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Supporting Information for

Late Stage Modification of Receptors Identified from Dynamic Combinatorial Libraries

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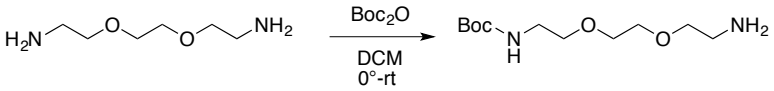
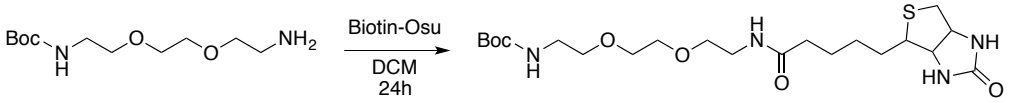
Synthesis of Biotin-Receptors

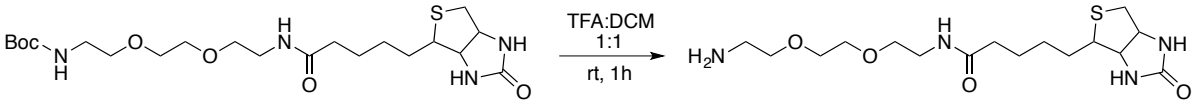
Biotin-PEG_2-NH_2



The mono-Boc protected PEG_2 diamine was synthesized according to a published procedure by stirring the diamine (1g, 6.76 mmol) with Boc anhydride (0.221g, 1.01 mmol) in 70 mL DCM for 24 hours. After 24 hours, the DCM solution was extracted four times with water and once with brine, then the organic layer was dried with $MgSO_4$ and filtered. The DCM was removed yield the product as a yellowish oil (0.245 g, 98%).



The mono-Boc protected PEG diamine (125 mg, 0.5 mmol) was coupled to Biotin-Osu (188 mg, 0.55 mmol) by stirring in a mixture of 9:1 DCM:MeOH (5 mL) for 24 hours. The solvent was then evaporated and the product purified by column chromatography using a gradient of 0-10% MeOH in DCM (130 mg, 54%).

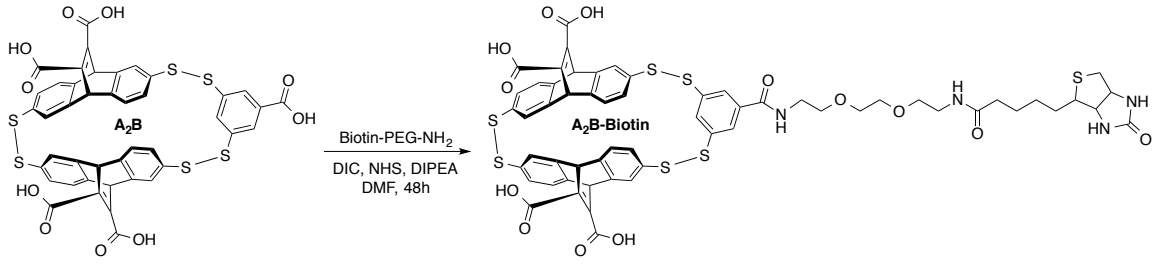


The Boc group was removed by stirring 130 mg (0.27 mmol) of the protected starting material in a 1:1 solution of TFA:DCM (3 mL) for 1 hour. The solvent was then blown off under a stream of N_2, and the residue dried under vacuum to give the free amine in quantitative yield. The product was confirmed by ESI-MS. MS (calculated) = 375.21 $[M+H]^{1+}$; MS (observed) = 375.21 $[M+H]^{1+}$.

General Approach for Coupling Biotin-PEG-NH_2 to A_2X receptors

The coupling of biotin to all receptors was achieved by stirring each receptor (2-4 μmol, 1 eq.) with Biotin-PEG-NH_2 (10 eq. PEG_2 / 7.5 eq. PEG_{11}), DIC (7.5 eq. with PEG_2, 5 eq. with PEG_{11}), NHS (7.5 eq. with PEG_2, 5 eq. with PEG_{11}), and DIPEA (12 eq. with PEG_2, 10 eq. with PEG_{11}) in 1 mL of anhydrous DMF for 48 hours. The DMF was then removed under vacuum, and the residue dissolved into 3 mL of 30%MeOH:H_2O. To ensure solubility of the product, the solution is adjusted to pH > 8 with dilute NaOH. The coupled product is purified by reverse phase HPLC using a linear gradient of 10-100% B in 45 minutes (A: 10 mM NH_4OAc in H_2O; B: 10 mM NH_4OAc in 9:1 ACN:H_2O). All receptors were purified using an Atlantis PrepT3 5 μm 10 x 150 mm C18 column.

A_2B-Biotin:



Scheme S1. Synthesis of **A_2B-Biotin**.

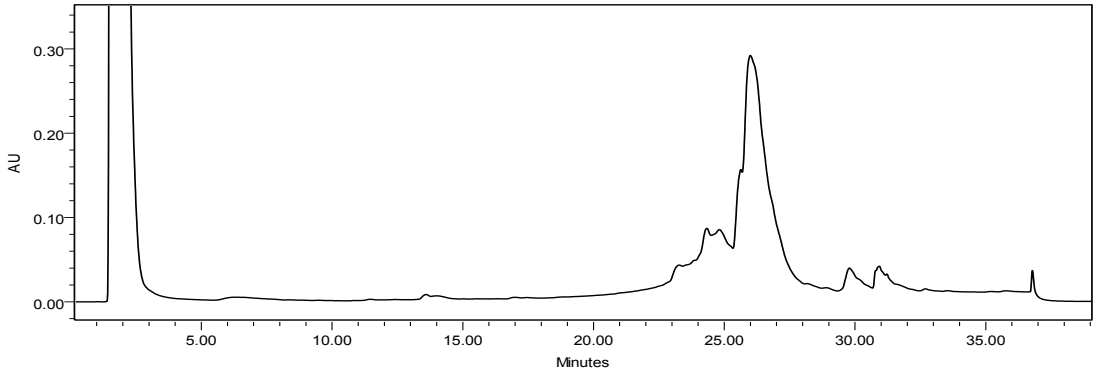


Figure S1. HPLC trace for the crude **A_2B-Biotin**, which elutes at ~26 minutes. **A_2B-Biotin** was formed in approximately 46% yield, by peak area.

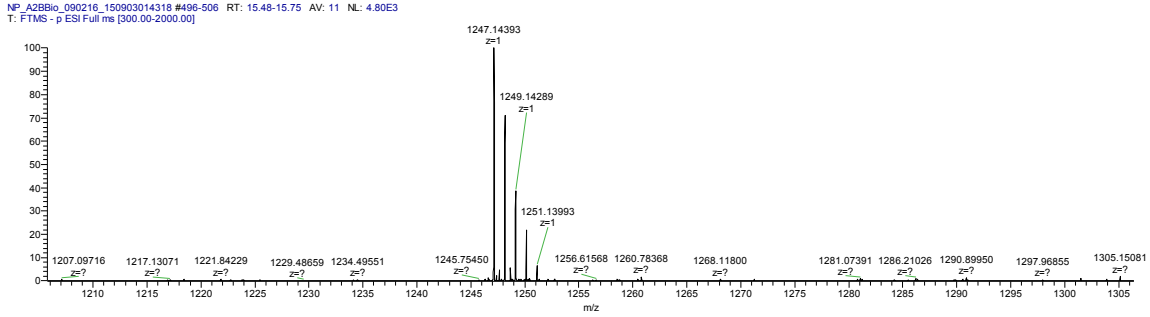
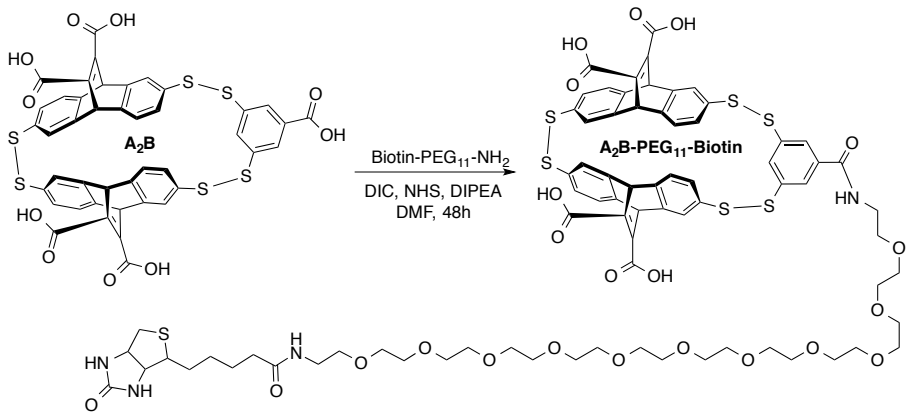


Figure S2. HRMS (-) of **A_2B-Biotin**. Theoretical $[M-H]^{1-}$ = 1247.15031; Observed $[M-H]^{1-}$ = 1247.14393.

A_2B-PEG_{11}-Biotin



Scheme S2. Synthesis of **A_2B-PEG_{11}-Biotin**.

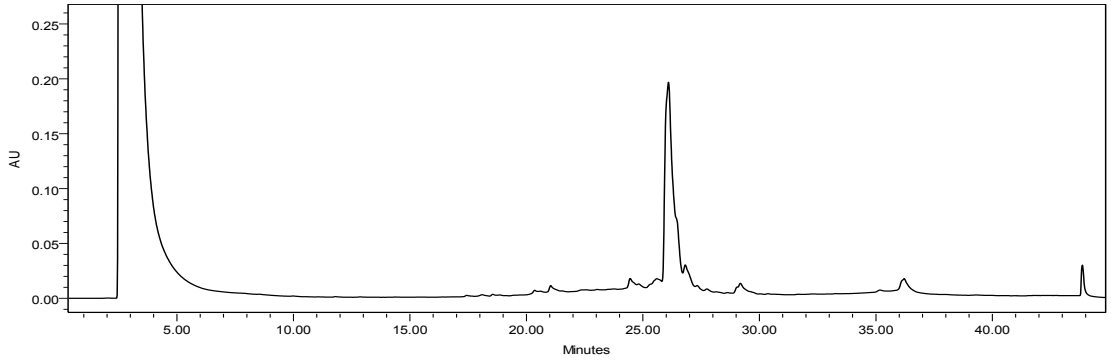


Figure S3. HPLC trace for the crude **A_2B-PEG_{11}-Biotin**, which elutes at ~26 minutes. **A_2B-PEG_{11}-Biotin** was formed in approximately 60% yield, by peak area.

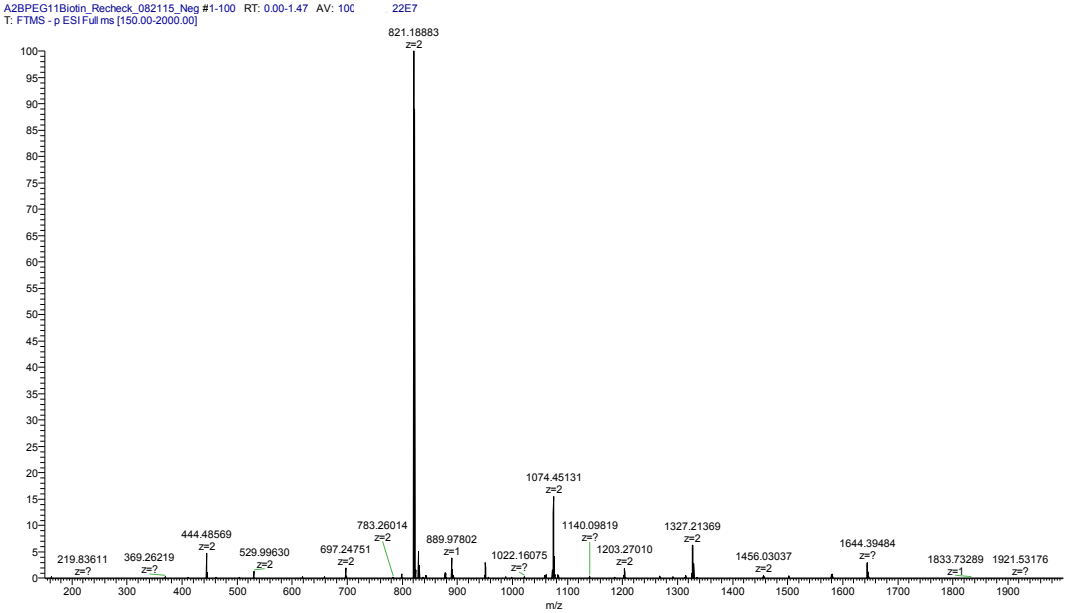
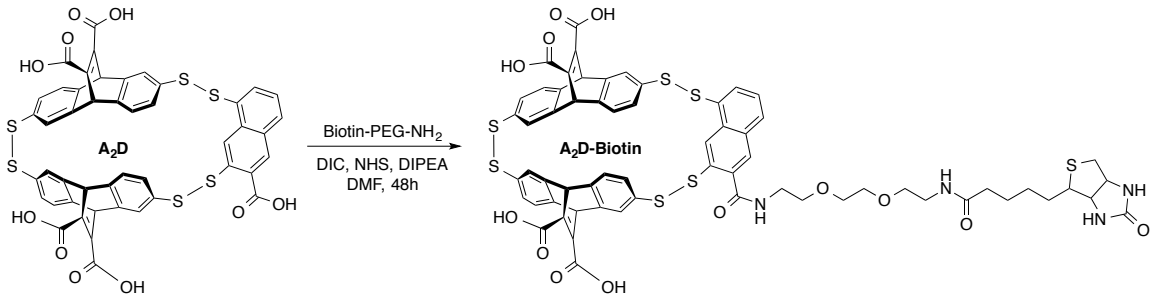


Figure S4. HRMS (-) of **A_2B-PEG_{11}-Biotin**. Theoretical $[M-2H]^{2-}$ = 821.18948; Observed $[M-2H]^{2-}$ = 821.18883.

A_2D-Biotin



Scheme S3. Synthesis of **A_2D-Biotin**.

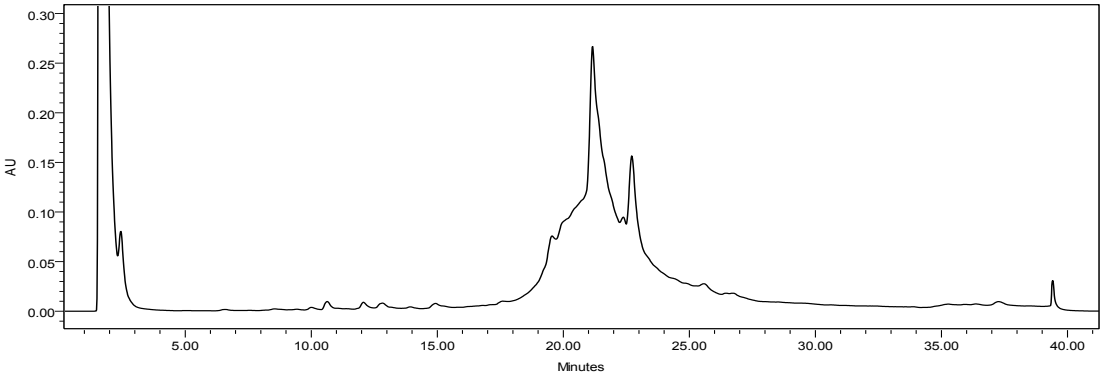


Figure S5. HPLC trace for the crude **A_2D-Biotin**, which elutes at ~23 minutes. **A_2D-Biotin** was formed in approximately 13% yield, by peak area.

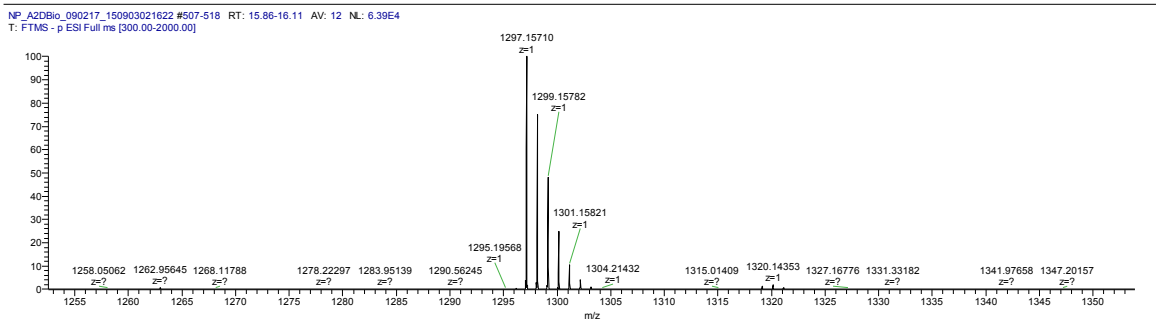
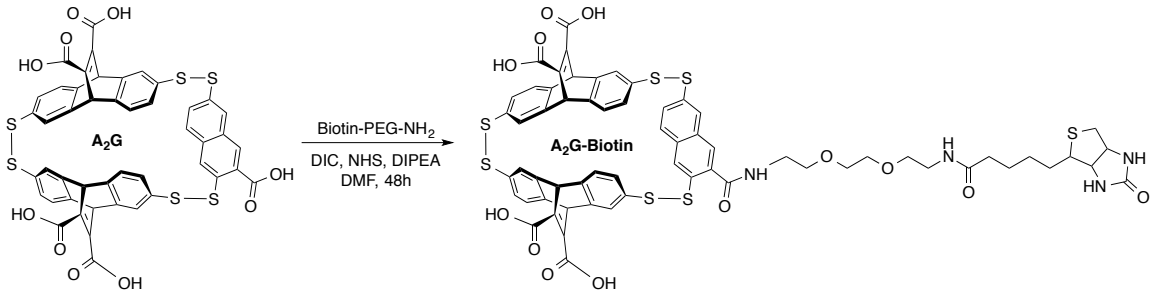


Figure S6. HRMS (-) of **A_2D-Biotin**. Theoretical $[M-H]^{1-}$ = 1297.16596; Observed $[M-H]^{1-}$ = 1297.15710.

A_2G-Biotin



Scheme S4. Synthesis of **A_2G-Biotin**.

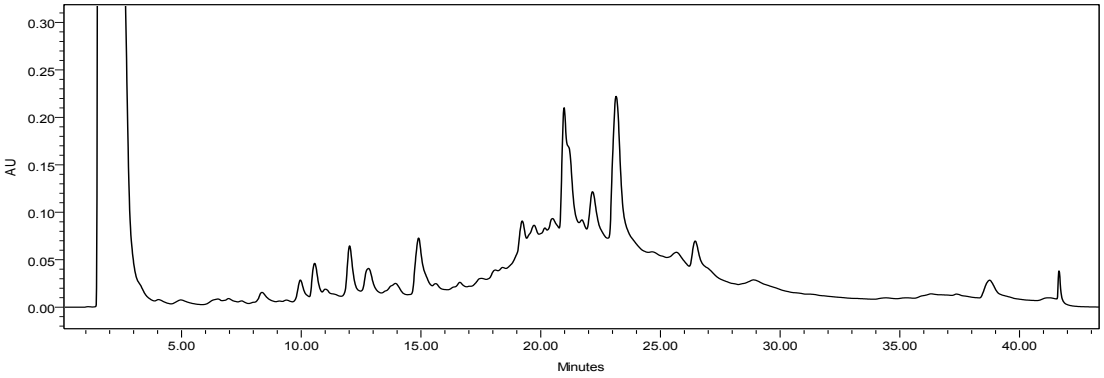


Figure S7. HPLC trace for the crude **A_2G-Biotin**, which elutes at ~23 minutes. **A_2G-Biotin** was formed in approximately 17% yield, by peak area.

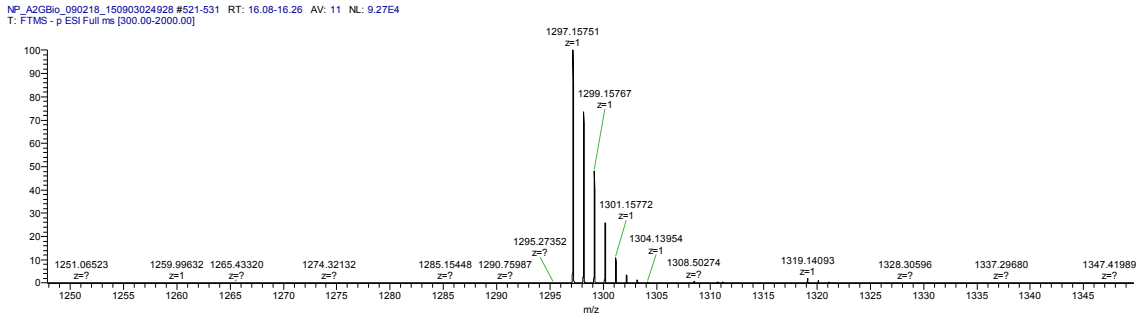
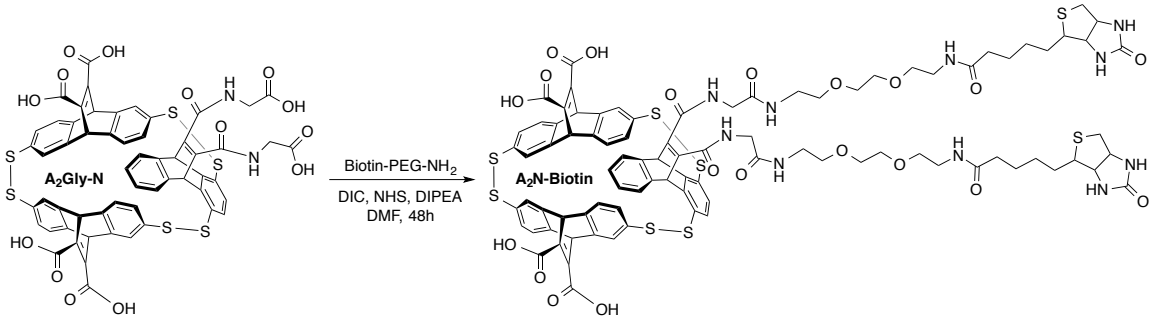


Figure S8. HRMS (-) of **A_2G-Biotin**. Theoretical $[M-H]^{1-}$ = 1297.16596; Observed $[M-H]^{1-}$ = 1297.15751.

A_2N-Biotin



Scheme S5. Synthesis of **A_2N-Biotin**.

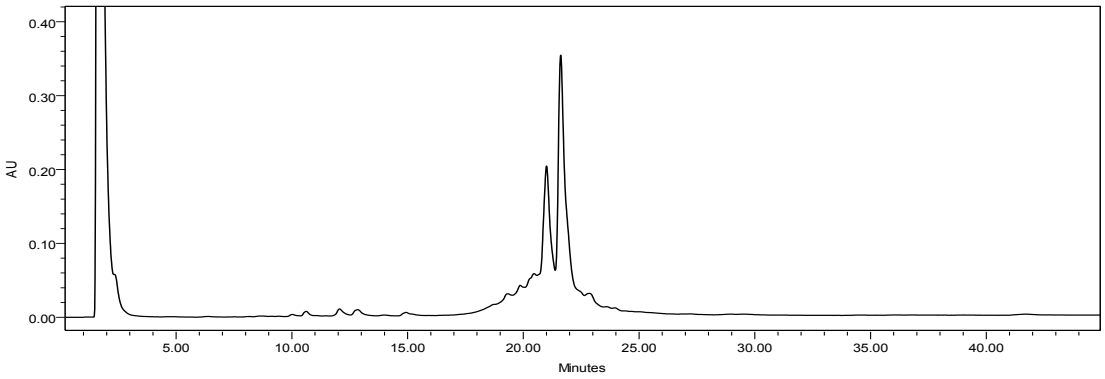


Figure S9. HPLC trace for the crude **A_2N-Biotin**, which elutes at ~22 minutes. **A_2N-Biotin** was formed in approximately 43% yield, by peak area.

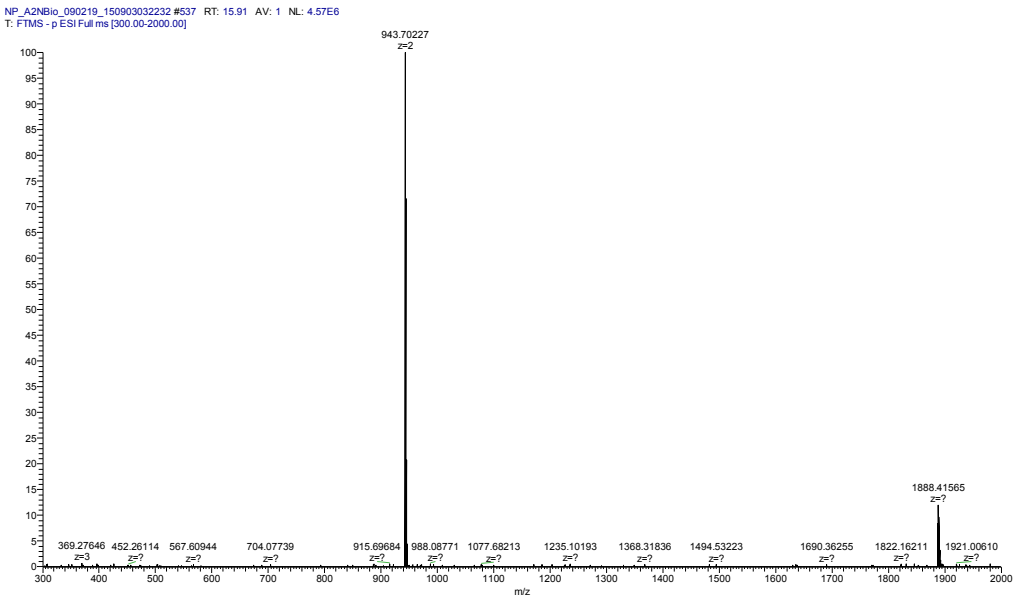
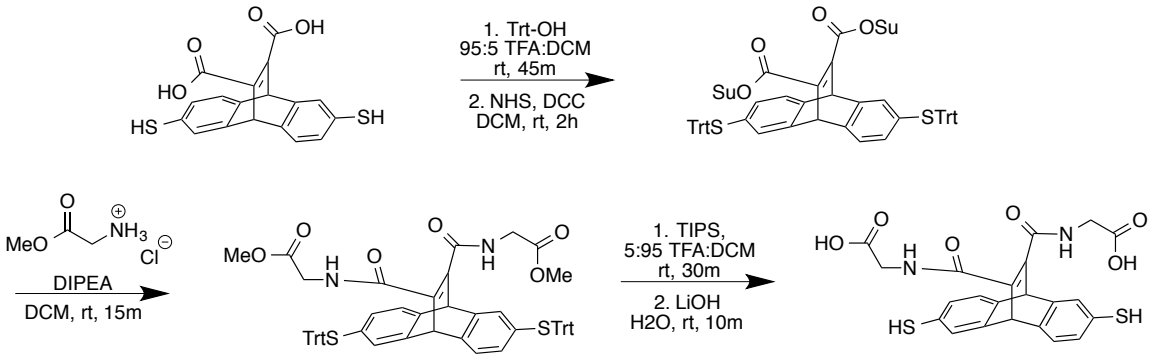


Figure S10. HRMS (-) of **A_2N-Biotin**. Theoretical $[M-2H]^{2-}$ = 943.20547; Observed $[M-2H]^{2-}$ = 943.70227.

Synthesis of Gly-A/N:



Scheme S6. General synthesis of carboxylate spaced monomers Gly-A and Gly-N. The synthesis is shown for monomer **A**, but is identical for monomer **N**.

The synthesis for **Gly-A** is described, but is identical for **Gly-N**.

Monomer **A** (1 g, 2.8 mmol) and triphenylmethanol (1.61 g, 6.2 mmol) were added to a flask and dissolved in 10 mL of 95:5 TFA:DCM. The reaction mixture was placed under N_2 and was allowed to stir for 45 minutes, after which the TFA and DCM were evaporated with a steady stream of N_2. The remaining oil was taken up into 20 mL of DCM and then rotovapped to remove any residual TFA. Saturated $NaHCO_3$ was added to the remaining solid, and the product was extracted into DCM. The organic layer was washed once with saturated $NaHCO_3$, once with brine, then was dried with $MgSO_4$. The solution was filtered and the filtrate evaporated to yield a brown solid. This solid was taken on without purification to the next step.

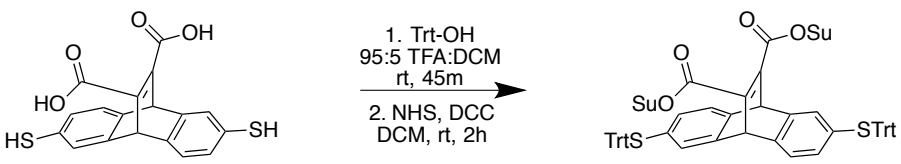
Crude trityl-**A** was dissolved into 20 mL of DCM, then N-hydroxysuccinimide (1.29 g, 11.2 mmol) and dicyclohexylcarbodiimide (1.15g, 5.6 mmol) were added. The reaction was placed under N_2 and was allowed to stir at room temperature for 2 hours. The reaction mixture was then cooled in an ice bath and filtered to remove the insoluble DCU side product. The filtrate was evaporated to give an orange solid. To purify, silica is first washed with 2% triethylamine in DCM, then the product is loaded in 0.5% TEA in DCM. The product is eluted by increasing the polarity gradually to 2% MeOH in 0.5% increments. After purification, 1.0 g of clean product was recovered (35% yield over two steps for **A**, 21% over two steps for **N**). There is typically partial degradation of the product on silica gel; to avoid this, the crude product can be taken on to the next step to improve the overall yield.

To couple to glycine (Gly-OMe), Trityl-**A**-OSu (500 mg, 0.484 mmol) was dissolved in 20 mL of DCM, and an excess of the methyl ester protected amino acid was added (242 mg, 1.93 mmol). Because Gly was used as a hydrochloride salt, an equimolar amount of DIPEA was also added (337 mg, 1.93 mmol). After addition of the amine and DIPEA, the reaction was allowed to stir for 1.5 hours, after which TLC shows the transformation is complete (1:1 EtOAc/Hexanes, Rf (SM) = 0.1, Rf (P) = 0.3). The solvent was then evaporated and the product precipitated into dH_2O with sonication. The

product was filtered and washed to give 430 mg of a white solid (Trt-A-Gly-OMe, 91% yield).

The deprotection was performed in two steps, starting with the removal of the trityl groups. The trityl-protected functionalized monomer (180 mg, 0.183 mmol) was dissolved in DCM and a small amount (~5%) of TFA was added. Triisopropylsilane (0.237 mL, 1.16 mmol) was added to scavenge the trityl cation. The reaction was allowed to stir for 30 minutes under a gentle stream of N_2, and then the solvent was removed by evaporating with a stronger stream of N_2. The product was precipitated into Et_2O, filtered, and washed with Et_2O to give 60 mg of product (66% yield, recovered). The methyl ester protected monomer was hydrolyzed using LiOH. A solution of 106 mg LiOH in 5 mL of dH_2O was degassed for two hours, and then the protected monomer was added in one portion (60 mg, 0.120 mmol). As the hydrolysis occurred, the product dissolved into the water to give a light red solution. After 10 minutes, the solution was acidified with 1M HCl, which precipitated the product as a white solid. The product was extracted into ethyl acetate and was washed with water and brine. The organic layer was collected and dried over $MgSO_4$, then was filtered and evaporated to give a tan solid (44 mg, 78% yield).

Trt-A-OSu (bis(2,5-dioxopyrrolidin-1-yl)-2,6-bis(tritylthio)-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate)



^{1}H NMR: ($CDCl_3$, 600 MHz): δ 7.365 (6H, doublet), δ 7.17-7.11 (9H, multiplet), δ 7.01 (2H, doublet), δ 6.95 (2H, doublet), δ 6.57 (2H, singlet), δ 5.12 (2H, singlet), δ 2.79 (8H, singlet)
^{13}C NMR: ($CDCl_3$, 150 MHz): δ 168.48, δ 159.80, δ 145.28, δ 144.24, δ 141.91, δ 141.84, δ 132.56, δ 131.88, δ 131.24, δ 129.89, δ 127.71, δ 126.75, δ 123.82, δ 71.41, δ 51.95, δ 25.66
HRMS: *Trt-A-OSu did not ionize for HRMS; instead the HRMS of the intermediate Trt-A is included:* Theoretical $[M-H]^{1-}$ = 839.2295; Observed $[M-H]^{1-}$ = 839.23010

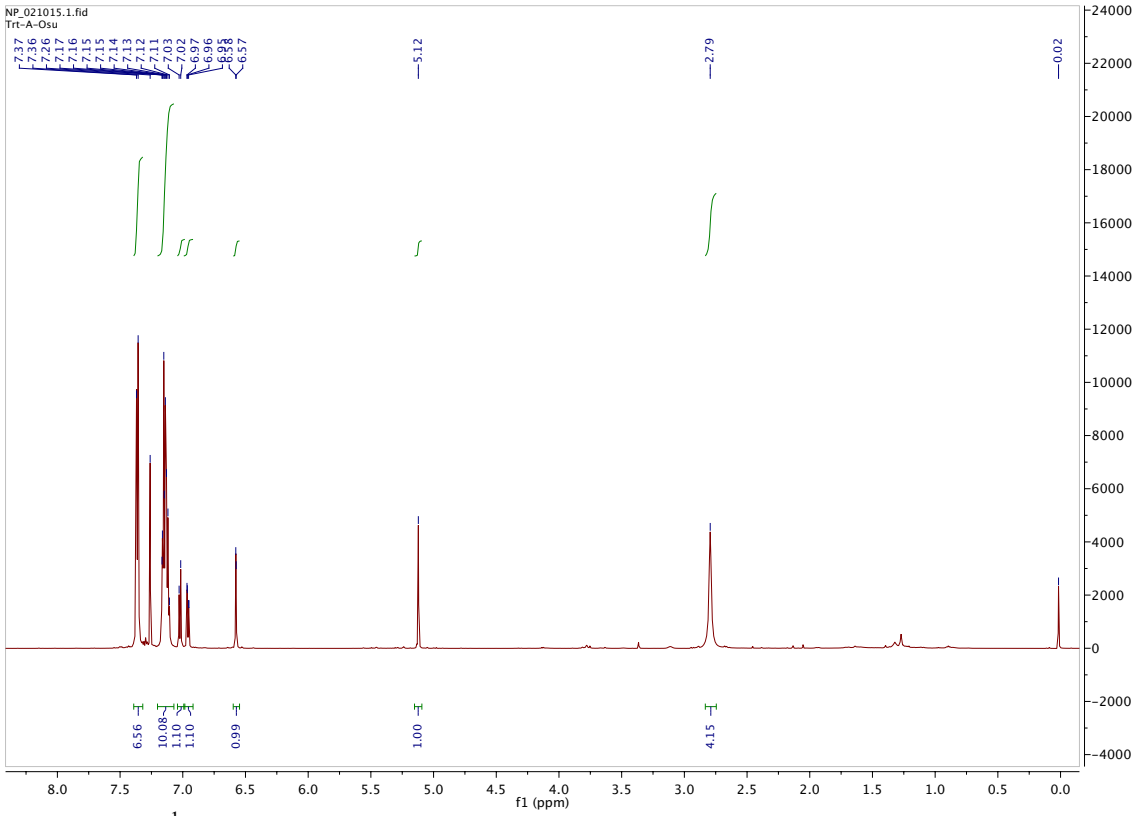


Figure S11. ^{1}H NMR Spectrum of Trt-A-Osu.

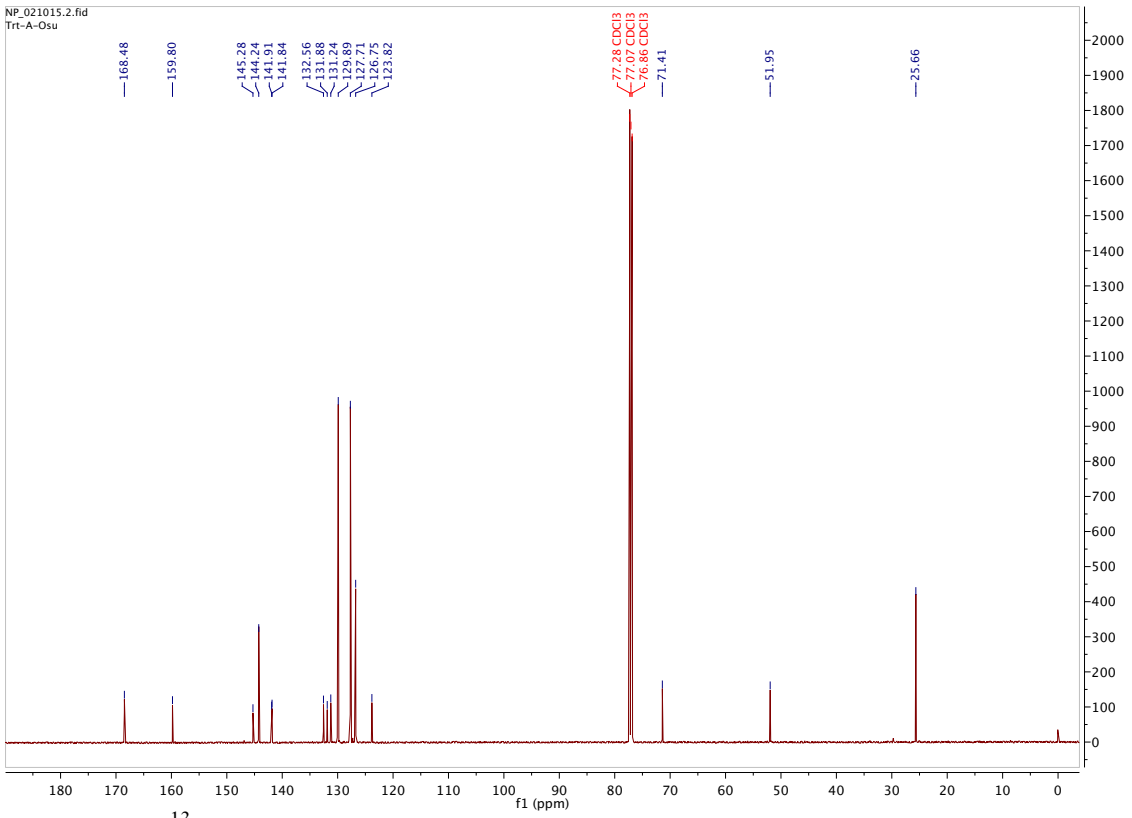


Figure S12. ^{13}C NMR Spectrum of Trt-A-OSu.

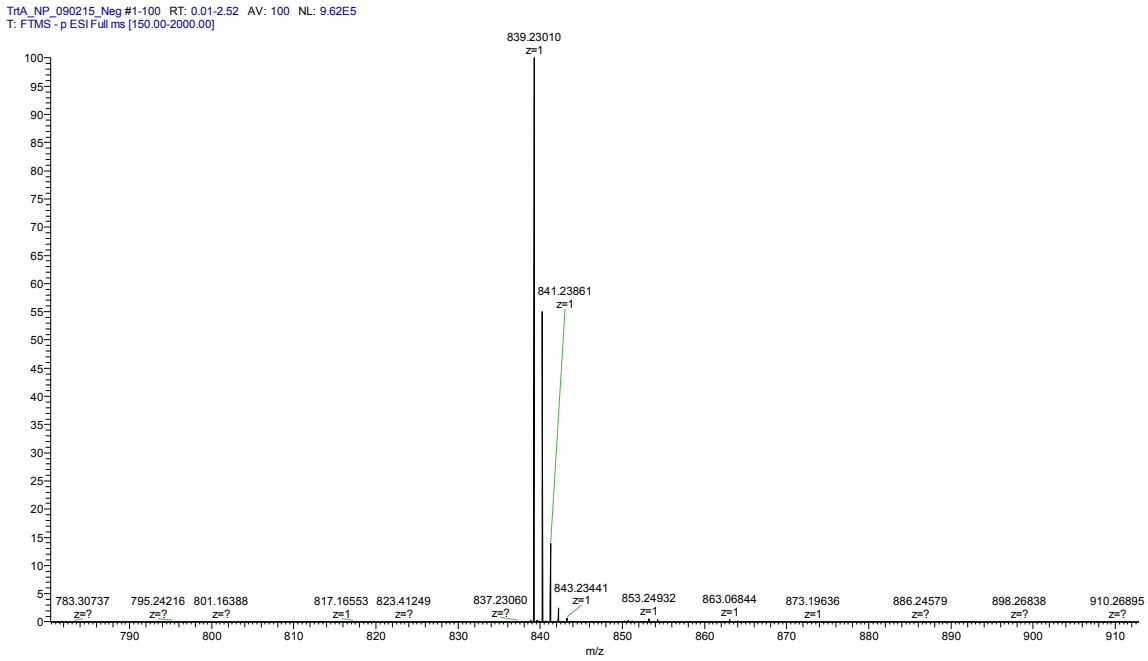
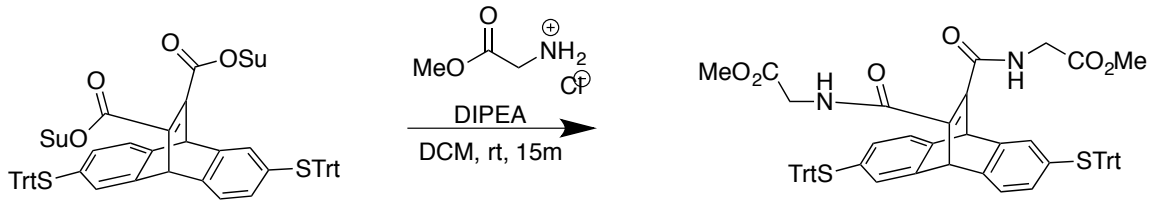


Figure S 13. HRMS (-) of Trt-A.

Trt-A-Gly-OMe (dimethyl 2,2'-((-2,6-bis(tritylthio)-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonyl)bis(azanediyl))diacetate):



^{1}H NMR: ($CDCl_3$, 600 MHz): δ 7.40 (2H, singlet), δ 7.36 (6H, doublet), δ 7.15-7.09 (9H, multiplet), δ 7.04 (2H, doublet), δ 6.95 (2H, doublet), δ 6.57 (2H, singlet), δ 5.18 (2H, doublet), δ 4.03 (4H, doublet of doublets), δ 3.71 (3H, singlet)
^{13}C NMR: ($CDCl_3$, 150 MHz): δ 170.86, δ 165.59, δ 145.74, δ 144.37, δ 143.87, δ 143.44, δ 132.17, δ 130.84, δ 130.74, δ 129.95, δ 127.65, δ 126.65, δ 123.38, δ 71.16, δ 52.54, δ 52.47, δ 41.68
HRMS: Theoretical $[M+Na]^{1+}$ = 1005.3002; Observed $[M+Na]^{1+}$ = 1005.29896

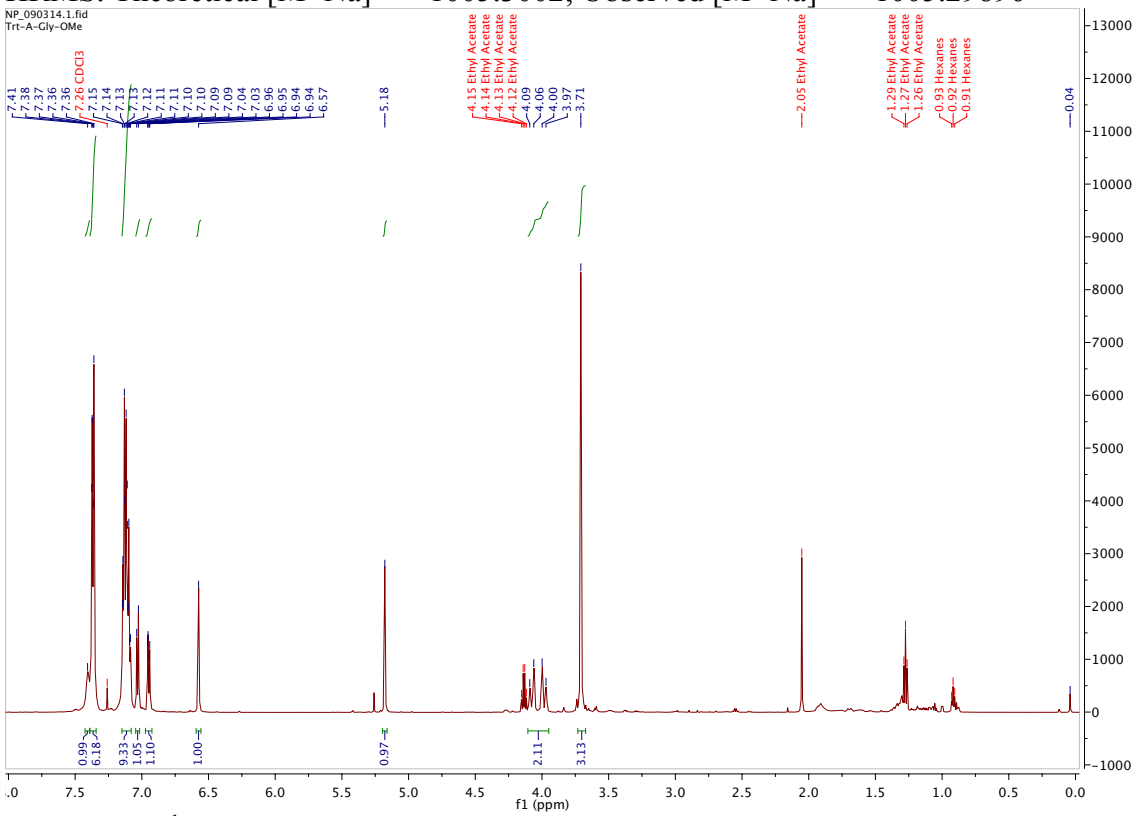


Figure S14. ^{1}H NMR Spectrum of Trt-A-Gly-OMe.

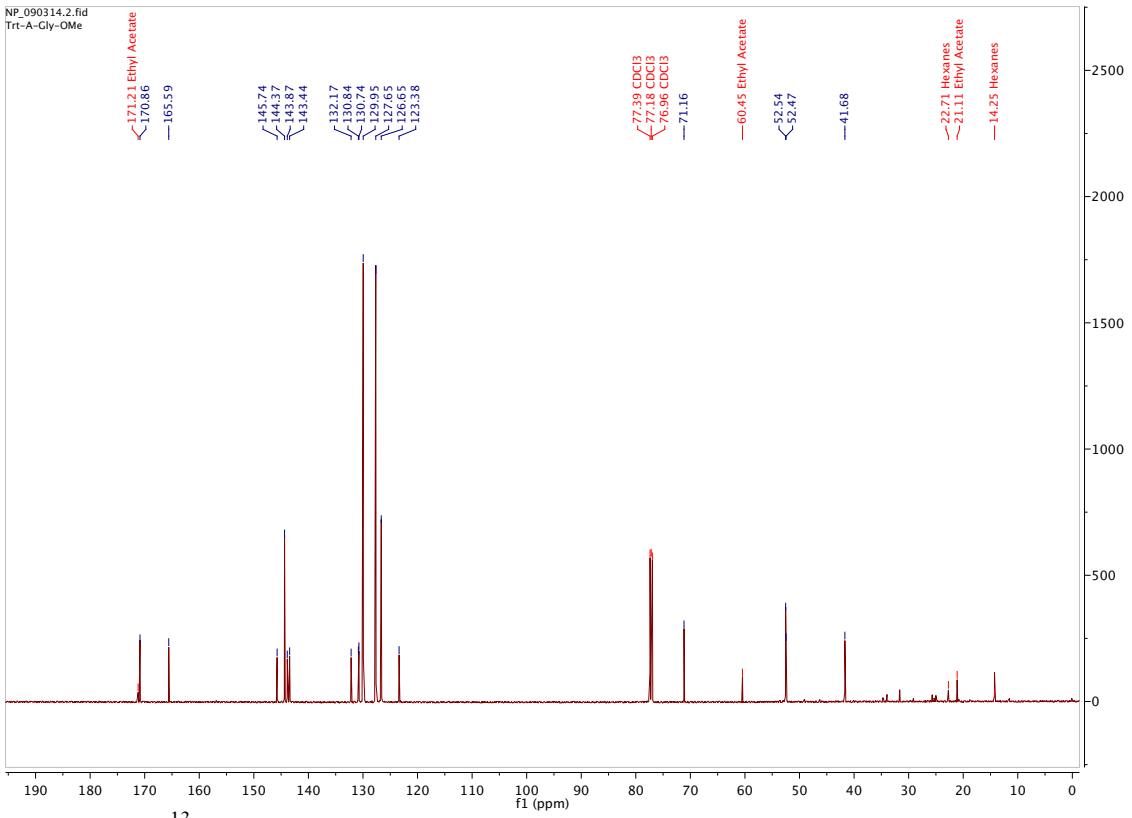


Figure S15. ^{13}C NMR Spectrum of Trt-A-Gly-OMe.

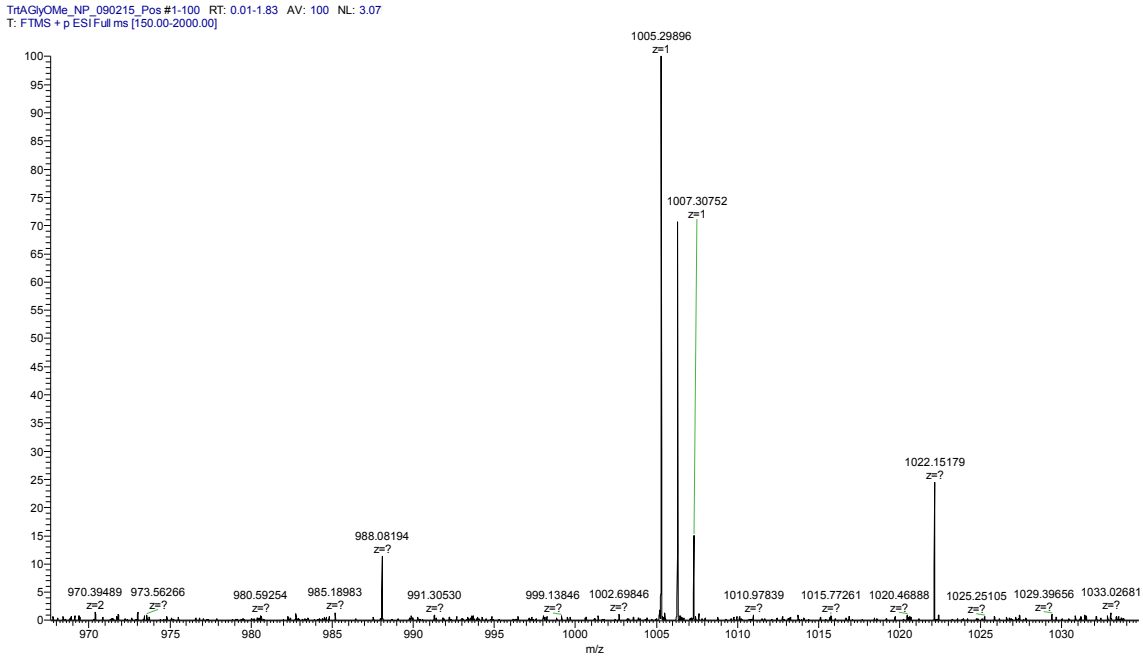


Figure S 16. HRMS (+) of Trt-A-Gly-OMe.

Gly-A-OMe (dimethyl 2,2'-((-2,6-dimercapto-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonyl)bis(azanediyl))diacetate):

^{1}H NMR: ($CDCl_3$, 600 MHz): δ 7.42 (2H, triplet), δ 7.33 (2H, singlet), δ 7.24 (2H, doublet), δ 6.95 (2H, doublet), δ 5.52 (2H, singlet), δ 4.04 (4H, multiplet), δ 3.71 (3H, singlet), δ 3.38 (2H, singlet)
^{13}C NMR: ($CDCl_3$, 150 MHz): δ 171.00, δ 165.59, δ 145.94, δ 145.09, δ 141.43, δ 127.58, δ 126.45, δ 125.33, δ 124.31, δ 52.56, δ 52.48, δ 41.69
HRMS: Theoretical $[M+TFA^-]^{1-}$ = 611.0775; Observed $[M+TFA^-]^{1-}$ = 611.07778

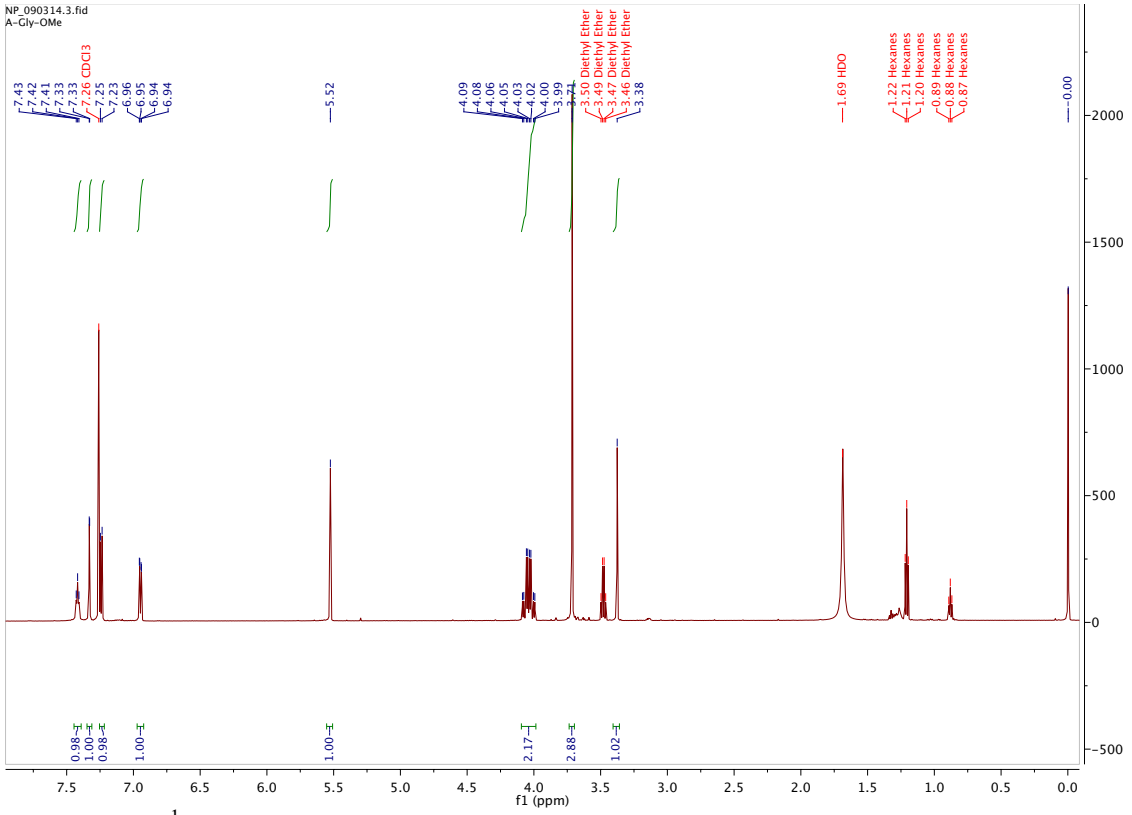


Figure S17. ^{1}H NMR Spectrum of Gly-A-OMe.

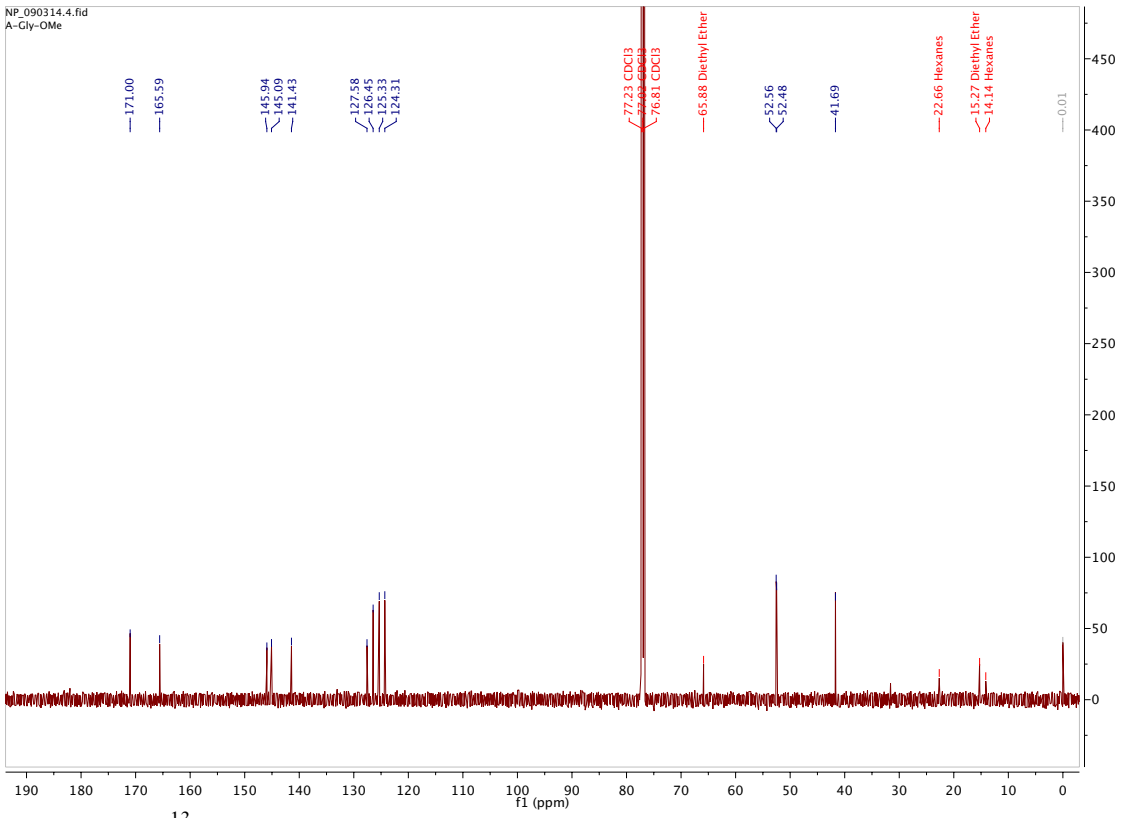


Figure S18. ^{13}C NMR Spectrum of Gly-A-OMe.

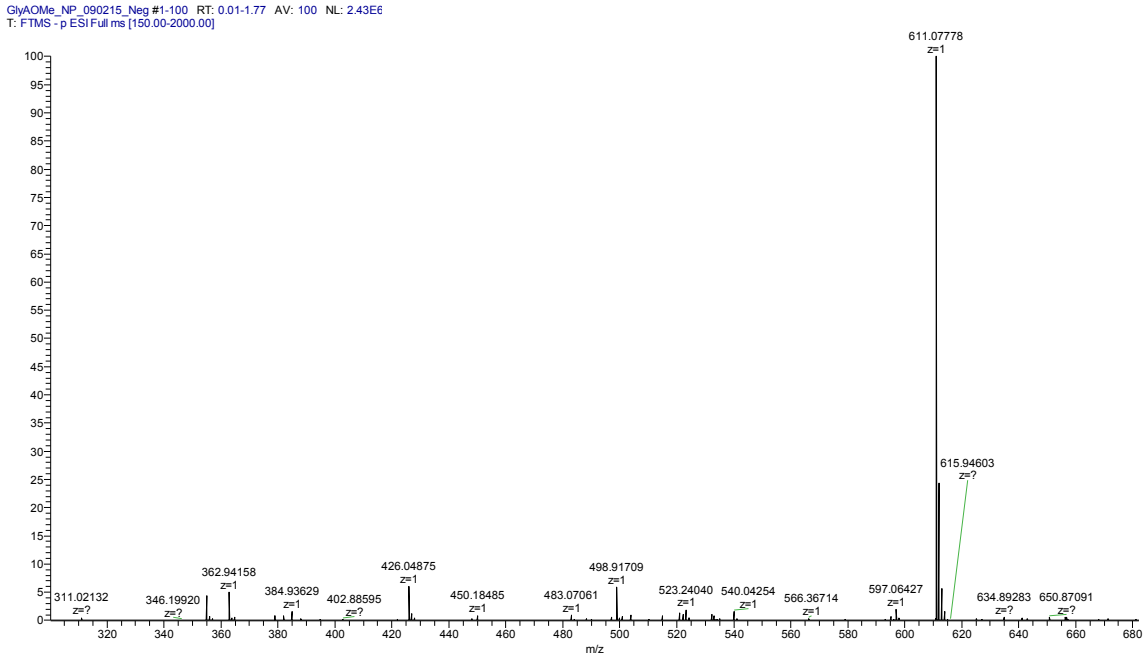
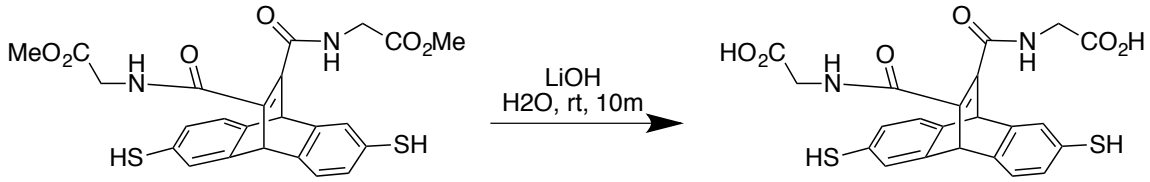


Figure S 19. HRMS (-) of Gly-A-OMe.

Gly-A (2,2'-((-2,6-dimercapto-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonyl)bis(azanediyl))diacetic acid):



^{1}H NMR: (CD_3OD, 600 MHz): δ 7.38 (2H, singlet), δ 7.29 (2H, doublet), δ 6.96 (2H, doublet), δ 5.48 (2H, singlet), δ 3.94 (4H, singlet)
^{13}C NMR: (CD_3OD, 150 MHz): δ 166.56, δ 146.23, δ 145.49, δ 141.40, δ 128.24, δ 125.22, δ 124.29, δ 123.78, δ 52.10, δ 40.75
HRMS: Theoretical $[M-H]^{1-}$ = 469.0534; Observed $[M-H]^{1-}$ = 469.05326

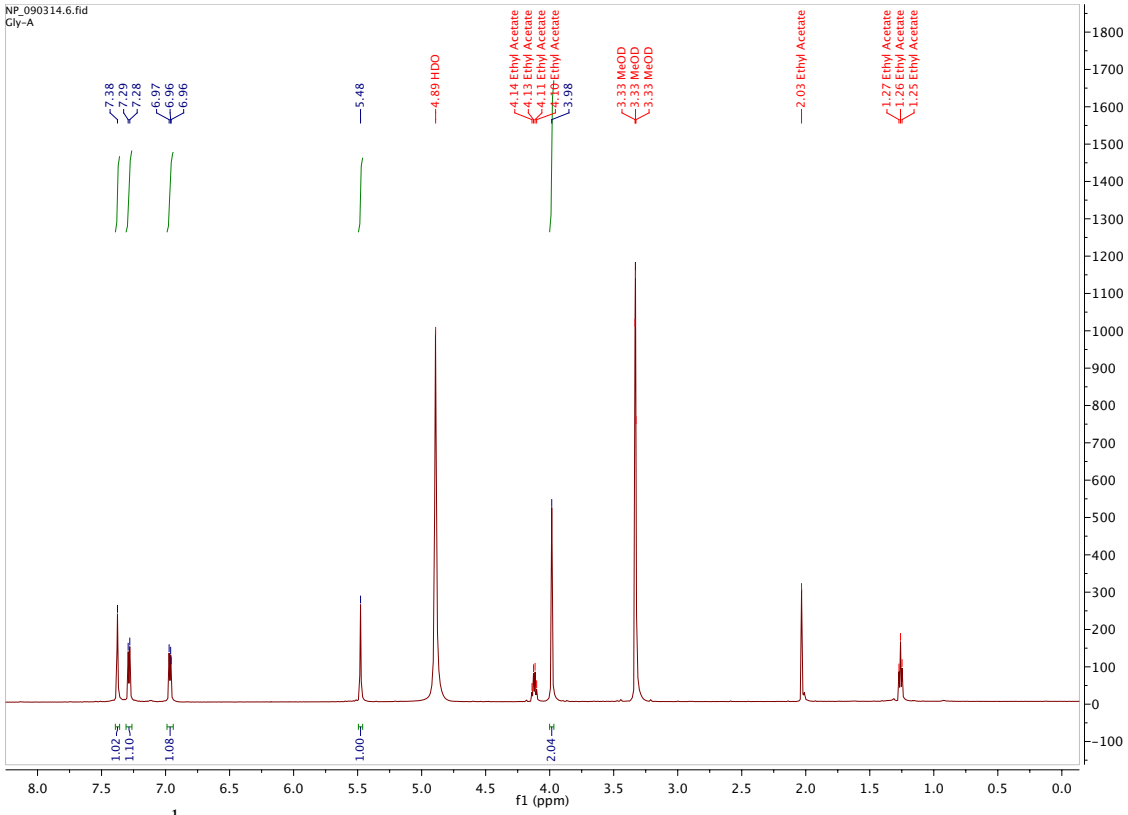


Figure S20. ^{1}H NMR Spectrum of Gly-A.

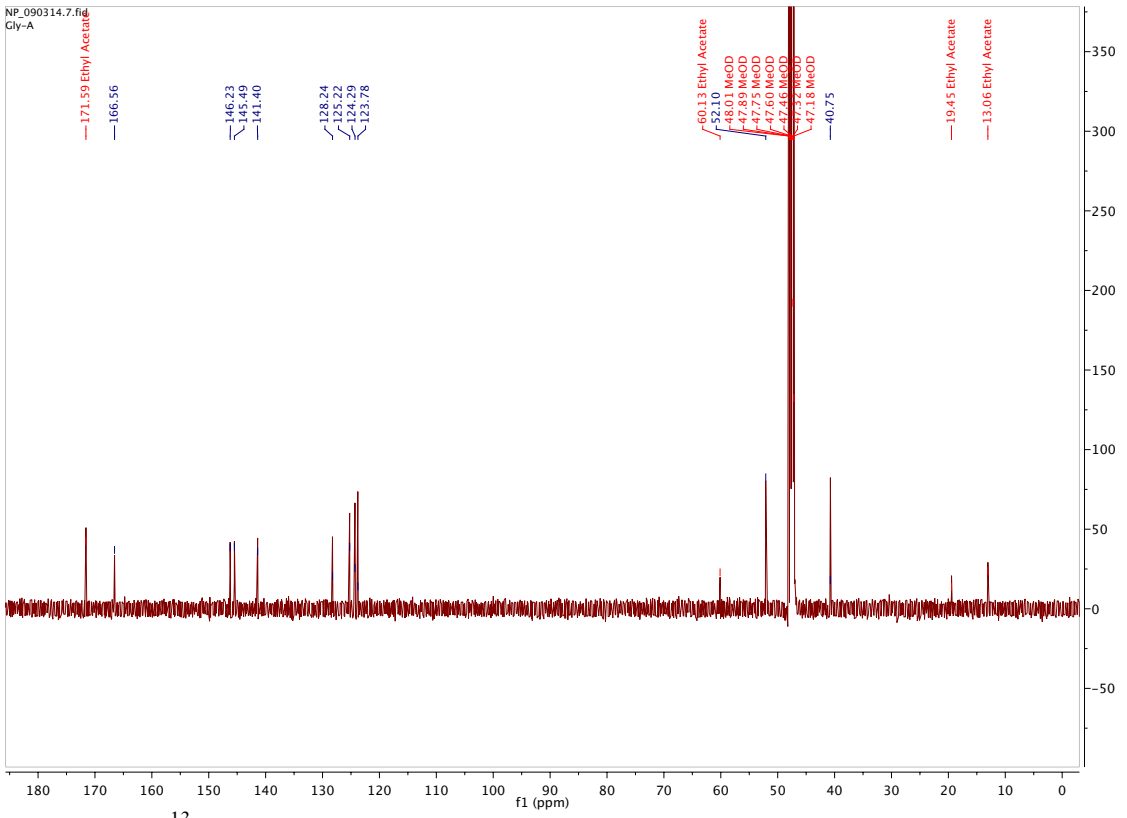


Figure S21. ^{13}C NMR Spectrum of Gly-A.

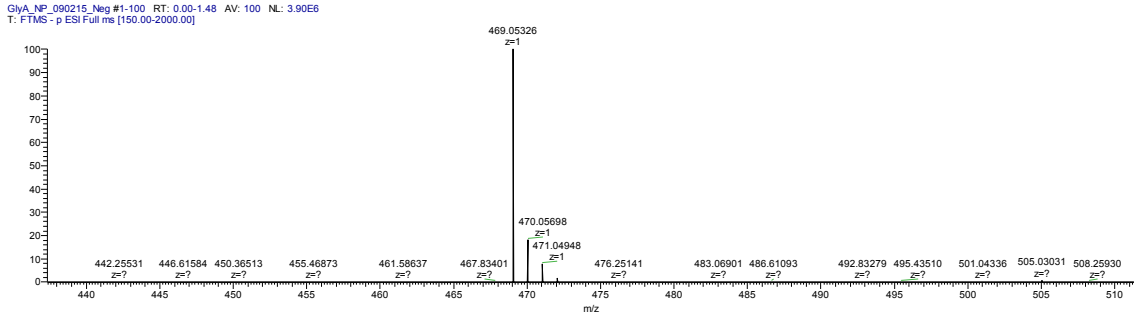
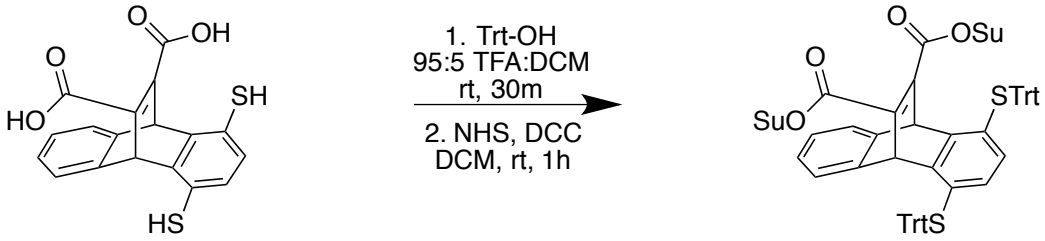


Figure S22. HRMS (-) of Gly-A.

Trt-N-OSu (bis(2,5-dioxopyrrolidin-1-yl)-1,4-bis(tritylthio)-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate):



^{1}H NMR: ($CDCl_3$, 600 MHz): δ 7.24-7.23 (12H, multiplet), δ 7.14-7.11 (18H, multiplet), δ 6.99 (4H, singlet), δ 6.29 (2H, singlet), δ 5.95 (2H, singlet), δ 2.78 (8H, multiplet)
^{13}C NMR: ($CDCl_3$, 150 MHz): δ 168.46, δ 159.87, δ 146.26, δ 144.63, δ 144.20, δ 141.98, δ 131.00, δ 130.17, δ 127.69, δ 126.93, δ 125.76, δ 124.75, δ 71.16, δ 50.54, δ 25.66
HRMS: *Trt-N-OSu did not ionize for HRMS; instead the HRMS of the intermediate Trt-N is included:* Theoretical $[M-H]^{1-}$ = 839.2295; Observed $[M-H]^{1-}$ = 839.23059

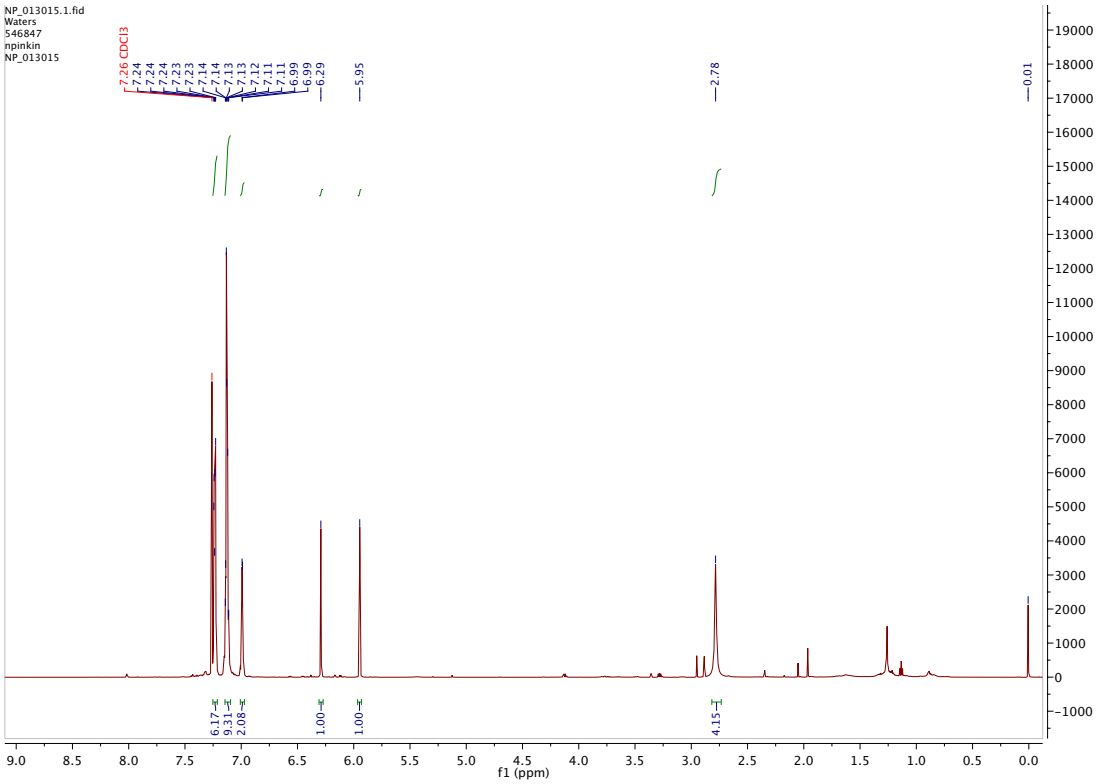


Figure S23. ^{1}H NMR Spectrum of Trt-N-Osu.

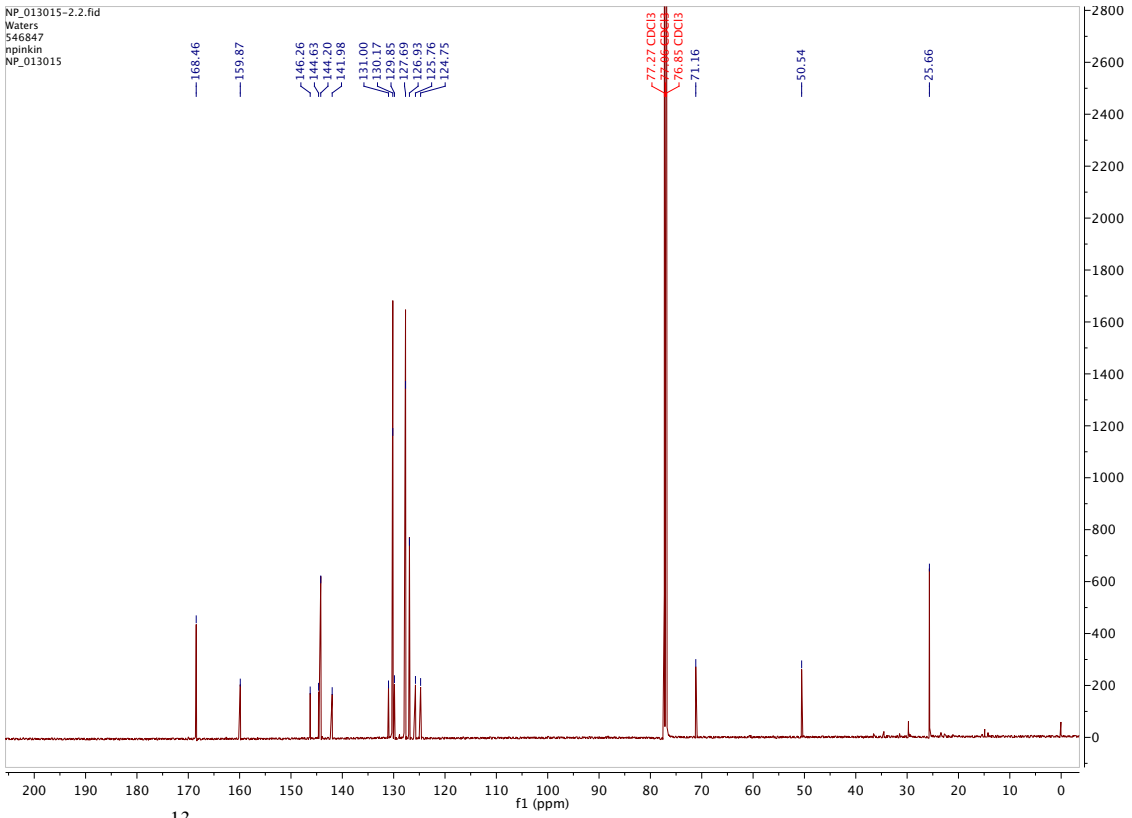


Figure S24. ^{13}C NMR Spectrum of Trt-N-OSu.

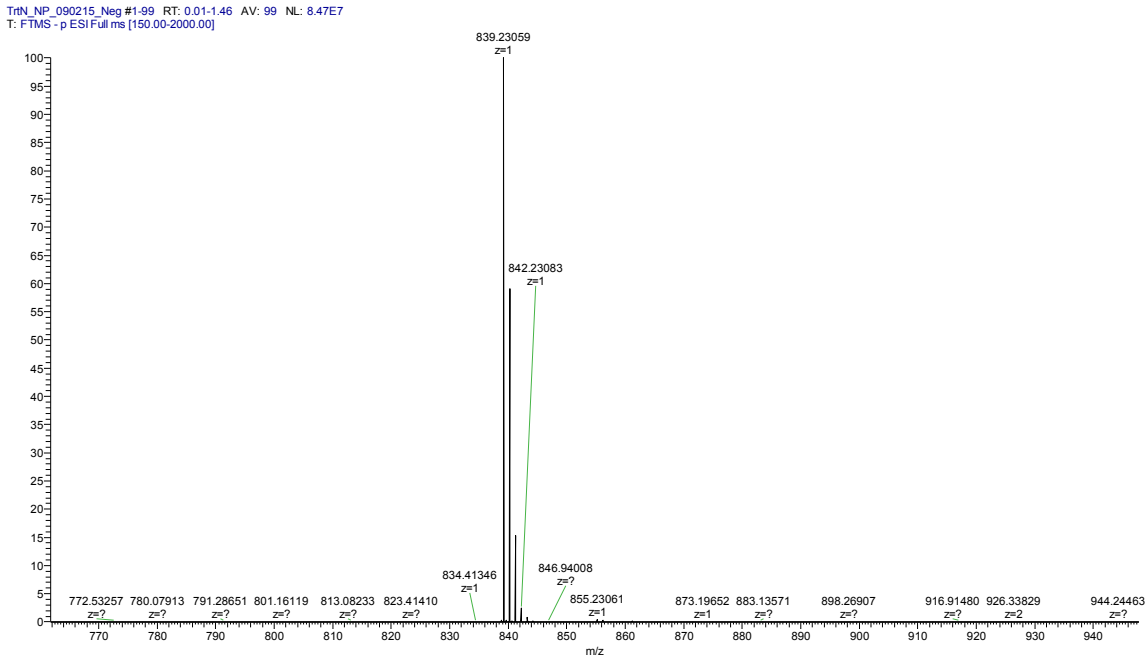
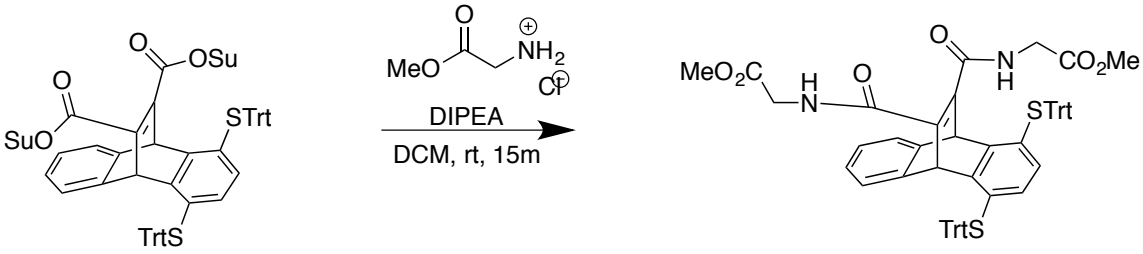


Figure S 25. HRMS (-) of Trt-N.

Trt-N-Gly-OMe (dimethyl 2,2'-((-1,4-bis(tritylthio)-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonyl)bis(azanediyl))diacetate):



^{1}H NMR: ($CDCl_3$, 600 MHz): δ 7.78 (2H, triplet), δ 7.23-7.21 (12H, multiplet), δ 7.14-7.09 (18H, multiplet), δ 6.98 (4H, singlet), δ 6.29 (2H, singlet), δ 5.88 (2H, singlet), δ 4.03 (4H, multiplet), δ 3.72 (6H, singlet)
^{13}C NMR: ($CDCl_3$, 150 MHz): δ 170.27, δ 165.45, δ 147.38, δ 146.24, δ 144.32, δ 143.25, δ 130.22, δ 129.24, δ 127.64, δ 126.89, δ 125.21, δ 124.26, δ 71.12, δ 52.39, δ 51.16
HRMS: Theoretical $[M+Na]^{1+}$ = 1005.3002; Observed $[M+Na]^{1+}$ = 1005.30096

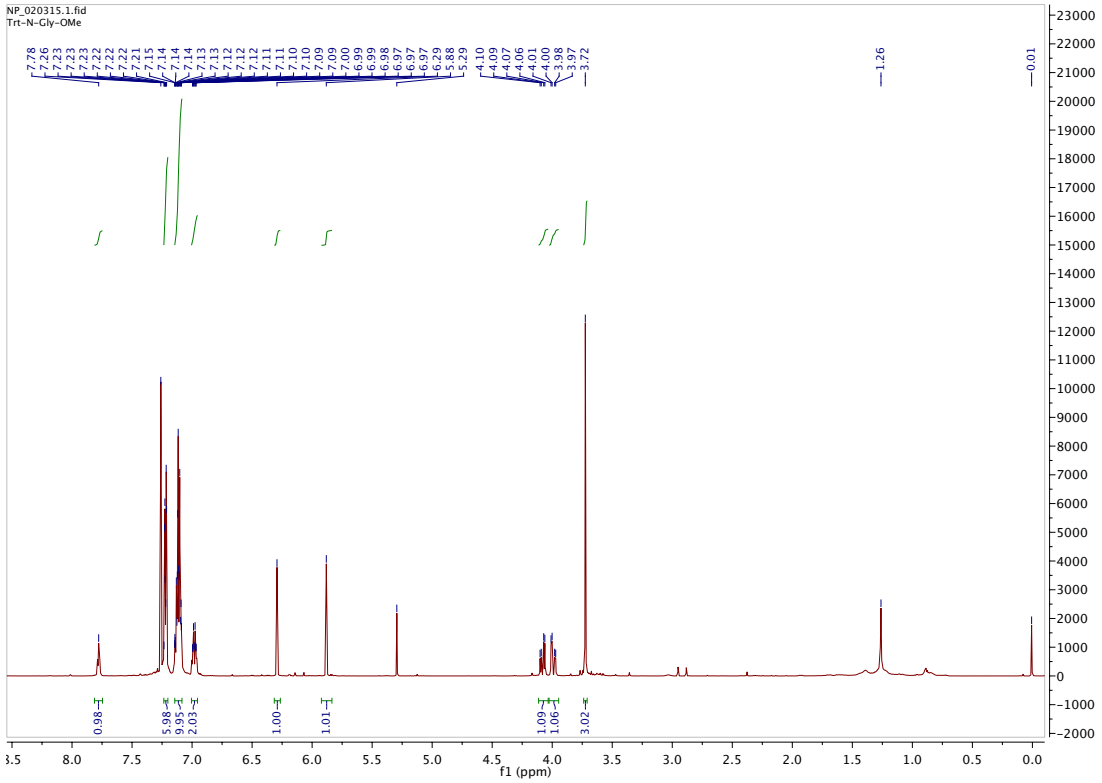


Figure S26. ^{1}H NMR Spectrum of Trt-N-Gly-OMe.

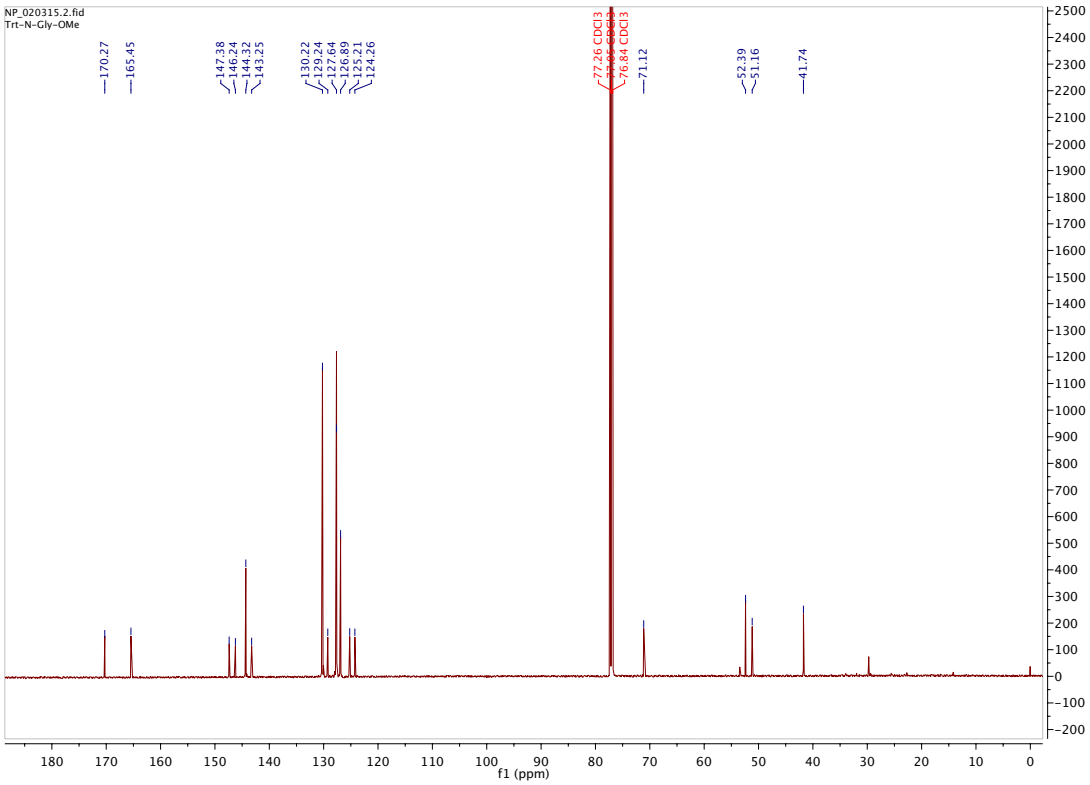


Figure S27. ^{13}C NMR Spectrum of Trt-N-Gly-OMe.

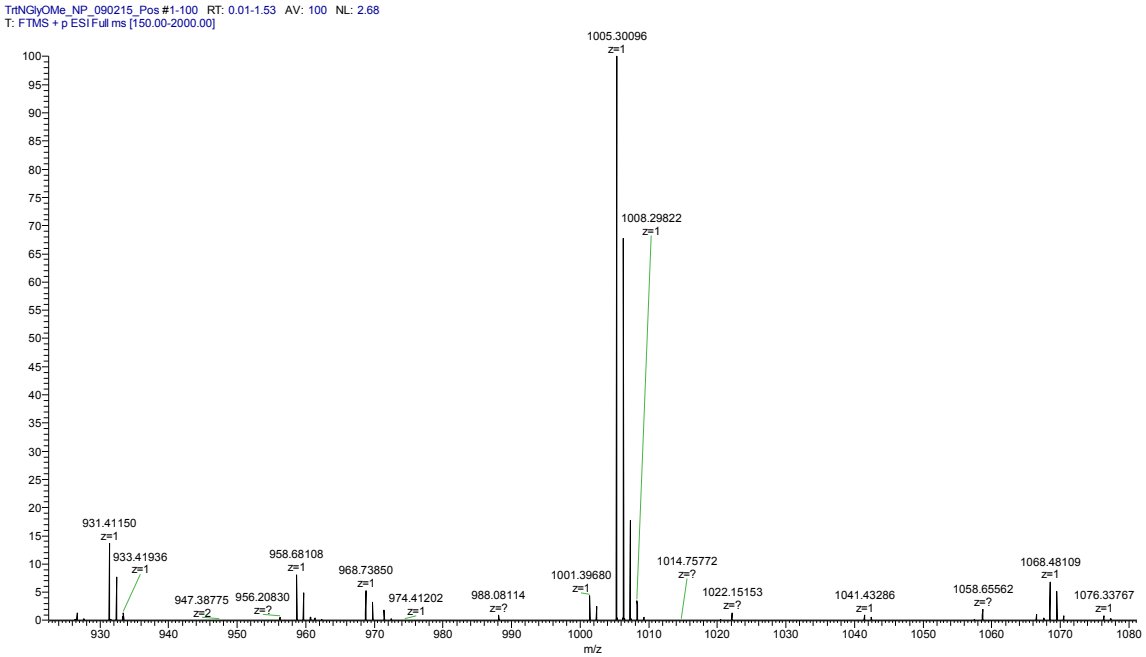
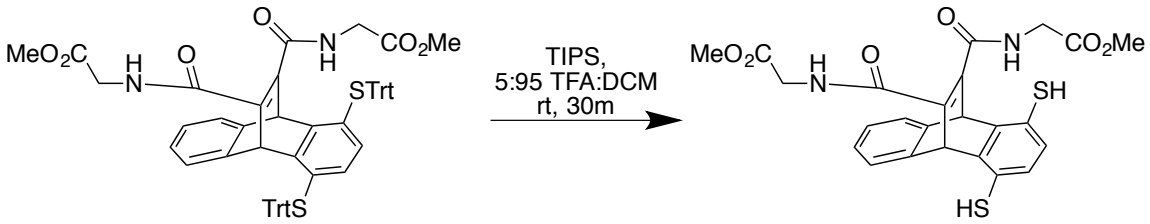


Figure S 28. HRMS (+) of Trt-N-Gly-OMe.

Gly-N-OMe (dimethyl 2,2'-((-1,4-dimercapto-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonyl)bis(azanediyl))diacetate):



^{1}H NMR: ($CDCl_3$, 600 MHz): δ 7.75 (2H, triplet), δ 7.45 (2H, multiplet), δ 7.07 (2H, multiplet), δ 6.93 (2H, singlet), δ 6.10 (2H, singlet), δ 4.09 (4H, multiplet), δ 3.73 (6H, singlet), δ 3.60 (2H, singlet)
^{13}C NMR: ($CDCl_3$, 150 MHz): δ 170.57, δ 165.43, δ 146.81, δ 144.86, δ 142.89, δ 129.08, δ 125.86, δ 124.24, δ 123.69, δ 52.54, δ 51.75, δ 41.79
HRMS: Theoretical $[M-H]^{1-}$ = 497.0847; Observed $[M-H]^{1-}$ = 497.08405

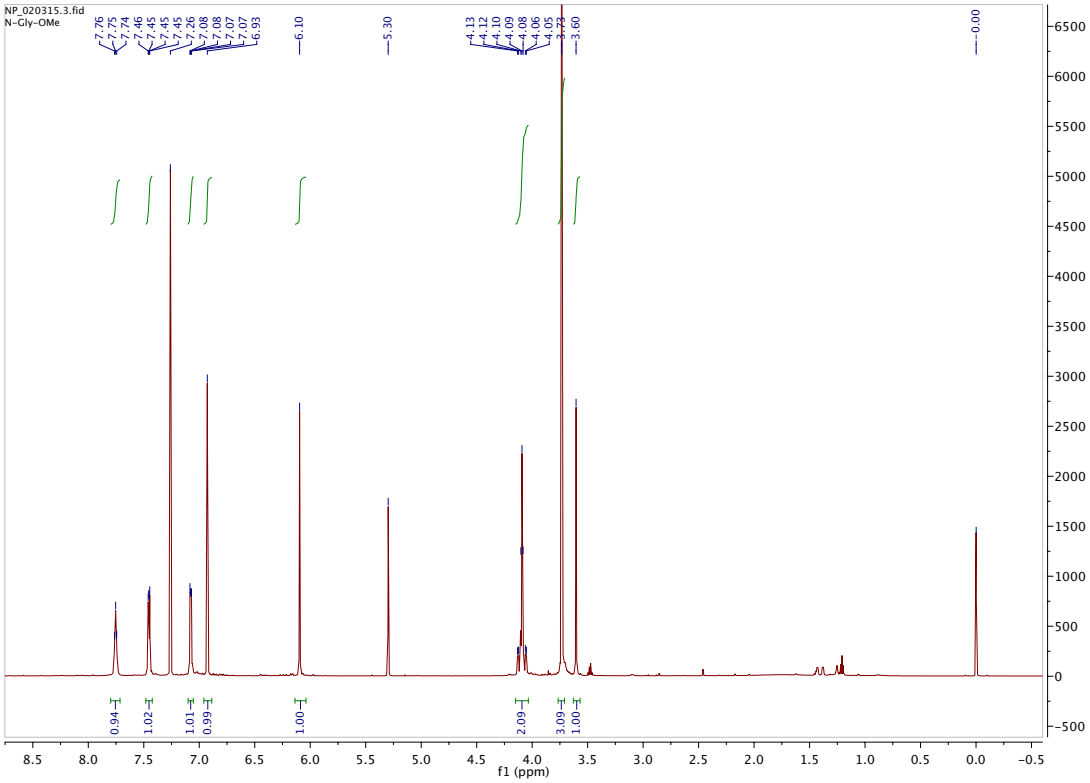


Figure S 29. ^{1}H NMR Spectrum of Gly-N-OMe.

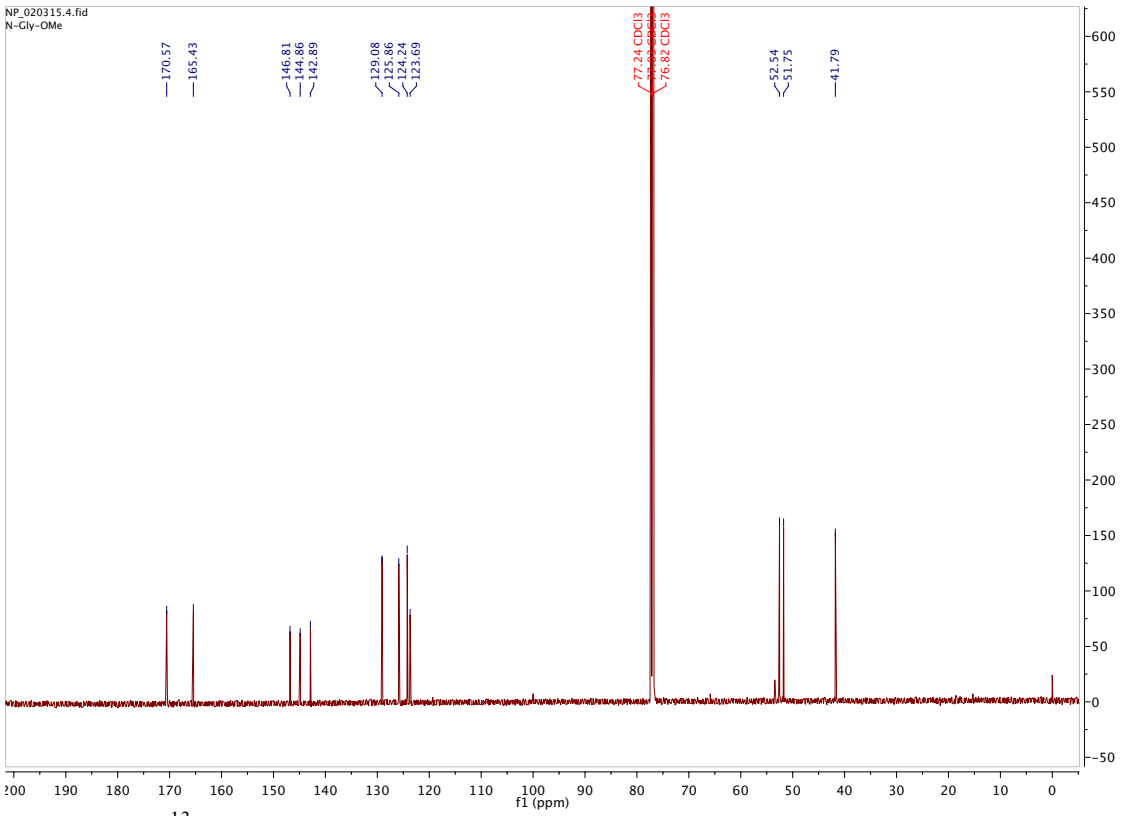


Figure S30. ^{13}C NMR Spectrum of Gly-N-OMe.

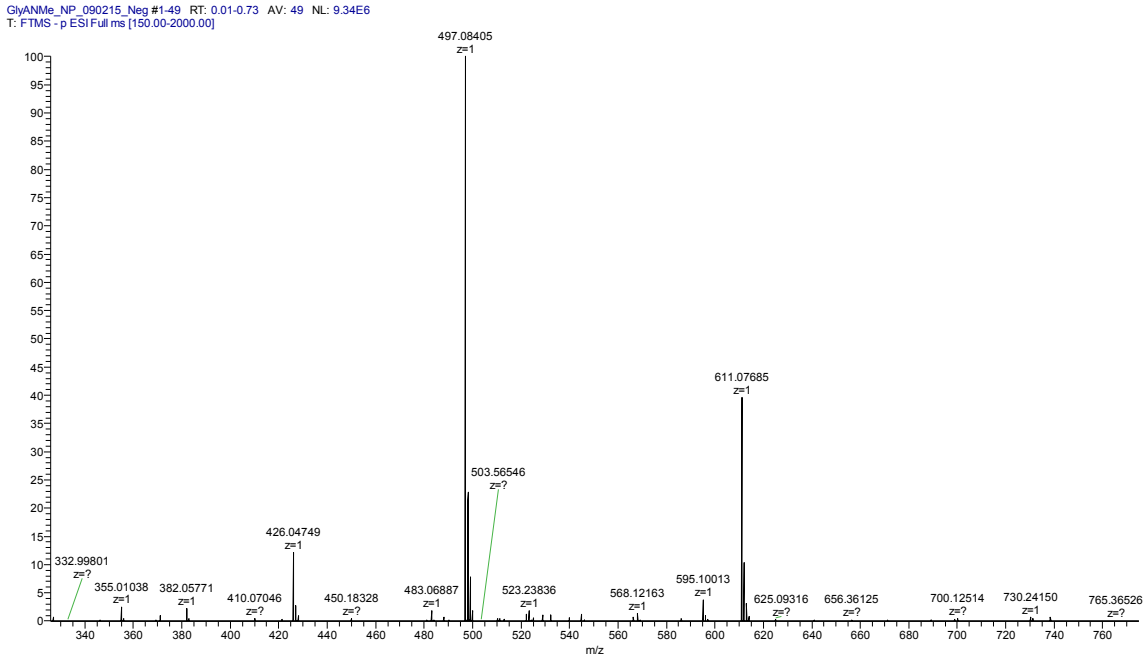
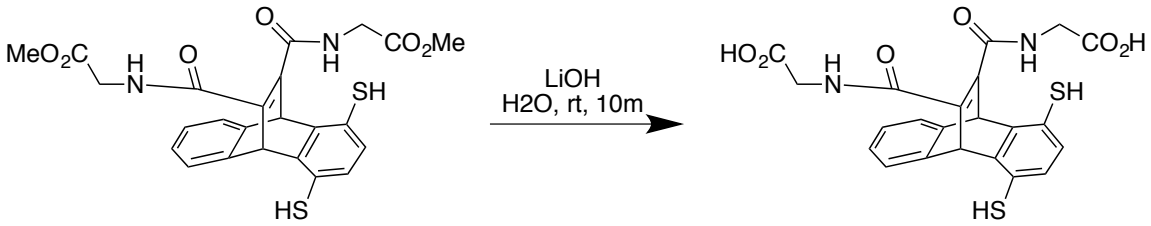


Figure S 31. HRMS (-) of Gly-N-OMe.

Gly-N (2,2'-((-1,4-dimercapto-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonyl)bis(azanediyl))diacetic acid):



^{1}H NMR: (CD_3OD, 600 MHz): δ 7.48 (2H, multiplet), δ 7.08 (2H, multiplet), δ 6.96 (2H, doublet), δ 6.01 (2H, singlet), δ 4.00 (4H, singlet)
^{13}C NMR: (CD_3OD, 150 MHz): δ 171.61, δ 166.35, δ 146.19, δ 144.39, δ 128.15, δ 125.25, δ 123.79, δ 123.63, δ 52.12, δ 40.81
HRMS: Theoretical $[M-H]^{1-}$ = 469.0534; Observed $[M-H]^{1-}$ = 469.05314

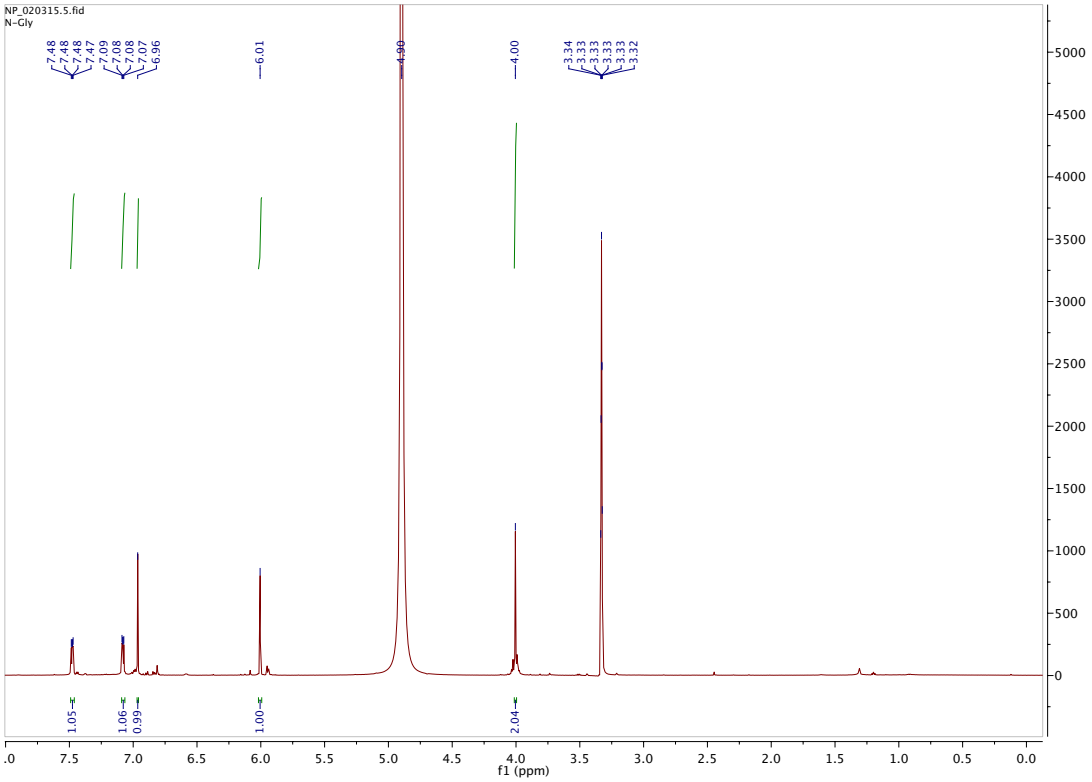


Figure S 32. ^{1}H NMR Spectrum of Gly-N.

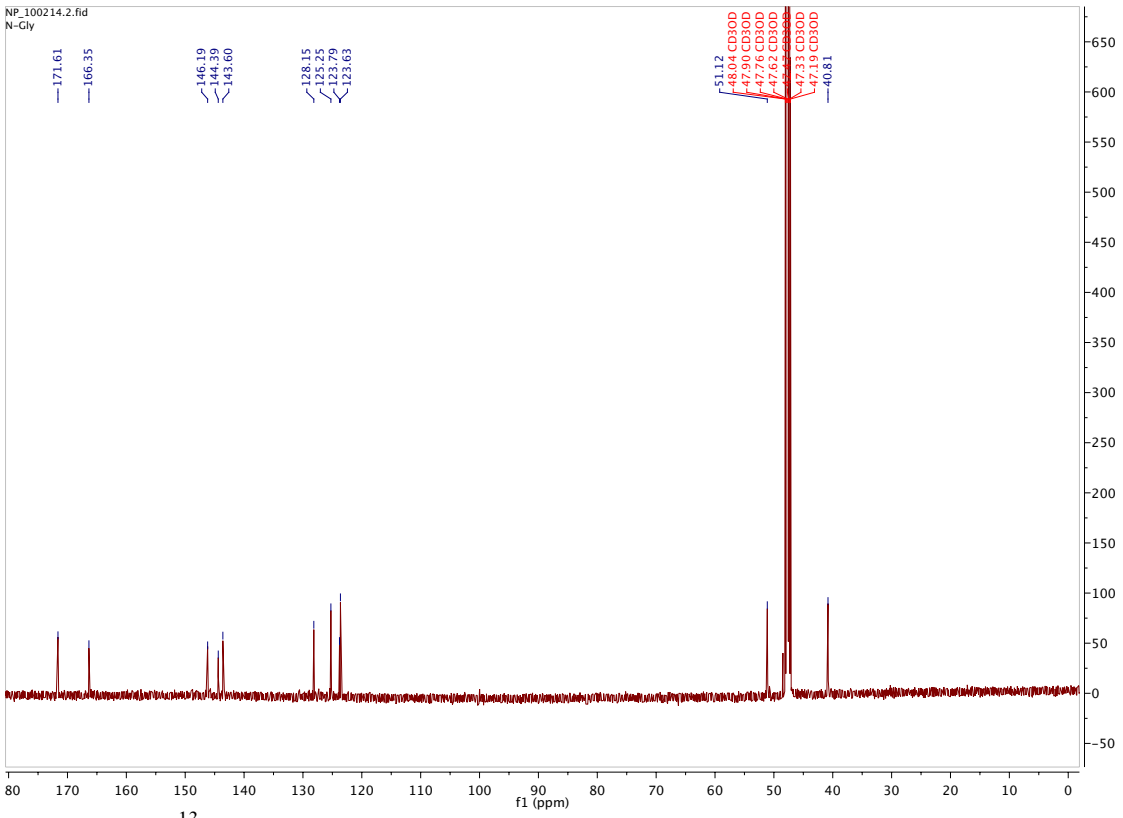


Figure S 33. ^{13}C NMR Spectrum of Gly-N.

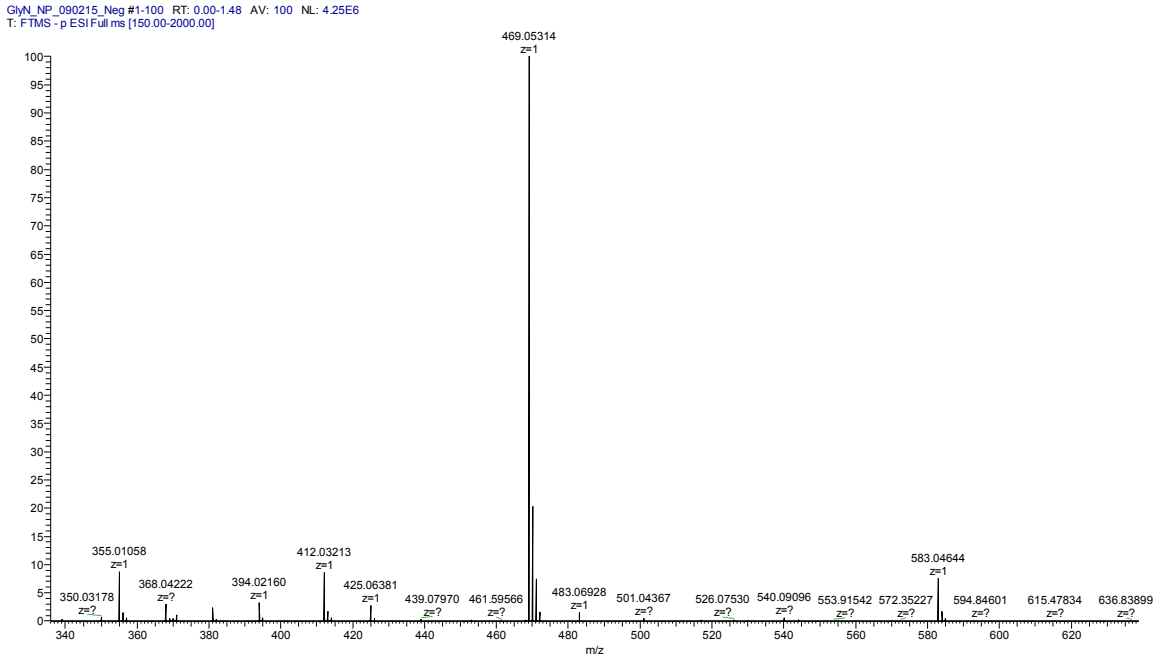
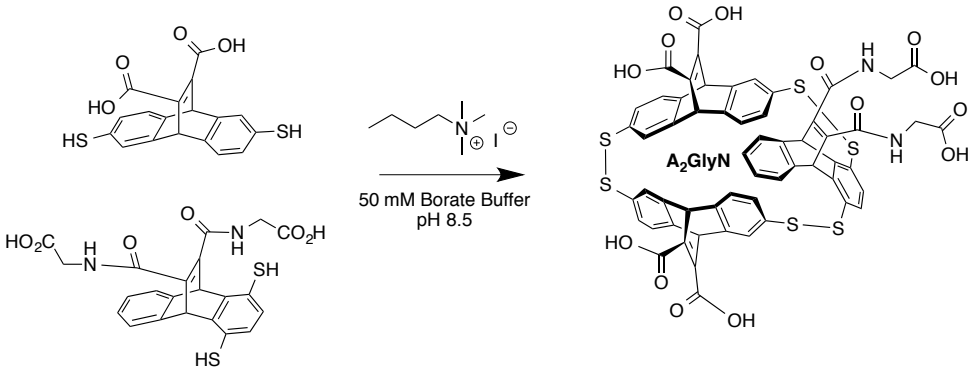


Figure S 34. HRMS (-) of Gly-N.

A_2Gly-N:



Scheme S7. Synthesis of **A_2Gly-N**.

A_2Gly-N was synthesized in a preparative DCL by equilibrating 2 mM **A**, 1.5 mM **Gly-N**, and 10 mM $BuNme_3^+\mathbf{I}^-$ in 20 mL of pH 8.5 50 mM borate buffer for five days. The receptor was purified by RP-HPLC using an Atlantis PrepT3 5 μm 10 x 150 mm C18 column. Using a linear gradient of 0-100% B in 45 minutes (A: 10 mM NH_4OAc in H_2O, B: 10 mM NH_4OAc in 9:1 ACN:H_2O), *rac*- and *meso*$_1$-**A_2Gly-N** were collected together at 22 minutes in 20% yield (by peak area), and *meso*$_2$-**A_2Gly-N** was collected at 23 minutes in 20% yield (by peak area).

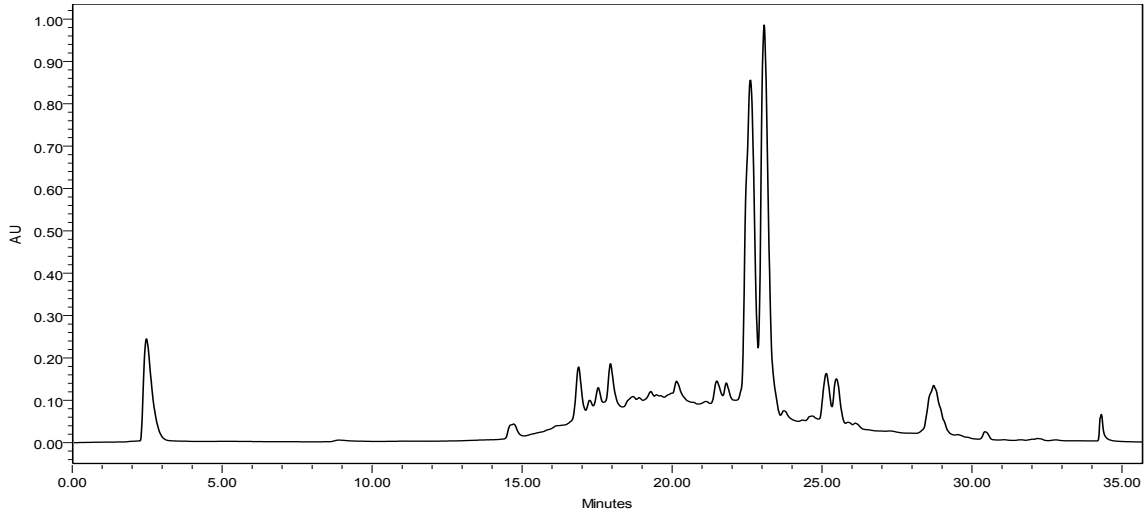


Figure S35. Preparative DCL for the formation of **A_2Gly-N** monitored at 254 nm. The *rac*- and *meso*$_1$- isomers of **A_2Gly-N** elute at 22 minutes and the *meso*$_2$- isomer elutes at 23 minutes.

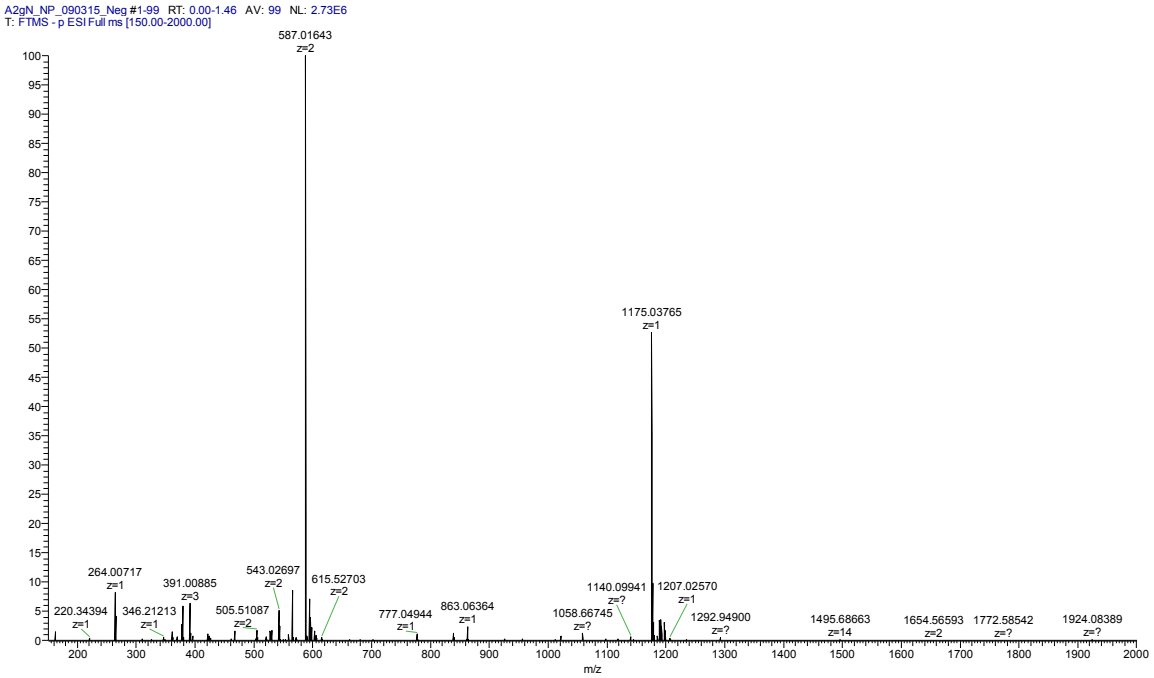
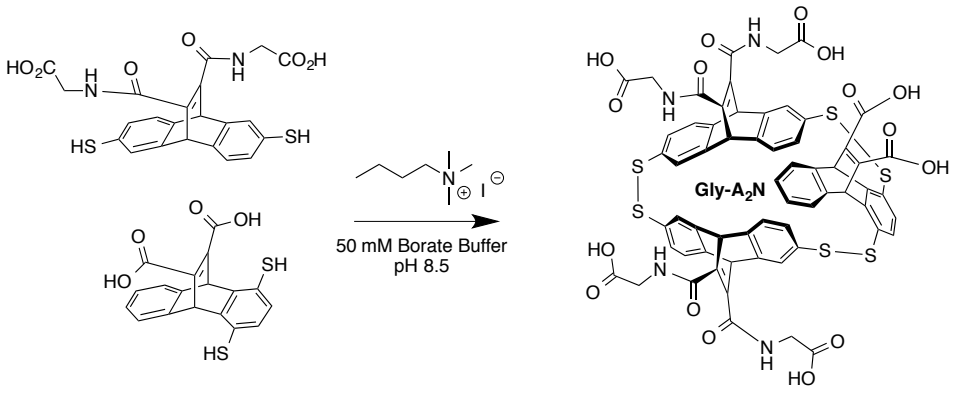


Figure S36. HRMS (-) of **A_2Gly-N**. Theoretical $[M-H]^{1-}$ = 1175.04180, Observed $[M-H]^{-}$ = 1175.03765.

Gly-A_2N:



Scheme S8. Synthesis of **Gly-A_2N**.

Gly-A_2N was synthesized in a preparative DCL by equilibrating 2 mM **Gly-A**, 2 mM **N**, and 10 mM $BuNme_3^+$**I**$^-$ in 20 mL of pH 8.5 50 mM borate buffer for five days. The receptor was purified by RP-HPLC using an Atlantis PrepT3 5 μm 10 x 150 mm C18 column. Using a linear gradient of 0-100% B in 45 minutes (A: 10 mM NH_4OAc in H_2O, B: 10 mM NH_4OAc in 9:1 ACN:H_2O), the three isomers of **Gly-A_2N** were collected in two parts at ~20 minutes in approximately 35% total yield (by peak area).

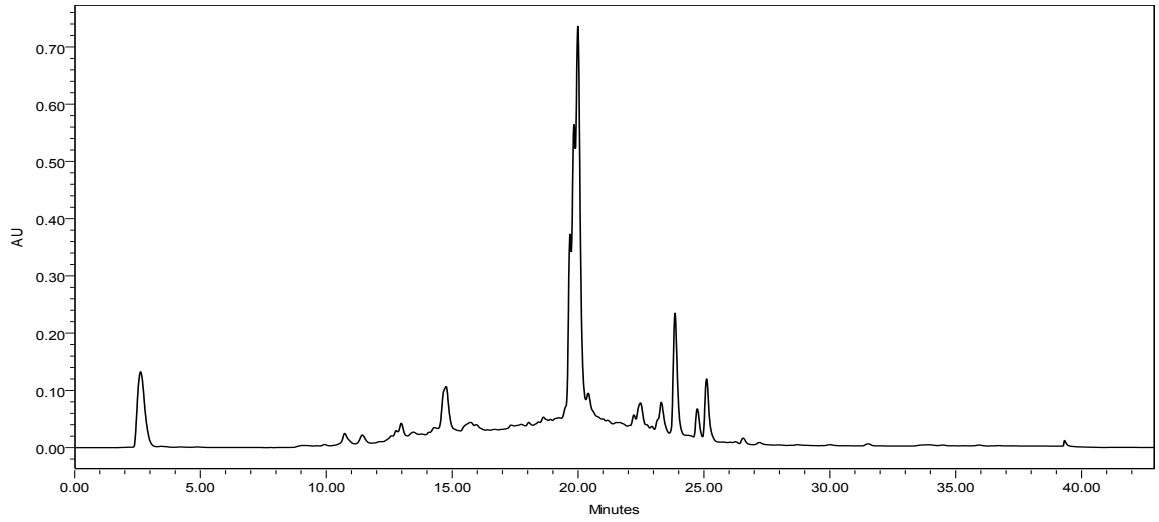


Figure S37. Preparative DCL for the formation of **Gly-A_2N** monitored at 254 nm. The three isomers of **Gly-A_2N** nearly co-elute at ~20 minutes.

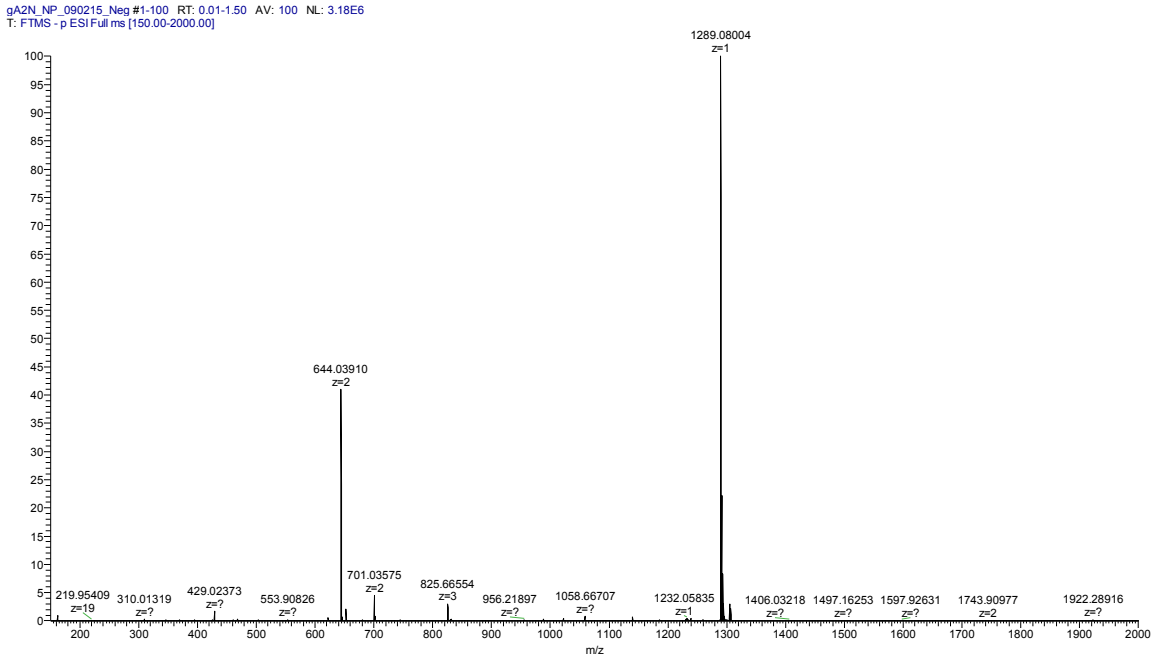
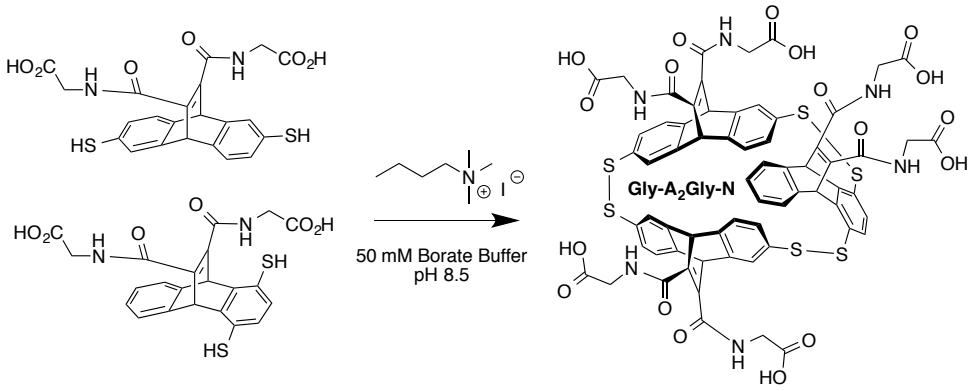


Figure S38. HRMS (-) of **Gly-A_2N**. Theoretical $[M-H]^{1-}$ = 1289.0847, Observed $[M-H]^{1-}$ = 1289.08004

Gly-A$_2$Gly-N:



Scheme S9. Synthesis of **Gly-A$_2$Gly-N**.

Gly-A$_2$Gly-N was synthesized in a preparative DCL by equilibrating 4 mM Gly-**A**, 2 mM **Gly-N**, and 10 mM $BuNme_3^+\mathbf{I}^-$ in 10 mL of pH 8.5 50 mM borate buffer for five days. The receptor was purified by RP-HPLC using an Atlantis PrepT3 5 μm 10 x 150 mm C18 column. Using a linear gradient of 0-100% B in 45 minutes (A: 10 mM NH_4OAc in H_2O, B: 10 mM NH_4OAc in 9:1 ACN:H_2O), three isomers of **GlyA$_2$Gly-N** were collected at 16, 17, and 18 minutes in 12%, 16%, and 25% yield, by peak area. Assuming the isomers elute in the same order as observed for **A$_2$N**, the order of elution is *rac*-, *meso$_1$*-, and then *meso$_2$*-**Gly-A$_2$Gly-N**. An NMR degradation of all of the isomers showed the same 2:1 proportion of **Gly-A** and **Gly-N** (Figure S41).

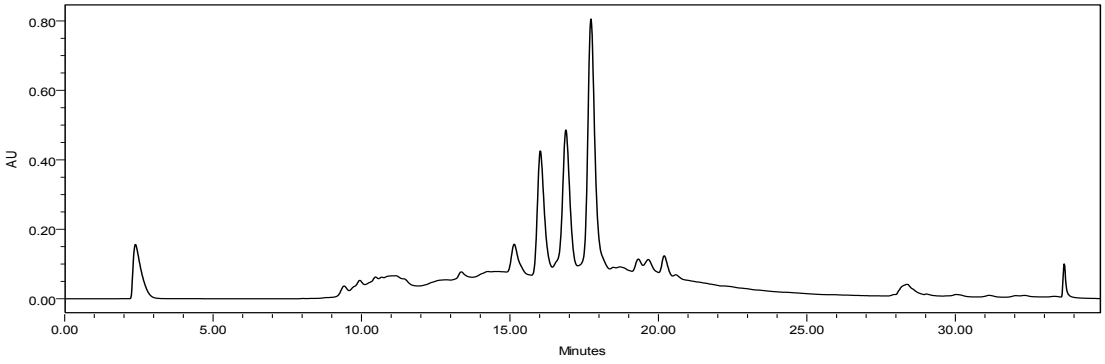


Figure S39. Preparative DCL for the formation of **GlyA$_2$Gly-N** monitored at 254 nm. *Rac*-, *meso$_1$*-, and *meso$_2$*-**GlyA$_2$Gly-N** elute at approximately 16, 17, and 18 minutes, respectively.

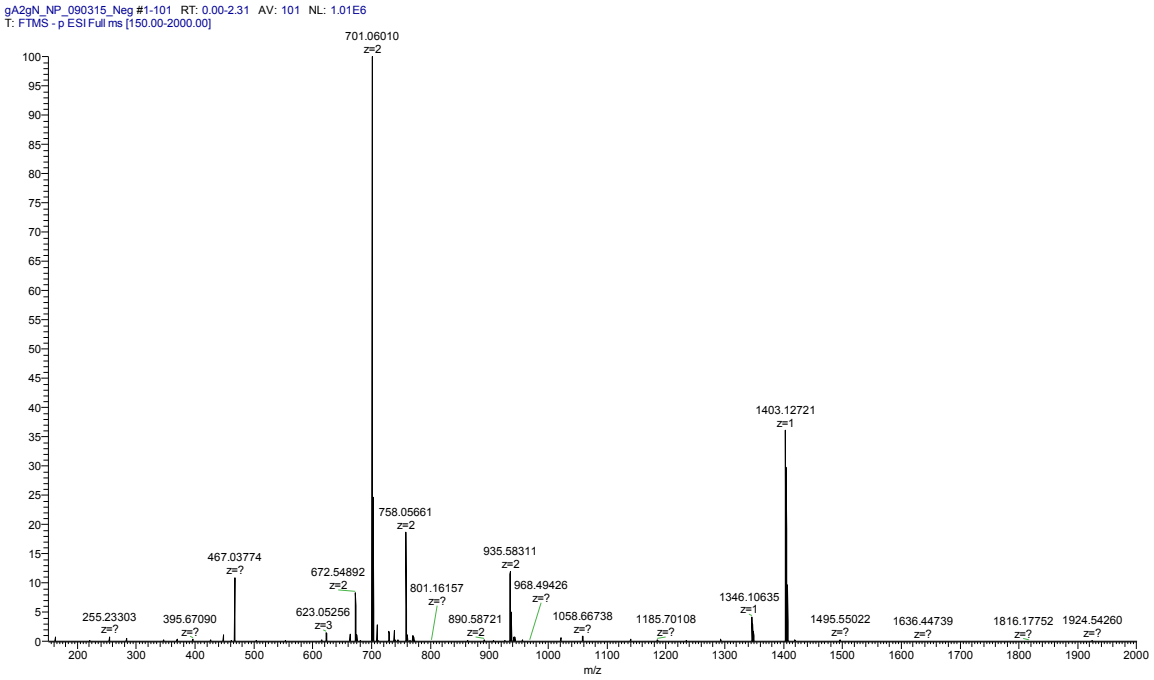


Figure S40. HRMS (-) of **Gly-A$_2$Gly-N**. Theoretical $[M-H]^{1-}$ = 1403.12766, Observed $[M-H]^{1-}$ = 1403.12721.

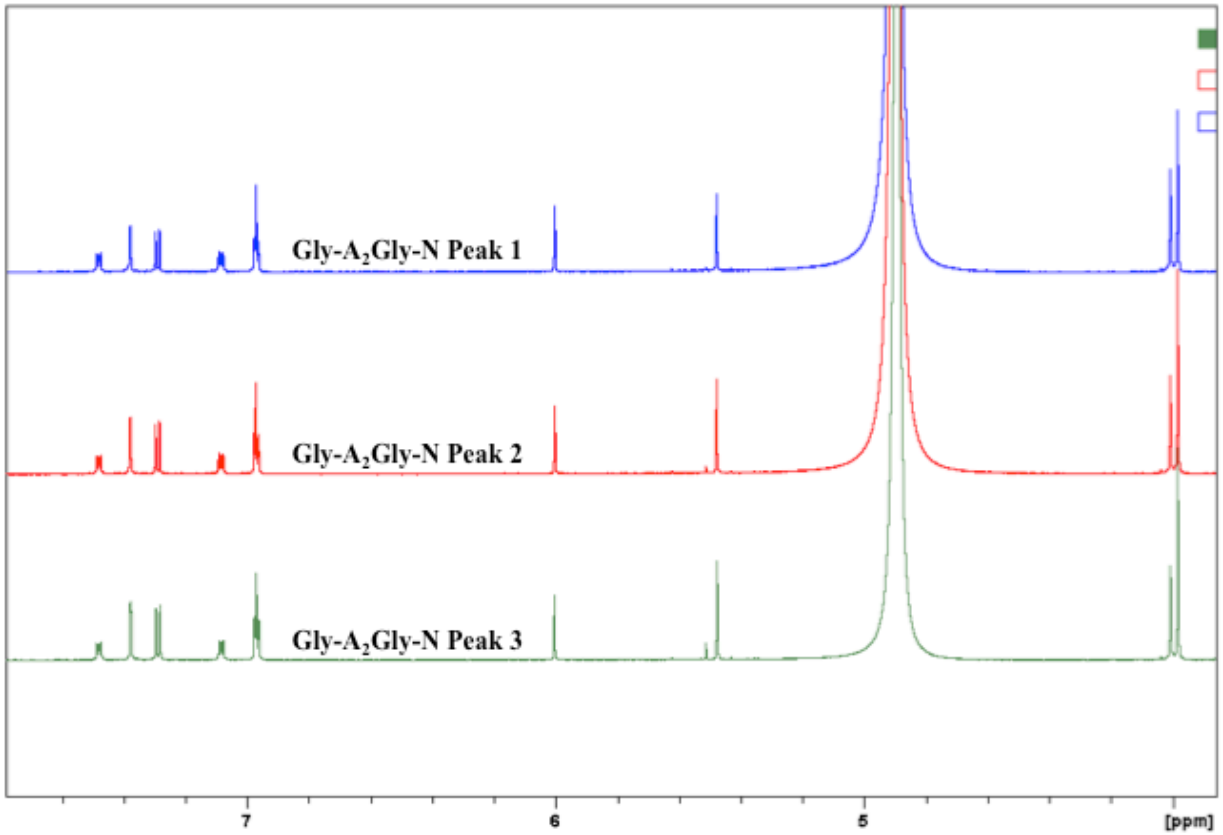


Figure S41. Overlaid ^{1}H NMR spectra of each of the three isomers of **Gly-A$_2$Gly-N** treated with TCEP, clearly showing the 2:1 ratio of **GlyA** : **GlyN**.

NMR Studies:

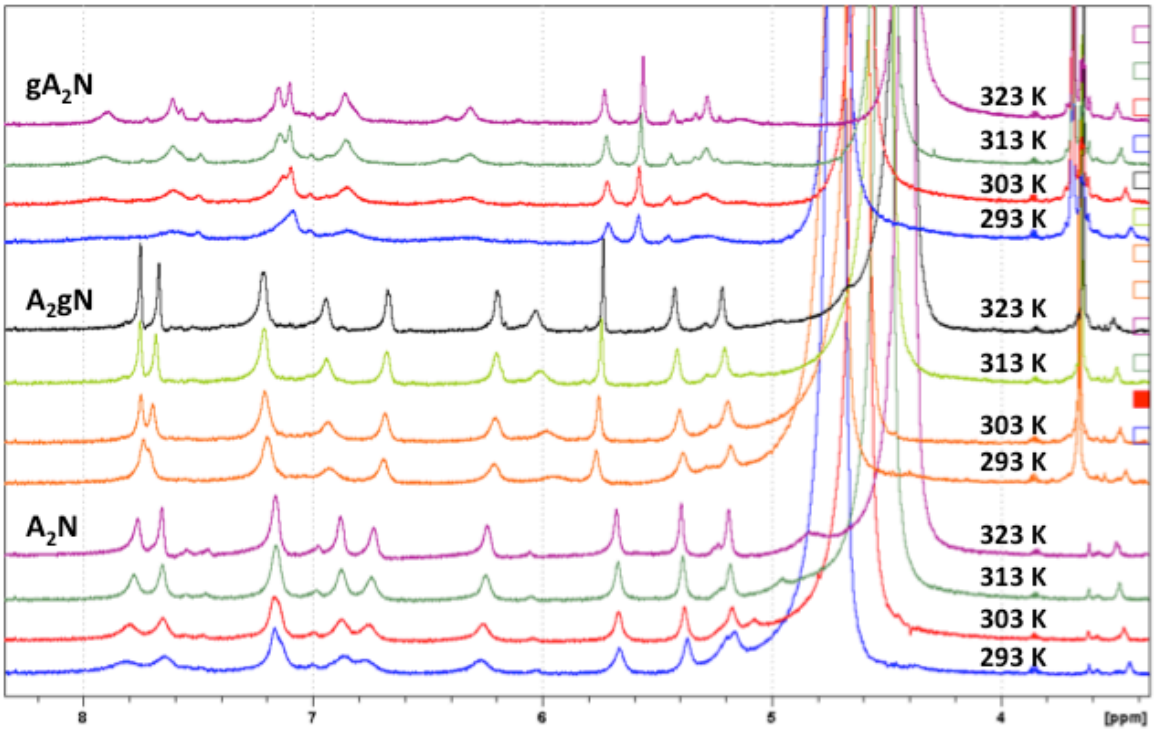


Figure S 42. Overlaid ^{1}H NMR spectra of **A_2N**, **A_2Gly-N (A_2gN)** and **Gly-A_2N (gA_2N)** in 10 mM Borate Buffer in D_2O (pH 8.5) at various temperatures.

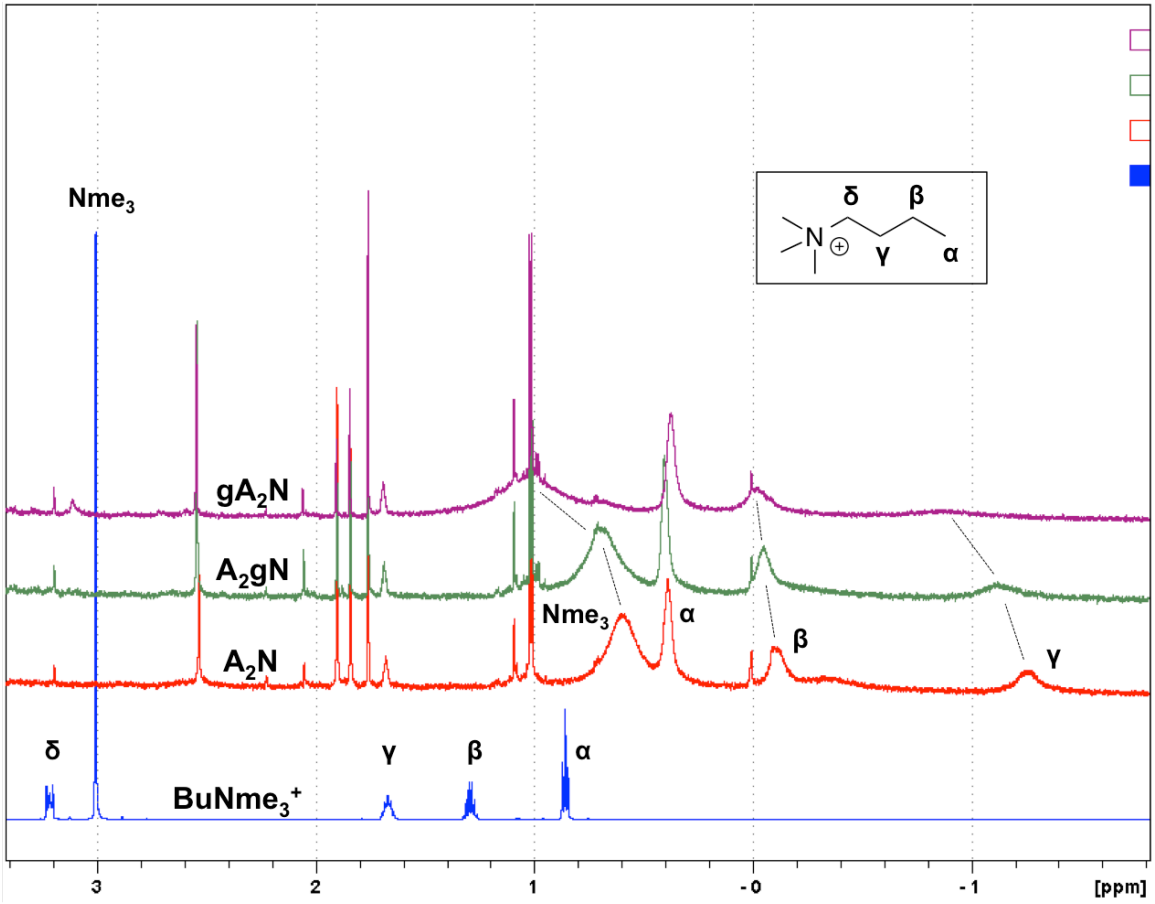


Figure S43. Overlaid ^{1}H NMR spectra of the simple guest butyltrimethylammonium ($BuNme_3^+$) alone (bottom), and bound to **A_2N**, **A_2Gly-N (A_2gN)**, and **Gly-A_2N (gA_2N)** in 10 mM Borate Buffer in D_2O (pH 8.5). For all spectra, [$BuNme_3^+$] = 370 μM and [receptor] = 480 μM. The δ-methylene could not be assigned in the bound spectra.

Isothermal Titration Calorimetry:

A_2GlyN:

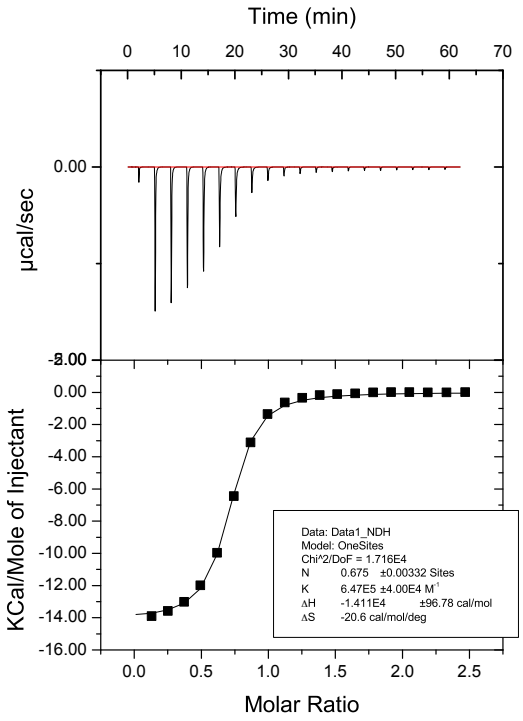


Figure S44. One of two trials of $RKme_3$ (WGGG-QTARKme_3STG-NH_2) (1.23 mM) titrated into *meso*$_2$-**A_2Gly-N** (101 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

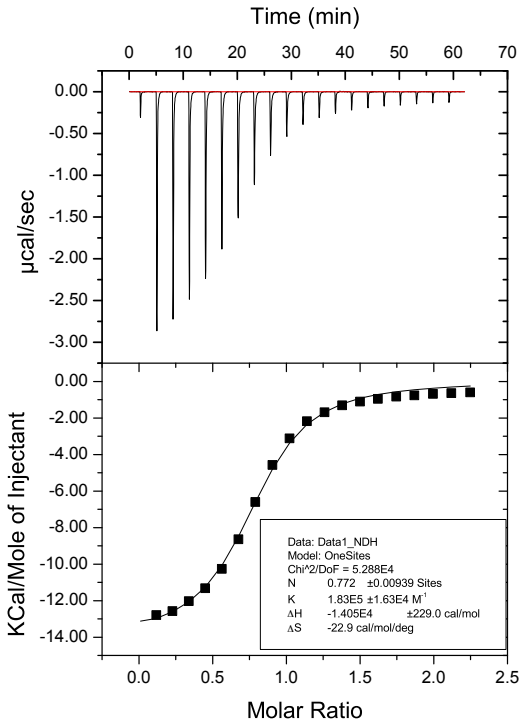


Figure S45. One of two trials of $RKme_2$ (WGGG-QTARKme_2STG-NH_2) (1.12 mM) titrated into *meso*$_2$-**A$_2$Gly-N** (101 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

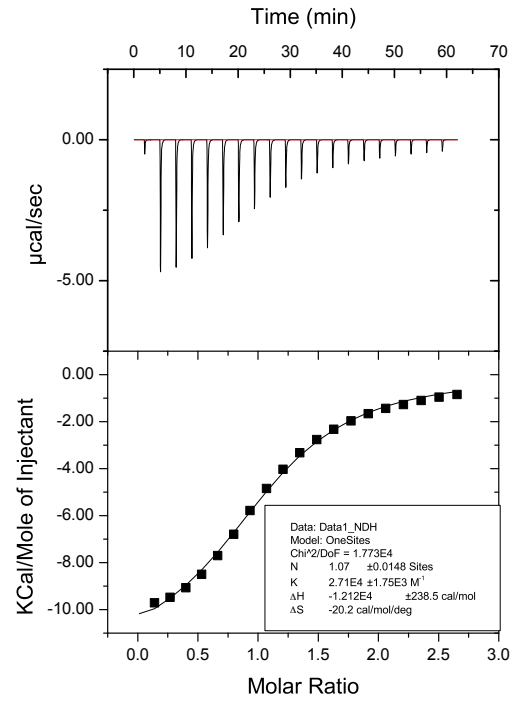


Figure S46. One of two trials of RKme (WGGG-QTARKmeSTG-NH_2) (2.39 mM) titrated into *meso*$_2$-**A$_2$Gly-N** (183 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

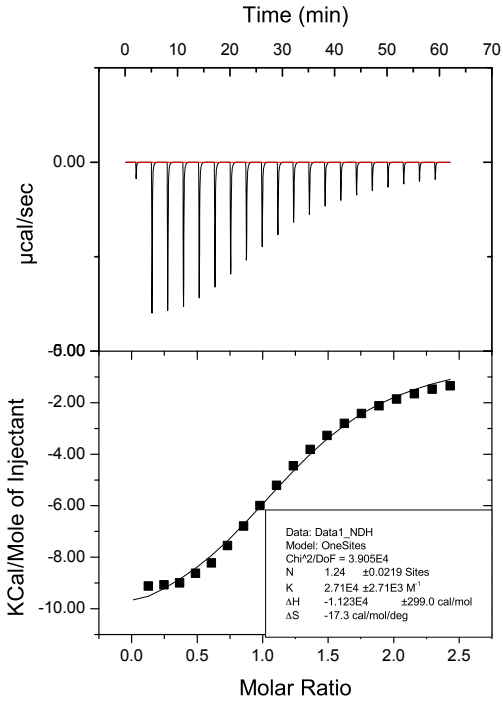


Figure S47. One of two trials of RK (WGGG-QTARKSTG-NH_2) (2.19 mM) titrated into *meso*$_2$-**A$_2$Gly-N** (183 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

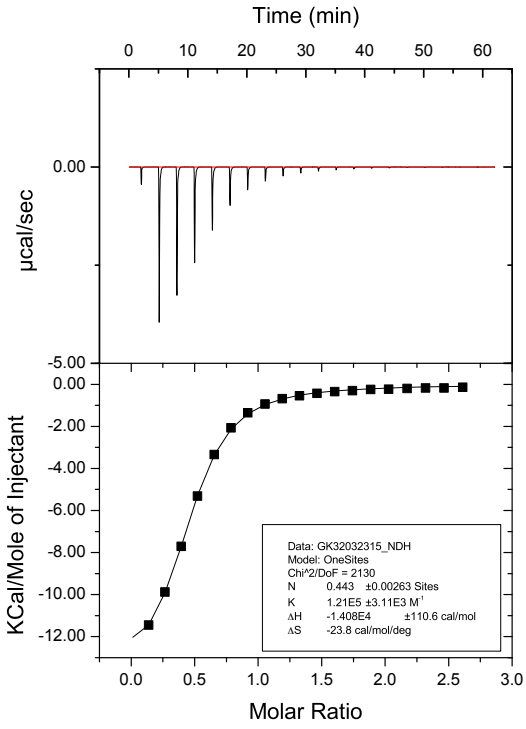


Figure S48. One of two trials of GKme$_3$ (WGGG-QTAGKme$_3$STG-NH_2) (1.46 mM) titrated into *meso*$_2$-**A$_2$Gly-N** (113 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

Gly-A_2N: (used as a mixture of isomers containing predominantly *meso*$_2$-**GlyA_2N**)

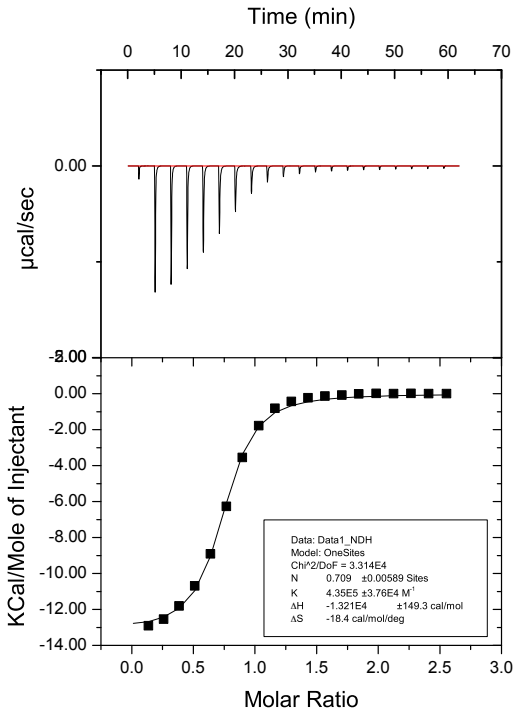


Figure S49. One of two trials of $RKme_3$ (WGGG-QTARKme_3STG-NH_2) (1.23 mM) titrated into *meso*$_2$-**Gly-A_2N** (98 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

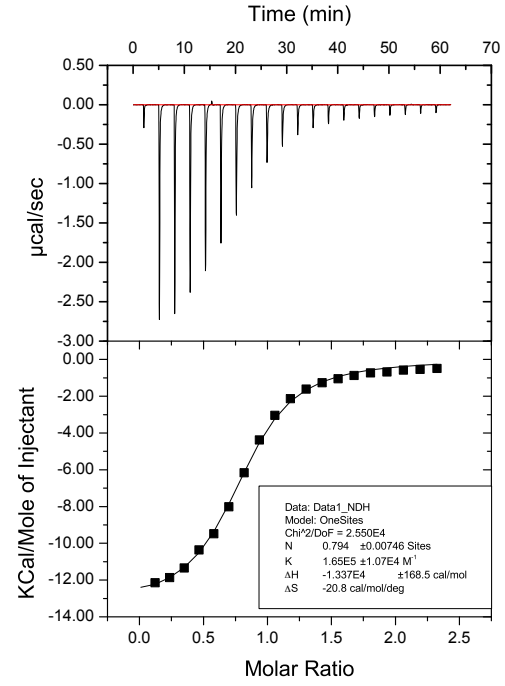


Figure S50. One of two trials of $RKme_2$ (WGGG-QTARKme_2STG-NH_2) (1.12 mM) titrated into *meso*$_2$-**Gly-A_2N** (98 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

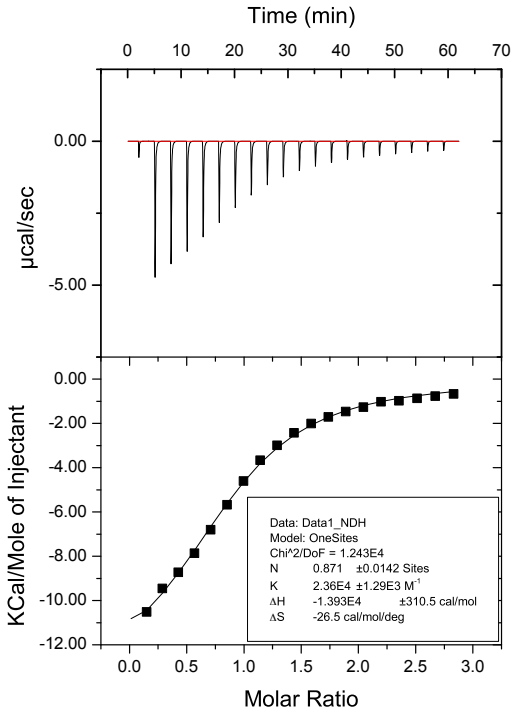


Figure S51. One of two trials of RKme (WGGG-QTARKmeSTG-NH_2) (2.39 mM) titrated into *meso*$_2$-**Gly-A$_2$N** (172 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

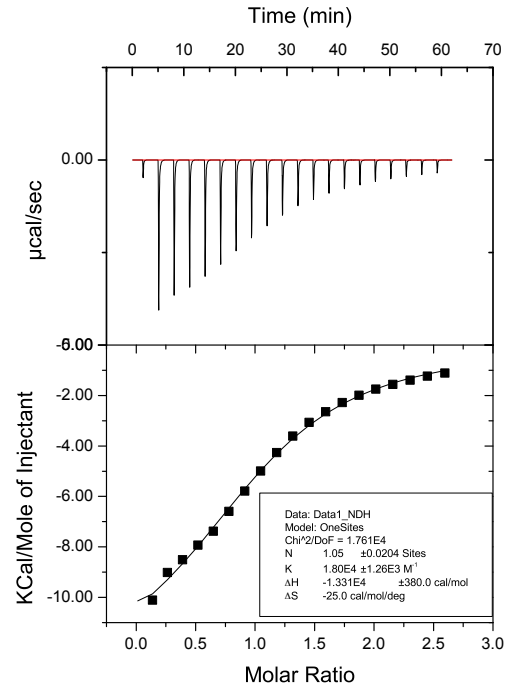


Figure S52. One of two trials of RK (WGGG-QTARKSTG-NH_2) (2.19 mM) titrated into *meso*$_2$-**Gly-A$_2$N** (172 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.

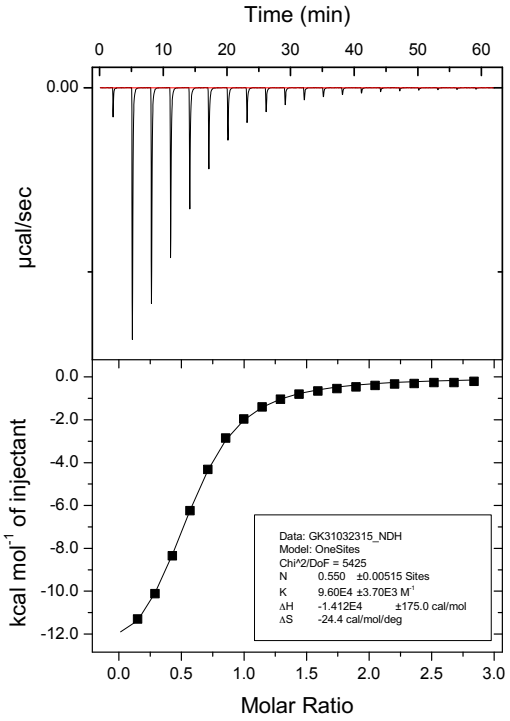


Figure S53. One of two trials of $GKme_3$ (WGGG-QTAGKme_3STG-NH_2) (1.46 mM) titrated into *meso*$_2$-**Gly-A$_2$N** (104 µM) at 26 ºC in 10 mM borate buffer, pH 8.5.