Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Total Synthesis of Teixobactin and Its Stereoisomers

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1. General Methods and Materials

All commercial materials were used as received unless otherwise noted. DCM was dried by distillation over CaH_2. THF and toluene were dried by distillation over sodium/benzophenone. TLC were performed on silica gel Huanghai HSGF254 plates and visualization of the developed chromatogram was performed by fluorescence quenching (λ_{max} = 254 nm). Flash chromatography was performed using Silica gel (200-300 mesh) purchased from Qingdao Haiyang Chemical Co., China.

Fmoc protected amino acids, HATU, DIPEA, CH_3NO_2, NMM were purchased from TCI Chemical. $Pd(PhP_3)_4$, Ph_3SiH, TFA, DIC, Et_3SiH, $Pd(OH)_2$, HCOOH, 6-TAMRA, 2-CTC Resin, H-Ala-2-CTC Resin and PyBop were purchased from *J&K* Chemical. KOtBu, Tf_2O, Alloc-OSu, TEA and AcOH were purchased from Bide Pharmatech Ltd.

^{1}H-NMR spectra were obtained using a Bruker AVANCE AV 400 at frequencies of 400 MHz respectively in $CDCl_3$ or DMSO-d_6. Chemical shifts are reported in parts per million (ppm) and coupling constants in Hertz (Hz). The residual solvent peaks were used as internal standards. ^{1}H-NMR data is reported as follows: chemical shift values (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant and relative integral. ^{13}C-NMR spectra were obtained using a Bruker AVANCE AV 400 at 100 MHz in $CDCl_3$, DMSO-d_6. ^{13}C-NMR data is reported as chemical shift values (ppm).

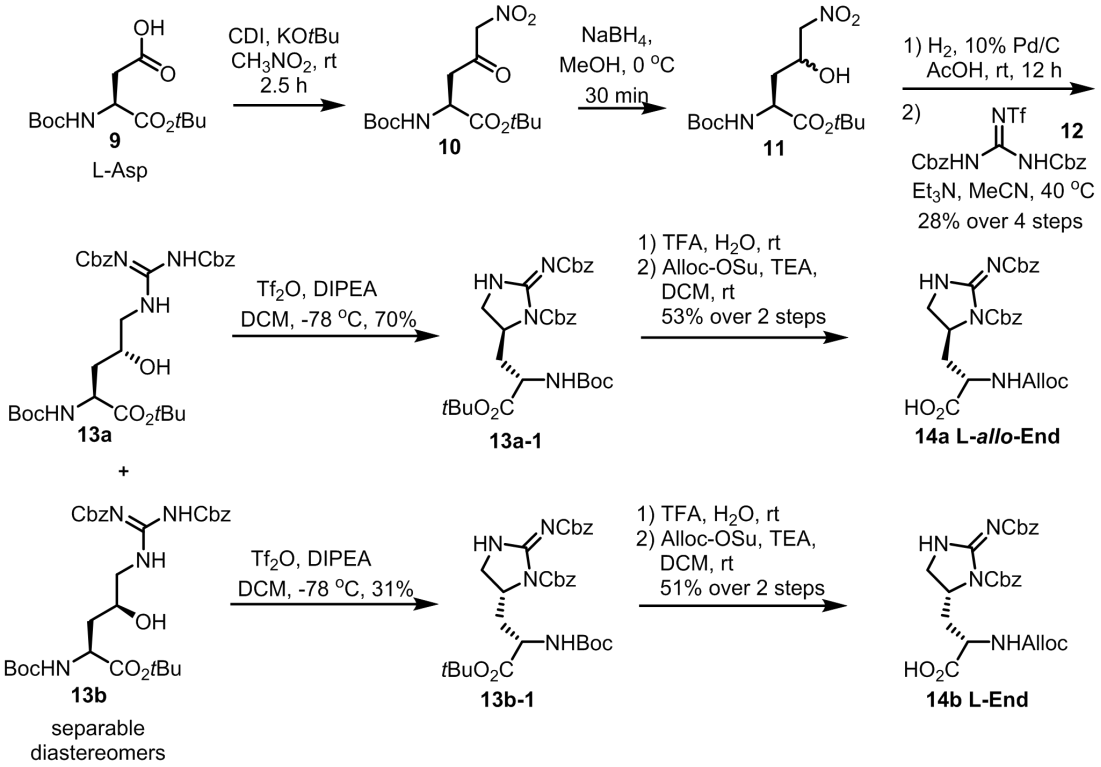
LC-MS was performed on a Thermo Scientific MSQ instrument with the spectrometer operating in positive mode. Separations on the LC-MS system were performed on two methods using a thermo accucore C18 (2.6 μm, 100 x 2.1 mm) column. Method **A**: Linear gradient of 10-90% CH_3CN/H_2O and 0.1% TFA over 40 min was applied at a flow rate of 1.0 mL/min and detection at 220 nm. Method **B**: Linear gradient of 10-90-90-10% CH_3CN/H_2O and 0.1% TFA over 10 min (10-90 vol% MeCN over 6 min, 90-90 vol% over 3 min, 90-10 vol% MeCN over 1min) was applied at a flow rate of 1.0 mL/min and detection at 220 nm. Preparative reverse-phase HPLC was performed using Thermo Scientific Ultimate 3000 equipped

with a Thermo Hypersil Gold (5 μm, 150 x 21.2 mm) column using the following buffer systems: A: 0.1% TFA in water. B: 0.1% TFA in MeCN using a 10-90-90-10 vol% MeCN gradient (10-90 vol% MeCN over 30 min, 90-90 vol% over 10 min, 90-10 vol% MeCN over 10 min) at a flow rate of 8 mL/min.

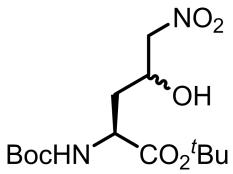
2. Experimental and Analytical Data

2.1 Synthesis of Alloc-L-*allo*-End(Cbz)$_2$-OH/Alloc-L-End(Cbz)$_2$-OH

Alloc-L-*allo*-End(Cbz)$_2$-OH and Alloc-L-End(Cbz)$_2$-OH were synthesized using a modified procedure reported by Payne.[1] All data for known compounds are consistent with those reported in literature.



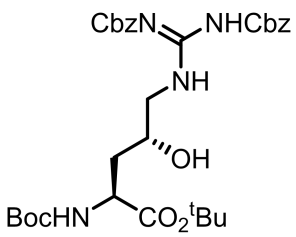
Scheme S1



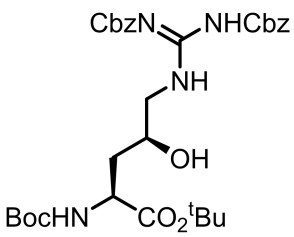
11

Boc-L-Asp-O^{t}Bu **9** (9.00 g, 31.1 mmol) and 1,1'-carbonyldiimidazole (7.56 g, 46.7 mmol) were dried *in vacuo* for 1 h then dissolved in nitromethane (53 mL). The reaction mixture was stirred at 0 ^{o}C for 45 min, then potassium *tert*-butoxide (6.72 g, 62.4 mmol) was slowly added to the reaction mixture. The reaction mixture was stirred at room temperature for an additional 2.5 h, then quenched with 0.5 M/L HCl (150 mL) and extracted with ethyl acetate (3 x 100 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (100 mL), water (100 mL) and brine (100 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated to afford nitro ketone **10** which was used without purification.

Crude nitro ketone **10** was dissolved in MeOH (500 mL) and cooled to 0 ^{o}C. To this solution was slowly added $NaBH_4$[2] (4.71 g, 124.4 mmol), the resulting reaction mixture was stirred at 0 ^{o}C for 30 min. The resulting mixture was concentrated to 30 mL, then poured onto 1 M/L HCl solution (150 mL) and diluted with water (350 mL). The resulting mixture was extracted with ethyl acetate (3 x 200 mL) and the combined organic phases were washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (300 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a yellow oil **11** which was used directly for the next step.



13a



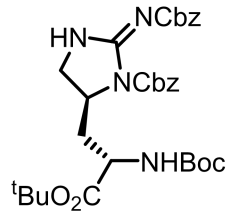
13b

Alcohol **11** was dissolved in anhydrous methanol (50 mL) and to this solution was added 10% w/w palladium on activated carbon (3.31 g, 3.11 mmol palladium),

and glacial acetic acid (1.78 mL, 31.1 mmol). The reaction vessel was filled with an atmosphere of hydrogen and stirred at room temperature for 12 h, then filtered through a pad of celite. The filtrate was concentrated to afford a crude beige foam. The foam was redissolved in MeCN (100 mL). Goodman's reagent **12**[3] (14.28 g, 31.1 mmol) and Et_3N (17.60 mL, 10.4 mmol) was added and the reaction mixture was stirred at 40 °C for 6 h. The mixture was concentrated to 30 mL, then poured onto a saturated aqueous NH_4Cl solution (100 mL). The mixture was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated to give a crude oil which was purified by flash chromatography (*n*-hexanes:EA = 5:1), affording compound **13a** (2.58 g, 14%) and **13b** (2.58 g, 14%) as white solid.

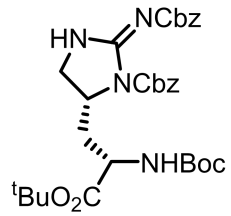
13a: ^{1}**H NMR:** ($CDCl_3$, 400 MHz) δ 11.69 (bs, 1H), 8.70 (t, *J* = 5.4 Hz, 1H), 7.47-7.24 (m, 10H), 5.42 (d, *J* = 7.1 Hz, 1H), 5.18 (s, 2H), 5.10 (s, 2H), 4.58 (s, 1H), 4.21 (d, *J* = 6.5 Hz, 1H), 4.02-3.88 (m, 1H), 3.72-3.57 (m, 1H), 3.40 (ddd, *J* = 13.4, 7.5, 4.9 Hz, 1H), 1.96 (d, *J* = 14.8 Hz, 1H), 1.89-1.77 (m, 1H), 1.43 (s, 18H); ^{13}**C NMR** ($CDCl_3$,100 MHz**)** δ 171.5, 163.2, 157.0, 155.7, 153.6, 136.5, 134.5, 128.8, 128.7, 128.5, 128.4, 128.1, 127.9, 82.2, 80.0, 68.7, 68.3, 67.1, 52.1, 47.2, 37.8, 28.3, 27.9; **HRMS:** (+ESI) Calc. for $C_{31}H_{43}N_4O_9$: 615.3025 $[M+H]^+$, Found: 615.3027 $[M+H]^+$.

13b: ^{1}**H NMR:** ($CDCl_3$, 400 MHz) δ 11.72 (bs, 1H), 8.73 (t, *J* = 5.3 Hz, 1H), 7.50-7.14 (m, 10H), 5.61 (d, *J* = 8.1 Hz, 1H), 5.13 (s, 2H), 5.09 (s, 2H), 4.76 (s, 1H), 4.38 (ddd, *J* = 11.4, 7.9, 3.3 Hz, 1H), 3.93-3.74 (m, 1H), 3.69 (ddd, 1H, *J* = 14.2, 6.6, 3.3 Hz, 1H), 3.27 (ddd, *J* = 13.2, 8.1, 4.0 Hz, 1H), 1.888 (ddd, *J* = 14.0, 10.6, 3.4 Hz, 1H), 1.59-1.52 (m, 1H), 1.43 (s, 9H), 1.41 (s, 9H); ^{13}**C NMR** ($CDCl_3$,100 MHz**)** δ 171.5, 163.4, 156.7, 156.3, 153.5, 136.7, 134.7, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 82.2, 80.2, 68.1, 67.0, 66.4, 51.2, 46.4, 38.7, 28.2, 27.9; **HRMS:** (+ESI) Calc. for $C_{31}H_{43}N_4O_9$: 615.3025 $[M+H]^+$, Found: 615.3028 $[M+H]^+$.



13a-1

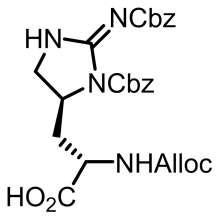
Compound **13a** (2.39 g, 3.89 mmol) was dissolved in anhydrous CH_2Cl_2 (140 mL) and the mixture was cooled to -78 °C. DIPEA (3.24 mL, 18.6 mmol) was added to this solution followed by dropwise addition of Tf_2O (669 µL, 4.66 mmol). The reaction mixture was stirred at -78 °C for 1 h, then warmed to room temperature for 15 min. This mixture poured onto water (150 mL) and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic phases was dried over Na_2SO_4, filtered and concentrated *in vacuo* to give brown oil which was purified by flash chromatography (*n*-hexanes:EA = 2:1), affording Boc-L-*allo*-End(Cbz)$_2$-O^{t}Bu (**13a-1**) (1.63 g, 70%) as a white foam. **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 7.51-7.29 (m, 10H), 5.29 (d, J = 2.5 Hz, 2H), 5.16 (d, J = 2.6 Hz, 2H), 4.55 (s, 1H), 4.15 (q, J = 7.2 Hz, 1H), 3.79 (d, J = 11.5 Hz, 1H), 3.64 (d, J = 9.8 Hz, 1H), 2.38-2.26 (m, 1H), 1.93-1.89 (m, 1H), 1.46 (s, 9H), 1.45 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 171.3, 155.9, 155.5, 153.0, 152.7, 135.1, 134.0, 129.1, 128.8, 128.7, 128.6, 128.54, 128.46, 128.3, 82.4, 80.1, 69.2, 68.5, 67.9, 51.9, 48.0, 37.3, 28.2, 27.8; **HRMS:** (+ESI) Calc. for $C_{31}H_{41}N_4O_8$: 597.2919 $[M+H]^+$, Found: 597.2922 $[M+H]^+$.



13b-1

Compound **13b** (2.39 g, 3.89 mmol) was dissolved in anhydrous CH_2Cl_2 (140 mL) and cooled to -78 °C. DIPEA (3.24 mL, 18.6 mmol) was added to this solution followed by dropwise addition of Tf_2O (669 µL, 4.66 mmol). The reaction mixture was stirred at -78 °C for 1 h, then warmed to room temperature for 15 min. This

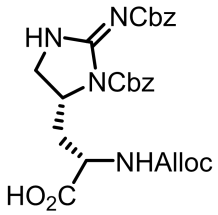
mixture poured onto water (150 mL) and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic phases was dried over Na_2SO_4, filtered and concentrated *in vacuo* to give brown oil which was purified by flash chromatography (*n*-hexanes:EA = 2:1), affording Boc-L-*allo*-End(Cbz)$_2$-O^{t}Bu (**13b-1**) (0.79 g, 31%) as a white foam. **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 7.48-7.27 (m, 10H), 5.27 (d, J = 2.9 Hz, 2H), 5.15 (d, J = 7.3 Hz, 2H), 4.43-4.31 (m, 1H), 4.14(td, J = 10.8, 7.2, 4.2 Hz, 1H), 3.88-3.77 (m, 1H), 3.58 (d, J = 11.4 Hz, 1H), 1.97 (dt, J = 10, 4.5 Hz, 2H), 1.44 (s, 9H), 1.42 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 170.6, 155.8, 150.8, 136.5, 135.1, 128.7, 128.6, 128.4, 128.3, 128.1, 127.9, 82.9, 80.2, 68.4, 67.4, 53.7, 50.6, 36.9, 28.2, 27.9; **HRMS:** (+ESI) Calc. for $C_{31}H_{41}N_4O_8$: 597.2919 $[M+H]^+$, Found: 597.2923 $[M+H]^+$.



14a L-*allo*-End$_{10}$

Boc-L-*allo*-End(Cbz)$_2$-O^{t}Bu (**13a-1)** (597 mg, 1 mmol) was dissolved in a mixture of TFA (10 mL) and water (1.0 mL). The mixture was stirred at room temperature for 3 h, then concentrated to give a brown oil. The resulting crude oil was azeotroped with toluene (3 x 10 mL) and concentrated *in vacuo* to remove any residual TFA. The concentrated crude material was then dissolved in a mixture of DCM (4 mL) and DIPEA (0.87 mL, 5 mmol), Alloc-OSu (299 mg, 1.5 mmol) was added to this mixture and the reaction mixture was stirred at room temperature for 3 h. The mixture was concentrated to give a crude white foam which was purified by flash chromatography (DCM:MeOH = 10:1) to afford Alloc-L-*allo*-End(Cbz)$_2$-OH **14a** (278 mg, 530 mmol, 53%) as a white foam. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.53 – 7.14 (m, 11H), 5.94-5.83 (m,2H), 5.36-5.01 (m, 6H), 4.63 (s, 1H), 4.50 (d, J = 5.5 Hz, 2H), 4.11 (t, J = 6.3 Hz, 1H), 3.74-3.60 (m, 2H), 2.36 (t, J = 7.1 Hz, 1H), 2.05 (dd, J = 16.8, 8.7 Hz, 1H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 173.8, 163.4, 156.4, 155.8, 153.6, 136.5, 134.5, 132.3, 128.8, 128.7, 128.6, 128.5, 128.2, 128.1, 118.2, 68.4, 67.3, 66.2,

51.3, 44.1, 32.8; **HRMS:** (+ESI) Calc. for $C_{26}H_{28}N_4O_8$: 525.1980 $[M+H]^+$, Found: 525.1984 $[M+H]^+$.

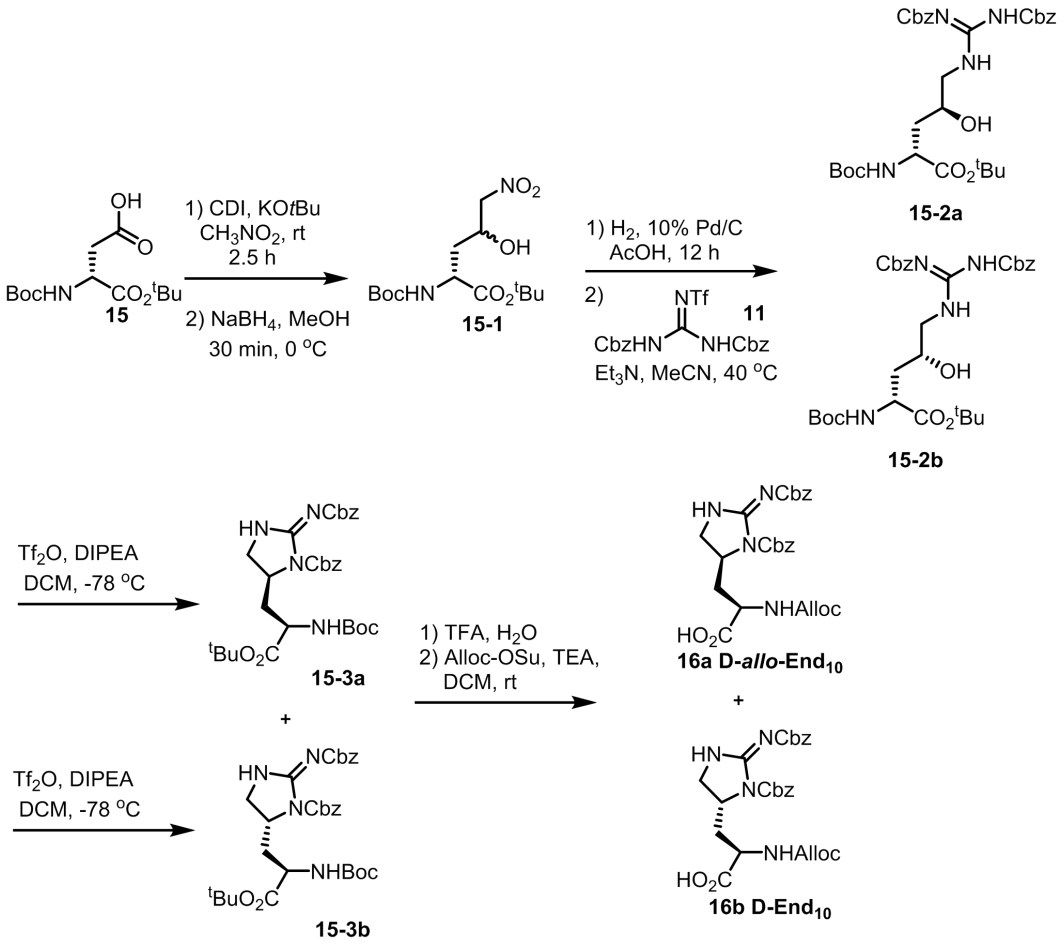


14b L-End$_{10}$

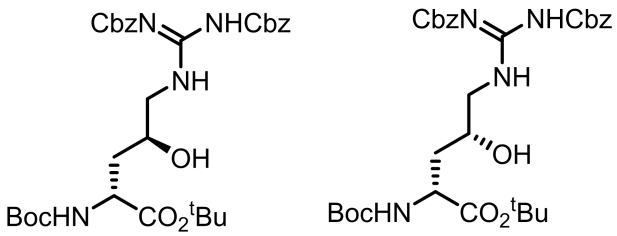
Boc-L-End(Cbz)$_2$-O^{t}Bu (**13b-1)** (597 mg, 1 mmol) was dissolved in a mixture of TFA (10 mL) and water (1.0 mL). The mixture was stirred at room temperature for 3 h, then concentrated to give brown oil. The resulting crude oil was azeotroped with toluene (3 x 10 mL) and concentrated *in vacuo* to remove any residual TFA. The concentrated crude material was then dissolved in a mixture of DCM (4 mL) and DIPEA (0.87 mL, 5 mmol). Alloc-OSu (299 mg, 1.5 mmol) was added to this mixture and the reaction was stirred at room temperature for 3 h. This mixture was concentrated *in vacuo* to give a crude white foam that was purified by flash chromatography (DCM:MeOH = 10:1) to afford Alloc-L-End(Cbz)$_2$-OH **14b** (278 mg, 530 mmol, 51%) as a white foam. ^{1}**H NMR** ($CDCl_3$, 400 MHz) δ 11.71 (s, 1H), 8.73 (d, *J* = 5.5 Hz, 1H), 7.45 – 7.24 (m, 10H), 5.96-5.87 (m, 1H), 5.34 – 5.05 (m, 6H), 4.54 (d, *J* = 5.6 Hz, 2H), 4.23 (d, *J* = 6.2 Hz, 1H), 3.96 (dt, *J* = 8.2, 4.1 Hz, 1H), 3.65 (m, 1H), 3.38 (t, *J* = 10.0 Hz, 1H), 2.08 – 1.87 (m, 2H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 176.2, 163.6, 156.3, 155.9, 153.5, 136.8, 134.8 133.1, 128.68, 128.63, 128.5, 128.4, 128.1, 127.8, 117.4, 68.0, 67.5, 67.1, 65.4, 53.1, 46.7, 38.0; **HRMS:** (+ESI) Calc. for $C_{26}H_{29}N_4O_8$: 525.1980 $[M+H]^+$, Found: 525.1983 $[M+H]^+$.

2.2 Synthesis of Alloc-D-*allo*-End(Cbz)$_2$-OH/Alloc-D-End(Cbz)$_2$-OH

Alloc-D-End(Cbz)$_2$-OH **16a** and Alloc-D-*allo*-End(Cbz)$_2$-OH **16b** were synthesized following the same procedure as Alloc-L-End(Cbz)$_2$-OH **14b** and Alloc-L-*allo*-End(Cbz)$_2$-OH **14a**.



Scheme S2

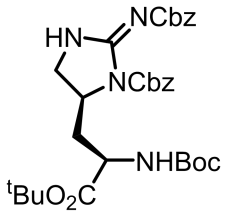


15-2a **15-2b**

15-2a: ^{1}**H NMR:** ($CDCl_3$, 400 MHz) δ 11.72 (bs, 1H), 8.74 (t, 1H, *J* = 5.0 Hz), 7.37-7.23 (m, 10H), 5.55 (d, 1H, *J* = 7.9 Hz), 5.14 (s, 2H), 5.10 (s, 2H), 4.80 (s, 1H), 4.38 (m, 1H), 3.79 (s, 1H,), 3.71 (dd, 1H, *J* = 14.6, 6.6, 14.6, 6.3 Hz, 1H), 3.27 (ddd, 1H, *J* = 13.2, 8.1, 3.9 Hz), 1.91-1.84 (m, 1H), 1.57-1.50 (m, 1H), 1.43 (s, 9H), 1.42 (s, 9H); ^{13}**C NMR** ($CDCl_3$,100 MHz**)** δ 171.5, 163.5, 156.8, 156.3, 153.5, 136.7, 134.7, 128.74, 128.65, 128.5, 128.4, 128.1, 127.9, 82.4, 80.4, 68.1, 67.1, 66.3, 51.1, 46.4,

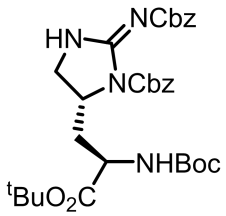
38.9, 28.3, 28.0; **HRMS:** (+ESI) Calc. for $C_{31}H_{43}N_4O_9$: 615.3025 $[M+H]^+$, Found: 615.3029 $[M+H]^+$;

15-2b: **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 9.34 (ddt, 1H, *J* = 6.8, 12.2 Hz), 7.41-7.25 (m, 10H), 5.61 (s, 1H), 5.19 (s, 2H), 5.14 (s, 2H), 4.21 (s, 1H), 4.01 (d, *J* = 7.1 Hz, 1H), 3.72 (d, *J* = 13.9 Hz, 1H), 3.52 (dd, 1H, *J* = 14.2, 7.4 Hz), 1.99-1.94 (m, 1H), 1.90-1.82 (m, 1H), 1.42 (s, 9H), 1.41 (s, 9H); **^{13}C NMR** ($CDCl_3$,100 MHz**)** δ 171.5, 163.2, 157.0, 155.8, 153.6, 136.5, 134.5, 128.8, 128.7, 128.5, 128.4, 128.1, 128.0, 82.3, 80.0, 68.7, 68.3, 67.1, 52.1, 47.2, 37.8, 28.3, 27.9; **HRMS:** (+ESI) Calc. for $C_{31}H_{43}N_4O_9$: 615.3025 $[M+H]^+$, Found: 615.3027 $[M+H]^+$.



15-3a

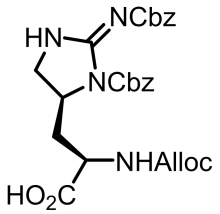
^{1}H NMR: ($CDCl_3$, 400 MHz) δ 8.66(s, 1H), 7.62-7.22 (m, 10H), 5.28 (s, 2H), 5.15 (d, *J* = 7.6 Hz, 2H), 4.37 (s, 1H), 4.15(q, *J* = 8.3 Hz, 1H), 3.80 (s, 1H), 3.56 (s, 1H), 1.98 (s, 2H), 1.44 (s, 9H), 1.42 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 170.6, 155.8, 150.8, 136.5, 135.1, 128.7, 128.6, 128.4, 128.3, 128.1, 127.9, 82.9, 80.1, 68.5, 68.4, 67.4, 53.7, 50.6, 36.9, 28.3, 27.9; **HRMS:** (+ESI) Calc. for $C_{31}H_{41}N_4O_8$: 597.2919 $[M+H]^+$, Found: 597.2923 $[M+H]^+$.



15-3b

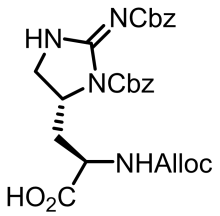
^{1}H NMR: ($CDCl_3$, 400 MHz) δ 7.49-7.24 (m, 10H), 5.27 (d, *J* = 2.8 Hz, 2H), 5.15 (d, *J* = 2.5 Hz, 2H), 4.53 (s, 1H), 4.13 (q, *J* = 7.2 Hz, 1H), 3.80 (d, *J* = 9.9 Hz, 1H), 3.63 (d, *J* = 11 Hz, 1H), 2.32-2.22 (m, 1H), 1.93-1.85 (m, 1H), 1.44 (s, 9H), 1.43 (s,

9H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 175.0, 163.4, 156.0, 155.9, 153.1, 137.2, 135.5, 133.8, 129.03, 128.99, 128.9, 128.8, 1.5, 128.3, 117.7, 75.1, 68.2, 66.9, 65.2, 59.9, 44.3, 31.5; **HRMS:** (+ESI) Calc. for $C_{31}H_{41}N_4O_8$: 597.2919 $[M+H]^+$, Found: 597.2922 $[M+H]^+$.



16a D-*allo*-End$_{10}$

^{1}H NMR (DMSO-d_6, 400 MHz) δ δ 11.60 (s, 1H), 8.61 (t, J = 5.8 Hz, 1H), 7.77 (d, J = 8.5 Hz, 1H), 7.52 – 7.26 (m, 10H), 5.91 (ddt, J = 17.4, 10.6, 5.4 Hz, 1H), 5.35 – 5.14 (m, 4H), 5.05 (s, 2H), 4.64 (dt, J = 8.0, 3.9 Hz, 1H), 4.59 – 4.43 (m, 3H), 3.74 – 3.52 (m, 2H), 2.45 (ddd, J = 12.0, 9.0, 5.7 Hz, 1H), 1.91 (q, J = 11.5 Hz, 1H); **^{13}C NMR** (DMSO-d_6, 100 MHz**)** δ 173.8, 1623.4, 156.4, 155.7, 153.6, 136.5, 134.5, 132.3, 128.8, 128.7, 128.6, 128.5, 128.2, 128.1, 118.2, 68.4, 67.3, 66.2, 51.3, 44.1, 32.8; **HRMS:** (+ESI) Calc. for $C_{26}H_{29}N_4O_8$: 525.1980 $[M+H]^+$, Found: 525.1983 $[M+H]^+$.

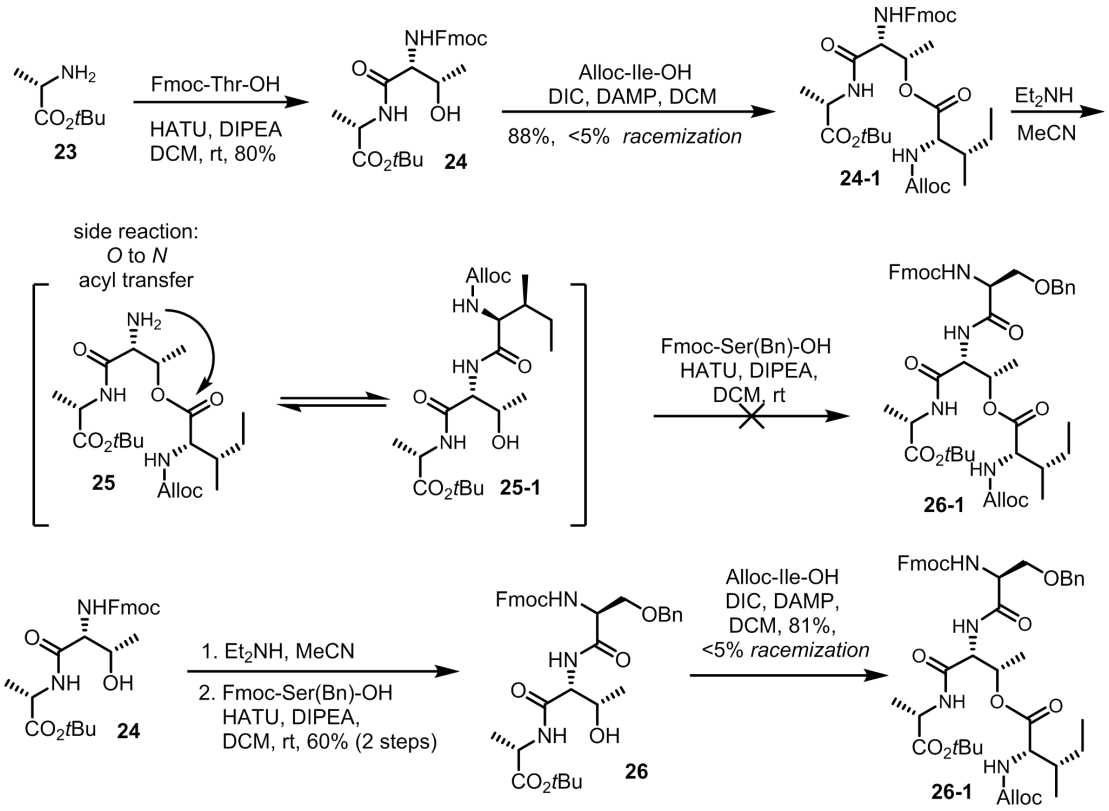


16b D-End$_{10}$

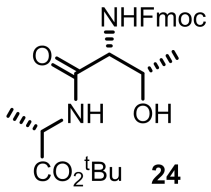
^{1}H NMR (DMSO-d_6, 400 MHz) δ δ 11.62 (s, 1H), 8.54 (t, J = 5.5 Hz, 1H), 7.54 – 7.27 (m, 10H), 5.90 (ddt, J = 16.2, 10.5, 5.3 Hz, 1H), 5.36 – 5.13 (m, 4H), 5.04 (s, 2H), 4.46 (d, J = 5.3 Hz, 2H), 4.12 (td, J = 8.8, 4.1 Hz, 1H), 3.67 (d, J = 8.6 Hz, 1H), 3.41 (dt, J = 13.5, 5.3 Hz, 1H), 3.25 (dt, J = 13.0, 6.1 Hz, 1H), 1.69 (dt, J = 10.6, 5.2 Hz, 2H); **^{13}C NMR** (DMSO-d_6, 100 MHz**)** δ 175.0, 163.5, 156.4, 155.8, 153.3, 137.3, 135.6, 134.1, 129.03, 128.98, 128.9, 128.8, 128.5, 128.3, 117.5, 68.1, 66.8, 65.3, 64.8,

51.4, 47.0, 36.3; **HRMS:** (+ESI) Calc. for $C_{26}H_{29}N_4O_8$: 525.1980 $[M+H]^+$, Found: 525.1985$[M+H]^+$.

2.3 Synthesis of tetrapeptide intermediate 26-1

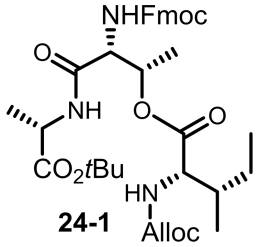


Scheme S3



H-Ala-O^{t}Bu **23** (1.5 g, 10 mmol), Fmoc-Thr-OH (3.4 g, 10 mmol) and DIPEA (5.2 ml, 30 mmol) was dissolved in 50 mL anhydrous DCM. HATU (5.7 g, 15 mmol) was added to the solution and the mixture was stirred at room temperature for 6 h. The reaction mixture was then washed by 1.0 M HCl (20 mL), aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried with anhydrous Na_2SO_4 and

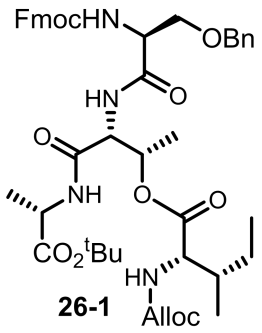
concentrated *in vacuo*. The crude residue was purified by flash column chromatography (DCM: MeOH=80:1) to afford compound **24** (3.7 g, 80%). ^{1}**H NMR** ($CDCl_3$, 400 MHz) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 6.99 (d, *J* = 7.6 Hz, 1H), 5.88 (d, *J* = 8.0 Hz, 1H), 4.53-4.35 (m, 4H), 4.27-4.13 (m, 2H), 3.58 (s, 1H), 1.44 (s, 9H), 1.38 (d, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 171.9, 170.7, 156.9, 143.8, 141.3, 127.7, 127.1, 125.0, 120.0, 82.3, 67.3, 67.0, 59.1, 49.0, 47.2, 27.9, 18.3, 18.0; **HRMS:** (+ESI) Calc. for $C_{26}H_{32}N_2NaO_6$: 491.2153 $[M+Na]^+$, Found: 491.2157 $[M+Na]^+$.



24-1

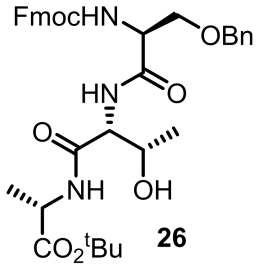
Compound **24** (3.7 g, 8 mmol) was dissolved in dry DCM (20 mL) at room temperature. Alloc-Ile-OH (2.5 g, 12 mmol), DIC (2.4 ml, 12 mmol) and DMAP (98 mg, 0.8 mmol) were added to the solution and the mixture was stirred at room temperature for 8 hours. The reaction mixture was washed by 1.0 M HCl (20 mL), aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (Hexane: EA=2:1) to afford compound **24-1** (4.7 g, 88% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.62 (d, *J* = 7.4 Hz, 2H), 7.40 (td, *J* = 7.4, 3.1 Hz, 2H), 7.33 (dt, *J* = 10.8, 5.2 Hz, 2H), 6.91 (d, *J* = 7.2 Hz, 1H), 5.90 (ddt, *J* = 16.4, 10.9, 5.6 Hz, 1H), 5.63 (d, *J* = 8.6 Hz, 1H), 5.54 – 5.42 (m, 1H), 5.41 – 5.25 (m, 2H), 5.20 (d, *J* = 10.5 Hz, 1H), 4.57 (d, *J* = 5.6 Hz, 2H), 4.48 (q, *J* = 8.8, 6.8 Hz, 2H), 4.39 (q, *J* = 9.0, 7.6 Hz, 2H), 4.27 (dt, *J* = 18.4, 5.7 Hz, 2H), 1.82 (s, 1H), 1.46 (s, 9H), 1.37 (d, *J* = 7.1 Hz, 4H), 1.25 (d, *J* = 6.5 Hz, 3H), 0.89 (q, *J* = 7.5 Hz, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 171.8, 170.7, 167.6, 156.4, 143.7, 141.3, 132.6, 127.8, 127.1, 125.0, 120.0, 117.8 , 82.4, 71.2, 67.4, 65.8, 58.6, 58.1,

48.9, 47.1, 37.8, 28.0, 24.7, 18.6, 16.3, 15.4, 11.5. **HRMS:** (+ESI) Calc. for $C_{36}H_{47}N_3NaO_9$: 688.3205 $[M+Na]^+$, Found: 688.3207 $[M+Na]^+$.



26-1

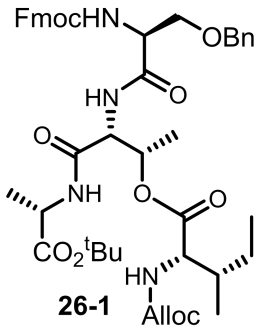
Compound **24-1** (4.7 g, 7 mmol) was dissolved in a mixture of 20% Et_2NH in MeCN (20 mL), and the resulting mixture was stirred at room temperature for 2 h. Then the solution was concentrated *in vacuo*, the resulting crude oil was azeotroped with n-heptane (3 x 10 mL) to remove any residual Et_2NH. The crude product was redissolved in DCM (30 mL). Fmoc-Ser(Bn)-OH (4.2 g, 10 mmol), DIPEA (5.2 ml, 30 mmol) and HATU (4.6 g, 12 mmol) were added to the solution and the reaction mixture was stirred at room temperature for 3 hours. No tetrapeptide product **26-1** was found by LC-MS analysis. The failure installation of Ser_7 on the N-terminus of the resulting tripeptide was problematic due to the facile acyl migration of the ester (O)-linked Ile group to the NH_2 group of Thr in **25**.



26

Compound **24** (3.7 g, 8 mmol) was dissolved in a mixture of 20% Et_2NH in MeCN (20 mL), and the resulting mixture was stirred at room temperature for 2 h. Then the solution was concentrated *in vacuo*, the resulting crude oil was azeotroped with n-heptane (3 x 10 mL) to remove any residual Et_2NH. The crude product was redissolved in DCM (30 mL). Fmoc-Ser(Bn)-OH (4.2 g, 10 mmol), DIPEA (5.2 ml, 30 mmol) and HATU (4.6 g, 12 mmol) were added to the solution and the resulting

mixture was stirred at room temperature for 3 hours. The reaction mixture was washed by 1.0 M HCl (20 mL), aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (DCM: MeOH=80:1) to afford compound **26** (3.1 g, 60% yield). ^{1}**H NMR** ($CDCl_3$, 400 MHz) δ 7.73-7.64 (m, , 2H), 7.51 (d, *J* = 7.6, 4.4 Hz, 2H), 7.47-7.36 (m, 1H), 7.32 (ddd, *J* = 8.8, 5.3, 1.8 Hz, 2H), 7.28-7.18 (m, 7H), 6.06-5.93 (m, 1H), 4.55 – 4.23 (m, 8H), 4.13 (t, *J* = 7.1 Hz, 1H), 3.87-3.72 (m, 2H), 3.59 (t, *J* = 8.0 Hz, 1H), 1.35 (s, 9H), 1.26 (d, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 172.2, 170.9, 170.2, 156.3, 143.8, 143.7, 141.3, 137.2, 128.5, 128.0, 127.9, 127.8, 127.2, 127.1, 125.1, 120.0, 82.1, 73.5, 69.7, 67.4, 66.9, 58.0, 55.0, 49.0, 47.1, 27.9, 18.4, 17.7; **HRMS:** (+ESI) Calc. for $C_{36}H_{43}N_3NaO_8$: 668.2942 $[M+Na]^+$, Found: 668.2947 $[M+Na]^+$.

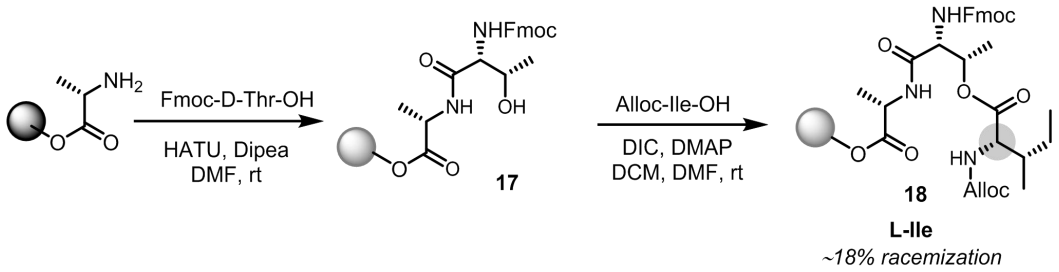


26-1

Compound **26** (3.1 g, 4.8 mmol) was dissolved in 20 mL dry DCM. Alloc-Ile-OH (1.5 g, 7.2 mmol), DIC (1.2 ml, 7.2 mmol) and DMAP (61 mg, 0.5 mmol) were added to the solution and the resulting mixture was stirred at room temperature for 8 hours. The reaction mixture was washed with 1.0 M HCl (20 mL), aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography on silica gel (Hexane: EA=2:1) to afford compound **26-1** (3.3 g, 81% yield). ^{1}**H NMR** ($CDCl_3$, 400 MHz) δ 7.80 – 7.72 (m, 2H), 7.59 (dd, *J* = 7.8, 4.3 Hz, 2H), 7.44 – 7.27 (m, 9H), 7.00 (s, 1H), 5.87 (ddt, *J* = 16.4, 10.8, 5.6 Hz, 1H), 5.77 (s, 1H), 5.52 (dt, *J* = 9.3, 4.6 Hz, 1H), 5.44 – 5.35 (m, 1H), 5.33 – 5.22 (m, 1H), 5.22 – 5.10 (m, 1H), 4.68 – 4.62 (m, 1H), 4.59 (d, *J* = 8.3 Hz, 2H), 4.56 – 4.50

(m, 2H), 4.48 – 4.32 (m, 4H), 4.29 – 4.17 (m, 2H), 3.91 (d, *J* = 7.4 Hz, 1H), 3.62 (s, 1H), 2.22 (d, *J* = 20.4 Hz, 1H), 1.80 (s, 1H), 1.43 (s, 9H), 1.33 (d, *J* = 7.1 Hz, 3H), 1.29 – 1.19 (m, 3H), 1.15 – 1.00 (m, 1H), 0.87 (d, *J* = 7.1 Hz, 6H); **^{13}C NMR** ($CDCl_3$, 100 MHz**)** δ 171.8, 170.7, 170.5, 167.2, 156.2 , 156.0, 143.8, 143.6, 141.3, 137.0, 132.6, 128.6, 128.1, 127.9, 127.8, 127.1, 125.1, 120.0, 117.8, 82.2, 73.5, 70.9, 69.3, 67.4, 65.8, 58.6, 56.4, 54.9, 48.8, 47.1, 37.7, 27.9, 24.8, 18.5, 16.4, 15.3, 11.5; **HRMS:** (+ESI) Calc. for $C_{46}H_{58}N_4N_aO_{11}$: 865.3994 $[M+Na]^+$, Found: 865.4000 $[M+Na]^+$.

2.4 Esterification of D-Thr$_8$ with L-Ile$_{11}$ at position 11 via SPPS.



Scheme S4

H-Ala-2-Chlorortritylchloride (CTC) resin (1 g, manufacturer's loading = 0.98 mmol/g) was swelled in DMF (20 mL) in a reactor. Fmoc-D-Thr-OH (835 mg, 2.5 mmol), HATU (950mg, 2.5 mmol) and DIPEA (855µL, 4.9 mmol) were added and the reactor was shaken for 1h at room temperature. Then the mixture was filtered, the resin was washed with MeOH (3 x 50 mL) and DCM (3 x 50 mL) to afford the resin-bound dipeptide **17**.

The resin-bound dipeptide **17** was swelled in DMF (5 mL) and DCM (5 mL) in a reactor, then Alloc-L-Ile-OH (2.1 g, 9.8 mmol), DIC (1.5 mL, 9.8 mmol) and DMAP (120 mg, 0.98 mmol) were added. The reactor was shaken at room temperature for 3h. Then the mixture was filtered, the resin was washed with MeOH (3 x 50 mL) and DCM (3 x 50 mL). Some of the resin (~1 mg) was treated with 0.5% TFA in DCM (0.5 mL) to cleavage the tripeptide from the resin. The resulting tripeptide was

analysed on a Thermo Scientific MSQ instrument (Lc-Ms method A), and ~18% racemization at Ile was observed (**Figure S1**).

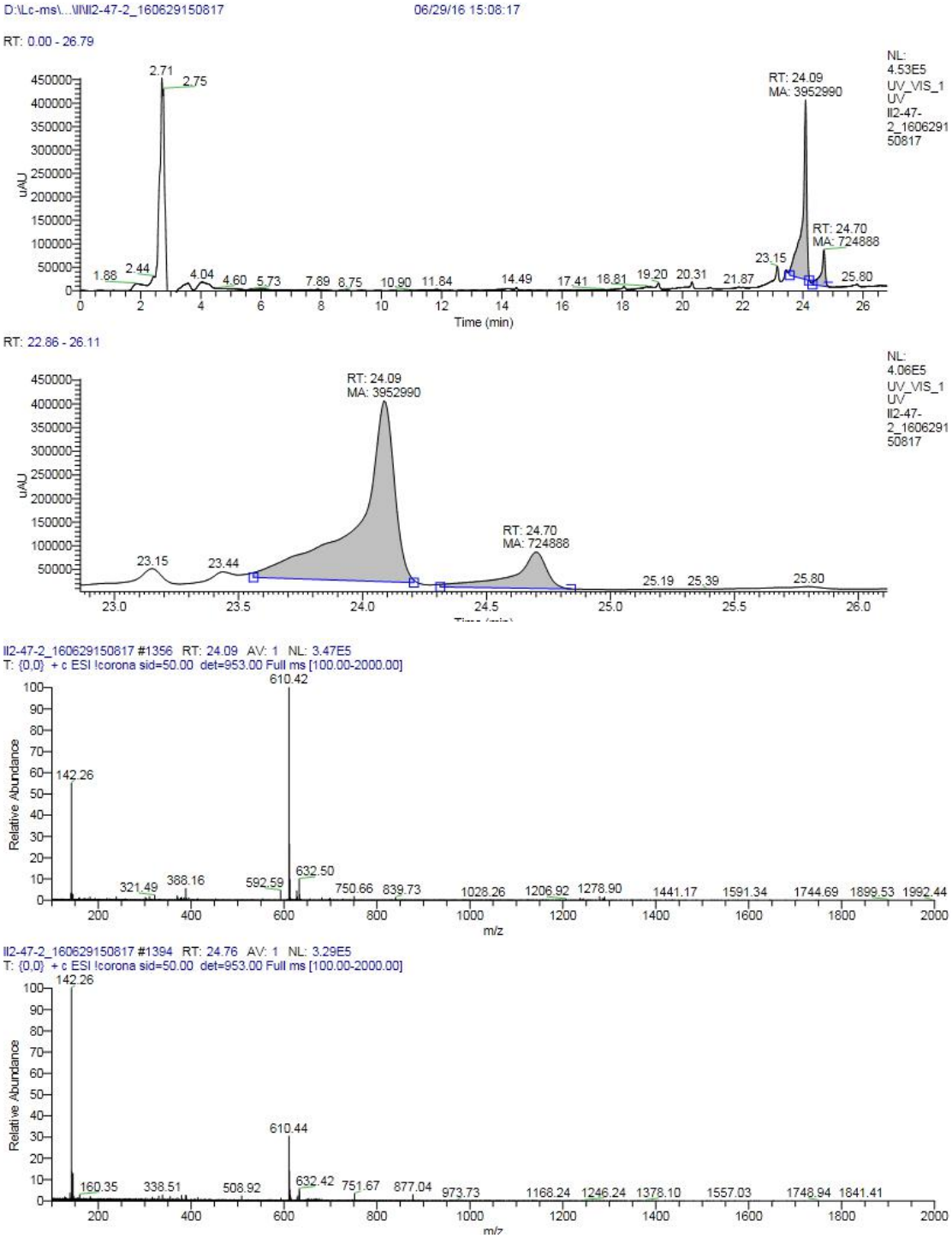
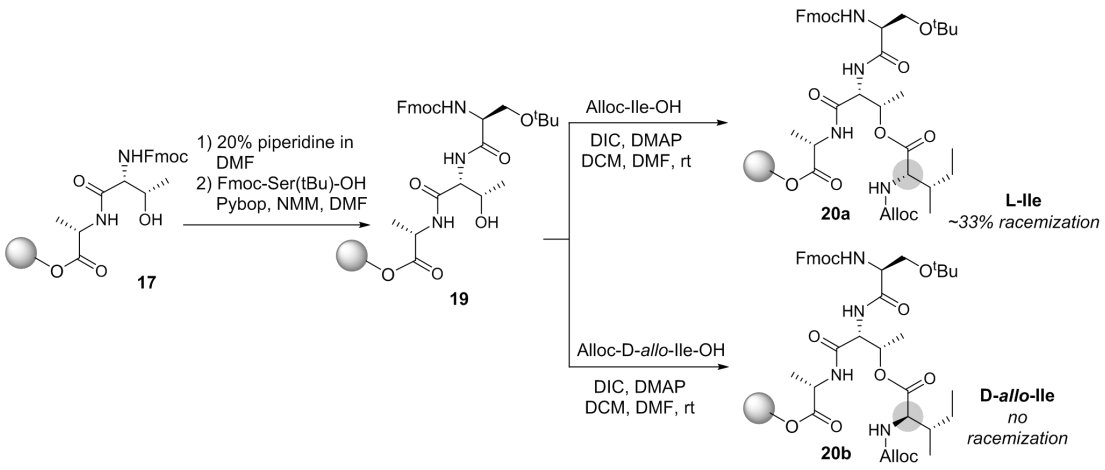


Figure S1. Lc-Ms Analysis of Tripeptide **18**



Scheme S5

The resin-bound dipeptide **17** was added to a mixture of 20% piperidine in DMF (20 mL), and the mixture was shaken to for 30 minutes. Then the mixture was filtered, the resin was washed with MeOH (3 x 20 mL) and DCM (3 x 20 mL). Fmoc-L-Ser(*t*Bu)-OH (958 mg, 2.5 mmol), Pybop (1.3 g, 2.5 mmol) and NMM (546 μL, 4.9 mmol) in DMF were added on the resin and the reactor was shaken for 1h at room temperature. Then the mixture was filtered, the resin was washed with MeOH (3 x 20 mL) and DCM (3 x 20 mL) to afford the resin-bound tripeptide **19**. The resin-bound tripeptide **19** was swelled in DMF (5 mL) and DCM (5 mL) in a reactor, then Alloc-L-Ile-OH (2.1 g, 9.8 mmol), DIC (1.5 mL, 9.8 mmol) and DMAP (120 mg, 0.98 mmol) were added. The reactor was shaken at room temperature for 3h. Then the mixture was filtered, the resin was washed with MeOH (3 x 50 mL) and DCM (3 x 50 mL). Some of the resin (~1 mg) was treated with 0.5% TFA in DCM (0.5 mL) to cleavage the tetrapeptide from the resin. The resulting tetrapeptide **20a** was analysed on a Thermo Scientific MSQ instrument (Lc-Ms method A), and ~33% racemization at Ile was observed (**Figure S2**).

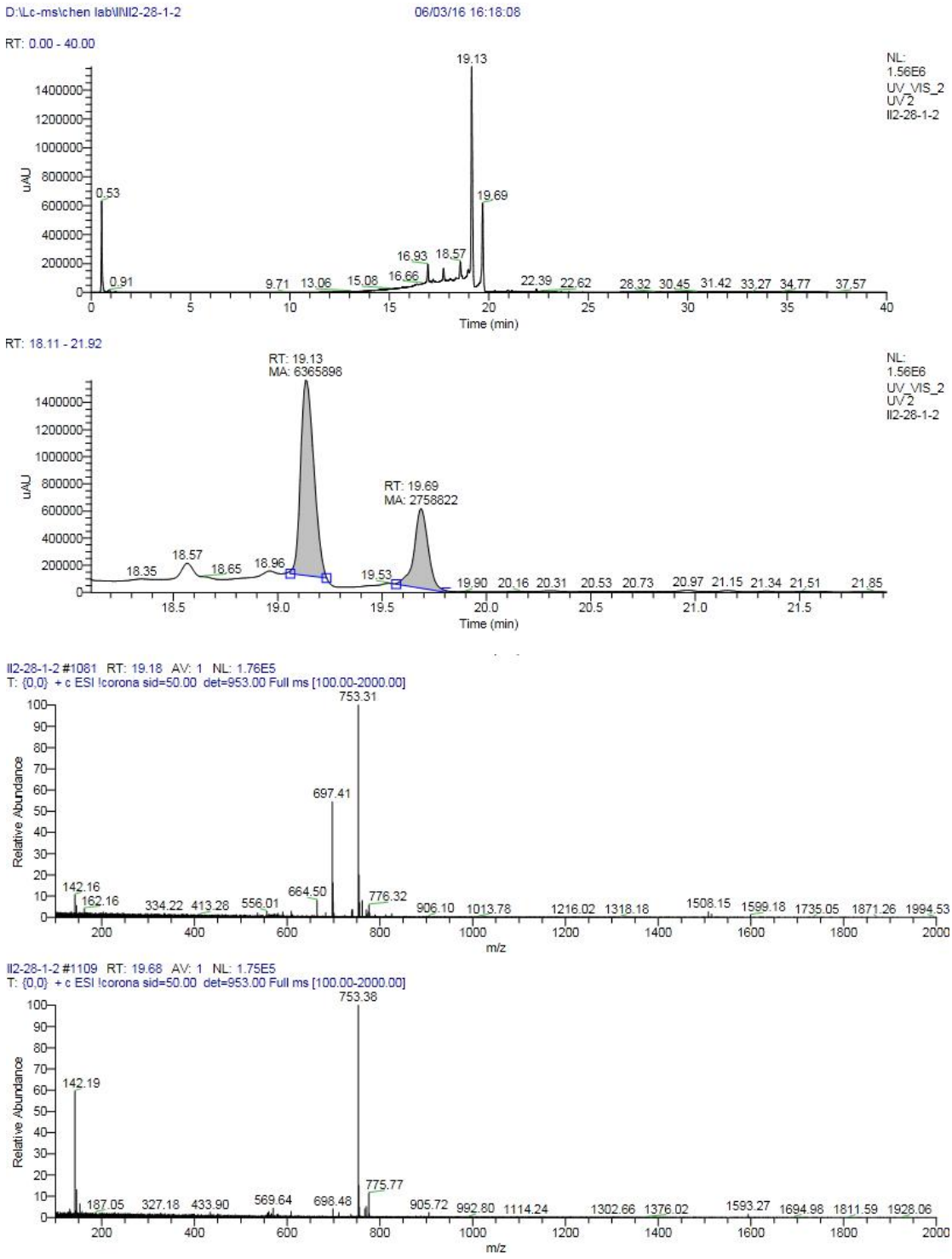


Figure S2. Lc-Ms Analysis of Tetrapeptide **20a**

Esterification of tripeptide **19** with Alloc-D-*allo*-Ile-OH was conducted following the same procedure above to afford tetrapeptide **20b**, and no racemization at D-*allo*-Ile was observed (**Figure S3**, Lc-MS method B).

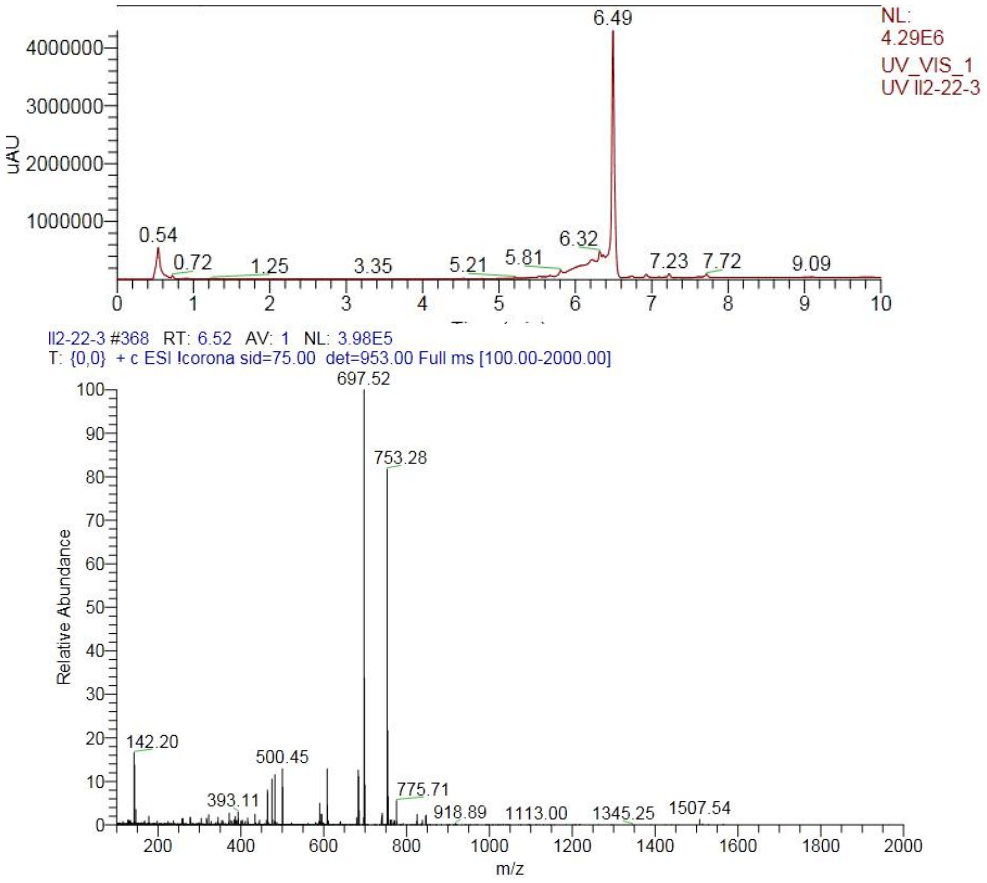
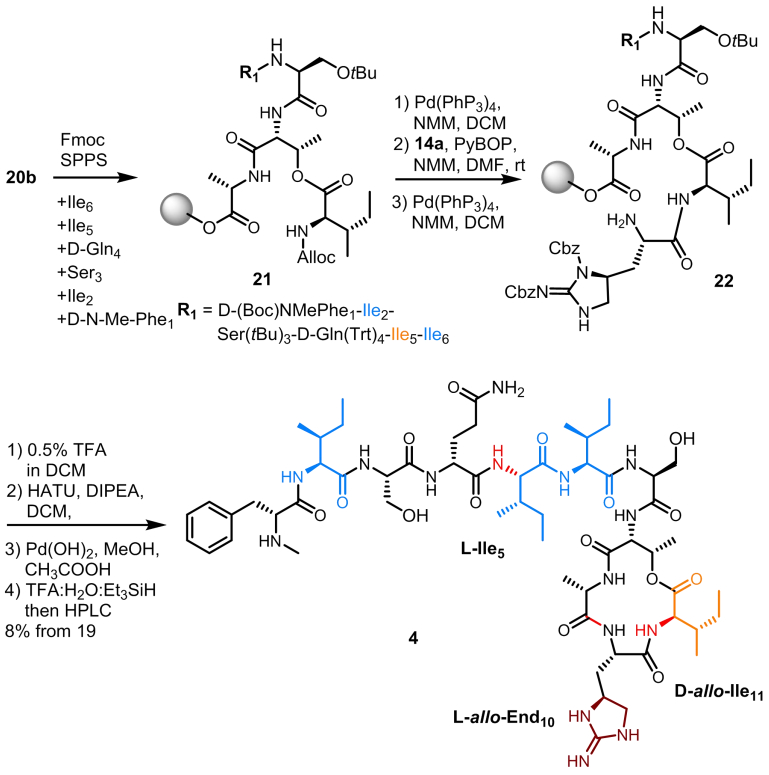


Figure S3. Lc-Ms Analysis of Tetrapeptide **20b**

2.5 Synthesis of teixobactin stereoisomer 4



Scheme S6

With the resin-bound tetrapeptide **20b** in hand, teixobactin stereoisomer **4** was synthesized using the standard SPPS (solid phase peptide synthesis) method:

1) General procedure for HATU coupling on resin: The loaded resin was shaken for 2 h at room temperature with a solution of the desired Fmoc-AA-OH (4 equiv), HATU (4 equiv) and DIPEA (8 equiv) in DMF (20 mL)). The coupling mixture was filtered and the resin was washed with CH_2Cl_2 (10 mL x 20) and CH3OH (10 mL x 20).

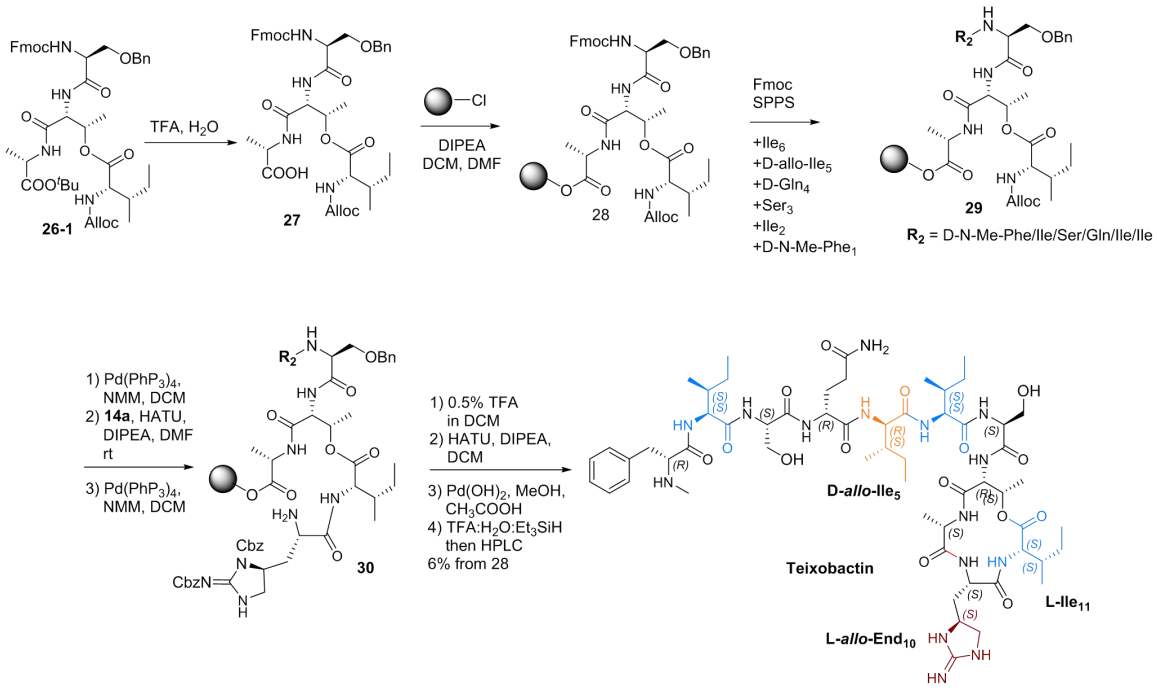
2) General procedure for deprotection of Fmoc: The loaded resin was treated with a solution of 20 vol% piperidine in DMF (20 mL) for 30 min and then filtered. The resin was washed with CH_2Cl_2 (20 mL x 5) and CH_3OH (20 mL x 5).

3) General procedure for cleavage the peptide from the resin: 0.5% TFA in DCM (20 mL) were added on the resin and the mixture was shaken for 2h before filtered. The resin was washed with CH_2Cl_2 (20 mL x 5) and CH_3OH (20 mL x 5).

The resin-bound decapeptide **21** was swell in DCM (20 mL), then $Pd(PPh_3)_4$ (115 mg, 0.1 mmol) and $PhSiH_3$ (1.2 mL, 9.8 mmol) was added. The reaction mixture was shaken under N_2 for 3 h, then filtered and the resin was washed with MeOH (3 x 20 mL), DCM (3 x 20 mL). Alloc-L-allo-End(Cbz)-OH 14a (514 mg, 0.98 mmol), Pybop (780 mg, 1.5 mmol) and NMM (223 µL, 2 mmol) in DMF (20 mL) were added on the resin and the reactor was shaken for 1h at room temperature. Afterward, the mixture was filtered and the resin was washed with MeOH (3 x 20 mL), DCM (3 x 20 mL). $Pd(PPh_3)_4$ (115 mg, 0.1 mmol) and $PhSiH_3$ (1.2 mL, 9.8 mmol) and dry DCM (20 mL) was added and the reaction mixture was shake nunder N_2 for 3 h to remove the Alloc protecting group. The resin was washed with MeOH (3 x 20 mL), DCM (3 x 20 mL). 0.5% TFA in DCM (20 mL) were added on the resin and the mixture was shaken for 2h to cleavage the peptide from the resin. The mixture was filtered and the filtrate was concentrated *in vacuo* to give a white foam. The peptide was redissolved in 500 mL of DCM, then HATU (372 mg, 0.98 mmol) and DIPEA (855µL, 4.9 mmol) were added. The reaction mixture was stirred for 24 h. The reaction mixture was washed with 1.0 M HCl (300 mL), aqueous $NaHCO_3$ (300 mL) and brine (300 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated *in vacuo* to give crude cyclized depsipeptide. The crude compound was dissolved in 10 mL of MeOH/HCOOH(*v/v*=9:1) and hydrogenized with $Pd(OH)_2$ (90 mg, 10% on carbon) under H_2 for 10 hours to remove the Cbz groups. The reaction mixture was filtered through a pad of celite and the filtrate was concentrated *in vacuo*. The residue was re-dissolved in a mixture of TFA:Et_3SiH:H_2O (10 mL, 95/2.5/2.5 v/v/v). The reaction mixture was stirred for 3 h, and then concentrated *in vacuo* to give teixobactin steroisomer **4** as a crude solid. This solid was further purified using RP-HPLC (General method) to give a white solid (11 mg, 8% yield). ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 9.05 (s, 3H), 8.58 (d, *J* = 9.9 Hz, 1H), 8.50 (d, *J* = 8.3 Hz, 2H), 8.36 (s, 1H), 8.23 (d, *J* = 4.8 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 2H), 7.93 (dd, *J* = 20.6, 8.6 Hz, 5H), 7.84 (d, *J* = 6.5 Hz, 3H), 7.76 (s, 4H), 7.36 – 7.27 (m, 3H), 7.24 (dd, *J* = 19.4, 6.9 Hz, 7H), 7.13 (d, *J* = 8.8 Hz, 2H), 6.76 (s, 2H), 5.39 – 5.21 (m, 3H), 4.74 (d, *J* = 12.4 Hz, 2H), 4.55 – 4.39 (m, 3H), 4.31 (td, *J* = 19.0, 16.8, 6.6 Hz, 6H), 4.23 – 4.10 (m, 6H),

4.05 – 3.94 (m, 2H), 3.75 (d, J = 6.6 Hz, 2H), 3.66 (dd, J = 13.1, 8.0 Hz, 6H), 3.30 – 3.21 (m, 4H), 3.16 – 3.03 (m, 4H), 2.96 (dd, J = 13.3, 9.5 Hz, 3H), 2.77 (d, J = 4.9 Hz, 3H), 2.68 (d, J = 6.3 Hz, 1H), 2.50 – 2.41 (m, 23H), 2.17 (s, 3H), 2.10 – 1.95 (m, 6H), 1.95 – 1.77 (m, 5H), 1.78 – 1.60 (m, 7H), 1.53 (s, 3H), 1.35 (dd, J = 16.1, 6.5 Hz, 9H), 1.26 (d, J = 25.4 Hz, 14H), 1.18 – 0.93 (m, 13H), 0.86 (q, J = 7.2 Hz, 8H), 0.82 – 0.69 (m, 23H), 0.63 (t, J = 7.1 Hz, 5H), 0.58 (d, J = 6.7 Hz, 4H). HRMS: (+ESI) Calc. for $C_{58}H_{96}N_{15}O_{15}$: 1242.7205 $[M+H]^+$, Found: 1242.7208 $[M+H]^+$.

2.6 Synthesis of teixobactin and its stereoisomer 2, 3, 5, 6, 7, 8.



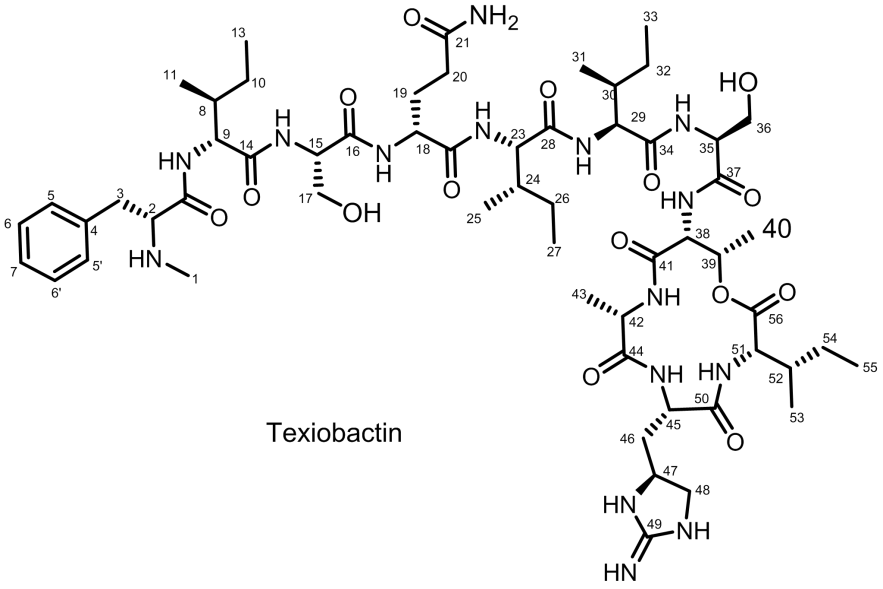
Scheme S7

The tetrapeptide **26-1** was dissolved in a mixture of TFA (10 mL) and water (1.0 mL). The mixture was stirred at room temperature for 3 h, then concentrated *in vacuo* to give crude **27** as a brown oil**.** The resulting crude oil was azeotroped with toluene (3 x 10 mL) and concentrated *in vacuo* to remove residual TFA. Compound **27** (1.57 g, 2 mmol) was then dissolved in a mixture of DCM (10 mL) and DMF (10 mL). DIPEA (1.7 mL, 10 mmol), 2-CTC resin (1 g) were added to this mixture and the

reaction was stirred at room temperature was for 3h. The resin was filtered and washed with MeOH (3 x 20 mL), DCM (3 x 20 mL). The unreacted resin was capped with MeOH in a mixture of MeOH:DIPEA:DCM (1:2:7, 10 mL) for 5 h. Fmoc protecting group was removed following the general procedure and the remain amino acids were successively coupled using the standard SPPS method.

The resin-bound decapeptide **29** was swell in DCM (20 mL), then $Pd(PPh_3)_4$ (115 mg, 0.1 mmol) and $PhSiH_3$ (1.2 ml, 9.8 mmol) was added. The reaction mixture was shaken under N_2 for 3 h, then filtered and the resin was washed with MeOH (3 x 20 mL), DCM (3 x 20 mL). Alloc-L-*allo*-End(Cbz)$_2$-OH **14a** (514 mg, 0.98 mmol), Pybop (780 mg, 1.5 mmol) and NMM (223 μL, 2 mmol) in DMF (20 mL) were added on the resin and the reactor was shaken for 1h at room temperature. Afterward, the mixture was filtered and the resin was washed with MeOH (3 x 20 mL), DCM (3 x 20 mL). $Pd(PPh_3)_4$ (115 mg, 0.1 mmol) and $PhSiH_3$ (1.2 ml, 9.8 mmol) and dry DCM (20 mL) was added and the reaction mixture was shake nunder N_2 for 3 h to remove the Alloc protecting group. The resin was washed with MeOH (3 x 20 mL), DCM (3 x 20 mL). 0.5% TFA in DCM (20 mL) were added on the resin and the mixture was shaken for 2h to cleavage the peptide from the resin. The mixture was filtered and the filtrate was concentrated *in vacuo* to give a white foam. The peptide was redissolved in 1 L of dry DCM, then HATU (372 mg, 0.98 mmol) and DIPEA (855μL, 4.9 mmol) were added. The reaction mixture was stirred for 24 h. The reaction mixture was washed with 1.0 M HCl (300 mL), aqueous $NaHCO_3$ (300 mL) and brine (300 mL). The organic phase was dried with anhydrous Na_2SO_4 and concentrated *in vacuo* to give crude cyclized depsipeptide. The crude compound was dissolved in 10 mL of MeOH/HCOOH(*v/v*=9:1) and hydrogenized with $Pd(OH)_2$ (90 mg, 10% on carbon) under H_2 for 10 hours to remove the Cbz and Bn groups. The reaction mixture was filtered through a pad of celite and the filtrate was concentrated *in vacuo*. The residue was re-dissolved in a mixture of TFA:Et_3SiH:H_2O (10 mL, 95/2.5/2.5 v/v/v). The reaction mixture was stirred for 3 h, and then concentrated *in vacuo*. The crude peptide was precipitated using cold Et_2O and centrifuged at 7000 rpm to give a white solid. This solid was further purified by RP-HPLC using protocols described in the

general method. Fractions were collected, concentrated and lyophilized to give teixobactin **1** as a white solid (10 mg, 2% yield). HRMS: (+ESI) Calc. for $C_{58}H_{96}N_{15}O_{15}$: 1242.7205 $[M+H]^+$, Found: 1242.7210 $[M+H]^+$; The ^1H NMR and ^{13}C NMR spectra of synthetic product were fully consistent with the data of isolated samples reported in the literature.[4] See table S1 and table S2 for details.



Scheme 8

Table S1. ^1H NMR (DMSO-d_6, 400 MHz) Spectroscopic Data Comparison with Natural teixobaction

Position	Natural	Synthetic (Organic Letters)[1]	Synthetic (Nature Communications)[5]	Our Synthetic	Δδ ($\delta_{synthetic}$ - $\delta_{natural}$)
2-NH	9.3	10.09	Not reported	9.02	-0.28
	9	9.08	Not reported	8.87	-0.13
9-NH	8.43	8.64	8.8	8.83	0.4
35-NH	8.37	8.99	8.7	8.74	0.4
45-NH	8.32	8.85	8.6	8.50	0.18

48-NH	8.1	8.05	9	8.16	0.06
42-NH	8.05	8.16	8.1	8.08	0.03
51-NH	8.01	8.75	9	8.06	0.05
15-NH	7.88	8.09	7.9	7.94	0.06
18-NH	7.85	8.02	7.9	7.90	0.05
29-NH	7.78	7.89	7.8	7.80	0.02
49-NH	7.76	7.8	7.9	7.78	0.02
23-NH	7.7	7.75	7.7	7.70	0
6,6’	7.31	7.28	7.3	7.31	0
7	7.27	7.22	7.3	7.26	-0.01
5,5’	7.24	7.21	7.2	7.22	-0.02
21-NH2	7.11	7.26	7.2	7.11	0
21-NH2	6.63	6.76	6.7	6.80	0.17
39	5.36	5.37	5.3	5.38	0.02
38	4.64	4.69	4.6	4.63	-0.01
35	4.47	4.64	4.4	4.41	-0.06
45	4.38	4.35	4.4	4.39	0.01
23	4.36	4.37	4.4	4.37	0.01
15	4.34	4.3	4.3	4.35	0.01
18	4.33	4.3	4.3	4.33	0
29	4.29	4.39	4.3	4.31	0.02
2	4.21	4.27	4.2	4.29	0.08
9	4.12	4.07	4.1	4.13	0.01
51	4.03	4.01	4	4.01	-0.02
42	3.97	3.89	3.9	3.98	0.01

47	3.9	3.82	3.9	3.90	0.08
36	3.8	3.87	3.8	3.80	-0.07
48	3.66	3.6	3.5	3.67	0.07
36	3.64	3.56	3.6	3.63	0.07
16	3.57	3.54	3.6	3.57	0.03
48	3.36	3.44	3.4	3.39	0.03
3	3.15	3.29	3	3.12	-0.03
3	3	2.95	3.1	2.96	-0.04
1	2.5	2.47	2.5	2.43	-0.07
20	2.1	2.08	2.2	2.07	-0.03
46	2.03	2.13	2	2.02	-0.01
19	1.92	1.87	2.2	1.93	0.01
30	1.83	1.82	1.8	1.81	-0.02
24	1.8	1.8	1.9	1.81	0.01
52	1.77	1.88	1.8	1.77	0
19	1.74	1.71	1.7	1.69	-0.05
10	1.56	1.56	1.5	1.53	-0.03
32	1.42	1.44	1.3	1.43	0.01
43	1.34	1.26	1.3	1.34	0
26	1.32	1.28	1.3	1.27	-0.05
40	1.13	1.05	1.1	1.26	0.13
32	1.11	1.08	1.1	1.23	0.12
26	1.09	1.06	1.1	1.14	0.05
12	1.07	1.02	1.1	1.06	-0.01
54	1.07	1.41	1.1	1.04	-0.03

33	0.85	0.77	0.8	0.88	0.03
31	0.84	0.88	0.8	0.85	0.01
25	0.82	0.77	0.8	0.83	0.01
27	0.82	0.82	0.8	0.81	-0.01
55	0.82	0.8	0.8	0.80	-0.02
53	0.81	0.78	0.8	0.79	-0.02
54	0.77	1.13	0.8	0.77	0
12	0.76	0.72	0.8	0.76	0
13	0.66	0.61	0.6	0.63	-0.03
11	0.62	0.53	0.6	0.57	-0.05

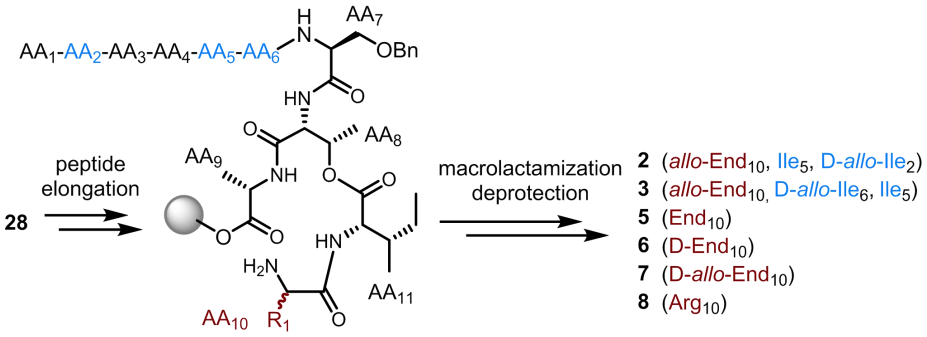
Table S2. ^{13}C NMR (DMSO-d_6, 125 MHz) Spectroscopic Data Comparison with Natural teixobaction

Position	Natural	Synthetic (Organic Letters)[1]	Synthetic (Nature Communications)[5]	Our Synthetic	Δδ ($\delta_{synthetic}$ - $\delta_{natural}$)
21	174.4	173.9	174.5	174.4	0
44	173.1	172.5	173.1	173.0	-0.1
50	171.8	172.5	171.9	171.8	0
37	171.7	171.4	171.6	171.5	-0.2
34	171.6	170.7	171.6	171.5	-0.1
28	171.4	170.8	171.3	171.2	-0.2
22	170.9	170.9	171.1	171.0	0.1
14	170.6	170.1	170.7	170.6	0
17	170.2	169.7	170.2	170.0	-0.2
56	169.3	169.3	169.3	169.7	0.4

41	168.9	167.9	168.5	168.4	-0.5
8	167.1	166.6	167.1	-	-
49	160	159	159.5	159.3	-0.7
4	135	134.7	135	135.2	0.2
5,5’	129.7	129	129.7	129.7	0
6,6’	128.9	128.3	128.9	128.9	0
7	127.5	126.8	127.7	127.5	0
39	71.2	70	70.8	70.7	-0.5
36	62.7	63.5	64.3	63.5	0.8
16	62.4	61.7	62.4	62.3	-0.1
2	61.9	61	61.8	61.9	0
9	57.9	57.4	57.9	57.7	-0.2
51	57.8	57	57.8	57.7	-0.1
29	57.3	56.6	57.3	57.2	-0.1
23	56.8	55.5	55.9	56.0	-0.8
35	56.5	55.5	56.2	55.9	-0.6
38	56.2	55.3	56.1	55.5	-0.7
15	55.6	55.2	55.6	55.5	-0.1
47	53.5	53.2	53.9	53.7	0.2
18	52.7	52	52.5	52.4	-0.3
42	52.2	51.6	52.3	52.2	0
45	52.2	51.9	52.3	52.2	0
48	48.3	47.7	48.5	48.4	0.1
24	37.4	36.7	37.6	37.5	0.1
46	37.2	36.2	37.5	37.4	0.2

30	36.9	36.7	37.2	36.9	0
10	36.5	35.8	36.7	36.6	0.1
3	36.4	35.5	36.4	36.6	0.2
52	36.3	35.2	35.9	35.8	-0.5
1	31.9	30.9	31.9	31.9	0
20	31.9	31.4	31.9	31.9	0
19	28.4	27.9	28.7	28.7	0.3
26	26.2	25.6	26.4	26.2	0
32	25.3	24.1	25.5	25.3	0
54	24.5	24.8	24.8	24.7	0.2
12	24.4	23.8	24.3	24.2	-0.2
43	17.1	16.5	17.3	17.1	0
53	16	15	16	15.9	-0.1
40	15.9	15.3	15.9	15.9	-0.1
11	15.5	14.9	15.6	15.8	0.3
31	15.4	15.4	15.6	15.5	0.1
25	14.7	14.3	14.7	14.6	-0.1
55	11.8	10.1	12	11.9	0.1
13	11.3	10.8	11.7	11.6	0.3
33	11.2	11.4	11.4	11.3	0.1
27	10.6	11.2	10.6	10.5	-0.1

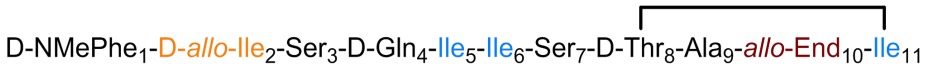
Products **2-3** and **5-8** were prepared using the corresponding amino acid units following the same procedure as teixobactin **1**. (Table S3)



Scheme 9

Table S3. Teixobactin analogs **2**, **3**, **5**, **6**, **7**, **8**

Teixobactin analogs	Yield	Chemical Formula	Calc. MW $[M+H]^+/[M+Na]^+$	HRMS $[M+H]^+/[M+Na]^+$
2	4%	$C_{58}H_{95}N_{15}O_{15}$	1242.7205	1242.7206
3	5%	$C_{58}H_{95}N_{15}O_{15}$	1242.7205	1242.7203
5	4%	$C_{58}H_{95}N_{15}O_{15}$	1242.7205	1242.7210
6	6%	$C_{58}H_{95}N_{15}O_{15}$	1264.7024 $[M+Na]^+$	1264.7028
7	4%	$C_{58}H_{95}N_{15}O_{15}$	1264.7024 $[M+Na]^+$	1264.7028
8	7%	$C_{58}H_{97}N_{15}O_{15}$	1243.7289	1243.7454



2

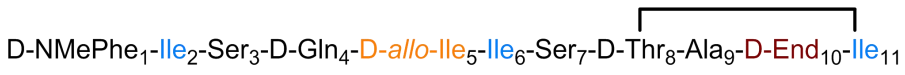
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.93 (s, 2H), 8.55 (s, 4H), 8.19 (m, 3H), 8.02 (d, 3H), 7.86 (s, 1H), 7.74 (s, 1H), 7.63 (s, 2H), 7.36 – 7.07 (m, 5H), 6.81 (s, 1H), 6.68 (s, 1H), 5.65 (s, 2H), 5.47 – 5.27 (m, 2H), 4.94 (d, J = 56.5 Hz, 2H), 4.66 (d, J = 8.1 Hz, 1H), 4.53 (s, 1H), 4.35 (d, J = 43.8 Hz, 4H), 4.13 (q, J = 5.2 Hz, 3H), 4.08 – 3.96 (m, 1H), 3.96 – 3.76 (m, 3H), 3.60 (s, 2H), 3.51 (d, J = 12.3 Hz, 1H), 3.16 (d, J = 5.0 Hz, 4H), 2.87 (s, 3H), 2.45 – 2.23 (m, 3H), 2.23 – 2.02 (m, 3H), 2.02 – 1.93 (m, 2H), 1.93 – 1.74 (m, 4H), 1.74 – 1.48 (m, 3H), 1.48 – 1.34 (m, 3H), 1.34 – 1.18 (m, 11H), 1.18 – 0.96 (m, 6H), 0.96 – 0.70 (m, 15H), 0.66 (t, J = 6.4 Hz, 5H); HRMS: (+ESI) Calc. for $C_{58}H_{96}N_{15}O_{15}$: 1242.7205 $[M+H]^+$, Found: 1242.7210 $[M+H]^+$.

3

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.22 (s, 1H), 9.06 (s, 1H), 8.55 (m, 2H), 8.38 (s, 1H), 8.28 – 8.10 (m, 2H), 8.08 (s, 3H), 8.00 – 7.71 (m, 8H), 7.35 – 7.13 (m, 8H), 7.13 – 6.95 (m, 1H), 5.42 – 5.19 (m, 2H), 4.74 (d, *J* = 11.0 Hz, 1H), 4.56 – 4.41 (m, 3H), 4.29 (td, *J* = 16.8, 15.8, 8.6 Hz, 5H), 4.13 (q, *J* = 7.0 Hz, 6H), 4.10 – 3.72 (m, 21H), 3.66 (dd, *J* = 11.5, 7.8 Hz, 5H), 3.58 – 3.40 (m, 4H), 3.29 – 3.14 (m, 2H), 3.17 – 3.00 (m, 2H), 2.96 (dd, *J* = 13.2, 9.5 Hz, 2H), 2.77 (d, *J* = 4.5 Hz, 2H), 2.18 (d, *J* = 9.0 Hz, 2H), 2.10 – 1.79 (m, 7H), 1.79 – 1.58 (m, 5H), 1.54 (d, *J* = 7.3 Hz, 2H), 1.37 (d, *J* = 7.3 Hz, 6H), 1.23 (s, 10H), 1.20 – 1.08 (m, 6H), 1.08 – 0.92 (m, 5H), 0.92 – 0.66 (m, 24H), 0.66 – 0.46 (m, 8H); HRMS: (+ESI) Calc. for $C_{58}H_{96}N_{15}O_{15}$: 1242.7205 $[M+H]^+$, Found: 1242.7203 $[M+H]^+$.

5

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.53 (m, 3H), 8.19 (m, 3H), 8.09 – 7.85 (m, 4H), 7.74 (m, 3H), 7.44 – 7.18 (m, 5H), 6.83 (s, 2H), 5.35 (s, 2H), 5.00 (s, 2H), 4.62 (s, 1H), 4.34 (d, *J* = 16.5 Hz, 5H), 4.18 – 3.98 (m, 3H), 3.89 (dt, *J* = 22.5, 7.2 Hz, 2H), 3.70 (d, *J* = 45.1 Hz, 3H), 3.05 (s, 2H), 2.99 – 2.86 (m, 1H), 2.04 (dt, *J* = 24.2, 7.6 Hz, 4H), 1.73 (d, *J* = 34.7 Hz, 5H), 1.48 (d, *J* = 50.9 Hz, 3H), 1.39 – 1.19 (m, 6H), 1.12 (d, *J* = 6.0 Hz, 6H), 0.91 – 0.68 (m, 13H), 0.68 – 0.44 (m, 6H); HRMS: (+ESI) Calc. for $C_{58}H_{96}N_{15}O_{15}$: 1242.7205 $[M+H]^+$, Found: 1242.7210 $[M+H]^+$.



6

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.91 (m, 1H), 8.27 (d, *J* = 7.7 Hz, 1H), 8.04 (m, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.80 – 7.56 (m, 3H), 7.56 – 7.24 (m, 1H), 7.14 – 6.90 (m, 5H), 6.86 (d, *J* = 8.9 Hz, 2H), 5.17 – 4.90 (m, 1H), 4.48 (d, *J* = 9.6 Hz, 1H), 4.28 – 4.10 (m, 2H), 4.10 – 4.01 (m, 2H), 3.92 (dq, *J* = 23.2, 8.0 Hz, 6H), 3.74 (dd, *J*

= 7.5, 5.2 Hz, 9H), 3.40 (q, *J* = 9.6, 7.3 Hz, 3H), 3.30 (dt, *J* = 10.8, 4.7 Hz, 3H), 2.87 – 2.64 (m, 3H), 1.95 (t, *J* = 8.4 Hz, 2H), 1.71 (dq, *J* = 36.5, 7.0, 6.6 Hz, 4H), 1.48 (d, *J* = 31.3 Hz, 3H), 1.13 (dd, *J* = 17.8, 6.9 Hz, 7H), 0.99 (s, 8H), 0.93 – 0.67 (m, 7H), 0.67 – 0.45 (m, 17H), 0.37 (dd, *J* = 21.1, 6.8 Hz, 6H); HRMS: (+ESI) $C_{58}H_{91}N_{15}NaO_{15}$: 1264.7024 $[M+Na]^+$, Found: 1264.7028 $[M+Na]^+$.

D-NMePhe$_1$-Ile$_2$-Ser$_3$-D-Gln$_4$-D-*allo*-Ile$_5$-Ile$_6$-Ser$_7$-D-Thr$_8$-Ala$_9$-D-*allo*-End$_{10}$-Ile$_{11}$

7

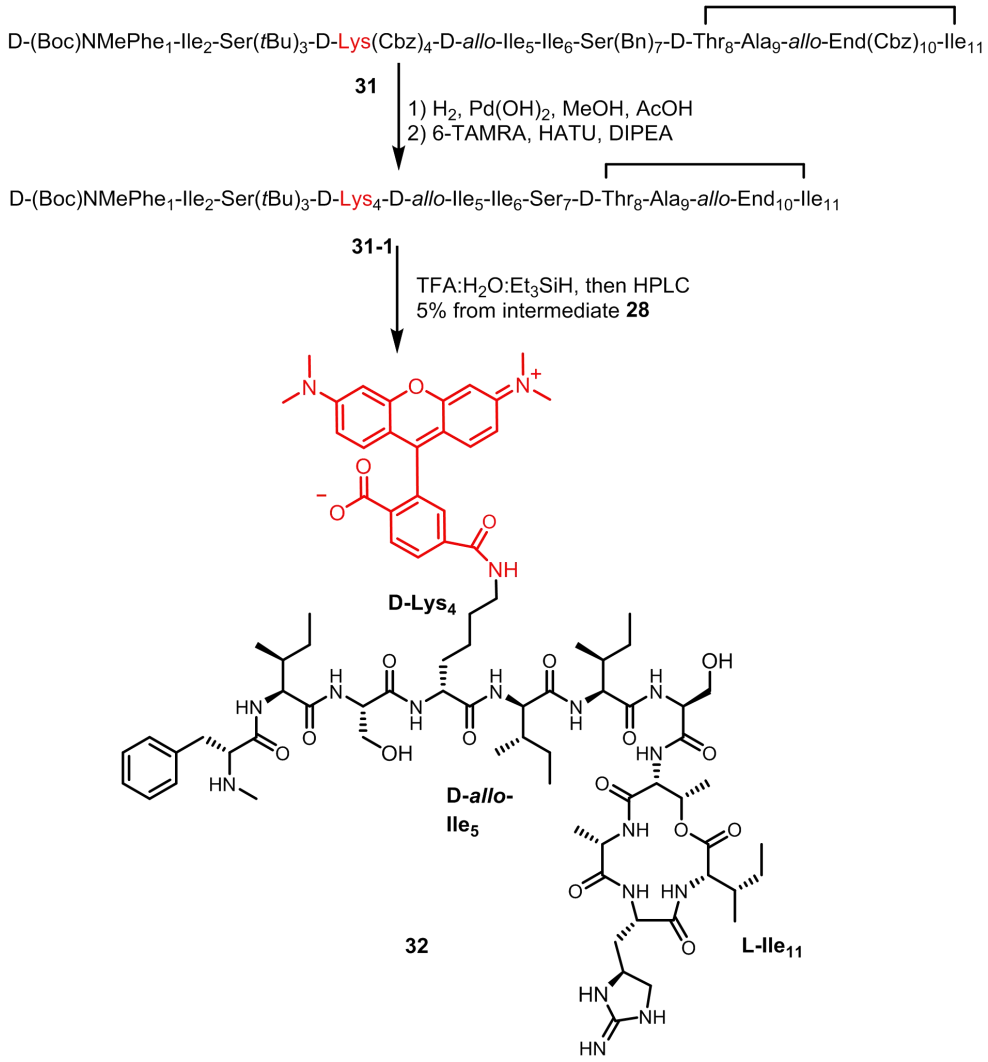
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.07 (s, 3H), 8.51 (d, *J* = 8.4 Hz, 2H), 8.26 (s, 3H), 8.09 (d, *J* = 15.5 Hz, 3H), 7.97 (d, *J* = 14.0 Hz, 2H), 7.95 – 7.80 (m, 2H), 7.74 (s, 2H), 7.44 – 7.17 (m, 5H), 6.75 (m, 3H), 5.32 (t, *J* = 4.7 Hz, 3H), 4.63 (s, 3H), 4.34 (dd, *J* = 12.5, 6.2 Hz, 6H), 4.15 (d, *J* = 7.6 Hz, 3H), 4.08 – 3.81 (m, 4H), 3.17 – 2.90 (m, 4H), 2.08 (d, *J* = 3.4 Hz, 2H), 1.99 (p, *J* = 7.0, 6.5 Hz, 4H), 1.94 – 1.65 (m, 6H), 1.41 (dd, *J* = 27.8, 7.1 Hz, 5H), 1.35 – 1.18 (m, 14H), 1.18 – 0.98 (m, 7H), 0.85 (ddt, *J* = 28.0, 14.6, 7.1 Hz, 15H), 0.61 (dd, *J* = 21.8, 6.7 Hz, 5H); HRMS: (+ESI) Calc. for $C_{58}H_{95}N_{15}NaO_{15}$: 1264.7024 $[M+Na]^+$, Found: 1264.7028 $[M+Na]^+$.

D-NMePhe$_1$-Ile$_2$-Ser$_3$-D-Gln$_4$-D-*allo*-Ile$_5$-Ile$_6$-Ser$_7$-D-Thr$_8$-Ala$_9$-Arg$_{10}$-Ile$_{11}$

8

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.12 (m, 1H), 8.52 (dd, *J* = 9.1, 6.1 Hz, 1H), 8.28 (m, 1H), 8.13 (d, *J* = 7.5 Hz, 1H), 8.03 – 7.81 (m, 2H), 7.74 – 7.50 (m, 1H), 7.43 – 7.14 (m, 5H), 7.11 (d, *J* = 8.9 Hz, 1H), 5.45 – 5.18 (m, 1H), 4.73 (dd, *J* = 9.9, 3.0 Hz, 1H), 4.50 – 4.24 (m, 3H), 4.24 – 4.08 (m, 4H), 4.08 – 3.92 (m, 2H), 3.69 (d, *J* = 30.0 Hz, 19H), 3.53 (td, *J* = 9.7, 7.5, 4.6 Hz, 4H), 2.96 (dd, *J* = 13.5, 9.7 Hz, 2H), 2.20 (t, *J* = 8.5 Hz, 2H), 2.08 – 1.81 (m, 3H), 1.68 (q, *J* = 12.3, 11.6 Hz, 3H), 1.38 (dd, *J* = 18.7, 7.7 Hz, 7H), 1.24 (s, 6H), 1.19 – 0.93 (m, 6H), 0.93 – 0.68 (m, 14H), 0.68 – 0.43 (m, 5H); HRMS: (+ESI) Calc. for $C_{58}H_{98}N_{15}O_{15}$: 1243.7289 $[M+H]^+$, Found: 1242.7454 $[M+H]^+$.

2.7 Synthesis of fluorescent labelled stereoisomer of teixobactin



Scheme 10

The compound **31** was synthesized using the similar strategy for compounds **1** with Gln replaced by Cbz-protected Lys residue. The crude compound **31** was dissolved in MeOH (10 mL), then CH_3COOH (0.1 mL) and $Pd(OH)_2$ (90 mg, 10% on carbon) were added to the solution. The reaction mixture was stirred under an atmosphere of H_2 for 10 hours to remove the Cbz and Bn groups. Then the reaction mixture was filtered through a pad of celite and the filtrated was concentrated *in vacuo* to give crude depsipeptide (30 mg, 0.02 mmol). Then **31-1** was redissolved in dry DMF (5 mL), 6-TAMRA (13 mg, 0.03 mmol), HATU (11 mg, 0.03 mmol) and DIPEA (16 µL, 0.09 mmol) were added to the solution. The reaction mixture was stirred at room temperature for 12 hours then concentrated *in vacuo*. The resulting

crude peptide was purified using RP-HPLC to give a red solid (18 mg, 33%). The red solid was dissolved in a mixture of TFA:Et_3SiH:H_2O (95:2.5:2.5 v/v/v, 10 mL) and the mixture was stirred for 3 h. Afterward, the mixture was concentrated *in vacuo*, and the rude peptide was precipitated with cold Et_2O and centrifuged at 7000 rpm to give a red solid. This solid was further purified by RP-HPLC (General method) to afford **32** as a red solid (6.6 mg, 5% from intermediate **28**). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.10 (m, 2H), 8.77 (t, *J* = 5.6 Hz, 1H), 8.53 (d, *J* = 8.2 Hz, 1H), 8.32 (d, *J* = 8.3 Hz, 1H), 8.26 (d, *J* = 8.3 Hz, 1H), 8.13 (d, *J* = 7.7 Hz, 1H), 8.00 (d, *J* = 7.4 Hz, 1H), 7.92 (q, *J* = 7.3, 6.1 Hz, 3H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 7.2 Hz, 3H), 7.27 (s, 1H), 7.23 (t, *J* = 9.2 Hz, 3H), 7.17 (s, 1H), 7.10 (d, *J* = 9.7 Hz, 2H), 7.07 – 6.97 (m, 4H), 6.69 (s, 1H), 5.33 (t, *J* = 4.9 Hz, 2H), 4.70 (p, *J* = 6.9 Hz, 2H), 4.42 – 4.28 (m, 3H), 4.18 (m, 4H), 3.97 (q, *J* = 7.1 Hz, 3H), 3.17 – 3.08 (m, 3H), 2.96 (ddt, *J* = 29.7, 12.1, 6.5 Hz, 5H), 2.09 – 1.91 (m, 8H), 1.82 – 1.62 (m, 4H), 1.62 – 1.53 (m, 3H), 1.46 (m, 10H), 1.24 (d, *J* = 3.7 Hz, 39H), 1.16 (dd, *J* = 13.4, 6.8 Hz, 5H), 1.10 – 0.94 (m, 4H), 0.86 (td, *J* = 6.9, 4.2 Hz, 7H), 0.83 – 0.68 (m, 11H), 0.68 – 0.50 (m, 4H); HRMS: (+ESI) Calc. for $C_{84}H_{121}N_{17}O_{18}$: 828.9533 $[M+2H]^{2+}$, Found: 828.9541 $[M+2H]^{2+}$.

3. Reference

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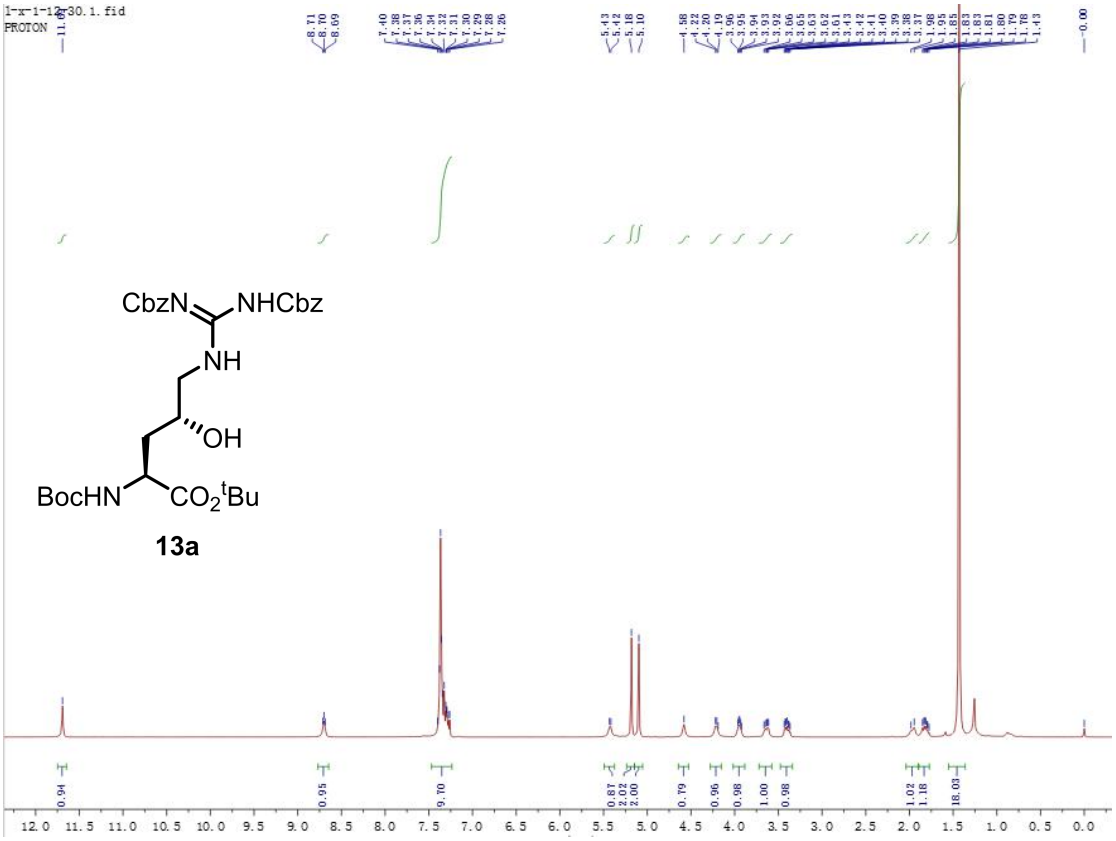
4. ^{1}H-NMR and ^{13}C-NMR Spectra



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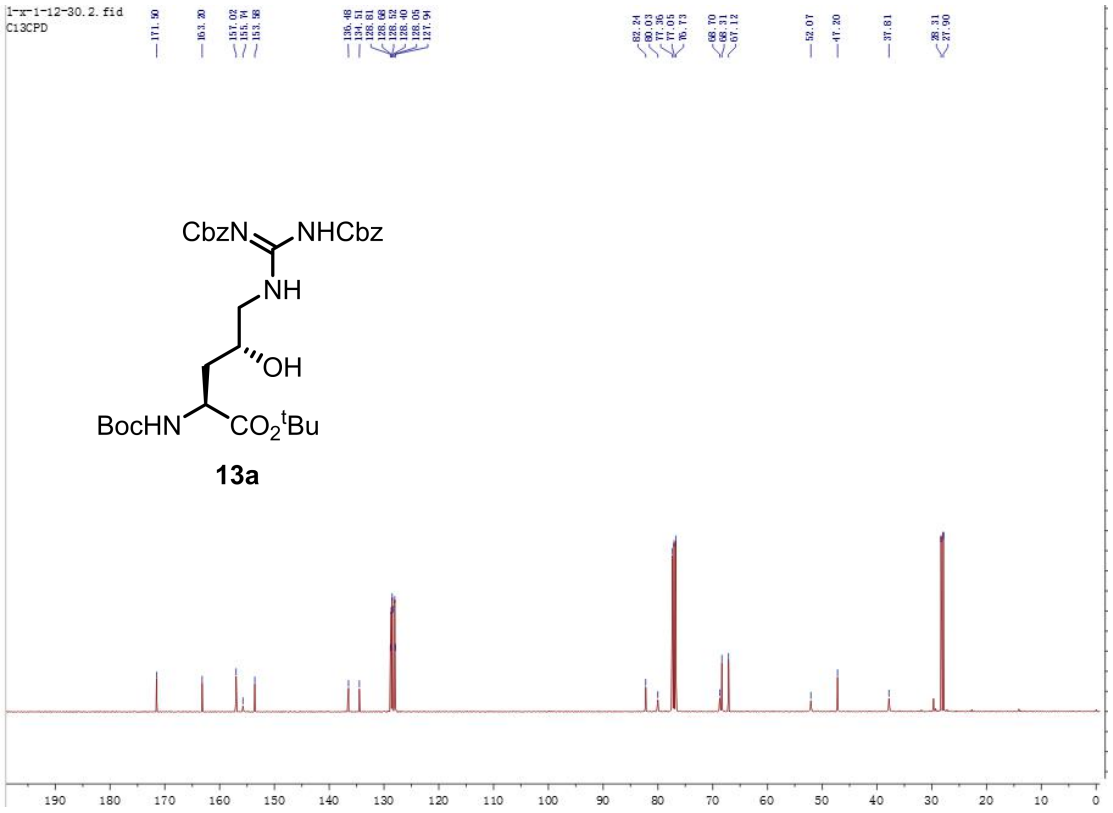

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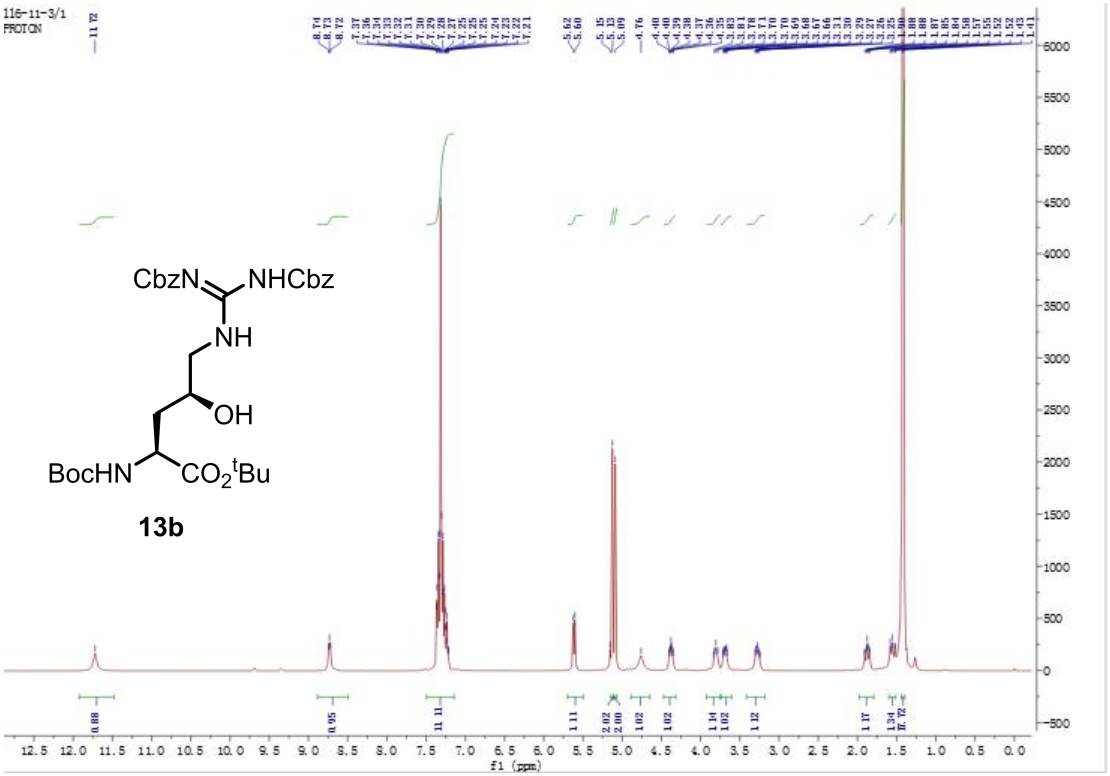
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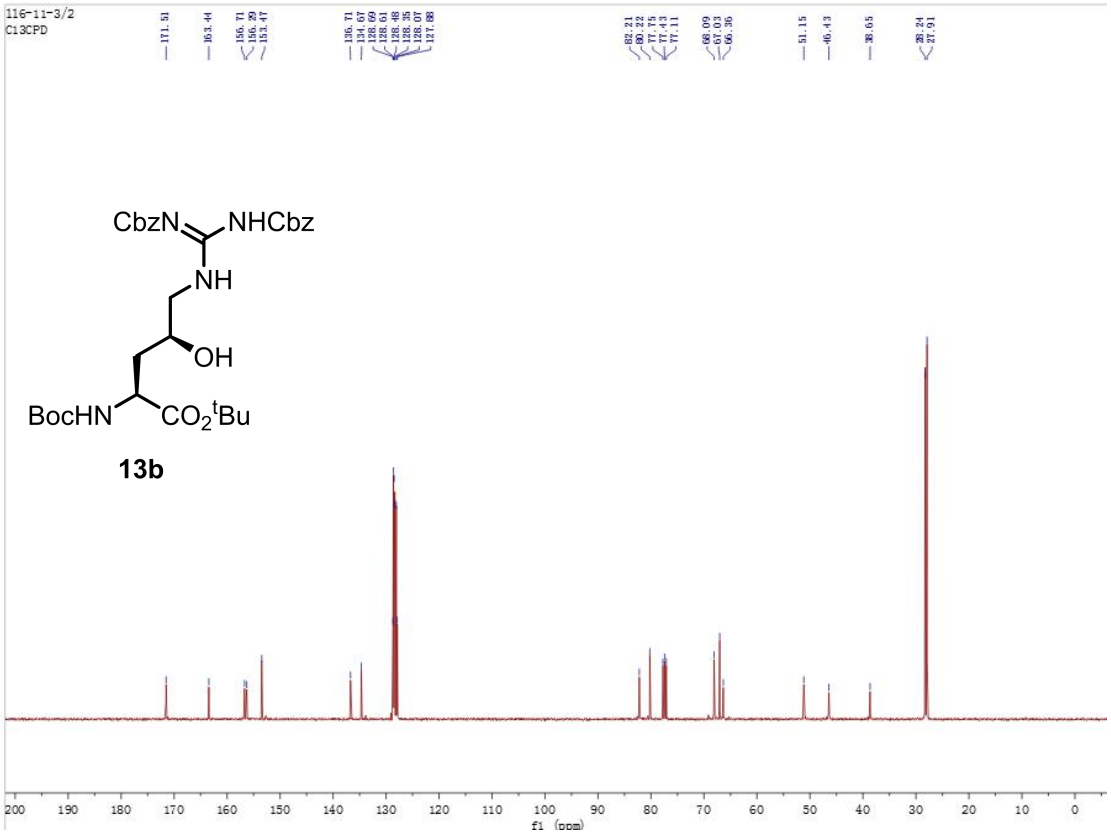
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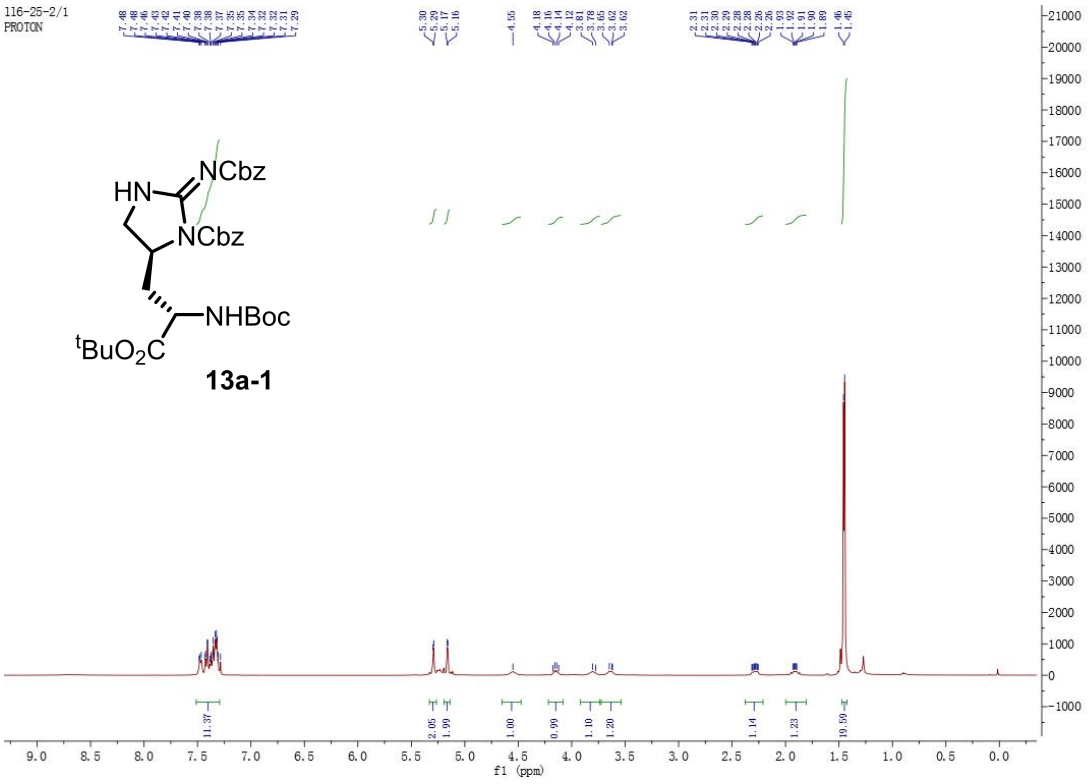
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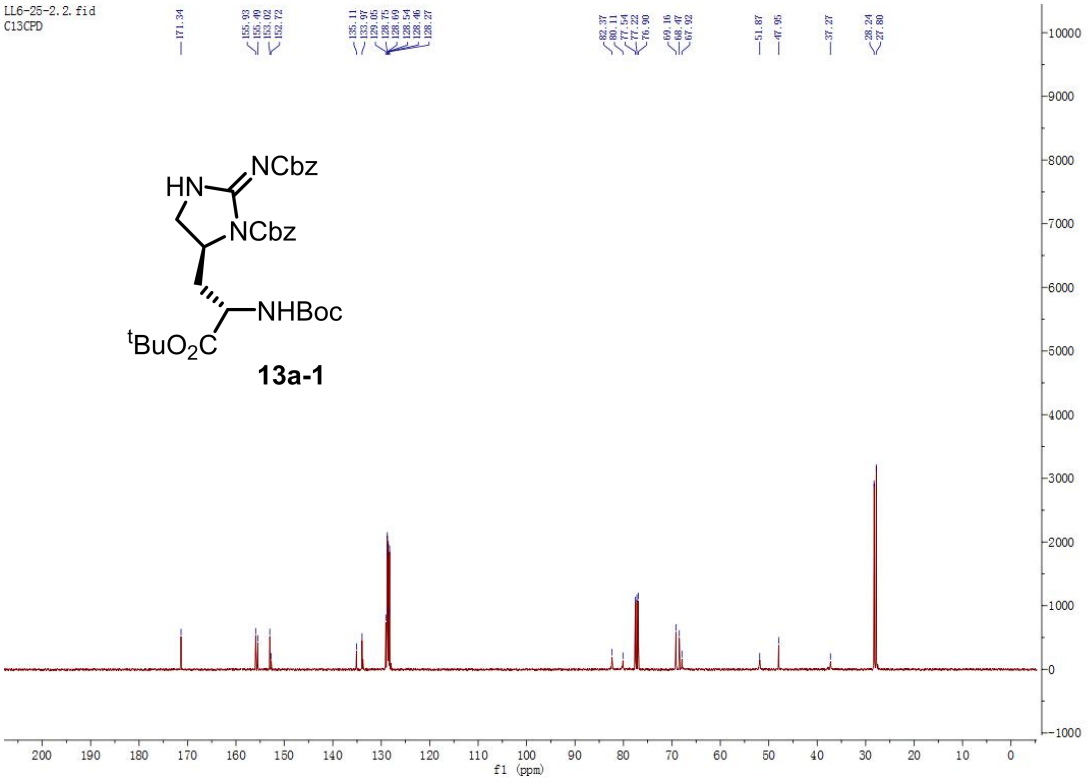
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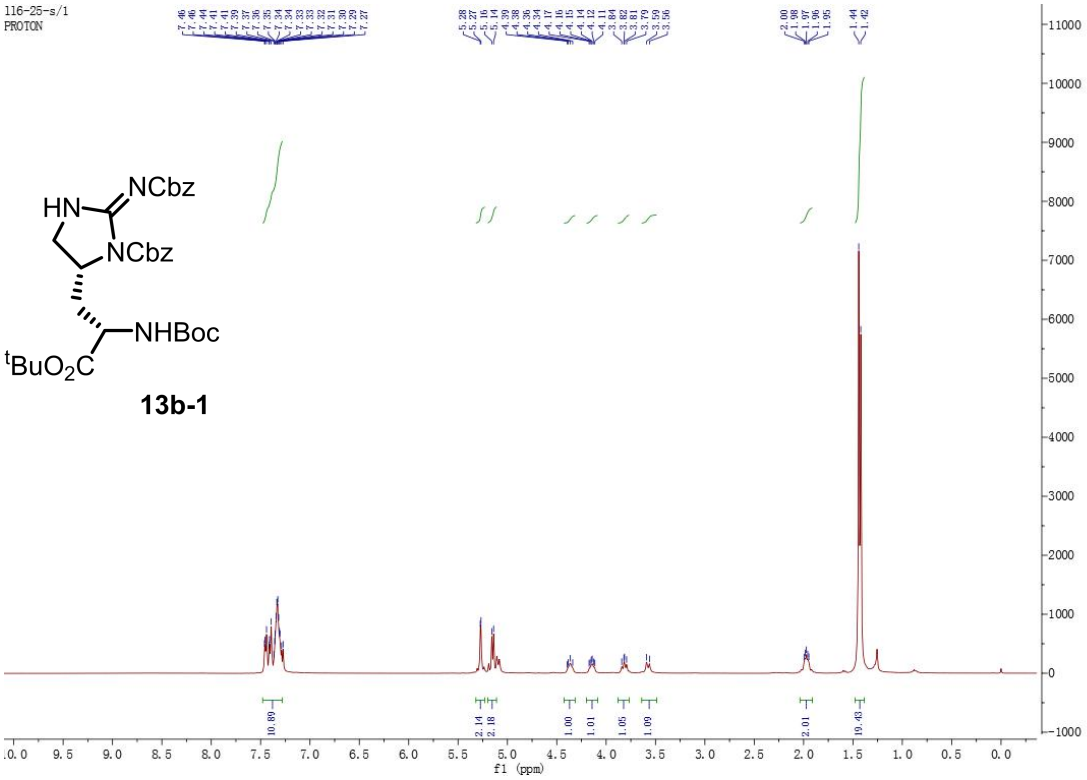
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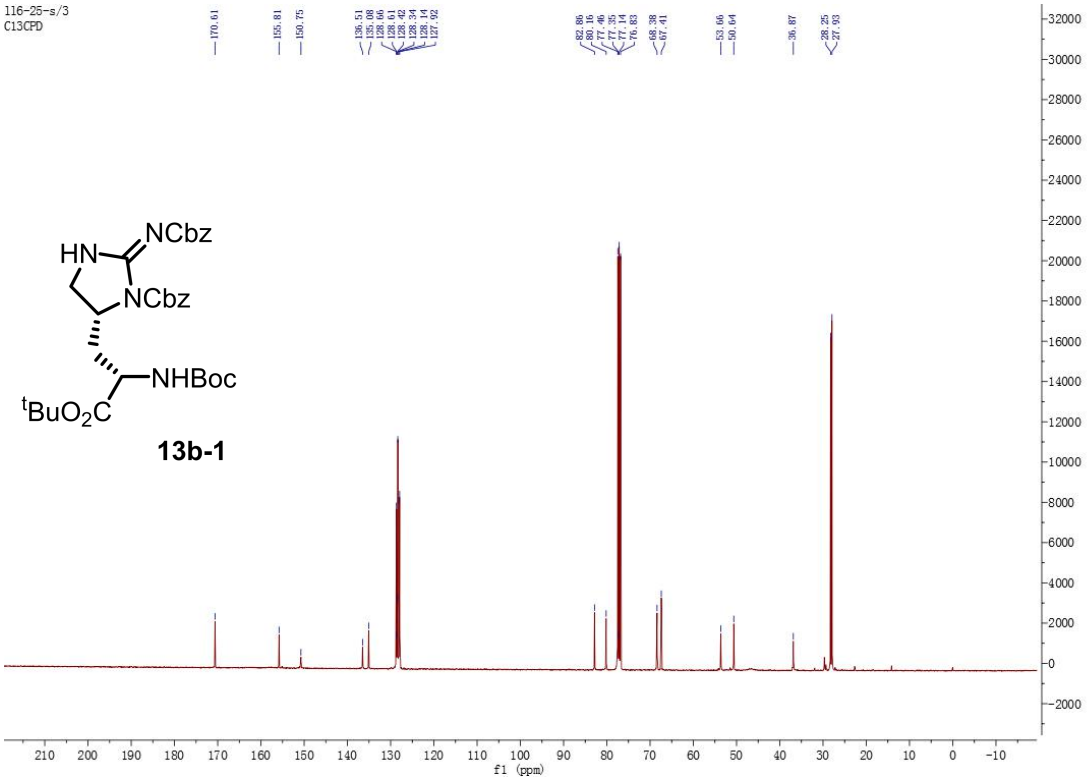
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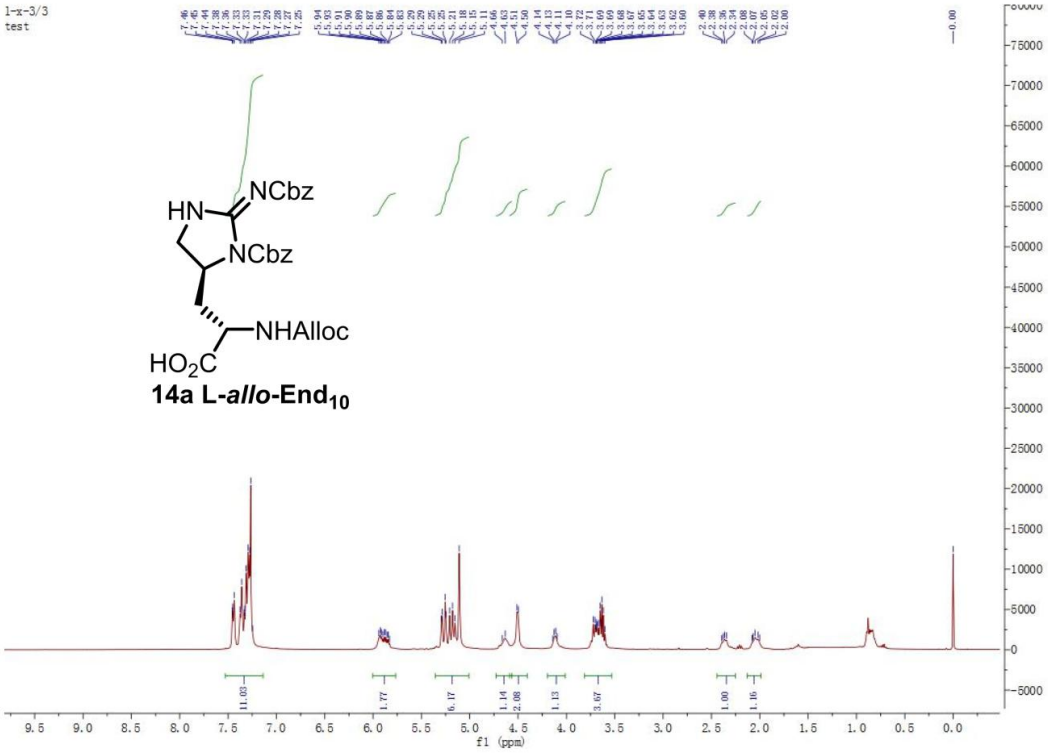
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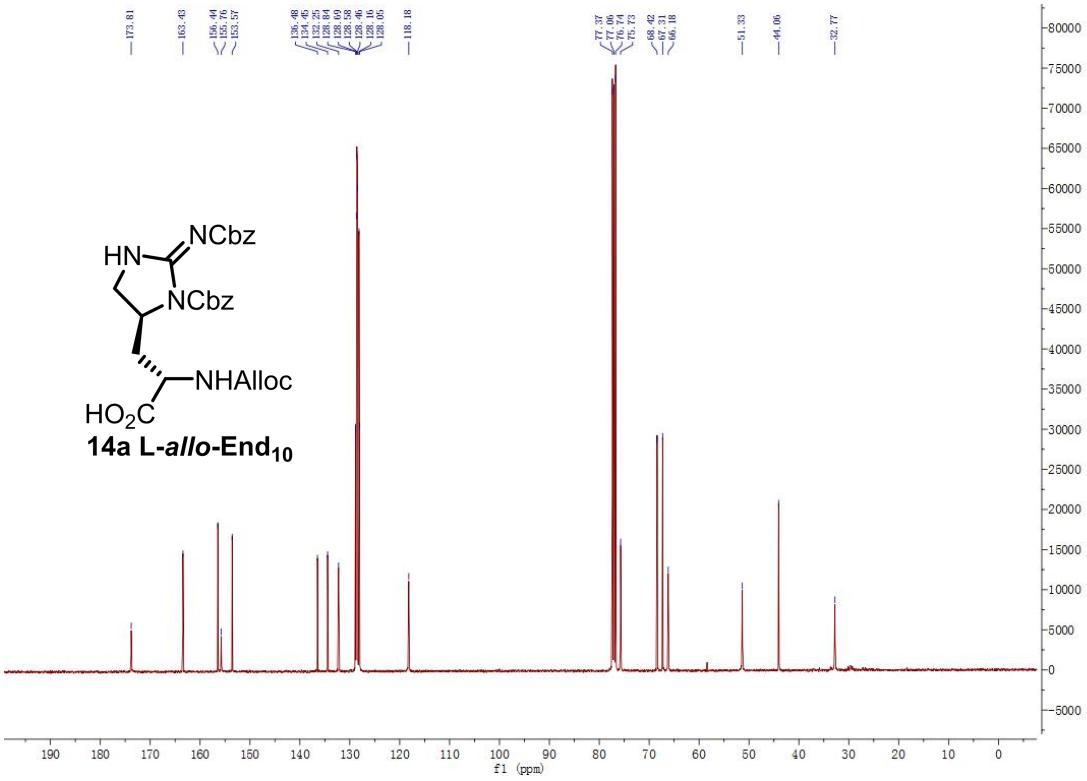
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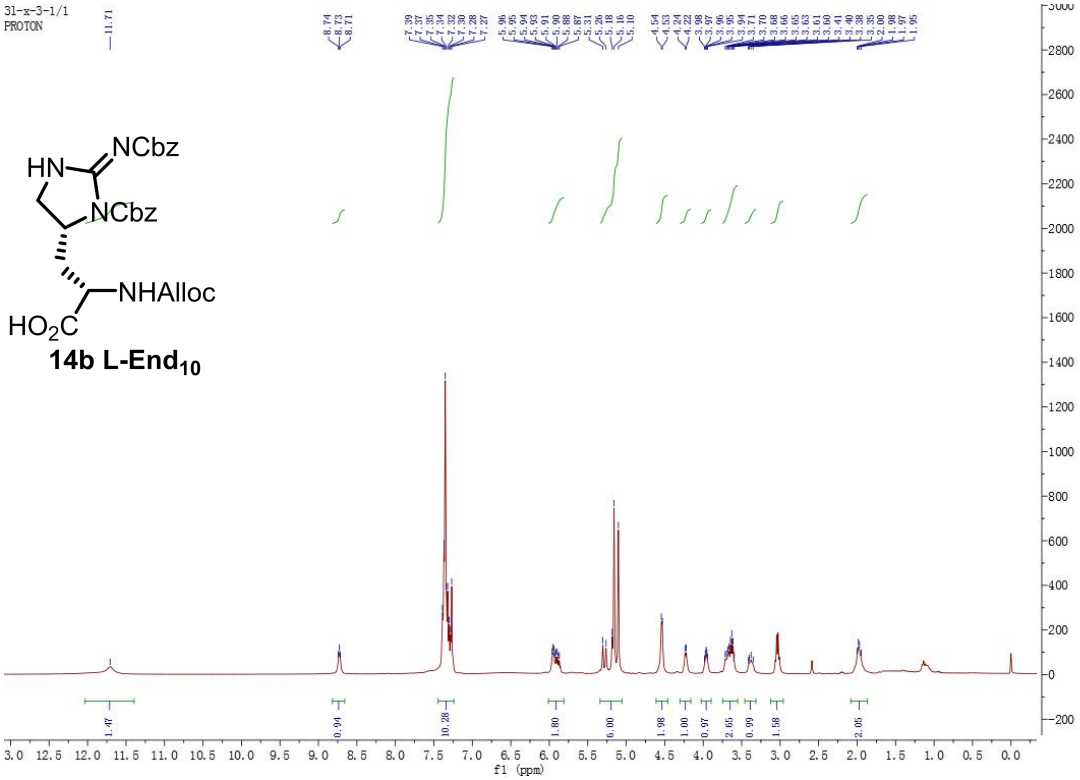
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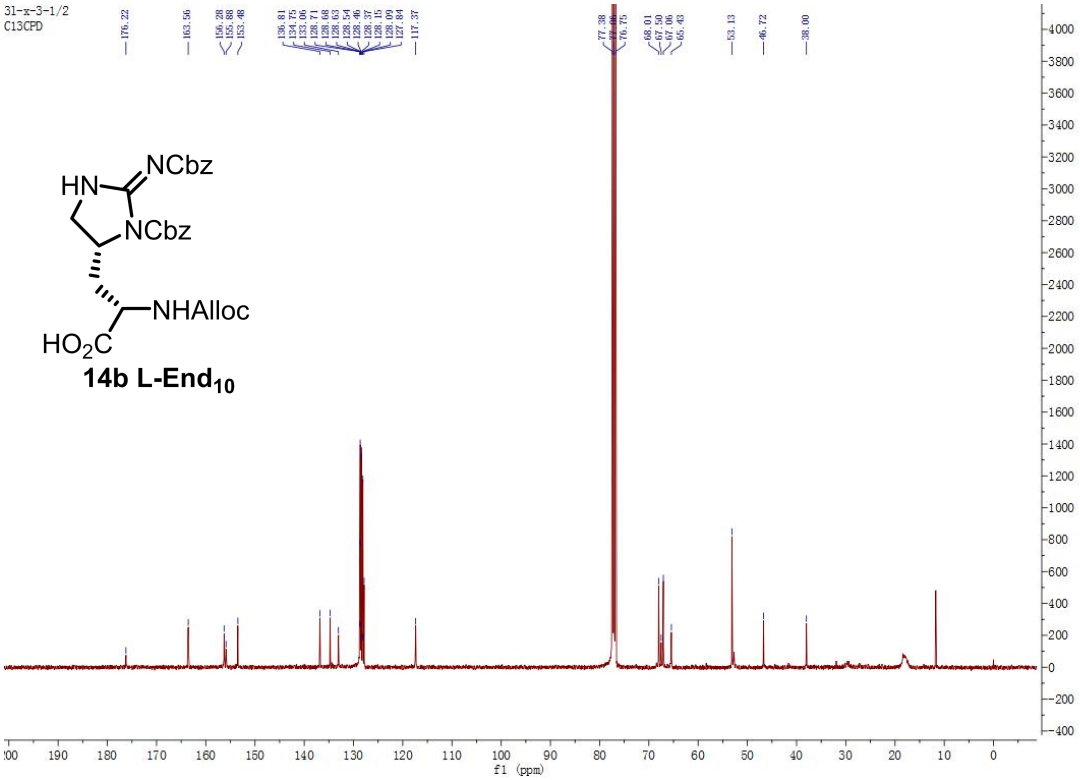
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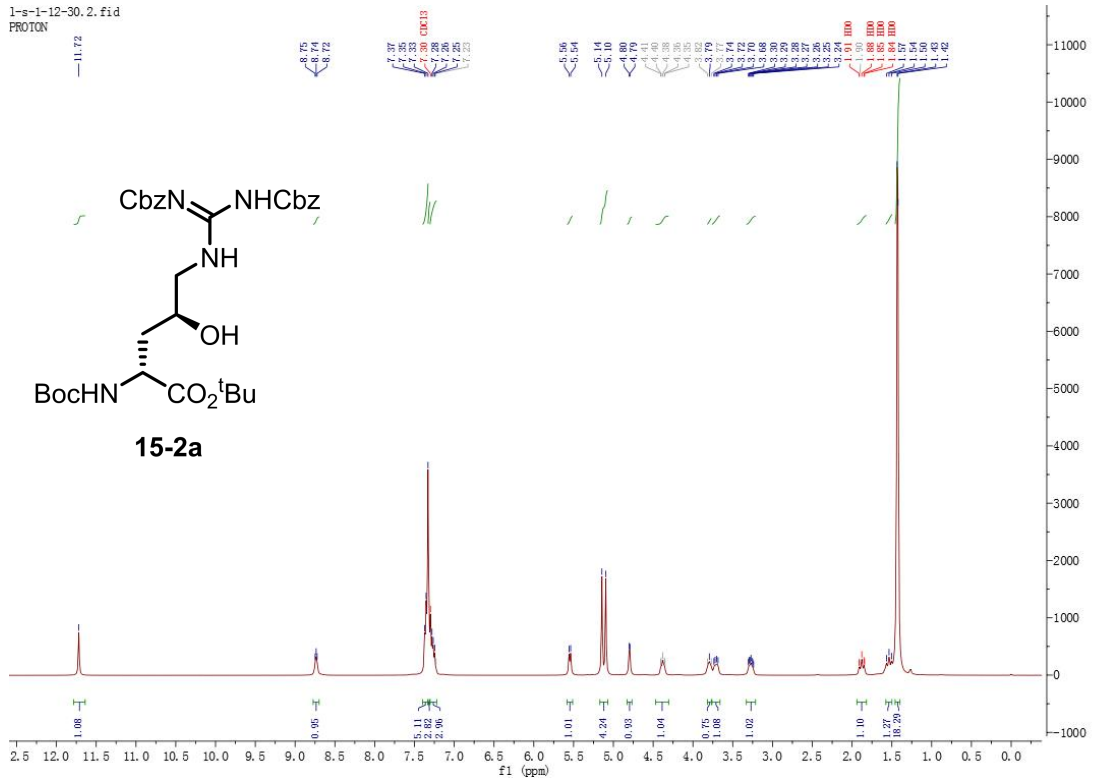
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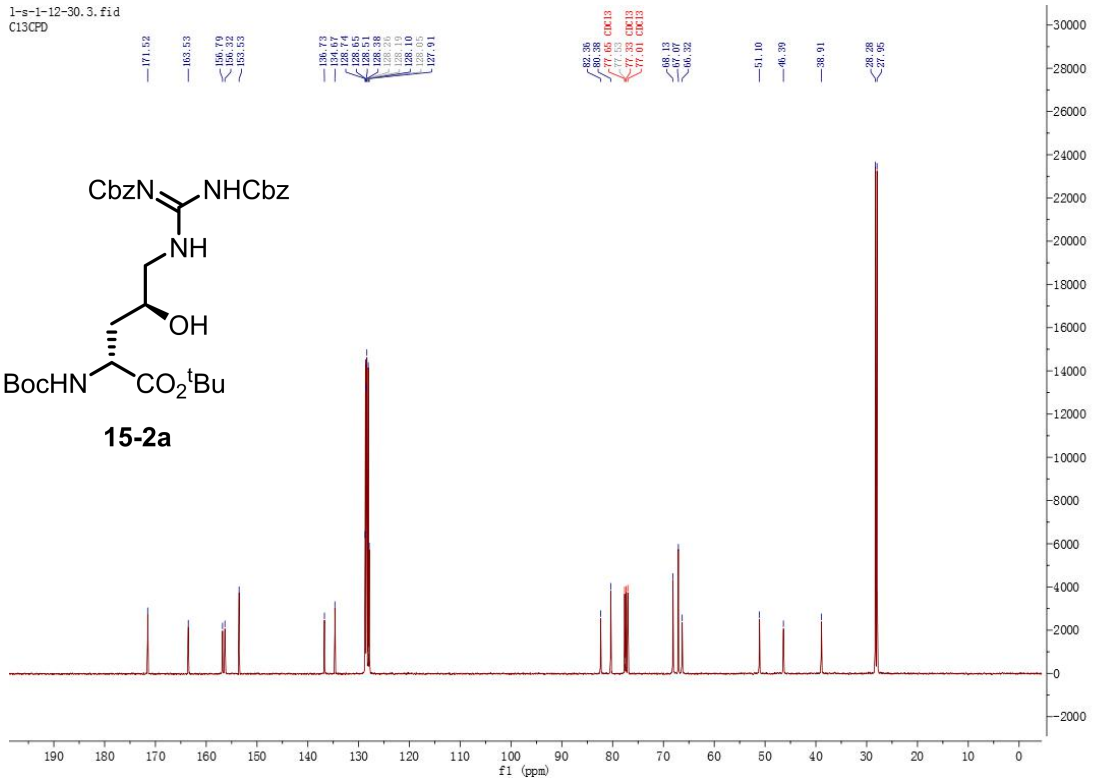
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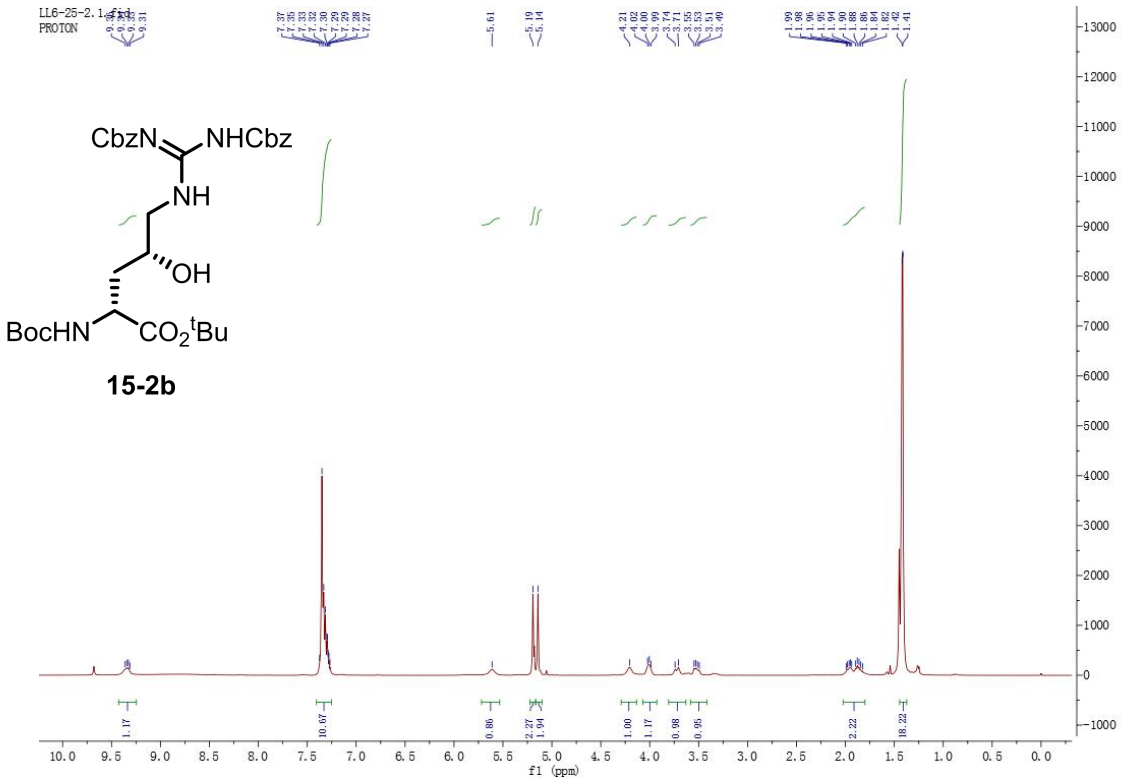
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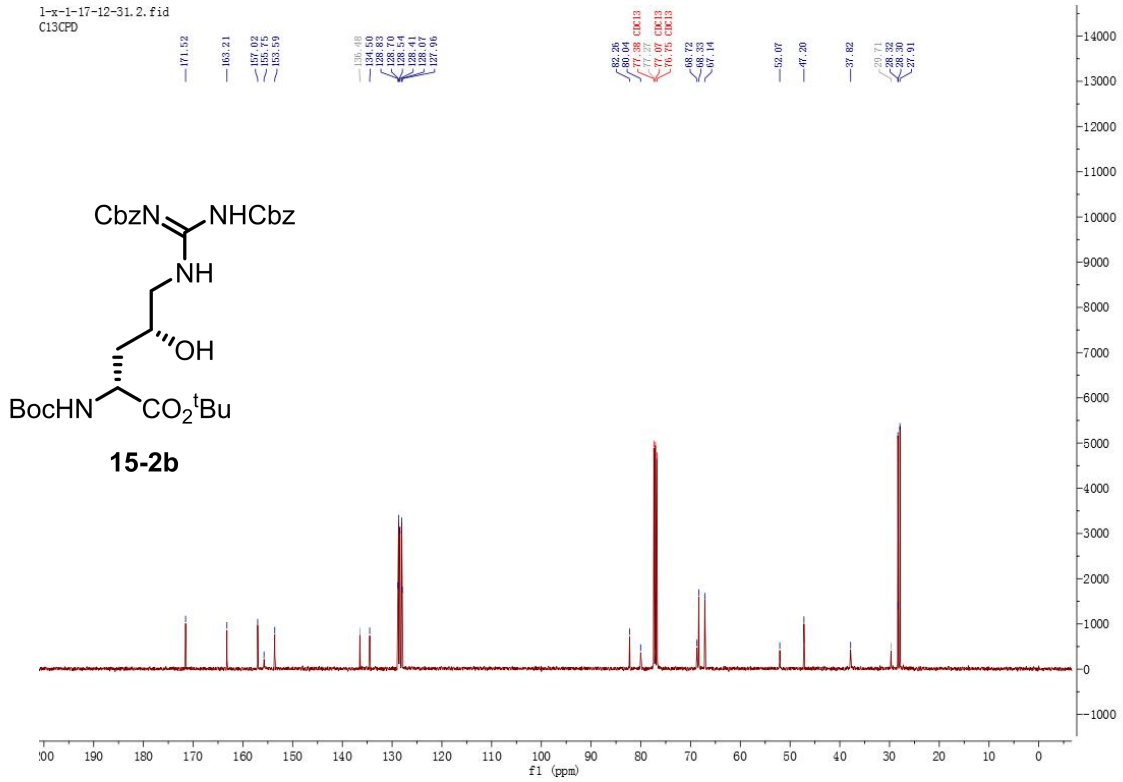
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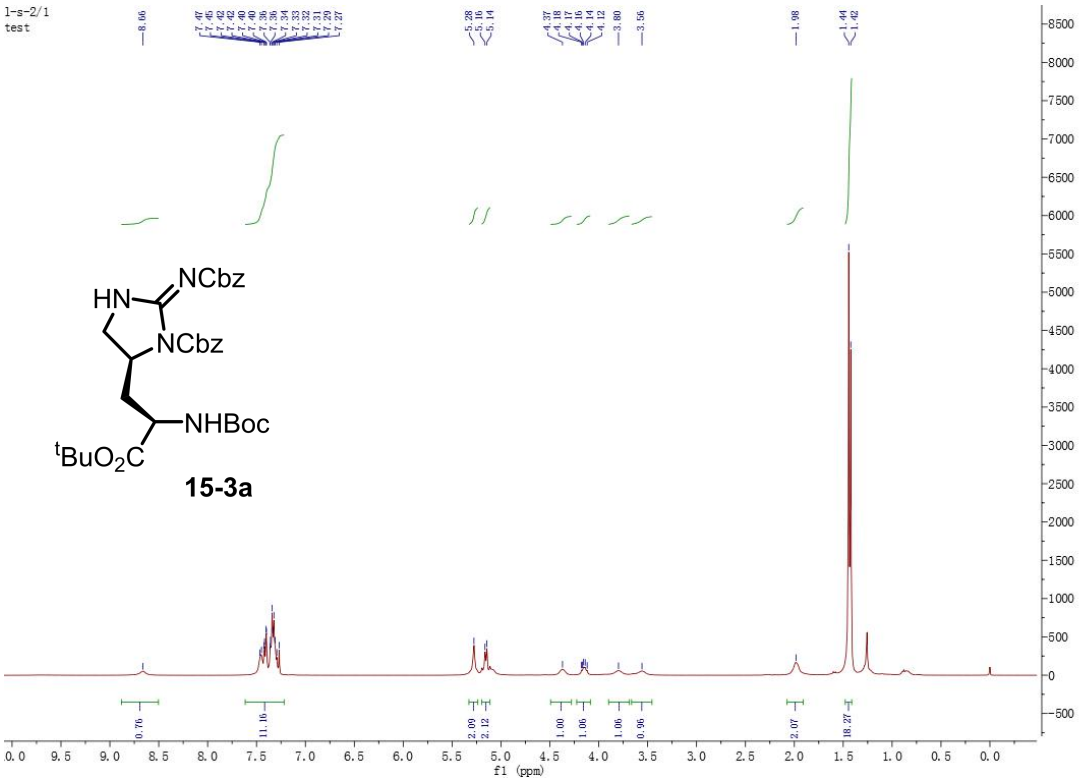
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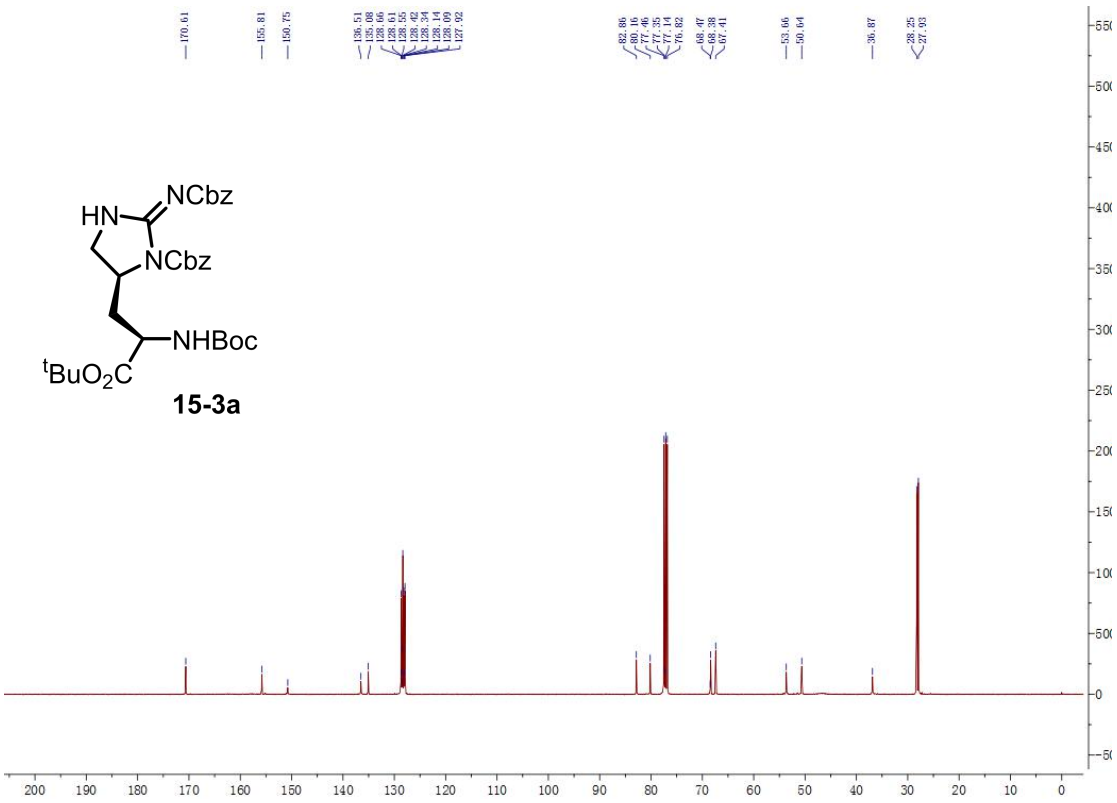
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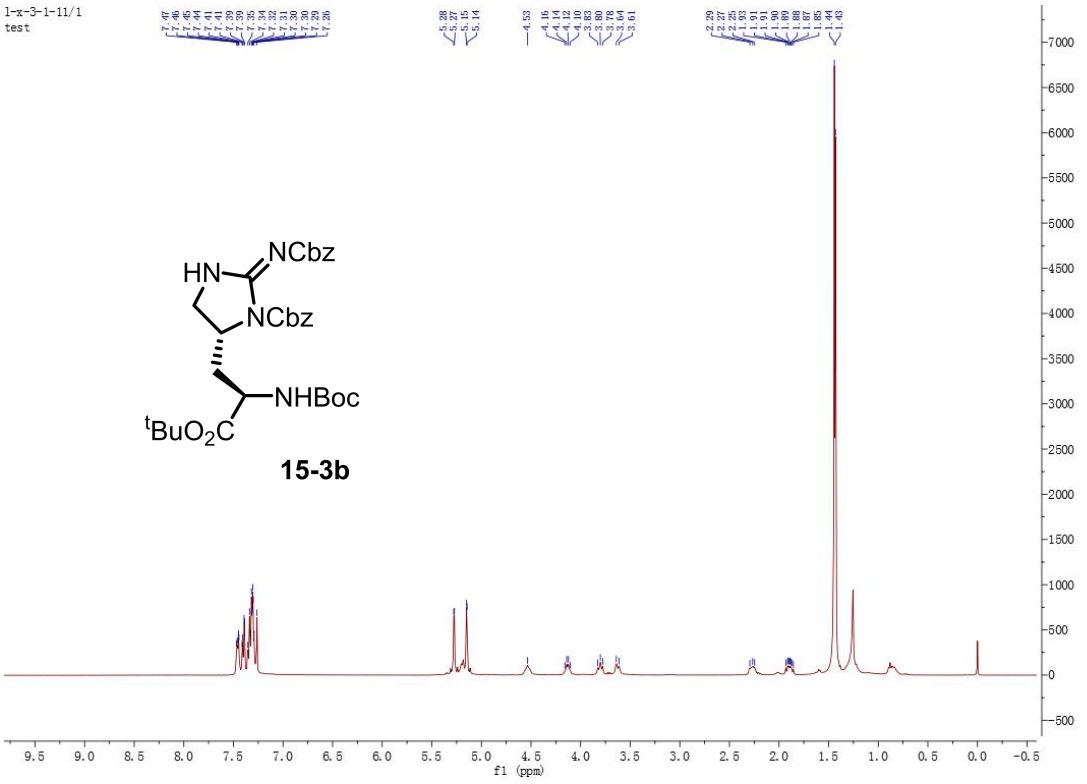
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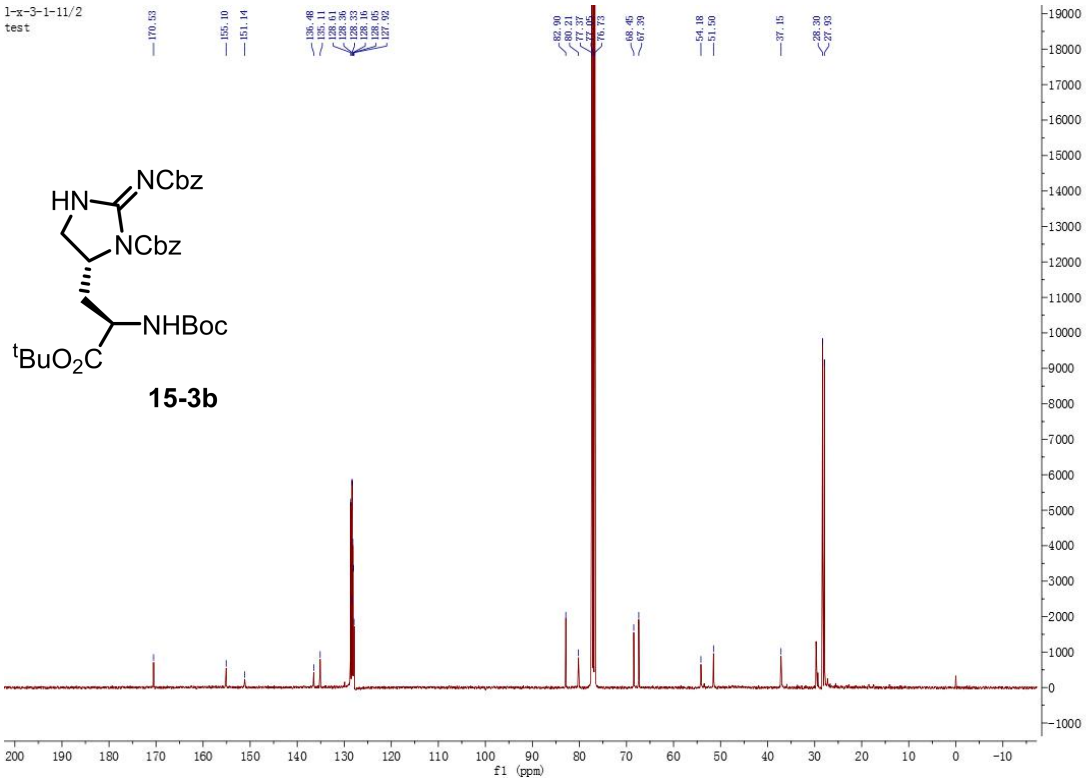
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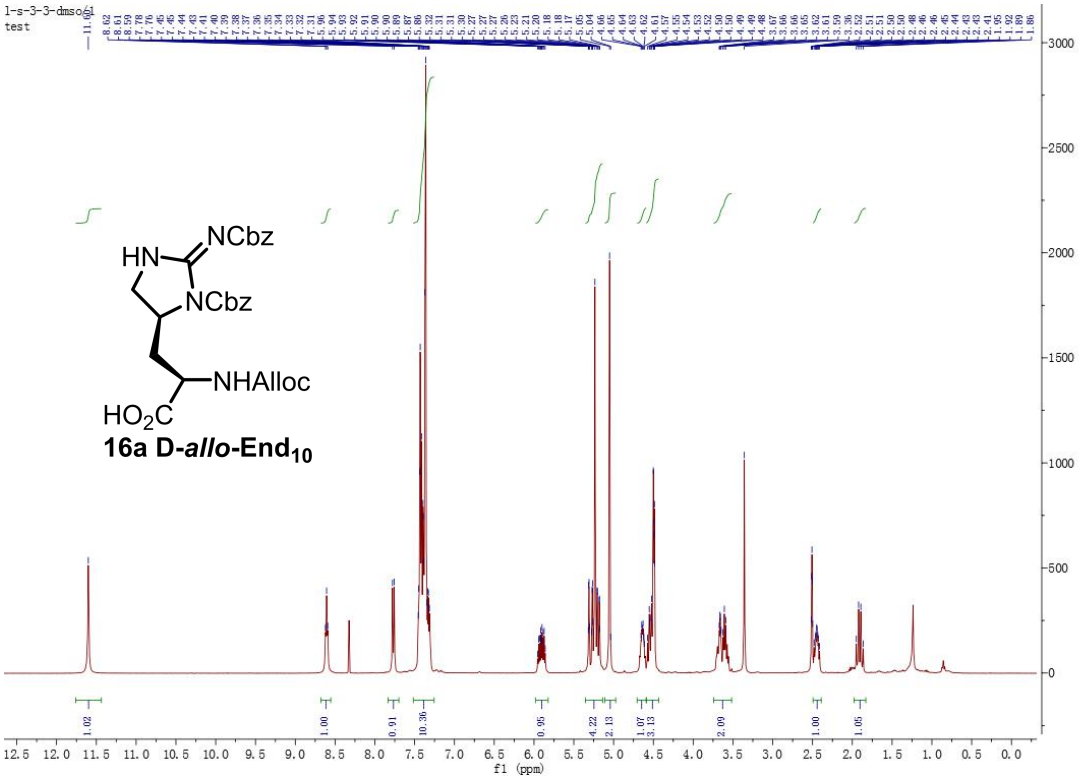
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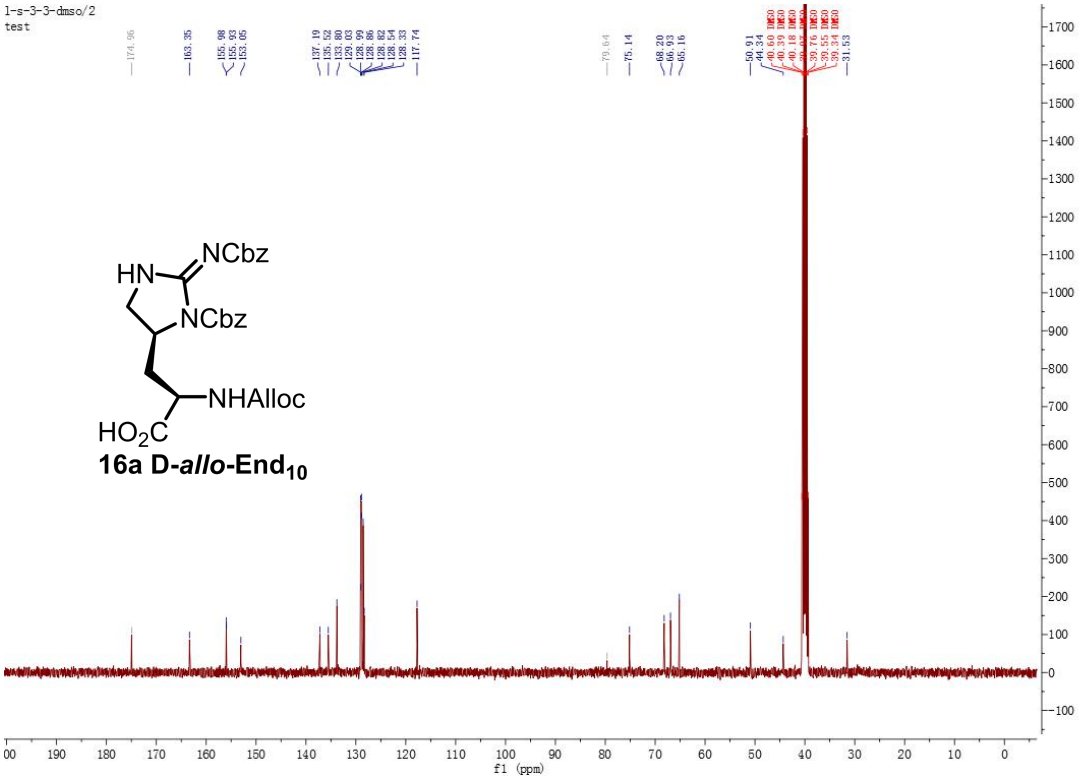
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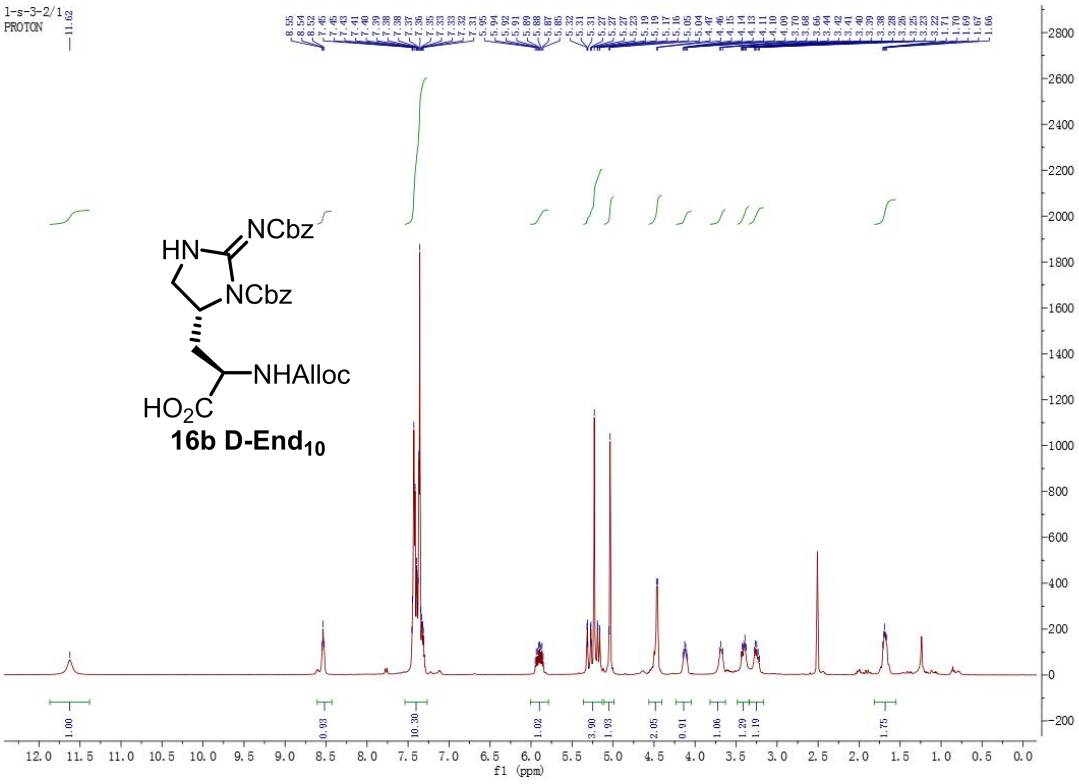
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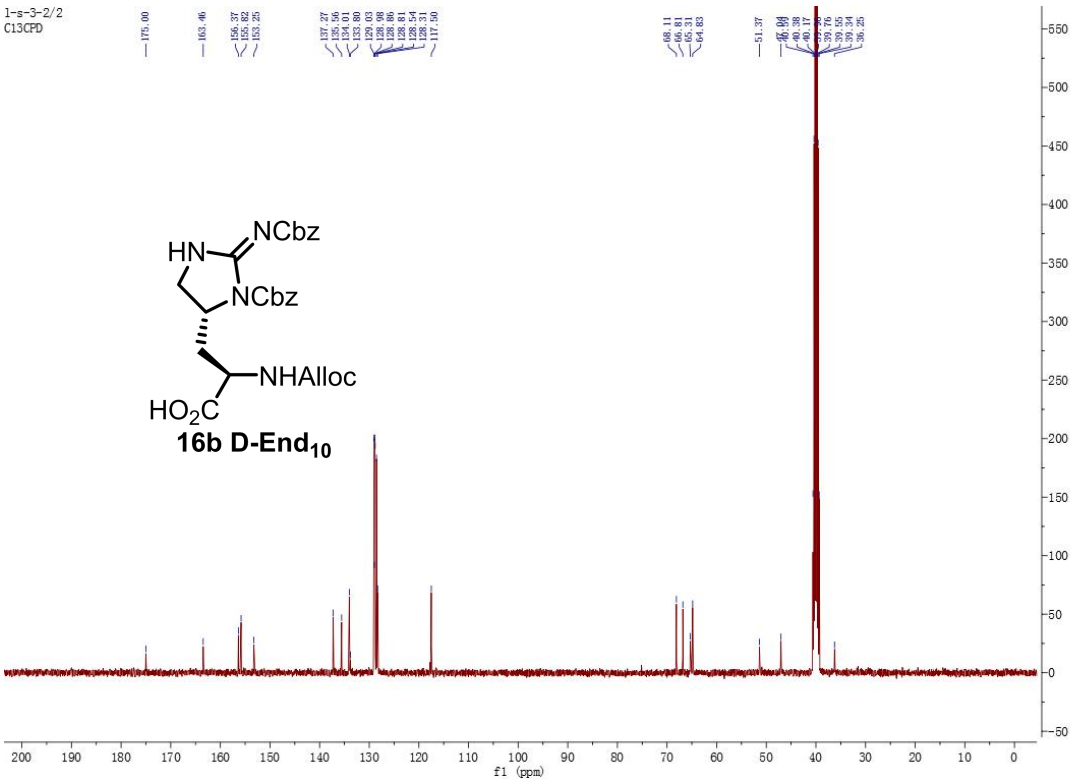
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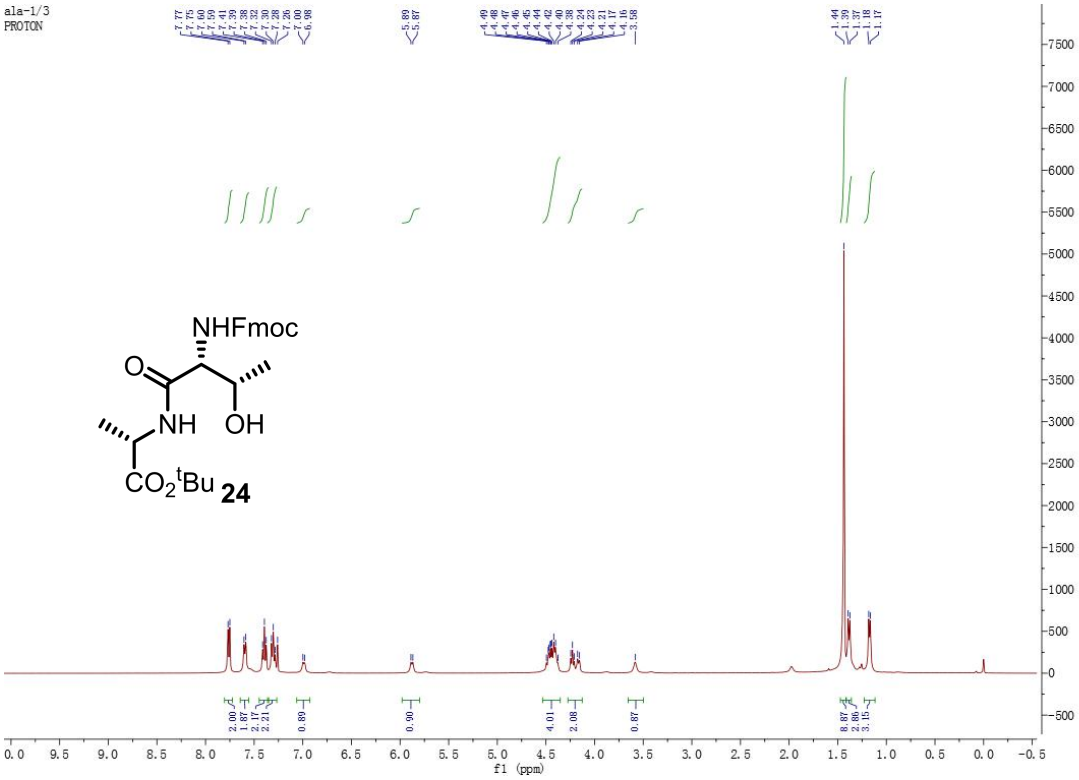
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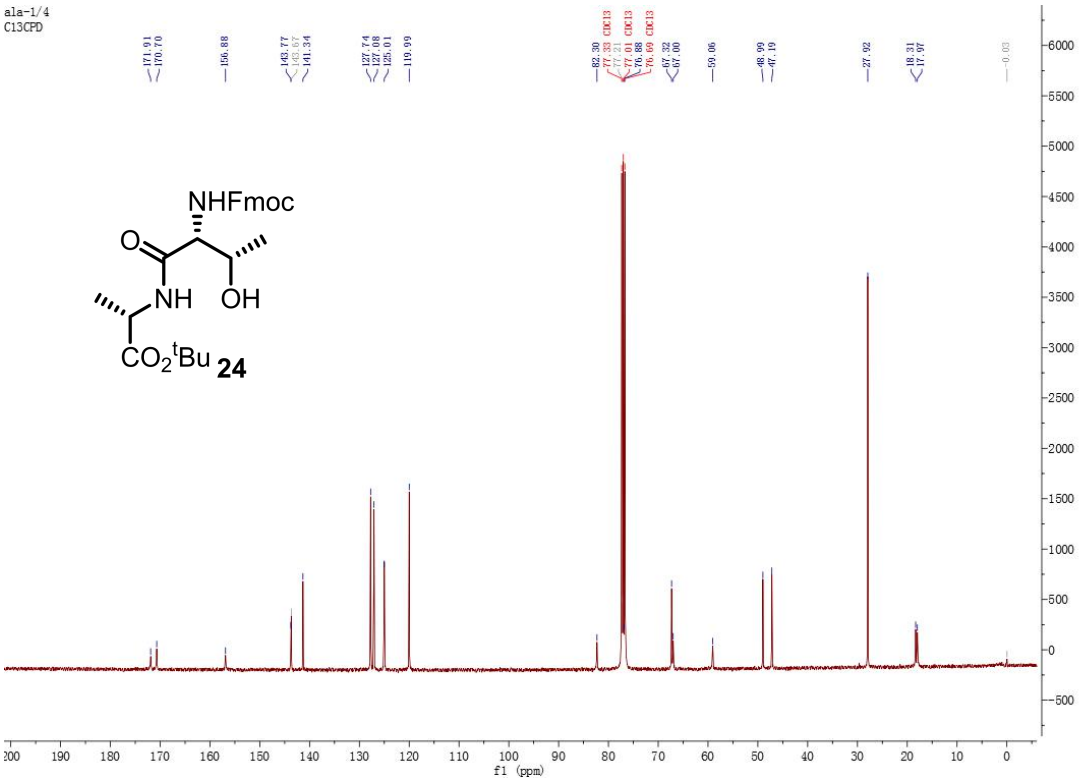
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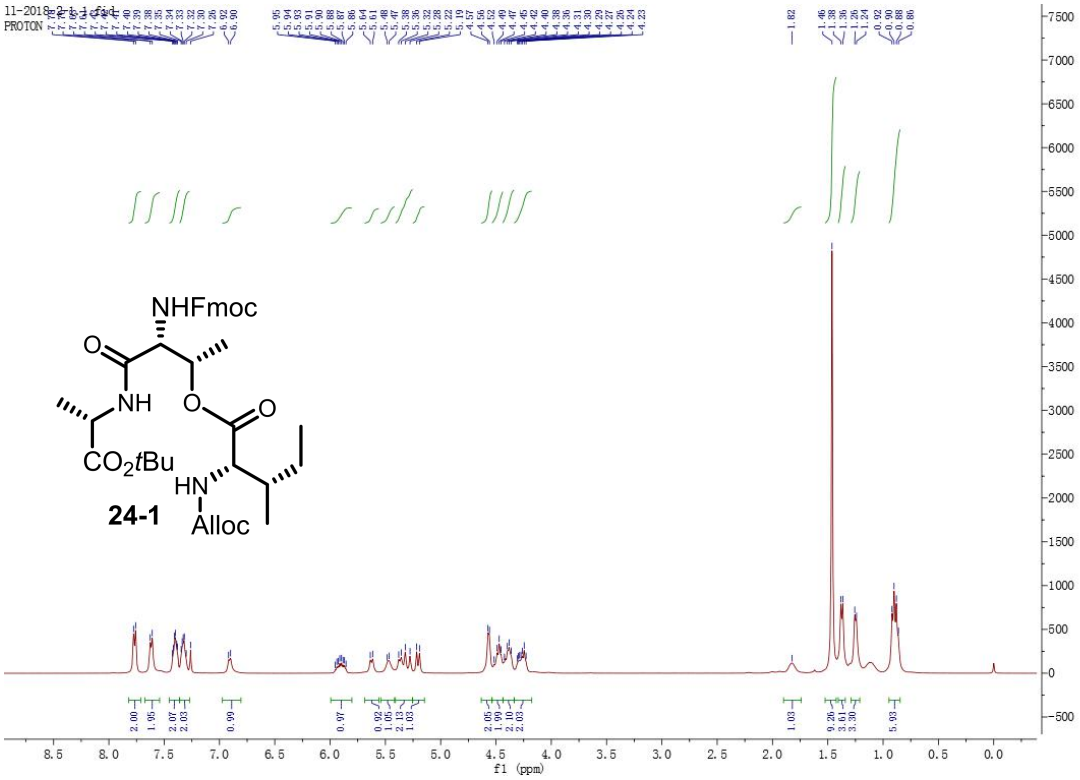
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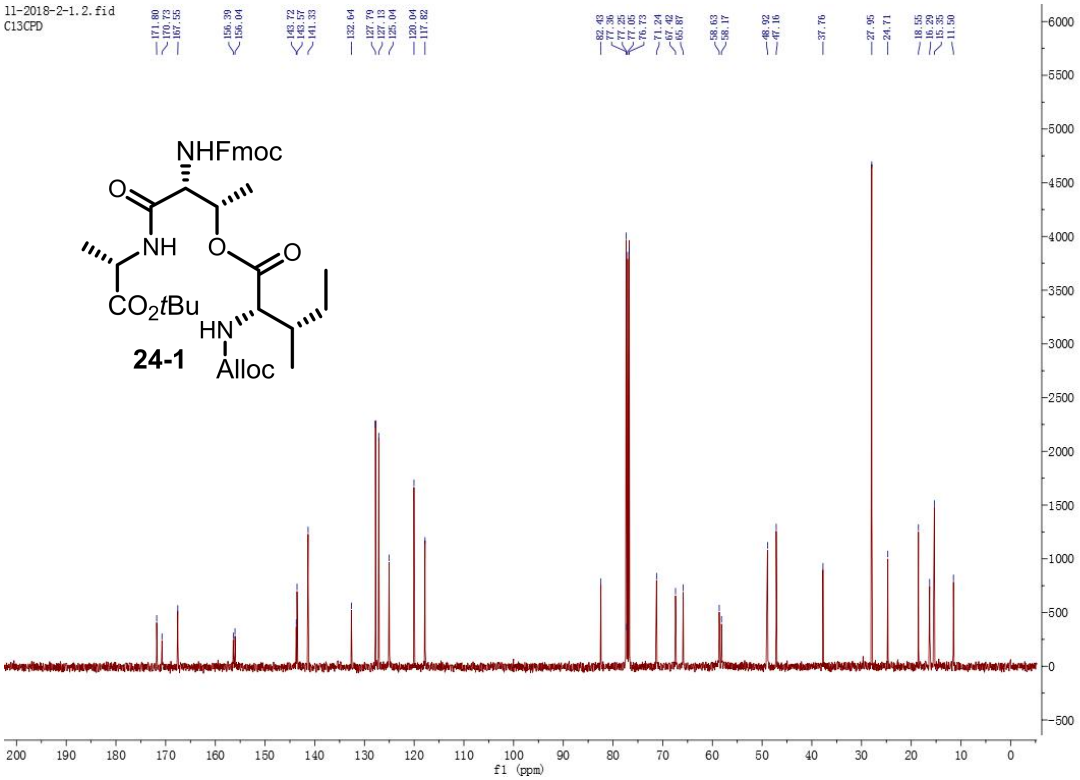
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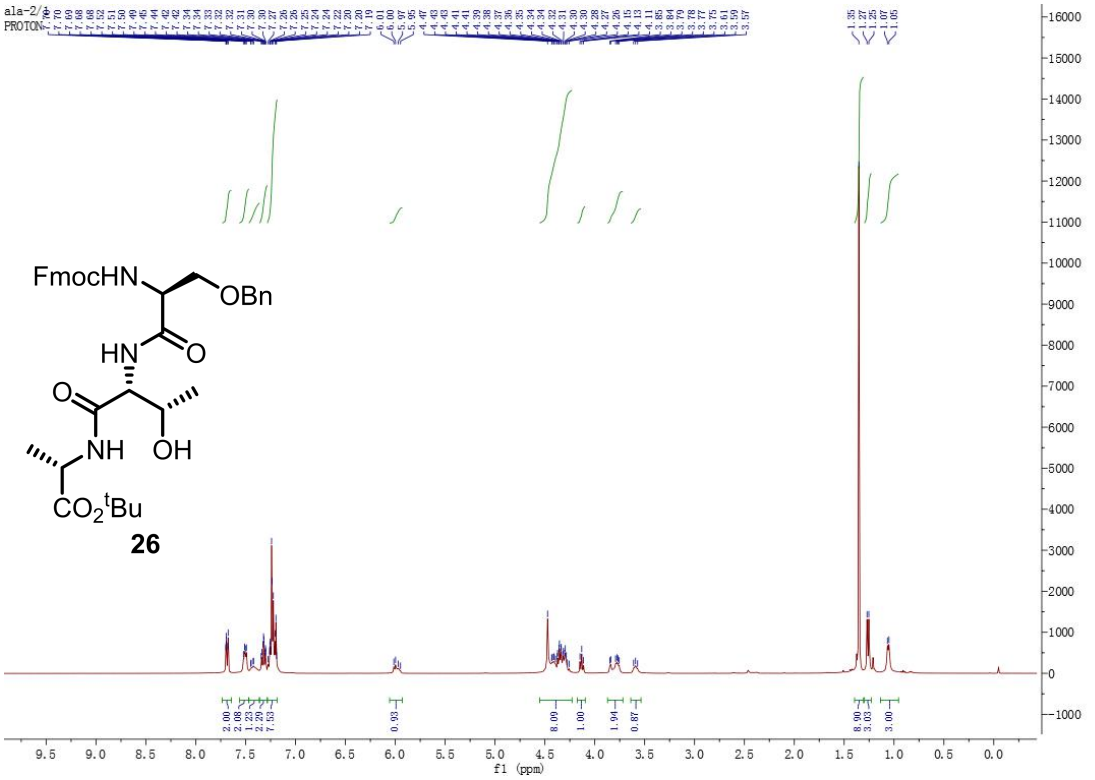
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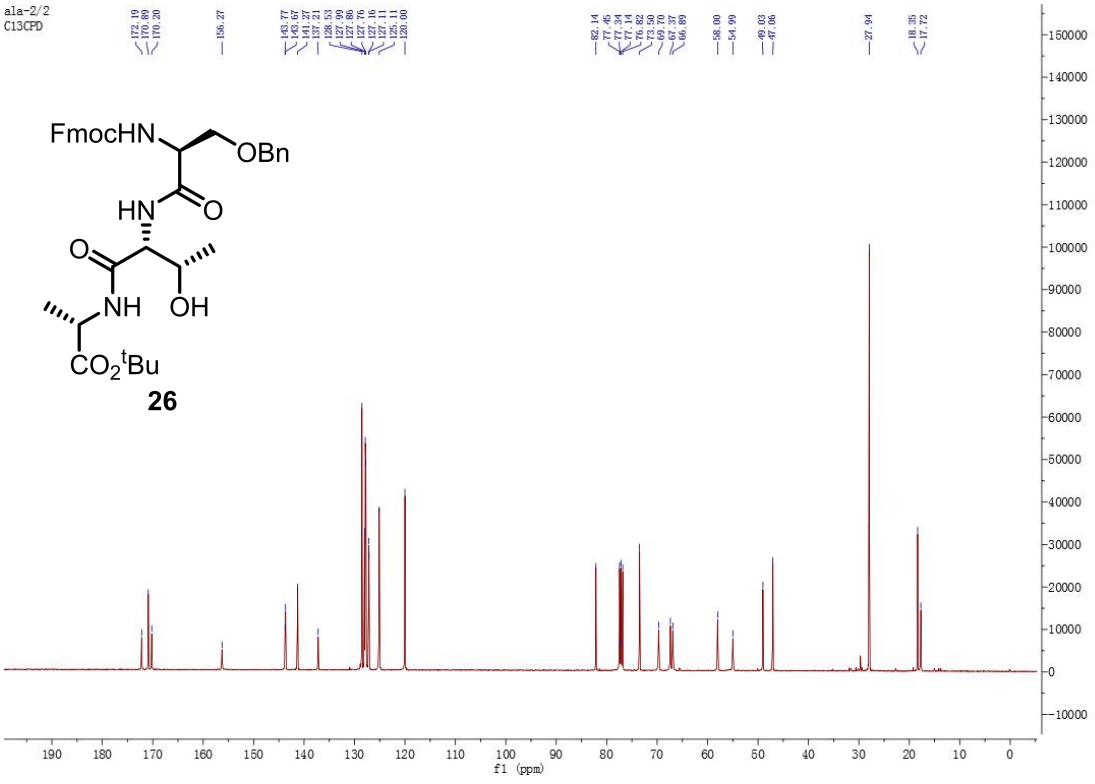
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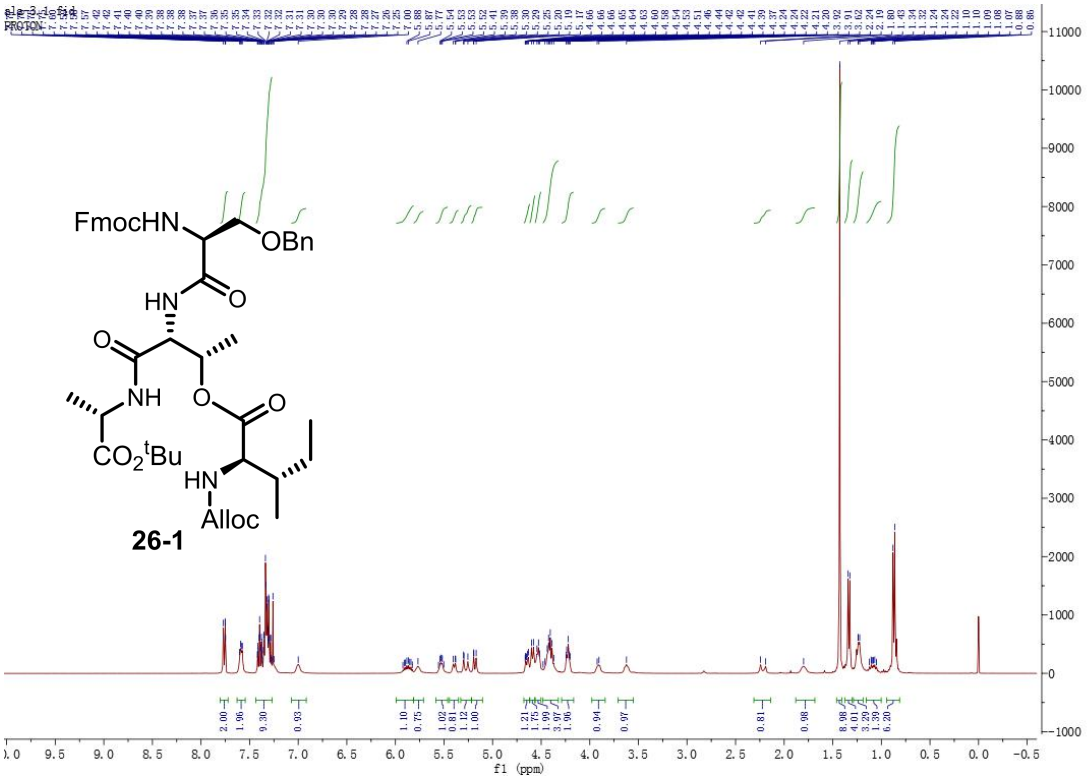
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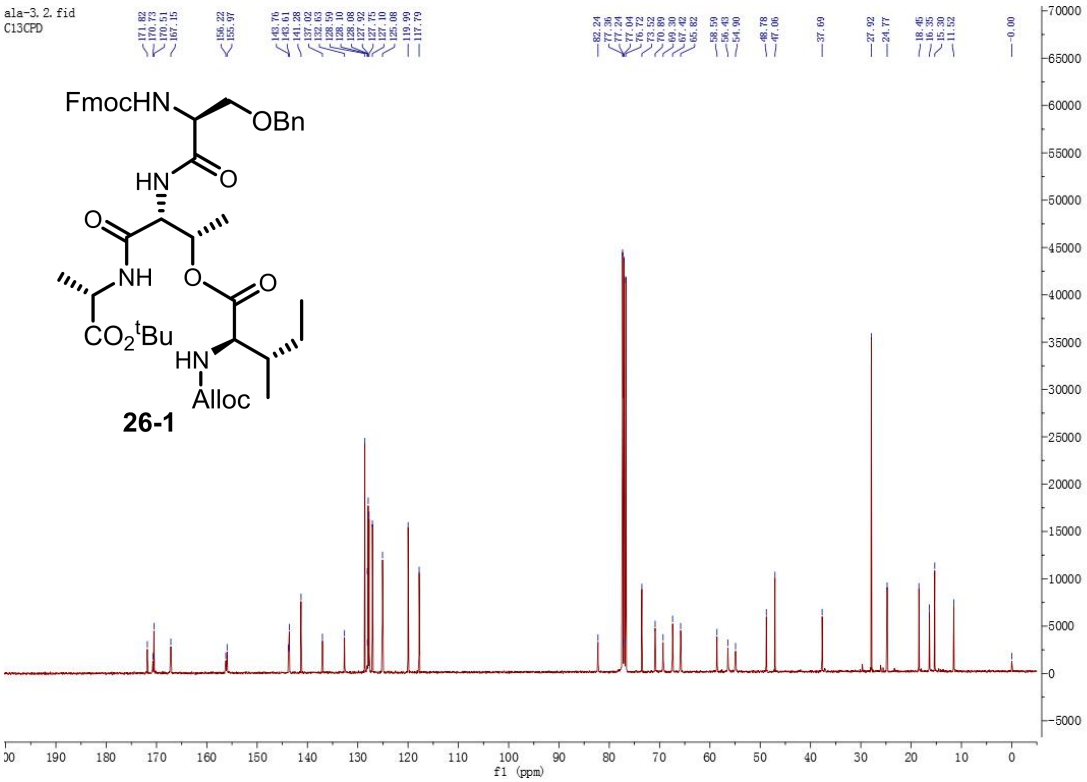
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5. ^{1}H-NMR spectra, high resolution mass spectra, and analytical HPLC spectra of teixobactin and its stereoisomers

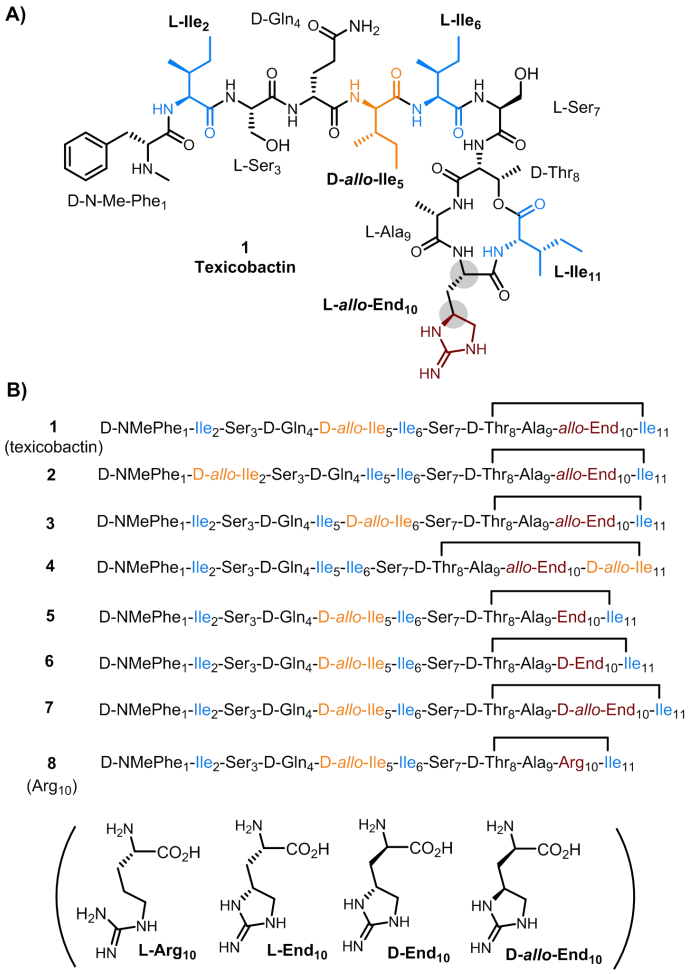
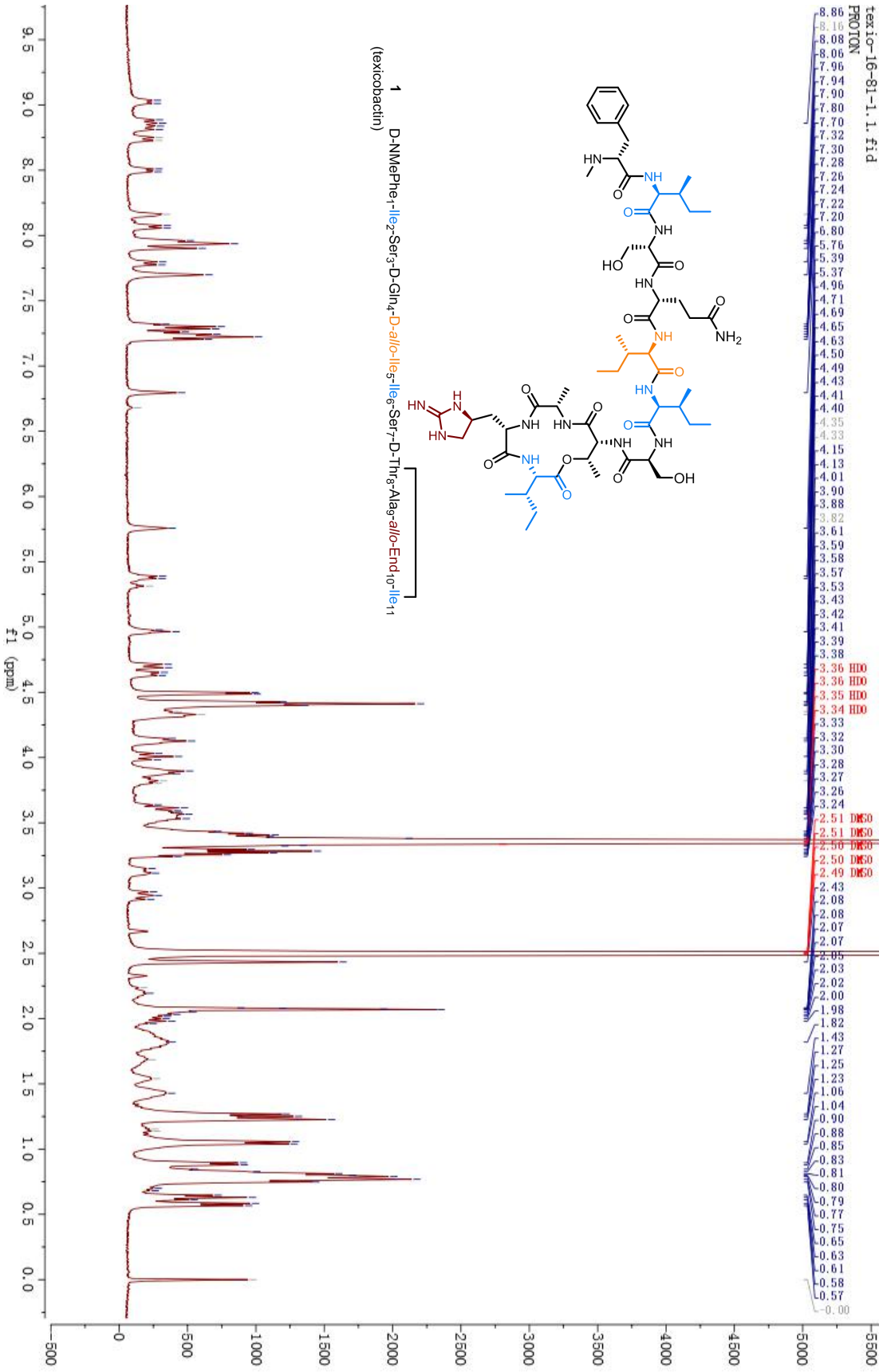


Figure S4. Structures of teixobactin and its synthetic stereoisomers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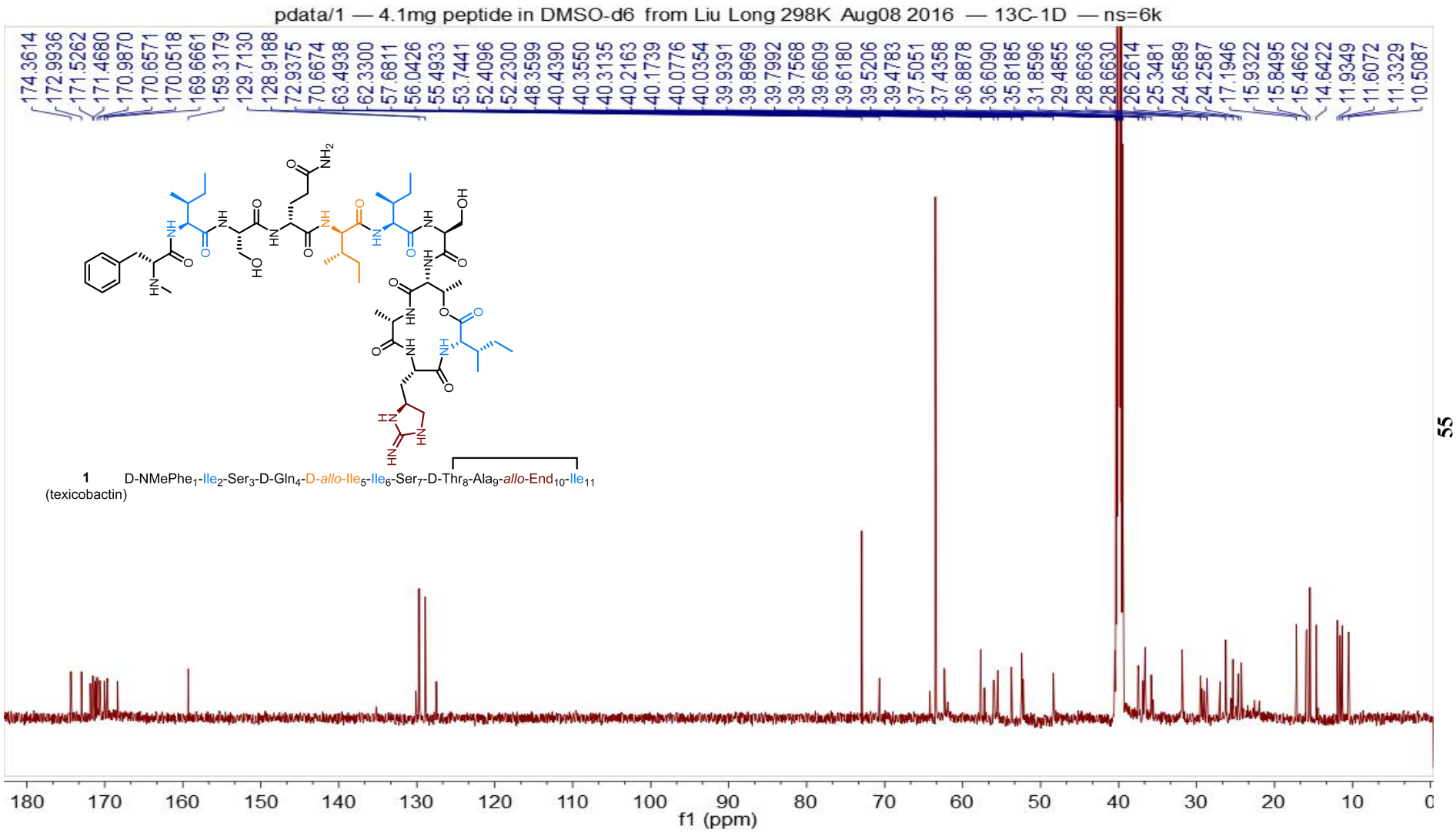
PROTON
1
(texicobactin)
D-NMePhe1-Ile2-Ser3-D-Gln4-D-allo-Ile5-Ile6-Ser7-D-Thr8-Ala9-allo-End10-Ile11
f1 (ppm)


pdata/1 — 4.1mg peptide in DMSO-d6 from Liu Long 298K Aug08 2016 — 13C-1D — ns=6k
174.3614
172.9936
171.5262
171.4680
170.9870
170.6571
170.0518
169.6661
159.3179
129.7130
128.9188
72.9375
70.6674
63.4938
62.3300
57.6811
56.0426
55.4933
53.7441
52.4096
52.2300
48.3599
40.4390
40.3550
40.3135
40.2163
40.1739
40.0776
40.0354
39.9391
39.8969
39.7992
39.7568
39.6609
39.6180
39.5206
39.4783
37.5051
37.4358
36.8878
36.6090
35.8185
31.8596
29.4855
28.6636
28.6630
26.2614
25.3481
24.6589
24.2587
17.1946
15.9322
15.8495
15.4662
14.6422
11.9349
11.6072
11.3329
10.5087
1 D-NMePhe1-Ile2-Ser3-D-Gln4-D-allo-Ile5-Ile6-Ser7-D-Thr8-Ala9-allo-End10-Ile11
(texicobactin)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

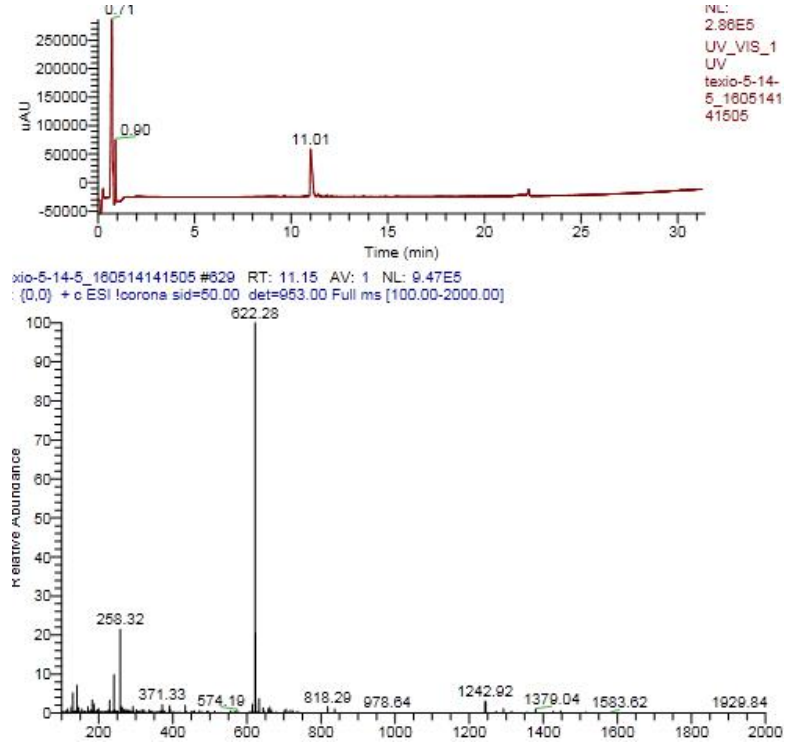


Figure S5. Analytical Lc-Ms trcae of teixobaction

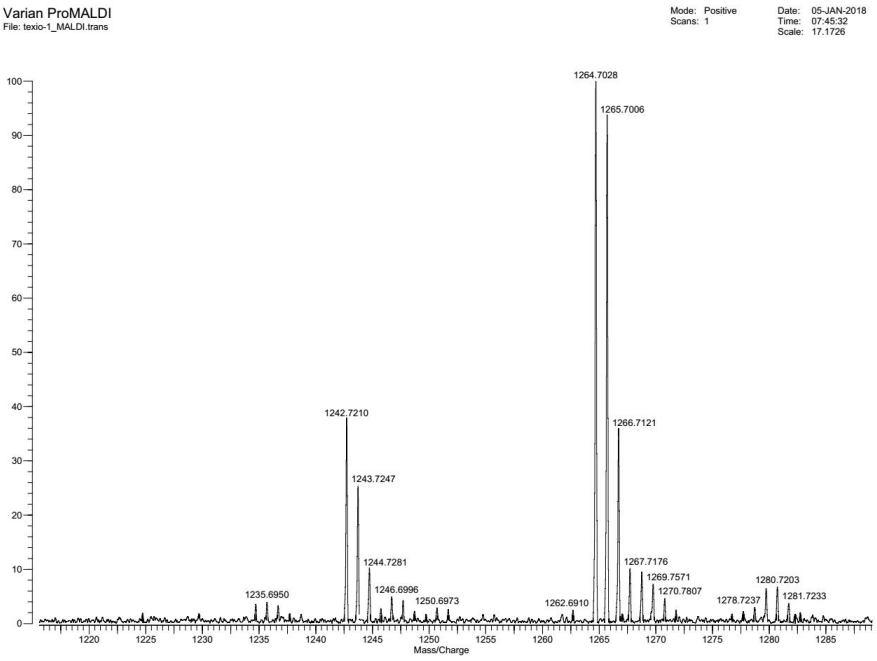
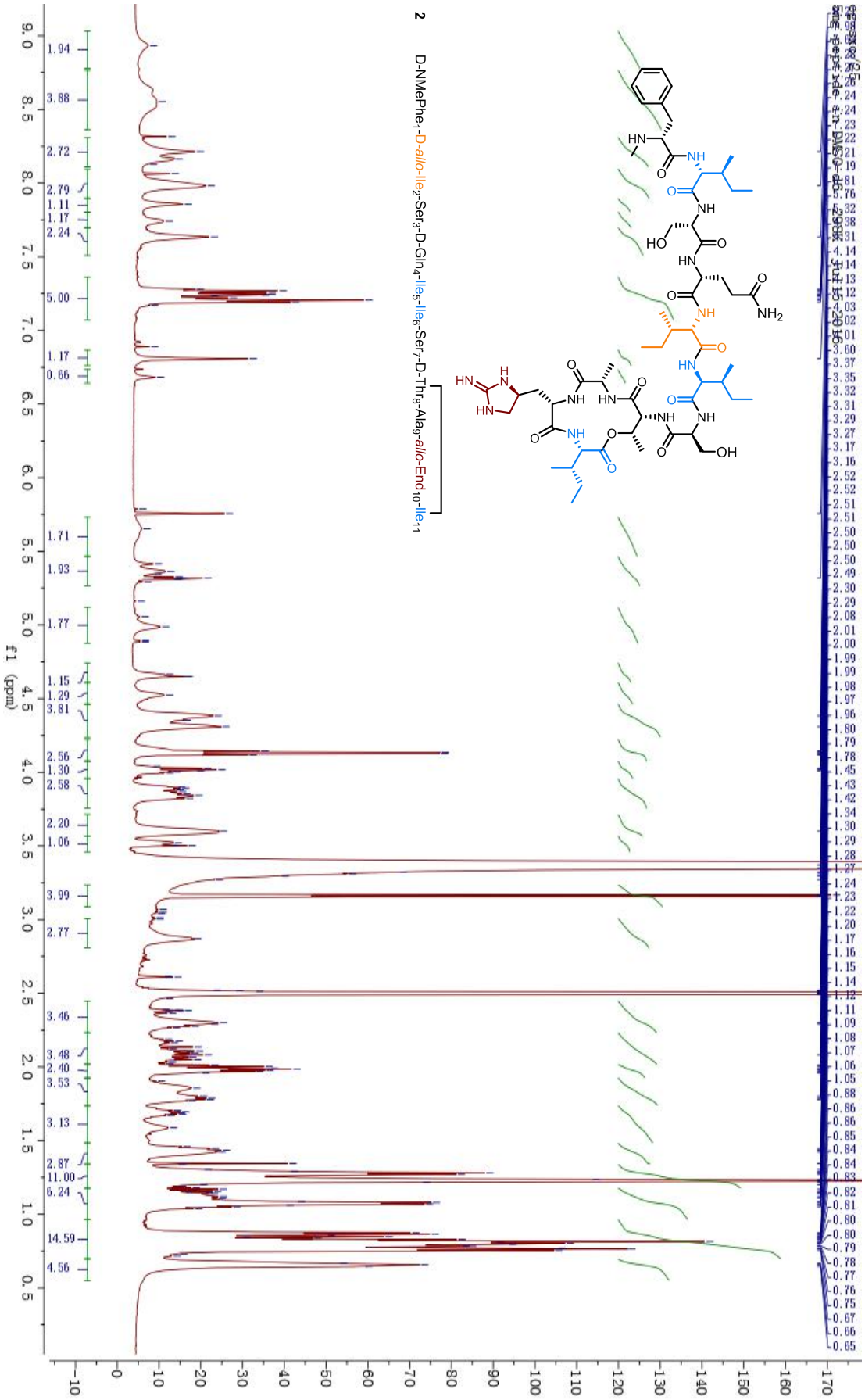


Figure S6. High Resolution Mass spectra of teixobaction


2
D-NMePhe1-D-allo-Ile2-Ser3-D-Gln4-Ile5-Ile6-Ser7-D-Thr8-Ala9-allo-End10-Ile11
f1 (ppm)

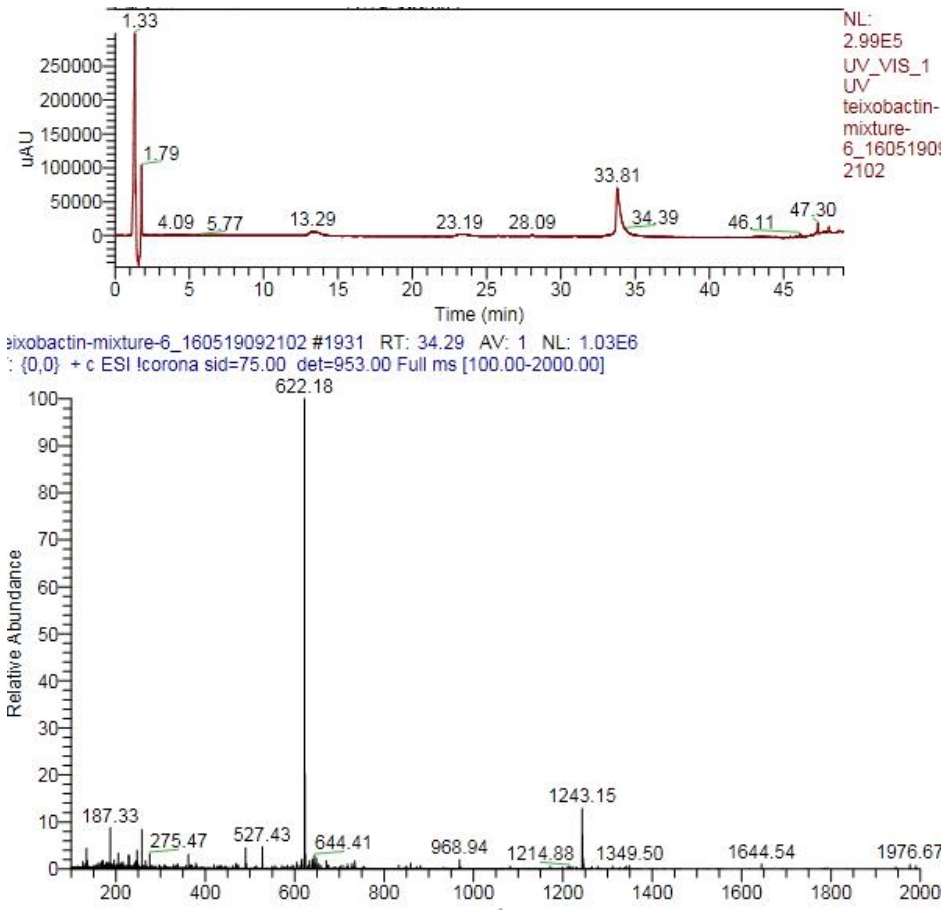


Figure S7. Analytical Lc-Ms trcae of teixobaction analog **2**

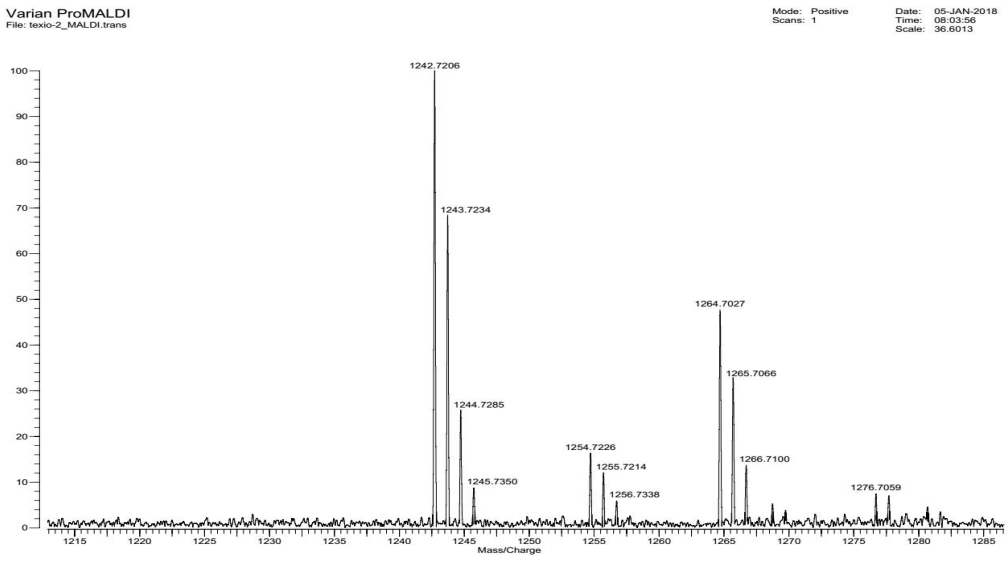
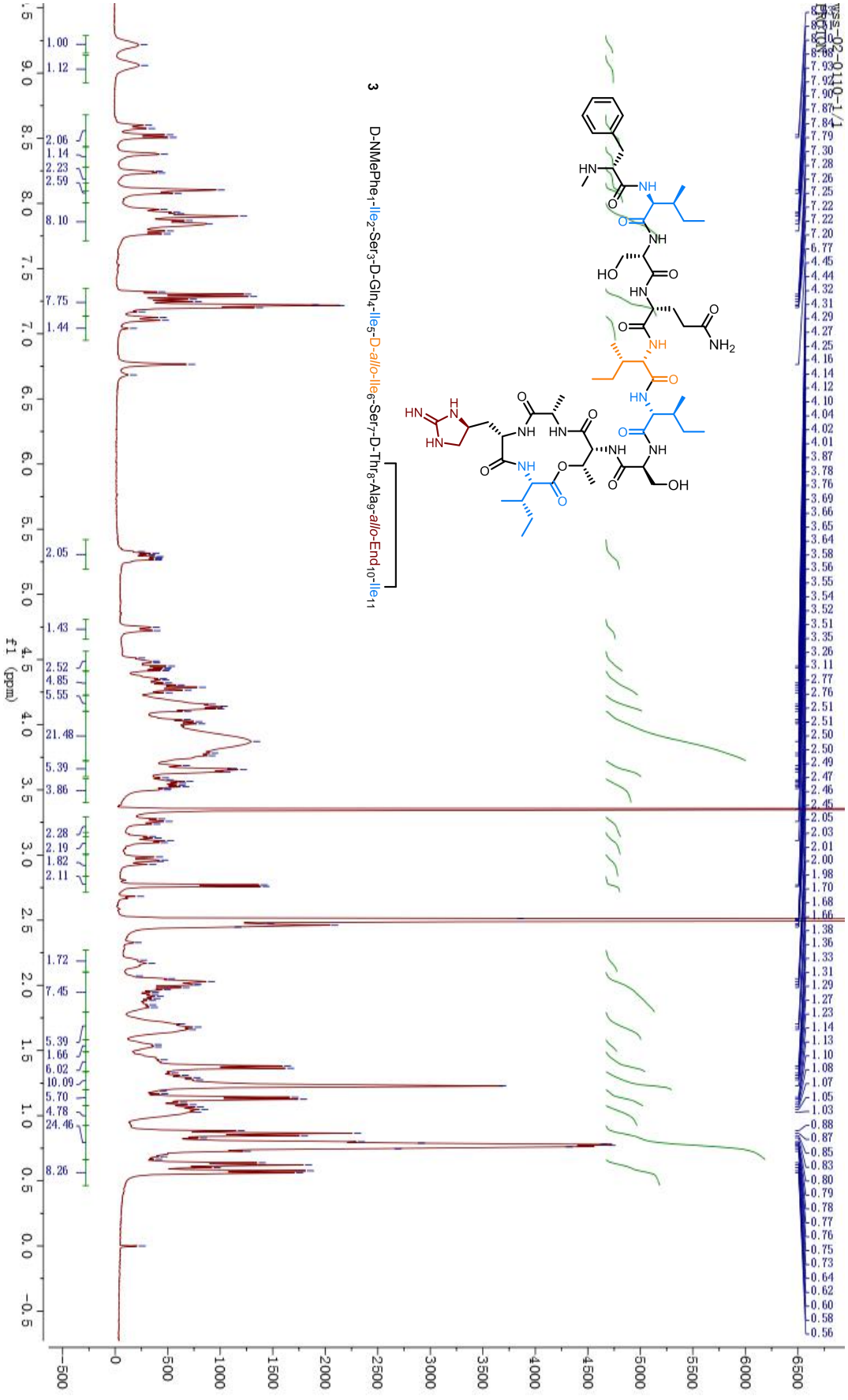


Figure S8. High Resolution Mass spectra of teixobactionanalog **2**


3
D-NMePhe1-Ile2-Ser3-D-Gln4-Ile5-D-allo-Ile6-Ser7-D-Thr8-Ala9-allo-End10-Ile11
f1 (ppm)

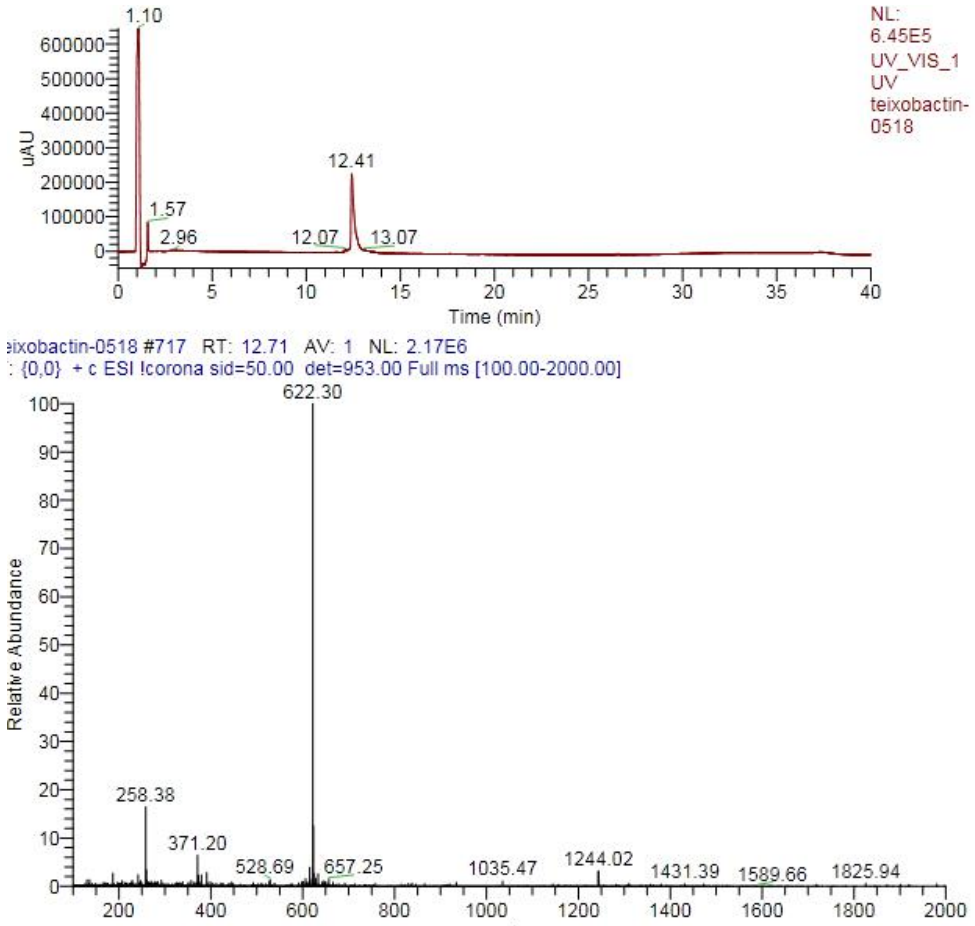


Figure S9. Analytical Lc-Ms trcae of teixobaction analog **3**

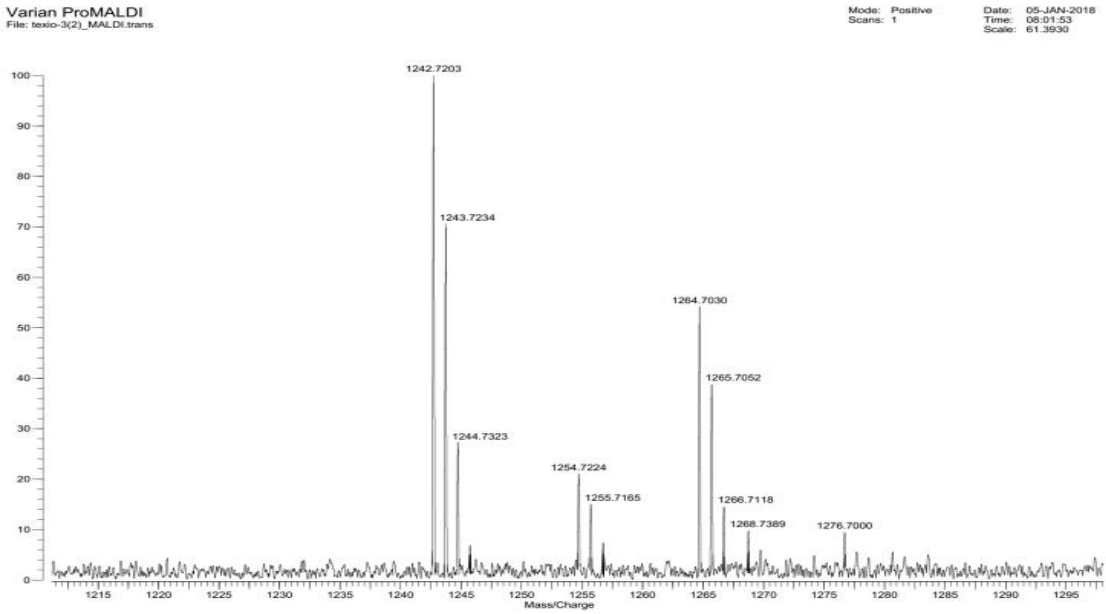
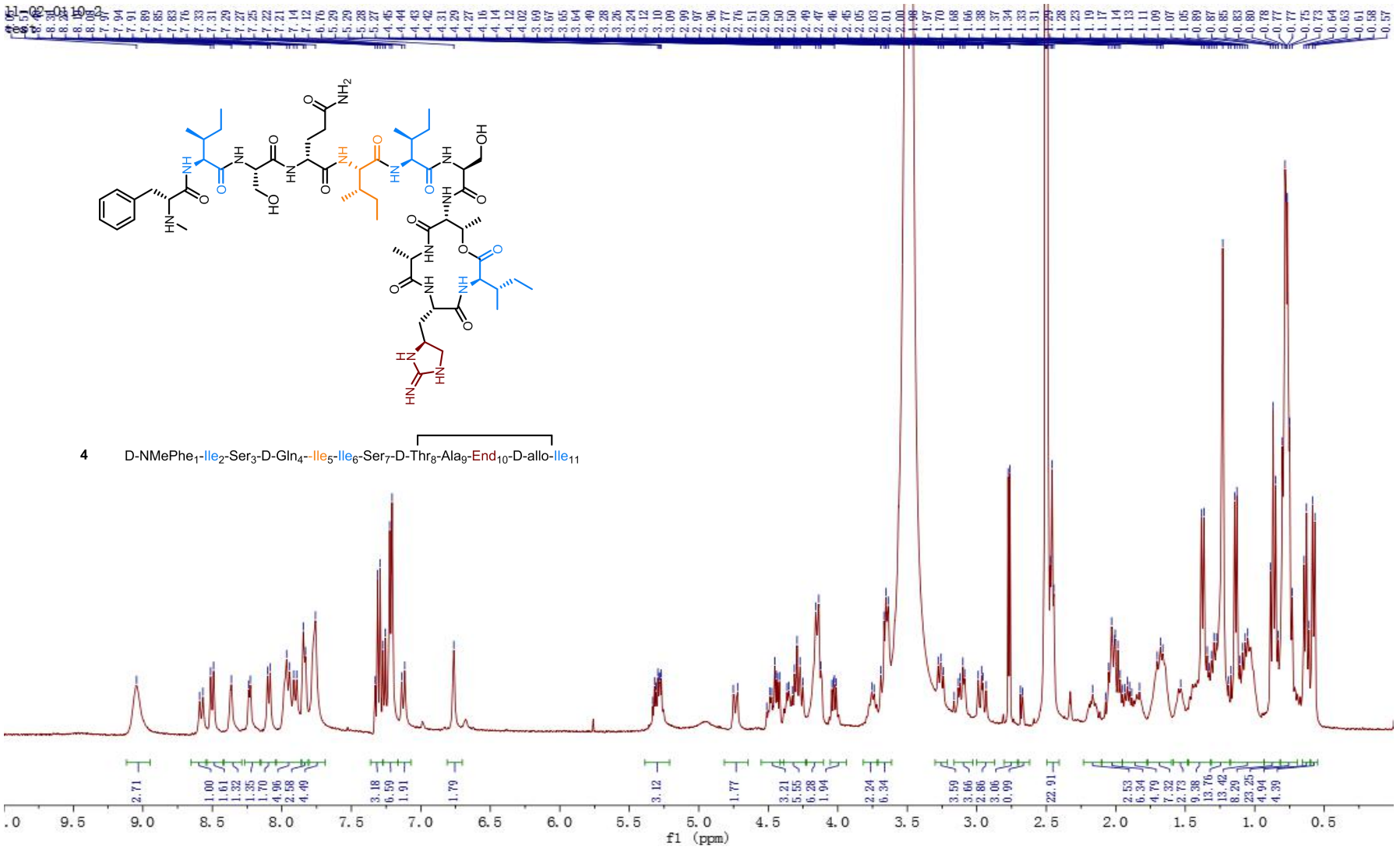


Figure S10. High Resolution Mass spectra of teixobactionanalog **3**


4
D-NMePhe1-Ile2-Ser3-D-Gln4--Ile5-Ile6-Ser7-D-Thr8-Ala9-End10-D-allo-Ile11
f1 (ppm)

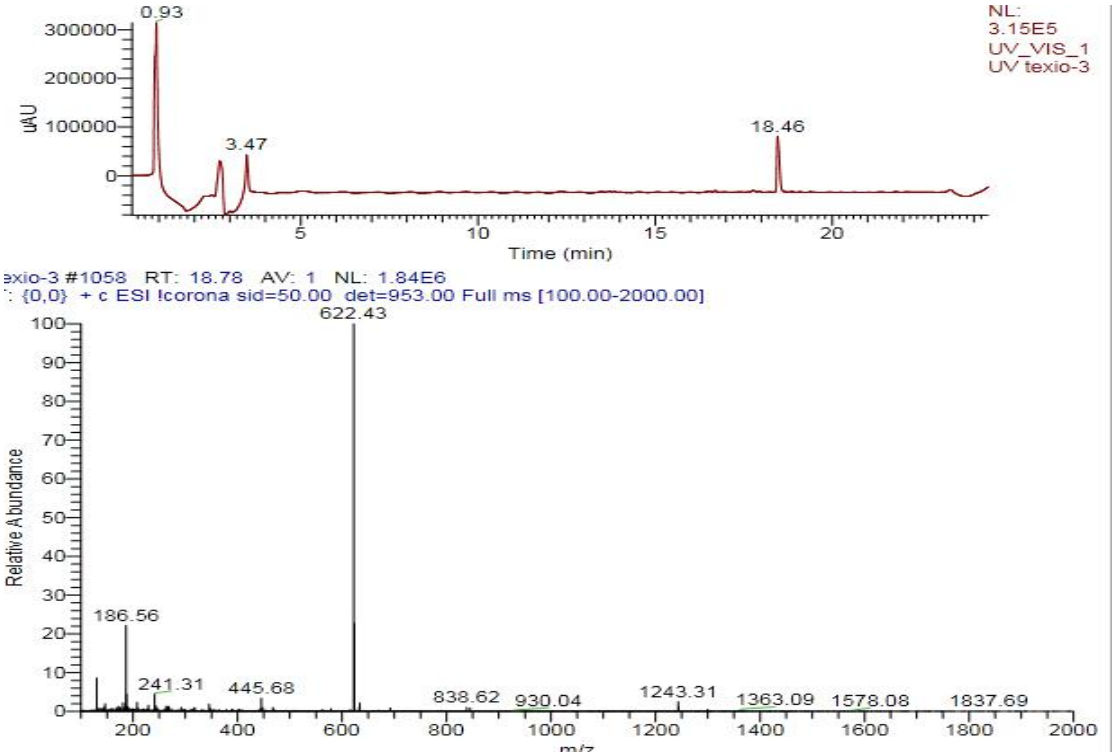


Figure S11. Analytical Lc-Ms trcae of teixobaction analog **4**

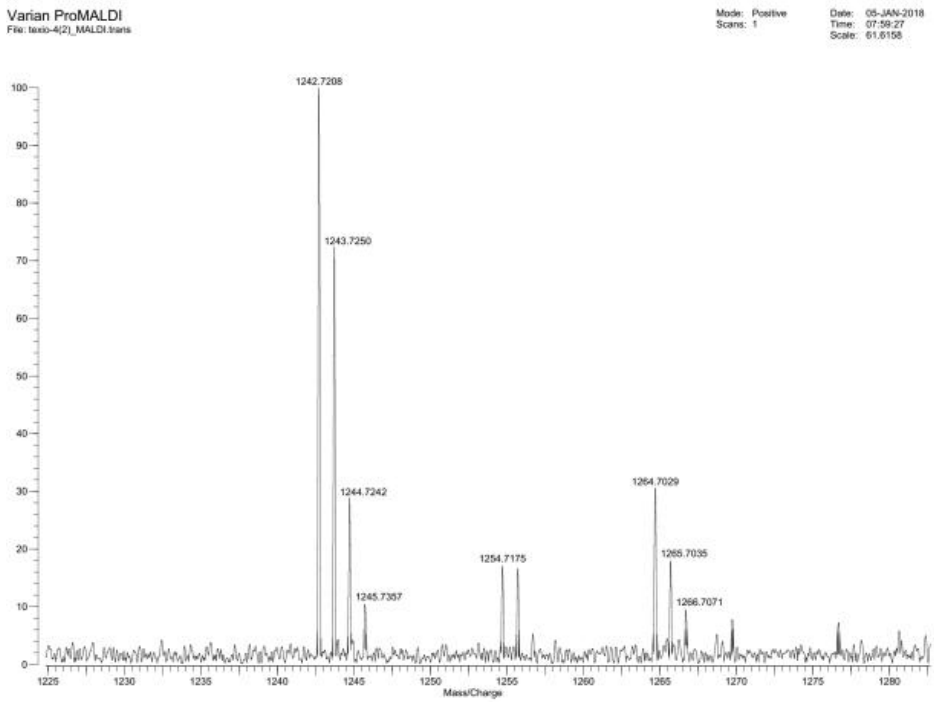
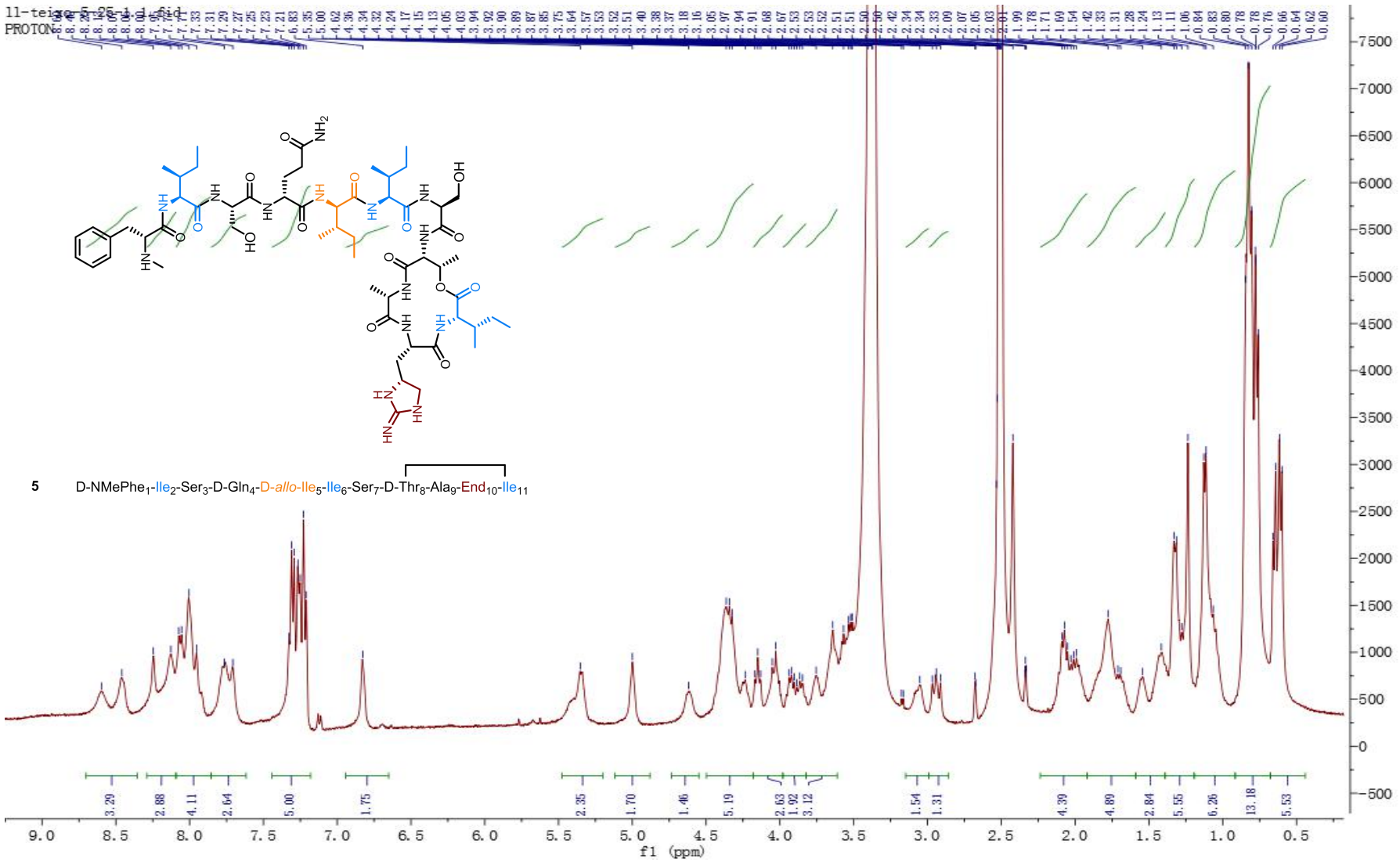


Figure S12. High Resolution Mass spectra of teixobactionanalog **4**


11-teige-5-25-1-1.fid
PROTON
5
D-NMePhe1-Ile2-Ser3-D-Gln4-D-allo-Ile5-Ile6-Ser7-D-Thr8-Ala9-End10-Ile11
f1 (ppm)

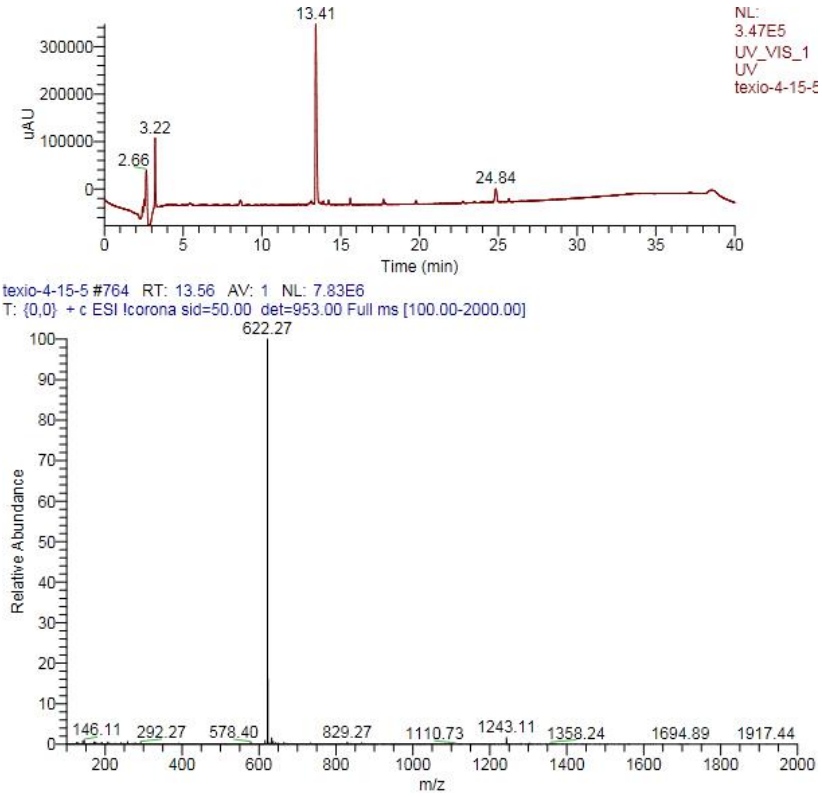


Figure S13. Analytical Lc-Ms trcae of teixobaction analog **5**

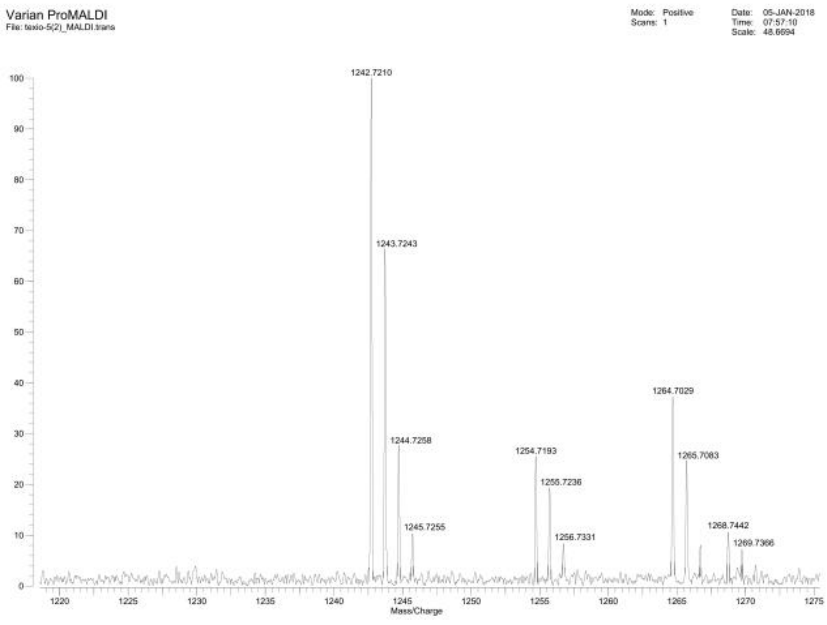
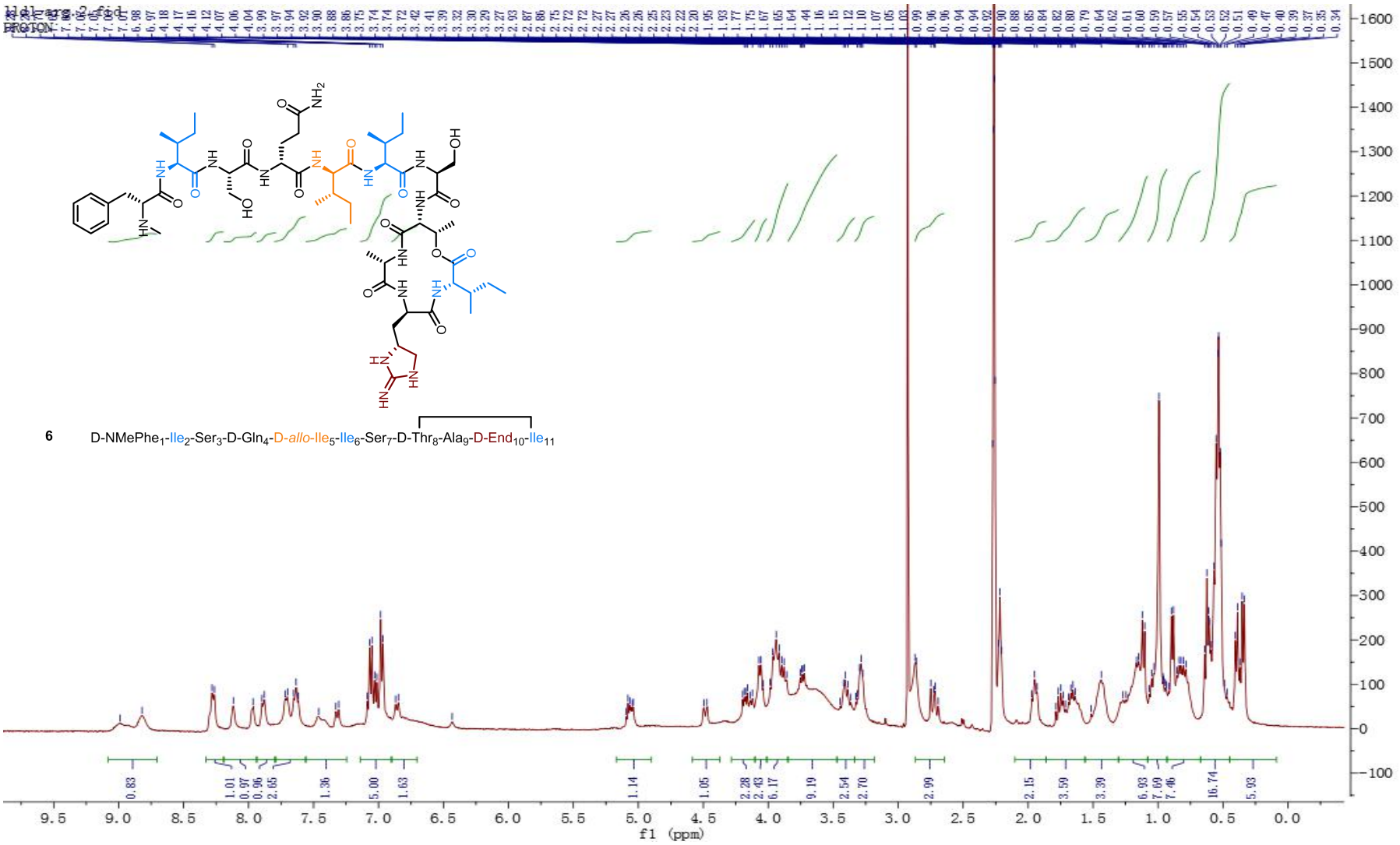


Figure S14. High Resolution Mass spectra of teixobactionanalog **5**



6 D-NMePhe$_1$-Ile$_2$-Ser$_3$-D-Gln$_4$-D-*allo*-Ile$_5$-Ile$_6$-Ser$_7$-D-Thr$_8$-Ala$_9$-D-End$_{10}$-Ile$_{11}$

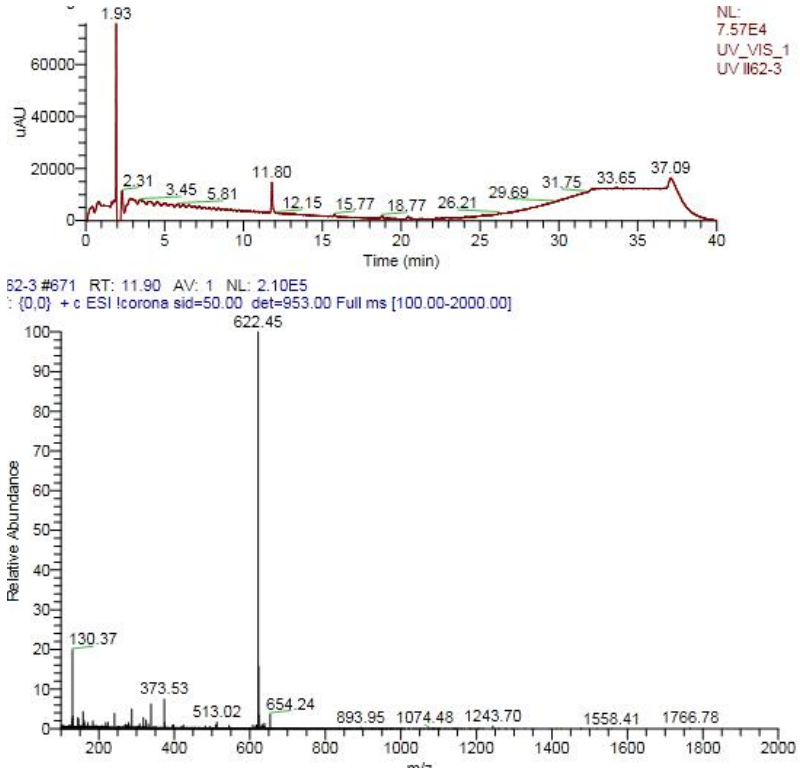


Figure S15. Analytical Lc-Ms trcae of teixobaction analog **6**

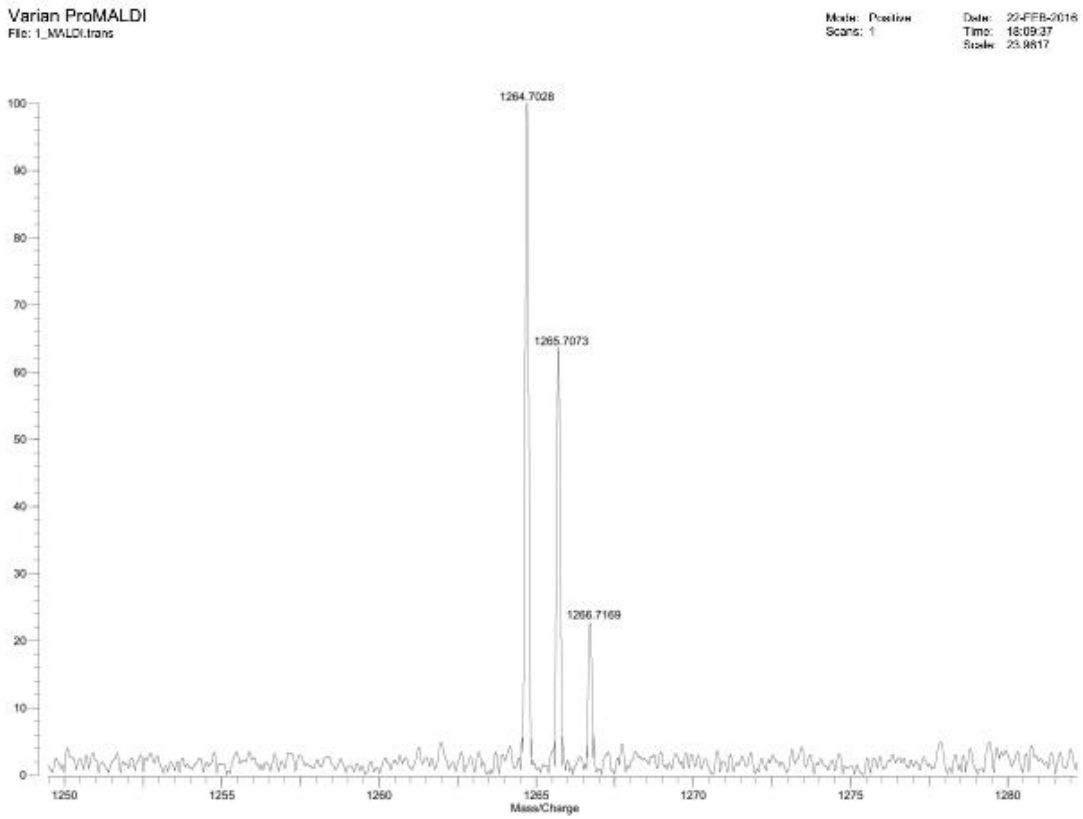
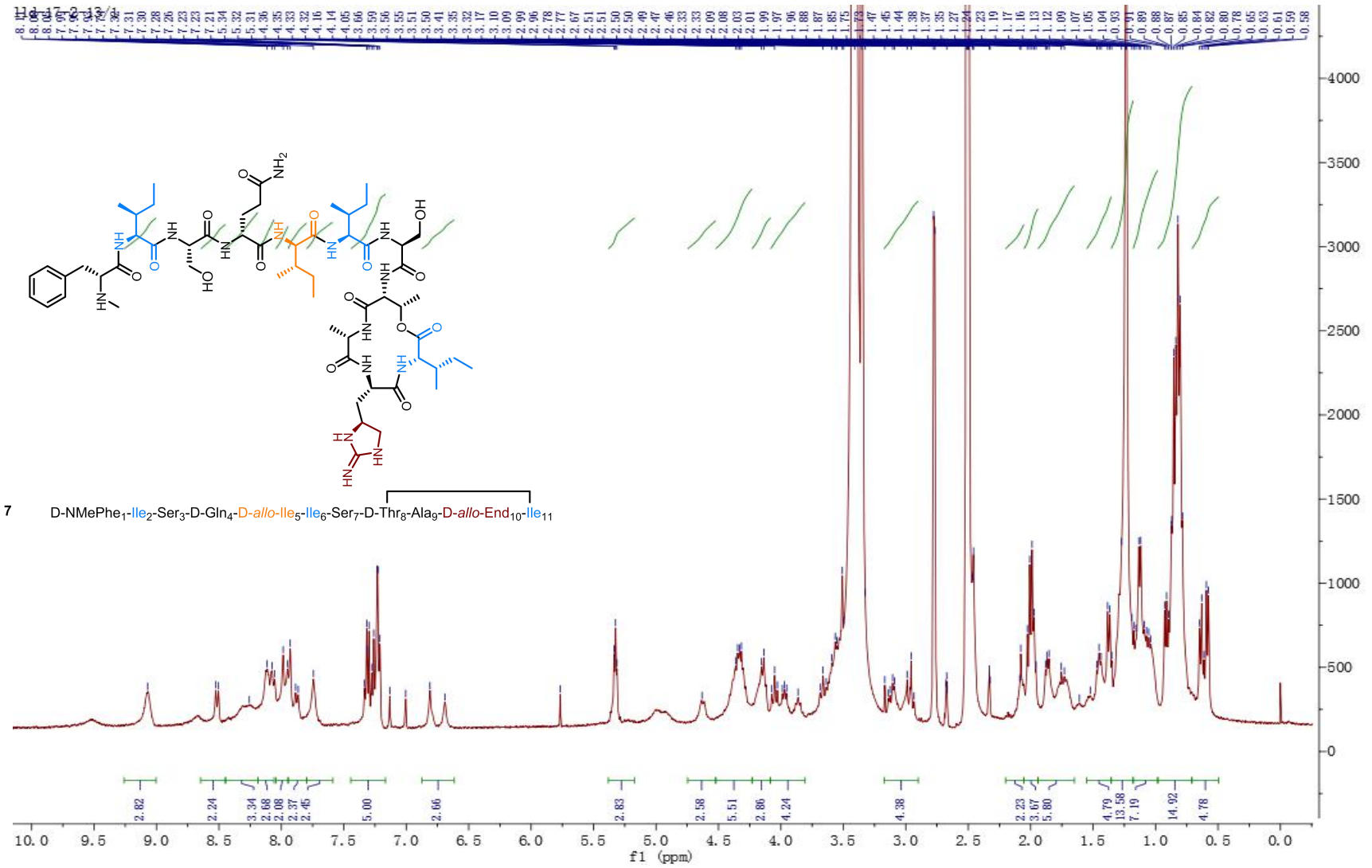


Figure S16. High Resolution Mass spectra of teixobactionanalog **6**


7
D-NMePhe1-Ile2-Ser3-D-Gln4-D-allo-Ile5-Ile6-Ser7-D-Thr8-Ala9-D-allo-End10-Ile11
f1 (ppm)

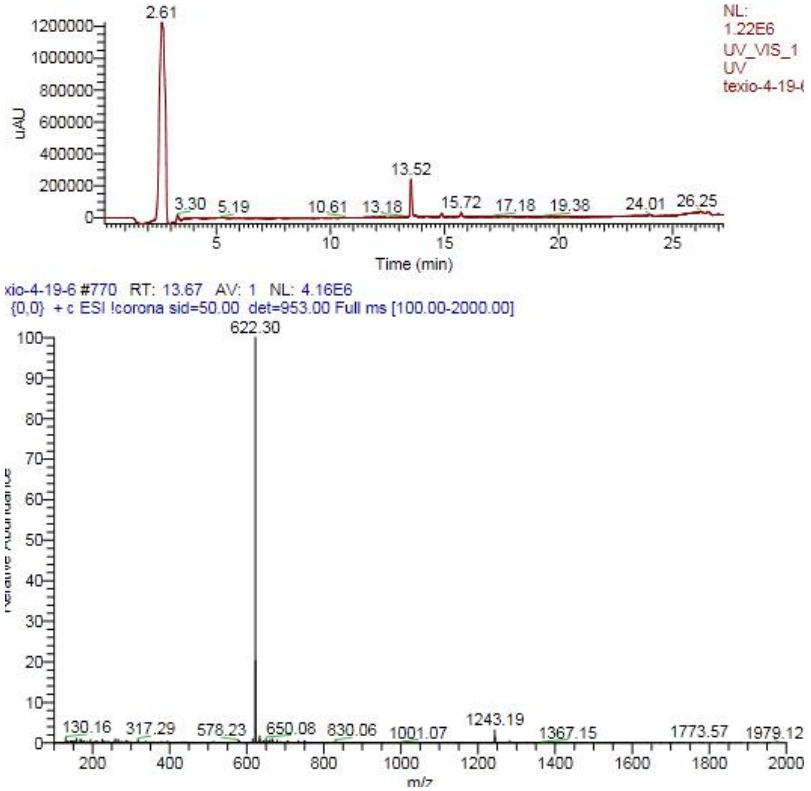


Figure S17. Analytical Lc-Ms trcae of teixobaction analog **7**

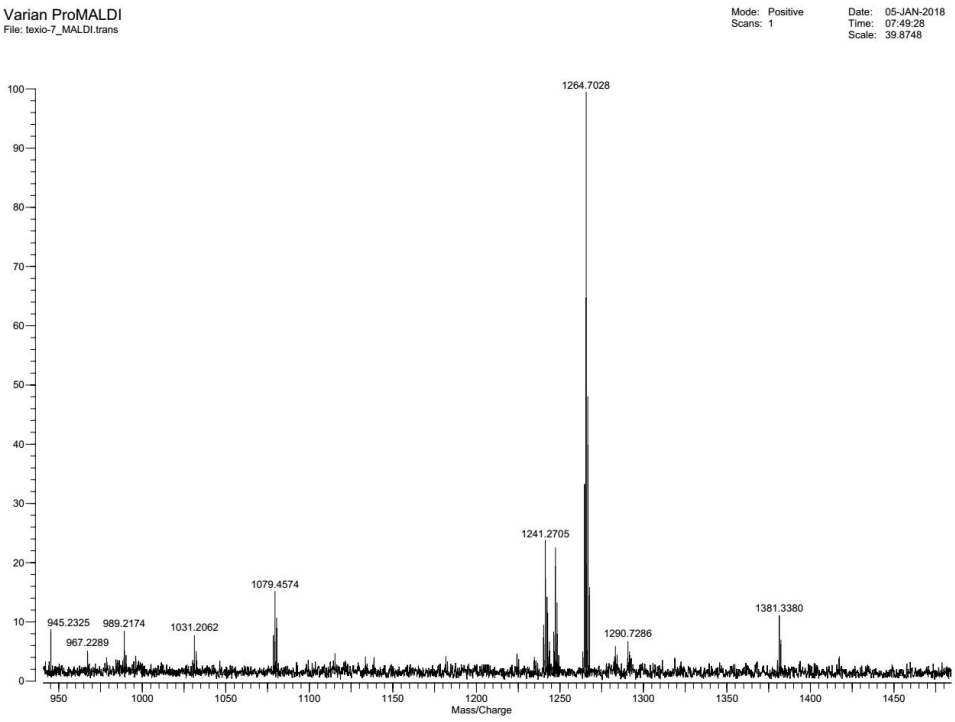
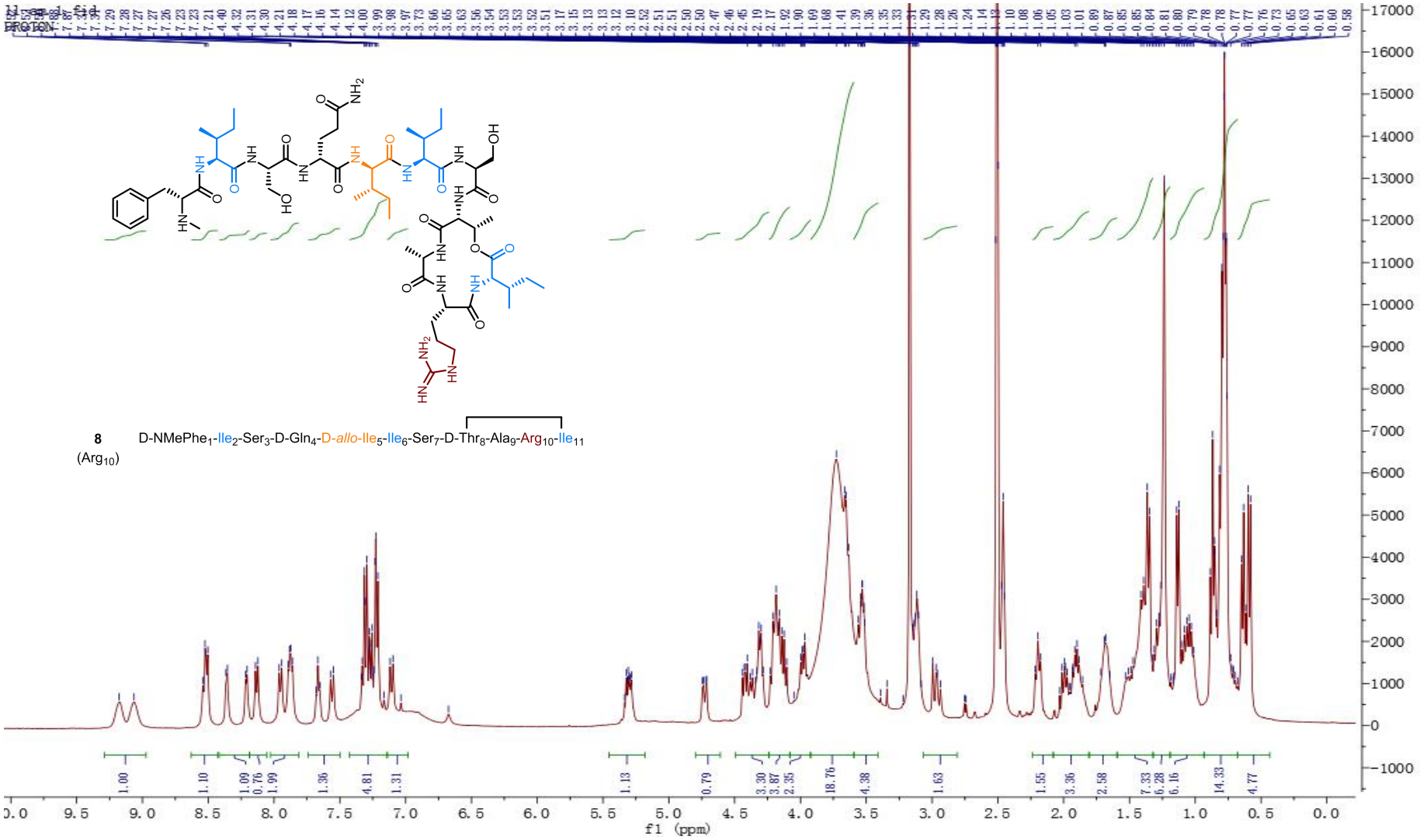


Figure S18. High Resolution Mass spectra of teixobaction analog **7**


PROTON
8
(Arg10)
D-NMePhe1-Ile2-Ser3-D-Gln4-D-allo-Ile5-Ile6-Ser7-D-Thr8-Ala9-Arg10-Ile11
f1 (ppm)

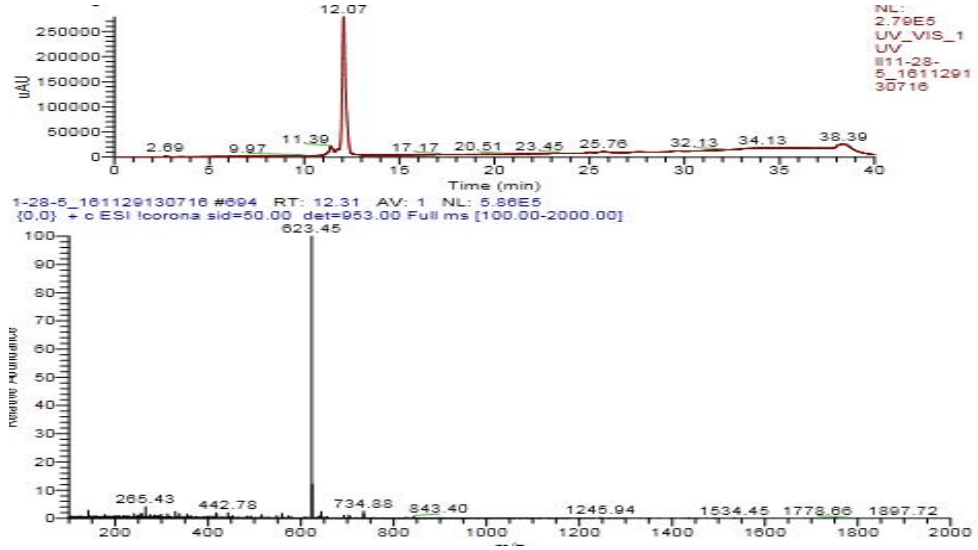


Figure S19. Analytical Lc-Ms trcae of teixobaction analog **8**

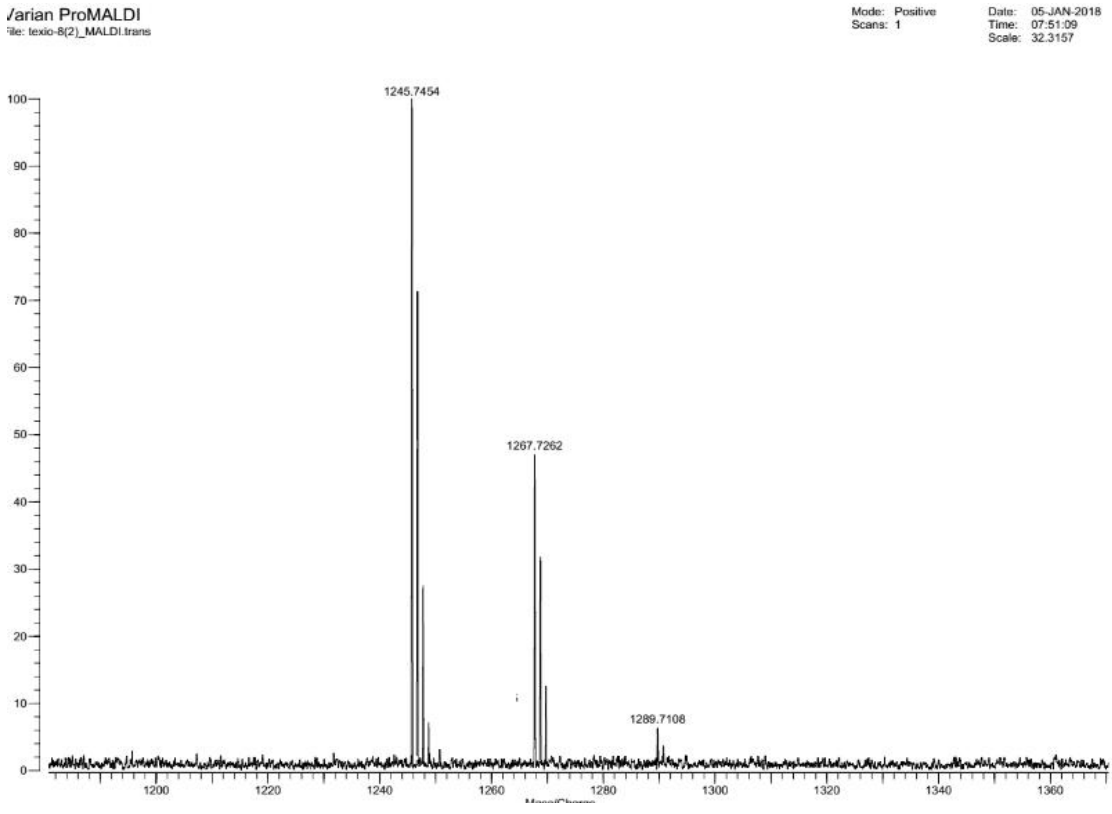
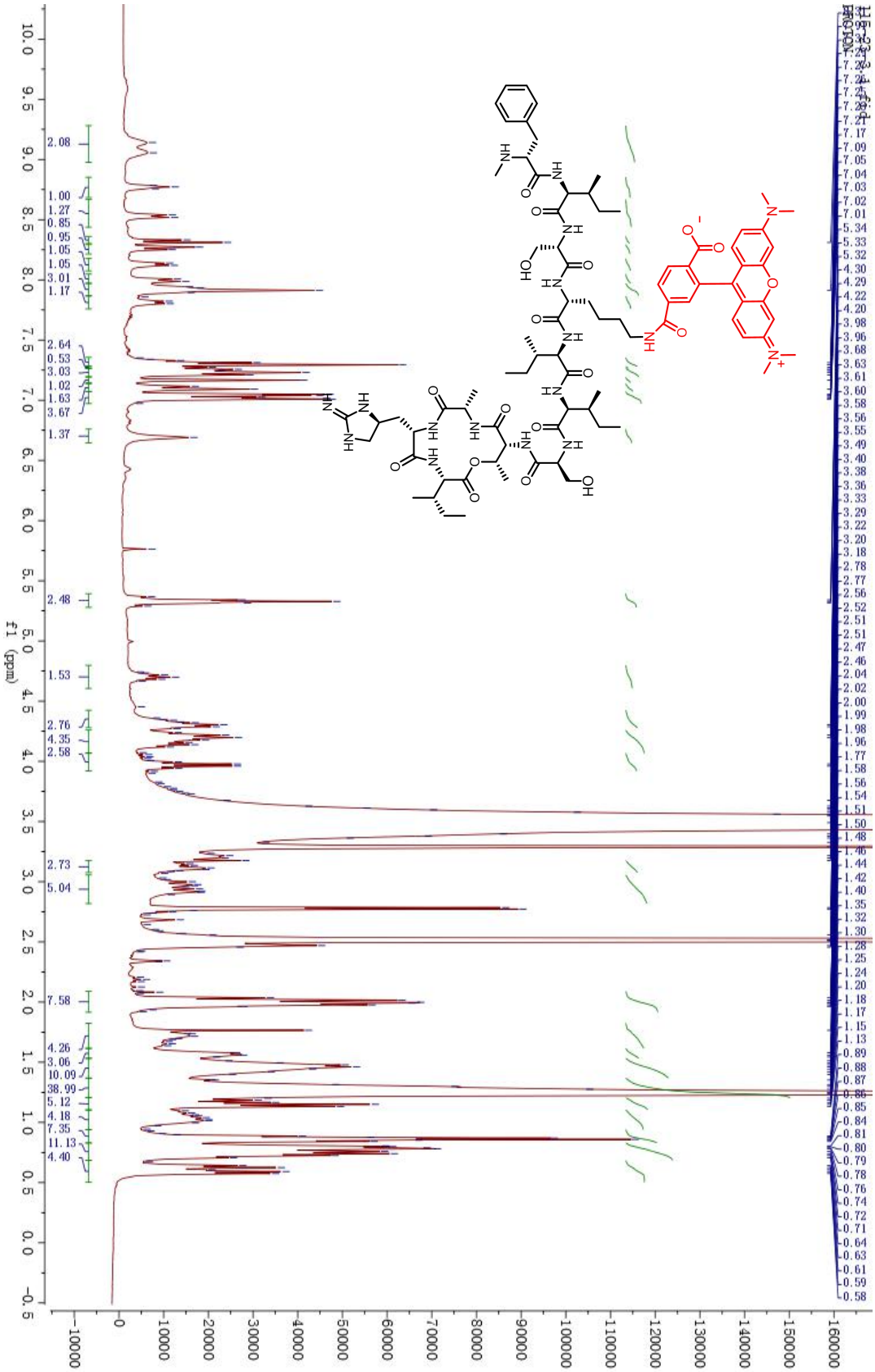


Figure S20. High Resolution Mass spectra of teixobactionanalog **8**



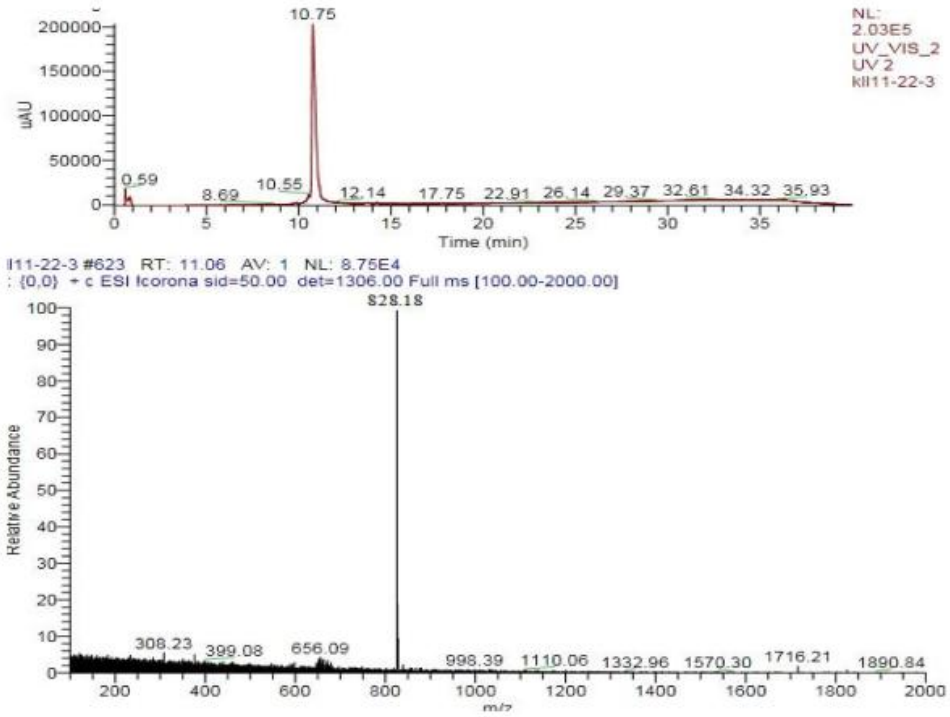


Figure S21. Analytical Lc-Ms trcae of fluorescent labelled analog of teixobactin **32**

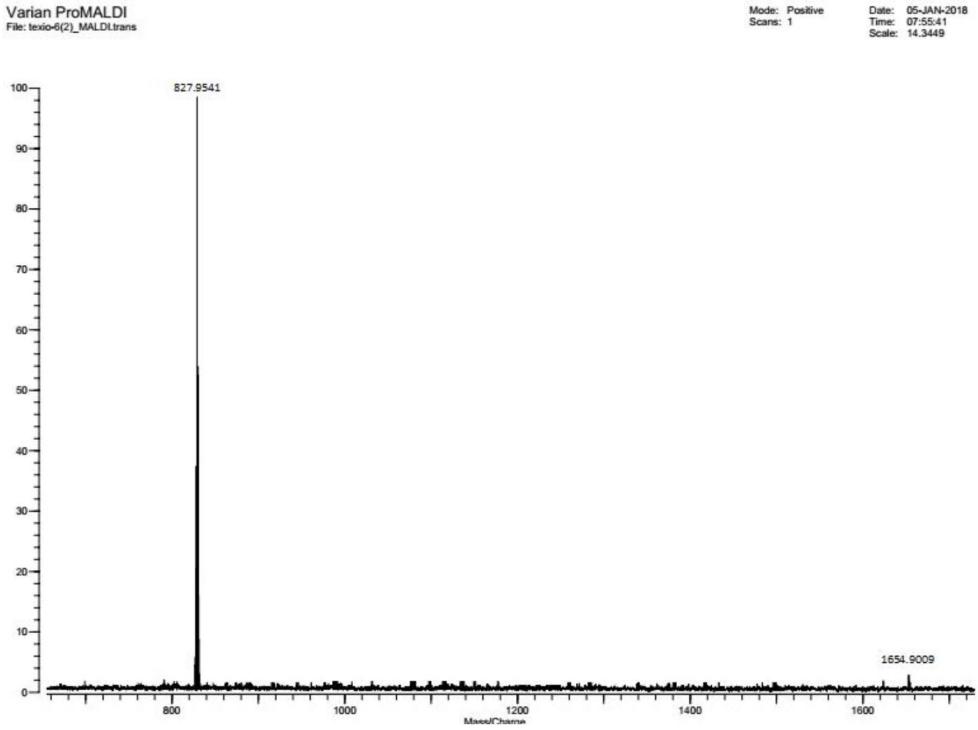


Figure S22 High Resolution Mass spectra of fluorescent labelled analog of teixobactin **32**