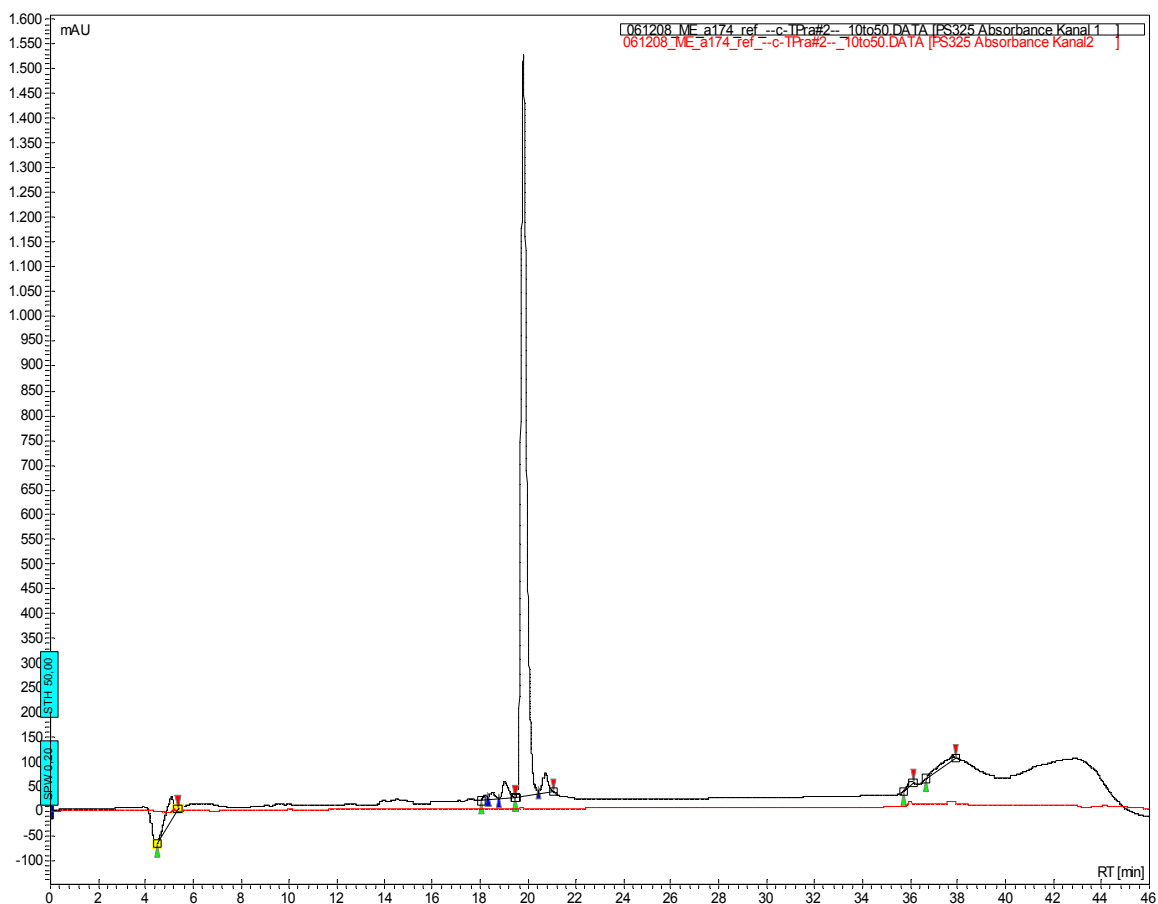
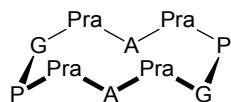
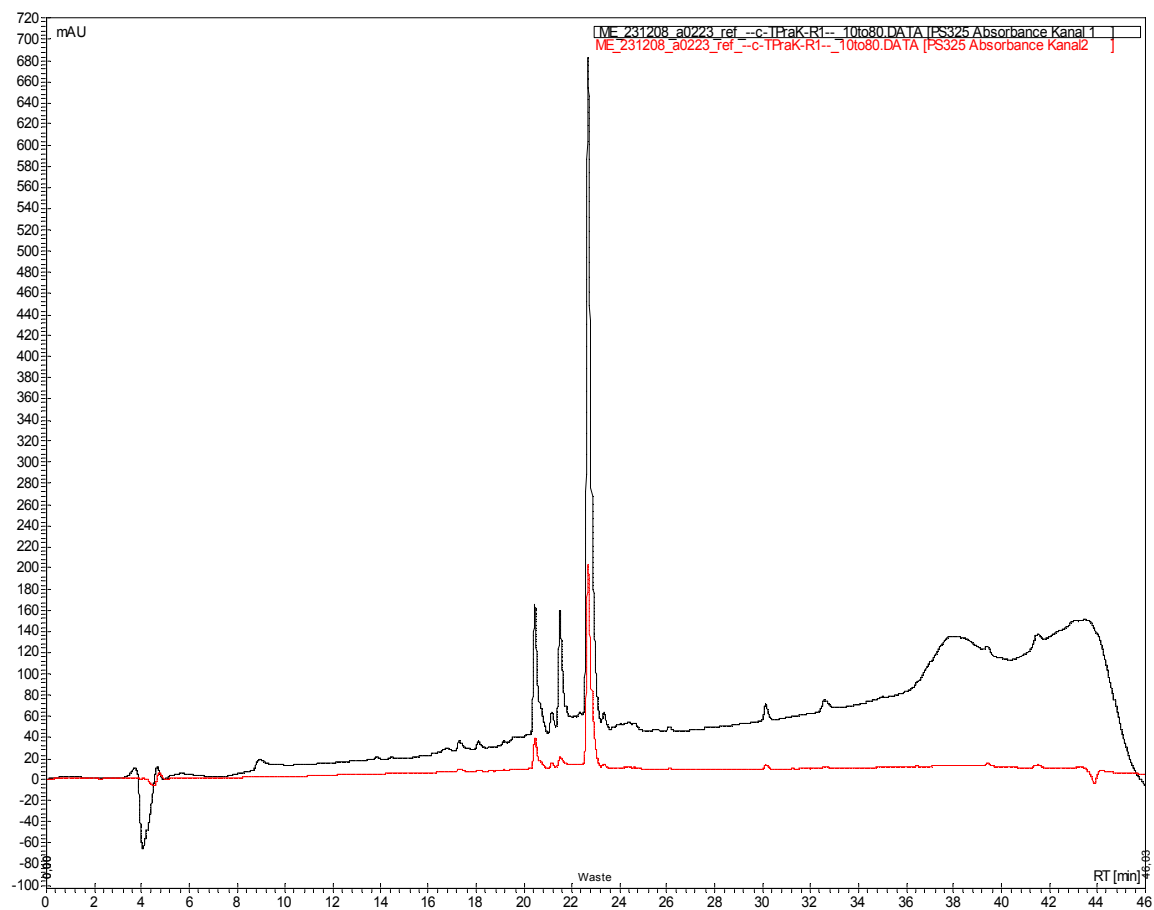
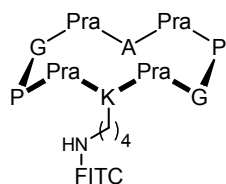


Supporting Information

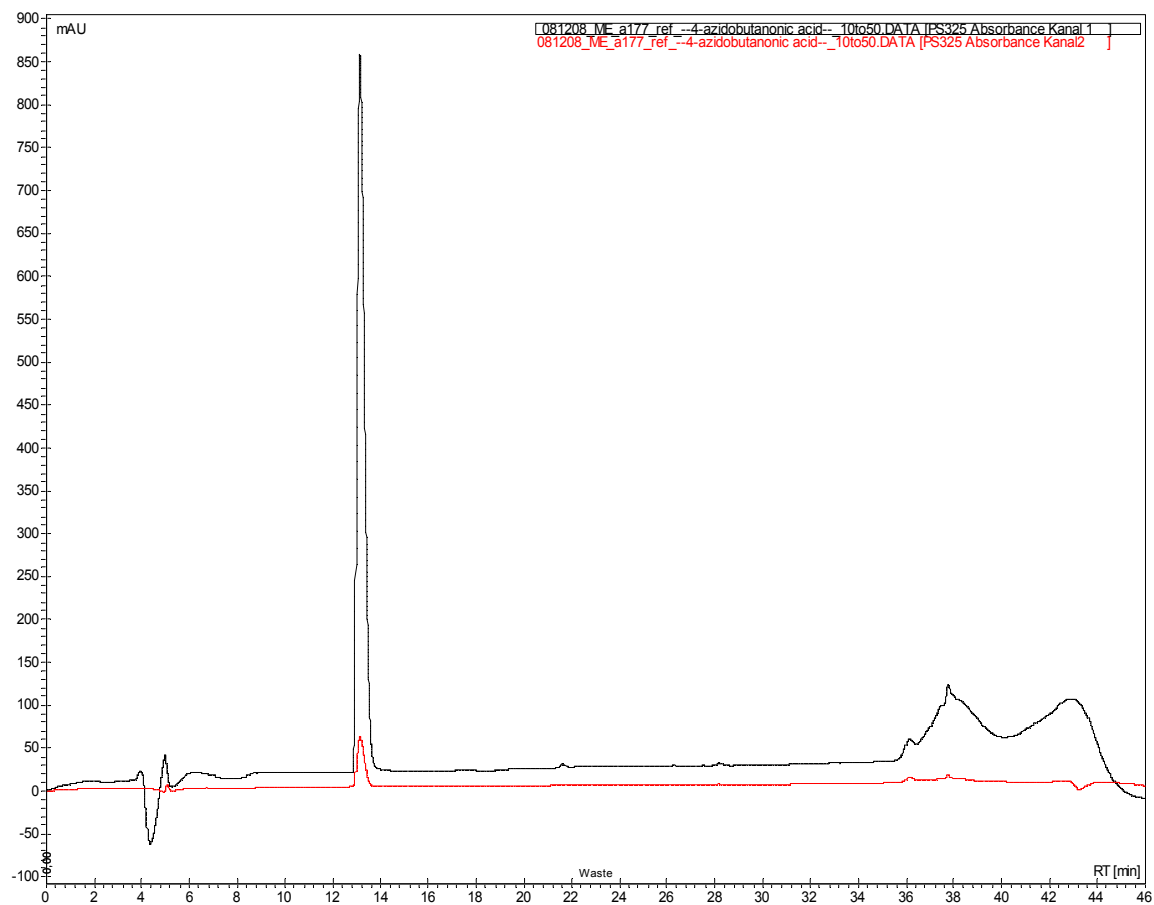
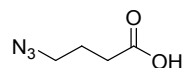
RP-HPLC traces for scaffolds and peptide ligands at 220 (black) and 280 (red) nm:



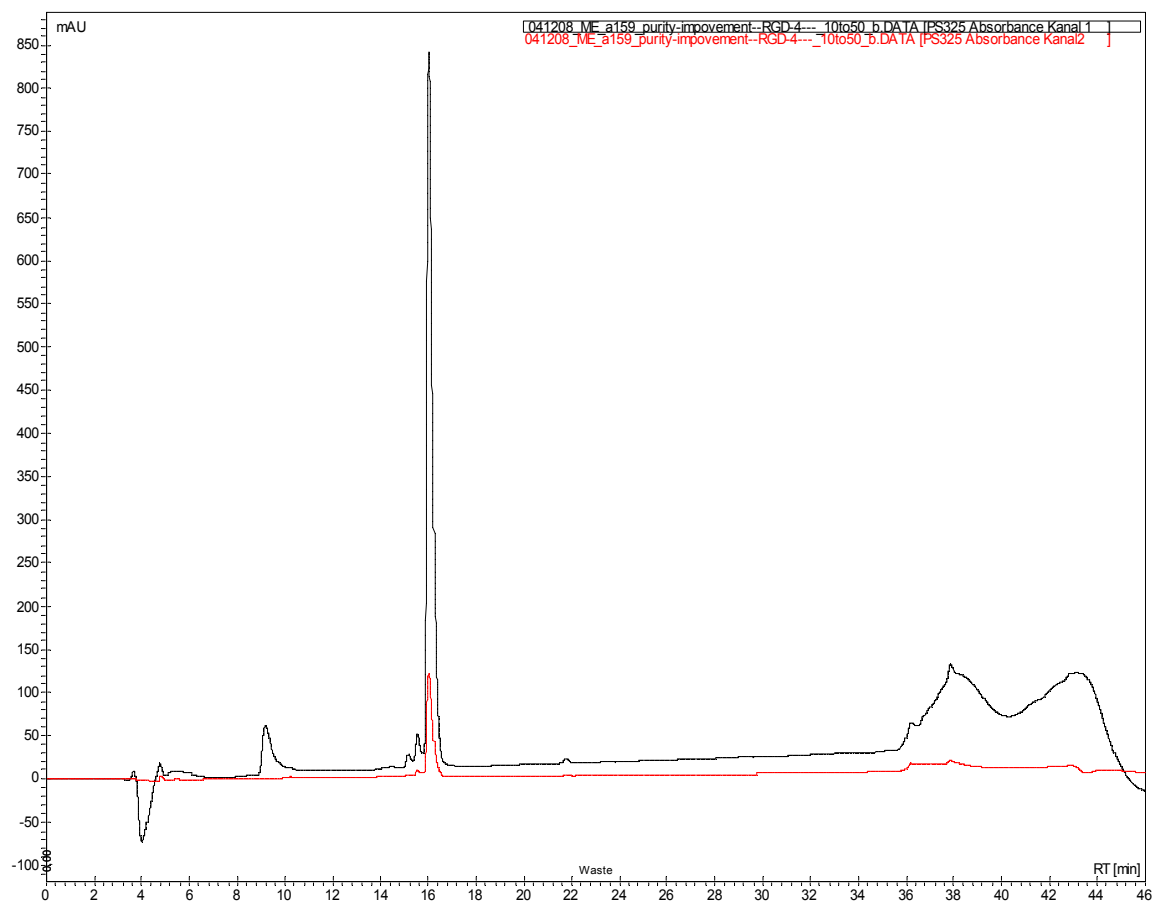
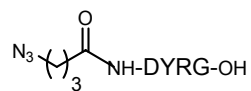
gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min



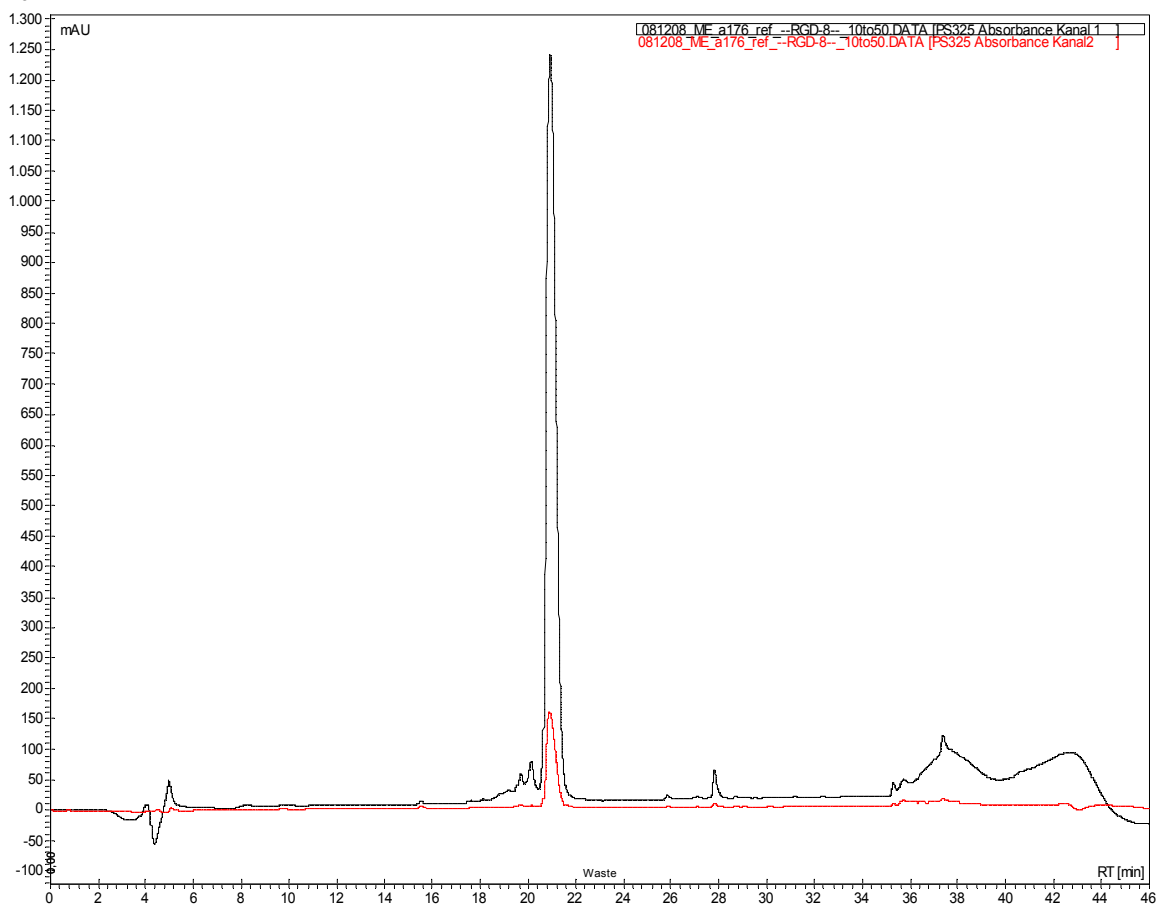
gradient: 9→72% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min.



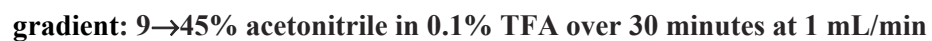
gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min

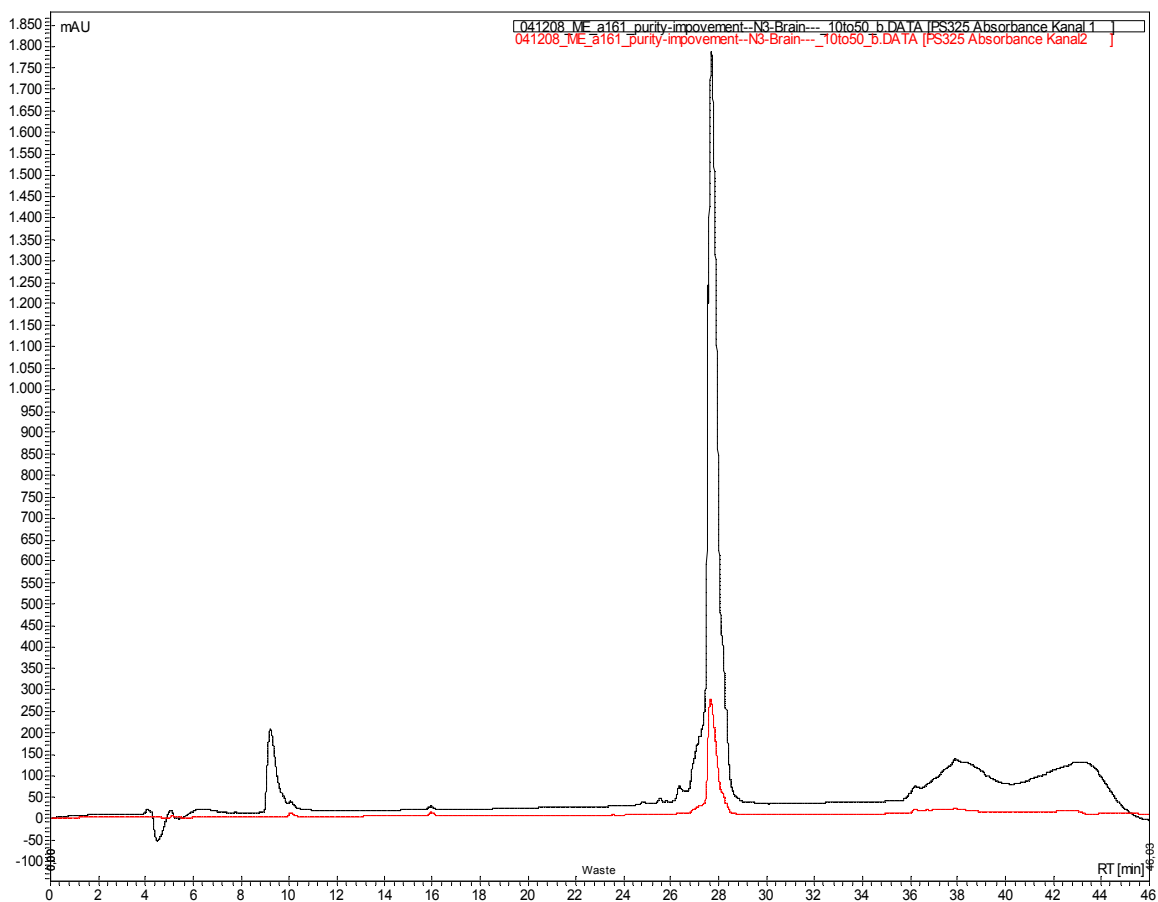


gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min

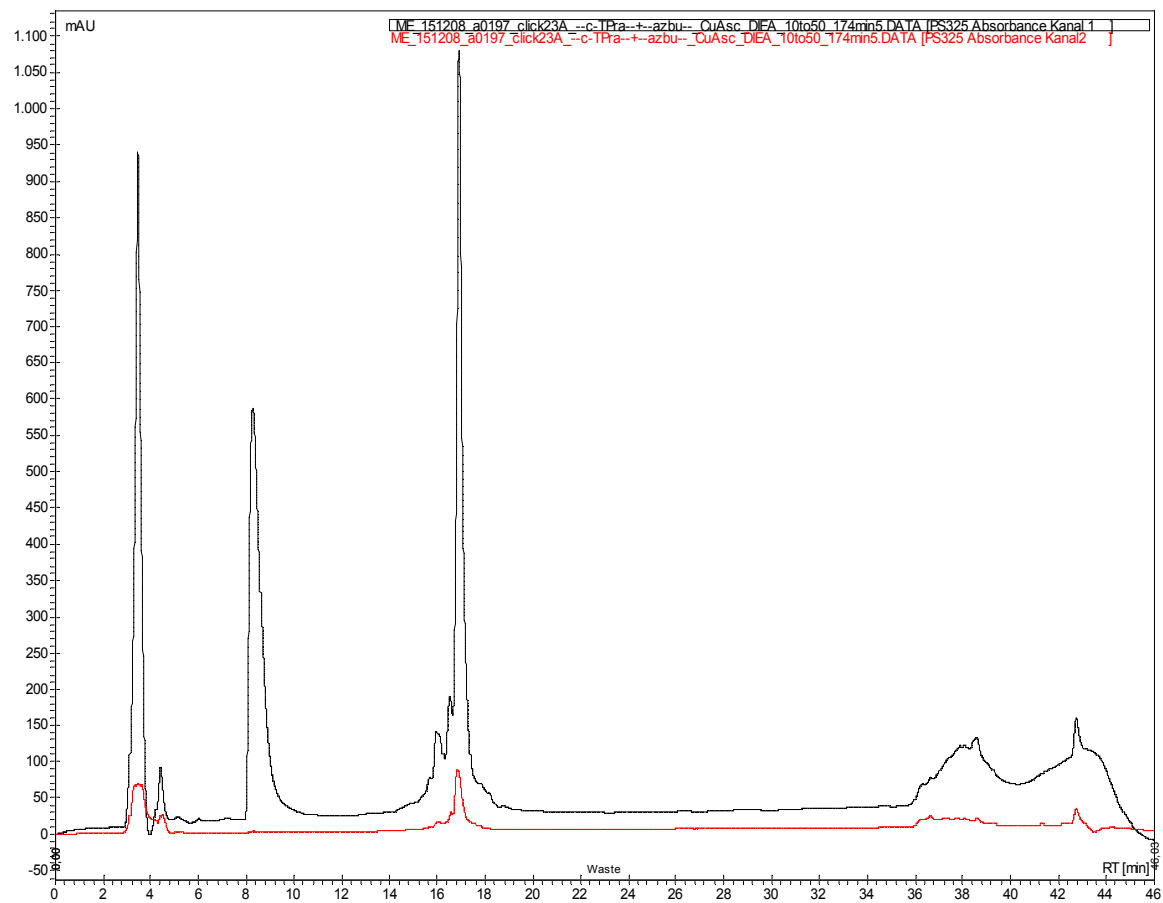
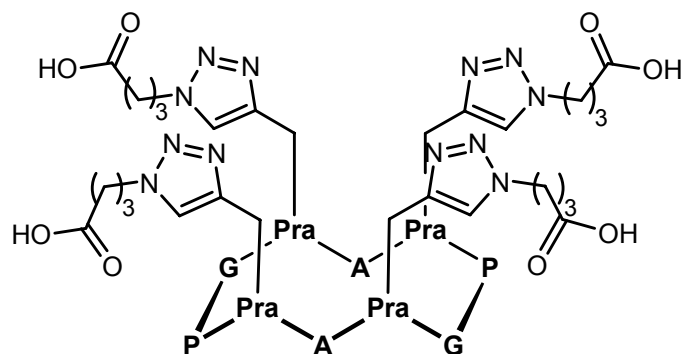


gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min

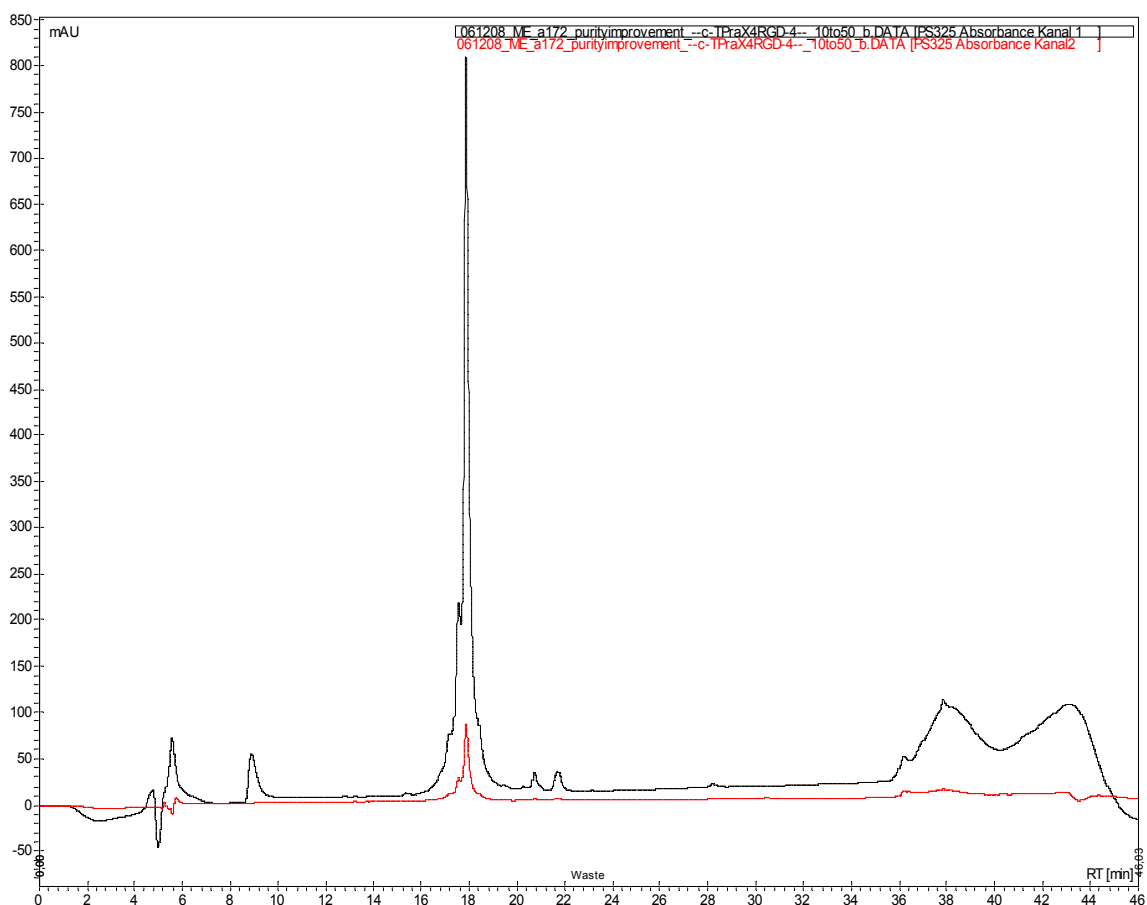
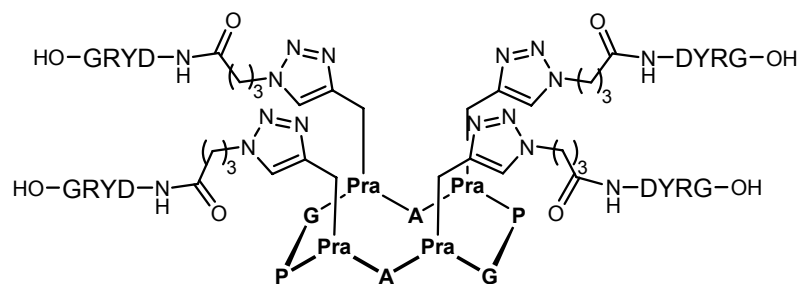




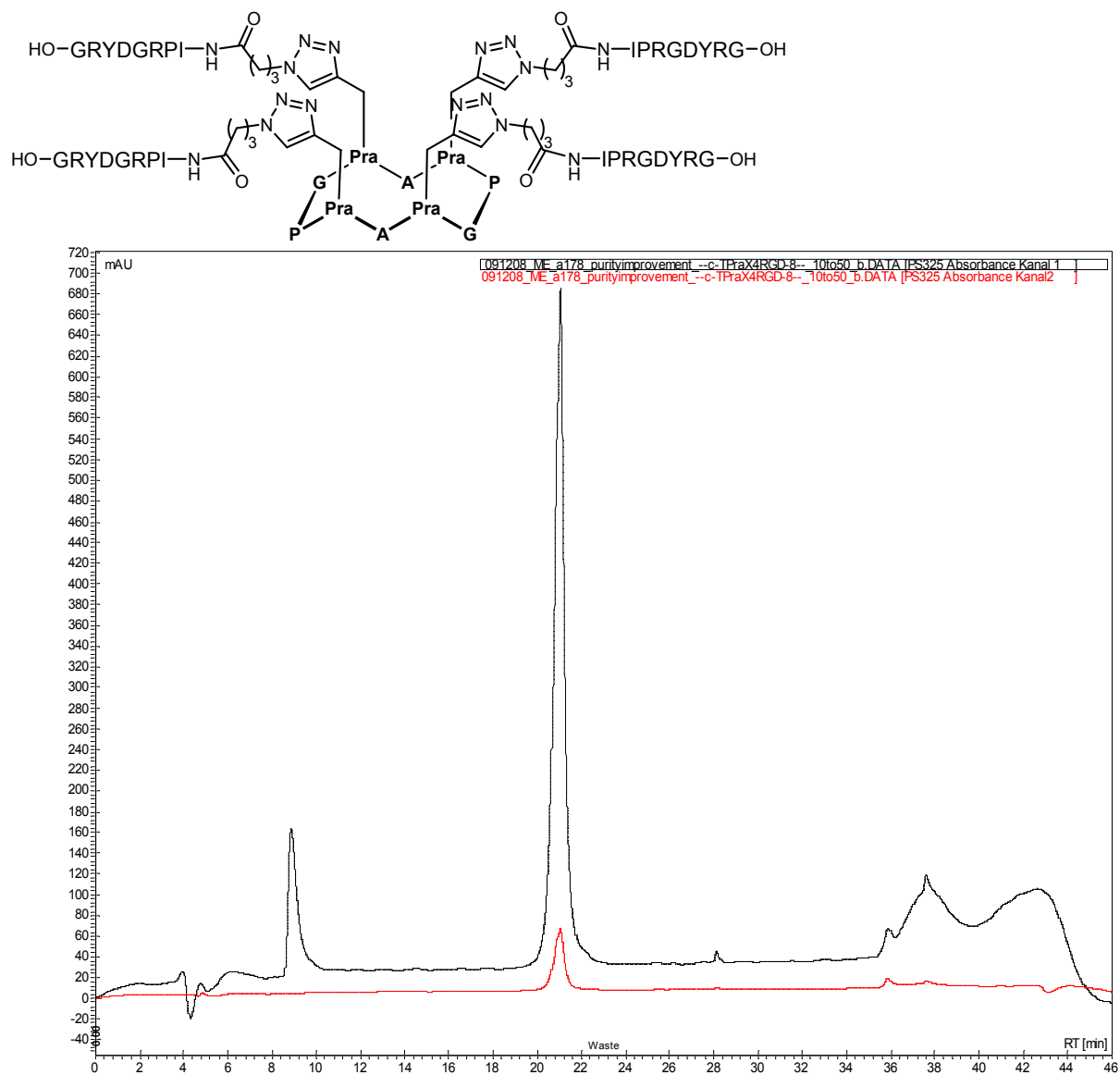
gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min



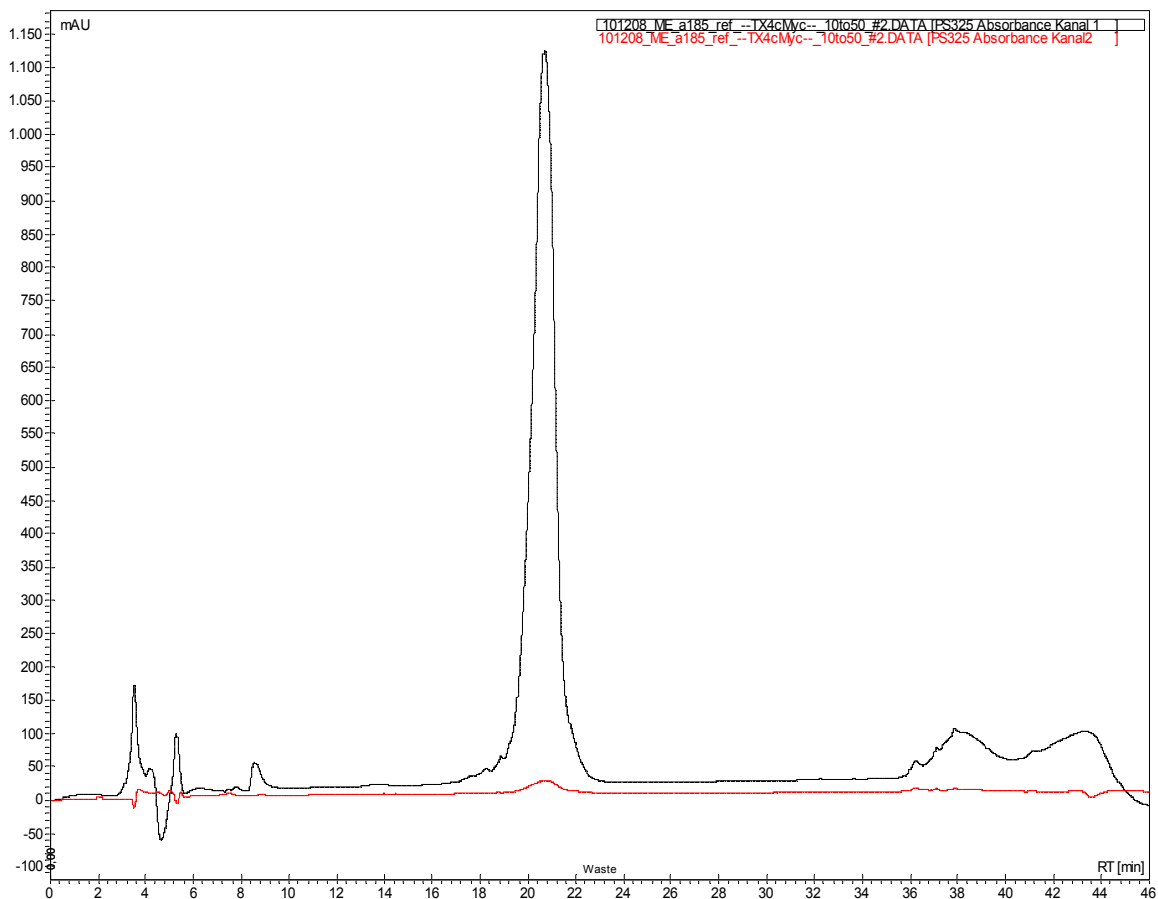
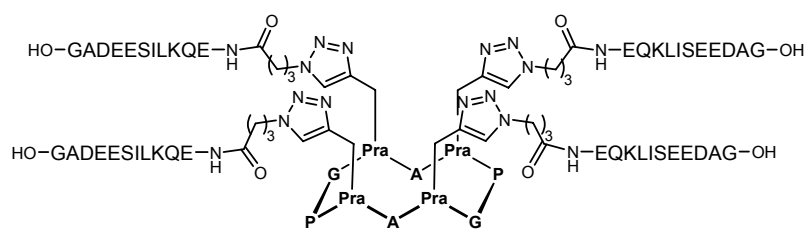
gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min



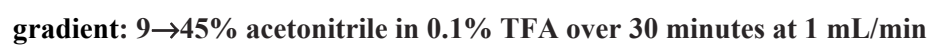
gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min

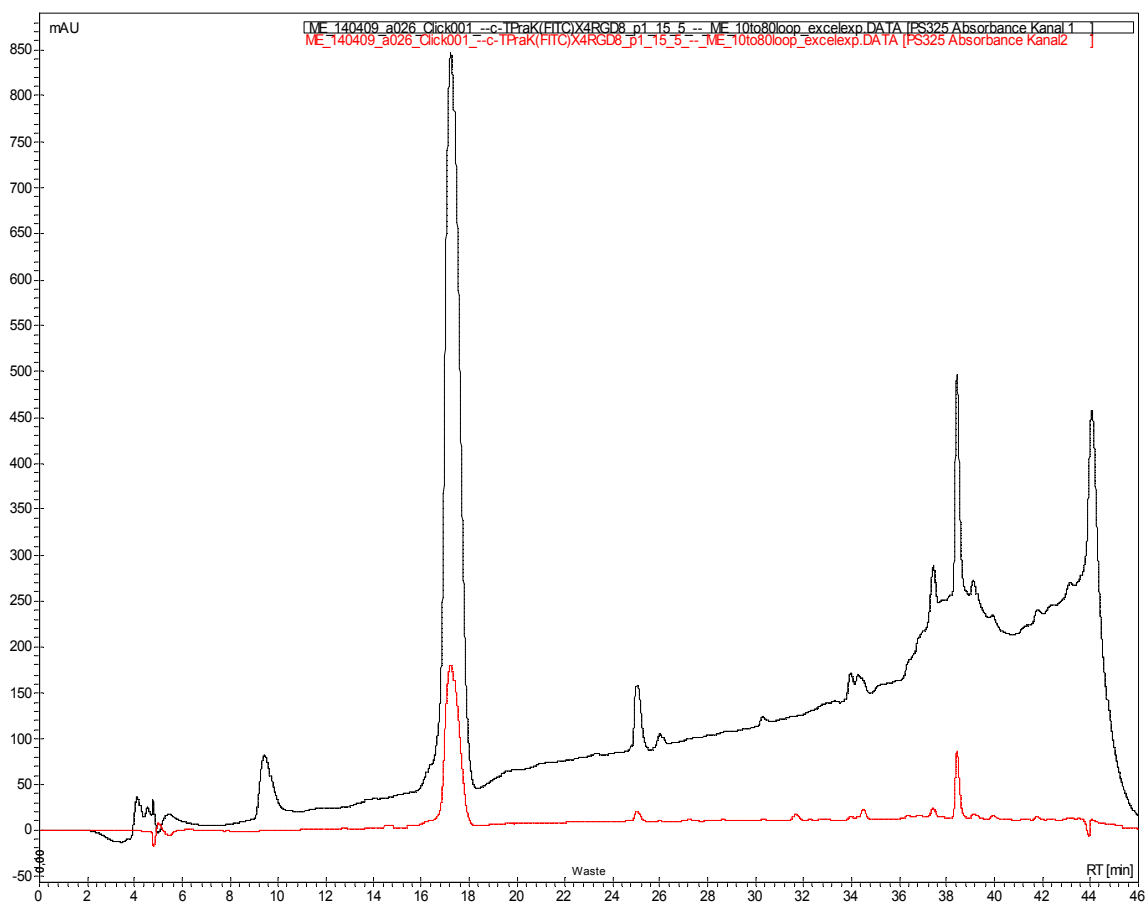
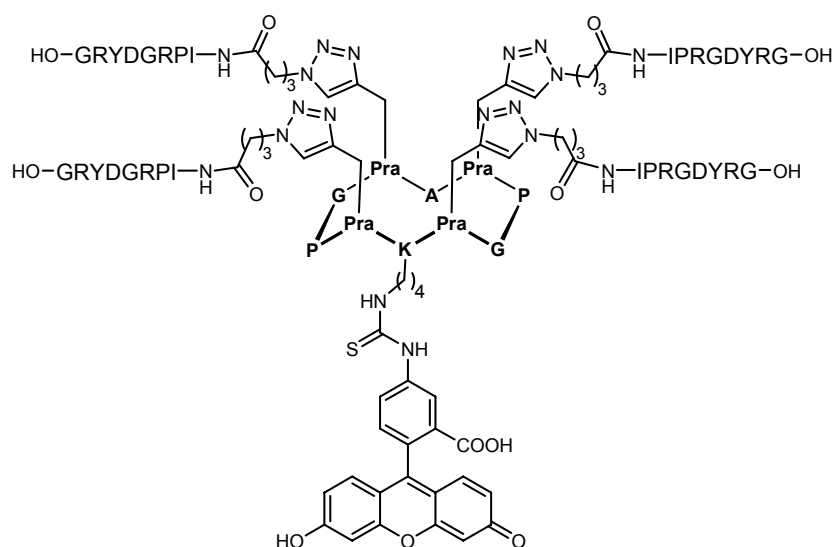


gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min



gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min

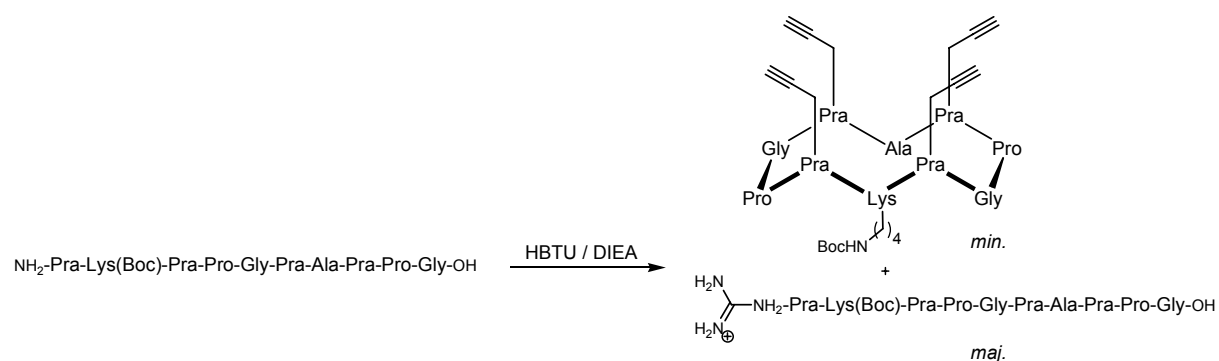




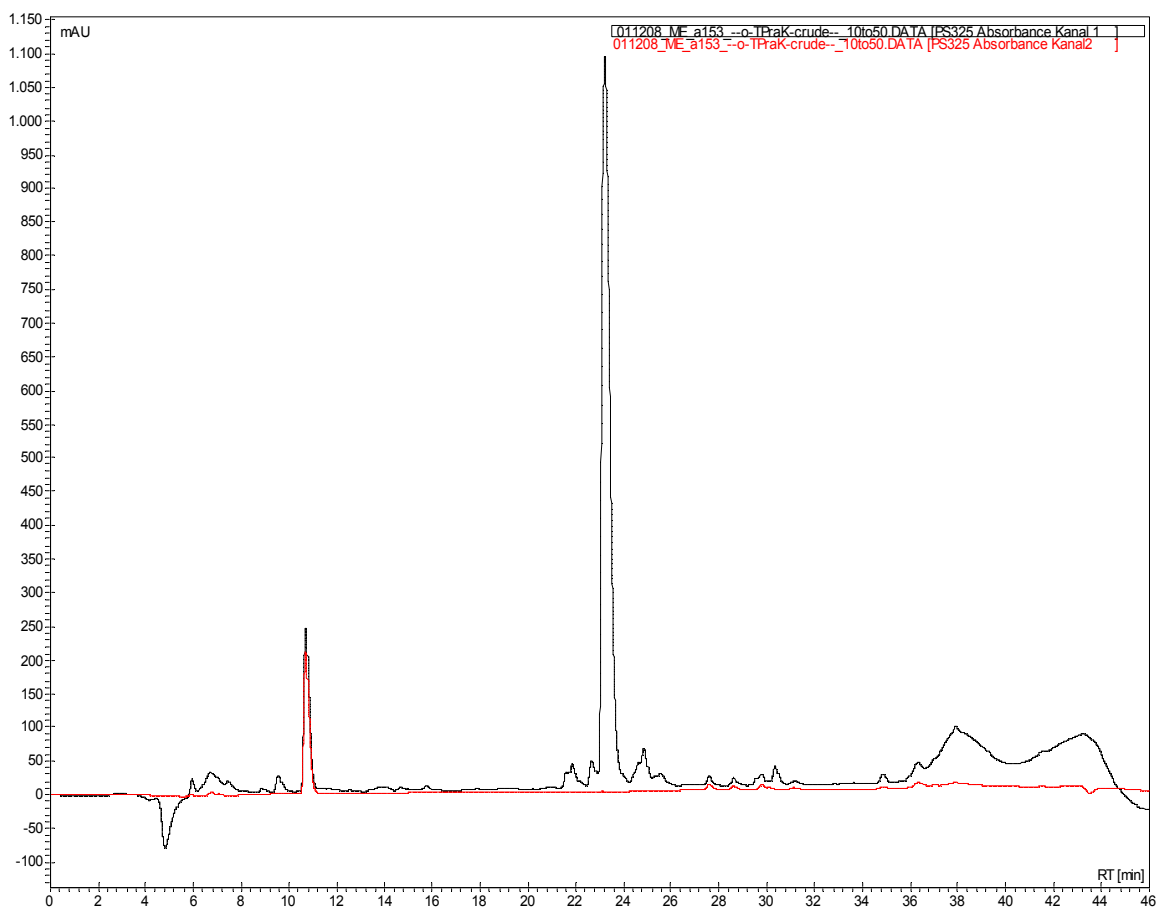
gradient: 9→72% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min.

RP-HPLC traces for the macrocyclization of NH₂-Pra-Lys(Boc)-Pra-Pro-Gly-Pra-Ala-Pra-Pro-Gly-OH to cyclo-(Pra-Lys(Boc)-Pra-Pro-Gly-Pra-Ala-Pra-Pro-Gly) using HBTU or at 220 (black) and 280 (red) nm:

HBTU activation:

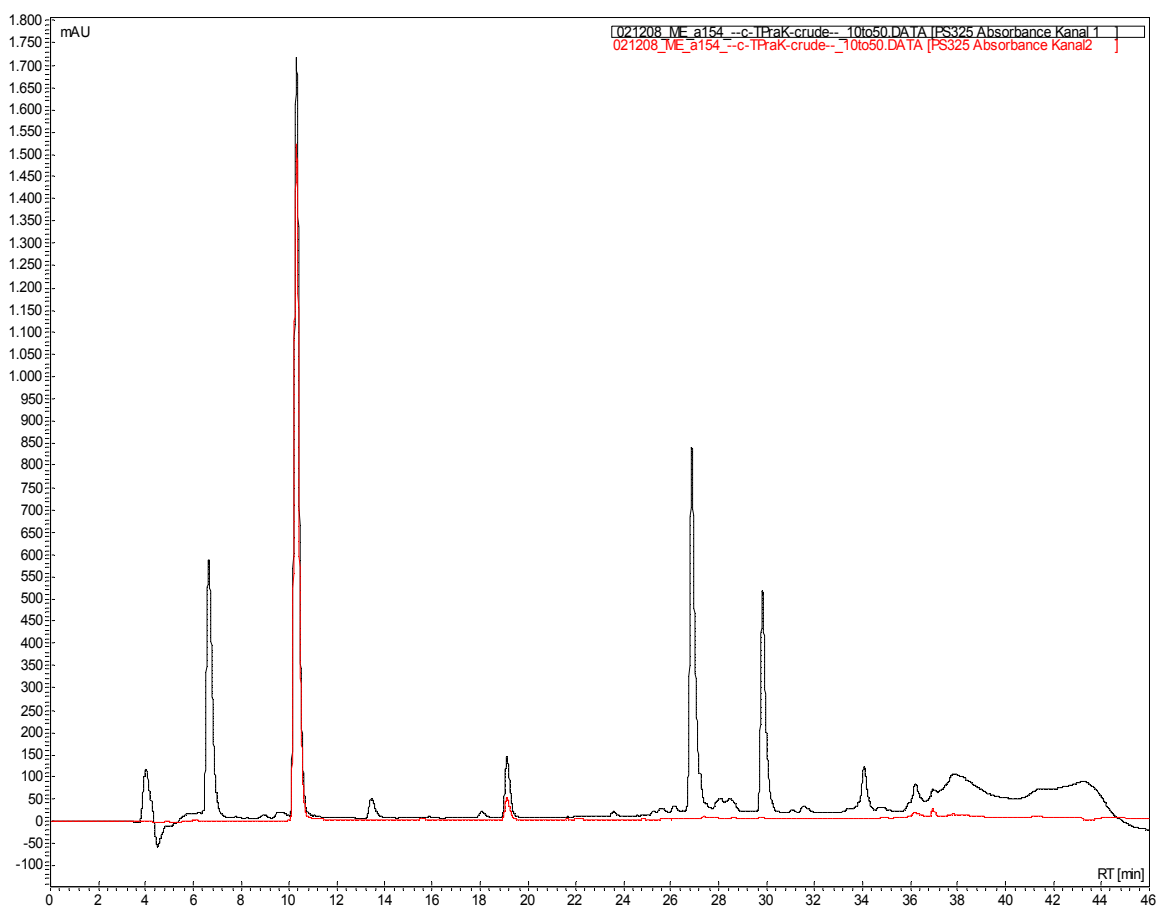


Reference: NH₂-Pra-Lys(Boc)-Pra-Pro-Gly-Pra-Ala-Pra-Pro-Gly-OH



gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min

Reaction mixture:

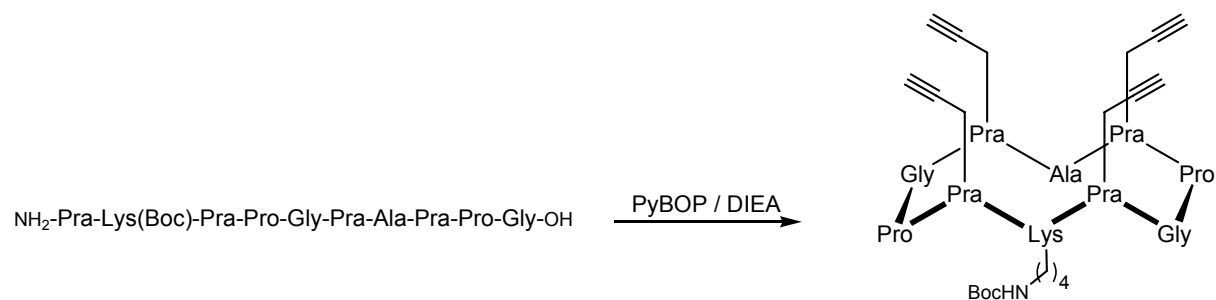


R_f = 26 min: guanidinated open chain precursor

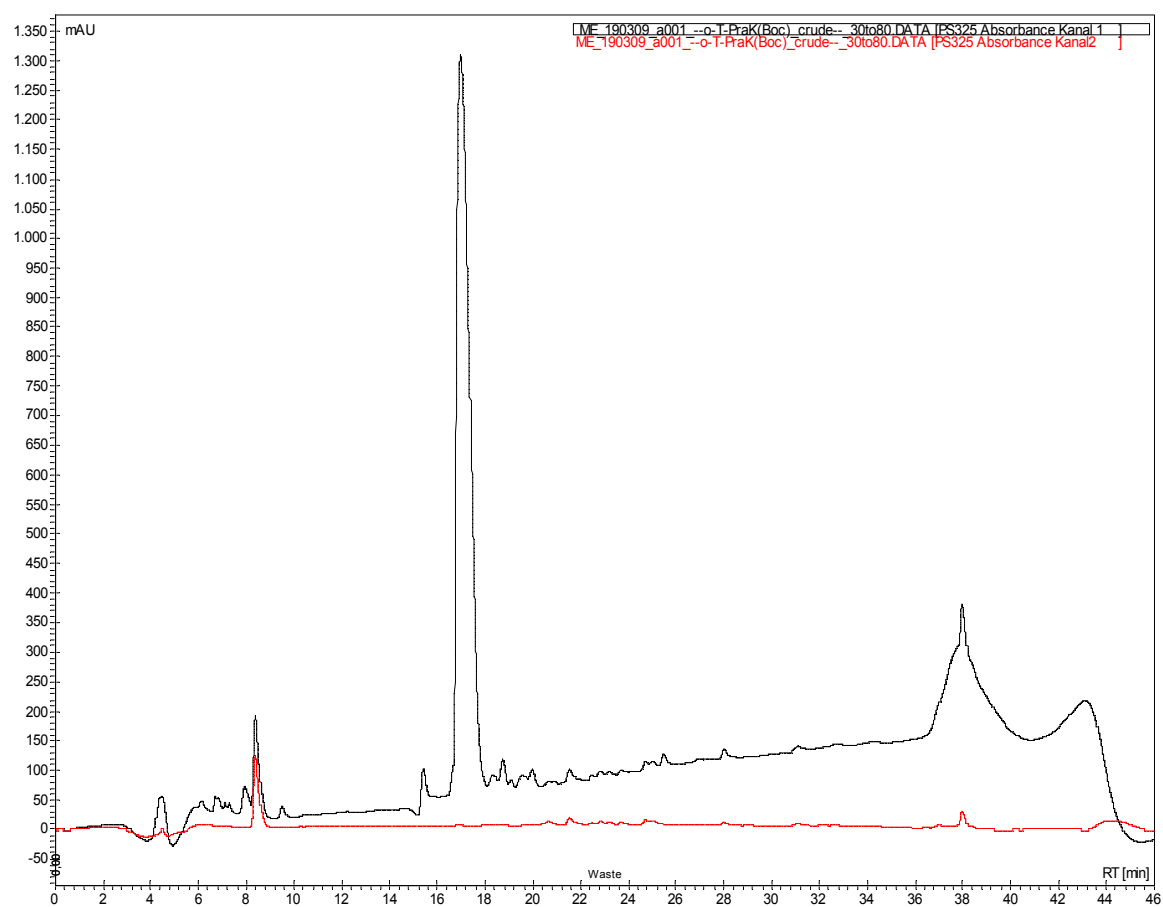
R_f = 30 min: *cyclo*-(Pra-Lys(Boc)-Pra-Pro-Gly-Pra-Ala-Pra-Pro-Gly)

gradient: 9→45% acetonitrile in 0.1% TFA over 30 minutes at 1 mL/min

PyBOP activation:

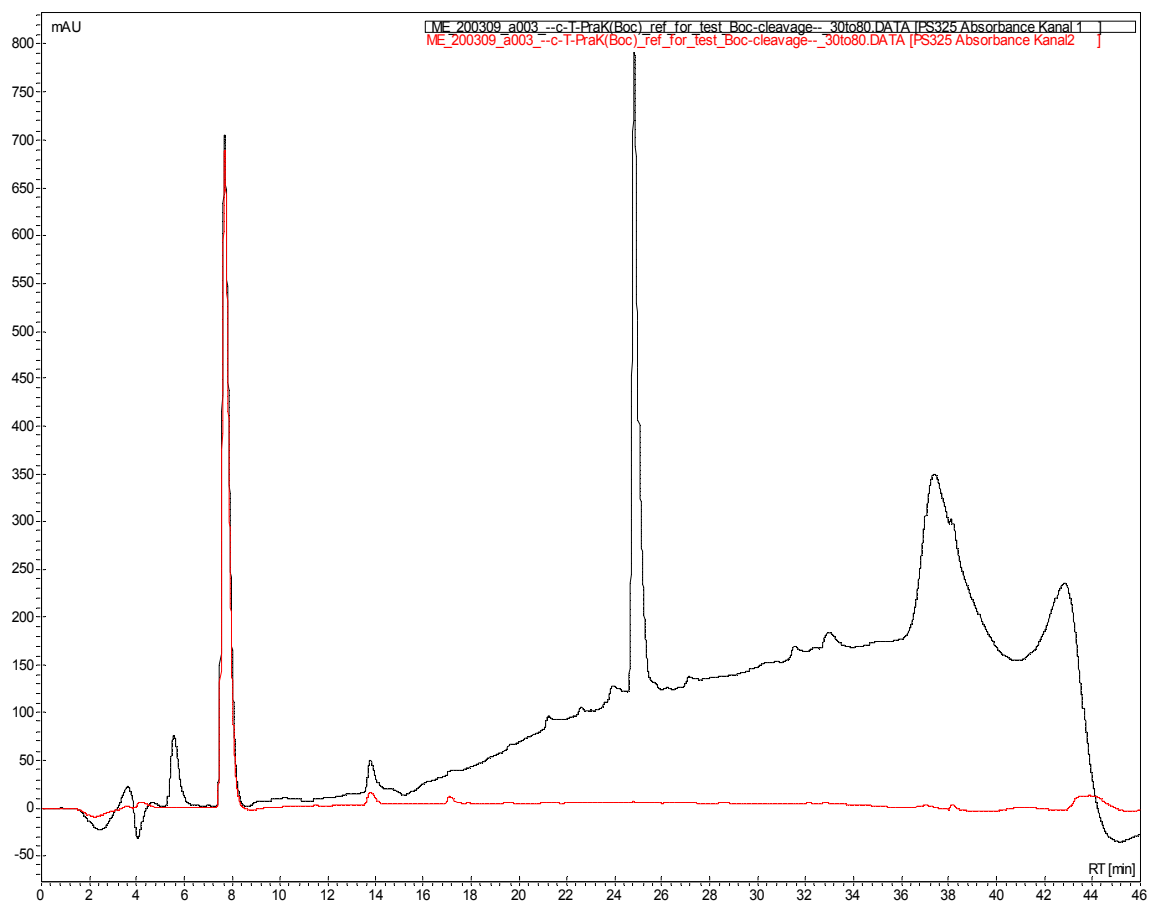


Reference: $\text{NH}_2\text{-Pra-Lys(Boc)-Pra-Pro-Gly-Pra-Ala-Pra-Pro-Gly-OH}$



gradient: 30→80% methanol in 0.1% TFA over 30 minutes at 1 mL/min

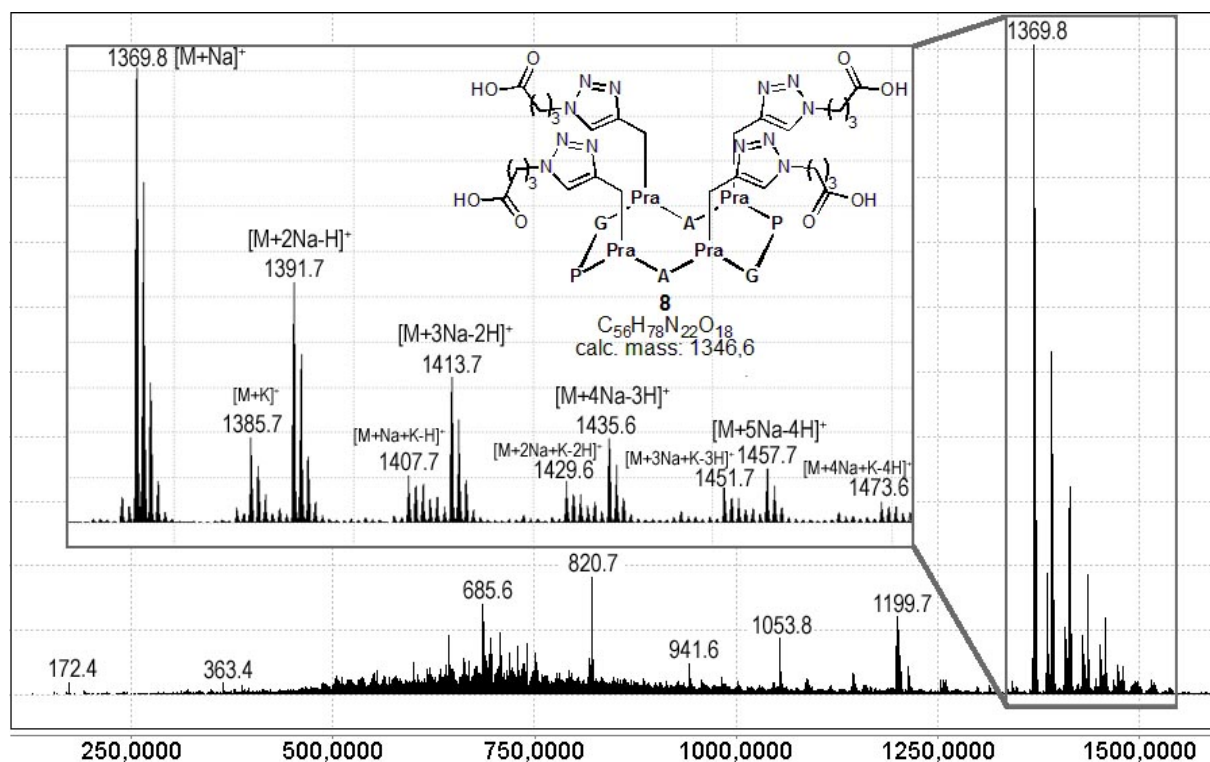
Reaction mixture:



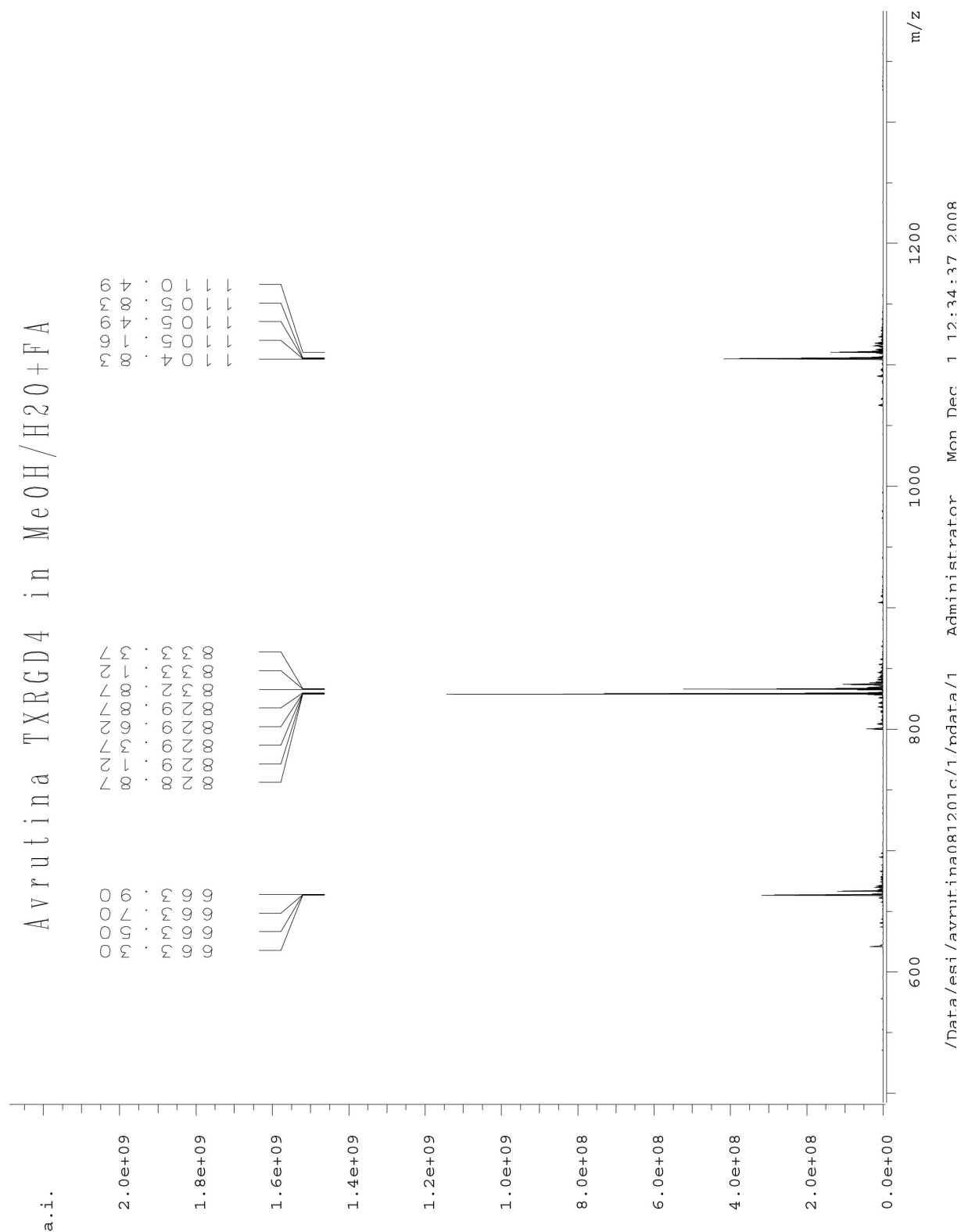
$R_t = 24$ min: *cyclo*-(Pra-Lys(Boc)-Pra-Pro-Gly-Pra-Ala-Pra-Pro-Gly)

gradient: 30→80% methanol in 0.1% TFA over 30 minutes at 1 mL/min

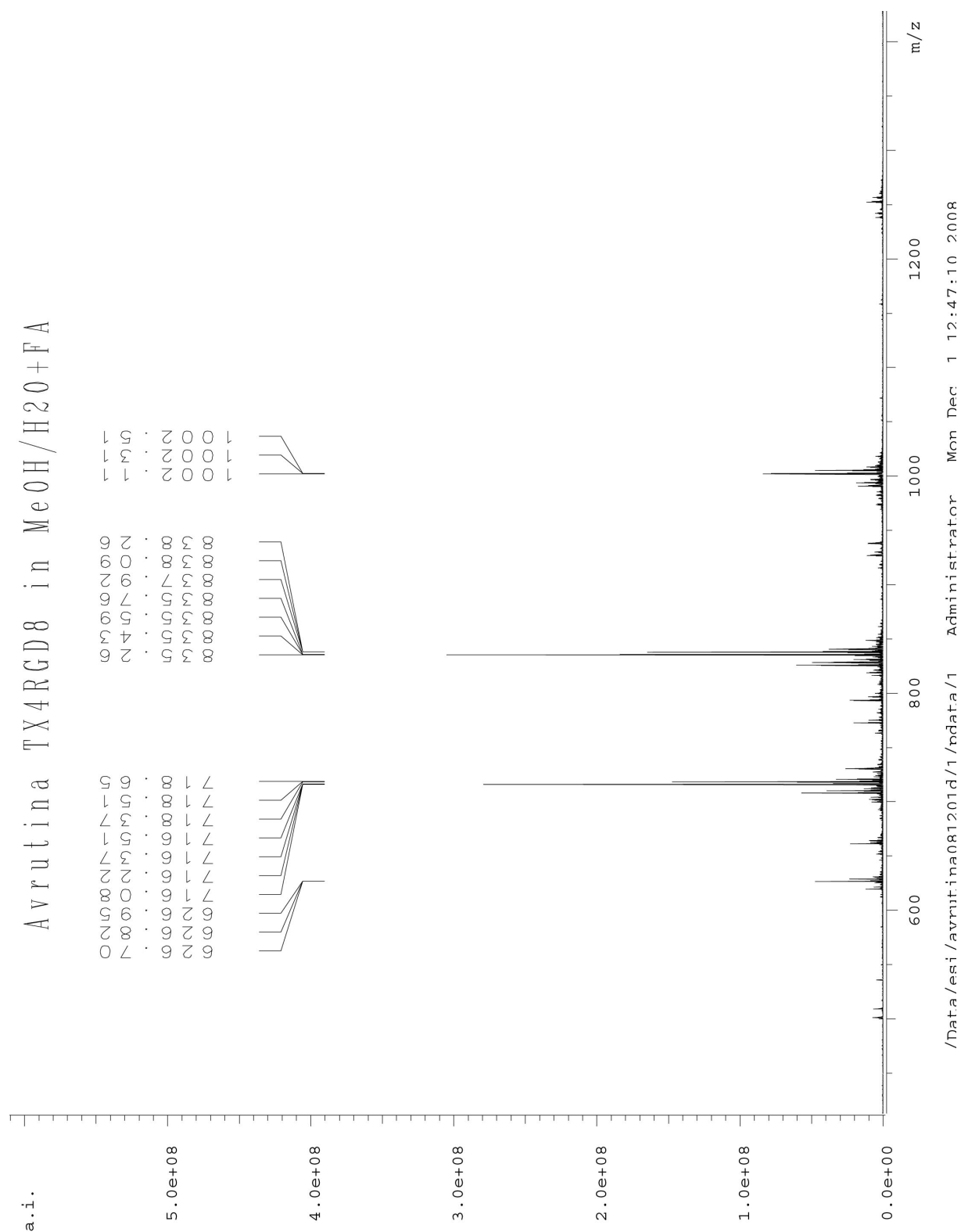
ESI-MS:



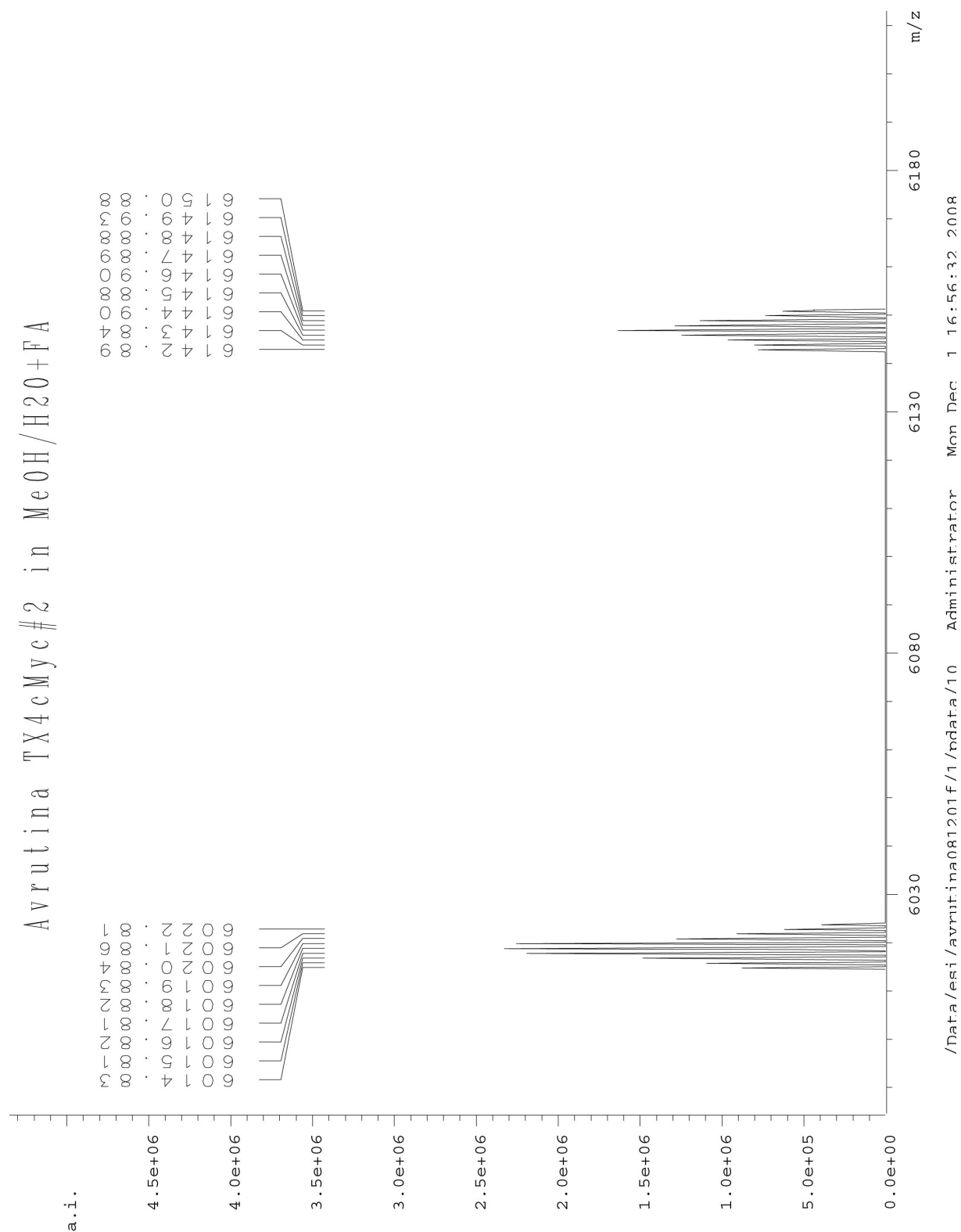
Conjugate 8: $C_{56}H_{78}N_{22}O_{18}$ Calc. Mass: 1346.6 ^{m/z}



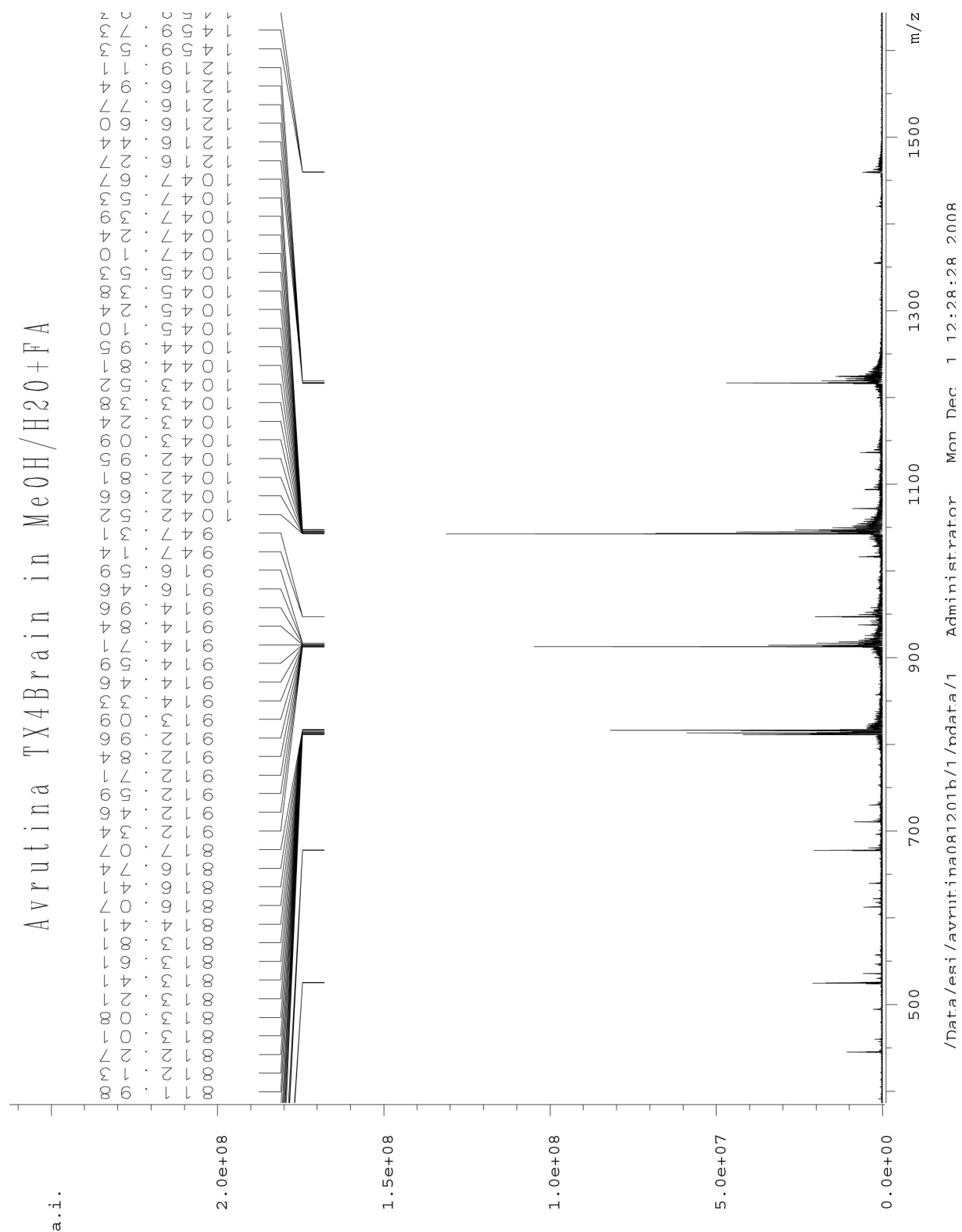
Conjugate 9: C₁₄₀H₁₉₄N₅₀O₄₆, Calc. Mass: 3311.4



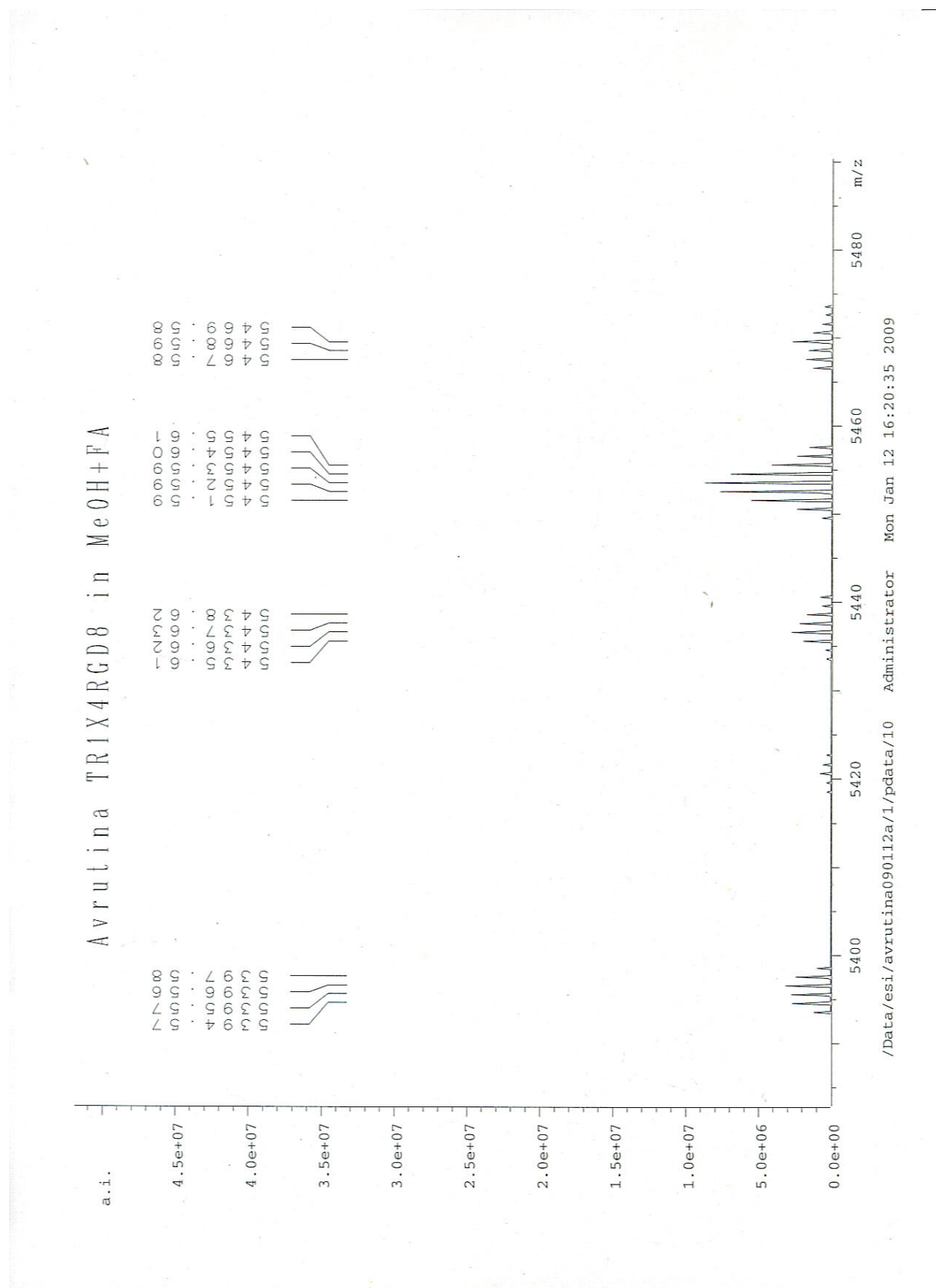
Conjugate 10: C₂₁₆H₃₂₆N₇₈O₆₂, Calc. Mass: 5004.5



Conjugate 11: C₂₅₆H₄₀₂N₇₄O₁₀₂, Calc. Mass: 6144.9



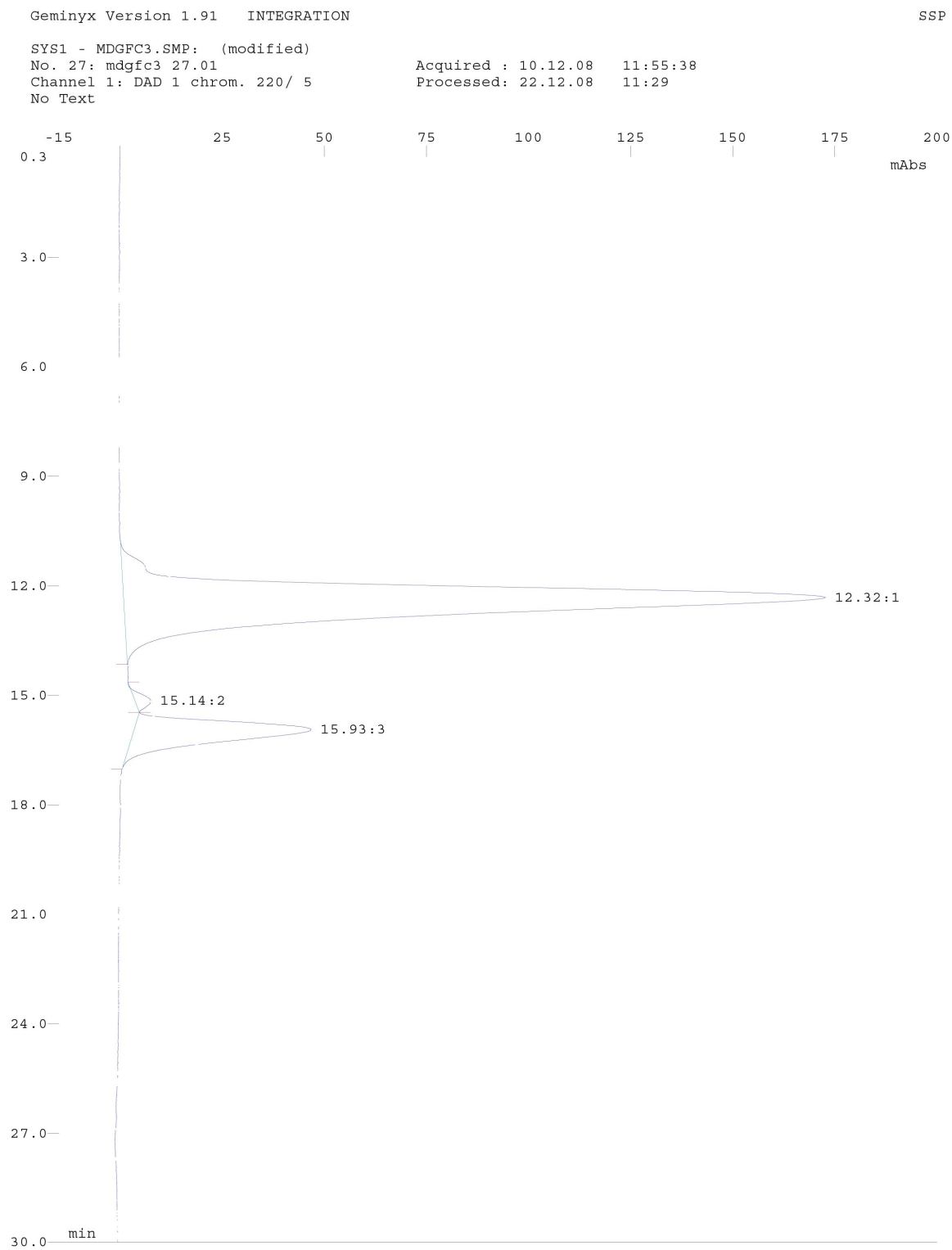
Conjugate 12: C₃₂₄H₄₇₄N₁₀₆O₉₀, Calc. Mass: 7289.6



Conjugate 13: $C_{240}H_{344}N_{80}O_{67}S$, Calc. Mass: 5450.6

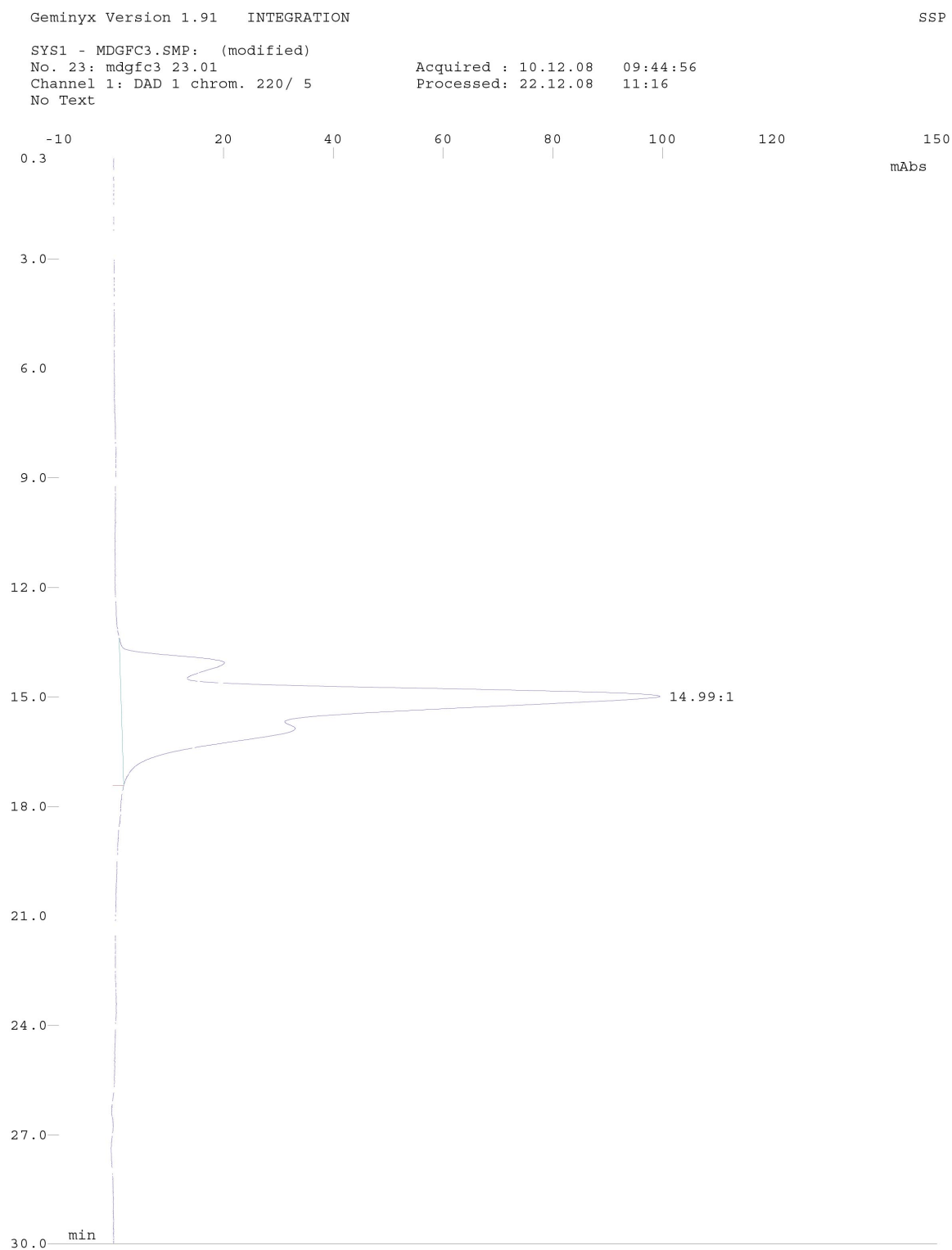
GFC traces at 220 nm: (eluent: 150 m aq. NaCl at flow rate 0.75 mL / min)

Conjugate 9:

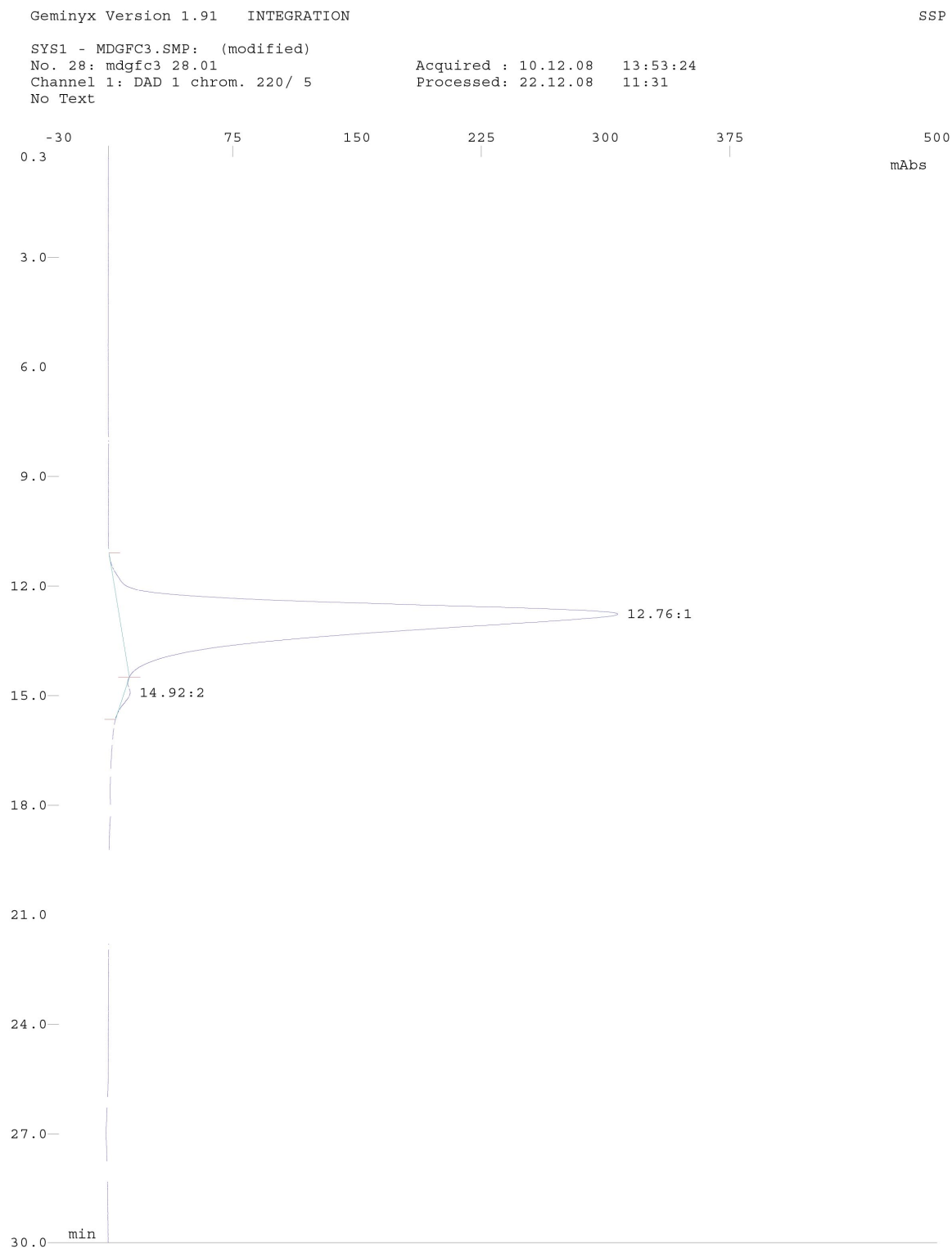


Conjugate 10:

Peptide ligand 5:

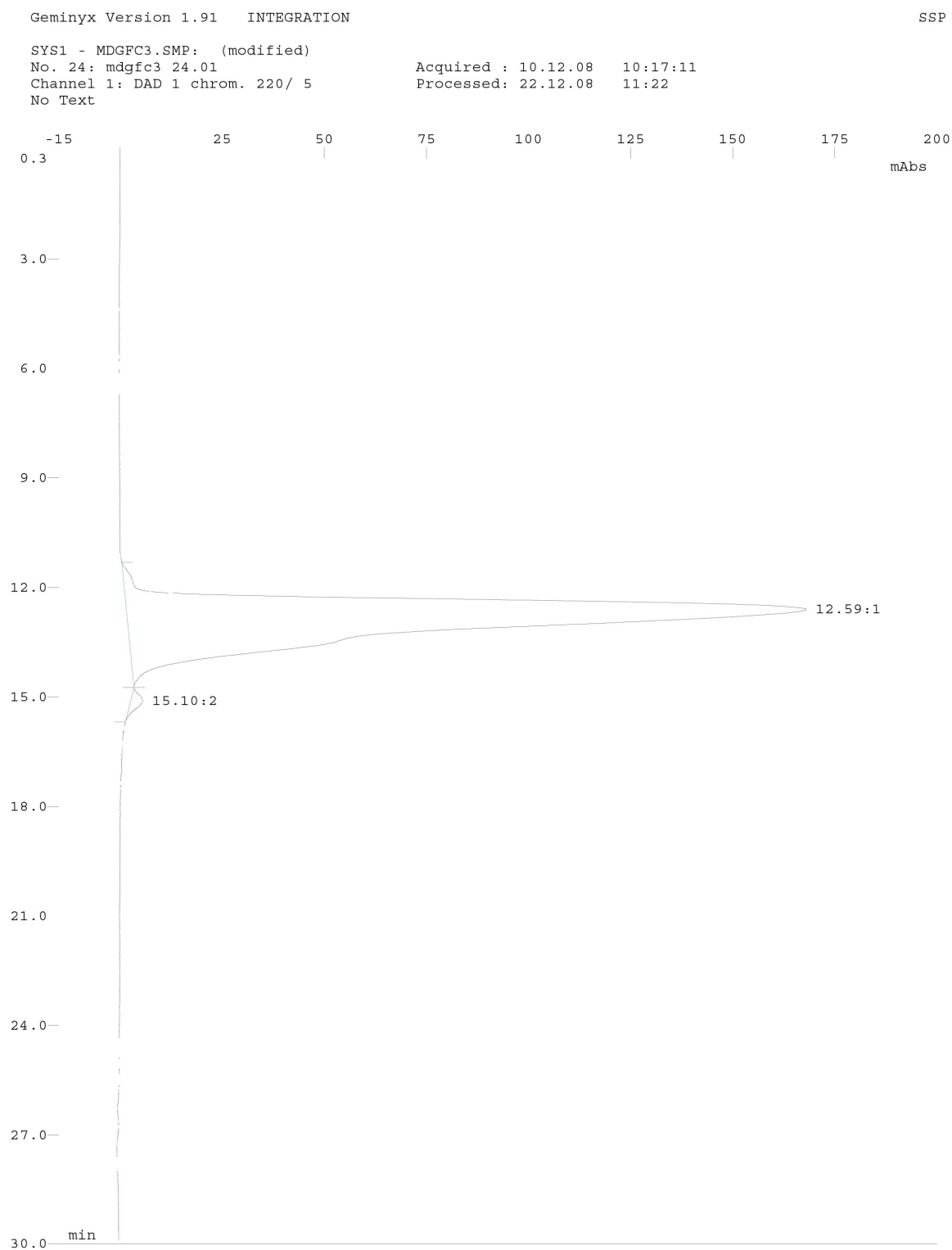


Conjugation product 10:

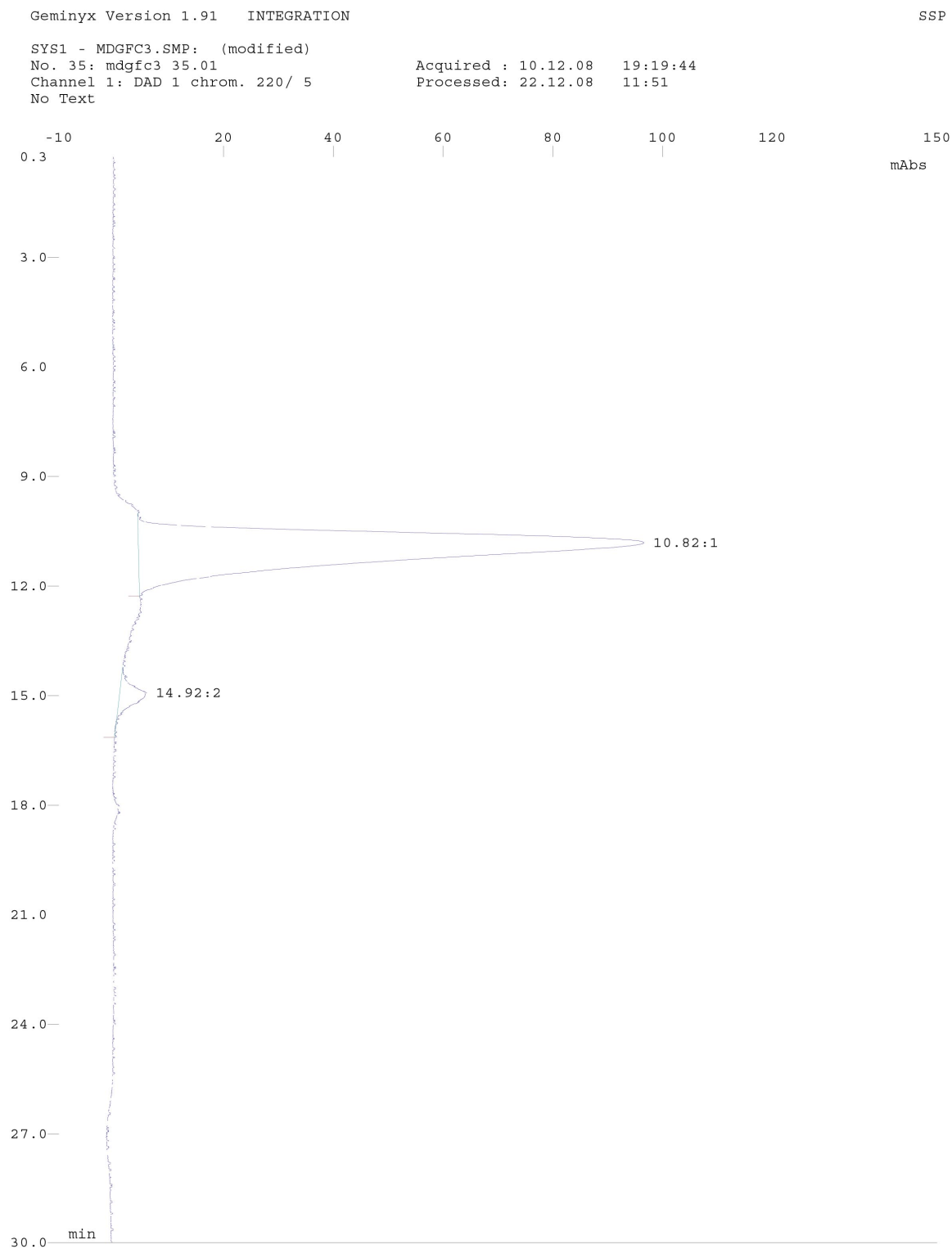


Conjugate 11:

Peptide ligand 6:

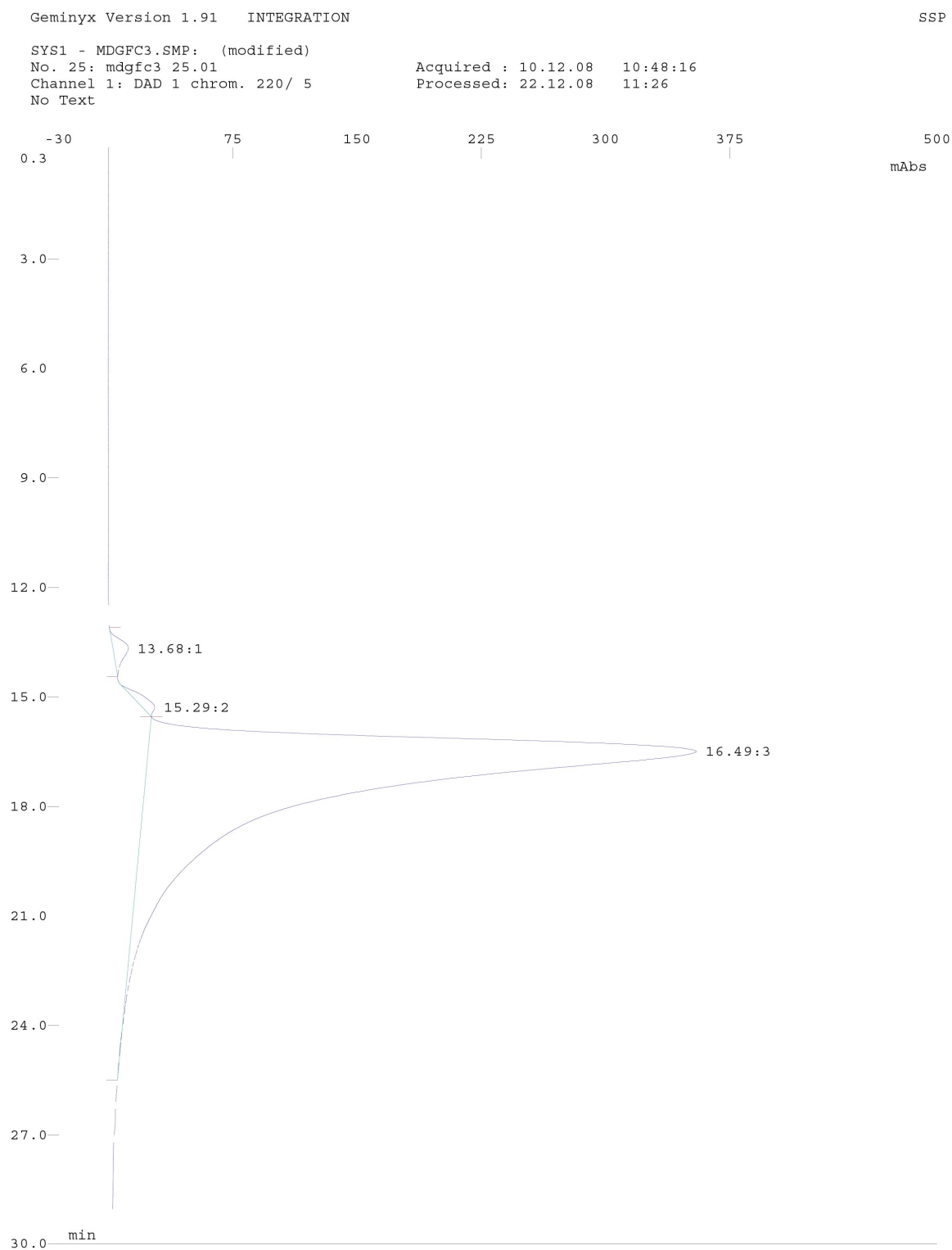


Conjugation product 11:

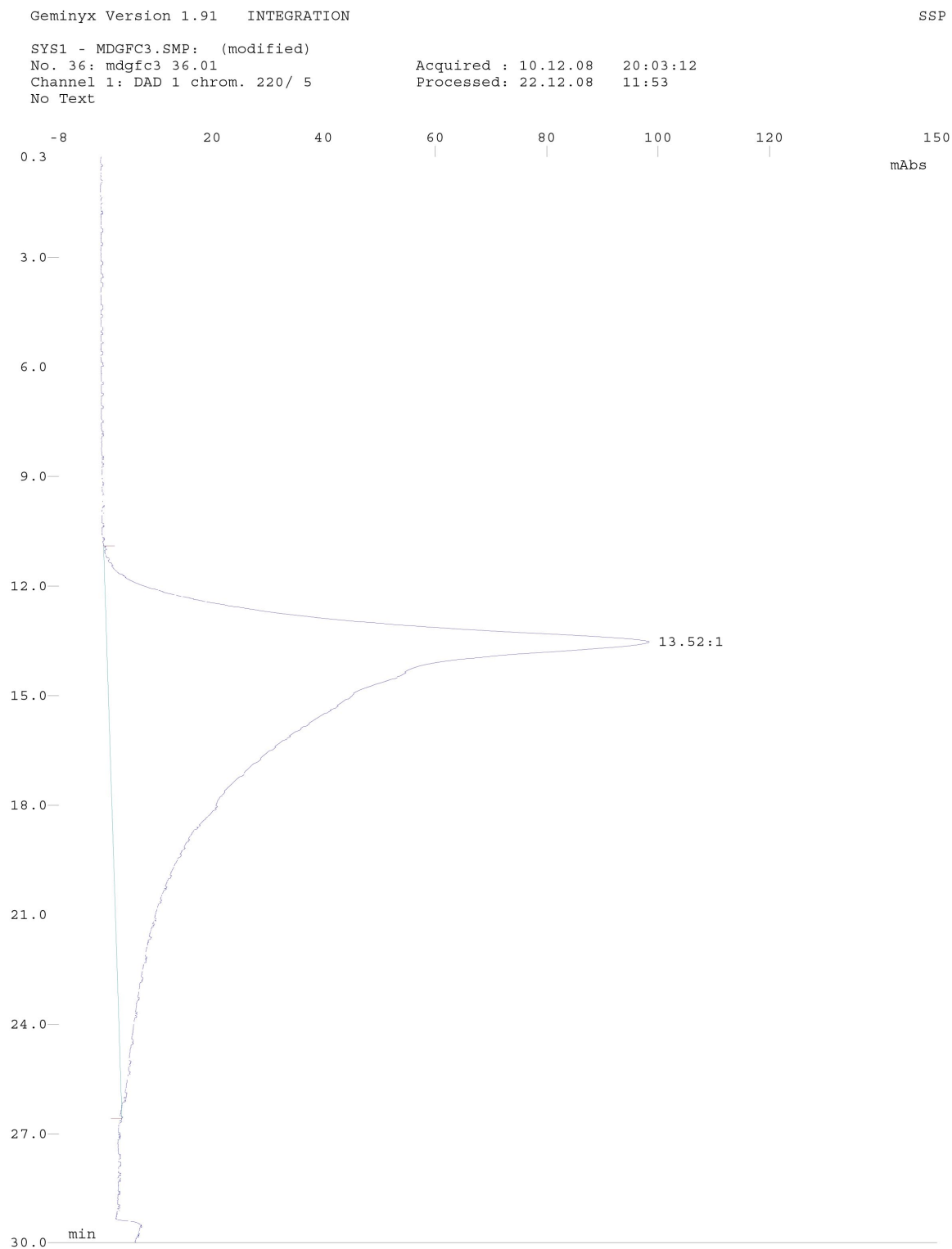


Conjugate 12:

Peptide ligand 7:



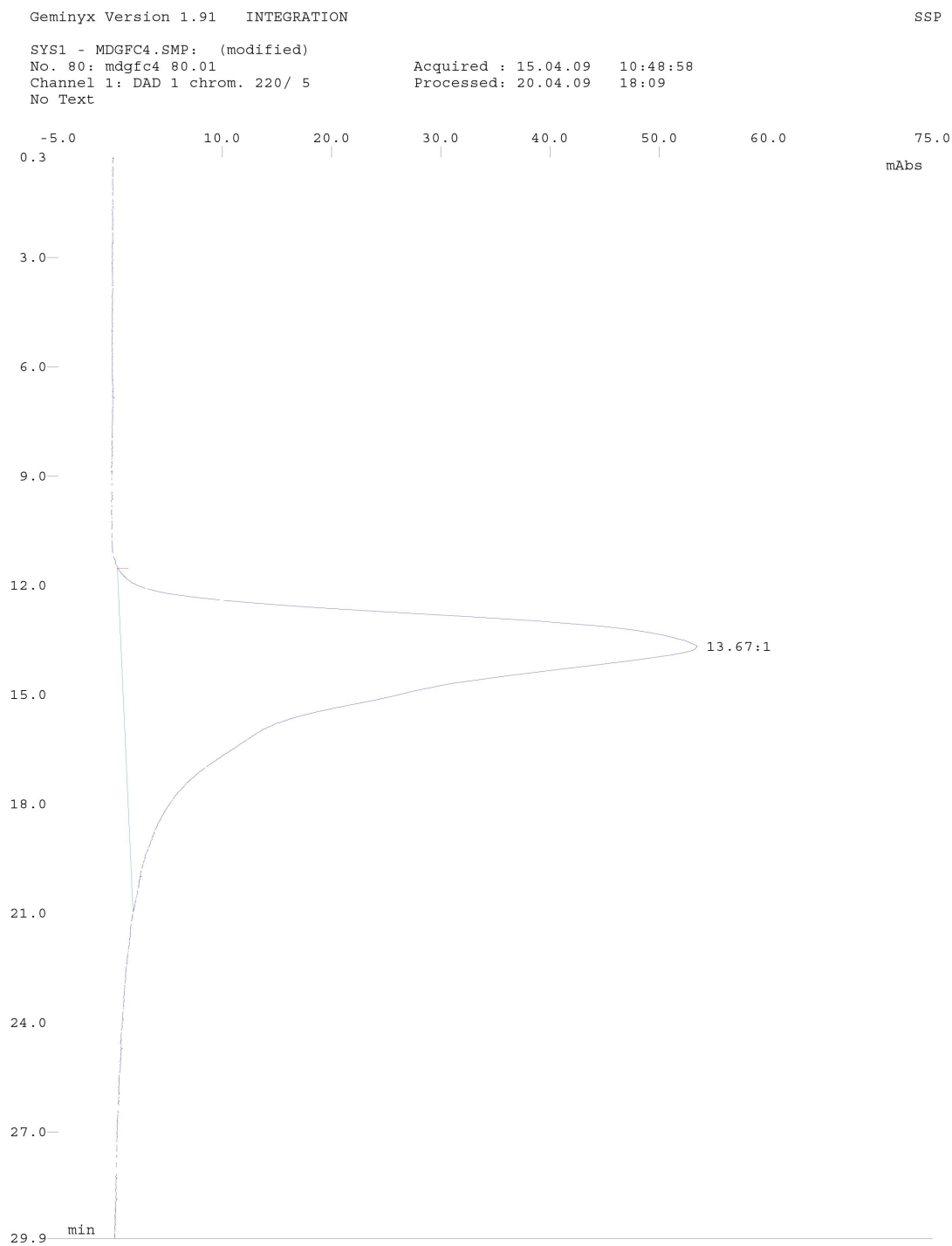
Conjugation product 12:



Conjugate 13:

Peptide ligand 5 see “conjugate 10”

Conjugation product 13:



GFC trace of 13 at 220 nm and 485 nm:

