Unraveling the Interplay of Backbone Rigidity and Electron Rich Side-Chains on Electron Transfer in Peptides: The Realization of Tunable Molecular Wires

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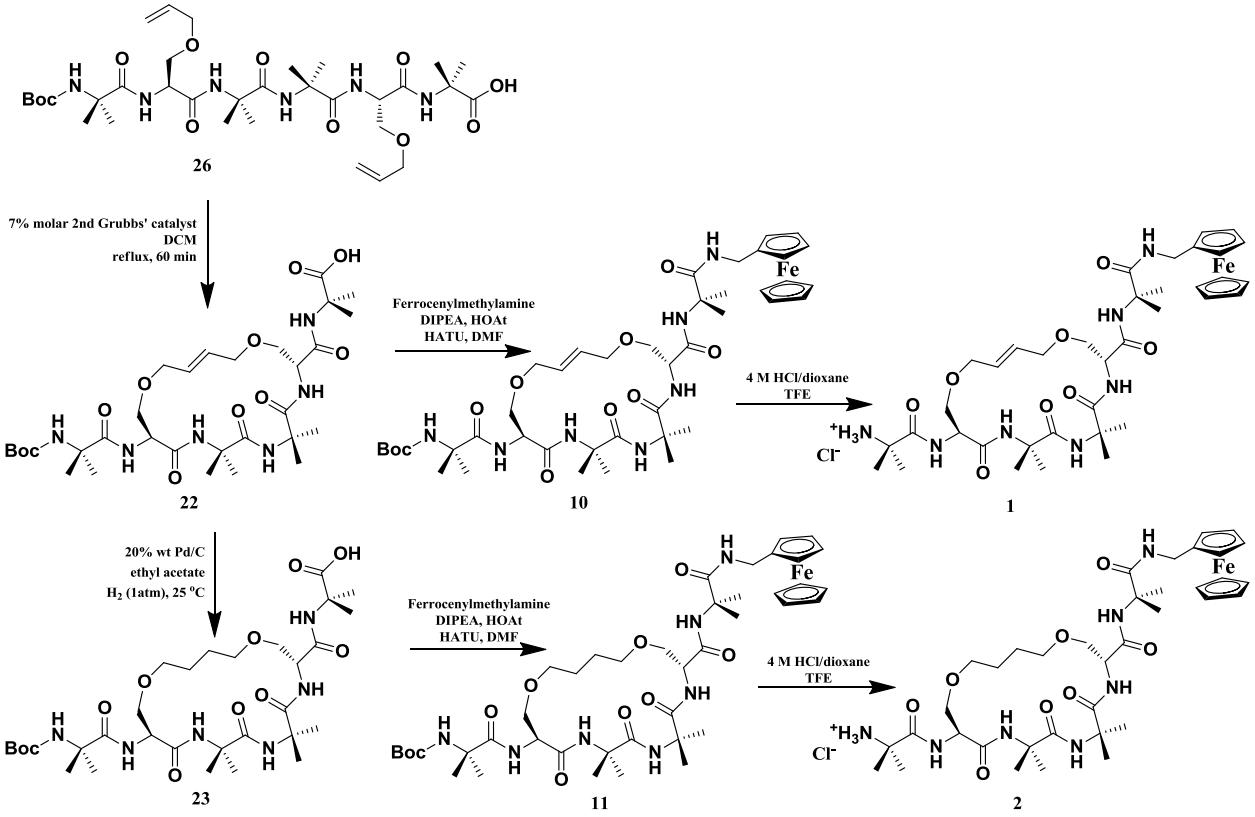
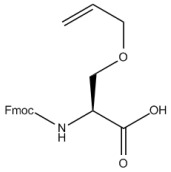
Table of Contents:

1. Synthesis of peptides

Scheme S1. The final synthetic steps for RCM macrocyclized 3_{10}-helical peptides



Fmoc-Ser(Al)-OH

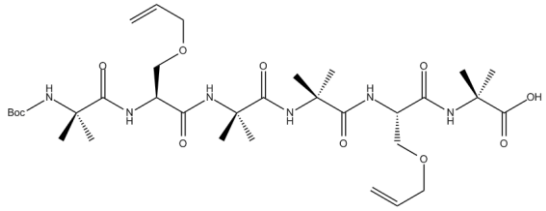


Boc-Ser(Al)-OH[1] (1.0 g, 4.1 mmol) was dissolved in DCM and cooled to 0 ^{o}C. TFA (2 ml) was added and the mixture was stirred at 0 ^{o}C for 30 min and then warmed to room temperature over an additional 30 min. The volatiles were removed and the resulting residue was dissolved in dioxane (5mL). A solution of 10% NaOH (163 mg in 1.63 mL H_2O, 4.1 mmol, 1 equiv.) was added followed by $NaHCO_3$ (343 mg, 4.1 mmol, 1 equiv.) and Fmoc-OSu (1.37 g, 4.1 mmol, 1 equiv.). The reaction mixture was stirred overnight at room temperature after which the volatiles were removed under reduced pressure. The residue was dissolved in 2.5% $NaHCO_3$ and washed with Et_2O (3x20 mL). The aqueous layer was then acidified to pH 3 by dropwise addition of 6 M aqueous HCl and extracted with EtOAc (3x20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4 and the solvent removed under reduced pressure to give the product as a white solid (1.36 g, 91%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, 2H, arom *H*, *J*=7.4 Hz), 7.61 (d, 2H, arom *H*, *J*=4.0 Hz), 7.41 (t, 2H, arom *H*), 7.32 (t, 2H, arom *H*), 5.79-5.93 (m, 1H, C*H*=CH_2), 5.70 (d, 1H, N*H*, *J*=8.2

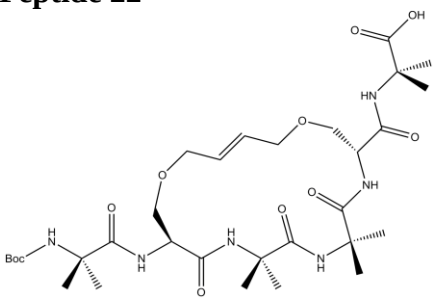
Hz), 5.19-5.30 (m, 2H, CH=CH_2), 4.56 (m, 1H, C*H*), 4.32-4.52 (m, 2H, CH_2), 4.24 (t, 1H, NHC*H*), 4.03 (d, 2H, CH_2O, *J*=5.7 Hz), 3.95 (dd, 1H, CH_2), 3.70 (dd, 1H, CH_2).
MS: $[M+Na]^+_{calcd}$=390.2, $[M+Na]^+_{found}$=390.2.

Peptide 26



Fmoc-Aib-OH loaded 2-chlorotrityl chloride resin (2.00 g, typically 0.5 mmol/ gram of resin) was transferred into a sintered funnel fitted with a Teflon stopcock, and then rinsed with DCM (2x20 mL). After air drying, the Fmoc group was removed by reaction with a solution of 25% piperidine in DMF (20 mL) for 30 min followed by washing successively with DCM (3x20 mL), DMF (3 x 20 mL), and DCM (3 x 20 mL). To a solution of Fmoc-Ser(Al)-OH (1.00 g, 2 equiv) in DMF (4 mL) was added a 0.5 M solution of HATU in DMF (2 mL) followed by DIPEA (1.2 mL, 4-fold excess) and the resulting solution was added to the deprotected resin. The mixture was left for 2 h, with occasional stirring. The resin was isolated by filtration and rinsed successively with DCM (3 x 50 mL), DMF (3 x 50 mL), and DCM (3 x 50 mL). The sequence was repeated 2 more times to ensure complete coupling. Following additions of Fmoc-Aib-OH and Fmoc-Ser(Al)-OH were carried out, using this protocol, to give the appropriate pentapeptide. The pentapeptide was capped with Boc-Aib-OH in the last cycle using the same protocol and the resulting hexapeptide was cleaved from the resin with 2% TFA / DCM (v/v). The crude products were purified by HPLC.
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (s, 1H, N*H*), δ 7.72 (s, 1H, N*H*), δ 7.71 (d, 1H, N*H*, *J*=9.0 Hz), δ 7.20 (s, 1H, N*H*), δ 7.17 (d, 1H, N*H*, *J*=5.3 Hz), δ 5.82 (m, 2H, 2xC*H*=CH_2), δ 5.30 (s, 1H, N*H*), δ 5.20 (m, 4H, 2xCH=CH_2), δ 4.53 (m, 2H, 2xNHC*H*CO), δ 3.99 (m, 4H, 2xCHCH_2O), δ 3.90-3.64 (m, 4H, 2xCH_2CH=CH_2), δ 1.65-1.35 (m, 33H, 8xCH_3, Boc).
MS: $[M+Na]^+_{calcd}$=735.4, $[M+Na]^+_{found}$=735.4.

Peptide 22

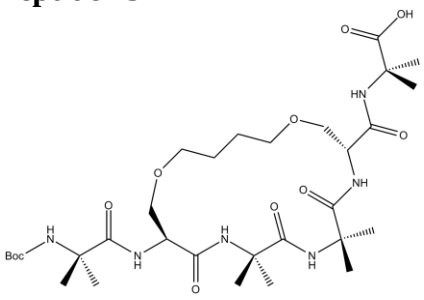


(*E* isomer)

Peptide **26** (0.839 g, 1.2 mmol) was dissolved in anhydrous DCM (60 mL) in a nitrogen-flushed flask equipped with a water-cooled condenser. Second-generation Grubbs' catalyst (0.071 g, 7 mol%) was added in a single portion and the flask was then immersed in an oil bath maintained at 50 °C. After refluxing for 30 min., the reaction was quenched by adding ethyl vinyl ether (400µL) directly to the flask after removing it from the oil bath. Stirring continued for 20 min., after which the solvent was removed under reduced pressure. The residue was purified by column

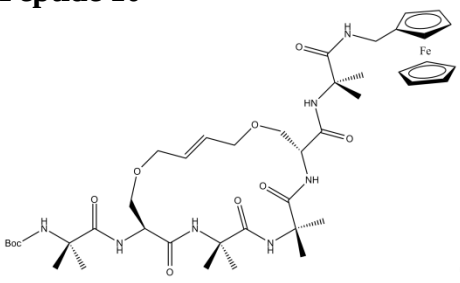
chromatography (DCM with 2% →10% methanol) to afford the *E*-selective isomer (475 mg, 57%).
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H, N*H*), δ 7.53 (d, 1H, N*H*, *J*=8.8 Hz), δ 7.42 (s, 1H, N*H*), δ 7.08 (d, 1H, N*H*, *J*=6.0 Hz), δ 6.98 (s, 1H, N*H*), δ 5.77-5.67 (m, 2H, C*H*=C*H*), δ 5.31 (s, 1H, N*H*), δ 4.75-4.47 (m, 2H, 2xNHC*H*CO), δ 4.28-3.60 (m, 8H, 2x CH_2-CH=CH, 2xCHCH_2O), δ 1.65-1.37 (m, 33H, 8xCH_3, Boc).
LRMS: $[M+Na]^+_{calcd}$=707.4, $[M+Na]^+_{found}$=707.4.

Peptide 23



To a solution of **22** (100 mg, 0.146 mmol) in anhydrous ethyl acetate (30 mL), was added 20 mg Pd/C (20% w/w). The reaction was purged with nitrogen and then placed under a hydrogen atmosphere. After stirring for 2 h, the reaction was filtered and concentrated *in vacuo* to reveal a white solid (100 mg, quant).
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (s, 1H, N*H*), δ 7.58 (d, 1H, N*H*, *J*=8.8Hz), δ 7.44 (s, 1H, N*H*), δ 7.18 (d, 1H, N*H*, *J*=4.0 Hz), δ 7.10 (s, 1H, N*H*), δ 5.45 (s, 1H, N*H*), δ 4.62 (m, 1H, NHC*H*CO), δ 4.51 (m, 1H, NHC*H*CO), δ 4.11 (m, 2H, CH_2CH_2O), δ 3.84 (m, 2H, CHCH_2O), δ 3.70 (m, 2H, OCH_2CH_2), δ 3.50 (m, 2H, CHCH_2O), δ 1.70-1.35 (m, 37H, 2xCH_2, 8xCH_3, Boc).
LRMS: $[M+Na]^+_{calcd}$=709.4, $[M+Na]^+_{found}$=709.4.

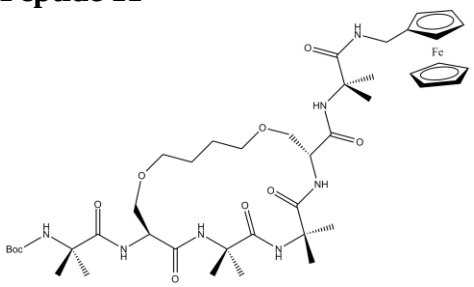
Peptide 10



(*E* isomer)
Peptide **22** (78 mg, 0.11 mmol) and ferrocenylmethylamine (35 mg, 0.16 mmol) were dissolved in anhydrous DMF (3 mL). DIPEA (80µL, 4 equiv.), HOAt (50mg, 2 equiv.) and HATU (4 equiv.) were added. Reaction mixture was stirred overnight under an N_2 atmosphere at rt. The solvent was removed *in vacuo* and the peptide purified using reverse phase HPLC.
^{1}H NMR (300 MHz, DMSO-d_6): δ 8.34 (s, 1H, N*H*), δ 7.99 (br s, 1H, N*H*), δ 7.77 (s, 1H, N*H*), δ 7.53 (s, 1H, N*H*), δ 7.49 (d, 1H, N*H*, *J*=8.1 Hz), δ 7.27 (s, 1H, N*H*), δ 7.07 (br s, 1H, N*H*), δ 5.68 (m, 2H, C*H*=C*H*), δ 4.44 (d, 1H, Cα*H*, *J*=6.4 Hz), 4.31 – 3.68 (m, 18H, Cp, Cα*H*, 4xCH_2), δ 3.58 – 3.49 (m, 2H, CαHCH_2), δ 1.42-1.28 (m, 33H, Boc, 8xCH_3).

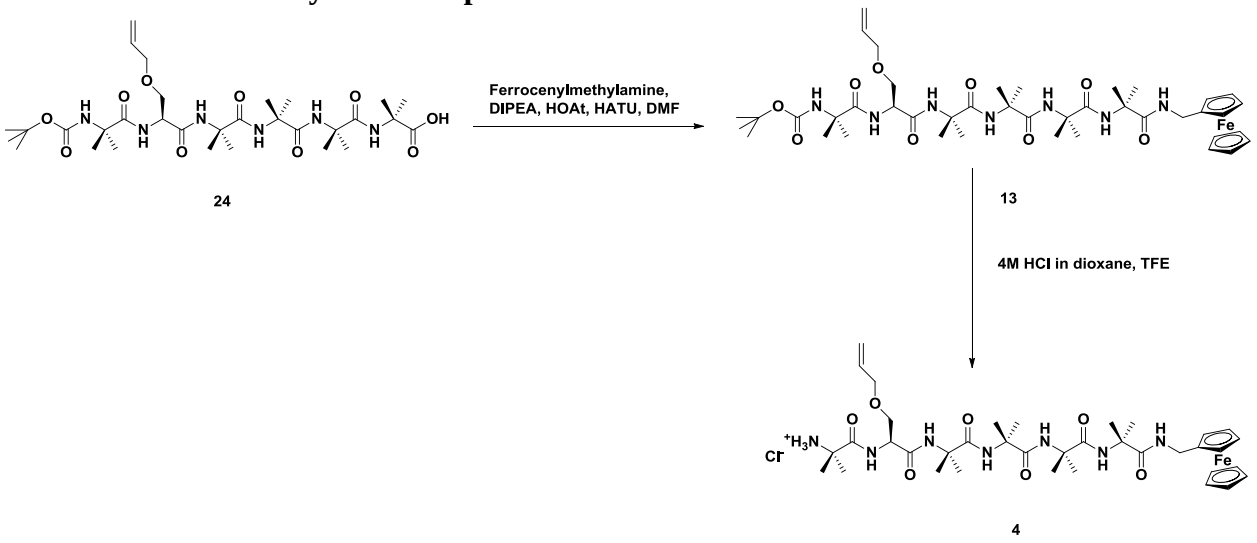
^{13}C NMR (150 MHz, DMSO-d_6): δ 175.18, 174.89, 174.81, 174.68, 174.28, 173.13, 171.23, 168.76, 158.26, 158.02, 155.04, 131.20, 128.30, 109.53, 78.87, 78.63, 68.57, 67.00, 66.04, 56.46, 56.26, 56.13, 55.76, 54.82, 52.64, 37.82, 28.17, 26.72, 25.47, 25.00, 24.68, 23.46, 22.88.
LRMS: $[M+Na]^+_{calcd}$=904.4, $[M+Na]^+_{found}$=904.4.

Peptide 11

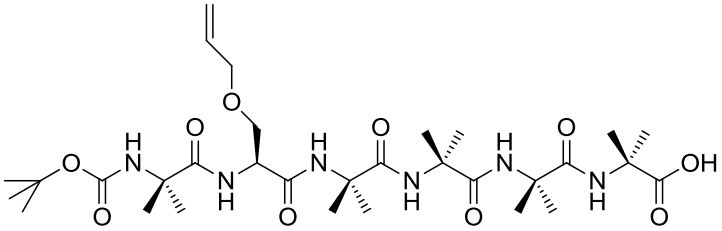


Peptide **23** (101 mg, 0.15 mmol) and ferrocenylmethylamine (35 mg, 0.16 mmol) were dissolved in anhydrous DMF (3 mL). DIPEA (100µL, 4 equiv.), HOAt (40mg, 2 equiv.) and HATU (110 mg, 4 equiv.) were added. Reaction mixture was stirred overnight under an N_2 atmosphere at room temperature. The solvent was removed *in vacuo* and the peptide purified using reverse phase HPLC.
^{1}H NMR (300 MHz, DMSO-d_6): δ 8.63 (s, 1H, N*H*), δ 8.06 (s, 1H, N*H*), δ 7.55 (s, 1H, N*H*), δ 7.35 (br s, 1H, N*H*), δ 7.33 (s, 1H, N*H*), δ 7.24 (br s, 1H, N*H*), δ7.15 (br s, 1H, N*H*), δ 4.45 (br s, 1H, Cα*H*), δ 4.24 – 3.90 (m, 12H, Cp, Cα*H*, CH_2 (Fc)), δ 3.81 (d, 1H, C*H*, *J*=6.9 Hz), δ 3.68 – 3.58 (m, 4H, 2xCH_2), δ 3.41 (dd, 1H, C*H*, *J*=9.6, 3.7 Hz), δ 3.21 (td, 1H, C*H*, *J*=9.2, 2.2 Hz), δ 1.75 (m, 1H, C*H*), δ 1.64 (m, 1H, C*H*), δ 1.53 (m, 1*H*, CH), δ 1.44-1.25 (m, 35H, Boc, CH_2, 8xCH_3).
^{13}C NMR (150 MHz, DMSO-d_6): δ 175.38, 174.76, 173.70, 173.40, 170.31, 168.84, 86.40, 78.24, 72.14, 70.83, 69.55, 68.91, 68.33, 67.01, 56.53, 56.44, 55.79, 55.75, 52.00, 37.88, 28.15, 27.43, 26.86, 26.46, 25.55, 24.03, 23.92, 23.18, 22.64.
LRMS: $[M+Na]^+_{calcd}$=906.4, $[M+Na]^+_{found}$=906.4.

Scheme S2. The final synthetic steps for helical control 4



Peptide 24



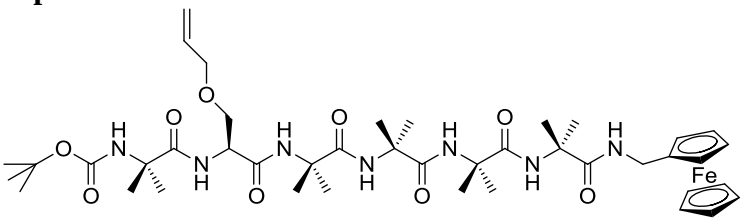
Fmoc-Aib-OH loaded 2-chlorotrityl chloride resin (2.0 g, typically 0.5 mmol/ gram of resin) was transferred into a sintered funnel fitted with a Teflon stopcock, and then rinsed with DCM (2x20 mL). After air drying, the Fmoc group was removed by reaction with a solution of 25% piperidine in DMF (20 mL) for 30 min followed by washing successively with DCM (3x20 mL), DMF (3 x 20 mL), and DCM (3 x 20 mL). To a solution of Fmoc-Aib-OH (1.0 g, 2 equiv) in DMF (4 mL) was added a 0.5 M solution of HATU in DMF (2 mL) followed by DIPEA (1.2 mL, 4-fold excess) and the resultant solution was added to the deprotected resin. The mixture was left for 2 h, with occasional stirring. The resin was isolated by filtration and rinsed successively with DCM (3 x 50 mL), DMF (3 x 50 mL), and DCM (3 x 50 mL). The sequence was repeated twice to ensure complete coupling. Successive additions of Fmoc Aib-OH were carried out to give the appropriate oligotetrapeptide. Following additions of Fmoc-Ser(Al)-OH were carried out, using this protocol, to give the appropriate pentapeptide. The pentapeptide was then capped with Boc-Aib-OH in the last cycle using the same protocol and the resulting hexapeptide was cleaved from the resin with 2% TFA / DCM (v/v). The crude products were purified using reverse phase HPLC.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (s, 1H, N*H*), δ 7.67 (s, 1H, N*H*), δ 7.65 (s, 1H, N*H*), δ 7.24 (s, 1H, N*H*), δ 7.19 (d, 1H, N*H*, *J*=4.7 Hz), δ 5.80 (ddd, 1H, C*H*=CH_2, *J*=15.9, 10.8, 5.6 Hz), δ 5.22 (m, 2H, CH=CH_2), δ 5.20 (s, 1H, N*H*), δ 4.13 (m, 1H, NHC*H*CO), δ 3.99 (m, 2H, CHCH_2O), δ 3.87 (dd, 1H, C*H*HCH=CH_2, *J*=10.0, 3.2 Hz), δ 3.72 (dd, 1H, CH*H*CH=CH_2, *J*=10.0, 3.5 Hz), δ 1.60-1.11 (m, 39H, 10xCH_3, Boc).

^{13}C NMR (150 MHz, $CDCl_3$) δ 176.24, 175.89, 175.48, 174.74, 170.72, 155.47, 133.56, 117.90, 81.46, 77.21, 77.00, 76.79, 72.22, 67.97, 59.53, 57.09, 56.90, 56.74, 56.18, 50.81, 31.91, 31.23,

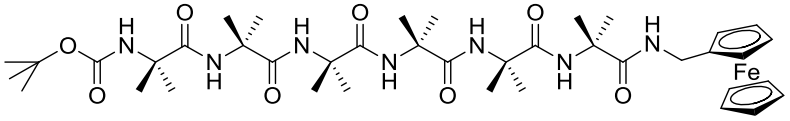
29.68, 29.64, 29.35, 28.29, 28.25, 27.23, 26.61, 26.45, 25.55, 24.65, 23.52, 23.43, 23.33, 23.64, 22.68, 14.10.
LRMS: $[M+Na]^+_{calcd}$=693.4, $[M+Na]^+_{found}$=693.4.

Peptide 13



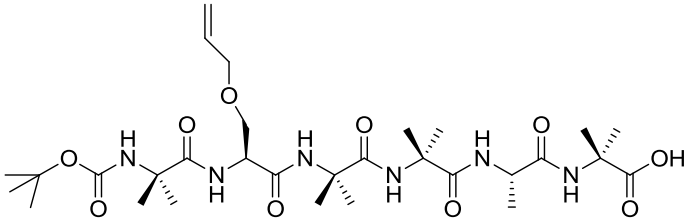
Peptide **24** (460 mg, 0.69 mmol) and ferrocenylmethylamine (163 mg, 0.76 mmol) were dissolved in anhydrous DMF (10 mL). DIPEA (480 µL, 4 equiv.), HOAt (190 mg, 2 equiv.) and HATU (4 equiv.) were added. Reaction mixture was stirred overnight under an N_2 atmosphere at room temperature. The solvent was removed *in vacuo* and the peptide purified using reverse phase HPLC.
^{1}H NMR (300 MHz, DMSO-d_6): δ 8.31 (br s, 1H, N*H*), δ 7.98 (br s, 1H, N*H*), δ 7.61 (s, 1H, N*H*), δ 7.56 (s, 1H, N*H*), δ 7.52 (br s, 1H, N*H*), δ 7.37 (s, 1H, N*H*), δ 7.31 (s, 1H, N*H*), δ 5.92-5.77 (ddd, 1H, C*H*=CH_2, *J*=22.5, 10.4, 5.2 Hz), δ 5.20 (m, 2H, CH=CH_2), δ 4.35-3.45 (m, 16H, Cp, NHC*H*CO, 2xCH_2), δ 1.65-1.05 (m, 39H, 10xCH_3, Boc).
LRMS: $[M+Na]^+_{calcd}$=890.5, $[M+Na]^+_{found}$=890.5.

Peptide 12 (Precursor to **3**)



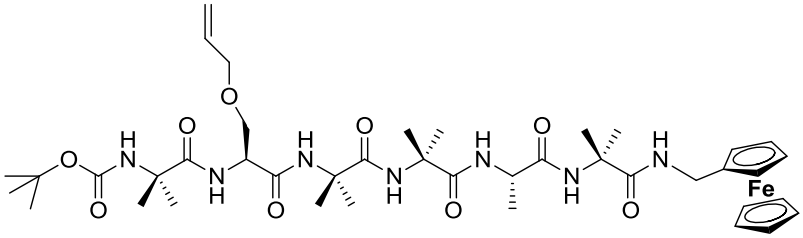
^{1}H NMR (300 MHz, DMSO-d_6), ^{13}C NMR (150 MHz, DMSO-d_6), LRMS: Previously reported.[2]

Peptide 25



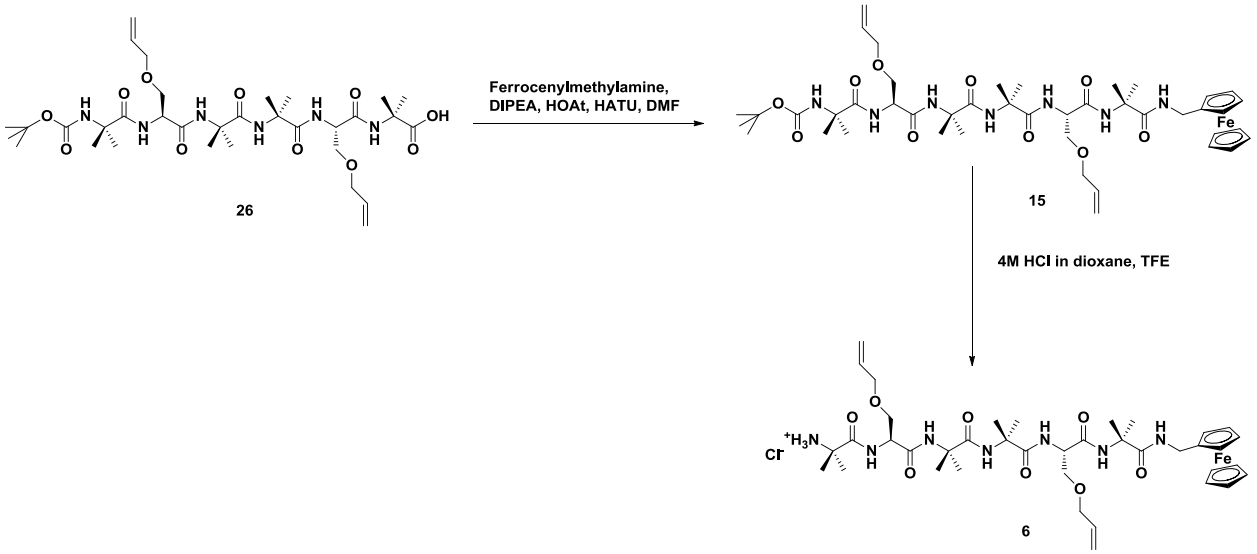
Peptide **25** was synthesized on SPPS using the protocol for peptide **24**, with an Fmoc-Ala-OH residue at position 2, in lieu of Fmoc-Aib-OH.
^{1}H NMR (300 MHz, DMSO-d_6): δ 8.22 (br s, 1H, N*H*), δ 7.94 (br s, 1H, N*H*), δ 7.42 (d, 1H, N*H*, *J*=3.5 Hz), δ 7.42 – 7.37 (m, 3H, N*H*), δ 5.83 (m, 1H, OCH$_2$C*H*), δ 5.23 (dd, 1H, CHC*H*H, *J*=17.3, 1.8 Hz), δ 5.13 (dd, 1H, CHCH*H*, *J*=10.5, 1.5 Hz), δ 4.10 (br s, 1H, Cα*H*), δ 3.96 (dd, 2H, OC*H*$_2$CH, *J*=3.5, 1.5 Hz), δ 3.68 (ddd, 2H, CαHC*H*$_2$, *J*=13.9, 9.9, 4.6 Hz), δ 1.39 – 1.29 (m, 33H, Boc, 4xAibs), δ 1.27 – 1.25 (d, 3H, C*H*$_3$ Alanine, *J*=7.3 Hz).
HRMS: $[M]^+_{calcd}$=657.3823, $[M]^+_{found}$=657.3891.

Peptide 14 (Precursor to **5**)

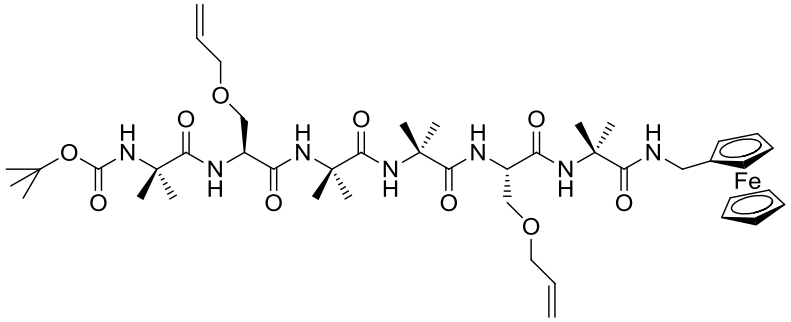


Peptide **25** (200 mg, 0.30 mmol) and ferrocenylmethylamine (72 mg, 0.33 mmol) were dissolved in anhydrous DMF (5 mL). DIPEA (212 µL, 4 equiv.), HOBt (37 mg, 0.9 equiv.) and HATU (1.1 equiv.) were added. Reaction mixture was stirred for 39 h under an N_2 atmosphere at room temperature. The solvent was removed *in vacuo* and the peptide purified using reverse phase HPLC.
^{1}H NMR (300 MHz, DMSO-d_6): δ 8.29 (br s, 1H, N*H*), δ 7.96 (br s, 1H, N*H*), δ 7.56 (d, 1H, N*H*, *J*=6.0 Hz), δ 7.50 (s, 1H, N*H*), δ 7.43 (s, 1H, N*H*), δ 7.39 (s, 1H, N*H*), δ 7.26 (t, 1H, N*H*, *J*=6.1 Hz), δ 5.87-5.80 (ddd, 1H, C*H*=CH$_2$, *J*=22.4, 10.4, 5.2 Hz), δ 5.23 (dd, 1H, CH=C*H*CH, *J*=17.3, 1.5 Hz), δ 5.14 (d, 1H, CH=CHC*H*, *J*=10.4 Hz), δ 4.20-4.02 (m, 10H, Cp, Cα*H*), δ 3.97-3.90 (m, 5H, Cα*H*, 2xC*H*$_2$), δ 3.74-3.65 (m, 2H, C*H*$_2$), δ 1.41-1.32 (m, 33H, 8xC*H*$_3$, Boc), δ 1.31-1.29 (m, 3H, C*H*$_3$ Alanine).
LRMS: $[M+Na]^+_{calcd}$=876.4, $[M+Na]^+_{found}$=876.4.

Scheme S3. The final synthetic steps for helical control 6



Peptide 15

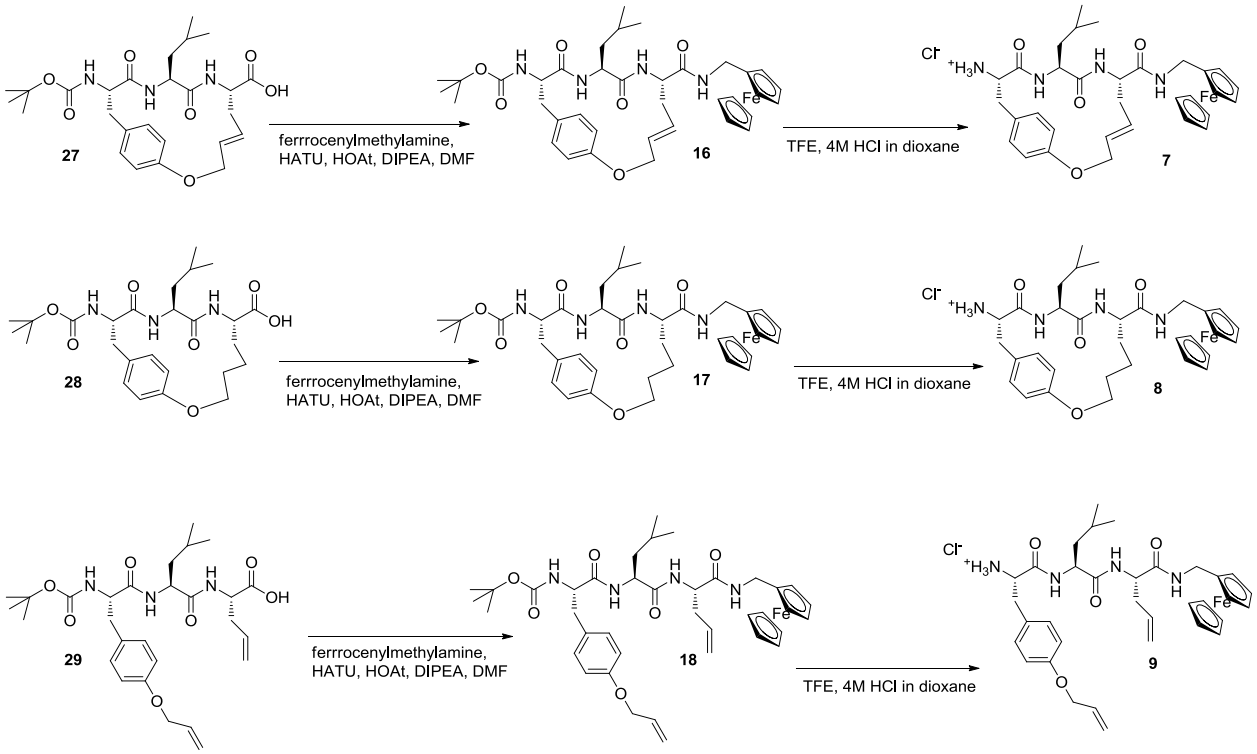


Peptide **26** (240 mg, 0.32 mmol) and ferrocenylmethylamine (88 mg, 0.41 mmol) were dissolved in anhydrous DMF (5 mL). DIPEA (240µL, 4 equiv.), HOAt (80 mg, 2 equiv.) and HATU (4 equiv.) were added. The reaction mixture was stirred overnight under an N_2 atmosphere at room temperature. The solvent was removed *in vacuo* and the peptide purified using reverse phase HPLC.

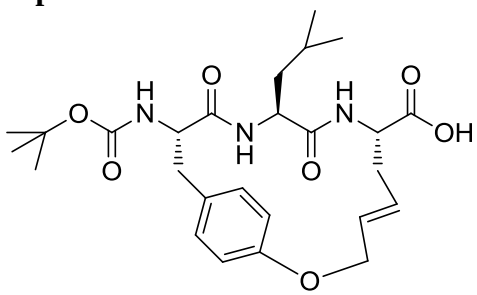
^{1}H NMR (300 MHz, DMSO-d_6): δ 8.27 (br s, 1H, N*H*), δ 8.05 (br s, 1H, N*H*), δ 7.62 (d, 1H, N*H*, *J*=6.4 Hz), δ 7.54 (s, 1H, N*H*), δ 7.49 (s, 1H, N*H*), δ 7.43 (br s, 1H, N*H*), δ 7.27 (t, 1H, N*H*, *J*=6.3 Hz), δ 5.90 – 5.78 (m, 2H, 2xC*H*=CH_2), δ 5.25 – 5.08 (m, 4H, 2xCH=CH_2), δ 4.25-3.65 (m, 21H, Cp, 2xCα*H*, 5xCH_2), δ 1.65-1.05 (m, 33H, 8xCH_3, Boc).

LRMS: $[M+Na]^+_{calcd}$=932.5, $[M+Na]^+_{found}$=932.5.

Scheme S4. The final synthetic steps for β-strand peptides



Peptide 27

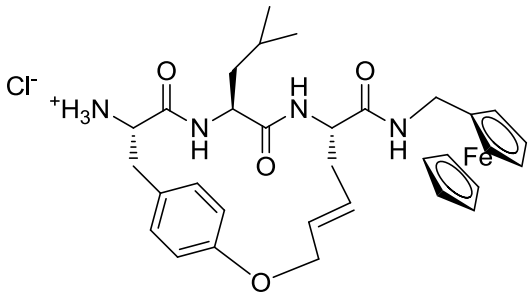


Methyl (4*E*,7S,10S,13S)-13-{[(tert-butoxy)carbonyl]amino}-10-(2-methylpropyl)-9,12-dioxo-2-oxa-8,11-diazabicyclo[13.2.2]nonadeca-1(17),4,15,18-tetraene-7-carboxylate[3] (584 mg, 1.13 mmol) was dissolved in THF (4 mL). To this stirring reaction 1.6M NaOH (1.2 mL) was added, followed by MeOH (2 mL). The solution was stirred at rt for 22 h, diluted with water (20 mL) and ethyl acetate (20 mL), and the pH adjusted to pH 3. The organic phase was separated, washed with brine (20 mL), and dried with $MgSO_4$. The solvent was removed *in vacuo* to yield a white crystalline solid (495 mg, 87%).

^{1}H NMR (600 MHz, d_6-DMSO) δ 7.97 (d, 1H, N*H* Gly, *J*=8.4 Hz), δ 7.19 (d, 1H, N*H* Leu, *J*=8.2 Hz), δ 6.97 (d, 2H, Ar*H*, *J*=7.3 Hz), δ 6.87 (d, 1H, N*H* Tyr, *J*=7.3 Hz), δ 6.68 (d, 2H, Ar*H*, *J*=8.7 Hz), δ 5.56 (d, 1H, $OCH_2CHCHCH_2$, *J*=15.7 Hz), δ 5.47 – 5.43 (m, 1H, $OCH_2CHCHCH_2$), δ 4.65 – 4.57 (m, 2H, $OCH_2CHCHCH_2$), δ 4.27 – 4.23 (m, 1H, Cα*H* Gly), δ 4.22 – 4.17 (m, 1H, Cα*H* Tyr), δ 4.09 – 4.06 (m, 1H, Cα*H* Leu), δ 2.80 – 2.77 (dd, 1H, CαH C*H*HPh, *J*=13.0, 5.2 Hz), δ 2.69 – 2.65 (m, 1H, CαH CH*H*Ph), δ 2.49 – 2.46 (m, 1H, $OCH_2CHCHCHH$), δ 2.25 – 2.20 (m,

1H, $OCH_2CHCHCH\mathit{H}$), δ 1.58 – 1.51 (m, 1H, CαH$CH_2C\mathit{H}(CH_3)_2$), δ 1.38 (s, 9H, $(CH_3)_3$), δ1.34 – 1.23 (m, 2H, CαH$C\mathit{H}_2CH(CH_3)_2$), δ 0.84 – 0.79 (m, 6H, CαH$CH_2CH(C\mathit{H}_3)_2$)
^{13}C NMR (150 MHz, d_6-DMSO) δ 172.7, 171.9, 171.0, 170.2, 169.8, 155.4, 154.6, 129.7, 128.9, 77.9, 72.2, 65.9, 60.2, 59.7, 55.3, 51.8, 50.4, 42.9, 32.6, 28.1, 23.4, 23.0, 22.4, 21.0, 20.7
LRMS (*m/z*) : $[M]^-$ calculated for $C_{26}H_{36}N_3O_7^-$, 502.2; found 502.2.

Peptide 7

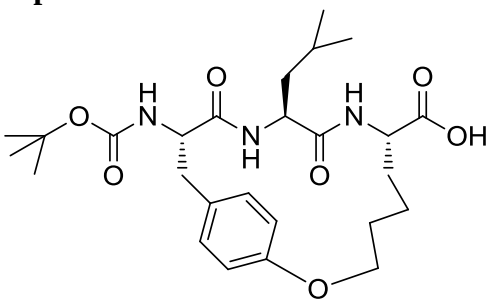


Peptide **27** (116 mg, 0.23 mmol) was dissolved in anhydrous DMF (3.85 mL) and the solution stirred at r.t. for 10 min. Ferrocenylmethylamine (54 mg, 0.25 mmol) was added, followed by DIPEA (119 mg, 0.92 mmol, 160 μL), HATU (95 mg, 0.25 mmol) and HOAt (34 mg, 0.25 mmol). The reaction mixture was stirred under an N_2 atmosphere at rt for 20 h, and subsequently diluted with water (20 mL) and ethyl acetate (20 mL), and the pH adjusted to pH 3. The organic phase was separated and washed with brine (2 x 20 mL) and dried with $MgSO_4$. The solvent was removed *in vacuo* to yield Peptide **16** as a pale brown solid (63 mg), that was used in the next step without further purification.
^{1}H NMR (600 MHz, d_6-DMSO) δ 7.97 (d, 1H, N*H* Gly, *J*=8.6 Hz), δ 7.90 (t, 1H, N*H* Fc, *J*=5.8 Hz), δ 7.07 (d, 1H, N*H* Leu, *J*=7.8 Hz), δ 6.97 (d, 2H, Ar*H*, *J*=7.7 Hz), δ 6.87 (d, 1H, N*H* Tyr, *J*=7.2 Hz), δ 6.68 (d, 2H, Ar*H*, *J*=8.6 Hz), δ 5.57- 5.54 (d, 1H, $OCH_2C\mathit{H}CHCH_2$, *J*=15.2 Hz), δ 5.49 – 5.44 (dd, 1H, $OCH_2CHC\mathit{H}CH_2$, *J*=14.6, 6.7 Hz), δ 4.63- 4.57 (m, 2H, $OC\mathit{H}_2CHCHCH_2$), δ 4.35 – 4.33 (m, 1H, Cα*H* Gly), δ 4.25 – 3.92 (m, 9H, Cp), δ 4.21 – 4.17 (m, 1H, Cα*H* Tyr), δ 4.07 – 4.05 (m, 1H, Cα*H* Leu), δ 3.96 (m, 2H, $C\mathit{H}_2$Fc), δ 2.81 – 2.77 (dd, 1H, CαHC*H*HPh, *J*=13.0, 5.2 Hz), δ 2.69 – 2.61 (dd, 1H, CαHCH*H*Ph, *J*=22.6, 11.4 Hz), δ 2.38 – 2.22 (m, 2H, $OCH_2CHCHC\mathit{H}_2$), δ 1.52 – 1.46 (tt, 1H, CαH$CH_2C\mathit{H}(CH_3)_2$, *J*=13.3, 6.6 Hz), δ 1.38 (s, 9H, $(CH_3)_3$), δ1.31 – 1.23 (m, 2H, CαH$C\mathit{H}_2CH(CH_3)_2$), δ 0.79 – 0.77 (m, 6H, CαH$CH_2CH(C\mathit{H}_3)_2$)
^{13}C NMR (150 MHz, d_6-DMSO) δ 170.9, 170.5, 162.2, 155.5, 129.7, 129.1, 127.3, 114.9, 85.9, 77.9, 72.2, 71.5, 70.3, 69.2, 68.9, 68.8, 68.7, 68.3, 68.2, 67.9, 67.3, 60.2, 52.6, 50.4, 43.1, 40.0, 38.2, 37.4, 35.7, 30.7, 28.1, 23.5, 23.1, 22.4
LRMS (*m/z*) : $[M + Na]^+$ calculated for $C_{37}H_{48}FeN_4O_6Na$, 723.2; found 723.2.

Peptide **16** (24 mg, 0.03 mmol) was dissolved in TFE (3 mL) and 4M HCl in dioxane (3mL) added. The mixture was stirred at rt for 30 min., and the solvent removed *in vacuo*. The crude product was purified using reverse phase HPLC to yield a brown solid (Peptide **7**, (5 mg, 25%)).
^{1}H NMR (600 MHz, d_6-DMSO) δ 8.30 (d, 3H, N*H* Tyr, *J*=3.4 Hz), δ 8.20 (d, 1H, N*H* Gly, *J*=8.7 Hz), δ 7.99 (t, 1H, N*H* Fc, *J*=5.8 Hz), δ 7.93 (d, 1H, N*H* Leu, *J*=8.0 Hz), δ 6.96 (d, 2H, Ar*H*, *J*=7.9 Hz), δ 6.72 (d, 2H, Ar*H*, *J*=8.7 Hz), δ 5.64 – 5.60 (dt, 1H, $OCH_2C\mathit{H}$, *J*=15.8, 4.3 Hz), δ 5.54 – 5.50 (m, 1H, $OCH_2CHC\mathit{H}$), δ 4.67 – 4.60 (m, 2H, $OC\mathit{H}_2CH$), δ 4.41 – 4.37 (ddd, 1H, Cα*H* Gly, *J*=11.8, 8.8, 2.7 Hz), δ 4.23 -4.18 (m, 1H, Cα*H* Tyr), δ 4.16 – 4.10 (m, 1H, Cα*H* Leu), δ 4.16 – 4.04 (m, 9H, Cp), δ 4.00 – 3.91 (ddd, 2H, $C\mathit{H}_2$Fc, *J*=30.9, 14.8, 5.8 Hz), δ 3.05 – 3.02 (dd, 1H,

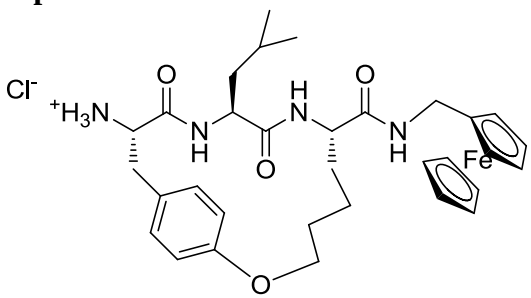
CαHC*H*HPh, *J*=13.1, 5.7 Hz), δ 2.71 – 2.67 (dd, 1H, CαHCH*H*Ph, *J*=12.9, 10.6 Hz), δ 2.35 (d, 1H, $OCH_2CHCHCH$, *J*=15.5 Hz), δ 2.27 – 2.21 (m, 1H, $OCH_2CHCHCH$), δ 1.54 – 1.48 (m, 1H, $C\alpha HCH_2CH(CH_3)_2$), δ 1.36 – 1.27 (m, 2H, $C\alpha HCH_2CH(CH_3)_2$), δ 0.84 – 0.82 (m, 6H, $C\alpha HCH_2CH(CH_3)_2$). ^{13}C NMR (150 MHz, d_6-DMSO) δ 170.5, 166.4, 156.0, 129.8, 129.2, 127.3, 114.9, 86.0, 72.9, 69.4, 69.3, 68.2, 67.3, 67.2, 67.1, 65.8, 52.6, 52.5, 50.8, 43.5, 37.3, 36.0, 33.6, 23.6, 22.8, 22.7. HRMS: $[M+H]^+$ calculated for $C_{32}H_{40}FeN_4O_4$, 600.23916; found 600.23935. IR : 1635 cm^{-1}, 1686 cm^{-1} (shoulder) (Amide I Band); 1513 cm^{-1}, 1529 cm^{-1} (Amide II Band); 3292 cm^{-1} (Amide A Band).

Peptide 28



Methyl (7S,10S,13S)-13-{[(tert-butoxy)carbonyl]amino}-10-(2-methylpropyl)-9,12-dioxo-2-oxa-8,11-diazabicyclo[13.2.2]nonadeca-1(17),15,18-triene-7-carboxylate[3] (558 mg, 1.08 mmol) was dissolved in THF (3.2 mL). To this stirring reaction, 1.6M NaOH (1.1 mL) was added, followed by MeOH (1.84 mL). The solution was stirred at rt for 22 h, diluted with water (20 mL) and ethyl acetate (20 mL), and the pH adjusted to pH 3-4. The organic phase was separated, washed with brine (20 mL), and dried with $MgSO_4$. The solvent was removed *in vacuo* to yield a white solid (400 mg, 73%).
^{1}H NMR (300 MHz, d_6-DMSO) δ 8.03 (d, 1H, N*H*, *J*=8.9Hz), δ 7.01 (d, 3H, N*H* and Ar*H*, *J*=7.6 Hz), δ 6.81 (d, 1H, N*H*, *J*=8.0 Hz), δ 6.75 (d, 2H, Ar*H*, *J*=8.6 Hz), δ 4.39 – 4.30 (d, 1H, Cα*H*, *J*=11.9 Hz), δ 4.25 -4.12 (m, 2H, $OCH_2CH_2CH_2$), δ 4.07 – 3.91 (dd, 2H, (2x Cα*H*), *J*=14.4, 7.3 Hz), δ 2.85 – 2.77 (dd, 1H, CαHC*H*HPh, *J*=12.4, 5.1 Hz), δ 2.67 – 2.54 (t, 1H, CαHCH*H*Ph, *J*=12.0 Hz), δ 1.78 – 1.62 (br s, 2H, $OCH_2CH_2CH_2$), δ 1.61 -1.45 (m, 3H, $C\alpha HCH_2CH(CH_3)_2$), δ 1.38 (s, 9H, $(CH_3)_3$), δ 1.35 – 1.20 (m, 4H, $OCH_2CH_2CH_2CH_2$), δ 0.81 – 0.76 (m, 6H, $C\alpha HCH_2CH(CH_3)_2$)
LRMS (*m/z*) : $[M + H]^+$ calculated for $C_{26}H_{40}N_3O_7$, 506.2; found 505.9.

Peptide 8

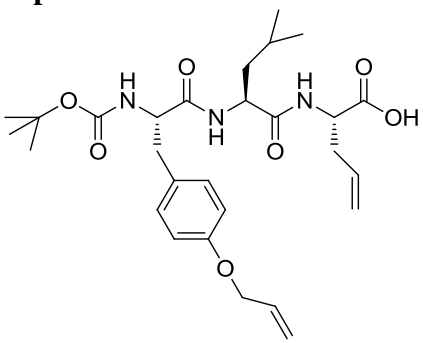


Peptide **28** (200 mg, 0.40 mmol) was dissolved in anhydrous DMF (6.7 mL) and stirred at rt for 10 min. Ferrocenylmethylamine (95 mg, 0.44 mmol) was added, followed by DIPEA (206 mg, 1.60 mmol, 280 μL), HATU (167 mg, 0.44 mmol) and HOAt (60 mg, 0.44 mmol). The reaction

mixture was stirred at r.t. under N_2 conditions for 24 h, and subsequently diluted with water (32 mL) and ethyl acetate (32 mL), and the pH adjusted to pH 3-4. The organic phase was separated and washed with $NaHCO_3$ (30 mL) and brine (2 x 30 mL), and dried with $MgSO_4$. The solvent was removed *in vacuo* to yield Peptide **17** as a pale brown solid (300 mg), that was used in the next step without further purification.
^{1}H NMR (600 MHz, d_6-DMSO) δ 7.96 (d, 1H, N*H* Gly, *J*=9.8Hz), δ 7.89 (m, 1H, N*H* Fc), δ 7.20 – 6.96 (m, 3H, Ar*H* and N*H* Tyr), δ 6.88 – 6.62 (m, 3H, Ar*H* and N*H* Leu), δ 4.34 – 4.02 (m, 2H, OC*H*$_2$CH$_2$CH$_2$), δ 4.29 – 4.25 (m, 1H, Cα*H* Gly), δ 4.23 – 3.96 (m, 9H, Cp), δ 4.20 – 3.96 (m, 2H, 2x Cα*H*), δ 3.96 (d, 2H, C*H*$_2$Fc, *J*=5.7Hz), δ 2.82 – 2.79 (dd, 1H, CαHC*H*HPh, *J*=12.6, 5.5 Hz), δ 2.64 – 2.59 (dd, 1H, CαHCH*H*Ph, *J*=23.9, 11.3 Hz), δ 1.77 – 1.68 (br s, 2H, OCH$_2$C*H*$_2$CH$_2$), δ 1.59 -1.42 (td, 3H, CαHC*H*$_2$C*H*(CH$_3$)$_2$, *J*=13.1, 6.4 Hz), δ 1.38 (s, 9H, (CH$_3$)$_3$), δ 1.34 – 1.19 (m, 4H, OCH$_2$CH$_2$C*H*$_2$C*H*$_2$), δ 0.88 – 0.74 (m, 6H, CαHCH$_2$CH(C*H*$_3$)$_2$)
^{13}C NMR (150 MHz, d_6-DMSO) δ 171.2, 170.8, 169.7, 162.2, 155.8, 128.5, 115.4, 86.0, 77.8, 73.0, 70.3, 69.4, 68.8, 68.7, 67.2, 67.1, 66.8, 59.7, 56.0, 50.8, 50.3, 43.2, 40.0, 38.2, 37.3, 36.6, 35.7, 31.2, 30.7, 28.0, 27.0, 23.5, 23.1, 22.6, 21.8, 20.7
LRMS (*m/z*) : $[M + Na]^+$ calculated for $C_{37}H_{50}FeN_4O_6Na$, 725.3; found 725.1.

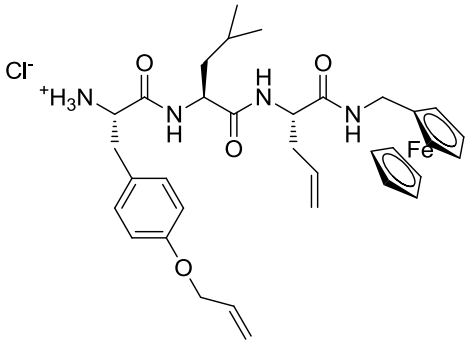
Peptide **17** (37 mg, 0.05 mmol) was dissolved in TFE (3 mL) and 4M HCl in dioxane (3mL) added. The mixture was stirred at rt for 25 min., and the solvent removed *in vacuo*. The crude product was purified using reverse phase HPLC to yield a brown solid (Peptide **8**, (14 mg, 44%)).
^{1}H NMR (600 MHz, d_6-DMSO) δ 8.32 (d, 3H, N*H* Tyr, *J*=4.1 Hz), δ 8.11 (d, 1H, N*H* Gly, *J*=9.1 Hz), δ 7.96 (t, 1H, N*H* Fc, *J*=5.8 Hz), δ 7.80 (d, 1H, N*H* Leu, *J*=7.8 Hz), δ 7.00 (d, 2H, Ar*H*, *J*=7.7 Hz), δ 6.79 (d, 2H, Ar*H*, *J*=8.6 Hz), δ 4.35 – 4.25 (m, 3H, OC*H*HC*H*$_2$CH$_2$, Cα*H* Gly, Cα*H* Tyr), δ 4.19 – 4.01 (m, 11H, Cp, C*H*$_2$), OCH*H*C*H*$_2$CH$_2$, Cα*H* Leu), δ 3.97 – 3.92 (dd, 2H, C*H*$_2$Fc, *J*=15.8, 6.1 Hz), δ 3.08 – 3.05 (dd, 1H, CαHC*H*HPh, *J*=12.8, 5.8 Hz), δ 2.65 – 2.61 (m, 1H, CαHCH*H*Ph), δ 1.78 – 1.70 (m, 1H, OCH$_2$C*H*HCH$_2$), δ 1.61 – 1.47 (m, 3H, OCH$_2$CH$_2$C*H*HC*H*H, CαHCH$_2$C*H*(CH$_3$)$_2$), δ 1.43 – 1.21 (m, 5H, OCH$_2$CH*H*CH*H*CH*H*, CαHC*H*$_2$CH(CH$_3$)$_2$), δ 0.83 – 0.81 (m, 6H, CαHCH$_2$CH(C*H*$_3$)$_2$). ^{13}C NMR (150 MHz, d_6-DMSO) δ 171.1, 170.2, 166.4, 156.3, 130.1, 126.2, 115.5, 86.1, 73.0, 69.4, 69.3, 68.7, 67.3, 67.2, 67.1, 66.2, 52.6, 50.8, 50.7, 43.6, 40.0, 37.3, 36.2, 31.2, 26.8, 23.6, 22.8, 22.7, 21.7. HRMS: $[M+H]^+$ calculated for $C_{32}H_{42}FeN_4O_4$, 602.25500; found 602.25488. IR : 1636 cm^{-1} (Amide I Band); 1511 cm^{-1} (Amide II Band); 3293 cm^{-1} (Amide A Band).

Peptide 29



Methyl(2S)-2-[(2S)-2-[(2S)-2-{[(tert-butoxy)carbonyl]amino}-3-[4-(prop-2-en-1-yloxy)phenyl] propanamido]-4-methylpentanamido]pent-4-enoate[3] (485 mg, 0.89 mmol) was dissolved in THF (3 mL). To this stirring reaction 1.6M NaOH (890 μL) was added, followed by MeOH (1.5 mL). The solution was stirred at rt for 23 h, diluted with water (20 mL) and ethyl acetate (20 mL), and the pH adjusted to pH 3-4. The organic phase was separated, washed with brine (20 mL), and dried over $MgSO_4$. The solvent was removed *in vacuo* to yield a white solid (405 mg, 86%).
^{1}H NMR (300 MHz, d_6-DMSO) δ 8.11 (d, 1H, N*H*, *J*=7.7 Hz), δ 7.87 (d, 1H, N*H*, *J*=8.4 Hz), δ 7.14 (d, 2H, Ar*H*, *J*=8.2 Hz), δ 6.88 (d, 1H, N*H*, *J*=8.9 Hz), δ 6.82 (d, 2H, Ar*H*, *J*=7.9 Hz), δ 6.09 – 5.96 (ddd, 1H, OCH_2CHCH_2, *J*=22.4, 10.4, 5.2 Hz), δ 5.82 – 5.68 (td, 1H, $C\alpha HCH_2CHCH_2$, *J*=16.9, 6.9 Hz), δ 5.34 (d, 1H, CH_2CHCHH, *J*=17.3 Hz), δ 5.22 (d, 1H, CH_2CHCHH, *J*=10.5 Hz), δ 5.07 (d, 1H, CH_2CHCHH, *J*=17.2 Hz), δ 5.02 (d, 1H, CH_2CHCHH, *J*=10.2 Hz), δ 4.51 (d, 1H, OCH_2CHCH_2, *J*=4.0 Hz), δ 4.42 – 4.35 (d, 1H, Cα*H*, *J*=7.6 Hz) δ 4.26 – 4.19 (dd, 1H, Cα*H*, *J*=13.0, 7.7 Hz) δ 4.13 – 3.97 (m, 1H, Cα*H*), δ 2.91 – 2.84 (d, 1H, $C\alpha HCHHPh$, *J*=10.3 Hz), δ 2.64 – 2.60 (m, 1H, $C\alpha HCHHPh$), δ 2.47 – 2.32 (m, 2H, $C\alpha HCH_2CHCH_2$), δ 1.70 – 1.24 (m, 3H, $CH_2CH(CH_3)_2$), δ 1.30 (s, 9H, $(CH_3)_3$), δ 0.90 – 0.84 (m, 6H, $C\alpha HCH_2CH(CH_3)_2$)

Peptide 9

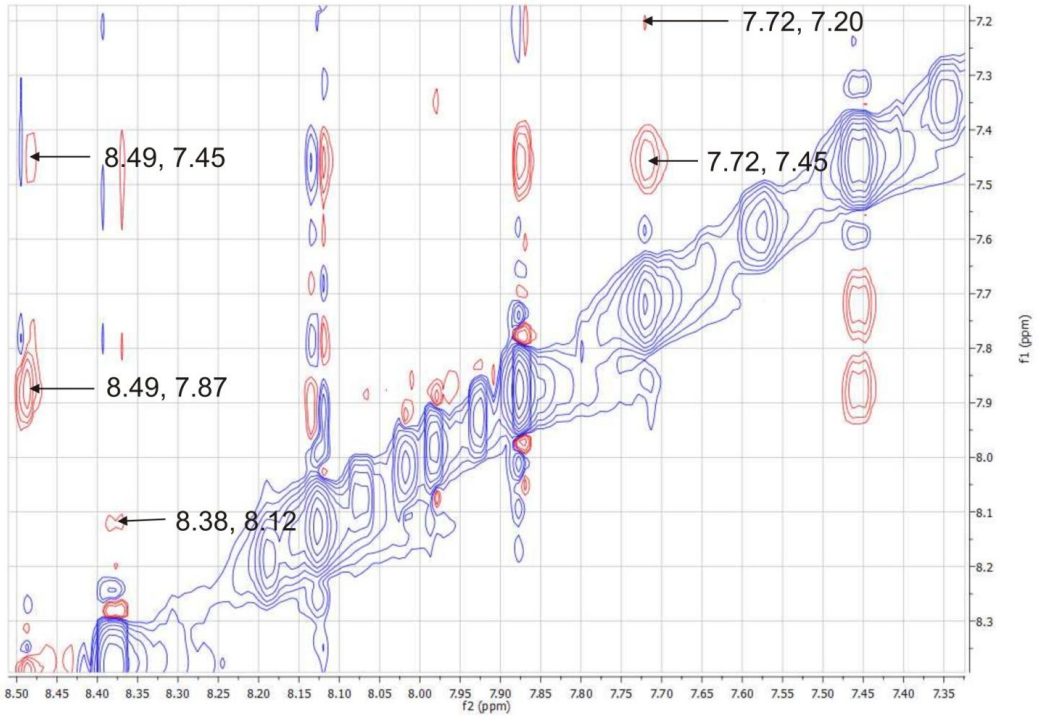


Peptide **29** (200 mg, 0.38 mmol) was dissolved in anhydrous DMF (6.4 mL). Ferrocenylmethylamine (90 mg, 0.42 mmol) was added, followed by DIPEA (196 mg, 1.52 mmol, 265 μL), HATU (160 mg, 0.42 mmol) and HOAt (57 mg, 0.42 mmol). The reaction mixture was stirred under an N_2 atmosphere at rt for 24 h, and subsequently diluted with water (30 mL) and ethyl acetate (30 mL), and the pH adjusted to pH 3-4. The organic phase was separated and washed with $NaHCO_3$ (30 mL) and brine (30 mL), and dried with $MgSO_4$. The solvent was removed *in vacuo* to yield Peptide **18** as a brown solid (280 mg), that was used in the next step without further purification.

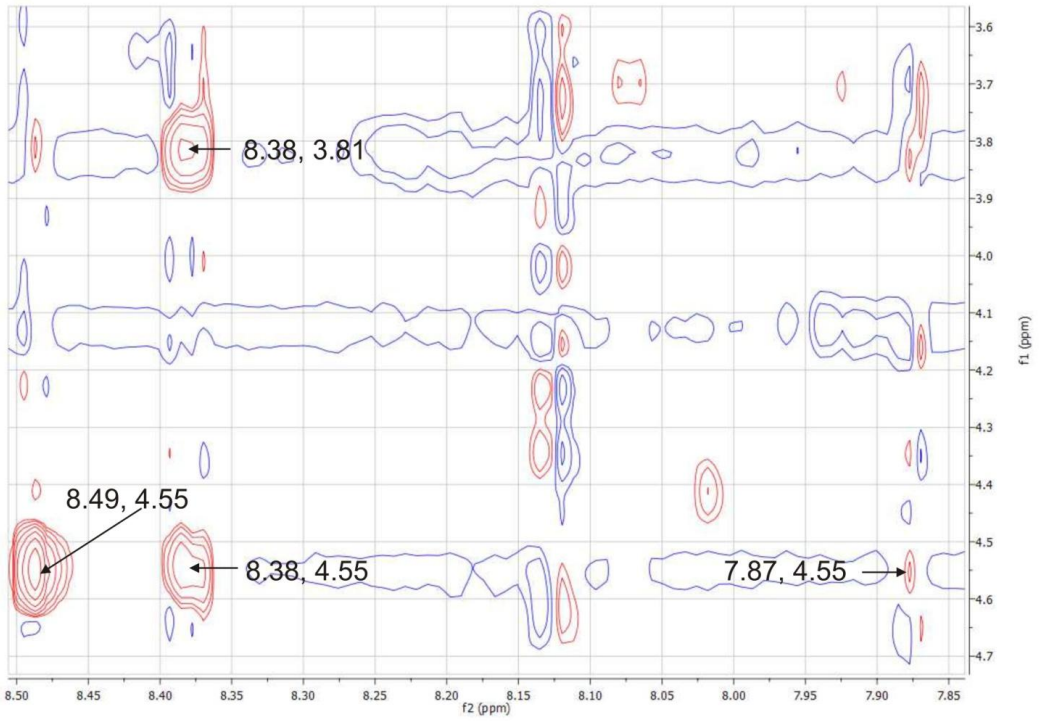
^{1}H NMR (300 MHz, d_6-DMSO) δ 8.11 – 7.91 (m, 3H, N*H*), δ 7.14 (d, 2H, Ar*H*, *J*=8.1 Hz), δ 6.88 (d, 1H, N*H*, *J*=8.9 Hz), δ 6.82 (d, 2H, Ar*H*, *J*=8.2 Hz), δ 6.08 – 5.96 (m, 1H, OCH_2CHCH_2), δ 5.76 – 5.66 (m, 1H, $C\alpha HCH_2CHCH_2$), δ 5.34 (d, 1H, CH_2CHCHH, *J*=17.3 Hz), δ 5.22 (d, 1H, CH_2CHCHH, *J*=10.3 Hz), δ 5.09 – 4.98 (m, 2H, CH_2CHCHH), δ 4.50 (d, 1H, OCH_2CHCH_2, *J*=4.0 Hz), δ 4.38 – 4.30 (m, 1H, Cα*H*), δ 4.21 – 4.02 (m, 11H, Cp and 2x Cα*H*), δ 3.96 (d, 2H, CH_2Fc, *J*=6.1 Hz), δ 2.93 – 2.60 (m, 2H, $C\alpha HCH_2$Ph), δ 2.47 – 2.27 (m, 2H, $C\alpha HCH_2CHCH_2$), δ 1.68 – 1.23 (m, 3H, $CH_2CH(CH_3)_2$), δ 1.30 (s, 9H, $(CH_3)_3$), δ 0.91 – 0.82 (m, 6H, $C\alpha HCH_2CH(CH_3)_2$)
LRMS (*m/z*) : $[M + Na]^+$ calculated for $C_{39}H_{52}FeN_4O_6Na$, 751.3; found 751.2.

Peptide **18** (37 mg, 0.05 mmol) was dissolved in TFE (3 mL) and 4M HCl in dioxane (2.5 mL) added. The mixture was stirred at rt for 25 min., and the solvent removed *in vacuo*. The crude product was purified using reverse phase HPLC to yield a brown solid (Peptide **9**, (15 mg, 46%)). ^{1}H NMR (600 MHz, d_6-DMSO) δ 8.60 (d, 1H, N*H* Leu, *J*=8.2 Hz), δ 8.21 (d, 1H, N*H* Gly, *J*=8.2 Hz), δ 8.11 (t, 1H, N*H* Fc, *J*=5.9 Hz), δ 8.02 (d, 3H, N*H* Tyr, *J*=4.1 Hz), δ 7.16 (d, 2H, Ar*H*, *J*=8.5 Hz), δ 6.88 (d, 2H, Ar*H*, *J*=8.6 Hz), δ 6.06 – 6.00 (dtt, 1H, OCH_2CHCH_2, *J*=15.8, 10.4, 5.2 Hz), δ 5.77 – 5.69 (m, 1H, $C\alpha HCH_2CHCH_2$), δ 5.37 (ddd, 1H, OCH_2CHCHH, *J*=17.3, 10.3, 1.6 Hz), δ 5.25 (dd, 1H, OCH_2CHCHH, *J*=10.5, 1.4 Hz), δ 5.08 (dd, 1H, $C\alpha HCH_2CHCHH$, *J*=17.1, 1.4 Hz), δ 5.00 (d, 1H, $C\alpha HCH_2CHCHH$, *J*=10.2 Hz), δ 4.53 (d, 2H, OCH_2CHCH_2, *J*=5.2 Hz), δ 4.46 – 4.37 (m, 2H, Cα*H* Leu, Cα*H* Gly), δ 4.19 – 3.94 (m, 12H, Cp, Cα*H* Tyr, CH_2Fc), δ 3.06 – 3.03 (dd, 1H, $C\alpha HCHHPh$, *J*=14.4, 4.7 Hz), δ 2.86 – 2.83 (dd, 1H, $C\alpha HCHHPh$, *J*=14.4, 8.1 Hz), δ 2.45 – 2.30 (m, 2H, $C\alpha HCH_2CHCH_2$), δ 1.66 – 1.59 (td, 1H, $CH_2CH(CH_3)_2$, *J*=13.5, 6.7 Hz), δ 1.50 – 1.45 (m, 2H, $CH_2CH(CH_3)_2$), δ 0.90 – 0.86 (m, 6H, $C\alpha HCH_2CH(CH_3)_2$). ^{13}C NMR (150 MHz, d_6-DMSO) δ 171.1, 170.1, 167.6, 157.3, 134.0, 133.7, 130.6, 126.6, 117.3, 114.6, 85.9, 71.5, 70.9, 70.3, 68.3, 68.1, 67.5, 67.4, 67.3, 67.2, 67.1, 53.2, 52.0, 51.0, 48.5, 41.1, 40.0, 37.4, 36.3, 36.0, 23.9, 22.9, 21.6. HRMS: $[M+H]^+$ calculated for $C_{34}H_{44}FeN_4O_4$, 628.27065; found 628.26923. IR : 1641 cm^{-1} (Amide I Band); 1512 cm^{-1} (Amide II Band); 3277 cm^{-1} (Amide A Band).

2. ROESY spectra for peptides **1, 4, 5, 6, 7, 8, 9.**

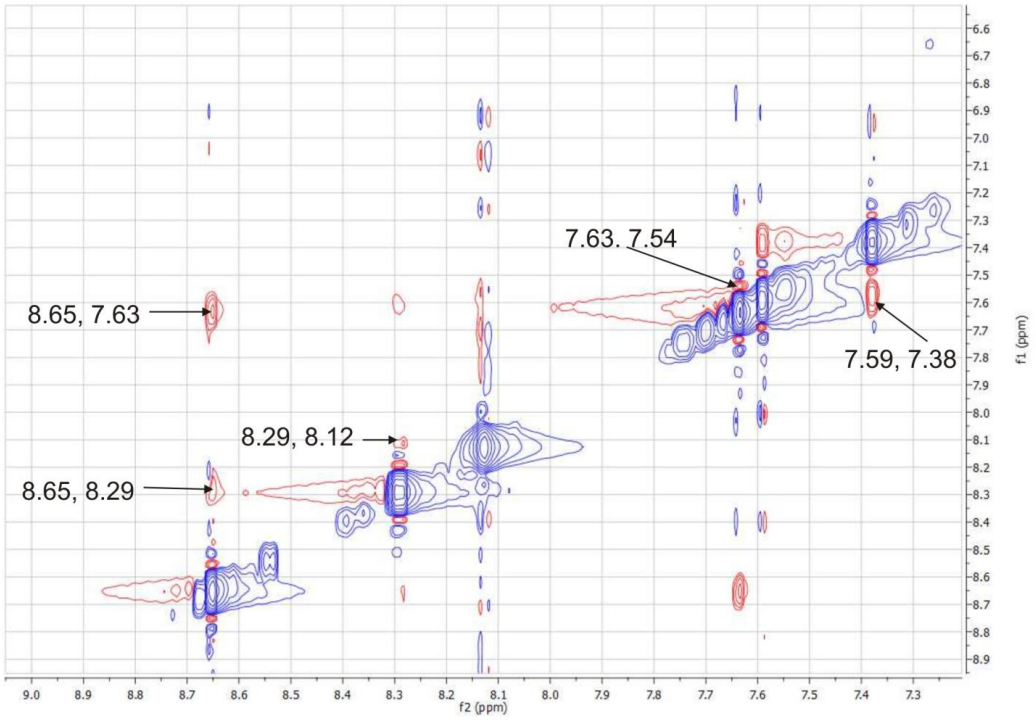


(a)

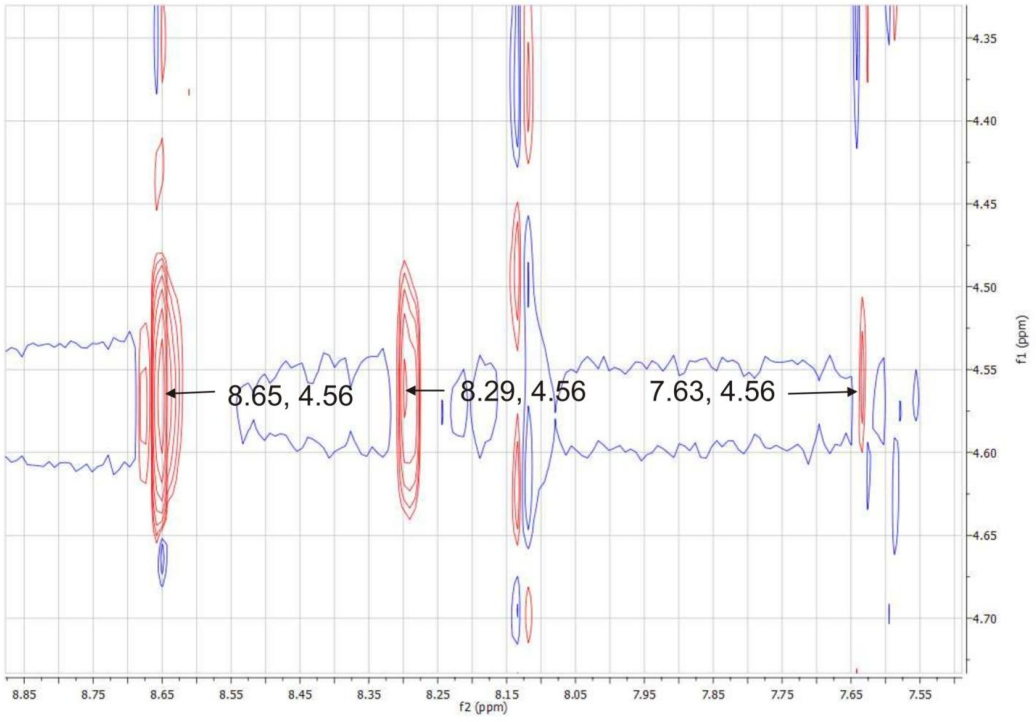


(b)

Figure S1. ROESY spectra of peptide **1,** showing (a) N*H* (*i*) to N*H* (*i*+1), (b) Cα*H* (*i*) to N*H* (*i*+1) and medium range Cα*H* (*i*) to N*H* (*i*+2) and CβH_2(*i*) and N*H* (*i*) correlations.



(a)



(b)

Figure S2. ROESY spectra of peptide **4,** showing (a) N*H* (*i*) to N*H* (*i*+1), (b) Cα*H* (*i*) to N*H* (*i*+1) and medium range Cα*H* (*i*) to N*H* (*i*+2) correlations.

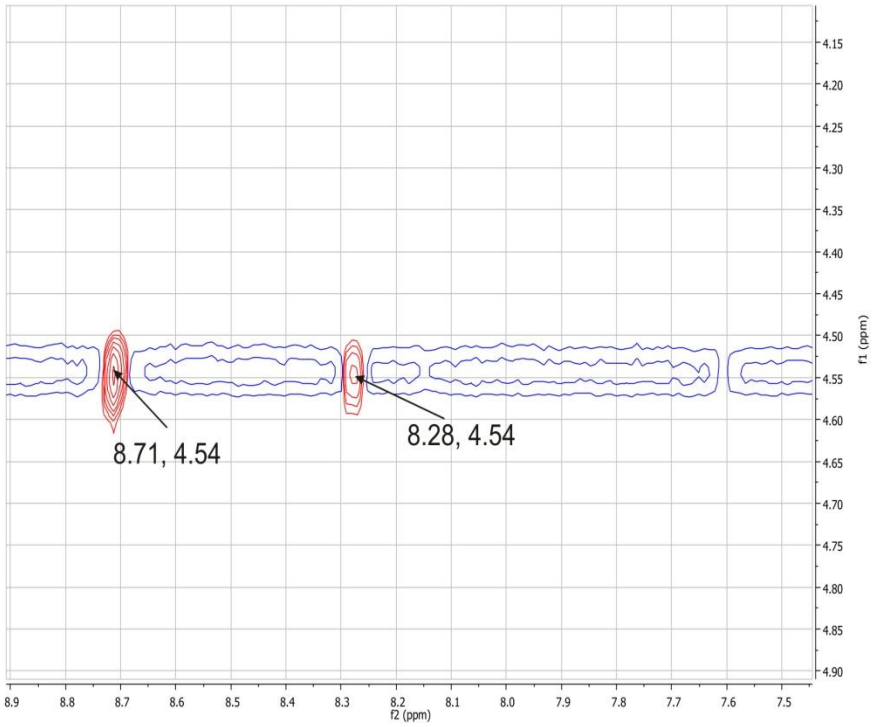
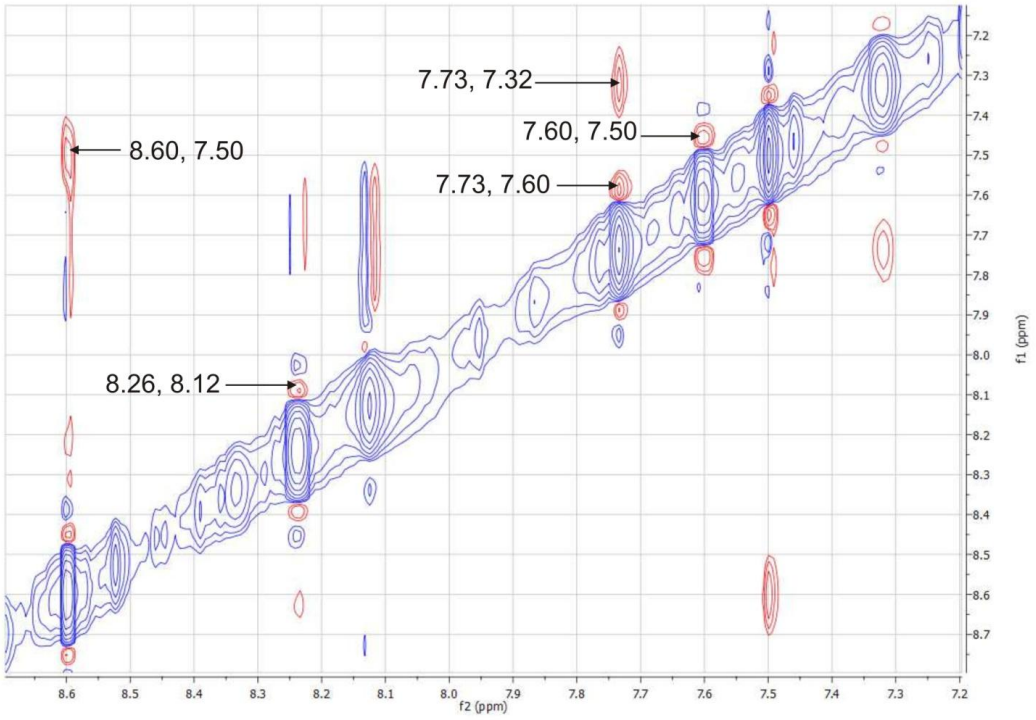
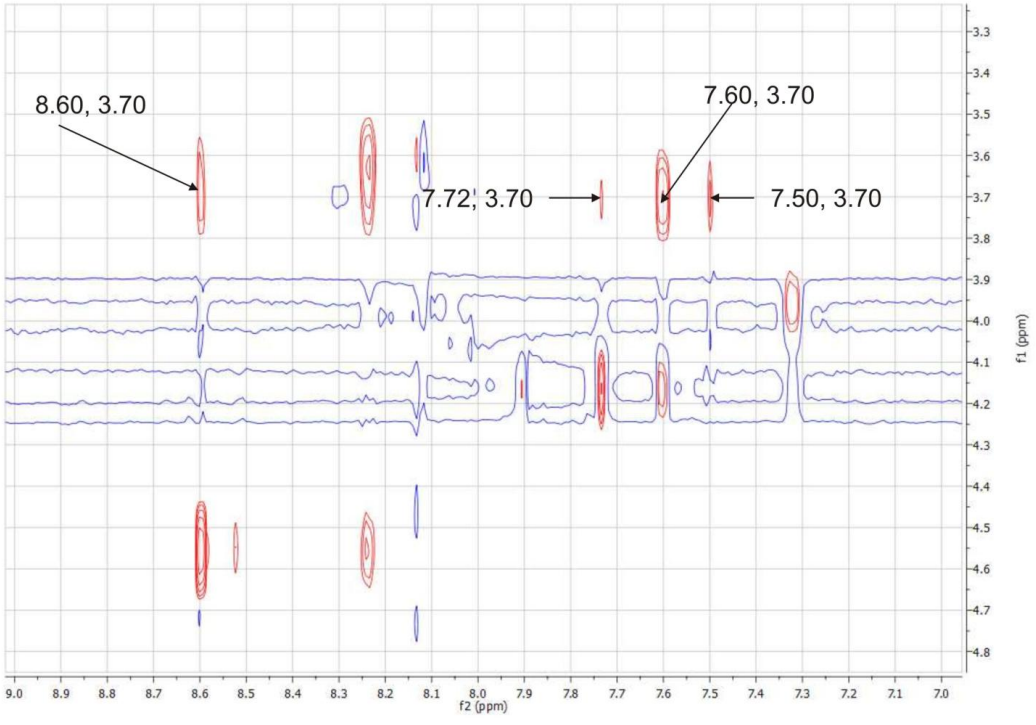


Figure S3. ROESY spectra of peptide **5,** showing Cα*H* (*i*) to N*H* (*i*+1) correlations.



(a)



(b)

Figure S4. ROESY spectra of peptide **6,** showing (a) N*H* (*i*) to N*H* (*i*+1), (b) C*αH* (*i*) to N*H* (*i*+1) and medium range C*αH* (*i*) to N*H* (*i*+2) correlations.

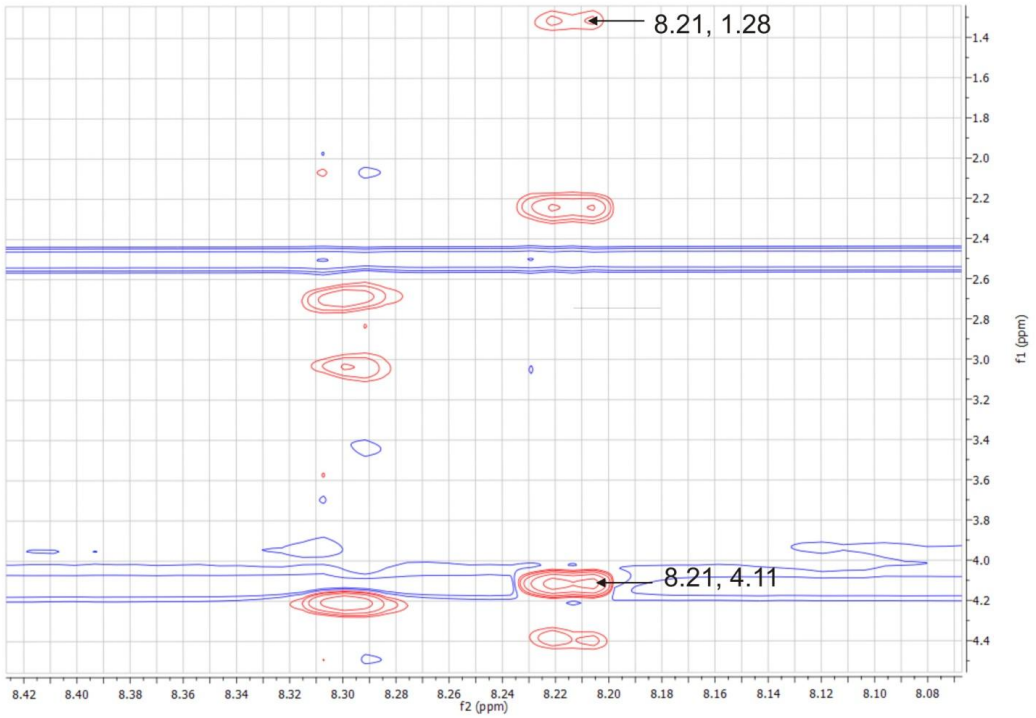


Figure S5. ROESY spectrum of peptide **7**, showing Cα*H* (*i*) to N*H* (*i*+1) and Cβ*H* (*i*) to N*H* (*i*+1) correlations.

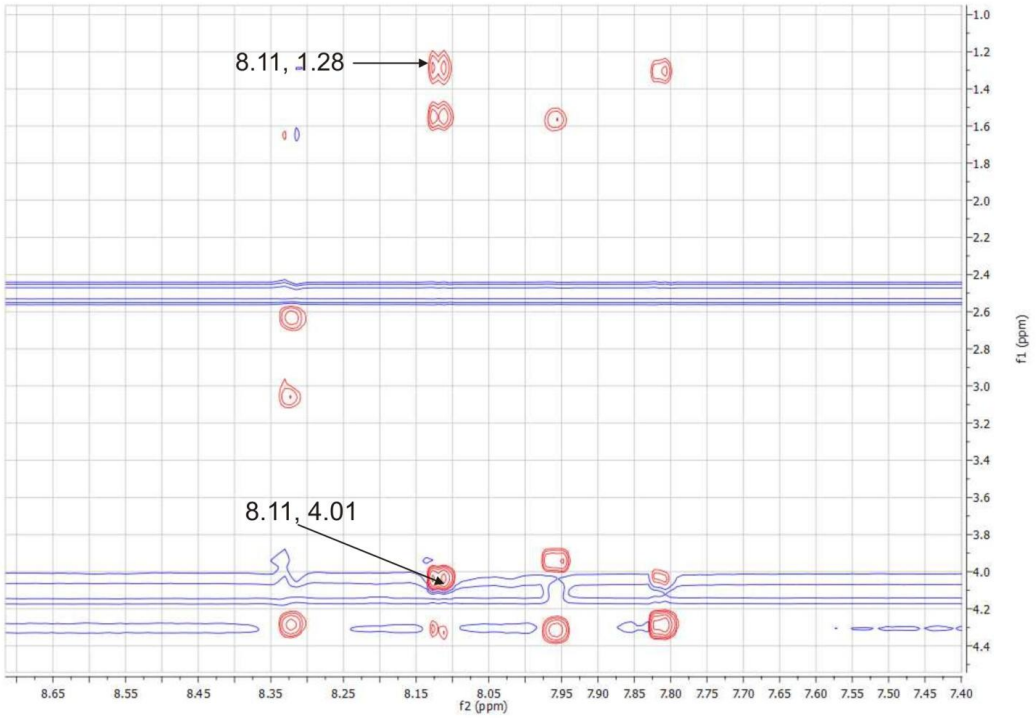


Figure S6. ROESY spectra of peptide **8,** showing Cα*H* (*i*) to N*H* (*i*+1) and Cβ*H* (*i*) to N*H* (*i*+1) correlations.

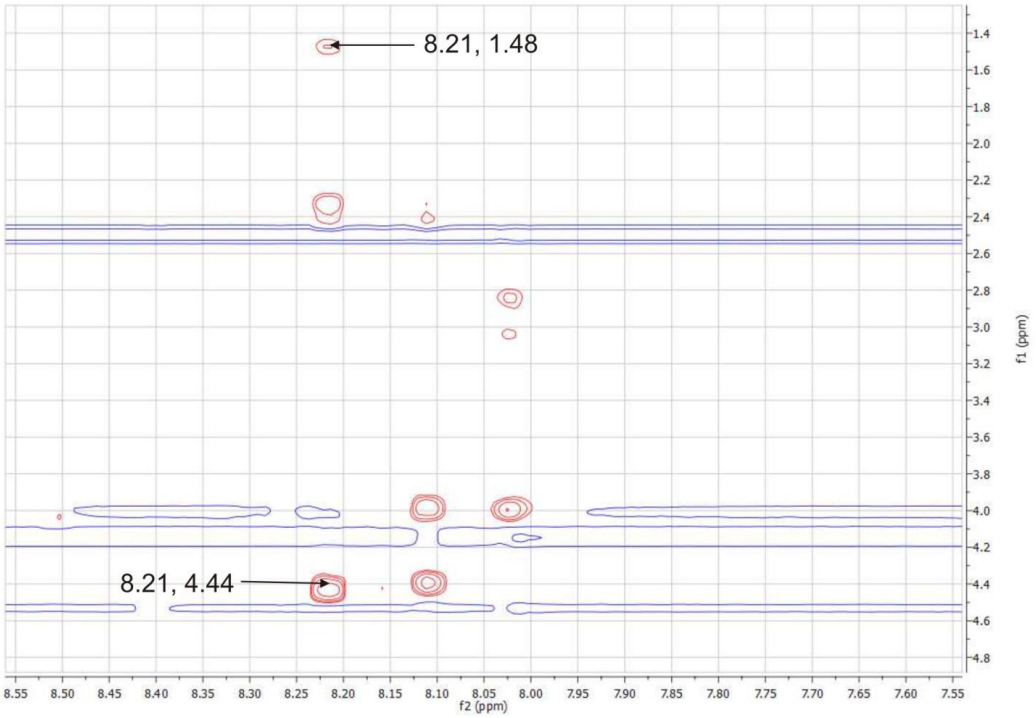


Figure S7. ROESY spectrum of **9,** showing Cα*H* (*i*) to N*H* (*i*+1) and Cβ*H* (*i*) to N*H* (*i*+1) correlations.

3. IR spectra for peptides **7-9**

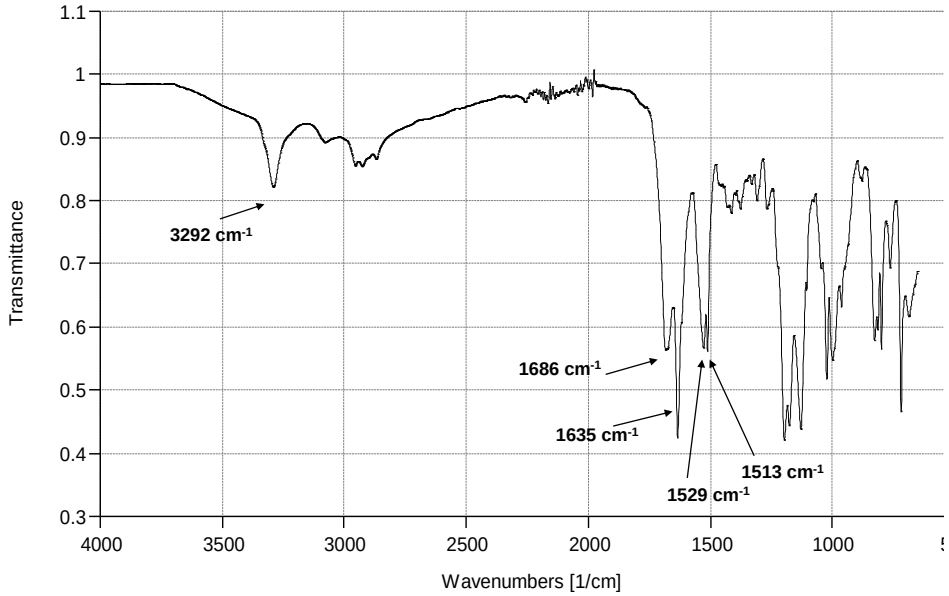


Figure S8. IR spectrum of peptide **7.**

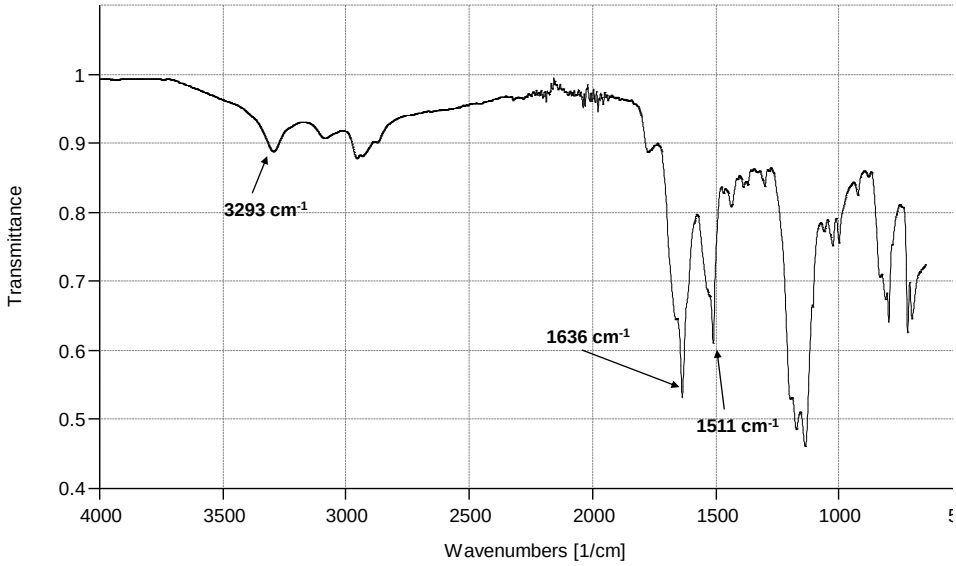


Figure S9. IR spectrum of peptide **8.**

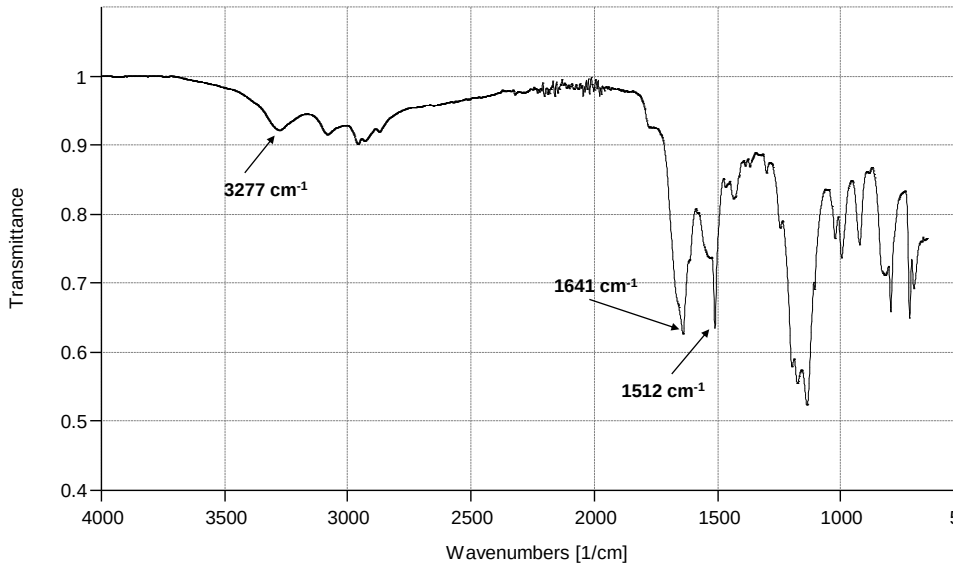


Figure S10. IR spectrum of peptide **9.**

4. Computational models of peptides **10, 11, 13, 14, 15, 16, 17** and **18.**

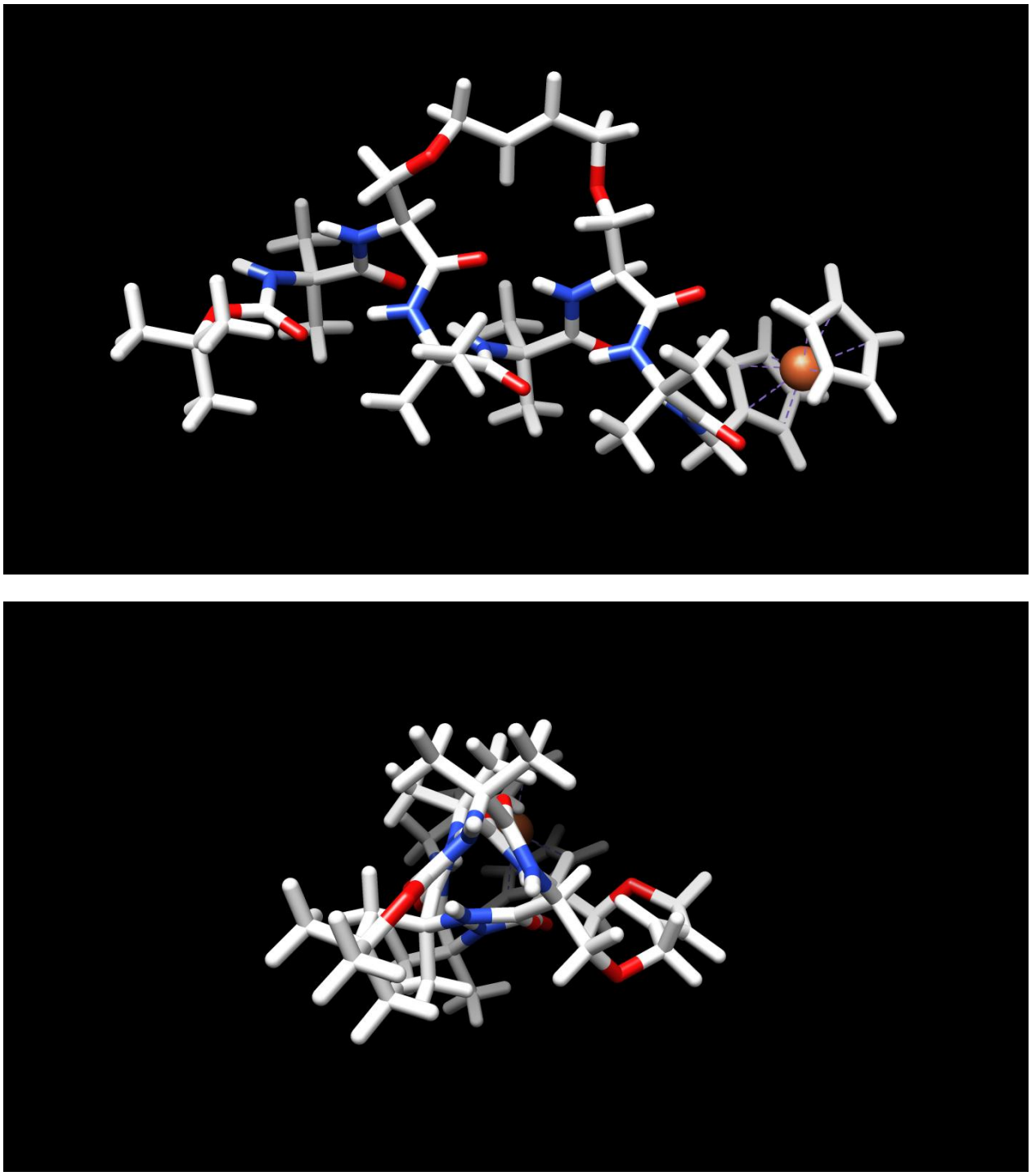


Figure S11. (Top) The lowest energy conformer for Peptide **10** optimized by the hybrid B3LYP method with 6-31G** basis set for all C, H, N, O atoms, and Lanl2dz basis set for Fe atom. (Bottom) Top view looking down helix showing the triangular shape, which is characteristic of a 3_{10}-helix.[1]

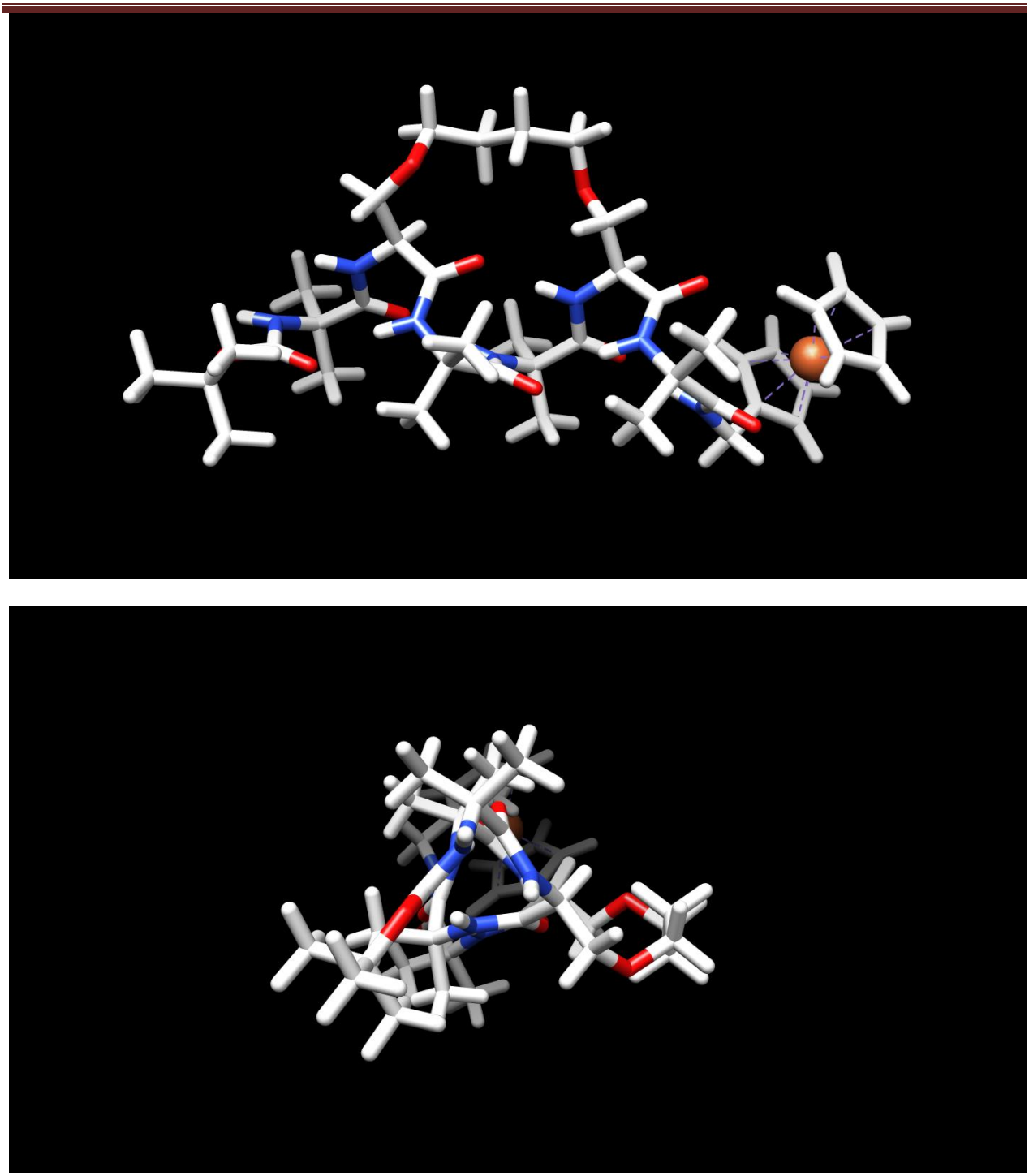


Figure S12. (Top) The lowest energy conformer for Peptide **11,** optimized by the hybrid B3LYP method with 6-31G** basis set for all C, H, N, O atoms, and Lanl2dz basis set for Fe atom. (Bottom) Top view looking down helix showing the triangular shape, which is characteristic of a 3_{10}-helix.[1]

****NB.** The lowest energy conformer for Peptide **12** previously reported[2].

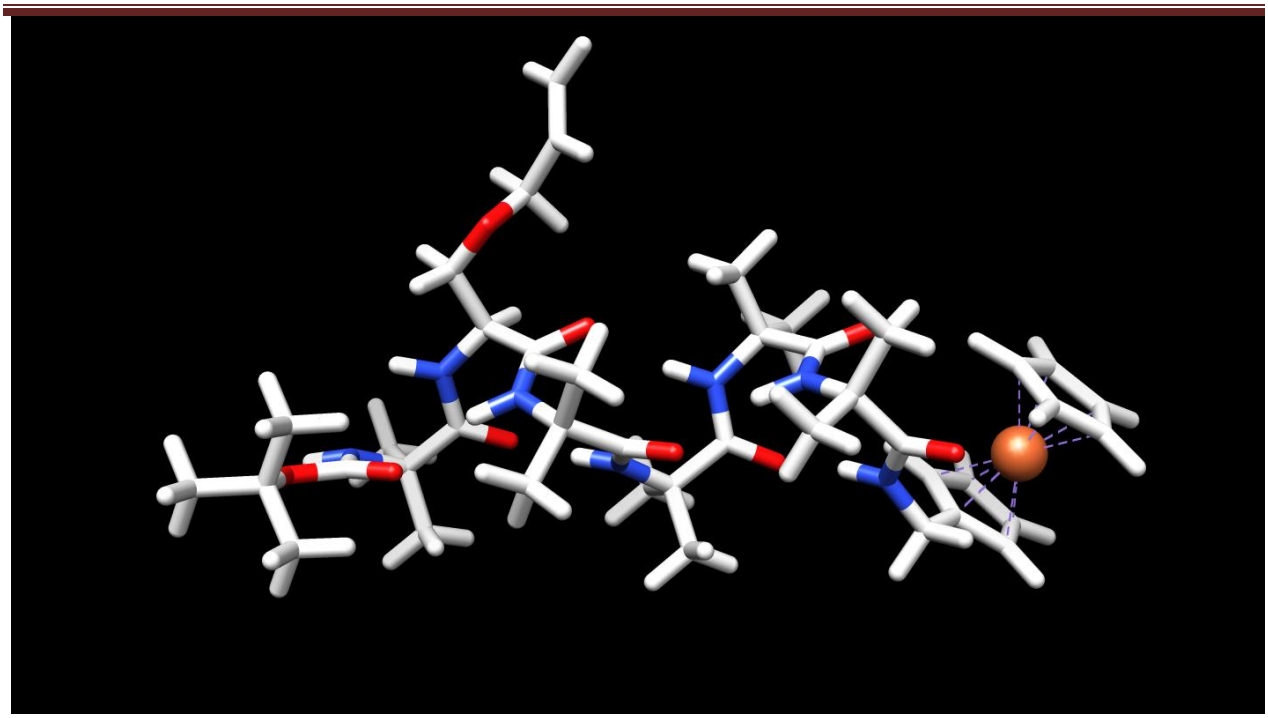


Figure S13. The lowest energy conformer for Peptide **13,** optimized by the hybrid B3LYP method with 6-31G** basis set for all C, H, N, O atoms, and Lanl2dz basis set for Fe atom.

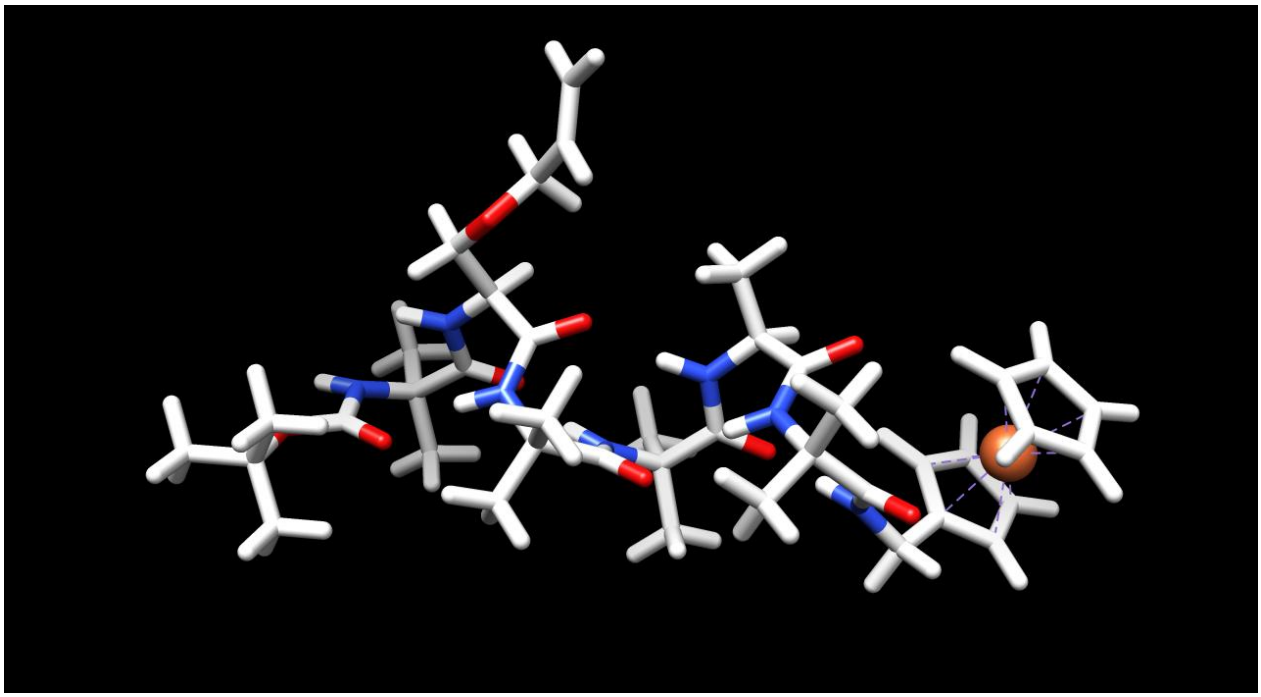


Figure S14. The lowest energy conformer for Peptide **14**, optimized by the hybrid B3LYP method with 6-31G** basis set for all C, H, N, O atoms, and Lanl2dz basis set for Fe atom.

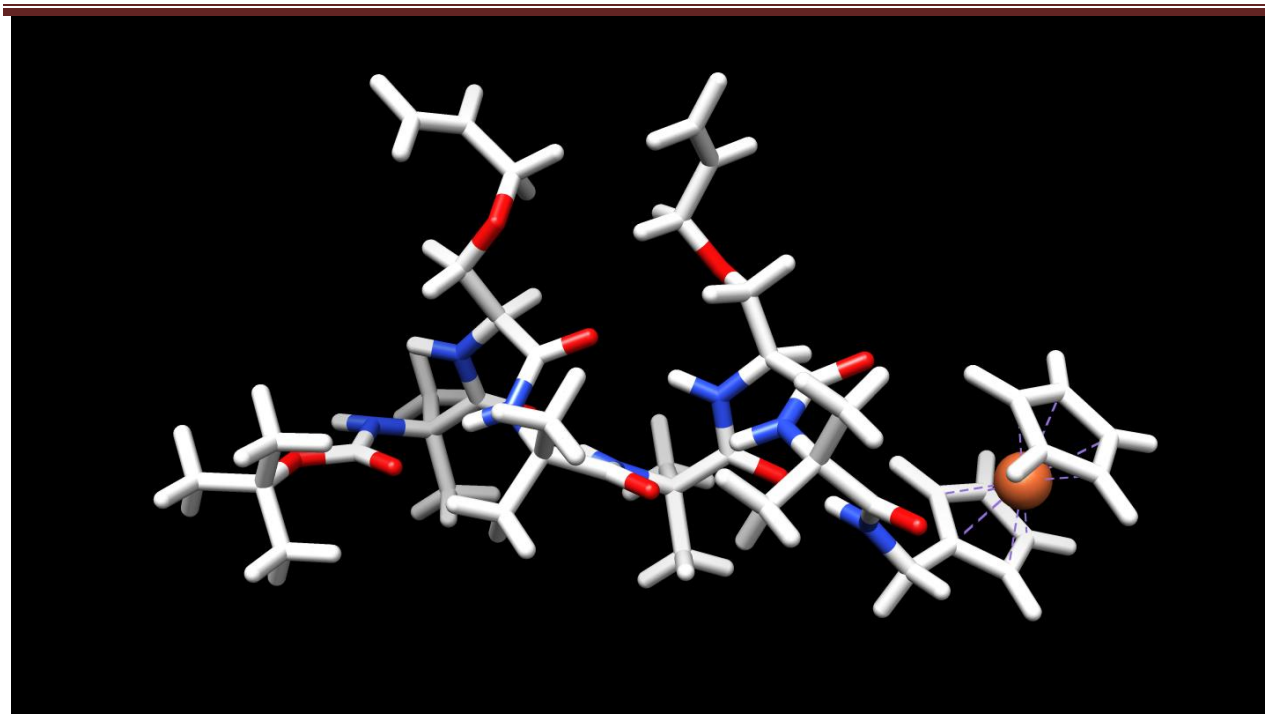


Figure S15. The lowest energy conformer for Peptide **15,** optimized by the hybrid B3LYP method with 6-31G** basis set for all C, H, N, O atoms, and Lanl2dz basis set for Fe atom.

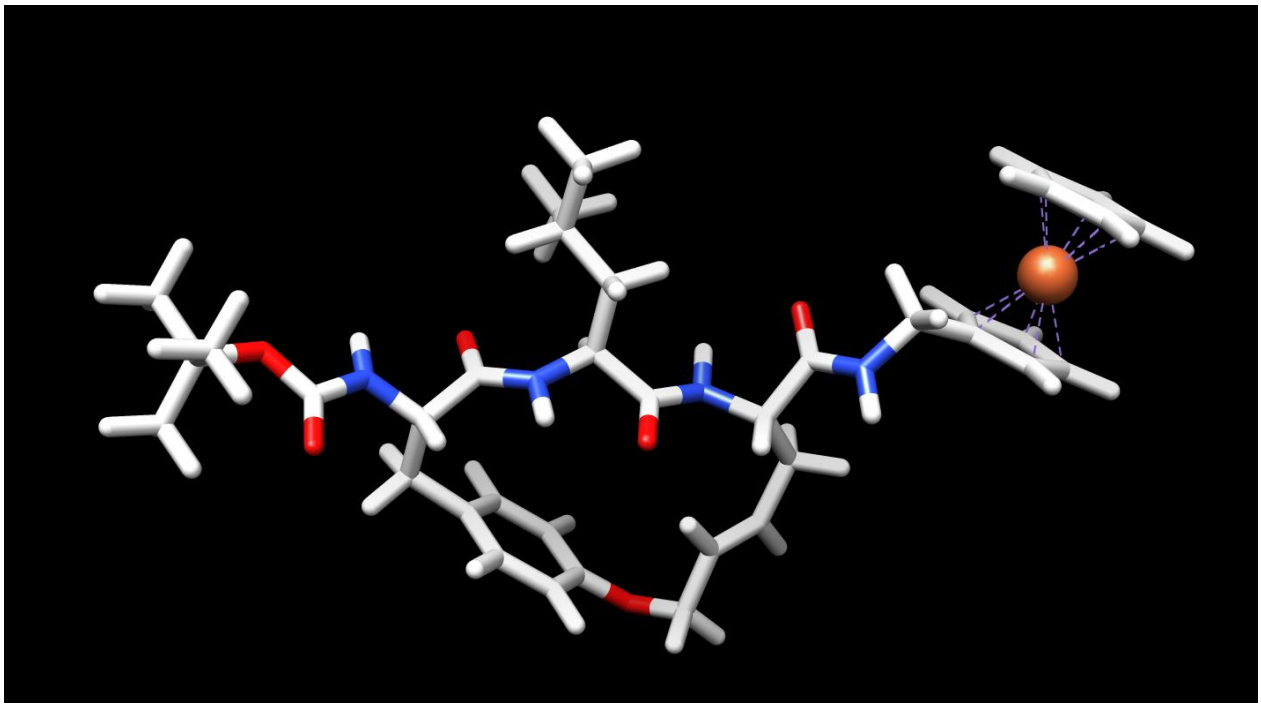


Figure S16. The lowest energy conformer for Peptide **16,** optimized by the hybrid B3LYP method with 6-31G** basis set for all C, H, N, O atoms, and Lanl2dz basis set for Fe atom.

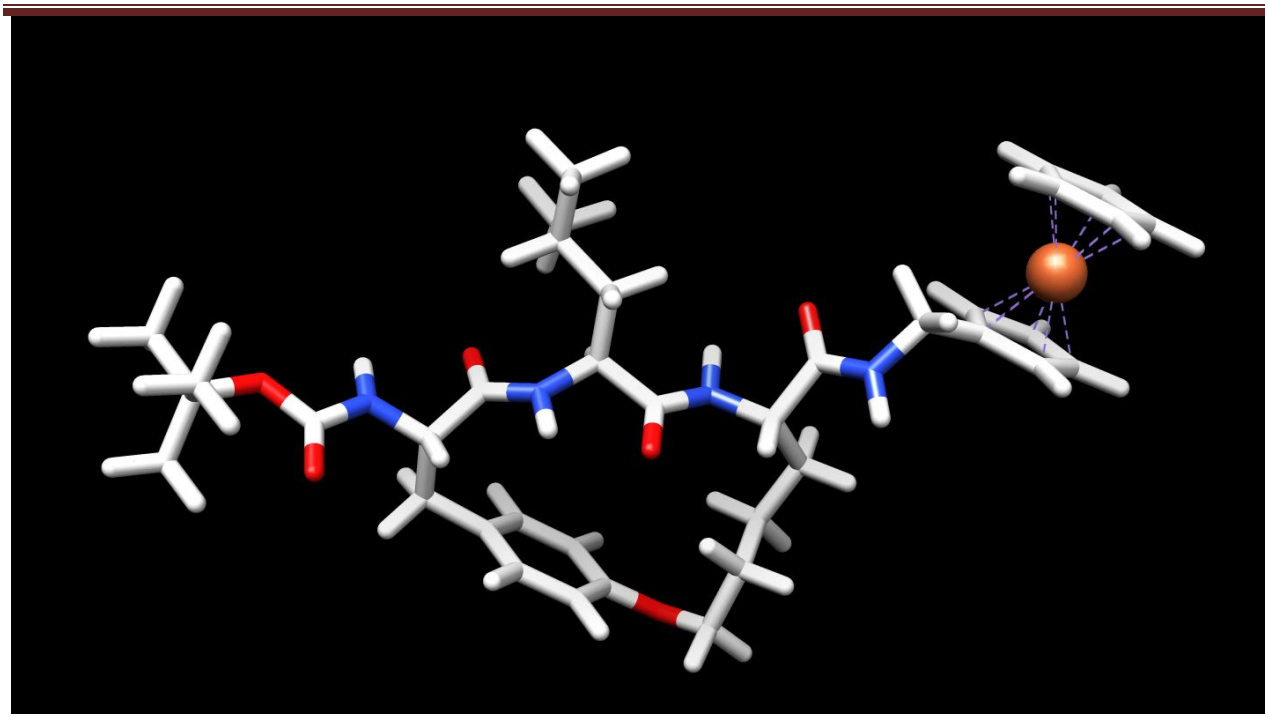


Figure S17. The lowest energy conformer for Peptide **17,** optimized by the hybrid B3LYP method with 6-31G** basis set for all C, H, N, O atoms, and Lanl2dz basis set for Fe atom.

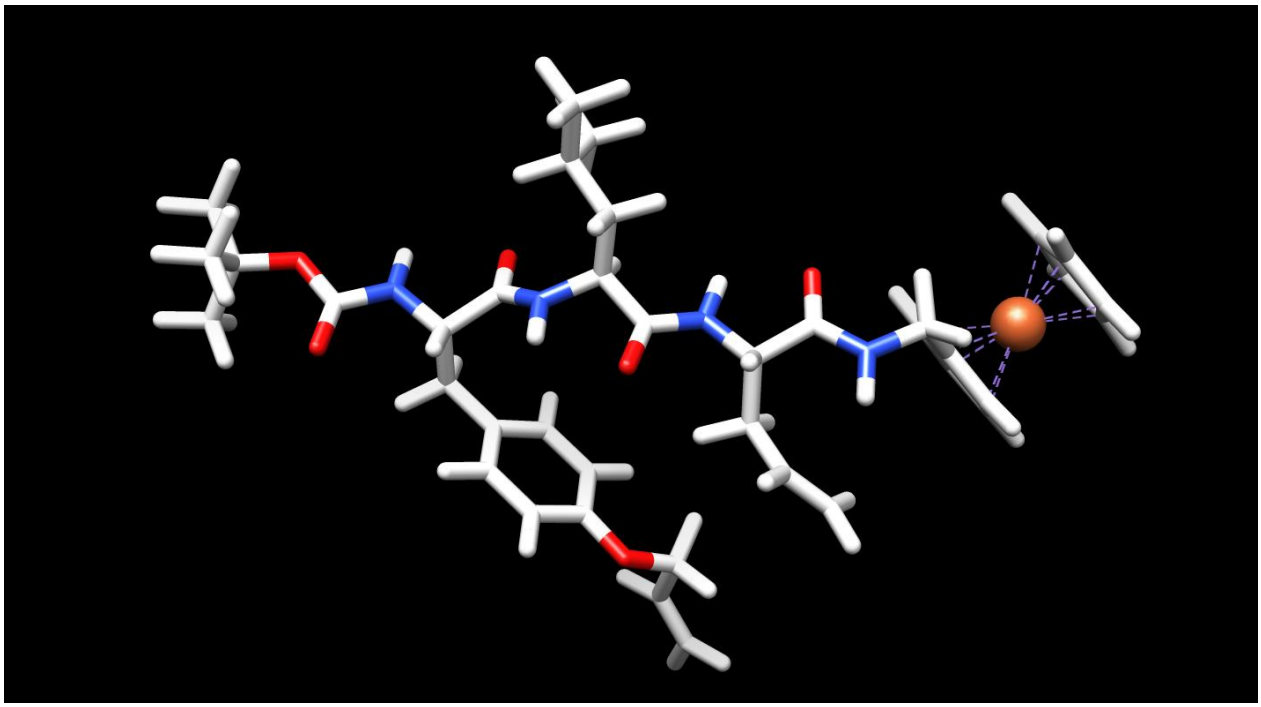


Figure S18. The lowest energy conformer for Peptide **18,** optimized by the hybrid B3LYP method with 6-31G** basis set for all C, H, N, O atoms, and Lanl2dz basis set for Fe atom.

4.1 Characteristics of *N*-protected helical peptides **(10 - 15).**

(Peptide **12 previously characterized[2]).

Table S1. Distances between dαN, dβN and dNN, characteristic of a 3_{10}-helix.

Distance	Peptide **10**	Peptide **11**	Peptide **13**	Peptide **14**	Peptide **15**	Ideal 3_{10} helix[4]
dαN (Å)	3.4	3.4	3.5	3.5	3.5	3.4
dβN (Å)	3.2-4.2	3.2-4.1	3.0-4.2	3.0-4.2	3.0-4.0	2.9-4.4
dNN (Å)	2.8	2.8	2.8	2.8	2.8	2.6

Table S2. Hydrogen bond lengths, N*H* to N*H* distances and total peptide length for **10**.

Residue	Hydrogen bond lengths (Å)	Distance (N*H* to N*H*) (Å)
1	2.093	2.984
2	2.195	2.778
3	2.001	2.828
4	2.105	2.845
5	2.128	2.749
6		2.618
• Distance from first to last carbonyl carbon 11.913 Å. • Length of π bond 1.332 Å.		

Table S3. Hydrogen bond lengths, N*H* to N*H* distances and total peptide length for **11**.

Residue	Hydrogen bond lengths (Å)	Distance (N*H* to N*H*) (Å)
1	2.116	2.986
2	2.178	2.763
3	2.051	2.802
4	2.076	2.851
5	2.087	2.831
6		2.644
• Distance from first to last carbonyl carbon 11.868 A. • Length of σ bond 1.531 A		

Table S4. Hydrogen bond lengths, N*H* to N*H* distances and total peptide length for **13**.

Residue	Hydrogen bond lengths (Å)	Distance (N*H* to N*H*) (Å)
1	2.103	2.983
2	2.160	2.812
3	2.113	2.795
4	2.164	2.791
5	2.055	2.791
6		2.678
• Distance from first to last carbonyl carbon 11.879 A.		

Table S5. Hydrogen bond lengths, N*H* to N*H* distances and total peptide length for **14**.

Residue	Hydrogen bond lengths (Å)	Distance (N*H* to N*H*) (Å)
1	2.101	2.983
2	2.166	2.818
3	2.059	2.797
4	2.150	2.789
5	2.134	2.745
6		2.630
• Distance from first to last carbonyl carbon 11.972 A.		

Table S6. Hydrogen bond lengths, N*H* to N*H* distances and total peptide length for **15**.

Residue	Hydrogen bond lengths (Å)	Distance (N*H* to N*H*) (Å)
1	2.120	2.983
2	2.136	2.814
3	2.159	2.792
4	2.142	2.798
5	2.090	2.849
6		2.634
• Distance from first to last carbonyl carbon 11.905 Å.		

Table S7. Average H-bond lengths for 3_{10}-helical structures, with comparison to literature.

Peptide	Average Hydrogen Bond Length (Å)
10	2.10
11	2.10
13	2.11
14	2.12
15	2.12
acyclic 1[5]	2.19
cyclic 2[5]	2.11
acyclic 1[1]	2.21
cyclic 2 (unsaturated)[1]	2.38
cyclic 3 (saturated)[1]	2.33
constrained peptide 1[2]	2.16
linear analogue 2[2]	2.11

Table S8. Dihedral angles for all residues in the lowest energy conformers for Peptides **10** and **11**.

	Peptide **10**		Peptide **11**	
	Φ	ψ	Φ	ψ
Residue 1	-65.153	-27.906	-65.256	-27.460
Residue 2	-61.747	**-18.790**	-61.850	**-19.727**
Residue 3	-50.604	-30.478	-52.681	-26.326
Residue 4	-52.937	-30.804	-51.882	-29.774
Residue 5	-67.187	**-13.261**	-61.661	**-19.943**
Residue 6	-66.123	-23.381	-65.619	-22.359

Table S9. Dihedral angles for all residues in the lowest energy conformers for Peptides **13, 14** and **15**.

	Peptide **13**		Peptide **14**		Peptide **15**	
	Φ	ψ	Φ	ψ	Φ	ψ
Residue 1	-64.784	-28.059	-64.796	-28.029	-64.728	-28.215
Residue 2	-54.912	-28.346	-54.987	-28.842	-54.803	-28.457
Residue 3	-54.245	-27.506	-54.745	-27.112	-53.786	-29.439
Residue 4	-53.957	-28.364	-53.382	-29.893	-54.411	-28.824
Residue 5	-53.760	-31.592	-62.276	-20.566	-64.622	-17.831
Residue 6	-66.636	-20.293	-65.788	-23.035	-66.056	-23.162

4.2 Characteristics of *N*-protected β-strand peptides **(16, 17** and **18).**

Table S10. N*H* to N*H* distances and total lengths for Peptides **16**, **17** and **18**.

N*H* to N*H* distance (Å)	Peptide **16**	Peptide **17**	Peptide **18**
1-2	4.248	4.257	4.271
2-3	4.273	4.278	4.327
3-4	4.312	4.314	4.258
Distance from first to last carbonyl carbon (Å)	10.673	10.732	10.974

Table S11. Dihedral angles for all residues in the lowest energy conformers for Peptides **16**, **17** and **18**.

	Peptide **16**		Peptide **17**		Peptide **18**	
	Φ	ψ	Φ	ψ	Φ	ψ
Residue 1	-158.308	130.980	-158.655	133.051	-161.288	135.778
Residue 2	-144.437	160.328	-142.642	161.648	-139.979	156.359
Residue 3	-114.878	150.830	-119.519	154.529	-159.222	177.500

Table S12. Important characteristic correlations for Peptides **16, 17** and **18**, with comparison to optimal β-strand values. (all distances in Å)

	Peptide **16** (unsaturated)	Peptide **17** (saturated)	Peptide **18** (unconstrained)	Optimal β-strand conformation
Length (first to last carbonyl)	10.673	10.732	10.974	
Distance*	8.0	8.0	8.3	8.0[6]
N-Leu to CO-Leu	2.4	2.4	2.4	2.5[4]
NH to NH (Average)	4.3	4.3	4.3	4.3[4]
αH to NH+1	2.2	2.2	2.2	2.2[4]
βH_2 to NH+1	4.1, 4.2	4.1, 4.1	4.0, 4.2	3.2 to 4.5[4]

Note: * This distance is defined between the C atom (*i*) and N (*i*+3). This is indicative of an optimal extended β-strand, as shown in Figure S19.

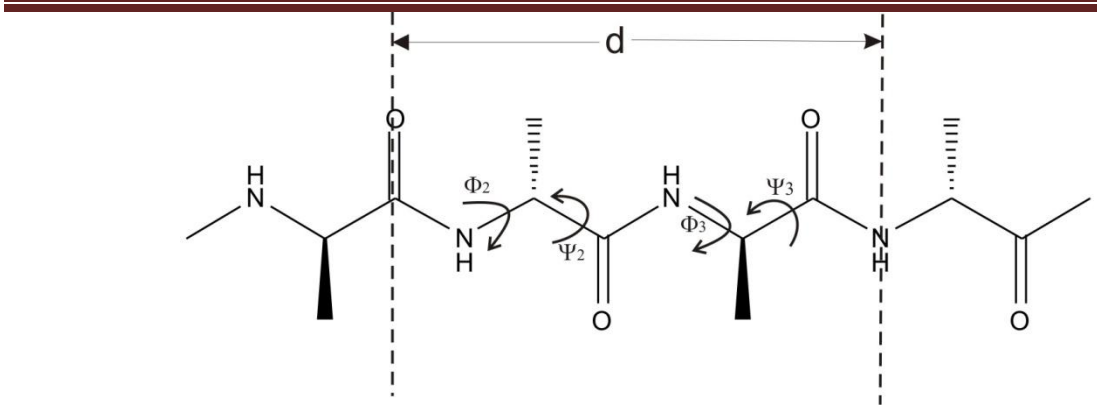


Figure S19. Peptide β-strand backbone with torsional angles Φ, Ψ, and optimal distance d = 8.0 Å[6].

5. Electrochemical measurements

P2-SWCNTs were functionalized using previously reported methods.[7] CNTs were then suspended in a solution of DMSO containing 0.2 mg mL^{-1} CNTs, 0.25 mg mL^{-1} DCC and 0.14 mg mL^{-1} DMAP. Polished flat gold disk electrodes (2 mm diameter) were cleaned in 25 % v/v H_2O_2/ KOH (50 mM) for 20 min and then electrochemically cleaned by cycling between 0 and 1.5 V vs. Ag/AgCl in 50 mM KOH. This cleaning process yielded clean gold surfaces with peak separations of 59 mV in 1 mM $Ru(NH_3)_6^{+3/}$ solution. The clean surfaces were then incubated in cysteamine for 24 h resulting in exposed amine groups. These substrates were then exposed to the functionalized SWCNTs/DMSO suspensions for 24 h, after which they were rinsed with propan-2-ol and dried under nitrogen flow. The surfaces were then exposed to 0.01 M ferrocene-derivatised peptide in DMF solution containing 0.5 M HATU and 0.5 M DIPEA for 48 h before being further rinsed and dried.

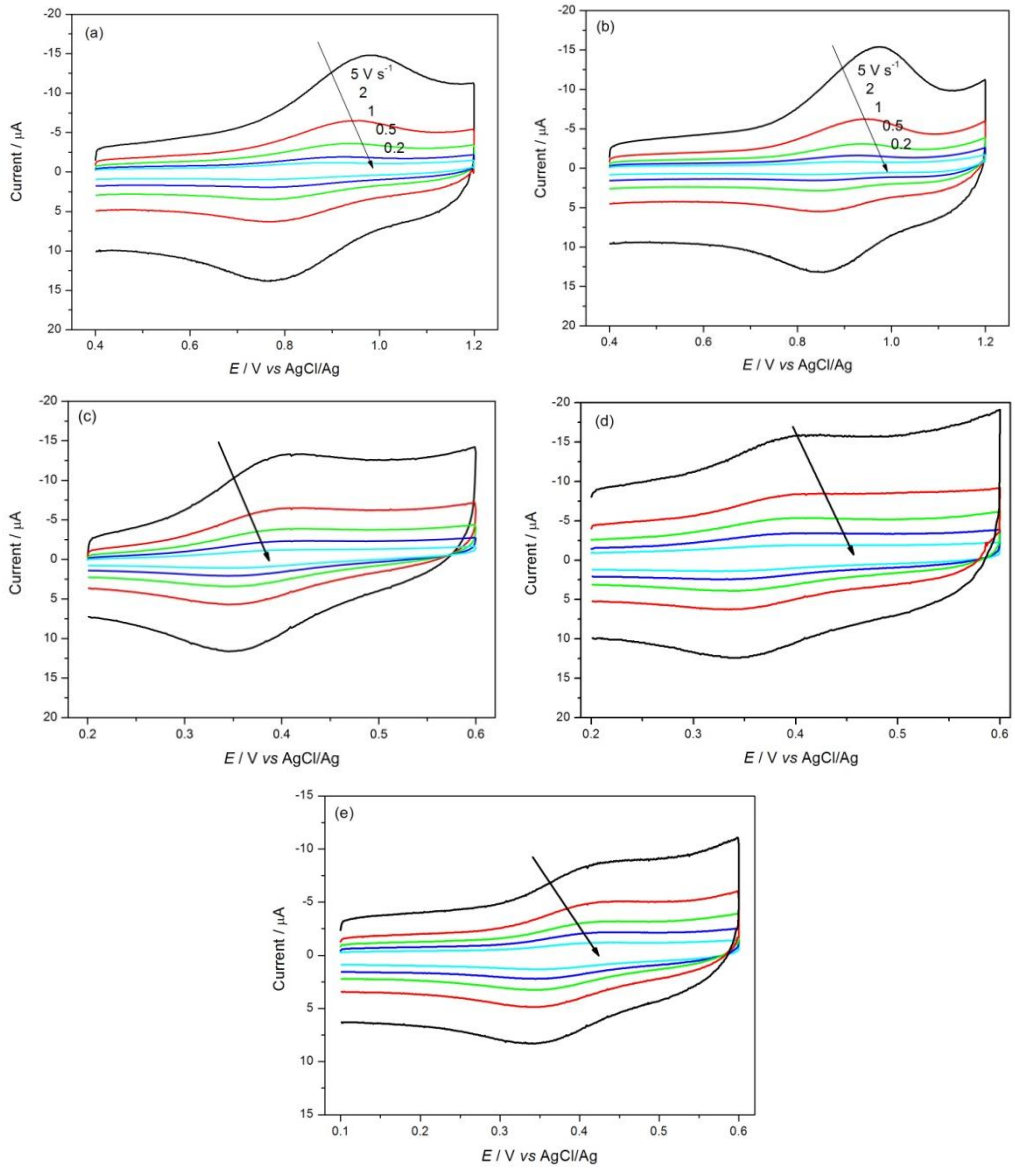


Fig. S20. Cyclic voltammograms for (a) Peptide **1**, (b) Peptide **2,** (c) Peptide **4**, (d) Peptide **5** and (e) Peptide **6** immobilized on SWCNTs/Au electrodes taken at 5, 2, 1, 0.5 and 0.2 V s^{-1} (from top to centre).

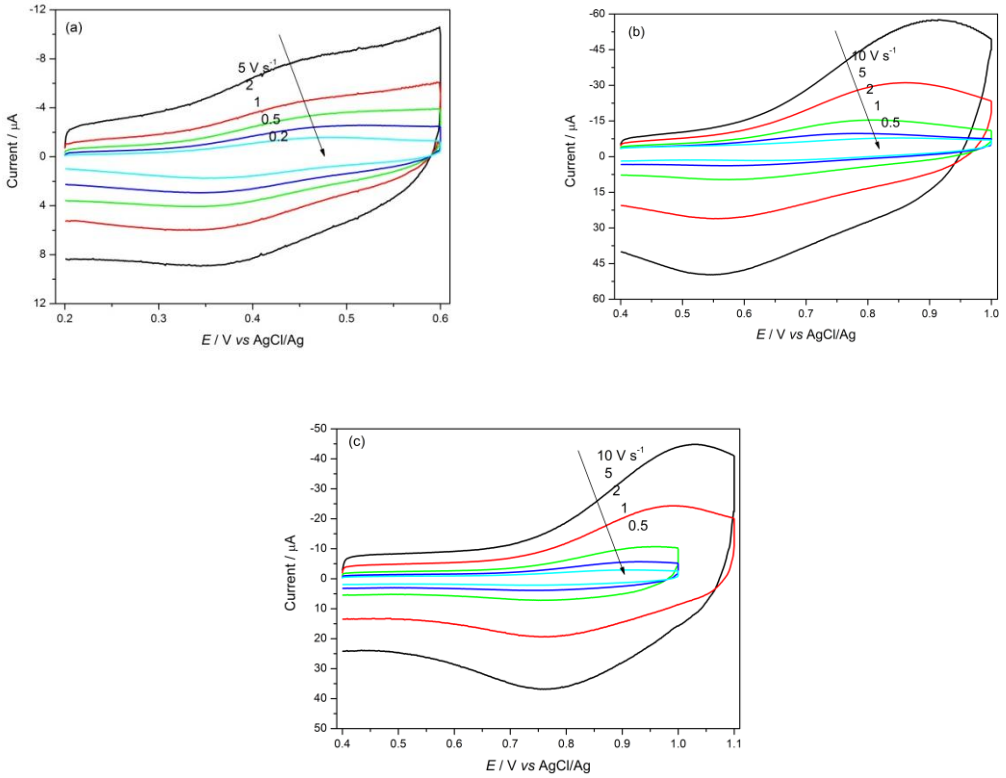


Fig. S21. Cyclic voltammograms for (a) Peptide **9** immobilized on SWCNTs/Au electrodes taken at 5, 2, 1, 0.5 and 0.2 V s^{-1} (from top to centre). (b) Peptide **7** and (c) Peptide **8** taken at 10, 5, 2, 1 and 0.5 V s^{-1} (from top to centre).

6. Diabatic potential profiles in the three model peptides

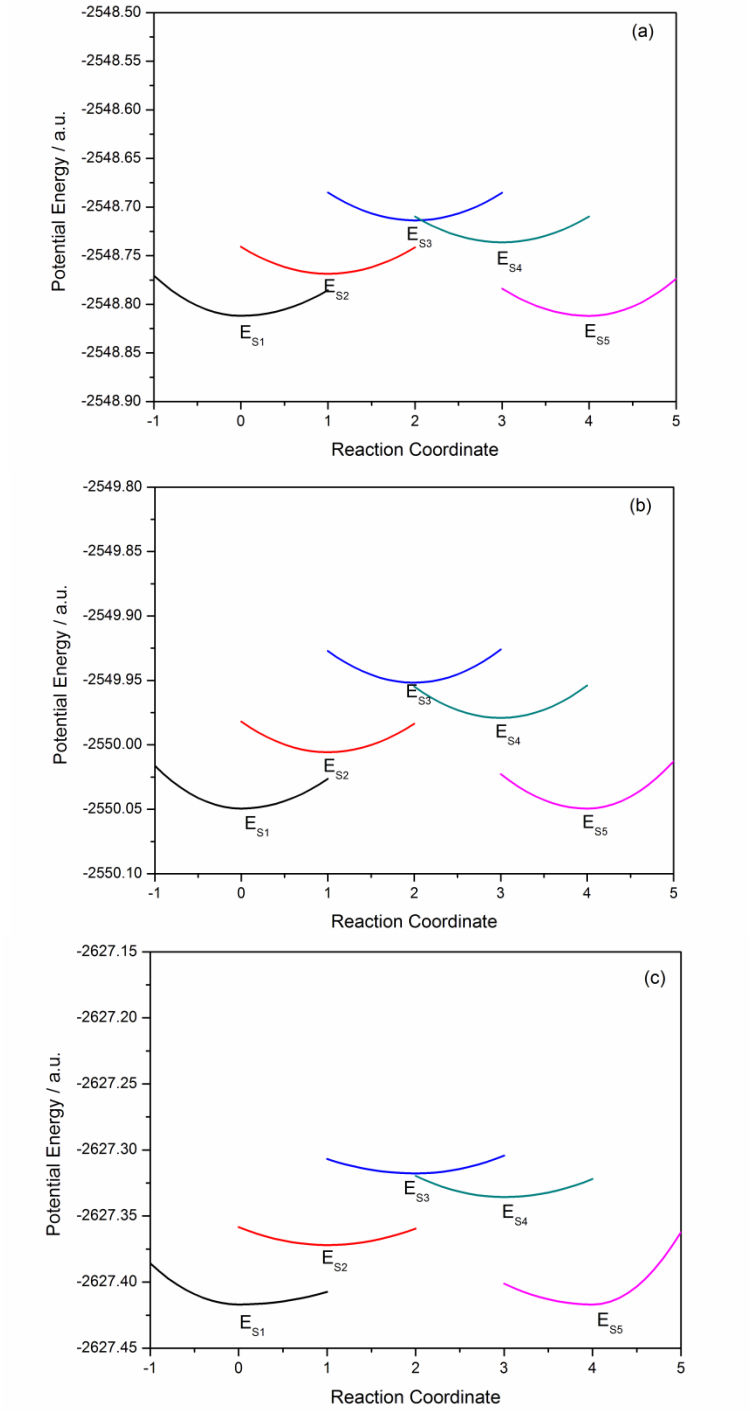
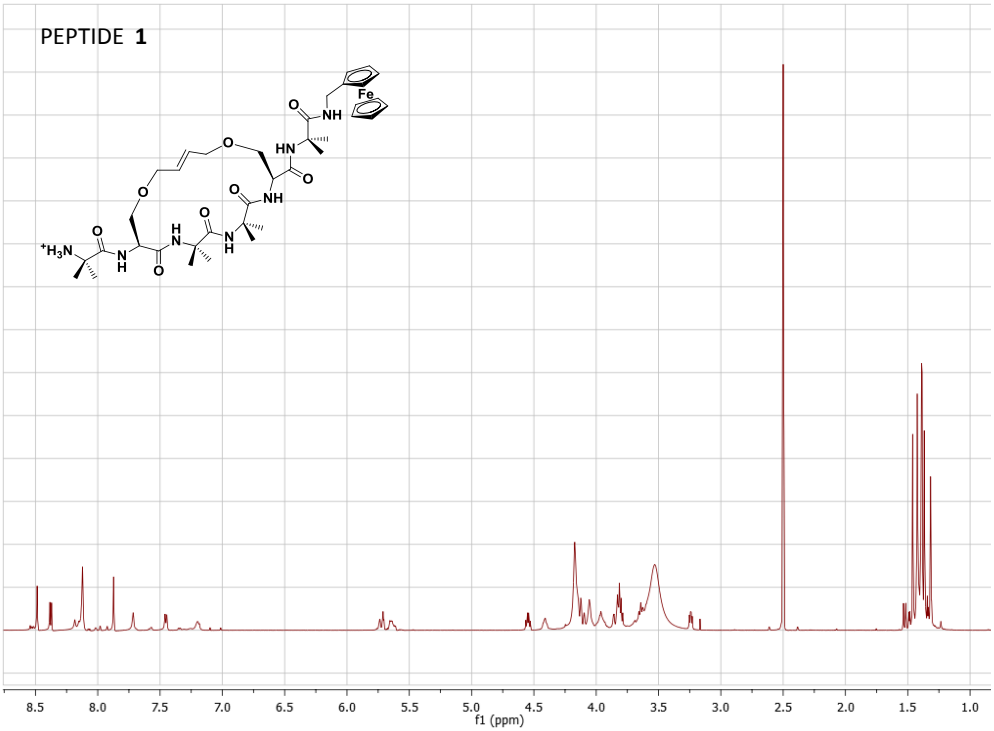


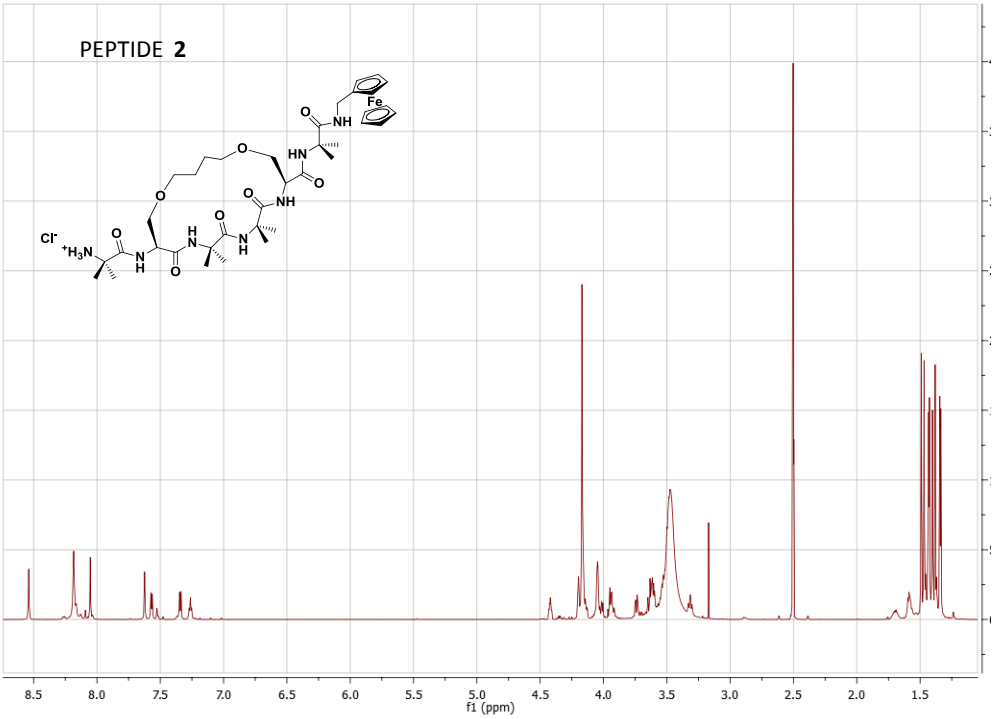
Fig. S22. Diabatic potential profiles in the three model peptides, (a) peptide **19**, (b) peptide **20** and (c) peptide **21**.

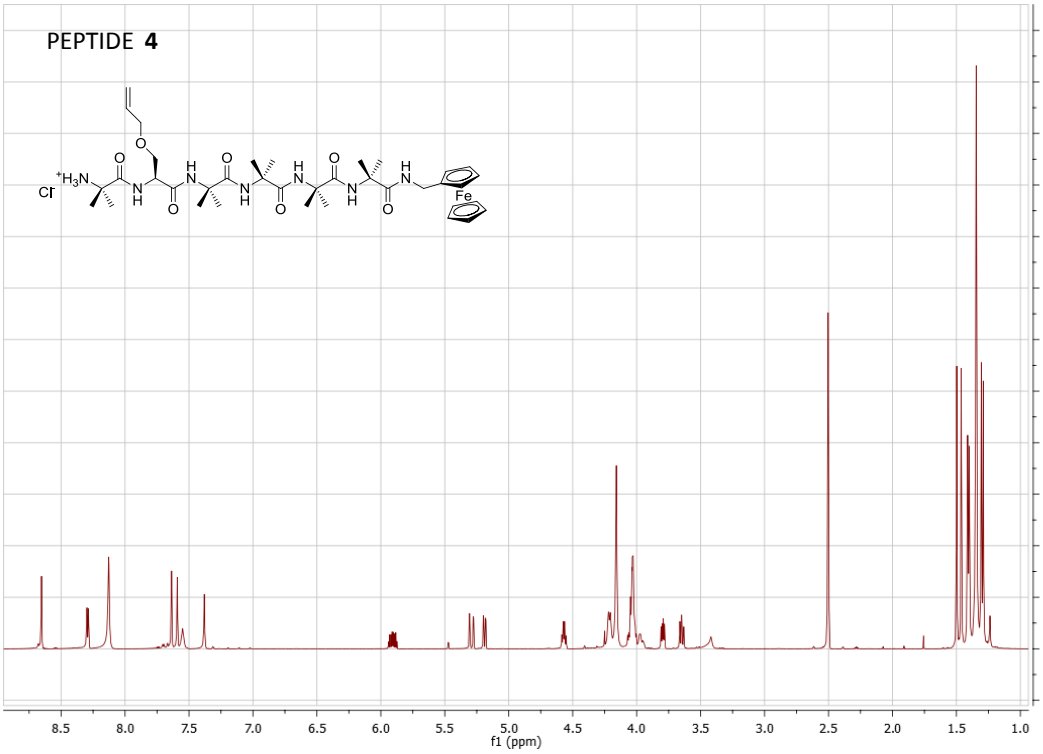
Table S13 Comparison of computed reorganization energies (λ) for electron hopping steps involving diabatic states S1 to S5 in the model peptides **19-21**.

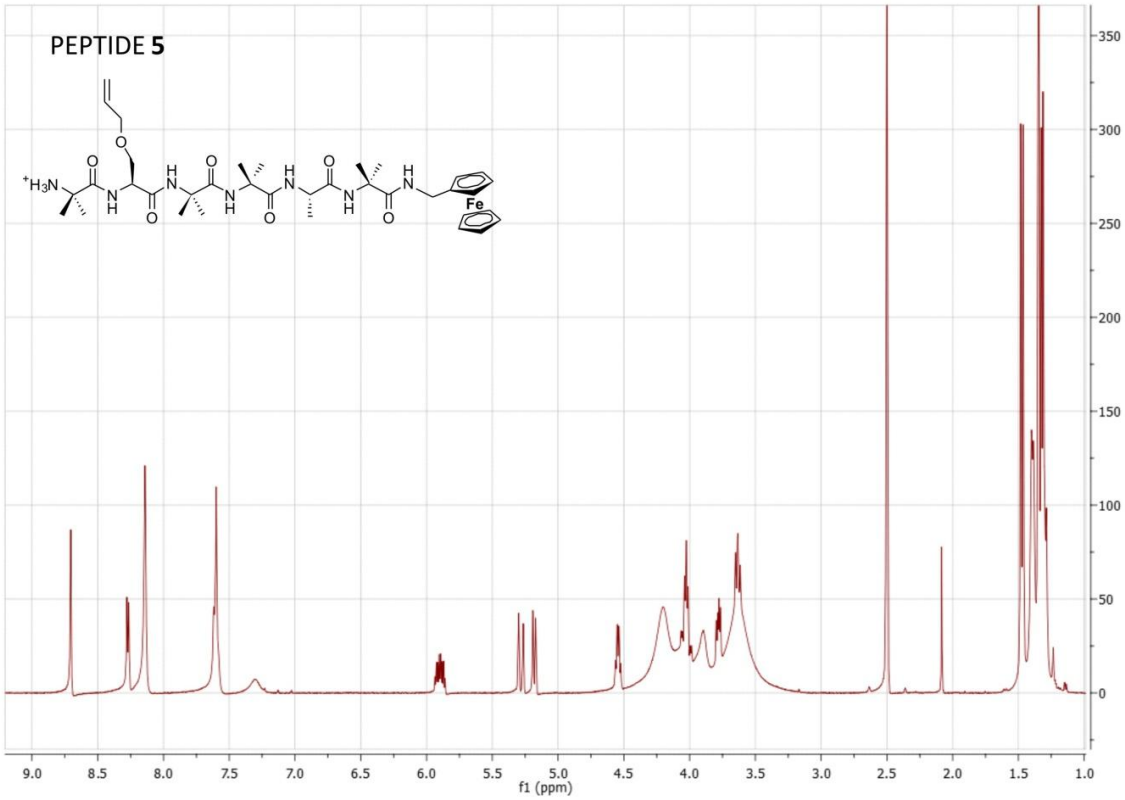
Hopping Step	Peptide **19** (eV)	Peptide **20** (eV)	Peptide **21** (eV)
S1 → S2	0.71	0.62	0.25
S2 → S1	0.76	0.64	0.37
S2 → S3	0.74	0.60	0.33
S3→ S2	0.78	0.67	0.29
S3 → S4	0.77	0.70	0.36
S4→ S3	0.72	0.66	0.44
S4→ S5	0.72	0.68	0.37
S5→ S4	0.76	0.72	0.43

7. ^{1}H NMR spectra for target peptides and their key synthetic intermediates

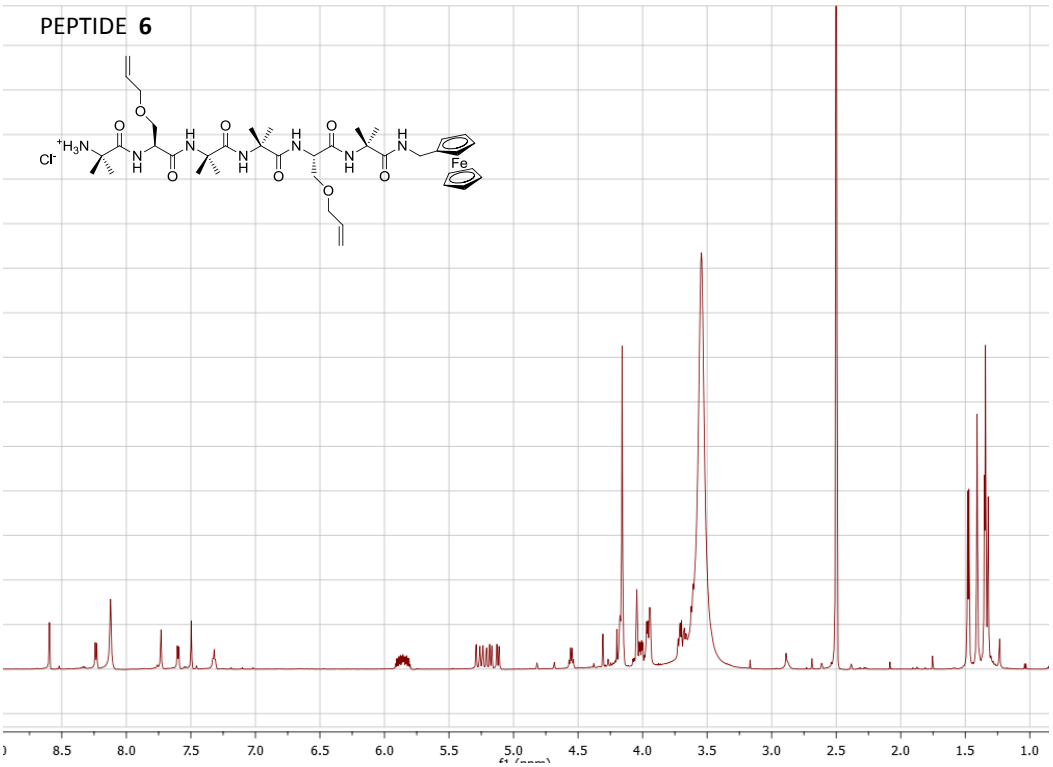




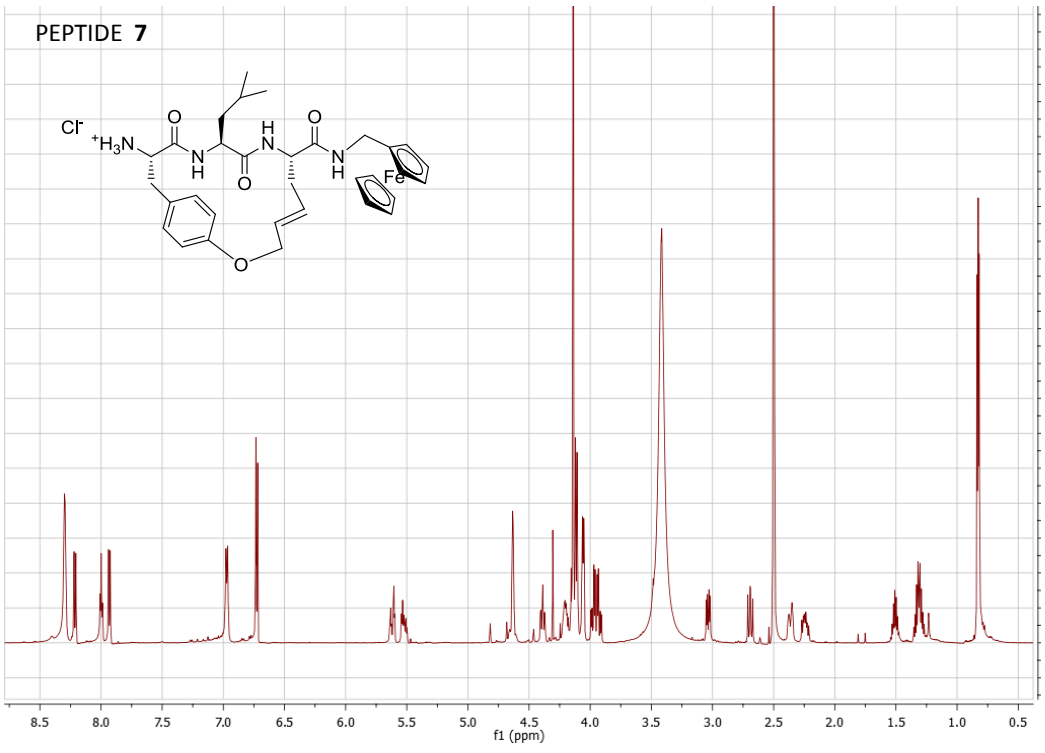

PEPTIDE 4
Cr
Fe
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


PEPTIDE 5
Fe
350
300
250
200
150
100
50
0
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

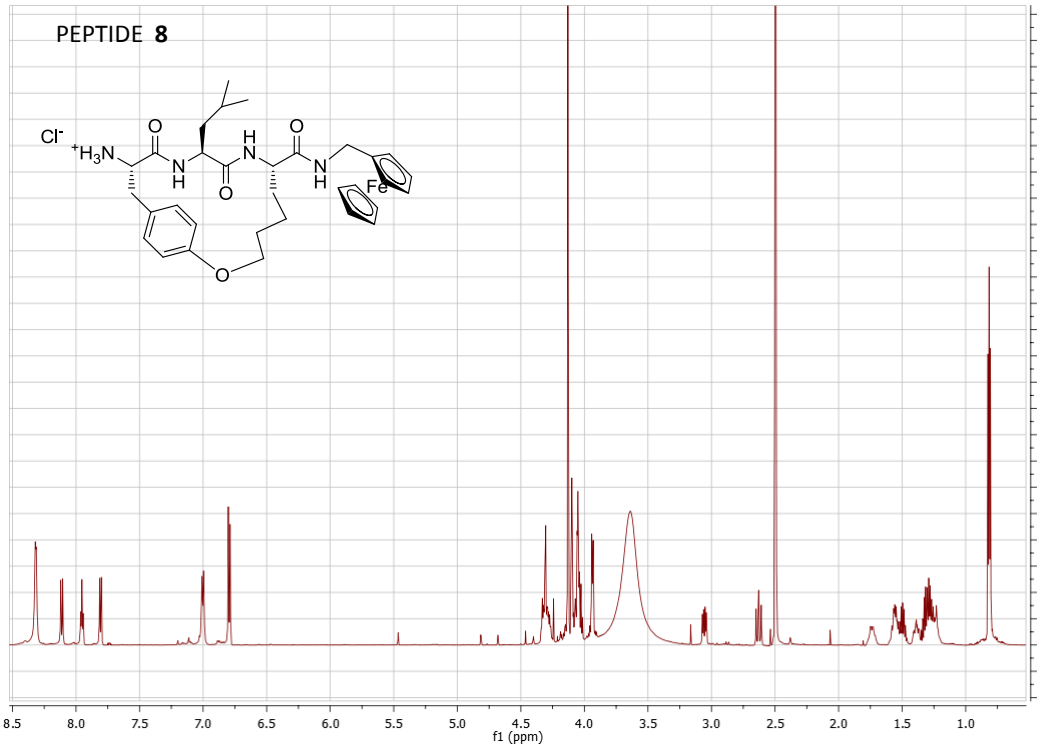
PEPTIDE **6**



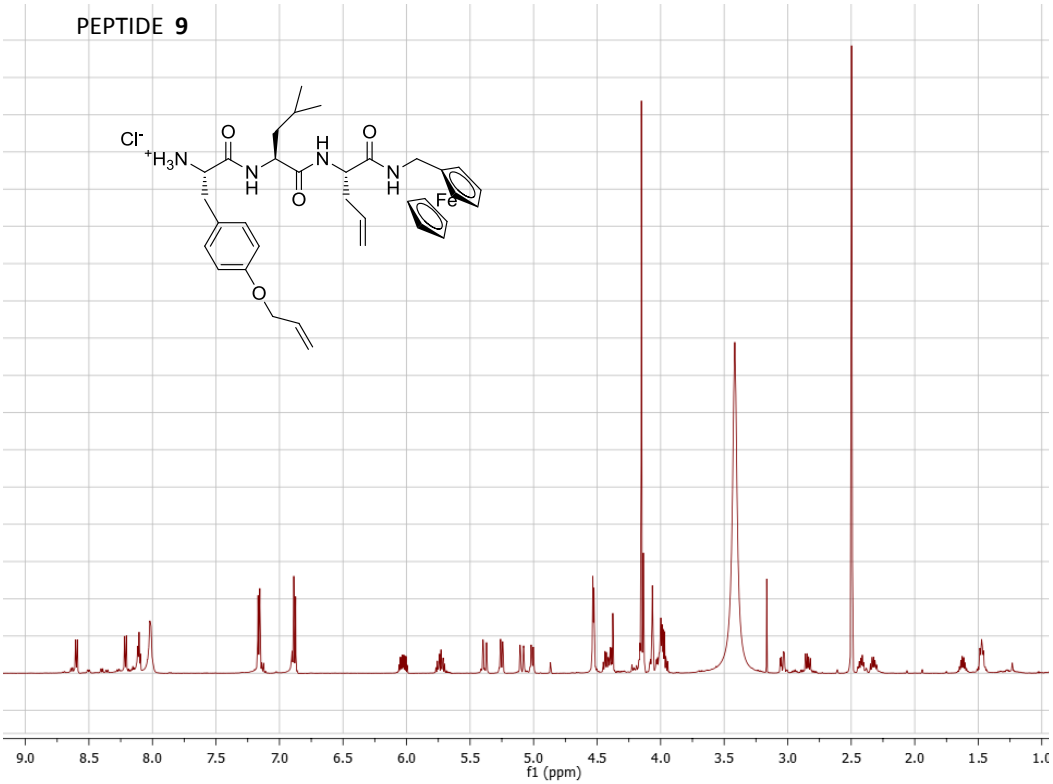
PEPTIDE **7**



PEPTIDE **8**



PEPTIDE **9**



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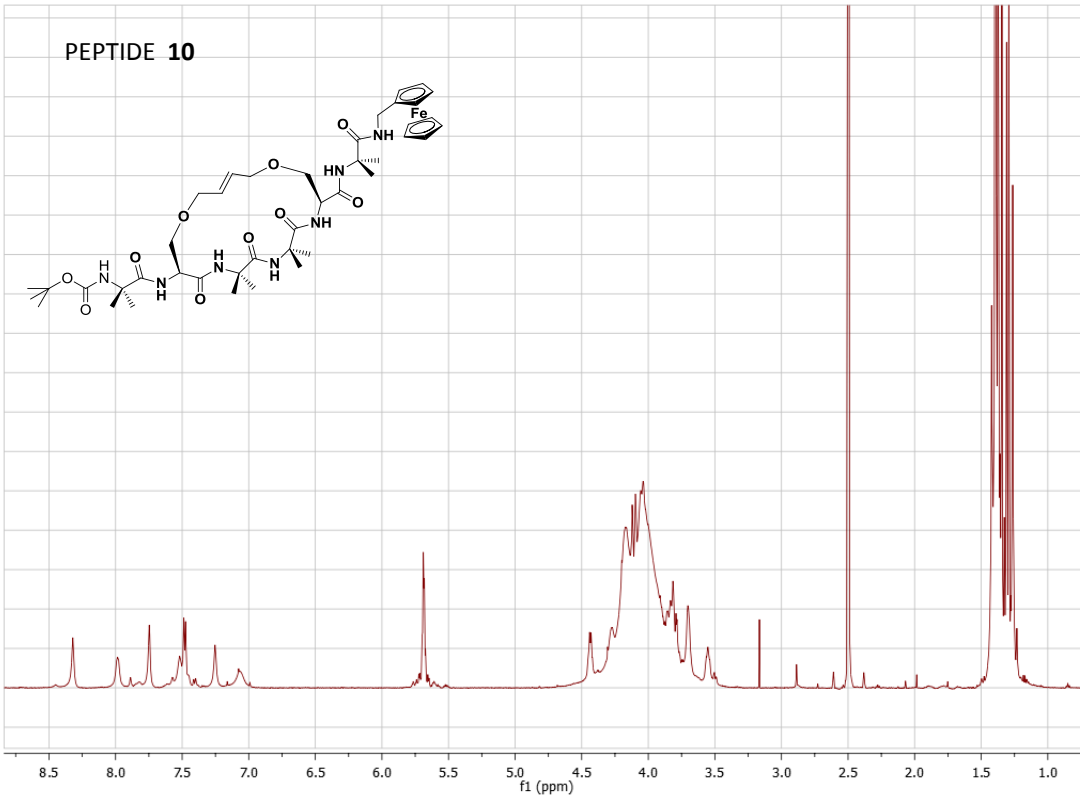
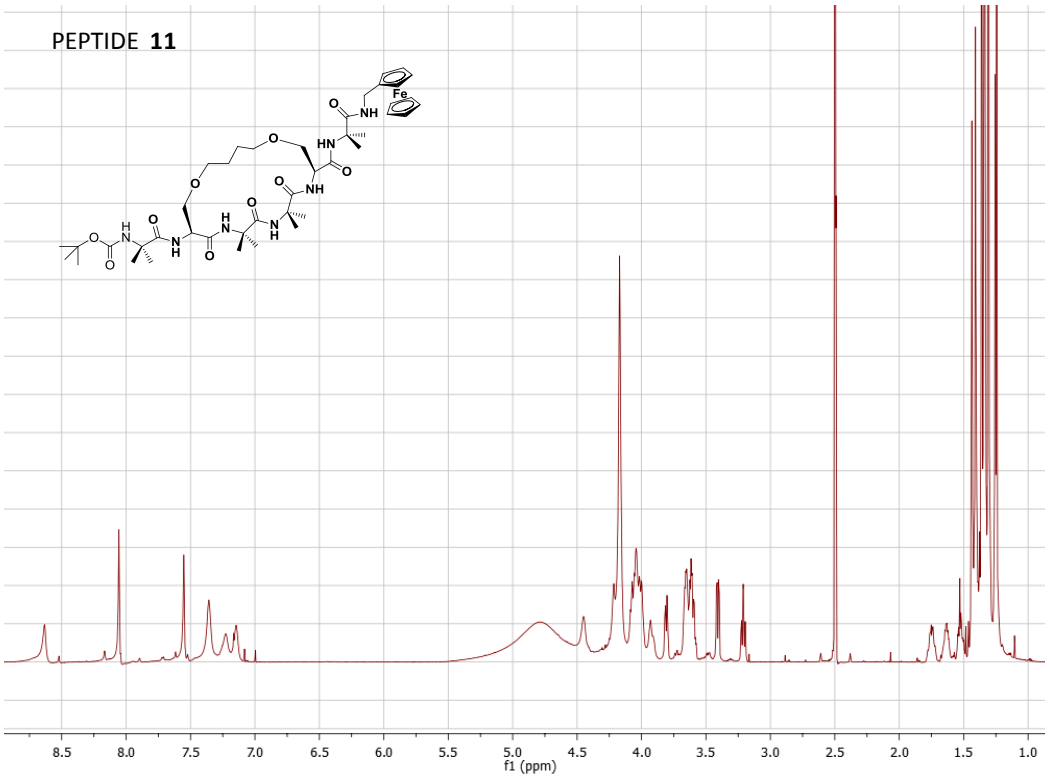


PEPTIDE **11**



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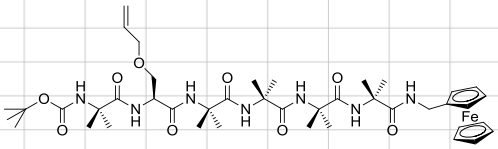

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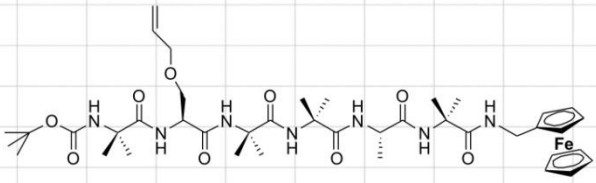

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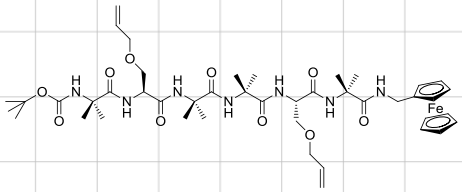

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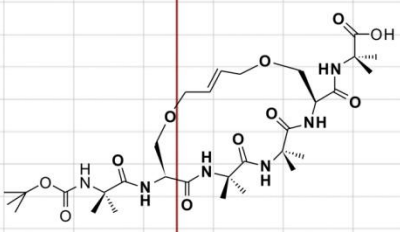

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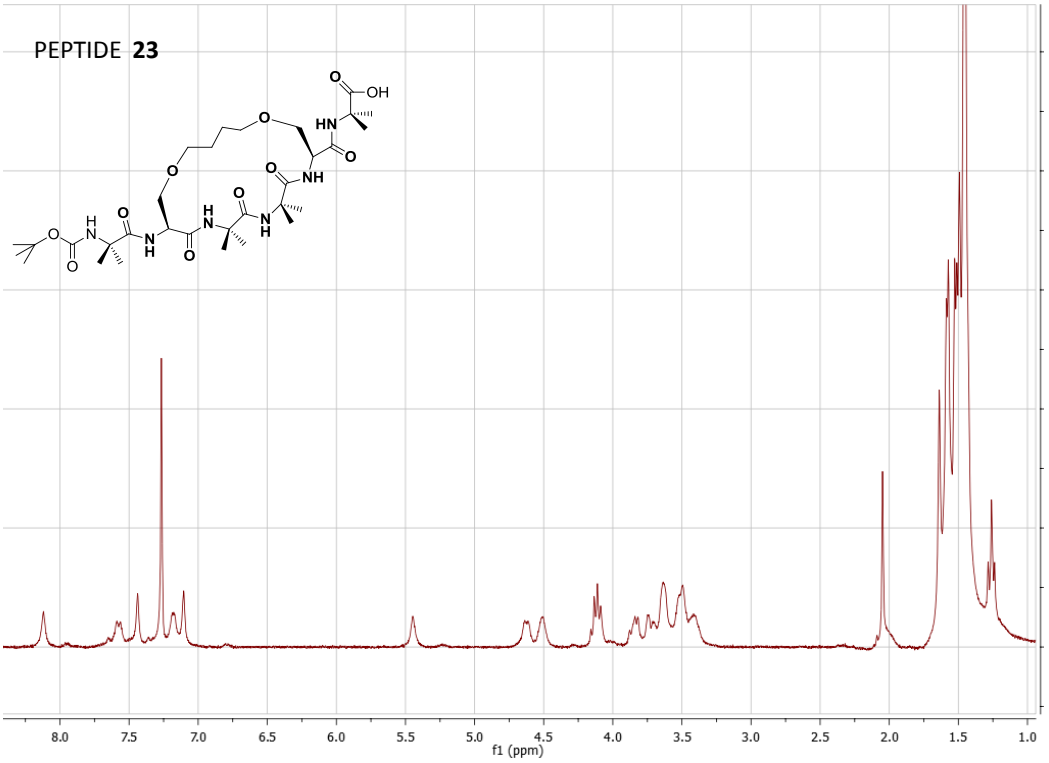

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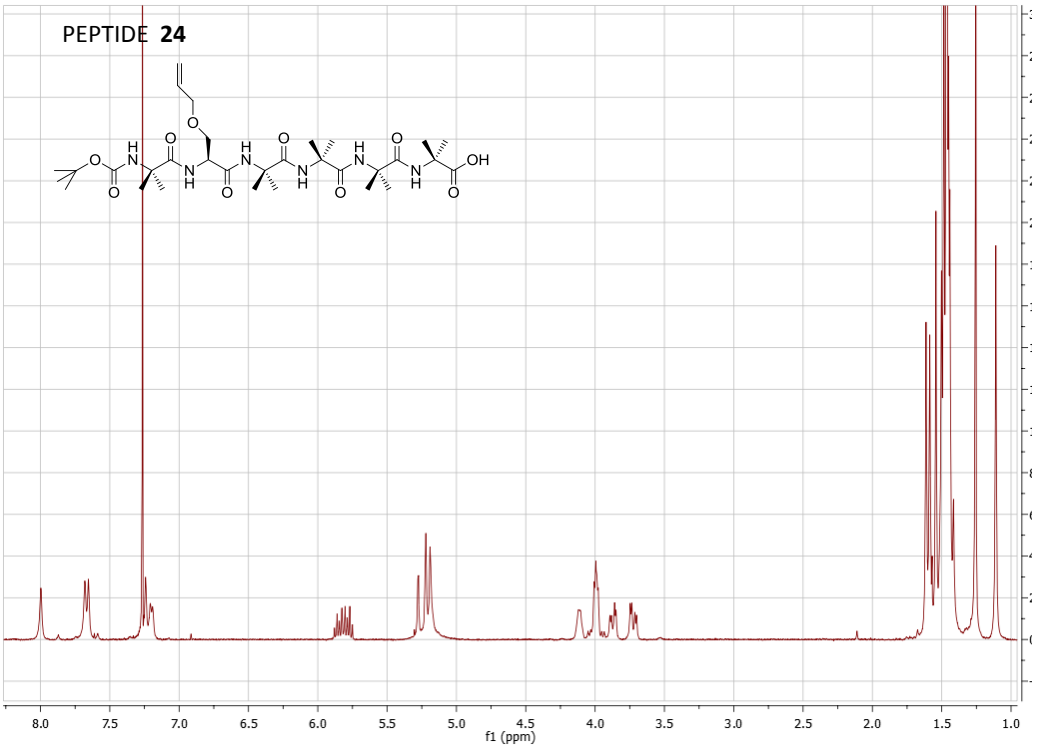
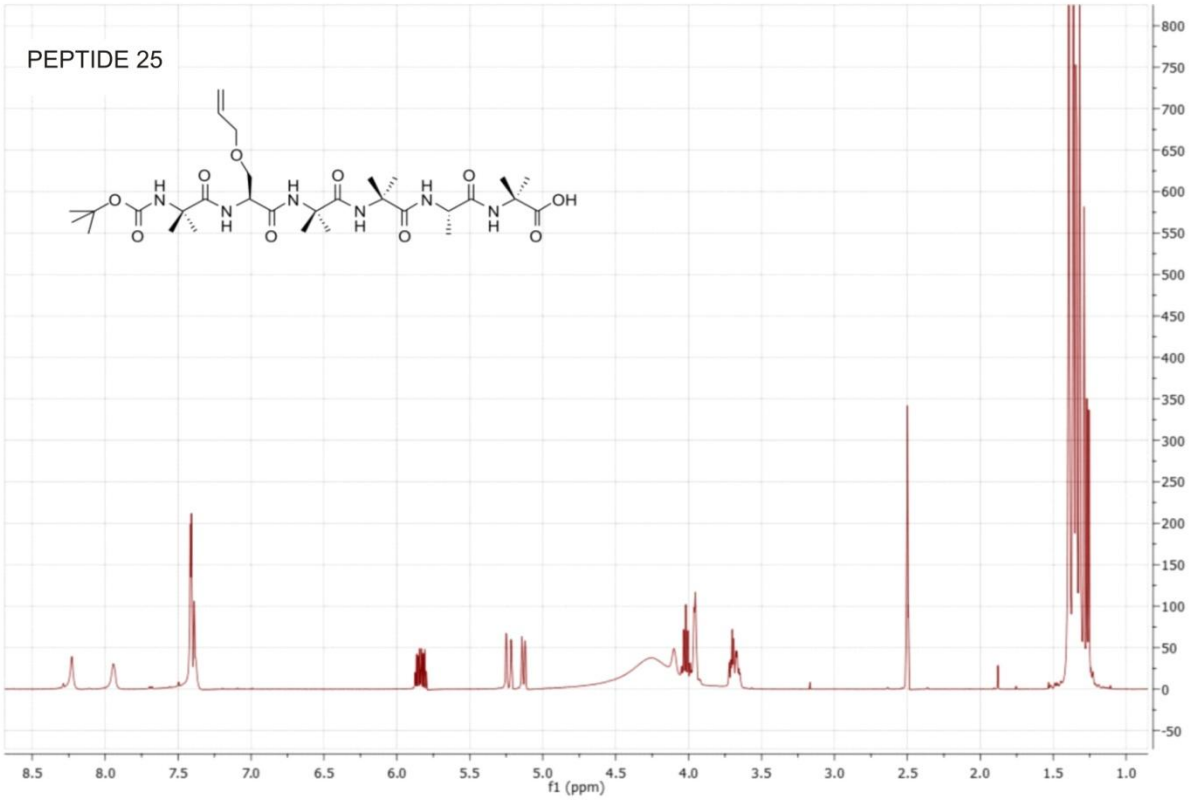
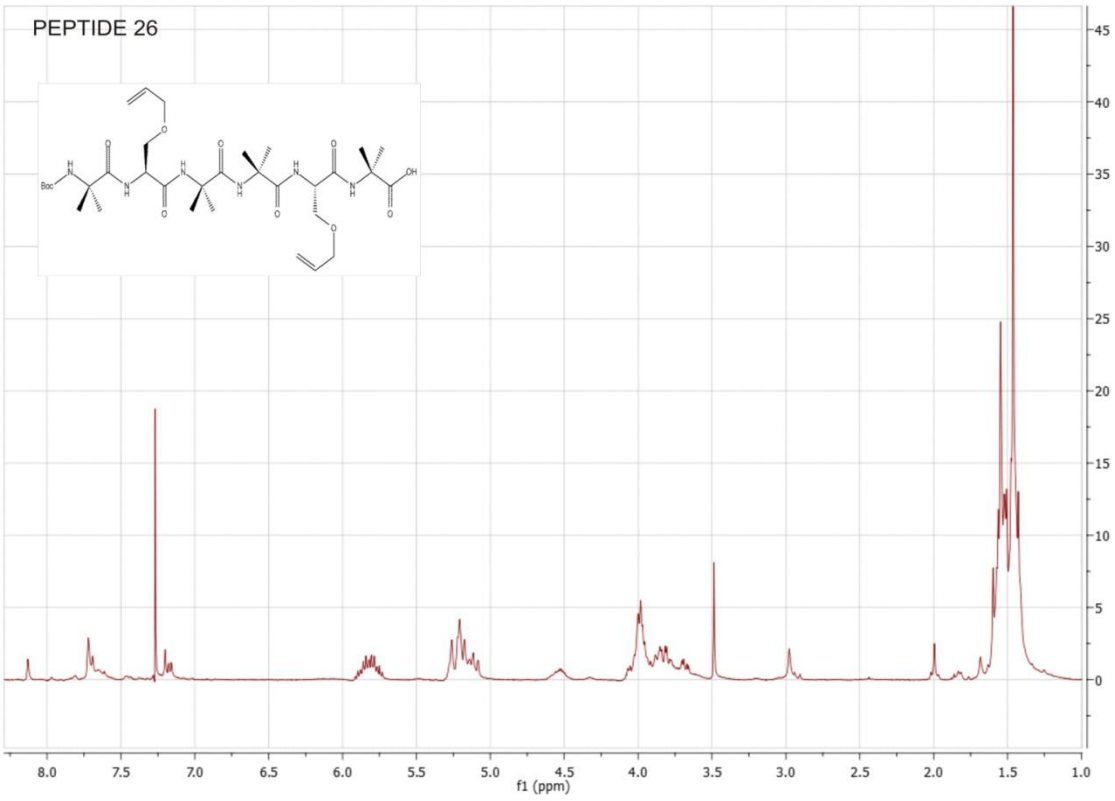
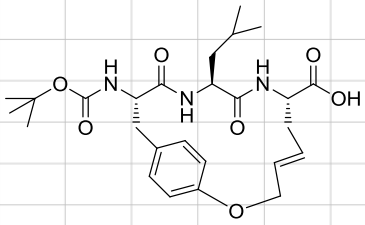



PEPTIDE 25
f1 (ppm)


PEPTIDE 26
f1 (ppm)

PEPTIDE **27**



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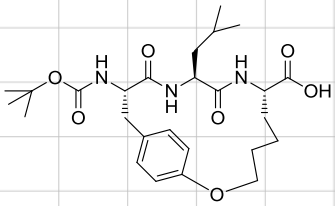

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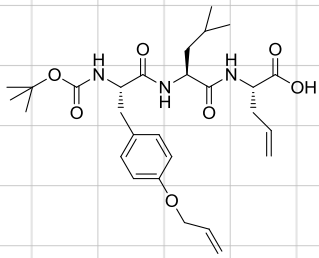

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