Transamidation of Primary Thioamides with Primary and Secondary Amines via C(S)–N Bond Cleavage and Formation by Hydroxylamine Hydrochloride Catalysis

Yu Gao,[†,‡] Fang Chai,[†] and Chengwei Liu*[,‡]

[†]*Key Laboratory for Photochemical Biomaterials and Energy Storage Materials of Heilongjiang Province, Key Laboratory for Photonic and Electronic Bandgap Materials of Ministry of Education, College of Chemistry and Chemical Engineering, Harbin Normal University, Harbin 150025, China*

[‡]*Department of Chemistry, Shanghai University, 99 Shangda Road, Shanghai 200444, China*

fangchai@gmail.com; liuchengwei@shu.edu.cn; liuchengwei2024@163.com

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Corresponding Authors:

Prof. Dr. F. Chai
Harbin Normal University
fangchai@gmail.com

Prof. Dr. C. Liu
Shanghai University
liuchengwei@shu.edu.cn
liuchengwei2024@163.com

List of Known Compounds/General Methods

Unless stated otherwise, all compounds reported in this manuscript have been previously reported. Spectroscopic data matched literature values. All solvents were purchased at the highest commercial grade and used as received or after purification by passing through activated alumina columns or distillation from sodium/benzophenone under nitrogen. All solvents were deoxygenated prior to use. All other chemicals were purchased at the highest commercial grade and used as received. Reaction glassware was oven-dried at 140 °C for at least 24 h or flame-dried prior to use, allowed to cool under vacuum and purged with argon (three cycles). All products were identified using ^{1}H NMR analysis and comparison with authentic samples. GC and/or GC/MS analysis was used for volatile products. All yields refer to yields determined by ^{1}H NMR and/or GC or GC/MS using an internal standard (optimization) and isolated yields (preparative runs) unless stated otherwise. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on JEOL spectrometers at 400 (^{1}H NMR) and 101 MHz (^{13}C NMR). All shifts are reported in parts per million (ppm) relative to residual $CHCl_3$ peak (7.27 and 77.2 ppm, ^{1}H NMR and ^{13}C NMR, respectively). All coupling constants (*J*) are reported in hertz (Hz). Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; brs, broad singlet. GC-MS chromatography was performed using Agilent HP6890 GC System and Agilent 5977C inert XL EI/CI MSD using helium as the carrier gas at a flow rate of 1 mL/min and an initial oven temperature of 45 °C. The injector temperature was 280 °C. The detector temperature was 280 °C. For runs with the initial oven temperature of 45 °C, temperature was increased with a 20 °C/min ramp after 45 °C hold for 2.5 min to a final temperature of 280 °C, then hold at 220 °C for 2 min (splitless mode of injection, total run time of 16.25 min). High-resolution mass spectra (HRMS) were measured on a 7T Bruker Daltonics FT-MS instrument (for HRMS). Melting point was measured on MeltEMP (laboratory devices). All flash chromatography was performed using silica gel, 60 Å, 300 mesh. TLC analysis was carried out on glass plates coated with silica gel 60 F254, 0.2 mm thickness. The plates were visualized using a 254 nm ultraviolet lamp or aqueous potassium permanganate solutions. ^{1}H NMR and ^{13}C NMR data are given for all compounds in the Supporting Information. ^{1}H NMR, ^{13}C NMR and HRMS data are reported for all new compounds.

Experimental Procedures

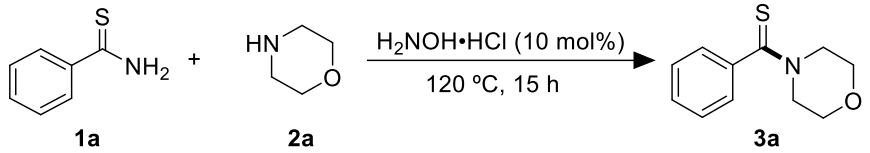
General Procedure for Transamidation of Primary Thioamides with Amines. An oven-dried microwave tube equipped with a stir bar was charged with primary thioamides (neat, 1.0 equiv), amines (neat, 0.1 mL per 0.1 mmol primary thioamides), hydroxylamine hydrochloride (typically, 10 mol%), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. The microwave tube was placed in a preheated oil bath at 120 °C, which was stirred for 15 h. After the indicated time, the reaction mixture was cooled down to room temperature. The reaction mixture was added dichloromethane (10 mL) and washed with saturated $NaHCO_3$ solution (2×10 mL). The obtained solution was dried with anhydrous sodium sulfate, filtrated, concentrated to get crude product. The sample was analyzed by ^1H NMR ($CDCl_3$, 400 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (hexane/ethyl acetate) afforded the title product. Caution: reactions involving high pressure must be carried out in a well-ventilated hood with appropriate pressure vessels, pressure relief equipment, and/or blast shields.

Representative Procedure for Transamidation of Primary Thioamides with Amines. An oven-dried microwave tube equipped with a stir bar was charged with benzothioamide (neat, 13.8 mg, 0.10 mmol, 1.0 equiv), morpholine (neat, 0.1 mL), hydroxylamine hydrochloride (0.7 mg, 0.01 mmol, 0.1 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. The microwave tube was placed in a preheated oil bath at 120 °C, which was stirred for 15 h. After the indicated time, the reaction mixture was cooled down to room temperature. The reaction mixture was added dichloromethane (10 mL) and washed with saturated $NaHCO_3$ solution (2×10 mL). The obtained solution was dried with anhydrous sodium sulfate, filtrated, concentrated to get crude product. The sample was analyzed by ^1H NMR ($CDCl_3$, 400 MHz) and GC-MS to obtain conversion, yield and selectivity using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (hexane/ethyl acetate) afforded the title product. Yield 82% (17.0 mg, 0.082 mmol). White Solid. Characterization data are included in the section below. Caution: reactions involving high pressure must be carried out in a well-ventilated hood with appropriate pressure vessels, pressure relief equipment, and/or blast shields.

Procedure for the synthesis *tert*-Butyl benzyl(phenylcarbonothioyl)carbamate: An oven-dried flask equipped with a stir bar was charged with *N*-benzylbenzothioamide (454.7 mg. 2.0 mmol, 1.0 equiv), dimethylaminopyridine (24.4 mg, 0.10 mmol, 5 mol%) and THF (10 mL, 0.20 M). Di-*tert*-butyl dicarbonate (480.1 mg, 1.1 equiv) was added dropwise to the reaction mixture with vigorous stirring at 0 ℃, and the reaction mixture was stirred for 15 h at 25 °C. After the indicated time, the reaction mixture was diluted with ethyl acetate (50 mL), the organic layer was washed with water (1 x 30 mL), dried over Na_2SO_4, and concentrated. The crude reaction mixture was purified by chromatography on silica gel (hexane/ethyl acetate = 40:1 to 5:1).

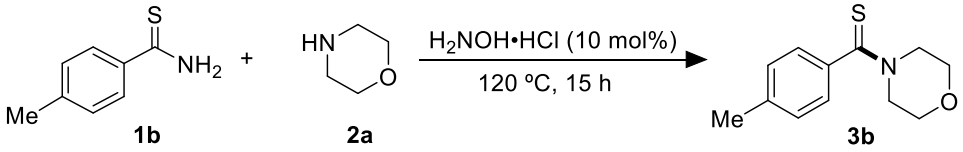
Characterization Data for Transamidation of Primary Thioamides

Morpholino(phenyl)methanethione (Scheme 1, 3a)[1]



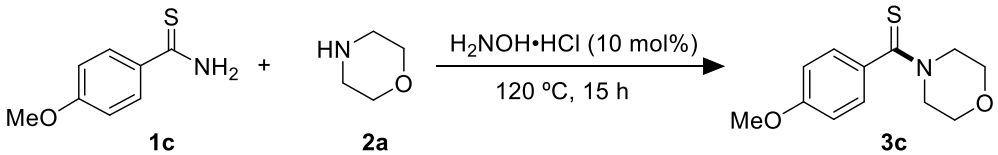
According to the general procedure, the reaction of benzothioamide (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 82% yield (17.0 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.27 (m, 3H), 7.23-7.20 (m, 2H), 4.38 (t, *J* = 4.9 Hz, 2H), 3.82 (t, *J* = 5.0 Hz, 2H), 3.59-3.52 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.01, 141.43, 127.86, 127.53, 124.85, 65.73, 65.52, 51.49, 48.51.

Morpholino(*p*-tolyl)methanethione (Scheme 1, 3b)[1]



According to the general procedure, the reaction of 4-methylbenzothioamide (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 56% yield (12.4 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.14-7.08 (m, 4H), 4.37 (t, *J* = 4.9 Hz, 2H), 3.81 (t, *J* = 5.0 Hz, 2H), 3.57 (s, 4H), 2.28 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.37, 138.63, 138.10, 128.09, 125.01, 65.75, 65.53, 51.55, 48.66, 20.24.

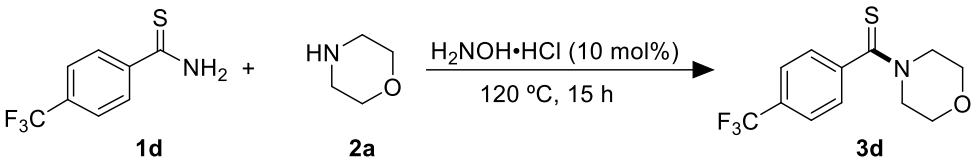
(4-Methoxyphenyl)(morpholino)methanethione (Scheme 1, 3c)[1]



According to the general procedure, the reaction of 4-methoxybenzothioamide (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C,

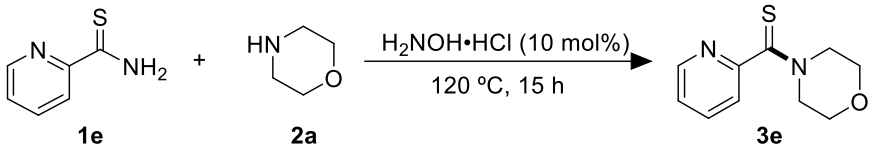
afforded after work-up and chromatography the title compound in 61% yield (14.5 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.23-7.20 (m, 2H), 6.82-6.79 (m, 2H), 4.36 (s, 2H), 3.81 (s, 2H), 3.75 (s, 3H), 3.60 (s, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.22, 159.28, 133.85, 127.07, 112.71, 65.75, 54.41, 49.00.

Morpholino(4-(trifluoromethyl)phenyl)methanethione (Scheme 1, 3d)[1]



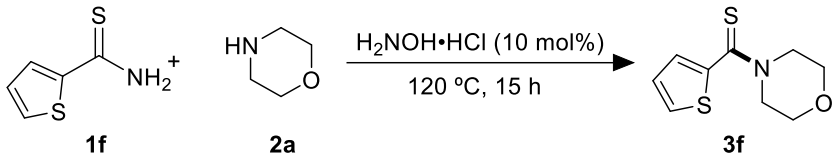
According to the general procedure, the reaction of 4-(trifluoromethyl)benzothioamide (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 69% yield (19.0 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.57 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 4.37 (t, *J* = 4.8 Hz, 2H), 3.83 (t, *J* = 5.0 Hz, 2H), 3.60-3.58 (m, 2H), 3.51-3.49 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.79, 144.62, 129.73 (q, J^F = 11.0 Hz), 125.11, 124.73 (q, J^F = 3.9 Hz), 121.32, 65.62, 65.46, 51.47, 48.30. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -62.74.

Morpholino(pyridin-2-yl)methanethione (Scheme 1, 3e)[2]



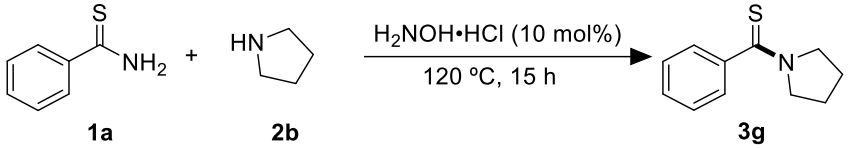
According to the general procedure, the reaction of pyridine-2-carbothioamide (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 87% yield (18.1 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.49 (d, *J* = 4.6 Hz, 1H), 7.83 (t, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 8.8 Hz, 1H), 7.33 (t, *J* = 5.9 Hz, 1H), 4.37 (t, *J* = 4.8 Hz, 2H), 3.87 (t, *J* = 5.0 Hz, 2H), 3.70 (t, *J* = 4.6 Hz, 2H), 3.55 (t, *J* = 4.6 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 218.91, 147.04, 145.81, 136.19, 122.82, 122.50, 65.72, 65.39, 51.40, 48.52.

Morpholino(thiophen-2-yl)methanethione (Scheme 1, 3f)[2]



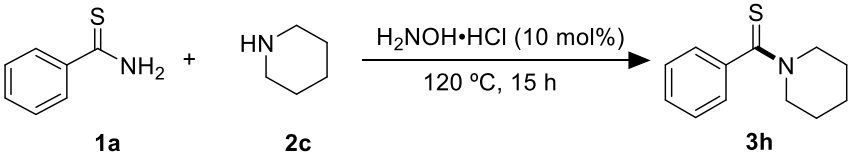
According to the general procedure, the reaction of thiophene-2-carbothioamide (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 53% yield (11.3 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36-7.35 (m, 1H), 7.01-7.00 (m, 1H), 6.93-6.91 (m, 1H), 4.10 (s, 4H), 3.74 (s, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 190.84, 143.28, 128.35, 125.60, 125.19, 65.65, 41.30.

Phenyl(pyrrolidin-1-yl)methanethione (Scheme 2, 3g)[1]



According to the general procedure, the reaction of benzothioamide (0.10 mmol, 1.0 equiv), pyrrolidine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 89% yield (17.0 mg). White solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30-7.25 (m, 5H), 3.91 (t, *J* = 7.0 Hz, 2H), 3.40 (t, *J* = 6.8 Hz, 2H), 2.06-1.98 (m, 2H), 1.94-1.87 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.26, 142.95, 127.70, 127.28, 124.60, 52.76, 52.38, 25.46, 23.64.

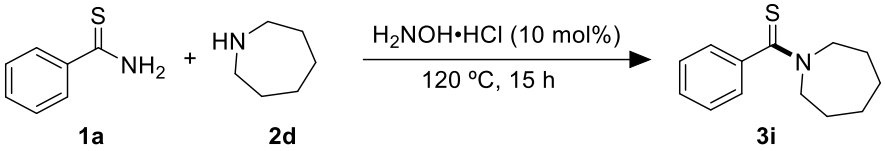
Phenyl(piperidin-1-yl)methanethione (Scheme 2, 3h)[1]



According to the general procedure, the reaction of benzothioamide (0.10 mmol, 1.0 equiv), piperidine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 82% yield (16.8 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.18 (m, 5H), 4.29 (t, *J* = 5.4 Hz, 2H), 3.45 (t, *J* = 5.6 Hz, 2H), 1.79-

1.73 (m, 2H), 1.71-1.65 (m, 2H), 1.53-1.47 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.56, 142.36, 127.38, 127.34, 124.39, 52.15, 49.59, 25.87, 24.48, 23.15.

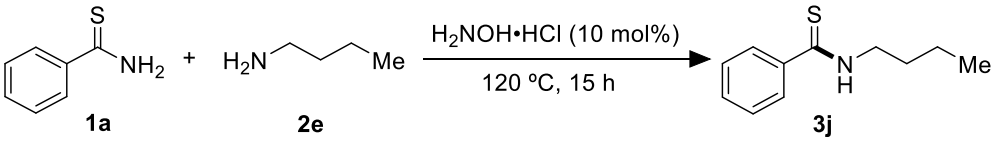
Azepan-1-yl(phenyl)methanethione (Scheme 2, 3i)[3]



1a **2d** **3i**

According to the general procedure, the reaction of benzothioamide (0.10 mmol, 1.0 equiv), azepane (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 49% yield (10.7 mg). White solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.22 (m, 3H), 7.18-7.16 (m, 2H), 4.16 (t, *J* = 6.0 Hz, 2H), 3.49 (t, *J* = 6.0 Hz, 2H), 1.98-1.92 (m, 2H), 1.63-1.61 (m, 2H), 0.83-0.77 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 199.33, 142.96, 127.34, 126.94, 124.08, 53.43, 52.67, 27.99, 26.39, 25.11, 24.34.

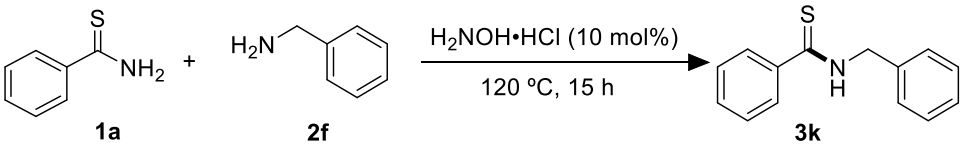
***N*-Butylbenzothioamide (Scheme 3, 3j)[4]**



1a **2e** **3j**

According to the general procedure, the reaction of benzothioamide (0.10 mmol, 1.0 equiv), butan-1-amine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 95% yield (18.4 mg). Yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.67-7.64 (m, 2H), 7.41-7.36 (m, 1H), 7.33-7.29 (m, 2H), 3.78-3.73 (m, 2H), 1.71-1.64 (m, 2H), 1.45-1.35 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.17, 141.09, 129.92, 127.48, 125.52, 45.62, 29.19, 19.27, 12.79.

***N*-Benzylbenzothioamide (Scheme 3, 3k)[4]**

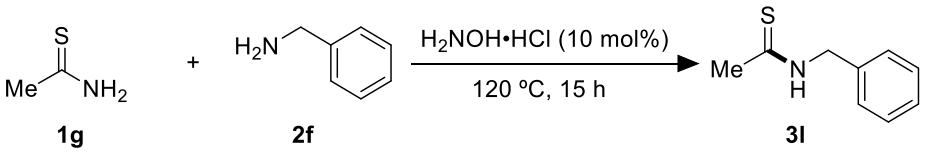


1a **2f** **3k**

According to the general procedure, the reaction of benzothioamide (0.10 mmol, 1.0 equiv), phenylmethanamine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C,

afforded after work-up and chromatography the title compound in 96% yield (21.8 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70-7.67 (m, 2H), 7.41-7.36 (m, 1H), 7.36-7.30 (m, 6H), 7.29-7.26 (m, 1H), 4.92 (d, *J* = 5.1 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.13, 140.59, 135.13, 130.17, 128.04, 127.52, 127.38, 127.25, 125.66, 50.09.

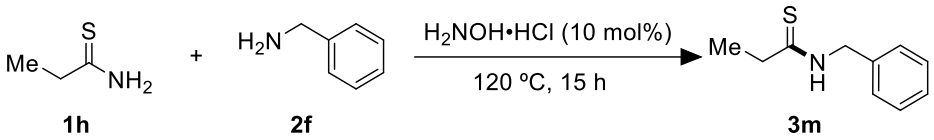
N-Benzylethanethioamide (Scheme 4, 3l)[4]



1g **2f** **3l**

According to the general procedure, the reaction of ethanethioamide (0.10 mmol, 1.0 equiv), phenylmethanamine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 95% yield (15.7 mg). White solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33-7.27 (m, 5H), 4.75 (d, *J* = 5.1 Hz, 2H), 2.52 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 199.81, 135.00, 127.97, 127.42, 127.23, 49.70, 33.17.

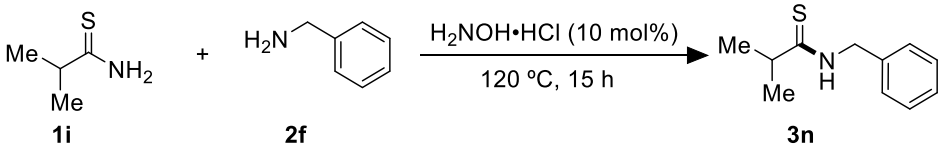
N-Benzylpropanethioamide (Scheme 4, 3m)[5]



1h **2f** **3m**

According to the general procedure, the reaction of propanethioamide (0.10 mmol, 1.0 equiv), phenylmethanamine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 98% yield (17.6 mg). White solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33-7.27 (m, 5H), 4.76 (d, *J* = 5.0 Hz, 2H), 2.64 (q, *J* = 7.5 Hz, 2H), 1.25 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 205.73, 135.13, 127.98, 127.35, 127.19, 49.36, 39.01, 12.58.

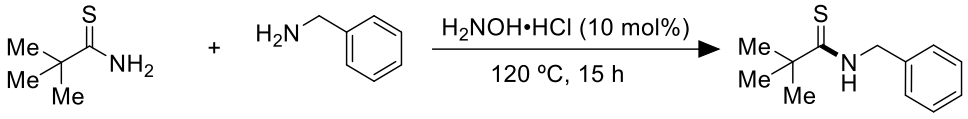
N-Benzyl-2-methylpropanethioamide (Scheme 4, 3n)[5]



1i **2f** **3n**

According to the general procedure, the reaction of 2-methylpropanethioamide (0.10 mmol, 1.0 equiv), phenylmethanamine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 70% yield (13.5 mg). Colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31-7.26 (m, 5H), 4.78 (d, *J* = 5.0 Hz, 2H), 2.81-2.70 (m, 1H), 1.22 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 210.51, 135.24, 127.98, 127.27, 127.15, 49.02, 43.56, 21.63.

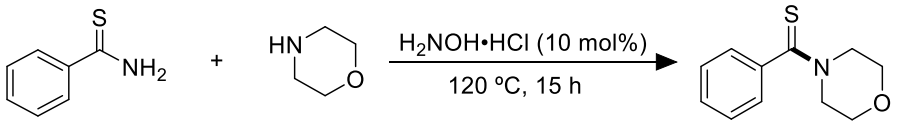
_N_-Benzyl-2,2-dimethylpropanethioamide (Scheme 4, 3o)[5]



1j **2f** **3o**

According to the general procedure, the reaction of 2,2-dimethylpropanethioamide (0.10 mmol, 1.0 equiv), phenylmethanamine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 48% yield (10.0 mg). Colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.34-7.24 (m, 5H), 4.77 (d, *J* = 4.8Hz, 2H), 1.31 (s, 9H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 212.38, 135.38, 128.02, 127.48, 127.12, 49.77, 43.52, 29.16.

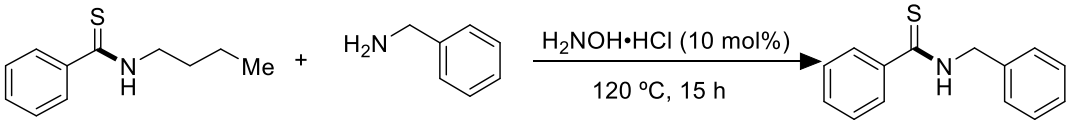
Morpholino(phenyl)methanethione (Scheme 5, 3a)[1]



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

According to the general procedure, the reaction of benzothioamide (7.5 mmol, 1.0 equiv), morpholine (10 mmol, 1.5 equiv) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 63% yield (979.4 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.27 (m, 3H), 7.23-7.20 (m, 2H), 4.38 (t, *J* = 4.9 Hz, 2H), 3.82 (t, *J* = 5.0 Hz, 2H), 3.59-3.52 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.01, 141.43, 127.86, 127.53, 124.85, 65.73, 65.52, 51.49, 48.51.

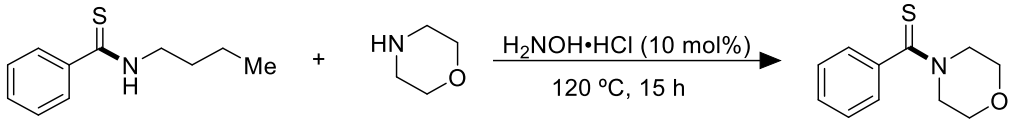
_N_-Benzylbenzothioamide (Scheme 5, 3k)[4]



3j **2f** **3k**

According to the general procedure, the reaction of *N*-butylbenzothioamide (0.10 mmol, 1.0 equiv), phenylmethanamine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, while no desired product was generated after work-up.

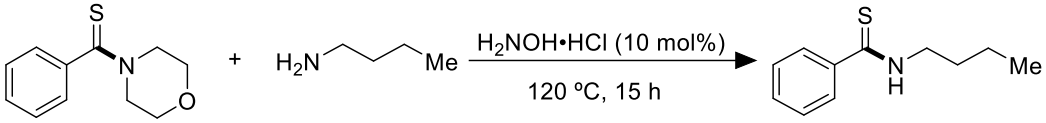
Morpholino(phenyl)methanethione (Scheme 5, 3a)[1]



3j **2a** **3a**

According to the general procedure, the reaction of *N*-butylbenzothioamide (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, while no desired product was generated after work-up.

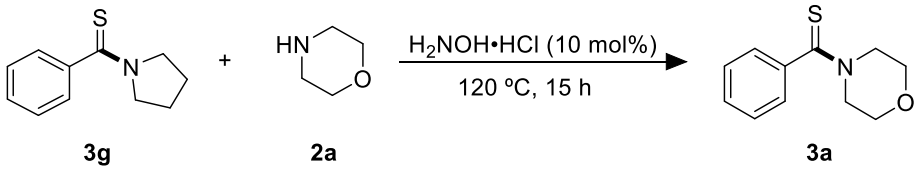
_N_-Butylbenzothioamide (Scheme 5, 3j)[4]



3a **2e** **3j**

According to the general procedure, the reaction of morpholino(phenyl)methanethione (0.10 mmol, 1.0 equiv), butan-1-amine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, while no desired product was generated after work-up.

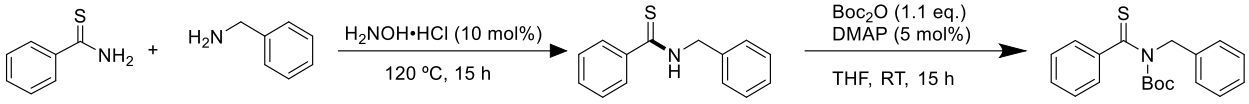
Morpholino(phenyl)methanethione (Scheme 5, 3a)[1]



3g **2a** **3a**

According to the general procedure, the reaction of phenyl(pyrrolidin-1-yl)methanethione (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 90% yield (18.7 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.27 (m, 3H), 7.23-7.20 (m, 2H), 4.38 (t, *J* = 4.9 Hz, 2H), 3.82 (t, *J* = 5.0 Hz, 2H), 3.59-3.52 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.01, 141.43, 127.86, 127.53, 124.85, 65.73, 65.52, 51.49, 48.51.

tert-Butyl benzyl(phenylcarbonothioyl)carbamate (Scheme 6, 3k')[6]

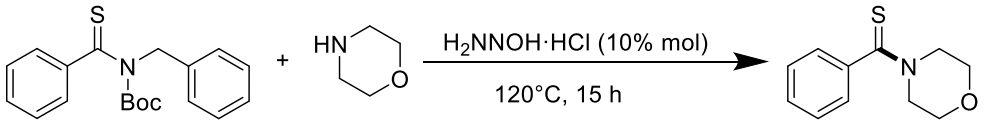


1a **2f** **3k** **3k'**

According to the general procedure, the reaction of benzothioamide (3 mmol, 1.0 equiv), phenylmethanamine (4.5 mmol, 1.5 equiv) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 90% yield (613.8 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70-7.67 (m, 2H), 7.41-7.36 (m, 1H), 7.36-7.30 (m, 6H), 7.29-7.26 (m, 1H), 4.92 (d, *J* = 5.1 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 198.13, 140.59, 135.13, 130.17, 128.04, 127.52, 127.38, 127.25, 125.66, 50.09.

According to the procedure, the reaction of *N*-benzylbenzothioamide (2.0 mmol, 1.0 equiv), dimethylaminopyridine (0.10 mmol, 5 mol%), THF (0.20 M) and di-*tert*-butyl dicarbonate (1.1 equiv) for 15 h at 25 °C, afforded after work-up and chromatography the title compound in 62% yield (406.0 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70-7.68 (m, 2H), 7.34-7.21 (m, 8H), 4.93 (d, *J* = 5.1 Hz, 2H), 1.40 (d, *J* = 26.2 Hz, 9H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 140.64, 135.17, 130.16, 128.05, 127.58, 127.53, 127.40, 127.26, 126.31, 125.68, 50.12, 27.39, 26.40.

Morpholino(phenyl)methanethione (Scheme 6, 3a)[1]

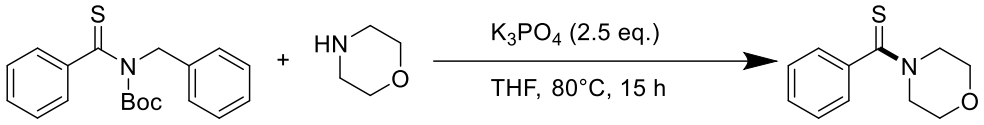


3k' **2a** **3a**

According to the general procedure, the reaction of *tert*-butyl benzyl(phenylcarbonothioyl)carbamate (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and

hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 78% yield (16.2 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.27 (m, 3H), 7.23-7.20 (m, 2H), 4.38 (t, *J* = 4.9 Hz, 2H), 3.82 (t, *J* = 5.0 Hz, 2H), 3.59-3.52 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.01, 141.43, 127.86, 127.53, 124.85, 65.73, 65.52, 51.49, 48.51.

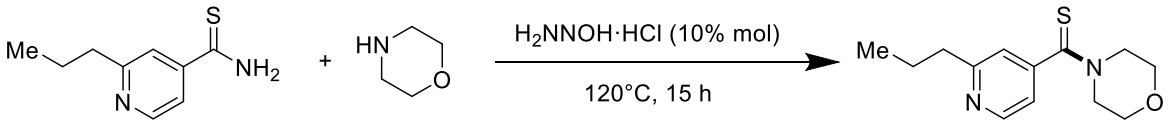
Morpholino(phenyl)methanethione (Scheme 6, 3a)[1]



3k' **2a** **3a**

According to the general procedure, the reaction of *tert*-butyl benzyl(phenylcarbonothioyl)carbamate (0.10 mmol, 1.0 equiv), morpholine (0.20 mmol, 2.0 equiv) and K_3PO_4 (2.5 equiv) for 15 h at 80 °C, afforded after work-up and chromatography the title compound in 46% yield (9.5 mg). Yellow solid. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32-7.27 (m, 3H), 7.23-7.20 (m, 2H), 4.38 (t, *J* = 4.9 Hz, 2H), 3.82 (t, *J* = 5.0 Hz, 2H), 3.59-3.52 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 200.01, 141.43, 127.86, 127.53, 124.85, 65.73, 65.52, 51.49, 48.51.

Morpholino(2-propylpyridin-4-yl)methanethione (Scheme 7, 3p)



1k **2a** **3p**

According to the general procedure, the reaction of 2-propylpyridine-4-carbothioamide (0.10 mmol, 1.0 equiv), morpholine (0.1 mL) and hydroxylamine hydrochloride (10 mol%) for 15 h at 120 °C, afforded after work-up and chromatography the title compound in 84% yield (21.0 mg). Yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.52 (d, *J* = 5.8 Hz, 1H), 7.15 (s, 2H), 4.33 (s, 2H), 3.84 (t, *J* = 4.8 Hz, 2H), 3.62 (s, 2H), 3.47 (s, 2H), 2.92 (t, *J* = 7.4 Hz, 2H), 1.83-1.74 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 134.65, 128.10, 127.51, 119.44, 117.03, 53.15, 50.00, 38.73, 21.97, 12.82.

References

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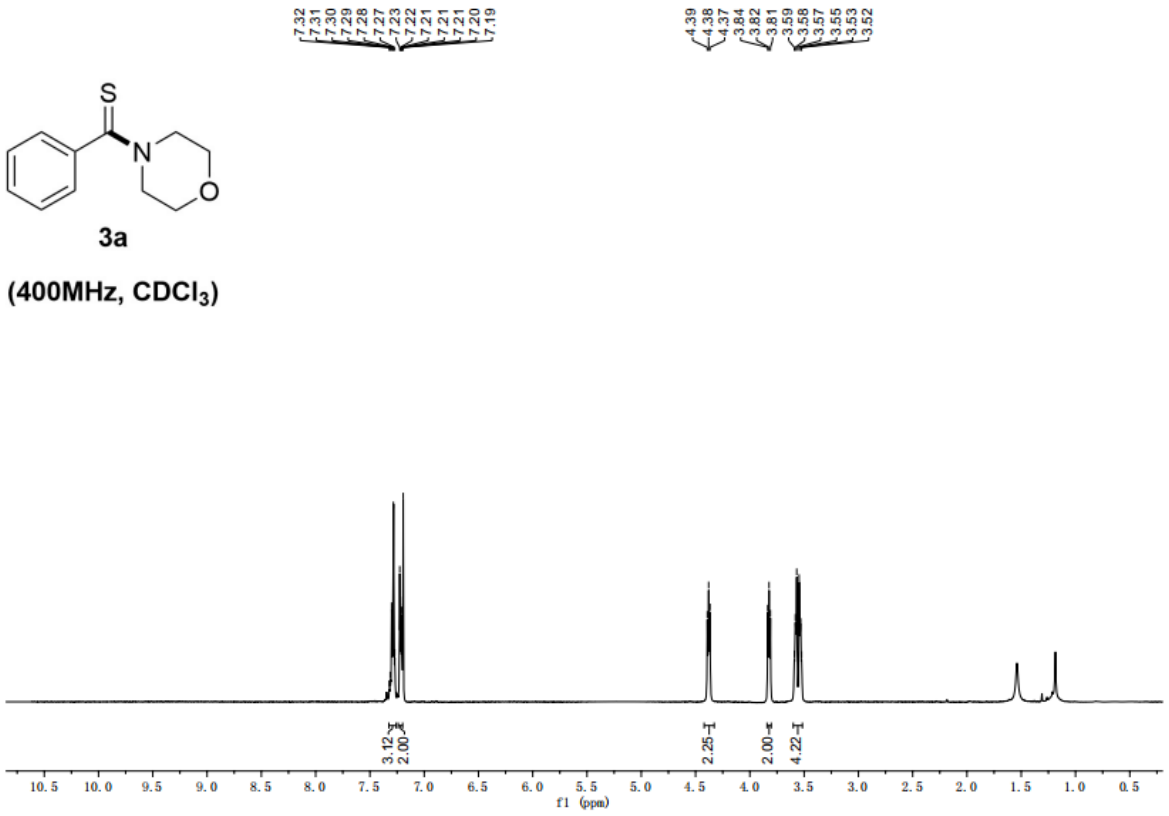
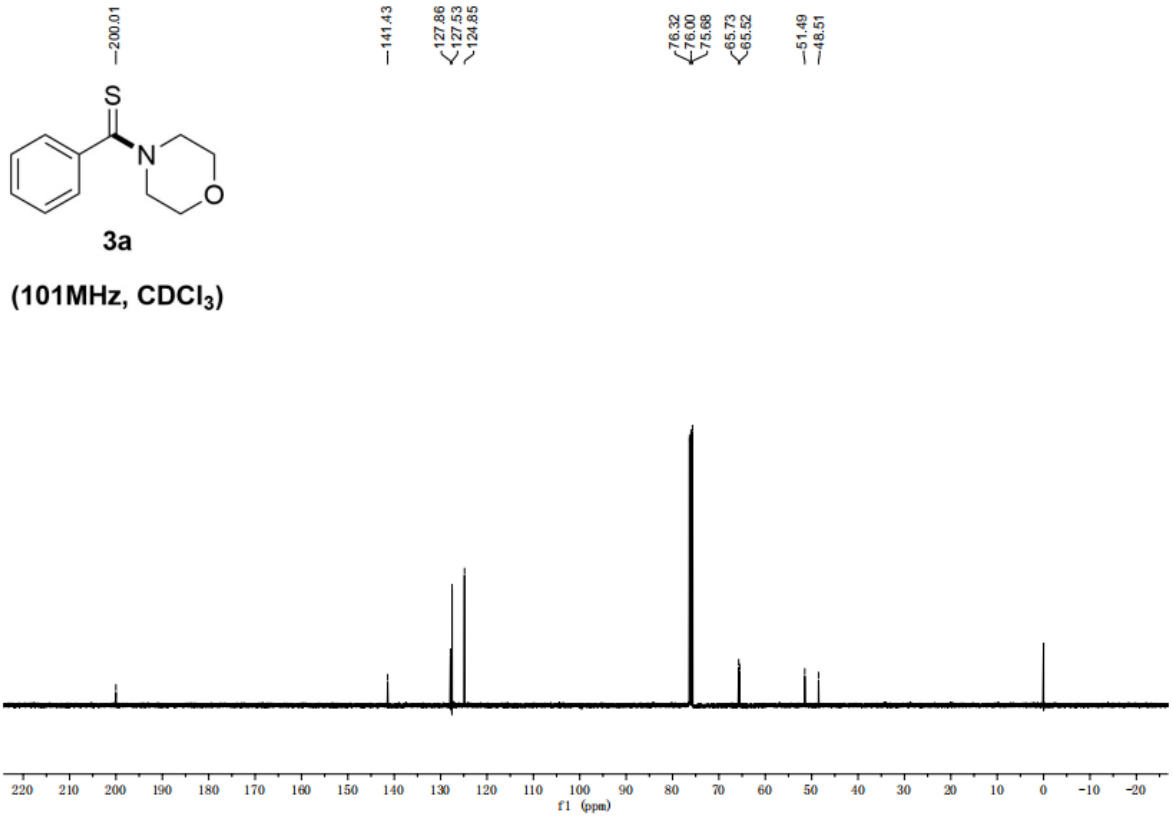
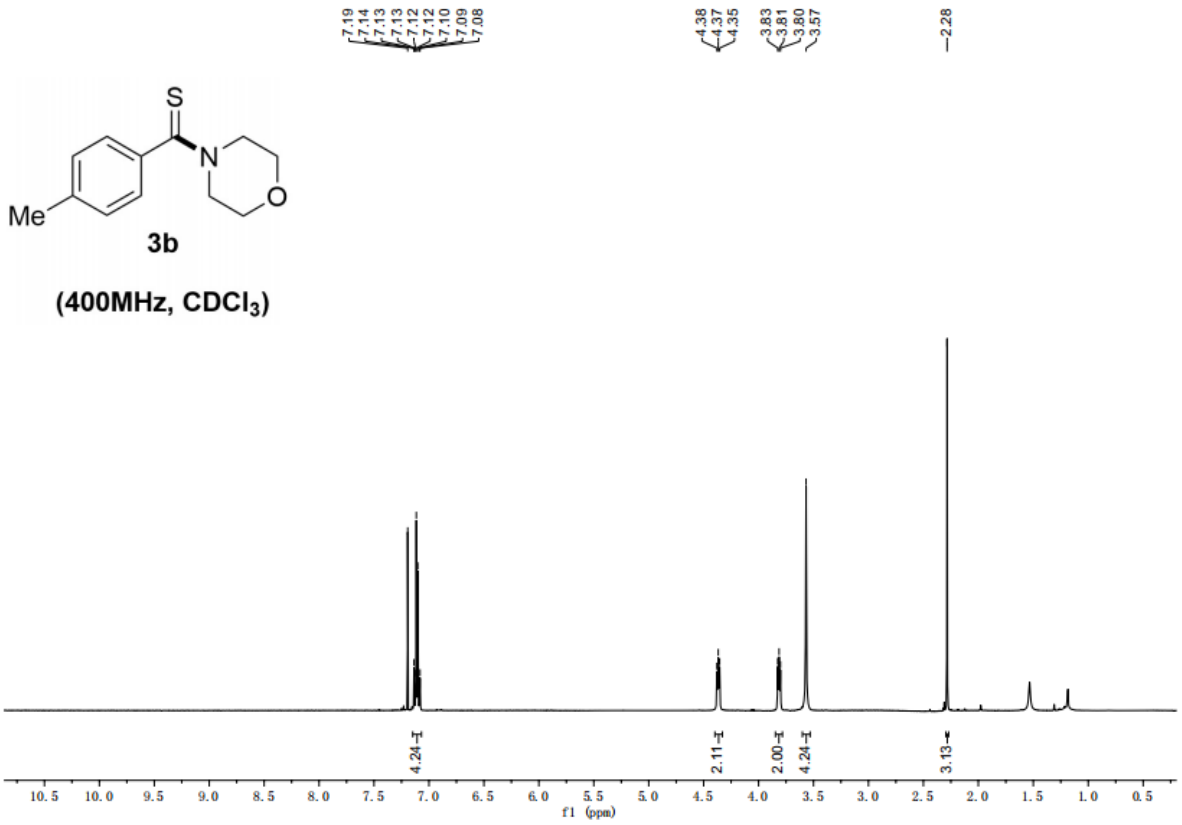
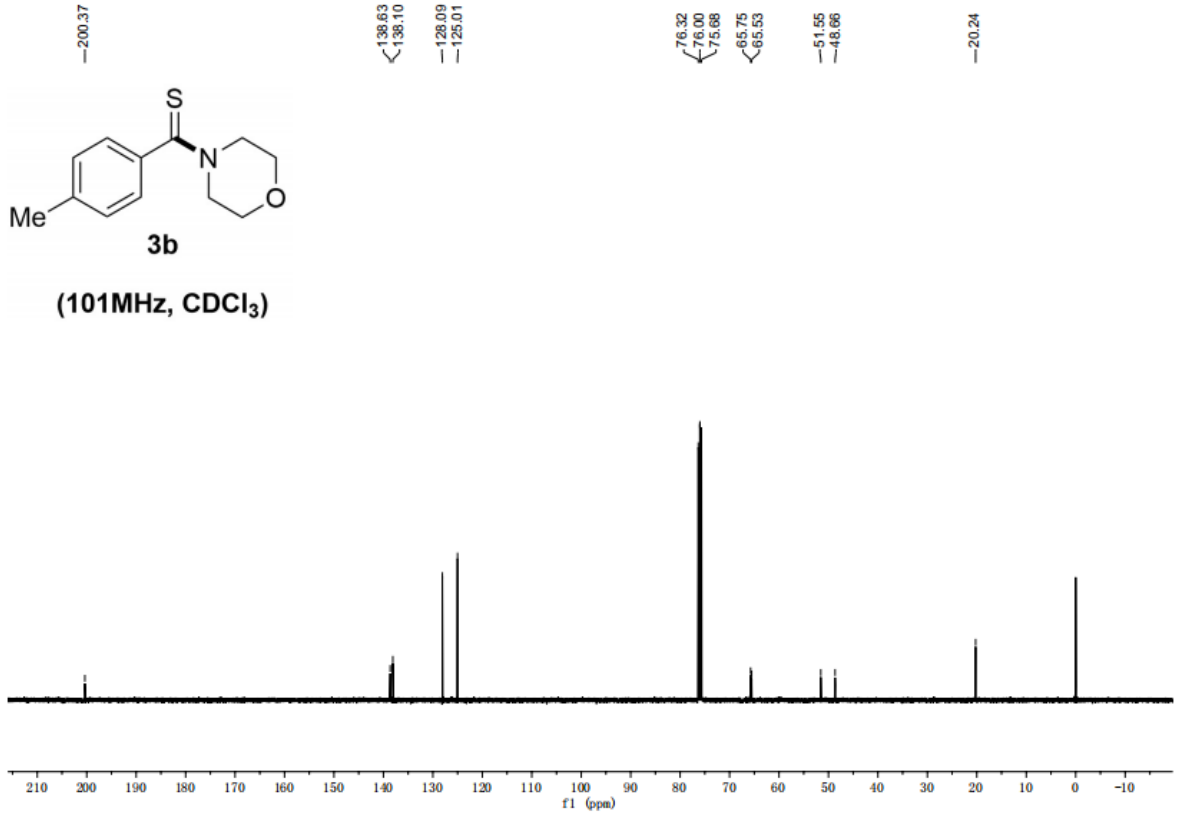
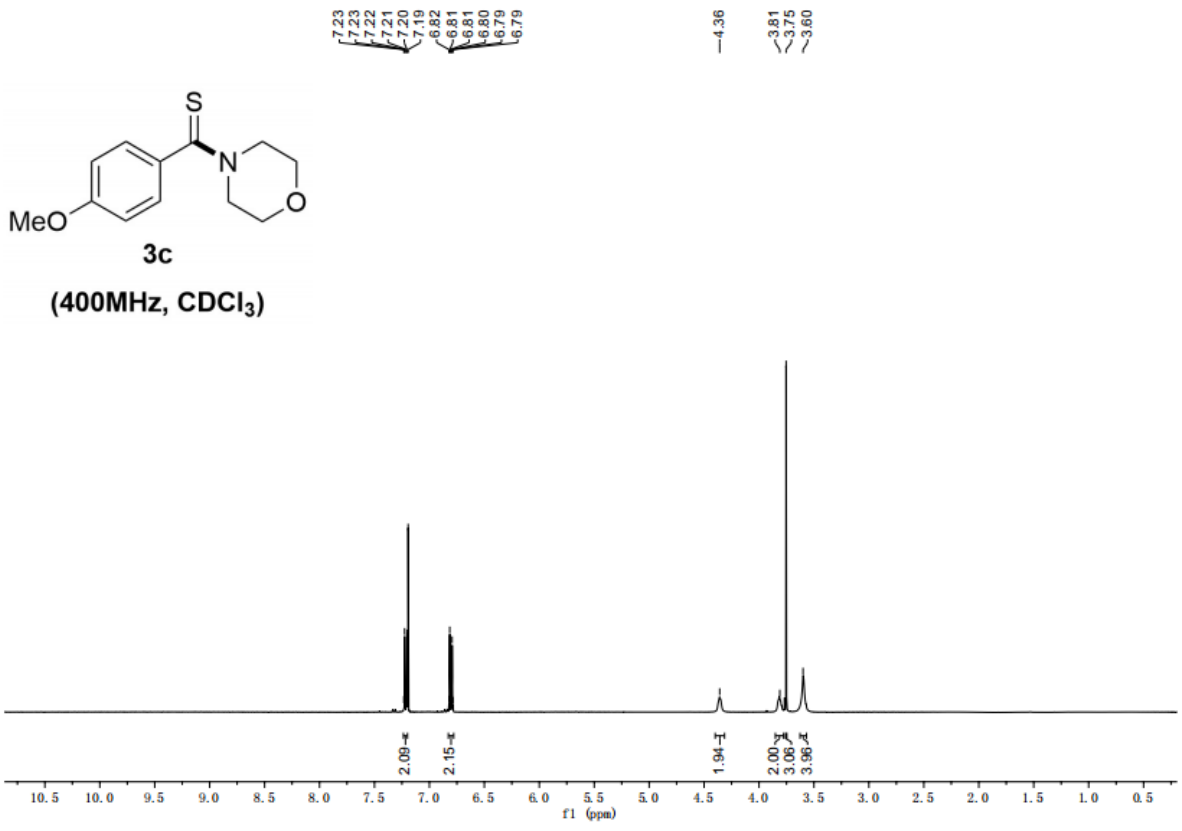
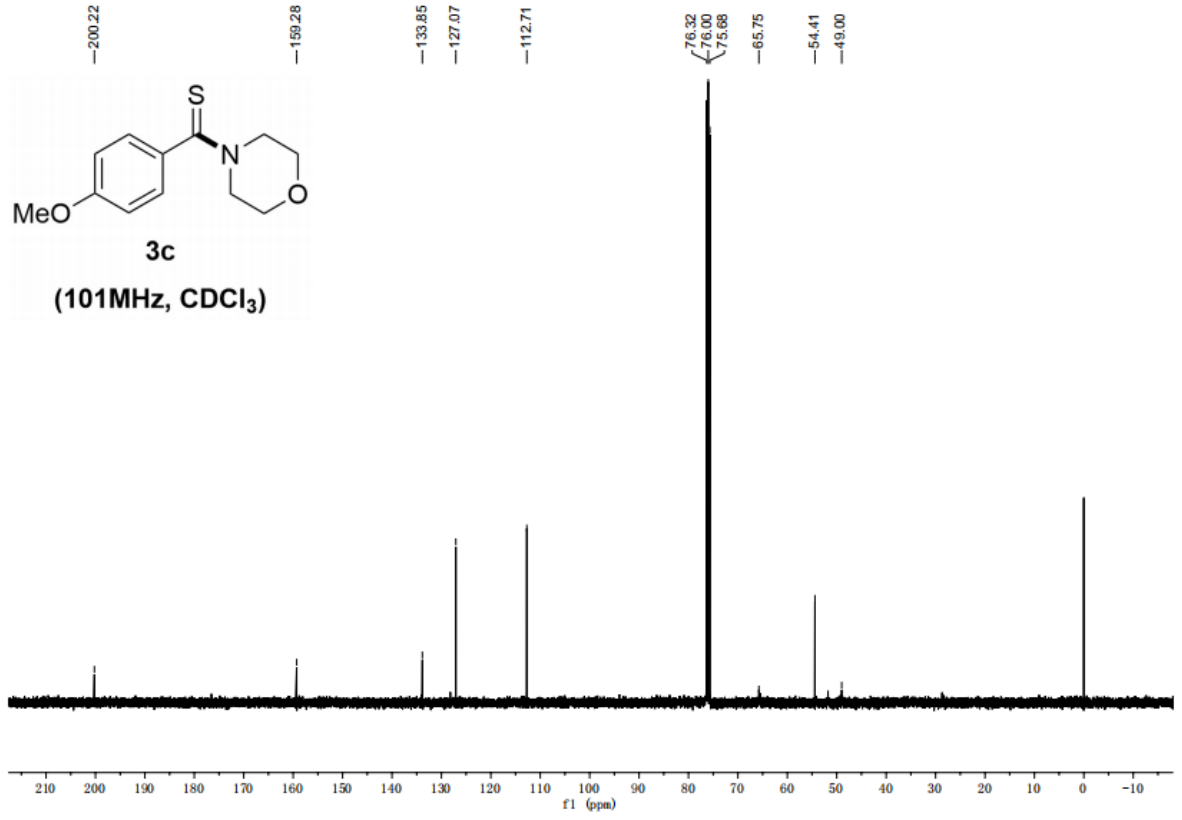

7.32
7.31
7.30
7.29
7.28
7.27
7.23
7.22
7.21
7.21
7.21
7.20
7.19
4.39
4.38
4.37
3.84
3.82
3.81
3.59
3.58
3.57
3.55
3.53
3.52
S
N
O
3a
(400MHz, CDCl3)
3.12
2.00
2.25
2.00
4.22
f1 (ppm)

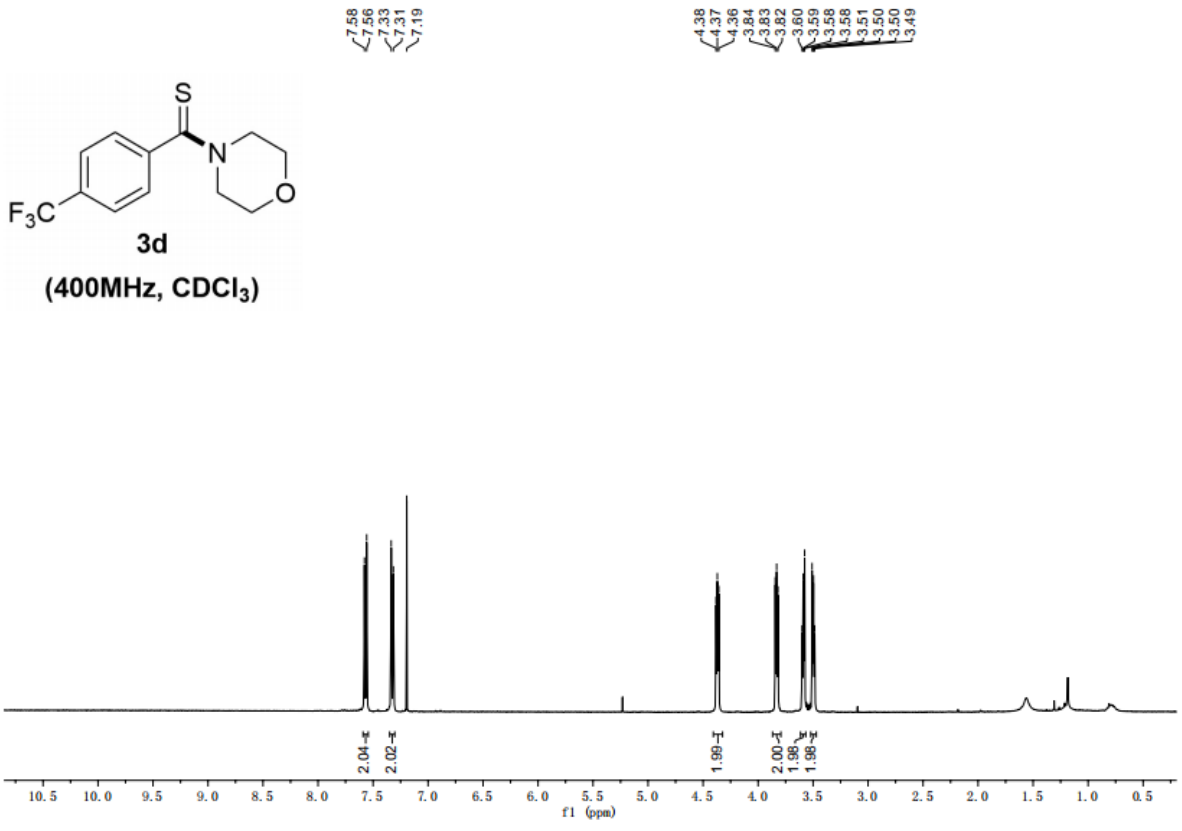

200.01
141.43
127.86
127.53
124.85
76.32
76.00
75.68
65.73
65.52
51.49
48.51
S
N
O
3a
(101MHz, CDCl3)
f1 (ppm)

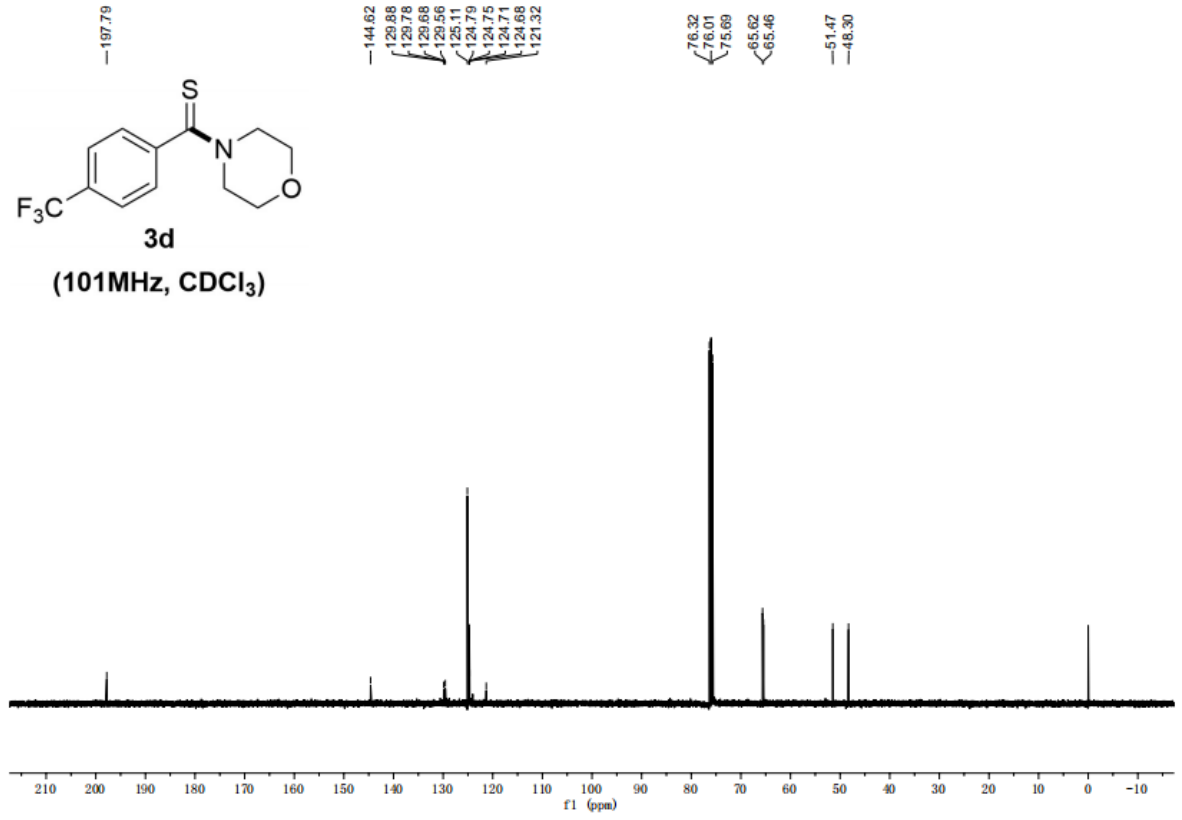

7.19
7.14
7.13
7.13
7.12
7.12
7.10
7.09
7.08
4.38
4.37
4.35
3.83
3.81
3.80
3.57
2.28
S
N
O
Me
3b
(400MHz, CDCl3)
4.24
2.11
2.00
4.24
3.13
f1 (ppm)


200.37
138.63
138.10
128.09
125.01
76.32
76.00
75.68
65.75
65.53
51.55
48.66
20.24
S
N
O
Me
3b
(101MHz, CDCl3)
f1 (ppm)


7.23
7.23
7.22
7.21
7.20
7.19
6.82
6.81
6.81
6.80
6.79
6.79
4.36
3.81
3.75
3.60
S
N
O
MeO
3c
(400MHz, CDCl3)
2.09
2.15
1.94
2.00
3.06
3.96
f1 (ppm)


200.22
159.28
133.85
127.07
112.71
76.32
76.00
75.68
65.75
54.41
49.00
S
N
O
MeO
3c
(101MHz, CDCl3)
f1 (ppm)


7.58
7.56
7.33
7.31
7.19
4.38
4.37
4.36
3.84
3.83
3.82
3.60
3.59
3.58
3.58
3.51
3.50
3.50
3.49
S
N
O
F3C
3d
(400MHz, CDCl3)
2.04
2.02
1.99
2.00
1.98
1.98
f1 (ppm)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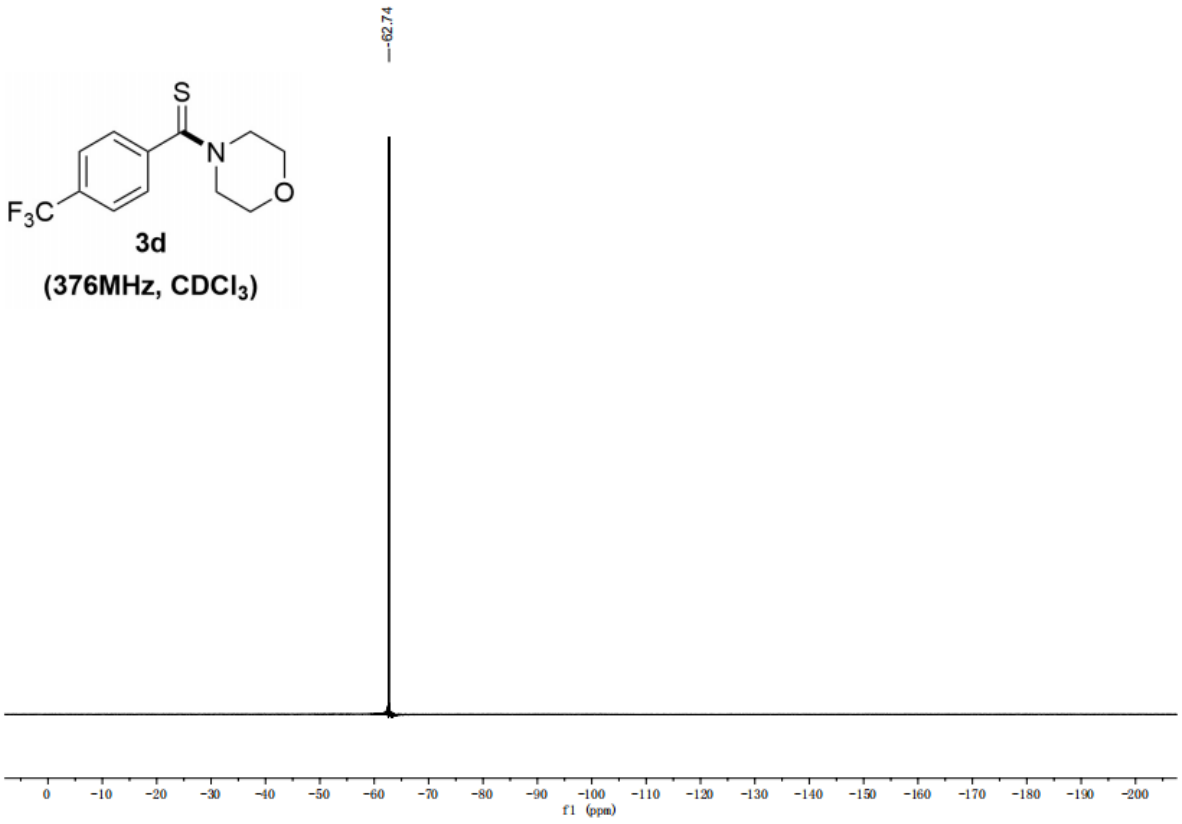
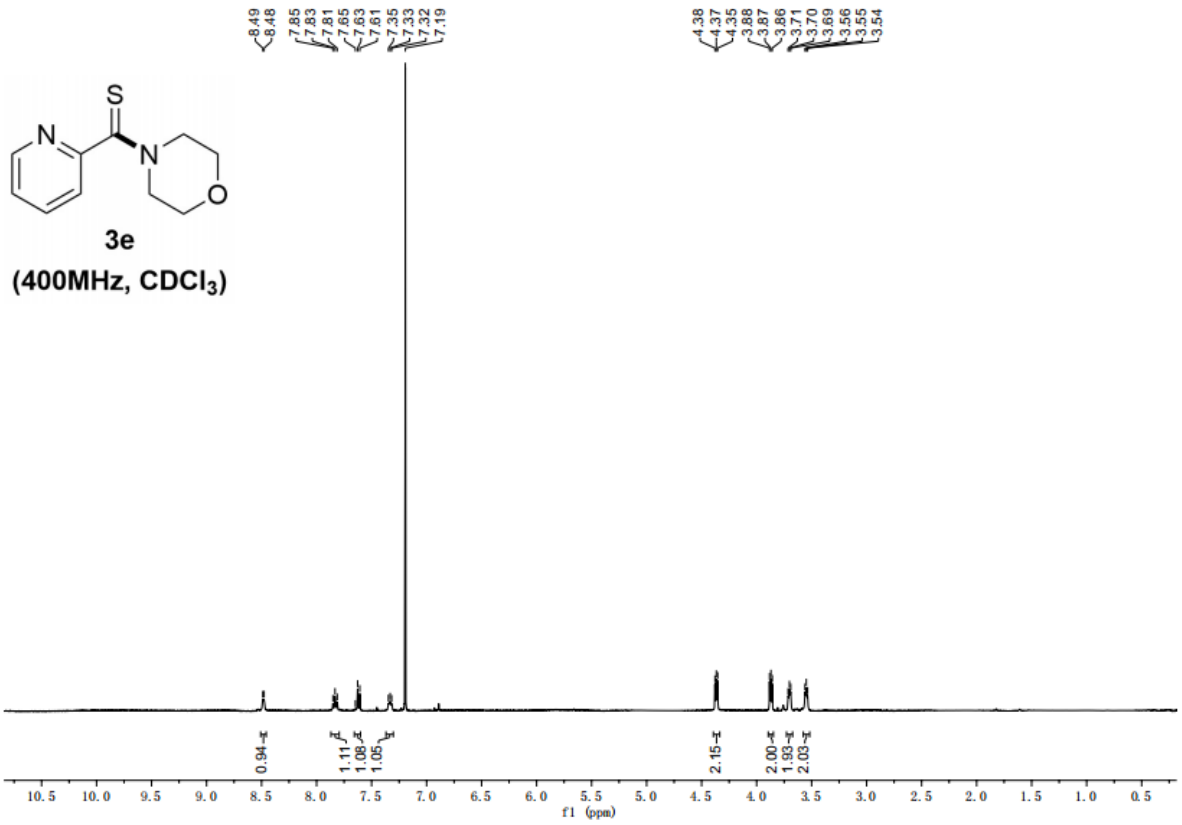
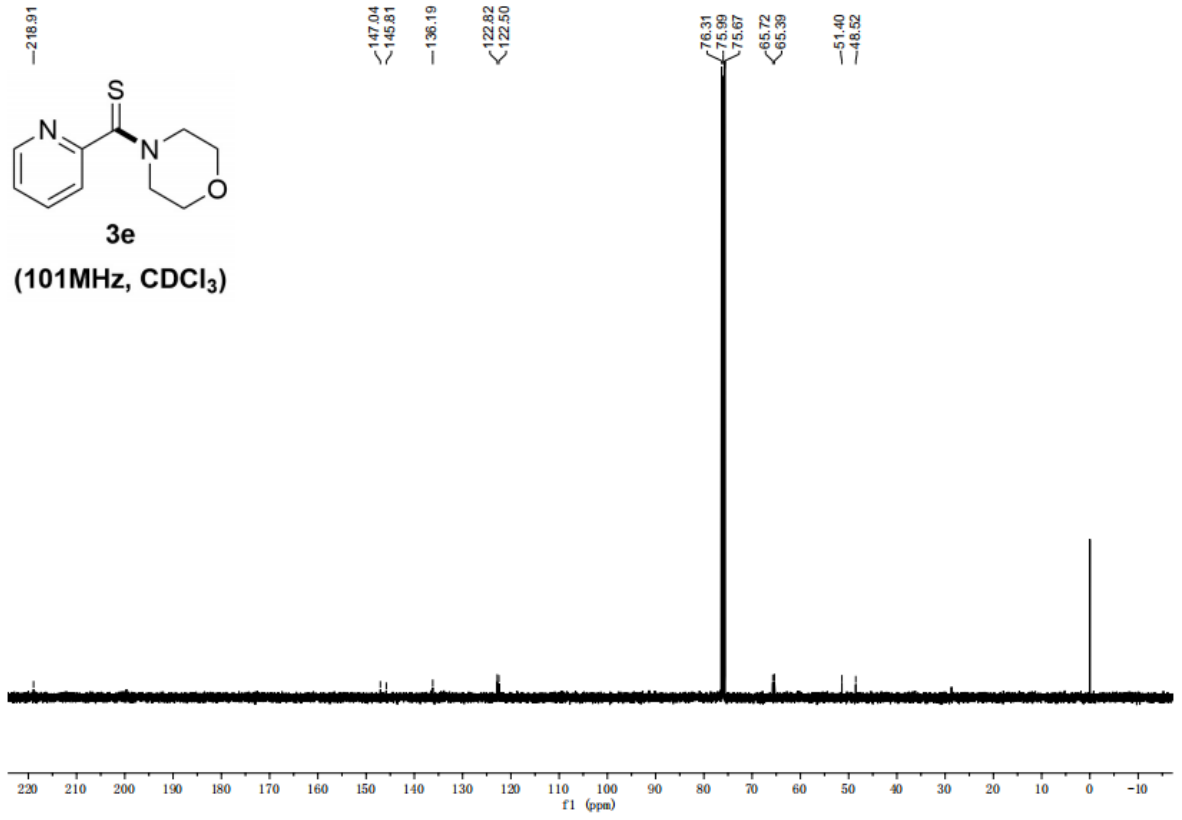
144.62
129.88
129.78
129.68
129.56
125.11
124.79
124.75
124.71
124.68
121.32
76.32
76.01
75.69
65.62
65.46
51.47
48.30
S
N
O
F3C
3d
(101MHz, CDCl3)
f1 (ppm)


S
N
O
F_3C
3d
(376MHz, $CDCl_3$)
-62.74
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)


8.49
8.48
7.85
7.83
7.81
7.65
7.63
7.61
7.35
7.33
7.32
7.19
4.38
4.37
4.35
3.88
3.87
3.86
3.71
3.70
3.69
3.56
3.55
3.54
S
N
N
O
3e
(400MHz, CDCl3)
0.94
1.11
1.08
1.05
2.15
2.00
1.93
2.03
f1 (ppm)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122.50
76.31
75.99
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65.39
51.40
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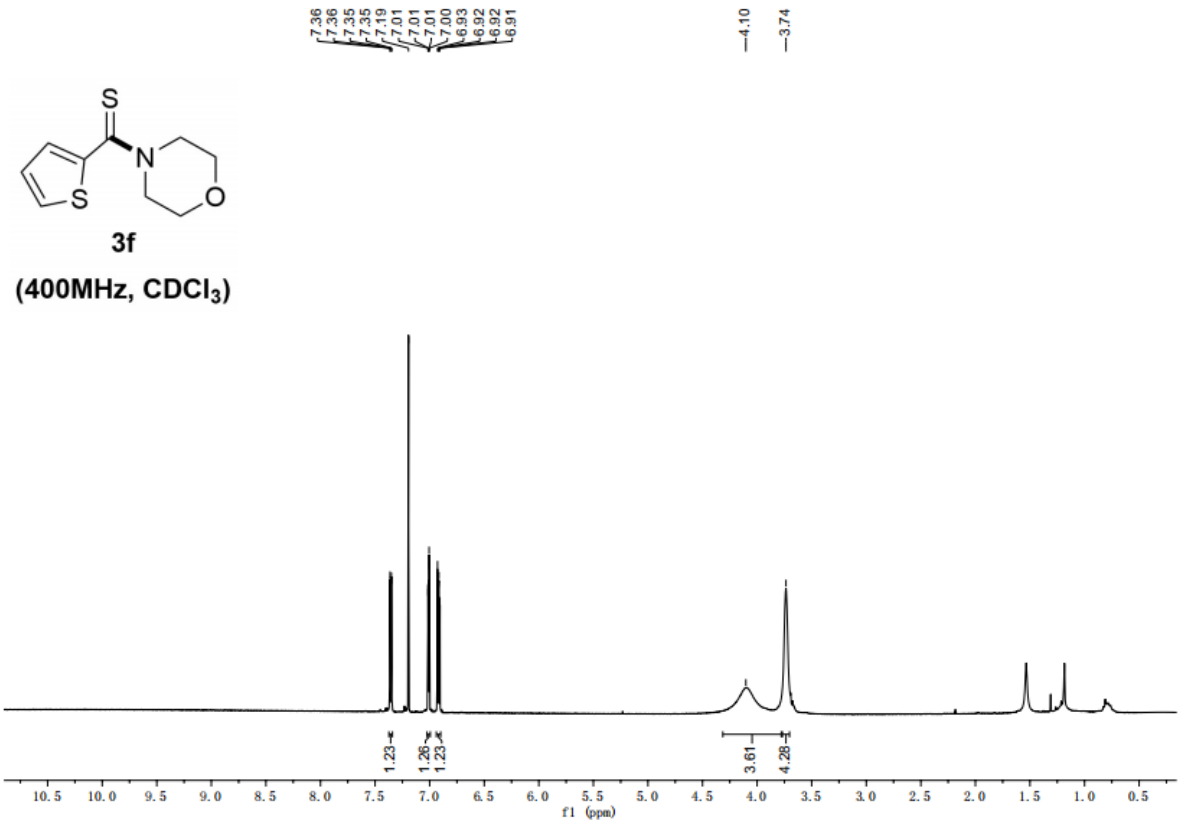
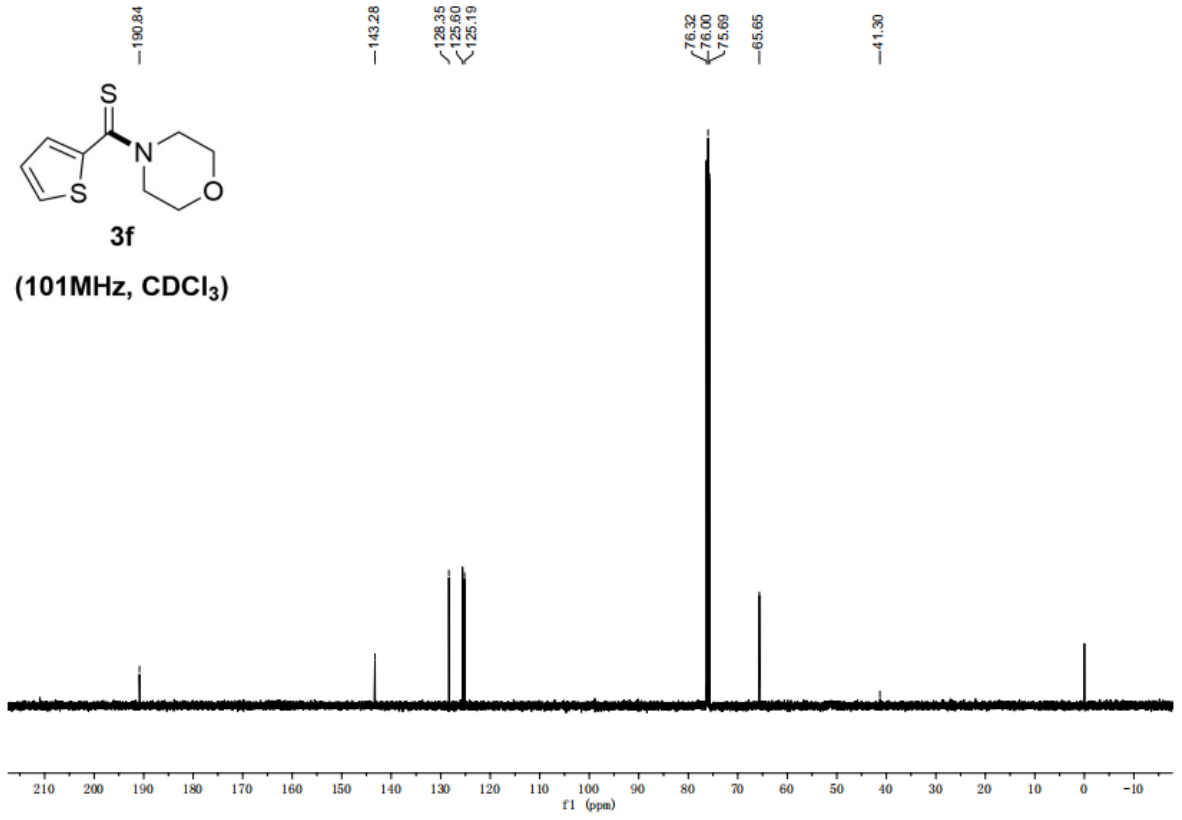
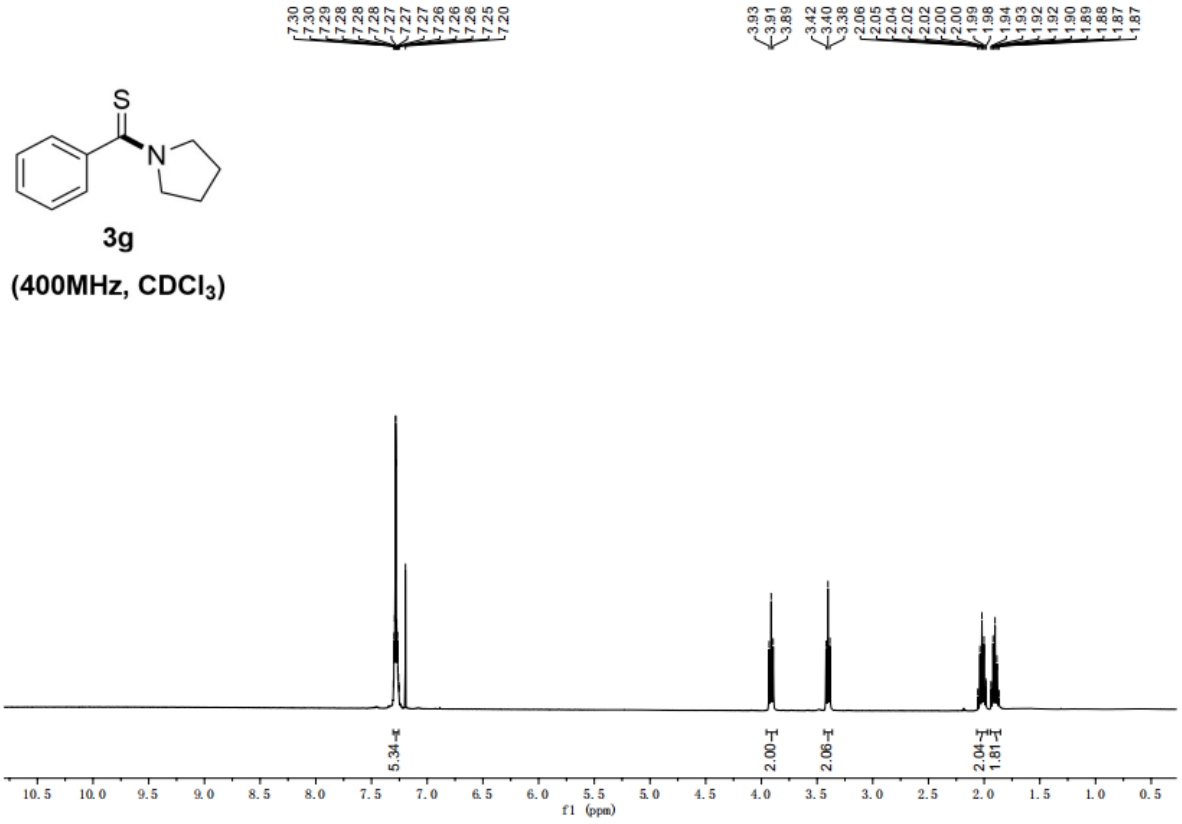
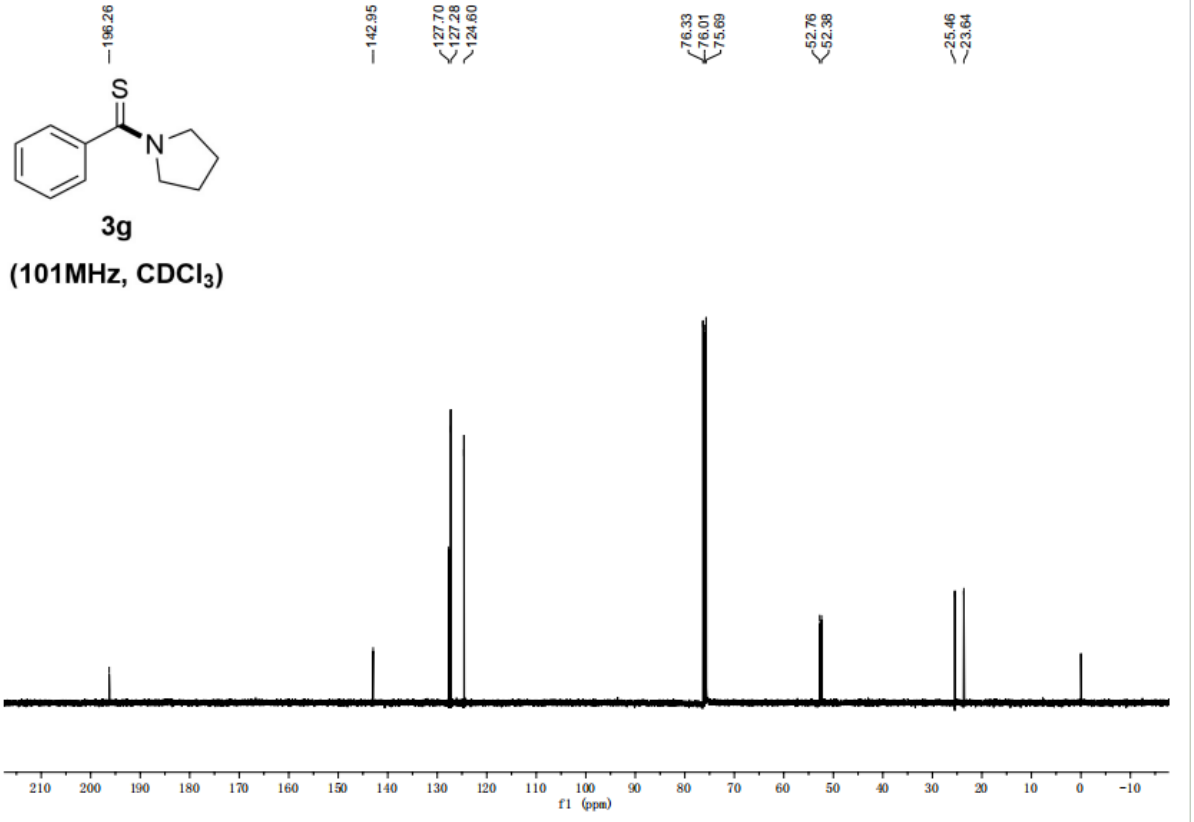
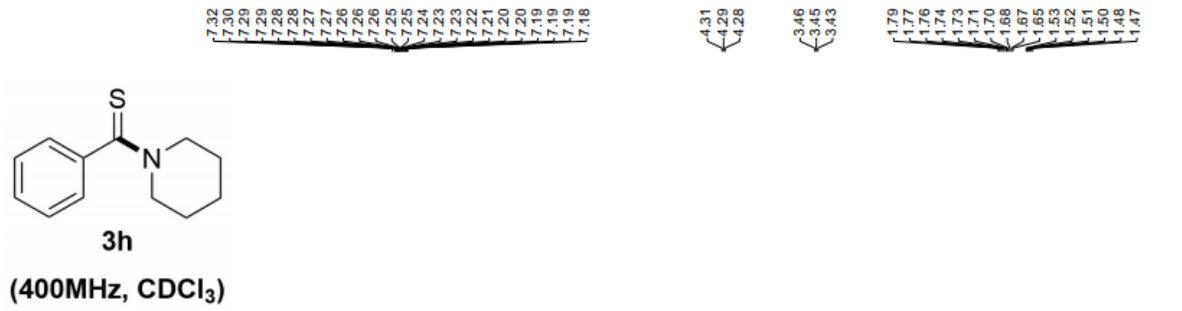
N
N
O
3e
(101MHz, CDCl3)
f1 (ppm)


7.36
7.36
7.35
7.35
7.19
7.01
7.01
7.01
7.00
6.93
6.92
6.92
6.91
4.10
3.74
S
N
O
S
3f
(400MHz, CDCl3)
1.23
1.26
1.23
3.61
4.28
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


190.84
143.28
128.35
125.60
125.19
76.32
76.00
75.69
65.65
41.30
S
N
O
S
3f
(101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

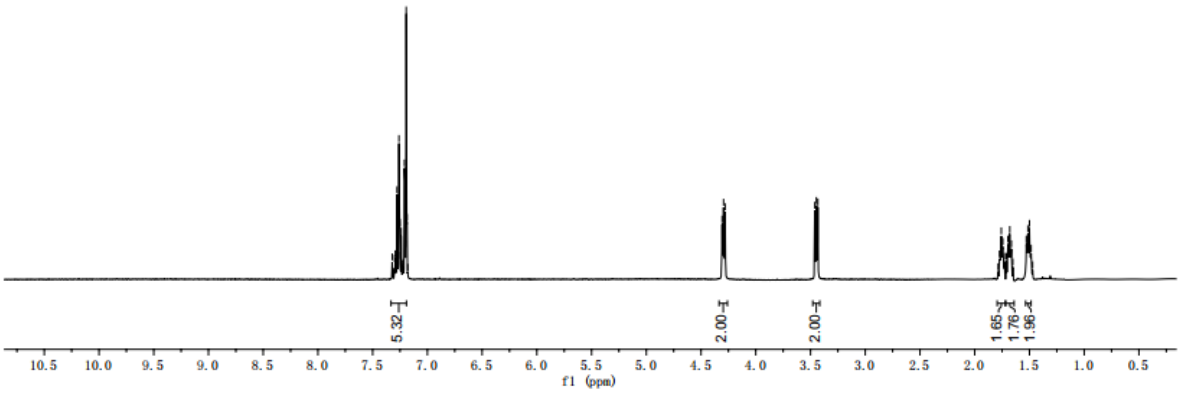

7.30
7.30
7.29
7.28
7.28
7.28
7.27
7.27
7.27
7.26
7.26
7.26
7.25
7.20
3.93
3.91
3.89
3.42
3.40
3.38
2.06
2.05
2.04
2.02
2.02
2.00
2.00
1.99
1.98
1.94
1.93
1.92
1.92
1.90
1.89
1.88
1.87
1.87
S
N
3g
(400MHz, CDCl3)
5.34
2.00
2.06
2.04
1.81
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

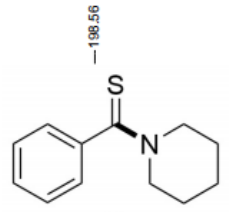

196.26
142.95
127.70
127.28
124.60
76.33
76.01
75.69
52.76
52.38
25.46
23.64
S
N
3g
(101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



3h

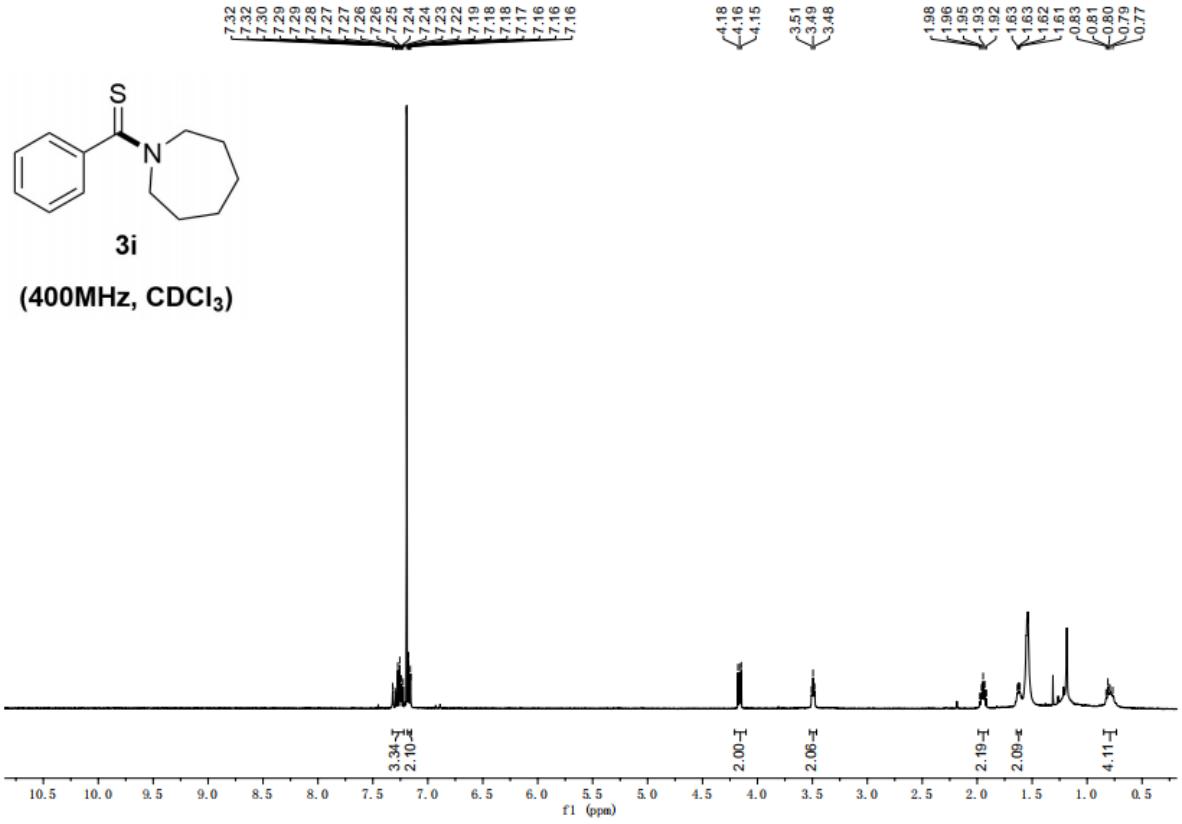
(400MHz, $CDCl_3$)

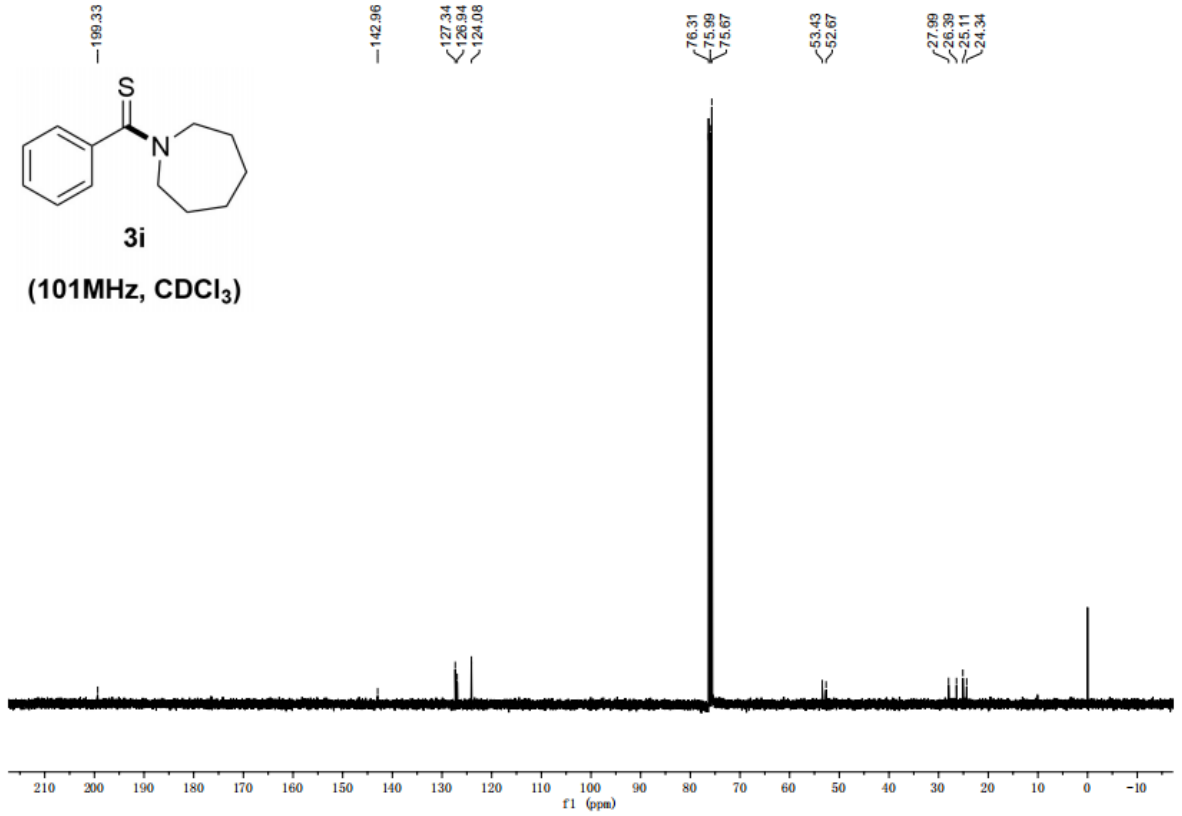


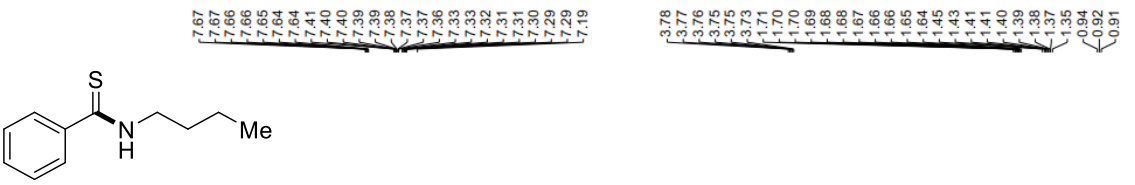


3h

(101MHz, $CDCl_3$)

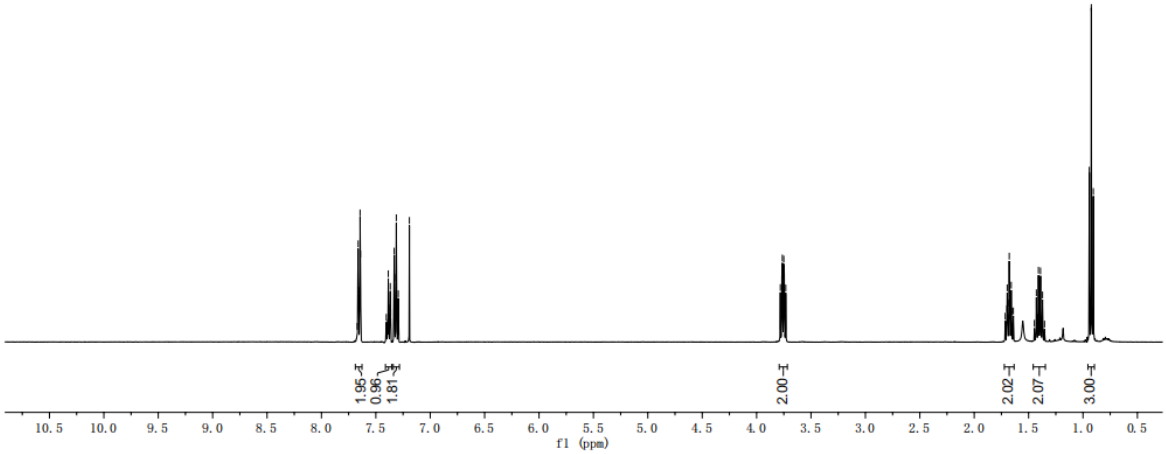

3i
(400MHz, CDCl3)
f1 (ppm)

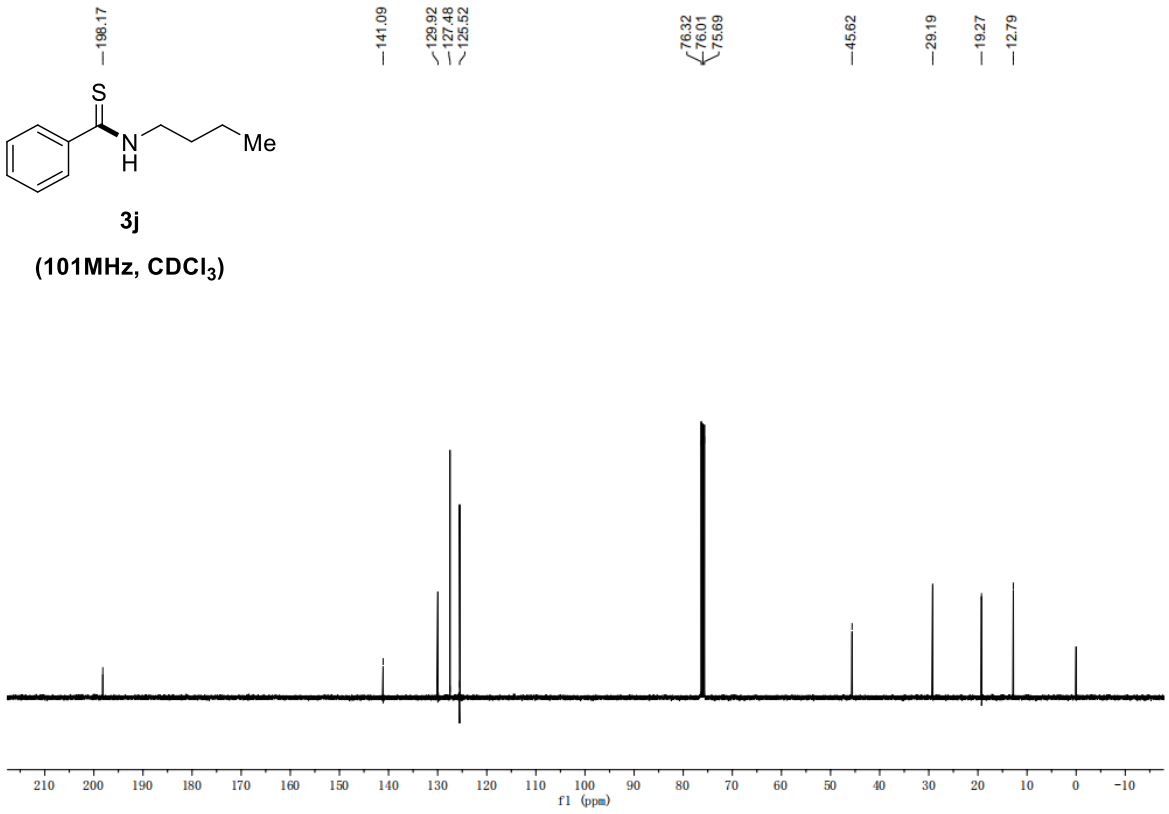

3i
(101MHz, CDCl3)
f1 (ppm)



3j

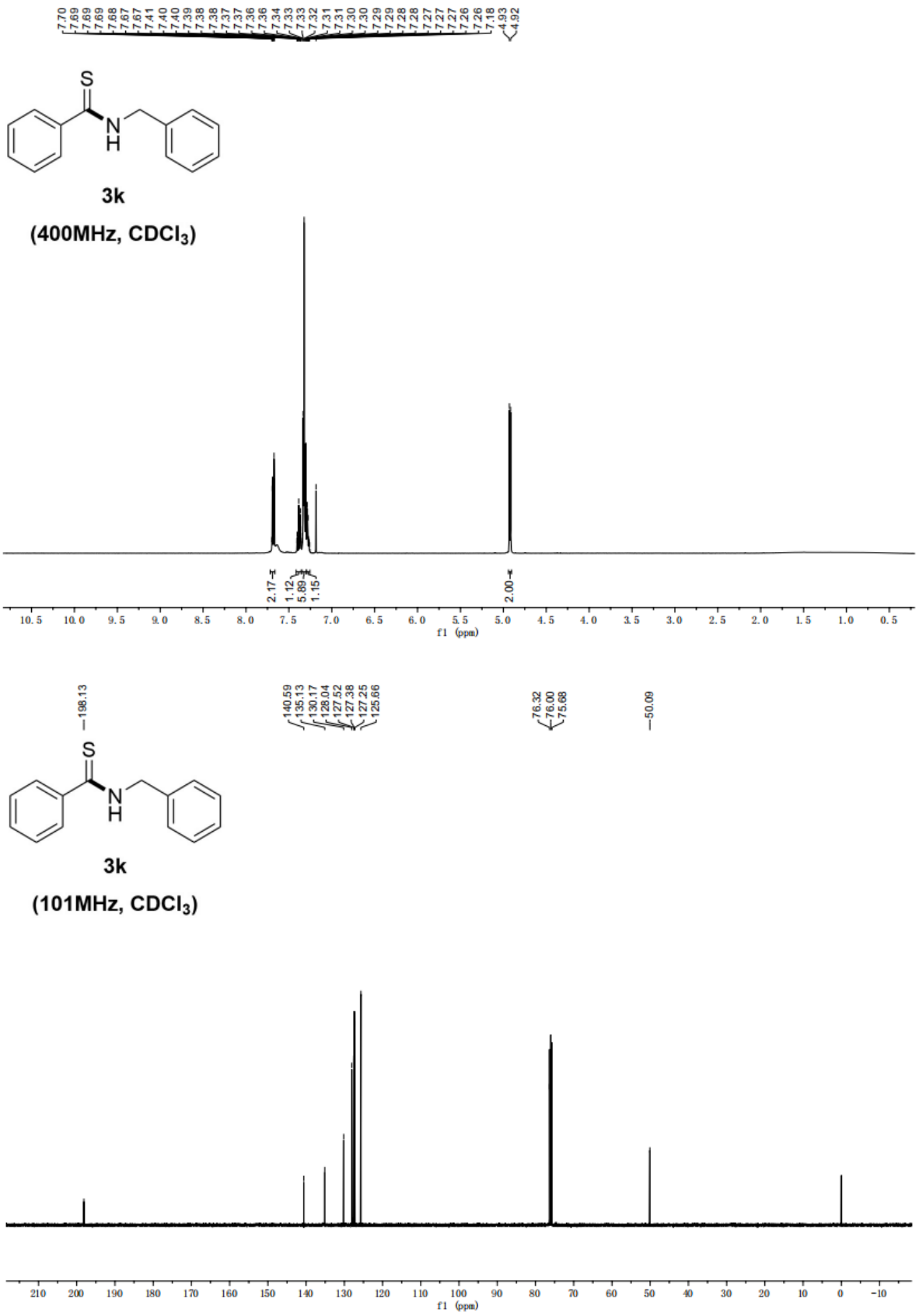
(400MHz, $CDCl_3$)

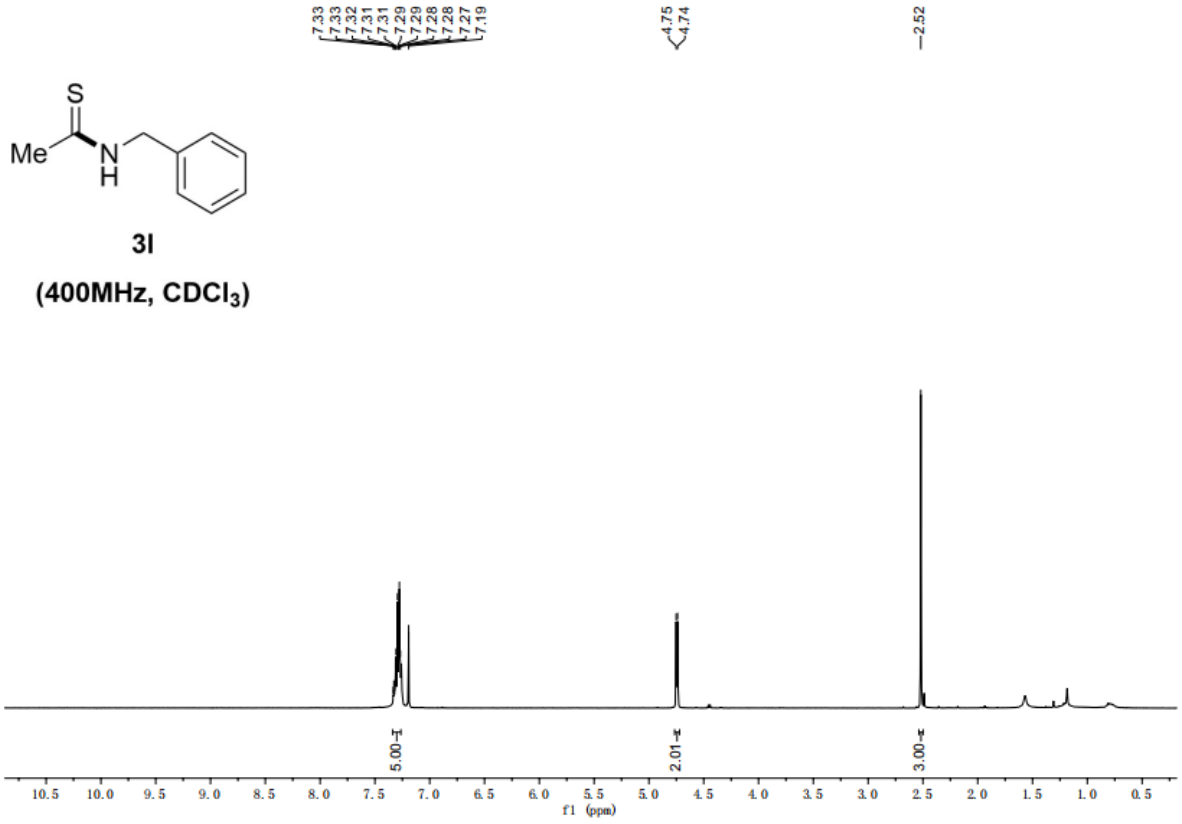




3j

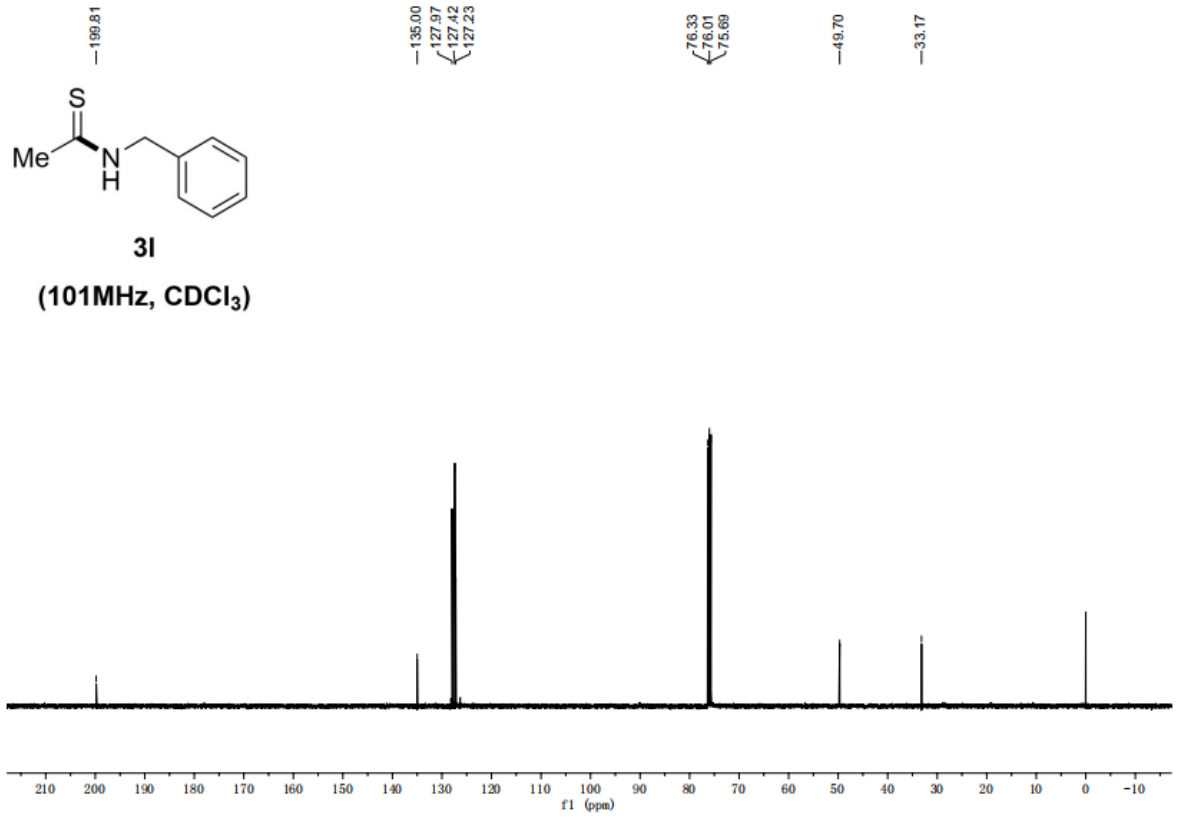
(101MHz, $CDCl_3$)


7.70
7.69
7.69
7.69
7.68
7.67
7.67
7.41
7.40
7.40
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.34
7.33
7.33
7.32
7.31
7.31
7.30
7.30
7.29
7.29
7.28
7.28
7.27
7.27
7.27
7.26
7.26
7.18
4.93
4.92
S
N
H
3k
(400MHz, CDCl3)
2.17
1.12
5.89
1.15
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
198.13
140.59
135.13
130.17
128.04
127.52
127.38
127.25
125.66
76.32
76.00
75.68
50.09
S
N
H
3k
(101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



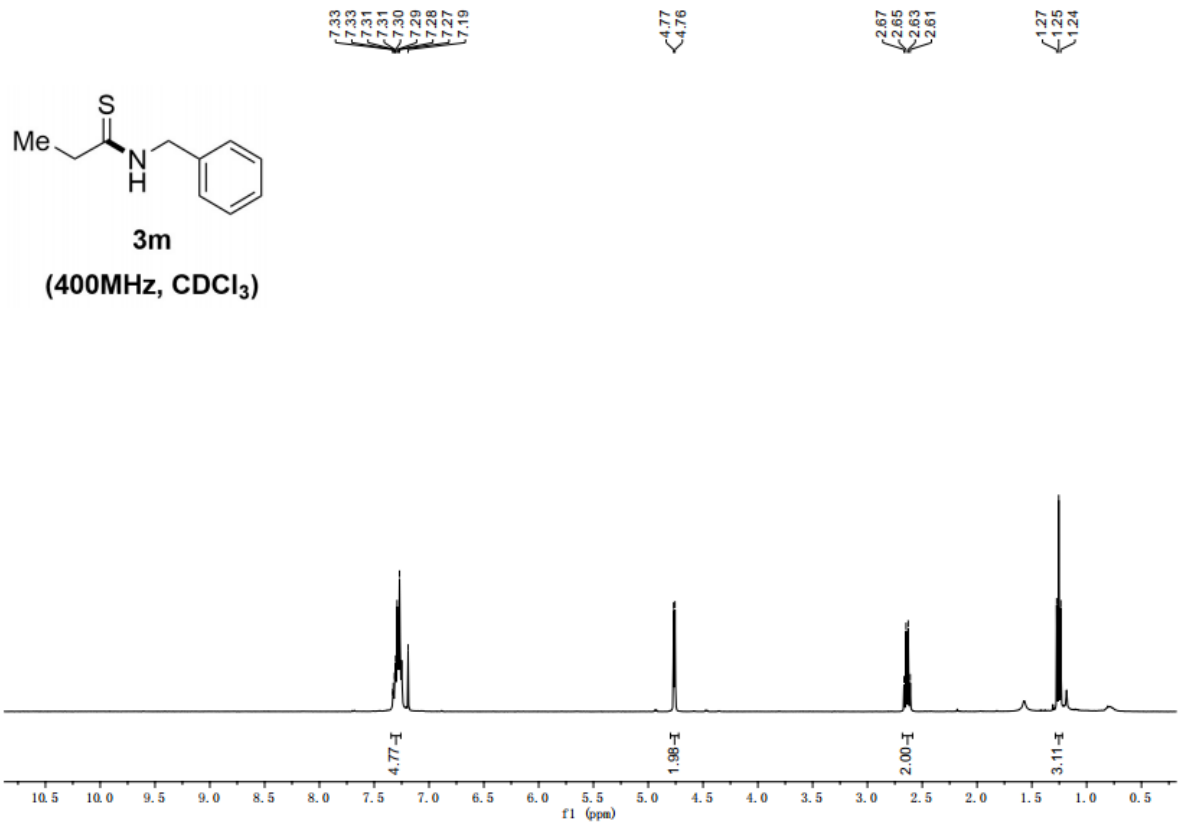
3l

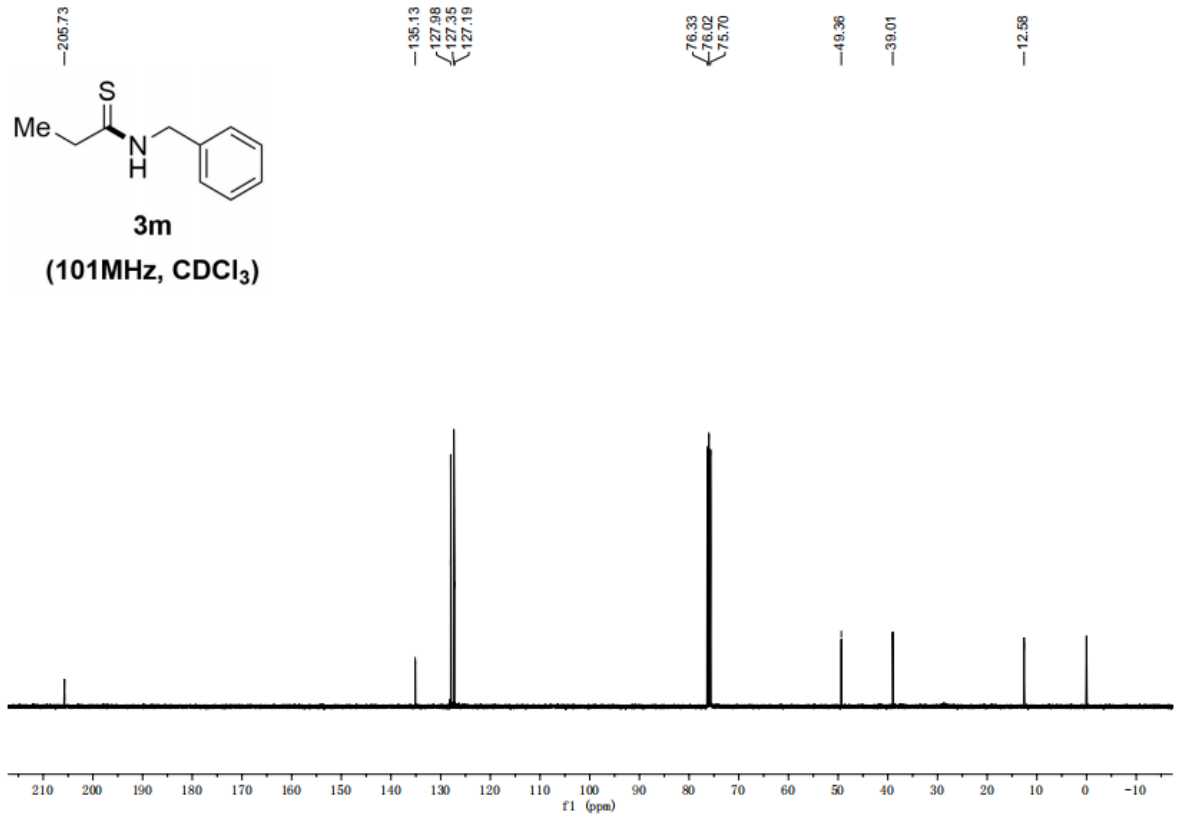
(400MHz, $CDCl_3$)

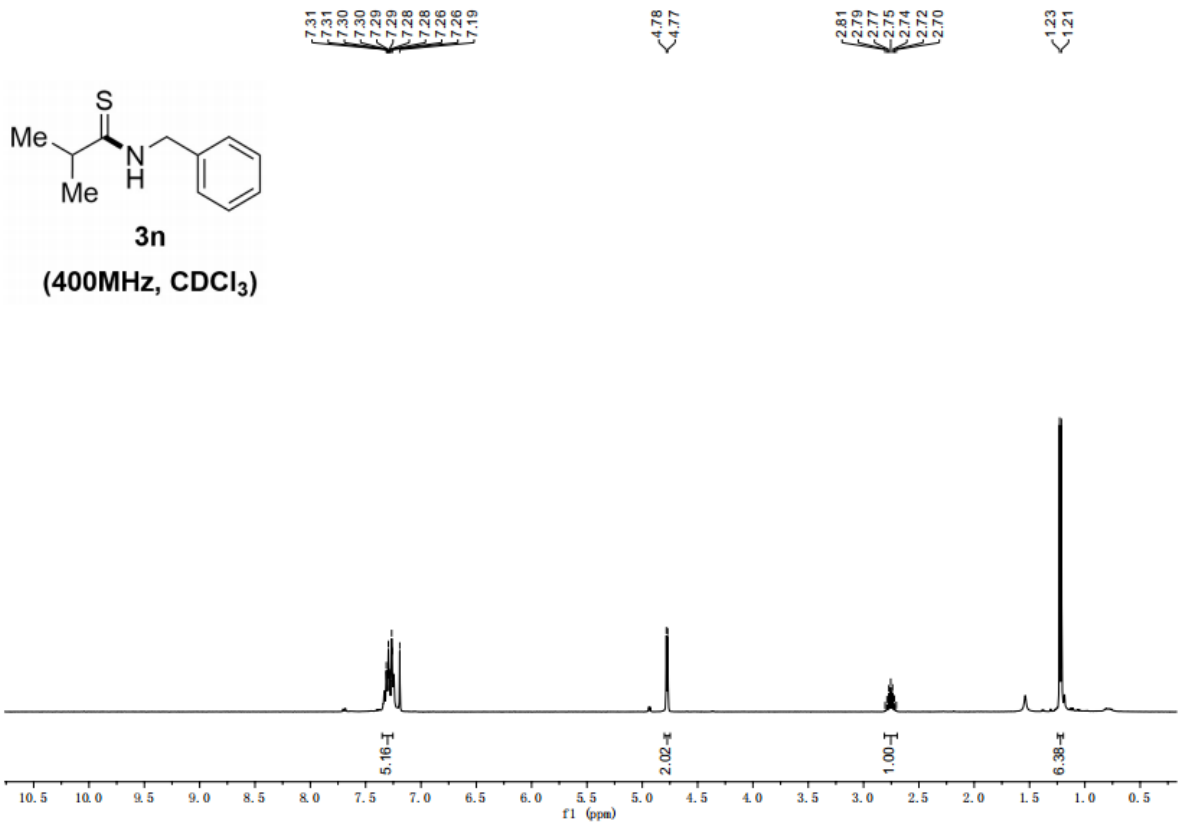


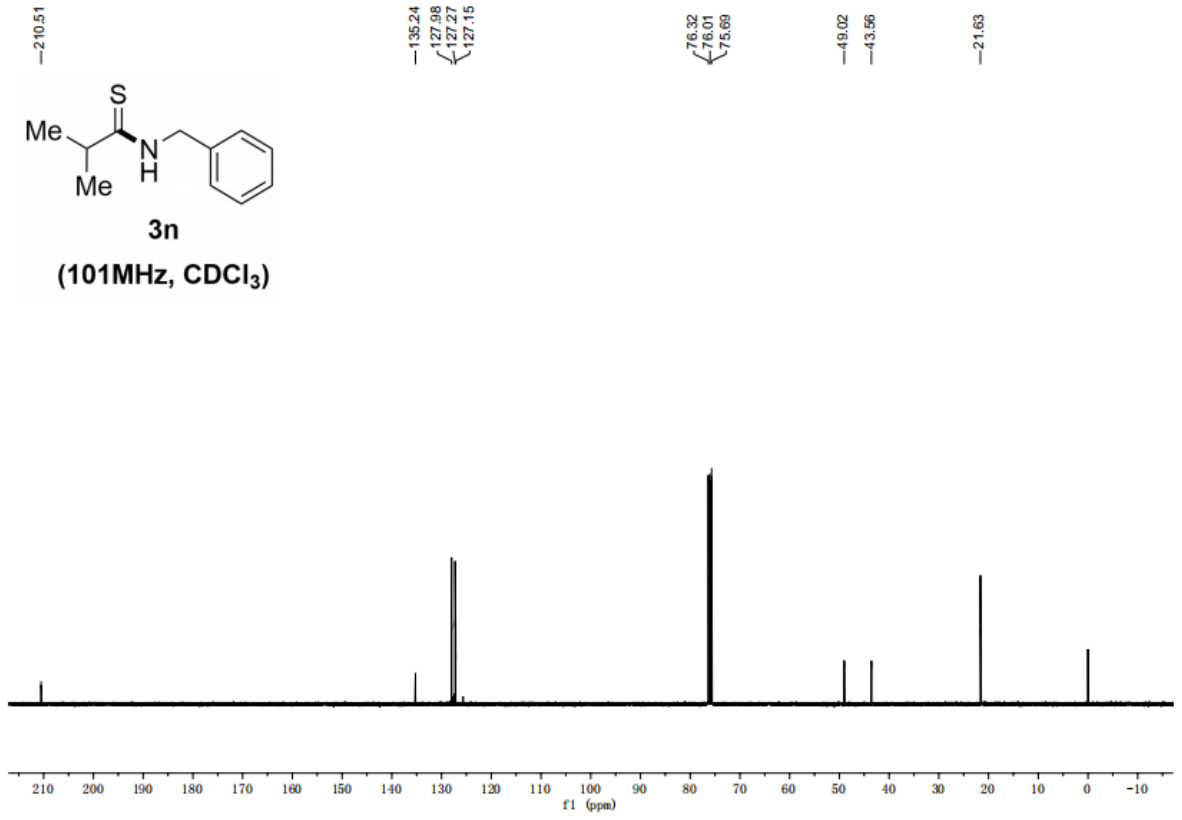
3l

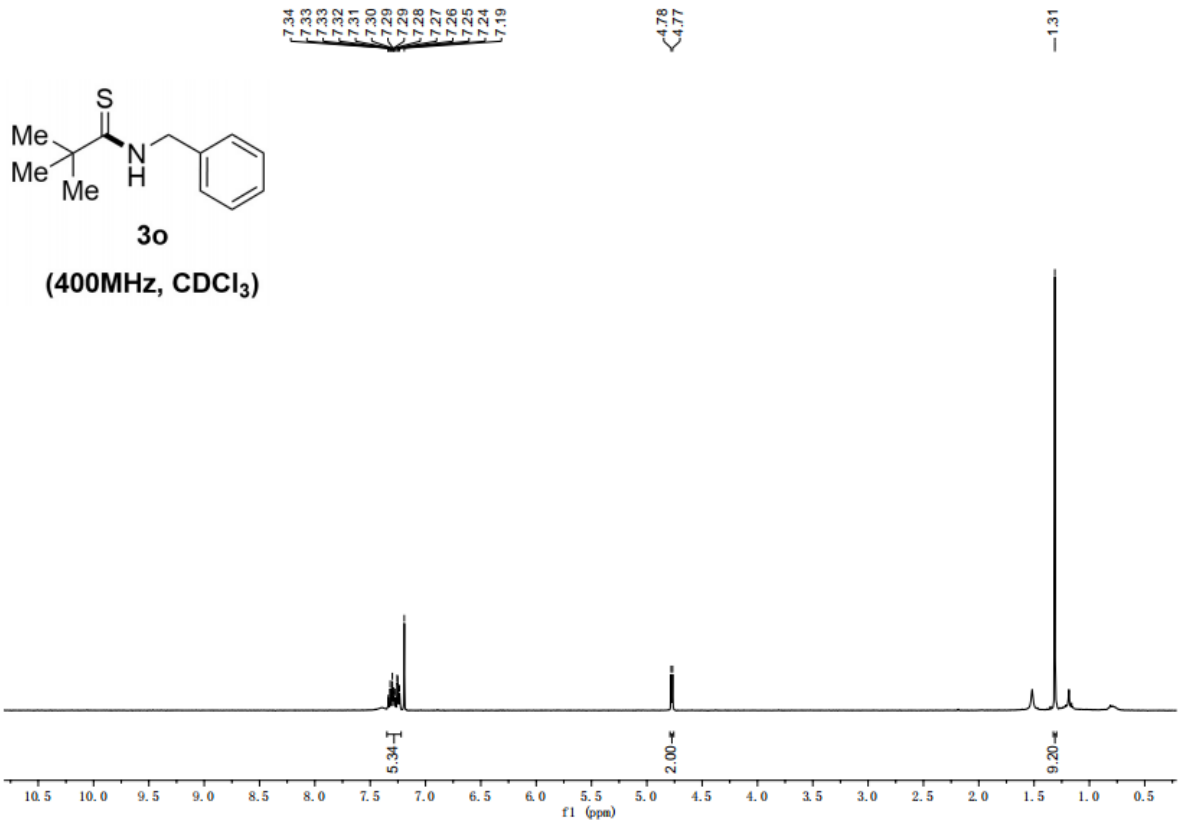
(101MHz, $CDCl_3$)

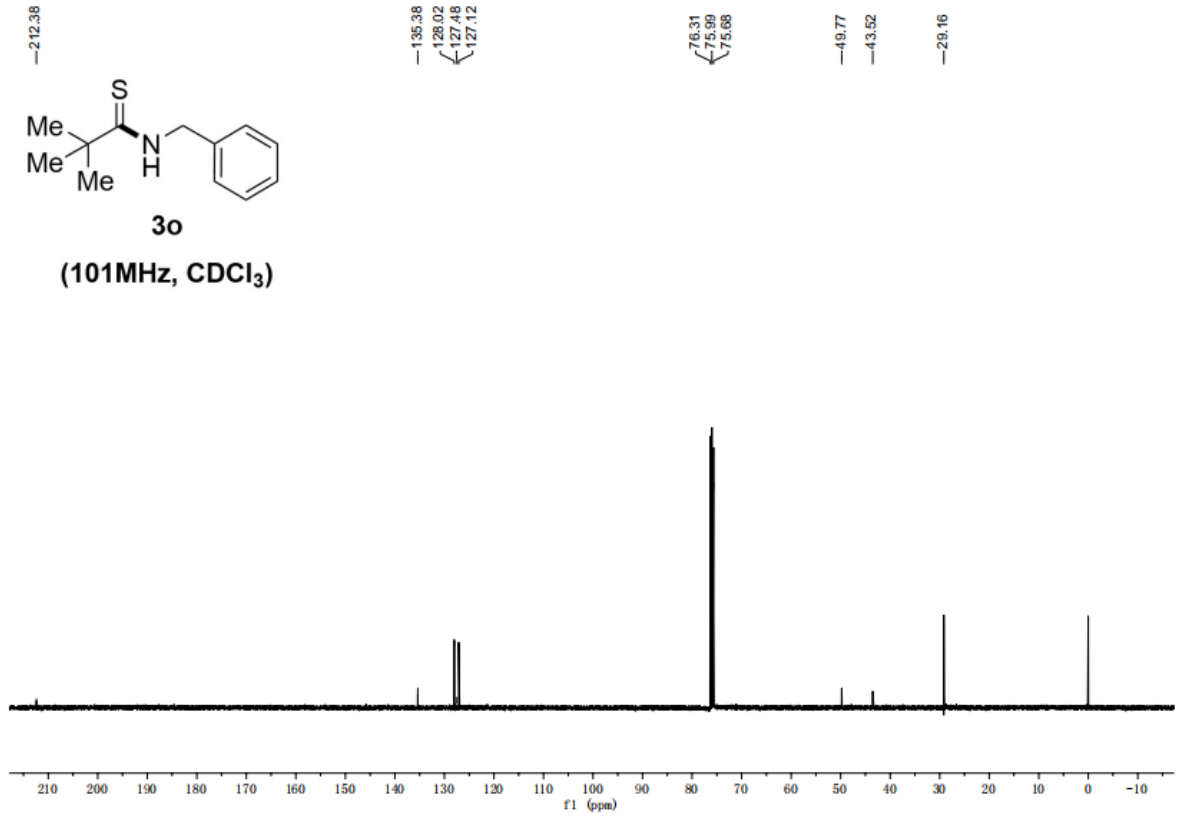

7.33
7.33
7.31
7.31
7.30
7.29
7.28
7.27
7.19
4.77
4.76
2.67
2.65
2.63
2.61
1.27
1.25
1.24
S
Me
N
H
3m
(400MHz, CDCl3)
4.77
1.98
2.00
3.11
f1 (ppm)

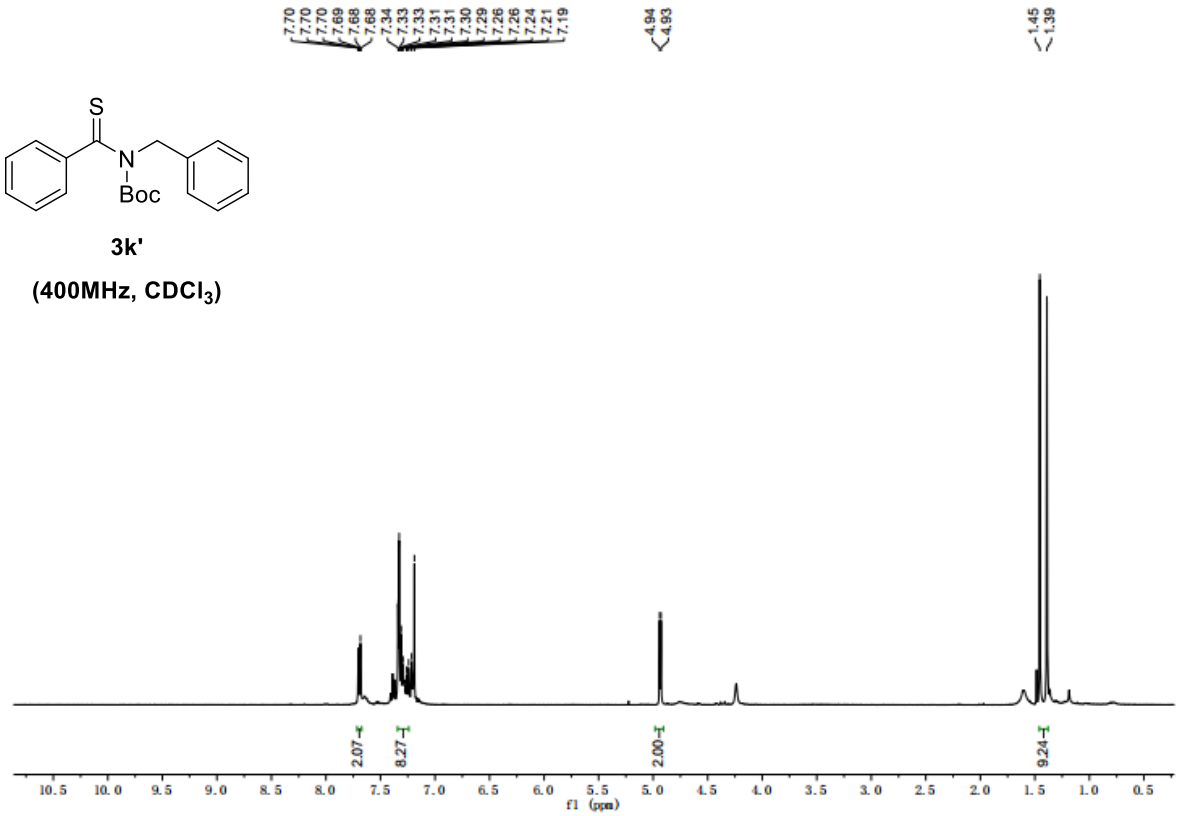

205.73
135.13
127.98
127.35
127.19
76.33
76.02
75.70
49.36
39.01
12.58
S
Me
N
H
3m
(101MHz, CDCl3)
f1 (ppm)


7.31
7.31
7.30
7.30
7.29
7.29
7.28
7.28
7.26
7.26
7.19
4.78
4.77
2.81
2.79
2.77
2.75
2.74
2.72
2.70
1.23
1.21
S
Me
N
H
Me
3n
(400MHz, CDCl3)
5.16
2.02
1.00
6.38
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


210.51
135.24
127.98
127.27
127.15
76.32
76.01
75.69
49.02
43.56
21.63
S
Me
N
H
Me
3n
(101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

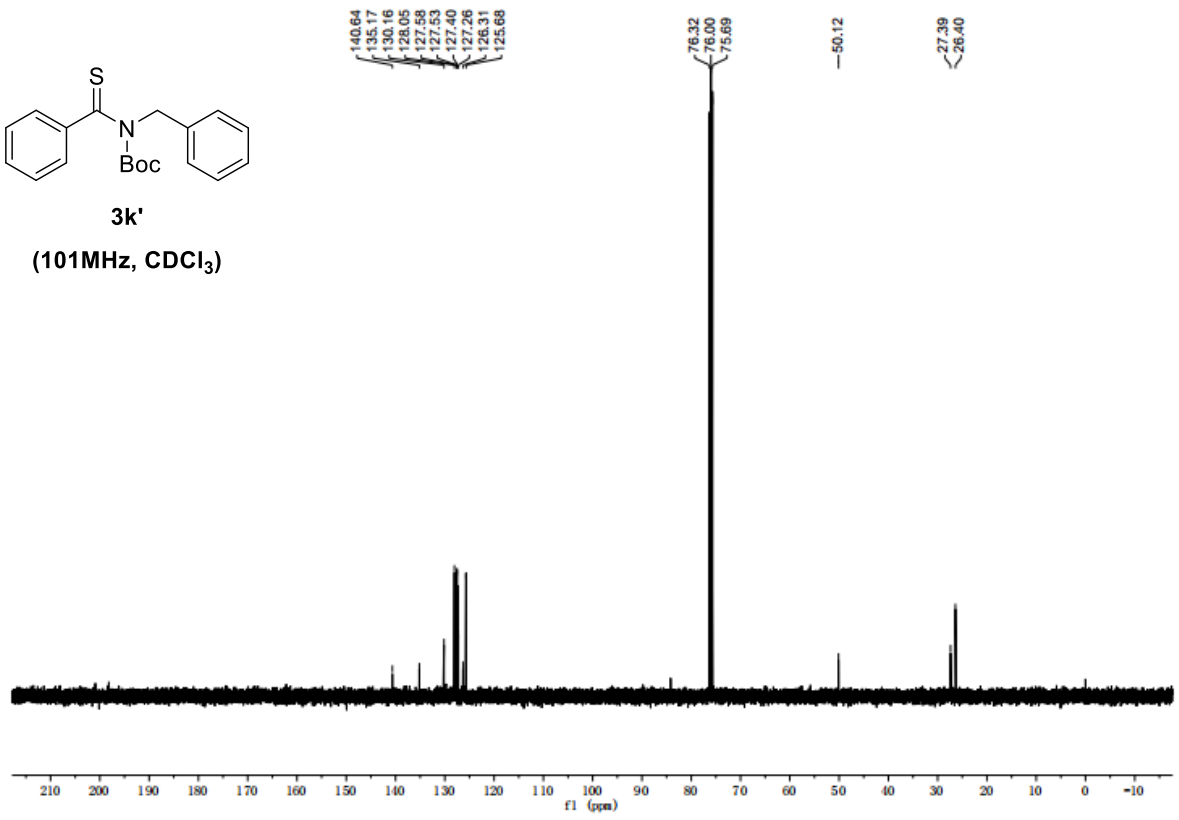

7.34
7.33
7.33
7.32
7.31
7.30
7.29
7.29
7.28
7.27
7.26
7.25
7.24
7.19
4.78
4.77
1.31
S
Me
Me
Me
N
H
3o
(400MHz, CDCl3)
5.34
2.00
9.20
f1 (ppm)


212.38
135.38
128.02
127.48
127.12
76.31
75.99
75.68
49.77
43.52
29.16
S
Me
Me
Me
N
H
3o
(101MHz, CDCl3)
f1 (ppm)



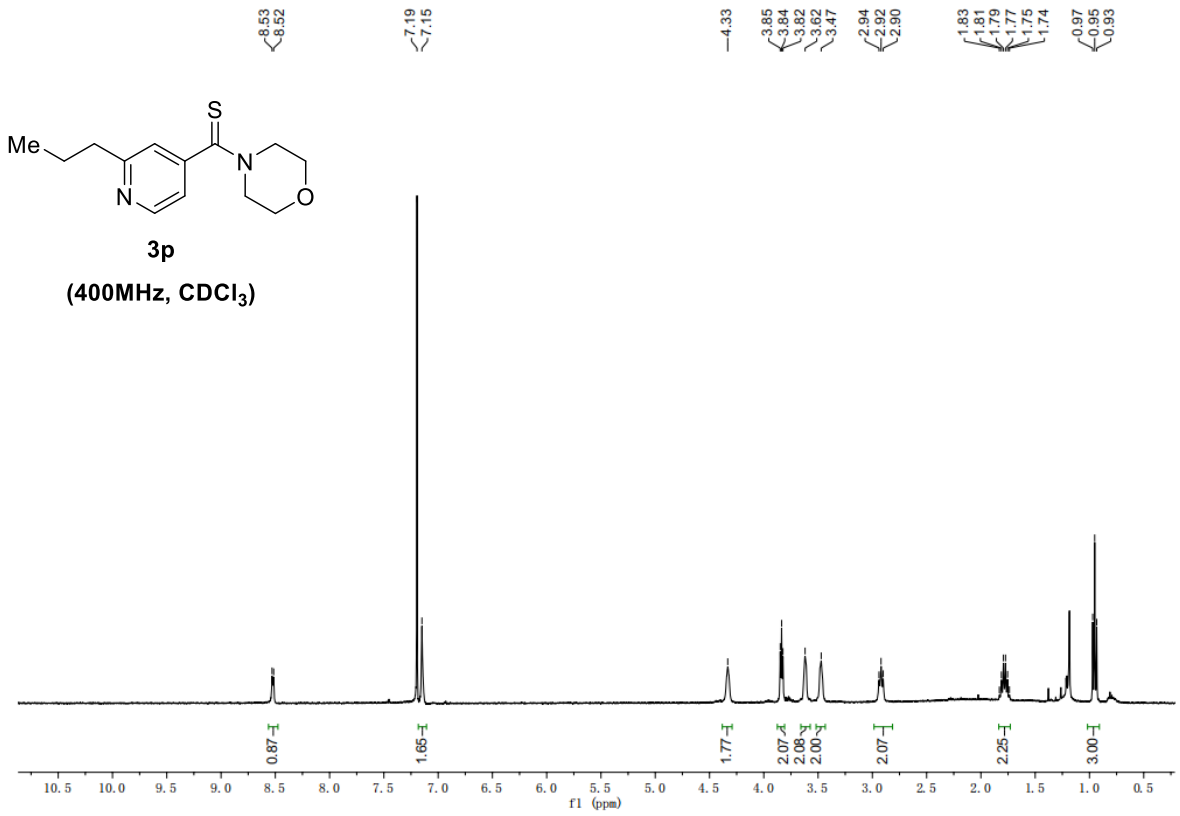
3k'

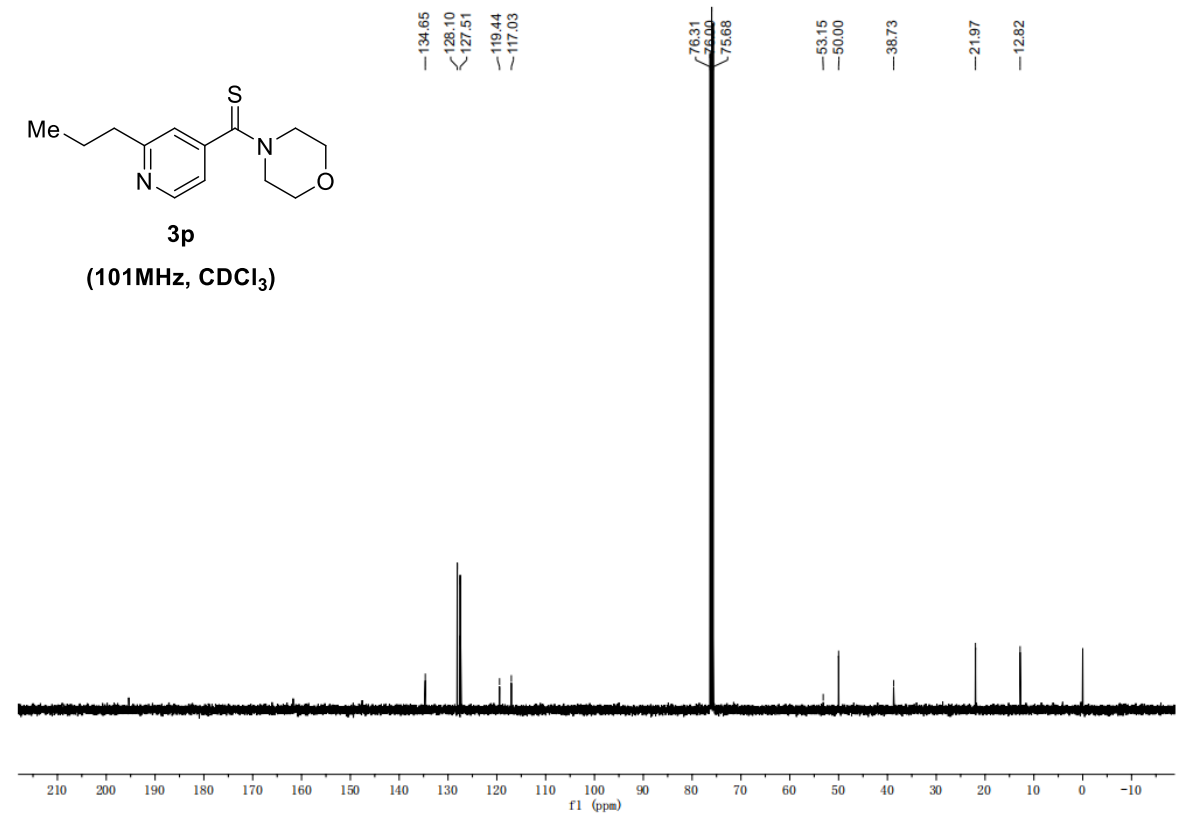
(400MHz, $CDCl_3$)



3k'

(101MHz, $CDCl_3$)


8.53
8.52
7.19
7.15
4.33
3.85
3.84
3.82
3.62
3.47
2.94
2.92
2.90
1.83
1.81
1.79
1.77
1.75
1.74
0.97
0.95
0.93
Me
S
N
N
O
3p
(400MHz, CDCl3)
0.87
1.65
1.77
2.07
2.08
2.00
2.07
2.25
3.00
f1 (ppm)


134.65
128.10
127.51
119.44
117.03
76.31
76.00
75.68
53.15
50.00
38.73
21.97
12.82
Me
S
N
N
O
3p
(101MHz, CDCl3)
f1 (ppm)