Thiol-Promoted Selective Addition of Ketones to Aldehydes

Regev Parnes, Sachin Narute and Doron Pappo*

Department of Chemistry, Ben-Gurion University of the Negev
Beer Sheva 84105, Israel

Email: pappod@bgu.ac.il

Supporting Information

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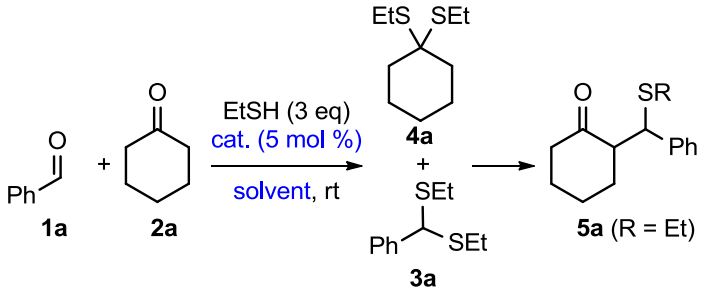
Experimental section

A. General information:

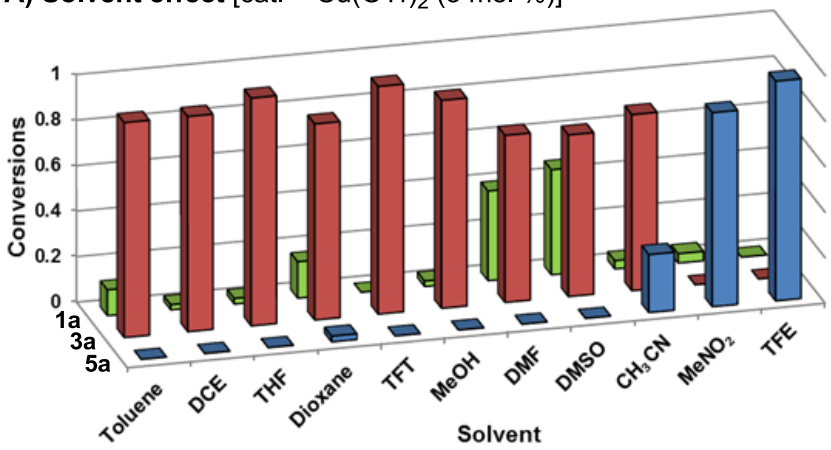
All reagents were of reagent grade quality, purchased commercially from Sigma-Aldrich, Alfa-Aesar, or Fluka, and used without further purification. $Cu(OTf)_2$ used was purchased from strem chemicals. Purification by column chromatography was performed on Merck chromatographic silica gel (40-60 μm). TLC analyses were performed using Merck silica gel glass plates 60 F254. NMR spectra were recorded on Bruker DPX400, or DMX500 instruments; chemical shifts, given in, are relative to Me_4Si as the internal standard or to the residual solvent peak. The microwave radiation reactions were performed on CEM Discover microwave synthesizer. HR-MS data were obtained using a Thermoscientific LTQU XL Orbitrap HRMS equipped with APCI (atmospheric-pressure chemical ionization). Gas chromatography data were obtained using an Agilent 7820A GC equipped with FID detector working under standard conditions and an Agilent HP-5 column. HPLC analysis was carried out on a Agilent 1260 instrument equipped with a G4212-60008 photodiode array detector, ES-MS Advion Expression unit and a Agilent reverse phase ZORBAX Eclipse plus C18 3.5 μm column (4.6 X 100 mm). IR spectra were recorded on a Nicolet 380 FTIR spectrometer. Copper(II)trifluoromethanesulfonate from Sterm [catalog number 29-5000] was used in this study.

B. Reaction parameters screening

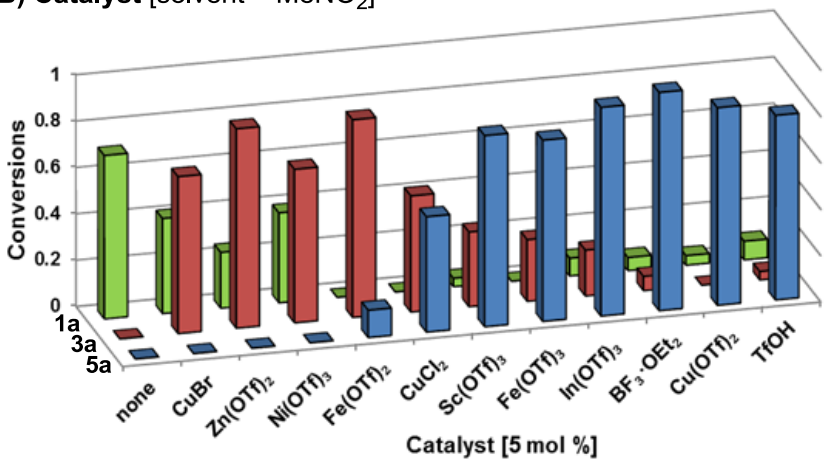
Figure 1S.



A) Solvent effect [cat. = $Cu(OTf)_2$ (5 mol %)]



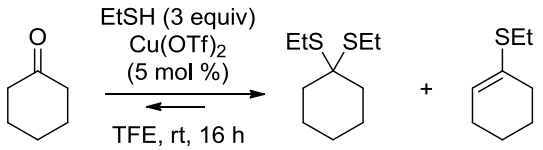
B) Catalyst [solvent = $MeNO_2$]



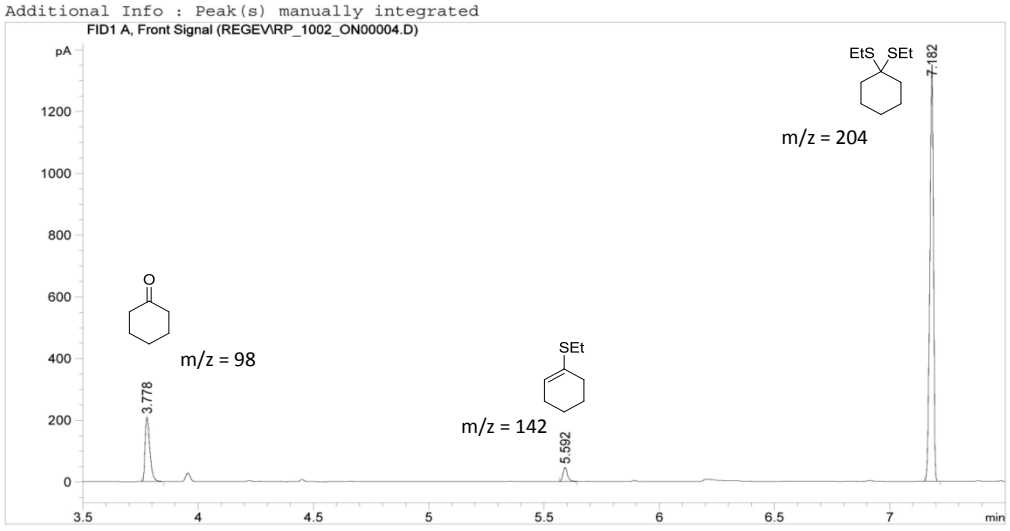
Conditions: 1a (0.2 mmol), **2a** (0.6 mmol), EtSH (0.6 mmol), catalyst (5 mol %), solvent (0.3 M), rt, 6 h; the products' molar ratios were determined by HPLC analysis using mesitylene as the internal standard. DCE = 1,2-dichloroethane, THF = tetrahydrofuran, TFT = α,α,α-trifluorotoluene, DMF = *N*,*N*-dimethylformamide, DMSO = dimethylsulfoxide, TFE = 2,2,2-trifluoroethanol.

C. Mechanistic study

(a) Evidence for the formation of vinyl sulfide under the reaction conditions (based on GC-MS and GC-FID chromatography):



GC spectrum of the crude reaction mixture:

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=====================================================================
                        Area Percent Report
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Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 A, Front Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [pA*s]      [pA]       %
----|-------|----|-------|----------|----------|--------|
   1   3.778 BB    0.0217  298.64658  208.20615 16.17427
   2   5.592 BB    0.0210   63.00315   45.88004  3.41216
   3   7.182 BB    0.0181 1484.78076 1323.97083 80.41357
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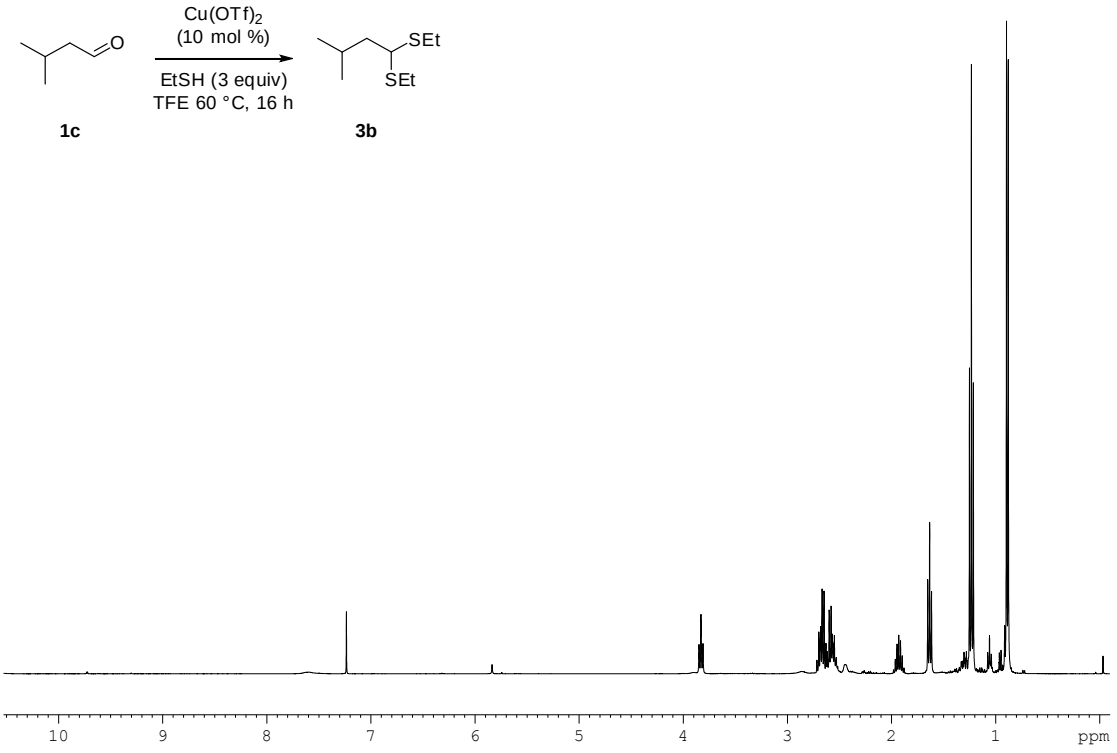
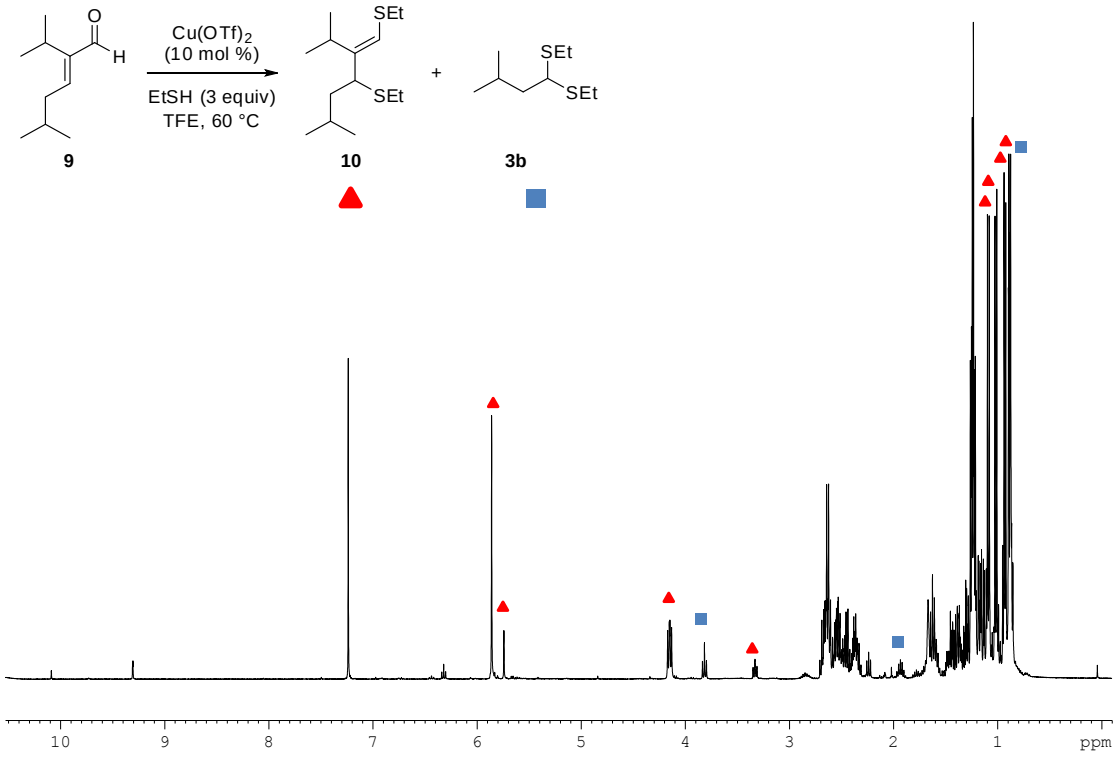
(b) The ^{1}H-NMR spectrum for the reaction mixture of aliphatic aldehyde **1c** with ethanethiol:

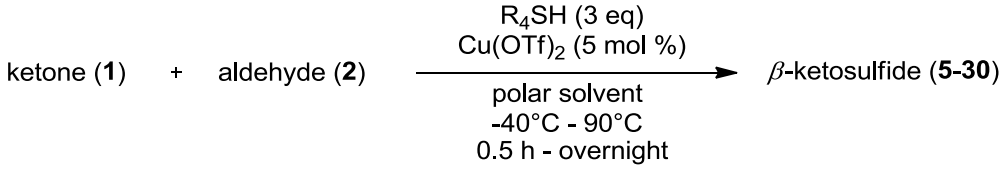


(c) The reaction of compound **9** with ethanethiol; evidence for the reversibility of the dimerization process (^{1}H-NMR spectrum of the reaction mixture):



D. General procedures

The Pummerer/aldol addition reaction of aldehydes and ketones

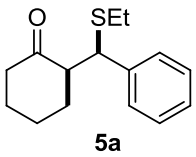


Method A (aromatic aldehydes): solution of aromatic aldehyde (1 equiv.), $Cu(OTf)_2$ (0.05 equiv.), ethanethiol (3 equiv.) and a ketone (3 equiv.) in a polar solvent (0.3 M) was stirred at required temperature. After completion of the reaction or when the reaction did not proceed any more, the volatiles were removed under reduced pressure and the crude residue purified over silica gel column chromatography affording the desired coupling product(s).

Method B (aliphatic aldehydes): A solution of aliphatic aldehyde (1 equiv.), $Cu(OTf)_2$ (0.05 equiv.) and ethanethiol (3 equiv.) in a polar solvent (0.3 M) was stirred at room temperature for 0.1 to 3 hours. Then, the ketone (3 equiv.) coupling partner was added and the mixture stirred at required temperature. After completion of the reaction or when the reaction did not proceed any more, the volatiles were removed under reduced pressure and the crude residue purified over silica gel column chromatography affording the desired coupling product(s).

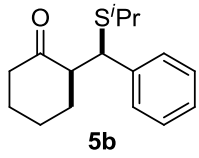
E. Experimental and data:

1] Compound 5a was prepared according to method A. A solution of Benzaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol) and ethanethiol (47 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at rt for 0.5 h. The mixture was cooled to -40 °C and cyclohexanone (74 mg, 0.75 mmol) was added using syringe. The reaction was kept at that temperature for 2 h, the volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **5a** (52.7 mg, 85% yield; d.r. = 11:1 based on HPLC analysis) as a colorless thick oil. Spectral data for compound **5a**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.36–7.31 (m, 2H), 7.28–7.23 (m, 2H), 7.17 (t, J = 7.3 Hz, 1H), 4.38 (d, J = 7.3 Hz, 1H), 2.76 (ddd, J = 5.4, 7.3, 11.9 Hz, 1H), 2.38–2.28 (m, 2H), 2.25 (t, J = 7.3 Hz, 1H), 2.22–2.15 (m, 1H), 2.01–1.94 (m, 1H), 1.91–1.86 (m, 1H), 1.73–1.65 (m, 3H), 1.61–1.55 (m, 1H), 1.11 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 210.1, 142.3, 128.3, 128.2, 126.8, 56.6, 48.4, 42.1, 30.6, 27.7, 25.3, 24.6, 14.2; HRMS (ESI): m/z calculated for $C_{15}H_{20}OS$ $[M+H]^+$ 249.1308, found 249.1305.



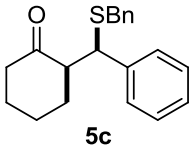
5a

2] Compound 5b was prepared according to method A. A solution of benzaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), isopropyl mercaptan (57 mg, 0.75 mmol) and cyclohexanone (74 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at rt for 6 h. The volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **5b** (55 mg, 84% yield; dr = 2.5:1) as a thick oil. Spectral data for compound **5b**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.36 (t, J = 9.5 Hz, 2H), 7.28–7.23 (m, 2H), 7.20–7.14 (m, 1H), 4.44 (d, J = 6.8 Hz, 1H), 2.75–2.68 (m, 1H), 2.57–2.49 (m, 1H), 2.38–2.25 (m, 1H), 2.24–2.22 (m,1H), 1.99–1.83 (m, 2H), 1.78–1.62 (m, 3H), 1.60–1.49 (m, 1H), 1.21 (d, J = 6.6 Hz, 3H), 1.05 (t, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 210.1, 142.9, 128.4, 128.2, 126.7, 57.0, 47.6, 42.2, 34.5, 30.3, 27.6, 24.6, 23.4, 23.2; HRMS (ESI): m/z calculated for $C_{16}H_{22}OS$ $[M+H]^+$ 285.1292, found 285.1284.



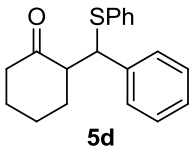
5b

3] Compound 5c was prepared according to method A. A solution of benzaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), benzyl mercaptan (93 mg, 0.75 mmol) and cyclohexanone (74 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 18 h. The volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 2:98) affording compound **5c** (49.9 mg, 64% yield; dr = 7.1:1) as a pale yellow thick oil. Spectral data for compound **5c**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.34–7.17 (m, 10H), 4.23 (d, J = 7.6 Hz, 1H), 3.48 (d, J = 13.8 Hz, 1H), 3.39 (d, J = 13.8 Hz, 1H), 2.79–2.70 (m, 1H), 2.33–2.24 (m, 2H), 2.14 (ddd, J = 1.1, 5.8, 11.7 Hz, 1H), 1.96–1.76 (m, 2H), 1.74–1.62 (m, 2H), 1.58–1.47 (m, 1H); ^{13}C NMR ($CDCl_3$/100MHz): δ 210.0, 141.8, 137.9, 129.1, 129.0, 128.5, 128.3, 128.2, 126.9, 56.4, 48.4, 42.1, 35.5, 30.8, 27.7, 24.4; HRMS (ESI): m/z calculated for $C_{20}H_{22}OS$ $[M+H]^+$ 311.1464, found 311.1479.



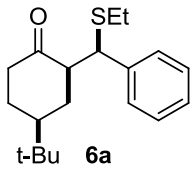
5c

4] Compound 5d was prepared according to method A. A solution of benzaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (9 mg, 0.0125 mmol) thiophenol (82.5 mg, 0.75 mmol) and cyclohexanone (74 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at rt for 6 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **5d** (37.7 mg, 51% yield; dr = 1:1) as a colorless oil. Spectral data for compound **5d**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.26–7.13 (m, 10H), 4.72 (d, J = 7.0 Hz, 0.5H), 4.66 (d, J = 8.0 Hz, 0.5H), 2.89–2.80 (m, 1H), 2.53–2.30 (m, 2H), 2.26–2.18 (m, 1H), 1.97–1.85 (m, 2H), 1.82–1.58 (m, 2H), 1.35–1.23 (m, 1H); ^{13}C NMR ($CDCl_3$/100MHz): δ 210.6, 139.8, 134.8, 132.2, 128.9, 128.6, 128.2, 128.1, 127.1, 126.8, 56.6, 53.0, 42.0, 31.6, 28.0, 24.6; HRMS (ESI): m/z calculated for $C_{19}H_{20}OS$ $[M+Na]^+$ 319.1127, found 319.1136.



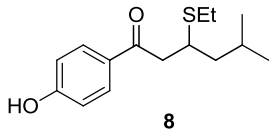
5d

5] Compound 6a was prepared according to method A. A solution of benzaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (93 mg, 0.75 mmol) and 4-*t*-butylcyclohexanone (116 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at 0 °C for 6 h. All volatiles were removed under reduce pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **6a** (92 mg, 71% yield; dr = 14:1) as a colorless syrup (which solidifies slowly). Spectral data for compound **6a**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.41– 7.37 (m, 2H), 7.27–7.31 (m, 2H), 7.20 (ddt, J = 1.3, 7.3 Hz, 1H), 4.44 (d, J = 6.6 Hz, 1H), 2.77–2.83 (m, 1H), 2.43–2.49 (m, 1H), 2.35–2.41 (m, 1H), 2.20–2.33 (m, 3H), 2.02–2.09 (m, 1H), 1.38–1.53 (m, 3H), 1.14 (t, J = 7.4 Hz, 3H), 0.92 (s, 9H); ^{13}C NMR ($CDCl_3$/100MHz): δ 210.4, 142.7, 128.3, 128.1, 126.6, 55.7, 48.6, 46.9, 41.6, 32.6, 31.4, 28.3, 27.6, 25.4, 14.2; HRMS (ESI): m/z calculated for $C_{19}H_{28}OS$ $[M+H]^+$ 305.1934, found 305.1933.



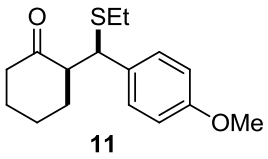
6a

6] Compound 8 was prepared according to method A. Into a sealed tube apparatus were added isovaleraldehyde (21.5 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 0.75 mmol) and 2,2,2-trifluoroethanol. The mixture was stirred at room temperature for 3 h, 4′-hydroxyacetophenone (102 mg, 0.75 mmol) was added and the tube was sealed. The reaction was stirred at 90 °C for 18 h, cooled to room temperature and all the volatiles removed under reduced pressure. The crude residue was purified over column chromatography (Silica gel 230–400; ethyl acetate /hexane 5:95) affording compound **8** (27 mg, 50% yield) as a thick oil. Spectral data for compound **8**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.89 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8, 2H), 3.40–3.33 (m, 1H), 3.26 (dd, J = 6.5, 16.4 Hz, 1H), 3.1 (dd, J = 6.8, 16.4 Hz, 1H), 2.59–2.48 (m, 2H), 1.85 (sex, J = 6.5 Hz, 1H), 1.51–1.37 (m, 2H), 1.21 (t, J = 7.4 Hz, 3H), 0.91 (d, J = 8.7 Hz, 3H), 0.89 (d, J = 8.8 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 198.5, 161.0, 130.9, 129.9, 115.6, 45.2, 39.1, 25.6, 24.7, 23.0, 22.0, 14.8; HRMS (ESI): m/z calculated for $C_{15}H_{22}O_2S$ $[M+H]^+$ 267.1413, found 267.1408.



8

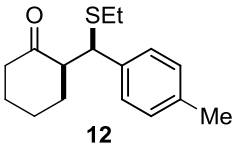
7] Compound 11 was prepared according to method A. A solution of 4-methoxybenzaldehyde



11

(34 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 1.5 mmol) and cyclohexanone (74 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at 10 °C for 0.5 h. All volatiles were removed and the crude residue was purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **11** (64 mg, 92% yield; dr = 4:1) as a colorless thick oil. Spectral data for compound **11**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.26–7.23 (m, 2H), 6.81–6.78 (m, 2H), 4.33 (d, J = 7.6 Hz, 1H), 3.74 (s, 3H), 2.76–2.68 (m, 1H), 2.36–2.26 (m, 2H), 2.25–2.14 (m, 2H), 2.01–1.93 (m, 1H), 1.91–1.85 (m, 1H), 1.80–1.62 (m, 3H), 1.61–1.53 (m, 1H), 1.10 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 210.4, 158.3, 134.2, 129.3, 113.5, 56.8, 55.1, 47.8, 42.1, 30.7, 27.8, 25.1, 24.4, 14.2; HRMS (ESI): m/z calculated for $C_{16}H_{22}O_2S$ $[M+Na]^+$ 301.1233, found 301.1193.

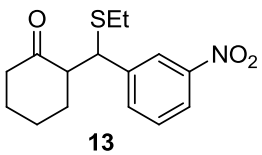
8] Compound 12 was prepared according to method A. A solution of 4-methylbenzaldehyde (30



12

mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 0.75 mmol) and cyclohexanone (74 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 4 h. All volatiles were removed and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **12** (57.3 mg, 88% yield, dr = 2.7:1) as a colorless thick oil. Spectral data of compound **12**: ^{1}H NMR ($CDCl_3$/400 MHz): δ 7.24 (d, J = 9 Hz, 2H), 7.10 (t, J = 7.5 Hz, 2H), 4.37 (d, J = 7.3 Hz, 1H), 2.80–2.74 (m, 1H), 2.30 (s, 3H), 2.39–2.17 (m, 4H), 2.00–1.82 (m, 2H), 1.82–1.67 (m, 3H), 1.64–1.53 (m, 1H), 1.14 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$/100 MHz): δ 210.3, 139.7, 136.4, 129.0, 128.2, 56.7, 48.2, 45.4, 42.2, 42.0, 30.7, 29.9, 27.8, 25.5, 24.6, 14.3.

9] Compound 13 was prepared according to method A. A solution of 3-nitrobenzaldehyde (76

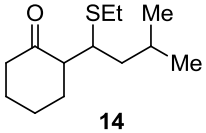


13

mg, 0.5 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol), ethanethiol (93 mg, 1.5 mmol) and cyclohexanone (147 mg, 1.5 mmol) in a solvent mixture of CH_3NO_2:HFIP (4:1) was stirred at 90 °C for 6 h. All volatiles were

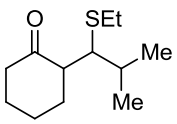
removed under reduce pressure and the crude residue was purified over column chromatography (Silica gel 230–400; ethyl acetate/hexane 12:88) affording compound **13** (98 mg, 67% yield; dr = 1:1.8) as a pale yellow solid. Spectral data for compound **13**: ^{1}H NMR ($CDCl_3$/400MHz): δ 8.21 (t, J = 2.2 Hz, 1H), 8.02 (ddd, J = 1.2, 2.2, 8.1 Hz, 1H), 7.70 (dt, J = 1.2, 7.9 Hz, 1H), 7.43 (t, J = 7.9 Hz, 1H), 4.36 (d, J = 8.1 Hz, 1H), 2.84–2.78 (m, 1H), 2.45–2.40 (m, 2H), 2.36–2.18 (m, 4H), 2.07–1.97 (m, 1H), 1.96–1.86 (m, 1H), 1.70–1.56 (m, 2H), 1.12 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 209.7, 145.3, 142.8, 134.7, 129.0, 122.9, 121.8, 56.3, 48.2, 42.4, 31.4, 27.9, 25.3, 24.9, 14.1; HRMS (ESI): m/z calculated for $C_{15}H_{19}NO_3S$ $[M+H]^+$ 294.1158, found 294.1158.

10] Compound 14 was prepared according to method B. A solution of isovaleraldehyde (43 mg, 0.5 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol) and ethanethiol (93 mg, 1.5 mmol) in a mixture of CH_3NO_2:HFIP (4:1) was stirred at room temperature for 1.5 h. Then to this, cyclohexanone (127 mg, 0.75 mmol) was added and stirring continued for 6 h. All volatiles were removed and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 2:98) affording compound **27** (58 mg, 50% yield; dr = 1:2.2) as a colorless oil. Spectral data for compound **27**: ^{1}H NMR ($CDCl_3$/400MHz): δ 3.21–3.12 (m, 1H), 2.57–2.50 (m, 2H), 2.49–2.42 (m, 1H), 2.40–2.34 (m, 1H), 2.28–2.19 (m, 2H), 2.06–1.70 (m, 5H), 1.67–1.57 (m, 2H), 1.31–1.23 (m, 1H), 1.19 (t, J = 7.5 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 211.3, 55.4, 42.6, 42.1, 41.1, 28.0, 27.2, 25.9, 25.6, 24.9, 23.7, 21.2, 14.9; HRMS (ESI): m/z calculated for $C_{13}H_{24}OS$ $[M+H]^+$ 229.1621, found 229.1597.



14

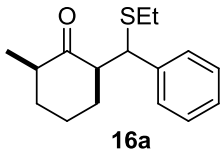
11] Compound 15 was prepared according to method B. A a solution of butyraldehyde (36 mg, 0.5 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol) and ethanethiol (93 mg, 1.5 mmol) in a mixture of CH_3NO_2:HFIP (4:1) was stirred at room temperature for 1.5 h. Then to this, cyclohexanone (147 mg, 1.5 mmol) was added and stirring continued for 4 h. All volatiles were removed under reduced pressure and the crude residue was purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 2:98) affording compound **28** (48 mg, 45% yield; dr = 1:1) as a colorless oil. Spectral data for compound **28**: ^{1}H NMR ($CDCl_3$/400MHz): δ 2.94 (t, J = 6.1 Hz, 1H), 2.68–2.49 (m, 2H), 2.44–2.35 (m, 1H), 2.33–2.15



15

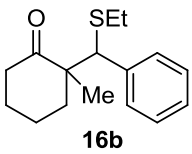
(m, 2H), 2.11–1.90 (m, 2H), 1.88–1.55 (m, 5H), 1.19 (t, *J* = 7.3 Hz, 3H), 0.96 (d, *J* = 5.3 Hz, 3H), 0.92 (d, *J* = 2.9 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 212.2, 55.7, 52.9, 42.5, 30.0, 28.8, 28.0, 25.1, 21.9, 19.0, 14.9; HRMS (ESI): m/z calculated for $C_{12}H_{22}OS$ $[M+H]^+$ 215.1464, found 215.1462.

12] Compound 16a was prepared according to method A. A solution of benzaldehyde (27 mg, 0.25 mmol), triflic acid (44 μL, 0.5 mmol), ethanethiol (47 mg, 0.75 mmol) and 2-methylcyclohexanone (84 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at -40 °C for 18 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **16a** (45.8 mg, 70% yield, dr =1:1:5:12) as a colorless oil. Spectral data for compound **16a**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.33–7.29 (m, 5H), 4.17 (d, *J* = 11.5 Hz, 1H), 2.81–2.76 (m, 1H), 2.74–2.68 (m, 1H), 2.20–2.14 (m, 2H), 2.06–2.00 (m, 1H), 1.87–1.75 (m, 2H), 1.63–1.49 (m, 2H), 1.41–1.30 (m, 1H), 1.09 (d, *J* = 6.5 Hz, 3H), 1.06 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 213.4, 140.2, 128.5, 128.3, 127.4, 55.8, 48.3, 42.0, 36.5, 30.6, 24.8, 20.5, 14.9, 14.1; HRMS (ESI): m/z calculated for $C_{16}H_{22}OS$ $[M+H]^+$ 263.1464, found 263.1478.



16a

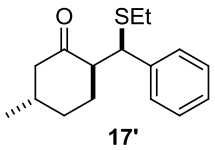
13] Compound 16b was prepared according to method A. A solution of benzaldehyde (53 mg, 0.5 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol), ethanethiol (93 mg, 1.5 mmol) and 2-methylcyclohexanone (168 mg, 1.5 mmol) in a mixture of CH_3NO_2:HFIP (4:1) was stirred at 40 °C for 18 h. All volatiles were removed under reduced pressure and the crude residue was purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 2:98) affording compound **16a** (44 mg, 34% yield, dr = 0:1:2:31) as a colorless oil and **16b** (32 mg, 24% yield) as a colorless oil. Spectral data for compound **16b**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.43 (br d, *J* = 7.3 Hz, 2H), 7.31–7.22 (m, 3H), 4.43 (s, 1H), 2.72–2.64 (m, 1H), 2.42–2.37 (m, 1H), 2.17 (dq, *J* = 2.0, 7.4 Hz, 2H), 2.10–1.97 (m, 2H), 1.70–1.59 (m, 3H), 1.30–1.22 (m, 1H), 1.07 (t, *J* = 7.4 Hz, 3H), 1.00 (s, 3H); ^{13}C NMR



16b

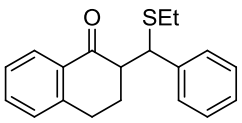
($CDCl_3$/100MHz): δ 213.2, 137.8, 130.2, 127.9, 127.4, 53.4, 52.4, 38.7, 38.4, 28.0, 25.4, 21.1, 18.9, 14.1; HRMS (ESI): m/z calculated for $C_{16}H_{22}OS$ $[M+H]^+$ 263.1464, found 263.1481.

14] Compound 17 was prepared according to method A. A solution of benzaldehyde (53 mg, 0.5 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol), ethanethiol (93 mg, 1.5 mmol) and 3-methylcyclohexanone (168 mg, 1.5 mmol) in a solvent of CH_3NO_2:HFIP (4:1) was stirred at room temperature for 20 h. All volatiles were removed and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 3:97) affording compound **17** (77 mg, 59% yield) as a colorless oil. Other diastereoisomers were isolated as inseparable mixture (24 mg, 18% yield) as colorless oil. Spectral data for compound **15** (major isomer): ^{1}H NMR ($CDCl_3$/400MHz): δ 7.37–7.31 (m, 2H), 7.27–7.23 (m, 2H), 7.17 (ddt, J = 1.3, 2.0, 7.3 Hz, 1H), 4.37 (d, J = 6.8 Hz, 1H), 2.71 (ddd, J = 5.6, 6.8, 12.7 Hz, 1H), 2.42–2.29 (m, 2H), 2.28–2.19 (m, 2H), 1.95–1.90 (m, 1H), 1.91–1.81 (m, 2H), 1.59 (dq, J = 3.4, 13.0 Hz, 1H), 1.35–1.24 (m, 1H), 1.11 (t, J = 7.5 Hz, 3H), 0.97 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 209.4, 142.8, 128.3, 128.1, 126.7, 55.8, 50.5, 48.2, 35.4, 33.8, 29.6, 25.3, 22.2, 14.2; HRMS (ESI): m/z calculated for $C_{16}H_{22}OS$ $[M+H]^+$ 263.1464, found 263.1480.



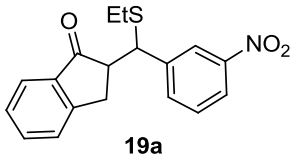
17'

15] Compound 18 was prepared according to method A. A solution of benzaldehyde (53 mg, 0.5 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol), ethanethiol (93 mg, 1.5 mmol) and α`-tetralone (88 mg, 0.6 mmol) in a mixture of CH_3NO_2:HFIP (4:1) was stirred at 60 °C for 5 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 2:98) affording compound **18** (97 mg, 66% yield; dr = 1.1:1) as a pale yellow thick oil. Spectral data for compound **18**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.98 (dd, J = 1.1, 7.4 Hz, 1H), 7.50–7.14 (m, 8H), 4.92 (d, J = 4.9 Hz, 1H), 3.00–2.91 (m, 2H), 2.85–2.77 (m, 1H), 2.42–2.28 (m, 2H), 2.22–2.16 (m, 1H), 1.71 (ddt, J = 7.7, 12.6, 15.3 Hz, 1H), 1.14 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 196.8, 143.6, 141.8, 133.3, 132.3, 129.5, 128.6, 128.5, 128.3, 128.0, 127.8, 127.1, 126.7, 53.4, 47.1, 28.6, 25.5, 25.1, 14.2; HRMS (ESI): m/z calculated for $C_{19}H_{20}OS$ $[M+H]^+$ 297.1308, found 297.1275.



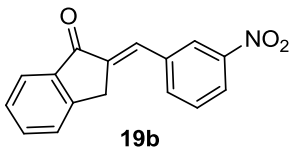
18

16] Compound 19a and **19b** were prepared according to method A. A solution of 3-nitrobenzaldehyde (113 mg, 0.75 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 0.75 mmol) and 1-indanone (33 mg, 0.25 mmol) in 2,2,2-trifluoroethanol was stirred at 60 °C for 16 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; ethyl acetate/hexane 10:90) affording compound **19a** (35.2 mg, 43% yield; dr = 1:1.6) as a brown oil and compound **19b** (12.7 mg, 19% yield) as a yellow solid.



19a

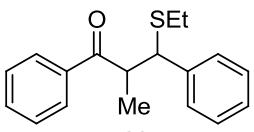
Spectral data for compound **19a**: ^{1}H NMR ($CDCl_3$/400MHz): δ 8.38 (t, J = 2.1 Hz, 1H), 8.12 (ddd, J = 1.0, 2.1, 8.1 Hz, 1H), 7.82 (dt, J = 1.5, 7.8 Hz, 1H), 7.75 (br d, J = 7.8 Hz, 1H), 7.47–7.59 (m, 3H), 7.23–7.36 (m, 1H), 4.65 (d, J = 4.0 Hz, 1H), 3.41 (dd, J = 4.4, 16.8 Hz, 1H), 3.25–3.32 (m, 1H), 3.16 (dd, J = 8.0, 16.8 Hz, 1H), 2.35 (q, J = 7.4 Hz, 2H), 1.11 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 204.4, 153.3, 144.7, 140.4, 135.7, 135.2, 134.1, 129.5, 127.6, 126.5, 124.2, 122.8, 122.3, 53.2, 49.5, 29.4, 26.0, 14.3; HRMS (ESI): m/z calculated for $C_{18}H_{17}NO_3S$ $[M+H]^+$ 328.1002, found 328.0999.



19b

Spectral data for compound **19b**: ^{1}H NMR ($CDCl_3$/400MHz): δ 8.54 (t, J = 1.8 Hz, 1H), 8.25 (ddd, J = 0.9, 2.2, 8.3 Hz, 1H), 7.94 (t, J = 7.4 Hz, 2H), 7.69–7.6 (m, 4H), 7.46 (t, J = 7.3 Hz, 1H), 4.12 (s, 1H), 4.11 (s, 1H),; ^{13}C NMR ($CDCl_3$/100MHz): δ 193.7, 149.3, 148.7, 137.6, 137.5, 137.1, 136.5, 135.2, 130.8, 130.0, 128.0, 126.3, 124.7, 124.3, 123.9, 32.2; HRMS (ESI): m/z calculated for $C_{18}H_{17}NO_3S$ $[M+H]^+$ 328.1002, found 328.0999.

17] Compound 20 was prepared according to method A. A solution of benzaldehyde (53 mg, 0.5 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol), ethanethiol (93 mg, 1.5 mmol) and propiophenone (168 mg, 1.5 mmol) in a mixture of CH_3NO_2:HFIP (4:1) was stirred at 60 °C for 8 h. all volatiles were removed under reduced pressure and the crude residue was purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **20** (102 mg, 72% yield; dr = 1:2.7) as a pale yellow oil. Spectral data for compound **20**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.74–7.71 (m, 1H), 7.58–7.43 (m, 2H), 7.38–7.23 (m, 6H), 7.17–7.13 (m, 1H), 4.16 (d, J = 10.7 Hz, 1H), 3.92 (dq, J

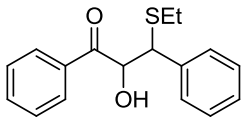


20

= 6.9, 10.7 Hz, 1H), 2.34–2.16 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 202.8, 140.9, 133.1, 128.6, 128.5, 128.4, 128.1, 128.0, 127.2, 51.8, 45.9, 25.9, 17.5, 14.1; HRMS (ESI): m/z calculated for $C_{18}H_{20}OS$ $[M+H]^+$ 285.1308, found 285.1307.

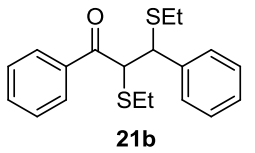
18] Compound 21a and **21b** were prepared according to method A. A solution of benzaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 0.75 mmol) and 2-hydroxyacetophenone (74 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at 50 °C for 16 h. All volatiles were removed and the crude residue purified over column chromatography (Silica gel 230–400; ethyl acetate/hexane 5:95) affording compound **21a** (36 mg, 50% yield; dr = 2.8:1) and compound **21b** (15.7 mg, 19% yield; dr = 1.8:1) as thick oil.

Spectral data for compound **21a**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.83–7.81 (m, 2H), 7.66–7.61 (m, 1H), 7.52–7.48 (m, 2H), 7.20–7.15 (m, 3H), 7.09–7.07 (m, 2H), 5.46 (d, *J* = 3.2 Hz, 1H), 4.28 (d, *J* = 3.2 Hz, 1H), 2.41–2.33 (m, 2H), 1.14 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 199.5, 140.3, 134.0, 128.9, 128.7, 128.6, 127.7, 76.6, 53.8, 25.3, 14.3; HRMS (ESI): m/z calculated for $C_{17}H_{18}O_2S$ $[M-(H_2O)+H]^+$ 269.0995, found 269.1002.



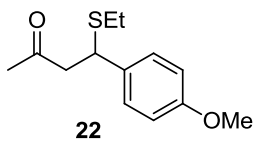
21a

Spectral data for compound **21b**: ^{1}H NMR ($CDCl_3$/400MHz): δ 8.08–8.03 (m, 2H), 7.61–7.56 (m, 1H), 7.53–7.48 (m, 2H), 7.44–7.40 (m, 3H), 7.39–7.36 (m, 1H), 7.33–7.29 (m, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.40 (d, *J* = 11.8 Hz, 1H), 2.42–2.31 (m, 2H), 2.30–2.17 (m, 2H), 1.07 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 193.9, 140.4, 136.6, 133.2, 128.7, 128.6, 128.5, 128.4, 127.6, 52.0, 49.1, 26.9, 23.9, 14.3, 13.7; HRMS (ESI): m/z calculated for $C_{19}H_{22}OS_2$ $[M+Na]^+$ 353.1014, found 353.1004.



21b

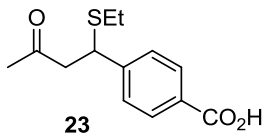
19] Compound 22 was prepared according to method A. A solution of anisaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 0.75 mmol) and acetone (55 μL, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 16 h. All volatiles were removed under



22

reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; ethyl acetate /hexane 8:92) affording compound **22** (39.2 mg, 66% yield) as a thick oil. Spectral data for compound **22**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.25 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.6 Hz, 2H), 4.3 (t, J = 7.3 Hz, 1H), 3.76 (s, 3H), 2.93 (d, J = 7.3 Hz, 2H), 2.36–2.22 (m, 2H), 2.07 (s, 3H), 1.14 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 205.8, 158.7, 133.8, 128.8, 113.9, 55.3, 50.3, 43.3, 30.8, 25.2, 14.3; HRMS (ESI): m/z calculated for $C_{13}H_{18}O_2S$ $[M+Na]^+$ 261.0920, found 261.0922.

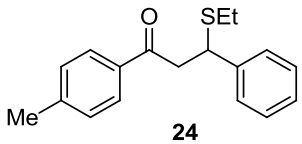
20] Compound 23 was prepared according to method A. A solution of 4-carboxybenzaldehyde



23

(75 mg, 0.5 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol), ethanethiol (93 mg, 1.5 mmol) and acetone (87 mg, 1.5 mmol) in a mixture of CH_3NO_2:HFIP (4:1) was stirred at 70 °C for 7 h. All volatiles were removed under reduced pressure and the crude residue was purified over column chromatography (Silica gel 230–400; acetone/hexane 30:70) affording compound **23** (66 mg, 52% yield) as an off-white solid. m.p = 82 ^{0}C. Spectral data for compound **23**: ^{1}H NMR ($CDCl_3$/400MHz): δ 8.02 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 4.37 (t, J = 7.3 Hz, 1H), 2.97 (d, J = 7.3 Hz, 1H), 2.35–2.21 (m, 2H), 2.08 (s, 3H), 1.12 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 205.0, 171.6, 148.4, 130.5, 128.2, 127.9, 49.6, 43.6, 30.6, 25.3, 14.2; HRMS (ESI): m/z calculated for $C_{13}H_{16}O_3S$ [M+H]+ 253.0893, found 253.0910.

21] Compound 24 was prepared according to method A. A solution of benzaldehyde (27 mg,

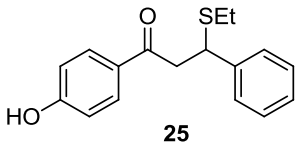


24

0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.025 mmol), ethanethiol (47 mg, 0.75 mmol) and 4-methylacetophenone (101 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 18 h. All volatiles were removed under reduced pressure and the crude residue was purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **24** (52.6 mg, 74% yield) as a white solid. m.p = 94 ^{0}C. Spectral data for compound **24**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.80–7.77 (m, 2H), 7.39 (br d, J = 7.7 Hz, 2H), 7.29–7.16 (m, 5H), 4.56 (t, J = 7.1 Hz, 1H), 3.48 (d, J = 7.1 Hz, 2H), 2.63 (s, 3H), 2.33 (q, J = 7.4 Hz, 2H), 1.14 (t, J = 7.4 Hz,

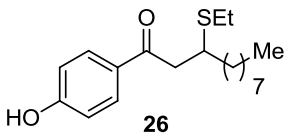
3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 196.5, 144.0, 142.3, 134.3, 129.2, 128.4, 128.2, 127.8, 127.1, 45.1, 44.0, 25.4, 21.6, 14.3; HRMS (ESI): m/z calculated for $C_{18}H_{20}OS$ $[M+H]^+$ 285.1229, found 285.1276.

22] Compound 25 was prepared according to method A. A solution of benzaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 0.75 mmol) and 4′-hydroxyacetophenone (102 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 16 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; ethyl acetate/hexane 15:85) affording compound **25** (61.5 mg, 86% yield) as a colorless crystal. m.p = 105 ^{0}C. Spectral data for compound **25**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.84 (d, J = 8.7 Hz, 1H), 7.4 (d, J = 7.3, 3H), 7.29 (t, J = 7.4, 2H), 7.2 (t, J = 7.3, 1H), 6.85 (d, J = 8.8, 2H), 4.55 (t, J = 7.1 Hz, 1H), 3.49 (d, J = 7.1 Hz, 2H), 2.41–2.27 (m, 2H), 1.15 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 196.3, 161.2, 142.1, 131.0, 129.4, 128.6, 127.8, 127.3, 115.6, 44.9, 44.4, 25.5, 14.3; HRMS (ESI): m/z calculated for $C_{17}H_{18}O_2S$ $[M+H]^+$ 311.1100, found 311.1107.



25

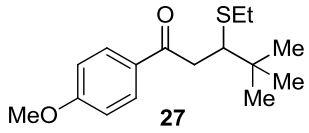
23] Compound 26 was prepared according to method B. A solution of nonylaldehyde (142 mg, 1 mmol), $Cu(OTf)_2$ (9 mg, 0.025 mmol) and ethanethiol (186 mg, 3 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 30 min. Then to this, 4-hydroxyacetophenone (68 mg, 0.5 mmol) was added and stirring continued at 60 °C for 48 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 4:96) affording compound **26** (64 mg, 40% yield) as a pale yellow oil. Spectral data of compound **26**: ^{1}H NMR ($CDCl_3$/400 MHz): δ 7.87 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 3.32–3.26 (m, 1H), 3.22 (dd, J = 6.5, 16.2 Hz, 1H), 3.08 (dd, J = 7.0, 16.2 Hz, 1H), 2.52 (q, J = 7.4 Hz, 2H), 1.61–1.53 (m, 2H), 1.22 (br s, 12H), 1.19 (t, J = 7.4 Hz, 3H), 0.83 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$/100 MHz): δ 198.2, 160.9, 130.8, 115.5, 44.5, 41.1, 35.4, 31.8, 29.4,



26

29.2, 25.0, 22.6, 14.7, 14.0; HRMS (ESI): m/z calcd for $C_{19}H_{30}O_2S$ [M+H]+ 323.2049, found 323.2039.

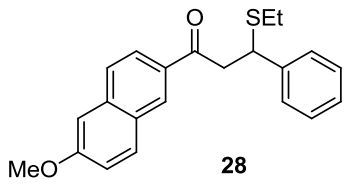
24] Compound 27 was prepared according to method B. A solution of trimethylacetaldehyde



27

(21.5 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol) and ethanethiol (47 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 3 h. Then to this, 4′-methoxyacetophenone (112.5 mg, 0.75 mmol) was added and stirring continued at 60 °C for 16 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; diethyl ether/hexane 5:95) affording compound **27** (17.5 mg, 25% yield) as a thick oil. Spectral data for compound **27**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.96 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 3.87 (s, 3H), 3.33–3.26 (m, 1H), 3.19–3.12 (m, 2H), 2.56 (q, J = 7.4 Hz, 2H), 1.16 (t, J = 7.4 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$/100MHz): δ 197.6, 163.4, 130.6, 130.5, 129.9, 113.7, 55.5, 52.8, 41.7, 35.5, 28.6, 27.7, 14.8; HRMS (ESI): m/z calculated for $C_{16}H_{24}O_2S$ $[M+H]^+$ 281.1569, found 281.1563.

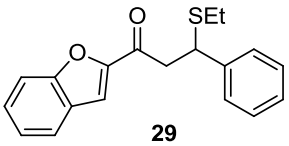
14] Compound 28 was prepared according to method A. A solution of benzaldehyde (27 mg,



28

0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 0.75 mmol) and 1-(6-methoxy-2-naphthyl)ethanone (150 mg, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 16 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; ethyl acetate/hexane 4:96) affording compound **28** (36 mg, 85% yield) as a white solid. m.p = 113 ^{0}C. Spectral data for compound **28**: ^{1}H NMR ($CDCl_3$/400MHz): δ 8.36 (s, 1H), 7.96 (dd, J = 1.6, 8.8 Hz, 1H), 7.83 (d, J = 9.0 Hz, 1H), 7.73 (d, J = 8.7 Hz, 1H), 7.46 (d, J = 7.4 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.24–7.18 (m, 2H), 7.13 (d, J = 2.1 Hz, 1H), 4.65 (t, J = 7.1 Hz, 1H), 3.93 (s, 3H), 3.64 (d, J = 7.1 Hz, 2H), 2.45–2.31 (m, 2H), 1.19 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 196.6, 159.8, 142.4, 137.4, 132.3, 131.2, 129.8, 128.5, 127.9, 127.8, 127.20, 127.17, 124.6, 119.8, 105.7, 55.4, 45.3, 44.3, 25.5, 14.4; HRMS (ESI): m/z calculated for $C_{22}H_{22}O_2S$ $[M+H]^+$ 351.1413, found 351.1417.

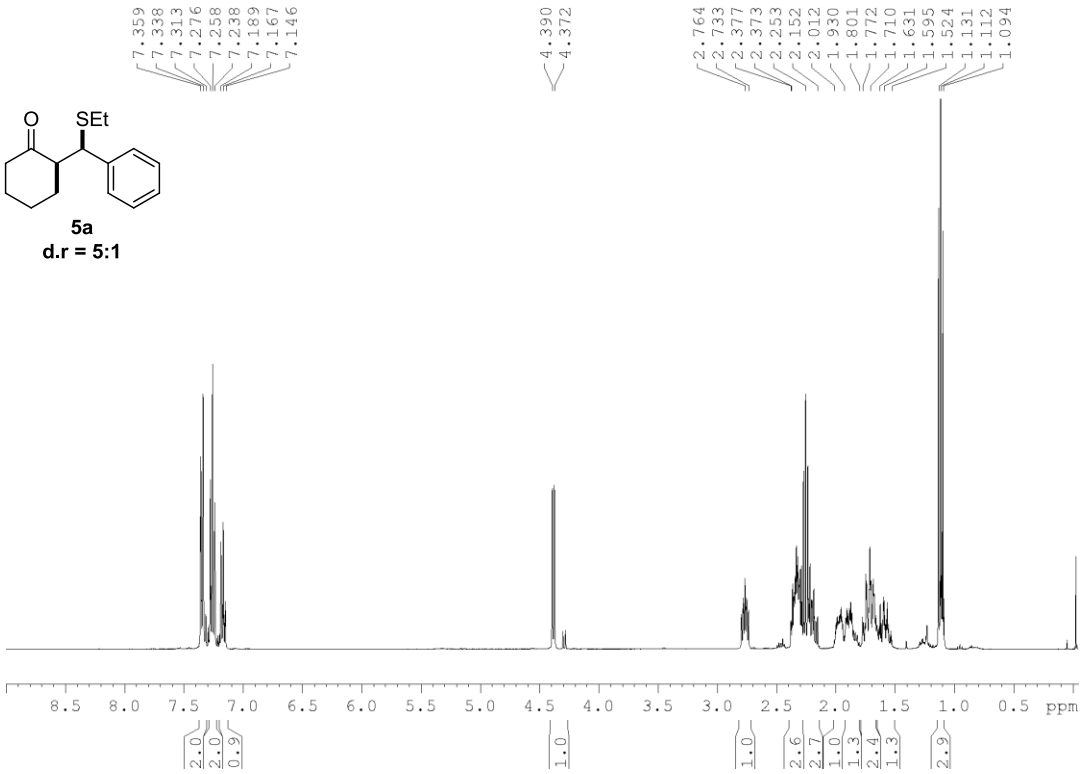
21] Compound 29 was prepared according to method A. A solution of benzaldehyde (27 mg, 0.25 mmol), $Cu(OTf)_2$ (4.5 mg, 0.0125 mmol), ethanethiol (47 mg, 0.75 mmol) and 1-(benzofuran-2-yl)ethanone (55 μL, 0.75 mmol) in 2,2,2-trifluoroethanol was stirred at room temperature for 16 h. All volatiles were removed under reduced pressure and the crude residue purified over column chromatography (Silica gel 230–400; ethyl acetate/hexane 4:96) affording compound **29** (39.2 mg, 66% yield) as a thick oil. Spectral data for compound **29**: ^{1}H NMR ($CDCl_3$/400MHz): δ 7.69 (d, J = 7.9 Hz, 1H), 7.56 (d, J = 8.6 Hz, 1H), 7.49 (s, 1H), 7.48–7.42 (m, 3H), 7.33–7.28 (m, 3H), 7.24–7.19 (m, 1H), 4.59 (t, J = 7.3 Hz, 1H), 3.54 (dd, J = 7.1, 16.3 Hz, 1H), 3.49 (d, J = 7.6, 16.3 Hz, 1H), 2.44–2.31 (m, 2H), 1.17 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$/100MHz): δ 188.1, 155.7, 152.5, 141.8, 128.6, 128.4, 127.8, 127.4, 127.0, 124.0, 123.4, 113.3, 112.5, 45.6, 44.1, 25.5, 14.3; HRMS (ESI): m/z calculated for $C_{19}H_{18}O_2S$ $[M+H]^+$ 311.1100, found 311.1107.



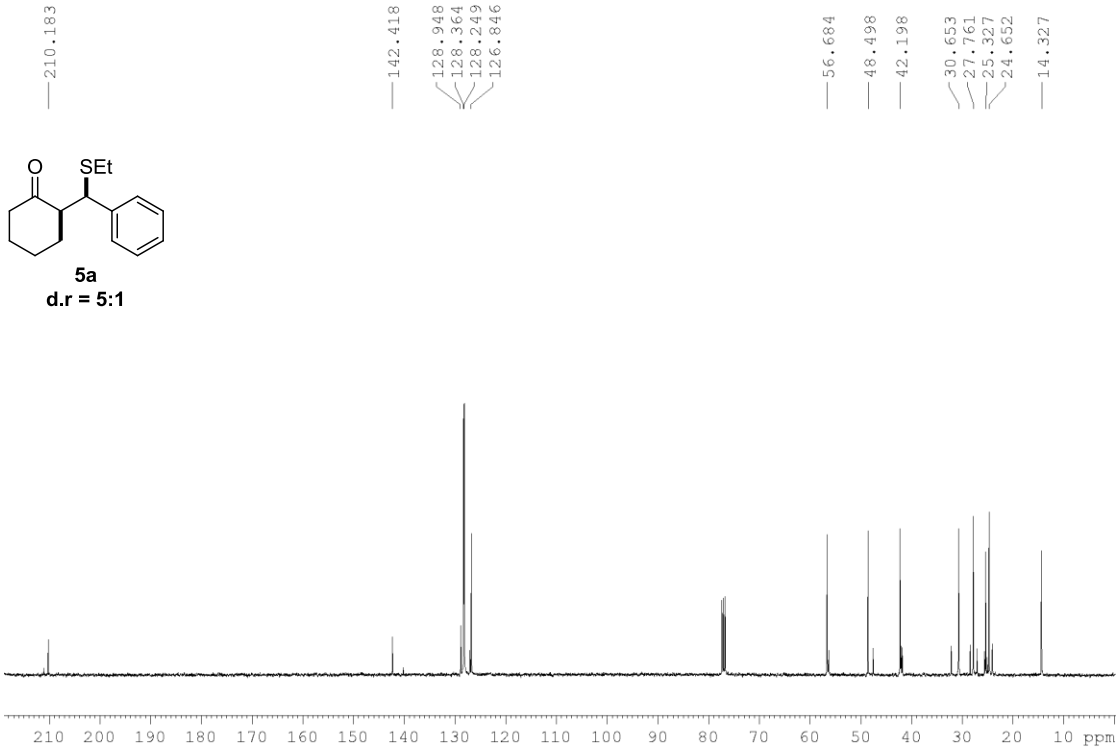
29

E] ^{1}H and ^{13}C NMR spectra for compounds 5 – 30:

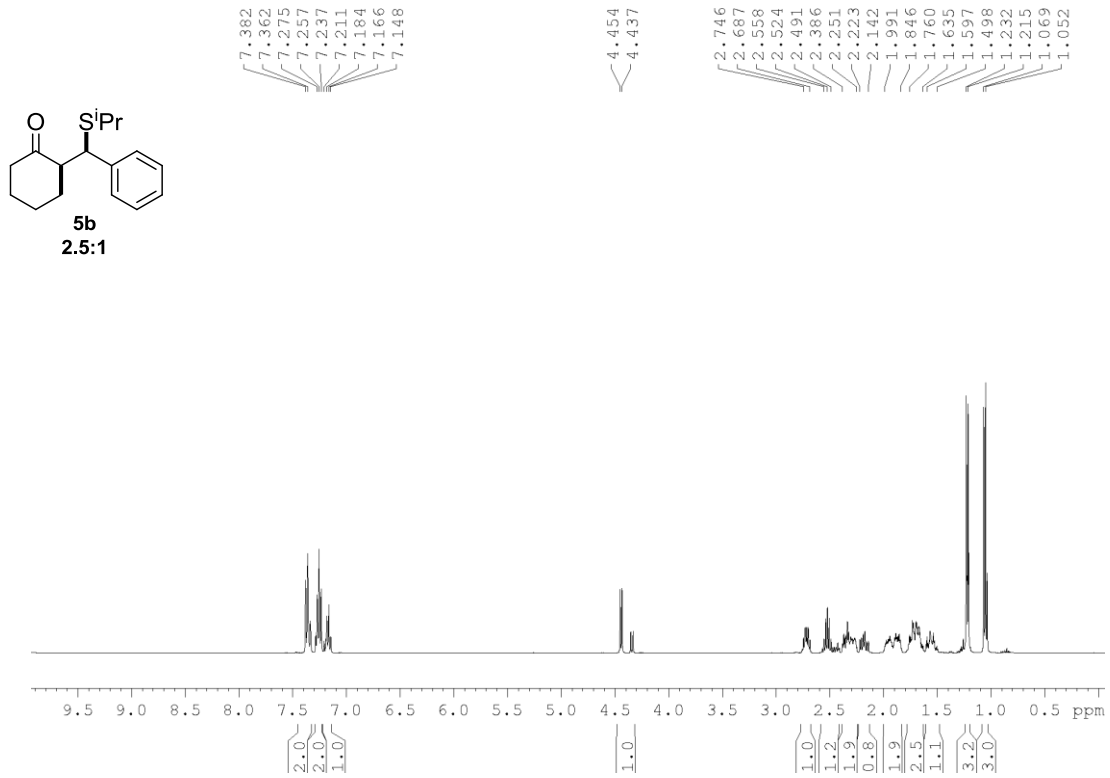
^{1}H - NMR spectrum of compound **5a** ($CDCl_3$, 400 MHz):



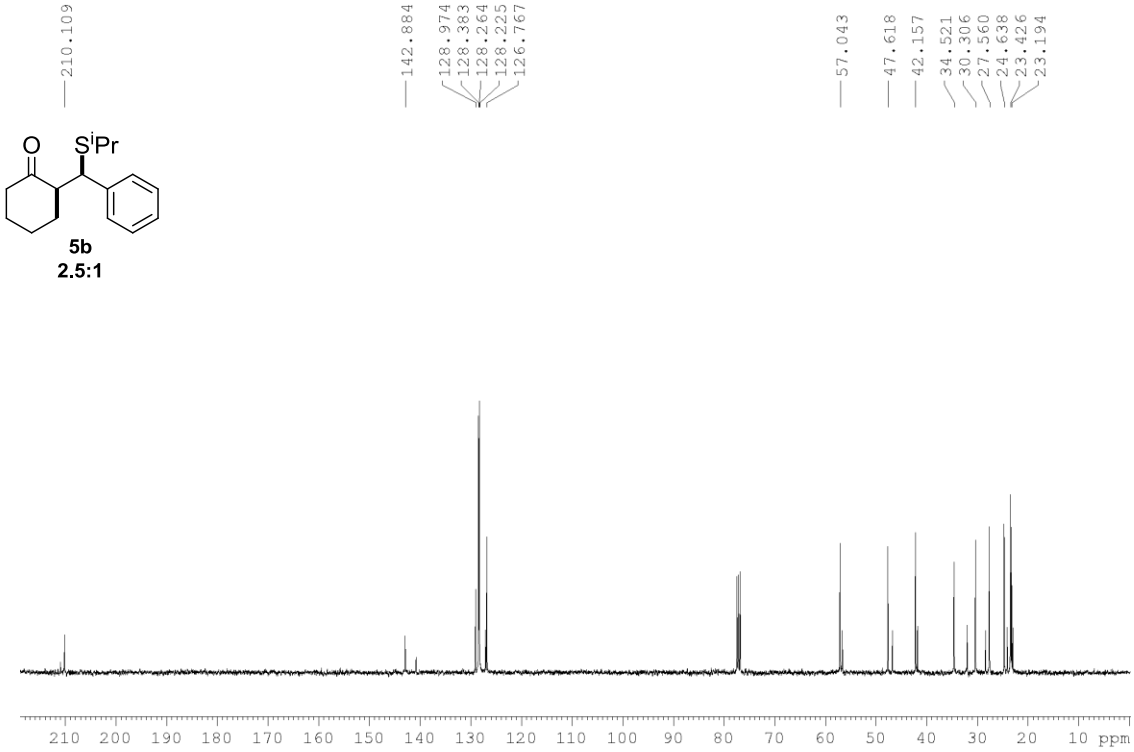
^{13}C - NMR spectrum of compound **5a** ($CDCl_3$, 400 MHz):



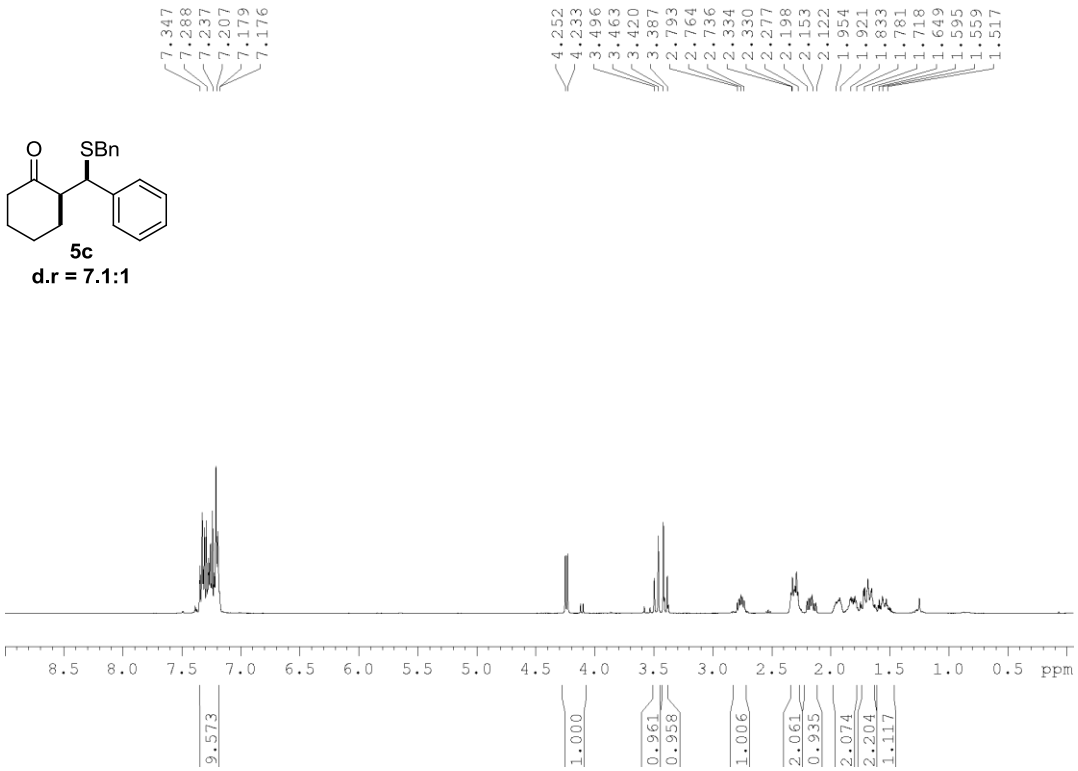
^{1}H - NMR spectrum of compound **5b** ($CDCl_3$, 400 MHz):



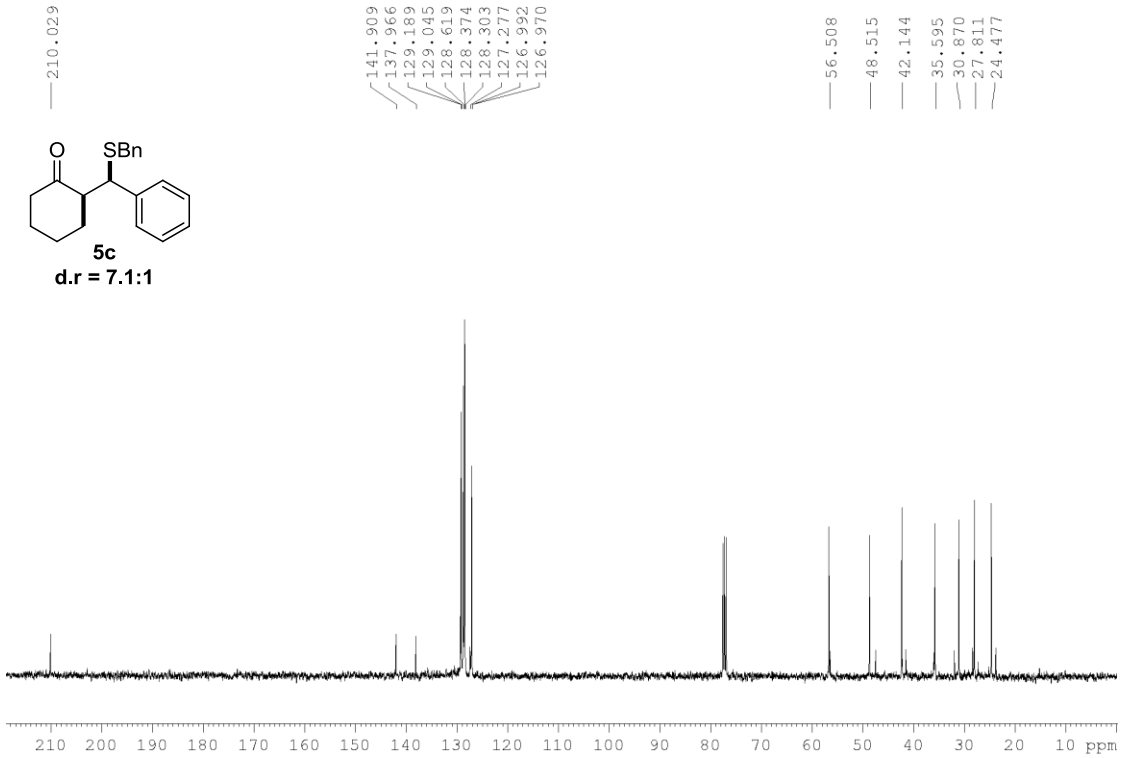
^{13}C - NMR spectrum of compound **5b** ($CDCl_3$, 400 MHz):



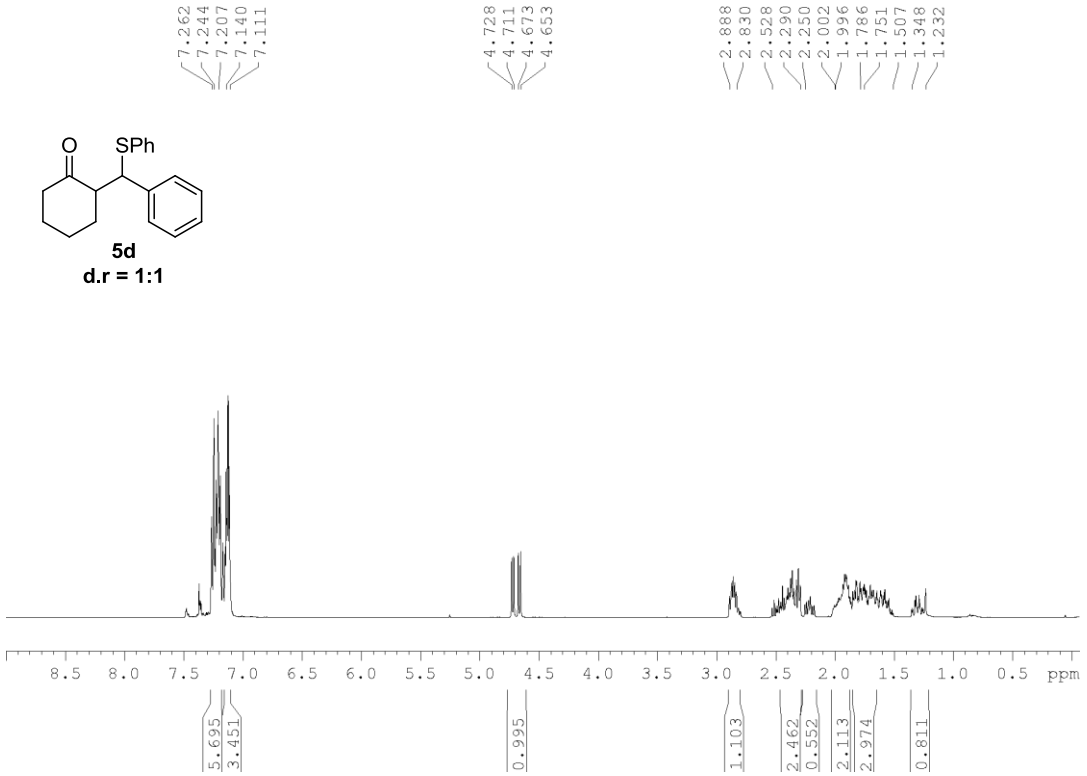
^{1}H - NMR spectrum of compound **5c** ($CDCl_3$, 400 MHz):



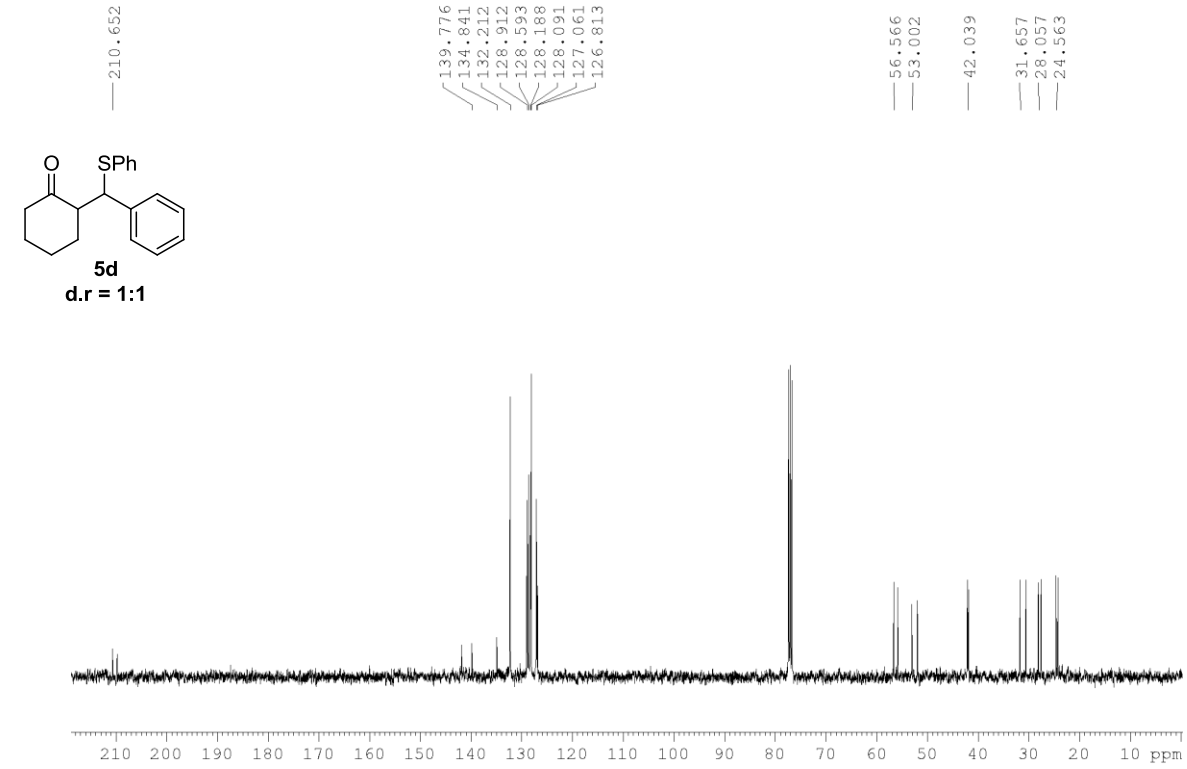
^{13}C - NMR spectrum of compound **5c** ($CDCl_3$, 400 MHz):



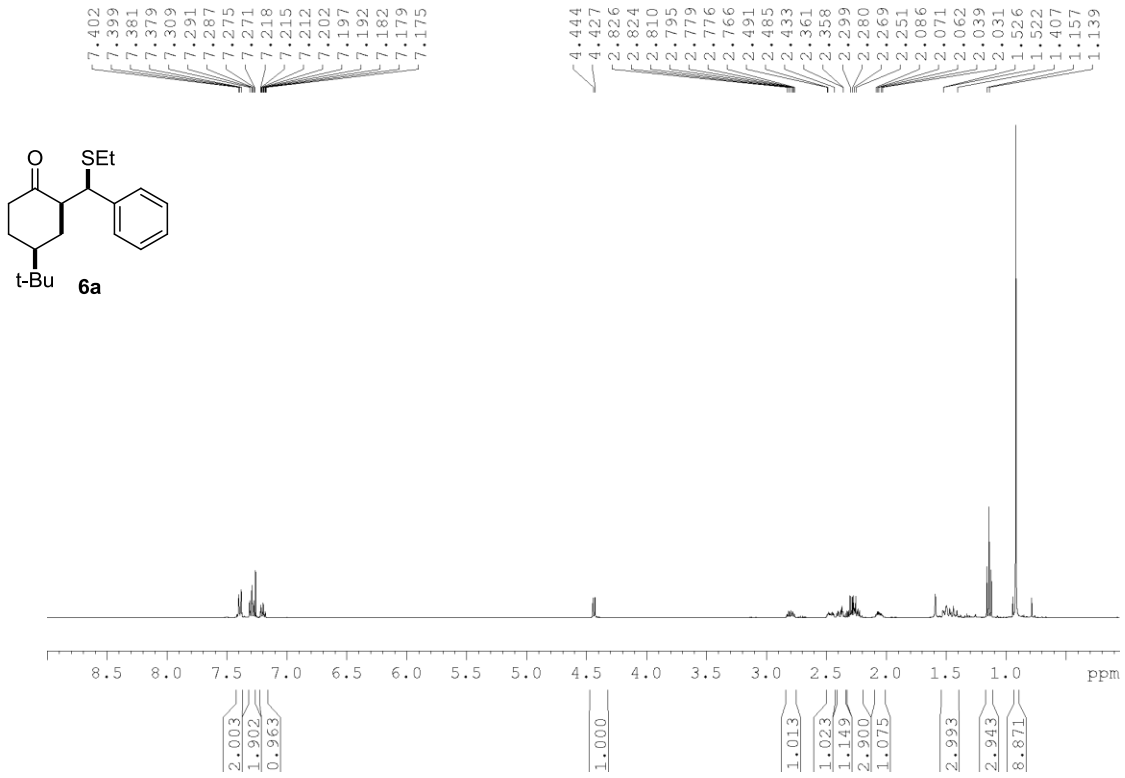
^{1}H - NMR spectrum of compound **5d** ($CDCl_3$, 400 MHz):



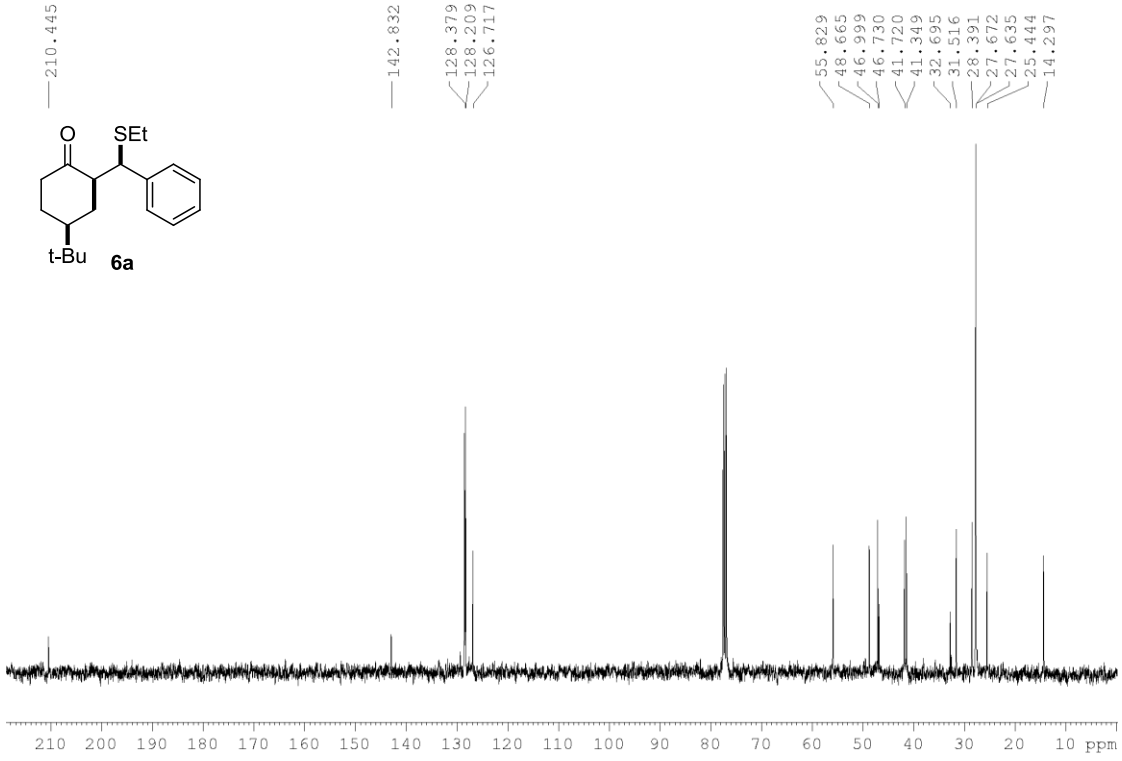
^{13}C - NMR spectrum of compound **5d** ($CDCl_3$, 400 MHz):



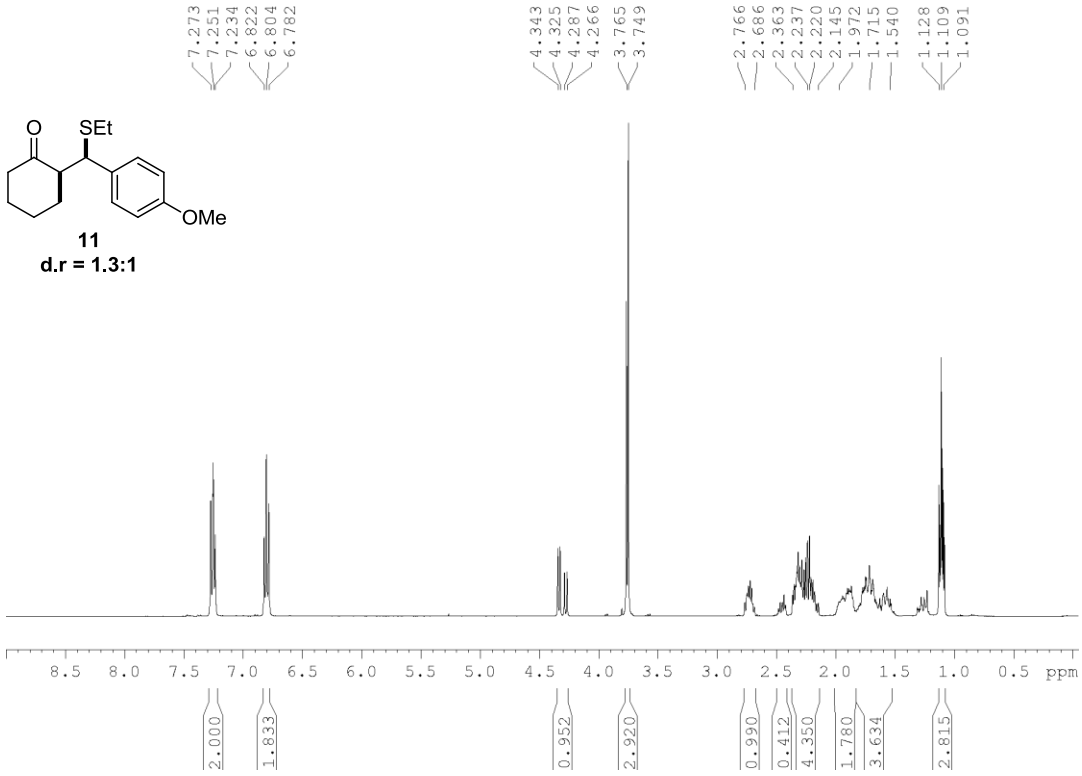
^{1}H - NMR spectrum of compound **6a** ($CDCl_3$, 400 MHz):



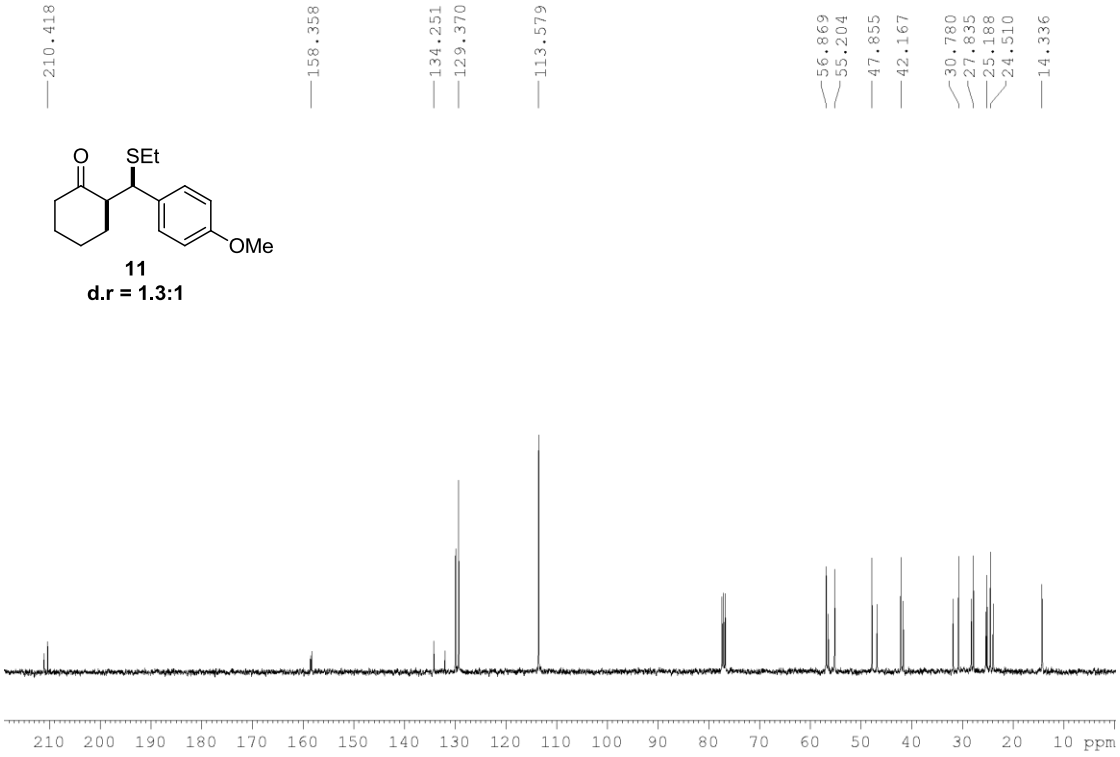
^{13}C - NMR spectrum of compound **6a** ($CDCl_3$, 400 MHz):



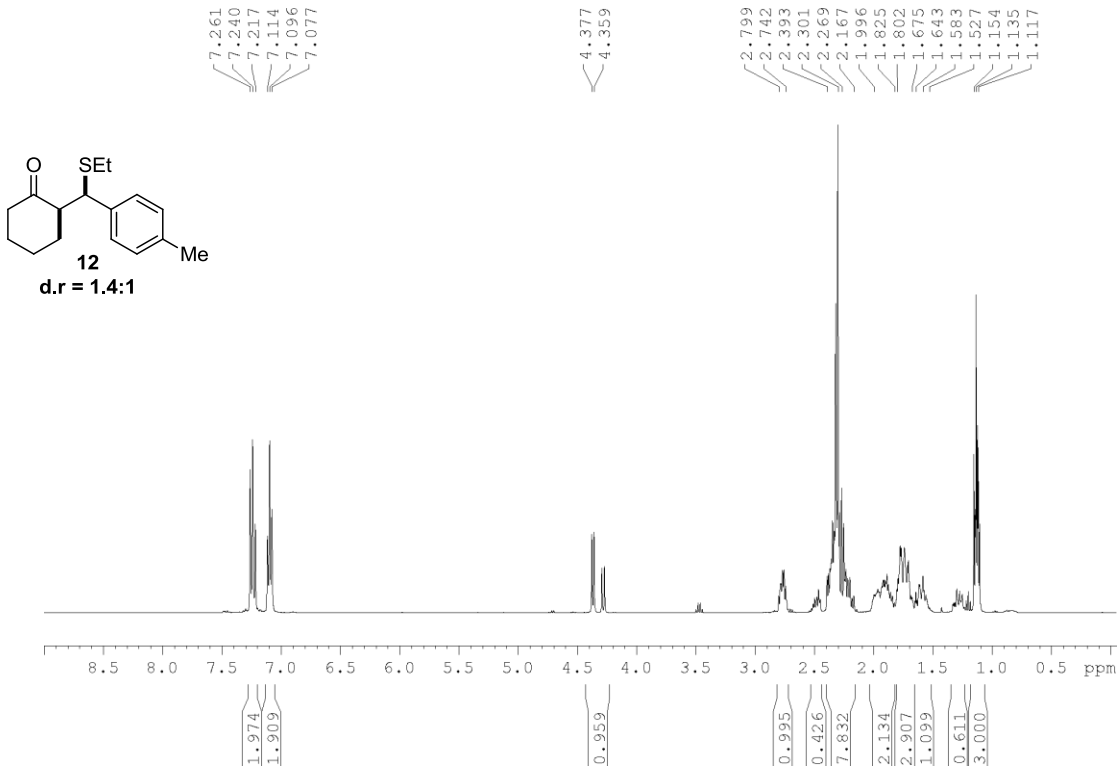
^{1}H - NMR spectrum of compound **11** ($CDCl_3$, 400 MHz):



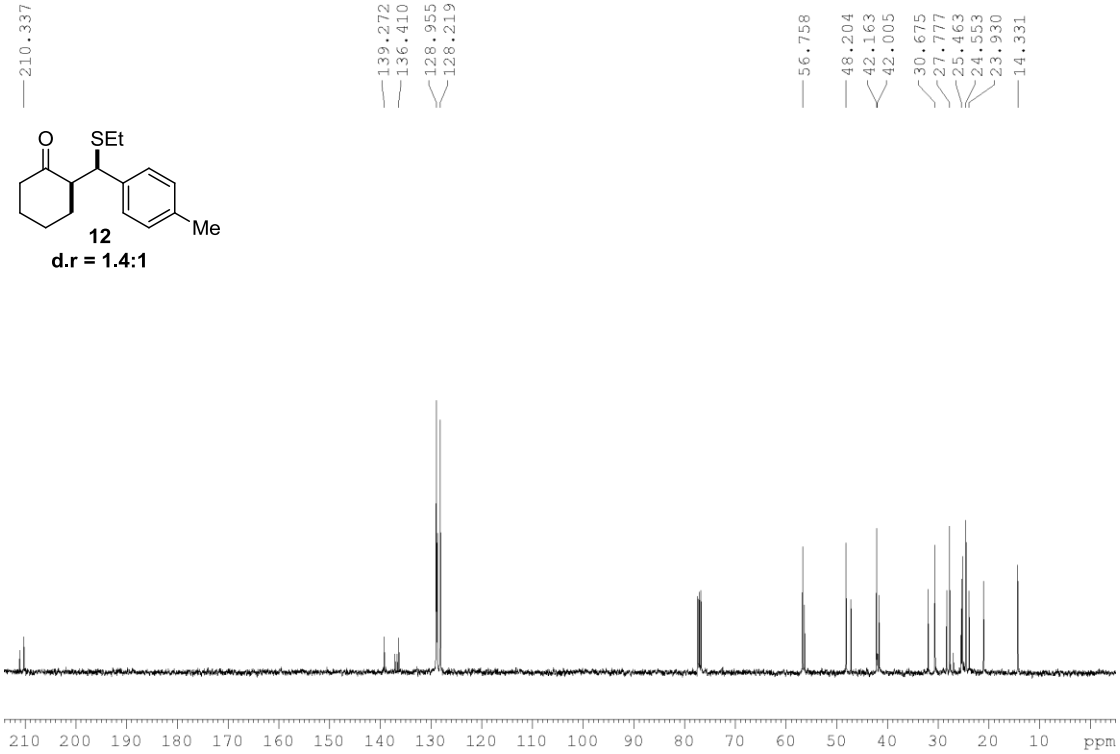
^{13}C - NMR spectrum of compound **11** ($CDCl_3$, 400 MHz):



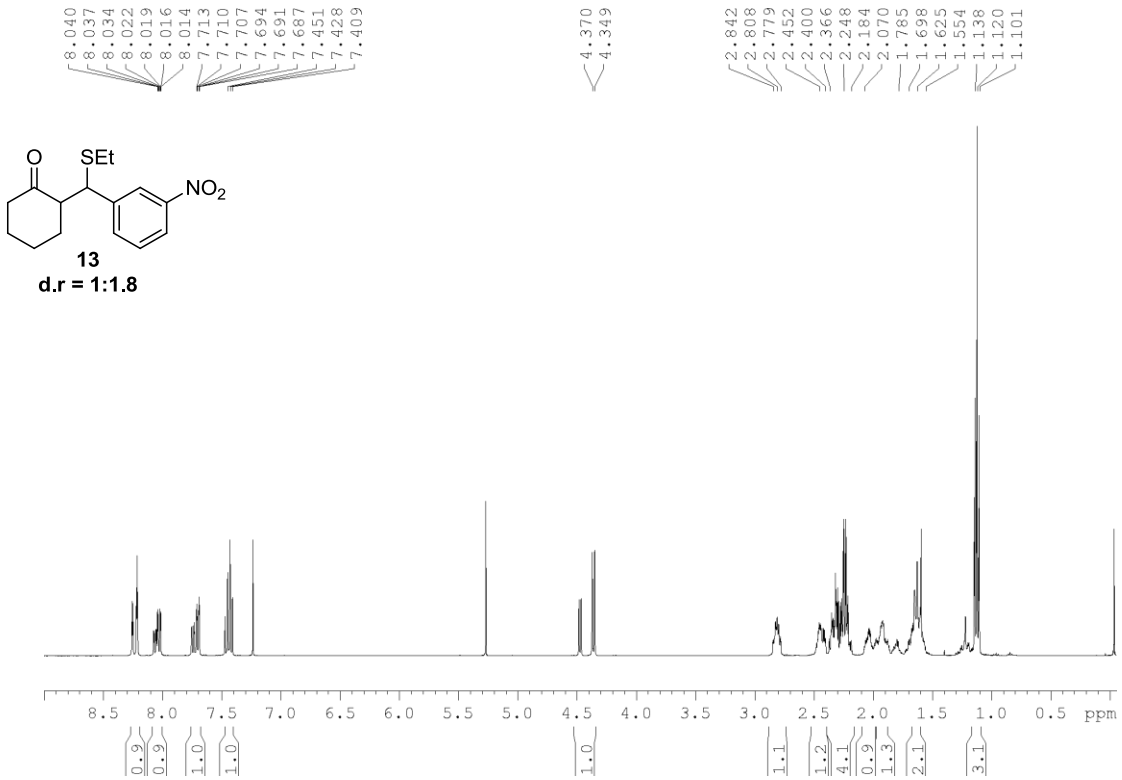
^{1}H - NMR spectrum of compound **12** ($CDCl_3$, 400 MHz):



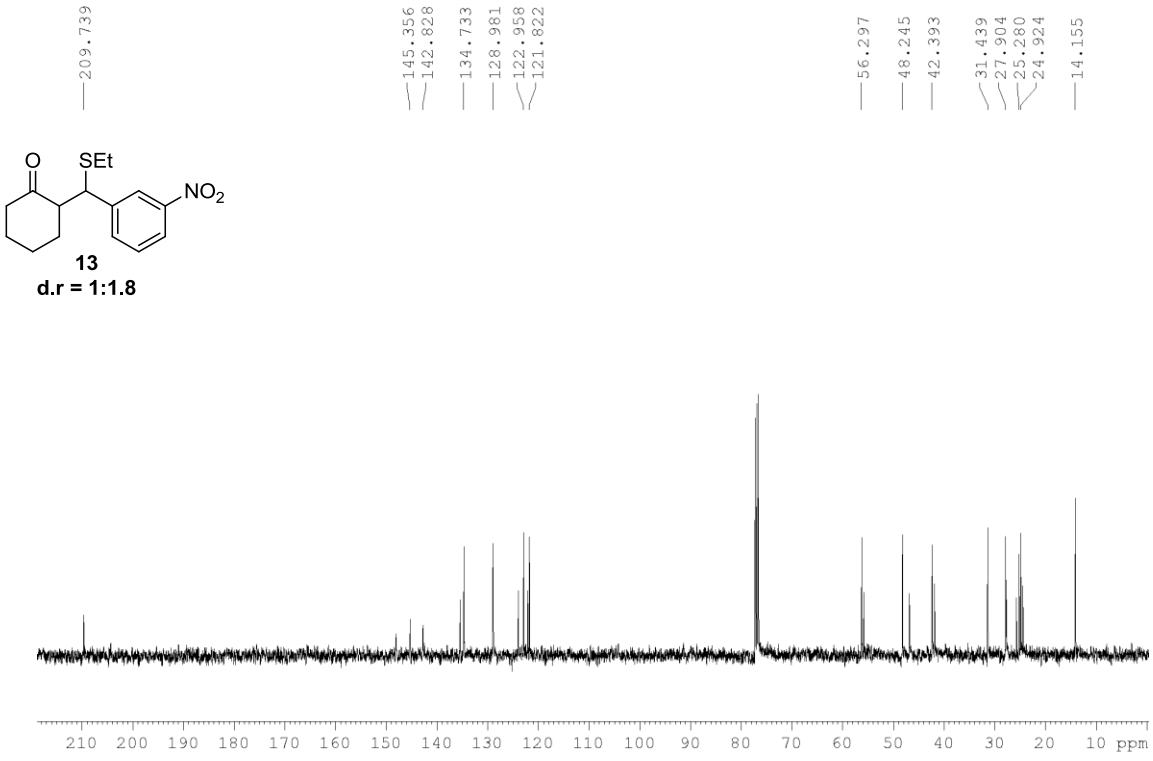
^{13}C - NMR spectrum of compound **12** ($CDCl_3$, 400 MHz):



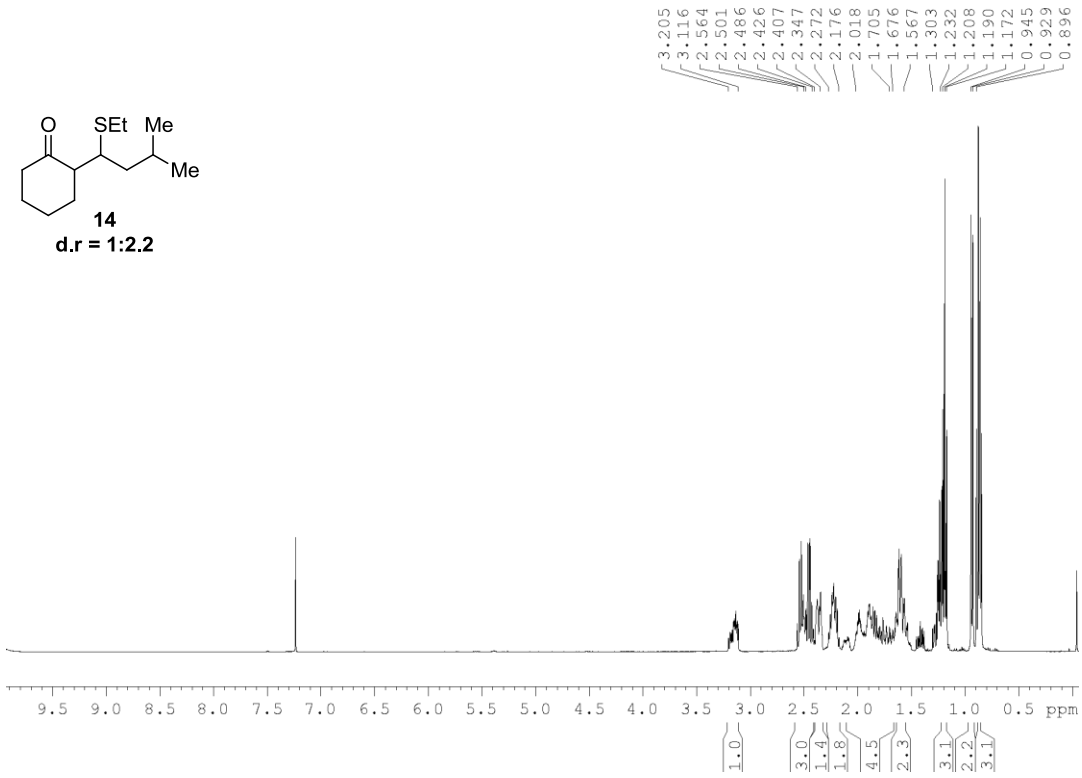
^{1}H - NMR spectrum of compound **13** ($CDCl_3$, 400 MHz):



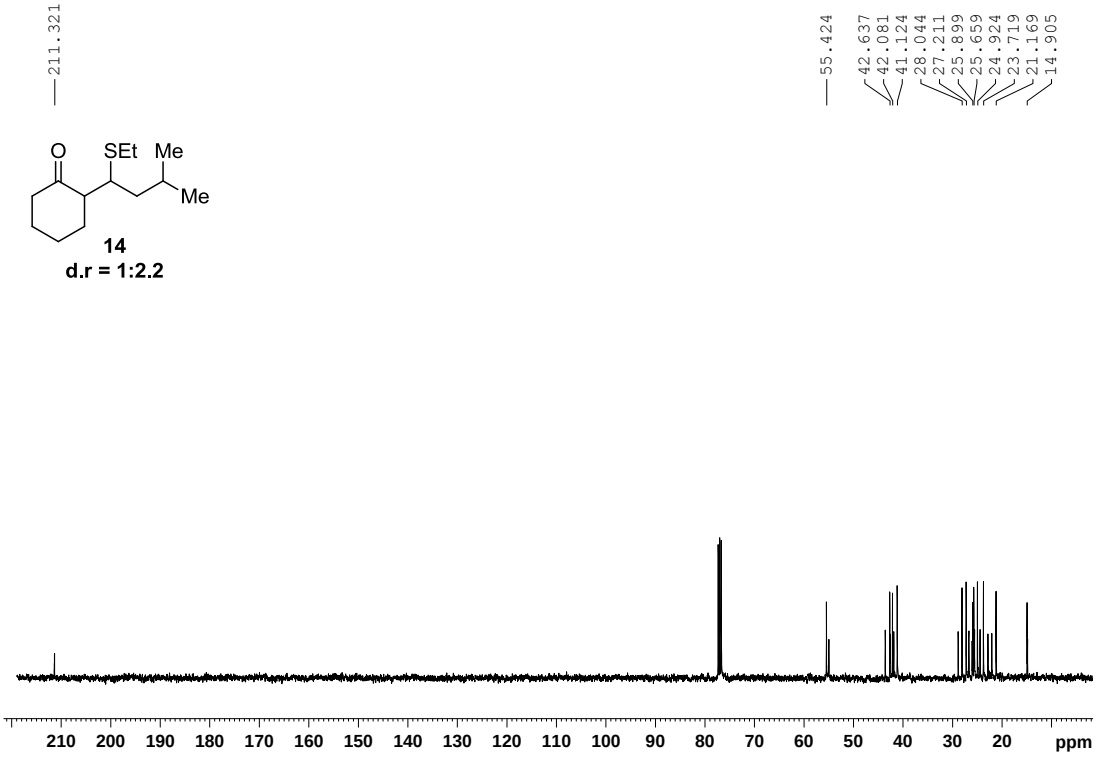
^{13}C - NMR spectrum of compound **13** ($CDCl_3$, 400 MHz):



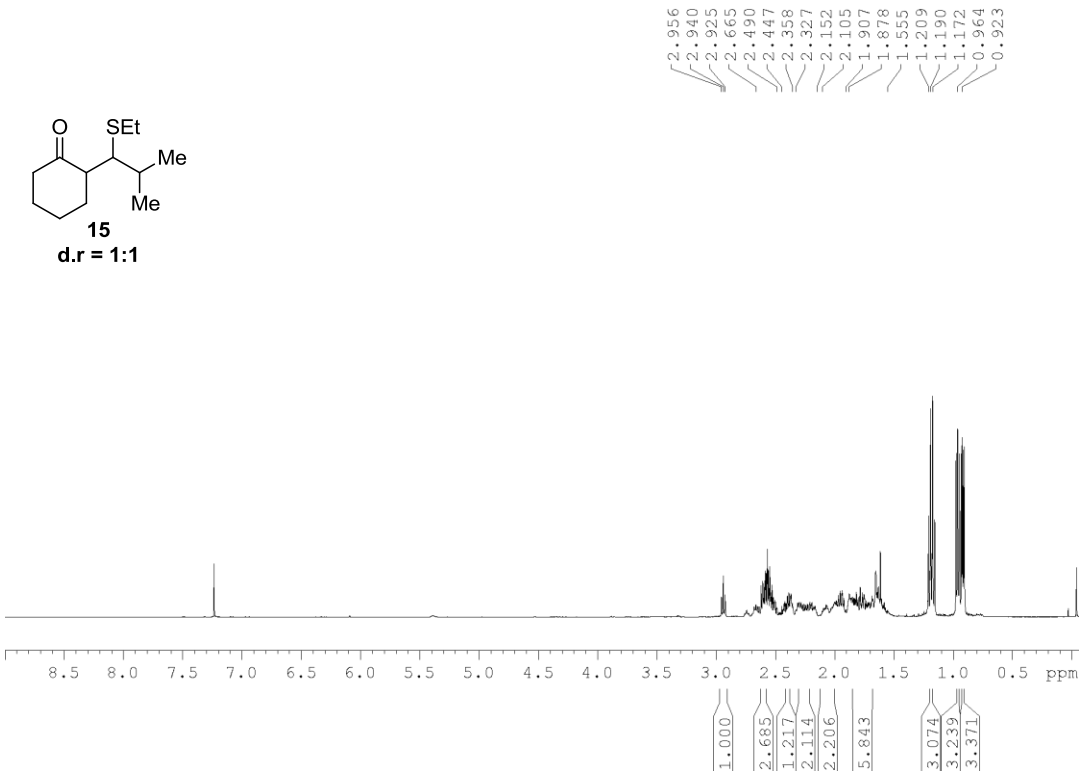
^{1}H - NMR spectrum of compound **14** ($CDCl_3$, 400 MHz):



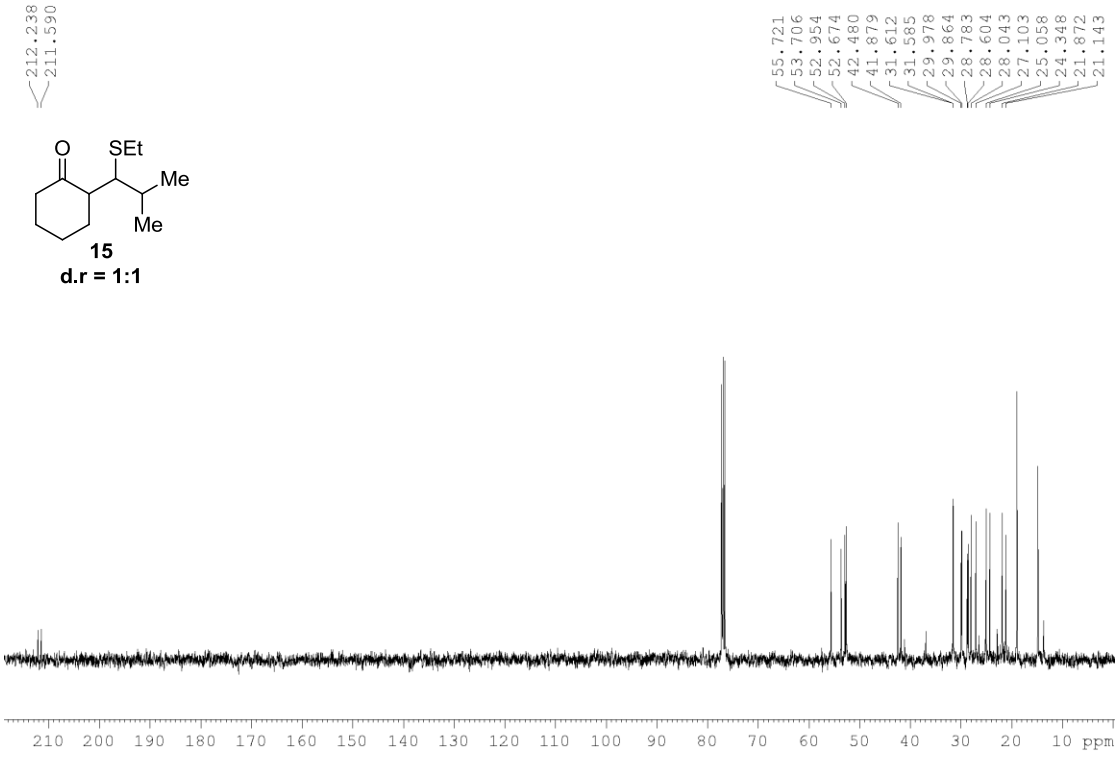
^{13}C - NMR spectrum of compound **14** ($CDCl_3$, 400 MHz):



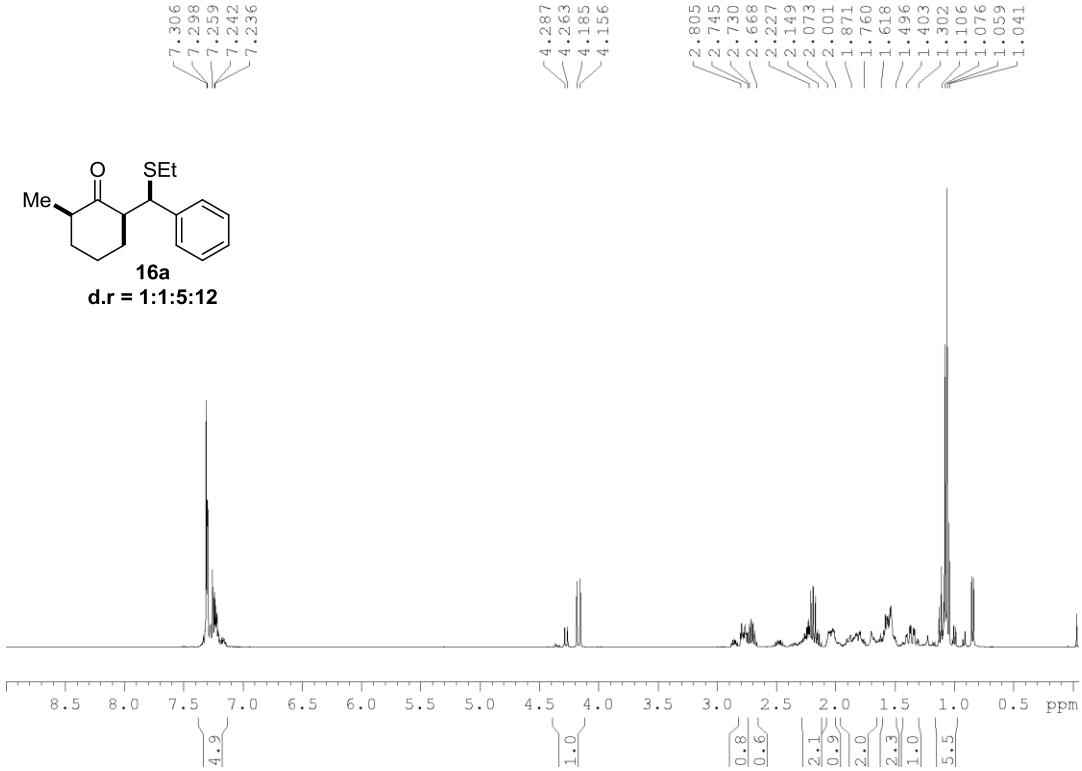
^{1}H - NMR spectrum of compound **15** ($CDCl_3$, 400 MHz):



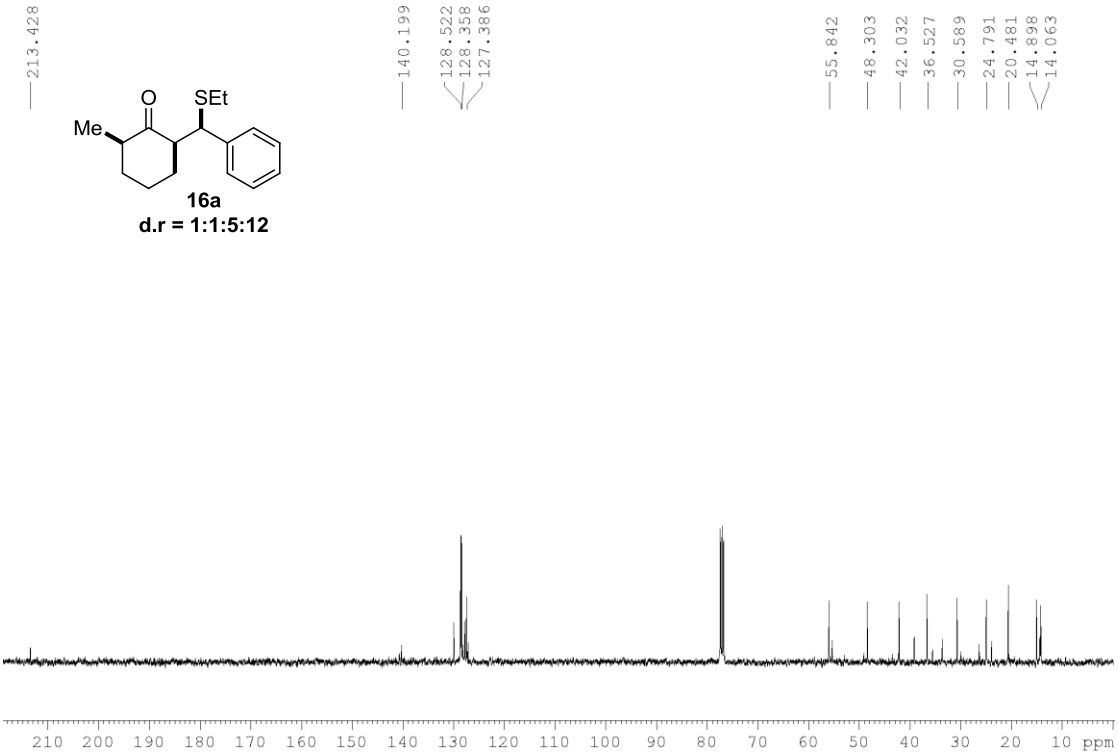
^{13}C - NMR spectrum of compound **15** ($CDCl_3$, 400 MHz):



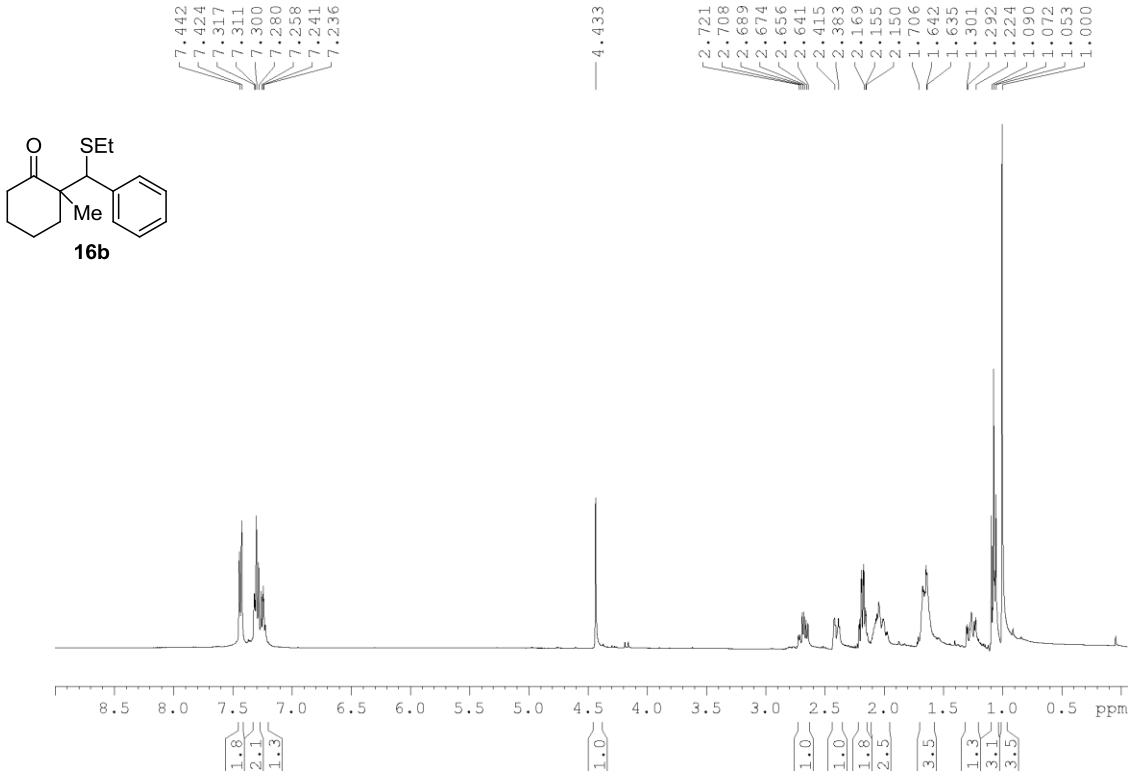
^{1}H - NMR spectrum of compound **16a** ($CDCl_3$, 400 MHz):



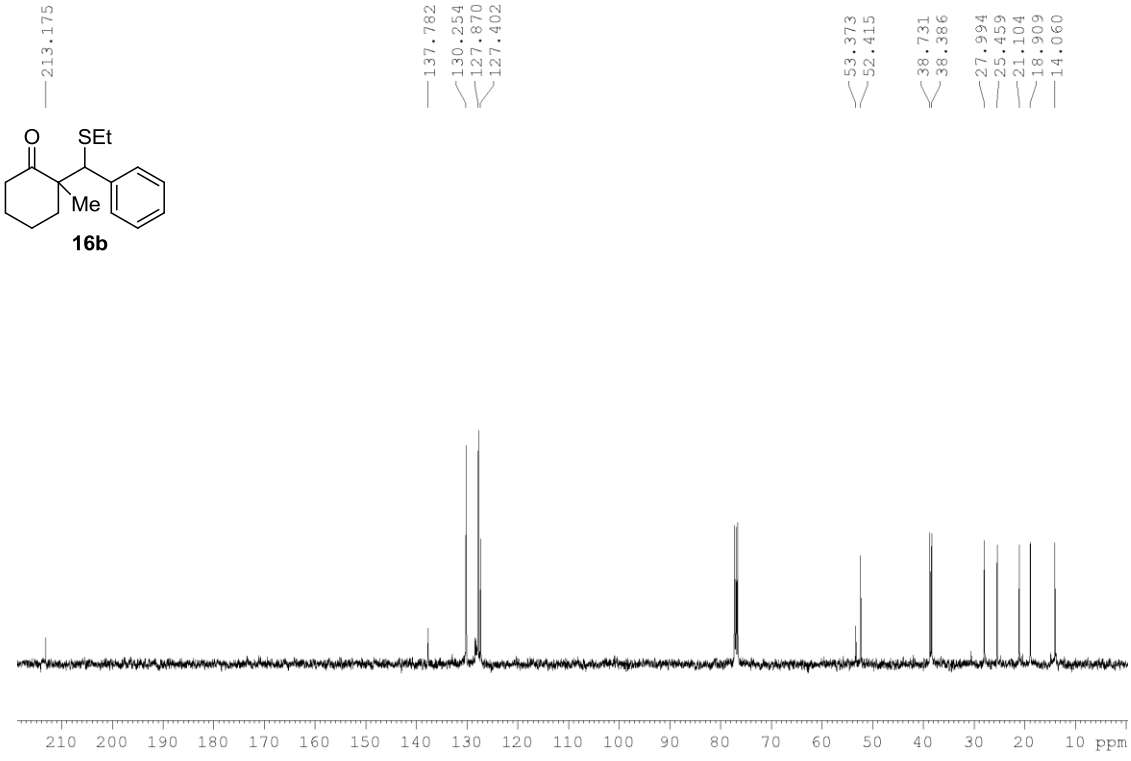
^{13}C - NMR spectrum of compound **16a** ($CDCl_3$, 400 MHz):



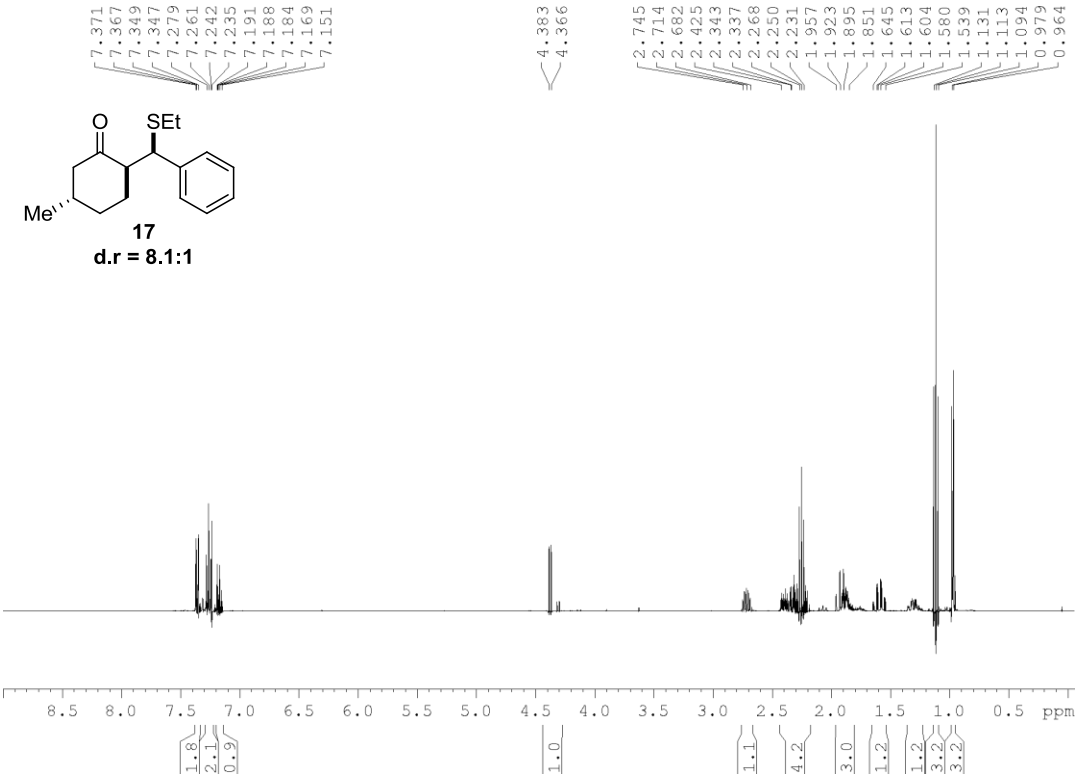
^{1}H - NMR spectrum of compound **16b** ($CDCl_3$, 400 MHz):



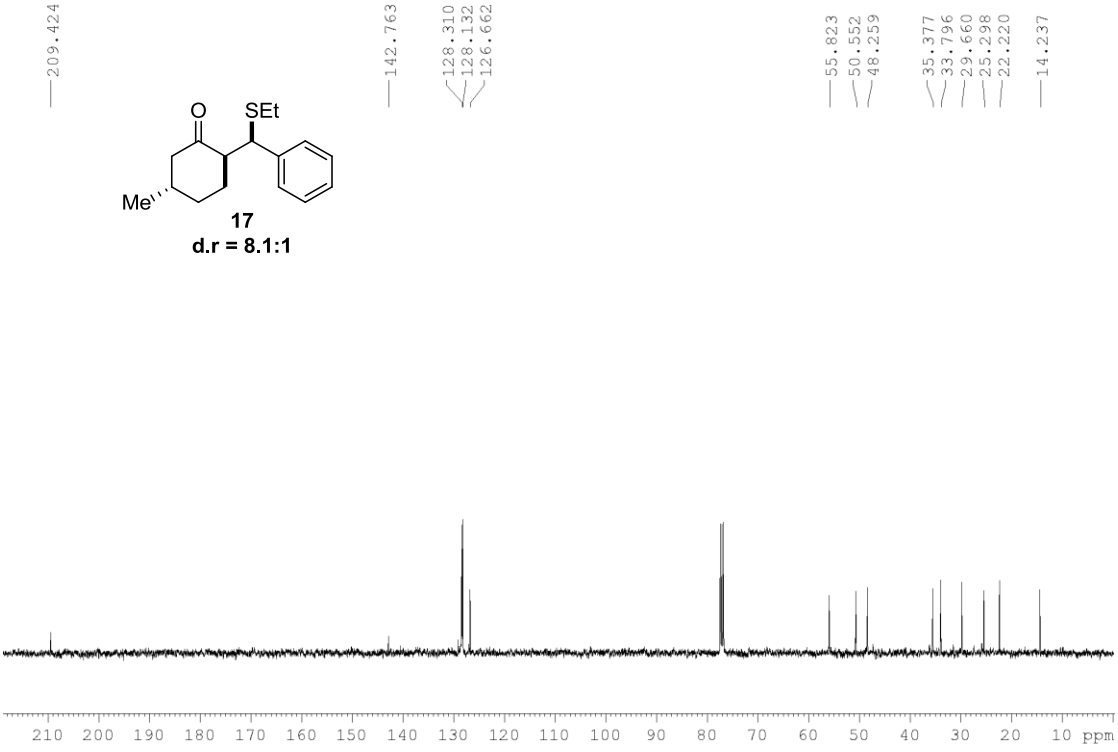
^{13}C - NMR spectrum of compound **16b** ($CDCl_3$, 400 MHz):



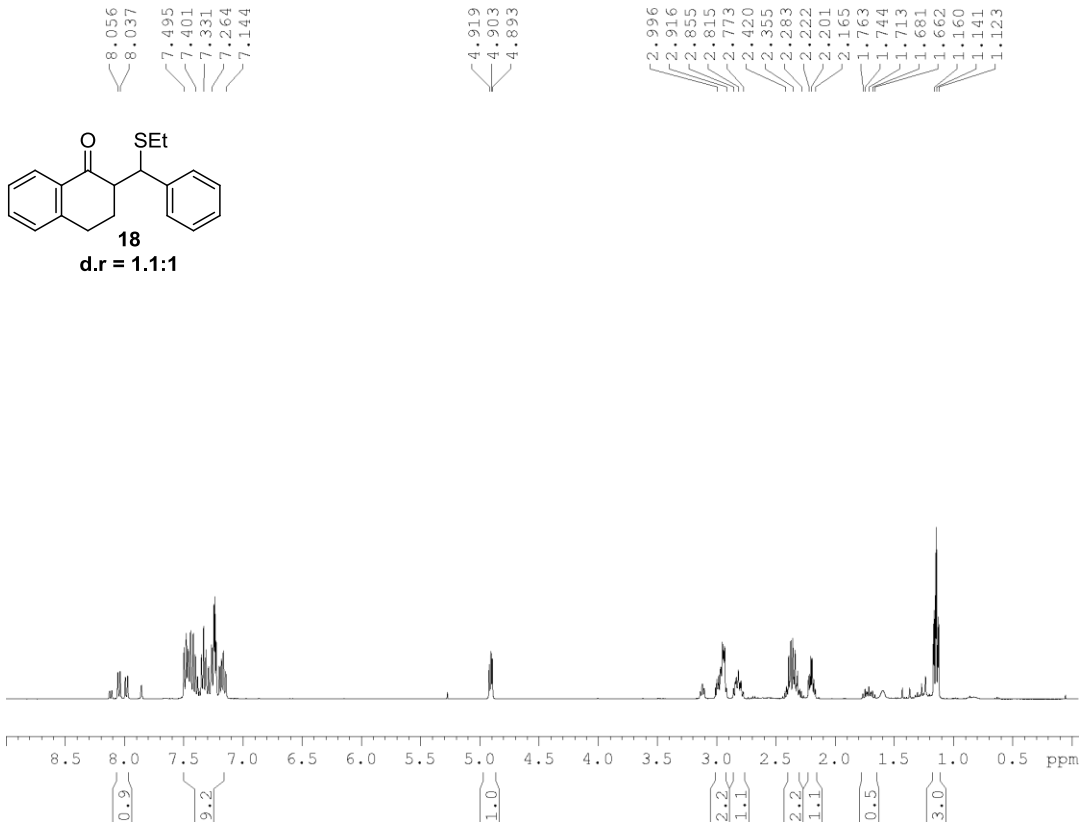
^{1}H - NMR spectrum of compound **17** ($CDCl_3$, 400 MHz):



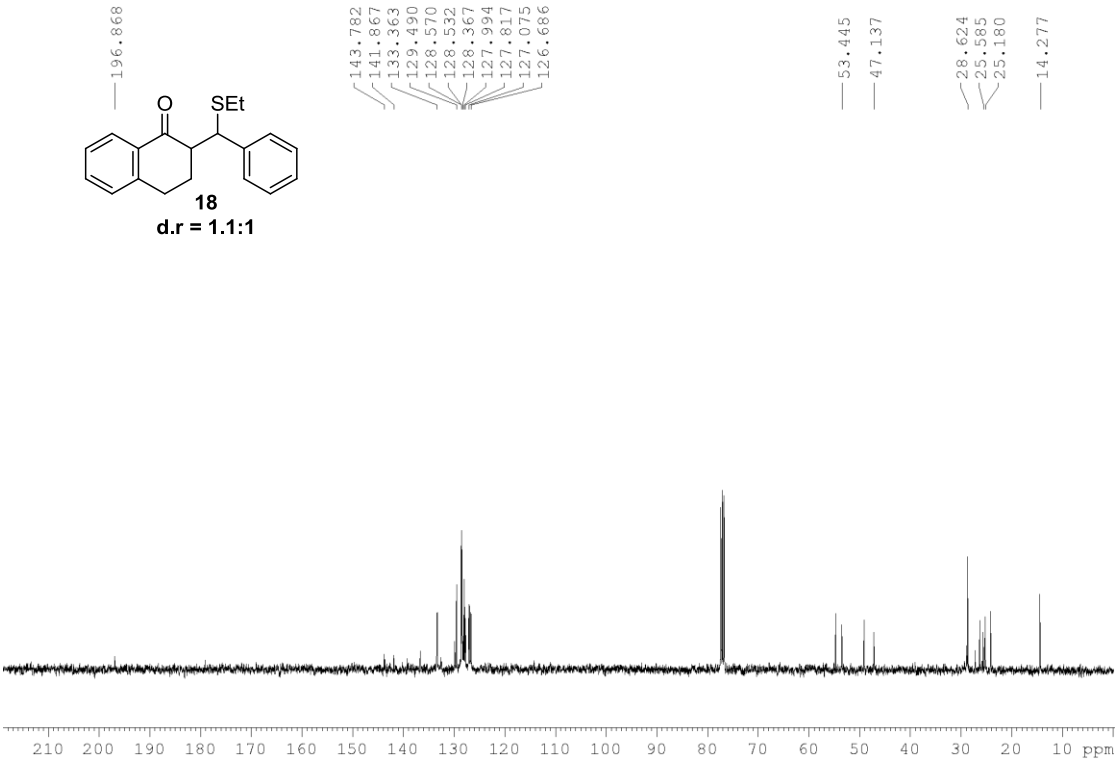
^{13}C - NMR spectrum of compound **17'** ($CDCl_3$, 400 MHz):



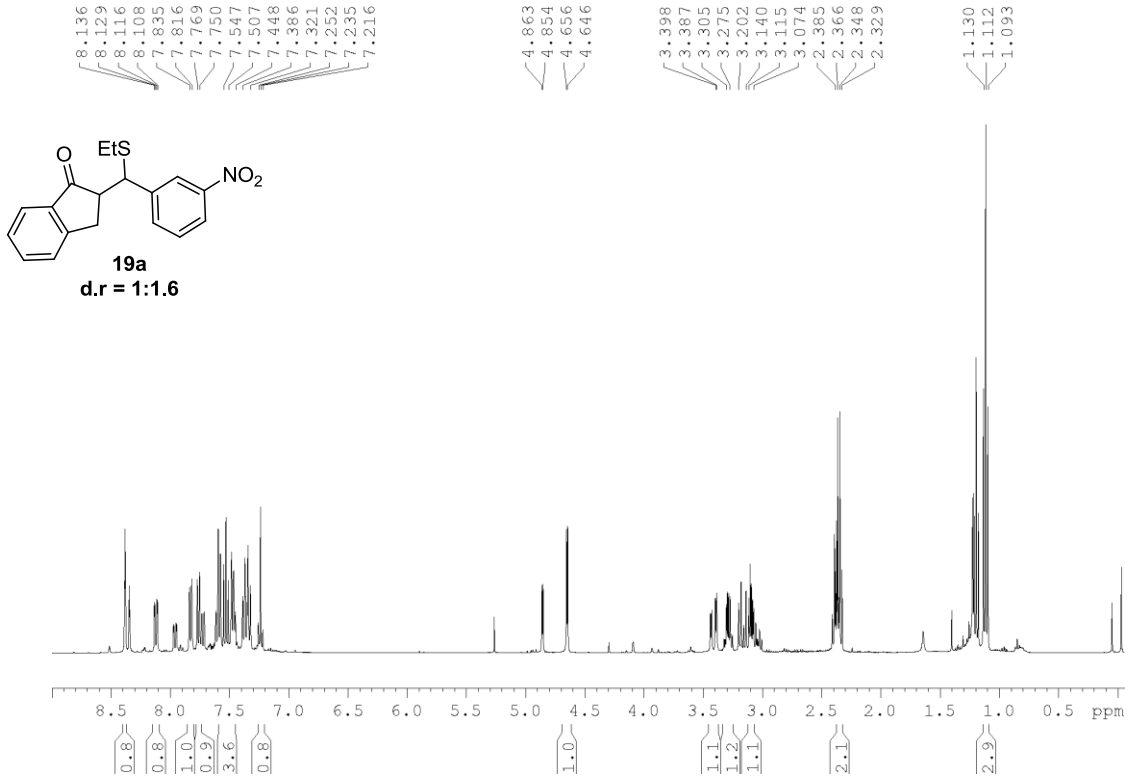
^{1}H - NMR spectrum of compound **18** ($CDCl_3$, 400 MHz):



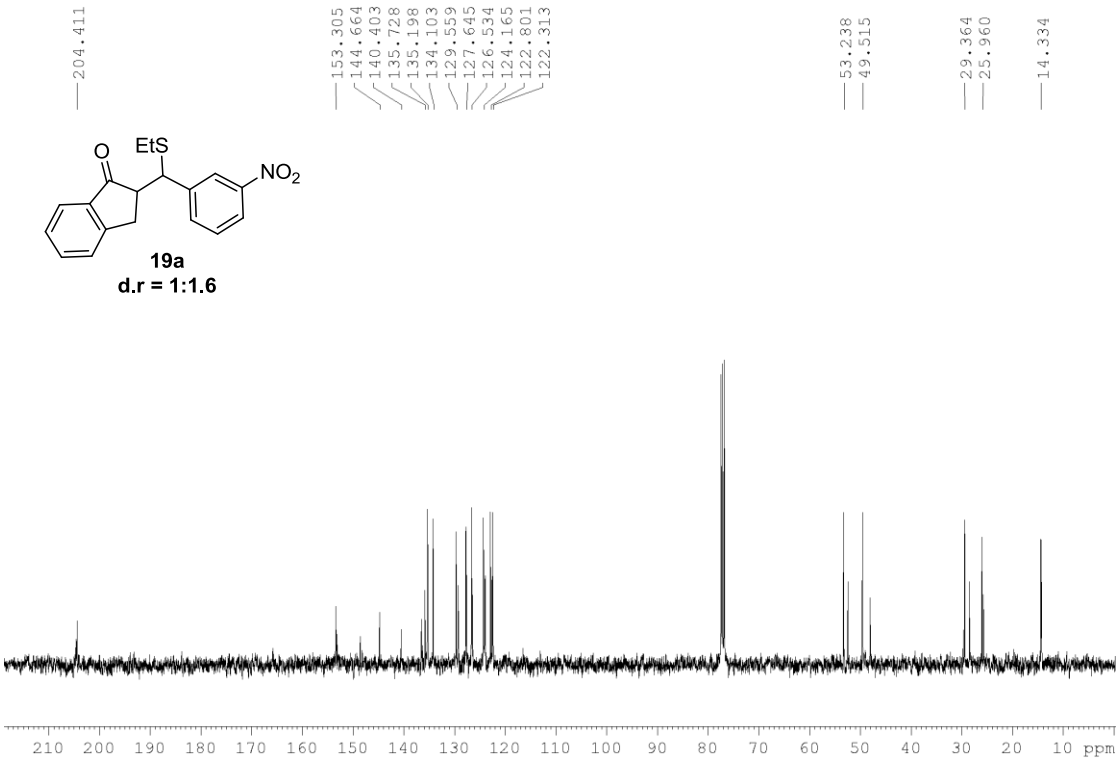
^{13}C - NMR spectrum of compound **18** ($CDCl_3$, 400 MHz):



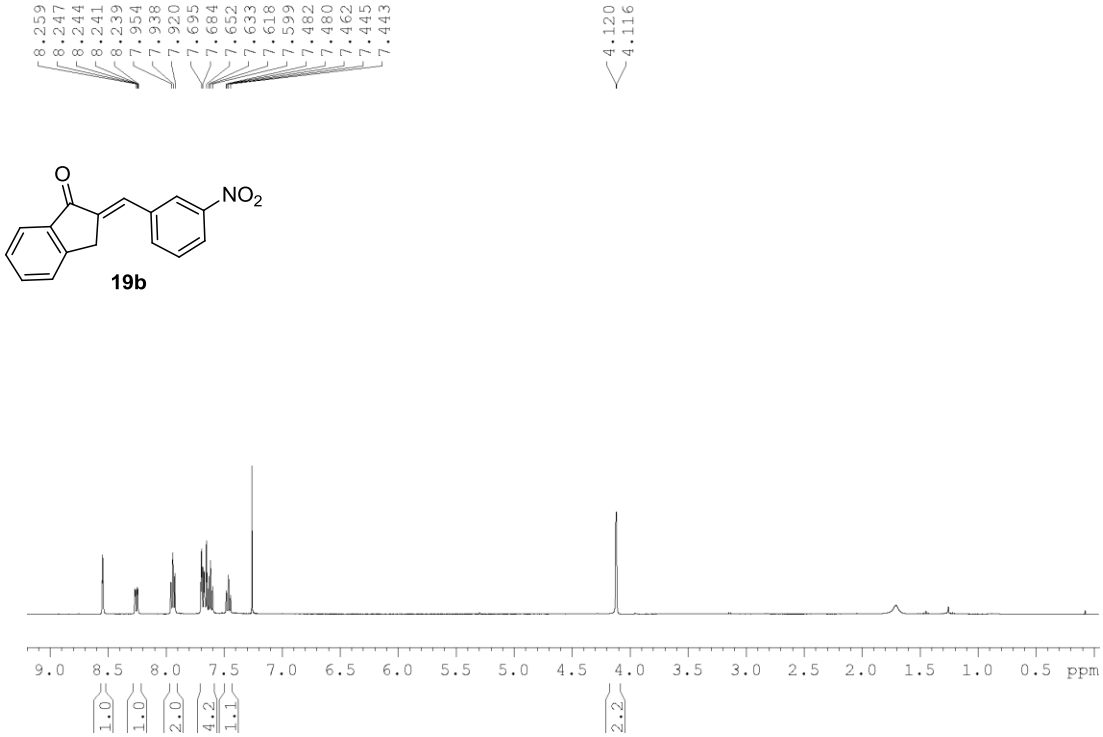
^{1}H - NMR spectrum of compound **19a** ($CDCl_3$, 400 MHz):



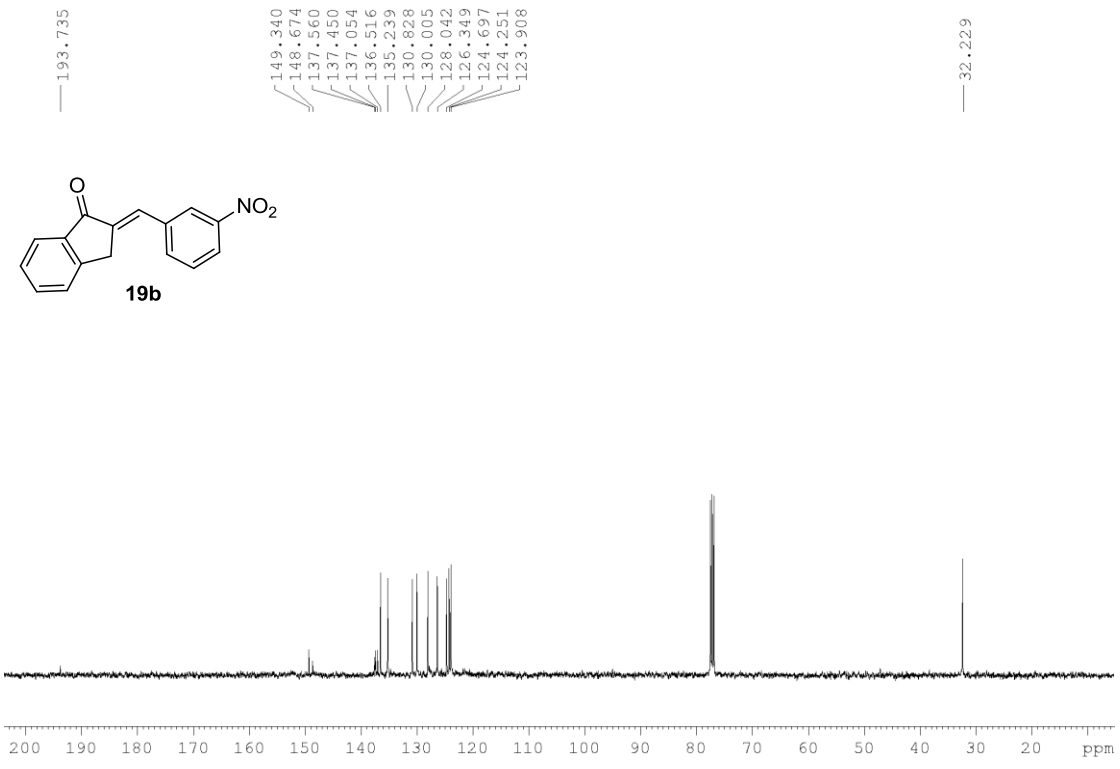
^{13}C - NMR spectrum of compound **19a** ($CDCl_3$, 400 MHz):



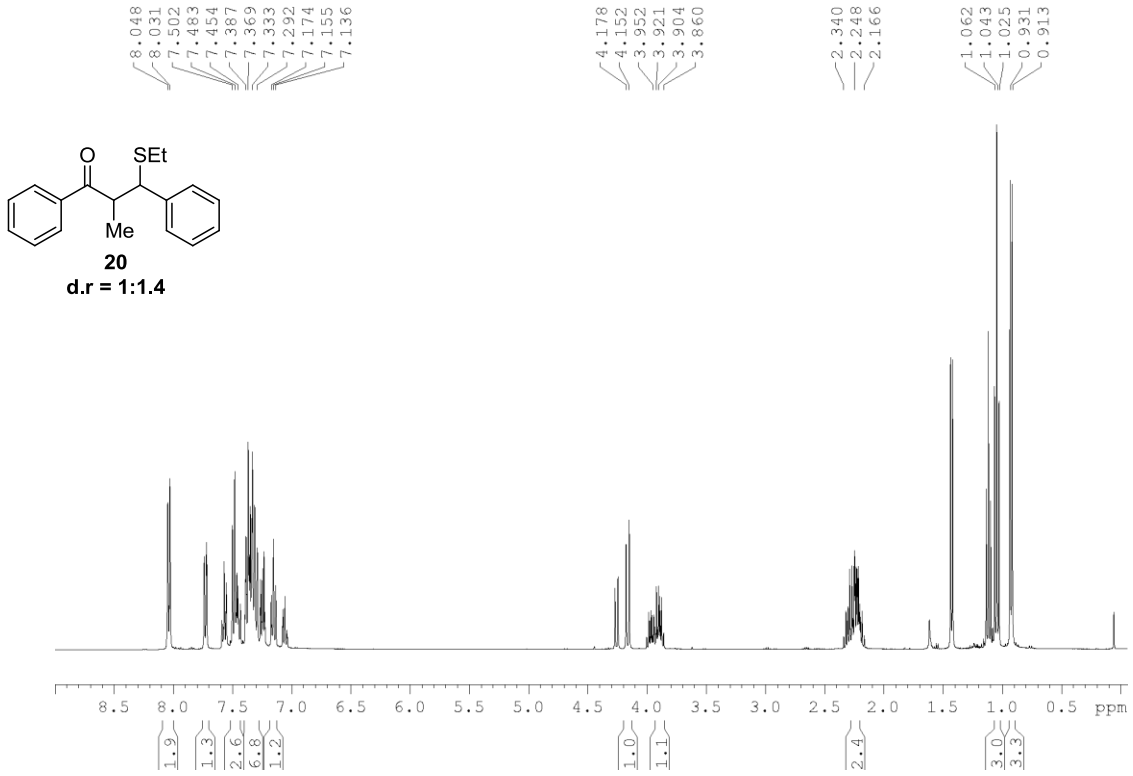
^{1}H - NMR spectrum of compound **19b** ($CDCl_3$, 400 MHz):



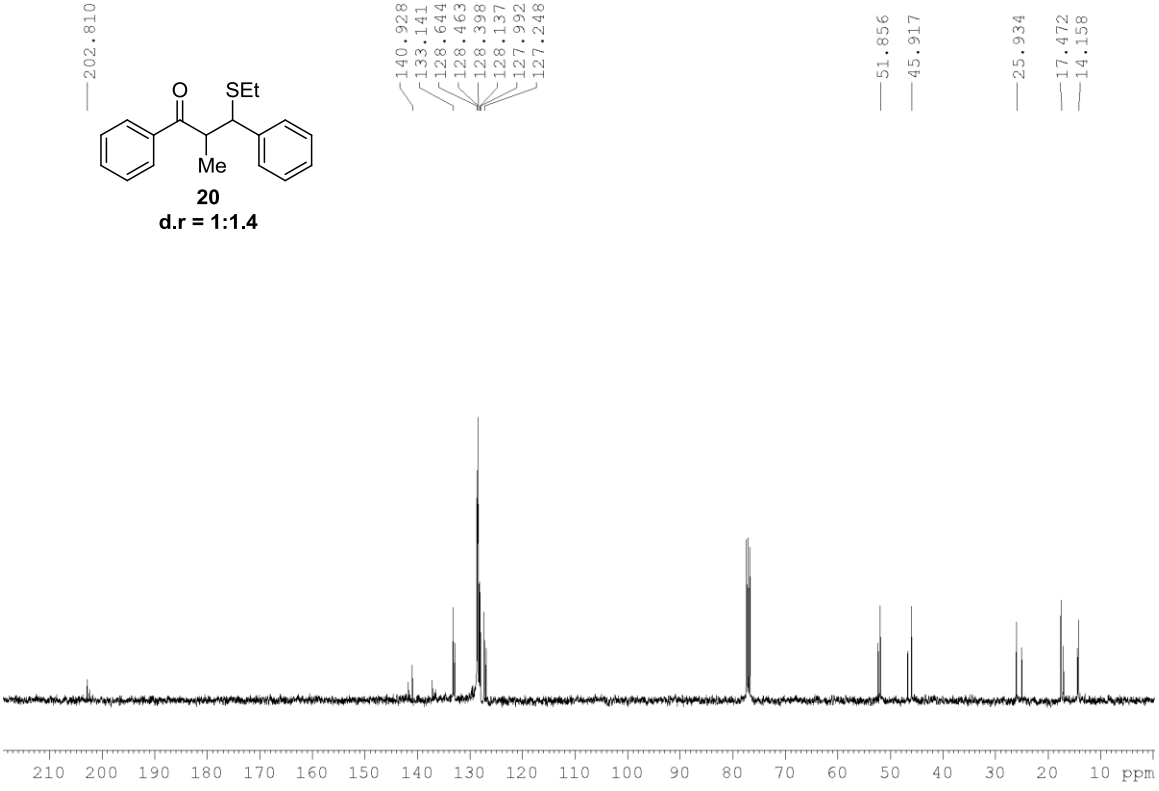
^{13}C - NMR spectrum of compound **19b** ($CDCl_3$, 400 MHz):



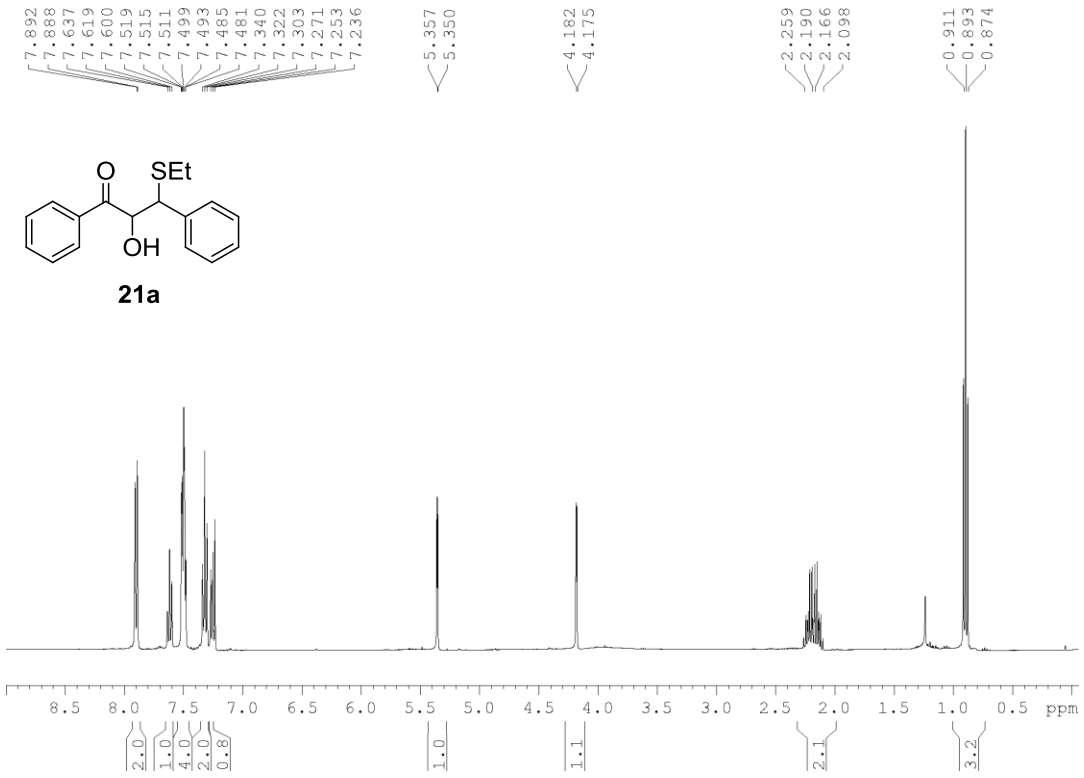
^{1}H - NMR spectrum of compound **20** ($CDCl_3$, 400 MHz):



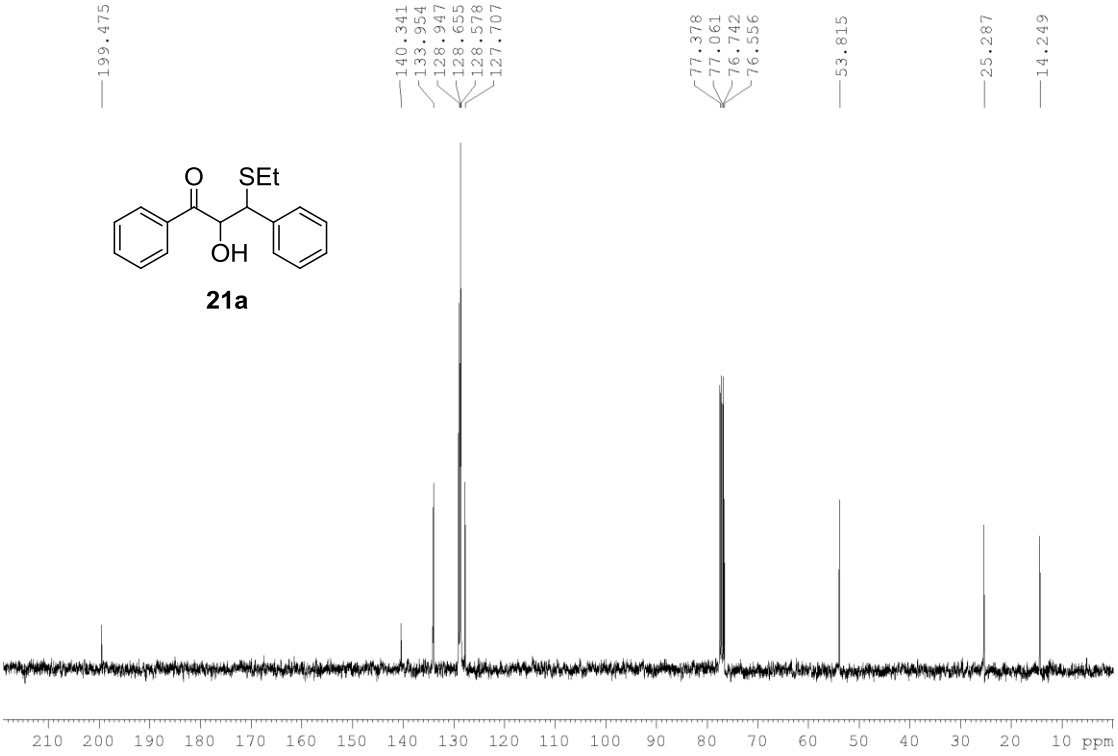
^{13}C - NMR spectrum of compound **20** ($CDCl_3$, 400 MHz):



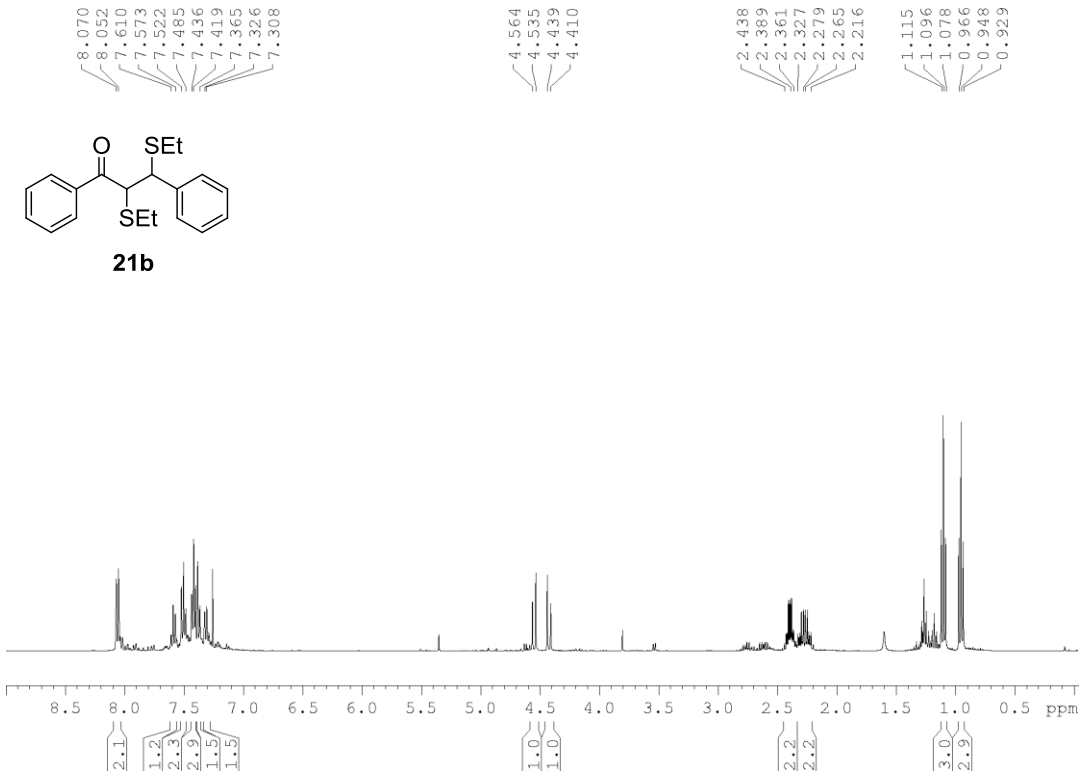
^{1}H - NMR spectrum of compound **21a** ($CDCl_3$, 400 MHz):



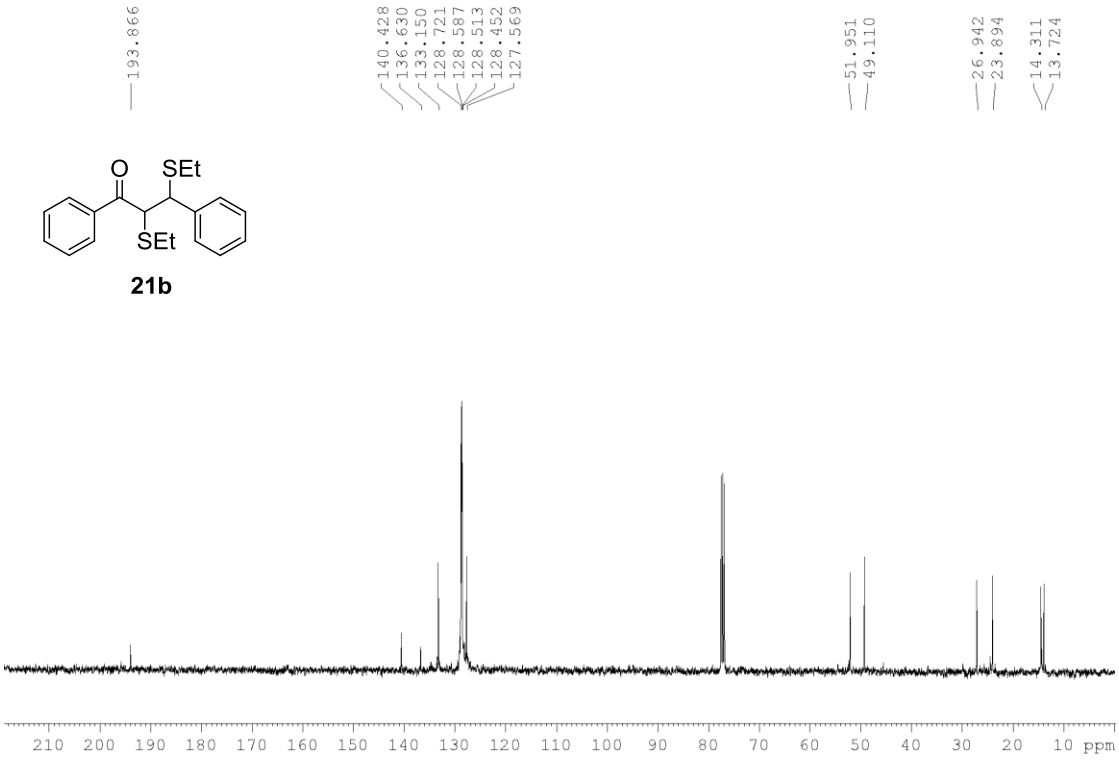
^{13}C - NMR spectrum of compound **21a** ($CDCl_3$, 400 MHz):



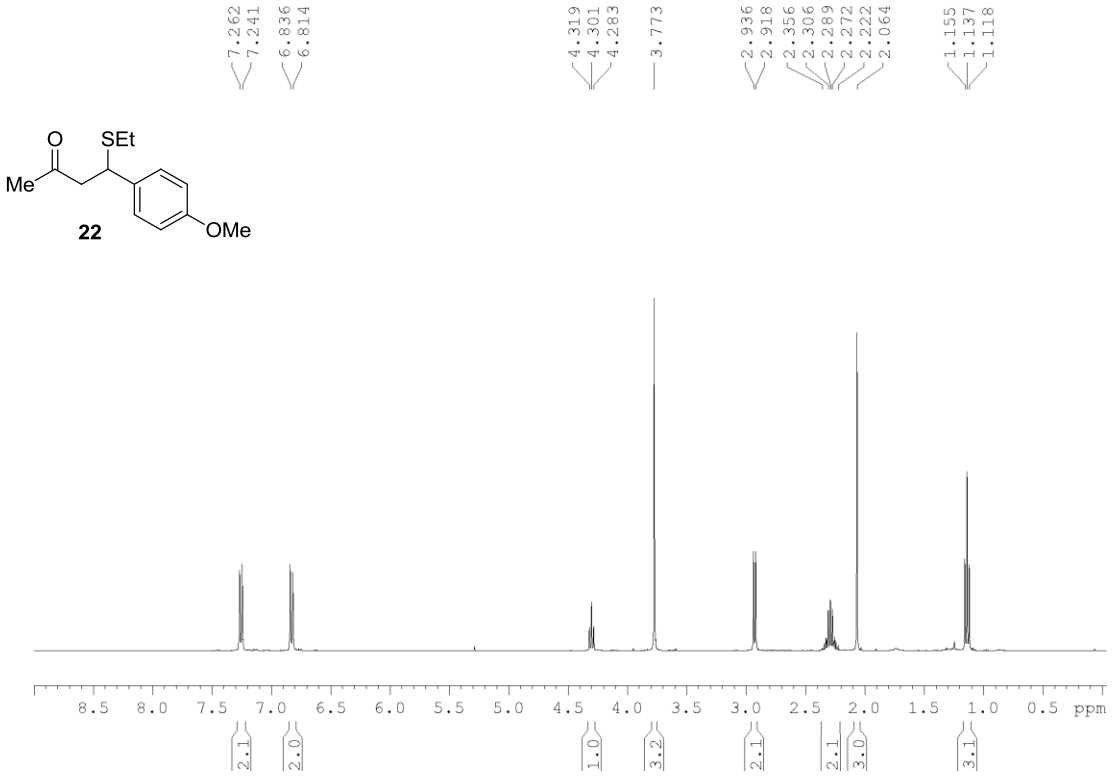
^{1}H - NMR spectrum of compound **21b** ($CDCl_3$, 400 MHz):



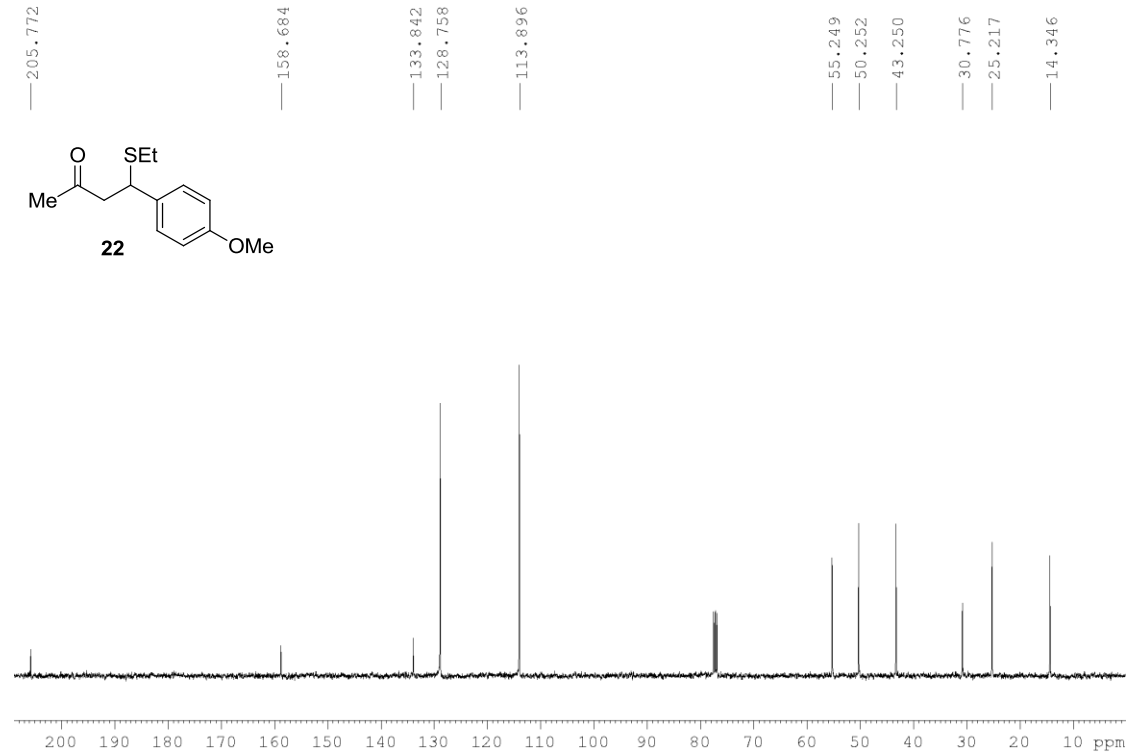
^{13}C - NMR spectrum of compound **21b** ($CDCl_3$, 400 MHz):



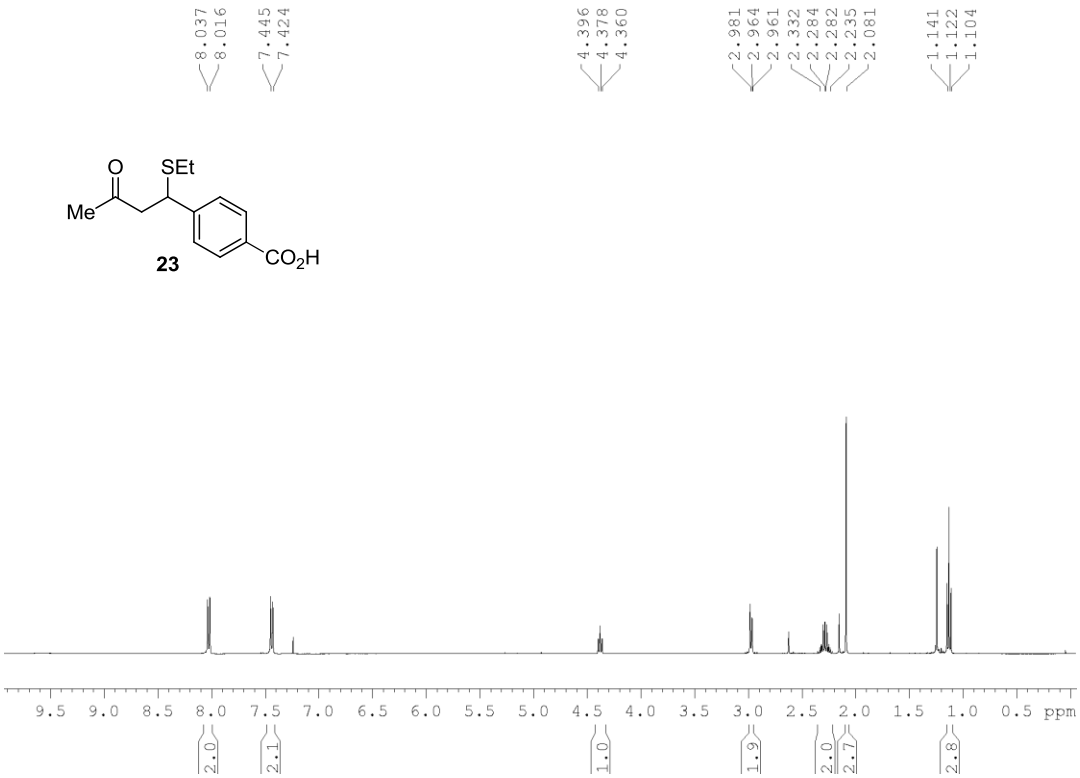
^{1}H - NMR spectrum of compound **22** ($CDCl_3$, 400 MHz):



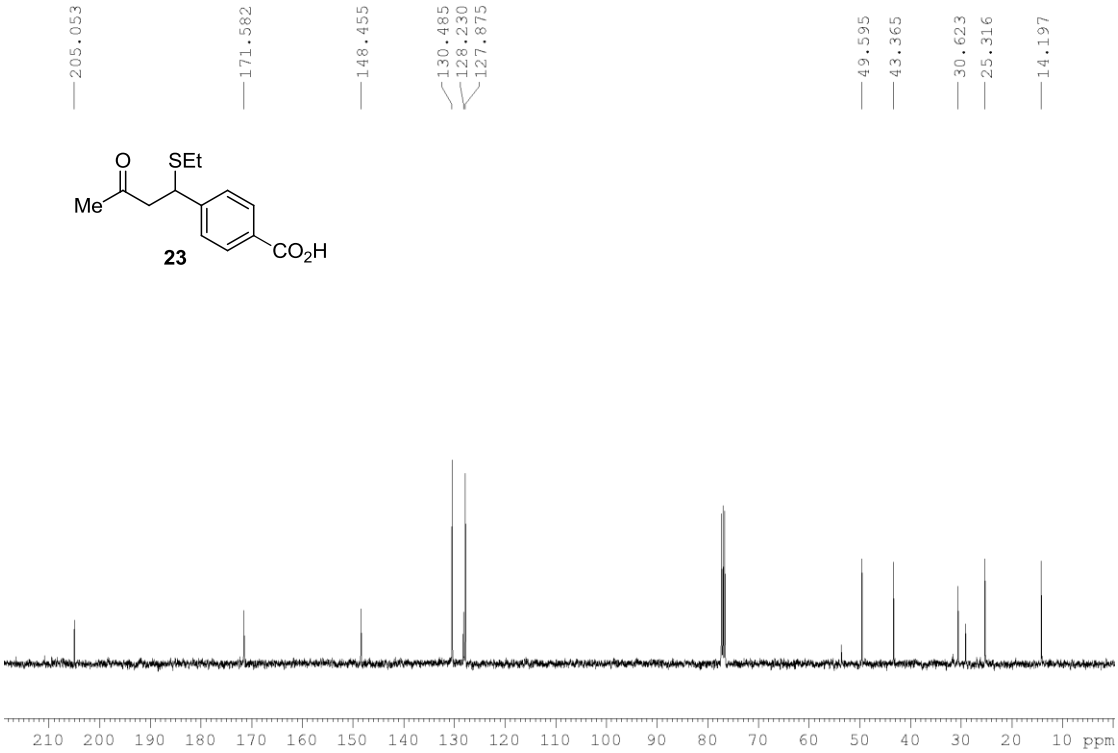
^{13}C - NMR spectrum of compound **22** ($CDCl_3$, 400 MHz):



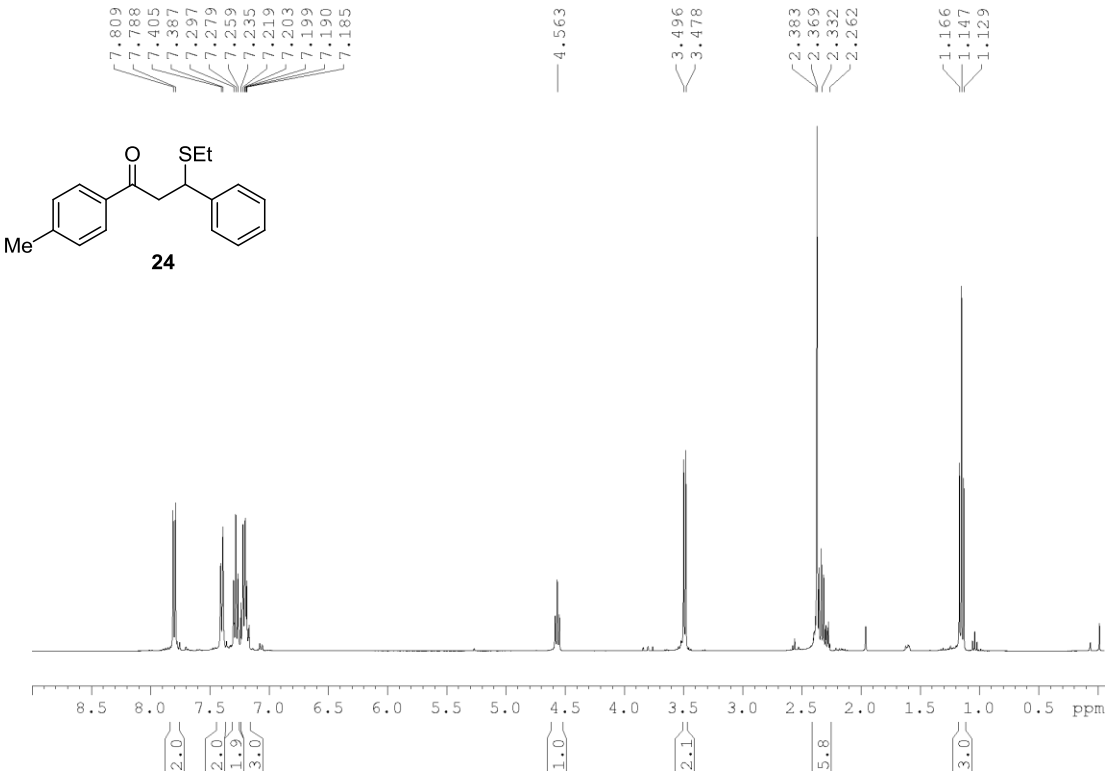
^{1}H - NMR spectrum of compound **23** ($CDCl_3$, 400 MHz):



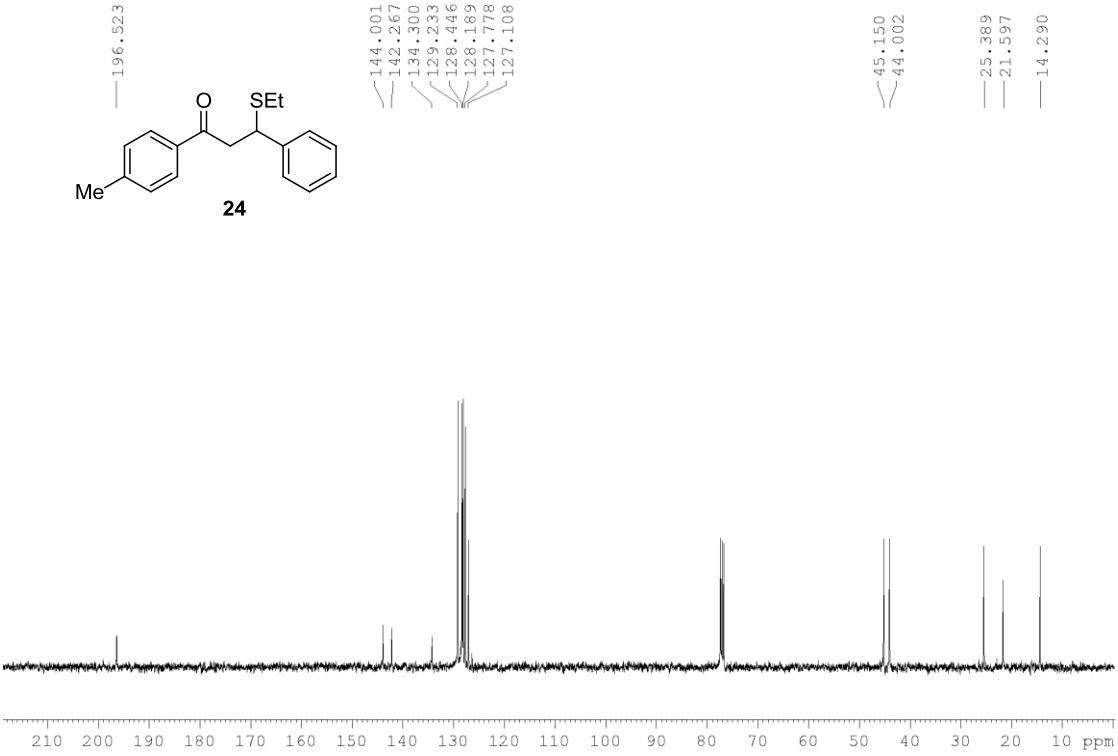
^{13}C - NMR spectrum of compound **23** ($CDCl_3$, 400 MHz):



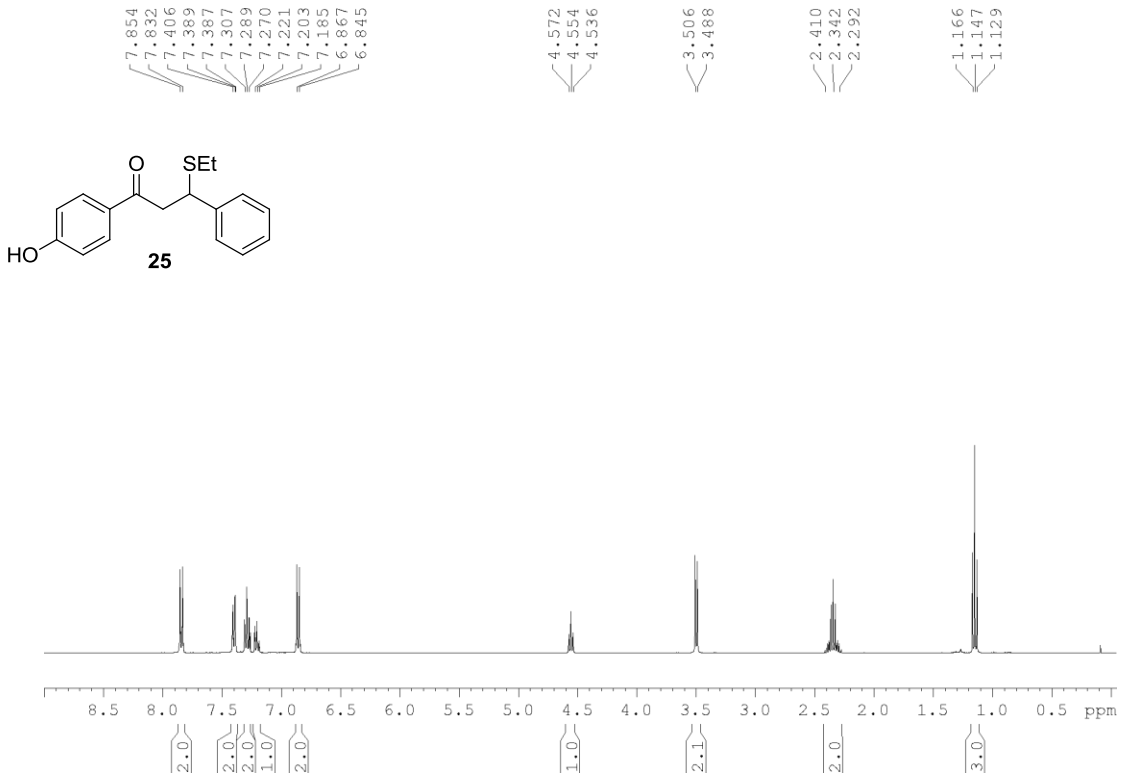
^{1}H - NMR spectrum of compound **24** ($CDCl_3$, 400 MHz):



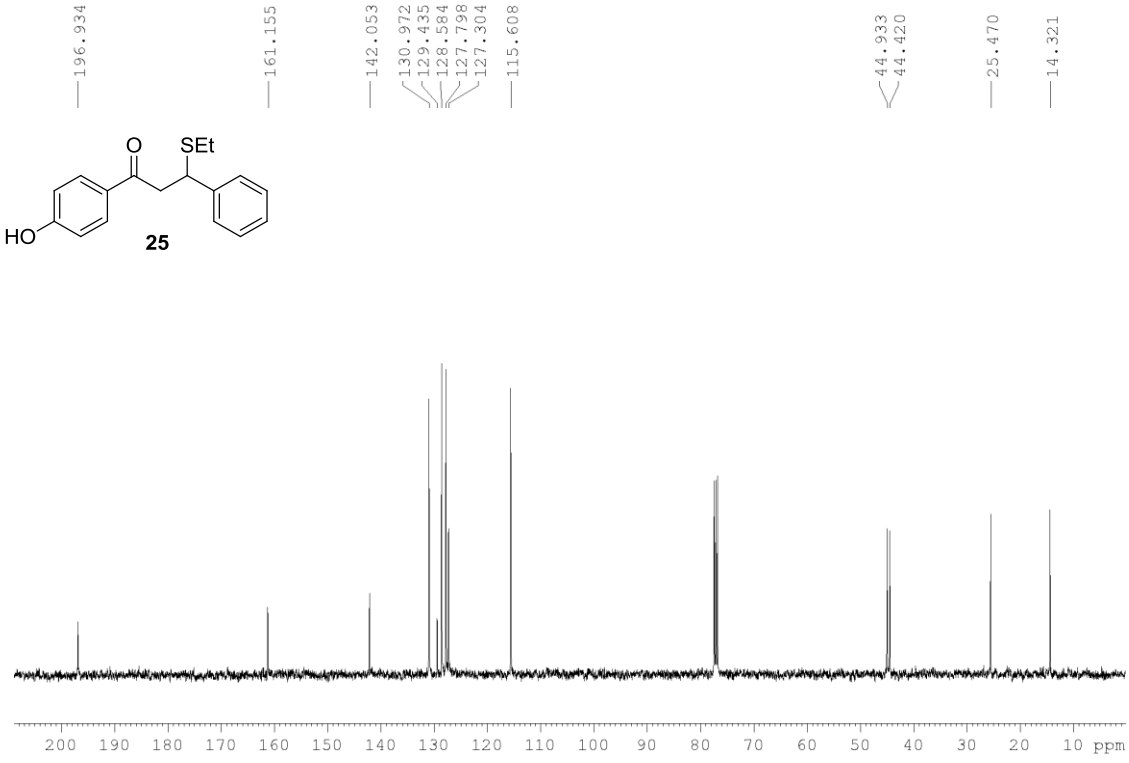
^{13}C - NMR spectrum of compound **24** ($CDCl_3$, 400 MHz):



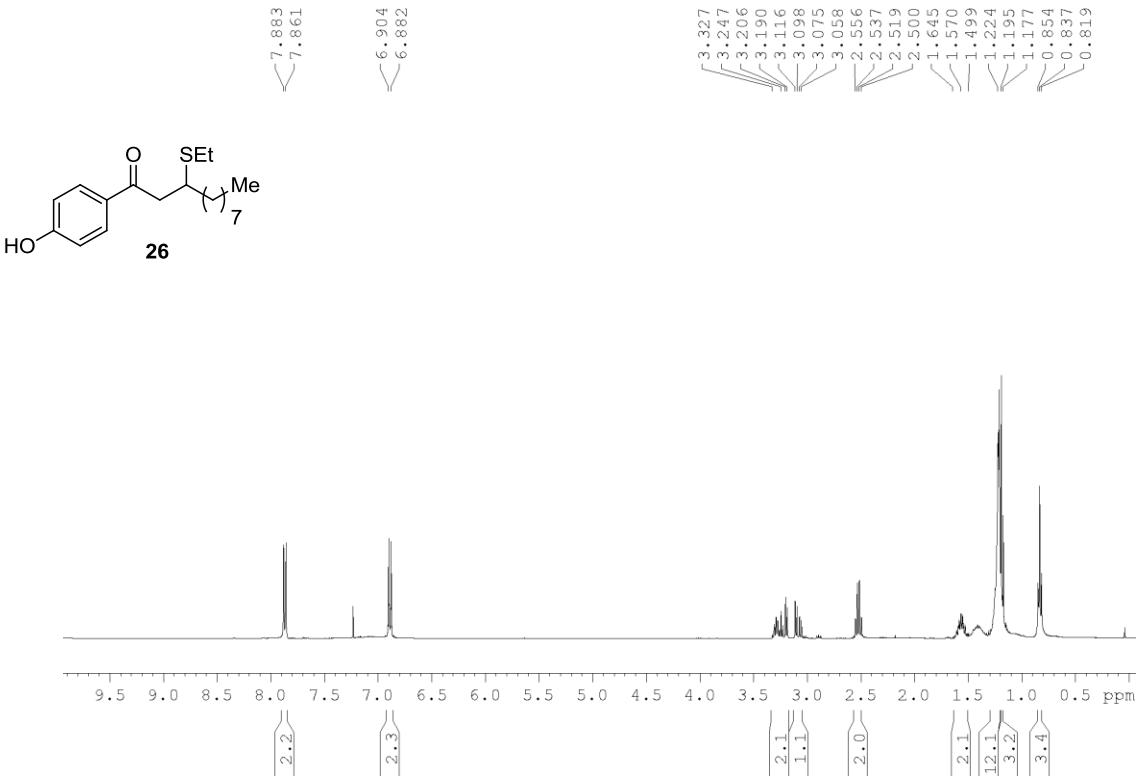
^{1}H - NMR spectrum of compound **25** ($CDCl_3$, 400 MHz):



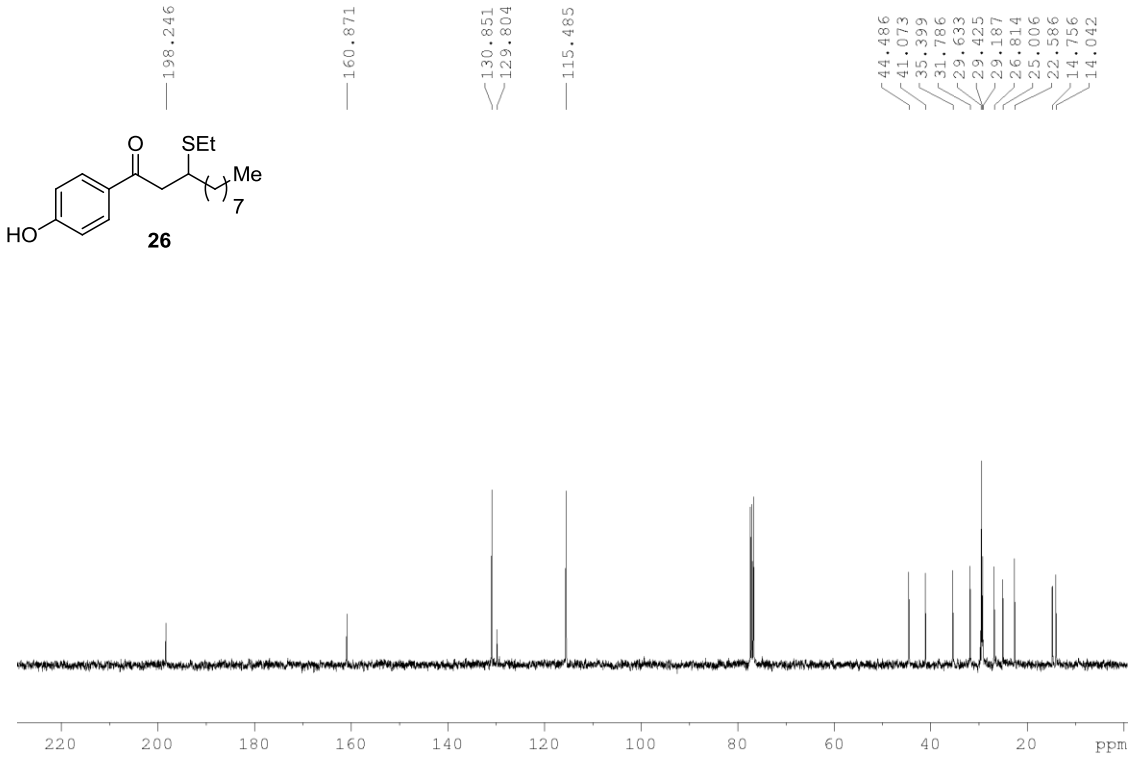
^{13}C - NMR spectrum of compound **25** ($CDCl_3$, 400 MHz):



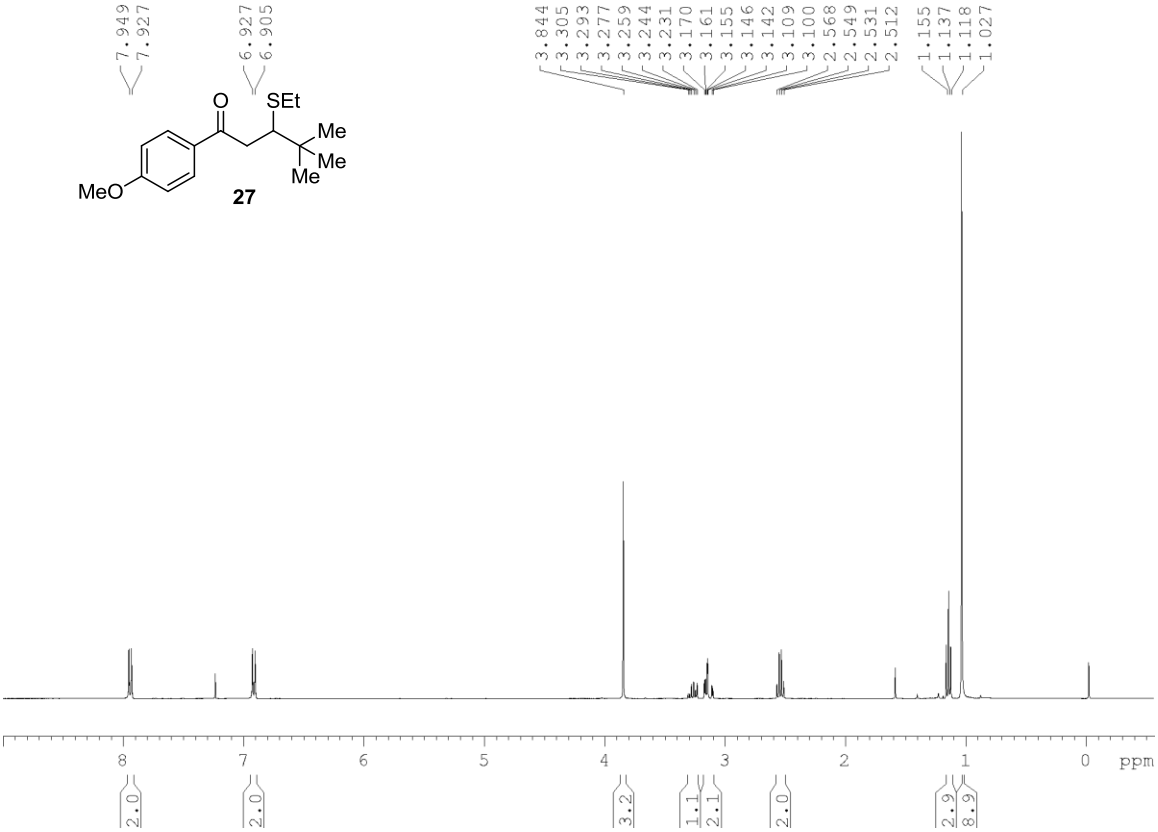
^{1}H - NMR spectrum of compound **26** ($CDCl_3$, 400 MHz):



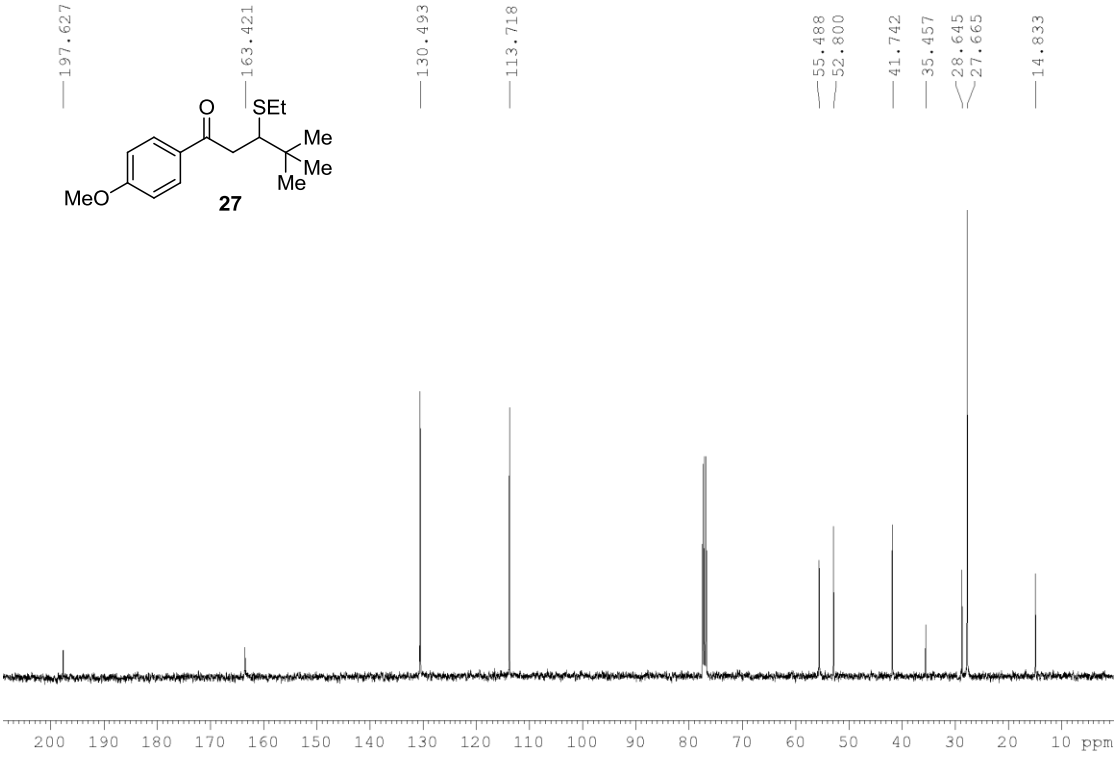
^{13}C - NMR spectrum of compound **26** ($CDCl_3$, 400 MHz):



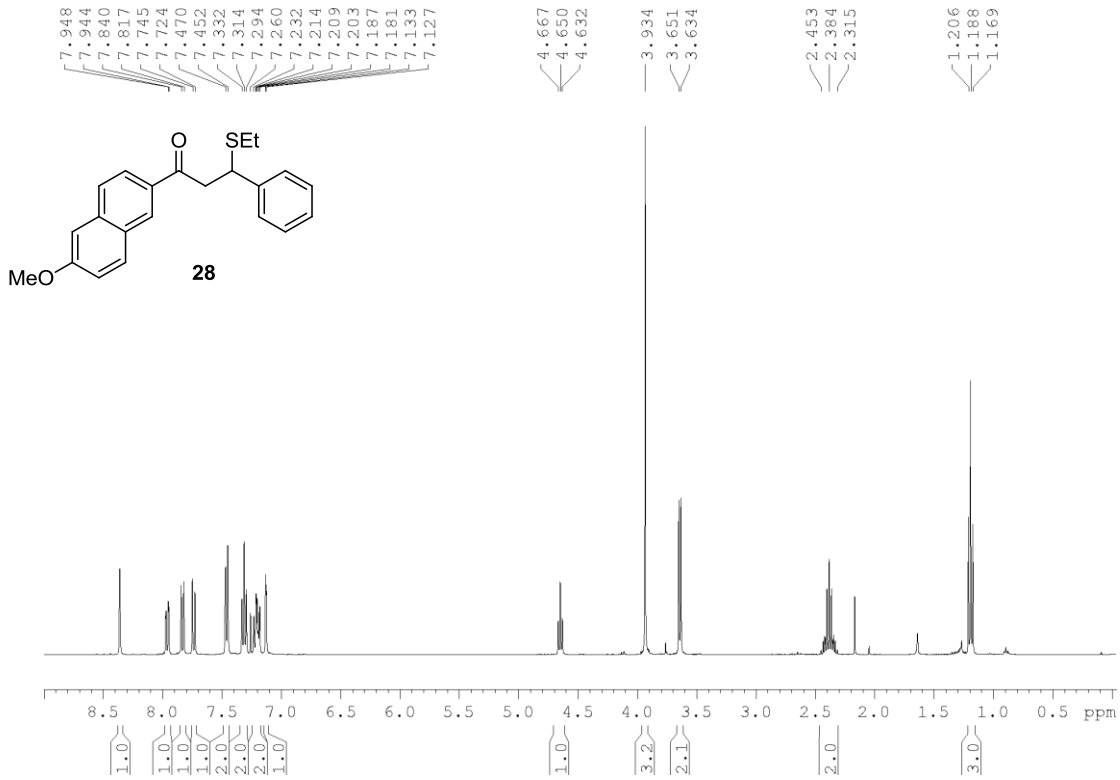
^{1}H - NMR spectrum of compound **27** ($CDCl_3$, 400 MHz):



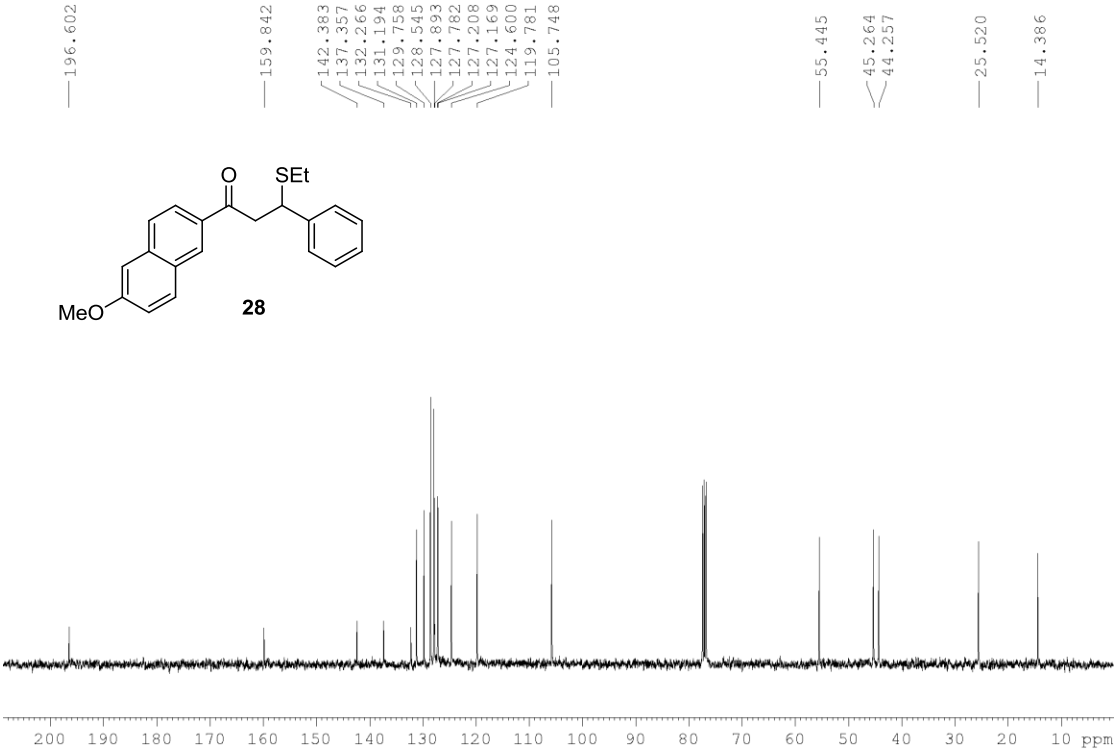
^{13}C - NMR spectrum of compound **27** ($CDCl_3$, 400 MHz):



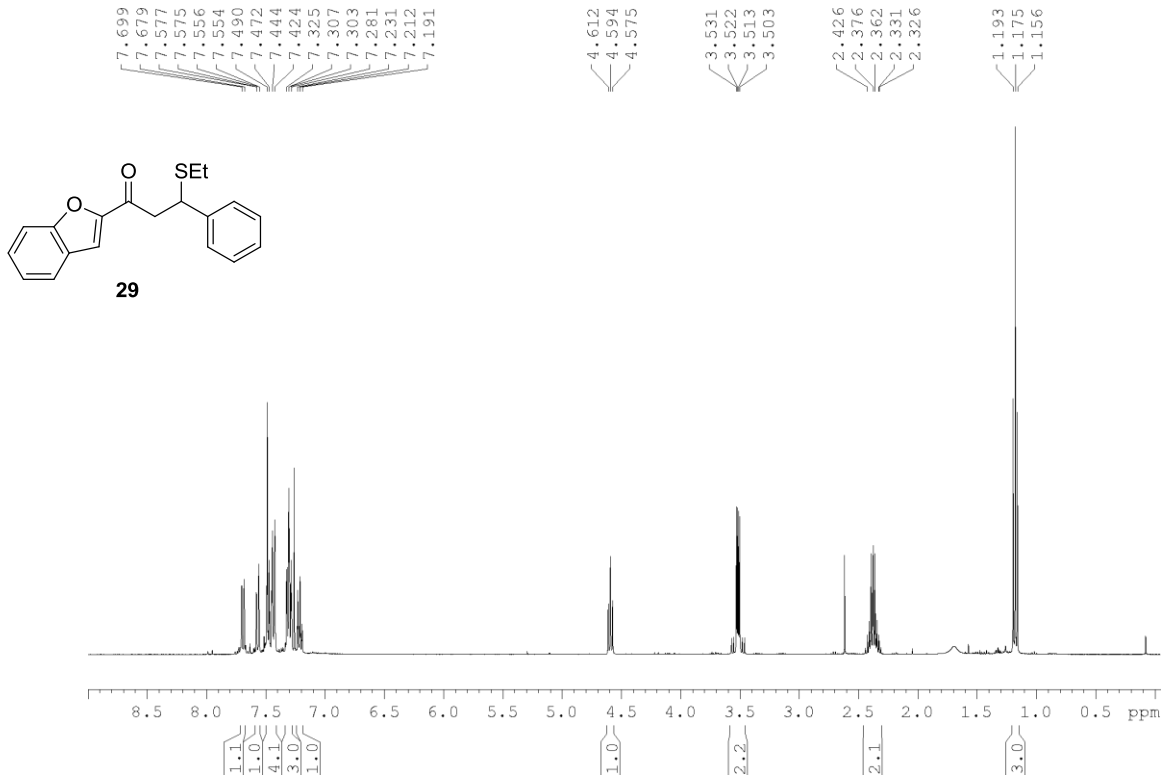
^{1}H - NMR spectrum of compound **28** ($CDCl_3$, 400 MHz):



^{13}C - NMR spectrum of compound **28** ($CDCl_3$, 400 MHz):



\\\$^{1}$H - NMR spectrum of compound **29** ($CDCl_3$, 400 MHz):



^{13}C - NMR spectrum of compound **29** ($CDCl_3$, 400 MHz):