Supporting Information for

Catalysis of thiol-thioester exchange by water soluble alkyldiselenols applied to the synthesis of peptide thioesters and SEA-mediated ligation

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1. Table of Contents

1. Kinetic studies

Step 1. Kinetic measurements for SEA amide-SEA thioester equilibrium (see Figure 1)

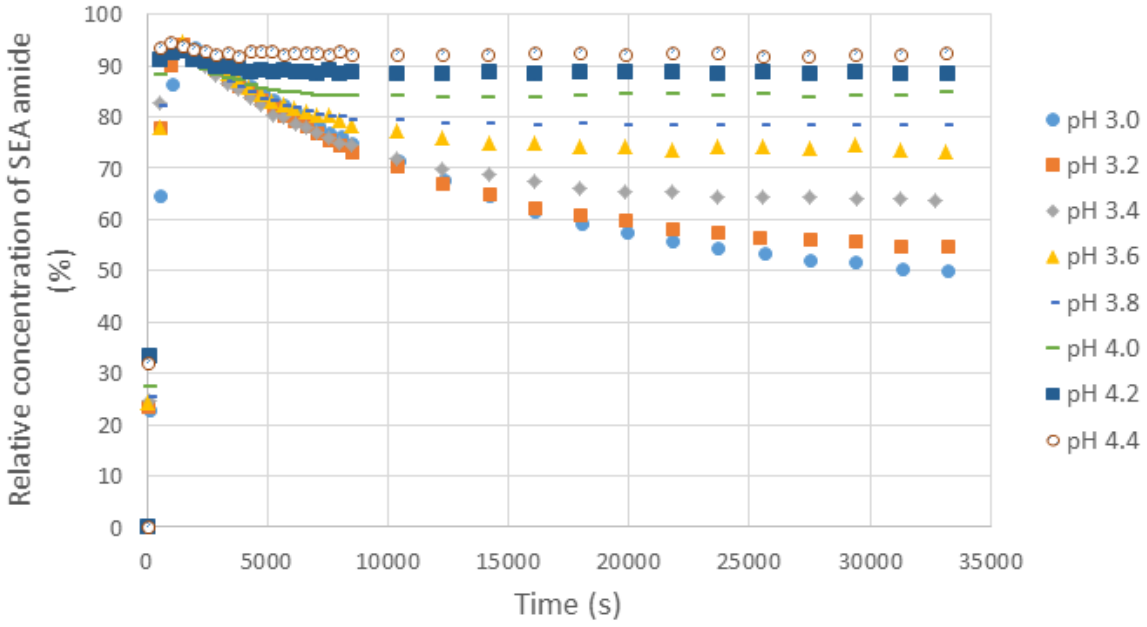


Figure S 1. Evolution of the relative concentration of SEA^{on} peptide **2a** at various pH (expressed as a percentage of total peptidic content).

Table S 1. Step 1. Determination of rate constants k_1, k_2 and k_{-2}.

pH	k_1	STDERR	k_{+2}	STDERR	k_{-2}	STDERR
3.0	0.0239	0.002414	4.08E-05	3.64E-06	3.29E-05	8.90E-06
3.2	0.0372	4.22E-03	4.80E-05	4.31E-06	5.60E-05	1.14E-06
3.4	0.0394	0.001472	5.59E-05	1.65E-06	0.0001	4.13E-05
3.6	0.0412	0.004287	5.53E-05	4.35E-06	0.000159	1.80E-05
3.8	0.042809	0.002441	7.40E-05	2.74E-06	0.000274	4.24E-05
4.0	0.0488	0.001274	8.38E-05	1.48E-06	0.000444	5.94E-05
4.2	0.065	0.001163	0.000101	8.07E-06	0.000803	6.87E-05
4.4	0.0718	0.00101	0.000123	6.39E-06	0.00154	7.13E-04

[a] k_1 in $M^{-1}.s^{-1}$; k_{+2} and k_{-2} in s^{-1}

Step 2. Kinetic study of the MPA - SEA thioester exchange (see Figure 2)

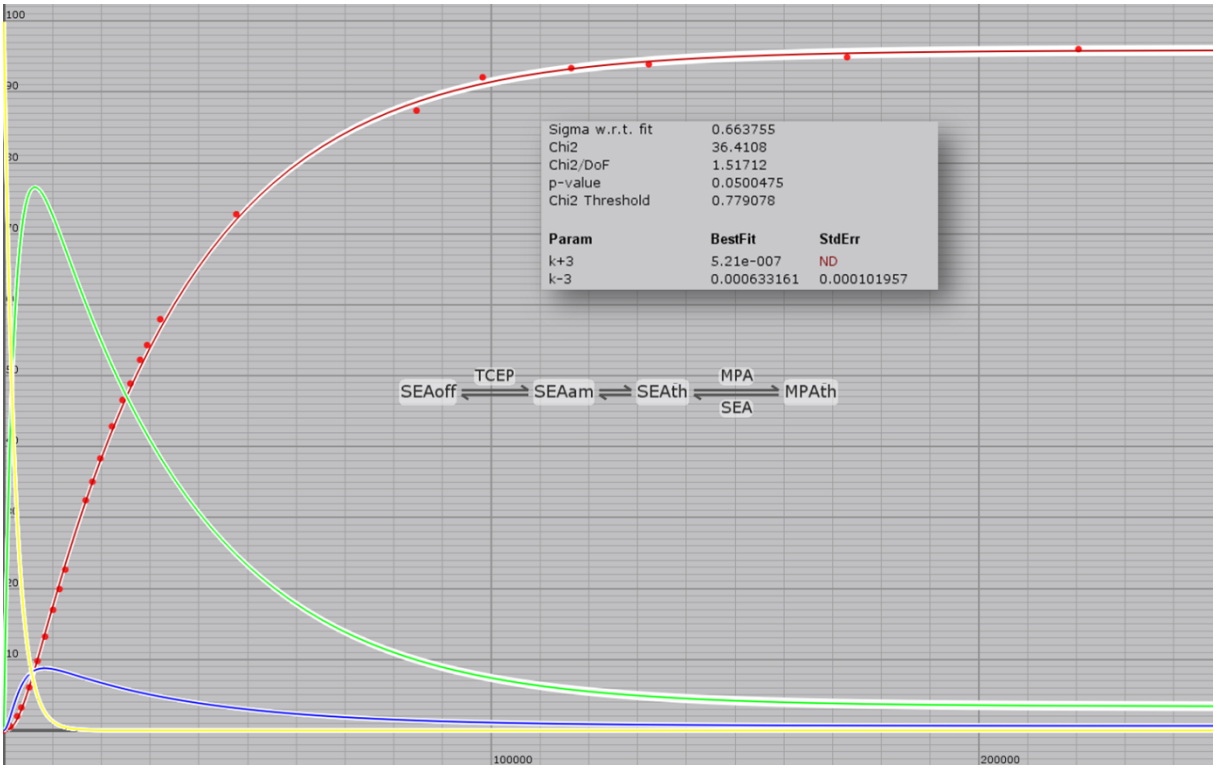


Figure S 2. Fitting of the uncatalyzed SEA –MPA exchange reaction using KinteK Explorer Software™ (Version 7.2.180216., Kintek Corporation - https://kintekcorp.com/software/). Red dots correspond to experimental values.

SEA thioester-MPA exchange for C-terminal Thr and Ile (see Table 1)

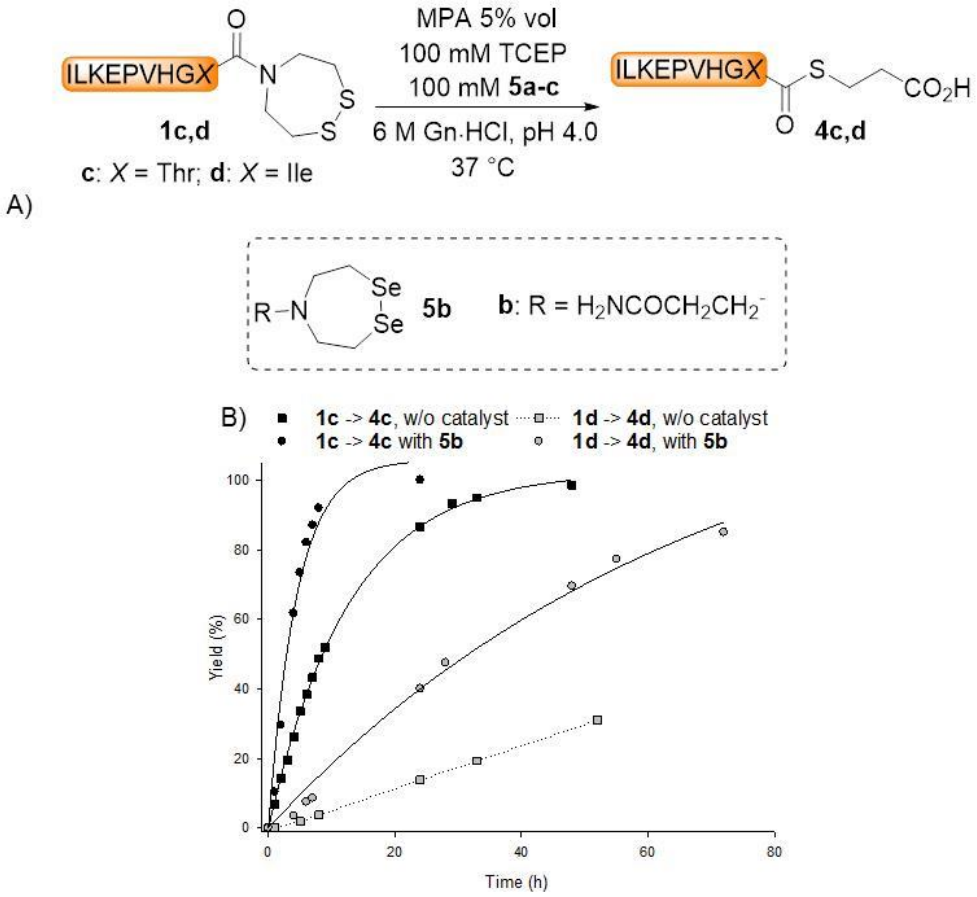


Figure S 3. Exchange of the SEA group by MPA catalyzed by diselenide **5b**. Conversion of peptide **1c,d** into **4c,d**. The continuous curves correspond to the fitting to a pseudo first order kinetic law from which t½ were extracted (see Table 1 in the manuscript).

2. Characterizations of synthesized compounds

*Characterization of peptide **1e***

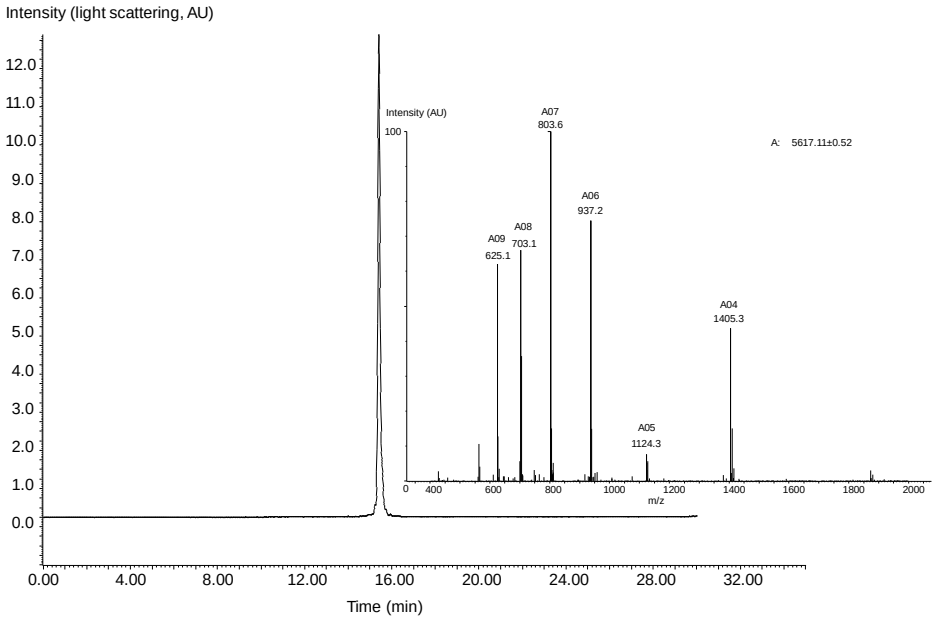


Figure S 4. LC-MS analysis of peptide **1e**. LC trace. Chromatography conditions: eluent A 0.10% TFA in water, eluent B 0.10% TFA in CH_3CN/water: 4/1 by vol. C3 Zorbax 300SB Å 3.5 μm (4.6 × 150 mm) column, gradient 0-100% B in 30 min, 60 °C, 1 mL/min, detection at 215 nm. MS trace. m/z = 1405.3 ($[M+4H]^{4+}$), 1124.3 ($[M+5H]^{5+}$), 937.2 ($[M+6H]^{6+}$), 803.6 ($[M+7H]^{7+}$), 703.1 ($[M+8H]^{8+}$), 625.1 ($[M+9H]^{9+}$). Calcd. for M: 5617.5 (average), found: 5617.1.

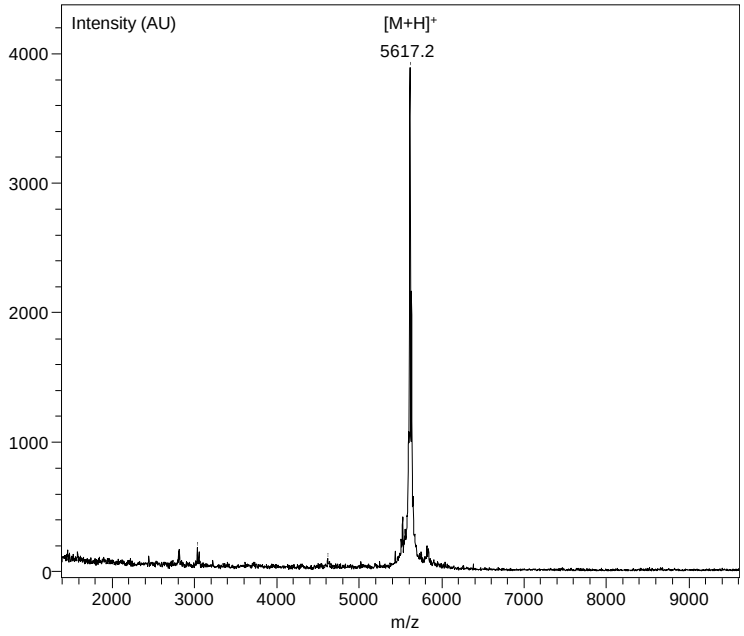


Figure S 5. MALDI-TOF of peptide **1e**. Matrix = sinapinic acid, positive detection mode, m/z calcd for $[M+H]^+$ (average): 5618.5, found: 5617.2.

*Characterization of peptide **1f***

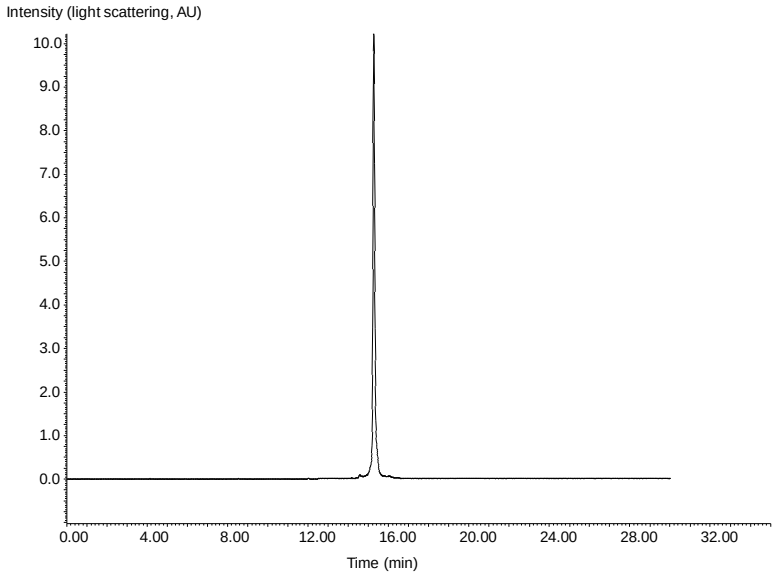


Figure S 6. LC analysis of peptide **1f**. LC trace. Chromatography conditions: eluent A 0.10% TFA in water, eluent B 0.10% TFA in CH_3CN/water: 4/1 by vol. C3 Zorbax 300SB Å 3.5 μm (4.6 × 150 mm) column, gradient 0-100% B in 30 min, 60 °C, 1 mL/min, detection at 215 nm.

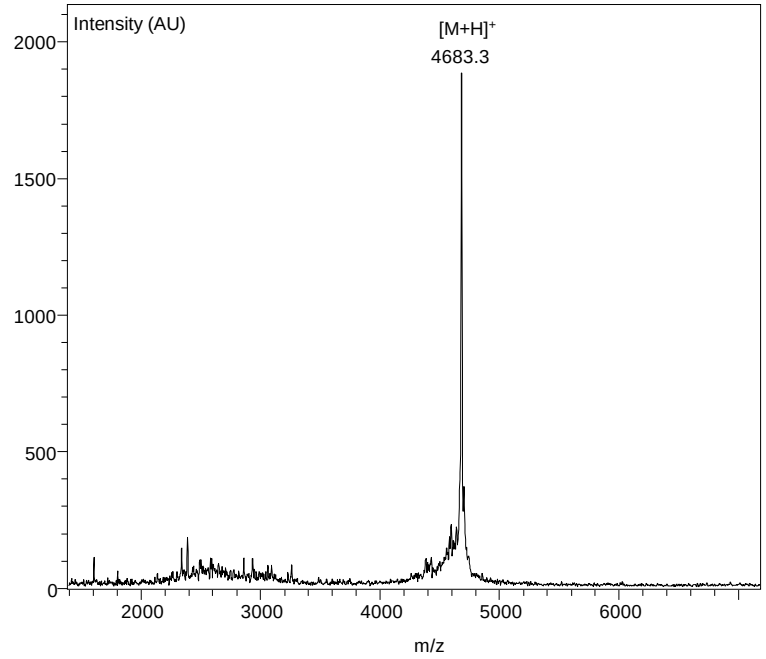


Figure S 7. MALDI-TOF of peptide **1f**. Matrix = sinapinic acid, positive detection mode, m/z calcd for $[M+H]^+$ (average): 4683.8, found: 4683.3.

*Characterization of peptide **1g***

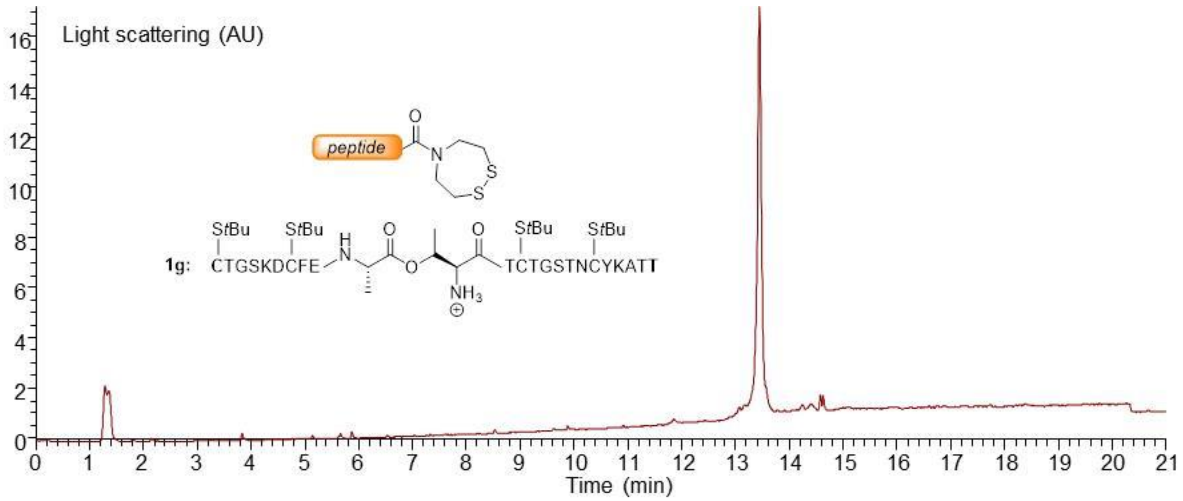


Figure S 8. LC analysis of peptide **1g**. LC trace. Chromatography conditions: eluent A 0.10% TFA in water, eluent B 0.10% TFA in CH_3CN/water: 4/1 by vol. C3 Zorbax 300SB Å 3.5 µm (4.6 × 150 mm) column, gradient 0-100% B in 30 min, 60 °C, 1 mL/min, detection at 215 nm.

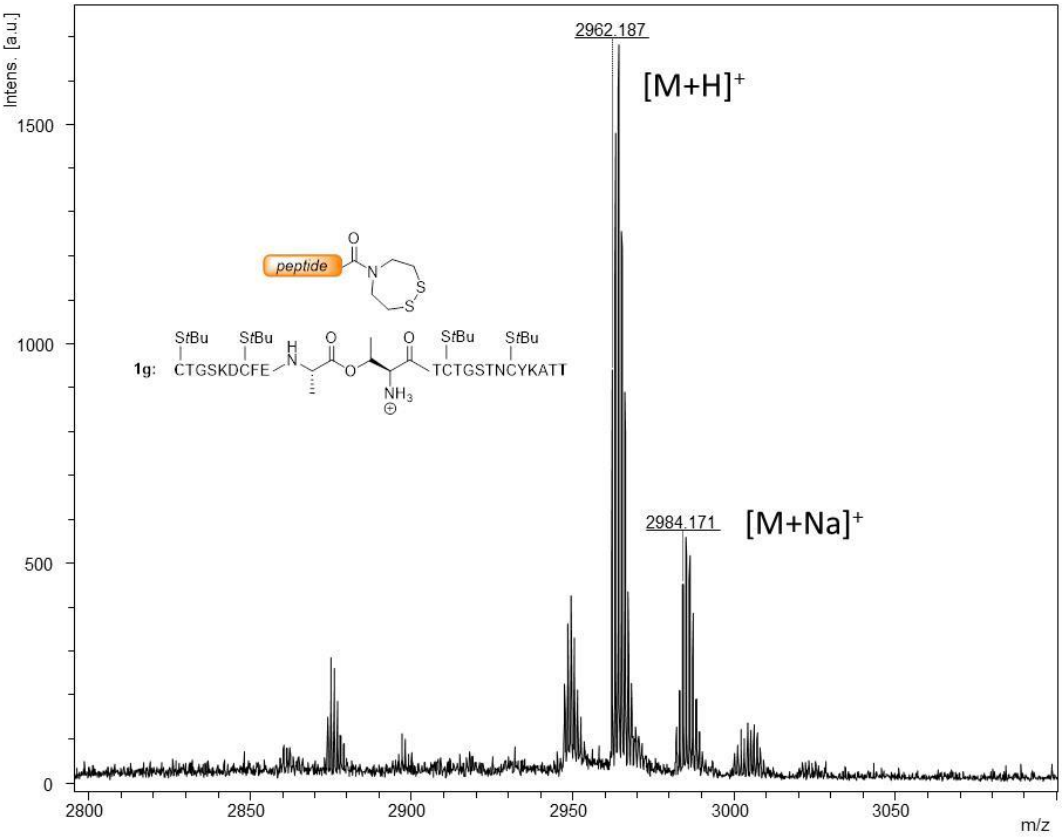


Figure S 9**.** MALDI-TOF of peptide **1g**. Matrix = sinapinic acid, positive detection mode, m/z calcd for $[M+H]^+$ (monoisotopic): 2962.14, found: 2962.19

*Characterization of peptide **4b***

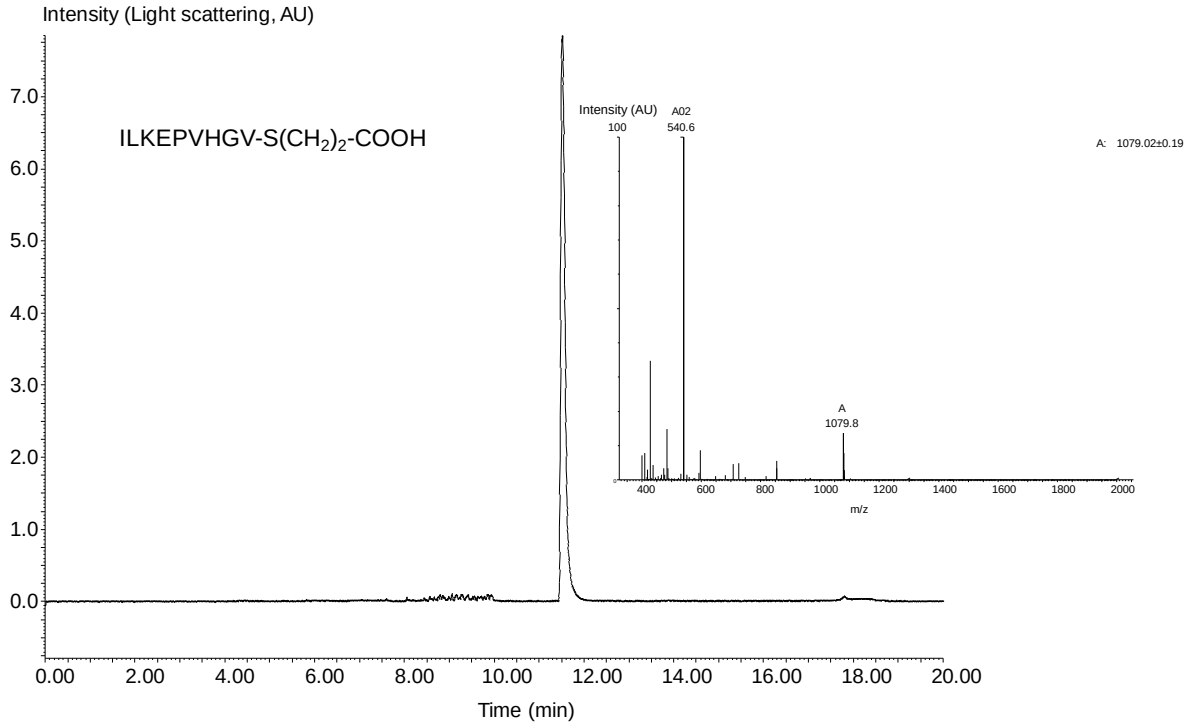


Figure S 10. LC-MS analysis of peptide **4b**. LC trace. Chromatography conditions: eluent A 0.1% TFA in water, eluent B 0.1% TFA in CH_3CN/water: 4/1 by vol. C18 Xbridge BEH 300 Å 5 μm (4.6 × 250 mm) column, gradient 0-50% B in 15 min, 1 mL/min, detection at 215 nm. MS trace. m/z = 1079.8 ($[M+H]^+$), 540.6 ($[M+2H]^{2+}$). Calcd. for M (average): 1079.3, found: 1079.0.

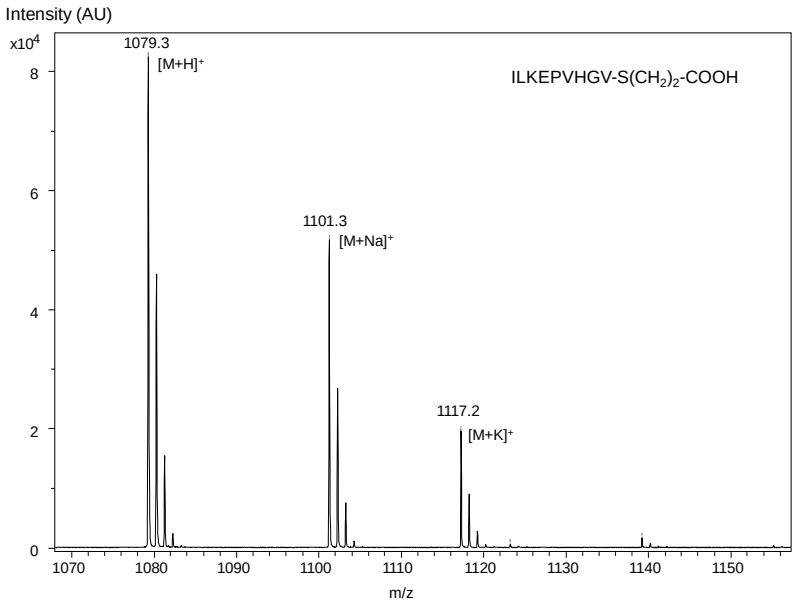


Figure S 11. MALDI-TOF of peptide **4b**. Matrix = α-cyano-4-hydroxycinnamic acid, positive detection mode, m/z calcd for $[M+H]^+$ (monoisotopic): 1079.6, found: 1079.3.

*Characterization of peptide **4e***

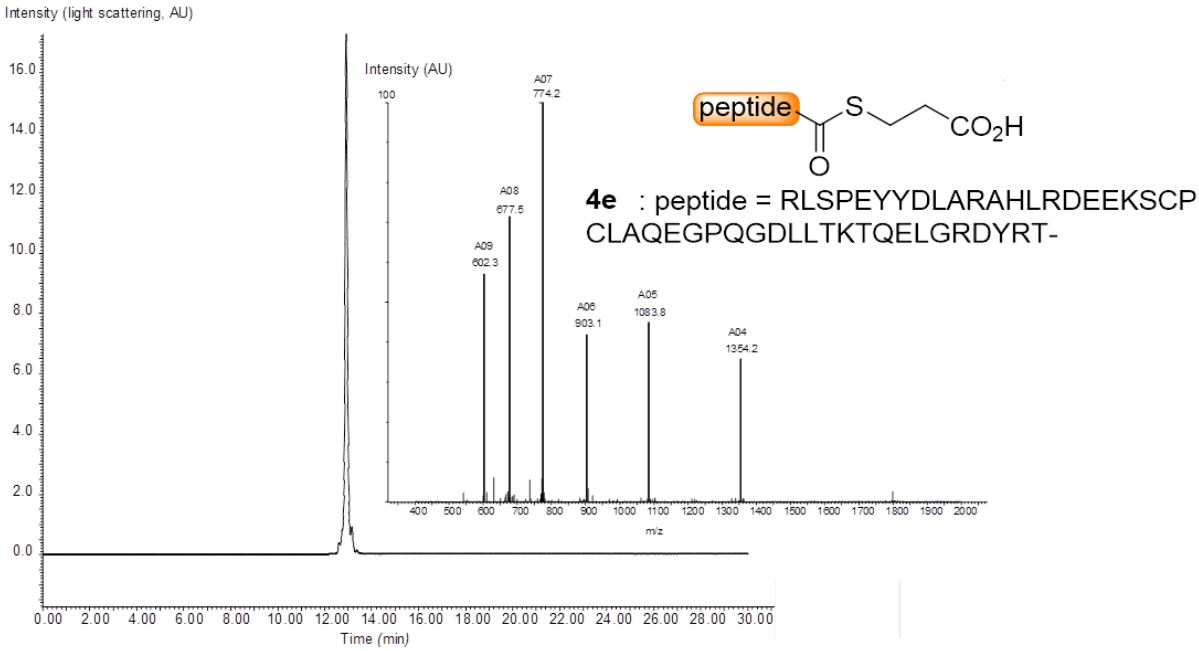


Figure S 12. LC-MS analysis of peptide **4e**. LC trace. Chromatography conditions: eluent A 0.10% TFA in water, eluent B 0.10% TFA in CH_3CN/water: 4/1 by vol. C3 Zorbax 300SB Å 3.5 µm (4.6 × 150 mm) column, gradient 0-100% B in 30 min, 60 °C, 1 mL/min, detection at 215 nm. MS trace. m/z = 1354.2 ($[M+4H]^{4+}$), 1083.8 ($[M+5H]^{5+}$), 903.1 ($[M+6H]^{6+}$), 774.2 ($[M+7H]^{7+}$), 677.5 ($[M+8H]^{8+}$), 602.3 ($[M+9H]^{9+}$). Calcd. for M (average): 5412.04, found 5412.50.

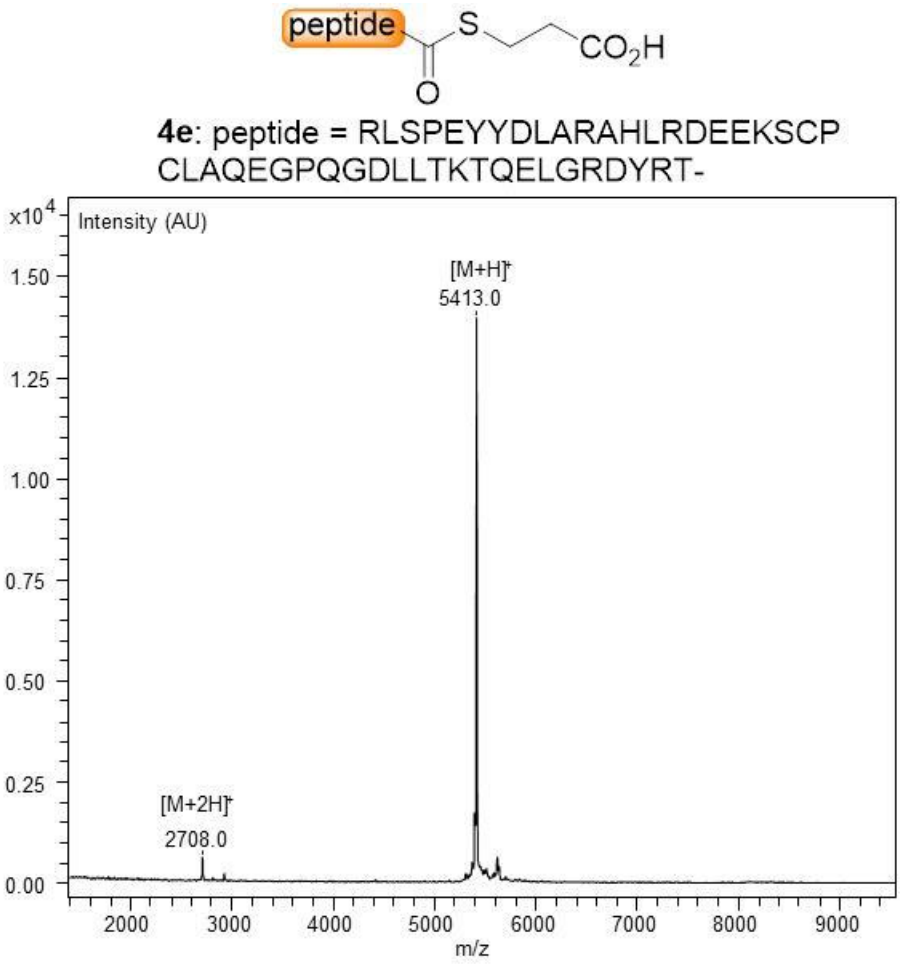
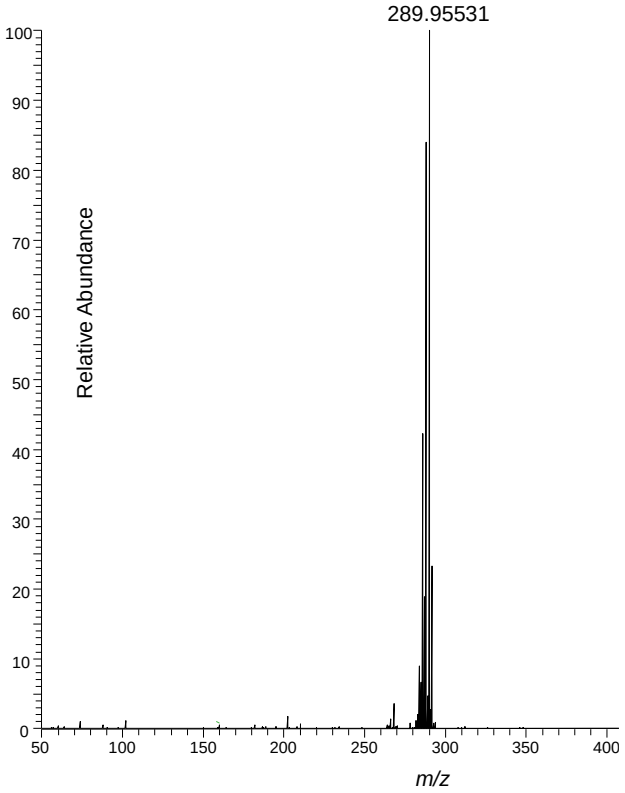
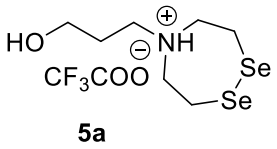


Figure S 13. MALDI-TOF of peptide **4e**. Matrix = sinapinic acid, positive detection mode, m/z calcd for $[M+H]^+$ (average): 5413.0, found: 5413.0.

*Characterization of diselenide **5a***



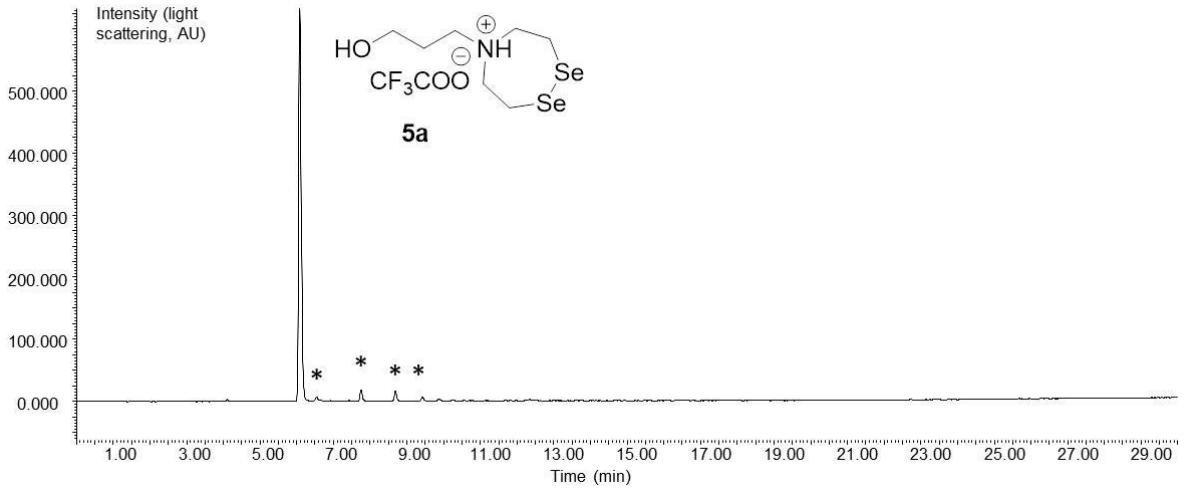


5a

m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	RDB equiv	Composition
285,9579	7890467	44,41	285,9584	-1,72	0,5	C7 H16 O N [76]Se Se
286,9588	3286462	18,5	286,9591	-0,85	0,5	C7 H16 O N [77]Se Se
287,9562	14460140	81,39	287,9565	-1,13	0,5	C7 H16 O N [78]Se Se
289,9552	**17765790**	**100**	**289,9557**	**-1,67**	**0,5**	**C7 H16 O N Se2**
291,9553	4317527	24,3	291,9559	-1,95	0,5	C7 H16 O N Se [82]Se

Figure S 14. HRMS analysis for catalyst **5a**. m/z calcd. for $[M+H]^+$ (monoisotopic): 289.9559, found: 289.9552.

A)



B)

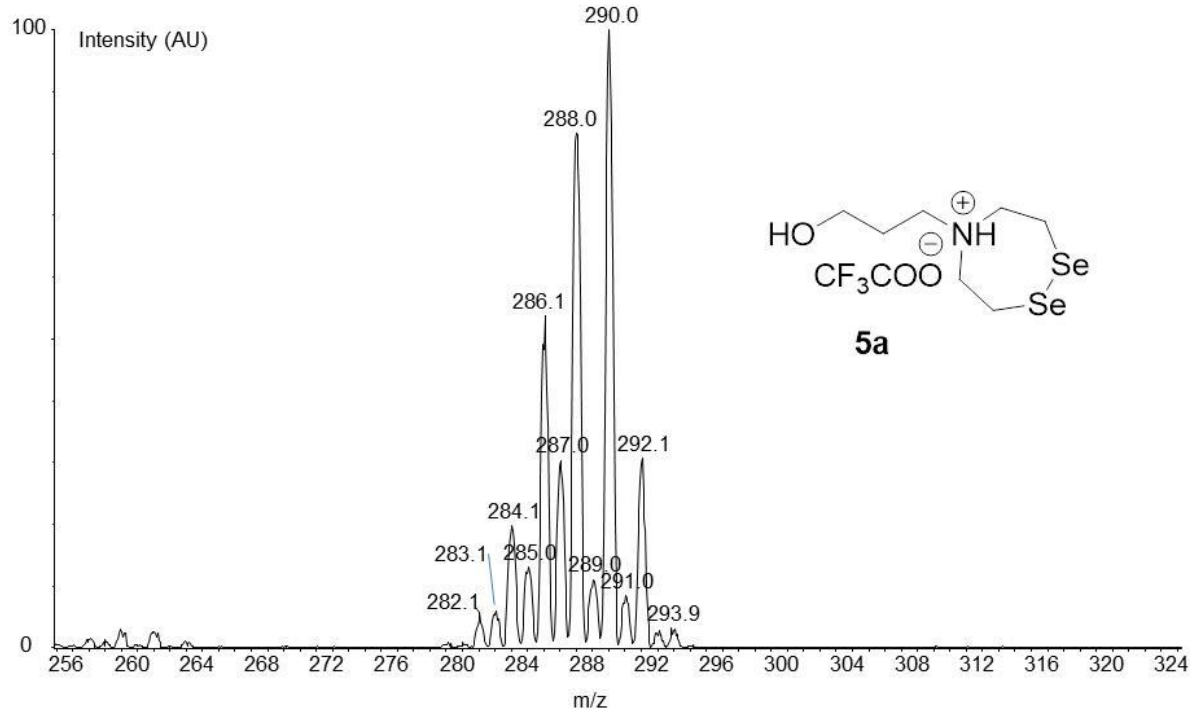


Figure S 15. LC-MS analysis of diselenide **5a**. A) LC trace. Chromatography conditions: eluent A 0.1% TFA in water, eluent B 0.1% TFA in CH3CN/water: 4/1 by vol. C18 Xbridge BEH 300 Å 5 μm (4.6 × 250 mm) column, gradient 0-50% B in 15 min, 1 mL/min, detection at 215 nm. The peaks marked by a star correspond to aggregates of diselenide **5a**. All display the same MS trace as **5a**. The capacity of diselenide **5a** to aggregate is reminiscent of the aggregation properties of 1,2,5-diselenazepane. B) MS trace. m/z calcd. for $[M+H]^+$: 290.0 (peak of highest intensity, monoisotopic), found: 290.0.

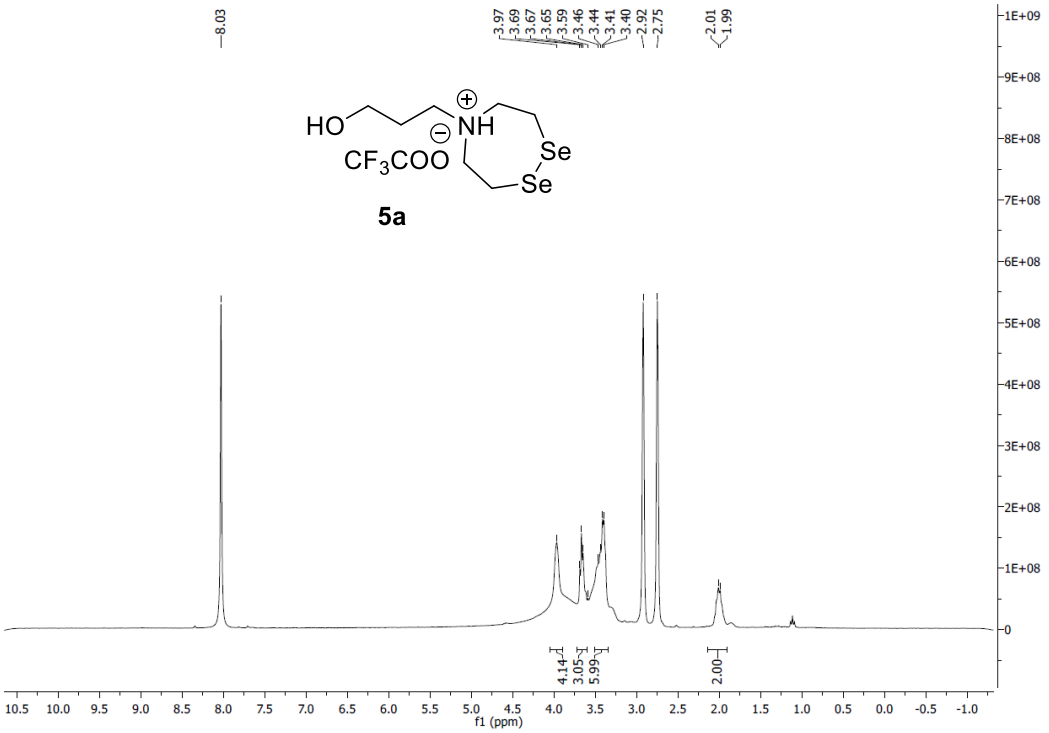


Figure S 16. ^{1}H NMR (300 MHz) spectrum for compound **5a** (DMF-d7, 300 K). δ 3.97 (m, 4H), 3.69-3.65 (m, 3H), 3.46-3.40 (m, 6H), 2.00 (m, 2H) ppm. The ^{1}H NMR spectrum of **5a** is large due to conformational effects, a behavior shared by other catalysts (see the ^{1}H NMR of **5c** at different temperatures).

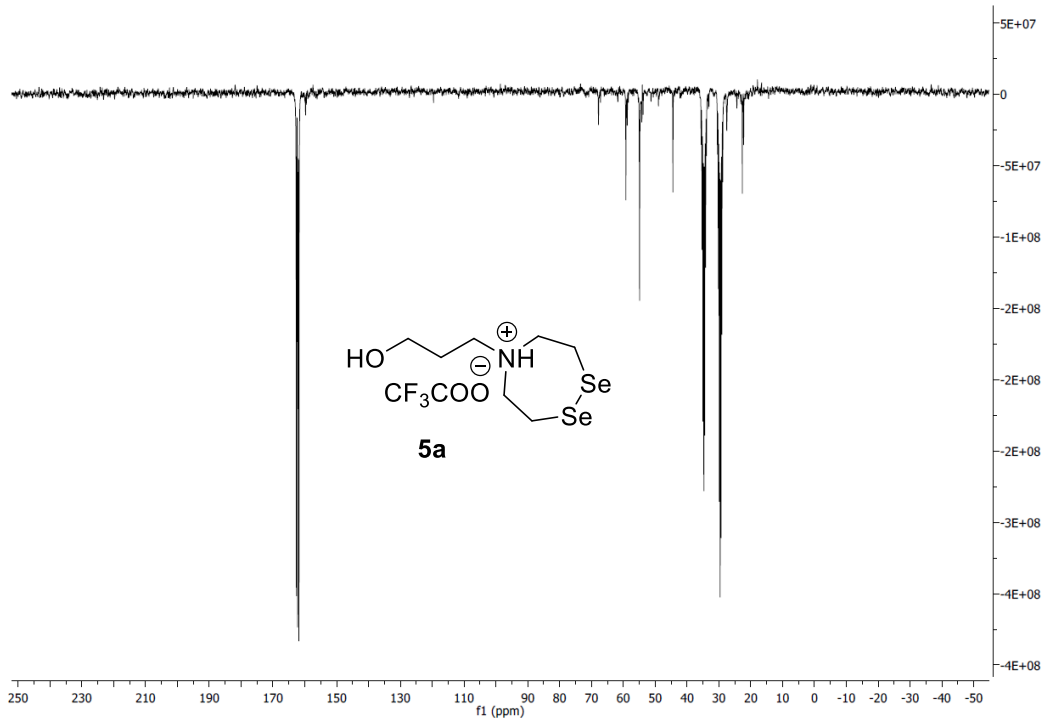


Figure S 17. ^{13}C JMOD NMR (75 MHz) spectrum for compound **5a** (DMF-d7, 300 K). δ 59.2 (CH_2), 54.6 (4 × CH_2), 22.3 (CH_2) ppm. One ^{13}C signal is not seen due to overlap with the residual signal from the solvent.

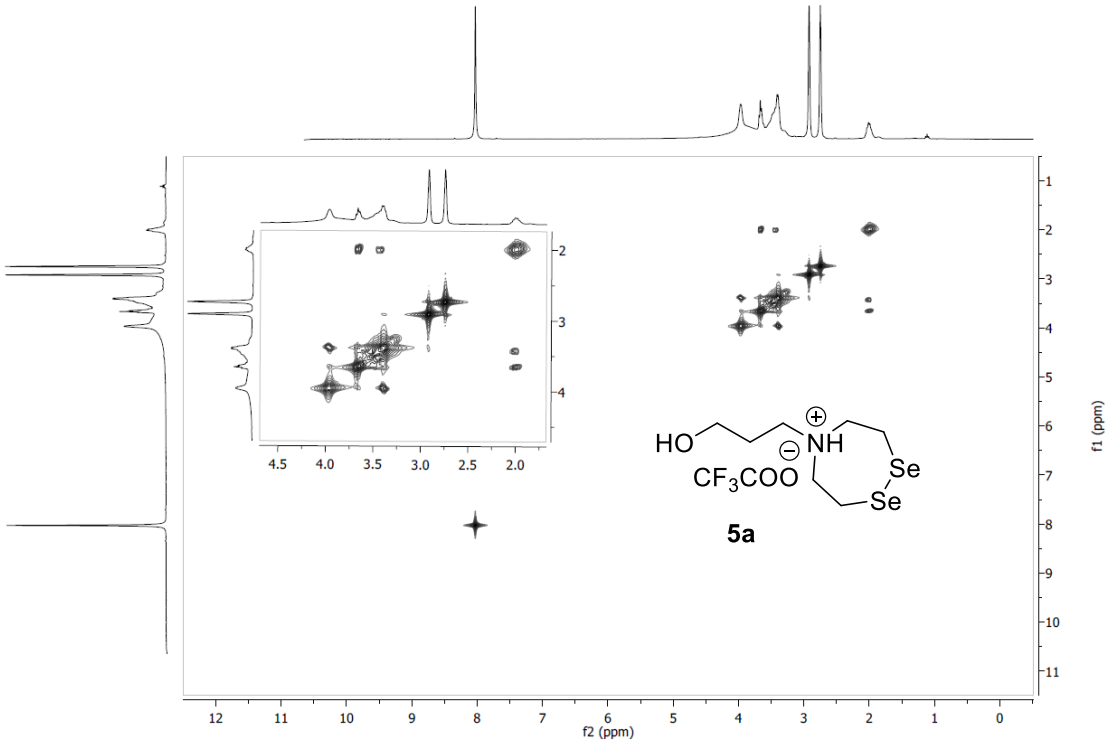


Figure S 18. ^{1}H-^{1}H COSY spectrum for compound **5a** (DMF-d7, 300 K).

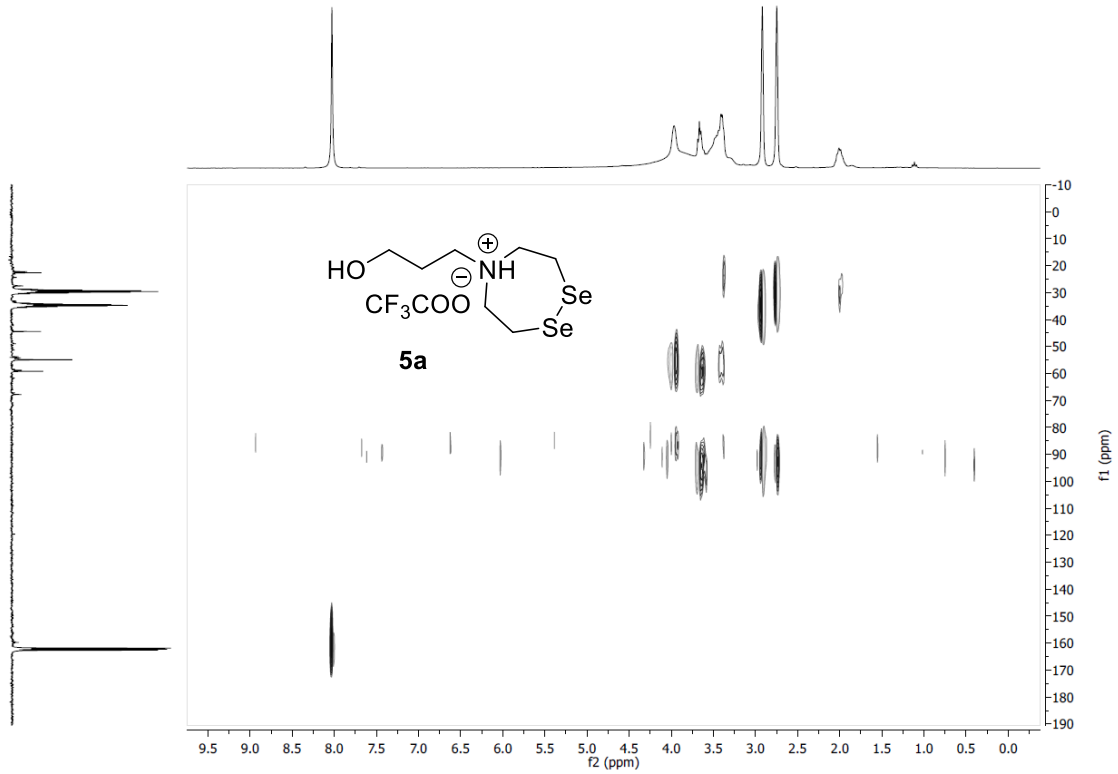
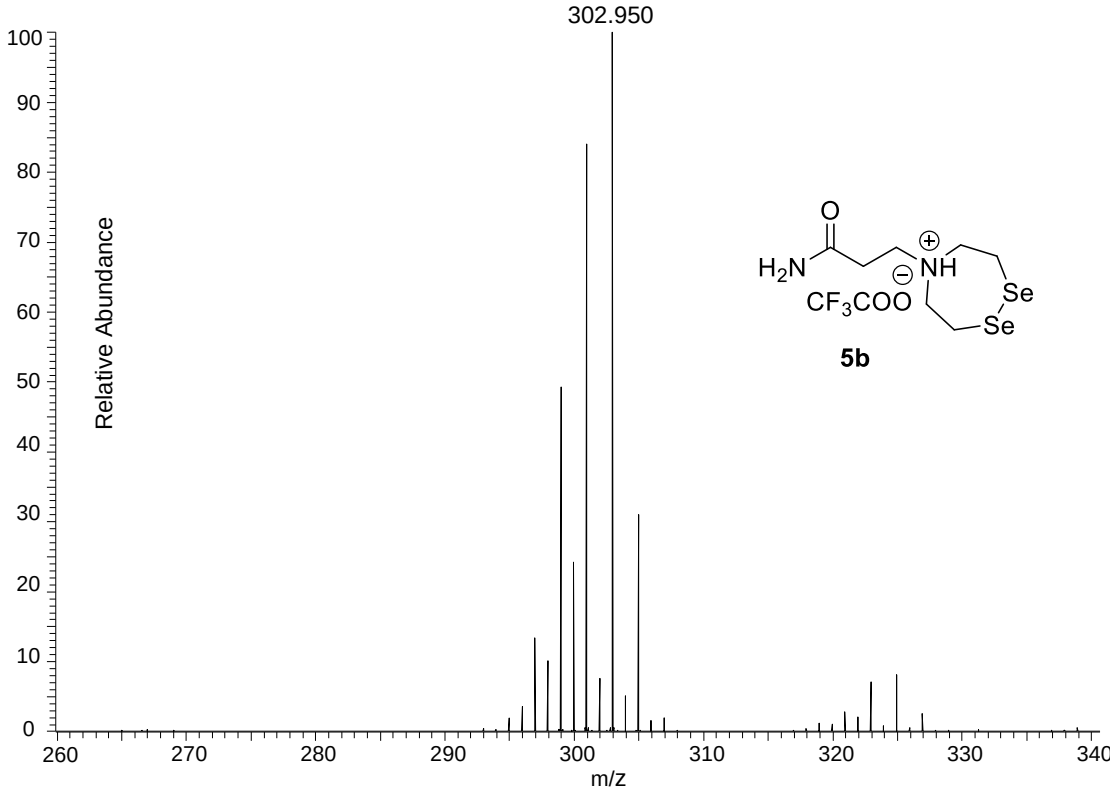


Figure S 19. ^{1}H-^{13}C HSQC spectrum for compound **5a** (DMF-d7, 300 K).

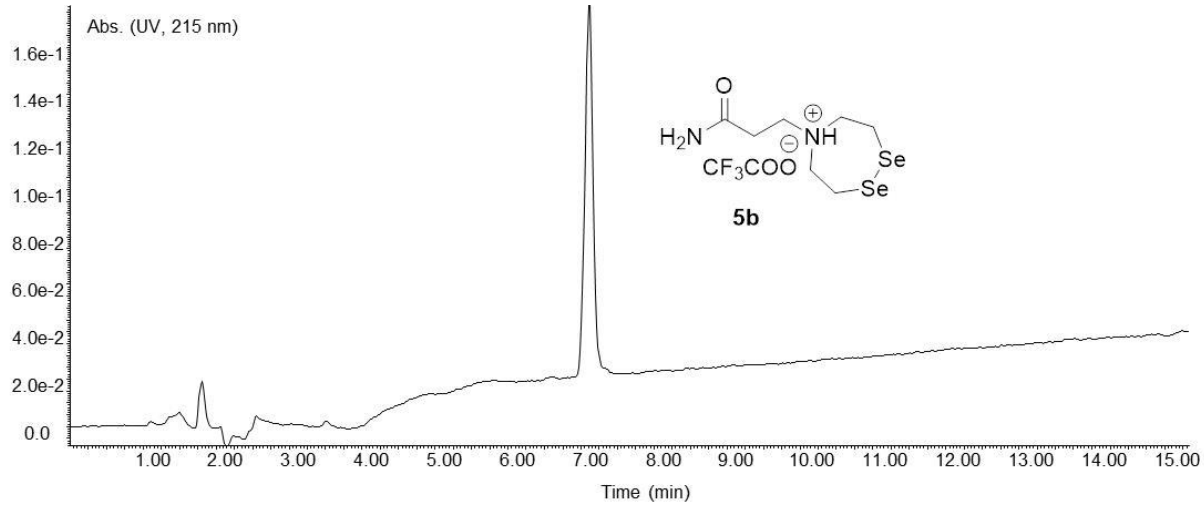
*Characterization of diselenide **5b***



m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	RDB equiv	Composition
298,9531	61619380	50,61				
299,9541	30622960	25,15				
300,9513	103122168	84,7				
302,9503	**121743136**	**100**	**302,9509**	**-1,98**	**1,5**	**C7 H15 O N2 Se2**
304,9504	38553024	31,67				

Figure S 20. HRMS analysis for catalyst **5b**. m/z calcd. for $[M+H]^+$ (monoisotopic) 302.9509, found: 302.9503.

A)



B)

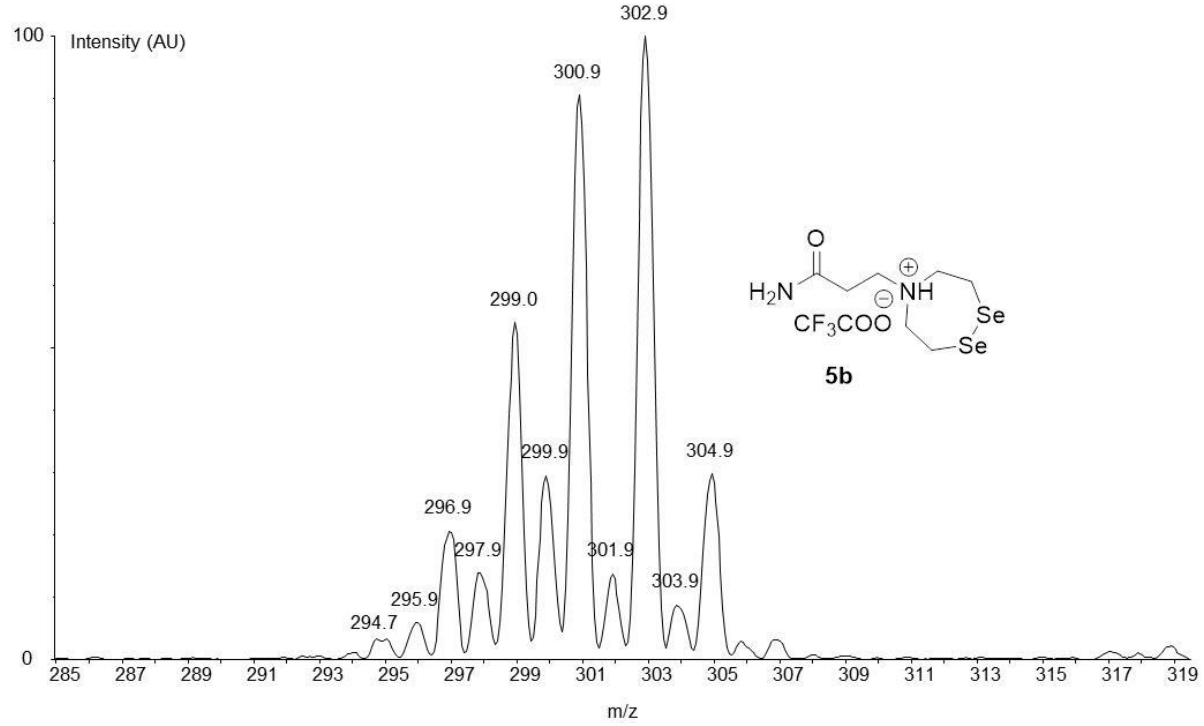


Figure S 21. LC-MS analysis of diselenide **5b**. A) LC trace. Chromatography conditions: eluent A 0.1% TFA in water, eluent B 0.1% TFA in CH3CN/water: 4/1 by vol. C18 Xbridge BEH 300 Å 5 μm (4.6 × 250 m) column, gradient 0-50% B in 15 min, 1 mL/min, detection at 215 nm. B) MS trace. m/z calcd. for $[M+H]^+$: 303.0 (peak of highest intensity, monoisotopic), found: 302.9.

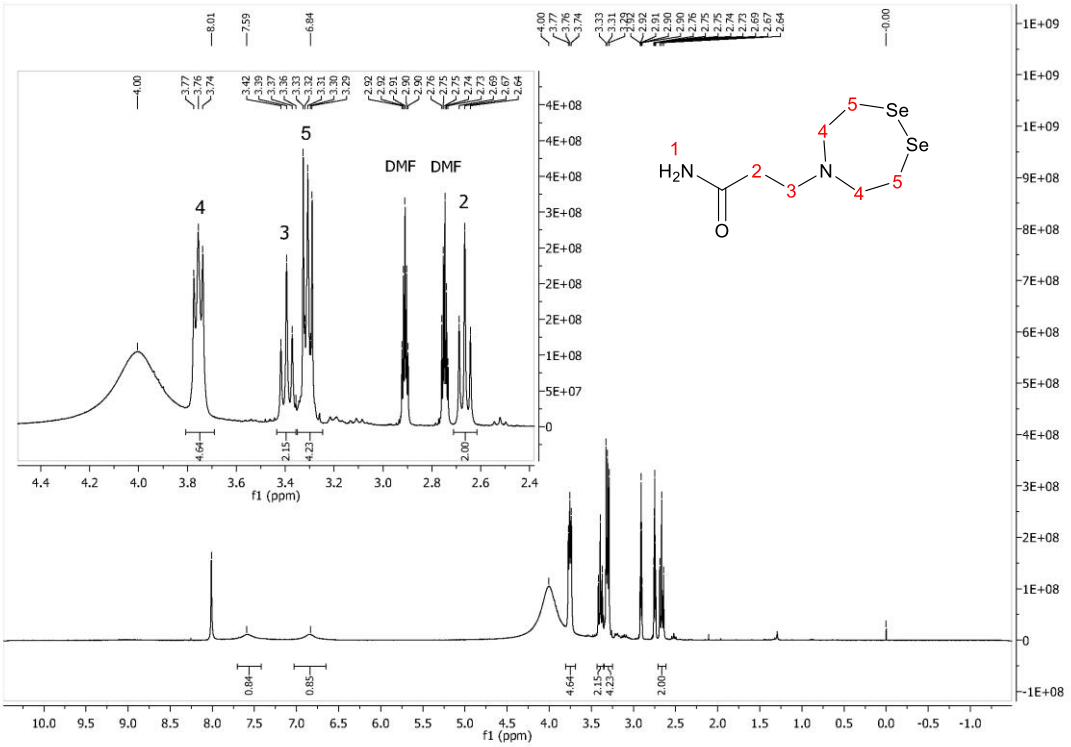


Figure S 22. ^{1}H NMR (300 MHz) spectrum for compound **5b** (DMF-d7, 333 K). δ 7.59 (s, 1H), 6.84 (s, 1H), 3.77-3.74 (m, 4H), 3.42-3.36 (t, *J* = 6.9 Hz, 2H), 3.33-3.29 (m, 4H), 2.73-2.64 (t, *J* = 6.9 Hz, 2H) ppm.

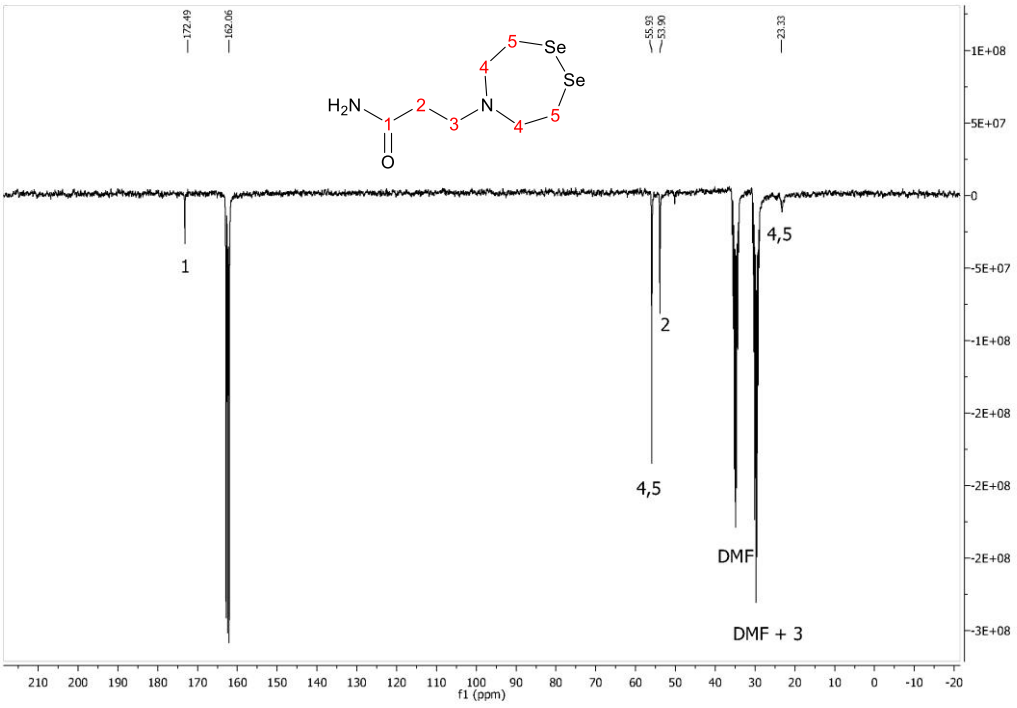


Figure S 23. ^{13}C JMOD NMR (75 MHz) spectrum for compound **5b** (DMF-d7, 291 K). δ 172.49 (C), 55.93 (2 × CH_2), 53.90 (CH_2), 23.33 (2 × CH_2) ppm. One ^{13}C signal is not visible due to the overlapping with the residual signal of the solvent.

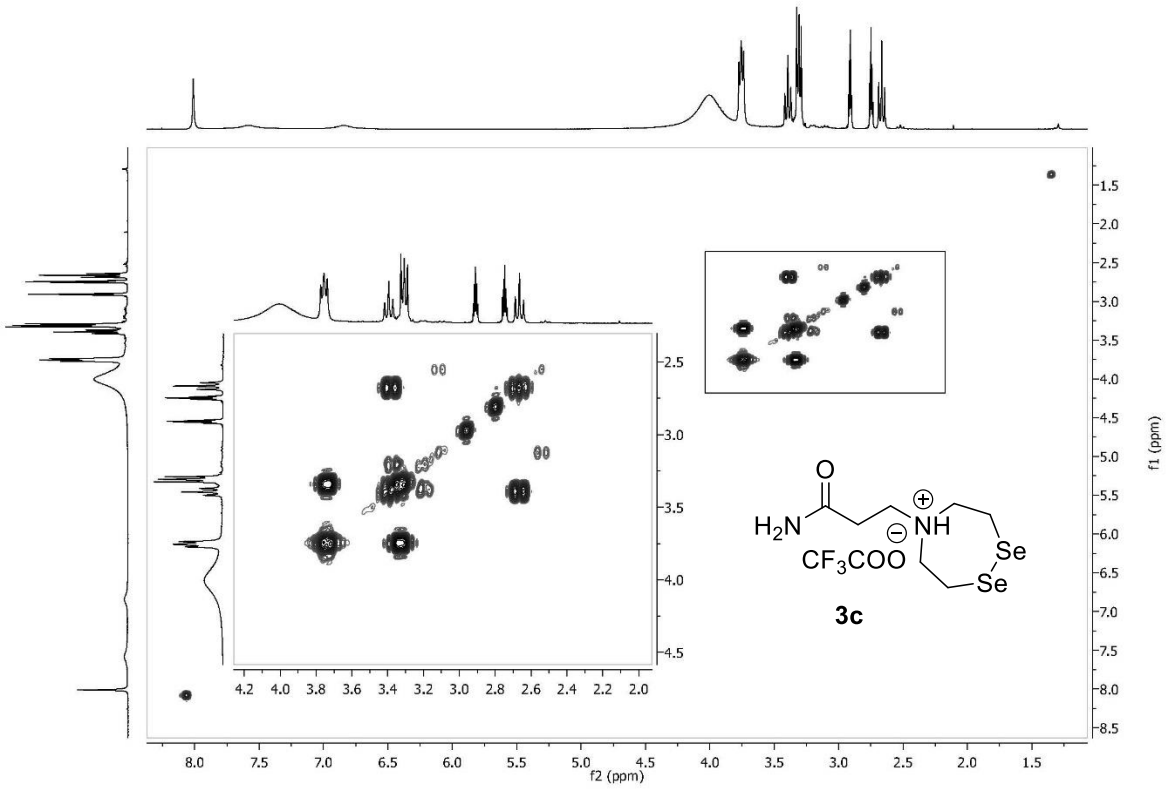


Figure S 24. ^{1}H-^{1}H COSY spectrum for compound **5b** (DMF-d7, 333 K).

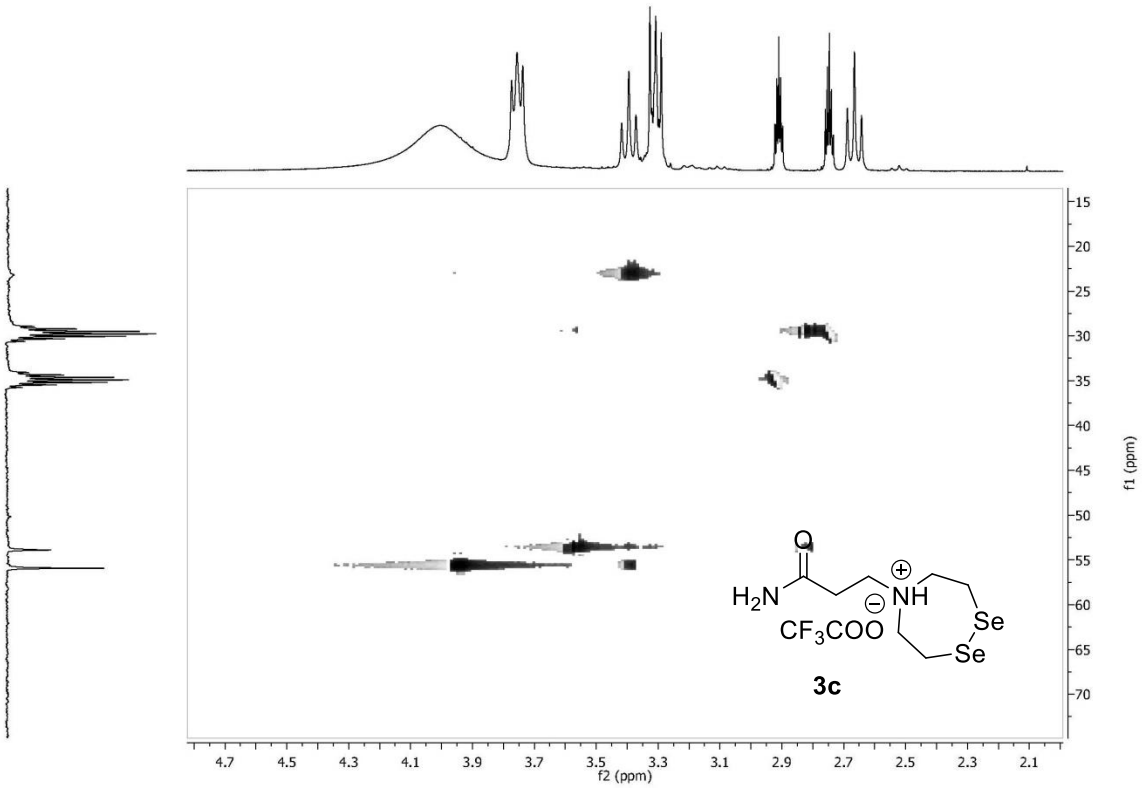
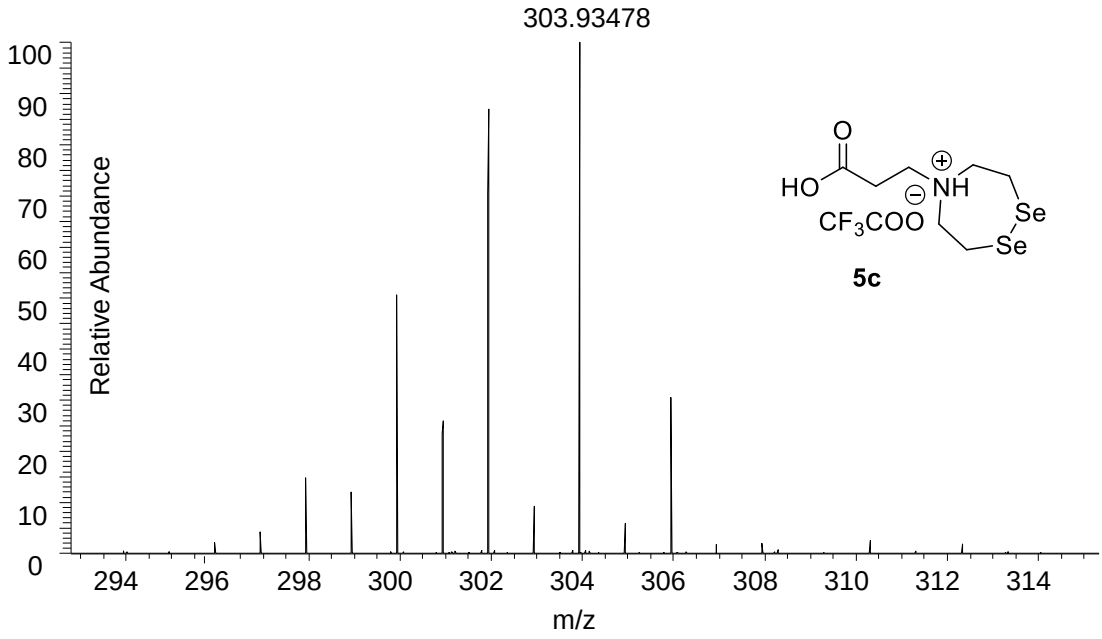


Figure S 25. ^{1}H-^{13}C HSQC spectrum for compound **5b** (DMF-d7, 291K).

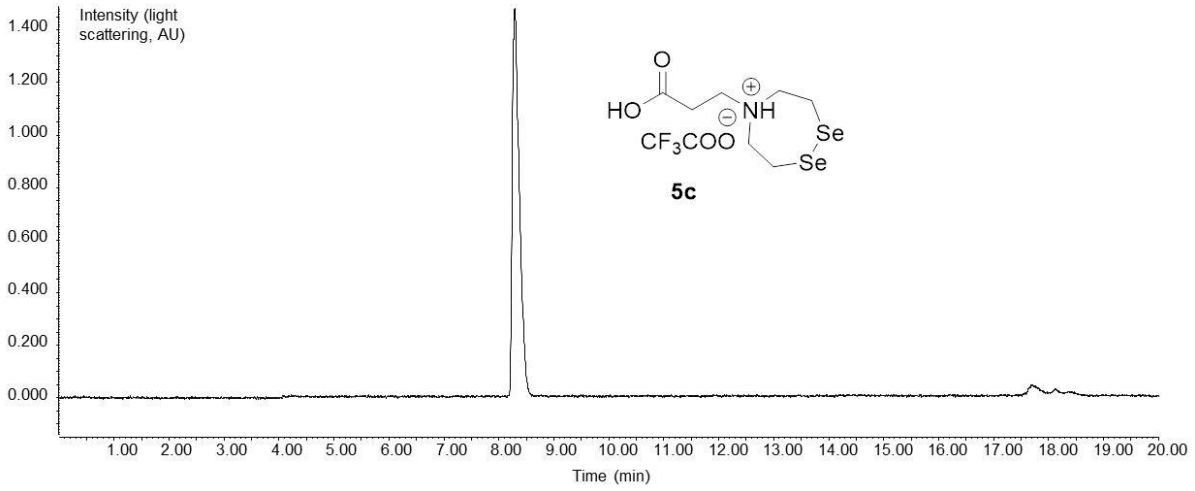
*Characterization of diselenide **5c***



m/z	Intensity	Relative	Theo. Mass	Delta (ppm)	RDB equiv	Composition
299,9375	2139153,3	52,61				
300,9385	1105033	27,18				
301,9358	3534280,3	86,92				
303,9348	**4066237,8**	**100**	**303,9350**	**-0,13**	**1,5**	**C7 H14 O2 N Se2**
305,9348	1315523,8	32,35				

Figure S 26. HRMS analysis for catalyst **5c**. m/z calcd. for $[M+H]^+$ (monoisotopic): 303.9350, found: 303.9348.

A)



B)

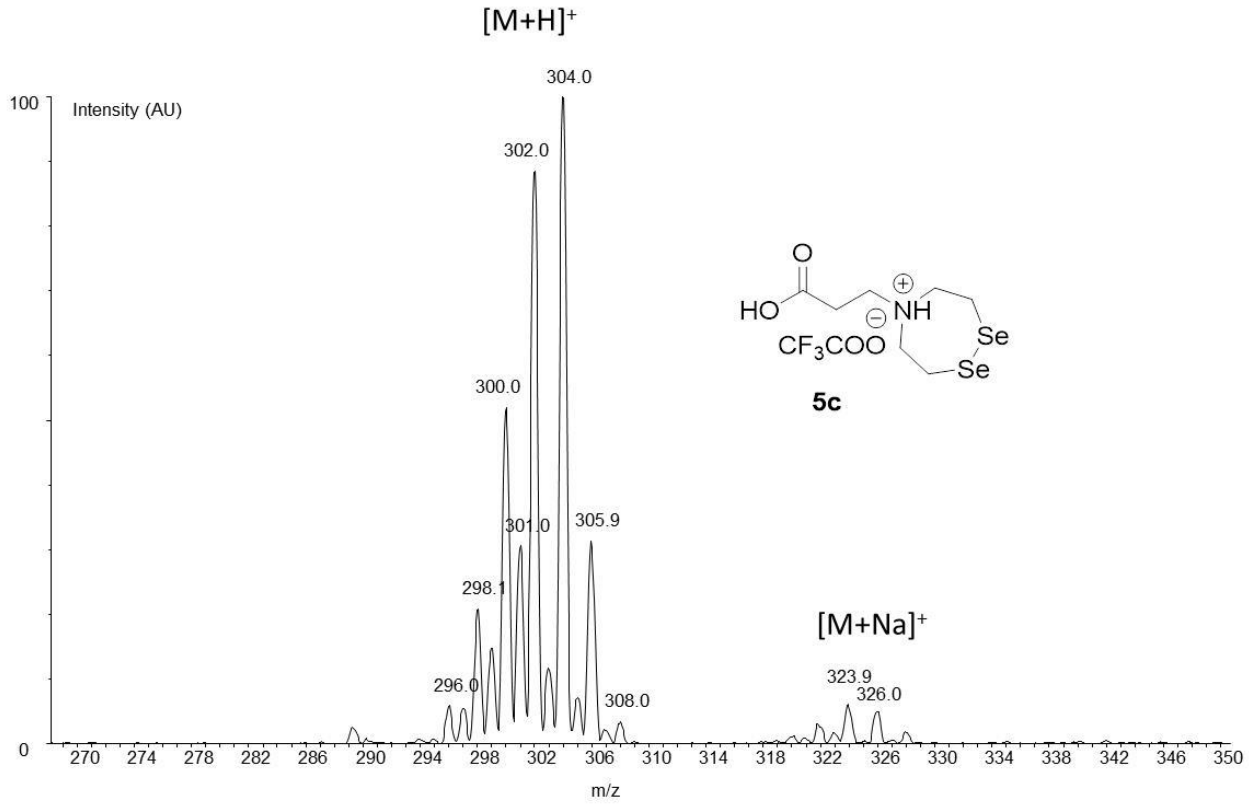


Figure S 27. LC-MS analysis of diselenide **5c** A) LC trace. Chromatography conditions: eluent A 0.1% TFA in water, eluent B 0.1% TFA in CH3CN/water: 4/1 by vol. C18 Xbridge BEH 300 Å 5 μm (4.6 × 250 mm) column, gradient 0-50% B in 15 min, 1 mL/min, detection at 215 nm. B) MS trace. m/z calcd. for $[M+H]^+$: 303.9 (peak of highest intensity, monoisotopic), found: 304.0.

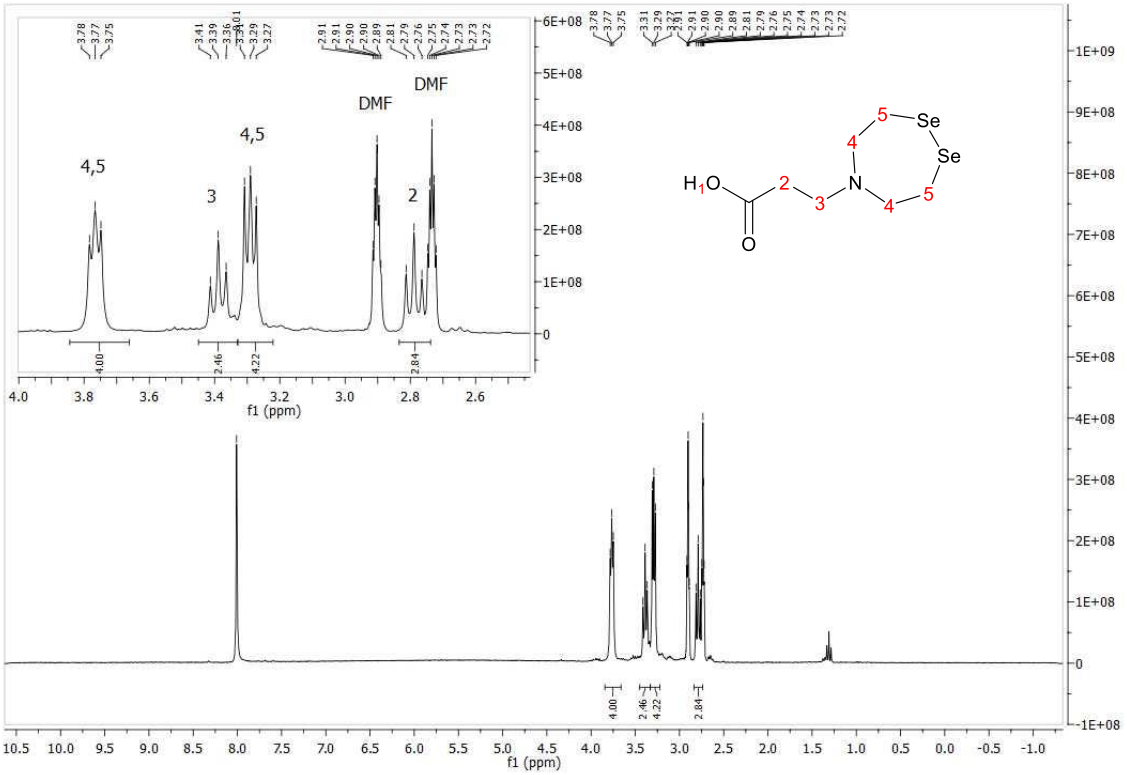


Figure S 28. ^{1}H NMR (300 MHz) spectrum for compound **5c** (DMF-d7, 310 K). δ 3.78-3.75 (t, *J* = 5.3 Hz, 4H), 3.41-3.36 (t, *J* = 7.2 Hz, 2H), 3.31-3.27 (t, *J* = 5.4 Hz, 4H), 2.81-2.76 (t, *J* = 7.2 Hz, 2H) ppm.

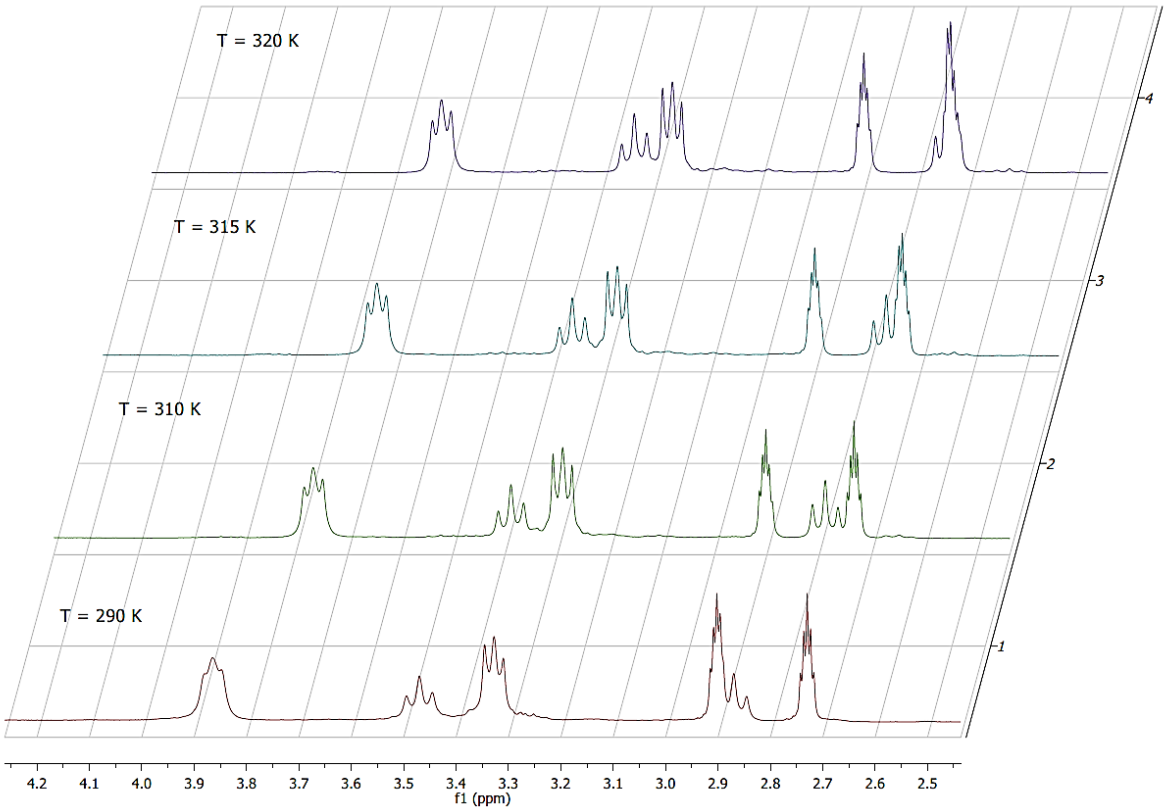


Figure S 29. ^{1}H NMR (300 MHz) spectrum for compound **5c** (DMF-d7). Effect of the temperature.

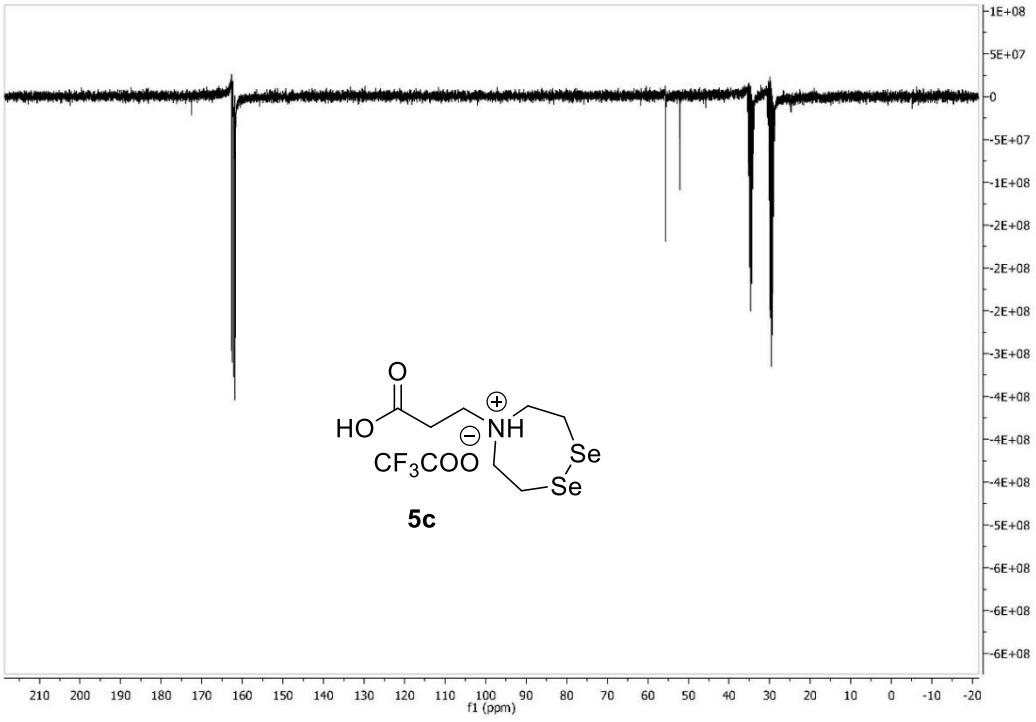


Figure S 30. ^{13}C JMOD NMR (75 MHz) spectrum for compound **5c** (DMF-d7, 310 K). δ 172.50 (C), 55.66 (2 × CH_2), 52.16 (CH_2), 24.61 (2 × CH_2) ppm. One ^{13}C signal is not visible due to the overlapping with the residual signal of the solvent.

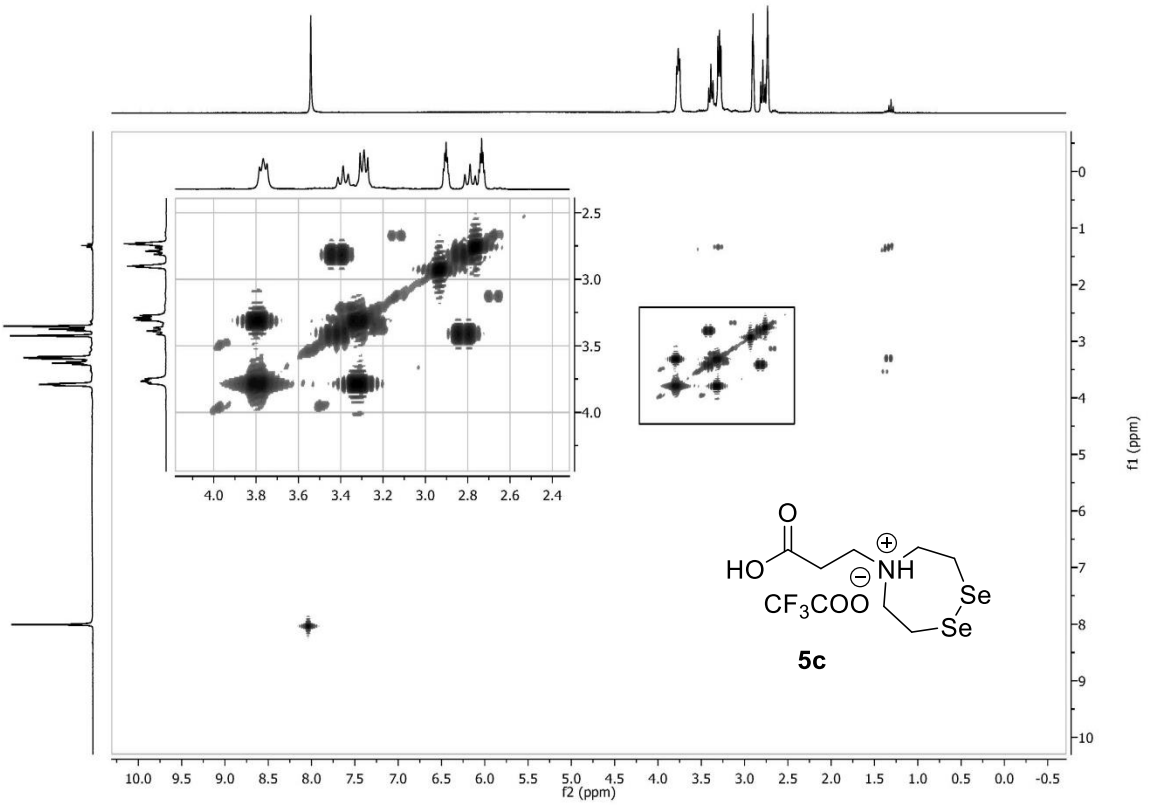


Figure S 31. ^{1}H-^{1}H COSY spectrum for compound **5c** (DMF-d7, 310 K).

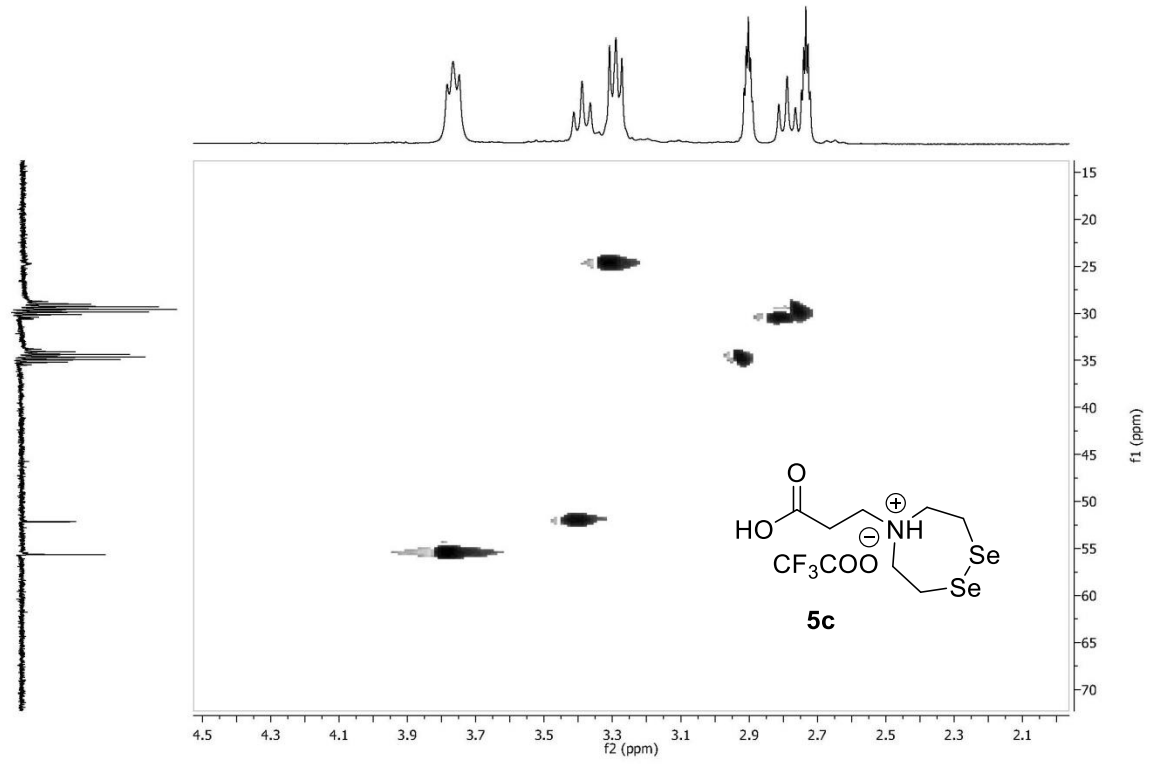


Figure S 32. ^{1}H-^{13}C HSQC spectrum for compound **5c** (DMF-d7, 310K).

*Characterization of compound **6***

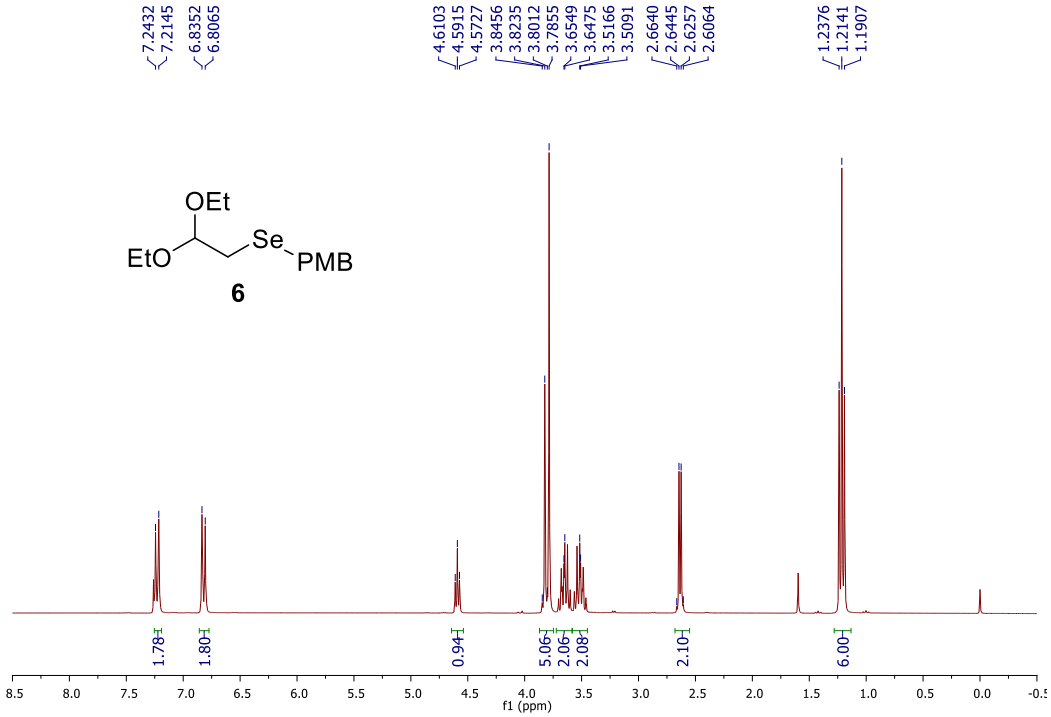


Figure S 33. ^{1}H NMR (300 MHz) spectrum for compound **6** ($CDCl_3$, 293 K). δ 7.23 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 4.59 (t, *J* = 5.6 Hz, 1H), 3.82 (s, 2H), 3.78 (s, 3H), 3.59-3.71 (m, 2H), 3.45-3.57 (m, 2H), 2.63 (d, *J* = 5.6 Hz, 2H), 1.21 (d, *J* = 7.0 Hz, 6H) ppm.

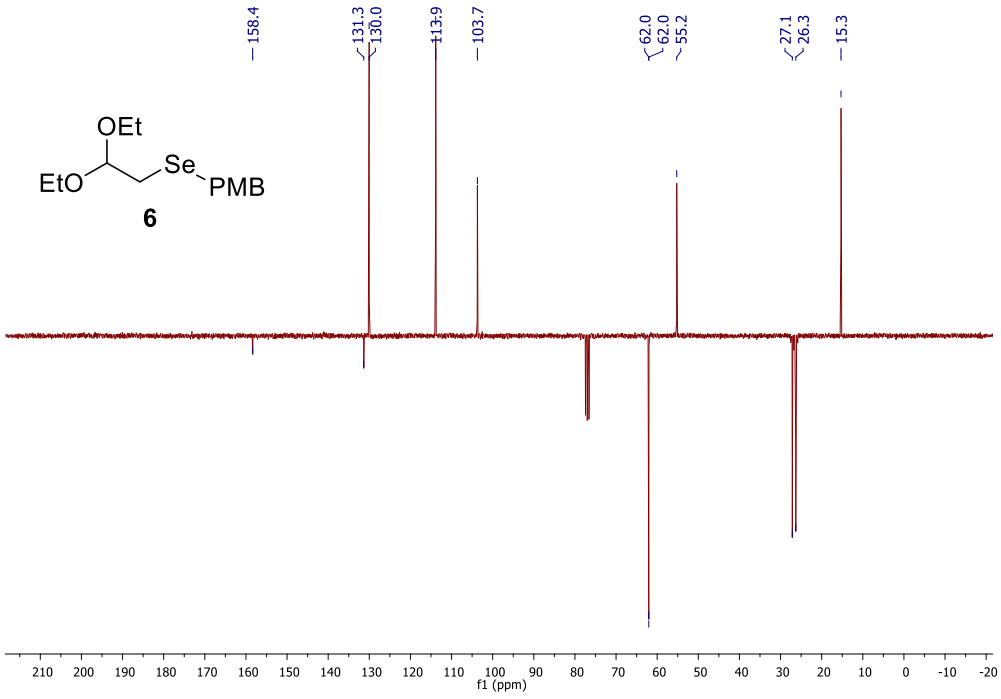


Figure S 34. ^{13}C JMOD NMR (75 MHz) spectrum for compound **6** ($CDCl_3$, 293 K). δ 158.4 (C), 131.3 (C), 130.0 (2 × CH), 113.9 (2 × CH), 103.7 (CH), 62.0 (2 × CH_2), 55.2 (CH_3), 27.1 (CH_2), 26.3 (CH_2), 15.3 (2 × CH_3) ppm.

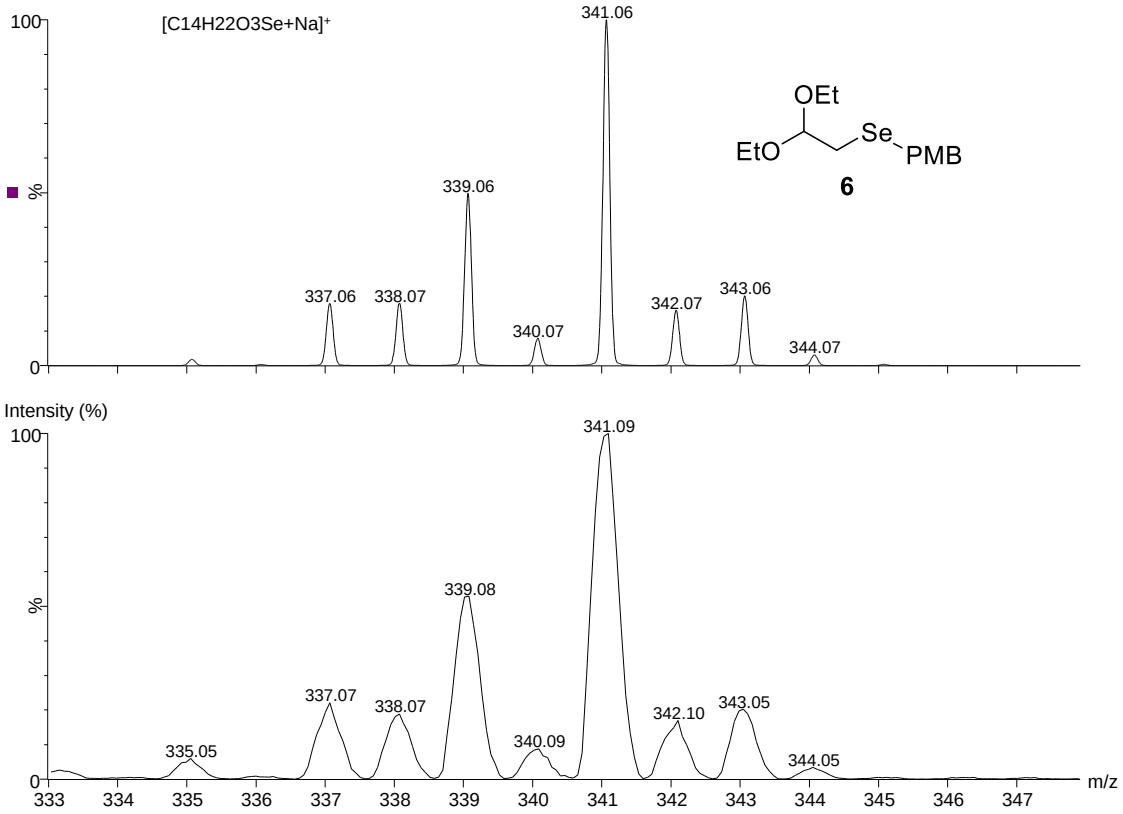


Figure S 35. MS analysis of compound **6** (bottom) and theorical profil (top).

*Characterization of compound **8***

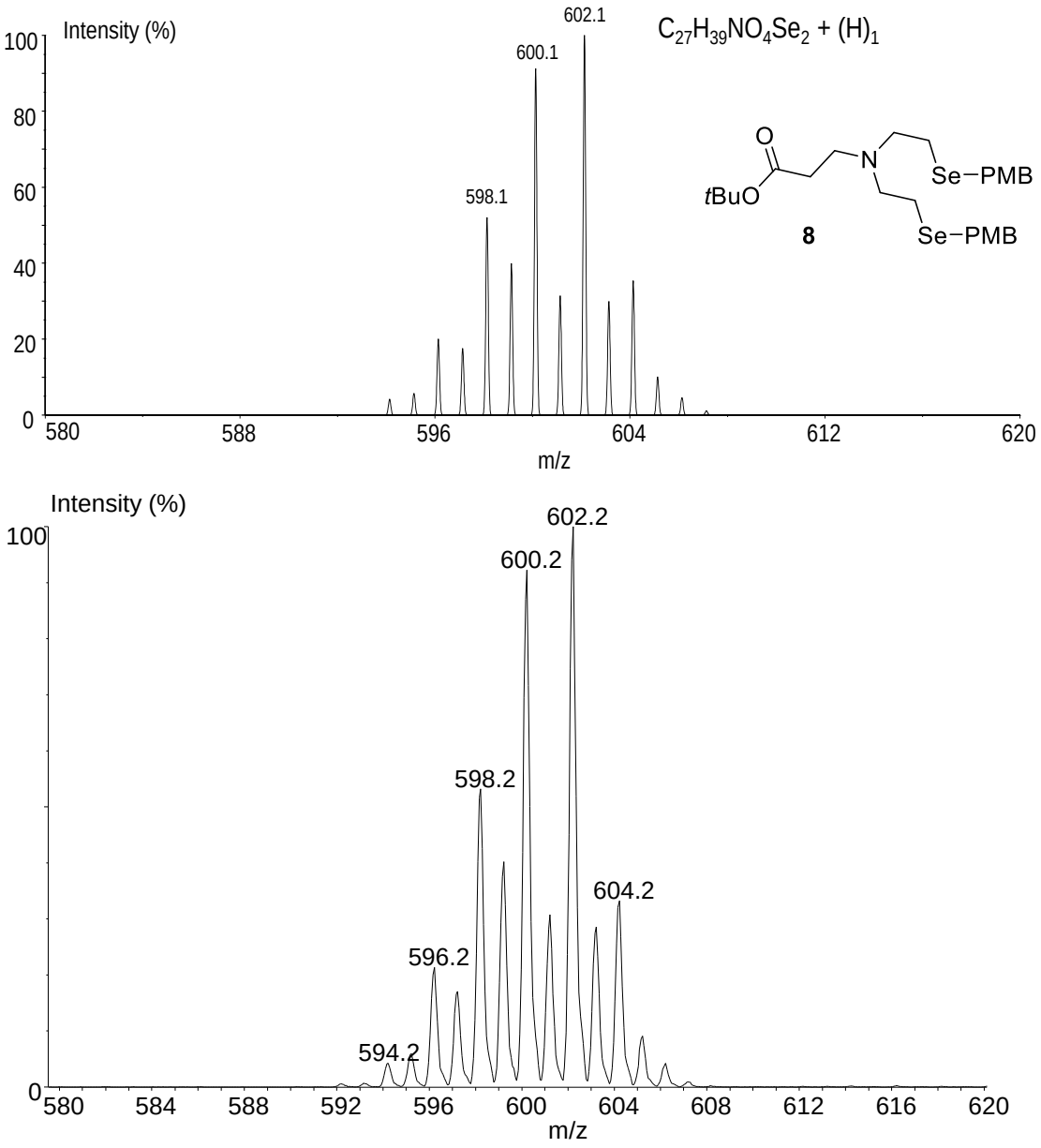


Figure S 36. MS analysis of compound **8** (bottom) and theorical profil (top).

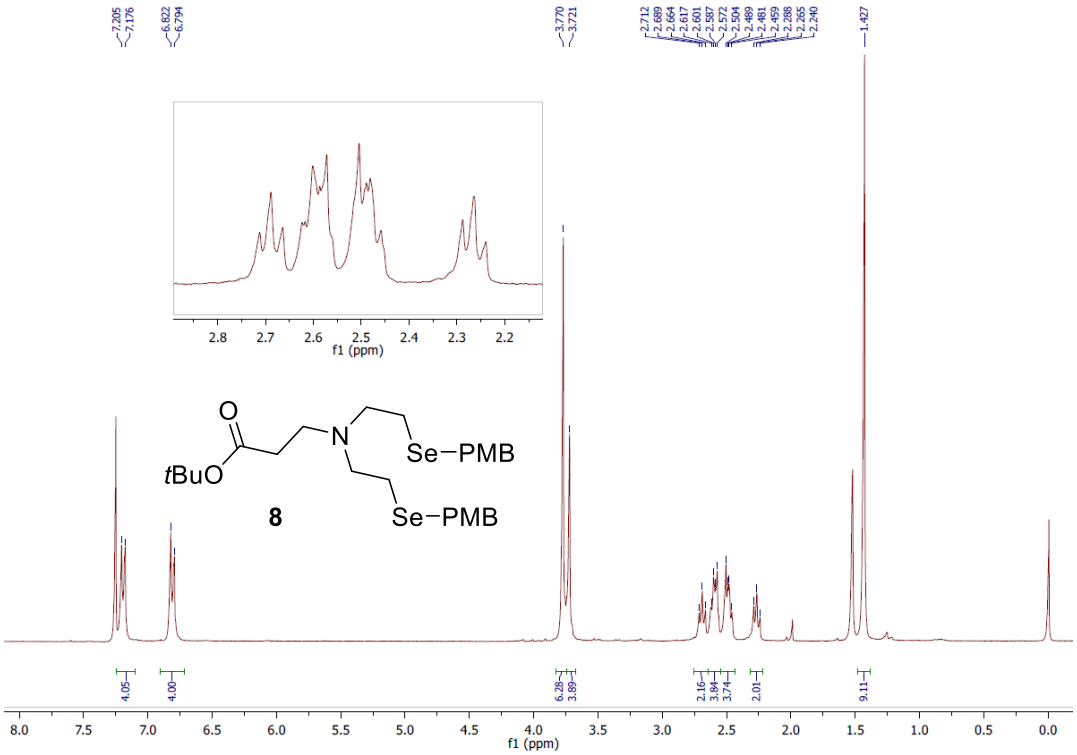


Figure S 37. ^{1}H NMR (300 MHz) spectrum for compound **8** ($CDCl_3$, 305 K). δ 7.20 (d, *J* = 8.7 Hz, 4H), 6.82 (d, *J* = 8.4 Hz, 4H), 3.77 (s, 6H), 3.72 (s, 4H), 2.69 (t, *J* = 6.9 Hz, 2H), 2.60 (m, 4H), 2.48 (m, 4H), 2.26 (t, *J* = 6.9 Hz, 2H), 1.42 (s, 9H) ppm.

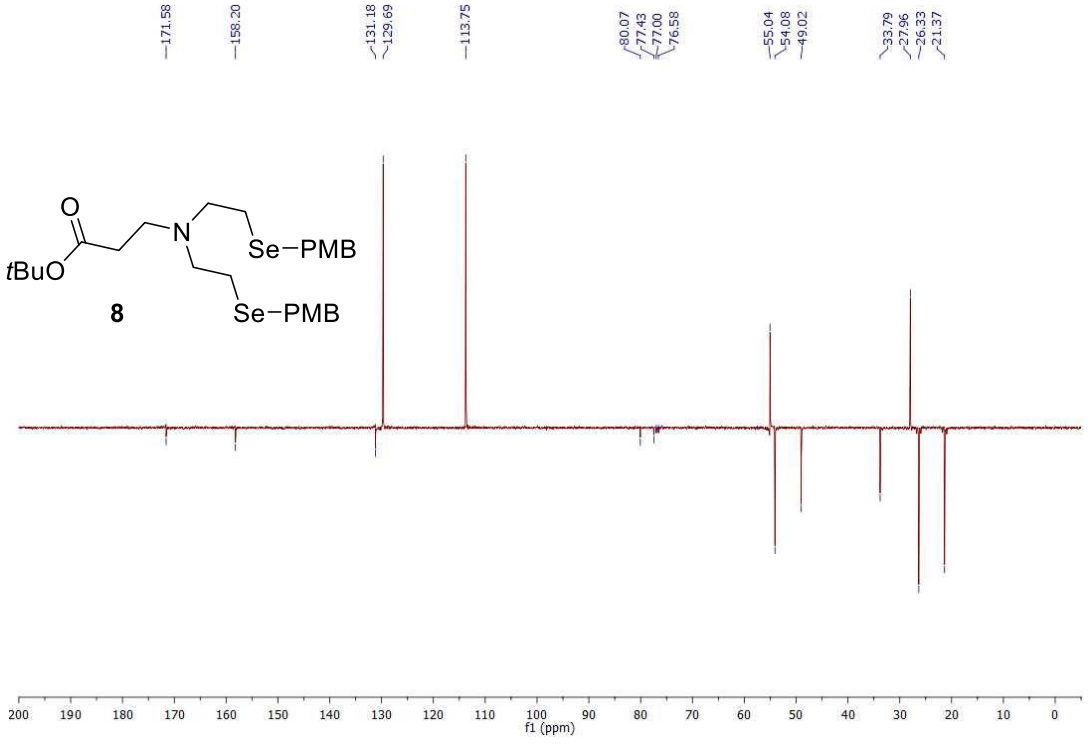


Figure S 38. ^{13}C JMOD NMR (75 MHz) spectrum for compound **8** ($CDCl_3$, 293 K). δ 171.6 (C), 158.2 (2 × C), 131.1 (2 × C), 129.7 (4 × CH), 113.7 (4 × CH), 80.1 (C), 55.0 (2 × CH_3), 54.1 (2 × CH_2), 49.0 (CH_2), 33.8 (CH_2), 28.0 (3 × CH_3), 26.3 (2 × CH_2), 21.4 (2 × CH_2) ppm.

*Characterization of peptide **10***

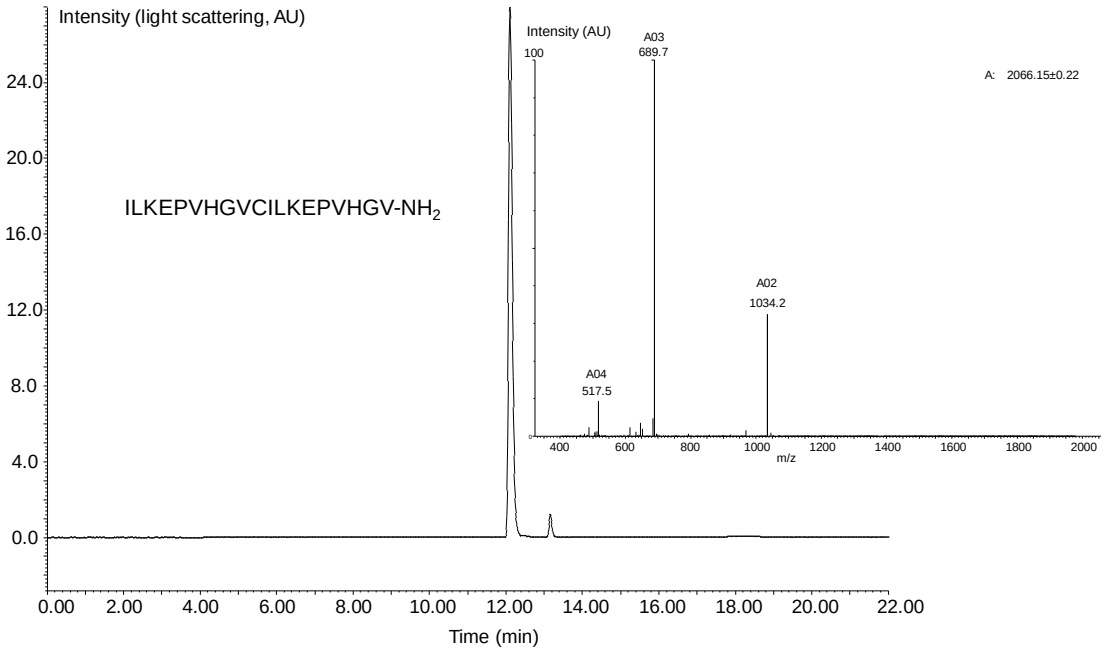


Figure S 39. LC-MS analysis of peptide **10**. LC trace. Chromatography conditions: eluent A 0.10% TFA in water, eluent B 0.10% TFA in CH_3CN/water: 4/1 by vol. C18 Xbridge BEH 300 Å 5 μm (4.6 × 250 mm) column, gradient 0-50% B in 15 min, 1 mL/min, detection at 215 nm. MS trace. m/z = 1034.2 ($[M+2H]^{2+}$), 689.7 ($[M+3H]^{3+}$), 517.5 ($[M+4H]^{4+}$). Calcd. for M (average): 2066.5, found 2066.1.

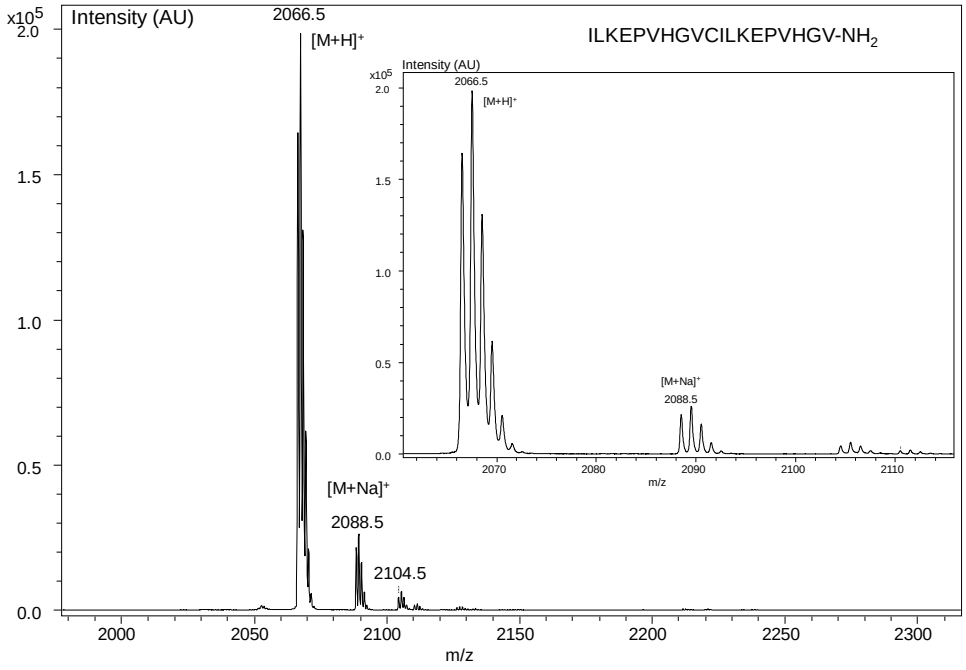


Figure S 40. MALDI-TOF analysis of peptide **10**. Matrix = α-cyano-4-hydroxycinnamic acid, positive detection mode. m/z calcd for $[M+H]^+$ (monoisotopic): 2066.2, found: 2066.5.

*Characterization of peptide **11***

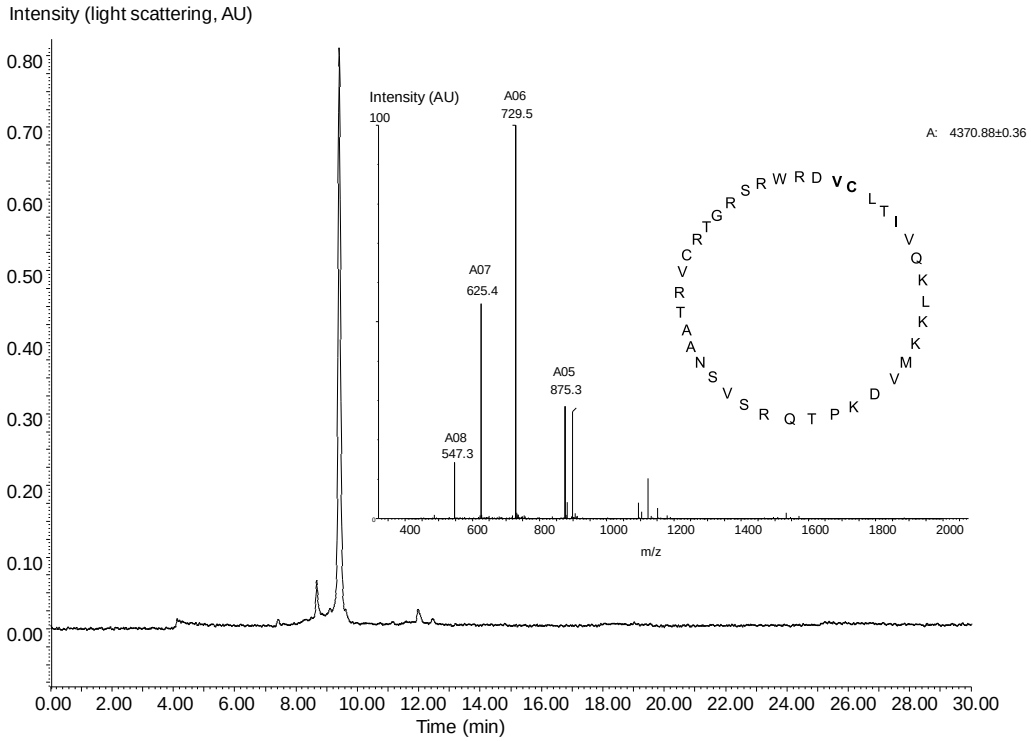


Figure S 41. LC-MS analysis of peptide **11**. LC trace. Chromatography conditions: eluent C 0.10% FA (formic acid) in water, eluent D 0.10% FA in CH_3CN/water: 4/1 by vol. C3 Zorbax 300SB Å 3.5 µm (4.6 × 150 mm) column, gradient 0-100% D in 30 min, 60 °C, 1 mL/min, detection at 215 nm. MS trace. m/z = 875.3 ($[M+5H]^{5+}$), 729.5 ($[M+6H]^{6+}$), 625.4 ($[M+7H]^{7+}$), 547.3 ($[M+8H]^{8+}$). Calcd. for M (average): 4371.2, found 4370.9.

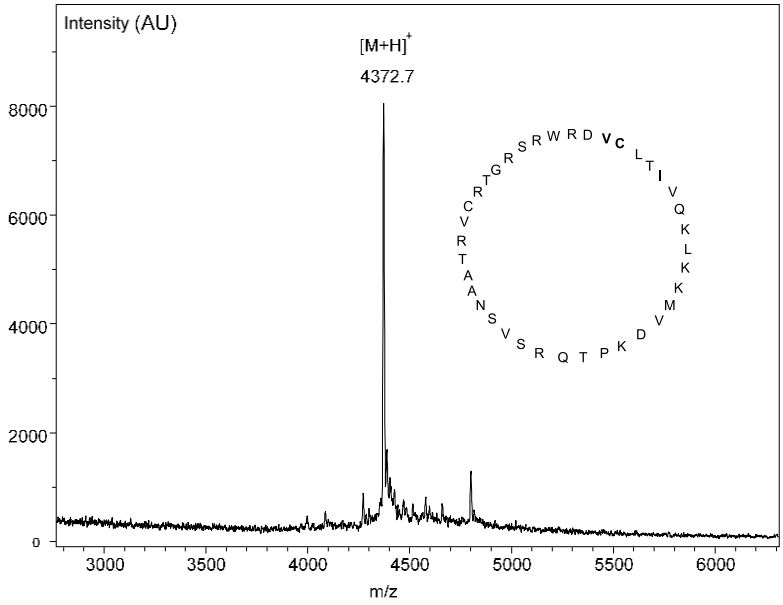


Figure S 42. MALDI-TOF analysis of peptide **11**. Matrix = sinapinic acid, positive detection mode, m/z calcd for $[M+H]^+$ (average): 4372.2, found: 4372.7.

Proteomic analysis of peptide 11

Reduction-alkylation

Peptide **11** (10 µg) was diluted with dithiothreitol (1 mg/mL in 0.025 M ammonium bicarbonate, 10 µL) and treated with iodoacetamide (10 mg/mL in 0.025 M ammonium bicarbonate, 10 µL) for 10 min. The alkylation step was monitored by MALDI-TOF mass spectrometry as shown below.

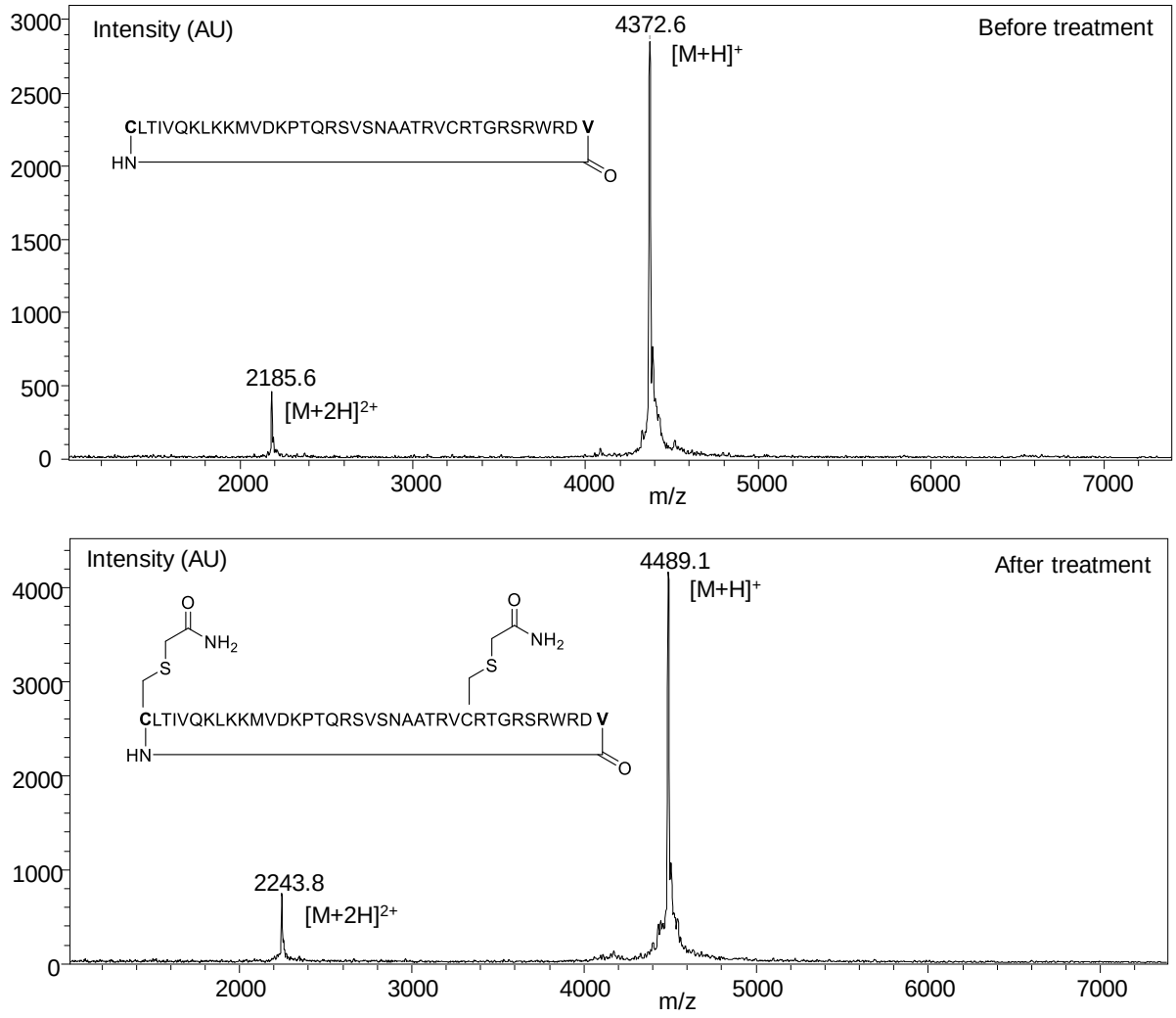
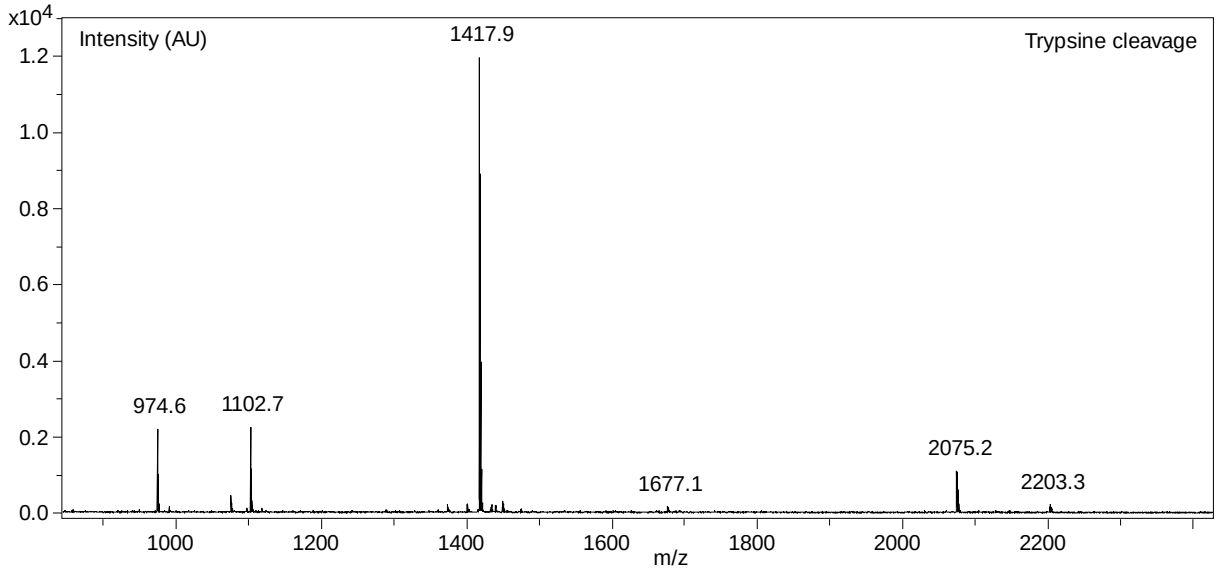


Figure S 43. Monitoring of the alkylation of cyclic peptide **11** by MALDI-TOF mass spectrometry (matrix: α-cyano-4-hydroxycinnamic acid).

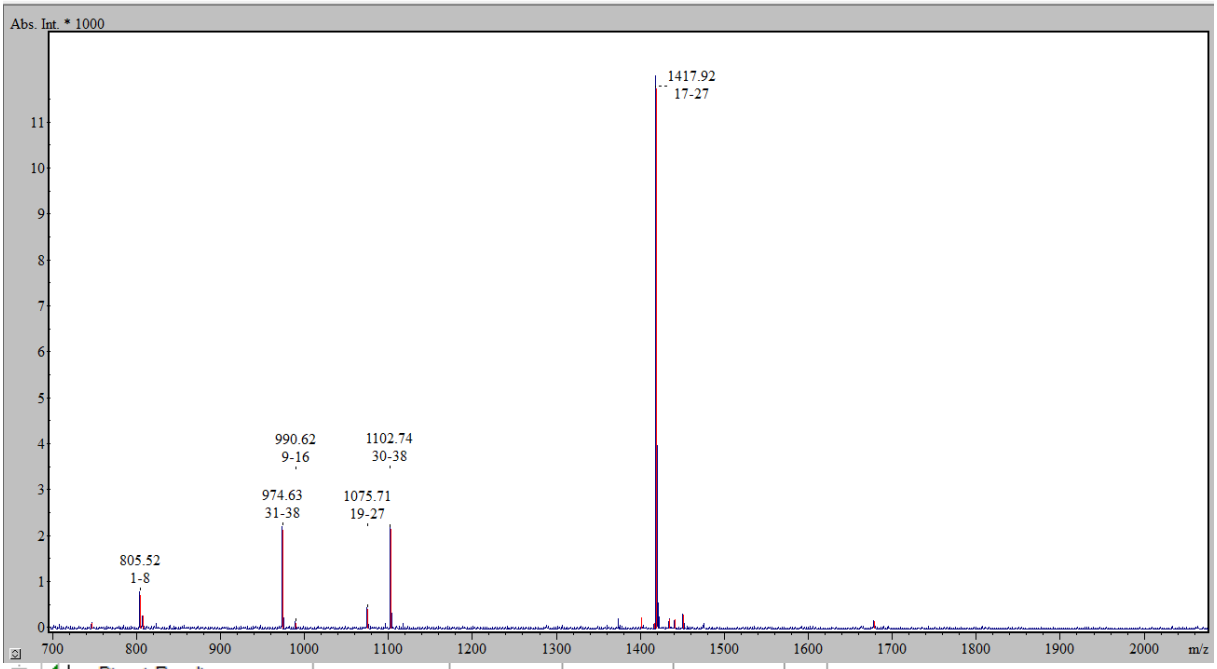
Trypsin cleavage

Then, trypsin (0.1 mg/mL, 1 µL) was added to the mixture to cleave the alkylated cyclic peptide. The formed peptide fragments were identified by MALDI-TOF MS-MS.

A)



B)



Digest Results						
Modifications: Global: ...						
Search Parameter: Tit...						
peak 2	805.52	805.42	741.83	1 - 8	0	SVSNAATR
peak 4	974.63	974.51	2147.42	31 - 38	0	MVDKPTQR
peak 5	990.62	991.52	139.60	9 - 16	2	VCRTGRSR 2: Carbamidomethyl (C)
peak 6	1075.71	1075.58	436.33	19 - 27	0	DVCLTIVQK 3: Carbamidomethyl (C)
peak 7	1102.74	1102.60	2165.79	30 - 38	1	KMVDKPTQR
peak 10	1417.92	1417.76	11693.75	17 - 27	1	WRDVCLTIVQK 5: Carbamidomethyl (C)

C)

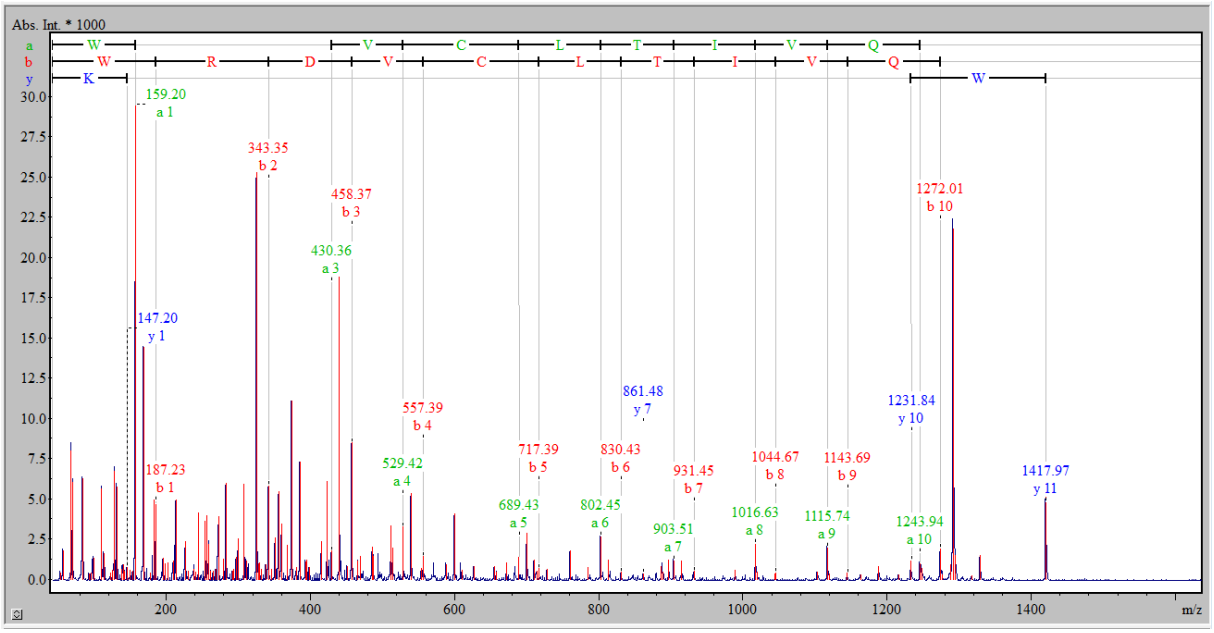
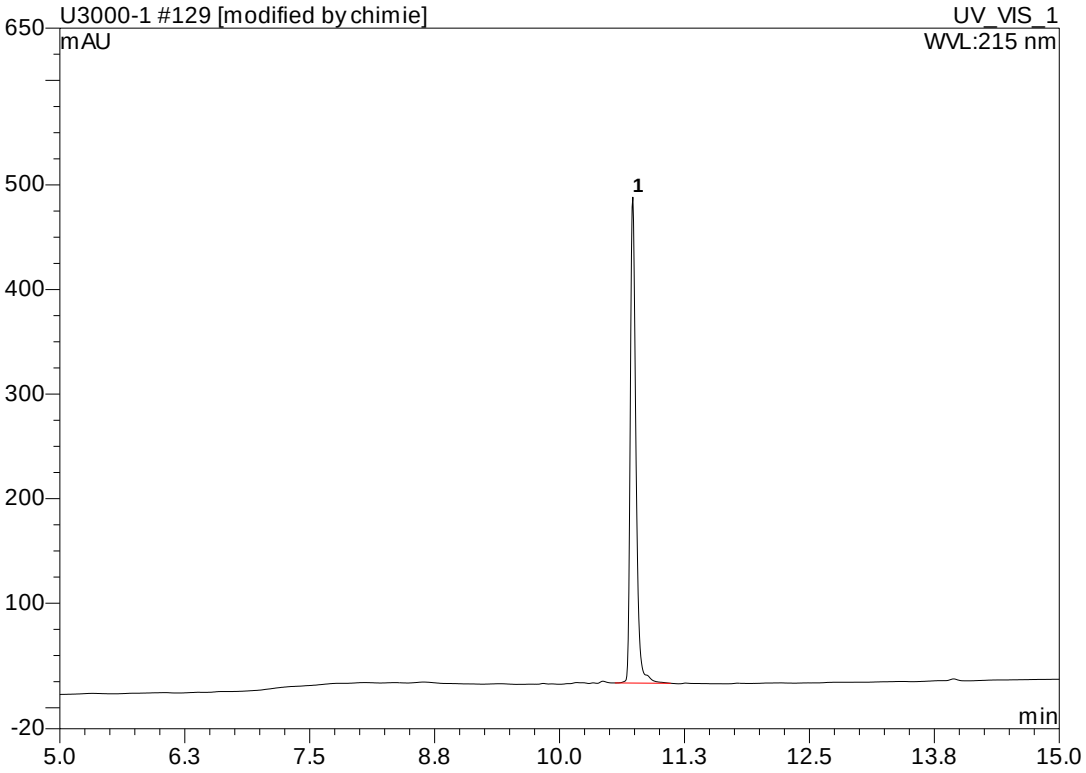


Figure S 44. In source MALDI-TOF sequencing of peptide **11** after alkylation and trypsin cleavage using α-cyano-4-hydroxycinnamic acid as matrix (positive reflector mode). A) Global spectrum. B) MS-MS sequencing of the peptides. C) MS-MS sequencing of the ion at m/z 1417.97 shows the presence of the Val-Cys peptide bond (…RD**VC**LT…).

*Characterization of peptide **12***

A)



B)

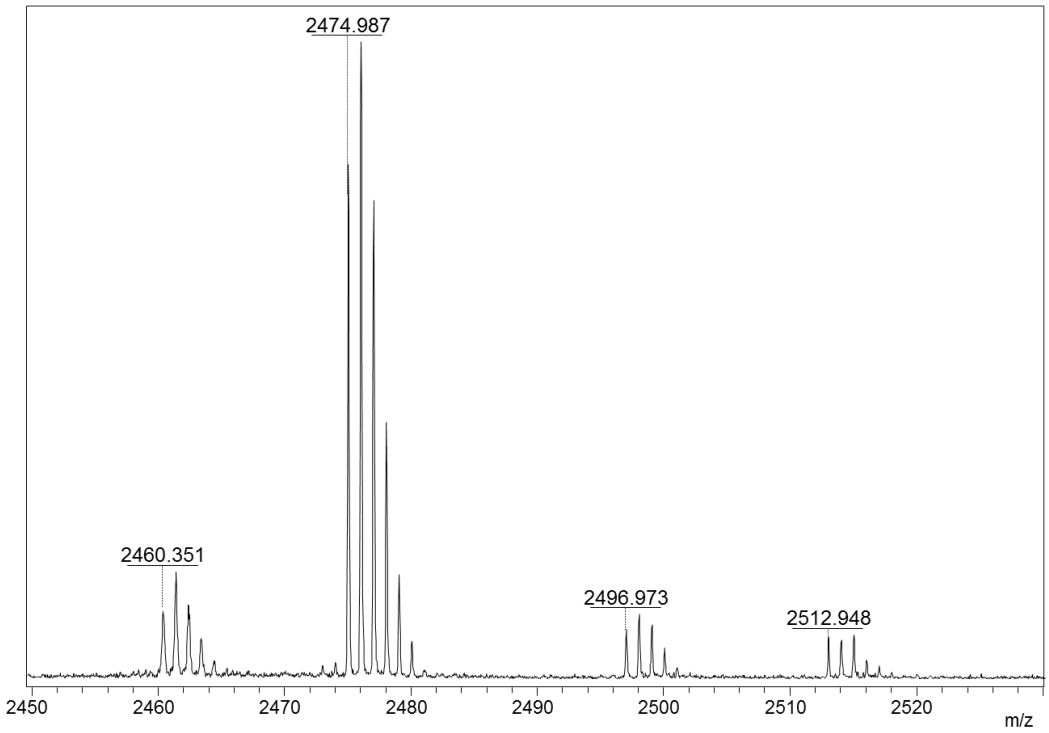
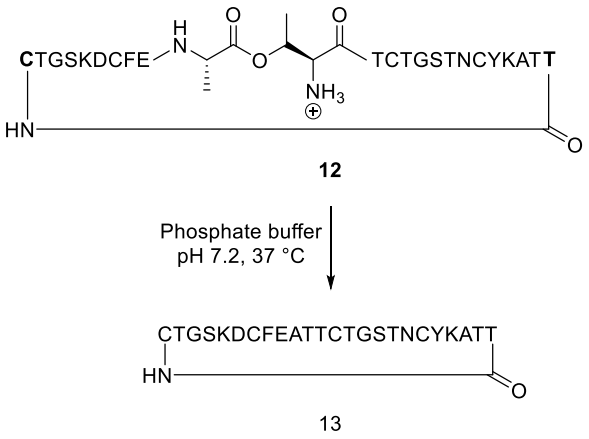


Figure S 45. Peptide **12**. A) HPLC trace, eluent A 0.10% TFA in water, eluent B 0.10% TFA in CH_3CN/water: 4/1 by vol. C18 Zorbax 300 Å 3.5 μm (4.6 × 150 mm) column, gradient 0-100% B in 30 min, 50 °C, 1 mL/min, detection at 215 nm. B)

Rearrangement of the O-acyl isopeptide unit

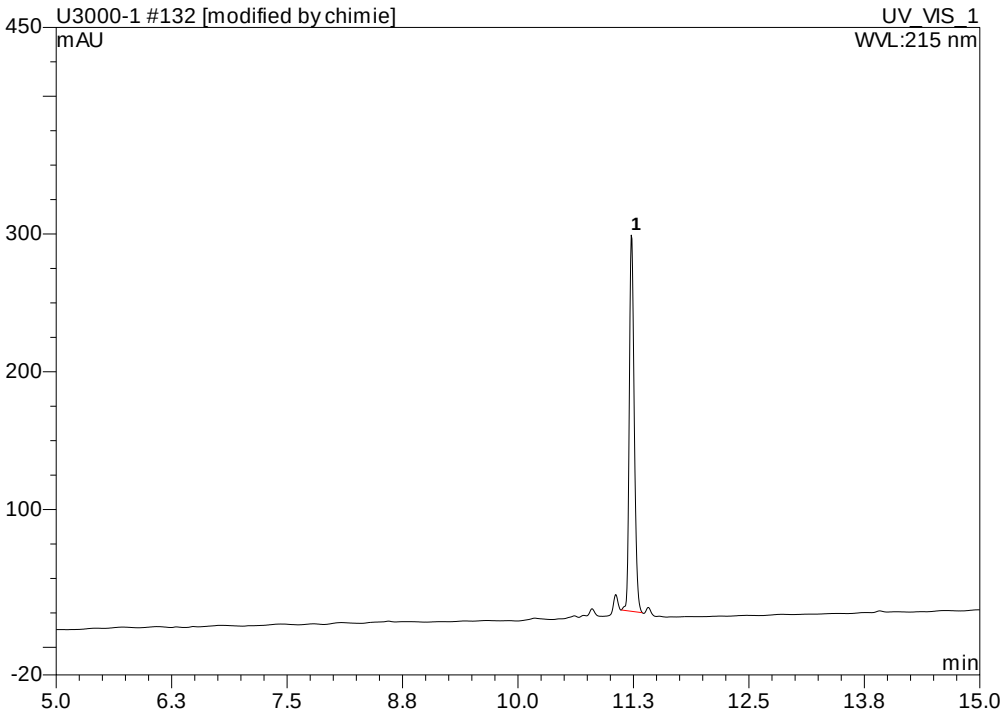


Scheme S 1. Rearrangement of peptide **12** into cyclic peptide **13**.

Peptide **12** (0.324 mg, 119 µmol, 1 mM) was dissolved in a 10 mM solution of TCEP in phosphate buffer at pH 7.2 (120 µL). The reaction mixture was immediately analyzed by HPLC to show the rearrangement of the *O*-acyl isopeptide unit (cyclic peptide **13**).

Peptide **13:** ESI-MS m/z 1238.7 ($[M+2H]^{2+}$), 826.0 ($[M+3H]^{3+}$), calcd. for M 2475.7 (average), found 2475.2. MALDI-TOF matrix sinapinic acid, positive detection mode, $[M+H]^{+}$ calcd (monoisotopic) 2474.99, observed mass: 2475.04 (monoisotopic).

A)



B)

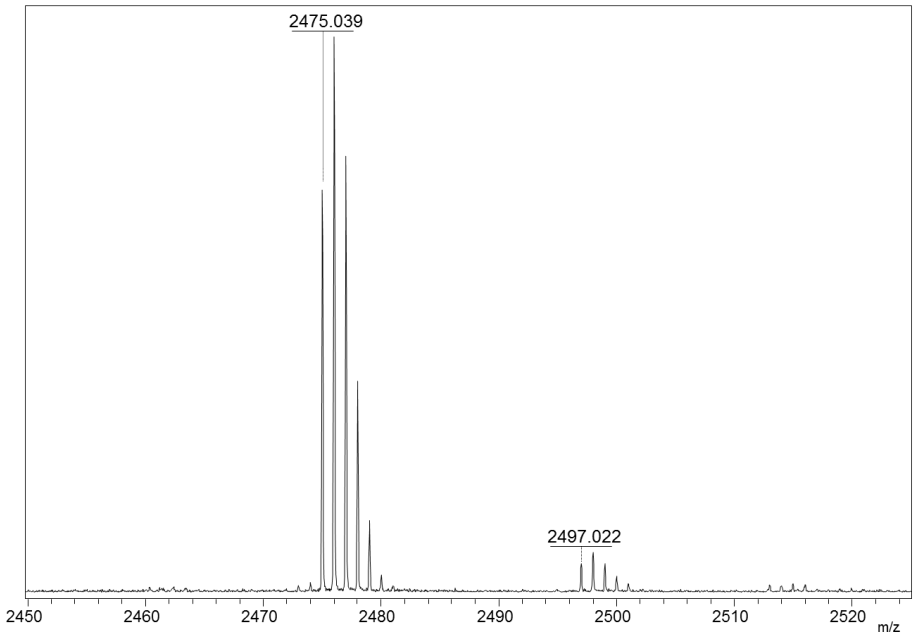


Figure S 46. Rearranged peptide **13**. A) HPLC trace, eluent A 0.10% TFA in water, eluent B 0.10% TFA in CH_3CN/water: 4/1 by vol. C18 Zorbax 300 Å 3.5 μm (4.6 × 150 mm) column, gradient 0-100% B in 30 min, 50 °C, 1 mL/min, detection at 215 nm. B) MALDI-TOF of peptide **13**. Matrix sinapinic acid, positive detection mode.

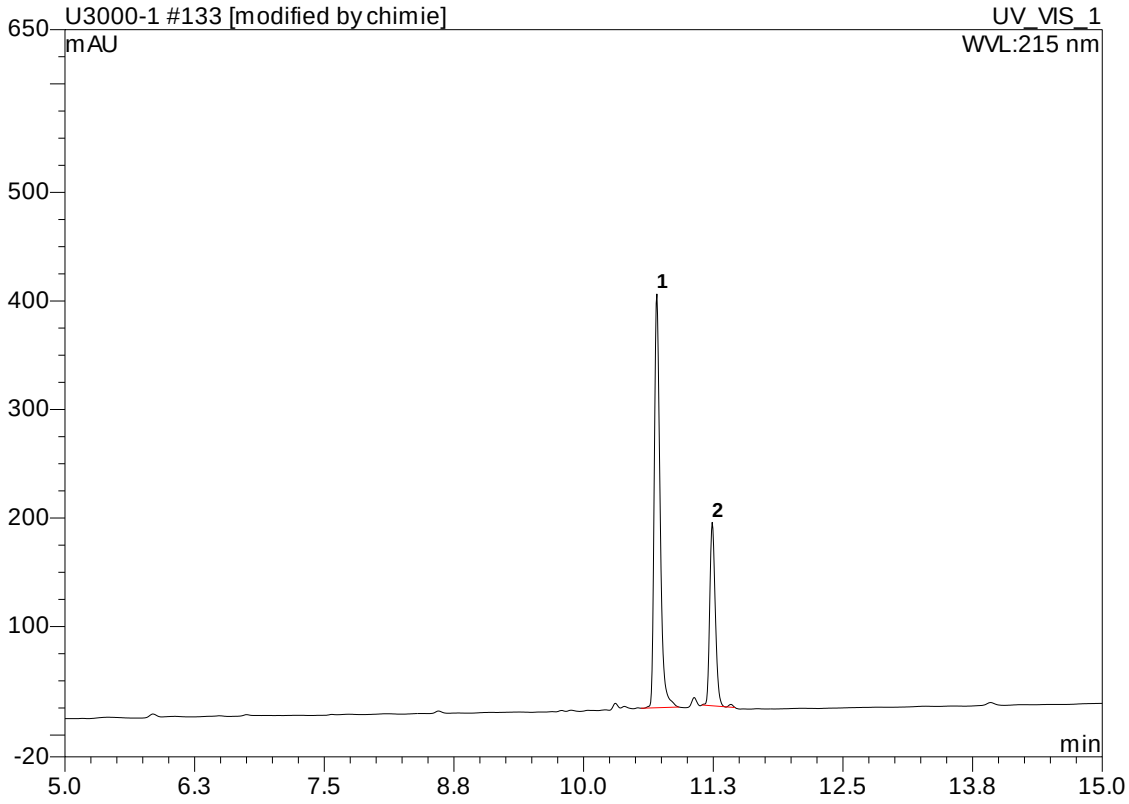


Figure S 47. Coelution control of *O*-acyl isopeptide containing peptide **12** (peak 1) with rearranged peptide **13** (peak 2). HPLC trace, eluent A 0.10% TFA in water, eluent B 0.10% TFA in CH_3CN/water: 4/1 by vol. C18 Zorbax 300 Å 3.5 µm (4.6 × 150 mm) column, gradient 0-100% B in 30 min, 50 °C, 1 mL/min, detection at 215 nm.

*Proteomic analysis of rearranged peptide **13***

Reduction – Alkylation - Trypsin cleavage

Peptide **13** (~10 µg) was diluted with dithiothreitol (1 mg/mL in 0.025 M ammonium bicarbonate, 10 µL) and treated with iodoacetamide (10 mg/mL in 0.025 M ammonium bicarbonate, 10 µL) for 10 min. The alkylation step was monitored by MALDI-TOF mass spectrometry (Figure S 48B).

Then, trypsin (0.1 mg/mL, 1 µL) was added to the mixture to cleave the alkylated cyclic peptide (Figure S 48C,D). The formed peptide fragments were identified by MALDI-TOF MS-MS.

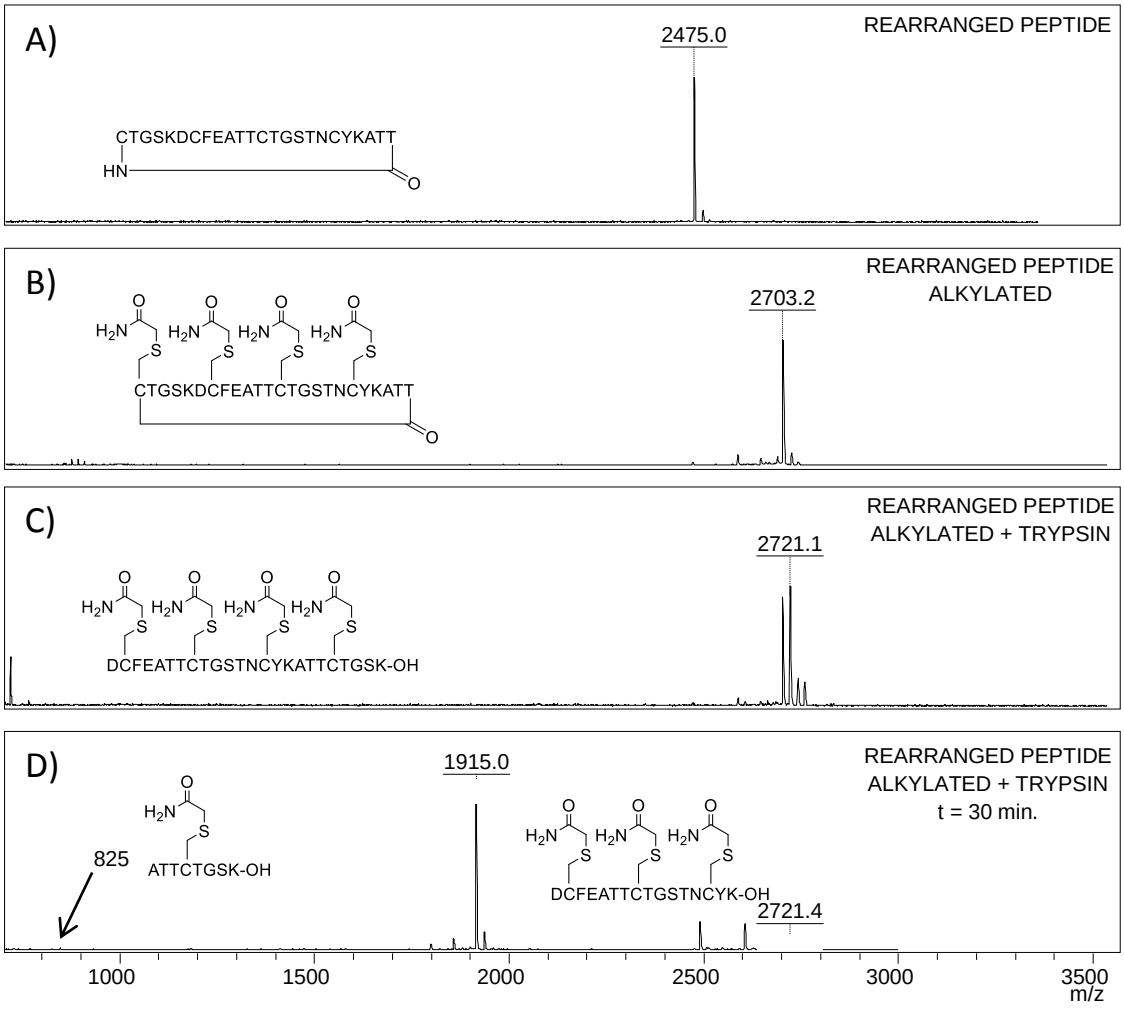


Figure S 48. A) & B). Monitoring of the alkylation of cyclic peptide **13** by MALDI-TOF mass spectrometry (matrix: alpha-cyano-4-hydroxycinnaminic acid). C) & D) MALDI-TOF Monitoring of trypsic digestion of alkylated peptide **13**.

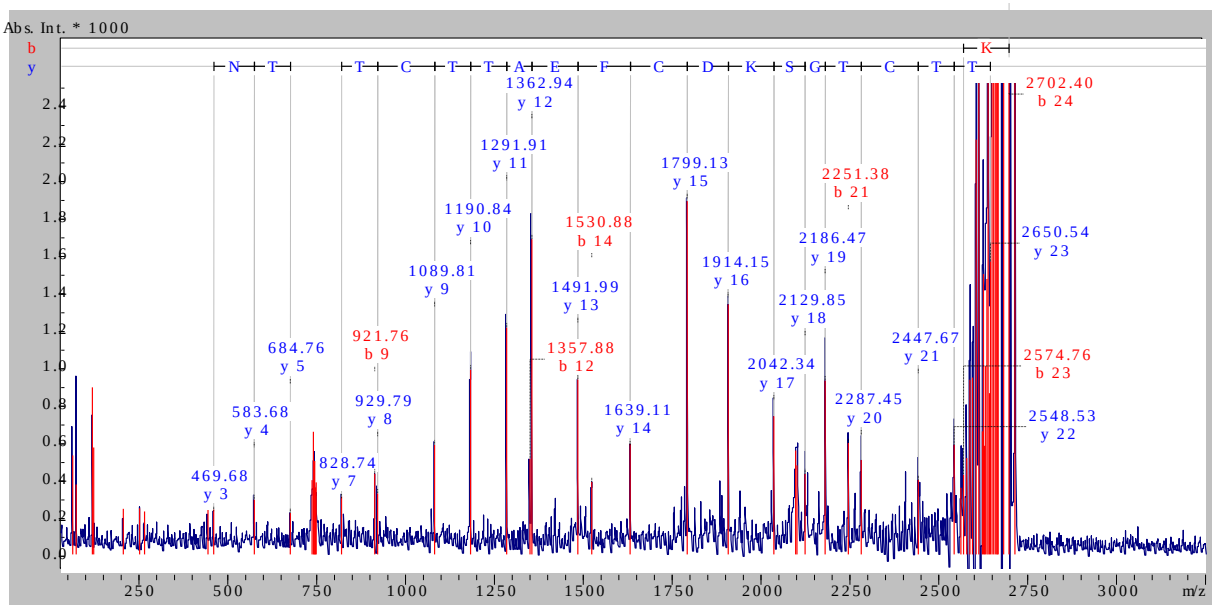


Figure S 49. In source MALDI-TOF sequencing of peptide **13** after alkylation and trypsin cleavage using alpha-cyano-4-hydroxycinnaminic acid as matrix (positive reflector mode). MS-MS sequencing of the ion at m/z 1915.0 shows the presence of the Thr-Cys peptide bond (…SG**TC**TT…).

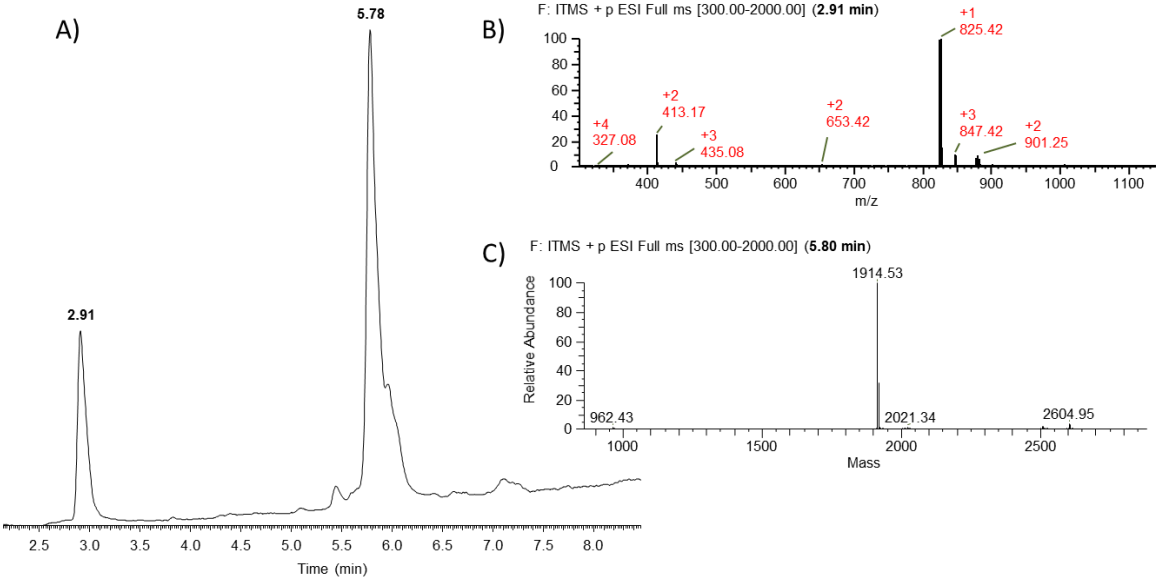


Figure S 50. UPLC-MS analysis of the trypsin digest of alkylated peptide **13**. A) LC trace, eluent A 0.1% TFA in water, eluent B 0.1% TFA in CH_3CN/water: 4/1 by vol. C18 BEH (3.0 × 100 mm) column, gradient 0-100% B in 15 min, 50 °C, 0.7 mL/min, detection at 215 nm ; B) MS trace of peptide fragment at 2.91 min. $[M+H]^+$ m/z calcd. (average) 825.92, found

825.42; C) MS trace of peptide fragment at 5.80 min. $[M+H]^+$ m/z calcd. (average) 1915.05, found 1914.53.

*Study of the deselenization of catalyst **5c** during the SEA-thiol exchange reaction at pH 4.0*

We quantified the deselenization of catalyst **5c** during the SEA-thiol exchange reaction at pH 4.0 by monitoring the appearance of selenophosphine $Se=P(CH_2CH_2CO_2H)_3$ in the reaction mixture by HPLC, see manuscript for experimental details.

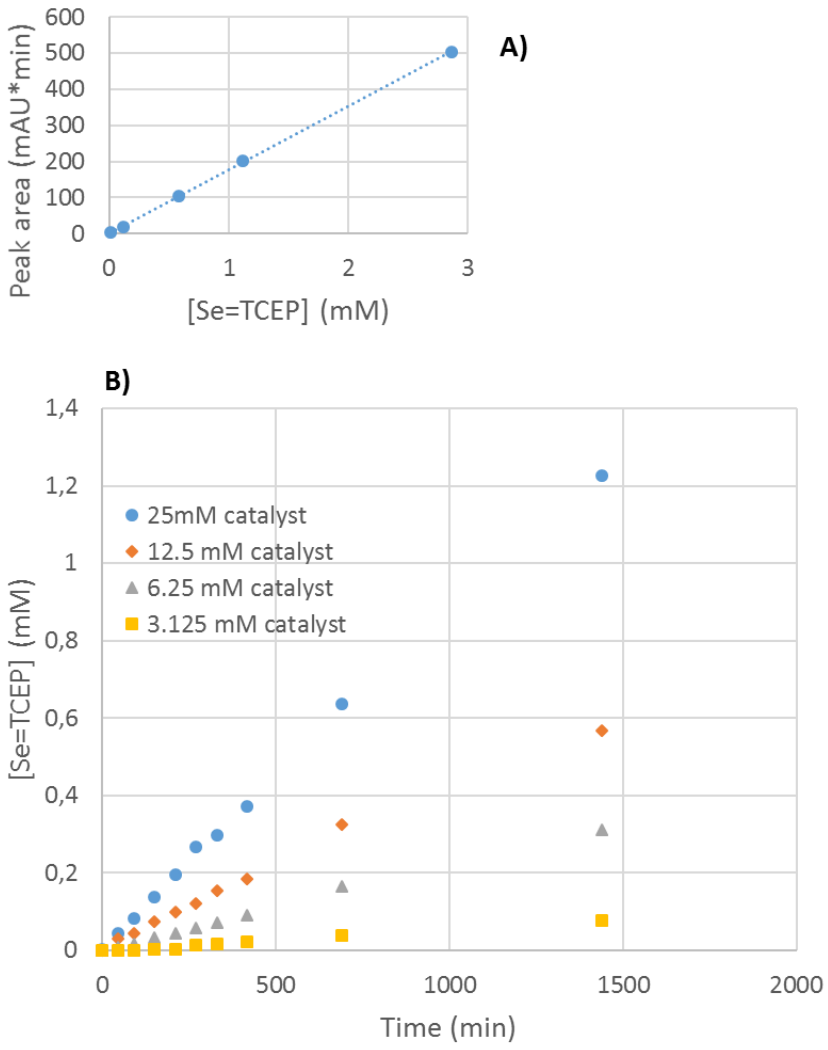


Figure S 51. A) Standard calibration curve of [TCEP=Se]; B) Evolution of selenophosphine concentration [TCEP=Se] at different catalyst concentration.