Supporting Information for

Synthesis of Isothiocyanates and Unsymmetrical Thioureas with the Bench-Stable Solid Reagent $(Me_4N)SCF_3$

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1. General experimental details

Reagents. $(Me_4N)SCF_3$ was prepared according to the corresponding literature procedure.[1] Anhydrous tetramethylammonium fluoride and (trifluoromethyl)trimethylsilane were purchased from ABCR and sulfur from Sigma Aldrich. Unless otherwise stated, all starting materials were commercially available and used as received.

Solvents. CH_2Cl_2, hexane, pentane were of technical grade.

Characterization. All ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at ambient temperature either on Varian V-NMRS 600 or Varian V-NMRS 400 spectrometers. Chemical shifts (δ) are quoted in parts per million (ppm) and were referenced to the residual solvent peak in the case of ^1H and ^{13}C NMR spectra. Coupling constants (J) are given in Hz. The resonance multiplicity is described as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sex (sextet), hept (heptet), m (multiplet), dd (doublet of doublets) and br (broad). ^{19}F NMR spectra were recorded using the F-H decoupled pulse sequence from the Varian program library. The peak observed at 83.3 ppm in ^{13}C NMR measured at 151 MHz is an artifact from the instrument.

High Resolution Mass Spectrometric analysis were performed on a Thermo Scientific LTQ Orbitrap XL (ESI), and on a Finnigan SSQ 7000, EI: 70 eV (EI).

Reactions were followed with an Agilent Technologies 5975 series MSD mass spectrometer coupled with an Agilent Technologies 7820A gas chromatograph (with an Agilent 19091s-433 HP-SMS column (30 m x 0.250 µm x 0.25 µm)).

(GC-MS Conditions: Front inlet mode: split; Temperature: 250°C; Pressure: 10.42 psi; Total flow 22.7 ml/min; Split ratio: 20:1; Split flow: 20 ml/min; Run time: 25.5 min; Oven Program: 60°C for 0.5 min then 10°C/min to 280°C for 3 min; Flow 1.2 ml/min.)

2. General experimental procedures and compounds characterization data

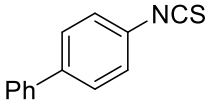
General procedure for the synthesis of compounds from Scheme 1, Figure 2 and Scheme 2:

Under air atmosphere, the amine (0.2 mmol, 1 equiv.) and triethylamine (42 μL, 0.3 mmol, 1.5 equiv.) were mixed in CH_2Cl_2 (1.5 mL) at room temperature. To this solution was added at once $(Me_4N)SCF_3$ salt (39 mg, 0.22 mmol, 1.1 equiv.). After the indicated time, pentane (or hexane) (0.75 mL) was added to the reaction mixture which was then filtered through a pad of celite (2 cm). Subsequent wash of the celite pad with a 1/1 mixture of CH_2Cl_2 / pentane (or hexane) (1 mL) was performed. The filtrate was then concentrated under reduced pressure to afford the expected product. Unless otherwise stated no further purification was necessary.

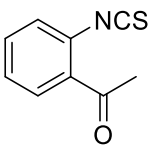
Procedure for the 10 mmol scale experiment:

Under air atmosphere, methyl 4-aminobenzoate (1.51 g, 10 mmol, 1 equiv.) and triethylamine (2.1 mL, 15 mmol, 1.5 equiv.) were mixed in CH_2Cl_2 (50 mL) at room temperature. To this solution was added at once $(Me_4N)SCF_3$ salt (1.93 g, 11 mmol, 1.1 equiv.). After 30 minutes, hexane (50 mL) was added to the reaction mixture which was then filtered through celite. Subsequent wash of the celite pad with a 1/1 mixture of CH_2Cl_2 / hexane was performed. The filtrate was then concentrated under reduced pressure to afford the expected product in 92% yield (1.78 g) as a pale yellow solid.

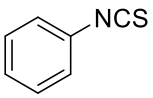
Compounds from Scheme 1:



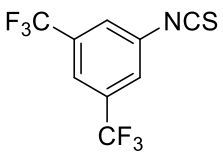
4-Isothiocyanato-1,1'-biphenyl 1 : The title compound was obtained as a white solid after 15 minutes in 93% yield (39.2 mg) using 4-amino-1,1'-biphenyl after filtration over celite following the general procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 – 7.54 (m, 4H), 7.48 – 7.43 (m, 2H), 7.40 – 7.35 (m, 1H), 7.32 – 7.28 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 140.3, 139.7, 135.5, 130.2, 128.9, 128.2, 127.8, 127.0, 126.1. *m/z* (EI) 211 (M, 100), 152 (35). The analytical data are in agreement with those reported previously in the literature.[2]



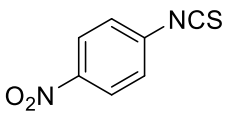
1-(2-Isothiocyanatophenyl)ethan-1-one 2 : The title compound was obtained as a brown liquid after 60 minutes in 88% yield (31.3 mg) using 2-aminoacetophenone after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.34 – 7.30 (m, 2H), 2.64 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 137.2, 133.4, 133.1, 130.1, 129.6, 128.7, 127.0, 29.7. HRMS (ESI) calculated for C_9H_8ONS: 178.0321 $[M+H]^+$, Found: 178.0321.



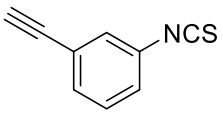
Isothiocyanatobenzene 3 : The title compound was obtained as a colorless liquid after 10 minutes in 92% yield (24.8 mg) using aniline after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 2H), 7.29 – 7.23 (m, 1H), 7.23 – 7.18 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.4, 131.2, 129.5, 127.3, 125.7. *m/z* (EI) 135 (M, 100), 77 (58), 51 (19). The analytical data are in agreement with those reported previously in the literature.[3]



1-Isothiocyanato-3,5-bis(trifluoromethyl)benzene 4 : The title compound was obtained as a pale yellow liquid after 60 minutes in 88% yield (47.5 mg) using 3,5-bis(trifluoromethyl)aniline after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.64 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2. ^{13}C NMR (151 MHz, $CDCl_3$) δ 140.8 , 133.9 , 133.3 (q, *J* = 34.1 Hz), 126.1 – 125.4 (m), 122.4 (q, *J* = 273.1 Hz), 120.6 – 120.2 (m). *m/z* (EI) 271 (M, 100), 252 (28), 213 (31), 163 (19), 69 (10). The analytical data are in agreement with those reported previously in the literature.[4]

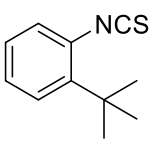


1-Isothiocyanato-4-nitrobenzene 5 : The title compound was obtained as a yellow solid after 15 hours in 97% yield (34.8 mg) using 4-nitroaniline after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.19 (m, 2H), 7.36 – 7.29 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8, 140.3, 137.9, 126.3, 125.2. *m/z* (EI) 180 (M, 100), 150 (49), 134 (47), 90 (42). The analytical data are in agreement with those reported previously in the literature.[5]

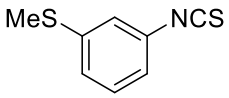


1-Ethynyl-3-isothiocyanatobenzene 6 : The title compound was obtained as a pale yellow liquid after 30 minutes in 88% yield (28.0 mg) using 3-ethynylaniline after filtration over celite following the general procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ

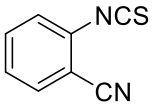
7.39 – 7.36 (m, 1H), 7.34 – 7.32 (m, 1H), 7.32 – 7.28 (m, 1H), 7.21 – 7.18 (m, 1H), 3.13 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.7, 131.6, 130.8, 129.6, 129.1, 126.1, 123.8, 81.8, 78.8. *m/z* (EI) 159 (M, 100), 101 (29), 75 (18). The analytical data are in agreement with those reported previously in the literature.[6]



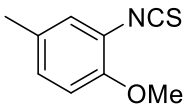
1-(*tert*-Butyl)-2-isothiocyanatobenzene 7 : The title compound was obtained as a pale yellow liquid after 15 minutes in 81% yield (31.0 mg) using 2-*tert*-butylaniline after filtration over celite following the general procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 1H), 7.31 – 7.28 (m, 1H), 7.25 – 7.18 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.8, 135.2, 129.7, 129.2, 127.3, 127.1, 126.8, 35.1, 29.8. HRMS (EI) calculated for $C_{11}H_{13}NS$: 191.0763 $[M]^+$, Found: 191.0765.



(3-Isothiocyanatophenyl)(methyl)sulfane 8 : The title compound was obtained as a yellow oil after 15 minutes in 86% yield (31.2 mg) using 3-(methylthio)aniline after filtration over celite following the general procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.23 (m, 1H), 7.16 – 7.13 (m, 1H), 7.08 – 7.06 (m, 1H), 7.00 – 6.97 (m, 1H) 2.48 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.6, 136.6, 132.6, 130.4, 125.7, 123.5, 122.7, 15.5. HRMS (ESI) calculated for $C_8H_8NS_2$: 182.0093 $[M+H]^+$, Found: 182.0092.

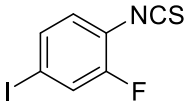


2-Isothiocyanatobenzonitrile 9 : The title compound was obtained as a yellow solid after 60 minutes in 81% yield (26.0 mg) using 2-aminobenzonitrile after filtration over celite following the general procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.36 – 7.31 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.0, 134.8, 133.9, 133.4, 127.0, 127.0, 115.4, 109.6. *m/z* (EI) 160 (M, 100), 102 (28), 75 (13). The analytical data are in agreement with those reported previously in the literature.[7]

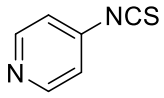


2-Isothiocyanato-1-methoxy-4-methylbenzene 10 : The title compound was obtained as a yellow liquid after 10 minutes in 99% yield (35.7 mg) using 2-methoxy-5-methylaniline after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 – 6.99 (m, 1H), 6.93 (d, *J* = 2.0 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 2.25

(s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8, 139.3, 130.3, 128.6, 126.0, 120.2, 111.4, 56.0, 20.2. HRMS (ESI) calculated for $C_9H_{10}ONS$: 180.0478 $[M+H]^+$, Found: 180.0477.

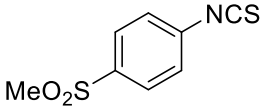


2-Fluoro-4-iodo-1-isothiocyanatobenzene 11 : The title compound was obtained as a slightly yellow solid after 30 minutes in 82% yield (45.9 mg) using 2-fluoro-4-iodoaniline after filtration over celite following the general procedure. M.p. = 43 – 45 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.46 – 7.43 (m, 1H), 6.92 – 6.88 (m, 1H). ^{19}F NMR (564 MHz, $CDCl_3$) δ -117.3 (t, *J* = 8.3 Hz). ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.0 (d, *J* = 258.9 Hz), 142.3, 134.0 (d, *J* = 4.1 Hz), 127.4, 125.7 (d, *J* = 20.9 Hz), 120.6 (d, *J* = 13.4 Hz), 90.7 (d, *J* = 6.9 Hz). HRMS (EI) calculated for C_7H_3NFIS: 278.9010 $[M]^+$, Found: 278.9018.



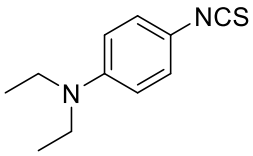
4-Isothiocyanatopyridine 12 : The title compound was obtained as a orange liquid after 30 minutes in 92% yield (24.9 mg) using 4-aminopyridine after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 2.1 Hz, 1H), 8.50 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.52 (ddd, *J* = 8.2, 2.5, 1.5 Hz, 1H), 7.31 (ddd, *J* = 8.2, 4.8, 0.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 147.1, 139.2, 132.3, 129.6, 123.9. HRMS (ESI) calculated for $C_6H_5N_2S$: 137.0168 $[M+H]^+$, Found: 137.0169.

7-Isothiocyanato-1*H*-indole 13 : The title compound was obtained as a colorless liquid after 30 minutes in 93% yield (32.3 mg) using 7-amino-1*H*-indole after column chromatography on silica gel with EtOAc/hexane (10/90, R_f = 0.43) following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (brs, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.26 – 7.21 (m, 1H), 7.13 – 7.01 (m, 2H), 6.62 – 6.57 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6, 131.5, 129.6, 124.9, 120.5, 120.2, 119.1, 115.1, 103.9. HRMS (EI) calculated for $C_9H_6N_2S$: 174.0246 $[M]^+$, Found: 174.0249.

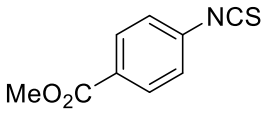


1-Isothiocyanato-4-(methylsulfonyl)benzene 14 : The title compound was obtained as an off-white solid after 30 minutes in 90% yield (38.6 mg) using 4-(methylsulfonyl)aniline after filtration over celite following the general procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.41 – 7.34 (m, 2H), 3.06 (s, 3H). ^{13}C NMR (151 MHz,

$CDCl_3$) δ 139.6, 138.7, 137.0, 129.1, 126.5, 44.5. *m/z* (EI) 213 (M, 88), 198 (40), 150 (47), 134 (100), 90 (24). The analytical data are in agreement with those reported previously in the literature.[8]

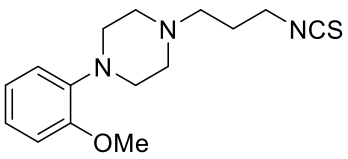


***N,N*-diethyl-4-isothiocyanatoaniline 15 :** The title compound was obtained as a colorless liquid after 10 minutes in 91% yield (37.5 mg) using *N,N*-diethylbenzene-1,4-diamine after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 – 7.05 (m, 2H), 6.57 – 6.52 (m, 2H), 3.34 (q, *J* = 7.1 Hz, 4H), 1.16 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.8, 126.9, 117.5, 115.0, 111.6, 44.5, 12.4. *m/z* (EI) 206 (M, 60), 191 (100), 163 (32), 134 (18). The analytical data are in agreement with those reported previously in the literature.[9]



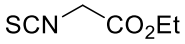
Methyl 4-isothiocyanatobenzoate 16 : The title compound was obtained as a colorless liquid after 30 minutes in 93% yield (36.0 mg) using methyl 4-aminobenzoate after filtration over celite following the general procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 – 7.96 (m, 2H), 7.25 – 7.20 (m, 2H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 137.9, 135.6, 131.0, 128.6, 125.6, 52.3. *m/z* (EI) 193 (M, 66), 162 (100), 134 (42), 90 (15). The analytical data are in agreement with those reported previously in the literature.[10]

1-Isothiocyanatoadamantane 17 : The title compound was obtained as a white solid after 15 minutes in 96% yield (37.2 mg) using 1-adamantanamine after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (s, 3H), 1.97 – 1.94 (m, 6H), 1.68 – 1.58 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 115.0, 58.4, 43.7, 35.5, 29.2. *m/z* (EI) 193 (M, 12), 135 (100), 79 (27). The analytical data are in agreement with those reported previously in the literature.[11]

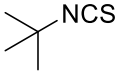


1-(3-Isothiocyanatopropyl)-4-(2-methoxyphenyl)piperazine 18 : The title compound was obtained as a sticky yellow oil after 10 minutes in 93% yield (54.0 mg) using 1-(3-aminopropyl)-4-(2-methoxyphenyl)piperazine after filtration over a pad of silica (2 cm) following a modified general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 – 6.82 (m, 4H), 3.84 (s, 3H), 3.61 (t, *J* = 6.7 Hz, 2H), 3.07

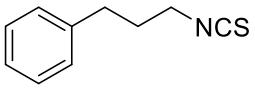
(s, 4H), 2.63 (s, 4H), 2.51 (t, J = 6.7 Hz, 2H), 1.88 (p, J = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 141.2, 130.0, 122.9, 120.9, 118.2, 111.2, 55.3, 54.8, 53.4, 50.6, 43.1, 27.2. HRMS (ESI) calculated for $C_{15}H_{22}ON_3S$: 292.1478 $[M+H]^+$, Found: 292.1477.



Ethyl 2-isothiocyanatoacetate 19 : The commercial starting material was available as a hydrochloride salt, therefore 2.5 equiv. of triethylamine (70 μL, 0.5 mmol, 2.5 equiv.) was used instead of 1.5 equiv. The title compound was obtained as a pale yellow liquid after 10 minutes in 91% yield (26.4 mg) using glycine ethyl ester hydrochloride after filtration over a pad of silica (2 cm) following a modified general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.26 (q, J = 7.1 Hz, 2H), 4.19 (s, 2H), 1.30 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 138.5, 62.6, 46.4, 14.1. *m/z* (EI) 145 (M, 86), 72 (100). The analytical data are in agreement with those reported previously in the literature.[12]

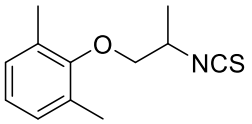


***tert*-Butyl isothiocyanate 20 :** The title compound was obtained as a colorless liquid after 15 minutes in 86% yield (19.8 mg) using *tert*-butylamine after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 115.0, 58.3, 30.7. *m/z* (EI) 115 (M, 100), 100 (30), 57 (75). The analytical data are in agreement with those reported previously in the literature.[13]

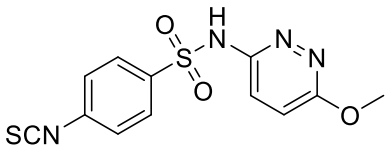


(3-Isothiocyanatopropyl)benzene 21 : The title compound was obtained as a colorless liquid after 10 minutes in 87% yield (30.9 mg) using 3-phenylpropan-1-amine after filtration over celite following the general procedure. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H), 7.25 – 7.21 (m, 1H), 7.21 – 7.18 (m, 2H), 3.50 (t, J = 6.5 Hz, 2H), 2.76 (t, J = 7.4 Hz, 2H), 2.06 – 1.98 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.9, 130.2, 128.6, 128.5, 126.4, 44.1, 32.5, 31.4. *m/z* (EI) 177 (M, 85), 117 (100), 91 (89). The analytical data are in agreement with those reported previously.[10]

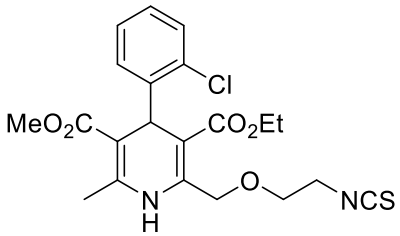
Compounds from Figure 2:



2-(2-Isothiocyanatopropoxy)-1,3-dimethylbenzene 22 : The commercial starting material was available as a hydrochloride salt, therefore 2.5 equiv. of triethylamine (70 μL, 0.5 mmol, 2.5 equiv.) was used instead of 1.5 equiv. The title compound was obtained as a pale yellow liquid after 15 minutes in 96% yield (42.4 mg) using 1-(2,6-dimethylphenoxy)-2-propanamine hydrochloride after filtration over a pad of silica following a modified general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, *J* = 7.2 Hz, 2H), 6.96 – 6.91 (m, 1H), 4.14 (h, *J* = 6.6 Hz, 1H), 3.79 (d, *J* = 5.6 Hz, 2H), 2.29 (s, 6H), 1.49 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 132.8, 130.7, 129.0, 124.3, 74.1, 53.6, 18.4, 16.3. HRMS (EI) calculated for $C_{12}H_{15}ONS$: 221.0869 $[M]^+$, Found: 221.0875.

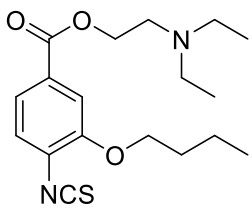


4-Isothiocyanato-*N*-(6-methoxypyridazin-3-yl)benzenesulfonamide 23 : The title compound was obtained as a slightly yellow solid after 30 minutes in 75% yield (48.3 mg) using sulfamethoxypyridazine after column chromatography on silica gel with MeOH/CH_2Cl_2 (2.5/97.5, R_f = 0.26) following a modified general procedure. M.p. = 143 – 145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.79 (brs, 1H), 7.97 – 7.86 (m, 2H), 7.31 – 7.23 (m, 2H), 7.18 (d, *J* = 9.7 Hz, 1H), 7.04 (d, *J* = 9.7 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 151.8, 140.8, 138.4, 135.1, 132.7, 127.9, 127.1, 126.0, 55.0. HRMS (ESI) calculated for $C_{12}H_{10}O_3N_4NaS_2$: 345.0087 $[M+Na]^+$, Found: 345.0082.



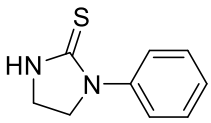
3-Ethyl 5-methyl 4-(2-chlorophenyl)-2-((2-isothiocyanatoethoxy)-methyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate 24 : The title compound was obtained as a white solid after 15 minutes in 94% yield (85.2 mg) using amlopidine after column chromatography on silica gel with MeOH/CH_2Cl_2 (1/99, R_f = 0.22) following a modified general procedure. M.p. = 167 – 169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.22 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.16 – 7.10 (m, 1H), 7.06 – 7.00 (m, 1H), 6.98 (s, 1H), 5.40 (s, 1H), 4.82 (d, *J* = 15.7 Hz, 1H), 4.75 (d, *J* = 15.7 Hz, 1H), 4.12 – 3.95 (m, 2H), 3.82 – 3.75 (m, 2H), 3.75 – 3.69 (m, 2H), 3.60 (s, 3H), 2.37 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 167.1, 145.6, 144.3,

143.9, 133.9, 132.3, 131.4, 129.2, 127.4, 126.9, 104.0, 101.8, 69.1, 67.9, 59.9, 50.8, 45.2, 37.1, 19.6, 14.2. HRMS (ESI) calculated for $C_{21}H_{23}O_5N_2ClNaS$: 473.0908 $[M+Na]^+$, Found: 473.0908.

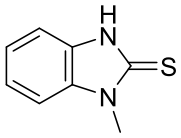


2-(Diethylamino)ethyl 3-butoxy-4-isothiocyanatobenzoate 25 : The commercial starting material was available as a hydrochloride salt, therefore 2.5 equiv. of triethylamine (70 μL, 0.5 mmol, 2.5 equiv.) was used instead of 1.5 equiv. The title compound was obtained as a yellow oil after 30 minutes in 90% yield (62.8 mg) using oxybuprocaine hydrochloride after column chromatography on silica gel with MeOH/CH_2Cl_2 (5/95, R_f = 0.32) following a modified general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.51 (m, 2H), 7.07 – 7.03 (m, 1H), 4.36 (t, *J* = 6.3 Hz, 2H), 4.07 (t, *J* = 6.3 Hz, 2H), 2.82 (t, *J* = 6.2 Hz, 2H), 2.61 (q, *J* = 7.1 Hz, 4H), 1.88 – 1.76 (m, 2H), 1.54 (sex, *J* = 7.4 Hz, 2H), 1.05 (t, *J* = 7.1 Hz, 6H), 0.97 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 155.6, 143.5, 129.5, 125.5, 124.2, 121.9, 112.6, 68.9, 63.7, 50.9, 47.9, 31.0, 19.1, 13.7, 12.0. HRMS (ESI) calculated for $C_{18}H_{27}O_3N_2S$: 351.1737 $[M+H]^+$, Found: 351.1737.

Compounds from Scheme 2:

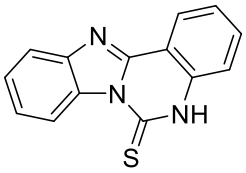


1-Phenylimidazolidine-2-thione 26: The title compound was obtained as a white solid after 15 minutes in 88% yield (31.4 mg) using *N*-phenylethane-1,2-diamine after column chromatography on silica gel with EtOAc/hexane (70/30, R_f = 0.37) following a modified general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.53 (m, 2H), 7.42 – 7.35 (m, 2H), 7.26 – 7.21 (m, 1H), 6.33 (brs, 1H), 4.21 – 4.11 (m, 2H), 3.75 – 3.68 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.9, 139.9, 128.8, 126.4, 124.4, 52.1, 41.6. *m/z* (EI) 178 (M, 96), 106 (100), 77 (38), 51 (13). The analytical data are in agreement with those reported previously in the literature.[14]

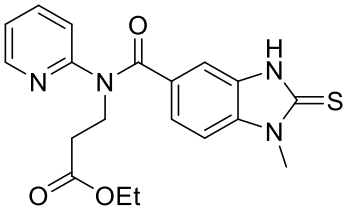


1-Methyl-1,3-dihydro-(2*H*)-benzo[*d*]imidazole-2-thione 27: The title compound was obtained as a pale yellow solid after 30 minutes in 85% yield (27.9 mg) using *N*-methylbenzene-1,2-diamine after column chromatography on silica gel with EtOAc/hexane (20/80, R_f = 0.24) following a modified general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.21 (brs, 1H), 7.30 – 7.10 (m, 4H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 133.3, 130.4,

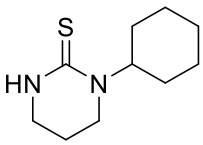
123.4, 122.9, 110.0, 109.1, 30.5. HRMS (ESI) calculated for $C_8H_9N_2S$: 165.0481 $[M+H]^+$, Found: 165.0481. The analytical data are in agreement with those reported previously in the literature.[15]



Benzo[4,5]imidazo[1,2-c]quinazoline-6(5*H*)-thione 28: The title compound was obtained as a pale yellow solid after 30 minutes in 93% yield (46.6 mg) using 2-(1*H*-benzo[*d*]imidazol-2-yl)aniline after filtration over celite following the general procedure. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.47 (brs, 1H), 9.37 (d, *J* = 8.2 Hz, 1H), 8.37 (d, *J* = 7.0 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.73 – 7.67 (m, 1H), 7.61 – 7.52 (m, 2H), 7.49 – 7.43 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.7, 145.6, 144.6, 136.2, 133.0, 132.6, 126.4, 125.6, 124.8, 123.7, 119.7, 117.4, 116.4, 113.7. HRMS (ESI) calculated for $C_{14}H_{10}N_3S$: 252.0590 $[M+H]^+$, Found: 252.0590. The analytical data are in agreement with those reported previously in the literature.[16]

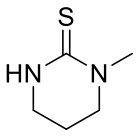


Ethyl 3-(1-methyl-N-(pyridin-2-yl)-2-thioxo-2,3-dihydro-1*H*-benzo[d]imidazole-5-carboxamido)propanoate 29: The title compound was obtained as a pale yellow solid after 30 minutes in 90% yield (69.3 mg) using ethyl 3-(3-amino-4-(methylamino)-*N*-(pyridin-2-yl)benzamido)propanoate after column chromatography on silica gel with EtOAc/hexane (70/30, R_f = 0.37) following a modified general procedure. M.p. = 145 – 147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.20 (brs, 1H), 8.44 – 8.35 (m, 1H), 7.43 – 7.36 (m, 1H), 7.29 – 7.26 (m, 1H), 7.11 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.02 (dd, *J* = 7.4, 4.9 Hz, 1H), 6.87 (d, *J* = 8.3 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 4.39 (t, *J* = 7.1 Hz, 2H), 4.04 (q, *J* = 7.1 Hz, 2H), 3.65 (s, 3H), 2.77 (t, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 170.2, 170.0, 155.9, 149.0, 137.6, 134.6, 131.0, 130.0, 124.0, 122.4, 121.4, 110.7, 108.1, 60.6, 44.9, 33.2, 30.5, 14.1. HRMS (ESI) calculated for $C_{19}H_{20}O_3N_4NaS$: 407.1148 $[M+Na]^+$, Found: 407.1146.



1-Cyclohexyltetrahydropyrimidine-2(1*H*)-thione 30: The title compound was obtained as a white solid after 10 minutes in 89% yield (35.3 mg) using *N*-cyclohexylpropane-1,3-diamine after column chromatography on silica gel with EtOAc/hexane (70/30, R_f = 0.26) following a modified general procedure. M.p. = 166 – 168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (brs, 1H), 5.16 (tt, *J* = 11.7, 3.6 Hz, 1H), 3.25 – 3.19 (m, 4H), 1.92 (quint, *J* = 6.0 Hz, 2H), 1.84 – 1.73 (m, 4H), 1.68 – 1.60 (m, 1H), 1.49 – 1.25 (m, 4H), 1.04 (qt, *J* = 12.9, 3.6 Hz, 1H). ^{13}C

NMR (101 MHz, $CDCl_3$) δ 177.0, 60.0, 40.7, 40.4, 29.4, 25.5, 25.5, 21.2. HRMS (ESI) calculated for $C_{10}H_{19}N_2S$: 199.1264 $[M+H]^+$, Found: 199.1263.



1-Methyltetrahydropyrimidine-2(1*H*)-thione 31: The title compound was obtained as a white solid after 15 minutes in 83% yield (21.5 mg) using *N*-methylpropane-1,3-diamine after filtration over celite following the general procedure. M.p. = 123 – 125 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58 (brs, 1H), 3.40 (s, 3H), 3.36 (t, *J* = 6.0 Hz, 2H), 3.31 – 3.27 (m, 2H), 2.03 (quint, *J* = 6.0 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 177.8, 48.4, 42.1, 40.7, 21.1. HRMS (ESI) calculated for $C_5H_{11}N_2S$: 131.0638 $[M+H]^+$, Found: 131.0638.

3. References

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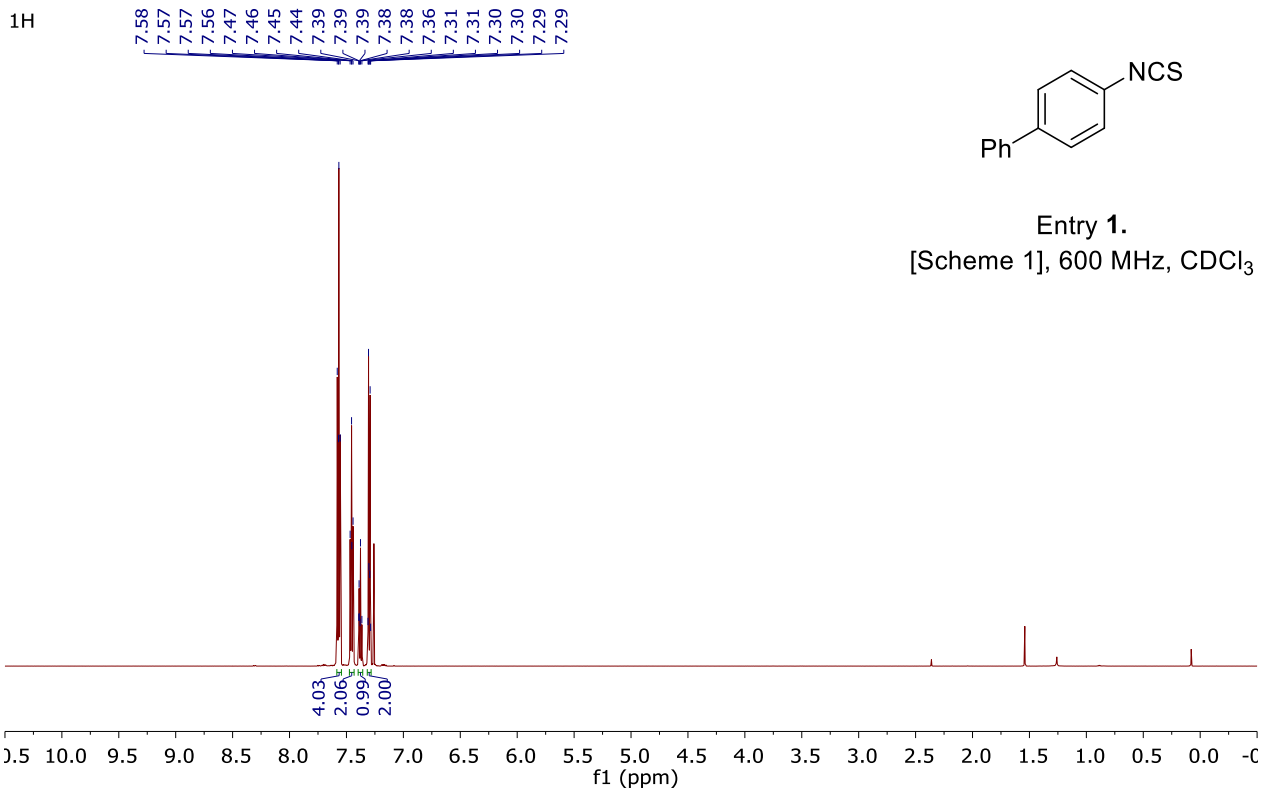
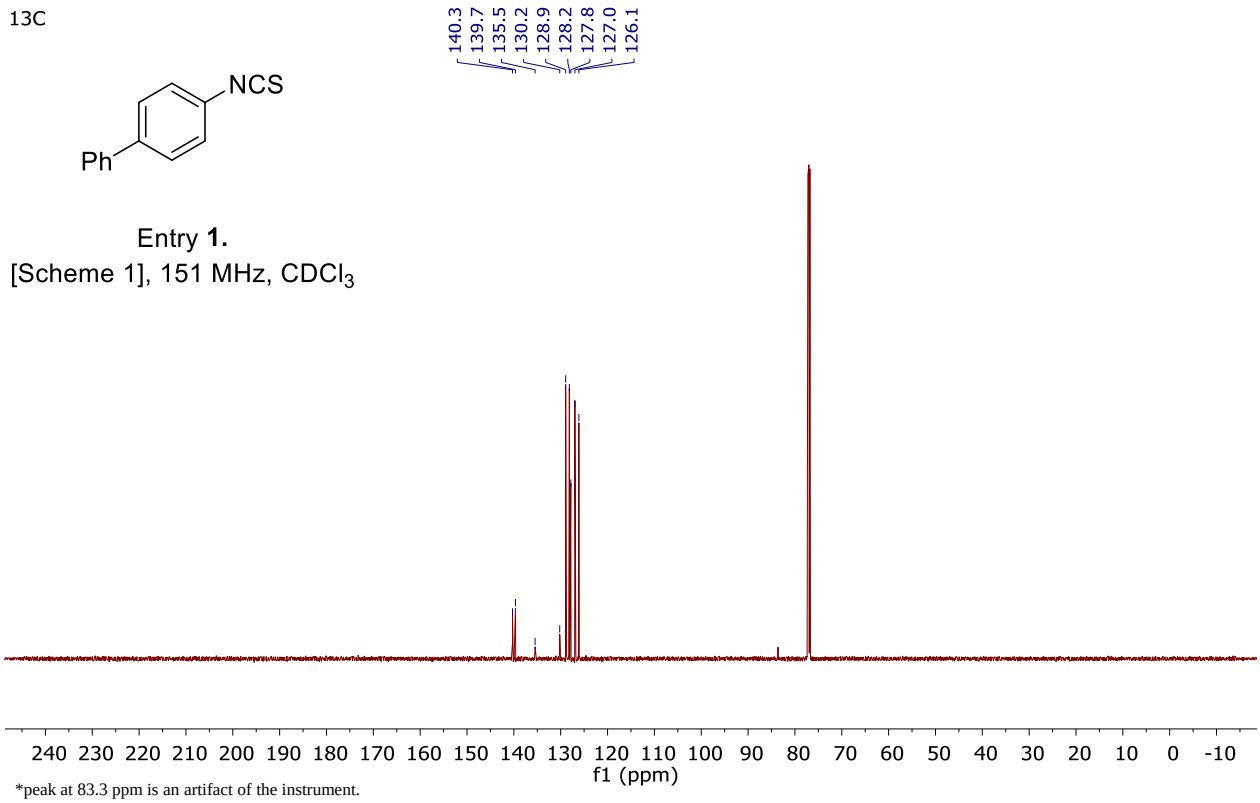
4. NMR spectra

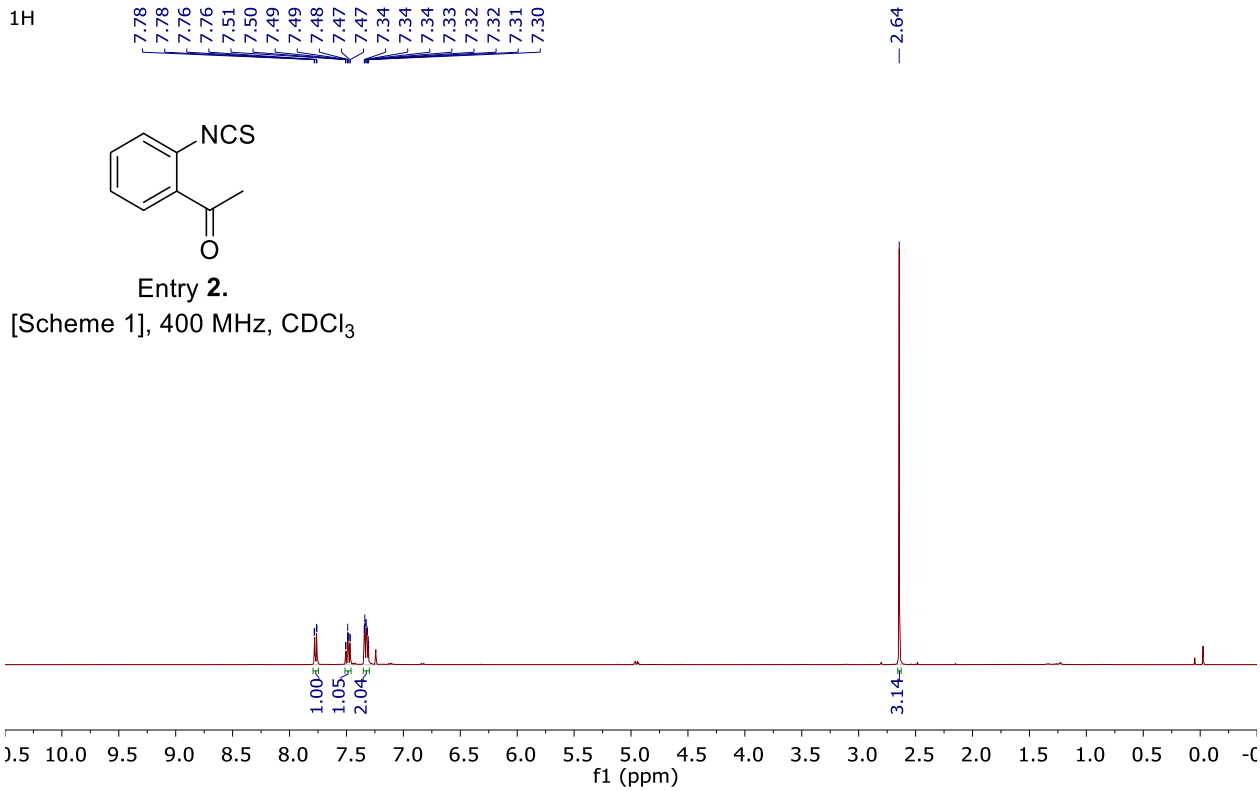


Entry **1.**
[Scheme 1], 600 MHz, $CDCl_3$

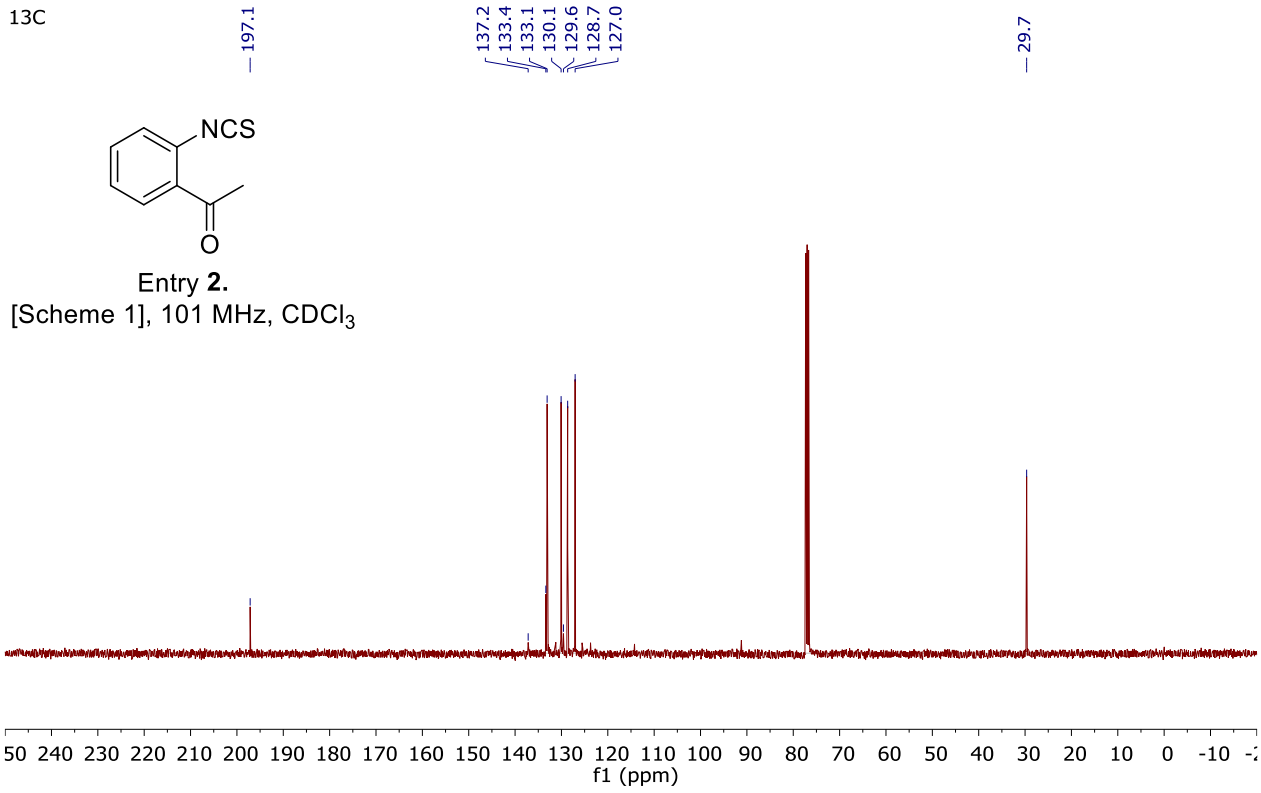


Entry **1.**
[Scheme 1], 151 MHz, $CDCl_3$

*peak at 83.3 ppm is an artifact of the instrument.

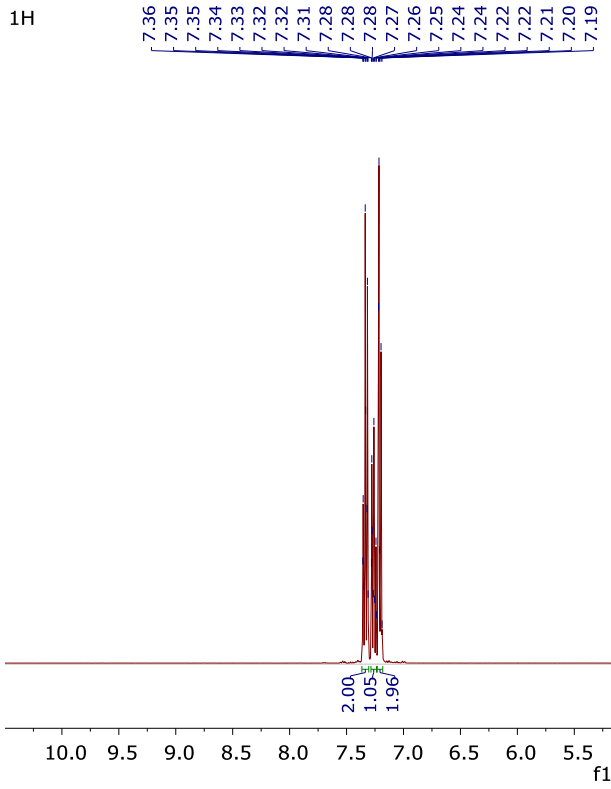


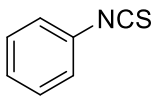
Entry **2.**
[Scheme 1], 400 MHz, $CDCl_3$



Entry **2.**
[Scheme 1], 101 MHz, $CDCl_3$

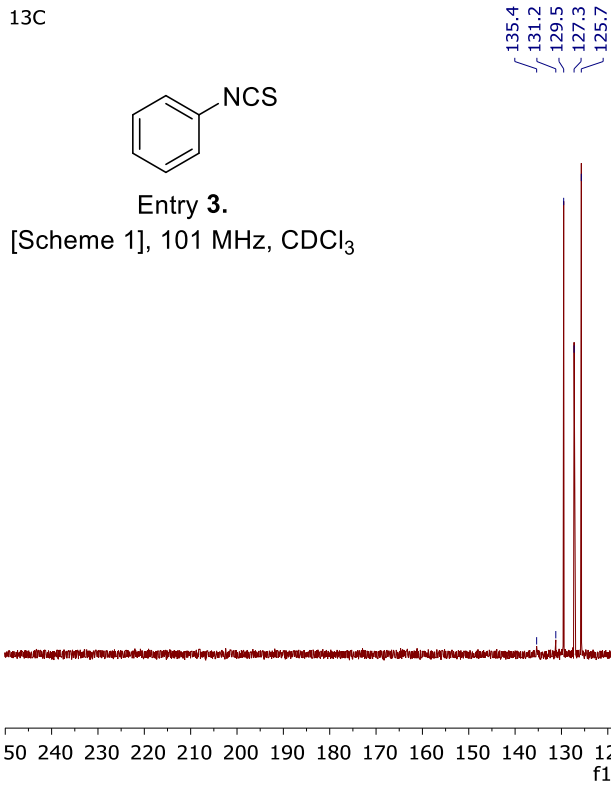
1H





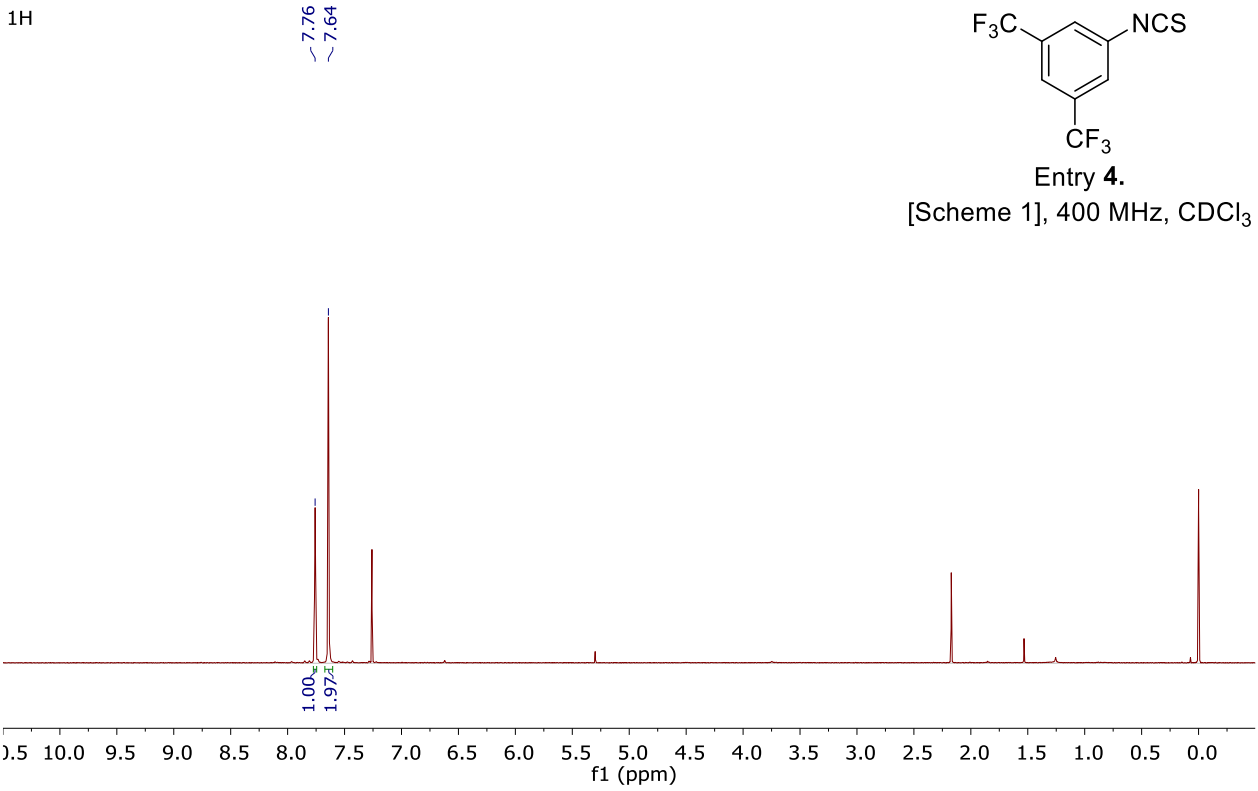
Entry **3.**
[Scheme 1], 400 MHz, $CDCl_3$

13C



Entry **3.**
[Scheme 1], 101 MHz, $CDCl_3$

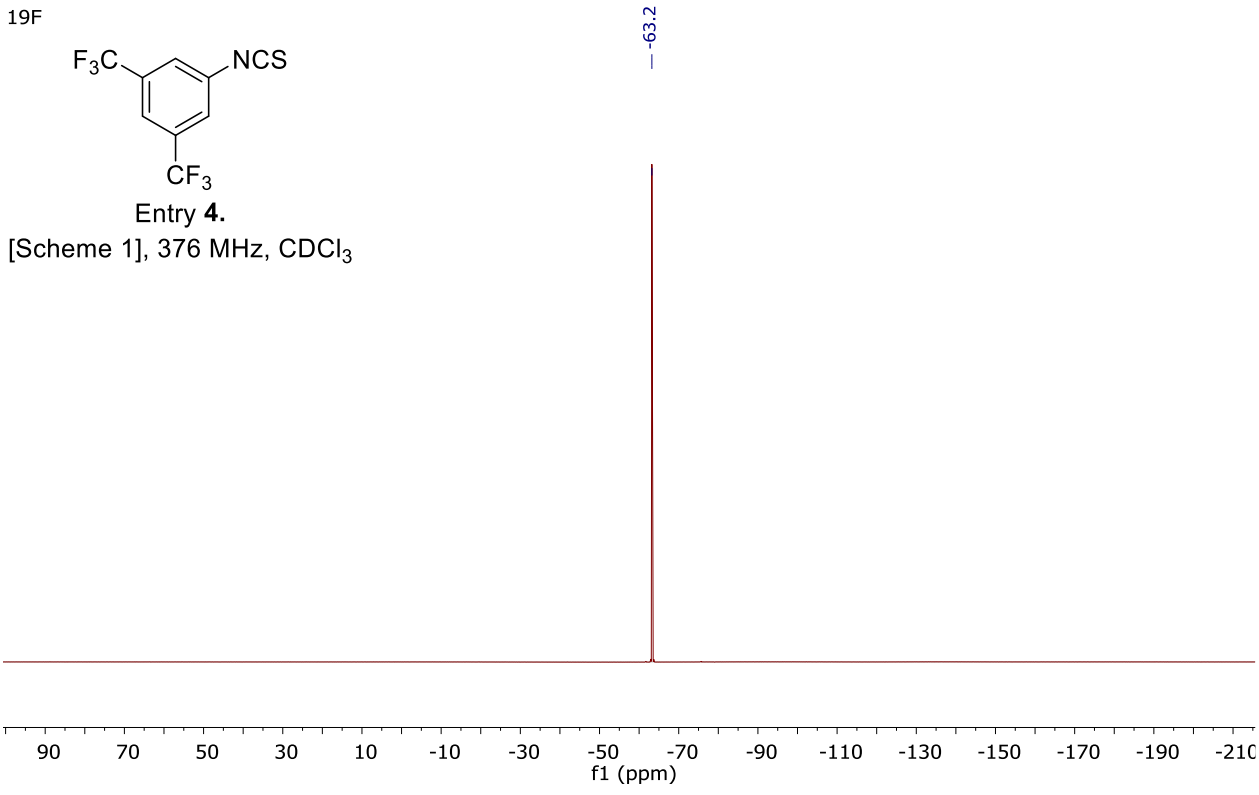
1H



Entry **4.**

[Scheme 1], 400 MHz, $CDCl_3$

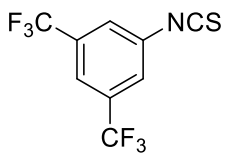
19F



Entry **4.**

[Scheme 1], 376 MHz, $CDCl_3$

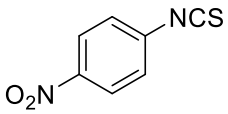
13C



Entry **4.**

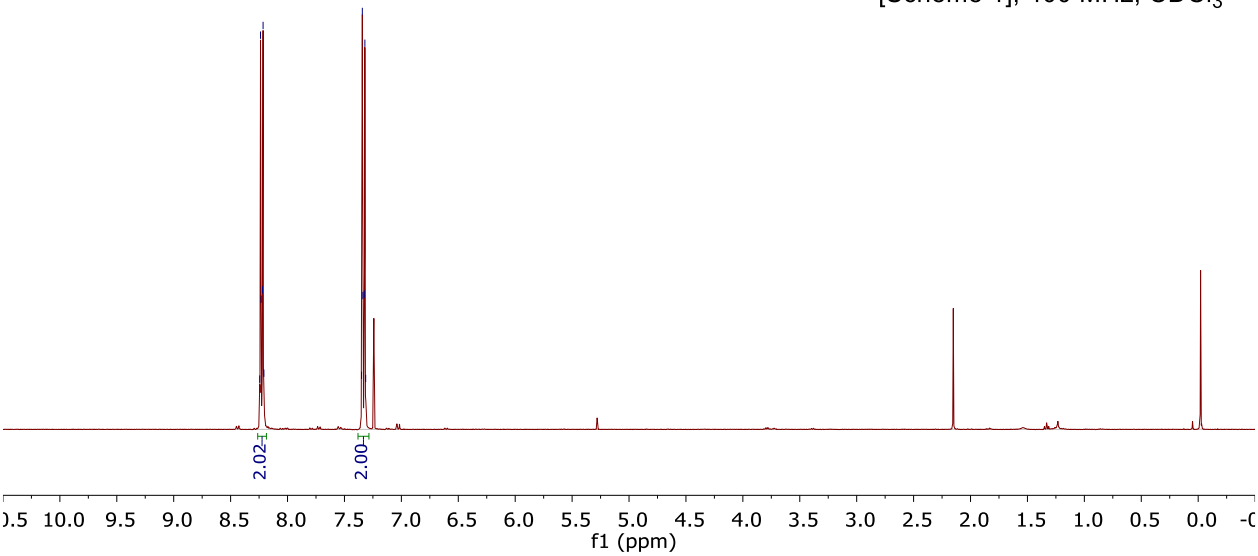
[Scheme 1], 151 MHz, $CDCl_3$

1H

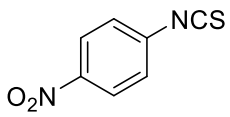


Entry **5.**

[Scheme 1], 400 MHz, $CDCl_3$

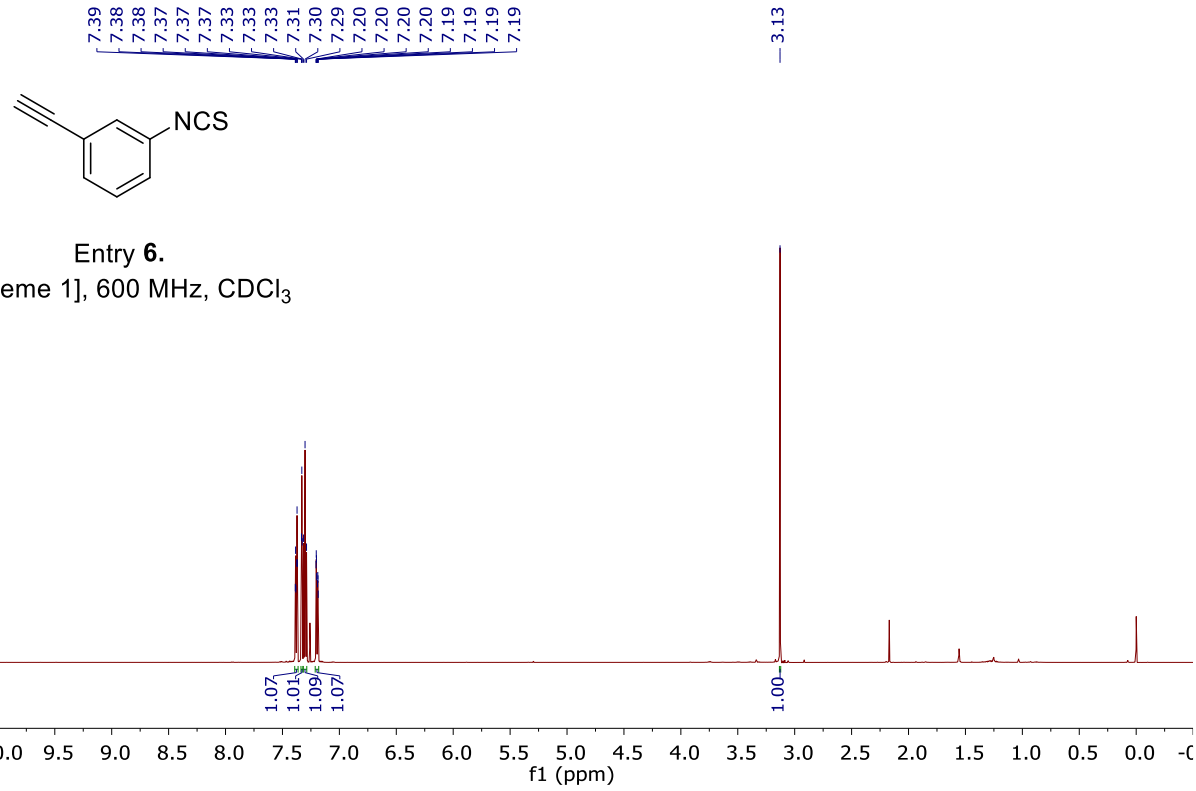


13C



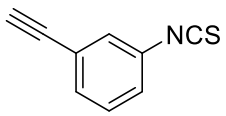
Entry **5.**
[Scheme 1], 101 MHz, $CDCl_3$

1H



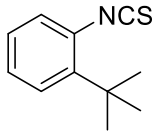
Entry **6.**
[Scheme 1], 600 MHz, $CDCl_3$

13C



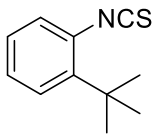
Entry **6.**
[Scheme 1], 151 MHz, $CDCl_3$

1H



Entry **7.**
[Scheme 1], 600 MHz, $CDCl_3$

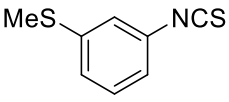
13C



Entry **7.**
[Scheme 1], 151 MHz, $CDCl_3$

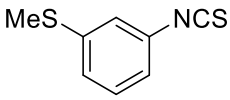
*peak at 83.3 ppm is an artifact of the instrument.

1H



Entry **8.**
[Scheme 1], 600 MHz, $CDCl_3$

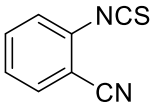
13C



Entry **8.**

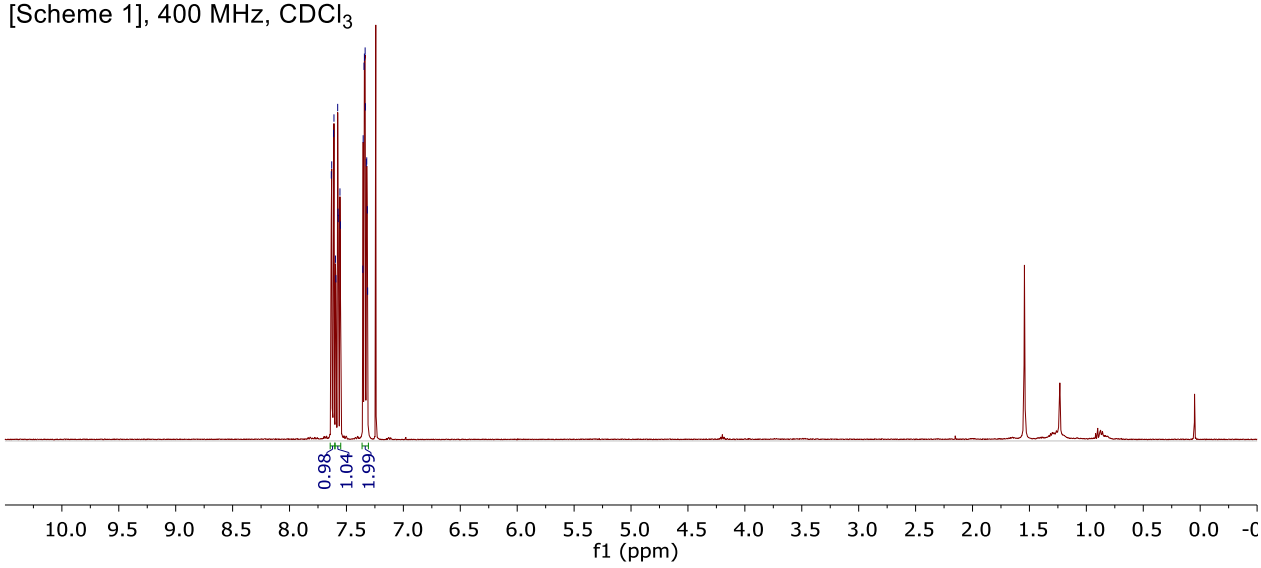
[Scheme 1], 151 MHz, $CDCl_3$

1H

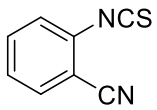


Entry **9.**

[Scheme 1], 400 MHz, $CDCl_3$



13C



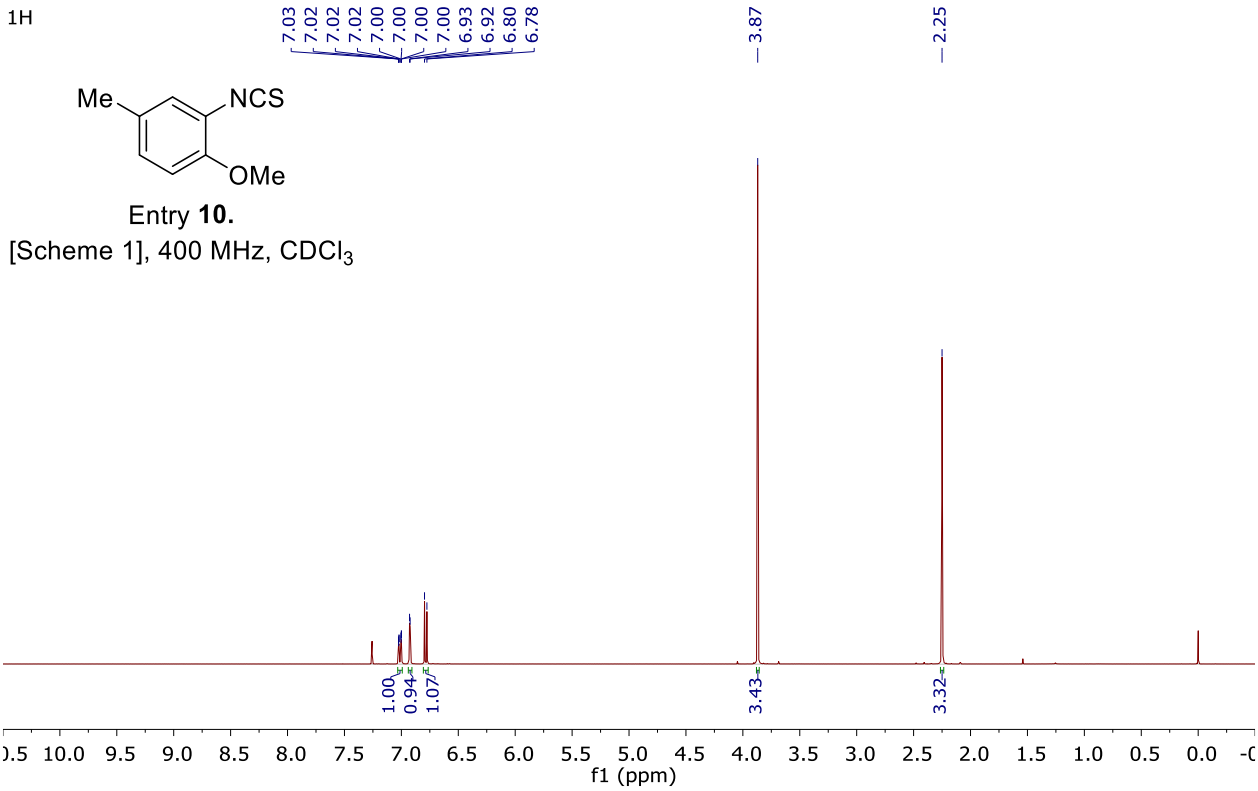
Entry **9.**

[Scheme 1], 101 MHz, $CDCl_3$

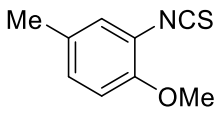
1H

Entry **10.**

[Scheme 1], 400 MHz, $CDCl_3$



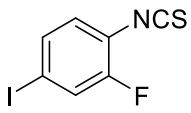
13C



Entry **10.**

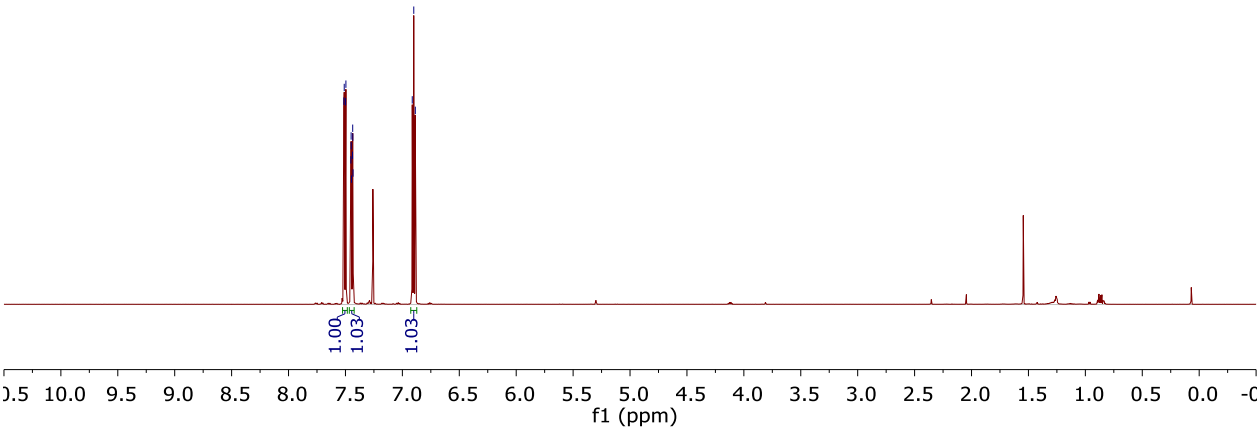
[Scheme 1], 101 MHz, $CDCl_3$

1H

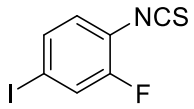


Entry **11.**

[Scheme 1], 600 MHz, $CDCl_3$

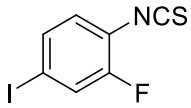


19F



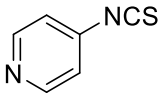
Entry **11.**
[Scheme 1], 564 MHz, $CDCl_3$

13C

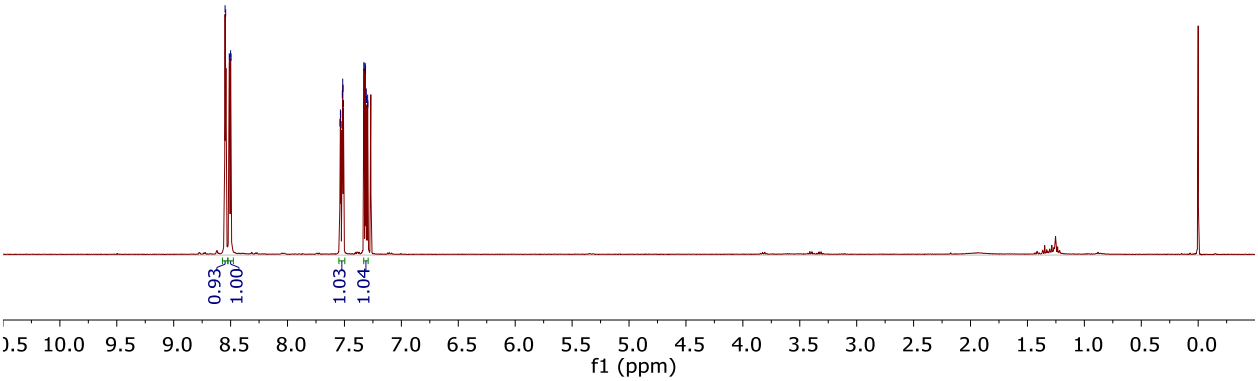


Entry **11.**
[Scheme 1], 151 MHz, $CDCl_3$

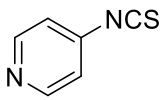
1H



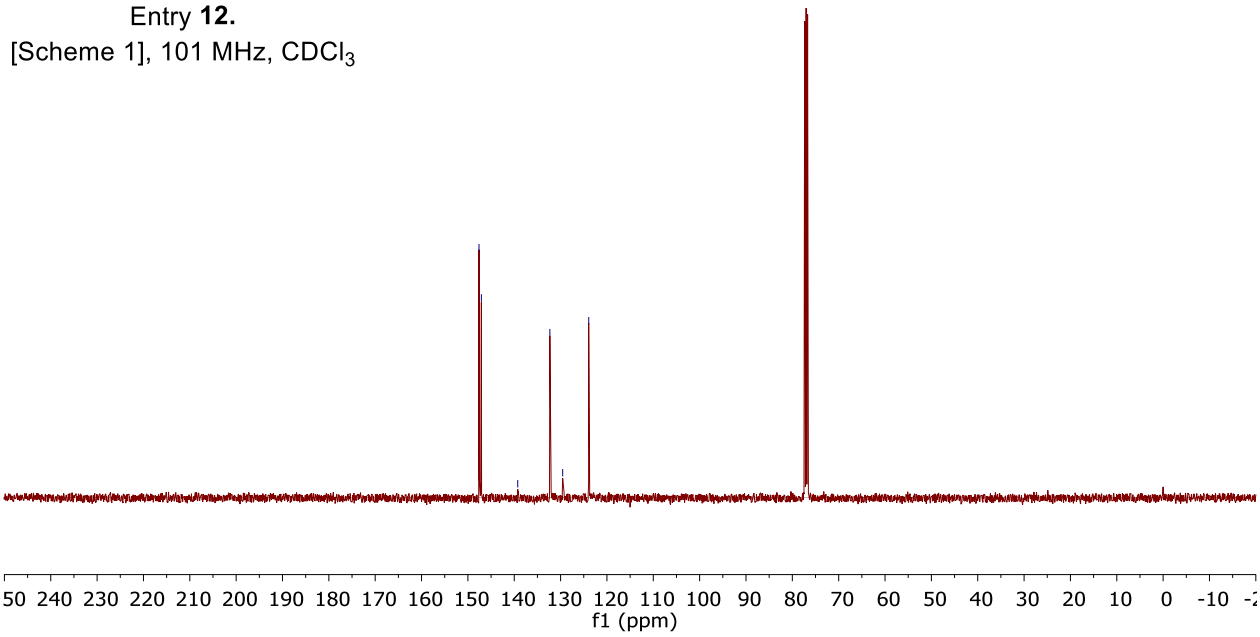
Entry **12.**
[Scheme 1], 400 MHz, $CDCl_3$



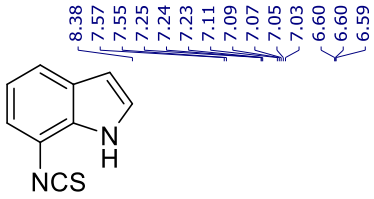
13C



Entry **12.**
[Scheme 1], 101 MHz, $CDCl_3$

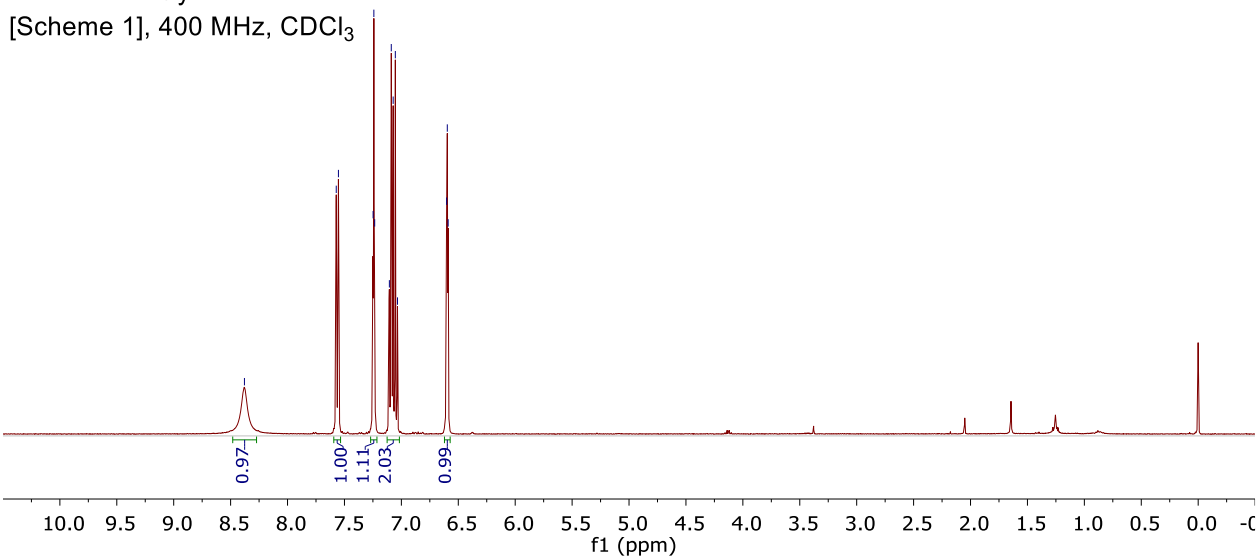


1H

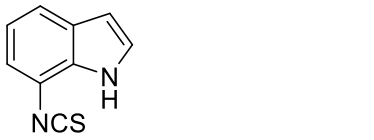


Entry **13.**

[Scheme 1], 400 MHz, $CDCl_3$

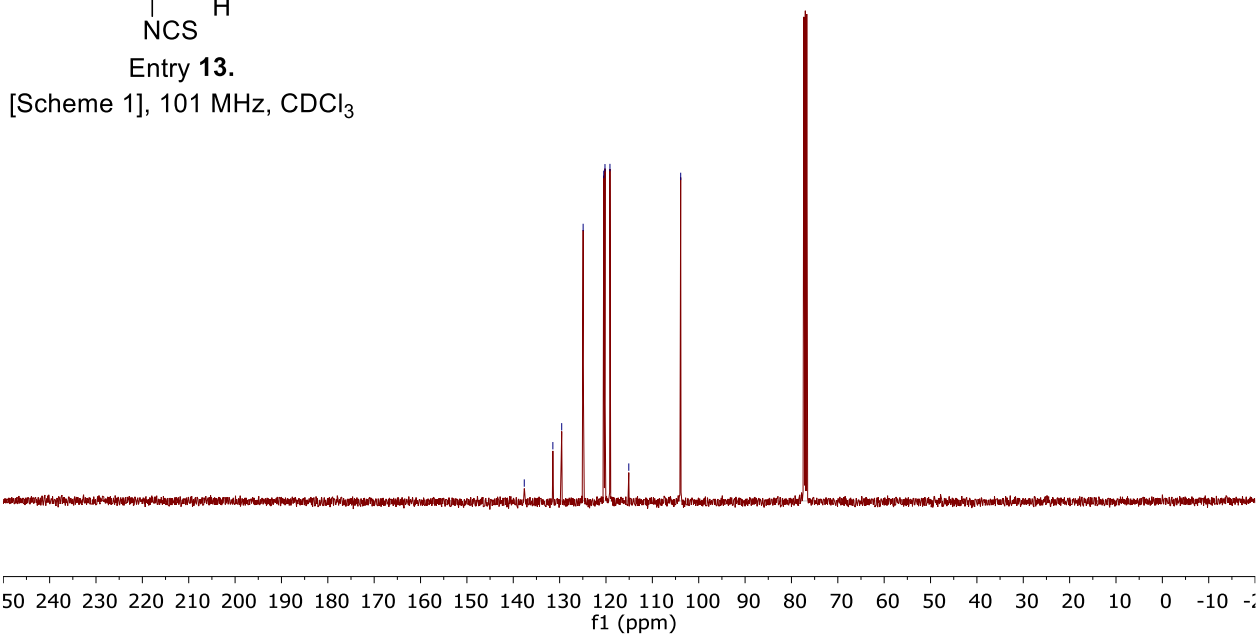


13C

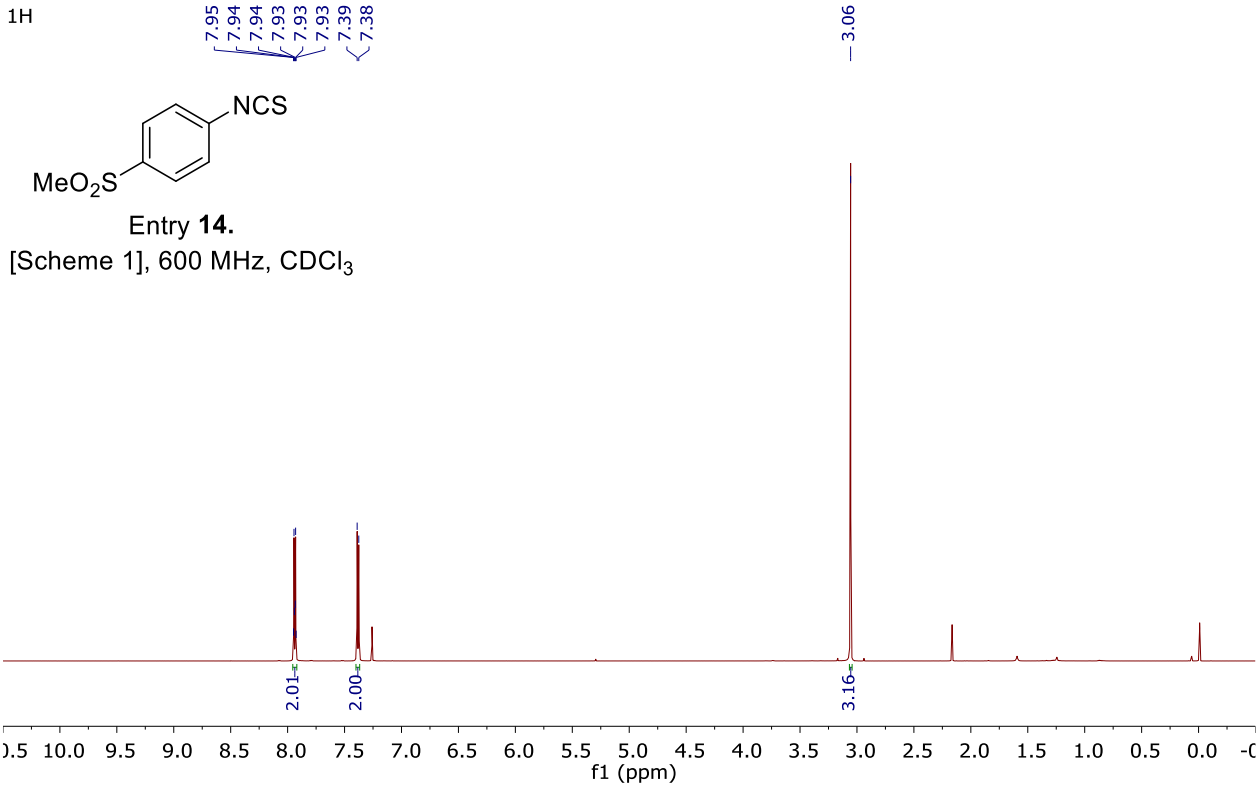


Entry **13.**

[Scheme 1], 101 MHz, $CDCl_3$

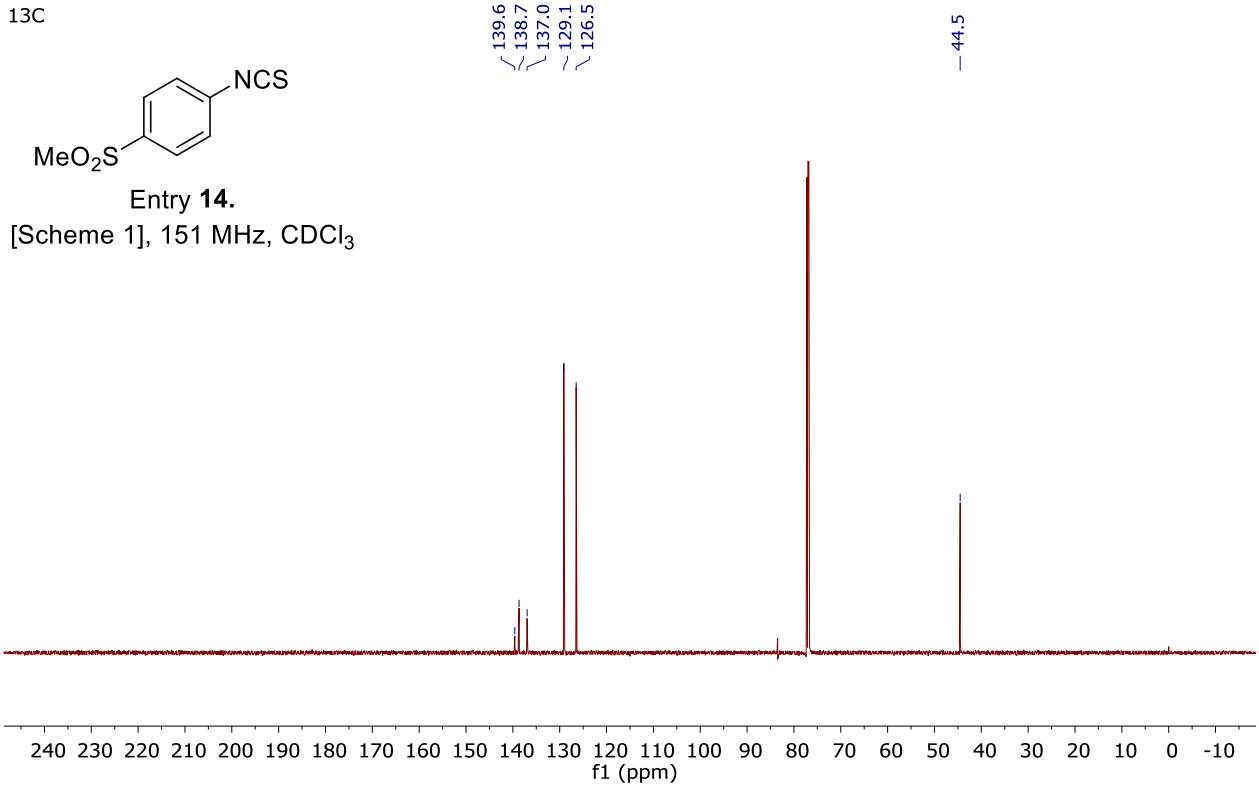


1H



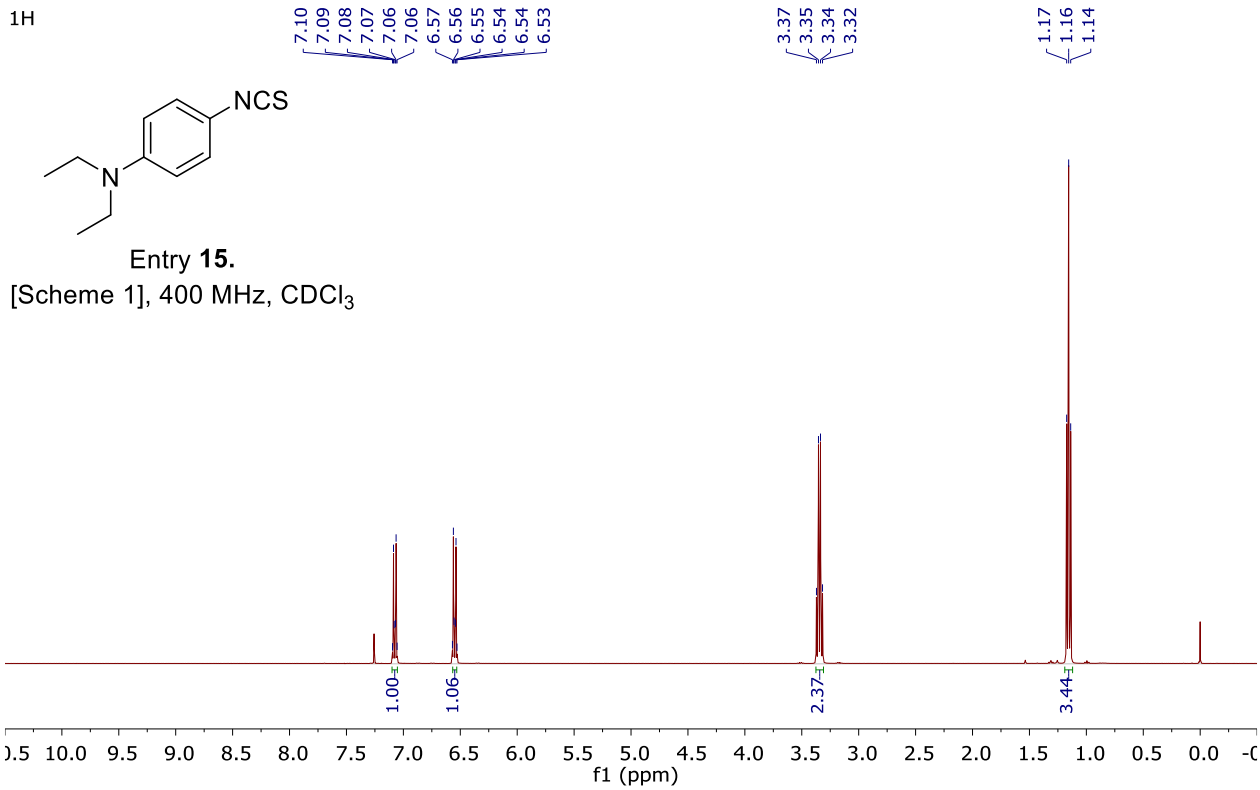
Entry **14.**
[Scheme 1], 600 MHz, $CDCl_3$

13C

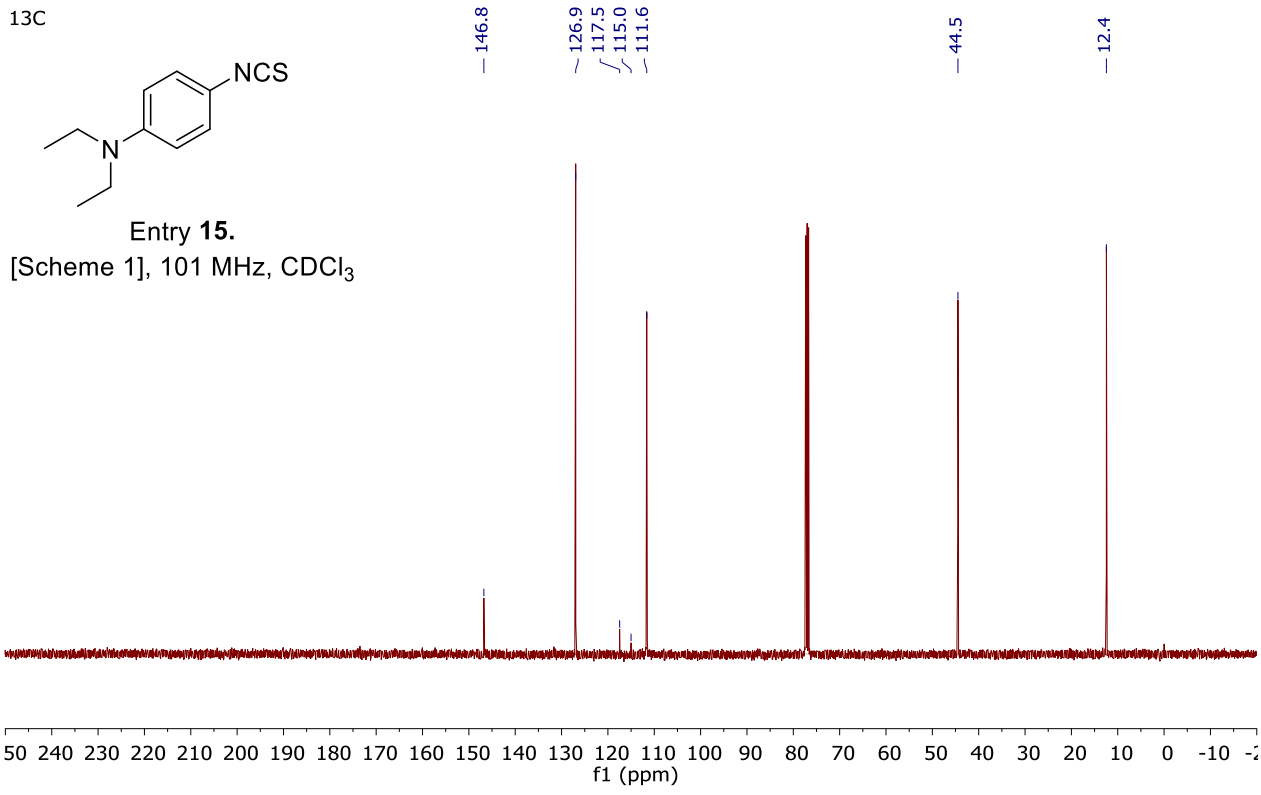


Entry **14.**
[Scheme 1], 151 MHz, $CDCl_3$

*peak at 83.3 ppm is an artifact of the instrument.

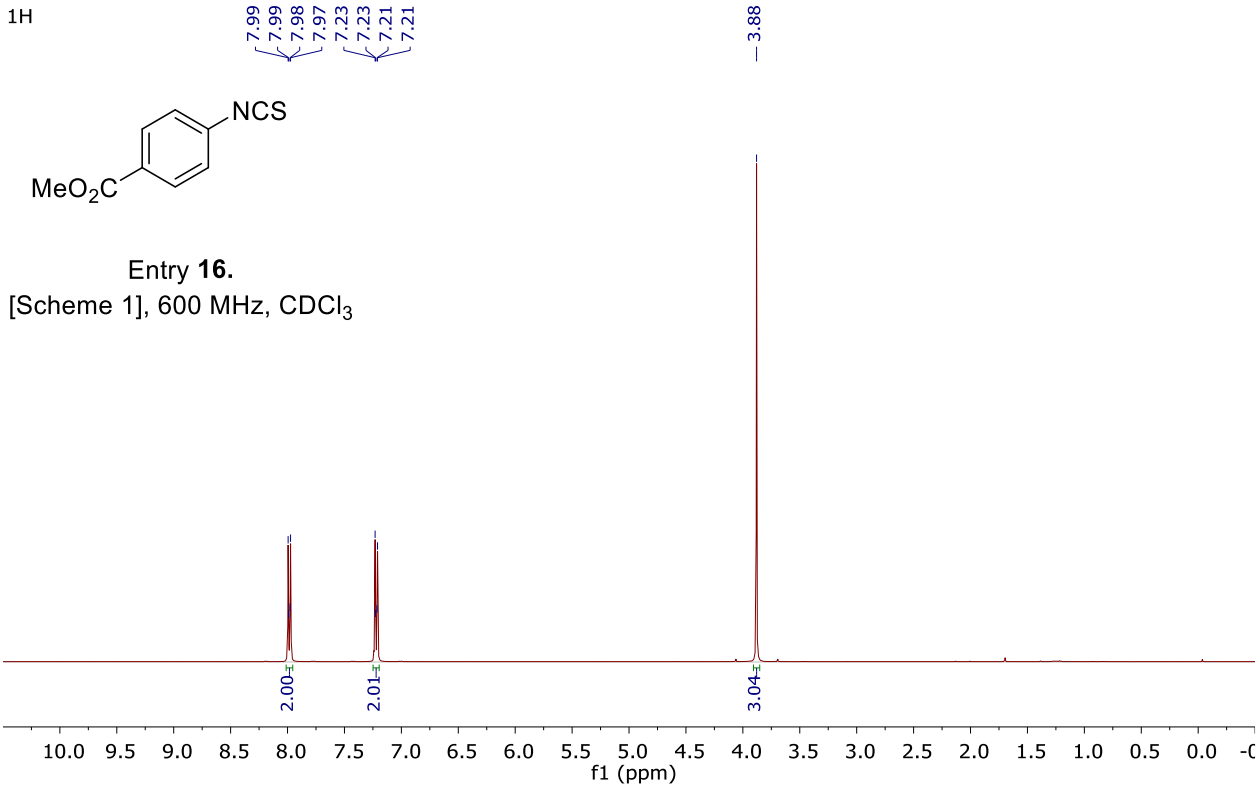


Entry **15.**
[Scheme 1], 400 MHz, $CDCl_3$



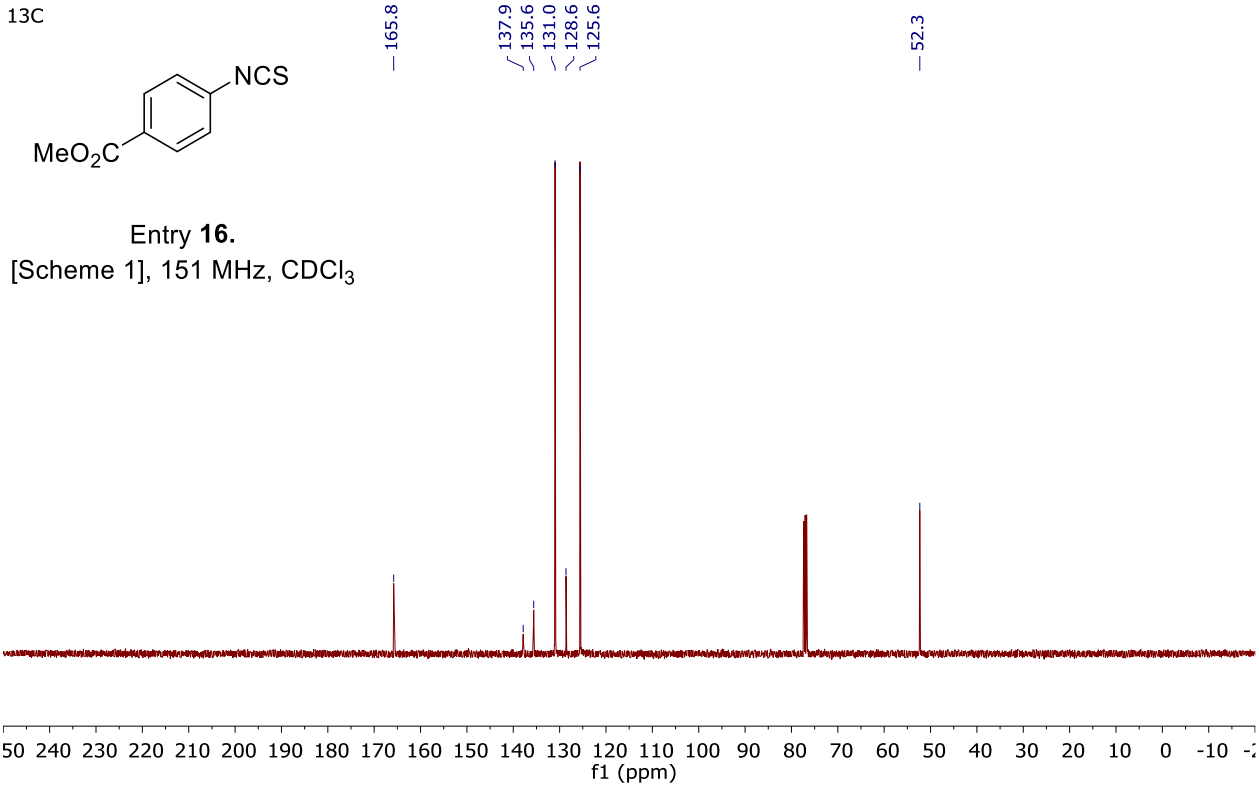
Entry **15.**
[Scheme 1], 101 MHz, $CDCl_3$

1H



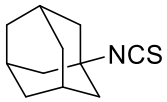
Entry **16.**
[Scheme 1], 600 MHz, $CDCl_3$

13C



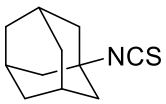
Entry **16.**
[Scheme 1], 151 MHz, $CDCl_3$

1H



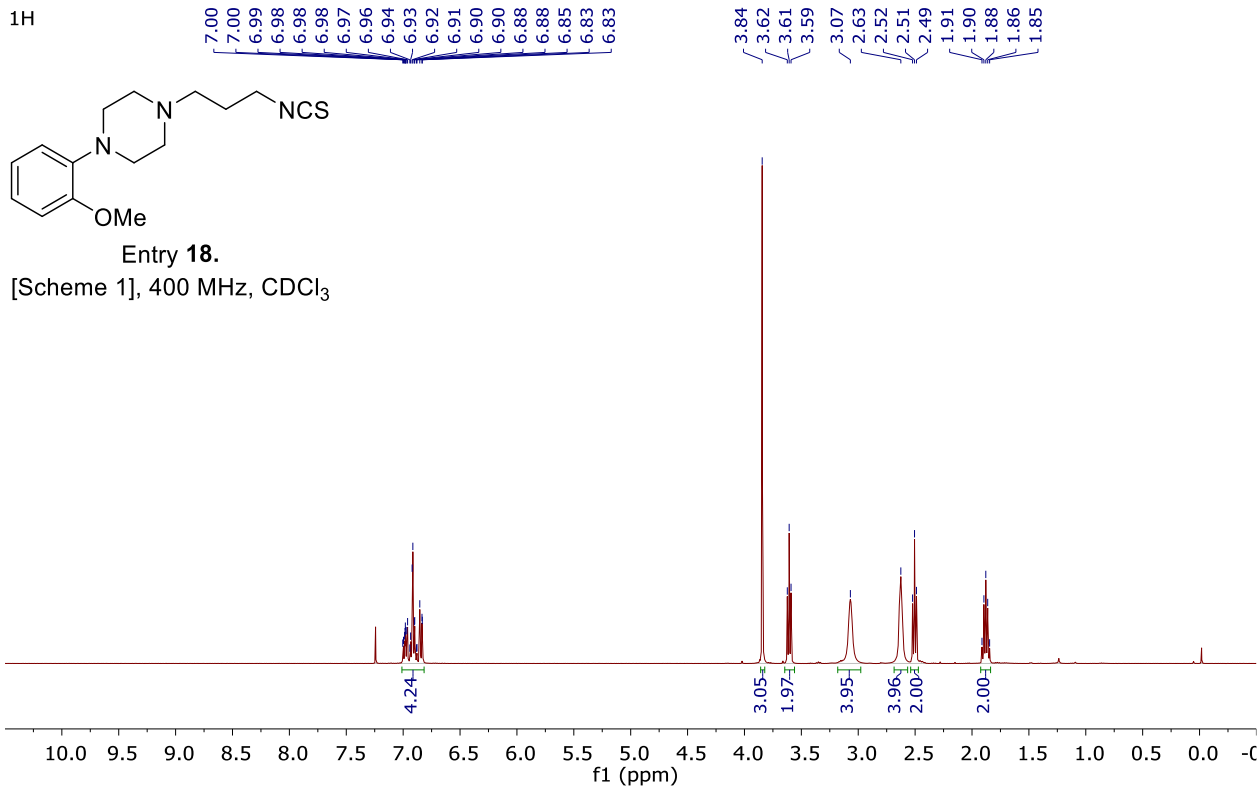
Entry **17.**
[Scheme 1], 400 MHz, $CDCl_3$

13C



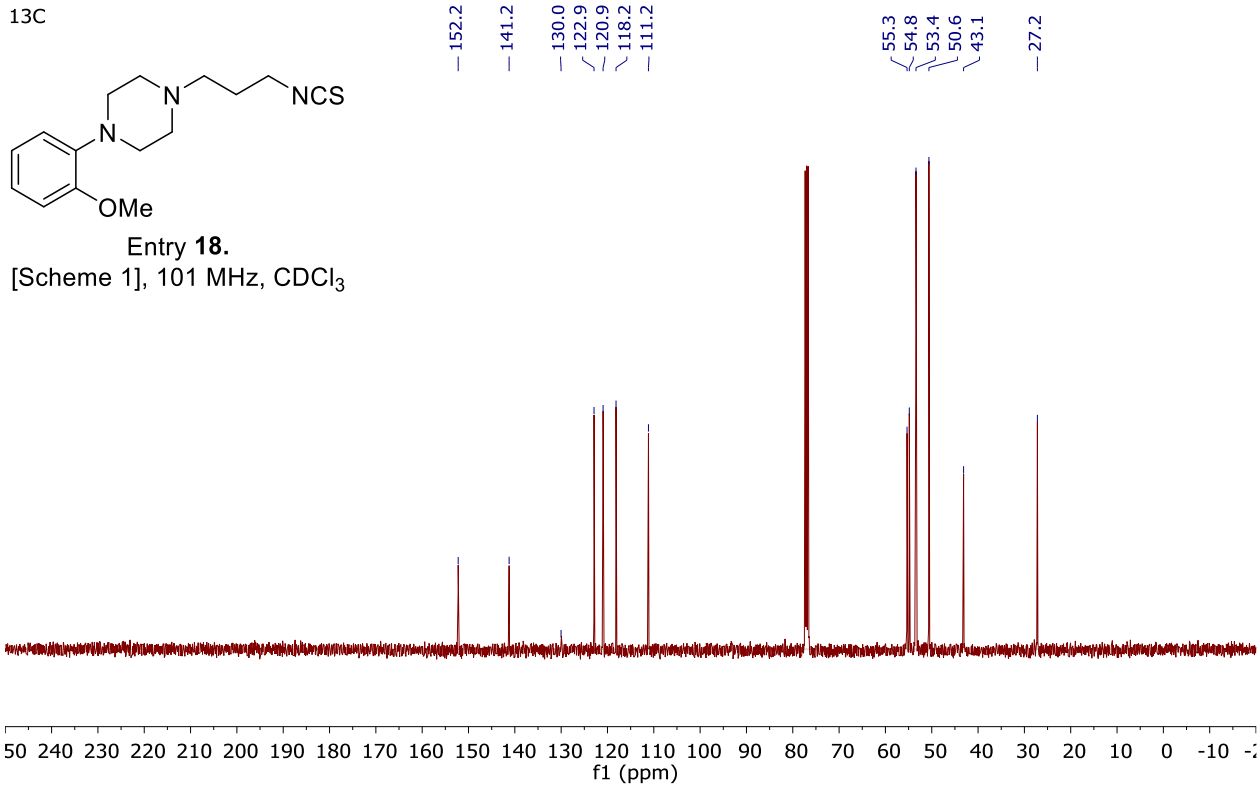
Entry **17.**
[Scheme 1], 101 MHz, $CDCl_3$

1H



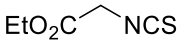
Entry **18.**
[Scheme 1], 400 MHz, $CDCl_3$

13C



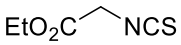
Entry **18.**
[Scheme 1], 101 MHz, $CDCl_3$

1H



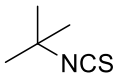
Entry **19.**
[Scheme 1], 400 MHz, $CDCl_3$

13C



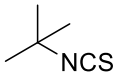
Entry **19.**
[Scheme 1], 101 MHz, $CDCl_3$

1H



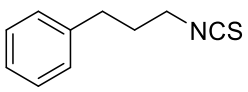
Entry **20.**
[Scheme 1], 400 MHz, $CDCl_3$

13C



Entry **20.**
[Scheme 1], 101 MHz, $CDCl_3$

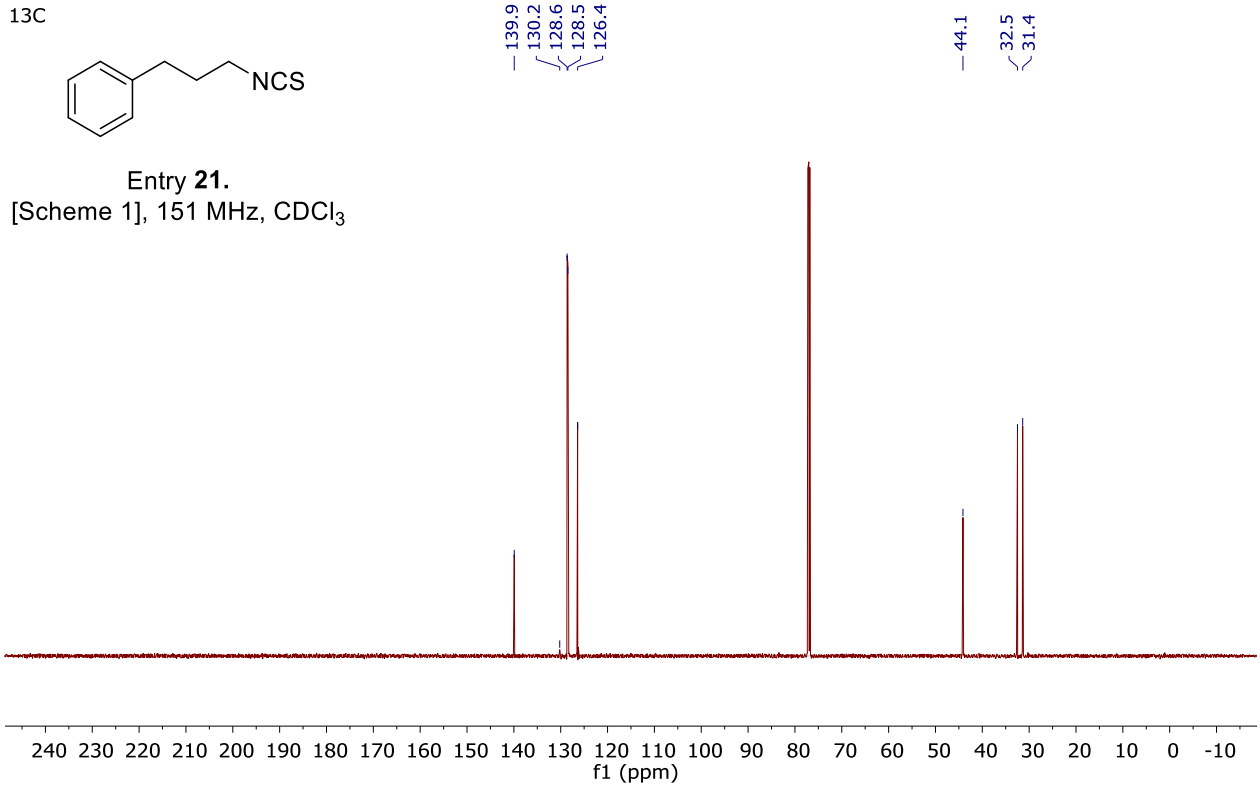
1H



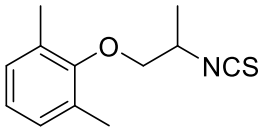
Entry **21.**
[Scheme 1], 600 MHz, $CDCl_3$

13C

Entry **21.**
[Scheme 1], 151 MHz, $CDCl_3$

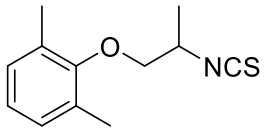


1H

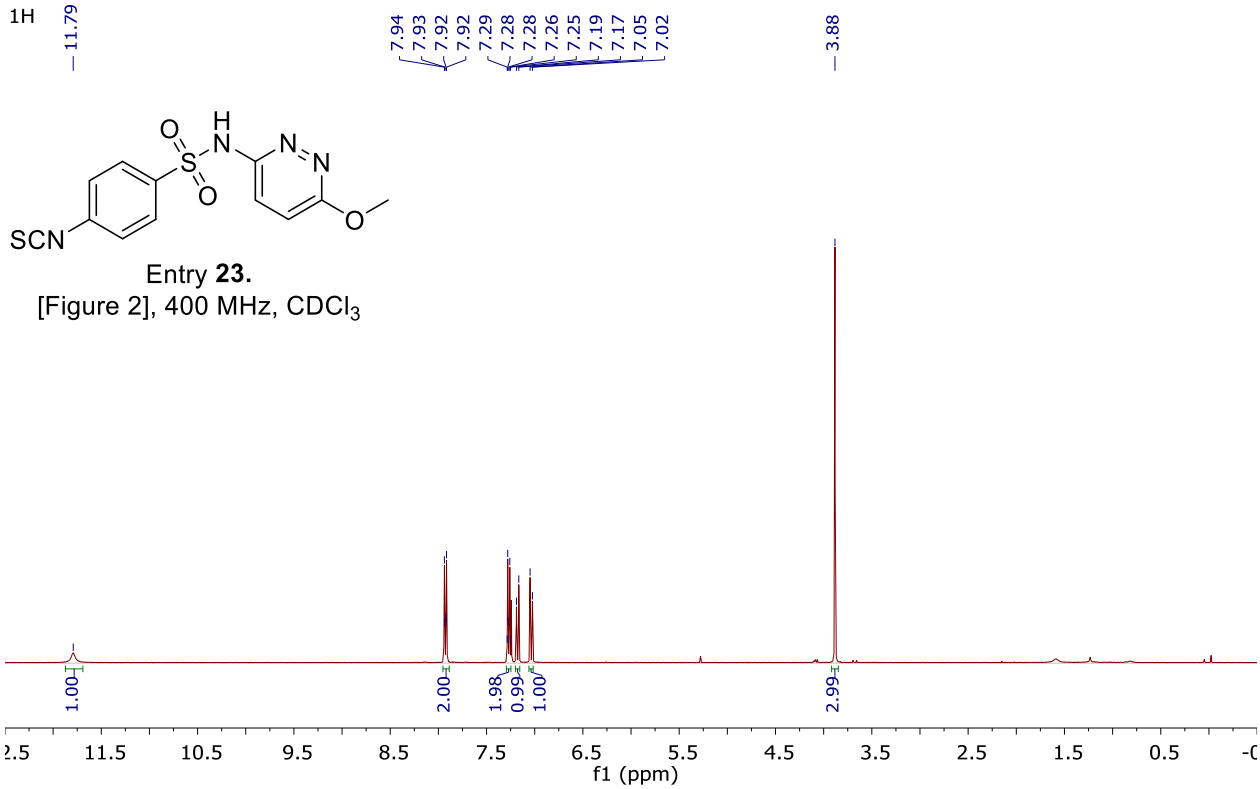


Entry **22.**
[Figure 2], 400 MHz, $CDCl_3$

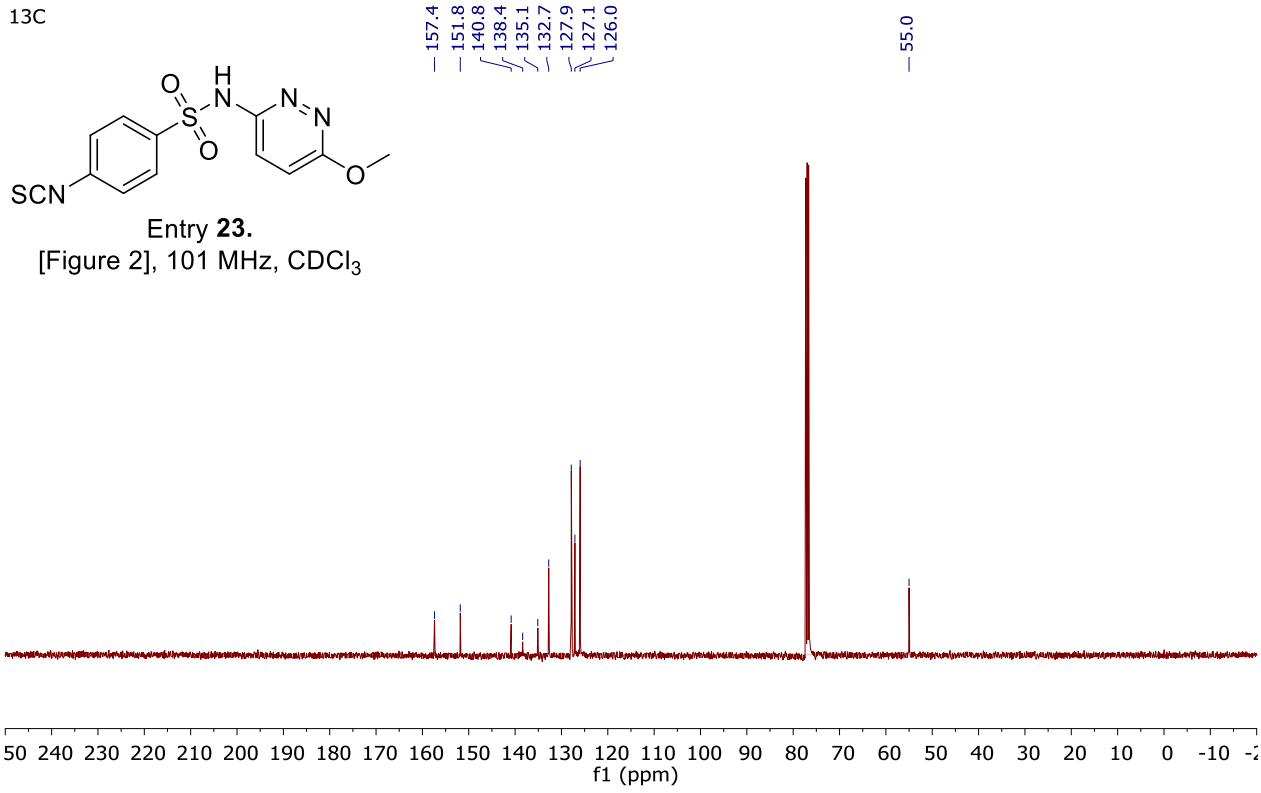
13C



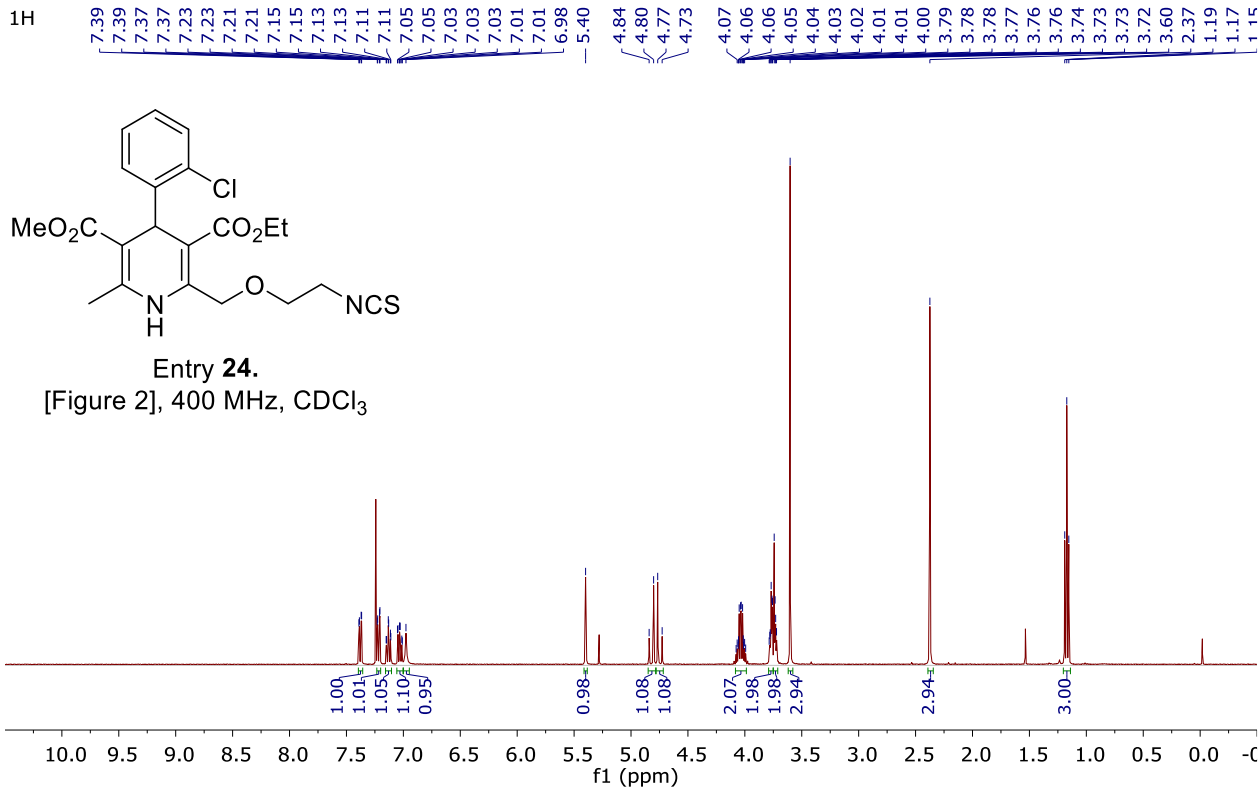
Entry **22.**
[Figure 2], 101 MHz, $CDCl_3$



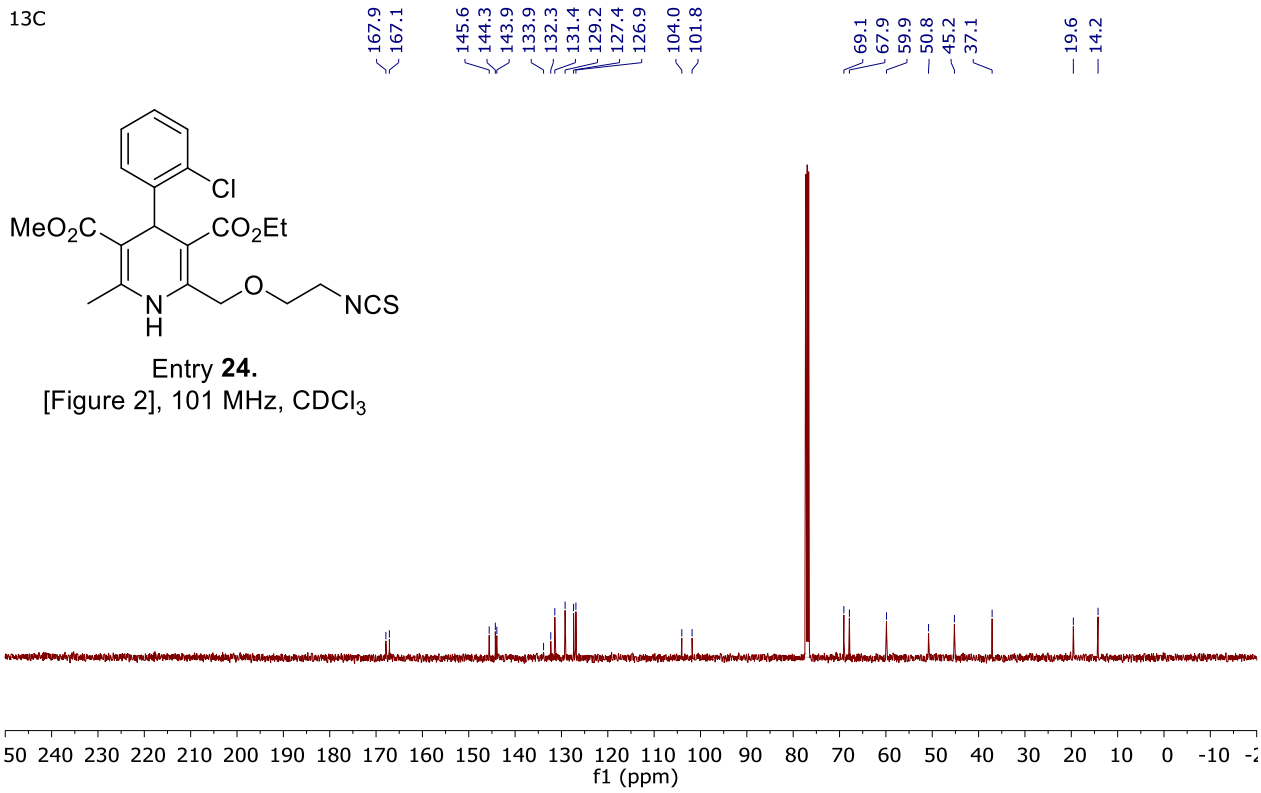
Entry **23.**
[Figure 2], 400 MHz, $CDCl_3$



Entry **23.**
[Figure 2], 101 MHz, $CDCl_3$

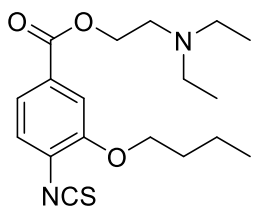


Entry **24.**
[Figure 2], 400 MHz, $CDCl_3$



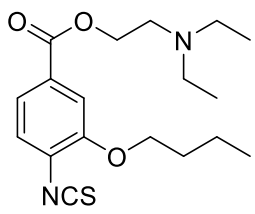
Entry **24.**
[Figure 2], 101 MHz, $CDCl_3$

1H

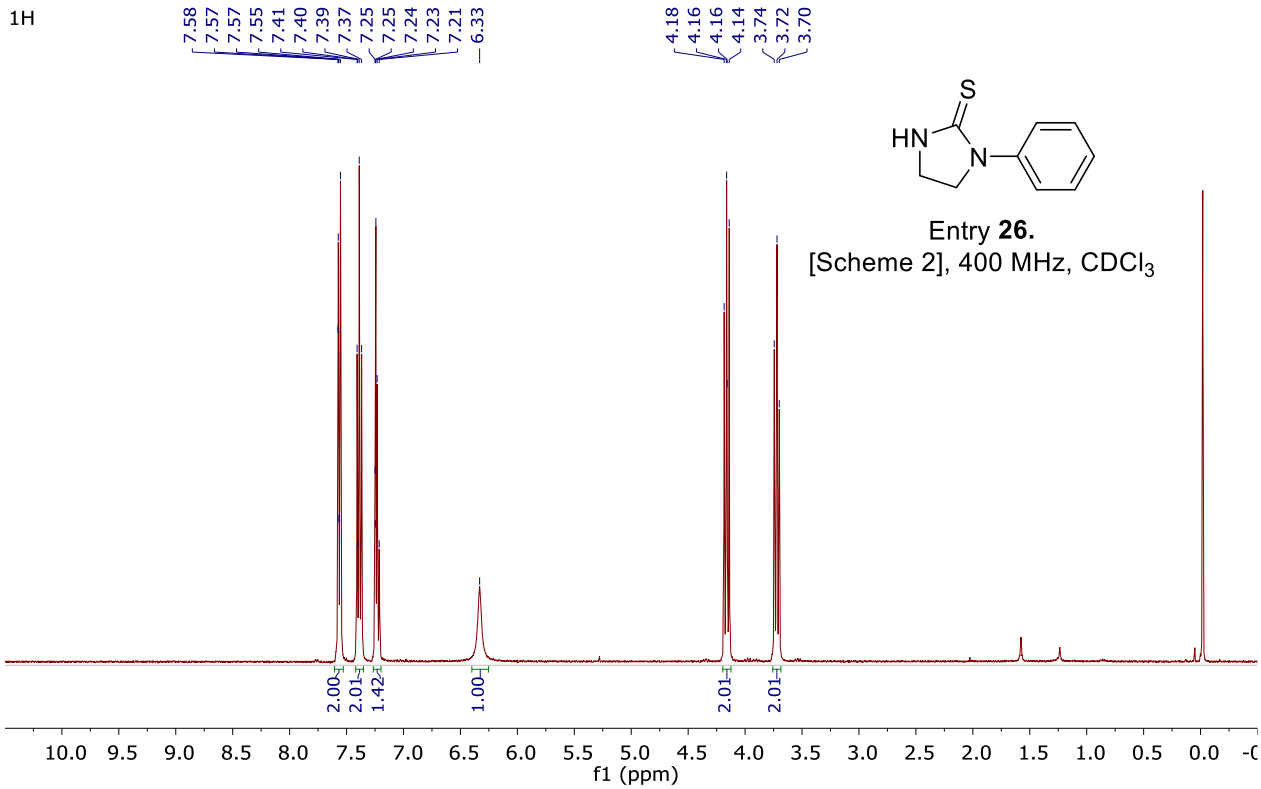


Entry **25.**
[Figure 2], 400 MHz, $CDCl_3$

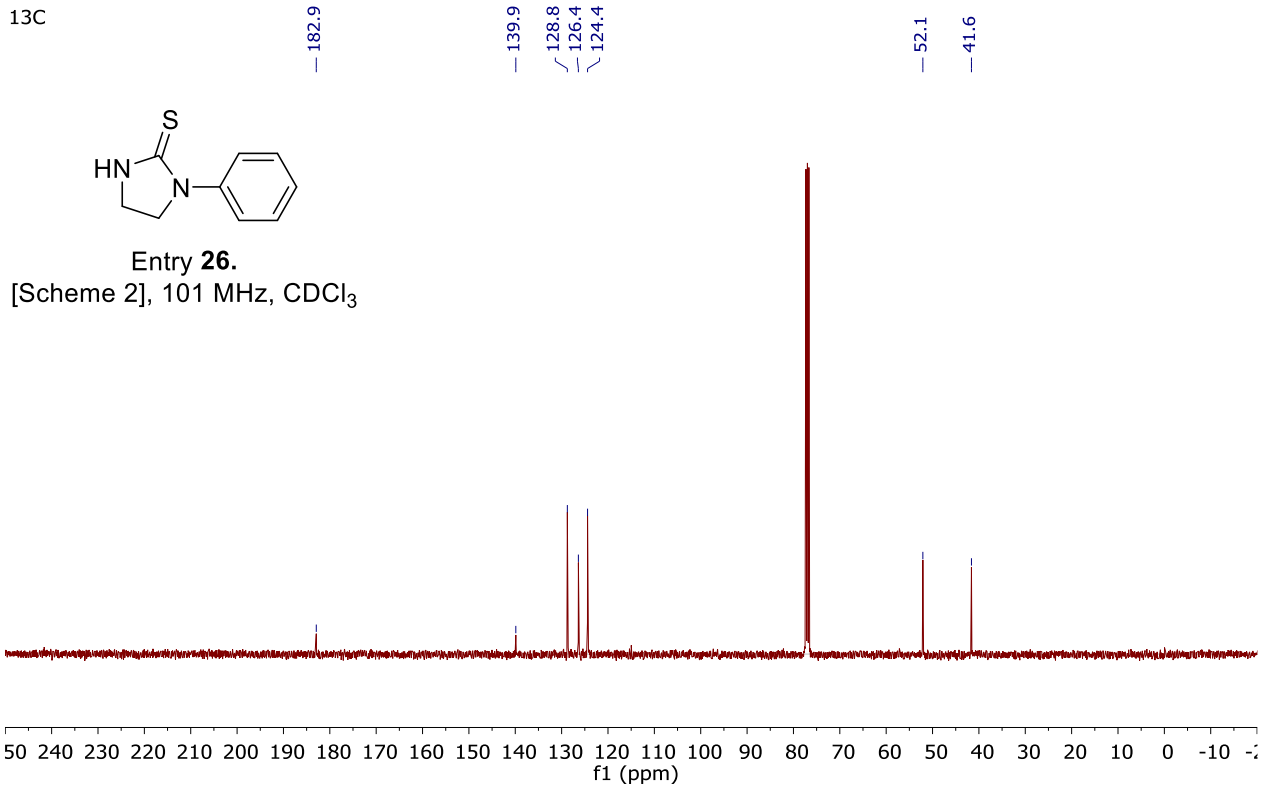
13C



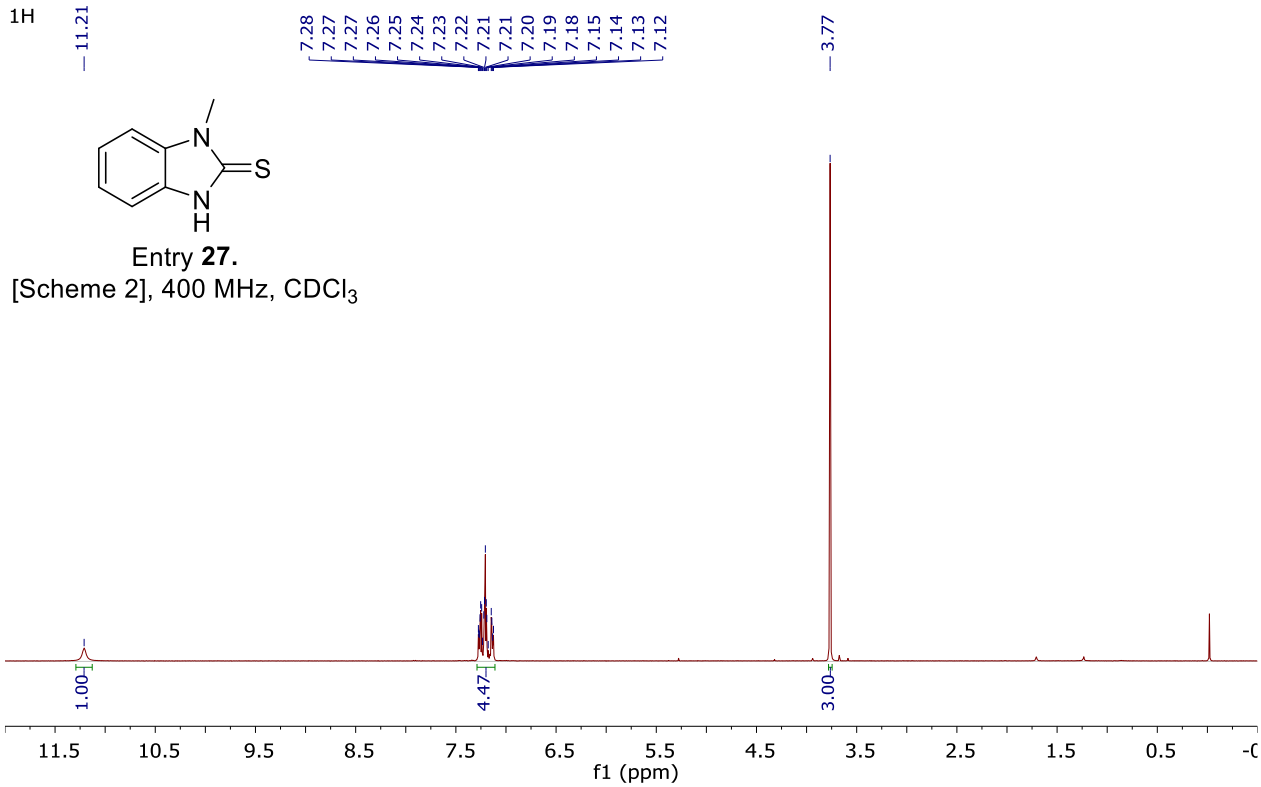
Entry **25.**
[Figure 2], 101 MHz, $CDCl_3$



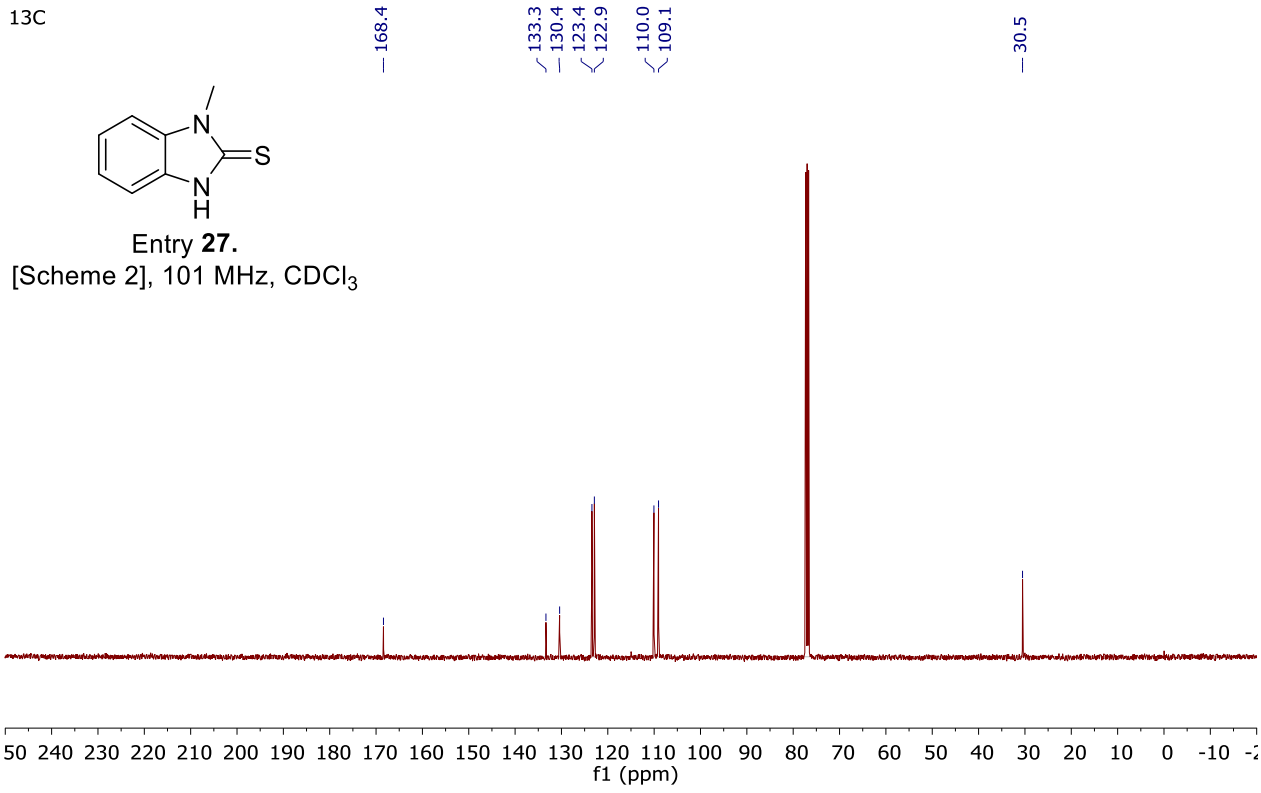
Entry **26.**
[Scheme 2], 400 MHz, $CDCl_3$



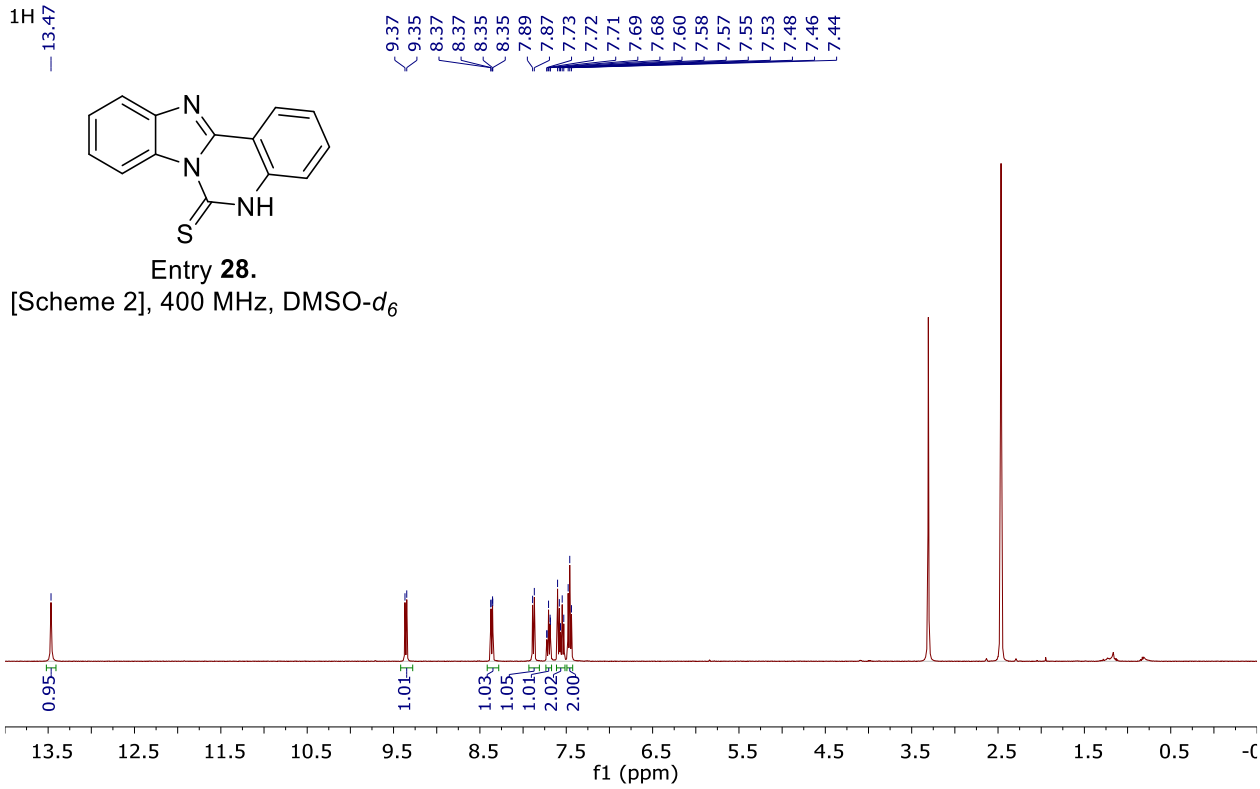
Entry **26.**
[Scheme 2], 101 MHz, $CDCl_3$



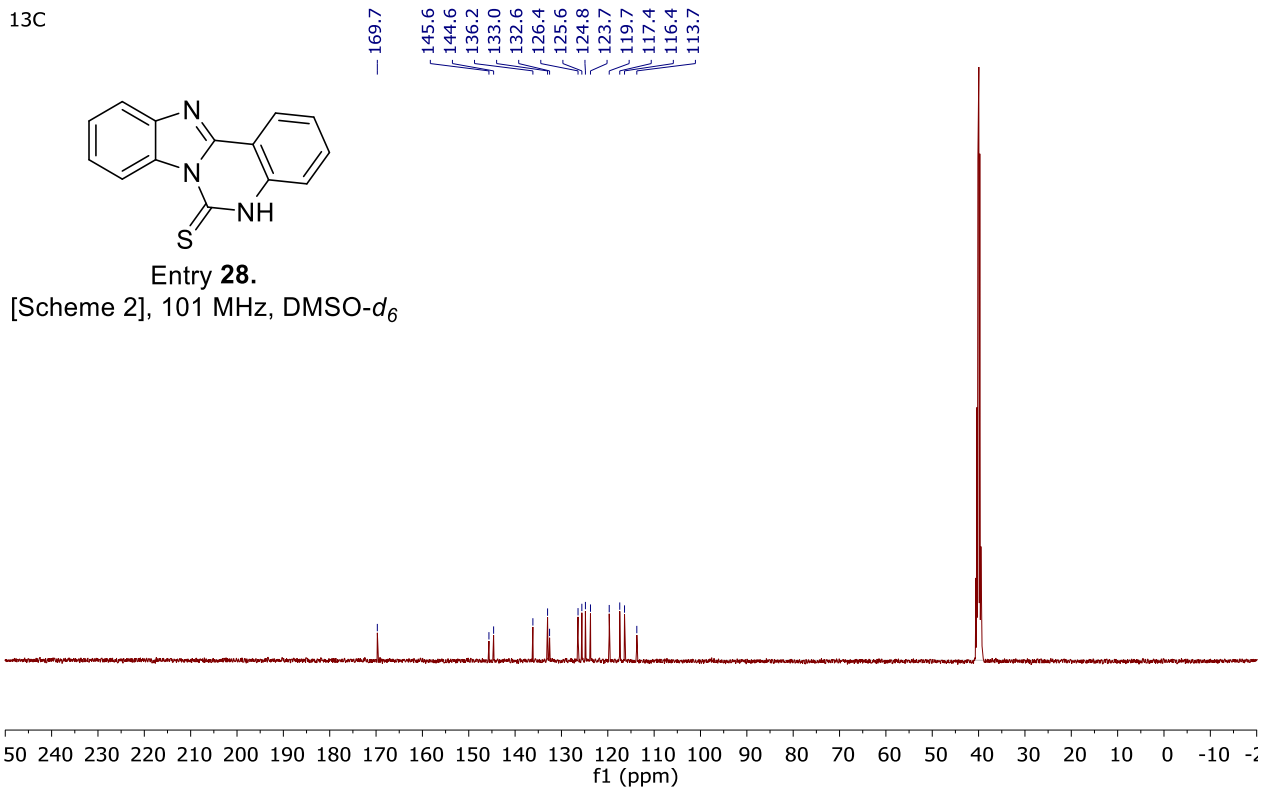
Entry **27.**
[Scheme 2], 400 MHz, $CDCl_3$



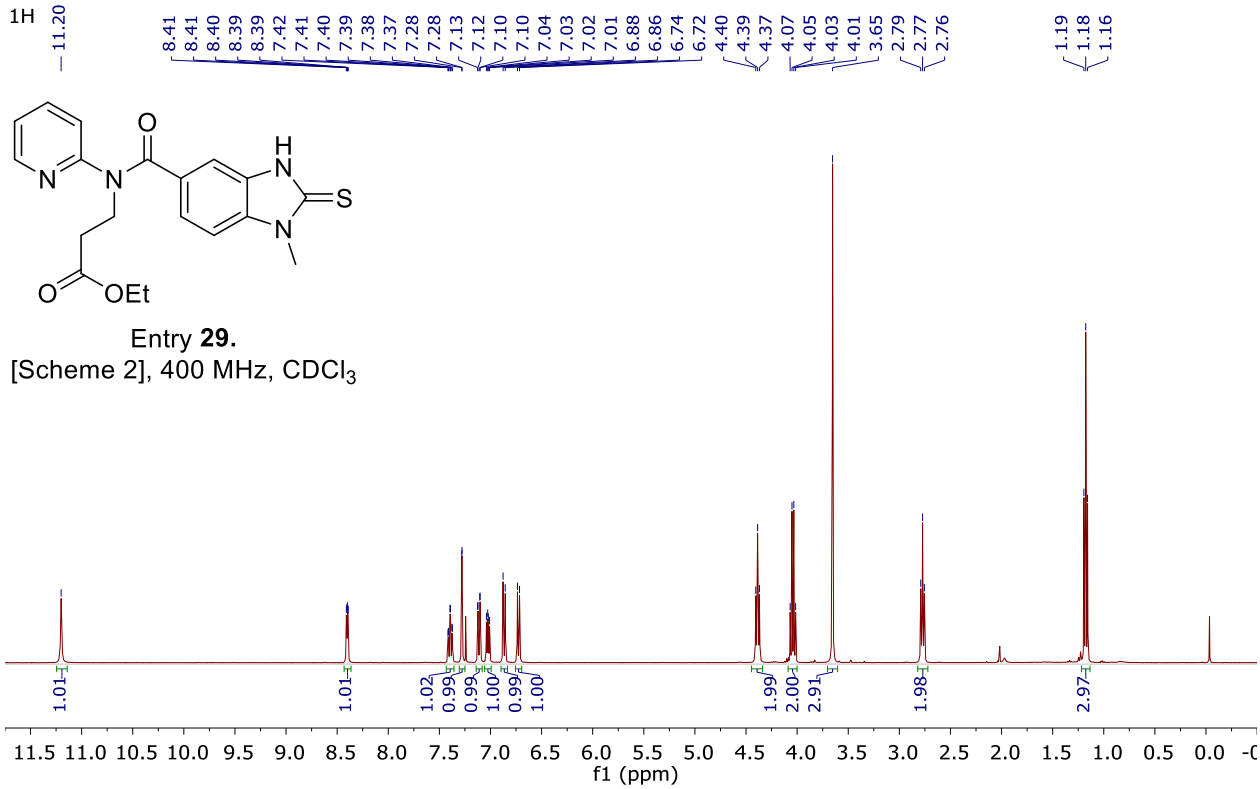
Entry **27.**
[Scheme 2], 101 MHz, $CDCl_3$



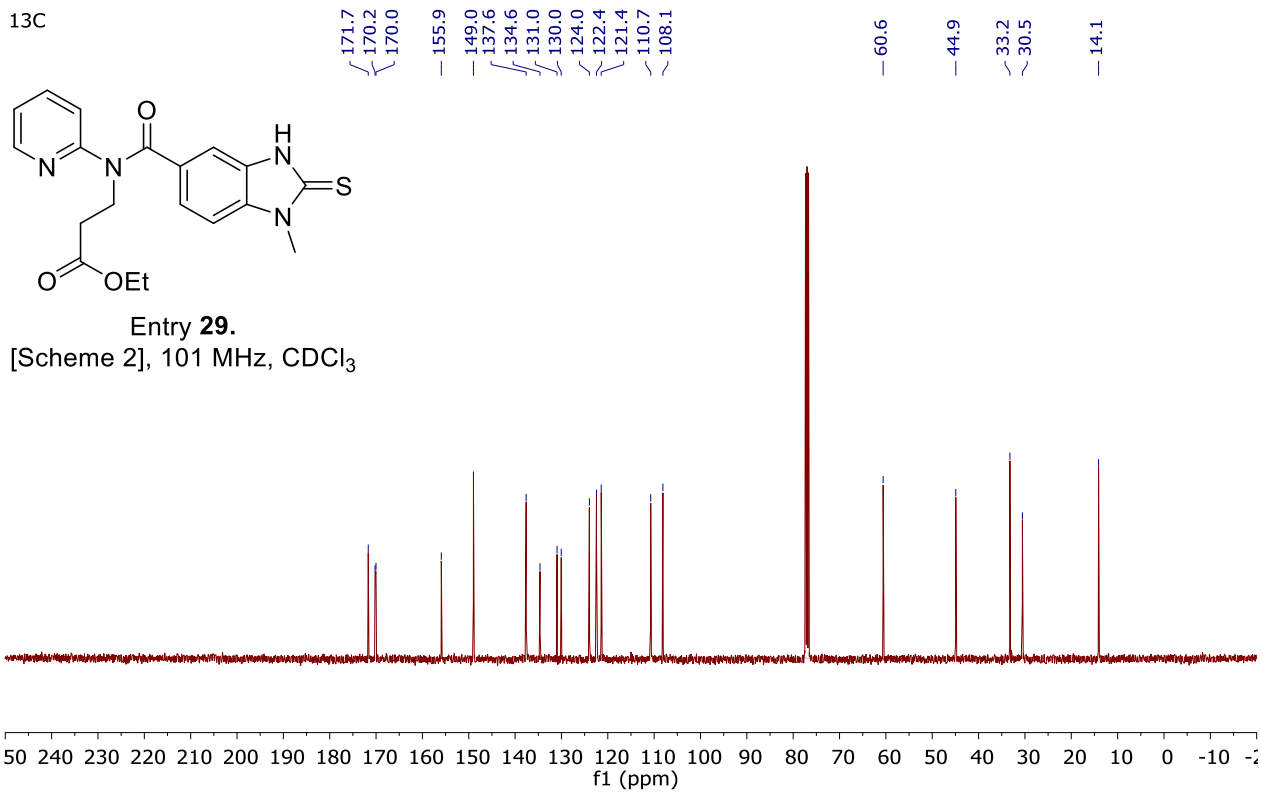
Entry **28.**
[Scheme 2], 400 MHz, DMSO-d_6



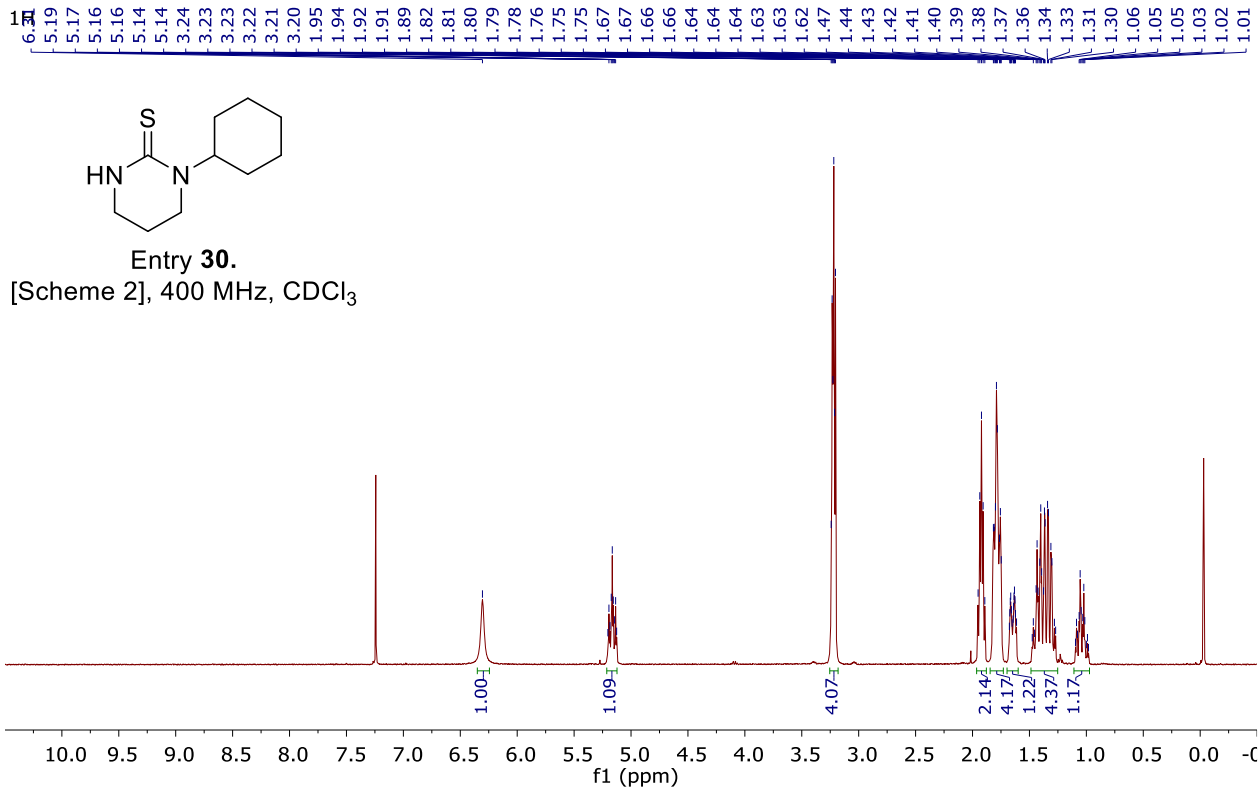
Entry **28.**
[Scheme 2], 101 MHz, DMSO-d_6



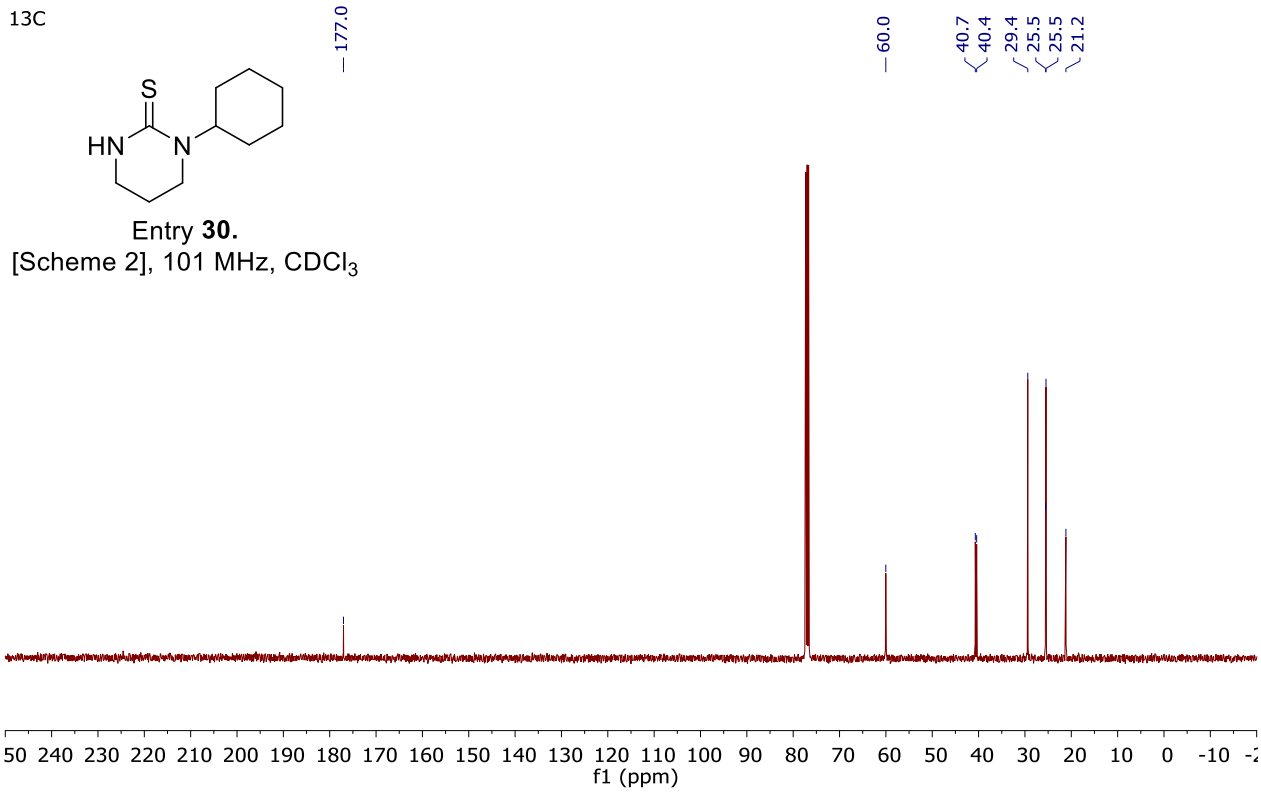
Entry **29.**
[Scheme 2], 400 MHz, $CDCl_3$



Entry **29.**
[Scheme 2], 101 MHz, $CDCl_3$

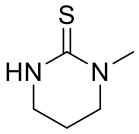


Entry **30.**
[Scheme 2], 400 MHz, $CDCl_3$



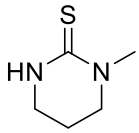
Entry **30.**
[Scheme 2], 101 MHz, $CDCl_3$

1H



Entry **31.**
[Scheme 2], 600 MHz, $CDCl_3$

13C



Entry **31.**
[Scheme 2], 151 MHz, $CDCl_3$