Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Expedient Synthesis of α-Substituted Fluoroethenes

Samir K. Mandal, Arun K. Ghosh, Rakesh Kumar and Barbara Zajc*

Department of Chemistry, The City College and The City University of New York, 160 Convent Avenue, New York, New York 10031

TABLE OF CONTENTS

General Experimental Methods

THF was distilled over $LiAlH_4$, and then over sodium, methylene chloride was distilled over CaH_2 powder, and acetone over anhydrous K_2CO_3. Toluene was distilled over sodium. DMF was obtained from commercial sources and was used without further purification. For reactions, which were performed under a nitrogen atmosphere, glassware was flame dried under vacuum. LDA (2.0 M solution in heptane/THF/EtPh) was obtained from commercial sources. Fluorinating reagent *N*-fluorobenzenesulfonimide (NFSI) was a gift from Honeywell (Dr. Andrew Poss), but is also commercially available. Thin layer chromatography was typically performed on aluminum foil-backed silica gel plate (200 μm), except for **3h**, where glass-backed silica gel plate (250 μm layer thickness) was used. All other reagents were obtained from commercial sources and used without further purification. ^{1}H NMR spectra were recorded at 500 MHz in $CDCl_3$, DMSO-d_6, and are referenced to the residual protonated solvent resonance. ^{13}C NMR spectra were recorded at 125 MHz and were referenced to $CDCl_3$ or DMSO-d_6. ^{19}F NMR spectra were recorded at 282 MHz using $CFCl_3$ as internal standard. Chemical shifts (δ) are reported in parts per million and coupling constants (J) are in hertz.

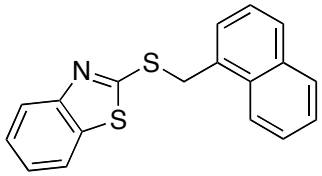
Synthesis of 2-[(Aryl)methylthio]benzo[*d*]thiazoles

Synthesis of 2-(benzylthio)benzo[*d*]thiazole,[1] 2-[(naphthalen-2-yl)methylthio]benzo[*d*]thiazole,[1] and 2-{[2-(thiophen-2-yl)thiazol-4-yl]methylthio}benzo[*d*]thiazole[1] has previously been reported by us.

From Halomethyl Arenes: General Procedure

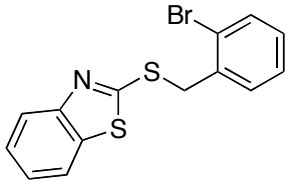
To a solution of halomethyl arene (1 molar equiv) in DMF (5.5 mL per mmol of halomethyl arene), the sodium salt of 2-mercapto-1,3-benzothiazole (1.2 molar equiv) was added. The reaction mixture was stirred overnight at rt (unless stated otherwise), and complete consumption of the starting material was observed by TLC. The reaction mixture was diluted with water and extracted 3 times with ethyl acetate. The combined organic layer was thoroughly washed with water and finally with brine, dried over anhydrous Na_2SO_4 and the solvent evaporated under reduced pressure. The products were either used in the next step as crude, or were purified by column chromatography on silica gel (100-200 mesh, for eluting solvent see specific headings) to give the corresponding sulfide.

2-[(Naphthalen-1-yl)methylthio]benzo[d]thiazole



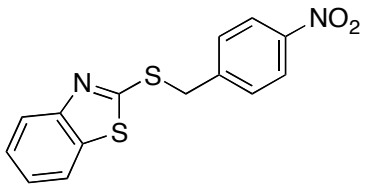
Reaction mixture was heated overnight at 60-65 ºC. 1-(Chloromethyl)naphthalene: 2.00 g (11.3 mmol); sodium salt of 2-mercapto-1,3-benzothiazole: 2.57 g (13.6 mmol, 1.2 molar equiv); DMF: 63.0 mL. Yield of 2-[(naphthalen-1-yl)methylthio]benzo[*d*]thiazole:[2] 3.45 g (99%, a white solid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.46. Crude product was subjected to oxidation. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.96 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.89 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.83 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.77 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.65 (d, 1H, *J* = 6.8 Hz, Ar-H), 7.59-7.51 (m, 2H, Ar-H), 7.48-7.41 (m, 2H, Ar-H), 7.32 (t, 1H, *J* = 7.3 Hz, Ar-H), 5.13 (s, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.7, 153.3, 135.5, 134.1, 131.7, 131.5, 129.1 (2 C), 128.3, 126.7, 126.24, 126.18, 125.6, 124.5, 123.8, 121.7, 121.2, 35.8.

2-[(2-Bromobenzyl)thio]benzo[d]thiazole



1-Bromo-2-(bromomethyl)benzene: 2.00 g (8.00 mmol); sodium salt of 2-mercapto-1,3-benzothiazole: 1.81 g (9.58 mmol, 1.2 molar equiv); DMF: 44.0 mL. Yield of 2-[(2-bromobenzyl)thio]benzo[*d*]thiazole:[3] 2.60 g (97%, a white). R_f (SiO_2, 10% EtOAc in hexanes) = 0.49. Crude product was subjected to oxidation. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, 1H, *J* = 8.1 Hz, Ar-H), 7.75 (d, 1H, *J* = 8.1 Hz, Ar-H), 7.62 (d, 1H, *J* = 7.5 Hz, Ar-H), 7.59 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.43 (t, 1H, *J* = 7.5 Hz, Ar-H), 7.30 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.25 (t, 1H, *J* = 7.5 Hz, Ar-H), 7.14 (td, 1H, *J* = 7.5; 1.5 Hz, Ar-H), 4.75 (s, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 153.3, 136.3, 135.7, 133.2, 131.6, 129.6, 127.9, 126.3, 125.0, 124.5, 121.8, 121.2, 38.1.

2-[(4-Nitrobenzyl)thio]benzo[d]thiazole

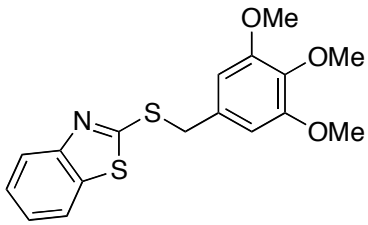


1-(Bromomethyl)-4-nitrobenzene: 2.16 g (10.0 mmol); sodium salt of 2-mercapto-1,3-benzothiazole: 2.27 g (12.0 mmol, 1.2 molar equiv); DMF: 55.0 mL. Purification by column chromatography, CH_2Cl_2 eluting solvent. Yield of 2-[(4-nitrobenzyl)thio]benzo[*d*]thiazole:[4] 2.75 g (91%, a yellowish solid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.36. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, 2H, *J* = 8.3 Hz, Ar-H), 7.89 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.76 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.65 (d, 2H, *J* = 8.3 Hz, Ar-H), 7.44 (t, 1H, *J* = 7.8 Hz, Ar-H), 7.32 (t, 1H, *J* = 7.8 Hz, Ar-H), 4.67 (s, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.0, 153.1, 147.5, 144.7, 135.7, 130.2 (2C), 126.4, 124.8, 124.0 (2C), 121.8, 121.3, 36.6.

FROM HYDROXYMETHYL ARENES: GENERAL PROCEDURE

A solution of 2-mercaptobenzothiazole (1.80 g, 10.8 mmol, 1.2 molar equiv) and diethyl azodicarboxylate (1.88 g, 10.8 mmol, 1.2 molar equiv) in THF (40 mL) was added slowly to a well stirred solution of hydroxymethyl arene (9 mmol) and PPh_3 (2.83 g, 10.8 mmol, 1.2 molar equiv) in THF (10 mL) at 0 ºC. The mixture was stirred for another 15 min at 0 ºC, then warmed to rt and stirred for 6 h. The reaction mixture was concentrated and purified by column chromatography on silica gel (100-200 mesh) using 20% EtOAc in hexanes to give the corresponding sulfide.

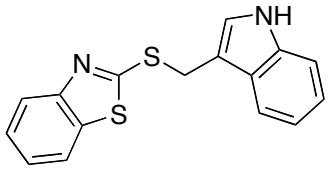
2-[(3,4,5-Trimethoxybenzyl)thio]benzo[d]thiazole



(3,4,5-Trimethoxyphenyl)methanol: 1.78 g (9.0 mmol). Yield of 2-[(3,4,5-trimethoxybenzyl)thio]benzo[d]thiazole:[5] 3.10 g (99%, a colorless liquid). R_f (SiO_2, 20% EtOAc in hexanes) = 0.27. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, 1H, *J* = 8.3 Hz, Ar-H), 7.76 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.43 (t, 1H, *J* = 7.8 Hz, Ar-H), 7.31 (t, 1H, *J* = 7.8 Hz, Ar-H), 6.70 (s, 2H, Ar-H), 4.55 (s, 2H, CH_2), 3.84 (s, 6H, OCH_3), 3.83 (s, 3H, OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ

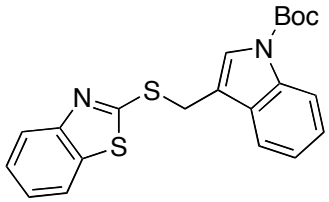
166.4, 153.5 (2C), 153.3, 135.6, 131.9 (2C), 126.3, 124.6, 121.6, 121.3, 106.4 (2C), 61.0, 56.3 (2C), 38.4.

2-[(1H-Indol-3-yl)methylthio]benzo[d]thiazole



(1*H*-Indol-3-yl)methanol: 1.33 g (9.0 mmol). Yield of 2-[(1*H*-indol-3-yl)methylthio]benzo[*d*]thiazole:[6] 2.56 g (96%, a light yellow viscous liquid). R_f (SiO_2, 20% EtOAc in hexanes) = 0.24. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (br s, 1H, NH), 7.93 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.75 (t, 2H, *J* = 7.1 Hz, Ar-H), 7.44 (t, 1H, *J* = 7.2 Hz, Ar-H), 7.37 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.32-7.29 (m, 2H, Ar-H), 7.24 (t, 1H, *J* = 7.5 Hz, Ar-H), 7.18 (t, 1H, *J* = 7.3 Hz, Ar-H), 4.86 (s, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.6, 153.3, 136.3, 135.4, 126.8, 126.2, 124.3 (2C), 122.7, 121.5, 121.2, 120.1, 119.1, 111.6, 110.2, 29.6.

Synthesis of tert-Butyl 3-[(benzo[d]thiazol-2-ylthio)methyl]-1H-indole-1-carboxylate



Di-*tert*-butyl dicarbonate (1.22 g, 5.58 mmol) was added to a well-stirred solution of 2-[(1*H*-indol-3-yl)methylthio]benzo[*d*]thiazole (1.10 g, 3.71 mmol) and DMAP (46.0 mg, 0.377 mmol) in dry acetonitrile (19.0 mL) at rt and the reaction mixture was allowed to stir for 2 h. After completion of the reaction, solvent was removed under reduced pressure and the residue was purified by column chromatography using 10% EtOAc in hexanes to afford *tert*-butyl 3-[(benzo[*d*]thiazol-2-ylthio)methyl]-1*H*-indole-1-carboxylate (1.37 g, 93%, a white solid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.28. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (br d, 1H, Ar-H), 7.93 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.76 (d, 1H, *J* = 8.3 Hz, Ar-H), 7.71 (s, 1H, Ar-H), 7.68 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.44 (td, 1H, *J* = 7.7; 1.0 Hz, Ar-H), 7.37-7.28 (m, 3H, Ar-H), 4.77 (s, 2H, CH_2), 1.66 (s, 9H, $3CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4, 153.3, 149.5, 135.6, 135.4, 129.5, 126.1, 125.4, 124.9, 124.4, 122.9, 121.6, 121.1, 119.3, 115.5, 115.2, 83.9, 28.4, 28.3 (3C). HRMS (ESI) calcd for $C_{21}H_{21}N_2O_2S_2$ [M + H]+ 397.1039, found 397.1032.

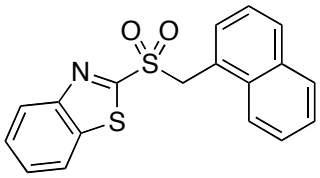
SYNTHESIS OF 2-[(ARYL)METHYLSULFONYL]BENZO[*d*]THIAZOLES

Synthesis of 2-(benzylsulfonyl)benzo[*d*]thiazole (**1b**),[1] 2-[(naphthalen-2-yl)methylsulfonyl]benzo[*d*]thiazole (**1f**),[1] and 2-{[2-(thiophen-2-yl)thiazol-4-yl]methylsulfonyl}benzo[*d*]thiazole (**1h**)[1] has previously been reported by us.

OXIDATION OF 2-[(ARYL)METHYLTHIO]BENZO[*d*]THIAZOLES: GENERAL PROCEDURE

To a vigorously stirred solution of sulfide (1 mmol) in $CHCl_3$ (3.0 mL per mmol of sulfide) at –10 ºC (ice-salt cooling) a solution of *m*-CPBA (either 70%, or purified, 2.5 mmol, 2.5 molar equiv) in $CHCl_3$ (8.0 mL per mmol of sulfide) was added dropwise. After complete addition, the mixture was stirred for an additional 10 min at –10 ºC, allowed to warm to room temperature and stirred at room temperature for 8 h. The reaction mixture was then poured into saturated aqueous $NaHCO_3$ and vigorously stirred for 15 min. After layer separation, the aqueous layer was extracted with organic solvent (see specific procedure), and the combined organic layer was washed with aqueous $NaHCO_3$, water and brine. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was purified either by column chromatography on silica gel (100-200 mesh), or by precipitation (see specific procedure). For each product, the amounts of sulfide precursor, reagents, solvent, purification protocol, and product yield are given under the specific compound headings below. Routinely, although the products can be chromatographically purified, use of material obtained by precipitation (providing better yields) proved to be more than adequate.

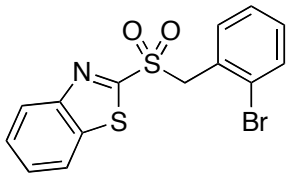
2-[(Naphthalen-1-yl)methylsulfonyl]benzo[d]thiazole (1a)



2-[(Naphthalen-1-yl)methylthio]benzo[*d*]thiazole (3.45 g, 11.2 mmol); *m*-CPBA (4.84 g, 28.0 mmol); $CHCl_3$: 124 mL. Extraction solvent in workup: CH_2Cl_2. Eluting solvent for column chromatography: CH_2Cl_2. Yield of 2-[(naphthalen-1-yl)methylsulfonyl]benzo[*d*]thiazole (**1a**):[7] 3.18 g (84%, a white solid). R_f (SiO_2, 20% EtOAc in hexanes) = 0.42. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (d, 1H, J = 8.3 Hz, Ar-H), 8.06-8.04 (m, 1H, Ar-H), 7.89 (d, 1H, J = 7.8 Hz, Ar-H), 7.86-7.81 (m, 2H, Ar-H), 7.65 (t, 1H, J = 7.4 Hz, Ar-H), 7.56 (t, 1H, J = 7.4 Hz, Ar-H), 7.45-7.43 (m, 3H, Ar-H), 7.36 (t, 1H, J = 7.4 Hz, Ar-H), 5.27 (s, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.5, 152.8, 137.4, 134.0, 132.4, 131.3, 130.5, 128.9, 128.2, 127.8, 127.1, 126.3, 125.6, 125.4,

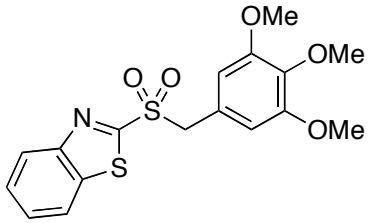
123.8, 122.9,122.4, 58.4.

2-[(2-Bromobenzyl)sulfonyl]benzo[d]thiazole (1c)



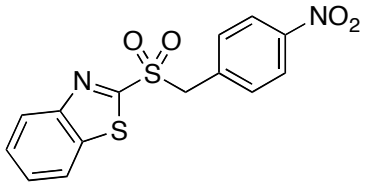
2-[(2-Bromobenzyl)thio]benzo[*d*]thiazole: 2.60 g (7.74 mmol); *m*-CPBA (4.78 g of 70% *m*-CPBA, 19.4 mmol of *m*-CPBA, 2.5 molar equiv); $CHCl_3$: 86.0 mL. Extraction solvent in workup: CH_2Cl_2. Crude **1c** was purified by precipitation from CH_2Cl_2 solution by addition of hexanes. Yield of 2-[(2-bromobenzyl)sulfonyl]benzo[*d*]thiazole (**1c**):[3b] 2.81 g (98%, a white solid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.11. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (dd, 1H, *J* = 8.5; 1.5 Hz, Ar-H), 7.98 (dd, 1H, *J* = 7.3; 1.0 Hz, Ar-H), 7.66 (td, 1H, *J* = 7.7; 1.1 Hz, Ar-H), 7.60 (td, 1H, *J* = 7.6; 1.0 Hz, Ar-H), 7.53 (dd, 1H, *J* = 7.8; 1.0 Hz, Ar-H), 7.46 (dd, 1H, *J* = 7.6; 1.7 Hz, Ar-H), 7.30 (td, 1H, *J* = 7.4; 1.1 Hz, Ar-H), 7.22 (td, 1H, *J* = 7.8; 1.5 Hz, Ar-H), 5.00 (s, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.0, 152.9, 137.5, 133.5, 133.3, 131.1, 128.3, 128.1, 127.9, 127.1, 126.3, 125.8, 122.5, 60.7. HRMS (ESI) calcd for $C_{14}H_{11}BrNO_2S_2$ $[M + H]^+$ 369.9388, found 369.9393.

2-[(3,4,5-Trimethoxybenzyl)sulfonyl]benzo[d]thiazole (1d)



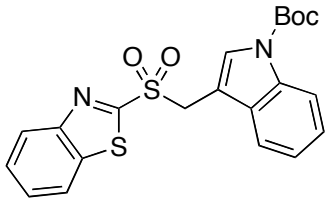
2-[(3,4,5-Trimethoxybenzyl)thio]benzo[*d*]thiazole: 3.10 g (8.93 mmol); *m*-CPBA (5.49 g of 70% *m*-CPBA, 22.3 mmol of *m*-CPBA, 2.5 molar equiv); $CHCl_3$: 98.0 mL. Extraction solvent in workup: EtOAc. Eluting solvent for column chromatography: 20% EtOAc in hexanes, followed by CH_2Cl_2. Yield of 2-[(3,4,5-trimethoxybenzyl)sulfonyl]benzo[*d*]thiazole (**1d**): 3.05 g (90%, a colorless liquid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.09. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (d, 1H, *J* = 8.2 Hz, Ar-H), 7.96 (d, 1H, *J* = 8.2 Hz, Ar-H), 7.65 (t, 1H, *J* = 8.2 Hz, Ar-H), 7.59 (t, 1H, *J* = 8.2 Hz, Ar-H), 6.41 (s, 2H, Ar-H), 4.67 (s, 2H, CH_2), 3.78 (s, 3H, OCH_3), 3.61 (s, 6H, OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4, 153.4 (2C), 152.6, 138.8, 137.2, 128.2, 127.8, 125.4, 122.5, 121.7, 108.3 (2C), 61.5, 60.9, 56.0 (2C). HRMS (ESI) calcd for $C_{17}H_{17}NO_5S_2Na$ $[M + Na]^+$ 402.0440, found 402.0446.

2-[(4-Nitrobenzyl)sulfonyl]benzo[d]thiazole (1e)



2-[(4-Nitrobenzyl)thio]benzo[*d*]thiazole: 2.60 g (8.61 mmol); *m*-CPBA (5.29 g of 70% *m*-CPBA, 21.5 mmol of *m*-CPBA, 2.5 molar equiv); $CHCl_3$: 95.0 mL. Extraction solvent in workup: CH_2Cl_2. Upon solvent concentration, pure product precipitated. Yield of 2-[(4-nitrobenzyl)sulfonyl]benzo[*d*]thiazole (**1e**):[8] 2.52 g (88%, a yellowish solid). R_f (SiO_2, CH_2Cl_2) = 0.35. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.30 (t, 2H, *J* = 7.6 Hz, Ar-H), 8.21 (d, 2H, *J* = 8.8 Hz, Ar-H), 7.75 (td, 1H, *J* = 7.8; 1.0 Hz, Ar-H), 7.71 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.60 (d, 2H, *J* = 8.7 Hz, Ar-H), 5.35 (s, 2H, CH_2). ^{13}C NMR (125 MHz, DMSO-d_6): δ 181.7, 165.3, 152.0, 147.8, 136.5, 134.8, 132.7 (2C), 128.4, 128.2, 125.0, 123.6 (2C), 59.0.

tert-Butyl 3-[(benzo[d]thiazol-2-ylsulfonyl)methyl]-1H-indole-1-carboxylate (1g)



tert-Butyl 3-[(benzo[*d*]thiazol-2-ylthio)methyl]-1*H*-indole-1-carboxylate: 1.32 g (3.33 mmol); *m*-CPBA (2.05 g of 70% *m*-CPBA, 8.32 mmol of *m*-CPBA, 2.5 molar equiv); $CHCl_3$: 39.0 mL. Extraction solvent in workup: EtOAc. Eluting solvent for column chromatography: 20% EtOAc in hexanes. Yield of *tert*-butyl 3-[(benzo[*d*]thiazol-2-ylsulfonyl)methyl]-1*H*-indole-1-carboxylate (**1g**): 0.995 g (70%, a white solid). R_f (SiO_2, 20% EtOAc in hexanes) = 0.23. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (d, 1H, *J* = 8.3 Hz, Ar-H), 8.09 (br d, 1H, *J* = 8.3 Hz, Ar-H), 7.91 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.64 (td, 1H, *J* = 7.8; 1.0 Hz, Ar-H), 7.58-7.55 (m, 2H, Ar-H), 7.45 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.25 (td, 1H, *J* = 7.8; 1.0 Hz, Ar-H), 7.09 (td, 1H, *J* = 7.6; 1.0 Hz, Ar-H), 4.92 (s, 2H, CH_2), 1.59 (s, 9H, 3 CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.4, 152.7, 149.1, 137.2, 135.3, 129.3, 128.1 (2C), 127.8, 125.5, 125.1, 123.1, 122.4, 119.0, 115.3, 106.0, 84.4, 52.4, 28.2 (3C). HRMS (ESI) calcd for $C_{21}H_{21}N_2O_4S_2$ $[M + H]^+$ 429.0937, found 429.0938.

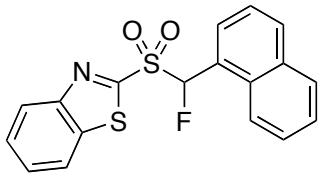
FLUORINATION OF 2-[(ARYL)METHYLSULFONYL]BENZO[*d*]THIAZOLES

Synthesis of 2-[fluoro(phenyl)methylsulfonyl]benzo[*d*]thiazole (**2b**),[1] 2-[fluoro(naphthalen-2-yl)methylsulfonyl]benzo[*d*]thiazole (**2f**),[1] and 2-{fluoro[2-(thiophen-2-yl)thiazol-4-yl]methylsulfonyl}benzo[*d*]thiazole (**2h**)[1] has previously been reported by us.

SYNTHESIS OF 2a, 2c, 2d, 2e, 2h: GENERAL PROCEDURE

A stirred solution of sulfone **1a**, **1c**, **1d**, **1e**, **1h** (1 molar equiv) in dry toluene (unless stated otherwise, see specific headings, also for the amount), was cooled to –78 ºC (dry-ice/*iso*-PrOH) under nitrogen. LDA (1.20 molar equiv of a 2 M solution in heptane/THF/EtPh) was added to the reaction mixture. After 20 min solid NFSi (1.20 molar equiv) was added. The mixture was allowed to stir at –78 ºC for 50 min, then warmed to rt and stirring was continued for an additional 50 min. Sat aq NH_4Cl was added to the mixture and the layers were separated. The aqueous layer was extracted with EtOAc (3 x), and the combined organic layer was washed with sat aq $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude reaction mixtures were purified by column chromatography on 100-200 mesh silica gel. For each substrate, the amount of substrate, reagents and solvent, eluting solvent for chromatography and product yield are given under the specific compound heading below.

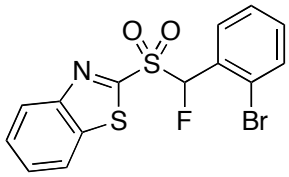
2-[Fluoro(naphthalen-1-yl)methylsulfonyl]benzo[d]thiazole (2a)



Sulfone **1a**: 0.700 g (2.07 mmol); NFSI: 0.781 g (2.48 mmol); toluene: 70.0 mL; LDA: 1.24 mL (2 M, 2.48 mmol). Eluting solvent for column chromatography: CH_2Cl_2. Yield of **2a**: 0.617 g (84%, a white solid). R_f (SiO_2, 20% EtOAc in hexanes) = 0.26. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, 1H, J = 8.2 Hz, Ar-H), 8.27 (d, 1H, J = 8.5 Hz, Ar-H), 8.04 (t, 2H, J = 7.7 Hz, Ar-H), 7.93 (d, 1H, J = 8.2 Hz, Ar-H), 7.89 (d, 1H, J = 7.2 Hz, Ar-H), 7.70 (td, 1H, J = 7.1; 1.0 Hz, Ar-H), 7.67-7.63 (m, 2H, Ar-H), 7.60-7.56 (m, 2H, Ar-H), 7.48 (d, 1H, $^2J_{HF}$ = 45.2 Hz, CHF). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4, 153.1, 137.8, 133.8, 132.5 (d, J_{CF} = 1.8 Hz), 131.4 (d, J_{CF} = 2.7 Hz), 129.1, 128.6, 128.5 (d, $^3J_{CF}$ = 9.6 Hz), 128.1, 127.8, 126.7, 126.0, 125.2, 123.5, 122.55, 122.54 (d, $^2J_{CF}$

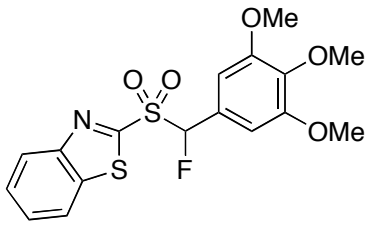
= 17.9 Hz), 99.8 (d, $^{1}J_{CF}$ = 220.6 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –171.58 (d, $^{2}J_{HF}$ = 45.7 Hz). HRMS (ESI) calcd for $C_{18}H_{12}FNO_2S_2Na$ $[M + Na]^+$ 380.0186, found 380.0191.

2-[(2-Bromophenyl)fluoromethylsulfonyl]benzo[d]thiazole (2c)



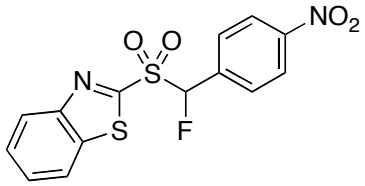
Sulfone **1c**: 0.500 g (1.36 mmol); NFSI: 0.513 g (1.63 mmol); toluene: 50 mL; LDA: 0.82 mL (2 M, 1.64 mmol). Eluting solvent for column chromatography: 25% EtOAc in hexanes. Yield of **2c**:[3b] 0.456 g (87%, a white solid). R_f (SiO_2, 20% EtOAc in hexanes) = 0.29. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33 (d, 1H, J = 8.3 Hz, Ar-H), 8.06 (d, 1H, J = 7.8 Hz, Ar-H), 7.75 (d, 1H, J = 7.8 Hz, Ar-H), 7.71-7.64 (m, 3H, Ar-H), 7.47 (t, 1H, J = 7.3 Hz, Ar-H), 7.41 (t, 1H, J = 7.6 Hz, Ar-H), 7.19 (d, 1H, $^{2}J_{HF}$ = 45.4 Hz, CHF). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9, 153.1, 137.8, 133.7, 133.2, 130.6 (d, $^{3}J_{CF}$ = 6.4 Hz), 128.7, 128.1 (2C), 127.0 (d, $^{2}J_{CF}$ = 20.6 Hz), 126.1, 124.9 (d, $^{3}J_{CF}$ = 4.6 Hz), 122.5, 100.6 (d, $^{1}J_{CF}$ = 222.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –170.34 (d, J = 45.8 Hz). HRMS (ESI) calcd for $C_{14}H_9FBrNO_2S_2Na$ $[M + Na]^+$ 407.9134, found 407.9137.

2-[Fluoro(3,4,5-trimethoxyphenyl)methylsulfonyl]benzo[d]thiazole (2d)



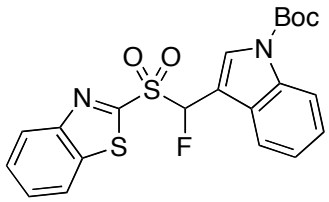
Sulfone **1d**: 1.52 g (4.00 mmol); NFSI: 1.51 g (4.79 mmol); toluene: 160 mL; LDA: 2.40 mL (2 M, 4.80 mmol). Eluting solvent for column chromatography: 35% EtOAc in hexanes. Yield of **2d**: 1.21 g (76%, a white solid). R_f (SiO_2, 30% EtOAc in hexanes) = 0.28. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (d, 1H, J = 8.3 Hz, Ar-H), 8.05 (d, 1H, J = 7.8 Hz, Ar-H), 7.71-7.63 (m, 2H), 6.81 (s, 2H, Ar-H), 6.54 (d, 1H, J = 45.4 Hz), 3.88 (s, 3H), 3.85 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.7, 153.5 (2C), 152.7, 140.6, 137.5, 128.4, 127.9, 125.6, 122.3, 121.4 (d, $^{2}J_{CF}$ = 20.1 Hz), 105.6 (d, 2C, $^{3}J_{CF}$ = 6.4 Hz), 102.2 (d, $^{1}J_{CF}$ = 223.8 Hz), 60.8, 56.2 (2C). ^{19}F NMR (282 MHz, $CDCl_3$): δ –170.40 (d, $^{2}J_{HF}$ = 45.8 Hz). HRMS (ESI) calcd for $C_{17}H_{16}FNO_5S_2Na$ $[M + Na]^+$ 420.0346, found 420.0350.

2-[Fluoro(4-nitrophenyl)methylsulfonyl]benzo[d]thiazole (2e)



Sulfone **1e**: 1.34 g (4.00 mmol); NFSI: 1.51 g (4.79 mmol); THF:toluene 3:2 (v/v): 160 mL; LDA: 2.40 mL (2 M, 4.80 mmol). Crude reaction mixture: 1.40 g. 2-[Fluoro(4-nitrophenyl)methylsulfonyl]benzo[*d*]thiazole (**2e**) could not be separated chromatographically from starting sulfone **1e** and difluorinated byproduct 2-[difluoro(4-nitrophenyl)methylsulfonyl]benzo[*d*]thiazole. Crude reaction mixture was used in the condensation with paraformaldehyde, to give 1-(1-fluorovinyl)-4-nitrobenzene in 71%-78% yield over two steps (depending on the method used, *vide infra*). 2-[Fluoro(4-nitrophenyl)methylsulfonyl]benzo[*d*]thiazole (**2e**): R_f (SiO_2, CH_2Cl_2) = 0.61. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36 (d, 2H, J = 8.3 Hz), 8.30 (d, 1H, J = 7.8 Hz), 8.07 (d, 1H, J = 7.8 Hz), 7.84 (d, 2H, J = 8.8 Hz), 7.73-7.66 (m, 2H), 6.76 (d, 1H, J = 46.4 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –175.59 (d, $^2J_{HF}$ = 45.8 Hz). HRMS (ESI) calcd for $C_{14}H_9FN_2O_4S_2Na$ $[M + Na]^+$ 374.9880, found 374.9887.

tert-Butyl 3-[(benzo[d]thiazol-2-ylsulfonyl)fluoromethyl]-1H-indole-1-carboxylate (2g)



Sulfone **1g**: 0.856 g (2.00 mmol); NFSI: 0.756 g (2.40 mmol); toluene: 60.0 mL; LDA: 1.20 mL (2 M, 2.40 mmol). Eluting solvent for column chromatography: CH_2Cl_2. Yield of **2g**: 0.805 g (90%, a light brownish solid). R_f (SiO_2, 20% EtOAc in hexanes) = 0.35. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (d, 1H, J = 8.3 Hz, Ar-H), 8.20 (d, 1H, J = 7.8 Hz, Ar-H), 8.05 (d, 1H, J = 7.8 Hz, Ar-H), 8.00 (d, 1H, J = 2.0 Hz, Ar-H), 7.80 (d, 1H, J = 7.8 Hz, Ar-H), 7.70-7.63 (m, 2H, Ar-H), 7.38 (t, 1H, J = 7.8 Hz, Ar-H), 7.28 (t, 1H, J = 8.1 Hz, Ar-H), 6.90 (d, 1H, J = 45.4 Hz), 1.68 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0, 153.0, 148.9, 137.6, 135.6, 129.0 (d, $^3J_{CF}$ = 8.2 Hz), 128.5, 128.0, 127.6, 125.8, 125.6, 123.7, 122.4, 120.5, 115.5, 106.9 (d, $^2J_{CF}$ = 22.4 Hz), 98.7 (d, $^1J_{CF}$ = 220.2 Hz), 85.1, 28.2 (3C). ^{19}F NMR (282 MHz, $CDCl_3$): δ –171.05 (d, $^2J_{HF}$ = 42.6 Hz). HRMS (ESI) calcd for $C_{21}H_{19}FN_2O_4S_2Na$ $[M + Na]^+$ 469.0662, found 469.0675.

SYNTHESIS OF 2-[(EWG)METHYLTHIO]BENZO[*d*]THIAZOLES

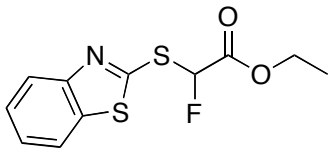
EWG: ELECTRON WITHDRAWING GROUP

Synthesis of ethyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate[9] (synthesis from commercial ethyl bromofluoroacetate also shown below), 2-[fluoro(phenylsulfonyl)methylsulfonyl]benzo[*d*]thiazole (**5a**),[10] ethyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-fluoroacetate (**5b**),[9] and 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-fluoro-*N*-methoxy-*N*-methylacetamide (**5e**)[11] has previously been reported by us. We have previously reported the ^{1}H NMR data for **5b** and **5e**, their ^{13}C NMR data are as follows.

5b: ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.3, 160.2 (d, $^{2}J_{CF}$ = 24.3 Hz), 152.9, 137.8, 129.0, 128.3, 126.2, 122.6, 96.7 (d, $^{1}J_{CF}$ = 234.8 Hz), 64.3, 14.1.

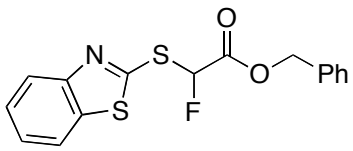
5e: ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.6, 159.6 (d, $^{2}J_{CF}$ = 23.8 Hz), 152.7, 137.9, 128.8, 128.1, 126.1, 122.5, 94.8 (d, $^{1}J_{CF}$ = 226.1 Hz), 62.2, 32.9.

Synthesis of Ethyl 2-(Benzo[d]thiazol-2-ylthio)-2-fluoroacetate[9]



To a solution of ethyl bromofluoroacetate (1.00 g, 5.41 mmol) in DMF (21.0 mL) at rt, the sodium salt of 2-mercapto-1,3-benzothiazole (1.22 g, 6.49 mmol) was added and the reaction mixture was allowed to stir until complete consumption of the starting material was observed by TLC (within 1 hr). The reaction mixture was diluted with water and extracted with EtOAc (3 x 150 mL). The combined organic layer was thoroughly washed with water, brine, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure to get crude product that was purified by column chromatography using 25% ethyl acetate in hexanes as eluent to get 1.20 g (82%) of ethyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate. R_f (SiO_2, 25% EtOAc in hexanes) = 0.43. The spectral data of ethyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate were in agreement with those previously reported by us.[9]

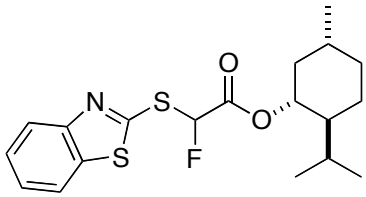
Synthesis of Benzyl 2-(Benzo[d]thiazol-2-ylthio)-2-fluoroacetate



Catalytic amount of potassium *tert*-butoxide (49.6 mg, 0.44 mmol, 0.1 molar equiv) was added

to a well stirred solution of ethyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate (1.2 g, 4.43 mmol) and benzyl alcohol (2.39 g, 22.14 mmol, 5 molar equiv) in dry benzene (44.0 mL) at 0 ºC. The stirring was continued at 0 ºC for 10 min then the reaction mixture was allowed to stir at rt for 1h, another 0.1 molar equiv (49.6 mg, 0.44 mmol) of *tert*-butoxide was added and the stirring was continued for 1 h. The reaction was quenched with 10% HCl (30 mL) and diluted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using 230-400 mesh silica gel and CH_2Cl_2 as eluent to yield (1.09 g, 73%) of benzyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate as a low melting colorless solid. R_f (SiO_2, CH_2Cl_2) = 0.51. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (br d, 1H, J = 7.9 Hz, Ar-H), 7.80 (br d, 1H, J = 7.9 Hz, Ar-H), 7.47 (td, 1H, J = 7.9; 1.0 Hz, Ar-H), 7.38 (td, 1H, J = 7.9; 1.0 Hz, Ar-H), 7.35-7.33 (m, 5H, Ar-H), 6.97 (d, 1H, $^2J_{HF}$ = 50.7 Hz, CHF), 5.30 (s, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.9 ($^2J_{CF}$ = 27.9 Hz), 159.5, 152.8, 136.4, 134.4, 128.9, 128.8 (2C), 128.7 (2C), 126.7, 125.5, 122.8, 121.4, 92.0 ($^1J_{CF}$ = 236.0 Hz), 68.6. ^{19}F NMR (282 MHz, $CDCl_3$): δ –161.76 (d, $^2J_{HF}$ = 51.9 Hz). HRMS (ESI) calcd for $C_{16}H_{13}FNO_2S_2$ $[M + H]^+$ 334.0366, found 334.0369.

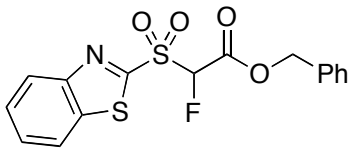
Synthesis of (1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 2-(Benzo[d]thiazol-2-ylthio)-2-fluoroacetate *(mixture of two diastereomers in a 1.1:1 ratio)*



Catalytic amount of potassium *tert*-butoxide (62.0 mg, 0.55 mmol) was added to a well stirred solution of ethyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate (1.00 g, 3.69 mmol) and (–)-menthol (2.90 g, 18.6 mmol) in dry hexanes (15.0 mL) at 0 ºC. The stirring was continued at 0 ºC for 10 min then the reaction mixture was allowed to stir at rt for 1.5 h. The reaction was quenched with water and diluted with diethyl ether. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using 10% ethyl acetate in hexanes as eluent to yield (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate (1.12 g, 79%, a low melting colorless solid) as a mixture of two diastereomers in a 1.1:1 ratio. R_f (SiO_2, 10% EtOAc in hexanes) = 0.43. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, 1H-both isomers, J = 8.3 Hz, Ar-H), 7.82 (d, 1H-both isomers, J = 7.8 Hz, Ar-H), 7.48 (t, 1H-both isomers, J = 7.8 Hz, Ar-H), 7.39 (t, 1H-both isomers, J = 7.8 Hz, Ar-H), 6.90 (d, 1H-one isomer,

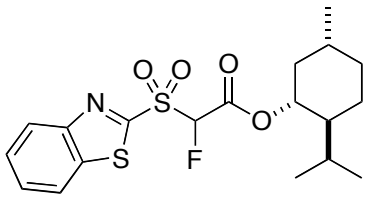
$^2J_{HF}$ = 51.8 Hz), 6.88 (d, 1H-one isomer, $^2J_{HF}$ = 51.3 Hz), 4.85-4.78 (m, 1H-both isomers), 2.03-0.68 (menthyl protons, 18 H-both isomers). ^{13}C NMR (125 MHz, $CDCl_3$; for very close signals, chemical shifts are reported to two decimal points, to differentiate between them): δ 164.6 (d, $^2J_{CF}$ = 27.0 Hz), 164.5 (d, $^2J_{CF}$ = 27.0 Hz), 159.90, 159.88, 152.9, 136.45, 136.40, 126.70, 126.68, 125.55, 125.52, 122.9, 121.40, 121.37, 92.3 (d, $^1J_{CF}$ = 236.6 Hz), 92.2 (d, $^1J_{CF}$ = 236.6 Hz), 77.88, 77.86, 47.0, 46.9, 40.6, 40.4, 34.19, 34.16, 31.6, 31.5, 26.4, 26.2, 23.5, 23.3, 22.09, 22.05, 20.88, 20.85, 16.4, 16.2. ^{19}F NMR (282 MHz, $CDCl_3$): δ –161.04 (d, $^2J_{HF}$ = 48.8 Hz, one isomer), –161.22 (d, $^2J_{HF}$ = 48.8 Hz, one isomer). HRMS (ESI) calcd for $C_{19}H_{25}FNO_2S_2$ $[M + H]^+$ 382.1305, found 382.1311.

Synthesis of Benzyl 2-(Benzo[d]thiazol-2-ylsulfonyl)-2-fluoroacetate (5c)



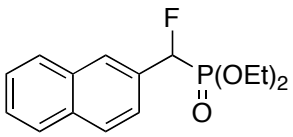
To a vigorously stirred solution of benzyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate (1.00 g, 3.00 mmol) in $CHCl_3$ (9 mL) at –10 ºC (ice-salt cooling) a solution of *m*-CPBA (3.68 g of 70% *m*-CPBA, 15 mmol of *m*-CPBA, 5 molar equiv) in $CHCl_3$ (26 mL) was added dropwise. After complete addition, the mixture was stirred for an additional 10 min at –10 ºC, allowed to warm to room temperature and stirred at room temperature for 48 h. The reaction mixture was then poured into saturated aqueous $NaHCO_3$ and vigorously stirred for 15 min. After layer separation, the aqueous layer was extracted with $CHCl_3$, and the combined organic layer was washed with aqueous $NaHCO_3$, water and brine. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (100-200 mesh) using dichloromethane to yield 0.962 (88%) of benzyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-fluoroacetate (**5c**) as a white solid. R_f (SiO_2, CH_2Cl_2) = 0.44. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (dd, 1H, *J* = 8.8; 1.5 Hz, Ar-H), 8.01 (dd, 1H, *J* = 8.8; 1.5 Hz, Ar-H), 7.68-7.63 (m, 2H, Ar-H), 7.35-7.33 (m, 5H, Ar-H), 6.08 (d, 1H, *J* = 47.3 Hz), 5.34 (s, 2H, CH_2). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 160.2 ($^2J_{CF}$ = 23.3 Hz), 152.8, 137.8, 133.8, 129.2, 129.0, 128.9 (2C), 128.8 (2C), 128.3, 126.2, 122.6, 96.7 ($^1J_{CF}$ = 235.7 Hz), 69.6. ^{19}F NMR (282 MHz, $CDCl_3$): δ –181.83 (d, $^2J_{HF}$ = 48.8 Hz). HRMS (ESI) calcd for $C_{16}H_{13}FNO_4S_2$ $[M + H]^+$ 366.0265, found 366.0270.

Synthesis of (1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 2-(benzo[d]thiazol-2-ylsulfonyl)-2-fluoroacetate (5d)



To a vigorously stirred solution of benzyl 2-(benzo[*d*]thiazol-2-ylthio)-2-fluoroacetate (1.05 g, 2.76 mmol) in $CHCl_3$ (8.3 mL) at –10 ºC (ice-salt cooling) a solution of *m*-CPBA (1.70 g of 70% *m*-CPBA, 6.89 mmol of *m*-CPBA, 2.5 molar equiv) in $CHCl_3$ (22.0 mL) was added dropwise. After complete addition, the mixture was stirred for an additional 10 min at –10 ºC, allowed to warm to room temperature and stirred overnight at room temperature. The reaction mixture was then poured into saturated aqueous $NaHCO_3$ and vigorously stirred for 15 min. After layer separation, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was washed with aqueous $NaHCO_3$, water and brine. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude product was purified first by column chromatography on silica gel (100-200 mesh) using 10% EtOAc in hexanes, followed by second column chromatography using CH_2Cl_2 to yield 0.970 g (85%) of (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-fluoroacetate (**5d**) as a gummy oil, that solidifies to white solid on storage. R_f (SiO_2, CH_2Cl_2) = 0.61. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (d, 1H-both isomers, Ar-H, J = 8.3 Hz), 8.05 (d, 1H-both isomers, Ar-H, J = 7.8 Hz), 7.70-7.64 (m, 2H-both isomers, Ar-H), 6.07 (d, 1H-one isomer, $^2J_{HF}$ = 47.4 Hz), 6.01 (d, 1H-one isomer, $^2J_{HF}$ = 47.4 Hz), 4.93-4.87 (m, 1H-both isomers), 2.12-0.71 (menthyl protons, 18H-both isomers). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.6, 161.4, 159.82 (d, $^2J_{CF}$ = 22.9 Hz), 159.78 (d, $^2J_{CF}$ = 23.3 Hz), 152.84, 152.81, 137.8, 137.7, 128.94, 128.91, 128.22, 128.19, 126.17, 126.13, 122.6, 96.8 (d, $^1J_{CF}$ = 236.2 Hz), 96.5 (d, $^1J_{CF}$ = 234.8 Hz), 79.4, 79.3, 46.8, 46.7, 40.5, 40.2, 34.1, 31.6, 26.3, 25.7, 23.4, 23.1, 22.07, 22.05, 20.9, 20.8, 16.2, 16.0. ^{19}F NMR (282 MHz, $CDCl_3$): δ –180.55 (d, $^2J_{HF}$ = 48.8 Hz, one isomer), –181.82 (d, $^2J_{HF}$ = 45.8 Hz, one isomer). HRMS (ESI) calcd for $C_{19}H_{25}FNO_4S_2$ $[M + H]^+$ 414.1204, found 414.1206.

Synthesis of Diethyl Fluoro(naphthalen-2-yl)methylphosphonate (**4**)



To a stirring solution of diethyl naphthalen-2-ylmethylphosphonate[12] (100.0 mg, 0.359 mmol, 1 molar equiv) in dry tetrahydrofuran (20.0 mL) cooled to –78 °C (dry ice/isopropanol) under nitrogen, LDA (1.2 molar equiv of a 2.0 M solution in heptane/THF/EtPh) was added. After 13 min, solid NFSI (176.0 mg, 0.431 mmol, 1.2 molar equiv) was added. The reaction mixture was allowed to stir at –78 °C for 50 min then warmed to room temperature and the stirring was continued for an additional 50 min. Saturated aq NH_4Cl was added to the reaction mixture and the layers were separated. The aqueous layer was extracted with EtOAc (3 times), and the combined organic layer was washed with water, saturated aq $NaHCO_3$ and brine. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude reaction mixture was purified by column chromatography (SiO_2, mesh 200-300, 40% EtOAc in hexanes) to yield 40.2 mg (38 %) of **4** as light yellow oil (unoptimized procedure). R_f (SiO_2, 50% CH_2Cl_2 in hexanes) = 0.29. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (br s, 1H, Ar-H), 7.89-7.84 (m, 3H, Ar-H), 7.60 (d, 1H, Ar-H, J = 8.3 Hz), 7.52-7.50 (m, 2H, Ar-H), 5.86 (dd, 1H, CHF, J = 44.7; 7.8 Hz), 4.19-4.00 (m, 4H, CH_{2A}, CH_{2B}), 1.29 (t, 3H, CH_{3A}, J = 7.4 Hz), 1.26 (t, 3H, CH_{3B}, J = 6.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 133.8, 133.1, 130.6 (d, $^2J_{CF}$ = 18.4 Hz), 128.53 (d, J = 1.8 Hz), 128.45, 128.0, 126.9, 126.7, 126.6 (app t, J = 7.8 Hz), 124.2 (app t, J = 4.8 Hz), 89.9 (dd, J = 184.2; 170.0 Hz), 64.0 (d, $^2J_{CP}$ = 6.9 Hz, CH_{2A}), 63.6 (d, $^2J_{CP}$ = 6.9 Hz, CH_{2B}), 16.61 (d, $^3J_{CP}$ = 5.5 Hz, CH_{3A}), 16.58 (d, $^3J_{CP}$ = 6.0 Hz, CH_{3B}). ^{19}F NMR (282 MHz, $CDCl_3$): δ –200.6 (dd, $^2J_{FP}$ = 83.9 Hz, $^2J_{FH}$ = 44.3 Hz). HRMS (ESI) calcd for $C_{15}H_{19}FO_3P$ $[M + H]^+$ 297.1050, found 297.1059.

CONDENSATION REACTIONS OF FLUOROSULFONES 2a-2e AND 5a-5e WITH PARAFORMALDEHYDE: GENERAL PROCEDURE

For each substrate, synthesis via one method is shown. The amounts of reactants and solvent, eluting solvent for chromatography, and product yield are given under the specific compound headings below.

Method A:

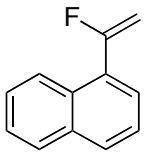
In a 20 mL pressure vial, DBU (1,52 g: 10 mmol, or 0.456 g: 3 mmol, see specific headings) in freshly distilled CH_2Cl_2 (6 mL per mmol of sulfone) was added to a well-stirrred solution of fluoro sulfone (1 mmol) and paraformaldehyde (300 mg, 10 mmol, 10 molar equiv) in freshly distilled CH_2Cl_2 (4 mL per mmol of sulfone) at room temperature. After stirring overnight, the reaction solvent was concentrated, the reaction mixture was directly loaded on silica gel (100-200 mesh, unless stated otherwise) column and fluorovinyl compound was eluted (for eluent, see specific

headings).

Method B:

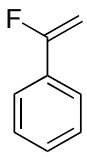
In a 20 mL pressure vial, caesium carbonate (652 mg, 2 mmol, 2 molar equiv) was added to a well-stirrred solution of fluoro sulfone (1 mmol) and paraformaldehyde (300 mg, 10 mmol, 10 molar equiv) in freshly distilled solvent (10 mL, CH_2Cl_2 or THF, see specific headings) at room *temperature*. The reaction was allowed to stir overnight, solids were removed by filtering through filtering funnel and the filtrate was concentrated. The fluorovinyl products were isolated by column chromatography (100-200 mesh silica gel, unless stated otherwise); for eluent, see specific headings. For each substrate, synthesis via one method is shown, and the amounts of substrate, reagents and solvent, and product yield are given under the specific compound headings below.

1-(1-Fluorovinyl)naphthalene (3a)



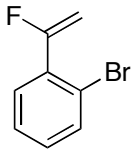
Method A. 2-[Fluoro(naphthalen-1-yl)methylsulfonyl]benzo[*d*]thiazole (**2a**): 286 mg (0.800 mmol); paraformaldehyde: 240 mg (8.00 mmol, 10 molar equiv); DBU: 1.22 g (8.00 mmol, 10 molar equiv); CH_2Cl_2: 8.0 mL. Eluting solvent: 10% EtOAc in hexanes. Yield of 1-(1-fluorovinyl)naphthalene (**3a**):[13] 92.0 mg (67%, a colorless liquid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.60. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (d, 1H, J = 8.2 Hz, Ar-H), 7.91-7.87 (m, 2H, Ar-H), 7.62 (d, 1H, J = 7.1 Hz, Ar-H), 7.58-7.51 (m, 2H, Ar-H), 7.46 (t, 1H, J = 7.5 Hz, Ar-H), 5.16 (dd, 1H, J = 16.1; 2.9 Hz), 4.89 (dd, 1H, J = 48.1; 2.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.2 (d, $^1J_{CF}$ = 255.0 Hz), 133.8, 130.9, 130.8 (d, $^2J_{CF}$ = 26.1 Hz), 130.5 (d, J_{CF} = 1.4 Hz), 128.6, 127.5 (d, J_{CF} = 4.6 Hz), 127.0 (d, J_{CF} = 0.9 Hz), 126.4, 125.7 (d, J_{CF} = 4.1 Hz), 125.1, 95.2 (d, $^2J_{CF}$ = 22.9 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –88.2 (dd, $^3J_{HF}$ = 48.8; 15.3 Hz).

(1-Fluorovinyl)benzene (3b)



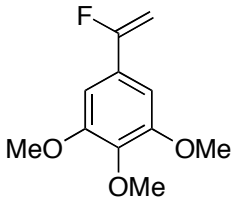
Method B. 2-[Fluoro(phenyl)methylsulfonyl]benzo[*d*]thiazole (**2b**): 307 mg (1.00 mmol); paraformaldehyde: 300 mg (10.0 mmol, 10 molar equiv); Cs_2CO_3: 652 mg (2.00 mmol, 2 molar equiv); CH_2Cl_2: 10.0 mL. Eluting solvent: CH_2Cl_2. Product is volatile and solvent needs to be removed cautiously! Yield of 1-(1-fluorovinyl)benzene (**3b**):[14] 105 mg (86%, a colorless liquid). R_f (SiO_2, CH_2Cl_2) = 0.81. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57-7.55 (m, 2H), 7.38-7.37 (m, 3H), 5.04 (dd, 1H, J = 49.7; 3.4 Hz), 4.85 (dd, 1H, J = 17.7; 3.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2 (d, $^1J_{CF}$ = 249.5 Hz), 132.2 (d, $^2J_{CF}$ = 29.3 Hz), 129.6, 128.7, 124.8 (d, $^3J_{CF}$ = 6.9 Hz), 89.7 (d, $^2J_{CF}$ = 22.4 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –108.47 (dd, $^3J_{HF}$ = 51.9; 18.3 Hz).

1-Bromo-2-(1-fluorovinyl)benzene (3c)



Method B. 2-[(2-Bromophenyl)fluoromethylsulfonyl]benzo[*d*]thiazole (**2c**): 386 mg (1.00 mmol); paraformaldehyde: 300 mg (10.0 mmol, 10 molar equiv); Cs_2CO_3: 652 mg (2.00 mmol, 2 molar equiv); THF: 10.0 mL. Eluting solvent: CH_2Cl_2. Yield of 1-bromo-2-(1-fluorovinyl)benzene (**3c**): 109 mg (54%, a colorless liquid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.61. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, 1H, J = 7.9 Hz, Ar-H), 7.48 (d, 1H, J = 7.6 Hz, Ar-H), 7.33 (t, 1H, J = 7.6 Hz, Ar-H), 7.24 (t, 1H, J = 7.9 Hz, Ar-H), 5.09 (dd, 1H, J = 16.5; 3.3 Hz), 4.97 (dd, 1H, J = 48.4; 3.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.1 (d, $^1J_{CF}$ = 253.6 Hz), 133.9 (d, $^2J_{CF}$ ~ 29 Hz, partially superimposed with resonance at 133.8), 133.8, 130.9, 130.7 (d, $^3J_{CF}$ = 4.1 Hz), 127.4, 121.7, 95.8 (d, $^2J_{CF}$ = 22.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –92.00 (dd, $^3J_{HF}$ = 48.8; 15.3 Hz). HRMS (EI) calcd for C_8H_6FBr M^+ 199.9637, found 199.9647.

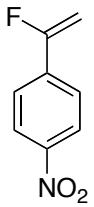
5-(1-Fluorovinyl)-1,2,3-trimethoxybenzene (3d)



Method A. 2-[Fluoro(3,4,5-trimethoxyphenyl)methylsulfonyl]benzo[*d*]thiazole (**2d**): 220 mg (0.554 mmol); paraformaldehyde: 166 mg (5.54 mmol, 10 molar equiv); DBU: 842 mg (5.54 mmol, 10 molar equiv); CH_2Cl_2: 5.5 mL. Eluting solvent: 20% EtOAc in hexanes. Yield of 5-(1-fluorovinyl)-1,2,3-trimethoxybenzene (**3d**): 108 mg (92%, an off white solid). R_f (SiO_2, CH_2Cl_2) =

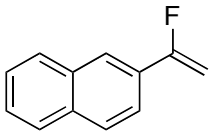
0.61. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.77 (s, 2H, Ar-H), 4.95 (dd, 1H, J = 49.6; 3.4 Hz), 4.82 (dd, 1H, J_{HF}= 17.6; 3.4 Hz), 3.89 (s, 6H, OCH_3), 3.87 (s, 3H, OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.8 (d, $^{1}J_{CF}$ = 249.9 Hz), 153.3 (2C), 139.4, 127.6 (d, $^{2}J_{CF}$ = 29.8 Hz), 102.2 (d, 2C, $^{3}J_{CF}$ = 7.3 Hz), 89.2 (d, $^{2}J_{CF}$ = 22.9 Hz), 61.0, 56.3 (2C). ^{19}F NMR (282 MHz, $CDCl_3$): δ –107.12 (dd, $^{3}J_{HF}$ = 48.8; 18.3 Hz). HRMS (ESI) calcd for $C_{11}H_{14}FO_3$ $[M + H]^+$ 213.0921, found 213.0924.

1-(1-Fluorovinyl)-4-nitrobenzene (3e)



Method B. Crude reaction mixture of 2-[fluoro(4-nitrophenyl)methylsulfonyl]benzo[*d*]thiazole (**2e**, along with starting sulfone **1e** and difluorinated byproduct, *vide supra*): 352 mg (1.00 mmol, calculated on pure **2e**); paraformaldehyde: 300 mg (10.0 mmol, 10 molar equiv); Cs_2CO_3: 652 mg (2.00 mmol, 2 molar equiv); THF: 10.0 mL. Eluting solvent: CH_2Cl_2. Yield of 1-(1-fluorovinyl)-4-nitrobenzene (**3e**):[13,15] 118 mg (70%, a light yellow solid) <u>*over two steps*</u> (fluorination and condensation step). R_f (SiO_2, CH_2Cl_2) = 0.87. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.24 (d, 2H, J = 8.8 Hz, Ar-H), 7.71 (d, 2H, J = 8.8 Hz, Ar-H), 5.26 (dd, 1H, J = 48.8; 3.9 Hz), 5.10 (dd, 1H, J = 17.1; 3.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0 (d, $^{1}J_{CF}$ = 250.8 Hz), 148.3, 138.0 (d, $^{2}J_{CF}$ = 29.7 Hz), 125.6 (d, $^{3}J_{CF}$ = 7.3 Hz), 124.0 (d, 2C, $^{4}J_{CF}$ = 2.3 Hz), 93.9 (d, $^{2}J_{CF}$ = 22.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –108.73 (dd, $^{3}J_{HF}$ = 48.8; 18.3 Hz).

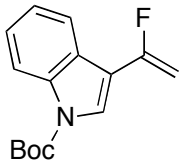
2-(1-Fluorovinyl)naphthalene (3f)



Method A. 2-[Fluoro(naphthalen-2-yl)methylsulfonyl]benzo[*d*]thiazole (**2f**): 2.70 g (7.56 mmol); paraformaldehyde: 2.28 g (75.9 mmol, 10 molar equiv); DBU: 3.45 g (22.7 mmol, 3 molar equiv); CH_2Cl_2: 76.0 mL (tightly stoppered round bottom flask was used instead of pressure vial). Eluting solvent: CH_2Cl_2. Yield of 2-(1-fluorovinyl)naphthalene (**3f**): 1.20 g (92%, a light yellow solid). R_f (SiO_2, CH_2Cl_2) = 0.97. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (s, 1H, Ar-H), 7.88-7.82 (m, 3H, Ar-H), 7.62 (d, 1H, J = 8.6 Hz, Ar-H), 7.52-7.50 (m, 2H, Ar-H), 5.17 (dd, 1H, J = 49.8; 3.5 Hz), 4.95 (dd, 1H, J = 18.0; 3.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2 (d, $^{1}J_{CF}$ =

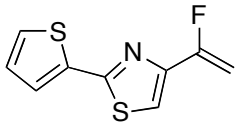
249.9 Hz), 133.8, 133.2, 129.4 (d, $^{2}J_{CF}$ = 28.8 Hz), 128.8, 128.5 (d, J_{CF} = 2.3 Hz), 127.9, 127.0, 126.8, 124.1 (d, $^{3}J_{CF}$ = 7.3 Hz), 122.4 (d, $^{3}J_{CF}$ = 6.9 Hz), 90.3 (d, $^{2}J_{CF}$ = 22.6 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –108.64 (dd, $^{3}J_{HF}$ = 48.8; 18.3 Hz). HRMS (ESI) calcd for $C_{12}H_9F$ M^+ 172.0683, found 172.0683.

***tert*-Butyl 3-(1-fluorovinyl)-1H-indole-1-carboxylate (3g)**



Method B. *tert*-Butyl 3-[(benzo[*d*]thiazol-2-ylsulfonyl)fluoromethyl]-1*H*-indole-1-carboxylate (**2g**): 223 mg (0.500 mmol); paraformaldehyde: 150 mg (5.00 mmol, 10 molar equiv); Cs_2CO_3: 326 mg (1.00 mmol, 2 molar equiv); THF: 5.0 mL. Eluting solvent: CH_2Cl_2. Yield of *tert*-butyl 3-(1-fluorovinyl)-1*H*-indole-1-carboxylate (**3g**): 82.0 mg (63%, a light yellow solid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.60. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.81 (s, 1H, Ar-H), 7.73 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.38 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.32 (t, 1H, *J* = 7.8 Hz, Ar-H), 5.00 (dd, 1H, *J* = 50.8; 3.4 Hz), 4.97 (dd, 1H, *J* = 19.5; 3.4 Hz), 1.68 (s, 9H, *tert*-Bu). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.7 (d, $^{1}J_{CF}$ = 245.0 Hz), 149.5, 136.1, 126.7 (d, $^{3}J_{CF}$ = 6.4 Hz), 125.2, 124.8 (d, $^{3}J_{CF}$ = 6.0 Hz), 123.6, 120.3 (d, J_{CF} = 1.4 Hz), 115.8, 113.9 (d, $^{2}J_{CF}$ = 32.5 Hz), 90.9 (d, $^{2}J_{CF}$ = 21.5 Hz), 84.6, 28.4 (3C). ^{19}F NMR (282 MHz, $CDCl_3$): δ –100.70 (dd, $^{3}J_{HF}$ = 51.9; 18.3 Hz). HRMS (EI) calcd for $C_{15}H_{16}FNO_2$ M^+ 261.1165, found 261.1182.

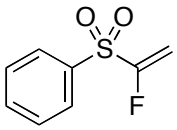
***4*-(1-Fluorovinyl)-2-(thiophen-2-yl)thiazole (3h)**



Method B. 2-{Fluoro[2-(thiophen-2-yl)thiazol-4-yl]methylsulfonyl}benzo[*d*]thiazole (**2h**): 198 mg (0.50 mmol); paraformaldehyde: 150 mg (5.00 mmol, 10 molar equiv); Cs_2CO_3: 326 mg (1.00 mmol, 2 molar equiv); THF: 5.0 mL. Eluting solvent: CH_2Cl_2. Yield of 4-(1-fluorovinyl)-2-(thiophen-2-yl)thiazole (**3h**): 88.0 mg (83%, a white solid). R_f (SiO_2, CH_2Cl_2) = 0.66. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, 1H, *J* = 3.6 Hz, Ar-H); 7.42 (d, 1H, *J* = 4.9 Hz, Ar-H), 7.32 (s, 1H, Ar-H), 7.09 (t, 1H, *J* = 4.6 Hz, Ar-H), 5.49 (dd, 1H, *J* = 49.7; 3.0 Hz), 4.97 (dd, 1H, *J* = 17.1; 3.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.5 (d, J_{CF} = 3.7 Hz), 158.6 (d, $^{1}J_{CF}$ = 243.5 Hz), 148.7 (d, $^{2}J_{CF}$ = 40.7 Hz), 136.9, 128.4, 128.1, 127.4, 114.7, 92.1 (d, $^{2}J_{CF}$ = 16.9 Hz). ^{19}F NMR (282 MHz,

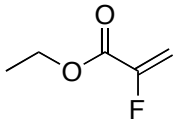
$CDCl_3$): δ –113.42 (dd, $^3J_{HF}$ = 48.8; 15.3 Hz). HRMS (ESI-APCI) calcd for $C_9H_7FNS_2$ $[M + H]^+$ 211.9998, found 212.0000.

(1-Fluorovinylsulfonyl)benzene (6a)



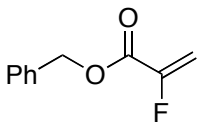
Method B. 2-[Fluoro(phenylsulfonyl)methylsulfonyl]benzo[*d*]thiazole (**5a**): 371 mg (1.00 mmol); paraformaldehyde: 300 mg (10.0 mmol, 10 molar equiv); Cs_2CO_3: 652 mg (2.00 mmol, 2 molar equiv); CH_2Cl_2: 10.0 mL. Eluting solvent: CH_2Cl_2. Yield of (1-fluorovinylsulfonyl)benzene (**6a**):[10,16] 140 mg (75%, a white solid). R_f (SiO_2, CH_2Cl_2) = 0.73. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, 2H, *J* = 7.8 Hz, Ar-H), 7.71 (t, 1H, *J* = 7.3 Hz, Ar-H), 7.60 (t, 2H, *J* = 7.8 Hz, Ar-H), 5.87 (dd, 1H, *J* = 42.0; 4.9 Hz), 5.43 (dd, 1H, *J* = 12.6; 4.7 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.7 (d, $^1J_{CF}$ = 302.1 Hz), 136.9, 134.9, 129.7 (2C), 129.0 (2C), 100.8 (d, $^2J_{CF}$ = 9.6 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ –115.6 (dd, $^3J_{HF}$ = 42.7; 12.2 Hz).

Ethyl 2-Fluoroacrylate (6b)



Method B. Ethyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-fluoroacetate (**5b**): 303 mg (1.00 mmol); paraformaldehyde: 300 mg (10.0 mmol, 10 molar equiv); Cs_2CO_3: 652 mg (2.00 mmol, 2 molar equiv); CH_2Cl_2: 10.0 mL. Eluting solvent: CH_2Cl_2. Product is volatile and solvent needs to be removed cautiously, yield lower due to volatility. Yield of ethyl 2-fluoroacrylate (**6b**):[17] 76 mg (64%, a volatile, colorless liquid). R_f (SiO_2, CH_2Cl_2) = 0.72. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.67 (dd, 1H, *J* = 43.5; 3.4 Hz), 5.31 (dd, 1H, *J* = 13.2; 3.4 Hz), 4.30 (q, 2H, *J* = 7.2 Hz), 1.34 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.6 (d, $^2J_{CF}$ = 36.1 Hz), 153.7 (d, $^1J_{CF}$ = 262.3 Hz), 102.7 (d, $^2J_{CF}$ = 14.6 Hz), 62.1, 14.3. ^{19}F NMR (282 MHz, $CDCl_3$): δ –117.72 (d, $^3J_{HF}$ = 42.7 Hz).

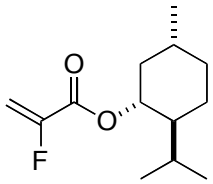
Benzyl 2-Fluoroacrylate (6c)



Method B. Benzyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-fluoroacetate (**5c**): 183 mg (0.500 mmol);

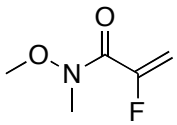
paraformaldehyde: 150 mg (5.00 mmol, 10 molar equiv); Cs_2CO_3: 326 mg (1.00 mmol, 2 molar equiv); CH_2Cl_2: 5.0 mL. Silica gel: 200-300 mesh; eluting solvent: CH_2Cl_2. Volatile compound, drying under vacuum decreases yield. Yield of benzyl 2-fluoroacrylate (**6c**):[18] after solvent evaporation and careful drying under vacuum: 59.0 mg (66%, a volatile, colorless liquid). R_f (SiO_2, CH_2Cl_2) = 0.61. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40-7.35 (m, 5H, Ar-H), 5.71 (dd, 1H, J = 43.3; 3.1 Hz), 5.34 (dd, 1H, J = 13.1; 3.4 Hz), 5.28 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.5 ($^2J_{CF}$ = 36.6 Hz), 153.5 ($^1J_{CF}$ = 262.3 Hz), 135.1, 128.9 (2C), 128.8, 128.6 (2C), 103.2 ($^2J_{CF}$ = 15.1 Hz), 67.7. ^{19}F NMR (282 MHz, $CDCl_3$): δ –117.50 (dd, $^3J_{HF}$ = 42.7; 12.2 Hz).

(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 2-Fluoroacrylate (6d)



Method B. (1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-fluoroacetate (**5d**): 413 mg (1.00 mmol); paraformaldehyde: 300 mg (10.0 mmol, 10 molar equiv); Cs_2CO_3: 652 mg (2.00 mmol, 2 molar equiv); CH_2Cl_2: 10.0 mL. Eluting solvent: CH_2Cl_2. Yield of (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-fluoroacrylate (**6d**): 156 mg (68%, a colorless oil). R_f (SiO_2, 10% EtOAc in hexanes) = 0.71. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.65 (dd, 1H, J = 43.7; 3.2 Hz), 5.30 (dd, 1H, J = 12.9; 3.2 Hz), 4.82 (td, 1H, J = 11.0; 4.4 Hz), 2.05 (br d, 1H, J = 11.7 Hz), 1.86 (hept d, 1H, J = 6.8; 2.4 Hz), 1.70 (br d, 2H, J = 11.2 Hz), 1.54-1.45 (m, 2H), 1.13-1.03 (m, 2H), 0.93-0.85 (m, 7H), 0.78 (d, 3H, J = 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.2 (d, $^2J_{CF}$ = 36.2 Hz), 153.9 (d, $^1J_{CF}$ = 262.7 Hz), 102.4 (d, $^2J_{CF}$ = 15.1 Hz), 76.5, 47.2, 40.8, 34.3, 31.6, 26.6, 23.8, 22.2, 20.8, 16.6. ^{19}F NMR (282 MHz, $CDCl_3$): δ –117.2 (dd, $^3J_{HF}$ = 42.7; 12.2 Hz). HRMS (ESI) calcd for $C_{13}H_{21}FO_2Na$ $[M + Na]^+$ 251.1418, found 251.1421. Optical rotation: $[\alpha]_D^{25}$ = –75.5° (c = 1.00 g/100 mL, MeOH).

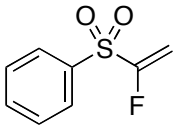
2-Fluoro-N-methoxy-N-methylacrylamide (6e)



Method B. 2-(Benzo[*d*]thiazol-2-ylsulfonyl)-2-fluoro-*N*-methoxy-*N*-methylacetamide (**5e**): 159 mg (0.500 mmol); paraformaldehyde: 150 mg (5.00 mmol, 10 molar equiv); Cs_2CO_3: 326 mg (1.00 mmol, 2 molar equiv); CH_2Cl_2: 5.0 mL. Eluting solvent: CH_2Cl_2. Product is volatile and

solvent needs to be removed cautiously. Yield of 2-fluoro-*N*-methoxy-*N*-methylacrylamide (**6e**): 59 mg (89%, a volatile colorless liquid). R_f (SiO_2, CH_2Cl_2) = 0.49. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.42 (dd, 1H, J = 46.4; 3.4 Hz), 5.17 (dd, 1H, J = 16.6; 3.4 Hz), 3.74 (s, 3H), 3.25 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.1 (d, $^2J_{CF}$ = 29.7 Hz), 156.6 (d, $^1J_{CF}$ = 269.6 Hz), 100.6 (d, $^2J_{CF}$ = 15.5 Hz), 61.9, 33.7. ^{19}F NMR (282 MHz, $CDCl_3$): δ –110.79 (dd, $^3J_{HF}$ = 45.8; 12.2 Hz). HRMS (ESI) calcd for $C_5H_9FNO_2$ $[M + H]^+$ 134.0612, found 134.0612.

Reaction of Diethyl Fluoro(phenylsulfonyl)methylphosphonate with Paraformaldehyde

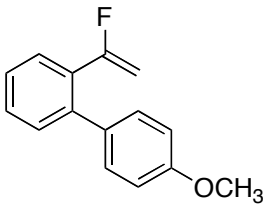


Method B. Diethyl fluoro(phenylsulfonyl)methylphosphonate: 310 mg (1.00 mmol); paraformaldehyde: 300 mg (10.0 mmol, 10 molar equiv); Cs_2CO_3: 652 mg (2.00 mmol, 2 molar equiv); CH_2Cl_2: 10.0 mL. Eluting solvent: CH_2Cl_2. Yield of (1-fluorovinylsulfonyl)benzene (**6a**):[10,16] 165 mg (89%) of low-melting, light brown solid.

SUZUKI COUPLING OF 1-BROMO-2-(1-FLUOROVINYL)BENZENE (3c): GENERAL PROCEDURE

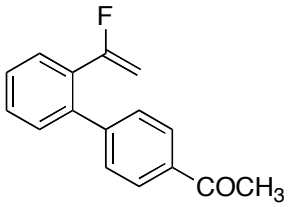
Into an oven-dried vial, purged with argon, 1-bromo-2-(1-fluorovinyl)benzene (**3c**), (0.10 mmol), arylboronic acid (0.10 mmol), caesium fluoride (0.30 mmol), tris(dibenzylideneacetone) dipalladium ($Pd_2(dba)_3$, 5 mol%) and 2'-(dicyclohexylphosphino)-*N*,*N*-dimethylbiphenyl-2-amine (10 mol%) were weighed. The mixture was purged again with argon and 1,4-dioxane (0.3 mL, 0.33 M solution of **3c**) was added. The reaction mixture was stirred at rt for ca 1 min in order to become homogeneous, and then heated under stirring at 80 °C for 2h. The reaction mixture was diluted with dichloromethane, filtered through celite and the filtrate was concentrated under vacuum. The crude reaction mixture was purified by column chromatography using 100-200 mesh silica gel (for eluting solvent see specific headings). The amounts of substrate, reagents and solvent, and product yield are given under the specific compound headings below.

2-(1-Fluorovinyl)-4'-methoxybiphenyl (7)



1-Bromo-2-(1-fluorovinyl)benzene (**3c**): 20.1 mg (0.1 mmol); 4-methoxyphenylboronic acid: 15.2 mg (0.1 mmol); caesium fluoride: 45.6 mg (0.3 mmol); $Pd_2(dba)_3$: 4.6 mg (0.005 mmol, 5 mol%); 2'-(dicyclohexylphosphino)-*N*,*N*-dimethylbiphenyl-2-amine: 3.9 mg (0.01 mmol, 10 mol%); 1,4-dioxane: 0.3 mL (0.33 M solution of **3c**). Eluting solvent for column chromatography: 2% EtOAc in hexanes. Yield of 2-(1-fluorovinyl)-4'-methoxybiphenyl (**7**): 18.6 mg (82%, a colorless liquid). R_f (SiO_2, 5% EtOAc in hexanes) = 0.36. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, 1H, J = 7.8 Hz, ArH), 7.42 (t, 1H, J = 7.3 Hz, ArH), 7.36-7.31 (m, 4H, ArH), 6.95 (d, 2H, J = 8.8 Hz, ArH), 4.81 (dd, 1H, J = 17.1; 2.9 Hz), 4.48 (dd, 1H, J = 49.3; 2.9 Hz), 3.85 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.8 (d, $^1J_{CF}$ = 254.0 Hz), 159.2, 140.6, 133.9, 131.5 (d, $^2J_{CF}$ = 26.1 Hz), 130.9, 129.9 (d, 2C, $^5J_{CF}$ = 1.4 Hz), 129.7 (d, J_{CF} = 0.9 Hz), 129.3 (d, $^3J_{CF}$ = 5.0 Hz), 127.1, 113.9 (2C), 94.7 (d, $^2J_{CF}$ = 22.0 Hz), 55.5. ^{19}F NMR (282 MHz, $CDCl_3$): δ –91.52 (dd, $^3J_{HF}$ = 46.9; 14.7 Hz). HRMS (ESI) calcd for $C_{15}H_{14}FO$ $[M + H]^+$ 229.1023, found 229.1025.

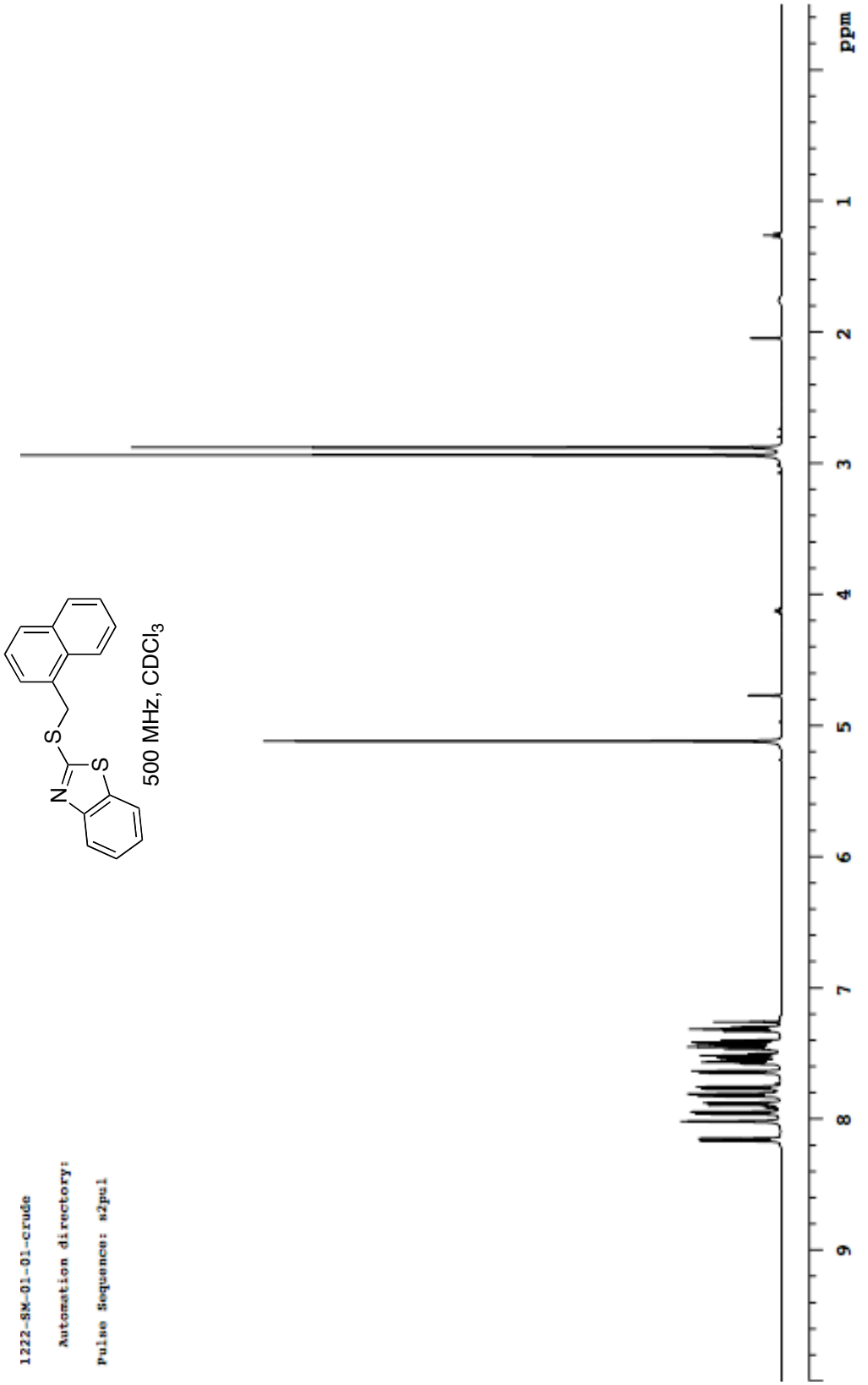
1-[2'-(1-Fluorovinyl)biphenyl-4-yl]ethanone (8)

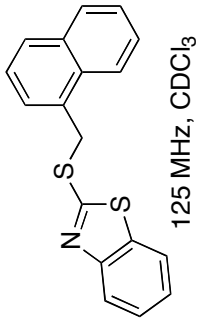


1-Bromo-2-(1-fluorovinyl)benzene (**3c**): 20.1 mg (0.1 mmol); 4-acetylphenylboronic acid: 16.4 mg (0.1 mmol); caesium fluoride: 45.6 mg (0.3 mmol); $Pd_2(dba)_3$: 4.6 mg (0.005 mmol, 5 mol%); 2'-(dicyclohexylphosphino)-*N*,*N*-dimethylbiphenyl-2-amine: 3.9 mg (0.01 mmol, 10 mol%); 1,4-dioxane: 0.3 mL (0.33 M solution of **3c**). Eluting solvent for column chromatography: trace amounts of unreacted 1-bromo-2-(1-fluorovinyl)benzene (**3c**) were first eluted with 2% EtOAc in hexanes, product **8** was subsequently eluted with 4% EtOAc in hexanes. Yield of 1-[2'-(1-fluorovinyl)biphenyl-4-yl]ethanone (**8**): 14.2 mg (59%, a colorless liquid). R_f (SiO_2, 10% EtOAc in hexanes) = 0.29. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (d, 2H, J = 8.3 Hz, ArH), 7.57 (d, 1H, J = 7.8 Hz, ArH), 7.52 (d, 2H, J = 8.3 Hz, ArH), 7.46 (t, 1H, J = 7.3 Hz, ArH), 7.41 (t, 1H, J = 7.8 Hz, ArH), 7.33 (d, 1H, J = 7.8 Hz, ArH), 4.82 (dd, 1H, J = 16.6; 2.9 Hz), 4.53 (dd, 1H, J = 48.8; 2.9 Hz), 2.64 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.0, 163.4 (d, $^1J_{CF}$ = 254.0 Hz), 146.4, 139.7, 136.2, 131.5 (d, $^2J_{CF}$ = 26.1 Hz), 130.6, 129.9 (d, J_{CF} = 0.9 Hz), 129.5 (d, $^3J_{CF}$ = 4.6 Hz), 129.0 (d, 2C, J_{CF} = 1.8 Hz), 128.6 (2C), 128.1, 95.1 (d, $^2J_{CF}$ = 22.9 Hz), 26.9. ^{19}F NMR (282 MHz, $CDCl_3$): δ –90.89 (dd, $^3J_{HF}$ = 46.9; 14.7 Hz). HRMS (ESI) calcd for $C_{16}H_{14}FO$ $[M + H]^+$ 241.1023, found 241.1026.

REFERENCES

1. A. K. Ghosh, B. Zajc, *Org. Lett.*, 2006, **8**, 1553–1556.
2. (a) A. Gaplovsky, R. Hercek, P. Kuran, *Chem. Pap.*, 2001, **55**, 45–48. (b) L. Zahajska, V. Klimesova, J. Koci, K. Waisser, J. Kaustova, *Arch. Pharm.*, 2004, **337**, 549–555.
3. (a) V. K. Ramanatham, V. S. R. S. K. Kotha, R. G. Kotarkonda, *J. Heterocyclic Chem.*, 2005, **42**, 153–156. (b) N. Allendörfer, M. Es-Sayed, M. Nieger, S. Bräse, *Synthesis*, 2010, 3439–3448.
4. J. Koí, V. Klimešová, K. Waisser, J. Kaustová, H.-M. Dahse, U. Möllmann, *Bioorg. Med. Chem. Lett.*, 2002, **12**, 3275–3278.
5. Commercially available. CAS Registry Number: 401598-07-0.
6. O. Minoru, F. Kiyoshi, I. Katsuaki, Patent: Jpn. Kokai Tokkyo Koho (1982), JP 57135945 A 19820821.
7. V. Sutoris, P. Foltinova, Patent: Czech. (1983), CS 203790 B1 19810331.
8. M. T. Makhija, R. T. Kasliwal, V. M. Kulkarni, N. Neamati, *Bioorg. Med. Chem.,* 2004, **12**, 2317–2333.
9. M. del Solar, A. K. Ghosh, B. Zajc, *J. Org. Chem.,* 2008, **73**, 8206–8211.
10. M. He, A. K. Ghosh, B. Zajc, *Synlett,* 2008, 999–1004.
11. A. K. Ghosh, S. Banerjee, S. Sinha, S. B. Kang, B. Zajc, *J. Org. Chem.,* 2009, **74**, 3689–3697.
12. C. F. Schwender, S. A. Beers, E. Malloy, K. Demarest, L. Minor, K. H. W. Lau, *Bioorg. Med. Chem. Lett.*, 1995, **5**, 1801–1806.
13. T. Hanamoto, T. Kobayashi**,** *J. Org. Chem.*, 2003, **68**, 6354–6359.
14. O. A. Wong, Y. Shi, *J. Org. Chem.*, 2009, **74**, 8377–8380.
15. T. Hanamoto, T. Kobayashi, M. Kondo, *Synlett*, 2001, 281–283.
16. (a) T. Koizumi, T. Hagi, Y. Horie, Y. Takeuchi, *Chem. Pharm. Bull.*, 1987, **35**, 3959-3962. (b) D. P. Matthews, J. R. McCarthy, *J. Org. Chem.*, 1990, **55**, 2973–2975.
17. See for example: (a) M. Hudlicky, *Tetrahedron Lett.*, 1960, **1**, 21-22. (b) A. Thenappan, D. J. Burton, *J. Fluorine Chem.*, 1990, **48**, 153-157. (c) C. Grison, N. Boulliung, P. Coutrot, Eur. Pat. Appl.: (1993), EP 521752 A1 19930107.
18. (a) Y. Usuki, M. Iwaoka, S. Tomoda, *J. Chem. Soc., Chem. Commun.*, 1992, 1148–1150. (b) K. W. Laue, G. Haufe, *Synthesis*, 1998, 1453–1456.





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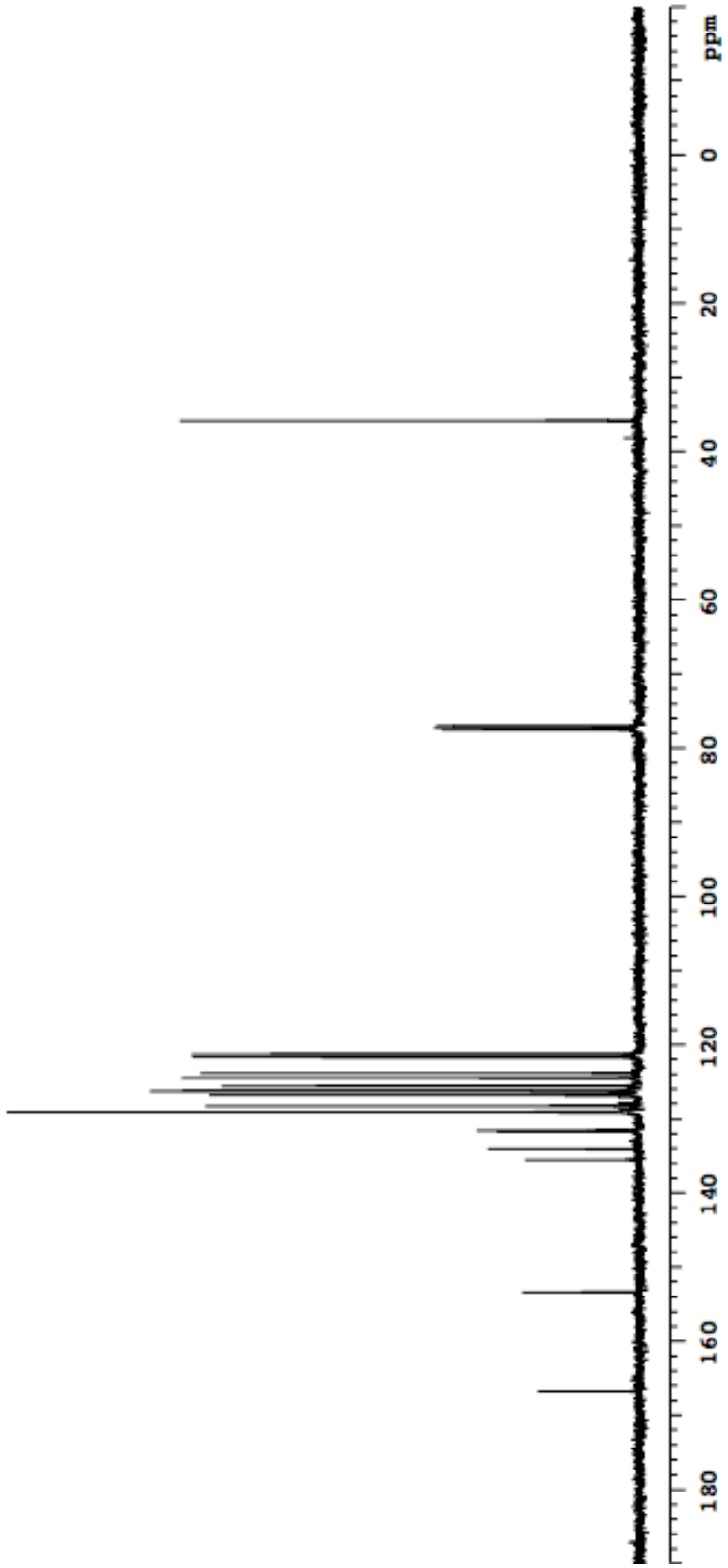

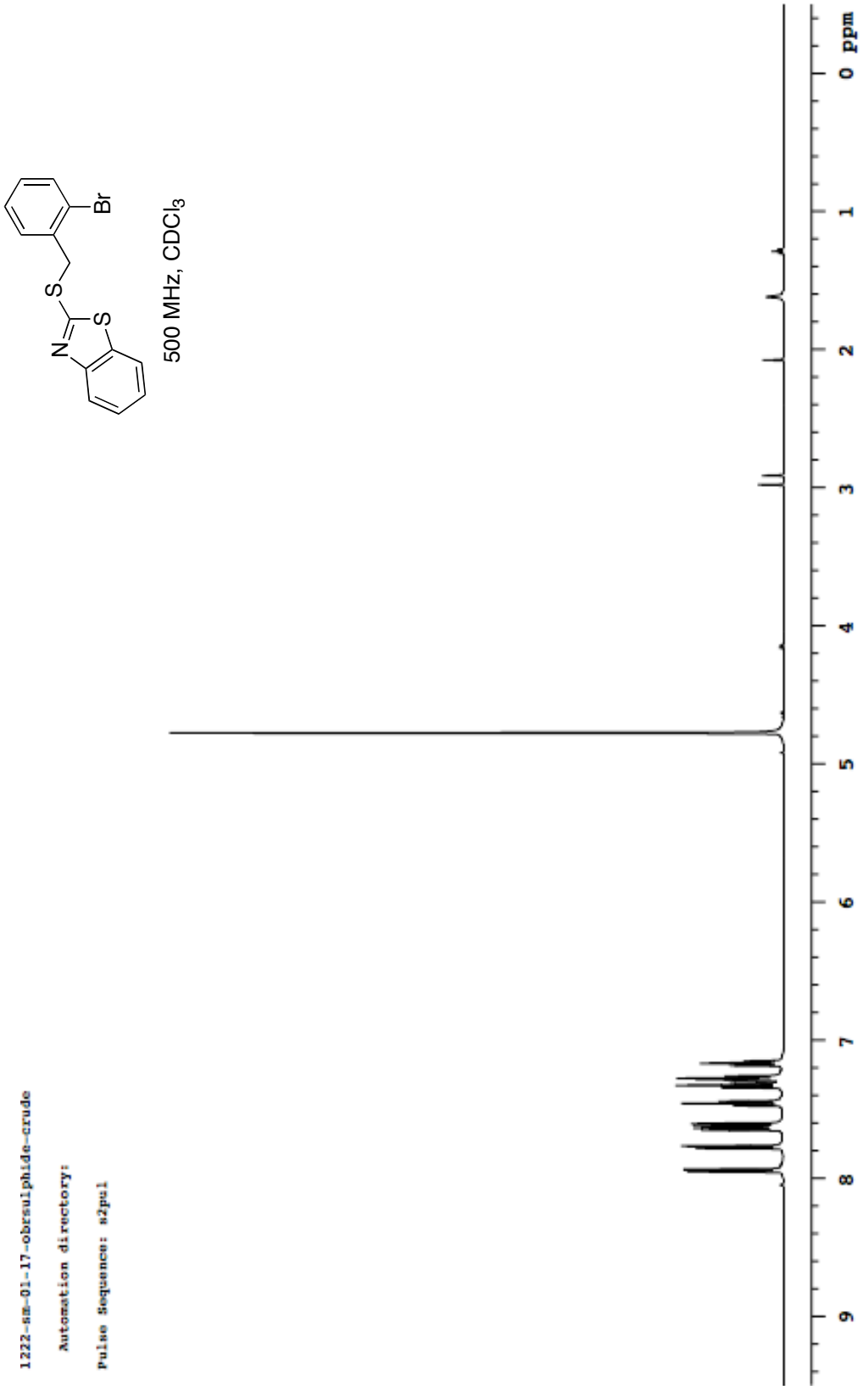

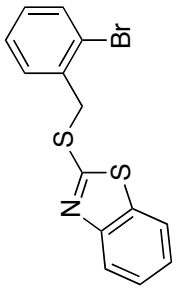

125 MHz, $CDCl_3$

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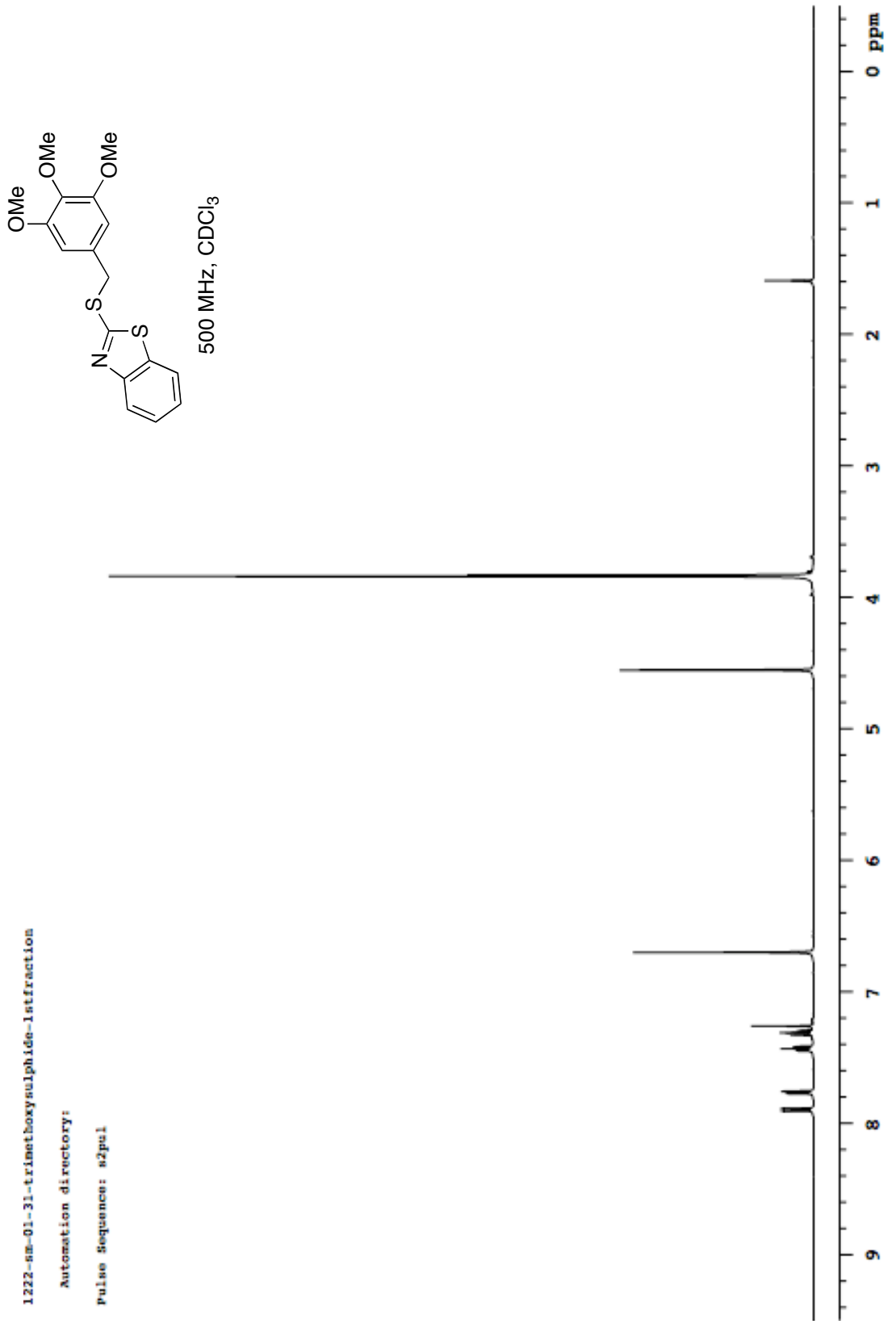
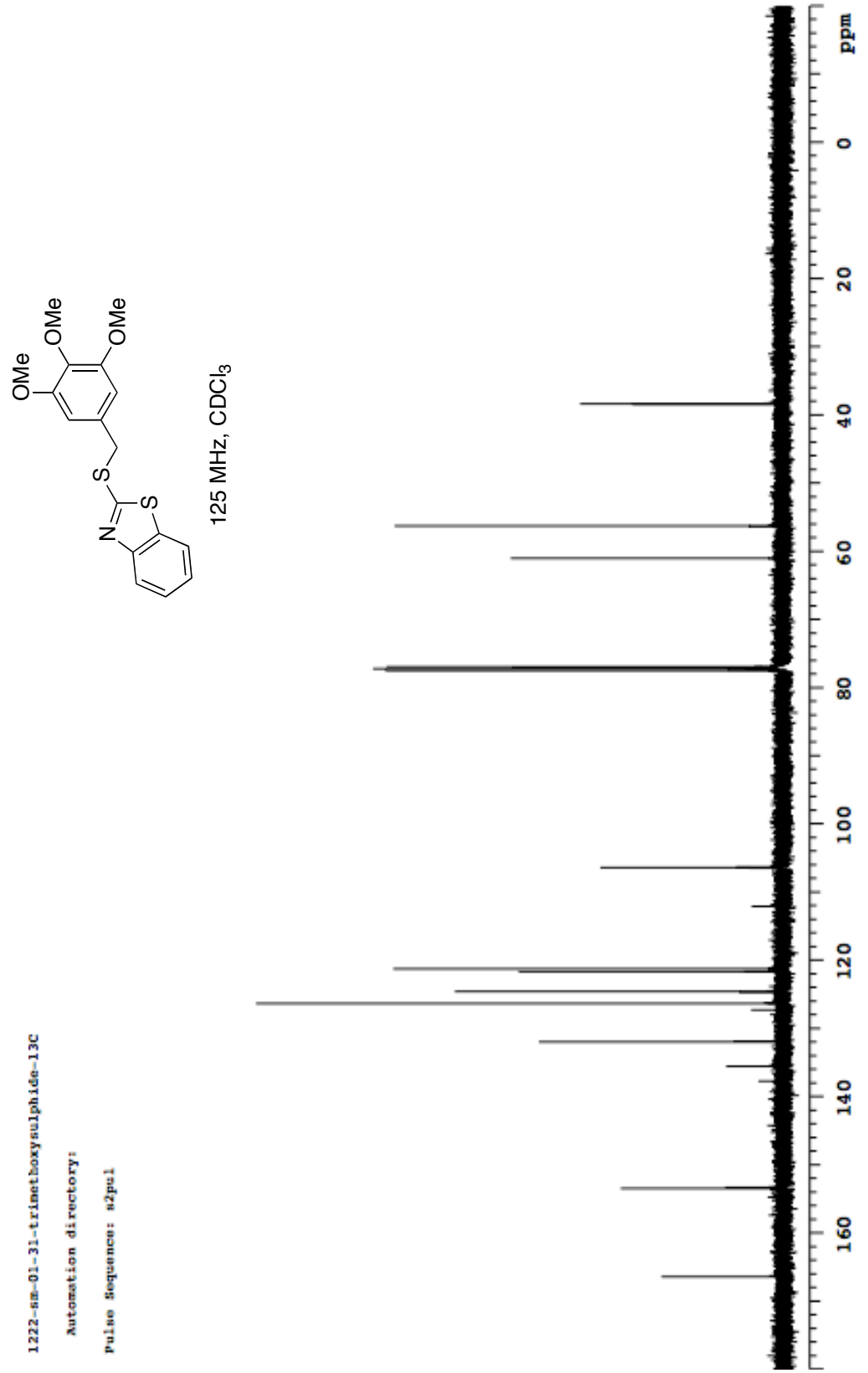
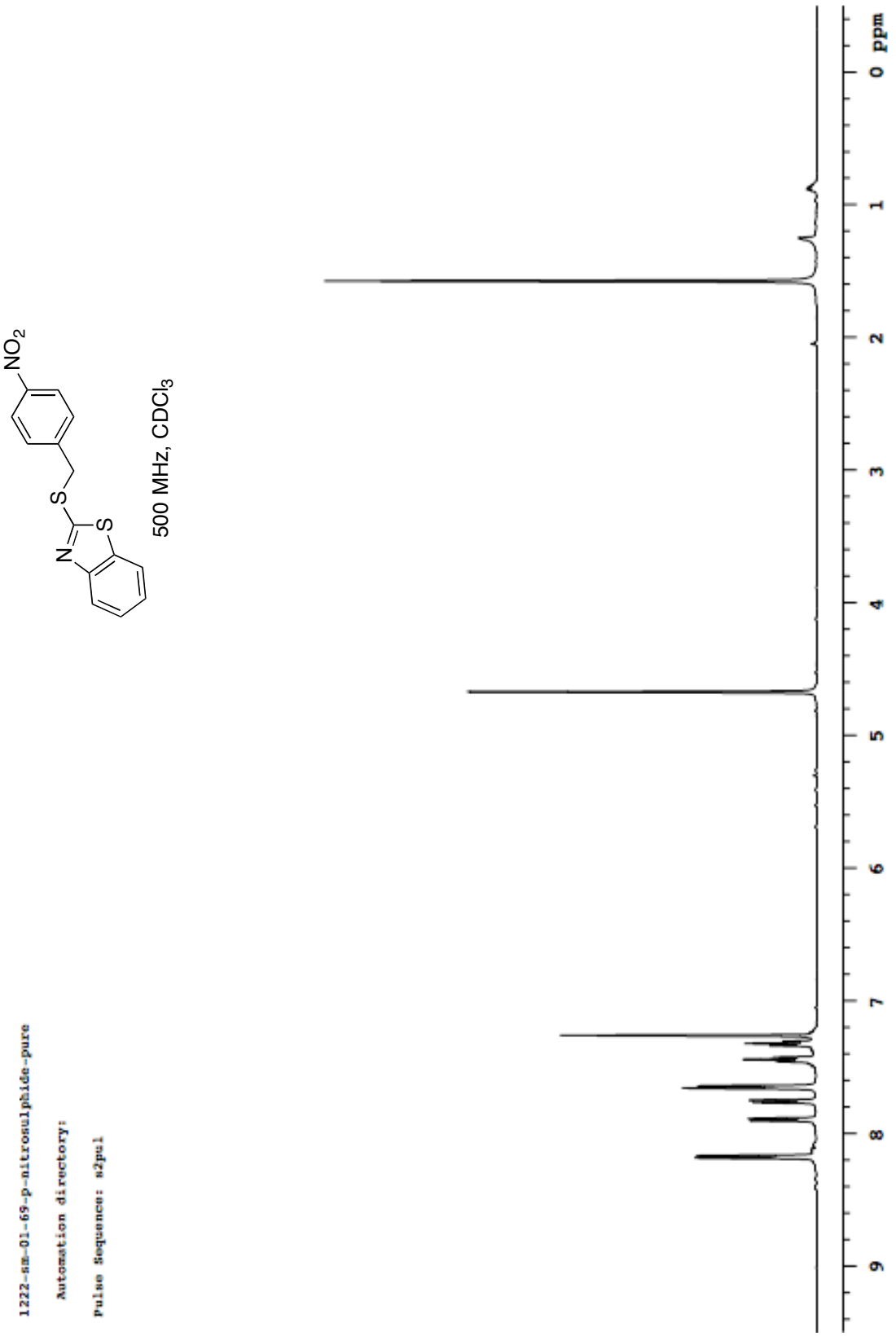
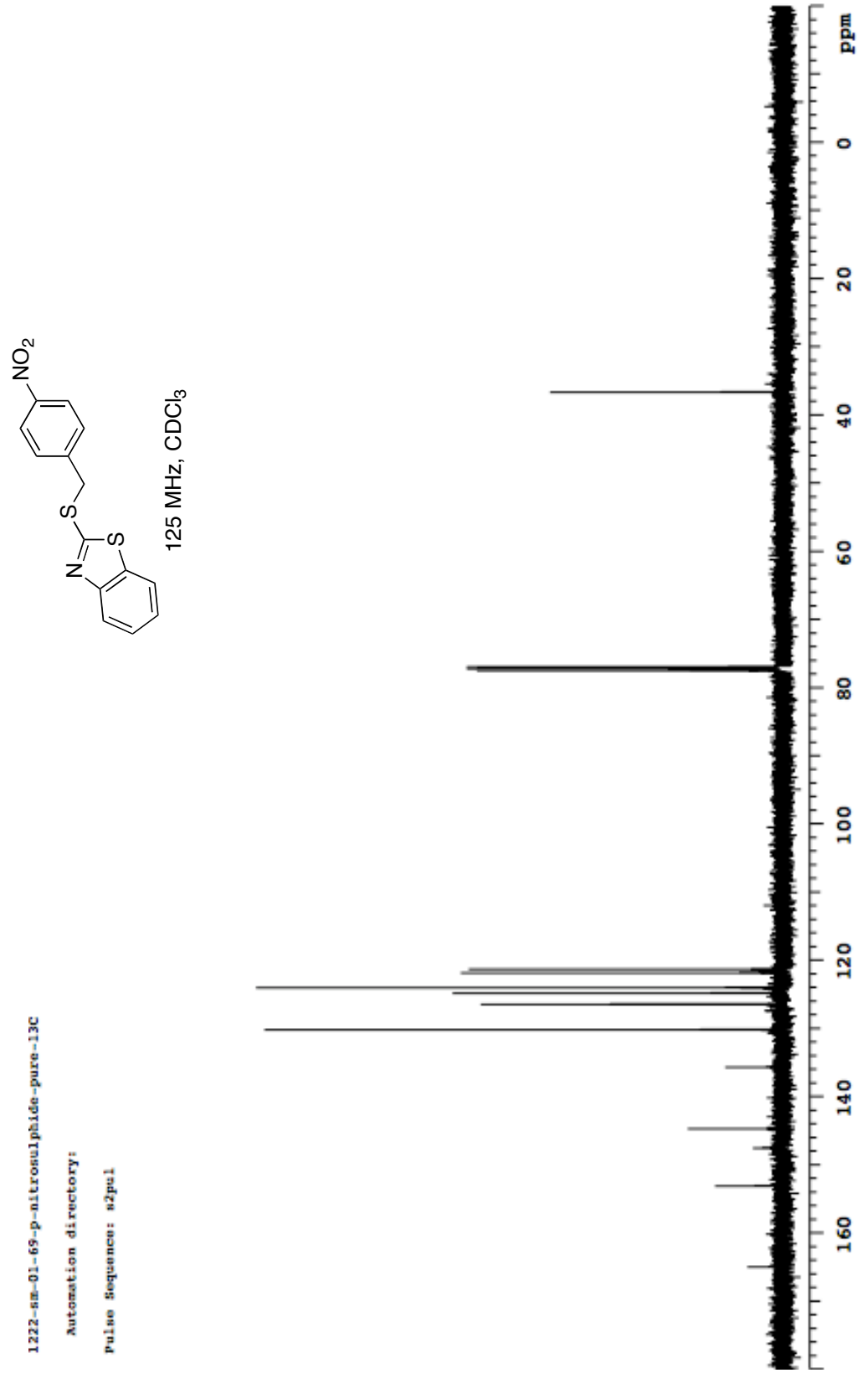
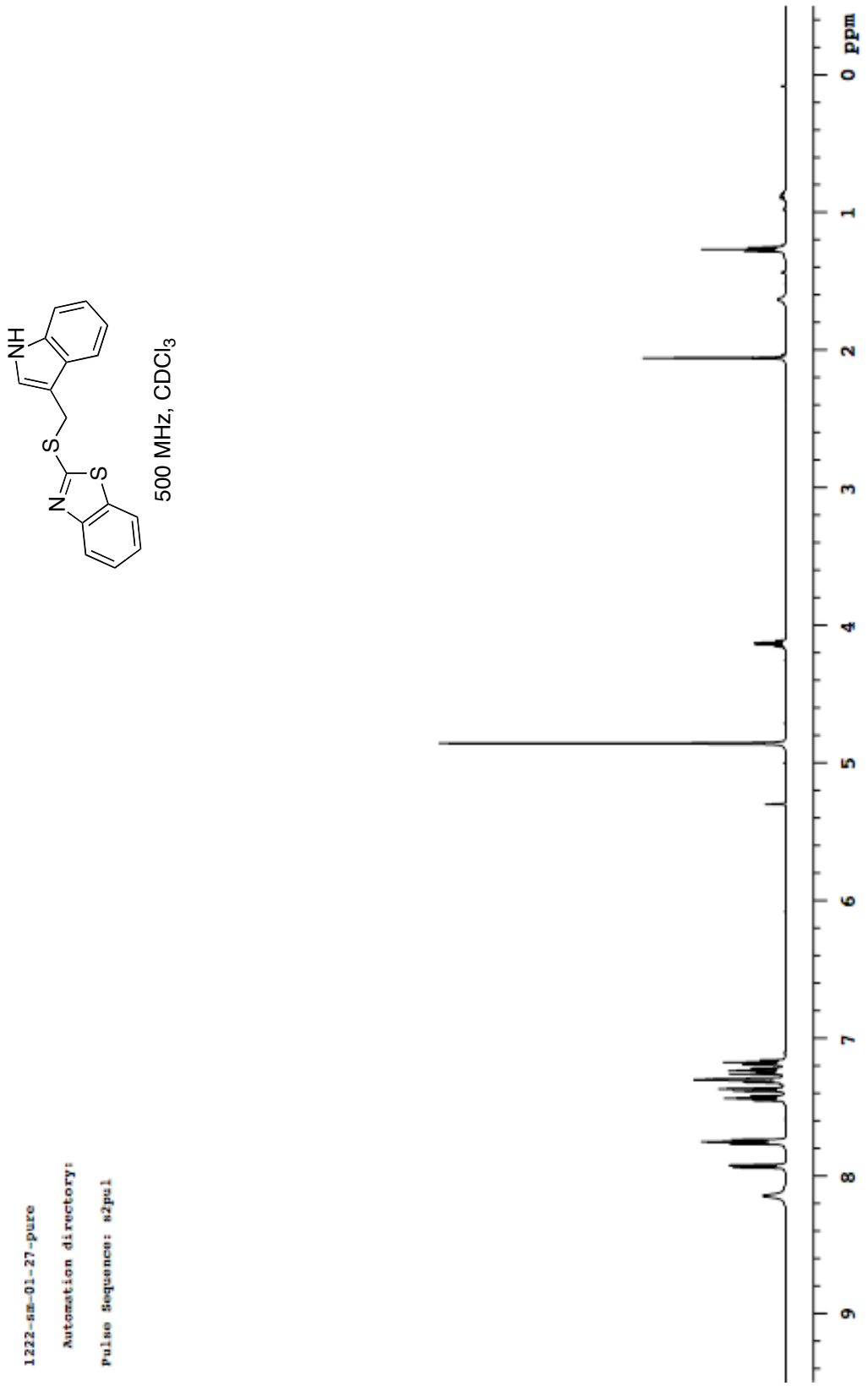
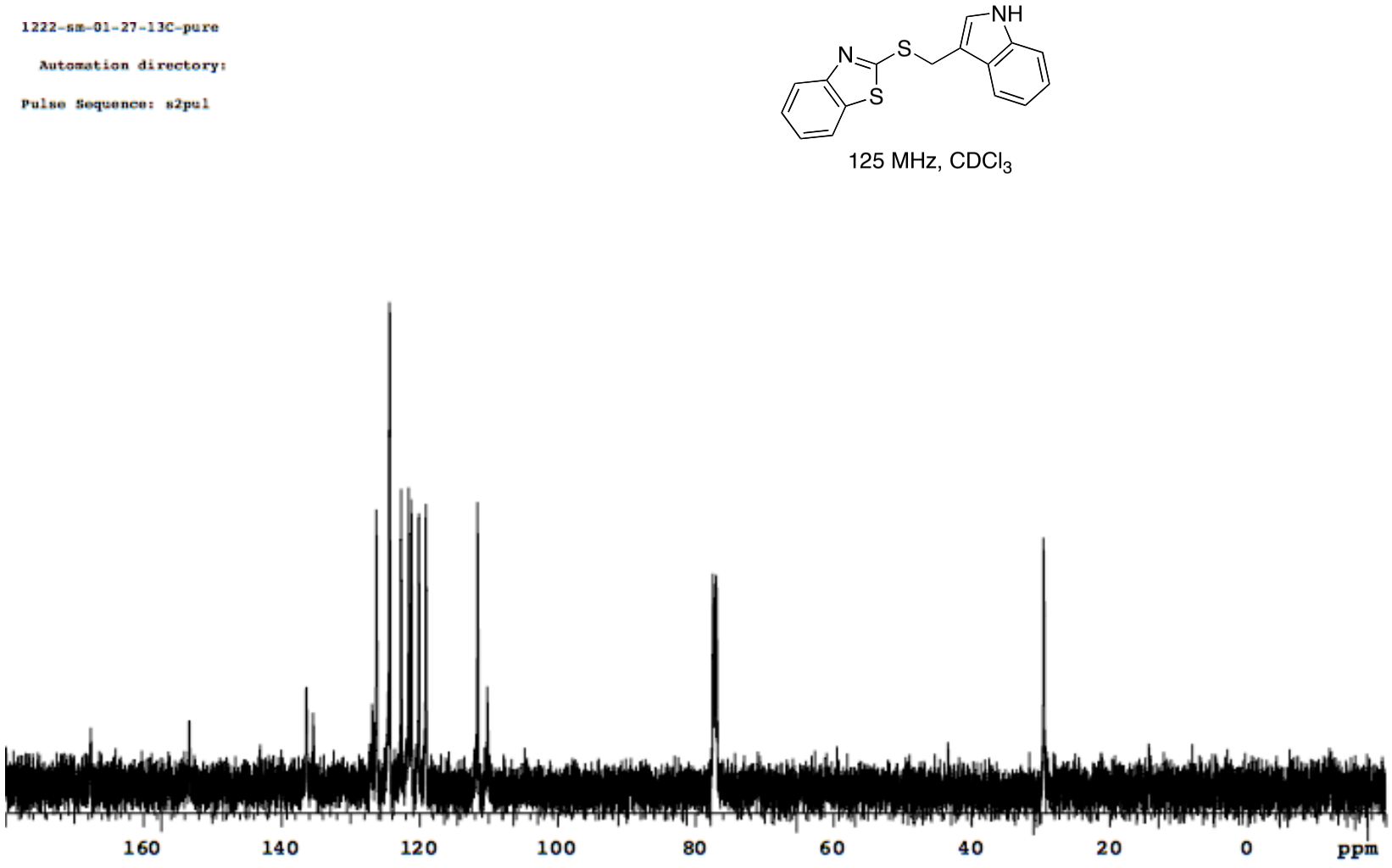


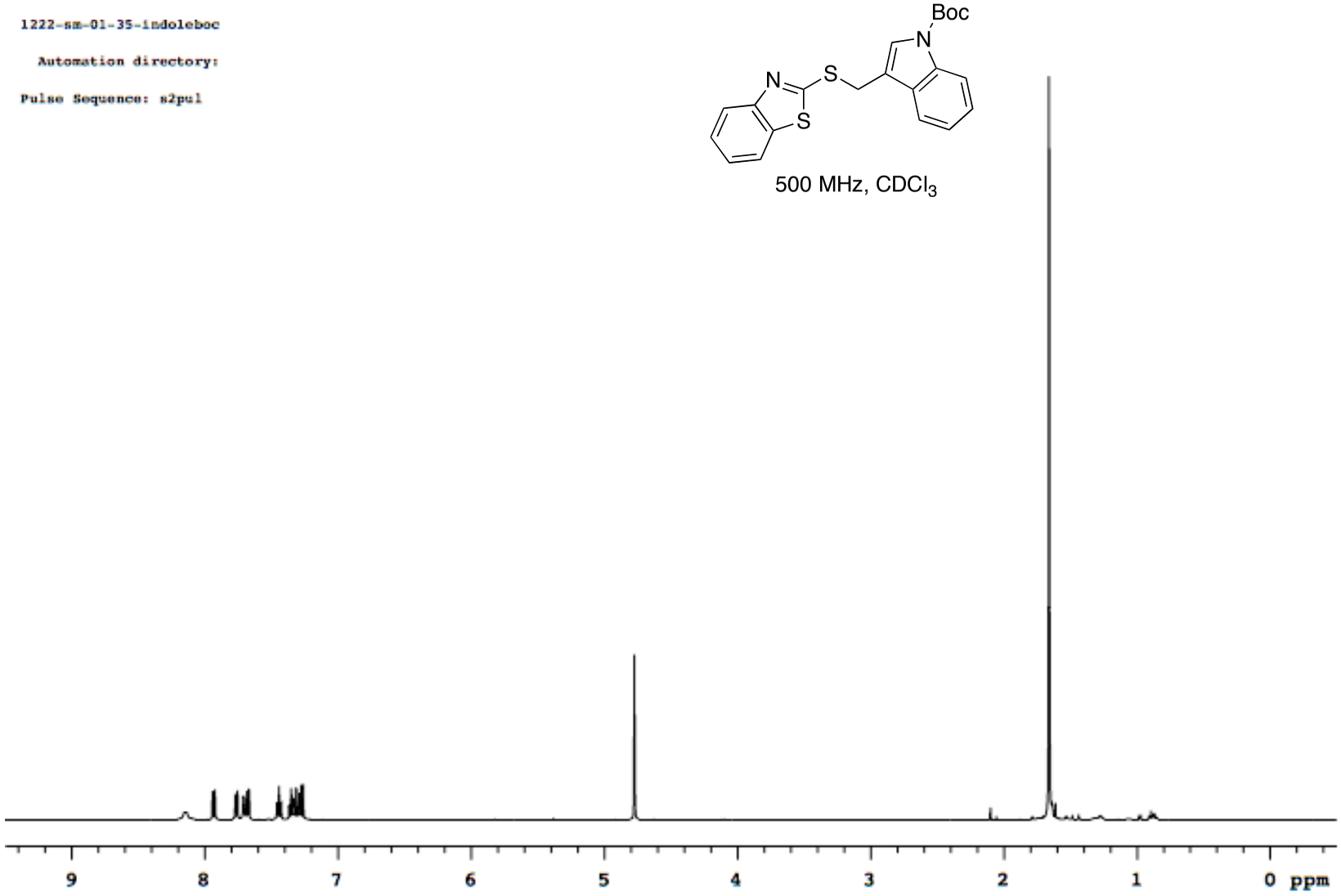


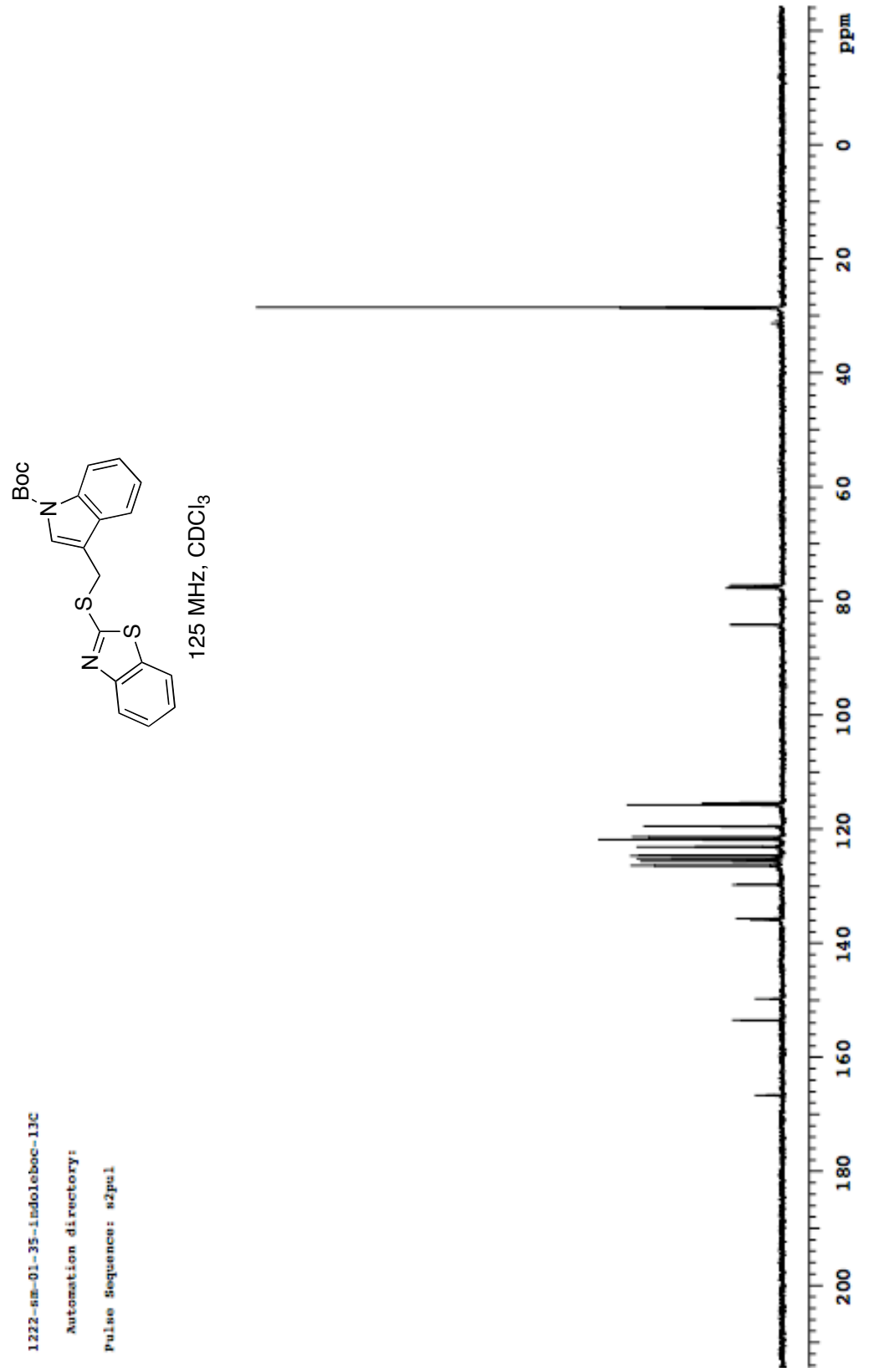


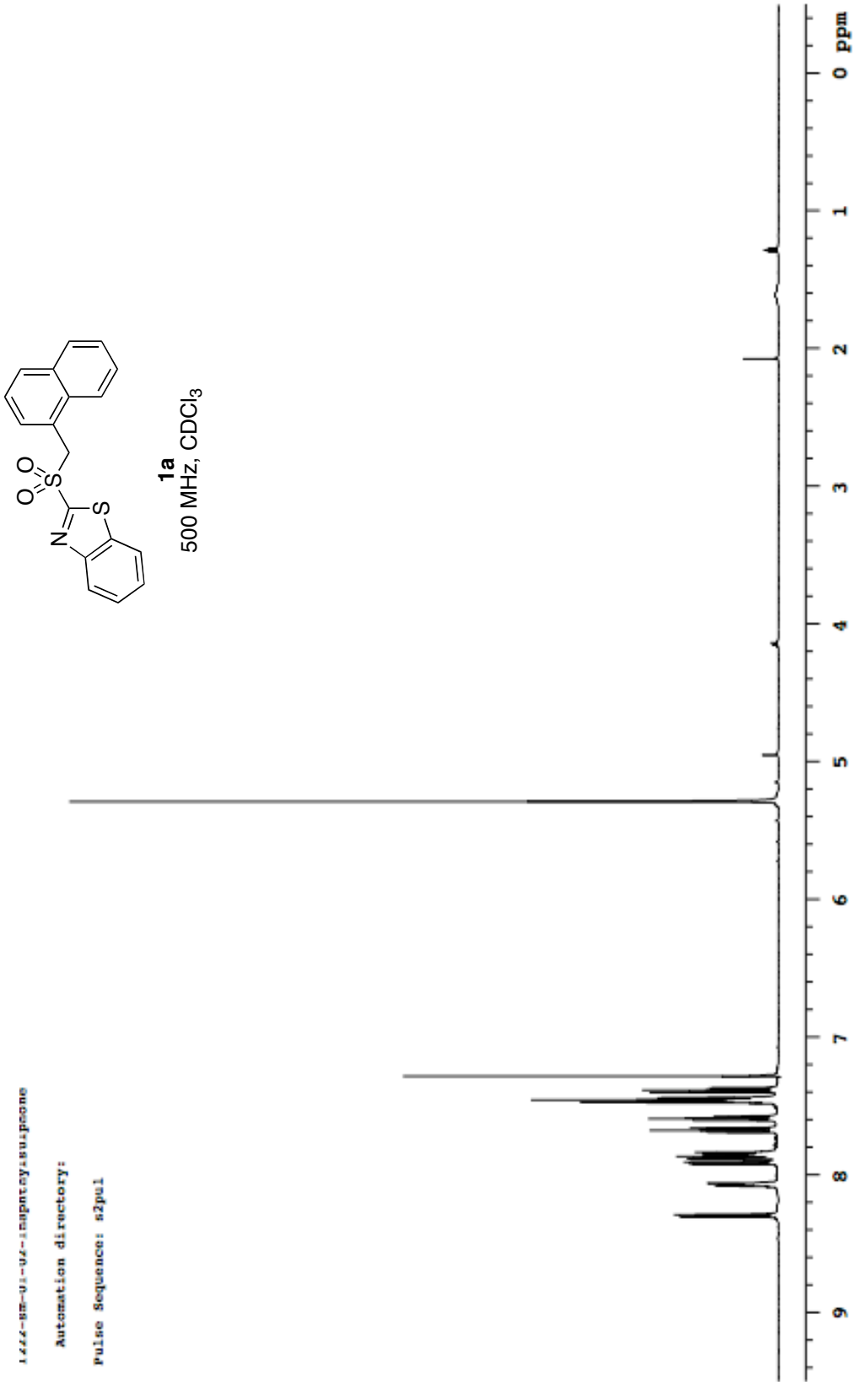


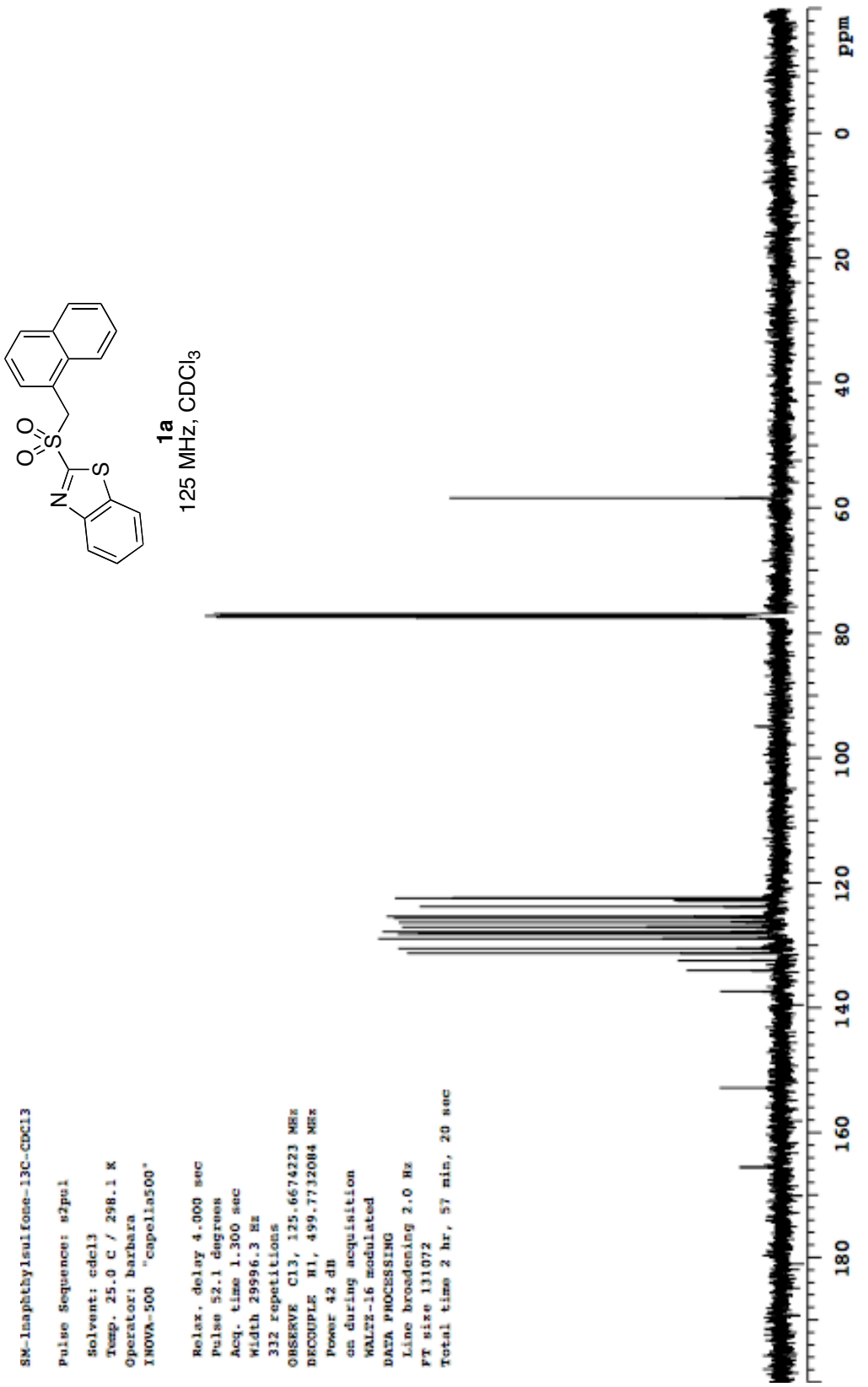


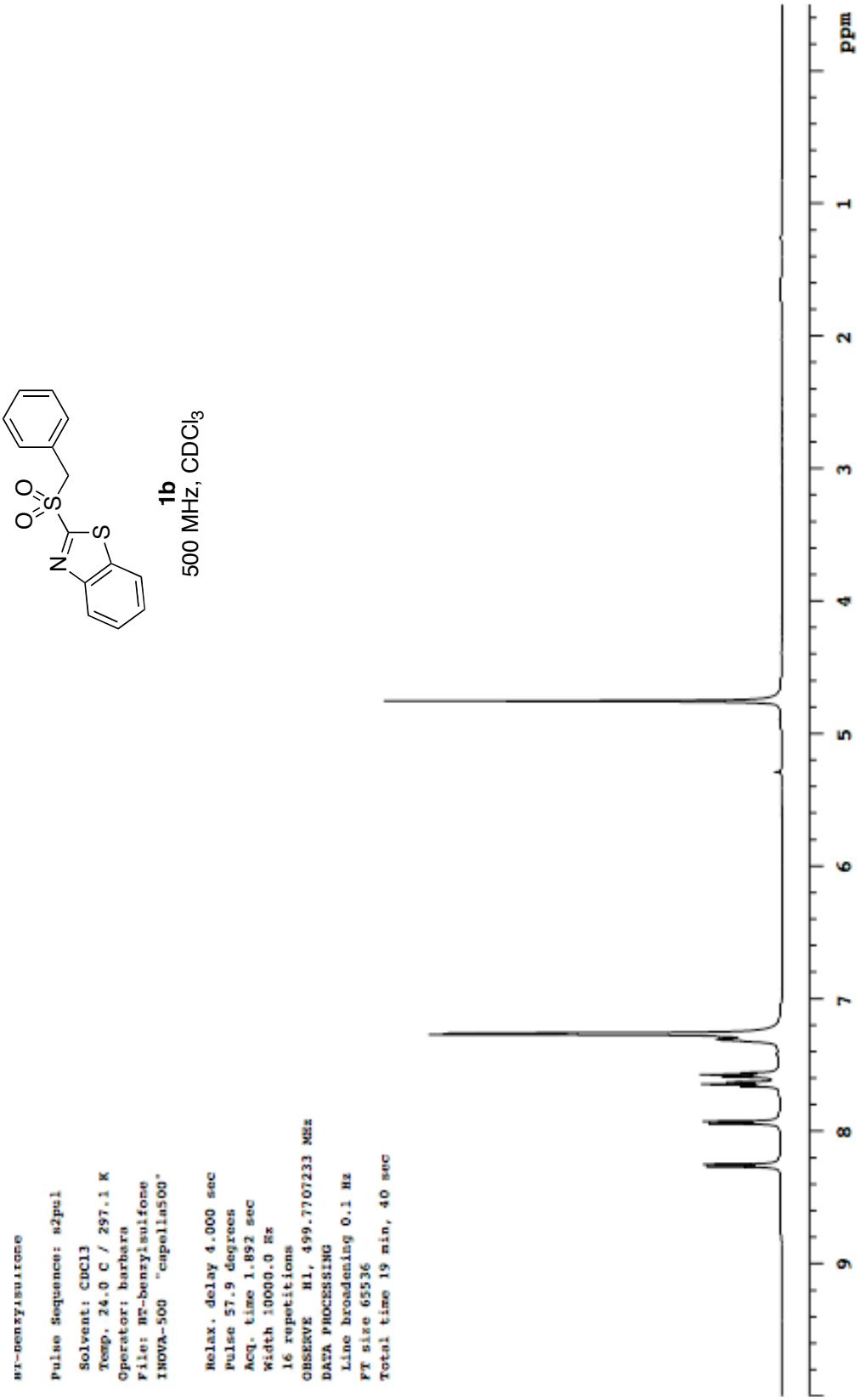


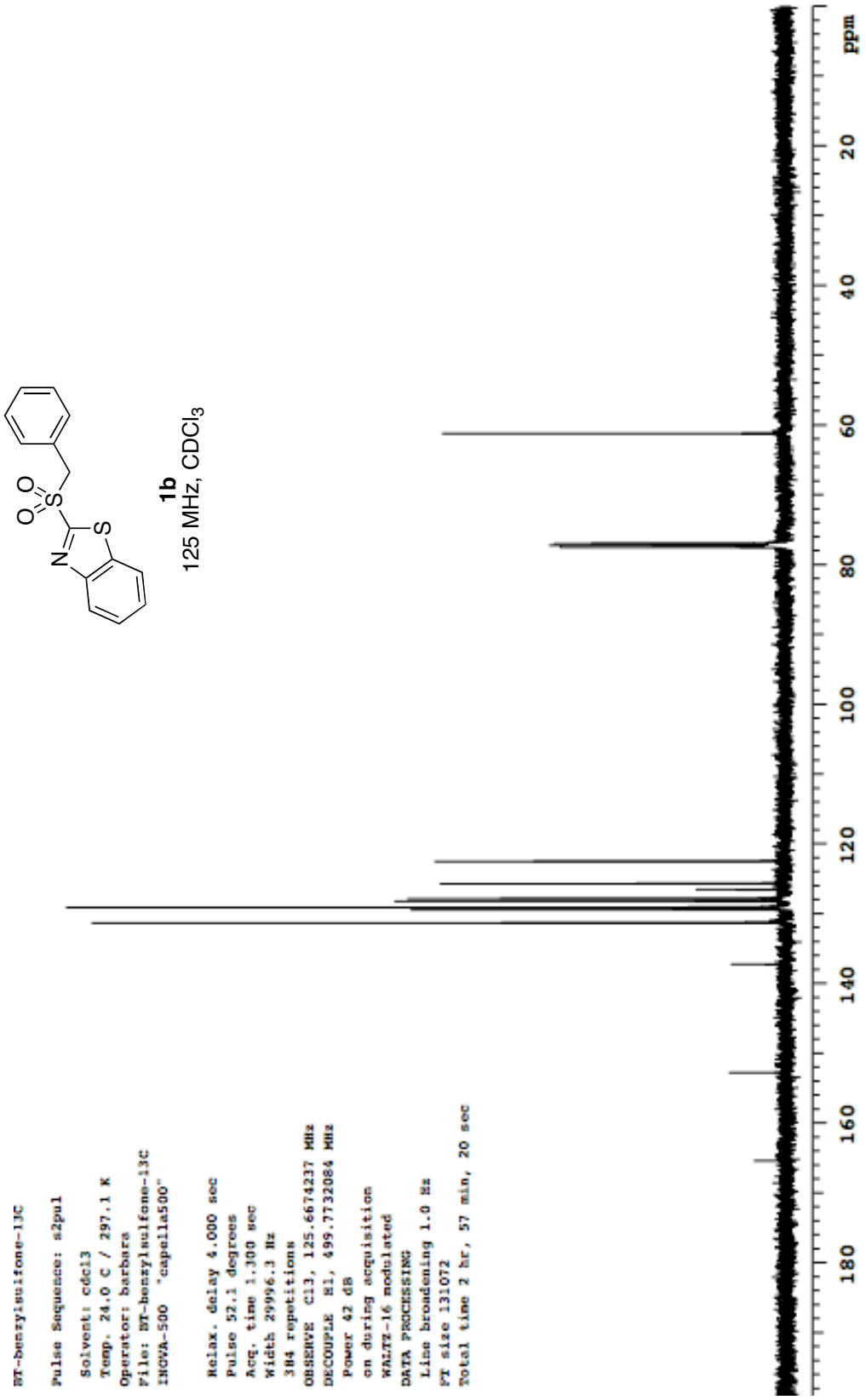


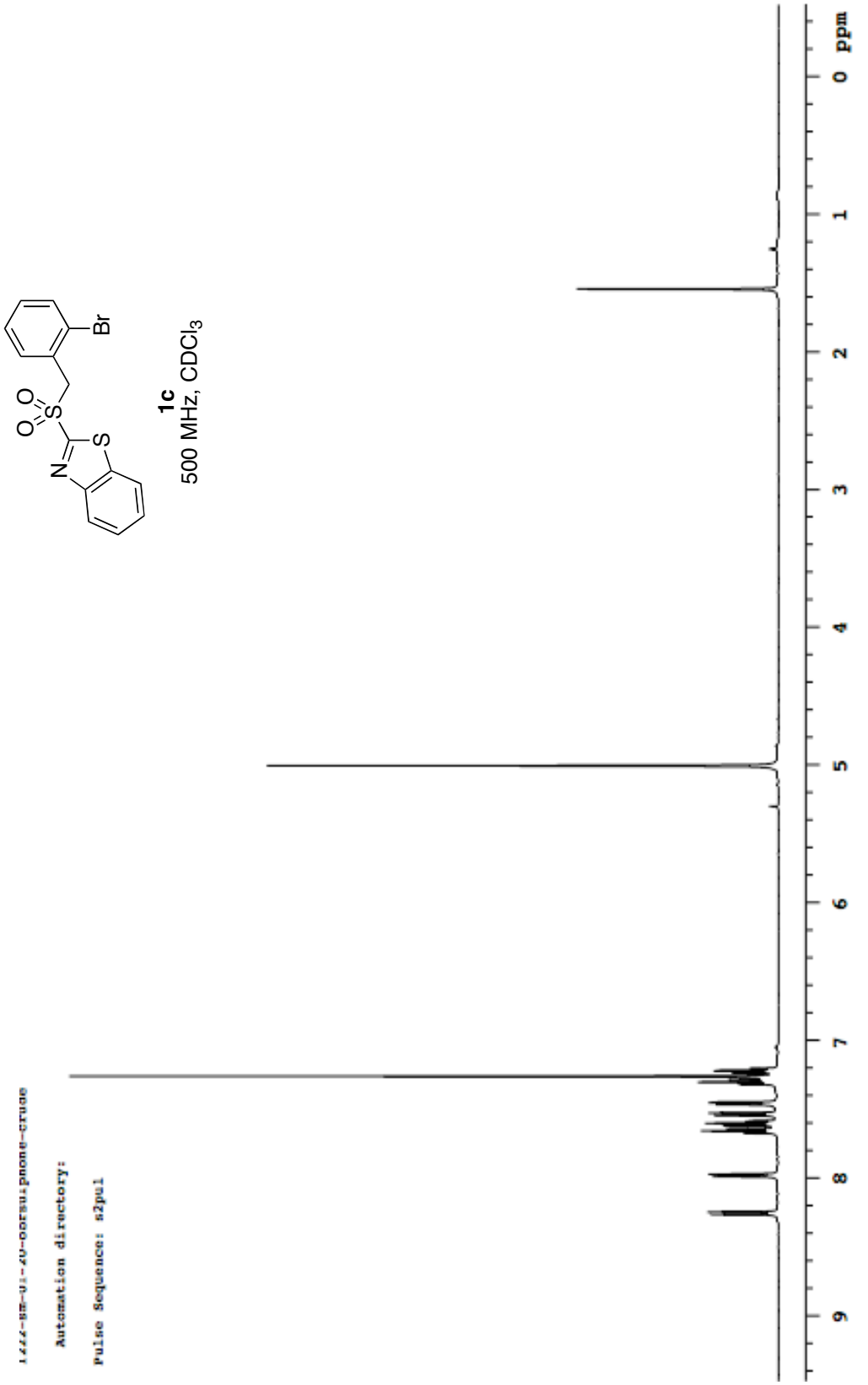


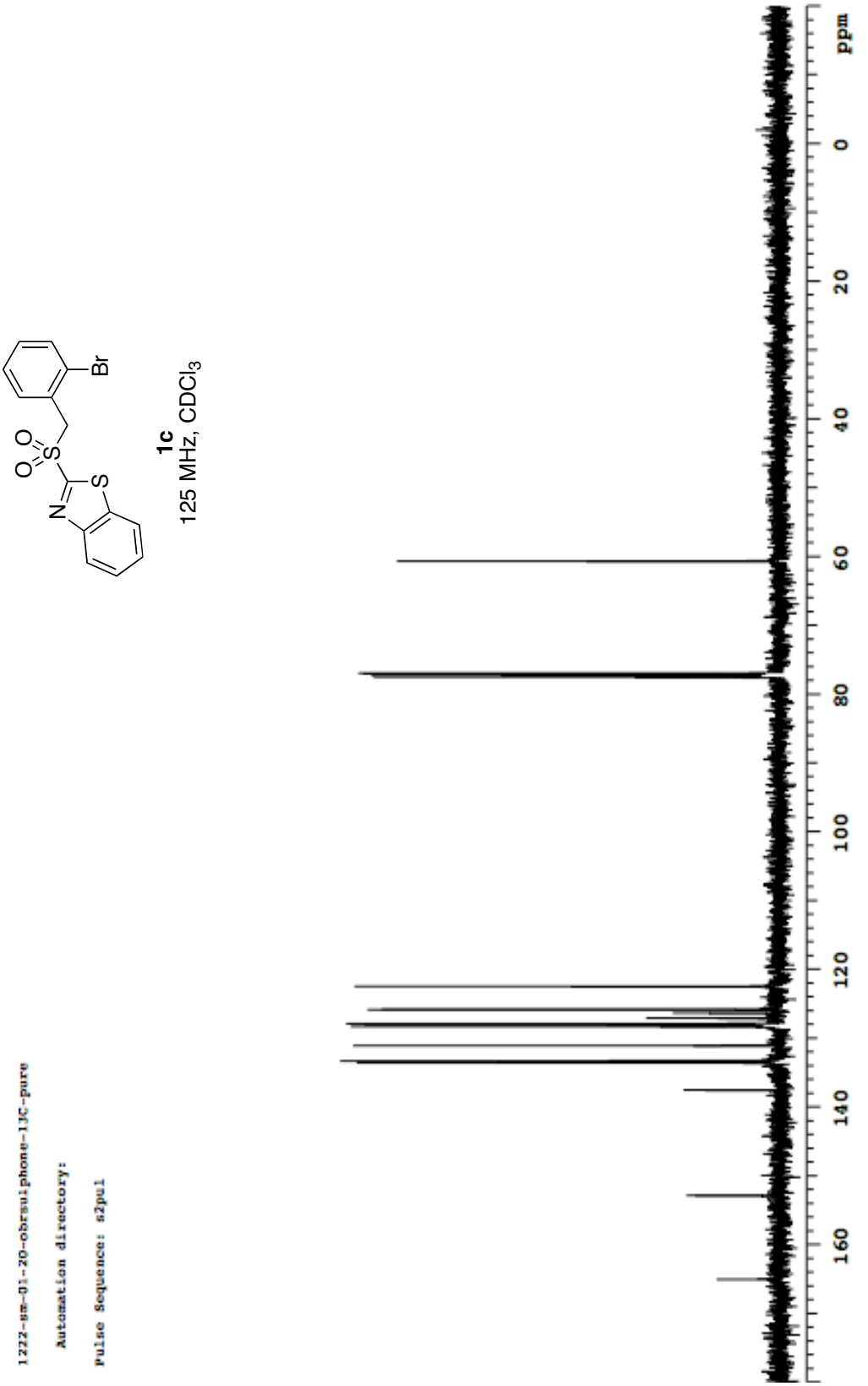


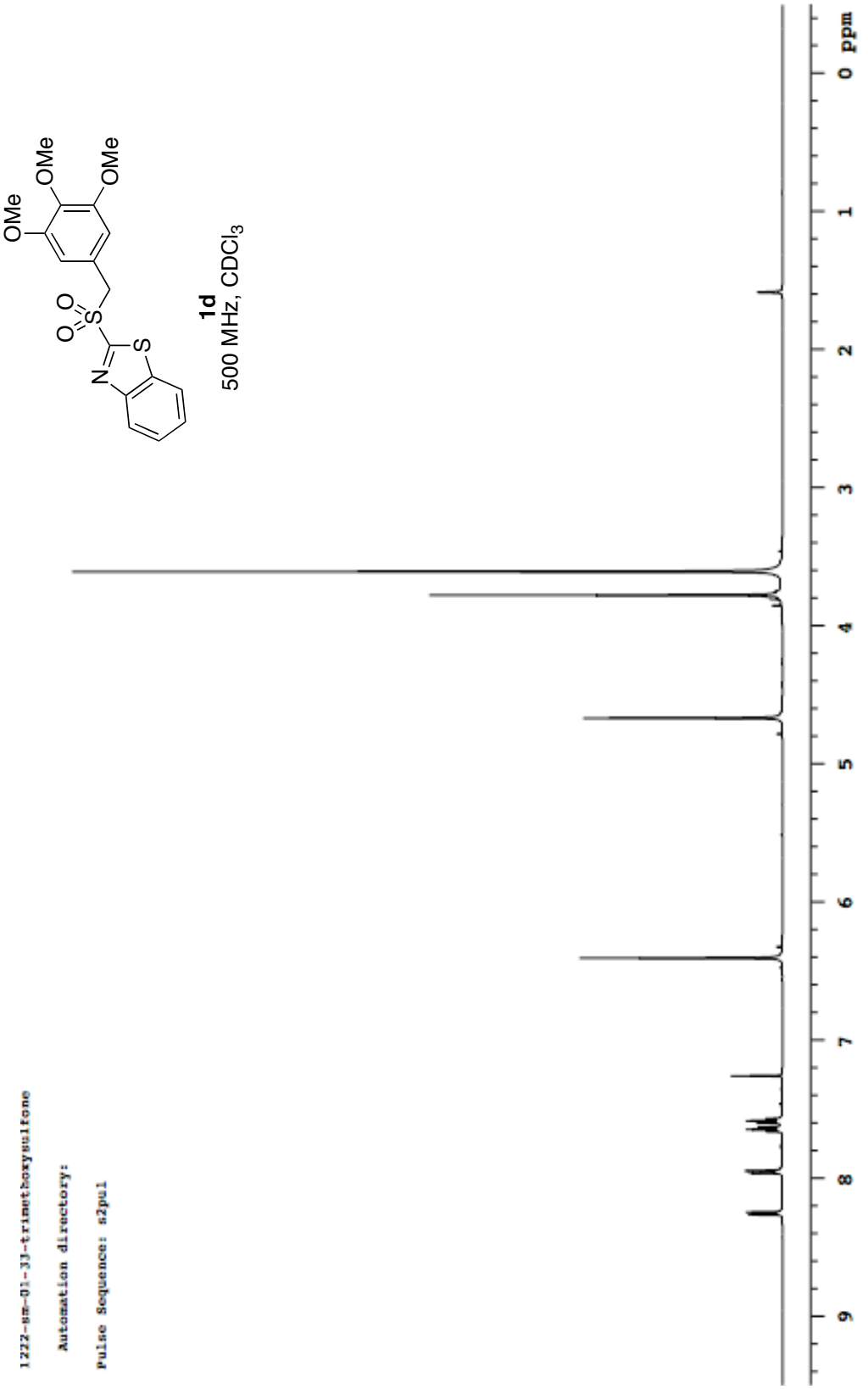






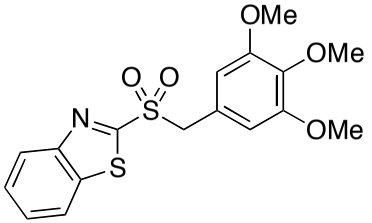




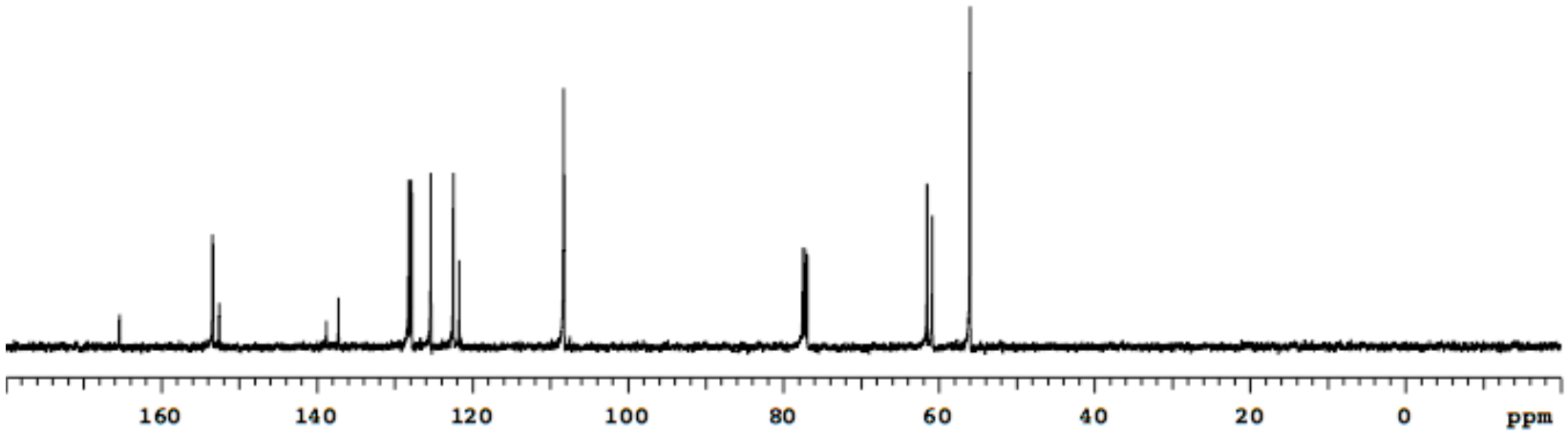


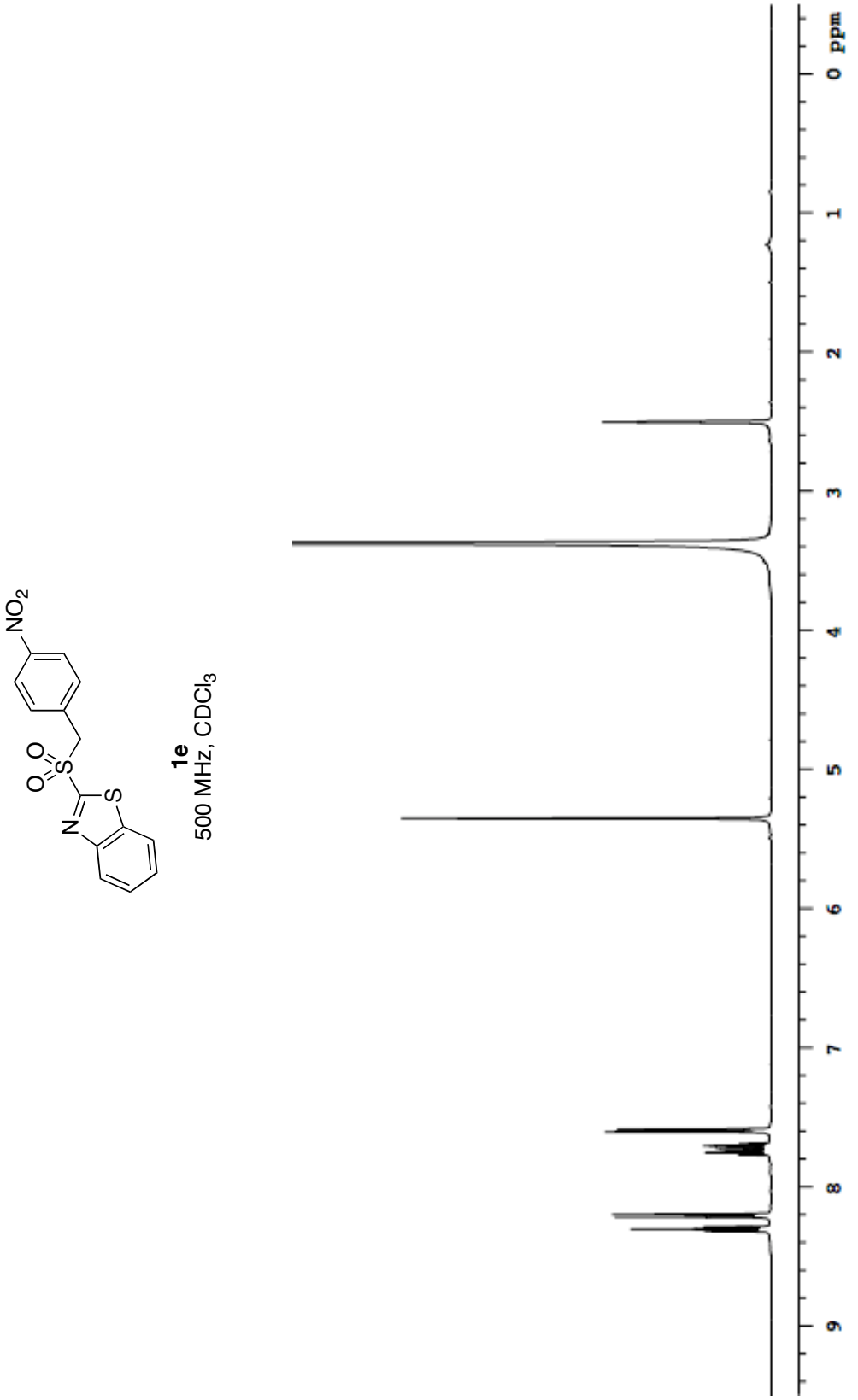
Automation directory:

Pulse Sequence: s2pul



1d
125 MHz, $CDCl_3$

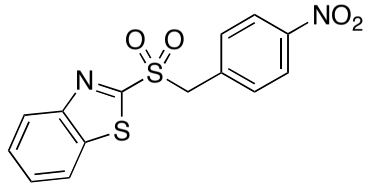




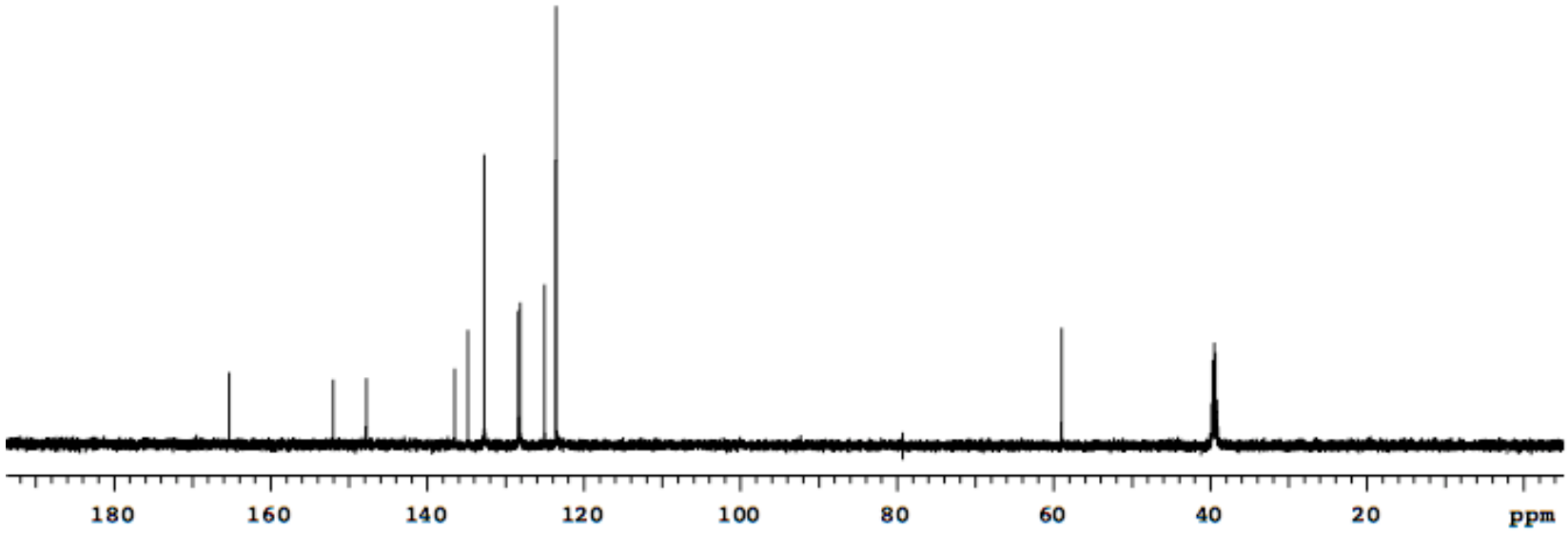
1222-sm-01-73-13C-dmso

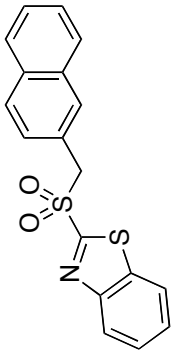
Automation directory:

Pulse Sequence: s2pul

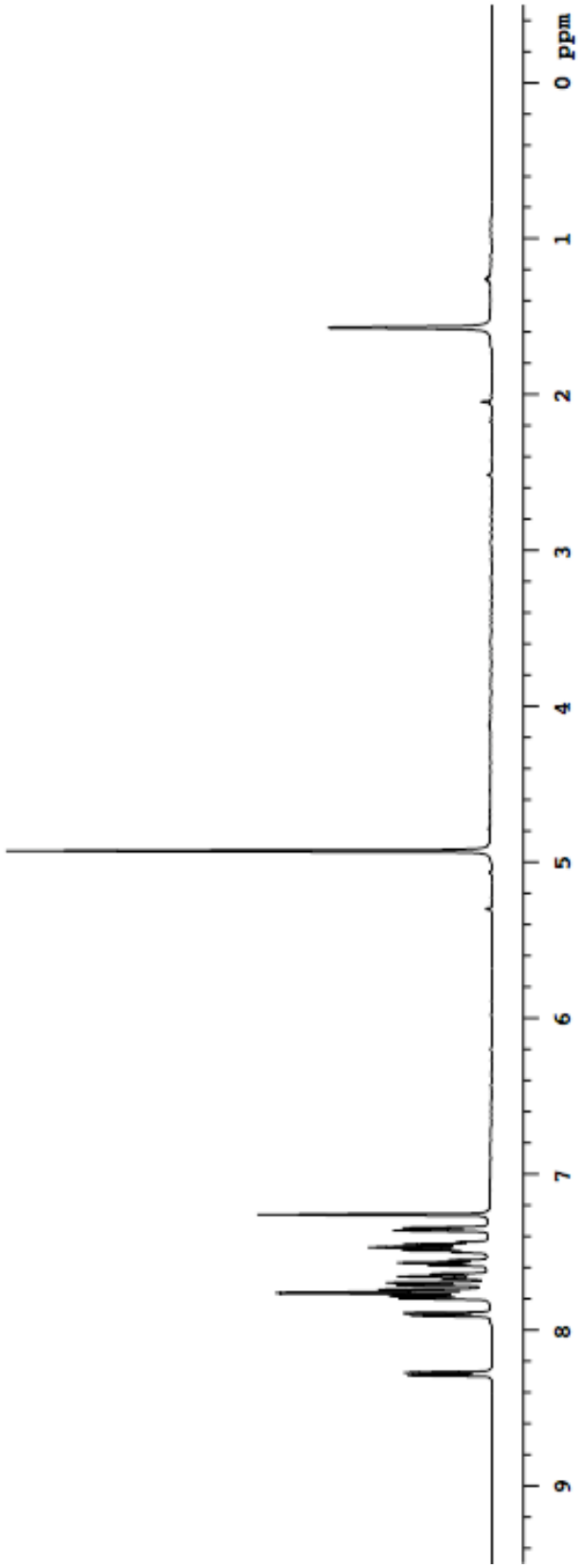


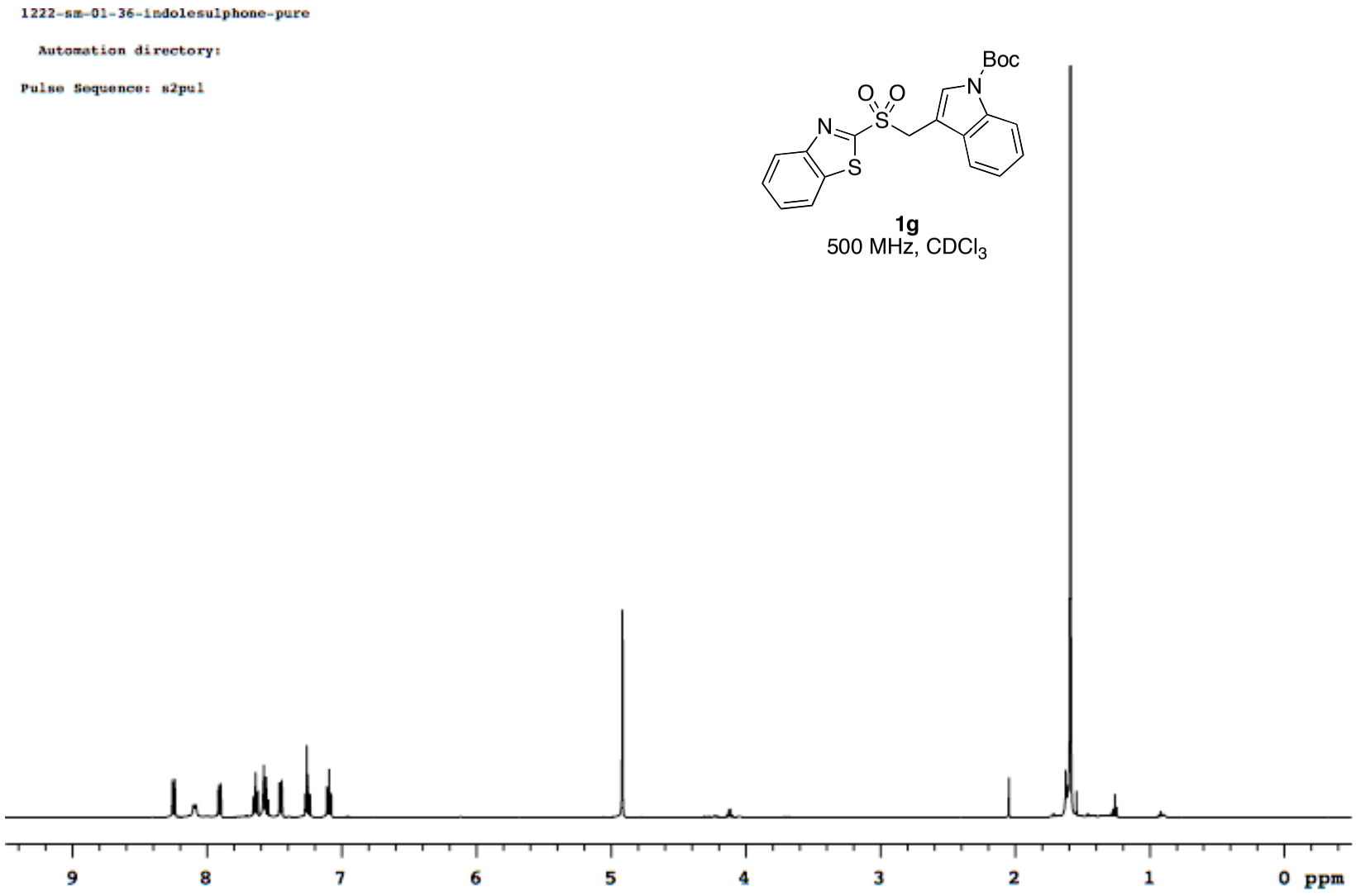
1e
125 MHz, $CDCl_3$

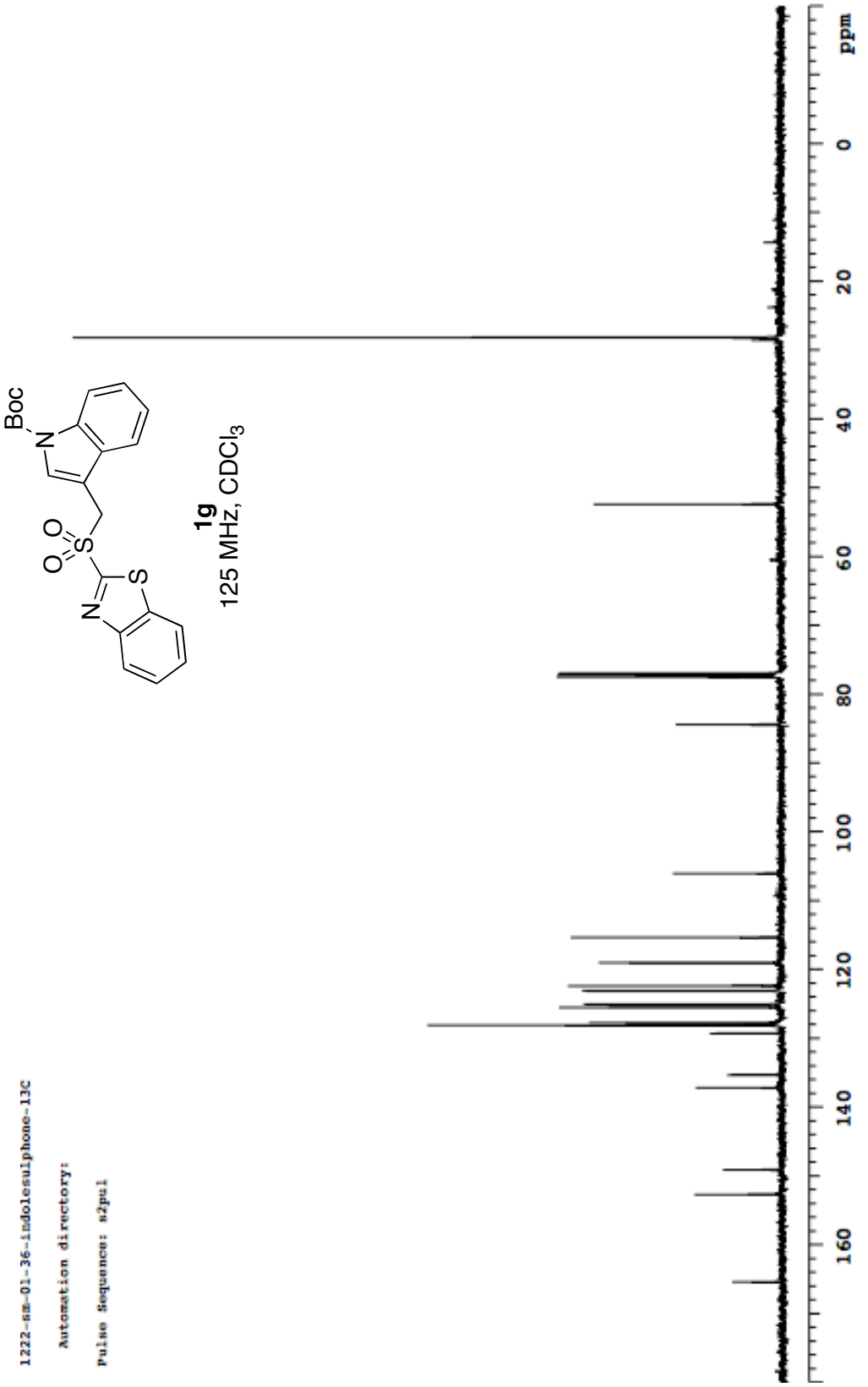


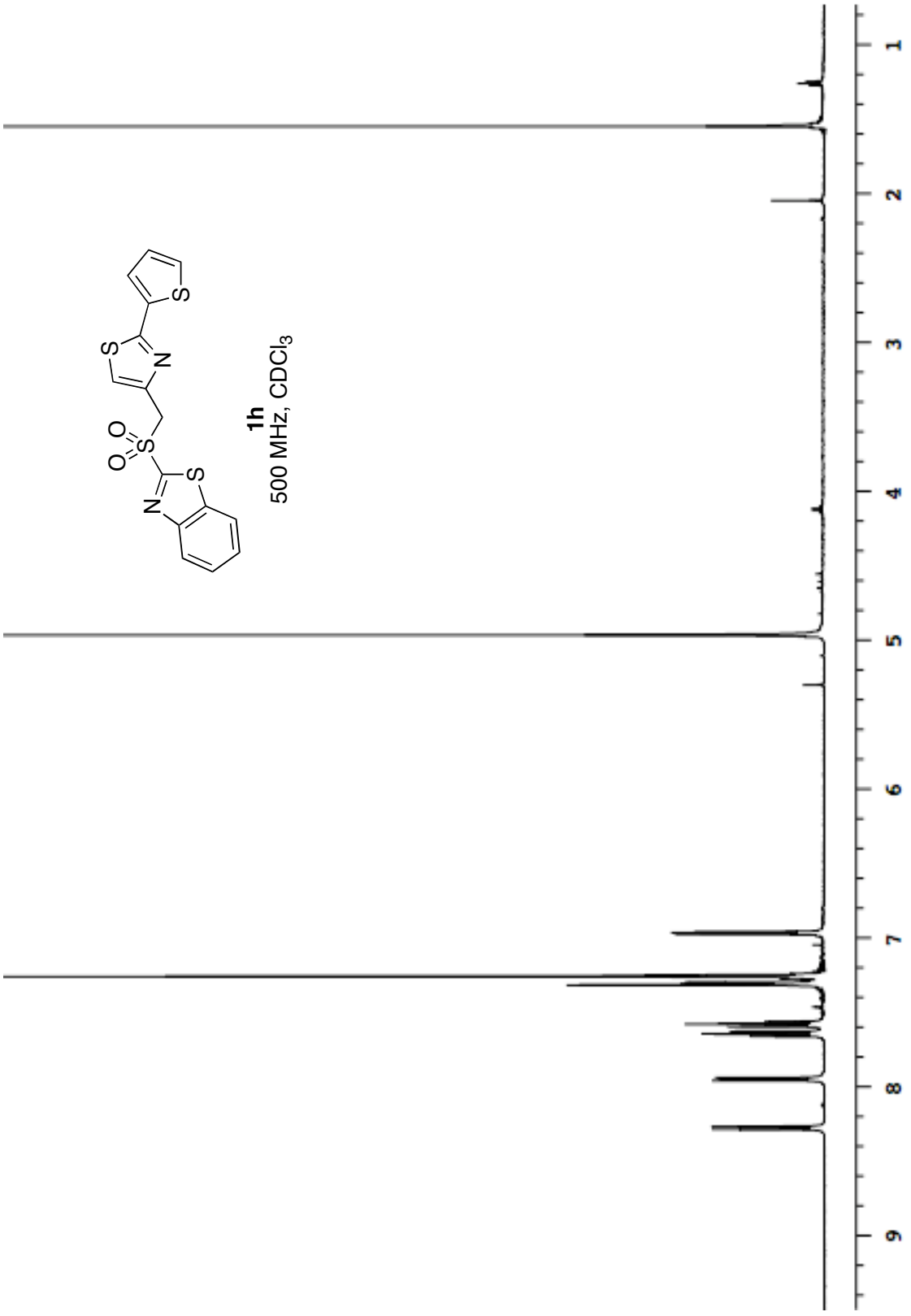


1f
500 MHz, $CDCl_3$





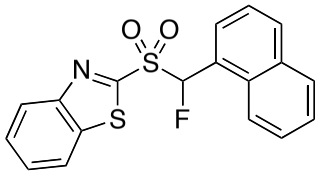




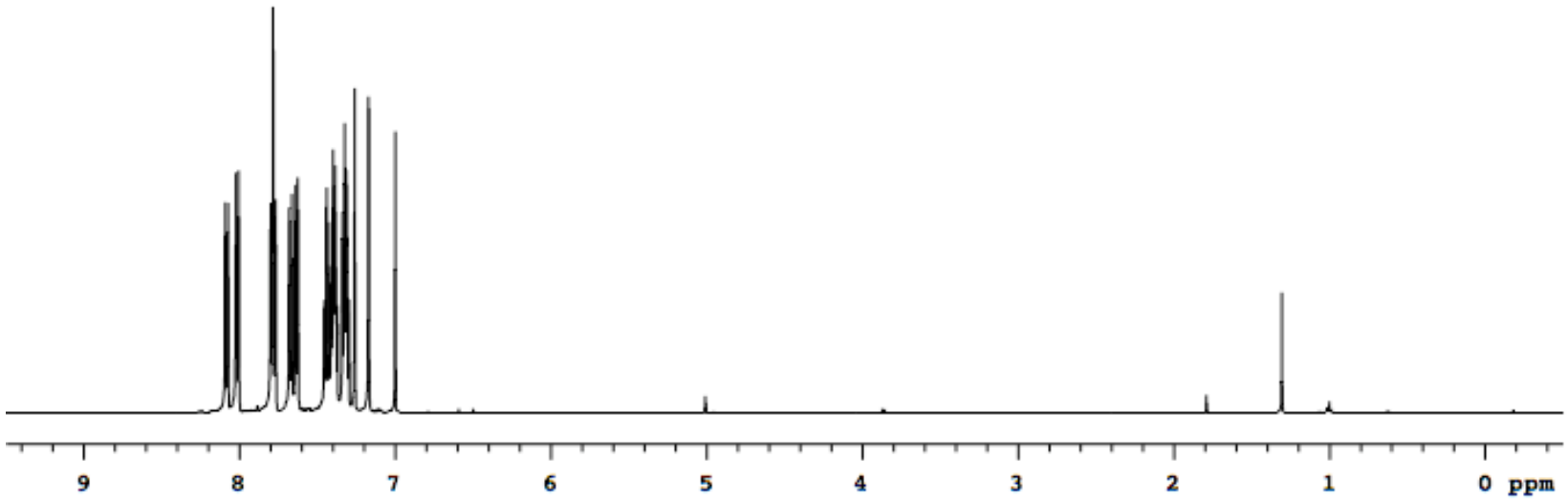
1222-sm-01-19-2NaphthylFsulfone-pure

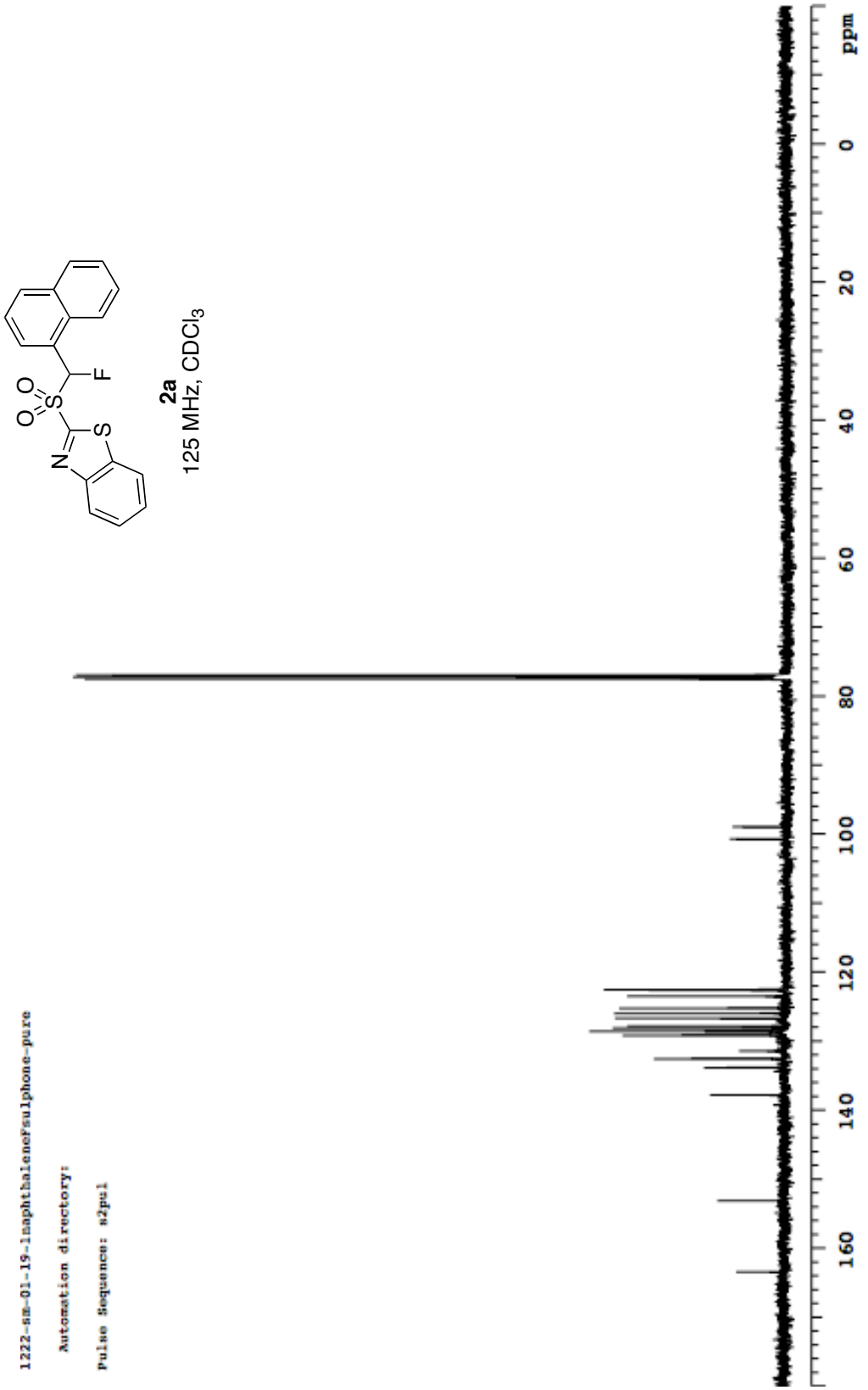
Automation directory:

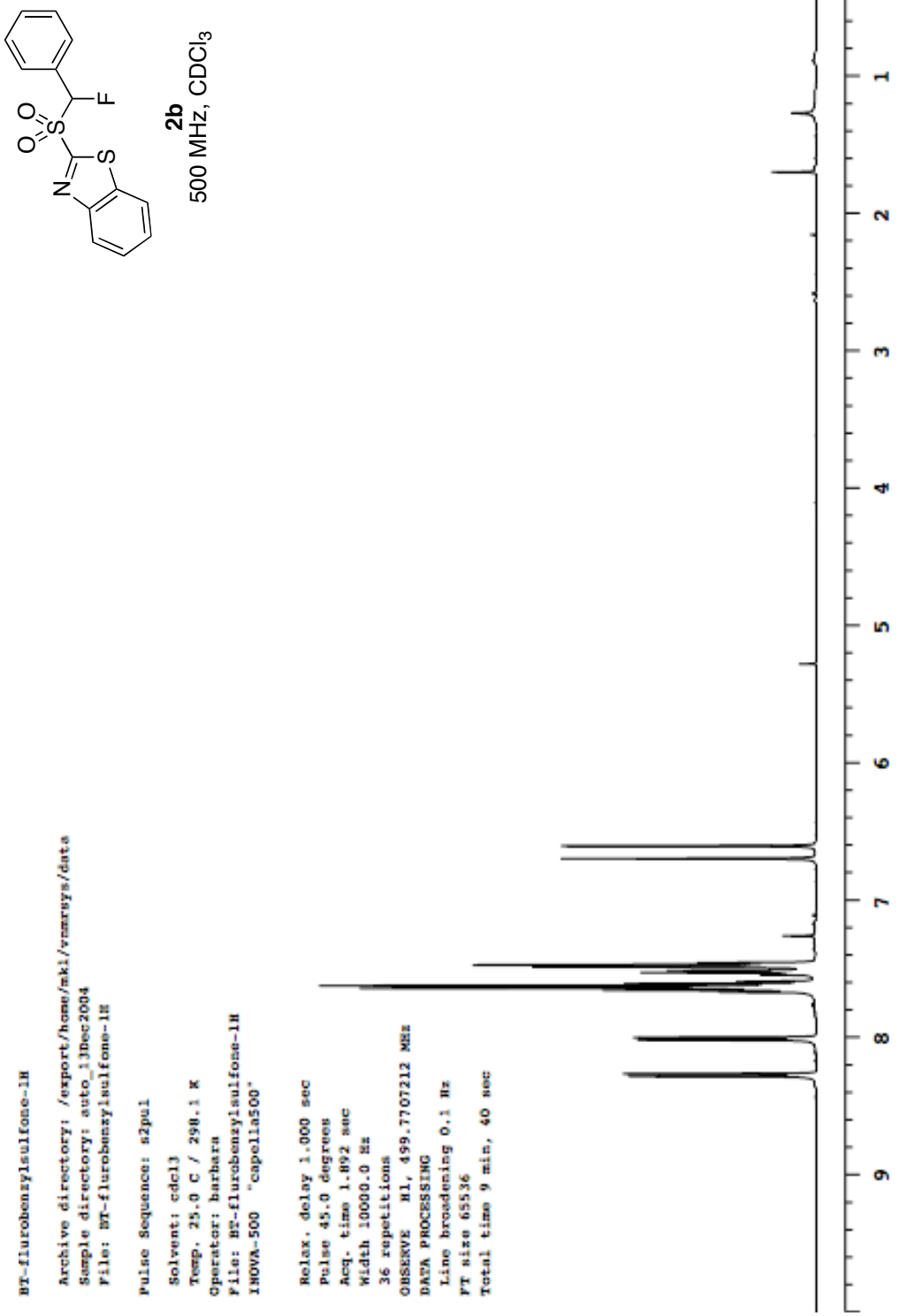
Pulse Sequence: s2pul

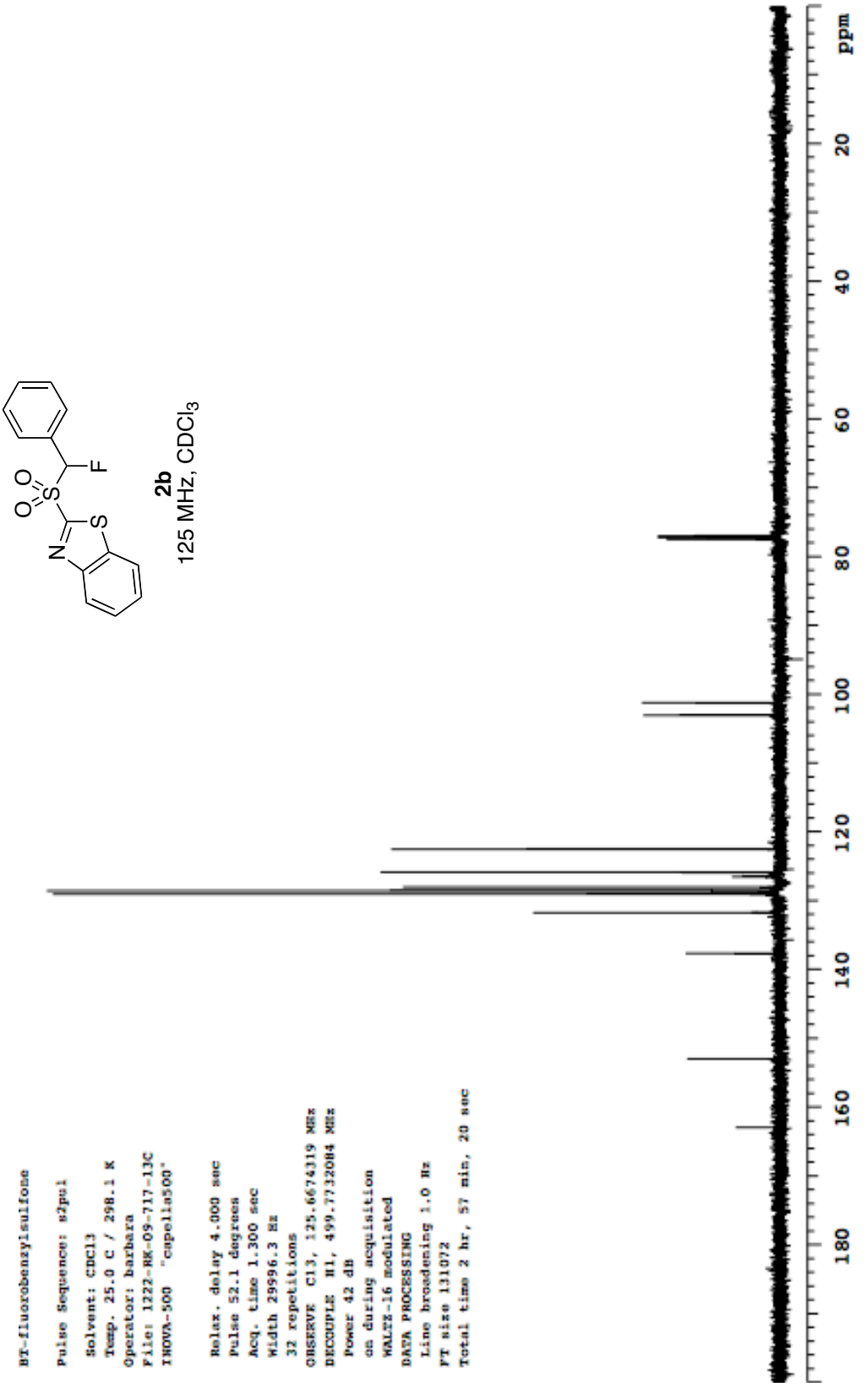


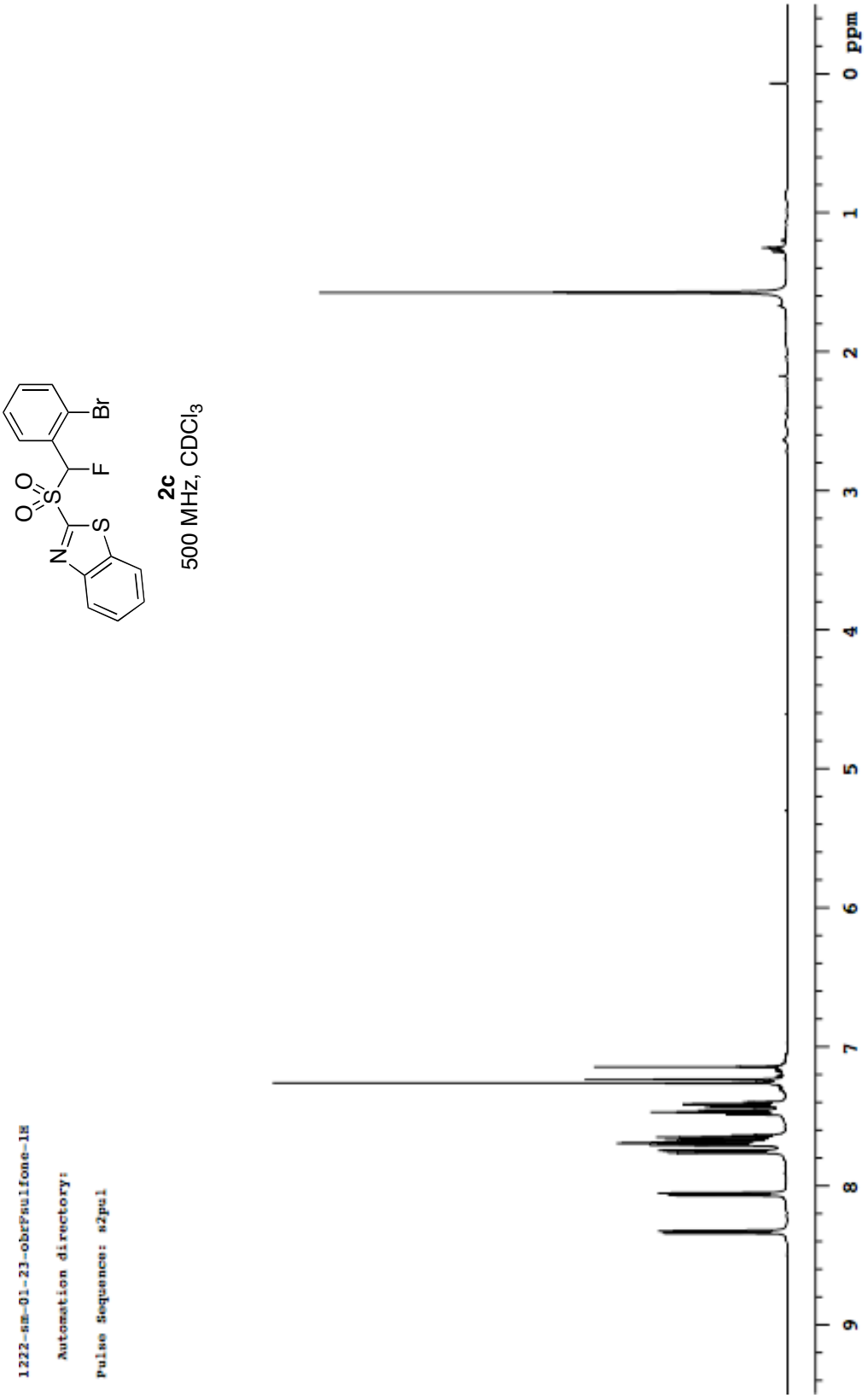
2a
500 MHz, $CDCl_3$

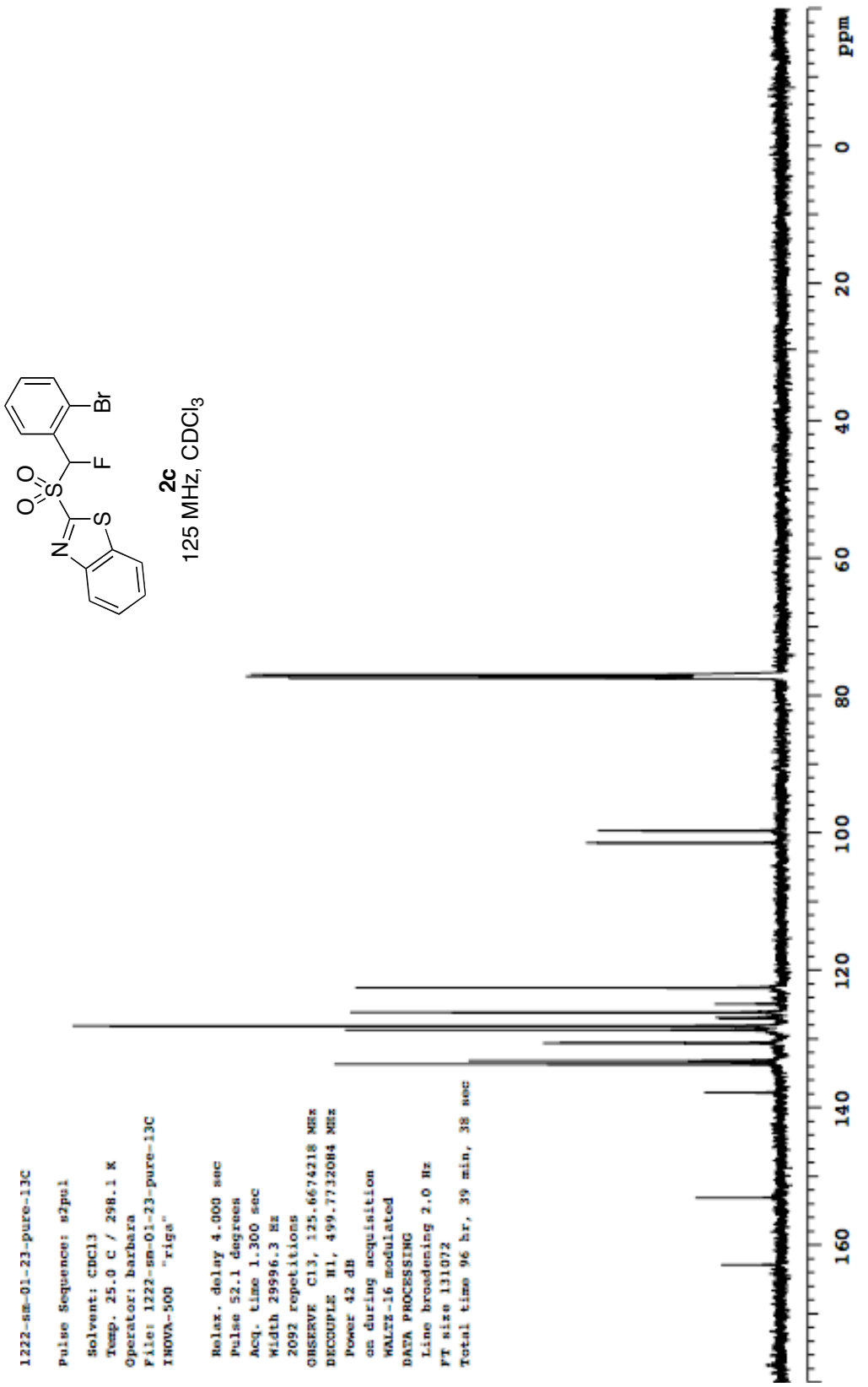


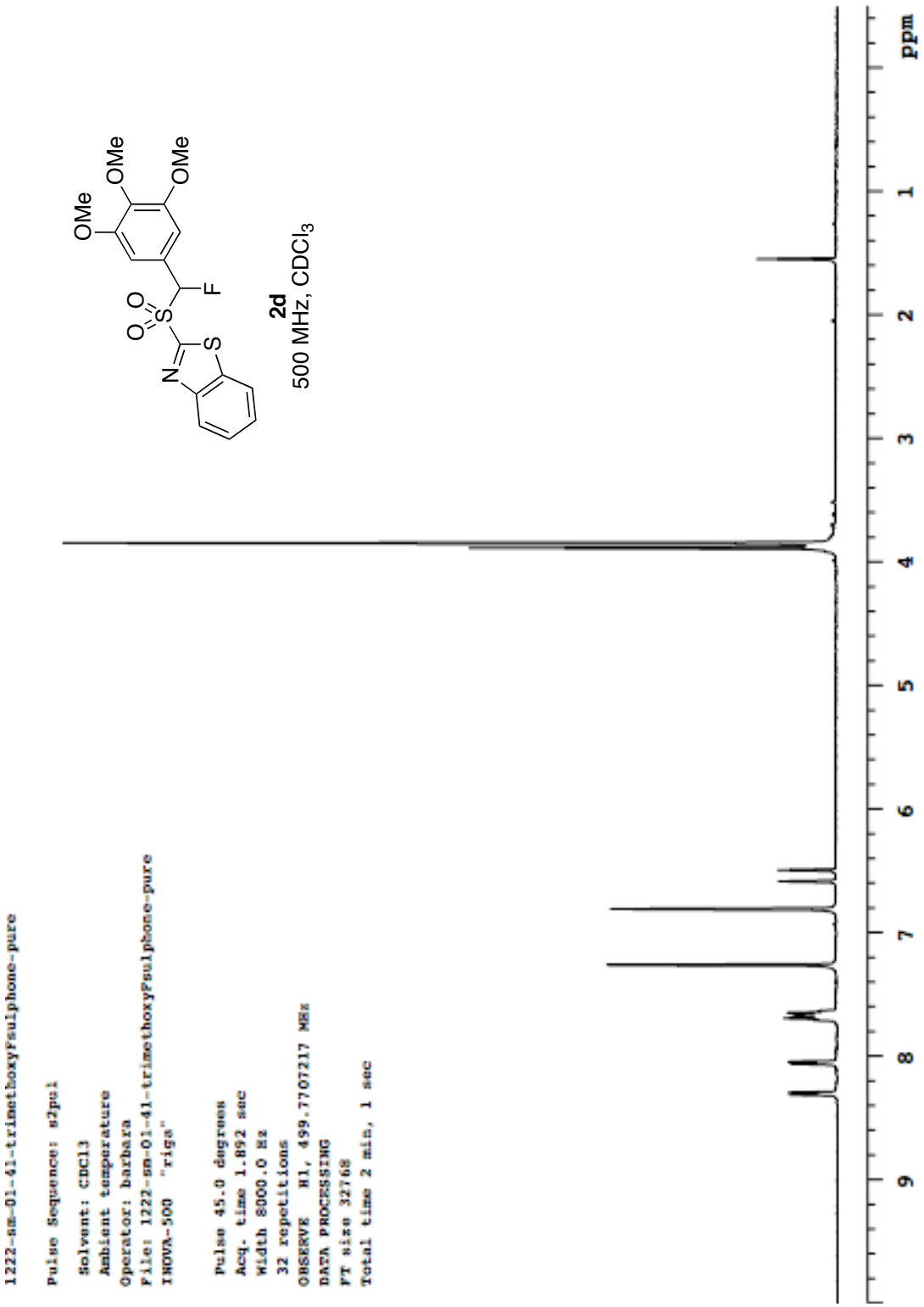



BT-flurobenzylsulfone-1H
Archive directory: /export/home/mki/vnmrsys/data
Sample directory: auto_13Dec2004
File: BT-flurobenzylsulfone-1H
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: barbara
File: BT-flurobenzylsulfone-1H
INOVA-500 "capella500"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.892 sec
Width 10000.0 Hz
36 repetitions
OBSERVE H1, 499.7707212 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 9 min, 40 sec
O
O
S
F
N
S
2b
500 MHz, CDCl3
9
8
7
6
5
4
3
2
1
ppm





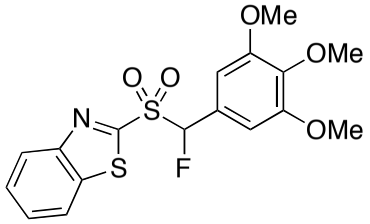




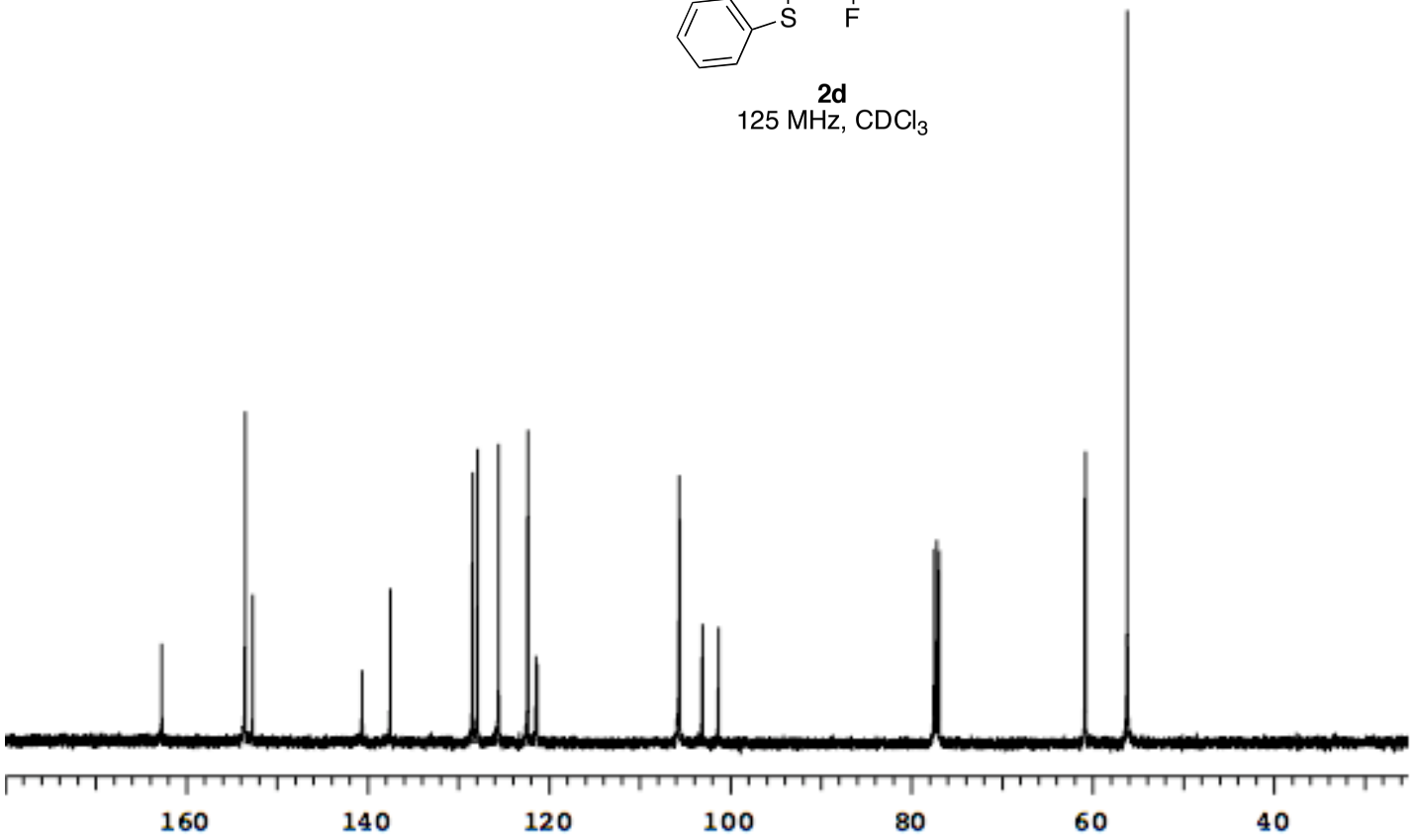
1222-sm-01-41-trimethoxyFsulphone-13C

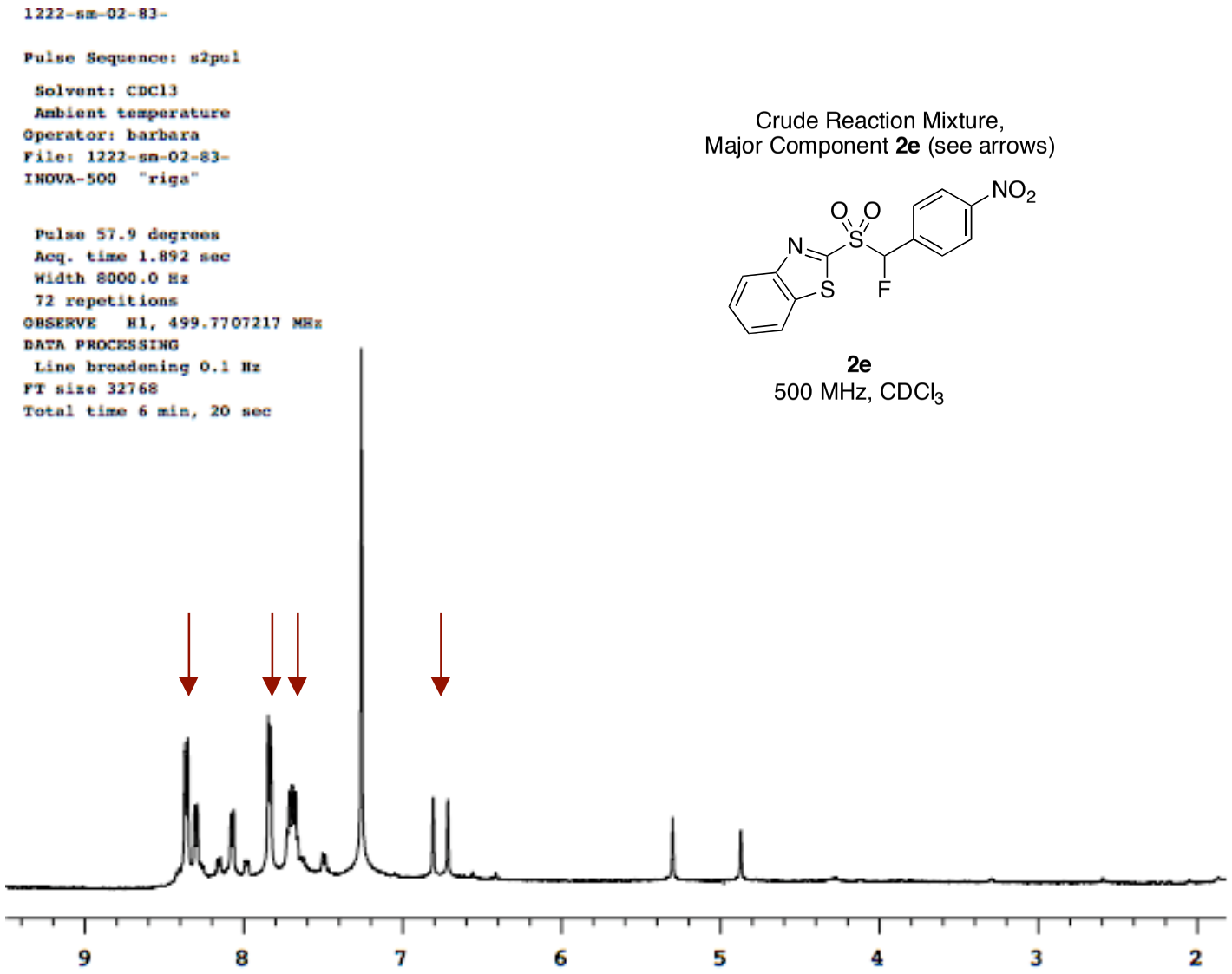
Automation directory:

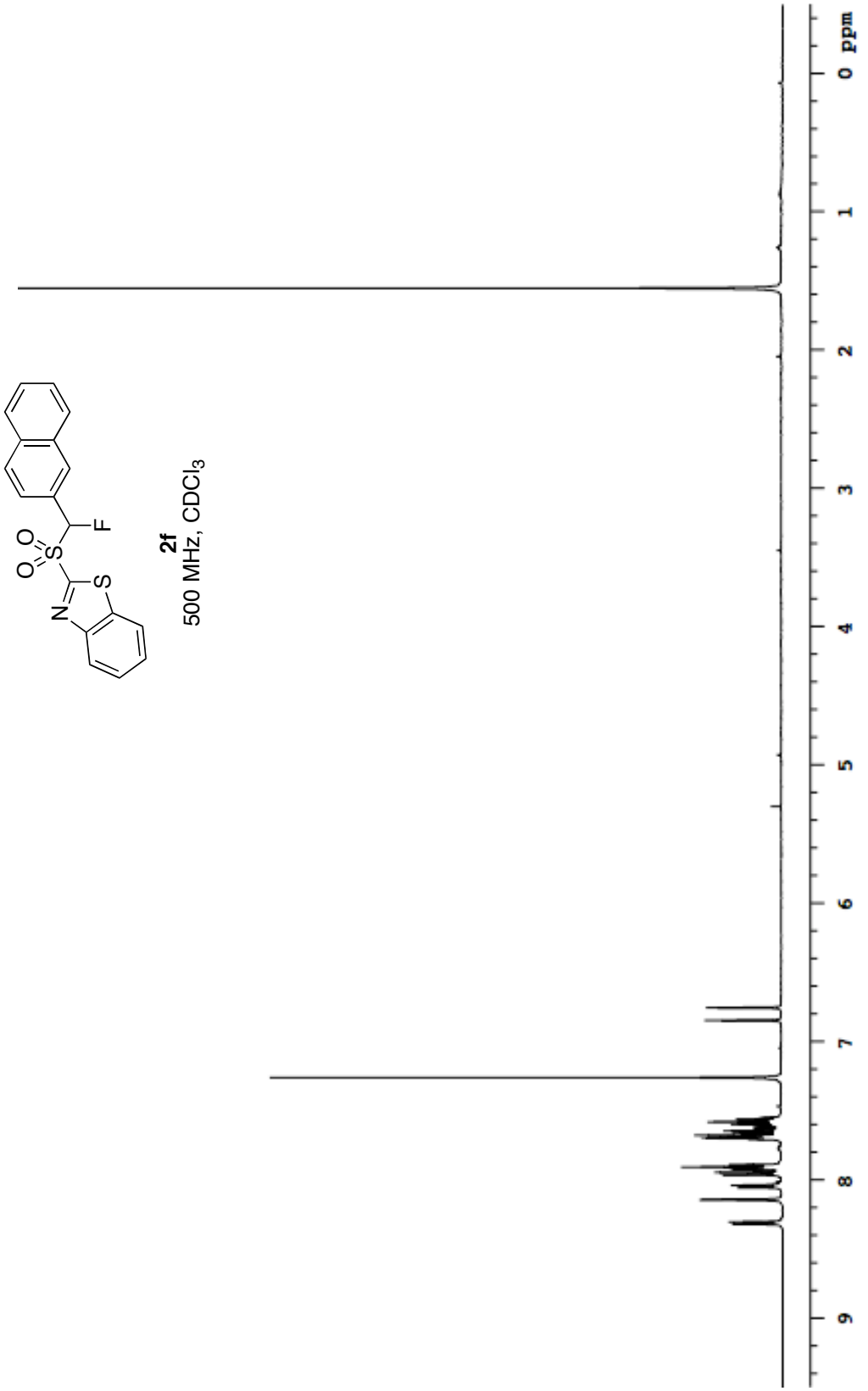
Pulse Sequence: s2pul

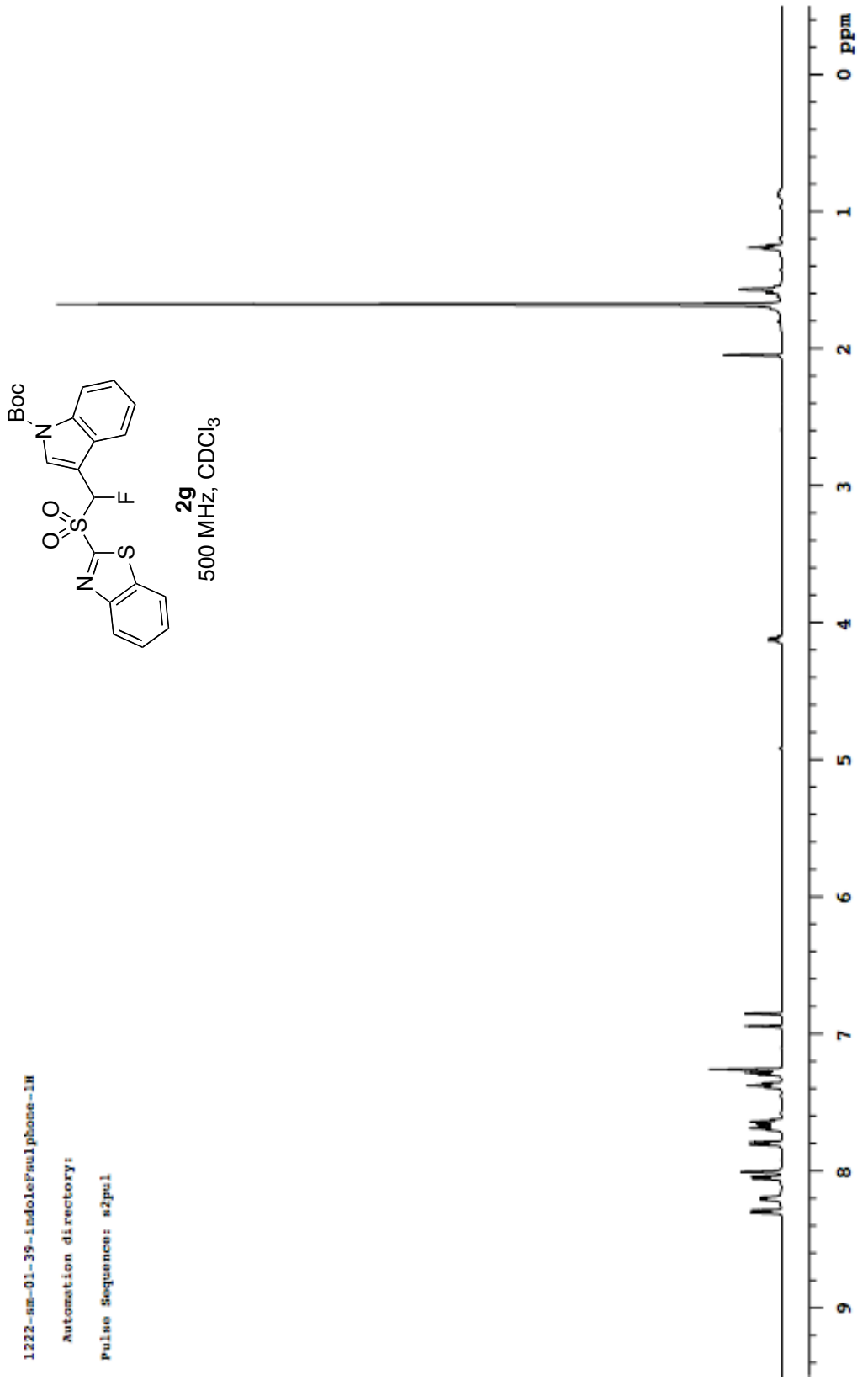


2d
125 MHz, $CDCl_3$





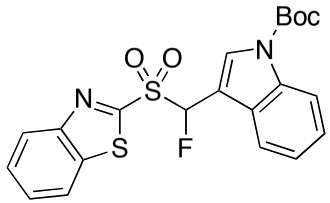




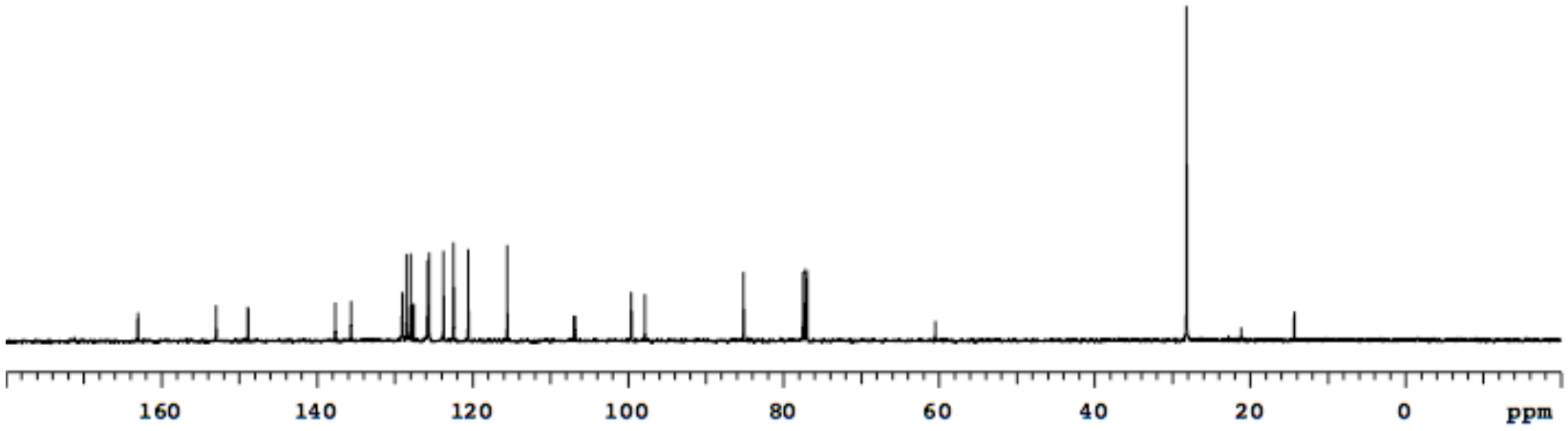
1222-sm-01-39-indolePsulphone-13C

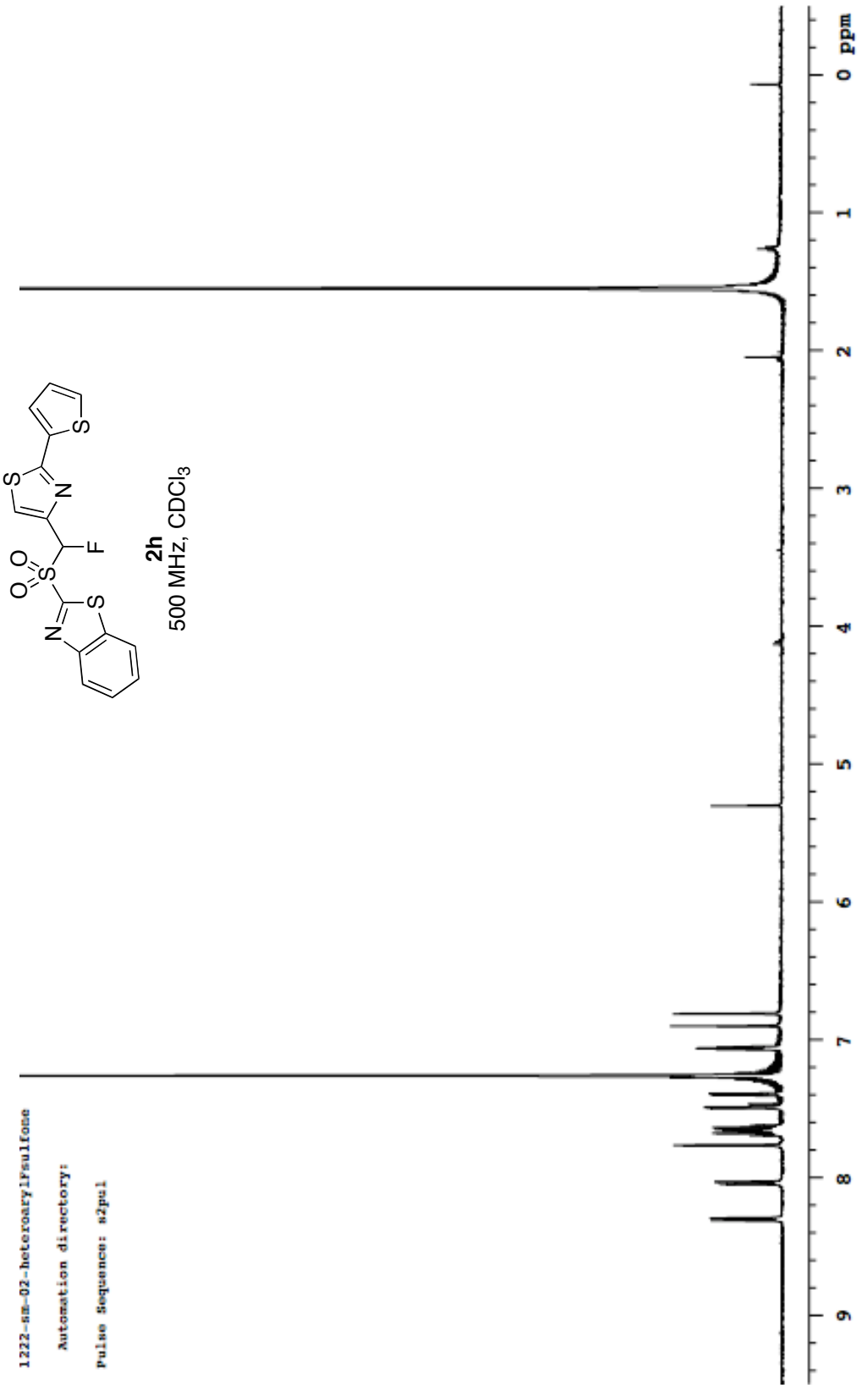
Automation directory:

Pulse Sequence: s2pul



2g
125 MHz, $CDCl_3$

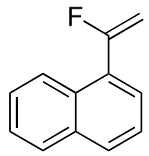




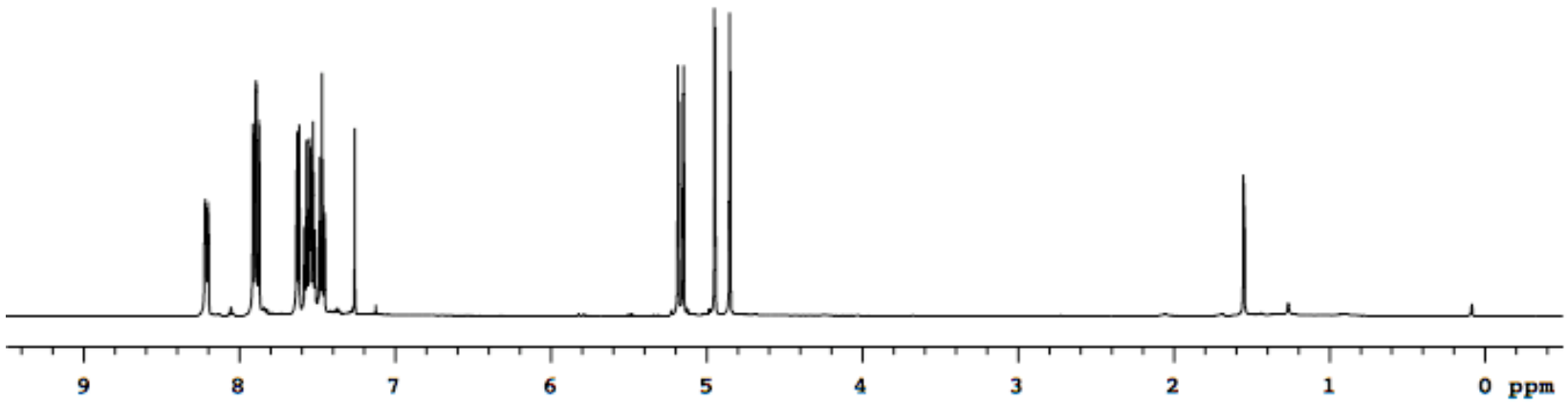
1222-sm-01-25-1naphthyl-pure-1H

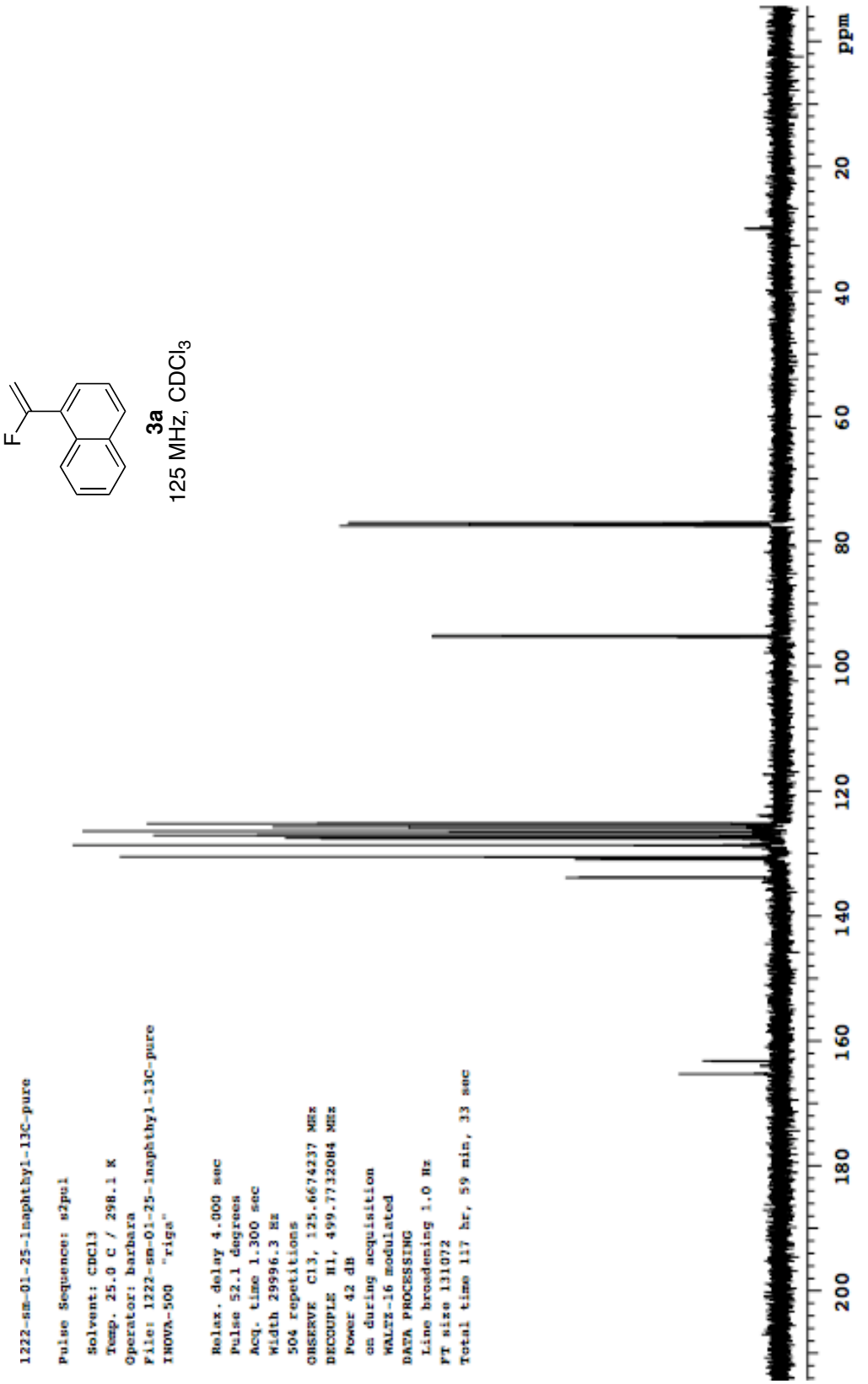
Automation directory:

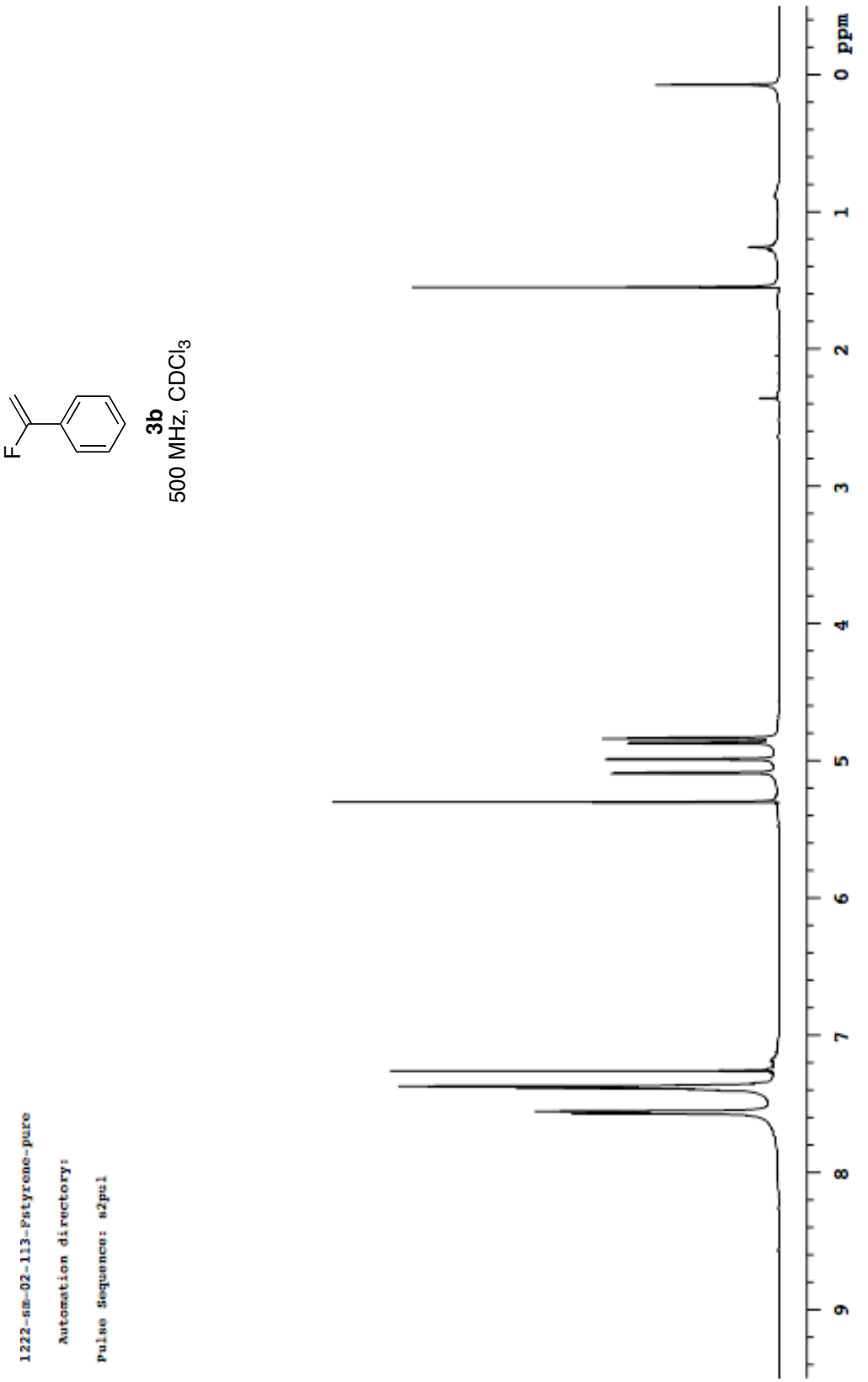
Pulse Sequence: s2pul

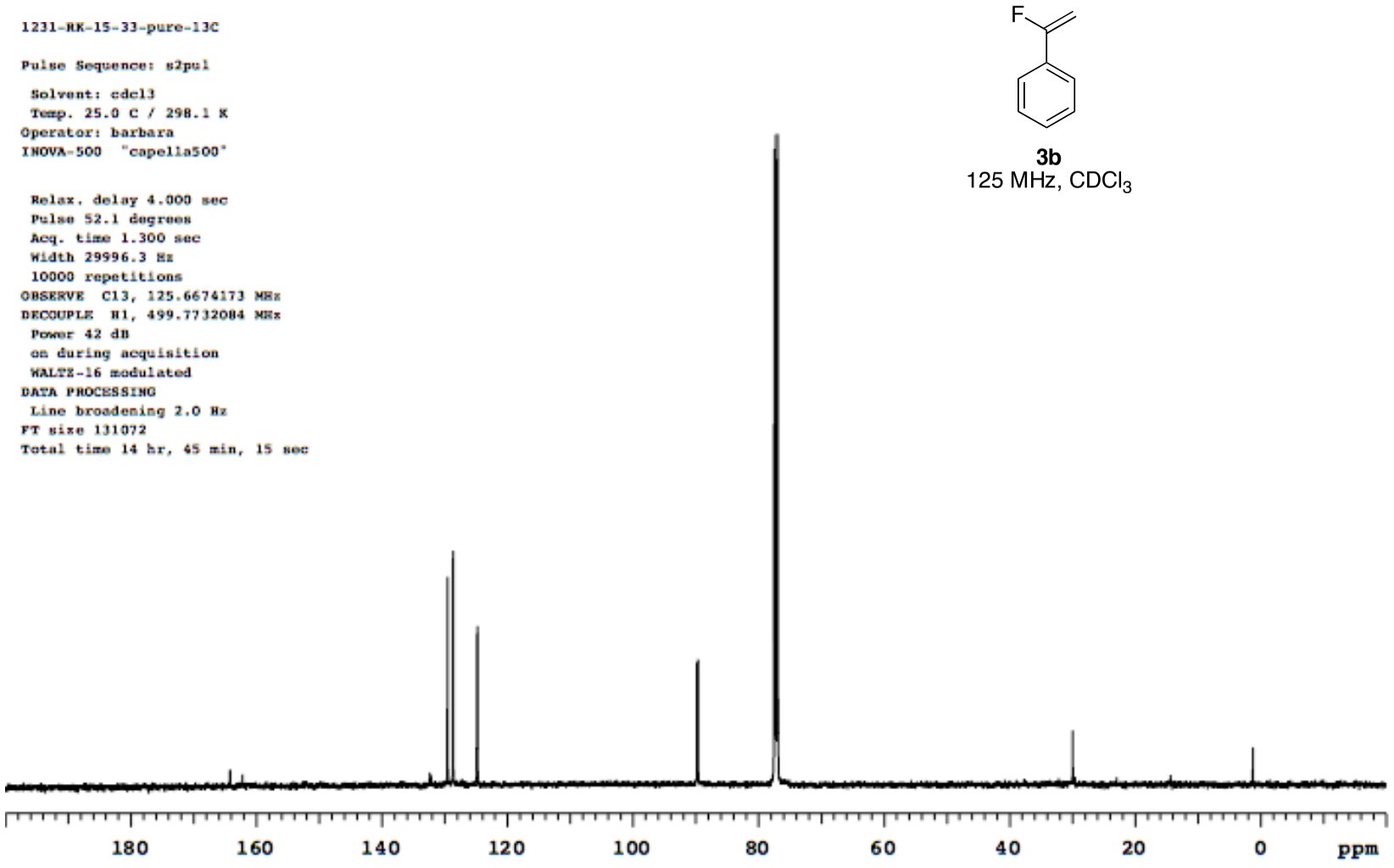


3a
500 MHz, $CDCl_3$





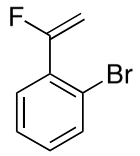




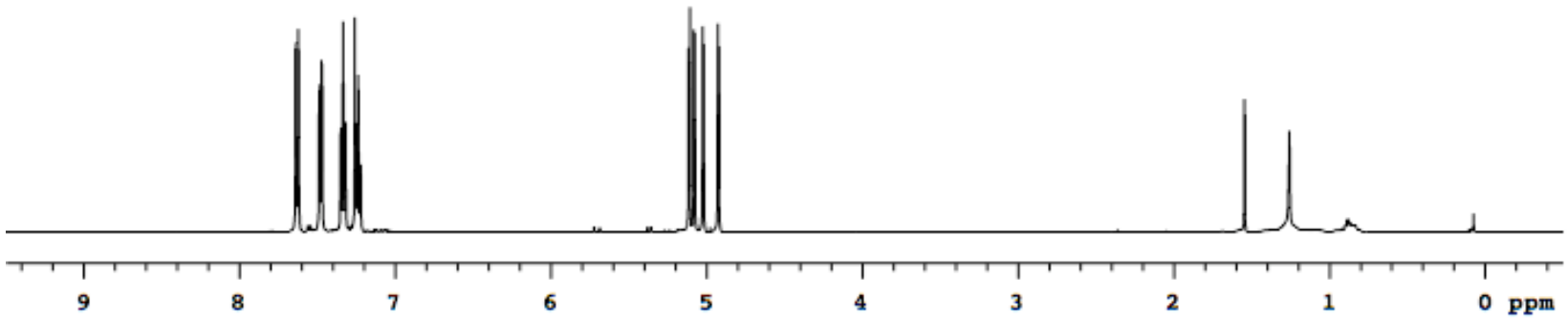
1222-sm-01-26-obr-2ndtime-pure

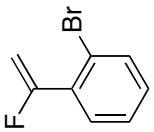
Automation directory:

Pulse Sequence: s2pul

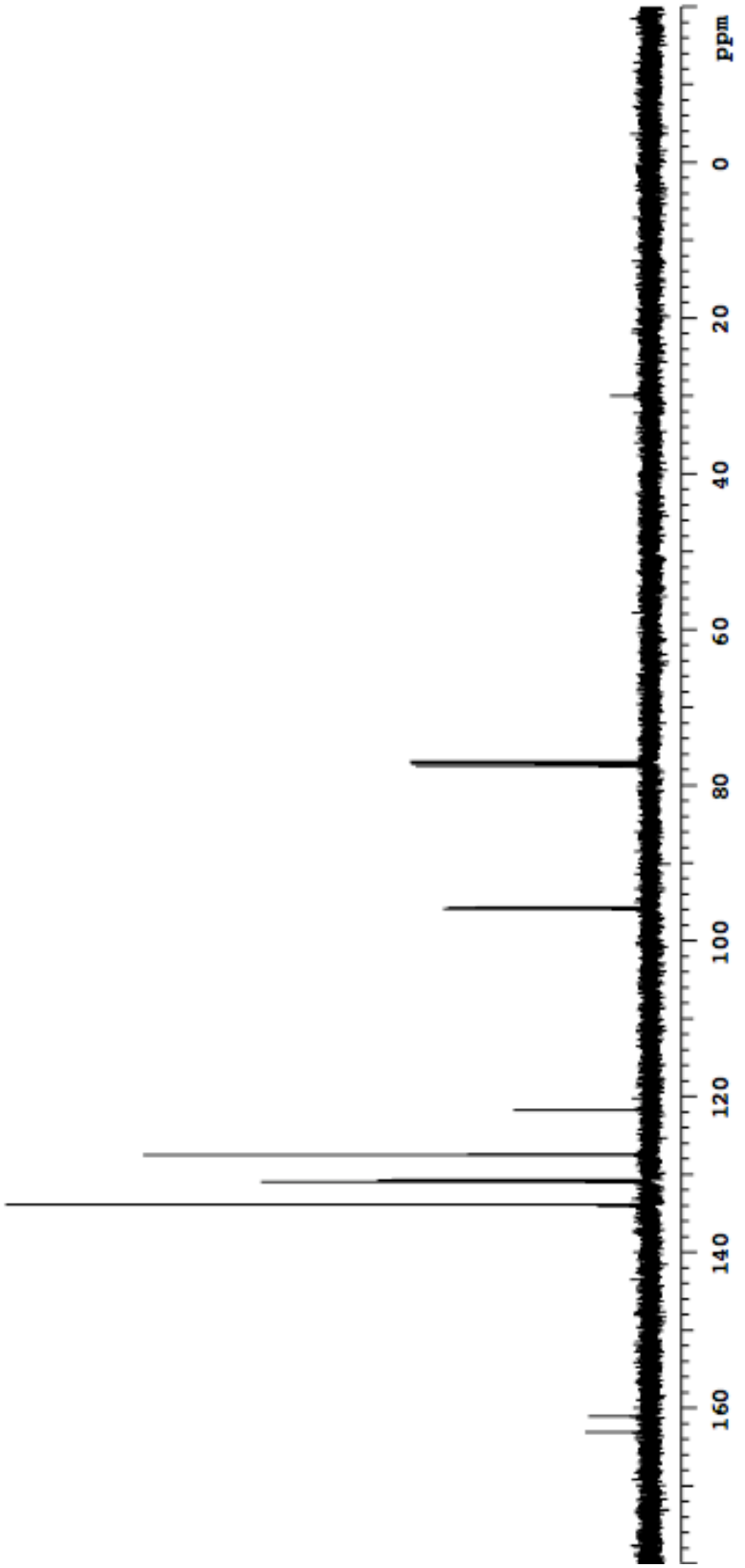


3c
500 MHz, $CDCl_3$

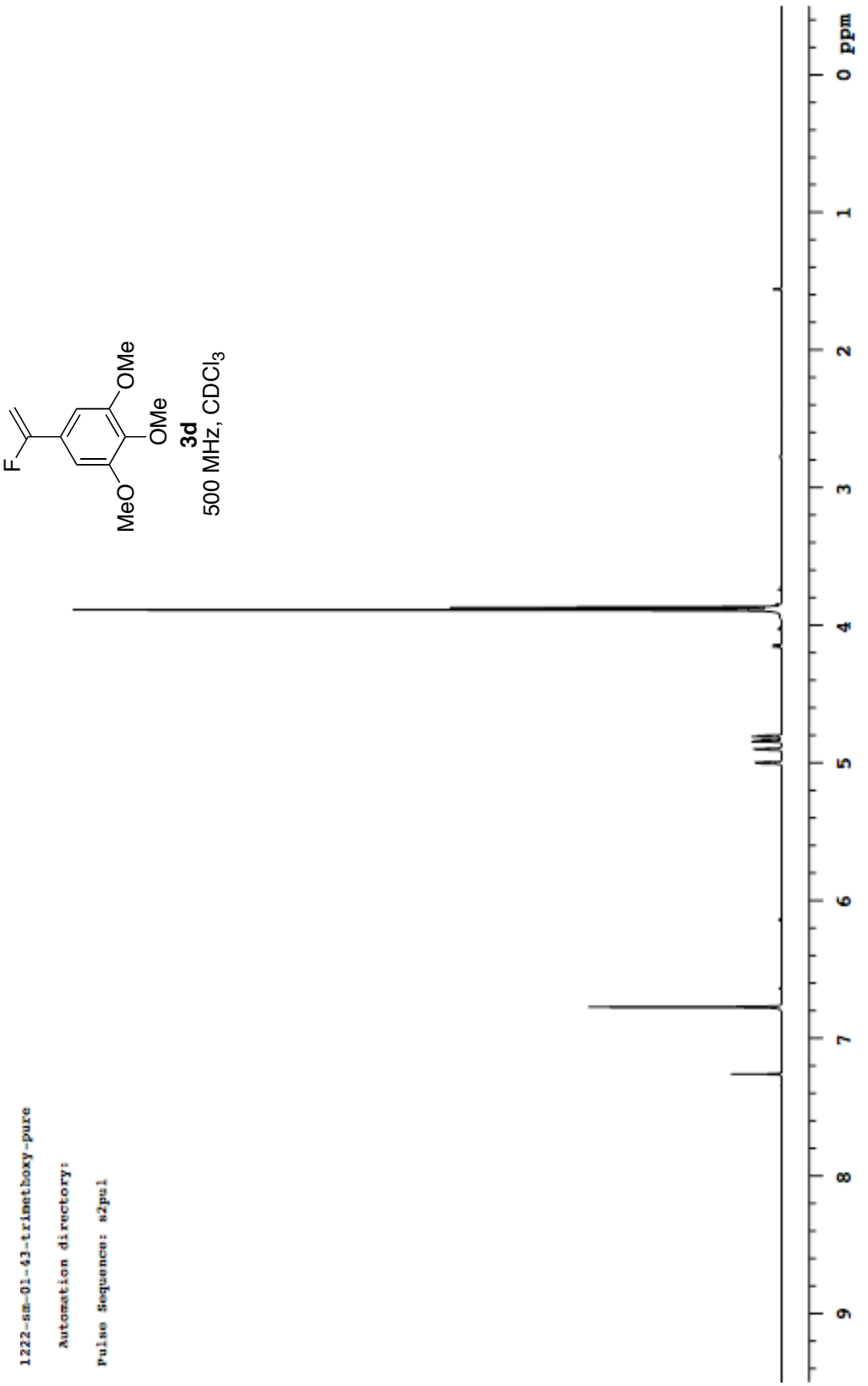


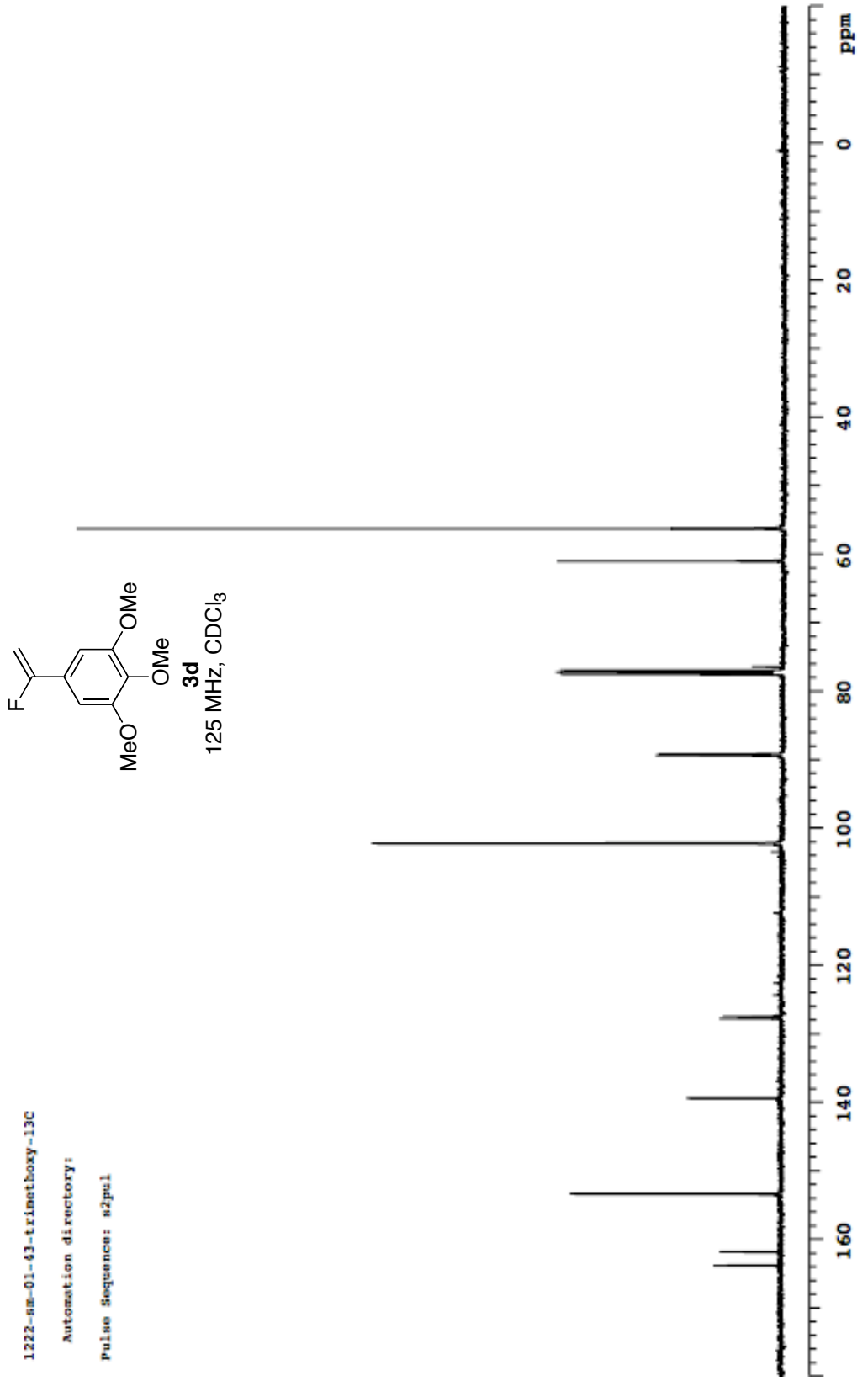


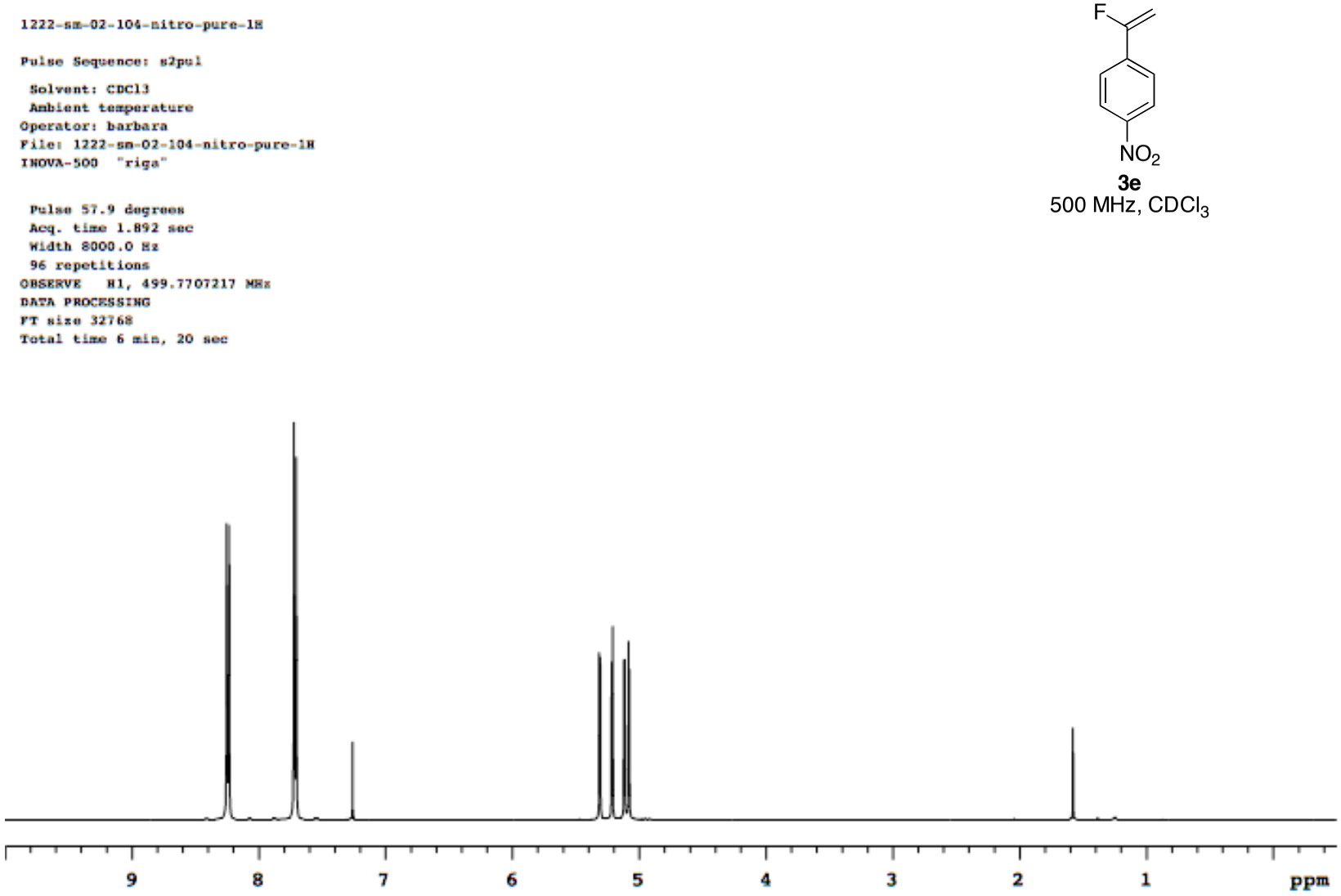
3c
125 MHz, $CDCl_3$

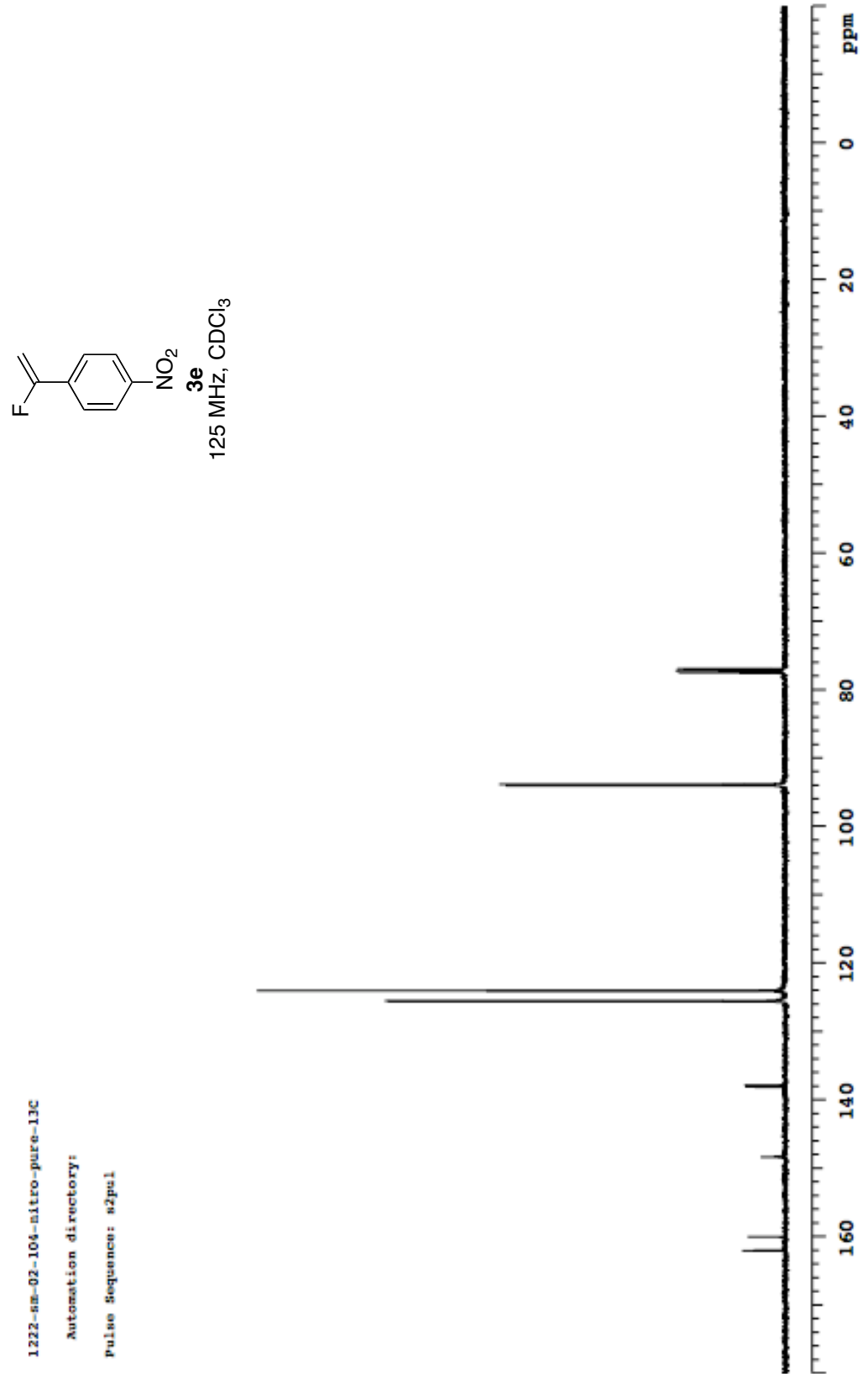


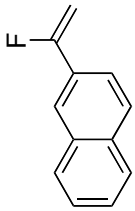
1222-sm-01-26-obr-13C-pure
Automation directory:
Pulse Sequence: s2pul



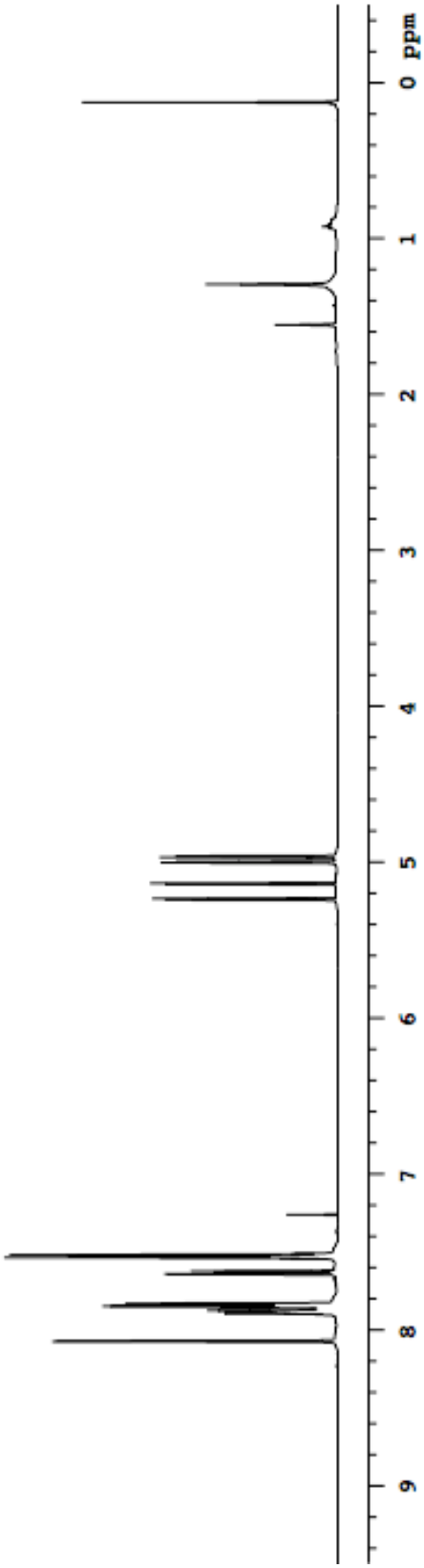


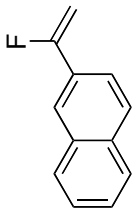




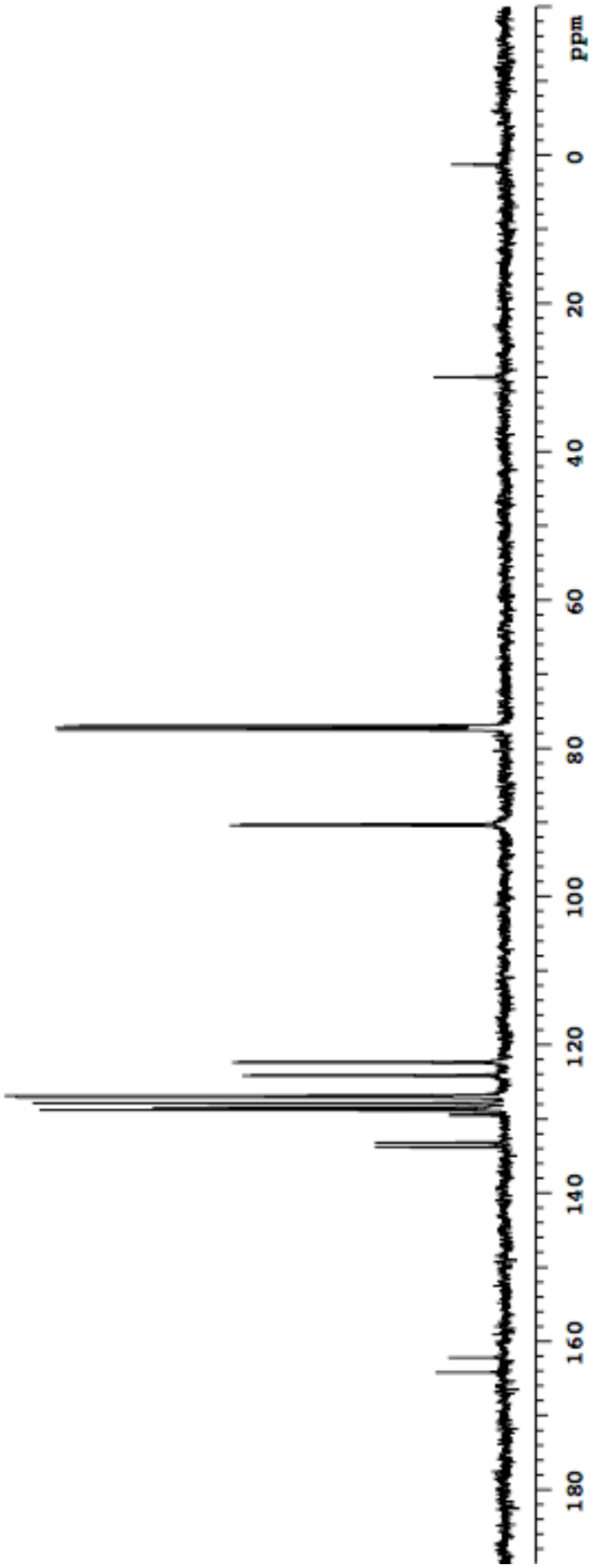


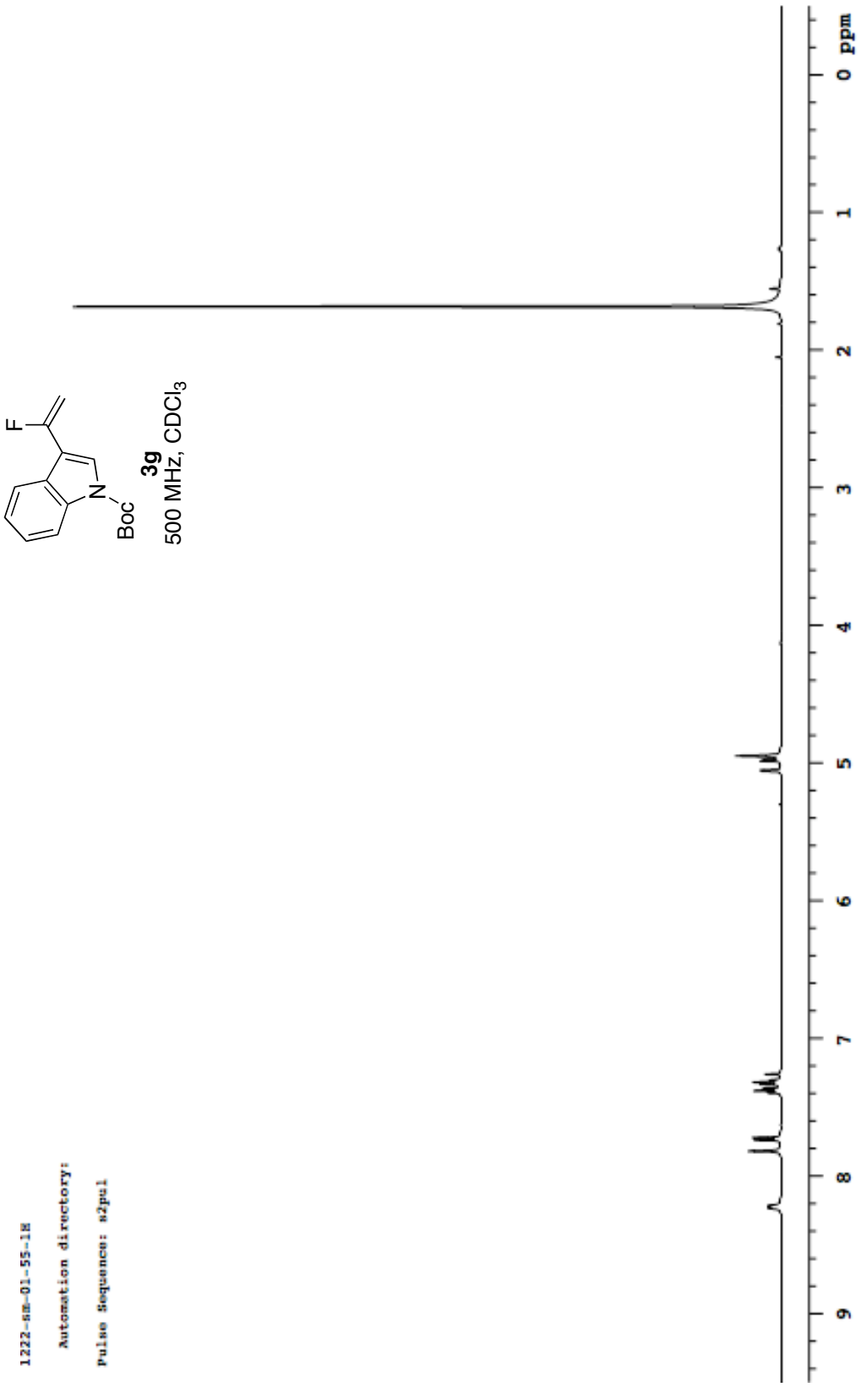
3f
500 MHz, $CDCl_3$





3f
125 MHz, $CDCl_3$

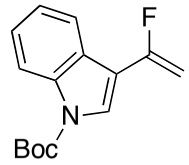




1222-sm-01-55-13C-pure

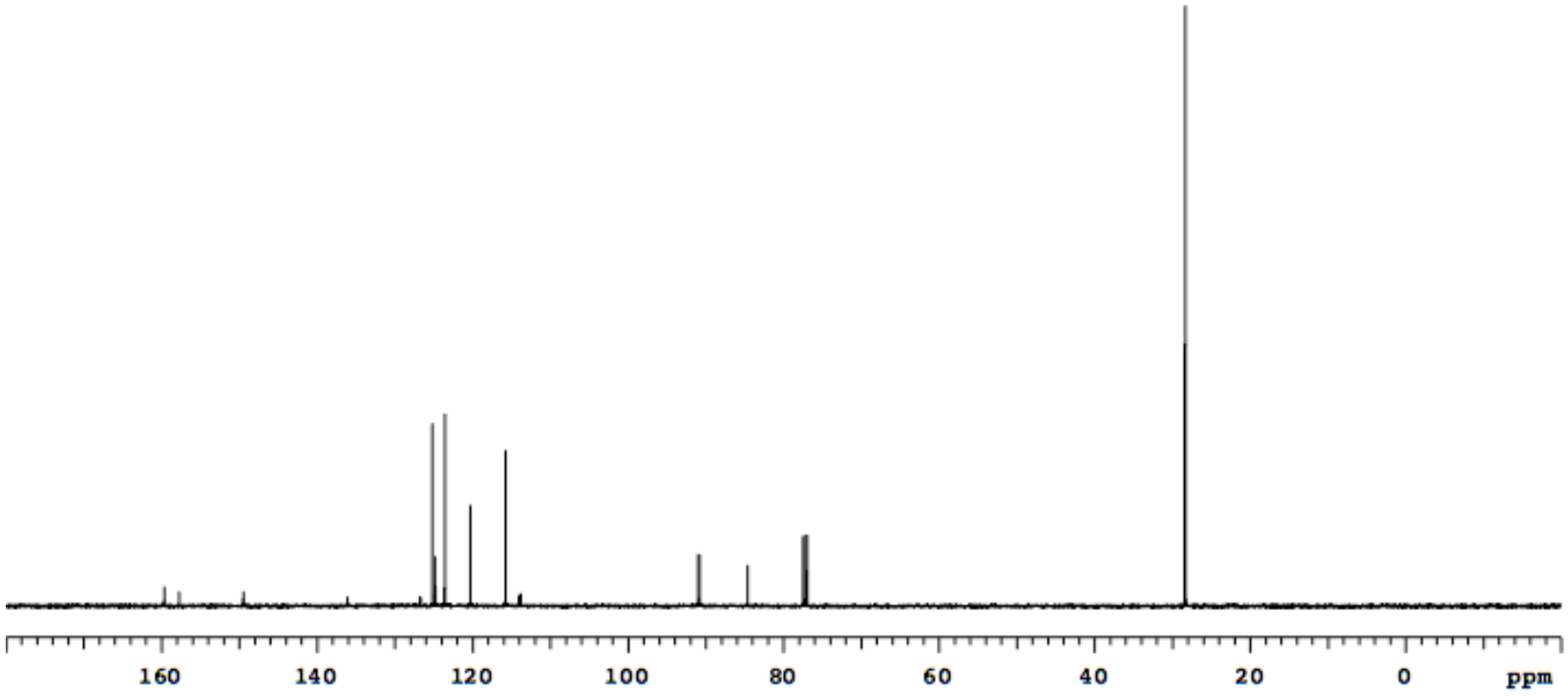
Automation directory:

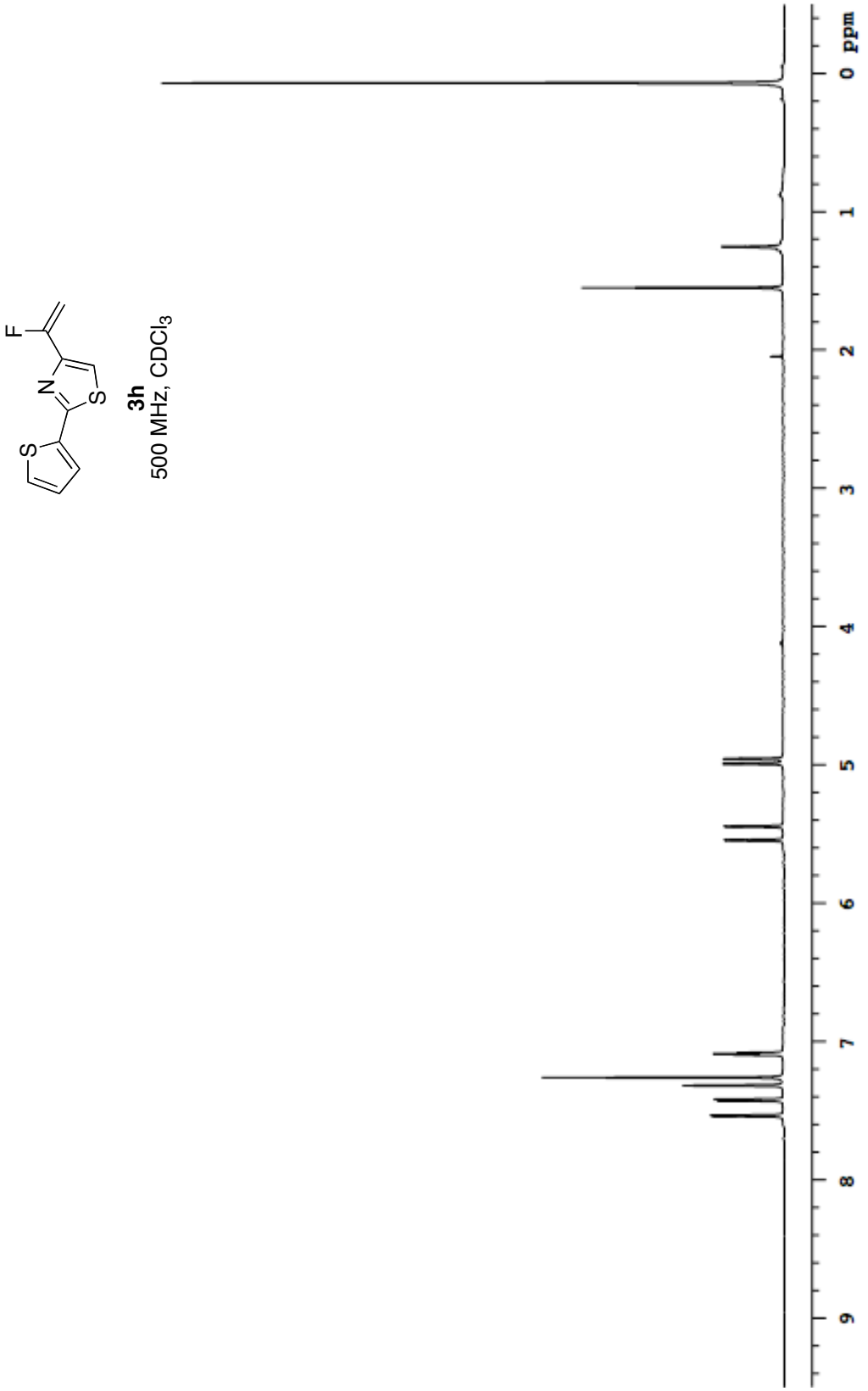
Pulse Sequence: s2pul

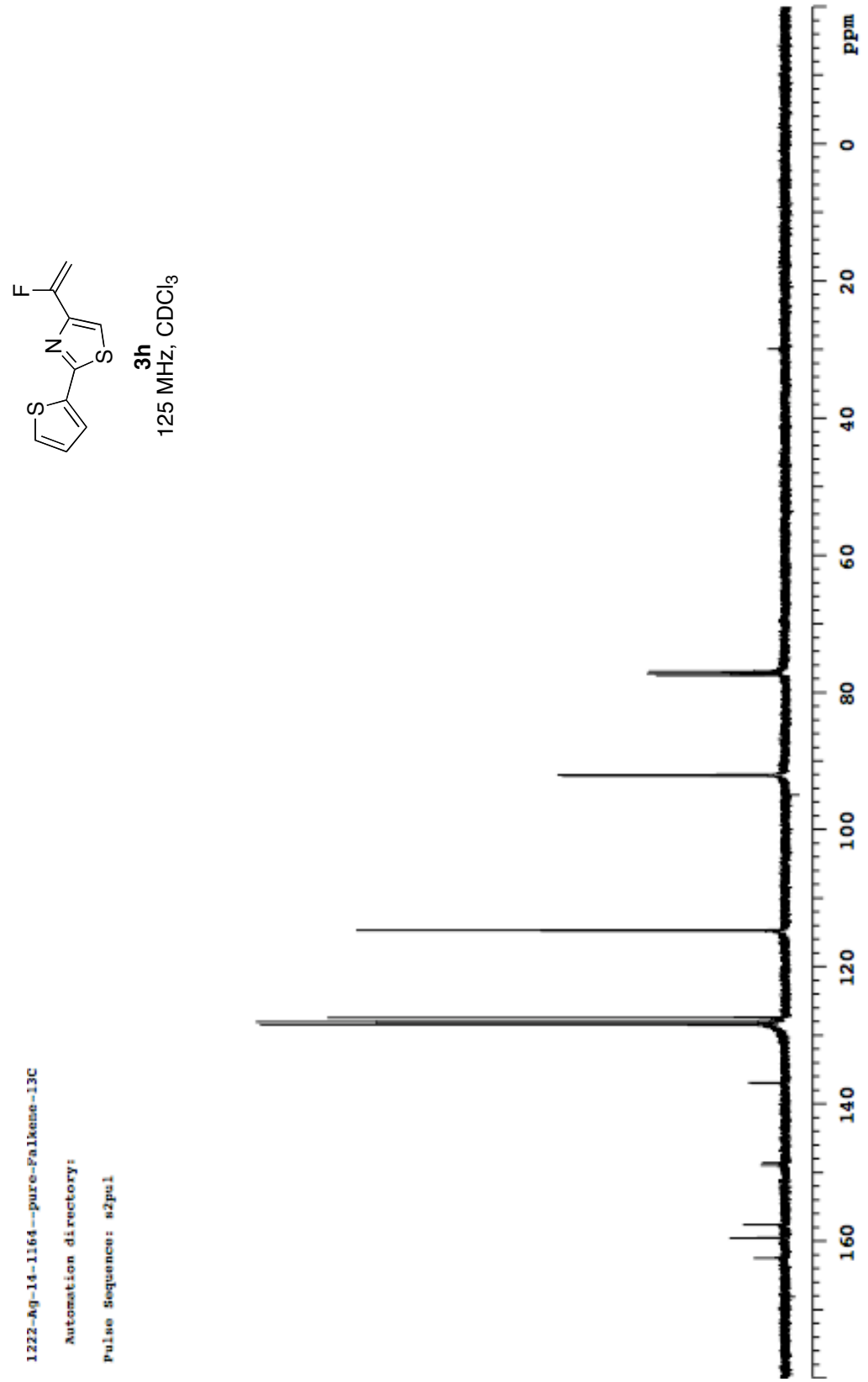


3g

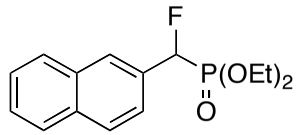
125 MHz, $CDCl_3$





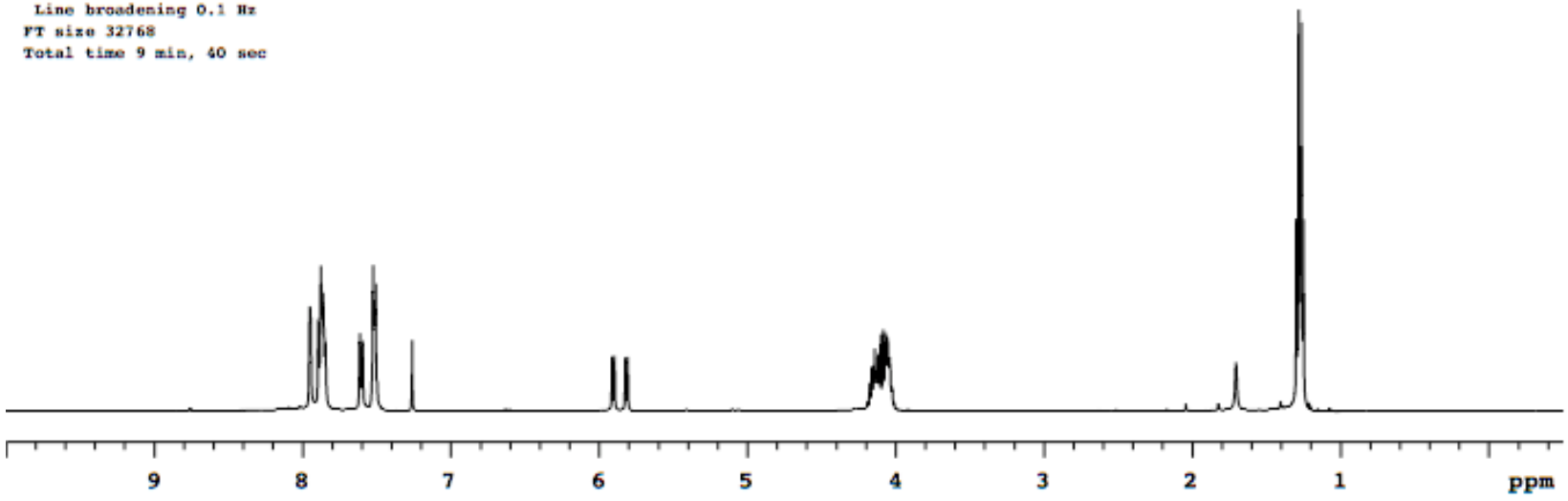


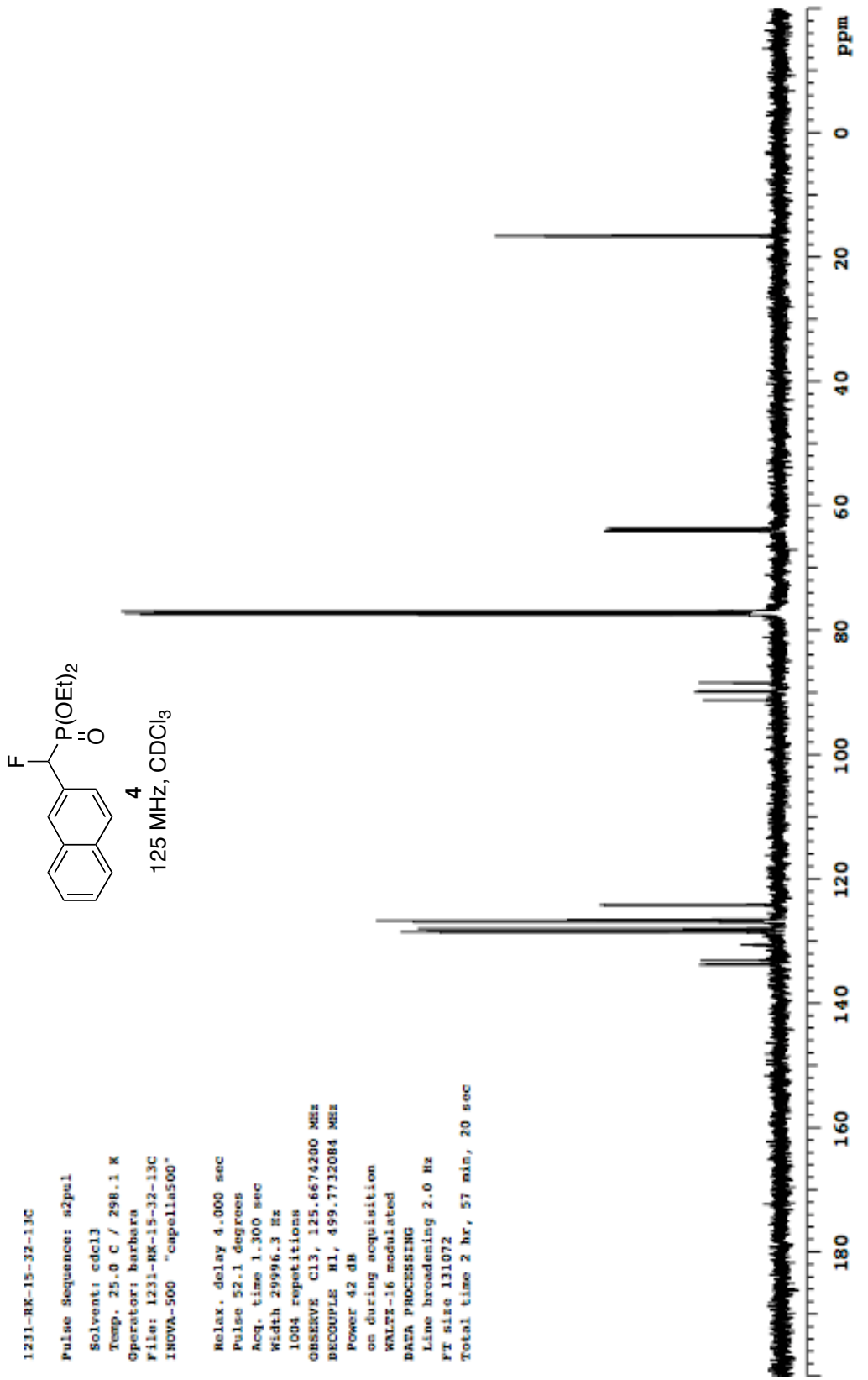
```
1231-RK-15-32-pure

 Archive directory: /export/home/mkl/vnmrsys/data
 Sample directory: auto_13Dec2004
 File: 1231-RK-15-32-pure

Pulse Sequence: s2pul

 Solvent: cdcl3
 Temp. 25.0 C / 298.1 K
Operator: barbara
File: 1231-RK-15-32-pure
INOVA-500  "capella500"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.892 sec
 Width 7544.3 Hz
 28 repetitions
OBSERVE   H1, 499.7707216 MHz
DATA PROCESSING
 Line broadening 0.1 Hz
FT size 32768
Total time 9 min, 40 sec
```

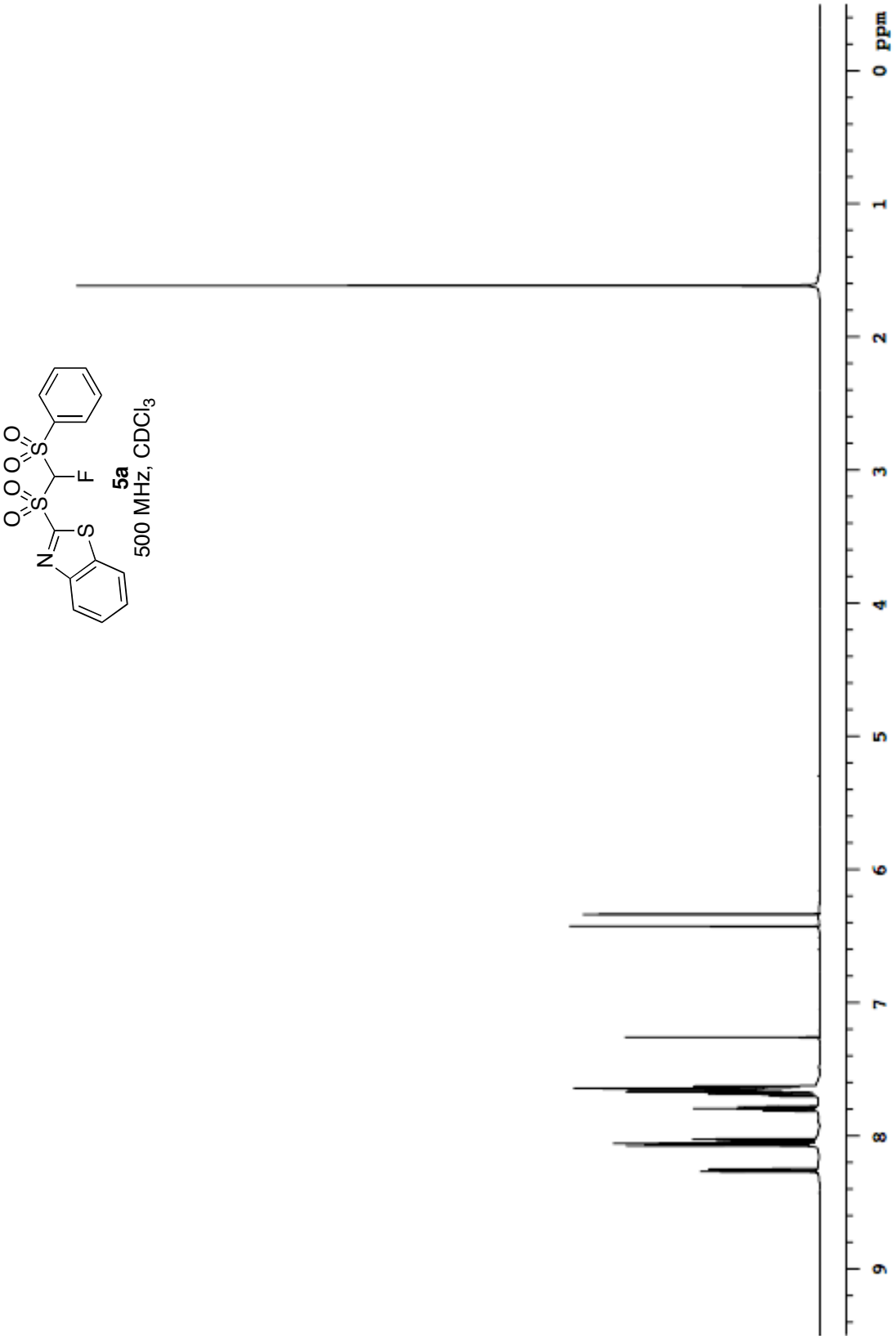


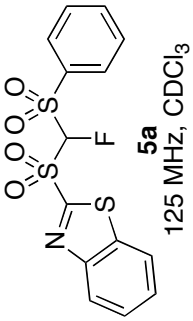
4

500 MHz, $CDCl_3$

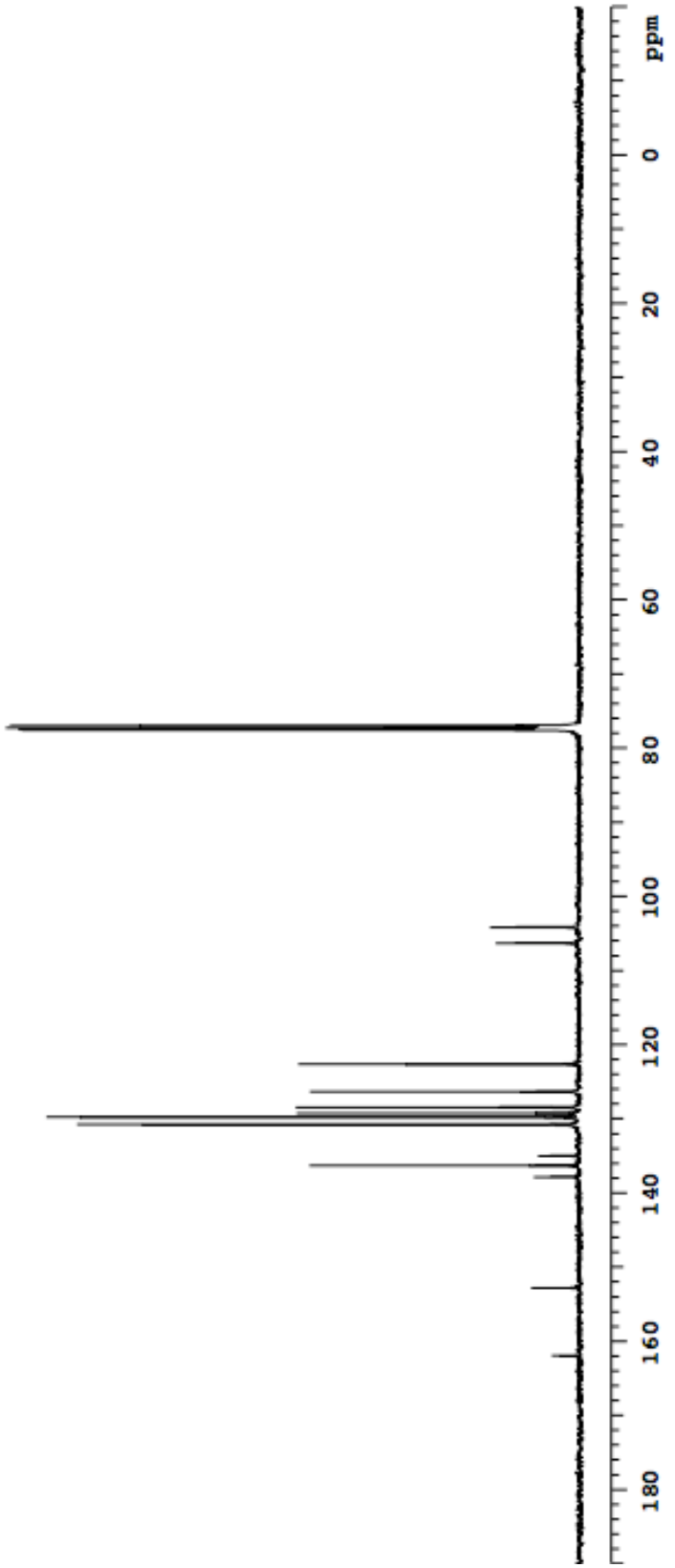


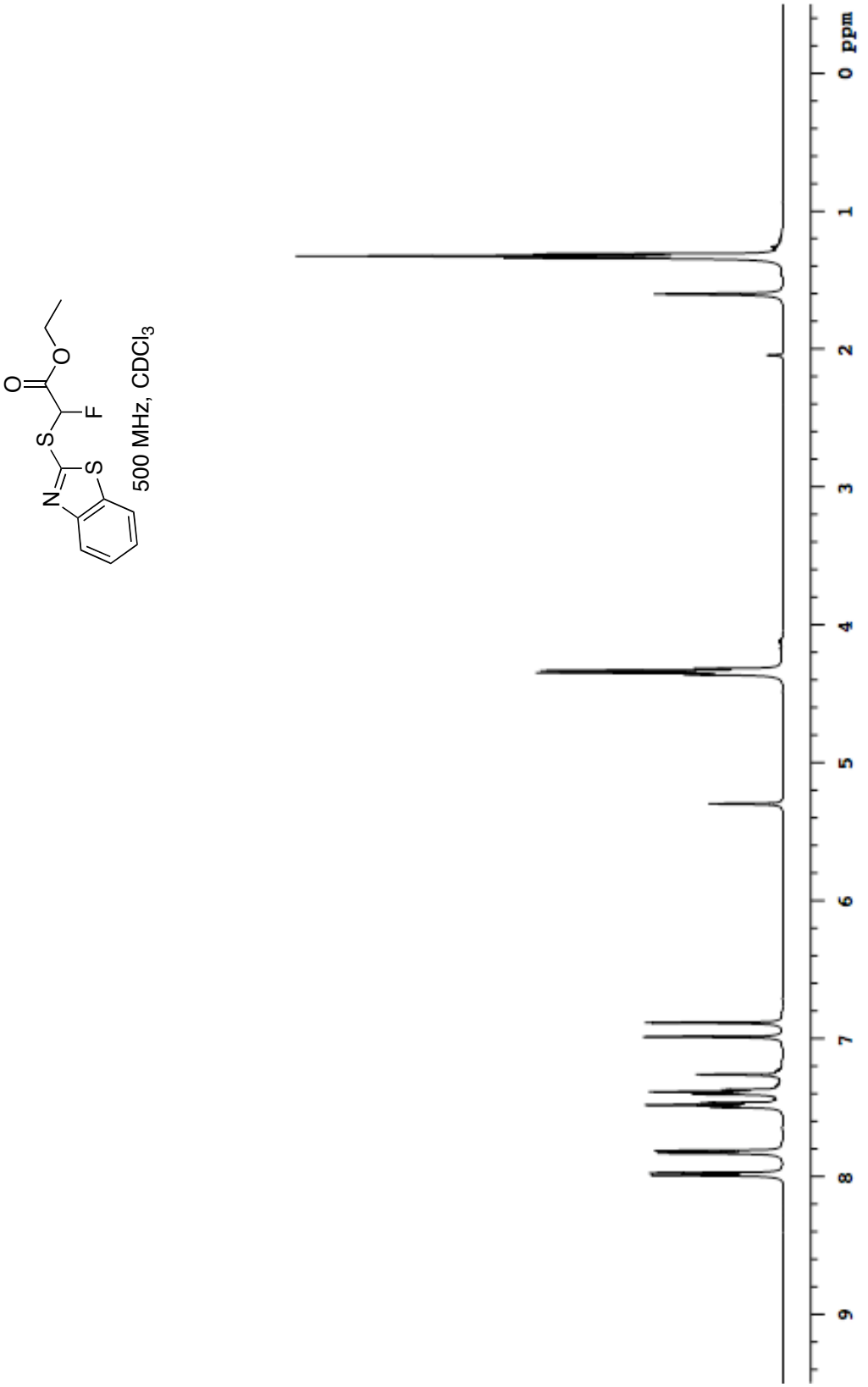


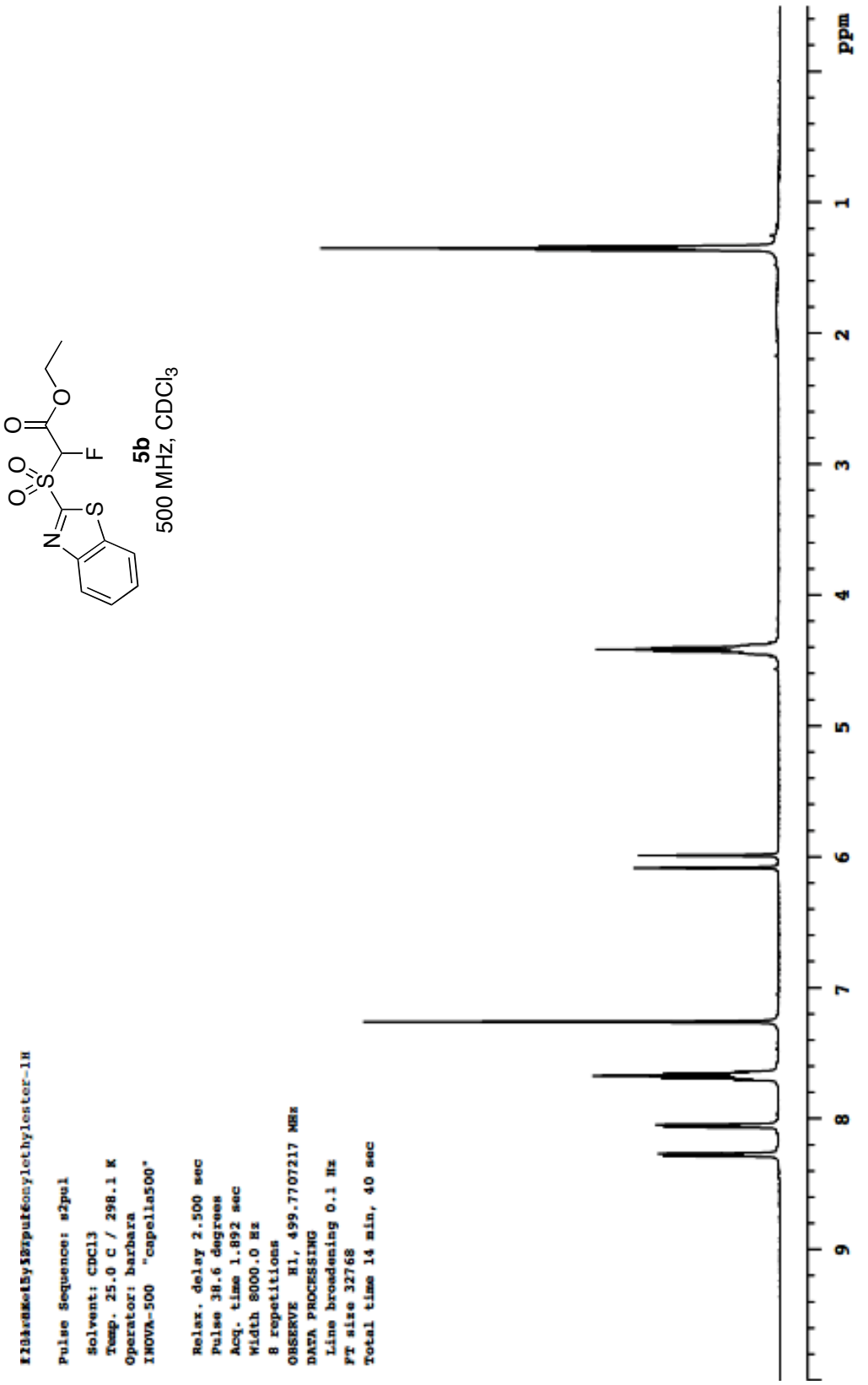


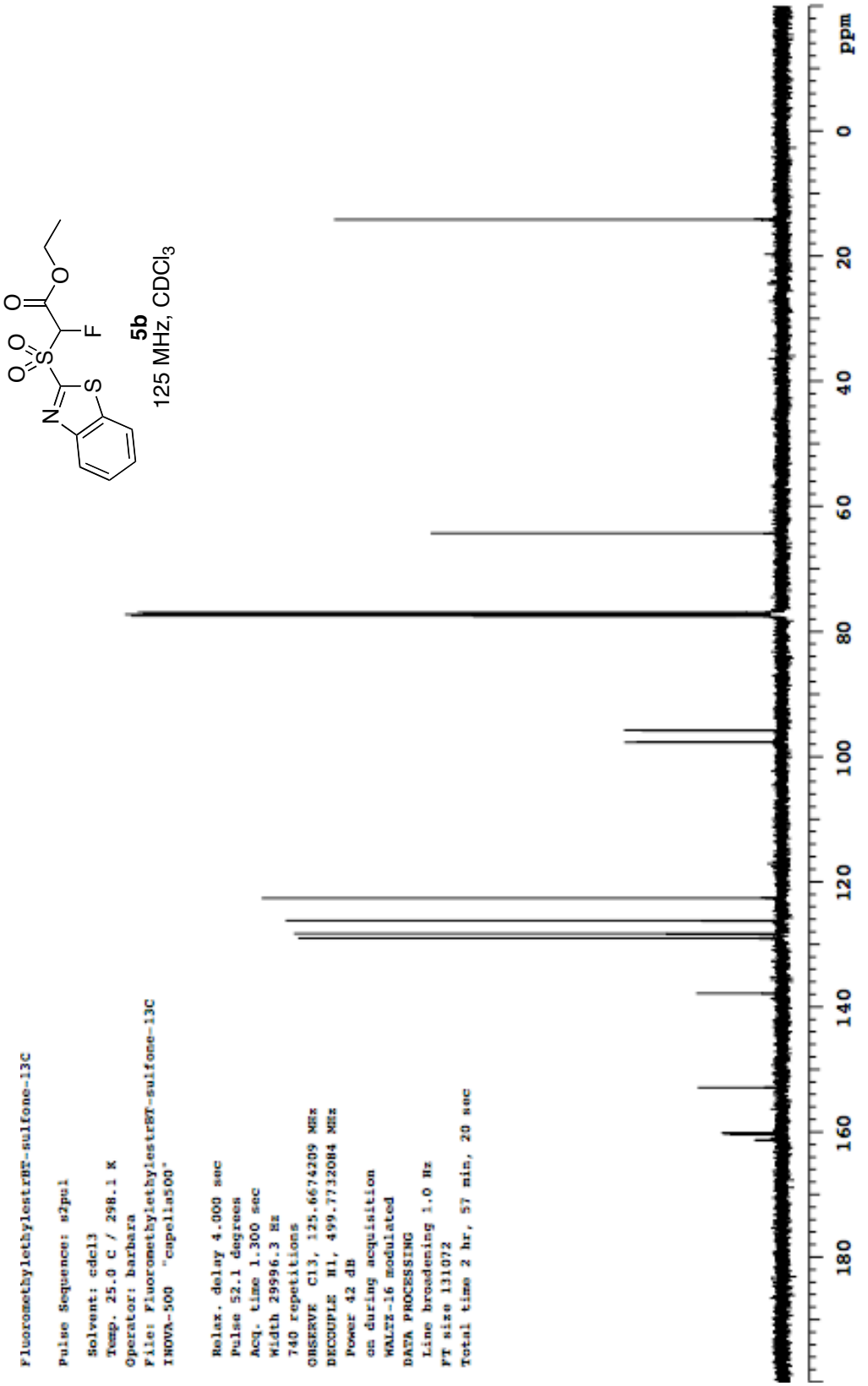


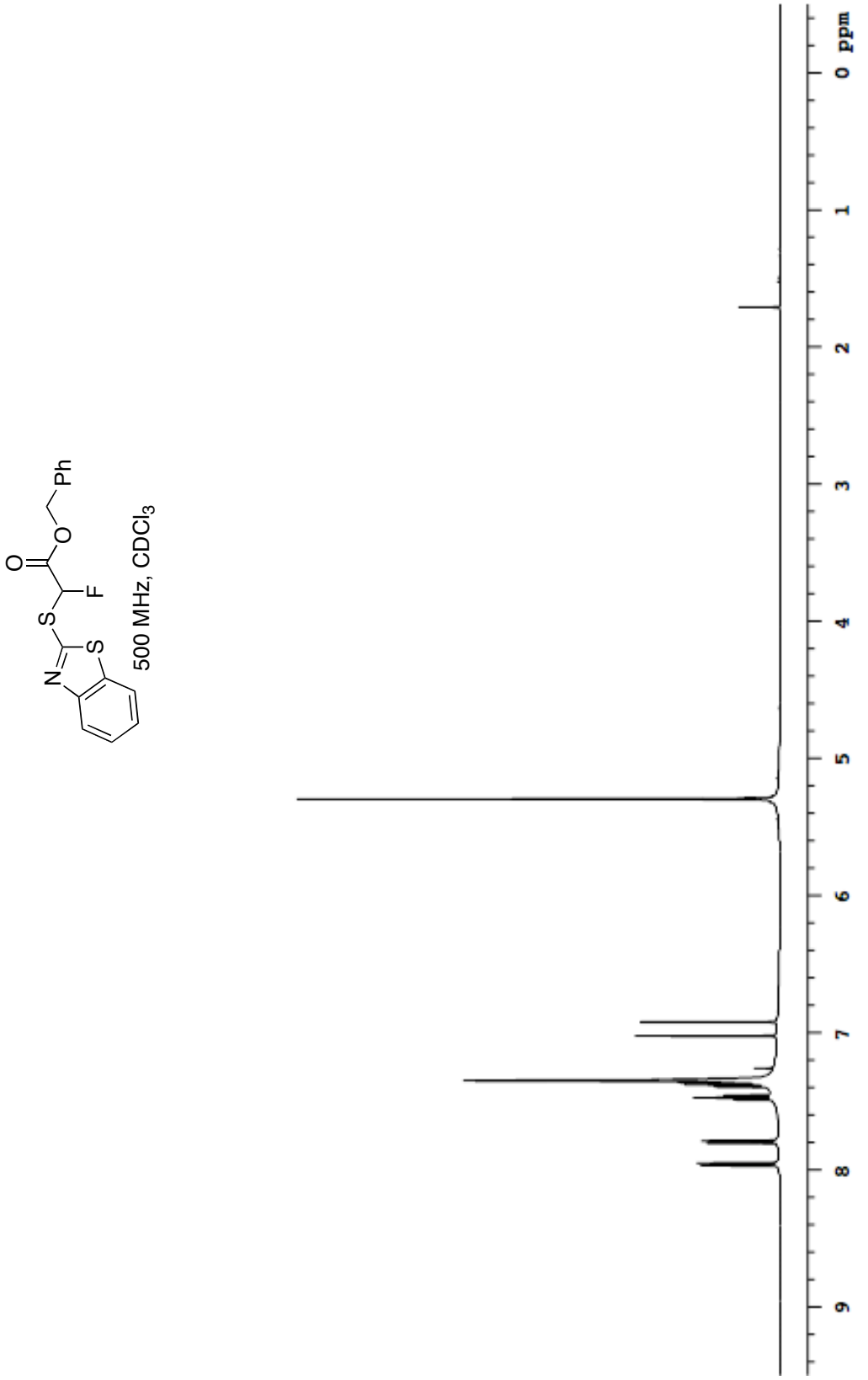
5a
125 MHz, $CDCl_3$

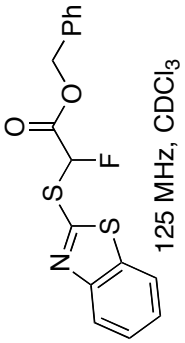




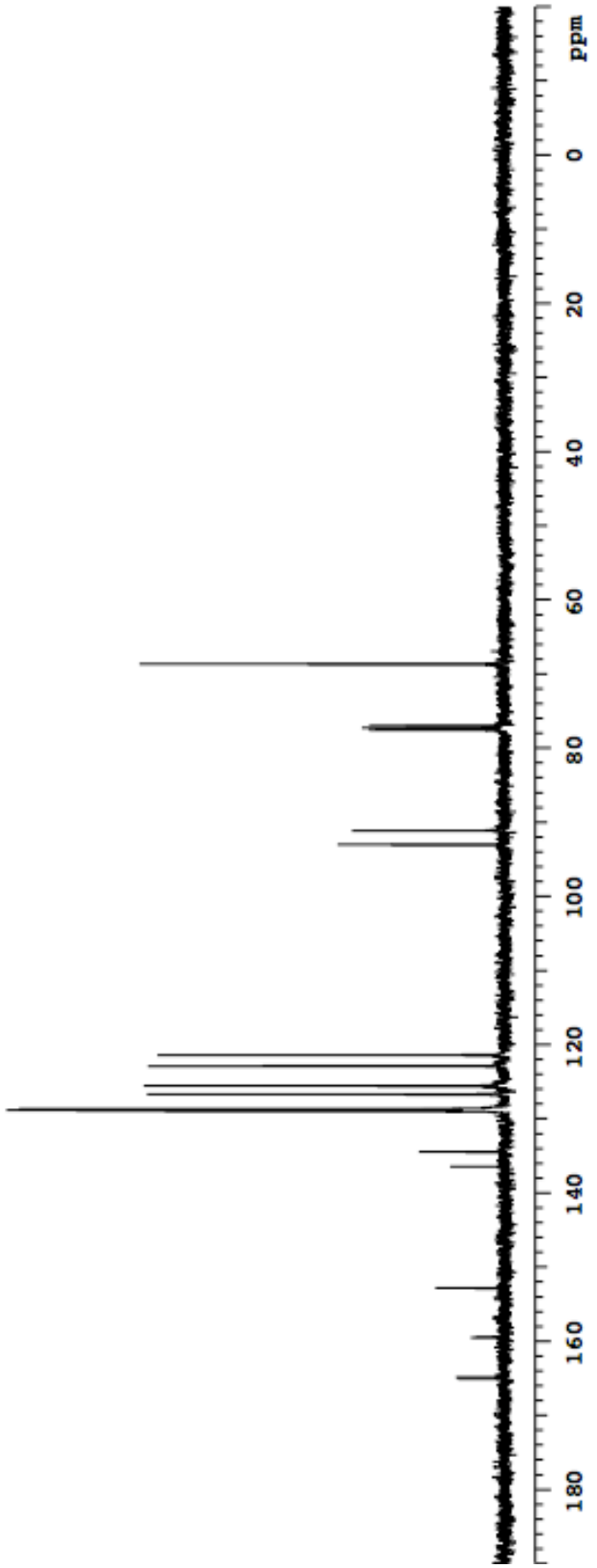


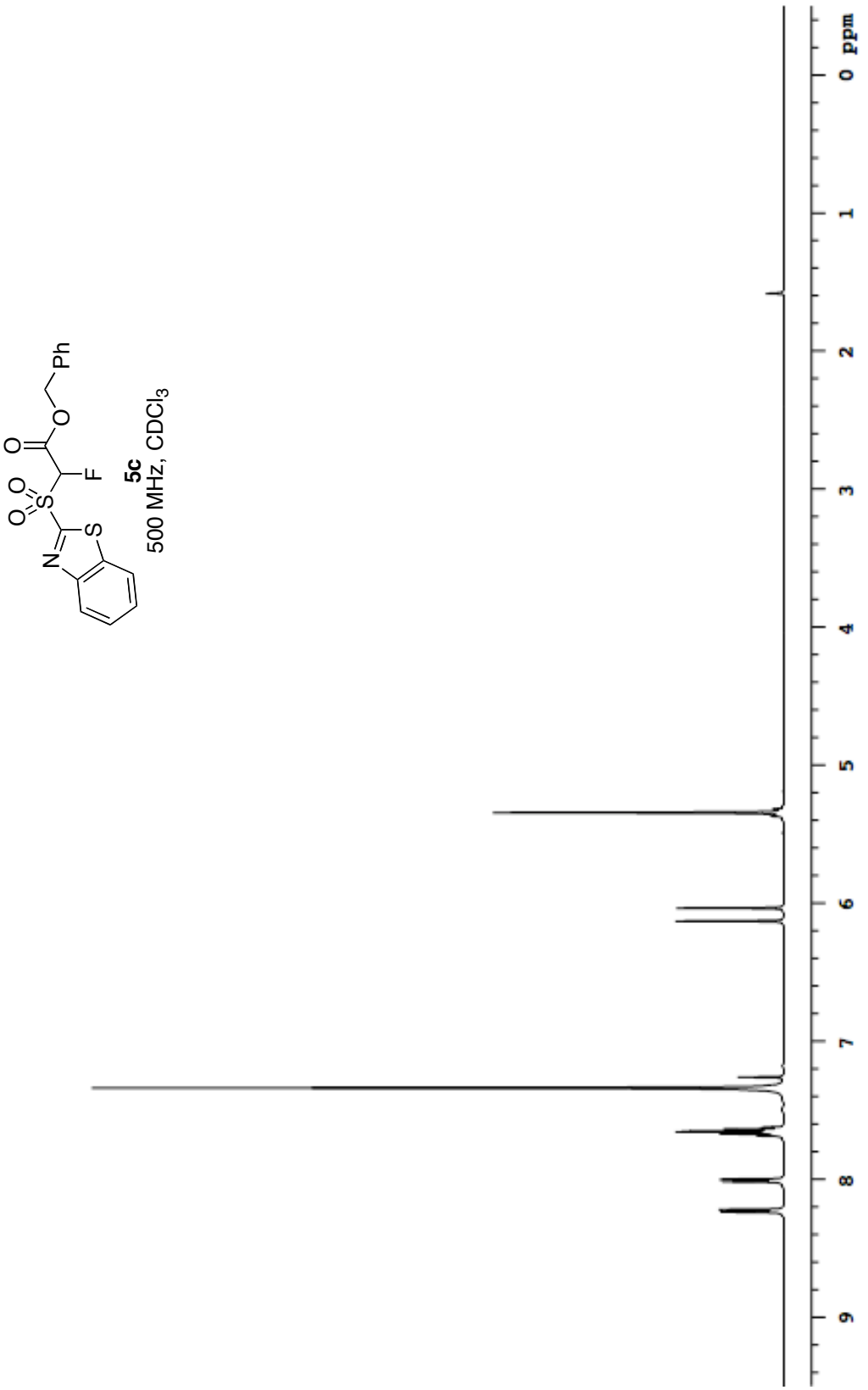


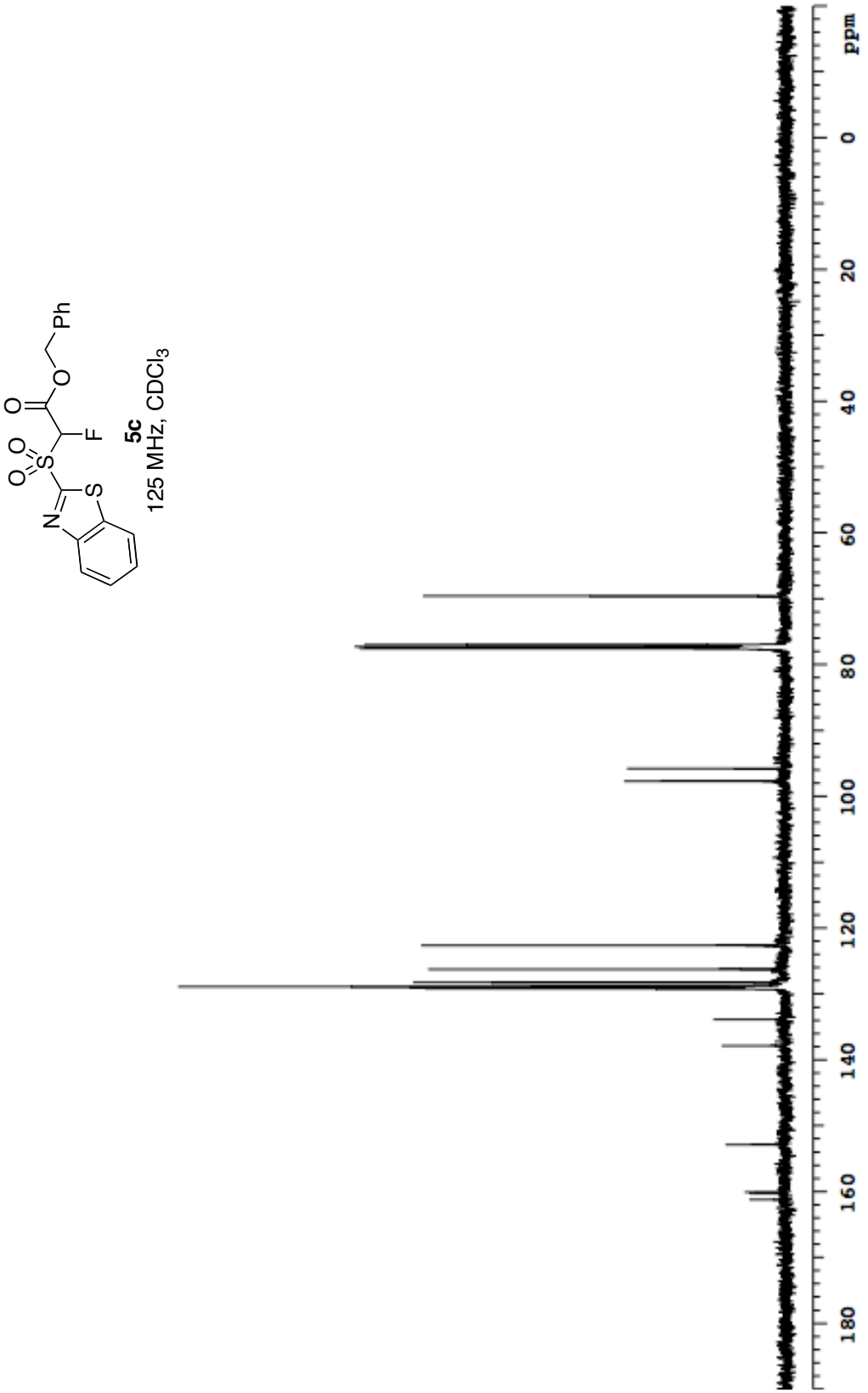


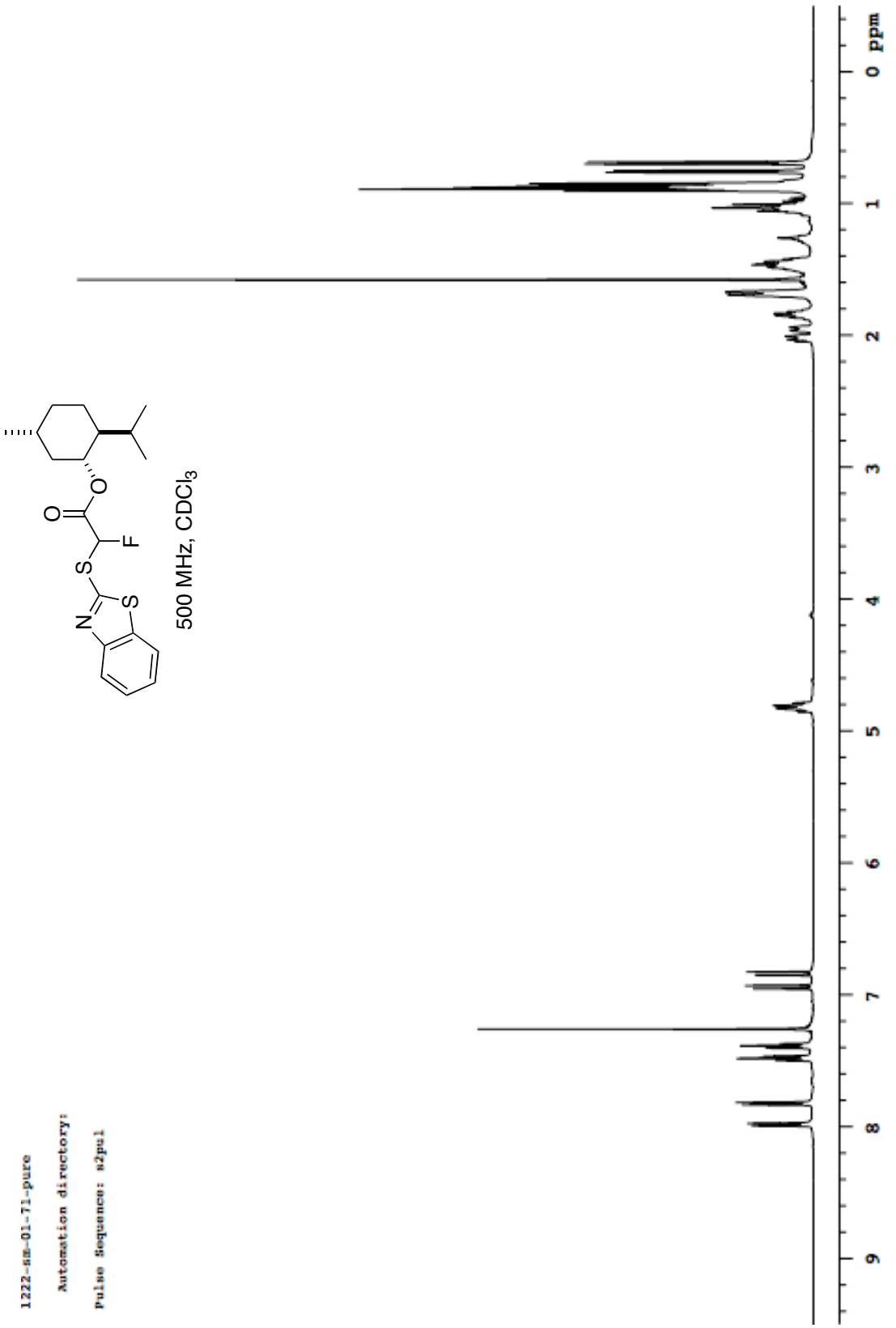


125 MHz, $CDCl_3$





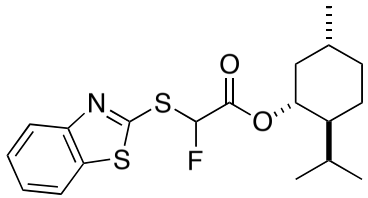




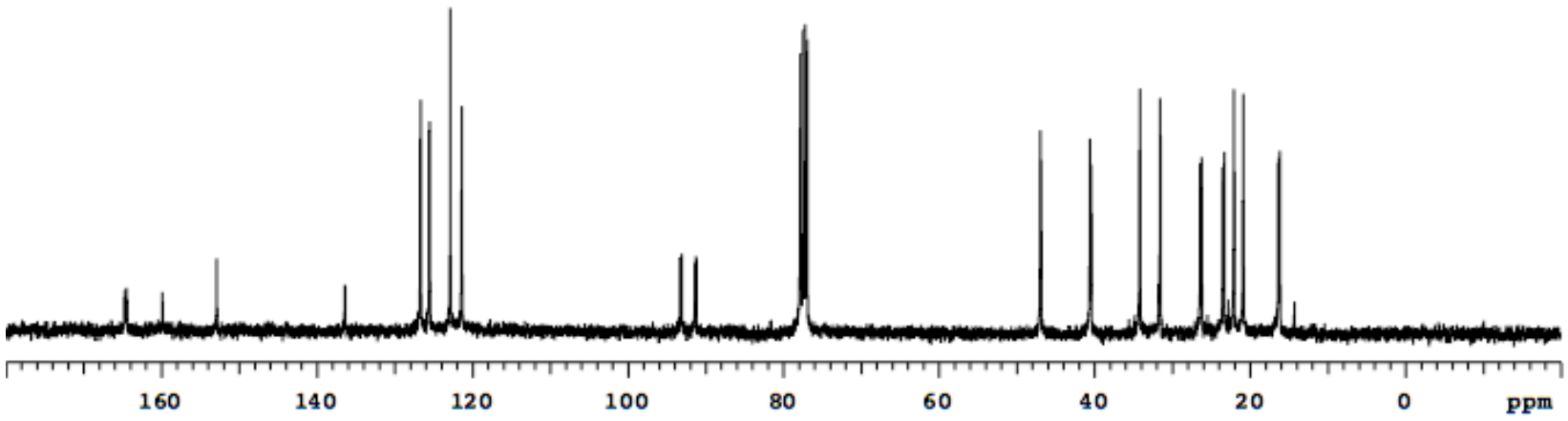
1222-sm-01-71-pure-13C

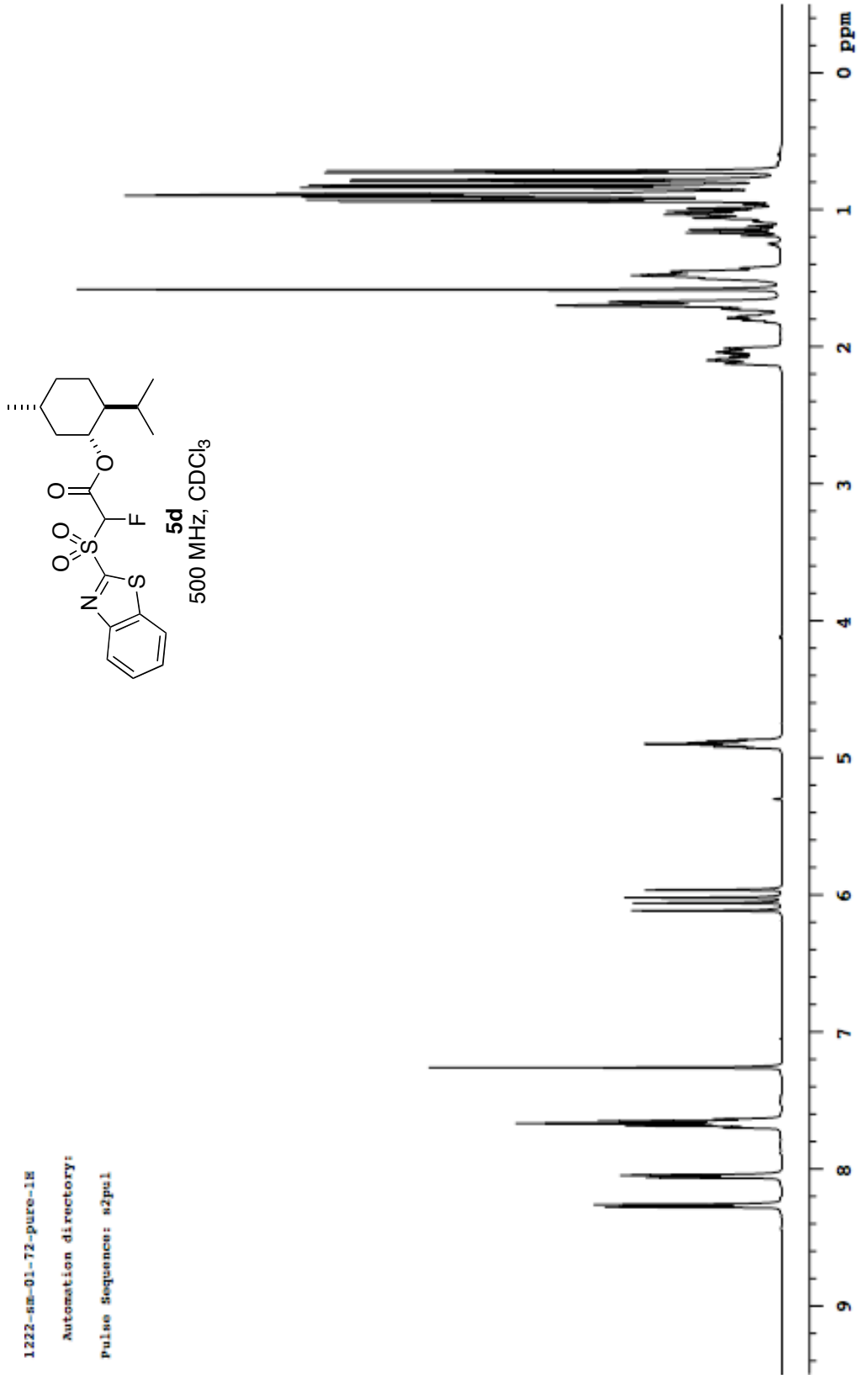
Automation directory:

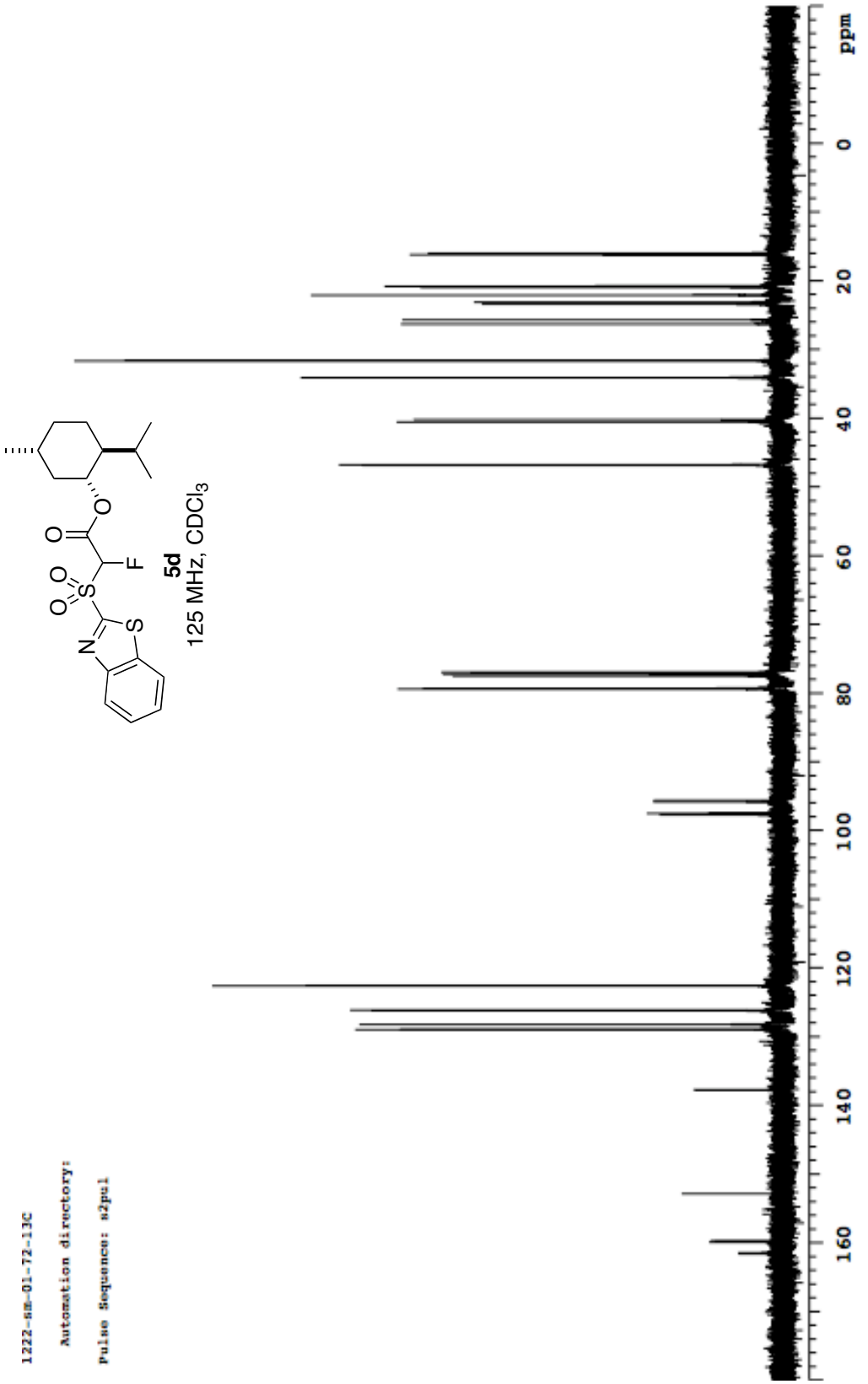
Pulse Sequence: s2pul

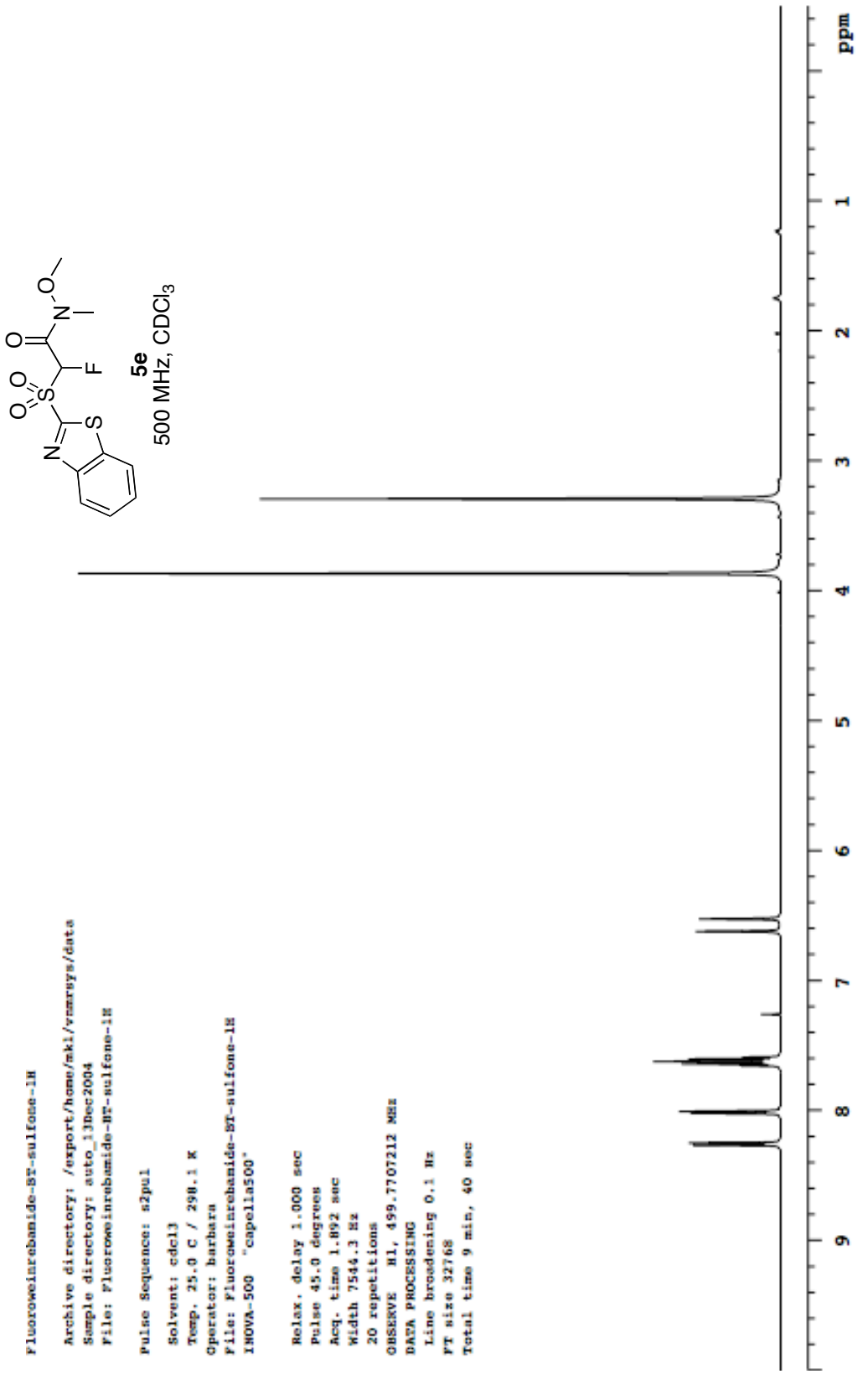


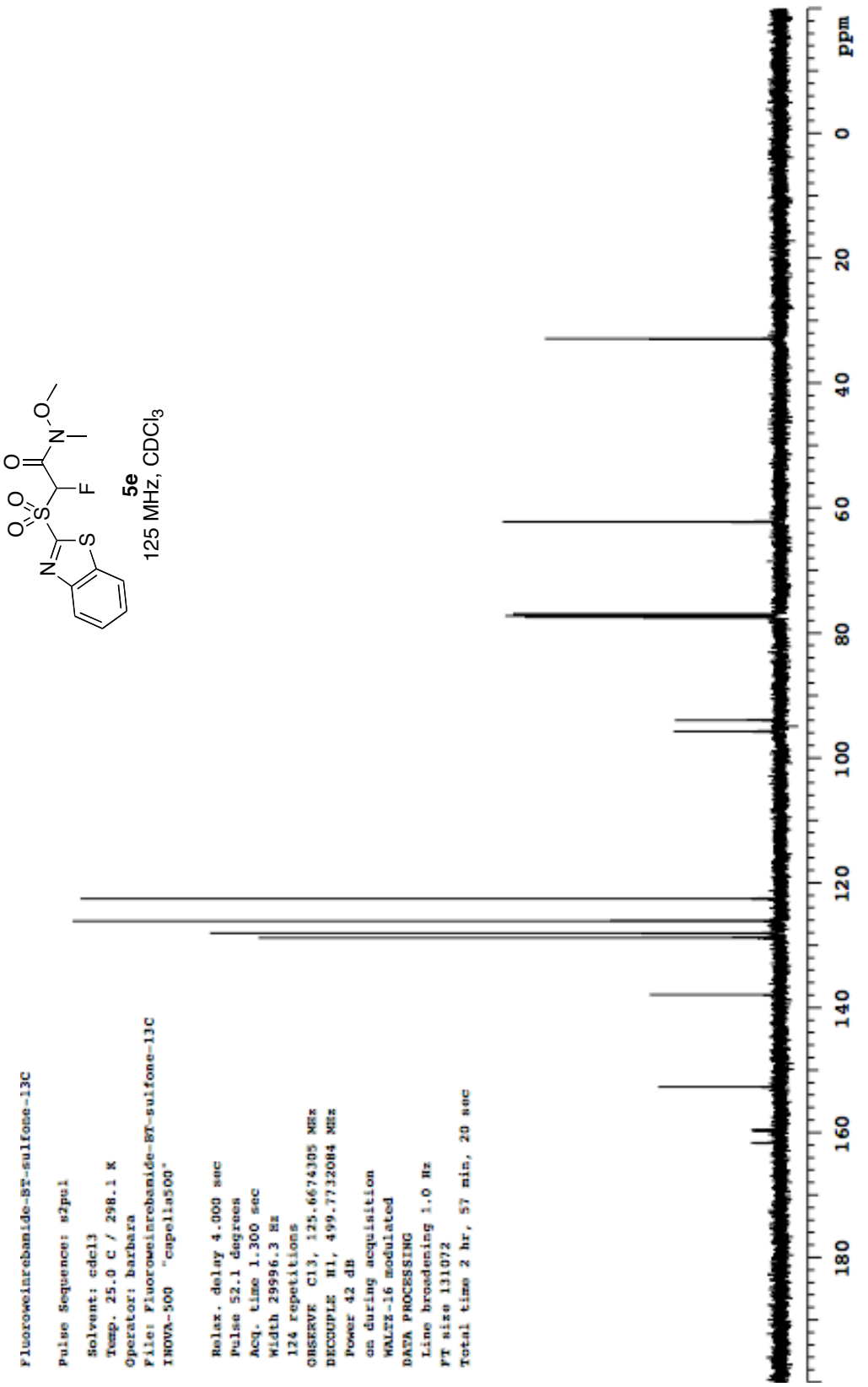
125 MHz, $CDCl_3$

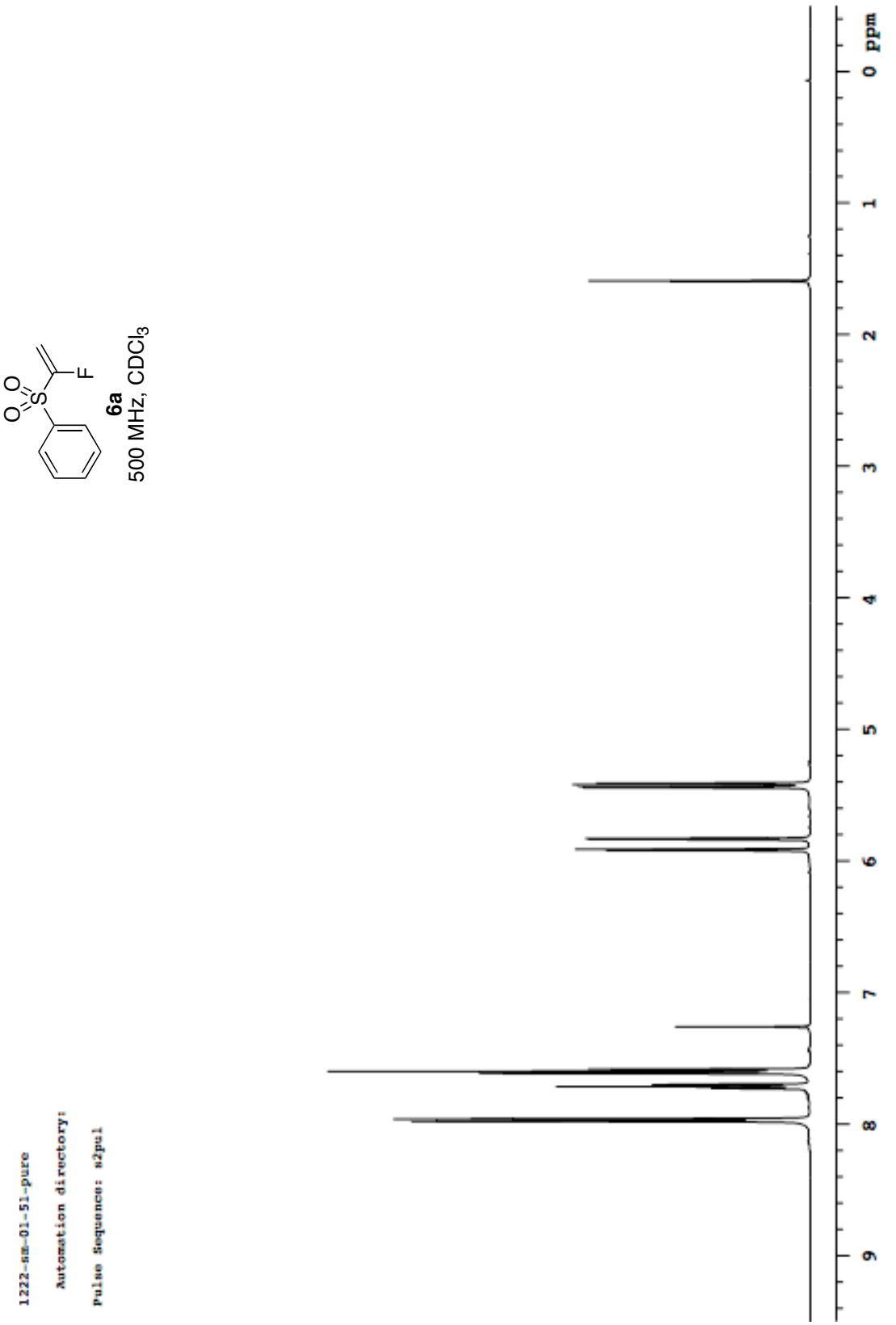


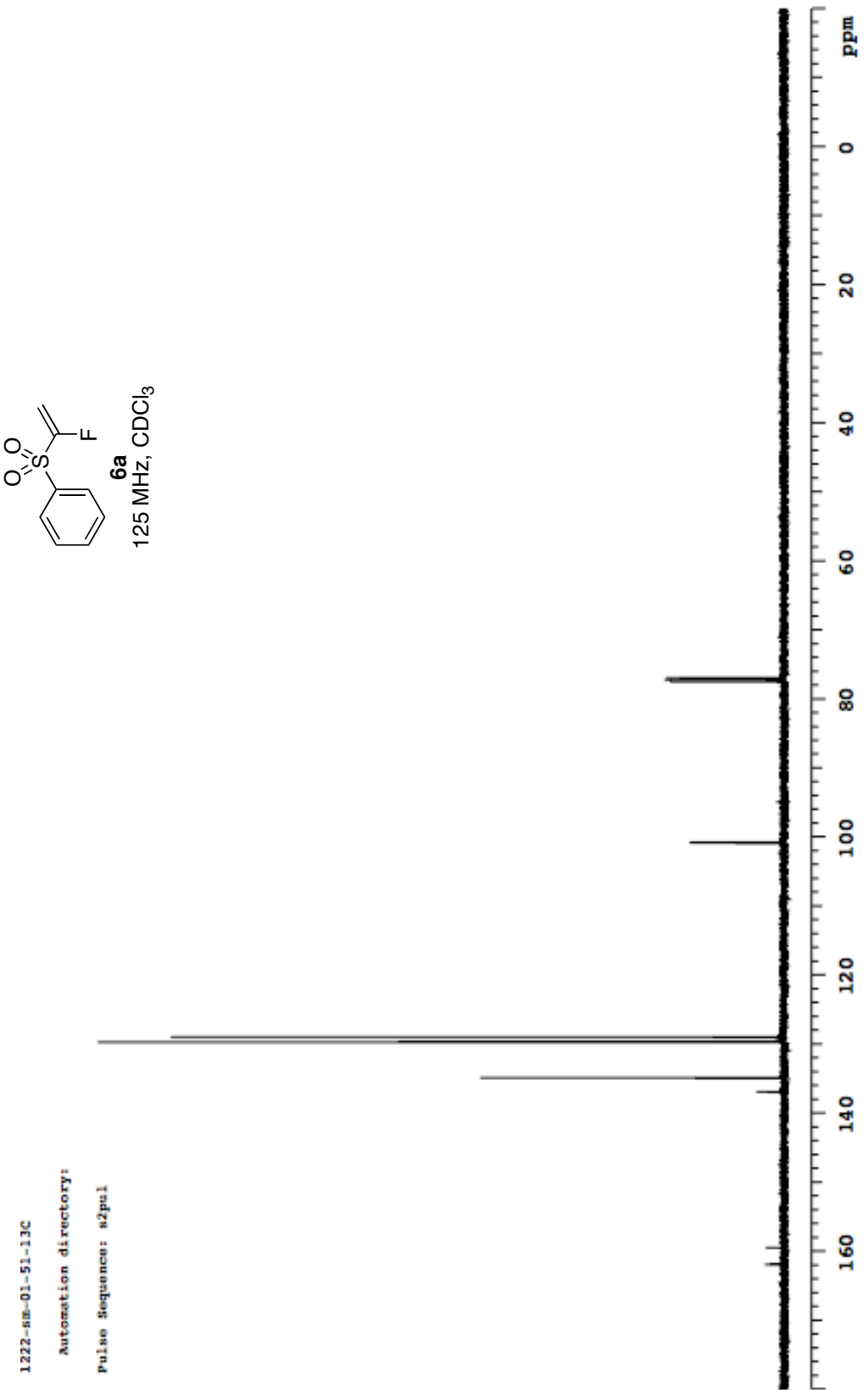


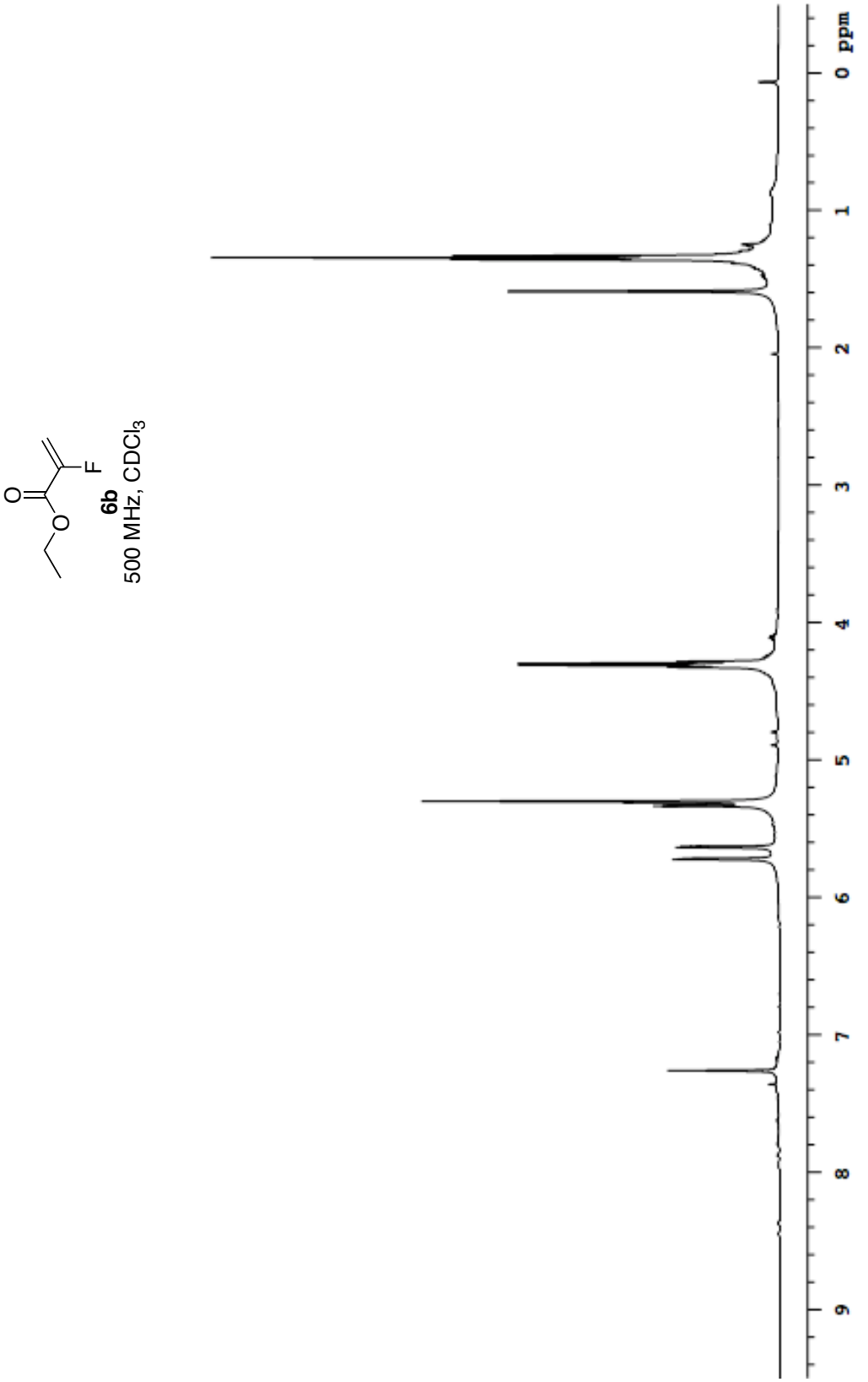


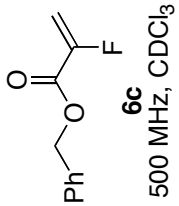






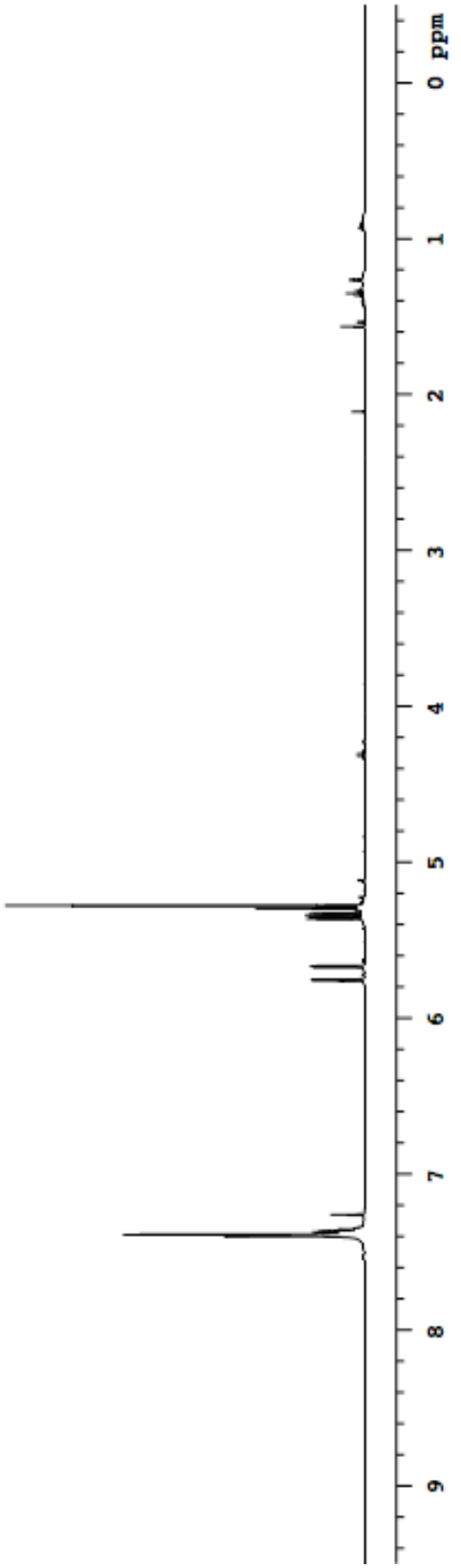


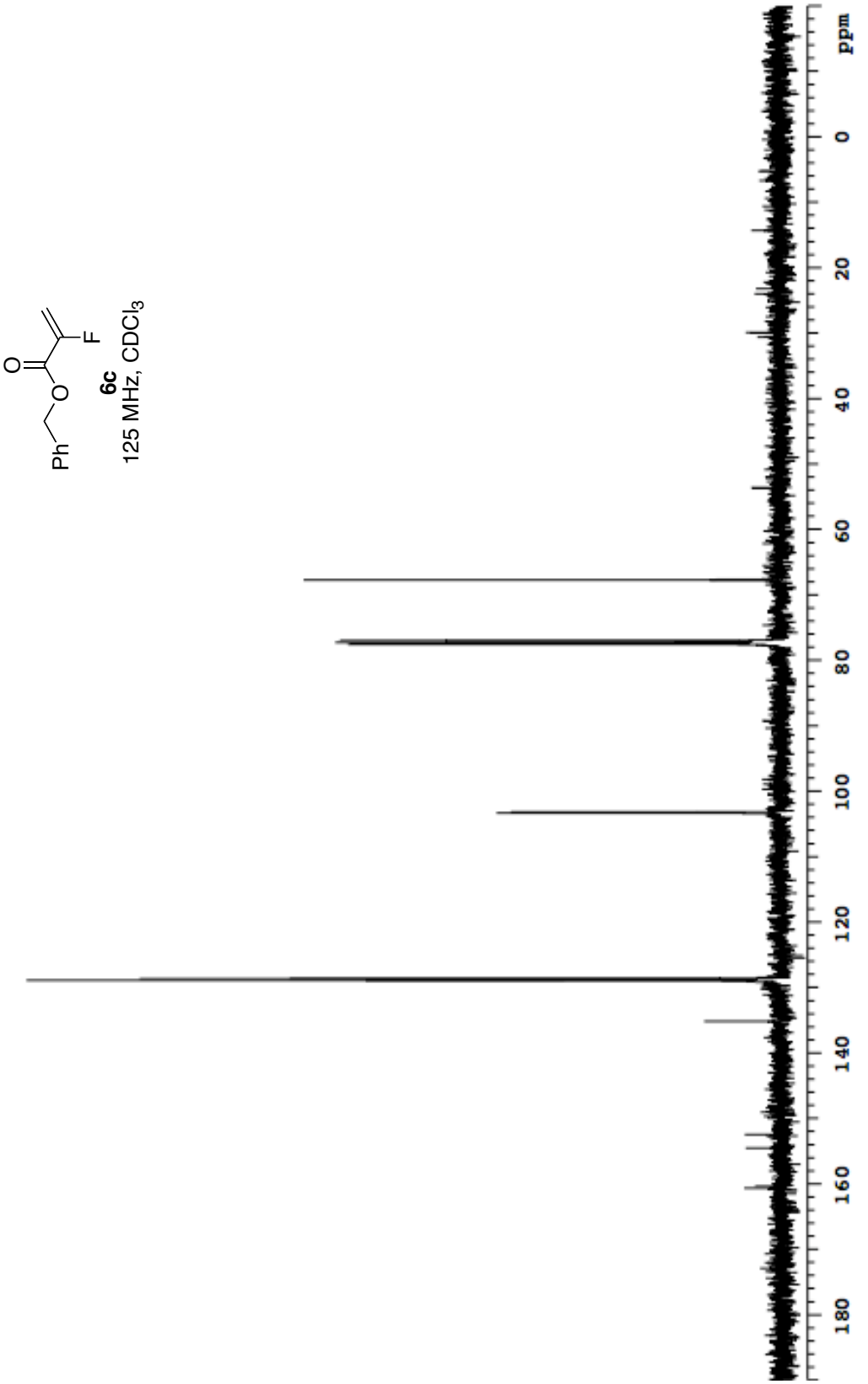




6c

500 MHz, $CDCl_3$

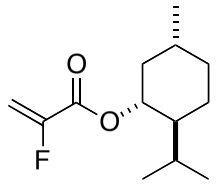




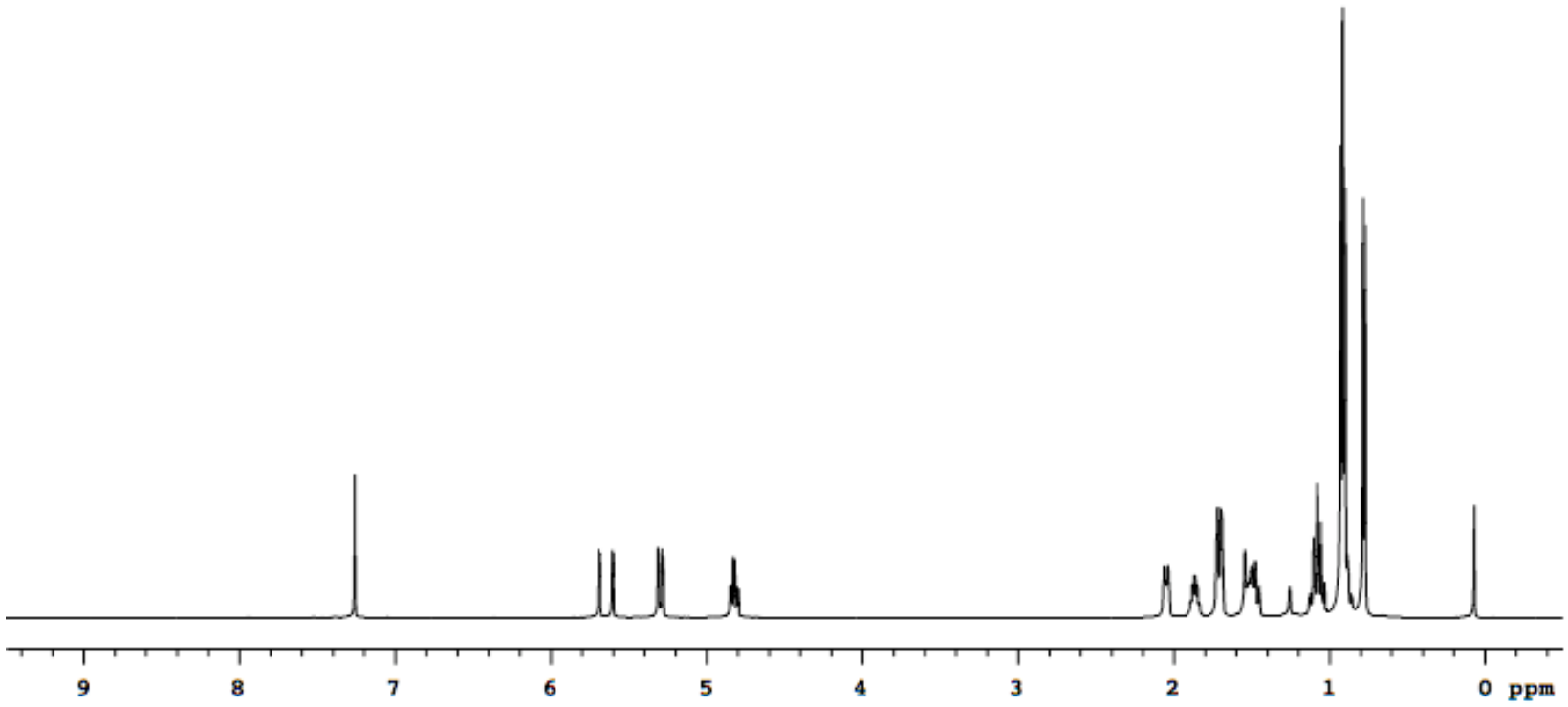
1222-sm-01-75-pure

Automation directory:

Pulse Sequence: s2pul



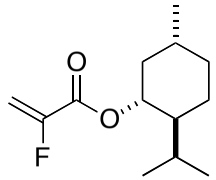
6d
500 MHz, $CDCl_3$



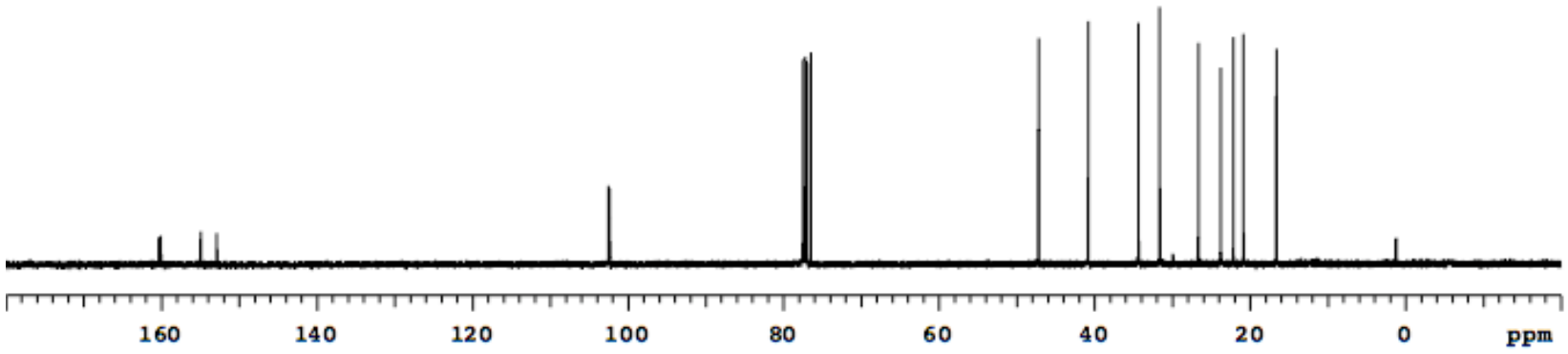
1222-sm-01-75-pure-13C

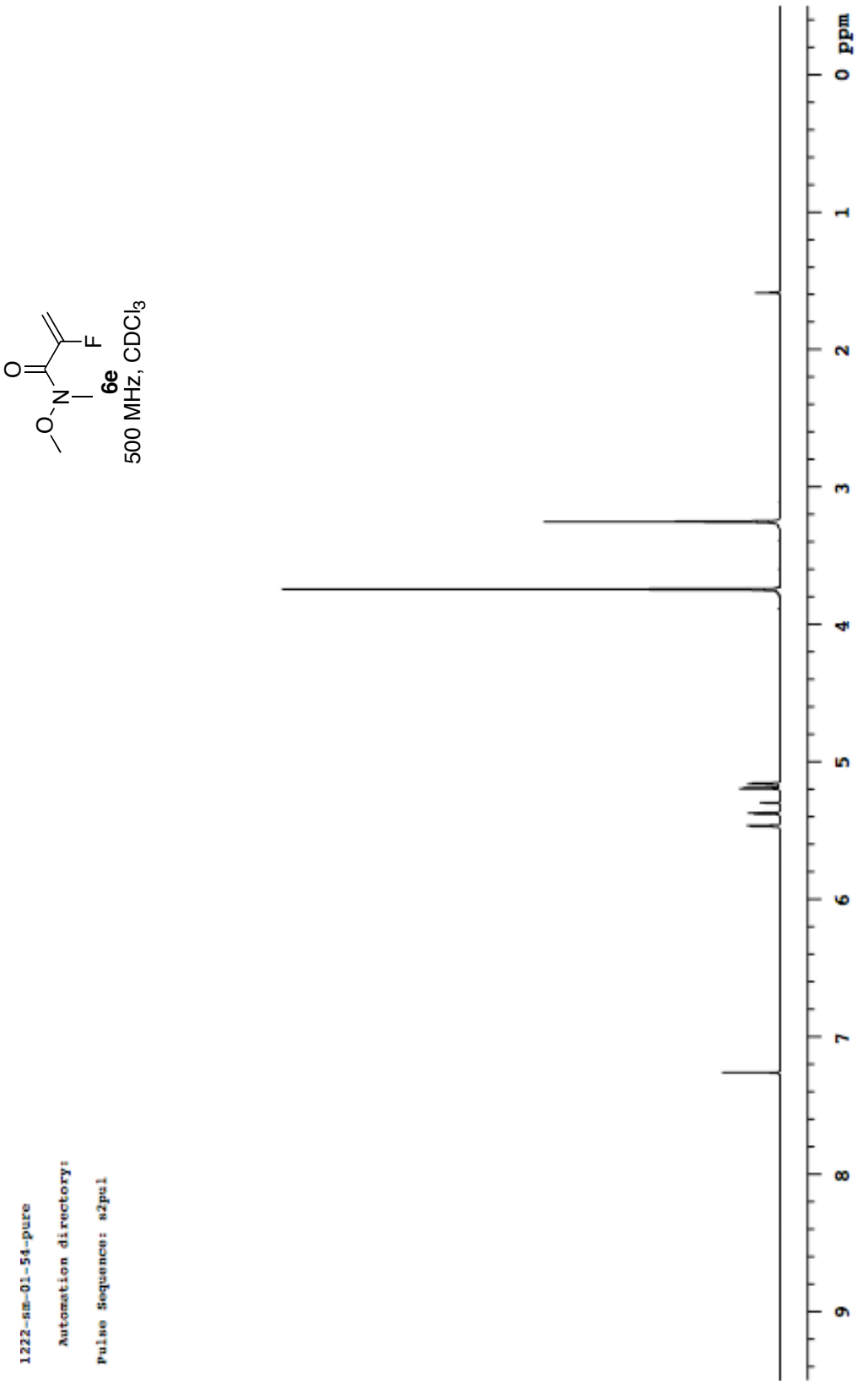
Automation directory:

Pulse Sequence: s2pul



6d
125 MHz, $CDCl_3$

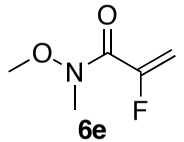




1222-sm-01-54-13C

Automation directory:

Pulse Sequence: s2pul



6e

125 MHz, $CDCl_3$