Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Transition-Metal-Free Cleavage of C-C Double Bond: Three-Component Reaction of Aromatic Alkenes with S_8 and Amides towards Aryl Thioamides

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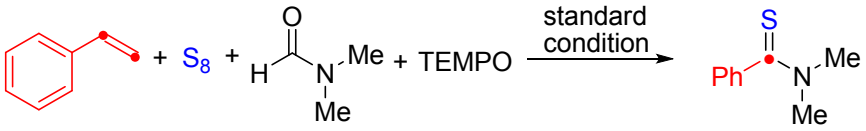
Contents

General Information

^{1}H, ^{13}C, and ^{19}F NMR spectra was recorded on a Bruker DPX-400 spectrometer at room temperature with $CDCl_3$ as the solvent and TMS as an internal standard. Analytical thin layer chromatography was performed on 0.25 mm silica gel plates. Silica gel (200-300 mesh) was used for flash chromatography. 1-methoxy-4-styrylbenzene was synthesized according to the reported literature.[1] Solvents and chemicals were bought from commercial sources and used directly unless otherwise stated.

Supplementary controlling experiments (Scheme 1)

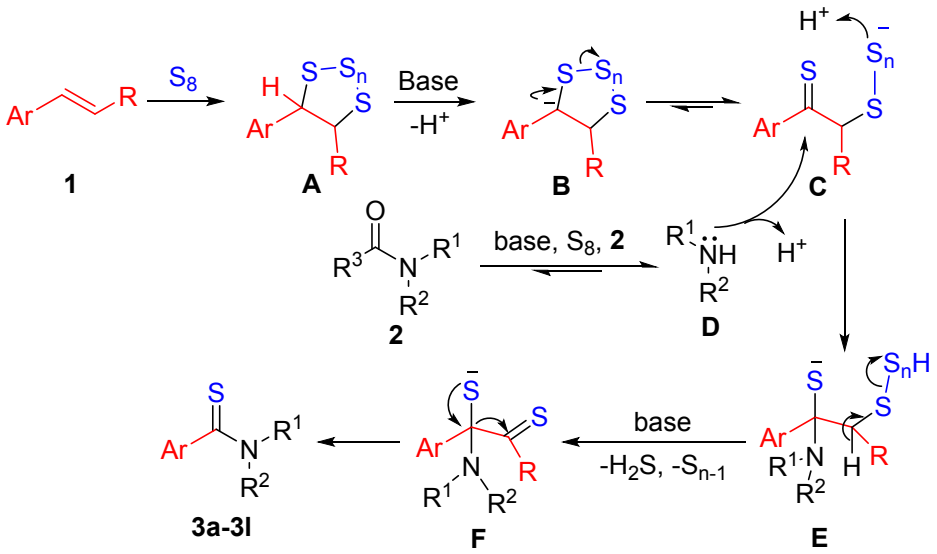


TEMPO (1 equiv) **3a**: 86%
TEMPO (24 equiv) **3a:** inferior yield
(an inseparable mixture including **3a**)

Under the standard condition, yield was constant with the addition of an equivalent amount of TEMPO, but yield significantly declined with the addition of TEMPO (24 equiv), suggesting that radical pathway was involved to some extent (Scheme 1).

Proposed mechanism (Scheme 2)

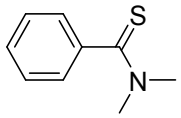
Cycloaddition between S_8 and aromatic alkene gives the cyclic polysulfides A. Subsequently, proton at the benzylic position is readily released under alkaline environment along with the formation of intermediate B. Next, the isomerization of intermediate B might be inclined to take place to form intermediate C with high regio-selectivity which might be resulted from the π-π conjugated effect between C=S bond and the aromatic ring. Then the nucleophilic addition of intermediate D, which is generated in situ from the corresponding aimde, to intermediate C furnishes intermediate E. Again, with the assistance of base, intermediate F might be formed along with release of H_2S. Finally, elimination of thioxo moiety from intermediate F leads to final product through C-C bond cleavage.



General procedure for the synthesis of aryl thioamides

A solution of aromatic alkene (0.4 mmol), S_8 (0.307 g, 9.6 mmol) and K_2CO_3 (0.166 g, 1.2 mmol) in amide (2 mL) was stirred in a 10 mL well-sealed thick-walled glass tube at 115 °C for 20 h. The reaction mixture was cooled down and added into H_2O (25 mL) and extracted with dichloromethane (10 mL) for three times. Then the combined organic layer was dried over anhydrous Na_2SO_4 and filtered. After removal of the solvent in vacuum,

the crude products were washed with methanol (10 mL) for three times. The filtrate was evaporated to dryness again and the final residue was purified by flash chromatography on silica gel (ethyl acetate/hexane) to give the pure product.



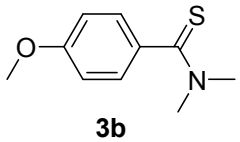
3a

***N,N*-dimethylbenzothioamide (3a)[2]**

Yellow solid, yield: 86% (57 mg) for **3a1**, 45% (30 mg) for **3a2**, 82% (54 mg) for **3a3**, 41% (27 mg) for **3a4** and 55% (36 mg) for **3a5** (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.30 (m, 5H), 3.60 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.2, 143.4, 128.6, 128.4, 125.7, 44.2, 43.3.

1.2 mmol-scale synthesis of 3a1

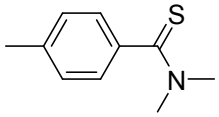
A solution of phenylethylene (0.123 g, 1.2 mmol), S_8 (0.922 g, 28.8 mmol) and K_2CO_3 (0.498 g, 3.6 mmol) in amide (6 mL) was stirred in a 10 mL well-sealed thick-walled glass tube at 115 ^{o}C for 20 h. The reaction mixture was cooled down and added into H_2O (75 mL) and extracted with dichloromethane (30 mL) for three times. Then the combined organic layer was dried over anhydrous Na_2SO_4 and filtered. After removal of the solvent in vacuum, the crude products were washed with methanol (30 mL) for three times. The filtrate was evaporated to dryness again and the final residue was purified by flash chromatography on silica gel (ethyl acetate/hexane = 1/4) to give the *N,N*-dimethylbenzothioamide as a yellow solid (165 mg, 83% yield).



3b

4-methoxy-*N,N*-dimethylbenzothioamide (3b)[2]

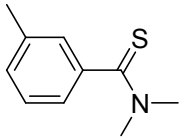
Yellow solid, yield: 94% (73 mg) (Scheme 2). R_f = 0.4 (ethyl acetate/hexane = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J*=8.0 Hz, 2H), 6.86 (d, *J*=8.4 Hz, 2H), 3.81 (s, 3H), 3.58 (s, 3H), 3.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.2, 160.0, 135.8, 127.9, 113.5, 55.4, 44.4, 43.6.



3c

***N,N*-dimethyl-4-(methyl)benzothioamide (3c)[2]**

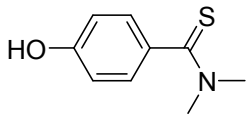
Pale yellow solid, yield: 87% (62 mg) for **3c1**, 46% (33 mg) for **3c2** (Scheme 2) and 84% (60 mg) for **3c3** (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J*=7.6 Hz, 2H), 7.14 (d, *J*=6.4 Hz, 2H), 3.57 (s, 3H), 3.16 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.4, 140.6, 138.7, 128.9, 125.9, 44.3, 43.4, 21.3.



3d

N,N-dimethyl-3-(methyl)benzothioamide (3d)[2]

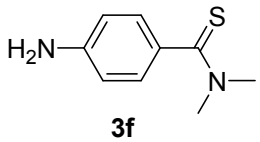
Yellow solid, yield: 80% (57 mg) (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.05 (m, 4H), 3.59 (s, 3H), 3.16 (s, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.4, 143.4, 138.2, 129.3, 128.2, 126.4, 122.6, 44.2, 43.2, 21.4.



3e

4-hydroxy-*N,N*-dimethylbenzothioamide (3e)[3]

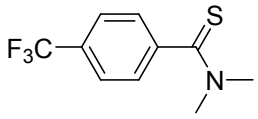
Yellow solid, yield: 83% (60 mg) (Scheme 2). R_f = 0.4 (ethyl acetate/hexane = 1/1); ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.78 (s, 1H), 7.18–7.17 (m, 2H), 6.73 (d, *J*=5.2 Hz, 2H), 3.46 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($(CD_3)_2SO$, 100 MHz) δ 200.0, 158.3, 134.4, 128.6, 114.9, 44.5, 43.7.



3f

4-amino-*N,N*-dimethylbenzothioamide (3f)[3]

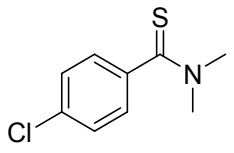
Yellow solid, yield: 92% (66 mg) (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J*=7.6 Hz, 2H), 6.58 (d, *J*=7.2 Hz, 2H), 3.88 (s, 2H), 3.56 (s, 3H), 3.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.8, 147.6, 133.0, 128.3, 114.0, 44.6, 43.8.



3g

***N,N*-dimethyl-4-(trifluoromethyl)benzothioamide (3g)[2]**

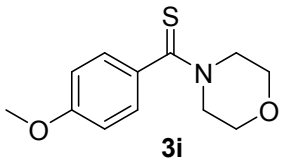
Yellow solid, yield: 56% (52 mg) for **3g1** and 72% (67 mg) for **3g2** (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J*=7.6 Hz, 2H), 7.41 (d, *J*=7.6 Hz, 2H), 3.60 (s, 3H), 3.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.2, 146.6, 130.4 (q, *J*=32.5 Hz), 126.0, 125.5 (q, *J*=3.7 Hz), 123.8 (q, *J*=270.6 Hz), 44.1, 43.1; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -62.79.



3h

4-chloro-*N,N*-dimethylbenzothioamide (3h)[2]

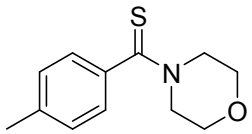
Yellow solid, yield: 52% (41 mg) (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J*=8.0 Hz, 2H), 7.25 (d, *J*=8.4 Hz, 2H), 3.58 (s, 3H), 3.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.9, 141.7, 134.6, 128.6, 127.3, 44.2, 43.3.



3i

(4-methoxyphenyl)(morpholino)methanethione (3i)[4]

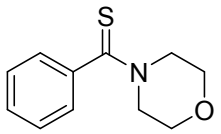
Yellow solid, yield: yield: 71% (67 mg) for **3i1** and 84% (80 mg) for **3i2** (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J=8.0 Hz, 2H), 6.87 (d, J=7.2 Hz, 2H), 4.42 (s, 2H), 3.89–3.82 (m, 5H), 3.67 (s, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.2, 160.3, 134.9, 128.1, 113.7, 66.8, 66.6, 55.4, 52.8, 50.0.



3j

Morpholino(*p*-tolyl)methanethione (3j)[5]

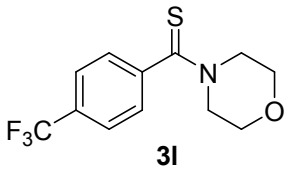
Pale yellow solid, yield: 84% (74 mg) for **3j1** and 96% (85 mg) for **3j2** (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J=4.4 Hz, 4H), 4.43 (s, 2H), 3.88 (s, 2H), 3.63 (s, 4H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.4, 139.7, 139.1, 129.1, 126.1, 66.8, 66.6, 52.6, 49.7, 21.3.



3k

Morpholino(phenyl)methanethione (3k)[2]

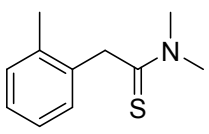
Pale yellow solid, yield: 85% (70 mg) for **3k1,** 80% (66 mg) for **3k2** and 65% (54 mg) for **3k3** (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.29 (m, 5H), 4.45 (s, 2H), 3.89 (s, 2H), 3.64–3.61 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.0, 142.5, 128.9, 128.6, 125.9, 66.8, 66.6, 52.5, 49.6.



3l

Morpholino(4-(trifluoromethyl)phenyl)methanethione (3l) [6]

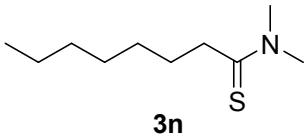
Yellow solid, yield: 53% (58 mg) for **3l1** and 51% (56 mg) for **3l2** (Scheme 2). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J=7.2 Hz, 2H), 7.40 (d, J=6.8 Hz, 2H), 4.44 (s, 2H), 3.90 (s, 2H), 3.66–3.56 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.8, 145.7, 130.7 (q, J=32.6 Hz), 126.2, 125.8 (q, J=3.7 Hz), 123.7 (q, J=270.6 Hz), 66.6, 66.5, 52.5, 49.3; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -62.82.



3m

***N*,*N*-dimethyl-2-*o*-tolylethanethioamide (3m)[7]**

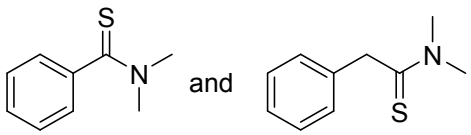
Yellow solid, yield: 32% (25 mg) (Scheme 3, eq 1). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.16 (m, 4H), 4.20 (s, 2H), 3.56 (s, 3H), 3.15 (s, 3H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.1, 135.8, 134.4, 130.2, 126.9, 126.9, 126.5, 48.1, 44.7, 42.2, 19.7.



3n

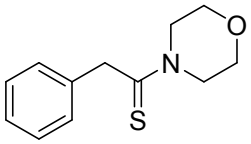
***N,N*-dimethyloctanethioamide (3n)[6]**

Pale yellow oil, yield: 56% (42 mg) (Scheme 3, eq 2). R_f = 0.4 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.49 (s, 3H), 3.32 (s, 3H), 2.83–2.79 (m, 2H), 1.83–1.61(m, 2H), 1.51–1.01 (m, 8H), 0.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.5, 44.5, 43.9, 41.6, 31.7, 29.4, 29.1, 29.0, 22.6, 14.1.



3a and **3o**

Mixture of 3a and 3o 62 mg (molar ratio of **3a** and **3o** is 0.298:1 based on ^{1}H NMR), yield: 20% (13 mg, **3a**), 68% (49 mg, **3o**) (Scheme 4, eq 3). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.24 (m, 5H), 4.31 (s, 1.64H), 3.59 (s, 0.67H), 3.48 (s, 2.25H), 3.19–3.15 (m, 2.91H).



3p

Morpholino-2-phenylethanethione (3p)[2]

Yellow solid, yield: 98% (87 mg) (Scheme 4, eq 4). R_f = 0.3 (ethyl acetate/hexane = 1/4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.25 (m, 5H), 4.35 (s, 4H), 3.72 (s, 2H), 3.62 (s, 2H), 3.38 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.9, 135.8, 129.0, 127.8, 127.1, 66.3, 66.1, 50.8, 50.6, 50.2.

References

[1] H. J. Xu, Y. Q. Zhao and X. F. Zhou, *J. Org. Chem.*, 2011, **76**, 8036.

[2] J. P. Wei, Y. M. Li and X. F. Jiang, *Org. Lett.*, 2016, **18**, 340.

[3] S. Kumar, R. Vanjari, T. Guntreddi and K. N. Singh, *Tetrahedron*, 2016, **72**, 2012.

[4] X. Wang, M. Ji, S. Lim and H. Y. Jang, *J. Org. Chem.*, 2014, **79**, 7256.

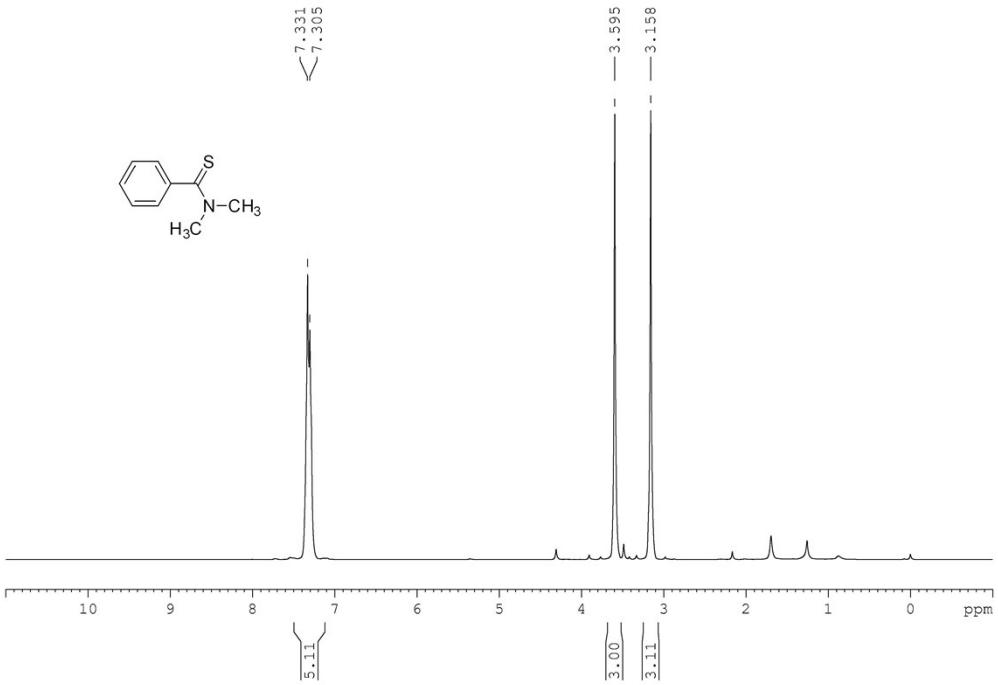
[5] T. Guntreddi, R. Vanjari and K. N. Singh, *Org. Lett.*, 2014, **16**, 3624.

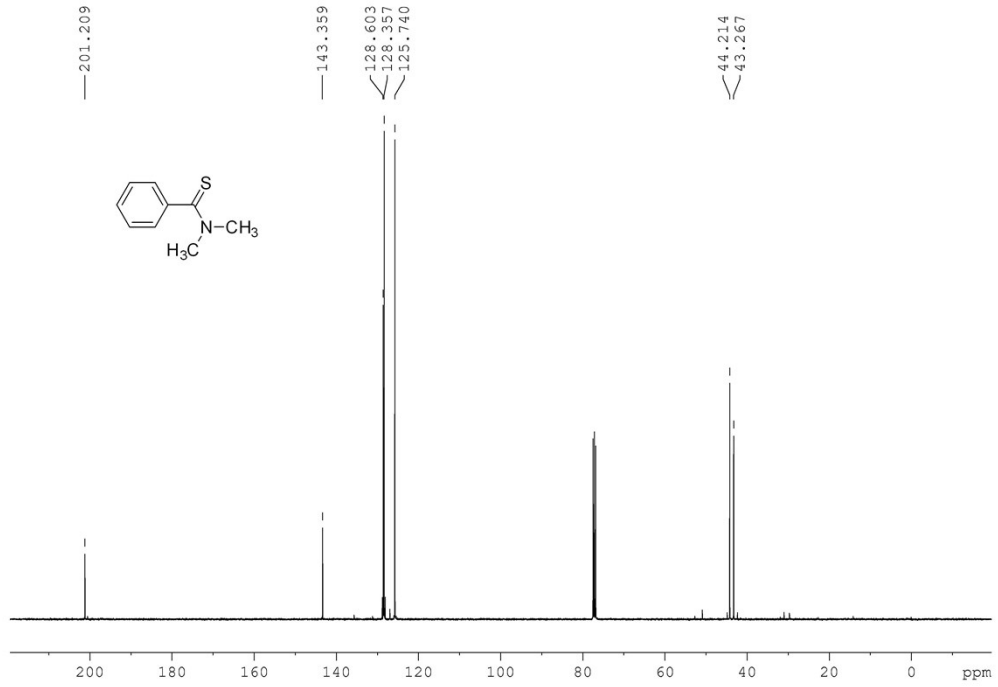
[6] K. Xu, Z. Y. Li, F. Y. Cheng, Z. Z. Zuo, T. Wang, M. C. Wang and L. T. Liu, *Org. Lett.*, 2018, **20**, 2228.

[7] Y. Qu, Z. K. Li, H. F. Xiang and X. G. Zhou, *Adv. Synth. Catal.*, 2013, **355**, 3141.

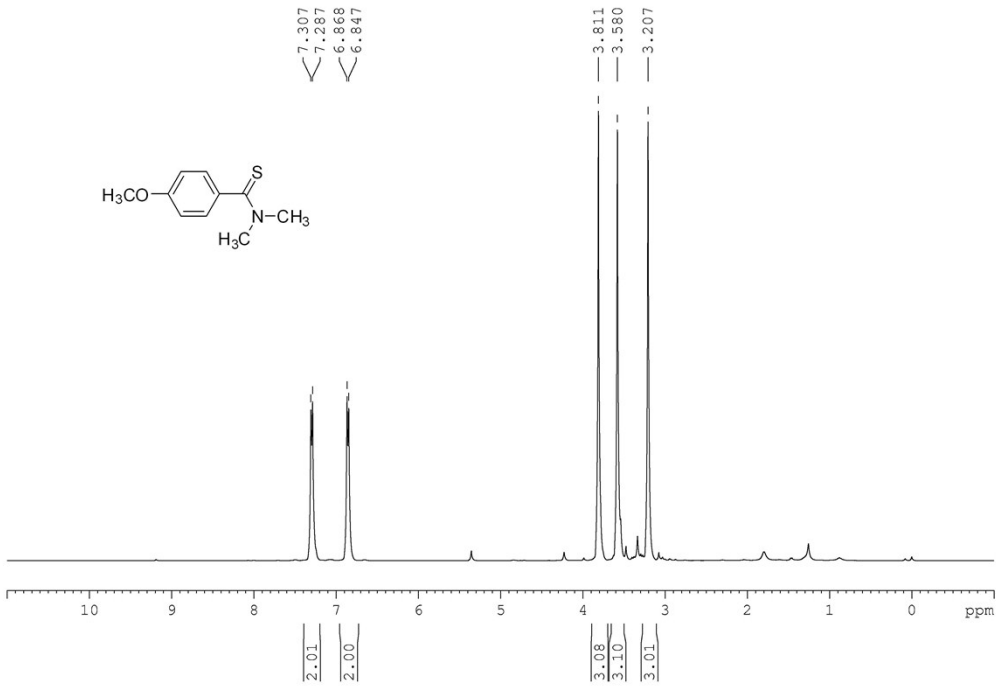
^{1}H, ^{13}C and ^{19}F NMR spectra for all the compounds

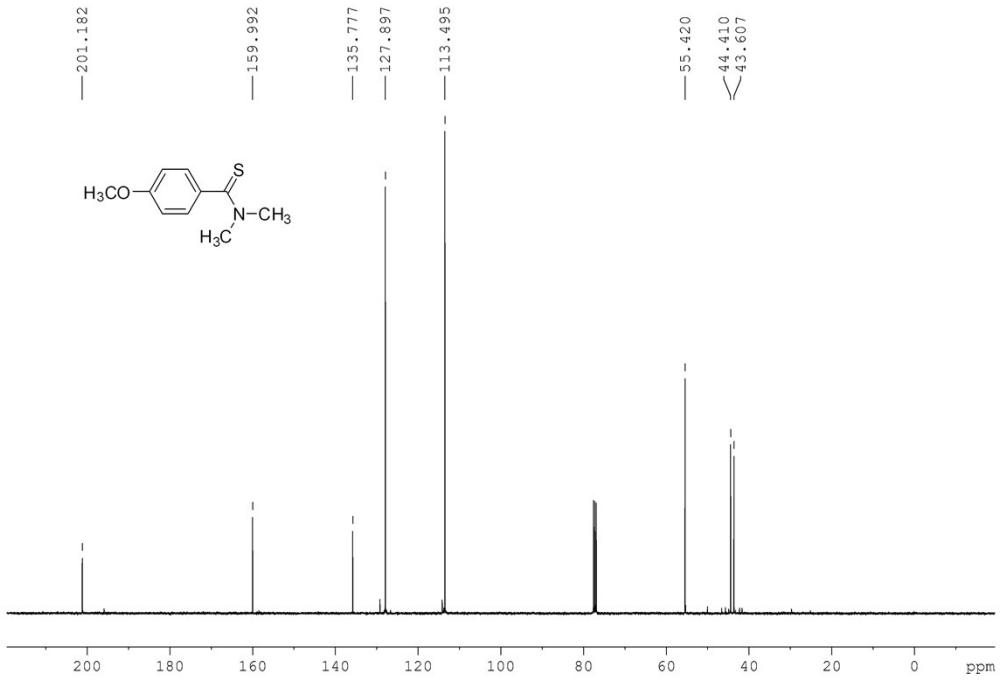
NMR spectra of **3a**



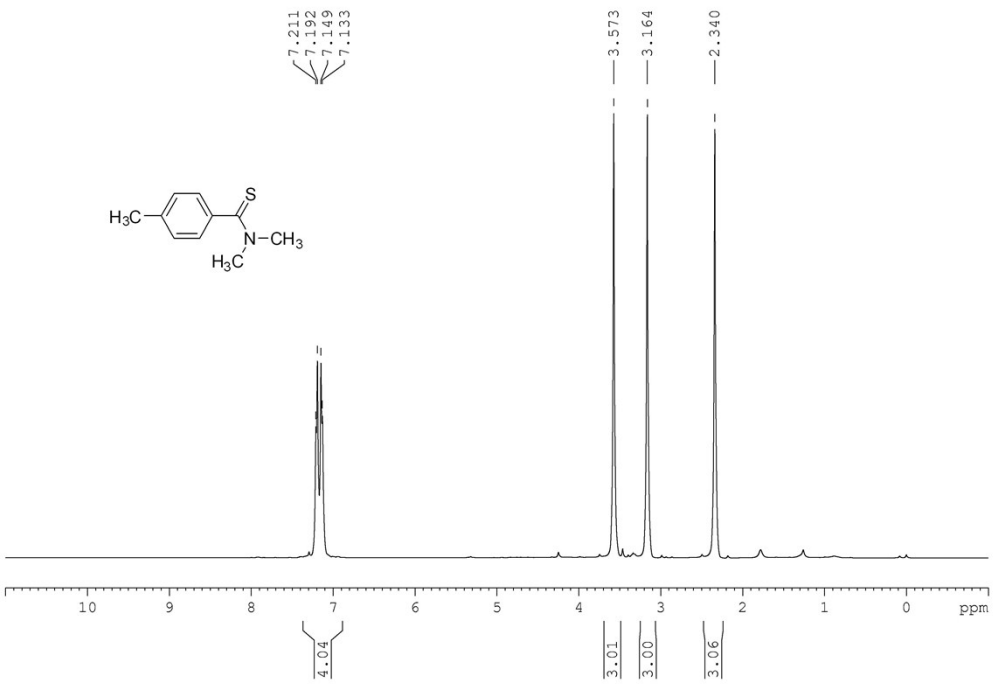


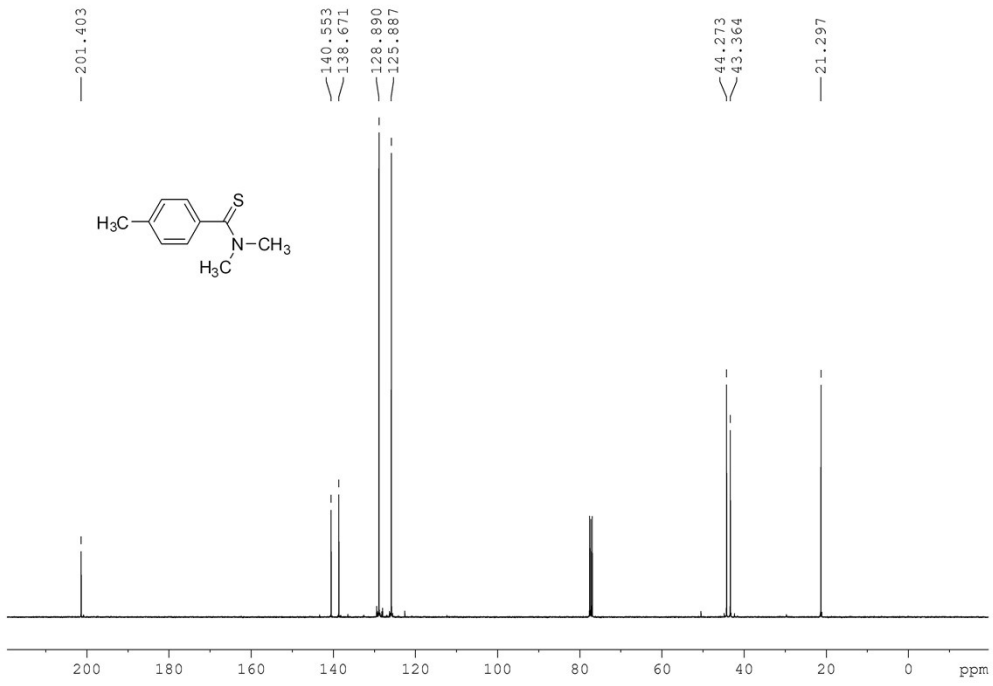
NMR spectra of **3b**



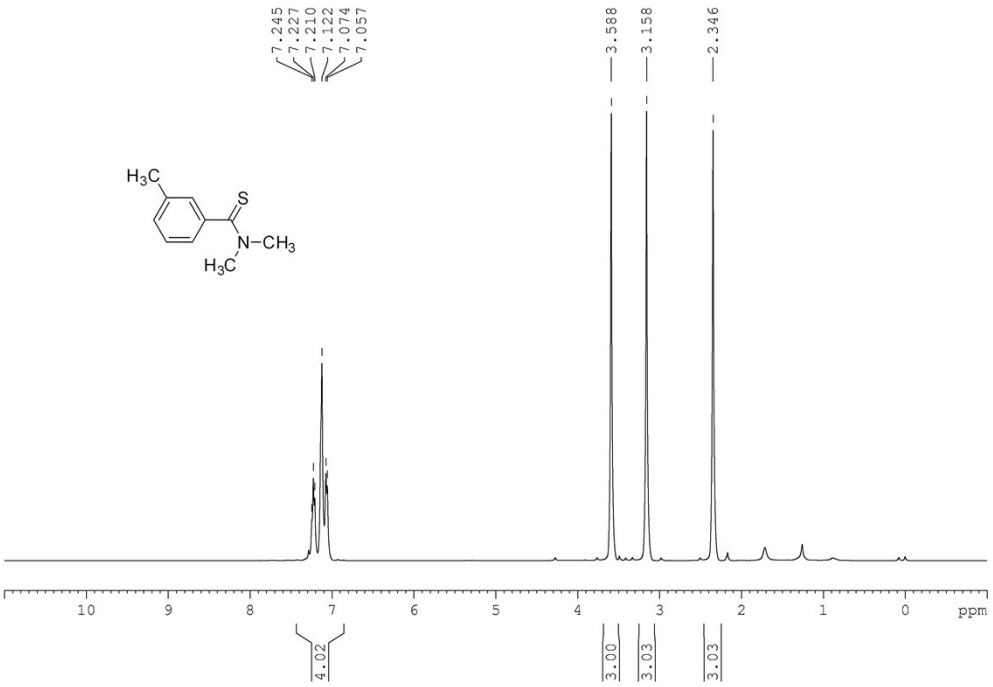


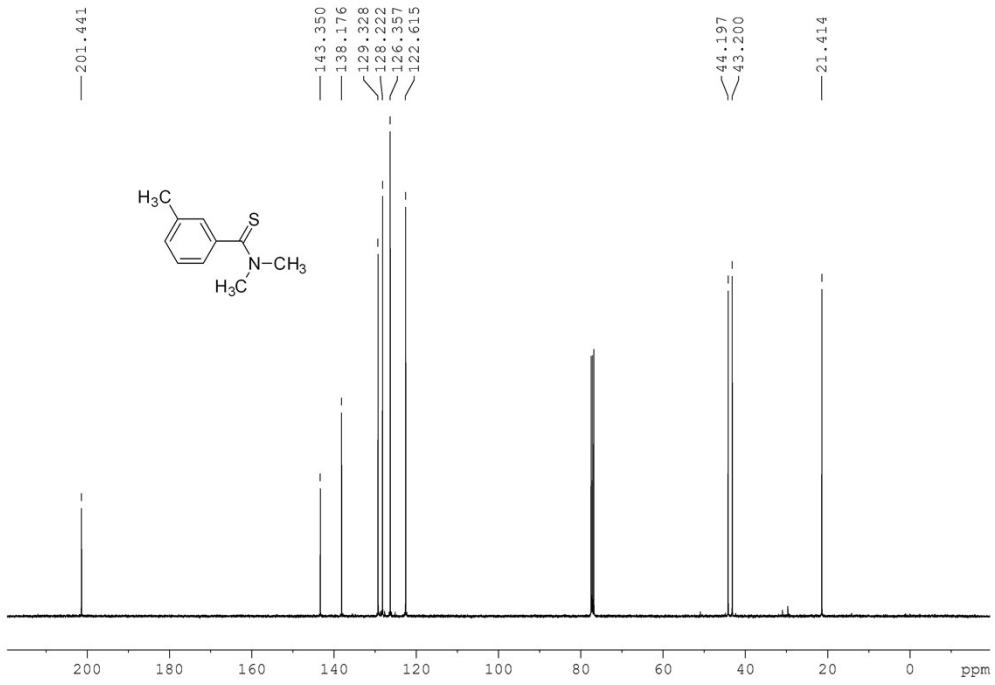
NMR spectra of **3c**



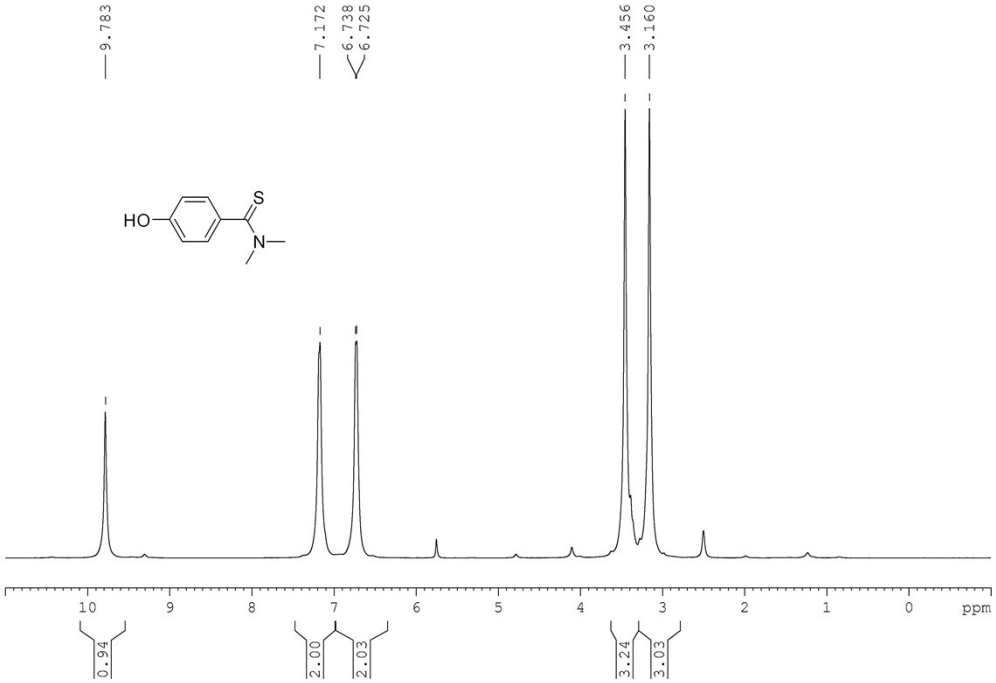


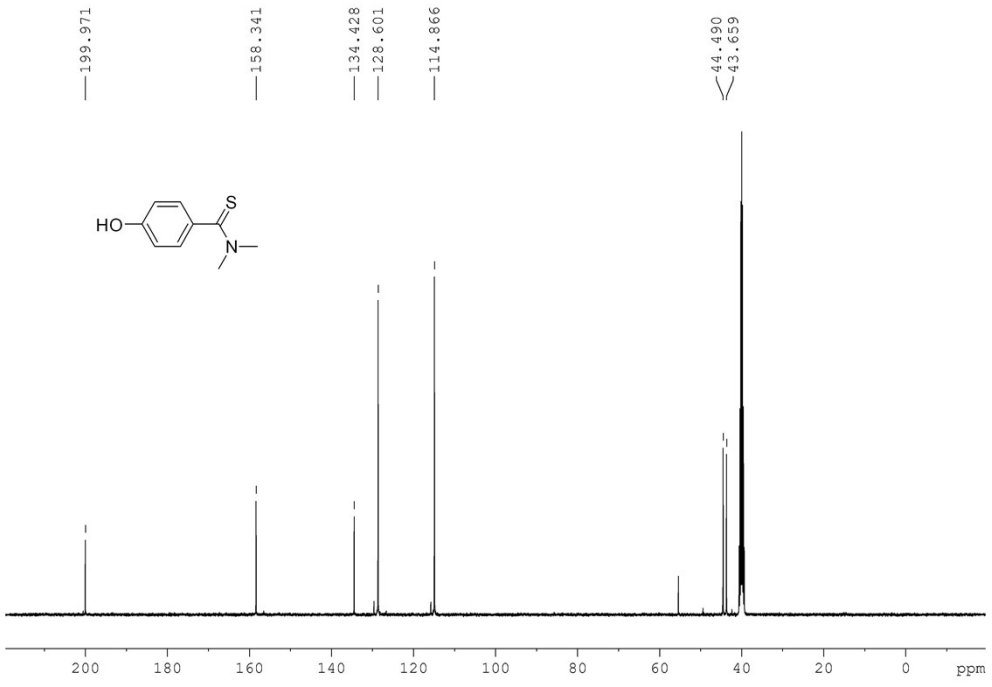
NMR spectra of **3d**



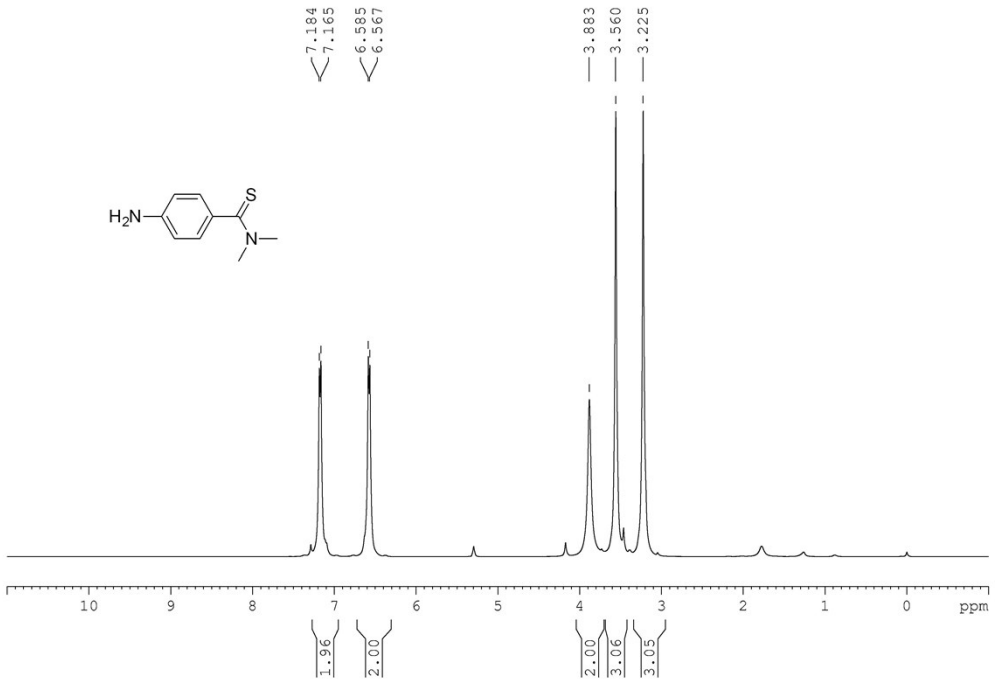


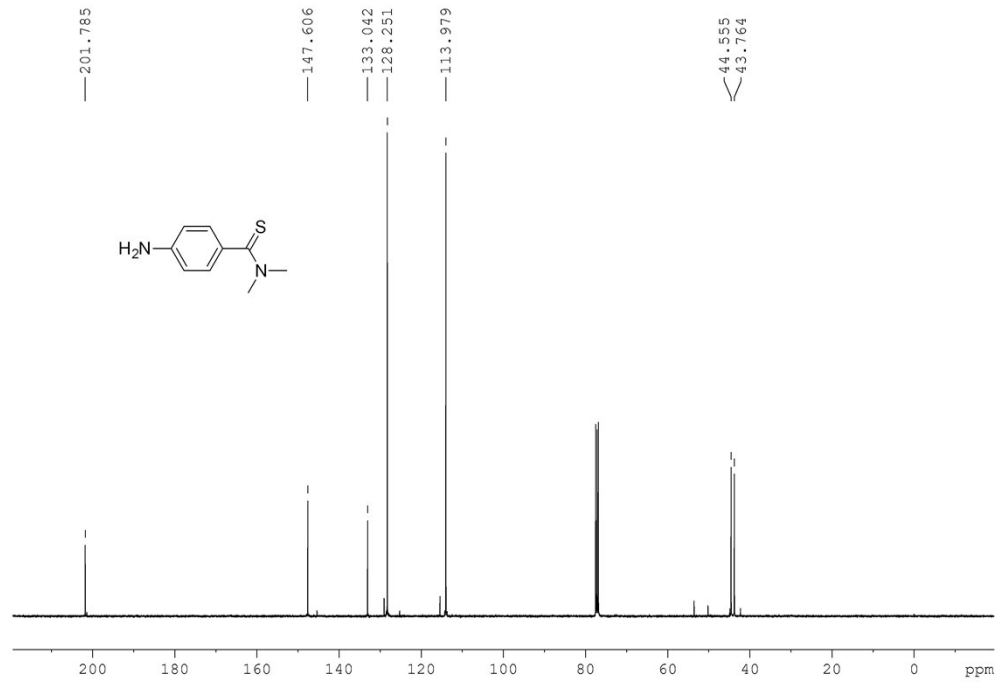
NMR spectra of **3e**



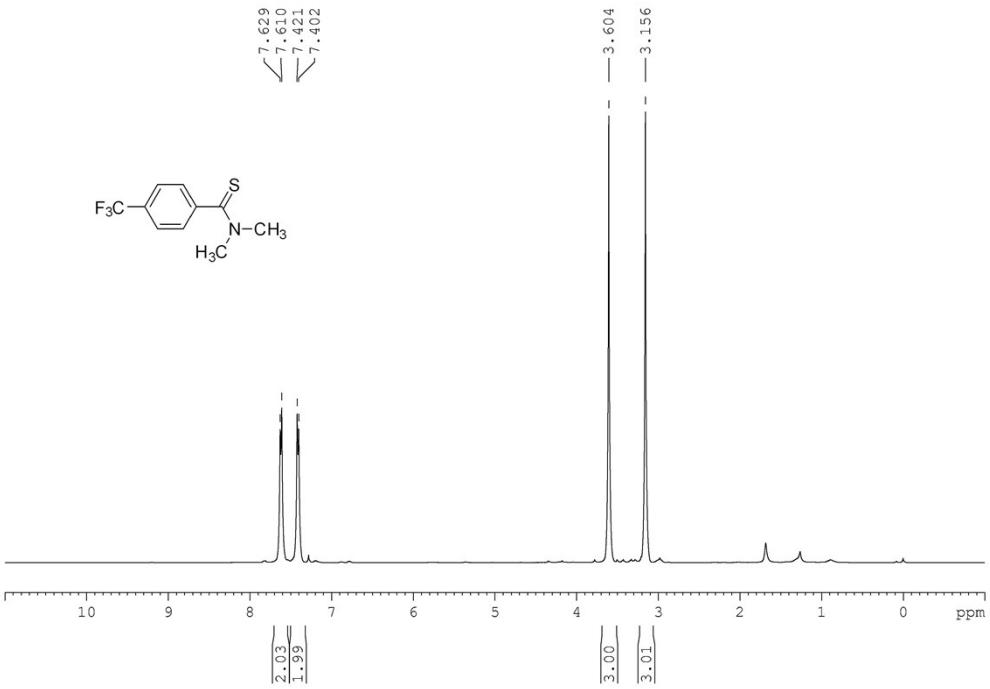


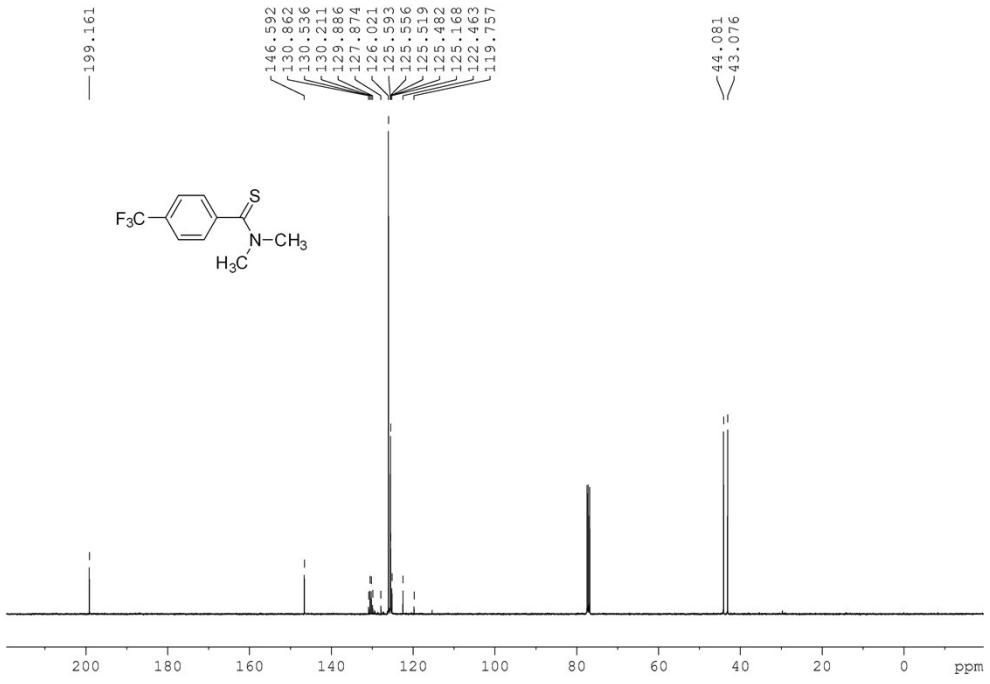
NMR spectra of **3f**

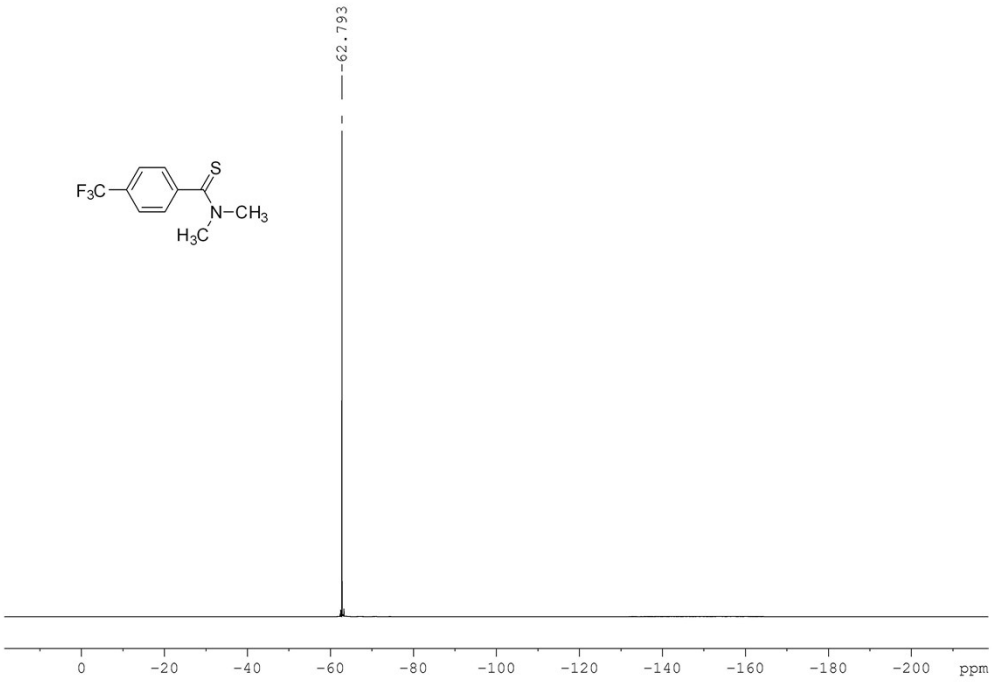




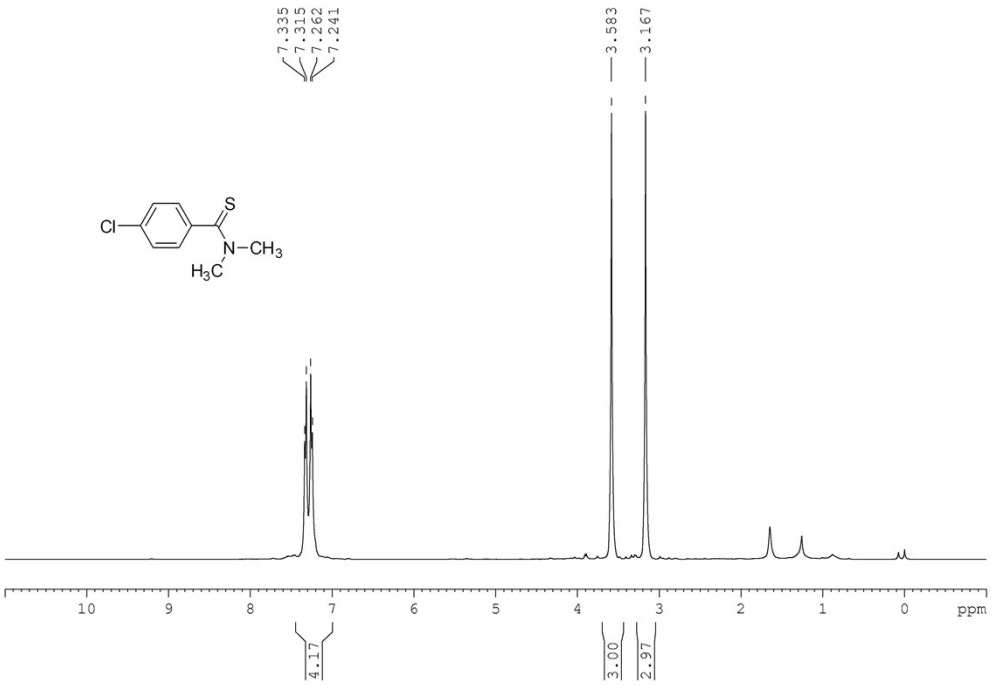
NMR spectra of **3g**

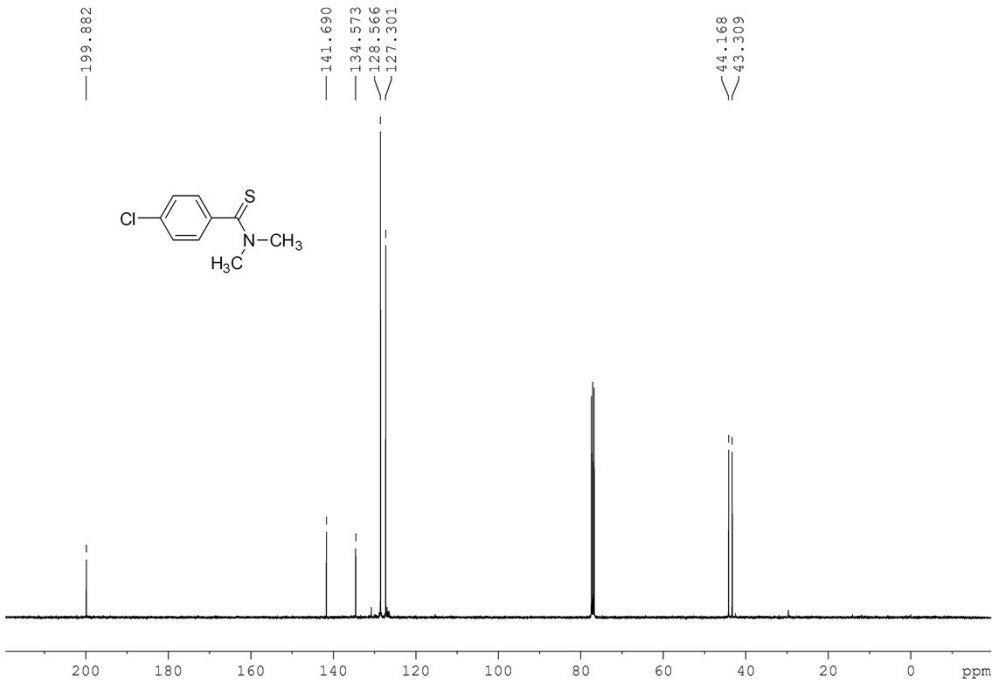




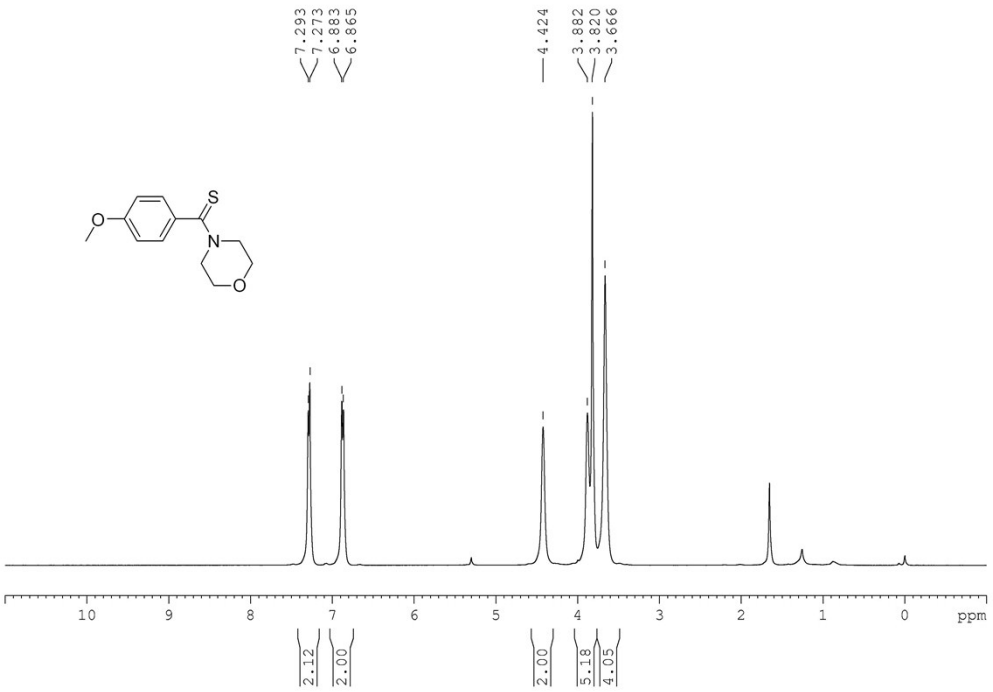

-62.793
S
F3C
N–CH3
H3C
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

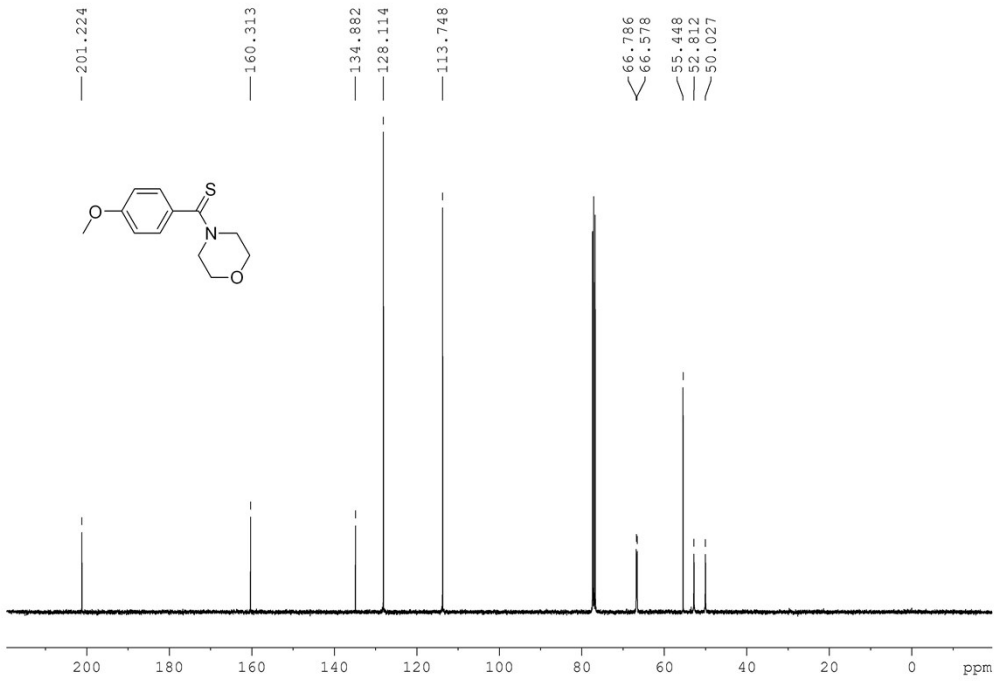
NMR spectra of **3h**



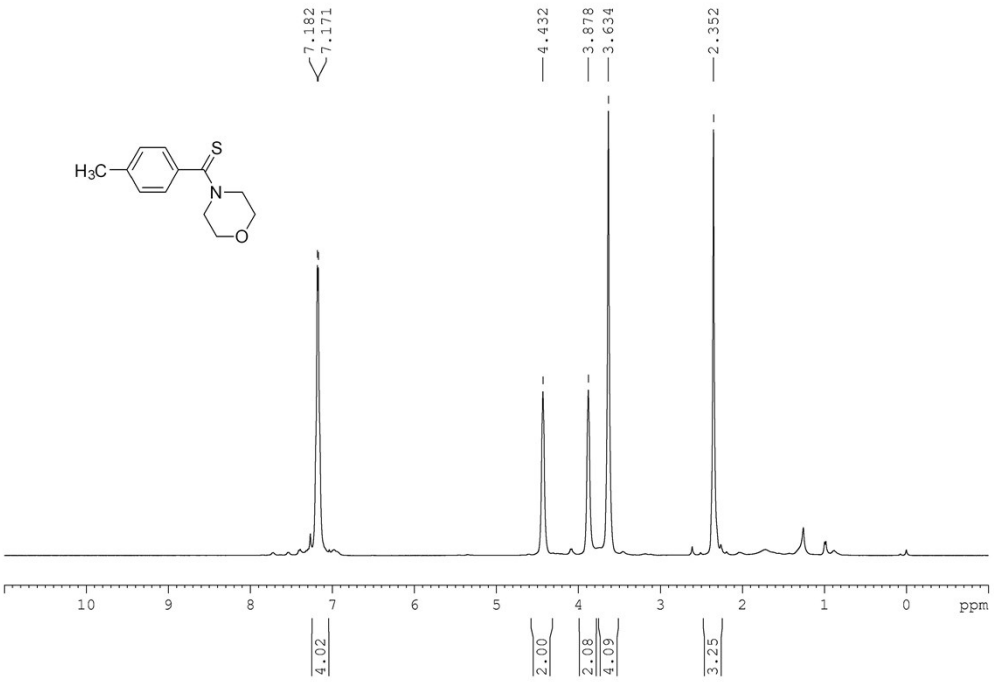


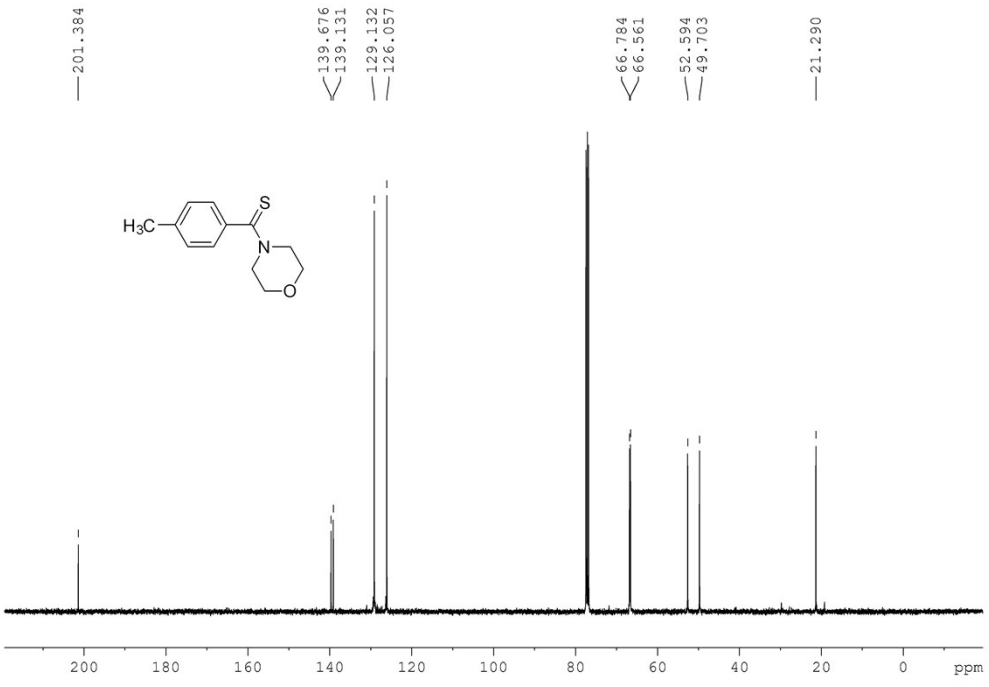
NMR spectra of **3i**



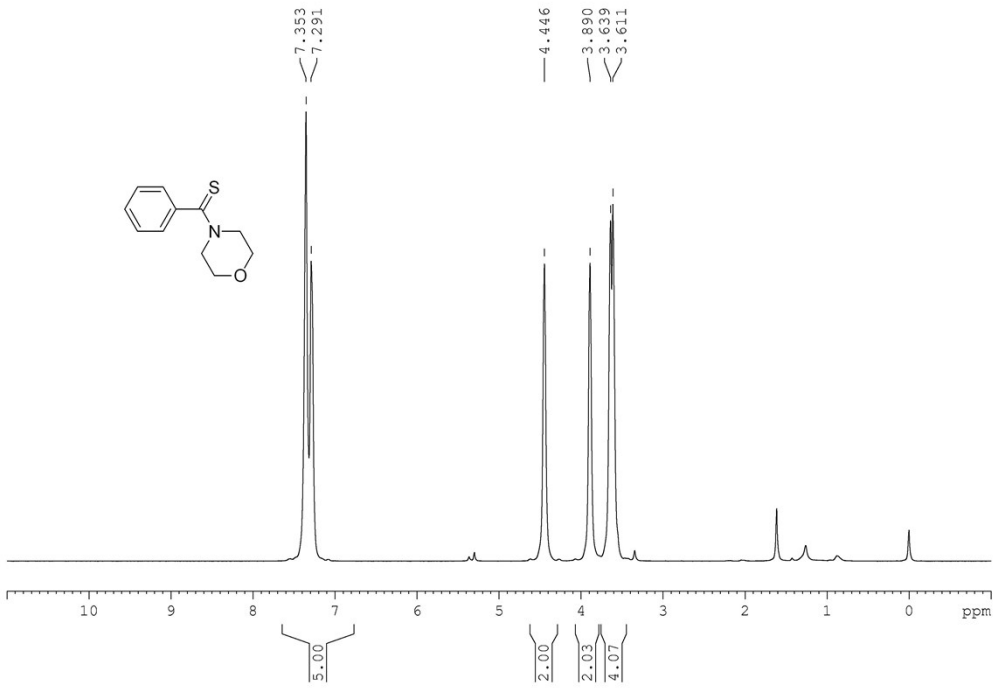


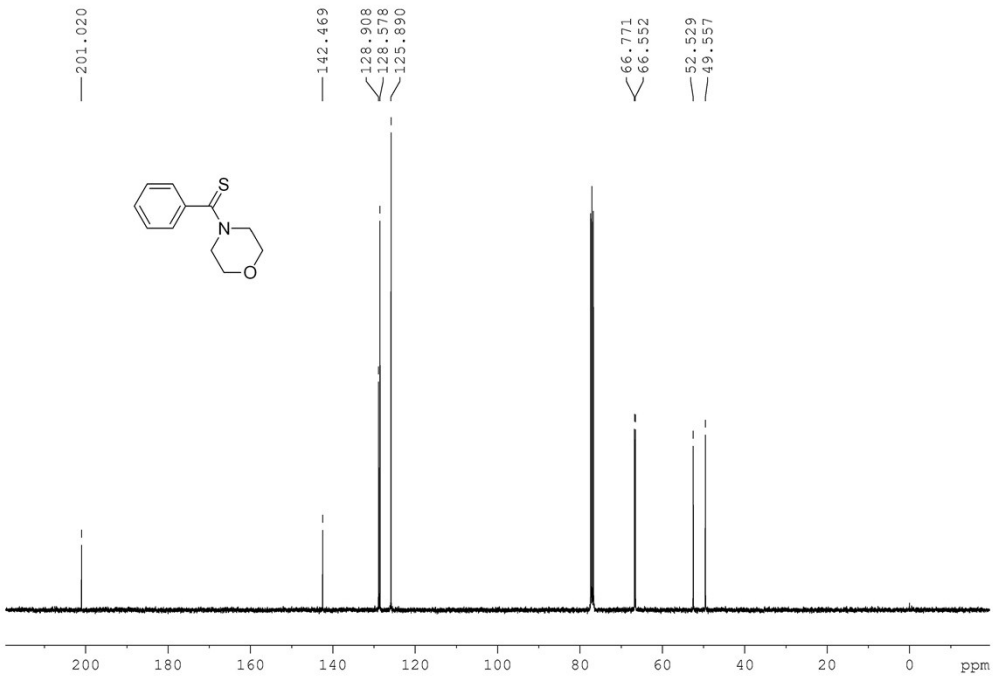
NMR spectra of **3j**



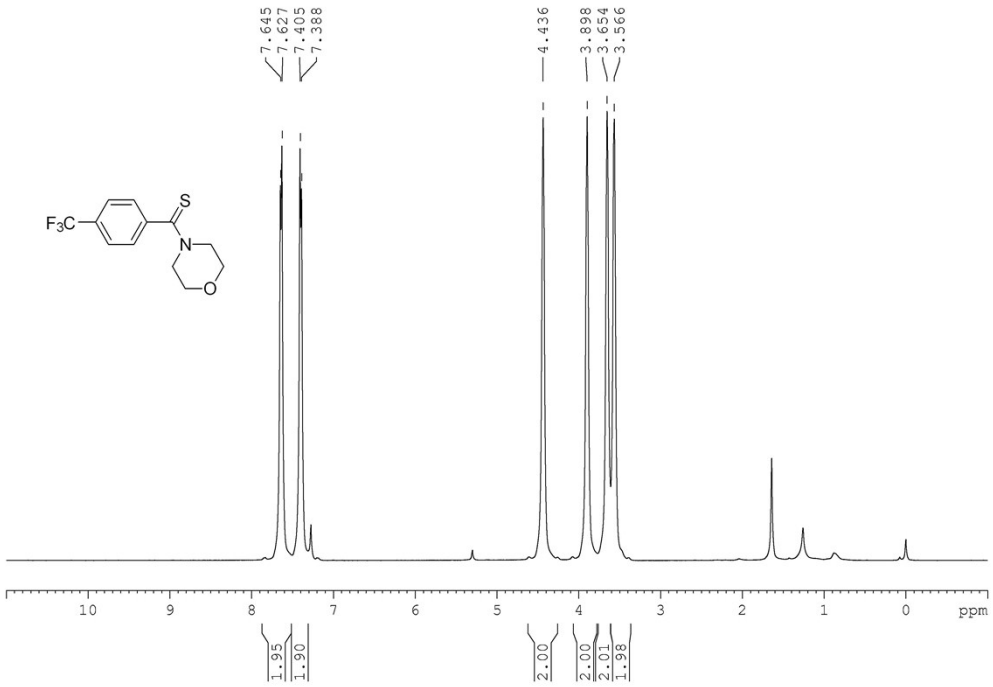


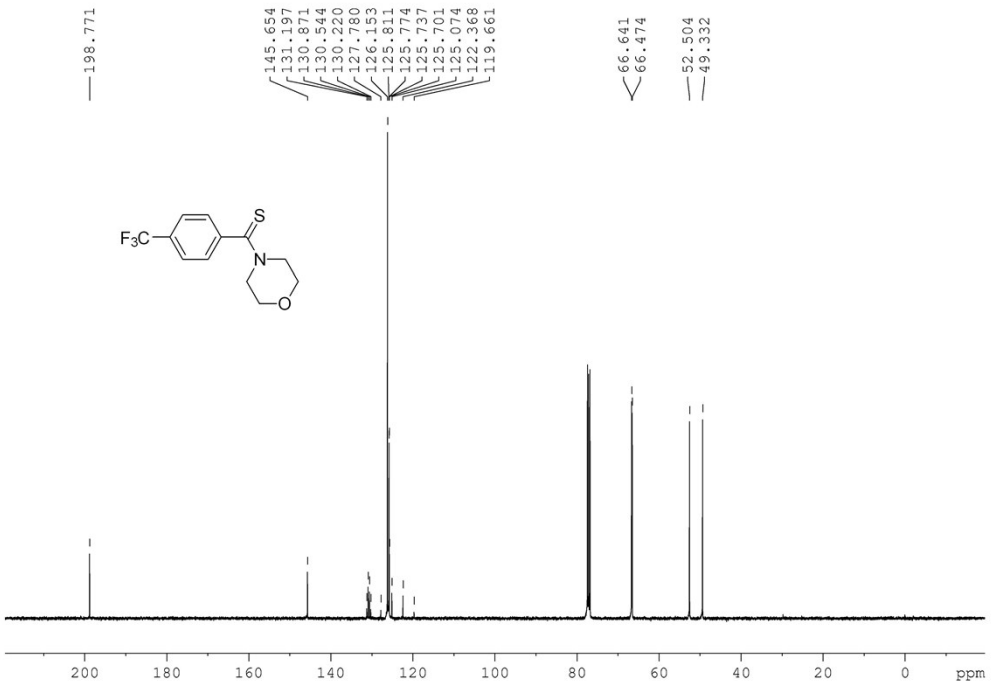
NMR spectra of **3k**

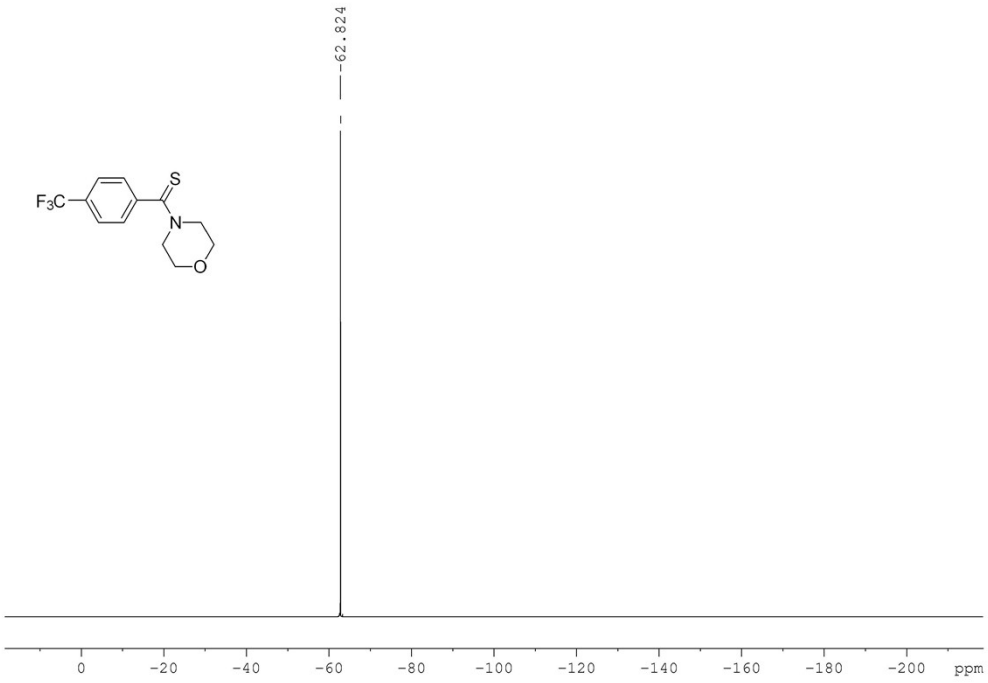




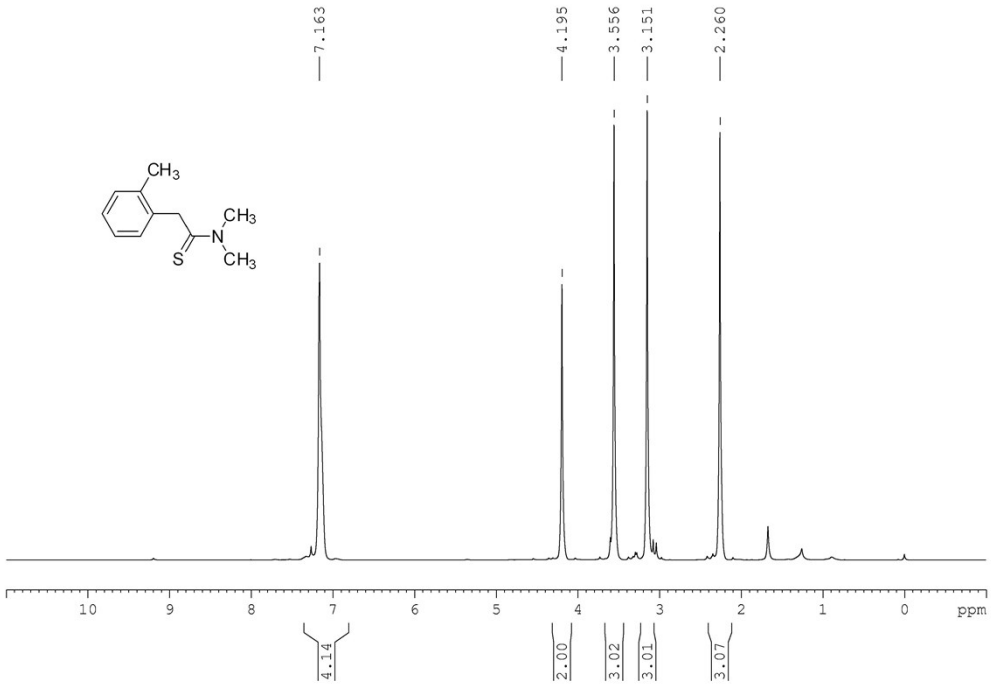
NMR spectra of **3l**

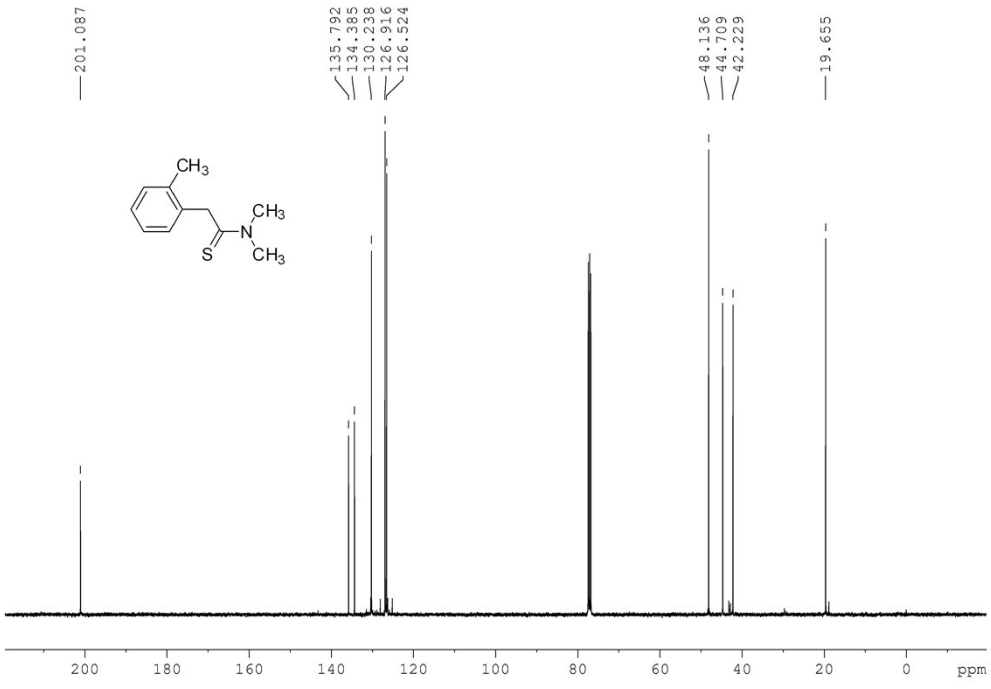




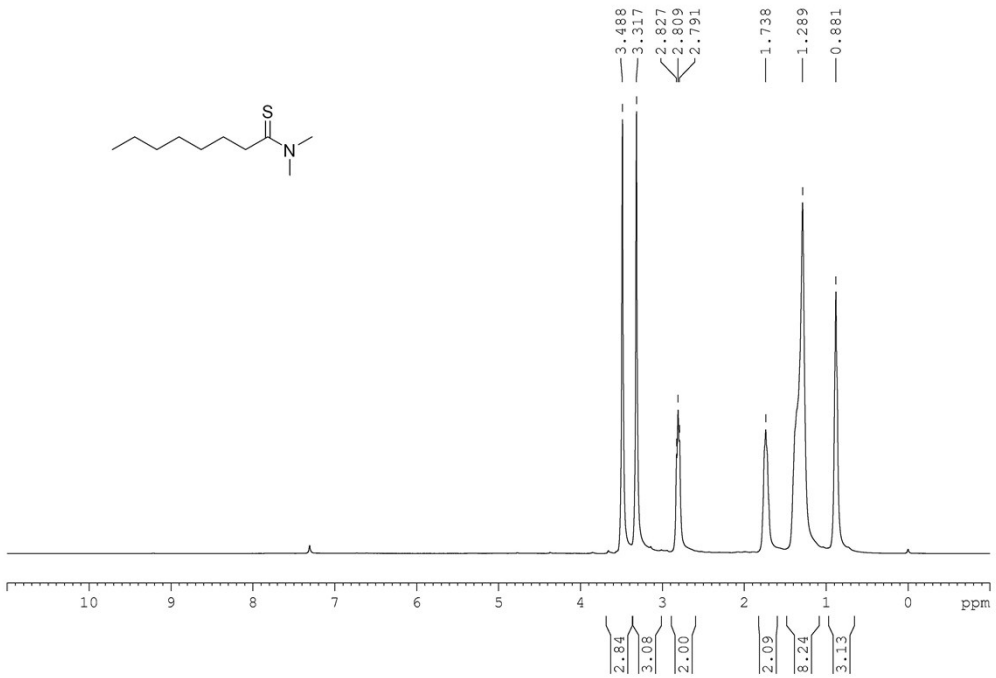

-62.824
F3C
S
N
O
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm

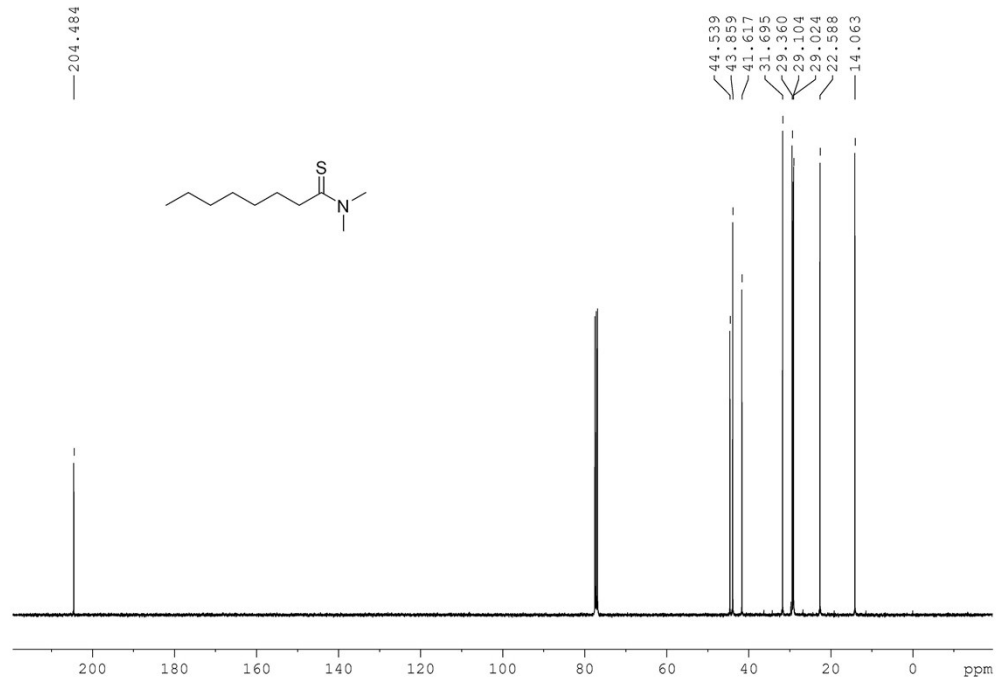
NMR spectra of **3m**



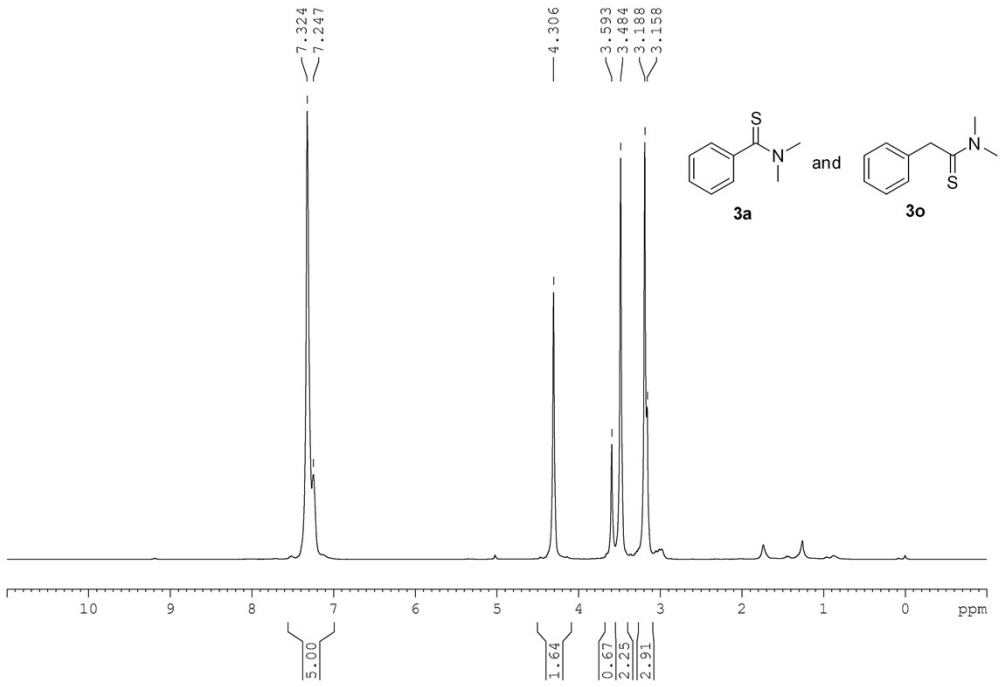


NMR spectra of **3n**





NMR spectra of mixture (**3a** and **3o**)



NMR spectra of **3p**