Electronic Supplementary Information

A phosphine-based redox method for direct conjugation of disulfides

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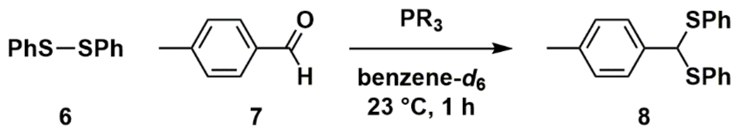
Contents

General Information

All solvents for the synthesis were purified by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Reactions were monitored by TLC or LC-MS and the products were purified by flash column chromatography unless otherwise mentioned. NMR spectra were recorded on a Bruker AN400 or AN600 instrument. The chemical shifts for ^{1}H and ^{13}C NMR spectra are reported in ppm (δ) relative to the ^{1}H and ^{13}C signals in the solvent ($CDCl_3$: δ 7.26, 77.16 ppm; DMSO-*d6*: δ 2.50, 39.51 ppm; CD_3CN: δ 1.94, and 1.32, 118.26 ppm; benzenz-*d6*: δ 7.16, 128.06 ppm) and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, m = multiplet. LC-MS was performed on an Agilent 1260 HPLC machine coupled to a 6120 single quadrupole MS detector using an Agilent Eclipse XDB-C18 5 μm 4.6×150 mm column.

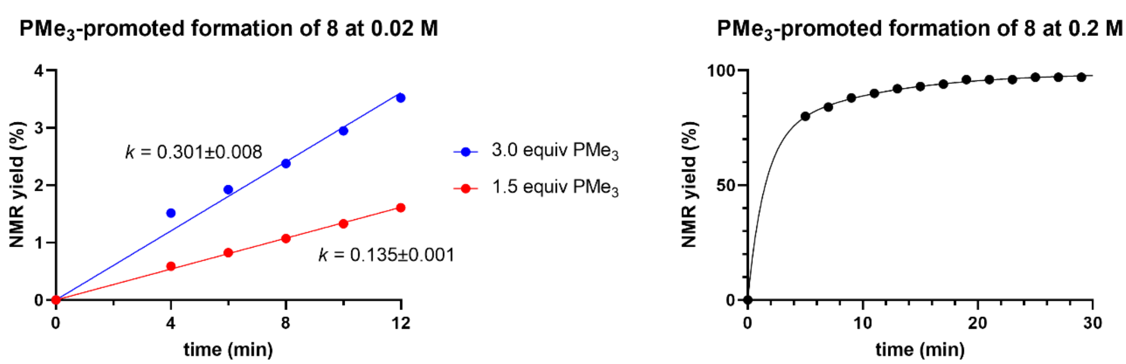
General Procedures and Characterization Data



PMe_3	94%	PCy_3	no reaction
PEt_3	78%	PEt_2Ph	12% (ether)
P^nBu_3	46%	$PEtPh_2$	no reaction
P^tBu_3	no reaction	PPh_3	no reaction
PMe^tBu_2	no reaction	$P(OMe)_3$	no reaction

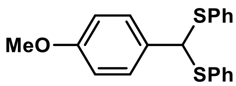
*General procedure for **Fig. 2***

Benzene-d_6 was degassed with argon for 5 times and then bubbled with argon for 30 min. To a vial charged with internal standard 1,3,5-trimethoxybenzene (5.60 mg, 0.033 mmol, 0.33 equiv) under an argon atmosphere was added a solution of **6** (1.0 M in benzene-d_6, 0.15 mL, 0.15 mmol, 1.5 equiv) and a solution of **7** (1.0 M in benzene-d_6, 0.1 mL, 0.1 mmol, 1.0 equiv). After diluting with additional benzene-d_6 (0.75 mL) to reach a final concentration of 0.1 M for **7**, phosphine (1.5 eq) was added, and the mixture was stirred at 23 °C for 1 h before transferring to an argon-filled NMR tube. The ^{1}H NMR spectra were recorded with 10 s recycle delay and the yield of **8** was determined by with integration relative to 1,3,5-trimethoxybenzene. The progress of the reaction at 0.02 M or 0.2 M with 1.5 or 3.0 equiv trimethylphosphine was monitored by ^{1}H NMR in an NMR tube.

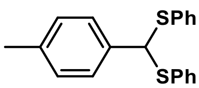


*General procedure for **Fig. 3***

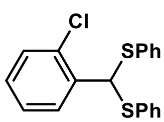
Toluene was degassed with argon for 5 times and then bubbled with argon for 30 min. To a vial charged with aldehyde (1.0 mmol, 1.0 equiv) and disulfide (1.5 mmol, 1.5 equiv) in toluene (2.0 mL) was added trimethylphosphine (0.13 mL, 1.5 mmol, 1.5 equiv). After stirring at 23 °C for 4 h, the crude reaction mixture was directly purified by silica gel column chromatography to give the dithioacetal. For the reaction between aliphatic aldehyde and dialkyl disulfide, 3.0 equiv disulfide and 3.0 equiv trimethylphosphine were used.



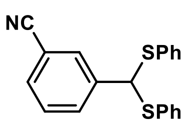
Yield: 98%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.29 (m, 6H), 7.28–7.22 (m, 6H), 6.81 (d, *J* = 8.8 Hz, 2H), 5.43 (s, 1H), 3.79 (s, 3H); MS (ESI) calculated for $C_{14}H_{13}OS$ $(M–SPh)^+$ 229.1, found 229.1



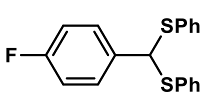
Yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.33 (m, 4H), 7.31–7.21 (m, 8H), 7.09 (d, *J* = 7.8 Hz, 2H), 5.43 (s, 1H), 2.32 (s, 3H); MS (ESI) calculated for $C_{14}H_{13}S$ $(M–SC_6H_6)^+$ 213.1, found 213.1.



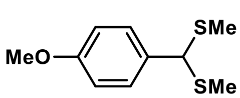
Yield: 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.39–7.34 (m, 4H), 7.32 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.26–7.23 (m, 6H), 7.22–7.14 (m, 2H), 6.04 (s, 1H); MS (ESI) calculated for $C_{13}H_{10}ClS$ $(M–SC_6H_6)^+$ 233.0, found 233.1.



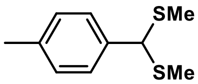
Yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.53 (m, 2H), 7.50 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.39–7.30 (m, 5H), 7.30–7.24 (m, 6H), 5.39 (s, 1H); MS (ESI) calculated for $C_{20}H_{15}NS_2Na$ $(M+Na)^+$ 356.1, found 356.0.



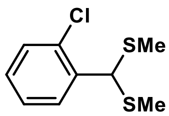
Yield: 93%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.28 (m, 6H), 7.26–7.22 (m, 6H), 6.94 (t, *J* = 8.6 Hz, 2H), 5.40 (s, 1H); ^{19}F NMR (376 MHz, $CDCl_3$): δ –113.73; MS (ESI) calculated for $C_{13}H_{10}FS$ $(M–SPh)^+$ 217.1, found 217.1.



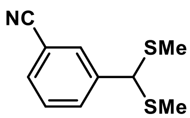
Yield: 91%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.77 (s, 1H), 3.80 (s, 3H), 2.09 (s, 6H); MS (ESI) calculated for $C_9H_{11}OS$ $(M–SMe)^+$ 167.1, found 167.1.



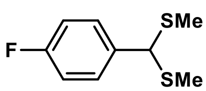
Yield: 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 7.7 Hz, 2H), 4.77 (s, 1H), 2.34 (s, 3H), 2.10 (s, 6H); MS (ESI) calculated for $C_9H_{11}S$ $(M–SMe)^+$ 151.1, found 151.1.



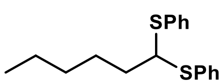
Yield: 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.38 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.29 (td, *J* = 7.6, 1.5 Hz, 1H), 7.24–7.18 (m, 1H), 5.33 (s, 1H), 2.13 (s, 6H); MS (ESI) calculated for C_8H_8ClS $(M–SMe)^+$ 171.0, found 171.0.



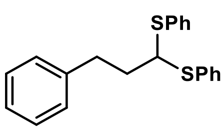
Yield: 76%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 1.9 Hz, 1H), 7.68 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.61–7.54 (m, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 4.77 (s, 1H), 2.11 (d, *J* = 0.9 Hz, 6H); MS (ESI) calculated for $C_{10}H_{12}NS_2$ $(M+H)^+$ 210.0, found 210.1.



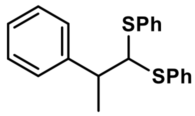
Yield: 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.36 (m, 2H), 7.07–6.99 (m, 2H), 4.77 (s, 1H), 2.10 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$): δ –114.17; MS (ESI) calculated for C_8H_8FS $(M–SMe)^+$ 155.0, found 155.1.



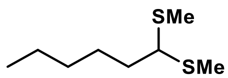
Yield: 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.42 (m, 4H), 7.33–7.22 (m, 6H), 4.39 (t, *J* = 6.6 Hz, 1H), 1.89–1.78 (m, 2H), 1.59 (dtd, *J* = 10.0, 7.6, 5.5 Hz, 2H), 1.32–1.19 (m, 4H), 0.86 (t, *J* = 7.0 Hz, 3H); MS (ESI) calculated for $C_{18}H_{23}S_2$ $(M+H)^+$ 303.1, found 303.3.



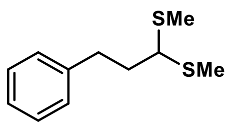
Yield: 94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.35 (m, 4H), 7.32–7.20 (m, 8H), 7.19–7.14 (m, 1H), 7.12–7.06 (m, 2H), 4.34 (t, *J* = 6.7 Hz, 1H), 2.90 (dd, *J* = 8.5, 6.6 Hz, 2H), 2.13 (ddd, *J* = 9.0, 7.5, 6.6 Hz, 2H); MS (ESI) calculated for $C_{21}H_{21}S_2$ $(M+H)^+$ 337.1, found 337.3.



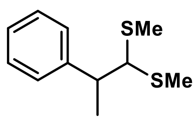
Yield: 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.32 (m, 2H), 7.30–7.19 (m, 8H), 7.17 (s, 5H), 4.55 (d, *J* = 4.4 Hz, 1H), 3.30 (qd, *J* = 7.0, 4.3 Hz, 1H), 1.54 (d, *J* = 7.0 Hz, 3H); MS (ESI) calculated for $C_{21}H_{21}S_2$ $(M+H)^+$ 337.1, found 337.3.



Yield: 44%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.63 (t, *J* = 7.2 Hz, 1H), 2.09 (s, 6H), 1.79–1.70 (m, 2H), 1.56–1.47 (m, 2H), 1.29 (dtd, *J* = 10.7, 6.9, 6.0, 4.0 Hz, 4H), 0.89 (t, *J* = 7.0 Hz, 3H); MS (ESI) calculated for $C_7H_{15}S$ $(M–SMe)^+$ 131.1, found 131.2.

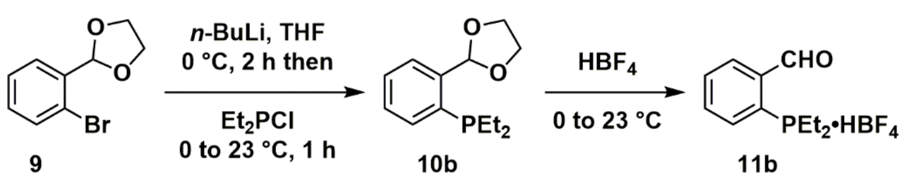


Yield: 52%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.27 (m, 2H), 7.24–7.18 (m, 3H), 3.60 (t, *J* = 7.2 Hz, 1H), 2.86 (dd, *J* = 8.6, 6.6 Hz, 3H), 2.14–2.03 (m, 8H); MS (ESI) calculated for $C_{10}H_{13}S$ $(M–SMe)^+$ 165.1, found 165.2.

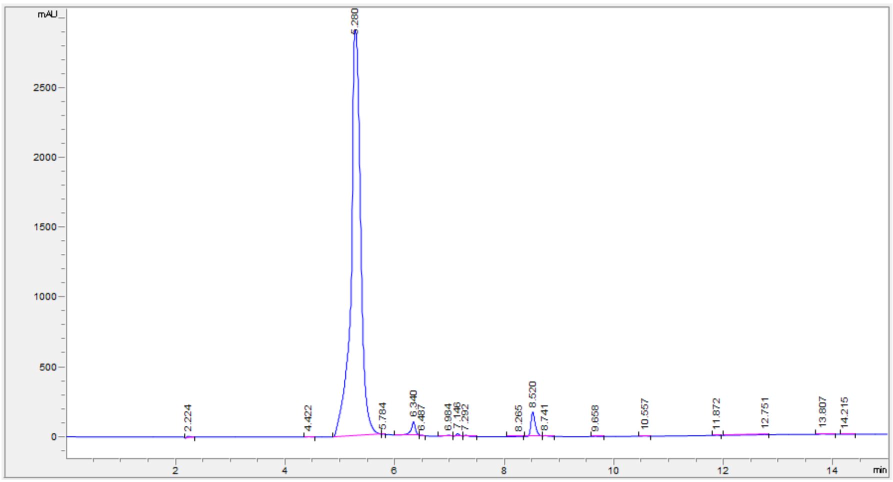


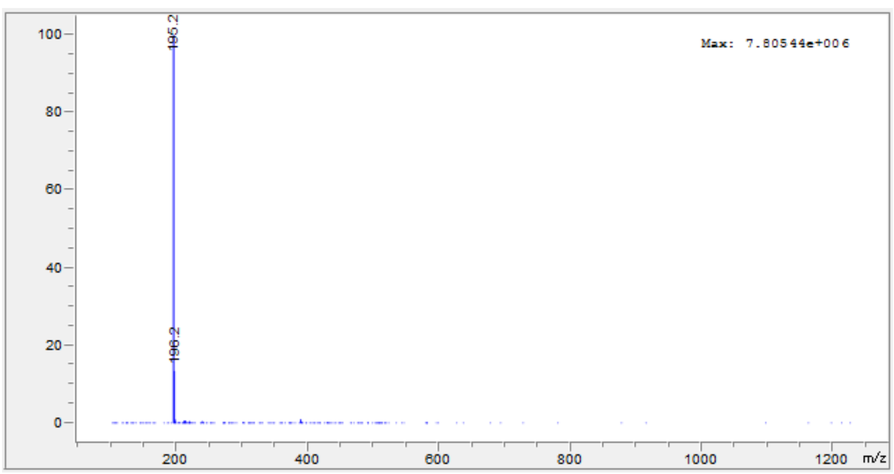
Yield: 61%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.23 (m, 5H), 3.80 (d, *J* = 7.6 Hz, 1H), 3.17–3.07 (m, 1H), 2.05 (d, *J* = 2.4 Hz, 6H), 1.49 (d, *J* = 7.0 Hz, 3H); MS (ESI) calculated for $C_{11}H_{16}S_2Na$ $(M+Na)^+$ 235.1, found 235.2.

*Synthesis of the **11b***



To a solution of **9** (1.54 g, 6.73 mmol, 1.0 equiv) in degassed diethyl ether (15 mL) was added *n*-butyllithium (1.6 M, 5.0 mL, 8.08 mmol, 1.2 equiv) at 0 °C. After stirring at the same temperature for 2 h, chlorodiethylphosphine (0.9 mL, 7.40 mmol, 1.1 equiv) was added and the mixture was stirred at 23 °C for 1 h before filtered under argon and washed with degassed diethyl ether (3 mL ×2) to afford **10b** as a diethyl ether solution. Tetrafluoroboric acid (48 wt. % in water, 1.34 mL, 10.1 mmol, 1.5 equiv) was then added and the mixture was stirred at 23 °C for 12 h before concentrated. The resulting residue was dissolved in water (5 mL), washed with methylene chloride (5 mL ×2) and lyophilized to give **11b** (1.71 g, 90% yield) as a colorless oil (96% pure by HPLC). [1]H NMR (400 MHz, CD_3CN, as a mixture of aldehyde and hydrate): δ 10.33 (s, 1H), 7.79–7.72 (m, 2H), 7.63–7.55 (m, 1H), 7.55–7.48 (m, 1H), 6.57 (d, *J* = 146.4 Hz, 1H, P•H), 2.15–1.99 (m, 4H), 1.04 (dt, *J* = 18.3, 7.7 Hz, 6H); [1]H NMR (600 MHz, D_2O, as a mixture of aldehyde and hydrate): δ 8.14–7.82 (m, 1H), 7.77–7.64 (m, 1H), 7.63–7.49 (m, 2H), 6.60 (d, *J* = 314.6 Hz, 1H, P•H), 2.87–2.55 (m, 4H), 1.61–1.31 (m, 3H), 1.11–1.00 (m, 3H); MS (ESI) calculated for $C_{11}H_{16}OP^+$ $(M+H)^+$ 195.1, found 195.2.



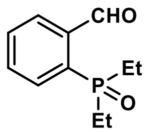


10b•HBF₄: [1]H NMR (400 MHz, D_2O): δ 8.00–7.85 (m, 2H), 7.84–7.72 (m, 2H), 5.99 (s, 1H), 4.30–4.12 (m, 4H), 2.65–2.52 (m, 4H), 1.23 (t, *J* = 7.6 Hz, 3H), 1.18 (t, *J* = 7.6 Hz, 3H); MS (ESI) calculated for $C_{13}H_{20}O_2P$ $(M+H)^+$ 239.1, found 239.1.

11a: [1]H NMR (400 MHz, D_2O, as a mixture of aldehyde and hydrate): δ 8.07–7.99 (m, 0.5H), 7.90–7.84 (m, 0.5H), 7.79–7.60 (m, 1.5H), 7.59–7.48 (m, 1.5H), 6.53 (d, *J* = 176.7 Hz, 1H, P•H), 2.50 (d, *J* = 13.4 Hz, 1.5H), 2.34 (dd, *J* = 13.9, 12.1 Hz, 3H), 2.17 (d, *J* = 12.8 Hz, 1.5H); MS (ESI) calculated for $C_9H_{12}OP$ $(M+H)^+$ 167.1, found 167.1.

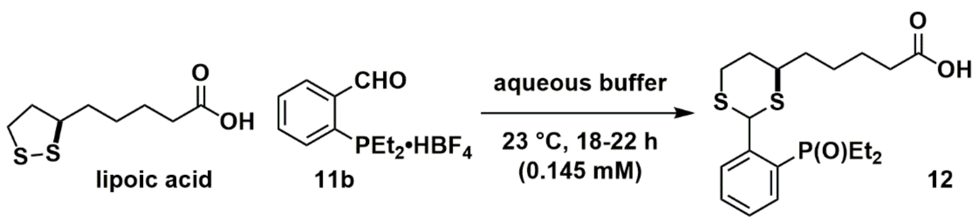
11c: ^{1}H NMR (400 MHz, D_2O, as a mixture of aldehyde and hydrate): δ 10.00 (s, 1H), 8.35–8.27 (m, 1H), 8.12–8.05 (m, 1H), 8.04–7.94 (m, 2H), 3.14 (dp, *J* = 12.6, 7.2 Hz, 2H), 1.38 (dd, *J* = 20.0, 7.0 Hz, 3H), 1.21 (dd, *J* = 19.3, 7.2 Hz, 3H), 1.08 (d, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 7.2 Hz, 3H); MS (ESI) calculated for $C_{13}H_{20}OP$ $(M+H)^+$ 223.1, found 223.2.

Characterization of the oxidation product of ***11b***



^{1}H NMR (400 MHz, DMSO-*d*6): δ 10.79 (s, 1H), 8.03–7.95 (m, 1H), 7.90 (ddd, *J* = 11.4, 6.7, 2.0 Hz, 1H), 7.79 (tdd, *J* = 9.0, 6.4, 3.8 Hz, 2H), 2.08 (dq, *J* = 11.5, 7.7 Hz, 4H), 0.96 (dt, *J* = 17.3, 7.6 Hz, 6H); ^{31}P NMR (162 MHz, DMSO-*d*6): δ 47.63; MS (ESI) calculated for $(M+H)^+$ 211.1, found 211.2.

RDDC of lipoic acid in aqueous buffers



Screening for buffer conditions:

To the aqueous buffer solution (25 mM, 82.5 μL) was added lipoic acid (1 μL, 3 mg/mL, 3 μg, 14.5 nmol, 1.0 equiv) in methanol followed by a solution of internal standard 1,3,5-trimethoxybenzene (2 μL, 5 mM, 0.01 μmol) in methanol and a solution of **11b** (10 mM, 14.5 μL, 10 equiv) in water. After stirring at 23 °C for 18–22 h, an aliquot of the reaction mixture was analyzed by LC-MS. Using a 1:1 mixture of purified **12** and **11b**, the relative absorption at 210 nm was determined to be 0.8529:1, which was used to estimate the yield of **12**.

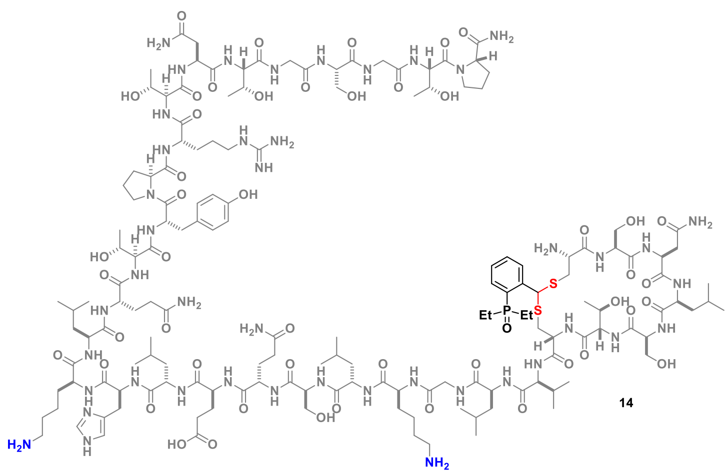
Procedure for ***Fig. 5***

To a solution of lipoic acid (20.6 mg, 0.1 mmol, 1.0 equiv) in aqueous buffer (25 mM, 5 mL) was added a solution of **11b** (282.0 mg, 10 equiv) in water (0.5 mL). After stirring at 23 °C for 20 h, the mixture was extract with ethyl acetate (5 mL ×3), dried over anhydrous sodium sulfate, concentrated, and purified by flash column chromatography to give **12** (32.1 mg, 80% yield). ^{1}H

NMR (600 MHz, CD_3CN): δ 7.86 (ddd, *J* = 7.9, 3.7, 1.2 Hz, 0.4H), 7.79 (ddd, *J* = 7.8, 3.7, 1.2 Hz, 0.6H), 7.62–7.49 (m, 2H), 7.44 (qdd, *J* = 7.5, 2.4, 1.3 Hz, 1H), 6.69 (s, 0.4H), 6.29 (s, 0.6H), 3.30 (ddd, *J* = 15.0, 13.0, 2.5 Hz, 0.4H), 3.08 (ddt, *J* = 14.2, 8.0, 2.1 Hz, 1H), 2.99–2.89 (m, 1H), 2.65 (ddd, *J* = 14.4, 4.6, 3.1 Hz, 0.6H), 2.42–2.22 (m, 2H), 2.22–2.04 (m, 6H), 1.79–1.36 (m, 6H), 1.19–0.96 (m, 6H). MS (ESI) calculated for $C_{19}H_{30}O_3PS_2$ $(M+H)^+$ 401.1, found 401.1.

*Disulfide stapling of **13** with **11b***

To a solution of salmon calcitonin (**13**) (1.0 mg, 0.292 μmol, 1.0 equiv) in pH 8.2 HEPES buffer (145 μL) was added a solution of **11b** in water (1.0 M, 0.9 μL, 3.0 equiv). After stirring at 23 °C for 18 h, excess **11b** was removed by a centrifugal filter (3 kDa MWCO), washed with water (300 μL ×3), incubated with (aminomethyl)polystyrene (15.0 mg, 50 equiv) for 12 h, and filtered to give a mixture of **13**, **14**, and **14'**. **13**: MS (ESI-QTOF) calculated for $C_{145}H_{241}N_{44}O_{48}PS_2$ $(M+H)^+$ 3431.72, found 3631.62. **14**: MS (ESI-QTOF) calculated for $C_{156}H_{256}N_{44}O_{49}PS_2$ $(M+H)^+$ 3625.81, found 3625.69 or 3625.76. **14'**: MS (ESI-QTOF) calculated for $C_{178}H_{282}N_{44}O_{49}P_3S_2$ $(M+H)^+$ 3977.96, found 3978.12 or 3978.19.



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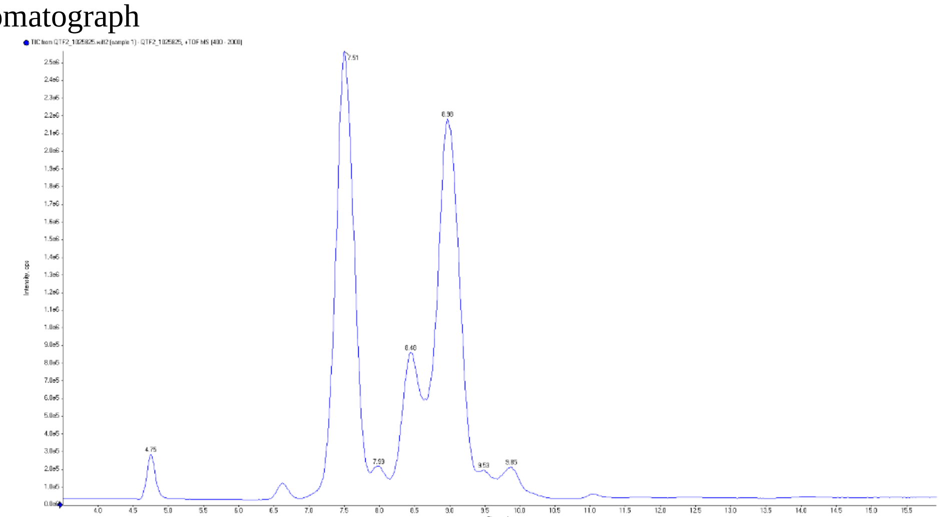
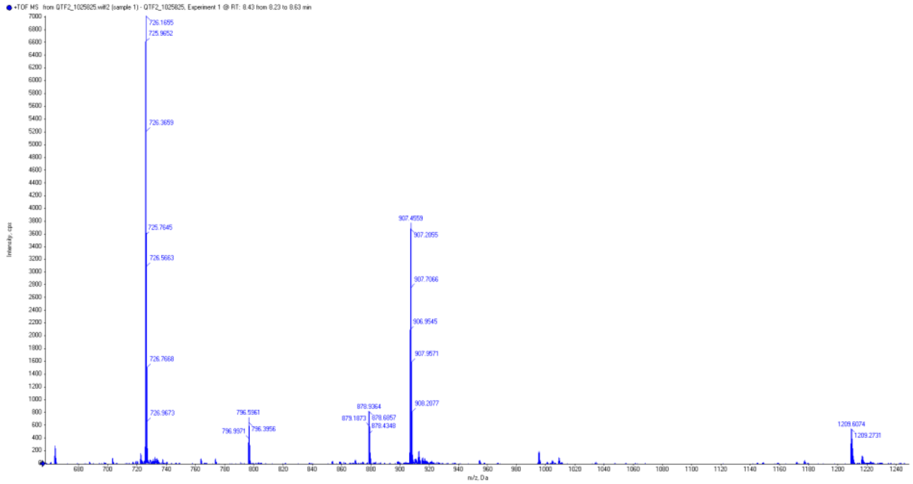
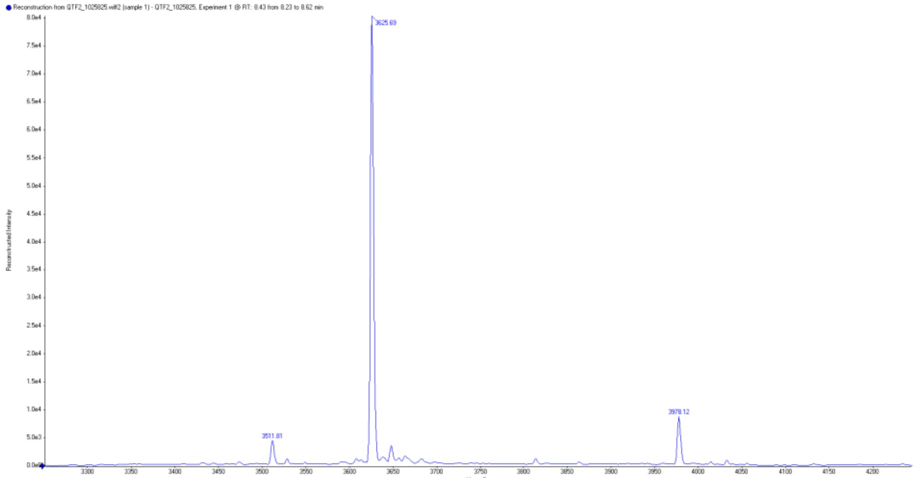
HPLC chromatograph



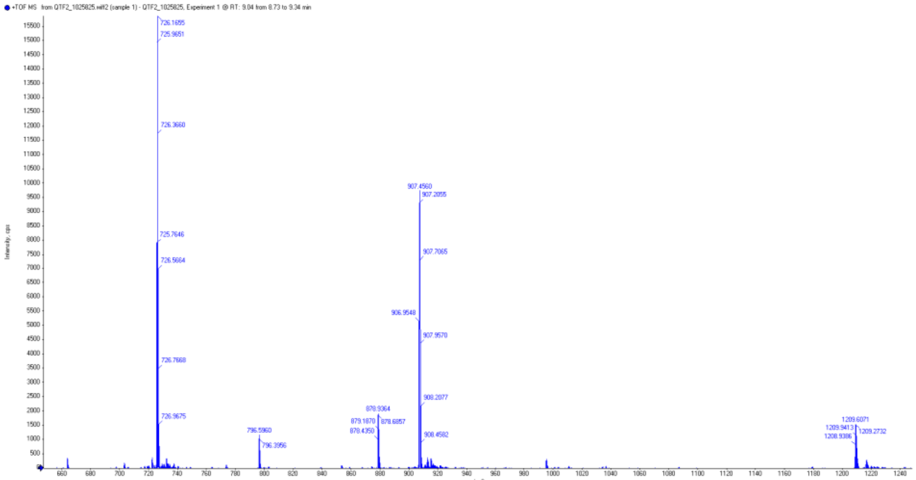
Mass spectrum at 8.43 min before deconvolution



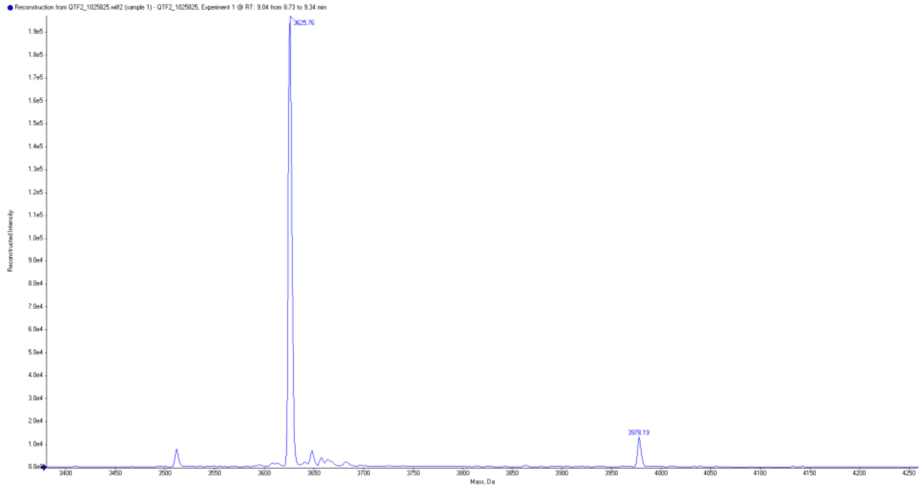
Mass spectrum at 8.43 min after deconvolution: *m/z* 3625.69 (**14**)



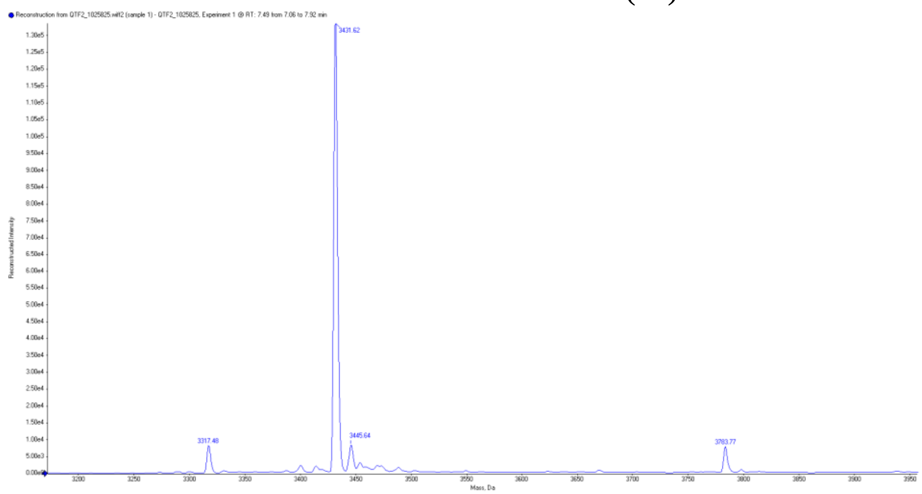
Mass spectrum at 9.04 min before deconvolution

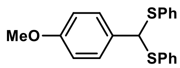


Mass spectrum at 9.04 min after deconvolution: *m/z* 3625.76 (**14**)

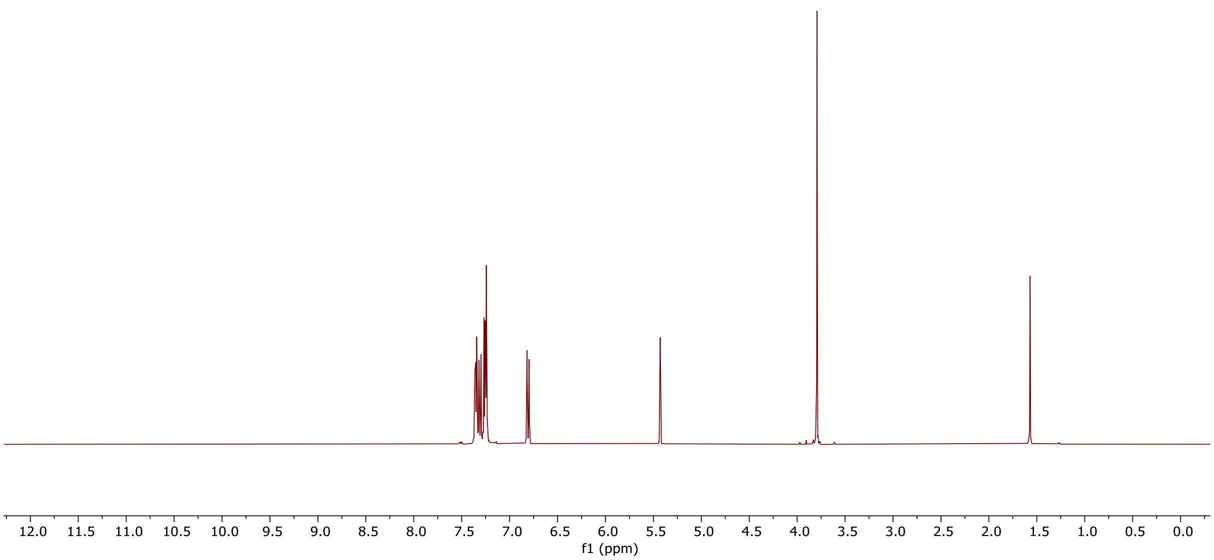


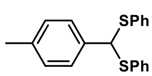
Mass spectrum at 7.49 min after deconvolution: *m/z* 3431.62 (**13**)



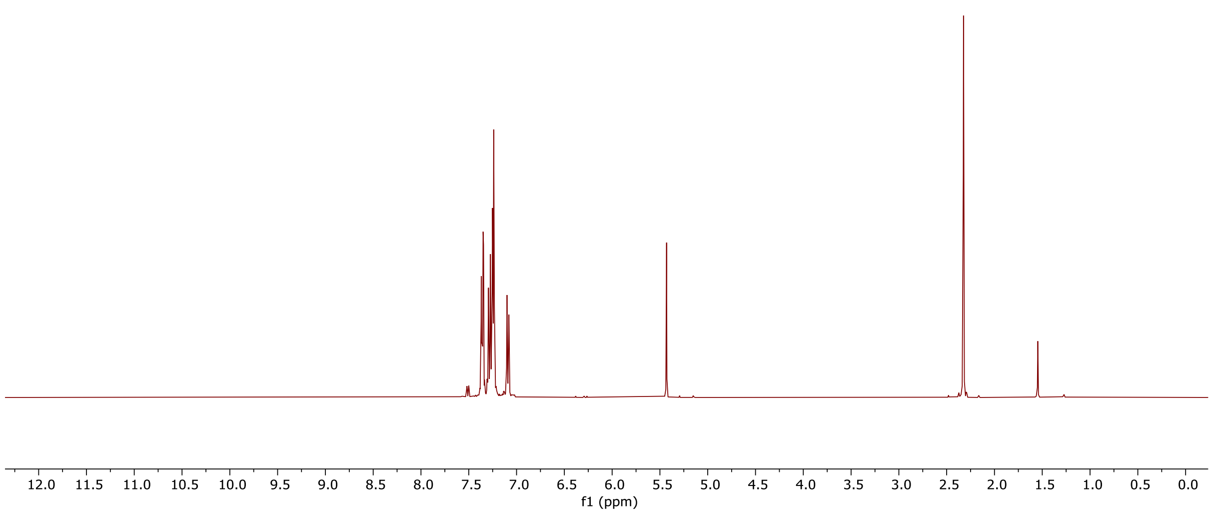


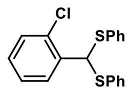
^{1}H NMR
$CDCl_3$, 400 MHz



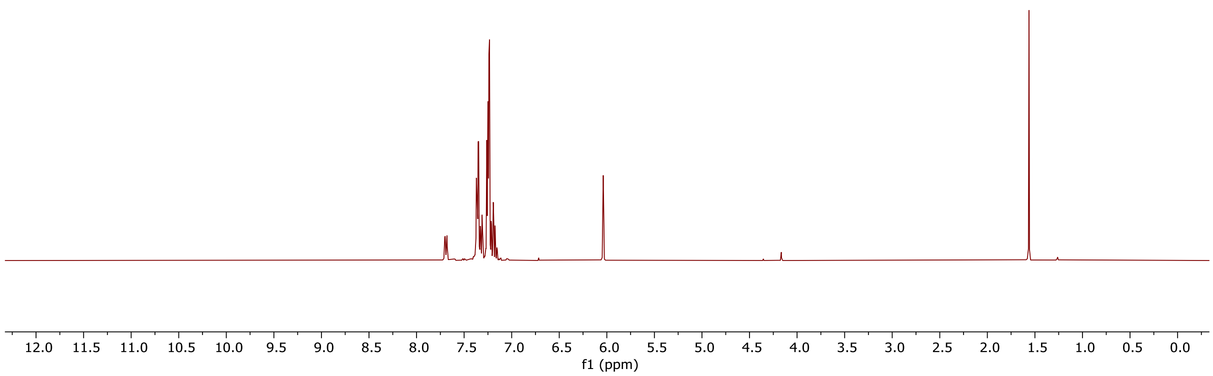


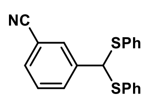
^{1}H NMR
$CDCl_3$, 400 MHz



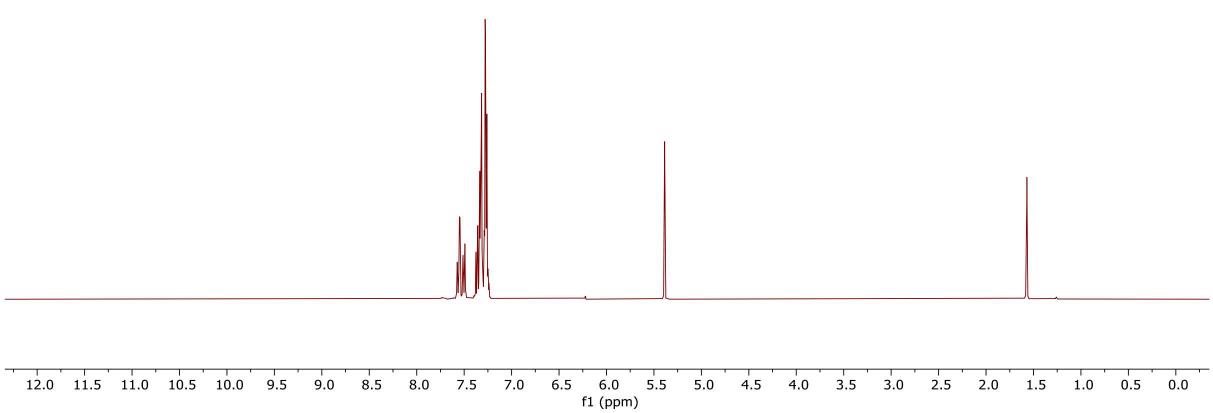


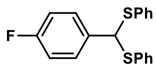
^{1}H NMR
$CDCl_3$, 400 MHz



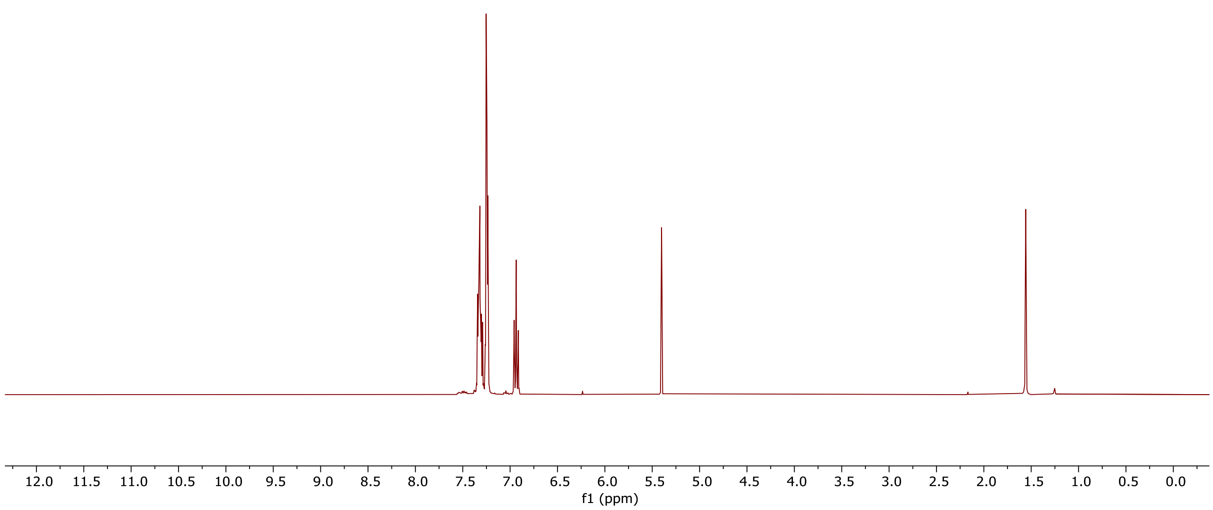


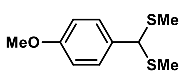
^{1}H NMR
$CDCl_3$, 400 MHz



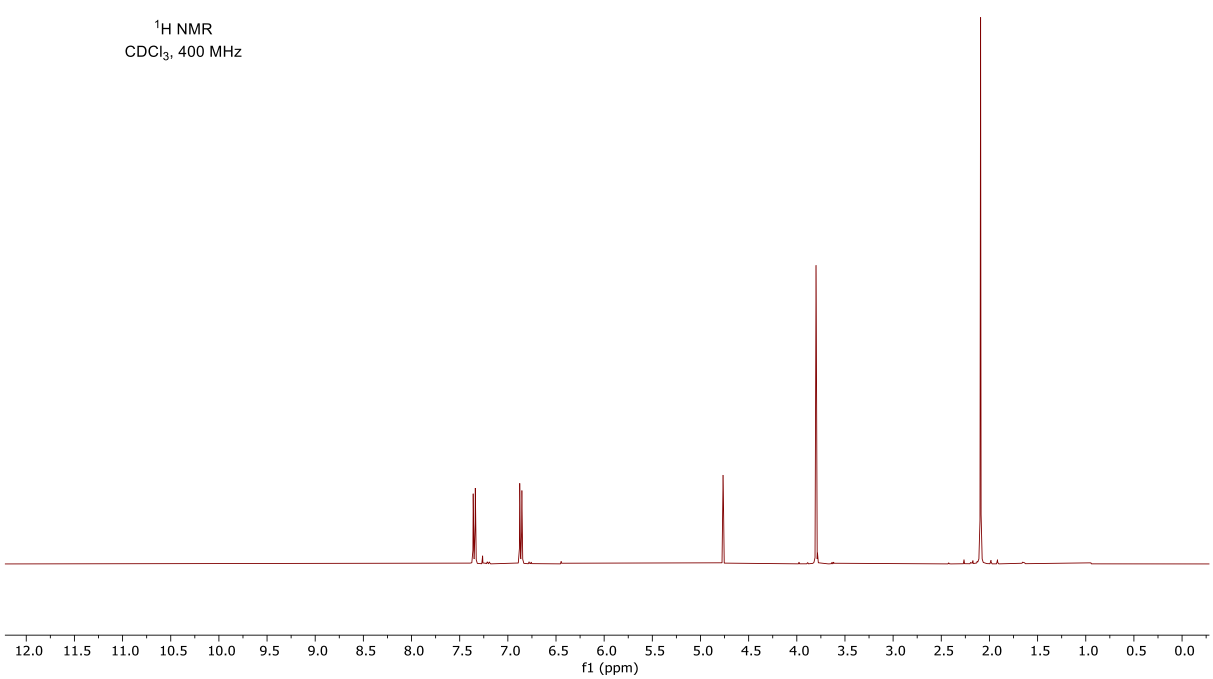


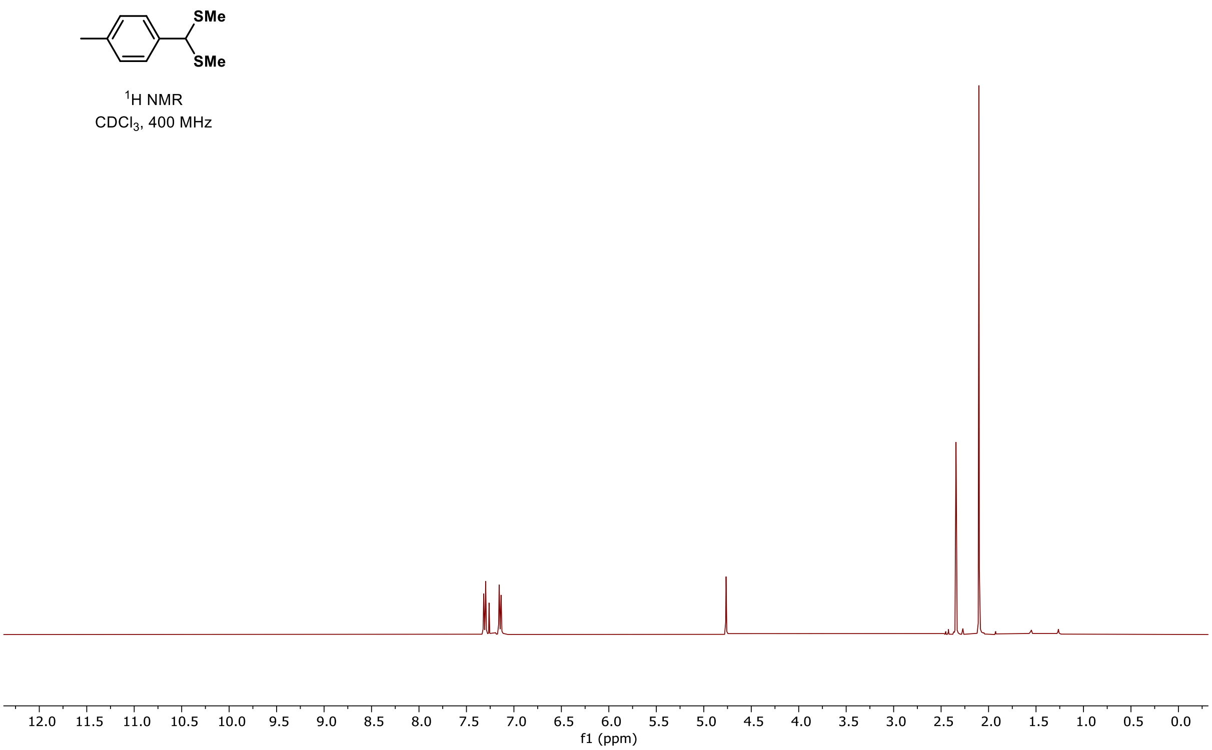
^1H NMR
$CDCl_3$, 400 MHz

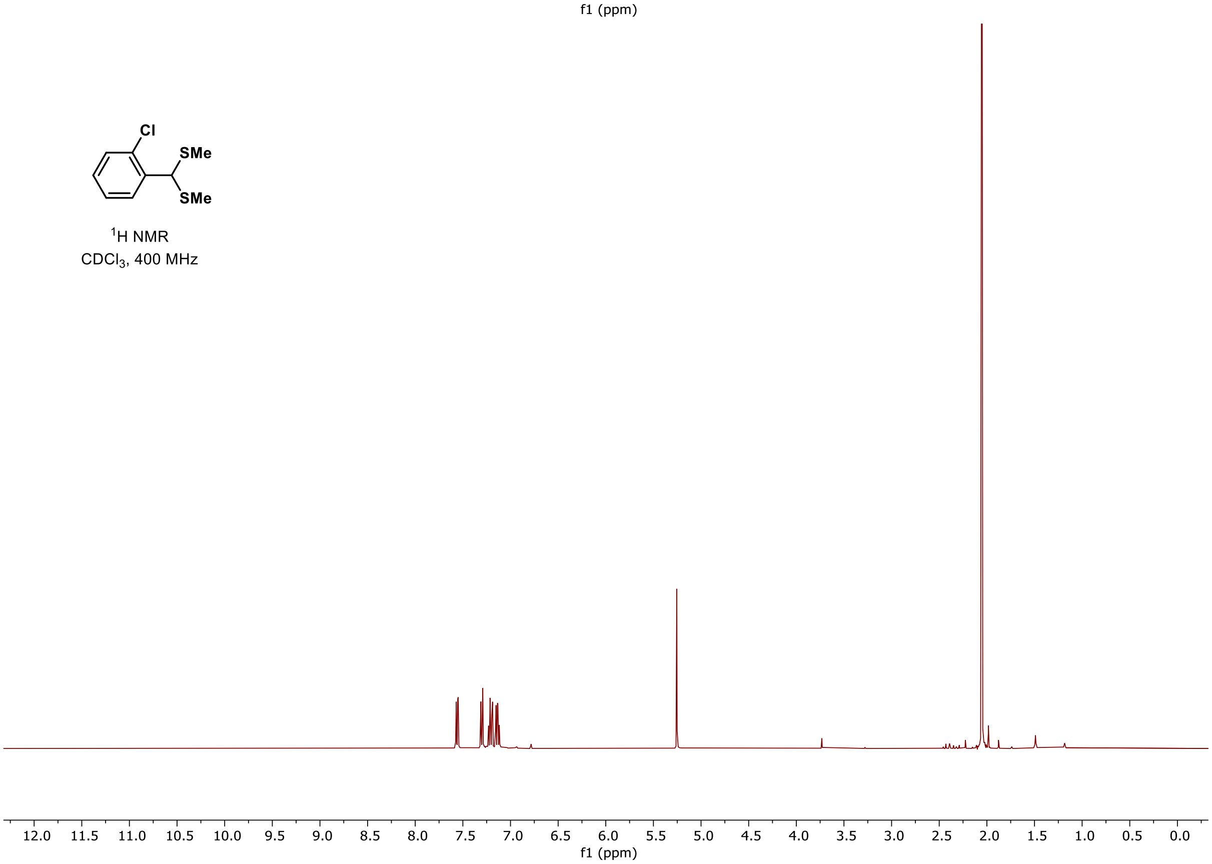


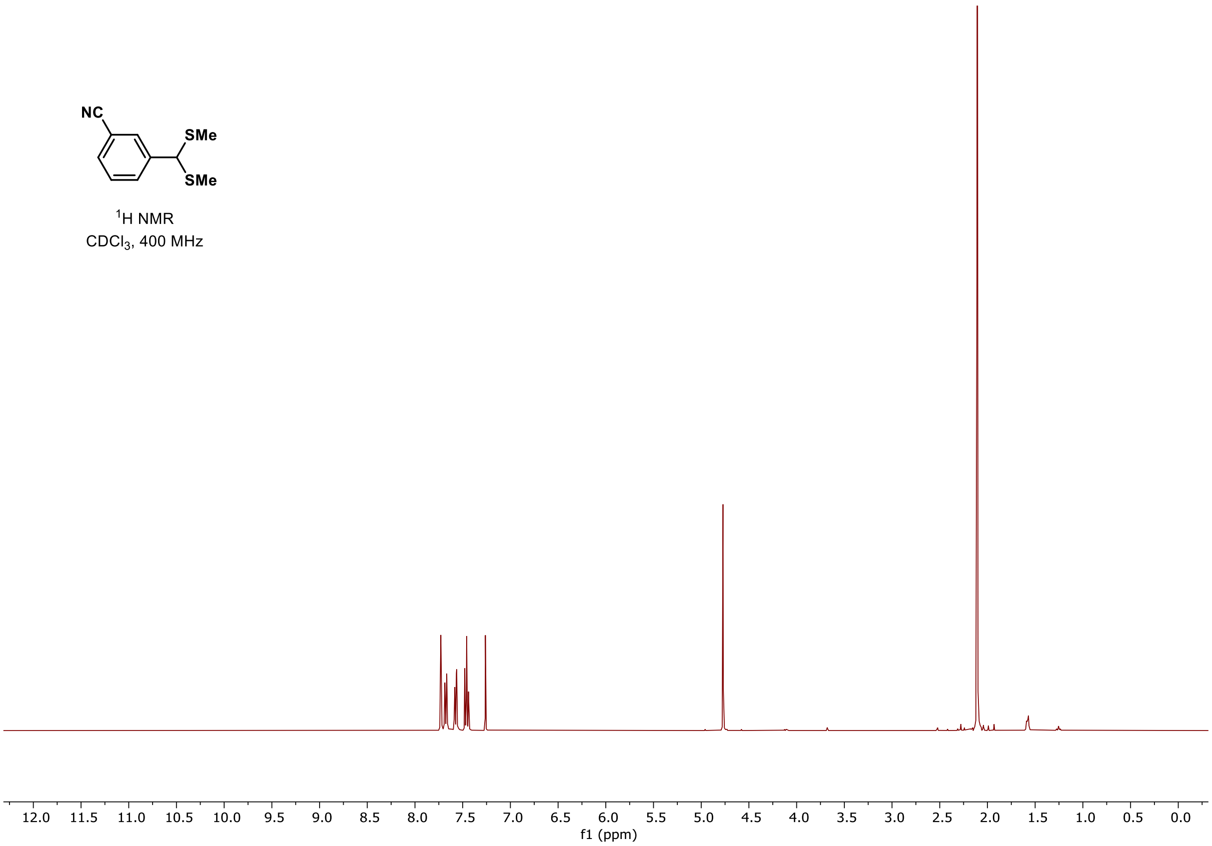


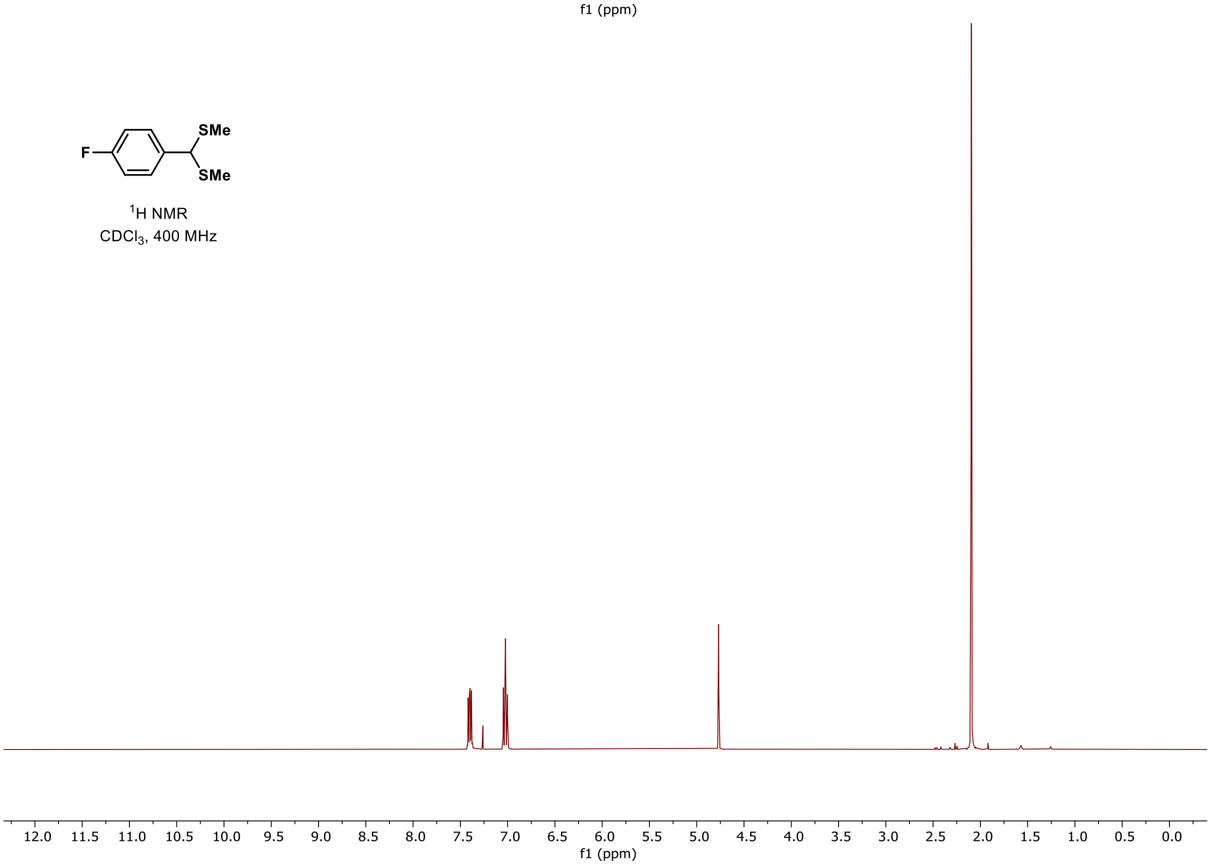
^1H NMR
$CDCl_3$, 400 MHz

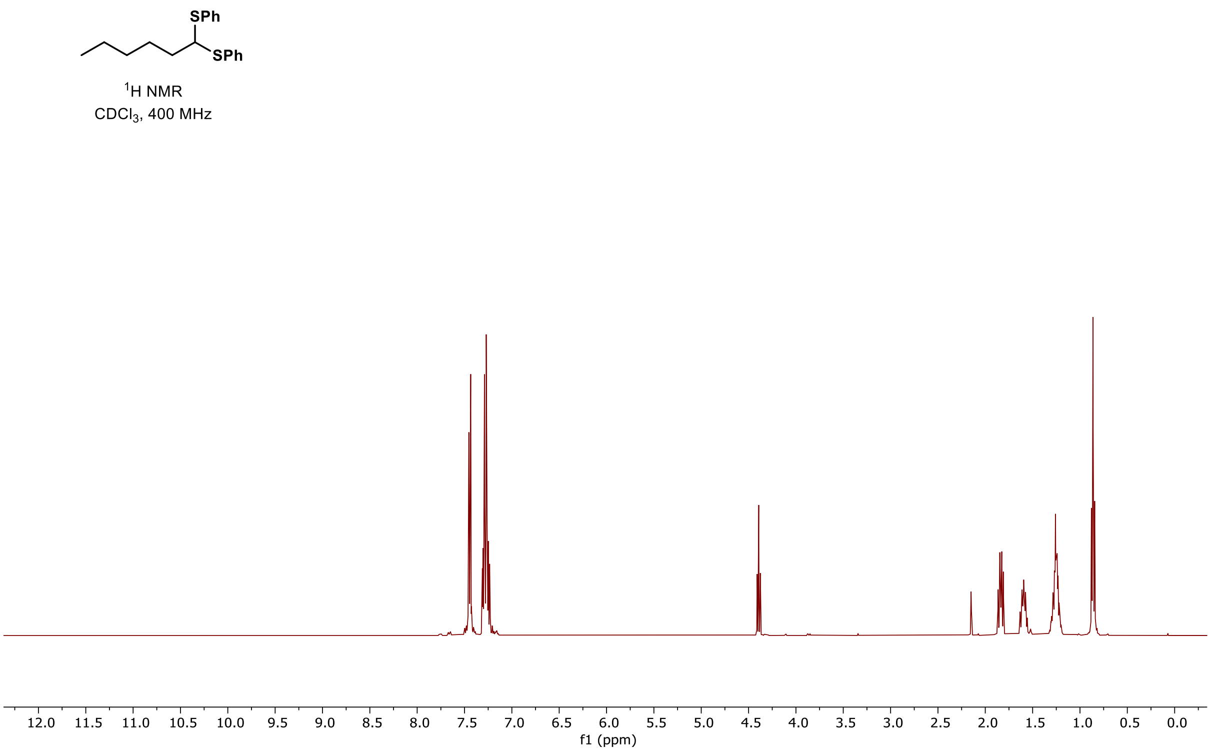


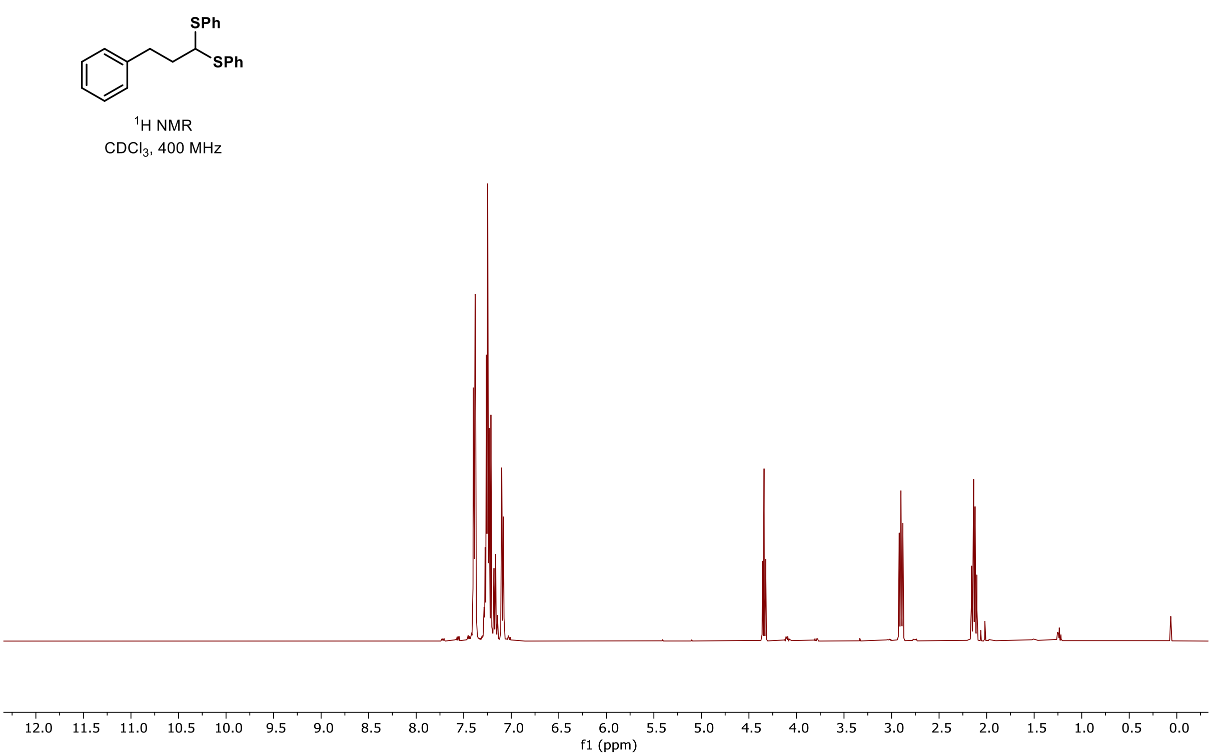

SMe
SMe
1H NMR
CDCl3, 400 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

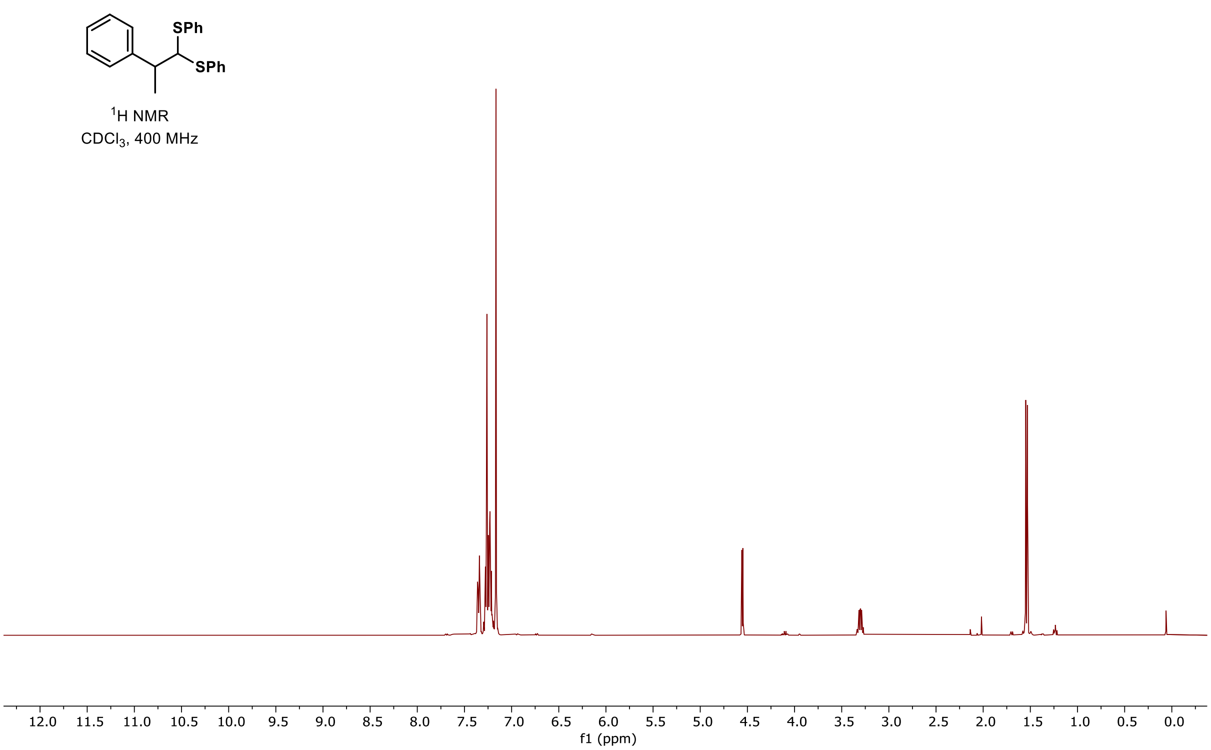

Cl
SMe
SMe
1H NMR
CDCl3, 400 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

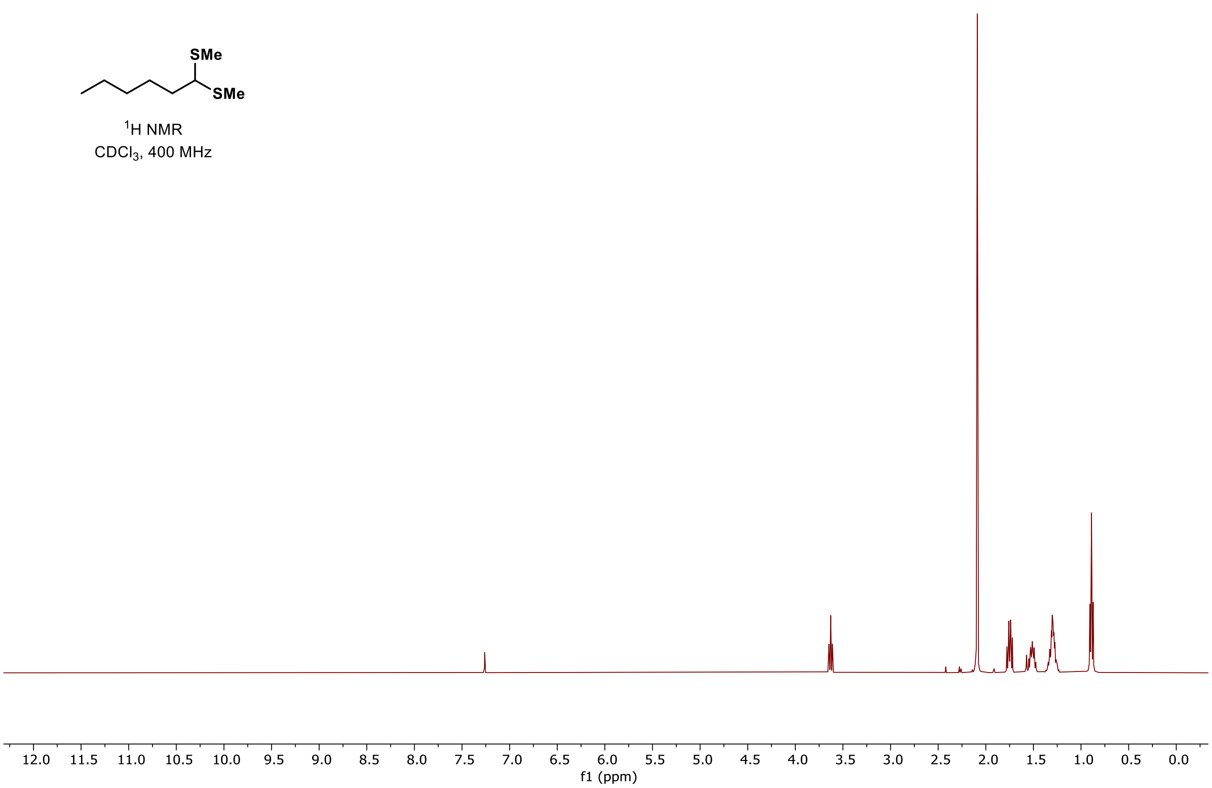

NC
SMe
SMe
1H NMR
CDCl3, 400 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

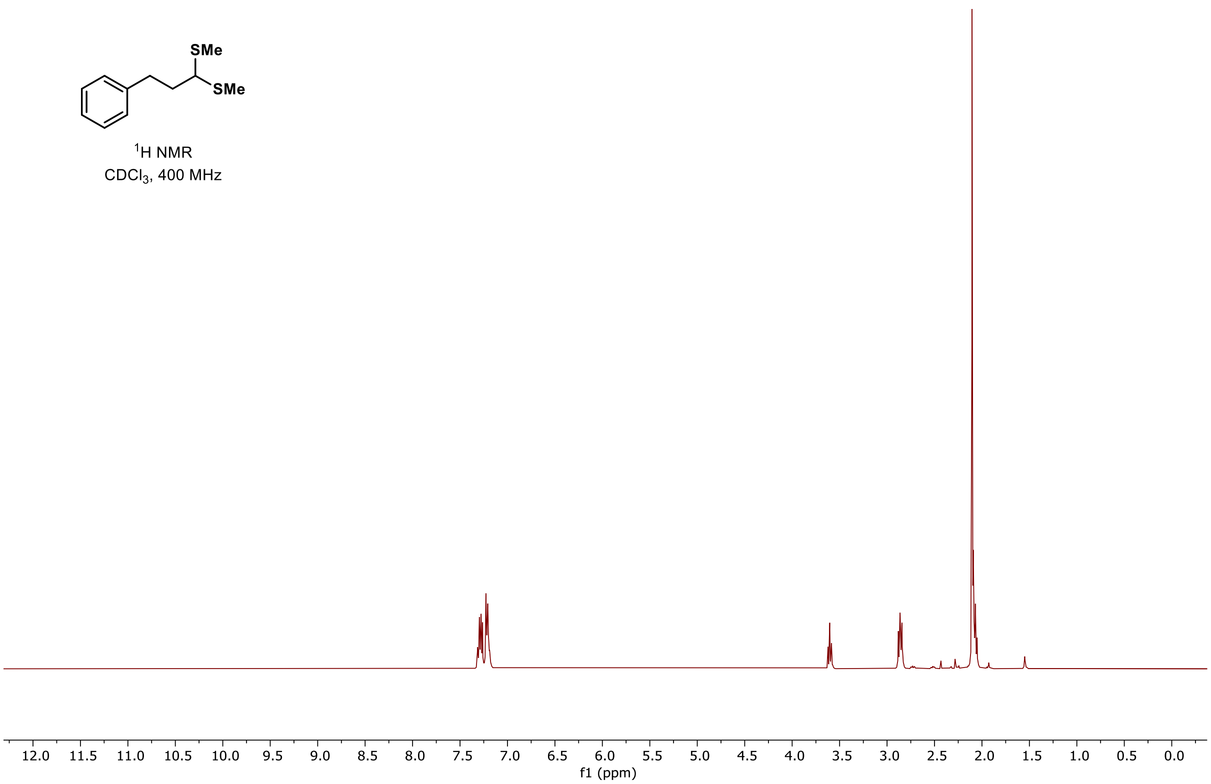

F
SMe
SMe
1H NMR
CDCl3, 400 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

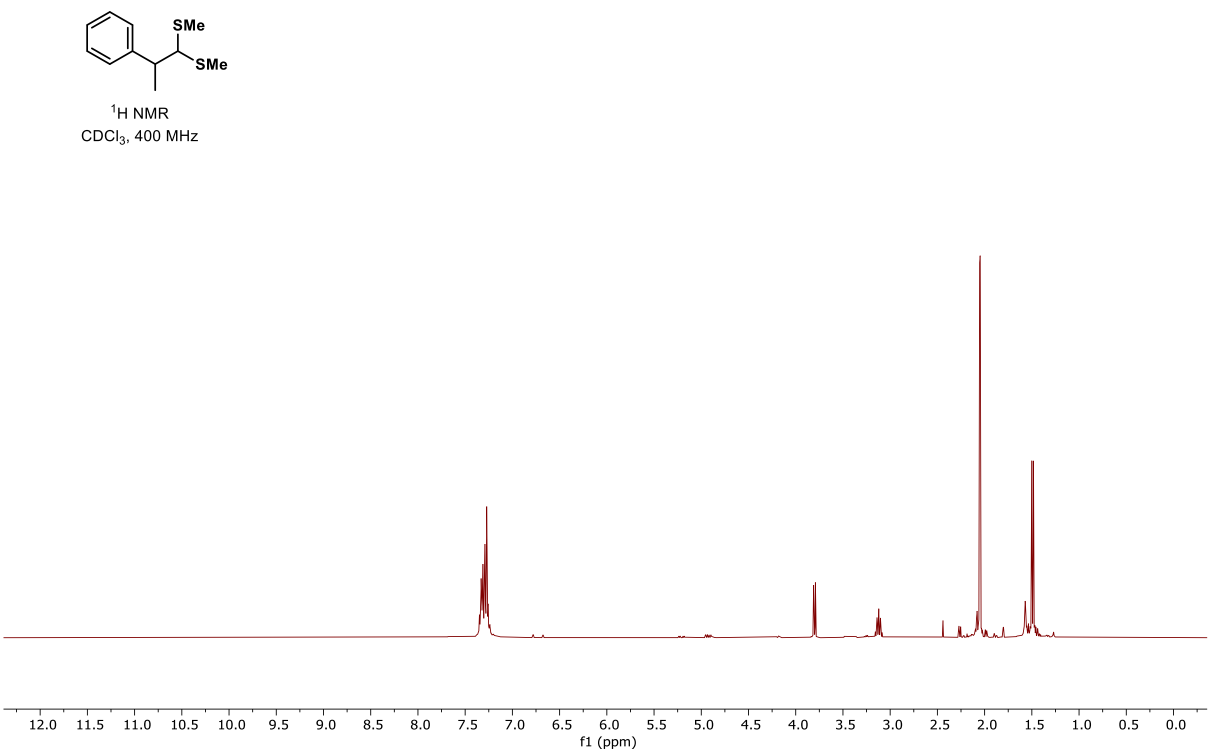

SPh
SPh
^{1}H NMR
$CDCl_3$, 400 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

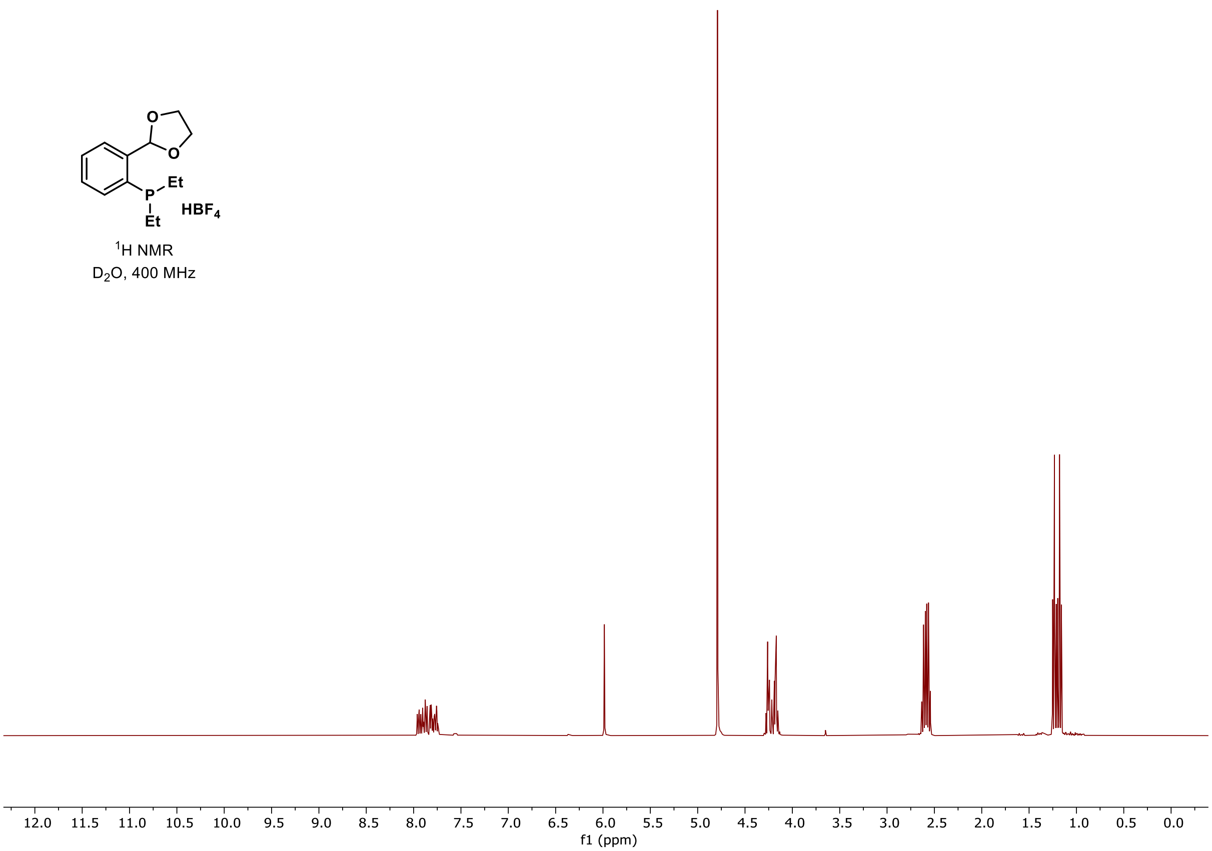

SPh
SPh
^{1}H NMR
$CDCl_3$, 400 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


SPh
SPh
1H NMR
CDCl3, 400 MHz
12.0 11.5 11.0 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 0.0
f1 (ppm)

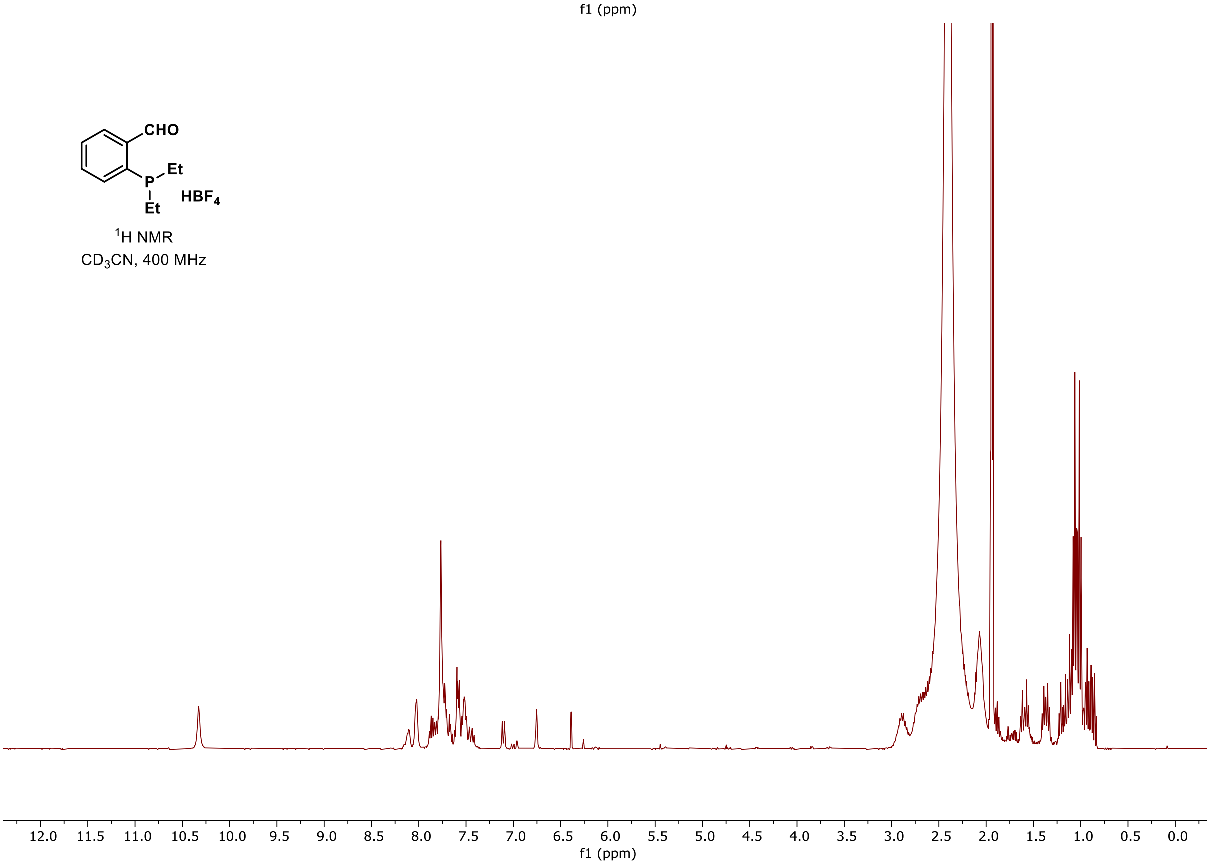

SMe
SMe
1H NMR
CDCl3, 400 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


SMe
SMe
1H NMR
CDCl3, 400 MHz
12.0 11.5 11.0 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 0.0
f1 (ppm)

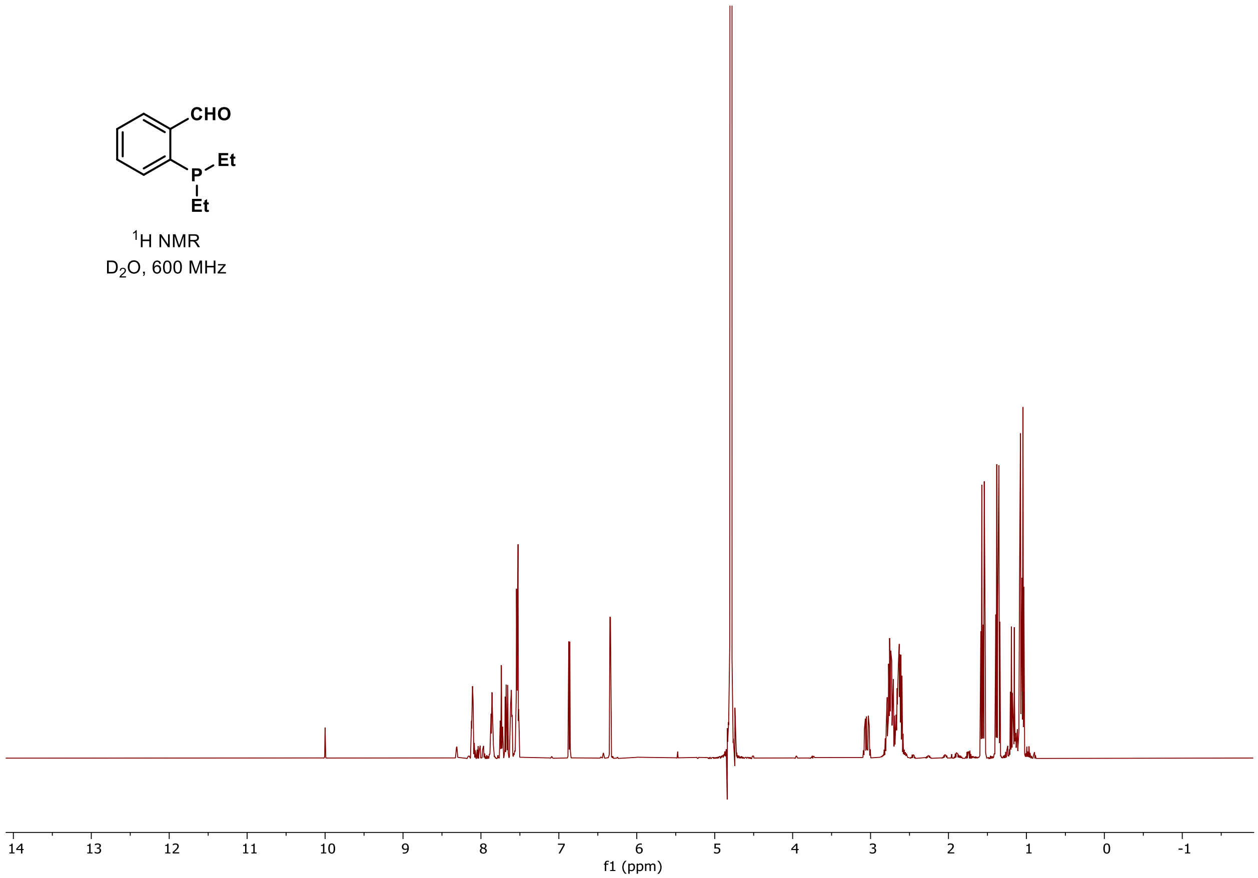

SMe
SMe
1H NMR
CDCl3, 400 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

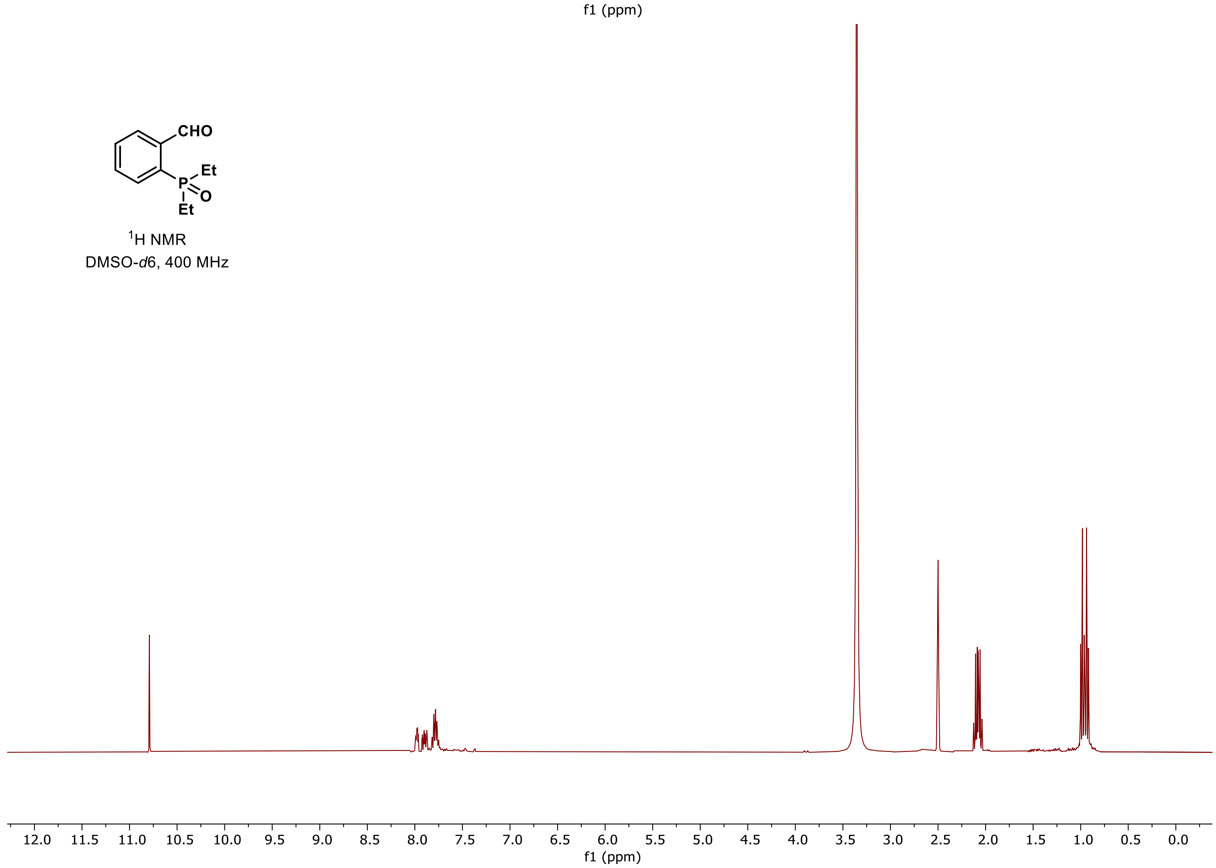


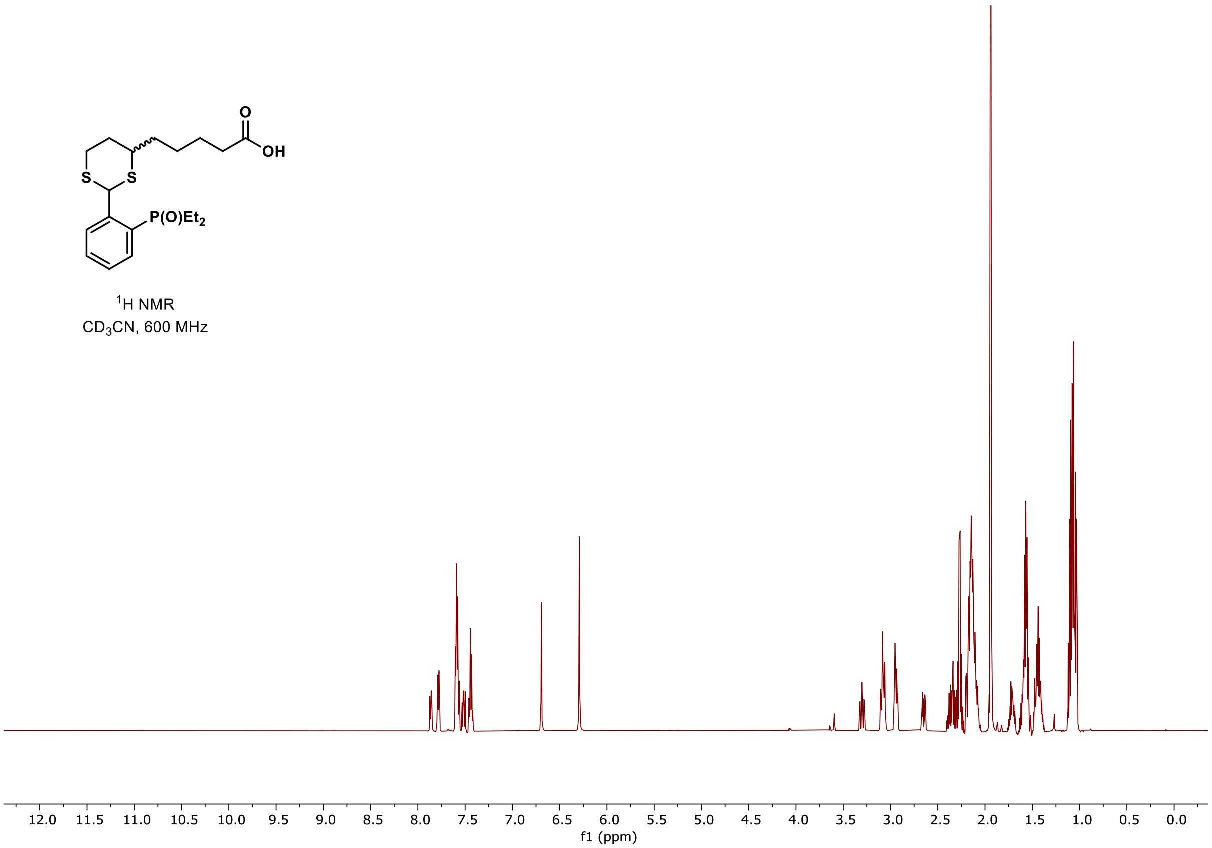
HBF4
1H NMR
D2O, 400 MHz
f1 (ppm)



CHO
HBF4
1H NMR
CD3CN, 400 MHz
f1 (ppm)


CHO
P
Et
Et
1H NMR
D2O, 600 MHz
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


CHO
P
Et
O
Et
1H NMR
DMSO-d6, 400 MHz
12.0 11.5 11.0 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 0.0
f1 (ppm)


O
OH
S
S
P(O)Et2
1H NMR
CD3CN, 600 MHz
12.0 11.5 11.0 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 0.0
f1 (ppm)