Supporting Information

Amine Capture Strategy for Peptide Bond Formation by Means of Quinolinium Thioester Salts

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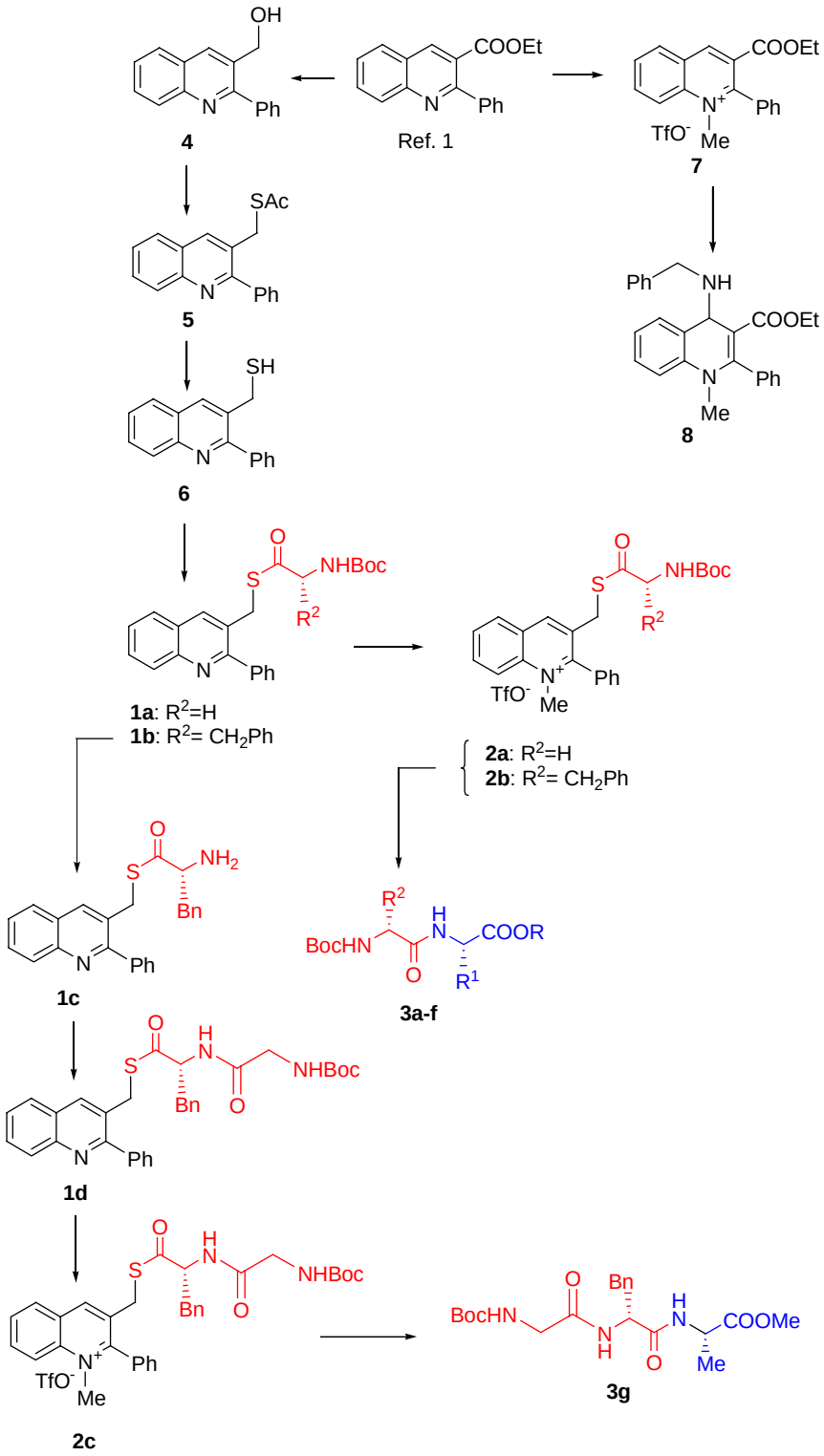
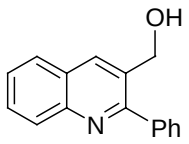
General synthetic scheme



General Experimental

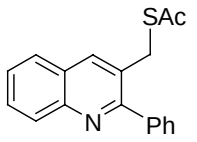
The NMR Spectra were recorded on 300 MHz spectrometers. ^{1}H at 300 MHz and ^{13}C at 75 MHz using $CDCl_3$ as solvent with the residual solvent signal (δ 7.26, ^{1}H; δ 77.0, ^{13}C) as internal standard unless otherwise indicated. The following abbreviations are used to describe peak pattern: s (singlet), d (doublet), t (triplet), q (quartet). Melting points are uncorrected. Analytical thin layer chromatographies were performed on silica gel plates with QF-254 indicator. Peptides were purified on preparative TLC (20x20 cm) with QF-254 indicator.



4

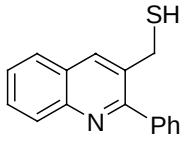
3-(hydroxymethyl)-2-phenylquinoline (4). Ethyl 2-phenylquinoline-3-carboxylate[1] (1.08 g, 4 mmol) in dry THF (80 mL) was slowly added to a suspension of $LiAlH_4$ (456 mg, 12 mmol) in dry THF (20 mL). The reaction mixture was stirred at room temperature during 2 hours and then slowly quenched with water (50 mL). The resulting solution was extracted with ether (3x100 mL). The organic layers were collected and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by flash chromatography on silica gel (CH_2Cl_2), affording a yellow oil (94 %). IR (KBr): 2923, 2852, 1689, 1618 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.83 (1H, t, *J* = 5.6 Hz), 4.75 (2H, d, *J* = 5.3 Hz), 7.4-7.7 (6H, m), 7.64 (1H, t, *J* = 7.1 Hz), 7.80 (1H, d, *J* = 8.3 Hz), 8.10 (1H, d, *J* = 8.7 Hz), 8.30 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 61.6, 125.6, 126.3, 126.4, 127.5, 127.6, 127.7, 128.3, 128.6, 131.1, 134.3, 138.9, 146.1, 157.9. Anal calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.58; H, 5.40; N, 5.85.

[1] Leleu, S.; Papamicaël, C.; Marsais, F.; Dupas, G.; Levacher, V. *Tetrahedron: Asymm.* **2004**, *15*, 3919.



5

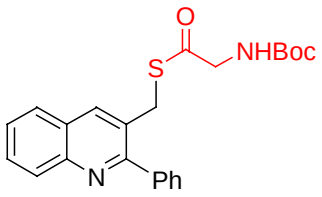
3-(Thiomethyl)-*S*-acetyl-2-phenylquinoline (5). Oxalyl chloride (0.371 mL, 4.32 mmol) and dimethylformamide (0.335 mL, 4.32 mmol) were added to a solution of 3-(hydroxymethyl)-2-phenylquinoline **4** (840 mg, 3.6 mmol) in CH_2Cl_2 (35 mL). The reaction mixture was stirred at room temperature for 2 hours. The solvent and oxalyl chloride in excess were evaporated. The residue was dissolved in CH_2Cl_2 (35 mL) and was added to a solution of potassium thioacetate (1.2 g, 10.8 mmol) in dimethylformamide (50 mL). The reaction mixture was stirred overnight. The solution was washed with water (2x100 mL). The organic layer was collected and dried ($MgSO_4$). The solvent was removed under *vacuum* and the residue was chromatographed on silica gel (cyclohexane/ethyl acetate: 80/20) to afford compound **5** as a yellow oil (62%). Mp: 102°C (cyclohexane). IR (KBr): 3351, 3055, 2346, 1605 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 2.24 (3H, s), 4.18 (2H, s), 7.3-7.7 (6H, m), 7.62 (1H, t, *J* = 8.7 Hz), 7.73 (1H, d, *J* =7.2 Hz), 8.04 (1H, d, *J* = 8.3 Hz), 8.19 (1H, s). ^{13}C NMR (50 MHz, $CDCl_3$) δ 30.7, 31.6, 127.7, 128.9, 129.0, 129.2, 129.7, 130.9, 137.8, 140.3, 160.4, 195.2. Anal. calcd for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77. Found: C, 73.55; H, 5.24; N, 5.01.



6

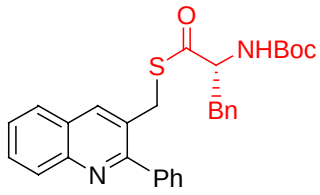
3-(Thiomethyl)-2-phenylquinoline (6). Potassium hydroxide (6.0 g, 0.107 mmol) was added to a solution of compound **5** (1.06 g, 3.6 mmol) in ethanol (60 mL). The reaction mixture was stirred at ambient temperature for 15 min. The solvent was evaporated and the resultant oil

was dissolved in water (20 mL). The aqueous layer was washed with Et_2O (3x15 mL) and then acidified to pH=5 with 1M aqueous HCl. The aqueous layer was extracted with Et_2O (4x20 mL). The organic layers were collected, dried ($MgSO_4$) and evaporated under vacuum affording compound **6** in 88% yield. Compound **6** was identified by ^{1}H NMR spectroscopy and used without further purification in the next step. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.68 (1H, t, *J* = 7.53 Hz), 3.82 (2H, d, *J* = 7.53 Hz), 7.3-7.7 (7H, m), 7.76 (1H, d, *J* = 7.96 Hz), 8.07 (1H, d, *J* = 8.66 Hz), 8.18 (1H, s).



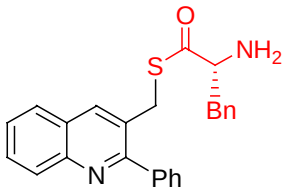
1a

3-(Thiomethyl)-S-(Boc-Gly)-2-phenylquinoline (1a). (General procedure A): Boc-GlyOH (175 mg, 1.12 mmol), EDCI (250 mg, 1.12 mmol) and HOBt (151 mg, 1.12 mmol), were added to a solution of quinoline **6** (104 mg, 0.56 mmol) in DMF (5 mL). The solution was stirred during 12 h and was then poured into water (50 mL). The precipitate was filtrated and the resulting crude solid was purified by flash chromatography on silica gel (cyclohexane/ethyl acetate: 80/20) to afford a white solid (60 %). Mp: 128°C (cyclohexane). IR (KBr): 3343, 3059, 3007, 2978, 2929, 1957, 1697 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (9H, s), 3.91 (2H, d, *J* = 6.02 Hz), 4.20 (2H, s), 5.09 (1H, s, broad, 7.37-7.50 (6H, m), 7.63 (1H, t, *J* = 8.29 Hz), 7.74 (1H, d, *J* = 8.3 Hz), 8.05 (1H, d, *J* = 8.3 Hz), 8.19 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7, 31.0, 50.5, 80.9, 127.2, 127.7 (x2), 128.9 (x2), 129.2 (x2), 129.7, 130.2, 137.9, 140.2, 147.4, 155.9, 160.3, 197.9. HRMS (IE): calcd for $C_{23}H_{24}N_2O_3S$ (M) 408. 15076; found: 408.15065.



1b

3-(Thiomethyl)-S-(Boc-D-Phe)-2-phenylquinoline (1b). The titled compound **1b** was prepared according to the general procedure A, from Boc-D-Phe-OH (690 mg, 2.6 mmol), EDCl (895 mg, 2.6 mmol) and 2-phenyl-3-(thiohydroxymethyl)quinoline **6** (680 mg, 2.6 mmol) in THF (10 mL). The crude solid was chromatographed on silica gel (cyclohexane/ethyl acetate: 98/2) to afford a white solid (68 %). Mp: 119°C (cyclohexane). $[\alpha]_D^{25}$ = +8° (c 0.004; CH_2Cl_2). IR (KBr): 3361, 3057, 3026, 2979, 1697 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.47 (9H, s), 3.12 (2H, m), 4.32 (2H, s), 4.69 (1H, q, *J* = 6.4 Hz), 4.97 (1H, d, *J* = 8.3 Hz), 7.10 (2H, d, *J* = 6.0 Hz), 7.13 (2H, m), 7.52-7.67 (6H,, m), 7.80 (1H, t, *J* = 7.5 Hz), 7.90 (1H, d, *J* = 7.9 Hz), 8.22 (1H, d, *J* = 8.7 Hz), 8.32 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7, 31.4, 38.6, 61.2, 80.9, 127.2, 127.5, 127.7, 127.75, 128.92, 128.95, 129.2, 129.3, 129.67, 129.72, 130.2, 135.7, 137.9, 140.3, 147.4, 155.3, 160.4, 200.6. Anal. calcd for $C_{30}H_{30}N_2O_3S$: C, 72.26; H, 6.06; N, 5.62. Found: C, 72.29; H, 6.15; N, 5.57.

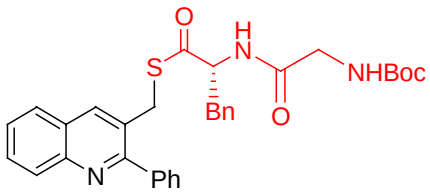


1c

3-(Thiomethyl)-S-(D-Phe)-2-phenylquinoline (1c).[2] Acetyl chloride (7.13 mL, 100 mmol) was added to a solution of methanol (2.9 mL, 100 mmol) in ethyl acetate (20 mL) and the

[2] Nudelman, A.; Bechor, Y.; Faib, E.; Fischer, B.; Wexler, B. A. *Synth. Comm.* **1998**, *28*, 471.

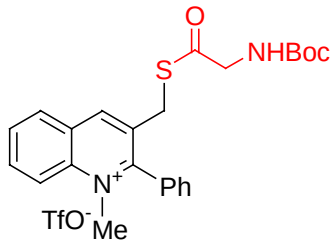
resulting solution was stirred for 1h. A solution of compound **1b** (1.0 g, 2.0 mmol) in ethyl acetate (5 mL), was added and the solution was stirred for 5 h at room temperature after which a precipitate was formed. The solid was filtrated and collected, dissolved in dichloromethane (50 mL) and DIEA (0.871 mL, 5.0 mmol) was added. After complete dissolution of the solid, the solvent was removed under reduced pressure. The crude oil was chromatographed on silica gel (CH_2Cl_2/AcOEt: 98/2) to afford compound **1c** as an oil (80%) IR (KBr): 3057, 2360, 2341, 1676, 1594 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.48 (2H 2H, s), 2.70 (1H, dd, *J* = 13.5 Hz and *J* = 8.3 Hz), 3.01 (1H, dd, *J* = 13.5 Hz and *J* = 4.5 Hz), 3.68 (1H, q, *J* = 4.5 Hz and *J* = 8.3 Hz), 4.16 (2H, s), 7.03-7.18 (2H, m), 7.39-7.50 (4H, m), 7.63 (1H, t, *J* = 7.5 Hz), 7.73 (1H, d, *J* = 7.91 Hz), 8.05 (1H, d, *J* = 8.66 Hz), 8.19 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.2, 41.6, 63.2, 127.2, 127.4, 127.7, 128.8, 128.9, 129.0 (x2), 129.3, 129.7, 129.8, 130.2, 137.0, 137.9, 140.4, 147.4, 160.4, 204.0. HRMS (IC): calcd for $C_{25}H_{23}N_2OS$ (M+H) 399.15311; found: 399.15306.



1d

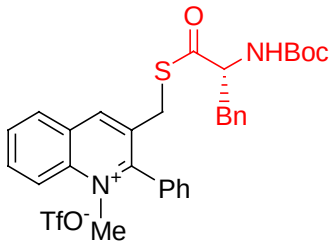
3-(Thiomethyl)-S-(Boc-Gly-D-Phe)-2-phenylquinoline (1d). To a solution of compound **1c** (108 mg, 0.24 mmol) in CH_2Cl_2 (5 mL) was added Boc-Gly-OH (42 mg, 0.24 mmol), EDCl (48 mg, 0.24 mmol) and diisopropylethylamine (0.42 mL, 0.24 mmol). The resulting solution was stirred overnight at room temperature and the solvent was then evaporated under vacuum. The residue was purified by flash chromatography on silica gel (cyclohexane/ethyl acetate: 80/20) to afford a white solid (88%). $[\alpha]_D^{25}$ +1.4° (c, 0.0035; CH_2Cl_2). IR (KBr): 3306, 3060, 2977, 2927, 2852, 1685, 1596 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.30 (9H, s), 2.99 (2H, d, *J*

= 5.65 Hz), 3.58-3.75 (2H, m), 4.17 (2H, s), 4.87 (1H, q, *J* = 7.55 Hz), 4.94 (1H, s), 6.48 (1H, d, *J* = 7.90 Hz), 6.92 (2H, d, *J* = 7.15 Hz), 7.01-7.11 (3H, m), 7.40-7.47 (5H, m), 7.50 (1H, t, *J* = 7.5 Hz), 7.66 (1H, t, *J* = 7.5 Hz), 7.76 (1H, d, *J* = 7.90 Hz), 8.07 (1H, d, *J* = 8.30 Hz), 8.16 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7, 30.5, 31.4, 38.5, 59.9, 127.2, 127.5, 127.6, 127.8, 128.9, 129.2, 129.6, 130.3, 135.7, 136.2, 137.9, 140.2, 147.4, 156.6, 160.2, 170.2, 199.1. HRMS (IC) calcd for $C_{32}H_{34}N_3O_4S$ (M+H) 556.2270; found: 556.2272.



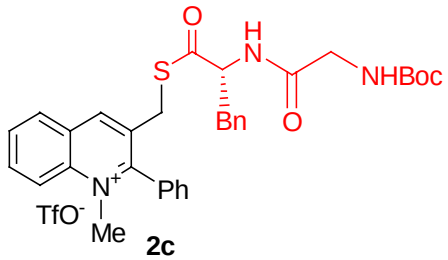
2a

3-(Thiomethyl)-*S*-(Boc-Gly)-2-phenylquinolinium triflate (2a). (General procedure B): Methyl trifluoromethanesulfonate (0.048 mL, 0.42 mmol) was added to a solution of compound **1a** (156 mg, 0.39 mmol) in dichloromethane (2 mL) under nitrogen atmosphere. The mixture was stirred for 2 h at room temperature after which the solvent was evaporated to afford quinolinium salt **2a** in 100 % yield. Mp: 98°C (dichloromethane/diethyle ether). IR (KBr): 3326, 3064, 2983, 2929, 2849, 1714, 1694 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (9H, s), 3.86-3.88 (4H, m), 4.23 (3H, s), 5.60 (1H, s broad), 7.53-7.64 (5H, m), 7.83 (1H, t, *J* = 7.5 Hz), 8.18 (1H, d, *J* = 8.3 Hz), 8.26 (1H, d, *J* = 9.0 Hz), 9.04 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7, 30.7, 43.1, 50.5, 80.7, 119.5, 122.9, 128.6, 129.1, 130.4, 130.5, 131.0, 131.1, 132.0, 133.5, 136.5, 139.2, 147.3, 156.4, 160.1, 199.2. HRMS (IE): calcd for $C_{24}H_{27}N_2O_3S$ (M): 423.1742; found: 423.1735.



2b

3-(Thiomethyl)-*S*-(Boc-D-Phe)-2-phenylquinolinium triflate (2b). The titled compound **2b** was prepared according to the general procedure B, from methyl trifluoromethanesulfonate (64 µL, 0.55 mmol) and quinoline **1b** (256 mg, 0.51 mmol), in dichloromethane (10 mL). Yield = 100 %. Mp: 166°C (dichloromethane/diethyl ether). $[\alpha]_D^{25}$ +4.7° (c 0.006; CH_2Cl_2). IR (KBr): 3307, 3062, 2980, 2933, 1702, 1624, 1603 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (9H, s), 2.89-3.01 (4H, m), 3.89 (2H, s), 4.27 (3H, s), 4.40-4.47 (1H, m), 5.00 (1H, d, *J* = 8.3 Hz), 6.99-7.20 (5H, m), 7.45-7.61 (5H, m), 7.88 (1H, t, *J* = 7.5 Hz), 7.90-8.14 (1H, d, *J* = 9.0 Hz), 8.99 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.6, 31.2, 37.9, 43.3, 61.6, 81.0, 119.8, 127.5, 128.4, 128.8, 129.0, 129.2, 129.6, 130.3, 130.5, 130.6, 130.7, 131.1, 132.0, 133.6, 135.9, 136.7, 139.3, 147.1, 160.1, 201.0. HRMS (FAB) calcd for $C_{31}H_{33}N_2O_3S$ (M) 513.2212; found: 513.2224.

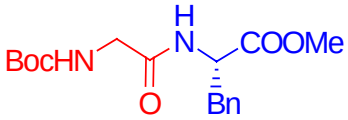


2c

3-(Thiomethyl)-*S*-(Boc-Gly-D-Phe)-2-phenylquinolinium triflate (2c). The titled compound **2c** was prepared according to the general procedure B, from methyl trifluoromethanesulfonate (64 µL, 0.55 mmol) and quinoline **1c** (256 mg, 0.51 mmol), dichloromethane (10 mL). Yield = 100 %. IR (CH_2Cl_2) 3054, 2986, 2305, 1686, 1508, 1421,

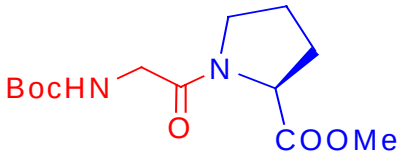
1265, 705 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (9H, s), 2.79-3.05 (4H, m), 3.53-3.95 (4H, m), 4.19 (3H, s), 4.68 (1H, m), 5.31 (1H, s broad), 7.00-7.19 (5H, m), 7.39-7.41 (2H, m), 7.53-7.60 (4H, m), 7.83 (1H, t, *J* = 7.55 Hz), 8.06 (1H, t, *J* = 7.7 Hz), 8.23 (2H, m), 9.01 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7, 30.1, 31.1, 37.4, 43.1, 60.4, 80.2, 119.4, 122.9, 127.3, 128.2, 128.8, 129.1, 129.5, 130.4, 130.6, 131.0, 131.1, 132.1, 133.4, 136.4, 136.6, 139.1, 147.4, 160.1, 170.8, 199.7. HRMS (FAB) calcd for $C_{33}H_{36}N_3O_4S$ (M) 570.2426; found; 570.2437.

Preparation of the dipeptides 3a-g by means of the quinolinium thioester salts 2a-c.



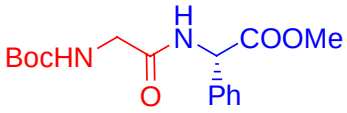
3a

Boc-Gly-L-Phe-OMe (3a). (General Procedure C): Methyl ester L-phenylalanine hydrochloride (43 mg, 0.2 mmol) and triethylamine (40 mg, 0.4 mmol) were added to a solution of quinolinium thioester salt **2a** (85 mg, 0.2 mmol) in acetonitrile (5 mL). The solution was stirred at least 6 h at room temperature. The reaction was quenched by addition of water (10 mL). The organic layer was collected, dried ($MgSO_4$) and the solvent was evaporated under vacuum. The resulting oil was purified by preparative TLC (SiO_2), using ethyl acetate as eluent. Yield = 50 %. IR (KBr): 3316, 3063, 3029, 2978, 2933, 1743, 1672 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (9H, s), 3.07-3.19 (2H, m), 3.73 (3H, s), 3.77-3.83 (2H, m), 4.90 (1H, m), 5.12 (1H, s broad), 6.56 (1H, s broad), 7.09-7.28 (5H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7, 38.2, 52.7, 53.5, 53.9, 80.5, 127.5, 129.0, 129.6, 136.1, 156.4, 169.6, 172.2. HRMS (IC): calcd for $C_{17}H_{25}N_2O_5$ (M+H) 337.1764; found: 337.1763.



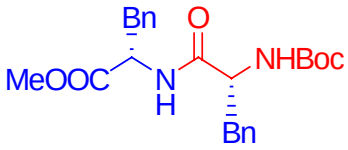
3b

Boc-Gly-L-Pro-OMe (3b). The titled compound **3b** was prepared according to the general procedure C, from methyl ester L-proline hydrochloride (33 mg, 0.2 mmol), triethylamine (40 mg, 0.4 mmol) and quinolinium thioester salt **2a** (85 mg, 0.2 mmol). Yield = 55 %. IR (KBr): 3408, 2996, 2974, 2949, 2878, 1753, 1720, 1658 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (9H, s), 1.64-1.98 (4H, m), 3.17-3.42 (2H, m), 3.48 (3H, s), 3.7 (2H, m), 4.27 (1H, d broad), 5.17 (1H, s broad). ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.0, 28.7, 29.4, 43.4, 46.2, 52.7, 58.8, 80.0, 156.2, 167.7, 172.8. HRMS (IC): calcd for $C_{13}H_{23}N_2O_5$ (M+H) 287.1607; found: 287.1611.



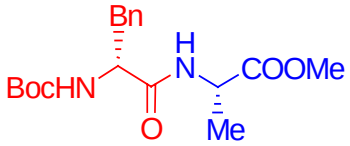
3c

Boc-Gly-L-Phg-OMe (3c). The titled compound **3c** was prepared according to the general procedure C, from methyl ester L-phenylglycine hydrochloride (40 mg, 0.2 mmol), triethylamine (40 mg, 0.4 mmol) and quinolinium thioester salt **2a** (85 mg, 0.2 mmol). Yield = 70 % . IR (KBr): 3315, 2978, 1744, 1675 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (9H, s), 3.60 (3H, s), 3.71 (2H, s broad), 5.05 (1H, s broad), 5.44 (1H, d broad), 7.02 (1H, s broad), 7.22 (5H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.6, 44.7, 53.3, 56.7, 80.1, 127.6, 129.0, 129.4, 136.5, 169.3, 171.5. HRMS (IC): calcd for $C_{16}H_{23}N_2O_5$ (M+H) 323.16.07; found: 323.1605.



3d

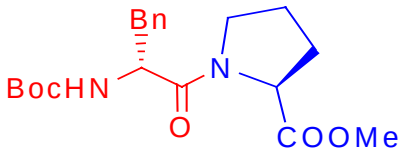
Boc-D-Phe-L-Phe-OMe (3d). The titled compound **3d** is prepared according to the general procedure C, from methyl ester L-phenylalanine hydrochloride (43 mg, 0.2 mmol), triethylamine (40 mg, 0.4 mmol) and quinolinium thioester salt **2b** (102 mg, 0.2 mmol). Yield = 55 %. IR (KBr): 3338, 3306, 3086, 3063, 3027, 2966, 2947, 2778, 1946, 1736, 1682, 1661 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (9H, s), 2.82-3.05 (4H, m), 3.59 (3H, s), 4.28 (1H, s broad), 4.7-4.8 (1H, m), 4.91 (1H, s, broad), 6.26 (0.5H, s, broad), 6.35 (0.5H, s, broad), 6.84-6.92 (2H, m), 7.07-7.21 (8H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.6, 38.2, 38.3, 38.6, 52.7, 53.4, 53.6, 56.1, 80.6, 127.4, 127.5, 127.6, 128.9, 129.0, 129.1, 129.5, 129.6, 129.7, 129.8, 135.9, 136.0, 155.7, 171.1, 171.2, 171.8. HRMS (IC): calcd for $C_{24}H_{31}N_2O_5$ (M+H) 427.2233; found: 427.2227.



3e

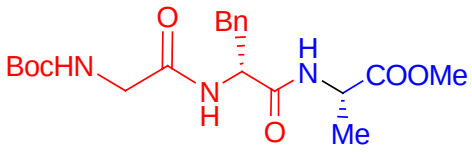
Boc-D-Phe-L-ala-OMe (3e). The titled compound **3e** was prepared according to the general procedure C, from methyl ester L-alanine hydrochloride (28 mg, 0.2 mmol), triethylamine (40 mg, 0.4 mmol) and quinolinium thioester salt **2b** (102 mg, 0.2 mmol). Yield = 66 %. IR (KBr): 3270, 3063, 3001, 2977, 2935, 1754, 1742, 1694, 1656 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (1.5H, d, *J* = 7.2 Hz), 1.27 (1.5 H, d, *J* = 7.2 Hz), 1.34 (9H, s), 2.99 (2H, m),

3.64 (3H, s), 4.28 (1H, s broad), 4.45 (1H, s broad), 4.95 (1H, s broad), 6.19 (0.5H, d), 6.35 (0.5 H, d), 7.12-7.43 (5H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5, 18.7, 28.6, 38.7, 39.1, 48.3, 48.5, 52.8, 56.1, 80.6, 127.3, 129.0, 129.1, 129.7 (x 2), 136.9, 137.0, 155.7, 171.0, 171.2, 173.3, 173.4. HRMS (IC): calcd for $C_{18}H_{27}N_2O_5$ (M+H) 351.1920; found: 351.1916.



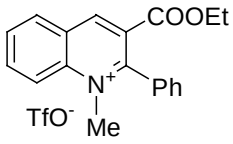
3f

Boc-D-Phe-L-Pro-OMe (3f). The titled compound **3f** was prepared according to the general procedure C, from the methyl ester L-proline hydrochloride (33 mg, 0.2 mmol), triethylamine (40 mg, 0.4 mmol) and quinolinium thioester salt **2b** (102 mg, 0.2 mmol). Yield = 75 %. IR (KBr): 3299, 2977, 2880, 1745, 1708 1643 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (0.5x9H, s), 1.29 (0.5x9H, s), 1.71-208 (4H, m), 2.47-2.53 (0.5x2H, m), 2.76-3.05 (4H, m), 3.36-3.49 (0.5x2H, m), 3.57 (0.5x3H, s), 3.60 (0.5x3H, s), 4.14-4.16 (0.5H, m), 4.33-4.37 (0.5H, m), 4.47-4.52 (1H, m), 5.19 (0.5H, d broad, *J* = 8.7 Hz), 5.29 (0.5H, d broad, *J* = 8.7 Hz), 7.08-7.14 (5H, m). ^{13}C NMR (7 MHz, $CDCl_3$) δ 24.8, 25.3, 28.69, 28.73, 29.3, 29.4, 40.8, 47.1, 47.2, 52.6, 53.6, 53.9, 59.1, 59.2, 80.1, 127.1, 127.3, 128.7, 128.75, 129.7, 129.8, 136.7, 136.8, 153.3, 155.5, 170.6, 171.0, 172.7. HRMS (IC): calcd for $C_{20}H_{29}N_2O_5$ (M+H) 377.2076; found: 377.2064.



3g

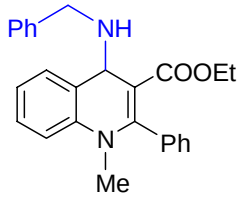
Boc-Gly-D-Phe-L-Ala-OMe (3g). The title compound **3g** was prepared according to the general procedure C, from methyl ester L-alanine hydrochloride (28 mg, 0.2 mmol), triethylamine (40 mg, 0.4 mmol) and quinolinium thioester salt **2c** (114 mg, 0.2 mmol). Yield = 75 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (3H, d, *J* = 7.2 Hz), 1.36 (9H, s), 2.97 (1H, dd, *J* = 13.5 Hz and 7.7 Hz), 3.08 (1H, dd, *J* = 13.5 Hz and 6.2 Hz), 3.62 (3H, s), 3.70 (2H, d, *J* = 5.6 Hz), 4.40 (1H, q, *J* = 7.3 Hz), 4.65 (1H, quint, *J* = 7.9 Hz), 5.11 (1H, t broad, *J* = 7.3 Hz), 6.46 (1H, d broad, *J* = 5.8 Hz), 6.70 (1H, d broad, *J* = 7.3 Hz), 7.12-7.25 (5H, m). ^{13}C NMR (7 MHz, $CDCl_3$) δ 28.65, 39.0, 44.35, 48.25, 52.7, 54.5, 60.8, 80.2, 127.2, 128.8, 129.8, 136.9, 156.6, 170.15, 171.05, 173.5. HRMS (IC): calcd for $C_{20}H_{30}N_3O_6$ (M+H) 408.2134; found: 408.2130.



7

Ethyl 2-phenylquinolinium-3-carboxylate triflate (7). To a solution of ethyl 2-phenylquinoline-3-carboxylate[1] (332 mg, 1.2 mmol) in dry CH_2Cl_2 was added methyl triflate (164 mg, 1.7 mmol). The resulting solution was stirred at room temperature for 2 h. Addition of Et_2O (10 mL) furnished a white precipitate which was filtered to give the desired quinolinium salt **7** in a quantitative yield. IR (KBr): 3065, 2991, 2364, 1720, 1624, 1591 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (3H, t, *J* = 7.15 Hz), 4.10 (2H, q, *J* = 7.15 Hz), 4.42 (3H, s), 7.63 (5H, m), 8.04 (1H, t, *J* = 7.5 Hz), 8.28 (1H, t, *J* = 7.5 Hz), 8.35 (1H, d, *J* = 2.3 Hz),

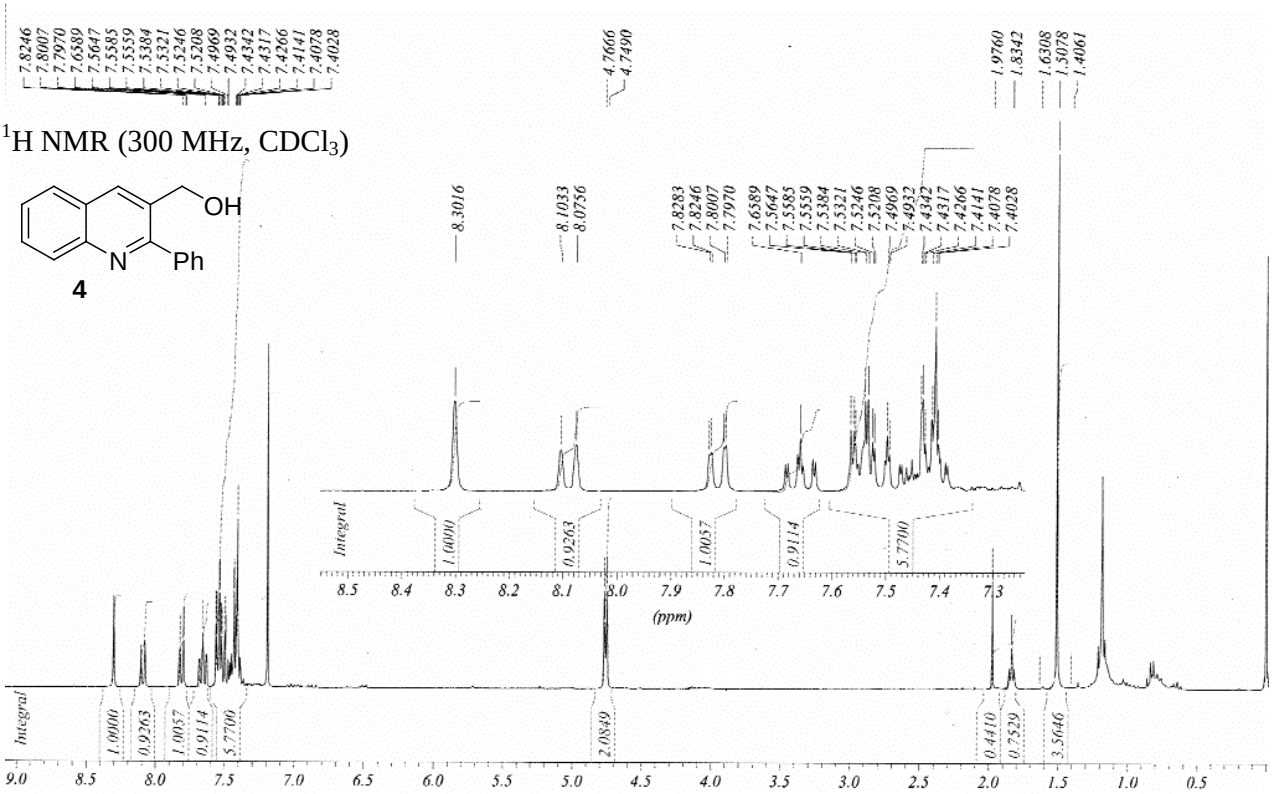
8.55 (1H, d, *J* = 9.05 Hz), 9.41 (1H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 43.5, 63.3, 120.6, 128.1, 128.5, 128.7, 129.6, 131.4, 131.7, 131.8, 132.2, 138.8, 141.0, 148.4, 159.4, 163.4. Anal calcd for $C_{20}H_{18}F_3NO_5S$: C, 54.42; H, 4.11; N, 3.17. Found: C, 54.22; H, 4.25; N, 3.12.



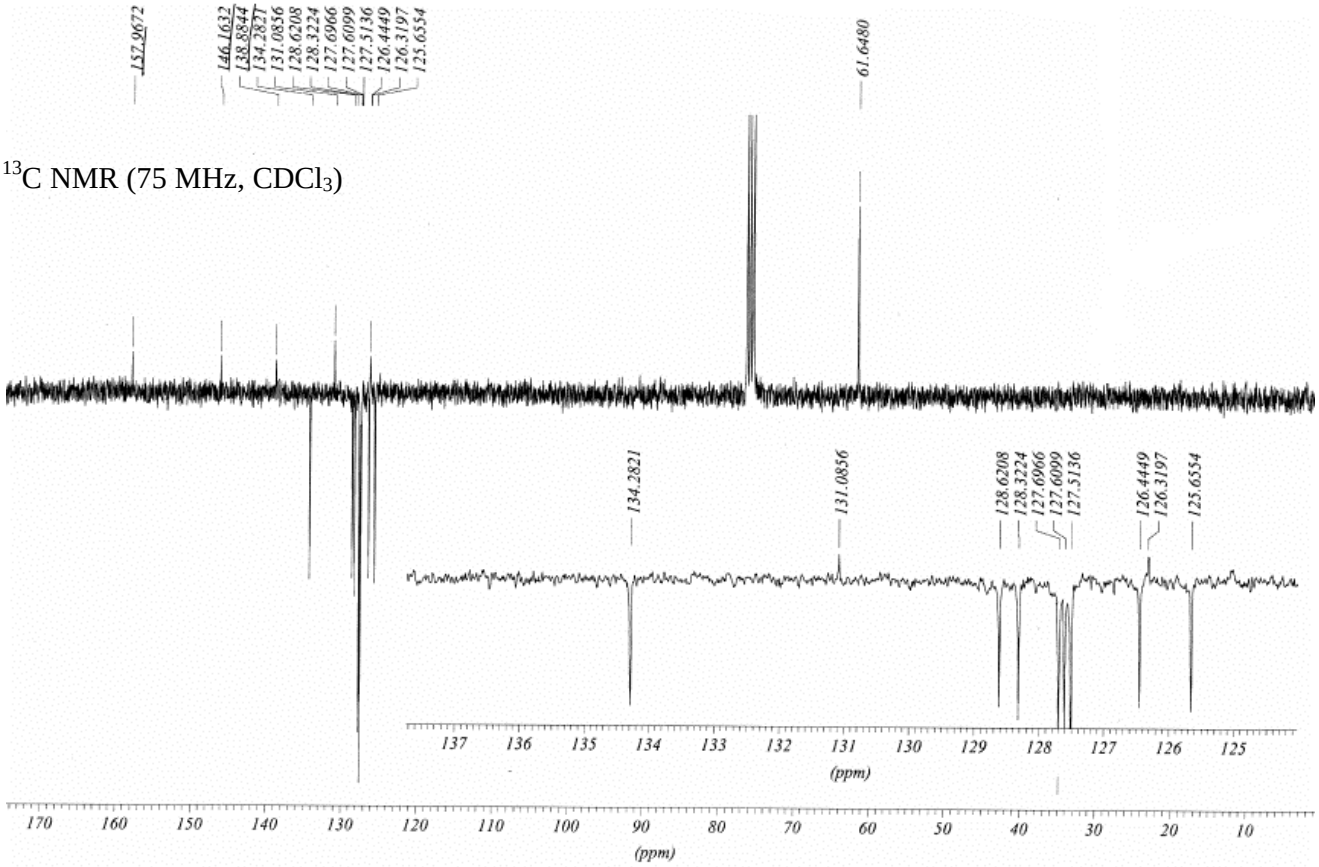
8

Ethyl 1-methyl-2-phenyl-4-benzylamino-1,4-dihydroquinoline-3-carboxylate (8). To a solution of quinolinium salt **7** (44 mg, 0.104 mmol) and NEt_3 (14.0 mg, 0.14 mmol) in CH_3CN (5 mL) was added benzylamine (12 µL, 0.114 mmol) at room temperature. The resulting solution was stirred for 1.5 h at 20°C. After evaporation of CH_3CN, water (5 mL) was added and the resulting aqueous phase was extracted with CH_2Cl_2 (3x5 mL). The organic layer was collected, dried ($MgSO_4$) and evaporated under vacuum at room temperature. The adduct product **8** was obtained in a quantitative yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (3H, t, *J* = 7.0 Hz), 3.37 (2H, q, *J* = 7.0 Hz), 3.75 (5H, broad s), 4.75 (1H, s), 7.12-7.30 (14H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 15.5, 46.5, 66.0, 123.0, 127.5, 127.7, 128.5, 128.7, 128.9, 129.3, 131.0, 134.0, 142.5, 157.0, 169.5.

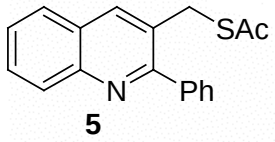
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



^{1}H NMR (300 MHz, $CDCl_3$)



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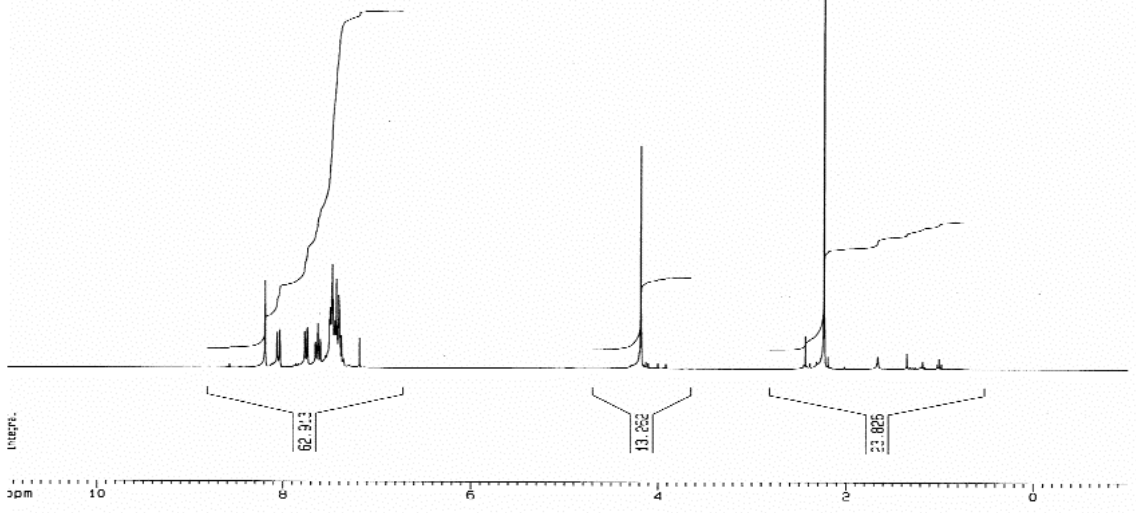
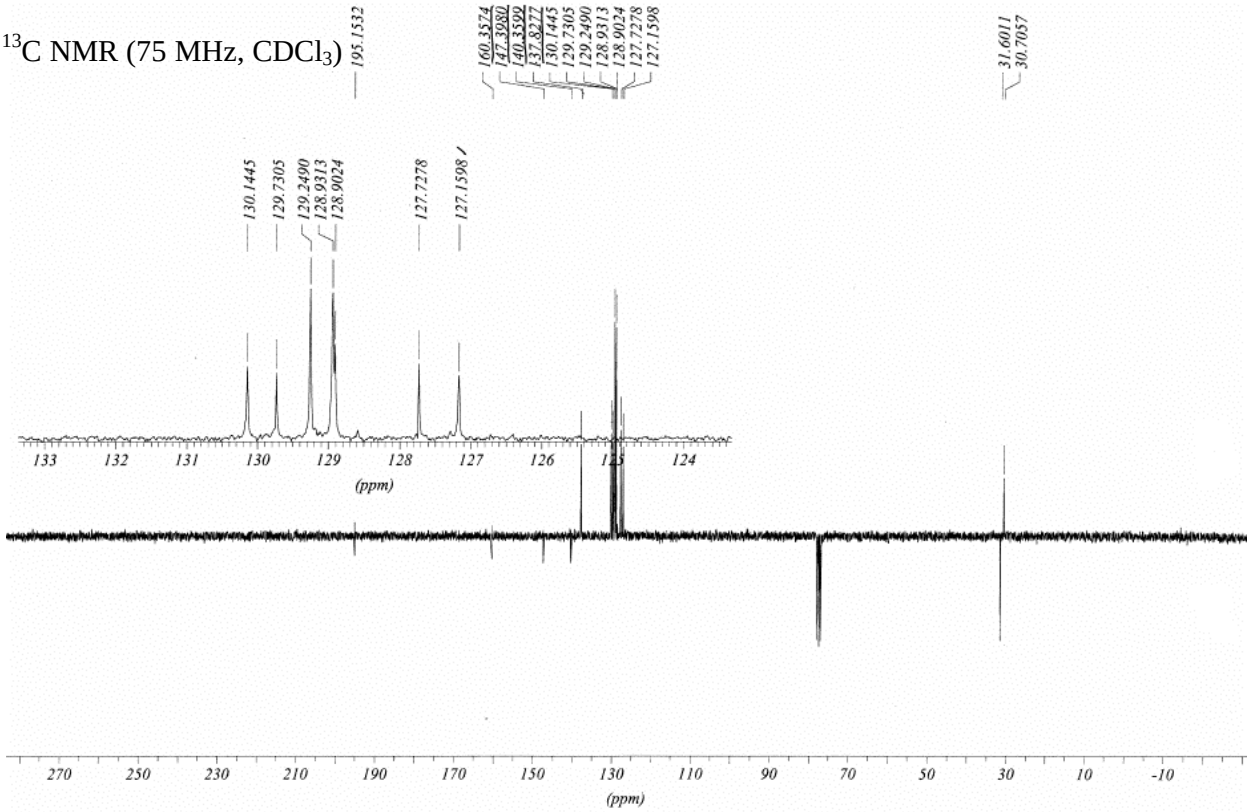
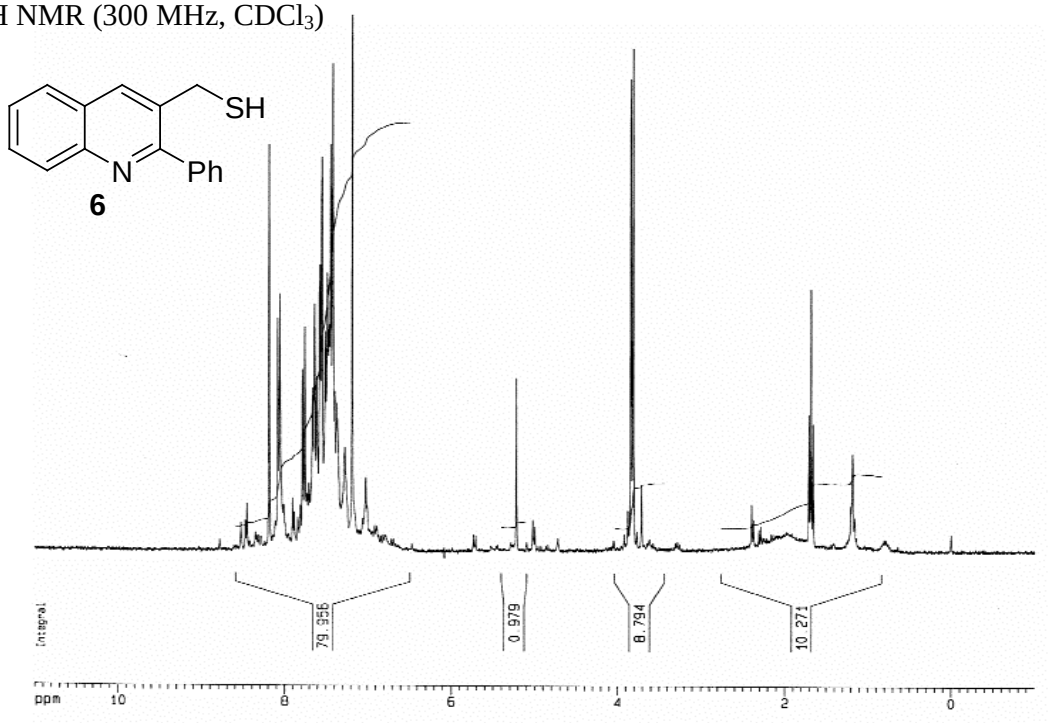
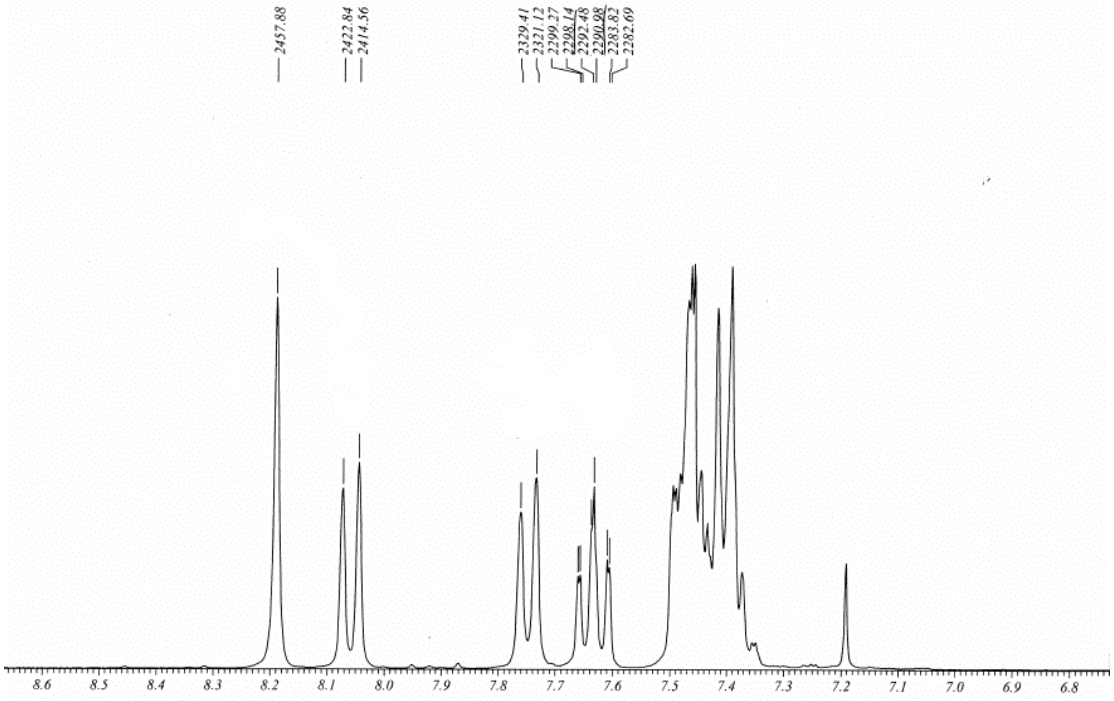


^{13}C NMR (75 MHz, $CDCl_3$)



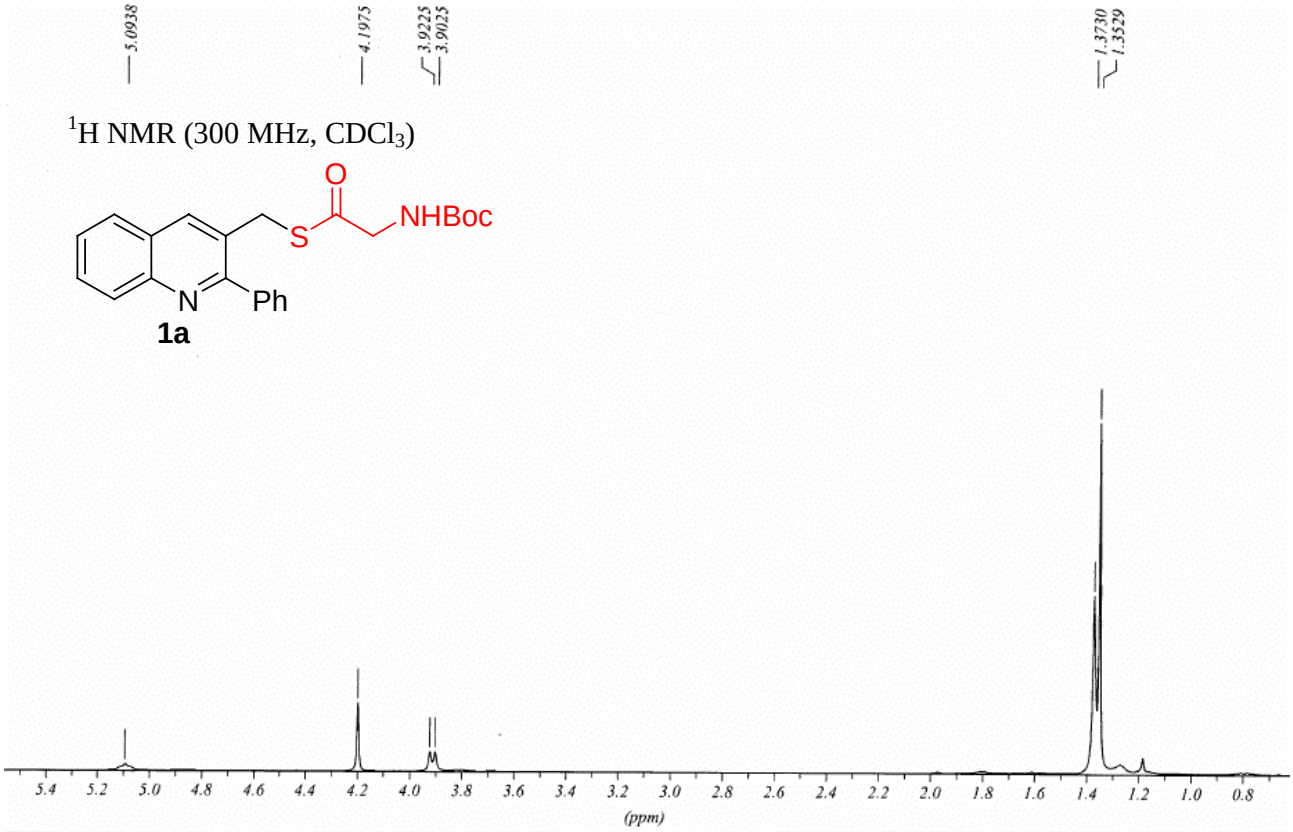
^{1}H NMR (300 MHz, $CDCl_3$)



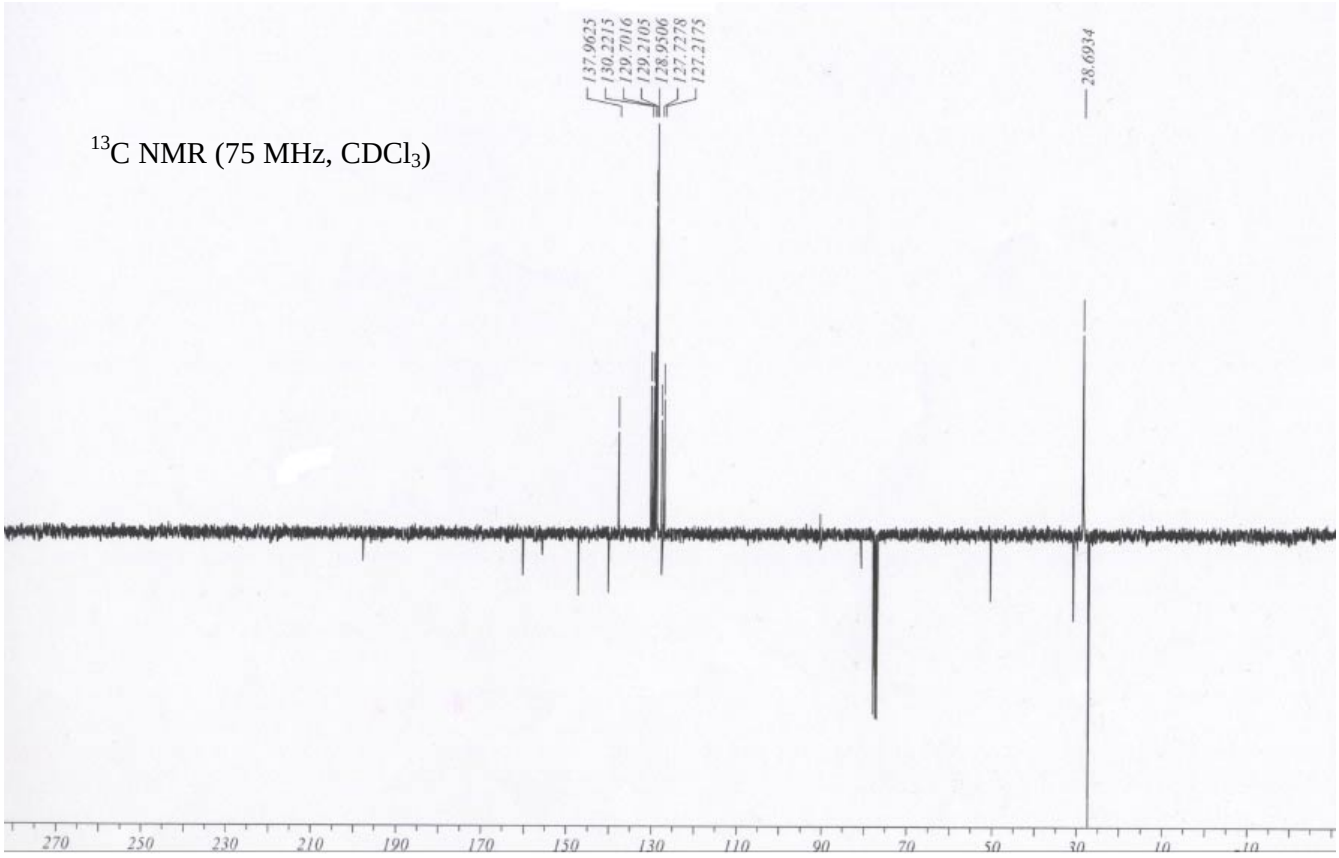


^{1}H NMR (300 MHz, $CDCl_3$)

1a

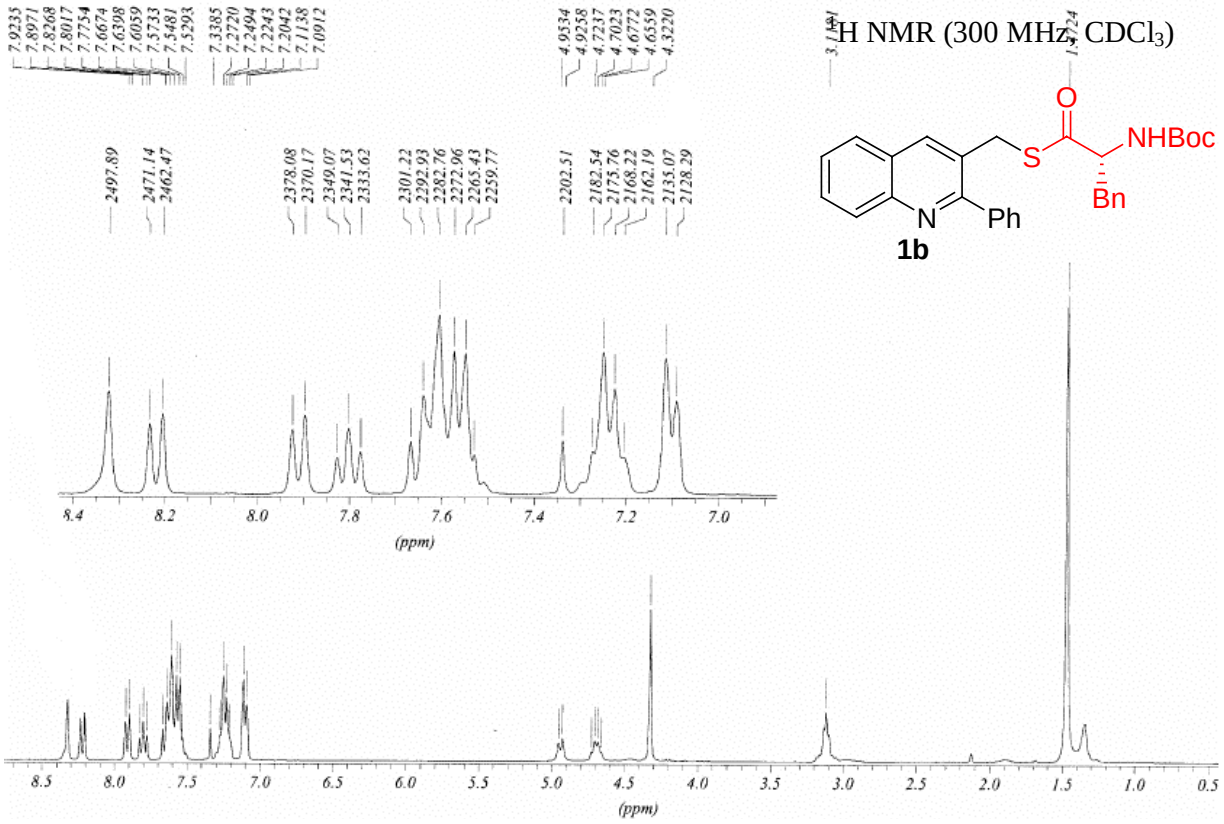


^{13}C NMR (75 MHz, $CDCl_3$)



^{1}H NMR (300 MHz, $CDCl_3$)

1b



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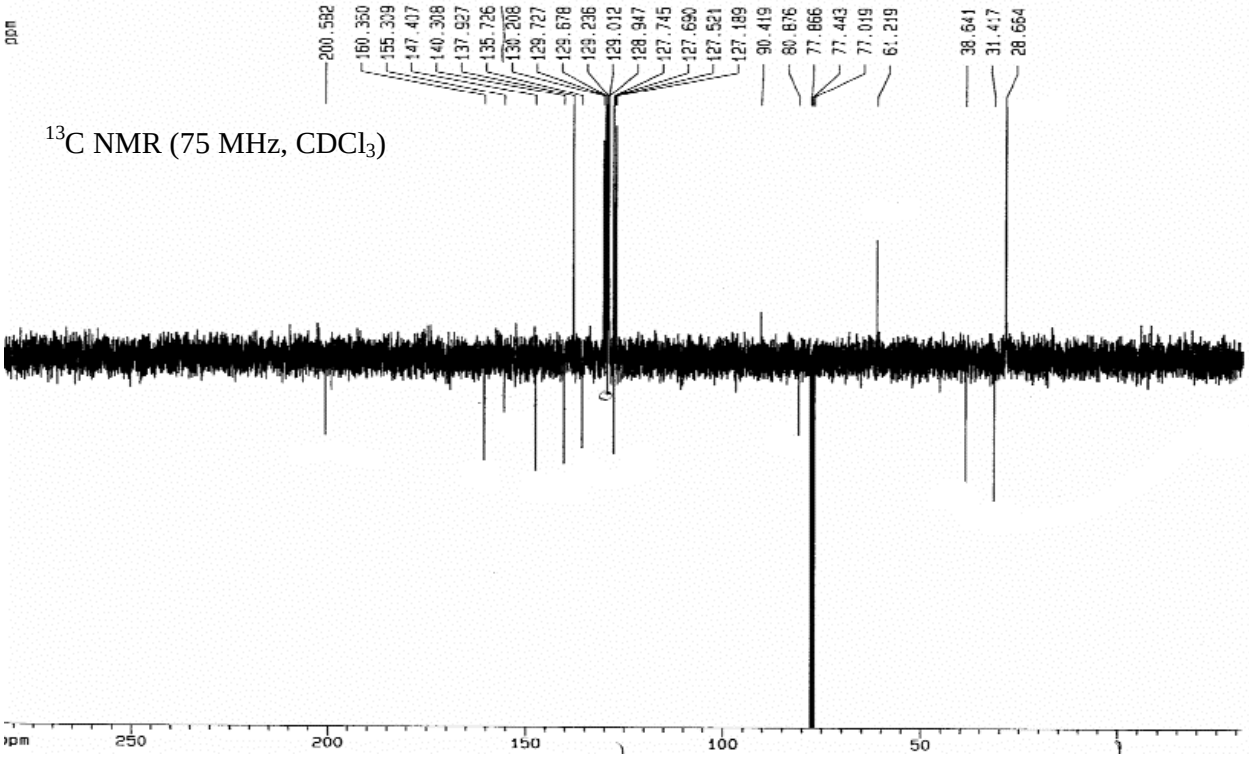
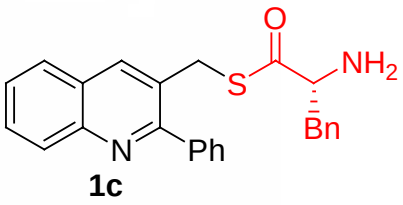
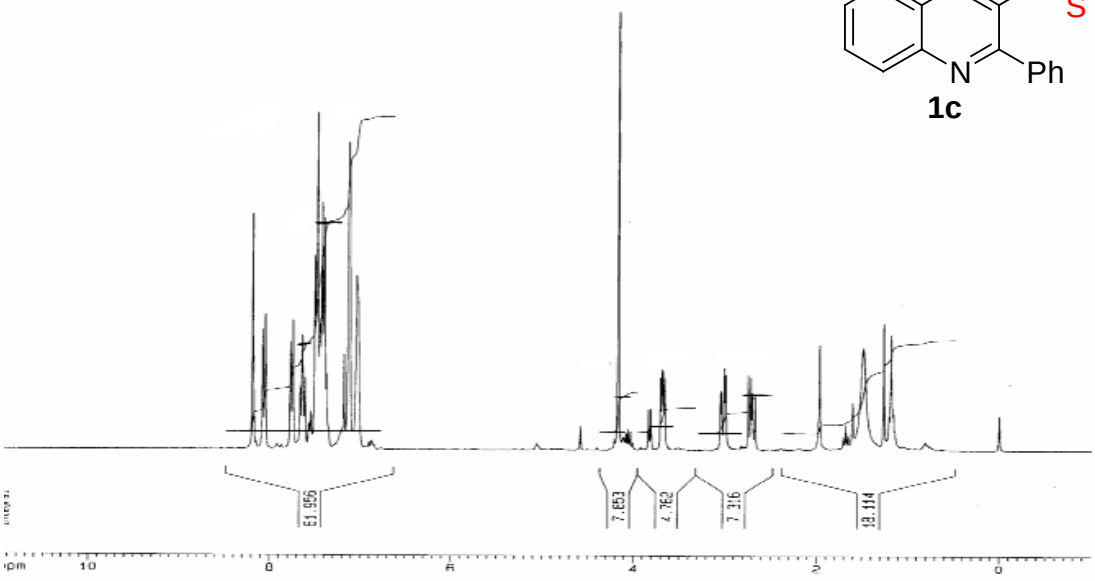


^{1}H NMR (300 MHz, $CDCl_3$)



1c



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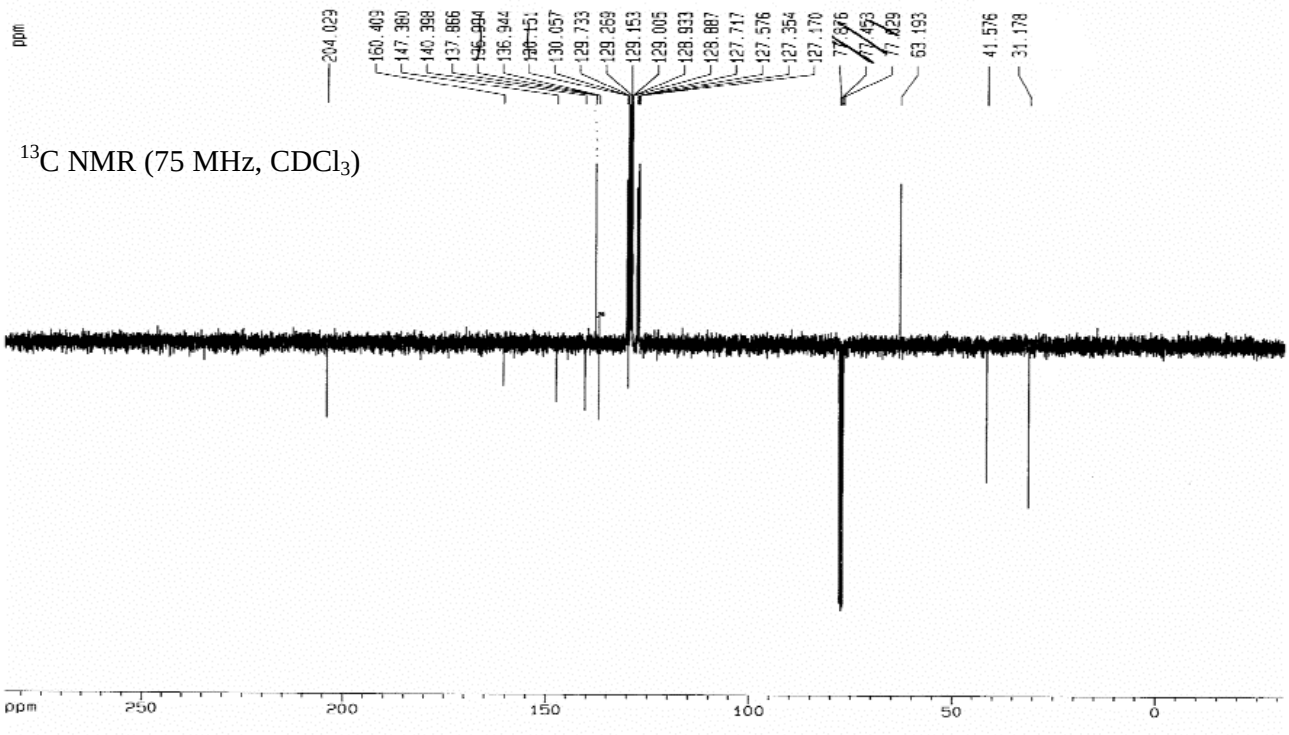
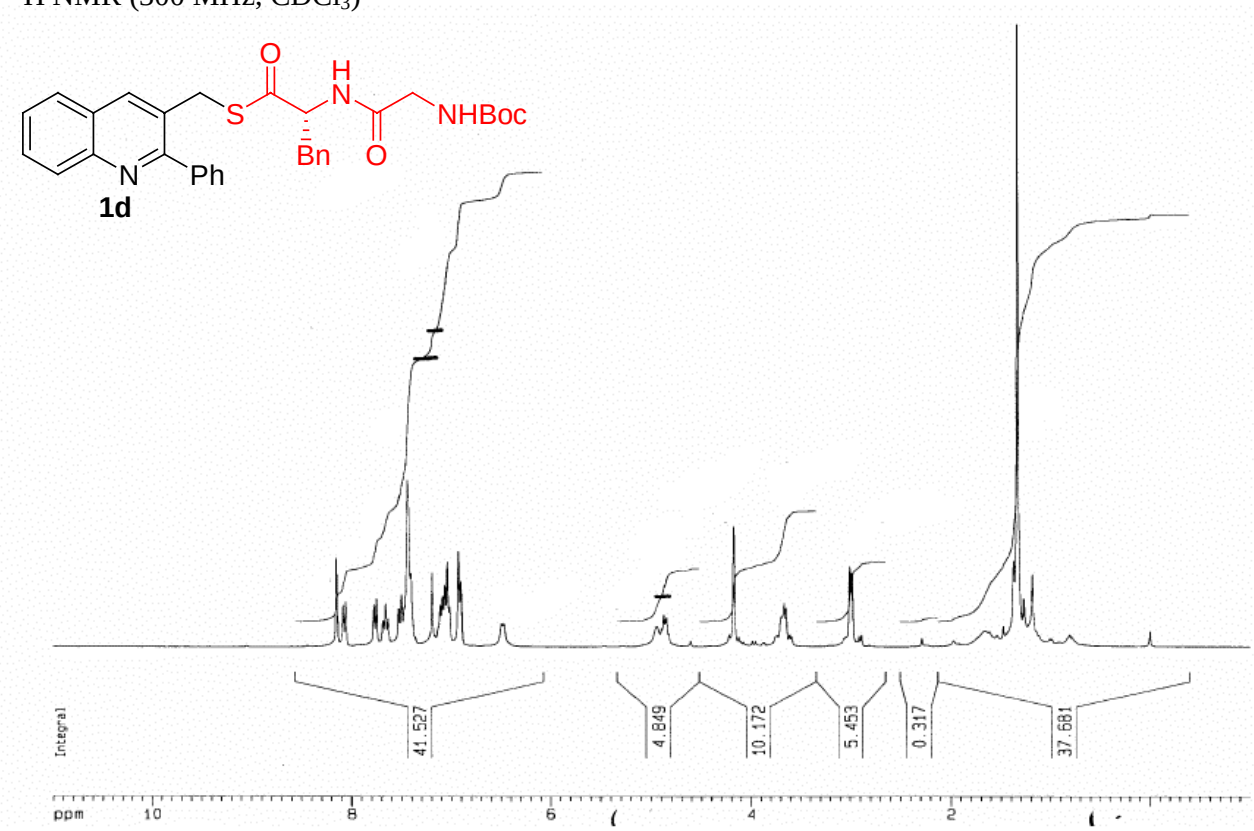
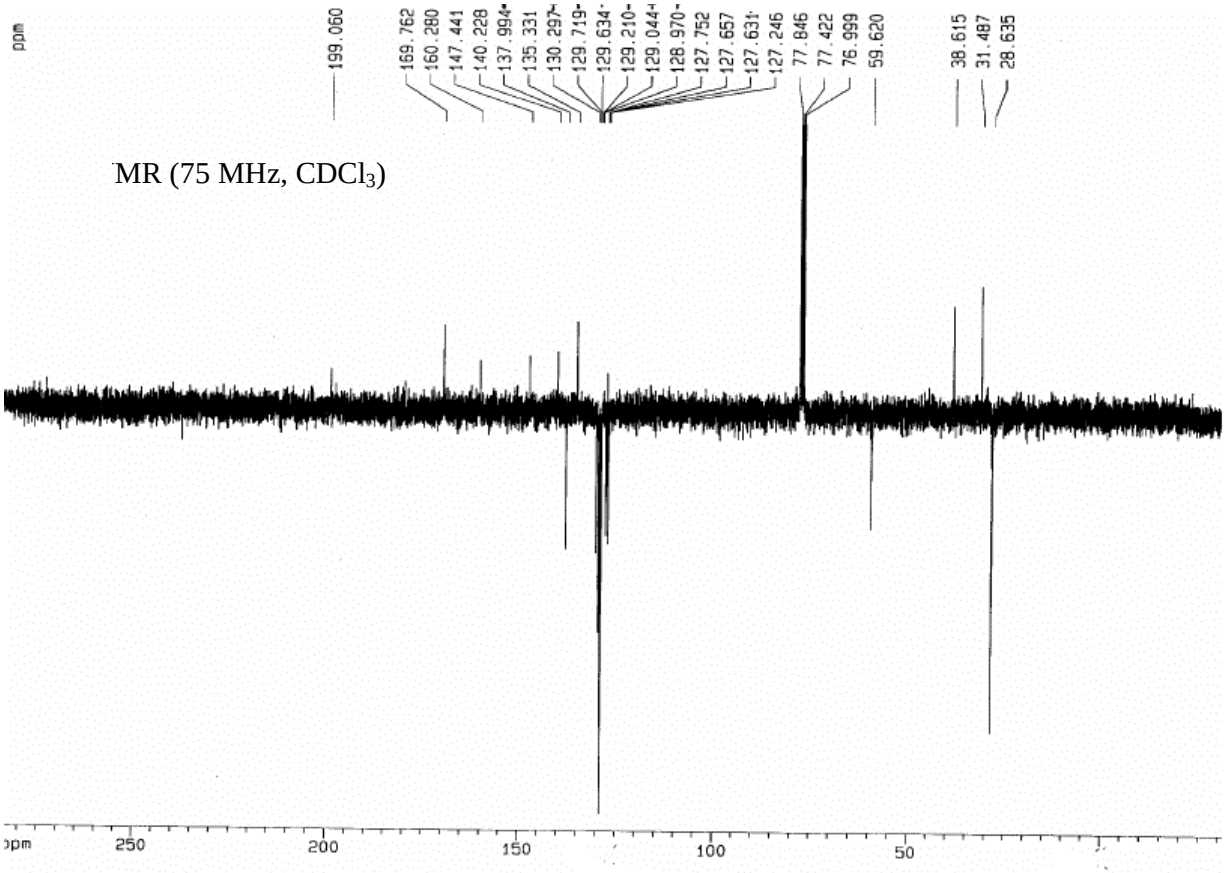


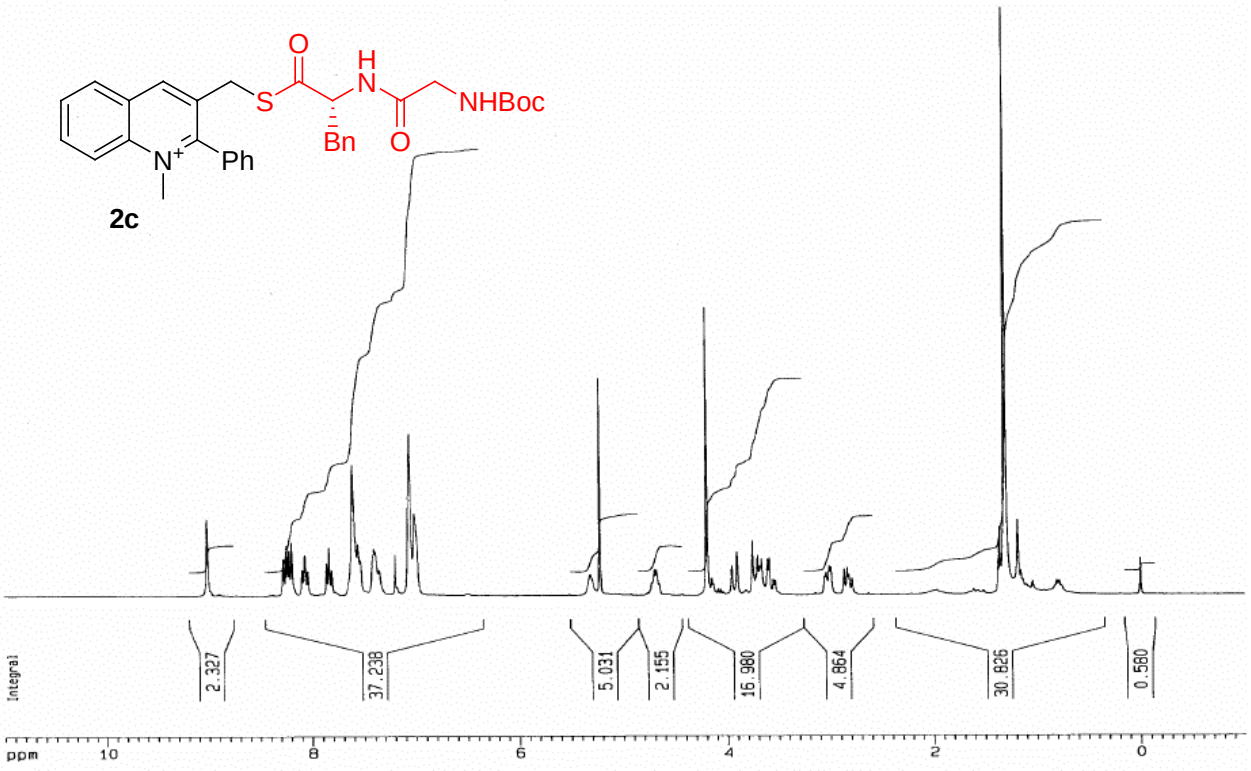
^{1}H NMR (300 MHz, $CDCl_3$)





MR (75 MHz, $CDCl_3$)

^{1}H NMR (300 MHz, $CDCl_3$)



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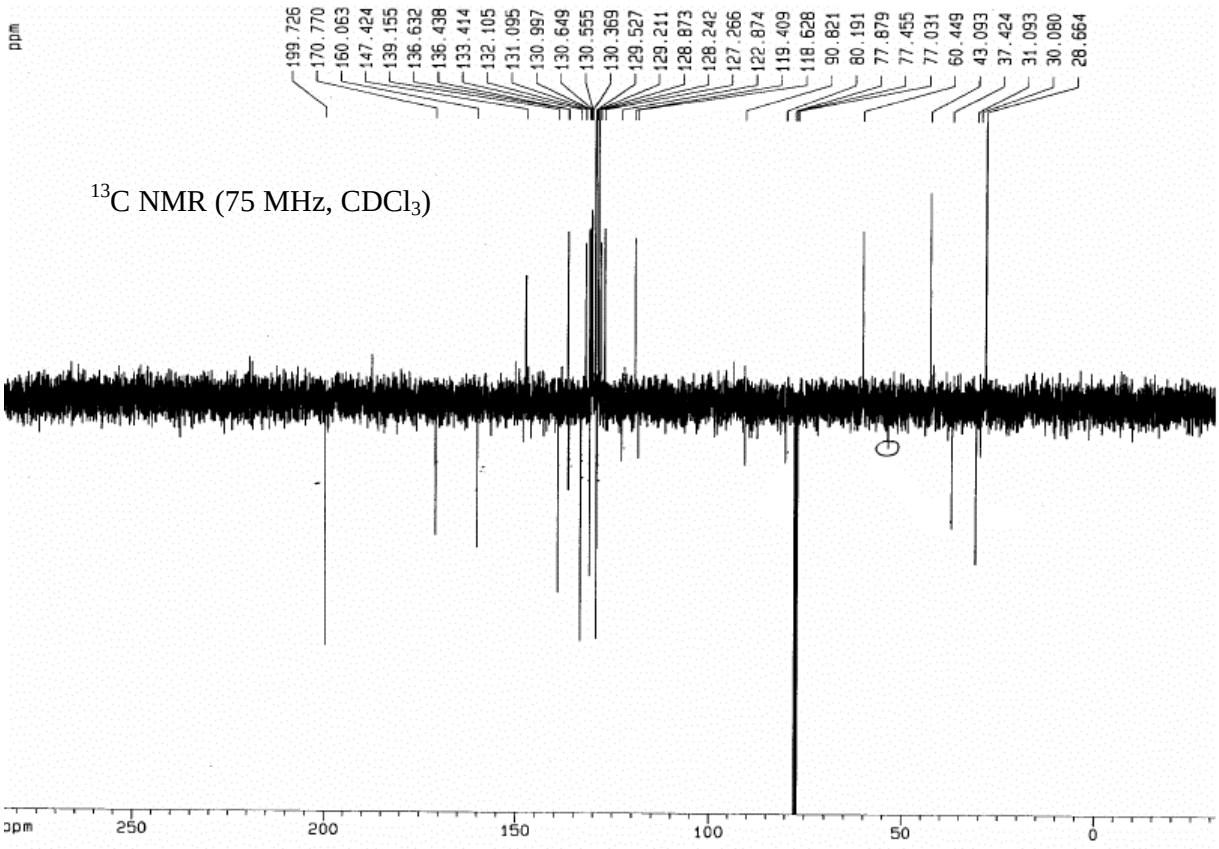
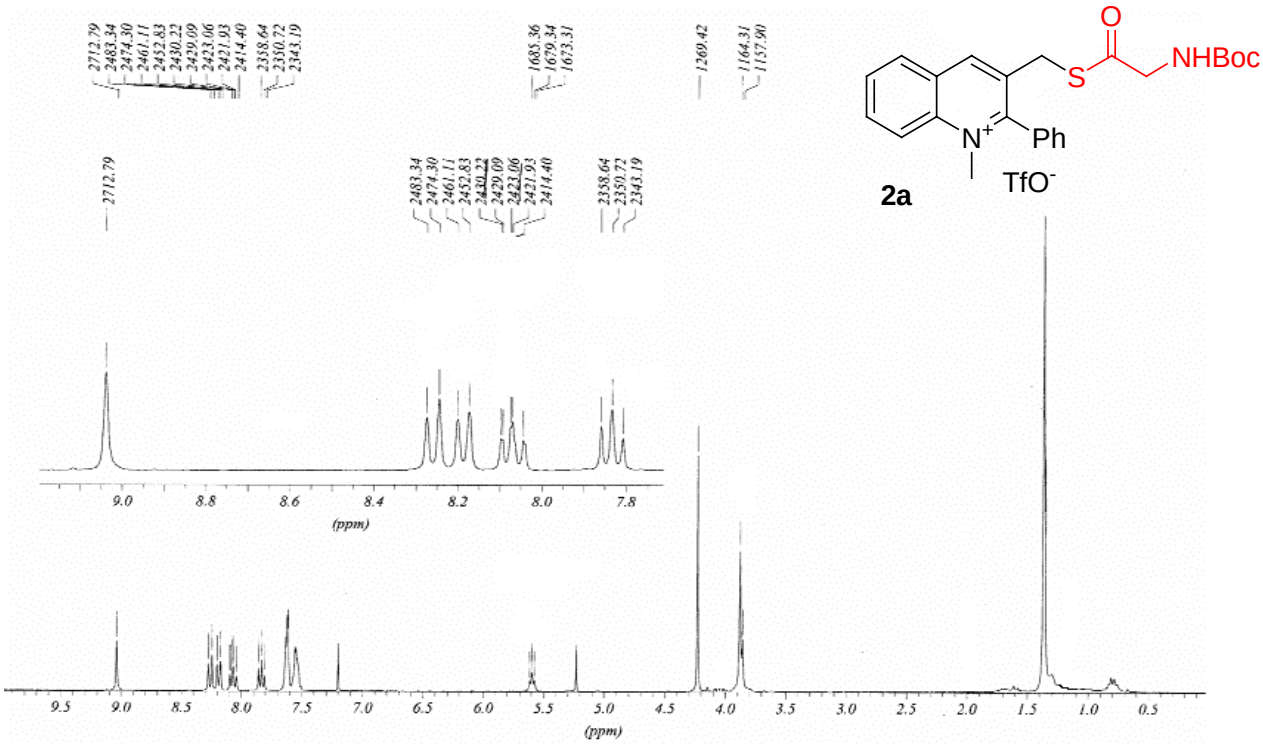
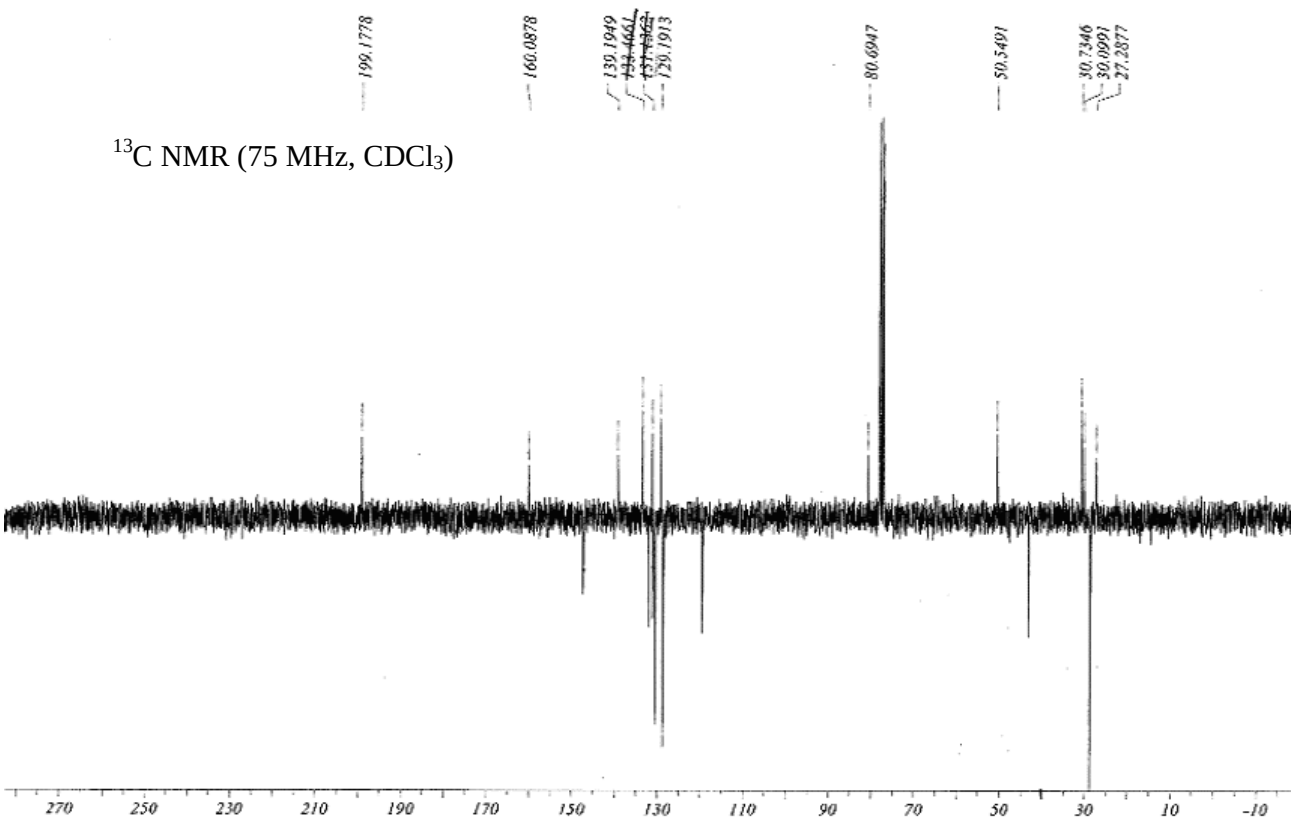


^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



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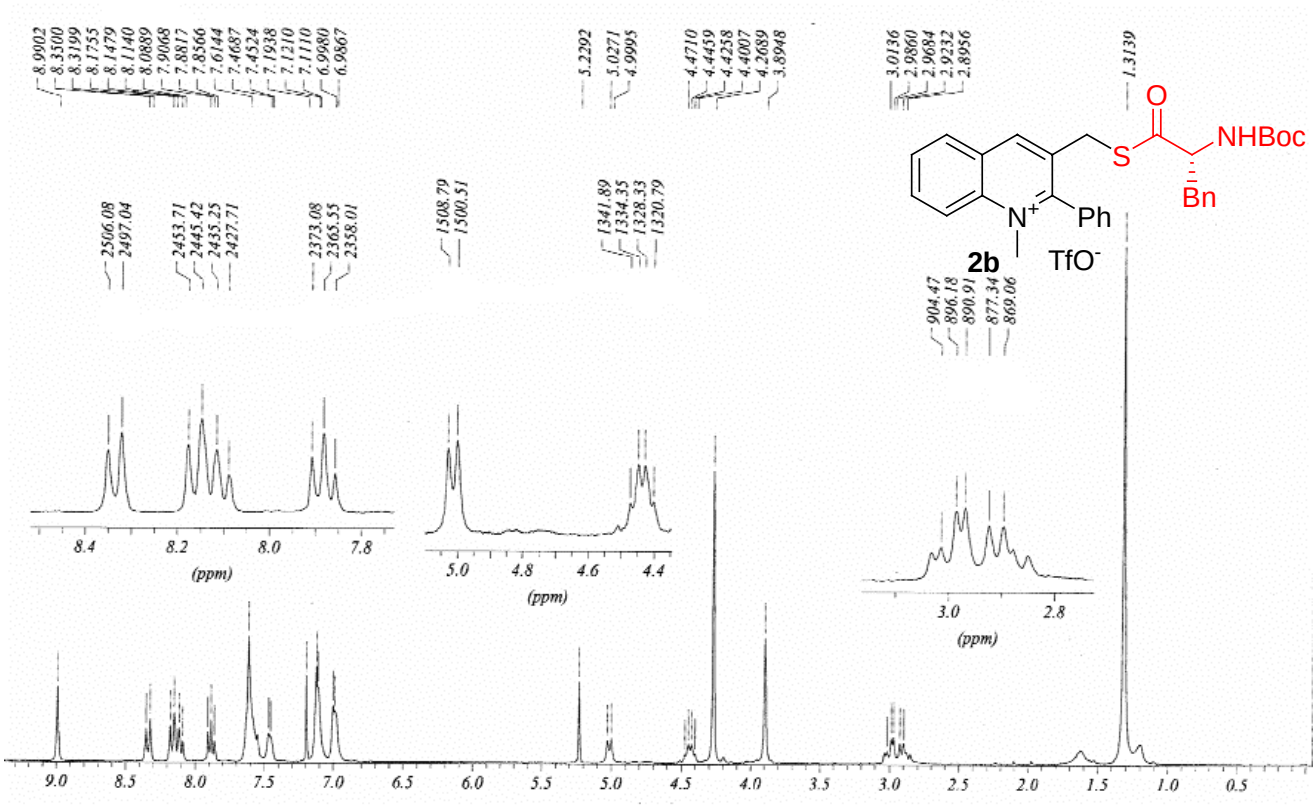
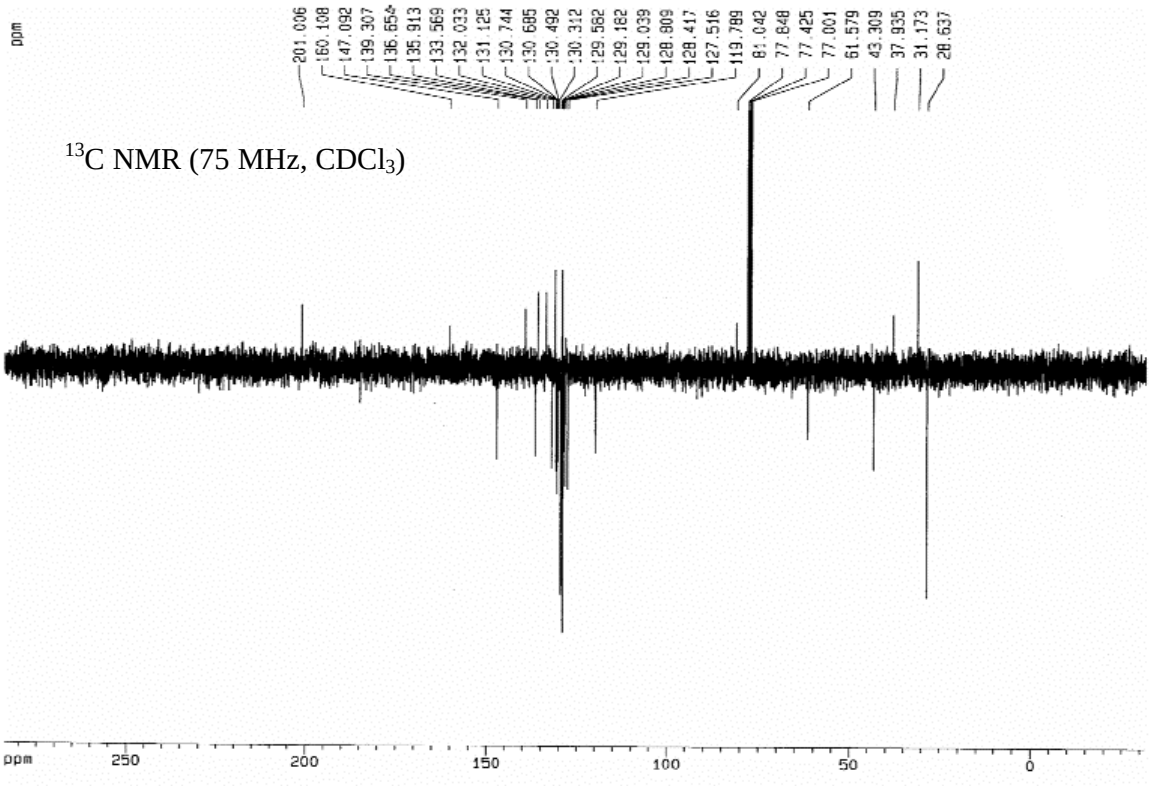
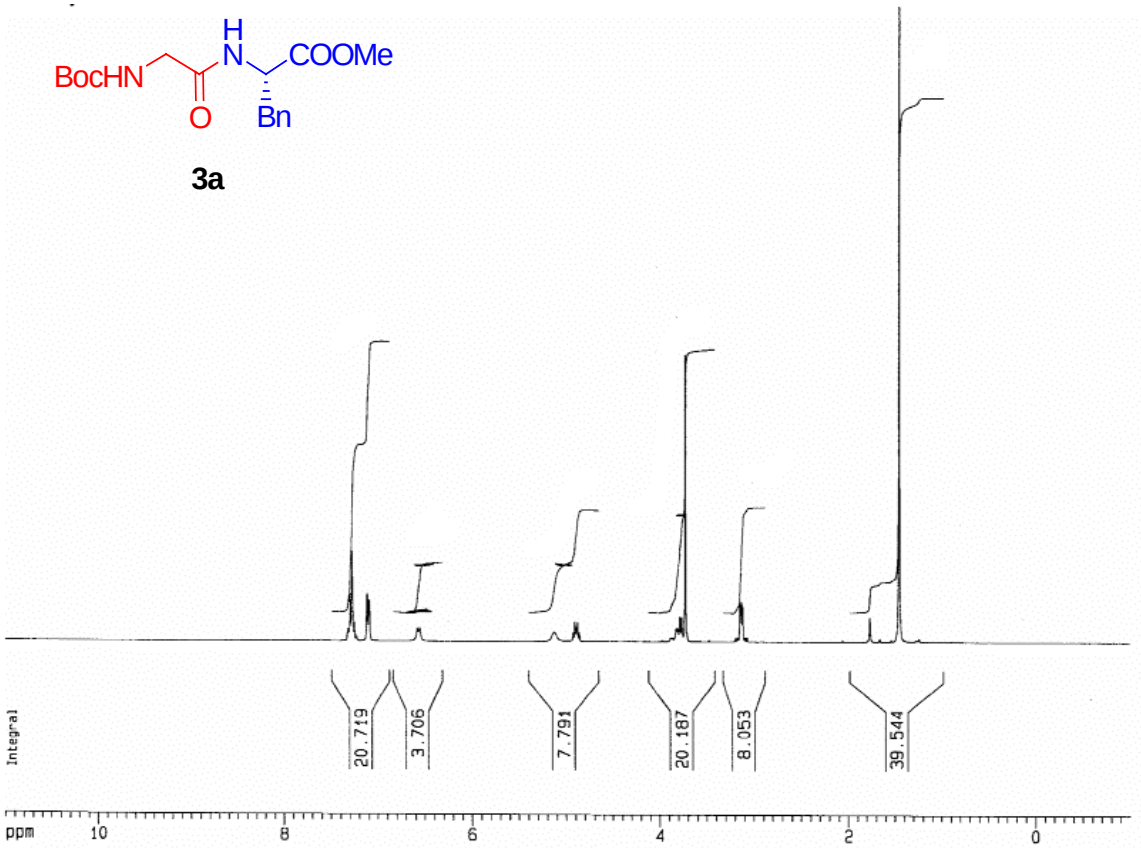


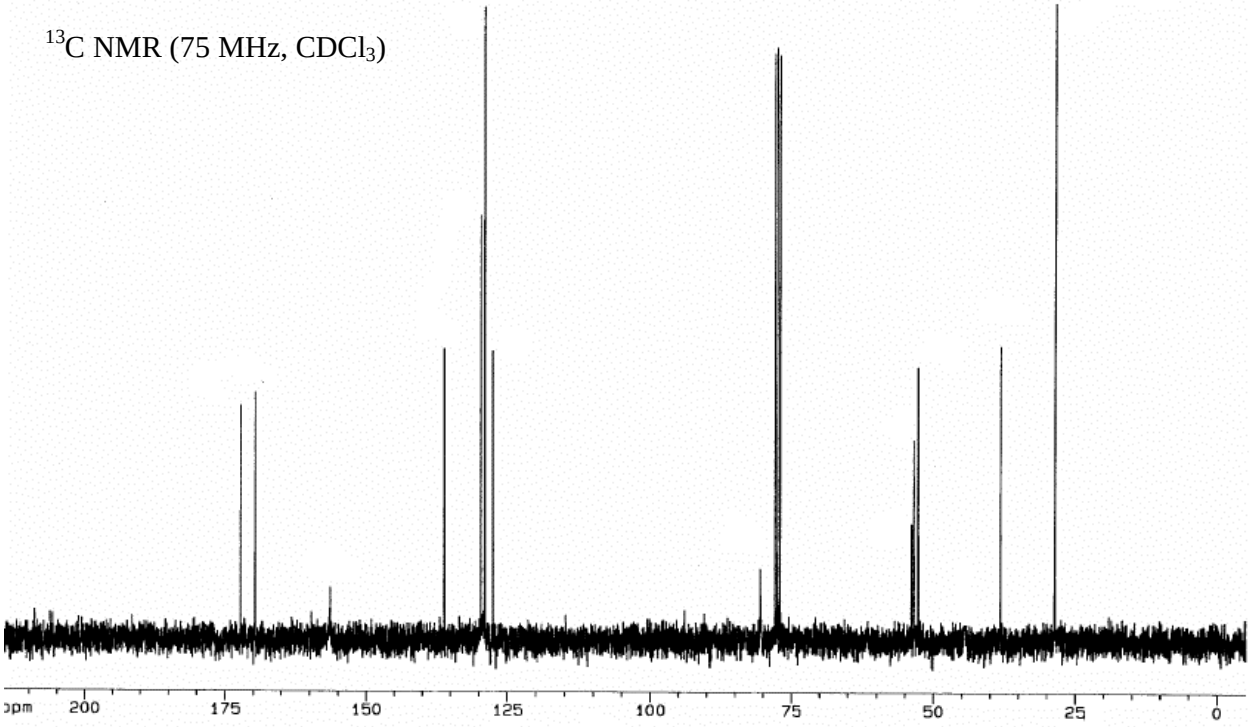


^{13}C NMR (75 MHz, $CDCl_3$)

^{1}H NMR (300 MHz, $CDCl_3$)

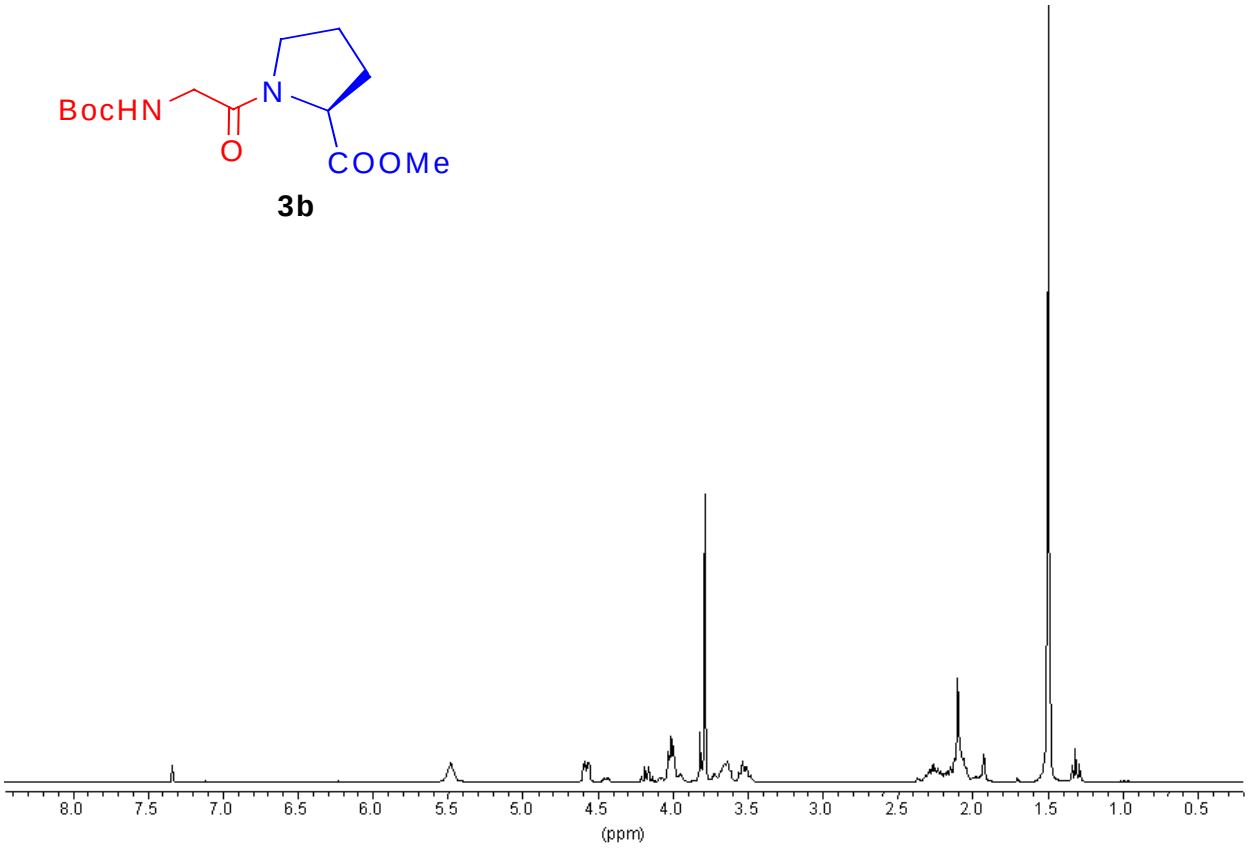


^{13}C NMR (75 MHz, $CDCl_3$)

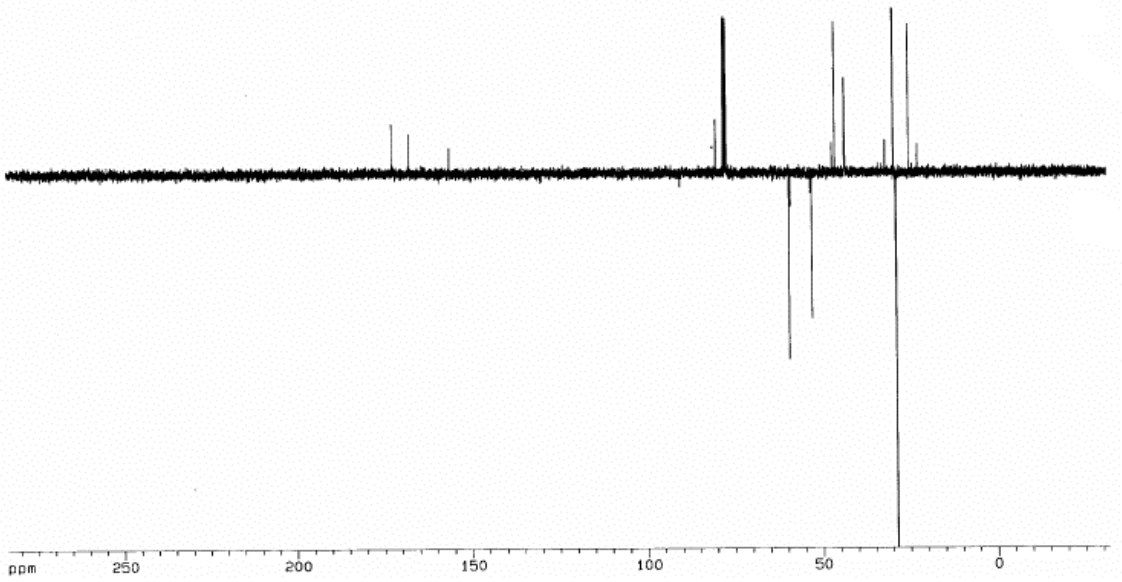


^{1}H NMR (300 MHz, $CDCl_3$)

3b

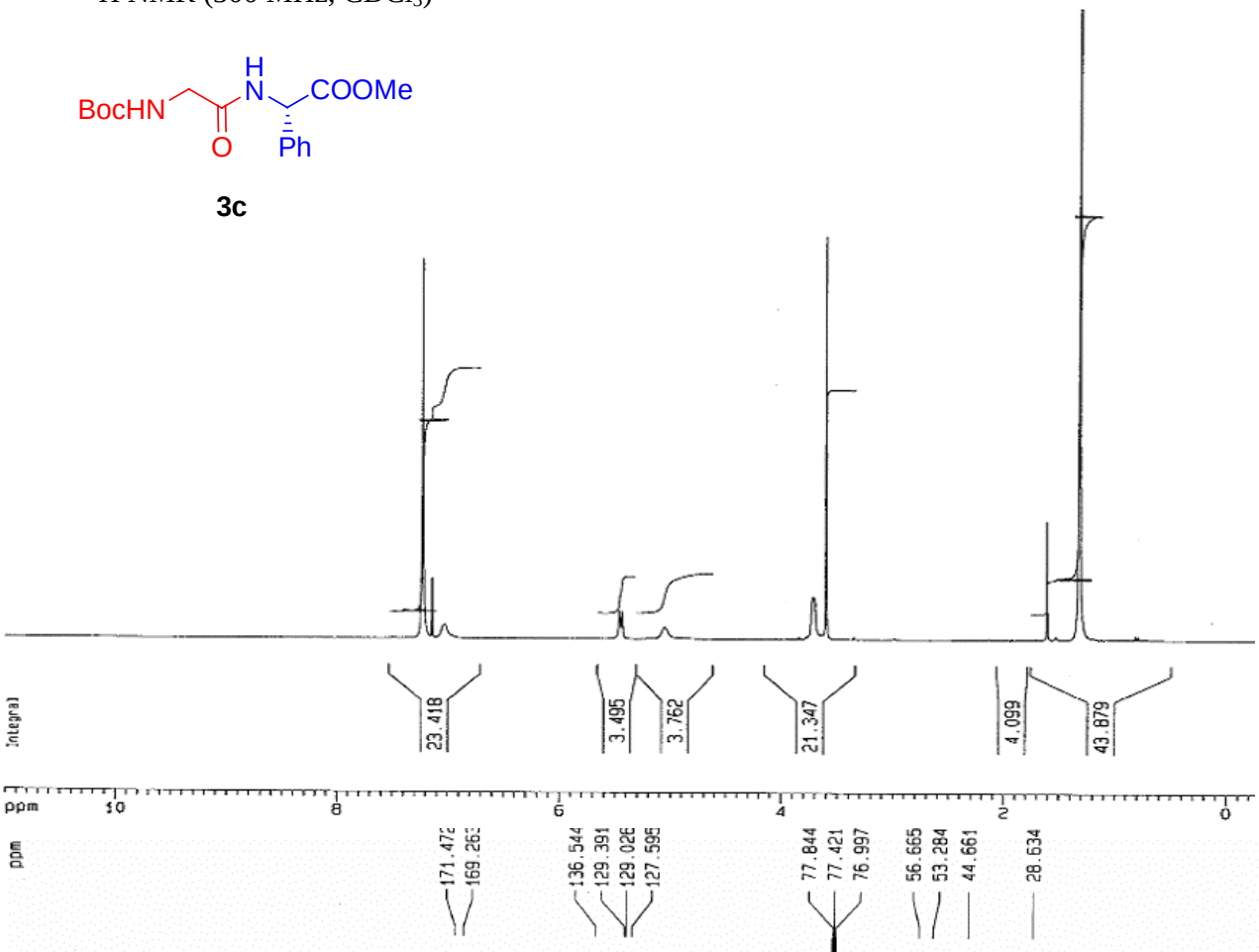


^{13}C NMR (75 MHz, $CDCl_3$)

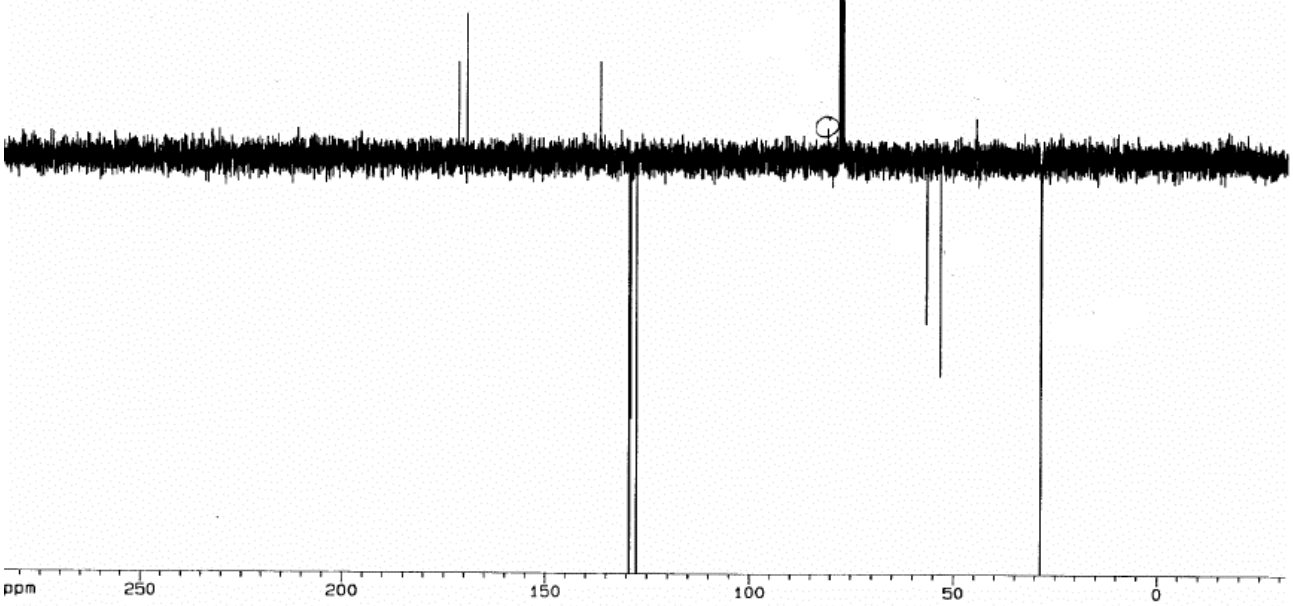


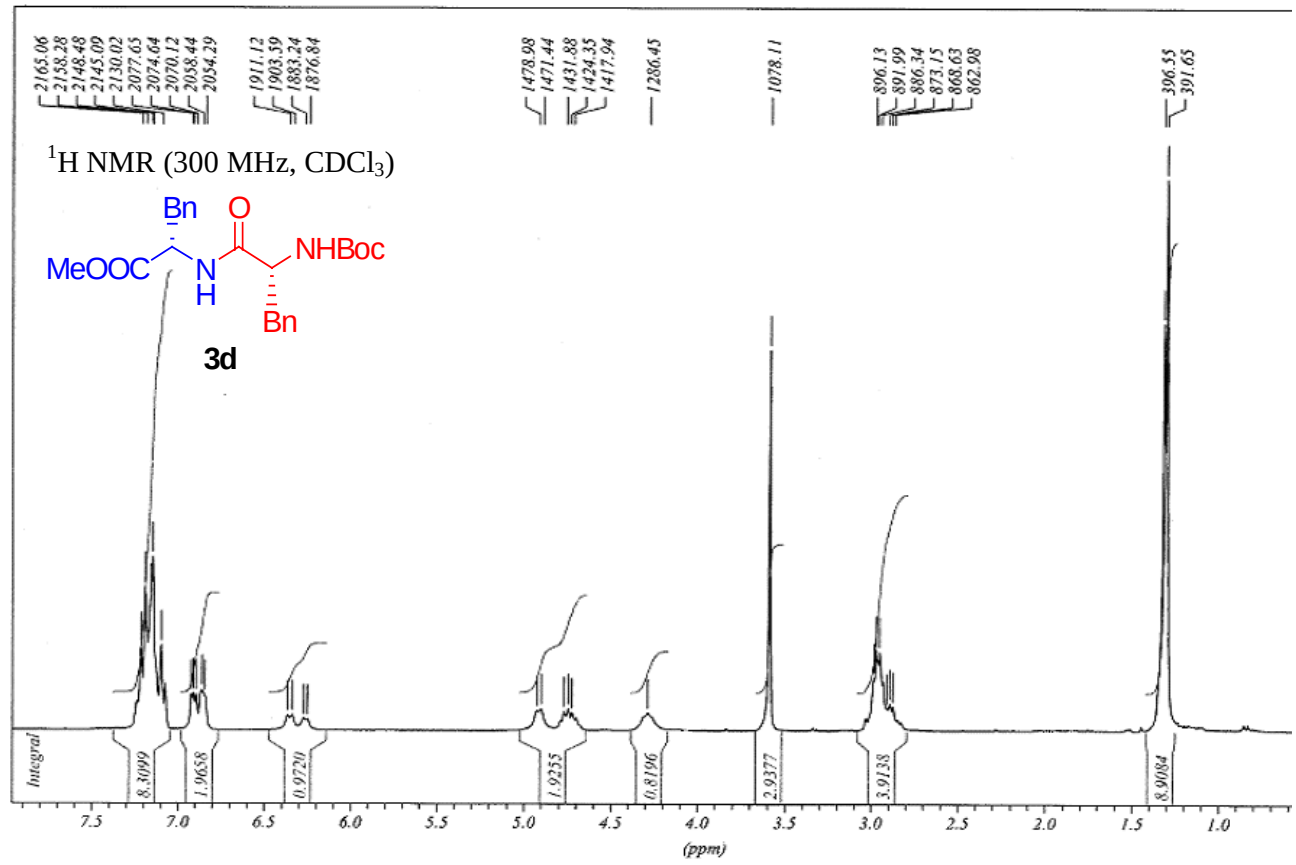
- ^{1}H NMR (300 MHz, $CDCl_3$)

3c



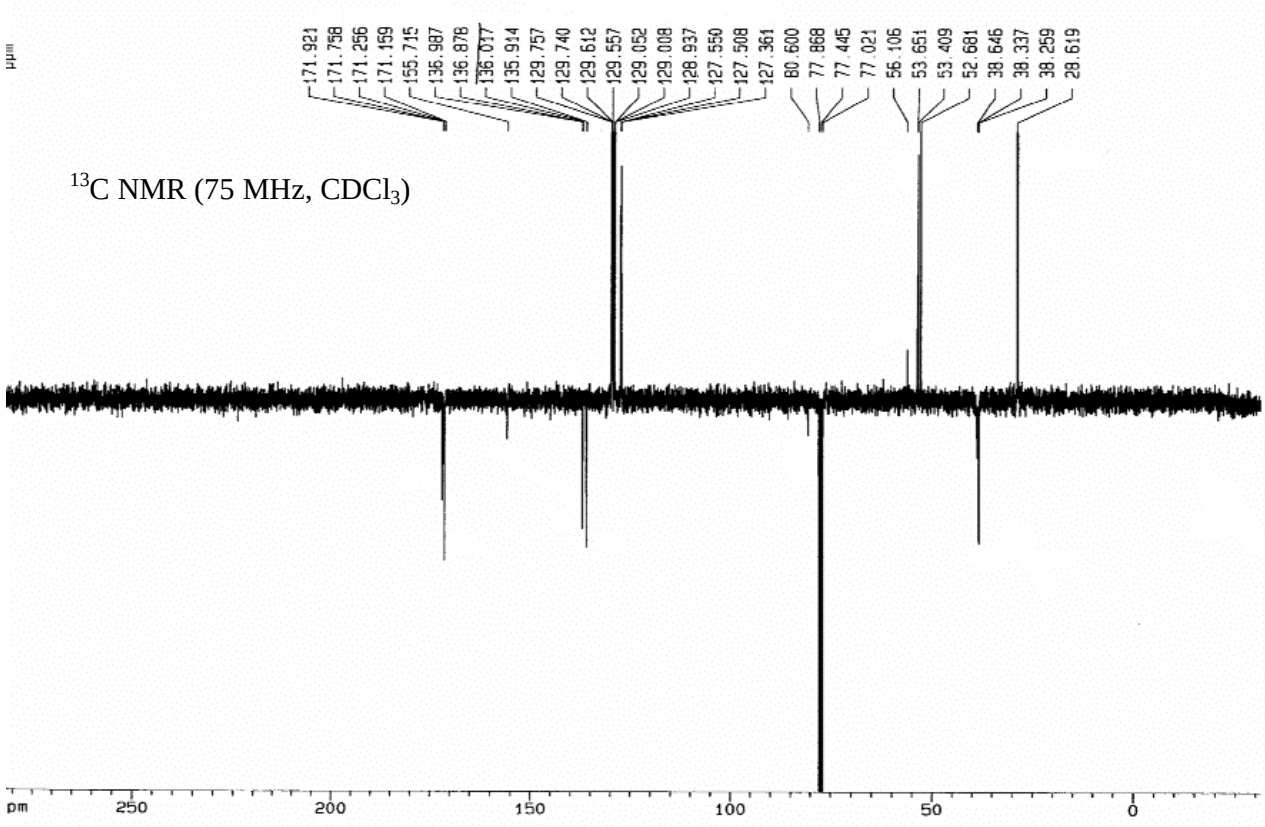
- ^{13}C NMR (75 MHz, $CDCl_3$)





^{1}H NMR (300 MHz, $CDCl_3$)

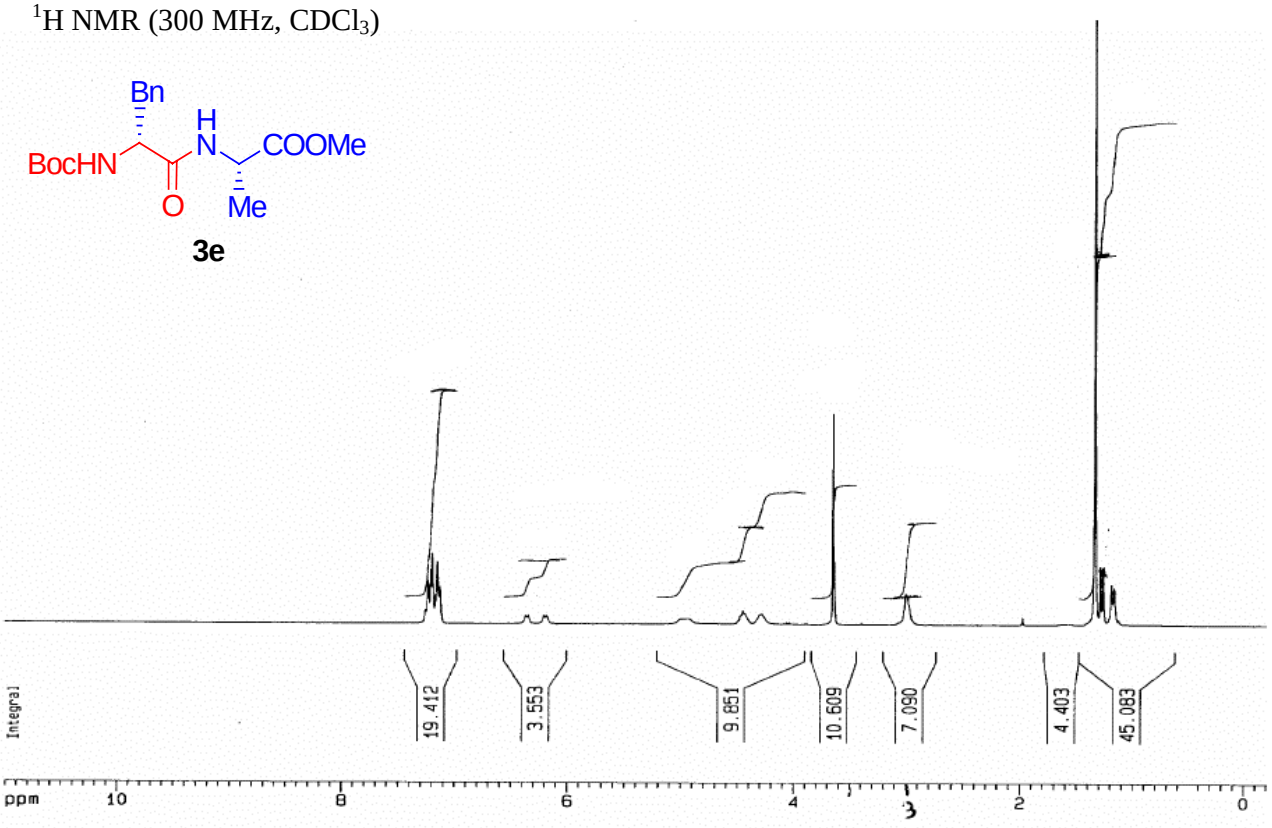
3d



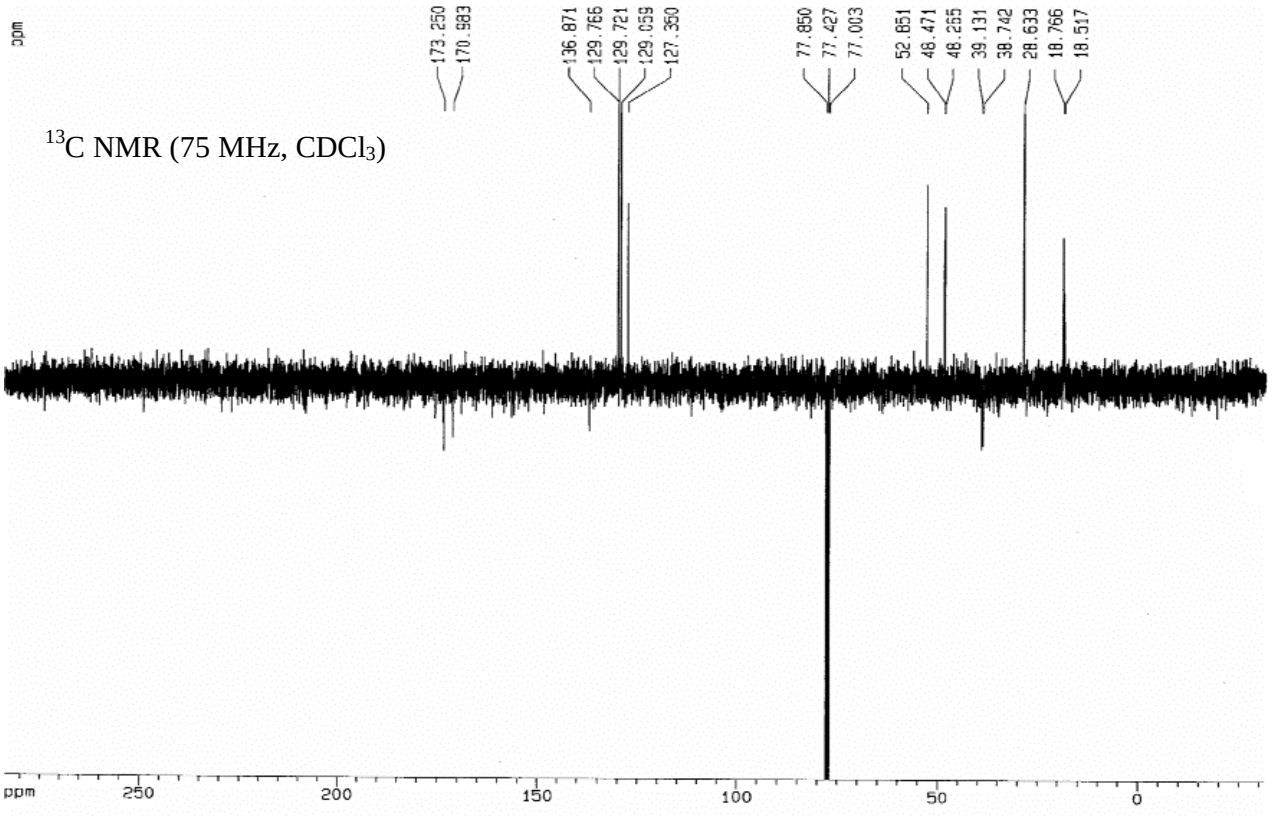
^{13}C NMR (75 MHz, $CDCl_3$)

^{1}H NMR (300 MHz, $CDCl_3$)

3e

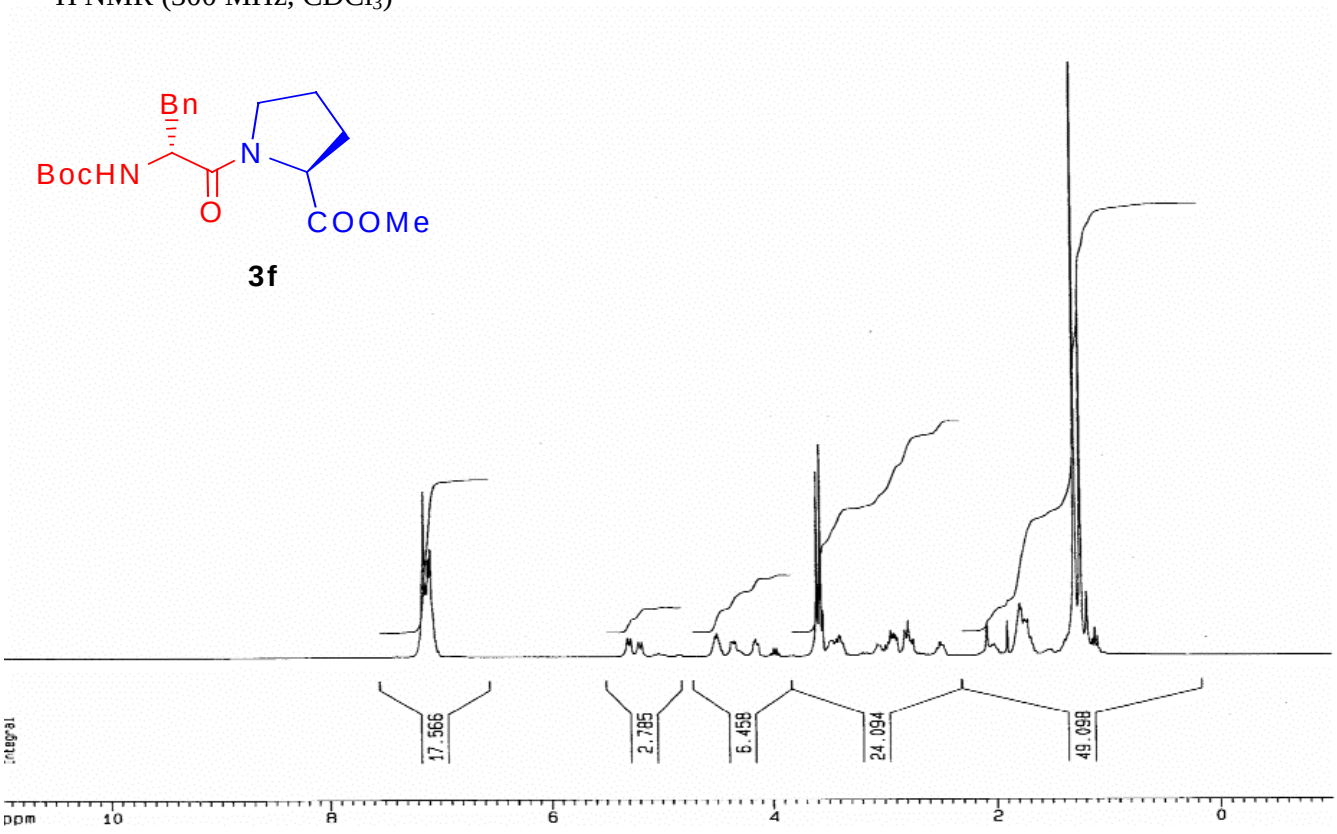


^{13}C NMR (75 MHz, $CDCl_3$)

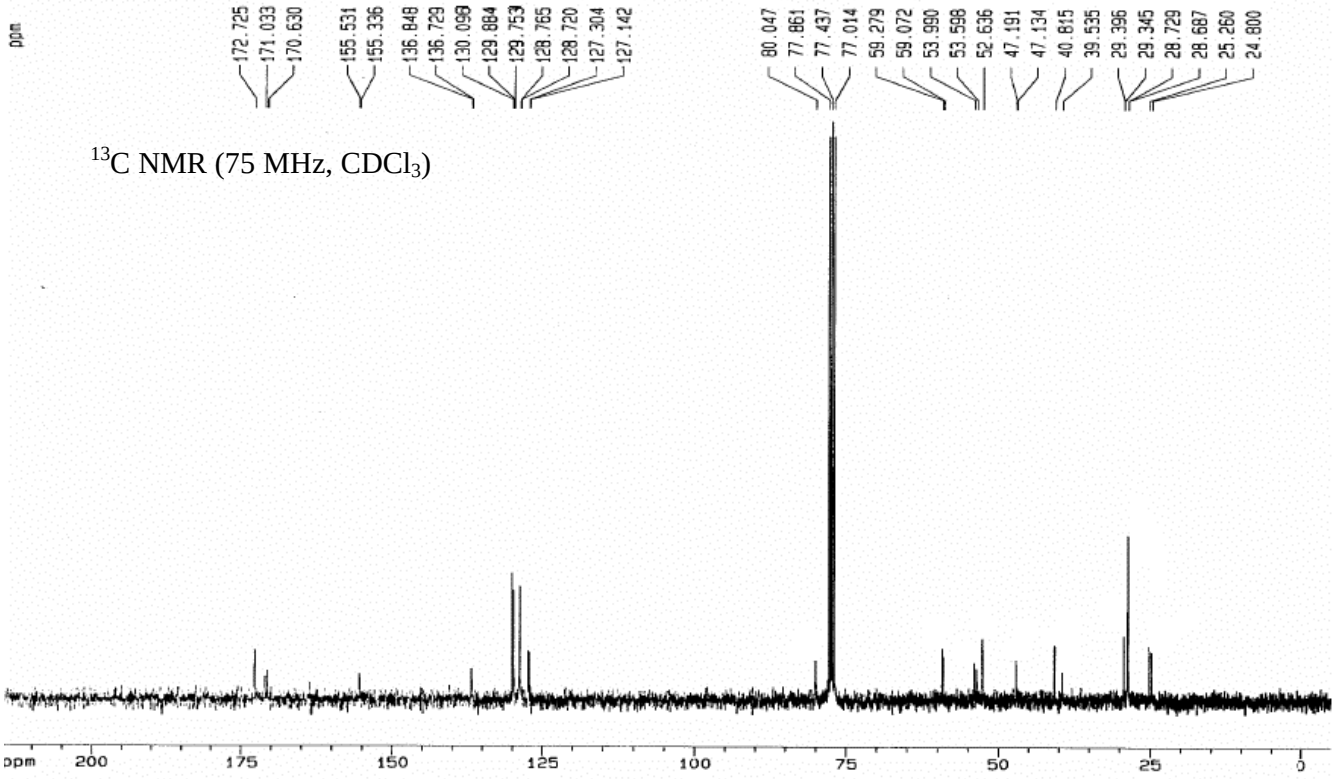


^{1}H NMR (300 MHz, $CDCl_3$)

3f



^{13}C NMR (75 MHz, $CDCl_3$)



^{1}H NMR (300 MHz, $CDCl_3$)

3g