Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.


# Supporting Information

## Cu-Catalyzed Arylation of S-Tosyl Peptides with Arylboronic Acids

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# 1. General Information

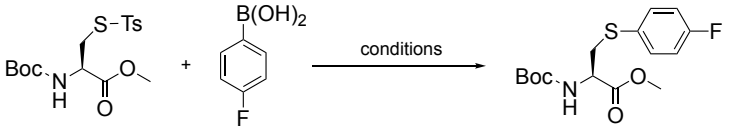
General Information: Unless otherwise stated, all reactions were set up under inert ($N_2$) atmosphere. Starting materials were purchased from commercial suppliers (Kaili Catalyst&materials Co. Ltd, Sigma Aldrich, Energy Chemical, Bidepharm, Tansoole) and used without further purifications unless otherwise stated. Basified silica gel was obtained by immersing silica in the 5% $Et_3N$/pentane overnight, and then the solvent was removed in vacuo. All solvents were dried according to standard procedures or purchased from commercial suppliers. Reaction was monitored using thin-layer chromatography (TLC) on *Merck silica gel aluminium plates* with *F254 indicator*. Visualization of the developed plates was performed under UV light (254 nm) or $KMnO_4$ stain (1.5 g $KMnO_4$, 1.25 mL 10% NaOH, 10 g $K_2CO_3$, 200 mL $H_2O$).

$^1H$, $^{13}C$, and $^{19}F$ NMR spectra were recorded on a Bruker AVIII 400 spectrometer. $^1H$ NMR and $^{13}C$ NMR chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane and $^{19}F$ NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. Coupling constants (*J*) are reported in Hertz (Hz). The residual solvent peak was used as an internal reference: $^1H$ NMR ($CDCl_3$ δ 7.26 ppm), $^{13}C$ NMR ($CDCl_3$ δ 77.16 ppm), $^1H$ NMR (DMSO-$d_6$ δ 2.50 ppm), $^{13}C$ NMR (DMSO-$d_6$ δ 39.50 ppm), $^1H$ NMR ($CD_3OD$ δ 4.87 ppm), $^{13}C$ NMR ($CD_3OD$ δ 49.00 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded using Nicolet iS50 spectrometer. HRMS data was recorded using HRMR Exactive Plus instrument. Melting point was measured using SGW X-4A instrument.

# 2. Optimization of Reaction Conditions

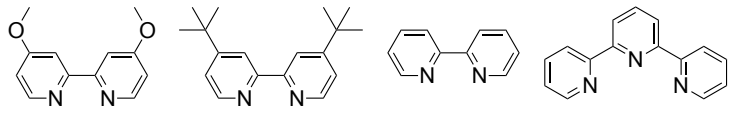
In a glove box filled with nitrogen, to an oven-dried 10 mL tube equipped with a stirring bar were added methyl *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteinate **1a** (0.1 mmol, 1.0 equiv.), (4-fluorophenyl)boronic acid **2a** (0.2 mmol, 2 equiv.), Cu catalyst, Ligand, base, solvent. The tube was sealed with a Teflon screw cap and the mixture was stirred at an indicated temperature. Upon completion, the yield was determined by $^{19}F$ NMR spectroscopy with (trifluromethoxy)benzene as an internal standard.

**Table S1: Optimization of catalyst and ligand**




1a 2a 3a

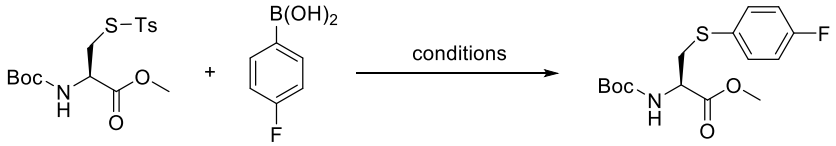
| Entry | Catalyst | Ligand | Yield (%)[a] |
|---|---|---|---|
| 1 | 20 mol% $Cu(OTf)_2$ | 20 mol% **L1** | 82 |
| 2 | 20 mol% $Cu(OAc)_2$ | 20 mol% **L1** | 96 |
| 3 | 20 mol% $CuSO_4$ | 20 mol% **L1** | 77 |
| 4 | 20 mol% $Cu(OAc)_2$ | 20 mol% **L2** | 91 |
| 5 | 20 mol% $Cu(OAc)_2$ | 20 mol% **L3** | 55 |
| 6 | 20 mol% $Cu(OAc)_2$ | 20 mol% **L4** | trace |
| 7 | 20 mol% $Cu(OAc)_2$ | 10 mol% **L1** | 73 |
| 8 | 10 mol% $Cu(OAc)_2$ | 20 mol% **L1** | 14 |
| 9 | 10 mol% $Cu(OAc)_2$ | 10 mol% **L1** | 67 |
| 10 | 5 mol% $Cu(OAc)_2$ | 5 mol% **L1** | 41 |




L1 L2 L3 L4

Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), **2a** (0.2 mmol, 2.0 equiv.), $NaHCO_3$ (0.2 mmol, 2.0 equiv.), 5-20 mol% catalyst, 5-20 mol% ligand in anhydrous MeOH (0.1 M) under $N_2$ atmosphere at 30℃ for 4 h. [a]Yield determined by crude $^{19}F$ NMR spectra analysis using trifluoromethoxy benzene as internal standard.

**Table S2: Optimization of solvent and base**

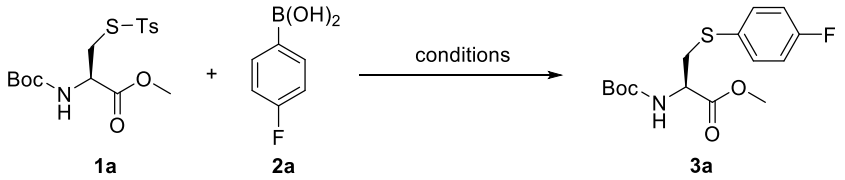



1a 2a 3a

| Entry | Base | Solvent | Yield (%)[a] |
|---|---|---|---|
| 1 | $NaHCO_3$ | MeOH | 96 |
| 2 | $Na_2CO_3$ | MeOH | 64 |
| 3 | $K_2CO_3$ | MeOH | 50 |
| 4 | $K_3PO_4$ | MeOH | trace |
| 5 | $NaHCO_3$ | EtOH | 14 |
| 6 | $NaHCO_3$ | DMF | trace |
| 7 | $NaHCO_3$ | $CH_3CN$ | 68 |

Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), **2a** (0.2 mmol, 2.0 equiv.), base (0.2 mmol, 2.0 equiv.), 20 mol% $Cu(OAc)_2$, 20 mol% **L1** in anhydrous solvent under $N_2$ atmosphere at 30℃ for 4 h. [a]Yield determined by crude $^{19}F$ NMR spectra analysis using trifluoromethoxy benzene as internal standard.

**Table S3: Control experiment**



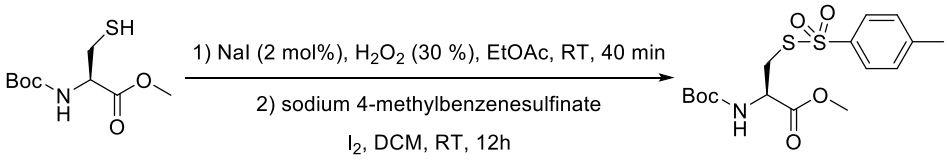

1a 2a 3a

| Entry | Deviation from standard condition | Yield (%)[a] |
|---|---|---|
| 1 | none | 96 |
| 2 | 1.5 equiv. Base | 98 |
| 3 | 1.5 equiv. **2a** | 53 |
| 4 | 1 equiv. **2a** | 23 |
| 5 | no Ligand | 77 |
| 6 | no Catalyst | N.R. |
| 7 | no Ligand and Catalyst | N.R. |
| 8 | no Base | 79 |
| 9 | ambient atmosphere | 42 |
| 10 | MeOH/$H_2O$ (80/20) | 88 |
| 11 | 0.01M **1a** | 98 |
| 12 | 0.005 M **1a** | 86 |

Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), **2a** (0.2 mmol, 2.0 equiv.), base (0.2 mmol, 2.0 equiv.), 20 mol% $Cu(OAc)_2$, 20 mol% **L1** in anhydrous MeOH (0.1 M) under $N_2$ atmosphere at 30℃ for 4 h unless otherwise noted. [a]Yield determined by crude $^{19}F$ NMR spectra analysis using trifluoromethoxy benzene as internal standard.

# 3. Procedure for the Synthesis of Starting Materials

## 3.1 **Procedure for the Synthesis of 1a**



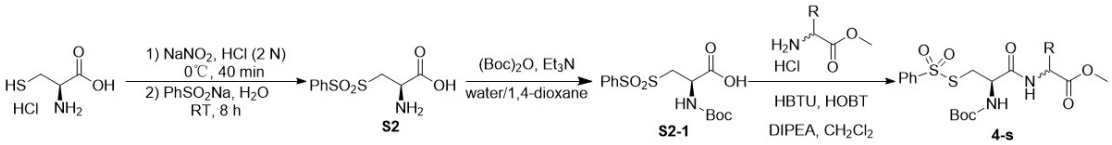

S1 1a

**Methyl *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteinate (1a):** To a stirred solution of a *N*-Boc-*L*-Cys-OMe (2 mmol, 470.6 mg) in ethyl acetate (6 mL) was added NaI (6 mg, 2 mol%) and 30% $H_2O_2$ (2 mmol, 0.22 mL) and the mixture was stirred at rt for 40 min. The solvent was removed under reduced pressure and the residue was directly used for the next step without further purification. To the mixture of sodium *p*-toluenesulfonate (3.2 mmol, 570 mg) and obtained crude disulfide in $CH_2Cl_2$ (6 mL) was added $I_2$ (2 mmol, 507.6 mg), and the mixture was stirred overnight. $CH_2Cl_2$ (50 mL) was added, followed by the addition of aq. $Na_2S_2O_3$ (1 M) with stirring until the $I_2$ color disappeared. The mixture was washed with $H_2O$ (2×50 mL). The organic layers were dried over anhydrous $Na_2SO_4$, followed by evaporation of solvent under vacuum. The residue was purified by flash column chromatography to afford the pure desired product **1a** (682.4 mg, 1.75

mmol, 88% yield) as a white solid;[1]

**$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 8.4 Hz, 2 H), 7.35 (d, *J* = 8.1 Hz, 2 H), 5.33 (d, *J* = 7.6 Hz, 1 H), 4.56 (q, *J* = 5.3 Hz, 1 H), 3.74 (s, 3 H), 3.51 (dd, *J* = 14.1, 4.8 Hz, 1 H), 3.40 (dd, *J* = 14.2, 5.6 Hz, 1 H), 2.45 (s, 3 H), 1.43 (s, 9 H) ppm.

### 3.2 General Procedure for the Synthesis of Dipeptide 4a-s to 4j-s (Method A)

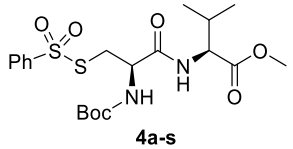



***S*-(phenylsulfonyl)-*L*-cysteine (S2)**: *L*-Cysteine monohydrochloride (6 mmol, 945.6 mg) was dissolved in 6 mL of 2 N HCl then cooled to 0 ℃ with ice-water bath. With stirring, a solution of sodium nitrite (6 mmol, 414 mg) in 4 mL of deionized water was added dropwise and the resulted deep red solution was stirred for 40 min under air atmosphere, solution of sodium 4-methylbenzenesulfinate (6 mmol, 1.97 g) in 4 mL deionized water was added dropwise with stirring. Precipitation of solids was observed immediately. The solution was warmed to room temperature to disperse solids (the product began collecting on the magnetic stirrer). Stirring was continued at rt about 12 h. The suspension was briefly cooled in an ice bath, then filtered, and washed with approximately 6 mL each of DI water, and diethyl ether to afford the target compound **S2** as a white solid (1.143 g, 4.4 mmol, 73%).[2] **S2** was directly used for the next step without further purification.

***N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteine (S2-1)**: To a solution of *S*-(phenylsulfonyl)-*L*-cysteine **S2** (2 mmol, 522.6 mg) in 4 mL of a mixture of water/dioxane (2 mL/2 mL, v/v). The mixture was added $(Boc)_2O$ (2 mmol, 436.6 mg) and $Et_3N$ (1.6 equiv., 0.44 mL), stirred overnight. After 12 h, the dioxane was removed under vacuum and the resulting aqueous layers was acidified to pH 6 and extracted with ethyl acetate for three times and was dried over $Na_2SO_4$. The resulting was concentrated under vacuum and was purified by column chromatography on silica-gel to afford the desired product as a pale yellow solid (363.5 mg, 1 mmol, 50%).[3]

Dipeptide **4-s**: To a 0.1 M solution of the *N*-Boc-*S*-(phenylsulfonyl)-*L*-Cys **S2-1** and methyl amino acids (1.1 equiv.) in anhydrous $CH_2Cl_2$ were added HBTU (1.1 equiv.), HOBT (0.37 equiv.) and DIPEA (2 equiv.). The reaction was monitored by analytical TLC. When **S2-1** was consumed, the solution was removed under vacuum and the resulting was dissolved in ethyl acetate. Organic layer was washed with saturated $NaHCO_3$×1, NaCl×2, and dried over anhydrous $Na_2SO_4$. The organic solvent was removed under vacuum and the residue was purified by column chromatography on silica-gel to afford the desired product **4-s**.[4]

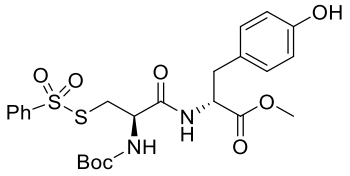
**Methyl *N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteinyl-*L*-valinate (4a-s)**




The title product compound was prepared according to the general procedure (Method A) with 0.5 mmol of *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteine for 10 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (200.3 mg, 84% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.8 Hz, 2 H), 7.60 (t, *J* = 7.4 Hz, 1 H), 7.51 (t, *J* = 7.7 Hz, 2 H), 7.07 (d, *J* = 8.5 Hz, 1 H), 5.63 (d, *J* = 8.1 Hz, 1 H), 4.50 (q, *J* = 7.0 Hz, 1 H), 4.41 (dd, *J* = 8.9, 4.9 Hz, 1 H), 3.66 (s, 3 H), 3.34-3.19 (m, 1 H), 2.18-2.06 (m, 1 H), 1.39 (s, 9 H), 0.88 (d, *J* = 6.9 Hz, 3 H), 0.84 (d, *J* = 6.9 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.78, 169.72, 155.57, 143.87, 134.01, 129.45, 127.09, 80.70, 57.35, 53.18, 52.21, 36.67, 31.02, 28.18, 18.98, 17.63 ppm; **IR (thin film, cm$^{-1}$):** 3348, 2963, 2928, 1670, 1513, 1447, 1392, 1367, 1326, 1257, 1213, 1143, 1078, 1018, 863, 795, 753, 715, 685, 664, 598, 537; **$[\alpha]_D^{25}$** = -35.1 (*c* = 0.39, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{20}H_{30}N_2NaO_7S_2$ ($M+Na^+$): 497.1387, found 497.1390; **M.p.**: 121.5-123.8 °C.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteinyl-*D*-tyrosinate (4c-s)**

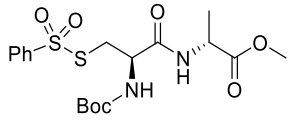


**4c-s**

The title product compound was prepared according to the general procedure (Method A) with 0.3 mmol of *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteine for 11 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:1, v/v) as the eluent, giving the titled compound as a white solid (138.5 mg, 86% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.4 Hz, 2 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 7.51 (t, *J* = 7.7 Hz, 2 H), 7.04 (d, *J* = 7.8 Hz, 1 H), 6.91 (d, *J* = 8.1 Hz, 2 H), 6.70 (d, *J* = 8.2 Hz, 2 H), 5.59 (d, *J* = 8.4 Hz, 1 H), 4.73 (q, *J* = 6.1 Hz, 1 H), 4.45 (q, *J* = 6.8 Hz, 1 H), 3.68 (s, 3 H), 3.34-3.17 (m, 2 H), 3.03 (dd, *J* = 14.1, 5.3 Hz, 1 H), 2.96 (dd, *J* = 14.0, 6.3 Hz, 1 H), 1.42 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.53, 169.63, 155.71, 155.55, 143.89, 134.14, 130.39, 129.56, 127.14, 126.77, 115.74, 81.09, 53.72, 53.42, 52.53, 37.02, 28.27 ppm; **IR (thin film, cm$^{-1}$):** 3346, 2958, 2926, 1666, 1614, 1515, 1446, 1367, 1324, 1257, 1216, 1161, 1142, 1077, 1018, 795, 756, 715, 684, 597, 537; **$[\alpha]_D^{25}$** = -33.0 (*c* = 0.44, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{24}H_{30}N_2NaO_8S_2$ ($M+Na^+$): 561.1336, found 561.1343; **M.p.**: 85.8-87.4°C.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteinyl-*D*-alaninate (4d-s)**



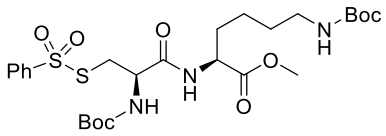
**4d-s**

The title product compound was prepared according to the general procedure (Method A) with 0. 5 mmol of *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteine for 12 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (2:5, v/v) as the eluent, giving the titled compound as a white solid (177 mg, 80% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.9 Hz, 2 H), 7.64 (t, *J* = 6.6 Hz, 1 H), 7.55 (t, *J* = 6.8 Hz, 2 H), 7.04 (d, *J* = 7.3 Hz, 1 H), 5.56-5.47 (m, 2 H), 4.59-4.45 (m, 2 H), 3.71 (s, 3 H), 3.34 (dd, *J* = 15.0, 5.6 Hz, 1 H), 3.25 (dd, *J* = 14.0, 5.1 Hz, 1 H), 1.44 (s, 9 H), 1.39 (d, *J* = 7.3 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.85, 169.30, 155.71, 144.05, 134.11, 129.56, 127.24, 80.99, 53.24, 52.63, 48.35, 36.91, 28.32, 18.20 ppm; **IR (thin film, cm$^{-1}$):** 3325, 2960, 2924, 2162, 1979, 1740, 1665, 1512, 1448, 1367, 1326, 1258, 1144, 1078, 1017, 864, 796, 716, 685, 600, 537, 432,

418; **[α]$_D^{25}$** = -29.5 (*c* = 0.38, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{18}H_{26}N_2NaO_7S_2$ ($M+Na^+$): 469.1074, found 469.1077; **M.p.**: 110.5-112.5 °C.

**Methyl *N*$^6$-(tert-butoxycarbonyl)-*N*$^2$-(*N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteinyl)-*L*-lysinate (4f-s)**

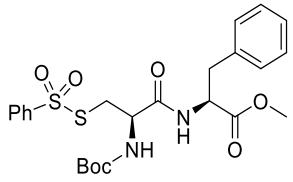


**4f-s**

The title product compound was prepared according to the general procedure (Method A) with 0.5 mmol of *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteine for 11 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (259.7 mg, 86% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.7 Hz, 2 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.51 (t, *J* = 7.7 Hz, 2 H), 7.12 (d, *J* = 8.0 Hz, 1 H), 5.71 (d, *J* = 6.5 Hz, 1 H), 4.80 (t, *J* = 5.9 Hz, 1 H), 4.45 (q, *J* = 7.8 Hz, 1 H), 3.66 (s, 3 H), 3.27 (qd, *J* = 14.6, 5.7 Hz, 2 H), 3.00 (q, *J* = 6.8 Hz, 2 H), 1.84-1.73 (m, 1 H), 1.68-1.56 (m, 1 H), 1.46-1.32 (m, 20 H), 1.30-1.22 (m, 2 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.29, 172.09, 169.65, 156.01, 155.52, 143.88, 133.99, 129.44, 127.07, 80.63, 78.96, 52.41, 52.14, 40.05, 36.86, 31.67, 29.23, 28.38, 28.19, 22.33 ppm; **IR (thin film, cm$^{-1}$):** 3332, 3019, 2962, 1694, 1508, 1367, 1260, 1214, 1144, 1094, 1013, 805, 747, 684, 665, 600, 537; **[α]$_D^{25}$** = -38.6 (*c* = 0.85, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{26}H_{41}N_3NaO_9S_2$ ($M+Na^+$): 626.2176, found 626.2181; **M.p.**: 144.5-146 °C.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteinyl-*L*-phenylalaninate (4g-s)**

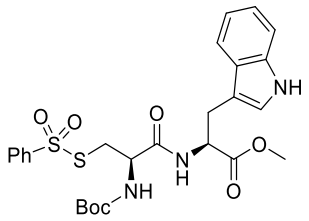


**4g-s**

The title product compound was prepared according to the general procedure (Method A) with 0.3 mmol of *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteine for 19 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a pale yellow syrup (108 mg, 69% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.6 Hz, 2 H), 7.65 (t, *J* = 7.4 Hz, 1 H), 7.60-7.52 (m, 2 H), 7.26 (dd, *J* = 14.2, 7.0 Hz, 3 H), 7.12 (d, *J* = 6.4 Hz, 2 H), 6.98 (d, *J* = 7.5 Hz, 1 H), 5.49 (d, *J* = 8.2 Hz, 1 H), 4.81 (q, *J* = 6.4 Hz, 1 H), 4.49 (q, *J* = 7.7 Hz, 1 H), 3.35 (dd, *J* = 14.0, 5.6 Hz, 1 H), 3.22 (dd, *J* = 14.1, 4.9 Hz, 1 H), 3.15 (dd, *J* = 13.9, 5.8 Hz, 1 H), 3.06 (dd, *J* = 13.9, 6.5 Hz, 1 H), 1.45 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.31, 169.43, 155.52, 143.95, 135.62, 134.05, 129.49, 129.28, 128.66, 127.23, 127.17, 80.80, 53.48, 53.36, 52.43, 37.83, 36.94, 28.26 ppm; **IR (thin film, cm$^{-1}$):** 3312, 2959, 2926, 2649, 2323, 2287, 2049, 1979, 1741, 1665, 1512, 1446, 1367, 1326, 1259, 1143, 1079, 1018, 863, 796, 715, 686, 600, 537, 417; **[α]$_D^{25}$** = -30.2 (*c* = 0.44, $CHCl_3$); **HRMS (ESI-TOF):** calculated for $C_{24}H_{30}N_2NaO_7S_2$ ($M+Na^+$): 545.1387, found 545.1392.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteinyl-*L*-tryptophanate (4h-s):**

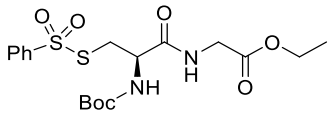


**4h-s**

The title product compound was prepared according to the general procedure (Method A) with 0.5 mmol of *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteine for 6 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (222 mg, 79% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.77 (s, 1 H), 7.81 (d, *J* = 7.5 Hz, 2 H), 7.56 (t, *J* = 7.5 Hz, 1 H), 7.50 (d, *J* = 7.8 Hz, 1 H), 7.42 (t, *J* = 7.7 Hz, 2 H), 7.31 (d, *J* = 7.9 Hz, 1 H), 7.19 -7.06 (m, 2 H), 7.05-6.97 (m, 2 H), 5.55 (d, *J* = 8.4 Hz, 1 H), 4.83 (q, *J* = 5.5 Hz, 1 H), 4.56-4.44 (m, 1 H), 3.62 (s, 3 H), 3.35-3.15 (m, 4 H), 2.80 (s, 1 H), 1.40 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.77, 169.50, 155.49, 143.81, 136.22, 133.96, 129.41, 127.37, 127.04, 123.47, 122.08, 119.50, 118.33, 111.57, 109.04, 80.67, 53.11, 52.45, 38.61, 37.29, 28.17, 27.39 ppm; **IR (thin film, cm$^{-1}$):** 3357, 2955, 2926, 1666, 1512, 1457, 1446, 1367, 1324, 1256, 1214, 1161, 1142, 1095, 1076, 1048, 1020, 862, 797, 746, 715, 684, 597, 536, 427; **$[\alpha]_D^{25}$** = -28.6 (*c* = 0.51, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{26}H_{31}N_3NaO_7S_2$ ($M+Na^+$): 584.1496, found 584.1499; **M.p.**: 87.9-90.1 °C.

**Ethyl *N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteinylglycinate (4j-s)**

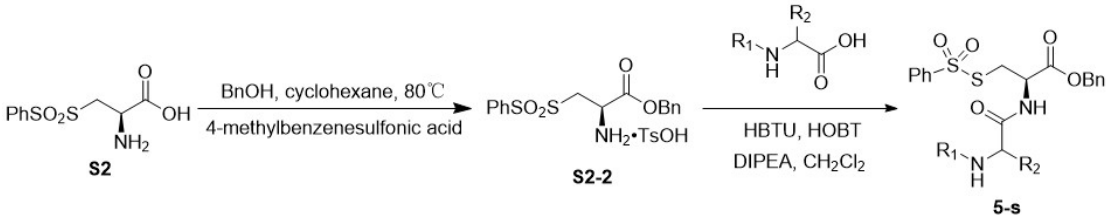


**4j-s**

The title product compound was prepared according to the general procedure (Method A) with 0.5 mmol of *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteine for 12 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:3, v/v) as the eluent, giving the titled compound as a white solid (192.6 mg, 86% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.8 Hz, 2 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.54 (t, *J* = 7.6 Hz, 2 H), 7.13 (t, *J* = 5.4 Hz, 1 H), 5.63 (d, *J* = 8.4 Hz, 1 H), 4.55 (q, *J* = 7.1 Hz, 1 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 4.04-3.90 (m, 2 H), 3.40-3.24 (m, 2 H), 1.42 (s, 9 H), 1.24 (t, *J* = 7.1 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.08, 169.32, 155.61, 143.94, 134.03, 129.48, 127.16, 80.81, 61.61, 53.20, 41.44, 37.07, 28.26, 14.13 ppm; **IR (thin film, cm$^{-1}$):** 3308, 2961, 2926, 2162, 1979, 1674, 1512, 1367, 1326, 1259, 1143, 1078, 1019, 863, 798, 716, 686, 600, 537, 457; **$[\alpha]_D^{25}$** = -36.9 (*c* = 0.52, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{18}H_{26}N_2NaO_7S_2$ ($M+Na^+$): 469.1074, found 469.1075; **M.p.**: 114.5-116.1 °C.

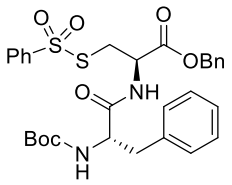
### 3.3 General Procedure for Synthesis of Dipeptide 5a-s to 5g-s (Method B)




**Benzyl *S*-(phenylsulfonyl)-*L*-cysteinate (S2-2):** A mixture of *S*-(phenylsulfonyl)-*L*-cysteine **S2** (2 mmol, 522.6 mg), benzyl alcohol (10 mmol, 1.03 mL), *p*-toluene sulfonic acid monohydrate (2.4 mmol, 413.3 mg) and cyclohexane (20 mL) was refluxed at 80℃ for 4 h using a Dean-Stark apparatus to separate water that was azeotroped out as it formed. The reaction mixture was cooled to room temperature and ethyl acetate (50 mL) was added. After stirring for 1 h, the precipitate was collected by filtration and dried to give the corresponding benzyl ester *p*-toluenesulfonate as a white solid. The crude product was used for next step without further purification.

To a 0.1 M solution of the benzyl *S*-(phenylsulfonyl)-*L*-cysteinate **S2-2** (1.1 equiv.) and protected amino acids (1 equiv.) in anhydrous $CH_2Cl_2$ were added HBTU (1.1 equiv.), HOBT (0.37 equiv.) and DIPEA (2 equiv.). Reaction monitored by analytical TLC. When material was consumed, the solvent was removed under vacuum and the resulting was dissolved in ethyl acetate. Organic layer was washed with saturated $NaHCO_3$×1, brine×2 and dried over $Na_2SO_4$. After filtration, organic solvent was removed under vacuum and the residue was purified by column chromatography on silica-gel to afford the desired product.[5]

**Benzyl *N*-((tert-butoxycarbonyl)-*L*-phenylalanyl)-*S*-(phenylsulfonyl)-*L*-cysteinate（5a-s)**

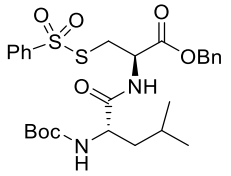



**5a-s**

The title product compound was prepared according to the general procedure (Method B) with 0.55 mmol of benzyl *S*-(phenylsulfonyl)-*L*-cysteinate for 5.5 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (215.9 mg, 72% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.3 Hz, 2 H), 7.62 (t, *J* = 7.5 Hz, 1 H), 7.51 (t, *J* = 7.7 Hz, 2 H), 7.39-7.29 (m, 5 H), 7.27-7.11 (m, 6 H), 5.14 (d, *J* = 4.5 Hz, 2 H), 5.09 (d, *J* = 8.1 Hz, 1 H), 4.80 (q, *J* = 5.5 Hz, 1 H), 4.50-4.39 (m, 1 H), 3.50 (dd, *J* = 14.5, 4.8 Hz, 1 H), 3.39 (dd, *J* = 14.5, 5.5 Hz, 1 H), 3.17 (dd, *J* = 14.0, 5.8 Hz, 1 H), 2.96 (dd, *J* = 14.2, 8.1 Hz, 1 H), 1.37 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.73, 168.92, 155.45, 143.94, 136.65, 134.78, 134.13, 129.50, 129.35, 128.71, 128.64, 128.51, 127.17, 126.90, 80.28, 67.98, 55.62, 51.89, 38.12, 36.94, 28.26 ppm; **IR (thin film, cm$^{-1}$):** 3300, 2959, 2924, 2323, 2160, 2049, 1983, 1665, 1497, 1447, 1366, 1327, 1258, 1166, 1144, 1078, 1019, 798, 752, 715, 698, 685, 599, 537, 427; **$[\alpha]_D^{25}$** = -29.2 (*c* = 0.36, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{30}H_{34}N_2NaO_7S_2$ ($M+Na^+$): 621.1700, found 621.1702; **M.p.**: 90.7-92.5 °C.

**Benzyl *N*-((tert-butoxycarbonyl)-*L*-leucyl)-*S*-(phenylsulfonyl)-*L*-cysteinate (5b-s)**

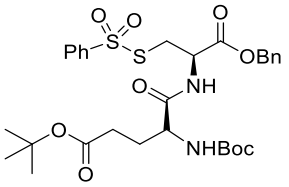


**5b-s**

The title product compound was prepared according to the general procedure (Method B) with 0.55 mmol of benzyl *S*-(phenylsulfonyl)-*L*-cysteinate for 11 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white syrup (185.7 mg, 76% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.8 Hz, 2 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.51 (t, *J* = 7.7 Hz, 2 H), 7.39-7.28 (m, 4 H), 7.26 (d, *J* = 8.2 Hz, 1 H), 5.19-5.10 (m, 2 H), 4.98 (d, *J* = 8.2 Hz, 1 H), 4.87-4.78 (m, 1 H), 4.19 (t, *J* = 11.0 Hz, 1 H), 3.47 (qd, *J* = 14.5, 5.1 Hz, 2 H), 1.71-1.62 (m, 2 H), 1.44 (s, 9 H), 0.90 (d, *J* = 3.6 Hz, 6 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.94, 169.12, 155.72, 143.92, 134.81, 134.14, 129.52, 128.72, 128.54, 127.23, 80.24, 67.99, 53.10, 51.82, 41.08, 37.01, 28.77, 24.76, 23.06, 21.82 ppm; **IR (thin film, cm$^{-1}$):** 3323, 2958, 2925, 2323, 2160, 2049, 1664, 1512, 1447, 1366, 1326, 1259, 1165, 1144, 1078, 1020, 796, 753, 715, 697, 685, 598, 537, 433; **$[\alpha]_D^{25}$** = -41.6 (*c* = 0.50, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{27}H_{36}N_2NaO_7S_2$ ($M+Na^+$): 587.1856, found 587.1859.

**Tert-butyl (*R*)-5-(((*R*)-1-(benzyloxy)-1-oxo-3-((phenylsulfonyl)thio)propan-2-yl)amino)-4-((tert-butoxycarbonyl)amino)-5-oxopentanoate (5d-s)**

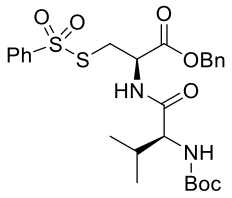


**5d-s**

The title product was prepared according to the general procedure (Method B) with 0.55 mmol of benzyl *S*-(phenylsulfonyl)-*L*-cysteinate for 11 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a chartreuse mucus (232.5 mg, 73% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.6 Hz, 2 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.50 (t, *J* = 7.9 Hz, 2 H), 7.46 (d, *J* = 8.1 Hz, 2 H), 7.38-7.29 (m, 5 H), 5.51 (d, *J* = 7.4 Hz, 1 H), 5.15 (s, 2 H), 4.81 (q, *J* = 6.1 Hz, 1 H), 4.25-4.15 (m, 1 H), 3.52 (dd, *J* = 14.5, 4.8 Hz, 1 H), 3.43 (dd, *J* = 14.4, 6.0 Hz, 1 H), 2.43-2.25 (m, 2 H), 2.17-2.05 (m, 1 H), 1.95-1.83 (m, 1 H), 1.44 (s, 18 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.45, 171.94, 168.90, 155.52, 143.79, 134.70, 133.97, 129.35, 128.51, 128.48, 128.32, 127.00, 80.58, 79.89, 67.74, 53.84, 51.70, 31.60, 28.20, 27.95, 27.23 ppm; **IR (thin film, cm$^{-1}$):** 3314, 2961, 2926, 1720, 1498, 1447, 1366, 1327, 1257, 1144, 1077, 1020, 795, 753, 715, 697, 685, 597, 537; **$[\alpha]_D^{25}$** = -28.2 (*c* = 0.51, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{30}H_{40}N_2NaO_9S_2$ ($M+Na^+$): 659.2067, found 659.2067.

**Benzyl *N*-((tert-butoxycarbonyl)-*L*-valyl)-*S*-(phenylsulfonyl)-*L*-cysteinate (5e-s)**

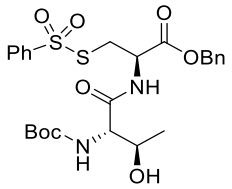


**5e-s**

The title product was prepared according to the general procedure (Method B) with 1.1 mmol of benzyl *S*-(phenylsulfonyl)-*L*-cysteinate for 24 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a chartreuse mucus (332.9 mg, 59% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.8 Hz, 2 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 7.49 (t, *J* = 7.7 Hz, 2 H), 7.44 (d, *J* = 7.7 Hz, 1 H), 7.37-7.28 (m, 5 H), 5.37 (d, *J* = 8.9 Hz, 1 H), 5.13 (d, *J* = 2.6 Hz, 2 H), 4.84 (q, *J* = 6.4 Hz, 1 H), 4.11-3.99 (m, 1 H), 3.49 (dd, *J* = 14.5, 4.9 Hz, 1 H), 3.43 (dd, *J* = 14.4, 6.5 Hz, 1 H), 2.18-2.06 (m, 1 H), 1.43 (s, 9 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.87 (d, *J* = 6.8 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.13, 169.21, 155.85, 143.81, 134.83, 134.14, 129.50, 128.63, 128.60, 128.48, 127.14, 79.83, 67.87, 59.68, 51.79, 36.86, 30.85, 28.35, 19.24, 17.69 ppm; **IR (thin film, cm$^{-1}$):** 3299, 2961, 2926, 2323, 2160, 1979, 1660, 1499, 1447, 1366, 1326, 1258, 1164, 1143, 1077, 1016, 867, 796, 753, 715, 696, 684, 597, 536; **$[\alpha]_D^{25}$** = -19.8 (*c* = 0.44, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{26}H_{34}N_2NaO_7S_2$ ($M+Na^+$): 573.1700, found 573.1700.

**Benzyl *N*-((tert-butoxycarbonyl)-*L*-threonyl)-*S*-(phenylsulfonyl)-*L*-cysteinate (5f-s)**

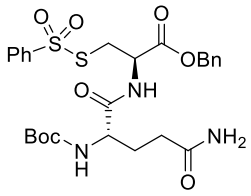


**5f-s**

The title product was prepared according to the general procedure (Method B) with 0.55 mmol of benzyl *S*-(phenylsulfonyl)-*L*-cysteinate for 14 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a chartreuse mucus (213.8 mg, 77% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.9 Hz, 2 H), 7.68 (d, *J* = 7.5 Hz, 1 H), 7.58 (t, *J* = 7.5 Hz, 1 H), 7.47 (t, *J* = 7.8 Hz, 2 H), 7.37-7.27 (m, 5 H), 5.73 (d, *J* = 7.7 Hz, 1 H), 5.13 (s, 2 H), 4.84 (q, *J* = 6.1 Hz, 1 H), 4.31 (d, *J* = 6.3 Hz, 1 H), 4.17 (d, *J* = 7.9 Hz, 1 H), 3.73 (s, 1 H), 3.54 (dd, *J* = 14.5, 4.6 Hz, 1 H), 3.44 (dd, *J* = 14.8, 5.9 Hz, 1 H), 1.44 (s, 9 H), 1.15 (d, *J* = 5.7 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.38, 168.98, 156.09, 143.77, 134.61, 133.99, 129.35, 128.53, 128.34, 126.96, 80.15, 67.85, 66.93, 58.76, 51.92, 36.64, 28.19, 18.30 ppm; **IR (thin film, cm$^{-1}$):** 3348, 2961, 2926, 2035, 1978, 1667, 1497, 1447, 1367, 1326, 1258, 1163, 1143, 1077, 1018, 874, 796, 752, 715, 697, 684, 597, 536; **$[\alpha]_D^{25}$** = -51.2 (c = 0.43, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{25}H_{32}N_2NaO_8S_2$ ($M+Na^+$): 575.1492, found 575.1492.

**Benzyl *N*-((tert-butoxycarbonyl)-*L*-glutaminyl)-*S*-(phenylsulfonyl)-*L*-cysteinate (5g-s)**

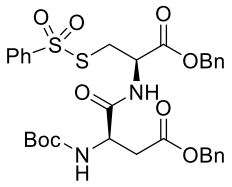


**5g-s**

The title product was prepared according to the general procedure (Method B) with 0.55 mmol of benzyl *S*-(phenylsulfonyl)-*L*-cysteinate for 10 h and isolated by column chromatography on silica gel using ethyl acetate as the eluent, giving the titled compound as a white solid (243.6 mg, 84% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.6 Hz, 1 H), 7.87 (d, *J* = 7.4 Hz, 2 H), 7.61 (t, *J* = 7.4 Hz, 1 H), 7.49 (t, *J* = 7.7 Hz, 2 H), 7.39-7.28 (m, 5 H), 6.36 (s, 1 H), 5.99 (s, 1 H), 5.69 (d, *J* = 7.6 Hz, 1 H), 5.13 (s, 2 H), 4.79 (q, *J* = 7.2 Hz, 1 H), 4.20 (q, *J* = 7.1 Hz, 1 H), 3.50 (dd, *J* = 14.4, 4.7 Hz, 1 H), 3.41 (dd, *J* = 14.4, 6.9 Hz, 1 H), 2.42-2.16 (m, 3 H), 2.12-2.01 (m, 1 H), 1.99-1.86 (m, 1 H), 1.43 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 175.40, 172.09, 169.39, 155.92, 143.96, 134.78, 133.66, 129.47, 128.69, 128.50, 127.14, 80.21, 67.97, 53.58, 51.86, 36.82, 31.74, 28.91, 28.33 ppm; **IR (thin film, cm$^{-1}$):** 3337, 2958, 2924, 2323, 2160, 1979, 1664, 1512, 1448, 1366, 1309, 1257, 1163, 1143, 1076, 1023, 861, 796, 753, 715, 696, 684, 590, 536, 491; **$[\alpha]_D^{25}$** = -15.7 (*c* = 0.35, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{26}H_{33}N_3NaO_8S_2$ ($M+Na^+$): 602.1601, found 602.1608; **M.p.**: 65.6-66.4 °C.

**Benzyl (*R*)-4-(((*R*)-1-(benzyloxy)-1-oxo-3-((phenylsulfonyl)thio)propan-2-yl)amino)-3-((tert-butoxycarbonyl)amino)-4-oxobutanoate (5h-s)**



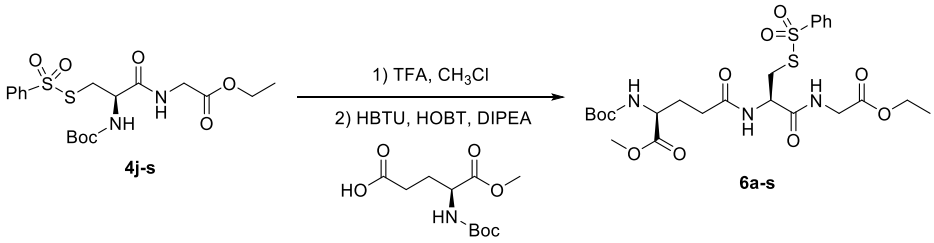
**5h-s**

The title product was prepared according to the general procedure (Method B) with 0.55 mmol of benzyl *S*-(phenylsulfonyl)-*L*-cysteinate for 5.5 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a chartreuse mucus (262 mg, 80% yield).

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.4 Hz, 2 H), 7.60 (t, *J* = 7.6 Hz, 1 H), 7.53-7.45 (m, 3 H), 7.38-7.26 (m, 10 H), 5.72 (d, *J* = 8.8 Hz, 1 H), 5.14 (s, 2 H), 5.11 (s, 2 H), 4.84-4.77 (m, 1 H), 4.61 (q, *J* = 6.6 Hz, 1 H), 3.51 (dd, *J* = 14.5, 4.8 Hz, 1 H), 3.42 (dd, *J* = 14.5, 5.7 Hz, 1 H), 2.93 (dd, *J* = 16.8, 5.4 Hz, 1 H), 2.80 (dd, *J* = 17.0, 5.9 Hz, 1 H), 1.45 (s, 9 H) ppm; $^{13}$C NMR (101 MHz, $CDCl_3$) δ 171.10, 170.91, 168.76, 155.39, 143.86, 135.38, 134.69, 133.96, 129.34, 128.55, 128.52, 128.46, 128.33, 128.21, 128.13, 127.02, 80.44, 67.81, 66.67, 51.89, 50.63, 36.62, 36.09, 28.18 ppm; IR (thin film, cm$^{-1}$): 3353, 2960, 2926, 2162, 1735, 1679, 1497, 1447, 1366, 1327, 1257, 1162, 1143, 1077, 1049, 1022, 909, 859, 798, 751, 715, 696, 684, 597, 536; $[\alpha]_D^{25}$ = -15.6 (*c* = 0.59, $CHCl_3$); HRMS (ESI-TOF): calculated for $C_{32}H_{36}N_2NaO_9S_2$ ($M+Na^+$): 679.1754, found 679.1752.

### 3.4 Procedure for Synthesis of Tripeptides

**Methyl $N^2$-(tert-butoxycarbonyl)-$N^5$-((*R*)-1-((2-ethoxy-2-oxoethyl)amino)-1-oxo-3-((phenylsulfonyl)thio)propan-2-yl)-*L*-glutaminate (6a-s)**

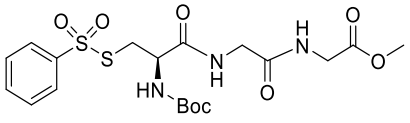



**4j-s** (150.2 mg, 0.34 mmol) was dissolved in 0.5 mL of dichloromethane, and TFA (0.5 mL) was added dropwise. After 1 h, solvent was removed under reduced pressure. The resulting residue as a brown yellow liquid for next step without further purification.

The residue and (*S*)-4-((tert-butoxycarbonyl)amino)-5-methoxy-5-oxopentanoic acid (80.8 mg, 0.31 mmol) in anhydrous $CH_2Cl_2$ were added HBTU (129 mg, 0.34 mmol), HOBT (15.5 mg, 0.11 mmol) and DIPEA (80 mg, 0.62 mmol). Reaction monitored by analytical TLC. When material was consumed, the solvent was removed under vacuum and the resulting was dissolved in ethyl acetate. Organic layer was washed with saturated $NaHCO_3$×1, brine×2 and dried over $Na_2SO_4$. After filtration, organic solvent was removed under vacuum and the residue was purified by column chromatography on silica-gel using ethyl acetate/petroleum ether (2:1, v/v) as the eluent to afford the desired product as a pale yellow mucus (78.4 mg, 43% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.4 Hz, 2 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.54 (t, *J* = 7.7 Hz, 2 H), 7.42 (t, *J* = 5.8 Hz, 1 H), 7.10 (d, *J* = 7.8 Hz, 1 H), 5.49 (d, *J* = 8.2 Hz, 1 H), 4.81 (q, *J* = 6.7 Hz, 1 H), 4.28 (q, *J* = 7.1 Hz, 1 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 4.02-3.87 (m, 2 H), 3.70 (s, 3 H), 3.38 (dd, *J* = 14.6, 6.7 Hz, 1 H), 3.28 (dd, *J* = 14.6, 5.3 Hz, 1 H), 2.35 (t, *J* = 7.2 Hz, 2 H), 2.19-2.10 (m, 1 H), 2.00-1.92 (m, 1 H), 1.38 (s, 9 H), 1.22 (t, *J* = 7.2 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.99, 172.90, 169.87, 169.51, 155.76, 143.81, 134.15, 129.57, 127.21, 80.15, 61.57, 52.79, 52.56, 52.14, 41.45, 36.40, 31.89, 28.33, 28.12, 14.15 ppm; **IR (thin film, cm$^{-1}$)**: 3312, 2957, 2927, 1738, 1660, 1527, 1445, 1368, 1324, 1255, 1207, 1144, 1075, 1020, 862, 794, 754, 715, 685, 597, 536; **$[\alpha]_D^{25}$** = -48.3 (*c* = 0.42, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{24}H_{35}N_3NaO_{10}S_2$ ($M+Na^+$): 612.1656, found 612.1652.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(phenylsulfonyl)-*L*-cysteinylglycylglycinate (6b-s)**



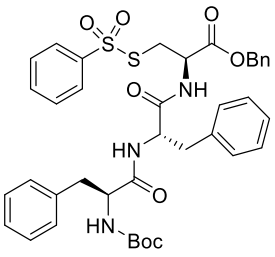
**6b-s**

The title product compound was prepared according to the general procedure (Method A) with 0.5 mmol of *N*-(tert-butoxycarbonyl)-*S*-tosyl-*L*-cysteine and 0.55mmol of methyl glycyl glycinate for 10 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (3:1, v/v) as the eluent, giving the titled compound as a white syrup (182 mg, 74% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.1 Hz, 2 H), 7.66 (t, *J* = 7.4 Hz, 1 H), 7.57 (t, *J* = 7.8 Hz, 2 H), 7.29 (d, *J* = 5.8 Hz, 1 H), 6.94 (s, 1 H), 5.71 (d, *J* = 7.6 Hz, 1 H), 4.51 (q, *J* = 6.2 Hz, 1 H), 4.09-3.94 (m, 4 H), 3.73 (s, 3 H), 3.43-3.30 (m, 2 H), 1.45 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.43, 170.25, 168.96, 155.93, 144.00, 134.27, 129.66, 127.32, 81.34, 53.93, 52.55, 43.21, 41.26, 36.95, 28.39 ppm; **IR (thin film, cm$^{-1}$)**: 3287, 3021, 2961, 2927, 1743, 1647, 1497,

1446, 1327, 1257, 1214, 1167, 1144, 1078, 1015, 795, 751, 697, 595, 536; **$[\alpha]_D^{25}$** = -30.0 (*c* = 0.32, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{19}H_{27}N_3NaO_8S_2$ ($M+Na^+$): 512.1132, found 512.1130.

**Benzyl *N*-(tert-butoxycarbonyl)-*L*-phenylalanyl-*L*-phenylalanyl-*S*-(phenylsulfonyl)-*L*-cysteinate (6c-s)**

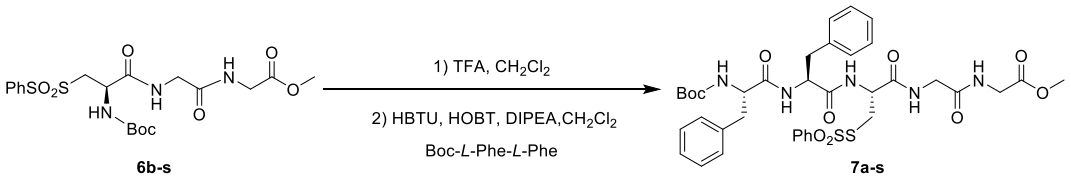


**6c-s**

The title product was prepared according to the general procedure (Method B) with 0.55 mmol of benzyl *S*-(phenylsulfonyl)-*L*-cysteinate and 0.5 mmol of (tert-butoxycarbonyl)-*L*-phenylalanyl-*L*-phenylalanine for 16 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a pale yellow solid (150.2 mg, 40% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.4 Hz, 2 H), 7.61 (t, *J* = 7.4 Hz, 1 H), 7.50 (t, *J* = 7.7 Hz, 3 H), 7.43-7.16 (m, 15 H), 7.07 (d, *J* = 6.7 Hz, 2 H), 6.78 (d, *J* = 8.2 Hz, 1 H), 5.16 (s, 2 H), 4.87-4.73 (m, 2 H), 4.45-4.36 (m, 1 H), 3.47 (dd, *J* = 14.4, 5.3 Hz, 1 H), 3.37 (dd, *J* = 14.4, 6.2 Hz, 1 H), 3.12-2.89 (m, 4 H), 1.37 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.30, 170.82, 168.82, 155.60, 144.01, 136.49, 136.05, 134.87, 134.00, 129.42, 129.33, 129.31, 128.66, 128.62, 128.58, 128.54, 128.46, 127.97, 127.10, 126.96, 80.27, 67.81, 55.85, 53.83, 52.00, 37.92, 36.79, 28.25 ppm; **IR (thin film, cm$^{-1}$)**: 3316, 2957, 2926, 1662, 1527, 1444, 1408, 1368, 1323, 1255, 1214, 1142, 1076, 1017, 862, 793, 754, 714, 685, 597, 536; **$[\alpha]_D^{25}$** = -19.0 (*c* = 0.20, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{39}H_{43}N_3NaO_8S_2$ ($M+Na^+$): 768.2384, found 768.2380; **M.p.**: 122.5-124.5 °C.

**Methyl *N*-(tert-butoxycarbonyl)-*L*-phenylalanyl-*L*-phenylalanyl-*S*-(phenylsulfonyl)-*L*-cysteinylglycylglycinate (7a-s)**




**6b-s** **7a-s**

**6b-s** (123.6 mg, 0.25 mmol) was dissolved in 3 mL of dichloromethane, and TFA (1 mL) was added dropwise. After 20 min, solvent was removed under reduced pressure. The resulting residue as a brown yellow liquid for next step without further purification.

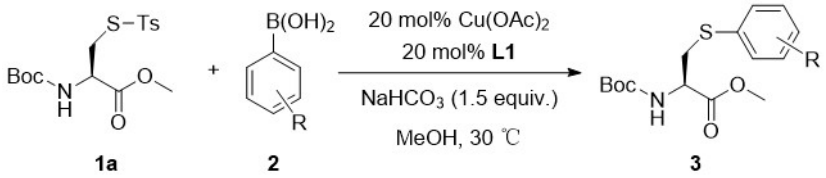
The residue and (tert-butoxycarbonyl)-*L*-phenylalanyl-*L*-phenylalanine (82.5 mg, 0.2 mmol) in anhydrous $CH_2Cl_2$ were added HBTU (83.4 mg, 0.22 mmol), HOBT (10 mg, 0.07 mmol) and DIPEA (77.6 mg, 0.4 mmol). Reaction monitored by analytical TLC. When material was consumed, the solvent was removed under vacuum and the resulting was dissolved in $CHCl_3$. Organic layer was washed with saturated $NaHCO_3$×1, brine×2 and dried over $Na_2SO_4$. After filtration, organic solvent was removed under vacuum and the residue was purified by column chromatography on basified silica-gel using ethyl acetate/petroleum ether (2:1, v/v) as the eluent to afford the desired

product as a colorless mucus (101.6 mg, 65% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.4 Hz, 2 H), 7.67 (t, *J* = 7.4 Hz, 1 H), 7.58 (t, *J* = 7.6 Hz, 2 H), 7.51 (d, *J* = 8.1 Hz, 1 H), 7.38 (s, 1 H), 7.36-7.27 (m, 5 H), 7.16 (d, *J* = 6.2 Hz, 2 H), 7.10 (d, *J* = 6.7 Hz, 2 H), 7.00-6.95 (m, 1 H), 6.70-6.58 (d, 1 H), 4.85 (d, *J* = 4.3 Hz, 1 H), 4.76-4.64 (m, 1 H), 4.54 (dd, *J* = 12.1, 5.8 Hz, 1 H), 4.32-4.24 (m, 1 H), 4.17-4.00 (m, 2 H), 3.88 (td, *J* = 17.0, 5.5 Hz, 2 H), 3.69 (s, 3 H), 3.48 (dd, *J* = 13.9, 4.1 Hz, 1 H), 3.33-3.16 (m, 2 H), 3.14-3.00 (m, 2 H), 2.87 (dd, *J* = 14.0, 8.4 Hz, 1 H), 1.28 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 173.30, 171.89, 170.40, 169.74, 169.28, 156.84, 144.11, 135.68, 135.63, 134.27, 129.69, 129.35, 129.29, 129.26, 129.08, 127.73, 127.60, 127.34, 81.77, 56.69, 55.34, 52.94, 52.36, 43.43, 41.11, 37.36, 36.57, 36.37, 28.37 ppm; **IR (thin film, cm$^{-1}$):** 3278, 2958, 2923, 2852, 1698, 1632, 1514, 1446, 1392, 1365, 1328, 1258, 1215, 1145, 1078, 1016, 798, 753, 715, 698, 684, 596, 536; **$[\alpha]_D^{25}$** = -34.3 (*c* = 0.87, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{37}H_{45}N_5NaO_{10}S_2$ ($M+Na^+$): 806.2500, found 806.2488.

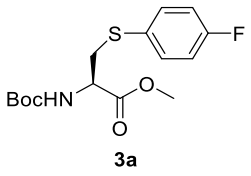
# 4. General Procedure for Copper-Catalyzed *S*-Arylation

## 4.1 General Procedure for Copper-Catalyzed *S*-Arylation of 1a (Method C)




The mixture of **1a** (0.1 mmol, 38.9 mg), **2** (0.2 mmol, 2 equiv.), $NaHCO_3$ (0.15 mmol, 12.6 mg), $Cu(OAc)_2$ (20 mol%, 4 mg), **L1** (20 mol%, 4.3 mg) in 1 mL of dry methanol was stirred at 30℃ under $N_2$ atmosphere. After 4 h, the solvent was removed under vacuum and the residue was purified by flash column chromatography to afford the pure desired product.

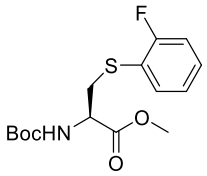
**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-fluorophenyl)-*L*-cysteinate (3a)**




**3a** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:7, v/v) as the eluent, giving the titled compound as a white solid (32.2 mg, 98% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.44-7.37 (m, 2 H), 6.98 (t, *J* = 8.6 Hz, 2 H), 5.34 (d, *J* = 8.0 Hz, 1 H), 4.57-4.46 (m, 1 H), 3.54 (s, 3 H), 3.23-3.35 (m, 2 H), 1.40 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.12 (m, 1 F) ppm. The data is in accordance to the literature.[6]

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(2-fluorophenyl)-*L*-cysteinate (3b)**

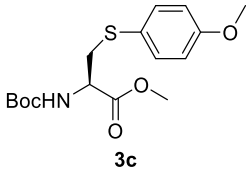



**3b**

**3b** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5, v/v) as the eluent, giving the titled compound as a white mucus (32.5 mg, 81% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.43 (t, *J* = 7.6 Hz, 1 H), 7.28-7.20 (m, 1 H), 7.08 (d, *J* = 7.4 Hz, 1 H), 7.04 (d, *J* = 8.4 Hz, 1 H), 5.37 (d, *J* = 8.1 Hz, 1 H), 4.59-4.50 (m, 1 H), 3.52 (s, 3 H), 3.42-3.28 (m, 2 H), 1.41 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -107.87 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.85, 162.18 (d, $J_{C\text{-}F}$ = 247.4 Hz), 154.95, 134.27, 129.72, 129.68 (d, $J_{C\text{-}F}$ = 8.02 Hz), 124.51 (d, $J_{C\text{-}F}$ = 3.81 Hz), 115.91 (d, $J_{C\text{-}F}$ = 22.80 Hz), 80.12, 53.24, 52.34, 36.38, 28.25; **IR (thin film, cm$^{-1}$):** 3368, 2956, 2925, 1746, 1712, 1499, 1473, 1437, 1366, 1349, 1258, 1219, 1162, 1052, 1012, 859, 796, 755, 673, 548, 457; **$[\alpha]_D^{25}$** = 61.7 (*c* = 0.47, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{15}H_{20}FNNaO_4S$ ($M+Na^+$): 352.0989, found 352.0989.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-methoxyphenyl)-*L*-cysteinate (3c)**

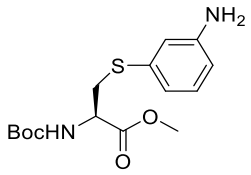



**3c**

**3c** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5, v/v) as the eluent, giving the titled compound as a white mucus (33.5 mg, 98% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.38 (dt, *J* = 8.8, 3.2 Hz, 2 H), 6.82 (dt, *J* = 8.7, 3.2 Hz, 2 H), 5.33 (d, *J* = 7.9 Hz, 1 H), 4.56-4.44 (m, 1 H), 3.78 (s, 3 H), 3.53 (s, 3 H), 3.24 (d, *J* = 4.8 Hz, 2 H), 1.41 (s, 9 H) ppm. The data is in accordance to the literature.[6]

**Methyl *S*-(3-aminophenyl)-*N*-(tert-butoxycarbonyl)-*L*-cysteinate (3d)**



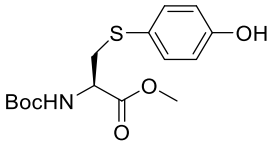

**3d**

**3d** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a brown yellow mucus (28.8 mg, 88% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.06 (t, *J* = 7.8 Hz, 1 H), 6.77 (d, *J* = 7.4 Hz, 1 H), 6.72 (s, 1 H), 6.52 (d, *J* = 5.7 Hz, 1 H), 5.35 (d, *J* = 8.0 Hz, 1 H), 4.50-4.62 (m, *J* = 9.2, 5.0 Hz, 1 H), 3.58 (s, 3 H), 3.34 (d, *J* = 4.9 Hz, 2 H), 1.42 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.13, 155.03, 146.93, 135.54, 129.83, 120.70, 117.04, 113.82, 80.10, 53.24, 52.35, 36.94, 28.28 ppm; **IR (thin**

**film, cm$^{-1}$):** 3367, 2956, 2924, 2852, 1741, 1701, 1623, 1591, 1500, 1482, 1438, 1391, 1365, 1305, 4257, 1215, 1161, 1051, 1012, 860, 777, 686, 498, 448, 421; **[α]$_D^{25}$** = 43.6 (*c* = 0.55, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{15}H_{22}N_2NaO_4S$ ($M+Na^+$): 349.1192, found 349.1193.

**Methyl N-(tert-butoxycarbonyl)-S-(4-hydroxyphenyl)-L-cysteinate (3e)**

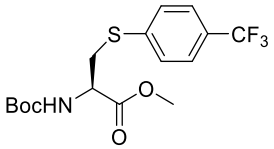



**3e**

**3e** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:1, v/v) as the eluent, giving the titled compound as a yellow mucus (32.7 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.1 Hz, 2 H), 6.98 (s, 1 H) 6.75 (d, *J* = 8.2 Hz, 2 H), 5.43 (d, *J* = 8.4 Hz, 1 H), 4.40-4.52 (m, 1 H), 3.52 (s, 3 H), 3.20 (d, *J* = 5.2 Hz, 2 H), 1.42 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.53, 156.49, 155.48, 135.02, 123.94, 116.37, 80.65, 53.21, 52.57, 38.96, 28.41 ppm; **IR (thin film, cm$^{-1}$):** 3353, 2955, 2926, 1683, 1600, 1582, 1495, 1435, 1392, 1366, 1258, 1216, 1161, 1094, 1054, 1011, 829, 796, 756, 659, 638, 523; **[α]$_D^{25}$** = 63.0 (*c* = 0.50, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{15}H_{21}NNaO_5S$ ($M+Na^+$): 350.1033, found 350.1033.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-(trifluoromethyl)phenyl)-*L*-cysteinate (3f)**

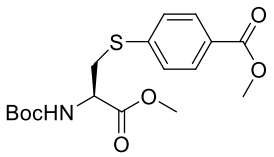



**3f**

**3f** was synthesized according to general procedure (Method C) for 6 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5, v/v) as the eluent, giving the titled compound as a white solid (37.9 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.3 Hz, 2 H), 7.46 (d, *J* = 8.1 Hz, 2 H), 5.31 (d, *J* = 8.0 Hz, 1 H), 4.57-4.67 (m, 1 H), 3.62 (s, 3 H), 3.49 (dd, *J* = 13.7, 4.4 Hz, 1 H), 3.40 (dd, *J* = 14.1, 4.6 Hz, 1 H), 1.40 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.58 (s, 3 F) ppm. The data is in accordance to the literature.[6]

**Methyl (*R*)-4-((2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)thio)benzoate (3g)**



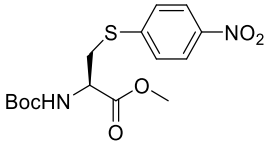

**3g**

**3g** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5, v/v) as the eluent, giving the titled compound as a brown yellow mucus (32.5 mg, 88% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.3 Hz, 2 H), 7.37 (d, *J* = 7.4 Hz, 2 H), 5.35 (d, *J* = 7.9

Hz, 1 H), 4.62 (q, *J* = 6.9, 6.1 Hz, 1 H), 3.89 (s, 3 H), 3.61 (s, 3 H), 3.49 (dd, *J* = 13.7, 4.4 Hz, 1 H), 3.42 (dd, *J* = 13.9, 4.3 Hz, 1 H), 1.41 (s, 9 H). ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.88, 166.67, 155.03, 142.06, 130.11, 128.32, 127.89, 80.40, 53.30, 52.65, 52.22, 35.63, 28.33 ppm; **IR (thin film, cm$^{-1}$):** 3362, 2953, 2925, 2853, 1746, 1716, 1594, 1492, 1454, 1435, 1392, 1366, 1351, 1284, 1274, 1258, 1162, 1106, 1089, 1052, 1013, 794, 759, 691, 523, 485, 424; **$[\alpha]_D^{25}$** = 50.9 (*c* = 0.57, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{17}H_{23}NNaO_6S$ ($M+Na^+$): 392.1138, found 392.1138.

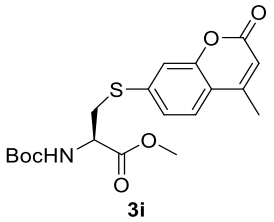
**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-nitrophenyl)-*L*-cysteinate (3h)**




**3h**

**3h** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a pale yellow solid (35.6 mg, quant. yield).
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.9 Hz, 2 H), 7.42 (d, *J* = 8.9 Hz, 2 H), 5.34 (d, *J* = 7.1 Hz, 1 H), 4.64 (q, *J* = 5.7 Hz, 1 H), 3.70 (s, 3 H), 3.57 (dd, *J* = 14.0, 5.0 Hz, 1 H), 3.43 (dd, *J* = 13.9, 5.0 Hz, 1 H), 1.41 (s, 9 H) ppm. The data is in accordance to the literature.[6]

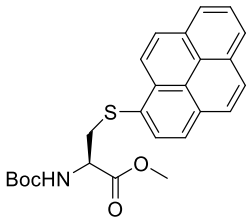
**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-methyl-2-oxo-2H-chromen-7-yl)-*L*-cysteinate (3i)**




**3i**

**3i** was synthesized according to general procedure (Method C) for 20 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a brown yellow mucus (39.4 mg, quant. yield).
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.2 Hz, 1 H), 7.27-7.20 (m, 2 H), 6.22 (s, 1 H), 5.34 (d, *J* = 7.9 Hz, 1 H), 4.67-4.56 (m, 1 H), 3.68 (s, 3 H), 3.51 (dd, *J* = 13.8, 4.7 Hz, 2 H), 3.38 (dd, *J* = 14.0, 5.2 Hz, 2 H), 2.39 (s, 3 H), 1.40 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.87, 160.52, 155.03, 153.78, 152.07, 141.20, 124.92, 124.38, 118.12, 116.19, 114.57, 80.50, 53.23, 52.80, 35.77, 28.35, 18.68 ppm; **IR (thin film, cm$^{-1}$):** 3345, 2955, 2925, 2853, 1713, 1619, 1600, 1503, 1436, 1386, 1366, 1314, 1245, 1216, 1162, 1095, 1053, 1011, 954, 853, 800, 751, 705, 664, 571, 537, 520, 439; **$[\alpha]_D^{25}$** = 20.4 (*c* = 0.50, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{19}H_{23}NNaO_6S$ ($M+Na^+$): 416.1138, found 416.1137; **M.p.**: 87.2-88.3 °C.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(pyren-1-yl)-*L*-cysteinate (3j)**

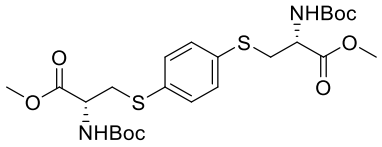



**3j**

**3j** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:3, v/v) as the eluent, giving the titled compound as a brown yellow mucus (43.6 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 9.2 Hz, 1 H), 8.26-8.16 (m, 4 H), 8.09 (t, *J* = 7.72 Hz, 2 H), 8.03 (t, *J* = 6.8 Hz, 2 H), 5.33 (d, *J* = 8.0 Hz, 1 H), 4.63-4.55 (m, 1 H), 3.56 (qd, *J* = 14.0, 4.6 Hz, 1 H), 3.37 (s, 3 H), 1.23 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.01, 154.81, 132.05, 131.47, 131.24, 131.22, 130.90, 129.03, 128.42, 128.00, 127.18, 126.30, 125.58, 125.53, 125.25, 124.90, 124.63, 124.44, 79.91, 53.77, 52.29, 38.75, 28.07 ppm; **IR (thin film, cm$^{-1}$):** 3366, 2955, 2923, 2852, 1744, 1711, 1593, 1497, 1455, 1436, 1365, 1349, 1257, 1213, 1161, 1051, 1013, 844, 817, 796, 756, 713, 680, 664, 600, 495; **$[\alpha]_D^{25}$** = 66.7 (*c* = 0.51, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{25}H_{25}NNaO_4S$ ($M+Na^+$): 458.1397, found 458.1397.

**Dimethyl 3,3'-(1,4-phenylenebis(sulfanediyl))(2*R*,2*′R*)-bis(2-((tert-butoxycarbonyl)amino)propanoate) (3k)**

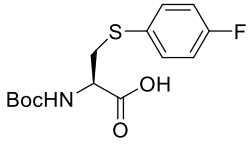



**3k**

**3k** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5, v/v) as the eluent, giving the titled compound as a colorless mucus (18.0 mg, 66% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.30 (s, 2 H), 5.32 (d, *J* = 7.8 Hz, 1 H), 4.55 (q, *J* = 5.4 Hz, 1 H), 3.58 (s, 3 H), 3.34 (p, *J* = 11.3, 8.6 Hz, 2 H), 1.42 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.07, 155.08, 131.31, 80.35, 53.35, 52.59, 37.25, 28.40 ppm; **IR (thin film, cm$^{-1}$):** 2954, 2927, 2854, 1745, 1711, 1500, 1478, 1437, 1391, 1365, 1350, 1310, 1253, 1214, 1162, 1102, 1050, 1009, 918, 858, 799, 775, 758, 653, 626, 585; **$[\alpha]_D^{25}$** = 63.488 (*c* = 0.43, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{24}H_{36}N_2NaO_8S_2$ ($M+Na^+$): 567.1805, found 567.1796.

***N*-(tert-butoxycarbonyl)-*S*-(4-fluorophenyl)-*L*-cysteine (3l)**

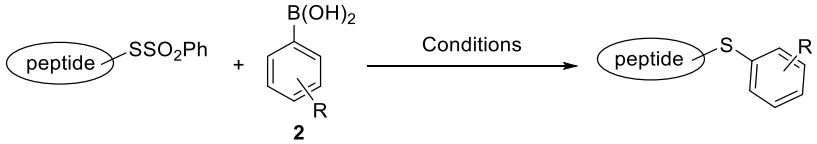



**3l**

**3l** was synthesized according to general procedure (Method C) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:1, v/v) as the eluent, giving the titled compound as a colorless mucus (21.7 mg, 69% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 8.5, 5.3 Hz, 2 H), 6.99 (t, *J* = 8.5 Hz, 2 H), 5.28 (d, *J* = 7.8 Hz, 1 H), 4.51 (d, *J* = 8.0 Hz, 1H), 3.38 (dd, *J* = 13.8, 4.4 Hz, 1 H), 3.29 (dd, *J* = 14.1, 4.7 Hz, 1 H), 1.41 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -113.88 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 174.72, 162.55 (d, $J_{C-F}$ = 248.7 Hz), 155.43, 134.21 (d, $J_{C-F}$ = 8.2 Hz), 129.68 (d, $J_{C-F}$ = 3.0 Hz), 116.39 (d, $J_{C-F}$ = 22.0 Hz), 80.75, 53.53, 38.04, 28.39 ppm; **IR (thin film, cm$^{-1}$):** 2955, 2926, 2858, 1714, 1589, 1557, 1490, 1456, 1393, 1367, 1336, 1292, 1257, 1228, 1157, 1090, 1054, 1013, 867, 794, 660, 623, 600, 563; **$[\alpha]_D^{25}$** = 15.357 (*c* = 0.28, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{14}H_{18}FNNaO_4S$ ($M+Na^+$): 338.0833, found 338.0828.

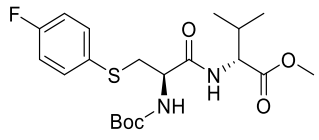
### 4.2 General Procedure for Copper-Catalyzed S-Arylation of Dipeptide and Tripeptide (Method D)




**2**

General procedure (Method D): In a 10 mL reactor, the mixture of dipeptide (0.1 mmol), **2** (0.2 mmol, 2equiv.), $NaHCO_3$ (0.15 mmol, 12.6 mg), $Cu(OAc)_2$ (20 mol%, 4 mg), **L1** (20 mol%, 4.3 mg) in 1 mL of dry methanol was stirred at 30℃ under $N_2$ atmosphere. After 4 h, the solvent was removed under vacuum and the residue was purified by flash column chromatography to afford the pure desired product.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-fluorophenyl)-*L*-cysteinyl-*D*-valinate (4a)**

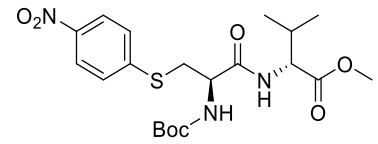



**4a**

**4a** was synthesized according to general procedure (Method D) in 0.05 mmol scale **4a-s** and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5, v/v) as the eluent, giving the titled compound as a white solid (21.4 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 8.0, 5.0 Hz, 2 H), 6.98 (t, *J* = 8.1 Hz, 2 H), 6.82 (d, *J* = 8.4 Hz, 1 H), 5.35 (d, *J* = 7.5 Hz, 1 H), 4.46 (dd, *J* = 9.0, 4.7 Hz, 1 H), 4.24 (s, 1 H), 3.71 (s, 3 H), 3.24 (d, *J* = 6.4 Hz, 2 H), 2.20-2.05 (m, 1 H), 1.42 (s, 9 H), 0.91 (d, *J* = 6.9 Hz, 3 H), 0.86 (d, J = 6.8 Hz, 3 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.34 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.15, 170.23, 162.30 (d, $J_{C-F}$ = 248.31 Hz), 133.28 (d, $J_{C-F}$ = 8.11 Hz), 129.41, 116.38 (d, $J_{C-F}$ = 22.14 Hz), 80.67, 57.20, 52.29, 37.10, 31.37, 28.31, 19.03, 17.70 ppm; **IR (thin film, cm$^{-1}$):** 3321, 2960, 2926, 1673, 1590, 1490, 1437, 1392, 1367, 1258, 1215, 1156, 1089, 1013, 864, 795, 752, 665, 627, 516; **$[\alpha]_D^{25}$** = -24.9 (*c* = 0.45, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{20}H_{29}FN_2NaO_5S$ ($M+Na^+$): 451.1673, found 451.1673; **M.p.**: 76.0-77.9 °C.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-nitrophenyl)-*L*-cysteinyl-*D*-valinate (4b)**

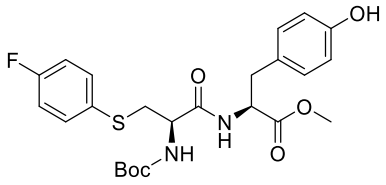


**4b**

**4b** was synthesized according to general procedure (Method D) for 10 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5, v/v) as the eluent, giving the titled compound as yellow mucus (45.6 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.8 Hz, 2 H), 7.46 (d, *J* = 8.5 Hz, 2 H), 6.81 (d, *J* = 8.8 Hz, 1 H), 5.42 (d, *J* = 7.8 Hz, 1 H), 4.48 (dd, *J* = 8.8, 4.8 Hz, 1 H), 4.41 (d, *J* = 6.8 Hz, 1 H), 3.71 (s, 3 H), 3.42 (s, 1 H), 2.21-2.09 (m, 1 H), 1.43 (s, 9 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.87 (d, *J* = 6.9 Hz, 3 H); **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.06, 169.81, 155.44, 145.69, 145.51, 127.21, 124.22, 81.01, 57.43, 52.38, 34.15, 31.31, 28.33, 19.07, 17.75 ppm; **IR (thin film, cm$^{-1}$):** 3019, 2961, 2927, 1677, 1517, 1340, 1260, 1214, 1090, 1012, 854, 804, 748, 665, 522; **$[\alpha]_D^{25}$** = -21.5 (*c* = 0.48, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{20}H_{29}N_3NaO_7S$ ($M+Na^+$): 478.1618, found 478.1620.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-fluorophenyl)-*L*-cysteinyl-*L*-tyrosinate (4c)**

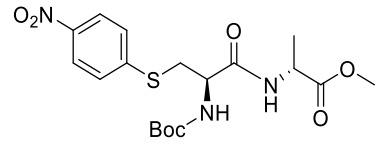


**4c**

**4c** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:3, v/v) as the eluent, giving the titled compound as a white mucus (47.4 mg, 96% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 8.5, 5.2 Hz, 2 H), 7.17 (s, 1 H), 6.98 (s, 1 H), 6.93 (t, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.1 Hz, 2 H), 6.65 (d, *J* = 7.9 Hz, 2 H), 5.40 (d, *J* = 8.2 Hz, 1 H), 4.80-4.71 (m, 1 H), 4.28-4.13 (m, 1 H), 3.72 (s, 3 H), 3.27-3.07 (m, 2 H), 3.06-2.94 (m, 2 H), 1.43 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.03 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.69, 170.23, 162.33 (d, $J_{C-F}$ = 248.5 Hz), 155.64, 155.50, 133.69 (d, $J_{C-F}$ = 8.3 Hz), 130.43, 129.27 (d, $J_{C-F}$ = 2.7 Hz), 126.72, 116.36 (d, $J_{C-F}$ = 22.1 Hz), 115.61, 80.89, 53.80, 53.60, 52.53, 37.44, 37.10, 28.34 ppm; **IR (thin film, cm$^{-1}$):** 3318, 2953, 2925, 2853, 1661, 1614, 1590, 1514, 1490, 1444, 1392, 1392, 1367, 1221, 1158, 1113, 1090, 1047, 1014, 827, 754, 664, 627, 514; **$[\alpha]_D^{25}$** = 11.3 (*c* = 0.47, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{24}H_{29}FN_2NaO_6S$ ($M+Na^+$): 515.1623, found 515.1627.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-nitrophenyl)-*L*-cysteinyl-*D*-alaninate (4d)**



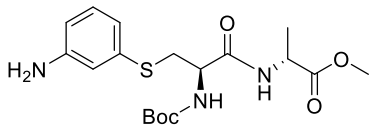
**4d**

**4d** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the

titled compound as yellow solid (39.9 mg, 93% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.9 Hz, 2 H), 7.44 (d, *J* = 8.5 Hz, 2 H), 6.89 (d, *J* = 7.6 Hz, 1 H), 5.44 (d, *J* = 8.2 Hz, 1 H), 4.51 (p, *J* = 7.3 Hz, 1 H), 4.41 (s, 1 H), 3.72 (s, 3 H), 3.41 (d, *J* = 5.7 Hz, 2 H), 1.42 (s, 9 H), 1.37 (d, *J* = 7.2 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 218.41, 173.07, 169.37, 155.46, 145.75, 145.60, 127.12, 124.19, 80.95, 53.53, 52.70, 48.35, 34.28, 28.33, 18.23 ppm; **IR (thin film, cm$^{-1}$):** 3312, 2954, 2925, 1740, 1660, 1595, 1578, 1512, 1453, 1366, 1336, 1255, 1215, 1160, 1089, 1049, 1019, 852, 795, 755, 742, 682, 664, 524, 470; **$[\alpha]_D^{25}$** = -18.6 (*c* = 0.49, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{18}H_{25}N_3NaO_7S$ ($M+Na^+$): 450.1305, found 450.1308; **M.p.**: 112.5-114.0 °C.

**Methyl *S*-(3-aminophenyl)-*N*-(tert-butoxycarbonyl)-*L*-cysteinyl-*D*-alaninate (4e)**

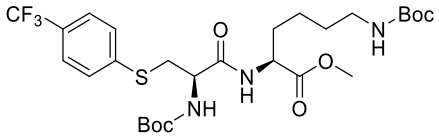


**4e**

**4e** was synthesized according to general procedure (Method D) for 5 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a brown red mucus (39.3 mg, 99% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 8.0 Hz, 1 H), 6.82 (d, *J* = 7.2 Hz, 1 H), 6.77-6.71 (m, 2 H), 6.50 (d, *J* = 7.8 Hz, 1 H), 5.36 (d, *J* = 7.8 Hz, 1 H), 4.50 (p, *J* = 7.2 Hz, 1 H), 4.29 (s, 1 H), 3.72 (s, 3 H), 3.35-3.16 (m, 2 H), 1.43 (s, 9 H), 1.36 (d, *J* = 7.2 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 173.15, 169.95, 155.50, 147.31, 135.57, 130.03, 119.73, 115.99, 113.68, 80.56, 52.60, 48.29, 35.74, 28.36, 27.01, 18.27 ppm; **IR (thin film, cm$^{-1}$):** 3363, 3018, 2960, 2927, 1739, 1701, 1671, 1592, 1483, 1453, 1367, 1259, 1214, 1162, 1088, 1047, 1012, 864, 797, 749, 686, 665, 528, 506; **$[\alpha]_D^{25}$** = -16.9 (*c* = 0.49, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{18}H_{27}N_3NaO_5S$ ($M+Na^+$): 420.1564, found 420.1566.

**Methyl $N^6$-(tert-butoxycarbonyl)-$N^2$-(*N*-(tert-butoxycarbonyl)-*S*-(4-(trifluoromethyl)phenyl)-*L*-cysteinyl)-*L*-lysinate (4f)**



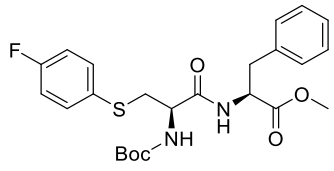
**4f**

**4f** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (59.0 mg, 97% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.3 Hz, 2 H), 7.45 (d, *J* = 8.3 Hz, 2 H), 6.91 (d, *J* = 7.9 Hz, 1 H), 5.48 (d, *J* = 8.0 Hz, 1 H), 4.70 (t, *J* = 5.7 Hz, 1 H), 4.50 (q, *J* = 7.7 Hz, 1 H), 4.39-4.27 (m, 1 H), 3.71 (s, 3 H), 3.43-3.30 (m, 2 H), 3.05 (q, *J* = 6.8 Hz, 2 H), 1.87-1.75 (m, 1 H), 1.72-1.59 (m, 1 H), 1.50-1.37 (m, 20 H), 1.31-1.21 (m, 2 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.51 (s, 3 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.34, 170.02, 156.14, 155.43, 140.62, 128.39, 128.24 (q, $J_{C-F}$ = 98.3 Hz), 128.08, 127.75, 125.94 (q, $J_{C-F}$ = 3.8 Hz), 124.12 (q, $J_{C-F}$ = 271.8 Hz), 80.72, 79.28, 53.90, 52.57, 52.19, 40.18, 34.81, 31.96, 29.37, 28.51, 28.31, 22.35 ppm; **IR (thin film, cm$^{-1}$):** 3324,

2927, 2865, 1740, 1685, 1606, 1512, 1455, 1392, 1366, 1326, 1253, 1215, 1163, 1123, 1094, 1063, 1012, 864, 822, 795, 755, 664, 590, 492; **$[\alpha]_D^{25}$** = -6.7 (*c* = 0.52, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{27}H_{40}F_3N_3NaO_7S$ ($M+Na^+$): 630.2431, found 630.2434; **M.p.**: 82.8-84.0 °C.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-fluorophenyl)-*L*-cysteinyl-*L*-phenylalaninate (4g)**

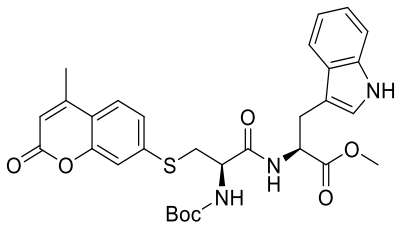



**4g**

**4g** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (47.7 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 8.6, 5.3 Hz, 2 H), 7.28 (q, *J* = 9.0, 7.7 Hz, 2 H), 7.10 (d, *J* = 6.3 Hz, 2 H), 7.00 (t, *J* = 8.6 Hz, 2 H), 6.74 (d, *J* = 7.7 Hz, 1 H), 5.24 (d, *J* = 7.6 Hz, 1 H), 4.84-4.74 (m, 1 H), 4.20 (s, 1 H), 3.72 (s, 3 H), 3.21 (d, *J* = 6.3 Hz, 2 H), 3.11 (qd, *J* = 13.9, 5.9 Hz, 2 H), 1.44 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.30 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.51, 169.91, 162.31 (d, $J_{C-F}$ = 248.4 Hz), 155.28, 135.72, 133.36 (d, $J_{C-F}$ = 8.1 Hz), 129.38, 128.68, 127.28, 116.38 (d, $J_{C-F}$ = 22.0 Hz), 80.58, 53.93, 53.42, 52.46, 37.94, 37.41, 28.33 ppm; **IR (thin film, cm$^{-1}$):** 3315, 2956, 2926, 1741, 1663, 1589, 1490, 1455, 1392, 1367, 1256, 1216, 1159, 1089, 1046, 1014, 865, 794, 752, 700, 664, 627, 510; **$[\alpha]_D^{25}$** = 10.3 (*c* = 0.59, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{24}H_{29}FN_2NaO_5S$ ($M+Na^+$): 499.1673, found 499.1677; **M.p.**: 73.3-75.6 °C.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-methyl-2-oxo-2H-chromen-7-yl)-*L*-cysteinyl-*L*-tryptophanate (4h)**



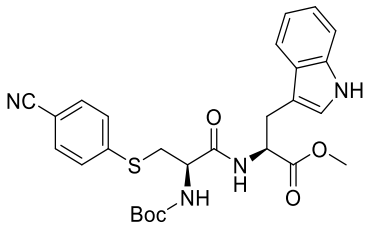

**4h**

**4h** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a colorless wax (56.3 mg, 97% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.69 (s, 1 H), 7.47 (d, *J* = 7.9 Hz, 1 H), 7.38 (d, *J* = 8.4 Hz, 1 H), 7.29 (d, *J* = 8.1 Hz, 1 H), 7.17 (d, *J* = 8.5 Hz, 1 H), 7.14-7.09 (m, 2 H), 7.05 (t, *J* = 7.4 Hz, 1 H), 7.00 (d, *J* = 2.3 Hz, 1 H), 6.98-6.91 (m, 1 H), 6.15 (s, 1 H), 5.41 (d, *J* = 8.1 Hz, 1 H), 5.28 (s, 1 H), 4.88-4.79 (m, 1 H), 4.36 (q, *J* = 7.2 Hz, 1 H), 3.66 (s, 3 H), 3.38-3.14 (m, 4 H), 2.31 (s, 3 H), 1.39 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.91, 169.86, 160.79, 155.34, 153.57, 152.37, 141.30, 136.20, 127.55, 124.95, 123.67, 123.15, 122.18, 119.56, 118.39, 117.77, 115.31, 114.13, 111.54, 109.39, 80.56, 53.55, 53.20, 52.58, 35.09, 29.76, 28.29, 27.43, 18.58 ppm; **IR (thin film, cm$^{-1}$):** 3330, 2954, 2923, 2853, 1712, 1685, 1600, 1512, 1457, 1438, 1386, 1366, 1257, 1214, 1163, 1095, 1053, 1011, 957, 854, 794, 754, 664, 437, 420; **$[\alpha]_D^{25}$** = 8.7 (*c* = 0.53, $CHCl_3$); **HRMS** (ESI-

TOF): calculated for $C_{30}H_{33}N_3NaO_7S$ ($M+Na^+$): 602.1931, found 602.1941.

**Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-cyanophenyl)-*L*-cysteinyl-*L*-tryptophanate (4i)**

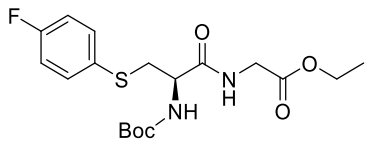



**4i**

**4i** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (2:3, v/v) as the eluent, giving the titled compound as a white solid (52.3 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.38 (s, 1 H), 7.48 (d, *J* = 7.9 Hz, 1 H), 7.45 (d, *J* = 8.0 Hz, 2 H), 7.31 (t, *J* = 9.7 Hz, 3 H), 7.16 (t, *J* = 7.6 Hz, 1 H), 7.07 (t, *J* = 7.6 Hz, 1 H), 6.95 (s, 1 H), 6.80 (d, *J* = 7.8 Hz, 1 H), 5.37-5.26 (m, 1 H), 4.82 (q, *J* = 5.5 Hz, 1 H), 4.29 (d, *J* = 8.0 Hz, 1 H), 3.67 (s, 3 H), 3.38-3.17 (m, 3 H), 1.41 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.82, 169.57, 155.25, 142.92, 136.17, 132.42, 127.74, 127.63, 123.09, 122.37, 119.76, 118.78, 118.44, 111.54, 109.55, 108.97, 80.71, 53.65, 53.41, 52.58, 34.46, 28.30, 27.47 ppm; **IR (thin film, cm$^{-1}$):** 3342, 2953, 2924, 2853, 2226, 1661, 1592, 1486, 1456, 1437, 1366, 1255, 1214, 1161, 1087, 1047, 1014, 819, 793, 746, 664, 581, 544, 427; **$[\alpha]_D^{25}$** = 12.0 (*c* = 0.49, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{27}H_{30}N_4NaO_5S$ ($M+Na^+$): 545.1829, found 545.1835; **M.p.**: 78.9-80.8 °C.

**Ethyl *N*-(tert-butoxycarbonyl)-*S*-(4-fluorophenyl)-*L*-cysteinylglycinate (4j)**

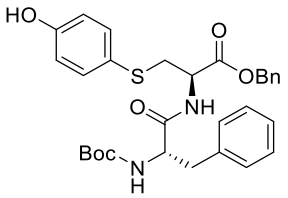



**4j**

**4j** was synthesized according to general procedure (Method D) in 0.067 mmol scale and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5, v/v) as the eluent, giving the titled compound as a colorless mucus (22.2 mg, 83% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 8.4, 5.2 Hz, 2 H), 6.98 (t, *J* = 8.4 Hz, 2 H), 6.86 (t, *J* = 5.3 Hz, 1 H), 5.38 (d, *J* = 8.0 Hz, 1 H), 4.28 (s, 1 H), 4.19 (q, *J* = 7.2 Hz, 2 H), 4.03-3.84 (m, 2 H), 3.25 (d, *J* = 6.4 Hz, 2 H), 1.42 (s, 9 H), 1.26 (t, *J* = 7.2 Hz, 3 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -114.30 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.55, 169.57, 162.29 (d, $J_{C-F}$ = 248.4 Hz), 155.49, 133.41 (d, $J_{C-F}$ = 8.1 Hz), 129.59, 116.35 (d, $J_{C-F}$ = 22.0 Hz), 80.67, 61.72, 53.83, 41.48, 37.54, 28.35, 14.21 ppm; **IR (thin film, cm$^{-1}$):** 3324, 2960, 2926, 1741, 1670, 1590, 1490, 1393, 1367, 1258, 1214, 1158, 1090, 1014, 864, 796, 751, 665, 627, 516; **$[\alpha]_D^{25}$** = -10.6 (*c* = 0.54, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{18}H_{25}FN_2NaO_5S$ ($M+Na^+$): 423.1360, found 423.1363.

**Benzyl *N*-((tert-butoxycarbonyl)-*L*-phenylalanyl)-*S*-(4-hydroxyphenyl)-*L*-cysteinate (5a)**

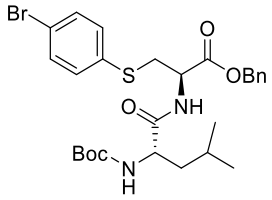


**5a**

**5a** was synthesized according to general procedure (Method D) for 6 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:3, v/v) as the eluent, giving the titled compound as a white solid (44.2 mg, 80% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.41-7.21 (m, 10 H), 7.17 (d, *J* = 7.3 Hz, 2 H), 6.79 (d, *J* = 8.1 Hz, 2 H), 6.66 (d, *J* = 7.6 Hz, 1 H), 5.21-4.71 (m, 4 H), 4.26 (q, *J* = 7.5 Hz, 1 H), 3.30 (dd, *J* = 14.3, 4.6 Hz, 1 H), 3.17 (dd, *J* = 14.0, 4.5 Hz, 1 H), 3.11-3.01 (m, 1 H), 2.94-2.81 (m, 1 H), 1.44 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.04, 169.69, 156.48, 155.43, 136.27, 134.92, 132.96, 129.31, 128.70, 128.63, 128.57, 128.38, 127.01, 124.16, 116.78, 80.55, 67.55, 55.54, 52.85, 38.42, 38.06, 28.27 ppm; **IR (thin film, cm$^{-1}$):** 3317, 3018, 2961, 2926, 2323, 2050, 1670, 1600, 1582, 1495, 1455, 1368, 1260, 1214, 1167, 1092, 1011, 799, 749, 699, 665, 520; **$[\alpha]_D^{25}$** = 14.1 (*c* = 0.41, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{30}H_{34}N_2NaO_6S$ ($M+Na^+$): 573.2030, found 573.2039; **M.p.**: 159.7-161.6 °C.

**Benzyl *S*-(4-bromophenyl)-*N*-((tert-butoxycarbonyl)-*L*-leucyl)-*L*-cysteinate (5b)**

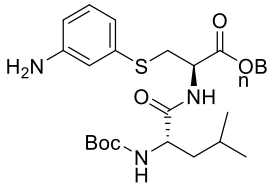


**5b**

**5b** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (57.6 mg, 99% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.40-7.31 (m, 5 H), 7.29-7.21 (m, 4 H), 6.98 (d, *J* = 7.3 Hz, 1 H), 5.08 (d, *J* = 12.2 Hz, 1 H), 4.94 (d, *J* = 12.2 Hz, 1 H), 4.82 (q, *J* = 5.0 Hz, 1 H), 4.75 (d, *J* = 7.9 Hz, 1 H), 4.11 (s, 1 H), 3.42 (dd, *J* = 14.1, 4.9 Hz, 1 H), 3.33 (dd, *J* = 14.1, 5.0 Hz, 1 H), 1.68-1.56 (m, 2 H), 1.45 (s, 9 H), 1.38-1.28 (m, 1 H), 0.91 (t, *J* = 6.6 Hz, 6 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.48, 169.87, 155.65, 134.89, 134.13, 132.65, 132.23, 128.70, 128.65, 128.39, 121.17, 80.28, 67.63, 52.31, 41.06, 36.74, 28.40, 24.78, 23.08, 21.90 ppm; **IR (thin film, cm$^{-1}$):** 3327, 2957, 2924, 2868, 1736, 1663, 1532, 1517, 1473, 1384, 1367, 1323, 1293, 1258, 1237, 1214, 1169, 1093, 1073, 1022, 1005, 908, 863, 802, 756, 696, 664, 478; **$[\alpha]_D^{25}$** = -4.7 (*c* = 0.47, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{27}H_{36}BrN_2O_5S$ ($M+H)^+$: 579.1523, found 579.1536; **M.p.**: 127.3-128.7 °C.

**Benzyl *S*-(3-aminophenyl)-*N*-((tert-butoxycarbonyl)-*L*-leucyl)-*L*-cysteinate (5c)**

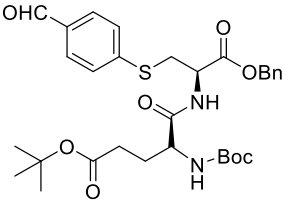


**5c**

**5c** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a yellow mucus (51.6 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5 H), 7.05 (t, *J* = 7.8 Hz, 1 H), 6.82 (d, *J* = 6.8 Hz, 1 H), 6.78 (d, *J* = 7.7 Hz, 1 H), 6.74 (s, 1 H), 6.53 (d, *J* = 8.0 Hz, 1 H), 5.12 (d, *J* = 12.2 Hz, 1 H), 5.00 (d, *J* = 12.2 Hz, 1 H), 4.91-4.87 (m, 1 H), 4.72 (d, *J* = 8.0 Hz, 1 H), 4.06 (d, *J* = 10.7 Hz, 1 H), 3.41 (dd, *J* = 14.3, 4.2 Hz, 1 H), 3.32 (dd, *J* = 14.4, 4.8 Hz, 1 H), 1.65-1.53 (m, 2 H), 1.45 (s, 9 H), 1.32-1.23 (m, 1 H), 0.89 (t, *J* = 5.5 Hz, 6 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.30, 169.99, 155.66, 147.24, 135.84, 135.12, 130.11, 128.72, 128.61, 128.48, 121.19, 117.38, 114.08, 80.22, 67.61, 53.00, 41.18, 36.53, 28.44, 24.78, 23.15, 21.80 ppm; **IR (thin film, cm$^{-1}$):** 3317, 3018, 2961, 2926, 1670, 1600, 1582, 1495, 1455, 1368, 1260, 1214, 1167, 1092, 1011, 799, 749, 699, 665, 521; **$[\alpha]_D^{25}$** = -6.6 (*c* = 0.29, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{27}H_{38}N_3O_5S$ $(M+H)^+$: 516.2527, found 516.2534.

**Tert-butyl (*R*)-5-(((*R*)-1-(benzyloxy)-3-((4-formylphenyl)thio)-1-oxopropan-2-yl)amino)-4-((tert-butoxycarbonyl)amino)-5-oxopentanoate (5d)**

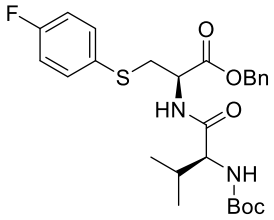


**5d**

**5d** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (2:5, v/v) as the eluent, giving the titled compound as a white solid (51.2 mg, 85% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.91 (s, 1 H), 7.74 (d, *J* = 7.8 Hz, 2 H), 7.41 (d, *J* = 8.0 Hz, 2 H), 7.38-7.23 (m, 6 H), 5.26 (d, *J* = 7.7 Hz, 1 H), 5.13 (d, *J* = 12.2 Hz, 1 H), 5.05 (d, *J* = 12.2 Hz, 1 H), 4.90 (q, *J* = 5.6 Hz, 1 H), 4.11 (q, *J* = 7.4 Hz, 1 H), 3.58 (dd, *J* = 13.9, 4.9 Hz, 1 H), 3.45 (dd, *J* = 13.9, 5.4 Hz, 1 H), 2.43-2.24 (m, 2 H), 2.13-1.98 (m, 1 H), 1.88-1.76 (m, 1 H), 1.55-1.35 (m, 18 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 191.25, 172.86, 171.89, 169.68, 155.71, 144.28, 134.81, 134.15, 130.20, 128.71, 128.43, 128.18, 81.10, 80.27, 67.80, 54.06, 52.21, 34.56, 31.79, 28.37, 28.14, 27.41 ppm; **IR (thin film, cm$^{-1}$):** 3325, 2963, 2926, 1697, 1591, 1561, 1498, 1455, 1390, 1366, 1256, 1214, 1167, 1087, 1047, 1013, 836, 796, 753, 696, 664, 608, 484; **$[\alpha]_D^{25}$** = -9.5 (*c* = 0.38, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{31}H_{40}N_2NaO_8S$ $(M+Na^+)$: 623.2398, found 623.2405; **M.p.**: 121.8-122.9 °C.

**Benzyl *N*-((tert-butoxycarbonyl)-*L*-valyl)-*S*-(4-fluorophenyl)-*L*-cysteinate (5e)**

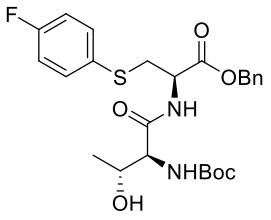


**5e**

**5e** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (50.5 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.42-7.29 (m, 5 H), 7.25 (d, $J$ = 4.5 Hz, 2 H), 6.96 (t, $J$ = 7.6 Hz, 2 H), 6.74 (d, J = 7.6 Hz, 1 H), 5.06 (d, $J$ = 12.2 Hz, 1 H), 5.00 (d, $J$ = 8.9 Hz, 1 H), 4.90 (d, $J$ = 12.2 Hz, 1 H), 4.82 (q, $J$ = 6.7, 6.3 Hz, 1 H), 3.95 (t, $J$ = 7.4 Hz, 1 H), 3.40-3.25 (m, 2 H), 2.19-2.06 (m, 1 H), 1.45 (s, 9 H), 0.93 (d, $J$ = 6.7 Hz, 3 H), 0.87 (d, $J_{C\text{-}F}$ = 6.9 Hz, 3 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ-113.51 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.48, 169.98, 162.46 (d, $J_{C\text{-}F}$ = 249.0 Hz), 155.82, 134.91, 134.25 (d, $J_{C\text{-}F}$ = 8.1 Hz), 129.50 (d, $J_{C\text{-}F}$ = 3.4 Hz), 128.71, 128.67, 128.42, 116.36 (d, $J_{C\text{-}F}$ = 22.0 Hz), 80.09, 67.62, 59.85, 52.13, 37.97, 30.95, 28.42, 19.28, 17.71 ppm; **IR (thin film, cm$^{-1}$):** 3018, 2961, 2926, 1675, 1590, 1490, 1367, 1259, 1214, 1157, 1090, 1013, 866, 800, 749, 697, 665, 628, 517; **$[\alpha]_D^{25}$** = 13.0 ($c$ = 0.47, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{26}H_{33}FN_2NaO_5S$ ($M+Na^+$): 527.1986, found 527.1993; **M.p.**: 142.9-144.9 °C.

**Benzyl *N*-((tert-butoxycarbonyl)-*L*-threonyl)-*S*-(4-fluorophenyl)-*L*-cysteinate (5f)**

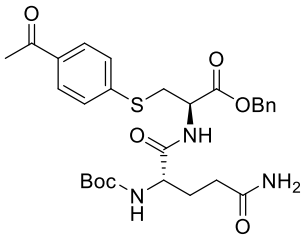


**5f**

**5f** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (48.9 mg, 96% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.46-7.31 (m, 6 H), 7.29-7.23 (m, 2 H), 6.96 (t, $J$ = 8.6 Hz, 2 H), 5.47 (d, $J$ = 9.4 Hz, 1 H), 5.06 (d, $J$ = 12.2 Hz, 1 H), 4.92 (d, $J$ = 12.2 Hz, 1 H), 4.78 (q, $J$ = 5.9 Hz, 1 H), 4.35-4.27 (m, 1 H), 4.10 (d, $J$ = 7.8 Hz, 1 H), 3.36 (dd, $J$ = 14.1, 4.8 Hz, 1 H), 3.32-3.19 (m, 2 H), 1.46 (s, 9 H), 1.16 (d, $J$ = 6.5 Hz, 3 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -113.39 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.29, 169.94, 162.50 (d, $J_{C\text{-}F}$ = 249.2 Hz), 156.39, 134.90, 134.32 (d, $J_{C\text{-}F}$ = 8.2 Hz), 129.24 (d, $J_{C\text{-}F}$ = 3.4 Hz), 128.73, 128.69, 128.42, 116.37 (d, $J_{C\text{-}F}$ = 21.9 Hz), 80.54, 67.68, 67.04, 58.29, 52.19, 37.74, 28.42, 18.15 ppm; **IR (thin film, cm$^{-1}$):** 3414, 3017, 2961, 2926, 1740, 1668, 1590, 1490, 1456, 1367, 1259, 1215, 1158, 1089, 1012, 872, 796, 750, 696, 665, 627, 514; **$[\alpha]_D^{25}$** = -9.4 ($c$ = 0.48, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{25}H_{31}FN_2NaO_6S$ ($M+Na^+$): 529.1779, found 529.1785; **M.p.**: 115.6-117.0 °C.

**Benzyl *S*-(4-acetylphenyl)-*N*-((tert-butoxycarbonyl)-*L*-glutaminyl)-*L*-cysteinate (5g)**

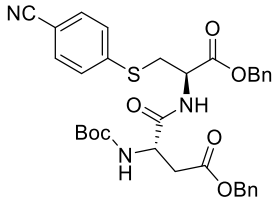


**5g**

**5g** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate as the eluent, giving the titled compound as a white solid (36.7 mg, 66% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.2 Hz, 1 H), 7.82 (d, *J* = 8.4 Hz, 2 H), 7.41-7.32 (m, 5 H), 7.32-7.26 (m, 2 H), 6.38 (s, 1 H), 6.02 (s, 1 H), 5.64 (d, *J* = 7.6 Hz, 1 H), 5.30 (s, 2 H), 5.08 (q, *J* = 12.2 Hz, 2 H), 4.86 (q, *J* = 6.4 Hz, 1 H), 4.18 (q, *J* = 7.2 Hz, 1 H), 3.53 (dd, *J* = 14.0, 5.0 Hz, 1 H), 3.40 (dd, *J* = 14.0, 6.5 Hz, 1 H), 2.55 (s, 3 H), 2.38-2.28 (m, 2 H), 2.07-1.97 (m, 1 H), 1.95-1.84 (m, 1 H), 1.43 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 197.35, 175.47, 172.00, 170.24, 155.95, 142.26, 134.87, 129.01, 128.74, 128.70, 128.41, 128.21, 80.22, 67.78, 53.56, 52.27, 34.58, 31.87, 29.26, 28.40, 26.61 ppm; **IR (thin film, cm$^{-1}$):** 3018, 2961, 1675, 1590, 1499, 1367, 1260, 1214, 1167, 1096, 1011, 798, 748, 665; **$[\alpha]_D^{25}$** = -15.3 (*c* = 0.43, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{28}H_{35}N_3NaO_7S$ ($M+Na^+$): 580.2088, found 580.2092; **M.p.**: 125.0-126.3 °C.

**Benzyl (*S*)-4-(((*R*)-1-(benzyloxy)-3-((4-cyanophenyl)thio)-1-oxopropan-2-yl)amino)-3-((tert-butoxycarbonyl)amino)-4-oxobutanoate (5h)**

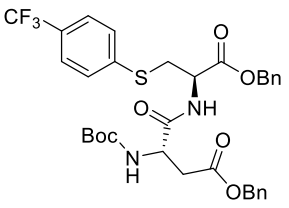


**5h**

**5h** was synthesized according to general procedure (Method D) for 10 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (40.2 mg, 65% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.5 Hz, 2H), 7.39-7.32 (m, 10 H), 7.31-7.27 (m, 2 H), 5.58 (d, *J* = 8.2 Hz, 1 H), 5.15-5.01 (m, 4 H), 4.90-4.81 (m, 1 H), 4.56-4.47 (m, 1 H), 3.47 (dd, *J* = 14.1, 5.2 Hz, 1 H), 3.40 (dd, *J* = 14.0, 5.1 Hz, 1 H), 3.03 (dd, *J* = 17.4, 4.4 Hz, 1 H), 2.69 (dd, *J* = 17.3, 6.0 Hz, 1 H), 1.44 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.85, 170.92, 169.50, 155.61, 142.67, 135.39, 134.75, 132.51, 128.82, 128.80, 128.75, 128.57, 128.49, 128.45, 128.34, 118.72, 109.48, 80.92, 67.90, 67.06, 52.32, 50.58, 35.86, 34.60, 28.38 ppm; **IR (thin film, cm$^{-1}$):** 3346, 2960, 1926, 2226, 1734, 1678, 1593, 1486, 1455, 1390, 1367, 1257, 1212, 1163, 1086, 1015, 793, 750, 696, 664, 579, 544; **$[\alpha]_D^{25}$** = 3.8 (*c* = 0.45, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{33}H_{35}N_3NaO_7S$ ($M+Na^+$): 640.2088, found 640.2094; **M.p.**: 127.9-128.8 °C.

**Benzyl (*S*)-4-(((*R*)-1-(benzyloxy)-1-oxo-3-((4-(trifluoromethyl)phenyl)thio)propan-2-yl)amino)-3-((tert-butoxycarbonyl)amino)-4-oxobutanoate (5i)**

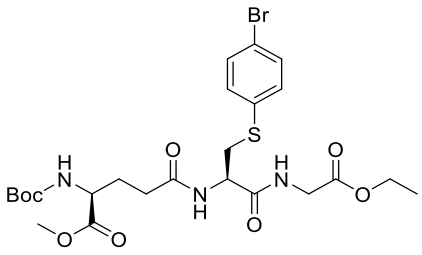


**5i**

**5i** was synthesized according to general procedure (Method D) for 5 h and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (59 mg, 89% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.2 Hz, 2 H), 7.44-7.30 (m, 11 H), 7.28-7.23 (m, 2 H), 5.57 (d, *J* = 8.7 Hz, 1 H), 5.13 (s, 2 H), 5.07 (d, *J* = 12.3 Hz, 1 H), 4.95 (d, *J* = 12.2 Hz, 1 H), 4.89-4.77 (m, 1 H), 4.59-4.49 (m, 1 H), 3.50-3.36 (m, 2 H), 3.00 (dd, *J* = 17.1, 4.5 Hz, 1 H), 2.70 (dd, *J* = 17.1, 6.1 Hz, 1 H), 1.45 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.50 (s, 3 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.74, 170.83, 169.62, 155.61, 140.31, 135.47, 134.84, 129.40, 128.74, 128.72, 128.63 (q, $J_{C-F}$ = 32.8 Hz), 128.51, 128.39, 128.35, 125.93 (q, $J_{C-F}$ = 3.8 Hz), 124.10 (q, $J_{C-F}$ = 272.9 Hz), 80.83, 67.74, 67.01, 52.35, 50.66, 35.96, 35.43, 28.37 ppm; **IR (thin film, cm$^{-1}$):** 3333, 2958, 2924, 2853, 1739, 1669, 1607, 1536, 1522, 1455, 1391, 1368, 1331, 1302, 1255, 1212, 1162, 1108, 1096, 1065, 1012, 822, 795, 758, 732, 694, 664, 509, 493; **$[\alpha]_D^{25}$** = 11.1 (*c* = 0.37, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{33}H_{35}F_3N_2NaO_7S$ ($M+Na^+$): 683.2009, found 683.2012; **M.p.**: 127.6-128.8 °C.

**Methyl *N*$^5$-((*R*)-3-((4-bromophenyl)thio)-1-((2-ethoxy-2-oxoethyl)amino)-1-oxopropan-2-yl)-*N*$^2$-(tert-butoxycarbonyl)-*L*-glutaminate (6a)**

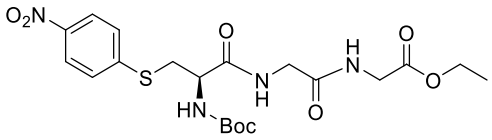


**6a**

**6a** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a pale yellow solid (40.3 mg, 66% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.6 Hz, 2 H), 7.27 (d, *J* = 8.6 Hz, 2 H), 7.13-7.07 (m, 1 H), 7.00 (d, *J* = 7.5 Hz, 1 H), 5.41 (d, *J* = 7.9 Hz, 1 H), 4.59 (q, *J* = 7.0 Hz, 1 H), 4.42-4.34 (m, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 3.98 (dd, *J* = 18.2, 5.5 Hz, 1 H), 3.89 (dd, *J* = 18.2, 5.2 Hz, 1 H), 3.72 (s, 3 H), 3.30 (d, *J* = 6.7 Hz, 2 H), 2.30 (t, *J* = 7.0 Hz, 2 H), 2.21-2.09 (m, 1 H), 1.96-1.81 (m, 1 H), 1.41 (s, 9 H), 1.26 (t, *J* = 7.1 Hz, 3 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.91, 172.47, 170.13, 169.61, 155.97, 133.93, 132.35, 131.65, 120.96, 80.52, 61.79, 52.72, 52.63, 41.57, 38.75, 35.35, 32.25, 29.06, 28.43, 14.26 ppm; **IR (thin film, cm$^{-1}$):** 3301, 2959, 2923, 2852, 1740, 1651, 1524, 1473, 1454, 1366, 1258, 1207, 1164, 1090, 1009, 861, 794, 660, 481; **$[\alpha]_D^{25}$** = -16.5 (*c* = 0.20, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{24}H_{34}BrN_3NaO_8S$ ($M+Na^+$): 626.1142, found 626.1146; **M.p.**: 158.8-160.2 °C.

**Ethyl *N*-(tert-butoxycarbonyl)-*S*-(4-nitrophenyl)-*L*-cysteinylglycylglycinate (6b)**

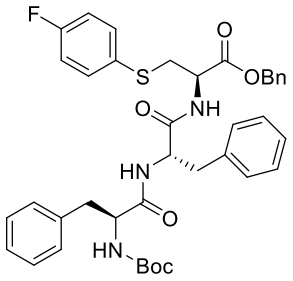


**6b**

**6b** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (2:1, v/v) as the eluent, giving the titled compound as a yellow solid (38.2 mg, 81% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 2.1 Hz, 2 H), 7.49 (t, *J* = 5.6 Hz, 1 H), 7.43 (d, *J* = 8.6 Hz, 2 H), 7.18 (t, *J* = 5.5 Hz, 1 H), 5.71 (d, *J* = 7.8 Hz, 1 H), 4.43 (q, *J* = 7.0 Hz, 1 H), 4.07-3.96 (m, 3 H), 3.91 (dd, *J* = 16.8, 5.3 Hz, 1 H), 3.72 (s, 3 H), 3.52-3.33 (m, 2 H), 2.36-2.23 (m, 2 H), 1.89-1.81 (m, 1 H), 1.40 (s, 9 H) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.77, 170.32, 169.15, 155.65, 145.82, 145.50, 127.16, 124.10, 80.84, 53.69, 52.50, 43.00, 41.18, 34.44, 28.31 ppm; **IR (thin film, cm$^{-1}$):** 3312, 2958, 2926, 1747, 1654, 1577, 1511, 1437, 1367, 1336, 1256, 1213, 1161, 1089, 1014, 853, 791, 754, 742, 682, 664, 523, 471; **$[\alpha]_D^{25}$** = -1.1 (*c* = 0.56, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{19}H_{26}N_4NaO_8S$ ($M+Na^+$): 493.1364, found 493.1362; **M.p.**: 87.4-88.9 °C.

**Benzyl *N*-(tert-butoxycarbonyl)-*L*-phenylalanyl-*L*-phenylalanyl-*S*-(4-fluorophenyl)-*L*-cysteinate (6c)**



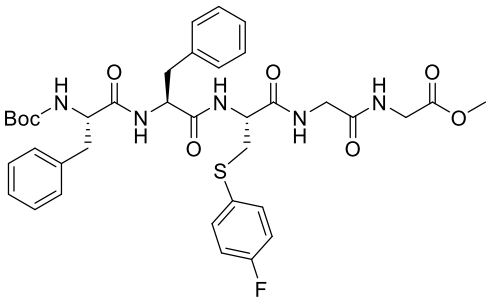
**6c**

**6c** was synthesized according to general procedure (Method D) and isolated by column chromatography on silica gel using ethyl acetate/petroleum ether (1:2, v/v) as the eluent, giving the titled compound as a white solid (54.2 mg, 77% yield).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 6 H), 7.31-7.23 (m, 5 H), 7.26-7.18 (m, 4 H), 7.21-7.14 (m, 2 H), 7.06 (d, *J* = 5.6 Hz, 2 H), 7.00-6.90 (m, 2 H), 6.69 (s, 1 H), 6.46 (d, *J* = 7.7 Hz, 1 H), 5.06 (d, *J* = 12.2 Hz, 1 H), 4.93-4.83 (m, 2 H), 4.70-4.57 (m, 2 H), 4.33 (d, *J* = 7.1 Hz, 1 H), 3.29 (dd, *J* = 14.0, 5.3 Hz, 1 H), 3.18 (dd, *J* = 14.0, 5.7 Hz, 1 H), 3.09-2.89 (m, 4 H), 1.36 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -113.71 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.16, 170.29, 169.60, 162.40 (d, $J_{C-F}$ = 248.9 Hz), 155.58, 136.48, 136.16, 135.02, 134.09 (d, $J_{C-F}$ = 8.2 Hz), 129.51, 129.48, 129.40, 129.37, 128.90, 128.81, 128.71, 128.69, 128.65, 128.42, 128.34, 116.34 (d, $J_{C-F}$ = 21.9 Hz), 80.59, 67.52, 54.19, 52.32, 38.00, 37.58, 28.33 ppm; **IR (thin film, cm$^{-1}$):** 3283, 2925, 1741, 1690, 1645, 1589, 1521, 1490, 1454, 1391, 1366, 1257, 1216, 1168, 1089, 1014, 795, 752, 697, 664, 627, 507; **$[\alpha]_D^{25}$** = 4.7 (*c* = 0.47, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{39}H_{42}FN_3NaO_6S$ ($M+Na^+$): 722.2671, found 722.2678; **M.p.**: 187.5-189.0 °C.

**Methyl *N*-(tert-butoxycarbonyl)-*L*-phenylalanyl-*L*-phenylalanyl-*S*-(4-fluorophenyl)-*L*-**

**cysteinylglycylglycinate (7a)**

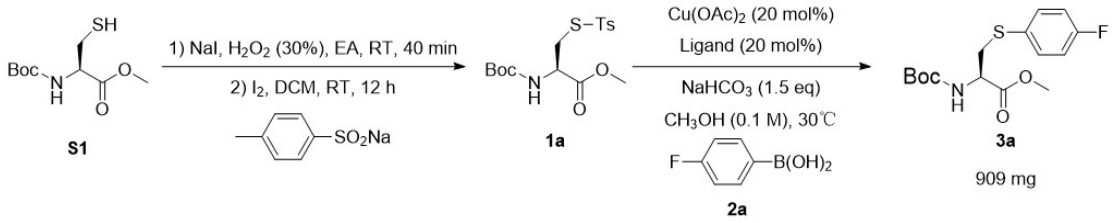


**7a**

**7a** was synthesized according to general procedure (Method D) in 0.06 mmol and isolated by column chromatography on basified silica gel using ethyl acetate as the eluent, giving the titled compound as a white mucus (46.5 mg, quant. yield).

**$^1$H NMR** (400 MHz, $CD_3OD$) δ 7.44 (dd, $J$ = 8.5, 5.2 Hz, 2 H), 7.29-7.14 (m, 10 H), 7.04 (t, $J$ = 8.6 Hz, 2 H), 4.65 (t, $J$ = 7.2 Hz, 1 H), 4.39 (t, $J$ = 7.1 Hz 1 H), 4.37-4.30 (m, 1 H), 3.97-3.75 (m, 4 H), 3.68 (s, 3 H), 3.37 (dd, $J$ = 13.9, 5.8 Hz, 1 H), 3.17-3.07 (m, 2 H), 3.07-2.93 (m, 2 H), 2.75 (dd, $J$ = 14.0, 9.8 Hz, 1 H), 1.33 (s, 9 H) ppm; **$^{19}$F NMR** (376 MHz, $CD_3OD$) δ -116.70 (m, 1 F) ppm; **$^{13}$C NMR** (101 MHz, $CD_3OD$) δ 174.42, 173.54, 172.37, 171.67, 171.58, 163.59 (d, $J_{C\text{-}F}$ = 248.6 Hz), 157.69, 138.57, 138.03, 134.60 (d, $J_{C\text{-}F}$ = 8.2 Hz), 131.39 (d, $J_{C\text{-}F}$ = 3.3 Hz), 130.51, 130.35, 129.58, 129.38, 127.76 (d, $J_{C\text{-}F}$ = 22.9 Hz), 117.22, 117.00, 80.74, 57.37, 55.92, 54.45, 52.66, 43.43, 41.81, 39.05, 38.68, 37.37, 28.69 ppm; **IR (thin film, cm$^{-1}$)**: 3276, 2924, 2853, 1748, 1630, 1518, 1490, 1438, 1392, 1365, 1259, 1221, 1168, 1013, 802, 745, 698; **$[\alpha]_D^{25}$** = -45.2 ($c$ = 0.56, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{37}H_{44}FN_5NaO_8S$ ($M+Na^+$): 760.2787, found 760.2781.

# 5. Gram-scale Synthesis of Arylated Cysteine 3a



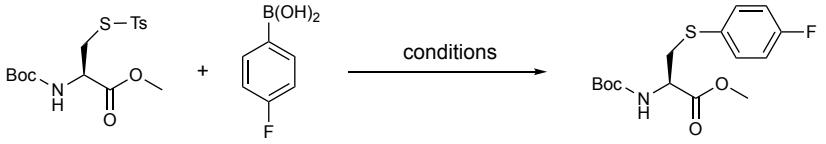

To a stirred solution of a *N*-Boc-*L*-Cys-OMe **S1** (5 mmol, 1.177 g) in ethyl acetate (10 mL) was added NaI (25 mg, 2 mol%) and 30% $H_2O_2$ (5 mmol, 0.55 mL) and the mixture was stirred at rt for 40 min. The solvent was removed under reduced pressure and the residue was directly used for the next step without further purification. To the mixture of sodium *p*-toluenesulfonate (8 mmol, 1.426 g) and obtained crude disulfide in $CH_2Cl_2$ (10 mL) was added $I_2$ (3 mmol, 761.4 mg), and the mixture was stirred overnight. $CH_2Cl_2$ (60 mL) was added, followed by the addition of aq. $Na_2S_2O_3$ (1 M) with stirring until the $I_2$ color disappeared. The mixture was washed with $H_2O$ (2×50 mL). The organic layers were dried over anhydrous $Na_2SO_4$, followed by evaporation of solvent under vacuum to afford 1.8 g of crude product **1a**. The residue without purification for next step.

In a 100 mL round-bottom flask, the mixture of the residue (2.76 mmol, 1.075 g), **2a** (5.52 mmol, 772.2 mg), $NaHCO_3$ (4.14 mmol, 347.8 mg), $Cu(OAc)_2$ (20 mol%, 110.2 mg), **L1** (20 mol%, 119.4 mg) in 28 mL of dry methanol was stirred at 30 ℃ under $N_2$ atmosphere. After 4 h, the solvent was

removed under vacuum and the residue was purified by flash column chromatography to afford the pure desired product **3a** (2.76 mmol, 909 mg, quant. yield).

# 6. Control Experiments

**Table S4: Influence of additives**




**1a** **2a** **3a**

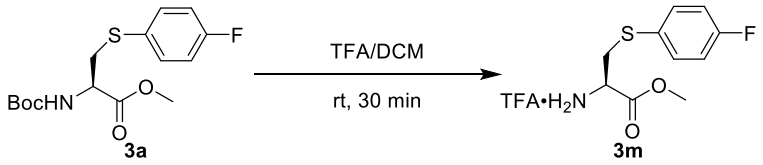
| Entry | Additive | equiv. | Yield (%)[a] |
|---|---|---|---|
| 1 | *D*-Glu(OMe)-OMe | 0.5 equiv. | 19 |
| 2 | | 1 equiv. | 10 |
| 3 | Boc-*L*-Pro | 0.5 equiv. | 61[b] |
| 4 | | 1 equiv. | 57[c] |
| 5 | Boc-*L*-Lys | 0.5 equiv. | 46 |
| 6 | | 1 equiv. | 16 |
| 7 | *N*-Boc-*L*-Met | 0.5 equiv. | 49[b] |
| 8 | | 1 equiv. | 52[c] |
| 9 | *N*-Boc-*L*-Arg | 0.5 equiv. | 61[b] |
| 10 | | 1 equiv. | 58[c] |
| 11 | *L*-Asn | 0.5 equiv. | trace[b] |
| 12 | | 1 equiv. | trace[c] |
| 13 | Ac-*L*-His-OMe | 0.5 equiv. | 75[b] |
| 14 | | 1 equiv. | 48[c] |
| 15 | Ac-*L*-Phe-OMe | 0.5 equiv. | quant. |
| 16 | | 1 equiv. | quant. |
| 17 | Bz-*L*-Arg-OEt | 0.5 equiv. | 95[b] |
| 18 | | 1 equiv. | 73[c] |

Conditions: 0.1 M solution of the **1a** (0.1 mmol, 1.0 equiv.), **2a** (0.2 mmol, 2.0 equiv.), $NaHCO_3$ (0.2 mmol, 2.0 equiv.), 1 or 0.5 equiv. of additive, 20 mol% $Cu(OAc)_2$, 20 mol% **L1** in anhydrous solvent under $N_2$ atmosphere at 30°C for 4 h**.** [a]Yield determined by crude $^{19}F$ NMR spectra analysis using trifluoromethoxy benzene as an internal standard. [b] 2 equiv. of base. [c] 2.5 equiv. of base.

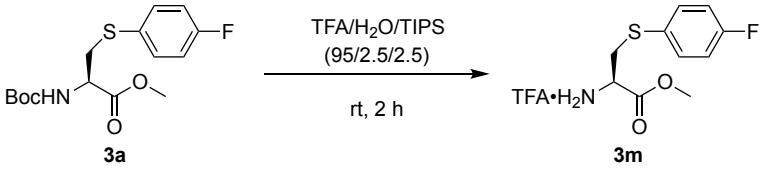
# 7. Studies on the Stability of Arylated Products

The stability of arylated products was studied by subjecting S-arylated cysteine or peptides to commonly used deprotection reactions in the field of peptide chemistry, including acidic, basic, and reductive conditions.

### 7.1 Stability under Acidic Conditions



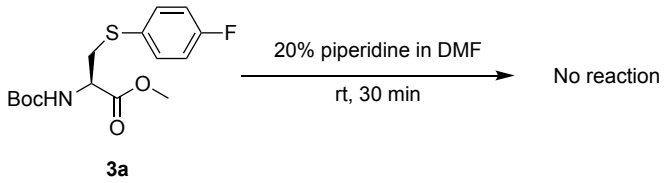

2 mL of trifluoroacetic acid (TFA) was added dropwise to the solution of **3a** (164.7 mg, 0.5 mmol) in 5 mL of dichloromethane. After stirred at room temperature for 30 min, the solvent was removed under reduced pressure. The crude product was analyzed by NMR. Modification or decomposition of thioether motif was not observed. Boc-deprotected compound **3m** was obtained as a colorless oil (163.7 mg, quant. yield). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.77 (s, 3 H), 7.45 (dd, $J$ = 8.5, 5.1 Hz, 2 H), 7.00 (t, $J$ = 8.5 Hz, 2 H), 4.17 (t, $J$ = 5.4 Hz, 1 H), 3.50 (s, 3 H), 3.46 (d, $J$ = 5.4 Hz, 2 H) ppm**; $^{19}$F NMR** (376 MHz, $CDCl_3$) δ -75.86, -112.32 ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 168.24, 162.92 (d, $J_{C\text{-}F}$ = 249.3 Hz), 135.00 (d, $J_{C\text{-}F}$ = 8.4 Hz), 127.31 (d, $J_{C\text{-}F}$ = 3.4 Hz), 116.63 (d, $J_{C\text{-}F}$ = 22.0 Hz), 53.35, 52.18, 35.91 ppm; **IR (thin film, cm$^{-1}$):** 2957, 2292, 2851, 1749, 1670, 1589, 1531, 1491, 1440, 1199, 1134, 1089, 832, 799, 722; **$[\alpha]_D^{25}$** = 38.364 ($c$ = 0.55, $CHCl_3$); **HRMS** (ESI-TOF): calculated for $C_{10}H_{13}FNO_2S$ ($M+H^+$): 230.0646, found 230.0634.



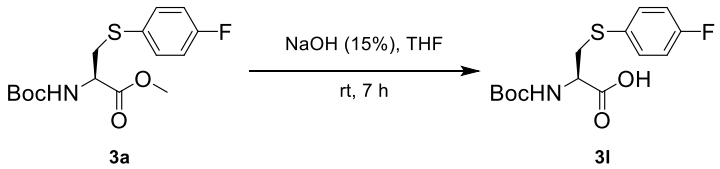

0.1 mmol of **3a** was treated with 0.1 mL of TFA/$H_2O$/TIPS (95/2.5/2.5). The solution was stirred at room temperature for 2 h. The solvent was removed under reduce pressure. The crude product was analyzed by NMR. Modification or decomposition of thioether motif was not observed. Boc-deprotected compound **3m** was obtained as a colorless oil (31.2 mg, quant. yield).

These results indicate that the thioether motif formed by S-arylation is stable under acidic conditions.

### 7.2 Stability under Basic Conditions



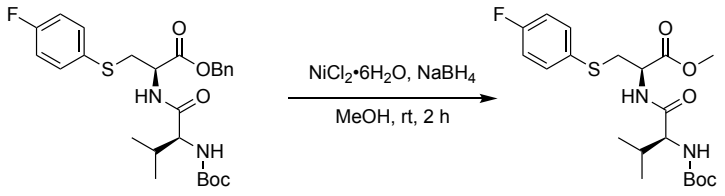

0.1 mmol **3a** was dissolved in 20% piperidine in DMF, and the solution was stirred at room temperature for 30 min. **3a** stay intact after the reaction.




0.6 mL of 15% NaOH aqueous solution was added dropwise to the solution of **3a** (0.2 mmol) in

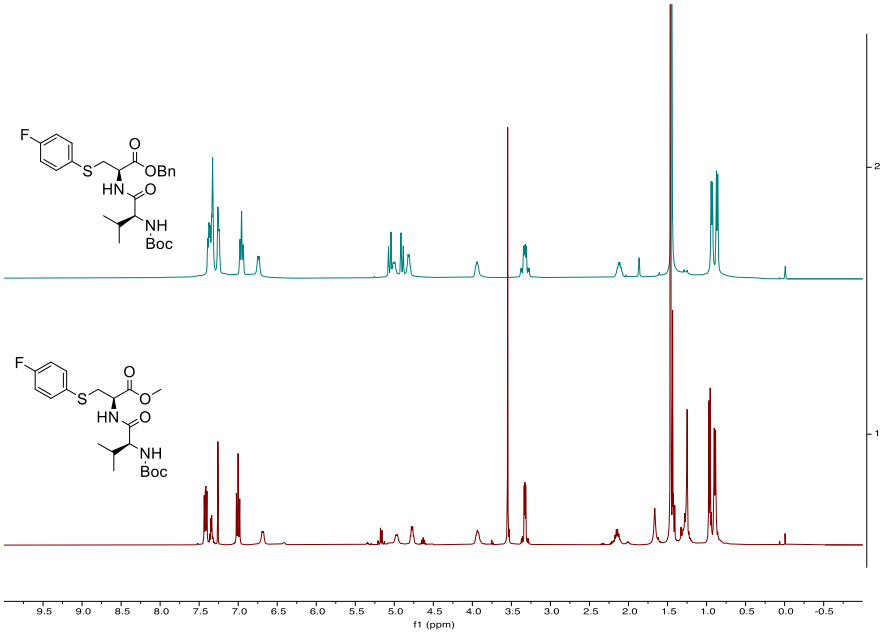
THF (0.3 mL). The reaction was stirred at room temperature for 7 hours, and the solution was acidified to pH 2 with 1 N HCl. The aqueous phase was extracted with $CH_2Cl_2$ for 3 times. The combined organic layers were dried over $NaSO_4$. The organic solvent was removed under reduced pressure. The crude product was analyzed by NMR. Hydrolysis compound **3l** was obtained in 87 % yield. Modification or decomposition of thioether motif was not observed.
These results indicate that the thioether motif formed by S-arylation is stable under basic conditions.

### 7.3 Stability under Reductive Conditions




**5e** **5e'**

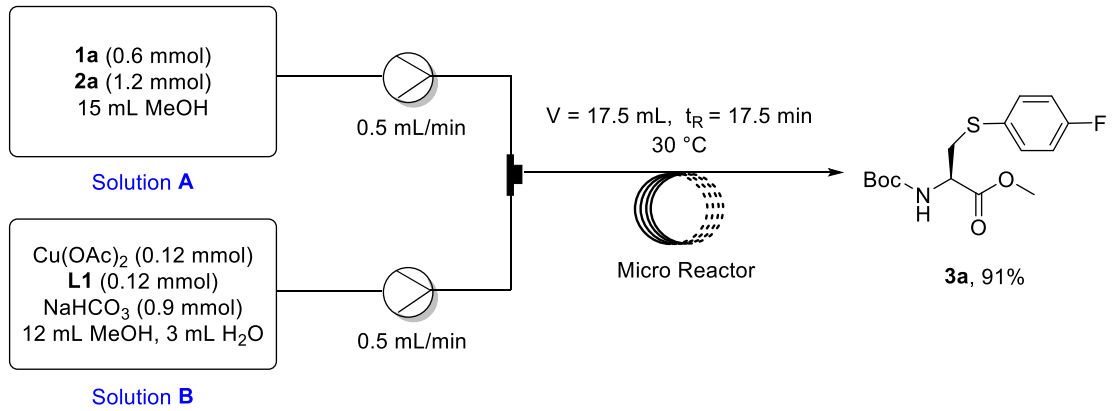
0.15 mmol $NiCl_2 \cdot 6H_2O$ was added to the solution of 0.05 mmol **5e** in MeOH (0.5 mL). 0.45 mmol of $NaBH_4$ was added portionwise to the green solution with stirring. The mixture turned black, and was stirred for another 2 h. The reaction mixture was filtered through celite, and the residue was washed with methanol. The resulting solution was concentrated *in vacuo* and purified by column chromatography on silica gel using ethyl acetate/petroleum ether = 1:2 as the eluent. Modification or decomposition of thioether motif was not observed. Ester exchange compound **5e'** was obtained as a white solid in 53% yield. **$^1$H NMR** (400 MHz, $CD_3Cl$) δ 7.42 (dd, *J* = 8.8, 5.2 Hz, 2 H), 7.00 (t, *J* = 8.6 Hz, 2 H), 6.68 (d, *J* = 7.5 Hz, 1 H), 4.97 (d, *J* = 7.6 Hz, 1 H), 4.82 – 4.73 (m, 1 H), 3.98 – 3.89 (m, 2 H), 3.55 (s, 2 H), 3.33 (dd, *J* = 5.0, 2.8 Hz, 1 H), 2.21 – 2.10 (m, 1 H), 1.46 (s, 9 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 0.89 (d, *J* = 6.9 Hz, 3 H) ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -113.51 ppm.

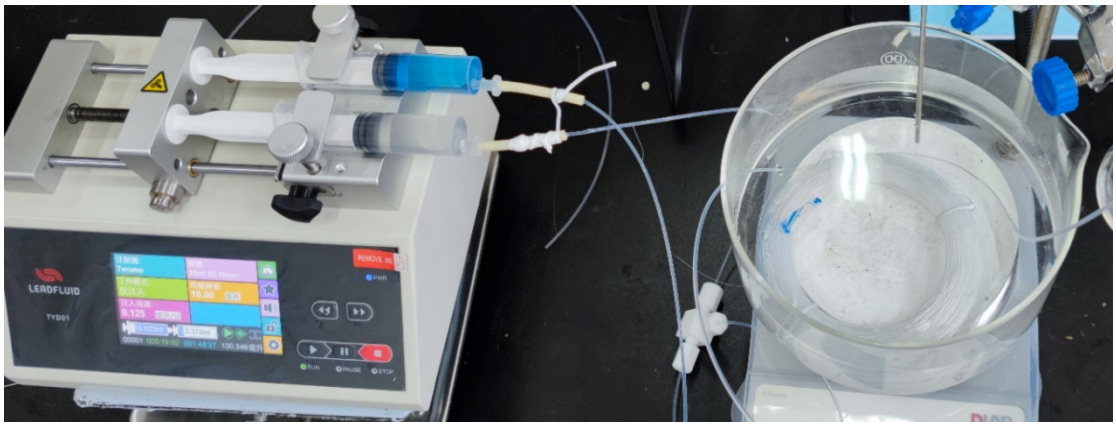



**Scheme S1. $^1$H NMR of S-arylated dipeptide after deprotection of benzyl group.**

These results indicate that the thioether motif formed by S-arylation is stable under reductive conditions.

## 8. Continuous-flow Process for Synthesis of Arylated Cysteine 3a



**Scheme S2. Details of the micro reactor for the arylated cysteine 3a (0.6 mmol scale)**

**1a** (233.7 mg, 0.6 mmol, 1 equiv.), **2a** (167.9 mg, 1.2 mmol, 2 equiv.) were dissolved in MeOH (15 mL) as Solution **A**. $NaHCO_3$ (75.6 mg, 0.9 mmol, 1.5 equiv.), $Cu(OAc)_2$ (24 mg, 0.12 mmol, 20 mol%), 4,4'-dimethoxy-2,2'-bipyridine (26 mg, 0.12 mmol, 20 mol%) were dissolved in 12 mL MeOH and 3 mL $H_2O$ as Solution **B**. The Solution **A** and **B** were transferred into 20 mL syringes separately. The two liquid streams were merged with a T-Mixer, then flowed into PFA tubing (Volume = 17.5 mL, O'D = 1/16 inch, I'D' = 0.8 mm) at 0.5 mL/min respectively. The collection was directly quenched with $H_2O$. Upon being emptied, two syringes were recharged with MeOH (8 mL), which were pumped at 0.5 mL/min to evacuate the tubing residue. All collection was combined, then extracted with $CH_2Cl_2$×3, and the organic layer was collected, dried with $Na_2SO_4$ and evaporated under reduced pressure. The resulting crude compound was purified by column chromatography using ethyl acetate/petroleum ether (1:7, v/v) as the eluent, giving the titled compound **3a** (180 mg, 91%).

# 9. Characterization Data

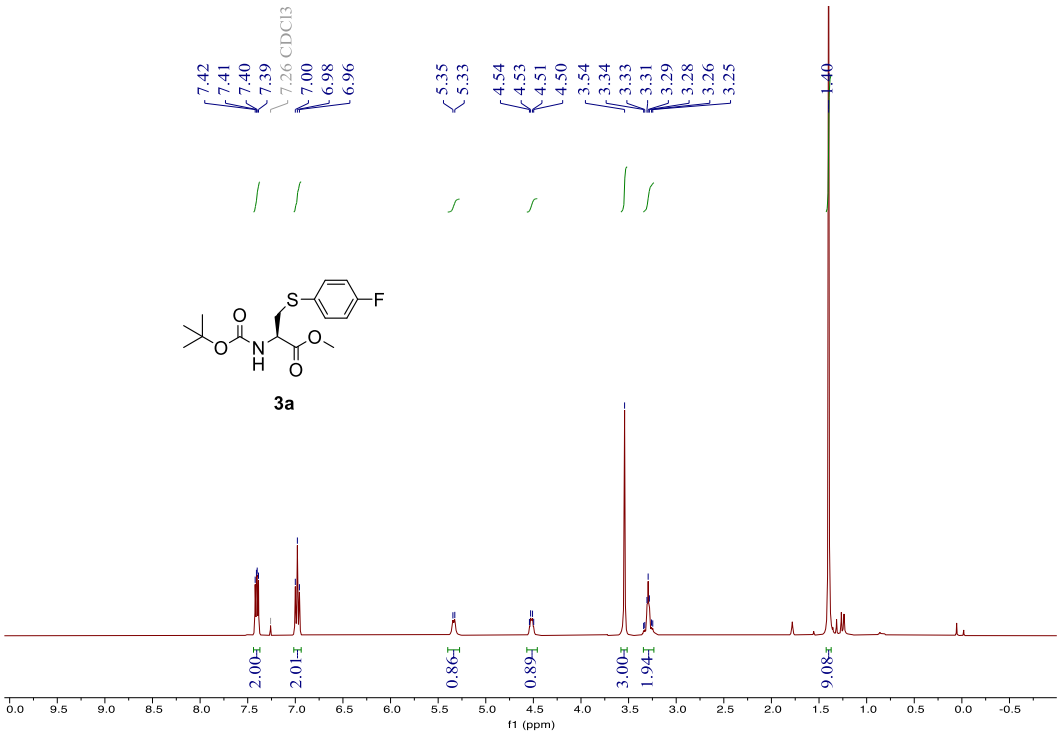



**Figure S1. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3a**

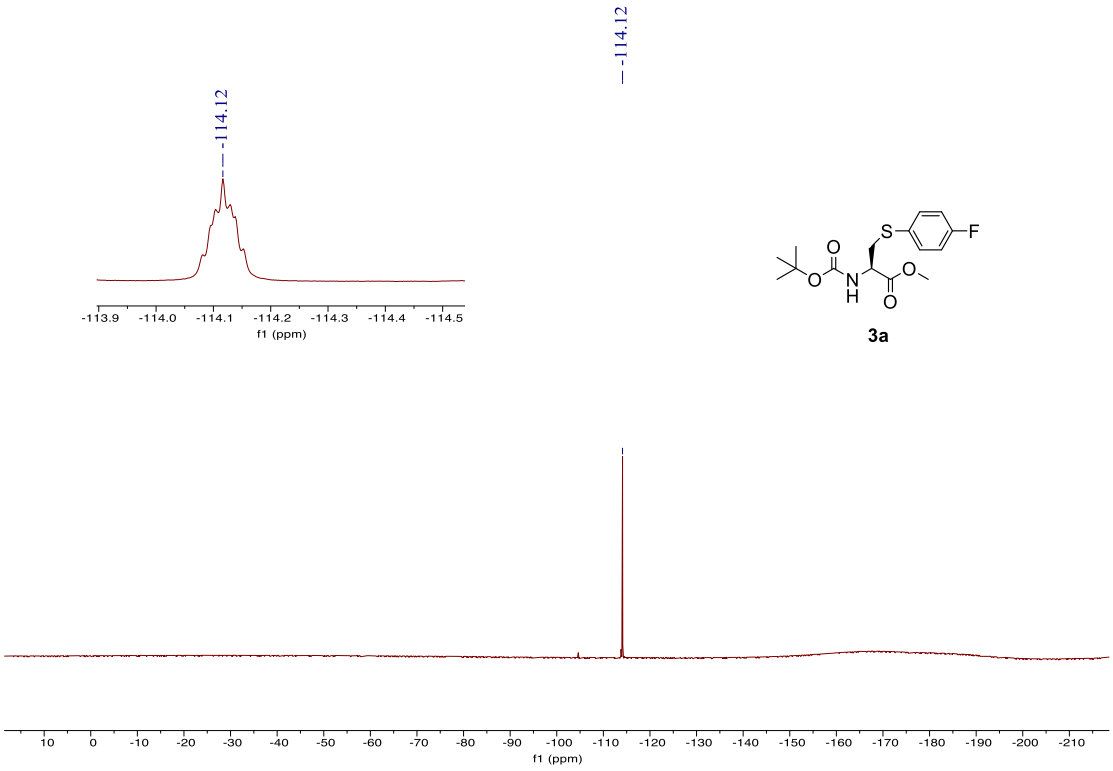



**Figure S2. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 3a**

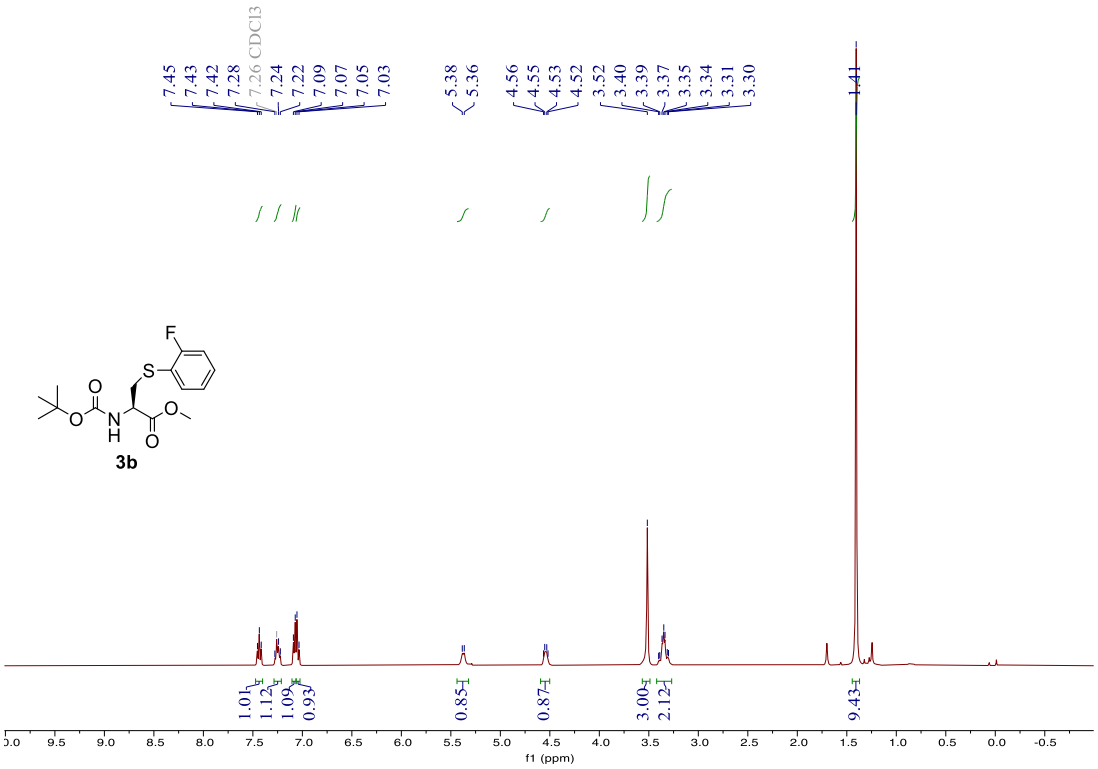



**Figure S3. $^{13}C$ NMR (101 MHz, $CDCl_3$) spectra for compound 3b**

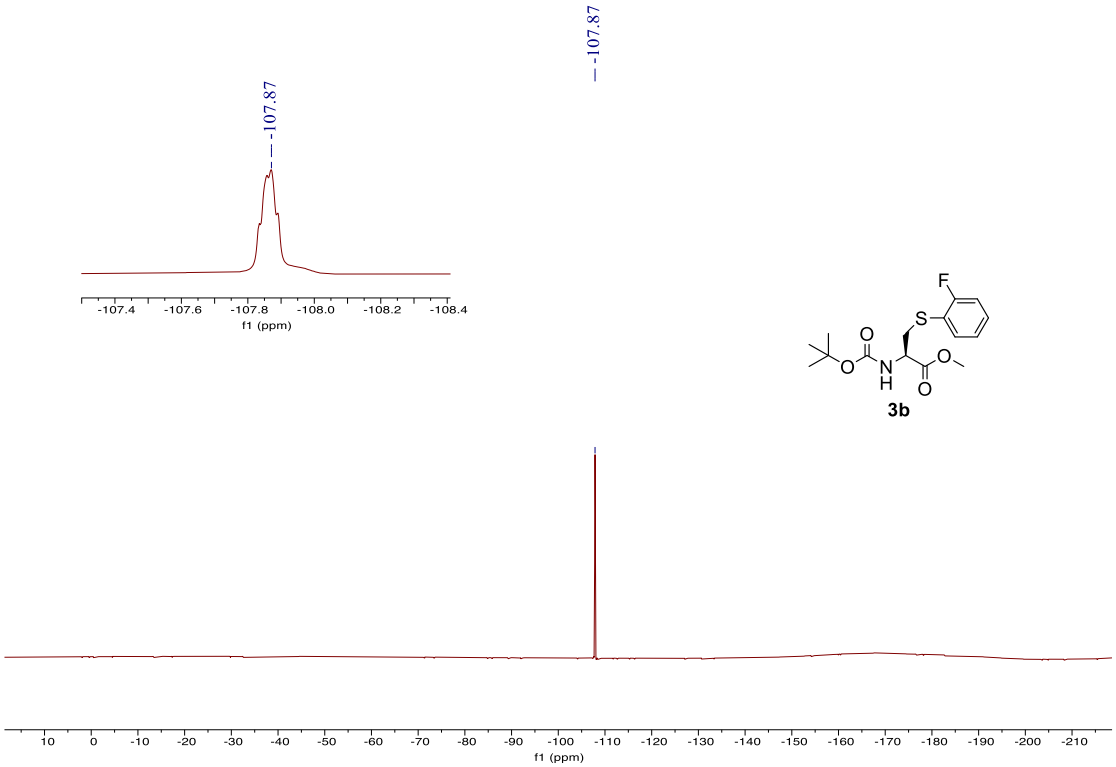



**Figure S4. $^{19}F$ NMR (376 MHz, $CDCl_3$) spectra for compound 3b**

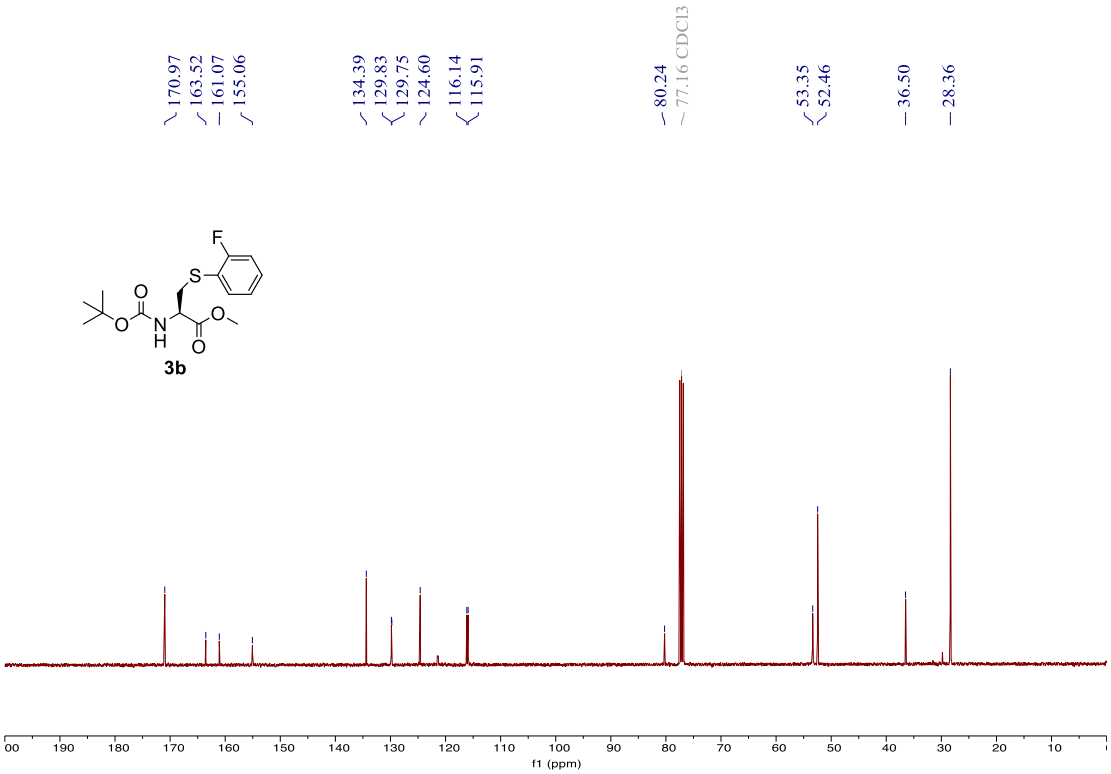



**Figure S5. $^{13}C$ NMR (101 MHz, $CDCl_3$) spectra for compound 3b**

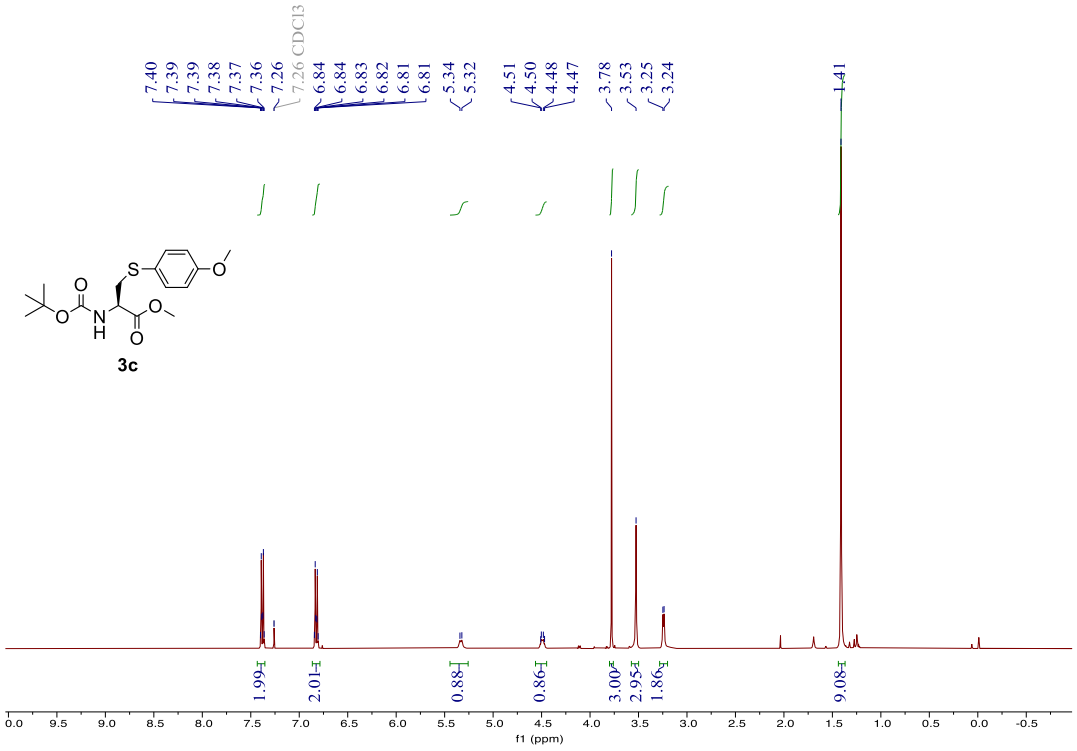



**Figure S6. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectra for compound 3c**

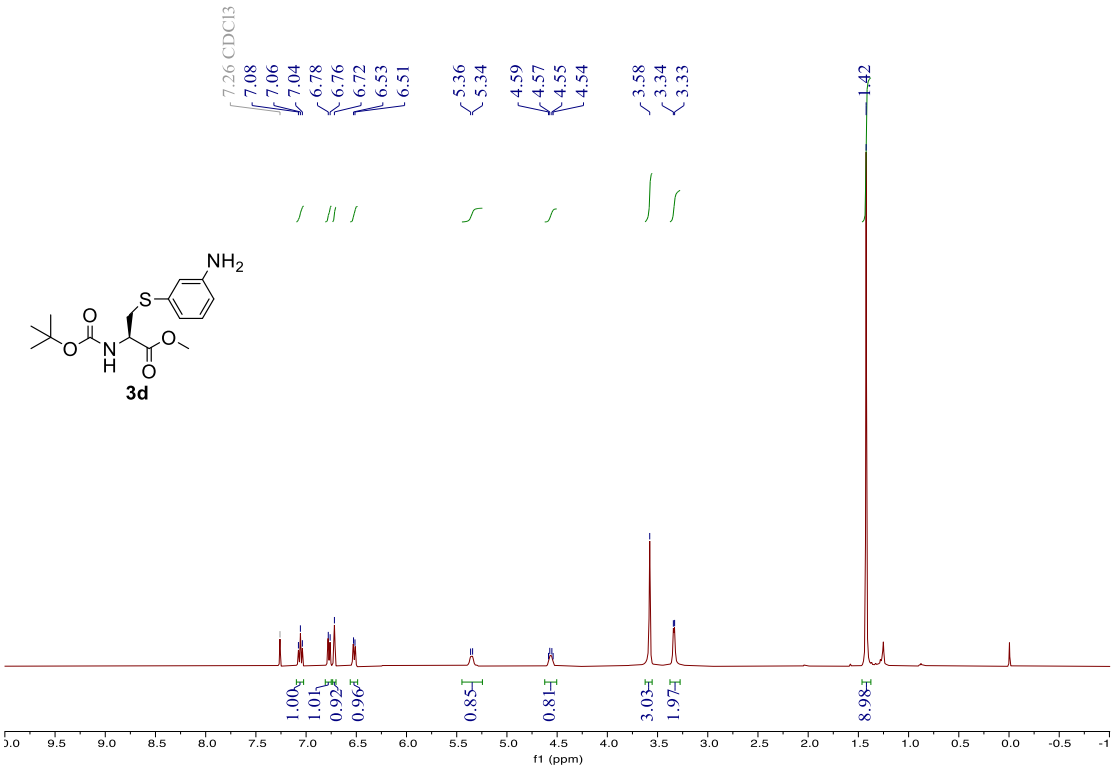



**Figure S7. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3d**

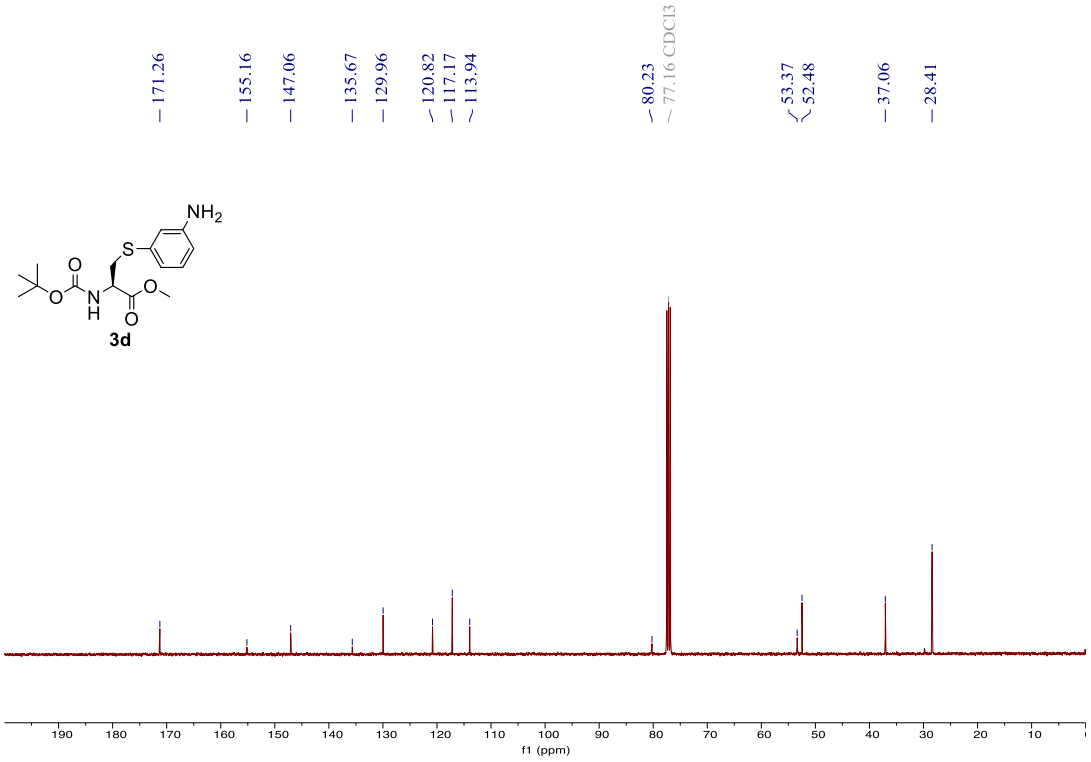



**Figure S8. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 3d**

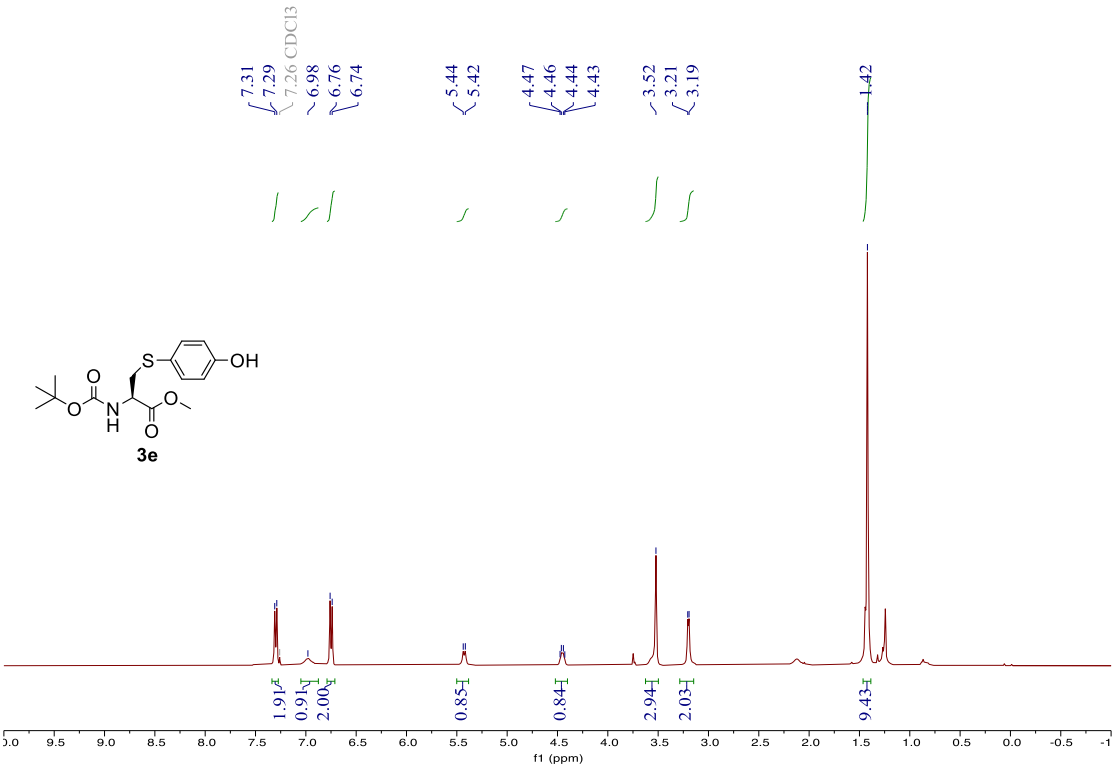



**Figure S9. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3e**

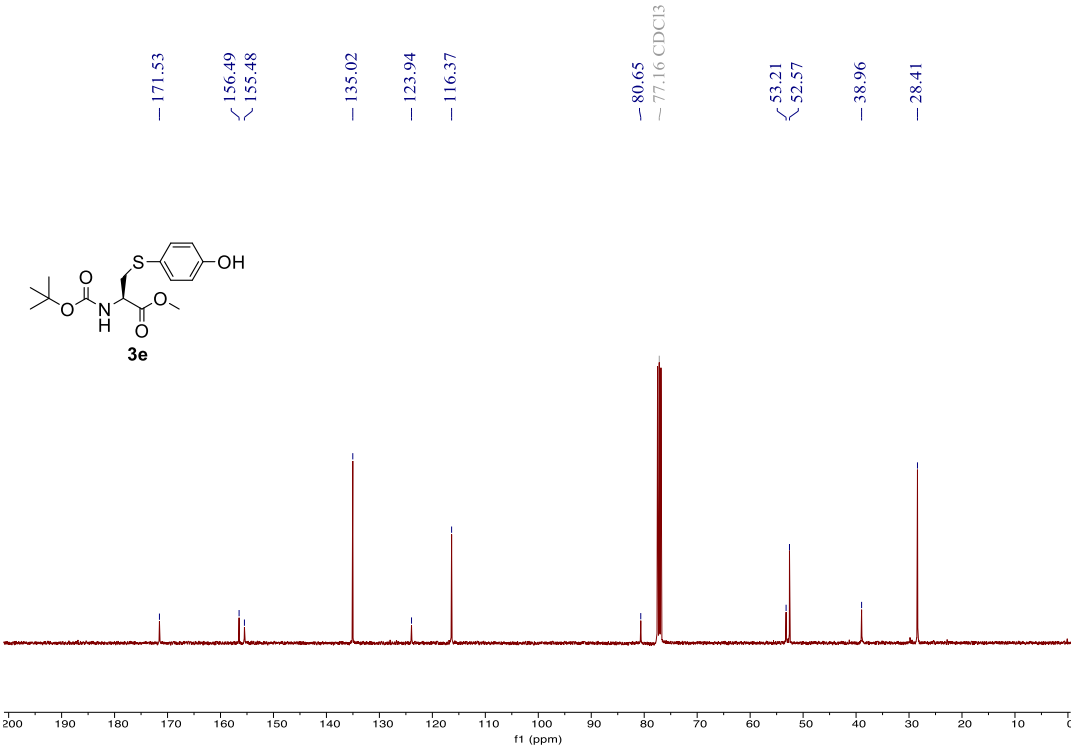



**Figure S10. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 3e**

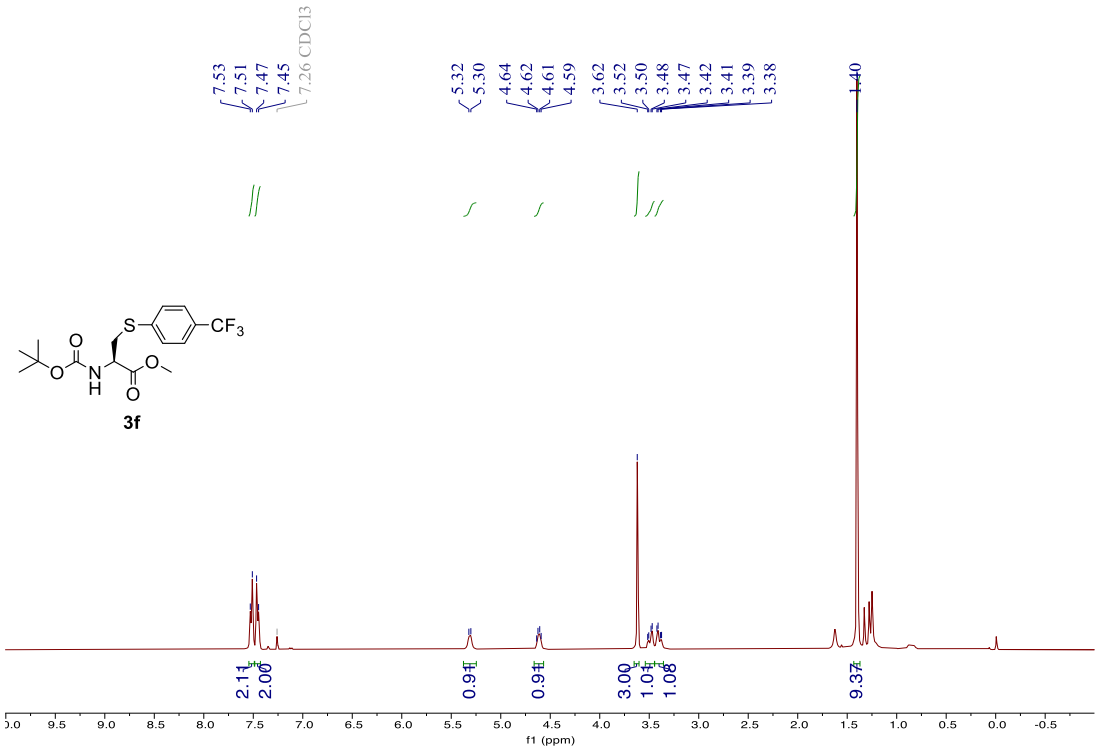



**Figure S11. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3f**

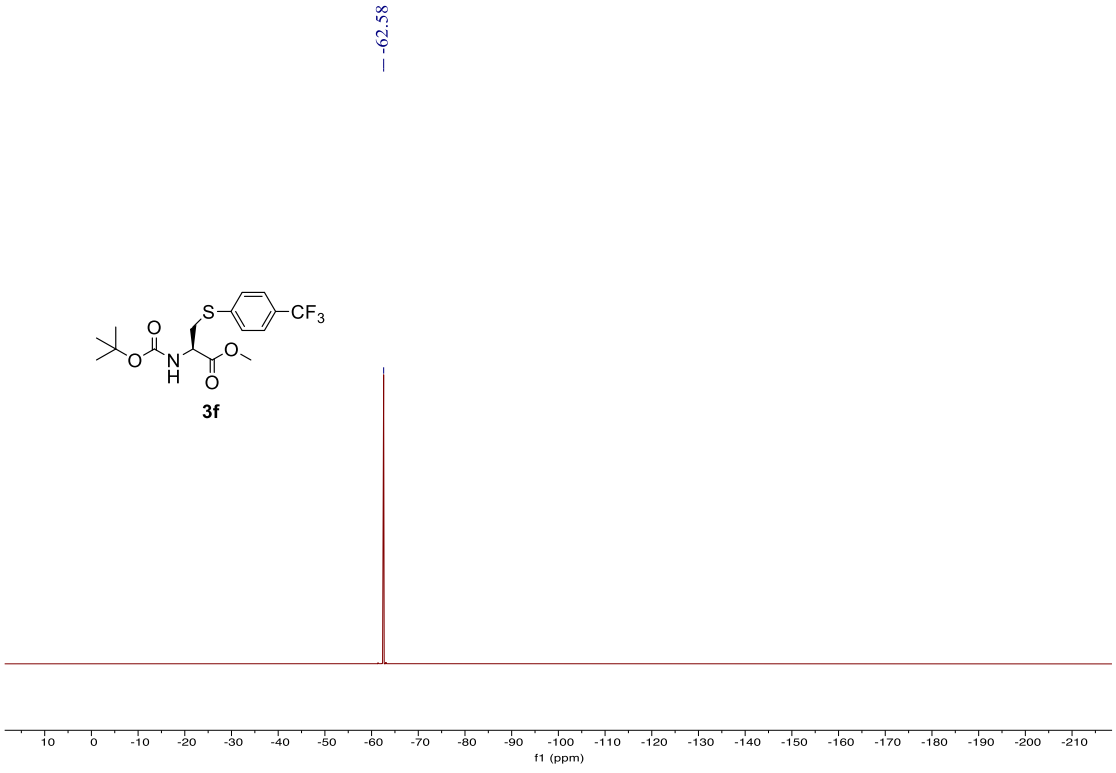



**Figure S12. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 3f**

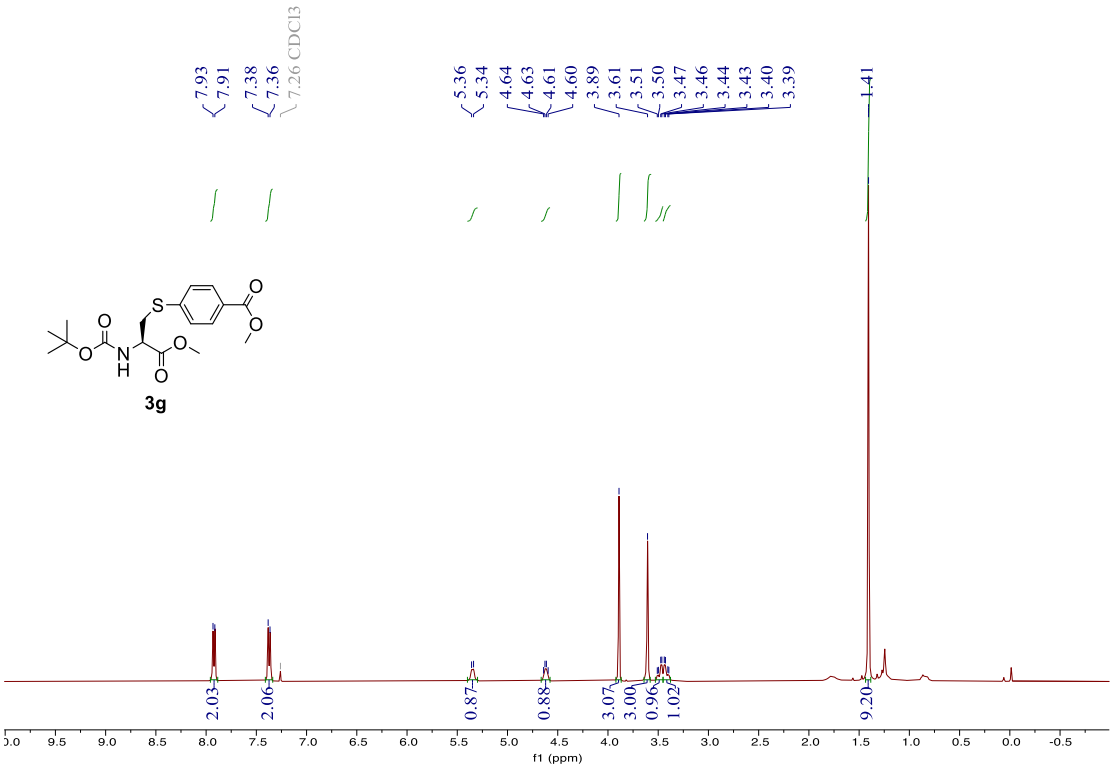



**Figure S13. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3g**

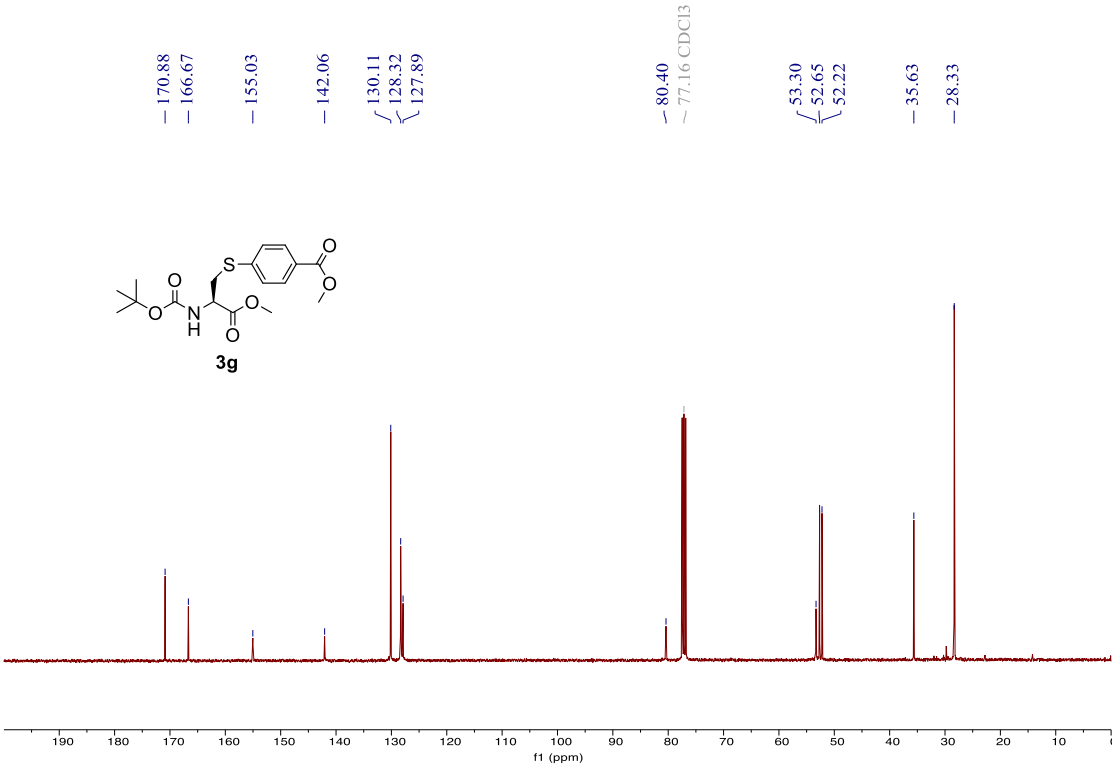



**Figure S14. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 3g**

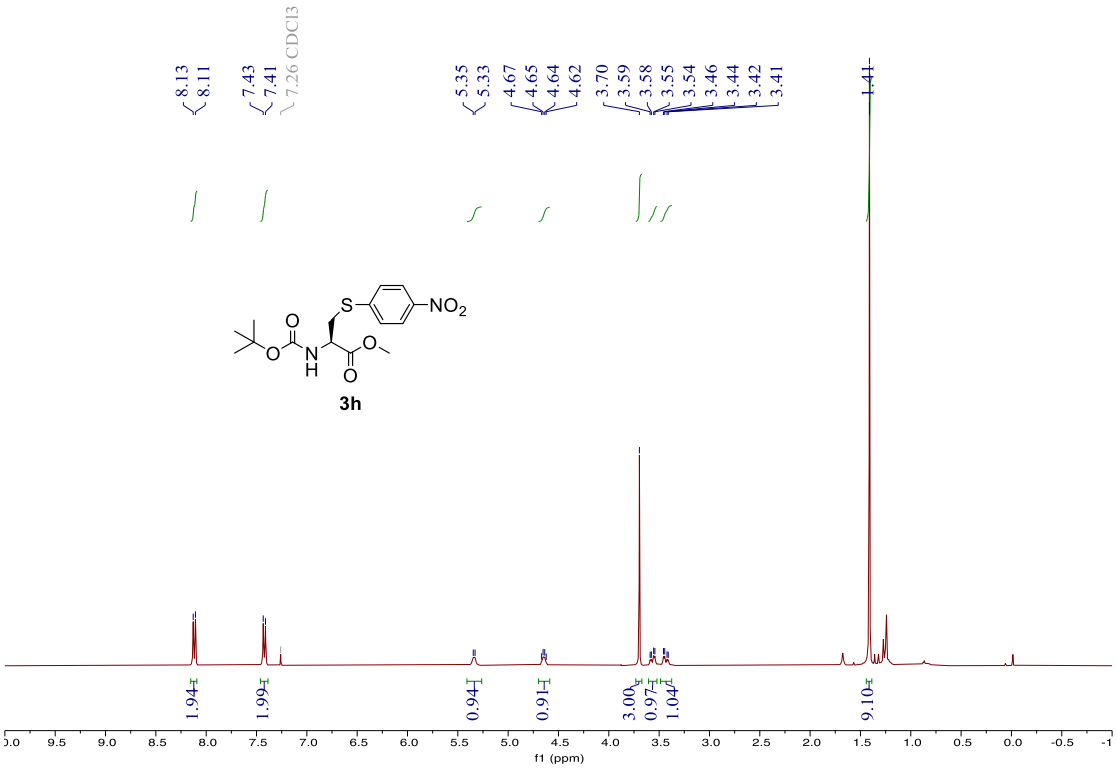



**Figure S15. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3h**

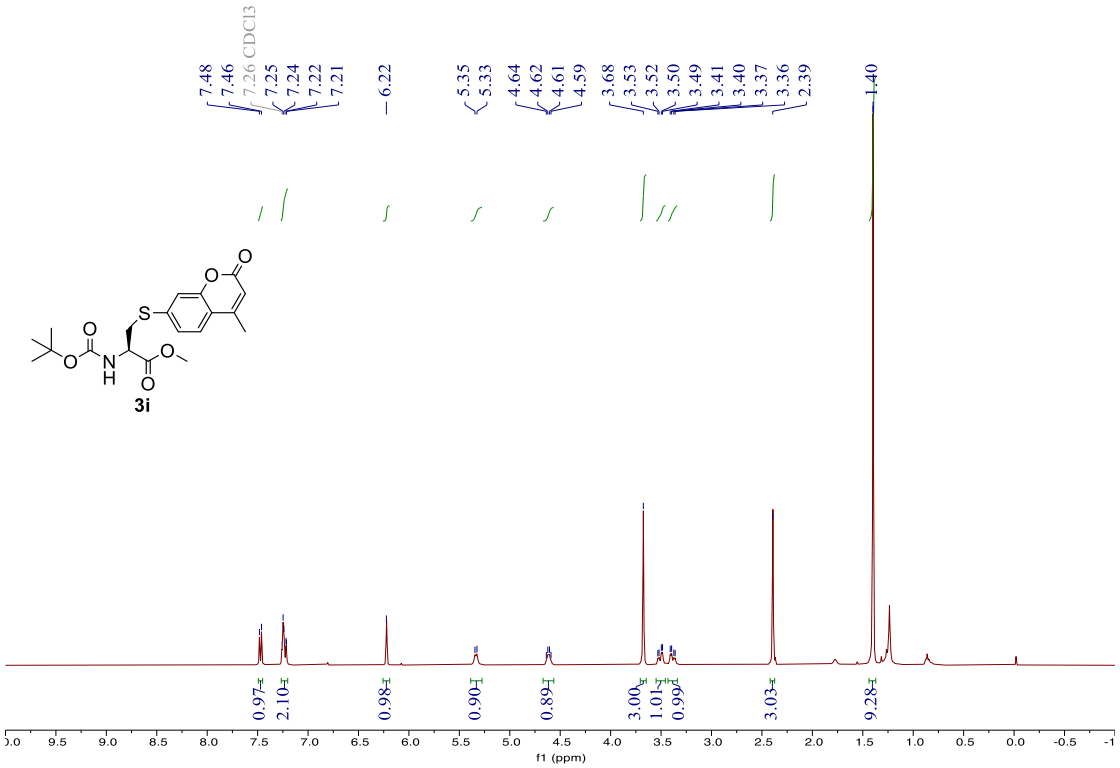



**Figure S16. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3i**

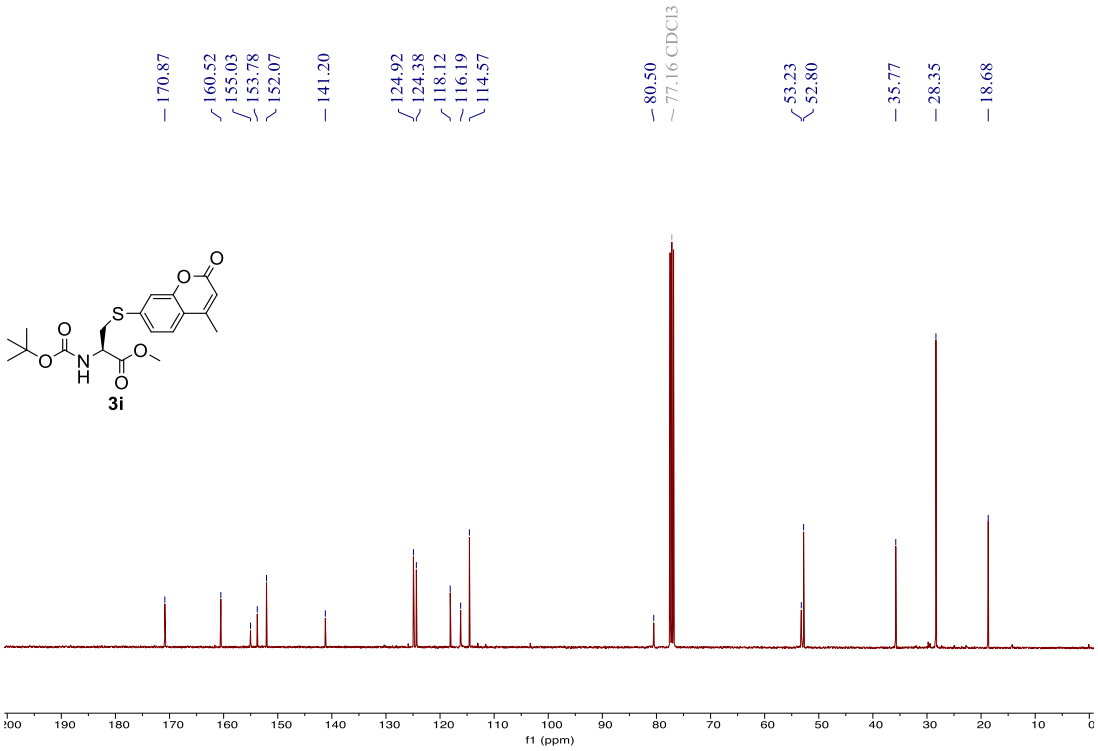



**Figure S17. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 3i**

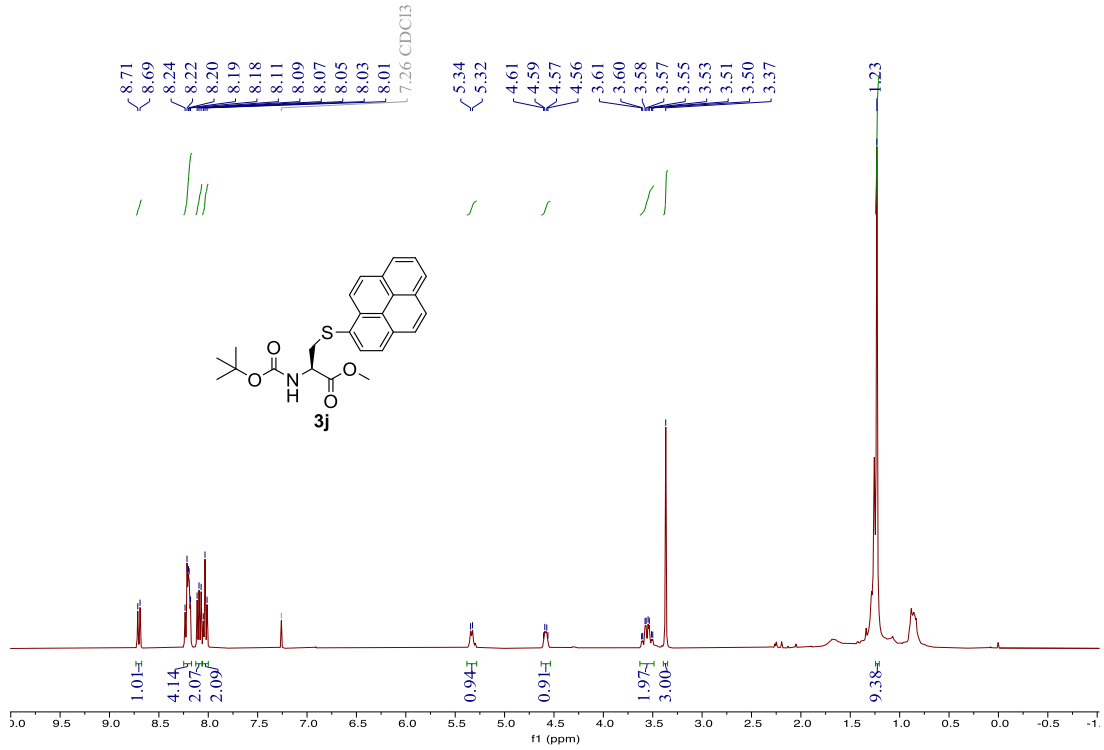



**Figure S18. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3j**

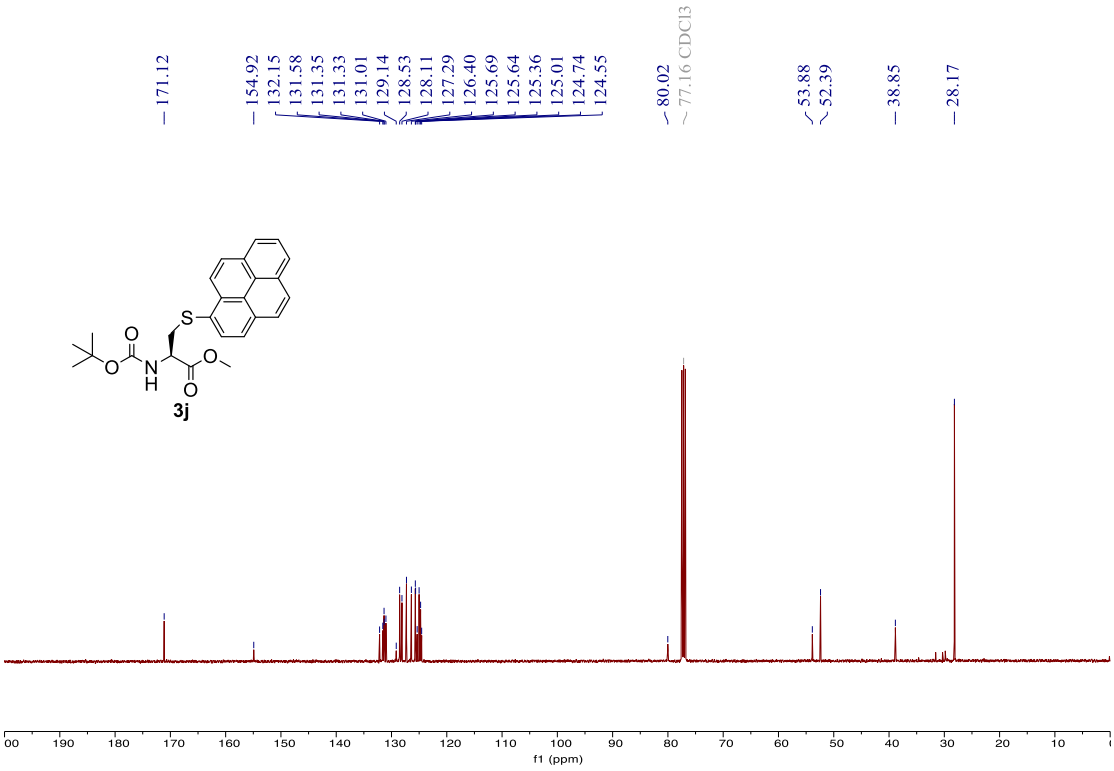



**Figure S19. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 3j**

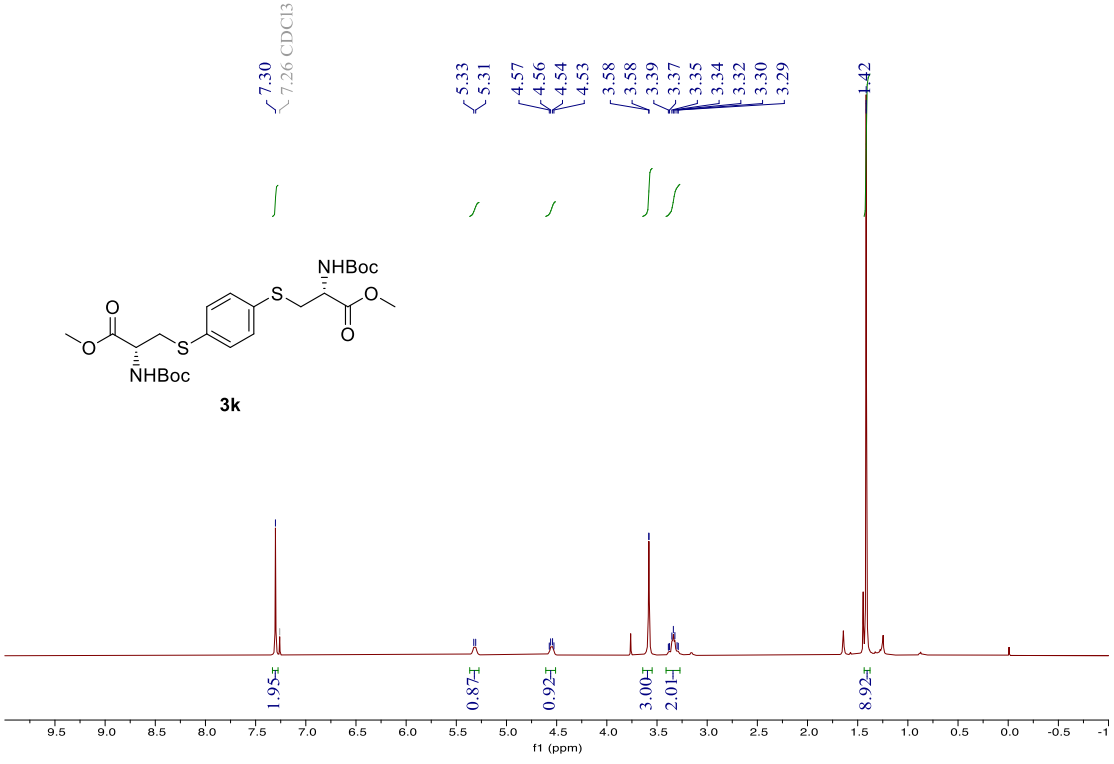



**Figure S20. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3k**

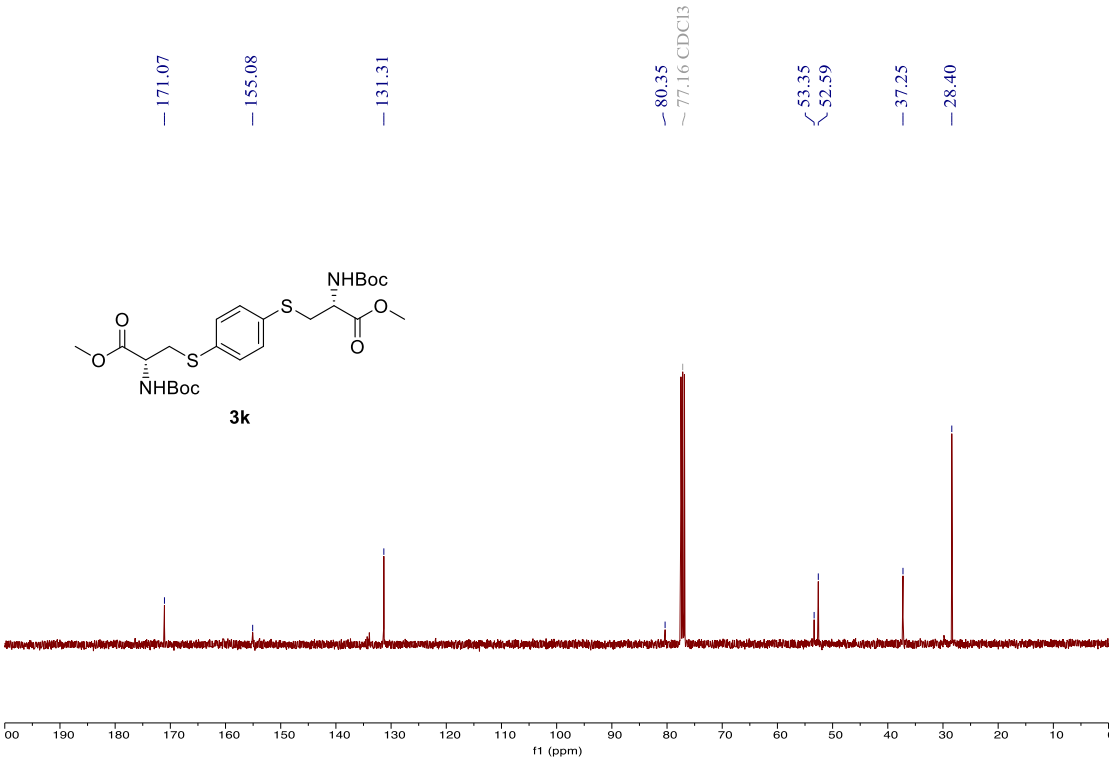



**Figure 21. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 3k**

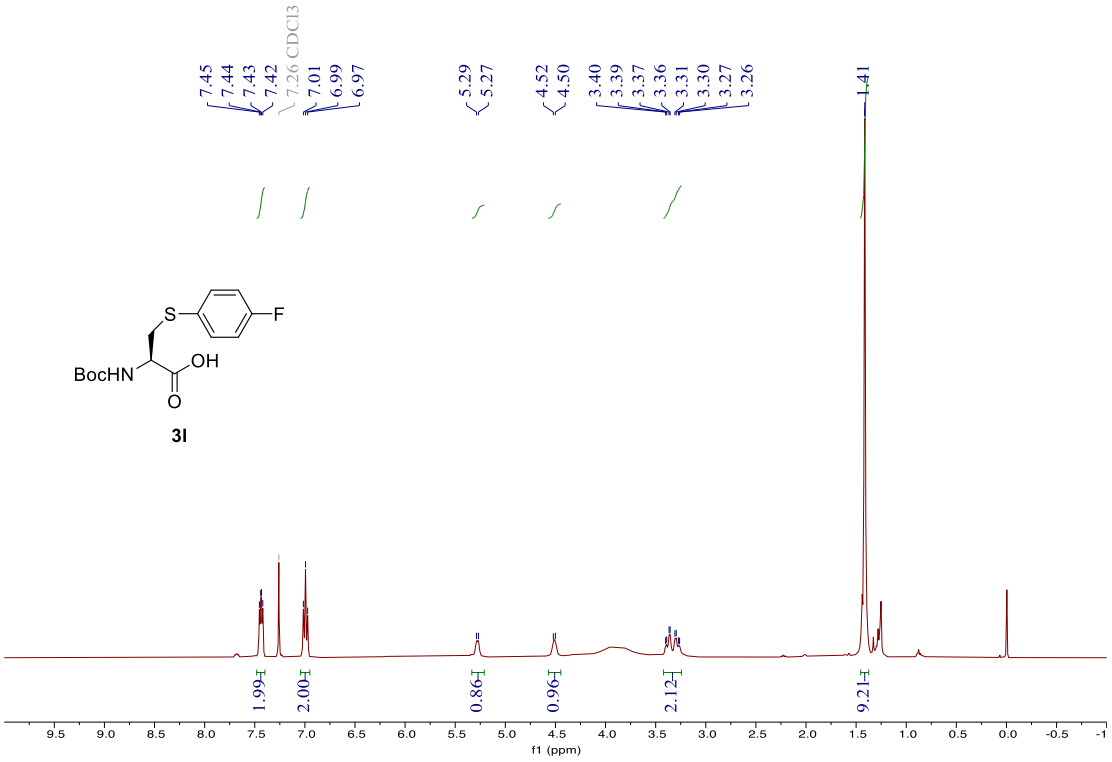



**Figure S22. $^{1}$H NMR (400 MHz, $CDCl_3$) Spectra for compound 3l**

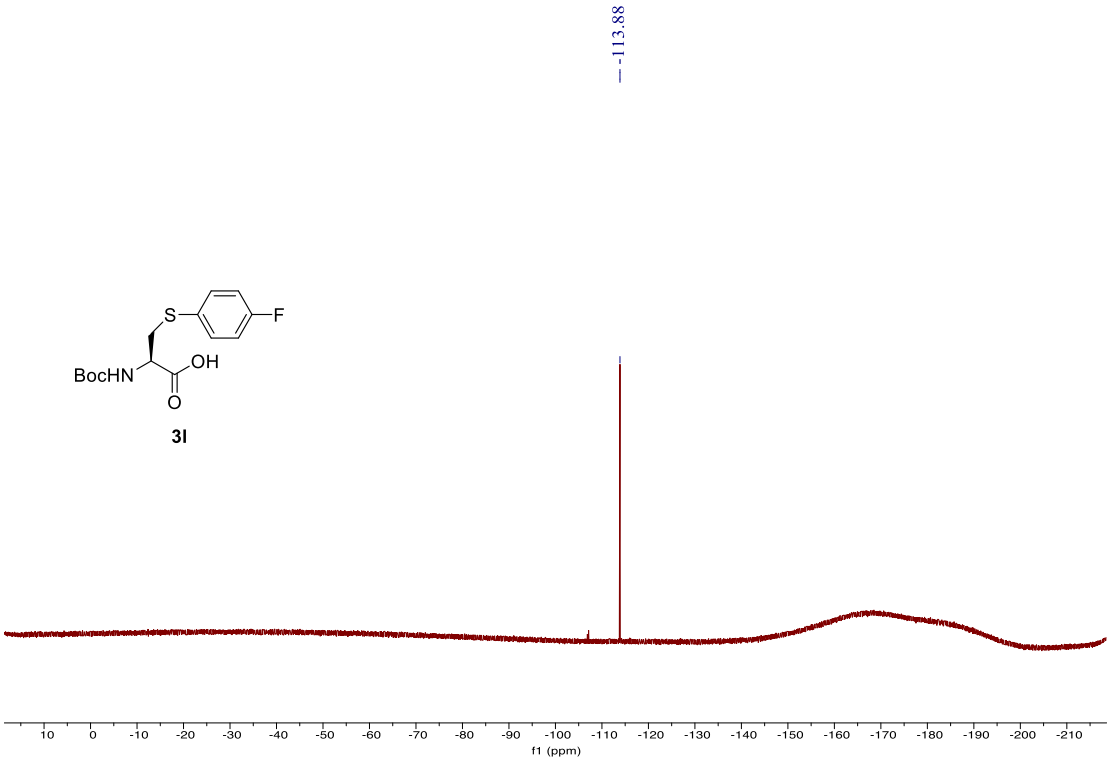



**Figure S23. $^{19}$F NMR (376 MHz, $CDCl_3$) Spectra for compound 3l**

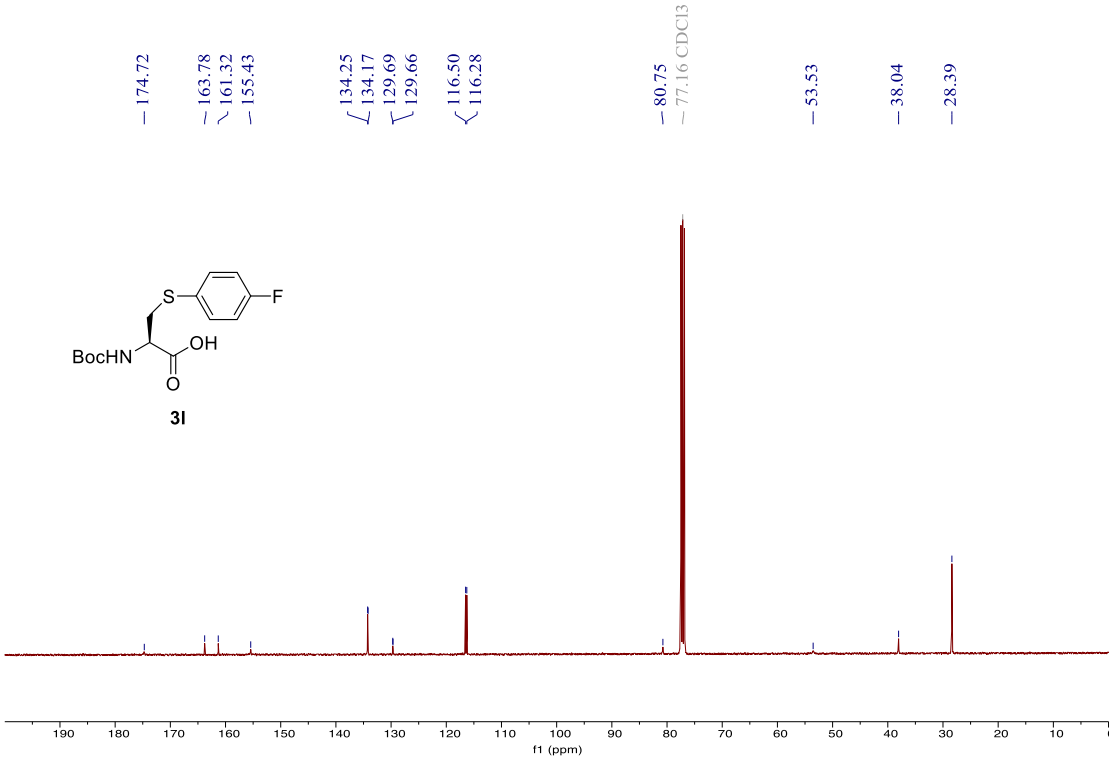



**Figure S24. $^{13}$C NMR (101 MHz, $CDCl_3$) Spectra for compound 3l**

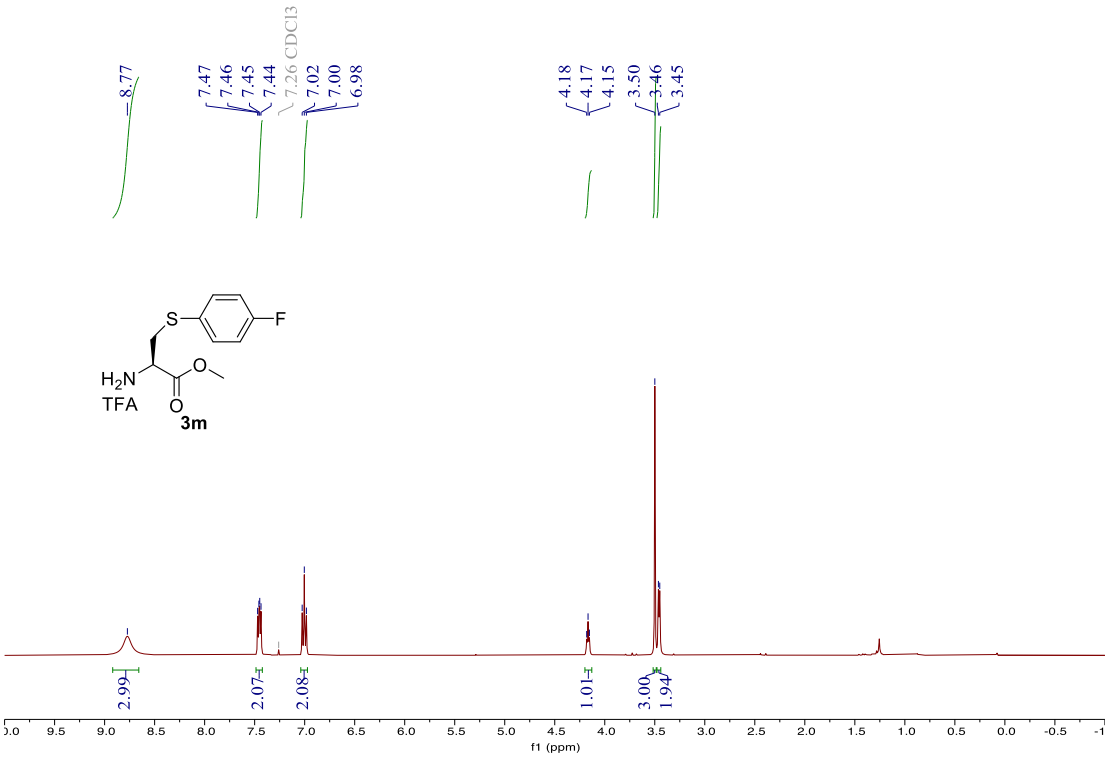



**Figure 25. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 3m**

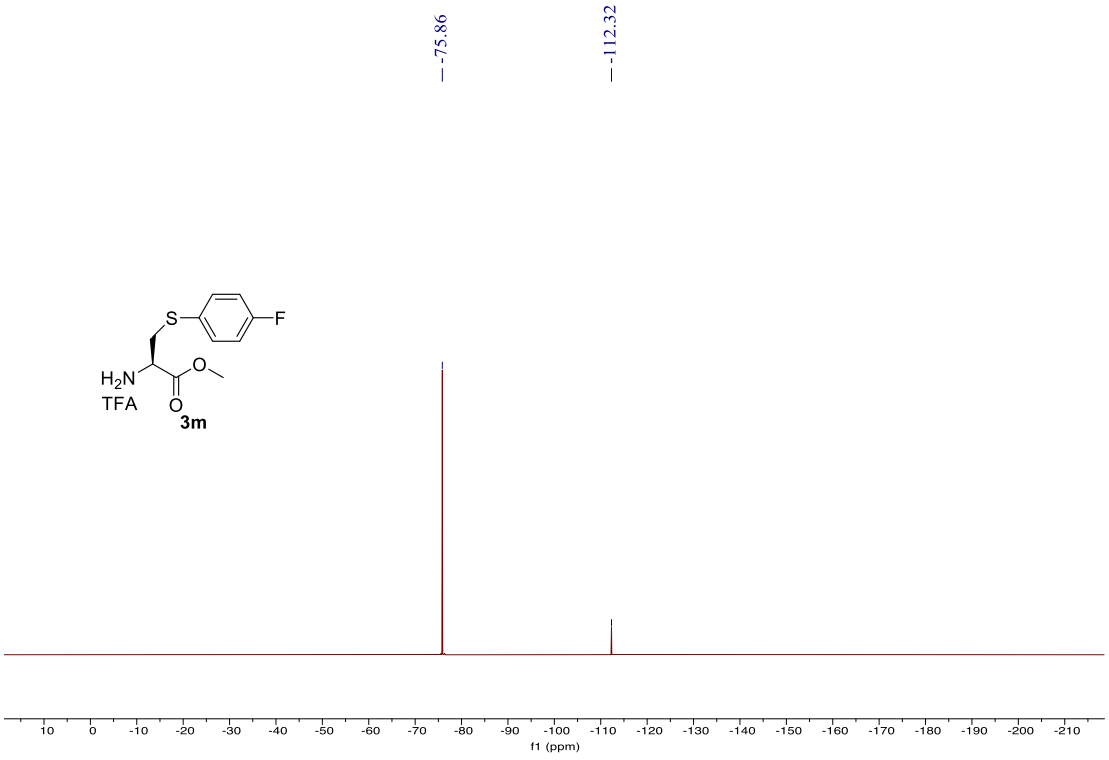



**Figure 26. $^{19}$F NMR (376 MHz, $CDCl_3$) Spectra for compound 3m**

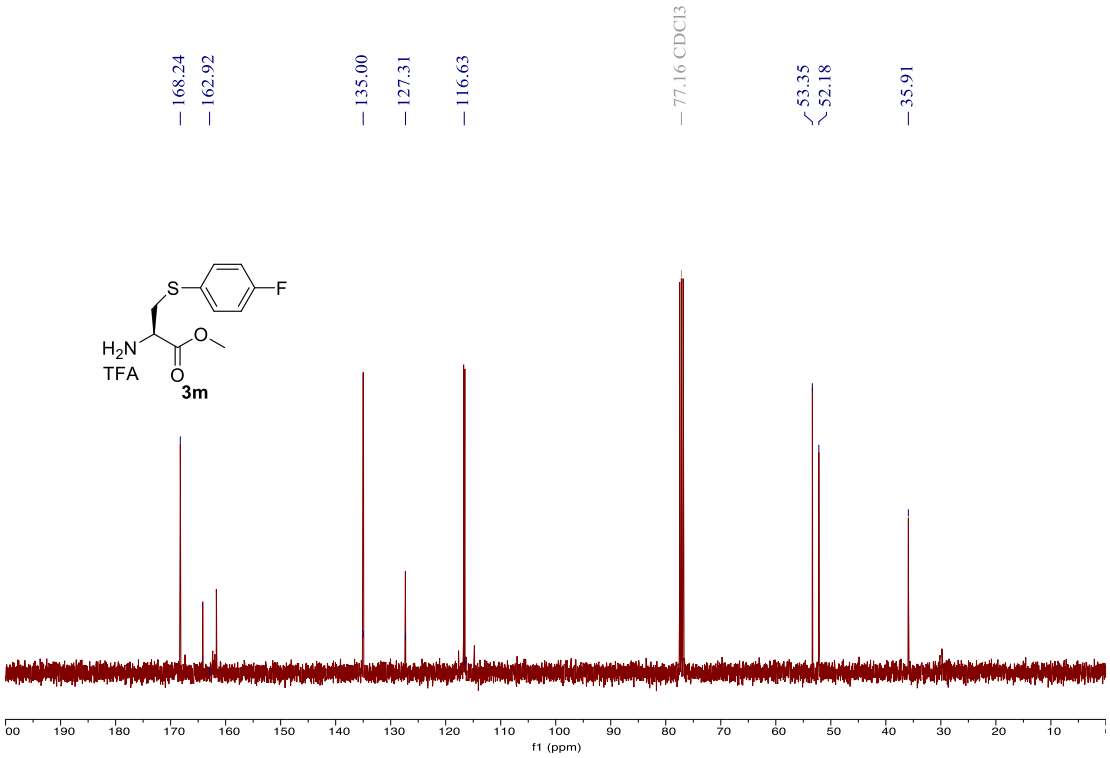



**Figure 27. $^{13}$C NMR (101 MHz, $CDCl_3$) Spectra for compound 3m**

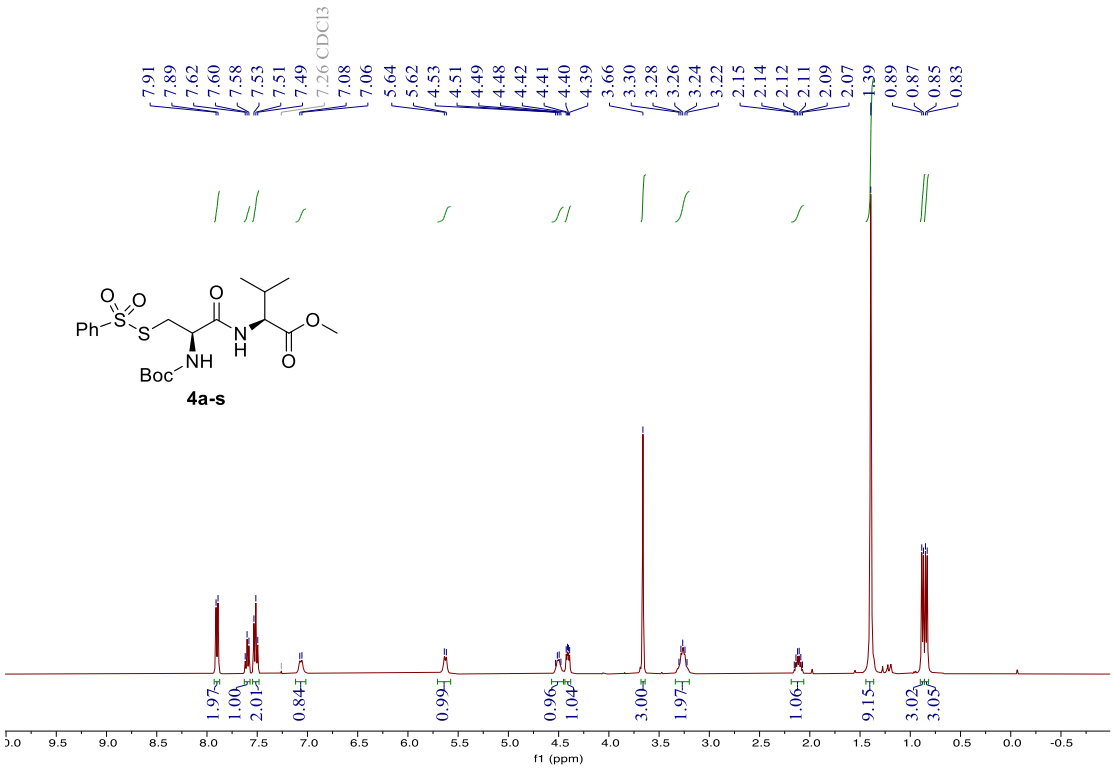



**Figure S28. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4a-s**

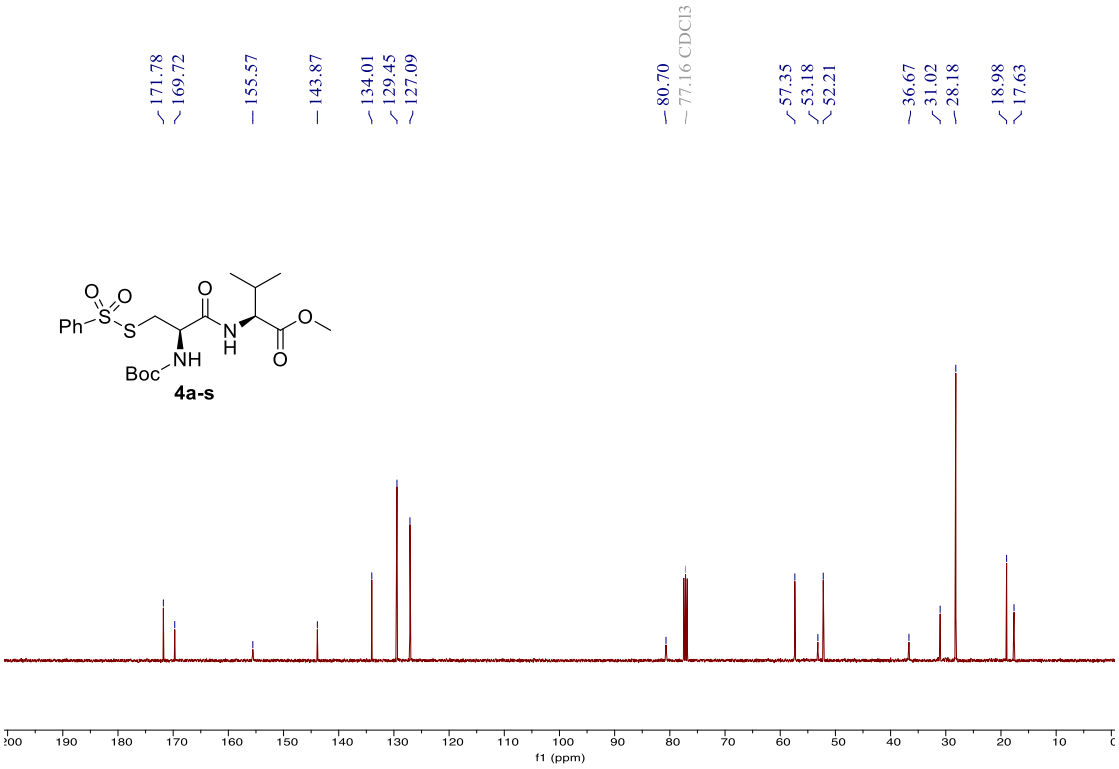



**Figure S29. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4a-s**

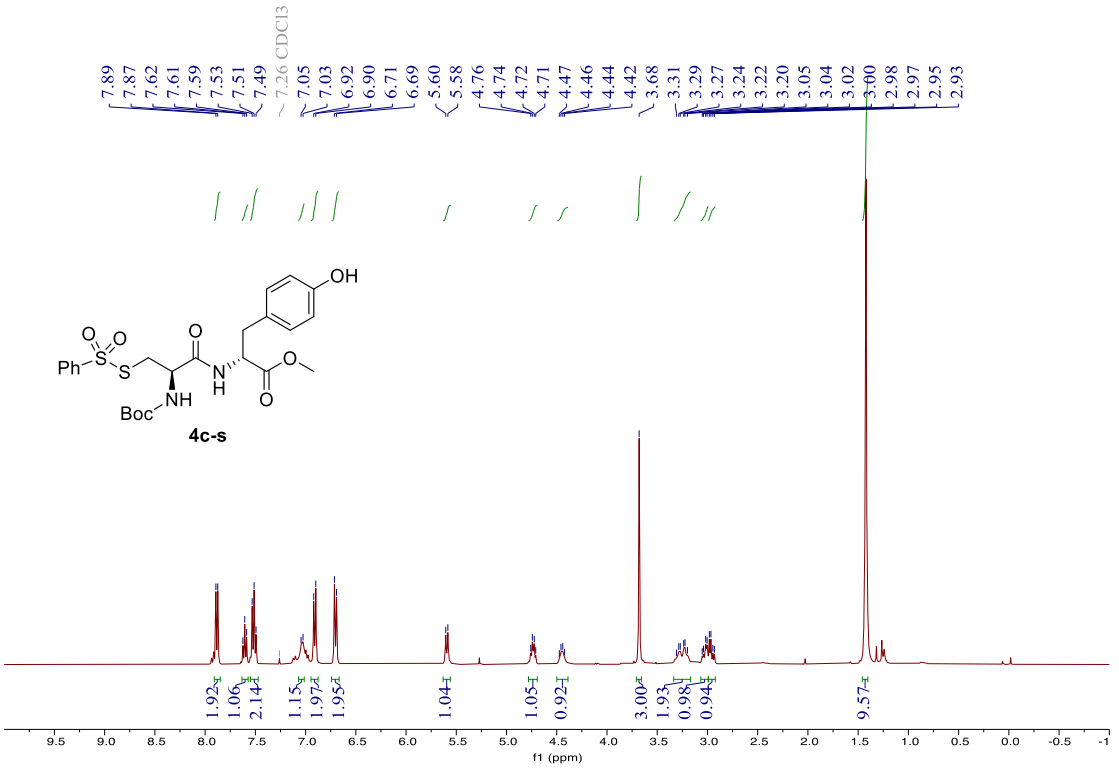



**Figure S30. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4c-s**

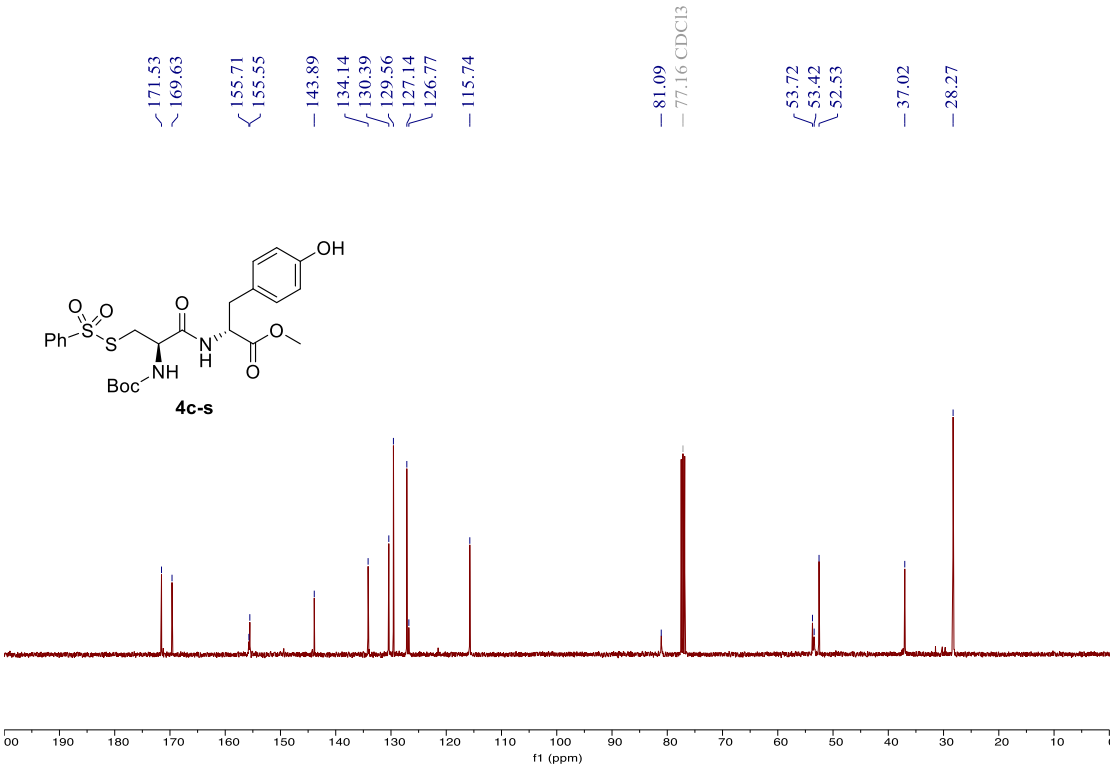



**Figure S31. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4c-s**

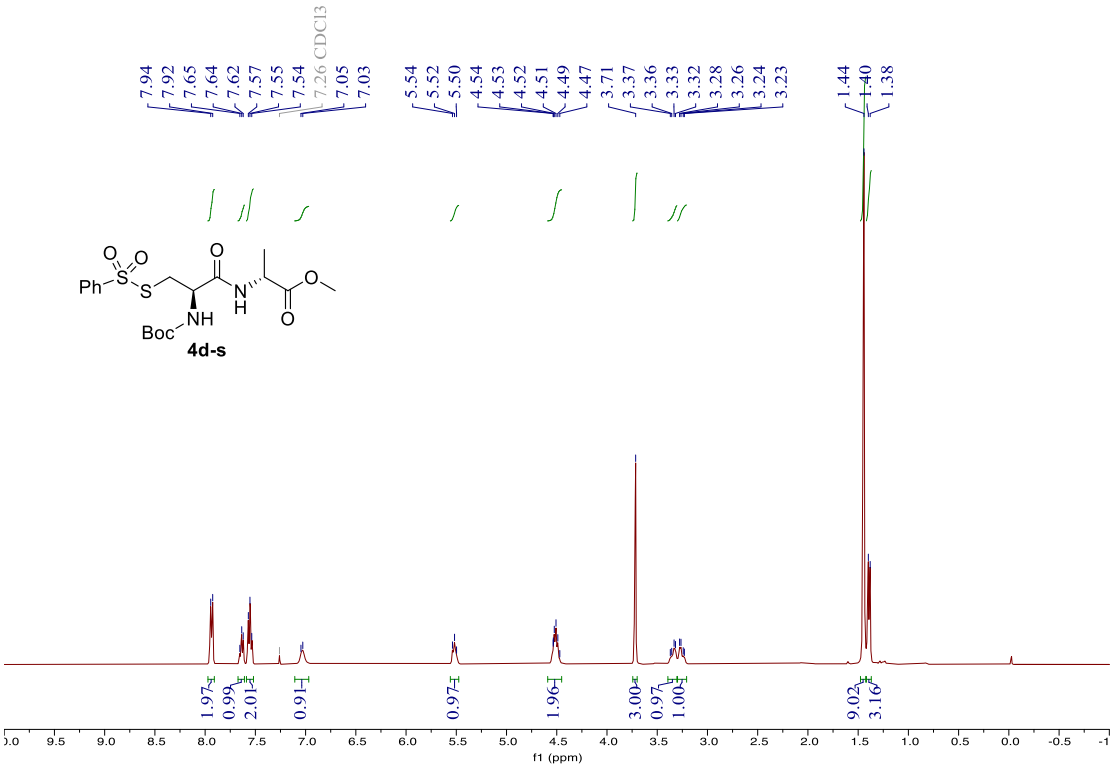



**Figure S32. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4d-s**

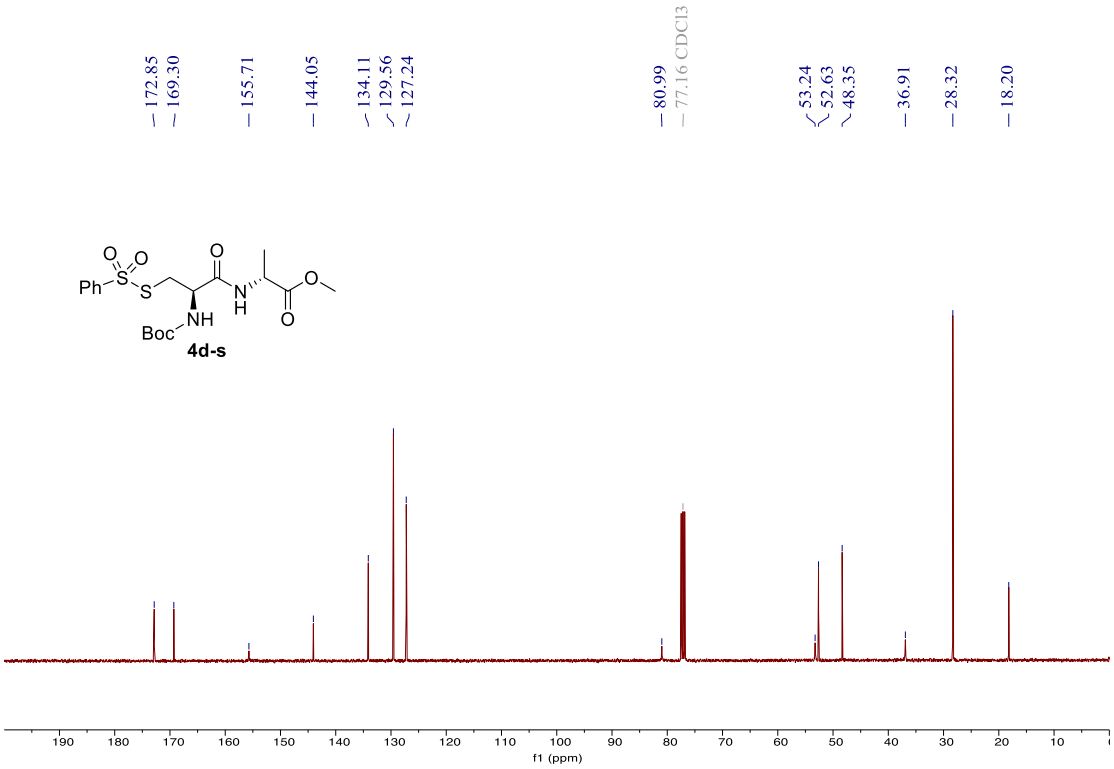



**Figure S33. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4d-s**

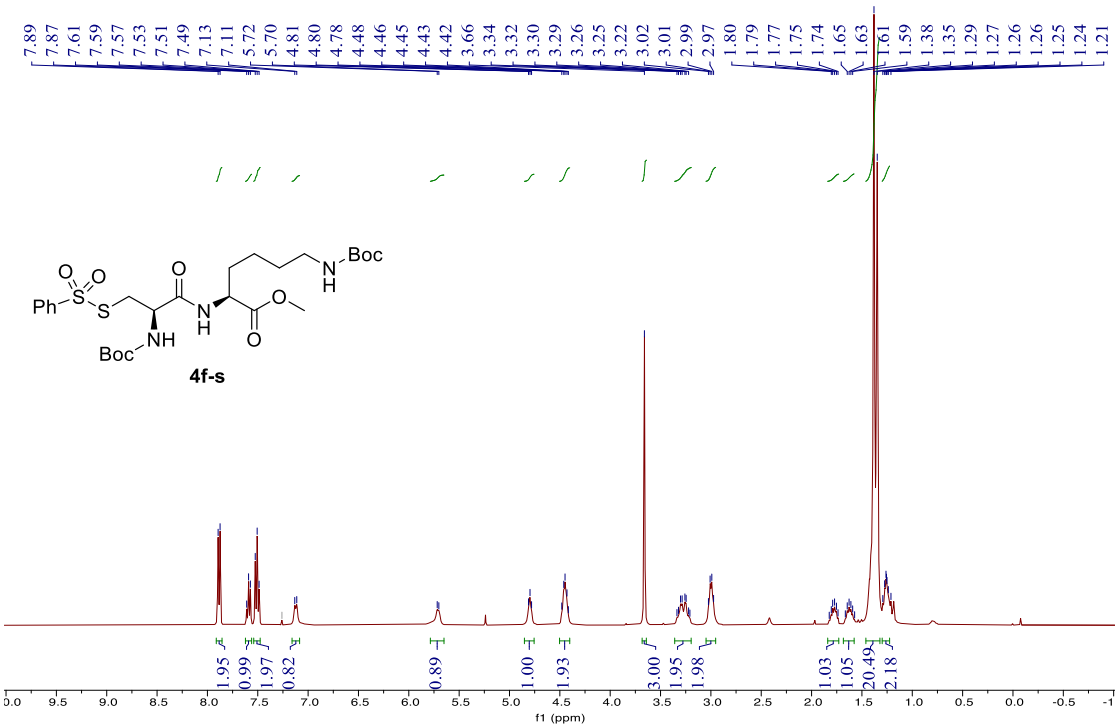



**Figure S34. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4f-s**

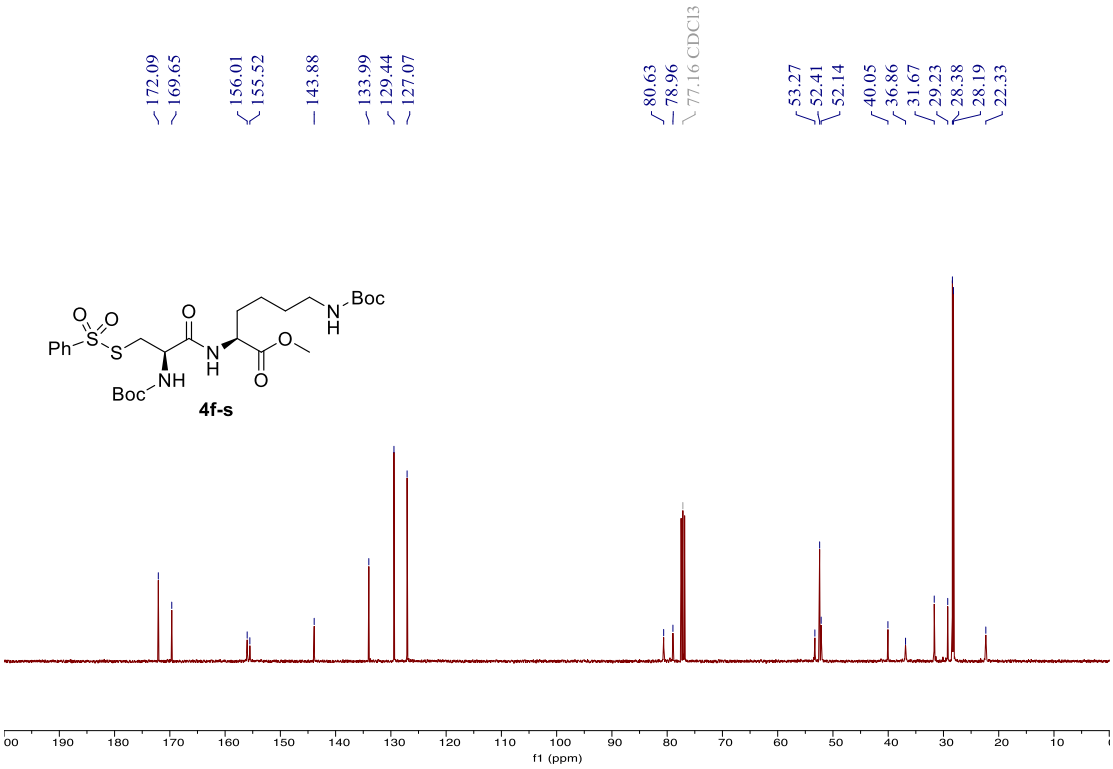



**Figure S35. $^{13}C$ NMR (101 MHz, $CDCl_3$) spectra for compound 4f-s**

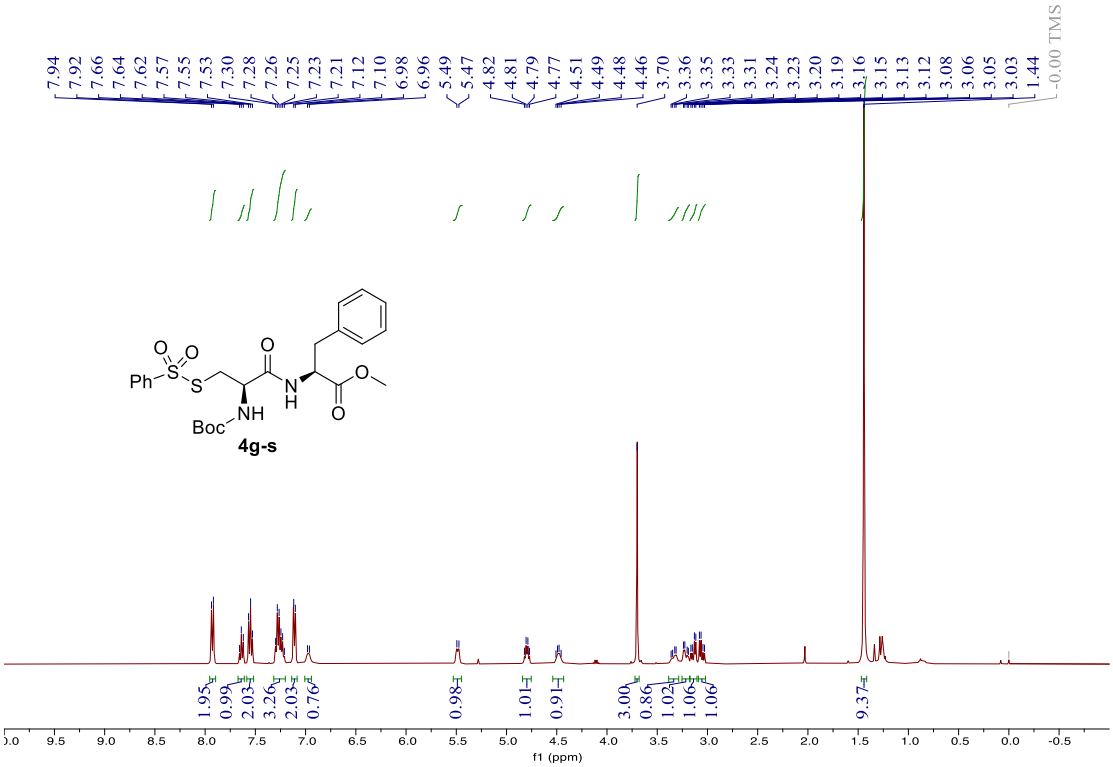



**Figure S36. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectra for compound 4g-s**

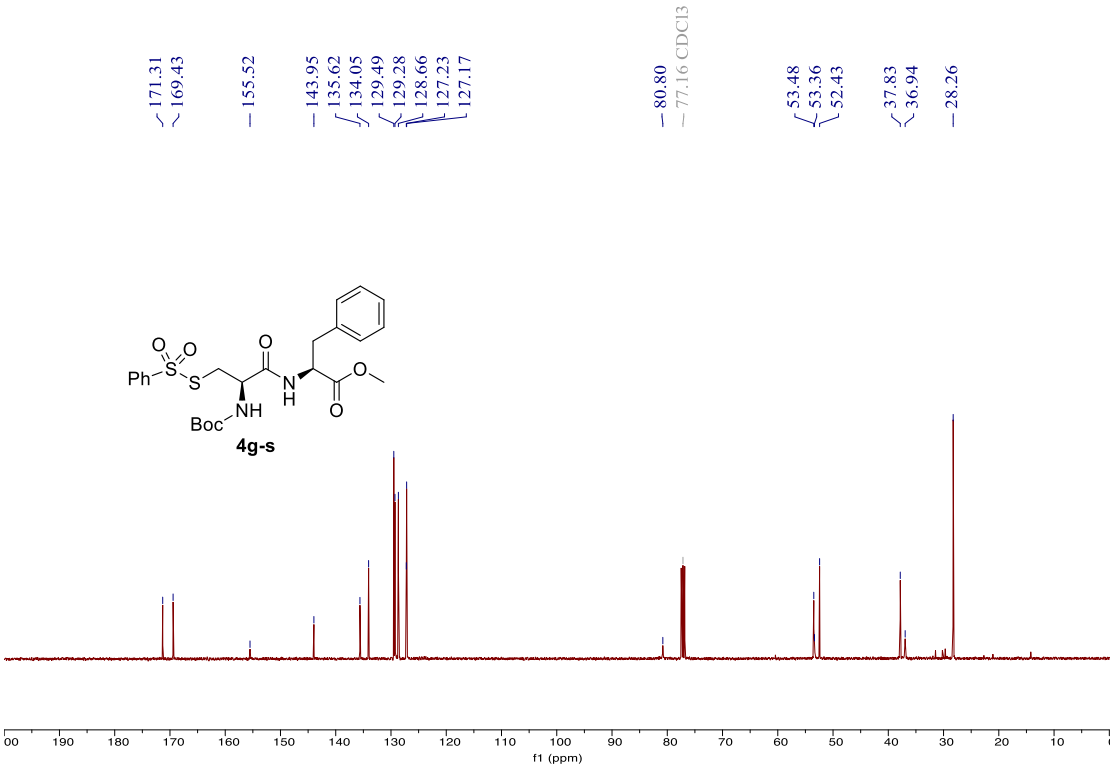



**Figure S37. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4g-s**

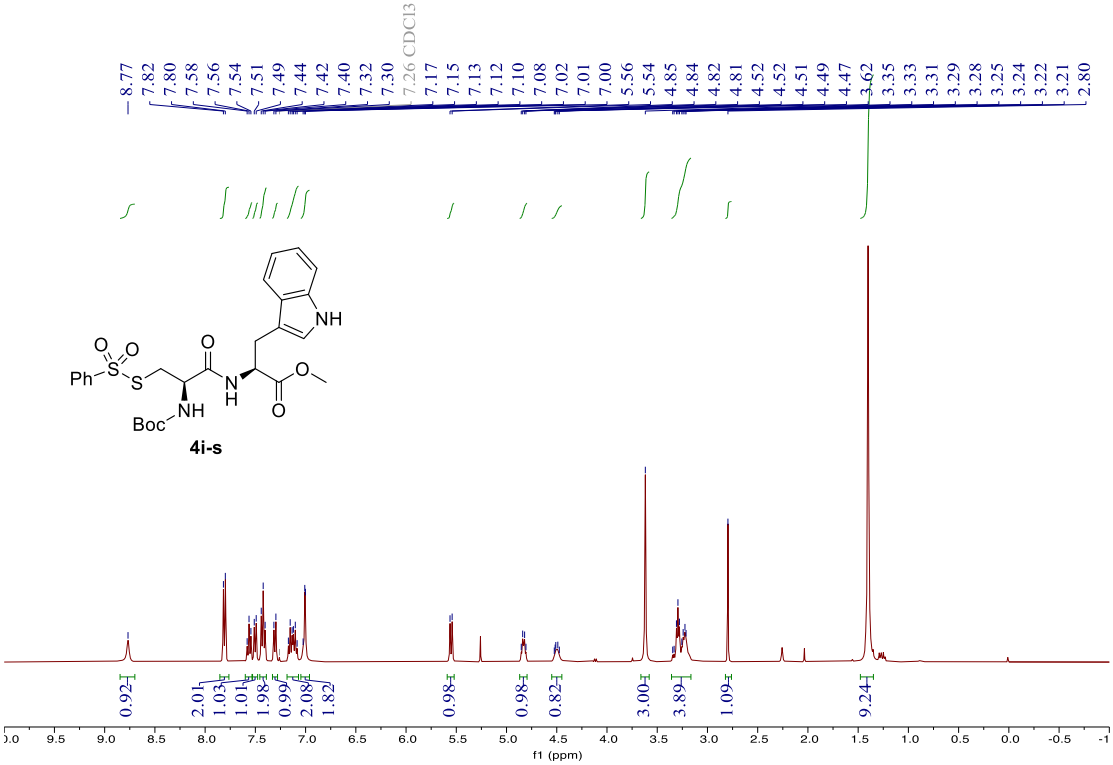



**Figure S38. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4i-s**

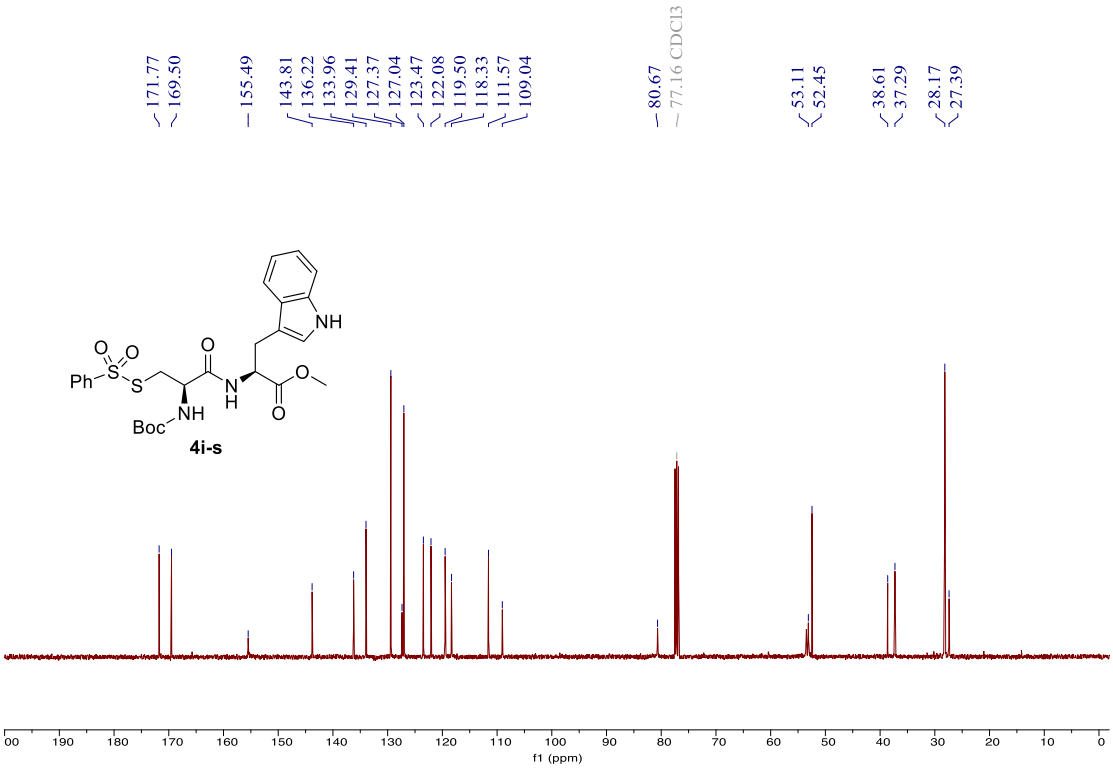



**Figure S39. $^{13}C$ NMR (101 MHz, $CDCl_3$) spectra for compound 4i-s**

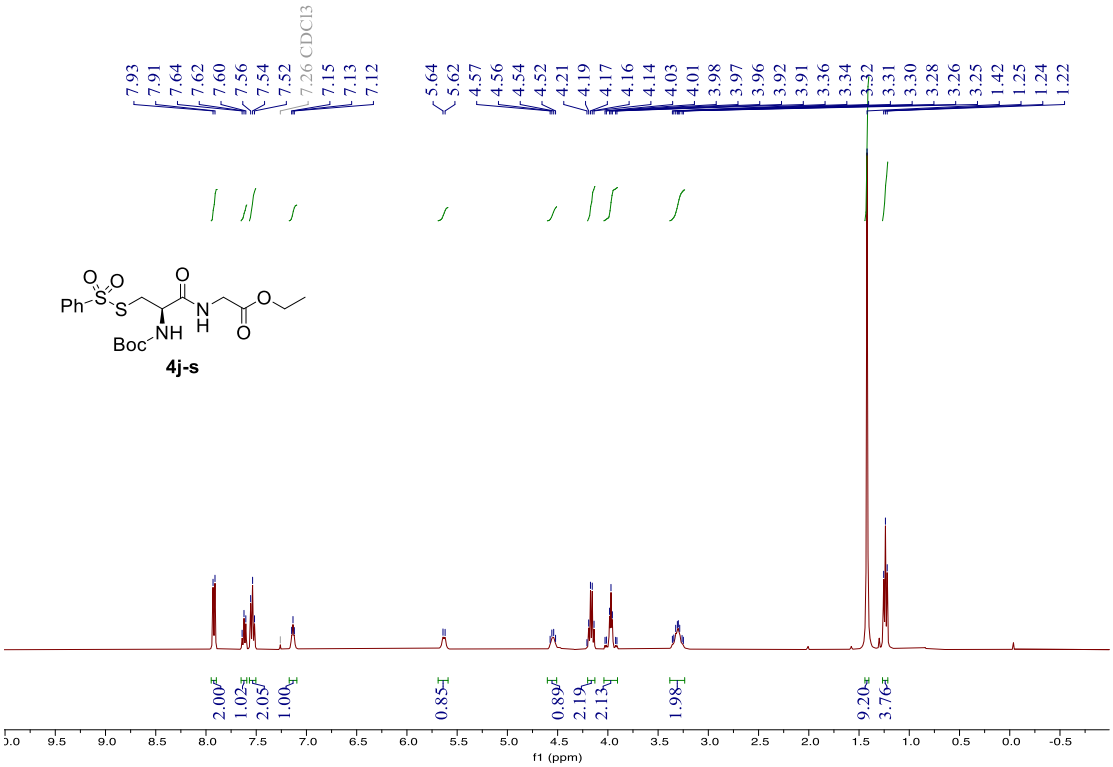



**Figure S40. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectra for compound 4j-s**

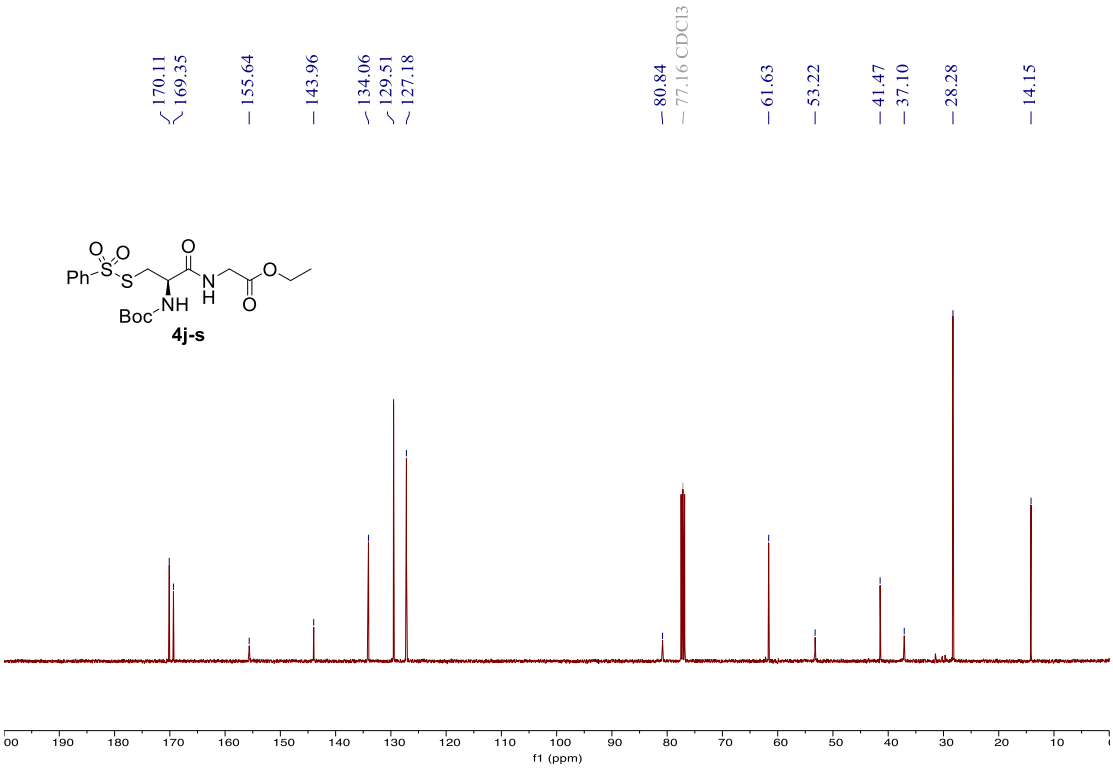



**Figure S41. $^{13}C$ NMR (101 MHz, $CDCl_3$) spectra for compound 4j-s**

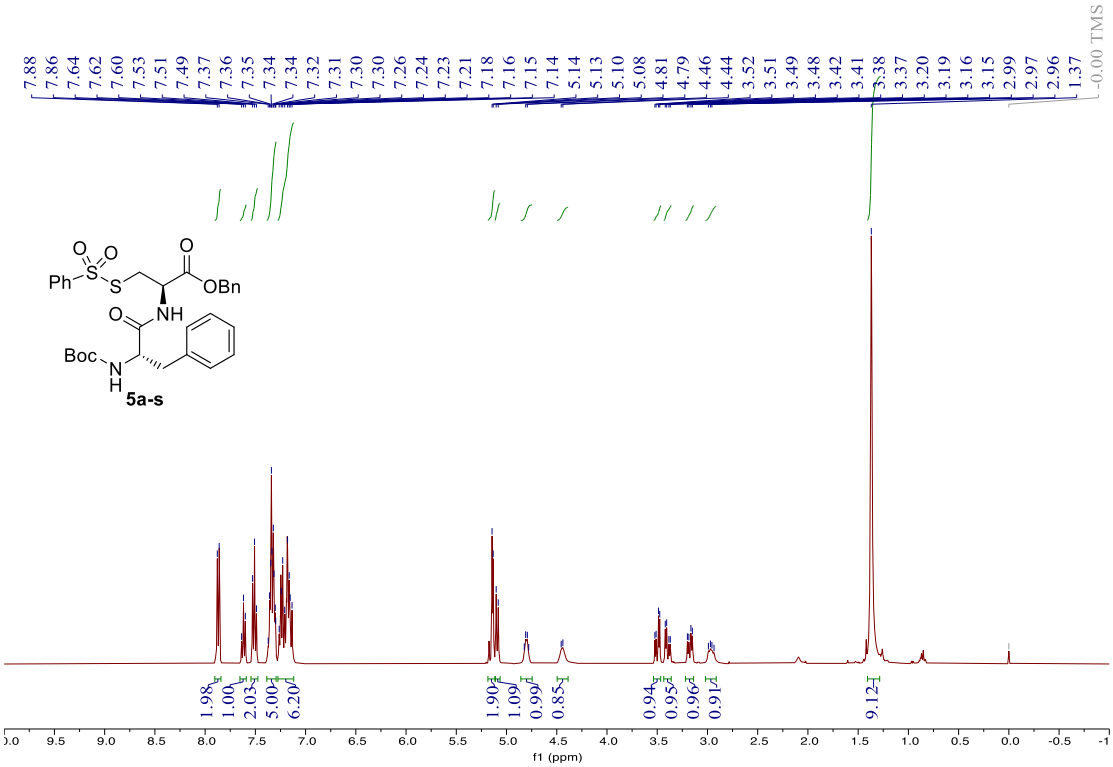



**Figure S42. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectra for compound 5a-s**

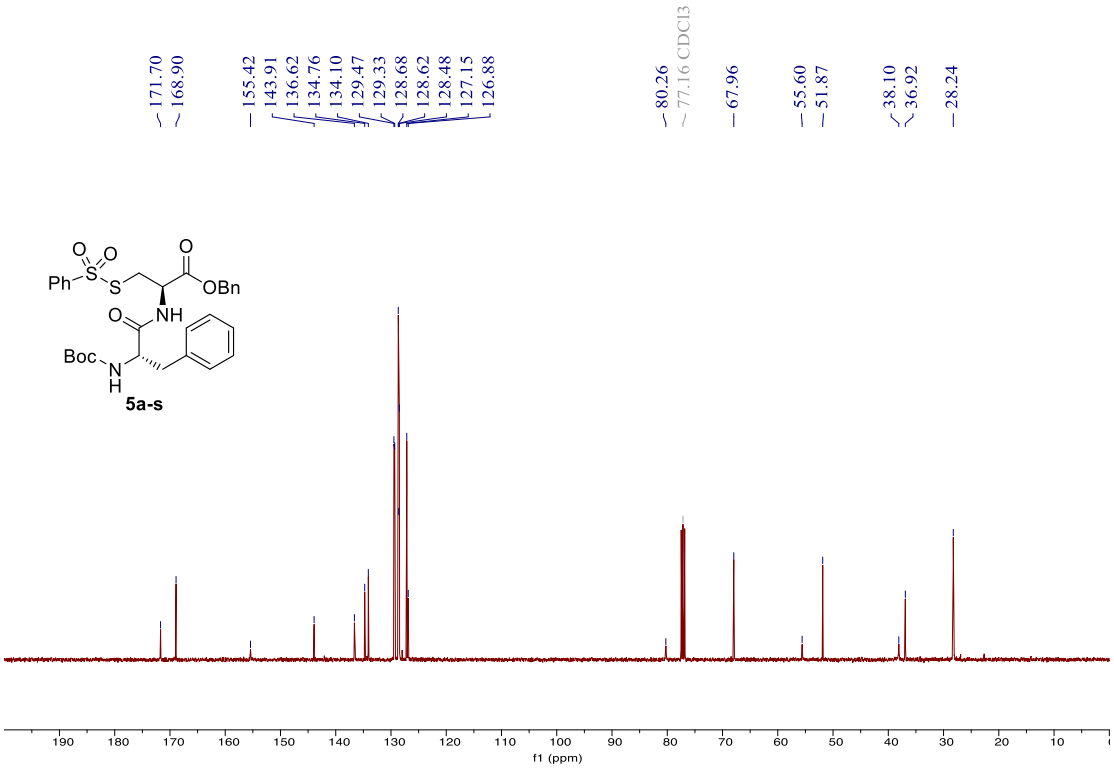



**Figure S43. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5a-s**

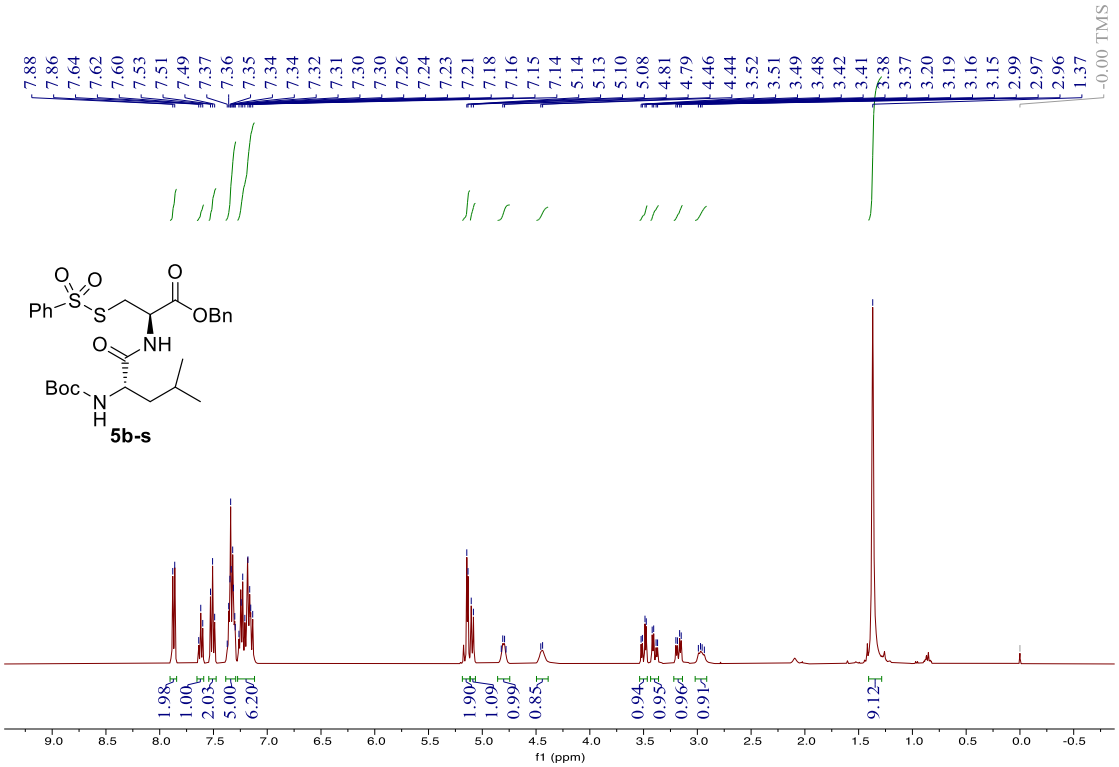



**Figure S44. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5b-s**

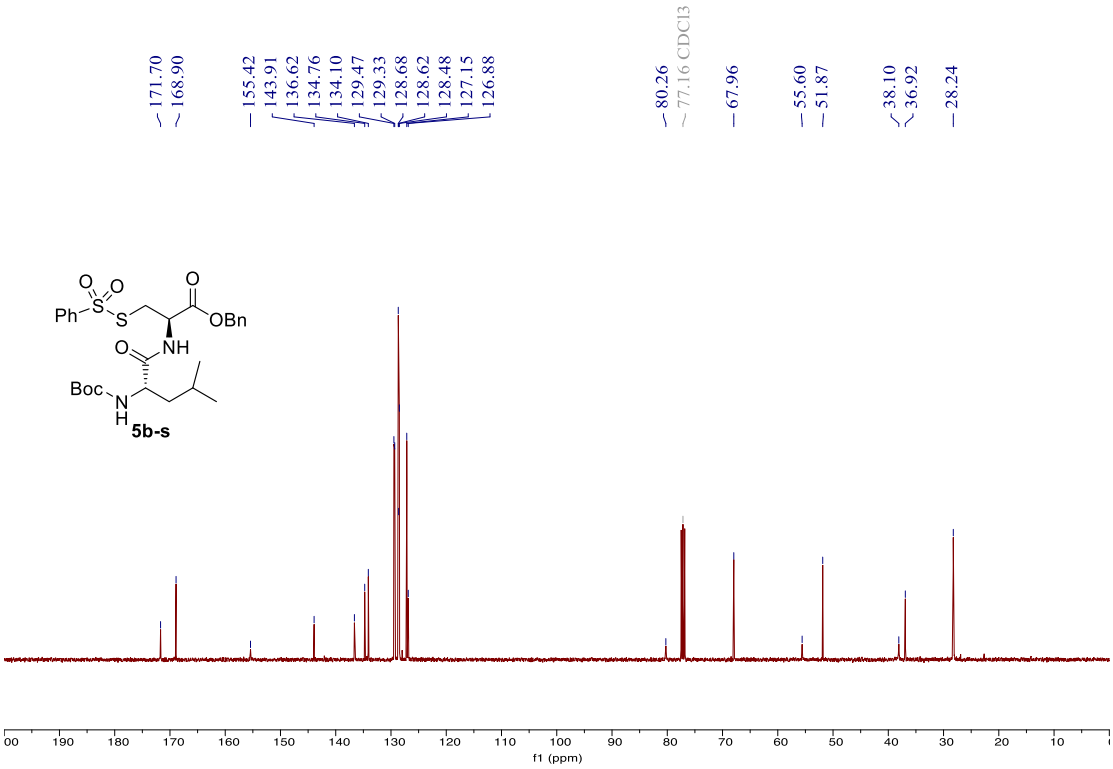



**Figure S45. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5b-s**

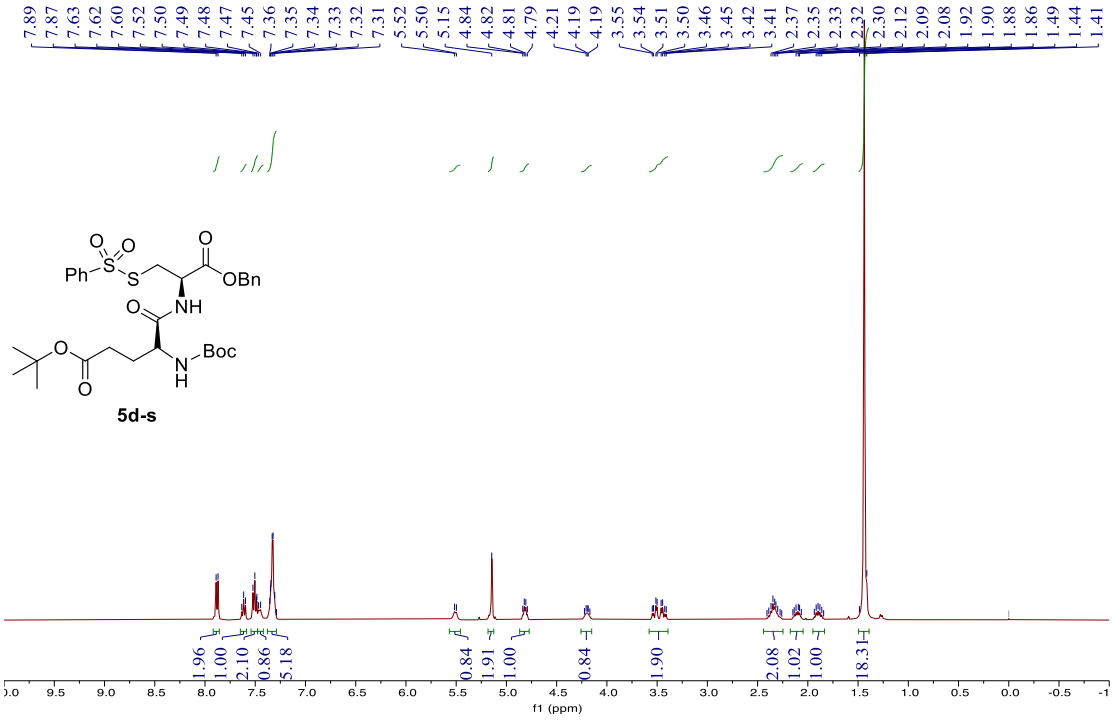



**Figure S46. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5d-s**

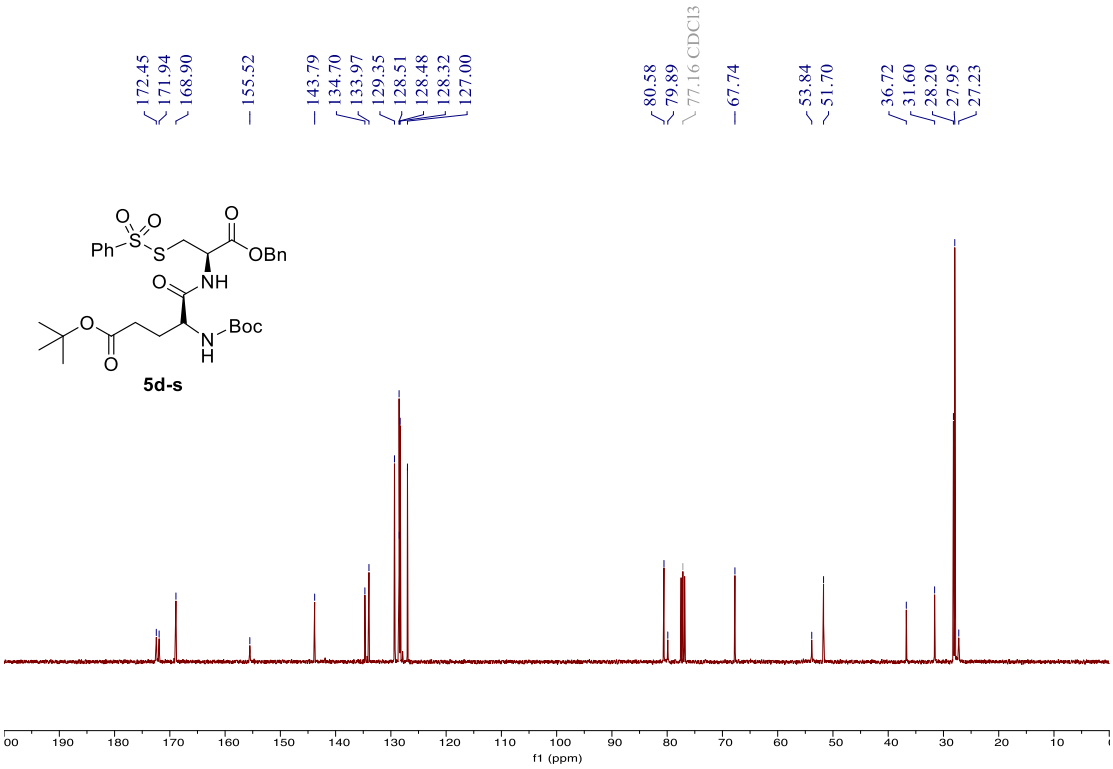



**Figure S47. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5d-s**

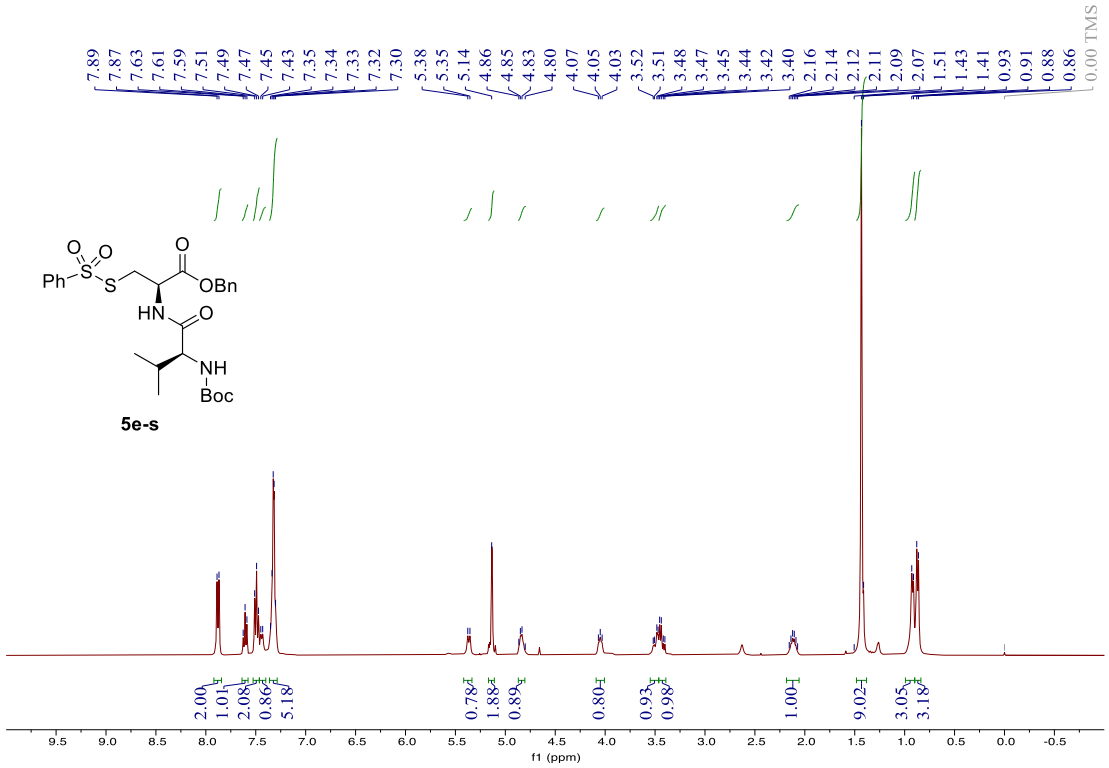



**Figure S48. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5e-s**

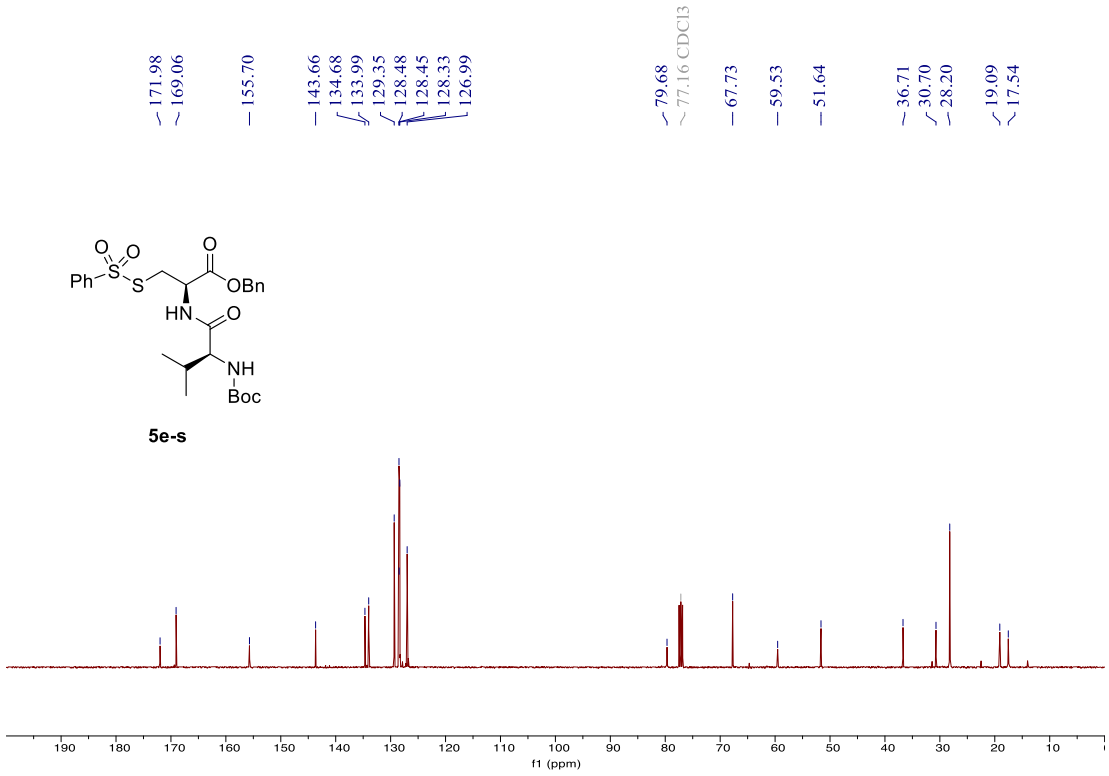



**Figure S49. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5e-s**

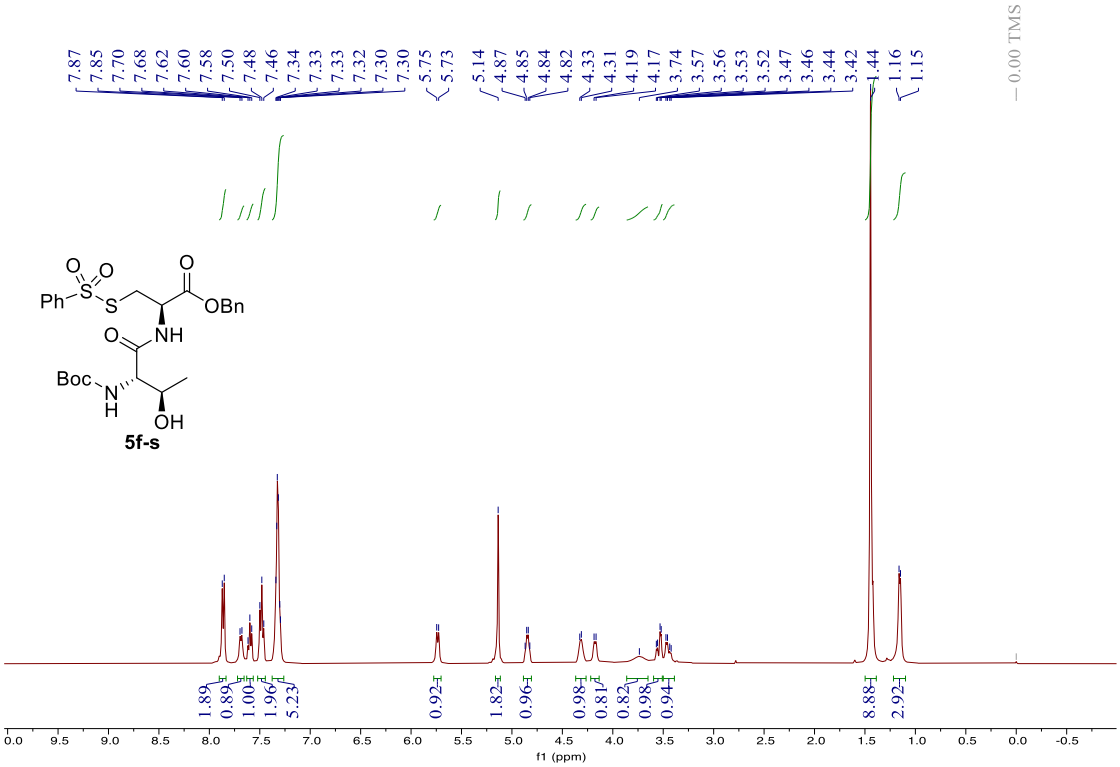



**Figure S50. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5f-s**

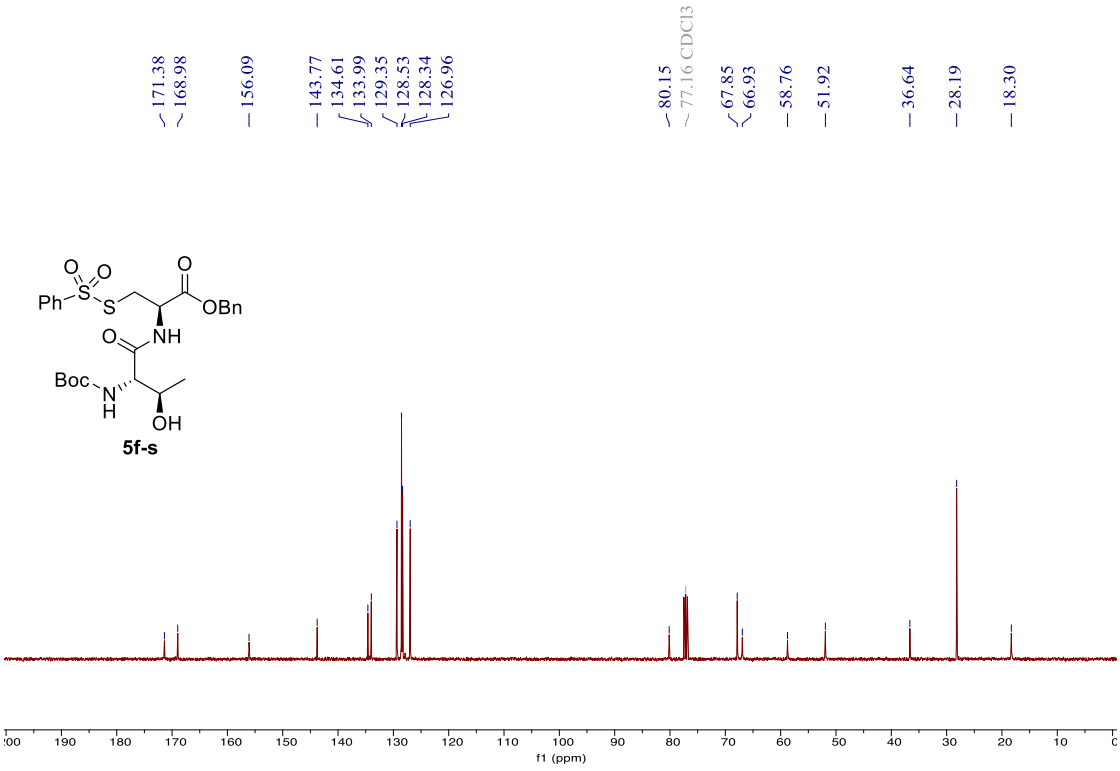



**Figure S51. $^{13}C$ NMR (101 MHz, $CDCl_3$) spectra for compound 5f-s**

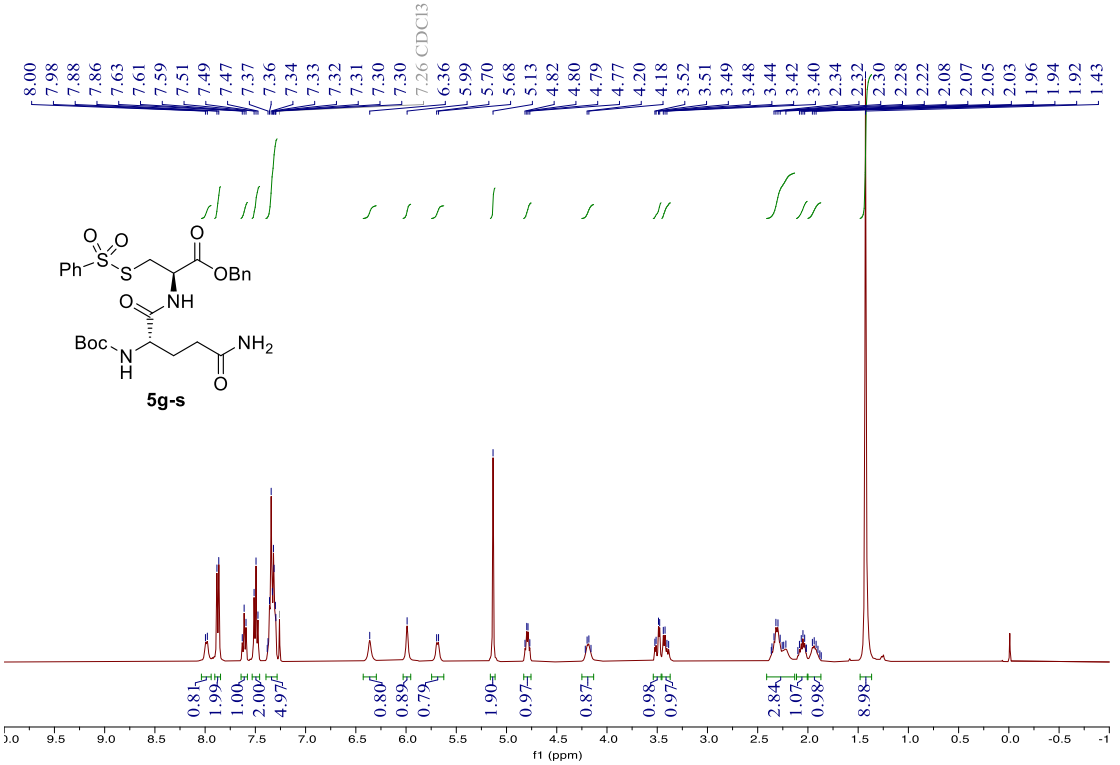



**Figure S52. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectra for compound 5g-s**

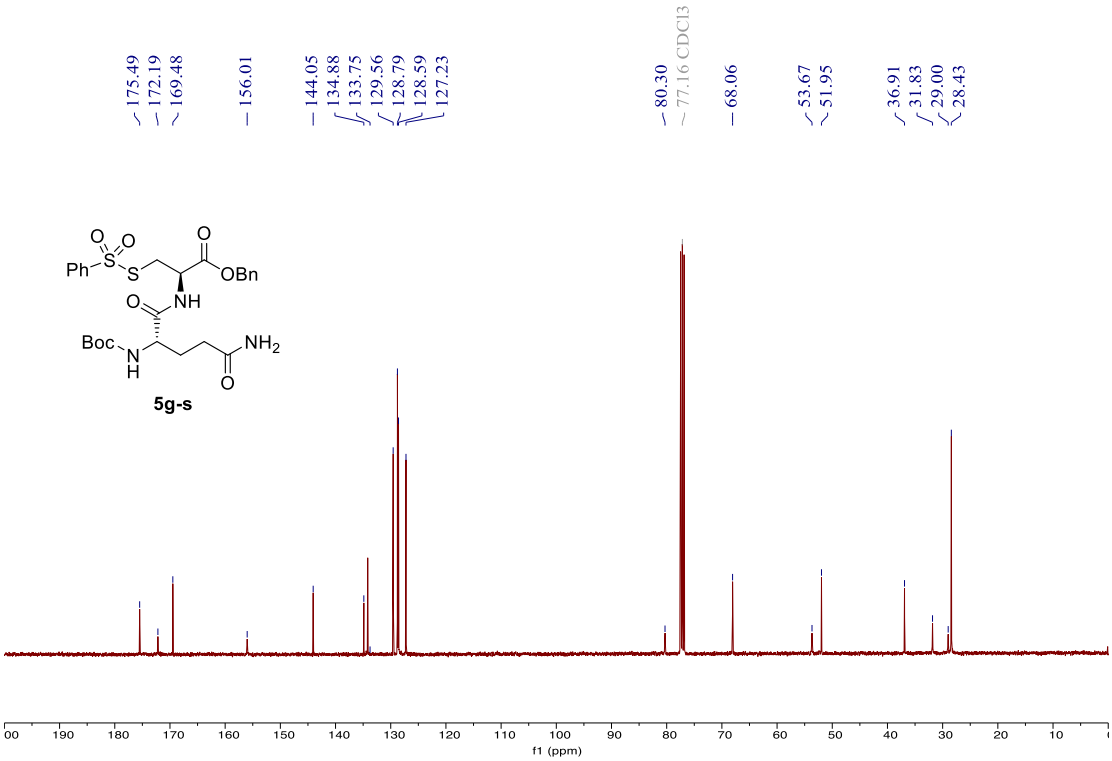



**Figure S53. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5g-s**

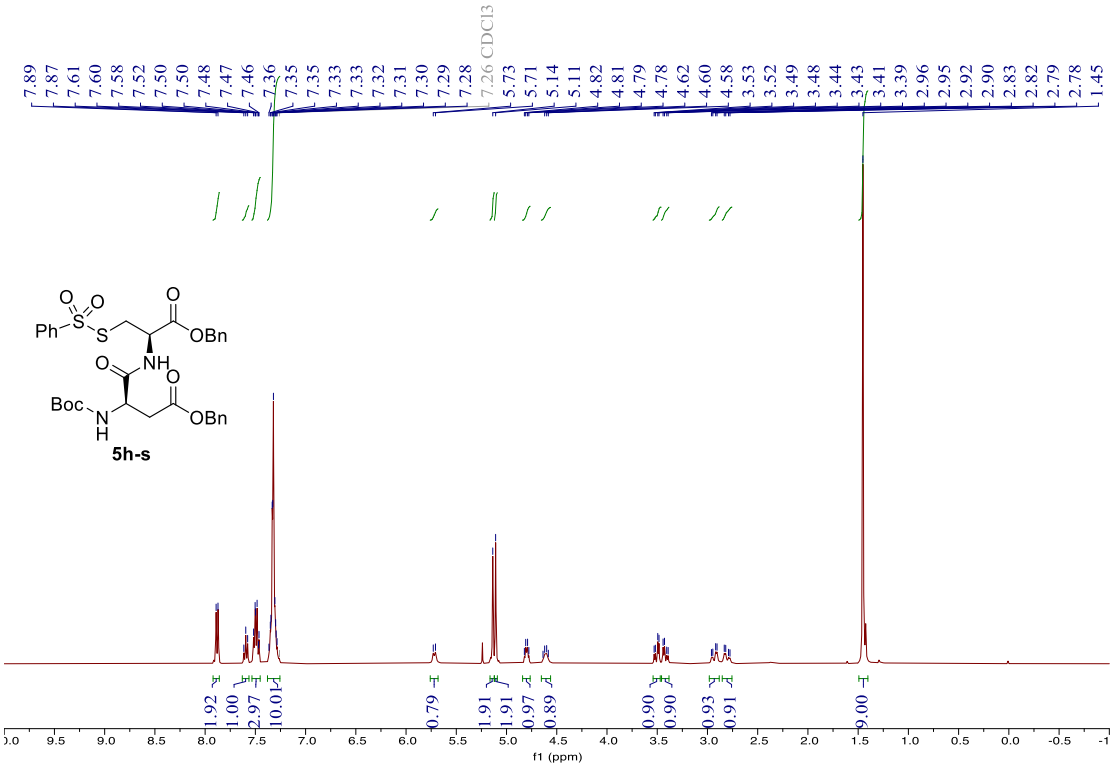



**Figure S54. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5h-s**

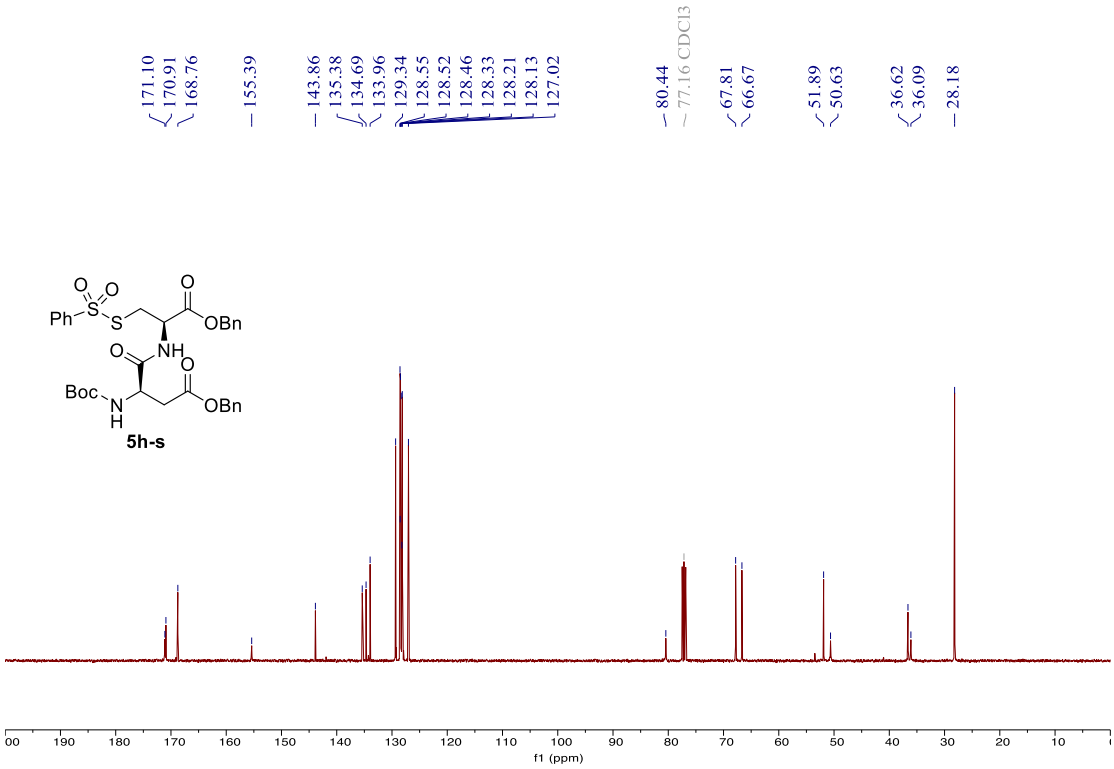



**Figure S55. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5h-s**

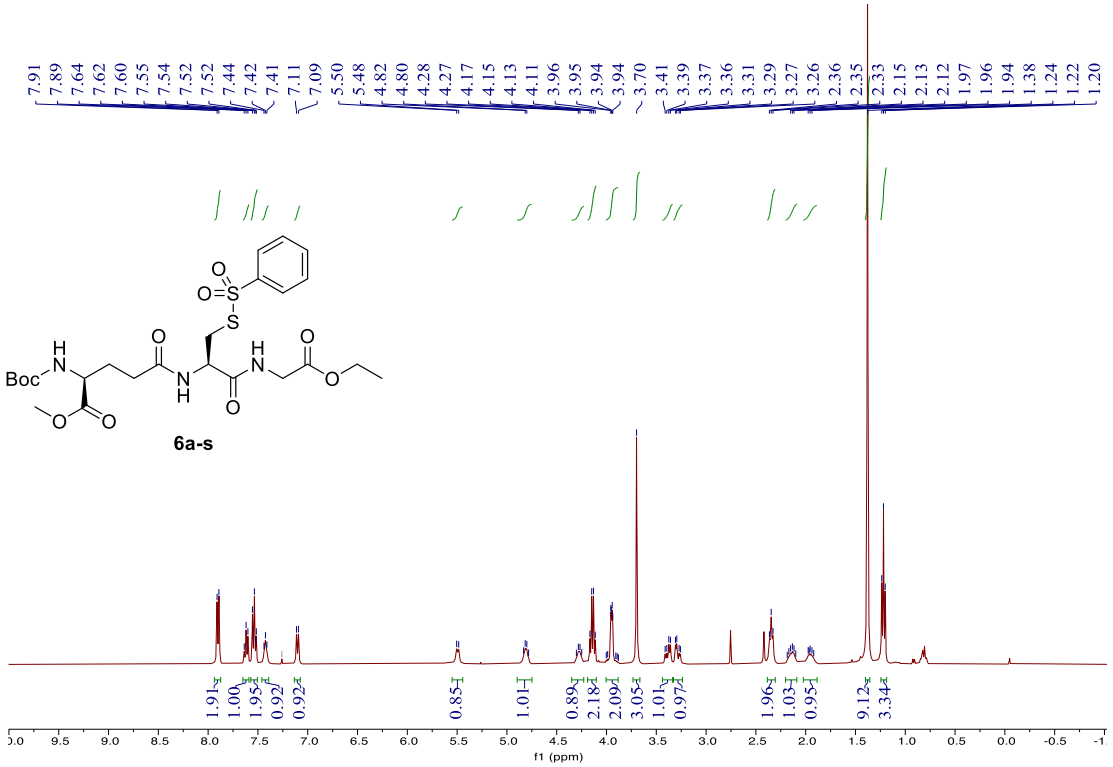



**Figure S56. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 6a-s**

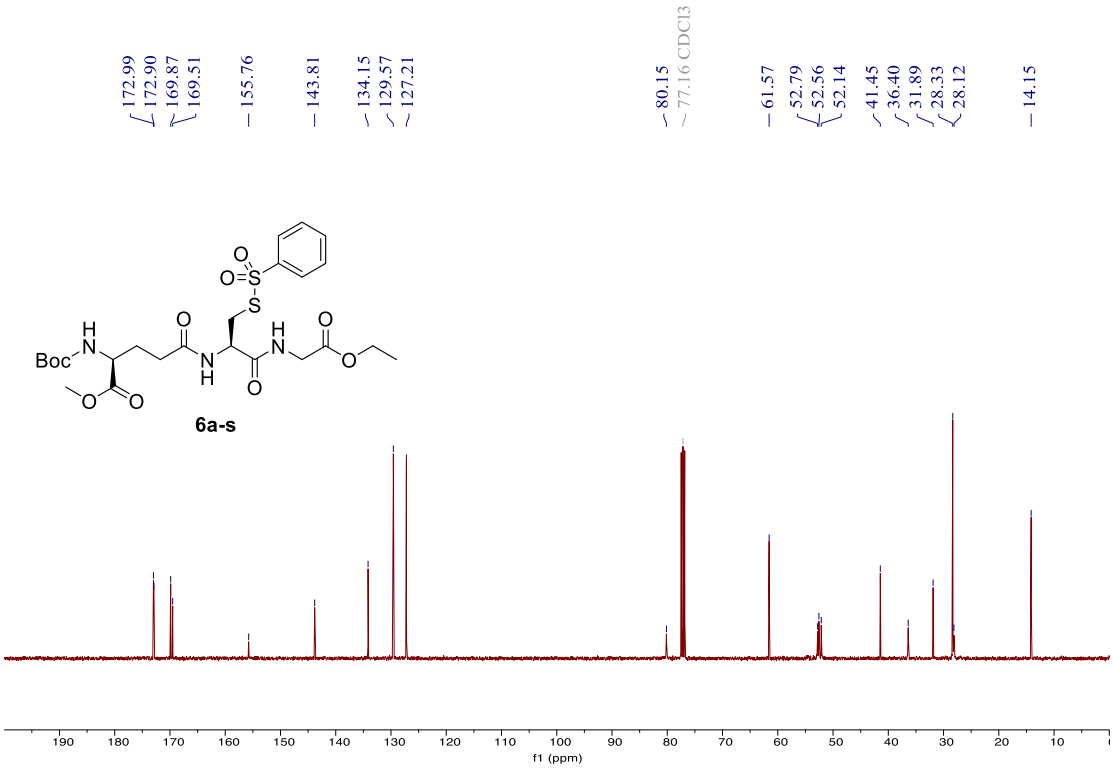



**Figure S57. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 6a-s**

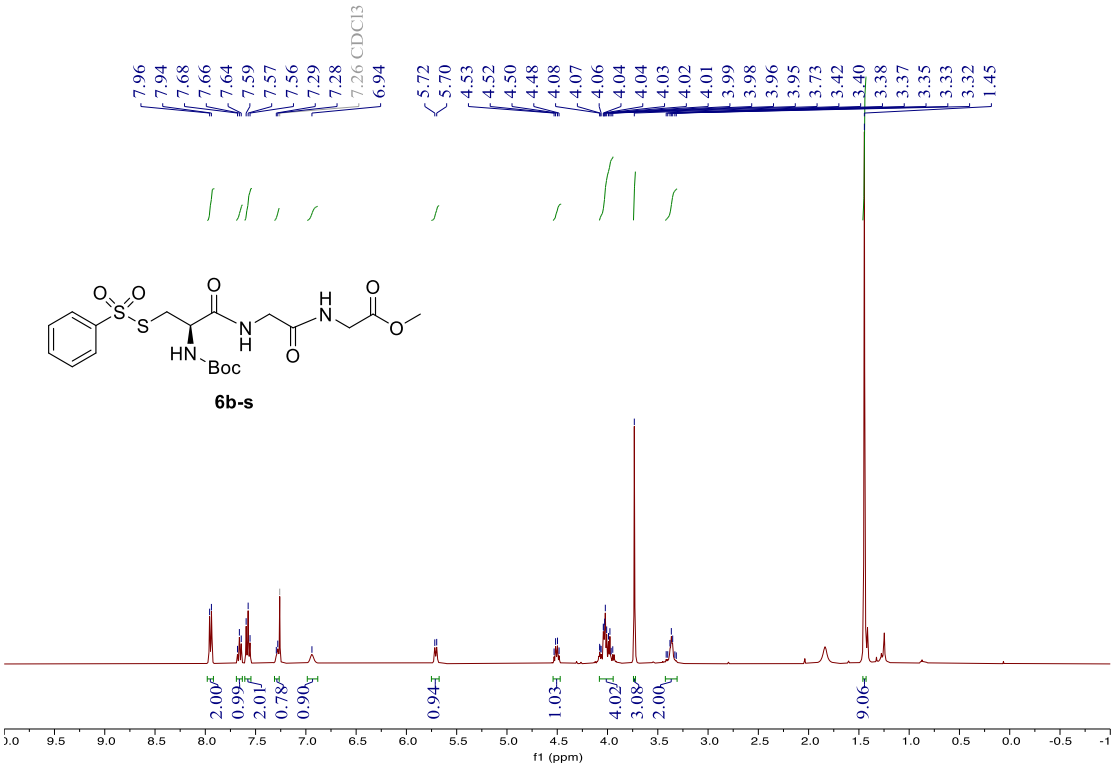



**Figure S58. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 6b-s**

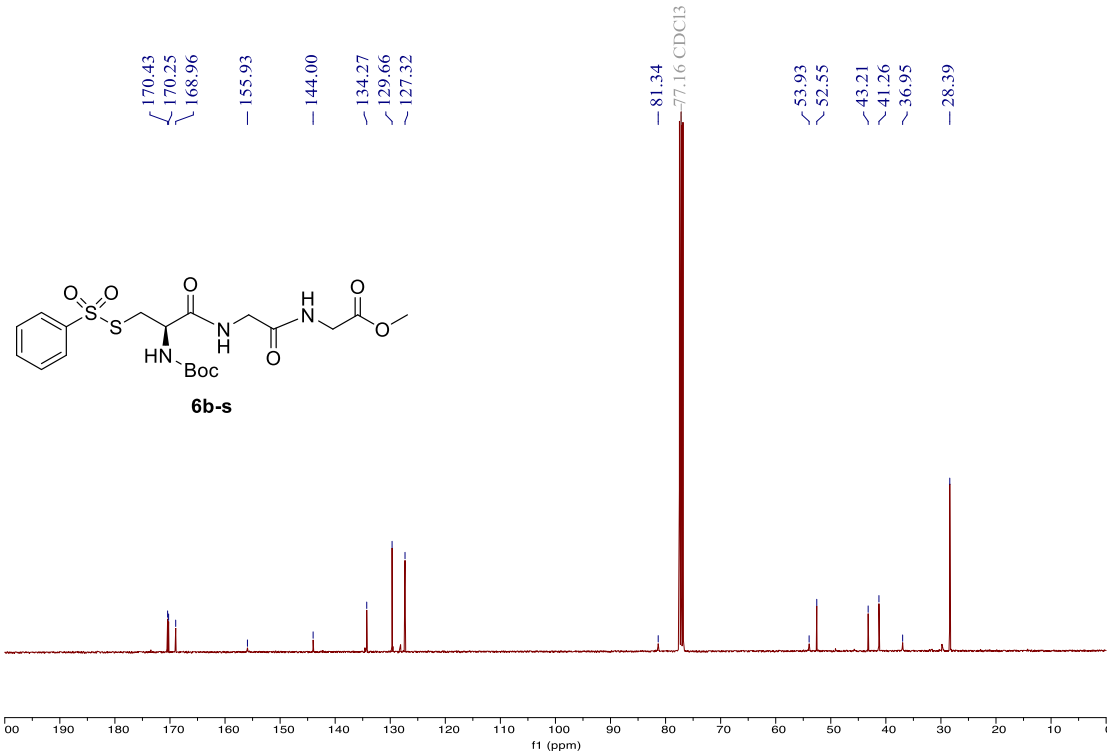



**Figure S59. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 6b-s**

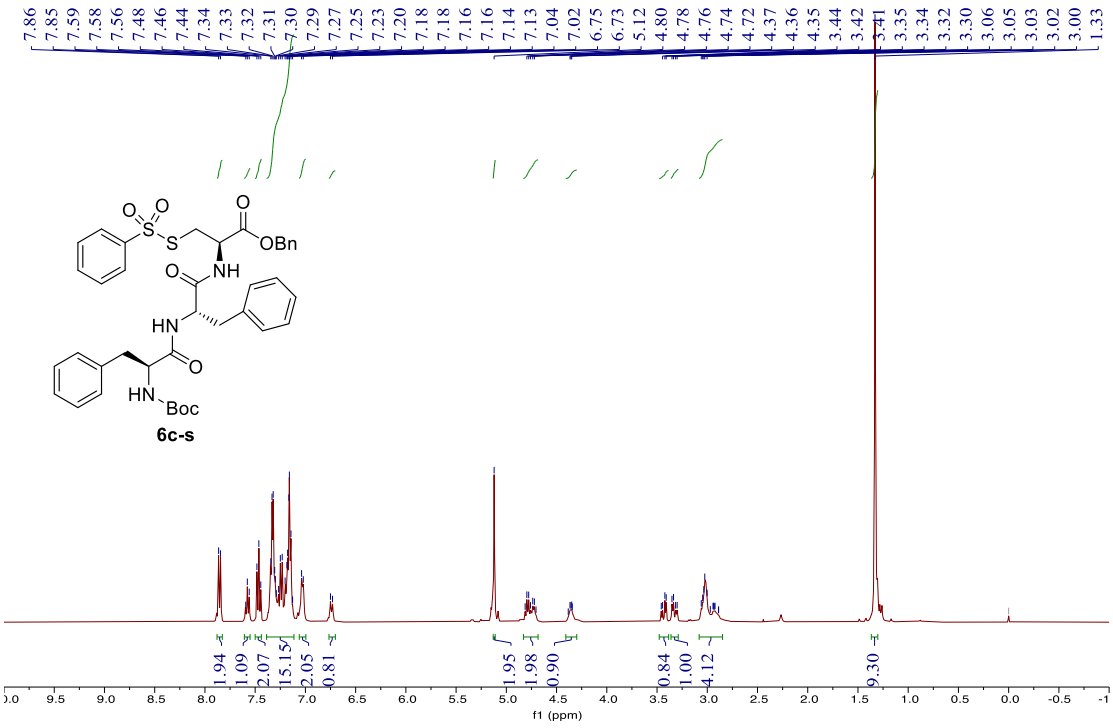



**Figure S60. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 6c-s**

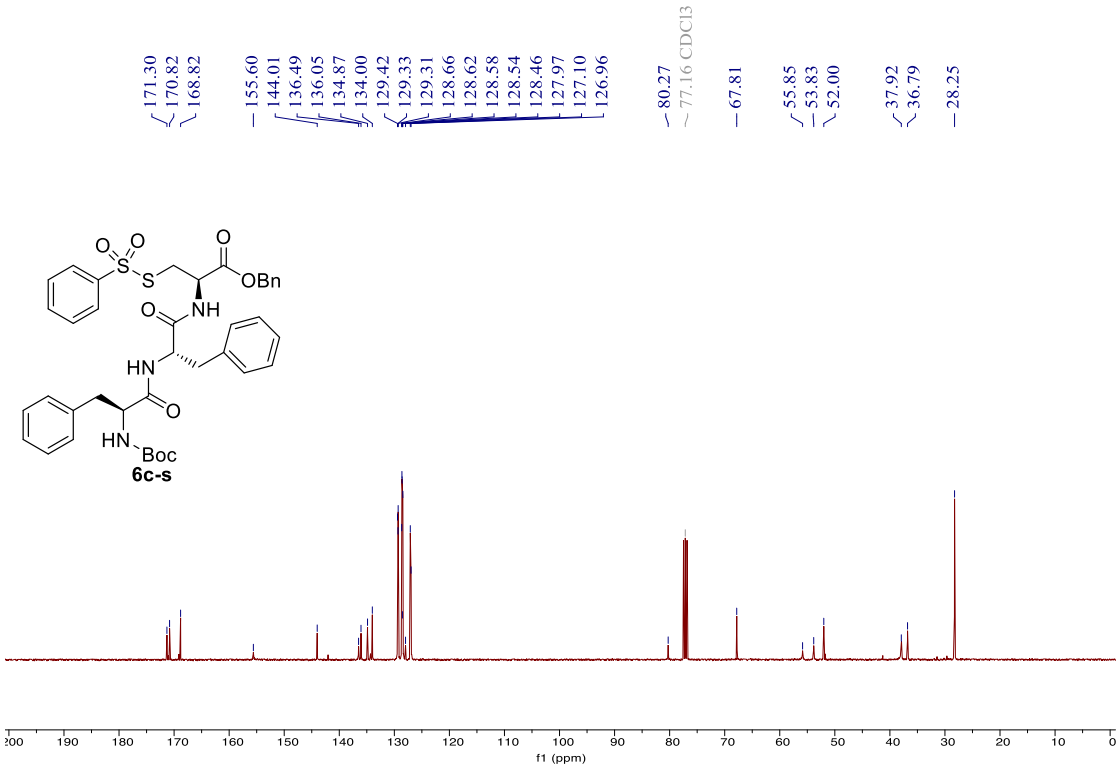



**Figure S61. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 6c-s**

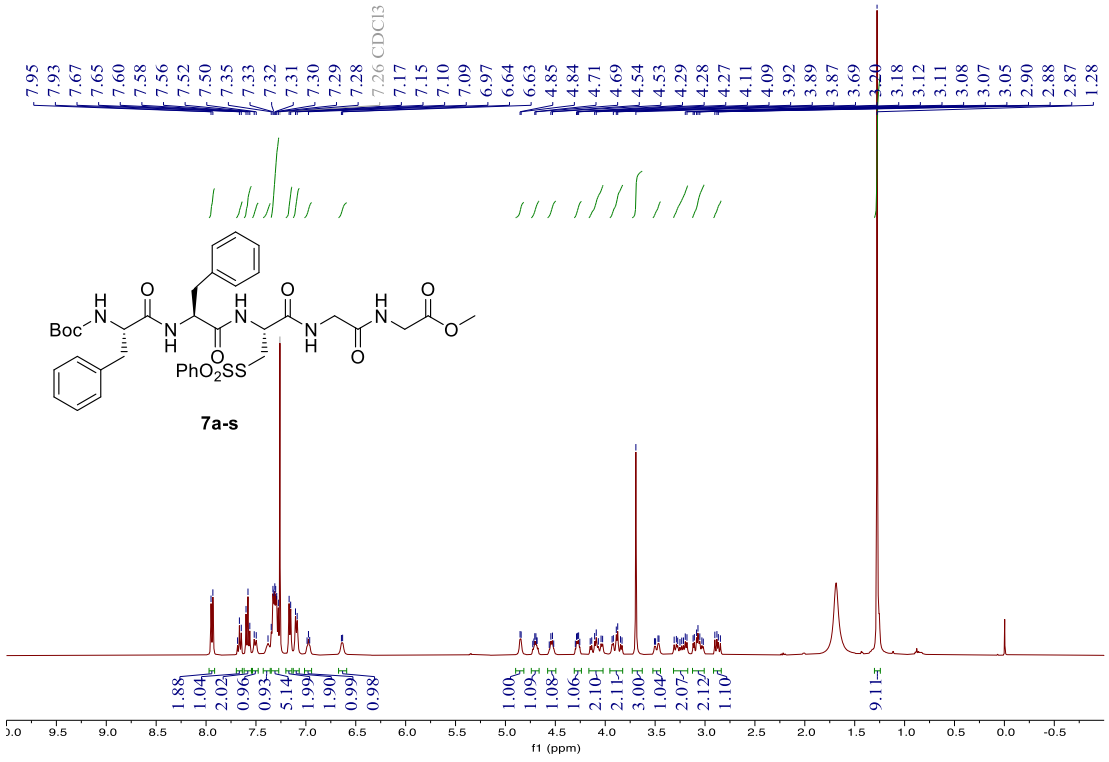



**Figure 62. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 7a-s**

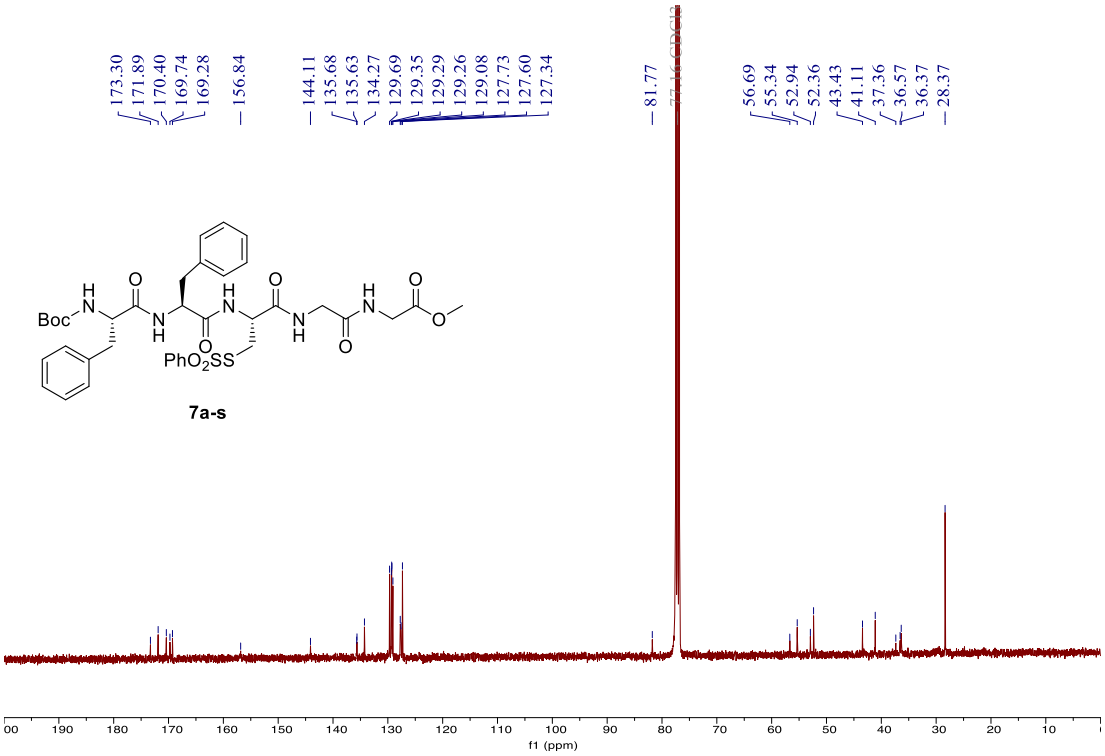



**Figure 63. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 7a-s**

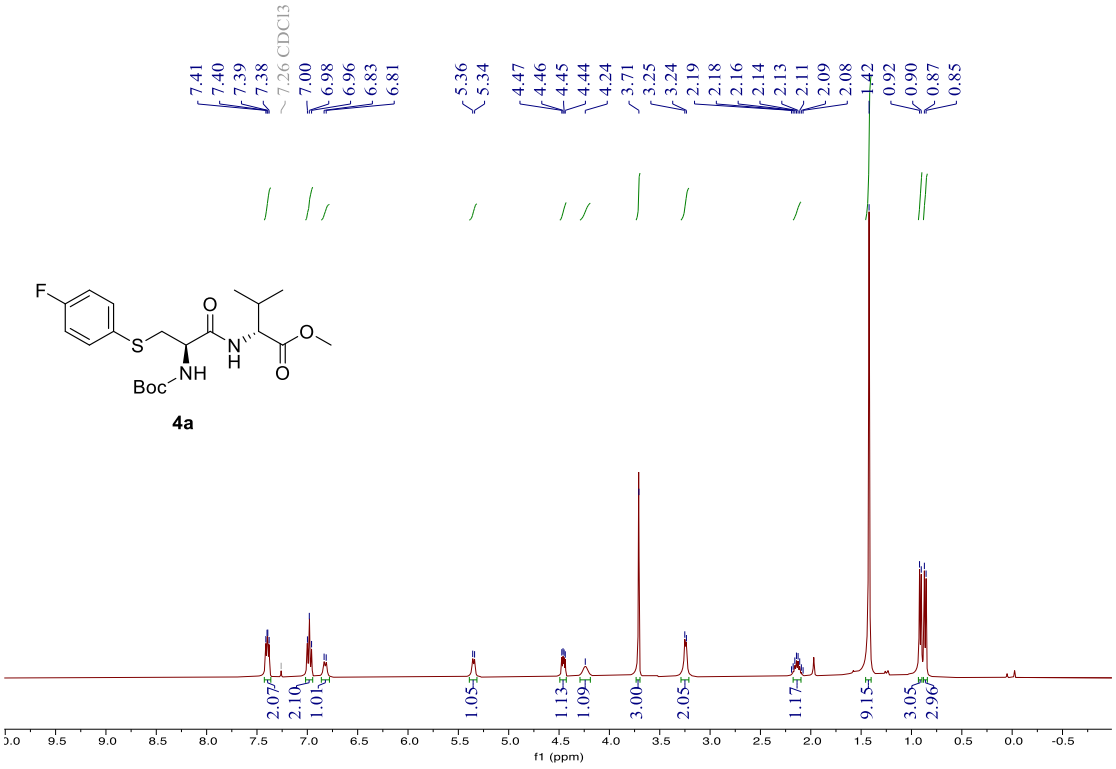



**Figure S64. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4a**

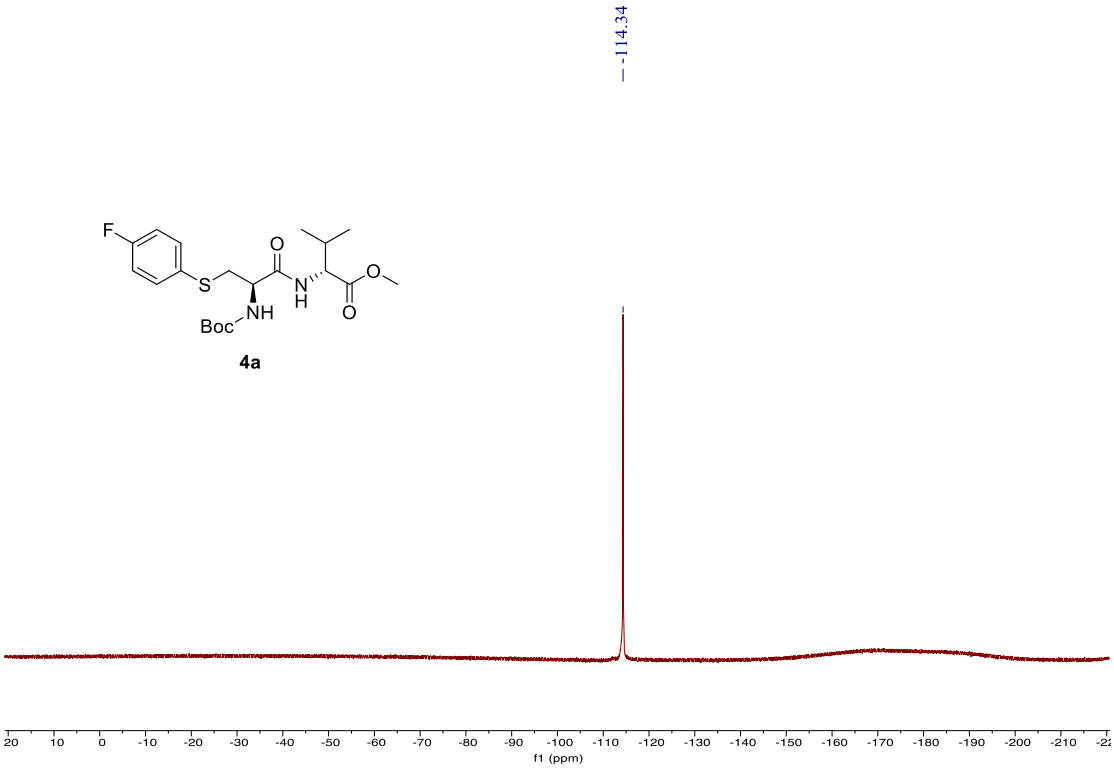



**Figure S65. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 4a**

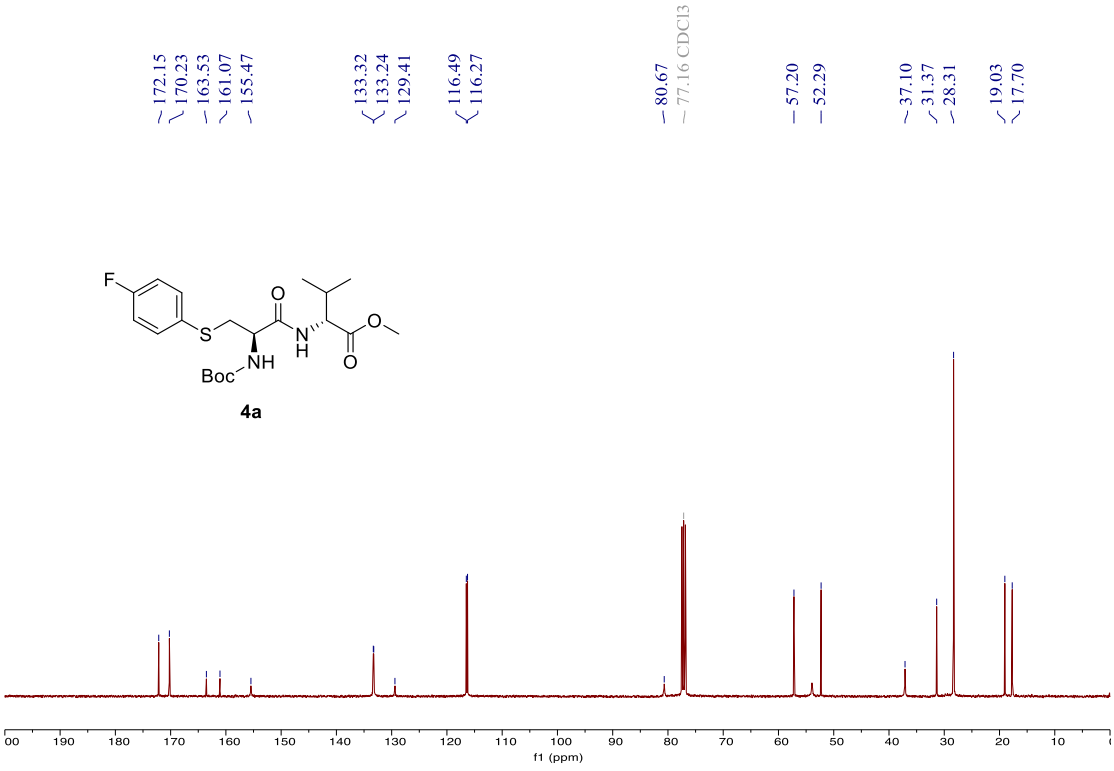



**Figure S66. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4a**

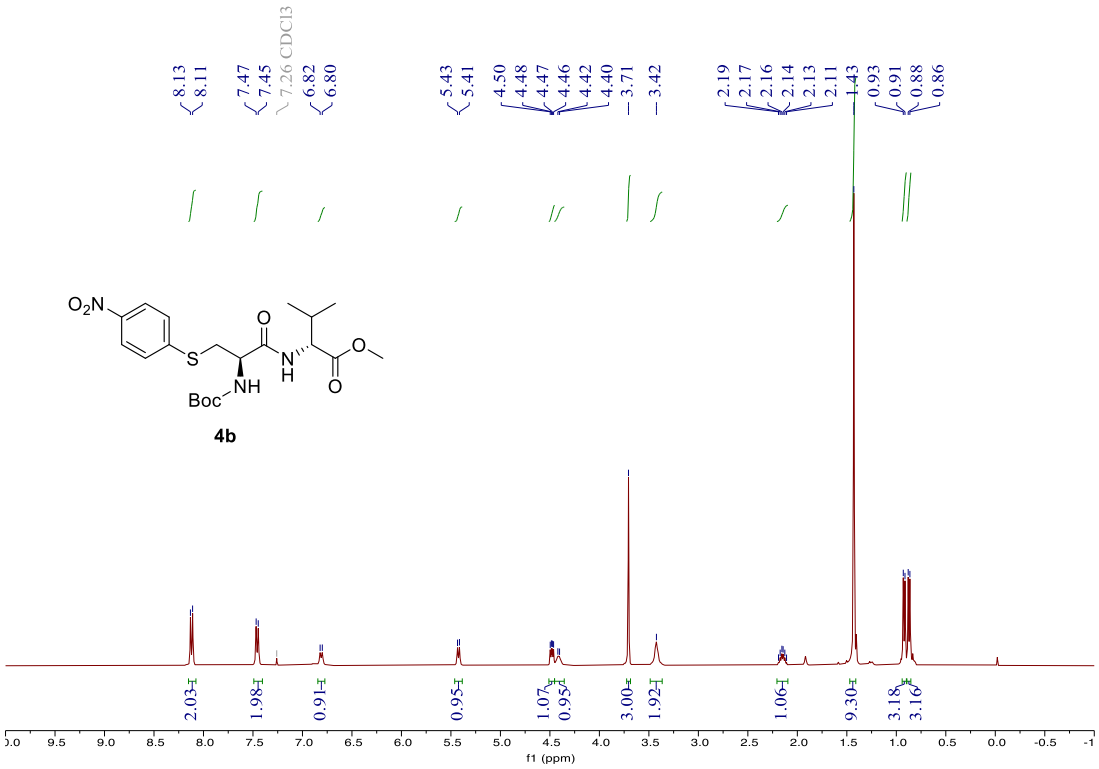



**Figure S67. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4b**

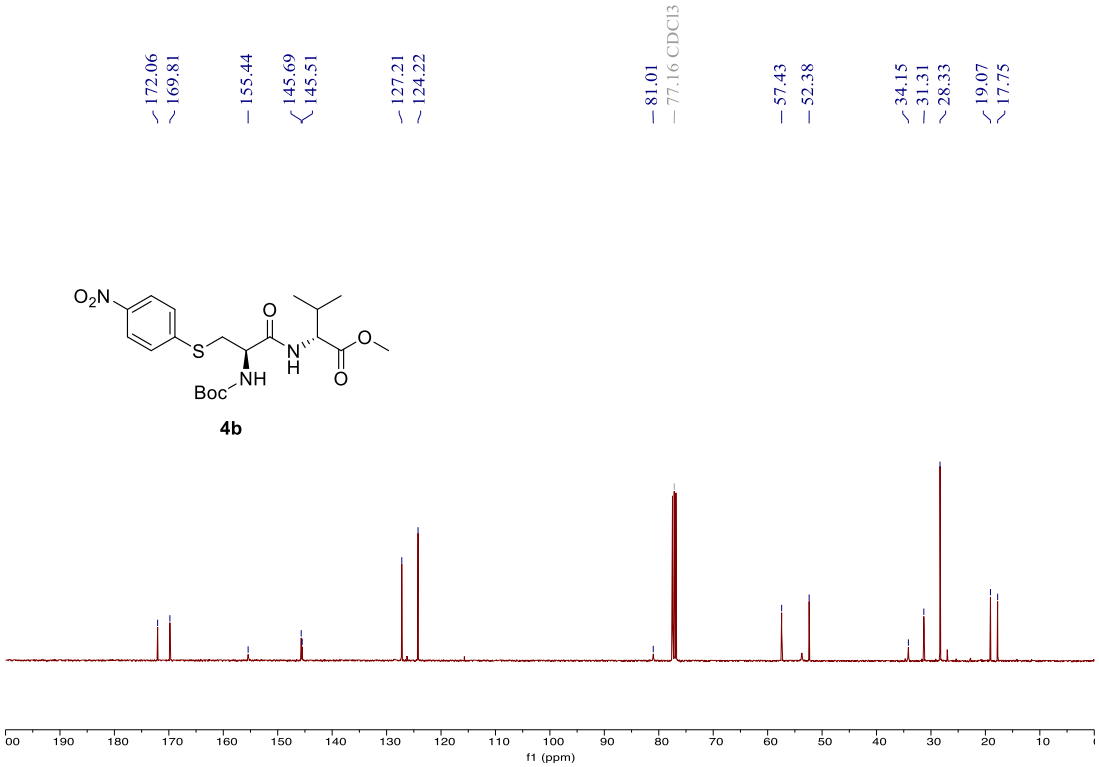



**Figure S68. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4b**

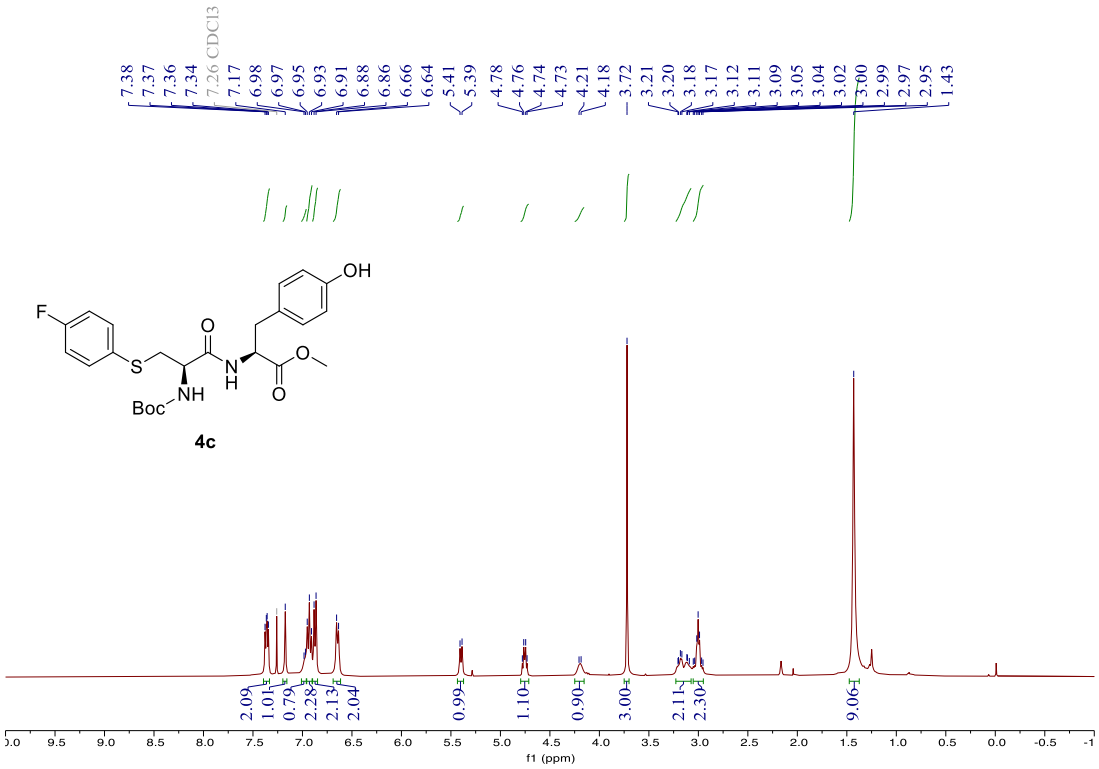



**Figure S69. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4c**

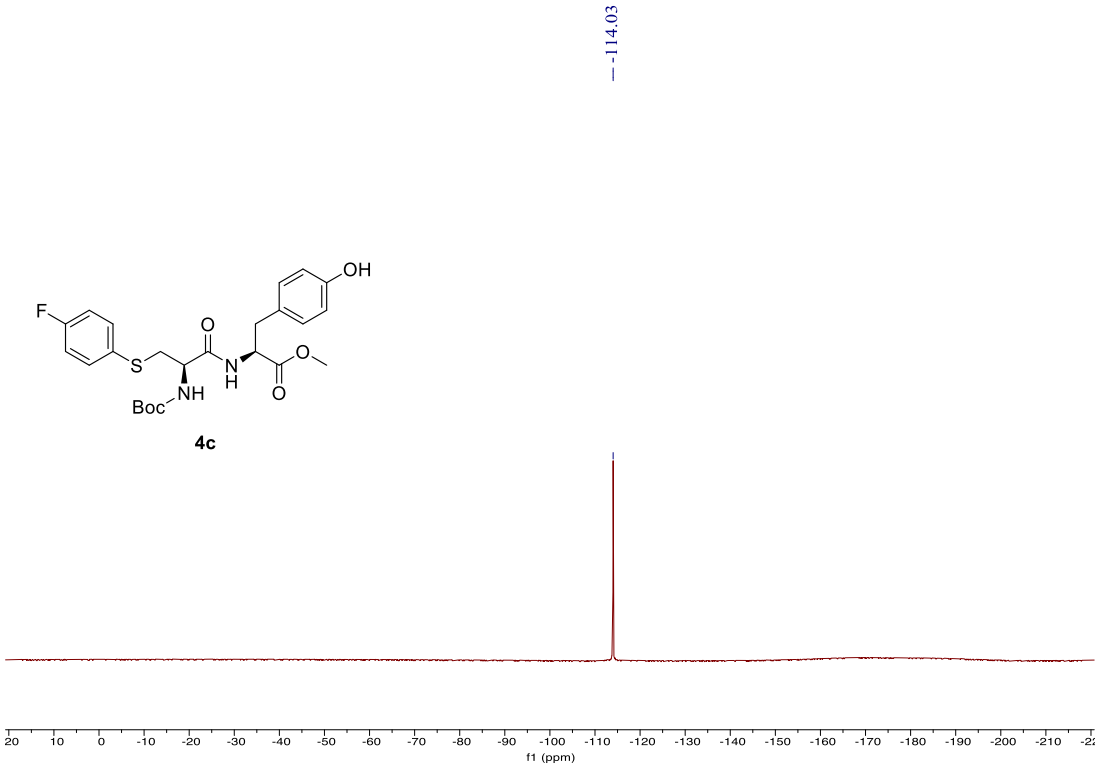



**Figure S70. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 4c**

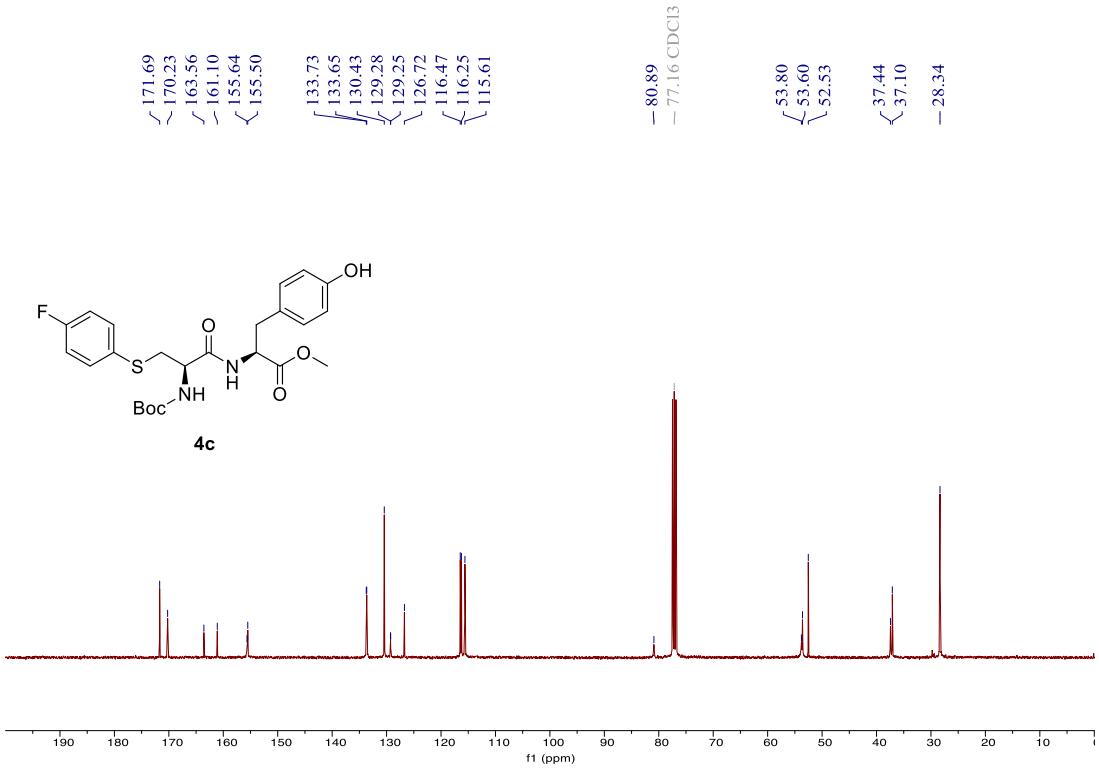



**Figure S71. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4c**

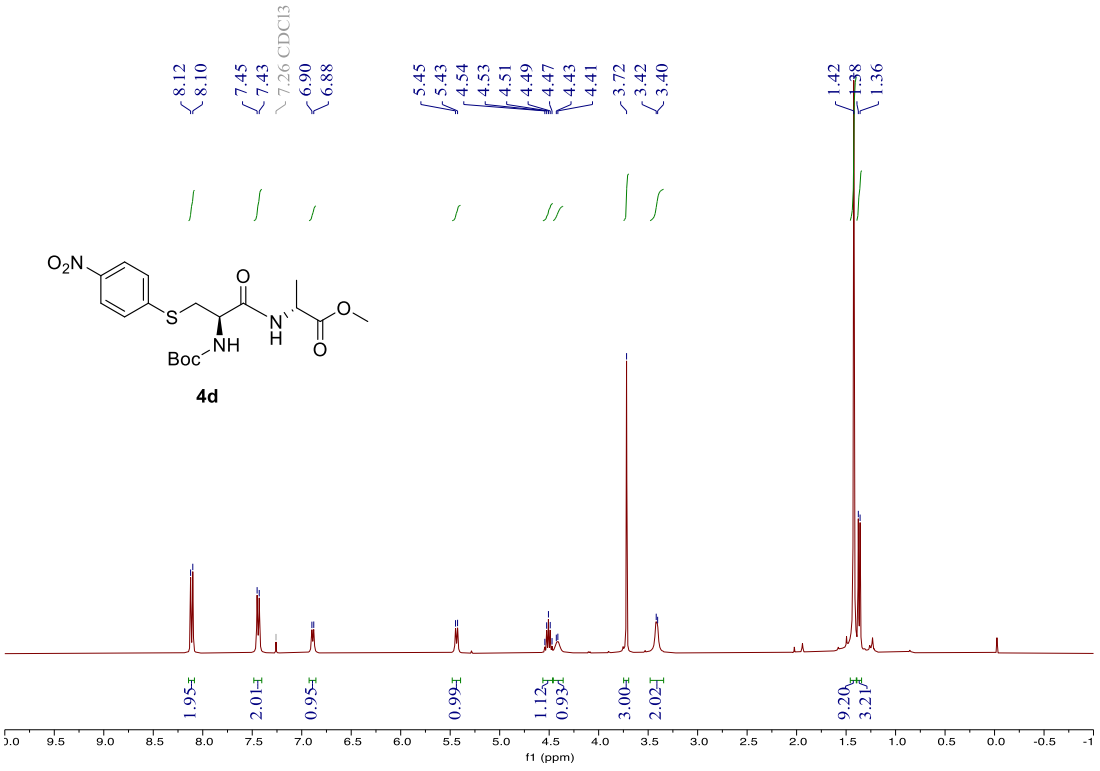



**Figure S72. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4d**

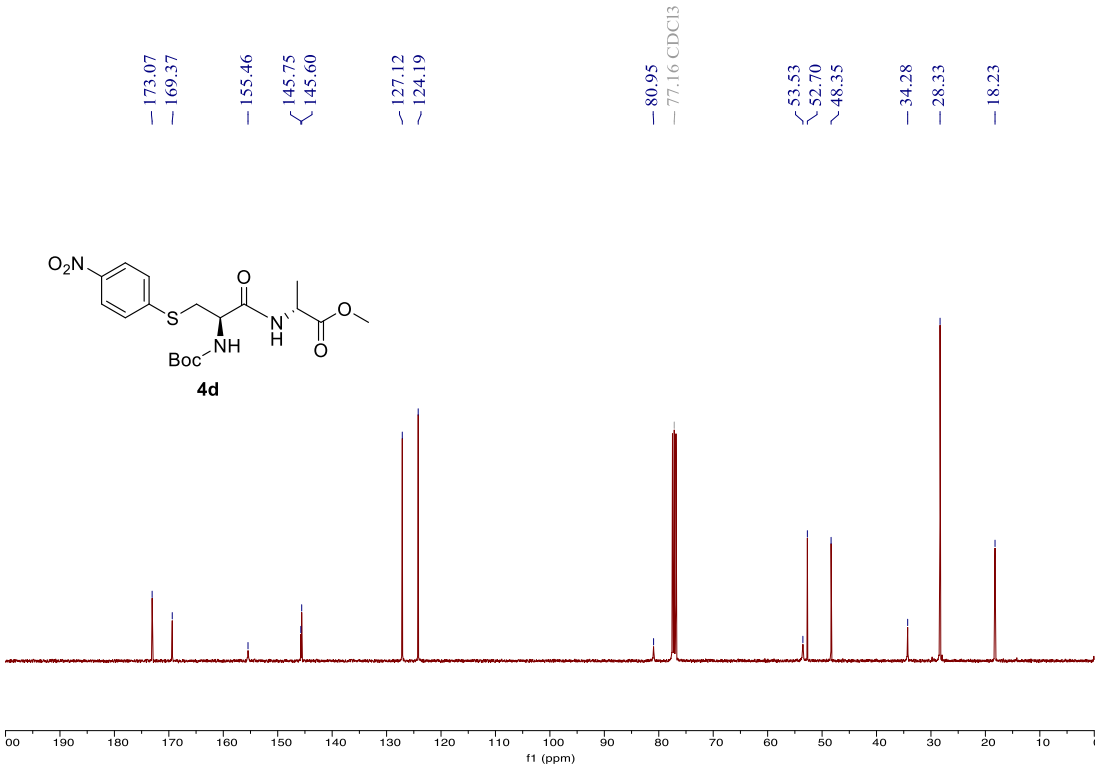



**Figure S73. $^{13}C$ NMR (101 MHz, $CDCl_3$) spectra for compound 4d**

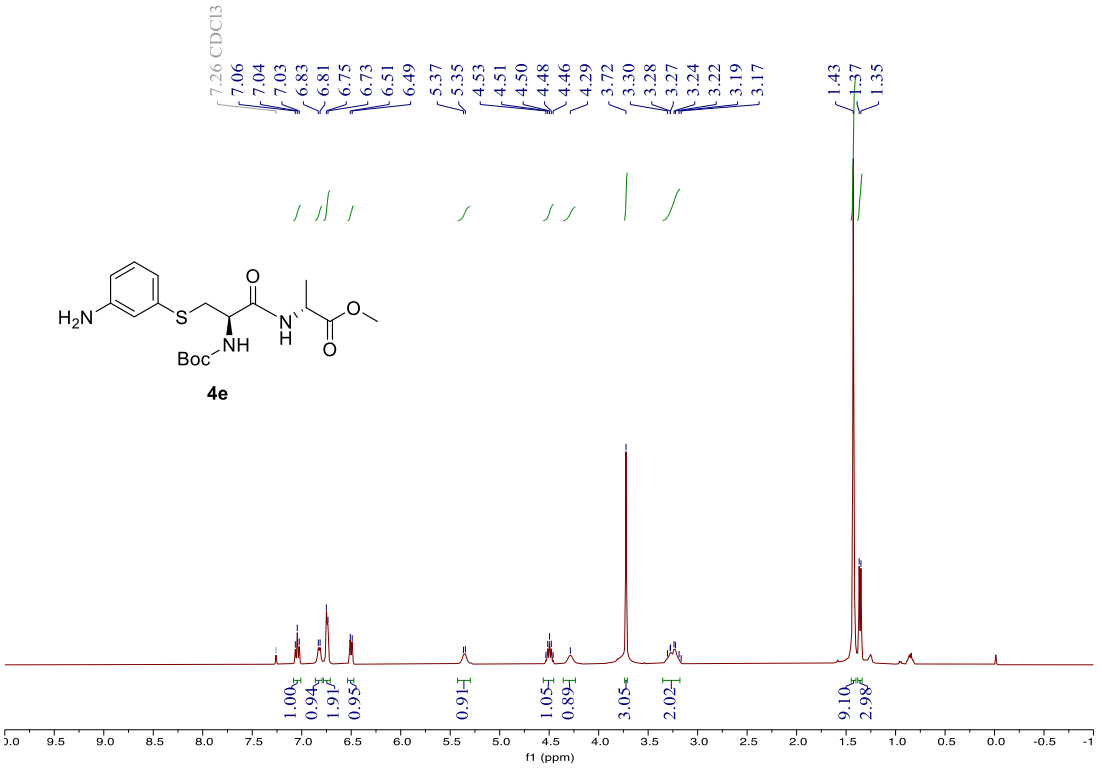



**Figure S74. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectra for compound 4e**

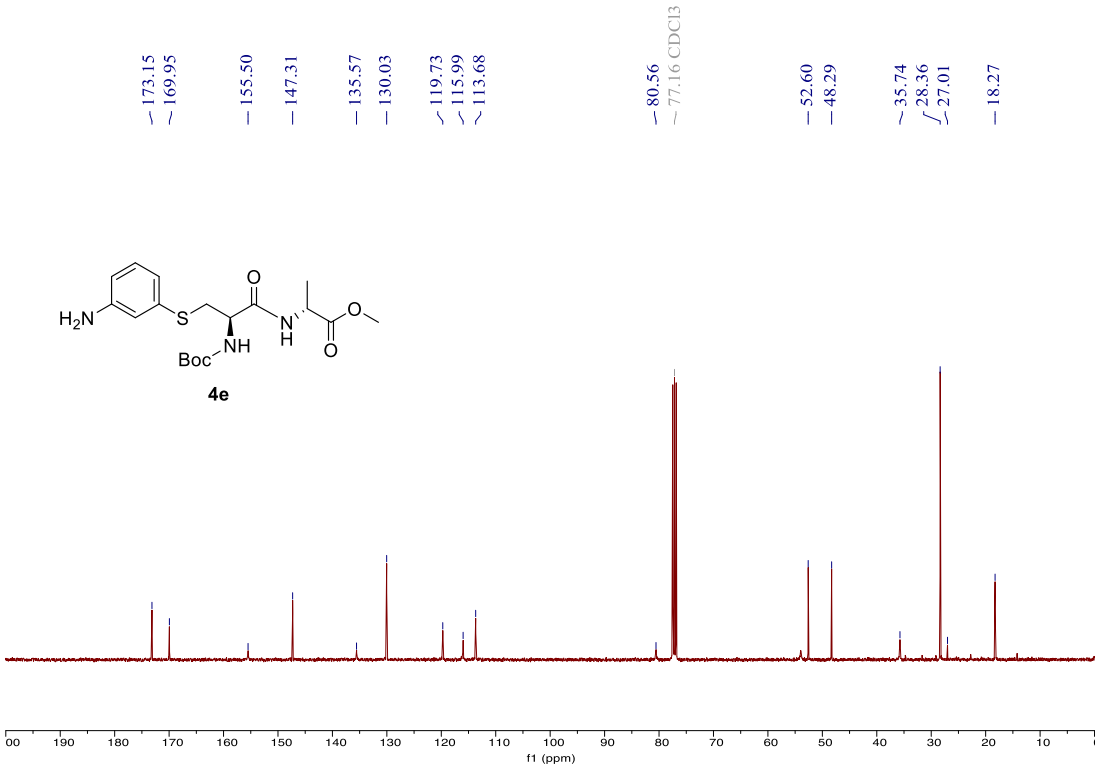



**Figure S75. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4e**

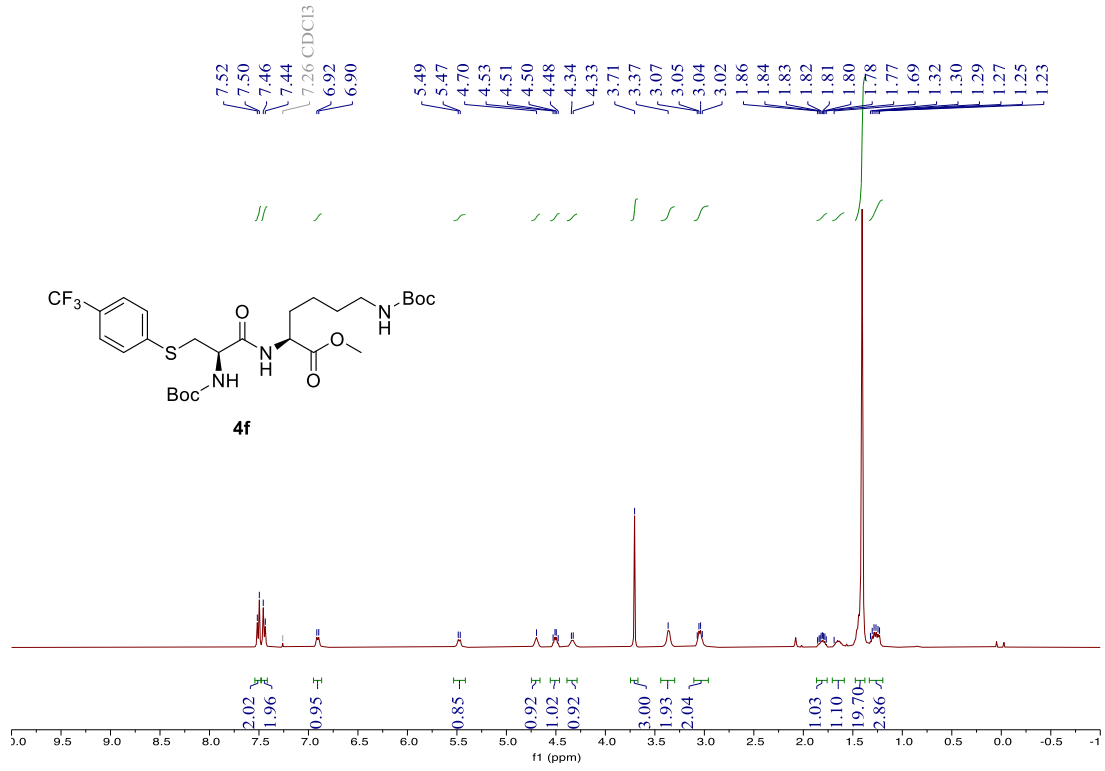



**Figure S76. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4f**

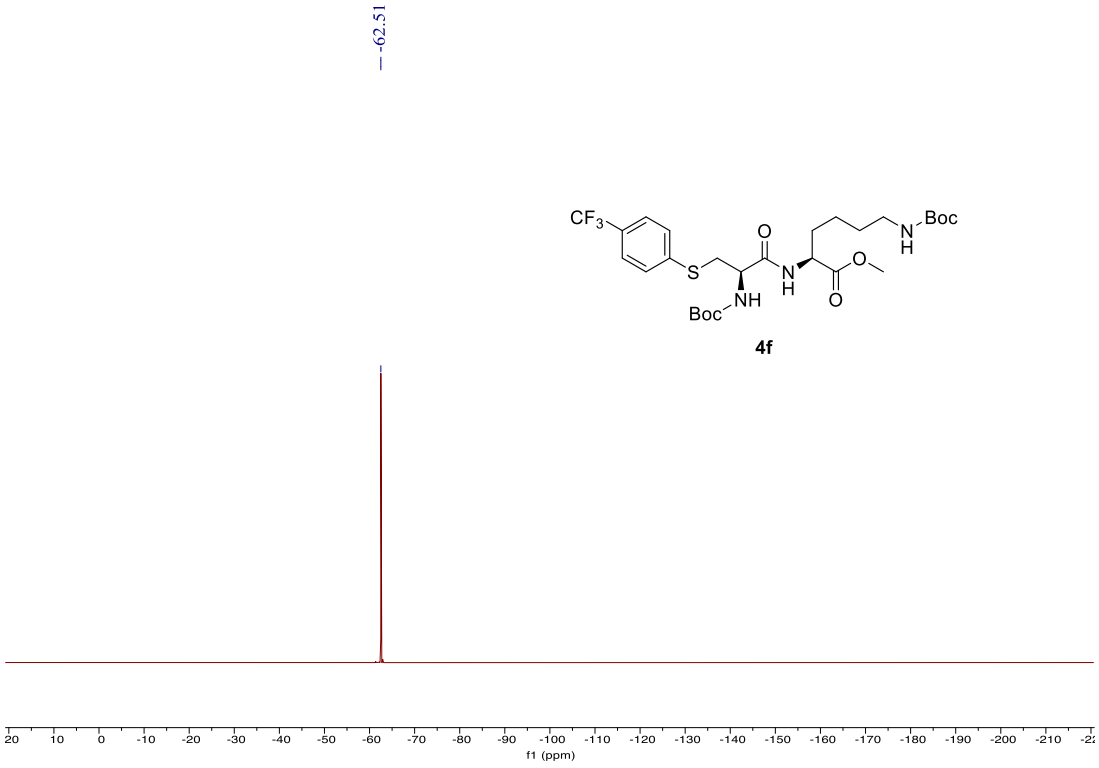



**Figure S77. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 4f**

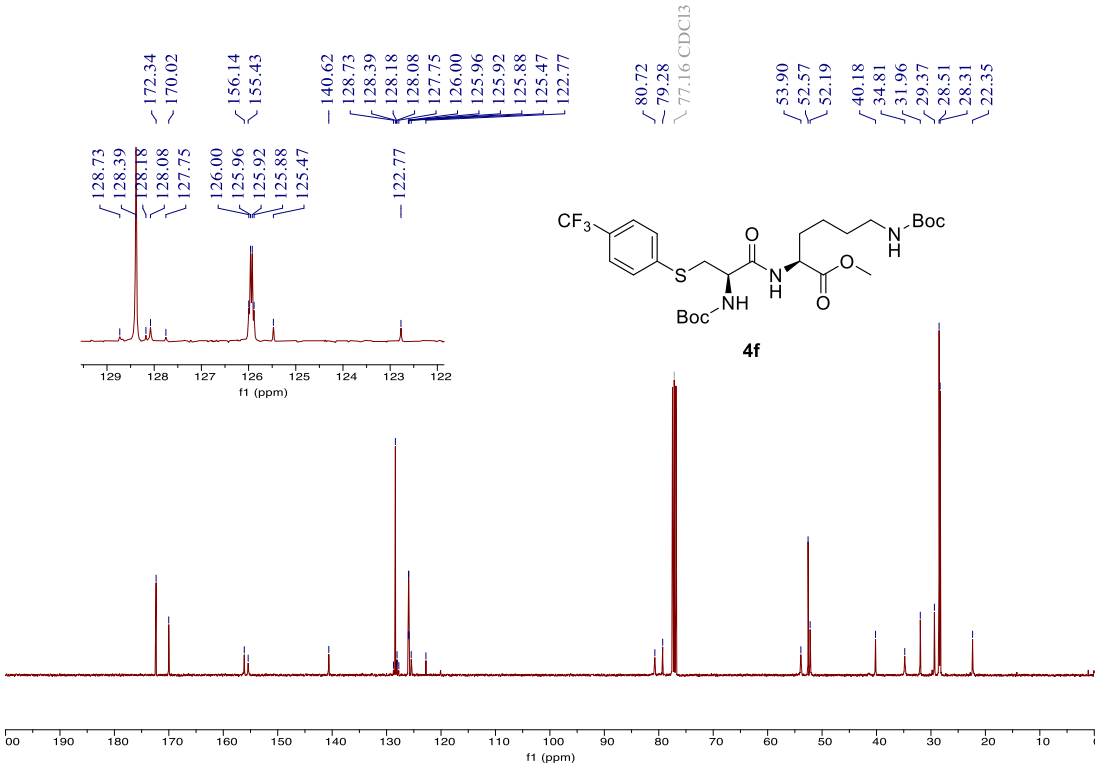



**Figure S78. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4f**

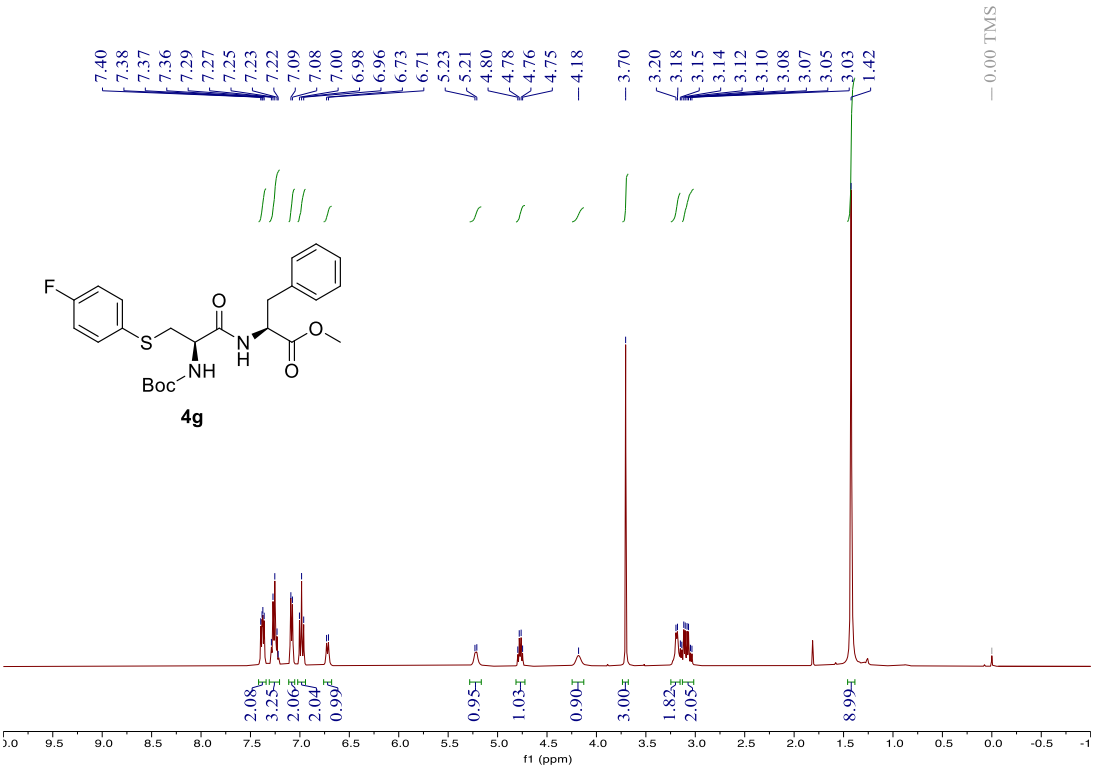



**Figure S79. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4g**

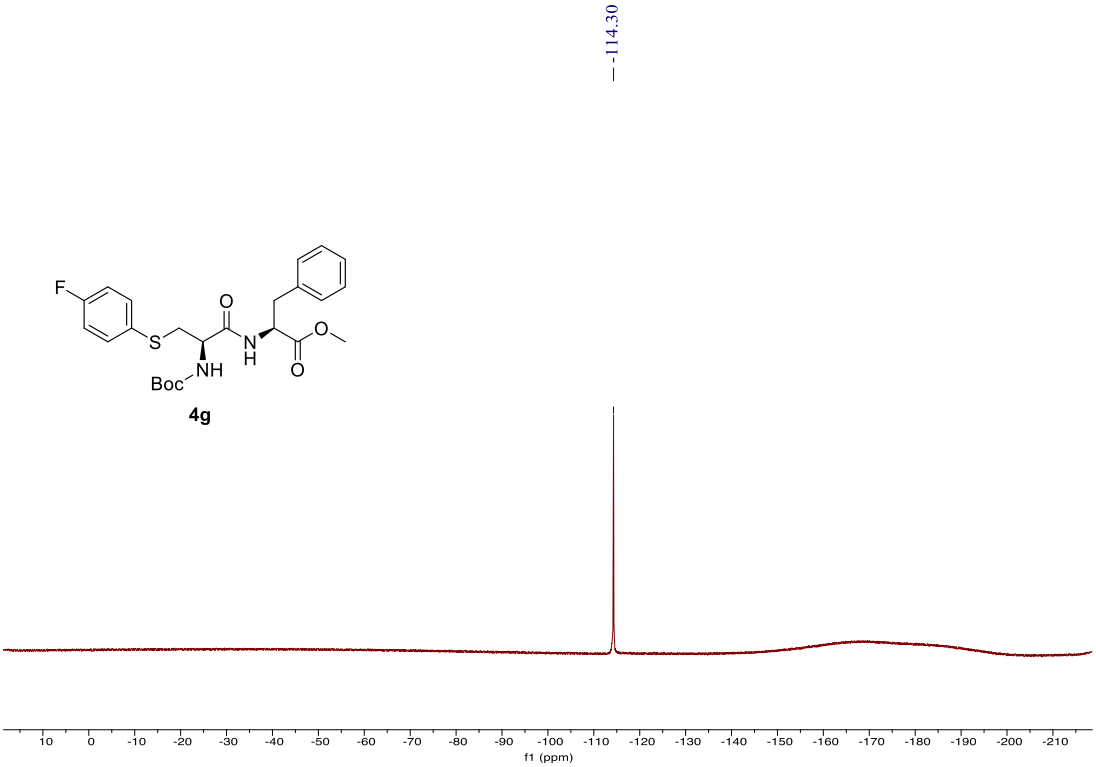



**Figure S80. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 4g**

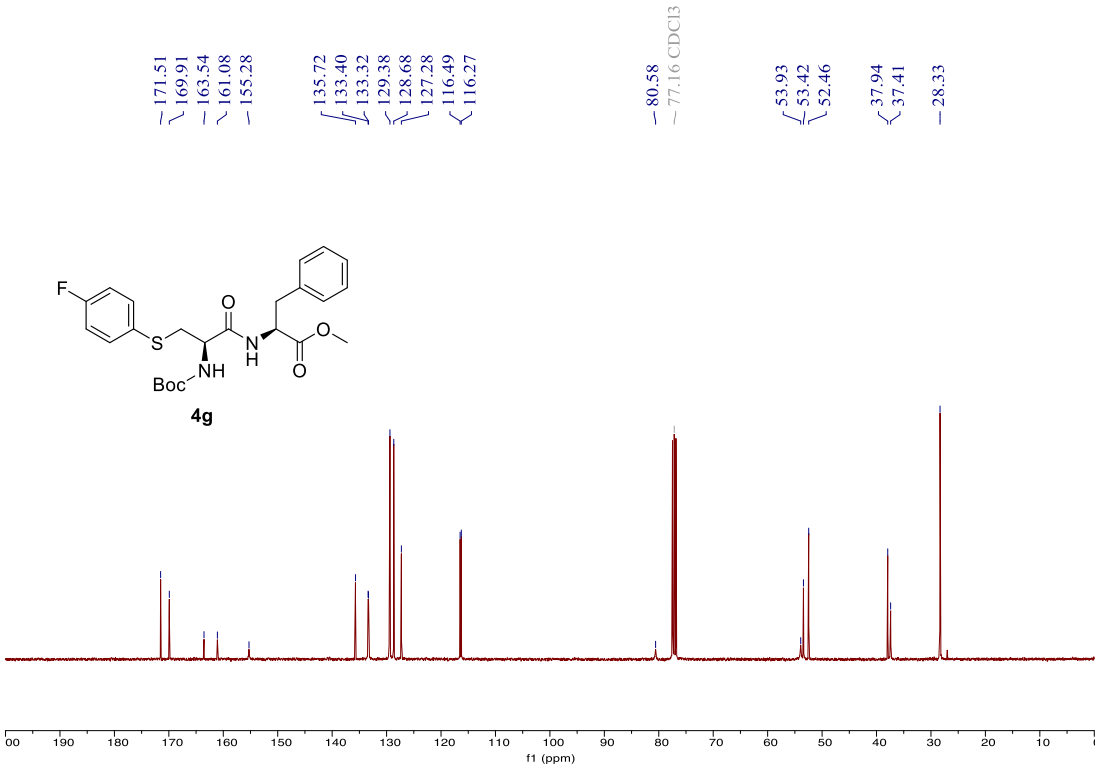



**Figure S81. $^{13}C$ NMR (101 MHz, $CDCl_3$) spectra for compound 4g**

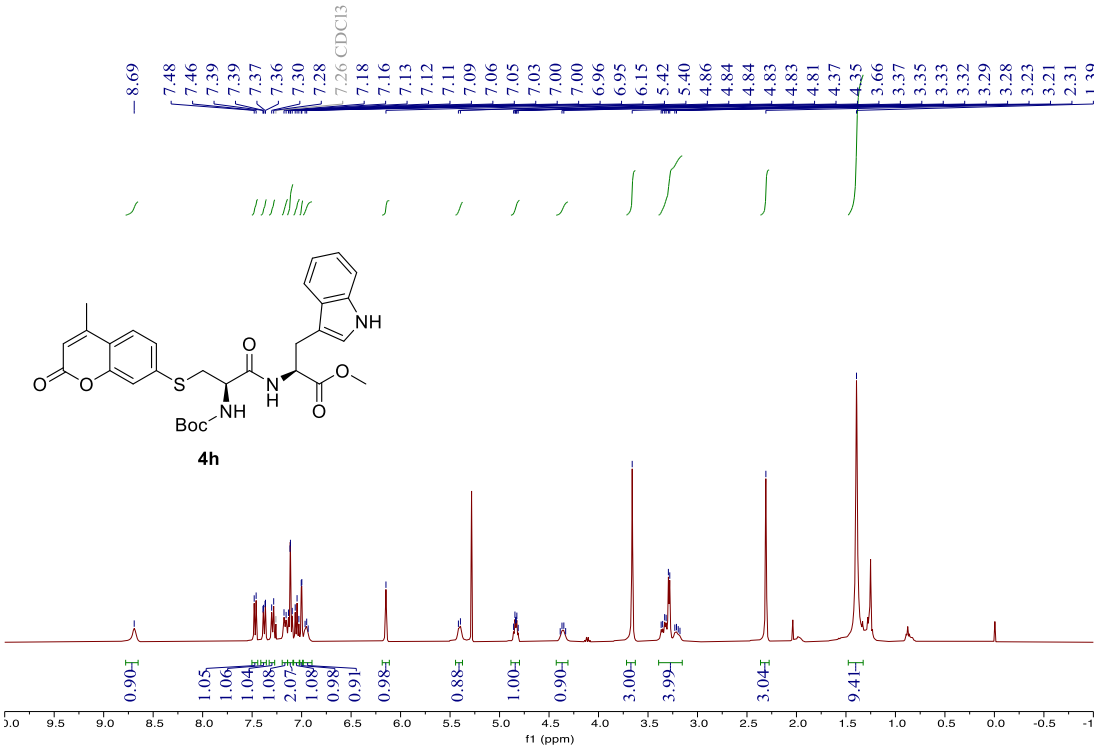



**Figure S82. $^{1}H$ NMR (400 MHz, $CDCl_3$) spectra for compound 4h**

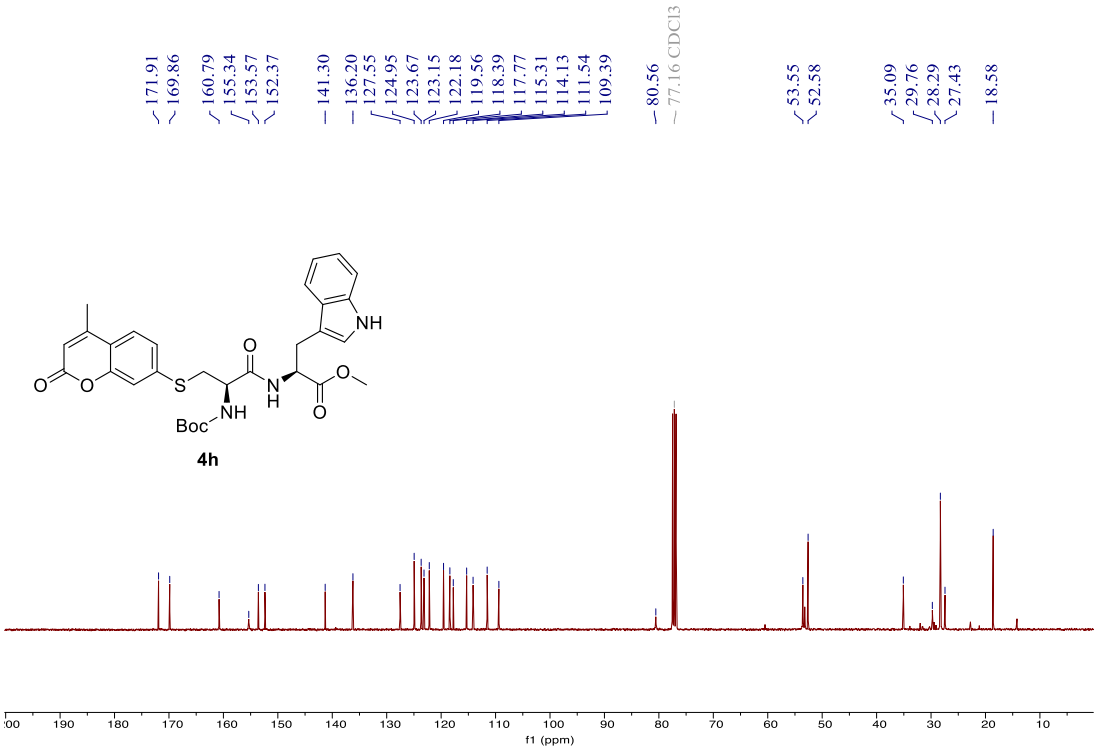



**Figure S83. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4h**

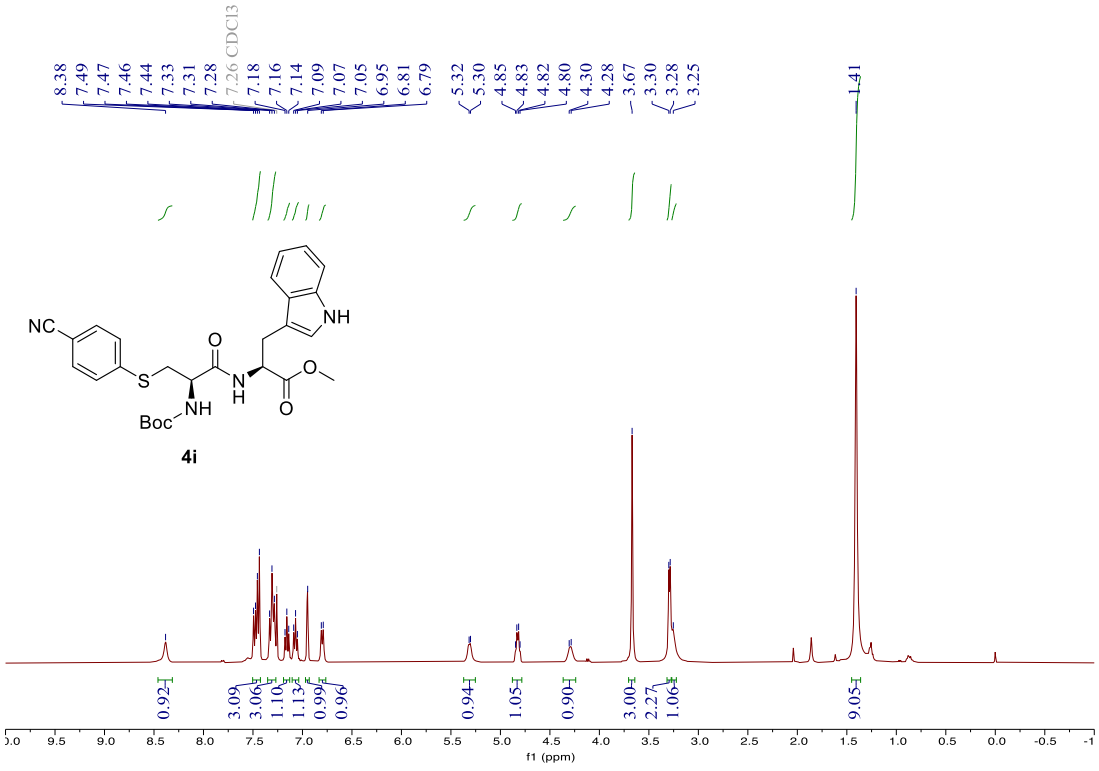



**Figure S84. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4i**

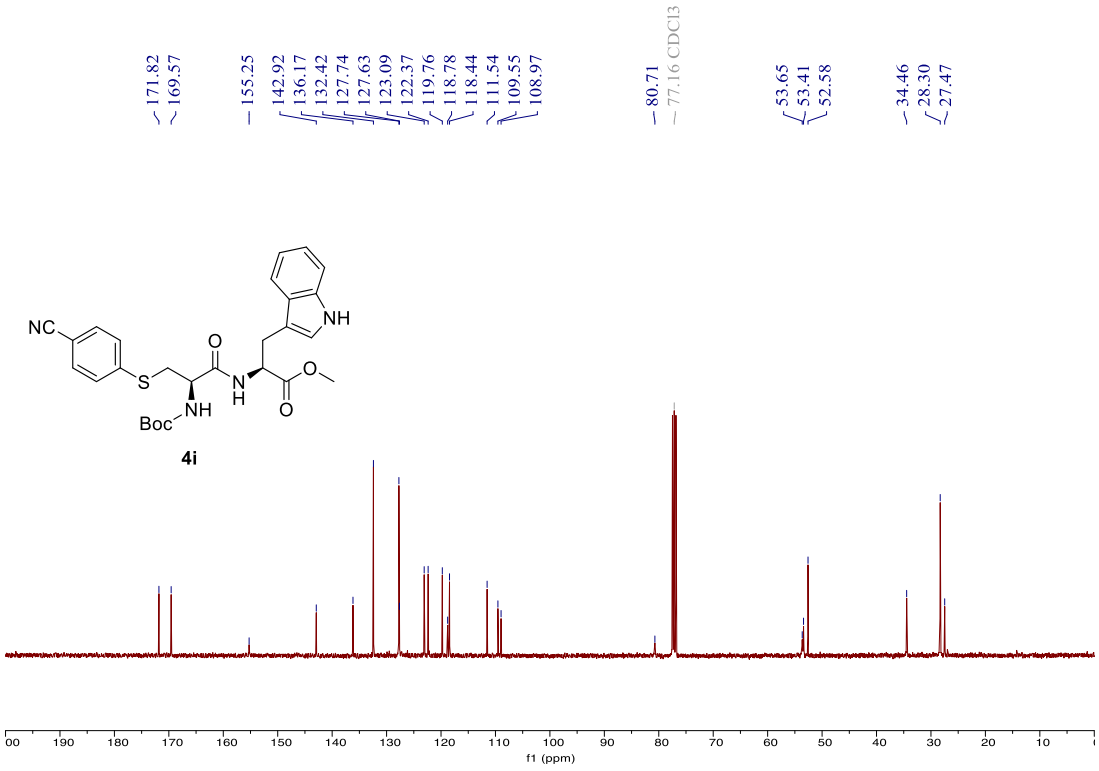



**Figure S85. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4i**

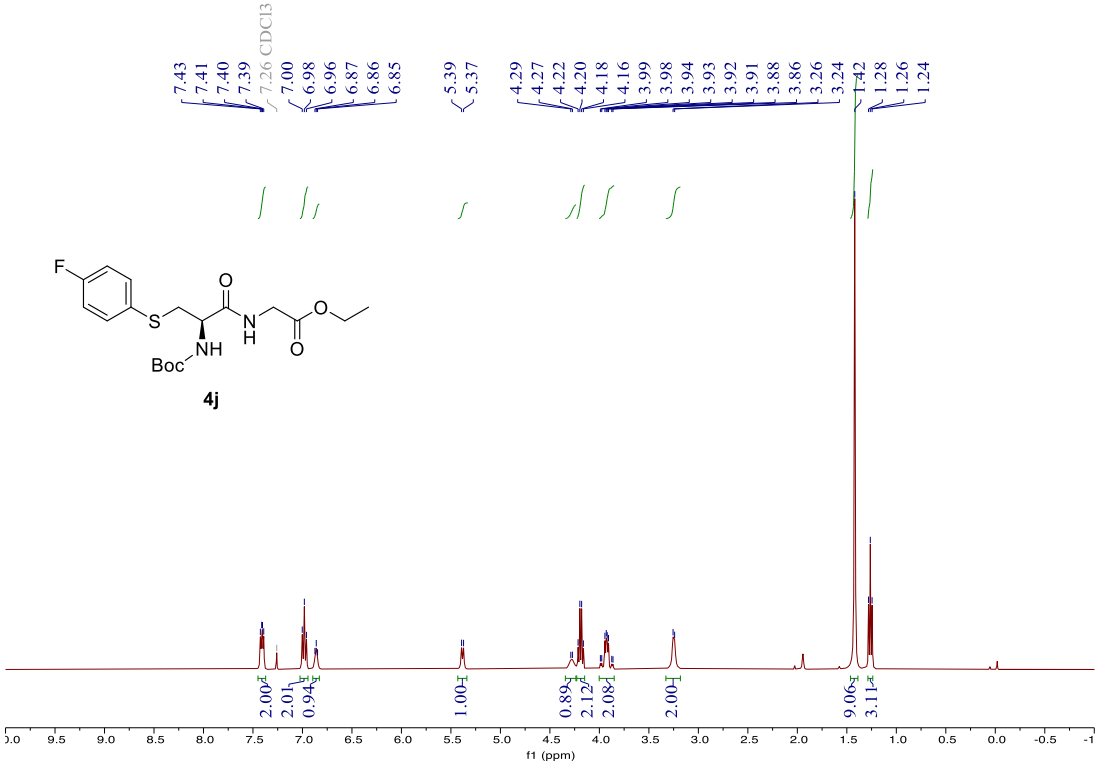



**Figure S86. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 4j**

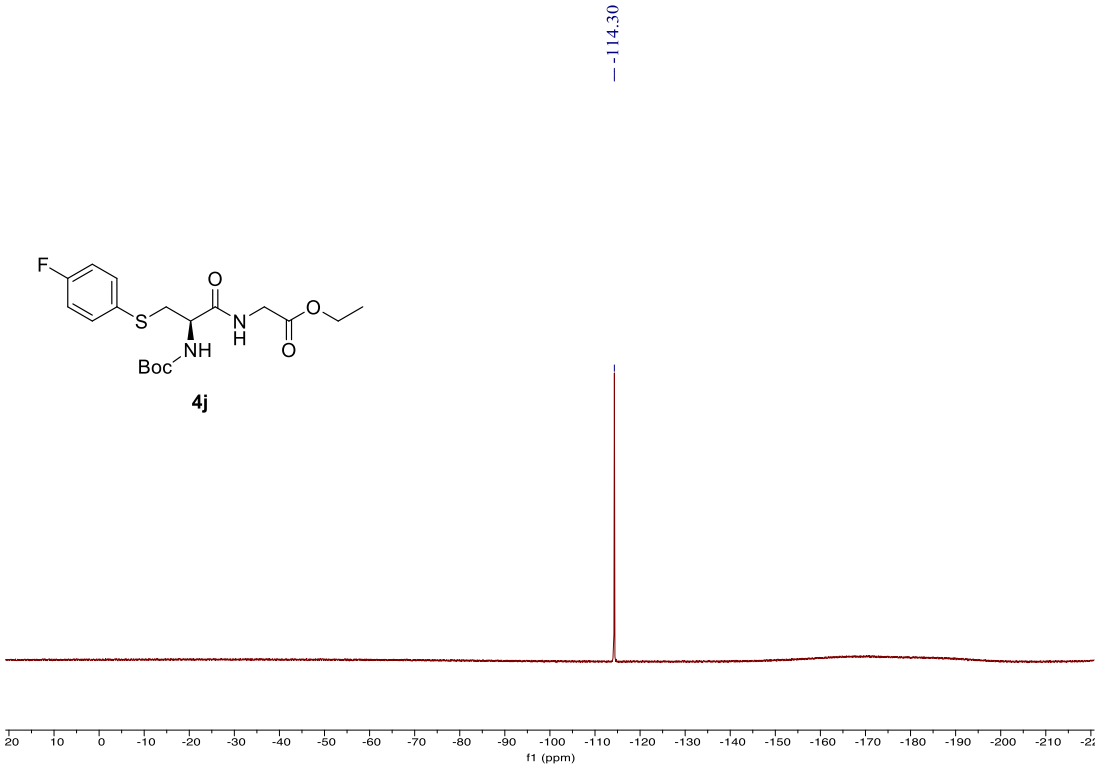



**Figure S87. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 4j**

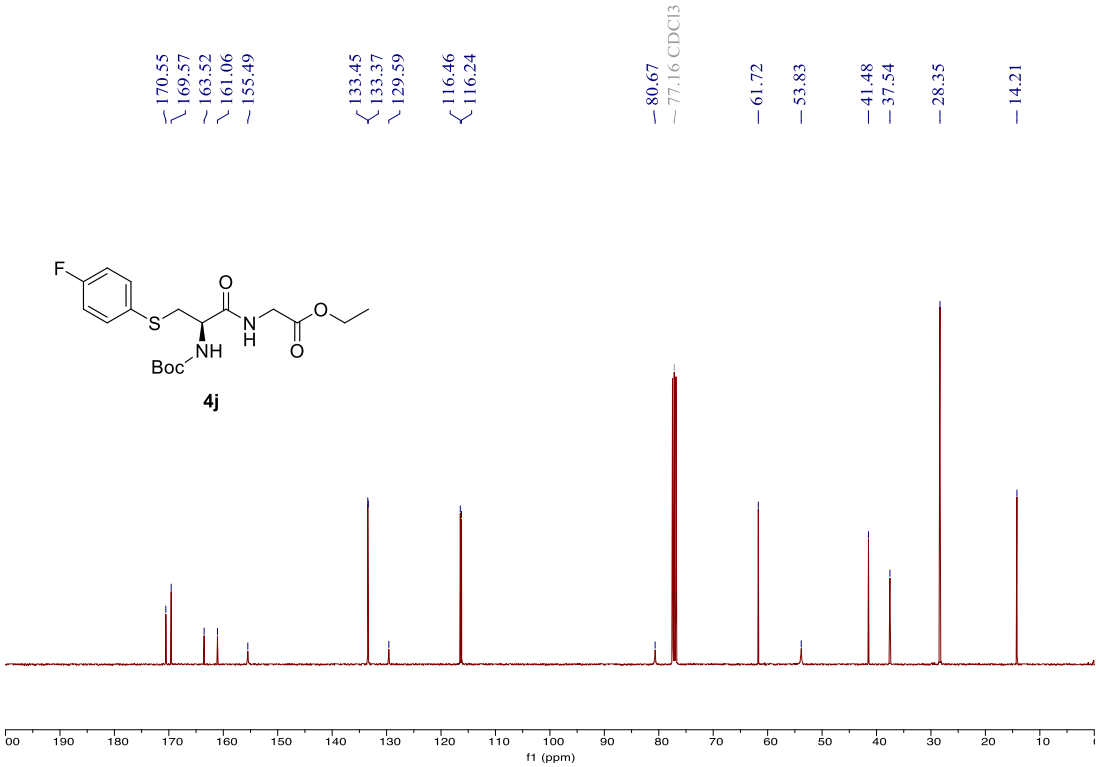



**Figure S88. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 4j**

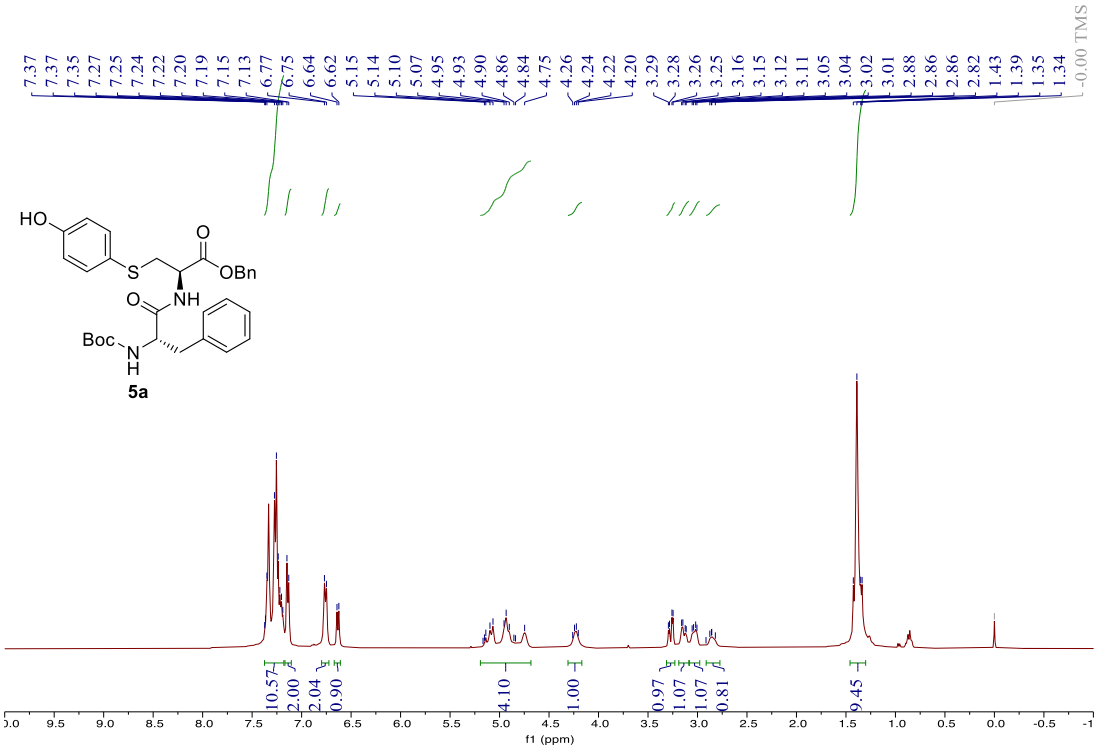



**Figure S89. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5a**

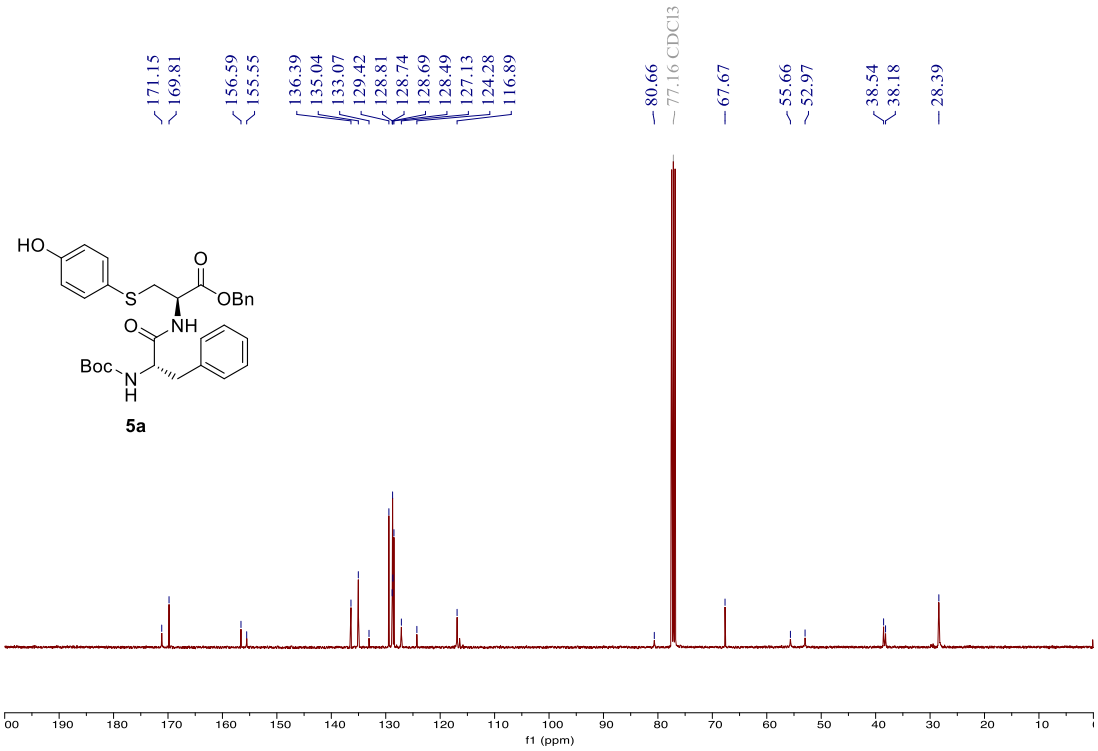



**Figure S90. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5a**

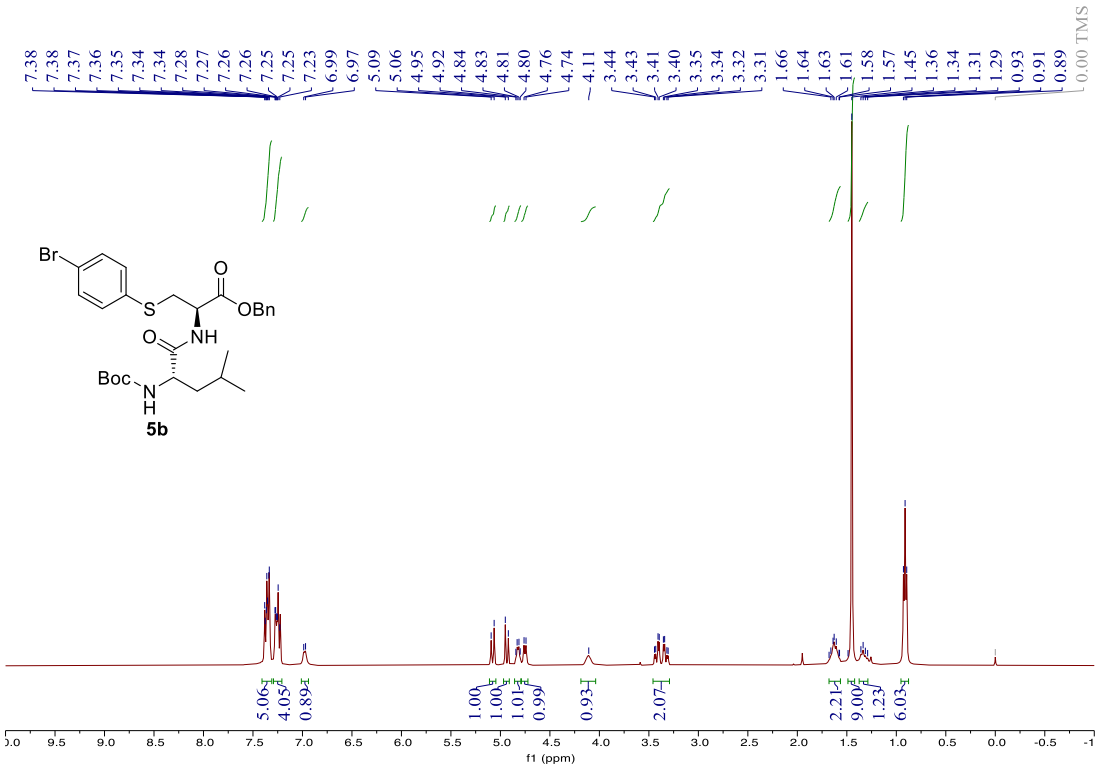



**Figure S91. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5b**

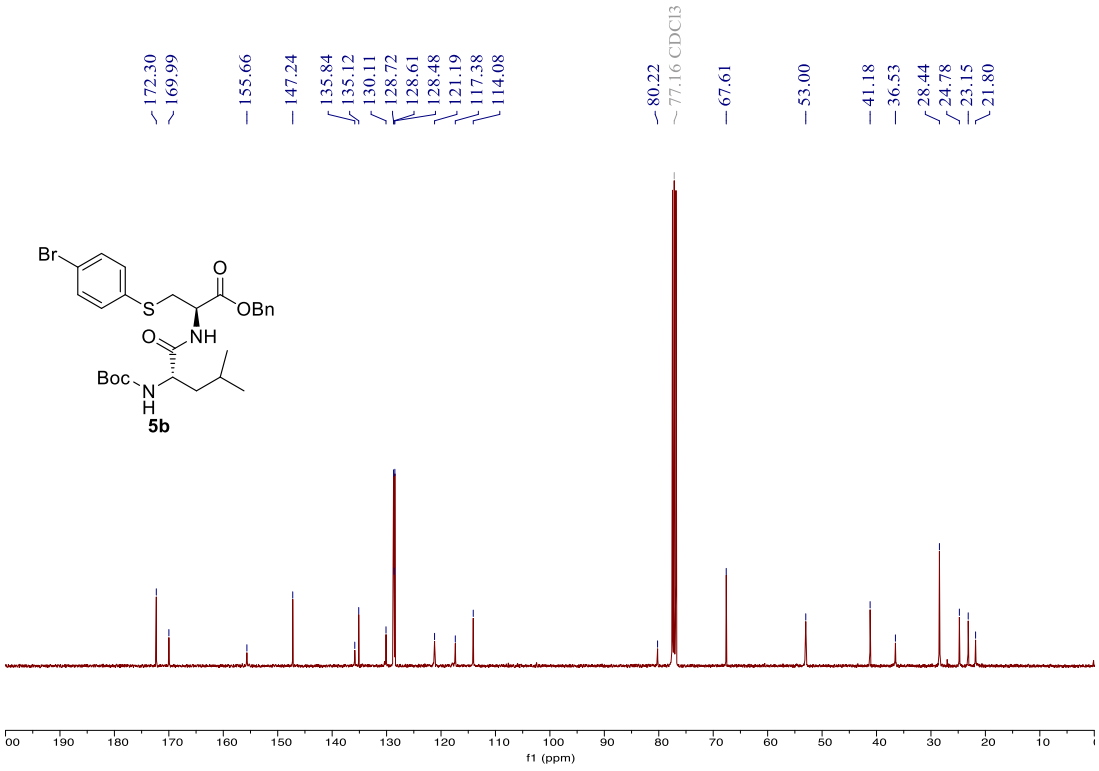



**Figure S92. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5b**

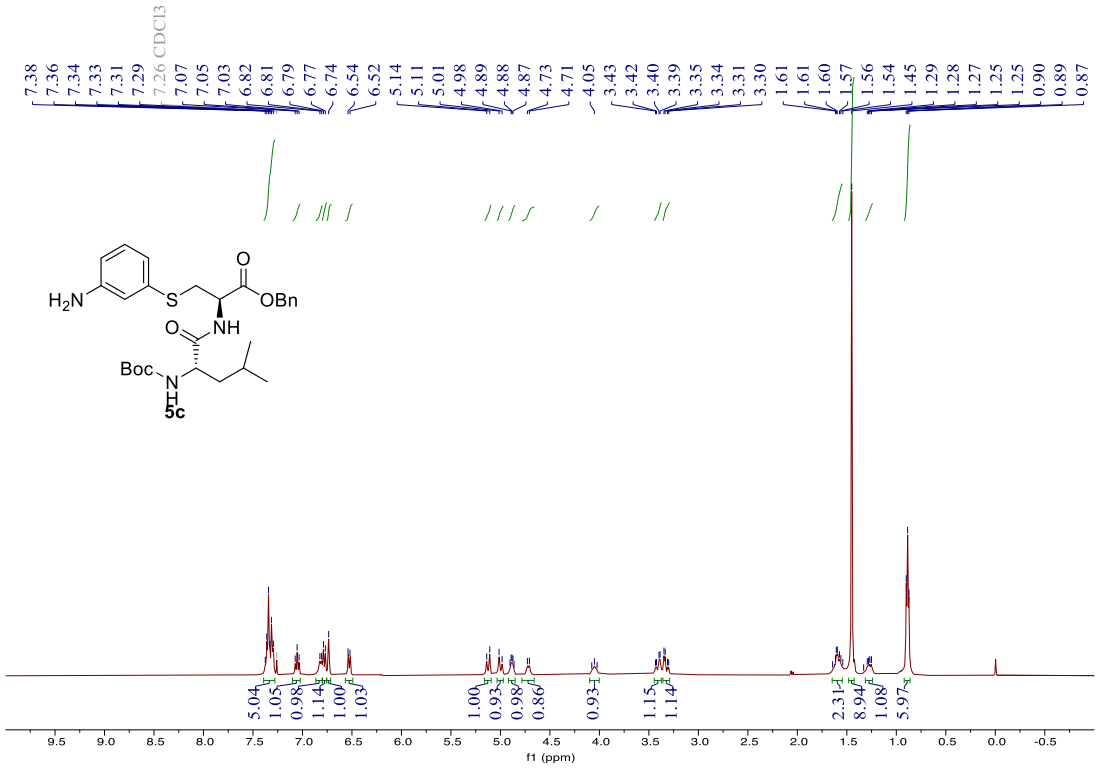



**Figure S93. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5c**

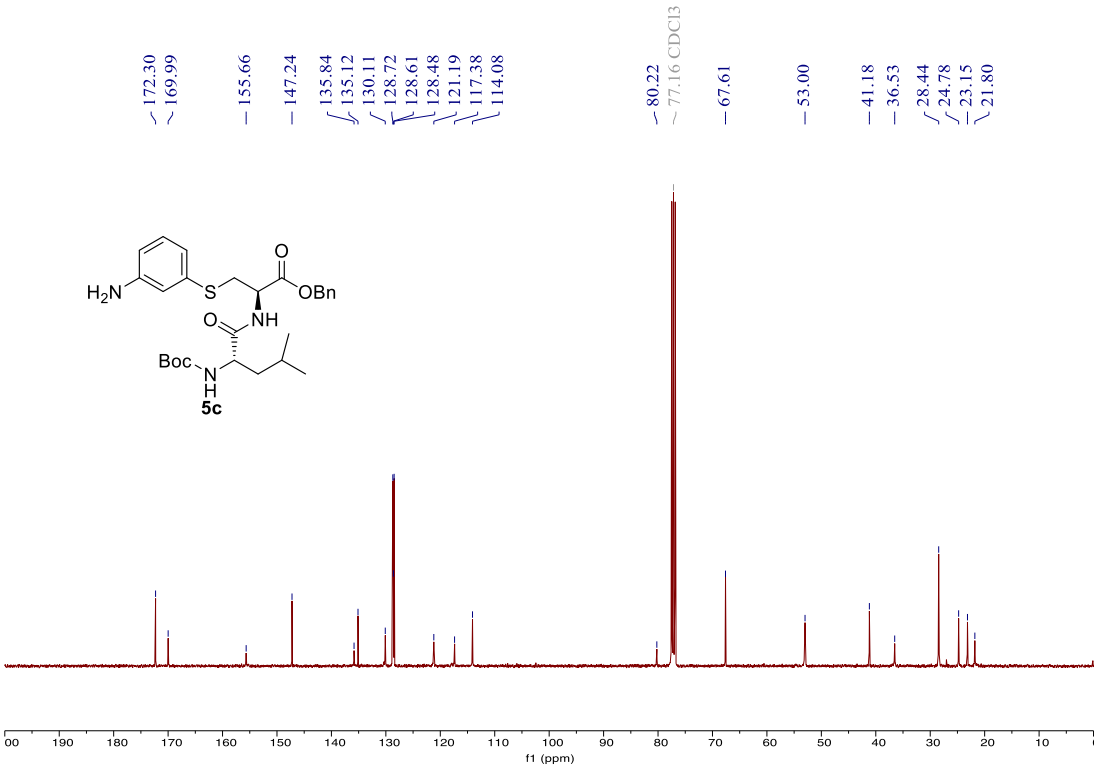



**Figure S94. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5c**

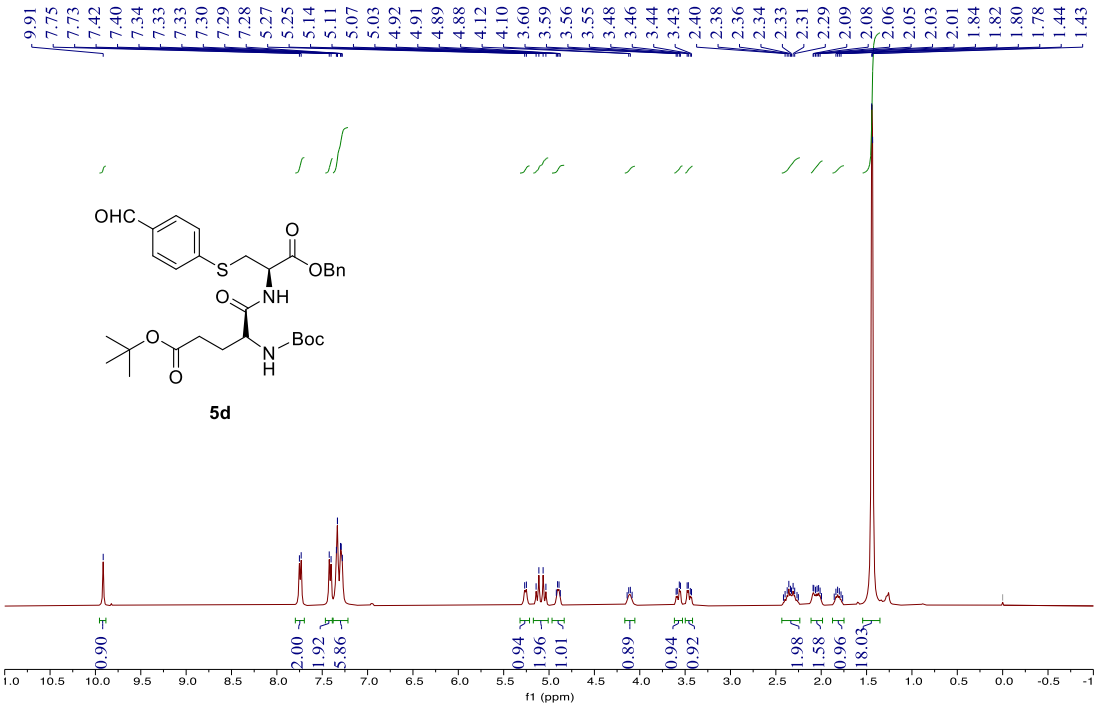



**Figure S95. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5d**

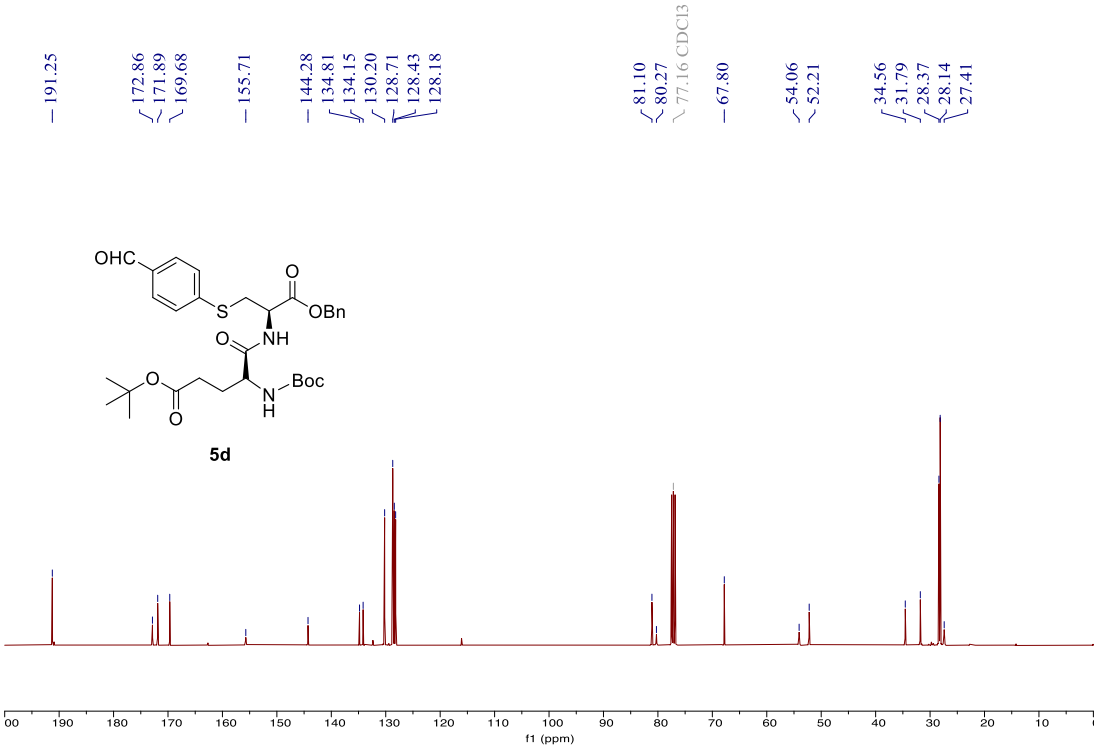



**Figure S96. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5d**

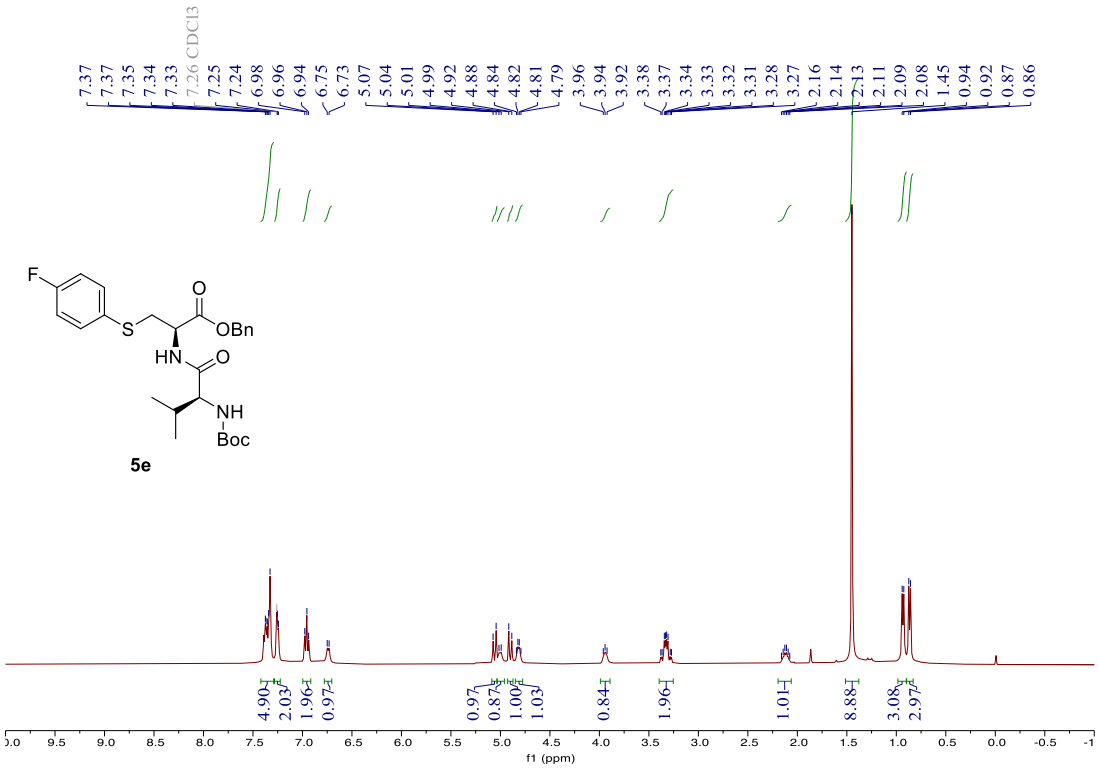



**Figure S97. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5e**

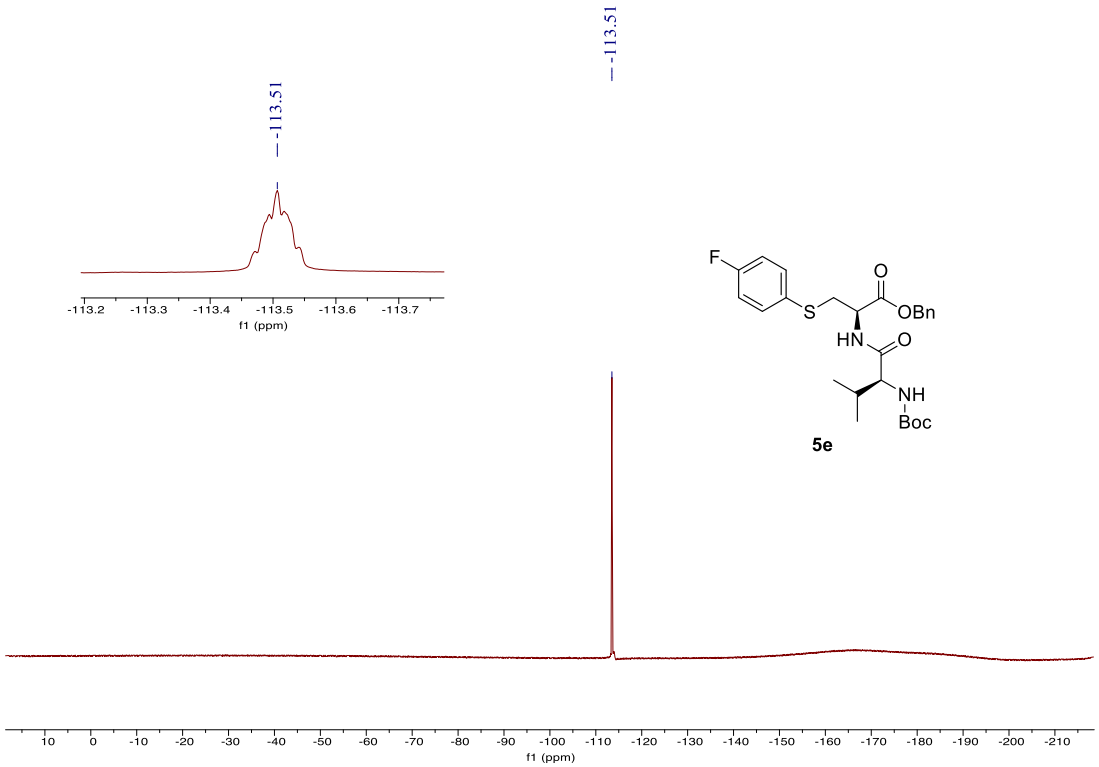



**Figure S98. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 5e**

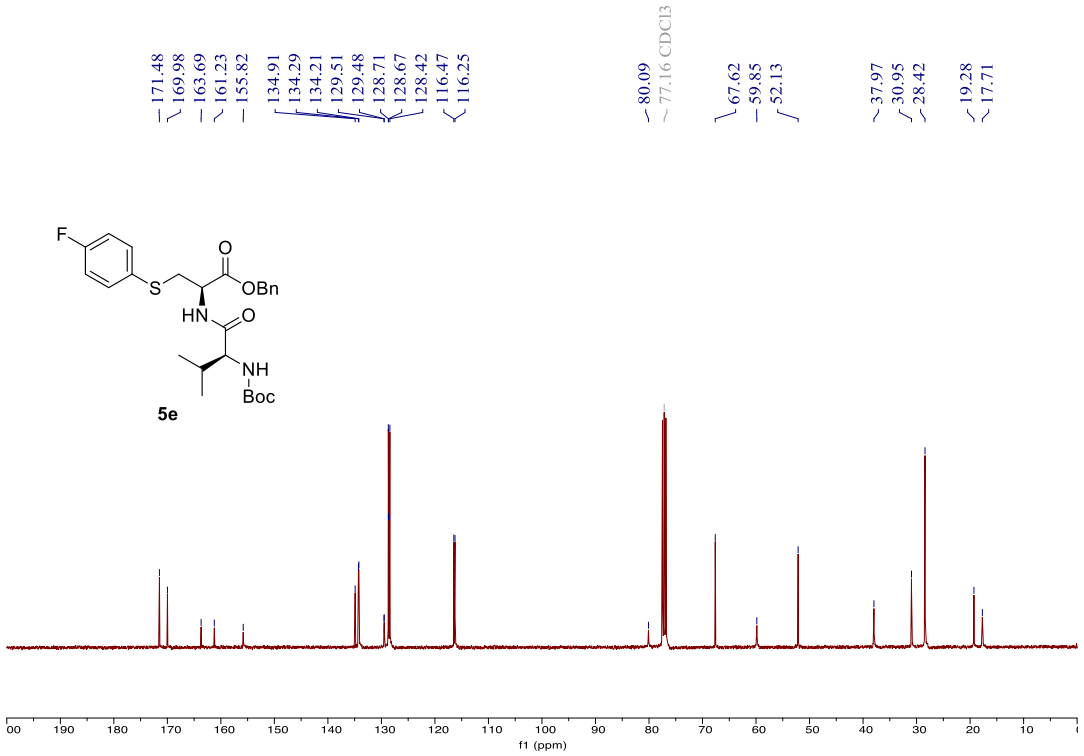



**Figure S99. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5e**

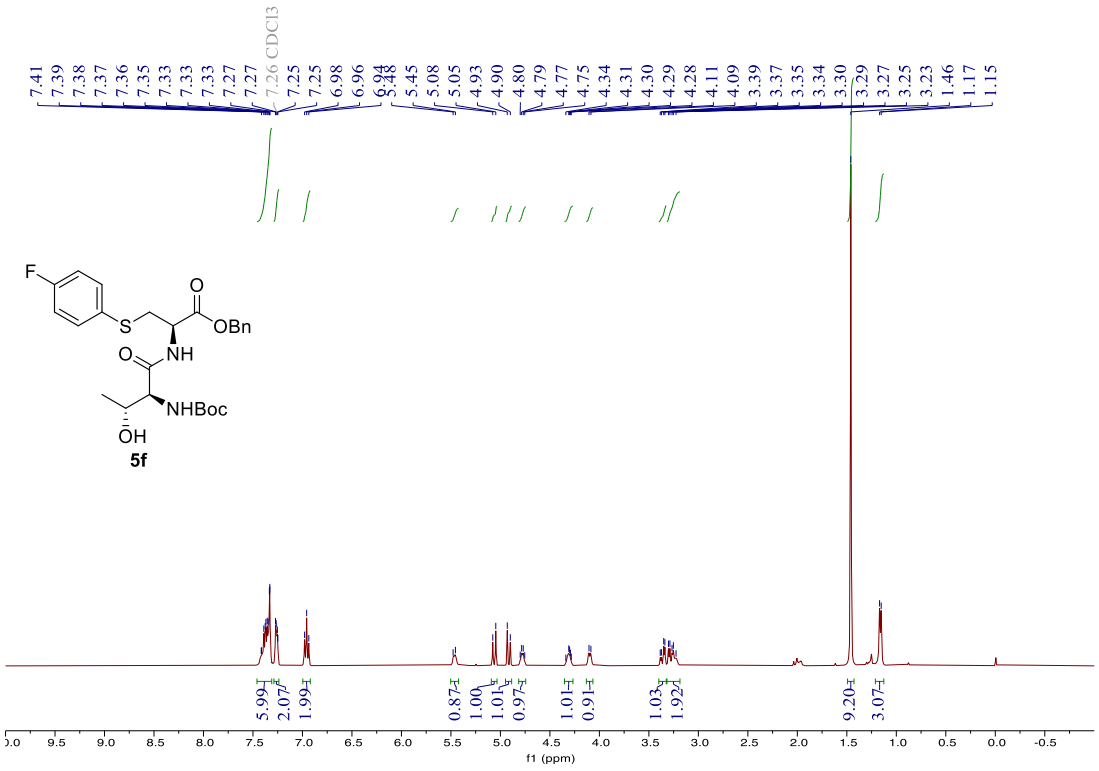



**Figure S100. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5f**

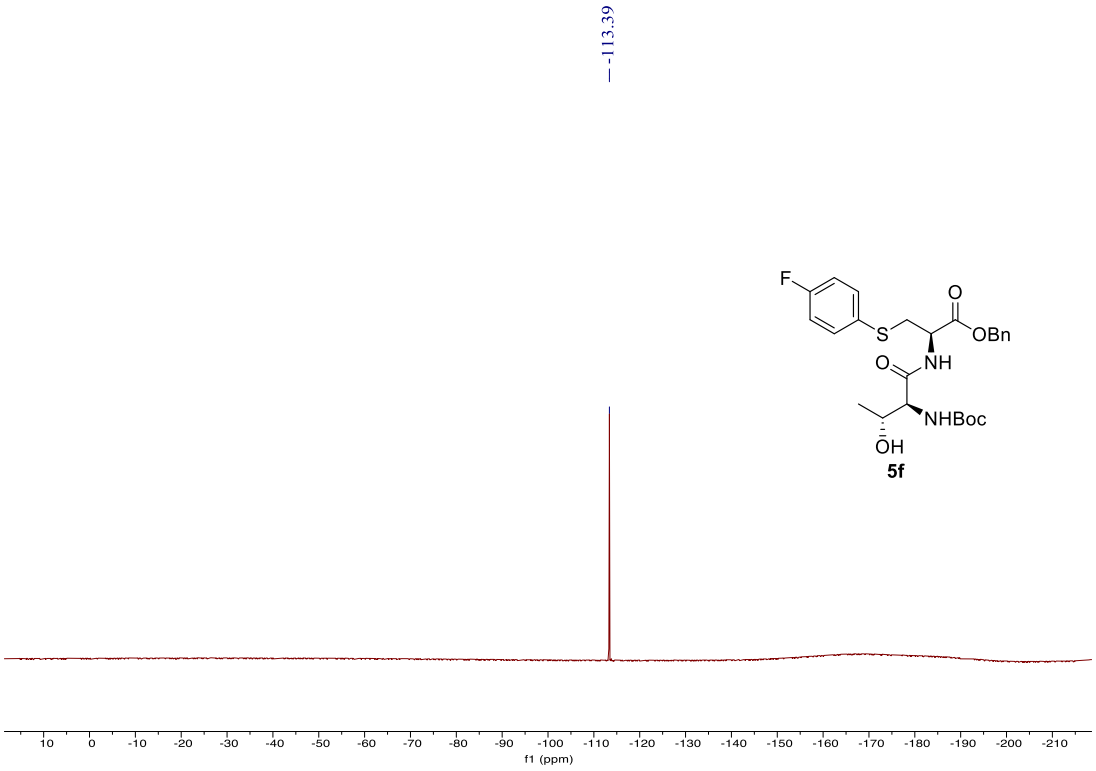



**Figure S101. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 5f**

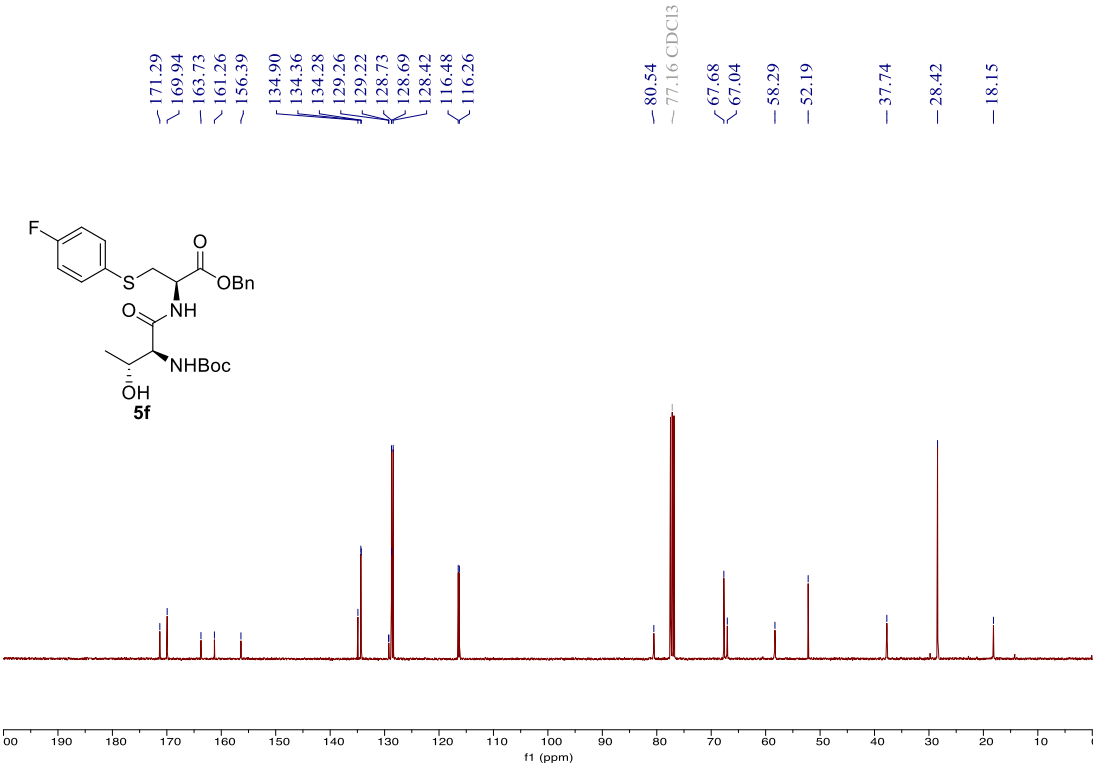



**Figure S102. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5f**

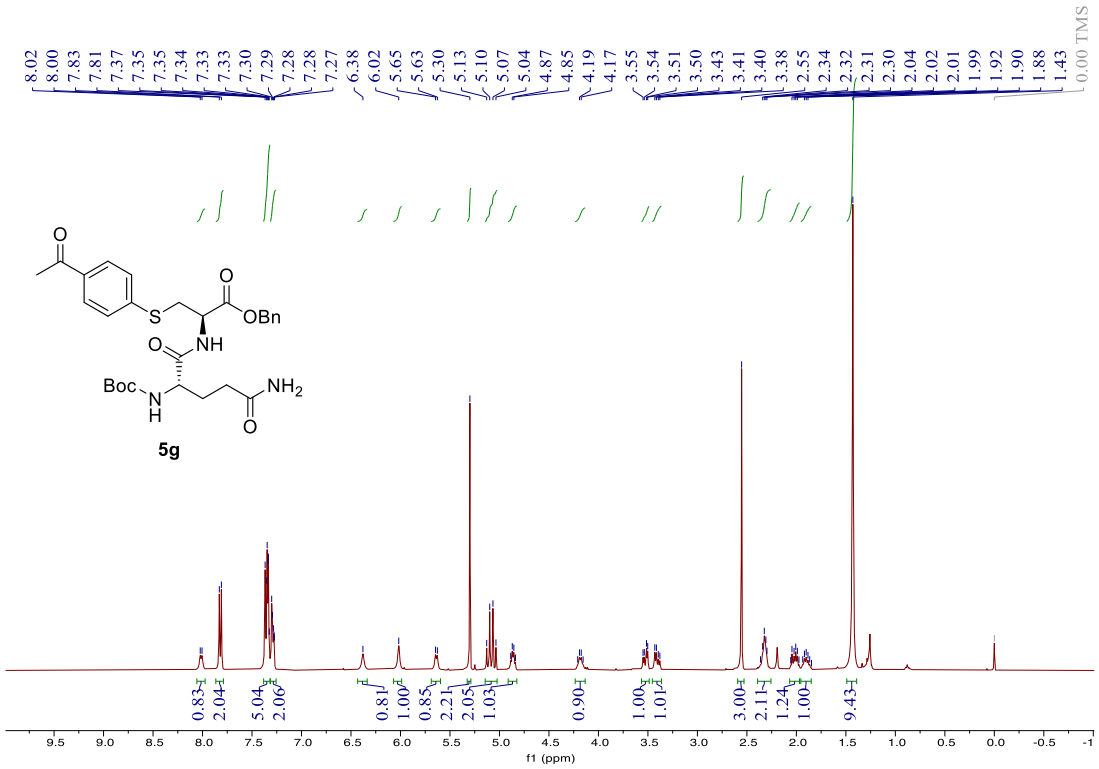



**Figure S103. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5g**

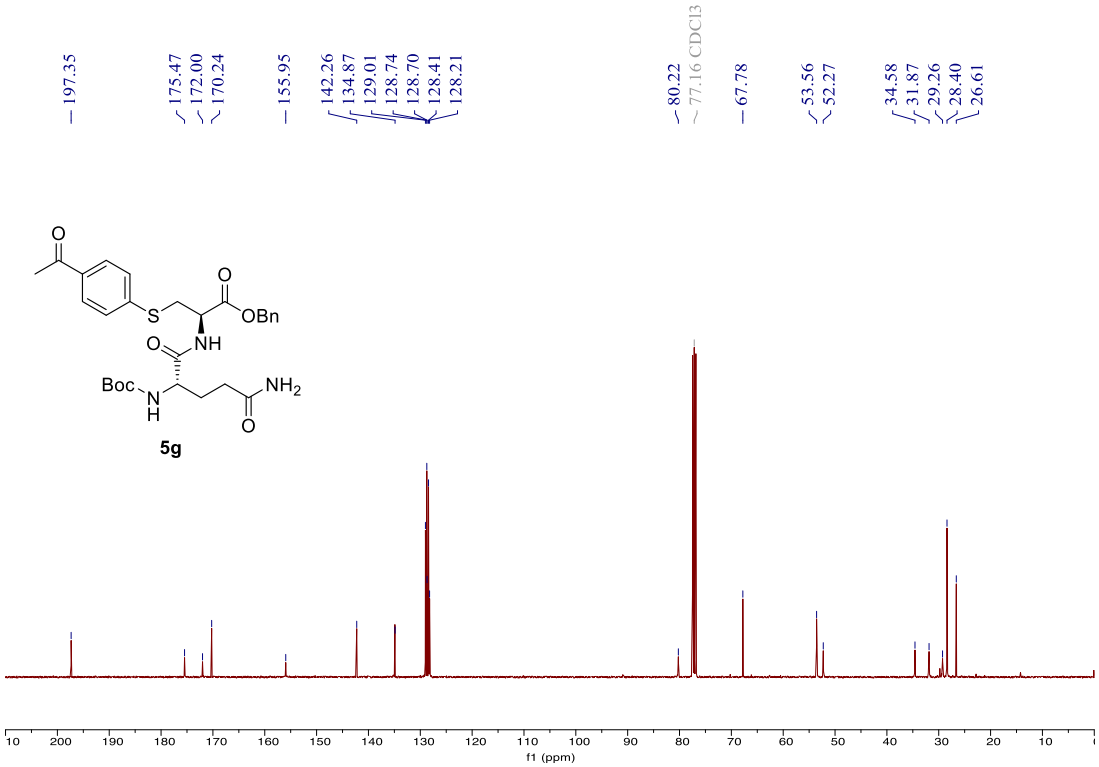



**Figure S104. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5g**

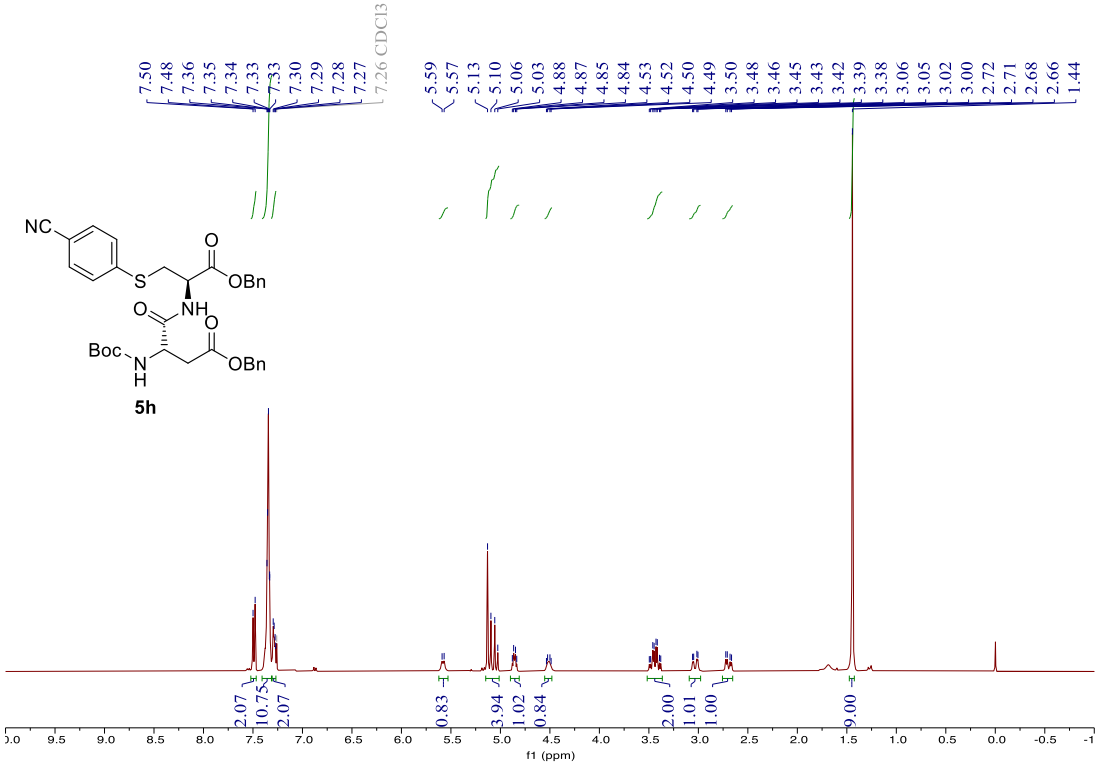



**Figure S105. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5h**

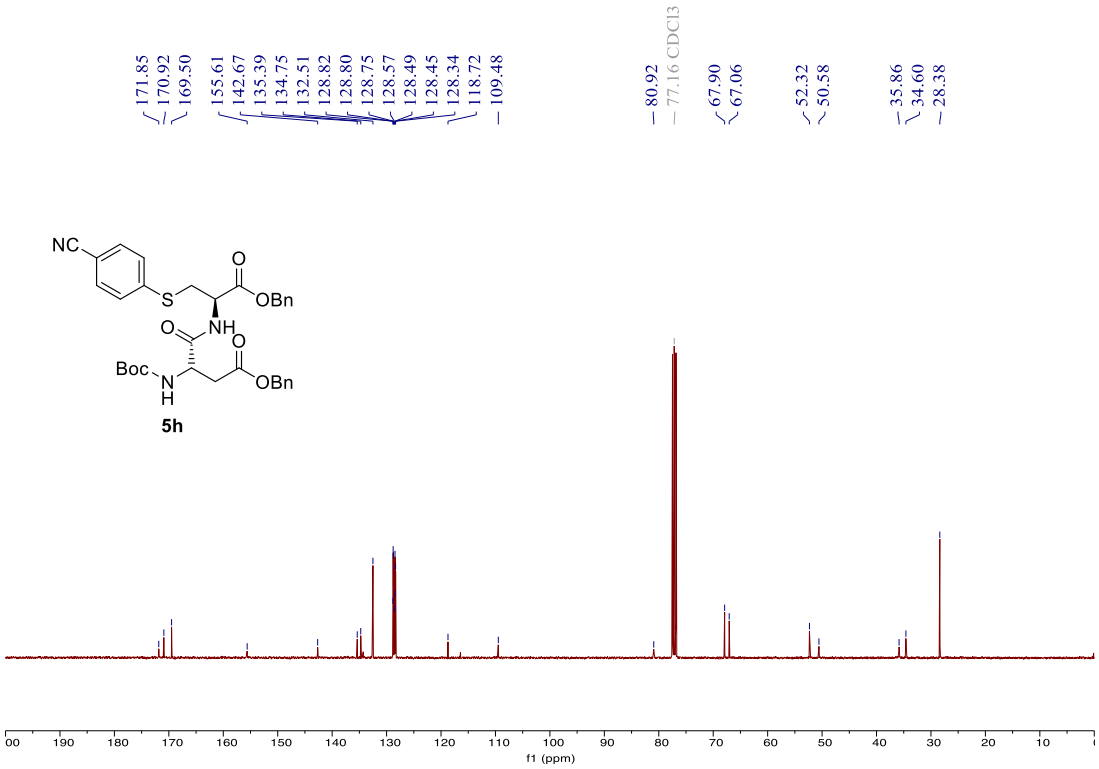



**Figure S106. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5h**

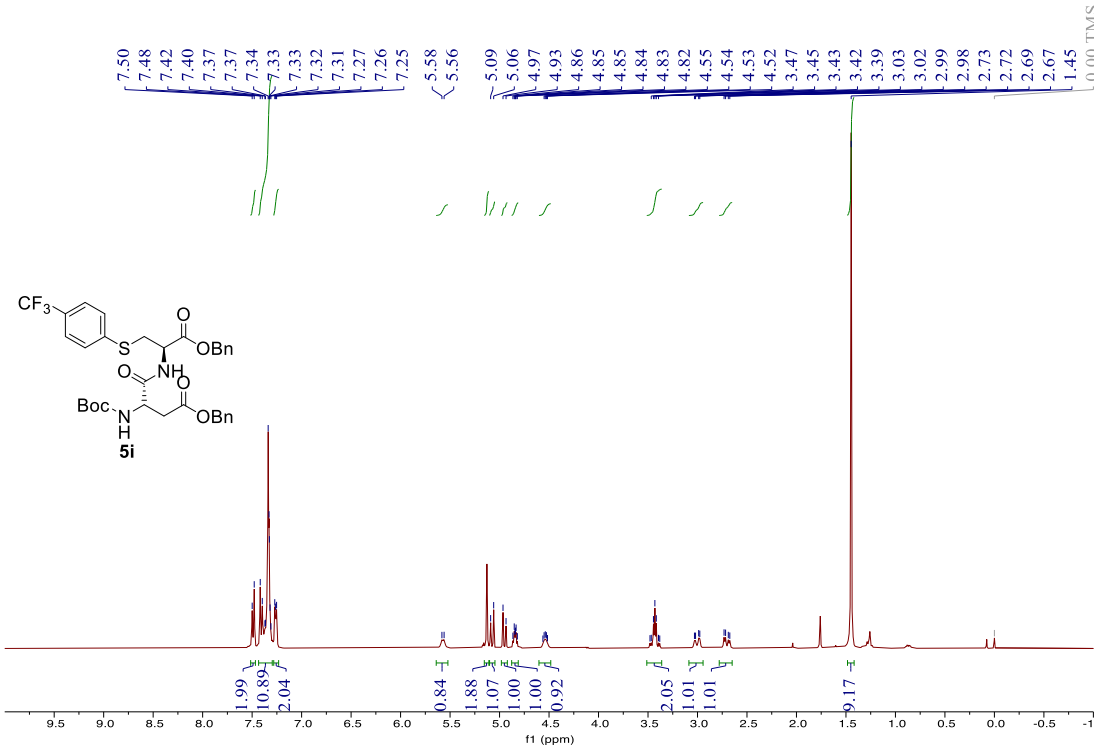



**Figure S107. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 5i**

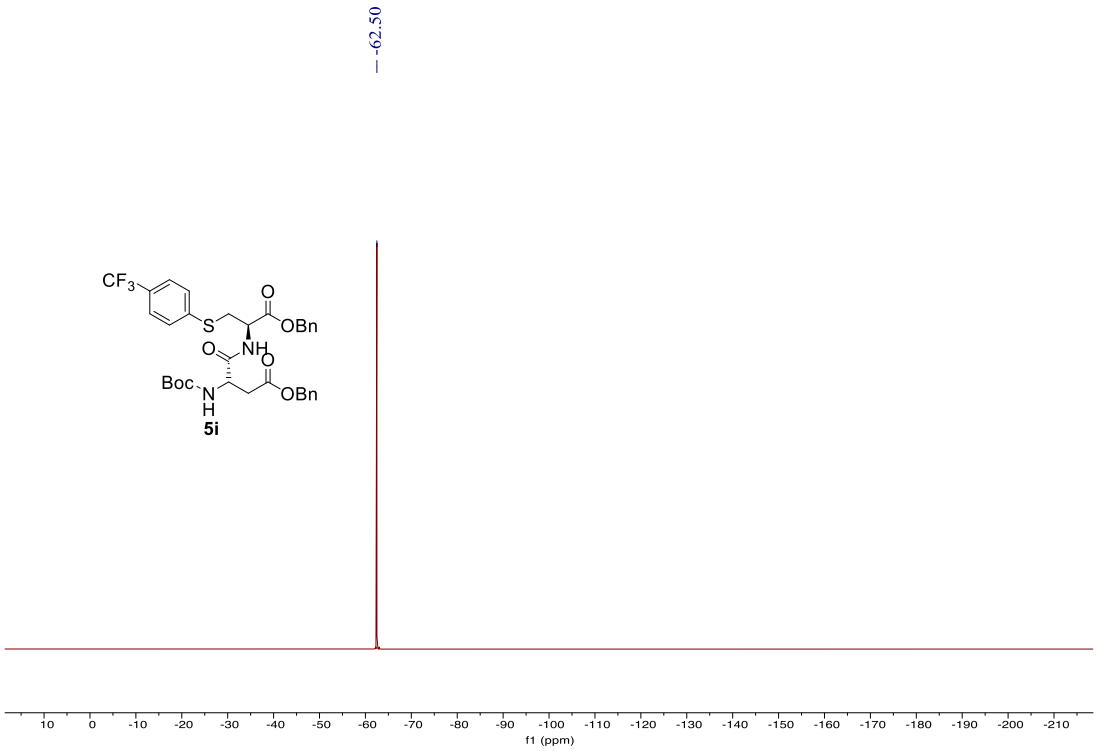



**Figure S108. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 5i**

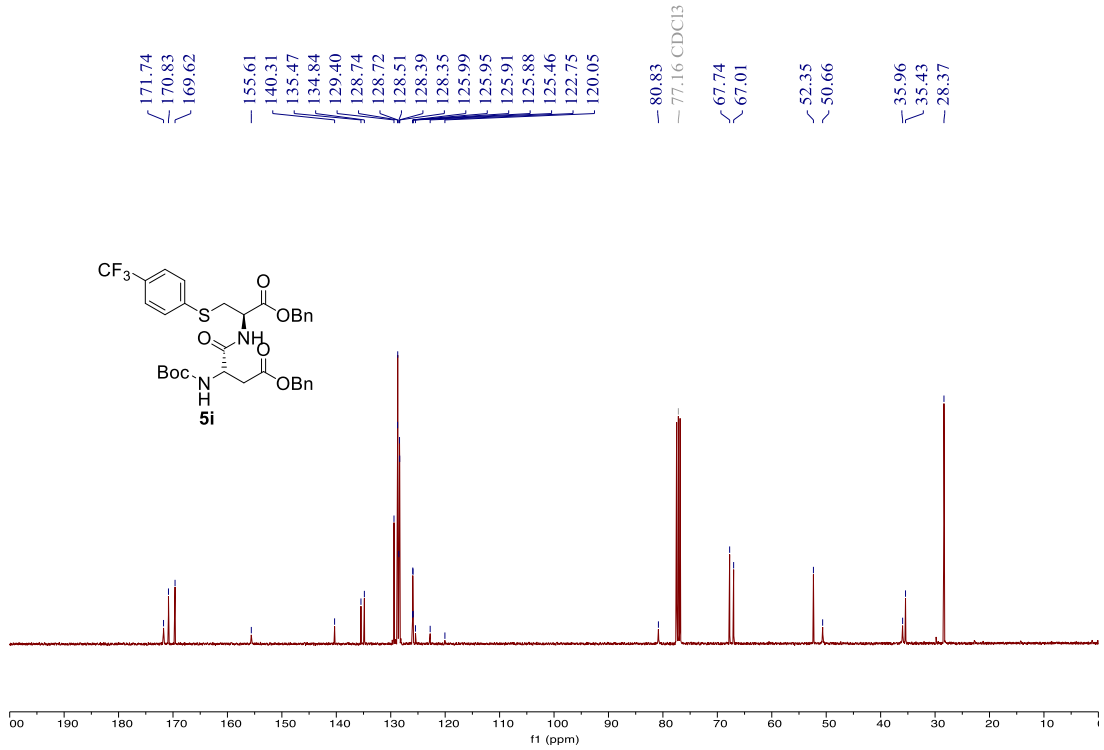



**Figure S109. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 5i**

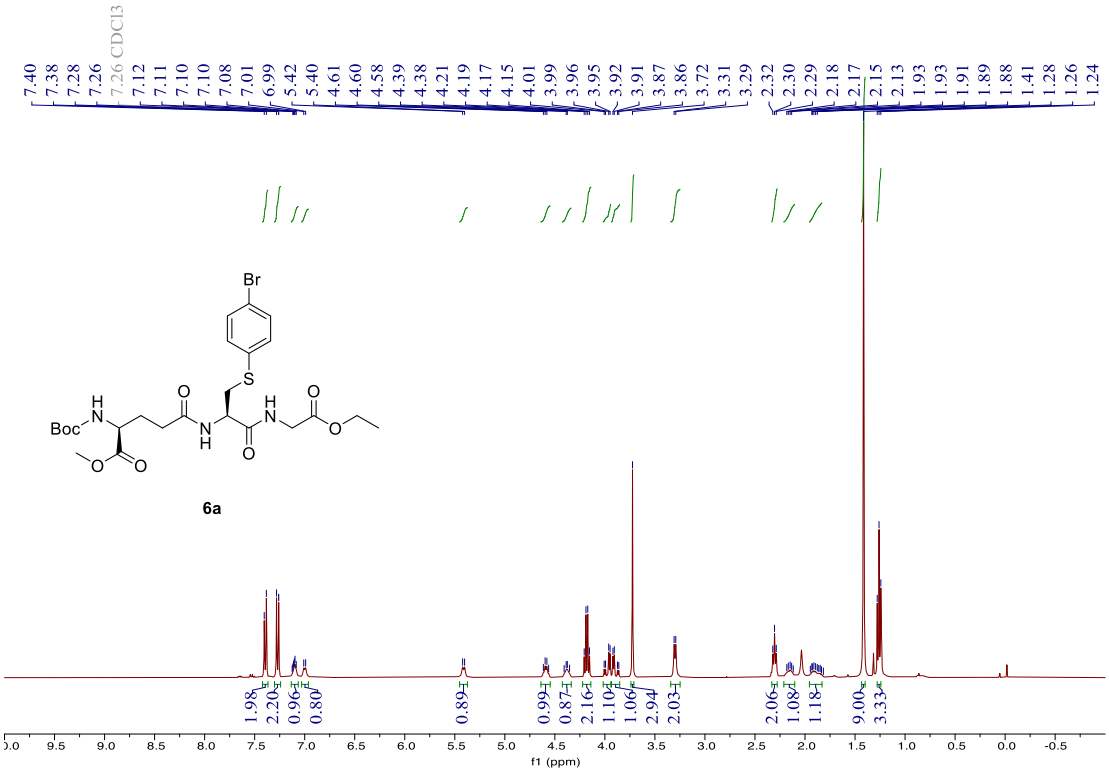



**Figure S110. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 6a**

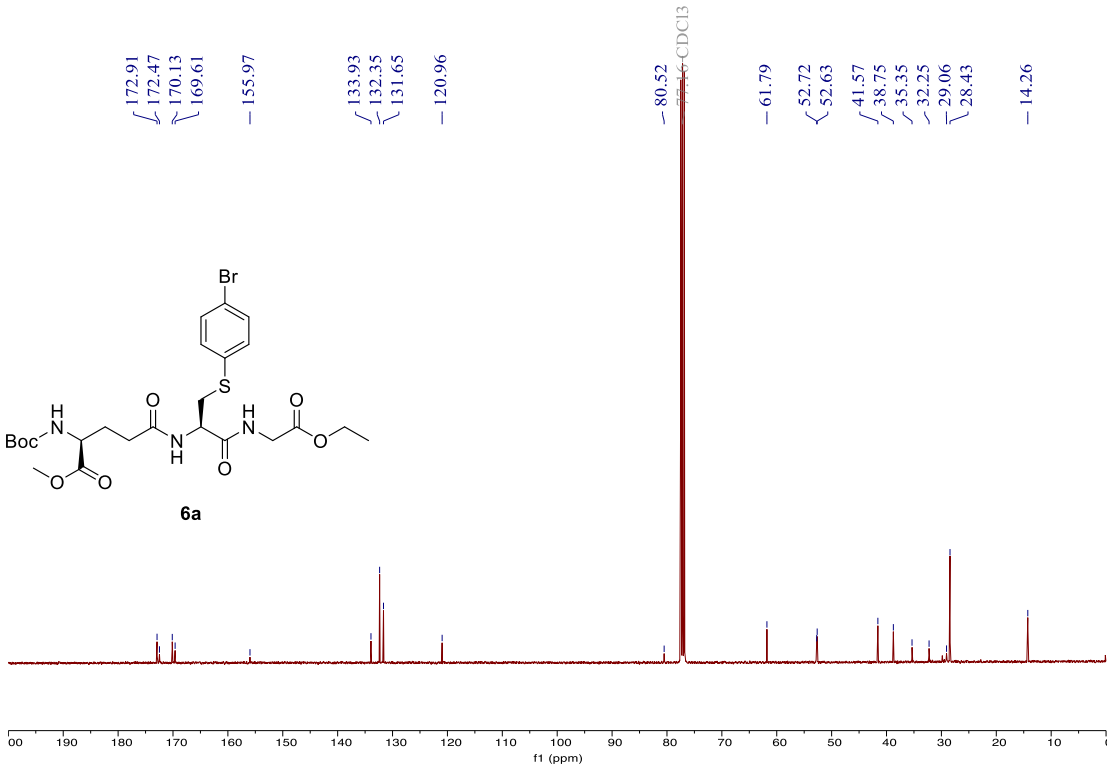



**Figure S111. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 6a**

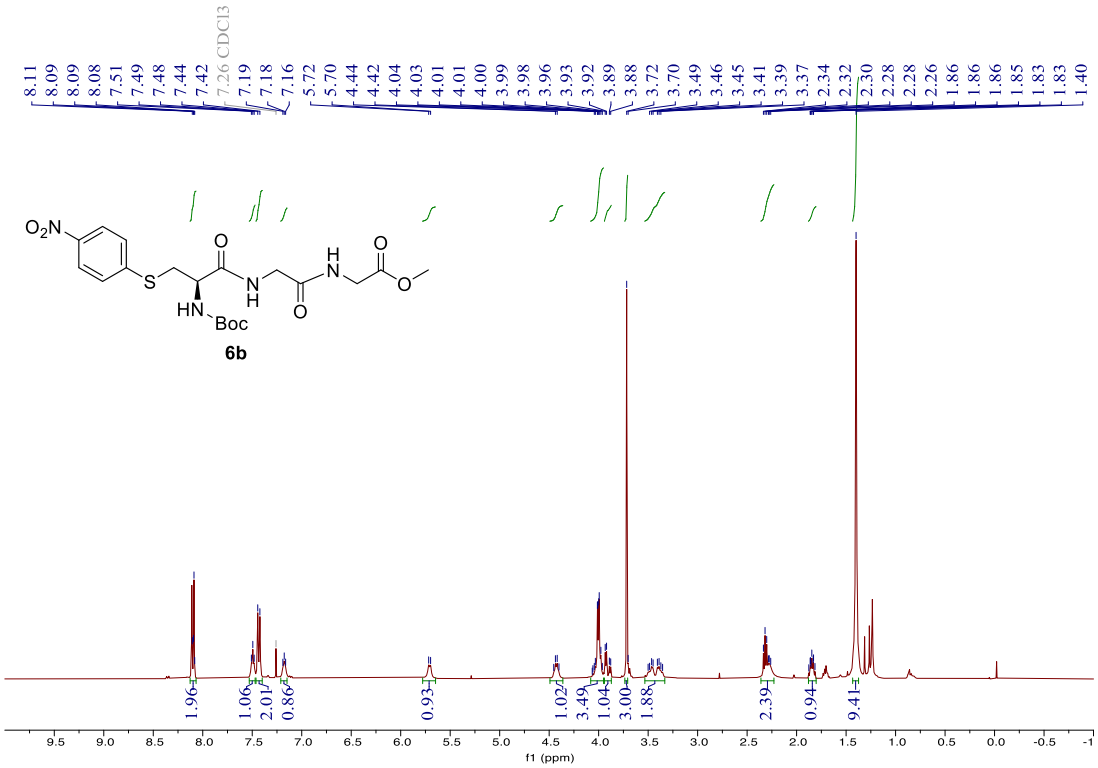



**Figure S112. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 6b**

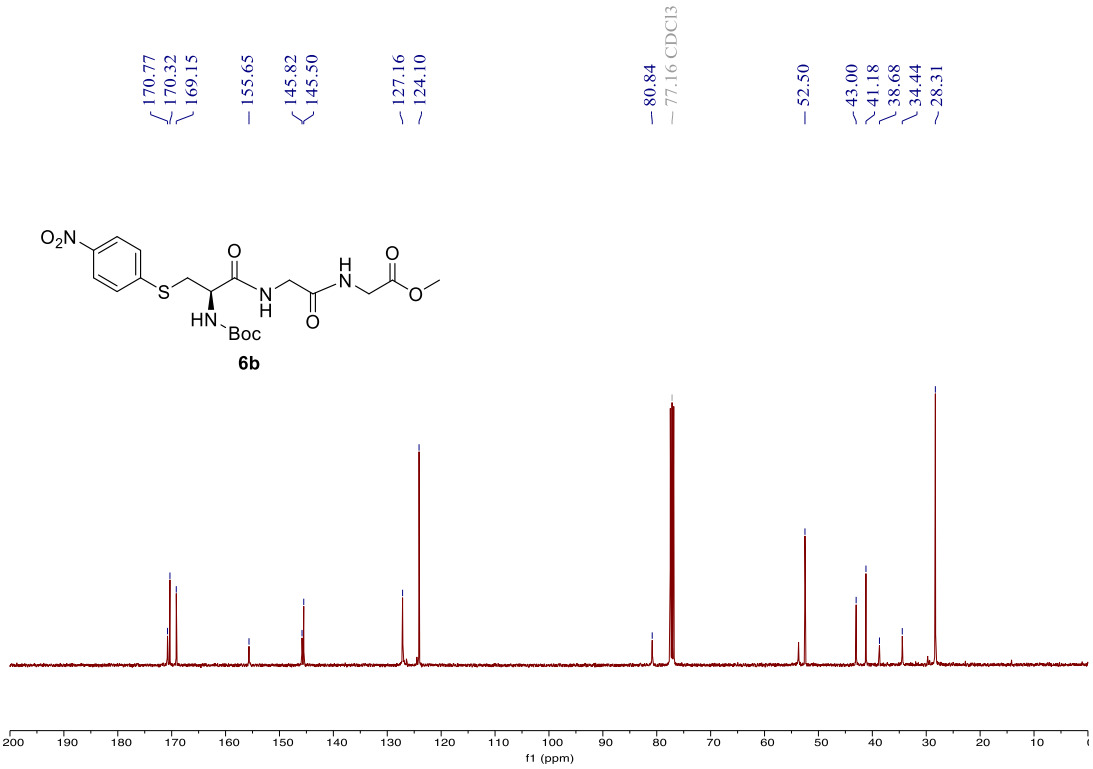



**Figure S113. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 6b**

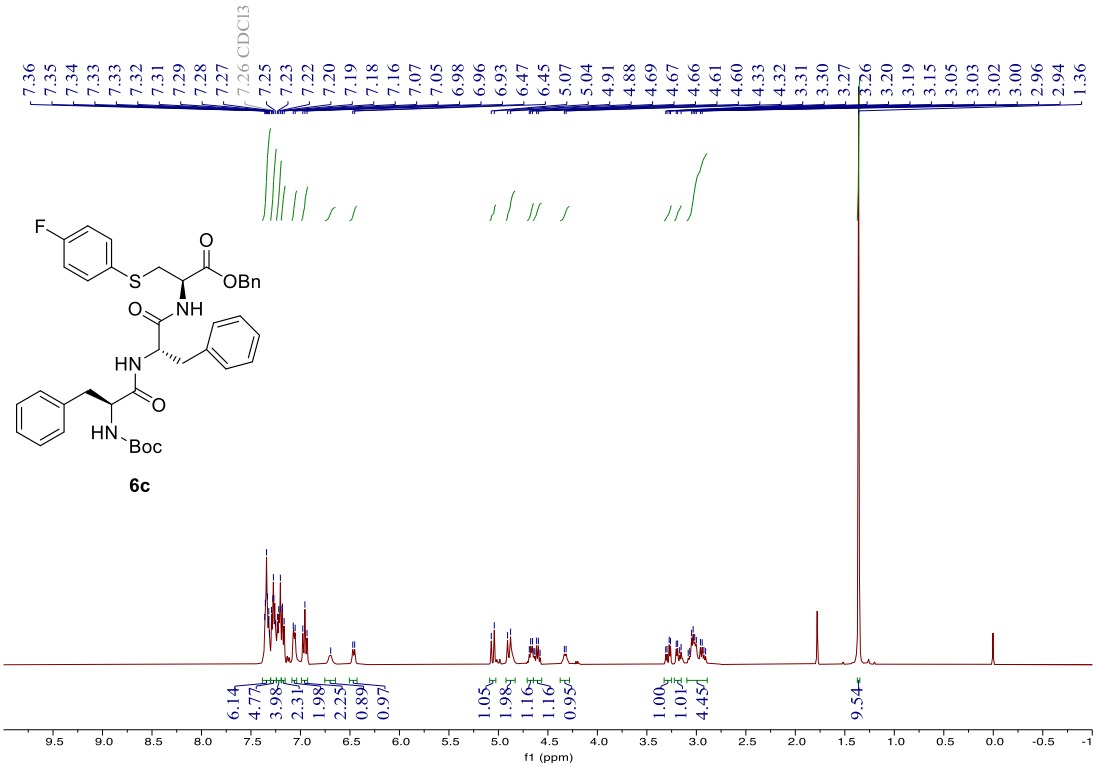



**Figure S114. $^{1}$H NMR (400 MHz, $CDCl_3$) spectra for compound 6c**

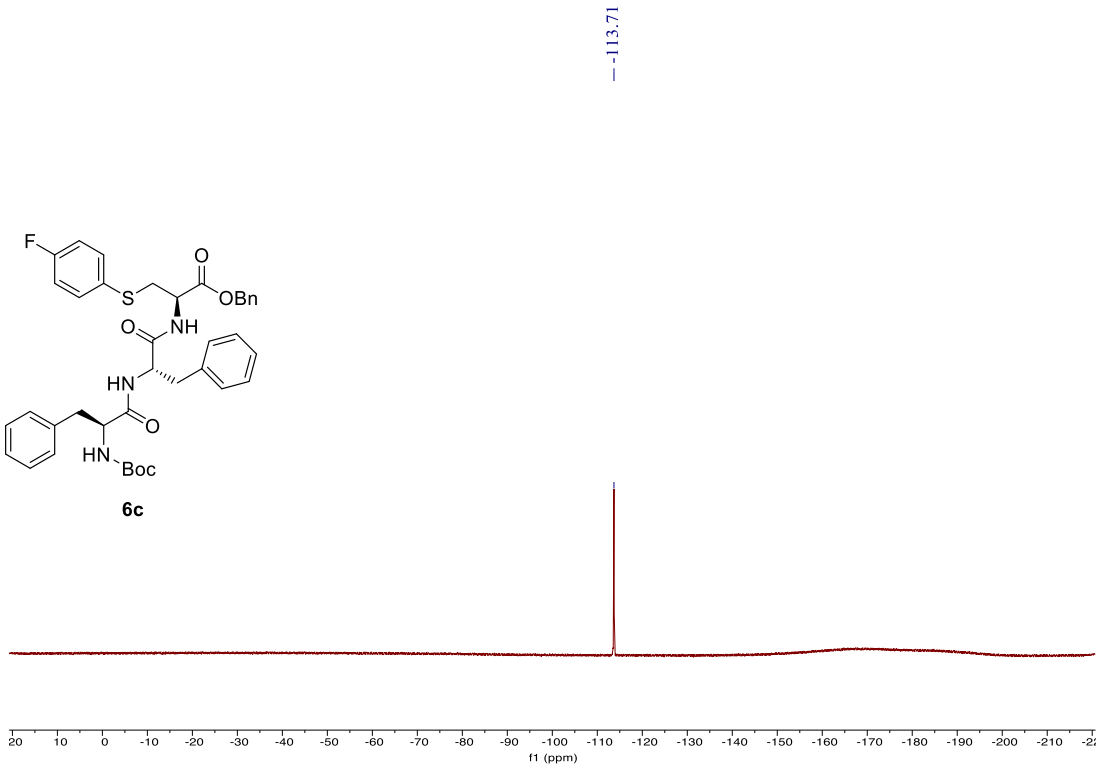



**Figure S115. $^{19}$F NMR (376 MHz, $CDCl_3$) spectra for compound 6c**

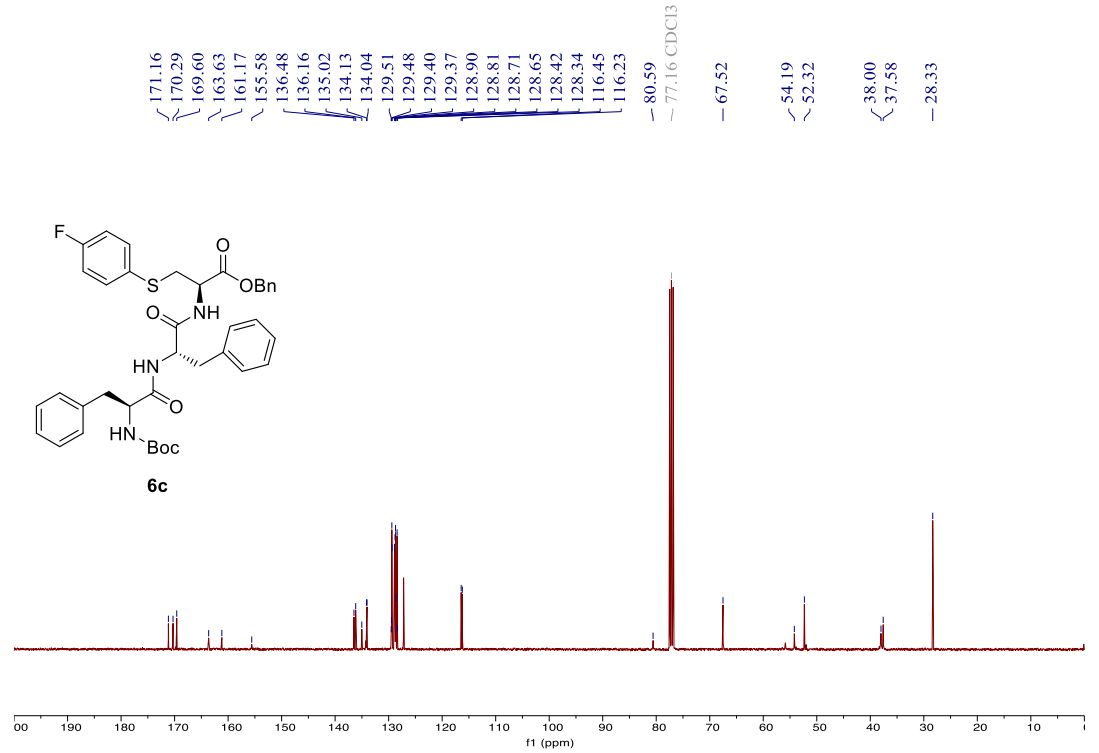



**Figure S116. $^{13}$C NMR (101 MHz, $CDCl_3$) spectra for compound 6c**

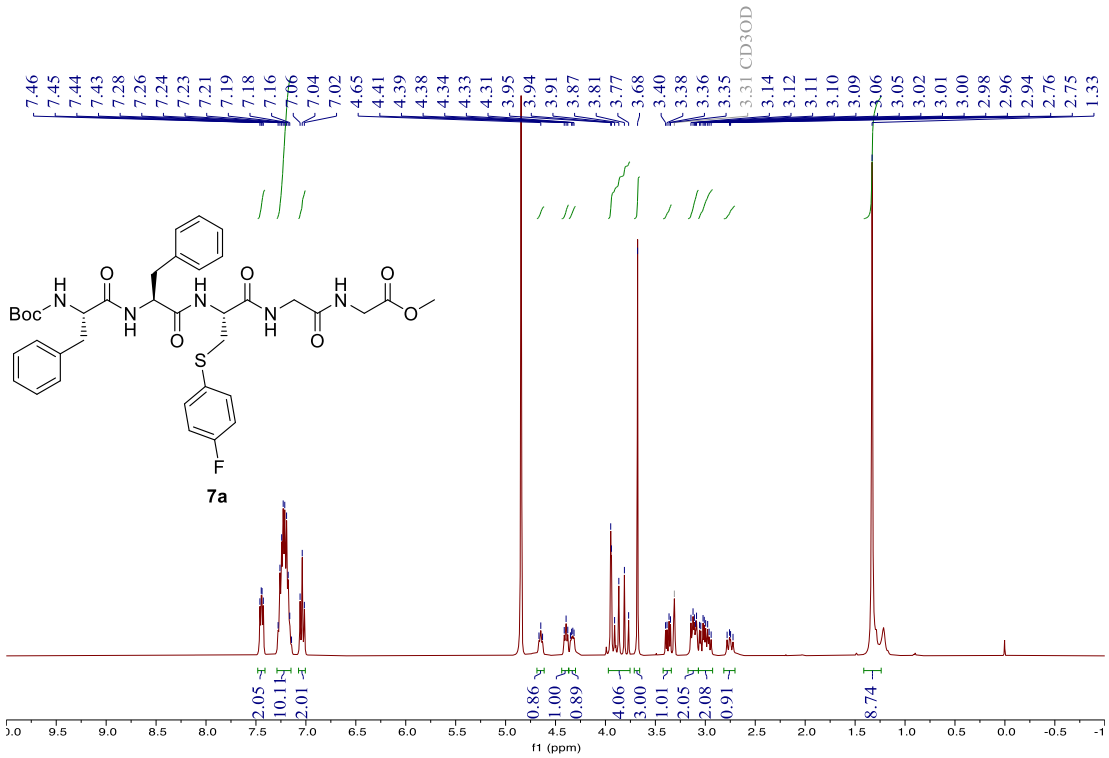



**Figure 117. $^{1}$H NMR (400 MHz, $CD_3OD$) spectra for compound 7a**

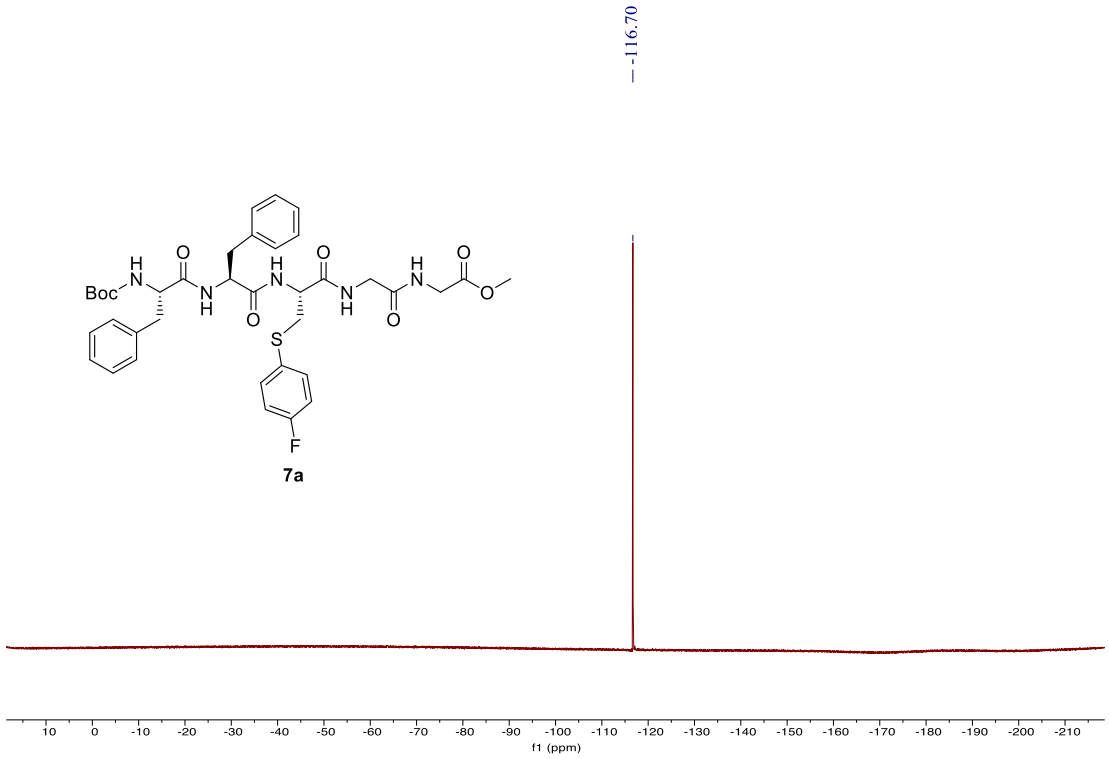



**Figure 118. $^{19}$F NMR (376 MHz, $CD_3OD$) spectra for compound 7a**

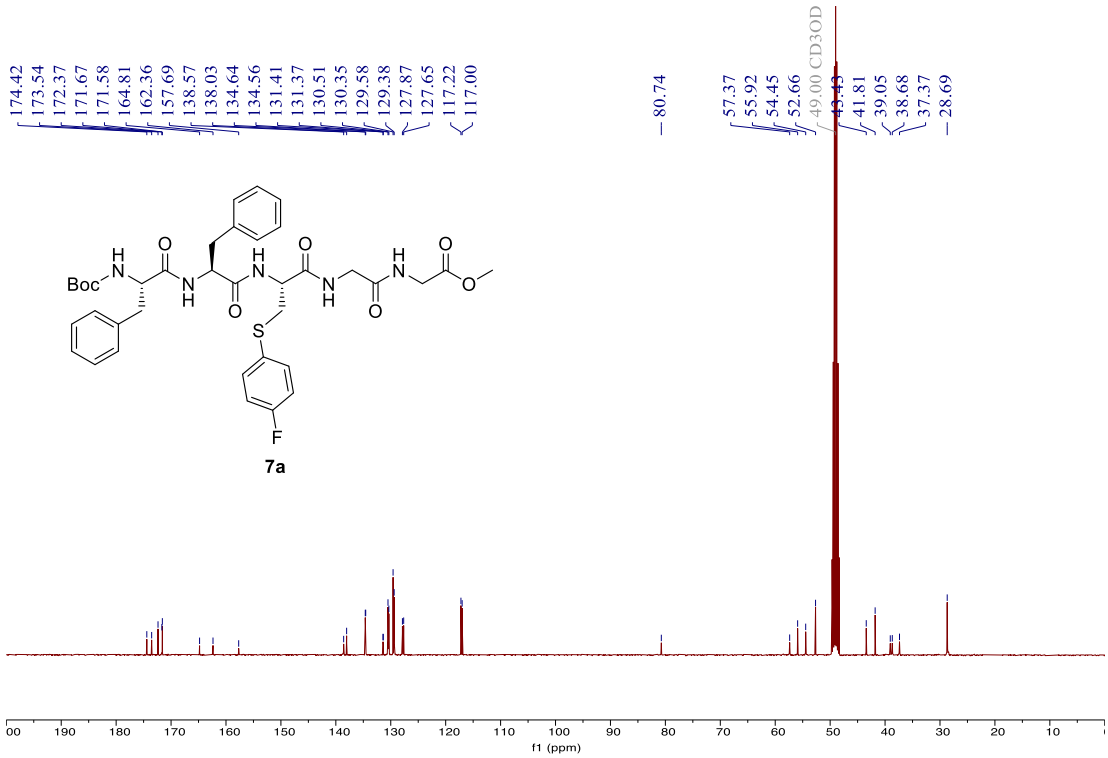



**Figure 119. $^{13}$C NMR (101 MHz, $CD_3OD$) spectra for compound 7a**

# 10. References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