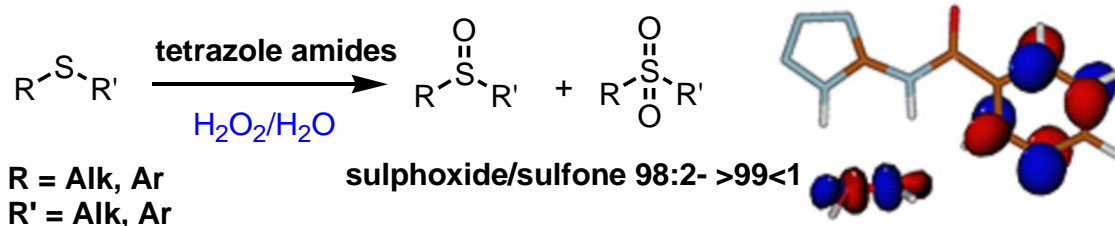


Supporting Information

New Aminotetrazole Derivatives as Hydrogen Bonding Catalysts. A Green and Selective Oxidation of Organosulphides with H₂O₂ in H₂O



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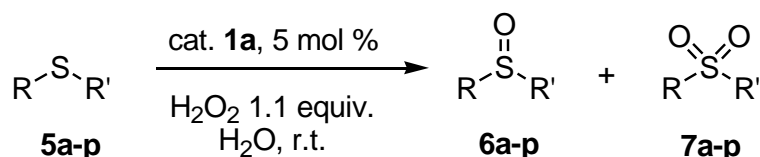
1. Synthesis

1.1 General methods

¹H NMR spectra were recorded on 400 and 500 MHz Varian spectrometers at 27°C using CDCl₃, DMF-*d*₇ or DMSO-*d*₆ as solvent. ¹³C NMR were recorded at 100 and 125 MHz at 27°C using CDCl₃, DMF-*d*₇ or DMSO-*d*₆ as solvent. Chemical shifts (δ) are given in ppm. Coupling constants (*J*) are reported in Hz. Infrared spectra were recorded on a FT-IR Bruker spectrophotometer and are reported in wavenumbers. Low Mass spectra analysis were recorded on an Agilent-HP GC-MS (E.I. 70eV).

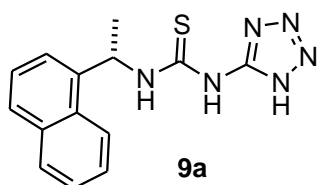
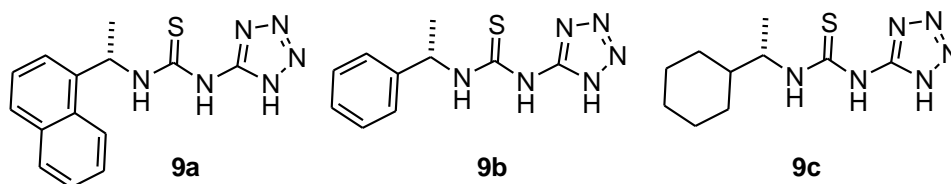
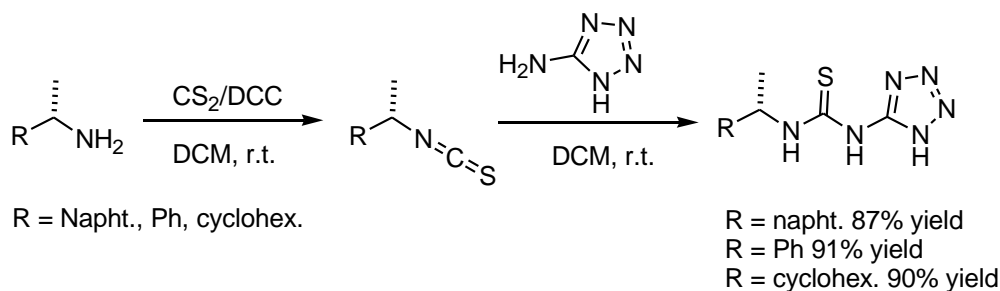
Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Flash chromatography was performed using 70-200 mesh silica gel. Yields refer to chromatography and spectroscopically pure materials.

1.2 General procedure for the oxidation of sulphides **5a-p** to sulphoxides **6a-6p** using cat. **1a**-H₂O₂

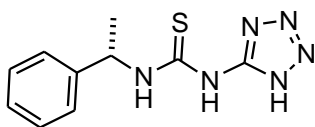


To a 3 M solution of sulphide **5a** (100 mg, 0.8 mmol) and tetrazole **1a** (5 mol. %) in water (2.7 mL), H₂O₂ (30% v/v in water, 1.1 equiv.) was added in one injection and the resulting mixture was stirred at room temperature and followed by Gc-MS until completion (**6a/7a** ratio 98:2). The reaction mixture was filtered and the water solution was extracted with. The organic phase was dried on Na₂SO₄, filtered and concentrated under reduced pressure. The catalyst was recovered by washing up the filtered solid with Ethyl acetate and dried. Pure sulphoxide **6a** was obtained after flash column chromatography (silica gel, 80:20 hexane/ether) in 92% yield. Colorless oil. ¹H NMR (500 MHz, CDCl₃) δ: 7.62-7.60 (m, 2 H), 7.48-7.46 (m, 3 H), 2.68 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ: 145.6, 130.8, 129.2, 123.3, 43.8. Ms *m/z*: (M+140, (100%), 125 (98%), 97 (60%), 77 (50%), 51 (35%).

1.3 Synthesis of aminotetrazole-thiourea ligands 9a-c

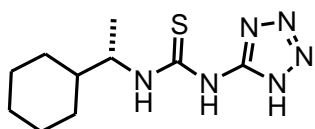


Synthesis of catalyst 9a. To a stirred solution of CS₂ (2.22 mL) and DCC (1.20g, 5.84 mmol) at -10°C, in dry Et₂O, (5 mL), (*S*)- 1-Naphthalen-2-yl-ethylamine (1.0g, 5.84 mmol), in Et₂O (3 mL), was added dropwise. After 1 hour the reaction mixture was warmed to room temperature and stirred for additional 12 hours. The reaction mixture was filtered and the resulting solid was washed with Et₂O. The organic phase was passed through a pad of silica, washed with hexane and concentrated under reduced pressure to afford the isothiocyanate intermediate as a colorless liquid which was used in the next step without further manipulations. Isothiocyanate was diluted in DCM (20 mL) and aminotetrazole-1H₂O (0.381g, 3.70 mmol) was added at room temperature. The resulting suspension was stirred for 48 h and concentrated under reduced pressure. The crude solid was chromatographed using EtOAc/EtOH 3:1 to afford compound **9a** as a white solid in 87% yield (1.51g). Mp = 108-112°C, [α]^{21°C}_D = -107.46 (*c.* 1.488 in MeOH). ¹H NMR (500 MHz, DMSO-*d*₆) δ: 8.12 (d, 1 H, *J* = 8.5Hz), 7.99 (d, 1 H, *J* = 8.0Hz), 7.94 (d, 1H, *J* = 8.5Hz), 6.45 (br.s, 2H), 6.05 (q, 1H, *J* = 6.5Hz), 1.77 (d, 3 H, *J* = 6.5Hz); ¹³C NMR (125 MHz, DMSO-*d*₆) δ: 156.3, 135.3, 133.3, 130.1, 129.1, 128.7, 128.6, 126.6, 125.9, 125.4, 122.9, 122.6, 110.5, 53.3, 22.9.



9b

Synthesis of catalyst 9b. To a stirred solution of CS₂ (3.13 mL) and DCC (1.69g, 8.26 mmol) at -10°C, in dry Et₂O, (5 mL), (*S*)- 1-1-Phenyl-ethylamine (1.0g, 8.26 mmol), in Et₂O (5 mL), was added dropwise. After 1 hour the reaction mixture was warmed to room temperature and stirred for additional 12 hours. The reaction mixture was filtered and the resulting solid was washed with Et₂O. The organic phase was passed through a pad of silica, washed with hexane and concentrated under reduced pressure to afford the isothiocyanate intermediate as a colorless liquid which was used in the next step without further manipulations. Isothiocyanate was diluted in DCM (35 mL) and aminotetrazole-1H₂O (0.851g, 8.25 mmol) was added at room temperature. The resulting suspension was stirred for 48 h and concentrated under reduced pressure. The crude solid was chromatographed using EtOAc/EtOH 3:1 to afford compound **9b** as a white solid in 91% yield (1.85g). Mp = 53-55°C, [α]^{21°C}_D = -7.03 (c. 2.274 in MeOH). ¹H NMR (500 MHz, DMF-*d*₇) δ: 7.62-7.60 (m, 2 H), 7.62-7.59 (m, 4 H), 7.55-7.52 (m, 1 H), 6.67 (br.s, 2H), 5.42 (q, 1H, *J* = 6.5Hz), 3.65 (br.s, 1H), 1.83 (d, 3H, *J* = 6.5Hz); ¹³C NMR (125 MHz, DMF-*d*₇) δ: 158.7, 142.0, 132.4, 130.3, 129.8, 129.6, 127.7, 127.1, 58.3, 25.3

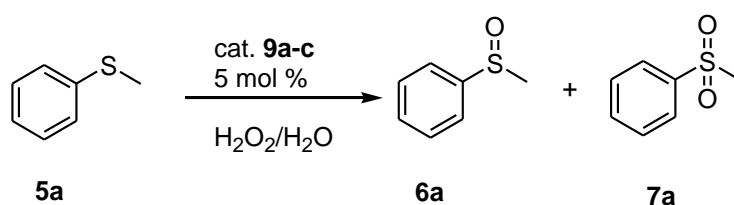


9c

Synthesis of catalyst 9c. To a stirred solution of CS₂ (3.13 mL) and DCC (1.69g, 8.26 mmol) at -10°C, in dry Et₂O, (5 mL), (*S*)- 1-1-cyclohexyl-ethylamine (1.05g, 8.26 mmol), in Et₂O (5 mL), was added dropwise. After 1 hour the reaction mixture was warmed to room temperature and stirred for additional 12 hours. The reaction mixture was filtered and the resulting solid was washed with Et₂O. The organic phase was passed through a pad of silica, washed with hexane and concentrated under reduced pressure to afford the isothiocyanate intermediate as a colorless liquid which was used in the next step without further manipulations. Isothiocyanate was diluted in DCM (35 mL) and aminotetrazole-1H₂O (0.851g, 8.25 mmol) was added at room temperature. The resulting

suspension was stirred for 48 h and concentrated under reduced pressure. The crude solid was chromatographed using EtOAc/EtOH 3:1 to afford compound **9c** as a white solid in 90% yield (1.88g). Mp = 68-70°C, $[\alpha]_{\text{D}}^{22} = +31.83$ (c. 2.764 in DMSO). $^1\text{H NMR}$ (500 MHz, DMSO- d_6) δ : 6.40 (br.s., 2 H), 3.75 (quint, 1 H, $J = 6.5\text{Hz}$), 1.76-1.67 (m, 3 H), 1.63-1.58 (m, 2H), 1.45-1.38 (m, 1H), 1.24 (d, 3H, $J = 6.5\text{Hz}$), 1.22-1.14 (m, 2H), 1.11-1.03 (m, 1H), 1.00 (dd, 1H, $J = 3.0\text{Hz}$, $J = 14.0\text{Hz}$), 0.95 (dd, 1H, $J = 2.5\text{Hz}$, $J = 12.0\text{Hz}$); $^{13}\text{C NMR}$ (125 MHz, DMSO- d_6) δ : 156.6, 128.2, 58.5, 42.9, 29.0, 27.5, 25.7, 25.4, 25.3, 18.5.

1.4 General procedure for the oxidation of sulphide **5a** using catalysts **9a-c**/ H_2O_2 .



Method A (room temperature oxidation) To a 3 M solution of sulphide **5a** (100 mg, 0.8 mmol) and tetrazole thiourea **9a** (5 mol. %) in water (2.7 mL), H_2O_2 (30% v/v in water, 1.1 equiv.) was added in one injection and the resulting mixture was stirred at room temperature and followed by Gc-Ms until completion (**6a/7a** ratio $>99<1$). The reaction mixture was filtered and the water solution was extracted with. The organic phase was dried on Na_2SO_4 , filtered and concentrated under reduced pressure. The catalyst was recovered by washing up the filtered solid with Ethyl acetate and dried. Pure sulphoxide **6a** was obtained after flash column chromatography (silica gel, 80:20 hexane/ether) in 92% yield. Colorless oil. HPLC chiral column: Phenomenex IPA/Hex 90:10, 1.0 mL/min, $\lambda = 254\text{ nm}$, $R_t = 14.10$, $R_t = 18.33$ (e.r. 49:51).

Method B (0°C oxidation) To a 3 M solution of sulphide **5a** (100 mg, 0.8 mmol) and tetrazole thiourea **9a** (5 mol. %) in water (2.7 mL), H_2O_2 (30% v/v in water, 1.1 equiv.) was added in one injection and the resulting mixture was stirred at room temperature and followed by Gc-Ms until completion (**6a/7a** ratio $>99<1$). The reaction mixture was filtered and the water

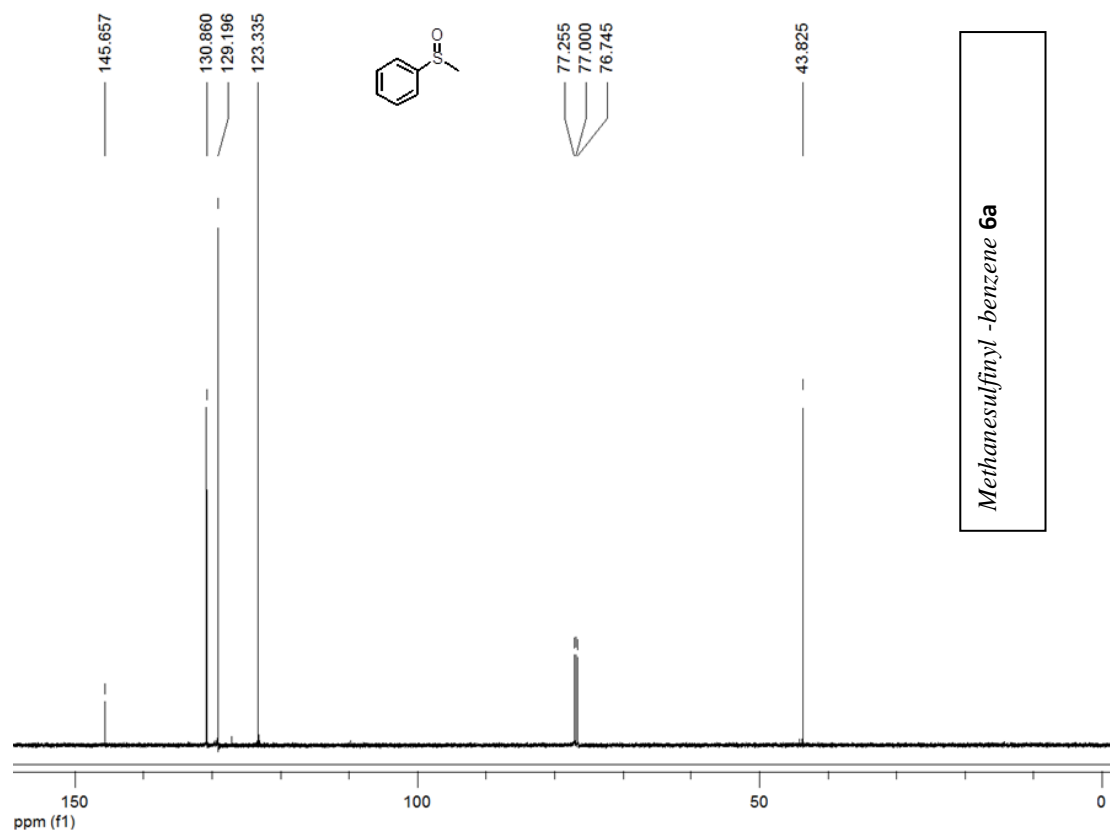
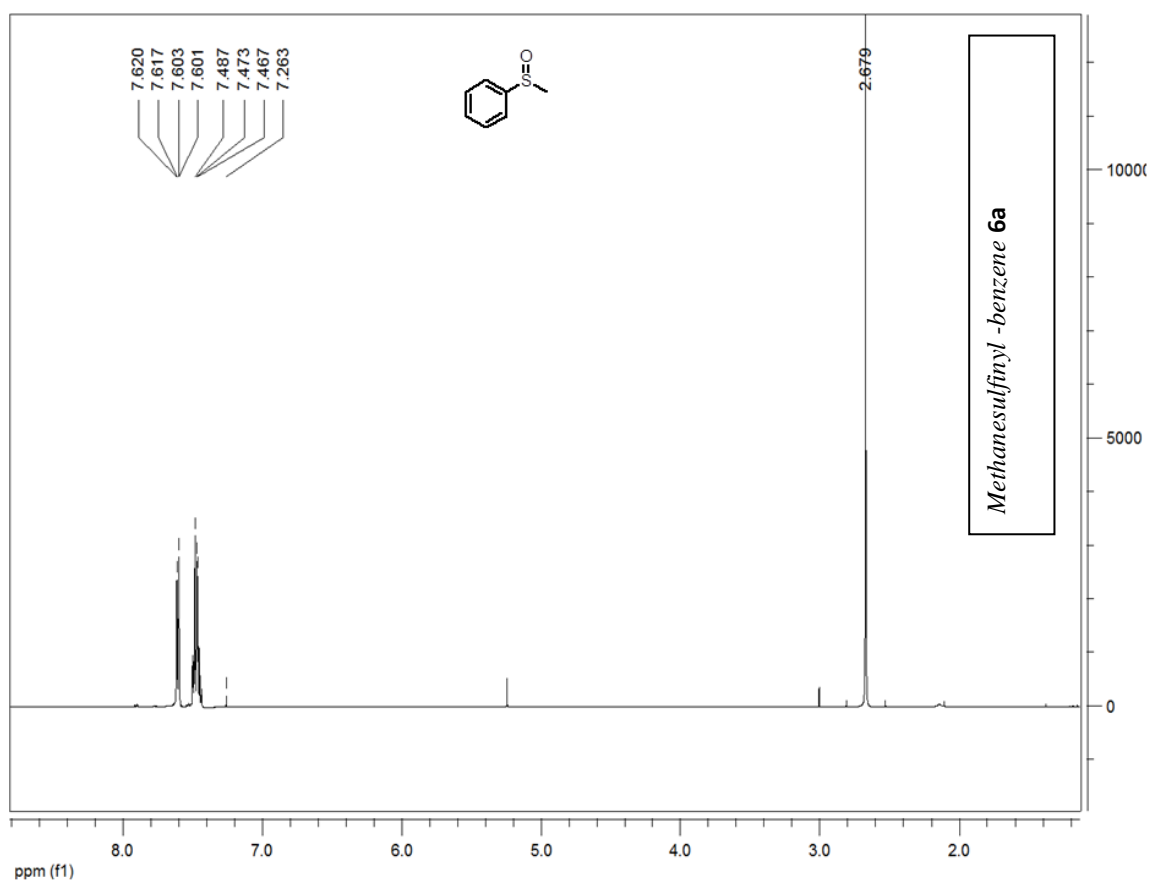
solution was extracted with. The organic phase was dried on Na₂SO₄, filtered and concentrated under reduced pressure. The catalyst was recovered by washing up the filtered solid with Ethyl acetate and dried. Pure sulphoxide **6a** was obtained after flash column chromatography (silica gel, 80:20 hexane/ether) in 90% yield. Colorless oil. Colorless oil. HPLC chiral column: Phenomenex IPA/Hex 90:10, 1.0 mL/min, $\lambda = 254$ nm, Rt = 14.10, Rt = 18.33 (e.r. 48:52).

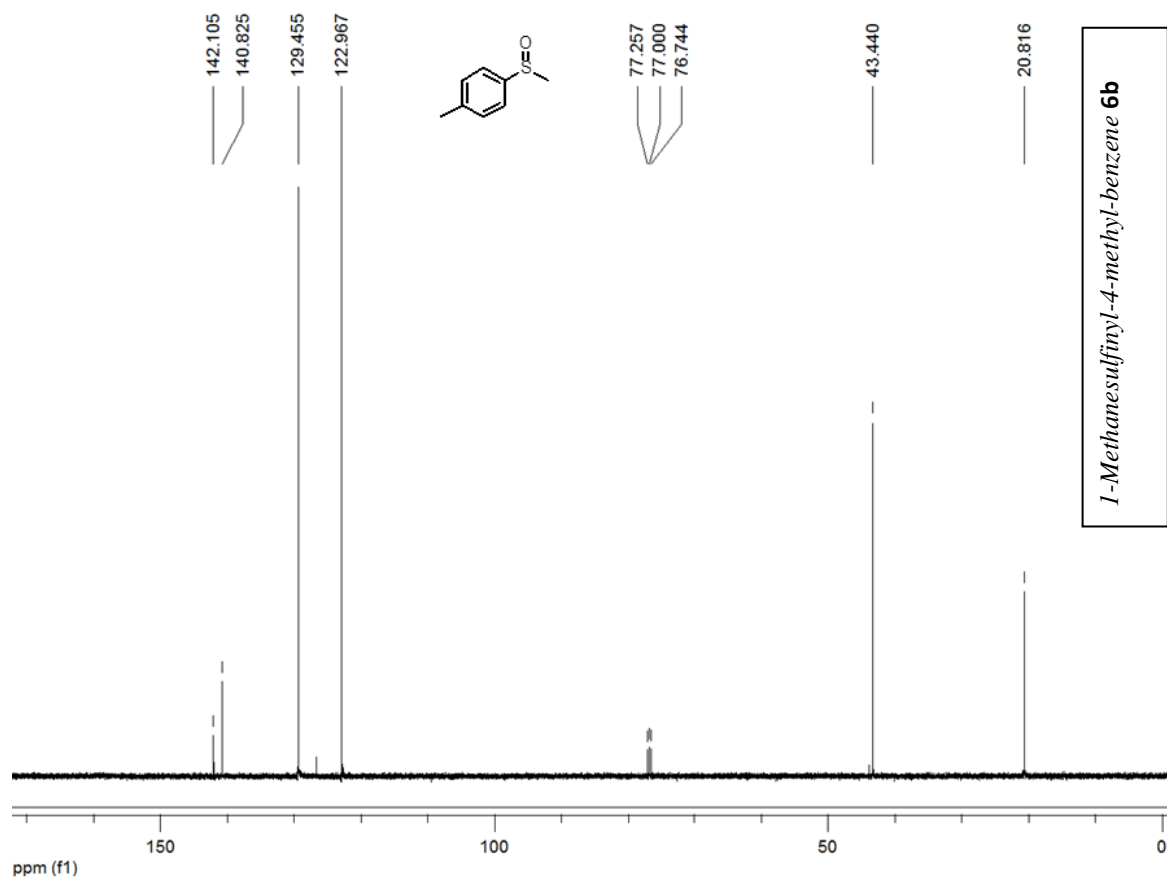
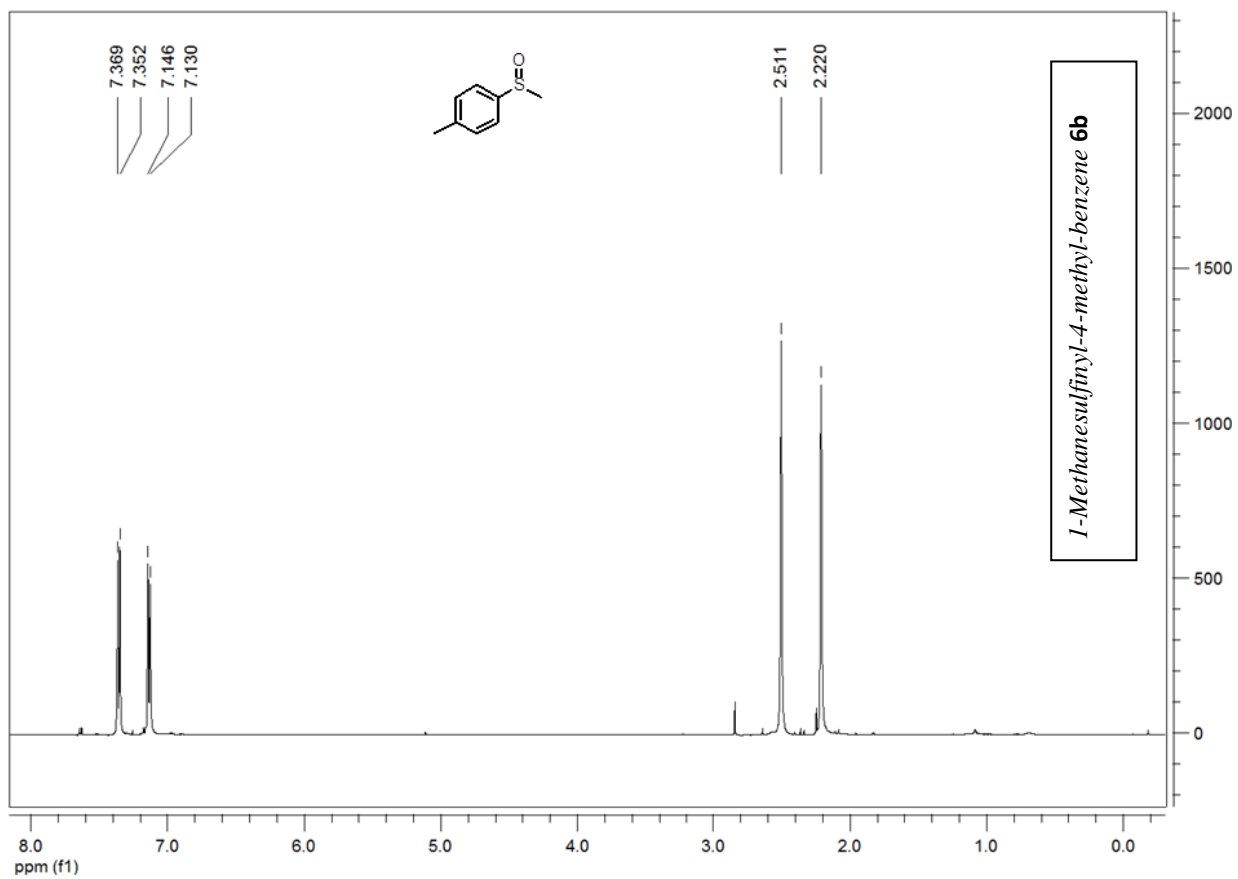
1.5 Catalyst recovery procedure

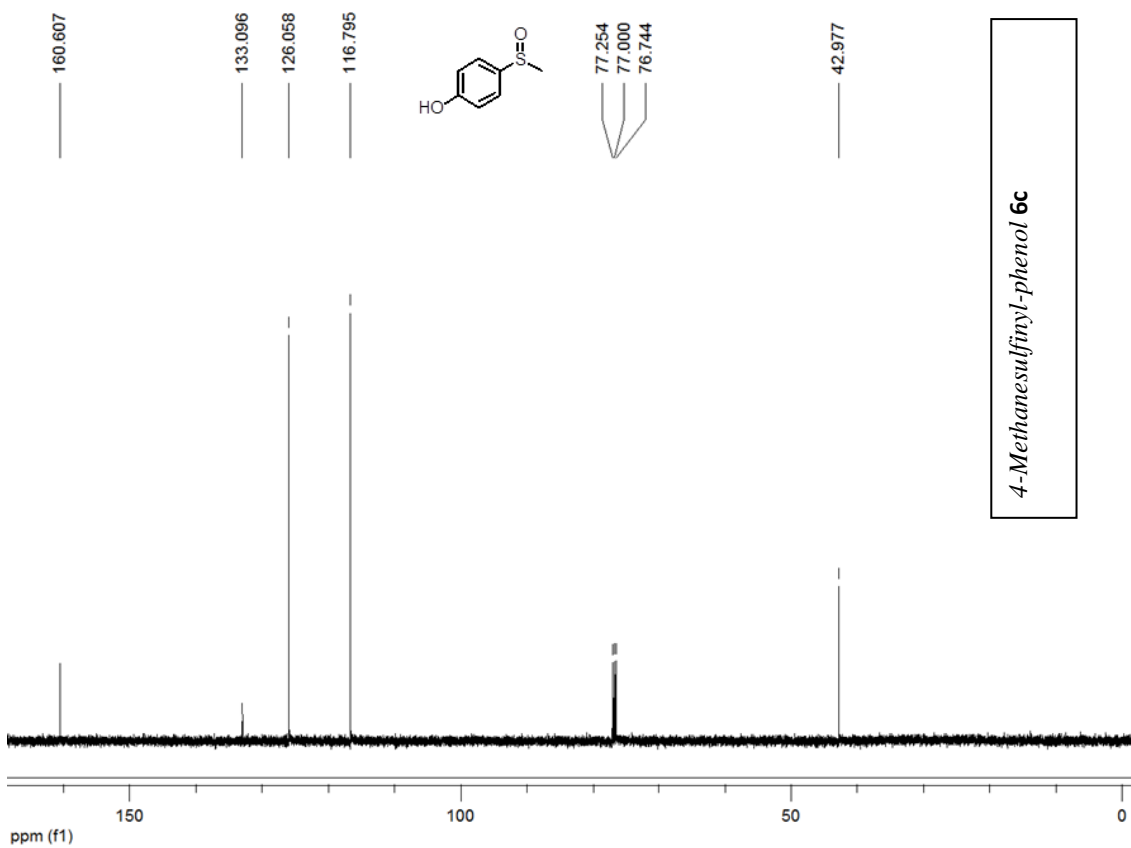
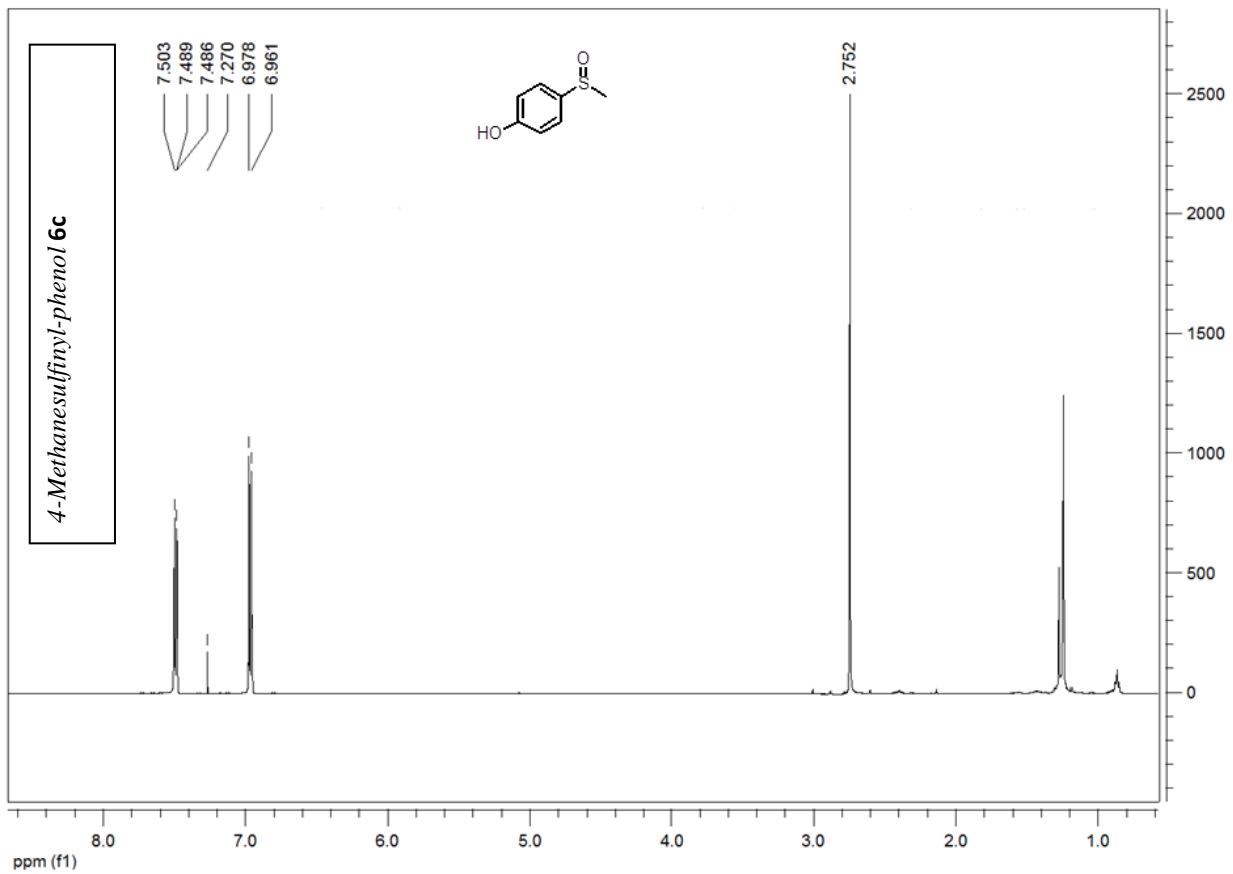
To value the catalyst recovery, we carried out a set of experiments as reported:

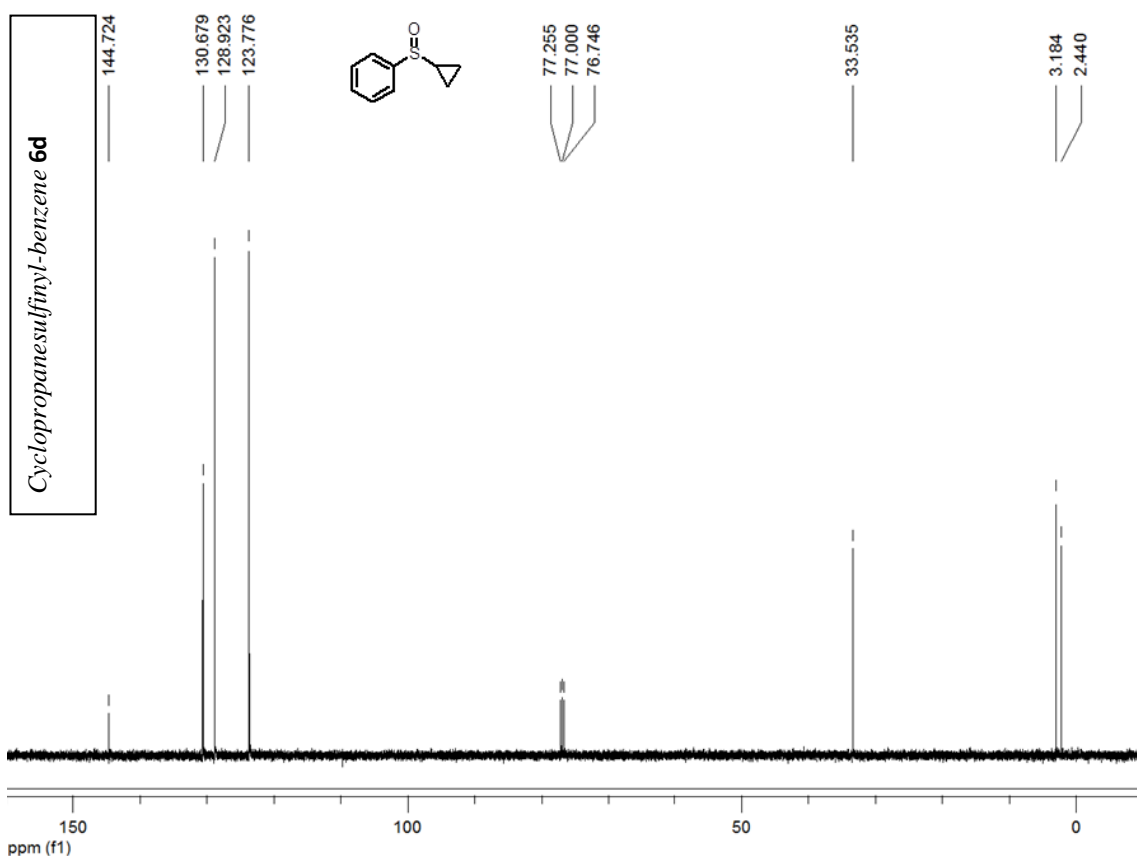
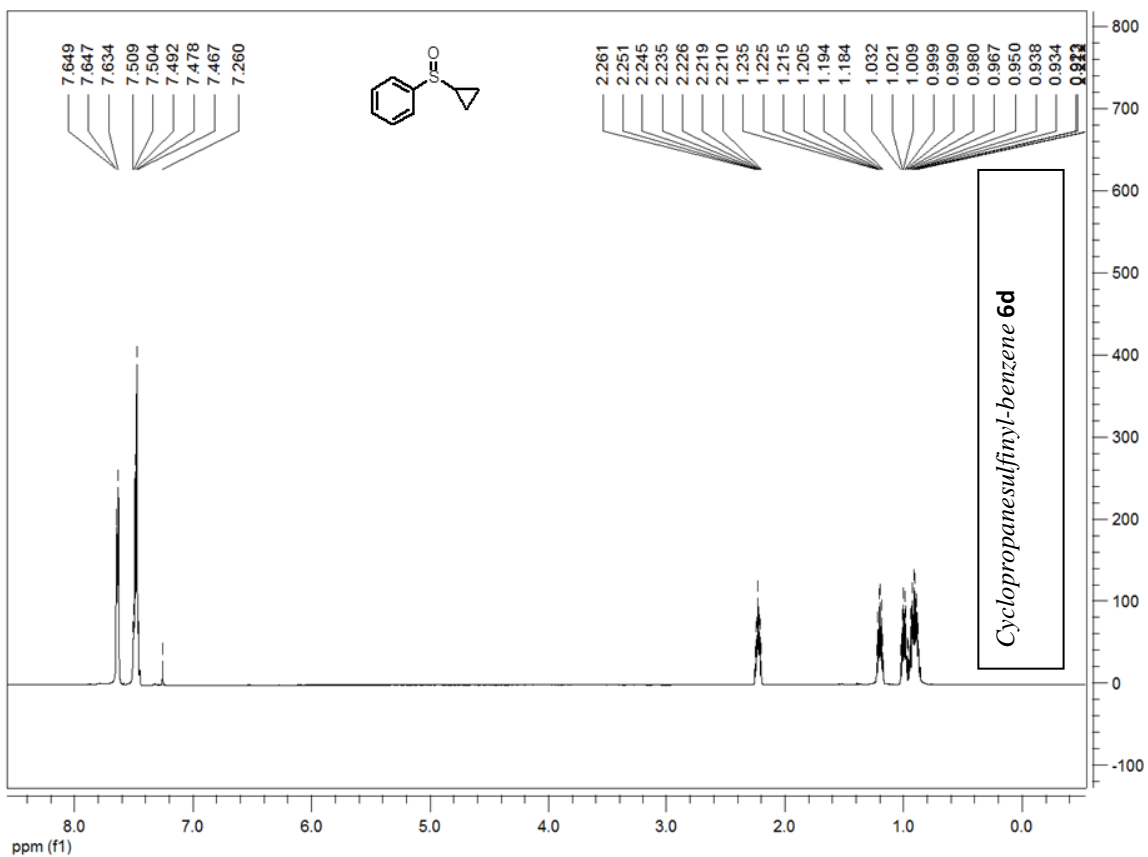
- 1) 150 mg of cat. **2a** were loaded for the oxidation of 2 g of sulphide **5a**. At completion, the reaction mixture was filtered and washed with EtOAc (2 x 30 mL). Cat. **2a** was collected and dried under reduced pressure for 12h at room temperature. The catalyst recovery % was determined by weighting of the dried white solid. (132 mg of catalyst, 88% recovered).
- 2) 130 mg of cat. **2a** were loaded for the oxidation of 1.73 g of sulphide **5a**. After filtration and drying, the catalyst recovery % was determined by weighting of the dried white solid. (113 mg of catalyst, 87% recovered).
- 3) 100 mg of cat. **2a** were loaded for the oxidation of 1.33 g of sulphide **5a**. After filtration and drying, the catalyst recovery % was determined by weighting of the dried white solid. (76 mg of catalyst, 76% recovered).

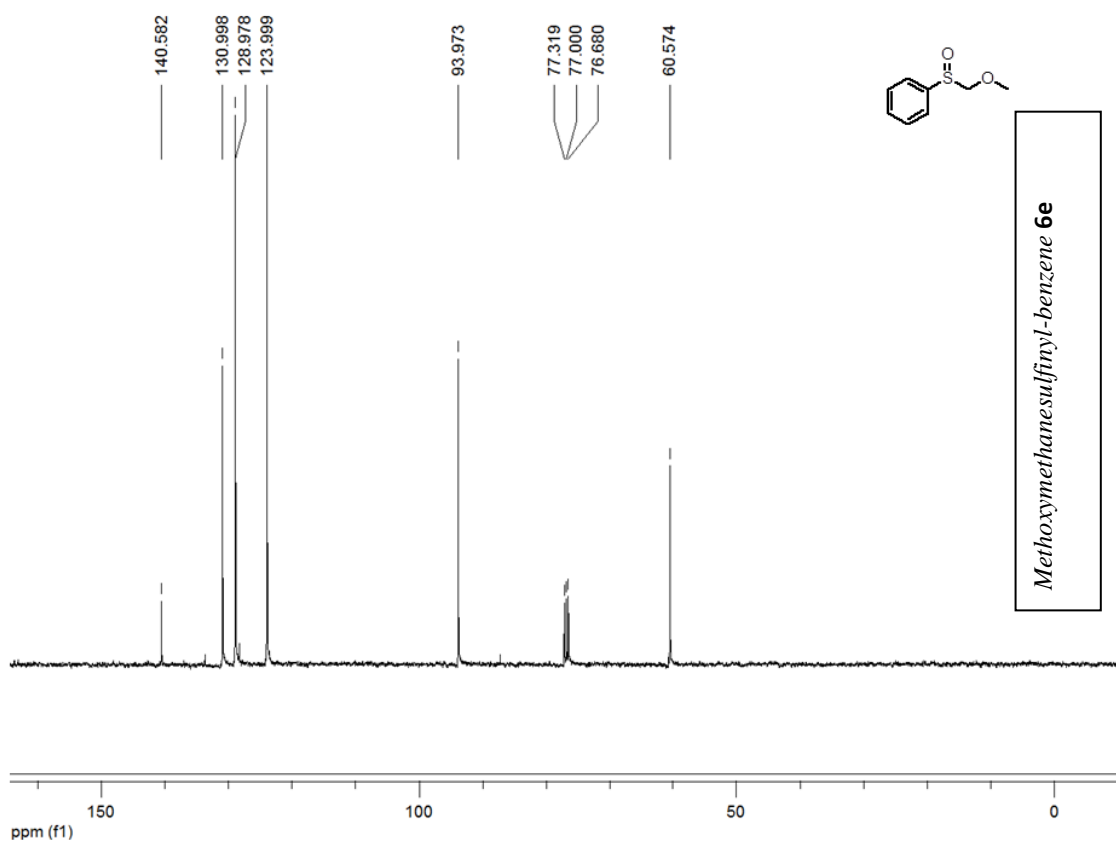
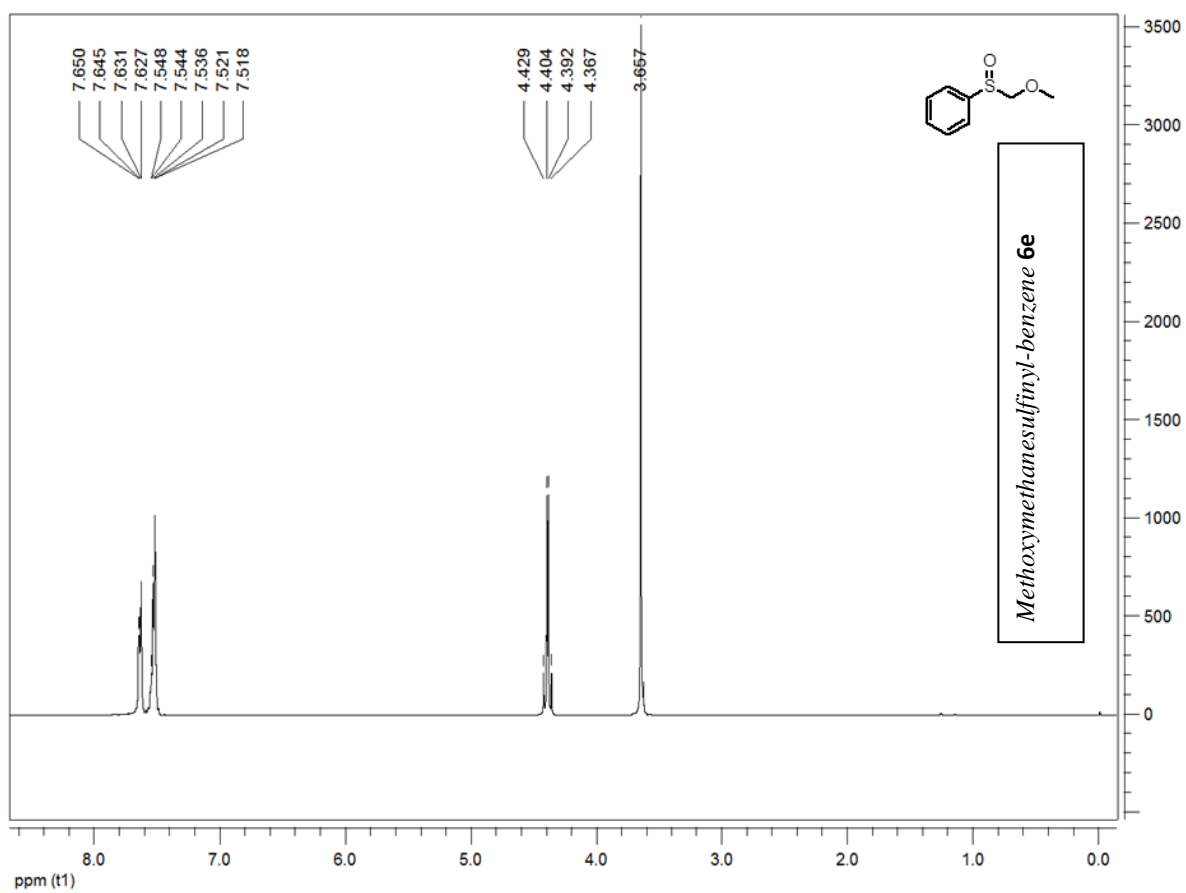
^1H and ^{13}C NMR spectra of compound 6a-p

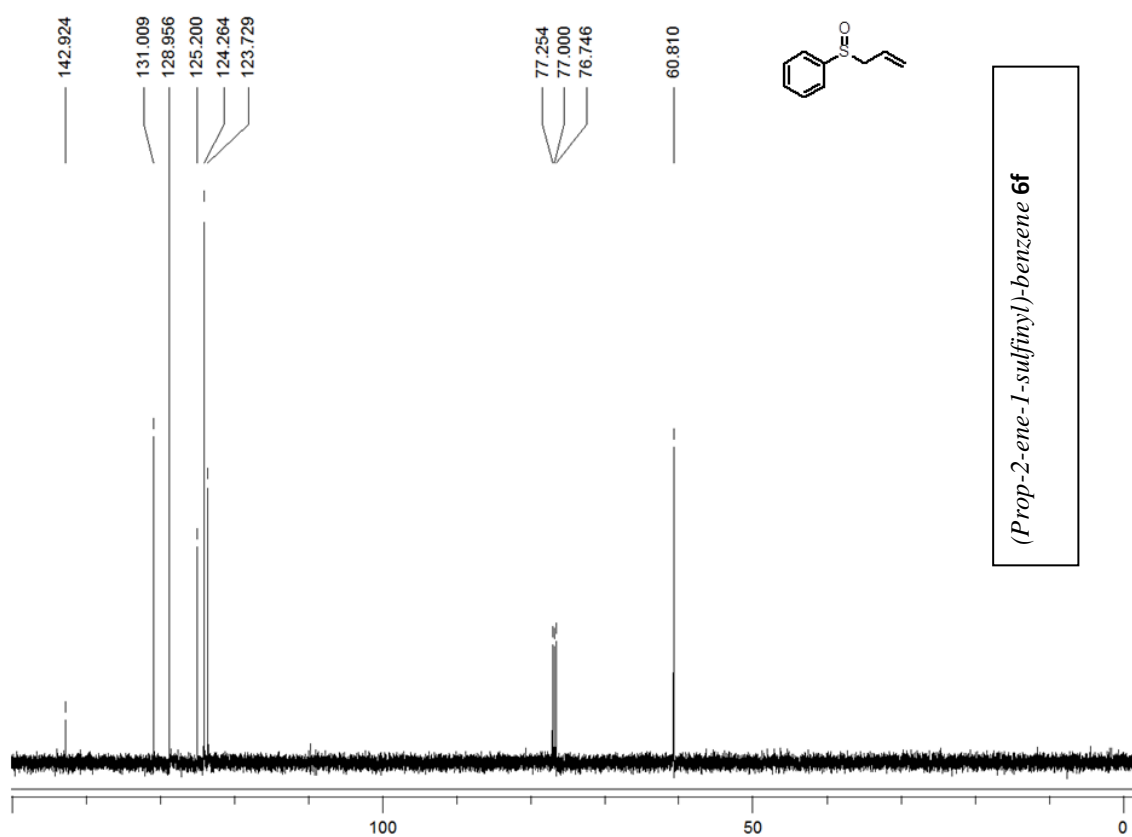
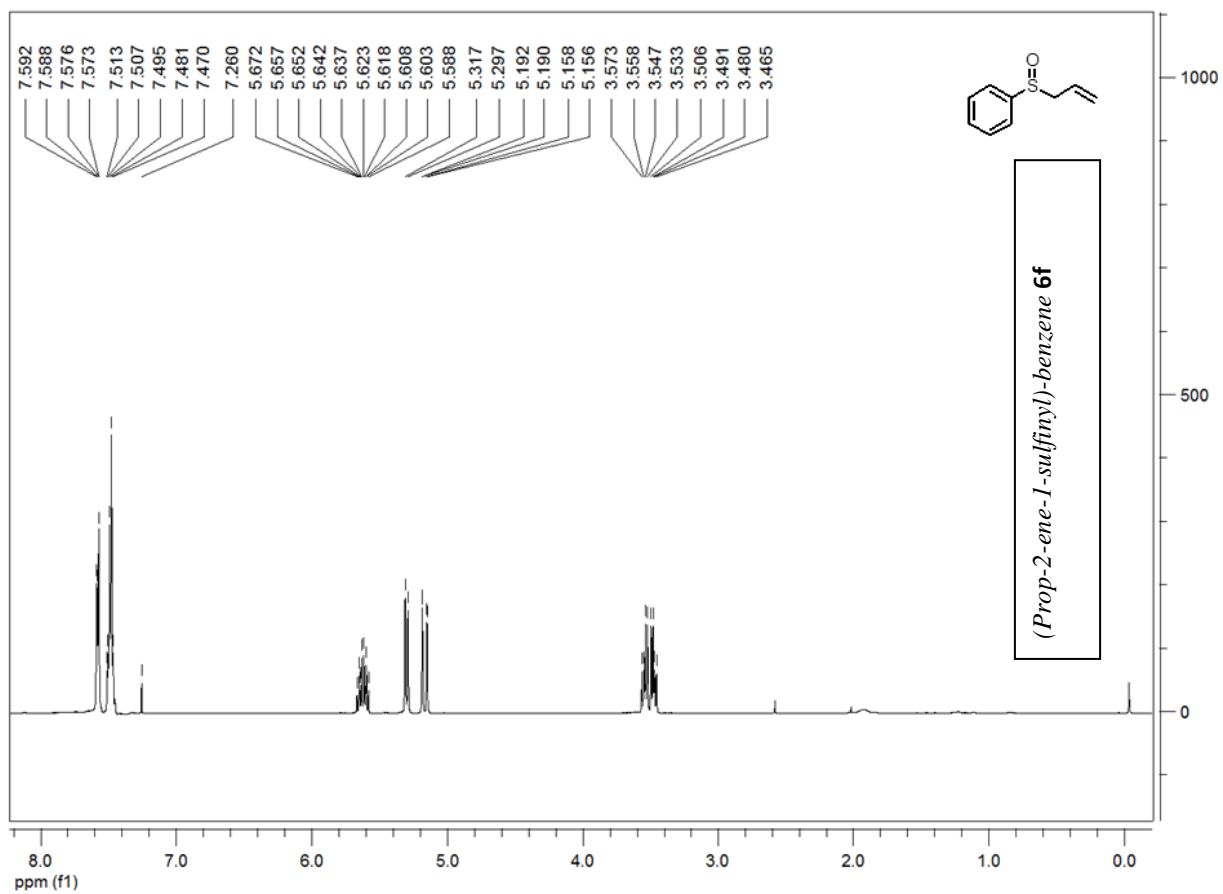


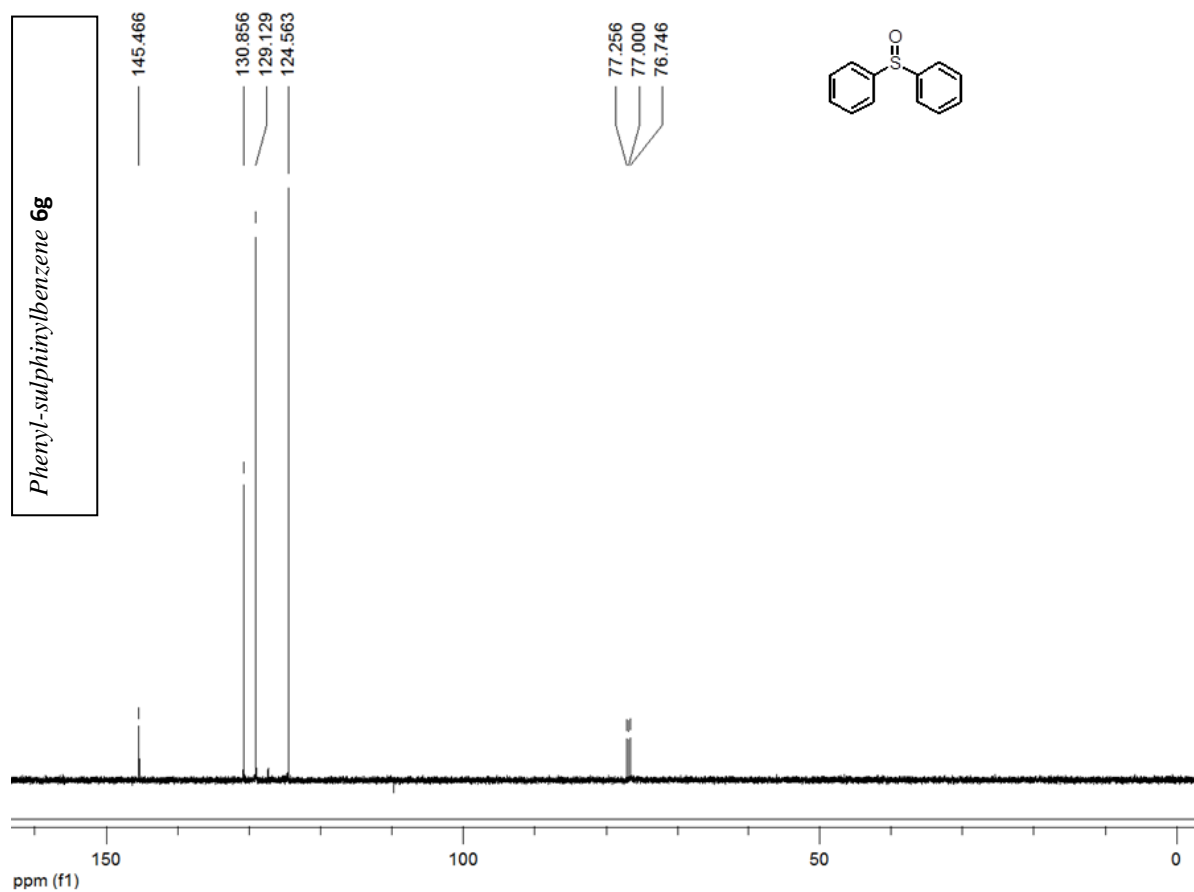
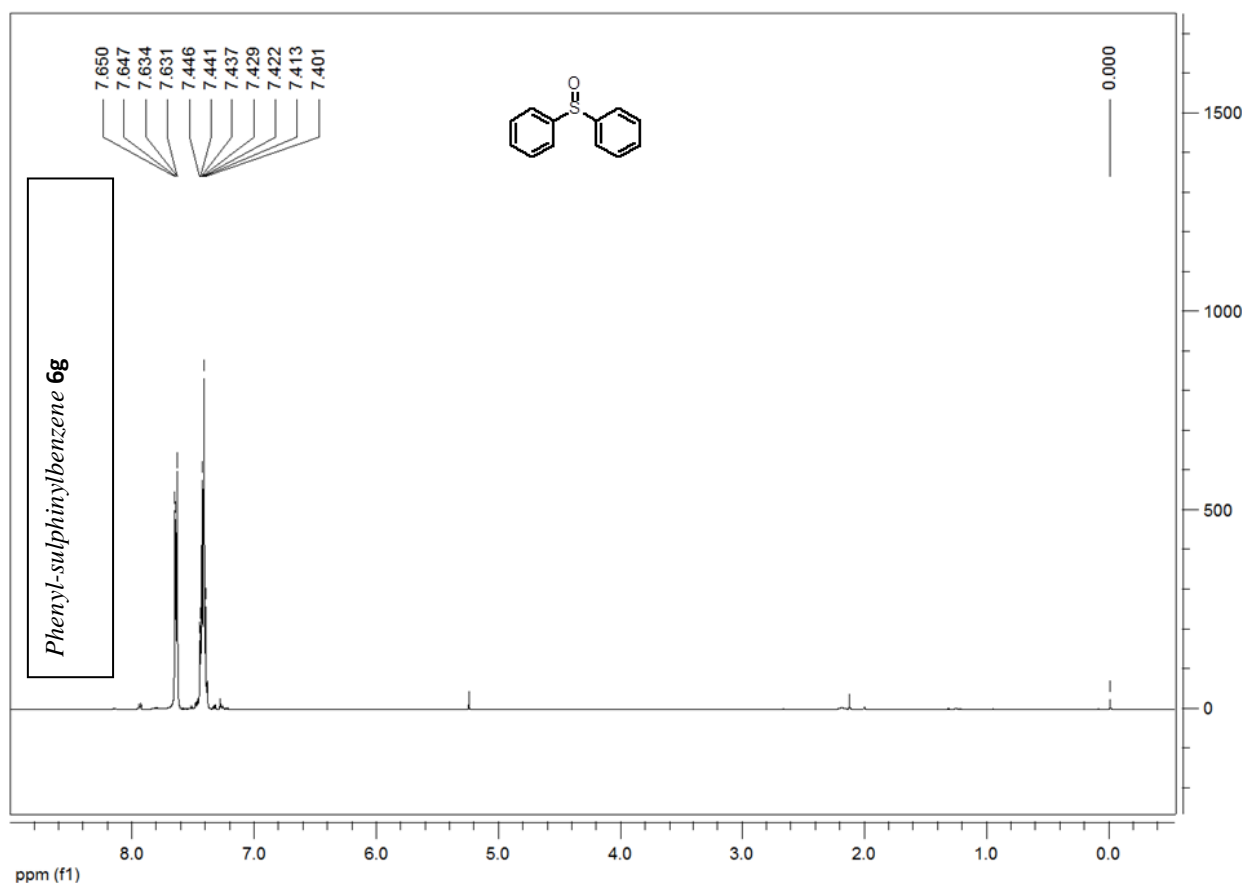


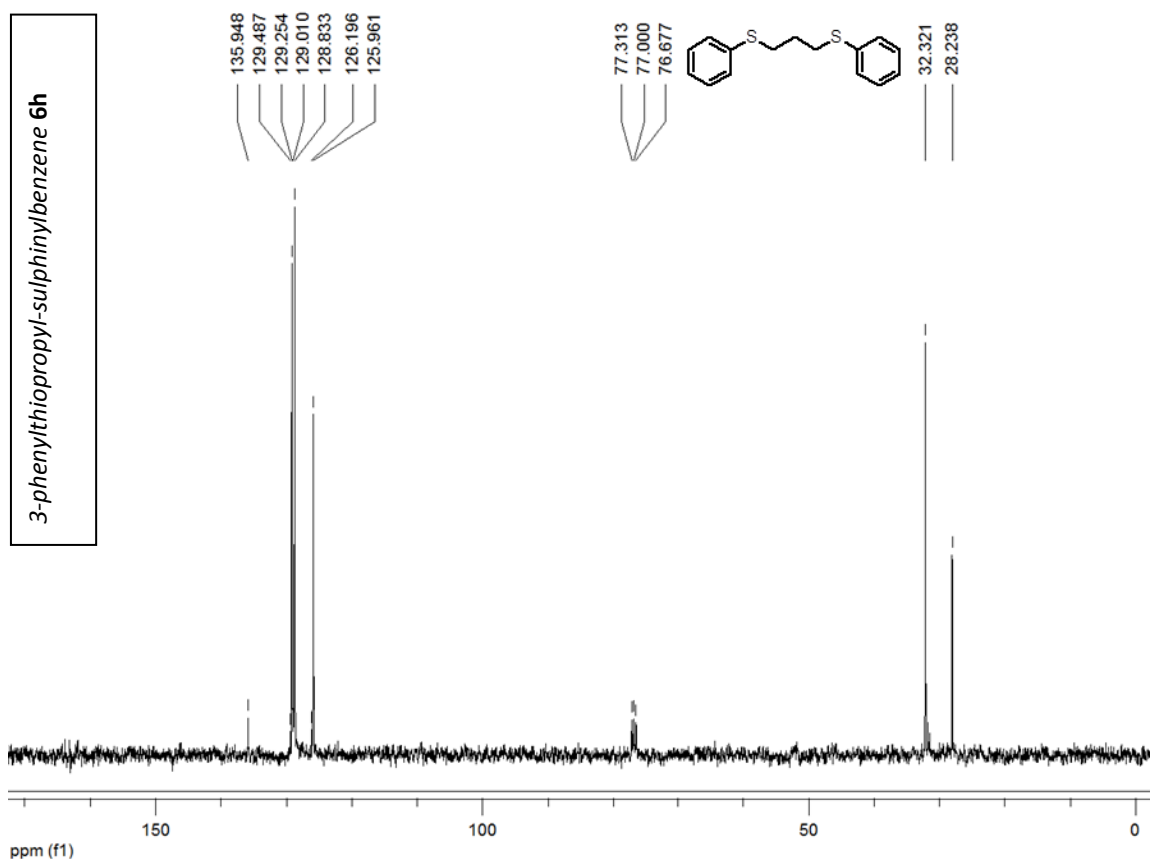
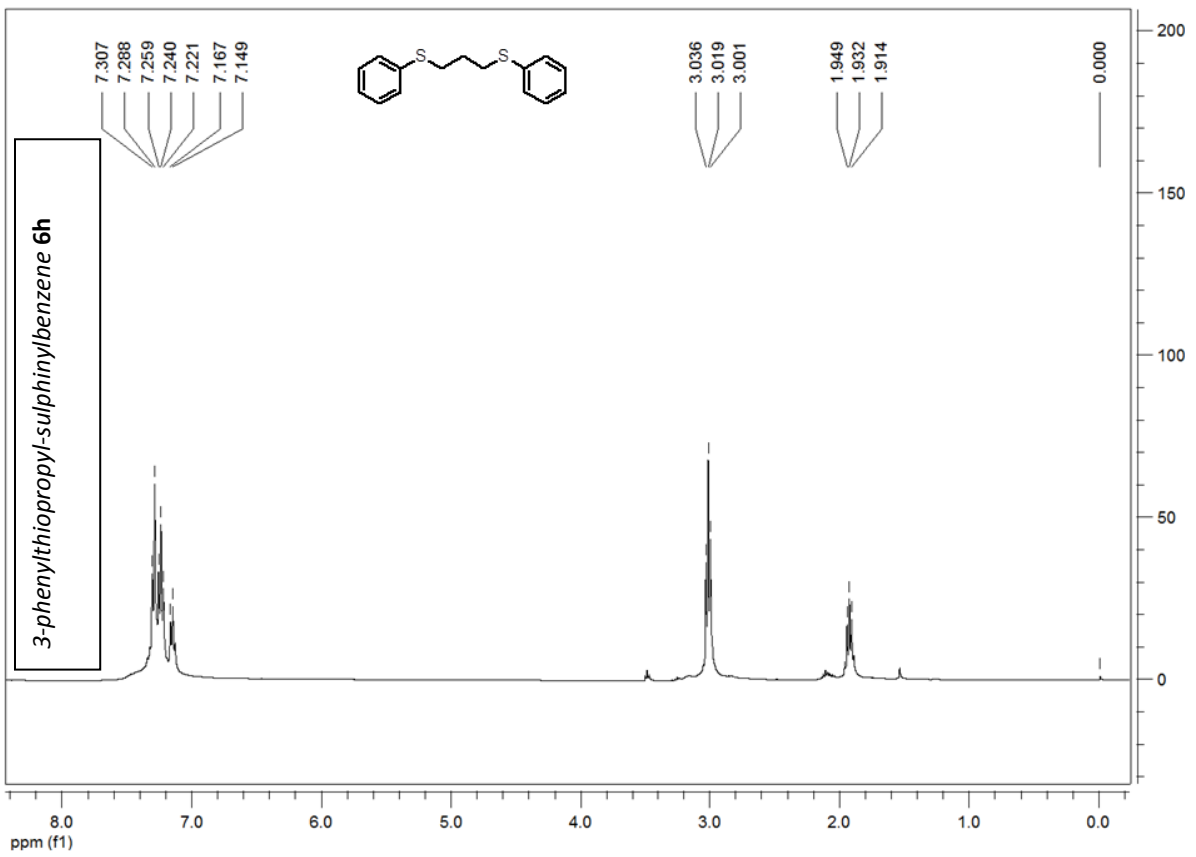


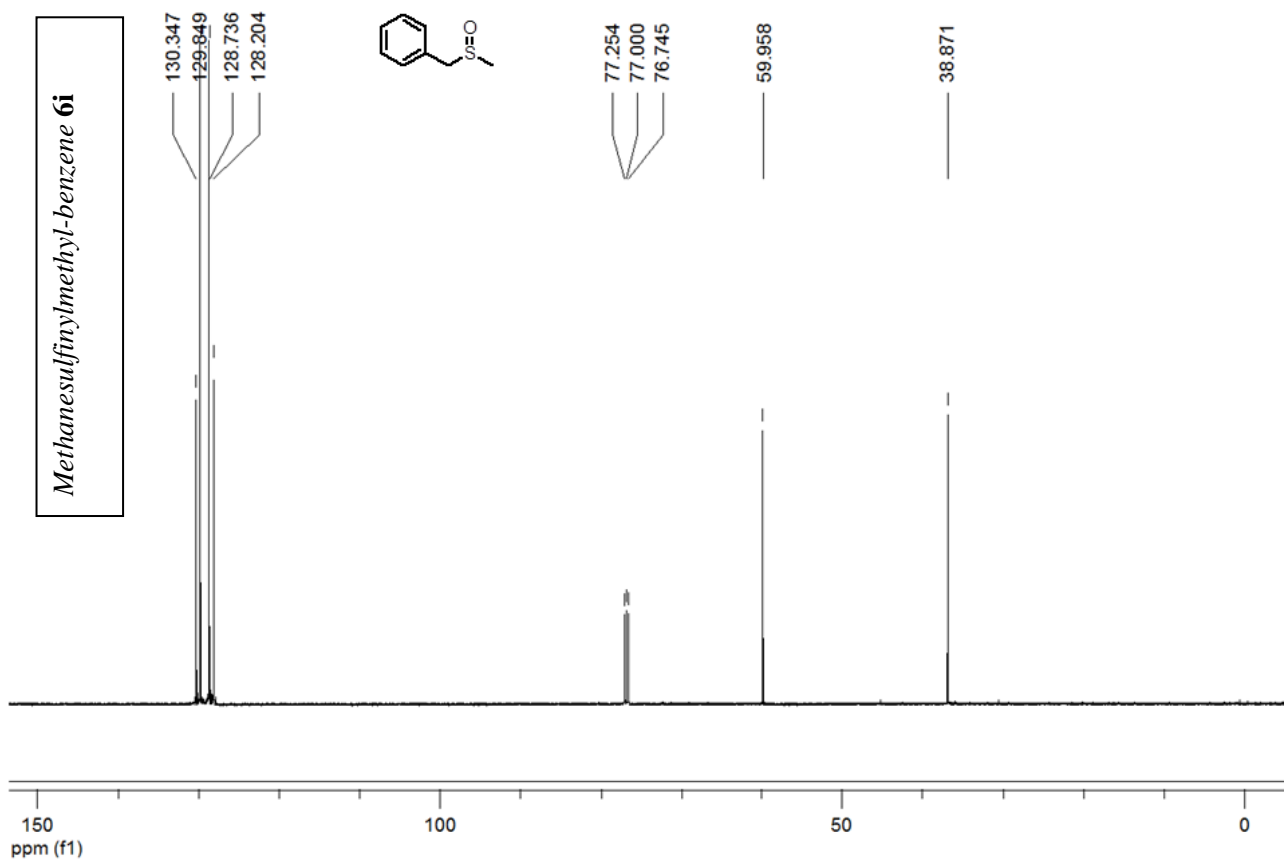
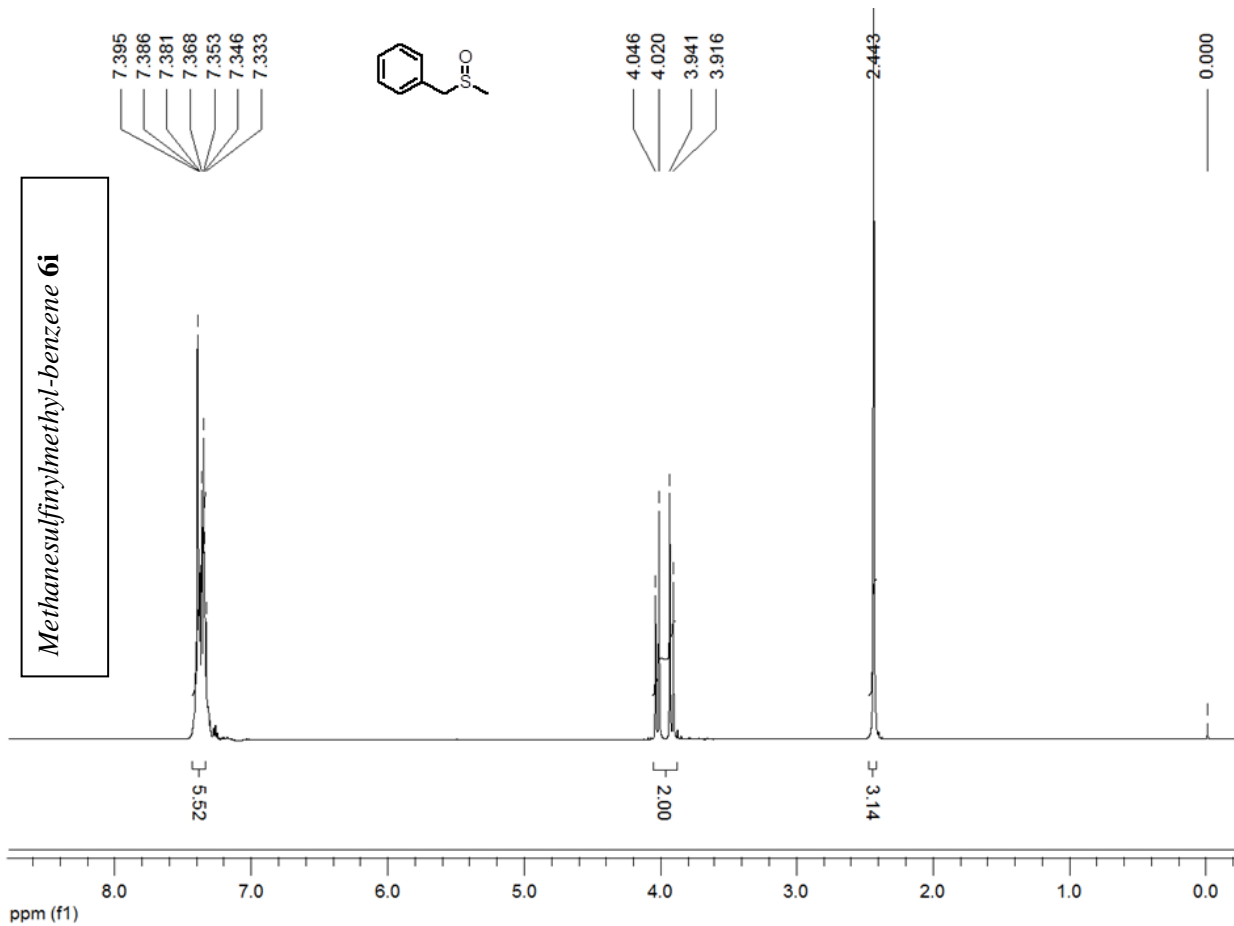


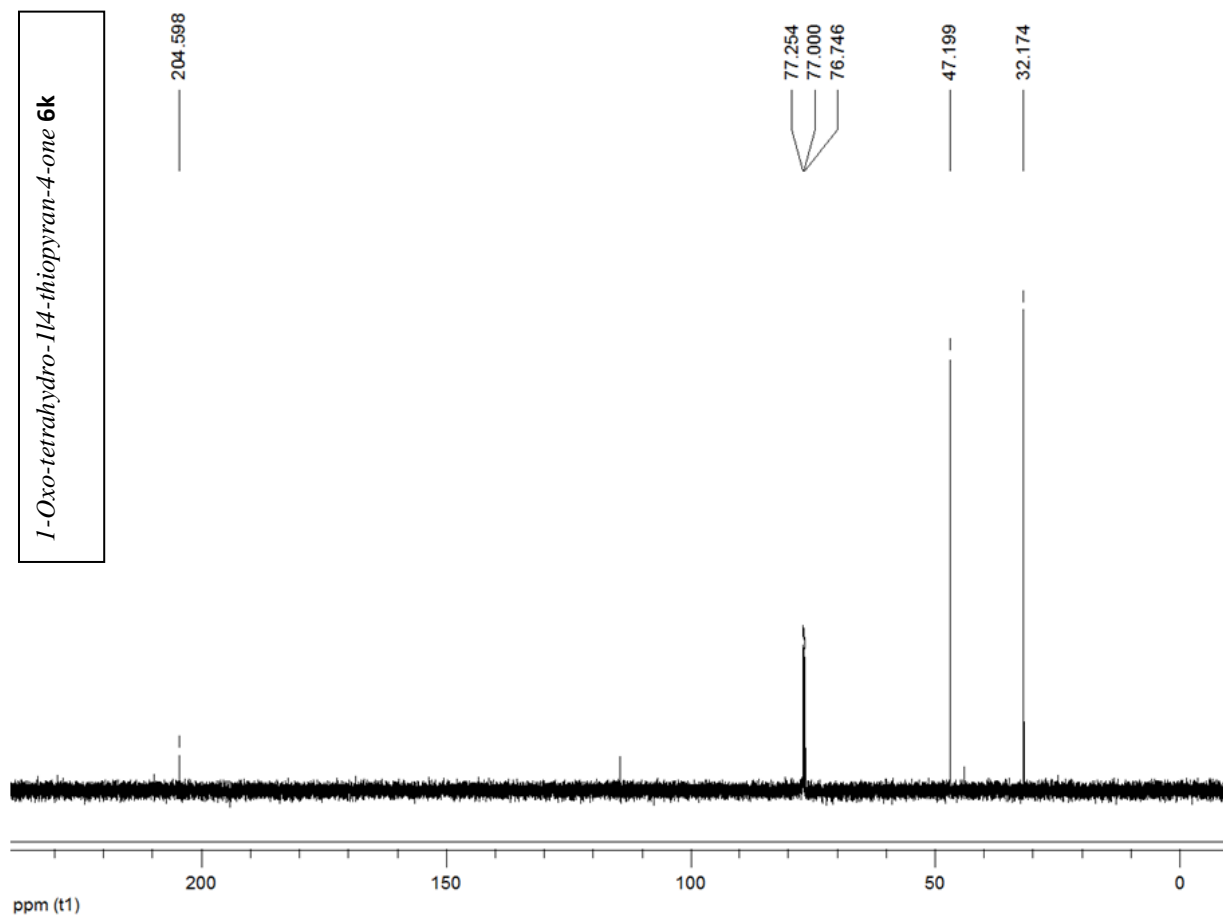
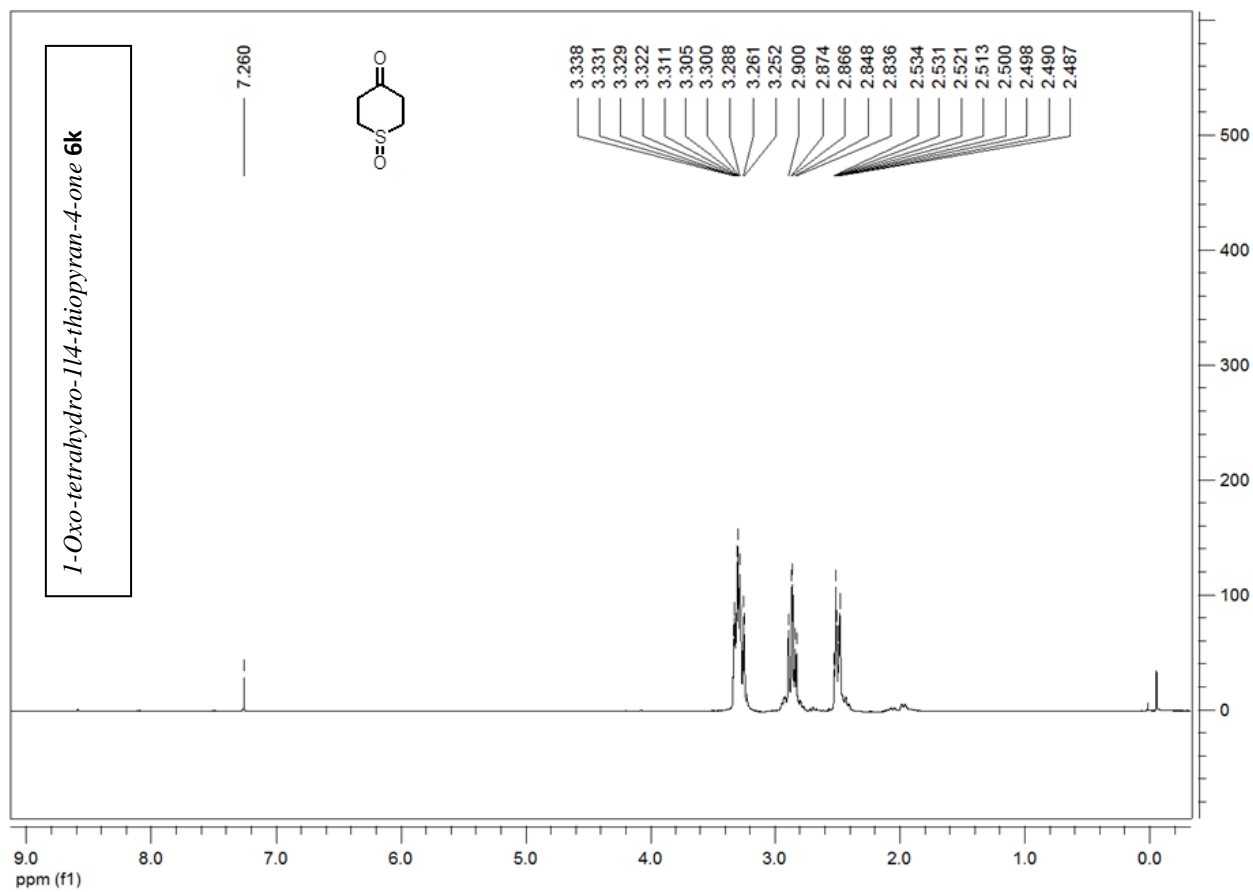


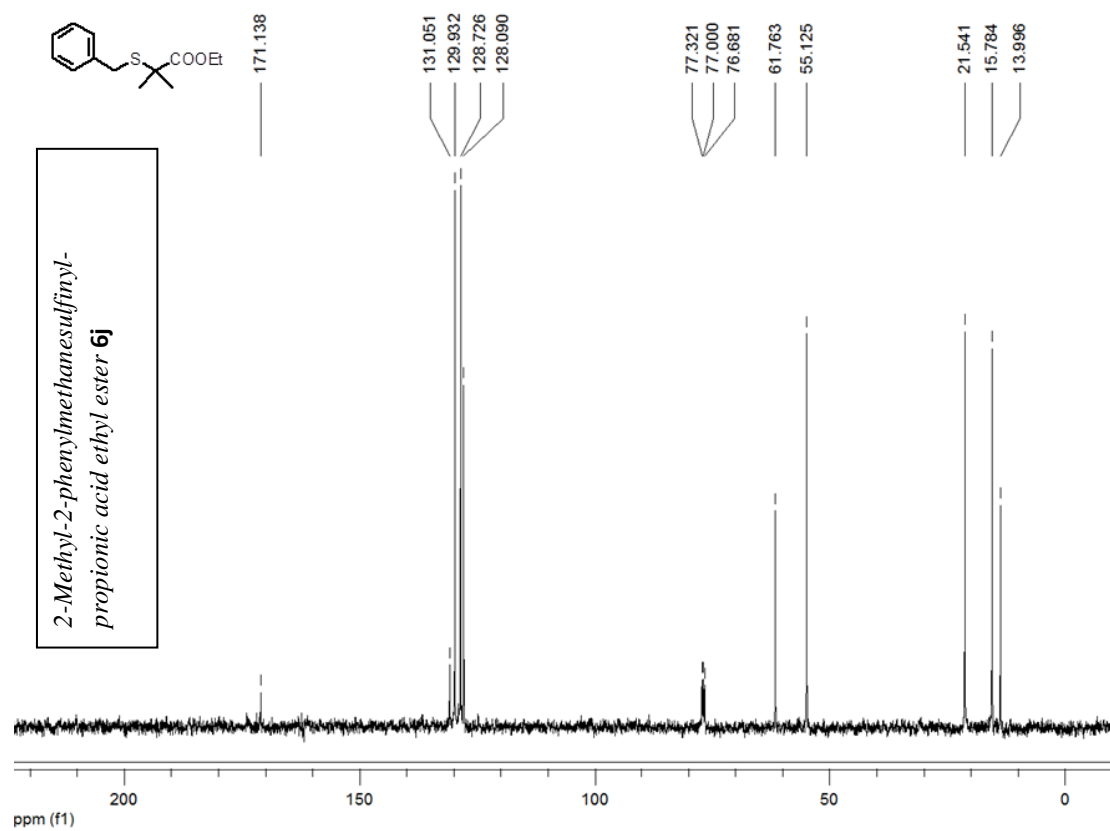
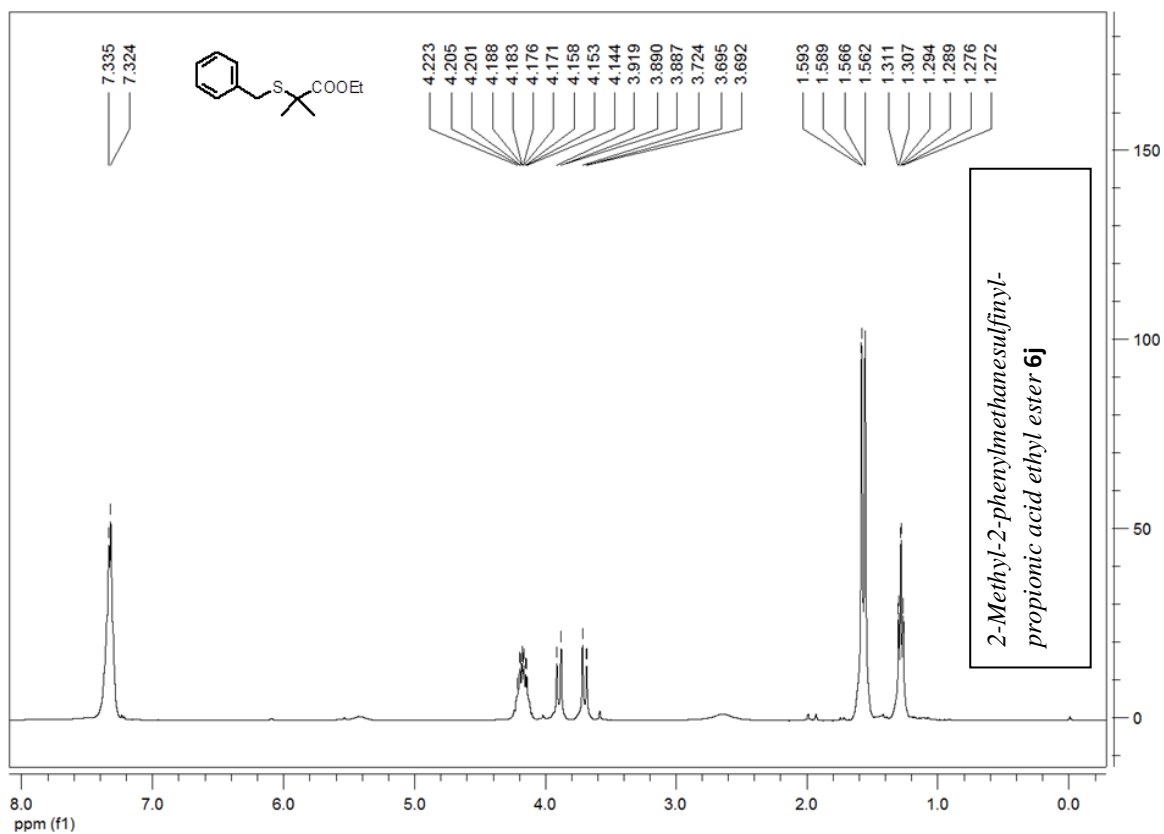


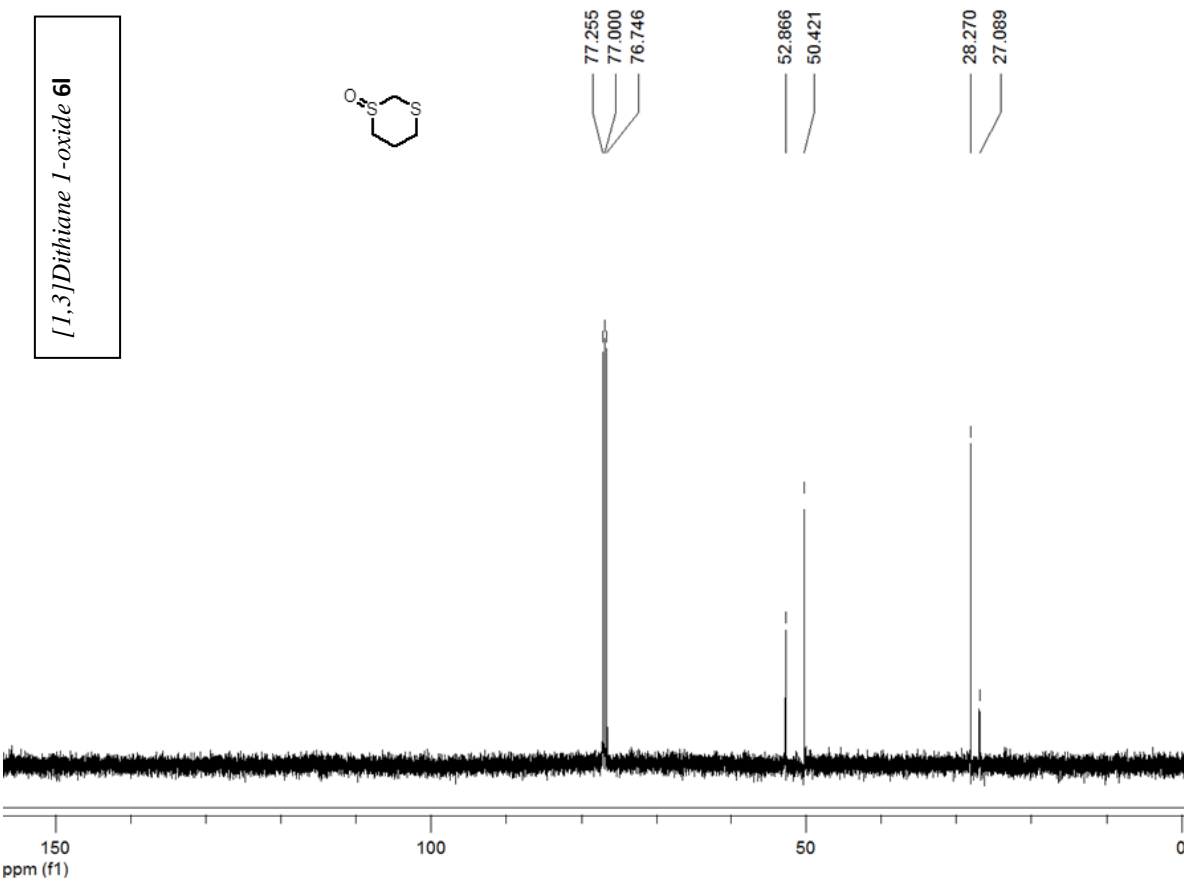
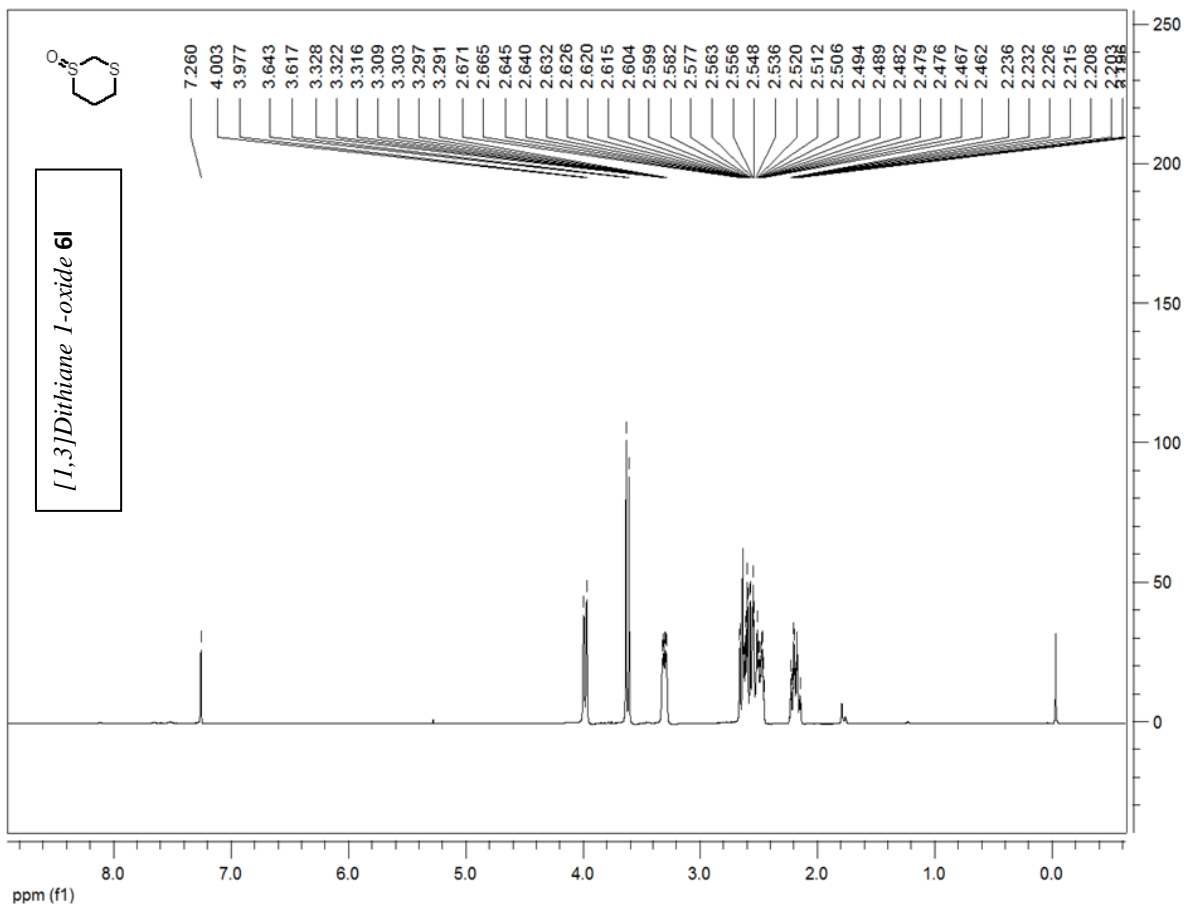


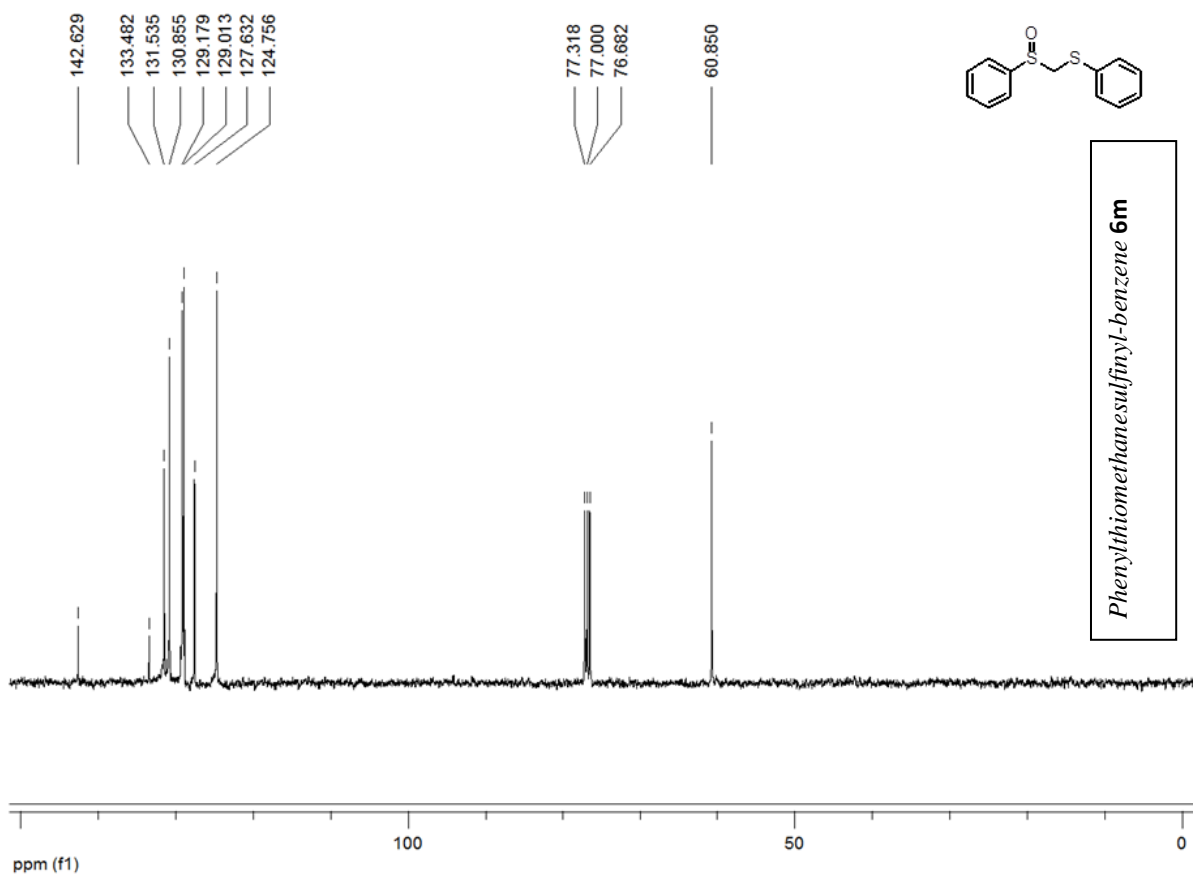
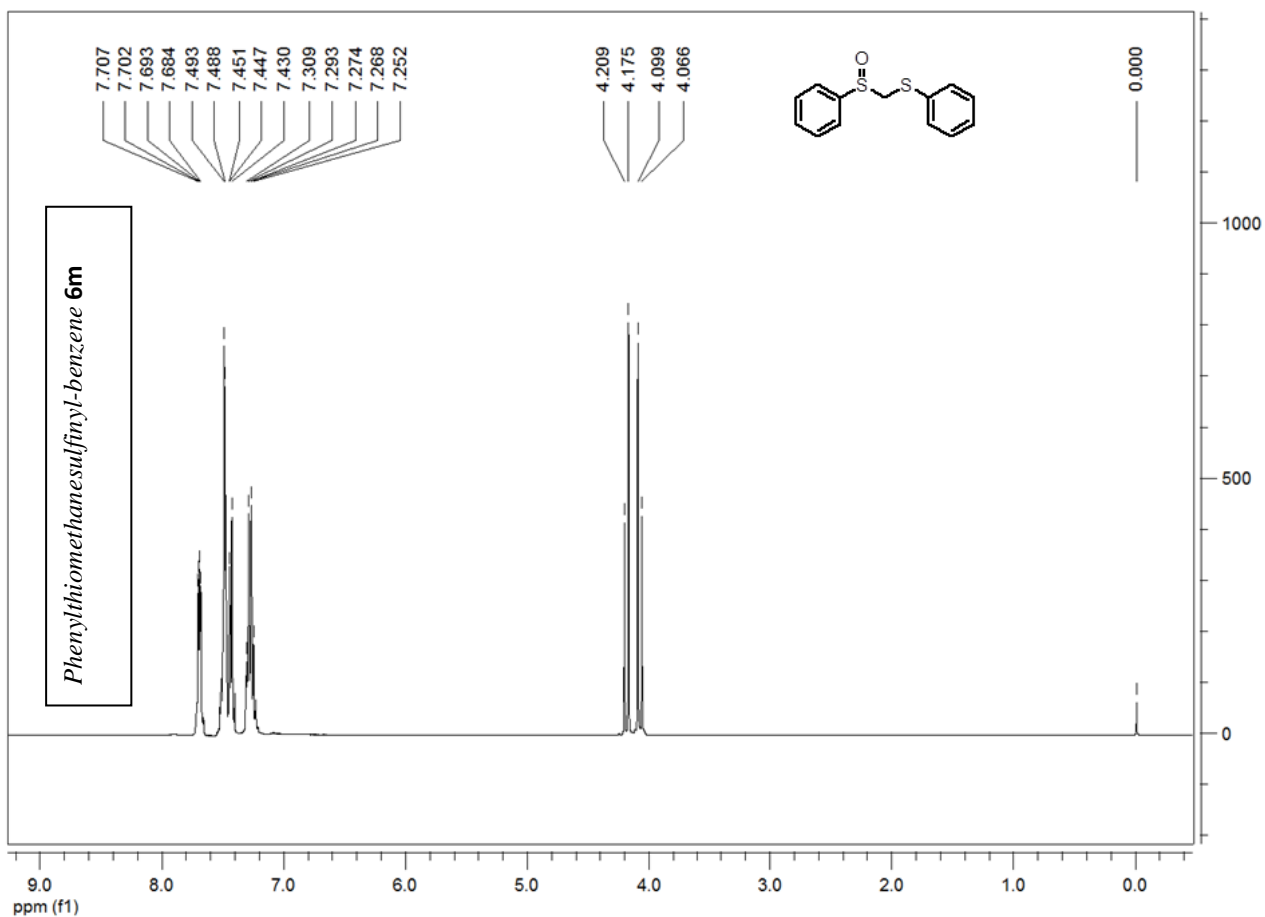


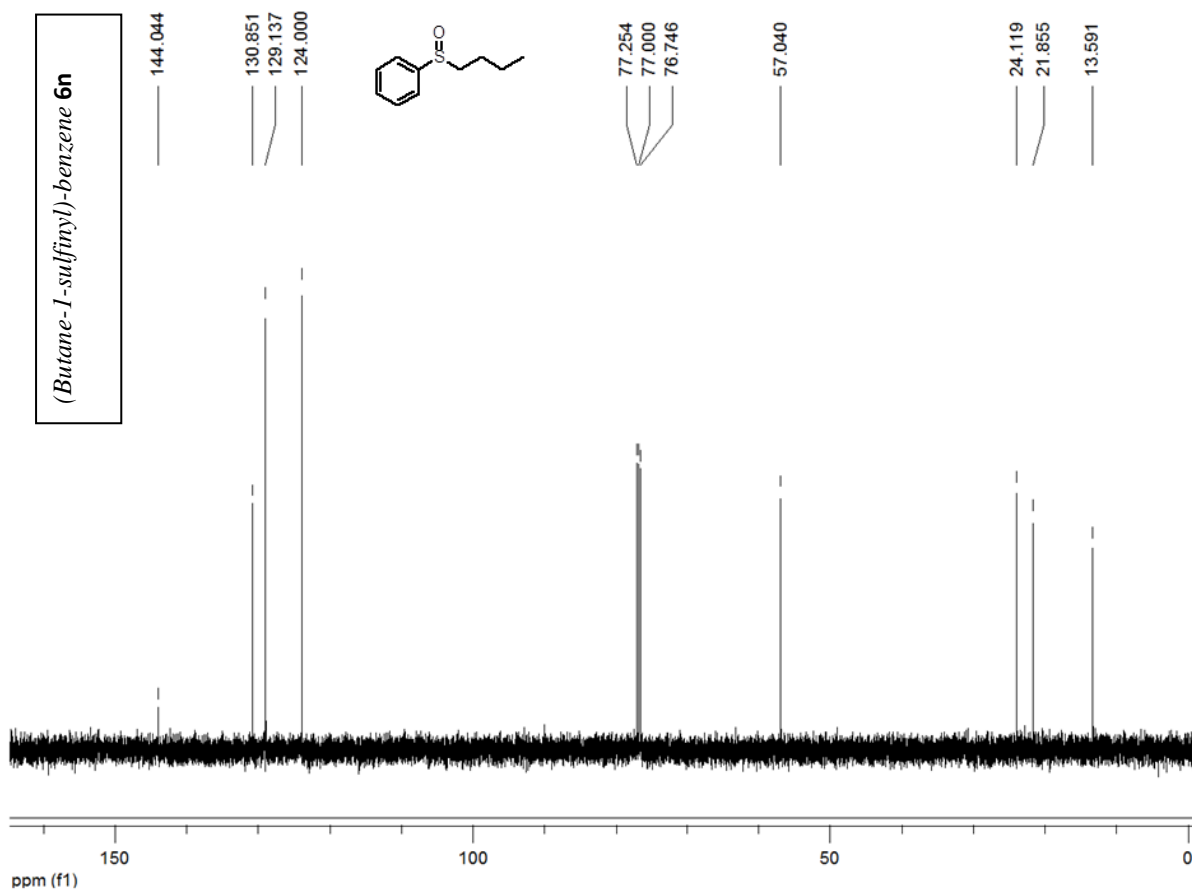
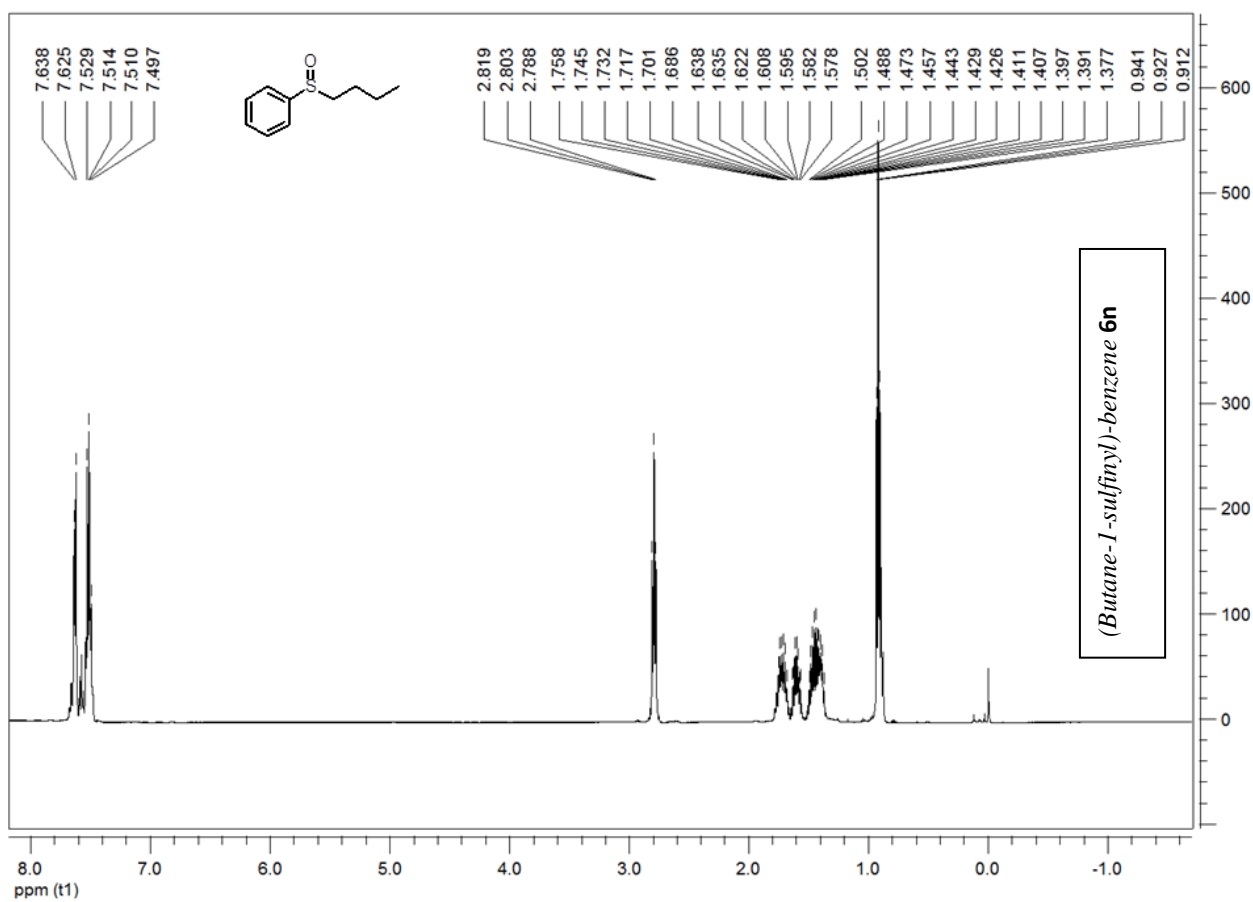


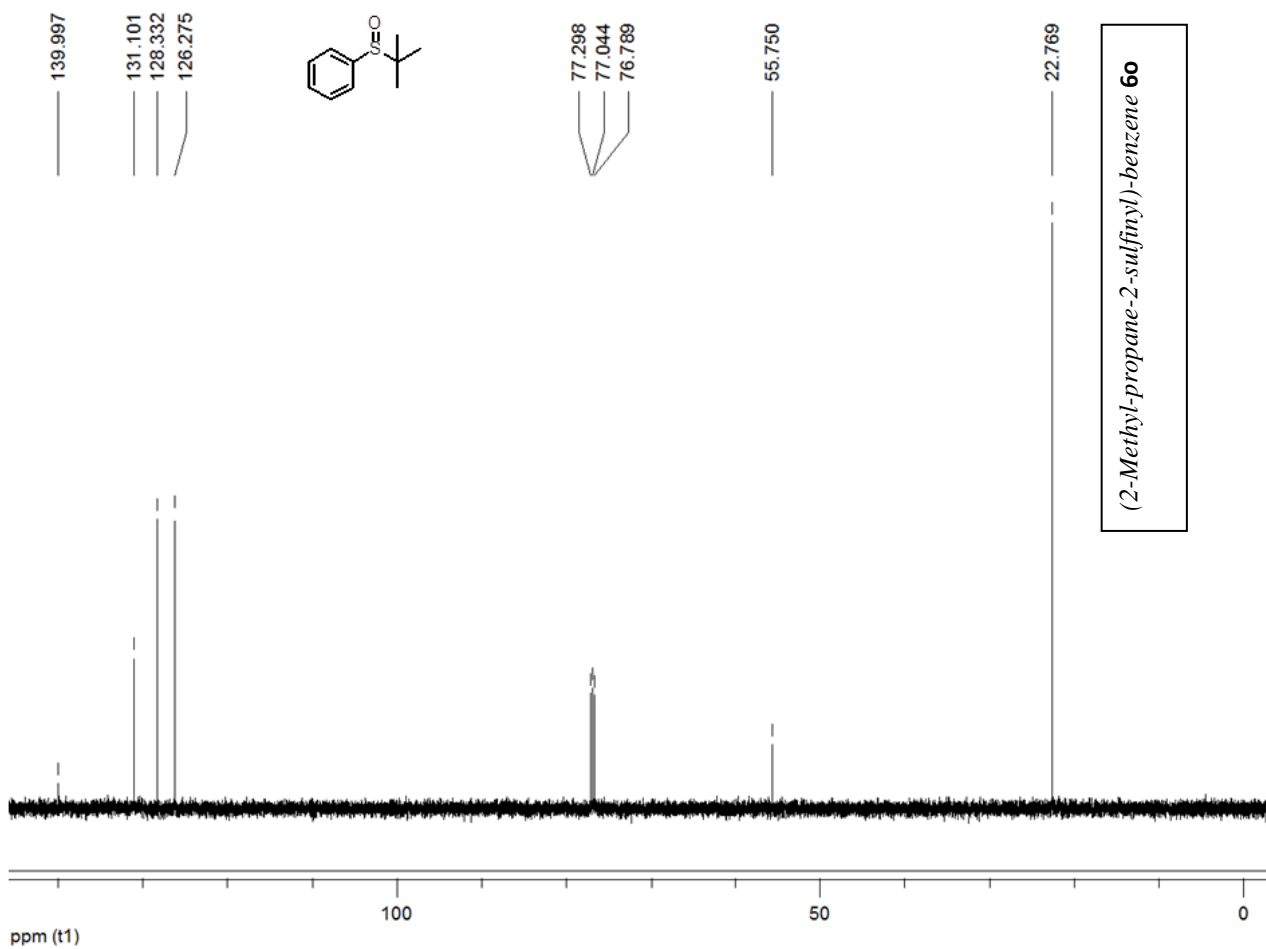
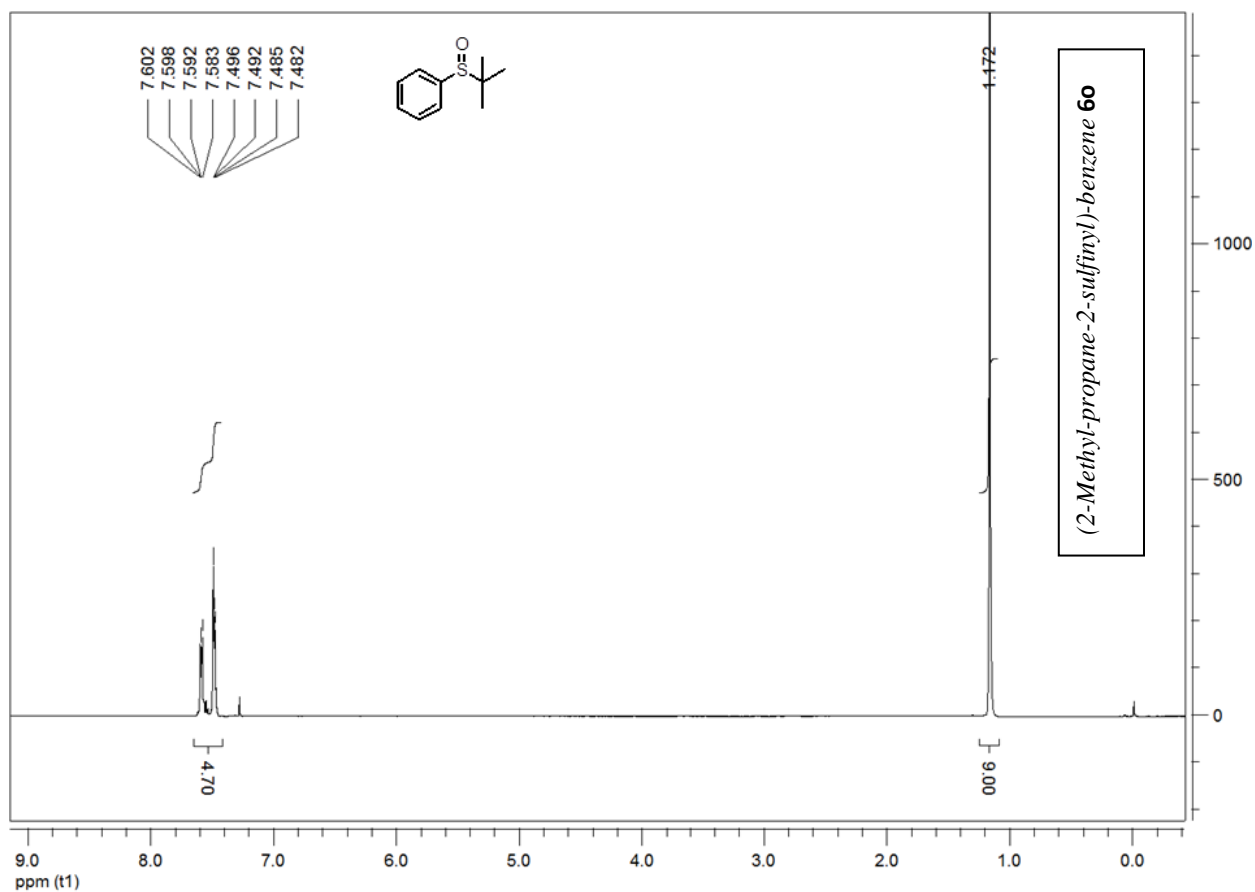


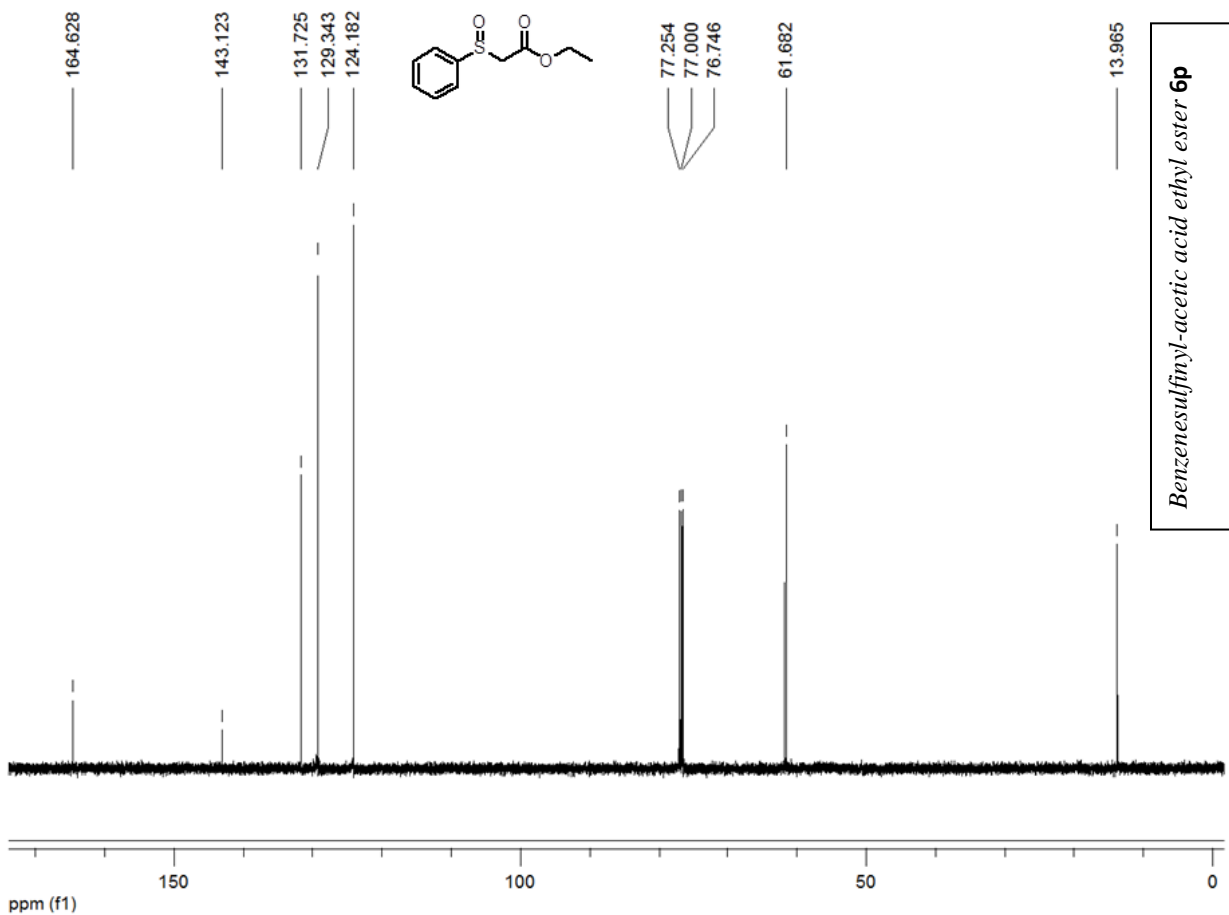
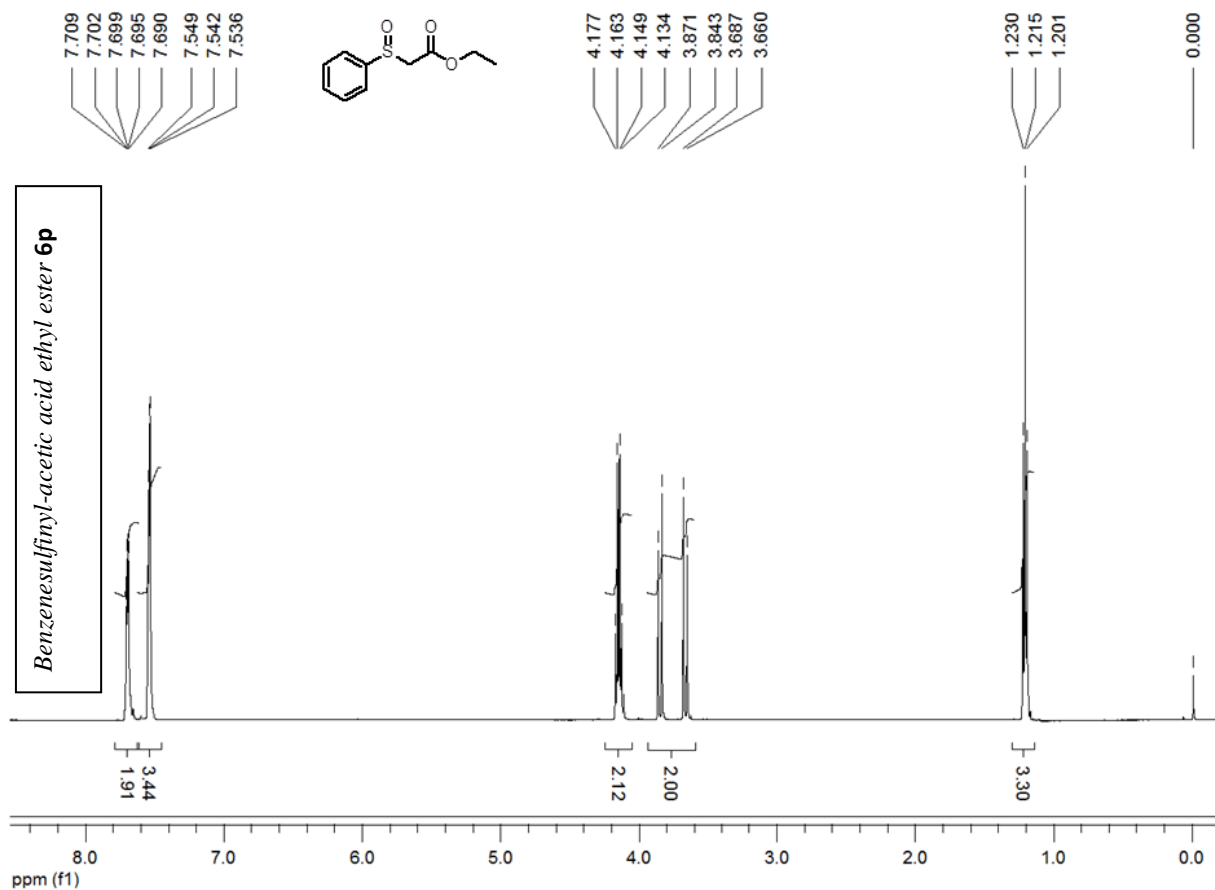












^1H and ^{13}C NMR spectra of catalysts 9a-c

