

A Microwave Enhanced Cross-Metathesis Approach to Peptidomimetics

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Supporting Information

General information: All reactions were carried out under an argon atmosphere, using oven-dried glassware. All chemicals were purchased from commercial sources and were used as received without further purification. Peptide coupling reactions were monitored in some cases using a Micromass Platform LC instrument. Acryloylations were monitored by thin-layer chromatography (app tLC) on pre-coated silica gel plates (254mm) and in some cases using a using a Micromass Platform LC instrument. All yields quoted are isolated yields unless otherwise stated. ¹H NMR spectra were recorded at 300MHz and ¹³C at 75MHz on a Bruker AMX 300 at ambient temperature unless otherwise stated. The chemical shifts for ¹H and ¹³C are quoted in ppm relative to residual protiated signals of the solvent. Mass spectra were obtained on a VG70-SE or a MAT 900 XP mass spectrometer. Infrared spectra were obtained on a Shimadzu FTIR 8700 Spectrophotometer. Optical rotations were measured using monochromatic light at 589 nm with a 1 dm cell and either a model AA-1000 polarimeter, at 294 K or a polAAR 2000 polarimeter at ambient temperatures. Melting points were measured, where appropriate, with a Gallenkamp apparatus and are uncorrected.

A note on the assignment of ¹H NMR – Superscript a and b distinguish between diastereotopic protons on the same carbon and thus are not intended to uniquely define protons within the same molecule.

Protocol I

Protected amino acid [3.4 mmol] and HOBt [455 mg, 3.4 mmol] were dissolved in DCM [15 ml] and the mixture stirred vigorously. EDC [1.2 g, 6.8 mmol], DIPEA [1.18 ml, 6.8 mmol] and homoallyl amine [0.31 ml, 3.4 mmol] were added, in this

order, and the resultant mixture stirred for 4 h. The mixture was then diluted with DCM [15 ml], and washed with HCl [2x10 ml, 0.5 M], NaHCO₃ [2x10 ml, 0.5 M], water [2x10 ml] and saturated brine [10 ml], dried with anhydrous MgSO₄, and purified by column chromatography [petroleum ether and ethyl acetate].

Protocol II

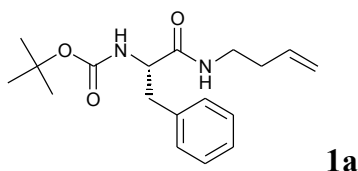
An amino acid ester [1.7 mmol, as the HCl salt] and Et₃N [0.5 ml, 3.7 mmol] were stirred in DCM [10 ml] under anhydrous conditions. Acryloyl chloride [2 mmol, as a 1 M solution in DCM] was added over 1 h, and the resultant mixture stirred overnight. The DCM was removed under reduced pressure, and ethyl acetate added [80 ml]. The solid was filtered off and the filtrate was washed with HCl [10 ml, 0.5 M], NaHCO₃ [2x10 ml, 0.5 M], water [10 ml] and saturated brine [10 ml], dried with anhydrous MgSO₄, and purified by column chromatography [petroleum ether and ethyl acetate].

Protocol III – optimised microwave cross metathesis

An electron deficient olefin [0.1 mmol] and the more reactive cross metathesis partner olefin [1.3 equivalents] were stirred in DCM in a microwave vial. Grubb's 2nd generation catalyst [18 mol%] was added, and the mixture stirred and subjected to microwave radiation [300 W, 100°C] for 30 mins. The reaction mixture was then degassed with argon for approximately 1 min, and the mixture stirred and subjected to microwave radiation [300 W, 100°C] for a further 30 mins. The mixture was then purified by column chromatography.

Compound 1a

BocPheOH [1.7g, 6.4 mmol] was reacted with homoallyl amine hydrochloride according to protocol I. purification yielded a waxy solid [1.3g, 64%, mp 64 – 66°C].



¹H NMR (CDCl₃) – 7.17-7.29 (m, 5 H, Ar-H); 5.99 (br, 1 H, NH); 5.61 (ddt, *J* = 17.1, *J* = 10.7, *J* = 6.7, 1 H, H₂CCH=CH₂); 5.20 (br, 1 H, NH); 4.91-4.98 (m, 2 H,

H₂CCH=CH₂); 4.29 (app q, *J* = 7.0, 1 H, NHCH); 3.13 (m, 2 H, NHCH₂); 3.01 (m, 2 H, CHCH₂); 2.02-2.16 (m, 2 H, CH₂CHCH₂); 1.38 (s, 9 H, C(CH₃)₃).

¹³C NMR (CDCl₃) – 171.1 (C=O); 155.4 (C=O); 136.9 (C); 134.9 (CH); 129.3 (CH); 128.6 (CH); 126.9 (CH); 117.1 (CH₂); 80.0 (C); 56.0 (CH); 38.9 (CH₂); 38.4 (CH₂); 33.4 (CH₂); 28.3 (CH₃).

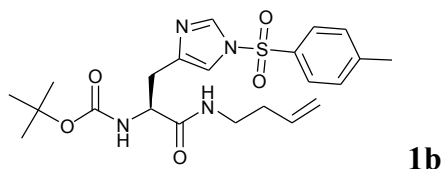
HRMS calc. for C₁₉H₂₈N₂O₄– 319.20216 (M+H); found 319.20270.

IR, solution cell, DCM (cm⁻¹) – 3427; 2978; 2934; 1709; 1676.

[α]²⁵_D +4.9 (*c* 0.50, CHCl₃)

Compound 1b

BocHis(Tos)OH [654 mg, 0.48 mmol] was reacted with homoallyl amine according to protocol I. Purification yielded a highly viscous clear liquid [537 mg, 73%].



¹H NMR (CDCl₃) – 8.00 (br s, 1 H, N=CH[?]); 7.92 (d, *J* = 8.2, 2 H, Ts-*H*); 7.35 (d, *J* = 8.0, 2 H, Ts-*H*); 7.09 (s, 1 H, NCH=C); 6.61 (br s, 1 H, NH); 5.86 (d, *J* = 7.3, 1 H, Ts-*H*); 5.63 (app ddt, 1 H, *J* = 17.3, *J* = 10.6, *J* = 6.8, H₂CCH=CH₂); 4.96-5.02 (m, 2 H, CH=CH₂); 4.40 (br s, 1 H, HNCH); 3.17 (app q, *J* = 5.9, 2 H, NHCH₂); 3.03 (dd, *J* = 5.6, *J* = 14.8, 1 H CH^aH^bIm); 2.90 (dd, *J* = 4.3, *J* = 14.6, 1 H CH^aH^bIm); 2.34 (s, 3 H, ArCH₃); 2.09 (app q, *J* = 6.7, 2 H, CH₂CH₂CHCH₂); 1.40 (s, 9 H, C(CH₃)₃).

¹³C NMR (MeOH *d*₄) – 173.7 (C=O); 157.5 (C=O); 148.0 (C); 141.7 (C); 138.1 (CH); 136.5 (CH); 136.2 (CH); 131.7 (CH); 128.7 (CH); 117.5 (CH₂); 116.4 (CH); 80.6 (C); 55.5 (CH); 39.8 (CH₂); 34.6 (CH₂); 31.7 (CH₂); 30.7 (CH₂); 28.7 (CH₂); 21.7 (CH₃).

IR, solution cell, DCM (cm⁻¹) – 3423; 2978; 2934; 1711; 1672; 1593.

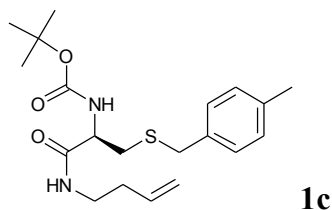
HRMS calc. for C₂₂H₃₀N₄O₅S – 463.20097 (M+H); found 463.200480.

[α]¹⁴_D +21.2 (*c* 0.62, CHCl₃)

Compound 1c

BocCys(4-MeBzl)OH [2.0 g, 6.2 mmol], HOBt [873 mg, 6.5 mmol], HBTU [2.3 g, 6.1 mmol] and DIPEA [1.1 ml, 6.2 mmol] were stirred in DCM [5 ml] and DMF [5 ml] for 20 min. Homoallyl amine hydrochloride [335 mg, 3.1 mmol] and DIPEA [0.6 ml, 3.4 mmol] in DCM [2 ml] were added, and the resultant mixture stirred for 3 h.

The majority of the solvent was removed under reduced pressure. DCM [20 ml] was then added, and the mixture washed with HCl [2x10 ml, 1 M], LiCl [2 x 10ml, 10%], NaHCO₃ [2x10 ml, 0.5 M], water [2x10 ml] and saturated brine [10 ml], dried with anhydrous MgSO₄, and purified by column chromatography [petroleum ether and ethyl acetate], yielding a waxy solid [989 mg, 84%].



¹H NMR (CDCl₃) – 7.22 (d, *J* = 8.0, 2 H, Ph-*H*); 7.12 (d, *J* = 7.8, 2 H, Ph-*H*); 6.26 (br t, NHCH₂); 5.75 (app ddt, *J* = 17.1, *J* = 10.3, *J* = 6.8, 1 H, H₂CCH=CH₂); 5.26 (br, 1 H, NHCH); 5.06 – 5.13 (m, 2 H, H₂C=CH); 4.18 (br app q, *J* = 6.0, 1 H, NHCH); 3.71 (s, 2 H, SCH₂Ar); 3.29 – 3.36 (m, 2 H, NHCH₂); 2.86 (dd, *J* = 5.6, *J* = 13.9, 1 H, CHCH^aH^bS); 2.70 (dd, *J* = 9.6, *J* = 13.9, 1 H, CHCH^aH^bS); 2.32 (s, 3 H, ArCH₃); 2.22 – 2.29 (m, 2 H, NHCH₂CH₂); 1.45 (s, 9 H, C(CH₃)₃).

¹³C NMR (CDCl₃) – 170.5 (C=O); 155.4 (C=O); 136.9 (C); 135.0 (CH); 134.9 (C); 129.3 (CH); 128.9 (CH); 117.4 (CH₂); 80.3 (C); 53.8 (CH); 38.6 (CH₂); 36.2 (CH₂); 33.8 (CH₂); 33.6 (CH₂); 28.3 (CH₃); 21.1 (CH₃).

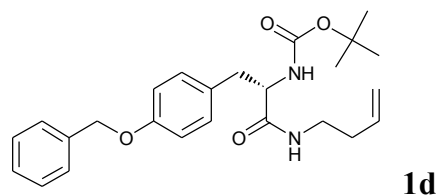
IR, solution cell, DCM (cm⁻¹) – 3423; 2974; 2930; 2330; 1713; 1676; 1489.

HRMS calc. for C₂₀H₃₀N₂O₃S- 379.20553 (M+H); found 379.20468.

[α]¹⁹_D +3.9 (*c* 0.42, CHCl₃)

Compound 1d

BocTyr(Bzl)OH [594 mg, 1.6 mmol] was reacted with homoallyl amine according to protocol I. Purification yielded a waxy solid [417 mg, 61%].



¹H NMR (DMSO *d*₆) – 7.86 (app t, *J* = 5.6, 1 H, NHCH₂); 7.30-7.43 (m, 5 H, CH₂Ar-*H*); 7.13 (d, *J* = 8.5, 2 H, *H* ortho to O); 6.89 (d, *J* = 8.5, 2 H, *H* meta to O); 6.82 (d, *J* = 8.5, 1 H, NHCH); 5.73 (app ddt, 1 H, *J* = 17.2, *J* = 10.3, *J* = 6.7, H₂CCH=CH₂); 5.04 (s, 2 H, OCH₂Ph); 4.96-5.02 (m, 2 H, CH=CH₂); 4.02 (app dt, *J* = 4.6, *J* = 9.1, 1

H, NHCH); 3.00-3.20 (m, 2 H, NHCH₂); 2.79 (dd, *J* = 8.9, *J* = 13.7, 1 H CHCH^aH^bAr); 2.64 (dd, *J* = 9.8, *J* = 13.5, 1 H CHCH^aH^bAr); 2.10 (app q, *J* = 6.9, 2 H, CH₂CH₂CHCH₂); 1.29 (s, 9 H, C(CH₃)₃).

¹³C NMR (DMSO *d*₆) – 171.4 (C=O); 156.8 (C=O); 155.1 (C); 137.2 (C); 135.9 (CH); 130.2 (C); 130.1 (CH); 128.3 (CH); 127.7 (CH); 127.5 (CH); 116.1 (CH₂); 114.3 (CH); 77.9 (C); 69.0 (CH₂); 55.9 (CH); 37.9 (CH₂); 36.8 (CH₂); 33.3 (CH₂); 28.1 (CH₃).

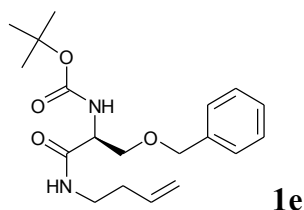
IR, solution cell, DCM (cm⁻¹) – 3427; 2977; 2934; 1711; 1676; 1611; 1506.

HRMS calc. for C₂₅H₃₂N₂O₄ - 425.24402 (M+H); found 425.24476.

[α]¹⁶_D +14.7 (*c* 0.63, CHCl₃)

Compound 1e

BocSer(Bzl)OH [1.0 g, 3.4 mmol] was reacted with homoallyl amine according to protocol I. Purification yielded a clear liquid [541 mg, 46%].



¹H NMR (CDCl₃) – 7.26-7.40 (m, 5 H, Ar-*H*); 6.49 (br t, *J* = 5.4, 1 H, NHCH₂); 5.71 (ddt, *J* = 17.1, *J* = 10.2, *J* = 6.7, 1 H, H₂CCH=CH₂); 5.41 (br, 1 H, NH); 4.92-5.00 (m, 2 H, H₂CCH=CH₂); 4.48 (d, *J* = 11.8, 1 H, OCH^aH^bPh); 4.42 (d, *J* = 11.8, 1 H, OCH^aH^bPh); 4.19 (br, 1 H, NHCH); 3.81 (dd, *J* = 4.0, *J* = 9.1, 1 H, NHCHCH^aH^b); 3.50 (dd, *J* = 9.4, *J* = 6.4, 1 H, NHCHCH^aH^b); 3.17-3.34 (m, 2 H, NHCH₂); 2.16 (app q, *J* = 6.4, 2 H, CH₂CH₂CHCH₂); 1.39 (s, 9 H, C(CH₃)₃).

¹³C NMR (MeOH *d*₄) – 172.8 (C=O); 157.6 (C=O); 139.2 (C); 136.6 (CH); 129.4 (CH); 128.9 (CH); 128.8 (CH); 117.1 (CH₂); 80.9 (C); 74.1 (CH₂); 71.1 (CH₂); 56.2 (CH); 39.9 (CH₂); 34.6 (CH₂); 28.7 (CH₃).

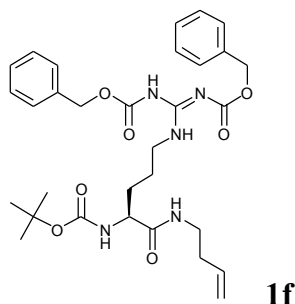
HRMS calc. for C₂₂H₃₀N₄O₅S – 371.19413 (M+Na); found 371.19302

IR, solution cell, DCM (cm⁻¹) – 3425; 2978; 2872; 1713; 1674.

[α]¹⁹_D +9.4 (*c* 0.64, CHCl₃).

Compound 1f

BocArg(diZ)OH [869 mg, 1.6 mmol] was reacted with homoallyl amine according to protocol I. Purification yielded a waxy solid [520 mg, 54%].



^1H NMR (DMSO d_6) – 9.18 (br s, $(\text{HN})_2\text{C}=\text{N}$); 7.78 (app t, $J = 5.5$, HNCH_2); 7.26-7.43 (m, 10 H, Ar-H); 6.77 (d, $J = 8.1$, 1 H, NHCH); 5.71 (app ddt, $J = 17.1$, $J = 10.3$, $J = 6.7$, 1 H, $\text{H}_2\text{CCH}=\text{CH}_2$); 5.23 (s, 2 H, CH_2Ph); 5.05 (s, 2 H, CH_2Ph); 4.99 (d, $J = 17.1$, 1 H, $\text{CH}=\text{CH}_{\text{trans}}$); 4.95 (d, $J = 9.5$, 1 H, $\text{CH}=\text{CH}_{\text{cis}}$); 3.85 (br d, 3 H, $\text{NHCHCH}_2\text{CH}_2\text{CH}_2\text{NH}$); 2.95-3.20 (m, 2 H, CONHCH_2); 2.10 (app q, $J = 6.5$, 2 H, CH_2CHCH_2); 1.4-1.7 (m, 4 H, $\text{NHCHCH}_2\text{CH}_2\text{CH}_2\text{N}$); 1.35 (s, 9 H, $\text{C}(\text{CH}_3)_3$).

^{13}C NMR (DMSO d_6) – 171.6 (C=O); 162.8 (C=O); 159.5 (app t, C=N); 155.1 (C=O); 154.9 (C=O); 137.0 (C); 135.8 (CH); 135.2 (CH); 128.4 (CH); 128.2 (CH); 128.19 (CH); 127.8 (CH); 127.78 (CH); 127.6 (CH); 116.1 (CH₂); 77.9 (C); 68.1 (CH₂); 66.0 (CH₂); 54.0 (CH); 44.3 (CH₂); 37.8 (CH₂); 33.3 (CH₂); 29.3 (CH₂); 28.1 (CH₃); 25.1 (CH₂).

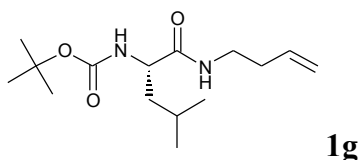
IR, solution cell, DCM (cm^{-1}) – 3665; 3391; 3281; 3038; 2974; 2941; 1715; 1668; 1612; 1506.

HRMS calc. for $\text{C}_{31}\text{H}_{41}\text{N}_5\text{O}_7$ – 596.30788 (M+H); found 596.308514.

$[\alpha]_{\text{D}}^{25} +15.1$ (c 0.29, CHCl_3).

Compound 1g

BocLeuOH [1.0 g, 4.0 mmol], HATU [1.5 g, 3.9 mmol] and DIPEA [2 ml, 11.5 mmol] were stirred for 10 minutes in DMF [5 ml] and DCM [10 ml]. Homoallyl amine hydrochloride [395 mg, 3.66 mmol] and DIPEA [0.5 ml, 2.9 mmol] in DCM [2 ml] were added and the mixture monitored by LCMS. After 2 h the relative intensities of the peaks had stabilized. The solvent was removed under reduced pressure, DCM was added and worked up as described in Protocol I yielding a white waxy solid [940 mg, 89%].



^1H NMR (MeOH d_4 , 400 MHz) – 5.81 (app ddt, $J = 17.1$, $J = 10.3$, $J = 6.8$, 1 H, $\text{H}_2\text{CCH}=\text{CH}_2$); 5.10 (dd, $J = 17.2$, $J = 1.6$, 1 H, $\text{H}_2\text{C}=\text{CH}$); 5.05 (d, $J = 10.3$, 1 H, $\text{H}_2\text{C}=\text{CH}$); 4.05 (dd, $J = 8.8$, $J = 6.1$, 1 H, NHCH); 3.15 – 3.33 (m, 2 H, NHCH_2); 2.26 (app q, $J = 6.9$, 2 H, NHCH_2CH_2); 1.61 – 1.72 (m, 1 H, $\text{CH}(\text{CH}_3)_2$); 1.46 – 1.52 (m, 2 H, CHCH_2CH); 1.52 (s, 9 H, $\text{C}(\text{CH}_3)_3$); 0.93 – 0.97 (m, 6 H, $\text{CH}(\text{CH}_3)_2$).

^{13}C NMR (MeOH d_4 , 100 MHz) – 176.1 (C=O); 137.0 (CH); 117.5 (CH_2); 81.0 (C); 55.1 (CH); 42.9 (CH_2); 40.2 (CH_2); 35.1 (CH_2); 29.1 (CH_3); 26.3 (CH); 23.8 (CH_3); 22.4 (CH_3).

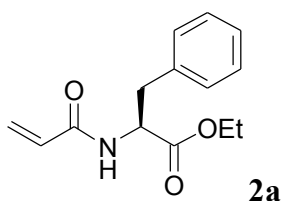
IR, solution cell, DCM (cm^{-1}) – 3431; 3342; 3055; 2966; 2876; 1707; 1676; 1501.

HRMS calc. for $\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_3$ – 285.21781 (M+H); found 285.21729.

$[\alpha]_D^{25}$ –39.2 (c 0.47, CHCl_3).

Compound 2a

PheOEt HCl [3.0 g, 13 mmol] was reacted with acryloyl chloride according to protocol II. In this case no column chromatography was required; two recrystallizations from ethyl acetate and petroleum ether proved sufficient, yielding white, needle-like crystals [78%].



^1H NMR (MeOH d_4) – 7.17-7.29 (m, 5 H, Ar- H); 6.26 (dd, $J = 9.5$, $J = 17.1$, 1 H, H_2CCH); 6.17 (dd, $J = 2.5$, $J = 17.1$, 1 H, H_2CCH); 5.64 (dd, $J = 2.5$, $J = 9.5$, 1 H, H_2CCH); 4.70 (dd, $J = 6.1$, $J = 8.6$, 1 H, HNCH); 4.12 (app q, $J = 7.3$, 2 H, OCH_2); 3.15 (dd, $J = 6.1$, $J = 13.8$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 2.99 (dd, $J = 8.6$, $J = 13.8$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 1.18 (app t, $J = 7.1$, 3 H, CH_2CH_3).

^{13}C NMR (MeOH d_4) – 173.0 (C=O); 167.9 (C=O); 138.1 (C); 131.4 (CH); 130.2 (CH); 129.5 (CH); 127.9 (CH); 127.4 (CH_2); 62.4 (CH_2); 55.5 (CH); 38.5 (CH_2); 14.4 (CH_3).

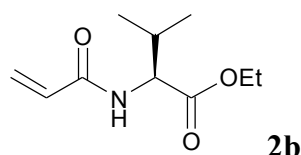
IR, solution cell, DCM (cm^{-1}) – 3420; 2986; 2359; 1735; 1676; 1632; 1506.

HRMS calc. for $C_{14}H_{17}NO_3$ – 270.11061 (M+Na); found 270.11119.

$[\alpha]_D^{25} +133.6$ (*c* 0.24, $CHCl_3$).

Compound **2b**

ValOEt HCl [1.7 g, 9.4 mmol] was reacted with acryloyl chloride according to protocol II. Purification yielded a yellow liquid [1.0 g, 54%].



1H NMR (MeOH d_4) – 6.40 (dd, $J = 10.1$, $J = 17.1$, 1 H, H_2CCH); 6.24 (dd, $J = 2.0$, $J = 17.1$, 1 H, H_2CCH); 5.68 (dd, $J = 2.0$, $J = 10.1$, 1 H, H_2CCH); 4.37 (d, $J = 6.1$, 1 H, $HNCH$); 4.14-4.23 (m, 2 H, OCH_2); 2.16 (app oct, $J = 6.7$, 1 H, $CH(CH_3)_2$); 1.26 (app t, $J = 7.1$, CH_2CH_3); 0.96 (d, $J = 6.8$, 6 H, $CH(CH_3)_2$).

^{13}C NMR (MeOH d_4) – 173.0 (C=O); 168.2 (C=O); 131.5 (CH); 127.5 (CH_2); 62.2 (CH_2); 59.4 (CH); 31.8 (CH); 19.5 (CH_3); 18.5 (CH_3); 14.5 (CH_3).

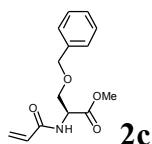
IR, solution cell, DCM (cm^{-1}) – 3678; 3425; 2972; 1732; 1678; 1626; 1510.

HRMS calc. for $C_{10}H_{17}NO_3$ – 222.11061 (M+Na); found 222.11040.

$[\alpha]_D^{16} +19.7$ (*c* 1.24, $CHCl_3$).

Compound **2c**

BocSer(Bzl)OH [1.8 g, 6.1 mmol] was stirred in methanol [10 ml] and toluene [10 ml]. 2 M TMS diazomethane in hexanes [3.1 ml, 6.2 mmol] was added. Acetic acid was then dripped in until the yellow colour disappeared. The solvent was removed under reduced pressure, and a further 20 ml of toluene added. This was removed under reduced pressure in order to azeotrope off impurities. TFA [5 ml] and DCM [12 ml] were then added and the mixture monitored by LCMS until the Boc protected material could no longer be seen. Toluene [10 ml] was added and the solvents removed under reduced pressure. This was repeated once. The resultant material was dissolved in DCM [40 ml] and triethylamine [0.12 ml, 0.76 mmol] added. Acryloyl chloride in DCM [0.17 mmol per ml] was slowly added until the starting free amine was no longer visible by LCMS. The solvent was removed under reduced pressure and the material worked up as described in protocol II, yielding a clear viscous liquid [1.24 g, 77%].



^1H NMR (CDCl_3 , 400 MHz) – 7.25 – 7.36 (m, 5 H, Ph-*H*); 6.47 (d, $J = 7.3$, 1 H, NH); 6.34 (dd, $J = 1.4$, $J = 17.0$, 1 H, $H^aH^b\text{C}=\text{CH}$); 6.16 (dd, $J = 10.2$, $J = 17.0$, 1 H, $\text{H}_2\text{C}=\text{CH}$); 5.69 (dd, $J = 1.4$, $J = 10.2$, 1 H, $H^aH^b\text{C}=\text{CH}$); 4.84 (app dt, $J = 3.1$, $J = 8.2$, 1 H, NHCH); 4.51 (AB q, 2 H, $\text{CH}_2\text{OCH}_2\text{Ph}$); 3.93 (dd, $J = 3.1$, $J = 9.5$, 1 H, CHCH^aH^bO); 3.94 (s, 3 H, OMe); 3.93 (dd, $J = 3.1$, $J = 9.5$, 1 H, CHCH^aH^bO).

^{13}C NMR (CDCl_3 , 100 MHz) – 171.1 (C=O); 165.6 (C=O); 137.9 (C); 130.7 (CH); 128.9 (CH); 128.3 (CH); 128.0 (CH); 127.7 (CH_2); 73.7 (CH_2); 70.1 (CH_2); 53.1 (CH); 53.0 (CH_3).

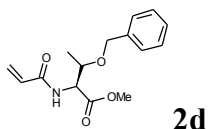
IR, solution cell, DCM (cm^{-1}) – 3427; 3071; 3034; 2951; 2872; 1747; 1678; 1626; 1506.

HRMS calc. for $\text{C}_{14}\text{H}_{17}\text{NO}_4$ - 264.12358 (M+H); found 264.12226.

$[\alpha]_D^{25} +47.2$ (c 0.46 CHCl_3)

Compound **2d**

BocThr(Bzl)OH [472 mg, 1.5 mmol] treated with a series of reagents, as described for Compound **2c**. The product was obtained as a clear viscous liquid [414 mg, 99%].



^1H NMR (CDCl_3 , 400 MHz) – 7.20 – 7.32 (m, 5 H, Ph-*H*); 6.30 (dd, $J = 1.5$, $J = 17.0$, 1 H, $H^aH^b\text{C}=\text{CH}$); 6.25 (br s, 1 H, NH); 6.16 (dd, $J = 10.2$, $J = 17.0$, 1 H, $\text{H}_2\text{C}=\text{CH}$); 5.66 (dd, $J = 1.5$, $J = 10.2$, 1 H, $H^aH^b\text{C}=\text{CH}$); 4.66 (dd, $J = 2.3$, $J = 9.3$, 1 H, NHCH); 4.54 (d, $J = 11.8$, 1 H, CH^aH^bPh); 4.34 (d, $J = 11.8$, 1 H, CH^aH^bPh); 4.13 (dq, $J = 2.3$, $J = 6.3$, 1 H, $\text{CH}(\text{CH}_3)\text{OCH}_2$); 3.63 (s, 3 H, OMe); 1.19 (d, $J = 6.3$, 3 H, $\text{CH}_3\text{CHOCH}_2$).

^{13}C NMR (CDCl_3 , 100 MHz) – 171.4 (C=O); 166.1 (C=O); 138.1 (C); 130.7 (CH); 128.8 (CH); 128.3 (CH); 128.2 (CH); 127.8 (CH_2); 74.8 (CH); 71.3 (CH_2); 57.0 (CH_3); 52.7 (CH_3); 16.7 (CH_3).

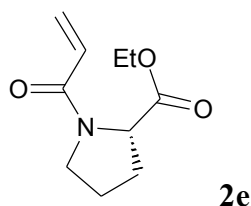
IR, solution cell, DCM (cm^{-1}) – 3427; 3069; 3034; 2984; 2947; 2874; 1746; 1678; 1628; 1508.

HRMS calc. for $\text{C}_{15}\text{H}_{19}\text{NO}_4$ - 278.13923 (M+H); found 278.13839.

$[\alpha]_D^{25} +13.0$ (*c* 0.70, CHCl₃)

Compound **2e**

ProOMe HCl [415 mg, 2.5 mmol] was reacted with acryloyl chloride according to protocol II. Purification yielded a clear liquid [340 mg, 72%]. This consisted of a 3:1 mix of rotamers, clearly visible by NMR. Heating did not result in coalescence of peaks and thus the spectrum for each compound is reported separately.



Conformation 1 (75%)

¹H NMR (CDCl₃, 400 MHz) – 6.44 (dd, *J* = 10.0, *J* = 16.8, 1 H, CHCH₂); 6.35 (dd, *J* = 2.2, *J* = 16.8, 1 H, CHCH₂); 5.67 (dd, *J* = 10.0, *J* = 2.2, 1 H, CHCH₂); 4.51 (dd, *J* = 4.0, *J* = 8.6, 1 H, NCH); 3.69 (s, 3 H, OMe); 3.55-3.77 (m, 2 H, NCH₂); 1.91-2.27 (m, 4 H, NCH₂CH₂CH₂).

¹³C NMR (CDCl₃, 100 MHz) – 172.6 (C=O); 164.4 (C=O); 128.4 (CH₂); 128.0 (CH); 58.8 (CH₃); 52.1 (CH); 46.9 (CH₂); 29.1 (CH₂); 24.7 (CH₂).

Conformation 2 (25%)

¹H NMR (CDCl₃, 400 MHz) – 6.33 (dd, *J* = 2.0, *J* = 16.9, 1 H, CHCH₂); 6.20 (dd, *J* = 10.3, *J* = 16.7, 1 H, CHCH₂); 5.62 (dd, *J* = 2.0, *J* = 10.2, 1 H, CHCH₂); 4.48 (dd, *J* = 2.8, *J* = 8.6, 1 H, NCH); 3.70 (s, 3 H, OMe); 3.55-3.77 (m, 2 H, NCH₂); 1.91-2.27 (m, 4 H, NCH₂CH₂CH₂).

¹³C NMR (CDCl₃, 100 MHz) – 172.5 (C=O); 164.8 (C=O); 128.1 (CH₂); 128.0 (CH); 59.2 (CH₃); 52.5 (CH); 46.4 (CH₂); 31.3 (CH₂); 22.5 (CH₂).

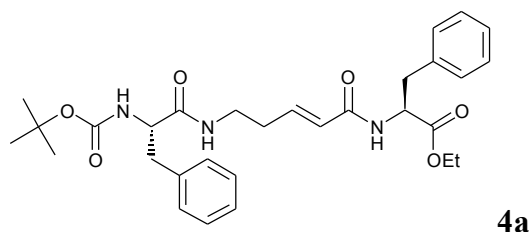
IR, solution cell, DCM (cm⁻¹) – 3476; 2959; 2883; 1744; 1649; 1609.

HRMS calc. for C₉H₁₃NO₃ – 206.07931 (M+Na); found 206.07928.

$[\alpha]_D^{14} -54.0$ (*c* 0.84, MeCN)

Compound **4a**

1a [80 mg, 0.25 mmol], **2a** [50 mg, 0.2 mmol] and Grubbs second generation catalyst [32 mg, 19 mol%] were subjected to microwave radiation [300 W, 80 °C] for 2 h. purification by column chromatography yielded a brown waxy solid [92 mg, 86%].



¹H NMR (CDCl₃, 400 MHz) – 7.14 – 7.28 (m, 5 H, Ph-*H*); 6.68 (br, 1 H, NH); 6.62 (app quintet, *J* = 7.9, 1 H, CH₂CH=CH); 6.45 (br, 1 H, NH); 5.64 (d, *J* = 15.4, 1 H, CH₂CH=CH); 5.53 (br, 1 H, NH); 4.90 (app dd, *J* = 6.3, *J* = 14.0, 1 H, NCHCOOEt); 4.48 (br app q, *J* = 6.6, 1 H, BocNCH); 4.16 (app q, *J* = 7.1, 2 H, OCH₂CH₃); 3.17 – 3.25 (br m, 2 H, NHCH₂); 3.06 – 3.17 (m, 2 H, EtO₂CHCH₂); 2.99 (d, *J* = 7.3, 2 H, BocNHCHCH₂); 2.10 – 2.30 (br m, 2 H, NHCH₂CH₂); 1.36 (s, 9 H, C(CH₃)₃); 1.22 (app t, *J* = 7.1, 2 H, OCH₂CH₃).

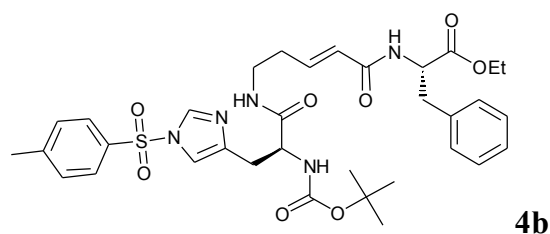
¹³C NMR (CDCl₃) – 172.2 (C=O); 171.8 (C=O); 165.1 (C=O); 155.7 (C=O); 141.1 (CH); 137.0 (C); 136.1 (C); 129.5 (CH); 129.3 (CH); 128.5 (2CH); 127.0 (CH); 126.8 (CH); 124.9 (CH); 80.0 (C); 61.5 (CH₂); 55.8 (CH); 53.9 (CH); 39.2 (CH₂); 38.1 (CH₂); 37.6 (CH₂); 31.9 (CH₂); 28.3 (CH₃); 14.1 (CH₃).

IR, solution cell, DCM (cm⁻¹) – 3425; 2980; 2936; 1726; 1678; 1501.

HRMS calc. for C₃₀H₃₉N₃O₆ – 538.29170 (M+H); found 538.29181.

Compound **4b**

1b, **2a** and DMF (3 drops) were reacted according to protocol III, except without degassing and for two 15-minute periods. Purification yielded a red waxy solid [28 mg, 41%].



¹H NMR (DMSO *d*₆, 353 K, 400 MHz) – 8.02 (d, *J* = 7.5, 1 H, N-*H*); 7.75 (app t, *J* = 5.8, 1 H, N-*H*); 7.27 (d, *J* = 8.0, 2 H, Ts-*H*); 7.19-7.27 (m, 5 H, Phe-*H*); 7.09 (d, *J* =

7.8, 5 H, Ts-*H*); 6.65 (br, 1 H, N-*H*); 6.57 (dt, $J = 15.5$, $J = 7.0$, 1 H, CH₂CH=CH); 6.00 (d, $J = 15.5$, 1 H, CH₂CH=CH); 4.57 (dt, $J = 6.7$, $J = 8.0$, 1 H, NHCHCH₂Ph); 4.24 (dt, $J = 5.7$, $J = 8.4$, 1 H, NHCHCH₂Im); 4.05 (app q, $J = 7.0$, 2 H, OCH₂CH₃); 3.10-3.22 (m, 2 H, CONCH₂); 3.10 (dd, $J = 15.1$, $J = 5.3$, 1 H, CH^aH^bAr); 3.05 (dd, $J = 14.2$, $J = 6.2$, 1 H, CH^aH^bAr); 2.95 (dd, $J = 13.9$, $J = 8.5$, 1 H, CH^aH^bAr); 2.90 (dd, $J = 15.1$, $J = 8.7$, 1 H, CH^aH^bAr); 2.29 (s, 3 H, ArCH₃); 1.34 (s, 9 H, C(CH₃)₃); 1.12 (app t, $J = 7.1$, 3 H, OCH₂CH₃).

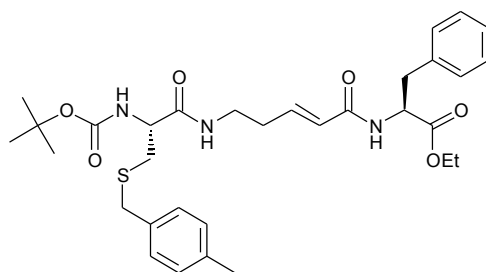
¹³C NMR (CDCl₃) – 171.9 (C=O); 171.2 (C=O); 165.1 (C=O); 155.6 (C=O); 146.5; 141.4; 140.5; 136.4; 136.1; 134.7; 130.5 (CH); 129.3 (CH); 128.5 (CH); 127.5 (CH); 127.0 (CH); 125.2 (CH); 114.9; 80.2 (C); 61.5 (CH₂); 54.1 (CH); 53.3 (CH); 38.0 (CH₂); 37.9 (CH₂); 32.1 (CH₂); 30.3 (CH₂); 28.3 (CH₃); 21.7 (CH₃); 14.1 (CH₃).

IR, solution cell, DCM (cm⁻¹) – 3422; 3296; 2932; 1762; 1674; 1501.

HRMS calc. for C₃₄H₄₃N₅O₈S – 682.29051 (M+H); found 682.291967.

Compound 4c

1c and **2a** were reacted according to protocol III. Purification yielded a pale brown waxy solid [31 mg, 51%].



¹H NMR (CDCl₃) – 7.09 – 7.30 (m, 9 H, Ar-*H*); 6.74 (dt, $J = 15.2$, $J = 6.9$, 1 H, CH₂CH=CH); 6.55 (br t, 1 H, NHCH₂); 6.34 (br d, $J = 6.8$, 1 H, NH(Phe)); 5.82 (d, $J = 15.4$, 1 H, CH₂CH=CH); 5.45 (br, 1 H, NH(Cys)); 4.91 (dt, $J = 7.6$, $J = 6.1$, 1 H, NHCH(Phe)); 4.27 (br m, 1 H, NHCH(Cys)); 4.14 (app q, $J = 7.1$, 2 H, OCH₂CH₃); 3.30 – 3.40 (m, 2 H, CHCH₂S); 3.10 – 3.14 (m, 2 H, CHCH₂Ph); 2.80 (dd, $J = 6.0$, $J = 13.9$, 1 H, CHCH^aH^bS); 2.70 (dd, $J = 6.8$, $J = 13.9$, 1 H, CHCH^aH^bS); 2.36 (app q, $J = 6.5$, 2 H, NHCH₂CH₂); 2.35 (s, 3 H, PheMe); 1.44 (s, 9 H, C(CH₃)₃); 1.22 (app t, $J = 7.1$, OCH₂CH₃).

¹³C NMR (CDCl₃) – 171.9 (C=O); 171.0 (C=O); 165.1 (C=O); 155.6 (C=O); 141.1 (CH); 136.9 (C); 136.0 (C); 134.9 (C); 129.33 (CH); 129.29 (CH); 128.9 (CH); 128.5 (CH); 127.1 (CH); 125.2 (CH); 80.3 (C); 61.6 (CH₂); 53.8 (CH); 53.3 (CH); 38.0

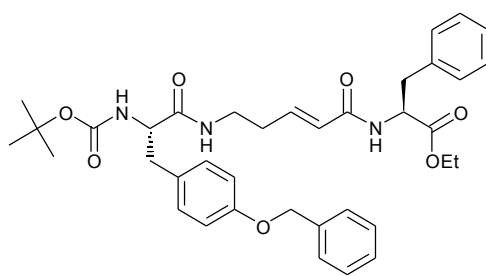
(CH₂); 36.1 (CH₂); 33.9 (CH₂); 32.0 (CH₂); 30.3 (CH₂); 28.3 (CH₃); 21.1 (CH₃); 14.1 (CH₃).

IR, solution cell, DCM (cm⁻¹) – 3422; 2980; 2932; 2332; 1726; 1678; 1504.

HRMS calc. for C₃₂H₄₃N₃O₆S – 598.29507 (M+H); found 598.29373.

Compound 4d

1d and **2a** were reacted according to protocol III. Purification yielded a pale brown waxy solid [53 mg, 82%].



4d

¹H NMR (MeOH *d*₄, 400 MHz, 333 K) – 7.16-7.39 (m, 10 H, Ar-H); 7.10 (d, *J* = 8.7, 2 H, *H* ortho to O); 6.89 (d, *J* = 8.7, 2 H, *H* meta to O); 6.64 (app dt, *J* = 15.5, *J* = 7.0, 1 H, CH₂CH=CH); 5.94 (d, *J* = 15.5, 1 H, CH₂CH=CH); 5.03 (s, 2 H, OCH₂Ph); 4.71 (dd, 1 H, *J* = 6.4, *J* = 8.0, NHCHCH₂Ar); 4.18 (app t, *J* = 7.1, BocNHCHCH₂Ar); 4.10 (app q, *J* = 7.1, 2 H, OCH₂CH₃); 3.15-3.24 (m, 2 H, CONCH₂); 3.11 (dd, *J* = 6.4, *J* = 14.1, 1 H, CH^aH^bAr); 2.99 (dd, *J* = 7.9, *J* = 14.1, 1 H CH^aH^bAr); 2.95 (dd, *J* = 6.4, *J* = 13.9, 1 H, CH^aH^bAr); 2.67 (dd, *J* = 8.1, *J* = 13.7, 1 H CH^aH^bAr); 2.27 (app q, *J* = 6.9, 2 H, H₂CCH=C); 1.35 (s, 9 H, C(CH₃)₃); 1.18 (app t, *J* = 7.1, 3 H, OCH₂CH₃).

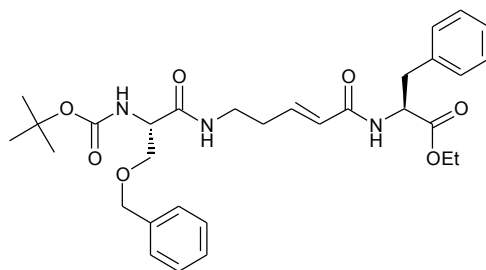
¹³C NMR (CDCl₃) – 172.0 (C=O); 171.7 (C=O); 165.1 (C=O); 157.7 (C=O); 155.6 (C); 141.1 (CH); 137.0 (C); 136.1 (C); 130.4 (C); 130.4 (CH); 129.3 (CH); 128.6 (CH); 128.5 (CH); 128.0 (CH); 127.5 (CH); 127.0 (CH); 125.0 (CH); 115.0 (CH₂); 80.0 (C); 70.1 (CH₂); 61.5 (CH₂); 53.4 (CH₂); 56.0 (CH); 53.4 (CH); 38.2 (CH₂); 38.0 (CH₂); 37.6 (CH₂); 32.0 (CH₂); 28.3 (CH₃); 14.1 (CH₃).

IR, solution cell, DCM (cm⁻¹) – 3425; 2979; 2933; 1726; 1678; 1506.

HRMS calc. for C₃₇H₄₅N₃O₇ – 666.31497 (M+Na); found 666.314246.

Compound 4e

1e [39 mg, 0.11 mmol] and **2a** [25 mg, 0.10 mmol] were reacted according to protocol III. Purification yielded a brown waxy solid [43 mg, 73%].



4e

^1H NMR (MeOH d_4 , 400 MHz) – 7.21 – 7.36 (m, 10 H, Ph-*H*); 6.72 (app dt, $J = 15.5$, $J = 6.9$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 6.01 (d, $J = 15.5$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 4.71 (dd, $J = 8.4$, $J = 6.2$, 1 H, NCHCOOEt); 4.47 – 4.57 (m, 2 H, $\text{CH}_2\text{OCH}_2\text{Ph}$); 4.26 (m, 1 H, BocNHCH); 4.13 (app q, $J = 7.1$, 2 H, OCH_2CH_3); 3.63 – 3.72 (m, 2 H, CHCH_2O); 3.23 – 3.35 (m, 2 H, NHCH_2); 3.15 (dd, $J = 6.2$, $J = 13.8$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 3.01 (dd, $J = 8.5$, $J = 13.8$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 2.38 (app q, $J = 6.6$, 2 H, NHCH_2CH_2); 1.45 (s, 9 H, $\text{C}(\text{CH}_3)_3$); 1.17 (app t, $J = 7.1$, OCH_2CH_3).

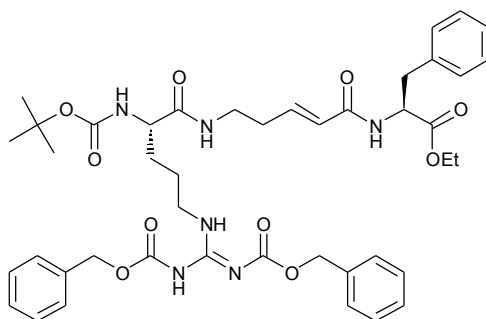
^{13}C NMR (MeOH d_4 , 100 MHz) – 173.5 (C=O); 173.4 (C=O); 168.5 (C=O); 158.1 (C=O); 143.3 (CH); 139.7 (C); 138.5 (C); 130.7 (CH); 130.0 (CH); 129.8 (CH); 129.3 (CH); 129.2 (CH); 128.3 (CH); 126.3 (CH); 81.3 (C); 74.5 (CH_2); 71.5 (CH_2); 62.8 (CH_2); 56.5 (CH); 55.9 (CH); 39.7 (CH_2); 39.0 (CH_2); 31.1 (CH_2); 29.1 (CH_3); 14.8 (CH_3).

IR, solution cell, DCM (cm^{-1}) – 3423; 3059; 2980; 2936; 2870; 1722; 1678; 1499.

HRMS calc. for $\text{C}_{31}\text{H}_{41}\text{N}_3\text{O}_7$ – 568.30226 (M+H); found 568.30133.

Compound 4f

1f [134 mg, 0.23 mmol], **2a** [52 mg, 0.21 mmol] and grubbs catalyst [21 mg, 12 mol%] were refluxed in DCM for 96 h, by which time **3** was no longer visible. Purification yielded a brick red waxy solid [120 mg, 70%].



4f

^1H NMR (400 MHz, 353 K) (DMSO d_6) – 8.98 (s, 2 H, $(\text{HN})_2\text{C}=\text{N}$); 7.93 (d, 1 H, NHCHCH_2Ph); 7.56 (br t, 1 H, NHCH_2); 7.19-7.40 (m, 15 H, Ar-*H*); 6.57 (app dt, 1

H, $J = 15.5$, $J = 6.9$, $\text{CH}_2\text{CH}=\text{CH}$); 6.23 (br d, 1 H, $\text{NHCHCH}_2\text{CH}_2$); 5.98 (d, $J = 15.5$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 5.25 (app s, 2H, OCH_2Ph); 5.07 (app s, 2H, OCH_2Ph); 4.58 (ddd, $J = 8.4$, $J = 7.8$, $J = 6.2$, 1 H, NHCHCH_2Ph); 4.05 (app q, $J = 7.1$, 2 H, OCH_2); 3.87 (m, 3 H, $\text{NHCHCH}_2\text{CH}_2\text{CH}_2\text{N}=\text{C}$); 3.12 (m, 2 H, CONCH_2); 3.05 (dd, $J = 6.2$, $J = 12.9$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 2.98 (dd, $J = 8.4$, $J = 14.0$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 2.23 (app q, 2 H, $J = 6.8$, $\text{H}_2\text{CCH}=\text{C}$); 1.45-1.65 (m, 4 H, $\text{NHCHCH}_2\text{CH}_2\text{CH}_2\text{N}=\text{C}$); 1.36 (s, 9 H, $\text{C}(\text{CH}_3)_3$); 1.12 (app t, $J = 7.1$, 3 H, OCH_2CH_3).

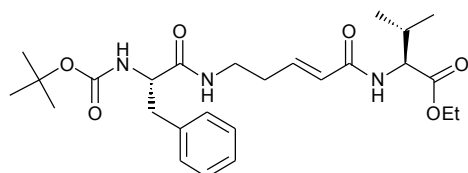
^{13}C NMR (CDCl_3) – 172.0 (C=O); 171.7 (C=O); 165.1 (C=O); 163.4 (C=O); 160.9 (C=N); 155.8 (C=O); 155.5 (C=O); 141.3 (CH); 136.4 (C); 136.0 (C); 134.6 (C); 129.3 (CH); 128.8 (CH); 128.6 (CH); 128.5 (CH); 128.3 (CH); 128.2 (CH); 127.0 (CH); 124.9 (CH); 79.6 (C); 69.0 (CH_2); 67.2 (CH_2); 61.5 (CH_2); 53.5 (CH); 53.2 (CH); 44.1 (CH_2); 37.9 (CH_2); 37.7 (CH_2); 31.9 (CH_2); 29.0 (CH_2); 28.4 (CH_3); 24.5 (CH_2); 14.1 (CH_3).

IR, solution cell, DCM (cm^{-1}) – 3391; 2976; 2939; 1719; 1676; 1611; 1504.

HRMS calc. for $\text{C}_{43}\text{H}_{54}\text{N}_6\text{O}_{10}$ – 815.39742 (M+H); found 815.397854.

Compound 4g

1a [70 mg, 0.22 mmol] and **2b** [40 mg, 0.20 mmol] were reacted according to protocol III. Purification yielded a brown waxy solid [33 mg, 34%].



4g

^1H NMR (CDCl_3 , 400 MHz) – 7.22 – 7.32 (m, 5 H, Ph-H); 6.68 (dt, $J = 15.2$, $J = 6.7$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 6.52 (br d, 1 H, $\text{NH}(\text{Phe})$); 6.29 (br t, 1 H, $\text{NH}(\text{Val})$); 4.65 (dd, $J = 4.9$, $J = 8.8$, 1 H, $\text{NHCH}(\text{Val})$); 4.42 (br m, 1 H, $\text{NHCH}(\text{Phe})$); 4.18 – 4.42 (m, 2 H, OCH_2CH_3); 3.20 – 3.40 (m, 2 H, NHCH_2); 3.04 (d, $J = 7.1$, CHCH_2); 2.15 – 2.35 (m, 3 H, NHCH_2CH_2 and $\text{CH}(\text{CH}_3)_2$ superimposed); 1.40 (s, 9 H, $\text{C}(\text{CH}_3)_3$); 1.32 (app t, $J = 7.1$, OCH_2CH_3); 0.98 (app t, $J = 7.2$, $\text{CH}(\text{CH}_3)_2$).

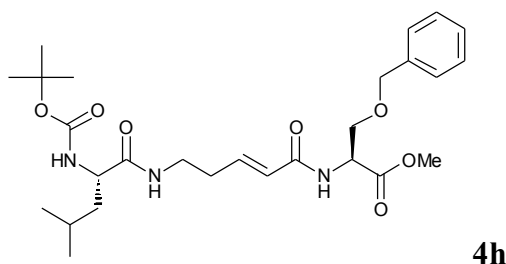
^{13}C NMR ($\text{MeOH } d_4$, 100 MHz) – 174.8 (C=O); 173.5 (C=O); 168.8 (C=O); 158.0 (C=O); 143.26 (CH); 139.0 (C); 130.8 (CH); 129.8 (CH); 128.1 (CH); 126.4 (CH); 81.0 (C); 62.6 (CH_2); 59.7 (CH); 58.0 (CH); 40.0 (CH_2); 39.5 (CH_2); 33.2 (CH_2); 32.3 (CH); 29.1 (CH_3); 19.9 (CH_3); 19.0 (CH_3); 15.0 (CH_3).

IR, solution cell, DCM (cm^{-1}) – 3427; 3329; 3057; 2974; 2936; 1726; 1678; 1504.

HRMS calc. for $\text{C}_{26}\text{H}_{39}\text{N}_3\text{O}_6$ – 490.29170 (M+H); found 490.29253.

Compound 4h

1g [32 mg, 0.11 mmol] and **2c** [26 mg, 0.10 mmol] were reacted according to protocol III. Purification yielded a pale brown waxy solid [39 mg, 75%].



^1H NMR (CDCl_3 , 400 MHz) – 7.19 – 7.29 (m, 5 H, Ph-*H*); 6.70 (app dt, $J = 15.3$, $J = 6.9$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 6.70 (br s, 1 H, $\text{NH}(\text{Ser})$); 6.59 (br s, 1 H, NHCH_2); 5.84 (d, $J = 15.4$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 5.14 (br d, $J = 5.9$, 1 H, $\text{NH}(\text{Leu})$); 4.77 (app dt, $J = 4.8$, $J = 3.4$, 1 H, $\text{NHCH}(\text{Ser})$); 4.48 (d, $J = 12.2$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 4.41 (d, $J = 12.2$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 4.08 (br s, $\text{NHCH}(\text{Leu})$); 3.84 (dd, $J = 3.4$, $J = 9.6$, 1 H, $\text{CHCH}^a\text{H}^b\text{O}$); 3.67 (s, 3 H, OMe); 3.64 (dd, $J = 3.4$, $J = 9.6$, 1 H, $\text{CHCH}^a\text{H}^b\text{O}$); 3.24 – 3.37 (m, 2 H, NHCH_2); 2.31 (app q, $J = 6.5$, 2 H, NHCH_2CH_2); 1.51 – 1.60 (m, 2 H, CHCH_2CH); 1.35 – 1.45 (m, 1 H, $\text{CH}(\text{CH}_3)_2$); 1.35 (s, 9 H, $\text{C}(\text{CH}_3)_3$); 0.83 – 0.86 (m, 6 H, $\text{CH}(\text{CH}_3)_2$).

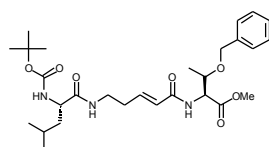
^{13}C NMR (CDCl_3 , 100 MHz) – 173.4 (C=O); 171.4 (C=O); 170.7 † (C=O); 165.7 (C=O); 164.2 † (C=O); 141.8 (CH); 137.9 (C); 137.8 † (C); 133.5 † (CH); 128.9 † (CH); 128.8 (CH); 128.4 † (CH); 128.3 (CH); 138.1 † (CH); 128.0 (CH); 125.6 (CH); 80.4 (C); 73.74 † (CH_2); 73.66 (CH_2); 70.1 (CH_2); 69.8 † (CH_2); 53.3 (CH); 53.04 (CH); 52.96 (CH_3); 42.5 † (CH_2); 41.8 (CH_2); 38.2 (CH_2); 32.5 (CH_2); 28.7 (CH_3); 25.2 (CH); 23.3 (CH_3); 22.4 (CH_3). † Minor peaks resulting from diastereoisomer.

IR, solution cell, DCM (cm^{-1}) – 3429; 2957; 2873; 1746; 1678; 1504.

HRMS calc. for $\text{C}_{27}\text{H}_{41}\text{N}_3\text{O}_7$ - 520.30226 (M+H); found 520.30055.

Compound 4i

1g [32 mg, 0.11 mmol] and **2d** [28 mg, 0.10 mmol] were reacted according to protocol III. Purification yielded a pale brown waxy solid [33 mg, 61%].



4i

^1H NMR (CDCl_3 , 400 MHz) – 7.16 – 7.29 (m, 5 H, Ph-*H*); 6.72 (app dt, $J = 15.1$, $J = 7.0$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 6.45 (br s, 1 H, NH); 6.40 (br d, $J = 8.7$, 1 H, NH); 5.88 (d, $J = 15.4$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 5.05 (br s, 1 H, NH); 4.69 (dd, $J = 2.3$, $J = 9.3$, 1 H, NHCHCO_2Me); 4.51 (d, $J = 11.8$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 4.32 (d, $J = 11.8$, 1 H, $\text{CH}^a\text{H}^b\text{Ph}$); 4.09 (dq, $J = 2.3$, $J = 6.3$, 1 H, $\text{CH}(\text{CH}_3)\text{OCH}_2$); 4.06 (br s, 1 H, NHCHCH_2); 3.60 (s, 3 H, OMe); 3.23 – 3.38 (m, 2 H, NHCH_2); 2.32 (app q, $J = 6.7$, 2 H, NHCH_2CH_2); 1.51 – 1.60 (m, 2 H, CHCH_2CH); 1.37 - 1.44 (m, 1 H, $\text{CH}(\text{CH}_3)_2$); 1.36 (s, 9 H, $\text{C}(\text{CH}_3)_3$); 1.16 (d, $J = 6.3$, 3 H, $\text{CH}_3\text{CHOCH}_2$); 0.83 – 0.86 (m, 6 H, $\text{CH}(\text{CH}_3)_2$).

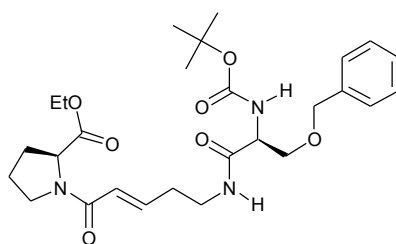
^{13}C NMR (CDCl_3 , 100 MHz) – 173.3 (C=O); 171.6 (C=O); 166.3 (C=O); 156.3 (C=O); 141.9 (CH); 138.2 (C); 128.8 (CH); 128.2 (CH); 128.2 (CH); 125.6 (CH); 80.4 (C); 74.7 (CH); 71.2 (CH_2); 57.0 (CH_3); 53.4 (CH); 52.8 (CH); 41.7 (CH_2); 38.2 (CH_2); 32.6 (CH_2); 28.7 (CH_3); 25.2 (CH); 23.3 (CH_3); 22.4 (CH_3); 16.7 (CH_3).

IR, solution cell, DCM (cm^{-1}) – 3429; 2959; 2874; 1744; 1680; 1504.

HRMS calc. for $\text{C}_{28}\text{H}_{43}\text{N}_3\text{O}_7$ - 534.31791 (M+H); found 534.31871.

Compound 4j

1e and **2e** were reacted according to protocol III. Purification yielded a pale brown waxy solid [25 mg, 50%].



4j

^1H NMR (CDCl_3 , 400 MHz) – 7.23-7.33 (m, 5 H, Ph-*H*); 6.81 (app quintet, $J = 7.1$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 6.51 (br, 1 H, NH); 6.15 (d, $J = 15.2$, 1 H, $\text{CH}_2\text{CH}=\text{CH}$); 5.29 (d, $J = 5.7$, 1 H, NHCH); 4.51 (AB q, 2 H, OCH_2Ph); 4.41 – 4.52 (br, 1 H, CHCO_2Me); 4.20 (dt, $J = 4.4$, $J = 6.6$, 1 H, NHCH); 3.84 (dd, $J = 9.4$, $J = 4.3$, 1 H, $\text{CHCH}^a\text{H}^b\text{O}$); 3.68 (s, 3 H, OMe); 3.64 (br t, 1 H, $\text{NCH}^a\text{H}^b\text{CH}_2\text{CH}_2$); 3.56 (dd, $J = 6.5$, $J = 9.4$, 1 H, $\text{CHCH}^a\text{H}^b\text{O}$); 3.51 – 3.57 (obs, 1 H, $\text{NCH}^a\text{H}^b\text{CH}_2\text{CH}_2$); 3.32-3.42 (m, 2 H, NHCH_2);

2.37 (app q, $J = 6.1$, 2 H, NHCH_2CH_2); 1.86-2.20 (m, 4 H, $\text{NCH}_2\text{CH}_2\text{CH}_2$); 1.41 (s, 9 H, $\text{C}(\text{CH}_3)_3$).

^{13}C NMR (CDCl_3) – 172.7 (C=O); 170.3 (C=O); 164.4 (C=O); 155.5 (C=O); 142.6 (CH); 137.5 (C); 128.5 (CH); 127.9 (CH); 127.7 (CH); 123.0 (CH); 80.2 (C); 73.4 (CH₂); 69.9 (CH₂); 59.2^{*}; 58.9 (CH₃); 52.6^{*}; 54.0 (CH); 52.2 (CH); 46.8 (CH₂); 46.5^{*}; 38.2 (CH₂); 32.3 (CH₂); 31.3^{*}; 29.1 (CH₂); 28.3 (CH₃); 24.8 (CH₂); 22.5^{*}.

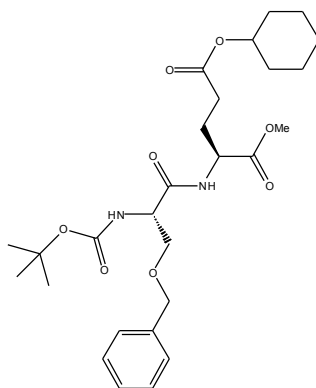
^{*}Smaller peaks corresponding to a different conformation of the proline portion of the compound. Directly analogous to those seen in **2e**.

IR, solution cell, DCM (cm^{-1}) – 3886; 3425; 2978; 2949; 2878; 1715; 1672; 1616.

HRMS calc. For $\text{C}_{26}\text{H}_{36}\text{N}_3\text{O}_7$ – 504.27096 (M+H); found 504.27143.

Compound **5a**

BocGlu(OcHex)OH [2.0 g, 6.2 mmol] was stirred in methanol [10 ml] and toluene [10 ml]. 2 M TMS diazomethane in hexanes [3.1 ml, 6.2 mmol] was added. Acetic acid was then dripped in until the yellow colour disappeared. The solvent was removed under reduced pressure, and a further 20 ml of toluene added. This was removed under reduced pressure in order to azeotrope off impurities. TFA [8 ml] and DCM [11 ml] were then added and the mixture monitored by LCMS until the Boc protected material could no longer be seen. Toluene [10 ml] was added and the solvents removed under reduced pressure. This was repeated once. The resultant material was dissolved in DMF [\sim 5 ml] and added to a mixture of BocSer(Bzl)OH [502 mg, 1.7 mmol], HATU [646 mg, 1.7 mmol] and DIPEA [1 ml, 4 mmol] in DCM [4 ml] and DMF [8 ml]. This mixture had been left to preactivate for 10 minutes prior to this addition. The resultant mixture was monitored by LCMS, and the starting material (GluO^cHexOMe) was consumed after 0.5 h. The solvent was removed under reduced pressure, DCM was added and worked up as described in Protocol I yielding a viscous clear liquid [717 mg, 89%].



5a

^1H NMR (CDCl_3 , 400 MHz) – 7.29 – 7.38 (m, 5 H, Ph-*H*); 7.15 (br d, $J = 5.4$, 1 H, NH(Glu)); 5.42 (br s, 1 H, NH(Ser)); 4.75 (m, 1 H, OCH(CH₂)₂); 4.67 (dt, $J = 5.1$, $J = 8.0$, 1 H, NHCH(Glu)); 4.55 – 4.61 (m, 2 H, CH₂OCH₂Ph); 3.74 (br s, NHCH(Ser)); 3.93 (dd, $J = 3.2$, $J = 9.3$, 1 H, CHCH^aH^bO); 3.74 (s, 3 H, OMe); 3.59 (dd, $J = 6.3$, $J = 9.2$, 1 H, CHCH^aH^bO); 2.17 – 2.42 (m, 3 H, CH^aH^bCH₂CO₂^cHex); 1.96 (app ddt, $J = 14.2$, $J = 5.8$, $J = 8.6$, 1 H, CH^aH^bCH₂CO₂^cHex); 1.80 – 1.87 (br m, 2 H, O^cHex); 1.67 – 1.76 (br m, 2 H, O^cHex); 1.50 – 1.59 (br m, 1 H, O^cHex); 1.47 (s, 9 H, C(CH₃)₃); 1.38 (br m, 2 H, O^cHex); 1.21 – 1.32 (br m, 1 H, O^cHex).

^{13}C NMR (CDCl_3 , 100 MHz) – 172.4 (C=O); 172.3 (C=O); 170.7 (C=O); 155.8 (C=O); 137.8 (C); 128.9 (CH); 128.9 (CH); 128.3 (CH); 128.25 (CH); 80.7 (C); 72.9 (CH₂); 73.4 (CH); 70.2 (CH₂); 54.4 (CH); 52.9 (CH); 52.1 (CH₃); 32.0 (CH₂); 30.9 (CH₂); 28.7 (CH₃); 28.0 (CH₂); 25.7 (CH₂); 24.1 (CH₂).

IR, solution cell, DCM (cm^{-1}) – 3425; 2941; 2864; 1719; 1680; 1493.

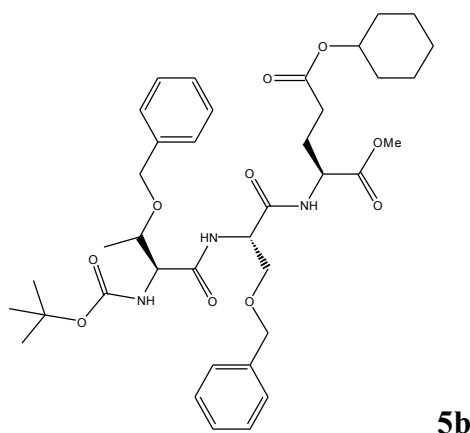
HRMS calc. for C₂₇H₄₀N₂O₈ - 521.28628 (M+H); found 521.28751.

$[\alpha]_D^{25} +11.2$ (c 0.59 CHCl₃)

Compound **5b**

5a [808 mg, 1.6 mmol] was dissolved in DCM [7 ml] and TFA [5 ml]. The mixture monitored by LCMS until the Boc protected material could no longer be seen. Toluene [10 ml] was added and the solvents removed under reduced pressure. This was repeated once. The resultant material was dissolved in DCM [~20 ml] and a mixture of BocThr(Bzl)OH [525 mg, 1.7 mmol], HATU [646 mg, 1.7 mmol] and DIPEA [1 ml, 4 mmol] in DMF [2 ml] was added. This mixture had been left to preactivate for 10 minutes prior to this addition. The resultant mixture was monitored by LCMS, and the starting material (Ser(Bzl)GluO^cHexOMe) was consumed after 20

min. The solvent was removed under reduced pressure, DCM was added and worked up as described in Protocol I yielding a white waxy solid [644 mg, 58%].



^1H NMR (CDCl_3 , 400 MHz) – 7.24 – 7.37 (m, 10 H, Ph-*H*); 7.20 (d, $J = 7.2$, 1 H, *NH*); 7.18 (d, $J = 7.8$, 1 H, *NH*); 5.49 (d, $J = 6.7$, 1 H, *NH*); 4.71 – 4.79 (m, 1 H, $\text{OCH}(\text{CH}_2)_2$); 4.64 (d, $J = 11.4$, 1 H, $\text{OCH}^a\text{H}^b\text{Ph}$); 4.16 (dt, $J = 2.8$, $J = 7.6$, 1 H, *NHCH*); 4.58 – 4.66 (obs., 1 H, *NHCH*); 4.55 (d, $J = 11.8$, 1 H, $\text{OCH}^a\text{H}^b\text{Ph}$); 4.51 (d, $J = 11.4$, 1 H, $\text{OCH}^a\text{H}^b\text{Ph}$); 4.45 (d, $J = 11.8$, 1 H, $\text{OCH}^a\text{H}^b\text{Ph}$); 4.30 (br d, 1 H, *NHCH*(app thr)); 4.20 (br, 1 H, *NHCHCH*(app thr)); 3.94 (dd, 1 H, $J = 2.4$, $J = 8.9$, $\text{CHCH}^a\text{H}^b\text{O}$); 3.27 (s, 3 H, OMe); 3.50 (dd, 1 H, $J = 5.9$, $J = 9.1$, $\text{CHCH}^a\text{H}^b\text{O}$); 2.08 – 2.39 (m, 3 H, $\text{CH}^a\text{H}^b\text{CH}_2\text{CO}_2^c\text{Hex}$); 1.67 – 1.89 (br m, 5 H, $\text{CH}^a\text{H}^b\text{CH}_2\text{CO}_2^c\text{Hex}$, O^cHex superimposed); 1.50 – 1.60 (br m, 1 H, O^cHex); 1.44 (s, 9 H, $\text{C}(\text{CH}_3)_3$); 1.30 – 1.41 (m, 4 H, O^cHex); 1.25 – 1.30 (obs., 1 H, O^cHex); 1.25 (d, $J = 6.4$, 3 H, $\text{CH}_3\text{CHOCH}_2$).

^{13}C NMR (CDCl_3 , 100 MHz) – 171.9 (C=O); 171.7 (C=O); 169.81 (C=O); 169.75 (C=O); 155.8 (C=O); 137.8 (C); 137.3 (C); 128.5 (CH); 128.4 (CH); 128.0 (CH); 127.9 (CH); 127.8 (CH); 127.6 (CH); 80.3 (C); 74.8 (CH); 73.5 (CH_2); 72.9 (CH); 71.7 (CH_2); 69.3 (CH_2); 58.2 (CH); 52.9 (CH); 52.4 (CH); 51.7 (CH_3); 31.6 (CH_2); 30.5 (CH_2); 28.3 (CH_3); 27.3 (CH_2); 25.3 (CH_2); 23.7 (CH_2); 15.6 (CH_3).

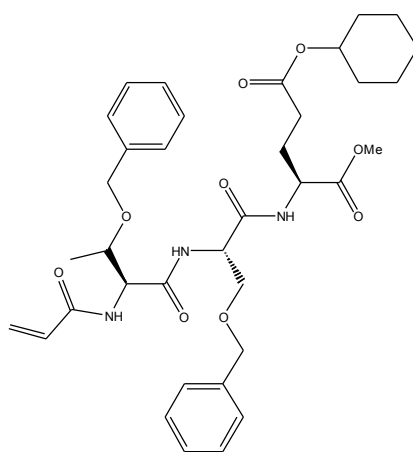
IR, solution cell, DCM (cm^{-1}) – 3422; 3360; 2939; 2894; 1719; 1680; 1495.

HRMS calc. for $\text{C}_{38}\text{H}_{53}\text{N}_3\text{O}_{10}$ - 712.38090 (M+H); found 712.38141.

$[\alpha]_D^{25} +11.3$ (c 0.23 CHCl_3)

Compound 5

5b [490 mg, 0.69 mmol] was dissolved in DCM [8 ml] and TFA [6 ml]. The mixture monitored by LCMS until the Boc protected material could no longer be seen. Toluene [10 ml] was added and the solvents removed under reduced pressure. This was repeated once. The resultant material was dissolved in DCM [40 ml] and triethylamine [0.12 ml, 0.76 mmol] added. Acryloyl chloride in DCM [0.17 mmol per ml] was slowly added until the starting free amine was no longer visible by LCMS. The solvent was removed under reduced pressure and the material worked up as described in protocol II, yielding a white solid [359 mg, 78%].



^1H NMR (CDCl_3 , 400 MHz) – 7.27 – 7.38 (m, 10 H, Ph-*H*); 7.20 (d, $J = 7.5$, 1 H, NH); 7.18 (d, $J = 7.8$, 1 H, NH); 6.64 (d, $J = 6.5$, 1 H, NH); 6.34 (dd, $J = 1.2$, $J = 17.0$, 1 H, $H^aH^b\text{C}=\text{CH}$); 6.19 (dd, $J = 10.2$, $J = 17.0$, 1 H, $\text{H}_2\text{C}=\text{CH}$); 5.71 (dd, $J = 1.2$, $J = 10.2$, 1 H, $H^aH^b\text{C}=\text{CH}$); 4.72 – 4.79 (m, 1 H, $\text{OCH}(\text{CH}_2)_2$); 4.73 (d, $J = 11.6$, $\text{OCH}^a\text{H}^b\text{Ph}$); 4.69 (dd, $J = 3.5$, $J = 6.6$, 1 H, $\text{NHCH}(\text{app thr})$); 4.59 – 4.66 (obs., 1 H, NHCH); 4.63 (dt, $J = 2.7$, $J = 7.6$, 1 H, NHCH); 4.60 (d, $J = 11.7$, 1 H, $\text{OCH}^a\text{H}^b\text{Ph}$); 4.49 – 4.57 (m, 2 H, OCH_2Ph); 4.23 (dq, $J = 6.3$, $J = 3.7$, 1 H, $\text{NHCHCH}(\text{app thr})$); 3.95 (dd, $J = 3.3$, $J = 9.1$, 1 H, $\text{CHCH}^a\text{H}^b\text{O}$); 3.23 (s, 3 H, OMe); 3.53 (dd, $J = 5.7$, $J = 9.1$, 1 H, $\text{CHCH}^a\text{H}^b\text{O}$); 2.08 – 2.35 (m, 3 H, $\text{CH}^a\text{H}^b\text{CH}_2\text{CO}_2^c\text{Hex}$); 1.65 – 1.90 (br m, 5 H, $\text{CH}^a\text{H}^b\text{CH}_2\text{CO}_2^c\text{Hex}$, O^cHex superimposed); 1.50 - 1.65 (br m, 1 H, O^cHex); 1.30 – 1.45 (br m, 4 H, O^cHex); 1.23 – 1.30 (obs., 1 H, O^cHex); 1.23 (d, $J = 6.4$, 3 H, $\text{CH}_3\text{CHOCH}_2$).

^{13}C NMR (CDCl_3 , 100 MHz) – 172.22 (C=O); 172.17 (C=O); 170.1 (C=O); 169.6 (C=O); 166.0 (C=O); 138.1 (C); 137.8 (C); 130.6 (CH); 128.83 (CH); 128.78 (CH); 128.23 (CH); 128.21 (CH); 128.11 (CH); 128.09 (CH); 127.8 (CH₂); 75.0 (CH); 73.8 (CH₂); 73.3 (CH); 72.1 (CH₂); 69.9 (CH₂); 56.9 (CH); 53.4 (CH); 52.7 (CH); 52.1 (CH₃); 32.0 (CH₂); 30.9 (CH₂); 27.6 (CH₂); 25.7 (CH₂); 24.1 (CH₂); 15.7 (CH₃).

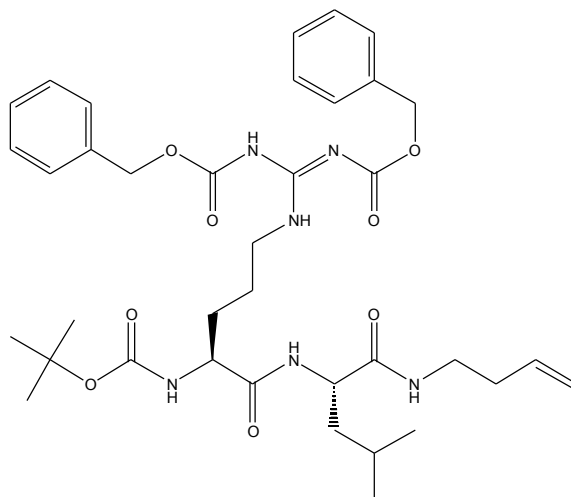
IR, solution cell, DCM (cm^{-1}) – 3406; 2939; 2864; 1734; 1674; 1497.

HRMS calc. for $\text{C}_{36}\text{H}_{47}\text{N}_3\text{O}_9$ - 666.33904 (M+H); found 666.33701.

$[\alpha]_D^{25} +11.9$ (c 0.25 CHCl_3)

Compound 6

1h [500 mg, 1.76 mmol] was dissolved in DCM [10 ml] and TFA [10 ml]. The mixture monitored by LCMS until the Boc protected material could no longer be seen. Toluene [20 ml] was added and the solvents removed under reduced pressure. This was repeated once. The resultant material was dissolved in DCM [5 ml] and DMF [10 ml] and a mixture of BocThr(Bzl)OH [525 mg, 1.7 mmol], HATU [646 mg, 1.7 mmol] and DIPEA [1 ml, 4 mmol] in DMF [5 ml] was added. This mixture had been left to preactivate for 10 minutes prior to this addition. The resultant mixture was monitored by LCMS, and the free amine was consumed after 35 min. The solvent was removed under reduced pressure, DCM was added and worked up as described in Protocol I yielding a cream waxy solid. The mixture was triturated in ether to remove tetramethyl urea, yielding a cream waxy solid [413 mg, 33%].



^1H NMR (CDCl_3 , 400 MHz) – 9.96 (br s, (HN)C=N); 9.31 (br s, (HN)C=N); 7.30 – 7.45 (m, 10 H, Ph-H); 6.60 (d, $J = 8.2$, NH(Leu)); 6.28 (br s, 1 H, NH); 5.73 (app ddt, $J = 17.1$, $J = 10.3$, $J = 6.8$, 1 H, $\text{H}_2\text{CCH}=\text{CH}_2$); 5.58 (br s, 1H, NH(Arg)); 5.27 (s, 2 H, $(\text{CH}_2\text{Ph})_2$); 5.18 (AB q, 2 H, CH_2Ph); 5.04 – 5.09 (m, 2 H, $\text{H}_2\text{C}=\text{CH}$); 4.32 (app dt, $J = 8.9$, $J = 7.1$, 1 H, NHCH(Leu)); 4.15 (app q, $J = 6.6$, 1 H, NHCH(Arg)); 3.90 – 4.05 (m, 2 H, CH_2NCN_2); 3.16 – 3.37 (m, 2 H, $\text{NHCH}_2\text{CH}_2\text{CH}=\text{CH}_2$); 2.22 (m, 2 H, NHCH_2CH_2); 1.60 – 1.70 (m, 4 H, $\text{CHCH}_2\text{CH}_2\text{CH}_2$); 1.45 (s, 9 H, $\text{C}(\text{CH}_3)_3$); 1.50 –

1.60 (m, 1 H, $CH(CH_3)_2$); 1.30 – 1.40 (m, 2 H, $CHCH_2CH$); 0.80 – 0.90 (m, 6 H, $CH(CH_3)_2$).

^{13}C NMR ($CDCl_3$, 100 MHz) – 172.5 (C=O); 171.9 (C=O); 164.0 (C=O); 161.0 (C=O); 156.3 (C=N); 137.1 (C); 135.5 (CH); 135.0 (C); 129.32 (CH); 129.26 (CH); 128.9 (CH); 128.8 (CH); 128.4 (CH); 128.3 (CH); 117.4 (CH_2); 80.6 (C); 69.4 (CH_2); 67.5 (CH_2); 55.0 (CH); 52.3 (CH); 44.5 (CH_2); 40.8 (CH_2); 39.0 (CH_2); 34.0 (CH_2); 28.7 (CH_3); 28.4 (CH_2); 25.4 (CH_2); 25.1 (CH); 23.3 (CH_3); 22.2 (CH_3).

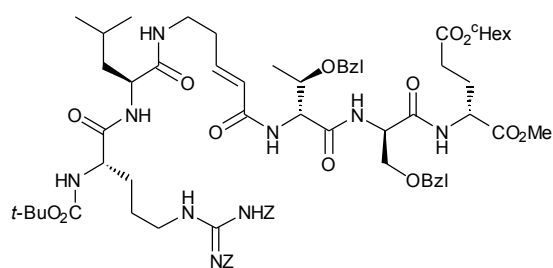
IR, solution cell, DCM (cm^{-1}) – 3391; 3281; 3072; 3036; 2961; 2875; 2330; 1717; 1672; 1612; 1508.

HRMS calc. for $C_{37}H_{52}N_6O_8$ - 425.24402 (M+H); found 425.24476.

$[\alpha]_D^{25}$ - 22.5 (*c* 0.18 $CHCl_3$)

Compound 7

6 [78 mg, 0.11 mmol] and **5** [67 mg, 0.10 mmol] were reacted according to protocol III. Purification yielded a pale brown waxy solid [51 mg, 38%]. Prior to this the HPLC yield was determined to be 67% by ELSD.



1H NMR ($CDCl_3$, 500 MHz) – 9.46 (br s, 1 H, $HNC=N$); 9.29 (br s, 1 H, $HNC=N$); 7.69 (d, $J = 8.0$, 1 H, $NH(Ser)$); 7.55 (br d, 1 H, $NH(app\ thr)$); 7.38 (obs., 1 H, $NH(Glu)$); 7.16 – 7.41 (m, 20 H, Ar-H); 6.76 (br t, 1 H, $NHCH_2$); 6.70 (ddd, $J = 6.0$, $J = 9.1$, $J = 15.4$, 1 H, $CH_2CH=CH$); 6.69 (d, $J = 8.9$, 1 H, $NH(Leu)$); 5.98 (d, $J = 15.4$, 1 H, $CH_2CH=CH$); 5.94 (br, 1 H, $NH(Arg)$); 5.15 - 5.25 (m, 4 H, $2CO_2CH_2$); 4.80 (m, 1 H, $NHCH(Ser)$); 4.72 (m, 1 H, $OCH(CH_2)_2$); 4.47, 4.51 (AB d, $J = 11.8$, 4 H, $2OCH_2Ph$); 4.52 (dd, $J = 2.1$, $J = 6.5$, 1 H, $NHCH(app\ thr)$); 4.57 (dt, $J = 8.3$, $J = 5.4$, 1 H, $NHCH(Glu)$); 4.20 – 4.30 (m, 2 H, $NHCH(Leu)$, $NHCHCH(app\ thr)$ superimposed); 4.05 (app q, $J = 6.5$, 1 H, $NHCH(Arg)$); 3.84 – 3.90 (m, 1 H, $CH^aH^bNCN_2$); 3.86 (dd, $J = 5.4$, $J = 9.5$, 1 H, $CHCH^aH^bO$); 3.72 – 3.79 (m, 1 H,

CH^aH^bNCN₂); 3.69 (s, 3 H, OMe); 3.63 (dd, *J* = 5.2, *J* = 9.5, 1 H, CHCH^aH^bO); 3.45 – 3.52 (m, 1 H, NH^aH^b); 2.97 – 3.07 (m, 1 H, NH^aH^b); 2.40 – 2.50 (m, 1 H, CH₂CH^aH^bCO₂^cHex); 2.21 – 2.37 (m, 3 H, NHCH₂CH₂, CH₂CH^aH^bCO₂^cHex superimposed); 2.09 – 2.20 (m, 1 H, CH^aH^bCH₂CO₂^cHex); 1.80 – 1.91 (m, 1 H, CH^aH^bCH₂CO₂^cHex); 1.77 – 1.85 (br m, 2 H, O^cHex); 1.68 – 1.72 (br m, 2 H, O^cHex); 1.45 – 1.55 (br m, 5 H, CHCH₂CH₂CH₂ (4 H), O^cHex (1 H) superimposed); 1.42 (s, 9 H, C(CH₃)₃); 1.2 – 1.4 (br m, 5 H, O^cHex); 1.22 (d, *J* = 6.4, 3 H, CH₃CHOCH₂); 0.82 (d, *J* = 6.2, 3 H, CHC^aH₃C^bH₃); 0.76 (d, *J* = 6.2, 3 H, CHC^aH₃C^bH₃).

¹³C NMR (CDCl₃, 125 MHz) – 172.7 (C=O); 172.3 (C=O); 171.84 (C=O); 171.77 (C=O); 170.3 (C=O); 170.0 (C=O); 166.9 (C=O); 163.6 (C=O); 160.9 (C=O); 156.1 (C=O); 155.7 (C=O); 140.6 (CH); 138.3 (C); 137.7 (C); 136.8 (C); 134.5 (C); 128.9 (CH); 128.8 (CH); 128.5 (CH); 128.4 (CH); 128.3 (CH); 128.2 (CH); 127.92 (CH); 127.87 (CH); 127.7 (CH); 127.6 (CH); 127.5 (CH); 127.3 (CH); 126.4 (CH); 80.3 (C); 74.5 (CH); 73.0 (CH); 72.8 (CH₂); 71.7 (CH₂); 69.2 (CH₂); 69.0 (CH₂); 67.0 (CH₂); 58.4 (CH); 55.5 (CH); 52.8 (CH); 52.3 (CH₃); 51.7 (CH); 51.4 (CH); 44.3 (CH₂); 40.3 (CH₂); 37.9 (CH₂); 31.5 (CH₂); 30.83 (CH₂); 30.76 (CH₂); 28.3 (CH₃); 27.34 (CH₂); 27.25 (CH₂); 25.3 (CH₂); 25.1 (CH₂); 24.6 (CH); 23.7 (CH₂); 22.8 (CH₃); 21.5 (CH₃); 16.1 (CH₃).

IR, solution cell, DCM (cm⁻¹) – 3387; 3055; 2936; 2862; 2307; 1719; 1670; 1612; 1504.

HRMS calc. for C₇₁H₉₅N₉O₁₇ - 1346.69238 (M+H); found 1346.69524.