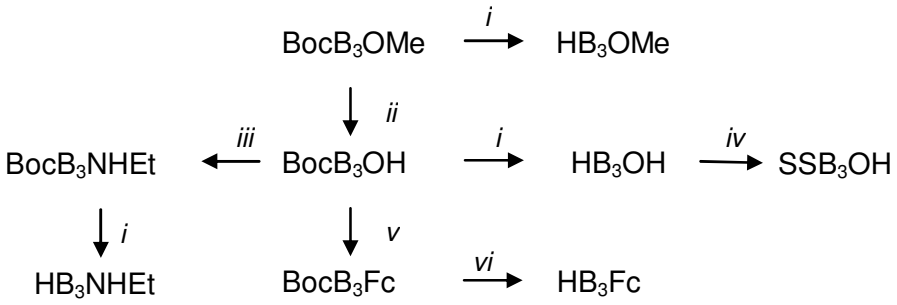
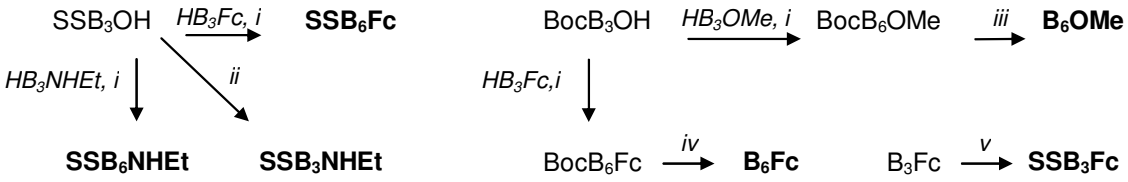
Supporting Information:

Electrochemistry of Ferrocenoyl β-Peptide Monolayers on Gold

Paula A. Brooksby, Kelly H. Anderson, Alison J. Downard, Andrew D. Abell.

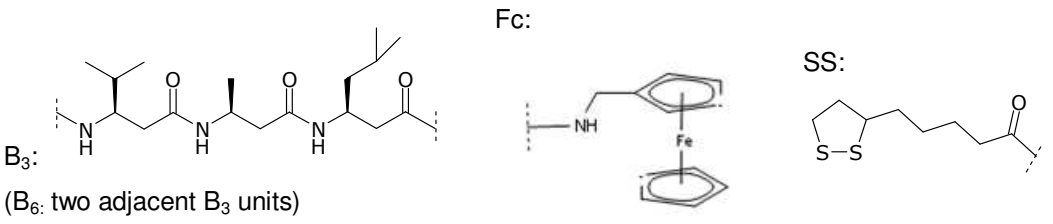


Scheme S1. Synthesis of β-tripeptides: (i)TFA, DCM, (ii) LiOH, THF, (iii) ethyl amine hydrochloride, HATU, DIEA, DMF, (iv) N-hydroxysuccinimide-activated lipoic acid, Et_3N, THF, H_2O, (v) ferrocene methyl amine, HATU, DIEA, DMF, (vii) 4M HCl in dioxane.



Scheme S2. Synthesis of β-peptides, with peptides mentioned directly in the manuscript highlighted in bold: (i) HATU, DIEA, DMF, (ii), ethyl amine hydrochloride,

HATU, DIEA, DMF, (iii)TFA, DCM, (iv) 4M HCl in dioxane, (v) N-hydroxysuccinimide-actived lipoic acid, THF, H_2O, DIEA.

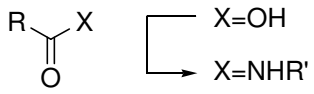


Scheme S3. Synthesis of β-tripeptides, with peptides mentioned directly in the manuscript highlighted in bold: (i) HATU, DIEA, DMF, (ii), ethyl amine hydrochloride, HATU, DIEA, DMF, (iii)TFA, DCM, (iv) 4M HCl in dioxane, (v) N-hydroxysuccinimide-actived lipoic acid, THF, H_2O, DIEA.

All NMR spectra are given at the end of this document. The synthesis of HB3OMe, BocB3OH, HB3OH, BocB6OMe, B6OMe[S1]; ferrocene methyl amine[S2,S3]; and N-hydroxysuccinimide-activated lipoic acid[S4] are published. Tetrahydrofuran was distilled from sodium benzophenone ketyl under an inert atmosphere immediately prior to use. Dichloromethane and triethylamine were distilled from calcium hydride under an inert atmosphere. Anhydrous dimethylformamide and 2,2,2-trifluoroethanol were obtained from commercial sources. Flash chromatography was carried out on Fluka Silica gel 100 C_{18}-reversed phase (fully endcapped) or lipophilic sephadex (Aldrich).

The following abbreviations apply: HATU: *O*-(7-azabenzotriazole-1-yl)-*N*,*N*,*N*',*N*'-tetramethyl uranium hexafluorophosphate; TFE: 2,2,2-trifluroethanol; TFA: trifluoroacetic acid; DCM: dichloromethane; DMF: N,N-dimethyl formamide; DIEA: diisopropylethylamine; THF: tetrahydrofuran

General Method A: Coupling with HATU

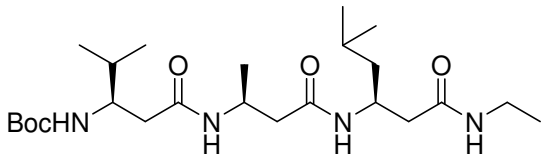


Primary amine (1.0 equiv) and carboxylic acid (1.0 equiv) were dissolved in dimethylformamide at rt, under N_2. First diisopropylethylamine (4.0 equiv) and then HATU (1.0 equiv) were added, and the reaction stirred for 16 h at rt. The reaction mixture was diluted with ethyl acetate, washed with saturated aqueous NH_4Cl, $NaHCO_3$, and NaCl, dried ($MgSO_4$), and the solvent removed *in vacuo*. The crude mixture was purified by column chromatography, as specified for each compound.

General Method B: Coupling with HATU (dimethylformamide-insoluble product)

Primary amine (1.0 equiv) and carboxylic acid (1.0 equiv) were dissolved in dimethylformamide at rt, under N_2. First diisopropylethylamine (4 equiv), and then HATU (1 equiv) were added, and the reaction stirred for 16 h. The solvent was removed *in vacuo* (high vacuum rotary evaporator), and the residue was sonicated in methanol for 10 min. The insoluble material was filtered, and washed with methanol and methanol/water (1:1) redissolved in 2,2,2-trifluoroethanol (to remove from the glass frit filter), and the solvent removed *in vacuo.* If necessary, the crude mixture was purified by column chromatography on lipophilic sephadex, as specified for each compound.

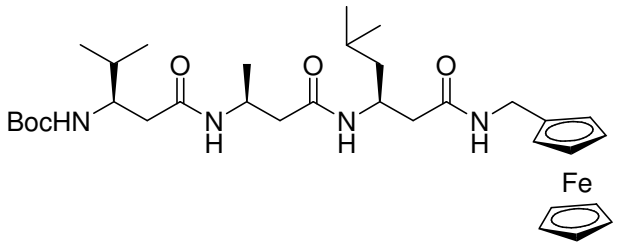
Boc-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-*N*-ethanamide (BocB_3NHEt)



Boc-β^3hVal-β^3hAla-β^3hLeu-OH (**BocB_3OH**) (76 mg, 0.17 mmol) and ethylamine hydrochloride (30 mg, 0.37 mmol) were coupled in dimethylformamide (5 mL) with HATU (65 mg, 0.17 mmol) and diisopropylethylamine (120 µL, 0.69 mmol) according to general method A. The crude residue was suspended in ethyl acetate (5 mL), sonicated, and filtered to give the product as a white solid (60 mg, 74%). mp = 208-210 ºC

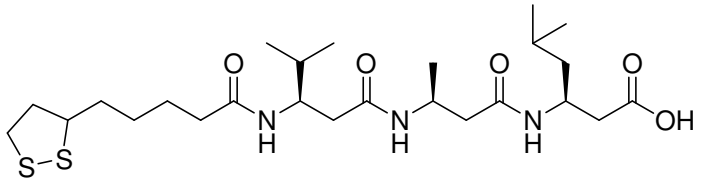
^{1}H NMR (TFE-d_3/CD_3OD 1:1) δ: 4.22 (m, 1H, NHC**H**CH_2CH), 4.10 (m, 1H, NHC**H**CH_3), 3.70 (m, 1H, NHC**H**CH), 3.13 (q, 2H, NHC**H$_2$**CH_3, *J*=7.2 Hz), 2.40-2.21 (m, 4H, NHCH($CH(CH_3)_2$C**H**H, NHCH(CH_3)C**H**H, NHCH($CHCH_2(CH_3)_2$C**H$_2$**), 2.17-2.11 (m, 2H, NHCH($CH(CH_3)_2$CH**H**, NHCH(CH_3)CH**H**), 1.68 (m, 1H, NHCHC**H**), 1.55 (m, 1H, NHCHCH_2C**H**), 1.39 (m, 1H, NHCHC**H**H), 1.36 (s, 9H, C(C**H$_3$**)$_3$), 1.23 (m, 1H, NHCHCH**H**), 1.11 (d, 3H, NHCHC**H$_3$**, *J*=6.7 Hz), 1.06 (t, 3H, NHCH_2C**H$_3$**, *J*=7.3 Hz), 0.85 (m, 12H, 2 x CH(C**H$_3$**)$_2$). ^{13}C NMR (TFE-d_3: CD_3OD 1:1) δ: 173.5, 173.3, 172.8, 158.2, 80.3, 55.9, 55.0, 46.7, 44.8, 44.6, 44.1, 43.1, 40.3, 35.3, 33.9, 28.8, 28.7, 26.0, 23.6, 22.0, 20.0, 19.5, 18.3, 14.6. HRMS calcd for $C_{24}H_{47}N_4O_5$ (MH^+) 471.3546; found 471.3534.

Boc-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-*N*-ferrocenyl methanamide (BocB$_3$Fc)



Boc-β^3hVal-β^3hAla-β^3hLeu-OH (**BocB$_3$OH**) (0.33 g, 0.75 mmol) and ferrocene methylamine (0.24 g, 1.1 mmol) were coupled in dimethylformamide (30 mL) with HATU (0.29 g, 0.76 mmol) and diisopropylethylamine (0.53 mL, 3.0 mmol), according to general method A. The product precipitated from the ethyl acetate and was filtered to give a yellow solid (0.24 g, 49%). mp = 210 ºC (dec). ^{1}H NMR (TFE-d$_3$) δ: 7.19 (t, 1H, N**H**CH$_2$, *J*=4.6 Hz), 7.04 (d, 1H, N**H**, *J*=8.6 Hz,), 6.99 (d, 1H, N**H,** *J*=8.2 Hz), 5.41 (d, 1H, N**H**CHCH**,** *J*=9.6 Hz,), 4.35-4.19 (m, 11H, Fc, FcC**H$_2$**), 4.12 (m, 1H, NHC**H**CH$_2$), 4.06 (m, 1H, NHCHC**H$_3$**), 3.67 (m, 1H, NHC**H**CH), 2.44-2.31 (m, 4H, CH(CH$_2$CH(CH$_3$)$_2$)C**H$_2$**, CH(CH(CH$_3$)$_2$)CH**H**, CH(CH$_3$)CH**H**), 2.25-2.19 (m, 2H, CH(CH(CH$_3$)$_2$)C**H**H, CH(CH$_3$)C**H**H), 1.73 (m, 1H, CHC**H**(CH$_3$)$_2$), 1.54 (m, 1H, NHCHCH$_2$C**H**), 1.44 (m, 1H, NHCHC**H**H), 1.42 (s, 9H, C(C**H$_3$**)$_3$), 1.28 (m, 1H, NHCHCH**H**), 1.15 (d, 3H, CHC**H$_3$** *J*=6.4 Hz,), 0.92-0.86 (m, 12H, 2 x CH(C**H$_3$**)$_2$). ^{13}C NMR (TFE-d$_3$) δ: 174.8, 174.3, 174.0, 159.4, 82.5, 72.3-71.6 (br, Fc), 55.6, 47.6, 45.5, 44.9, 44.3, 43.5, 41.1, 40.9, 34.4, 29.0, 26.5, 23.5, 22.2, 20.4, 19.7, 18.3. HRMS calcd for $C_{33}H_{53}FeN_4O_5$ (MH^+) 640.3287; found 640.3315.

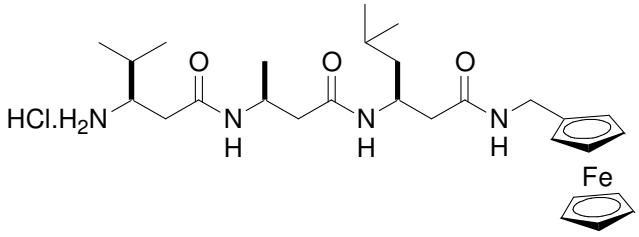
5-[1,2]Dithiolan-(3*S*/*R*)-3-yl-pentanoyl-β^3hVal-β^3hAla-β^3hLeu-OH (SSB$_3$OH)



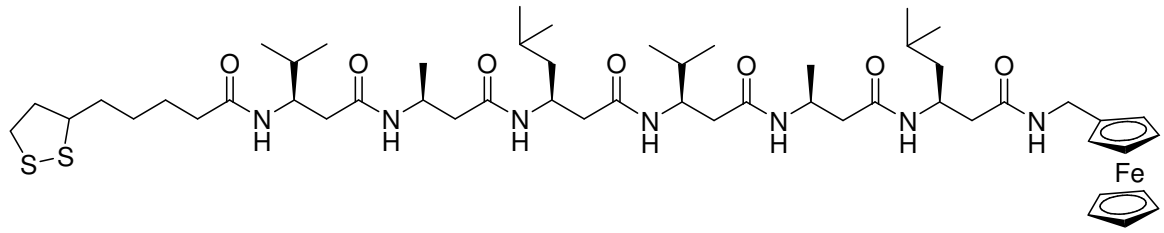
TFA·β^3hVal-β^3hAla-β^3hLeu-OH (**HB$_3$OH**) (140 mg, 0.31 mmol) and *N*-hydroxysuccinimide-activated lipoic acid (112 mg, 0.37 mmol) were dissolved in a mixture of tetrahydrofuran (30 mL), water (20 mL) and triethylamine (205 µL, 1.5 mmol) at rt. Triethylamine (~2 equiv) was added keeping the pH below 8.5 (universal indicator paper) and the reaction mixture was stirred for 16 h. The pH was adjusted to 3 (universal indicator paper) with 1 M aqueous citric acid and extracted twice with ethyl acetate (2 x 50 mL). The organic layers were combined, washed with water, dried ($MgSO_4$) and the solvent removed *in vacuo*. The product was obtained as a white solid (122 mg, 75%) that was not purified further. ^{1}H NMR ($CD_3OD/CDCl_3$ 2:1) δ: 7.76 (d, 1H, N**H**, *J*=9.4 Hz), 7.64 (d, 1H, N**H**, *J*=8.0 Hz), 7.55 (d, 1H, N**H**, *J*=9.0 Hz), 4.27 (m, 1H, NHC**H**CH_2), 4.12 (m, 1H, NHC**H**CH_3), 4.03 (m, 1H, NHC**H**CH), 3.54 (m, 1H, SC**H**), 3.18-3.06 (m, 2H, $SCH_2C\mathbf{H_2}$), 2.48-2.36 (m, 5H, $SCH_2C\mathbf{H}H$, $CH_2CHC\mathbf{H_2}CO$, $CHCHC\mathbf{H}HCO$, $CH_3CHC\mathbf{H}HCO$), 2.24-2.16 (m, 4H, $CH_2C\mathbf{H_2}CO$, $CHCHCH\mathbf{H}CO$, $CH_3CHCH\mathbf{H}CO$), 1.89 (m, 1H, $SCH_2CH\mathbf{H}$), 1.80-1.57 (m, 6H, NHCHC**H**, $NHCH_2C\mathbf{H}$, $CHC\mathbf{H_2}CH_2C\mathbf{H_2}$), 1.44 (m, 3H, $CHCH_2C\mathbf{H_2}CH_2$, C**H**HCH$(CH_3)_2$), 1.30 (m, 1H, CH**H**CH$(CH_3)_2$), 1.13 (d, 3H, $CHC\mathbf{H_3}$, *J*=6.7 Hz), 0.91-0.89 (m, 12H, 2 x C$(C\mathbf{H_3})_2$).

^{13}C NMR ($CD_3OD/CDCl_3$ 2:1) δ: 174.5, 174.2, 172.4, 172.0, 57.2, 52.9, 45.5, 44.1, 43.1, 41.0, 40.6, 39.5, 39.1, 36.9, 36.8, 35.4, 35.4, 32.9, 29.7, 29.6, 26.5, 26.0, 25.7, 23.5, 22.2, 19.9, 19.6, 18.6. HRMS calcd for $C_{25}H_{46}N_3O_5S_2$ (MH^+) 532.2879; found 532.2870.

5-[1,2]Dithiolan-(3*S*/*R*)-3-ylpentanoyl-(*R*)-*β*^{3}hVal-(*S*)-*β*^{3}hAla-(*S*)-*β*^{3}hLeu-(*R*)-*β*^{3}hVal-(*S*)-*β*^{3}hAla-(*S*)-*β*^{3}hLeu-1-ferrocenylmethanamide (SSB$_6$Fc)

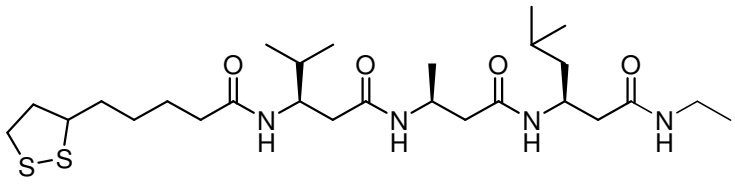


Boc-*β*^{3}hVal-*β*^{3}hAla-*β*^{3}hLeu-NHCH$_2$Fc (**BocB$_3$Fc**)(92 mg, 0.14 mmol) was first dissolved in trifluoroethanol (5 mL), then HCl (4 M in dioxane, 1 mL) was added. The reaction mixture was stirred for 5 min at rt, then the solvent was removed *in vacuo*. The product (HCl·*β*^{3}hVal-*β*^{3}hAla-*β*^{3}hLeu-NHCH$_2$Fc) was obtained as a glassy yellow solid and used without purification.



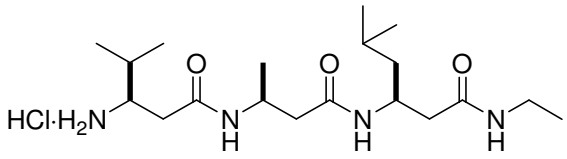
HCl·β^3hVal-β^3hAla-β^3hLeu-NHCH$_2$Fc (**HB$_3$Fc**) (83 mg, 0.14 mmol) and lipoamide-β^3hVal-β^3hAla-β^3hLeu-OH (**SSB$_3$OH**) (76 mg, 0.14 mmol) were coupled in dimethylformamide (5 mL) using HATU (54 mg, 0.14 mmol) and diisopropylethylamine (105 μL, 0.57 mmol) according to general method B. Chromatography (lipophilic sephadex; 1:0→1:9→1:1→0:1 methanol, trifluoroethanol) gave the product as a glassy yellow solid (107 mg, 71%). ^{1}H NMR (TFE-d_3) δ: 7.30- 7.01 (m, 6H, N**H**), 6.91 (d, 1H, N**H**, *J*=8.3 Hz), 4.06-4.38 (m, 17H, 6 x NHC**H**, **FcCH$_2$**), 3.59 (m, 1H, SC**H**), 3.18 (m, 1H, SC**H**H), 3.12 (m, 1H, SCH**H**), 2.52-2.21 (m, 15H, 7 x C**H$_2$**CO, SCH$_2$C**H**H), 1.93 (m, 1H, SCH$_2$C**H**H), 1.82-1.52 (m, 8H, 2 x NHCHC**H**(CH$_3$)$_2$, 2 x NHCHCH$_2$C**H,** C**H$_2$**CH$_2$C**H$_2$**CH$_2$CO), 1.45 (m, 4H, SCHCH$_2$C**H$_2$**(CH$_2$)$_2$, 2 x CHC**H**HCH(CH$_3$)$_2$), 1.29 (m, 2H, 2 x CHCH**H**CH(CH$_3$)$_2$), 1.15 (m, 6H, 2 x CHC**H$_3$**), 0.98-0.81 (m, 24H, 4 x CH(C**H$_3$**)$_2$). ^{13}C NMR (TFE-d_3) δ: 177.7, 174.5, 174.3, 174.1, 174.0, 173.9, 58.5, 54.4, 47.5, 47.4, 45.4, 44.0, 43.2, 42.0, 39.6, 38.0, 36.1, 34.0, 30.5, 30.5, 27.5, 26.7, 26.6, 23.7, 23.6, 22.7, 22.5, 20.7, 20.6, 19.8, 19.1, 19.0. HRMS calcd for $C_{53}H_{88}N_7O_7S_2Fe$ (MH^+) 1054.5536; found 1054.5511.

5-[1,2]Dithiolan-(3*S*/*R*)-3-yl-pentanoyl-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-N-ethanamide (SSB$_3$NHEt)



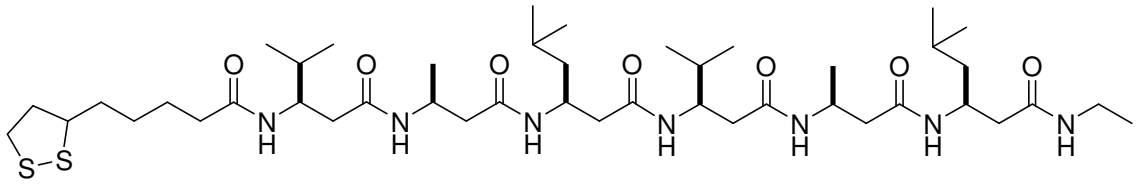
Lipoamide-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-OH (**SSB$_3$OH**) (50 mg, 94 μmol) and ethylamine hydrochloride (10 mg, 0.12 mmol) were coupled in dimethylformamide (10 mL) using HATU (36 mg, 95 μmol) and diisopropylethylamine (65 μL, 0.38 mmol). The reaction mixture was stirred for 16 h, at which time the solvent was removed *in vacuo*. The residue was sonicated in ethanol (5 mL) and filtered to give an off-white solid (36 mg, 68%). ^{1}H NMR (CD_3OD/TFE-d_3 2:1) δ: 4.25 (m, 1H, C**H**$CH_2CH(CH_3)_2$), 4.13 (m, 1H, C**H**CH_3), 4.07 (m, 1H, C**H**$CH(CH_3)_2$), 3.53 (m, 1H, SC**H**), 3.17-3.06 (m, 4H, SC**H$_2$**, C**H$_2$**CH_3), 2.46-2.17 (m, 9H, 3 x NHCHC**H$_2$**, SCHC**H**H, $(CH_2)_3$C**H$_2$**CO), 1.86 (m, 1H, SCHCH**H**), 1.78-1.44 (m, 9H, SCHC**H$_2$**C**H$_2$**C**H$_2$**, CHC**H**$(CH_3)_2$, CH**H**C**H**$(CH_3)_2$), 1.28 (m, 1H, C**H**HCH$(CH_3)_2$), 1.26 (m, 1H, C**H**HCH$(CH_3)_2$), 1.13-1.07 (m, 6H, CHC**H$_3$**, CH_2C**H$_3$**), 0.91-0.87 (m, 12H, 2 x CH(C**H$_3$**)$_2$). ^{13}C NMR (CD_3OD/TFE-d_3 2:1) δ: 176.9, 174.2, 174.1, 173.7, 58.4, 54.4, 47.6, 45.6, 45.4, 44.4, 43.9, 42.2, 40.8, 40.1, 38.0, 36.5, 36.3, 34.3, 30.8, 27.7, 26.9, 24.3, 22.9, 20.9, 20.3, 19.3, 15.4. HRMS calc for $C_{27}H_{51}N_4O_4S_2$ (MH^+) 559.3352; found 559.3332.

5-[1,2]Dithiolan-(3*S*/*R*)-3-yl-pentanoyl-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-ethanamide (SSB$_6$NHEt)



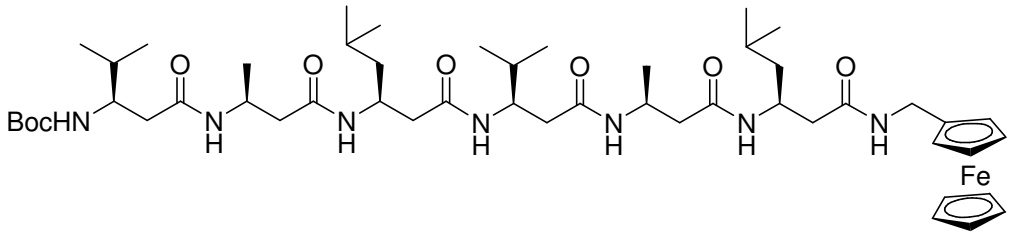
Boc-β^3hVal-β^3hAla-β^3hLeu-NHEt (**BocB$_3$NHEt**) (49 mg, 0.10 mmol) was dissolved in trifluoroacetic acid (2.5 mL) and dichloromethane (2.5 mL), then stirred for 2 h at rt. The solvent was removed *in vacuo*, twice co-evaporated *in vacuo* with

dichloromethane, and once with methanol to give the deprotected amine as a trifluoroacetate salt as a light yellow oil (50 mg, quant).



HCl·*β*3hVal-*β*3hAla-*β*3hLeu-NHEt (**HB$_3$NHEt**) (34 mg, 70 μmol) and lipoamide-*β*3hVal-*β*3hAla-*β*3hLeu-OH (**SSB$_3$OH**) (37 mg, 70 μmol) were coupled in dimethylformamide (5 mL) using HATU (27 mg, 70 μmol) and diisopropylethylamine (48 μL, 0.28 mmol) according to general method B. The product was obtained as an off-white solid (25 mg, 41%). mp = 292ºC (dec). ^{1}H NMR (TFE-d_3) δ: 7.24-6.93 (m, 7H, 7 x N**H**), 4.31-4.22 (m, 4H, 4 x NHC**H**), 4.08 (m, 2H, 2 x NHC**H**), 3.59-3.56 (m, 1H, SC**H**), 3.24-3.08 (m, 4H, C**H$_2$**S, NHC**H$_2$**), 2.47-2.30 (m, 15H, 6 x NHCHC**H$_2$**CO, $(CH_2)_3$C**H$_2$**CO, SCH_2C**H**H), 1.94-1.90 (m, 1H, SCH_2CH**H**), 1.81-1.53 (m, 8H, 2 x NHCHC**H**$(CH_3)_2$, 2 x $NHCHCH_2$C**H,** C**H$_2$**CH_2C**H$_2$**CH_2CO), 1.46 (m, 4H, SCHC**H$_2$**$CH_2(CH_2)_2$, 2 x CHC**H**HCH$(CH_3)_2$), 1.31 (m, 2H, 2 x CHCH**H**CH$(CH_3)_2$), 1.17-1.10 (m, 9H, 2 x CHC**H$_3$**, CH_2C**H$_3$**), 0.91- 0.90 (m, 24H, CH(C**H$_3$**)$_2$). ^{13}C NMR (TFE-d_3) δ:178.9, 176.0, 175.6, 175.4, 175.1, 175.0, 175.0, 59.6, 55.5, 48.7, 48.6, 46.5, 46.4, 45.1, 44.6, 44.4, 43.2, 41.4, 40.7, 39.2, 37.6, 37.2, 35.2, 35.1, 31.7, 31.6, 28.7, 27.8, 27.7, 24.9, 24.8, 23.8, 23.6, 21.9, 21.7, 21.0, 20.9, 20.2, 20.2, 15.9. HRMS calcd for $C_{44}H_{82}N_7O_7S_2$ (MH^+) 884.5717; found 884.5753.

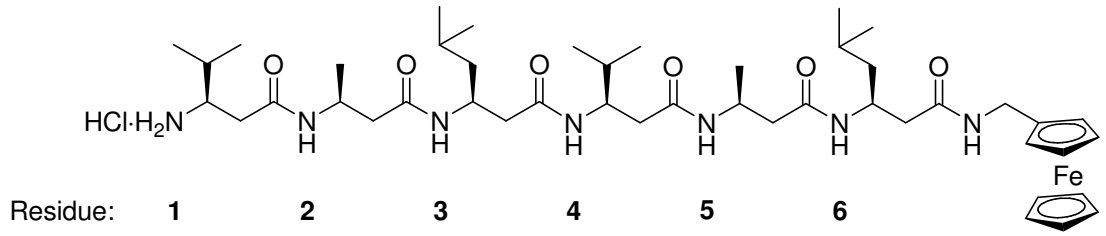
Boc-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3h-Leu-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3h-Leu-*N*-ferrocenylmethanamide (BocB$_6$Fc)



Boc-β^3hVal-β^3hAla-β^3hLeu-OH (**BocB$_3$OH**) (38 mg, 87 μmol) and HCl·β^3hVal-β^3hAla-β^3hLeu-NHCH$_2$Fc (**HB$_3$Fc**) (50 mg, 87 μmol) were coupled in DMF (50 mL) using HATU (33 mg, 87 μmol) and diisopropylethylamine (60 μL, 0.35 mmol) according to general method B to give a yellow powder (71 mg, 85%). mp = >250 ºC (dec). ^{1}H NMR (TFE-d_3) δ: 7.17-7.03 (m, 5H, 5 x N**H**), 6.98 (d, 1H, N**H**, *J*=8.7 Hz), 5.46 (d, 1H, N**H**, *J*=9.7 Hz), 4.54-4.12 (m, 15H, C**H$_2$Fc**, 2 x NHC**H**CH$_3$, 2 x NHC**H**CH$_2$), 4.04 (m, 1H, CH$_2$CONHC**H**CH), 3.69 (m, 1H, BocNHC**H**), 2.45-2.21 (m, 12H, 6 x C**H$_2$**CO), 1.80-1.69 (m, 2H, 2 x CHC**H**(CH$_3$)$_2$), 1.56 (m, 2H, 2 x NHCHCH$_2$C**H**), 1.47-1.42 (m, 11H, C(C**H$_3$**)$_3$, 2 x CHC**H**HCH(CH$_3$)$_2$), 1.29 (m, 2H, CHCH**H**CH(CH$_3$)$_2$), 1.18-1.13 (m, 6H, 2 x NHCHC**H$_3$**), 0.91-0.86 (m, 24H, 2 x CH(C**H$_3$**)$_2$).

^{13}C NMR (TFE-d_3) δ: 174.8, 174.2, 174.2, 174.1, 174.0, 173.9, 82.5, 74.4 (10C, Fc), 55.7, 54.4, 47.5, 47.5, 47.5, 47.5, 45.4, 45.4, 45.0, 44.9, 44.3, 44.0, 43.3, 43.3, 43.3, 41.1, 40.2, 40.2, 34.4, 33.6, 29.0, 26.6, 26.5, 23.7, 23.6, 22.4, 22.3, 20.5, 20.5, 19.7, 18.9, 18.4. HRMS calcd for $C_{50}H_{84}N_7O_8Fe$ (MH^+) 966.5731; found 966.5733.

HCl·(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-*N*-ferrocenylmethanamide (HB_6Fc)

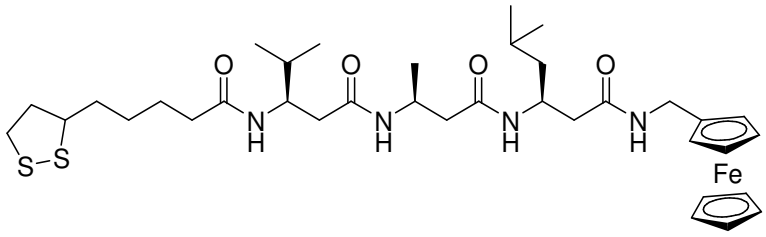


Boc-(β^3hVal-β^3hAla-β^3hLeu)$_2$-NHCH$_2$Fc (**BocB_6Fc**) (25 mg, 26 μmol) was stirred in 4M HCl/dioxane (0.5 mL) for 10 min at rt. The solvent was removed *in vacuo* and the residue passed through an alumina plug, eluting with methanol. The solvent was removed *in vacuo* and the resulting residue was purified by column chromatography (C_{18}-coated silica; 1:1→0:1 water, methanol) to give the product as a yellow solid (22 mg, 95%). ^{1}H NMR (CD_3OD) δ: 8.41 (d, 1H, *2*-N**H**, *J*=9.5 Hz), 8.32 (d, 1H, *3*-N**H**, *J*=9.1 Hz), 8.27 (d, 1H, N**H**, *J*=9.9 Hz), 8.07 (d, 1H, *4*-N**H**, *J*=9.3 Hz), 7.98 (d, 1H, N**H**CH$_2$Fc, *J*=8.4 Hz), 7.70 (d, 1H, *6*-N**H**, *J*=10.0 Hz), 7.55 (d, 1H, *5*-N**H**, *J*=8.4 Hz) 4.55 (m, 1H, *2*-NHC**H**), 4.46 (m, 1H, *5*-NHC**H**), 4.44 (m, 1H, *6*-NHC**H**), 4.37 (m, 1H, *3*-NHC**H**), 4.26 (m, 2H, C**H$_2$**Fc), 4.20 (m, 1H, *4*-NHC**H**), 3.52 (m, 1H, *1*-NHC**H**), 2.79 (dd, 1H, *1*-C**H**HCO, *J*=15.2, 11.6 Hz), 2.72 (dd, 1H, *2*-C**H**HCO, *J*=14.9, 11.6 Hz), 2.62 (m, 1H, *1*-CH**H**CO), 2.60 (m, 1H, *3*-C**H**HCO), 2.53 (m, 1H, *4*-C**H**HCO), 2.49 (m, 1H, *2*-CH**H**CO), 2.47 (m, 1H, *5*-C**H**HCO), 2.41 (m, 1H, *3*-CH**H**CO), 2.30 (m, 1H, *5*-CH**H**CO), 2.29 (m, 2H, *6*-C**H$_2$**CO), 2.20 (m, 1H, *4*-CH**H**CO), 1.76 (m, 1H, *4*-NHCHC**H**) 1.57 (m, 2H, 2 x NHCHCH$_2$C**H**), 1.42 (m, 1H, *3*-NHCHC**H**H), 1.36 (m, 1H, *6*-NHCHCH**H**), 1.25 (m, 2H, *3*,*6*-NHCHCH**H**), 1.18 (d, 3H, *2*-CHC**H$_3$**, *J*=6.7 Hz), 1.14 (d, 3H, *5*-CHC**H$_3$**, *J*=6.7 Hz),

1.09 (m, 6H, *1*-CH(C**H**$_3$)$_2$), 0.96 (d, 6H, 4-CH(C**H**$_3$)$_2$, *J*=6.5 Hz), 0.89 (m, 12H, *3*,*6*-CH(C**H**$_3$)$_2$). ^{13}C NMR (CD_3OD) δ: 173.2, 172.7, 172.1, 171.9, 171.6, 171.2, 70.4 (10 C, Fc), 56.4, 53.1, 46.5, 46.1, 45.8, 45.4, 43.7, 43.5, 43.3, 43.2, 42.0, 41.8, 39.4, 36.2, 34.5, 32.1, 26.1, 26.0, 26.0, 23.7, 23.4, 23.1, 22.9, 21.2, 20.9, 19.9, 19.8, 19.2, 18.2. HRMS calcd for $C_{45}H_{76}N_7O_6Fe$ (MH^+) 866.5206; found 866.5200.

$[\alpha]_D$ = -9 (c=0.75, methanol).

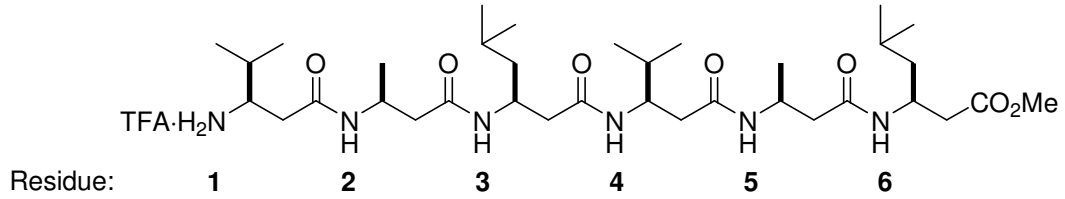
5-[1,2]Dithiolan-(3*S*/*R*)-3-yl-pentanoyl-(*R*)-*β*^{3}hVal-(*S*)-*β*^{3}hAla-(*S*)-*β*^{3}hLeu-*N*-ferrocenylmethanamide (SSB$_3$Fc)



N-Hydroxysuccinimide-activated lipoic acid (26 mg, 86 μmol) and HCl·(*R*)-*β*^{3}hVal-(*S*)-*β*^{3}hAla-(*S*)-*β*^{3}hLeu-*N*-ferrocenyl methanamide (**HB$_3$Fc**) (45 mg, 78 μmol) were dissolved in dimethylformamide (5 mL) followed by the addition of triethylamine (43 μL, 0.31 mmol). The reaction mixture was stirred under N_2 for 16 h, evaporated in vacuo, and the residue dried under high-vacuum for 30 min. Methanol (10 mL) was added and the suspension sonicated for 30 min. The suspension was filtered to give a yellow solid (51 mg, 89%). mp = 261 ºC (dec). ^{1}H NMR (TFE-d_3) δ: 7.16 (t, 1H, N**H**CH$_2$, *J*=5.3, 5.3 Hz), 7.07 (d, 1H, N**H**CHCH$_3$, *J*=8.3 Hz), 7.00 (d, 1H, N**H**CHCH$_2$CH(CH$_3$)$_2$, *J*=9.0 Hz), 6.83, (d, `H, N**H**CHCH(CH$_3$)$_2$, *J*=9.5 Hz), 4.25 (m, 1H, C**H**CH$_2$CH(CH$_3$)$_2$), 4.22-4.10 (m, 11H, **Fc**-C**H$_2$**), 4.14 (m, 1H, C**H**CH$_3$), 4.05 (m,

1H, C**H**CH$(CH_3)_2$) 3.58 (m, 1H, SC**H**), 3.18-3.06 (m, 2H, SC$\mathbf{H_2}$), 2.48-2.19 (m, 9H, 3 x C$\mathbf{H_2}$CO, SCHC**H**H, $(CH_2)_3$C$\mathbf{H_2}$CO), 1.93 (m, 1H, SCHCH**H**), 1.80-1.40 (m, 9H, SCHC$\mathbf{H_2}$C$\mathbf{H_2}$C$\mathbf{H_2}$, CHC**H**$(CH_3)_2$, CH**H**C**H**$(CH_3)_2$), 1.28 (m, 1H, C**H**HCH$(CH_3)_2$), 1.13 (d, 3H, CHC$\mathbf{H_3}$, *J*=6.6 Hz), 0.93-0.86 (m, 12H, 2 x CH(C$\mathbf{H_3}$)$_2$). ^{13}C NMR (TFE-d_3) δ: 177.5, 174.4, 174.2, 174.0, 71.2, 70.4, 58.4, 54.2, 47.5, 45.4, 44.9, 44.0, 43.4, 41.9, 41.0, 40.4, 39.5, 37.9, 35.9, 33.8, 30.4, 27.3, 26.5, 23.5, 22.3, 20.4, 19.8, 18.8. HRMS calc for $C_{36}H_{57}N_4O_4S_2Fe$ (MH^+) 729.3171; found 726.3161.

TFA-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu-(*R*)-β^3hVal-(*S*)-β^3hAla-(*S*)-β^3hLeu methyl ester (HB$_6$OMe)



Boc-(β^3hVal-β^3hAla-β^3hLeu)$_2$ methyl ester (**BocB$_6$OMe**) (21 mg, 27 μmol) was dissolved in trifluoroacetic acid (2 mL) and the solution stirred for 2 h at rt. The solvent was removed *in vacuo* and the residue twice resuspended in dichloromethane and concentrated *in vacuo*. The residue was redissolved in methanol and concentrated *in vacuo* to give a light brown solid (21 mg, quant.) that gave spectral and physical properties in agreement with those in the literature.[S1] mp= 214-216 ºC (220-222 ºC).[S1] *Where necessary, the chemical shift data is appended with the residue number indicated in the chemical structure above.* ^{1}H NMR (CD_3OD) δ: 8.74 (d, 1H, N**H**, *J*=4.8 Hz), 8.43

(d, 1H, N**H**, *J*=7.7 Hz), 8.39 (d, 1H, N**H**, *J*=9.3 Hz), 8.26 (d, 1H, N**H**, *J*=8.9 Hz), 7.80 (d, 1H, N**H**, *J*=7.0 Hz), 7.48 (d, 1H, N**H**, *J*=9.4 Hz), 4.54 (m, 1H, *2*-NHC**H**CH_3), 4.45 (m, 2H, *5*-NHC**H**CH_3, *6*-NHC**H**CH_2), 4.38 (m, 1H, *3*-NHC**H**CH_2), 4.22 (m, 1H, *4*-NHC**H**CH), 3.70 (s, 3H, OC**H$_3$**), 3.52 (m, *1*-NH_2C**H**CH), 2.76 (dd, 1H, *1*-NH_2CHC**H**H, *J*=15.4, 11.5 Hz), 2.69 (m, 1H, *2*-NHCHC**H**H), 2.64 (m, 1H, *6*-NHCHC**H**HCO), 2.59 (m, 1H, *1*-NHCHCH**H**), 2.52 (m, 1H, *6*-NHCHC**H**HCO), 2.50 (m, 2H, *3*-NHCHC**H**HCO, *4*-NHCHC**H**H), 2.47 (m, 1H, *2*-NHCHCH**H**), 2.45 (m, 1H, *5*-NHCHC**H**H), 2.39 (m, 1H, *3*-NHCHCH**H**CO), 2.33 (dd, 1H, *5*-NHCHCHH, *J*=15.1, 10.8 Hz), 2.22 (dd, 1H, *4*-NHCHCH**H**, *J*=14.7, 11.8 Hz), 2.07 (m, 1H, *1*-NH_2CHC**H**), 1.70 (m, 1H, *4*-NHCHC**H**), 1.56 (m, 2H, *3*,*6*-NHCHCH_2C**H**), 1.42 (m, 2H, *3*,*6*-NHCHC**H**H), 1.24 (m, 2H, *3*,*6*-NHCHC**H**H), 1.20 (d, 3H, *2*-NHCHC**H$_3$**, *J*=6.6 Hz), 1.14 (d, 3H, *5*-NHCHC**H$_3$**, *J*=6.7 Hz), 1.08 (d, 6H, *1*-CHCH(C**H$_3$**)$_2$, *J*=6.9 Hz), 0.92 (m, 12H, *4*-CHCH(C**H$_3$**)$_2$), 0.88 (m, 12H, *3*,*6*-CH_2CH(C**H$_3$**)$_2$).

S1. Seebach, D.; Overhand, M.; Kuehnle, F. N. M.; Martinoni, B., *Helvetica Chimica Acta* **1996,** 79, (4), 913-941.

S2. Beer, P. D.; Smith, D. K., *Journal of the Chemical Society, Dalton Transactions: Inorganic Chemistry* **1998**, (3), 417-423.

S3. Sun, H. W., Qingmin; Huang, Runqiu; Li, Heng; Li, Yonghong., *Journal of Organometallic Chemistry* **2002,** 655, (1-2), 182-185. 12.

S4. Gruzman, A.; Hidmi, A.; Katzhendler, J.; Haj-Yehie, A.; Sasson, S., *Bioorganic & Medicinal Chemistry* **2004,** 12, (5), 1183-1190.

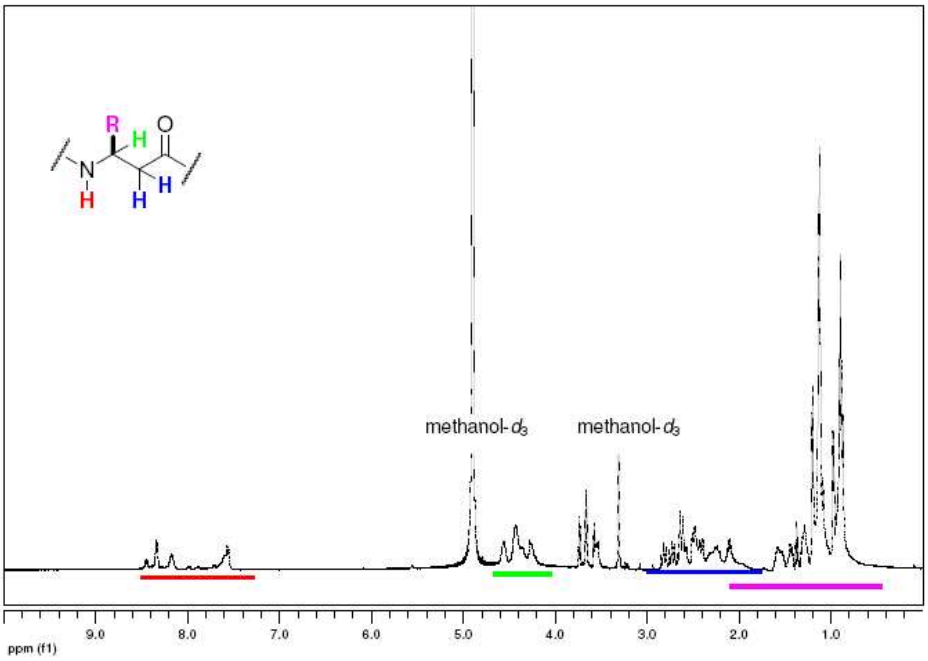


Figure S1 NMR spectrum of **B_6Fc** in d_3-methanol. The colored bands indicate the different proton environments of the peptide.

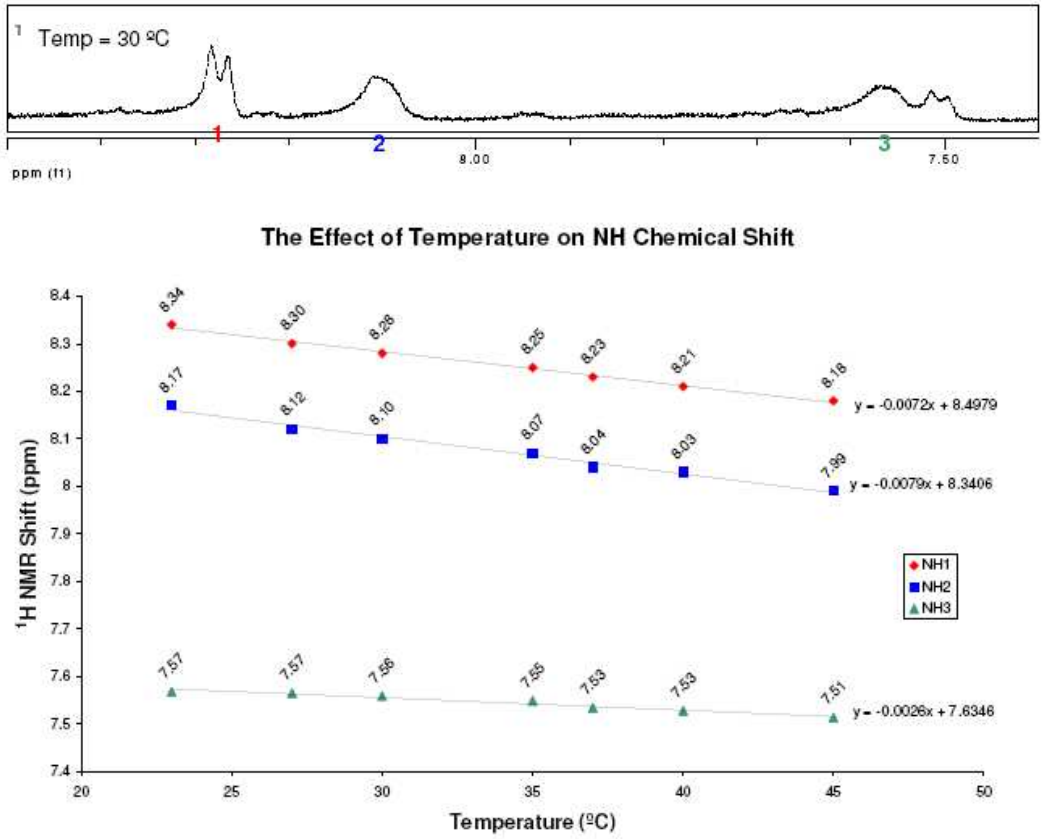


Figure S2 (top) NMR spectrum of **B_6Fc** in d_3-methanol at 30°C. (bottom) Chemical shift (ppm) of three NH protons of **B_6Fc** at different temperatures. The chemical shift values are shown next to the data points.

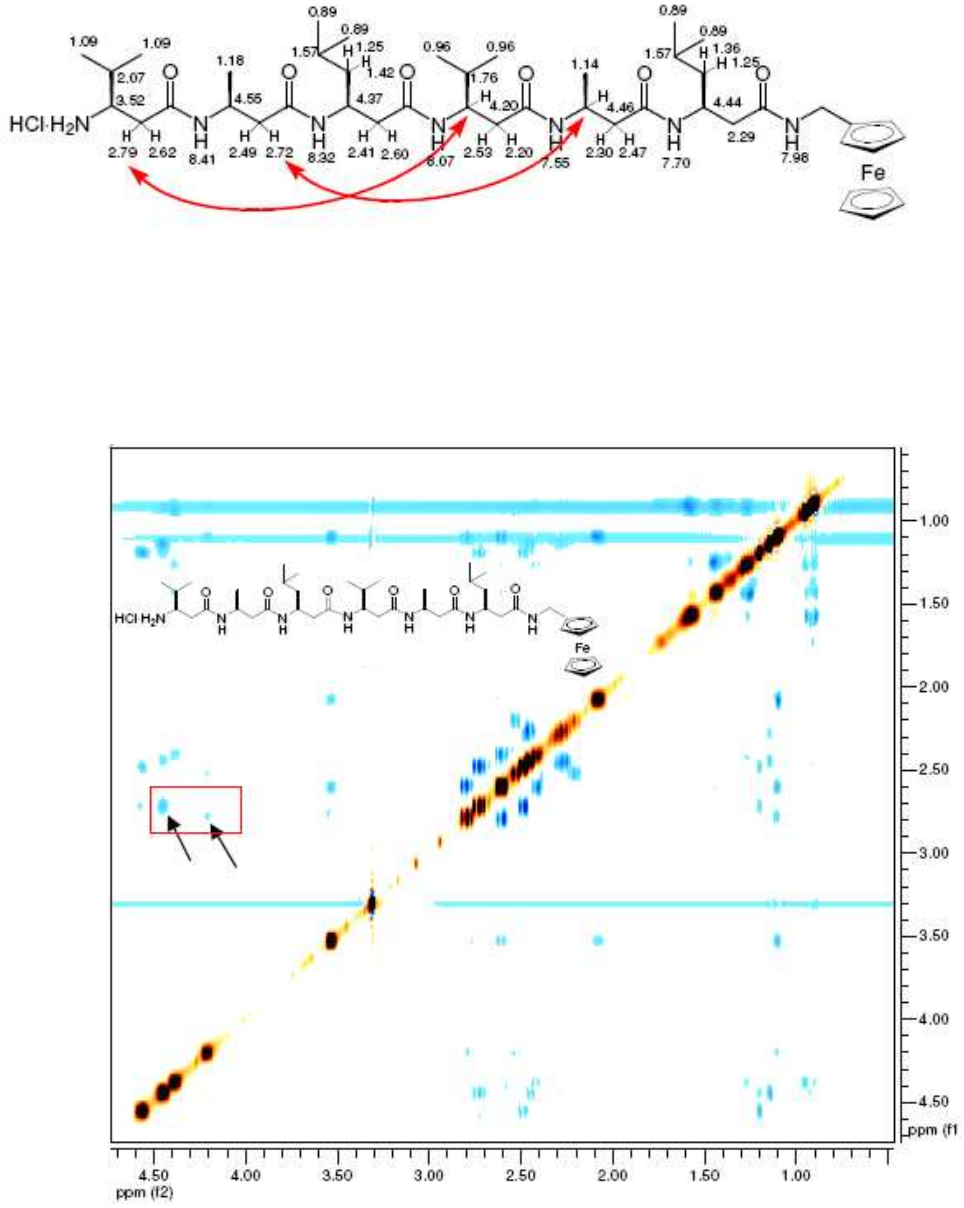


Figure S3 The partially assigned structure of **B_6Fc** showing: (top) NMR shifts, the red arrows indicate proton-proton correlations observed in the (bottom) 2D ROESY spectrum. The black arrows show the important structural correlations between backbone protons as illustrated above.

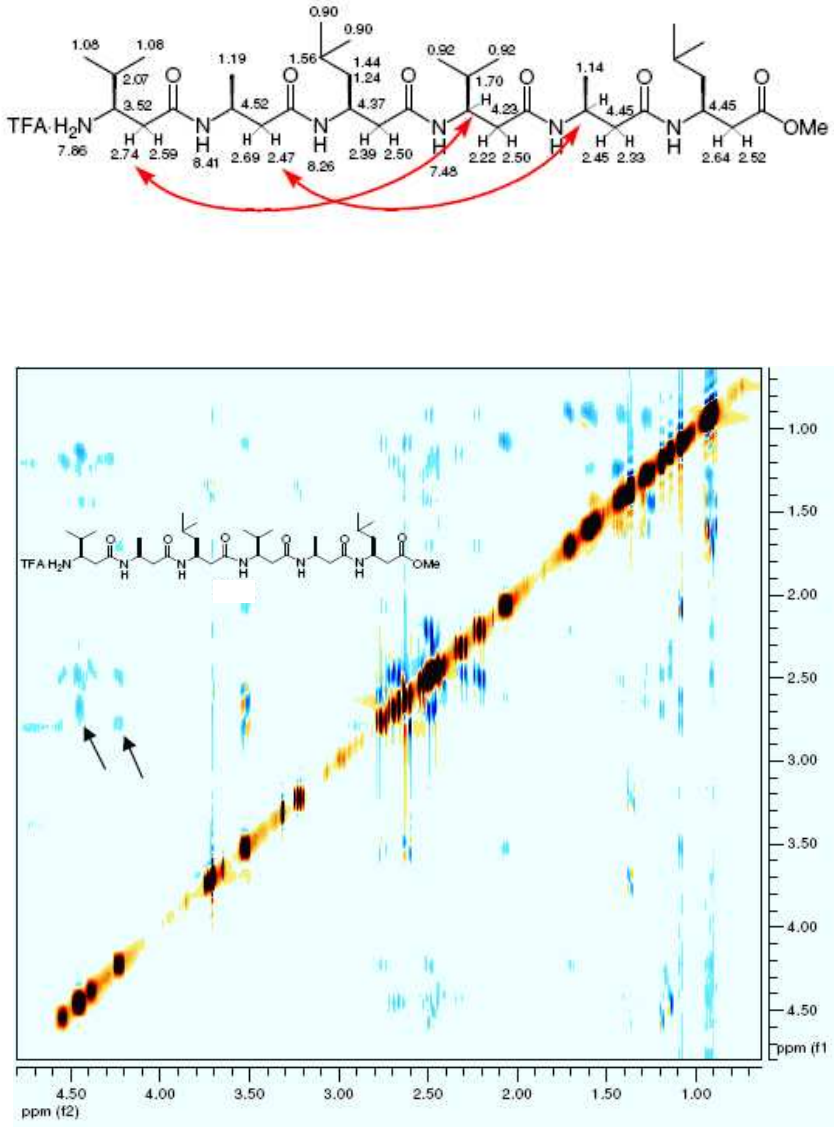
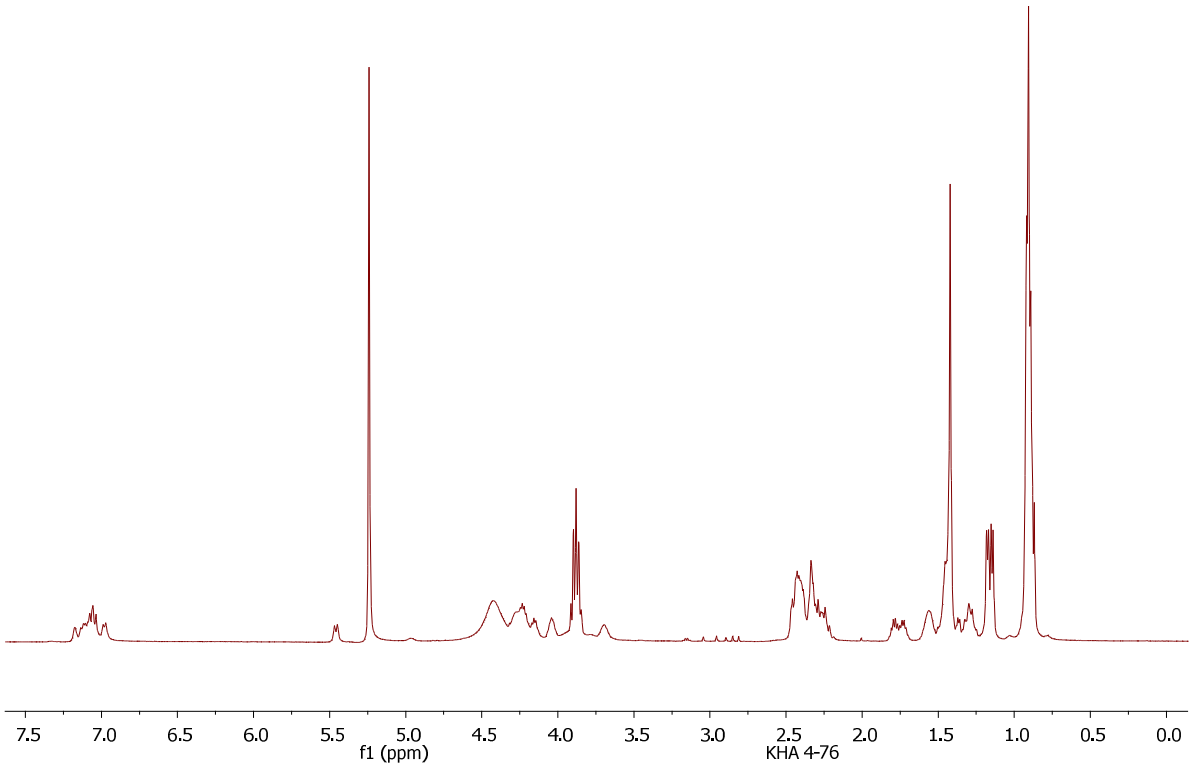
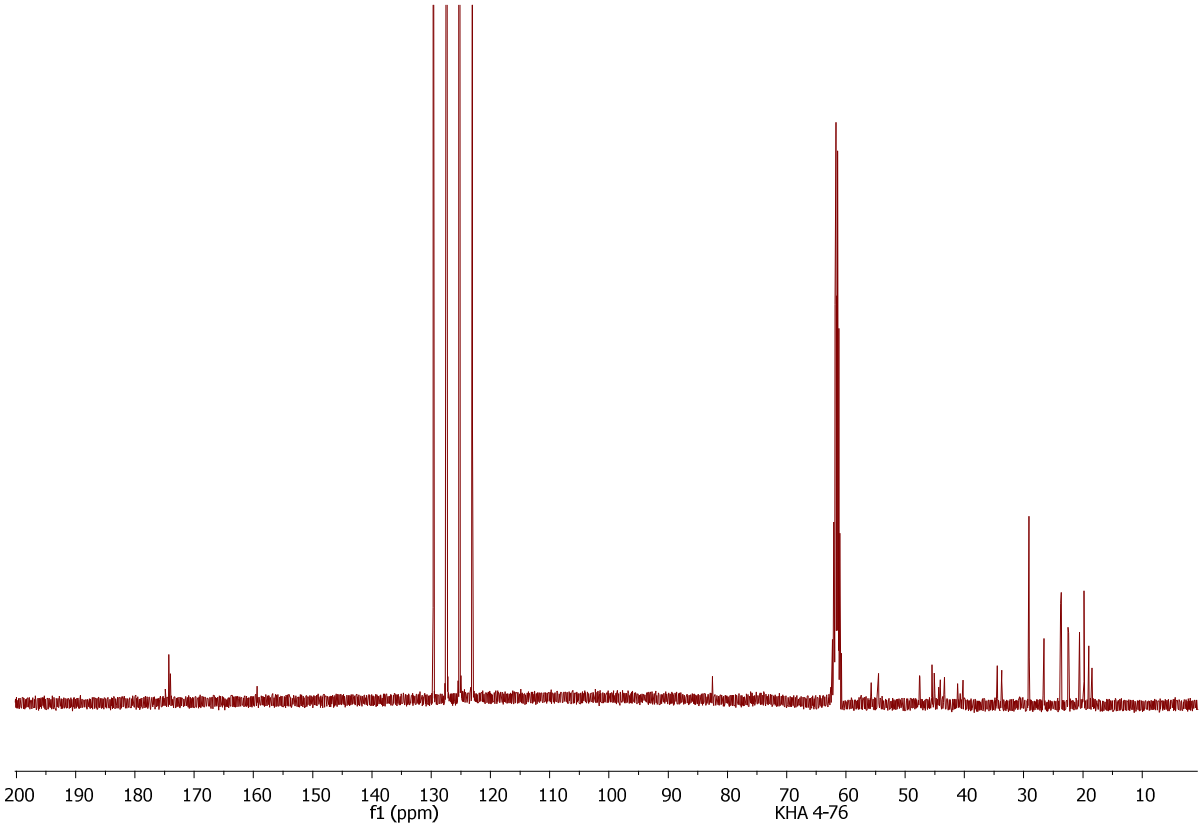


Figure S4 The partially assigned structure of **pB_6** showing: (top) NMR shifts, the red arrows indicate proton-proton correlations observed in the (bottom) 2D ROESY spectrum. The black arrows show the important structural correlations between backbone protons as illustrated above.

$BocB_6Fc$

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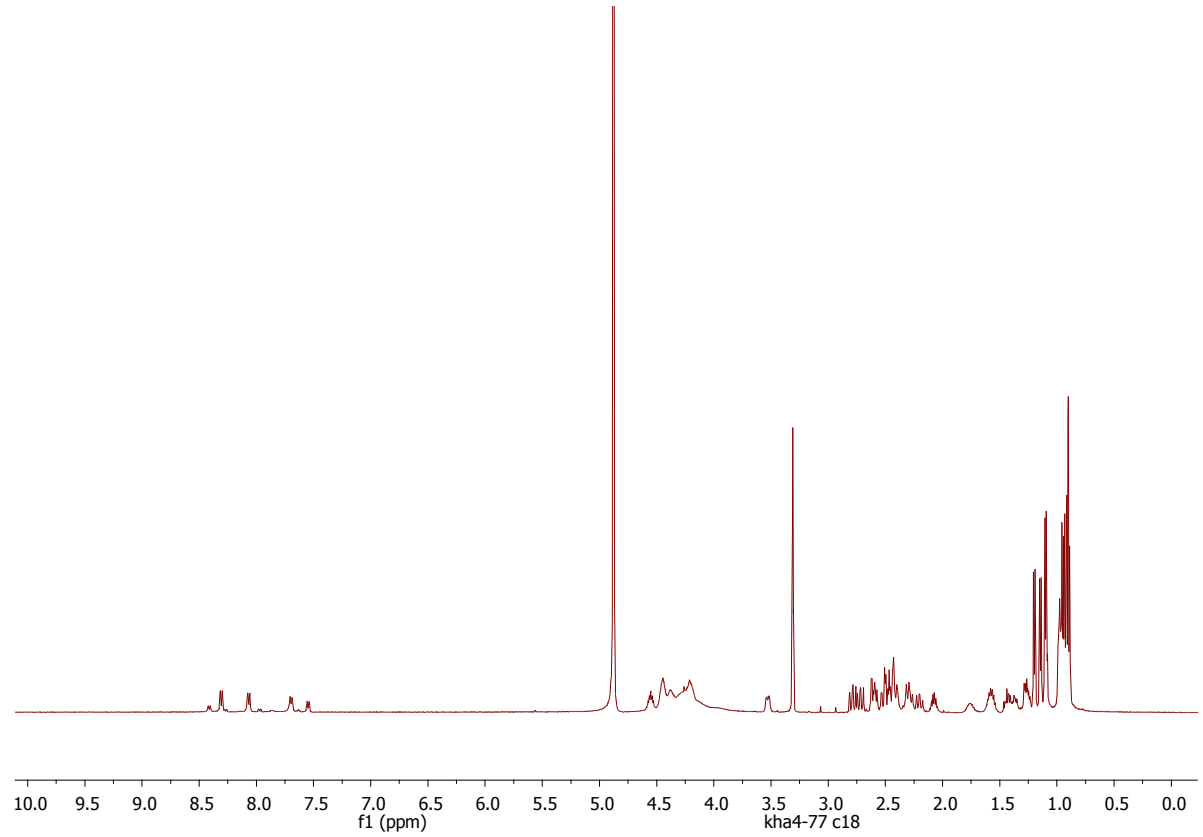
f1 (ppm)
KHA 4-76

B_6Fc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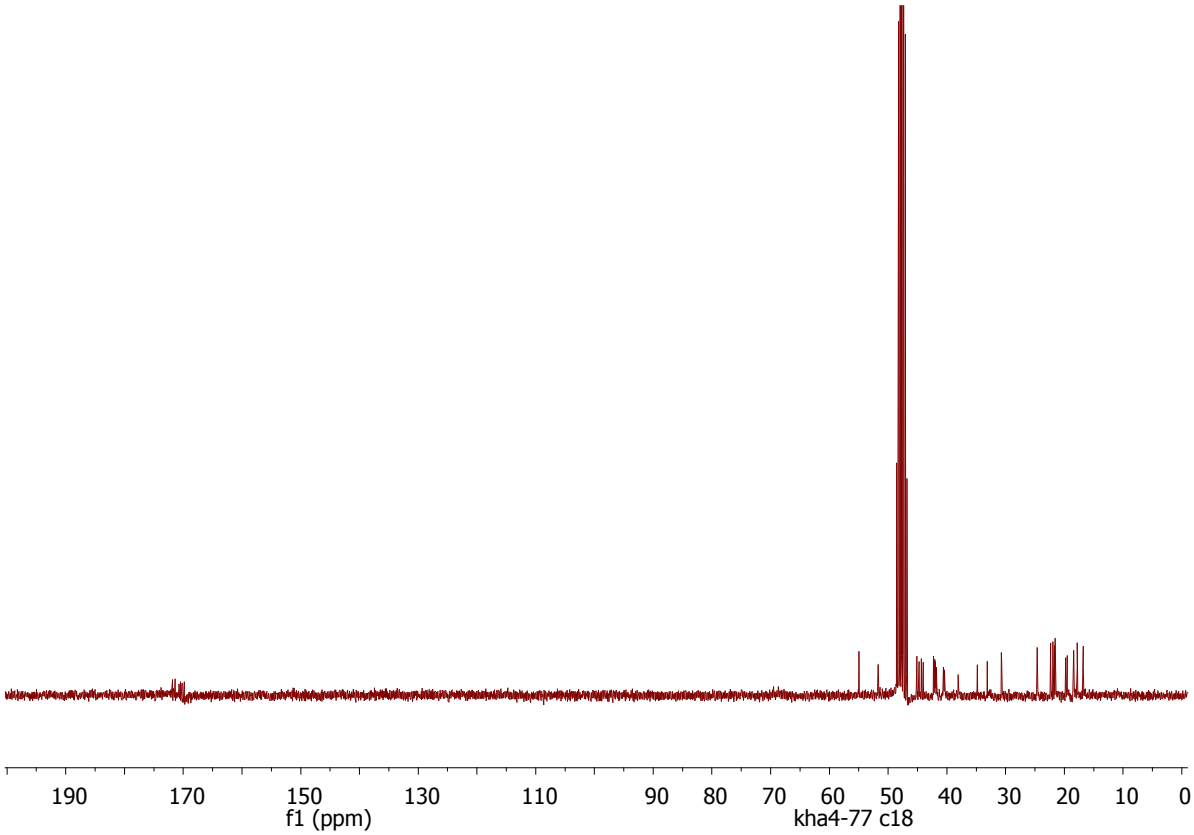
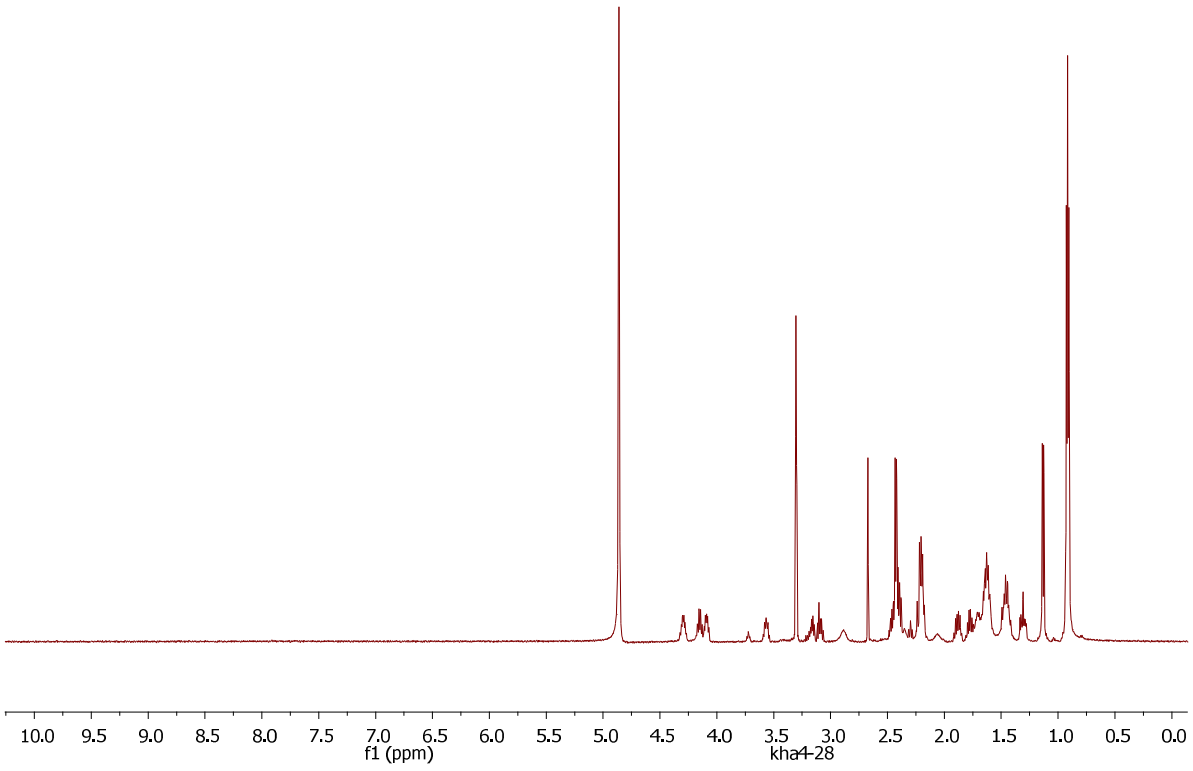
f1 (ppm)
kha4-77 c18


190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
kha4-77 c18

SSB_3OH


10.0
9.5
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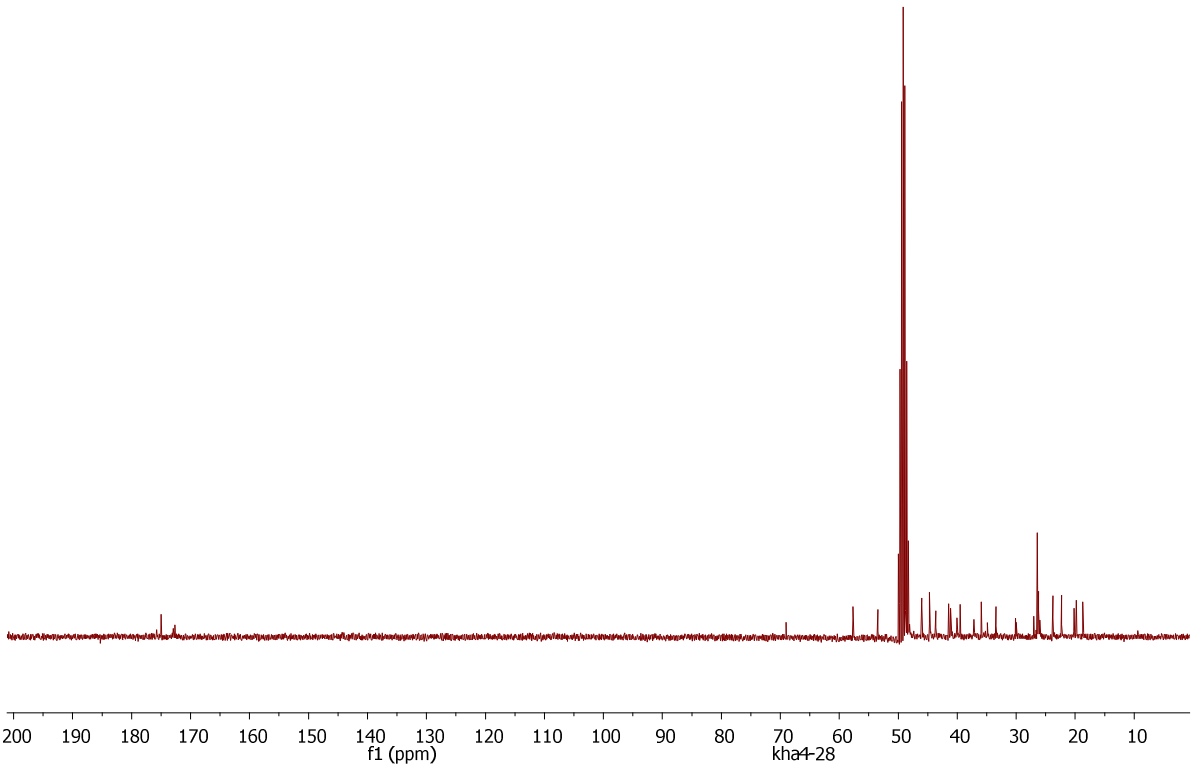
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
kha4-28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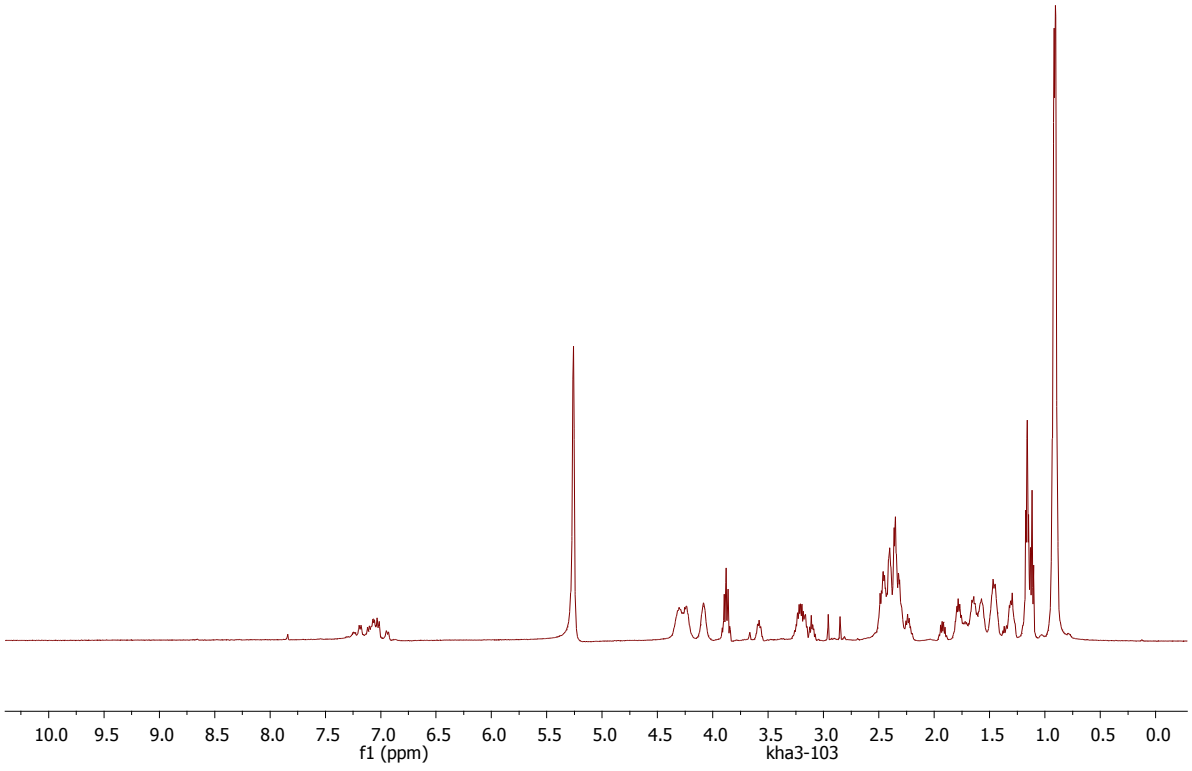
kha4-28

SSB_6Et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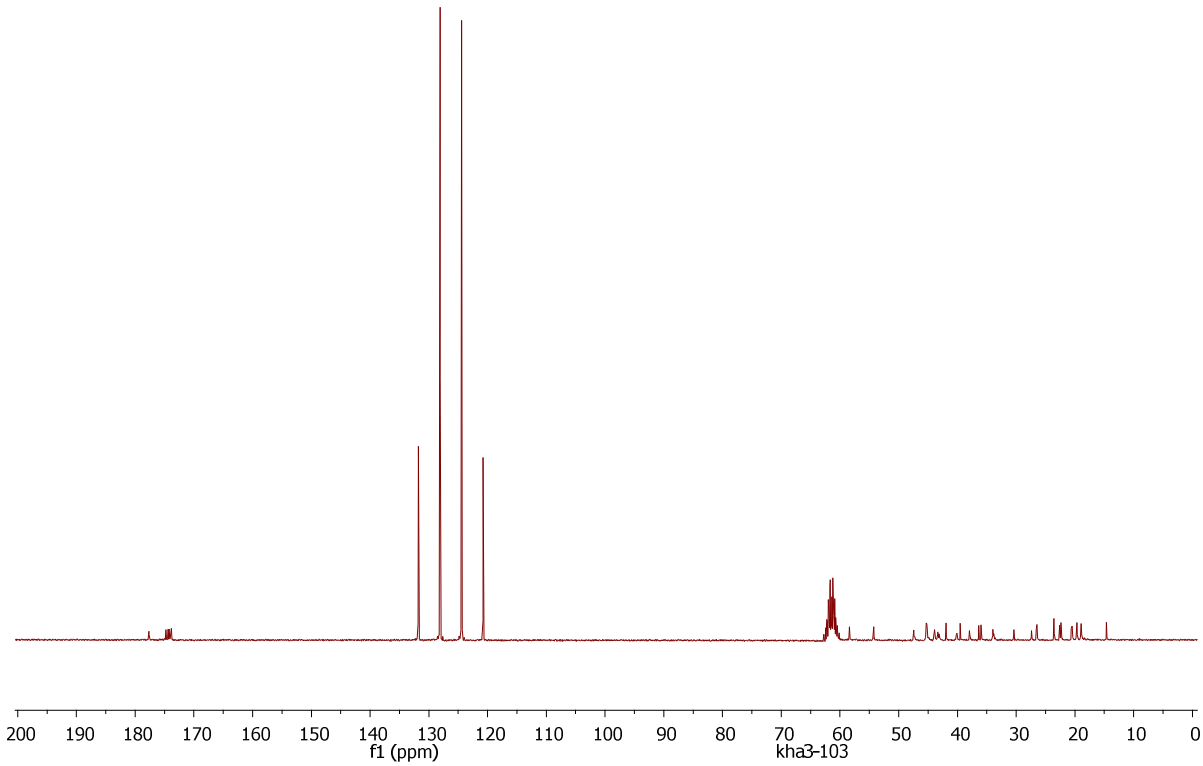
f1 (ppm)
kha3-103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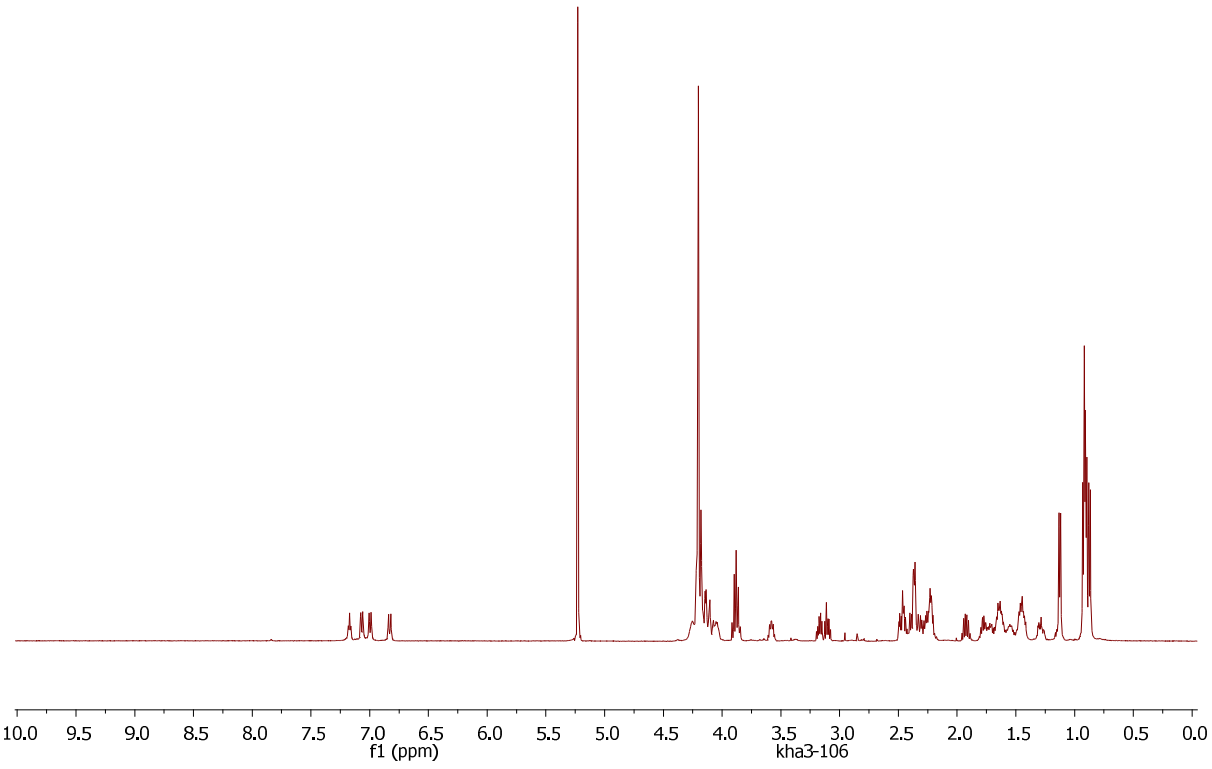
f1 (ppm)
kha3-103

SSB_3Fc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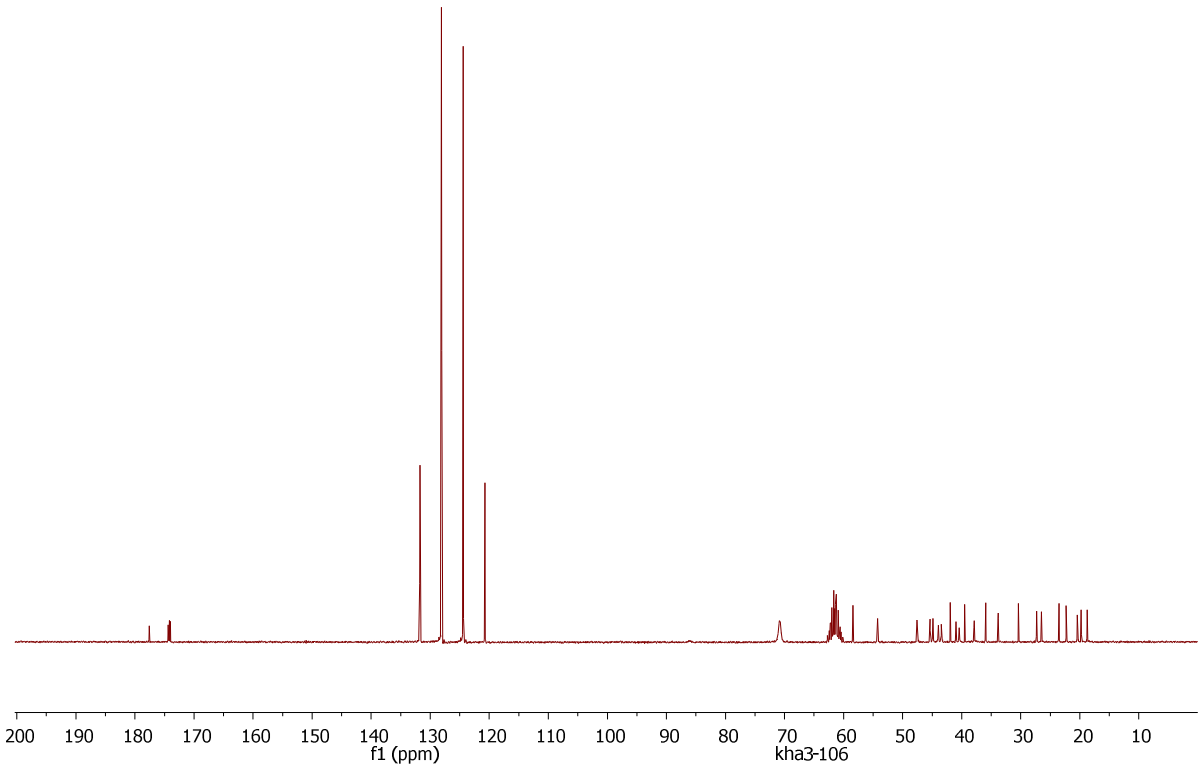
f1 (ppm)
kha3-106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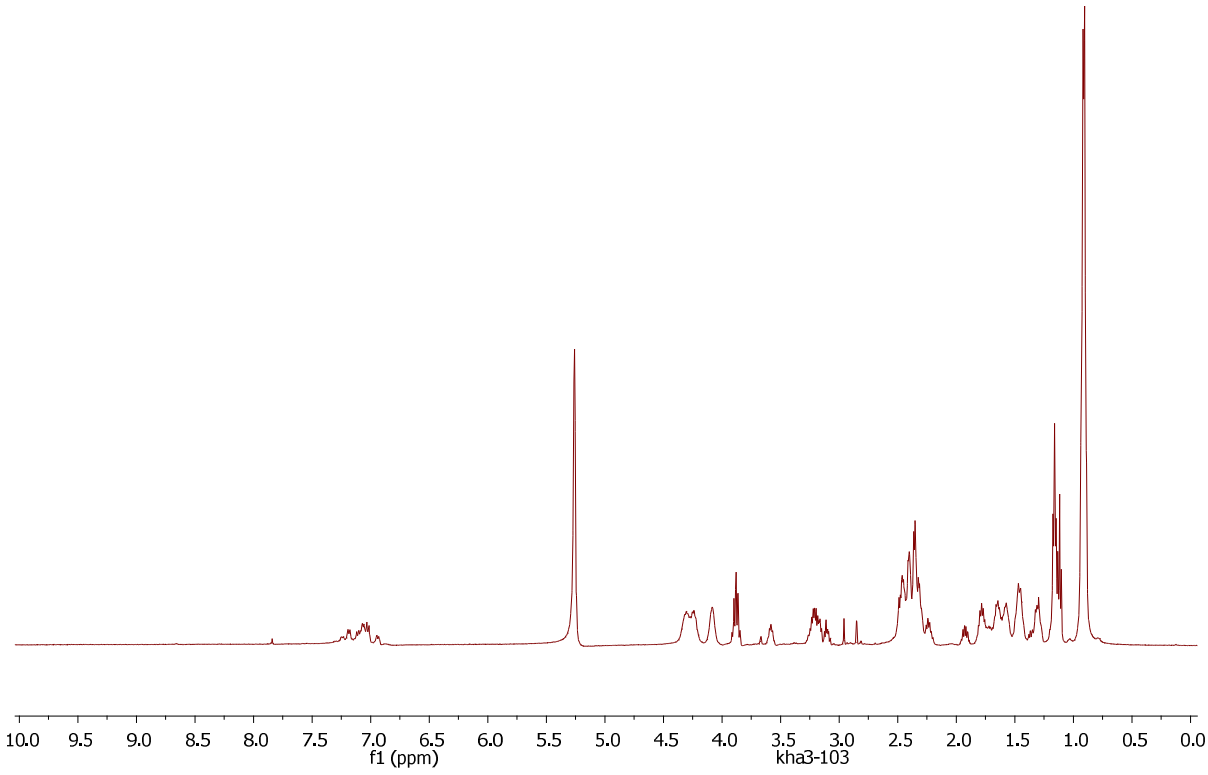
f1 (ppm)
kha3-106

SSB_6Et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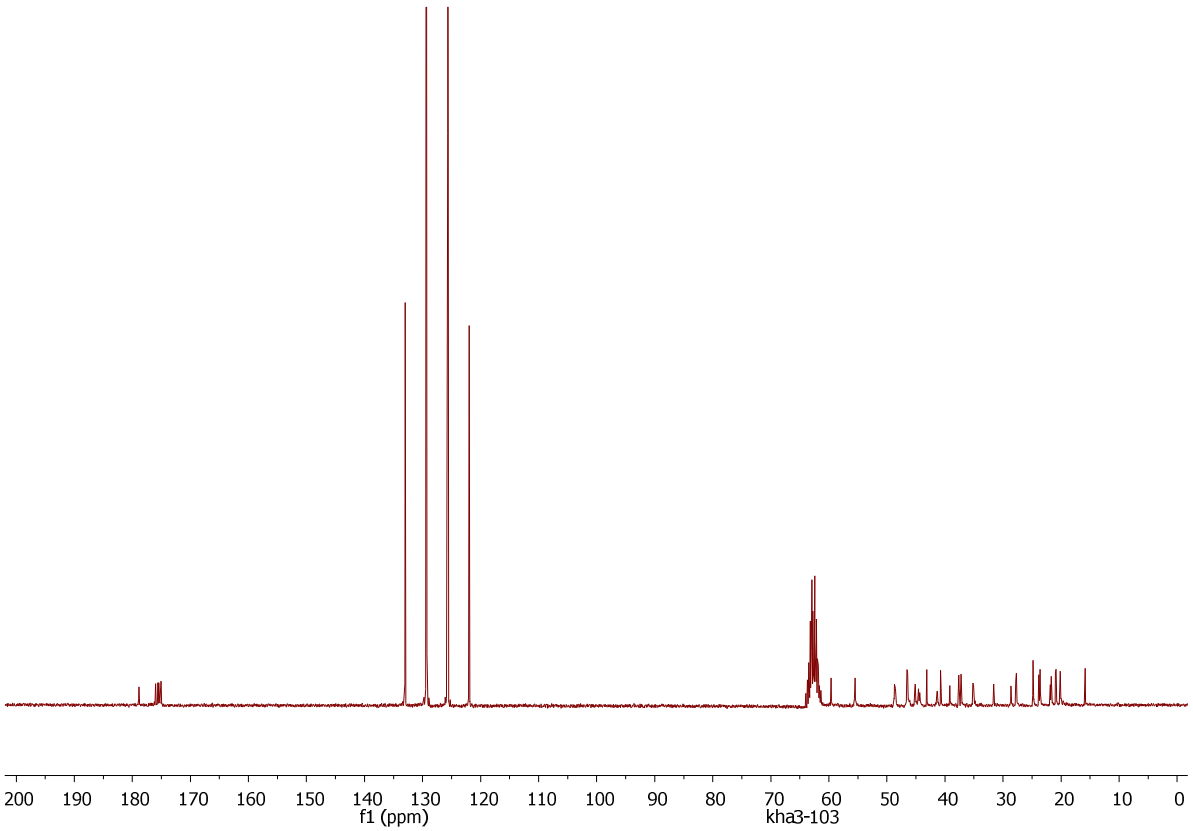
f1 (ppm)
kha3-103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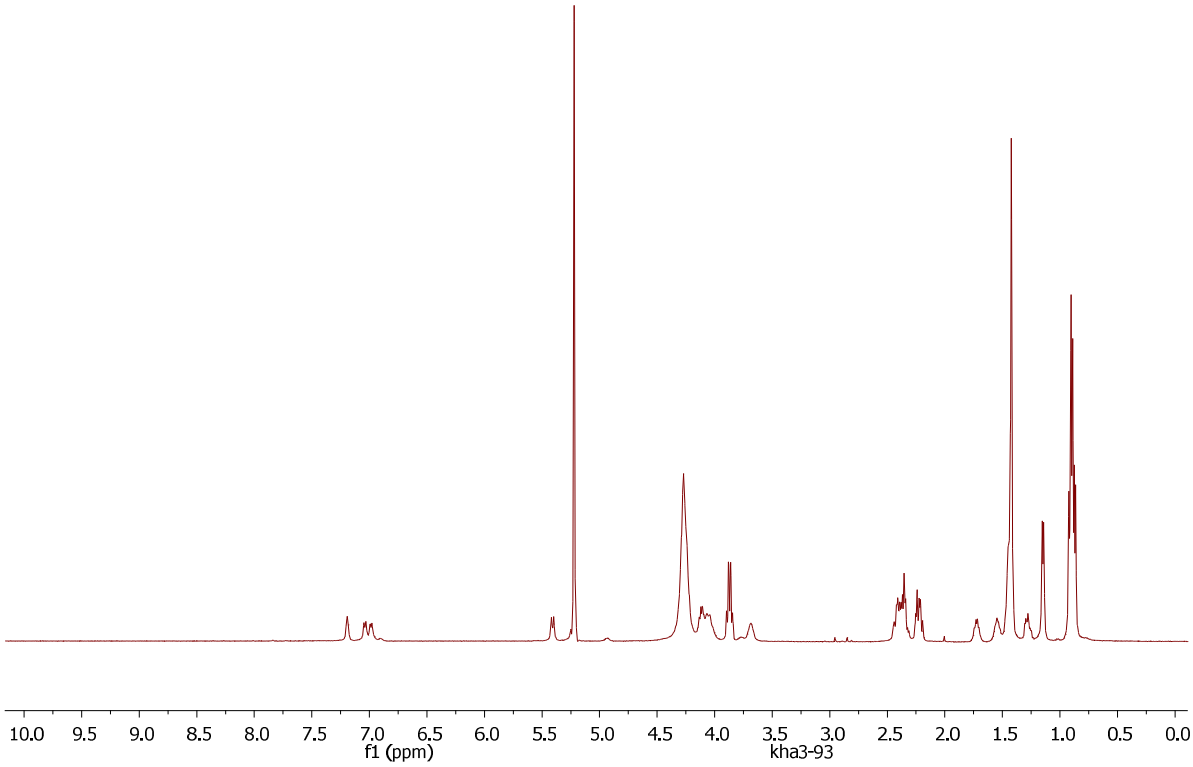
f1 (ppm)
kha3-103

$BocB_3Fc$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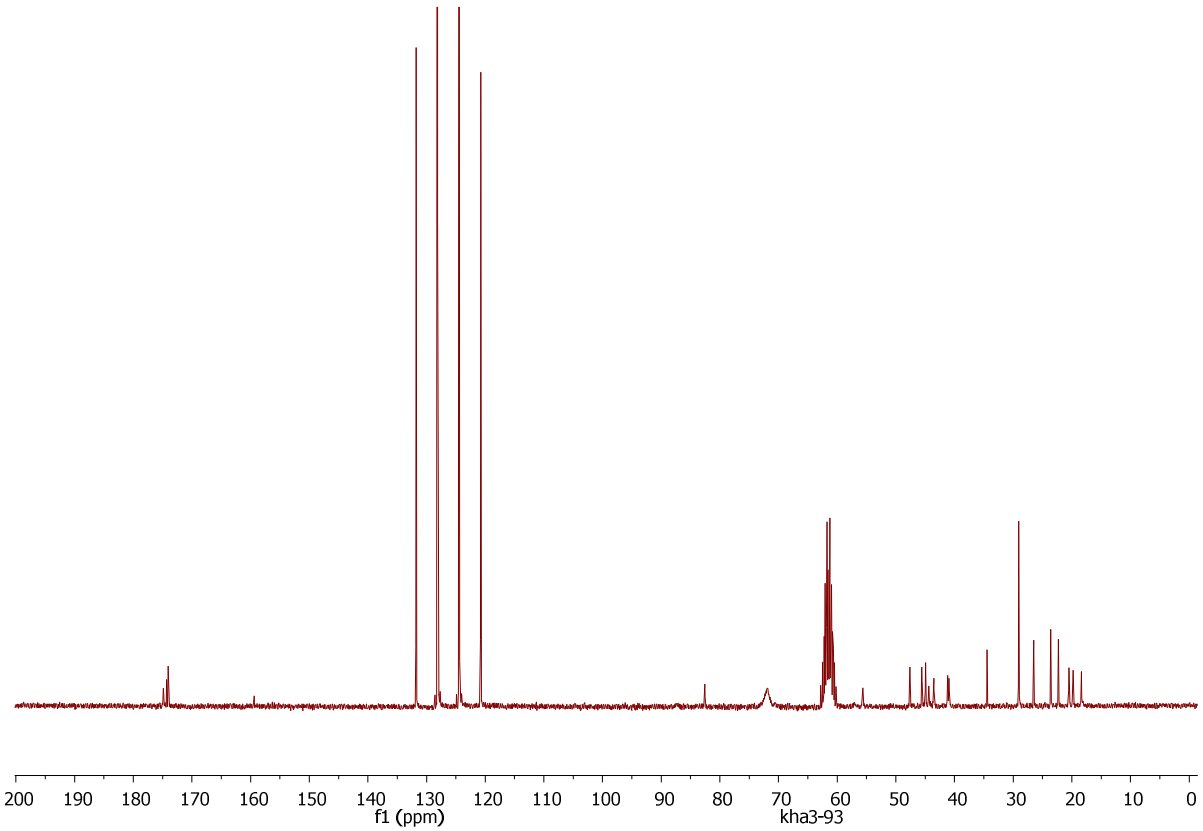
f1 (ppm)
kha3-93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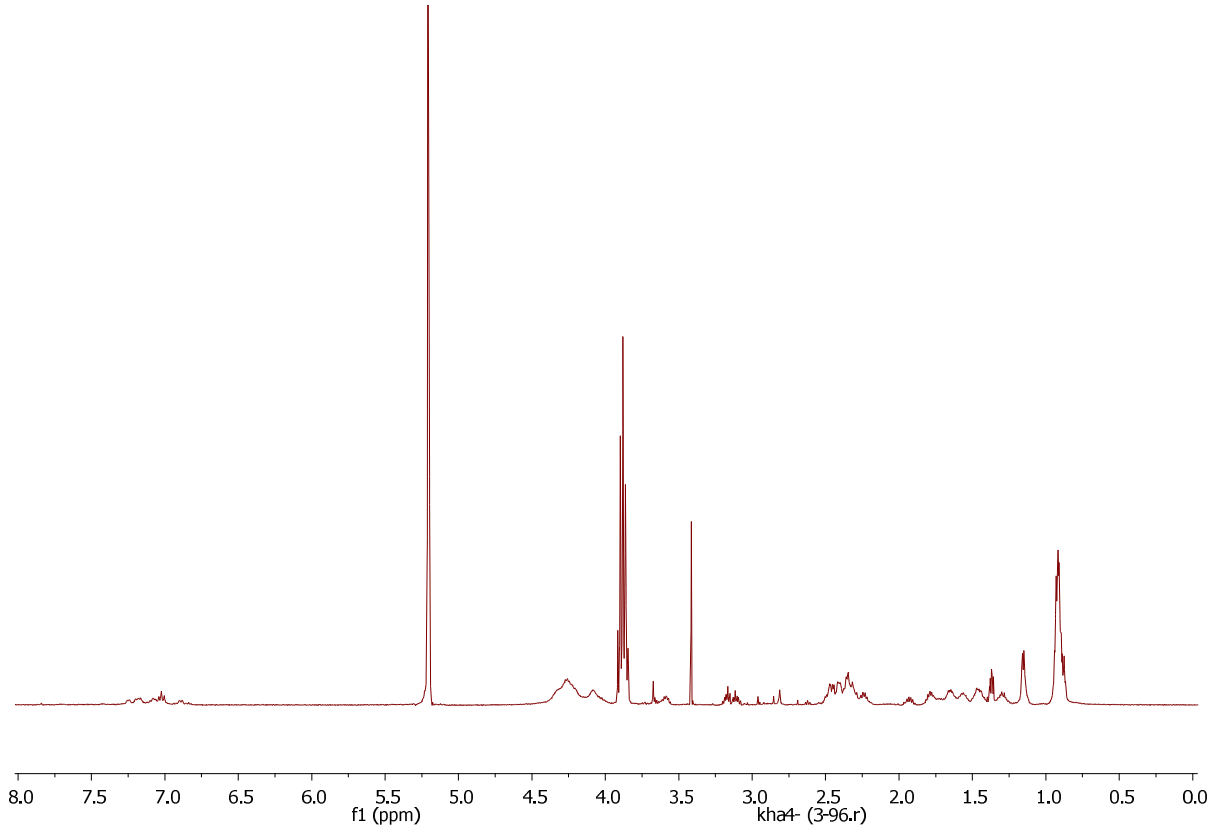
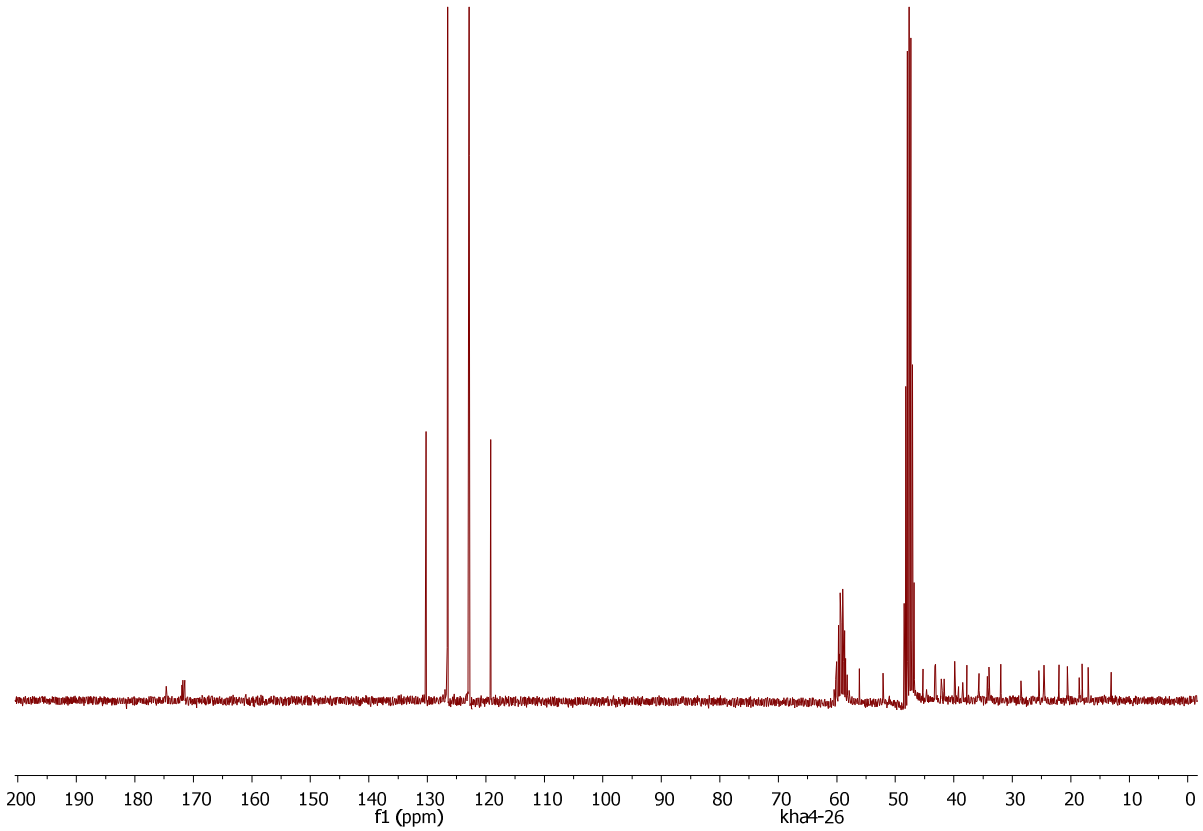
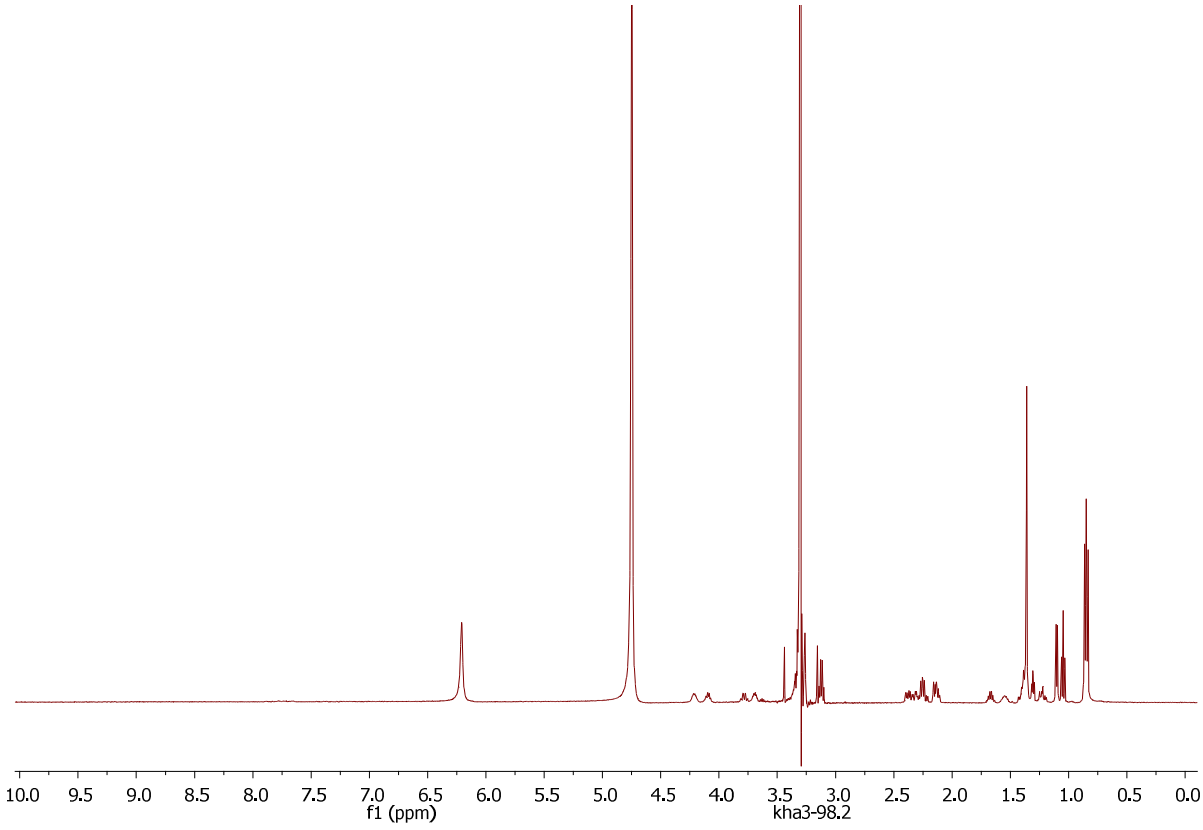
f1 (ppm)
kha3-93

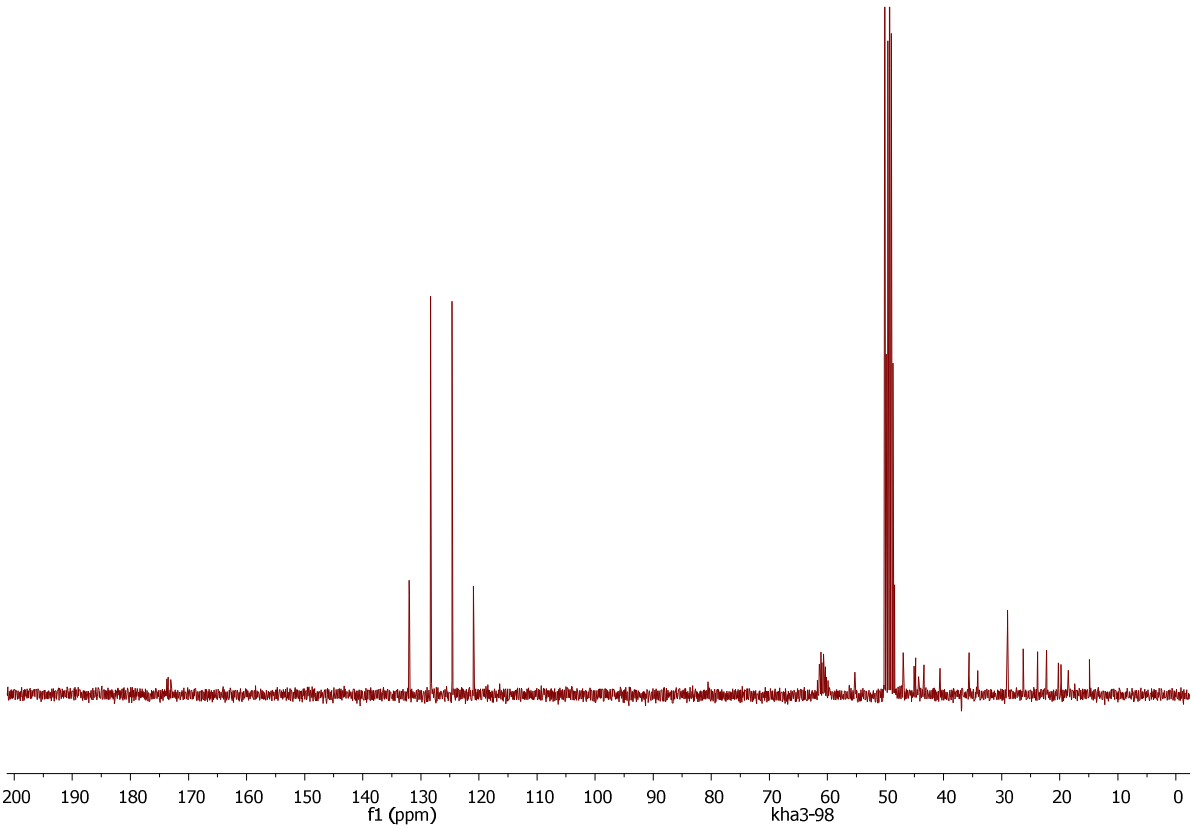
SSB_6Fc


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 0.5 0.0
f1 (ppm)
kha4- (3-96.r)

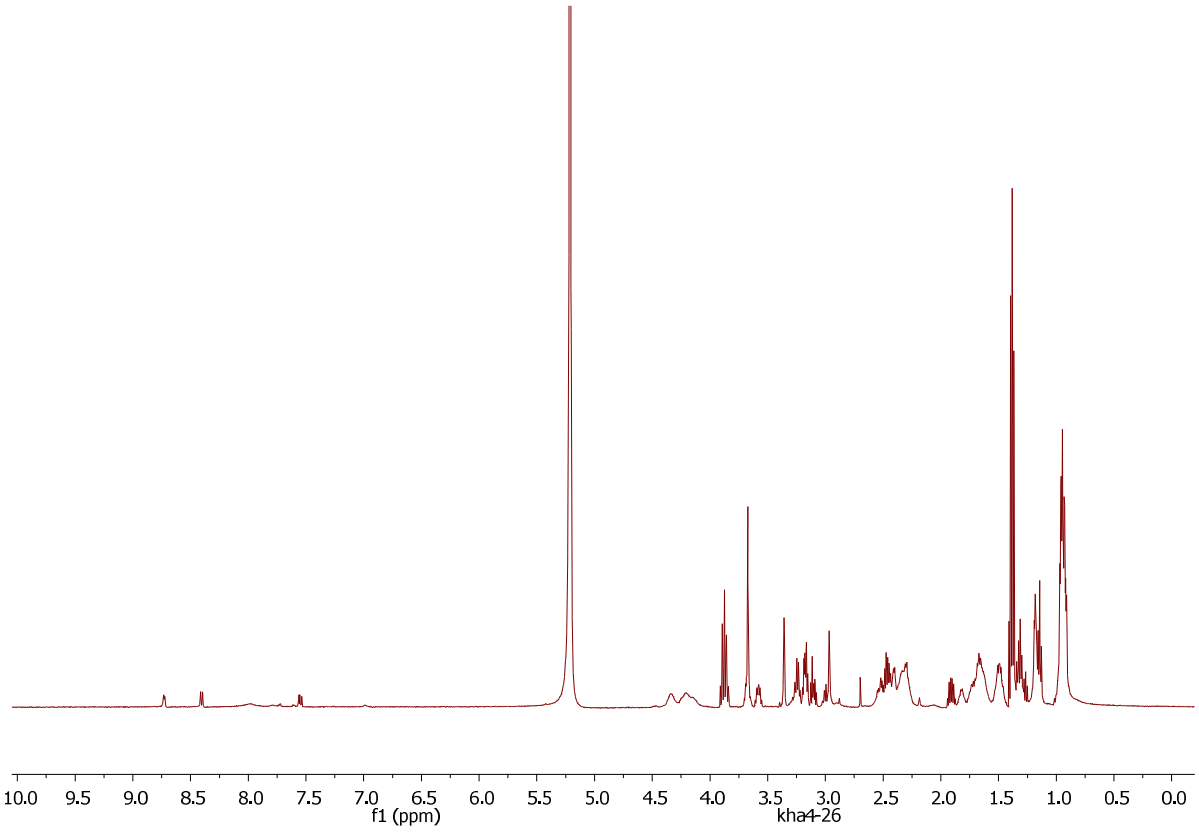

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
kha4-26

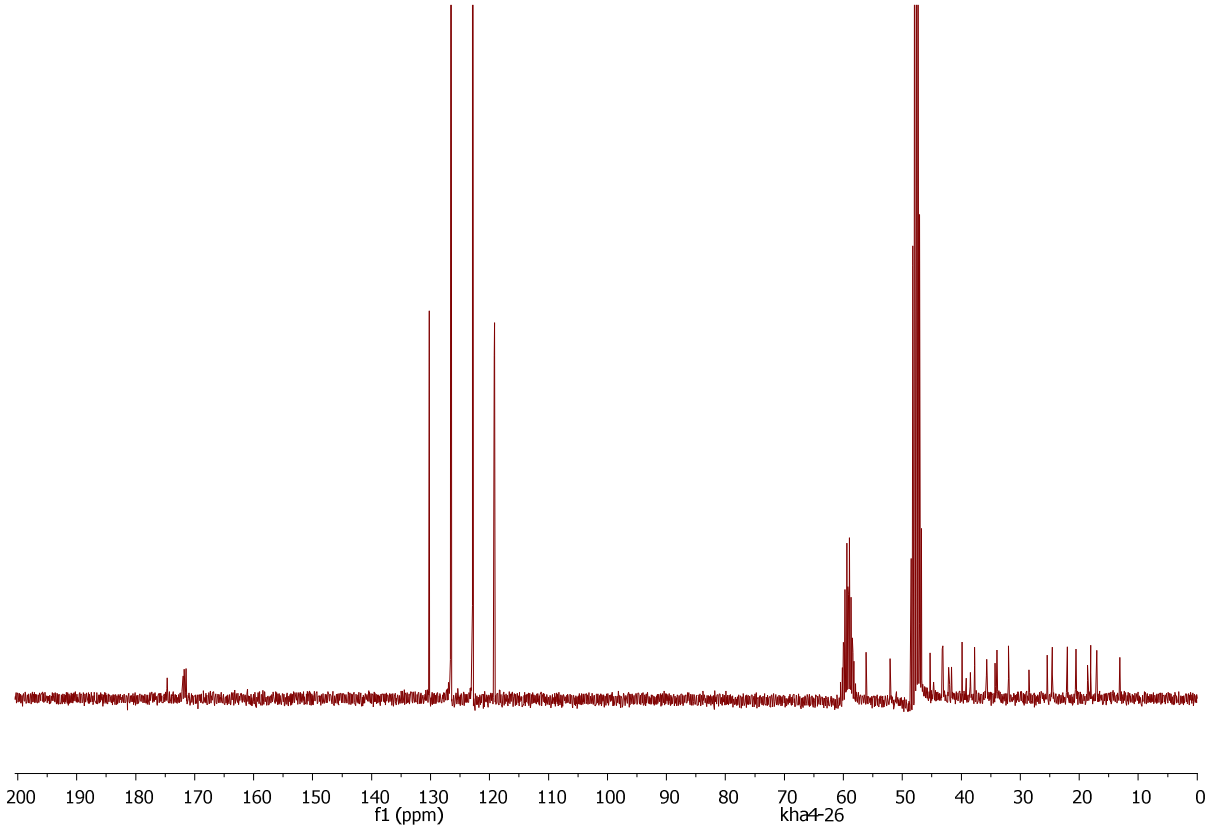
$BocB_3Et$


10.0 9.5 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 0.5 0.0
f1 (ppm)
kha3-98.2


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
kha3-98

SSB_3Et


10.0 9.5 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 0.5 0.0
f1 (ppm)
kha4-26


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
kha4-26

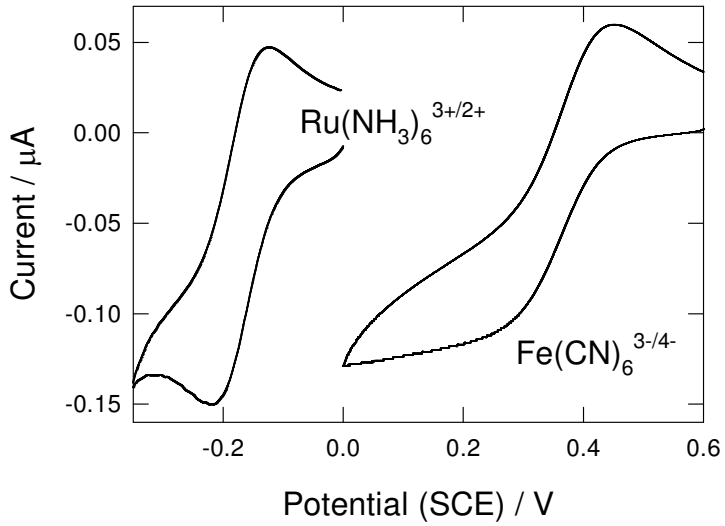

0.05
0.00
-0.05
-0.10
-0.15
Current / µA
Ru(NH3)6 3+/2+
Fe(CN)6 3-/4-
-0.2
0.0
0.2
0.4
0.6
Potential (SCE) / V

Figure S5 The cyclic voltammograms collected at 80 mV s^{-1} of aqueous 11.7 mM $Fe(CN)_6^{3-}$ + 0.1 M $HClO_4$ and 0.38 mM $Ru(NH_3)_6^{3+}$ + 0.1 M $HClO_4$ solutions at **SSB$_6$**. The ferricyanide current was scaled by 0.5.

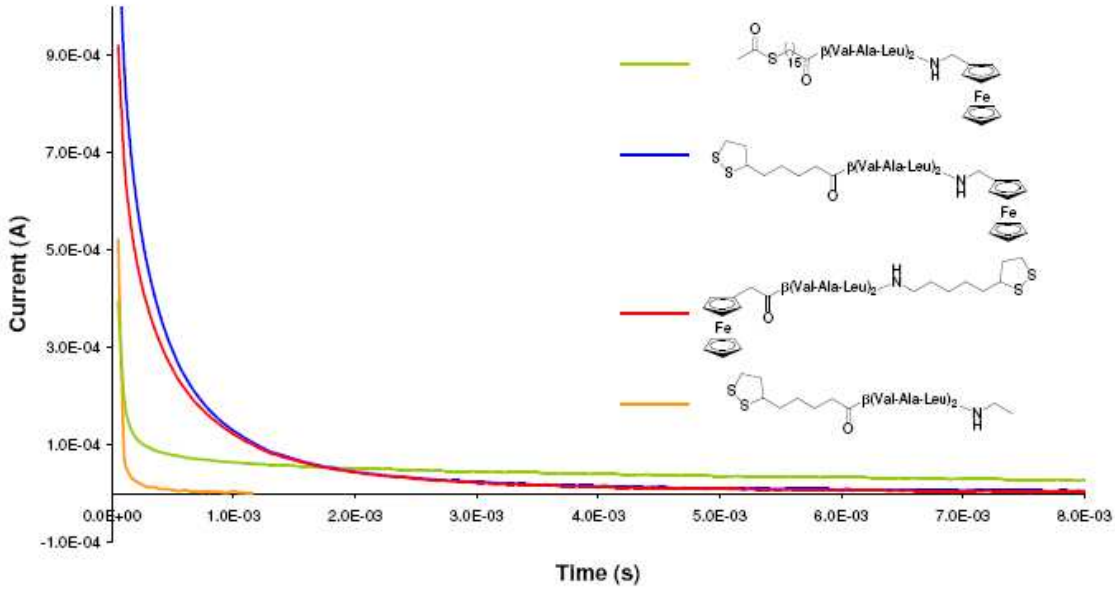


Figure S6 CA graphs of a variety of $\mathbf{B_6}$ analogues, including (blue) $\mathbf{SSB_6Fc}$ and (yellow) $\mathbf{SSB_6}$. Also shown are a reverse dipole (red) $\mathbf{SSB_6Fc}$ and a long chain alkanethiol peptide (green) $\mathbf{SC_{15}B_6Fc}$ not discussed in this article. The overpotential was 0.05 V (SCE) for each trace. The initial potential was 0.1 V for all species, and the step potential that equates to and overpotential = 0.05 V depends on the value of $E_{½}$ for each species.

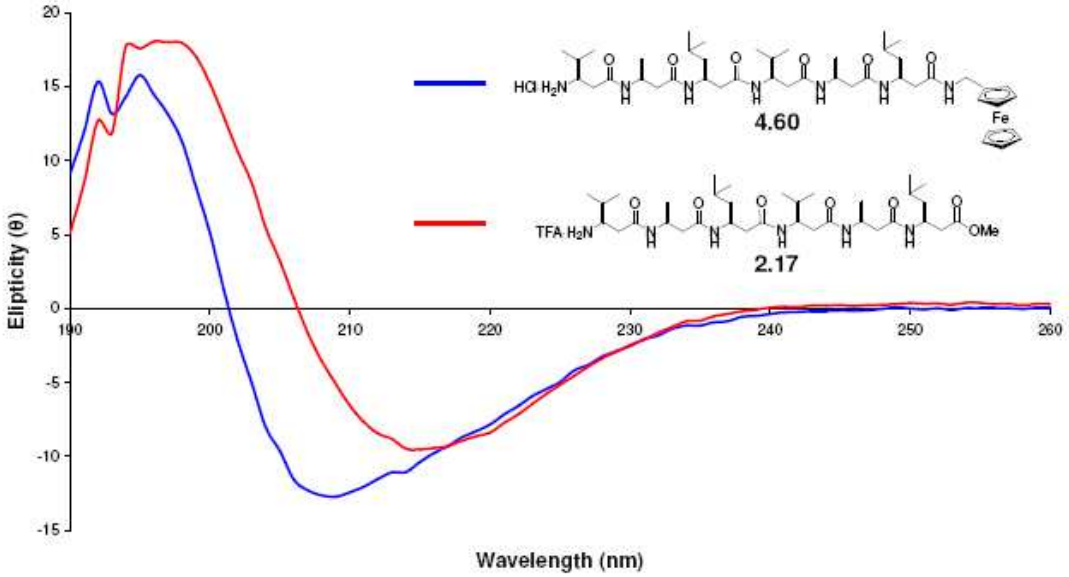


Figure S7 The CD spectra of 0.2 mM **B_6Fc** and **B_6** taken in methanol.