22 \text{ (m, 2 H, C(b)HH')}, 4.31 \text{ (m, 1 H, C(j)HH')}, 4.16 \text{ (m, 1 H, C(j)HH')}, 3.94 \text{ (d, 1 H, } J = 18 \text{ Hz, C(f)HH')}, 3.67 \text{ (d, 1 H, } J = 18 \text{ Hz, C(f)HH')}, 2.92 \text{ (d, 1 H, } J = 18 \text{ Hz, C(g)HH')}, 2.88 \text{ (m, 1 H, C(k)HH')}, 2.42 \text{ (d, 1 H, } J = 18 \text{ Hz, C(g)HH')}, 2.34 \text{ (s, 1 H, C(e)HH')}, 2.29 \text{ (s, 3 H, C(m)H)}, 2.27 \text{ (m, 1 H, C(k)HH')}, 2.09 \text{ (s, 1 H, C(e)HH')}, 1.28 \text{ (ap t, 3 H, } J = 6 \text{ Hz, 3 H, C(a)H)}

\[\text{13C NMR} \quad (150 \text{ MHz, CHLOROFORM-d}) \delta = 201.4 \text{ (C(l))}, 175.6 \text{ (C(i))}, 169.4 \text{ (C(c))}, 138.6 \text{ (C(Ar)ipso)}, 128.5 - 127.2 \text{ (C(Ar)H)}, 66.6 \text{ (C(j)HH')}, 61.7 \text{ (C(b)HH')}, 59.6 \text{ (C(h)HH')}, 56.1 \text{ (C(f)HH')}, 41.6 \text{ (C(d))}, 42.1 \text{ (C(e)HH')}, 37.0 \text{ (C(g)HH')}, 29.3 \text{ (C(k)HH')}, 25.9 \text{ (C(m)H)}, 14.1 \text{ (C(a)H)}

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C_{19}H_{24}NO_{5}; found: 346.164; deviation = -0.480 mmu.
**ethyl 1-benzyl-2-((((2-(trimethylsilyl)ethyl)thio)methyl)aziridine-2-carboxylate (4g)**

Synthesis: According to GPI, but the nucleophile and NaH were stirred for 25 min at low temperature, then 25 min at room temperature.

Yield: 51%, Rf: 0.30 (9/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.34 min

$^1$H NMR (400 MHz, CHLOROFORM-d) $\delta = 7.31 - 7.25$ (m, 5 H, C(Ar)$H$), 4.17 (m, 2 H, C(b)$HH'$), 3.75 (ap s, 2 H, C(f)$HH'$), 3.30 (d, $J = 16$ Hz, 1 H, C(g)$HH'$), 2.60 (ap t, $J = 8$ Hz, 2 H, C(h)$HH'$), 2.53 (d, $J = 16$ Hz, 1 H, C(g)$HH'$), 2.34 (s, 1 H, C(e)$HH'$), 2.11 (s, 1 H, C(e)$HH'$), 1.20 (ap t, $J = 8$ Hz, 3 H, C(a)$H_3$), 0.83 (m, 2 H, C(i)$HH'$), 0.00 (s, 9 H, C(j)$H_3$)

$^{13}$C NMR (100 MHz, CHLOROFORM-d) $\delta = 170.7$ (C(c)), 140.8 (C(Ar)ipso), 130.1 (C(Ar)$H$), 129.1 (C(Ar)$H$), 128.9 (C(Ar)$H$), 63.3 (C(b)$HH'$), 58.6 (C(f)$HH'$), 47.5 (C(d)), 41.3 (C(e)$HH'$), 38.2 (C(g)$HH'$), 30.5 (C(h)$HH'$), 19.4 (C(i)$HH'$), 15.9 (C(a)$H_3$), 0.0 (C(j)$H_3$)

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C$_{18}$H$_{30}$NO$_2$SSi; found: 352.176; deviation = 0.190 mnu.

**ethyl 1-benzyl-2-(((2-ethoxy-2-oxoethyl)thio)methyl)aziridine-2-carboxylate (4h)**

Synthesis: According to GPI, but the nucleophile and NaH were stirred for 25 min at low temperature, then 25 min at room temperature.

Yield: 64%, Rf: 0.21 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.05 min

$^1$H NMR (400 MHz, CHLOROFORM-d) $\delta = 7.24 - 7.15$ (m, 5 H, C(Ar)$H$), 4.15 - 4.05 (m, 4 H, C(b)$HH'$ and C(j)$HH'$), 3.75 (d, $J = 14$ Hz, 1 H, C(f)$HH'$), 3.69 (d, $J = 14$ Hz, 1 H, C(f)$HH'$), 3.26 - 3.16 (m, 3 H, C(g)$HH'$ and C(h)$HH'$), 2.70 (d, $J = 16$ Hz, 1 H, C(g)$HH'$), 2.27 (s, 1 H, C(e)$HH'$), 2.14 (s, 1 H, C(e)$HH'$), 1.20 (ap t, $J = 8$ Hz, 3 H, C(a)$H_3$ or C(k)$H_3$), 1.14 (ap t, $J = 6$ Hz, 3 H, C(a)$H_3$ or C(k)$H_3$)

S12
$^{13}$C NMR (100 MHz, CHLOROFORM-d) $\delta = 170.4$ (C(c) or C(i)), 168.8 (C(c) or C(i)), 138.9 (C(Ar)ipso), 128.4 (C(Ar)H), 128.0 (C(Ar)H), 127.1 (C(Ar)H), 61.6 (C(b)HH$'$ or C(j)HH$'$), 61.4 (C(b)HH$'$ or C(j)HH$'$), 56.6 (C(f)HH$'$), 44.9 (C(d)), 39.7 (C(e)HH$'$), 36.6 (C(g)HH$'$), 34.3 (C(h)HH$'$), 14.2 (C(a)H$_3$ or C(k)H$_3$), 14.1 (C(a)H$_3$ or C(k)H$_3$)

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C$_{13}$H$_{22}$NO$_4$S; found: 358.122; deviation = -0.010 mmu.

ethyl 1-benzyl-2-(((1-ethoxy-1-oxopropan-2-yl)thio)methyl)aziridine-2-carboxylate (4i)

Synthesis: According to GPI, but the nucleophile and NaH were stirred for 25 min at low temperature, then 25 min at room temperature

Yield: 70%, R$_f$: 0.32 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.15 min

Diastereomer A:

$^1$H NMR (600 MHz, CHLOROFORM-d) $\delta = 7.23 - 7.10$ (m, 5 H, C(Ar)H), 4.25 - 4.10 (m, 4 H, C(b)HH$'$ and C(j)HH$'$), 3.80 (d, $J = 8$ Hz, 1 H, C(f)HH$'$), 3.74 (d, $J = 8$ Hz, 1 H, C(f)HH$'$), 3.53 (q, $J = 8$ Hz, 1 H, C(h)H), 3.34 (d, $J = 12$ Hz, 1 H, C(g)HH$'$), 2.75 (d, $J = 12$ Hz, 1 H, C(g)HH$'$), 2.36 (s, 1 H, C(e)HH$'$), 2.27 (s, 1 H, C(e)HH$'$), 1.40 (d, $J = 8$ Hz, 3 H, C(l)H$_3$), 1.29 - 1.23 (m, 6 H, C(a)H$_3$ and C(k)H$_3$)

$^{13}$C NMR (150 MHz, CHLOROFORM-d) $\delta = 173.1$ or 173.2 (C(i)), 168.6 (C(c)), 138.9 (C(Ar)ipso), 128.3 (C(Ar)H), 128.0 (C(Ar)H), 127.1 (C(Ar)H), 61.6 (C(b)HH$'$ and C(j)HH$'$), 56.5 (C(f)HH$'$), 45.0 (C(d)), 40.9 (C(h)H), 39.7 (C(e)HH$'$), 35.1 (C(g)HH$'$), 17.2 (C(l)H$_3$), 14.2 (C(a)H$_3$ and C(k)H$_3$)

Diastereomer B:

$^1$H NMR (600 MHz, CHLOROFORM-d) $\delta = 7.23 - 7.10$ (m, 5 H, C(Ar)H), 4.25 - 4.10 (m, 4 H, C(b)HH$'$ and C(j)HH$'$), 3.84 (d, $J = 8$ Hz, 1 H, C(f)HH$'$), 3.78 (d, $J = 8$ Hz, 1 H, C(f)HH$'$), 3.48 (q, $J = 8$ Hz, 1 H, C(h)H), 3.35 (d, $J = 12$ Hz, 1 H, C(g)HH$'$), 2.75 (d, $J = 12$ Hz, 1 H, C(g)HH$'$), 2.35 (s, 1 H, C(e)HH$'$), 2.16 (s, 1 H, C(e)HH$'$), 1.42 (d, $J = 8$ Hz, 3 H, C(l)H$_3$), 1.29 - 1.23 (m, 6 H, C(a)H$_3$ and C(k)H$_3$)

$^{13}$C NMR (150 MHz, CHLOROFORM-d) $\delta = 173.1$ or 173.2 (C(i)), 168.8 (C(c)), 138.9 (C(Ar)ipso), 128.3 (C(Ar)H), 128.0 (C(Ar)H), 127.1 (C(Ar)H), 61.1 (C(b)HH$'$ and C(j)HH$'$), 56.6 (C(f)HH$'$), 44.8 (C(d)), 42.3 (C(h)H), 40.1 (C(e)HH$'$), 36.2 (C(g)HH$'$), 17.5 (C(l)H$_3$), 14.1 (C(a)H$_3$ and C(k)H$_3$)

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C$_{13}$H$_{22}$NO$_4$S; found: 352.158; deviation = 0.180 mmu.

S13
ethyl 1-benzyl-2-((benzylthio)methyl)aziridine-2-carboxylate (4j)

Synthesis: According to GPI, but the nucleophile and NaH were stirred for 25 min at low temperature, then 25 min at room temperature

Yield: 59%, Rf: 0.17 (9/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.18 min

$^1$H NMR (400 MHz, CHLOROFORM-d) $\delta = 7.23 - 7.10$ (m, 10 H, C(Ar)H), 4.10 (m, 2 H, C(b)H$H'$), 3.68 (ap s, 2 H, C(f)H$H'$ or C(h)H$H'$), 3.68 (ap s, 2 H, C(f)H$H'$ or C(h)H$H'$), 3.12 (d, $J = 12$ Hz, 1 H, C(g)H$H'$), 2.39 (d, $J = 12$ Hz, 1 H, C(g)H$H'$), 2.20 (s, 1 H, C(e)H$H'$), 1.92 (s, 1 H, C(e)H$H'$), 1.12 (ap t, $J = 6$ Hz, 3 H, C(a)H$_3$)

$^{13}$C NMR (100 MHz, CHLOROFORM-d) $\delta = 168.9 \text{ (C(c))}, 139.4 \text{ and } 138.4 \text{ (C(Ar)ipso)}, 128.9 \text{ (C(Ar)H)}, 128.5 \text{ (C(Ar)H)}, 128.3 \text{ (C(Ar)H)}, 128.0 \text{ (C(Ar)H)}, 127.1 \text{ (C(Ar)H)}, 127.1 \text{ (C(Ar)H)}, 61.5 \text{ (C(b)H$H'$)}, 56.7 \text{ (C(f)H$H'$)}, 45.4 \text{ (C(d))}, 39.6 \text{ (C(e)H$H'$)}, 37.1 \text{ (C(h)H$H'$)}, 35.6 \text{ (C(g)H$H'$)}, 14.2 \text{ (C(a)H$_3$)}

HRMS (ESI/FT - Orbitrap) $m/z$ calc’d for: C$_{20}$H$_{24}$NO$_2$S; found: 342.152; deviation = 0.090 mmu.

ethyl 1-benzyl-2-((2-oxopyrrolidin-1-yl)methyl)aziridine-2-carboxylate (4k)

Synthesis: According to GPI, but deprotonation of the nucleophile was done by stirring it with NaH for 1 h at room temperature

Yield: 38%, Rf: 0.43 (19/1 ethyl acetate/methanol), retention time (LCMS): 0.89 min

$^1$H NMR (400 MHz, CHLOROFORM-d) $\delta = 7.24 - 7.19$ (m, 5 H, C(Ar)H), 4.09 (m, 2 H, C(b)H$H'$), 3.22 (d, $J = 12$ Hz, 1 H, C(g)H$H'$), 3.22 (d, $J = 12$ Hz, 1 H, C(g)H$H'$), 2.25 (ap t, $J = 8$ Hz, 2 H, C(i)H$H'$), 2.21 (s, 1 H, C(e)H$H'$), 2.08 (s, 1 H, C(e)H$H'$), 1.86 (ap t, $J = 8$ Hz, 2 H, C(j)H$H'$), 1.13 (ap t, $J = 8$ Hz, 3 H, C(a)H$_3$)
$^{13}$C NMR (100 MHz, CHLOROFORM-d) $\delta = 175.3$ (C(h)), 168.9 (C(c)), 139.0 (C(Ar)ipso), 128.4 (C(Ar)H), 128.2 (C(Ar)H), 127.2 (C(Ar)H), 61.5 (C(b)HH’), 56.2 (C(f)HH’), 48.5 (C(g)HH’), 45.8 (C(k)HH’), 42.8 (C(d)), 38.9 (C(e)HH’), 30.8 (C(i)HH’), 18.2 (C(j)HH’), 14.1 (C(a)H$_3$)

**HRMS** (ESI/FT - Orbitrap) m/z calc’d for: C$_{17}$H$_{22}$N$_2$O$_3$; found: 303.179; deviation = -0.160 mmu.

**ethyl 1-benzyl-2-((1,3-dioxoisindolin-2-yl)methyl)aziridine-2-carboxylate (4l)**

Synthesis: According to GPI

Yield: 50%, R: 0.53 (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.07 min

$^1$H NMR (400 MHz, CHLOROFORM-d) $\delta = 7.84$ (dd, $J = 5$ Hz, 3 Hz, 2 H, C(j)H), 7.71 (dd, $J = 6$ Hz, 3 Hz, 2 H, C(k)H), 7.34 - 7.22 (m, 5 H, C(Ar)H), 4.45 (d, $J = 16$ Hz, 1 H, C(g)HH’), 4.13 (m, 2 H, C(b)HH’), 3.84 (ap d, $J = 16$ Hz, 2 H, C(f)HH’ and C(g)HH’), 3.75 (d, $J = 12$ Hz, 1 H, C(f)HH’), 2.29 (s, 1 H, C(e)HH’), 2.17 (s, 1 H, C(e)HH’), 1.15 (ap t, $J = 7$ Hz, 3 H, C(a)H$_3$)

$^{13}$C NMR (100 MHz, CHLOROFORM-d) $\delta = 176.0$ (C(c)), 168.1 (C(b)), 138.9 (C(Ar)ipso), 134.0 (C(k)H), 132.1 (C(i)H), 128.3 (C(Ar)H), 128.1 (C(Ar)H), 127.0 (C(Ar)H), 123.3 (C(j)H), 61.7 (C(b)HH’), 42.7 (C(d)), 40.4 (C(g)HH’), 39.1 (C(e)HH’), 14.0 (C(a)H$_3$)

**HRMS** (ESI/FT - Orbitrap) m/z calc’d for: C$_{21}$H$_{21}$N$_2$O$_4$; found: 365.152; deviation = -1.70 mmu.

**ethyl 2-(((1H-1,2,4-triazol-1-yl)methyl)-1-benzylaziridine-2-carboxylate (4m)**

Synthesis: According to GPII

Yield: 71%, R: 0.23 (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 0.72 min

$^1$H NMR (400 MHz, CHLOROFORM-d) $\delta = 8.00$ (s, 1 H, C(h)H), 7.81 (s, 1 H, C(i)H), 7.27 - 7.18 (m, 5 H, C(Ar)H), 4.75 (d, $J = 16$ Hz, 1 H, C(g)HH’), 4.14 - 4.00 (m, 3 H, C(b)HH’ and C(g)HH’), 3.91 (d, $J = 12$ Hz, 1
H, C(f)H'), 3.70 (d, J = 12 Hz, 1 H, C(f)HH'), 2.36 (s, 1 H, C(e)HH'), 2.81 (s, 1 H, C(e)HH'), 1.11 (ap t, J = 8 Hz, 3 H, C(a)H₃)

\(^{13}\)C NMR (100 MHz, CHLOROFORM-d) \(\delta = 167.9 (C(c)), 151.7 (C(i)H), 144.1 (C(h)H), 138.5 (C(Ar)ipso), 128.5 (C(Ar)H), 128.1 (C(Ar)H), 127.4 (C(Ar)H), 62.0 (C(b)HH'), 55.9 (C(f)HH'), 52.7 (C(g)HH'), 42.8 (C(d)), 39.6 (C(e)HH'), 14.1 (C(a)H₃)

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C\(_{15}\)H\(_{19}\)N\(_{4}\)O\(_{2}\); found: 287.150; deviation = -0.360 mmu.

ethyl 2-((1H-pyrazol-1-yl)methyl)-1-benzylaziridine-2-carboxylate (4n)

Synthesis: According to GPII

Yield: 70\%, R\(_f\): 0.43 (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 0.94 min

\(^1\)H NMR (400 MHz, CHLOROFORM-d) \(\delta = 7.40 (d, J = 2\, \text{Hz}, 1\, \text{H}, C(j)H), 7.34 (s, 1\, \text{H}, C(h)H), 7.27 - 7.16 (m, 5\, \text{H}, C(Ar)H), 6.12 (ap t, J = 4\, \text{Hz}, 1\, \text{H}, C(i)H), 4.80 (d, J = 12\, \text{Hz}, 1\, \text{H}, C(g)HH'), 4.11 - 3.99 (m, 3\, \text{H}, C(b)HH' and C(g)HH'), 3.87 (d, J = 12\, \text{Hz}, 1\, \text{H}, C(f)HH'), 3.68 (d, J = 12\, \text{Hz}, 1\, \text{H}, C(f)HH'), 2.31 (s, 1\, \text{H}, C(e)HH'), 2.13 (s, 1\, \text{H}, C(e)HH'), 1.08 (ap t, J = 8\, \text{Hz}, 3\, \text{H}, C(a)H₃)

\(^{13}\)C NMR (100 MHz, CHLOROFORM-d) \(\delta = 168.3 (C(c)), 139.4 (C(j)H), 138.8 (C(Ar)ipso), 130.2 (C(h)H), 128.4 (C(Ar)H), 128.0 (C(Ar)H), 127.2 (C(Ar)H), 106.3 (C(i)H), 61.6 (C(b)HH'), 56.1 (C(f)HH'), 55.0 (C(g)HH'), 43.8 (C(d)), 39.2 (C(e)HH'), 14.0 (C(a)H₃)

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C\(_{17}\)H\(_{20}\)N\(_{3}\)O\(_{2}\); found: 286.154; deviation = -0.230 mmu.

ethyl 1-benzyl-2-((diethoxyphosphoryl)methyl)aziridine-2-carboxylate (4o)

Synthesis: According to GPI, but THF was used as solvent and overnight stirring was done at 40 °C

Yield: 67\%, R\(_f\): 0.16 (ethyl acetate), retention time (LCMS): 0.98 min
\[ ^1H \text{NMR} (400 \text{ MHz, CHLOROFORM-d}) \delta = 7.26 - 7.16 (m, 5 H, C(Ar)H), 4.09 - 3.97 (m, 6 H, C(b)HH', C(h)HH' and C'(h)HH'), 3.69 (d, J = 16 Hz, 1 H, C(f)HH'), 3.63 (d, J = 16 Hz, 1 H, C(f)HH'), 2.91 (ap t, J = 18 Hz, C(g)HH'), 2.33 (s, 1 H, C(e)HH'), 2.22 (s, 1 H, C(e)HH'), 1.78 (dd, J = 18 Hz, 6 Hz, 1 H, C(g)HH'), 1.23 (m, 6 H, C(i)H$_3$ and C'(i)H$_3$), 1.11 (ap t, J = 3 Hz, 3 H, C(a)H$_3$) \]

\[ ^13C \text{NMR} (100 \text{ MHz, CHLOROFORM-d}) \delta = 168.4 (C(c)), 138.9 (C(Ar)ipso), 128.4 (C(Ar)H), 127.9 (C(Ar)H), 127.1 (C(Ar)H), 61.7 (C(h)HH' and C'(h)HH'), 61.6 (C(b)HH'), 56.5 (C(f)HH'), 40.9 (C(d)), 38.8 (C(e)HH'), 31.8 (d, J = 139 Hz, C(g)HH'), 16.5 (C(i)H$_3$), 16.4 (C'(i)H$_3$), 14.1 (C(a)H$_3$) \]

\[ ^31P \text{NMR} (160 \text{ MHz, CHLOROFORM-d}) \delta = 27.1 \]

**HRMS (ESI/FT - Orbitrap) m/z calc'd for: C$_{17}$H$_{27}$NO$_5$P; found: 356.161; deviation = -0.900 mmu.**

**ethyl 2-((benzylamino)methyl)-5-methyl-4-((trifluoromethyl)thio)-2,3-dihydrofuran-2-carboxylate (7a)**

**Synthesis:** According to GPI

**Yield:** 57%, $R_f$: 0.29 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 0.91 min

\[ ^1H \text{NMR} (600 \text{ MHz, BENZENE-d6}) \delta = 7.20 - 7.05 (m, 5 H, C(Ar)H), 3.93 (ap q, J = 8 Hz, 2 H, C(b)HH'), 3.54 (d, J = 18 Hz, 1 H, C(f)HH'), 3.48 (d, J = 18 Hz, 1 H, C(f)HH'), 3.04 (dq, J = 16 Hz, 2 Hz, 1 H, C(i)HH'), 2.98 (d, J = 14 Hz, 1 H, C(e)HH'), 2.84 (dq, J = 16 Hz, 2 H, 1 H, C(i)HH'), 2.75 (d, J = 14 Hz, 1 H, C(e)HH'), 1.72 (ap t, J = 2 Hz, 3 H, C(h)H$_3$), 0.89 (ap t, J = 8 Hz, 3 H, C(a)H$_3$) \]

\[ ^13C \text{NMR} (150 \text{ MHz, BENZENE-d6}) \delta = 170.9 (C(c)), 165.7 (C(g)), 140.2 (C(Ar)ipso), 130.2 (q, J = 189 Hz, C(k)), 128.2 - 126.9 (C(Ar)H), 89.3 (C(j)), 88.7 (C(d)), 61.1 (C(b)HH'), 54.2 (C(e)HH'), 53.5 (C(f)HH'), 41.9 (C(i)HH'), 13.7 (C(a)H$_3$), 11.9 (C(h)H$_3$) \]

\[ ^19F \text{NMR} (372 \text{ MHz, CHLOROFORM-d}) \delta = -43.7 \]

**HRMS (ESI/FT - Orbitrap) m/z calc'd for: C$_{17}$H$_{21}$F$_3$NO$_3$S; found: 376.119; deviation = 0.260 mmu.**
diethyl 2-((benzylamino)methyl)-5-methyl-2,3-dihydrofuran-2,4-dicarboxylate (7b)

Synthesis: According to GPI

Yield: 78%, Rf 0.17 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 0.76 min

$^1$H NMR (400 MHz, CHLOROFORM-d) δ = 7.25 - 7.15 (m, 5 H, C(Ar)H), 4.17 (m, 2 H, C(b)HH’ or C(l)HH’), 4.08 (ap q, J = 8 Hz, 2 H, C(b)HH’ or C(l)HH’), 3.79 (d, J = 14 Hz, 1 H, C(f)HH’), 3.73 (d, J = 14 Hz, 1 H, C(f)HH’), 3.04 (dq, J = 16 Hz, 4 Hz, 1 H, C(i)HH’), 3.02 (d, J = 12 Hz, 1 H, C(e)HH’), 2.90 (d, J = 12 Hz, 1 H, C(e)HH’), 2.85 (dq, J = 16 Hz, 4 Hz, 1 H, C(i)HH’), 2.15 (ap t, J = 4 Hz, 3 H, C(h)H$_3$), 1.20 (m, 6 H, C(a)H$_3$ and C(m)H$_3$)

$^{13}$C NMR (100 MHz, CHLOROFORM-d) δ = 171.8 (C(c)), 166.8 (C(k)), 165.5 (C(g)), 140.0 (C(Ar)ipso), 128.4 (C(Ar)H), 128.0 (C(Ar)H), 127.0 (C(Ar)H), 101.8 (C(j)), 89.0 (C(d)), 61.7 (C(b)HH’ or C(l)HH’), 59.7 (C(b)HH’ or C(l)HH’), 54.6 (C(e)HH’), 53.7 (C(f)HH’), 37.6 (C(i)HH’), 14.4 (C(a)H$_3$ or C(m)H$_3$), 14.1 (C(a)H$_3$ or C(m)H$_3$ and C(h)H$_3$)

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C$_{19}$H$_{26}$NO$_5$; found: 348.181; deviation = 0.380 mmu.

dimethyl 2-((2-(ethoxycarbonyl)aziridin-2-yl)methyl)malonate (8)

Synthesis: A two-necked flask (10 mL) equipped with a magnetic stirring bar (ellipsoidal), a rubber septum and an Ar-inlet was charged with a solution of starting material (93 mg, 0.27 mmol, 1.0 eq.) in MeOH (3.5 mL) by means of a syringe. 10% Pd/C catalyst (9 mg, 10 mol %) was added as solid. The Ar inlet was removed and hydrogen gas was bubbled through the reaction mixture while stirring for 10 min. Stirring was then continued overnight under hydrogen atmosphere at room temperature.

Work-up: The reaction mixture was filtered over a 1.5 cm thick Celite pad placed in a fritted glass (porosity 3, diameter 4 cm) on a piece of filter paper. The pad was washed with MeOH (30 mL). The filtrate was evaporated to dryness (bath temperature 35 °C) yielding the crude product as a yellow oil. The isolated material was purified
by flash column chromatography (stationary phase: 1.5 g 40-60 silica gel; mobile phase: cyclohexane/ethyl acetate from 10/0 to 0/10; fraction size: 10 mL; column diameter: 1 cm).

Yield: 51%, Rf: 0.17 (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 0.72 min

\textbf{1H NMR (400 MHz, CHLOROFORM-d)} \ δ = 4.15 (ap q, J = 8 Hz, 2 H, C(b)H₂), 3.67 (s, 3 H, C(i)H₃), 3.66 (s, 3 H, C'(i)H₃), 3.60 (ap t, 1 H, C(g)H), 2.64 (dd, J = 17 Hz, 6 Hz, 1 H, C(f)HH'), 2.08 (s, 1 H, C(e)HH'), 2.02 (dd, J = 16 Hz, 6 Hz, C(f)HH'), 1.66 (s, 1 H, C(e)HH'), 1.23 (t, J = 8 Hz, 3 H, C(a)H₃)

\textbf{13C NMR (150 MHz, CHLOROFORM-d)} \ δ = 172.8 (C(c)), 169.7 (C(h)), 169.6 (C'(h)), 62.1 (C(b)H₂), 52.7 (C(i)H₃), 52.6 (C'(i)H₃), 48.7 (C(g)HH'), 36.1 (C(d)HH'), 34.1 (C(e)HH'), 30.7 (C(f)), 14.1 (C(a)H₃)

\textbf{HRMS (ESI/FT - Orbitrap)} m/z calc'd for: C₁₁H₁₈NO₆; found: 260.113; deviation = 0.330 mmu.

ethyl 1-benzyl-8-hydroxy-5-methyl-6-oxo-1-azaspiro[2.5]oct-7-ene-5-carboxylate (9)

Synthesis: A two-necked flask (10 mL) equipped with a magnetic stirring bar (ellipsoidal), a rubber septum and an Ar-inlet was charged with a solution of SM (95 mg, 0.26 mmol, 1.0 eq.) in DMF (1.9 mL). While stirring, the reaction mixture was cooled in ice bath and NaH in oil (17 mg, 0.39 mmol, 1.5 eq.) was added as solid in one portion. The reaction mixture was stirred for 15 min at low temperature, then overnight at room temperature. Colour change to yellow observed.

Work-up: The reaction mixture was cooled in ice bath. Saturated NH₄Cl(aq.) (10 mL) was added first dropwise, then in one portion. 2.5 M HCl(aq.) was added dropwise till reaching pH=6-7 as indicated by pH-paper. The resulting mixture was extracted with diethyl ether (3 x 25 mL). Combined organic extracts were washed with water (30 mL), saturated NH₄Cl(aq.) (10 mL), dried over Na₂SO₄(anhydr.), filtered and evaporated to dryness (bath temperature 35 °C) yielding yellow solid.

Yield: 42%, dr = 1/1, Rf: 0.16 (200/80/40/40/10 toluene/ethanol/dioxane/triethylamine/water), retention time (LCMS): 0.70 min

Diastereomer A:

\textbf{1H NMR (400 MHz, CHLOROFORM-d)} \ δ = 7.30 - 7.15 (m, 5 H, C(Ar)H), 5.62 or 5.53 (s, 1 H, C(b)H), 4.10 (m, 2 H, C(j)HH'), 3.86 or 3.78 (d, J = 12 Hz, 1 H, C(f)HH'), 3.58 or 3.70 (d, J = 12 Hz, 1 H, C(d)HH'), 2.27 (d, J = 12 Hz, 1 H, C(g)HH'), 2.24 or 2.13 (s, 1 H, C(e)HH'), 2.17 (d, J = 12 Hz, 1 H, C(g)HH'), 1.99 or 1.94 (s, 1 H, C(e)HH'), 1.40 or 1.36 (s, 3 H, C(l)H₃), 1.21 - 1.14 (m, 3 H, C(k)H₃)

\textbf{13C NMR (150 MHz, CHLOROFORM-d)} \ δ = 196.4 or 196.2 (C(a)), 172.7 or 172.4 (C(i)), 170.6 or 170.3 (C(c)), 137.4 or 137.2 (C(Ar)ipso), 130.0 - 126.0 (C(Ar)H), 104.5 or 102.9 (C(b)H), 61.7 or 61.5 (C(j)HH'), 55.3
or 55.1 (C(f)H'H'), 54.7 or 53.3 (C(h)), 40.5 or 40.4 (C(e)H'H'), 39.3 or 38.9 (C(d)), 35.1 or 33.6 (C(g)H'H'), 22.1 or 20.0 (C(l)H₃), 14.0 (C(k)H₃)

Diastereomer B:

^1^H NMR (400 MHz, CHLOROFORM-d) δ = 7.30 - 7.15 (m, 5 H, C(Ar)H), 5.62 or 5.53 (s, 1 H, C(b)H), 4.10 (m, 2 H, C(j)H'H'), 3.86 or 3.78 (d, J = 12 Hz, 1 H, C(f)H'H'), 3.58 or 3.70 (d, J = 12 Hz, 1 H, C(f)H'H'), 2.24 or 2.13 (s, 1 H, C(e)H'H'), 1.99 or 1.94 (s, 1 H, C(e)H'H'), 1.70 (ap d, J = 12 Hz, 2 H, C(g)H'H'), 1.40 or 1.36 (s, 3 H, C(l)H₃), 1.21 - 1.14 (m, 3 H, C(k)H₃)

^1^3^C NMR (150 MHz, CHLOROFORM-d) δ = 196.4 or 196.2 (C(a)), 172.7 or 172.4 (C(i)), 170.6 or 170.3 (C(c)), 137.4 or 137.2 (C(Ar)ipso), 130.0 - 126.0 (C(Ar)H), 104.5 or 102.9 (C(b)H), 61.7 or 61.5 (C(j)H'H'), 55.3 or 55.1 (C(f)H'H'), 54.7 or 53.3 (C(h)), 40.5 or 40.4 (C(e)H'H'), 39.3 or 38.9 (C(d)), 35.1 or 33.6 (C(g)H'H'), 22.1 or 20.0 (C(l)H₃), 14.0 (C(k)H₃)

HRMS (ESI/FT - Orbitrap) m/z calc'd for: C₁₈H₂₂NO₄; found: 316.155; deviation = 0.330 mmu.

ethyl 4-((benzylamino)methyl)-3-hydroxythiophene-2-carboxylate (10)

Synthesis: According to GPIII, 0.25 mmol scale

Yield: 81%, Rf: 0.12 (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 0.72 min

^1^H NMR (400 MHz, CHLOROFORM-d) δ = 7.19 (broad s, 1 H, C(e)H), 7.19 - 7.08 (m, 6 H, C(Ar)H and NH), 4.22 (q, J = 7 Hz, 2 H, C(h)H₂), 3.67 (s, 2 H, C(d)H₂), 3.63 (s, 2 H, C(c)H₂), 1.23 (t, J = 7 Hz, 3 H, C(i)H₃)

^1^3^C NMR (150 MHz, CHLOROFORM-d) δ = 166.0 (C(g)), 162.1 (C(a)), 135.1 (C(Ar)ipso), 130.1 (broad, C(e)H), 129.0 (C(Ar)H), 128.7 (C(Ar)H), 128.0 (C(Ar)H), 127.4 (broad C(b)H), 104.8 (C(f)), 61.3 (C(b)H₂), 51.8 (C(d)H₂), 43.7 (C(c)H₂), 14.4 (C(i)H₃)

HRMS (ESI/FT - Orbitrap) m/z calc’d for: C₁₅H₁₈NO₃S; found: 192.100; deviation = 0.130 mmu.
ethyl 2-((hydroxy(1-phenylethyl)amino)methyl)acrylate (step 1 in synthesis of 12)

Synthesis: A 2-necked round-bottom flask (50 mL) was charged with ethyl 2-(bromomethyl)prop-2-enolate (0.050 g, 2.59 mmol, 1.0 eq.) and DCM (30 mL). The vessel was equipped with a magnetic stirring bar (ellipsoidal) and a low temperature thermometer. The reaction mixture was cooled in ice bath to 5 °C and N-(1-phenylethyl)hydroxylamine (0.36 g, 2.59 mmol, 1.0 eq.) was added as solid followed by liquid triethylamine (0.36 mL, 2.59 mmol, 1.0 eq.). The reaction vessel was equipped with a bubble counter and the reaction mixture was stirred for 30 min at low temperature.

Work-up: The reaction mixture was quenched with water (30 mL). DCM (20 mL) was added and phases were separated. The organic extract was washed with saturated NH₄Cl(aq.) (30 mL), brine (30 mL), dried over Na₂SO₄(anhdr.), filtered and evaporated to dryness (bath temperature 35 °C).

Yield: quantitative, Rf: 0.19 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 0.96 min

¹H NMR (400 MHz, CHLOROFORM-d) δ = 7.30 - 7.17 (m, 5 H, C(Ar)H), 6.21 (d, J = 4 Hz, 1 H, C(h)H'H'), 5.73 (d, J = 4 Hz, 1 H, C(h)H'H'), 4.13 (ap q, J = 8 Hz, 2 H, C(b)HH'), 3.79 (q, J = 8 Hz, 1 H, C(f)H), 3.38 (ap s, 2 H, C(e)HH'), 1.43 (d, J = 8 Hz, 3 H, C(g)H₃), 1.21 (ap t, J = 8 Hz, 3 H, C(a)H₃)

¹³C NMR (100 MHz, CHLOROFORM-d) δ = 166.9 (C(c)), 142.3 (C(Ar)ipso), 137.2 (C(d)), 128.4 (C(Ar)H), 128.0 (C(h)H'H'), 127.9 (C(Ar)H), 127.5 (C(Ar)H), 67.7 (C(f)H), 60.8 (C(b)HH'), 57.5 (C(e)HH'), 19.8 (C(g)H₃), 14.2 (C(a)H₃)

HRMS (ESI/FT - Orbitrap) m/z calc'd for: C₁₄H₂₀NO₃; found: 250.144; deviation = 0.000 mmu.

ethyl 2-(((1-phenylethyl)(pivaloyloxy)amino)methyl)acrylate (12)

Synthesis: A 2-necked round-bottom flask (25 mL) equipped with a magnetic stirring bar (ellipsoidal) and a low temperature thermometer was charged with a solution of starting material (0.53 g, 2.1 mmol, 1.0 eq.) in DCM (10 mL). While stirring, the reaction mixture was cooled in ice bath to 5 °C and triethylamine (0.29 mL, 2.1 mmol, 1.0 eq.) was injected in one portion. Stirring was continued for 10 min at room temperature. Then, pivaloyl chloride (0.26 mL, 2.1 mmol, 1 eq.) was added dropwise. Precipitation of a white solid (triethylamine hydrochloride) was observed. The ice bath was removed and stirring was continued at room temperature for 2 h.
Work-up: The reaction mixture was washed with water (10 mL) and brine (10 mL). The organic phase was dried over Na₂SO₄ (anhydr.), filtered and evaporated to dryness (bath temperature 35 °C). Purified by chromatographic separation on Rf-machine.

Yield: 71%, Rₜ: 0.40 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.26 min

**¹H NMR** (400 MHz, CHLOROFORM-d) δ = 7.42 - 7.23 (m, 5 H, C(Ar)H), 6.22 (d, J = 4 Hz, 1 H, C(h)H''), 5.89 (d, J = 4 Hz, 1 H, C(b)H'H'), 4.20 (ap q, J = 8 Hz, 2 H, C(b)H'H'), 4.07 (q, J = 8 Hz, 1 H, C(f)H), 3.60 (ap t, J = 16 Hz, 2 H, C(e)H'H'), 1.44 (d, J = 8 Hz, 3 H, C(g)H₃), 1.28 (ap t, J = 8 Hz, 3 H, C(a)H₃), 1.06 (s, 9 H, C(j)H₃)

**¹³C NMR** (100 MHz, CHLOROFORM-d) δ = 176.3 (C(i)), 166.4 (C(c)), 141.8 (C(Ar)ipso), 136.3 (C(d)), 128.6 - 127.1 (C(Ar)H and C(h)H'H'), 67.1 (C(f)H), 60.7 (C(b)H'H'), 56.1 (C(e)H'H'), 38.5 (C(j)), 27.2 (C(k)H₃), 19.8 (C(g)H₃), 14.2 (C(a)H₃)

**HRMS** (ESI/FT - Orbitrap) m/z calc’d for: C₁₉H₂₈NO₄; found: 334.202; deviation = 0.420 mmu.

dimethyl 2-((2-(ethoxycarbonyl)-1-(1-phenylethyl)aziridin-2-yl)methyl)malonate (13)

Synthesis: According to GPIV. The major diastereomer could be purified by recrystallization from tBuOMe followed by washing with pentane.

Yield: 48%, Rₜ: 0.29 (4/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.26 min (major); 1.73 min (minor)

Diastereomer A (major):

**¹H NMR** (400 MHz, CHLOROFORM-d) δ = 7.29 - 7.12 (m, 5 H, C(Ar)H), 3.84 (m, 1 H, C(b)H'H'), 3.64 (s, 3 H, C(k)H₃), 3.63 (s, 3 H, C'(k)H₃), 3.42 - 3.37 (m, 2 H, C(f)H and C(i)H), 2.60 (dd, J = 14 Hz, 4 Hz, 1 H, C(h)H'H'), 2.22 (s, 1 H, C(e)H'H'), 2.02 (dd, J = 14 Hz, 8 Hz, 1 H, C(b)H'H'), 1.99 (s, 1 H, C(e)H'H'), 1.33 (d, J = 4 Hz, 3 H, C(g)H₃), 0.85 (ap t, J = 8 Hz, 3 H, C(a)H₃)

**¹³C NMR** (100 MHz, CHLOROFORM-d) δ = 169.7 (C(c) or C(j) or C'(j)), 169.4 (C(c) or C(j) or C'(j)), 168.8 (C(c) or C(j) or C'(j)), 144.5 (C(Ar)ipso), 128.2 (C(Ar)H), 126.9 (C(Ar)H), 126.6 (C(Ar)H), 61.2 (C(b)H'H'), 61.2 (C(f)H), 52.6 (C(k)H₃), 52.5 (C'(k)H₃), 48.7 (C(i)H), 42.9 (C(d)), 39.0 (C(e)H'H'), 32.7 (C(h)H'H'), 24.3 (C(g)H₃), 13.7 (C(a)H₃)
Diastereomer B (minor):

**1H NMR** (400 MHz, CHLOROFORM-d) δ = 7.29 - 7.12 (m, 5 H, C(Ar)H), 4.21 (ap q, J = 8 Hz, 2 H, C(b)H'H'), 3.67 (s, 3 H, C(k)H3), 3.67 (s, 3 H, C'(k)H3), 3.50 - 3.44 (m, 2 H, C(f)H and C(i)H), 2.55 (dd, J = 16 Hz, 8 Hz, 1 H, C(h)H',), 2.44 (dd, J = 16 Hz, 8 Hz, 1 H, C(h)H'), 2.06 (s, 1 H, C(e)H'H'), 1.79 (s, 1 H, C(e)H'H'), 1.28 (ap t, J = 8 Hz, 3 H, C(a)H3) 1.15 (d, J = 4 Hz, 3 H, C(g)H3)

**13C NMR** (100 MHz, CHLOROFORM-d) δ = 169.8 (C(c) or C(j) or C'(j)), 169.5 (C(c) or C(j) or C'(j)), 168.8 (C(c) or C(j) or C'(j)), 144.8 (C(Ar)ipso), 128.3 (C(Ar)H), 127.1 (C(Ar)H), 126.6 (C(Ar)H), 61.6 (C(b)HH'), 60.4 (C(f)H), 52.6 (C(k)H3), 52.5 (C'(k)H3), 48.8 (C(i)H), 42.7 (C(d)), 38.9 (C(e)HH'), 32.2 (C(h)HH'), 23.4 (C(g)H3), 14.3 (C(a)H3)

**HRMS (ESI/FT - Orbitrap)** m/z calc'd for: C19H26NO6; found: 364.175; deviation = -0.160 mmu.

**ethyl 2-((benzylthio)methyl)-I-(1-phenylethyl)aziridine-2-carboxylate (14)**

**Synthesis:** According to GPI, but the nucleophile and NaH were stirred for 25 min at low temperature, then 25 min at room temperature.

**Yield:** 61%, Rf: 0.29 (9/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.28 min

Diastereomer A (major):

**1H NMR** (600 MHz, CHLOROFORM-d) δ = 7.40 - 7.21 (m, 10 H, C(Ar)H), 3.95 (m, 1 H, C(b)H'H'), 3.81 (m, 1 H, C(b)H'H'), 3.74 (ap s, 2 H, C(i)HH'), 3.88 (q, J = 6 Hz, 1 H, C(f)H), 3.28 (d, J = 12 Hz, 1 H, C(h)H',), 2.36 (d, J = 12 Hz, 1 H, C(h)H'), 2.33 (s, 1 H, C(e)H'H'), 2.03 (s, 1 H, C(e)H'H'), 1.41 (d, J = 6 Hz, 3 H, C(g)H3), 0.93 (ap t, J = 6 Hz, 3 H, C(a)H3)

**13C NMR** (150 MHz, CHLOROFORM-d) δ = 168.7 (C(c)), 144.6 or 144.5 (C(Ar)ipso), 138.4 (C(j)), 128.9 - 126.5 (C(Ar)H), 61.6 (C(b)HH'), 61.2 (C(f)H), 45.7 (C(d)), 39.1 (C(e)HH'), 37.1 (C(i)HH'), 35.8 (C(h)HH'), 24.3 (C(g)H3), 13.7 (C(a)H3)

Diastereomer B (minor):

**1H NMR** (600 MHz, CHLOROFORM-d) δ = 7.40 - 7.21 (m, 10 H, C(Ar)H), 4.32 (ap q, J = 6 Hz, 2 H, C(b)H'H'), 3.88 (d, J = 12 Hz, 1 H, C(i)HH'), 3.84 (d, J = 12 Hz, 1 H, C(i)HH'), 3.47 (q, J = 8 Hz, 1 H, C(f)H), 3.14 (d, J = 12 Hz, 1 H, C(h)H'H'), 2.63 (d, J = 12 Hz, 1 H, C(h)H'H'), 2.17 (s, 1 H, C(e)H'H'), 1.86 (s, 1 H, C(e)H'H'), 1.37 (ap t, J = 8 Hz, 3 H, C(a)H3), 1.33 (d, J = 6 Hz, 3 H, C(g)H3),
**13C NMR** (150 MHz, CHLOROFORM-d) δ = 169.3 (C(c)), 144.6 or 144.5 (C(Ar)ipso), 138.5 (C(j)), 128.9 - 126.5 (C(Ar)H), 61.6 (C(b)HH’), 60.8 (C(f)H), 46.0 (C(d)), 39.4 (C(e)HH’), 37.0 (C(i)HH’), 36.0 (C(h)HH’), 23.4 (C(g)H3), 14.3 (C(a)H3)

168.7 (C(c)), 144.5 or 144.6 (C(Ar)ipso), 138.5 or 138.3 (C(j)), 129.0 - 126.9 (C(Ar)H), 61.2 (C(b)HH’), 61.6 (C(f)H), 45.6 (C(d)), 39.3 (C(e)HH’), 37.4 (C(i)HH’), 36.0 (C(h)HH’), 23.4 (C(g)H3), 14.3 (C(a)H3)

**HRMS** (ESI/FT - Orbitrap) m/z calc’d for: C21H26NO2S; found: 356.168; deviation = -0.180 mmu.

ethyl 2-((1H-pyrazol-1-yl)methyl)-1-(1-phenylethyl)aziridine-2-carboxylate (15)

Synthesis: According to GPI.

Yield: 56%, Rf: 0.55 (major) and 0.48 (minor) (1/1 cyclohexane/ethyl acetate), retention time (LCMS): 1.05 min

Diastereomer A (major):

**1H NMR** (400 MHz, CHLOROFORM-d) δ = 7.39 (d, J = 2 Hz, 1 H, C(i)H or C(k)H), 7.29 (ap s, 1 H, C(i)H or C(k)H), 7.23 - 7.15 (m, 5 H, C(Ar)H), 6.10 (ap t, J = 4 Hz, 1 H, C(j)H), 4.76 (d, J = 12 Hz, 1 H, C(h)HH’), 3.88 (d, J = 12 Hz, 1 H, C(h)HH’), 3.85 (m, 1 H, C(b)HH’), 3.74 (m, 1 H, C(b)HH’), 3.45 (q, J = 6 Hz, 1 H, C(f)H), 2.34 (s, 1 H, C(e)HH’), 2.20 (s, 1 H, C(e)HH’), 1.36 (d, J = 6 Hz, 3 H, C(g)H3), 0.87 (ap t, J = 6 Hz, 3 H, C(a)H3)

**13C NMR** (100 MHz, CHLOROFORM-d) δ = 168.2 (C(c)), 144.5 (C(Ar)ipso), 139.3 (C(i)H or C(k)H), 130.2 (C(Ar)H or C(i)H or C(k)H), 128.3 (C(Ar)H or C(i)H or C(k)H), 126.7 (C(Ar)H or C(i)H or C(k)H), 126.6 (C(Ar)H or C(i)H or C(k)H), 105.2 (C(i)H), 61.3 (C(b)HH’), 61.2 (C(f)H), 55.0 (C(h)HH’), 44.2 (C(d)), 38.9 (C(e)HH’), 24.3 (C(g)H3), 13.8 (C(a)H3)

Diastereomer B (minor):

**1H NMR** (400 MHz, CHLOROFORM-d) δ = 7.46 (ap s, 1 H, C(i)H or C(k)H), 7.26 - 7.15 (m, 6 H, C(Ar)H and C(i)H or C(k)H), 6.16 (ap s, 1 H, C(j)H), 4.86 (d, J = 12 Hz, 1 H, C(h)HH’), 4.21 (m, 2 H, C(b)HH’), 4.12 (d, J = 12 Hz, 1 H, C(h)HH’), 3.45 (q, J = 6 Hz, 1 H, C(f)H), 2.16 (s, 1 H, C(e)HH’), 1.92 (s, 1 H, C(e)HH’), 1.23 (ap t, J = 8 Hz, 3 H, C(a)H3), 1.18 (d, J = 6 Hz, 3 H, C(g)H3)

**HRMS** (ESI/FT - Orbitrap) m/z calc’d for: C17H22N3O2; found: 300.171; deviation = 0.12 mmu.
4. $^1$H and $^{13}$C NMR spectra

Chemical Shift (ppm)

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8 1.9 2.0 2.1 2.2 2.3 2.4 2.5 2.6 2.7 2.8 2.9 3.0 3.1 3.2 3.3 3.4 3.5 3.6 3.7 3.8 3.9 4.0 4.1 4.2 4.3 4.4 4.5 4.6 4.7 4.8 4.9 5.0 5.1 5.2 5.3 5.4 5.5 5.6 5.7 5.8 5.9 6.0 6.1 6.2 6.3 6.4 6.5 6.6 6.7 6.8 6.9 7.0 7.1 7.2 7.3 7.4 7.5 7.6 7.7 7.8 7.9 8.0 8.1 8.2 8.3 8.4 8.5 8.6 8.7 8.8 8.9 9.0 9.1 9.2 9.3 9.4 9.5 9.6 9.7 9.8 9.9 10.0

3.34 2.07 2.05 2.22 0.99 1.00 6.61 7.30 7.29 7.27 7.27 7.19 6.26 6.25 5.78 5.77 4.17 4.15 4.13 4.11 3.81 1.23 1.21 1.19

$N_{OH}$
Chemical Shift (ppm)

1.7  1.6  1.5  1.4  1.3  1.2  1.1  1.0  0.9  0.8  0.05  0.10  0.15  0.20

3.09  1.36  1.14  1.12

0.92  0.52

N

S

OO

Chemical Shift (ppm)
Chemical Shift (ppm)

- 168.92
- 138.95
- 138.35
- 128.92
- 128.52
- 128.37
- 127.10
- 61.52
- 56.69
- 45.37
- 39.62
- 37.12
- 35.62
- 26.97
- 14.15

N
S
O
Chemical Shift (ppm)

4.2  4.1  4.0  3.9  3.8  3.7  3.6

0  0.1  0.2  0.3  0.4  0.5  0.6  0.7  0.8  0.9  1.0

1.15  5.82  2.00  4.17  4.15  4.14  4.12

3.67  3.66  3.61  3.60  3.60  3.60  3.58

N

H

OO

O

O

O
Chemical Shift (ppm)
### Table S2. Conditions for HPLC.

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<th>mobile phase</th>
<th>column temp. (°C)</th>
<th>flow rate (ml/min)</th>
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<tr>
<td>Table 2, all entries</td>
<td>Waters Acquity UPLC with PDA Detector and SQD MS Detector</td>
<td>Agilent ZORBAX RRHD Stablebond SB-C18; Column Length: 100 mm; Int. Diameter: 3.0 mm; Particle Size: 1.8 micron</td>
<td>A: Water/HCOOH 0.1% B: Acetonitrile gradient: 50-95% B in 5 min, then 95-50% B in 3 min</td>
<td>60</td>
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<tr>
<td>Table 3, entry 1</td>
<td>Waters Acquity UPC²/QDa with PDA Detector</td>
<td>Daicel SFC CHIRALPAK® IE; Column Length: 100 mm; Int. Diameter: 3.0 mm; Particle Size: 3 micron</td>
<td>A: CO₂ (1800 psi) B: MeOH; gradient: 0-5% B in 1.8 min</td>
<td>40</td>
<td>2.0</td>
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<tr>
<td>Table 3, entry 2</td>
<td>Waters Acquity UPC²/QDa with PDA Detector</td>
<td>Daicel SFC CHIRALPAK® IB; Column Length: 100 mm; Int. Diameter: 3.0 mm; Particle Size: 3 micron</td>
<td>A: CO₂ (1800 psi) B: EtOH; gradient: 0-5% B in 4.8 min</td>
<td>40</td>
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5.2. Traces for Table 2.

Table 2, entry 1, crude:

Table 2, entry 2, crude:
Table 2, entry 3, crude:

Table 2, entry 4, crude:
Table 2, entry 5, crude:
5.3. Traces for Table 3.

Table 3, entry 1, crude:

Table 3, entry 2, crude:
6. **X-ray Structure of 13a**

Diffraction-quality crystals of 13a were grown from t-BuOMe and pentane. X-ray data were collected on an Oxford Diffraction Xcalibur PX Ultra diffractometer using CuKα radiation. The structure was solved by full-matrix least squares refinement using CRYSTALS. Empirical formula: C₁₉H₂₅NO₆; formula weight: 363.41; T=100.0(2) K; crystal system: monoclinic; space group: P2(1)/n; Z = 4; cell parameters: a = 8.8078(5) Å, b= 8.1927(4) Å, c= 25.9170(13) Å, beta= 93.874(6)°; V = 1865.90(17) Å³ ; R1=0.1070; wR2=0.1726; max shift/e.s.d. = 0.00014. Crystallographic data for 13a have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-1528523 (http://www.ccdc.cam.ac.uk/data_request).

**Figure S1.** X-ray structure of 13a. This structure has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-1528523.
Bond precision: \( C-C = 0.0084 \, \text{A} \) \quad \text{Wavelength}=1.54184

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<td>( b = 8.1927(4) )</td>
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<td>9.9, 28</td>
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<td>( Npar )</td>
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</table>
7. Computational Methods

All calculations have been performed with Gaussian 03 package. The density functional theory (DFT) method was employed using M06-2X hybrid functional. The structures were optimized in gas phase using 6-311G** basis set. All stationary points were characterized by vibrational analysis, and were confirmed to be part of the intrinsic reaction coordinate (IRC) of the reported pathways. Relative energies are corrected for enthalpy and entropy factors.

Figure S1. Energy profiles (M06-2X/6-311G**, kcal/mol) of aziridine formation for the S,S-pathway (blue), the S,R-pathway (red) and the interconversion between the pro-S and the pro-R conformer reactants (green). The dotted lines are only schematic.
