Cs_2CO_3-promoted methylene insertion into disulfide bonds using acetone as a methylene source

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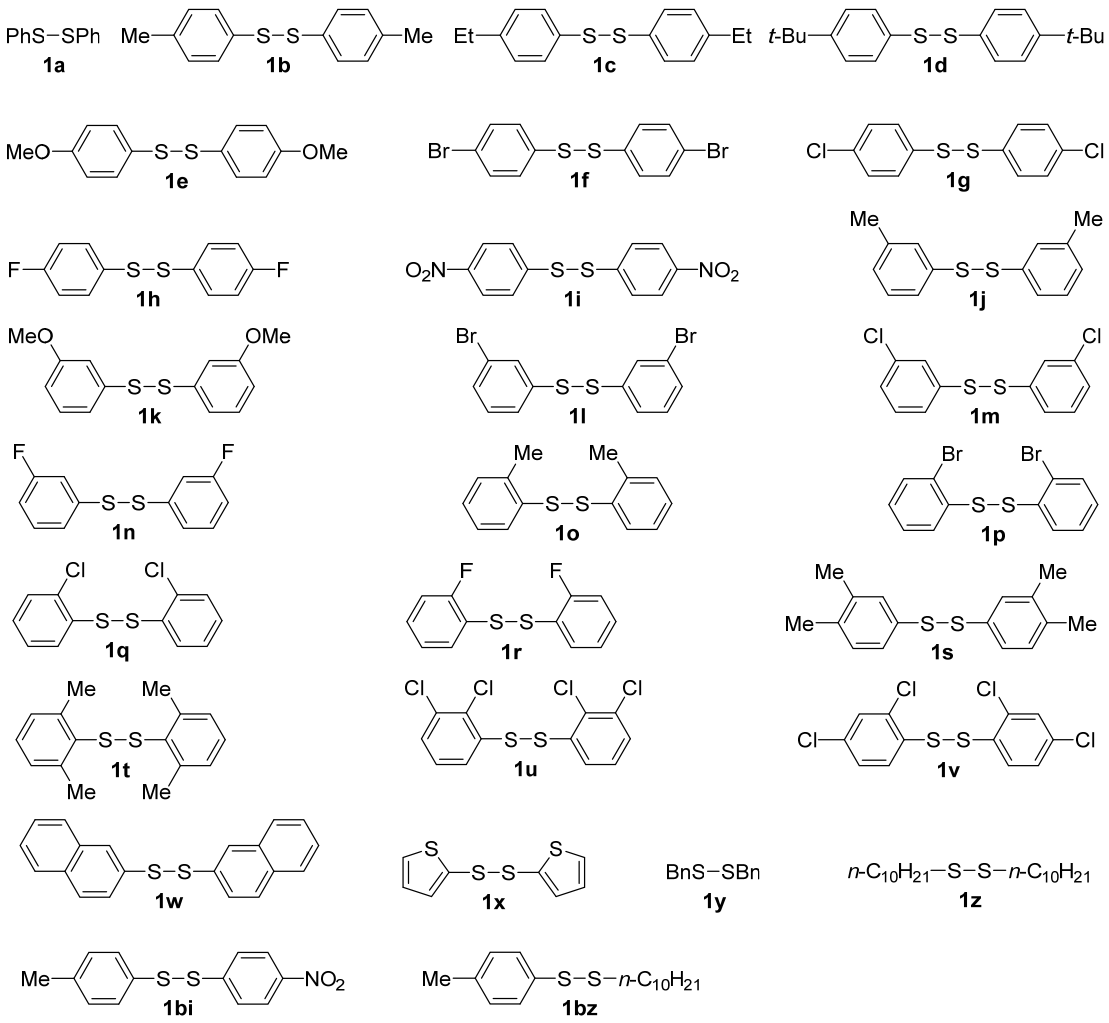
SUPPORTING INFORMATION

Content:

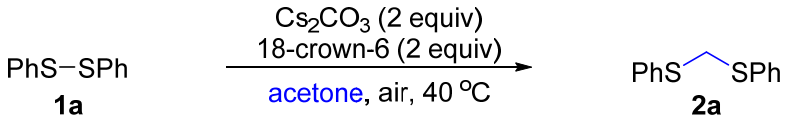
1. General Information

All reactions were carried out in an oven-dried Schlenk tube open to air using standard syringe/septa techniques. Petroleum ether refers to the petroleum fraction bp 40~60 °C. Acetone was dried over 4 Å molecular sieves. Commercial reagents were used without purification unless otherwise noted. Disulfides which were not commercially available were prepared according to the literature.[1] Flash chromatography was performed using the indicated solvent system on silica gel standard grade (200~300 mesh). ^{1}H NMR spectra were recorded on in $CDCl_3$ on Bruker 400/600 (400/600 MHz) spectrometers. ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker 400/600 (101/151 MHz) spectrometers. ^{19}F NMR spectra were recorded in $CDCl_3$ on Bruker 400 (376 MHz) spectrometer. Chemical shifts are reported relative to $CDCl_3$ (δ 7.26 ppm) for ^{1}H NMR and $CDCl_3$ (δ 77.16 ppm) for ^{13}C NMR. Multiplicities were indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Mass spectra were taken on a Waters UPLC H-class LC-MS instrument in the electrospray ionization (ESI) mode. Only molecular ions (M + H) were given for the ESI-MS analysis. Melting points (mp) were uncorrected and measured on micro melting point apparatus.

2. Overview of Substrates Numbering



3. General Procedure for the Methylene Insertion Reaction

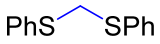


To a solution of diphenyl disulfide **1a** (87 mg, 0.4 mmol) in anhydrous acetone (6 mL) was added Cs_2CO_3 (260 mg, 0.8 mmol) and 18-crown-6 (210 mg, 0.8 mmol). The mixture was stirred at 40 ^{o}C in a Schlenk tube open to air for 24 h. The reactant was quenched with brine, extracted with EtOAc, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was then purified by flash column chromatography on silica gel with petroleum ether to give the desired **2a** (86 mg, 92%) as a white solid.

4. Characterizations of Compounds 2, 2a-*d*, 3a and 4a

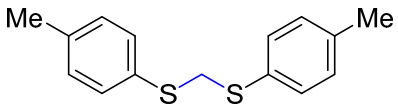
The known compounds **2a**,[2] **2b**,[2] **2e**,[2] **2f**,[2] **2g**,[2] **2h**,[2] **2i**,[3] **2j**,[4] **2o**,[4] **2q**,[3] **2w**,[5] **2x**,[2] **2y**,[2] **3a**,[6] and **4a**[7] showed characterization data in full agreement with previously reported data.

Bis(phenylthio)methane (2a)[2]



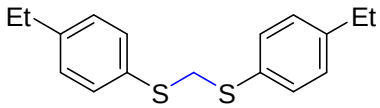
White solid (86 mg, 92%): mp 33−34 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.41 (m, 4H), 7.31−7.29 (m, 4H), 7.27−7.21 (m, 2H), 4.34 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.0, 130.7, 129.0, 127.1, 40.7. **2a-*d***: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.41 (m, 4H), 7.31−7.29 (m, 4H), 7.27−7.21 (m, 2H), 4.35 (s, 1H).

Bis(*p*-tolylthio)methane (2b)[2]



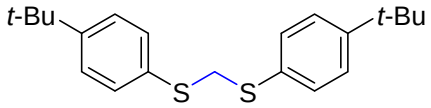
Yellow oil (89 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.0 Hz, 4H), 7.13 (d, J = 8.0 Hz, 4H), 4.27 (s, 2H), 2.34 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.4, 131.5, 131.3, 129.8, 42.0, 21.2.

Bis((4-ethylphenyl)thio)methane (2c)



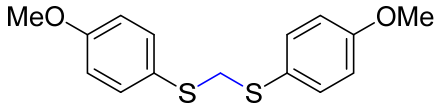
Colorless oil (68 mg, 59%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.2 Hz, 4H), 7.15 (d, J = 8.2 Hz, 4H), 4.28 (s, 2H), 2.64 (q, J = 7.6 Hz, 4H), 1.23 (t, J = 7.6 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.7, 131.6, 131.5, 128.6, 41.9, 28.5, 15.4; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{17}H_{21}S_2$ 289.1079; found 289.1039.

Bis((4-(*tert*-butyl)phenyl)thio)methane (2d)



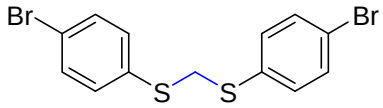
Yellow oil (114 mg, 83%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.6 Hz, 4H), 7.33 (d, J = 8.6 Hz, 4H), 4.30 (s, 2H), 1.32 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4, 131.6, 130.8, 126.0, 41.4, 34.6, 31.3; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{21}H_{29}S_2$ 345.1705; found 345.1666.

Bis((4-methoxyphenyl)thio)methane(2e)[2]



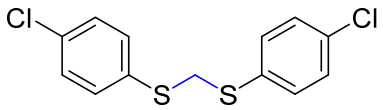
White solid (71 mg, 61%): mp 67−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.6 Hz, 4H), 6.85 (d, J = 8.6 Hz, 4H), 4.15 (s, 2H), 3.81 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.6, 134.5, 125.2, 114.6, 55.4, 44.5.

Bis((4-bromophenyl)thio)methane (2f)[2]



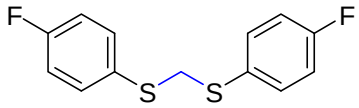
White solid (136 mg, 87%): mp 70−72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.5 Hz, 4H), 7.26 (d, J = 8.5 Hz, 4H), 4.27 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.7, 132.5, 132.2, 121.6, 40.8.

Bis((4-chlorophenyl)thio)methane (2g)[2]



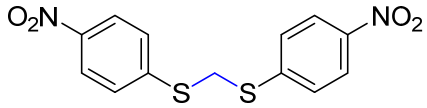
White solid (108 mg, 90%): mp 40−42 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.5 Hz, 4H), 7.28 (d, J = 8.5 Hz, 4H), 4.28 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.6, 133.0, 132.4, 129.2, 41.2.

Bis((4-fluorophenyl)thio)methane (2h)[2]



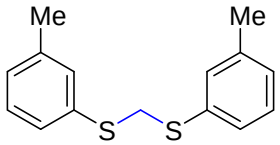
Yellow oil (101 mg, 94%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.30 (m, 4H), 7.04−7.00 (m, 4H), 4.22 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.5 (d, J = 248 Hz), 134.1 (d, J = 8.2 Hz), 129.5 (d, J = 3.3 Hz), 116.2 (d, J = 22.0 Hz), 43.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.6.

Bis((4-nitrophenyl)thio)methane (2i)[3]



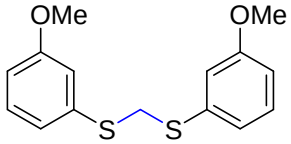
White solid (124 mg, 96%): mp 177−178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 9.0 Hz, 4H), 7.46 (d, J = 9.0 Hz, 4H), 4.54 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.3, 143.9, 128.2, 124.2, 36.4.

Bis(*m*-tolylthio)methane (2j)[4]



Colorless oil (57 mg, 55%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.18 (m, 6H), 7.05 (d, J = 7.0 Hz, 2H), 4.34 (s, 2H), 2.33 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4, 136.0, 132.6, 131.6, 130.2, 128.9, 41.9, 19.7.

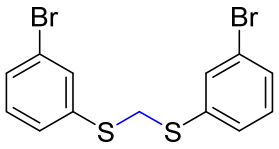
Bis((3-methoxyphenyl)thio)methane (2k)



Yellow oil (62 mg, 53%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.21 (m, 2H), 7.02−6.97 (m, 4H), 6.79 (d, J = 8.2 Hz, 2H), 4.36 (s, 2H), 3.79 (s, 6H); ^{13}C NMR (151

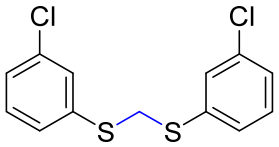
MHz, $CDCl_3$) δ 159.8, 136.3, 129.8, 122.6, 115.7, 112.9, 55.3, 40.1; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{17}O_2S_2$ 293.0664; found 293.0539.

Bis((3-bromophenyl)thio)methane (2l)



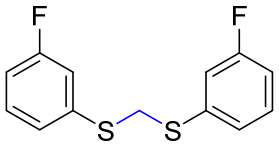
Colorless oil (94 mg, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54−7.53 (m, 2H), 7.40−7.37 (m, 2H), 7.34−7.31 (m, 2H), 7.20−7.16 (m, 2H), 4.33 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.8, 133.2, 130.4, 130.3, 129.2, 122.8, 40.3; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{13}H_{11}Br_2S_2$ 388.8663; found 388.8568.

Bis((3-chlorophenyl)thio)methane (2m)



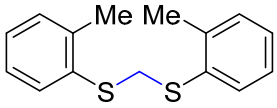
Colorless oil (78 mg, 65%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (s, 2H), 7.30−7.21 (m, 6H), 4.34 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.6, 134.8, 130.3, 130.1, 128.7, 127.5, 40.1; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{13}H_{11}Cl_2S_2$ 300.9674; found 300.9666.

Bis((3-fluorophenyl)thio)methane (2n)



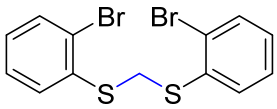
Blue oil (72 mg, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.24 (m, 2H), 7.17−7.09 (m, 4H), 6.96−6.91 (m, 2H), 4.34 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.7 (d, J = 249 Hz), 137.0 (d, J = 8.5 Hz), 130.3 (d, J = 7.8 Hz), 125.9 (d, J = 3.0 Hz), 117.1 (d, J = 22.9 Hz), 114.2 (d, J = 21.2 Hz), 39.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.8; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{13}H_{11}F_2S_2$ 269.0265; found 269.0154.

Bis(*o*-tolylthio)methane (2o)[4]



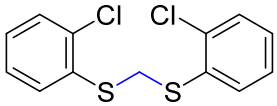
Colorless oil (73 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.3 Hz, 2H), 7.20−7.16 (m, 6H), 4.31 (s, 2H), 2.37 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 134.5, 130.3, 130.0, 126.9, 126.5, 38.7, 20.5.

Bis((2-bromophenyl)thio)methane (2p)



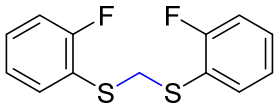
Colorless oil (111 mg, 71%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58−7.57 (m, 2H), 7.48−7.46 (m, 2H), 7.32−7.29 (m, 2H), 7.12−7.09 (m, 2H), 4.41 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.9, 133.2, 130.8, 128.1, 127.9, 125.1, 37.9; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{13}H_{11}Br_2S_2$ 388.8663; found 388.8564.

Bis((2-chlorophenyl)thio)methane (2q)[3]



White solid (92 mg, 76%): mp 68−69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.47 (m, 2H), 7.41−7.38 (m, 2H), 7.27−7.17 (m, 4H), 4.41 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.0, 133.7, 131.2, 129.9, 128.1, 127.2, 37.2.

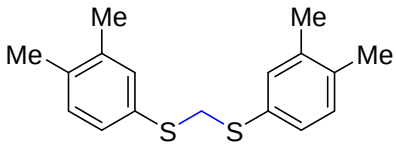
Bis((2-fluorophenyl)thio)methane (2r)



Colorless oil (96 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.37 (m, 2H), 7.24−7.21 (m, 2H), 7.07−6.99 (m, 4H), 4.29 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.0 (d, J = 246 Hz), 134.0 (d, J = 1.1 Hz), 129.8 (d, J = 8.0 Hz), 124.5 (d, J = 3.7

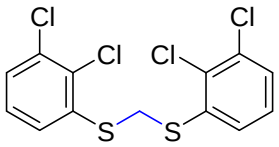
Hz), 121.0 (d, J = 17.7 Hz), 115.8 (d, J = 22.5 Hz), 38.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -108.5; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_{11}F_2S_2$ 269.0265; found 269.0423.

Bis((3,4-dimethylphenyl)thio)methane (2s)



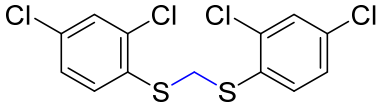
Colorless oil (58 mg, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−7.17 (m, 4H), 7.08−7.06 (m, 2H), 4.27 (s, 2H), 2.24 (s, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4, 136.0, 132.6, 131.6, 130.2, 128.9, 41.9, 19.7, 19.4; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{21}S_2$ 289.1079; found 289.1043.

Bis((2,3-dichlorophenyl)thio)methane (2u)



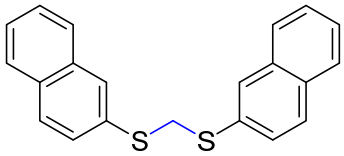
Yellow oil (83 mg, 56%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.36 (m, 4H), 7.22 (dd, J = 8.4, 2.2 Hz, 2H), 4.35 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.10, 135.08, 132.3, 130.5, 127.63, 127.62, 49.2; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_9Cl_4S_2$ 368.8894; found 368.8817.

Bis((2,4-dichlorophenyl)thio)methane (2v)



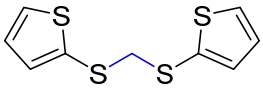
Colorless oil (93 mg, 63%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, J = 5.4, 1.2 Hz, 2H), 7.22 (dd, J = 3.6, 1.2 Hz, 2H), 7.02 (dd, J = 5.4, 3.6 Hz, 2H), 4.06 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.2, 133.9, 132.7, 131.8, 129.8, 127.5, 37.8; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{13}H_9Cl_4S_2$ 368.8894; found 368.8819.

Bis(naphthalen-2-ylthio)methane (2w)[5]



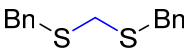
Colorless oil (76 mg, 57%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 2H), 7.82−7.70 (m, 6H), 7.52−7.44 (m, 6H), 4.54 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.6, 132.30, 132.27, 129.4, 128.6, 128.2, 127.7, 127.4, 126.6, 126.2, 40.6.

Bis(thiophen-2-ylthio)methane (2x)[2]



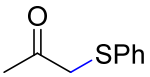
Colorless oil (59 mg, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.33 (m, 4H), 7.21−7.17 (m, 2H), 4.42 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.2, 128.8, 128.5, 127.5, 37.1.

Bis(benzylthio)methane (2y)[2]



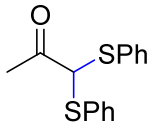
White solid (37 mg, 36%): mp 54−55 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.42 (m, 8H), 7.41−7.36 (m, 2H), 3.98 (s, 4H), 3.52 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 129.2, 128.6, 127.1, 34.6, 33.6.

1-(Phenylthio)propan-2-one (3a)[6]



Colorless oil (5 mg, 7%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.19 (m, 4H), 7.15−7.12 (m, 1H), 3.59 (s, 2H), 2.19 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.5, 134.7, 129.6, 129.2, 126.9, 44.7, 28.0.

1,1-Bis(phenylthio)propan-2-one (4a)[7]

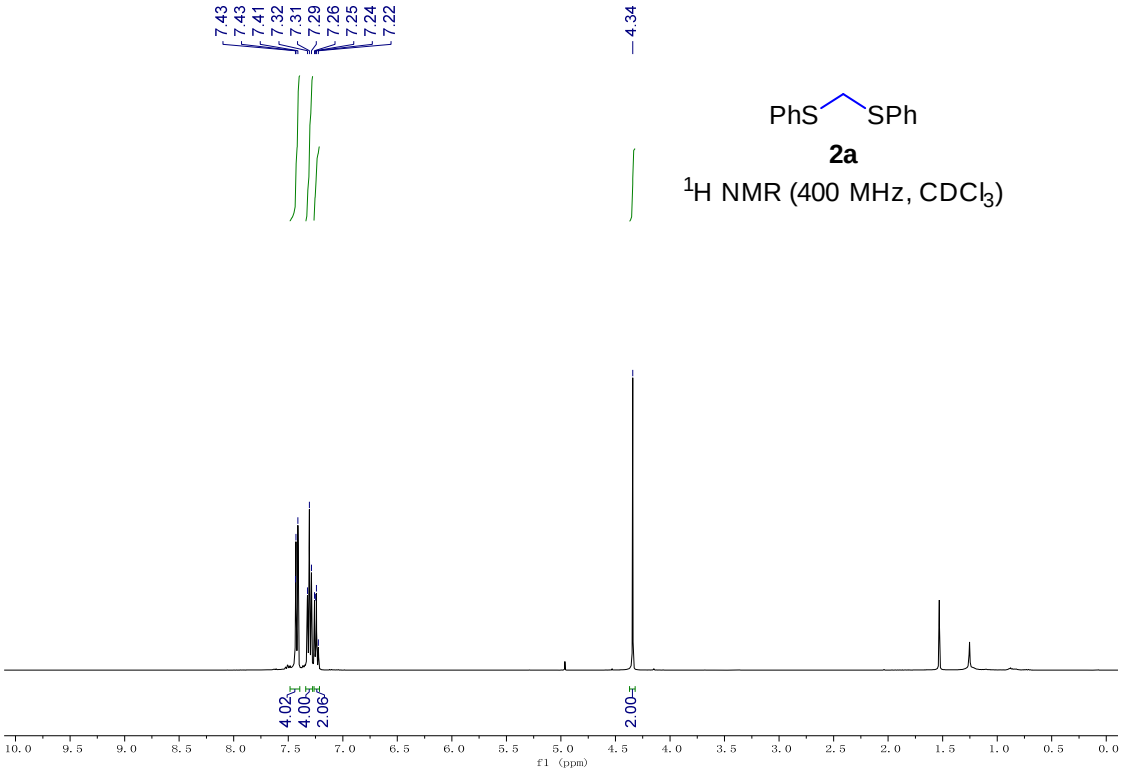


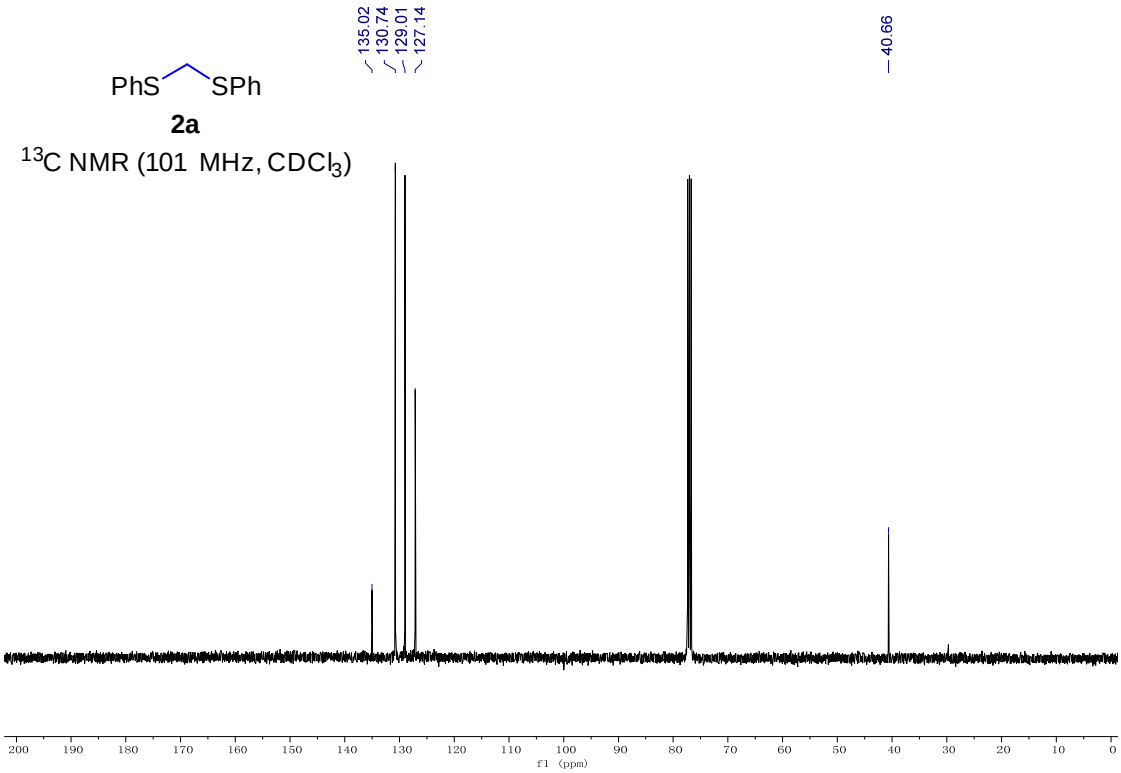
Colorless oil (19 mg, 17%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.44 (m, 4H), 7.33−7.32 (m, 6H), 4.88 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.0, 132.9, 132.5, 129.2, 128.6, 65.1, 25.9.

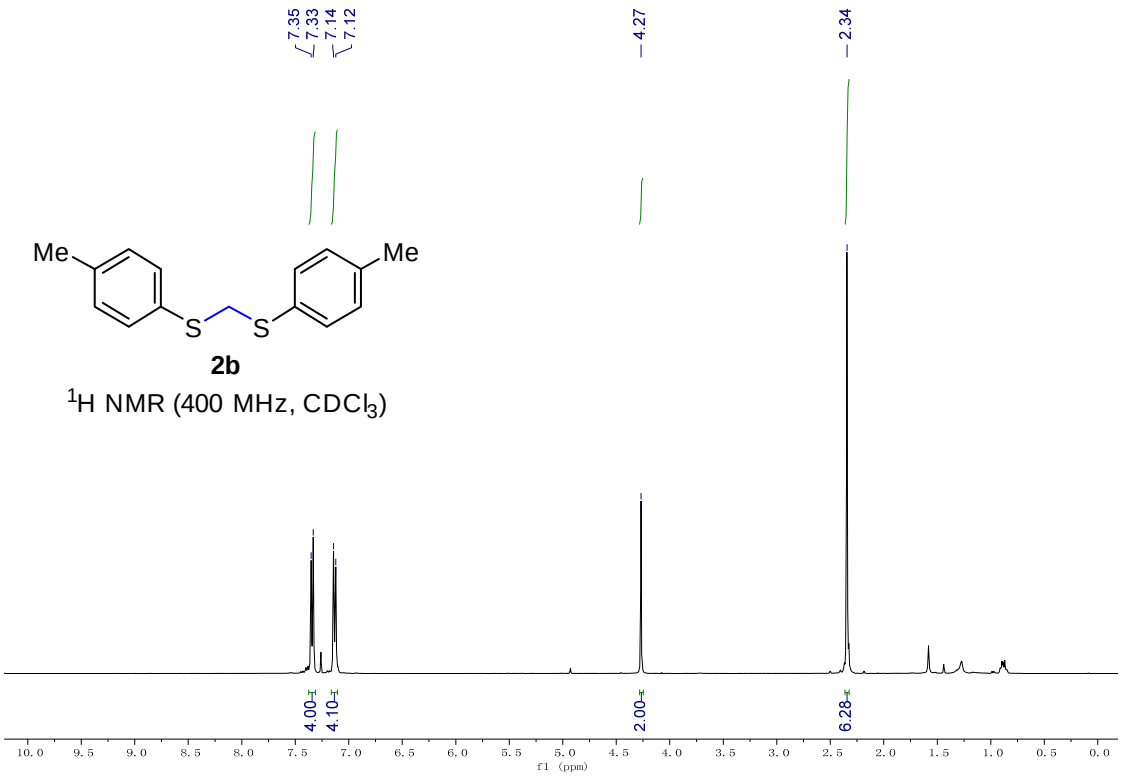
References:

1. W.-L. Dong, G.-Y. Huang, Z.-M. Li and W.-G. Zhao, Phosphorus, *Sulfur Silicon Relat. Elem*., 2009, **184**, 2058.
2. V. Pace, A. Pelosi and W. Holzer, *Chem. Commun.*, 2016, **52**, 2639.
3. R. F. Brookes, *J. Sci. Food Agr.*, 1957, **8**, 31.
4. T. Shigeo, *Bull. Inst. Chem. Res., Kyoto Univ.*, 1978, **56**, 297.
5. H. Hauptmann, *J. Am. Chem. Soc.*, 1950, **72**, 707.
6. X.-P. Gu, N. Nishida, I. Ikeda and M. Okahara, *J. Org. Chem.*, 1987, **52**, 3192.
7. F. A. Davis and P. A. Mancinelli, *J. Org. Chem.*, 1980, **45**, 2597.

5. Copies of ^{1}H and ^{13}C NMR Spectra for 2, 3a and 4a

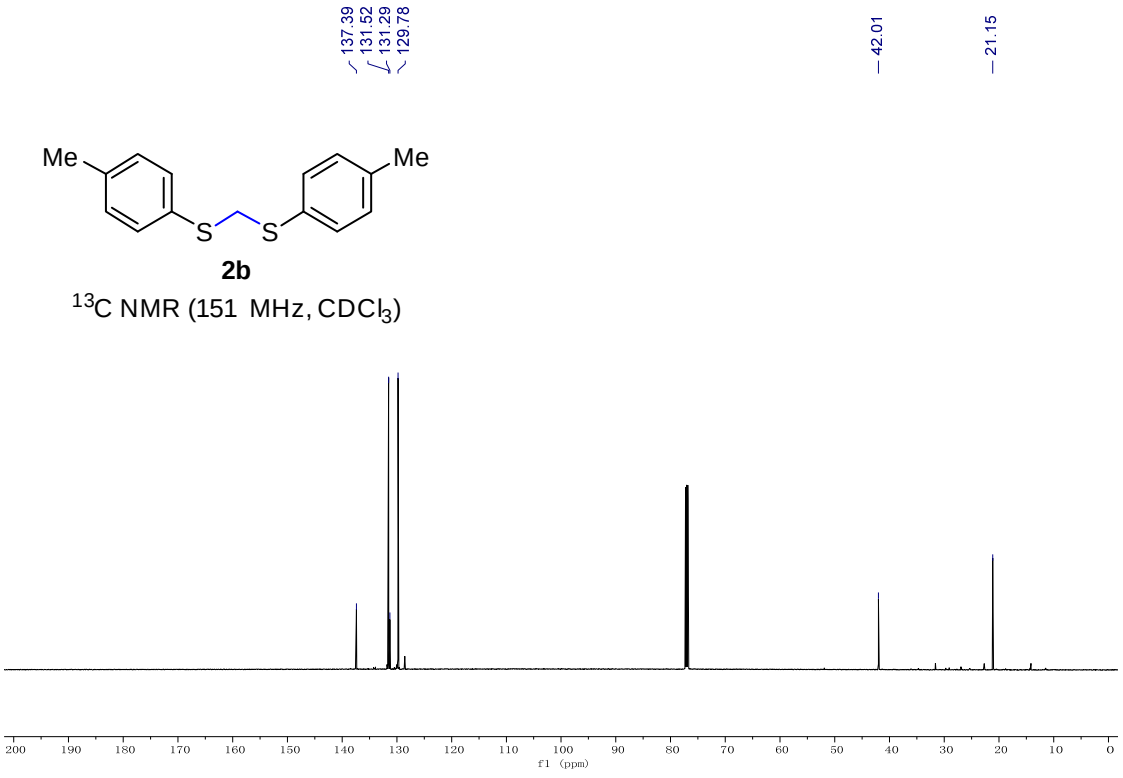






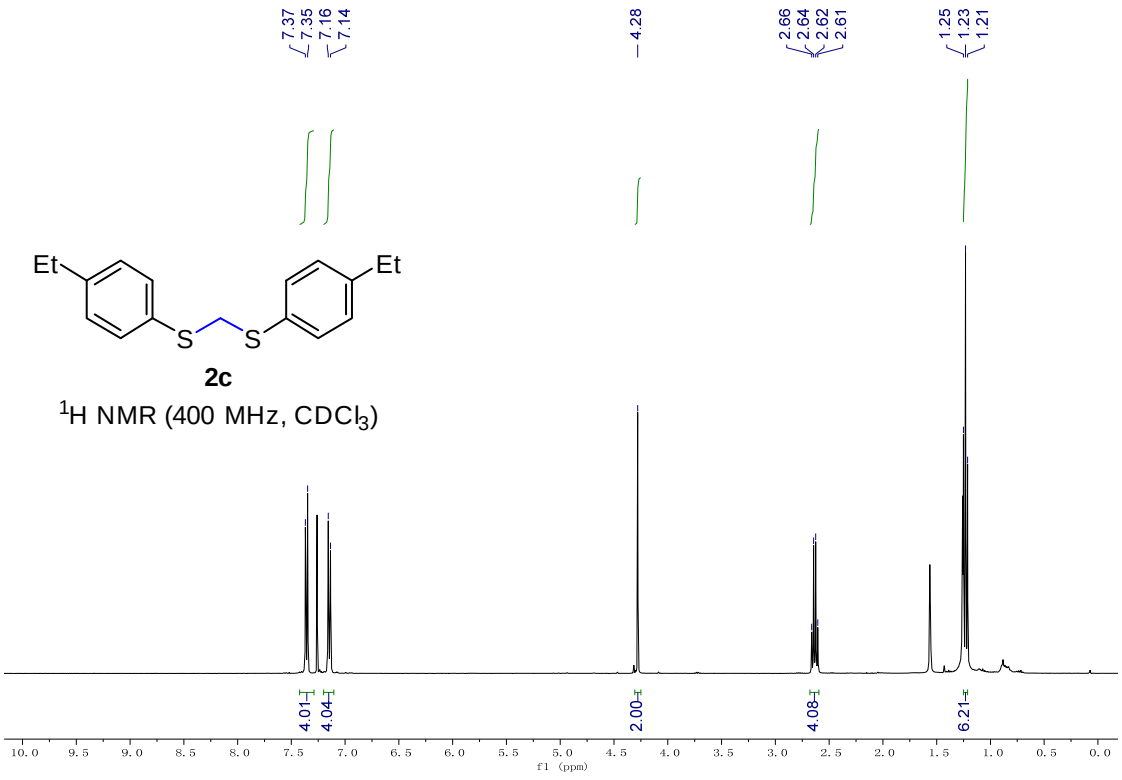
2b

^{1}H NMR (400 MHz, $CDCl_3$)



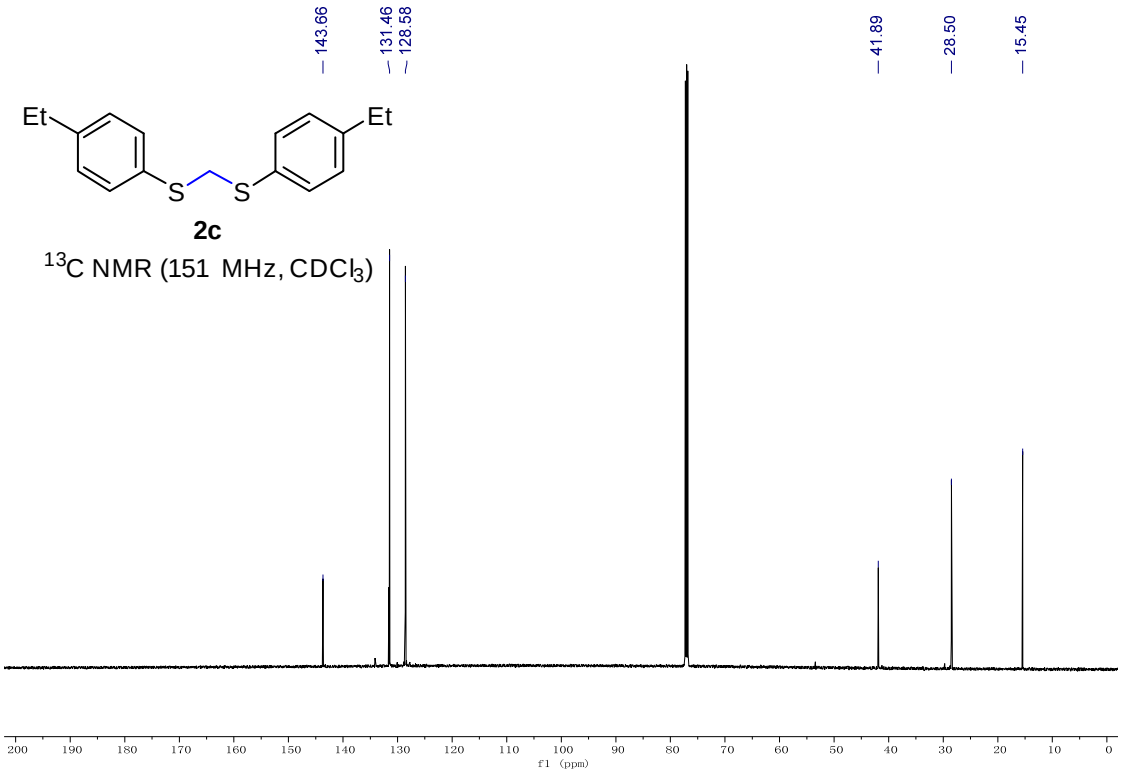
2b

^{13}C NMR (151 MHz, $CDCl_3$)



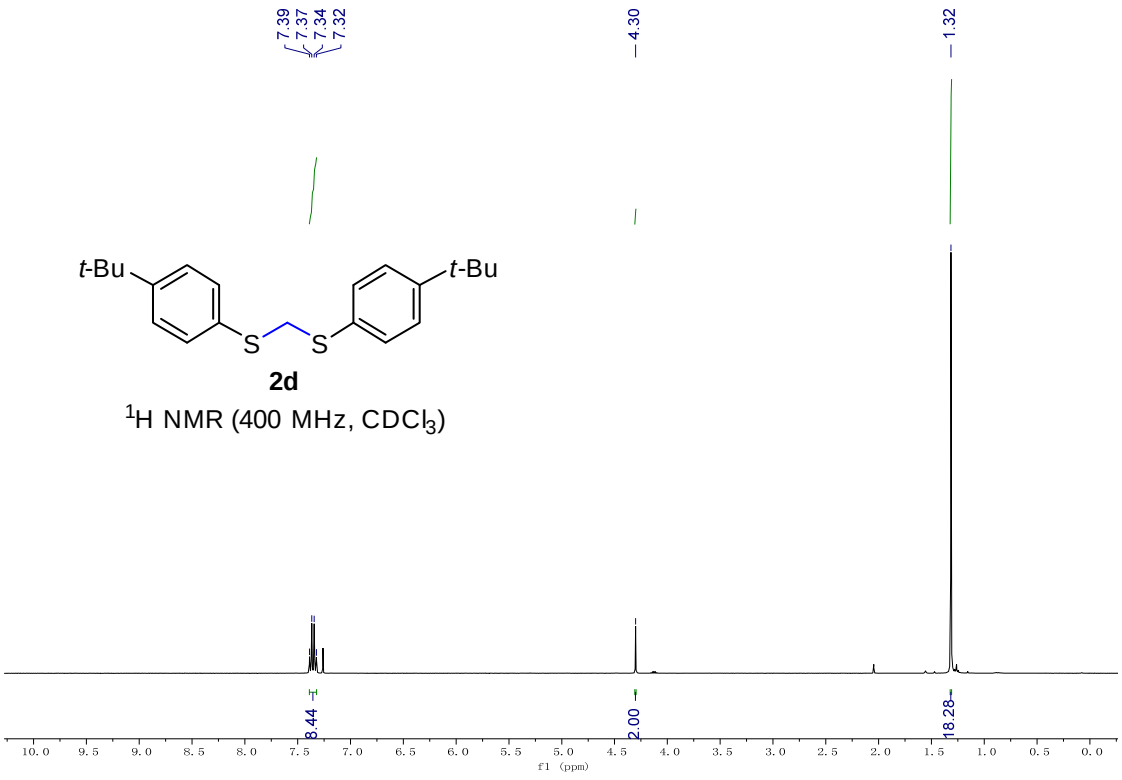
2c

^{1}H NMR (400 MHz, $CDCl_3$)



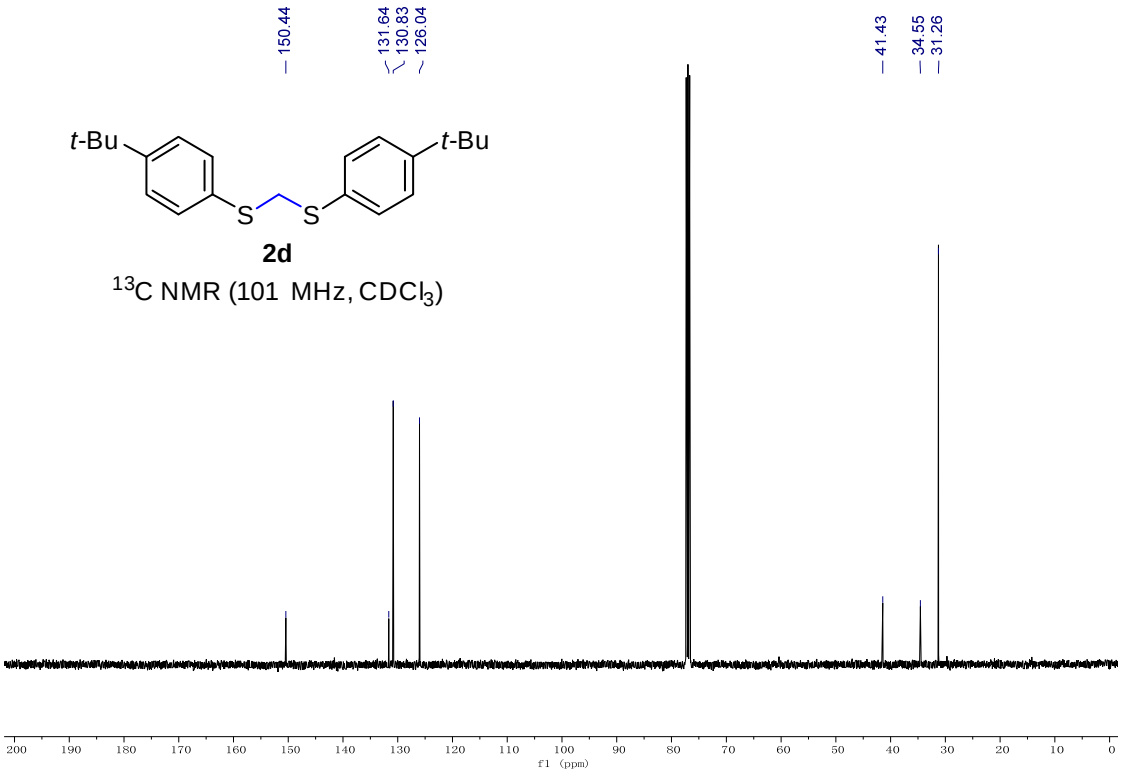
2c

^{13}C NMR (151 MHz, $CDCl_3$)



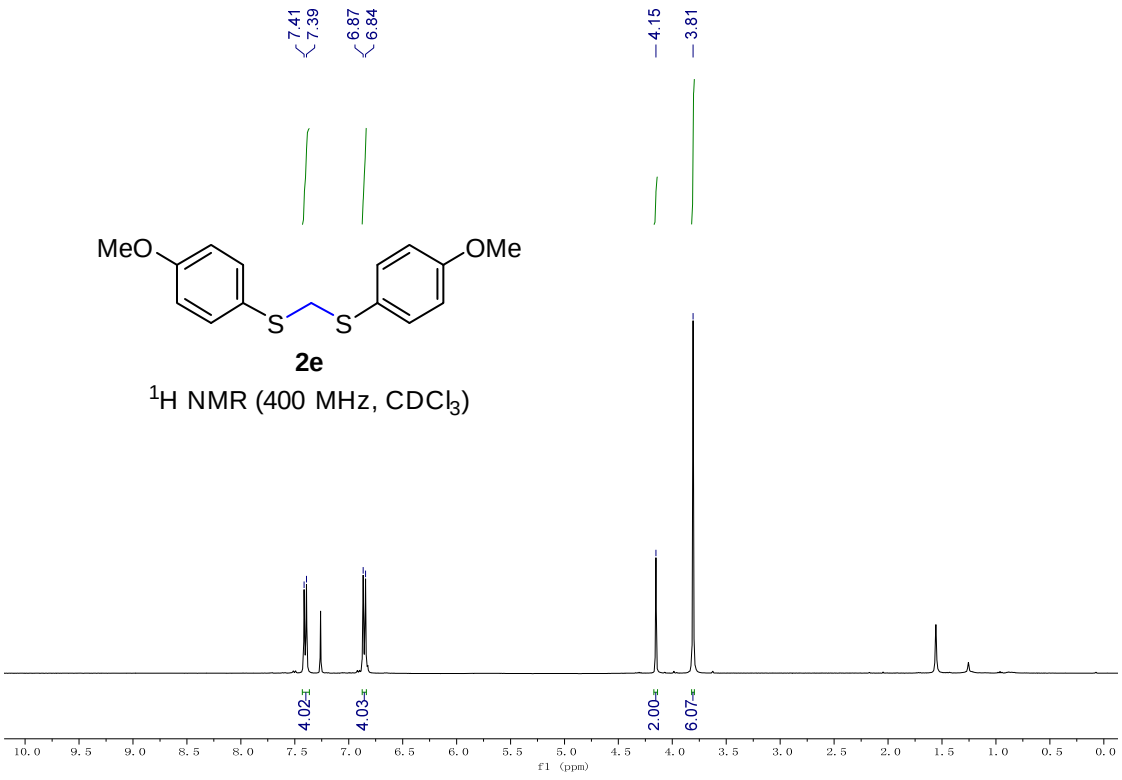
2d

^{1}H NMR (400 MHz, $CDCl_3$)



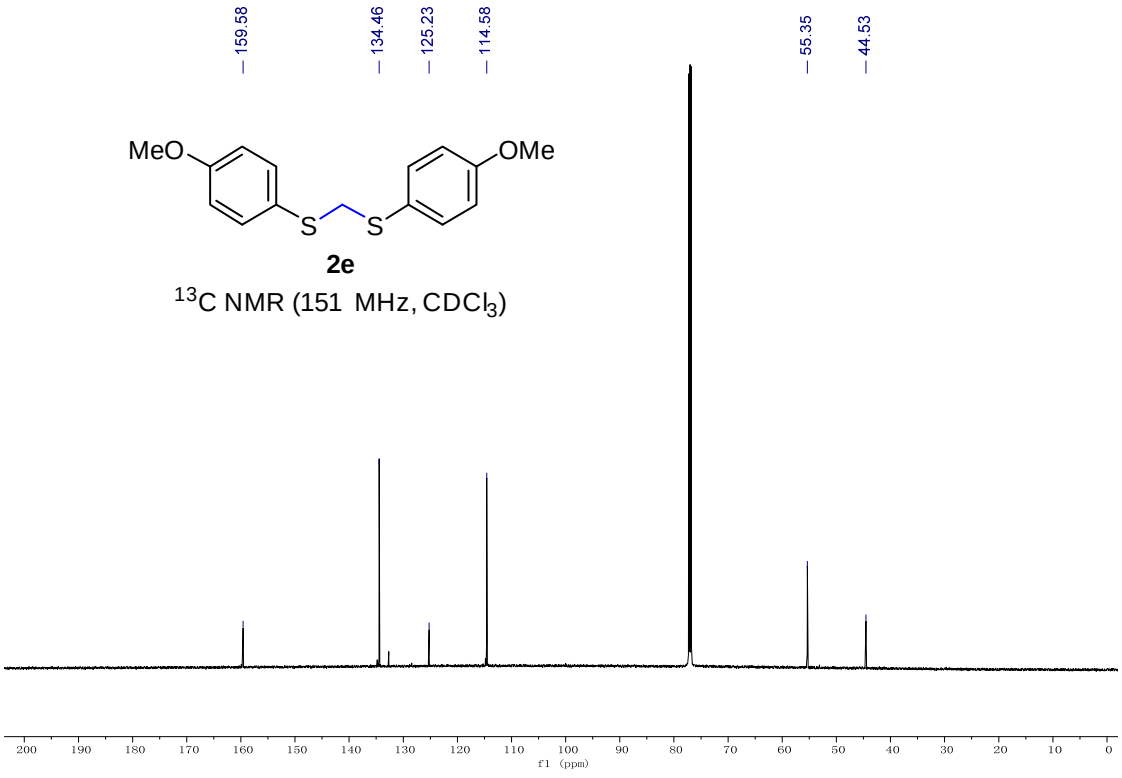
2d

^{13}C NMR (101 MHz, $CDCl_3$)



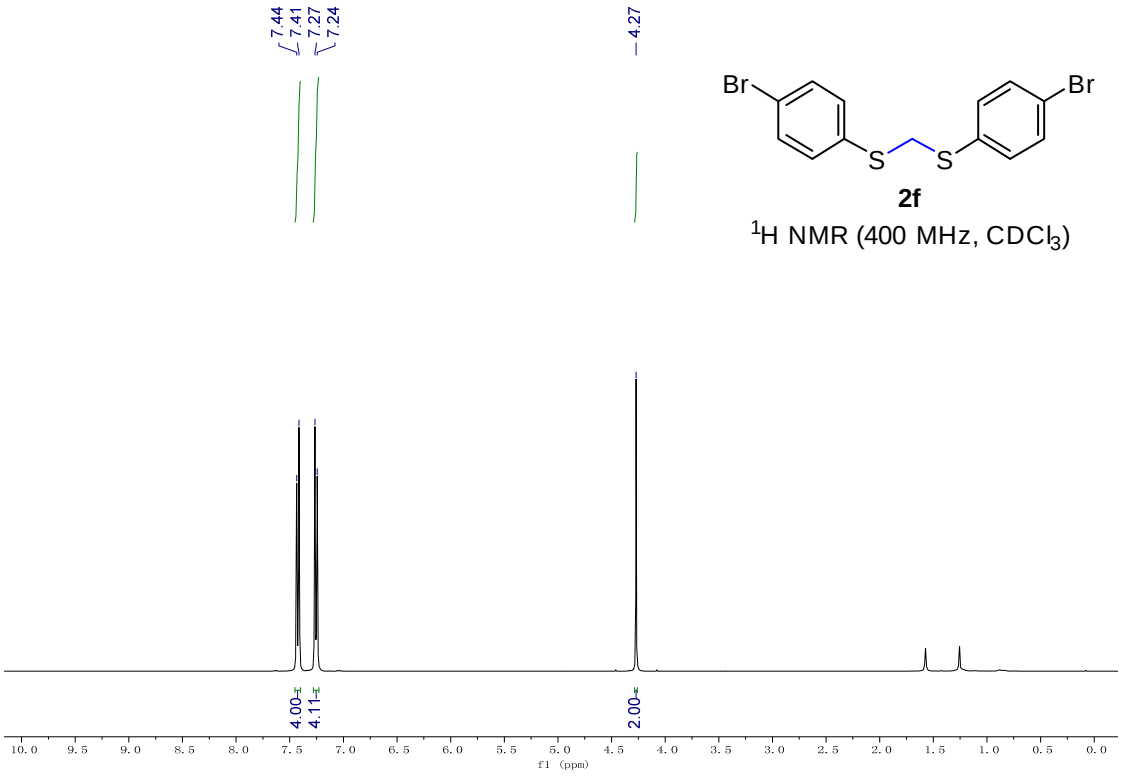
2e

^{1}H NMR (400 MHz, $CDCl_3$)



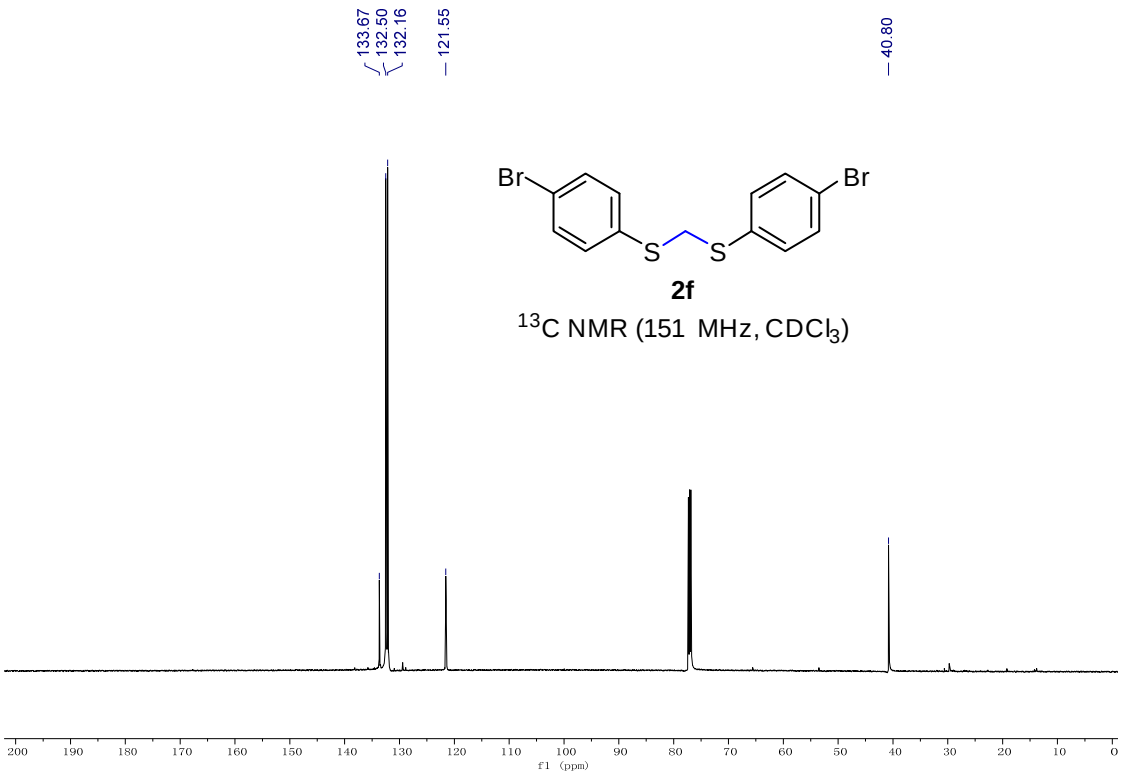
2e

^{13}C NMR (151 MHz, $CDCl_3$)



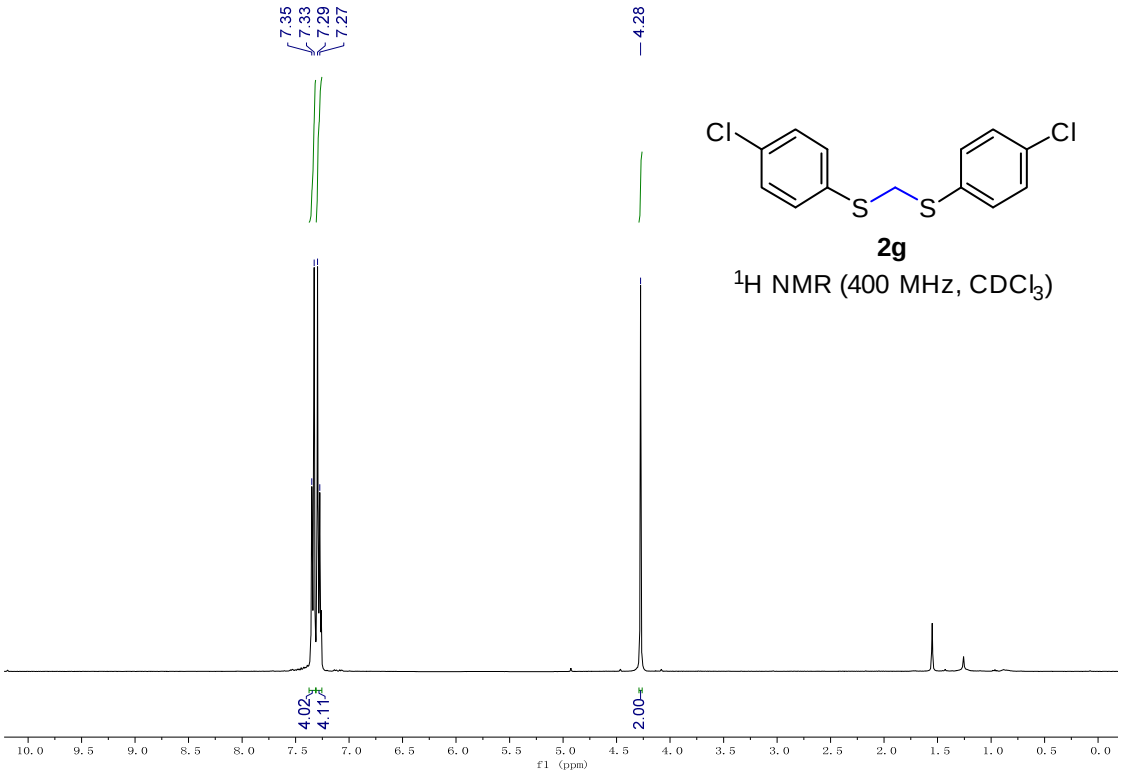
2f

^{1}H NMR (400 MHz, $CDCl_3$)



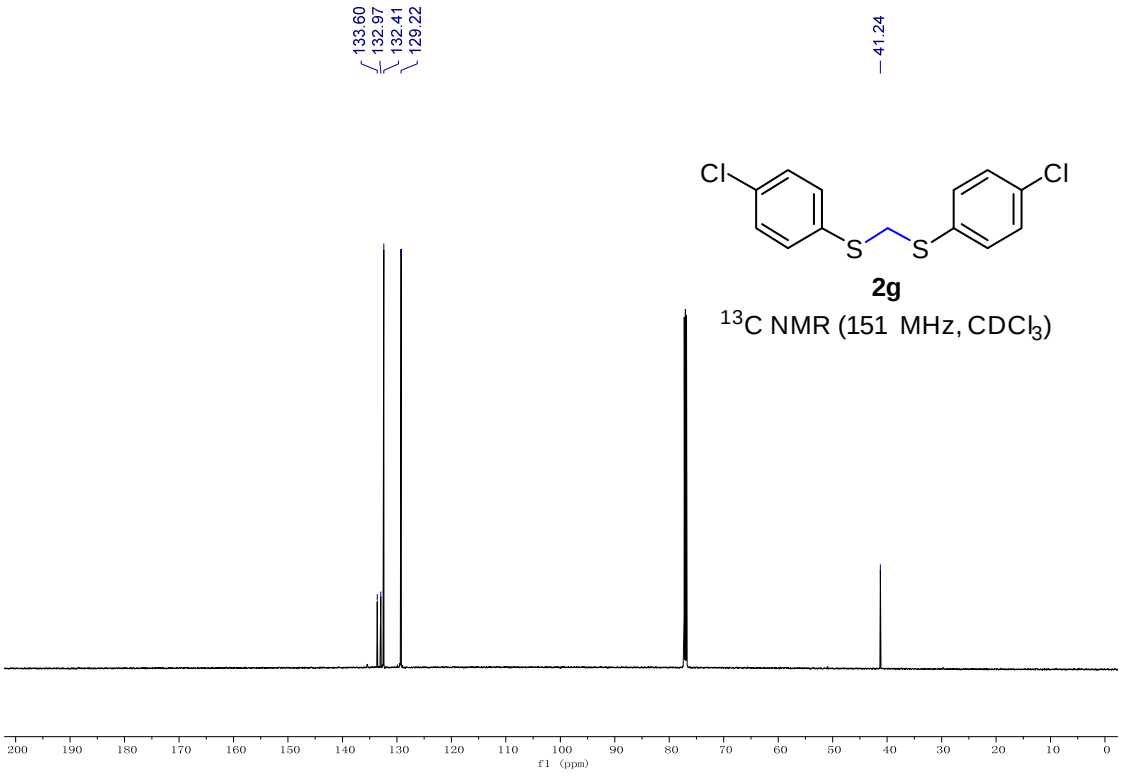
2f

^{13}C NMR (151 MHz, $CDCl_3$)



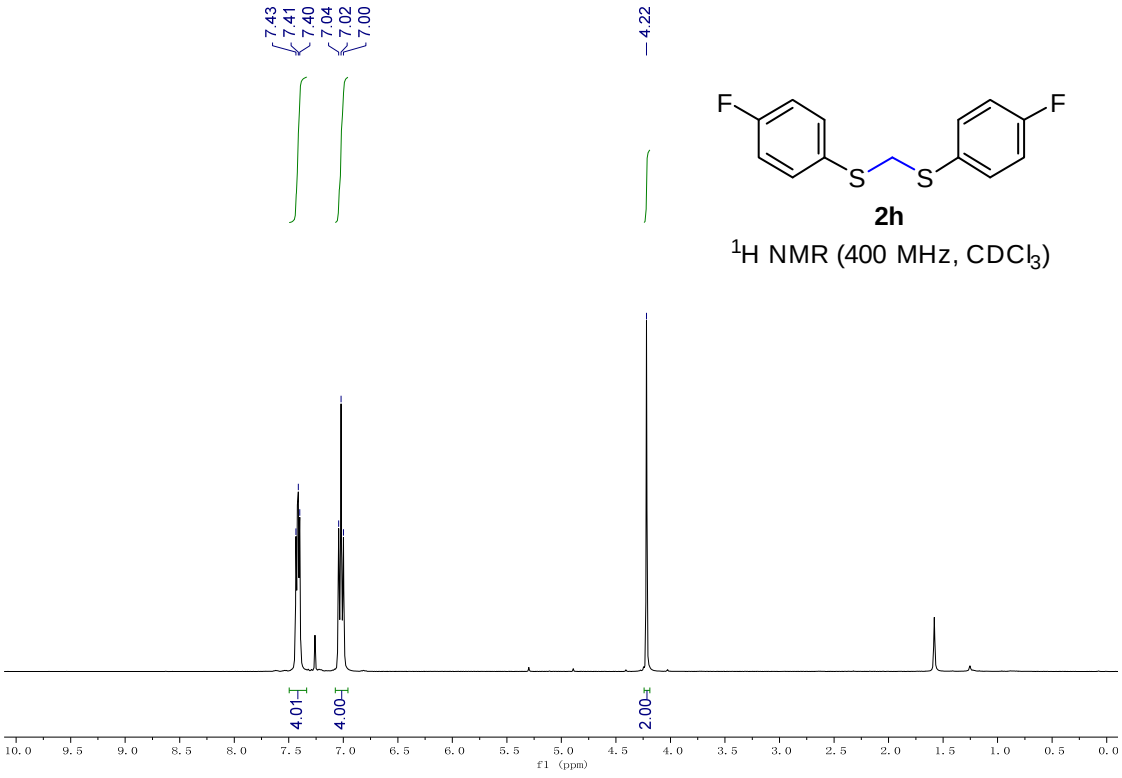
2g

^{1}H NMR (400 MHz, $CDCl_3$)



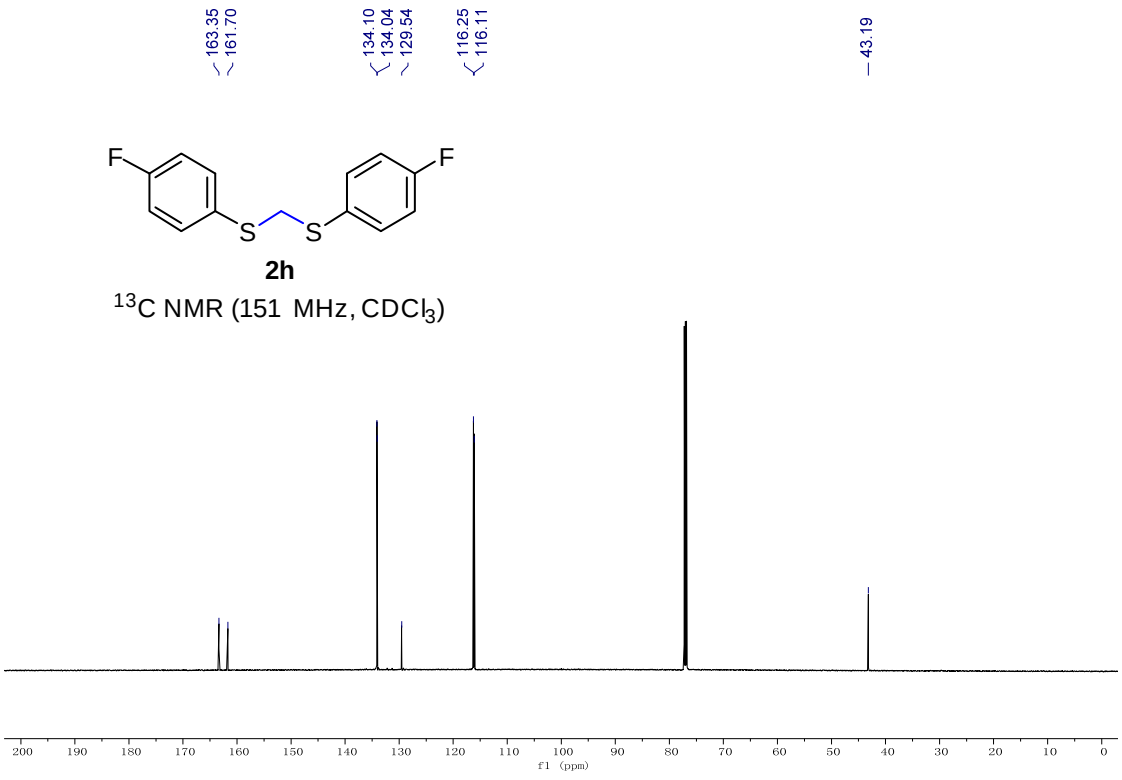
2g

^{13}C NMR (151 MHz, $CDCl_3$)



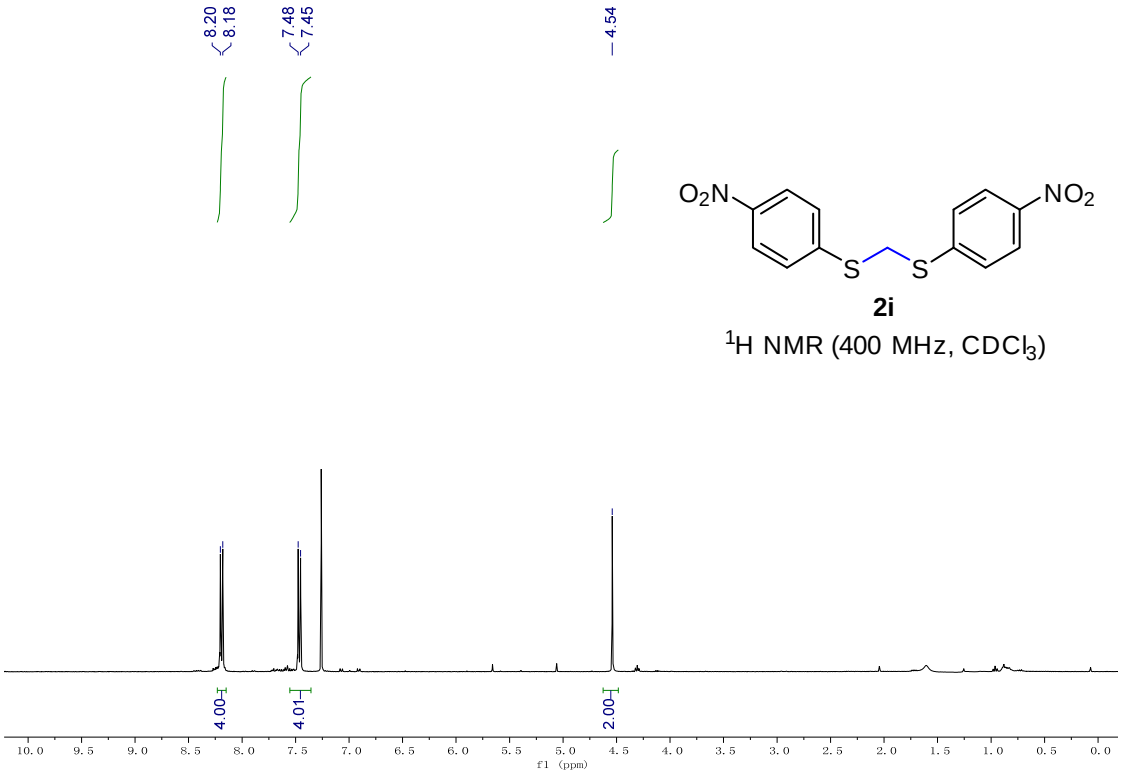
2h

^{1}H NMR (400 MHz, $CDCl_3$)



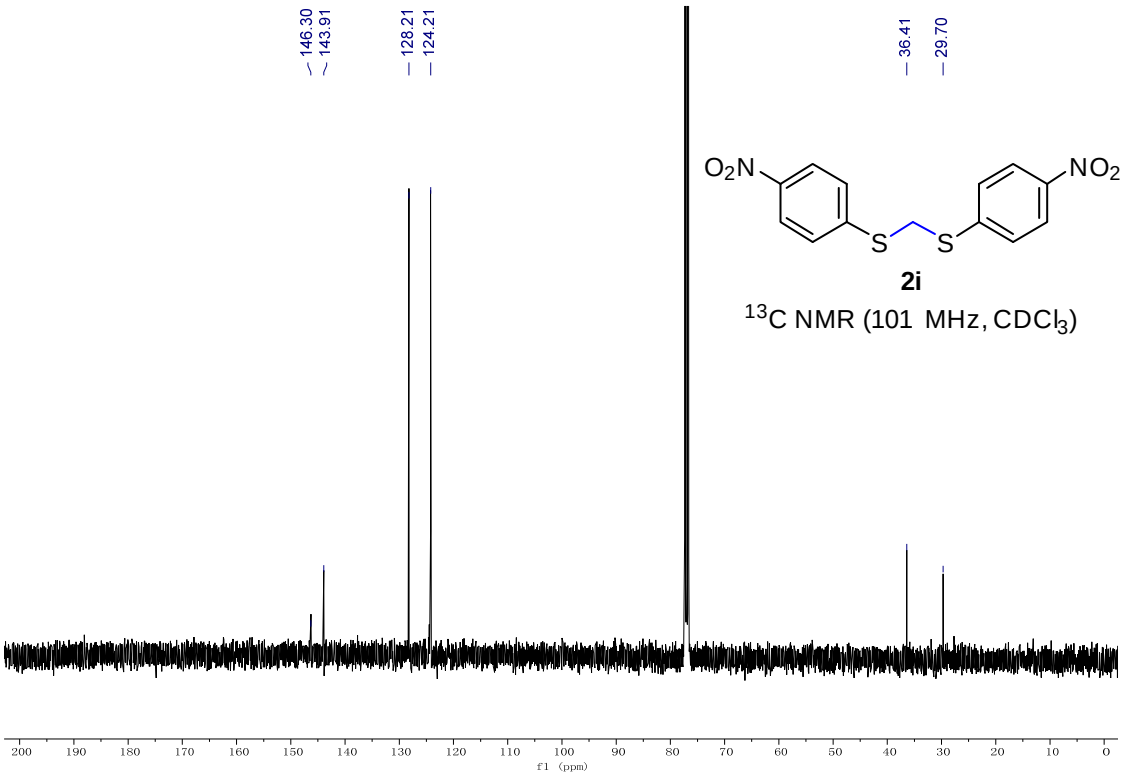
2h

^{13}C NMR (151 MHz, $CDCl_3$)



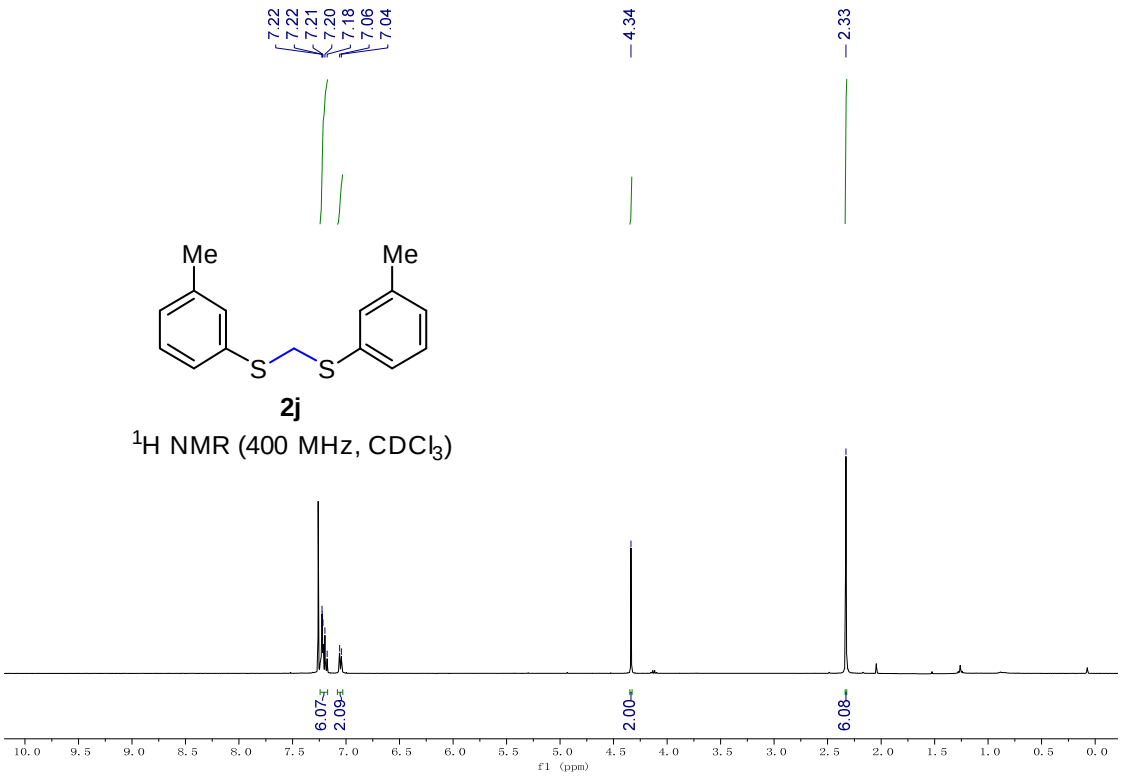
2i

^{1}H NMR (400 MHz, $CDCl_3$)



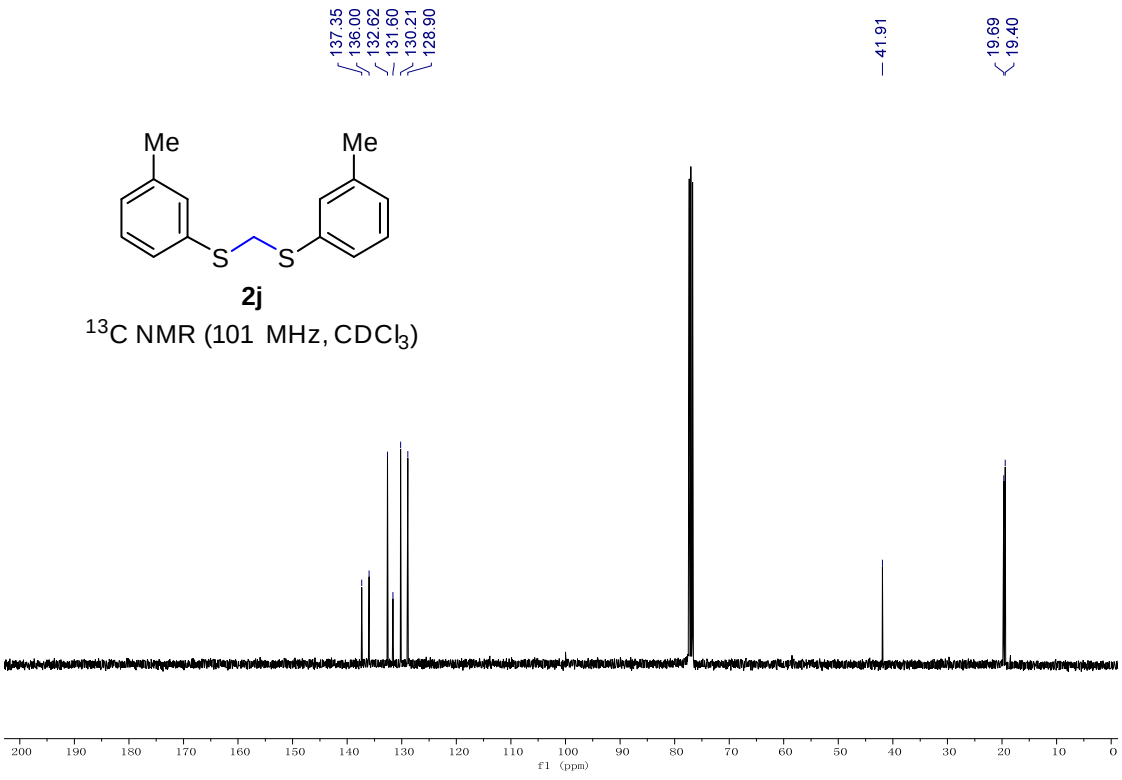
2i

^{13}C NMR (101 MHz, $CDCl_3$)



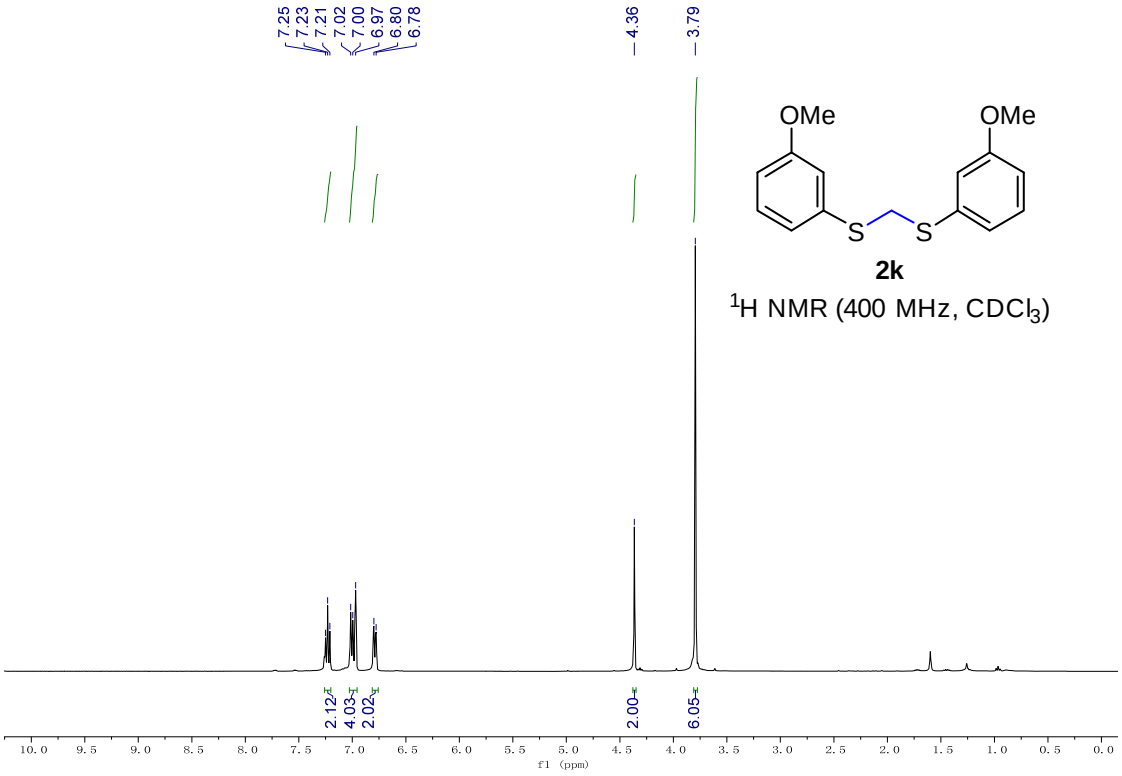
2j

^{1}H NMR (400 MHz, $CDCl_3$)



2j

^{13}C NMR (101 MHz, $CDCl_3$)



2k

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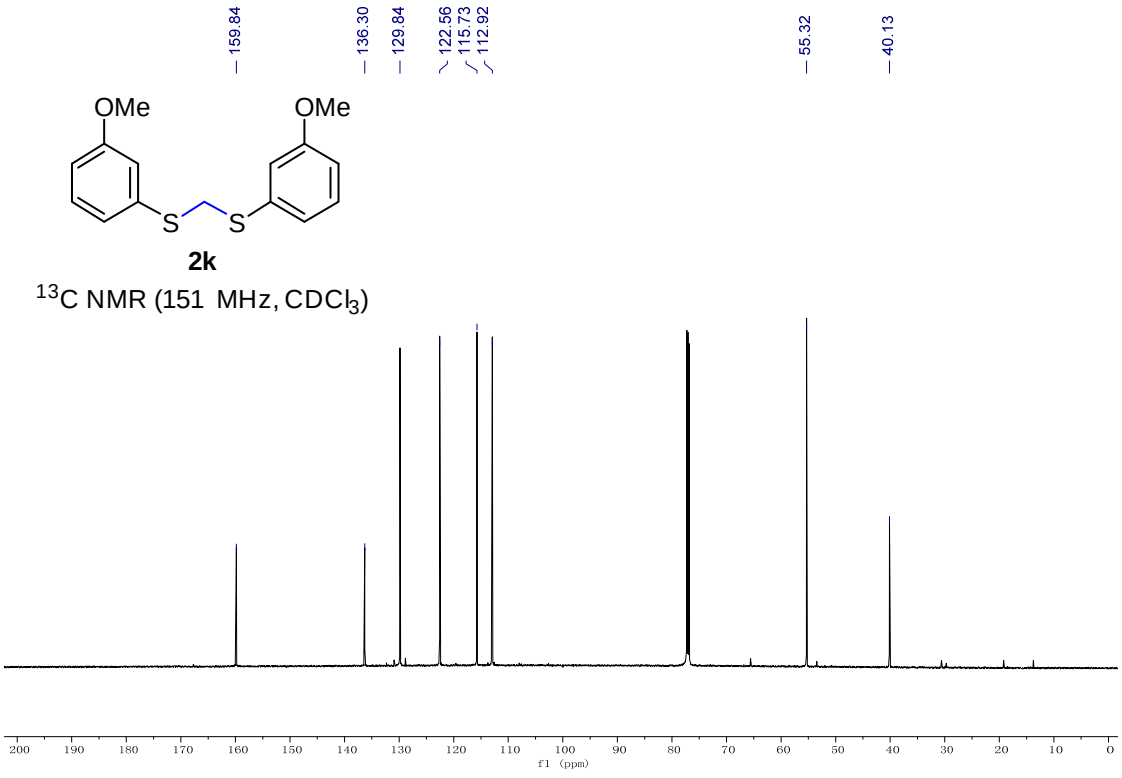

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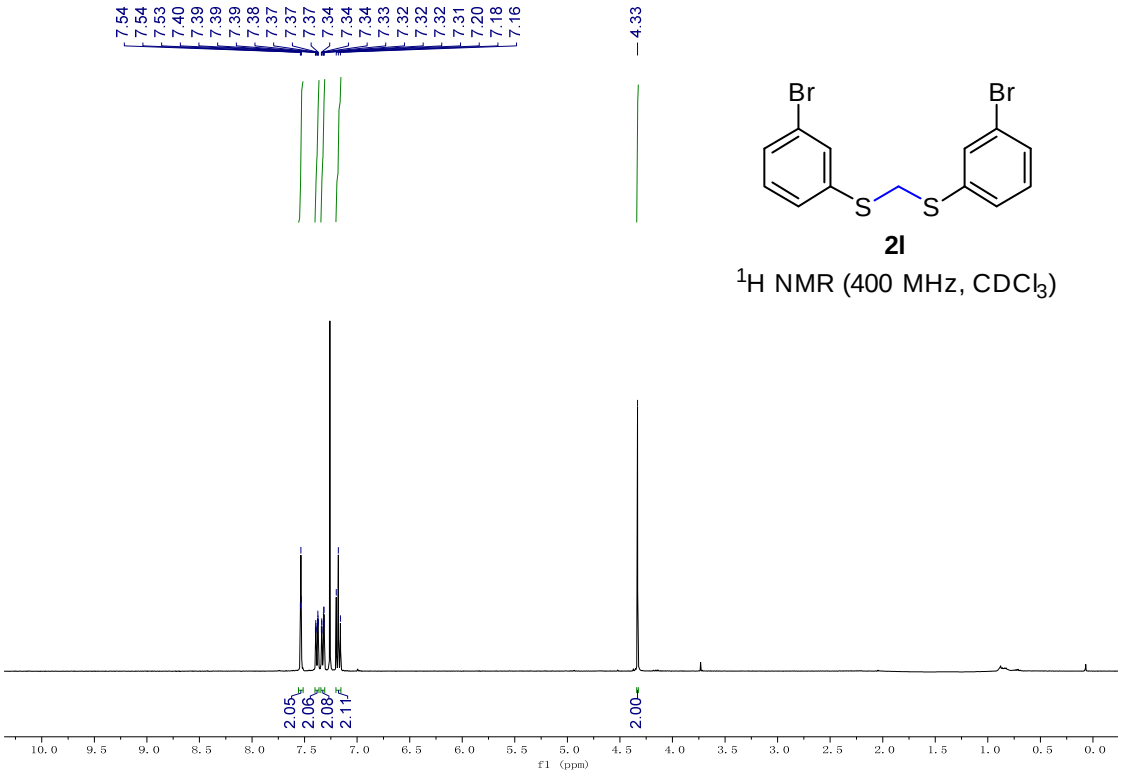

2l

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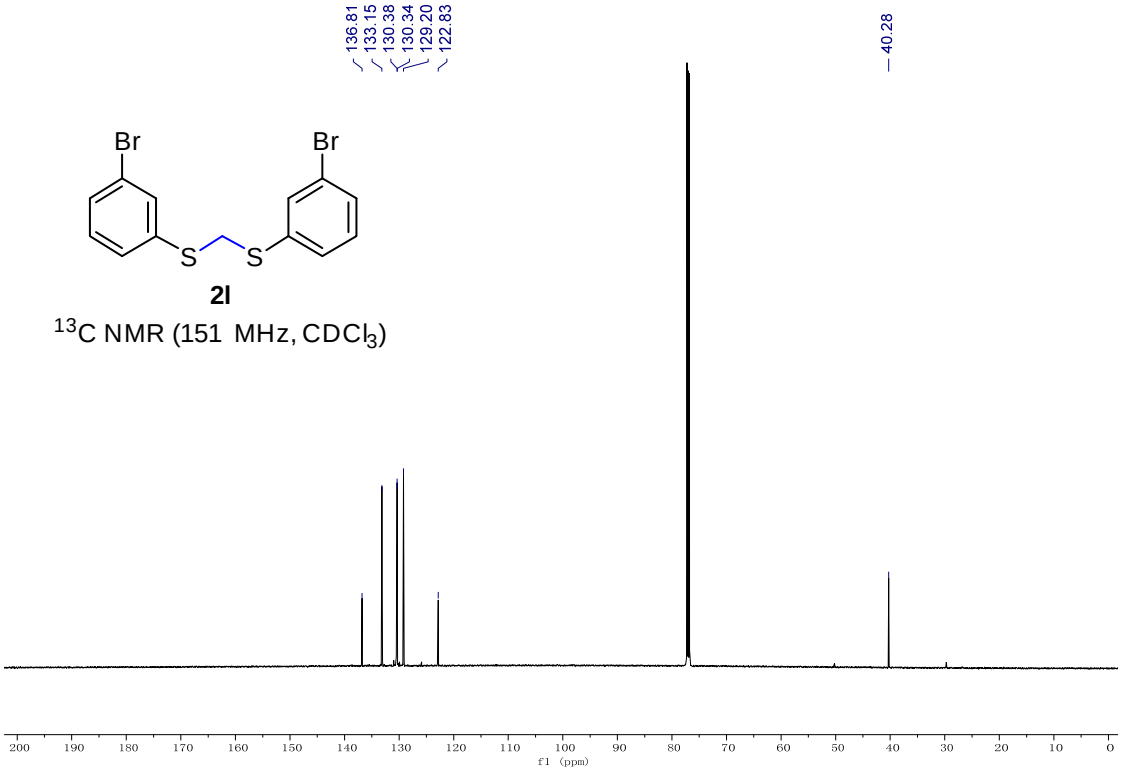
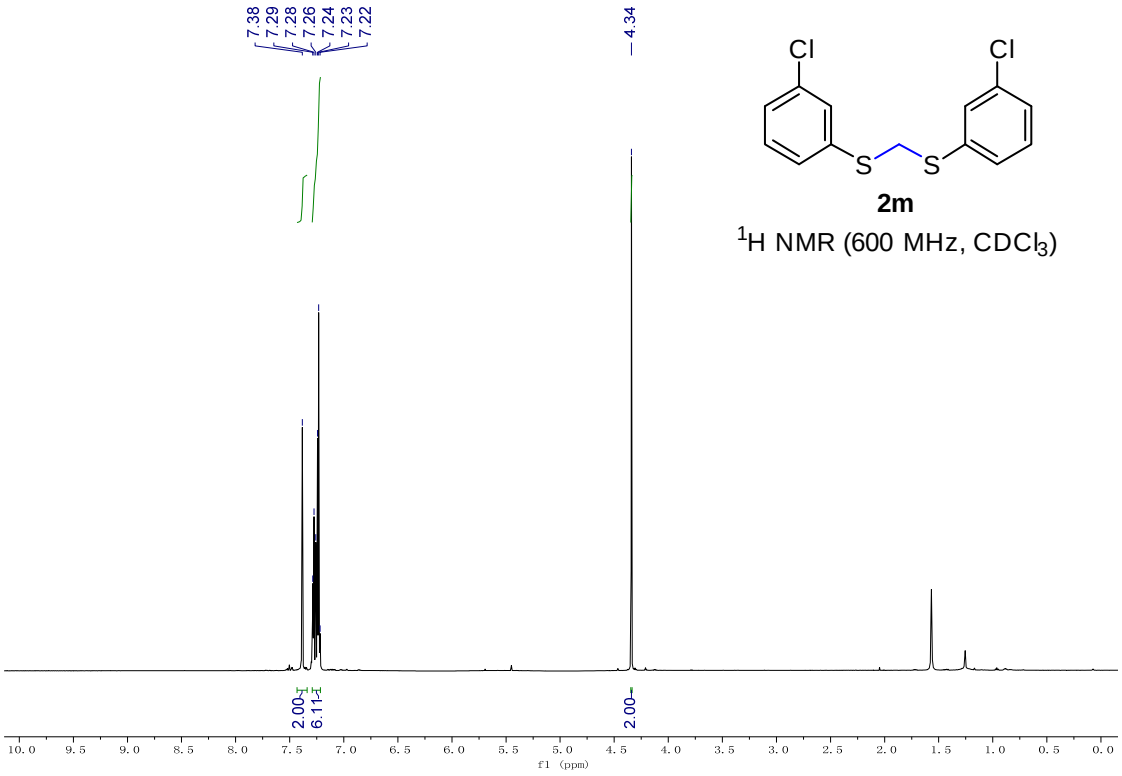


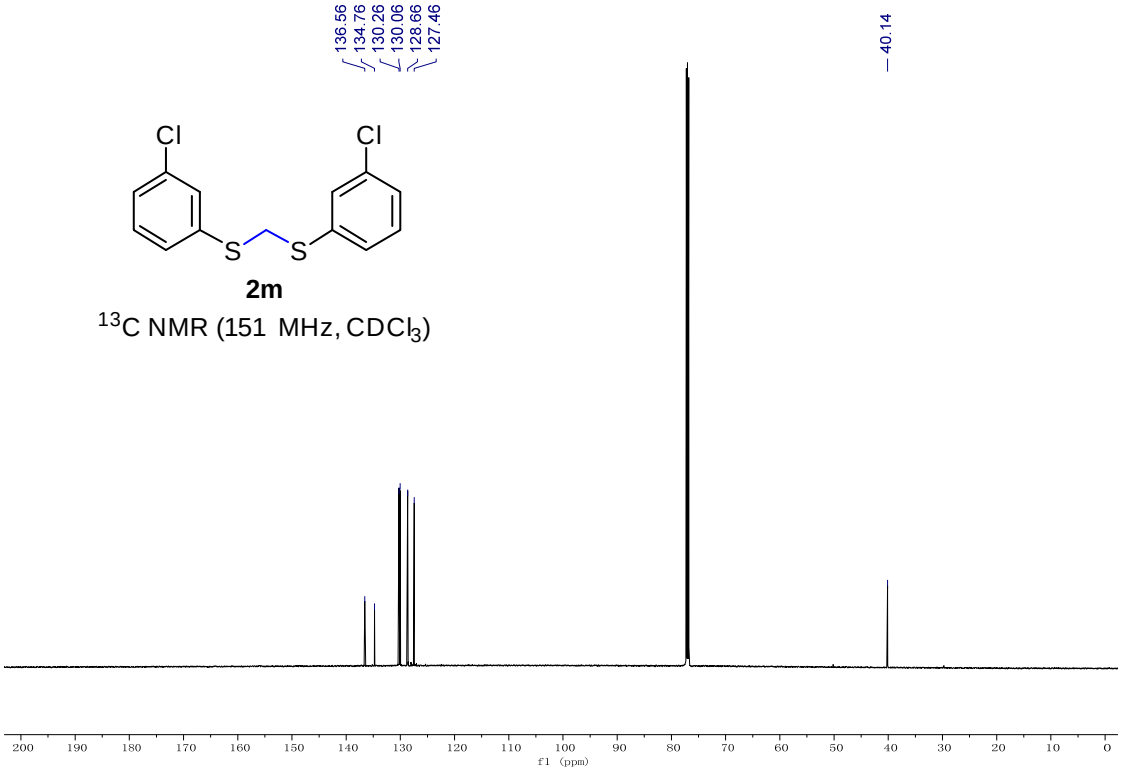
2l

^{13}C NMR (151 MHz, $CDCl_3$)



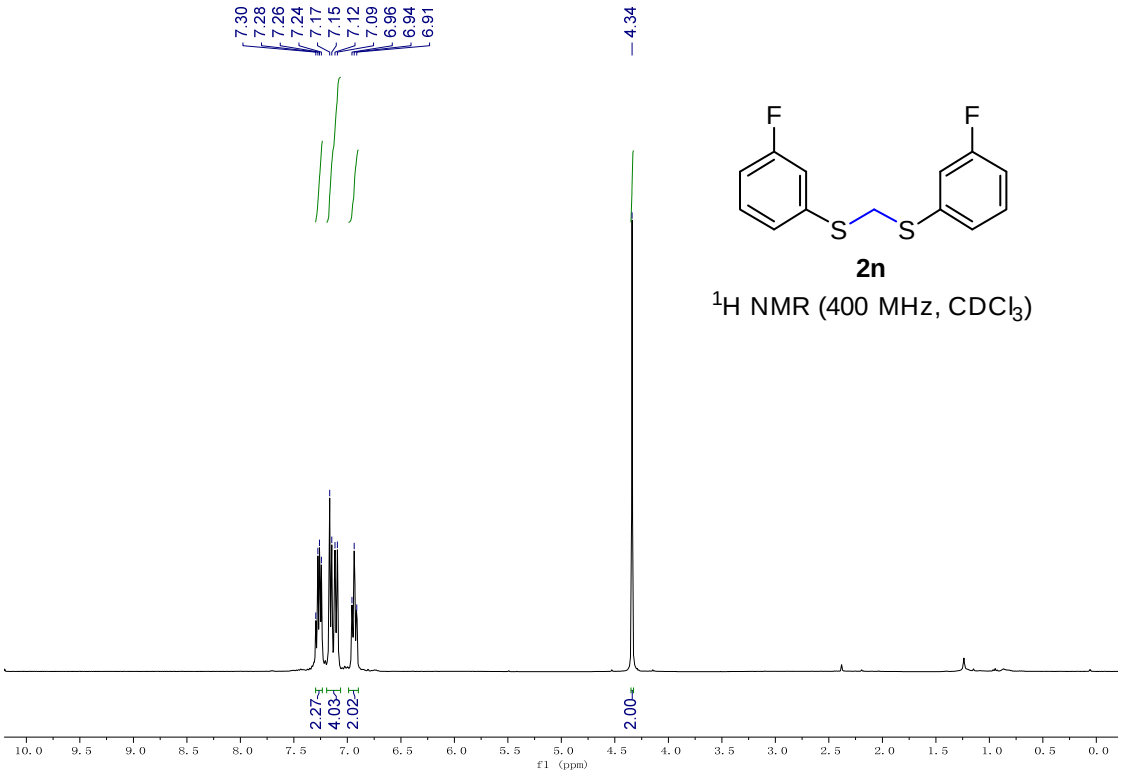
2m

^{1}H NMR (600 MHz, $CDCl_3$)



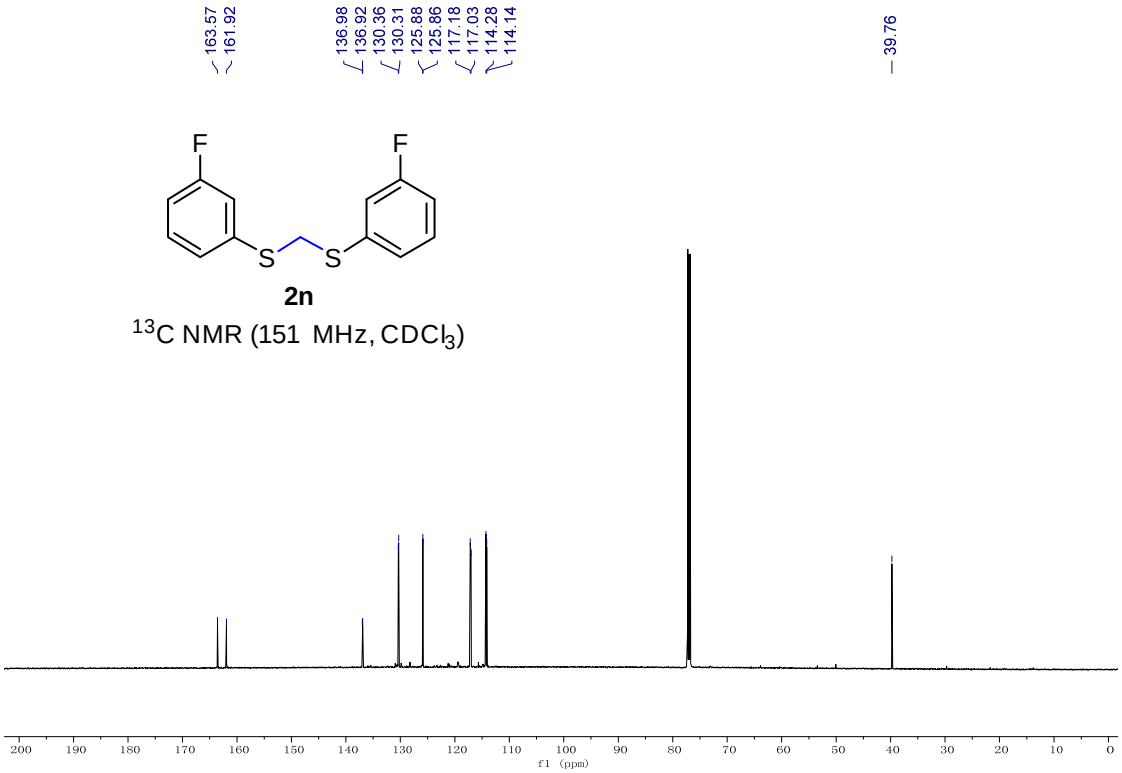
2m

^{13}C NMR (151 MHz, $CDCl_3$)



2n

^{1}H NMR (400 MHz, $CDCl_3$)



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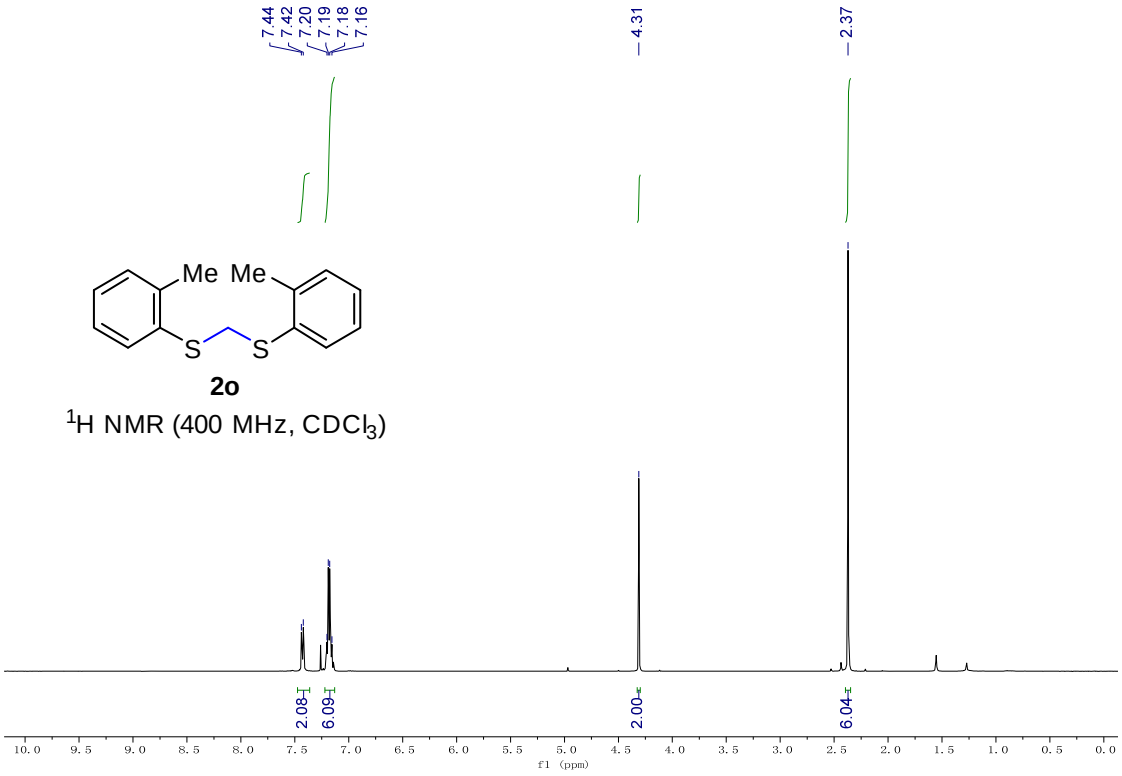
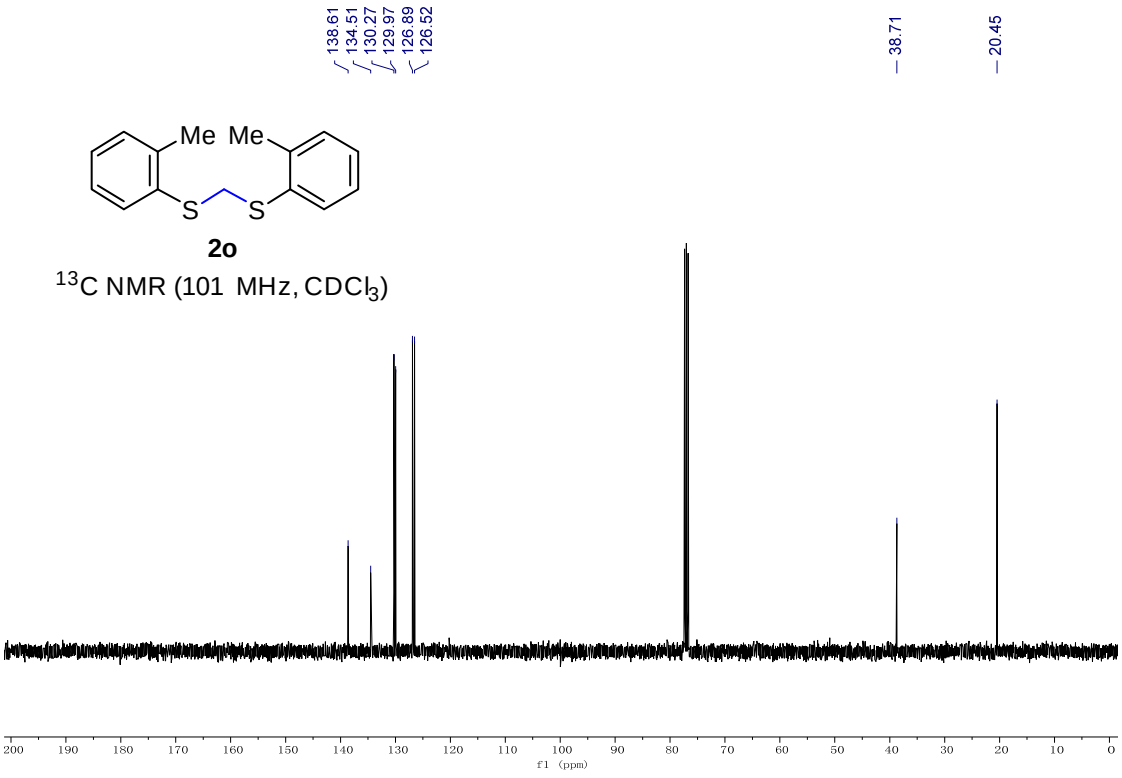


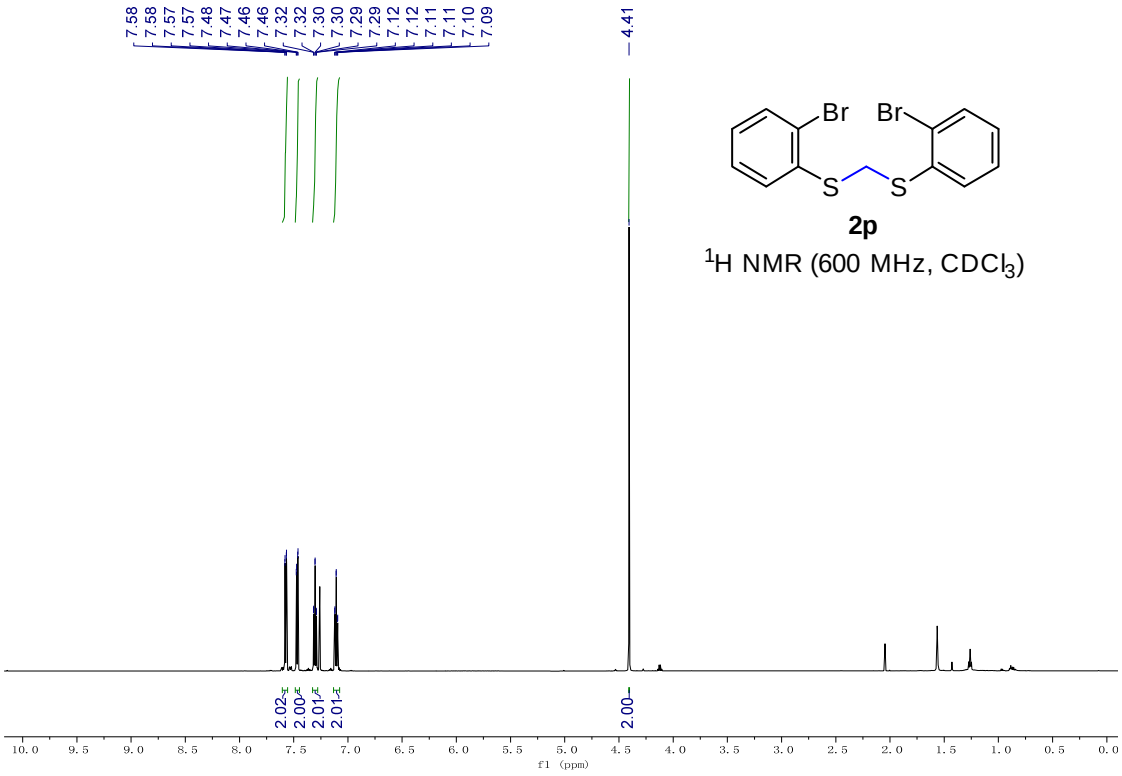
2o

^{1}H NMR (400 MHz, $CDCl_3$)



2o

^{13}C NMR (101 MHz, $CDCl_3$)



2p

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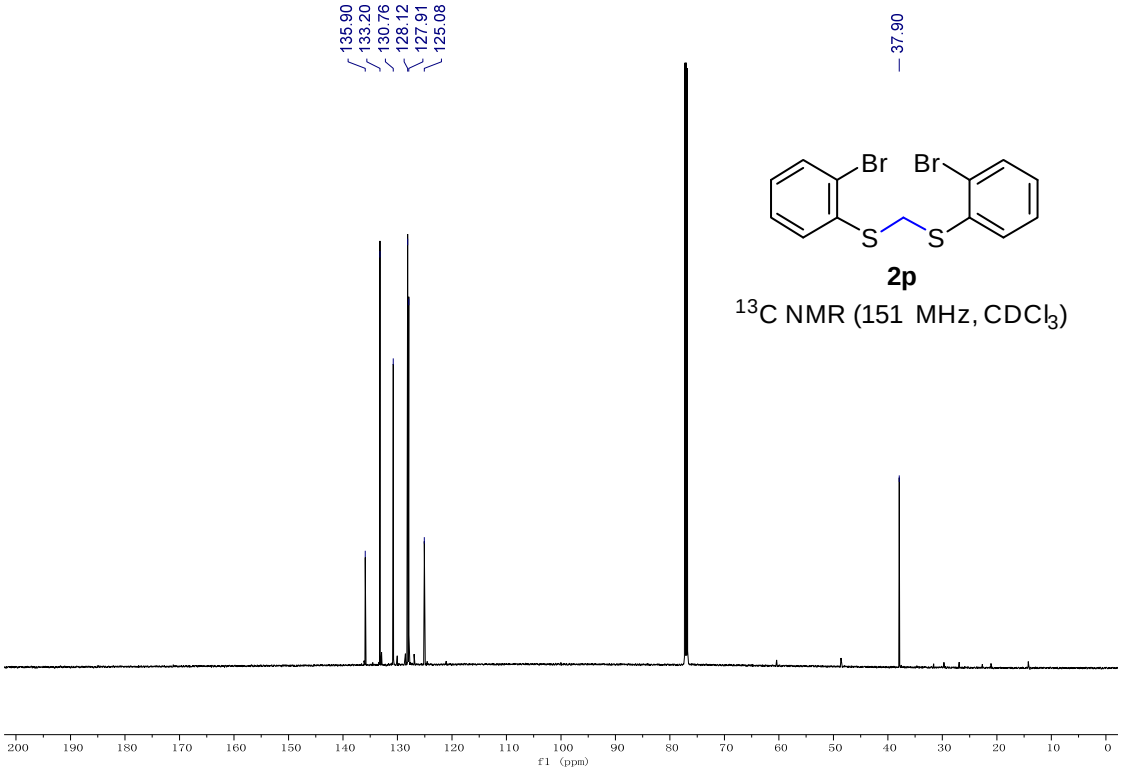
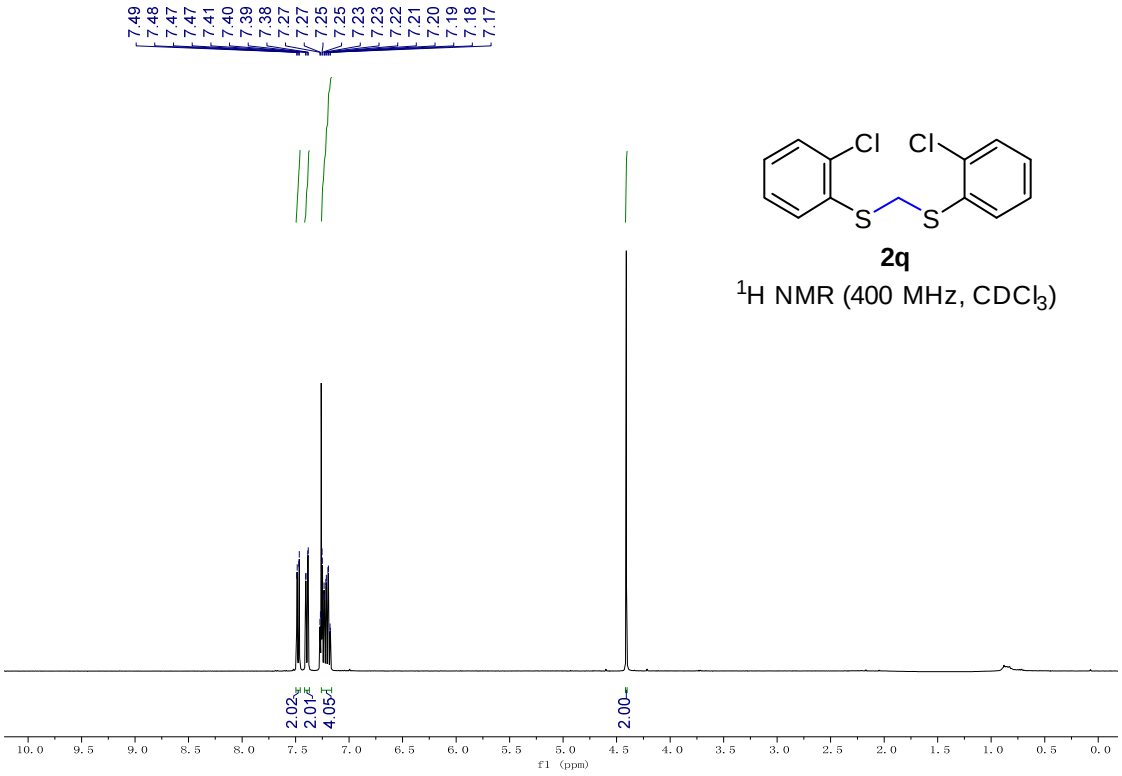


2p

^{13}C NMR (151 MHz, $CDCl_3$)



2q

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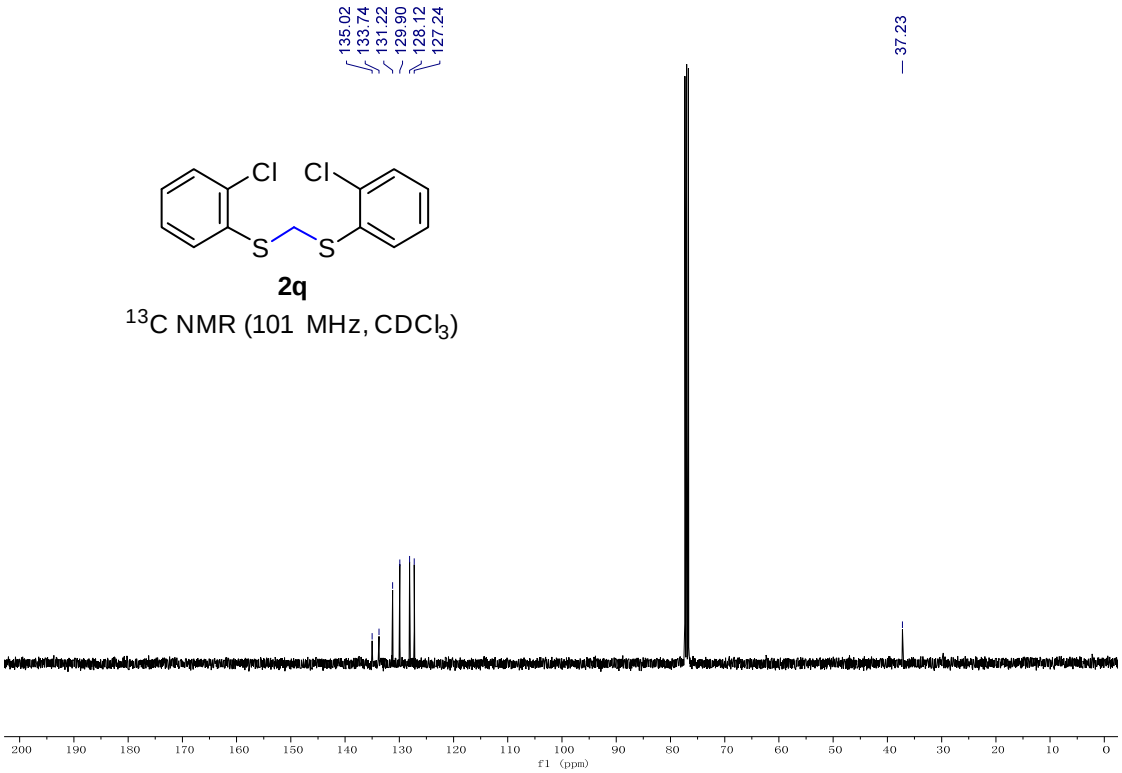

2q

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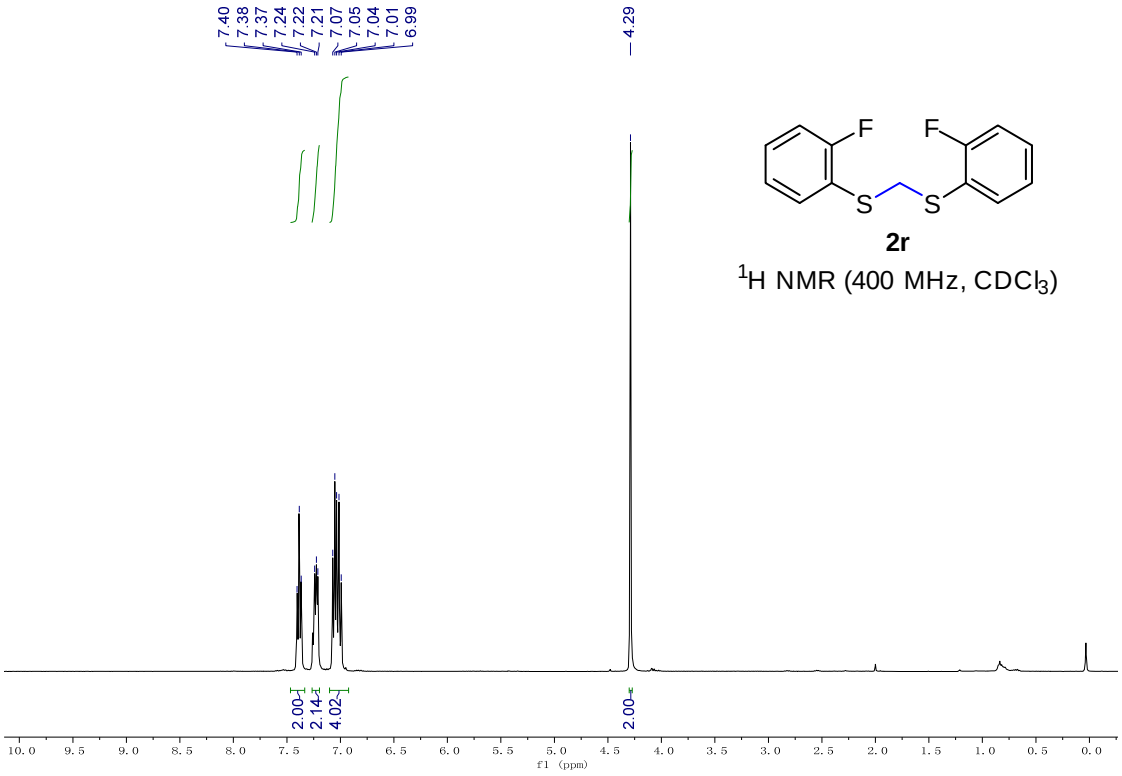

2r

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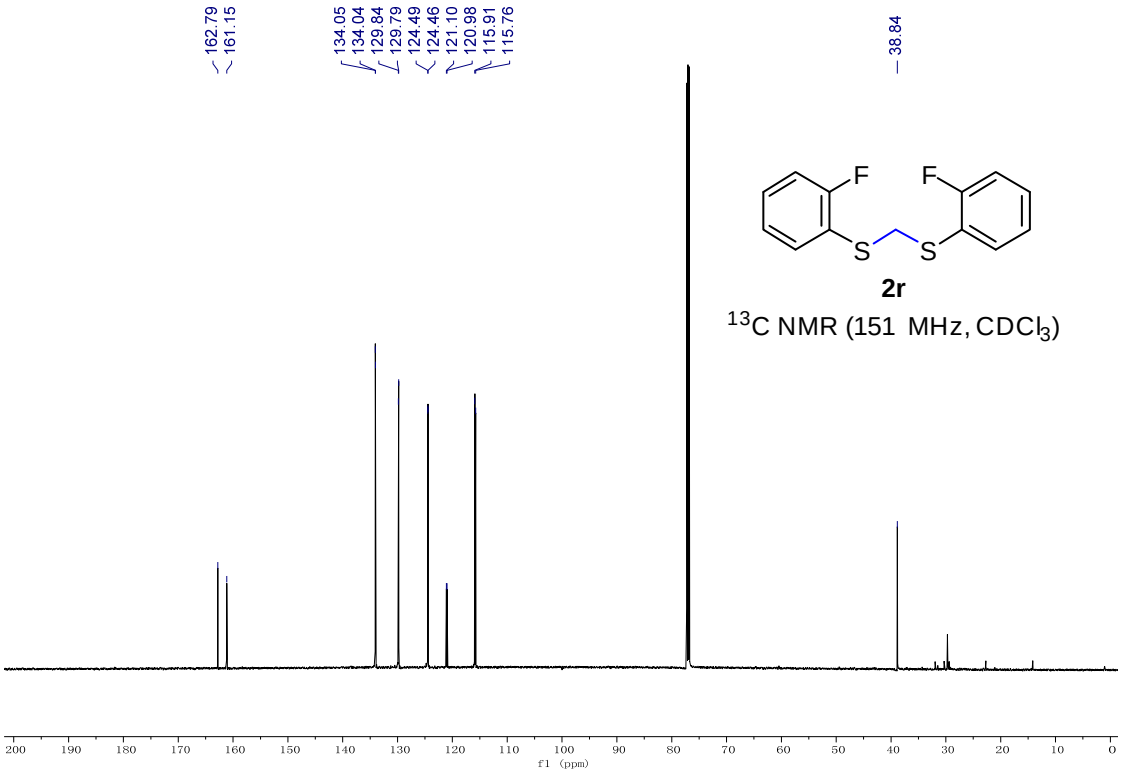

2r

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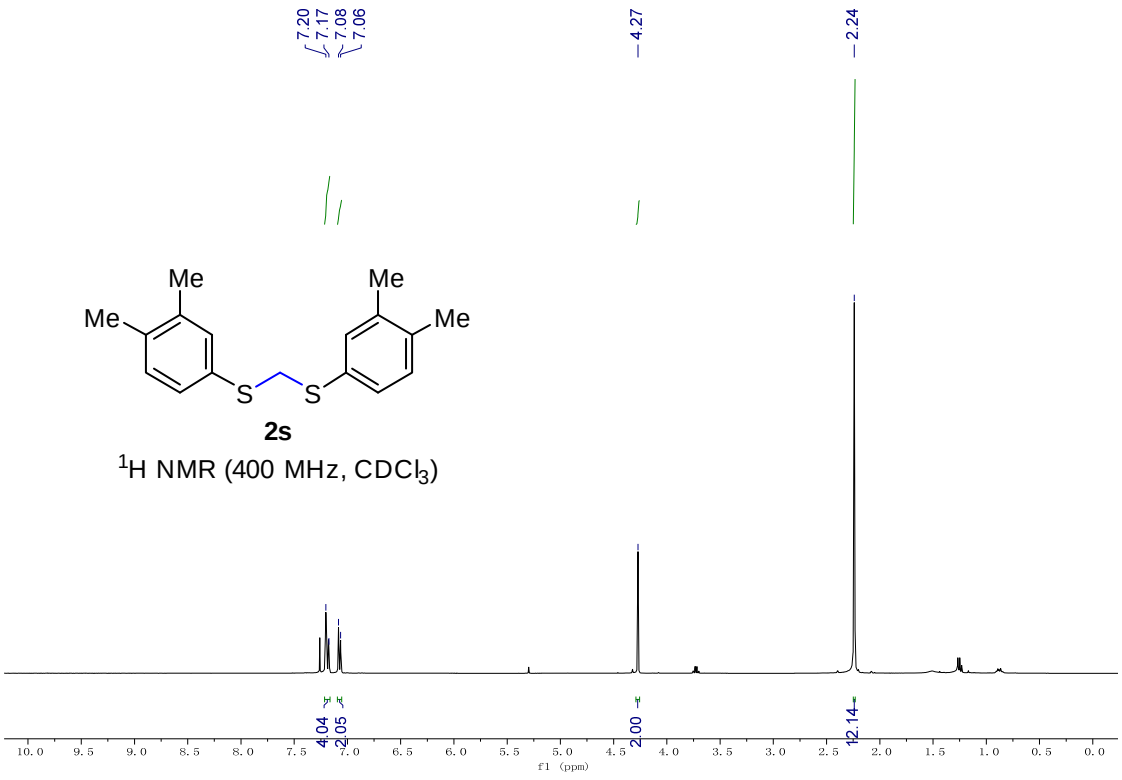

2s

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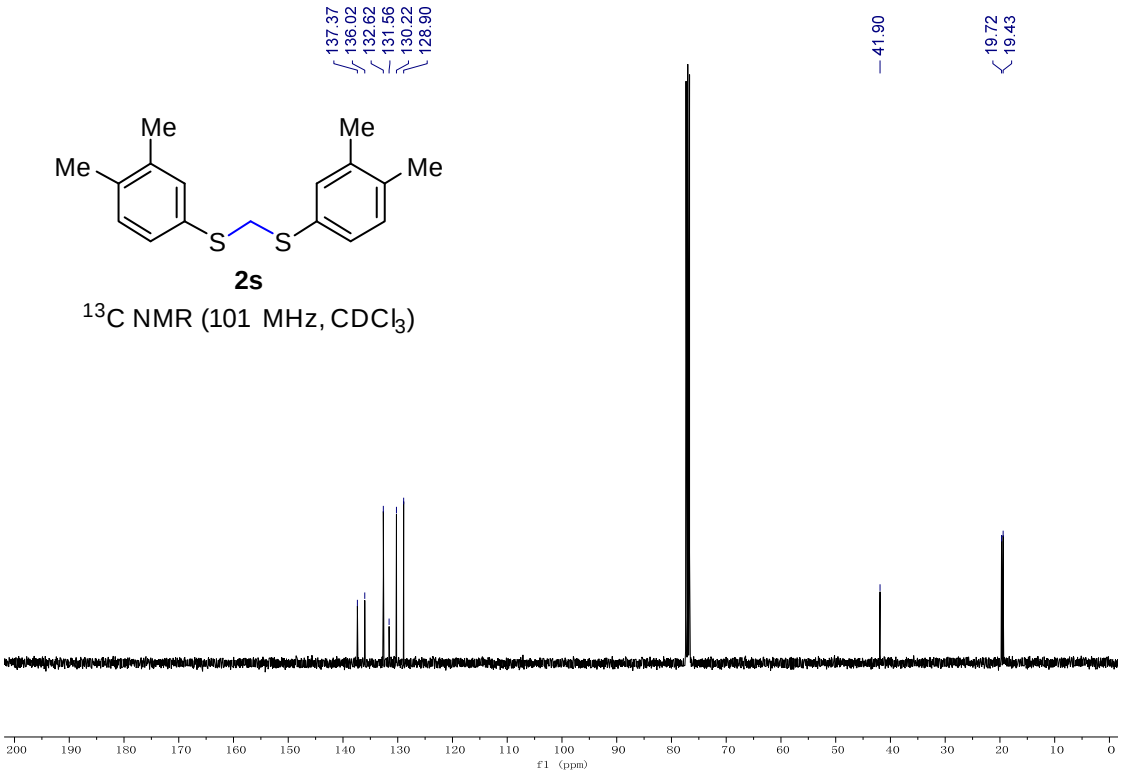
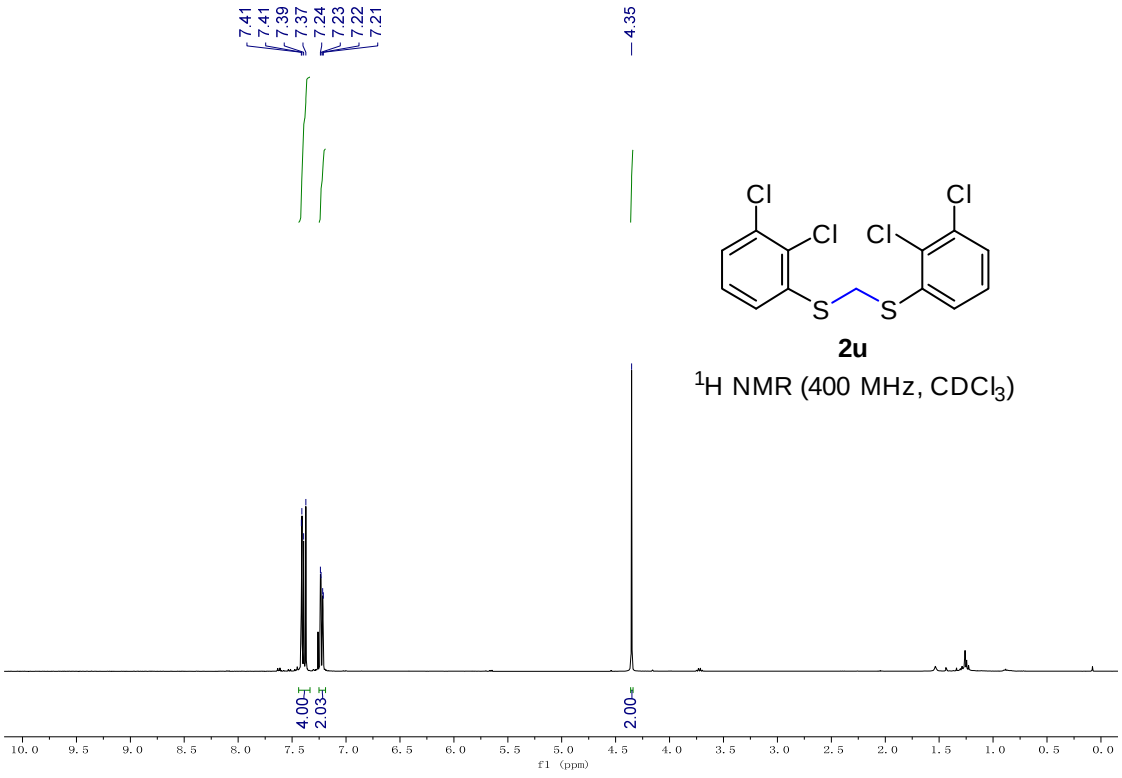


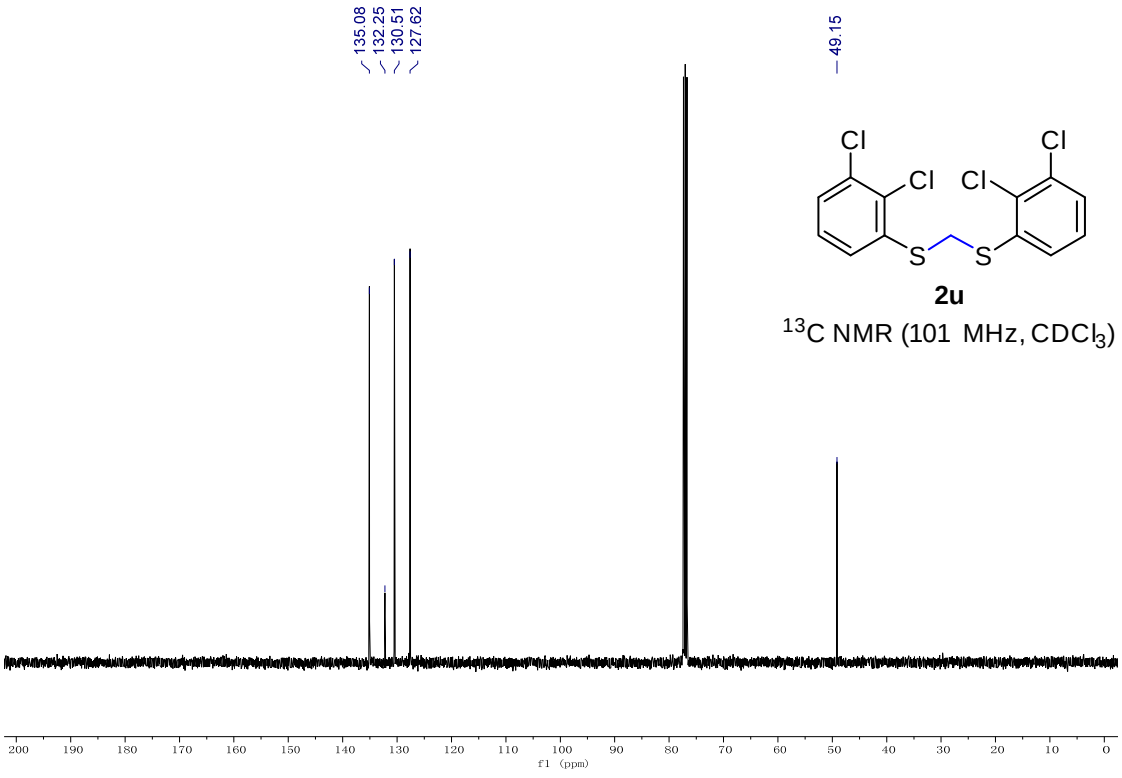
2s

^{13}C NMR (101 MHz, $CDCl_3$)



2u

^{1}H NMR (400 MHz, $CDCl_3$)



2u

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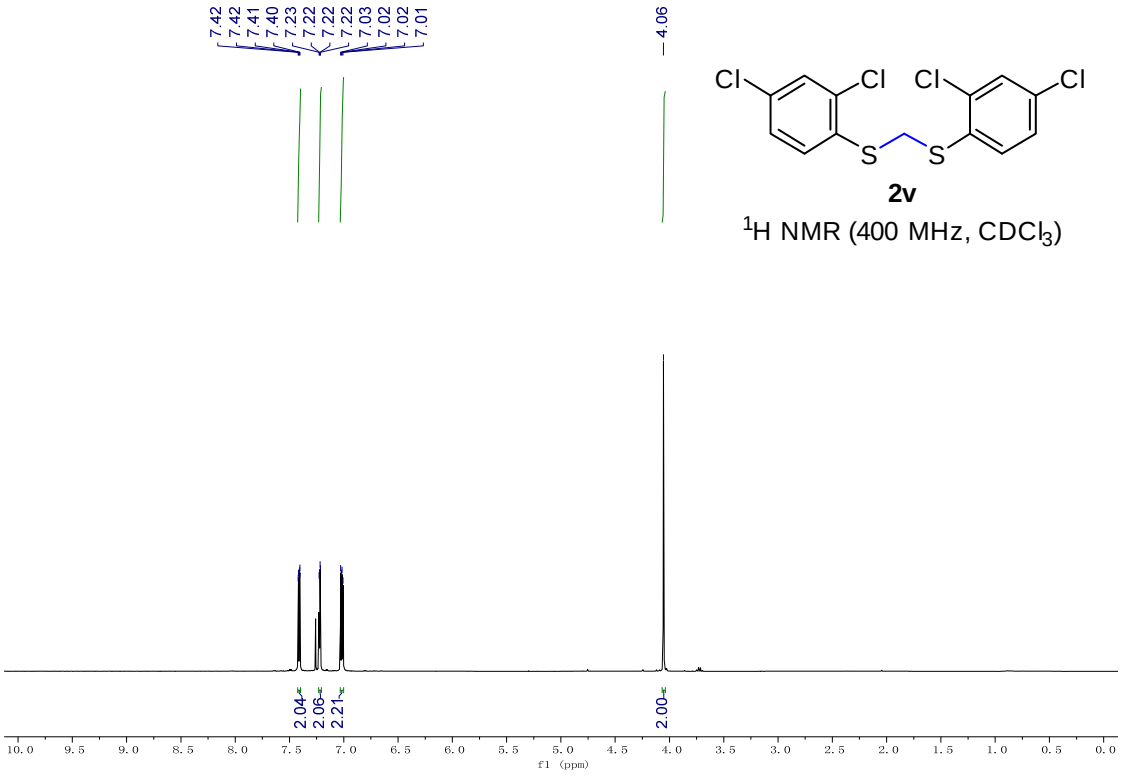
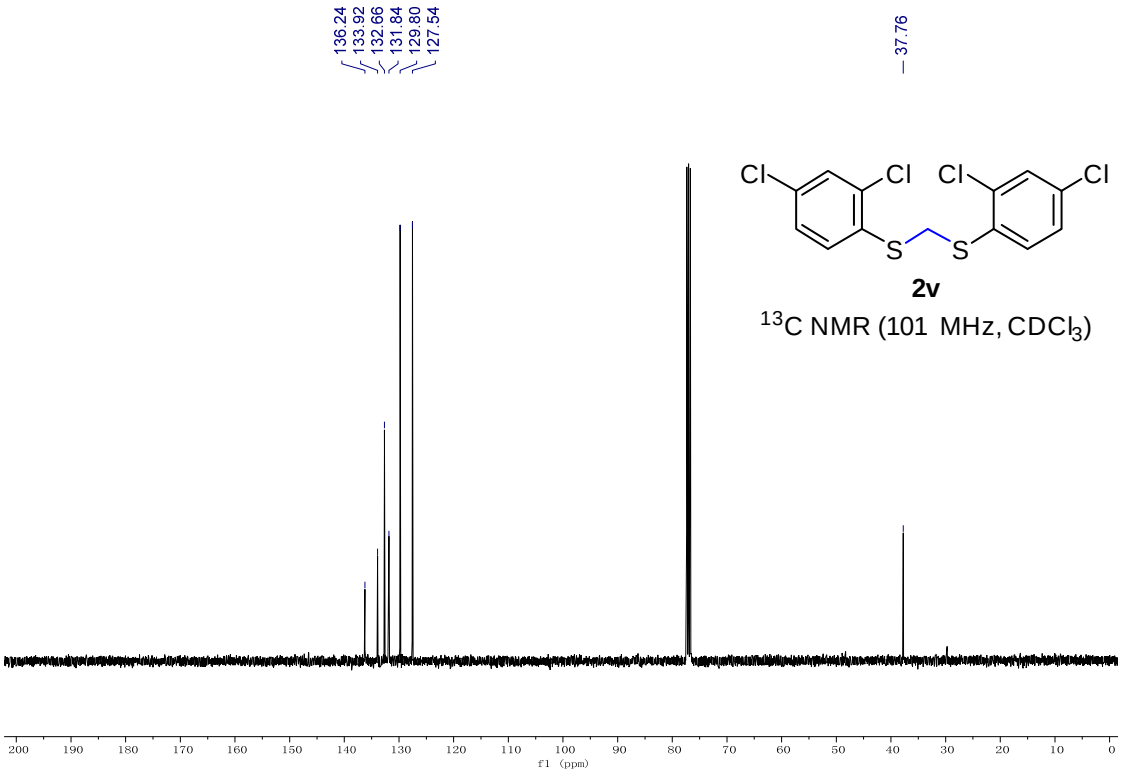


2v

^{1}H NMR (400 MHz, $CDCl_3$)



2v

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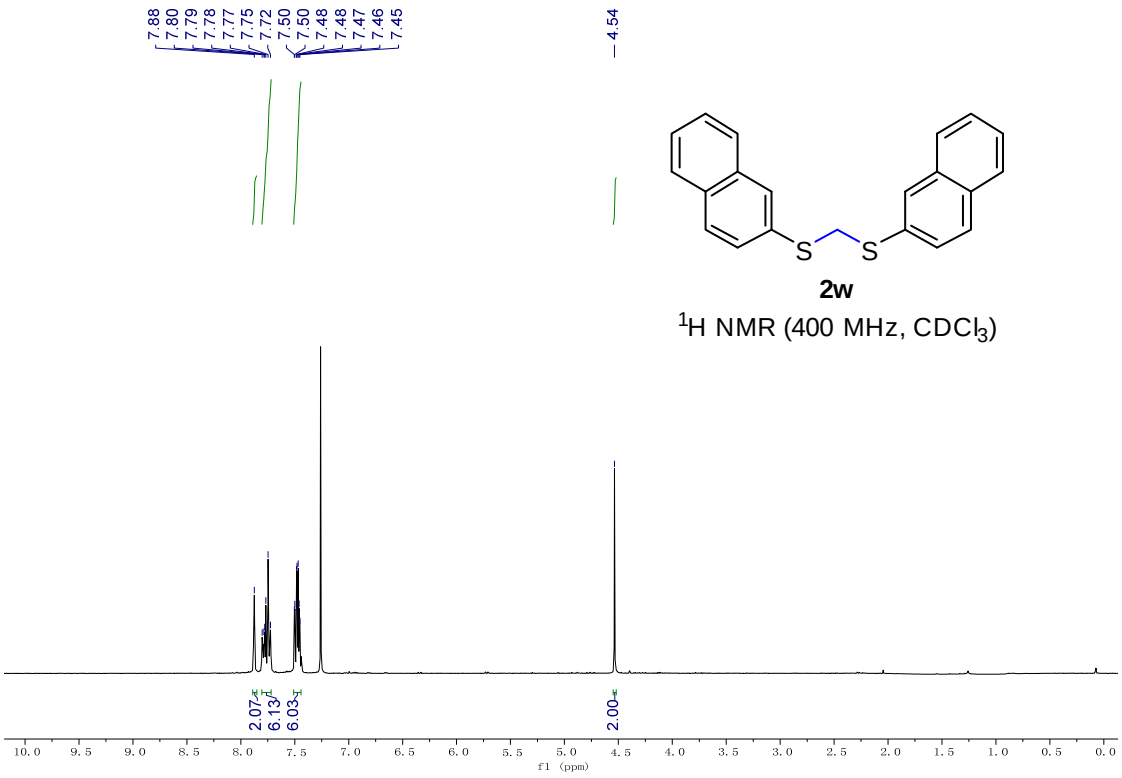

2w

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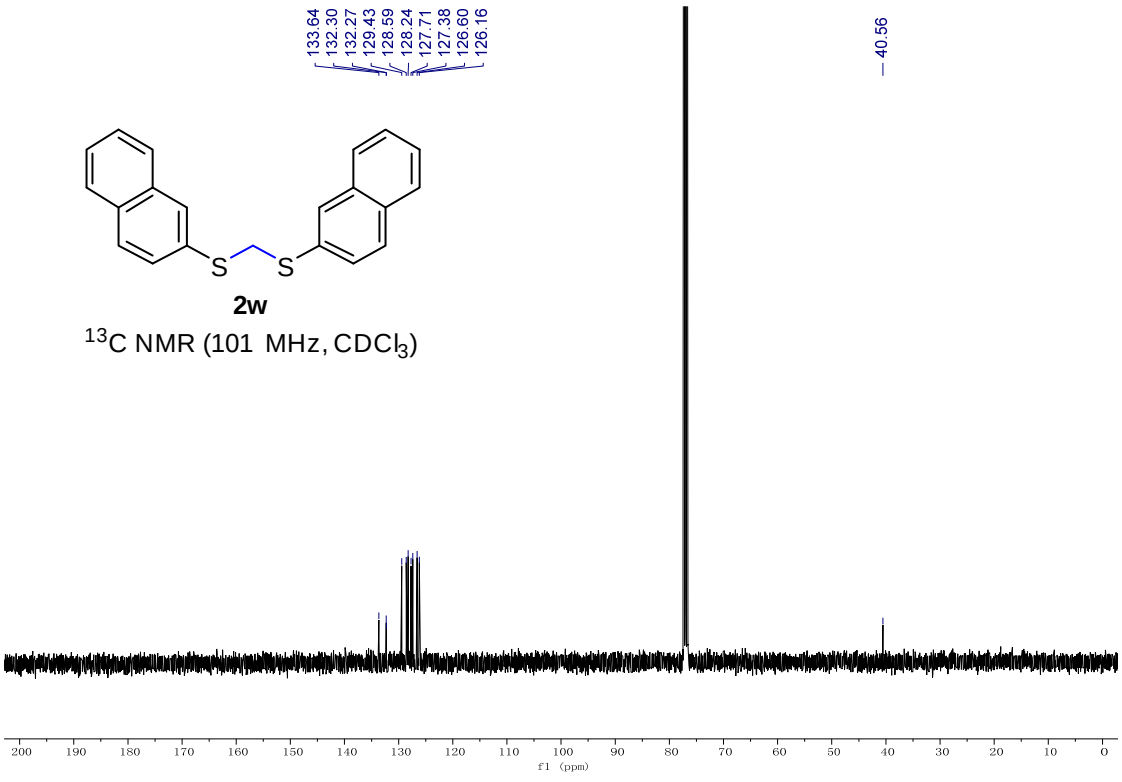
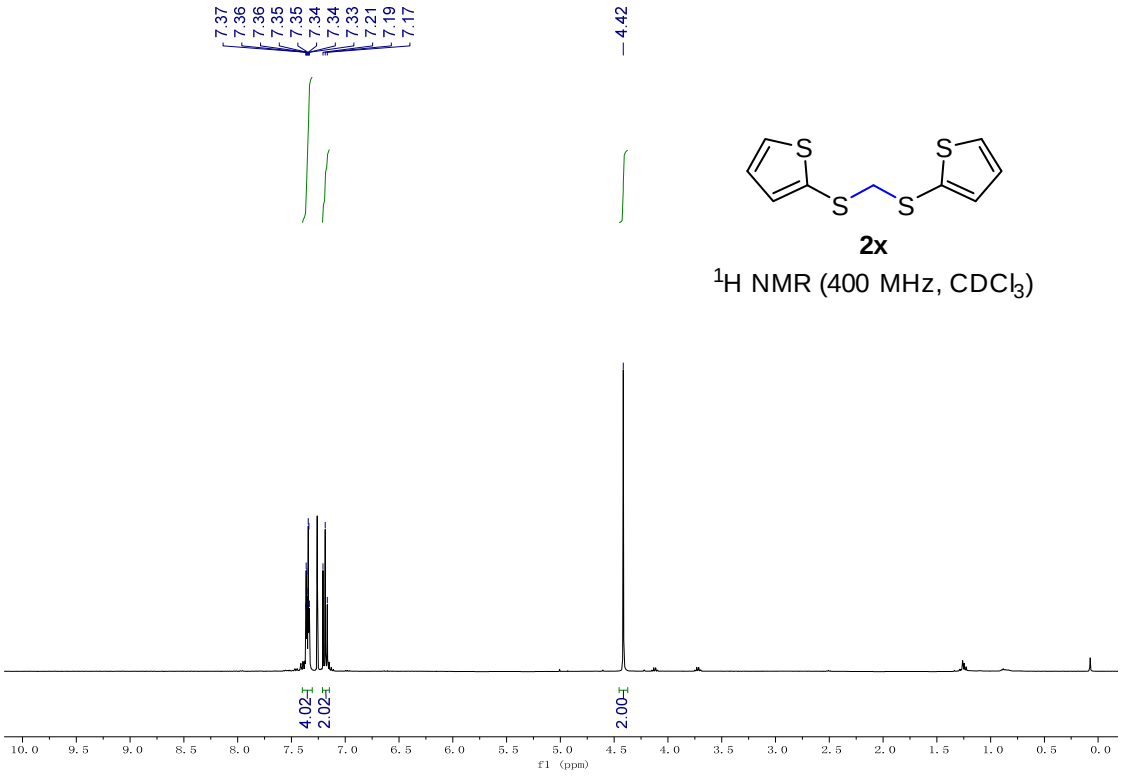


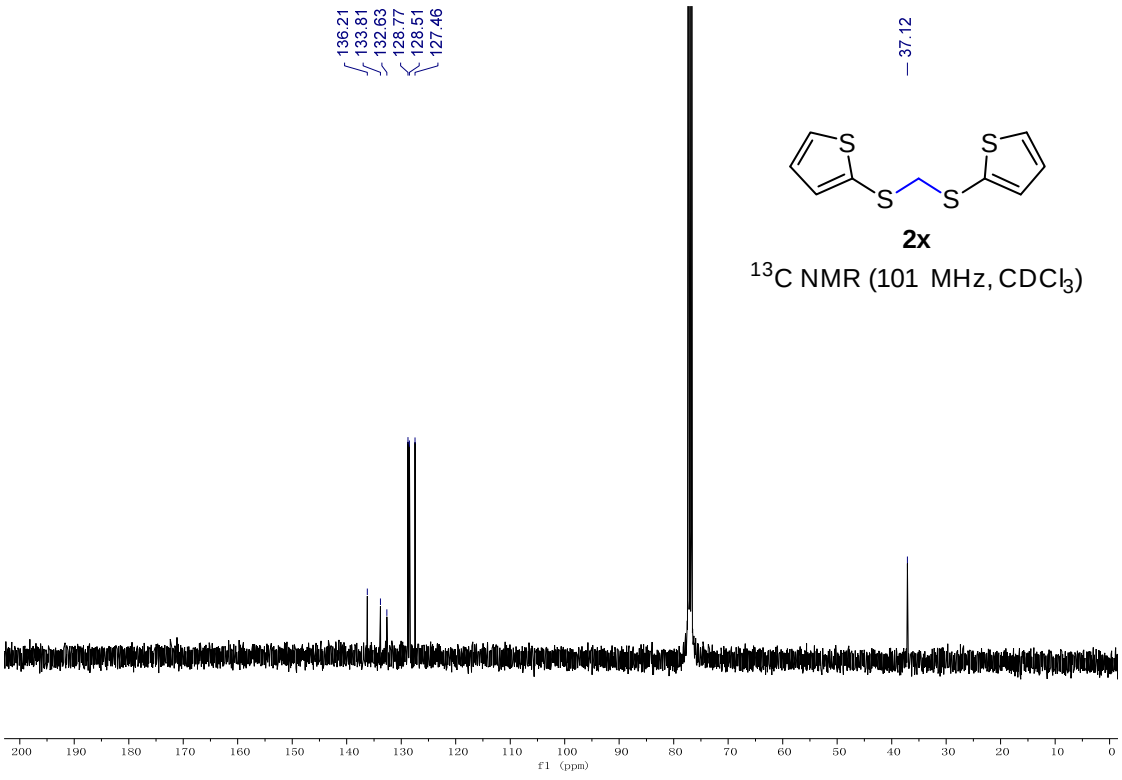
2w

^{13}C NMR (101 MHz, $CDCl_3$)



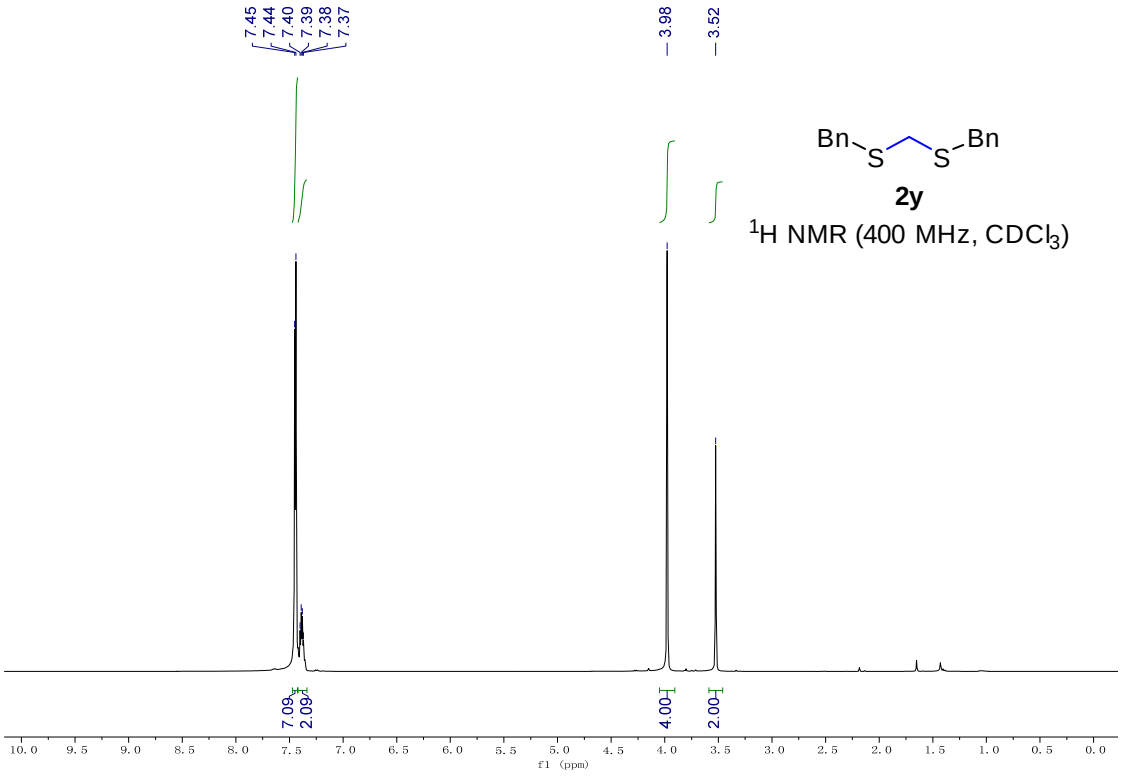
2x

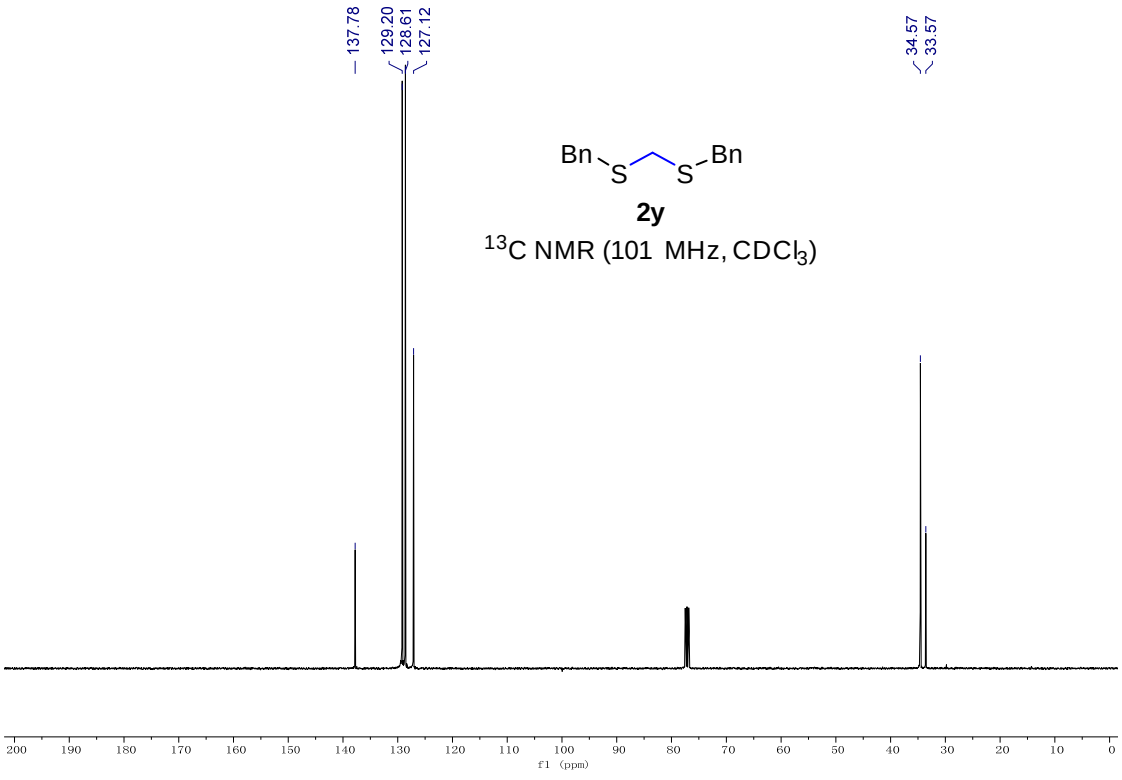
^{1}H NMR (400 MHz, $CDCl_3$)

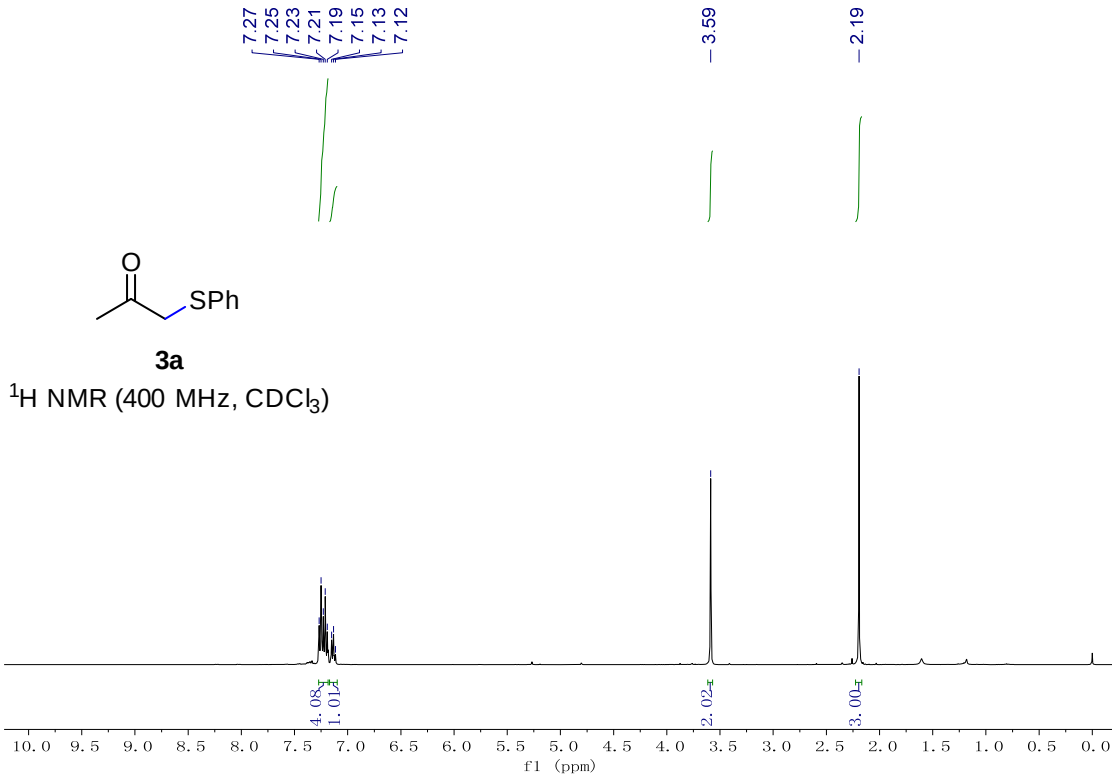


2x

^{13}C NMR (101 MHz, $CDCl_3$)

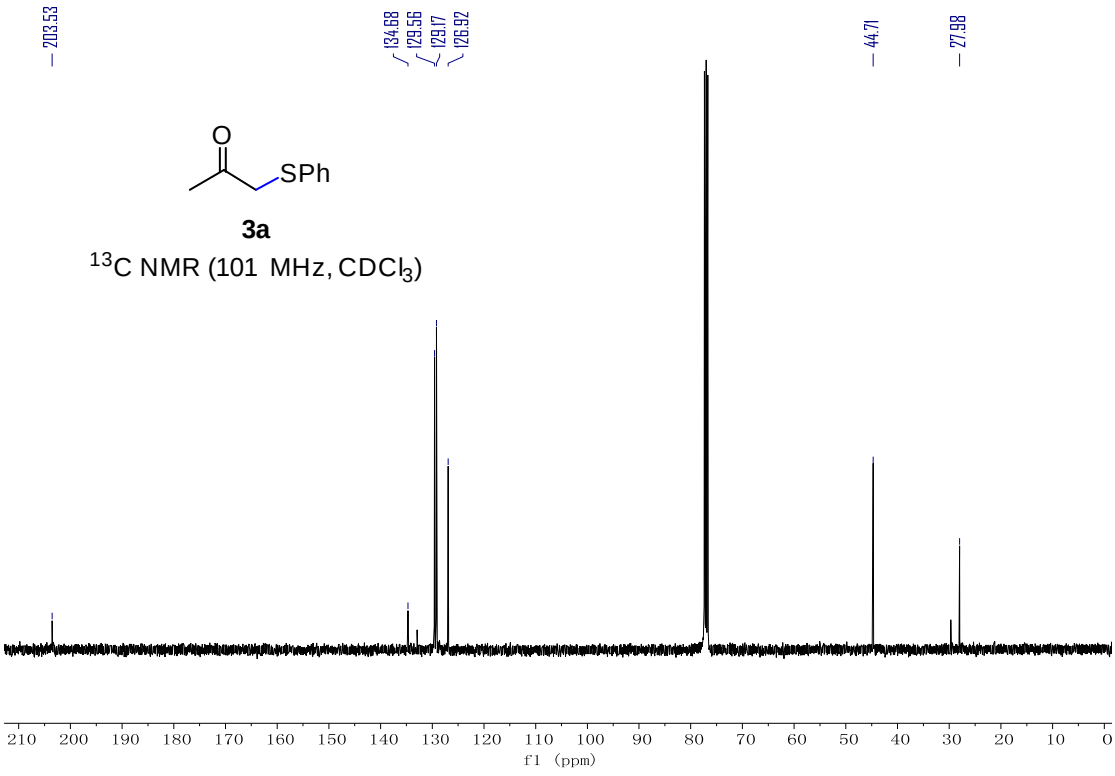

7.45
7.44
7.40
7.39
7.38
7.37
3.98
3.52
Bn
S
S
Bn
2y
1H NMR (400 MHz, CDCl3)
7.09
2.09
4.00
2.00
f1 (ppm)


137.78
129.20
128.61
127.12
34.57
33.57
Bn
S
S
Bn
2y
13C NMR (101 MHz, CDCl3)
f1 (ppm)



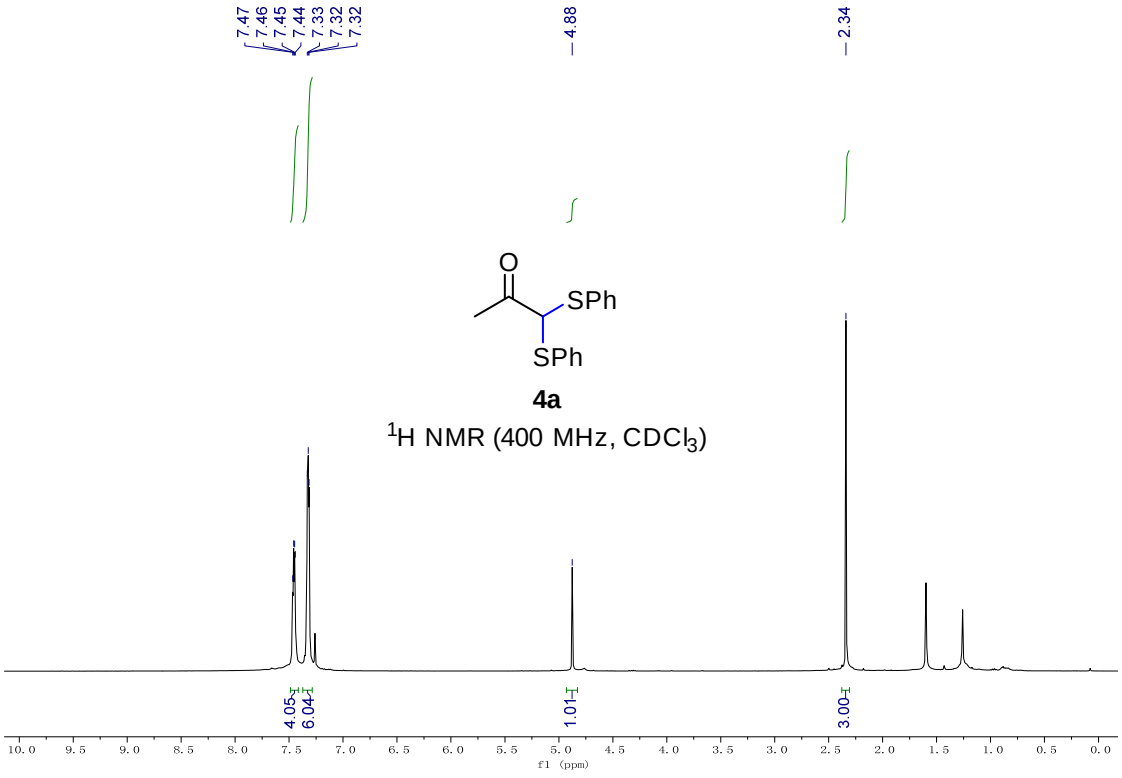
3a

^{1}H NMR (400 MHz, $CDCl_3$)



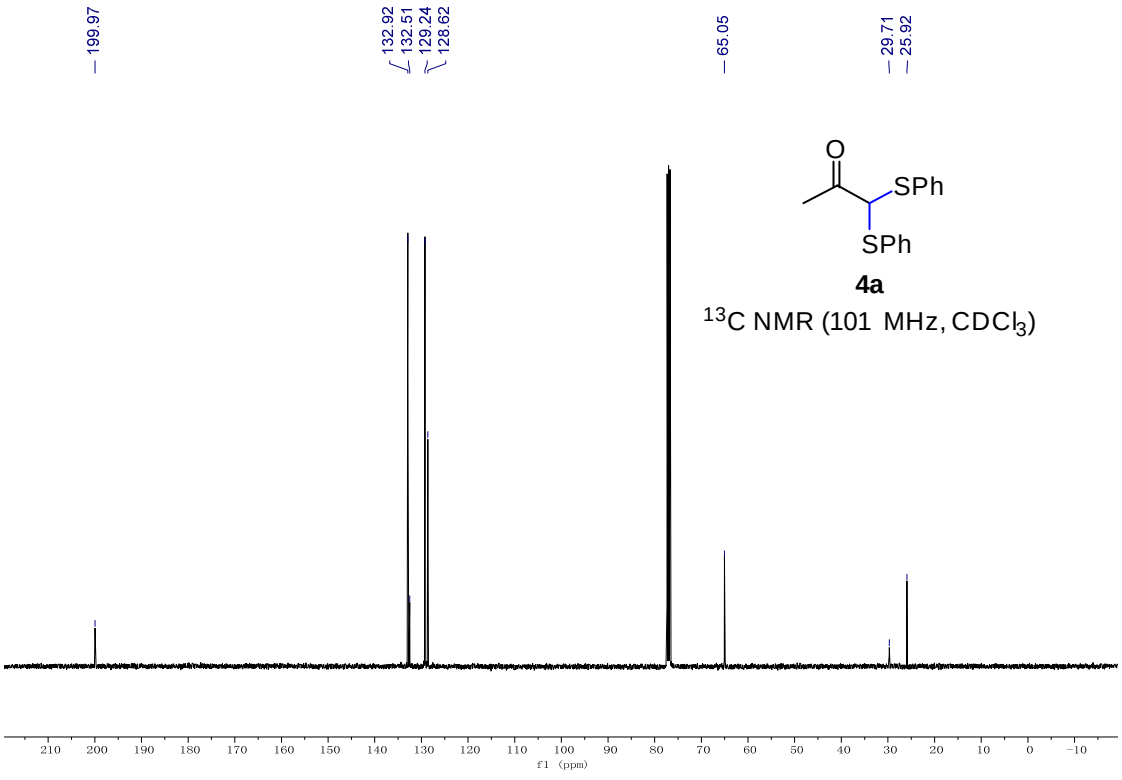
3a

^{13}C NMR (101 MHz, $CDCl_3$)



4a

^{1}H NMR (400 MHz, $CDCl_3$)



4a

^{13}C NMR (101 MHz, $CDCl_3$)

6. Copy of ^{1}H NMR Spectra for 2a-*d*