Supplementary Information (SI) for Organic Chemistry Frontiers.

Electrochemical diversification of cysteine derivatives and cysteine-containing peptides to phosphorothioates and sulfinates

Supporting Information

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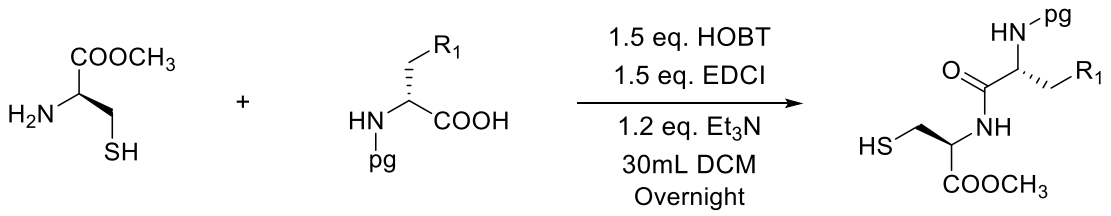
1. General Information

All glassware was oven dried at 110℃ for hours and cooled down under vacuum. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. The instrument for electrolysis was dual display potentiostat (DJS-292B) (made in China). The anodic electrode was platinum plate (15 mm×15 mm×0.3 mm) and cathodic electrode was platinum plate (15 mm×15 mm×0.3 mm). Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel. Gradient flash chromatography was conducted eluting with a continuous gradient from dichloromethane to the methanol. High resolution mass spectra (HRMS) for polypeptides were measured with an ABI 5800 instrument and accurate masses were reported for the molecular ion + Hydrogen (M+H) or molecular ion + Sodium (M+Na) or molecular ion + Potassium (M+Ka). The ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer. For ^{1}H NMR, chemical shifts (δ) were given in ppm relatives to internal standard (TMS at 0 ppm, DMSO-d_6 at 2.50 ppm, MeOH-d_4 at 3.31 ppm). For ^{13}C-NMR, chemical shifts (δ) were reported in ppm using solvent as internal standard (DMSO-d_6 at 39.50 ppm). HPLC analyses were performed on an Agilent 1260 Infinity LC system using a 100 mm Agilent Zorbax 300SB-C18 5 μm analytical column. All of the MALDI-TOF-MS and MALDI-TOF-MS/MS spectra were acquired using Orbitrap Exploris 480 and QE HF-X mass spectrometer (Thermo Fisher).

2. Synthesis of Starting Materials

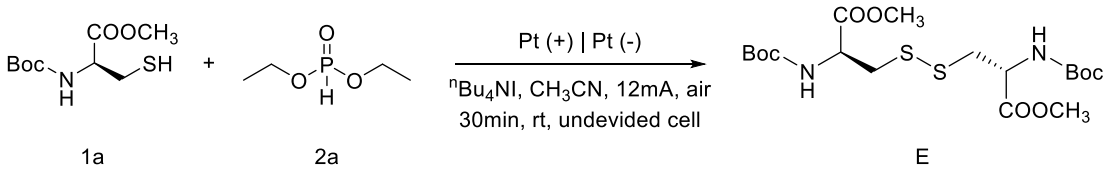
2.1 Synthesis of starting materials dipeptides 3aa-3aj[1]



peptideA peptideB Dipeptides 3aa-3aj

In a round bottomed flask, equipped with a stir bar, peptide **A** (5.0 mmol), peptide **B** (5.0 mmol), HOBT (1-hydroxybenzotriazole) (7.5 mmol), EDCI (1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride) (7.5 mmol), dichloromethane (30 mL) and triethylamine (6 mmol) were combined and added. The reaction was stirred overnight. After regular workup, the reaction mixture washed by saturated $NaHCO_3$ solution (40 mL x 3), 2M hydrochloric acid solution (40 mL x 3) and H_2O (40 mL x 3). The organic layers were combined, dried over Na_2SO_4, and concentrated. The resulting crude product was purified by flash chromatography (DCM/ MeOH) to afford corresponding dipeptides **3aa-3aj**.

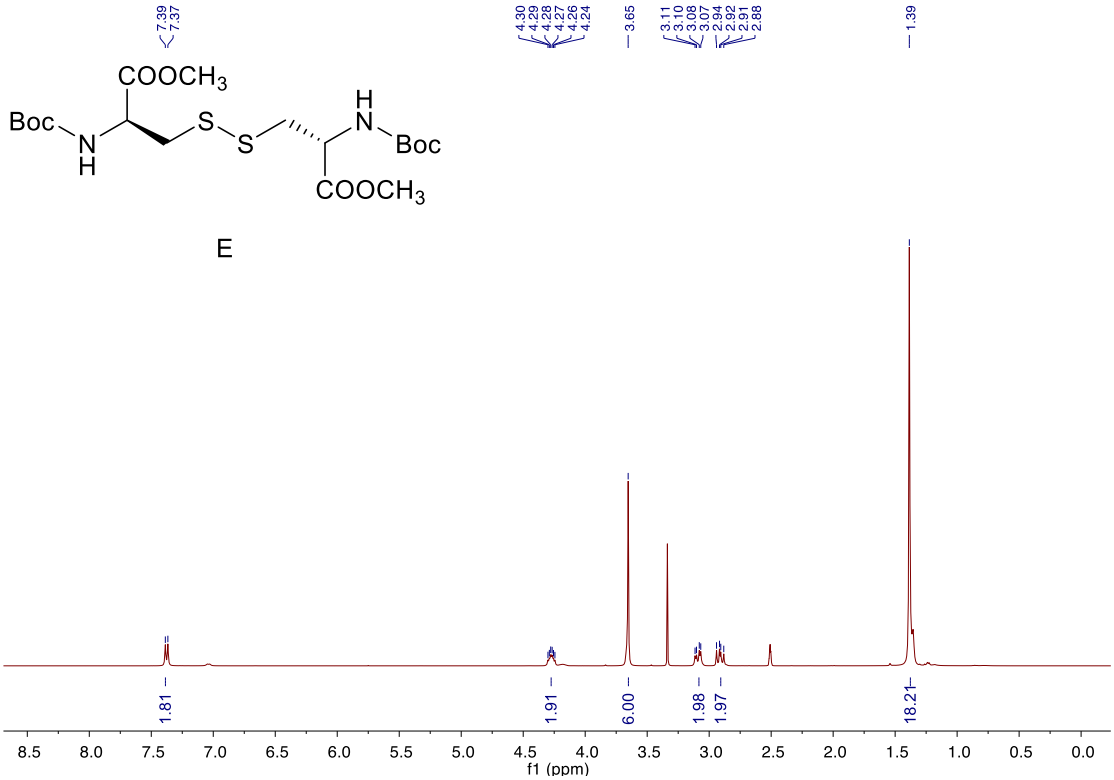
2.2 Synthesis of starting materials E

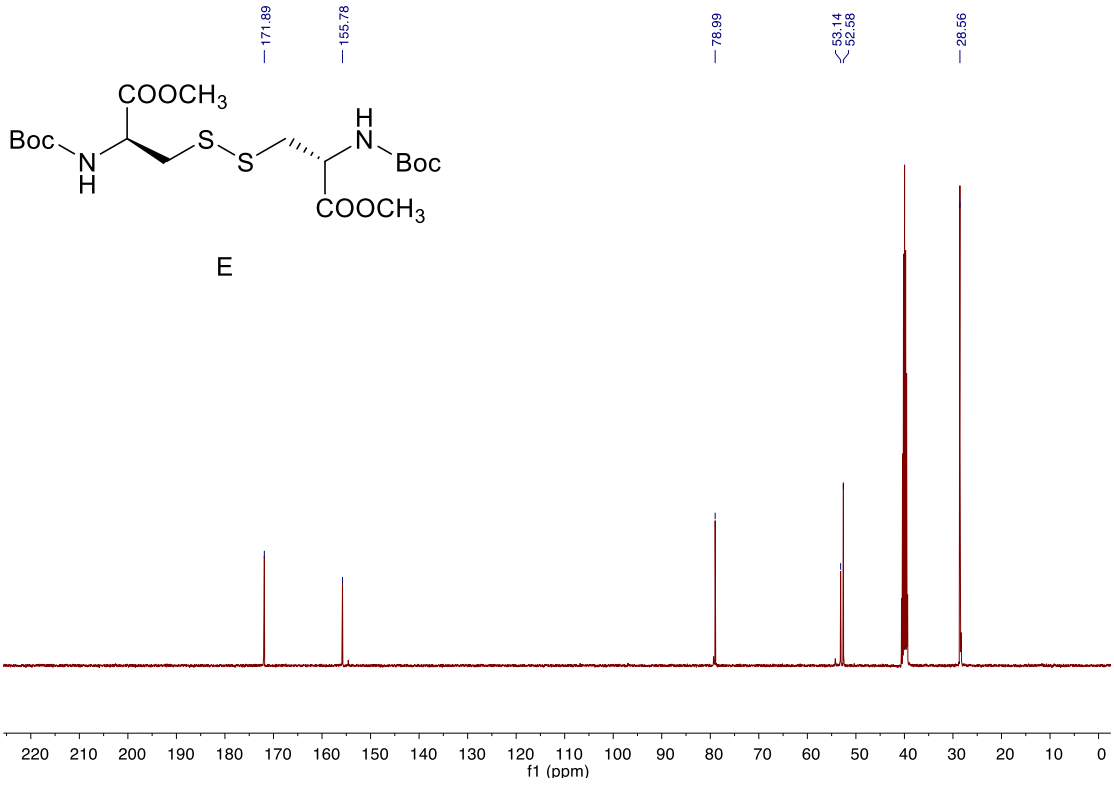


1a 2a E

In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, methyl (tert-butoxycarbonyl)-D-cysteinate (0.2 mmol), diethyl phosphonate (0.4 mmol), and $^nBu_4NI$ (0.2 mmol), Then, CH_3CN (8 mL) were added. The bottle was equipped with platinum plate (15 mm×15 mm×0.3 mm as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at constant current of 12 mA under 25℃ for 30 min. After completion of the reaction, as indicated by TLC, the pure product E was obtained by flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate= 4:1).

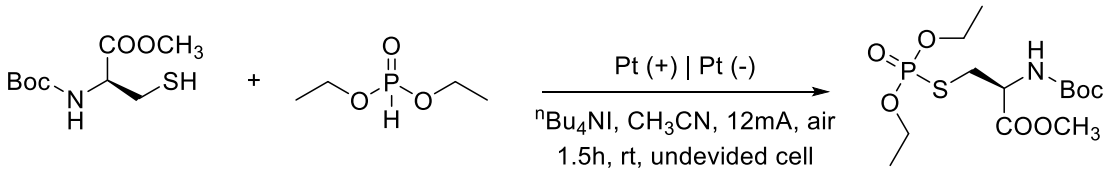
^{1}H NMR (400 MHz, DMSO-d6) δ 7.38 (d, *J* = 8.2 Hz, 2H), 4.27 (td, *J* = 8.9, 4.5 Hz, 2H), 3.65 (s, 6H), 3.09 (dd, *J* = 13.7, 4.7 Hz, 2H), 2.91 (dd, *J* = 13.7, 9.7 Hz, 2H), 1.39 (s, 18H). ^{13}C NMR (101 MHz, DMSO-d6) δ 171.89, 155.78, 78.99, 53.14, 52.58, 28.56.





3. General Procedure

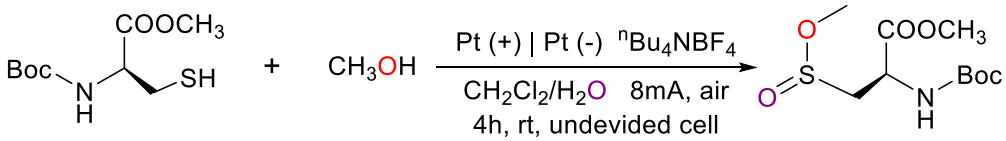
3.1.1 General Procedure for Phosphorothioates Synthesis



1a 2a 3a

General procedure for Gram-Scale Experiments: In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, methyl (tert-butoxycarbonyl)-D-cysteinate (0.2 mmol), diethyl phosphonate (0.4 mmol), and $^{n}Bu_4NI$ (0.2 mmol), Then, CH_3CN (8 mL) were added. The bottle was equipped with platinum plate (15 mm×15 mm×0.3 mm as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at constant current of 12 mA under 25℃ for 1.5 hours. After completion of the reaction, as indicated by TLC, the pure product (yield: 87%, 64.6 mg) was obtained by flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate= 2:1).

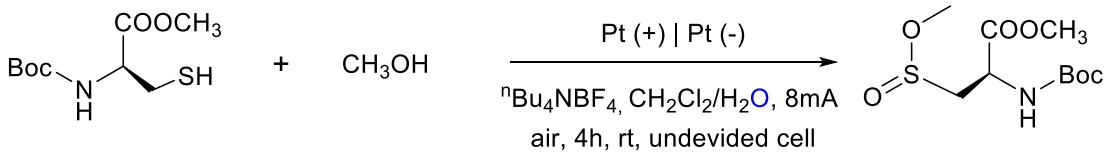
3.1.2 General Procedure for sulfinates Synthesis



1a 5a 6a

General procedure for Gram-Scale Experiments: In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, methyl (tert-butoxycarbonyl)-D-cysteinate (5.0 mmol), methanol (5.0 mmol), H_2O (10 uL) and $^{n}Bu_4NBF_4$ (5.0 mmol), Then, CH_2Cl_2 (6 mL) were added. The bottle was equipped with platinum plate (15 mm×15 mm×0.3 mm as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at constant current of 8 mA under 25℃ for 4 hours. After completion of the reaction, as indicated by TLC, the pure product (yield: 90%, 50.6 mg) was obtained by flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate= 2:1).

3.2 Table S1 Optimization of the reaction conditions



1a 5a 6a

Entry	variation from the standard conditions	yield(%)
1	none	90
2	6 mA instead of 8 mA	50
3	10 mA instead of 8 mA	73
4	$^{n}Bu_4NPF_6$ intead of $^{n}Bu_4NBF_4$	57
5	$^{n}Bu_4NI$ intead of $^{n}Bu_4NBF_4$	N.R
6	without $^{n}Bu_4NBF_4$	N.R
7	CH_3OH instead of CH_2Cl_2	78
8	CH_3CN instead of CH_2Cl_2	N.R
9	H_2O instead of CH_2Cl_2	N.R
10	graphite rod as the anode	64
11	Ni foam(-) as the cathode	85
12	no electricity	N.R

[a]Reaction conditions: undivided cell, Pt anode, Pt cathode, **1a** (0.2 mmol), **5a** (5.0 mmol), $^{n}Bu_4NBF_4$ (0.2 mmol), CH_2Cl_2 (6 mL), H_2O (10 uL), air, rt, 8 mA, 4 h. yield of isolated products. N.R = Not Reaction

4. Mechanistic Experiments

4.1 Cyclic voltammetry experiments of Phosphorothioates Synthesis

Cyclic voltammetry was performed in a three-electrode cell connected to a schlenk line at room temperature. Cyclic voltammograms of reactants and the mixtures in 2×10^{-3}M $^{n}Bu_4NI/CH_3CN$ using a glassy carbon-disk working electrode (diameter, 3 mm). Pt disk as counter; Ag/AgCl as reference electrode, at 100 mV/s scan rate.

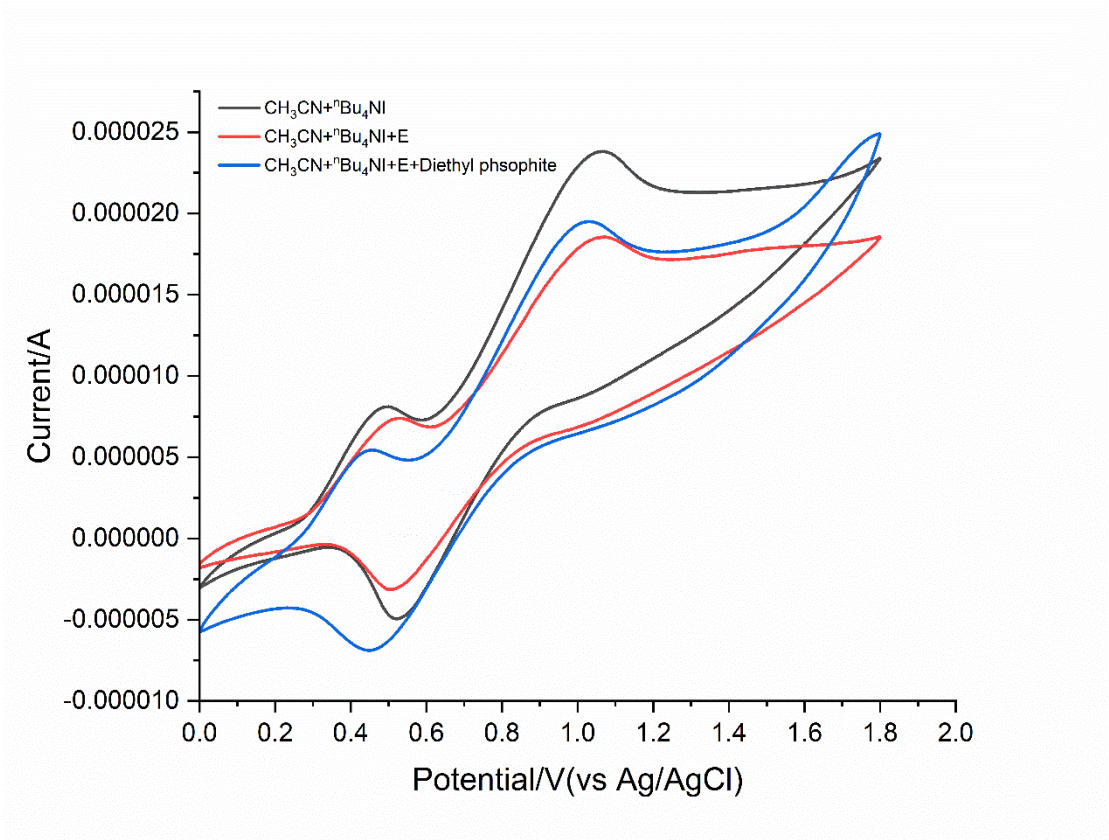


Figure S1. Cyclic voltammograms of substrate $CH_3CN+^{n}Bu_4NI$, $CH_3CN+^{n}Bu_4NI$+ **E**(10mmol/L), $CH_3CN+^{n}Bu_4NI$+**E**+**2a**, 0-2 V

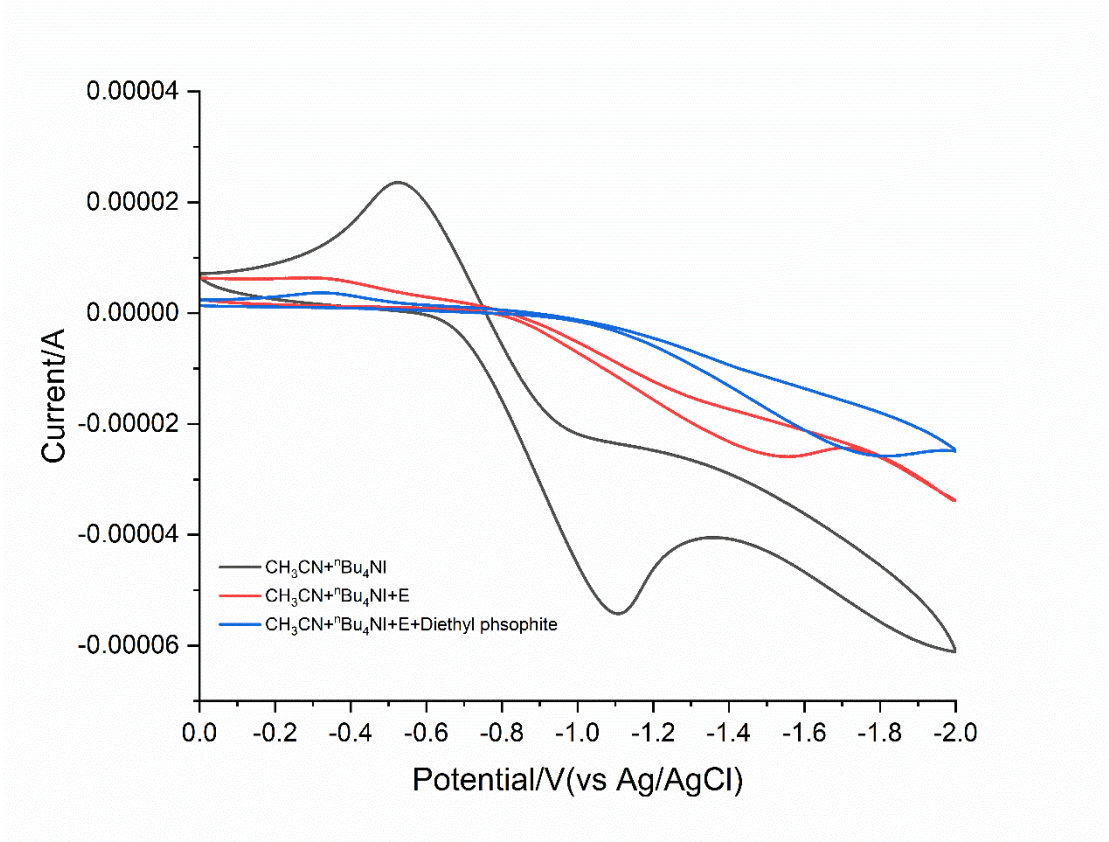


Figure S2. Cyclic voltammograms of substrate $CH_3CN+^nBu_4NI$, $CH_3CN+^nBu_4NI$+**E**, $CH_3CN+^nBu_4NI$+**E**+**2a**, -2-0V

4.2 Cyclic voltammetry experiments of sulfinates Synthesis

Cyclic voltammetry was performed in a three-electrode cell connected to a schlenk line at room temperature. Cyclic voltammograms of reactants and the mixtures in 2×10^{-3}M $^nBu_4NBF_4/CH_2Cl_2$ using a glassy carbon-disk working electrode (diameter, 3 mm). Pt disk as counter; Ag/AgCl as reference electrode, at 100 mV/s scan rate.

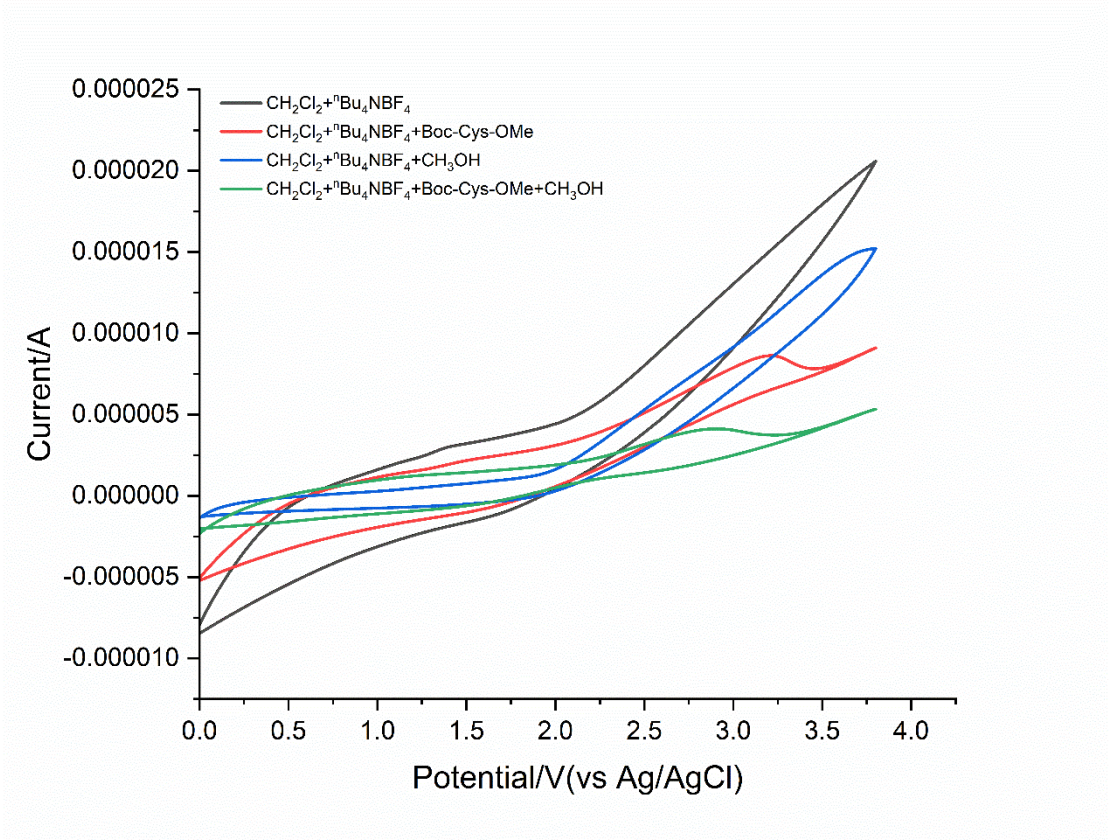


Figure S3. Cyclic voltammograms of substrate CH_3CN+$^{n}Bu_4NBF_4$, CH_3CN+$^{n}Bu_4NBF_4$ + **1a**(8mmol/L), CH_3CN+$^{n}Bu_4NBF_4$ +5a(50uL), CH_3CN+$^{n}Bu_4NBF_4$+1a+5a, 0-3.8V

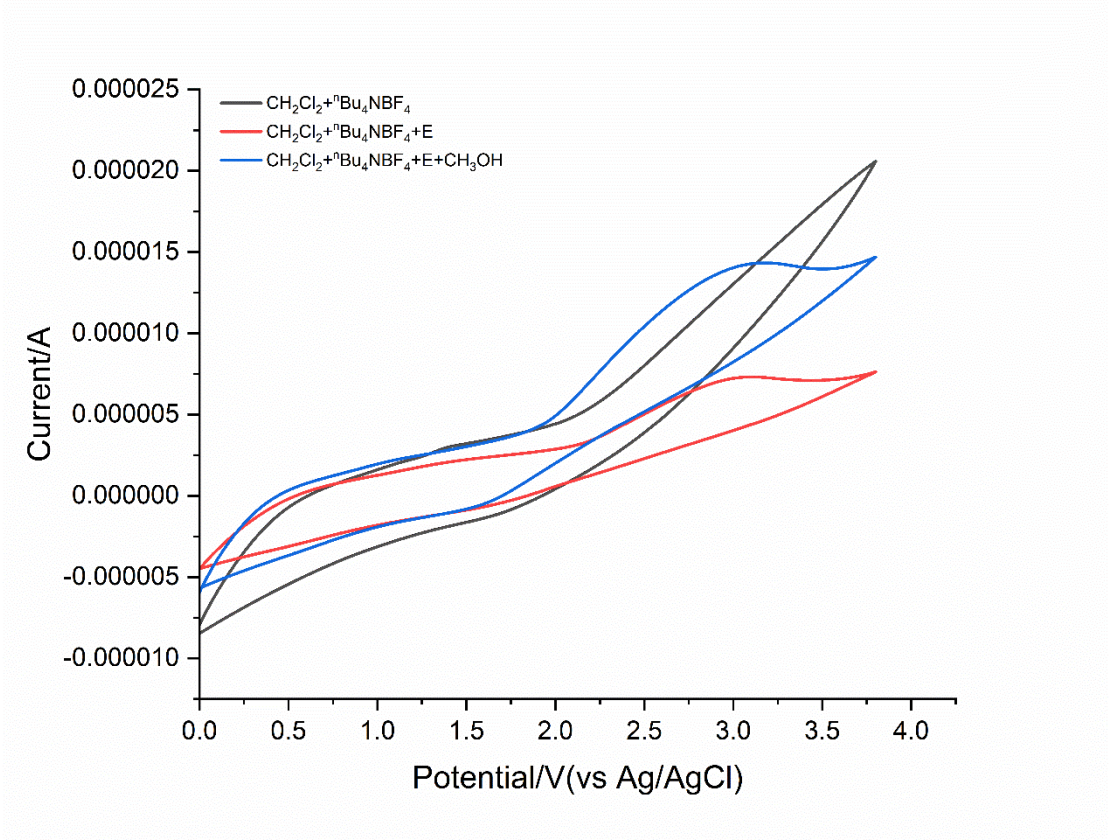


Figure S4. Cyclic voltammograms of substrate of substrate $CH_3CN+^nBuNBF_4$, $CH_3CN+^nBu_4NBF_4$+**E**(10mmol/L), $CH_3CN+^nBu_4NBF_4$+**E**+**5a**, 0-3.8V

4.3 General procedure for the electron paramagnetic resonance (EPR) experiment

Reagent was electrolyzed in CH_3CN (8.0 mL) for 20 min. The samples were taken out by a capillary (borosilicate glass, 0.8-1.1×100 mm), and then recorded by EPR spectrometer at indicated temperature and parameters.

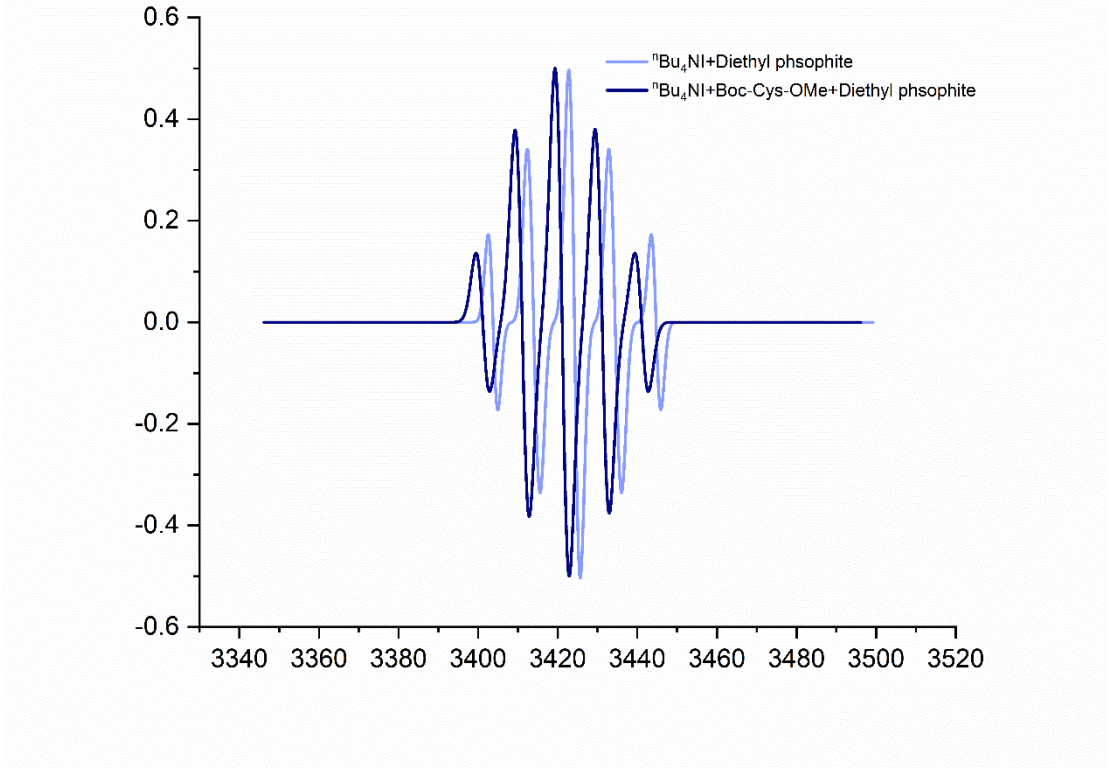


Figure S5

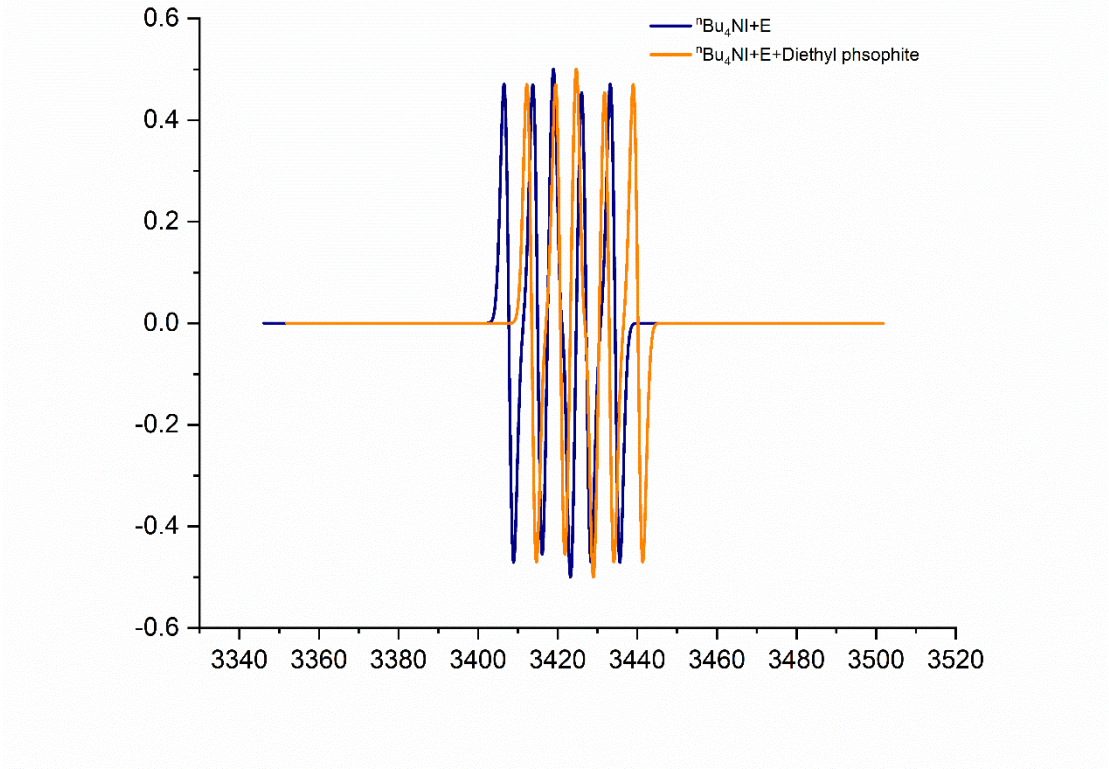
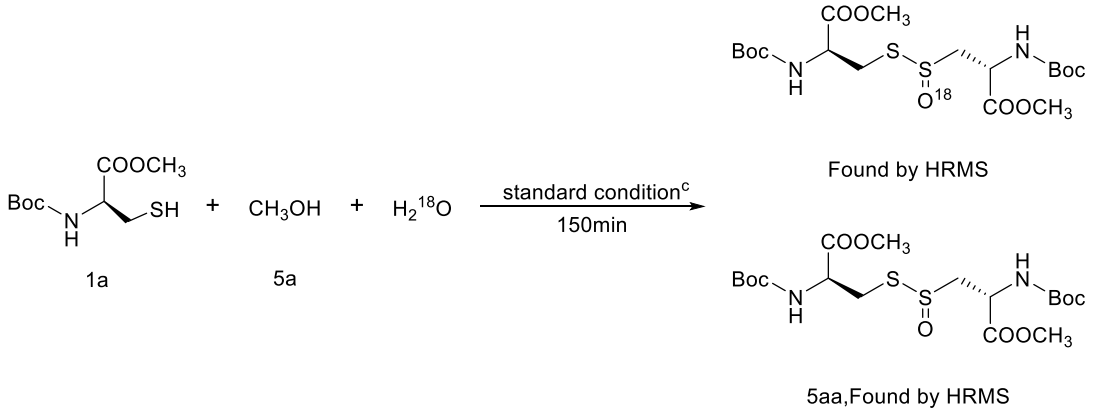


Figure S6

4.4 The isotope labeling experiment



We replace the water with water containing the isotope ^{18}O, and we let the reactant 1a and the reactant 5a react for 150 min under standard conditions, and finally get the intermediate 5aa and the 5aa mixture containing ^{18}O. The spectra of the intermediate 5aa and the 5aa mixture containing ^{18}O are listed below (Figure S7).

HRMS (ESI-TOF): m/z calculated for $C_{18}H_{32}N_2O_9S_2$, $[M+Na]^+$, 507.14414, found 507.14839.

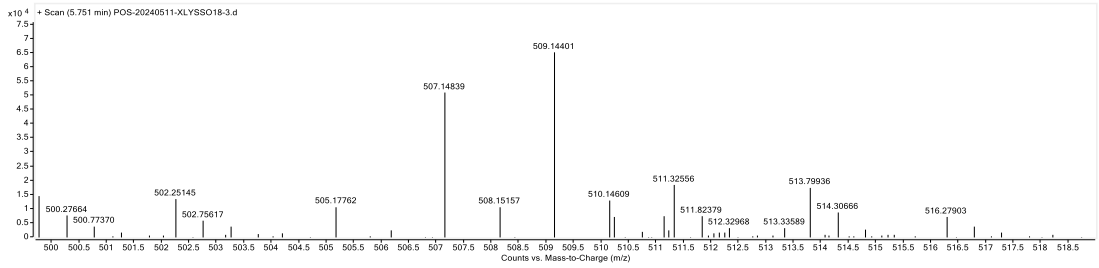
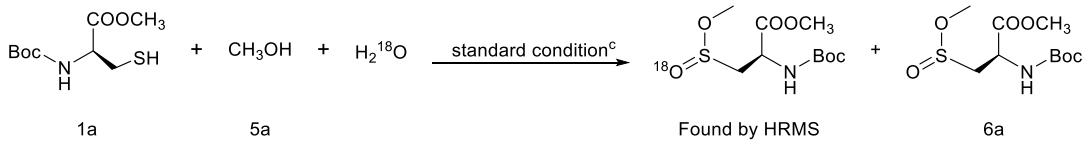


Figure S7. The HMRS spectra of the mixture of 5aa and [18O]-5aa.



we let the reactant 1a and the reactant 5a react under standard conditions, and finally get the intermediate 6a and the 6a mixture containing ^{18}O. The spectra of the intermediate 6a and the 6a mixture containing ^{18}O are listed below (Figure S8).

HRMS (ESI-TOF): m/z calculated for $C_{10}H_{19}NO_6S$, $[M+Na]^+$, 507.14414, found 507.14839.

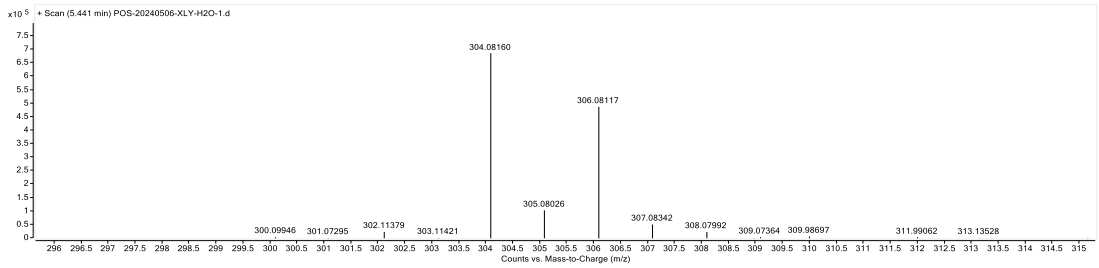


Figure S8. The HMRS spectra of the mixture of 6a and [18O]-6a.

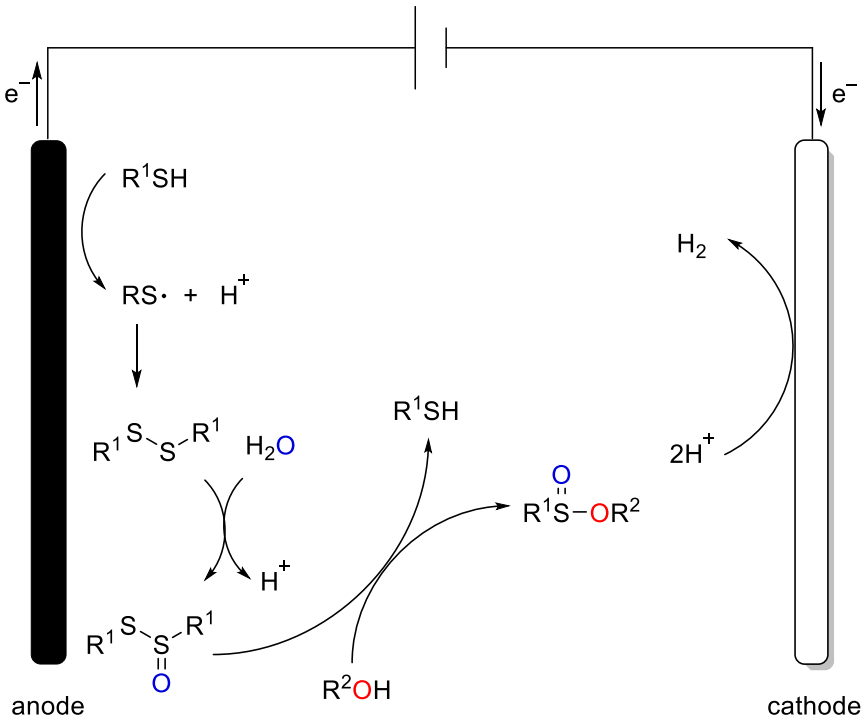


Figure S9. Proposed mechanism of 6a**.**

5. Gram-scale synthesis

5.1.1 Gram synthesis of 3a

General procedure for Gram-Scale Experiments: In an oven-dried undivided three-necked bottle (100 mL) equipped with a stir bar, methyl (tert-butoxycarbonyl)-D-cysteinate (5.0 mmol), diethyl phosphonate (10.0 mmol), and $^{n}Bu_4NI$ (5.0 mmol), Then, CH_3CN (40 mL) were injected into the tubes via syringes. The bottle was equipped with platinum plate (15 mm×15 mm×0.3 mm as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at constant current of 12 mA under 25℃ for 48 hours. The solvent was removed under vacuum. The crude product was purified by flash column chromatography on silica gel to afford pure product.

5.1.2 Antifungal experiment of 3a

Fungal plaque was inoculated into 2mL of Luria-Bertani liquid culture medium in 96-well plates and incubated at 28°C for 24 hours. Afterwards, the optical density at 600nm (OD_{600}) of each sample was determined.

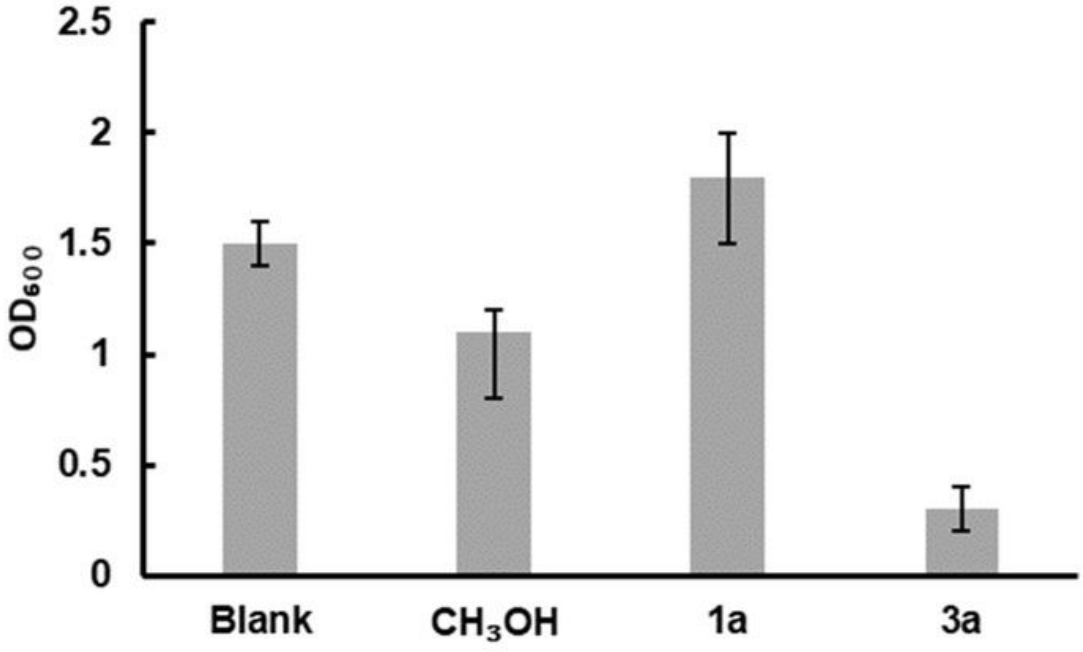


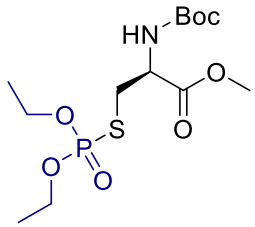
Figure S10. Optical density of treated fungal patches at 600 nm (OD_{600})

5.2 Gram-Scale Experiments with methanol

General procedure for Gram-Scale Experiments: In an oven-dried undivided three-necked bottle (100 mL) equipped with a stir bar, methyl (tert-butoxycarbonyl)-D-cysteinate (5.0 mmol), methanol (4.20 mL), H_2O (0.25 mL) and $^{n}Bu_4NBF_4$ (5.0 mmol), Then, CH_2Cl_2 (40 mL) were injected into the tubes via syringes. The bottle was equipped with platinum plate (15 mm×15 mm×0.3 mm as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at constant current of 8 mA under 25℃ for 96 hours. The solvent was removed under vacuum. The crude product was purified by flash column chromatography on silica gel to afford pure product.

6. Detailed descriptions for products

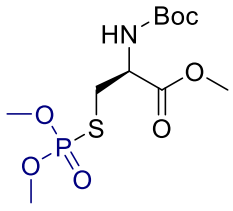
6.1 Phosphite ester and Thioglucose scope and characterization



3a

Metnyl N-(tert-butoxycarbonyl)-S-(diethoxyphosphory)-D-cysteinate (3a).

64.6 mg (yield: 87%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.44 (d, *J* = 8.4 Hz, 1H), 4.24 (ddd, *J* = 9.9, 8.3, 4.6 Hz, 1H), 4.08 (ddt, *J* = 9.0, 7.0, 2.0 Hz, 4H), 3.66 (s, 3H), 3.16 (td, *J* = 13.4, 4.7 Hz, 1H), 2.99 (ddd, *J* = 16.9, 13.3, 9.9 Hz, 1H), 1.39 (s, 9H), 1.27 (tt, *J* = 7.1, 1.2 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 171.25, 155.76, 79.11, 63.83 (dd, *J* = 5.7, 2.5 Hz), 54.30 (d, *J* = 4.1 Hz), 52.71, 40.30, 31.73 (d, *J* = 3.7 Hz), 28.53, 16.26 (dd, *J* = 7.1, 2.6 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 26.03. HRMS (ESI) calcd. For $(M+Na)^+$ $C_{13}H_{26}NO_7PS$: 394.10598 found, 394.10593.

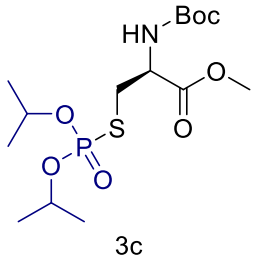


3b

Methyl N-(tert-butoxycarbonyl)-S-(dimethoxyphosphoryl)-D-cysteinate (3b).

51.5 mg (yield: 75%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.46 (d, *J* = 8.4 Hz, 1H), 4.24 (ddd, *J* = 9.9, 8.4, 4.6 Hz, 1H), 3.74 (d, *J* = 2.2 Hz, 3H), 3.70 (d, *J* = 2.2 Hz, 3H), 3.66 (s, 3H), 3.17 (td, *J* = 13.4, 4.7 Hz, 1H), 3.00 (ddd, *J* = 17.0, 13.3, 9.9 Hz, 1H), 1.39 (s, 9H), 3.37 – 3.35 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ 171.17, 155.76, 79.15, 54.24 (dd, *J* = 5.6, 2.3 Hz), 52.73, 31.66 (d, *J* = 3.7 Hz),

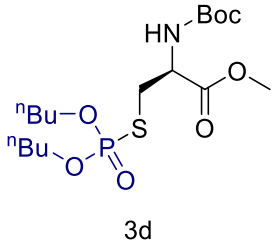
28.53. ^{31}P NMR (162 MHz, DMSO-d6) δ 29.70. HRMS (ESI) cald. for $(M+Na)^+$ $C_{11}H_{22}NO_7PS$: 366.07648, found, 366.07463.



3c

Methyl N-(tert-butoxycarbonyl)-S-(diisopropoxyphosphoryl)-D-cysteinate (3c).

57.6 mg (yield: 72%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.42 (d, *J* = 8.3 Hz, 1H), 4.62 (ddq, *J* = 12.6, 6.3, 3.6, 3.1 Hz, 2H), 4.30 – 4.23 (m, 1H), 3.66 (s, 3H), 3.20 – 3.11 (m, 1H), 2.99 (ddd, *J* = 16.1, 13.2, 9.9 Hz, 1H), 1.39 (s, 9H), 1.30 – 1.26 (m, 12H). ^{13}C NMR (101 MHz, DMSO-d6) δ 171.30, 155.73, 79.43, 79.07, 72.88 (dd, *J* = 9.2, 6.2 Hz), 55.60, 54.41 (d, *J* = 4.2 Hz), 52.70, 31.89 (d, *J* = 3.7 Hz), 29.47, 28.53, 23.95 (d, *J* = 3.8 Hz), 23.71 (d, *J* = 5.6 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 23.56. HRMS (ESI) cald. for $(M+Na)^+$ $C_{15}H_{30}NO_7PS$: 422.13728, found, 422.13765.

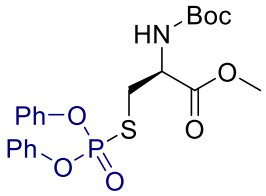


3d

Methyl N-(tert-butoxycarbonyl)-S-(dibutoxyphosphoryl)-D-cysteinate (3d).

56.4 mg (yield: 66%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.43 (d, *J* = 8.4 Hz, 1H), 4.24 (ddd, *J* = 10.0, 8.4, 4.6 Hz, 1H), 4.06 – 3.98 (m, 4H), 3.66 (s, 3H), 3.16 (td, *J* = 13.4, 4.6 Hz, 1H), 2.99 (ddd, *J* = 16.9, 13.3, 10.0 Hz, 1H), 1.65 – 1.58 (m, 4H), 1.39 (d, *J* = 3.1 Hz, 9H), 1.36 – 1.32 (m, 4H), 0.90 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 171.24, 155.76, 79.12, 67.32 (d, *J* = 6.3 Hz), 54.36 (d, *J* = 4.0 Hz), 52.72, 40.55 (d, *J* = 12.3 Hz), 31.99 (d, *J* = 6.5 Hz), 31.69 (d, *J* = 3.7

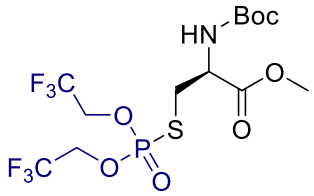
Hz), 28.52, 28.30, 18.66, 13.84. ^{31}P NMR (162 MHz, DMSO-d6) δ 26.33. HRMS (ESI) cald. for $(M+Na)^+$ $C_{17}H_{34}NO_7PS$: 428.18664, found, 428.18624.



3e

Methyl N-(tert-butoxycarbonyl)-S-(diphenoxyphosphoryl)-D-cysteinate (3e).

81.3 mg (yield: 87%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, Methanol-d4) δ 7.41 (dd, *J* = 8.6, 7.2 Hz, 4H), 7.31 – 7.24 (m, 6H), 4.42 (dd, *J* = 8.6, 4.8 Hz, 1H), 3.69 (s, 3H), 3.48 (ddd, *J* = 15.1, 13.3, 4.8 Hz, 1H), 3.33 – 3.23 (m, 1H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d6) δ 170.93, 155.71, 150.08 (dd, *J* = 8.4, 5.2 Hz), 130.65, 126.44, 120.91 (d, *J* = 4.7 Hz), 79.27, 54.15 (d, *J* = 5.3 Hz), 52.82, 32.36 (d, *J* = 3.9 Hz), 28.51. ^{31}P NMR (162 MHz, DMSO-d6) δ 20.28. HRMS (ESI) cald. for $(M+Na)^+$ $C_{21}H_{26}NO_7PS$: 490.10598, found, 490.10538.

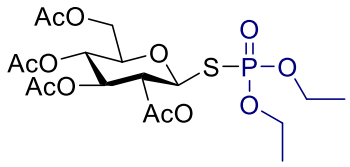


3f

Methyl S-(bis(trifluoromethoxy)phosphoryl)-N-(tert-butoxycarbonyl)-D-cysteinate (3f).

54.1 mg (yield: 60%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.52 (d, *J* = 8.6 Hz, 1H), 4.85 – 4.76 (m, 4H), 4.36 – 4.30 (m, 1H), 3.67 (s, 3H), 3.34 – 3.28 (m, 1H), 3.14 (ddd, *J* = 18.3, 13.2, 10.0 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d6) δ 170.87, 155.82, 127.46 (d, *J* = 11.2 Hz), 124.70 (d, *J* = 10.7 Hz), 121.94 (d, *J* = 10.8 Hz), 79.31, 63.73 (d, *J* = 5.0 Hz), 63.37 (dd, *J* = 8.0, 4.2 Hz), 63.01 (dd, *J* = 8.0, 4.2 Hz), 62.80 – 62.52 (m), 53.89 (d, *J* = 4.7 Hz), 52.80, 32.36 (d, *J* = 3.7 Hz), 28.45. ^{31}P NMR (162 MHz, DMSO-d6) δ 29.80. ^{19}F NMR (377 MHz, DMSO-d6) δ -

73.78 (q, J = 8.4 Hz). HRMS (ESI) cald. for $(M+Na)^+$ $C_{11}H_{16}F_6NO_7PS$: 502.04945, found, 502.04980.

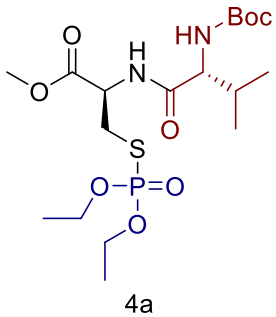


3g

(2R,3R,4S,5R,6S)-2-(acetoxymethyl)-6-((diethoxyphosphoryl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (3g).

72.7 mg (yield: 72%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 5.41 (t, J = 9.4 Hz, 1H), 5.21 (dd, J = 13.3, 10.0 Hz, 1H), 5.00 – 4.91 (m, 2H), 4.15 – 4.09 (m, 5H), 4.08 – 4.00 (m, 2H), 2.05 – 1.97 (m, 9H), 1.95 (s, 3H), 1.31 – 1.26 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 170.44, 169.83 (d, J = 19.1 Hz), 169.50 , 81.90 (d, J = 3.8 Hz), 75.23, 73.10, 70.97 (d, J = 9.2 Hz), 68.17, 64.14 (dd, J = 16.9, 5.3 Hz), 62.37, 61.59, 21.00 – 20.60 (m), 16.54 (d, J = 6.2 Hz), 16.20 (dd, J = 7.0, 3.4 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 21.47. HRMS (ESI)cald. for $(M+K)^+$ $C_{18}H_{29}O_{12}PS$: 539.07489, found, 539.07485.

6.2 Dipeptide scope and characterization

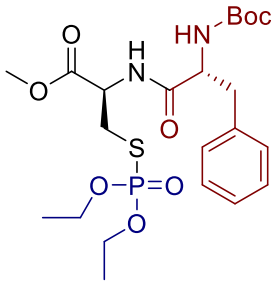


4a

Methyl N-((tertbutoxycarbonyl)-D-valyl)-S-(diethoxyphosphoryl)-L-cyteinate (4a).

45.2 mg (yield: 48%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.51 (d, J = 7.9 Hz, 1H), 6.63 (d, J = 9.0 Hz, 1H), 4.52 (td, J = 8.7, 4.9 Hz, 1H), 4.12 – 4.01 (m, 4H), 3.85 (dd, J = 9.2, 6.7 Hz, 1H), 3.65 (s, 3H), 3.21 (td, J = 13.3, 5.0 Hz,

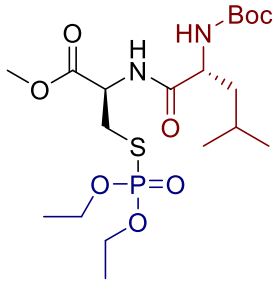
1H), 3.04 (ddd, *J* = 16.1, 13.2, 9.2 Hz, 1H), 1.96 (h, *J* = 6.6 Hz, 1H), 1.39 (s, 9H), 1.27 (t, *J* = 7.1 Hz, 6H), 0.85 (dd, *J* = 12.4, 6.8 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d6) δ 172.19, 170.64, 155.84, 78.47, 63.83 (d, *J* = 5.7 Hz), 59.98, 52.69 (d, *J* = 4.2 Hz), 31.61, 30.90, 28.60, 19.60, 18.33, 16.26 (d, *J* = 6.9 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 25.88. HRMS (ESI) cald. for $(M+Na)^+$ $C_{18}H_{35}N_2O_8PS$: 493.17439, found, 493.17486.



4b

Methyl N-((tert-butoxycarbonyl)-D-phenylalanyl)-S-(diethoxyphosphoryl)-L-cyteinate (4b).

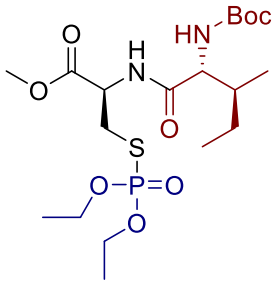
84.5 mg (yield: 77%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.58 (d, *J* = 7.9 Hz, 1H), 7.28 (d, *J* = 4.4 Hz, 4H), 7.20 (dt, *J* = 8.8, 4.3 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 4.58 (td, *J* = 8.4, 5.2 Hz, 1H), 4.21 (ddd, *J* = 10.3, 8.6, 4.2 Hz, 1H), 4.08 (ddt, *J* = 12.3, 6.0, 2.3 Hz, 4H), 3.66 (s, 3H), 3.22 (td, *J* = 13.4, 5.3 Hz, 1H), 3.12 – 3.03 (m, 1H), 3.02 – 2.95 (m, 1H), 2.75 (dd, *J* = 13.8, 10.3 Hz, 1H), 1.29 (d, *J* = 2.1 Hz, 9H), 1.27 (d, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.59, 170.73, 155.65, 138.49, 129.65, 128.49, 126.67, 78.48, 63.91 (d, *J* = 5.9 Hz), 56.04, 52.77 (d, *J* = 4.7 Hz), 37.76, 31.51 (d, *J* = 3.5 Hz), 28.56, 16.29 (d, *J* = 7.1 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 25.87. HRMS (ESI) cald. for $(M+Na)^+$ $C_{22}H_{35}N_2O_8PS$: 541.17439, found, 507.17439.



4c

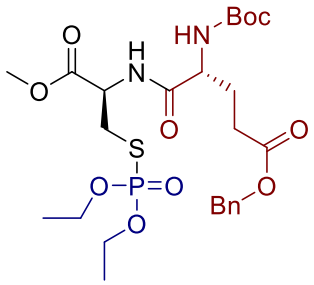
Methyl N-((tertbutoxycarbonyl)-D-leucyl)-S-(diethoxyphosphoryl)-L-cyteinate (4c).

49.4 mg (yield: 51%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.45 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.5 Hz, 1H), 4.52 (td, *J* = 8.6, 4.9 Hz, 1H), 4.06 (dddd, *J* = 17.4, 8.4, 4.9, 1.5 Hz, 5H), 3.66 (s, 3H), 3.20 (td, *J* = 13.2, 5.0 Hz, 1H), 3.05 (ddd, *J* = 16.0, 13.2, 9.1 Hz, 1H), 1.61 (dt, *J* = 13.4, 6.7 Hz, 1H), 1.43 (dd, *J* = 8.6, 6.0 Hz, 2H), 1.38 (s, 9H), 1.27 (t, *J* = 7.1 Hz, 6H), 0.87 (t, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 173.34, 170.69, 155.69, 78.41, 63.80 (d, *J* = 5.6 Hz), 53.04, 52.82 – 52.44 (m), 41.25, 31.73 (d, *J* = 3.5 Hz), 28.61, 24.67, 23.33, 22.01, 16.26 (d, *J* = 6.8 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 25.89. HRMS (ESI) cald. for $(M+H)^+$ $C_{19}H_{37}N_2O_8PS$: 485.20812, found, 485.20322.



4d

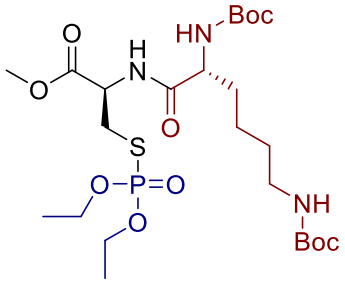
Methyl N-((tertbutoxycarbonyl)-D-alloisoleucyl)-S-(diethoxyphosphoryl)-L-cyteinate (4d). 54.3 mg (yield: 56%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.52 (d, *J* = 7.9 Hz, 1H), 6.66 (d, *J* = 9.0 Hz, 1H), 4.52 (tt, *J* = 8.7, 5.0 Hz, 1H), 4.07 (ddt, *J* = 12.5, 6.3, 2.3 Hz, 4H), 3.90 – 3.84 (m, 1H), 3.65 (s, 3H), 3.20 (td, *J* = 13.3, 5.0 Hz, 1H), 3.04 (ddd, *J* = 16.1, 13.2, 9.3 Hz, 1H), 1.70 (ddq, *J* = 14.3, 7.2, 3.5 Hz, 1H), 1.38 (s, 10H), 1.27 (t, *J* = 7.0 Hz, 6H), 1.08 (ddt, *J* = 14.2, 9.9, 7.2 Hz, 1H), 0.86 – 0.79 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.24, 170.64, 155.76, 78.47, 63.83 (d, *J* = 6.0 Hz), 59.08, 52.69 (d, *J* = 3.6 Hz), 40.20, 37.02, 31.59, 28.60, 24.64, 16.26 (d, *J* = 7.2 Hz), 15.76, 11.44. ^{31}P NMR (162 MHz, DMSO-d6) δ 25.90. HRMS (ESI) cald. for $(M+Na)^+$ $C_{19}H_{37}N_2O_8PS$: 507.19004, found, 507.19061.



4e

Benzyl (R)-4-((tert-butoxycarbonyl)amino)-5-((R)-3-((diethoxyphosphoryl)thio)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentanoate (4e).

79.1 mg (yield: 67%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.50 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.31 (m, 5H), 6.98 (d, *J* = 8.1 Hz, 1H), 5.09 (s, 2H), 4.54 (td, *J* = 8.6, 4.8 Hz, 1H), 4.11 – 3.98 (m, 5H), 3.65 (s, 3H), 3.22 (td, *J* = 13.2, 4.9 Hz, 1H), 3.07 (ddd, *J* = 16.3, 13.2, 9.2 Hz, 1H), 2.46 – 2.35 (m, 2H), 1.99 – 1.87 (m, 1H), 1.86 – 1.75 (m, 1H), 1.39 – 1.33 (m, 9H), 1.25 (td, *J* = 7.0, 1.8 Hz, 6H).^{13}C NMR (101 MHz, DMSO-d6) δ 172.67, 172.37, 170.61, 155.71, 136.66, 128.88, 128.36 (d, *J* = 14.4 Hz), 78.66, 65.91, 63.84 (d, *J* = 5.8 Hz), 53.82, 52.73 (d, *J* = 12.7 Hz), 40.44 (d, *J* = 1.1 Hz), 31.70, 30.46, 28.61, 27.63, 16.27 (d, *J* = 7.2 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 25.85. HRMS (ESI) cald. for $(M+Na)^+$ $C_{25}H_{39}N_2O_{10}PS$: 613.19552, found, 613.19428.

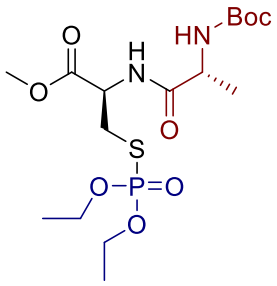


4f

Methyl N-(N^2,N^6-bis(tert-butoxycarbonyl)-D-lysyl)-S-(diethoxyphosphoryl)-L-cysteinate (4f).

82.8 mg (yield: 69%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.42 (d, *J* = 8.1 Hz, 1H), 6.83 – 6.66 (m, 2H), 4.59 (td, *J* = 8.2, 4.9 Hz, 1H), 4.20 – 4.05 (m, 4H), 3.99 (q, *J* = 7.7, 7.2 Hz, 1H), 3.71 (s, 3H), 3.30 – 3.05 (m, 2H), 2.97 – 2.89 (m, 2H), 1.69 – 1.53 (m, 2H), 1.43 (d, *J* = 3.6 Hz, 20H), 1.32 (t, *J* = 7.1 Hz, 8H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.95, 170.64, 156.03, 155.72, 78.49, 77.77, 63.85 (d,

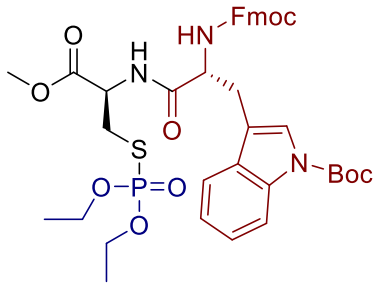
J = 5.8 Hz), 54.65, 52.65 (d, *J* = 7.0 Hz), 32.10, 31.79 (d, *J* = 3.6 Hz), 29.66, 28.68 (d, *J* = 8.8 Hz), 23.15, 16.25 (d, *J* = 6.8 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 25.84. HRMS (ESI) cald. for $(M+H)^+$ $C_{24}H_{46}N_3O_{10}PS$: 600.27143, found, 600.27098.



4g

Methyl N-((tertbutoxycarbonyl)-D-alanyl)-S-(diethoxyphosphoryl)-L-cyteinate (4g).

39.7 mg (yield: 45%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.39 (d, *J* = 8.1 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 4.54 (td, *J* = 8.6, 5.1 Hz, 1H), 4.12 – 3.96 (m, 5H), 3.66 (s, 3H), 3.20 (td, *J* = 13.3, 5.1 Hz, 1H), 3.05 (ddd, *J* = 16.1, 13.2, 9.0 Hz, 1H), 1.38 (s, 9H), 1.29 – 1.25 (m, 6H), 1.20 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ 173.56, 170.70, 155.44, 78.49, 63.84 (d, *J* = 5.8 Hz), 52.79, 52.54 (d, *J* = 4.6 Hz), 50.05, 39.52, 31.81, 28.64, 18.66, 16.28 (d, *J* = 6.8 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 25.87. HRMS (ESI) cald. for $(M+H)^+$ $C_{16}H_{31}N_2O_8PS$: 443.16115, found, 443.16163.

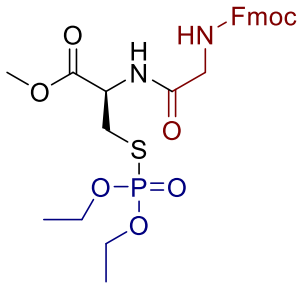


4h

Tert-butyl 3-((R)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(((R)-3-(((R)-3-((diethoxyphosphoryl)thio)-1-methoxy-1-oxopropan-2-yl)amino)-3-oxopropyl)-1H-indole-1-carboxyla-te (4h).

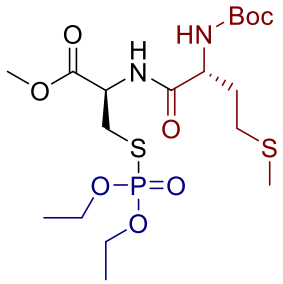
85.8 mg (yield: 55%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.83 (d, *J* = 8.1 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 2H), 7.80 (d, *J* =

7.8 Hz, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.66 – 7.57 (m, 3H), 7.40 – 7.30 (m, 3H), 7.25 (dq, *J* = 15.4, 7.5, 5.4 Hz, 3H), 4.63 (td, *J* = 8.4, 5.1 Hz, 1H), 4.49 (td, *J* = 9.3, 4.4 Hz, 1H), 4.22 – 4.14 (m, 2H), 4.05 (dddd, *J* = 15.3, 10.8, 7.1, 2.3 Hz, 5H), 3.69 (s, 3H), 3.26 – 2.95 (m, 4H), 1.57 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.22, 170.64, 156.32, 149.52, 144.18 (d, *J* = 3.4 Hz), 141.12 (d, *J* = 3.0 Hz), 135.20, 130.71, 128.04, 127.44, 125.73 (d, *J* = 10.2 Hz), 124.71 (d, *J* = 7.0 Hz), 122.85, 120.50, 119.93, 117.05, 115.13, 83.90, 66.30, 63.89 (d, *J* = 6.1 Hz), 54.85, 52.82 (d, *J* = 4.2 Hz), 47.05, 31.90 (d, *J* = 3.4 Hz), 28.12, 16.26 (d, *J* = 6.8 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 25.81. HRMS (ESI) cald. for $(M+Na)^+$ $C_{39}H_{46}N_3O_{10}PS$: 802.25337, found, 802.25121.



4i

Methyl N-(((9H-fluoren-9-yl)methoxy) carbonglcyl)-S-(diethoxyphosphoryl)-L-cyteinate (4i). 47.4 mg (yield: 43%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.54 (d, *J* = 7.9 Hz, 1H), 7.91 – 7.88 (m, 2H), 7.73 (d, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 6.2 Hz, 1H), 7.42 (td, *J* = 7.5, 1.2 Hz, 2H), 7.34 (td, *J* = 7.4, 1.2 Hz, 2H), 4.59 (dt, *J* = 8.3, 4.1 Hz, 1H), 4.30 (d, *J* = 7.7 Hz, 2H), 4.24 (d, *J* = 6.7 Hz, 1H), 4.07 (dtt, *J* = 8.4, 5.2, 1.6 Hz, 4H), 3.70 (d, *J* = 6.2 Hz, 2H), 3.67 (s, 3H), 3.21 (td, *J* = 13.5, 5.3 Hz, 1H), 3.07 (ddd, *J* = 15.9, 13.3, 8.6 Hz, 1H), 1.26 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 170.73, 169.93, 156.95, 144.30, 141.20, 128.11, 127.55, 125.73, 120.58, 66.23, 63.92 (d, *J* = 5.8 Hz), 52.92 – 52.60 (m), 47.09, 43.59, 31.66 (d, *J* = 3.8 Hz), 16.29 (d, *J* = 6.9 Hz). ^{31}P NMR (162 MHz, DMSO-d6) δ 25.85. HRMS (ESI) cald. for $(M+Na)^+$ $C_{25}H_{31}N_2O_8PS$: 573.14309, found, 573.14329.

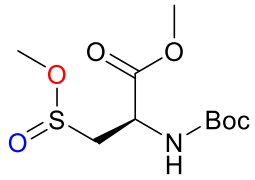


4j

Methyl N-((tert-butoxycarbonyl)-D-methionyl)-S-(diethoxyphosphoryl)-L-cyteinate (4j).

65.3 mg (yield: 65%, 0.2 mmol scale), yellow oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.47 (d, *J* = 8.1 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 1H), 4.55 (td, *J* = 8.6, 4.9 Hz, 1H), 4.11 – 4.02 (m, 5H), 3.66 (s, 3H), 3.22 (td, *J* = 13.1, 4.9 Hz, 1H), 3.07 (ddd, *J* = 16.1, 13.2, 9.2 Hz, 1H), 2.46 (dd, *J* = 9.0, 6.3 Hz, 2H), 2.04 (s, 3H), 1.92 – 1.76 (m, 2H), 1.39 (s, 9H), 1.27 (t, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.94, 172.52, 170.62, 155.75, 155.12, 78.60, 63.85 (d, *J* = 5.7 Hz), 53.90, 52.88 – 52.47 (m), 32.18, 31.78 (d, *J* = 3.7 Hz), 30.04, 28.61, 16.27 (d, *J* = 7.0 Hz), 15.05. ^{31}P NMR (162 MHz, DMSO-d6) δ 25.85. HRMS (ESI) cald. for $(M+Na)^+$ $C_{18}H_{35}N_2O_8PS_2$: 525.14647, found, 525.14598.

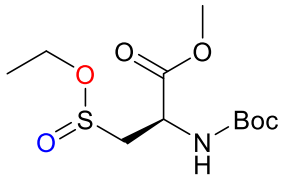
6.3 Alcohols substrate and characterization



6a

Methyl (tert-butoxycarbonyl)(methoxysulfinyl)-D-alaninate (6a).

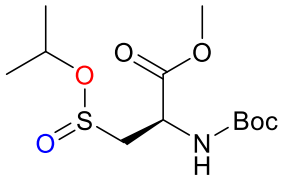
50.6 mg (yield: 90%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.59 (dd, *J* = 8.4, 2.7 Hz, 1H), 4.37 – 4.26 (m, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 3.22 – 3.14 (m, 1H), 3.05 – 2.96 (m, 1H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d6) δ 171.32 (d, *J* = 11.5 Hz), 155.52, 79.34 (d, *J* = 4.0 Hz), 57.68, 57.16, 54.28 (d, *J* = 3.1 Hz), 52.89, 49.03 (d, *J* = 10.1 Hz), 28.51. HRMS (ESI) cald. for $(M+Na)^+$ $C_{10}H_{19}NO_6S$: 304.08253, found, 304.08221.



6b

Methyl (tert-butoxycarbonyl)(ethoxysulfinyl)-D-alaninate (6b).

46.1 mg (yield: 78%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.58 (dd, *J* = 8.3, 2.4 Hz, 1H), 4.39 – 4.26 (m, 1H), 4.06 (ttd, *J* = 7.1, 4.3, 2.2 Hz, 2H), 3.66 (s, 3H), 3.21 – 3.09 (m, 1H), 3.06 – 2.94 (m, 1H), 1.39 (s, 9H), 1.25 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ 171.34 (d, *J* = 14.9 Hz), 155.54 (d, *J* = 12.8 Hz), 79.30 (d, *J* = 5.3 Hz), 64.86 (d, *J* = 17.2 Hz), 58.24, 57.70, 52.87, 49.12, 28.50, 16.19 (d, *J* = 7.2 Hz). HRMS (ESI) cald. for $(M+K)^+$ $C_{11}H_{21}NO_6S$: 334.07212, found, 334.07208.

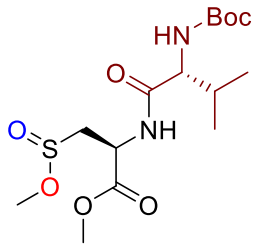


6c

Methyl (tert-butoxycarbonyl)(isopropoxysulfinyl)-D-alaninate (6c).

45.2 mg (yield: 73%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.58 (t, *J* = 9.2 Hz, 1H), 4.50 – 4.41 (m, 1H), 4.37 – 4.23 (m, 1H), 3.66 (s, 3H), 3.17 – 2.89 (m, 2H), 1.39 (d, *J* = 1.9 Hz, 9H), 1.26 (ddd, *J* = 17.2, 6.2, 3.0 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 171.36 (d, *J* = 19.2 Hz), 155.52 (d, *J* = 14.7 Hz), 79.28 (d, *J* = 7.0 Hz), 74.55 (d, *J* = 17.1 Hz), 58.57, 58.18, 52.86 (d, *J* = 3.4 Hz), 49.23 (d, *J* = 15.1 Hz), 39.49, 28.51 (d, *J* = 2.8 Hz), 24.05, 23.49, 23.27. HRMS (ESI) cald. for $(M+Na)^+$ $C_{12}H_{23}NO_6S$: 332.11383, found, 332.11330.

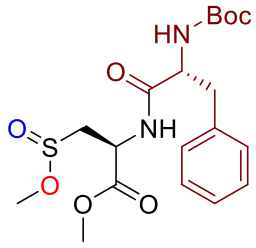
6.4 Dipeptide and Thioglucose scope and characterization



7a

Methyl ((tert-butoxycarbonyl)-D-valyl)(methoxysulfinyl)-L-alaninate (7a).

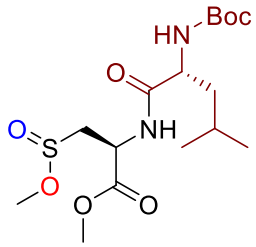
60.0 mg (yield: 67%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.66 (dd, *J* = 11.1, 7.8 Hz, 1H), 6.70 (d, *J* = 8.8 Hz, 1H), 4.64 – 4.51 (m, 1H), 3.80 (dt, *J* = 8.8, 6.4 Hz, 1H), 3.69 (s, 3H), 3.65 (d, *J* = 1.2 Hz, 3H), 3.28 – 3.19 (m, 1H), 3.10 – 3.01 (m, 1H), 1.98 – 1.87 (m, 1H), 1.39 (s, 9H), 0.84 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.11 (d, *J* = 19.3 Hz), 170.72 (d, *J* = 4.5 Hz), 155.89, 78.53, 60.07 (d, *J* = 4.7 Hz), 57.60, 57.36, 54.43, 54.20, 52.87, 47.43 (d, *J* = 18.3 Hz), 30.73 (d, *J* = 8.7 Hz), 28.61, 19.52, 18.37 (d, *J* = 3.2 Hz). HRMS (ESI) cald. for $(M+Na)^+$ $C_{15}H_{28}N_2O_7S$: 403.15094, found, 403.15013.



7b

Methyl ((tert-butoxycarbonyl)-D-phenylalanyl)(methoxysulfinyl)-L-alaninate (7b).

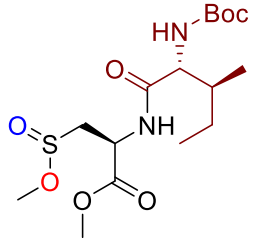
48.0 mg (yield: 56%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.69 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.28 (d, *J* = 5.3 Hz, 4H), 7.23 – 7.19 (m, 1H), 6.99 (dd, *J* = 8.6, 4.1 Hz, 1H), 4.69 – 4.58 (m, 1H), 4.21 – 4.14 (m, 1H), 3.70 (s, 3H), 3.67 – 3.64 (m, 3H), 3.29 – 3.18 (m, 1H), 3.14 – 3.04 (m, 1H), 3.02 – 2.95 (m, H), 2.74 (ddd, *J* = 13.9, 10.3, 1.8 Hz, 1H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.52, 172.32, 170.78 (d, *J* = 3.2 Hz), 155.67 (d, *J* = 3.7 Hz), 138.48, 129.65, 128.52, 126.69, 78.54, 57.60 (d, *J* = 18.3 Hz), 56.04 (d, *J* = 10.6 Hz), 54.59, 54.22, 52.95, 47.53 (d, *J* = 16.8 Hz), 37.59 (d, *J* = 6.8 Hz), 28.57. HRMS (ESI) cald. for $(M+Na)^+$ $C_{19}H_{28}N_2O_7S$: 429.16972, found, 429.16911.



7c

Methyl ((tert-butoxycarbonyl)-D-leucyl)(methoxysulfinyl)-L-alaninate (7c).

41.0 mg (yield: 52%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.51 (dd, *J* = 8.0, 3.3 Hz, 1H), 6.83 (d, *J* = 8.3 Hz, 1H), 4.60 (tdd, *J* = 9.4, 8.1, 4.9 Hz, 1H), 4.10 – 3.91 (m, 1H), 3.69 (d, *J* = 1.8 Hz, 3H), 3.66 (d, *J* = 3.7 Hz, 3H), 3.27 – 3.19 (m, 1H), 3.12 – 3.04 (m, 1H), 1.65 – 1.56 (m, 1H), 1.39 (s, 11H), 0.89 – 0.84 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 173.32, 173.10, 170.76 (d, *J* = 4.1 Hz), 155.72, 78.48, 57.71, 57.44, 54.40 (d, *J* = 19.5 Hz), 54.08, 52.98 (d, *J* = 16.7 Hz), 47.44 (d, *J* = 19.8 Hz), 40.97 (d, *J* = 6.0 Hz), 28.63, 24.64, 23.30, 22.04. HRMS (ESI) cald. for $(M+K)^+$ $C_{16}H_{30}N_2O_7S$: 395.18465, found, 395.18419.

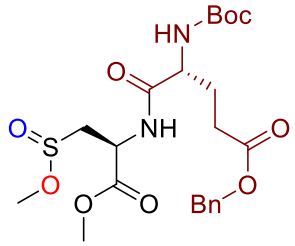


7d

Methyl ((tert-butoxycarbonyl)-D-isoleucyl)(methoxysulfinyl)-L-alaninate (7d).

44.6 mg (yield: 57%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.59 (t, *J* = 8.5 Hz, 1H), 6.63 (d, *J* = 8.7 Hz, 1H), 4.58 (ddt, *J* = 14.2, 10.0, 4.7 Hz, 1H), 3.87 – 3.78 (m, 1H), 3.68 (d, *J* = 1.2 Hz, 3H), 3.65 (d, *J* = 1.3 Hz, 3H), 3.26 – 3.20 (m, 1H), 3.10 – 3.02 (m, 1H), 1.69 (s, 1H), 1.38 (s, 10H), 1.09 (s, 1H), 0.81 (t, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.26, 172.05, 170.71 (d, *J* = 6.2 Hz), 155.80, 78.49, 59.07 (d, *J* = 6.6 Hz), 57.58, 57.34, 54.42, 54.18, 52.86, 47.44 (d, *J* = 13.9 Hz),

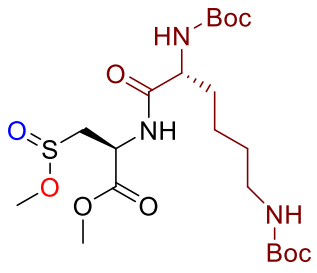
36.82 (d, J = 5.5 Hz), 28.61, 24.69, 15.67, 11.43 (d, J = 4.1 Hz).HRMS (ESI) cald. for $(M+K)^+$ $C_{16}H_{30}N_2O_7S$: 433.14053, found, 433.14027.



7e

Benzyl (4R)-4-((tert-butoxycarbonyl)amino)-5-(((2S)-1-methxoy-3-(methoxysulfinyl)-1-oxopropan-2-yl)amino-5-oxopentanoate (7e).

41.0 mg (yield: 62%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.64 (dd, J = 7.9, 4.6 Hz, 1H), 7.38 – 7.33 (m, 5H), 7.03 (d, J = 8.1 Hz, 1H), 5.10 (s, 2H), 4.69 – 4.51 (m, 1H), 3.98 (qd, J = 7.8, 5.5 Hz, 1H), 3.67 (s, 3H), 3.64 (d, J = 0.9 Hz, 3H), 3.25 (dt, J = 13.5, 7.7 Hz, 1H), 3.09 (ddd, J = 13.6, 6.8, 2.4 Hz, 1H), 2.42 (ddt, J = 12.4, 9.0, 4.9 Hz, 2H), 1.97 – 1.87 (m, 1H), 1.83 – 1.74 (m, 1H), 1.38 (d, J = 4.4 Hz, 9H). ^{13}C NMR (101 MHz, DMSO-d6) δ 172.65, 170.67 (d, J = 1.4 Hz), 136.69, 128.87, 128.52 – 128.16 (m), 78.73, 65.91, 57.60 (d, J = 15.6 Hz), 54.40, 54.05, 52.88, 47.59, 47.36, 30.38, 28.61, 27.39 (d, J = 4.8 Hz).HRMS (ESI) cald. for $(M+K)^+$ $C_{22}H_{32}N_2O_9S$: 539.14601, found, 539.14632.



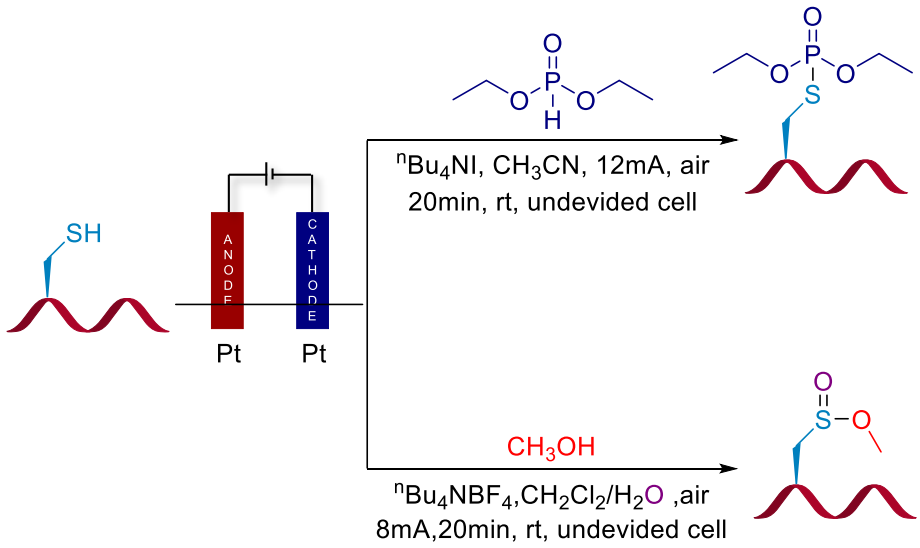
7f

Methyl N-(N^2,N^6-bis(tert-butoxycarbonyl)-D-lysyl)(methoxysulfinyl)-L-alaninate (7f).

73.4 mg (yield: 72%, 0.2 mmol scale), colorless oil. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.50 (dd, J = 8.0, 3.2 Hz, 1H), 6.85 – 6.59 (m, 2H), 4.66 – 4.57 (m, 1H), 3.93 – 3.85 (m, 1H), 3.69 (d, J = 2.4 Hz, 3H), 3.66 (s, 3H), 3.24 – 3.17 (m, 1H), 3.07 (ddd, J = 13.5,

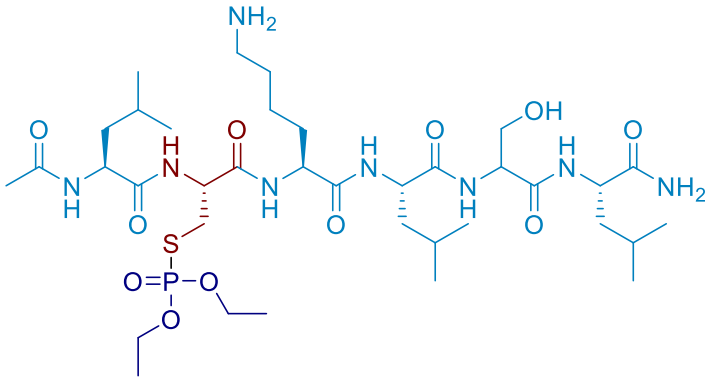
9.9, 6.6 Hz, 1H), 2.92 – 2.85 (m, 2H), 1.62 – 1.44 (m, 3H), 1.42 (s, 1H), 1.38 (d, J = 3.8 Hz, 20H). ^{13}C NMR (101 MHz, DMSO-d6) δ 170.73 (d, J = 4.0 Hz), 156.04, 155.73, 78.54, 77.80, 57.85, 57.64, 54.68 (d, J = 6.0 Hz), 54.40, 54.04, 52.85, 47.46 (d, J = 17.3 Hz), 40.11, 31.84 (d, J = 5.9 Hz), 29.64, 28.69 (d, J = 9.9 Hz), 28.40, 23.10. HRMS (ESI) cald. for $(M+H)^+$ $C_{21}H_{39}N_3O_9S$: 510.24798, found, 510.24786.

6.5 Polypeptide scope and characterization



General Procedure for Bioconjugation of cystein and diethyl phosphonate : In an oven-dried undivided three-necked bottle (15 mL) equipped with a stir bar, polypeptides (8 mg), diethyl phosphonate (10 mg), CH_3CN (3 mL), $^nBu_4NI$ (20.0 mg) were combined and added. The bottle was equipped platinum plate (10 mm×10 mm×0.3 mm) as the anode and platinum plate (10 mm×10 mm×0.3 mm) as the cathode and then charged. The reaction mixture was stirred and electrolyzed at constant current of 12 mA under room temperature for 15 min. General Procedure for Bioconjugation of cystein and CH_3OH : In an oven-dried undivided three-necked bottle (15 mL) equipped with a stir bar, polypeptides (8 mg), CH_3OH (50 uL), CH_2Cl_2 (3 mL), H_2O (10 uL), $^nBu_4NBF_4$ (20.0 mg) were combined and added. The bottle was equipped platinum plate (10 mm×10 mm×0.3 mm) as the anode and platinum plate (10 mm×10 mm×0.3 mm) as the cathode and then charged. The reaction mixture was stirred and electrolyzed at constant current of 8 mA under room temperature for 20 min. After completion of the reaction, the solution was analyzed by LC-MS/MS spectroscopy. The reaction was analyzed by

reversed-phase HPLC on a 250 mm long ChromCore C18 5µm column using a gradient of 40% buffer B within 22 minutes. HPLC analysis used buffers A (water + 0.1% TFA) and B (acetonitrile + 0.1% TFA). Conversion reported as a % conversion as determined.



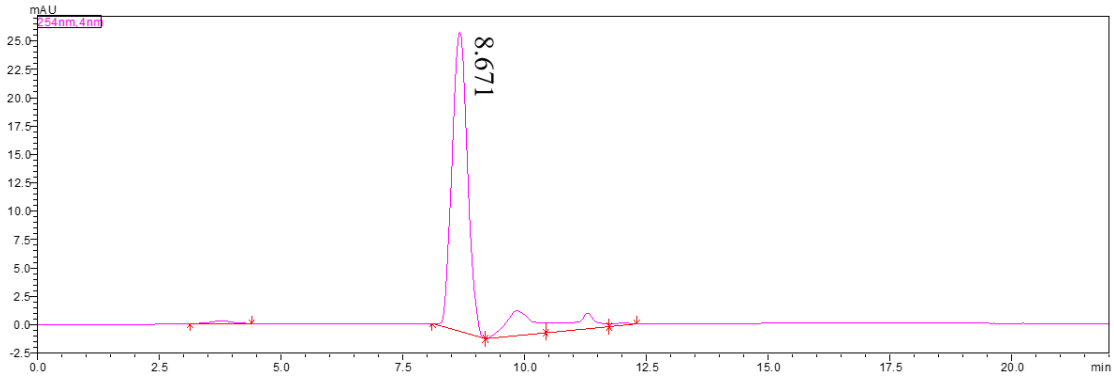
AnxA2 inhibitor:LCKLSL

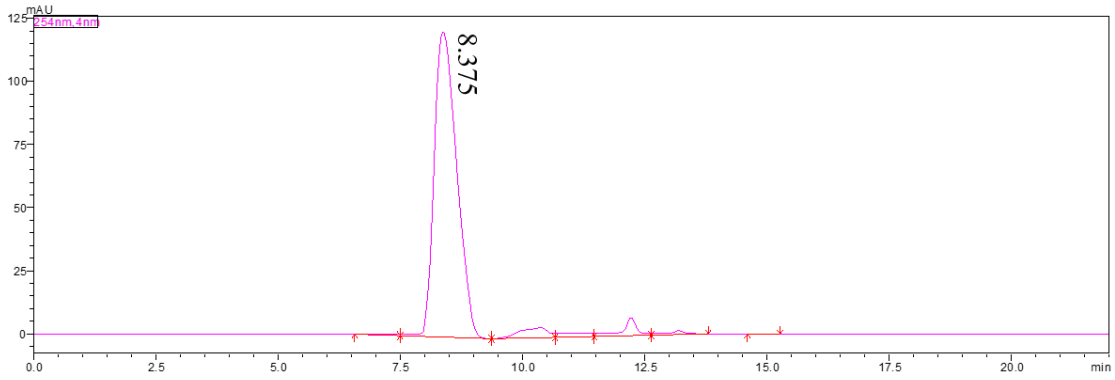
1HPLC: >99% conversion.

Product 8a is a peak that elute at 40% buffer B (acetonitrile + 0.1% TFA) with retention times of 8.375 min. Reactant is a peak that elutes at 40% buffer B with a retention time of 8.671min.

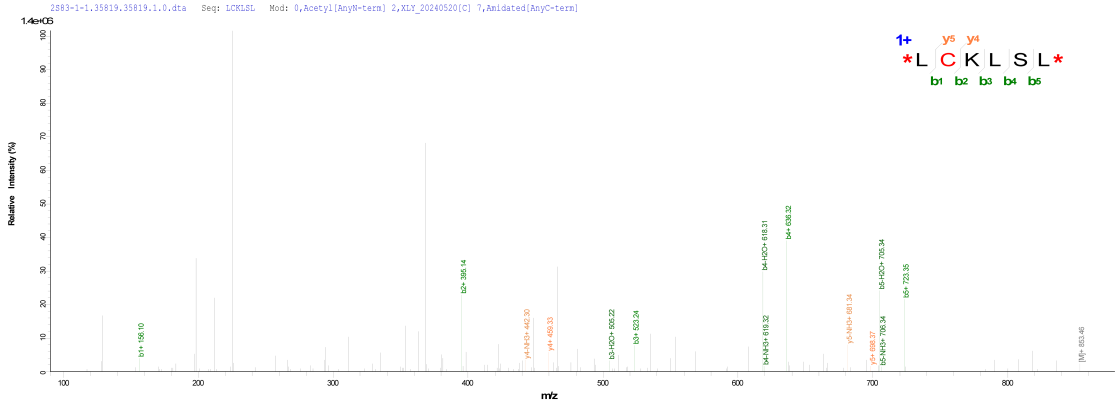
HRMS (ESI-TOF): m/z calculated for $C_{36}H_{69}N_8O_{11}PS$, $[M+H]^+$, 853.4617, found 853.4630.

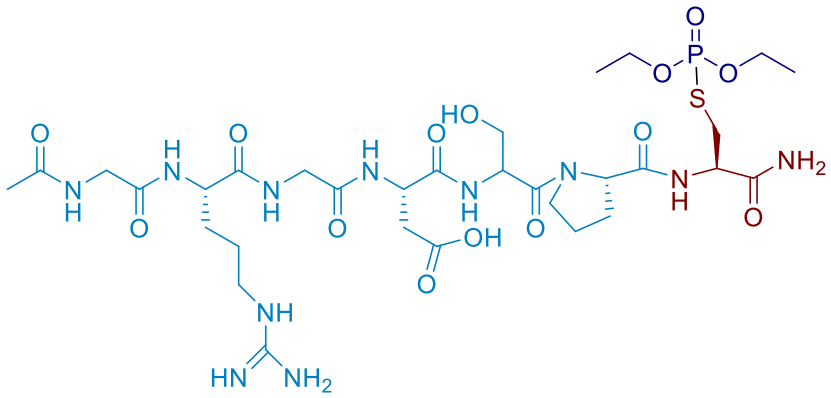
HPLC Spectra:





MALDI-TOF-MS/MS Spectra：





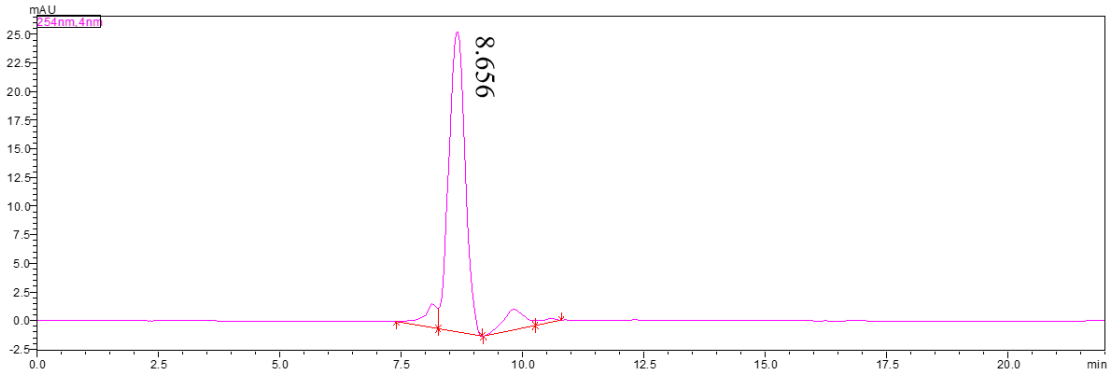
Cell adhesion peptide: GRGDSPC

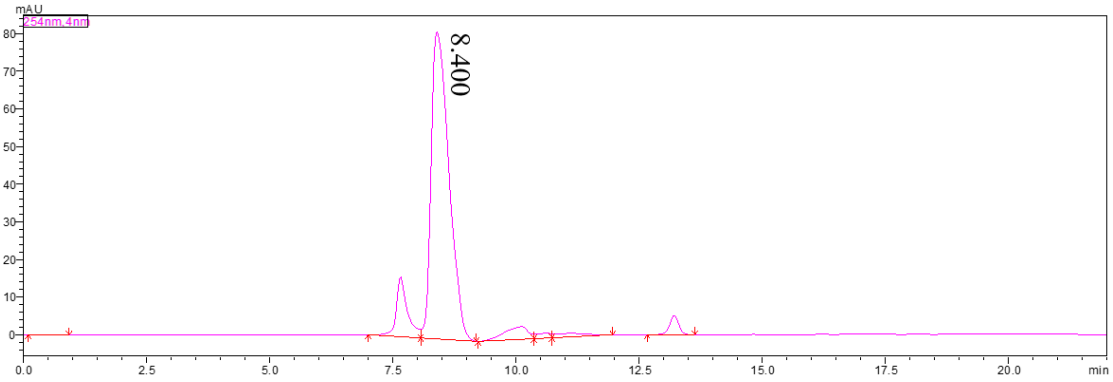
HPLC: >99% conversion.

Product 8b is a peak that elute at 40% buffer B (acetonitrile + 0.1% TFA) with retention times of 8.400 min. Reactant is a peak that elutes at 40% buffer B with a retention time of 8.656 min.

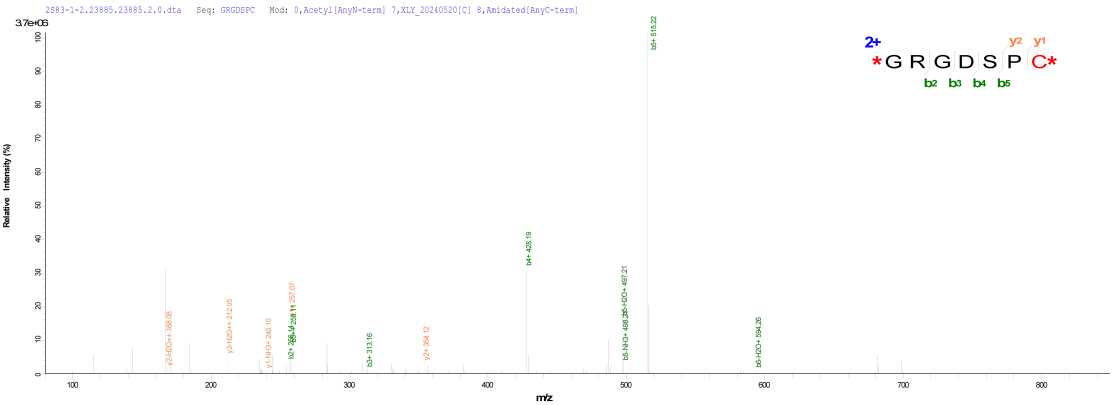
HRMS (ESI-TOF): m/z calculated for $C_{31}H_{54}N_{11}O_{14}PS$, $[M+H]^+$, 868.3383, found 868.3361.

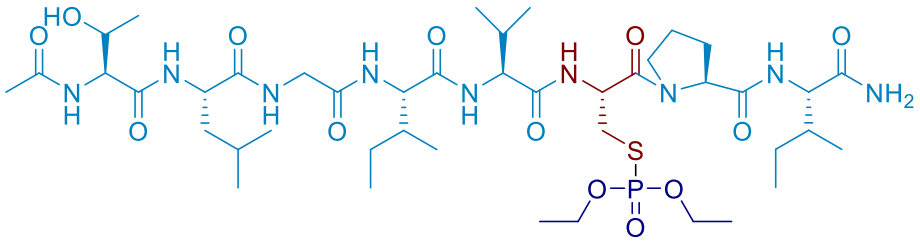
HPLC Spectra:





MALDI-TOF-MS/MS Spectra：





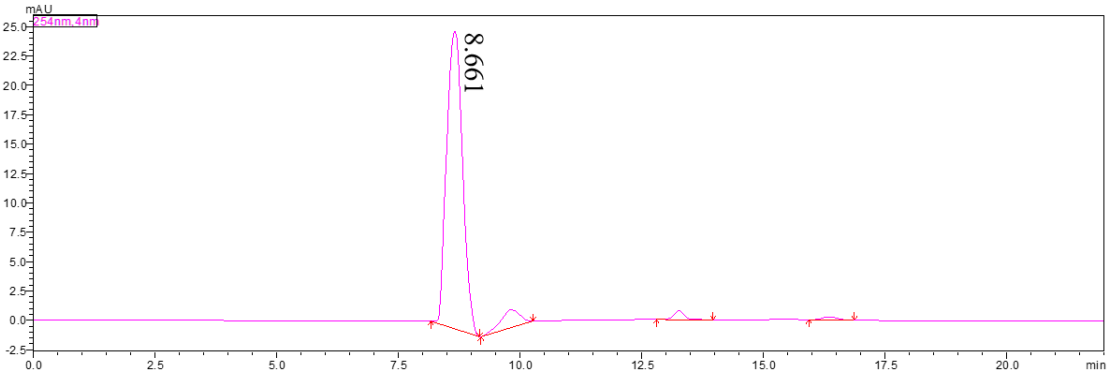
HPV16 E7(86-93): TLGIVCPI

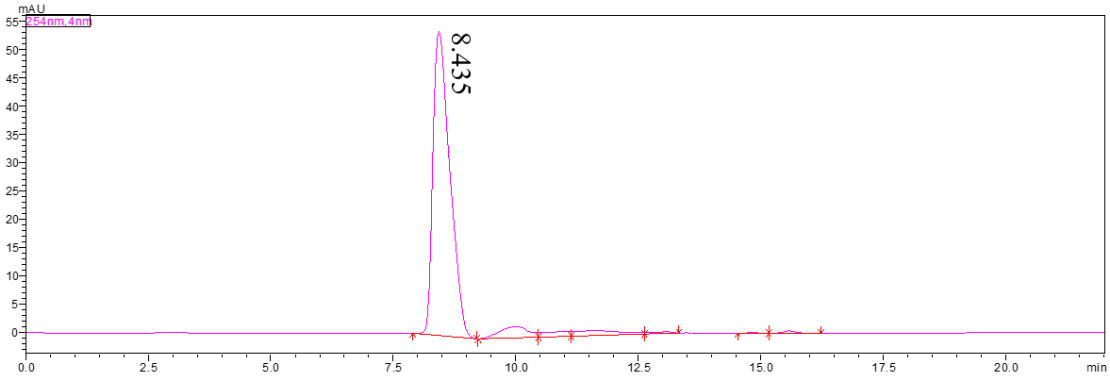
HPLC: >99% conversion.

Product 8c is a peak that elute at 40% buffer B (acetonitrile + 0.1% TFA) with retention times of 8.639 min. Reactant is a peak that elutes at 40% buffer B with a retention time of 8.661 min.

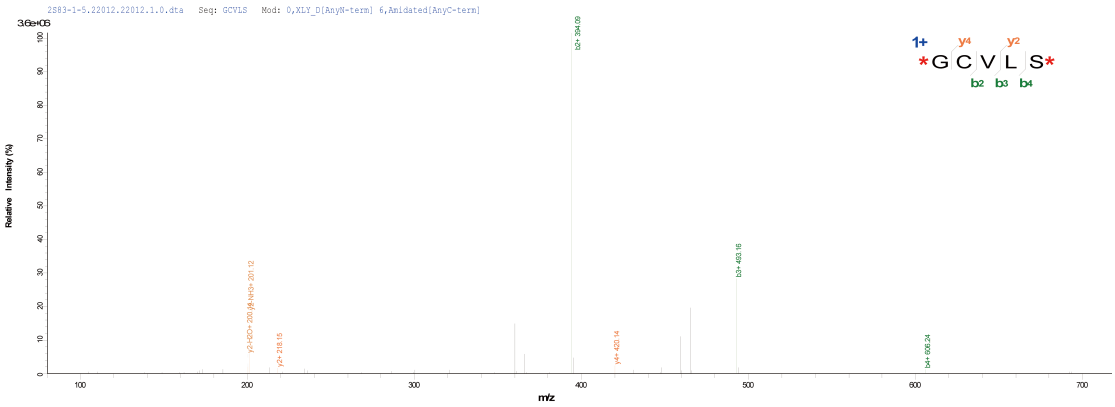
HRMS (ESI-TOF): m/z calculated for $C_{43}H_{78}N_9O_{13}PS$, $[M+H]^+$, 992.5250, found 992.5212.

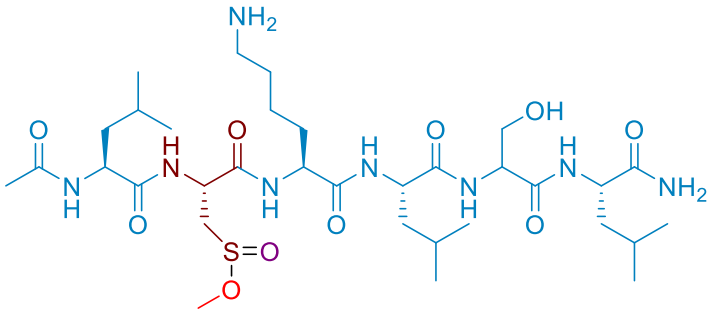
HPLC Spectra:





MALDI-TOF-MS/MS Spectra：





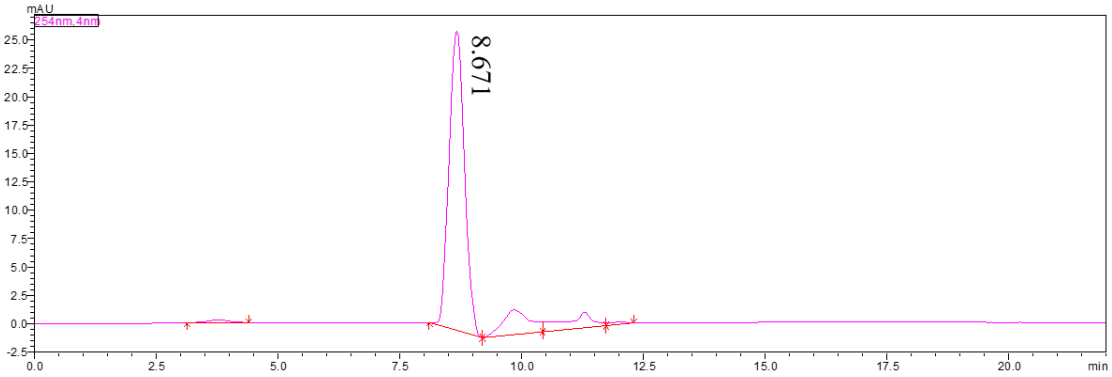
AnxA2 inhibitor:LCKLSL

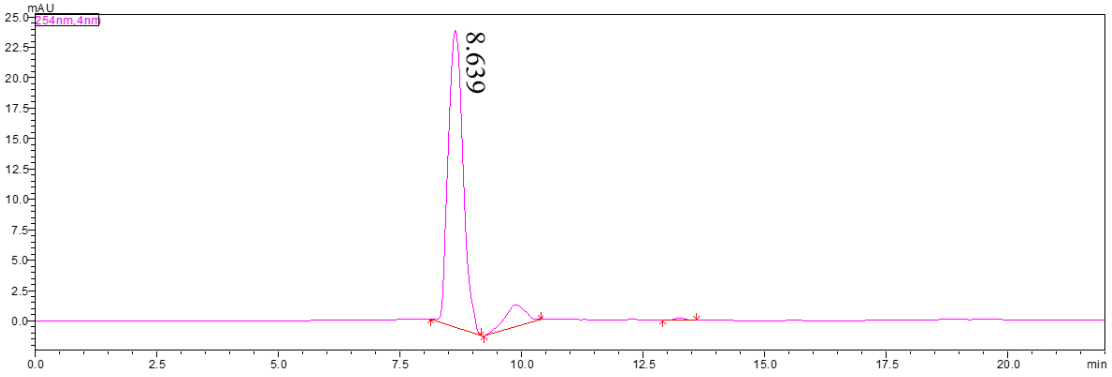
HPLC: >99% conversion.

Product 8d is a peak that elute at 40% buffer B (acetonitrile + 0.1% TFA) with retention times of 8.639 min. Reactant is a peak that elutes at 40% buffer B with a retention time of 8.671 min.

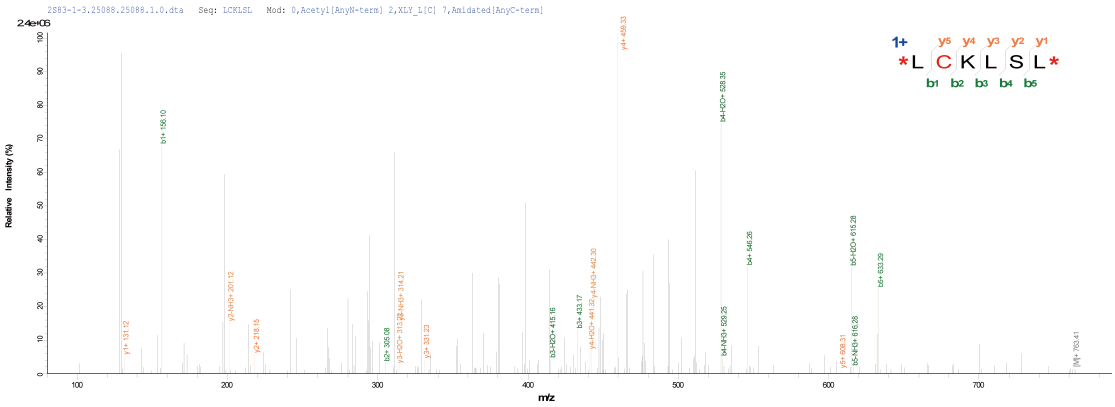
HRMS (ESI-TOF): m/z calculated for $C_{33}H_{62}N_8O_{10}S$, $[M+H]^+$, 763.4382, found 763.4372.

HPLC Spectra:



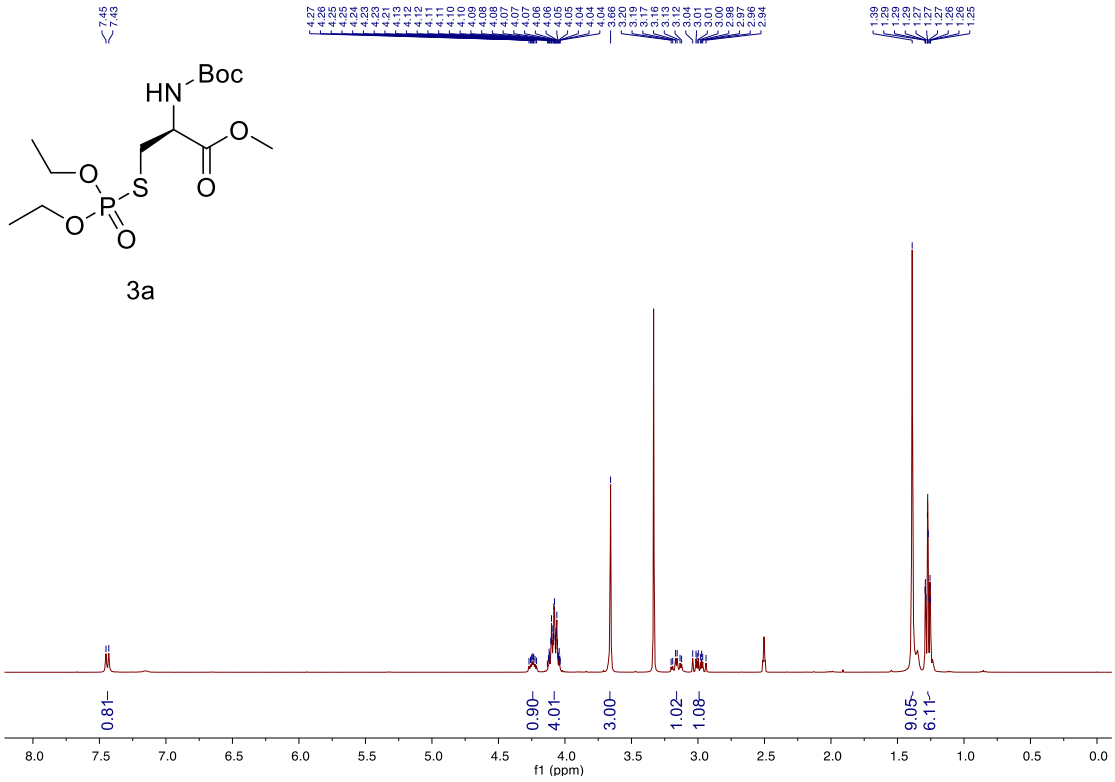


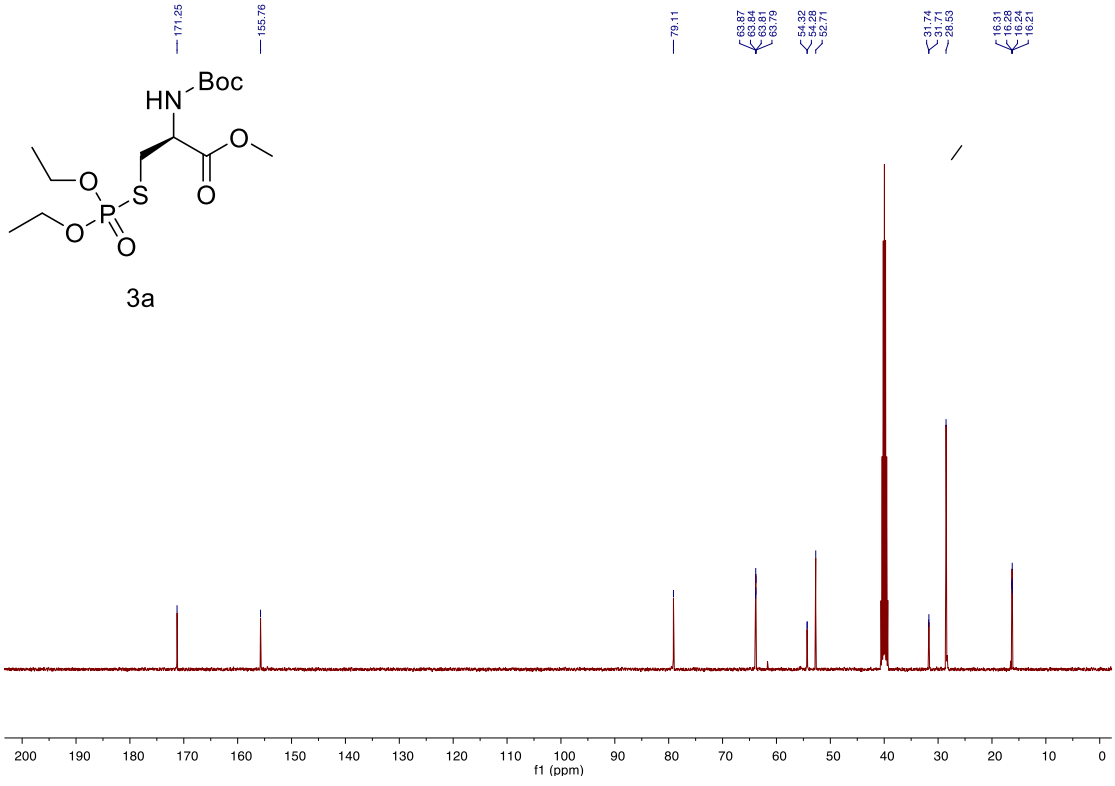
MALDI-TOF-MS/MS Spectra：

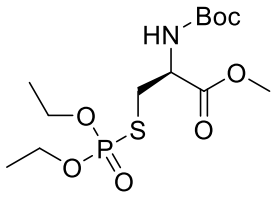


7. Spectra

7.1 NMR Spectra of Products

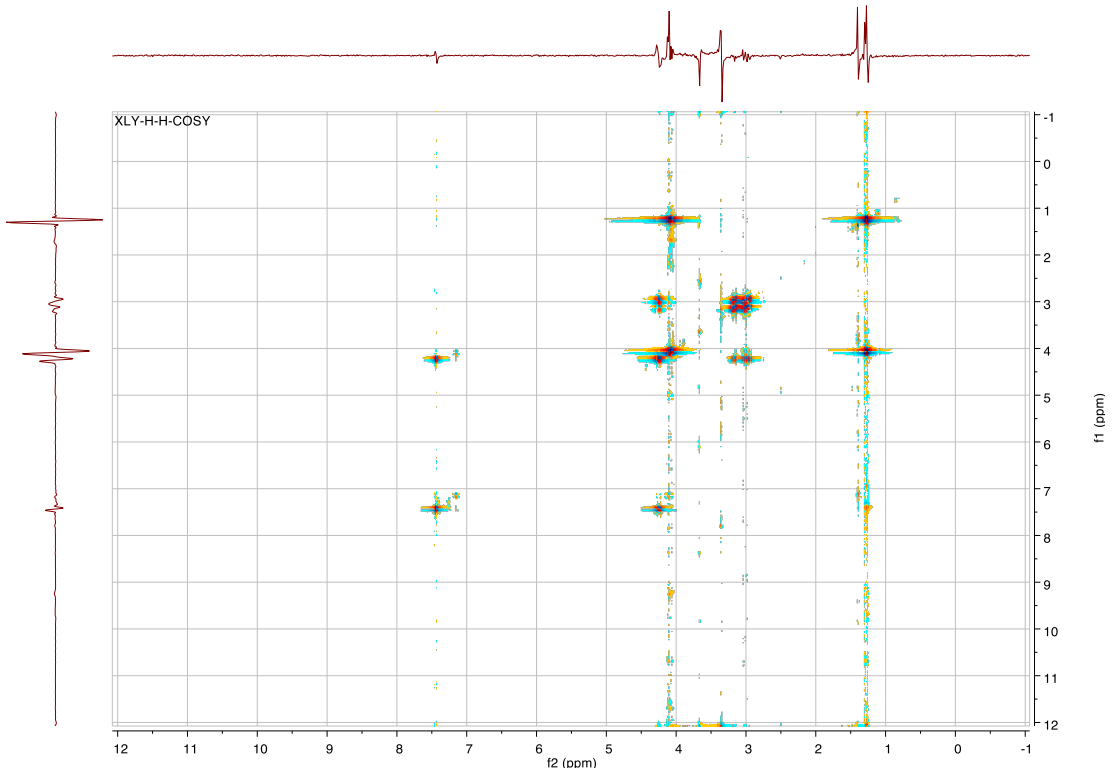


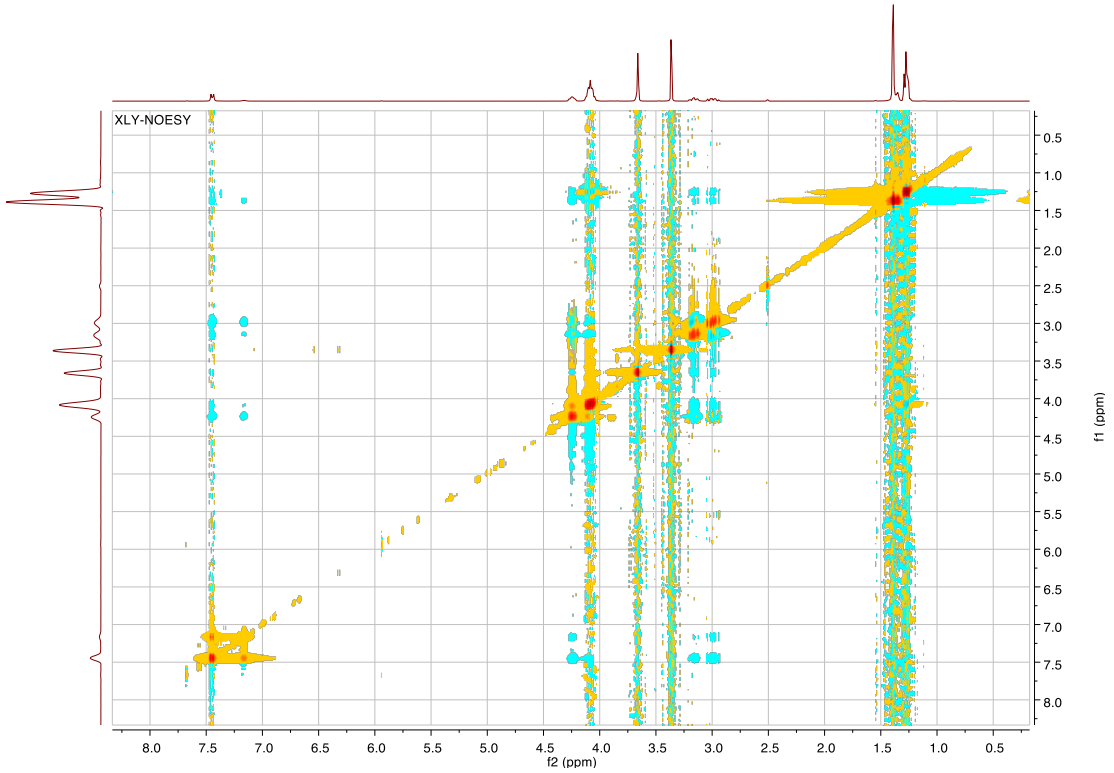


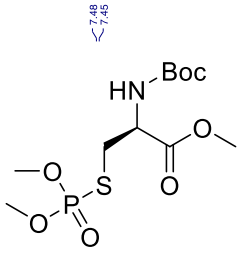

HN
Boc
O
O
S
O
P
O
O

3a

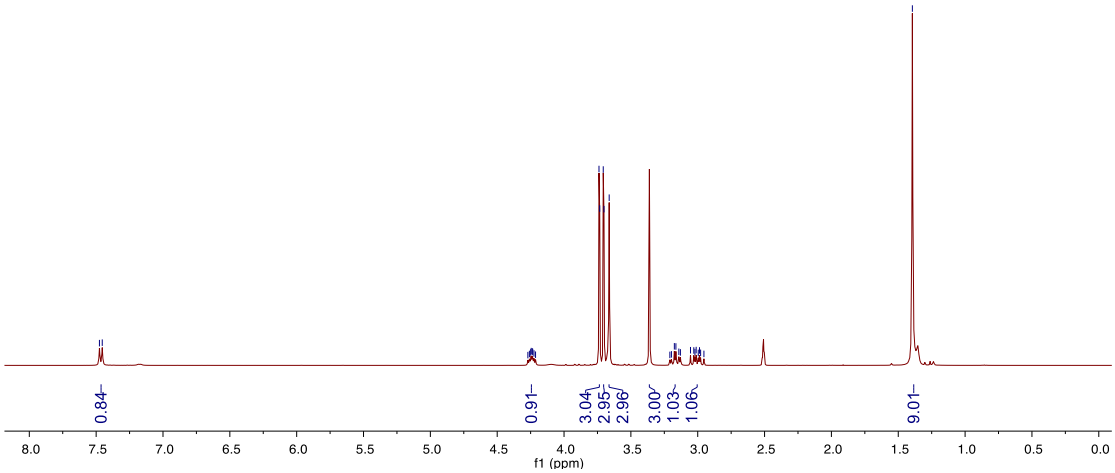
26.03
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

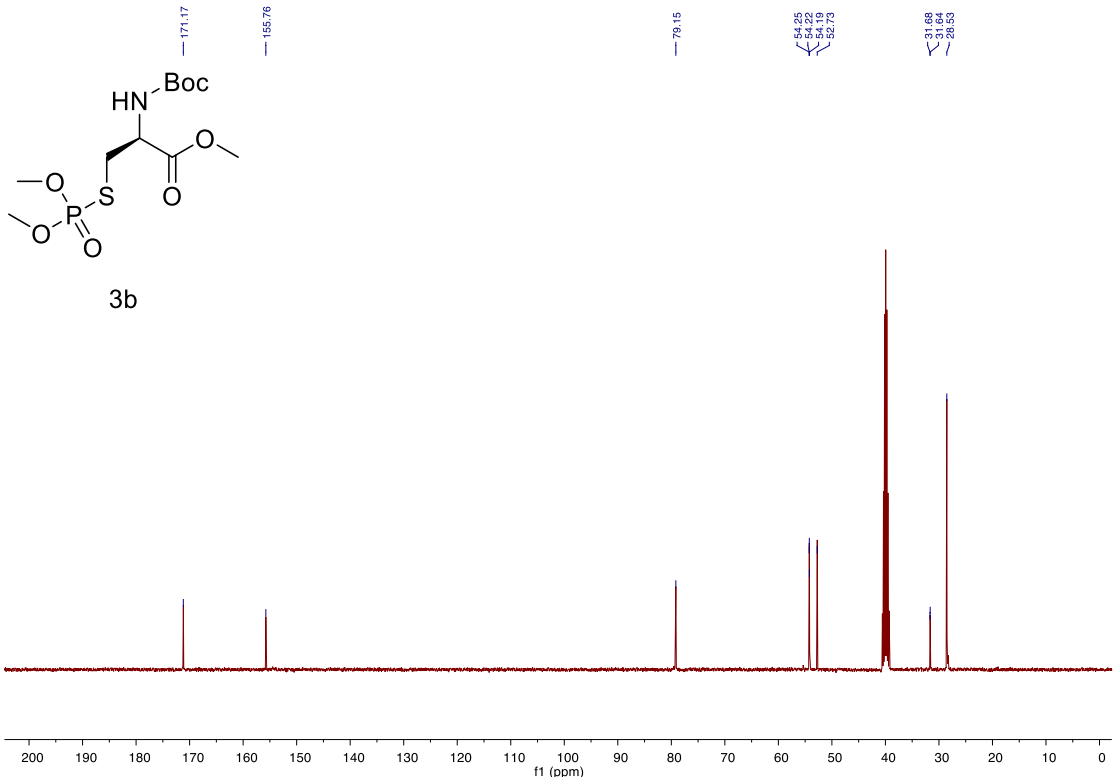

XLY-H-H-COSY
12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f2 (ppm)
-1 0 1 2 3 4 5 6 7 8 9 10 11 12
f1 (ppm)

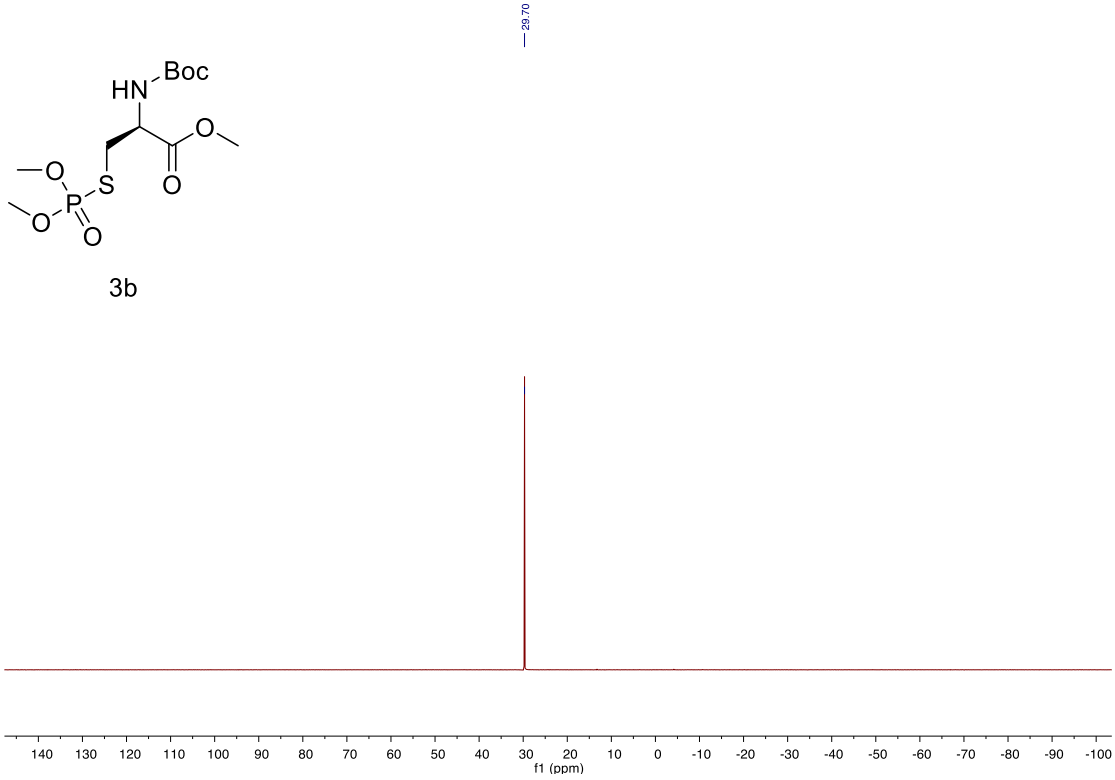

XLY-NOESY
f2 (ppm)
f1 (ppm)

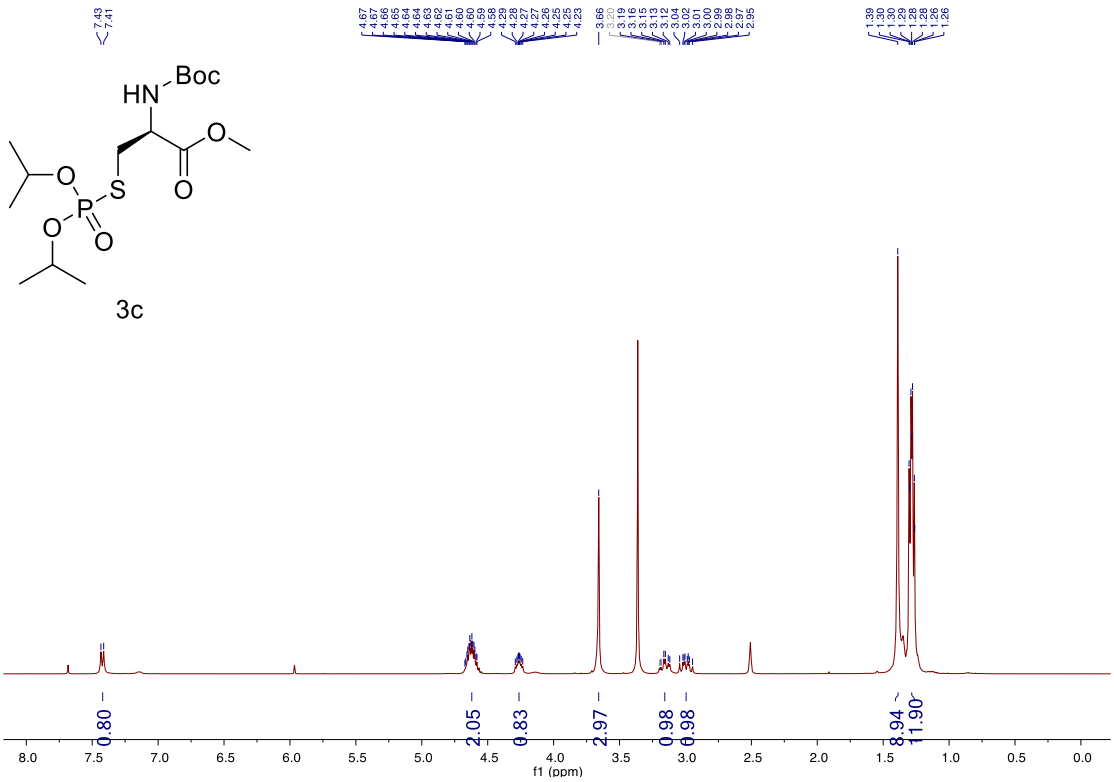

HN
Boc
O
O
S
O
P
O
O

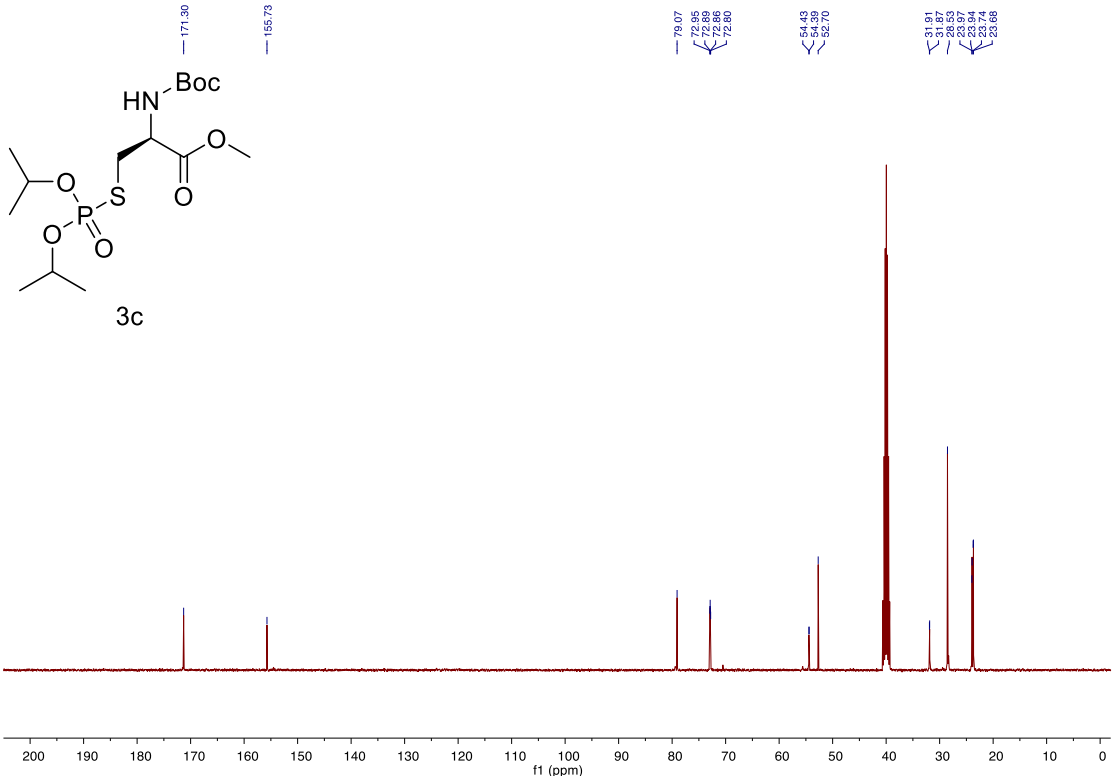
3b

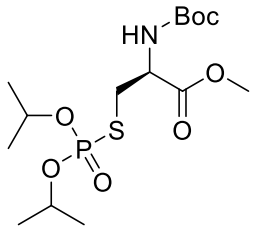

0.84
0.91
3.04
2.95
2.96
3.00
1.03
1.06
9.01
f1 (ppm)


171.17
155.76
79.15
54.25
54.22
54.19
52.73
31.68
31.64
28.53
HN
Boc
O
O
O
S
O
P
O
O
3b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


29.70
HN
Boc
O
O
O
S
O
P
O
O
3b
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

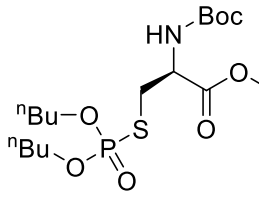

HN
Boc
O
O
S
P
O
O
O
3c
f1 (ppm)


HN
Boc
O
O
S
P
O
O
O
3c
f1 (ppm)


HN
Boc
O
O
S
O
P
O
O

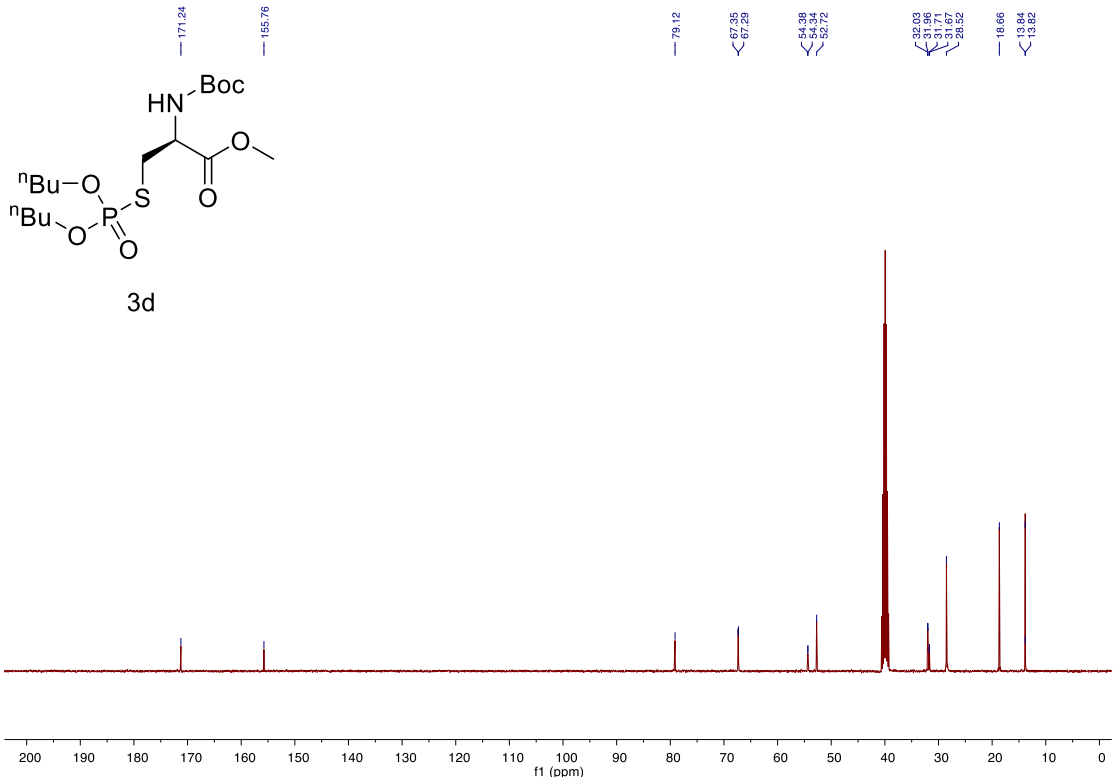
3c

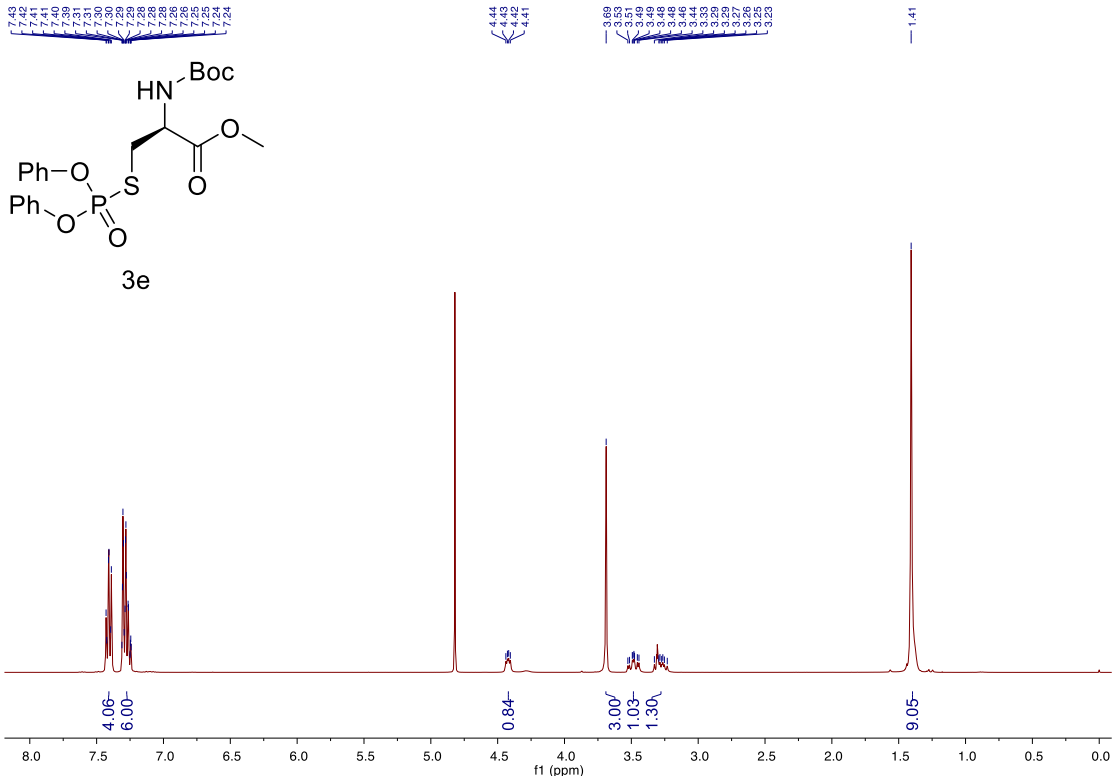
23.56
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

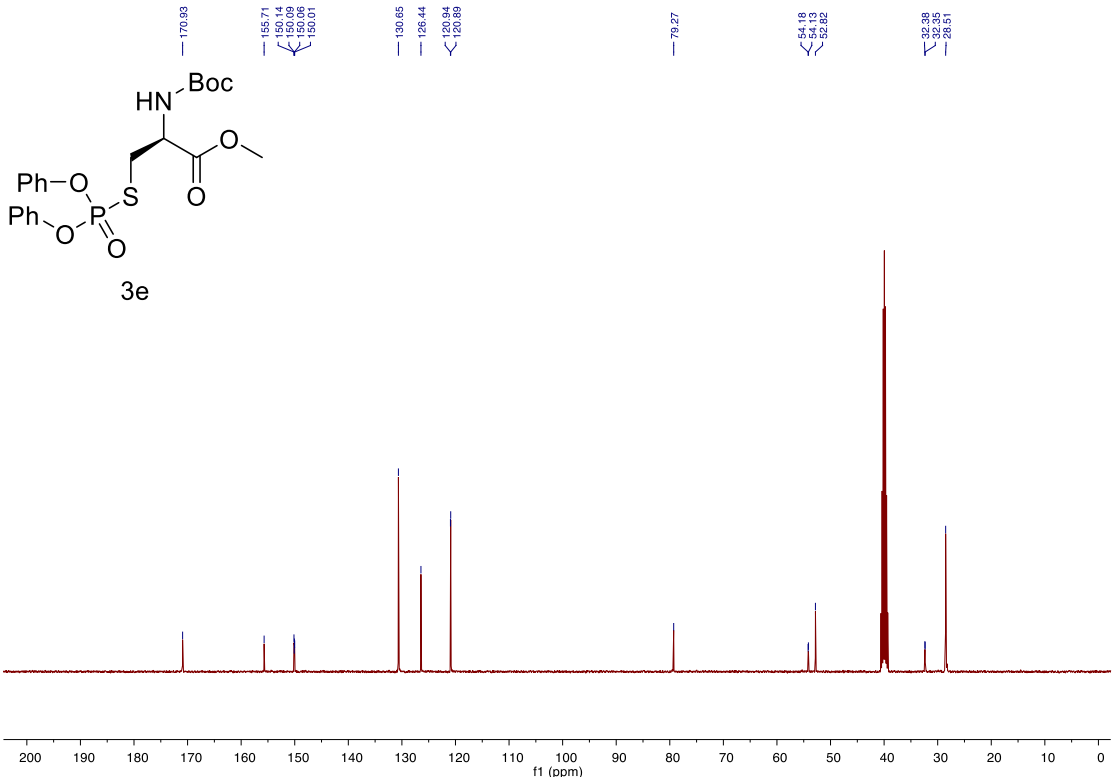

HN
Boc
O
O
nBu
O
S
nBu
O
P
O

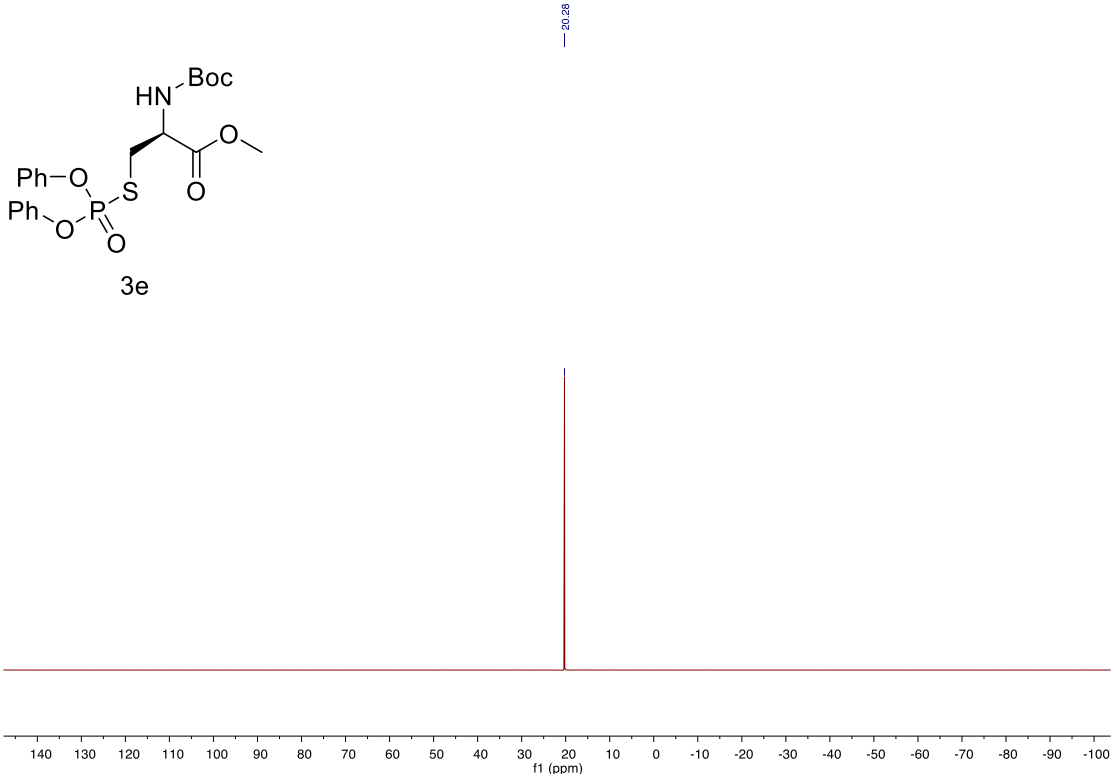
3d

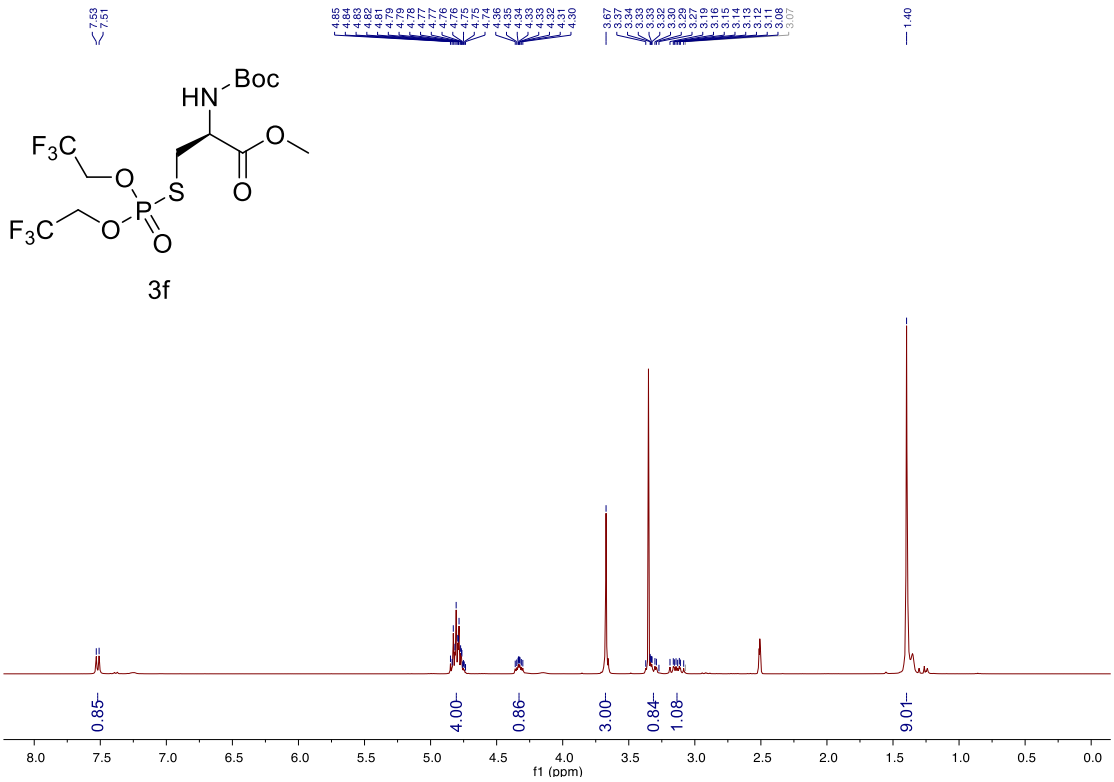
7.44
7.42
0.80
0.90
4.04
3.00
1.03
1.05
4.02
8.97
3.97
6.02
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

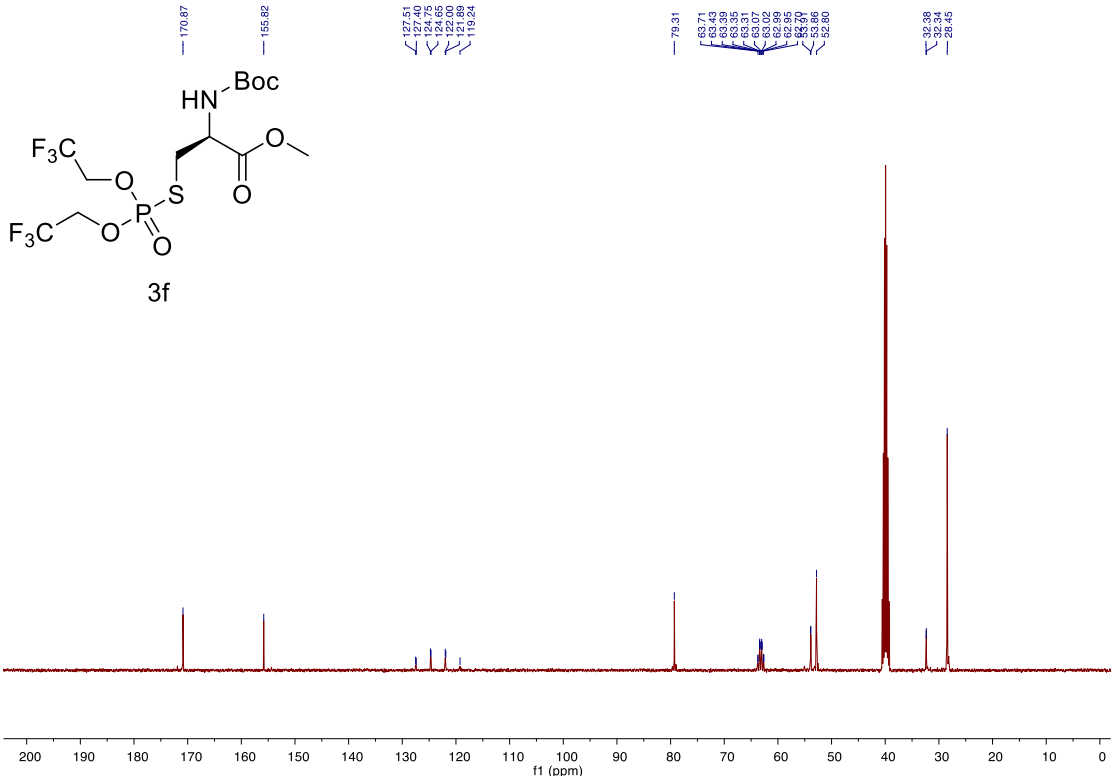

171.24
155.76
79.12
67.35
67.29
54.38
54.34
52.72
32.03
31.96
31.77
31.67
28.52
18.66
13.84
13.82
HN
Boc
O
O
nBu–O
nBu
O
P
S
O
3d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

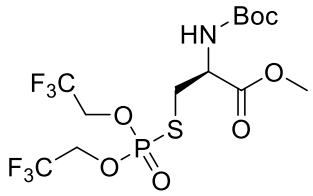

7.43
7.42
7.41
7.41
7.40
7.39
7.31
7.31
7.30
7.30
7.29
7.29
7.28
7.28
7.28
7.26
7.26
7.25
7.25
7.24
7.24
4.44
4.43
4.42
4.41
3.69
3.53
3.51
3.49
3.49
3.48
3.46
3.44
3.33
3.29
3.29
3.27
3.26
3.25
3.23
1.41
HN
Boc
O
O
Ph–O
Ph
O
P
S
O
3e
4.06
6.00
0.84
3.00
1.03
1.30
9.05
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


170.93
155.71
150.14
150.09
150.06
150.01
130.65
126.44
120.94
120.89
79.27
54.18
54.13
52.82
32.38
32.35
28.51
HN
Boc
O
Ph
O
S
O
Ph
O
P
O
3e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


20.28
HN
Boc
O
Ph
O
S
O
Ph
O
P
O
3e
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

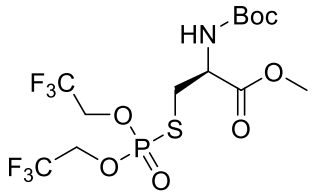

HN
Boc
F3C
O
S
O
O
F3C
O
P
O
3f
0.85
4.00
0.86
3.00
0.84
1.08
9.01
f1 (ppm)


HN
Boc
F3C
O
S
O
O
F3C
O
P
O
3f
f1 (ppm)


HN
Boc
O
O
S
P
O
O
F3C
O
F3C
O

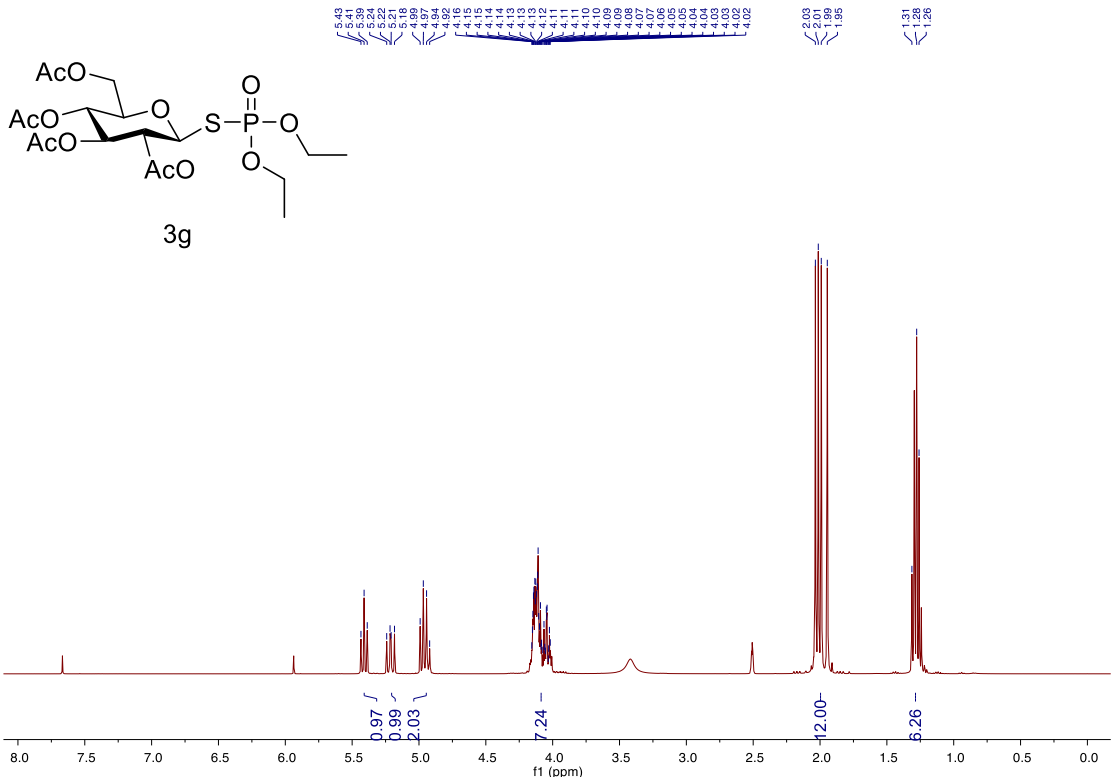
3f

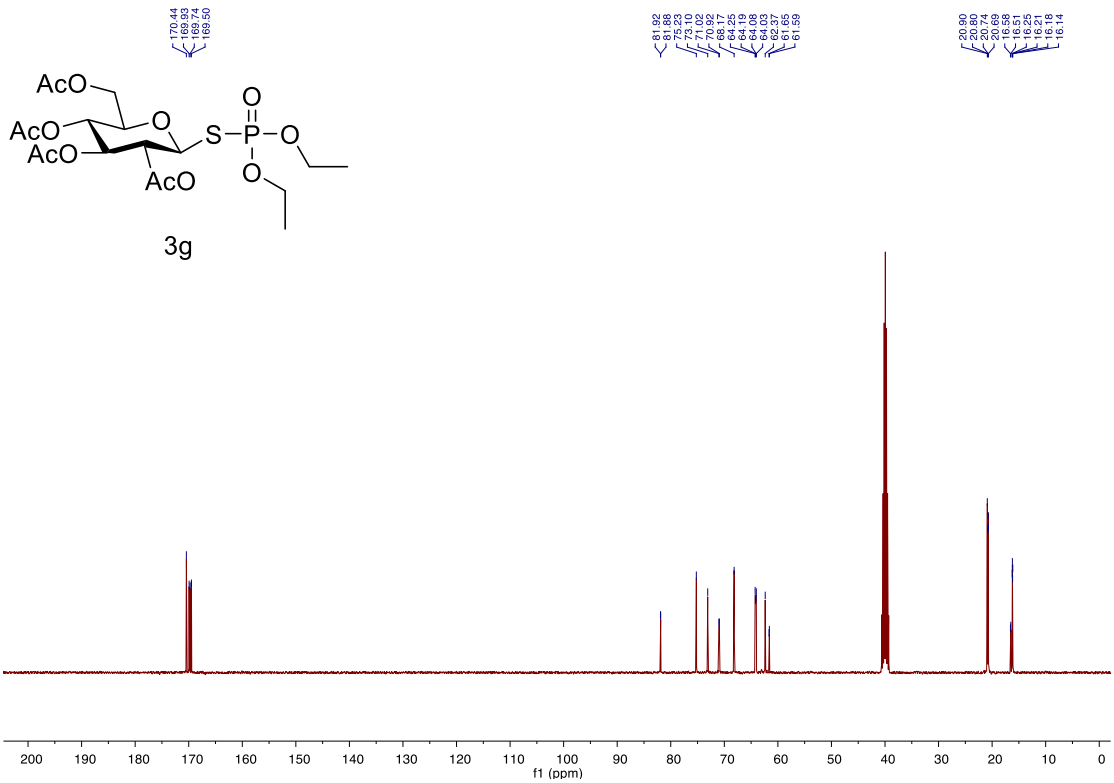
29.80
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
f1 (ppm)

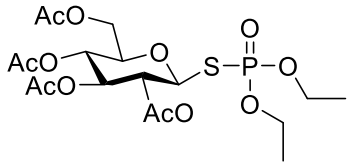

HN
Boc
O
O
S
P
O
O
F3C
O
F3C
O

3f

-73.75
-73.77
-73.79
-73.82
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)

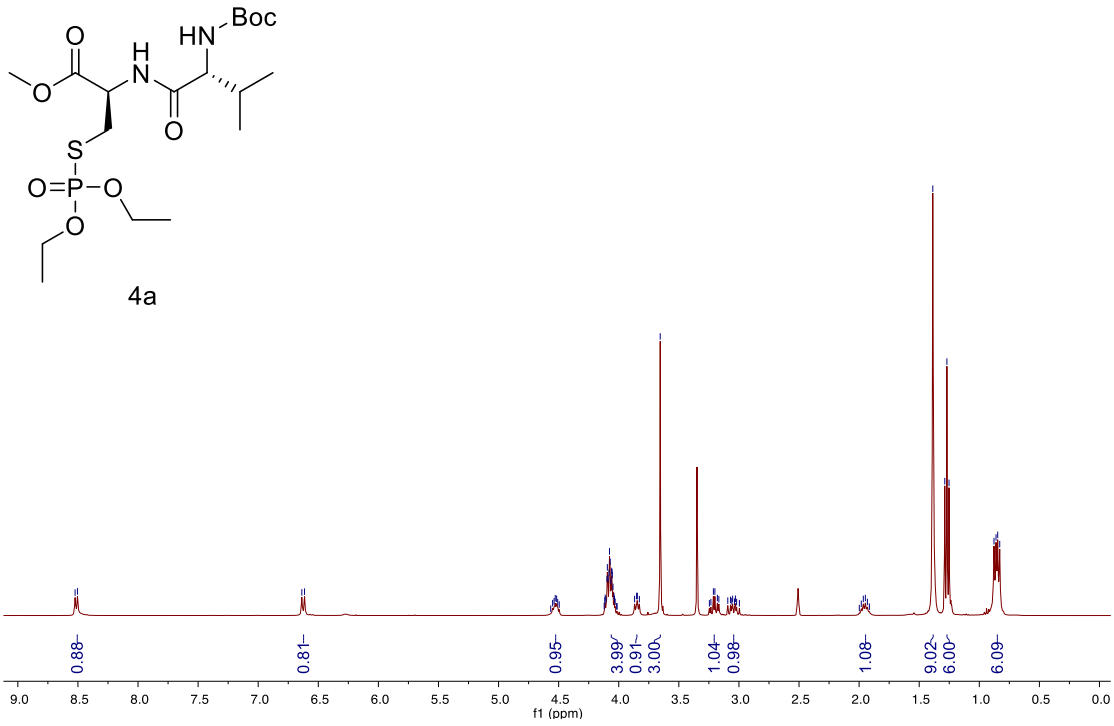

AcO
AcO
AcO
AcO
O
S
P
O
O
O
3g
0.97
0.99
2.03
7.24
12.00
6.26
f1 (ppm)


AcO
AcO
AcO
AcO
O
S
P
O
O
O
3g
f1 (ppm)

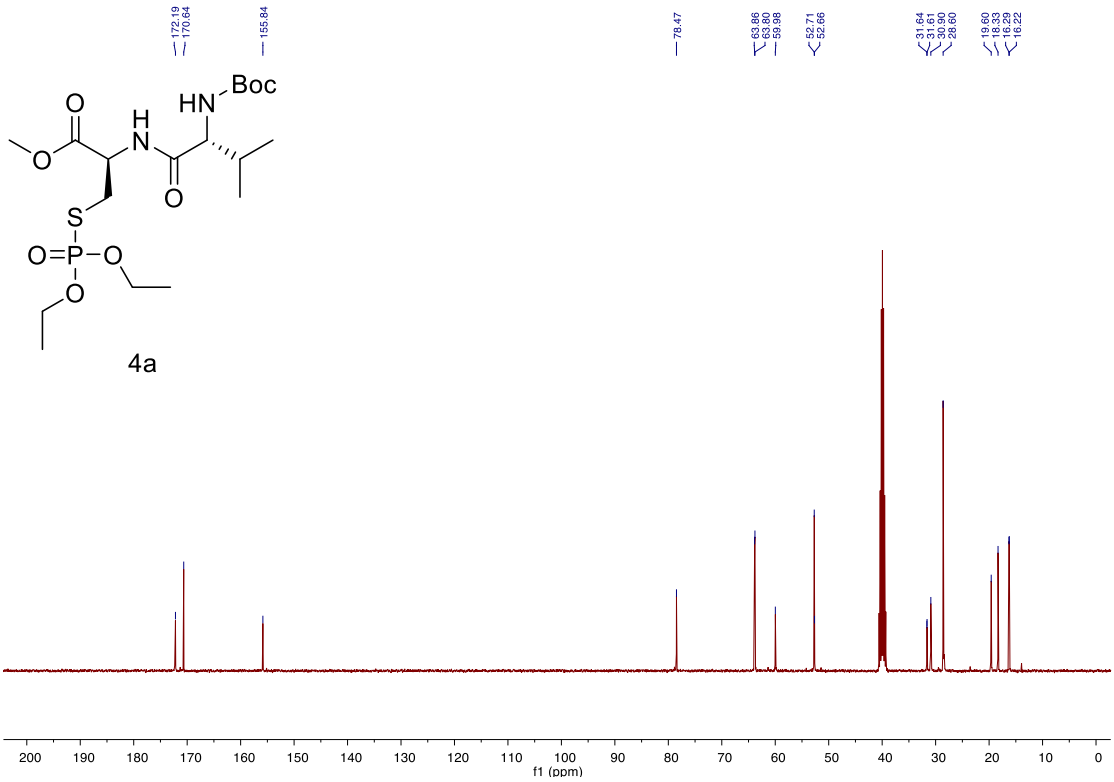

AcO
AcO
AcO
AcO
O
S
P
O
O
O

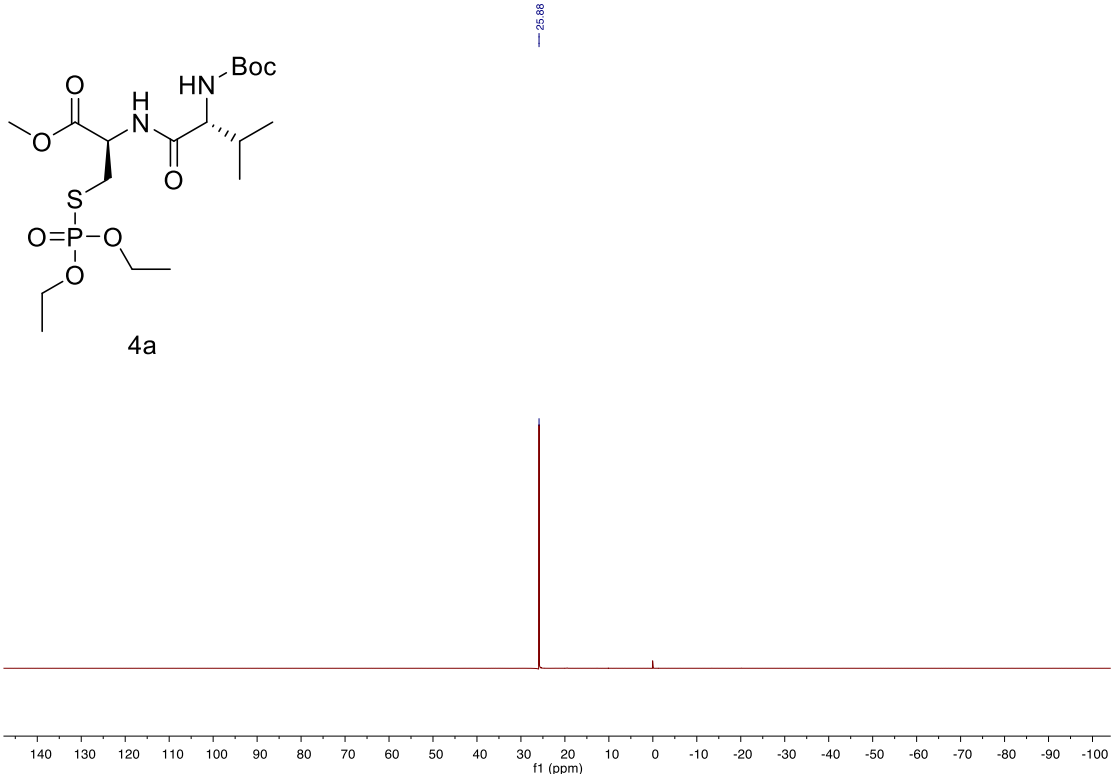
3g

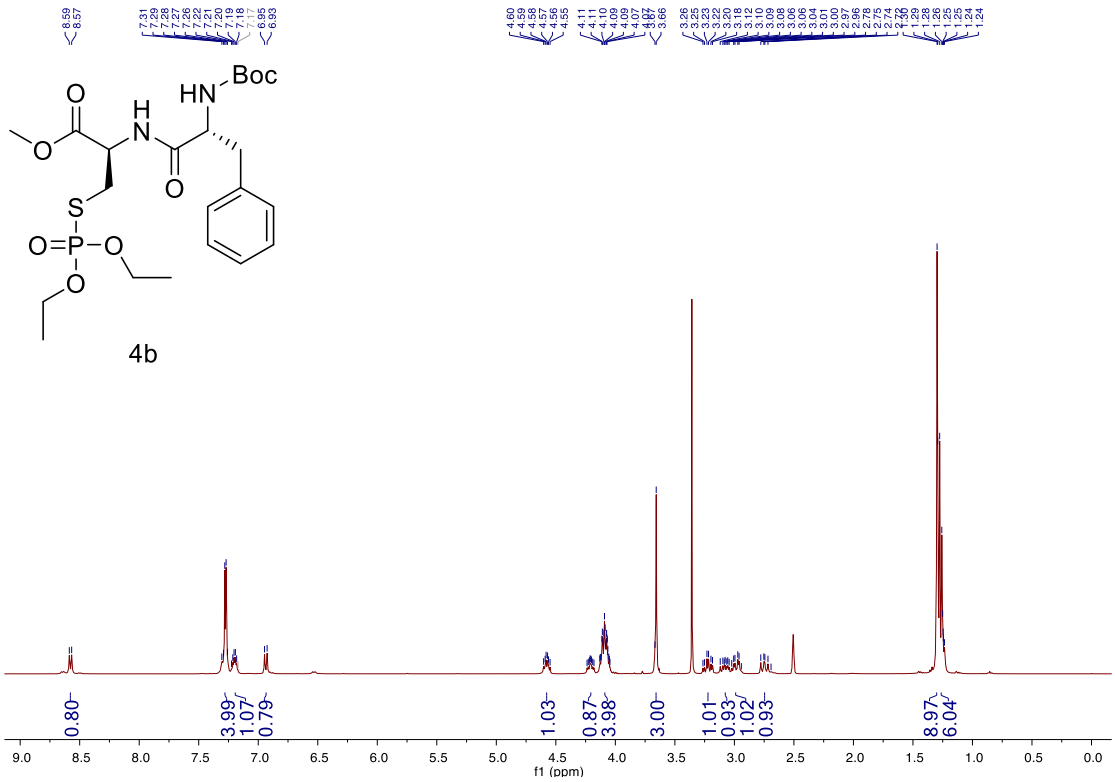
21.47
f1 (ppm)

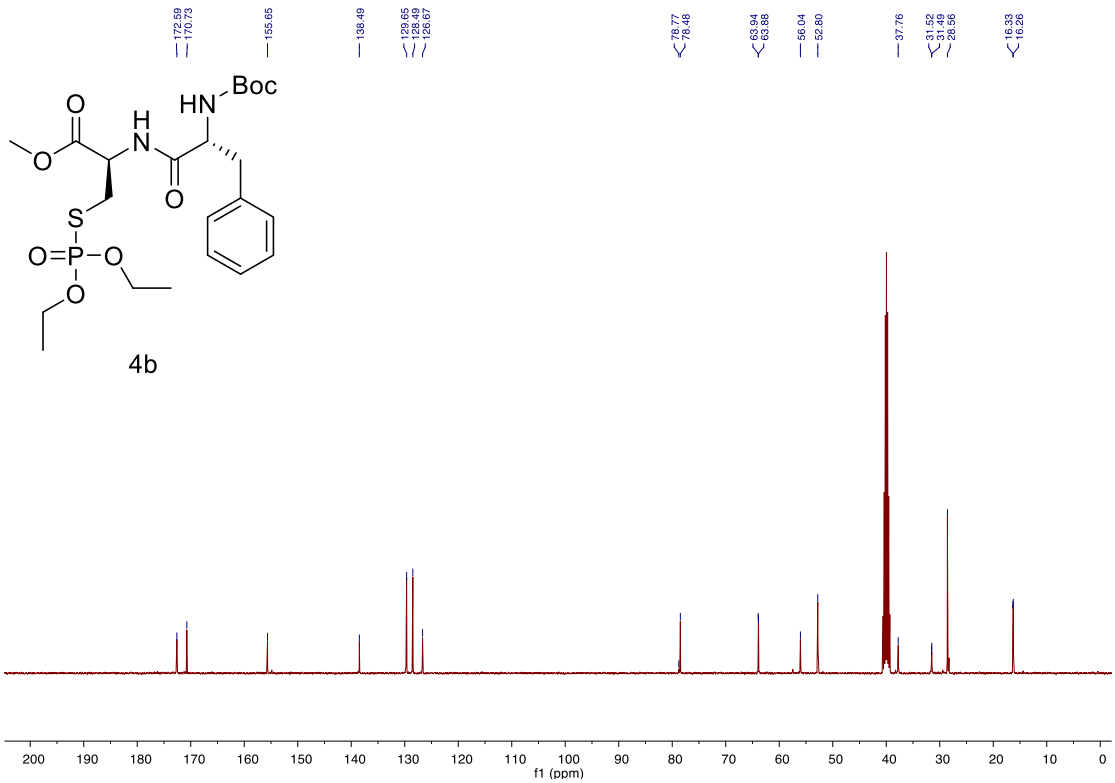

8.52
8.50
6.64
6.61
4.57
4.55
4.54
4.53
4.52
4.51
4.50
4.09
4.09
4.08
4.08
4.08
4.07
4.06
4.06
4.05
3.65
3.23
3.21
3.20
3.18
3.17
3.09
3.07
3.06
3.05
3.04
3.03
3.02
1.98
1.97
1.95
1.93
1.91
1.39
1.29
1.27
1.25
0.88
0.86
0.85
0.83
0.88
0.81
0.95
3.99
0.91
3.00
1.04
0.98
1.08
9.02
6.00
6.09
f1 (ppm)

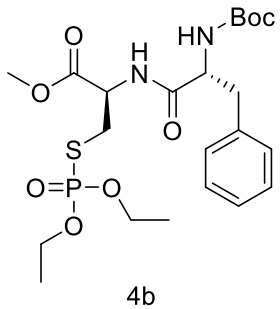
4a


172.19
170.64
155.84
78.47
63.86
63.80
59.98
52.71
52.66
31.64
31.61
30.90
28.60
19.60
18.33
16.20
16.22
Boc
HN
H
N
O
O
O
S
O=P−O
O
4a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


25.88
Boc
HN
H
N
O
O
O
S
O=P−O
O
4a
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

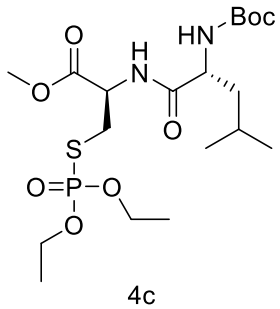

4b
f1 (ppm)


4b
f1 (ppm)



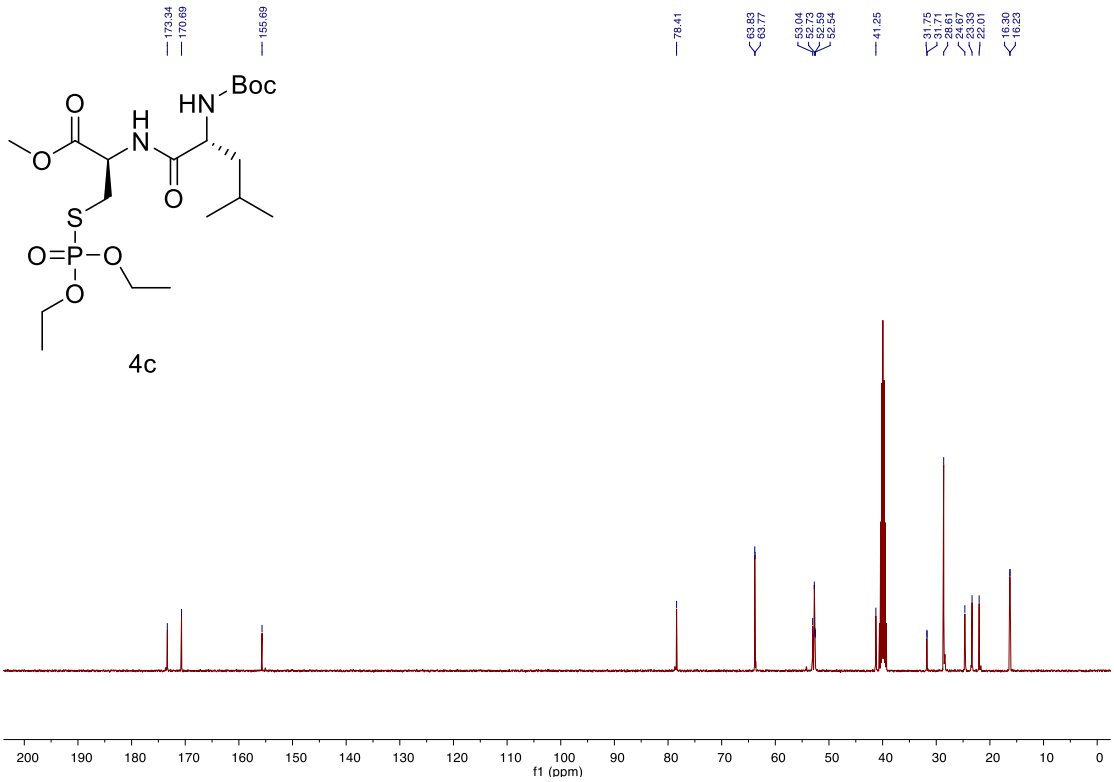
4b

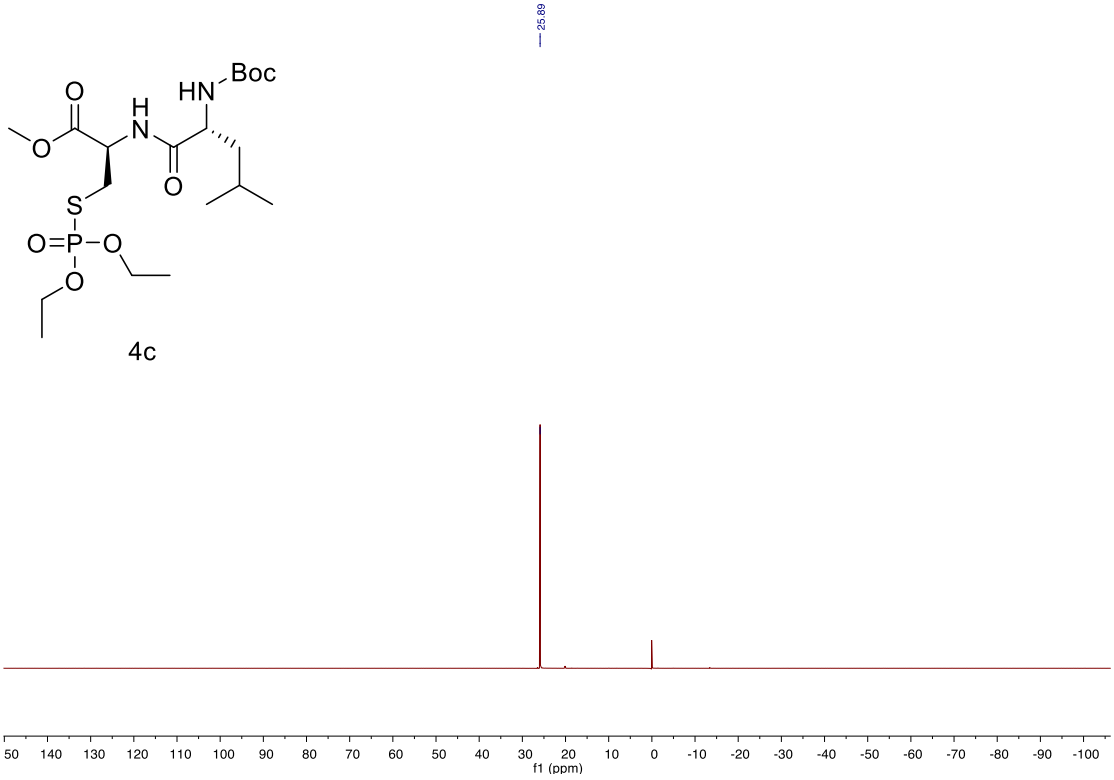
25.87
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

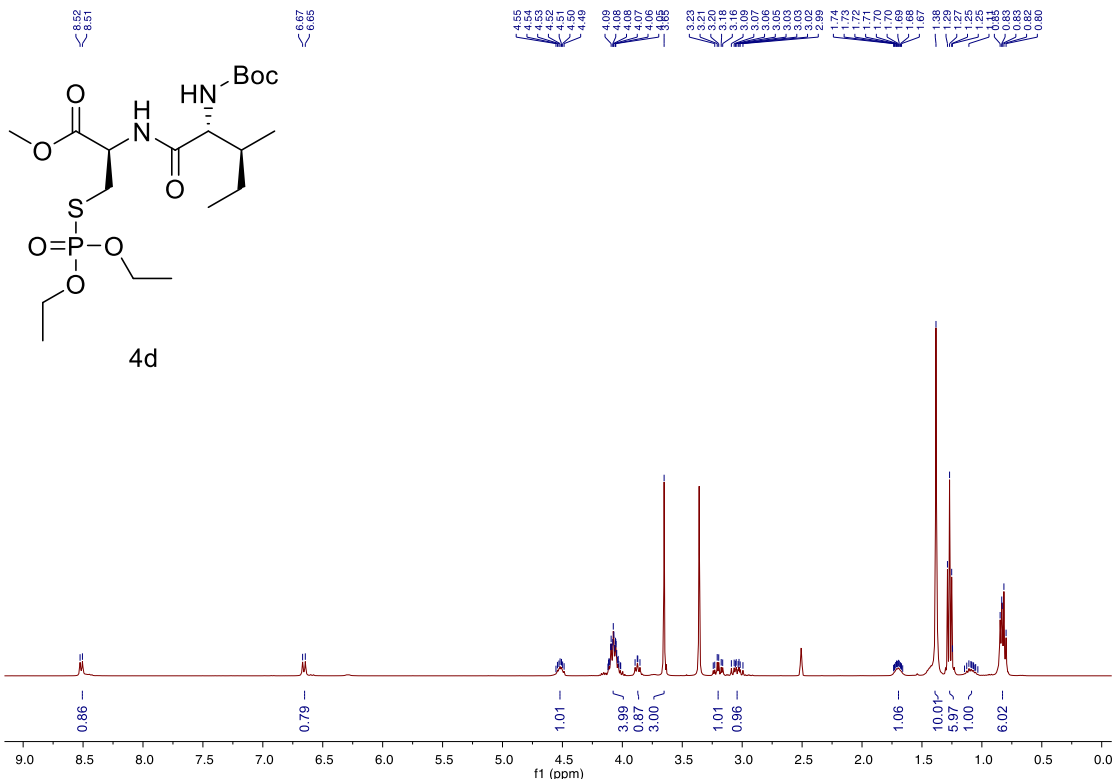


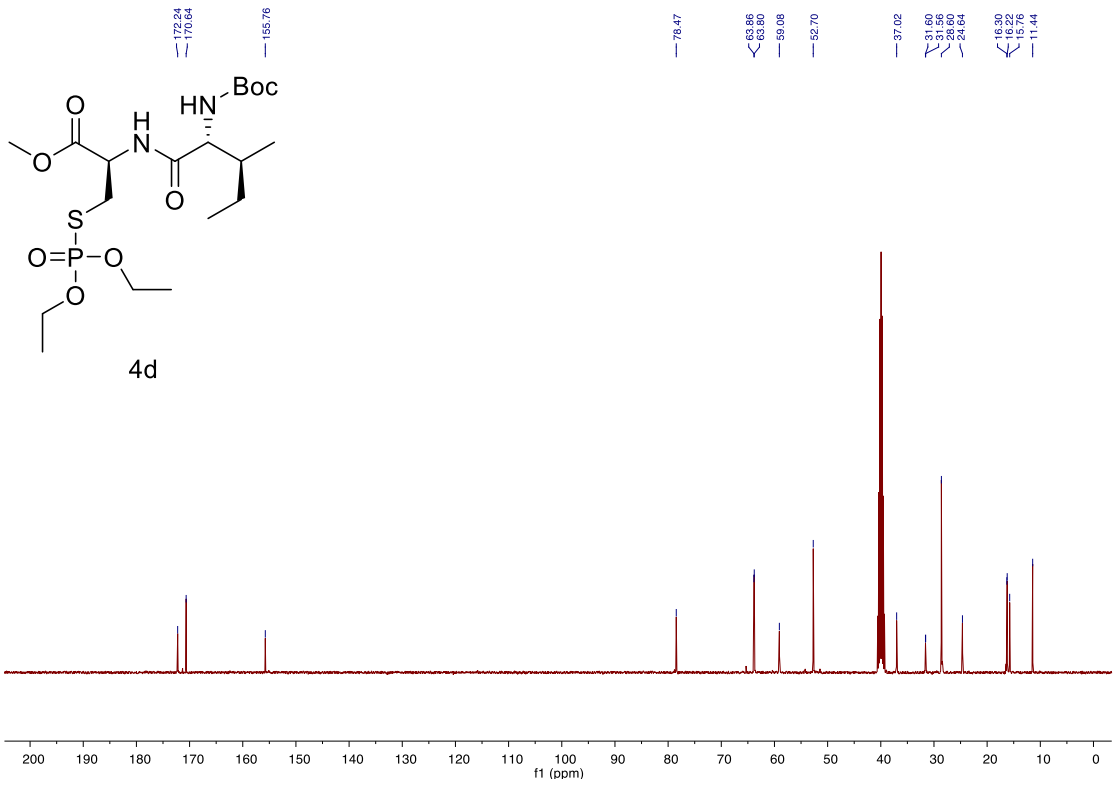
4c

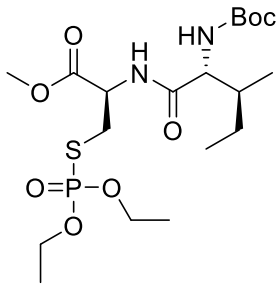
8.46
8.44
6.87
6.85
4.55 4.54 4.53 4.52 4.51 4.50
4.09 4.08 4.08 4.07 4.06 4.05
3.24 3.23 3.21 3.20 3.18 3.16 3.10 3.07 3.06 3.06 3.04 3.03 3.02 3.00
1.65 1.63 1.61 1.60 1.58 1.45 1.43 1.41 1.38 1.29 1.27 1.25 0.89 0.87 0.85
0.91 0.80 0.98 5.00 3.00 1.08 1.11 0.98 2.02 8.95 6.03 6.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


173.34
170.69
155.69
78.41
63.83
63.77
53.04
52.73
52.59
52.54
41.25
31.75
31.71
28.61
24.67
23.33
22.01
16.30
16.23
Boc
HN
H
N
O
O
O
O
S
O=P−O
O
4c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


25.89
Boc
HN
H
N
O
O
O
O
S
O=P−O
O
4c
50 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

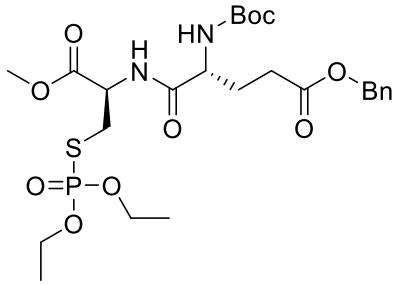

4d
f1 (ppm)


4d
f1 (ppm)



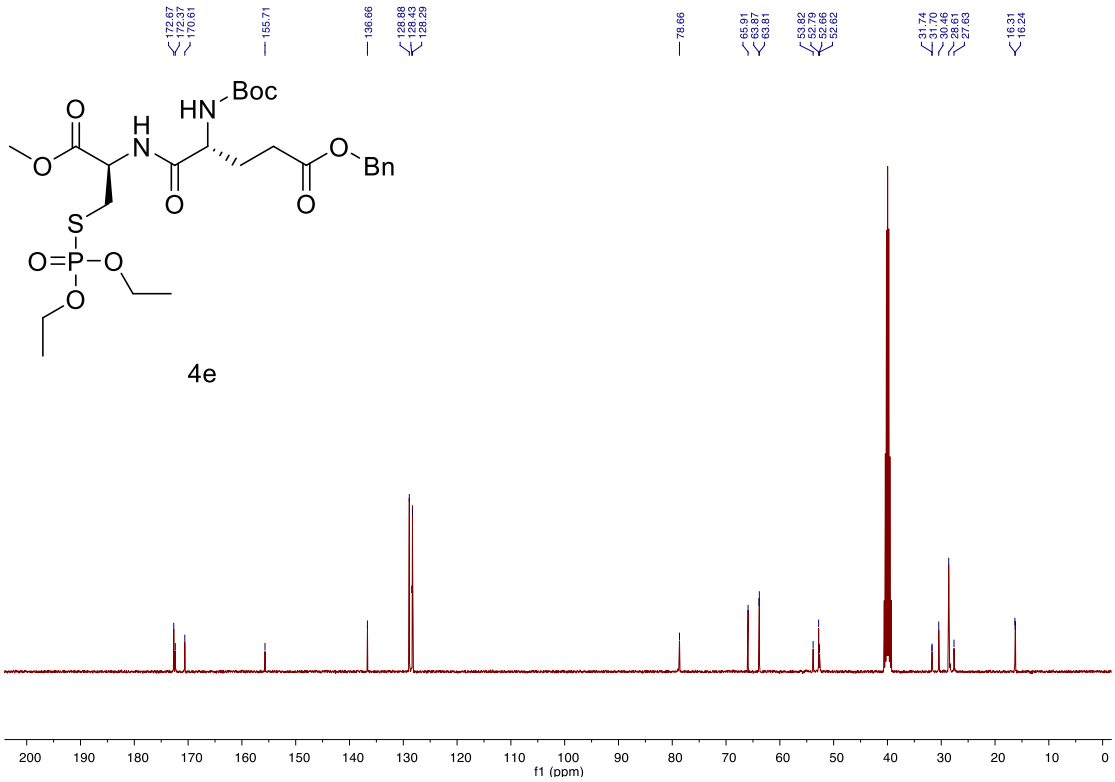
4d

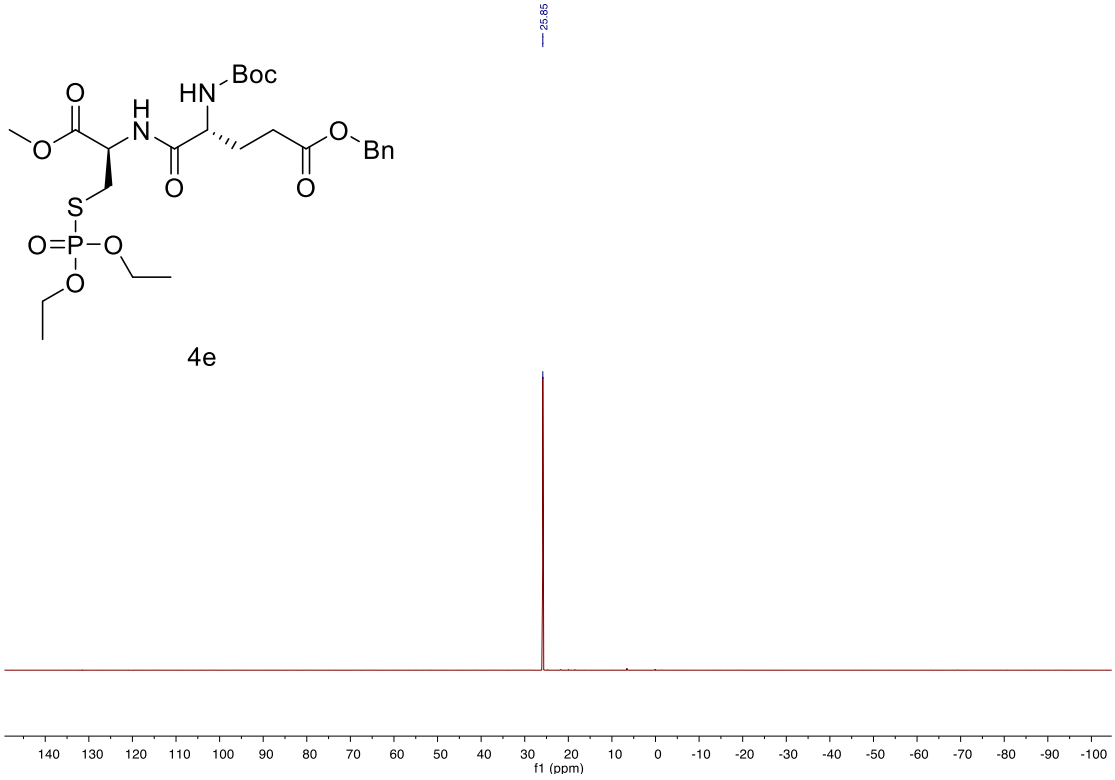
25.90
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

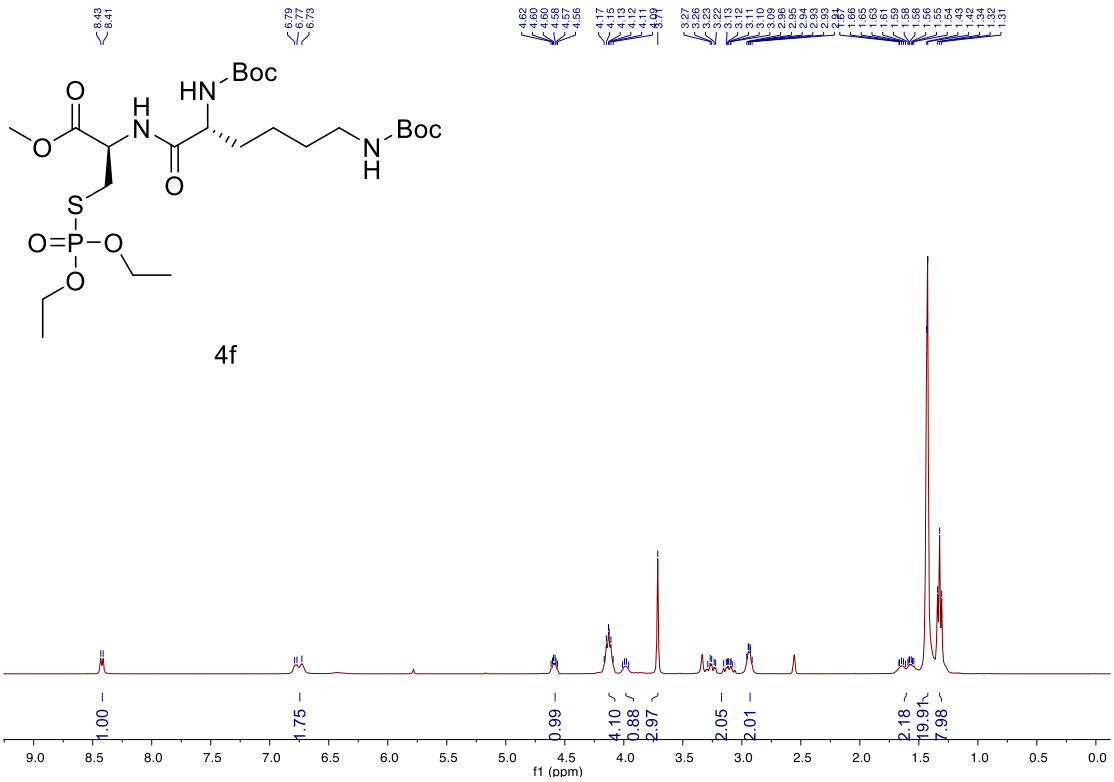


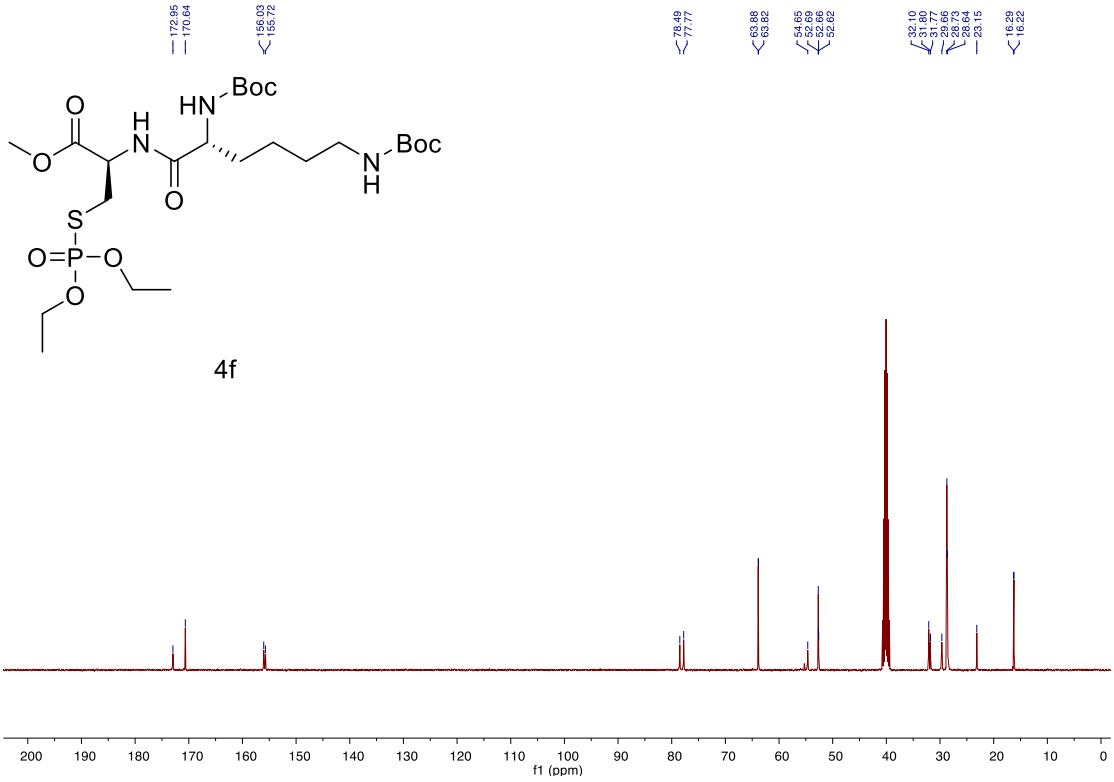
4e

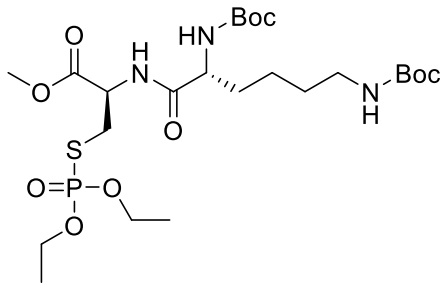
8.51 8.49 7.38 7.38 7.37 7.37 7.37 7.36 7.35 7.35 7.34 7.34 7.33 7.33 7.33 7.32 7.31 7.31 6.99 6.97
5.09 4.57 4.56 4.55 4.53 4.52 4.51 4.08 4.07 4.06 4.06 4.05 4.04 3.85 3.22 3.21 3.19 3.18 3.11 3.09 3.08 3.07 3.05 2.44 2.43 2.42 2.42 2.41 2.40 1.95 1.94 1.93 1.93 1.83 1.38 1.27 1.27 1.25 1.25 1.24 1.23
0.99 5.11 0.84 2.00 1.01 5.01 3.00 1.02 1.02 1.95 1.09 1.02 9.08 6.19
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


172.87
172.37
170.61
155.71
136.66
128.88
128.43
128.29
78.66
65.91
63.87
63.81
53.82
52.79
52.66
52.62
31.74
31.70
30.46
29.61
27.63
16.31
16.24
Boc
HN
Bn
S
O=P
4e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


25.85
Boc
HN
Bn
S
O=P
4e
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

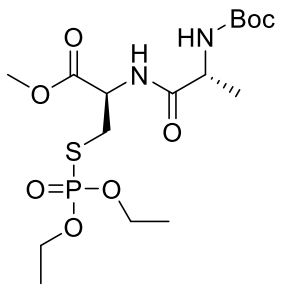

4f
f1 (ppm)


4f
f1 (ppm)



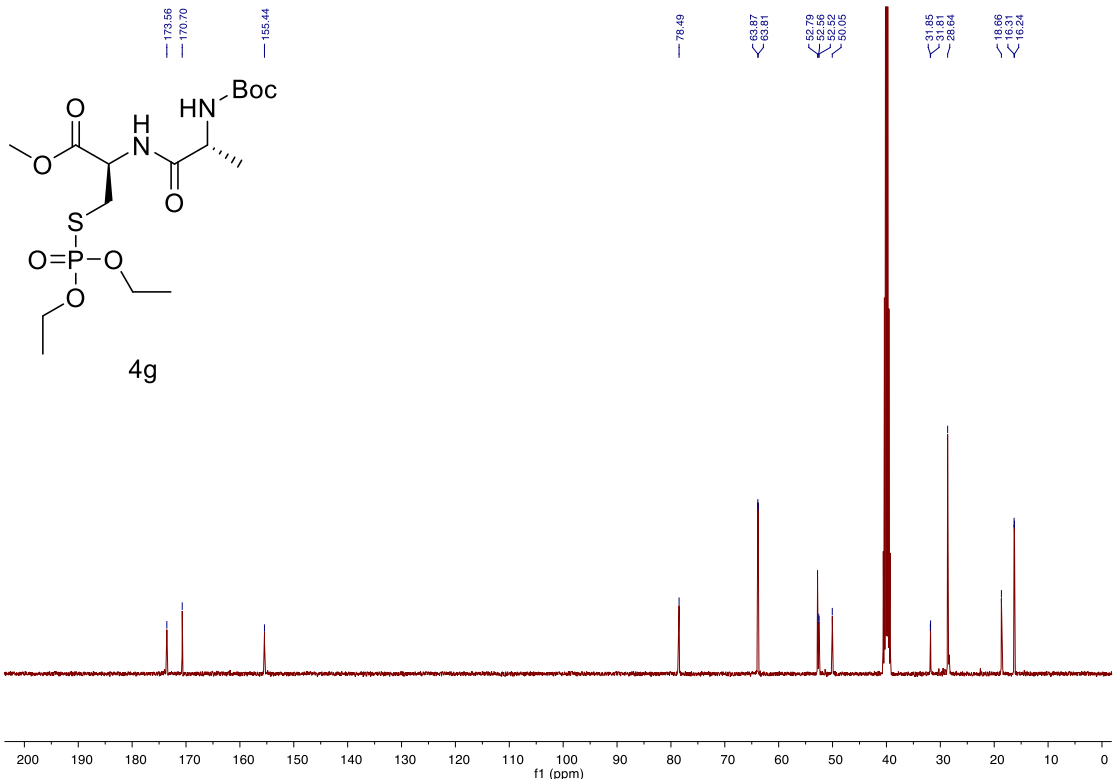
4f

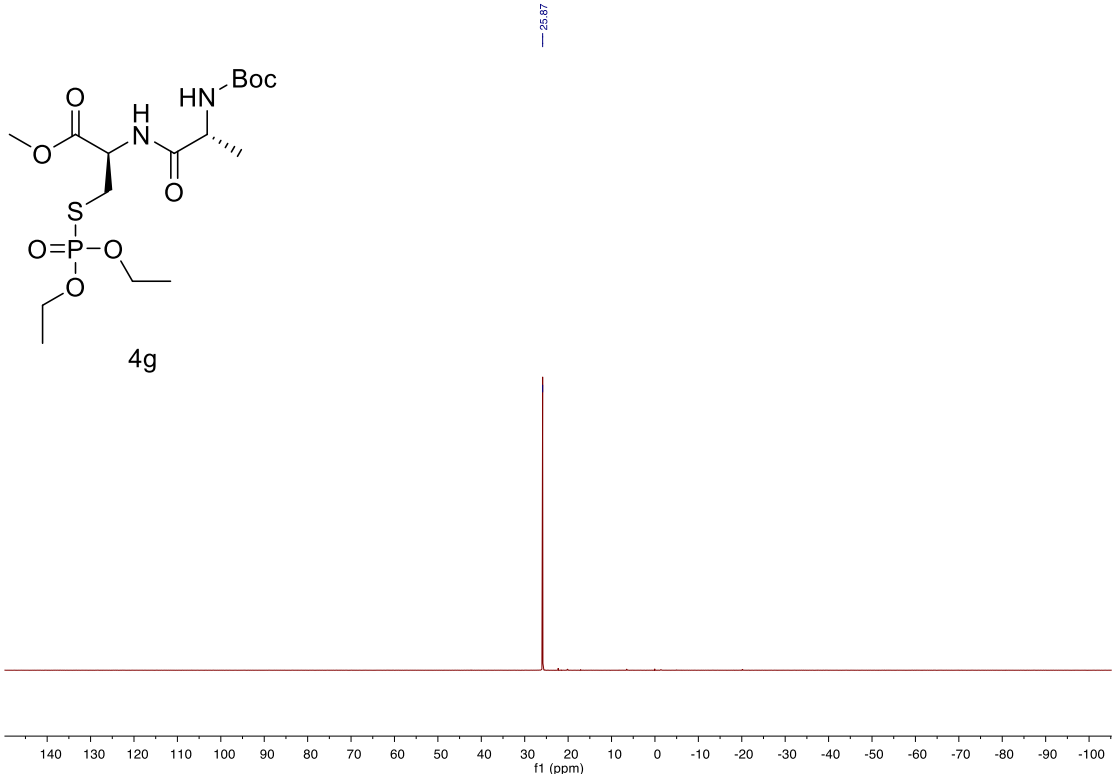
25.84
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

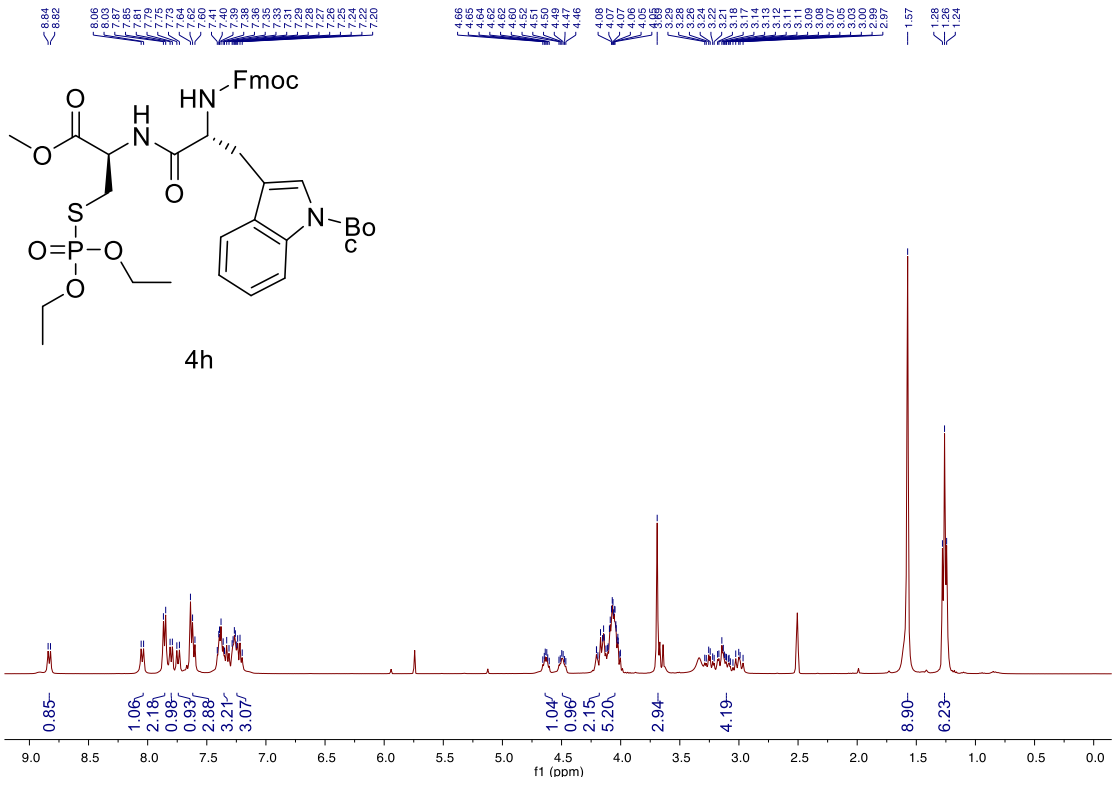


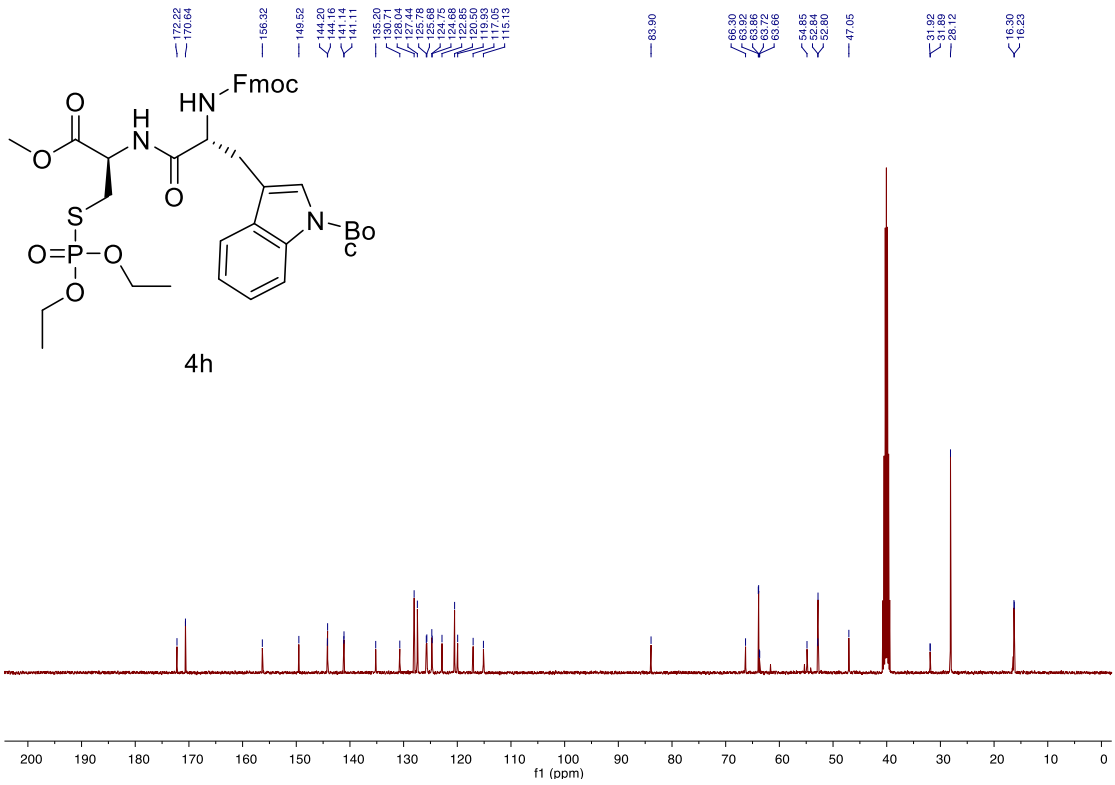
4g

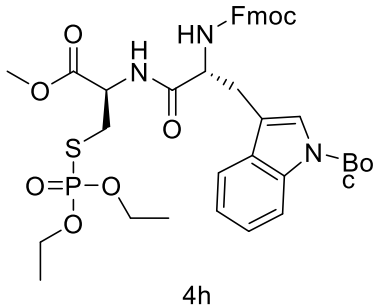
8.40
8.38
6.94
6.92
4.57
4.56
4.55
4.53
4.51
4.09
4.08
4.07
4.06
3.24
3.23
3.21
3.20
3.18
3.16
3.10
3.08
3.07
3.06
3.04
3.03
3.00
1.38
1.29
1.27
1.25
1.20
1.19
1.04
0.86
1.02
5.03
3.00
0.98
1.01
9.11
6.13
3.01
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


173.56
170.70
155.44
78.49
63.87
63.81
52.79
52.56
52.52
50.05
31.85
31.81
28.64
18.66
16.31
16.24
Boc
HN
H
N
O
O
O
S
O=P−O
O
4g
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


25.87
Boc
HN
H
N
O
O
O
S
O=P−O
O
4g
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

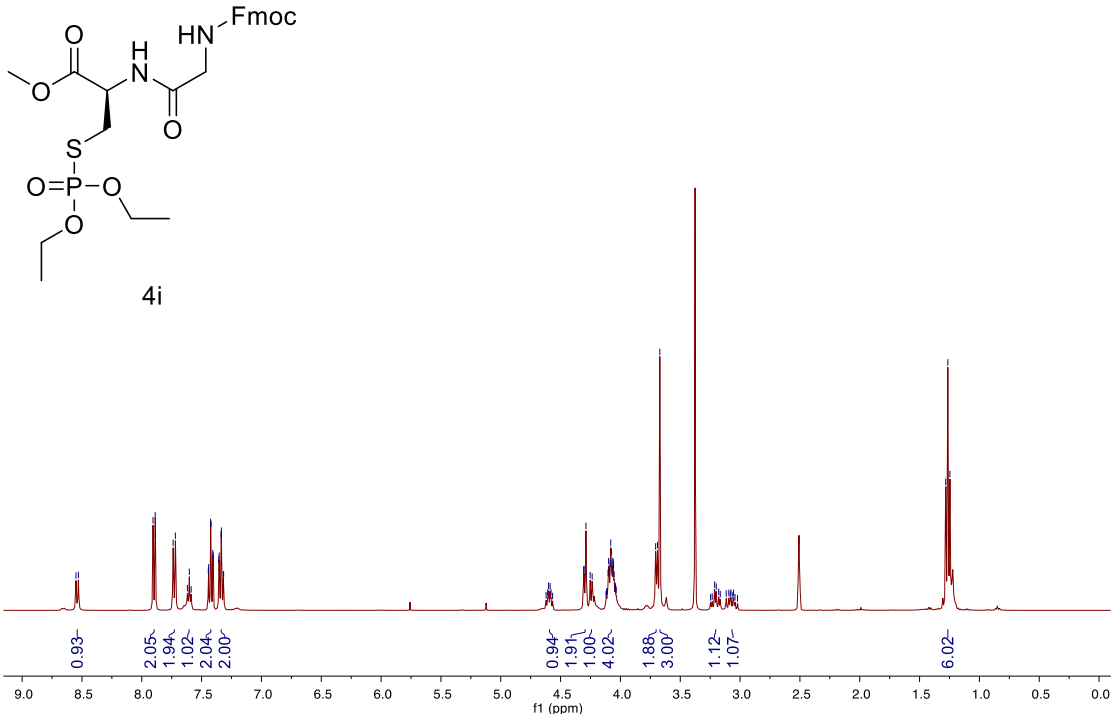

Fmoc
HN
O
H
N
O
O
S
O=P–O
O
N
Boc
4h
0.85
1.06
2.18
0.98
0.93
2.88
3.21
3.07
1.04
0.96
2.15
5.20
2.94
4.19
8.90
6.23
f1 (ppm)


Fmoc
HN
O
H
N
O
O
S
O=P–O
O
N
Boc
4h
f1 (ppm)


Fmoc
HN
H
N
O
O
O
S
O=P−O
O
N
Boc

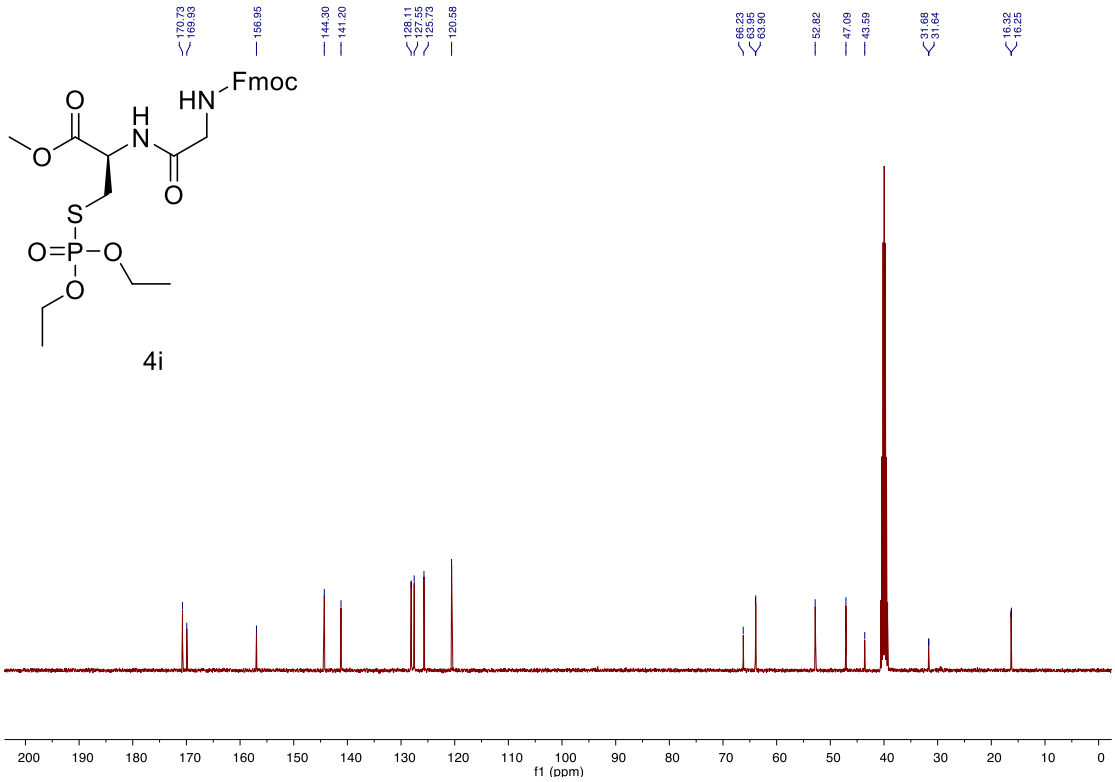
4h

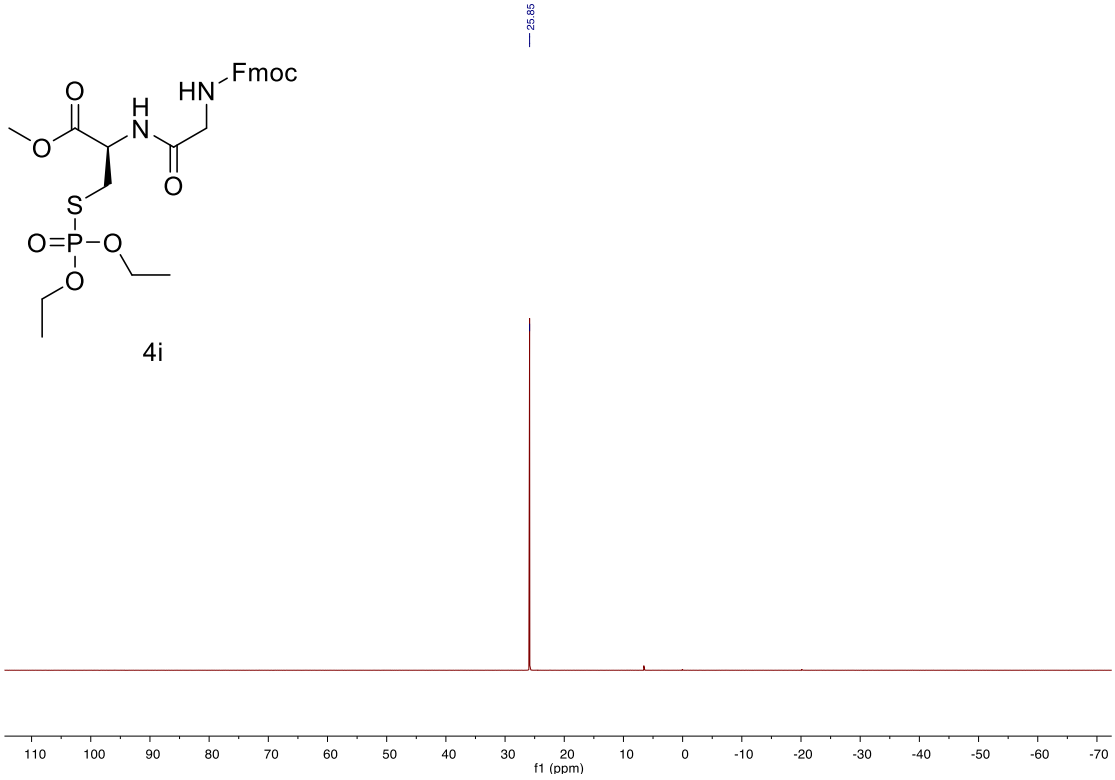
25.81
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

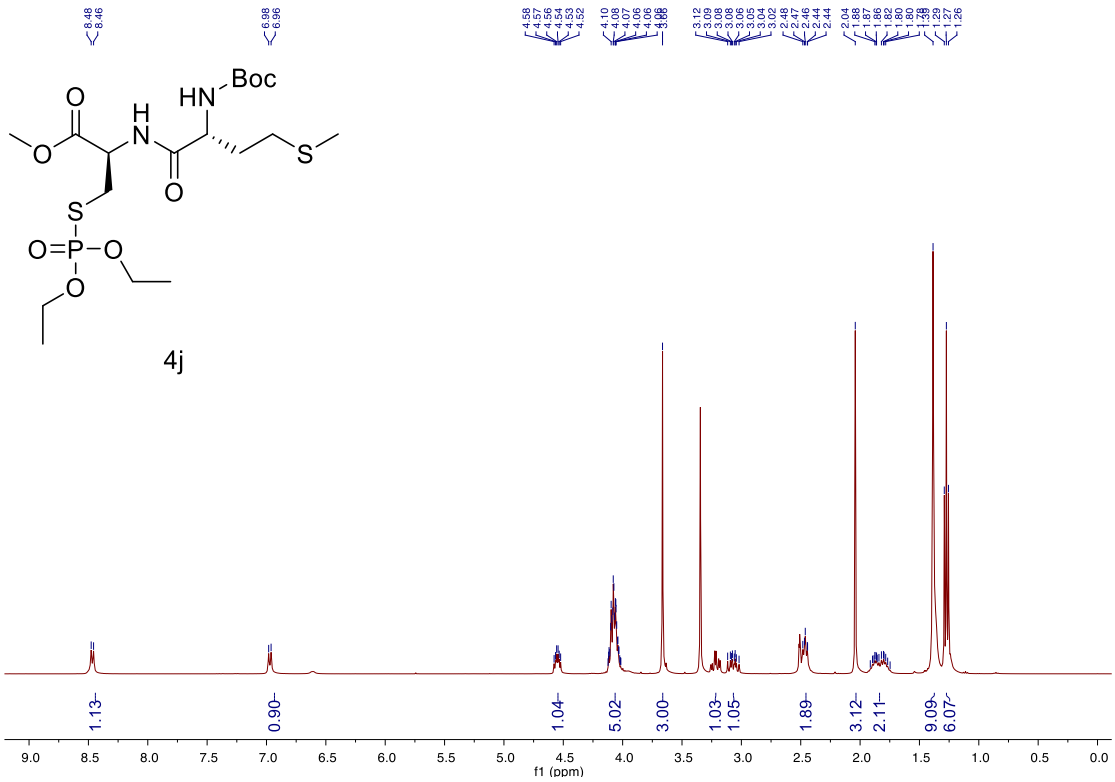

8.55
8.53
7.91
7.89
7.89
7.74
7.72
7.62
7.60
7.59
7.44
7.44
7.43
7.42
7.41
7.40
7.36
7.35
7.34
7.33
7.32
7.32
4.62
4.61
4.60
4.59
4.58
4.57
4.29
4.10
4.08
4.08
4.06
3.71
3.69
3.67
3.25
3.23
3.21
3.20
3.18
3.17
3.12
3.09
3.08
3.06
3.05
3.04
3.02
1.28
1.26
1.25
0.93
2.05
1.94
1.02
2.04
2.00
0.94
1.91
1.00
4.02
1.88
3.00
1.12
1.07
6.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

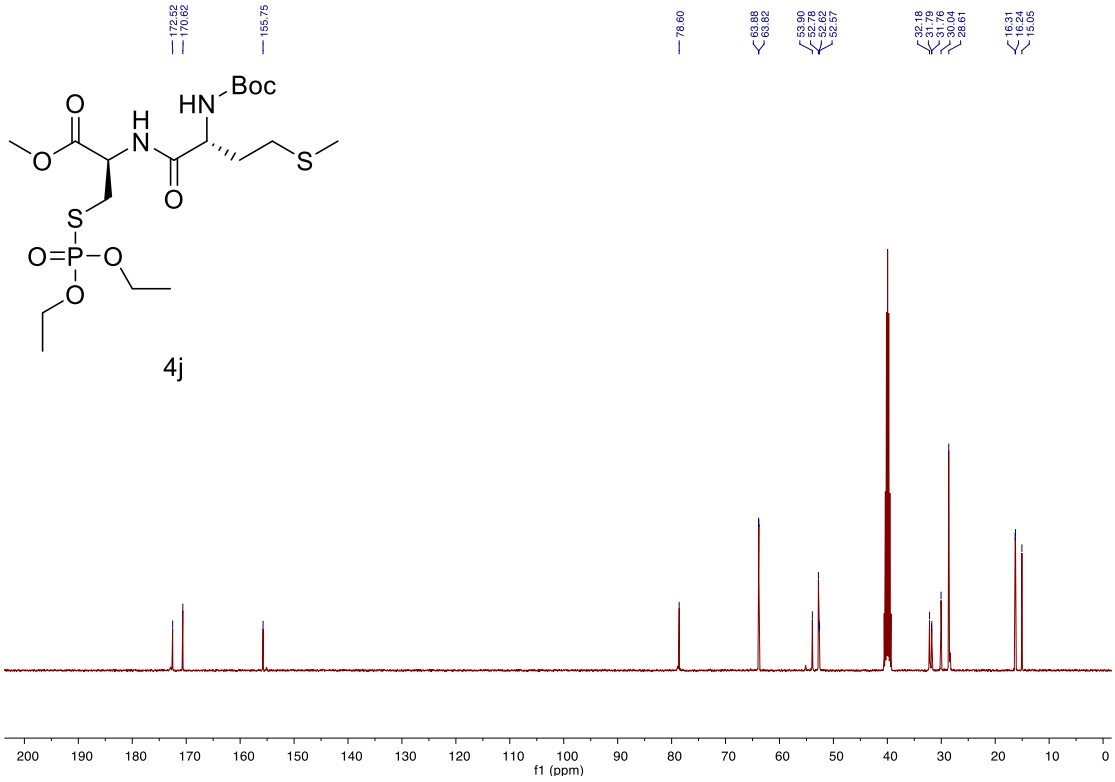
Fmoc
HN
H
N
O
O
O
S
O=P−O
O

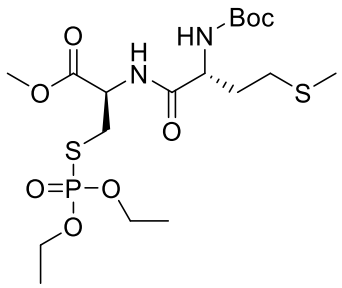
4i


170.73
169.93
156.95
144.30
141.20
128.11
127.55
125.73
120.58
66.23
63.95
63.90
52.82
47.09
43.59
31.68
31.64
16.32
16.25
Fmoc
HN
H
N
O
S
O=P
4i
f1 (ppm)


25.85
Fmoc
HN
H
N
O
S
O=P
4i
f1 (ppm)

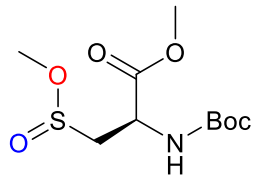

8.48
8.46
6.98
6.96
4.58
4.57
4.56
4.54
4.53
4.52
4.10
4.08
4.07
4.06
4.06
4.06
3.88
3.12
3.09
3.08
3.08
3.06
3.05
3.04
3.02
2.48
2.47
2.46
2.44
2.44
2.04
1.87
1.87
1.86
1.82
1.80
1.80
1.38
1.29
1.27
1.26
Boc
HN
H
N
O
O
O
S
S
O=P–O
O
4j
1.13
0.90
1.04
5.02
3.00
1.03
1.05
1.89
3.12
2.11
9.09
6.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


172.82
170.02
155.75
78.60
63.88
63.82
53.90
52.78
52.62
52.57
32.18
31.79
31.75
30.04
28.61
16.31
16.24
15.05
Boc
HN
H
N
O
O
O
S
S
O=P–O
O
4j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
HN
Boc
H
N
O
O
S
S
O=P−O
O

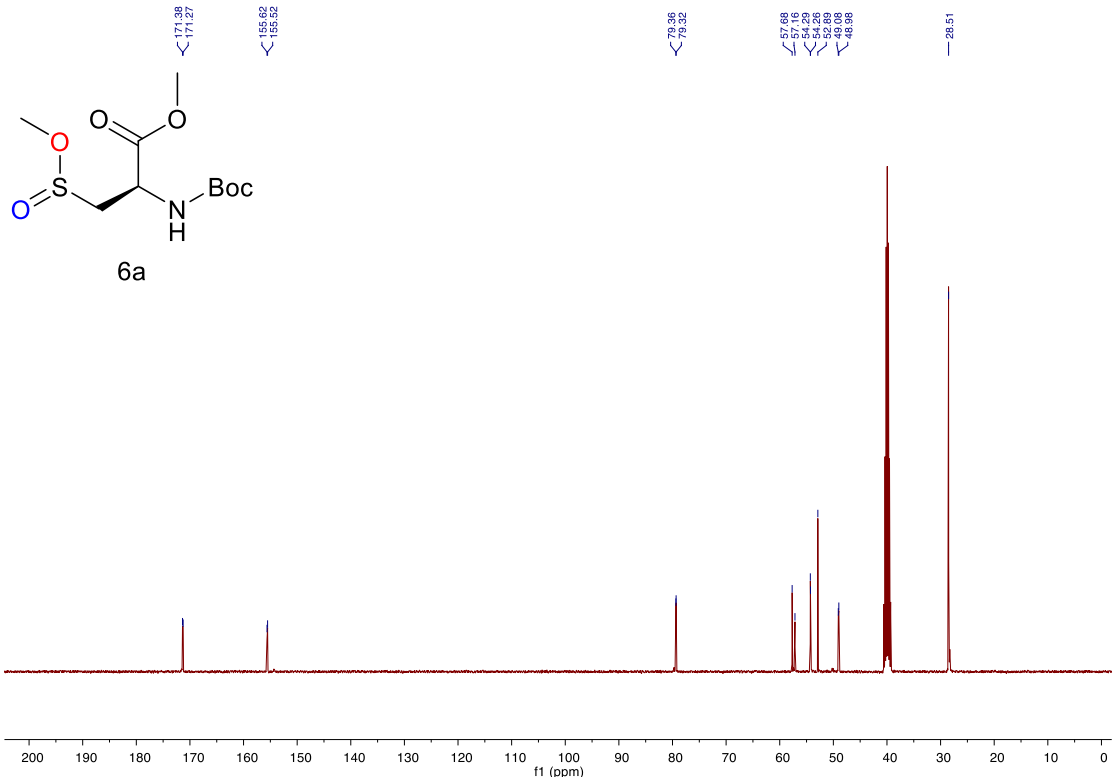
4j

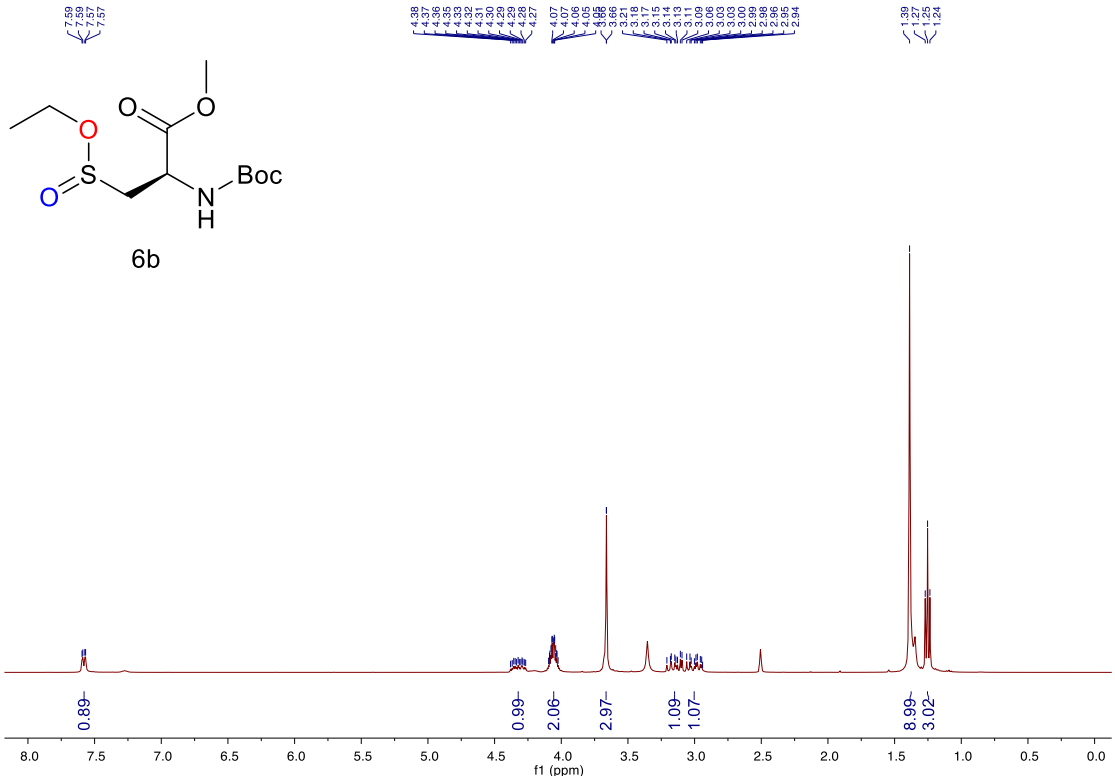
25.85
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100
f1 (ppm)

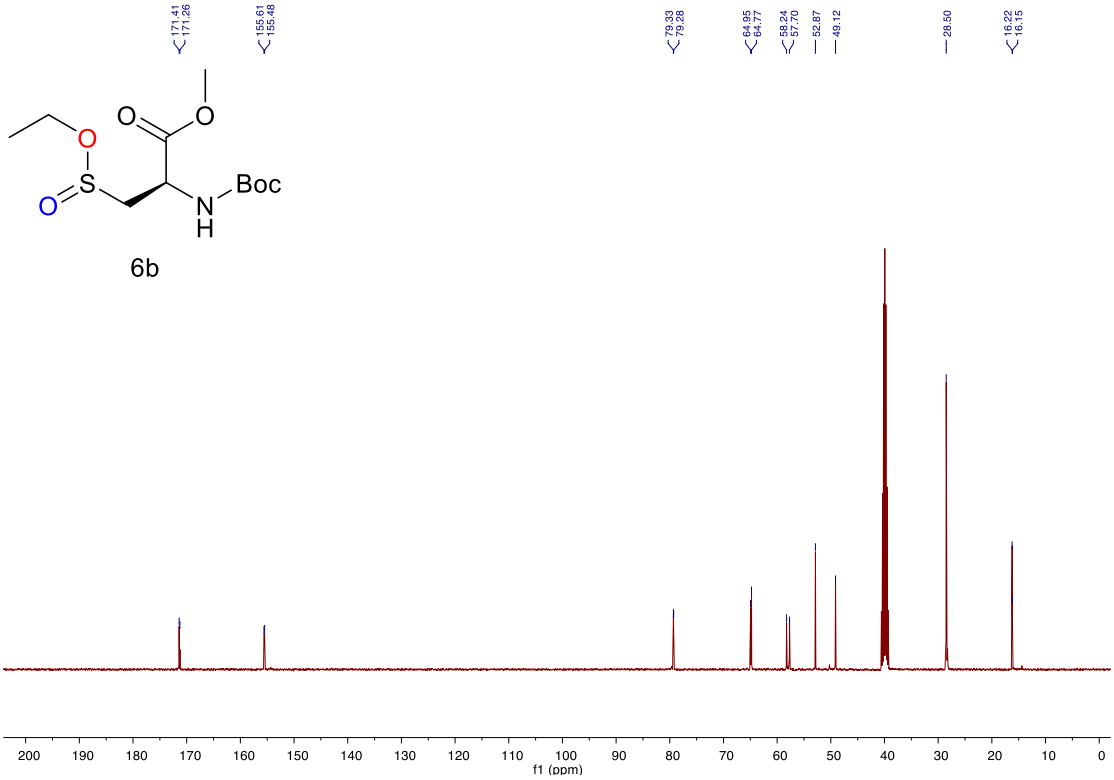

O
O
O
S
O
N
Boc
H

6a

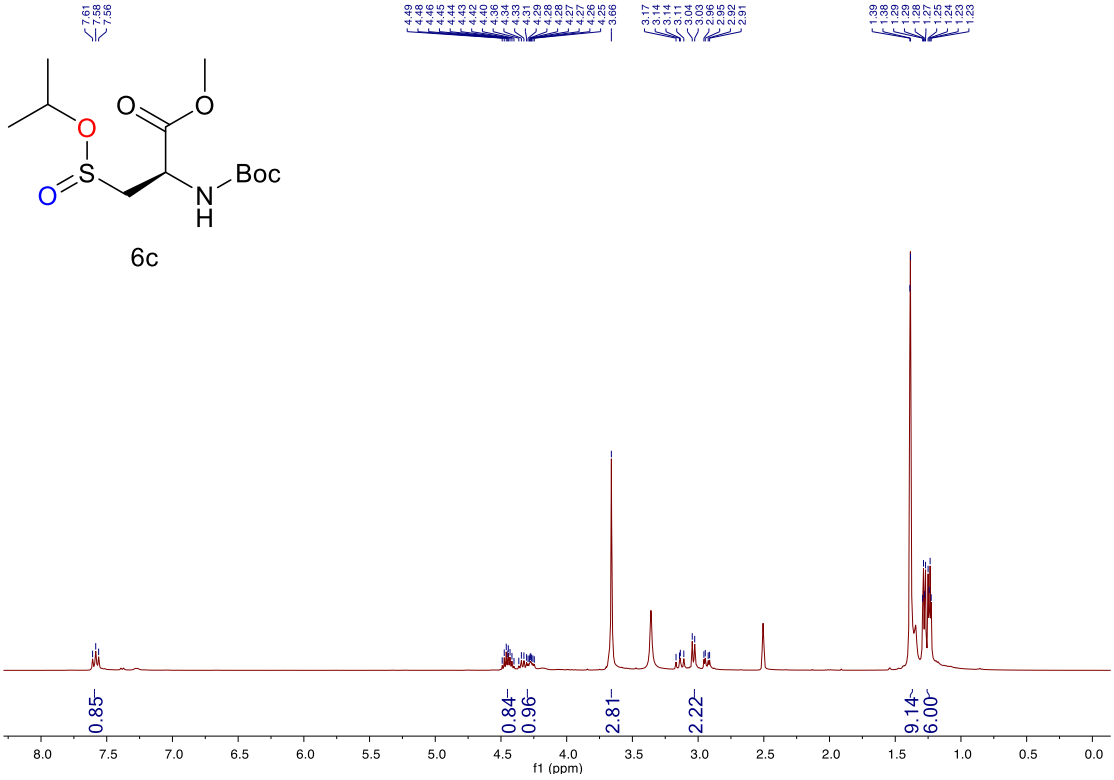
7.60
7.59
7.58
7.57
4.37
4.35
4.34
4.33
4.32
4.31
4.30
4.30
4.29
4.28
4.27
3.70
3.66
3.22
3.19
3.18
3.18
3.16
3.14
3.05
3.02
3.01
3.00
2.99
2.97
2.96
1.39
0.94
0.96
3.00
3.08
1.13
1.07
9.09
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


171.38
171.27
155.62
155.52
79.36
79.32
57.68
57.16
54.29
54.26
52.88
49.08
48.98
28.51
O
O
O
S
O
N
H
Boc
6a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

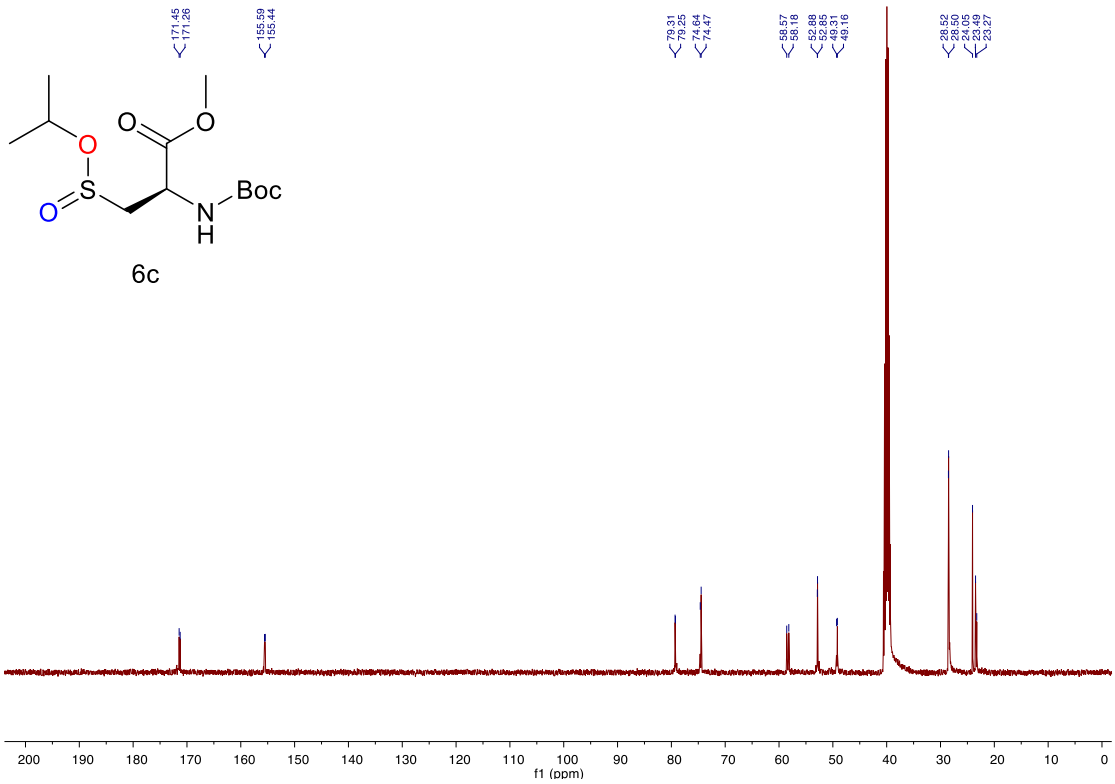

7.59
7.59
7.57
7.57
4.38
4.37
4.36
4.35
4.33
4.32
4.31
4.30
4.29
4.29
4.28
4.27
4.07
4.07
4.06
4.05
3.66
3.21
3.18
3.17
3.15
3.14
3.13
3.11
3.09
3.06
3.03
3.00
3.00
2.99
2.98
2.96
2.95
2.94
1.39
1.27
1.25
1.24
O
O
O
S
O
N
H
Boc
6b
0.89
0.99
2.06
2.97
1.09
1.07
8.99
3.02
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


171.41
171.26
155.61
155.48
79.33
79.28
64.95
64.77
58.24
57.70
52.87
49.12
28.50
16.22
16.15
O
O
O
S
O
N
H
Boc
f1 (ppm)

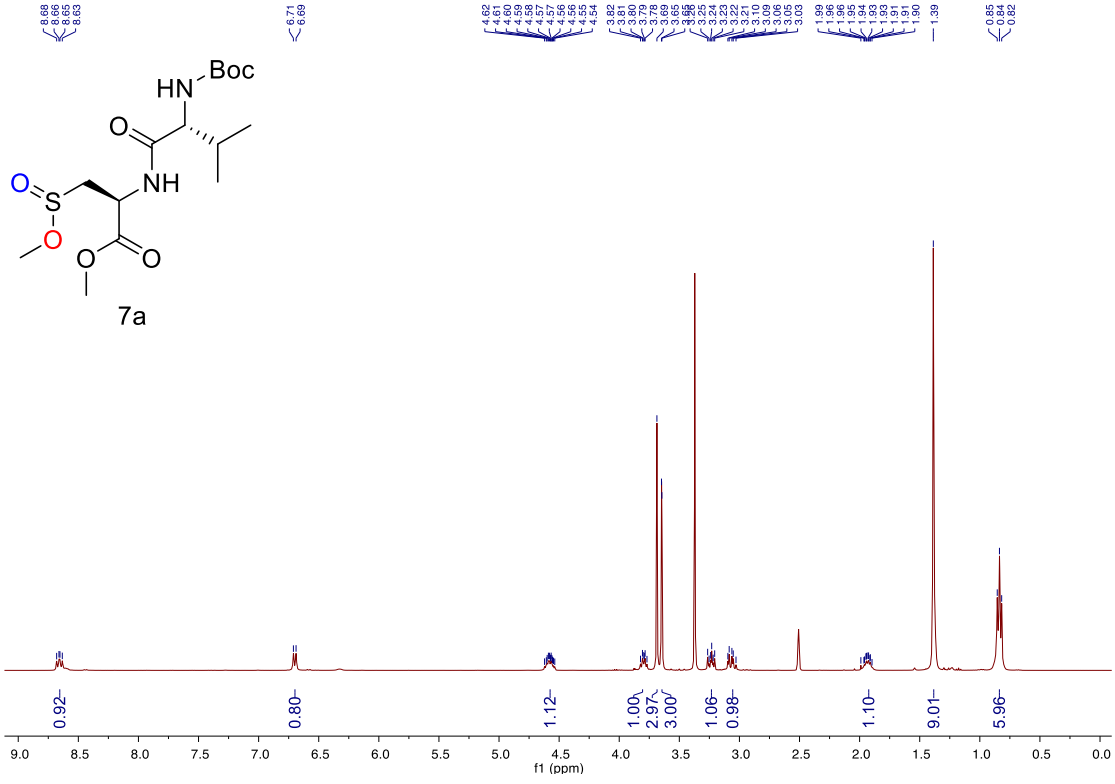
6b


7.61
7.58
7.56
3.66
3.17
3.14
3.11
3.04
3.00
2.96
2.95
2.92
2.91
1.39
1.38
1.29
1.28
1.27
1.25
1.24
1.23
1.23
O
O
O
S
O
N
H
Boc
0.85
0.84
0.96
2.81
2.22
9.14
6.00
f1 (ppm)

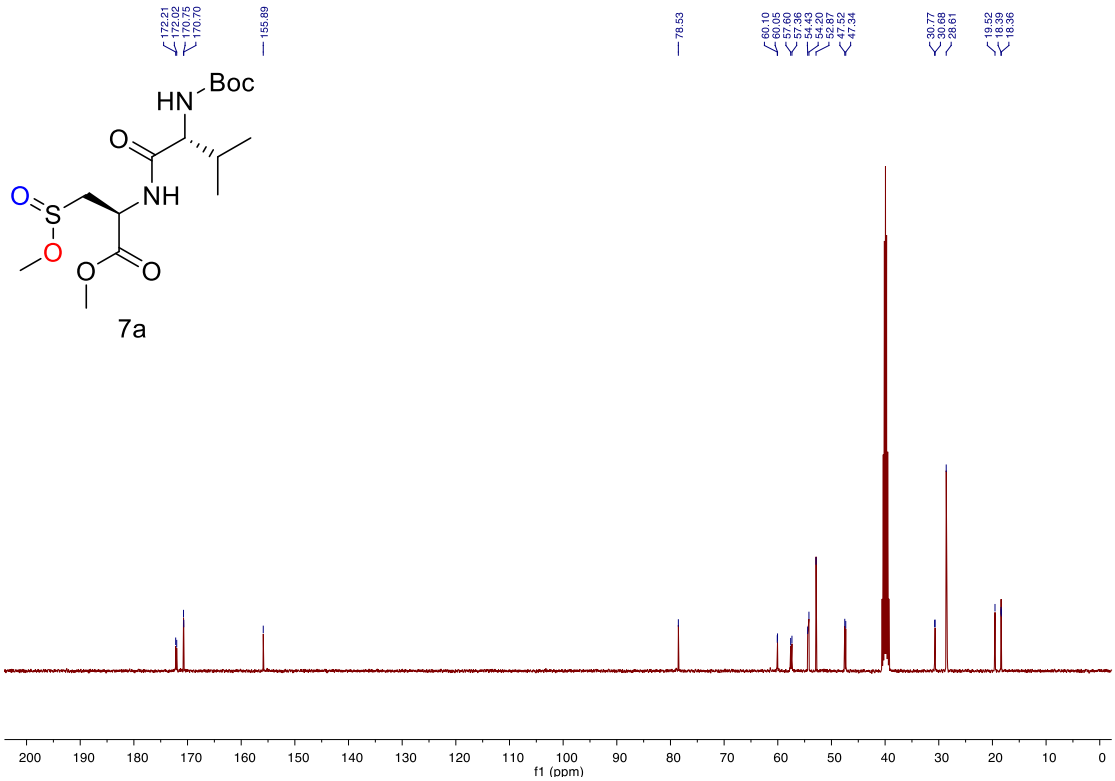
6c

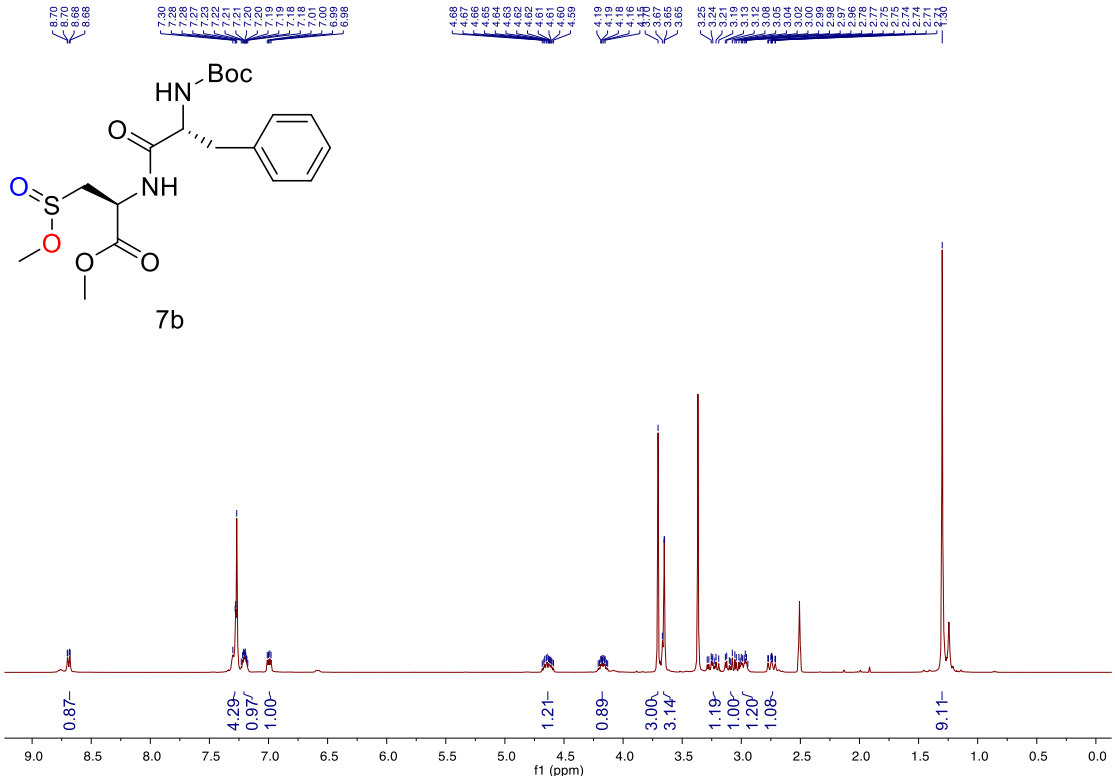

171.45
171.26
155.59
155.44
79.31
79.25
74.64
74.47
58.57
58.18
52.88
52.85
49.31
49.16
28.52
28.06
24.15
23.49
23.27
O
O
O
S
O
N
H
Boc
f1 (ppm)

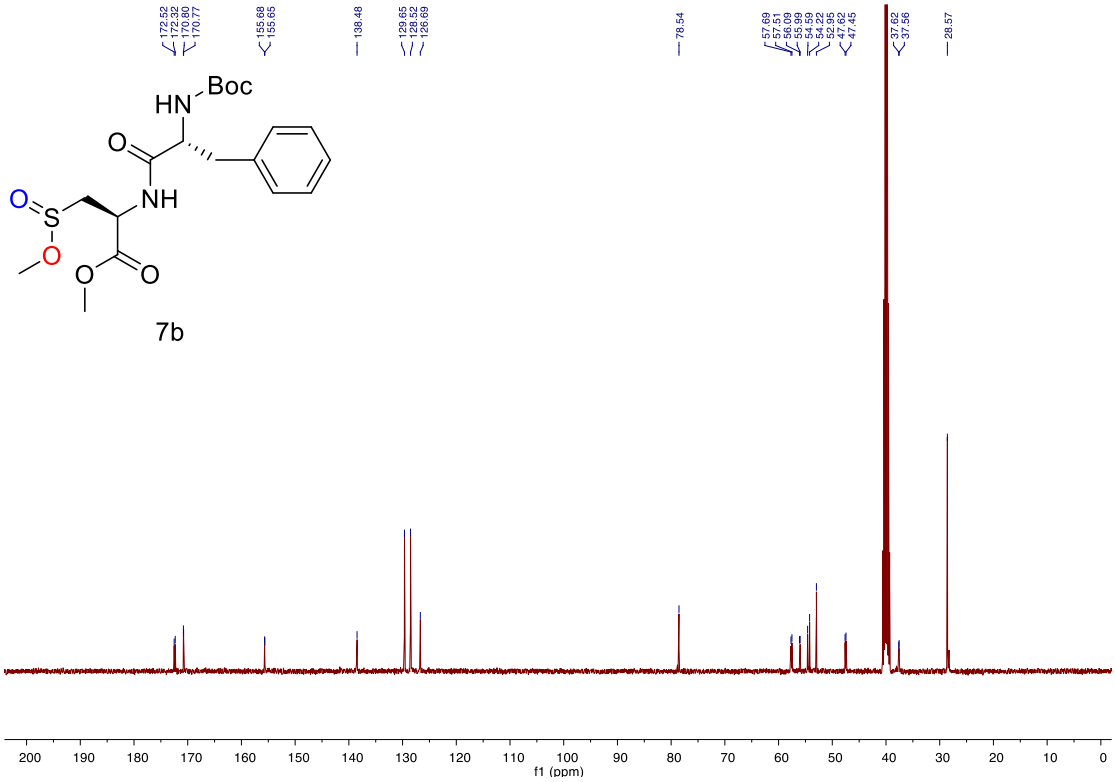
6c


8.68
8.66
8.65
8.63
6.71
6.69
4.62
4.61
4.60
4.59
4.58
4.57
4.57
4.56
4.56
4.55
4.54
3.82
3.81
3.80
3.79
3.78
3.69
3.65
3.26
3.25
3.24
3.23
3.22
3.21
3.10
3.09
3.06
3.05
3.03
1.99
1.96
1.96
1.95
1.94
1.93
1.93
1.91
1.91
1.90
1.39
0.85
0.84
0.82
HN
Boc
O
NH
O
S
O
O
O
0.92
0.80
1.12
1.00
2.97
3.00
1.06
0.98
1.10
9.01
5.96
f1 (ppm)

7a


172.21
172.02
170.75
170.70
155.89
78.53
60.10
60.05
57.86
57.38
54.43
54.20
52.87
47.82
47.34
30.77
30.68
28.61
19.52
18.39
18.36
HN
Boc
O
NH
O
S
O
O
O
7a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.70
8.70
8.68
8.68
7.30
7.28
7.28
7.27
7.23
7.22
7.21
7.21
7.20
7.20
7.19
7.19
7.18
7.01
7.00
6.99
6.98
4.68
4.67
4.65
4.64
4.63
4.62
4.62
4.61
4.61
4.60
4.59
4.19
4.19
4.18
4.16
4.15
3.67
3.65
3.25
3.24
3.21
3.19
3.13
3.12
3.08
3.05
3.04
3.02
3.00
2.99
2.98
2.97
2.96
2.78
2.77
2.75
2.74
2.74
2.71
1.30
HN
Boc
O
NH
O
S
O
O
O
7b
0.87
4.29
0.97
1.00
1.21
0.89
3.00
3.14
1.19
1.00
1.20
1.08
9.11
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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126.69
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56.09
55.89
54.59
54.22
52.95
47.82
47.45
37.62
37.56
28.57
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Boc
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NH
O
S
O
O
O
7b
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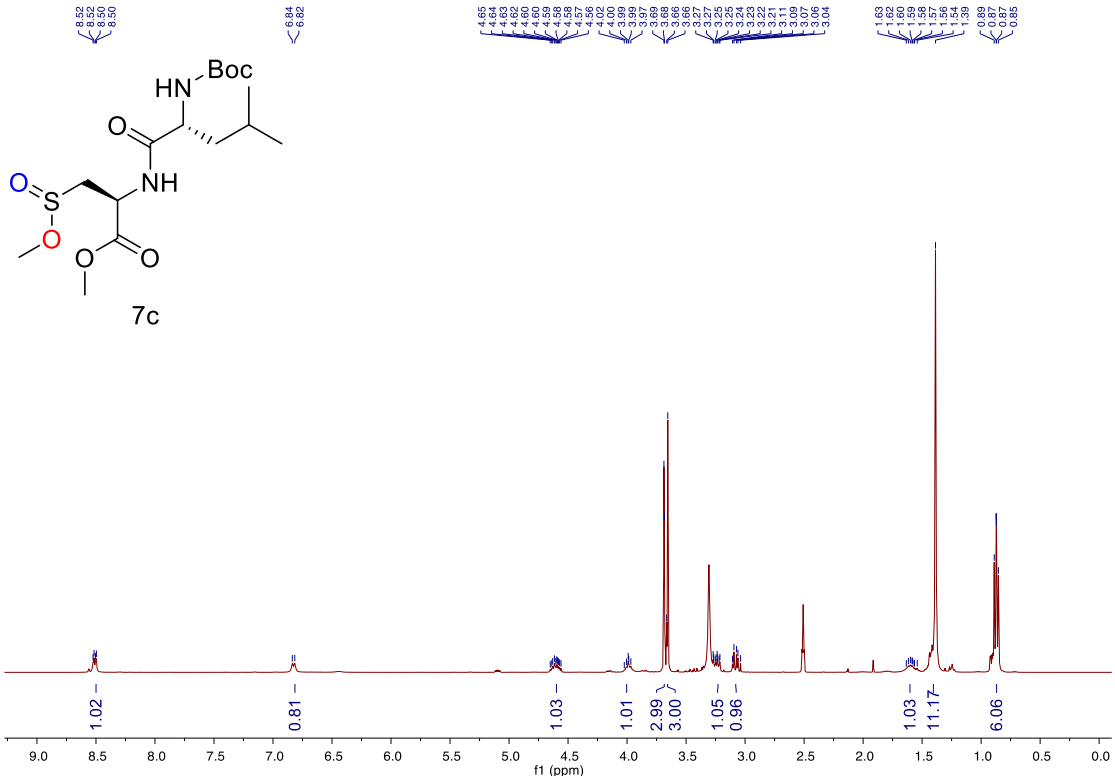
f1 (ppm)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6.82
4.65
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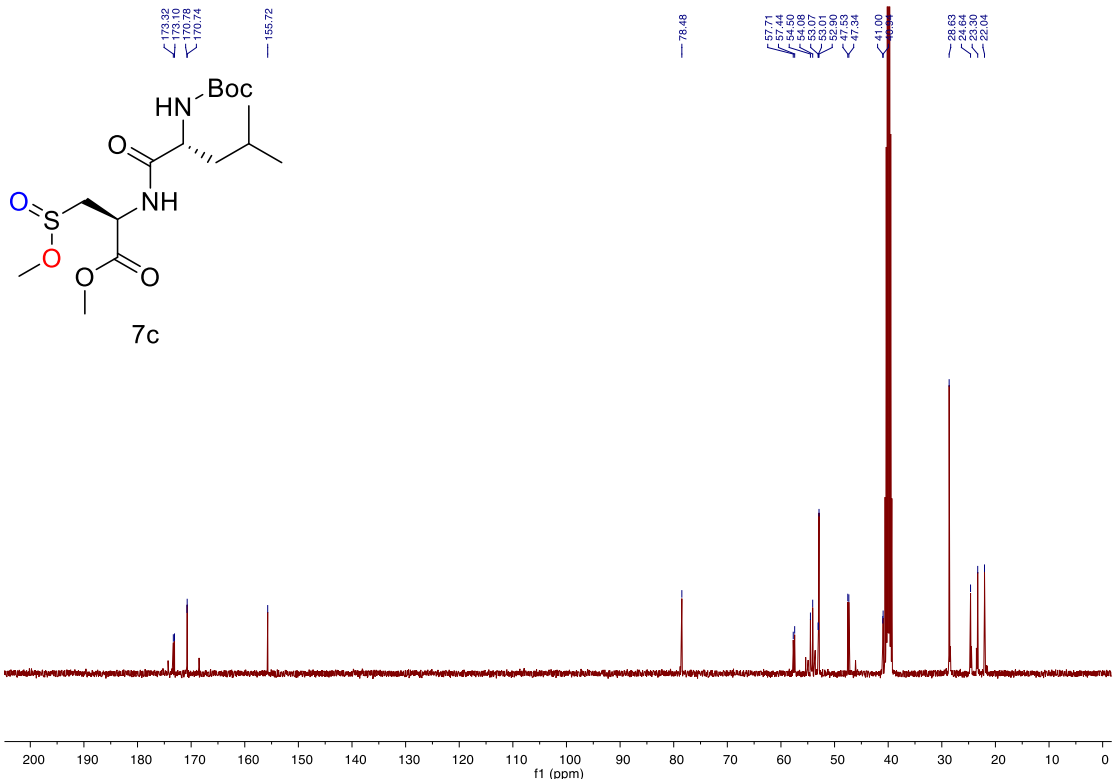
4.63
4.62
4.60
4.60
4.59
4.58
4.58
4.57
4.56
4.02
4.00
3.99
3.99
3.97
3.69
3.68
3.66
3.66
3.27
3.27
3.25
3.25
3.24
3.23
3.22
3.21
3.11
3.09
3.07
3.06
3.04
1.63
1.62
1.60
1.59
1.58
1.57
1.56
1.54
1.39
0.89
0.87
0.87
0.85
HN
Boc
O
NH
O
S
O
O
O
7c
1.02
0.81
1.03
1.01
2.99
3.00
1.05
0.96
1.03
11.17
6.06
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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170.74
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54.50
54.08
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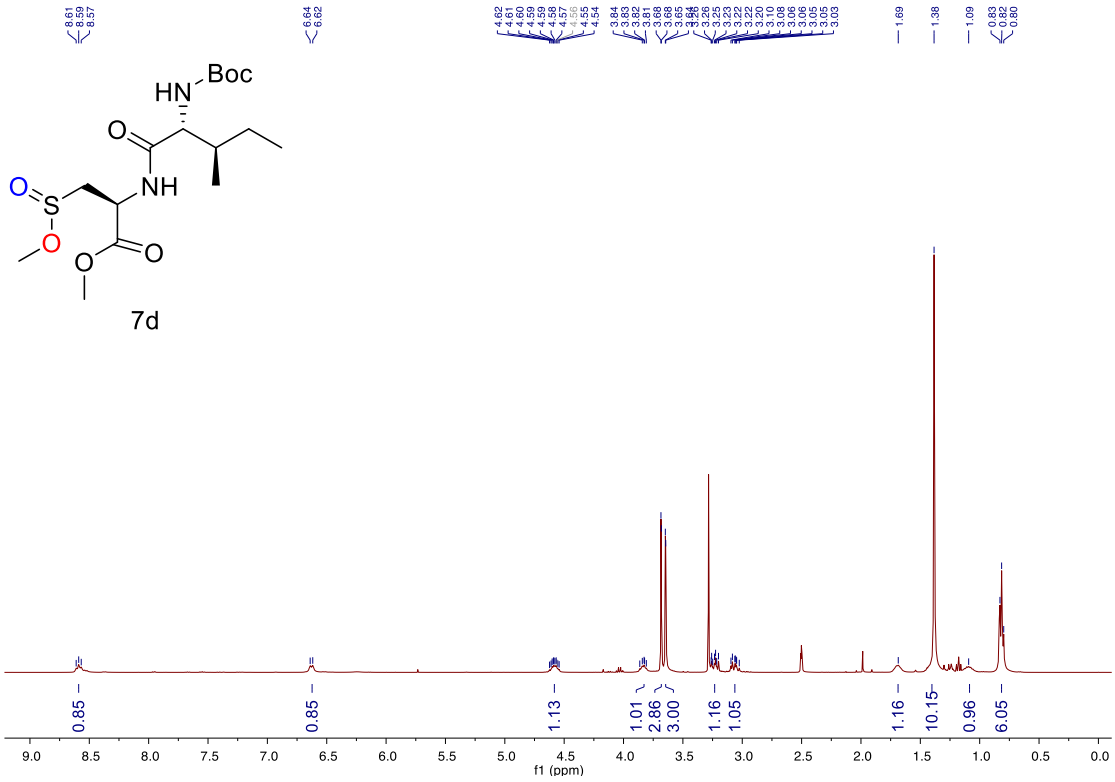
53.01
52.90
47.53
47.34
41.00
28.63
24.64
23.30
22.04
HN
Boc
O
NH
O
S
O
O
O
7c
f1 (ppm)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4.62
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4.60
4.59
4.59
4.58
4.57
4.55
4.54
3.84
3.83
3.82
3.81
3.68
3.65
3.26
3.25
3.23
3.22
3.10
3.08
3.06
3.05
3.03
1.69
1.38
1.09
0.83
0.82
0.80
HN
Boc
O
NH
O
S
O
O
O
7d
0.85
0.85
1.13
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2.86
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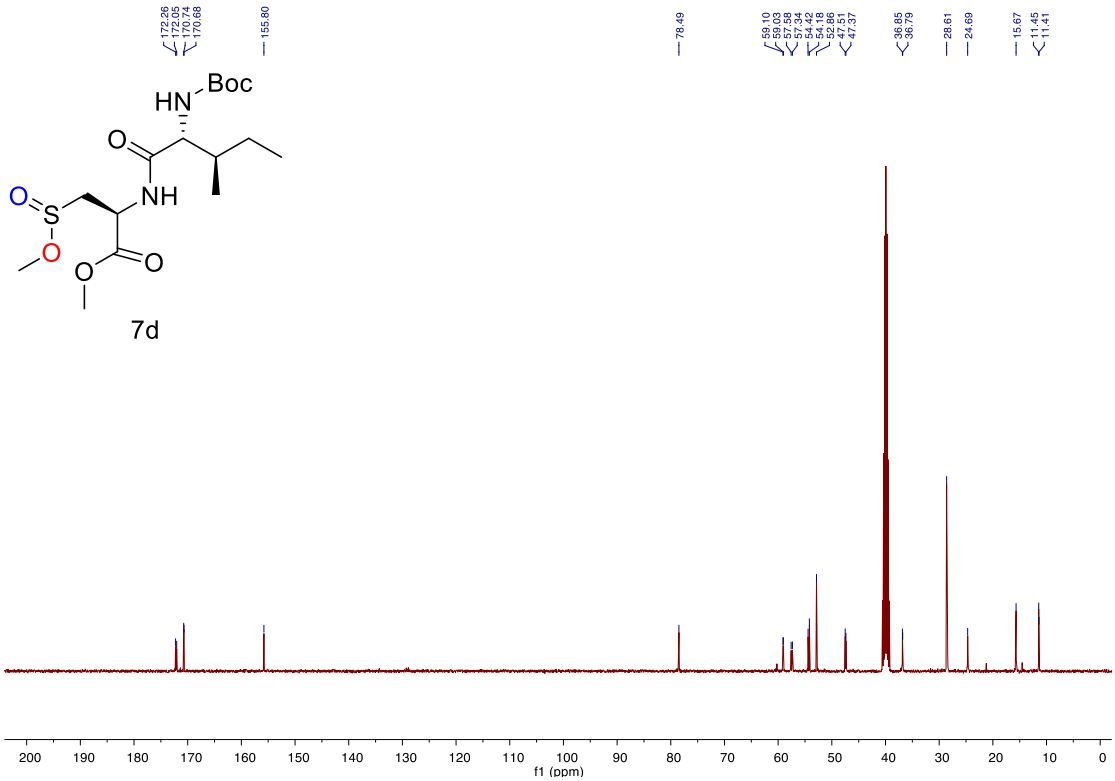
1.16
10.15
0.96
6.05
f1 (ppm)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78.49
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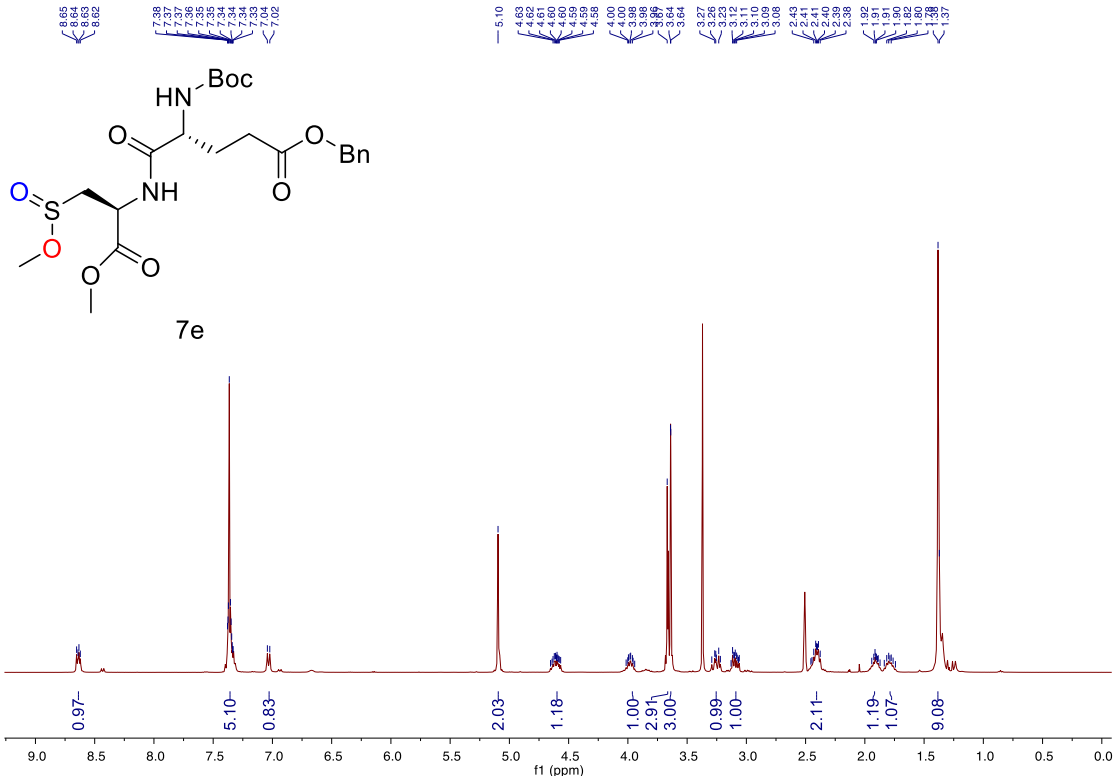
59.03
57.38
57.34
54.42
54.18
52.86
47.51
47.37
36.85
36.79
28.61
24.69
15.67
11.45
11.41
Boc
HN
O
NH
O
S
O
O
O
7d
f1 (ppm)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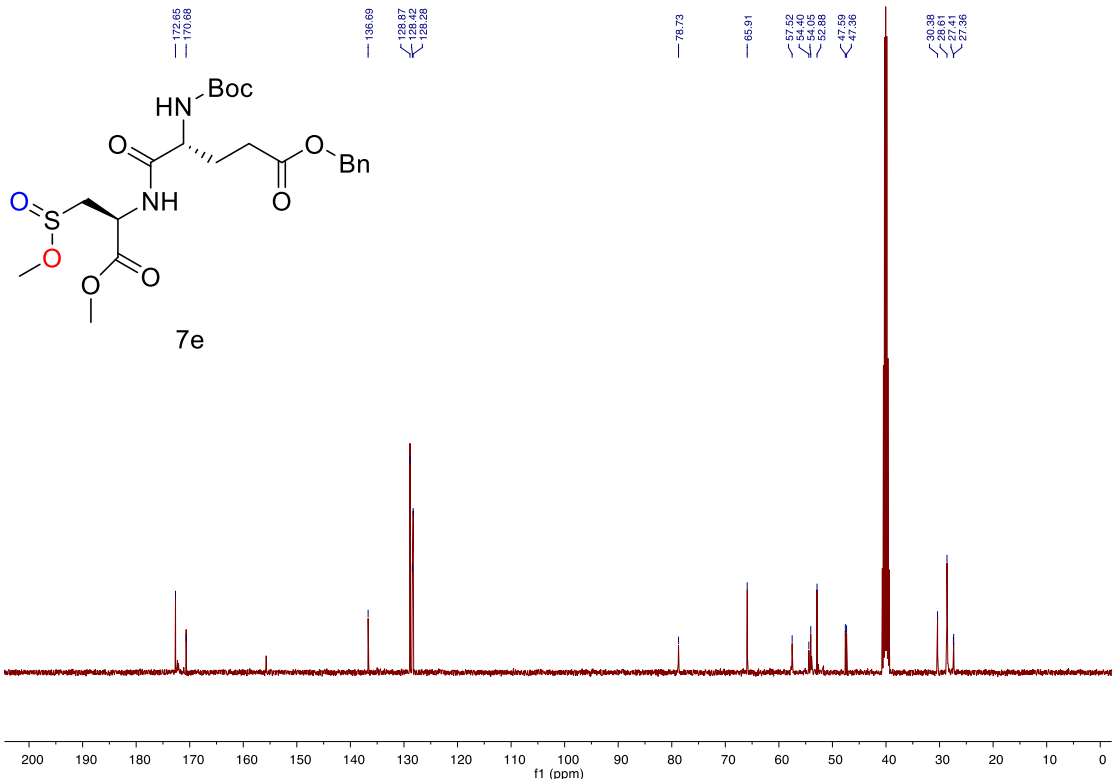
7.35
7.34
7.34
7.33
7.33
7.04
7.02
5.10
4.63
4.62
4.61
4.60
4.60
4.59
4.59
4.58
4.00
4.00
3.98
3.98
3.96
3.96
3.64
3.64
3.27
3.26
3.23
3.12
3.11
3.10
3.09
3.08
2.43
2.41
2.41
2.40
2.40
2.39
2.38
1.92
1.91
1.91
1.90
1.82
1.80
1.38
1.37
Boc
HN
O
NH
O
O
Bn
O
S
O
O
O
7e
0.97
5.10
0.83
2.03
1.18
1.00
2.91
3.00
0.99
1.00
2.11
1.19
1.07
9.08
f1 (ppm)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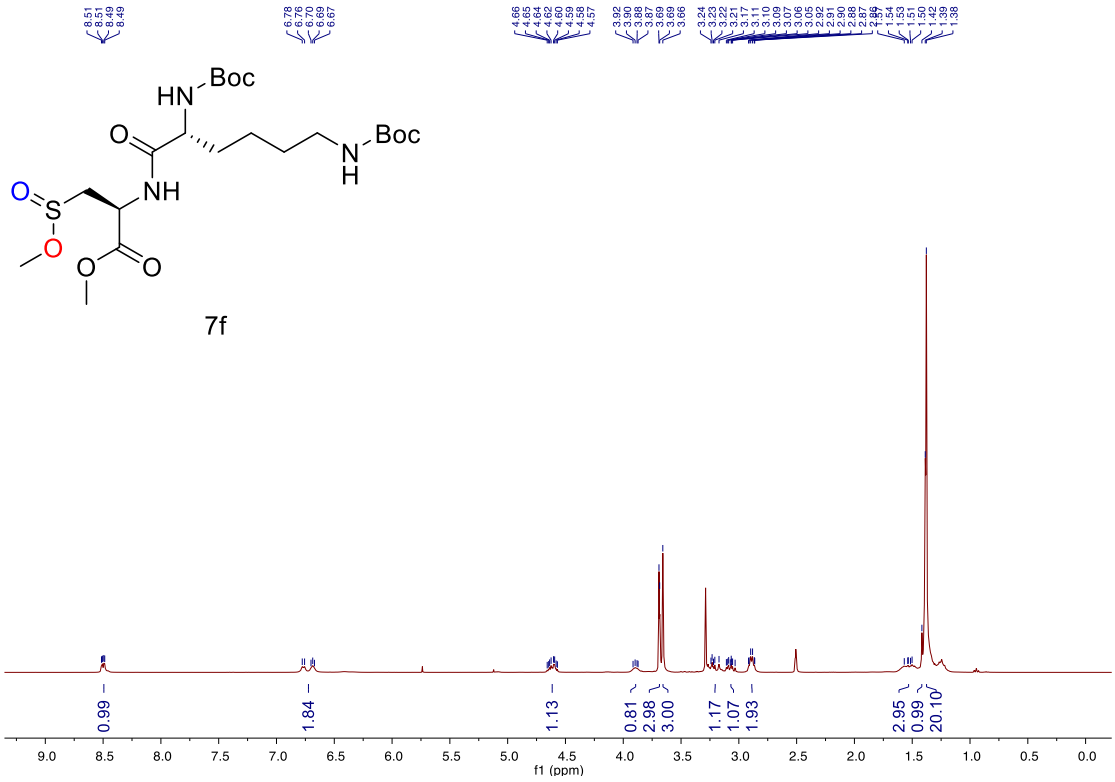
54.40
54.05
52.88
47.59
47.36
30.38
28.61
27.44
27.36
HN
Boc
O
O
O
Bn
NH
O
S
O
O
O
O
7e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.49
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6.76
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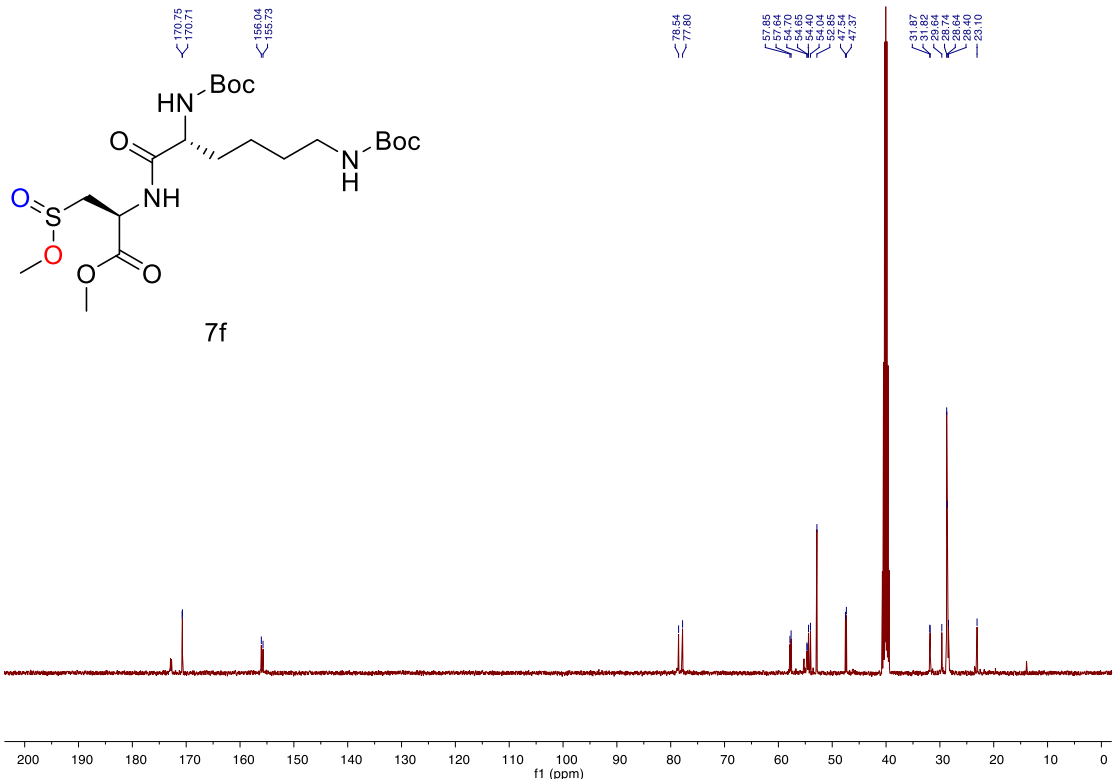
4.64
4.62
4.60
4.59
4.58
4.57
3.92
3.90
3.88
3.87
3.69
3.66
3.24
3.23
3.22
3.21
3.17
3.11
3.10
3.09
3.07
3.06
3.05
2.92
2.91
2.90
2.88
2.87
1.54
1.53
1.51
1.50
1.42
1.39
1.38
HN
Boc
O
O
N
H
Boc
NH
O
S
O
O
O
O
7f
0.99
1.84
1.13
0.81
2.98
3.00
1.17
1.07
1.93
2.95
0.99
20.10
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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77.80
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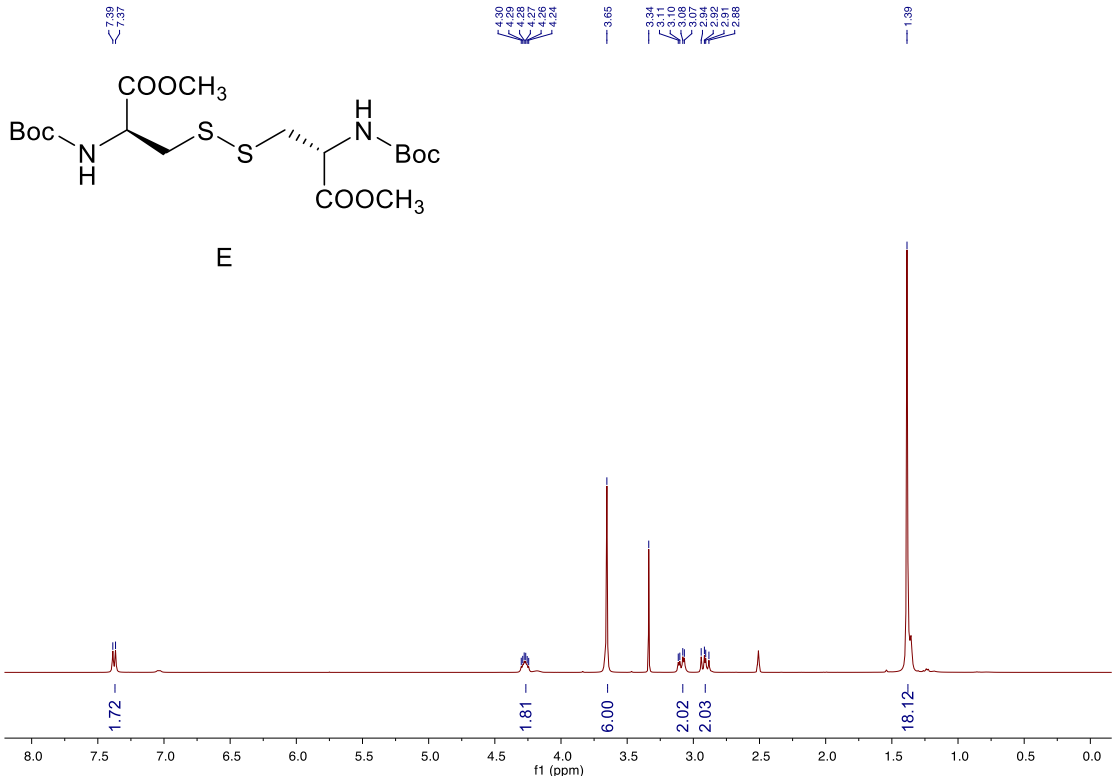
57.64
54.70
54.65
54.40
54.04
52.85
47.54
47.37
31.87
31.82
29.64
28.74
28.64
28.40
23.10
HN
Boc
O
NH
N
H
Boc
O
S
O
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

7f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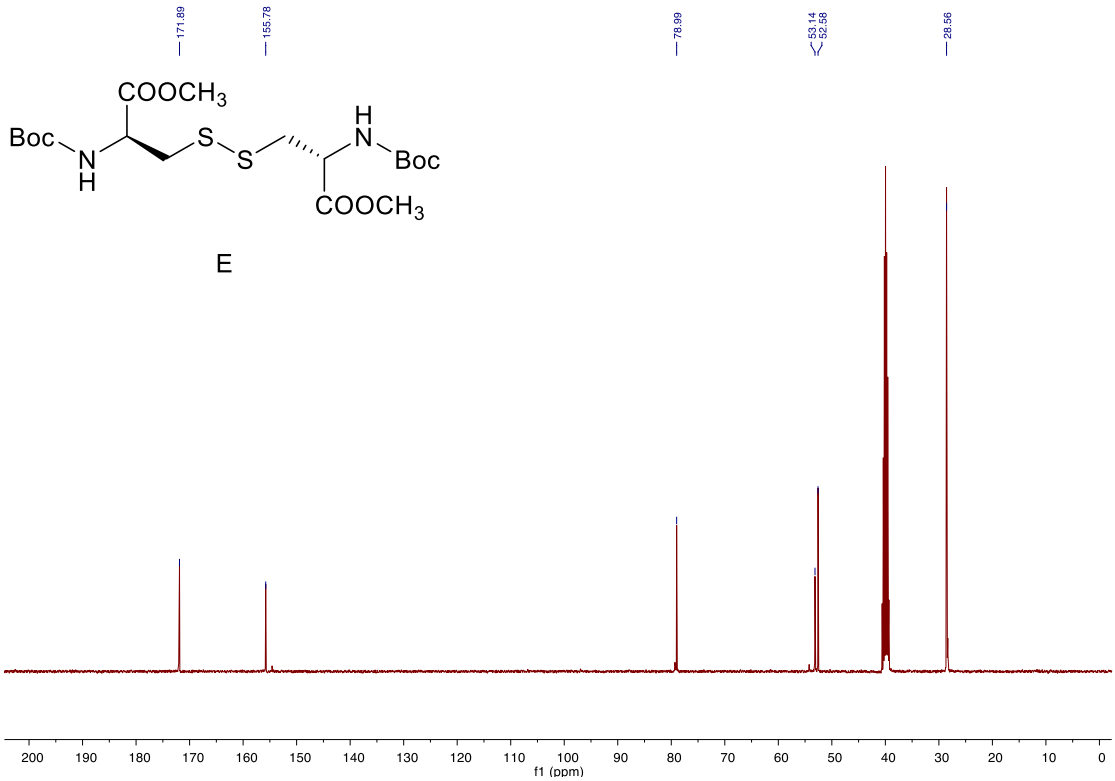
7.37
4.30
4.29
4.28
4.27
4.26
4.24
3.65
3.34
3.11
3.10
3.08
3.07
2.94
2.92
2.91
2.88
1.39
COOCH3
Boc
N
H
S
S
H
N
Boc
COOCH3
1.72
1.81
6.00
2.02
2.03
18.12
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

E


171.89
155.78
78.99
53.14
52.58
28.56
COOCH3
Boc
N
H
S
S
H
N
Boc
COOCH3
E
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

8. References

1. C. Loynd, S. J. Singha Roy, V. J. Ovalle, S. E. Canarelli, A. Mondal, D. Jewel, E. D. Ficaretta, E. Weerapana and A. Chatterjee, Electrochemical labelling of hydroxyindoles with chemoselectivity for site-specific protein bioconjugation, *Nat. Chem.*, 2024, **16**, 389-397.