Supporting Information

Sulfur-Switch Ugi-Reaction For Macrocyclic Disulfide-Bridged Peptidomimetics

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**General Information**

All reactions involving air-sensitive reagents were carried out with magnetic stirring and oven-dried glassware with rubber septa under argon, unless otherwise stated. All commercially available chemicals and reagent grade solvents were used directly without further purification, unless otherwise specified. Reactions were monitored by thin-layer chromatography (TLC) on Merck Silica Plates using UV-light (254 nm) detection or visualizing agents (e.g. iodine, KMnO₄ stain). Flash chromatography was conducted on a silica gel (230-400 mesh) using a Teledyne ISCO CombiFlash® Rf or Grace Reveleiris X2. NMR spectra were recorded at room temperature using a Bruker Avance 500 spectrometer (¹H NMR at 500 and ¹³C NMR at 126 MHz) with tetramethylsilane (TMS) as an internal standard. Mass spectra were measured on a Waters Investigator Supercritical Fluid Chromatograph with a 3100 MS Detector (ESI) using a solvent system of methanol and CO₂ on a Viridis silica gel column (4.6 × 250 mm, 5 μm particle size) or Ethyl pyridine column and reported as (m/z). The regioisomers (5a, 5b and 5c) were separated using Agilent 1200 series RP-HPLC system. Separation was carried out on a Zorbax C18 column at a flow rate of 5mL/min with a isocratic 42% Acetonitrile in Water. The eluent was detected on 254 nm. MS/MS was carried out on a 4000QTRAP tandem mass spectrometer.
1. Methyl S-trityl-L-cysteinate

To a stirred solution of S-trityl-L-cysteine (1.0 g, 2.76 mmol) in 50 mL of methanol at 0 °C was added thionyl chloride (1.50 mL, 0.206 mmol) in a drop wise fashion. The solution was allowed to warm up to room temperature and then refluxed at 80 °C for 5 h. The solvent was removed under reduced pressure and the crude product was extracted with ethyl acetate and washed with saturated sodium bicarbonate for several times. The organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated to give ester as pale yellow gum.

yield: 85% (0.865 g)

yellow gum

R_{f} 0.41 (PE/EtOAc, 1:1)

[α]_{D}^{20} = +30.4 (C1, CHCl_{3})

^{1}H NMR (500 MHz, CDCl_{3}) \delta 7.47 – 7.14 (m, 15H), 3.62 (s, 3H), 3.16–3.21 (m, 1H), 2.58 (dd, J = 12.4, 4.9 Hz, 1H), 2.47 (dd, J = 12.5, 7.7 Hz, 1H).

^{13}C NMR (126 MHz, CDCl_{3}) \delta 174.1, 144.4, 129.7, 129.5, 128.0, 127.9, 127.7, 126.8, 126.7, 66.8, 53.7, 52.1, 36.8.

MS (ESI) m/z calculated for C_{23}H_{23}NO_{2}S [M+Na]^{+} : 400.13; found [M+Na]^{+}: 400.10.

2. Methyl N-formyl-S-trityl-L-cysteinate
Amine 2 (1.0 g, 2.65 mmol) was dissolved in methyl formate (10 mL, solvent) and the solution was allowed to reflux at 60 °C until TLC showed complete consumption of the starting material (usually 24 h). The solvent was evaporated and the product was purified through flash column chromatography (0 to 80% EtOAc in PE for 20 min) to yield formyl ester 3 as white solid.

yield: 95% (1.03 g)
white solid, mp: 132–133 °C
R_f 0.50 (PE/EtOAc, 1:1)
[α]_D^20 = +18.8 (C1, CHCl_3).

^1H NMR (500 MHz, CDCl_3) δ 7.95 (d, J = 1.3 Hz, 1H), 7.50 – 7.11 (m, 16H), 6.14 (d, J = 8.1 Hz, 1H), 4.64 (dt, J = 8.2, 5.2 Hz, 1H), 3.68 (s, 3H), 2.77 (dd, J = 12.7, 5.8 Hz, 1H), 2.69 (dd, J = 12.9, 6.5 Hz, 1H).

^13C NMR (126 MHz, CDCl_3) δ 170.3, 160.4, 144.1, 129.4, 128.0, 128.0, 126.9, 126.8, 77.3, 77.1, 76.8, 67.0, 52.6, 49.7, 33.5.

MS (ESI) m/z calculated for C_{24}H_{23}NO_3S [M+Na]^+ : 428.12; found [M+Na]^+ : 428.20.

3. Methyl (R)-2-isocyano-3-(tritylthio)propanoate

To a solution of N-formyl Cys(Trt)--methyl ester 3 (30.0 g, 74.0 mmol) in CH_2Cl_2 (150.0 mL) at –78 °C, N-methylmorpholine (2.0 eq. 16.5 mL) was added. After 5 mins triphosgene (7.6 g, 0.35 eq.) in CH_2Cl_2 (50.0 mL) was added drop wise and the reaction mixture was stirred for 3h at –78 °C (TLC analysis). Saturated NaHCO_3 solution (10 mL) was added at same temperature
and allowed to warm to room temperature. The reaction mixture was extracted with CH₂Cl₂, the organic extracts were separated, dried over anhydrous Na₂SO₄, filtered, and concentrated. The solution was diluted with diethyl ether (10 mL) and stored at −15 °C for 5 h which resulted in pure solid of isocyanide 4 which was collected by filtration.

yield = 85% (24.3 g)

white solid, mp: 96–97 °C

Rf 0.42 (EtOAc/PE, 10:90)

[α]D²⁰ = +59.2 (C1, CHCl₃)

¹H NMR (500 MHz, CDCl₃) δ 7.57 – 7.06 (m, 16H), 3.70 (s, 3H), 3.34 (ddd, J = 7.7, 5.8, 1.6 Hz, 1H), 2.89 – 2.63 (m, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 165.6, 160.9, 143.9, 129.4, 129.2, 128.2, 128.0, 128.0, 127.9, 127.1, 77.3, 77.1, 76.8, 67.5, 55.3, 53.4, 34.2.

MS (ESI) m/z calculated for C₂₄H₂₁NO₂S [M+Na]+: 411.12; found [M+Na]+: 410.34.

4. Methyl S–trityl–R–cysteinate

To a stirred solution of S–trityl–R–cysteine 1b (1.0 g, 2.76 mmol) in 50 mL of methanol at 0 °C thionyl chloride (1.50 mL, 0.206 mmol) was added in a drop wise fashion. The solution was allowed to warm up to room temperature and then refluxed at 80 °C for 5 h. The solvent was removed under reduced pressure and the crude product was extracted with ethyl acetate and washed with saturated sodium bicarbonate for several times. The organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated to give ester 2b as pale yellow gum.
yield: 80% (0.830 g)
yellow gum
\[ R_f 0.40 \text{ (PE/EtOAc, 1:1)} \]
\[ [\alpha]^20_D = -102.4 \text{ (C1, CHCl}_3) \]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.50 – 7.39 (m, 6H), 7.32 (dd, $J = 8.5, 6.9$ Hz, 6H), 7.29 – 7.18 (m, 3H), 3.69 (s, 3H), 3.24 (dd, $J = 7.9, 4.8$ Hz, 1H), 2.63 (dd, $J = 12.5, 4.7$ Hz, 1H), 2.51 (dd, $J = 12.5$, 7.8 Hz, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 174.2, 144.5, 130.1, 130.1, 129.6, 129.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.1, 126.8, 77.4, 77.1, 76.8, 66.9, 53.8, 52.2, 36.9.

MS (ESI) m/z calculated for $\text{C}_{23}\text{H}_{23}\text{NO}_2\text{S}$ [M+Na]$^+$: 400.13; found [M+Na]$^+$: 400.04.

5. **Methyl N-formyl-S-trityl-R-cysteinate**

Amine 2b (1.0 g, 2.65 mmol) was dissolved in methyl formate (10 mL, solvent) and the assembly was allowed to reflux at 60 °C until TLC showed complete consumption of starting material (usually 24 h). The solvent was evaporated and the product was purified through column chromatography (0 to 80% EtOAc in PE) to yield formyl ester 3b as white solid.

yield: 78% (0.837 mg)
white solid, mp: 135–137 °C
\[ R_f 0.52 \text{ (PE/EtOAc, 1:1)} \]
\[ [\alpha]^20_D = -18.4 \text{ (C1, CHCl}_3) \]
1H NMR (500 MHz, CDCl₃) δ 8.01 (s, 1H), 7.52 – 7.43 (m, 6H), 7.29 (dt, J = 33.1, 7.5 Hz, 10H), 6.24 (t, J = 12.6 Hz, 1H), 4.69 (dt, J = 8.1, 5.2 Hz, 1H), 3.79 – 3.65 (m, 3H), 2.82 (dd, J = 12.7, 5.8 Hz, 1H), 2.69 (dd, J = 12.7, 4.7 Hz, 1H).

13C NMR (126 MHz, CDCl₃) δ 170.5, 160.6, 144.3, 129.6, 129.5, 128.2, 128.1, 127.1, 127.0, 52.8, 49.8, 33.7.

MS (ESI) m/z calculated for C₂₄H₂₃NO₅S [M+Na]+: 428.12; found [M+Na]+: 428.30.

6. Methyl (S)-2-isocyano-3-(tritylthio)propanoate

\[
\begin{align*}
\text{O} & \quad \text{Trt} \\
\text{N} & \quad \text{S} \\
\text{COOMe} & \quad \text{Triphosgene (0.35 eq.)} \\
\text{NMM (2.0 eq.)} & \quad \text{CH₂Cl₂, -78 °C} \\
\text{Trt} & \quad \text{S} \\
\text{CN} & \quad \text{COOMe}
\end{align*}
\]

To a solution of N-formyl Cys(Trt)-methyl ester 3b (2.0 g, 5.0 mmol) in CH₂Cl₂ (15.0 mL) was cooled to −78 °C. N-methylmorpholine (2.0 eq. 1.1 mL) was added. After 5 mins triphosgene (0.518 mg, 0.35 eq.) in CH₂Cl₂ (5.0 mL) was added drop wise and the reaction mixture was stirred for 3h at −78 °C (TLC analysis). Saturated NaHCO₃ solution (5 mL) was added at same temperature and allowed to warm to room temperature. The reaction mixture was extracted with CH₂Cl₂, the organic extracts were separated, dried over anhydrous Na₂SO₄, filtered, and concentrated. The solution was diluted with diethyl ether (10 mL) and stored at −15 °C for 5 h resulted in pure solid of isocyanide 4b which was collected by filtration.

yield = 85% (24.3 g)
white solid, mp: 101 –103 °C

R_f 0.42 (EtOAc/ PE, 10:90)

[α]_D^20 = -29.4 (C1, CHCl₃).

1H NMR (500 MHz, CDCl₃) δ 7.56 – 7.49 (m, 6H), 7.37 (dd, J = 8.5, 6.9 Hz, 6H), 7.35 – 7.26 (m, 3H), 3.76 (s, 3H), 3.43 (dd, J = 7.9, 5.8 Hz, 1H), 2.91 – 2.80 (m, 2H).
13C NMR (126 MHz, CDCl3) δ 165.7, 161.1, 144.0, 130.7, 129.5, 128.3, 128.0, 128.0, 127.7, 127.3, 127.2, 127.1, 67.6, 55.4, 53.5, 34.3.

MS (ESI) m/z calculated for C24H21NO2S [M+Na]+: 411.12; found [M+Na]+: 410.11.

7. 2-(Tritylsulfanyl)ethanamine

A solution of cysteamine hydrochloride (1.04 g, 9.17 mmol) and triphenylmethanol (2.18 g, 8.37 mmol) in TFA (5 mL) was stirred at room temperature for 1 h. After co-evaporation with acetonitrile the residue was dissolved in ethyl acetate and washed with NaOH (aq) 1 M, water and brine. The organic layer was dried over Na2SO4, filtered and the solvent was evaporated under reduced pressure to yield 2-(tritylsulfanyl)ethanamine which was used without further purification.

yield: 95% (5.9 g)
white solid, Mp: 144-146 °C
Rf 0.25 (MeOH/ CH2Cl2, 5:95)

1H NMR (500 MHz, MeOH-d4) δ 7.54 – 7.36 (m, 7H), 7.36 – 7.23 (m, 8H), 2.56 – 2.46 (m, 4H);

13C NMR (126 MHz, MeOH-d4) δ 144.5, 129.3, 127.7, 126.6, 67.0, 38.9, 30.8.

MS (ESI) m/z calculated for C21H21NS [M+Na]+: 342,12; found: 342,15.

8. Trityl thioacetic acid

To a mixture of mercaptoacetic acid (3.48 mL, 50.0 mmol) and triphenylmethanol (13.0 g, 50.0 mmol) in 50 chloroform was added trifluoroacetic acid (10 mL) in 5 min. After stirring at
room temperature for 1 h, the volatiles were removed in vacuo. The crude product was purified by recrystallization (CH$_2$Cl$_2$/Hexane = 1/2) to give tritylsulfanylacetic acid.

yield: 98% (16.37 g)

white solid, Mp: 159-161 °C

R$_f$ 0.38 (EtOAc/PE/AcOH, 30:70:1.0)

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.56 – 7.15 (m, 15H), 3.06 (s, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 175.5, 143.9, 129.5, 128.1, 127.9, 127.0, 67.3, 34.5.

MS (ESI) m/z calculated for C$_{21}$H$_{18}$O$_2$S [M+Na]$^+$: 357.09; found: 357.21.

9. N-methoxy-N-methyl-2-(tritylthio)acetamide

To a solution of acid (20.0 mmol), PyBOP (1.1 equiv.) and TEA (2.5 equiv.) in CH$_2$Cl$_2$ (50 mL) was added N,O-dimethylhydroxylamine hydrochloride (1.2 equiv.) and the solution was allowed to stir at RT overnight. The solution was then diluted with excess CH$_2$Cl$_2$ and washed consecutively with a 1 M HCl solution (3 x 10 mL), saturated aq. NaHCO$_3$ (3 x 10 mL), and water (1 x 10 mL). The organic phase was dried over MgSO$_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (0 to 100% EtOAc in PE) on silica gel to afford the desired Weinreb amide.

yield: 95% (7.16 g)

white solid, Mp: 125-127 °C

R$_f$ 0.32 (EtOAc/PE, 30:70)

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.52 – 7.44 (m, 7H), 7.32-7.31 (m, 8H), 3.49 (s, 3H), 3.14 (s, 3H), 3.11 (s, 2H).
13C NMR (126 MHz, CDCl3) δ 172.0, 144.3, 129.6, 128.0, 127.8, 126.8, 77.3, 77.0, 76.8, 66.9, 61.4, 33.7.

MS (ESI) m/z calculated for C23H23NO2S [M+Na]+: 400.13; found: 400.25.

10.3-(Tritylthio)propanoic acid

To a mixture of 2-mercaptopropanoic acid (4.35 mL, 50.0 mmol) and triphenylmethanol (13.0 g, 50.0 mmol) in 50 chloroform was added trifluoroacetic acid (10 mL) in 5 min. After stirring at room temperature for 1 h, the volatiles were removed in vacuo. The crude product was purified by recrystallization (CH2Cl2/Hexane = 1/2) to give 3-(tritylthio)propanoic acid.

yield: 98% (17.02 g)

white solid, Mp: 196-198 °C

Rf 0.52 (EtOAc/PE/AcOH, 30:70:1.0)

1H NMR (500 MHz, CDCl3) δ 7.50 – 7.42 (m, 6H), 7.39 – 7.29 (m, 6H), 7.29 – 7.21 (m, 4H), 2.49 (t, J = 7.3 Hz, 2H), 2.27 (d, J = 14.6 Hz, 2H).

13C NMR (126 MHz, CDCl3) δ 174.5, 144.5, 129.6, 128.0, 126.7, 60.5, 33.1, 26.5.

MS (ESI) m/z calculated for C22H20O2S [M+Na]+: 371.10; found: 371.26.

11. N-methoxy-N-methyl-3-(tritylthio)propanamide

To a solution of tritylsulfanylacetic acid (10.44g, 30 mmol), PyBOP (17.17 g, 33.0 mmol) and TEA (10.42 mL, 75.0 mmol) in CH2Cl2 (80 mL) was added N,O-dimethylhydroxylamine hydrochloride (3.51 g, 36.0 mmol) and the solution was allowed to stir at RT overnight.
solution was then diluted with excess CH₂Cl₂ (50 mL) and washed consecutively with a 1 M HCl solution (3 x 10 mL), saturated aq. NaHCO₃ (3 x 10 mL), and water (1 x 10 mL). The organic phase was dried over MgSO₄, filtered and concentrated in vacuo. The residue was purified by flash chromatography (0 to 80% EtOAc in PE) on silica gel to afford the desired Weinreb amide.

yield: 95% (11.14 g)

white solid, Mp: 145-147 °C

Rf 0.52 (EtOAc/ PE, 30:70)

1H NMR (500 MHz, CDCl3) δ 7.49 – 7.41 (m, 7H), 7.36 – 7.25 (m, 8H), 3.59 (s, 3H), 3.14 (s, 3H), 2.54 (t, J = 7.4 Hz, 2H), 2.41 (d, J = 8.5 Hz, 2H).

13C NMR (126 MHz, CDCl₃) δ 177.6, 144.8, 129.6, 127.9, 126.6, 61.2, 60.6, 32.1, 31.4, 26.7.

MS (ESI) m/z calculated for C₂₄H₂₅NO₂S [M+Na]⁺: 414.15; found: 414.23.

12. 2-(Tritylthio)acetaldehyde

A stirred solution of Weinreb amide 7 (10.0 mmol) in dry THF (50 mL) was cooled to 0 °C. Lithium aluminium hydride (LAH, 11.0 mmol) was added in portions and after 30 minutes 0.2 M KHSO₄ (30 mL) was added. The organic compounds were extracted with diethyl ether (3x 30 mL). The combined organic phases were washed with 1 M HCl (3x 10 mL), brine (3x 10 mL) and dried (MgSO₄). The solvent was evaporated under reduced pressure and the crude colorless oil was immediately used for Ugi reaction (analysis was done only with TLC analysis).

yield: 88% (2.8 g)

pale yellow gum
R_f 0.25 (EtOAc/ PE, 10:90)

**13.3-(Tritylthio)propanal**

\[
\text{TrtSCH(OH)}_2 \xrightarrow{\text{LAH, Ether, } 0 \, ^\circ \text{C}, 3 \text{h}} \text{TrtSC} = \text{OH}
\]

A stirred solution of Weinreb amide 9 (10.0 mmol) in dry THF (50 mL) was cooled to 0 °C. Lithium aluminium hydride (11.0 mmol) was added in portions and after 30 minutes 0.2 M KHSO_4 (30 mL) was added. The organic compounds were extracted with diethyl ether (3x 30 mL). The combined organic phases were washed with 1 M HCl (3x 10 mL), brine (3x 10 mL) and dried (MgSO4). The solvent was evaporated under reduced pressure and the crude colorless oil was immediately used for Ugi reaction (analysis was done only with TLC analysis).

yield: 95% (3.15 g)
pale yellow gum

R_f 0.31 (EtOAc/ PE, 10:90)

**14. N-(2-(tritylthio)ethyl)formamide**

\[
\text{H}_2\text{N} \xrightarrow{\text{Ethylformate reflux, } 48 \text{ h}} \xrightarrow{\text{STrt}} \text{O} \text{N} \xrightarrow{\text{STrt}}
\]

Amine (30.0 g, 93.92 mmol) was dissolved in methyl formate (150 mL) and CH_2Cl_2 (50 mL) the assembly was allowed to reflux at 60 °C until TLC showed complete consumption of starting material (usually 48 h). The solvent was evaporated and the crude product was dissolved in CH_2Cl_2 (200 mL) and passed through silica pad. The solvent was evaporated under reduced pressure followed by recrystallized in diethyl ether to yield formyl ester as white solid.
yield: 90% (29.34 g)
white solid, Mp: 131-133 °C
Rf 0.44 (EtOAc/ PE, 50:50)

1H NMR (500 MHz, CDCl₃) δ 8.02 (d, J = 1.5 Hz, 1H), 7.52 – 7.43 (m, 11H), 7.32-7.20(m, 6H), 5.51 (s, 1H), 3.13 (q, J = 6.2 Hz, 2H), 2.45 (dt, J = 30.0, 6.6 Hz, 2H).

13C NMR (126 MHz, CDCl₃) δ 160.1, 143.8, 128.8, 127.3, 126.2, 66.3, 39.9, 36.0, 32.7, 31.1.
MS (ESI) m/z calculated for C₂₂H₂₁NOS [M+Na]⁺: 370.12; found: 370.26.

15. 2-Isocyanoethyl)(trityl)sulfane

To a solution of N-(2-(tritylthio)ethyl)formamide (30.0 g, 80.1 mmol) in THF:CH₂Cl₂ (50:150 mL) was cooled to -20 °C. N-methylmorpholine (17.62 mL, 160.2 mmol) was added. After 5 mins triphosgene (9.49 g, 32.08 mmol) was added portion wise over 10 min. The reaction mixture was stirred for 6h at -20 °C (TLC analysis). Saturated NaHCO₃ solution (500 mL) was added at 0 °C and allowed to cool to room temperature and stirred for 30 min. The reaction mixture was extracted with CH₂Cl₂ (100 X 2), the organic extracts were separated, dried over anhydrous MgSO₄, filtered, and concentrated. The crude isocyanide was purified through flash column chromatography 20% CH₂Cl₂ in hexane.

yield: 75% (19.72 g)
pale yellow solid, Mp: 105-107 °C
Rf 0.55 (EtOAc/ PE, 10:90)

1H NMR (500 MHz, CDCl₃) δ 7.47 (dd, J = 7.7, 1.7 Hz, 7H), 7.35 (d, J = 7.3 Hz, 5H), 7.33 – 7.30 (m, 2H), 7.30 – 7.21 (m, 4H), 2.93 (t, J = 7.3 Hz, 2H), 2.60 (t, J = 7.2 Hz, 2H).
$^{13}$C NMR (126 MHz, CDCl$_3$) δ 156.8, 144.2, 129.7, 129.5, 128.1, 127.9, 127.3, 127.0, 67.3, 40.6, 31.1.

MS (ESI) m/z calculated for C$_{22}$H$_{19}$NS [M+Na]$^+$: 352.11; found: 352.24.
Optimization of Ugi Reaction

![Chemical diagram]

| Entry | Solvent (conc)                  | Time (h) | Temp (°C) | Yield (%)<sup>ab</sup> |
|-------|---------------------------------|----------|-----------|------------------------|
| a     | MeOH (1 M)                      | 48       | 25        | 5                      |
| b     | MeOH (0.2 M)                    | 24       | 40        | 20                     |
| b     | TFE (0.2 M)                     | 24       | 40        | 14                     |
| c     | HFIP (0.2 M)                    | 24       | 40        | 12                     |
| d     | THF (0.2 M)                     | 48       | 40        | 18                     |
| e     | DMF (0.2 M)                     | 48       | 40        | 20                     |
| f     | CH<sub>2</sub>Cl<sub>2</sub> (0.2 M) | 48       | 25        | 15                     |
| F     | MeOH:THF:DMF (0.2 M, 1:1:0.1)   | 24       | 25        | 52                     |
| G     | TFE:THF (0.2 M, 5:1)            | 24       | 25        | 50                     |

<sup>a</sup>All reactions were carried out in 1mmol scale; <sup>b</sup>Isolated yields after column purification.
**Synthetic procedure for Ugi reaction**

**Procedure A**: The amine (1.0 eq.), aldehyde (1.0 eq.), acid (1.0 eq.) and isocyanide (387.0 mg, 1.0 mmol.) were dissolved in MeOH, THF and few drops of DMF (0.1 M, 10 mL, 7:2.5:0.5). The resulting mixture was stirred at room temperature for 24-48 hours. The solvent was removed under reduced pressure and the residue was purified using flash column chromatography (ethyl acetate: petroleum ether from 0 to 60).

**Procedure B**: The amine (1.0 equiv), acid (1.0 eq.) and isocyanide (387.0 mg, 1.0 mmol.) in a mixture of TFE and THF (0.1 M, 10 mL, 8:2 mL) was added aldehyde (1.0 eq.). The resulting mixture was stirred at room temperature for 24-48 hours. The solvent was removed under reduced pressure and the residue was purified using flash column chromatography (ethyl acetate: petroleum ether from 0 to 60 in 20 min).

*Note*: Diastereomeric ratios were measured according to methyl group singlet of the C-terminal ester.
(5R,11R)-Methyl-7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3a

Procedure A

yield: 52% (0.56 g)
pale yellow solid, Mp: 85-87 °C

Rf 0.31 (EtOAc/ PE, 40:60)

dr ratio: 3:0

1H NMR (500 MHz, CDCl₃, mixture of rotamers) δ 7.80 (dd, J = 7.6, 4.7 Hz, 3H), 7.66 – 7.53 (m, 3H), 7.51 – 7.07 (m, 62H), 6.81 (d, J = 5.1 Hz, 0.5H), 6.73 (d, J = 8.1 Hz, 1H), 5.38 (dd, J = 11.8, 7.7 Hz, 2H), 4.53 (q, J = 7.3 Hz, 1H), 4.44 (ddt, J = 9.7, 6.6, 2.6 Hz, 1H), 4.39 – 4.35 (m, 1H), 4.35 – 4.29 (m, 3H), 4.26 (dt, J = 13.5, 4.2 Hz, 2H), 3.97 (d, J = 5.5 Hz, 1H), 3.94 – 3.77 (m, 5H), 3.67 (s, 2H), 3.65 (s, 3H), 2.74 – 2.69 (m, 0.5H), 2.68 – 2.63 (m, 5H), 2.61 (d, J = 4.7 Hz, 1H).

13C NMR (126 MHz, CDCl₃, mixture of rotamers) δ 172.2, 171.7, 171.2, 170.4, 167.8, 167.2, 160.3, 156.1, 155.9, 144.3, 144.2, 143.9, 143.7, 141.2, 137.4, 135.9, 135.0, 129.7, 129.6, 129.5, 129.2, 129.0, 128.7, 128.5, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.2, 127.1, 127.0, 126.9, 125.3, 125.2, 120.0, 119.9, 67.4, 67.3, 67.1, 67.0, 59.4, 56.1, 52.9, 52.6, 52.5, 51.8, 51.7, 51.2, 50.4, 49.6, 49.3, 47.1, 47.0, 33.1, 32.0, 23.9, 22.7.

HRMS (ESI) calculated for C₆₉H₆₁N₃O₆S₂ [M+Na]⁺: 1114.3899; found: 1114.3895.

(5R,11R)-Methyl 7-(3,4-dichlorobenzyl)-1-(9H-fluoren-9-yl)-8-isobutyl-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3b

Procedure A

yield: 61% (0.74 g)
pale yellow solid, Mp: 72-74 °C.
Rf 0.35 (EtOAc/ PE, 20:80)

dr ratio: 3:2.8

$^1$H NMR (500 MHz, CDCl$_3$, mixture of diastereomers and rotamers) $^1$H NMR (500 MHz, CDCl$_3$)

$^\delta$ 7.81 (dt, $J = 10.7$, 7.7 Hz, 7H), 7.68 – 7.55 (m, 8H), 7.55 – 7.15 (m, 150H), 7.12 – 7.03 (m, 3H), 7.03 – 6.98 (m, 2H), 5.31 (dt, $J = 13.7$, 5.8 Hz, 3H), 4.98 (tt, $J = 9.5$, 5.8 Hz, 2H), 4.91 – 4.77 (m, 2H), 4.60 – 4.54 (m, 2H), 4.54 – 4.48 (m, 2H), 4.48 – 4.40 (m, 3H), 4.37 (ddd, $J = 13.5$, 8.5, 4.9 Hz, 7H), 4.34 – 4.31 (m, 1H), 4.31 – 4.25 (m, 3H), 4.23 (td, $J = 8.0$, 2.8 Hz, 3H), 4.20 – 4.13 (m, 2H), 4.08 (t, $J = 15.6$ Hz, 2H), 3.64 (s, 1H), 3.62 (s, 1H), 3.55 (s, 3H), 3.54 (s, 3H), 2.79 – 2.72 (m, 1H), 2.70 (dd, $J = 10.6$, 4.4 Hz, 4H), 2.65 (dd, $J = 12.3$, 5.4 Hz, 2H), 2.62 – 2.59 (m, 2H), 2.58 – 2.54 (m, 3H), 2.54 – 2.50 (m, 1H), 1.64 – 1.51 (m, 2H), 1.48 – 1.29 (m, 5H), 0.97 (d, $J = 6.8$ Hz, 4H), 0.94 (d, $J = 6.8$ Hz, 7H), 0.92 (d, $J = 6.6$ Hz, 2H), 0.87 (d, $J = 6.6$ Hz, 4H), 0.85 (d, $J = 6.6$ Hz, 2H), 0.81 (d, $J = 6.3$ Hz, 2H), 0.77 (d, $J = 6.6$ Hz, 4H).

$^{13}$C NMR (126 MHz, CDCl$_3$, mixture of diastereomers and rotamers) $\delta$ 172.9, 172.8, 171.5, 170.7, 170.5, 170.4, 170.2, 170.1, 169.9, 169.7, 168.7, 168.1, 156.8, 156.7, 155.4, 155.3, 155.2, 144.5, 144.3, 144.2, 143.9, 143.8, 143.6, 143.5, 141.3, 138.5, 138.3, 137.1, 132.9, 132.2, 132.1, 131.6, 130.7, 130.6, 130.5, 130.2, 130.1, 129.9, 129.7, 129.6, 129.5, 129.3, 128.8, 128.5, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.2, 127.1, 127.0, 126.9, 126.8, 126.3, 126.1, 126.0, 125.3, 125.2, 120.1, 120.0, 68.0, 67.8, 67.6, 67.5, 67.4, 67.4, 67.2, 67.1, 67.0, 66.7, 59.1, 58.5, 56.1, 55.5, 52.6, 52.5, 52.4, 52.1, 51.9, 51.5, 51.4, 51.3, 51.0, 49.5, 49.3, 47.4, 47.0, 46.8, 46.4, 45.5, 43.0, 39.3, 39.2, 37.9, 36.7, 36.2, 34.6, 34.2, 34.0, 33.9, 33.5, 33.4, 25.1, 25.0, 24.9, 23.3, 23.0, 22.7, 22.5, 22.3, 22.2.

HRMS (ESI) calculated for $C_{73}H_{67}Cl_2N_3O_6S_2$ [M+H]$^+$: 1216.3881; found: 1216.3882.
(12R)-Methyl 8-(((S)-2-(((9H-fluoren-9-y1)methoxy)carbonyl)amino)-3-(tritylthio)propanoyl)-9-isopropyl-2,2-dimethyl-4,10-dioxo-12-((tritylthio)methyl)-3-oxa-5,8,11-triazatridecan-13-oate, 3c

Procedure A

yield: 63% (0.74 g)
yellow yellow solid, Mp: 94-96 °C

Rf 0.40 (EtOAc/ PE, 30:70)
dr ratio: 3:1.7

1H NMR (500 MHz, CDCl$_3$, mixture of diastereomers and rotamers) δ 7.85 – 7.75 (m, 5H), 7.73 – 7.61 (m, 4H), 7.58 – 7.05 (m, 107H), 5.65 – 5.47 (m, 2H), 5.45 – 5.39 (m, 1H), 5.31 (br, s, 0.5H), 5.30 – 5.26 (m, 1H), 5.25 (br, s, 1H), 4.78 – 4.50 (m, 3H), 4.50 – 4.36 (m, 4H), 4.33 (dd, J = 23.2, 5.1 Hz, 1H), 4.30 – 4.11 (m, 5H), 4.14 – 4.00 (m, 1H), 3.65 (s, 1H), 3.64 (s, 3H), 3.60 (s, 1H), 3.58 (s, 3H), 3.55 (d, J = 5.9 Hz, 1H), 3.51 – 3.17 (m, 8H), 3.16 – 2.74 (m, 10H), 2.68 – 2.42 (m, 2H), 2.42 – 2.26 (m, 1H), 1.52 (s, 9H), 1.49 (s, 3H), 1.46 (s, 9H), 1.43 (s, 3H), 1.03 (d, J = 11.7, 3H), 1.00 (d, J = 6.4 Hz, 3H), 0.88 (d, J = 6.3 Hz, 2H), 0.84 (d, J = 6.4 Hz, 1H), 0.76 – 0.72 (m, 6H).

13C NMR (126 MHz, CDCl$_3$, mixture of diastereomers and rotamers) δ 173.0, 172.6, 172.3, 172.1, 171.1, 170.8, 170.5, 170.1, 168.5, 168.4, 156.9, 156.8, 155.9, 155.8, 155.6, 155.5, 144.6, 144.5, 144.4, 144.3, 144.1, 144.0, 143.9, 143.9, 143.7, 143.5, 141.4, 141.3, 129.7, 129.6, 129.5, 128.1, 128.0, 127.9, 127.8, 127.7, 127.3, 127.2, 127.1, 127.0, 126.9, 126.7, 125.3, 125.2, 125.1, 120.1, 120.0, 79.3, 79.2, 78.9, 67.8, 67.4, 67.3, 67.1, 66.8, 66.4, 66.2, 52.5, 52.4, 52.1, 51.6, 51.3, 50.9, 49.4, 49.3, 47.2, 47.1, 47.0, 43.5, 40.3, 40.1, 39.8, 39.7, 39.5, 34.8, 34.5, 34.2, 34.1, 34.0, 33.7, 33.5, 33.2, 28.6, 28.5, 27.3, 27.2, 26.6, 26.4, 25.7, 20.0, 19.9, 19.7, 19.5, 19.2, 19.1, 18.9, 18.8.

HRMS (ESI) calculated for C$_{72}$H$_{74}$N$_4$O$_8$S$_2$ [M+H]$^+$: 1187.5099; found: 1187.5094.
(5R,11R)-Methyl 1-(9H-fluoren-9-yl)-8-isobutyl-3,6,9-trioxo-7-phenethyl-5,11-bis((tritylthio) methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3d

Procedure A

yield: 65% (0.75 g)
pale yellow solid, Mp: 94–96 °C
Rf 0.40 (EtOAc/ PE, 30:70)
dr ratio: 3:2

1H NMR (500 MHz, CDCl₃, mixture of diastereomers and rotamers) δ 7.81–7.53 (m, 9H) 7.51–7.13 (m, 106H), 6.72 (t, J = 15.3 Hz, 1H), 5.64 – 5.50 (m, 1H), 5.41 – 5.29 (m, 1H), 5.29 – 5.19 (m, 1H), 5.11 (d, J = 7.7 Hz, 1H), 4.80 – 4.62 (m, 4H), 4.49 – 4.39 (m, 1H), 4.34 (ddd, J = 9.8, 9.2, 3.7 Hz, 3H), 4.29 – 4.18 (m, 5H), 3.55 (s, 2H), 3.51 (s, 1H), 3.45 (s, 1H), 3.43 (s, 3H), 3.30 (d, J = 11.2 Hz, 1H), 3.24 – 3.10 (m, 3H), 2.84 – 2.76 (m, 2H), 2.69 – 2.47 (m, 3H), 2.13 – 2.02 (m, 9H), 1.93 (ddd, J = 18.1, 11.2, 4.7 Hz, 1H), 1.79 – 1.65 (m, 4H), 1.53 (td, J = 13.4, 6.8 Hz, 3H), 0.97 (dd, J = 5.8, 3.6 Hz, 4H), 0.97 – 0.95 (m, 6H), 0.94 (d, J = 8.7 Hz, 3H), 0.89 (d, J = 6.5 Hz, 3H).

13C NMR (126 MHz, CDCl₃, mixture of diastereomers and rotamers) δ 172.8, 172.1, 170.7, 170.6, 170.5, 170.4, 170.3, 170.2, 168.9, 168.6, 156.8, 156.7, 155.7, 155.6, 155.3, 144.4, 144.2, 144.1, 143.9, 143.8, 143.7, 143.6, 143.5, 141.3, 141.2, 139.4, 139.3, 137.9, 137.7, 137.6, 130.6, 129.6, 129.5, 129.4, 129.0, 128.9, 128.7, 128.4, 128.2, 128.1, 128.0, 127.8, 127.6, 127.2, 127.1, 127.0, 126.9, 126.8, 126.7, 126.2, 125.3, 125.2, 125.1, 120.0, 119.9, 67.7, 67.5, 67.4, 67.2, 67.1, 67.0, 66.9, 66.8, 58.5, 58.3, 54.4, 52.4, 52.3, 52.2, 52.1, 51.9, 51.7, 51.3, 51.2, 51.1, 50.9, 50.6, 49.3, 49.2, 47.1, 46.2, 46.0, 45.8, 38.8, 38.7, 37.4, 36.9, 36.8, 36.7, 36.4, 36.0, 35.0, 34.9, 34.7, 34.3, 34.0, 33.9, 33.6, 33.6, 33.3, 29.7, 25.0, 24.9, 24.8, 24.5, 23.2, 23.1, 22.6, 22.6, 22.5, 22.0.

HRMS (ESI) calculated for C₇₄H₇₁N₃O₆S₂ [M+Na]⁺: 1184.4682; found: 1184.4687.
(5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-propyl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3e

**Procedure A**

yield: 60% (0.62 g)

pale yellow solid, Mp: 115-117 °C

Rf 0.25 (EtOAc/ PE, 30:70)

dr ratio: 3:0

$^1$H NMR (500 MHz, CDCl$_3$, mixture of rotamers) $\delta$ 7.88 – 7.73 (m, 3H), 7.66 – 7.56 (m, 3H), 7.49 – 7.15 (m, 53H), 6.94 (d, $J$ = 8.1 Hz, 1H), 5.47 (d, $J$ = 21.2, 8.2 Hz, 1H), 5.30 (d, $J$ = 10.2 Hz, 0.26H), 4.53 (dd, $J$ = 14.0, 7.4 Hz, 1H), 4.44 – 4.36 (m, 2H), 4.36 – 4.25 (m, 3H), 4.21 (dd, $J$ = 14.5, 7.4 Hz, 1H), 4.18 – 4.10 (s, 0.28H), 4.03 (s, 2H), 3.62 (s, 1H), 3.54 (s, 3H), 3.27 – 3.13 (m, 1H), 3.13 – 3.02 (m, 1H), 2.77 – 2.56 (m, 6H), 1.58 (ddd, $J$ = 25.8, 12.8, 6.2 Hz, 1H), 1.54 – 1.44 (m, 1H), 0.99 – 0.89 (d, $J$ = 9.1 Hz, 1H), 0.85 (d, $J$ = 10.8 Hz, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$, mixture of rotamers) $\delta$ 171.5, 170.8, 170.5, 170.4, 168.4, 167.6, 156.4, 155.8, 144.4, 144.3, 144.0, 143.9, 143.7, 141.3, 129.6, 129.6, 129.5, 128.2, 128.1, 128.0, 127.8, 127.7, 127.2, 127.1, 127.0, 127.0, 126.9, 126.9, 125.3, 125.2, 120.0, 120.0, 77.0, 67.7, 67.5, 67.4, 67.2, 66.9, 52.5, 52.4, 51.9, 51.3, 50.8, 50.8, 50.5, 50.2, 49.2, 47.0, 34.4, 33.6, 33.2, 29.7, 23.9, 22.8, 22.0, 20.2, 14.2, 11.2, 11.1.

HRMS (ESI) calculated for C$_{65}$H$_{61}$N$_3$O$_6$S$_2$ [M+H]$^+$: 1044.4001; found: 1044.4001.

(5R,11R)-methyl 1-(9H-fluoren-9-yl)-8-isopropyl-7-methyl-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3f

**Procedure A**

yield: 40% (0.42 g)
pale yellow solid, Mp: 91-93 °C

Rf 0.42 (EtOAc/ PE, 30:70)

dr ratio: 3.8:2

^1^H NMR (500 MHz, CDCl$_3$, mixture of diastereomers and rotamers) δ 7.85 – 7.76 (m, 6H), 7.68 – 7.59 (m, 6H), 7.53 – 7.39 (m, 46H), 7.38 – 7.15 (m, 68H), 6.64 – 6.51 (m, 1H), 6.47 (d, J = 8.0 Hz, 1H), 4.59 (d, J = 11.0 Hz, 1H), 4.54 – 4.48 (m, 5H), 4.45 (dd, J = 10.5, 7.1 Hz, 1H), 4.42 – 4.35 (m, 4H), 4.35 – 4.19 (dd, J = 10.0, 6.9 Hz, 2H), 3.66 (s, 2H), 3.64 (s, 3H), 3.51 (s, 2H), 3.48 (s, 4H), = 12.4, 5.1 Hz, 1H), 2.81 (d, J = 2.6 Hz, 2H), 2.73 (d, J = 6.9 Hz, 2H), 2.72 – 2.68 (m, 2H), 2.67 – 2.62 (m, 4H), 2.45 – 2.33 (m, 1H), 2.31 – 2.17 (m, 2H), 1.05 – 0.94 (m, 9H), 0.85 – 0.75 (m, 6H), 0.70 (dd, J = 10.7, 6.9 Hz, 3H).

^1^C NMR (126 MHz, CDCl$_3$, mixture of diastereomers and rotamers) δ 172.2, 172.0, 171.3, 171.2, 170.6, 170.5, 170.3, 170.1, 169.5, 169.4, 169.2, 168.1, 156.9, 156.8, 155.7, 155.5, 144.6, 144.5, 144.4, 144.3, 144.0, 143.9, 143.7, 143.6, 143.4, 141.4, 141.3, 129.8, 129.7, 129.6, 129.5, 129.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.2, 127.1, 127.0, 126.9, 126.8, 125.3, 125.2, 125.1, 120.0, 67.7, 67.4, 67.3, 67.1, 67.0, 66.9, 66.2, 66.1, 62.3, 52.5, 52.4, 52.3, 52.0, 51.9, 51.8, 51.6, 51.0, 50.9, 50.7, 50.5, 49.1, 49.0, 47.2, 47.1, 47.0, 34.7, 34.5, 34.2, 34.1, 34.0, 33.7, 33.5, 33.4, 31.4, 30.9, 30.4, 30.1, 29.2, 29.1, 26.5, 26.4, 26.1, 25.9, 25.3, 25.1, 19.8, 19.7, 18.8, 18.7, 18.6, 18.3.

HRMS (ESI) calculated for C$_{66}$H$_{63}$N$_3$O$_6$S$_2$ [M+H]$^+$: 1058.4158; found: 1058.4157.

(5^R,11^R)-methyl 7-allyl-8-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3g

Procedure A

yield: 56% (0.63 g)
pale yellow solid, Mp: 80-82 °C
Rf 0.60 (EtOAc/ PE, 30:70)
dr ratio: 3:3

1H NMR (500 MHz, CDCl₃, mixture of diastereomers and rotamers) δ 7.59 – 7.55 (m, 15H), 7.54 – 7.39 (m, 15H), 7.38 – 7.11 (m, 94H), 6.15 (d, J = 5.4 Hz, 0.5H), 6.11(d, J = 4.4 Hz, 1.5H), 5.93 (d, J = 8.0 Hz, 1H), 5.81 – 5.76 (m,1.5H), 5.71 – 5.63 (m, 2H), 5.15 –5.10 (m, 1H), 5.09 – 4.97 (m, 3H), 4.92 (ddd, J = 39.0, 7.4, 1.5 Hz, 2H), 4.78 –4.77 (ddt, J = 16.2, 10.1, 6.0 Hz, 2H), 4.76 – 4.66 (m, 5H), 4.65 – 4.58b (dt, J = 8.0, 5.2 Hz, 1H), 4.57 – 4.55 (m, 4H), 4.52 – 4.43 (m, 1H), 4.20 – 4.15 (m 2H), 4.14 – 4.10 (m, 2H), 4.19 – 3.99 (m, 2H), 3.77 (s, 2H), 3.75 (s, 2H), 3.73 (s, 3H), 3.69 (s, 3H), 3.35 – 3.20 ((m, 8H), 3.18 – 3.11 (m, 5H), 3.09 – 2.96 (m, 6H).

13C NMR (126 MHz, CDCl₃, mixture of diastereomers and rotamers) δ 172.4, 172.1, 171.6, 171.4, 170.5, 168.8, 168.5, 157.4, 157.3, 156.3, 156.0, 144.8, 144.3, 141.0, 135.4, 132.8, 130.8, 130.7, 130.1, 129.6, 129.5, 128.8, 128.4, 128.0, 127.9, 126.0, 125.1, 122.7, 119.9, 119.2, 116.7, 70.6, 67.6, 63.1, 61.2, 57.3, 56.2, 55.5, 52.2, 51.3, 47.0, 41.9, 41.5, 40.6, 36.3, 35.7, 35.6, 35.05, 34.7, 33.2, 33.0, 28.4, 27.8, 26.8.

HRMS (ESI) calculated for C₇₂H₆₅N₆O₆S₂ [M+H]+: 1132.4330; found: 1132.4330.

(5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-trityl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3h

Procedure A

yield: 50% (0.62 g)
pale yellow solid, Mp: 110-112 °C
Rf 0.35 (EtOAc/ PE, 20:80)
dr ratio: 3:0
NMR (500 MHz, CDCl$_3$, mixture of rotamers) δ 7.79 (dt, $J = 7.6$, 3.6 Hz, 4H), 7.57 (t, $J = 7.5$ Hz, 4H), 7.49 – 7.34 (m, 17H), 7.31 – 7.19 (m, 46H), 5.43 (d, $J = 5.6$ Hz, 0.35H), 5.31(d, $J = 6.5$ Hz, 1H), 4.51 – 4.46 (m, 1H), 4.32 – 4.20 (m, 4H), 4.18 – 4.10 (m, 4H), 3.81 (s, 0.8H), 3.79 (s, 2H), 3.55 (s, 1H), 3.52 (s, 3H), 2.61 (dt, $J = 12.5$, 6.4 Hz, 3H), 2.30 – 2.15 (m, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$, mixture of rotamers) δ 169.71, 169.32, 167.82, 167.37, 152.46, 151.35, 145.06, 144.43, 143.67, 142.53, 141.27, 141.08, 129.69, 129.60, 129.45, 128.47, 127.99, 127.92, 127.85, 127.10, 126.69, 126.60, 126.48, 125.16, 124.93, 120.01, 70.73, 67.85, 57.01, 55.24, 53.02, 46.58, 32.35, 31.95, 30.90, 29.73, 29.39, 23.85, 22.72.

HRMS (ESI) calculated for C$_{81}$H$_{69}$N$_3$O$_6$S$_2$ [M+H$^+$]: 1244.5610; found: 1244.5617.

**(5R,14R)-methyl 10-benzyl-1-(9H-fluoren-9-yl)-11-isobutyl-3,6,9,12-tetraoxo-5,14-bis((tritylthio)methyl)-2-oxa-4,7,10,13-tetraazapentadecan-15-oate, 3i**

Procedure A

yield: 72% (0.86 g)
pale yellow solid, Mp: 70-72 °C

R$_f$ 0.22 (EtOAc/ PE, 30:70)
dr ratio: 3:2.7

$^1$H NMR (500 MHz, CDCl$_3$, mixture of diastereomers and rotamers) δ 7.78 – 7.12 (m, 135H) 6.81 – 6.66 (m, 6H), 6.60 (d, $J = 8.5$ Hz, 1H), 4.60 – 4.48 (m, 4H), 4.48 (d, $J = 7.1$ Hz, 2H), 4.43 – 4.40 (m, 4H), 4.28 (ddd, $J = 18.1$, 12.8, 9.2 Hz, 4H), 4.19 (dt, $J = 18.4$, 12.1 Hz, 2H), 4.18 – 4.15 (m, 2H), 3.91 – 3.78 (m, 8H), 3.67 (s, 2H), 3.66 (s, 3H), 3.64 (s, 3H), 3.61 (s, 2H), 2.70 – 2.51 (m, 7H), 1.91 – 1.79 (m, 4H), 1.35 – 1.20 (m, 4H), 1.01 – 0.96 (m, 5H), 0.95 – 0.90 (m, 4H), 0.89 – 0.85 (m, 4H), 0.84 – 0.77 (m, 7H).

$^{13}$C NMR (126 MHz, CDCl$_3$) (major diastereomer) δ 172.2, 170.1, 170.0, 169.8, 168.6, 164..5, 163.7, 157.0, 144.3, 141.3, 133.9, 133.3, 131.9, 129.9, 129.6, 128.9, 128.1, 128.0, 127.7, 127.1,
127.0, 126.9, 126.5, 125.1, 120.0, 119.6, 70.2, 70.1, 42.0, 41.0, 40.6, 37.2, 35.4, 34.4, 33.9, 33.2, 29.7, 27.8, 27.4, 25.6, 25.2, 22.7, 22.2, 22.0.

HRMS (ESI) calculated for C_{75}H_{72}N_{4}O_{7}S_{2} [M+H]⁺: 1205.5267; found: 1205.5269.

(R)-Methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-(2-(tritylthio)ethyl)-11-((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3j

Procedure B

yield: 65% (0.65 g)

white solid, Mp: 96-98 °C

Rᶠ 0.30 (EtOAc/ PE, 30:70)

¹H NMR (500 MHz, CDCl₃, mixture of rotamers) δ 7.80 (d, J = 7.6 Hz, 3H), 7.64 (dd, J = 7.8, 2.8 Hz, 2H), 7.52 – 7.37 (m, 20H), 7.37 – 7.21 (m, 45H), 6.54 (d, J = 7.8 Hz, 1H), 6.25 (d, J = 12.2 Hz, 0.3H), 5.75 (d, J = 5.5 Hz, 0.4H), 5.74 (d, J = 4.5 Hz, 1H), 4.51 – 4.46 (m, 2H), 4.45 – 4.32 (m, 3H), 4.25 (t, J = 7.2 Hz, 1H), 3.87 (s, 1H), 3.86 (s, 2H), 3.77 (d, J = 4.5 Hz, 0.6H), 3.75 (d, J = 6.4 Hz, 2H), 3.75 (s, 2H), 3.69 (s, 3H), 3.55 – 3.49 (m, 2H), 3.15 (t, J = 7.3 Hz, 1H), 3.11 (t, J = 11.4 Hz, 2H), 2.73 – 2.70 (m, 2.6H), 2.57 – 2.51 (m, 1.6H).

¹³C NMR (126 MHz, CDCl₃) δ 170.4, 170.1, 169.0, 167.4, 166.9, 156.0, 144.5, 144.3, 144.1, 143.2, 141.2, 129.5, 129.4, 129.3, 128.0, 127.9, 127.8, 127.6, 127.0, 126.0, 126.6, 125.1, 119.8, 67.8, 67.3, 57.7, 55.8, 51.4, 51.2, 50.4, 49.6, 47.5, 47.3, 44.4, 33.5, 33.4, 33.1, 29.7, 29.3.

HRMS (ESI) calculated for C_{63}H_{57}N_{3}O_{6}S_{2} [M+Na]⁺: 1038.3586; found: 1038.3587.

(11R)-Methyl 7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-8,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3k

Procedure B
yield: 45% (0.49 g)
white solid, Mp: 115-117 °C
Rf 0.40 (EtOAc/ PE, 30:70)
dr ratio: 3:2.5

$^1$H NMR (500 MHz, CDCl$_3$, mixture of diastereomers and rotamers) δ 7.80 (d, $J = 7.5$ Hz, 4H), 7.62 (dd, $J = 18.2$, 7.6 Hz, 5H), 7.49 – 7.18 (m, 119H), 7.06 – 6.97 (m, 5H), 6.52 (d, $J = 8.0$ Hz, 1H), 6.50 (d, $J = 8.0$ Hz, 1H), 5.70 (dd, $J = 9.9$, 6.2 Hz, 2H), 4.44 – 4.37 (m, 5H), 4.34 – 4.26 (m, 5H), 4.25 – 4.19 (m, 5H), 4.03 (d, $J = 4.5$ Hz, 2H), 3.97 (d, $J = 8.8$ Hz, 2H), 3.69 (s, 3H), 3.67 (s, 3H), 2.87 (dt, $J = 13.7$, 6.9 Hz, 2.5H), 2.77 (dt, $J = 12.1$, 6.0 Hz, 2H), 2.61 –2.49 (m, 5H).

$^{13}$C NMR (126 MHz, CDCl$_3$, mixture of diastereomers and rotamers) δ 170.7, 170.5, 169.6, 168.5, 156.6, 156.1, 155.8, 144.3, 144.2, 143.9, 143.6, 141.3, 135.5, 135.2, 129.5, 129.4, 129.3, 129.2, 129.0, 128.8, 128.1, 128.0, 127.9, 127.7, 127.6, 127.4, 127.1, 126.9, 126.5, 126.3, 125.2, 124.2, 120.0, 119.1, 67.3, 66.8, 66.5, 65.9, 58.2, 57.9, 57.3, 52.6, 52.2, 51.2, 50.0, 48.6, 46.8, 46.7, 43.0, 33.4, 33.3, 29.6, 29.5.

HRMS (ESI) calculated for C$_{69}$H$_{61}$N$_3$O$_6$S$_2$ [M+Na]$^+$: 1114.3899; found: 1114.3900.

(R)-Methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-(2-(tritylthio)ethyl)-5-((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3l

Procedure B

yield: 70% (0.71 g)
white solid, Mp: 89-91 °C
Rf 0.35 (EtOAc/ PE, 30:70)

$^1$H NMR (500 MHz, CDCl$_3$, mixture of rotamers) δ 7.81 (td, $J = 10.4$, 9.0, 5.7 Hz, 2H), 7.79 (dd, $J = 12.2$, 8.0 Hz, 2H), 7.71 – 7.54 (m, 26H), 7.56 – 7.30 (m, 30H), 7.02 (d, $J = 7.0$ Hz, 0.5H), 5.54 (d, $J = 7.3$ Hz, 1H), 5.54 (d, $J = 9.3$ Hz, 0.5H), 4.45 – 4.40 (m, 1.5H), 4.38 – 4.35 (m, 2.5H), 4.28 (t,
$J=8.5 \text{ Hz, } 0.5 \text{H}$, 4.25 (t, $J=12.5 \text{ Hz, } 1 \text{H}$), 3.81 (d, $J=5.4 \text{ Hz, } 0.8 \text{H}$), 3.78 (d, $J=4.0 \text{ Hz, } 2 \text{H}$), 3.77 (s, 0.7H), 3.76 (s, 2H), 3.66 (s, 1.5H), 3.65 (s, 3H), 3.18 (t, $J=6.7 \text{ Hz, } 0.7 \text{H}$), 3.16 (t, $J=8.0 \text{ Hz, } 2 \text{H}$), 2.81 (dd, $J=11.0, 3.5 \text{ Hz, } 0.5 \text{H}$), 2.77 (dd, $J=12.0, 6.5 \text{ Hz, } 0.7 \text{H}$), 2.49 (dd, $J=18.0, 8.5 \text{ Hz, } 1 \text{H}$), 2.38 (dd, $J=12.5, 6.9 \text{ Hz, } 1 \text{H}$).

$^{13}$C NMR (126 MHz, CDCl$_3$, mixture of rotamers) δ 171.5, 171.1, 169.8, 169.5, 161.3, 155.7, 155.2, 144.7, 144.5, 144.3, 143.8, 143.7, 143.5, 141.3, 141.0, 129.9, 129.8, 129.6, 129.5, 129.3, 128.2, 128.0, 127.8, 127.5, 127.2, 127.1, 126.9, 126.8, 125.3, 125.2, 125.1, 120.1, 120.0, 119.8, 67.5, 67.4, 67.2, 67.1, 64.4, 60.5, 53.6, 53.4, 52.3, 52.1, 50.1, 50.0, 49.5, 48.6, 47.2, 47.0, 40.6, 37.0, 34.6, 34.4, 30.2, 29.8, 29.1, 21.1.

HRMS (ESI) calculated for $C_{63}H_{57}N_3O_6S_2 [M+H]^+$: 1016.2731; found: 1016.2732.

**Methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7,8-bis(2-(tritylthio)ethyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3m**

Procedure B

yield: 52% (0.53 g)

white solid, Mp: 79-81 °C

R$_f$ 0.40 (EtOAc/ PE, 30:70)

$^1$H NMR (500 MHz, CDCl$_3$, mixture of rotamers) δ 7.80 (d, $J=7.5 \text{ Hz, } 2 \text{H}$), 7.78 (d, $J=12.5 \text{ Hz, } 2 \text{H}$) 7.65 – 7.38 (m, 17H), 7.36 – 7.13 (m, 52H), 6.70 (d, $J=5.6 \text{ Hz, } 1 \text{H}$), 5.60 (d, $J=4.6 \text{ Hz, } 1 \text{H}$), 4.45 (d, $J=6.7 \text{ Hz, } 2 \text{H}$), 4.33 (d, $J=8.1 \text{ Hz, } 2 \text{H}$), 2.25 (t, $J=12.6 \text{ Hz, } 1 \text{H}$), 4.23 (t, $J=9.4 \text{ Hz, } 1 \text{H}$), 4.15 – 3.98 (m, 2H), 3.97 (d, $J=12.4 \text{ Hz, } 1.5 \text{H}$), 3.95 (d, $J=8.4 \text{ Hz, } 2 \text{H}$), 3.91 (d, $J=16.4 \text{ Hz, } 2 \text{H}$), 3.88 (d, $J=6.5 \text{ Hz, } 1 \text{H}$), 3.75 (s, 3H), 3.69 (s, 3H), 3.24 (t, $J=18.2 \text{ Hz, } 2 \text{H}$), 3.22 (t, $J=16.4 \text{ Hz, } 2 \text{H}$), 2.81 – 2.69 (m, 4H), 2.46 (d, $J=12.1 \text{ Hz, } 2 \text{H}$), 2.43 (d, $J=6.7 \text{ Hz, } 2 \text{H}$), 2.05 (dt, $J=12.3, 7.3 \text{ Hz, } 2 \text{H}$), 1.97 (dt, $J=12.5, 6.8 \text{ Hz, } 2 \text{H}$).
\(^{13}\)C NMR (126 MHz, CDCl\(_3\), mixture of rotamers) \(\delta\) 170.2, 169.8, 169.5, 169.1, 164.3, 156.0, 144.8, 144.6, 143.9, 141.3, 129.6, 129.5, 129.3, 128.5, 128.0, 127.9, 127.7, 127.0, 126.8, 126.7, 126.6, 125.1, 120.0, 67.5, 67.1, 66.8, 62.1, 61.6, 52.3, 51.8, 47.1, 45.2, 42.9, 41.9, 41.0, 40.3, 30.4, 29.1, 28.1, 27.5, 26.5, 26.0.

HRMS (ESI) calculated for C\(_{64}\)H\(_{59}\)N\(_3\)O\(_6\)S\(_2\) [M+Na]\(^+\): 1052.3743; found: 1052.3741.

\((5R)\)-Methyl 7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,8-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3n

Procedure B

yield: 40\% (0.43 g)

white foam, Mp: 69-71 °C

R\(_f\) 0.35 (EtOAc/ PE, 30:70)

dr ratio: 3:2.7

\(^1\)H NMR (500 MHz, CDCl\(_3\), mixture of diastereomers and rotamers) \(\delta\) 7.81 – 7.79 (m, 5H), 7.74 – 7.63 (m, 7H), 7.73 – 7.11 (m, 130H), 5.48 (d, \(J = 8.2\) Hz, 2H), 4.63 (t, \(J = 12.2\) Hz, 1H), 4.52 (dt, \(J = 18.2, 8.6\) Hz, 1.6H), 4.51 –4.34 (m, 7H), 4.30 – 4.23 (m, 4H), 4.22 (d, \(J = 6.2\) Hz, 2H), 4.20 (d, \(J = 8.4\) Hz, 1.3 Hz), 3.97 – 3.83 (m, 3H) 3.67 (s, 1.5H), 3.65 (s, 1.5H), 3.63 (s, 3H), 3.60 (s, 2.8H), 2.80 – 2.77 (m, 2H), 2.76 – 2.73 (m, 0.8H), 2.70 – 2.66 (m, 1.5H), 2.65 – 2.58 (m, 2H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\), mixture of diastereomers and rotamers) \(\delta\) 172.5, 172.3, 171.7, 169.9, 169.6, 169.4, 169.0, 168.8, 168.0, 156.7, 155.6, 155.5, 144.5, 144.4, 144.3, 144.1, 143.8, 143.7, 143.6, 141.3, 141.2, 137.2, 135.8, 135.4, 129.7, 129.6, 129.5, 129.3, 128.9, 128.6, 128.2, 128.1, 127.9, 127.8, 127.7, 127.4, 127.1, 127.0, 126.9, 126.7, 125.3, 125.1, 120.1, 119.9, 119.8, 67.4, 67.3, 67.2, 59.3, 57.4, 52.1, 51.9, 51.2, 51.0, 49.0, 48.8, 47.1, 47.0, 40.9, 40.8, 34.7, 34.2, 33.6, 30.5, 30.3, 29.6.

HRMS (ESI) calculated for C\(_{69}\)H\(_{61}\)N\(_3\)O\(_6\)S\(_2\) [M+H]\(^+\): 1092.3691; found: 1092.3694.
**N₁-Methyl-N₁-(4-methyl-1-oxo-1-((2-(tritylthio)ethyl)amino)pentan-2-yl)-N₄-(2-(tritylthio) ethyl) succinamide, 3o**

Procedure A

yield: 80% (0.67 g)
white solid, Mp: 89 – 91 °C
Rf 0.35 (EtOAc/ PE, 30:70)

1H NMR (500 MHz, CDCl₃, mixture of rotamers) δ 7.52 – 7.37 (m, 1H), 7.37 – 7.14 (m, 26H), 6.52 (t, J = 5.9 Hz, 1H), 5.72 (d, J = 6.3 Hz, 1H), 5.13 (dd, J = 9.9, 5.7 Hz, 1H), 3.17 – 3.08 (m, 2H), 3.06 – 3.02 (m, 1H), 3.00 – 2.90 (m, 2H), 2.87 (s, 3H), 2.69 – 2.58 (m, 1H), 2.54 – 2.50 (m, 1H), 2.50 – 2.45 (m, 2H), 2.45 – 2.40 (m, 2H), 2.33 (dt, J = 12.8, 6.7 Hz, 2H), 1.63 – 1.55 (m, 2H), 1.48 – 1.36 (m, 2H), 0.94 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.5 Hz, 3H).

13C NMR (126 MHz, CDCl₃, mixture of rotamers) δ 173.3, 171.9, 170.6, 144.8, 144.6, 129.5, 128.1, 127.9, 126.9, 126.8, 126.7, 66.9, 58.8, 38.8, 38.2, 37.0, 36.0, 31.8, 31.3, 28.9, 28.5, 24.9, 23.3, 23.2, 21.9.

HRMS (ESI) calculated for C₅₃H₅₇N₃O₅S₂ [M+H]+: 848.1679; found: 848.1679.

(5S,13R)-Methyl 1-(9H-fluoren-9-yl)-5-(methoxycarbonyl)-3,8,11-trioxo-10,13-bis((tritylthio)methyl)-2-oxa-4,9,12-triazatetradecan-14-oate, 3p

Procedure B

yield: 21% (0.22 g)
white solid, Mp: 105 – 107 °C
Rf 0.60 (EtOAc/ PE, 50:50)

Single diastereomer isolated from column purification

1H NMR (500 MHz, CDCl₃) δ 7.85 – 7.69 (m, 2H), 7.67 – 7.01 (m, 38H), 6.46 (dd, J = 19.6, 11.5 Hz, 1H), 6.10 (t, J = 13.6 Hz, 1H), 5.66 (dd, J = 16.8, 8.0 Hz, 1H), 4.41 – 4.38 (m, 3H) 4.25 (t, J =
8.6 Hz, 1H), 4.07 (d, J = 11.9 Hz, 2H), 3.69 (s, 3H), 3.65 (s, 3H), 2.89 – 2.73 (m, 2H), 2.68 – 2.53 (m, 2H), 2.04 (t, J = 16.2 Hz, 2H), 1.93 (t, J = 22.2 Hz, 2H).

^1^C NMR (126 MHz, CDCl_3) δ 172.42, 171.76, 170.25, 169.65, 156.24, 144.41, 144.34, 144.32, 144.26, 143.88, 143.70, 141.34, 129.56, 129.52, 129.49, 128.17, 128.12, 128.03, 127.96, 127.93, 127.76, 127.25, 127.14, 126.90, 125.13, 120.02, 67.21, 67.06, 60.43, 53.30, 52.58, 52.56, 52.22, 52.06, 51.46, 47.21, 33.51, 33.35, 32.10, 28.46.

HRMS (ESI) calculated for C_{66}H_{61}N_{3}O_{8}S_{2} [M+H]^+: 1088.3358; found: 1088.3558.

(5R,11R)-Methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7,8-bis(2-(tritylthio)ethyl)-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3q

Procedure B

yield: 30% (0.48g)

white foam, Mp: 110 – 112 °C

R_f 0.42 (EtOAc/ PE, 30:70)

Single diastereomer isolated from column purification

^1^H NMR (500 MHz, CDCl_3, mixture of rotamers) δ 7.91 – 7.11 (m, 148H), 7.05 (d, J = 12.5 Hz, 0.8H), 4.81 (d, J = 6.4 Hz, 0.7H), 4.75 (d, J = 8.4 Hz, 0.2H), 4.45 – 4.42 (m, 1.6H), 4.41 – 4.35 (m, 3H), 4.34 – 4.24 (m, 2H), 4.22 – 4.16 (m, 2H), 3.49 (s, 3H), 3.47 (s, 0.7H), 3.15 – 2.98 (m, 2.5H), 2.71 – 2.65 (m, 2.6H), 2.61 – 2.52 (m, 2.5H), 2.49 – 2.37 (m, 2.6H), 2.31 – 2.18 (m, 2.8H), 1.77 – 1.59 (m, 2.8H).

^1^C NMR (126 MHz, CDCl_3, mixture of rotamers) δ 171.98, 170.46, 169.26, 155.71, 144.95, 144.84, 144.78, 144.70, 144.59, 144.54, 144.44, 144.37, 144.30, 144.26, 144.07, 143.53, 141.33, 141.23, 129.74, 129.67, 129.63, 129.58, 129.53, 128.19, 128.13, 128.09, 128.02, 127.96, 127.89, 127.77, 127.13, 127.09, 127.01, 126.96, 126.92, 126.86, 126.83, 126.77,
126.63, 126.58, 125.26, 125.09, 125.02, 120.03, 119.99, 77.35, 77.30, 77.10, 76.85, 67.35, 67.11, 66.81, 52.25, 51.72, 49.78, 47.12, 46.97, 33.74, 33.49, 33.34, 28.67, 27.73.

HRMS (ESI) calculated for $\text{C}_{104}\text{H}_{91}\text{N}_3\text{O}_6\text{S}_4 [\text{M}+\text{H}]^+$: 1607.1118; found: 1607.1113.
**Disulfide Synthesis**

To a solution of I₂ (10.0 equiv.) in 10:1 mixture of CH₂Cl₂: MeOH (150 mL) was added the Ugi product (1.0 equiv.) previously dissolved in CH₂Cl₂ (50 mL) dropwise over 10 min. The resulting mixture was stirred for 1 h and cooled then quenched the reaction mixture with saturated aqueous sodium bisulfite. The reaction mixture was concentrated and then partitioned between H₂O and EtOAc. The organic layer was washed with brine, dried over anhydrous Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography on silica gel (MeOH/CH₂Cl₂, 5:95).

Note: Diastereomeric ratios are given according to methyl group singlet of the C-terminal ester.

**(4R,10R)-Methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-benzyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4a**

yield: 82% (0.49 g)

white solid, Mp: 112-114 °C

Rf 0.41 (MeOH/ CH₂Cl₂, 3:97)

dr ratio: 3:0

\(^1\)H NMR (500 MHz, CDCl₃) δ 7.75 – 7.71 (m, 13H), 5.31 (br, d, J = 6.8 Hz, 1H), 5.15 – 4.86 (m, 1H), 4.81 – 4.68 (m, 1H), 4.42 (t, J = 8.2 Hz, 1H), 4.21 (d, J = 6.4 Hz, 2H), 4.16 (s, 2H), 3.86 (d, J = 12.2 Hz, 2H), 3.61 (s, 3H), 2.81 (dd, J = 6.8, 1.1 Hz, 1H), 2.79 (dd, J = 11.2, 6.2 Hz, 1H), 2.71 (dd, J = 8.5, 2.4 Hz, 1H), 2.65 (dd, J = 6.5, 2.5 Hz, 1H).

\(^13\)C NMR (126 MHz, CDCl₃) δ 169.3, 168.2, 168.0, 156.4, 143.4, 141.0, 135.6, 135.4, 128.7, 128.5, 127.9, 127.9, 127.7, 127.5, 126.9, 126.8, 124.8, 119.7, 77.3, 77.1, 76.8, 67.2, 53.0, 52.6, 52.5, 49.7, 48.8, 48.5, 48.2, 46.8, 40.1, 39.6.

HRMS (ESI) calculated for C₃₁H₃₁N₃O₆S₂ [M+H]^+: 606.1727; found: 606.1727.
(4R,10R)-Methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-(3,4-dichlorobenzyl)-7-isobutyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4b

yield: 75% (0.54 g)
white solid, Mp: 125-127 °C

Rf 0.60 (MeOH/ CH2Cl2, 5:95)

dr ratio: 3:2.3

1H NMR (500 MHz, CDCl3, mixture of diastereomers) δ 7.79 – 7.18 (m, 20H), 7.15 (d, J = 7.6 Hz, 1H), 7.11 (d, J = 6.6 Hz, 1H), 5.65 (d, J = 9.8 Hz, 1H), 5.31 (d, J = 11.8 Hz, 1H), 4.93 – 4.91 (m, 1H), 4.89 – 4.86 (m, 2H), 4.82 – 4.66 (m, 4H), 4.65 – 4.29 (m, 7H), 4.22 (d, J = 8.6 Hz, 2H), 4.11 (s, 1H), 4.08 (s, 2H), 3.77 (s, 2H), 3.75 (s, 3H), 3.49 – 3.38 (m, 2H), 3.30 – 3.21 (m, 3H), 3.18 – 2.93 (m, 2H), 1.74 – 1.63 (m, 3H), 1.56 – 1.32 (m, 2H), 1.01 – 1.32 (m, 2H), 1.01 – 0.86 (m, 5H), 0.83 (d, J = 4.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H).

13C NMR (126 MHz, CDCl3, mixture of diastereomers) δ 172.4, 172.1, 171.0, 170.1, 169.8, 169.6, 169.0, 168.8, 156.5, 155.6, 143.4, 141.3, 139.3, 137.8, 133.2, 132.7, 132.4, 132.0, 131.8, 130.9, 130.7, 130.3, 130.3, 129.0, 127.8, 127.5, 127.1, 126.5, 125.1, 120.2, 120.0, 67.3, 66.2, 60.9, 58.9, 55.8, 54.7, 53.0, 52.3, 51.2, 47.1, 46.9, 41.6, 41.2, 38.2, 36.7, 25.3, 22.9, 22.4, 22.3, 22.1, 21.9, 21.7, 21.5.

HRMS (ESI) calculated for C35H37Cl2N3O6S2 [M+H]+: 730.1573; found: 730.1575.

(4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-(2-((tert-butoxycarbonyl)amino)ethyl)-7-isopropyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4c

yield: 70% (0.49 g)
white solid, Mp: 110 – 112 °C

S33
Rf 0.55 (MeOH/ CH2Cl2, 5:95)

dr ratio: 3:2.1

1H NMR (500 MHz, CDCl3, mixture of diastereomers) δ 7.80 (d, J = 5.4 Hz, 2H), 7.61 (d, J = 7.4 Hz, 2H), 7.51 – 7.12 (m, 13H), 5.69 (br, s, 1.3H), 5.30 – 5.10 (m, 1.5H), 4.94 – 4.82 (m, 1.6H), 4.80 – 4.74 (m, 1.3H), 4.61 – 4.43 (m, 1.6H), 4.40 – 4.25 (m, 3H), 3.77 (s, 3H), 3.75 (s, 2H), 3.71 – 3.70 (m, 2H), 3.65 – 3.32 (m, 3H), 3.24 – 3.12 (m, 2H), 2.91 – 2.81 (m, 1.5H), 1.49 (s, 9H), 1.38 (s, 6H), 1.21 – 1.12 (m, 5H), 1.11 – 0.98 (m, 6H).

13C NMR (126 MHz, CDCl3, mixture of diastereomers) δ 174.7, 173.1, 172.0, 170.9, 170.7, 170.2, 170.0, 167.8, 156.9, 156.3, 155.4, 154.3, 153.0, 143.8, 142.7, 141.3, 129.0, 128.8, 127.9, 127.1, 126.1, 125.1, 123.9, 120.2, 120.0, 77.5, 77.3, 77.0, 76.8, 74.2, 73.5, 73.3, 72.6, 68.4, 68.1, 67.7, 66.8, 65.9, 58.3, 58.1, 54.0, 52.9, 52.7, 52.0, 51.4, 48.2, 47.5, 47.1, 47.0, 46.2, 45.0, 39.7, 38.6, 37.7, 35.9, 35.0, 33.9, 30.1, 29.4, 29.2, 28.5, 27.4, 27.1, 18.8, 18.4, 17.6.

HRMS (ESI) calculated for C34H44N4O8S [M+H]+: 701.2673; found: 701.2677.

(4R,10R)-Methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-7-isobutyl-6,9-dioxo-8-phenethyl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4d

yield: 85% (0.57 g)

white solid, Mp: 137-139 °C

Rf 0.55 (MeOH/ CH2Cl2, 5:95)

dr ratio: 3:2.8

1H NMR (500 MHz, CDCl3, mixture of diastereomers) δ 7.81 (d, J = 2.4 Hz, 0.6H), 7.79 (d, J = 4.4 Hz, 0.6H), 7.50 – 7.14 (m, 28H), 5.66 (d, J = 6.4 Hz, 0.9H), 5.33 9d, J = 7.2 Hz, 1H), 4.48 – 4.45 (m, 1.5H), 4.44 – 4.40 (m, 1.5H), 4.39 – 4.20 (m, 4H), 4.29 – 4.24 (m, 5.7H), 3.77 (s, 3H), 3.75 (s, 2.7H), 3.74 – 3.66 (m, 3.7H), 2.81 – 2.78 (m, 2.5H), 2.77 – 2.74 (m, 5H), 2.73 – 2.67 (m,
3.7H), 1.61 – 1.50 (m, 3.8H), 1.43 – 1.32 (m, 1.8H), 0.98 (d, \( J = 7.3 \) Hz, 2.7H), 0.90 (d, \( J = 8.8 \) Hz, 2.6H), 0.87 (d, \( J = 8.1 \) Hz, 3H), 0.85 (d, \( J = 2.1 \) Hz, 3H).

\(^{13}\)C NMR (126 MHz, CDCl₃, mixture of diastereomers) \( \delta \) 173.4, 172.5, 171.6, 170.4, 170.0, 157.6, 156.5, 146.4, 146.0, 145.3, 141.3, 139.9, 133.7, 132.8, 132.1, 131.0, 130.3, 128.7, 128.4, 128.3, 127.8, 127.2, 126.7, 125.0, 124.3, 122.0, 68.0, 68.1, 63.6, 62.9, 59.4, 52.7, 51.8, 51.3, 48.9, 48.7, 47.9, 43.9, 40.8, 36.8, 36.2, 35.3, 34.1, 30.3, 34.1, 30.4, 29.7, 25.1, 24.8, 22.7, 22.4.

HRMS (ESI) calculated for \( C_{36}H_{41}N_{3}O_{6}S_{2} \) [M+H]⁺: 676.2509; found: 676.2509.

\((4R,10R)\)-Methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6,9-dioxo-8-propyl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4e

yield: 70% (0.38 g)

white solid, Mp: 137-139 °C

Rᵥ 0.55 (MeOH/ CH₂Cl₂, 5:95)

dr ratio: 3:0

\(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 7.84 (d, \( J = 7.4 \) Hz, 1H), 7.74 – 7.21 (m, 8H), 5.75 (d, \( J = 9.0 \) Hz, 1H), 5.10 – 5.02 (m, 1H), 4.78 – 4.72 (m, 1H), 4.38 – 4.25 (m, 3H), 4.24 (t, \( J = 8.5 \) Hz, 2H), 3.77 (s, 3H), 3.53 (td, \( J = 12.1, 2.2 \) Hz, 2H), 3.18 – 2.81 (m, 4H), 1.71 (dd, \( J = 18.1, 7.6 \) Hz, 2H), 0.86 (t, \( J = 7.5 \) Hz, 3H).

\(^{13}\)C NMR (126 MHz, CDCl₃) \( \delta \) \(^{13}\)C NMR (126 MHz, CDCl₃) \( \delta \) 171.59, 170.21, 169.50, 156.52, 143.61, 143.55, 141.29, 141.23, 127.97, 127.76, 127.09, 125.23, 125.12, 124.94, 120.18, 120.14, 120.10, 119.91, 77.34, 77.08, 76.83, 67.33, 54.39, 52.91, 52.44, 51.52, 50.75, 47.13, 46.97, 34.11, 29.71, 20.93, 11.31.

HRMS (ESI) calculated for \( C_{27}H_{31}N_{3}O_{6}S_{2} \) [M+H]⁺: 558.1727; found: 558.1723.
(4R,10R)-Methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-7-isopropyl-8-methyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4f

yield: 82% (0.46 g)

white solid, Mp: 120-123 °C.

Rf 0.38 (MeOH/ CH2Cl2, 5:95)

dr ratio: 3:2

1H NMR (500 MHz, CDCl3, mixture of diastereomers) δ 7.79 (d, J = 7.8 Hz, 2H), 7.59 – 7.27 (m, 16H), 5.94 (d, J = 8.6 Hz, 1H), 5.76 (d, J = 9.4 Hz, 0.9H), 4.74 – 4.66 (m, 1.7H), 4.65 – 4.60 (m, 2H), 4.59 – 4.54 (m, 2H), 4.38 – 4.29 (m, 1.7H), 4.26 – 4.15 (m, 3.8H), 3.77 (s, 2.8H), 3.75 (s, 3H), 3.73 – 3.58 (m, 2.5H), 3.53 – 3.49 (m, 2H), 3.43 – 3.35 (m, 1.7H), 3.27 – 3.20 (m, 2H), 3.16 (s, 3H), 3.14 (s, 2H), 3.18 – 2.88 (m, 1H), 2.50 – 2.31 (m, 1.7H), 1.16 (d, J = 5.4 Hz, 3H), 1.10 (d, J = 6.5 Hz, 2H), 0.98 (d, J = 5.5 Hz, 3H), 0.96 (d, J = 6.2 Hz, 2H).

13C NMR (126 MHz, CDCl3, mixture of diastereomers) δ 171.1, 170.5, 169.6, 169.0, 168.8, 156.6, 155.9, 155.8, 144.1, 143.5, 143.4, 129.9, 129.0, 127.8, 127.1, 125.9, 125.1, 124.9, 123.6, 122.5, 120.7, 120.1, 119.9, 77.1, 68.5, 67.4, 66.7, 65.4, 56.4, 55.8, 51.1, 50.6, 49.5, 47.5, 46.6, 38.5, 37.8, 36.9, 33.0, 32.7, 32.3, 31.6, 28.4, 28.0, 27.8, 27.3, 20.2, 19.6, 19.4.

HRMS (ESI) calculated for C28H33N3O6S2 [M+H]+: 572.1883; found: 572.1882.

(4R,10R)-Methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-allyl-7-benzyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4g

yield: 74% (0.47 g)

white foamy solid, Mp: 103-105 °C

Rf 0.45 (MeOH/ CH2Cl2, 3:97)

dr ratio: 3:2
H NMR (500 MHz, CDCl₃, mixture of diastereomers) δ 7.63 – 7.10 (m, 23H), 5.91 (d, J = 6.4 Hz, 0.7H), 5.82 (d, J = 5.5 Hz, 0.9H), 5.65 (d, J = 18.4 Hz, 0.45H), 5.49 – 5.35 (m, 2H), 4.88 – 4.85 (m, 0.8H), 4.82 – 4.76 (m, 2H), 4.75 – 4.55 (m, 2.5H), 4.49 – 4.30 (m, 3H), 4.29 – 4.18 (m, 1.5H), 4.05 – 3.89 (m, 4H), 3.77 (s, 2H), 3.75 (s, 3H), 3.26 – 3.15 (m, 3H), 2.98 – 2.55 (m, 6H).

13C NMR (126 MHz, CDCl₃, mixture of diastereomers) δ 170.95, 170.65, 170.41, 170.09, 169.90, 169.57, 156.01, 155.64, 143.74, 143.62, 141.32, 138.03, 137.53, 137.05, 136.97, 129.30, 129.23, 129.12, 129.01, 128.69, 128.50, 128.19, 127.84, 127.78, 127.50, 127.15, 126.85, 125.82, 125.41, 125.21, 125.02, 120.18, 119.97, 77.42, 77.16, 76.91, 73.03, 69.48, 68.65, 67.30, 66.76, 54.87, 52.91, 52.61, 51.73, 47.60, 47.17, 47.09, 46.60, 40.78, 39.04, 33.50, 31.54, 29.72.

HRMS (ESI) calculated for C₃₄H₃₅N₃O₆S₂ [M+H]+: 646.2040; found: 646.2040.

(4R,10R)-Methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6,9-dioxo-8-trityl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4h

yield: 68% (0.51 g)
white solid, Mp: 137-139 °C
Rf 0.44 (MeOH/ CH₂Cl₂, 3:97)
dr ratio: 3:0

1H NMR (500 MHz, CDCl₃) δ 7.80 (d, J = 8.2 Hz, 1H), 7.61 – 7.15 (m, 25H), 5.48 (d, J = 7.5 Hz, 1H), 4.88 – 4.63 (m, 2H), 4.24 (d, J = 6.2 Hz, 2H), 4.16 (t, J = 12.2 Hz, 1H), 4.13 – 4.01 (m, 2H), 2.98 – 2.88 (m, 2H).

13C NMR (126 MHz, CDCl₃) δ 172.2, 171.1, 170.2, 156.3, 144.0, 143.5, 142.6, 141.3, 130.8, 129.7, 129.4, 128.8, 128.7, 127.9, 127.8, 127.2, 126.9, 126.3, 125.5, 124.8, 120.3, 120.1, 79.3, 77.3, 77.0, 76.8, 64.5, 60.1, 59.2, 54.4, 47.1, 45.7, 39.5, 36.8.

HRMS (ESI) calculated for C₁₁₅H₁₁₃N₇O₁₄S₄ [M+H]+:758.2353; found: 758.2356.
(4R,13R)-Methyl 13-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-benzyl-7-isobutyl-6,9,12-trioxo-1,2-dithia-5,8,11-triazacyclotetradecane-4-carboxylate, 4i

yield: 77% (0.55 g)

white solid, Mp: 109 – 111 °C.

Rf 0.61 (MeOH/ CH2Cl2, 5:95)

dr ratio: 3:2.7

1H NMR (500 MHz, CDCl3, mixture of diastereomers) δ 7.79 (d, J = 9.2 Hz, 2.8H), 7.60 (t, J = 10.3 Hz, 2.8H), 7.46 – 7.06 (m, 10H), 7.01 (br, s, 1H), 6.08 (br, s, 1H), 5.23 – 5.10 (m, 0.6H), 4.98 – 4.90 (m, 0.9H), 4.74 – 4.68 (m, 2.3H), 4.65 – 4.32 (m, 7H), 4.28 – 4.22 (m, 2.7H), 3.77 (s, 3H), 3.75 (s, 0.7H), 3.68 – 3.44 (m, 4.5H), 3.63 – 2.96 (m, 3.5H), 2.18 – 1.86 (m, 2.8H), 1.65 – 1.28 (m, 1.5H), 0.98 – 0.78 (m, 9H).

13C NMR (126 MHz, CDCl3) δ 172.0, 171.3, 170.7, 169.9, 159.0, 158.1, 157.2, 154.1, 143.6, 142.2, 141.3, 137.7, 130.9, 130.4, 129.7, 129.1, 127.8, 127.1, 126.7, 126.5, 125.9, 125.1, 124.1, 123.9, 120.2, 120.0, 77.3, 77.0, 76.8, 67.5, 67.0, 65.4, 64.7, 64.3, 63.6, 58.5, 57.4, 53.2, 52.4, 51.4, 50.9, 47.2, 46.8, 39.0, 38.2, 37.9, 37.2, 36.8, 35.9, 35.3, 35.0, 29.7, 25.6, 25.2, 23.1, 22.4, 22.0.

HRMS (ESI) calculated for C37H42N4O7S2 [M+H]+: 719.2567; found: 719.2568.

(R)-Methyl 8-((2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)acetyl)-6-oxo-1,2,5,8-dithiadiazacone-4-carboxylate, 4j

yield: 79% (0.41 g)

white solid, Mp: 115 – 117 °C

Rf 0.48 (MeOH/ CH2Cl2, 5:95)

1H NMR (500 MHz, CDCl3) δ 7.79 (t, J = 7.6 Hz, 2H), 7.65 (d, J = 7.6 Hz, 2H), 7.42 (q, J = 7.7 Hz, 2H), 7.35 (t, J = 7.5 Hz, 2H), 7.04 (d, J = 9.1 Hz, 1H), 5.89 – 5.80 (br, s, 1H), 4.51– 4.45 (m, 1H)
4.43 (t, J = 8.9 Hz, 1H), 4.21 (d, J = 8.2 Hz, 2H), 4.17 – 4.11 (m, 2H), 3.90 – 3.80 (m, 2H), 3.75 (s, 3H), 3.70 – 3.55 (m, 2H), 3.38 (d, J = 12.8 Hz, 1H, 1H), 3.31 (d, J = 15.3 Hz, 1H), 3.12 – 2.95 (m, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 170.3, 169.7, 169.5, 156.3, 143.8, 141.3, 127.8, 127.1, 125.1, 125.0, 120.0, 67.3, 60.4, 55.6, 52.6, 48.3, 47.1, 43.3, 42.9, 41.6, 39.3, 30.2.

HRMS (ESI) calculated for C$_{25}$H$_{27}$N$_3$O$_6$S$_2$ [M+H]$^+$: 530.1414; found: 530.1412.

($9$H-Fluoren-9-yl)methyl (2-(benzyl((4R)-4-((methylperoxy)methyl)-6-oxo-1,2,5-dithiazocan-7-yl)amino)-2-oxoethyl)carbamate, 4k

yield: 72% (0.43 g)

white solid, Mp: 101 – 103 °C

R$_f$ 0.38 (MeOH/ CH$_2$Cl$_2$, 5:95)

dr ratio: 3:2.3

$^1$H NMR (500 MHz, CDCl$_3$, mixture of diastereomers) δ 7.77 – 7.24 (m, 20H), 6.77 (d, J = 9.5 Hz, 1H), 5.82 (d, J = 21.3 Hz, 1H), 5.10 – 4.96 (m, 2H), 4.88 – 4.79 (m, 4H), 4.26 – 4.05 (m, 9H), 3.80 (s, 1.8H), 3.78 (s, 3H), 3.66 – 3.55 (m, 4H), 3.50 – 3.46 (m, 1H), 3.21 – 2.88 (m, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$, mixture of diastereomers) δ 172.8, 171.7, 170.6, 170.1, 169.8, 168.3, 164.4, 156.8, 156.3, 148.8, 143.8, 143.5, 141.2, 135.7, 135.2, 131.0, 130.1, 129.2, 126.5, 125.4, 125.3, 125.1, 119.6, 67.9, 67.1, 66.5, 66.3, 59.8, 59.4, 53.7, 55.2, 52.8, 51.8, 50.1, 49.3, 48.8, 48.4, 47.9, 47.1, 46.1, 45.7, 43.7, 43.1, 41.9, 40.3.

HRMS (ESI) calculated for C$_{31}$H$_{31}$N$_3$O$_6$S$_2$ [M+H]$^+$: 606.1724; found: 606.1724.

(R)-Methyl 2-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6-oxo-1,2,5-dithiazocan-5-yl)acetamido)acetate, 4l

yield: 71% (0.37 g)
white solid, Mp: 118-120 °C

Rf 0.31 (MeOH/ CH2Cl2, 3:97)

1H NMR (500 MHz, CDCl3 δ 7.78 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 7.5 Hz, 2H), 7.42 – 7.02 (m, 4H), 6.01 (br, s, 0.3 H), 4.51 – 4.41 (m, 1H), 4.40 (d, J = 2.2 Hz, 2H), 4.25 (t, J = 8.2 Hz, 1H), 4.08 (d, J = 16.1 Hz, 1H), 4.01 (t, J = 10.6 Hz, 2H), 3.81 – 3.77 (m, 2H), 3.74 (s, 3H), 3.02 – 2.09 (m, 3H), 2.75 – 2.55 (m, 1H).

13C NMR (126 MHz, CDCl3) δ 172.8, 169.9, 168.4, 155.3, 143.8, 143.6, 141.3, 127.8, 127.1, 125.1, 125.0, 124.5, 120.1, 77.3, 77.1, 76.8, 67.2, 54.1, 52.4, 50.8, 47.1, 45.9, 43.0, 41.2, 37.2.

HRMS (ESI) calculated for C25H27N3O6S2 [M+H]+: 530.1414; found: 530.1414.

Methyl 2-(5-(2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)acetyl)-1,2,5-dithiazocane-6-carboxamido)acetate, 4m

yield: 75% (0.40 g)

white solid, Mp: 141-143 °C

Rf 0.42 (MeOH/ CH2Cl2, 5:95)

1H NMR (500 MHz, CDCl3) δ 7.78 (d, J = 7.6 Hz, 2H), 7.62 (d, J = 7.6 Hz, 2H), 7.42 – 7.22 (m, 4H), 7.01 (br, d, J = 3.5 Hz, 1H), 5.93 (br, s, 1H), 4.39 (t, J = 10.9, 2H), 4.30 – 4.18 (m, 1H), 4.04 (dd, J = 7.5, 5.0 Hz, 2H), 3.91 (dd, J = 28.0, 11.3 Hz, 2H), 3.72 (s, 3H), 3.41 (t, J = 13.2 Hz, 2H), 3.11 – 3.04 (m, 2H), 2.80 – 3.02 (m, 2H), 2.49 – 2.29 (m, 2H).

13C NMR (126 MHz, CDCl3) δ 171.1, 170.8, 170.1, 156.6, 143.8, 143.7, 141.3, 127.8, 127.8, 127.1, 125.1, 124.8, 120.0, 67.3, 60.1, 52.5, 47.9, 46.7, 43.3, 41.2, 41.1, 31.9, 30.8, 29.7.

HRMS (ESI) calculated for C26H20N3O6S2 [M+H]+: 544.1570; found: 544.1569.

Methyl 2-((7R)-7-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-benzyl-6-oxo-1,2,5-dithiazocane-4-carboxamido)acetate, 4n
yield: 88% (0.53 g)
white solid, Mp: 121-123 °C
R_f 0.55 (MeOH/ CH_2Cl_2, 5:95)
dr ratio: 3:2.5

^1^H NMR (500 MHz, CDCl_3, mixture of diastereomers) δ 7.78 (dt, J = 9.6, 5.2 Hz, 2H), 7.66 – 7.16 (m, 19H), 6.38 (d, J = 6.4 Hz, 1H), 5.86 (d, J = 11.1 Hz, 0.8H), 5.23 – 5.15 (m, 1.5H), 5.0 – 4.80 (m, 1.2H), 4.78 – 4.73 (m, 1H), 4.61 – 4.50 (m, 0.9H), 4.48 – 4.40 (m, 2.2H), 4.38 – 4.26 (m, 3H), 4.24 – 4.16 (m, 4H), 3.82 (d, J = 6.2 Hz, 1.2H), 3.80 – 3.66 (m, 2.7H), 3.65 (s, 3H), 3.48 (s, 1.2H), 3.35 – 3.26 (m, 3H), 3.24 – 3.18 (m, 3H), 3.16 – 2.75 (m, 3H).

^13^C NMR (126 MHz, CDCl_3, mixture of diastereomers) δ 173.3, 173.1, 169.6, 169.5, 167.8, 155.8, 154.6, 143.4, 143.7, 143.6, 143.3, 141.0, 136.9, 136.7, 129.8, 129.7, 128.8, 128.7, 128.5, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.5, 127.2, 125.0, 124.8, 120.3, 120.1, 120.0, 119.1, 116.4, 67.2, 67.1, 60.9, 60.4, 58.7, 58.0, 57.6, 54.6, 52.8, 52.5, 52.2, 52.1, 52.0, 47.0, 46.9, 46.7, 46.6, 43.7, 43.6, 42.9, 41.7, 41.0, 40.5, 39.4, 39.1, 39.0.

HRMS (ESI) calculated for C_{31}H_{31}N_{3}O_{6}S_{2} [M+H]^+: 606.1727; found: 606.1723.

**7-Isobutyl-8-methyl-1,2-dithia-5,8,14-triazacyclohexadecane-6,9,13-trione, 4o**

yield: 82% (0.37 g)
white solid, Mp: 91-93 °C
R_f 0.30 (MeOH/ CH_2Cl_2, 5:95)

^1^H NMR (500 MHz, CDCl_3) δ 6.97 (t, J = 5.3 Hz, 1H), 5.21 (dd, J = 10.0, 5.5 Hz, 1H), 4.03 – 3.93 (m, 1H), 3.77 – 3.68 (m, 1H), 3.68 – 3.61 (m, 1H), 3.63 – 3.53 (m, 2H), 3.21 (s, 3H), 3.18 – 3.08 (m, 2H), 3.08 – 2.94 (m, 2H), 2.48 – 2.24 (m, 4H), 2.03 – 1.78 (m, 2H), 1.75 – 1.57 (m, 2H), 1.47 (ddddd, J = 13.2, 8.5, 6.7, 3.4 Hz, 1H), 0.99 (d, J = 8.5, 2H), 0.99 (d, J = 8.5, 3H), 0.91 (d, J = 12.8, 3H).
(4R)-Methyl 7-(((S)-4-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-methoxy-5-oxopentanamido)-6-oxo-1,2,5-dithiazocane-4-carboxylate, 4p

yield: 71% (0.42 g)
white solid, Mp: 105-107 °C
Rf 0.28 (MeOH/ CH2Cl2, 5:95)

Single diastereomer isolated from Ugi product is used for disulfide formation

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 7.78 (d, J = 7.5 \text{ Hz}, 2H), 7.68 (d, J = 12.5 \text{ Hz}, 2H), 7.45 - 7.26 (m, 6H), 7.19 (d, J = 6.0 \text{ Hz}, 1H), 6.67 (d, J = 11.6 \text{ Hz}, 1H), 5.76 (d, J = 7.4 \text{ Hz}, 1H), 5.05 - 4.91 (m, 1H), 4.85 - 4.71 (m, 1H), 4.54 - 4.48 (m, 1H), 4.42 (d, J = 8.6 \text{ Hz}, 2H), 4.23 (t, J = 7.1 Hz, 10H), 3.79 (s, 3H), 3.76 (s, 3H), 3.46 (dd, J = 11.1 Hz, 1H), 3.35 (dd, J = 10.5 Hz, 1H), 3.16 (d, J = 18.6 Hz, 1H), 3.06 (dd, J = 21.9 Hz, 1H), 2.86 (dt, J = 15.8, 6.5 Hz, 2H), 1.98 (td, J = 14.2, 7.8 Hz, 2H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta 172.48, 171.15, 169.70, 168.95, 155.93, 143.86, 143.72, 141.31, 127.74, 127.10, 125.12, 120.00, 77.30, 77.05, 76.79, 67.06, 54.49, 53.36, 53.14, 52.60, 52.23, 47.17, 42.40, 42.28, 31.92, 28.15.

HRMS (ESI) calculated for C\(_{28}H\(_{31}\)N\(_3\)O\(_8\)S\(_2\) [M+H]\(^+\): 602.1625; found: 602.1620.

Disulfide 5a, 5b and 5c (Mixture of regioisomers)

0.1 mmol scale
Yield: 75% (0.75 mg)
White solid, Mp: 125-128 °C
Rf 0.55 (MeOH/ CH₂Cl₂, 5:95)

¹H NMR (500 MHz, CDCl₃) δ 7.80 (d, J = 7.4 Hz, 4H), 7.61 (dd, J = 7.5, 2.4 Hz, 4H), 7.44 (t, J = 7.5 Hz, 4H), 7.41 – 7.30 (m, 4H), 7.30 (s, 2H), 7.11 (d, J = 8.1 Hz, 1H), 5.91 (s, 1H), 5.01 (d, J = 8.5 Hz, 1H). 4.93 (s, 1H), 4.77 – 4.71 (m, 1H), 4.53 – 4.40 (m, 4H), 4.25 (t, J = 7.2 Hz, 2H), 4.03 (d, J = 1.3 Hz, 1H), 3.82 (d, J = 2.6 Hz, 7H), 3.74 – 3.65 (m, 2H), 3.52 (t, J = 7.6 Hz, 2H), 3.39 (d, J = 15.0 Hz, 2H), 3.18 – 3.06 (m, 3H), 3.06 – 3.00 (m, 2H), 2.98 (s, 1H), 2.88 (d, J = 14.3 Hz, 2H), 2.69 – 2.59 (m, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 172.48, 171.15, 169.70, 156.31, 143.86, 143.72, 141.31, 127.74, 127.10, 125.12, 120.00, 77.30, 77.05, 76.79, 67.06, 53.36, 53.14, 52.60, 52.23, 47.17, 42.40, 42.28, 31.92, 28.15.

HRMS (ESI) calculated for C₂₇H₃₂N₃O₆S₄ [M+H]⁺: 634.1168; found: 634.1168.
Ms/Ms analysis of Disulfide Regioisomers 5a, 5a and 5c

Structural assignment based on MS/MS analysis:
All the regioisomers showed common m/z value at 412 (M+H-Fmoc+H)+ which can be rationalized by McLafferty-type rearrangement involving a γ-hydrogen migration from the fluorenyl moiety. Peak at 8.9 clearly shows the disulfide connectivity 5b due to distinct m/z values at 341.01 which can be attributed by the formation of dehydroalanine of the cysteine residues followed by N-terminal amide cleavage (see supporting information) which is not observed in other two. Also, the distinct m/z value at 367.02 corresponds to cleavage of C-N bond from the tertiary amide followed by H₂S liberation (see supporting information. Which also supports the peak at 8.9 was found to be regioisomer 5b. The detailed mechanistic investigation and MS/MS analysis of all the regioisomers are under investigation.
Proposed disulfide connectivity 5b from Ms/Ms fragmentation: HPLC Rt = 8.9 min

\[
\text{FmocHN} \quad \xrightarrow{\text{Tertiary amide cleavage and H}_2\text{S libration}} \quad \text{FmocHN} \quad \xrightarrow{-\text{MeOH}}
\]

\[
[M+H] = 634.2 \quad \rightarrow \quad [M-\text{Fme-CO}_2+H] = 412.04
\]

\[
[M-\text{B1-H}_2\text{S}+H] = 367.02 \quad \rightarrow \quad [M-\text{Fme-CO}_2-2\text{H}_2\text{S}-2\text{H}] = 341.01
\]

\[
[M-\text{Fme-CO}_2-\text{MeOH}] = 312.04
\]
Proposed disulfide 5c connectivity from Ms/Ms fragmentation: HPLC Rt: 9.6 min
MS/MS 634 @ RT8.9
MS/MS m/z 634 @ RT9.6
Msms m/z 634 @ RT10.7
$^1$H NMR of methyl S–trityl–L–cysteinate

$^{13}$C NMR of methyl S–trityl–L–cysteinate
SFC–HPLC and ESI–MS of methyl S-trityl–L-cysteinate
$^1$H NMR of methyl N-formyl-S-trityl-L-cysteinate

$^{13}$C NMR of methyl N-formyl-S-trityl-L-cysteinate
SFC-HPLC and ESI-MS of methyl N-formyl-S-trityl-L-cysteinate
$^1$H NMR of methyl (R)-2-isocyano-3-(tritylthio)propanoate

$^{13}$C NMR of methyl (R)-2-isocyano-3-(tritylthio)propanoate
SFC–HPLC and ESI–MS of methyl (R)-2-isocyano-3-(tritylthio)propanoate
$^1$H NMR of methyl S-trityl-D-cysteinate

$^{13}$C NMR of methyl S-trityl-D-cysteinate
SFC-HPLC and ESI-MS of methyl S-trityl-D-cysteinate
$^1$H NMR of methyl N-formyl-S-trityl-D-cysteinate

$^{13}$C NMR of methyl N-formyl-S-trityl-D-cysteinate
SFC-HPLC and ESI-MS of methyl N-formyl-S-trityl-D-cysteinate
$^1$H NMR of methyl (S)-2-isocyano-3-(tritylthio)propanoate

$^{13}$C NMR of methyl (S)-2-isocyano-3-(tritylthio)propanoate
SFC-HPLC and ESI-MS of methyl (S)-2-isocyano-3-(tritylthio)propanoate
Chiral SFC–HPLC chromatogram of enantiopure methyl (R)-2-isocyano-3-(tritylthio)propanoate. 

**Method:** Reprosil Chiral-AM column (4.6 × 250 mm, 5µm) with 5 - 30% MeOH in CO₂ for 9 min; γ = 254 nm.
Chiral SFC–HPLC chromatogram of enantiopure methyl (S)-2-isocyanopropylthio)propanoate
Method: Reprosil Chiral-AM column (4.6 × 250 mm, 5μm) with 5 - 30% MeOH in CO₂ for 9 min; γ = 254 nm.
Chiral SFC–HPLC chromatogram of 1:1 mixture of methyl (R+S)–2–isocyano–3–(tritylthio)propanoate, 4a and 4b

**Method:** Reprosil Chiral-AM column (4.6 × 250 mm, 5µm) with 5 - 30% MeOH in CO₂ for 9 min; γ = 254 nm.
$^1$H NMR of 2-(tritylsulfanyl)ethanamine

$^{13}$C NMR of 2-(tritylsulfanyl)ethanamine
SFC-HPLC and ESI-MS of 2-(tritylsulfanyl)ethanamine
$^1$H NMR of 2-(tritylsulfanyl)ethanamine 2-(tritylthio)acetic acid

$^{13}$C NMR of 2-(tritylsulfanyl)ethanamine 2-(tritylthio)acetic acid
SFC-HPLC and ESI-MS of 2-(tritylsulfanyl)ethanamine 2-(tritylthio)acetic acid
$^1$H NMR of N-methoxy-N-methyl-2-(tritylthio)acetamide

$^{13}$C NMR of N-methoxy-N-methyl-2-(tritylthio)acetamide
SFC-HPLC and ESI-MS of N-methoxy-N-methyl-2-(tritylthio)acetamide
$^1$H NMR of 3-(tritylthio)propanoic acid

$^{13}$C NMR of 3-(tritylthio)propanoic acid
SFC-HPLC and ESI-MS of 3-(tritylthio)propanoic acid
$^1$H NMR of N-methoxy-N-methyl-3-(tritylthio)propanamide

$^{13}$C NMR of N-methoxy-N-methyl-3-(tritylthio)propanamide
SFC-HPLC and ESI-MS of N-methoxy-N-methyl-3-(tritythio)propanamide
$^1$H NMR of N-(2-(tritylthio)ethyl)formamide

$^{13}$C NMR of N-(2-(tritylthio)ethyl)formamide
SFC-HPLC and ESI-MS of N-(2-(tritylthio)ethyl)formamide
$^1$H NMR of (2-isocyanethyl)(trityl)sulfane

$^{13}$C NMR of (2-isocyanethyl)(trityl)sulfane
SFC-HPLC and ESI-MS of (2-isocyanethyl)(trityl)sulfane
$^1$H NMR of (5R,11R)-methyl 7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3a

$^{13}$C NMR of (5R,11R)-methyl 7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3a
SFC-HPLC and HRMS of (5R,11R)-methyl 7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3a
$^1$H NMR of (5R,11R)-methyl 7-(3,4-dichlorobenzyl)-1-(9H-fluoren-9-yl)-8-isobutyl-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3b

$^{13}$C NMR of (5R,11R)-methyl 7-(3,4-dichlorobenzyl)-1-(9H-fluoren-9-yl)-8-isobutyl-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3b
SFC-HPLC and HRMS of (5R,11R)-methyl 7-(3,4-dichlorobenzyl)-1-(9H-fluoren-9-yl)-8-isobutyl-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3b
$^1$H NMR of (12R)-methyl 8-(((R)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(tritylthio)propanoyl)-9-isopropyl-2,2-dimethyl-4,10-dioxo-12-((tritylthio)methyl)-3-oxa-5,8,11-triazatridecan-13-oate, 3c

$^{13}$C NMR of (12R)-methyl 8-(((R)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(tritylthio)propanoyl)-9-isopropyl-2,2-dimethyl-4,10-dioxo-12-((tritylthio)methyl)-3-oxa-5,8,11-triazatridecan-13-oate, 3c
SFC-HPLC and HRMS of (12R)-methyl 8-(((R)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(tritylthio)propanoyl)-9-isopropyl-2,2-dimethyl-4,10-dioxo-12-((tritylthio)methyl)-3-oxa-5,8,11-triazatridecan-13-oate, 3c
$^1$H NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-8-isobutyl-3,6,9-trioxo-7-phenethyl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3d

$^{13}$C NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-8-isobutyl-3,6,9-trioxo-7-phenethyl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3d
SFC-HPLC and HRMS of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-8-isobutyl-3,6,9-trioxo-7-phenethyl-5,11-bis(tritythio)methyl)-2-oxa-4,7,10-triazadecan-12-oate, 3d
$^1$H NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-propyl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3e

$^{13}$C NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-propyl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3e
SFC-HPLC and HRMS of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-propyl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3e
$^1$H NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-8-isopropyl-7-methyl-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3f

$^{13}$C NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-8-isopropyl-7-methyl-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3f
SFC-HPLC and HRMS of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-8-isopropyl-7-methyl-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3f
$^1$H NMR of (5R,11R)-methyl 7-allyl-8-benzyl-1-{(9H-fluoren-9-y1)-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3g

$^{13}$C NMR of (5R,11R)-methyl 7-allyl-8-benzyl-1-{(9H-fluoren-9-y1)-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3g
SFC-HPLC and HRMS of (5R,11R)-methyl 7-allyl-8-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3g
$^1$H NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-trityl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3h

$^{13}$C NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-trityl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3h
SFC-HPLC and HRMS of $^1$H NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-trityl-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3h
$^1$H NMR of (5R,14R)-methyl 10-benzyl-1-(9H-fluoren-9-yl)-11-isobutyl-3,6,9,12-tetraoxo-5,14-bis((tritylthio)methyl)-2-oxa-4,7,10,13-tetraazapentadecan-15-oate, 3i

$^{13}$C NMR of (5R,14R)-methyl 10-benzyl-1-(9H-fluoren-9-yl)-11-isobutyl-3,6,9,12-tetraoxo-5,14-bis((tritylthio)methyl)-2-oxa-4,7,10,13-tetraazapentadecan-15-oate, 3i
SFC-HPLC and HRMS of (5R,14R)-methyl 10-benzyl-1-(9H-fluoren-9-yl)-11-isobutyl-3,6,9,12-tetraoxo-5,14-bis((tritylthio)methyl)-2-oxa-4,7,10,13-tetraazapentadecan-15-oate, 3i
$^1$H NMR of (R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-(2-(tritylthio)ethyl)-11-((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3j

$^{13}$C NMR of (R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-(2-(tritylthio)ethyl)-11-((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3j
SFC-HPLC and HRMS of (R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-{2-(tritylthio)ethyl}-11-((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3j
$^1$H NMR of (10R)-methyl 6-benzyl-1-(9H-fluoren-9-yl)-3,8-dioxo-7,10-bis((tritylthio)methyl)-2-oxa-4,6,9-triazaundecan-11-oate, 3k

$^{13}$C NMR of (10R)-methyl 6-benzyl-1-(9H-fluoren-9-yl)-3,8-dioxo-7,10-bis((tritylthio)methyl)-2-oxa-4,6,9-triazaundecan-11-oate, 3k
SFC-HPLC and HRMS of (10R)-methyl 6-benzyl-1-(9H-fluoren-9-yl)-3,8-dioxo-7,10-bis((tritylthio)methyl)-2-oxa-4,6,9-triazaundecan-11-oate, 3k
$^1$H NMR of (R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-(2-(tritylthio)ethyl)-5-((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3l

$^{13}$C NMR of (R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7-(2-(tritylthio)ethyl)-5-((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3l
SFC-HPLC and HRMS of (R)-methyl 1-([9H-fluoren-9-yl]-3,6,9-trioxo-7-(2-(tritylthio)ethyl)-5-((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3l
$^1$H NMR of methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7,8-bis(2-(tritylthio)ethyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3m

$^{13}$C NMR of methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7,8-bis(2-(tritylthio)ethyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3m
SFC-HPLC and HRMS of methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7,8-bis(2-(tritylthio)ethyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3m
H NMR of (5R)-methyl 7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,8-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadecan-12-oate, 3n

C NMR of (5R)-methyl 7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-trioxo-5,8-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadecan-12-oate, 3n
SFC-HPLC and HRMS of (5R)-methyl 7-benzyl-1-(9H-fluoren-9-yl)-3,6,9-triexo-5,8-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3n
$^1$H NMR of N1-methyl-N1-(4-methyl-1-oxo-1-((2-(tritylthio)ethyl)amino)pentan-2-yl)-N4-(2-(tritylthio)ethyl)succinamide, 3o

$^{13}$C NMR of N1-methyl-N1-(4-methyl-1-oxo-1-((2-(tritylthio)ethyl)amino)pentan-2-yl)-N4-(2-(tritylthio)ethyl)succinamide, 3o
SFC-HPLC and HRMS of N<sup>1</sup>-methyl-N<sup>4</sup>-(4-methyl-1-oxo-1-((2-(tritylthio)ethyl)amino)pentan-2-yl)-N<sub>4</sub>-(2-(tritylthio)ethyl)succinamide, 30
$^1$H NMR of (5S,13S)-methyl 1-(9H-fluoren-9-yl)-5-(methoxycarbonyl)-3,8,11-trioxo-10,13-bis((tritylthio)methyl)-2-oxa-4,9,12-triazatetradecan-14-oate, 3p

$^{13}$C NMR of (5S,13S)-methyl 1-(9H-fluoren-9-yl)-5-(methoxycarbonyl)-3,8,11-trioxo-10,13-bis((tritylthio)methyl)-2-oxa-4,9,12-triazatetradecan-14-oate, 3p
SFC-HPLC and HRMS of (5S,13S)-methyl 1-(9H-fluoren-9-yl)-5-(methoxycarbonyl)-3,8,11-trioxo-10,13-bis((tritylthio)methyl)-2-oxa-4,9,12-triazatetradecan-14-oate, 3p
$^1$H NMR of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7,8-bis(2-(tritylthio)ethyl)-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3q
SFC-HPLC and HRMS of (5R,11R)-methyl 1-(9H-fluoren-9-yl)-3,6,9-trioxo-7,8-bis(2-(tritylthio)ethyl)-5,11-bis((tritylthio)methyl)-2-oxa-4,7,10-triazadodecan-12-oate, 3q
$^1$H NMR of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-benzyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4a

$^{13}$C NMR of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-benzyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4a
SFC-HPLC and HRMS of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-benzyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4a
$\text{H NMR of } (4R,10R)\text{-methyl 10-}[[([9H-fluoren-9-yl]methoxy)carbonyl]amino)-8-(3,4-dichlorobenzyl)-7-isobutyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4b}$

$\text{13C NMR of } (4R,10R)\text{-methyl 10-}[[([9H-fluoren-9-yl]methoxy)carbonyl]amino)-8-(3,4-dichlorobenzyl)-7-isobutyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4b}$
SFC-HPLC and HRMS of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-(3,4-dichlorobenzyl)-7-isobutyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4b
$^1$H NMR of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-(2-((tert-butoxycarbonyl)amino)ethyl)-7-isopropyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4c

$^{13}$C NMR of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-(2-((tert-butoxycarbonyl)amino)ethyl)-7-isopropyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4c
SFC-HPLC and HRMS of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-9-{2-((tert-butoxycarbonyl)amino)ethyl}-7-isopropyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4c
$^1$H NMR of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-7-isobutyl-6,9-dioxo-8-phenethyl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4d

$^{13}$C NMR of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-7-isobutyl-6,9-dioxo-8-phenethyl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4d
SFC-HPLC and HRMS of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-7-isobutyl-6,9-dioxo-8-phenethyl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4d
\(^1\)H NMR of \((4R,10R)\)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6,9-dioxo-8-propyl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4e

\(^{13}\)C NMR of \((4R,10R)\)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6,9-dioxo-8-propyl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4e
SFC-HPLC and HRMS of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6,9-dioxo-8-propyl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4e
$^1$H NMR of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-7-isopropyl-8-methyl-6,9-dioxo-1,2-dithia-5,8-
diazacycloundecane-4-carboxylate, 4f

$^{13}$C NMR of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-7-isopropyl-8-methyl-6,9-dioxo-1,2-dithia-5,8-
diazacycloundecane-4-carboxylate, 4f
SFC-HPLC and HRMS of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-7-isopropyl-8-methyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4f
$^1$H NMR of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-allyl-7-benzyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4g

$^{13}$C NMR of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-allyl-7-benzyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4g
SFC-HPLC and HRMS of (4R,10R)-methyl 10-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-allyl-7-benzyl-6,9-dioxo-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4g
$^1$H NMR of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6,9-dioxo-8-trityl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4h

$^{13}$C NMR of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6,9-dioxo-8-trityl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4h
SFC-HPLC and HRMS of (4R,10R)-methyl 10-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6,9-dioxo-8-trityl-1,2-dithia-5,8-diazacycloundecane-4-carboxylate, 4h
\[ ^1H \text{ NMR of } (4R,13R) - \text{methyl } 13 - \text{(((9H-fluoren-9-yl)methoxy)carbonyl)amino} - 8\text{-benzyl-7-isobutyl-6,9,12-trioxo-1,2-dithia-5,8,11-triazacyclotetradecane-4-carboxylate, 4i} \]

\[ ^{13}C \text{ NMR of } (4R,13R) - \text{methyl } 13 - \text{(((9H-fluoren-9-yl)methoxy)carbonyl)amino} - 8\text{-benzyl-7-isobutyl-6,9,12-trioxo-1,2-dithia-5,8,11-triazacyclotetradecane-4-carboxylate, 4i} \]
SFC-HPLC and HRMS of (4R,13R)-methyl 13-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-8-benzyl-7-isobutyl-6,9,12-trioxo-1,2-dithia-5,8,11-triazacyclotetradecane-4-carboxylate, 4i
$^1$H NMR of (R)-methyl 8·(2·((((9H-fluoren-9-yl)methoxy)carbonyl)amino)acetyl)-6-oxo-1,2,5,8-dithiadiazecane-4-carboxylate, 4j

$^{13}$C NMR of (R)-methyl 8·(2·((((9H-fluoren-9-yl)methoxy)carbonyl)amino)acetyl)-6-oxo-1,2,5,8-dithiadiazecane-4-carboxylate, 4j
SFC-HPLC and HRMS of (R)-methyl 8-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)acetyl)-6-oxo-1,2,5,8-dithiadiazecane-4-carboxylate, 4j
$^1$H NMR of (4R)-methyl 7-{(2-{[(9H-fluoren-9-yl)methoxy]carbonyl}amino)-N-benzylacetamido)-6-oxo-1,2,5-dithiazocane-4-carboxylate, 4k

$^{13}$C NMR of (4R)-methyl 7-{2-{[(9H-fluoren-9-yl)methoxy]carbonyl}amino)-N-benzylacetamido)-6-oxo-1,2,5-dithiazocane-4-carboxylate, 4k
SFC-HPLC and HRMS of (4R)-methyl 7-{2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-N-benzylacetamido}-6-oxo-1,2,5-dithiazocane-4-carboxylate, 4k
$^{1}H$ NMR of (R)-methyl 2-\(2-\{7-(((9H\text{-fluoren-9-yl})\text{methoxy})\text{carbonyl]}\text{amino}\}-6\text{-oxo-1,2,5-dithiazocan-5-yl})\text{acetamido}\)acetate, 4l

$^{13}C$ NMR of (R)-methyl 2-\(2-\{7-(((9H\text{-fluoren-9-yl})\text{methoxy})\text{carbonyl]}\text{amino}\}-6\text{-oxo-1,2,5-dithiazocan-5-yl})\text{acetamido}\)acetate, 4l
SFC-HPLC and HRMS of (R)-methyl 2-(2-(7-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-6-oxo-1,2,5-dithiazocan-5-yl)acetamido)acetate, 4l
\(^1\)H NMR of methyl 2\(\cdot\)\((5\cdot\(2\cdot((9H\text{-}9\text{-yl})\text{-}9\text{yl})\text{methoxy} \text{carbonyl} \text{amino} \text{acetyl})\cdot1,2,5\text{-dithiazocane} \cdot6\text{-carboxamido} \text{acetate}, 4m

\(^{13}\)C NMR of methyl 2\(\cdot\)\((5\cdot\(2\cdot((9H\text{-}9\text{yl})\text{-}9\text{yl})\text{methoxy} \text{carbonyl} \text{amino} \text{acetyl})\cdot1,2,5\text{-dithiazocane} \cdot6\text{-carboxamido} \text{acetate}, 4m
SFC-HPLC and HRMS of methyl 2-(5-((9H-fluoren-9-yl)methoxy)carbonyl)amino)acetyl)-1,2,5-dithiazocane-6-carboxamido)acetate, 4m
$^1$H NMR of methyl 2-(((7R)-7-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-benzyl-6-oxo-1,2,5-dithiazocane-4-carboxamido)acetate, 4n

$^{13}$C NMR of methyl 2-(((7R)-7-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-benzyl-6-oxo-1,2,5-dithiazocane-4-carboxamido)acetate, 4n
SFC-HPLC and HRMS of methyl 2-(((7R)-7-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-benzyl-6-oxo-1,2,5-dithiazocane-4-carboxamido)acetate, 4n
$^1$H NMR of 7-isobutyl-8-methyl-1,2-dithia-5,8,14-triazacyclohexadecane-6,9,13-trione, 4o

$^{13}$C NMR of 7-isobutyl-8-methyl-1,2-dithia-5,8,14-triazacyclohexadecane-6,9,13-trione, 4o
SFC-HPLC and HRMS of 7-isobutyl-8-methyl-1,2-dithia-5,8,14-triazacyclohexadecane-6,9,13-trione, 4o
$^1$H NMR of (4R)-methyl 7-(((S)-4-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-methoxy-5-oxopentanamido)-6-oxo-1,2,5-dithiazocane-4-carboxylate, 4p

$^{13}$C NMR of (4R)-methyl 7-(((S)-4-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-methoxy-5-oxopentanamido)-6-oxo-1,2,5-dithiazocane-4-carboxylate, 4p
HPLC and HRMS of (4R)-methyl 7-(((S)-4-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-methoxy-5-oxopentanamido)-6-oxo-1,2,5-dithiazocane-4-carboxylate, 4p
$^1$H NMR of disulfide 5 (regioisomeric mixture)
$^{13}$C NMR of disulfide 5 (regioisomeric mixture)

HPLC and HRMS of NMR of disulfide 5 (regioisomeric mixture)