

Supporting Information

Ru-Catalyzed Chemo- and Enantioselective Hydrogenation of β -Diketones Assisted by the Neighboring Heteroatoms

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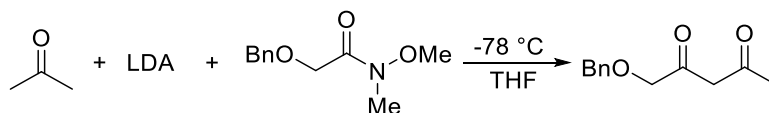
General and Materials

General: All reactions were carried out under an atmosphere of N₂ using standard Schlenk techniques unless otherwise noted. ¹H NMR, ¹³C NMR and ¹⁹F NMR spectra were obtained on a 400 MHz NMR spectrometer. The chemical shifts for ¹H NMR were recorded in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. The chemical shifts for ¹³C NMR were recorded in ppm downfield using the central peak of CDCl₃ (77.00 ppm) as the internal standard. Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplications. Flash column chromatography was performed on silica gel (300-400 mesh).

Materials: Commercially available reagents were used throughout without further purification other than those detailed below. The solvents used in catalyst preparation and hydrogenation reactions were pretreated by the following procedures: THF and 1,4-dioxane were distilled over sodium benzophenone ketyl under nitrogen. CH₂Cl₂ and DMF was distilled over calcium hydride. EtOH was distilled over magnesium under nitrogen. Acetone, MeCN and ethyl acetate was distilled over P₂O₅ under nitrogen.

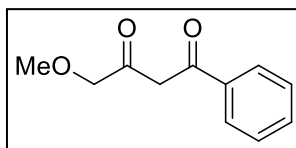
1. Preparation of 1a-k

(1a) 1-(Benzyloxy)pentane-2,4-dione^[1]



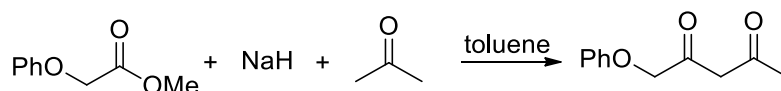
To a stirred solution of LDA (prepared from 6.0 g of *i*Pr₂NH and 32 mL of 2.4 M *n*-BuLi in hexane, 2.2 eq.) was added acetone (4.0 g, 68.9 mmol) dropwise at -78 °C. The mixture was maintained at -50 °C for 1 h before 2-(benzyloxy)-*N*-methoxy-*N*-methylacetamide (11.5 g, 55.1 mmol) was added dropwise. Then the mixture was warmed to room temperature and acidified with 10% HCl (aq.) to pH = 4-5. Then the solvent was removed under reduced pressure and the aqueous phase was extracted with ethyl acetate (20 mL × 3). The combined organic phase was washed with saturated brine and dried over Na₂SO₄. Column chromatography (PE/EA = 20:1) gave the product as light yellow liquid (6.5 g, 57%). **¹H NMR** (400 MHz, CDCl₃): mixture of keto:enol = 26:74, δ 7.42–7.27 (m, 5H), 5.86 (s, -CH=CO), 4.59 and 4.57 (s, PhCH₂O-, 2H), 4.09 and 4.06 (BnOCH₂-, s, 2H), 3.64 (s, -COCH₂-), 2.23 and 2.10 (s, -CH₃, 3H). **¹³C NMR** (100 MHz, CDCl₃): δ 202.8, 201.6, 191.8, 190.7, 137.1, 128.3, 127.9, 127.8, 127.7, 127.6, 97.2, 74.9, 73.4, 73.1, 70.9, 54.1, 30.7, 24.5.

(1b) 4-Methoxy-1-phenylbutane-1,3-dione^[2]



Prepared by the similar procedure to **1a** from *N*,2-dimethoxy-*N*-methylacetamide.^[3] **¹H NMR** (400 MHz, CDCl₃): mixture of keto:enol = 10:90, δ 7.95–7.89 (m, 2H), 7.58–7.50 (m, 1H), 7.50–7.41 (m, 2H), 6.49 (s, -CH=CO), 4.10 (s, OCH₂, 2H), 3.48 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃): δ 194.3, 182.7, 134.1, 132.3, 128.5, 128.4, 128.2, 126.9, 93.0, 74.0, 59.0, 49.5.

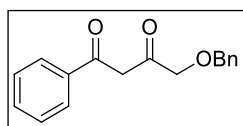
(1c) 1-Phenoxy-2,4-pentanedione^[4]



To a suspension of NaH (60% in mineral oil, 1.44 g, 36.1 mmol) in toluene (100 mL) was added methyl 2-phenoxyacetate^[5] (5.0 g, 30.1 mmol) in one portion at 80 °C, then acetone (2.6 g, 45.1 mmol) was added dropwise and reacted at this temperature for 5 h. The reaction was quenched with 50 mL of 10% HCl (aq.) and the aqueous phase was extracted with ethyl acetate for three times and the combined organic phase was washed with saturated brine and dried over Na₂SO₄. Column chromatography (PE/EA = 15:1) gave the product as light yellow liquid (4.1 g, 71%). **¹H NMR** (400 MHz, CDCl₃): mixture of keto:enol = 19:81, δ 7.35–7.28 (m, 2H), 7.01 (d, *J* = 7.4 Hz, 1H), 6.94–6.88 (m, 2H), 5.90 (s, -CH=CO), 4.60 and 4.57 (OCH₂, 2H), 3.76 (s, COCH₂), 2.28 and 2.09 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃): δ 201.2, 191.2, 190.1, 157.6, 129.4, 129.3, 121.3, 114.3, 114.2, 97.0, 72.3, 68.5, 53.7, 30.5, 24.0.

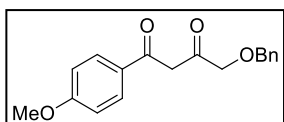
1(d-k) were prepared from various aryl methyl ketones with ethyl 2-benzyloxyacetate^[6] as **1c**.

(1d) 4-(Benzyloxy)-1-phenylbutane-1,3-dione



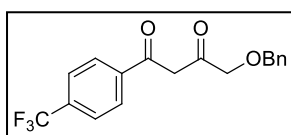
Light yellow liquid. **¹H NMR** (400 MHz, CDCl₃): mixture of keto:enol = 11:89, δ 7.98–7.84 (m, 2H), 7.53 (dd, *J* = 5.0, 3.8 Hz, 1H), 7.52–7.41 (m, 2H), 7.42–7.26 (m, 4H), 7.23–7.11 (m, 1H), 6.55 (s, -CH=CO), 4.66 (s, 2H), 4.56 (s, 1H), 4.18 (s, 2H). **¹³C NMR** (100 MHz, CDCl₃): δ 194.5, 183.0, 137.2, 134.4, 132.5, 128.6, 128.5, 128.2, 128.0, 127.8, 127.1, 93.4, 73.4, 71.7. **HRMS** Calculated for C₁₇H₁₆O₃Na (M+Na)⁺: 291.0997, found: 291.0994.

(1e) 4-(Benzyloxy)-1-(4-methoxyphenyl)butane-1,3-dione



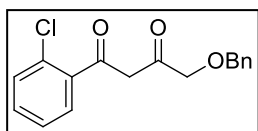
Light yellow liquid. ^1H NMR (400 MHz, CDCl_3): mixture of keto:enol = 15:85, δ 7.89 (d, J = 9.0 Hz, 2H), 7.42–7.24 (m, 5H), 6.95 (d, J = 9.0 Hz, 2H), 6.48 (s, -CH=CO), 4.65 and 4.56 (s, PhCH_2O , 2H), 4.17 and 4.12 (s, OCH_2CO , 2H), 3.87 (s, OMe, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 192.1, 183.6, 163.1, 137.2, 130.7, 129.1, 128.4, 128.3, 127.8, 127.7, 126.8, 113.8, 92.4, 74.9, 73.3, 73.2, 71.3, 55.3, 49.6. HRMS Calculated for $\text{C}_{18}\text{H}_{19}\text{O}_4$ ($\text{M}+\text{H}$) $^+$: 299.1283, found: 299.1280.

(1f) 4-(Benzyloxy)-1-(4-(trifluoromethyl)phenyl)butane-1,3-dione



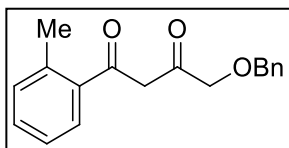
Light yellow solid, m.p.: 74.7–78.3 °C. ^1H NMR (400 MHz, CDCl_3): mixture of keto:enol = 15:85, δ 8.00 (d, J = 8.2 Hz, 2H), 7.71 (d, J = 8.2 Hz, 2H), 7.47–7.27 (m, 5H), 6.57 (s, CH=CO), 4.66 (s, 2H), 4.19 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 196.0, 180.4, 137.6, 137.0, 133.8, 133.5, 129.3, 128.8, 128.6, 128.1, 127.8, 127.3, 127.2, 125.6, 125.5, 125.0, 94.1, 73.5, 71.8. HRMS Calculated for $\text{C}_{18}\text{H}_{15}\text{F}_3\text{O}_3\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 359.0871, found: 359.0871.

(1g) 4-(Benzyloxy)-1-(2-chlorophenyl)butane-1,3-dione



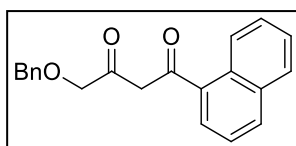
Light yellow liquid. ^1H NMR (400 MHz, CDCl_3) : mixture of keto:enol = 9:91, δ 7.95–7.27 (m, 9H), 6.55 (s, -CH=CO), 6.44 (s, 1H), 4.64 (s, 2H), 4.19 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 193.5, 183.8, 137.0, 134.9, 132.4, 131.8, 131.7, 130.6, 130.0, 128.5, 128.4, 127.9, 127.8, 127.7, 127.0, 126.8, 98.8, 93.4, 73.3, 71.3, 53.6. HRMS Calculated for $\text{C}_{17}\text{H}_{15}\text{ClO}_3\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 325.0607, found: 325.0600.

(1h) 4-(Benzyloxy)-1-(o-tolyl)butane-1,3-dione



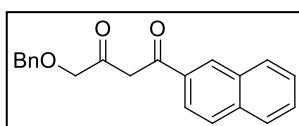
Light yellow liquid. ^1H NMR (400 MHz, CDCl_3): mixture of keto:enol = 17:83, δ 7.69–7.15 (m, 9H), 6.23 (s, CH=CO), 4.64 (s, 2H), 4.17 (s, 2H), 2.59 and 2.51 (s 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 193.6, 187.6, 137.2, 135.3, 131.0, 131.4, 130.8, 129.3, 128.5, 127.9, 127.7, 125.7, 125.6, 97.6, 73.3, 71.5, 20.8. HRMS Calculated for $\text{C}_{18}\text{H}_{18}\text{O}_3\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 305.1154, found: 305.1155.

(1i) 4-(Benzyloxy)-1-(naphthalen-1-yl)butane-1,3-dione



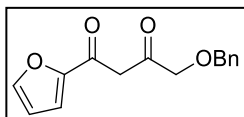
Yellow oil. ^1H NMR (400 MHz, CDCl_3): mixture of keto:enol = 20:80, δ 8.47 (s, 1H), 7.97–7.85 (m, 4H), 7.66–7.49 (m, 3H), 7.44–7.33 (m, 4H), 6.69 (s, CH=CO), 4.69 and 4.57 (s, 2H), 4.30 (s, 1H), 4.22 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 194.5, 182.8, 137.2, 135.3, 132.6, 131.6, 129.6, 129.3, 128.8, 128.6, 128.4, 128.1, 128.0, 127.9, 127.7, 127.4, 126.7, 126.4, 126.2, 126.0, 123.1, 93.8, 73.5, 71.8, 50.0. HRMS Calculated for $\text{C}_{21}\text{H}_{18}\text{O}_3\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 341.1154, found: 341.1147.

(1j) 4-(Benzyloxy)-1-(naphthalen-2-yl)butane-1,3-dione



Light yellow solid, m.p.: 41.2–42.4 °C. ^1H NMR (400 MHz, CDCl_3): mixture of keto:enol = 25:75, δ 8.56 (d, J = 8.4 Hz, 1H), 7.96–7.87 (m, 2H), 7.80 (dd, J = 7.2, 1.2 Hz, 1H), 7.65–7.47 (m, 3H), 7.51–7.22 (m, 5H), 6.47 (s, -CH=CO), 4.68 and 4.59 (s, 2H), 4.30 and 4.26 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 192.8, 187.8, 137.1, 133.7, 133.6, 131.8, 130.0, 128.4, 128.3, 127.9, 127.8, 127.7, 127.3, 127.2, 126.3, 125.4, 124.6, 98.5, 73.3, 71.3, 53.0. HRMS Calculated for $\text{C}_{21}\text{H}_{19}\text{O}_3$ ($\text{M}+\text{H}$) $^+$: 319.1334, found: 319.1328.

(1k) 4-(Benzyloxy)-1-(furan-2-yl)butane-1,3-dione



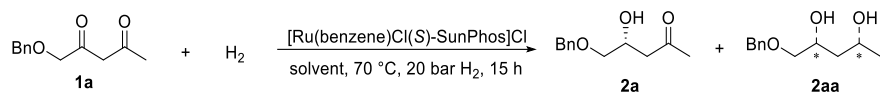
Yellow liquid. ^1H NMR (400 MHz, CDCl_3) : mixture of keto:enol = 25:75, δ 7.59 (dd, J = 1.6, 0.8 Hz, 1H), 7.41–7.25 (m, 5H), 7.21–7.15 (m, 1H), 6.59–6.48 (m, 1H), 6.41 (s, CH=CO), 4.64 and 4.56 (s, 2H), 4.18 (s, COCH_2), 4.15 and 4.03 (s, OCH_2 , 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 189.8, 175.5, 149.8, 146.8, 146.2, 137.0, 129.3, 128.3, 128.1, 127.8, 127.7, 118.2, 116.0, 112.4, 93.1, 70.5, 49.6. HRMS Calculated for $\text{C}_{15}\text{H}_{14}\text{O}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 281.0790, found: 281.0791.

2. Characterization data of compounds 2a-k

Typical procedure for asymmetric hydrogenation reactions: To a 20 mL Schlenk tube were added $[\text{Ru}(\text{benzene})\text{Cl}_2]_2$ (5.0 mg, 10.0 μmol) and (*S*)-SunPhos (15.1 mg, 22.6 μmol). The tube was vacuumed and purged with nitrogen three times before addition of freshly distilled and freeze-and-thaw degassed EtOH/ CH_2Cl_2 (1 mL/1 mL). The resulting mixture was heated at 50 °C for 1 h and then the solvent was removed under vacuum to give the catalyst as a brownish yellow solid. The catalyst was dissolved in degassed THF (10 mL) and then the solution was equally divided into 5 vials. Then the vials were taken into an autoclave. The autoclave was purged three times with H_2 and the required pressure of H_2 was set. Then the autoclave was stirred under specified reaction conditions. After being cooled to ambient

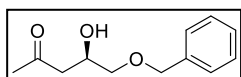
temperature and careful release of the hydrogen, the autoclave was opened, and the solvent was evaporated. The enantiomeric excess was determined by HPLC after passing the samples through a short pad of silica gel eluted with petroleum ether and ethyl acetate.

Table S1. Screening of the Other Solvents



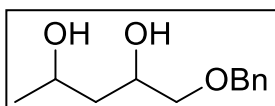
entry	solvent	conversion (%)	2a		2aa
			isolated yield (%)	ee (%)	isolated yield (%)
1	MeCN	<2	--	--	--
2	DMF	<2	--	--	--
3	dioxane	80	76	94.0	--
4	EtOAc	19	17	92.8	--
5	EtOH	99	--	--	95
6	DCM	95	--	--	90
7	Acetone	95	--	--	89
Conditions: 1a (103 mg, 0.5 mmol, solvent (2 mL), S/C = 200.					

(2a) (R)-5-(Benzyloxy)-4-hydroxypentan-2-one^[7]



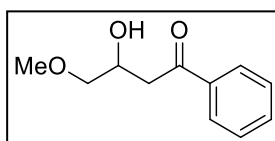
Purified by flash column chromatography (PE/EA = 5:1) as light yellow liquid (97 mg, 93%). ¹H NMR (400 MHz, CDCl₃): δ 7.39–7.27 (m, 5H), 4.55 (d, *J* = 1.3 Hz, 2H), 4.26 (dd, *J* = 7.0, 4.6 Hz, 1H), 3.47 (qd, *J* = 9.6, 5.4 Hz, 2H), 2.97 (d, *J* = 4.0 Hz, 1H), 2.72–2.59 (m, 2H), 2.18 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 207.9, 137.5, 127.9, 127.2, 73.0, 72.7, 66.1, 46.4, 30.2. HPLC (Chiralcel OJ-H column, hexane/ⁱPrOH = 94/6, 0.9 mL min⁻¹, 220 nm): *t*₁ = 25.9 min, *t*₂ = 27.6 min. [α]_D²⁵ = +16.4 (c 0.59, CH₂Cl₂); Reference value:^[7] [α]_D²⁵ = -13.8 (c 0.58, CH₂Cl₂) for (S)-**5a** with 98% ee.

(2aa) *anti*-1-(Benzyloxy)pentane-2,4-diol^[8]



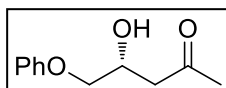
Purified by flash column chromatography (PE/EA = 5:1) as light yellow liquid (42 mg, 40%). The *anti*-configuration was determined by comparing the ¹³C NMR data with the literature value.^[8] **¹H NMR** (400 MHz, CDCl₃): δ 7.45–7.17 (m, 5H), 4.56 (s, 2H), 4.15–4.09 (m, 2H), 3.72–3.87 (m, 0.4H), 3.51–3.40 (m, 2H), 1.64–1.51 (m, 2H), 1.22 (d, *J* = 6.4 Hz, 3H). **¹³C NMR** (100 MHz, CDCl₃): δ 137.7, 128.2, 127.6, 74.4, 73.1, 67.5, 64.5, 40.8, 23.4.

(2b) 3-Hydroxy-4-methoxy-1-phenylbutan-1-one



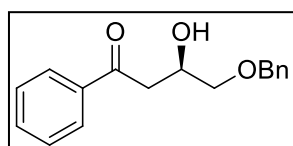
Purified by flash column chromatography (PE/EA = 4:1) as light yellow liquid (185 mg, 95%). **¹H NMR** (400 MHz, CDCl₃): δ 8.01–7.93 (m, 2H), 7.62–7.55 (m, 1H), 7.50–7.42 (m, 2H), 4.49–4.35 (m, 1H), 3.50 (t, *J* = 5.2 Hz, 2H), 3.41 (s, 3H), 3.21 (d, *J* = 1.0 Hz, 1H), 3.20 (d, *J* = 5.6 Hz, 2H). **¹³C NMR** (100 MHz, CDCl₃): δ 199.7, 136.6, 133.4, 128.5, 128.0, 75.7, 66.7, 59.1, 41.7. **HPLC** (ChiralPak AS-H column, hexane/*i*PrOH = 88/12, 0.8 mL min⁻¹, 220 nm): *t*₁ = 13.9 min, *t*₂ = 23.6 min. **HRMS** Calculated for C₁₁H₁₄O₃Na (M+Na)⁺: 217.0841, found: 217.0835.

(2c) (*R*)-4-Hydroxy-5-phenoxybutan-2-one^[9]



Purified by flash column chromatography (PE/EA = 5:1) as white solid (178 mg, 92%), m.p.: 53.3–55.3 °C. **¹H NMR** (400 MHz, CDCl₃): δ 7.34–7.20 (m, 2H), 7.01–6.93 (m, 1H), 6.93–6.86 (m, 2H), 4.50–4.35 (m, 1H), 3.97 (d, *J* = 5.4 Hz, 2H), 3.14 (dd, *J* = 4.2, 2.8 Hz, 1H), 2.80 (d, *J* = 6.0 Hz, 2H), 2.23 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃): δ 208.3, 158.2, 129.3, 120.8, 114.3, 70.6, 65.9, 46.4, 30.5. **HPLC** (Chiralcel OJ-H column, hexane/*i*PrOH = 94/6, 0.9 mL min⁻¹, 220 nm): *t*₁ = 28.4 min, *t*₂ = 31.5 min. **HRMS** Calculated for C₁₁H₁₄O₃Na (M+Na)⁺: 271.0841, found: 271.0842.

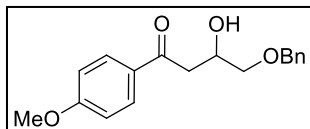
(2d) (*R*)-4-(Benzyloxy)-3-hydroxy-1-phenylbutan-1-one^[7]



Purified by flash column chromatography (PE/EA = 5:1) as light yellow oil (254 mg, 94%). **¹H NMR** (400 MHz, CDCl₃): δ 8.00–7.91 (m, 2H), 7.57 (d, *J* = 7.4 Hz, 1H), 7.47 (dd, *J* = 10.8, 4.5 Hz, 2H), 7.40–7.27 (m, 5H), 4.59 (d, *J* = 2.0 Hz, 2H), 4.50–4.40 (m, 1H), 3.59 (qd, *J* = 9.6, 5.2 Hz, 2H), 3.22 (d, *J* = 0.8 Hz, 1H), 3.20 (s, 2H). **¹³C NMR** (100 MHz, CDCl₃): δ 199.5, 137.8, 136.6, 133.2, 128.4, 128.2, 128.0, 127.6, 73.2, 66.9, 41.7. **HPLC** (Chiralcel AD-H column, hexane/*i*PrOH = 88/12, 0.8 mL min⁻¹, 220 nm): *t*₁ = 17.5 min, *t*₂ = 19.2

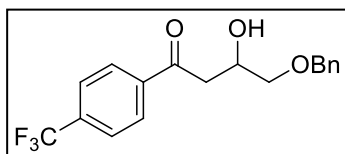
min. $[\alpha]_{\text{D}}^{25} = +24.6$ (*c* 0.47, CH₂Cl₂); Reference value:^[7] $[\alpha]_{\text{D}}^{25} = -21.4$ (*c* 0.46, CH₂Cl₂) for (*S*)-**2d** with 98% ee.

(2e) 4-(Benzyloxy)-3-hydroxy-1-(4-methoxyphenyl)butan-1-one



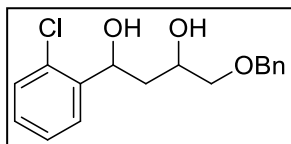
Purified by flash column chromatography (PE/EA = 4:1) as light yellow liquid (274 mg, 91%). ¹H NMR (400 MHz, CDCl₃): δ 8.02–7.85 (m, 2H), 7.38–7.26 (m, 5H), 7.01–6.89 (m, 2H), 4.58 (d, *J* = 1.6 Hz, 2H), 3.87 (s, 3H), 3.63–3.53 (m, 2H), 3.16 (s, 1H), 3.15 (d, *J* = 1.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 197.9, 163.4, 137.7, 130.2, 129.6, 128.0, 127.4, 127.3, 113.4, 73.2, 73.0, 66.8, 55.1, 41.2, 29.4. HPLC (ChiralPak IB-3 column, hexane/*i*PrOH = 85/15, 0.8 mL min⁻¹, 220 nm): *t*₁ = 13.4 min, *t*₂ = 14.5 min. HRMS Calculated for C₁₈H₂₁O₄ (M+H)⁺: 301.1440, found: 301.1444.

(2f) 4-(Benzyloxy)-3-hydroxy-1-(4-(trifluoromethyl)phenyl)butan-1-one



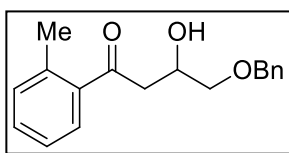
Purified by flash column chromatography (PE/EA = 5:1) as light yellow liquid (305 mg, 90%). ¹H NMR (400 MHz, CDCl₃): δ 8.05 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.39–7.27 (m, 5H), 4.58 (d, *J* = 2.8 Hz, 2H), 4.51–4.40 (m, 1H), 3.59 (qd, *J* = 9.6, 5.3 Hz, 2H), 3.29–3.16 (m, 2H), 3.03 (d, *J* = 4.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 198.6, 139.4, 137.7, 134.4, 128.4, 128.4, 127.8, 127.8, 126.0, 125.7, 125.6, 125.2, 124.8, 73.4, 73.1, 66.9, 42.2. HPLC (Chiralcel AD-H column, hexane/*i*PrOH = 88/12, 0.8 mL min⁻¹, 220 nm): *t*₁ = 14.9 min, *t*₂ = 17.7 min. HRMS Calculated for C₁₈H₁₇F₃O₂Na (M+Na)⁺: 361.1027, found: 361.1030.

(2gg) 4-(Benzyloxy)-1-(2-chlorophenyl)butane-1,3-diol



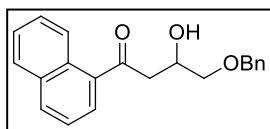
Purified by flash column chromatography (PE/EA = 5:1) as light yellow oil (282 mg, 92%). ¹H NMR (400 MHz, CDCl₃): δ 8.00–7.11 (m, 9H), 5.34 (d, *J* = 9.8 Hz, 1H), 4.57 (d, *J* = 10.4 Hz, 2H), 4.24 (s, 1H), 3.98 (s, 1H), 3.59–3.37 (m, 2H), 3.24–3.16 (m, 1H), 1.92 (d, *J* = 14.6 Hz, 1H), 1.68 (dt, *J* = 14.4, 10.0 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 141.6, 137.6, 131.1, 129.0, 128.5, 128.3, 128.2, 128.0, 127.7, 127.0, 74.2, 73.2, 73.2, 71.1, 70.6, 68.0, 66.9, 41.7, 39.9. HRMS Calculated for C₁₇H₁₉ClO₃Na (M+Na)⁺: 329.0920, found: 329.0925.

(2h) 4-(Benzyloxy)-3-hydroxy-1-(o-tolyl)butan-1-one



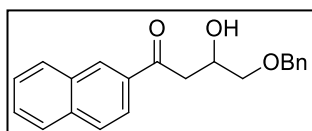
Purified by flash column chromatography (PE/EA = 5:1) as light yellow oil (271 mg, 95%). **¹H NMR** (400 MHz, CDCl₃): δ 7.67 (d, *J* = 7.8 Hz, 1H), 7.47–7.17 (m, 8H), 4.58 (d, *J* = 2.0 Hz, 2H), 4.42 (s, 1H), 3.56 (dd, *J* = 5.4, 4.2 Hz, 2H), 3.18 (d, *J* = 3.6 Hz, 1H), 3.16–3.09 (m, 2H), 2.50 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃): δ 203.5, 138.3, 137.8, 137.3, 131.9, 131.6, 128.8, 128.3, 127.6, 125.6, 73.3, 73.2, 67.2, 44.5, 21.3. **HPLC** (Chiralcel AS-H column, hexane/*i*PrOH = 88/12, 0.8 mL min⁻¹, 220 nm): *t*₁ = 12.5 min, *t*₂ = 16.5 min. **HRMS** Calculated for C₁₈H₂₀O₃Na (M+Na)⁺: 307.1310, found: 307.1311.

(2i) 4-(Benzyloxy)-3-hydroxy-1-(naphthalen-1-yl)butan-1-one



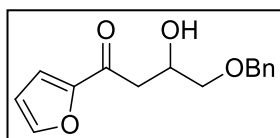
Purified by flash column chromatography (PE/EA = 5:1) as light yellow oil (296 mg, 92%). **¹H NMR** (400 MHz, CDCl₃): δ 8.47 (s, 1H), 8.06–7.84 (m, 4H), 7.66–7.52 (m, 2H), 7.40–7.27 (m, 5H), 4.61 (d, *J* = 1.8 Hz, 2H), 4.52 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.68–3.57 (m, 2H), 3.38–3.33 (m, 2H), 3.25 (d, *J* = 4.0 Hz, 1H). **¹³C NMR** (100 MHz, CDCl₃): δ 199.4, 137.8, 135.4, 133.9, 132.2, 129.9, 129.4, 128.4, 128.2, 127.6, 127.5, 126.6, 123.4, 73.2, 67.0, 41.8. **HPLC** (Chiralcel AD-H column, hexane/*i*PrOH = 88/12, 0.8 mL min⁻¹, 220 nm): *t*₁ = 26.1 min, *t*₂ = 28.0 min. **HRMS** Calculated for C₂₁H₂₀O₃Na (M+Na)⁺: 343.1310, found: 343.1301.

(2j) 4-(Benzyloxy)-3-hydroxy-1-(naphthalen-2-yl)butan-1-one



Purified by flash column chromatography (PE/EA = 5:1) as light yellow oil (304 mg, 95%). **¹H NMR** (400 MHz, CDCl₃): δ 8.64 (d, *J* = 8.6 Hz, 1H), 8.02–7.87 (m, 3H), 7.65–7.46 (m, 3H), 7.41–7.25 (m, 5H), 4.59 (d, *J* = 2.0 Hz, 2H), 4.57–4.48 (m, 1H), 3.66–3.56 (m, 2H), 3.38–3.24 (m, 2H), 3.22 (d, *J* = 4.2 Hz, 1H). **¹³C NMR** (100 MHz, CDCl₃): δ 203.4, 137.7, 135.2, 133.6, 132.8, 129.8, 128.2, 128.0, 127.8, 127.5, 126.2, 125.5, 124.1, 73.2, 73.1, 67.2, 45.0. **HPLC** (ChiralPak AS-H column, hexane/*i*PrOH = 88/12, 0.8 mL min⁻¹, 220 nm): *t*₁ = 20.6 min, *t*₂ = 22.2 min. **HRMS** Calculated for C₂₁H₂₀O₃Na (M+Na)⁺: 343.1310, found: 343.1299.

(2k) 4-(Benzyloxy)-1-(furan-2-yl)-3-hydroxybutan-1-one

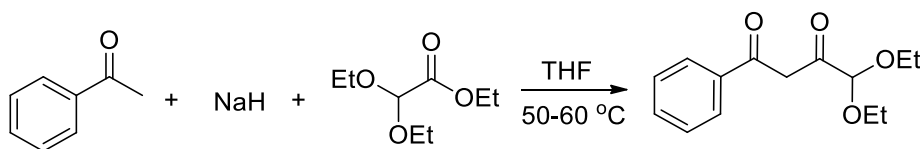


Purified by flash column chromatography (PE/EA = 5:1) as light yellow liquid (245 mg, 94%). Light yellow oil. **¹H NMR** (400 MHz, CDCl₃): δ 7.60 (d, *J* = 1.6 Hz, 1H), 7.40–7.26 (m, 5H), 7.22 (d, *J* = 3.6 Hz, 1H), 6.54 (dd, *J* = 3.6, 1.8 Hz, 1H), 4.58 (d, *J* = 1.6 Hz, 2H), 4.42 (s, 1H), 3.56 (qd, *J* = 9.6, 5.2 Hz, 2H), 3.13–3.00 (m, 2H), 3.06 (s, 1H). **¹³C NMR** (100 MHz, CDCl₃): δ 188.1, 152.4, 146.7, 137.8, 128.3, 127.6, 117.8, 112.3, 73.3, 73.2,

66.9, 41.6. **HPLC** (Chiralcel AS-H column, hexane/*i*PrOH (1% Et₂NH) = 86/14, 1.0 mL min⁻¹, 220 nm): *t*₁ = 18.6 min, *t*₂ = 27.4 min. **HRMS** Calculated for C₁₅H₁₆O₄Na (M+Na)⁺: 283.0946, found: 283.0953.

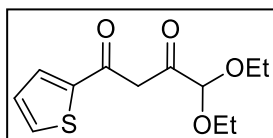
3. Preparation of 3a-j

(3a) 4,4-Diethoxy-1-phenylbutane-1,3-dione^[10]



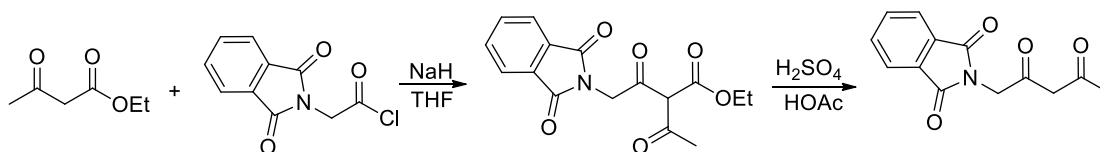
To a suspension of 60% NaH (2.9 g, 73.2 mmol) in THF (60 mL) was added a solution of acetophenone (4.0 g, 33.3 mmol) and ethyl 2,2-diethoxyacetate (5.9 g, 33.3 mmol) in THF (40 mL) at 50 °C and stirred overnight. Then poured the mixture into 50 mL cold 10% HCl (aq.) and the solvent was removed under reduced pressure. The aqueous phase was extracted with ethyl acetate for three times. The combined organic phase was washed with brine and dried over Na₂SO₄. Column chromatography (PE/EA = 10:1) gave **3a** as light yellow liquid (6.9 g, 84%). **¹H NMR** (400 MHz, CDCl₃): mixture of keto:enol = 5:95, δ 7.96–7.89 (m, 2H), 7.58–7.50 (m, 1H), 7.48–7.44 (m, 2H), 6.61–6.57 (m, 1H), 4.92–4.87 (m, 1H), 3.78–3.60 (m, 4H), 1.28 (t, *J* = 7.2 Hz, 6H). **¹³C NMR** (100 MHz, CDCl₃): δ 190.4, 184.4, 134.4, 132.6, 128.6, 127.2, 100.0, 93.7, 62.5, 15.1.

(3b) 4,4-Diethoxy-1-(thiophen-2-yl)butane-1,3-dione



Prepared from acetylthiophene (2.0 g, 15.8 mmol) and ethyl 2,2-diethoxyacetate (2.8 g, 15.8 mmol) with the same procedure as **3a**. Purified by flash column chromatography (PE/EA = 8:1) gave the product as light brown liquid (3.2 g, 79%). **¹H NMR** (400 MHz, CDCl₃): mixture of keto:enol = 17:83, δ 7.81–7.69 (m, 1H), 7.68–7.63 (m, 1H), 7.15–7.12 (m, 1H), 6.43 (s, 1H), 4.94 and 4.16 (s, 1H), 3.79–3.53 (m, 4H), 1.30–1.20 (m, 6H). **¹³C NMR** (100 MHz, CDCl₃): δ 183.2, 182.6, 141.2, 134.5, 133.1, 130.91, 128.2, 128.1, 102.1, 99.0, 94.2, 63.5, 62.2, 48.5, 29.5, 15.0, 14.9. **HRMS** Calculated for C₁₂H₁₆O₄SNa (M+Na)⁺: 279.0667, found: 279.0662.

(3c) 2-(2,4-Dioxopentyl)isoindoline-1,3-dione^[11]

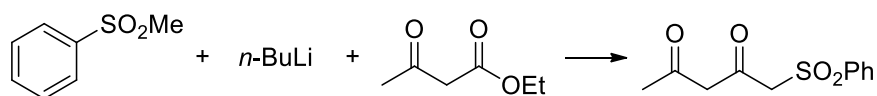


Ethyl 2-acetyl-4-(1,3-dioxoisindolin-2-yl)-3-oxobutanoate: To a suspension of 60% NaH (2.1 g, 50.7 mmol) in THF (50 mL) was added ethyl acetoacetate (6.0 g, 46.1 mmol) at room temperature. Then

2-(1,3-dioxoisindolin-2-yl)acetyl chloride (10.9 g, 48.0 mmol)^[12] in 100 mL of THF was added dropwise at 40 °C. After addition, the mixture was reacted at 70 °C overnight. The mixture was poured into 100 mL cold 10% HCl (aq.) and the solvent was removed under reduced pressure. The aqueous phase was extracted with ethyl acetate for three times. The combined organic phase was washed with saturated brine and dried over Na₂SO₄. The crude product was recrystallized from EtOH to give light yellow solid (11.3 g, 77%). ¹H NMR (400 MHz, CDCl₃): δ 7.89 (dd, *J* = 5.6, 3.0 Hz, 2H), 7.75 (dd, *J* = 5.4, 3.2 Hz, 2H), 4.99 (s, 2H), 4.34 (d, *J* = 7.2 Hz, 2H), 2.48 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 195.4, 194.7, 168.0, 165.9, 134.1, 132.1, 123.5, 106.3, 60.9, 44.7, 25.0, 14.3.

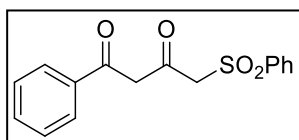
Ethyl 2-acetyl-4-(1,3-dioxoisindolin-2-yl)-3-oxobutanoate (6.8 g, 22.1 mmol) was dissolved in acetic acid (60 mL) containing several drops of concentrated sulfuric acid. The mixture was stirred under reflux for 2 h and the acetic acid was removed under reduced pressure to afford a brown crude mixture. Column chromatography (PE/EA = 3:1) gave the products as white solid (4.8 g, 88%). ¹H NMR (400 MHz, CDCl₃): mixture of keto:enol = 40:60, δ 7.90 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.75 (dd, *J* = 5.4, 3.0 Hz, 2H), 5.57 (s, CH=CO), 4.60 and 4.50 (s, 2H), 3.71 (s, COCH₂-), 2.29 and 2.04 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 191.3, 185.6, 167.6, 134.2, 134.1, 131.9, 123.5, 97.3, 55.4, 47.0, 43.4, 26.9, 23.0.

(3d) 1-(Phenylsulfonyl)pentane-2,4-dione ^[13]



To a solution of (methylsulfonyl)benzene (5.0 g, 32.0 mmol) in THF (70 mL) was added *n*-BuLi (30 mL, 2.4 M in hexane) under nitrogen at 0 °C. After 1 h, the mixture was cooled to -10 °C and ethyl acetoacetate (4.2 g, 32.0 mmol) was added dropwise and warmed to room temperature. After stirring overnight, the reaction was neutralized with cold 10% HCl aq. Then THF was removed under reduced pressure. The aqueous phase was extracted with ethyl acetate (30 mL × 3). Combined organic phase was washed with saturated brine, dried over Na₂SO₄. The crude product was purified by column chromatography (PE/EA = 3:1) to give white solid (5.7 g, 74%). m.p.: 105.3–106.1 °C. ¹H NMR (400 MHz, CDCl₃): mixture of keto:enol = 13:87, δ 7.92–7.86 (m, 2H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.60–7.54 (m, 2H), 5.73 (s, CH=CO), 4.01 (s, PhSO₂CH₂-, 2H), 2.26 and 2.10 (s, -COCH₃, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 192.4, 179.5, 138.4, 134.1, 129.1, 128.1, 102.5, 64.1, 57.5, 24.7.

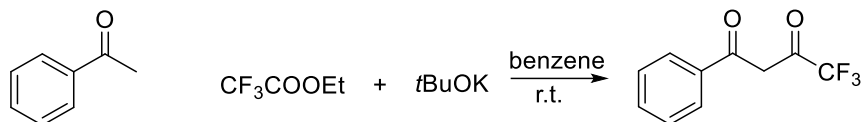
(3e) 1-Phenyl-4-(phenylsulfonyl)butane-1,3-dione



3e was prepared similarly as **3d**. White solid, m.p.: 120.6–122.5 °C. ¹H NMR (400 MHz, CDCl₃): mixture of keto:enol = 4:96, δ 7.94–7.84 (m, 4H), 7.74–7.61 (m, 1H), 7.57 (t, *J* = 7.6 Hz, 3H), 7.47 (t, *J* = 7.6 Hz, 2H), 6.40 (s, 1H),

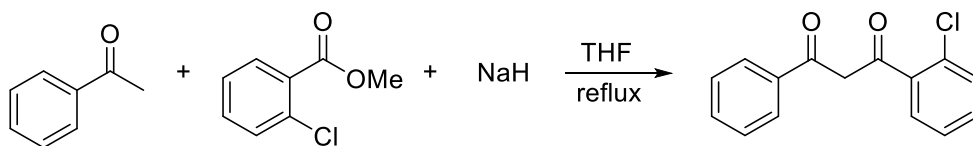
4.16 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ 184.3, 181.8, 138.4, 134.2, 133.6, 133.1, 129.2, 128.7, 128.3, 127.3, 98.6, 65.0. HRMS Calculated for $\text{C}_{16}\text{H}_{15}\text{O}_4\text{S}$ ($\text{M}+\text{H}$) $^+$: 303.0691, found: 303.0690.

(3f) 4,4,4-Trifluoro-1-phenylbutane-1,3-dione^[14]



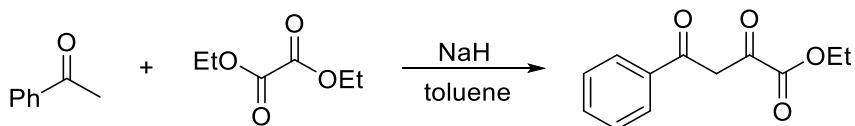
To a suspension of *t*-BuOK (1.4 g, 12.0 mmol) and acetophenone (1.2 g, 10.0 mmol) in benzene (10 mL) was added ethyl trifluoroacetate (1.7 g, 12.0 mmol) dropwise at 10 °C. The reaction mixture was stirred at room temperature for 15 h and acidified by 10% aq. H_2SO_4 to pH = 7 before extracted with ethyl ether (20 mL \times 3). The combined organic phase was washed with brine and dried over Na_2SO_4 . The crude product was purified by column chromatography (PE/EA = 10:1) to give **3f** as light yellow oil (1.5 g, 69%). ^1H NMR (400 MHz, CDCl_3): mixture of keto:enol = 4:96, δ 7.94–7.82 (m, 2H), 7.56 (ddd, J = 6.8, 4.0, 1.2 Hz, 1H), 7.45–7.39 (m, 2H), 6.51 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 186.2, 177.2 (q, $J_{\text{F-C}}$ = 36.6 Hz), 134.0, 132.7, 128.9, 128.4, 127.5, 118.6, 115.7, 92.2, 38.0.

(3g) 1-(2-Chlorophenyl)-3-phenylpropane-1,3-dione^[15]



3g was synthesized from acetophenone (1.8 g, 15.0 mmol) and methyl *o*-chlorobenzoate (2.6 g, 15.0 mmol) by using NaH (60% dispersed in mineral oil, 1.5 g, 37.5 mmol) according to the reported procedure.^[15] The crude product was purified by column chromatography (PE/EA = 15:1) to give yellow solid **3g** (3.3 g, 84%). ^1H NMR (400 MHz, CDCl_3): δ 8.09–7.78 (m, 2H), 7.71–7.67 (m, 1H), 7.59–7.27 (m, 6H), 6.76–6.66 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 186.8, 184.4, 136.1, 134.8, 132.6, 131.6, 130.6, 130.0, 128.6, 127.2, 126.9, 98.3.

(3h) Ethyl 2,4-dioxo-4-phenylbutanoate^[16]



To a solution of acetophenone (2.4 g, 20.0 mmol) in toluene (40 mL) was added NaH (60% in mineral oil, 1.0 g, 42.0 mmol) in portions and the mixture was warmed to 45–50 °C under stirring. At this temperature a solution of diethyl oxalate (3.5 g, 24.0 mmol) in toluene (20 mL) was added dropwise. The reaction mixture was refluxed for another 1.5 h. Then cooled to room temperature and acidified by 10%

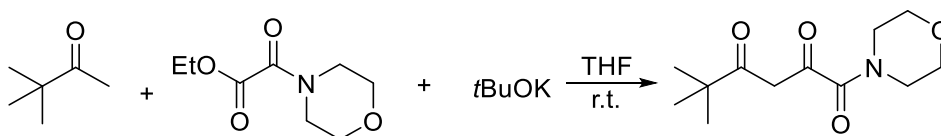
aq. H₂SO₄ to pH = 6 before extracted with ethyl acetate (20 mL × 3). The combined organic phase was washed with brine and dried over Na₂SO₄. The crude product was purified by column chromatography (PE/EA = 4:1) to give **3h** as light yellow liquid (4.1 g, 93%). ¹H NMR (400 MHz, CDCl₃): δ 8.08–7.90 (m, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.08 (s, 1H), 4.40 (q, *J* = 7.0 Hz, 2H), 1.41 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.6, 169.6, 162.0, 134.7, 133.76, 128.8, 127.7, 97.8, 62.5, 14.0.

(3i) Ethyl 2,4-dioxo-5-phenylpentanoate^[17]



To a stirred solution of NaOEt (prepared from 1.2 g of sodium in 25 mL of absolute EtOH) was added a mixture of 1-phenylpropan-2-one (5.4 g, 40.3 mmol) and diethyl oxalate (5.9 g, 40.3 mmol) at 0 °C. After 5 h at room temperature, the mixture was acidified by 10% aq. H₂SO₄ to pH = 6. Ethanol was removed under reduced pressure and the residue was extracted with ethyl acetate (20 mL × 3). The combined organic phase was washed with saturated brine and dried over Na₂SO₄. The crude product was purified by column chromatography (PE/EA = 3:1) to give **3i** as yellow oil (7.6 g, 81%). ¹H NMR (400 MHz, CDCl₃): mixture of keto:enol = 13:87, δ 7.39–7.19 (m, 5H), 6.36 (s, -CH=CO, 1H), 4.33–4.29 (m, 2H), 3.77 (s, 2H), 1.38–1.30 (m, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 200.5, 166.4, 161.6, 133.4, 129.2, 128.7, 127.2, 101.4, 62.3, 47.4, 13.8.

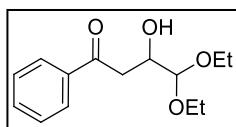
(3j) 5,5-Dimethyl-1-morpholinohexane-1,2,4-trione^[18]



A suspension of *t*-BuOK (2.3 g, 20.5 mmol) in THF (20 mL) was added via cannula to a solution of pinacolone (1.0 g, 10.0 mmol) and ethyl 2-morpholino-2-oxoacetate (1.9 g, 10.0 mmol) in THF (40 mL) over 40 min at 25 °C. After 3 h, AcOH (2.1 mL, 36.0 mmol) was added over 5 min and the resulting heterogeneous mixture was filtered and the solids were washed with CH₂Cl₂. The filtrate was washed with NaHCO₃ and brine, dried, filtered, and concentrated. Purification of the residue by flash chromatography (PE/EA = 1:1) provided the title compound as a yellow solid (1.8 g, 75%). ¹H NMR (400 MHz, CDCl₃): mixture of keto:enol = 31:69, δ 6.03 (s, 1H), 4.05 (s, 1H), 3.78–3.57 (m, 8H), 1.19 (s, 9H). ¹³C NMR (100 MHz, CDCl₃): δ 201.0, 184.6, 163.7, 95.4, 66.8, 66.6, 66.4, 66.3, 47.9, 46.5, 46.2, 42.1, 38.9, 27.0, 26.6, 25.8.

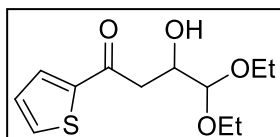
4. Characterization data of compounds 4a-j

(4a) 4,4-Diethoxy-3-hydroxy-1-phenylbutan-1-one



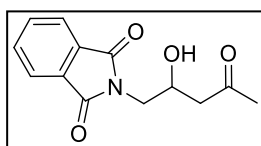
Purified by flash column chromatography (PE/EA = 6:1) as light yellow oil (225 mg, 89%). **¹H NMR** (400 MHz, CDCl₃): δ 8.01–7.94 (m, 2H), 7.60–7.52 (m, 1H), 7.48–7.44 (m, 2H), 4.52 (d, *J* = 4.8 Hz, 1H), 4.29 (s, 1H), 3.80–3.75 (m, 2H), 3.64–3.58 (m, 2H), 1.24–1.20 (m, 6H). **¹³C NMR** (100 MHz, CDCl₃): δ 197.4, 173.7, 136.3, 133.4, 128.5, 128.0, 67.0, 61.6, 42.1, 14.0. **HPLC** (Chiralcel AD-H column, hexane/*i*PrOH = 90/10, 0.8 mL min⁻¹, 220 nm): *t*₁ = 12.4 min, *t*₂ = 13.6 min. **HRMS** Calculated for C₁₄H₂₀O₄Na (M+Na)⁺: 275.1259, found: 275.1247.

(4b) 4,4-Diethoxy-3-hydroxy-1-(thiophen-2-yl)butan-1-one



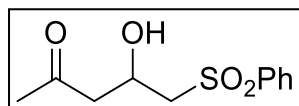
Purified by flash column chromatography (PE/EA = 3:1) as yellow oil (186 mg, 93%). **¹H NMR** (400 MHz, CDCl₃): δ 7.76 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.65 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.13 (dd, *J* = 4.9, 3.8 Hz, 1H), 4.51 (d, *J* = 4.8 Hz, 1H), 4.27 (d, *J* = 4.2 Hz, 1H), 3.80–3.75 (m, 2H), 3.64–3.58 (m, 2H), 3.26–3.11 (m, 2H), 2.94 (d, *J* = 4.4 Hz, 1H), 1.25–1.20 (m, 6H). **¹³C NMR** (100 MHz, CDCl₃): δ 192.6, 144.3, 134.0, 132.6, 128.1, 103.8, 69.1, 64.0, 63.6, 40.5, 15.3, 15.3. **HPLC** (ChiralPak AS-H column, hexane/*i*PrOH = 92/8, 0.7 mL min⁻¹, 254 nm): *t*₁ = 15.7 min, *t*₂ = 16.9 min. **HRMS** Calculated for C₁₂H₁₈O₄SNa (M+Na)⁺: 281.0832, found: 281.0829.

(4c) 2-(2-Hydroxy-4-oxopentyl)isoindoline-1,3-dione



Purified by flash column chromatography (PE/EA = 2:1) as white solid (223 mg, 90%), m.p.: 112.1–113.3 °C. **¹H NMR** (400 MHz, CDCl₃): δ 7.86 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.73 (dd, *J* = 5.4, 3.0 Hz, 2H), 4.39–4.35 (m, 1H), 3.88–3.72 (m, 2H), 3.23 (d, *J* = 4.4 Hz, 1H), 2.67 (dd, *J* = 10.0, 6.0 Hz, 2H), 2.19 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃): δ 208.2, 168.5, 134.0, 131.7, 123.3, 66.0, 47.3, 42.7, 30.6. **HPLC** (Chiralcel AD-H column, hexane/*i*PrOH = 82/18, 0.75 mL min⁻¹, 220 nm): *t*₁ = 25.2 min, *t*₂ = 29.8 min. **HRMS** Calculated for C₁₃H₁₃NO₄Na (M+Na)⁺: 270.0742, found: 270.0730.

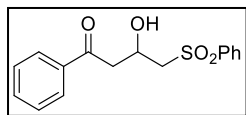
(4d) 4-Hydroxy-5-(phenylsulfonyl)pentan-2-one



Purified by flash column chromatography (PE/EA = 3:1) as yellow oil (221 mg, 91%). **¹H NMR** (400 MHz, CDCl₃): δ 7.93–7.86 (m, 2H), 7.68–7.61 (m, 1H), 7.58–7.52 (m, 2H), 4.54–4.41 (m, 1H), 3.61 (s, 1H), 3.37–3.22 (m, 2H), 2.75 (d,

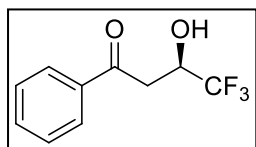
$J = 5.6$ Hz, 2H), 2.13 (s, 3H). **^{13}C NMR** (100 MHz, CDCl_3): δ 207.4, 139.2, 133.9, 129.3, 127.8, 62.7, 60.9, 48.5, 30.6. **HPLC** (ChiralPak IA-3 column, hexane/*i*PrOH = 82/18, 0.8 mL min⁻¹, 220 nm): $t_1 = 28.6$ min, $t_2 = 30.8$ min. **HRMS** Calculated for $\text{C}_{13}\text{H}_{17}\text{O}_4\text{S}$ ($\text{M}+\text{H}$)⁺: 243.0691, found: 243.0690.

(4e) 3-Hydroxy-1-phenyl-4-(phenylsulfonyl)butan-1-one



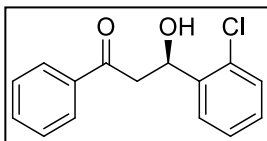
Purified by flash column chromatography (PE/EA = 3:1) as white solid (280 mg, 92%), m.p.: 100.4–101.5 °C. **^1H NMR** (400 MHz, CDCl_3): δ 8.00–7.89 (m, 4H), 7.67 (d, $J = 7.6$ Hz, 1H), 7.60 (t, $J = 7.8$ Hz, 3H), 7.47 (t, $J = 7.8$ Hz, 2H), 4.71–4.67 (m, 1H), 3.74 (d, $J = 3.6$ Hz, 1H), 3.46 (dd, $J = 6.0, 1.8$ Hz, 2H), 3.34 (d, $J = 5.8$ Hz, 2H). **^{13}C NMR** (100 MHz, CDCl_3): δ 198.6, 139.3, 136.2, 134.0, 133.8, 129.3, 128.7, 128.1, 128.0, 63.2, 61.2, 43.9. **HPLC** (ChiralPak IA-3 column, hexane/*i*PrOH = 81/19, 0.9 mL min⁻¹, 254 nm): $t_1 = 26.4$ min, $t_2 = 28.5$ min. **HRMS** Calculated for $\text{C}_{16}\text{H}_{16}\text{O}_4\text{SNa}$ ($\text{M}+\text{Na}$)⁺: 327.0667, found: 327.0657.

(4f) (R)-4,4,4-Trifluoro-3-hydroxy-1-phenylbutan-1-one^[19]



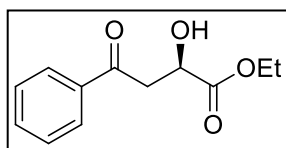
Purified by flash column chromatography (PE/EA = 8:1) as colorless liquid (208 mg, 95%). **^1H NMR** (400 MHz, CDCl_3): δ 7.97 (dd, $J = 8.2, 1.0$ Hz, 2H), 7.62 (d, $J = 7.8$ Hz, 1H), 7.51 (t, $J = 7.8$ Hz, 2H), 4.69 (s, 1H), 3.51 (d, $J = 4.6$ Hz, 1H), 3.43–3.27 (m, 2H). **^{13}C NMR** (100 MHz, CDCl_3): δ 197.5, 136.9, 134.1, 128.8, 128.2, 124.69 (q, $J = 280.0$ Hz), 67.03 (q, $J = 32.0$ Hz), 38.3. **HPLC** (Chiralcel OD-H column, hexane/*i*PrOH = 95/5, 1.0 mL min⁻¹, 237 nm): $t_1 = 9.5$ min, $t_2 = 10.7$ min.

(4g) (R)-3-(2-Chlorophenyl)-3-hydroxy-1-phenylpropan-1-one^[20]



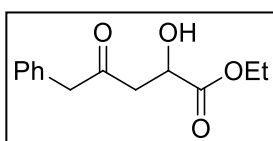
Purified by flash column chromatography (PE/EA = 5:1) as yellowoil (242 mg, 93%). **^1H NMR** (400 MHz, CDCl_3): δ 8.00–7.93 (m, 2H), 7.72 (d, $J = 7.8$ Hz, 1H), 7.59 (dd, $J = 10.7, 4.2$ Hz, 1H), 7.47 (t, $J = 7.7$ Hz, 2H), 7.35 (t, $J = 8.0$ Hz, 2H), 7.29–7.20 (m, 2H), 5.69 (d, $J = 9.6$ Hz, 1H), 3.84 (d, $J = 3.2$ Hz, 1H), 3.60–3.55 (m, 1H), 3.18–3.12 (m, 1H). **^{13}C NMR** (100 MHz, CDCl_3): δ 200.1, 140.3, 136.3, 133.6, 131.0, 129.2, 128.6, 128.5, 128.1, 127.2, 66.7, 45.3. **HPLC** (ChiralPak AS-H column, hexane/*i*PrOH = 90/10, 1.0 mL min⁻¹, 220 nm): $t_1 = 10.9$ min, $t_2 = 14.4$ min.

(4h) (R)-Ethyl 2-hydroxy-4-oxo-4-phenylbutanoate^[21]



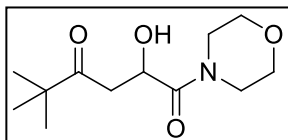
Purified by flash column chromatography (PE/EA = 6:1) as yellow oil (207 mg, 93%). ¹H NMR (400 MHz, CDCl₃): δ 8.00–7.90 (m, 2H), 7.63–7.53 (m, 1H), 7.52–7.42 (m, 2H), 4.66 (d, *J* = 3.8 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.57–3.43 (m, 2H), 3.35 (d, *J* = 5.8 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 197.4, 173.7, 136.3, 133.4, 128.5, 128.0, 67.0, 61.6, 42.1, 14.0. HPLC (ChiralPak AS-H column, hexane/*i*PrOH = 85/15, 1.0 mL min⁻¹, 254 nm): *t*₁ = 13.5 min, *t*₂ = 16.7 min.

(4i) Ethyl 2-hydroxy-4-oxo-5-phenylpentanoate



Purified by flash column chromatography (PE/EA = 5:1) as yellow oil (219 mg, 86%). ¹H NMR (400 MHz, CDCl₃) δ 7.39–7.13 (m, 5H), 4.44 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 2H), 3.18 (d, *J* = 5.4 Hz, 1H), 2.95 (dd, *J* = 9.0, 5.0 Hz, 2H), 1.24 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 205.6, 173.4, 133.2, 129.3, 128.5, 126.9, 66.7, 61.6, 50.2, 45.0, 13.8. HPLC (ChiralCel AD-H column, hexane/*i*PrOH = 85/15, 1.0 mL min⁻¹, 220 nm): *t*₁ = 11.3 min, *t*₂ = 12.4 min. HRMS Calculated for C₁₃H₁₆O₄Na (M+Na)⁺: 259.0946, found: 259.0955.

(4j) 2-Hydroxy-5,5-dimethyl-1-morpholinohexane-1,4-dione^[22]



Purified by flash column chromatography (PE/EA = 5:1) as yellow liquid (224 mg, 92%). ¹H NMR (400 MHz, CDCl₃): δ 4.83 (td, *J* = 7.6, 3.2 Hz, 1H), 3.86 (d, *J* = 7.4 Hz, 1H), 3.80–3.45 (m, 8H), 3.01–3.95 (m, 1H), 2.58–2.53 (m, 1H), 1.16 (s, 9H). ¹³C NMR (100 MHz, CDCl₃): δ 213.8, 171.5, 66.4, 66.3, 65.0, 45.4, 44.1, 42.4, 41.0, 25.7. HPLC (ChiralPak AS-H column, hexane/*i*PrOH = 80/20, 0.8 mL min⁻¹, 220 nm): *t*₁ = 8.8 min, *t*₂ = 9.5 min. HRMS Calculated for C₁₂H₂₁NO₄Na (M+Na)⁺: 266.1368, found: 266.1370.

5. Study of the enol structure of **1a** in THF.

The following ¹H NMR and ¹H-¹³C HMBC spectra were recorded on a Bruker-500 MHz NMR spectrometer at room temperature. The enol content in *d*₈-THF is 87% from the integrals of the H₍₁₎. The tautomerization equilibrium constant *K*_{eq} is calculated to be 6.7.^[23] An asymmetric β-diketone **1a** may exist in two possible enol forms (**B** and **C**), which could be identified by an HMBC experiment.^[24]

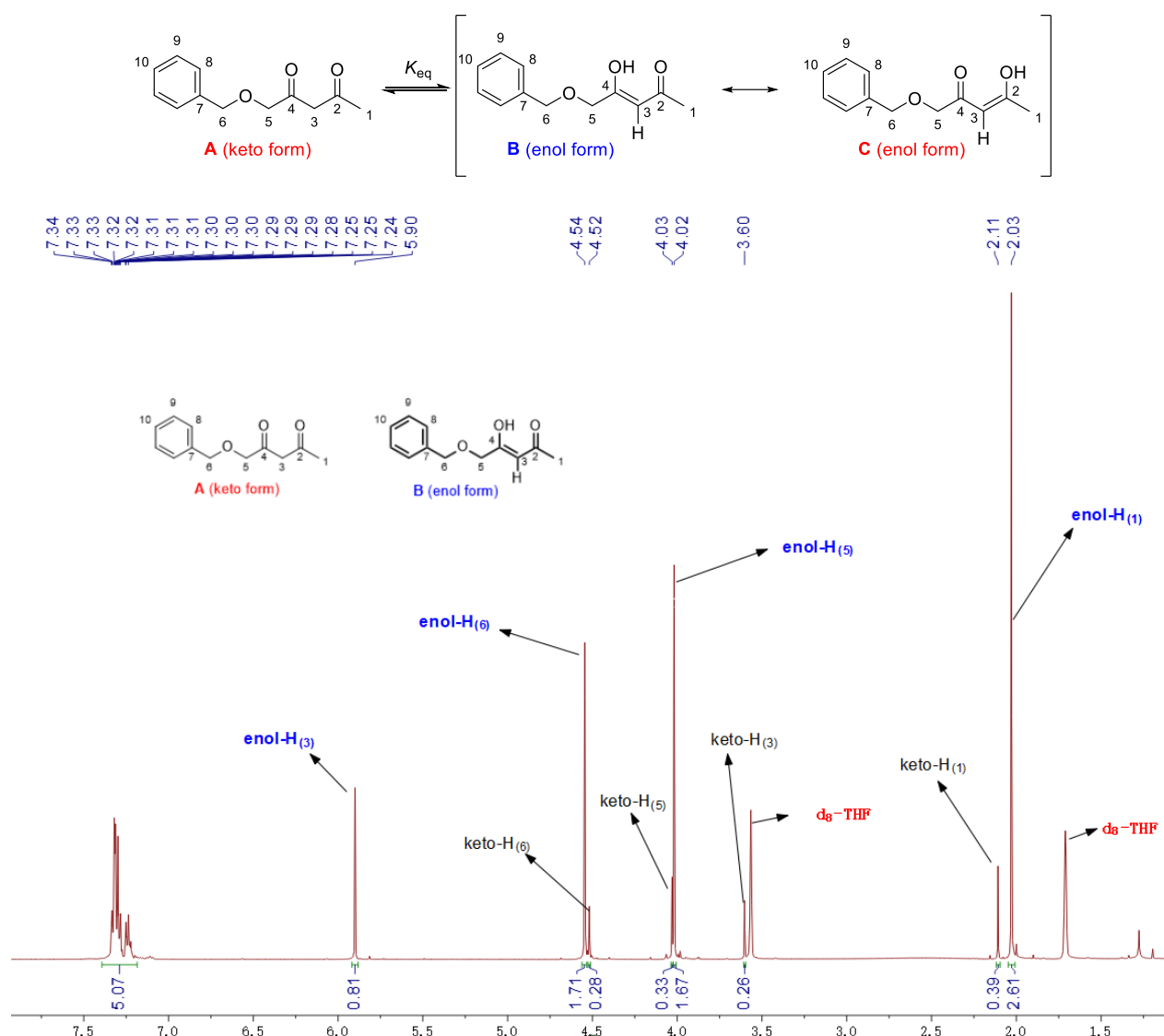


Figure S1. The Assignments of the ¹H NMR (d₈-THF, 500 MHz) Spectrum of **1a**.

From the ¹H-¹³C-HMBC spectrum, the enol form **B** is the predominant in THF.

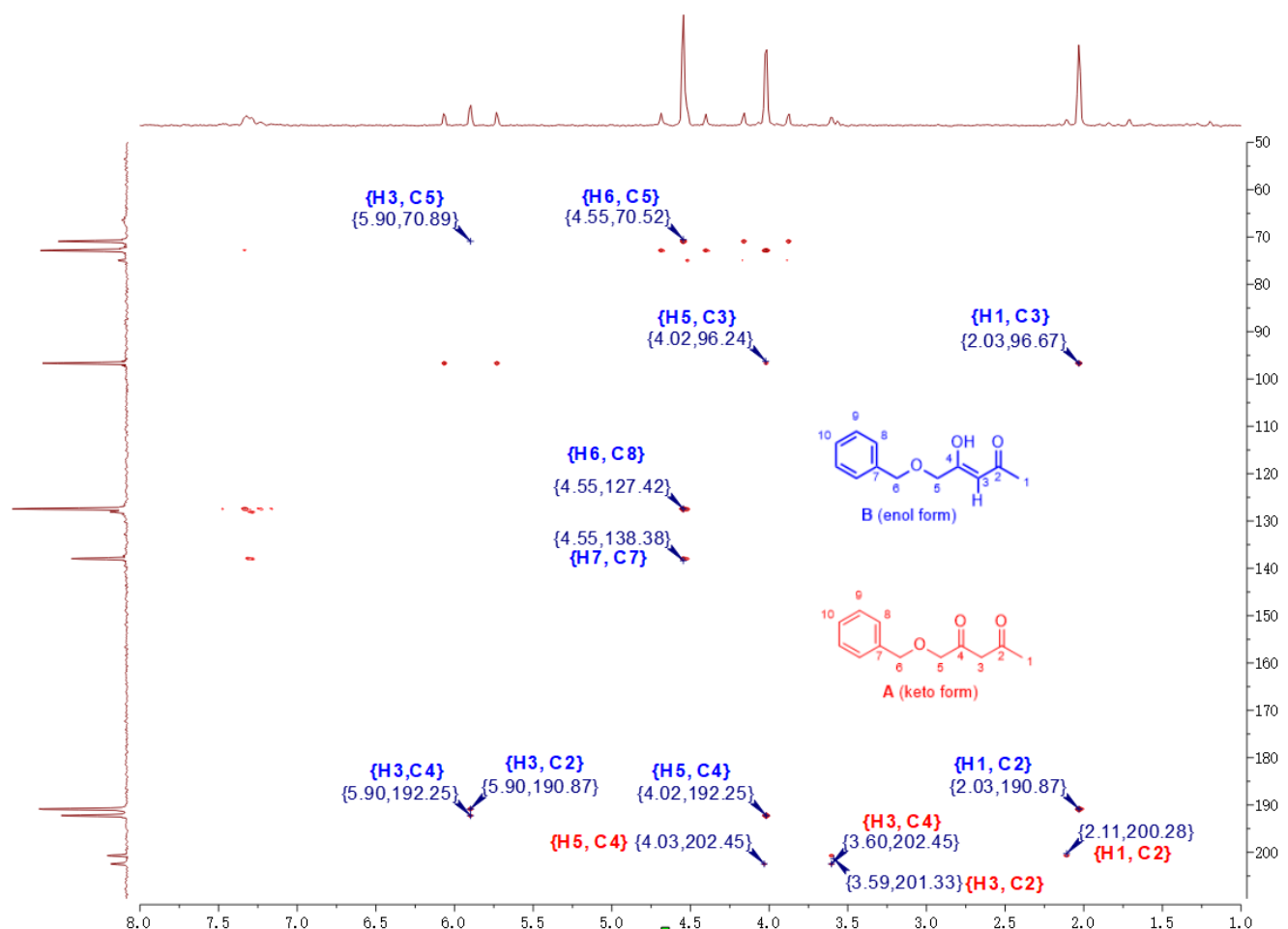


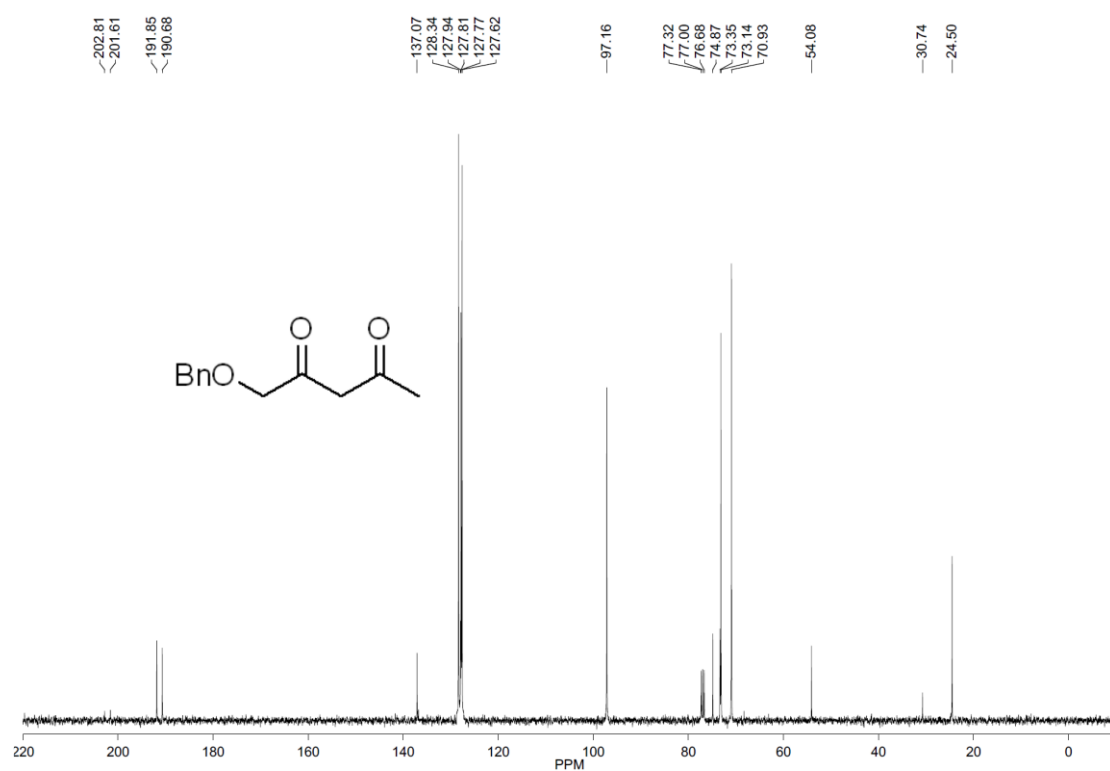
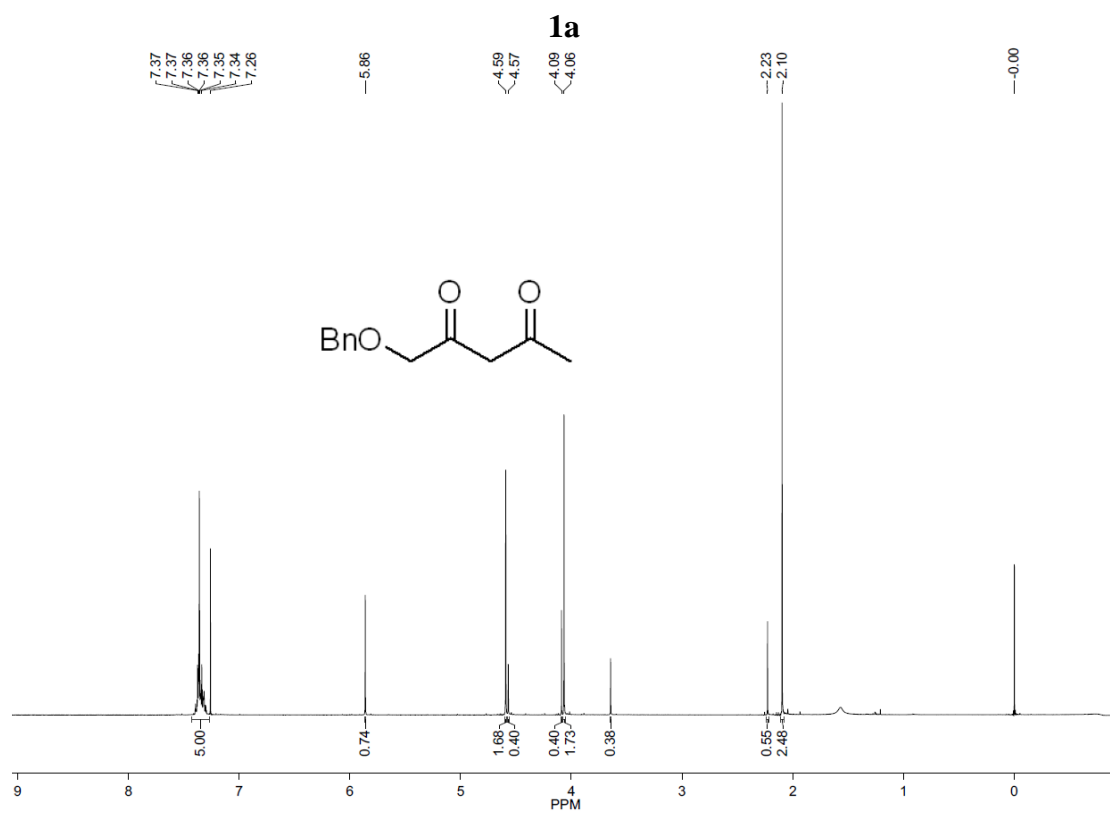
Figure S2. ^1H - ^{13}C HMBC (d_8 -THF, 500 MHz) Correlations for **1a**.

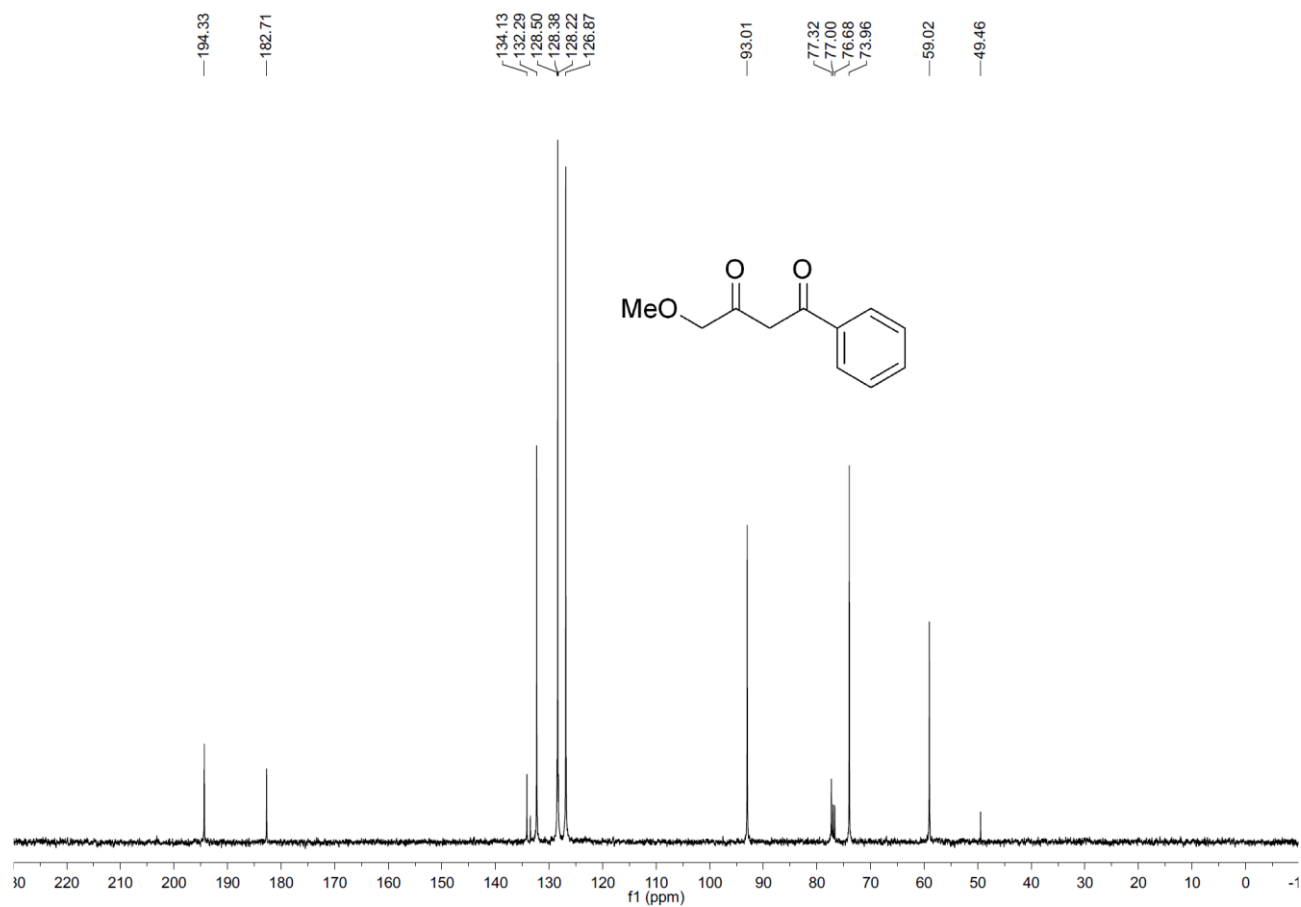
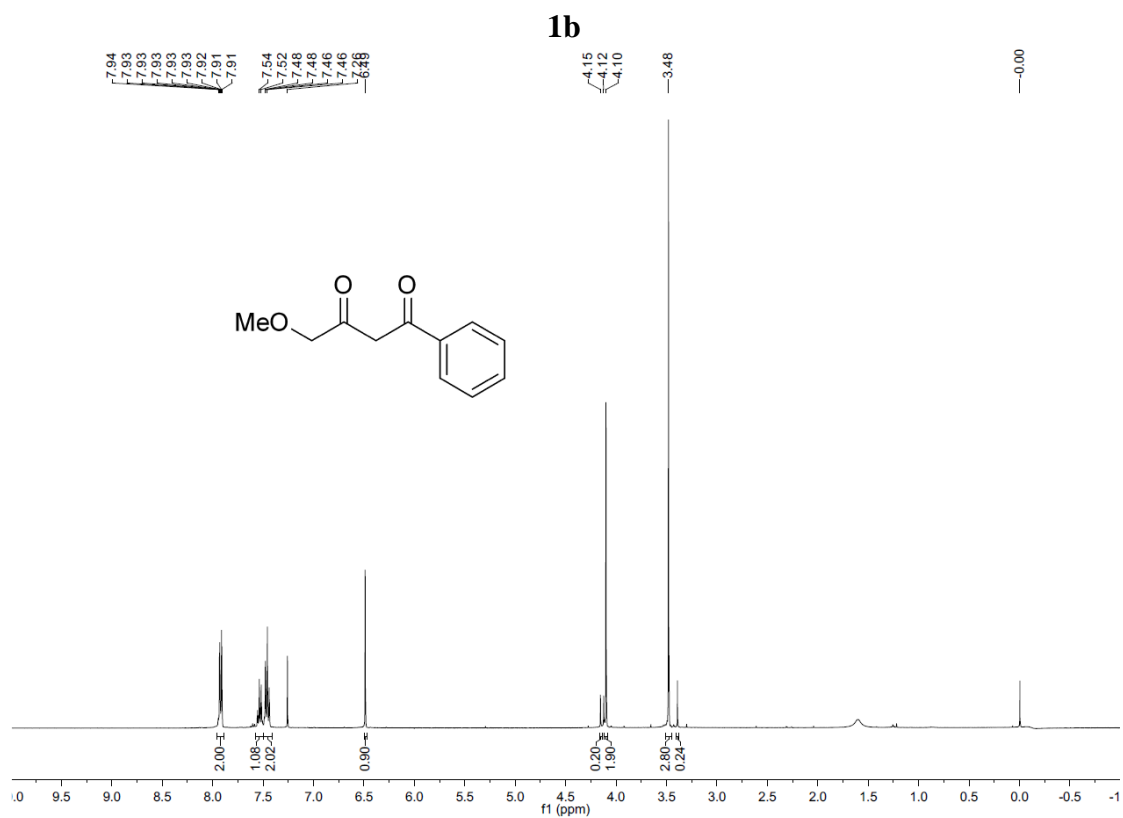
6. References

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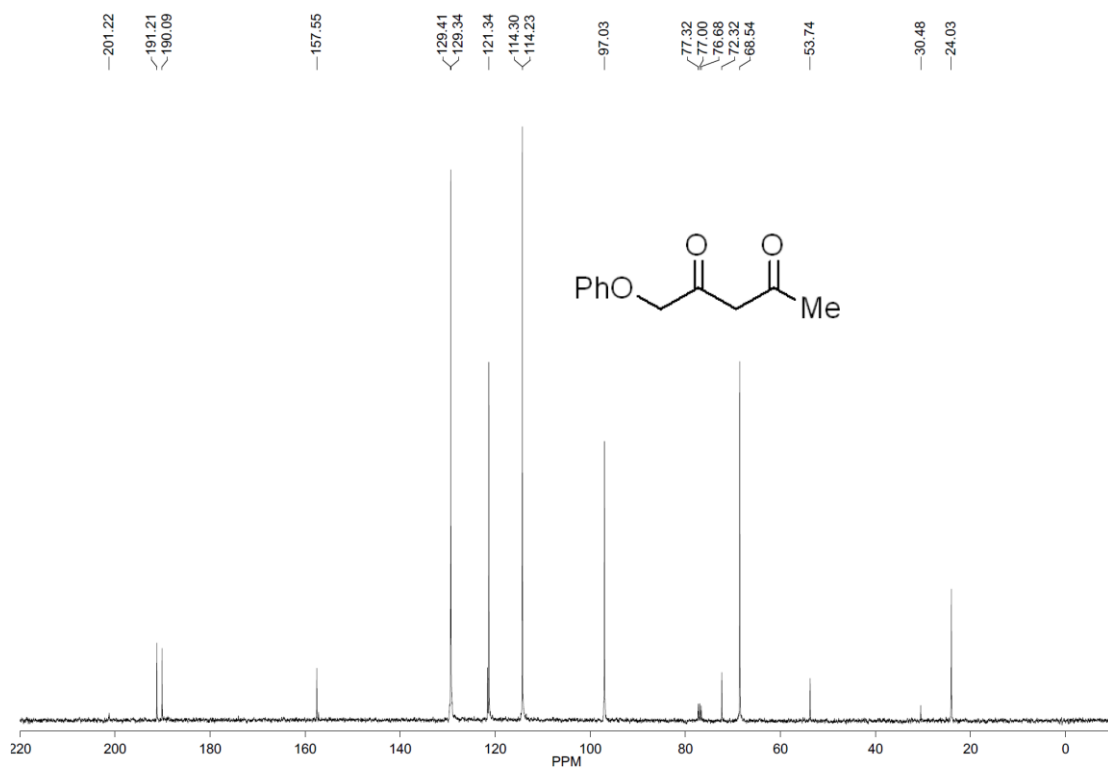
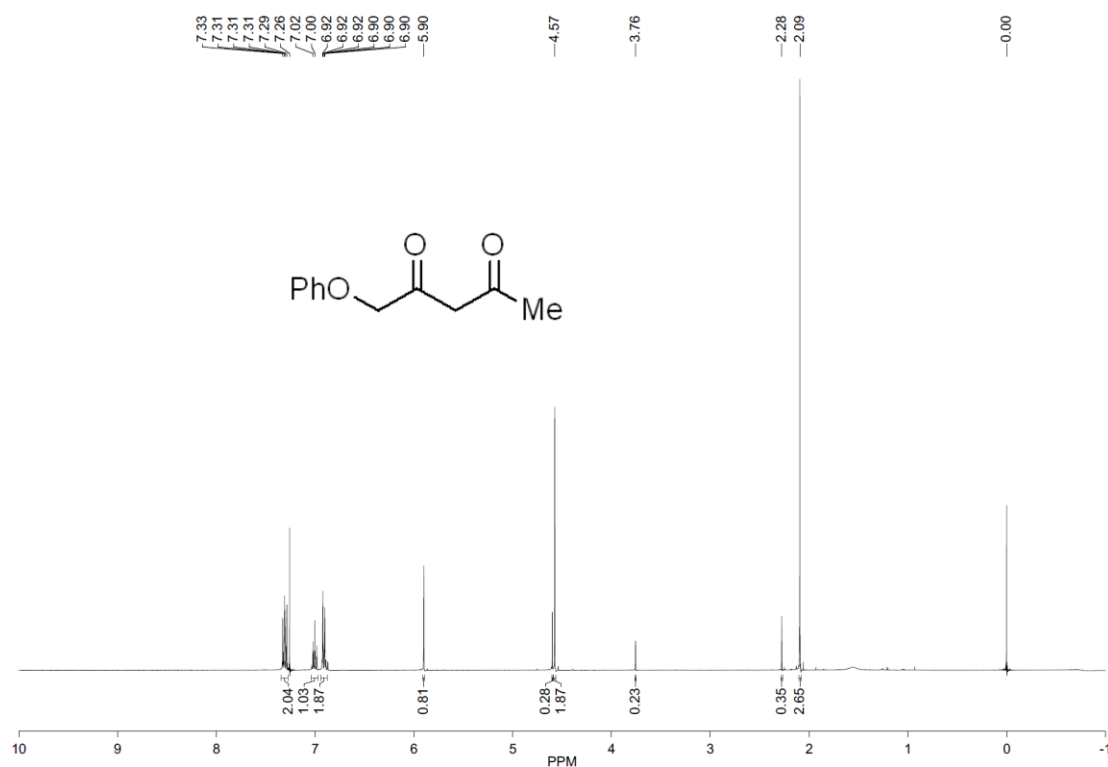
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7. NMR spectra of key substrates and all hydrogenation products

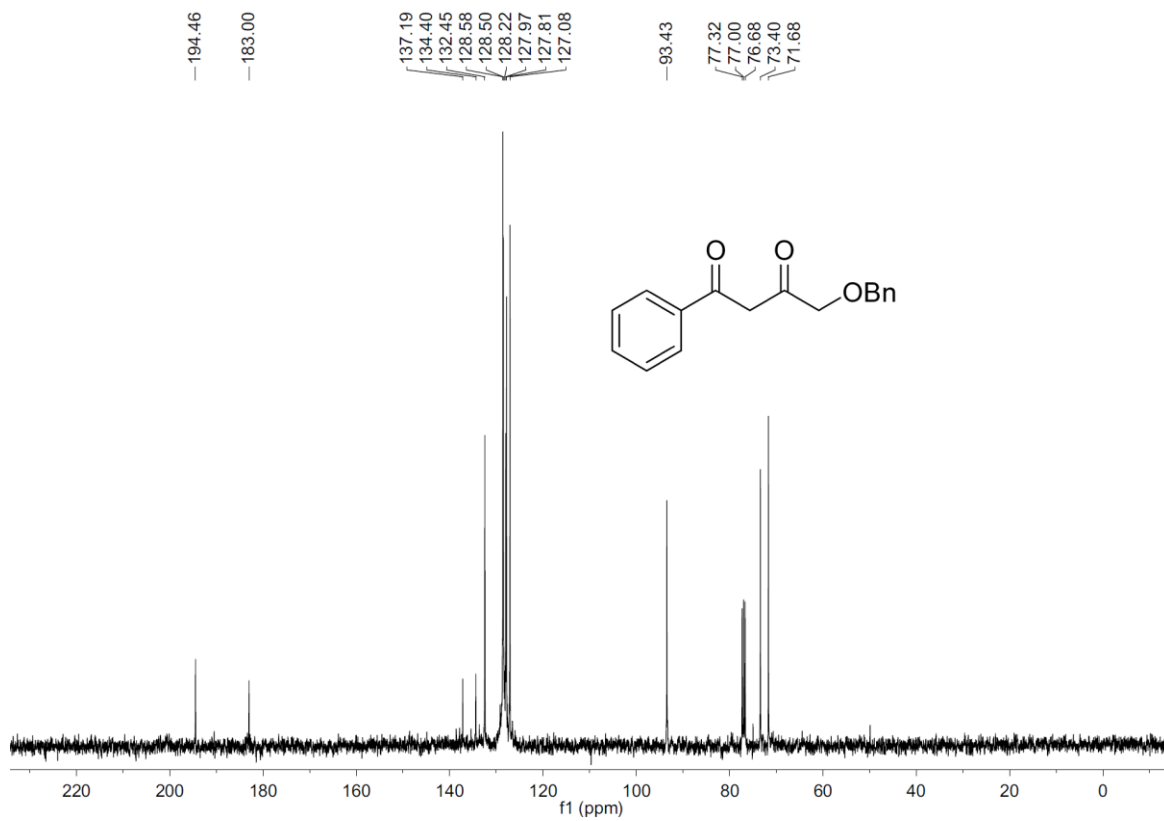
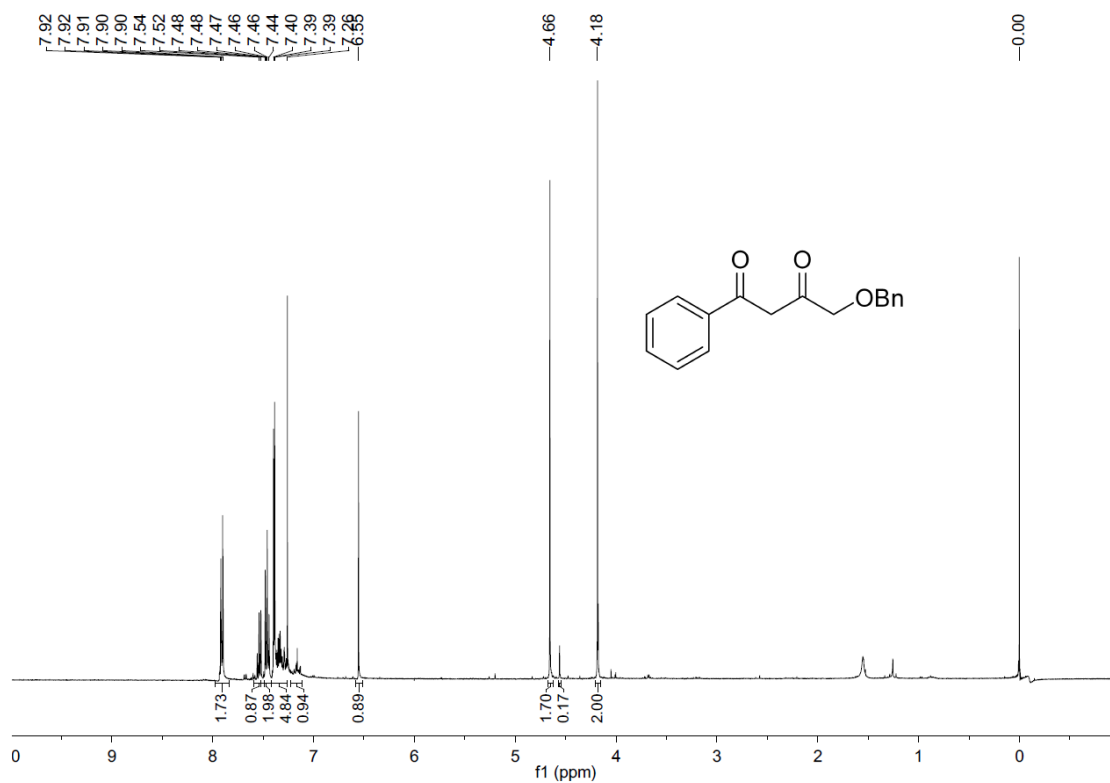


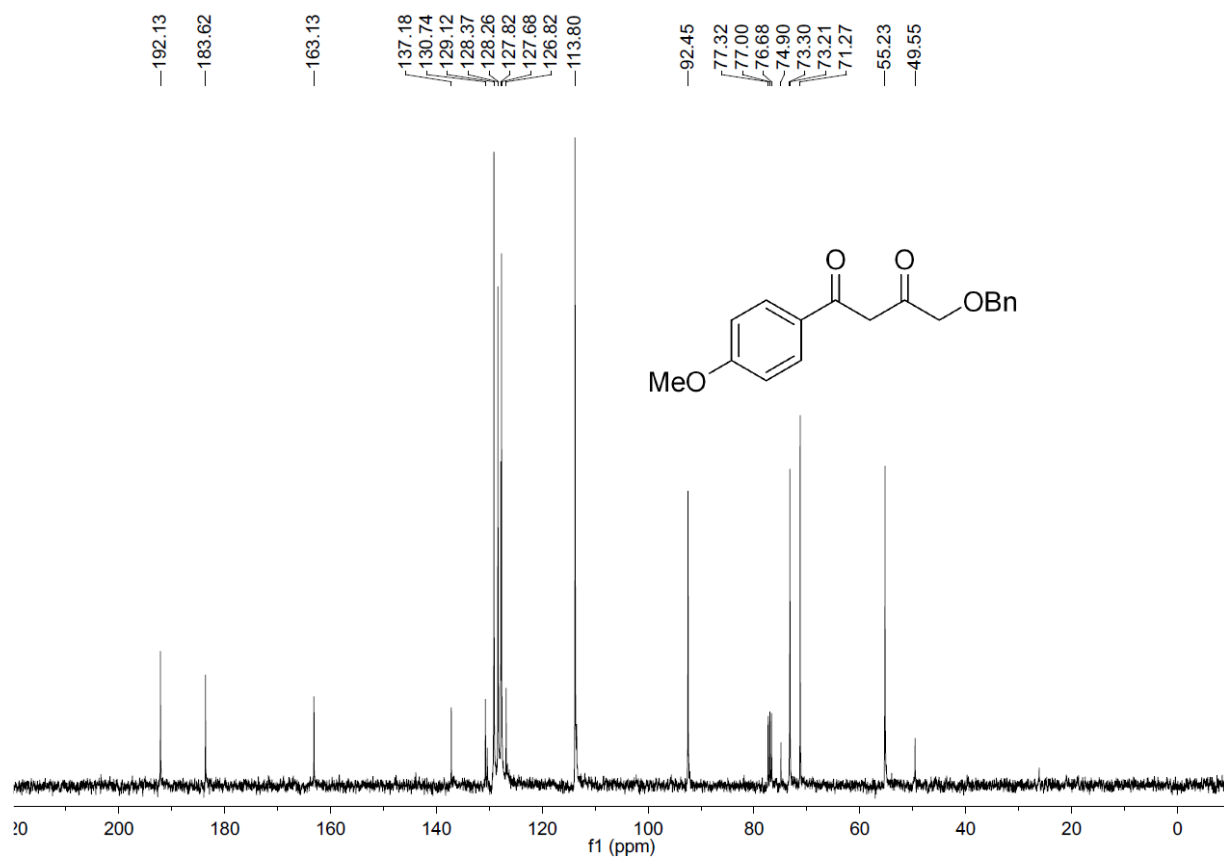
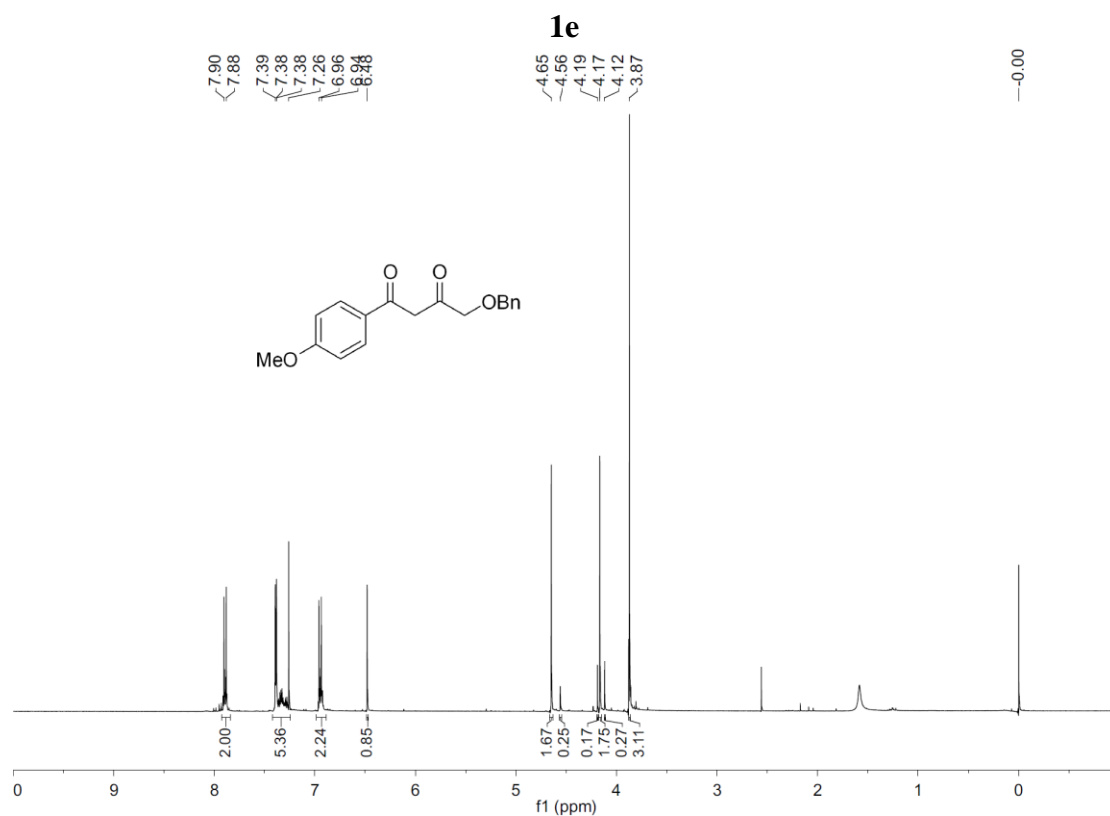


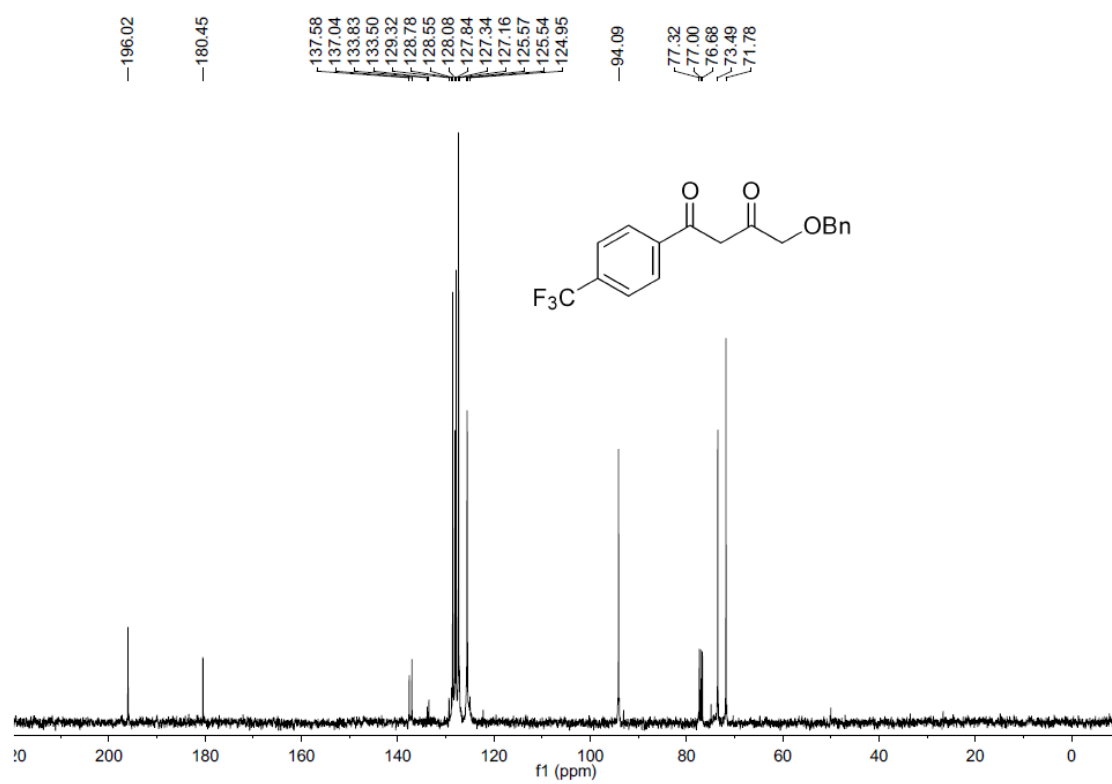
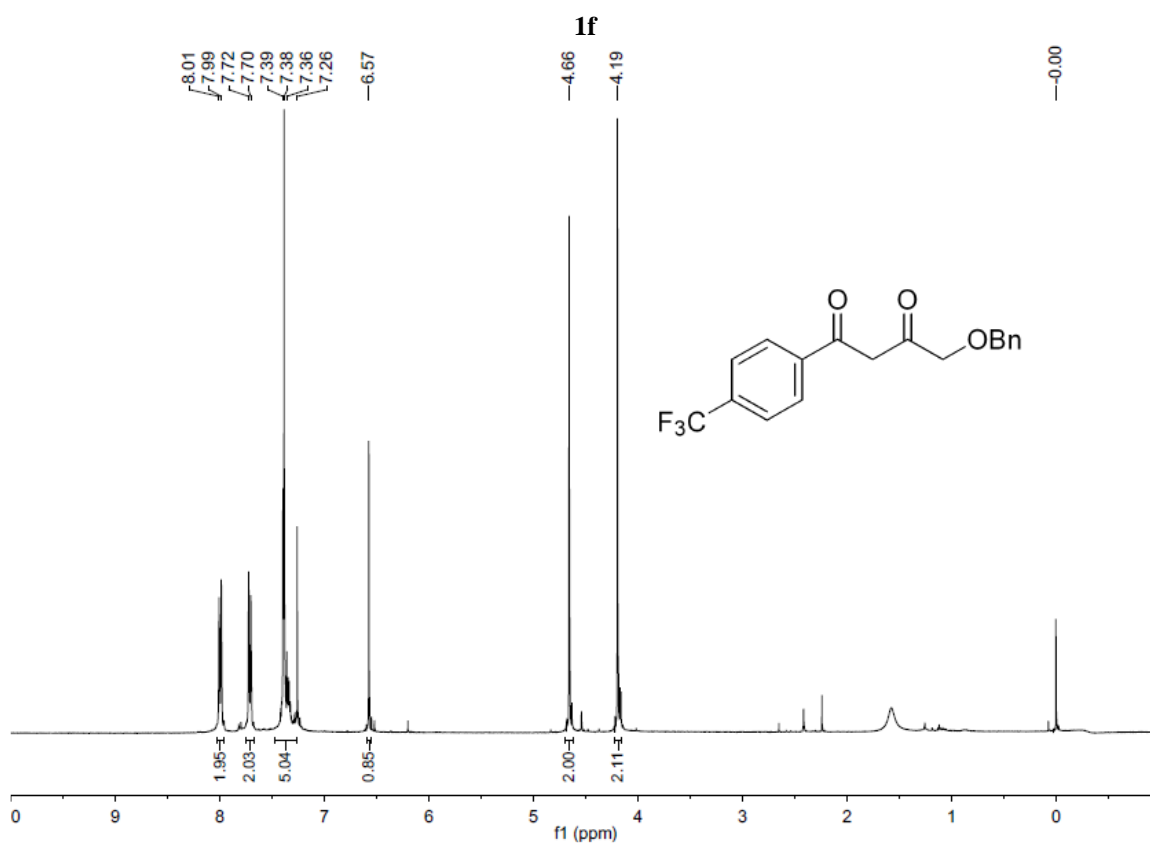
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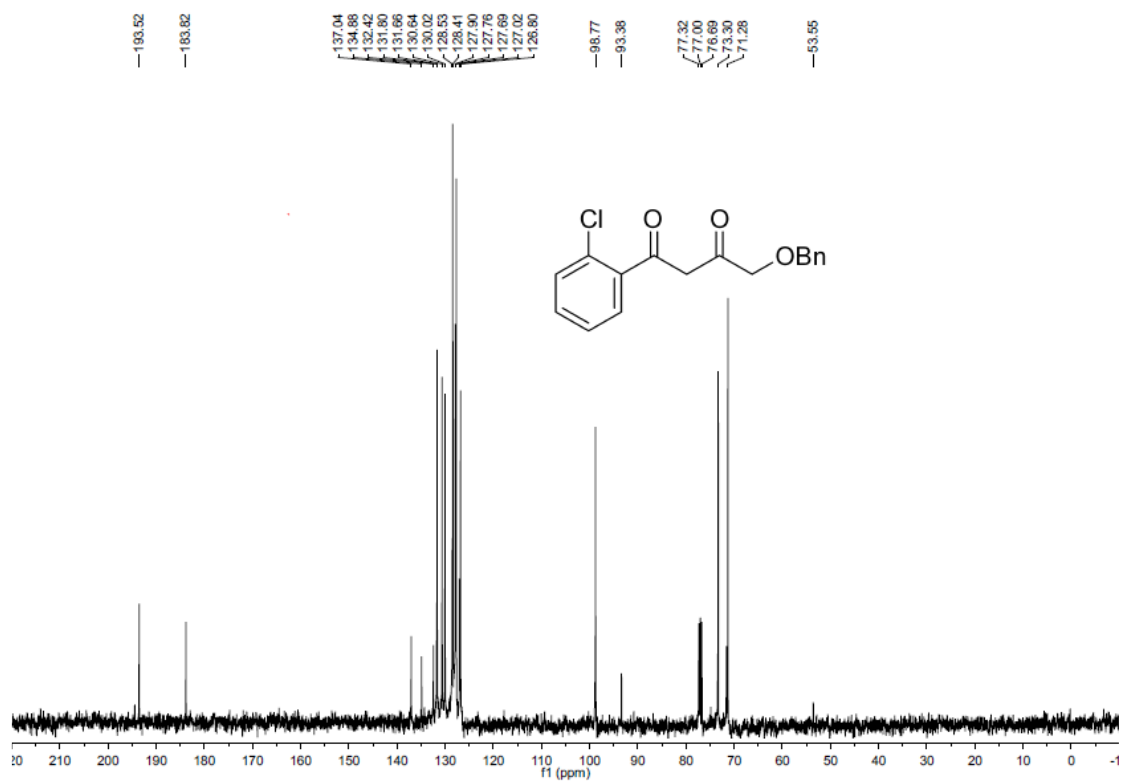
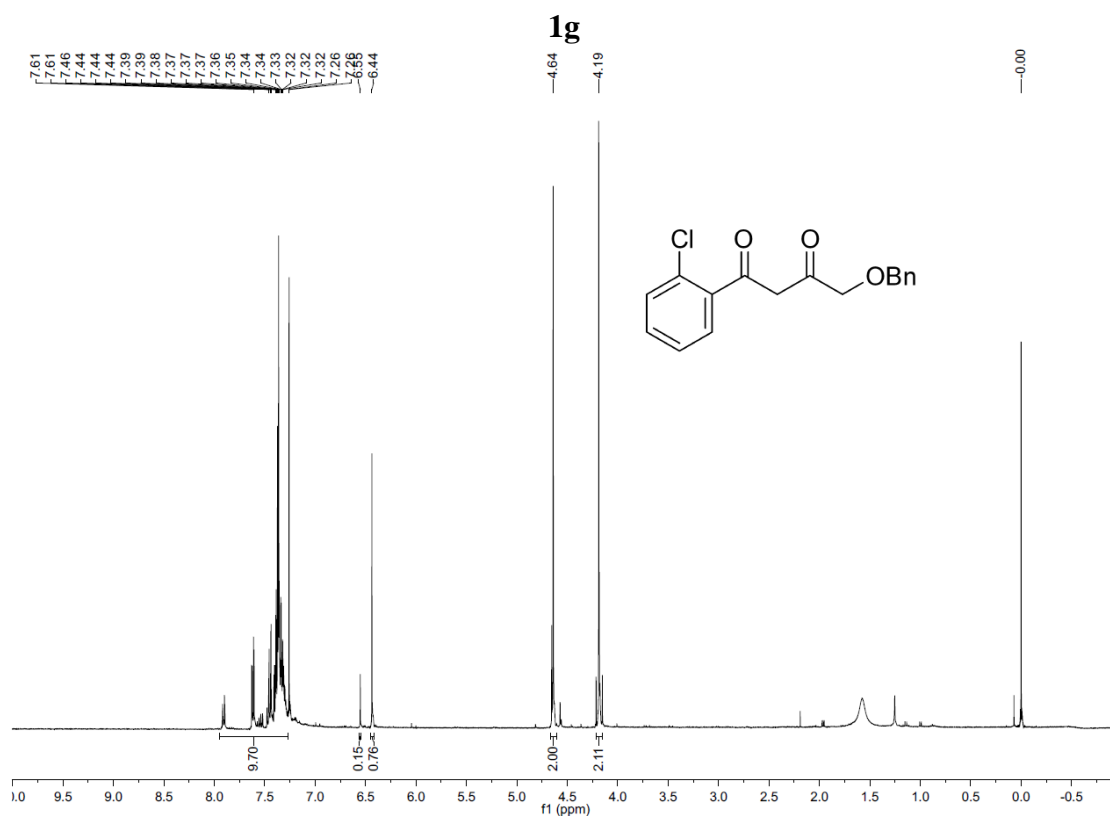


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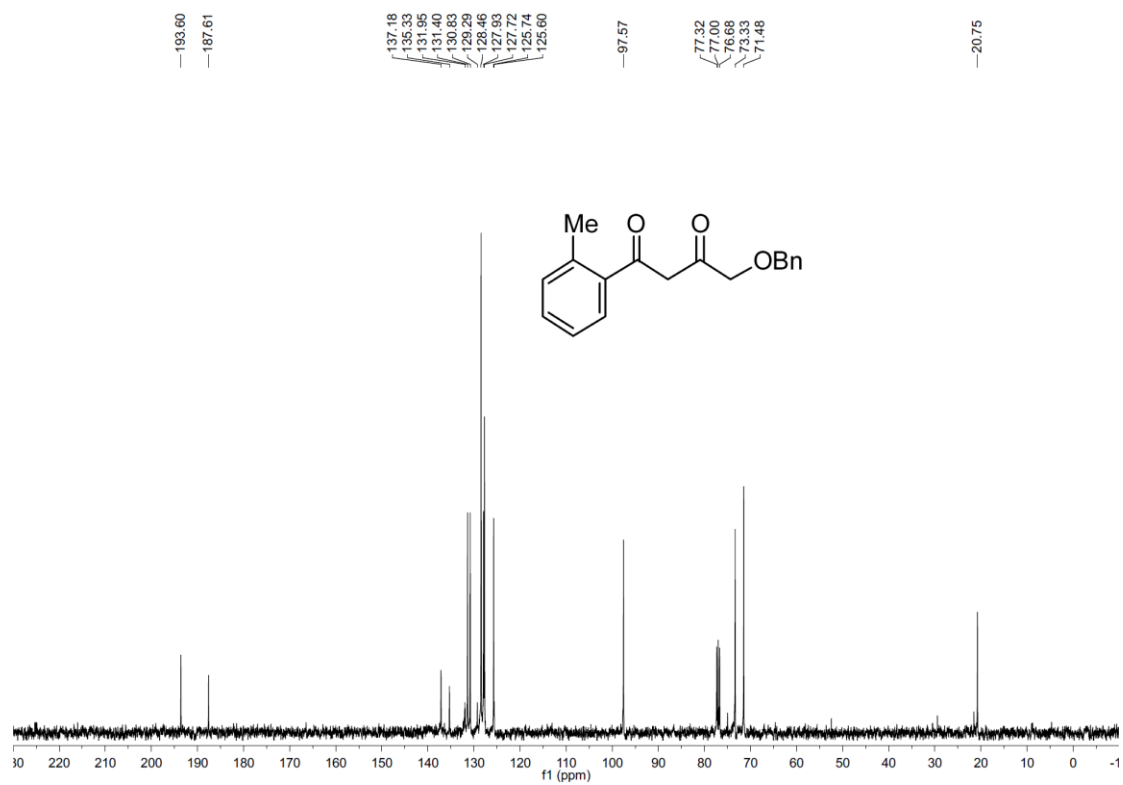
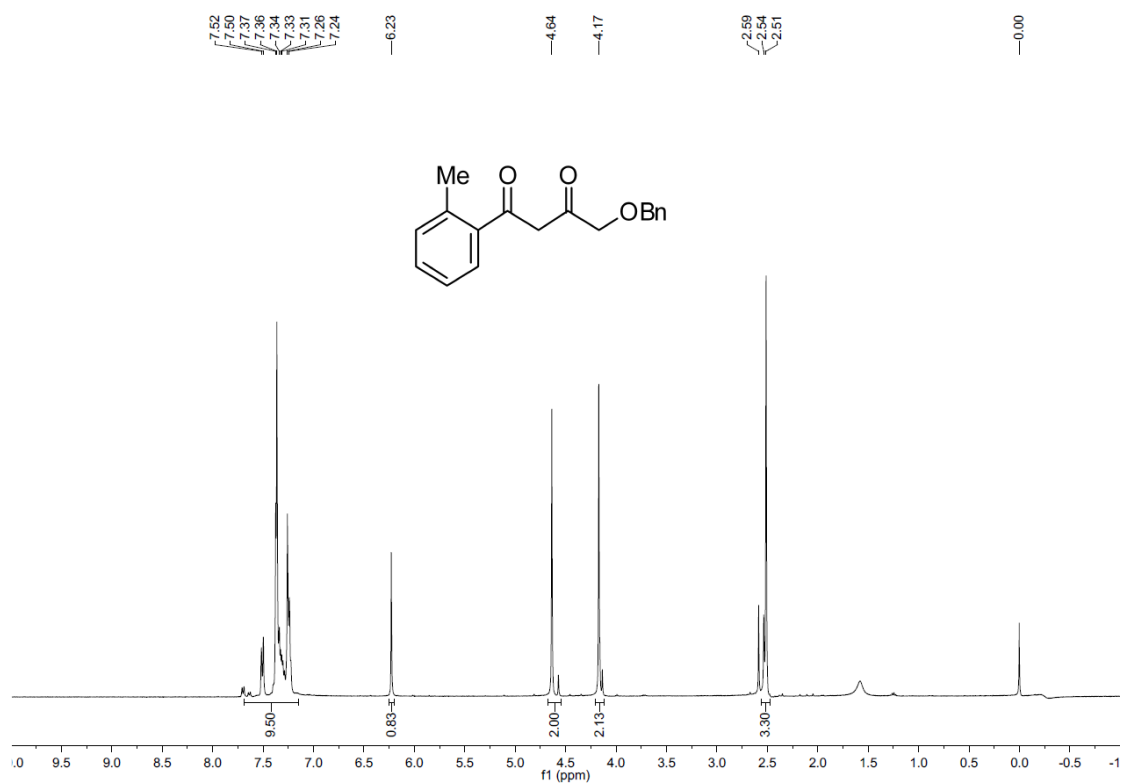


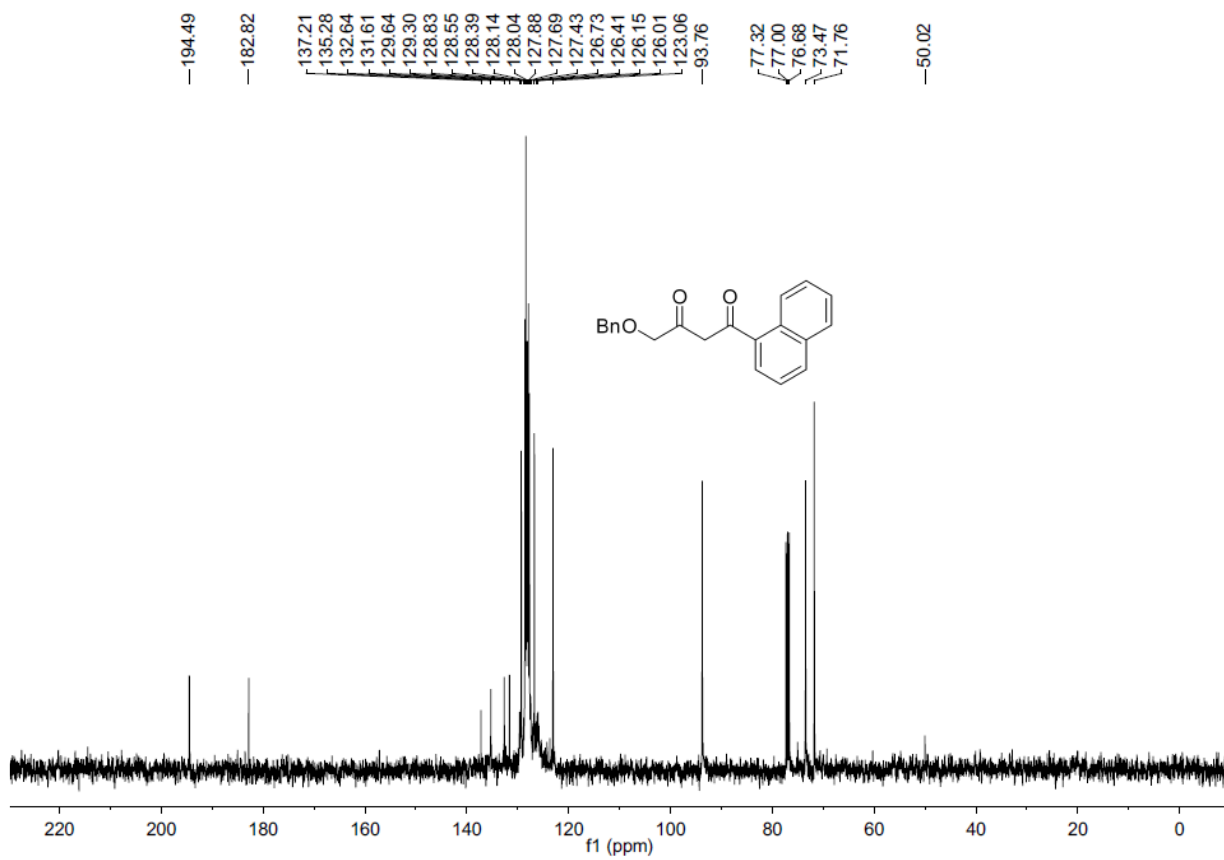
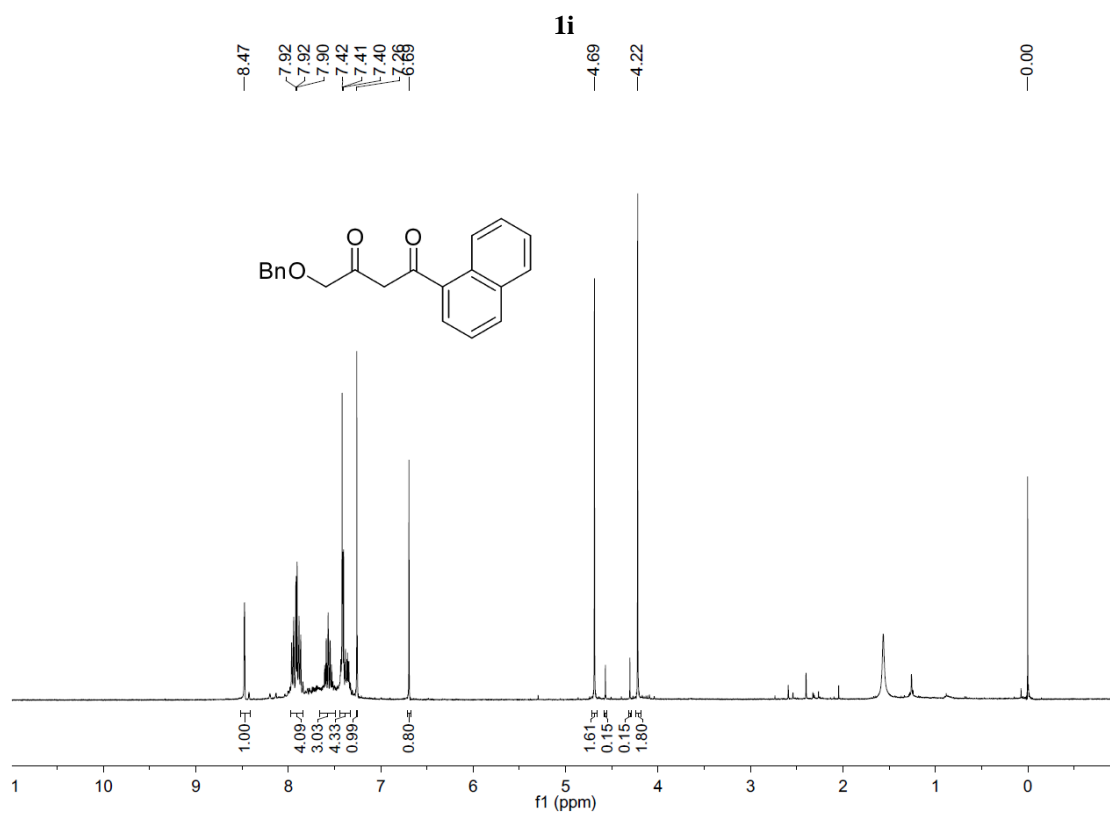


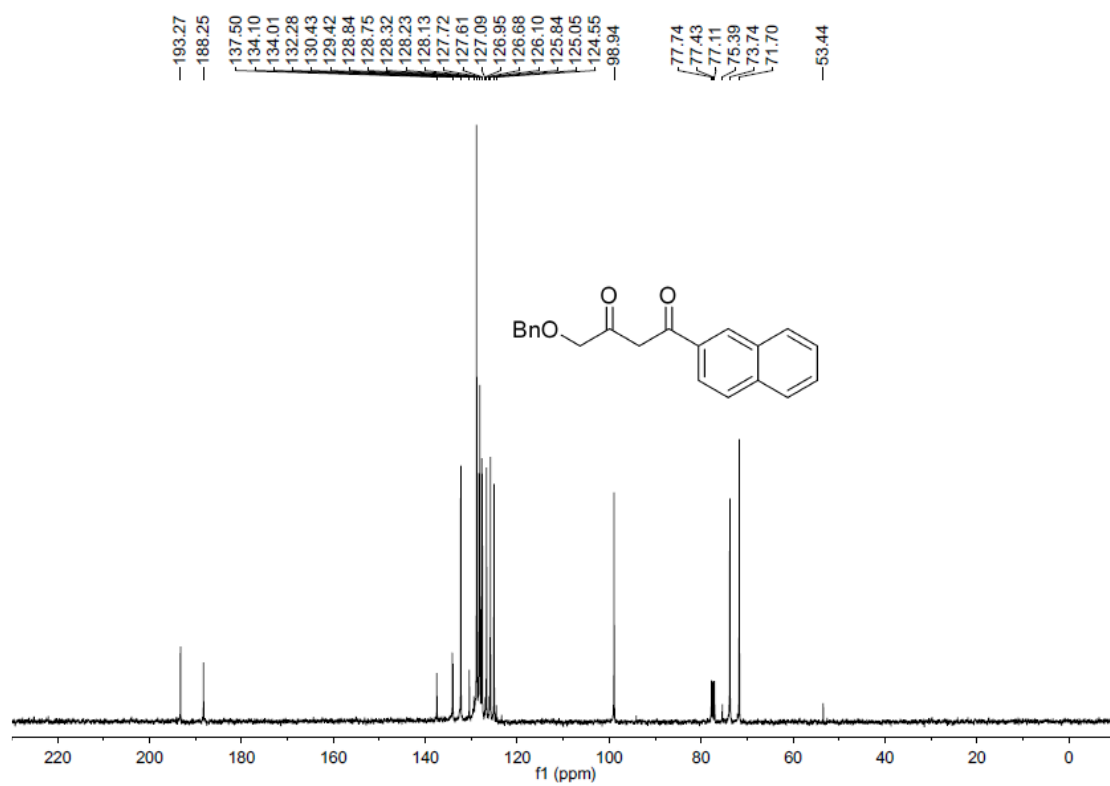
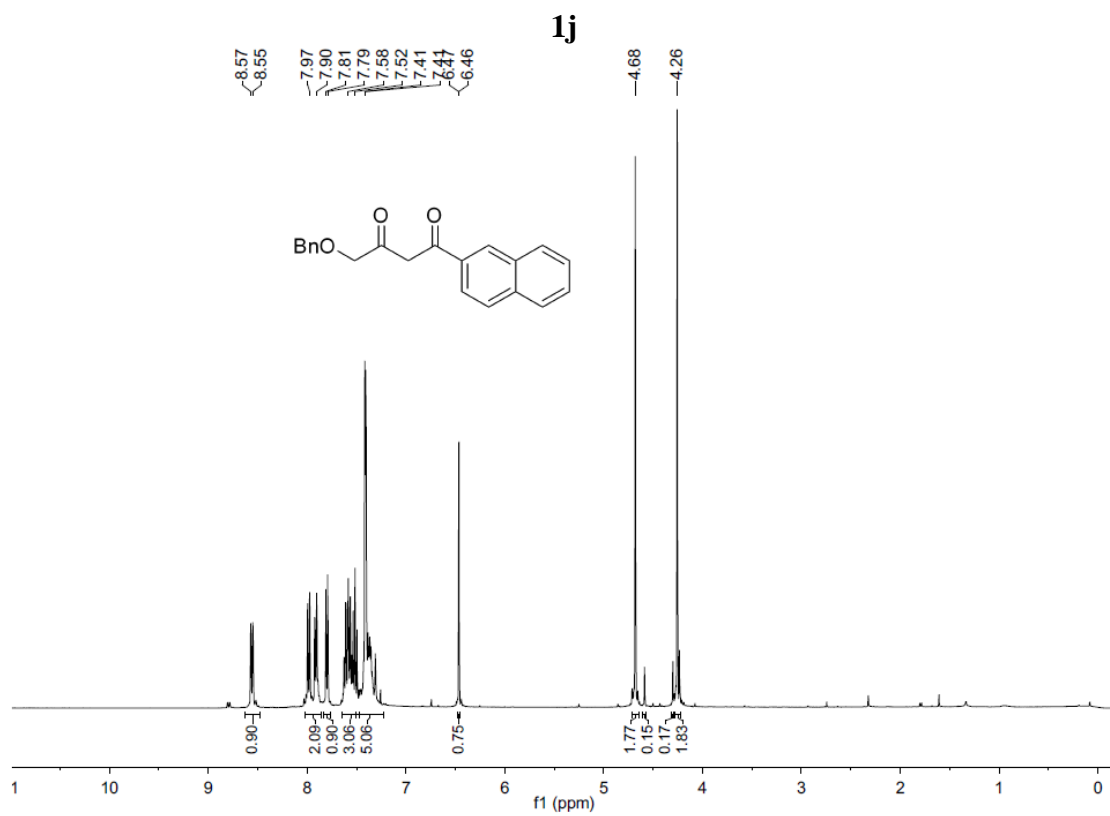


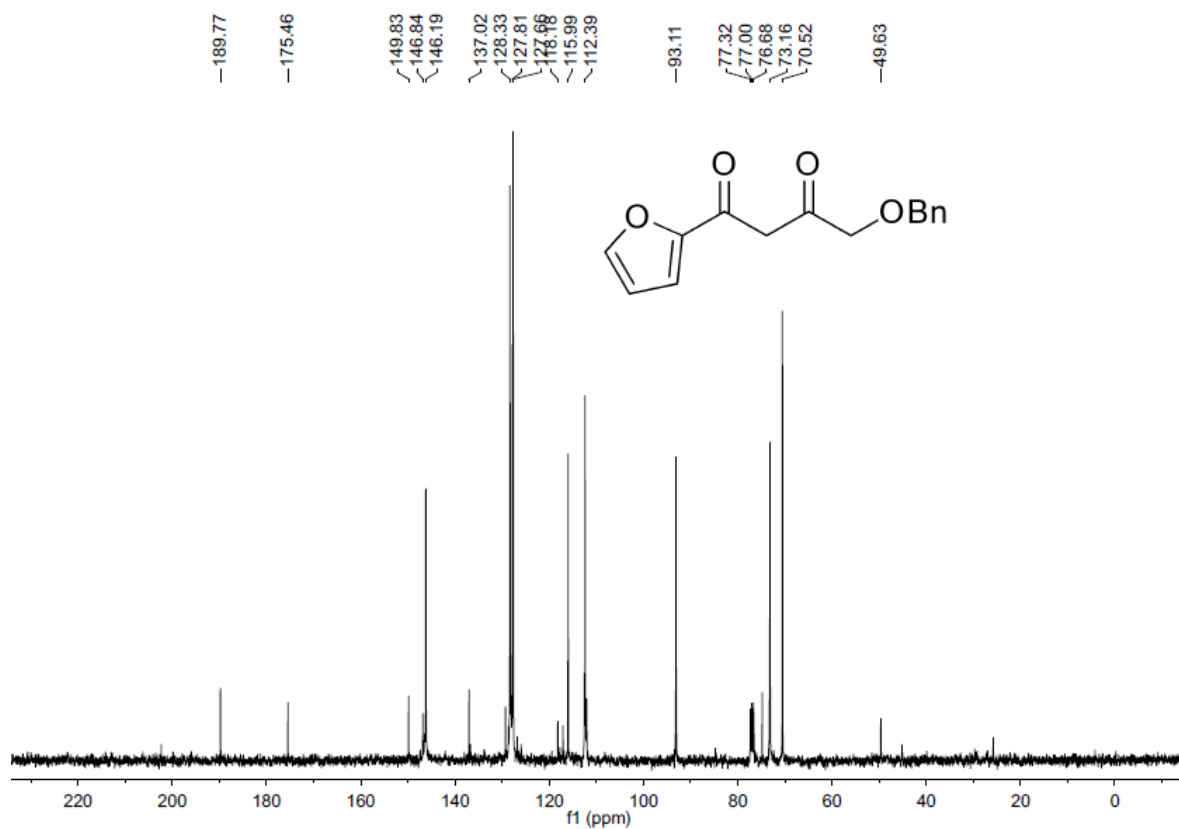
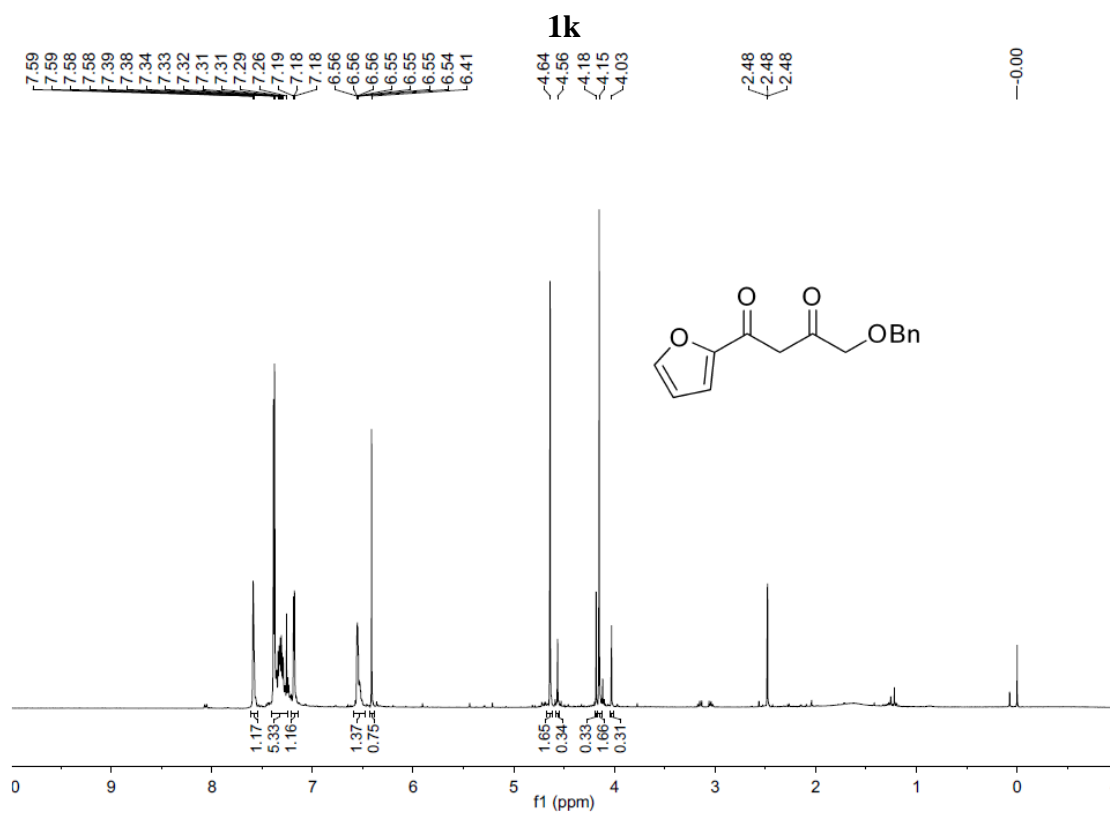


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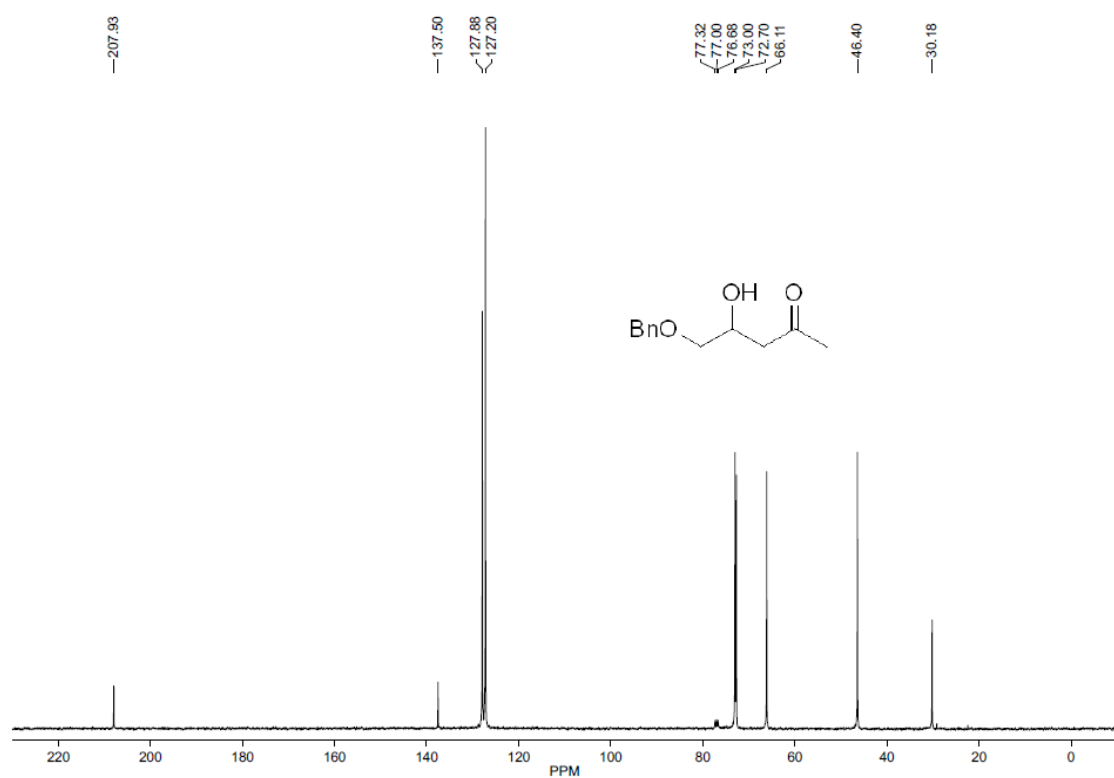
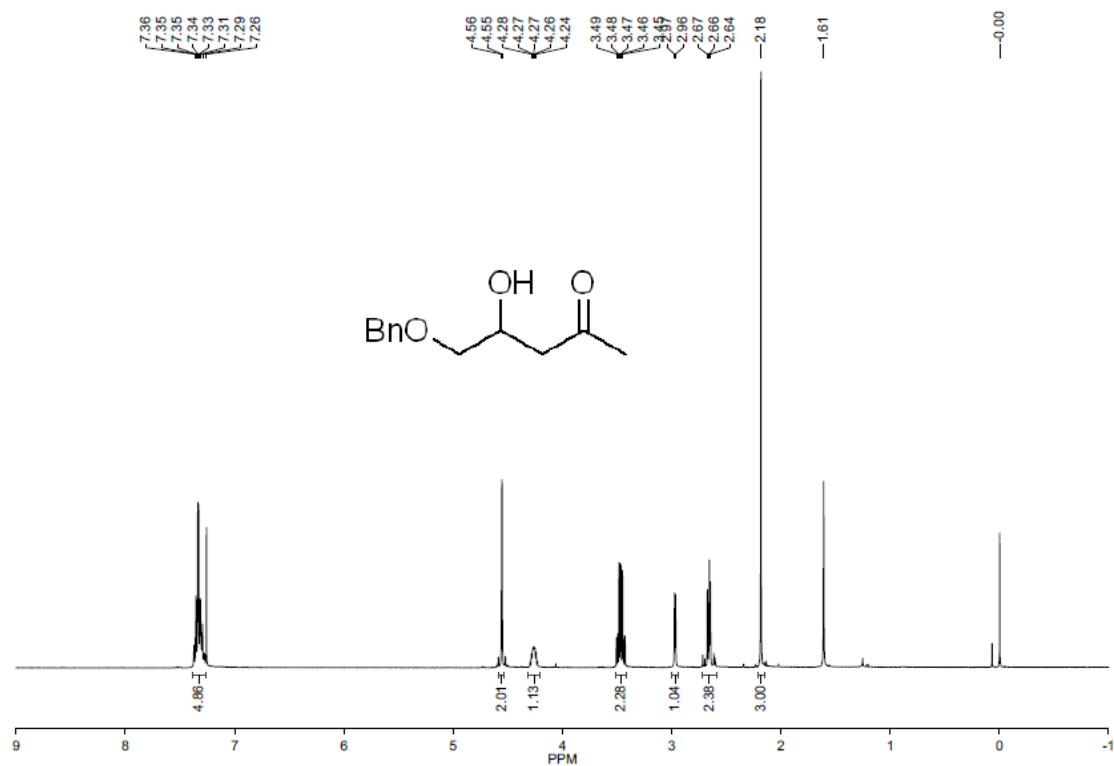


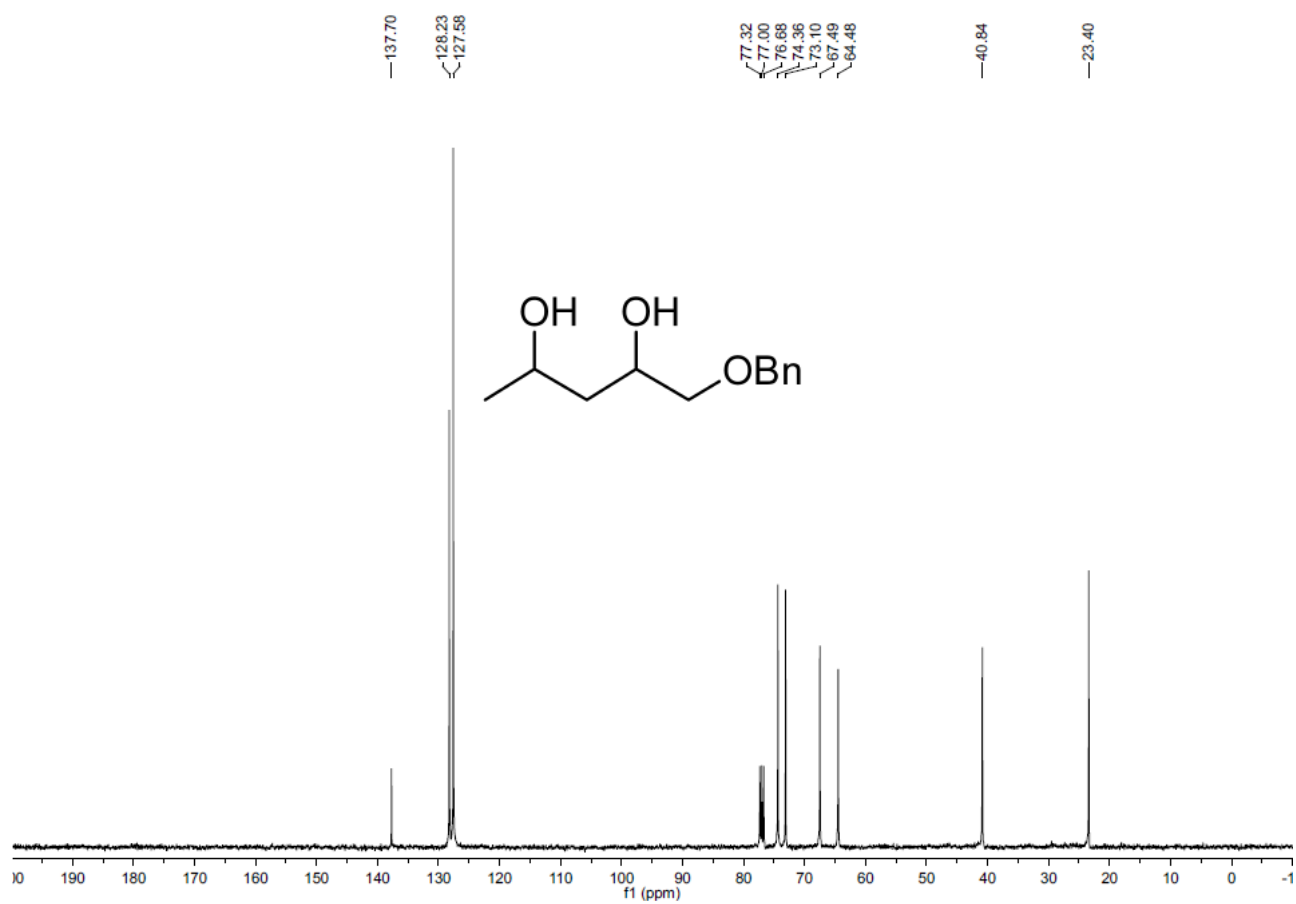
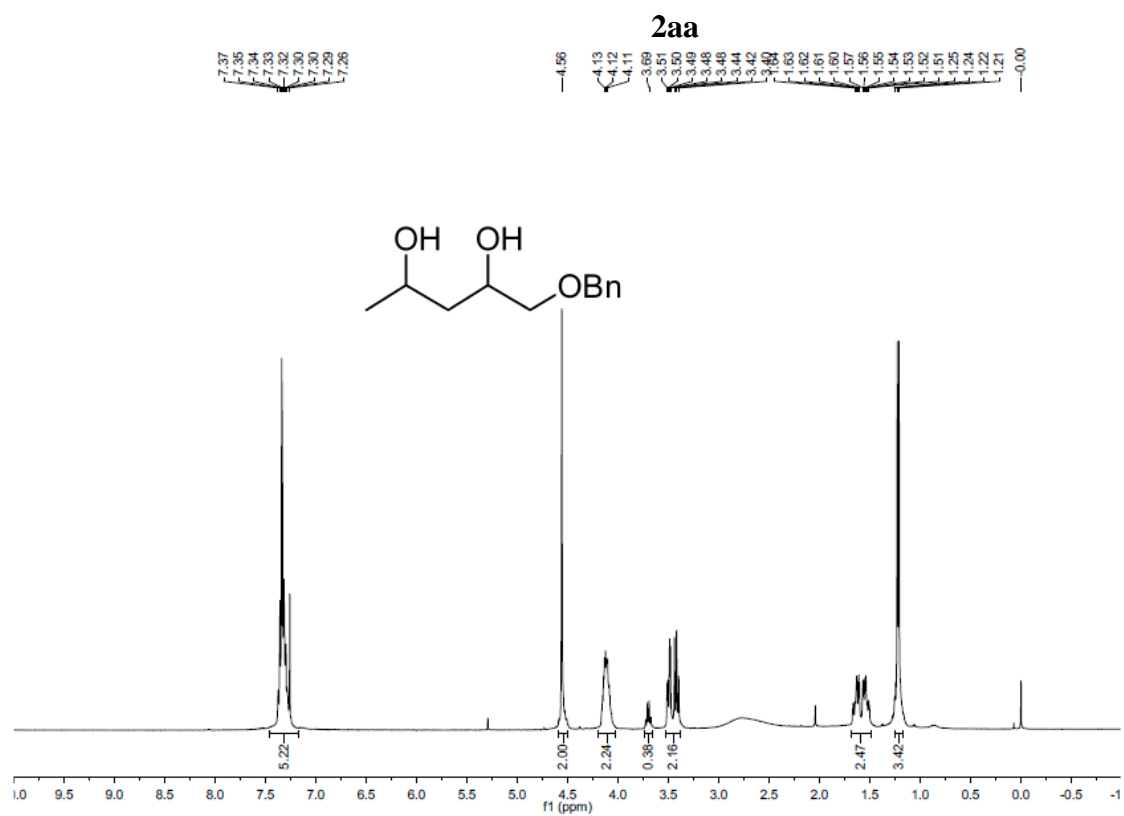


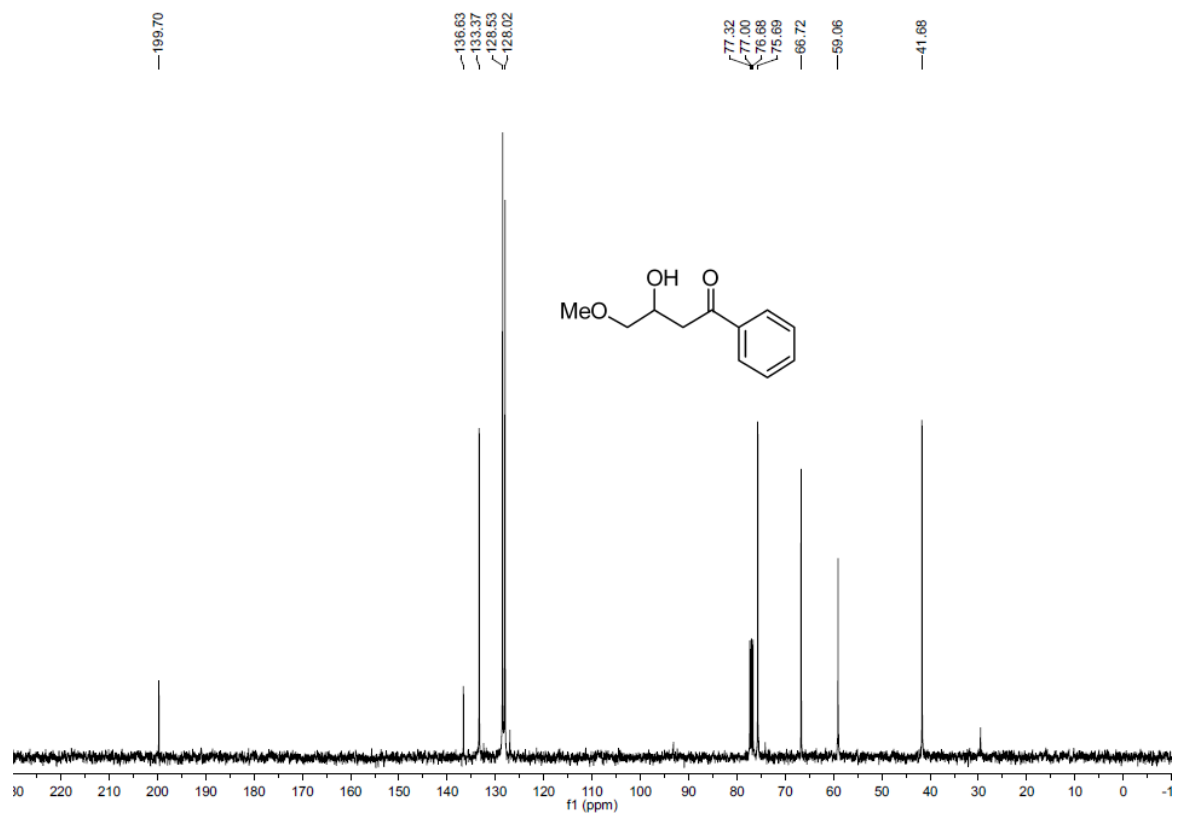
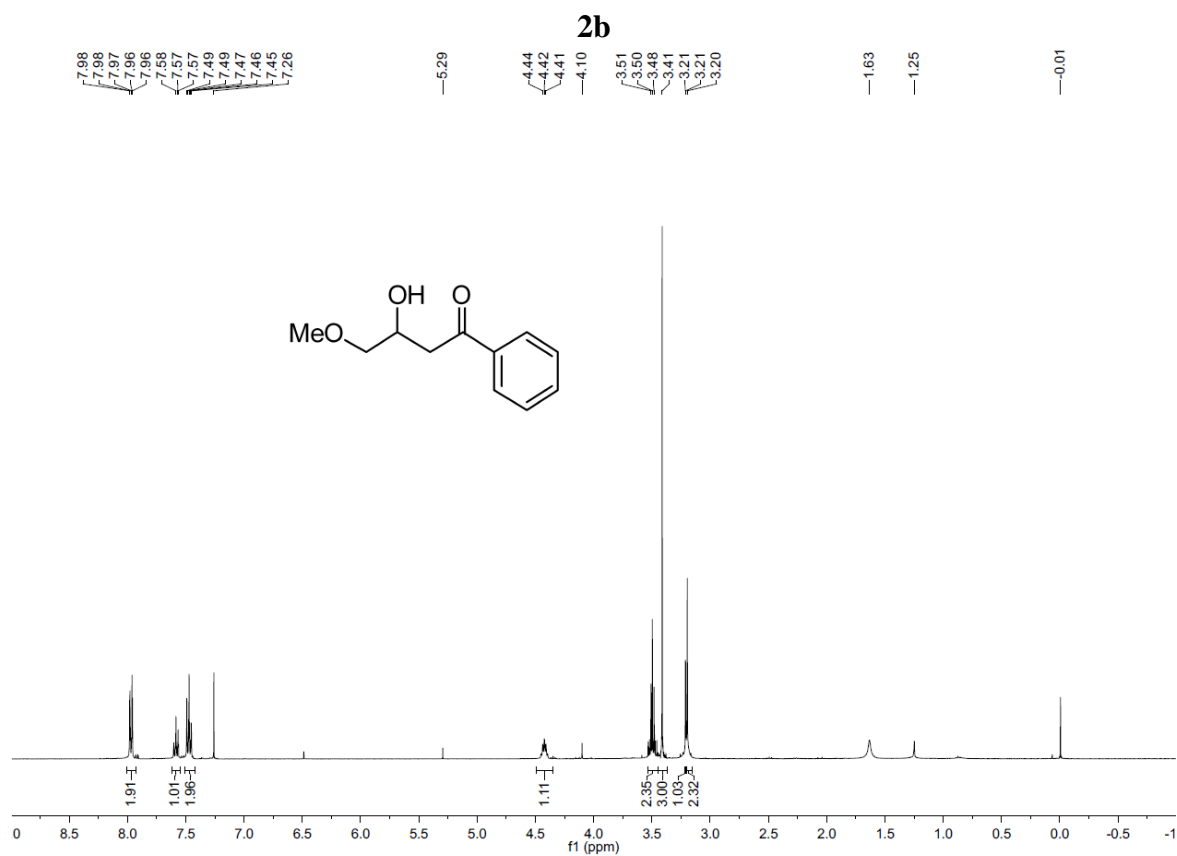


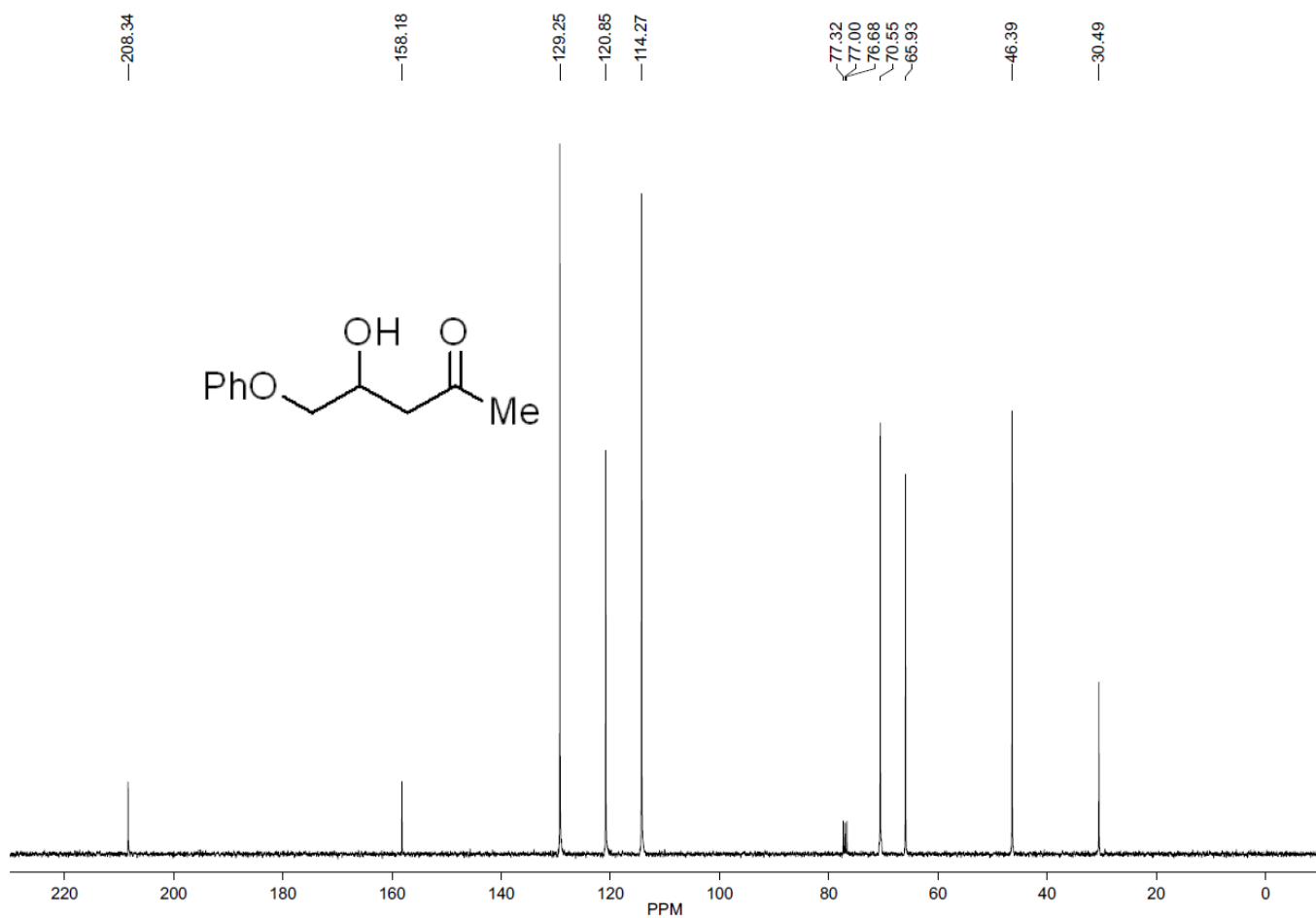
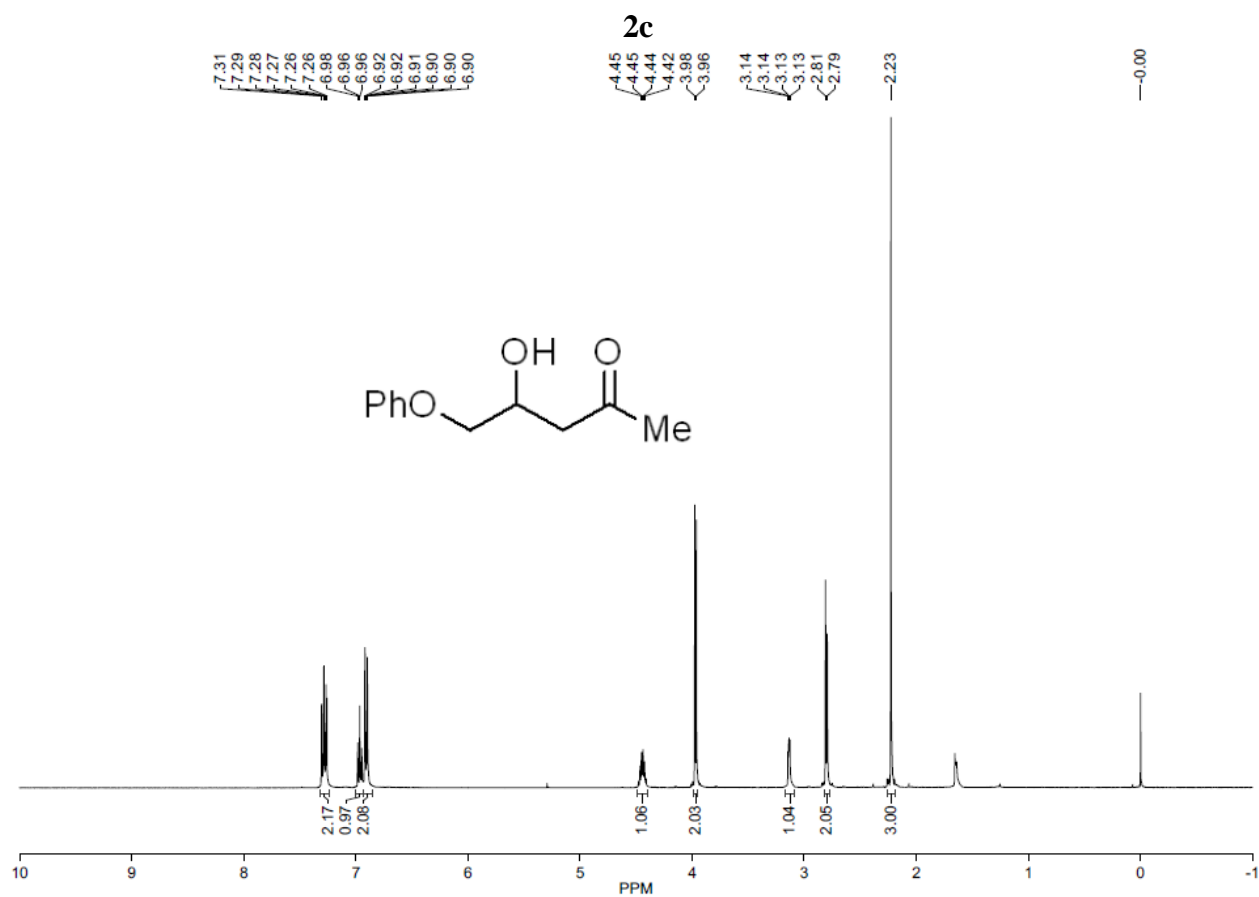


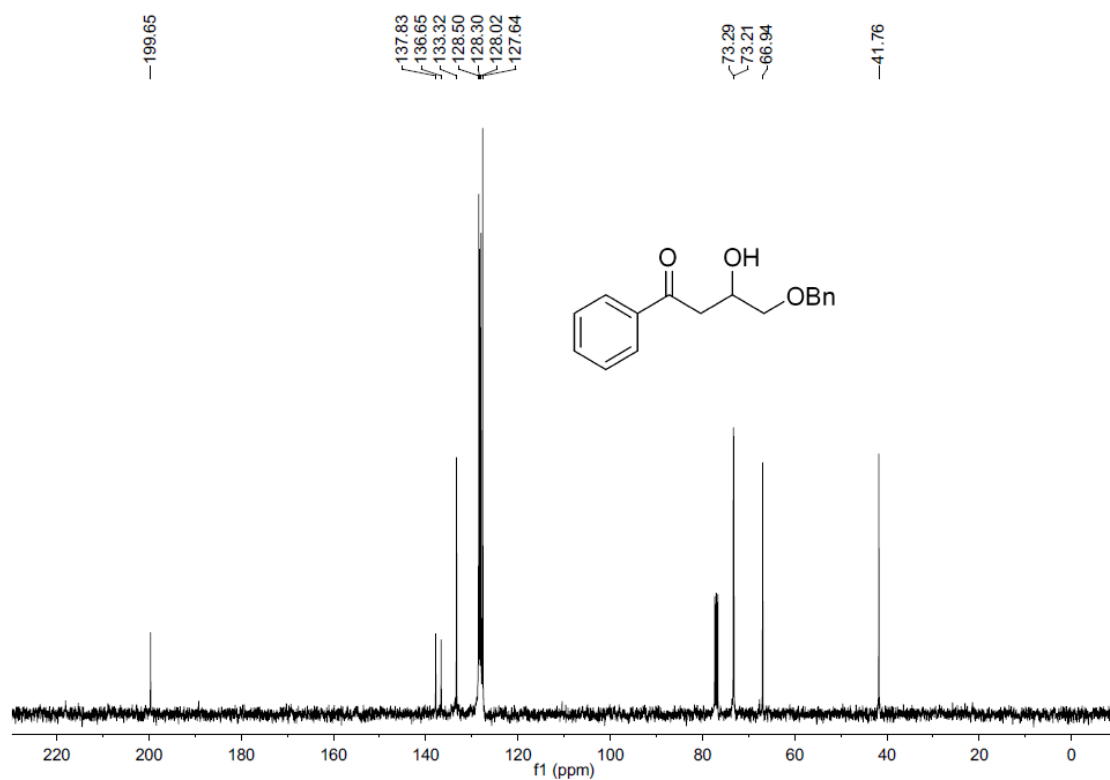
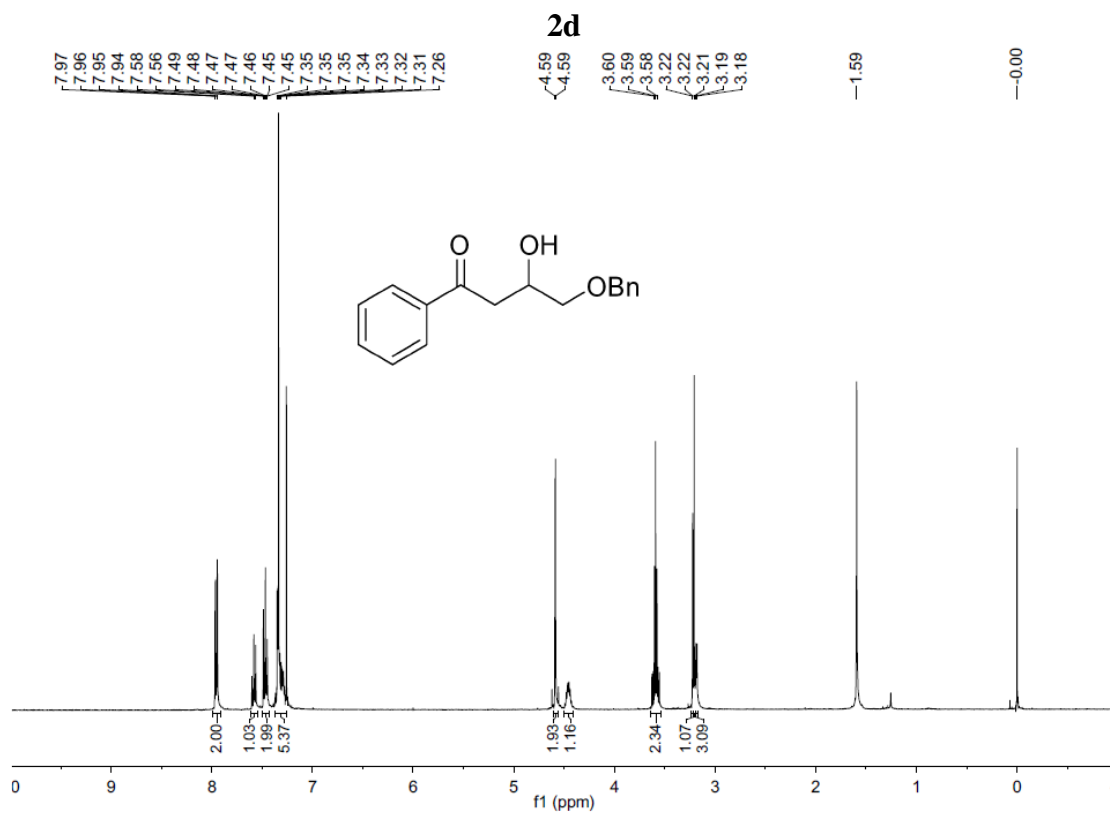
2a

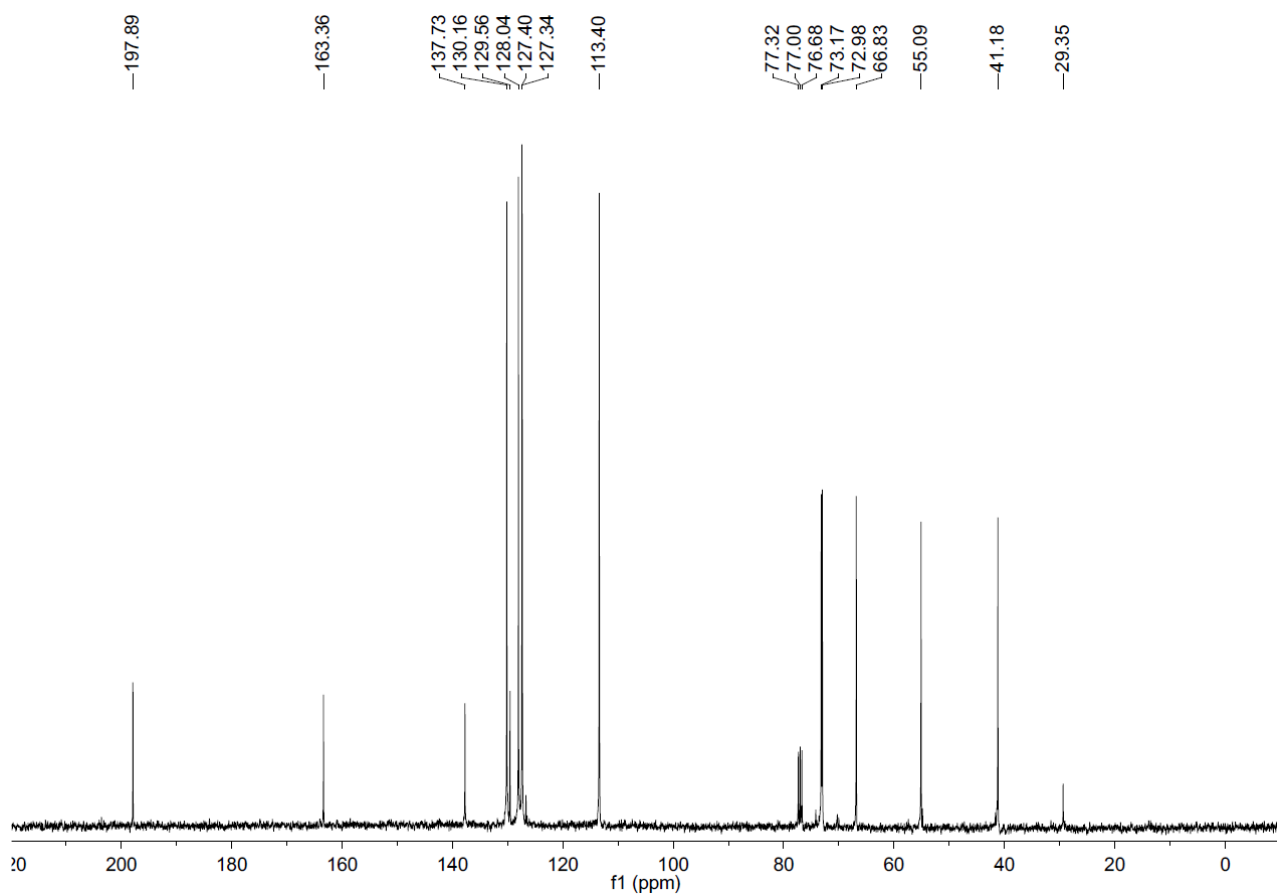
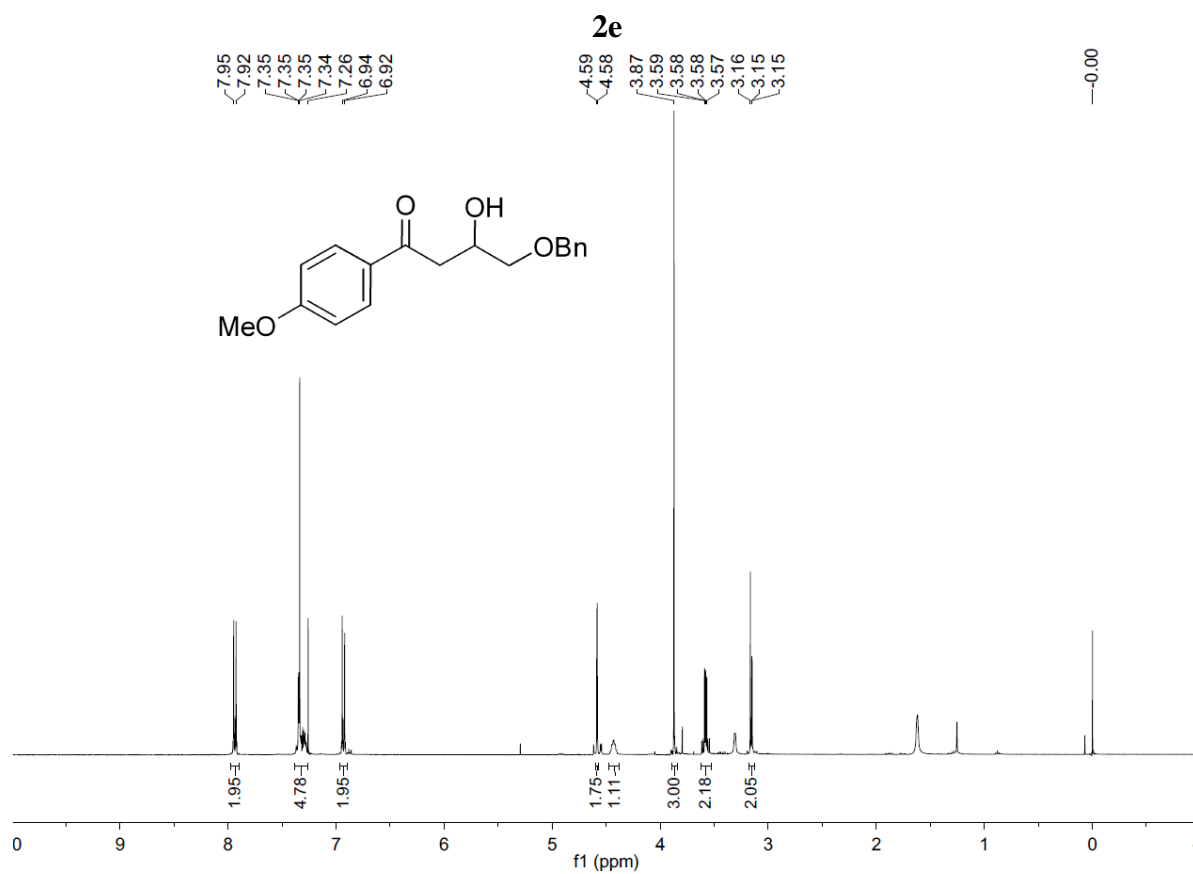


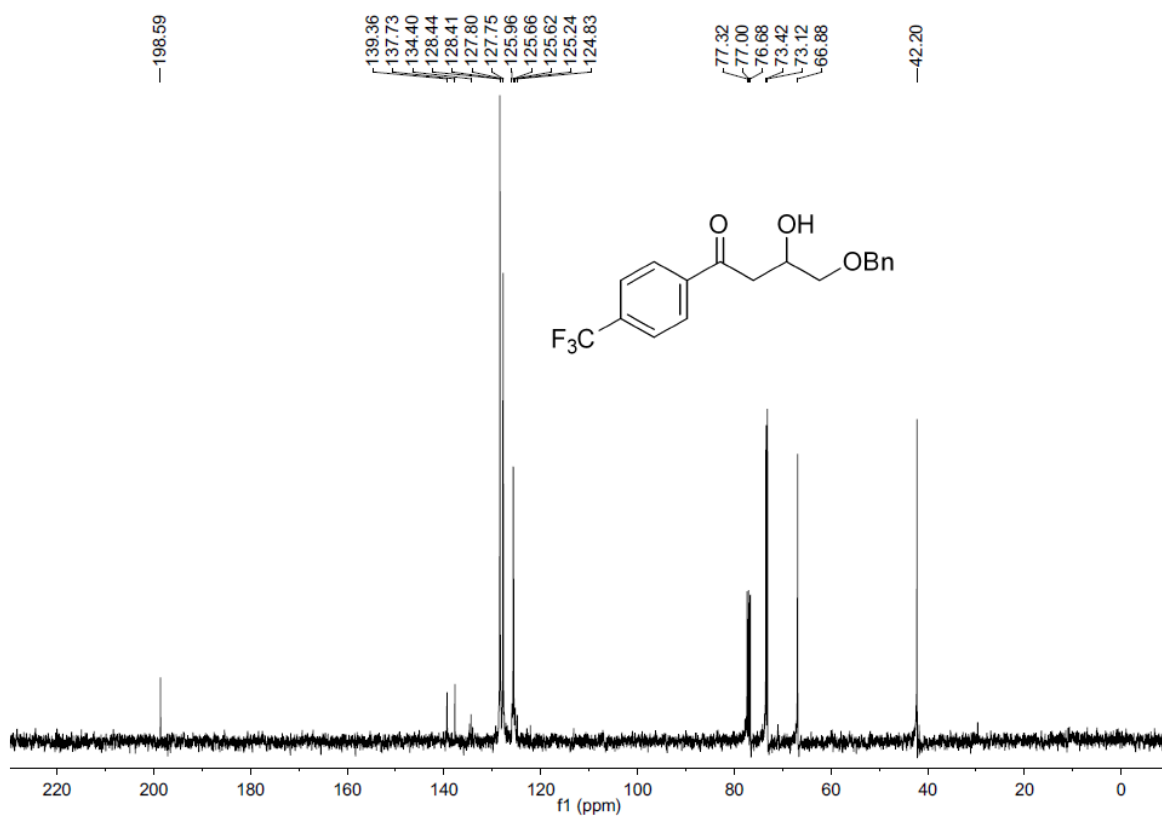
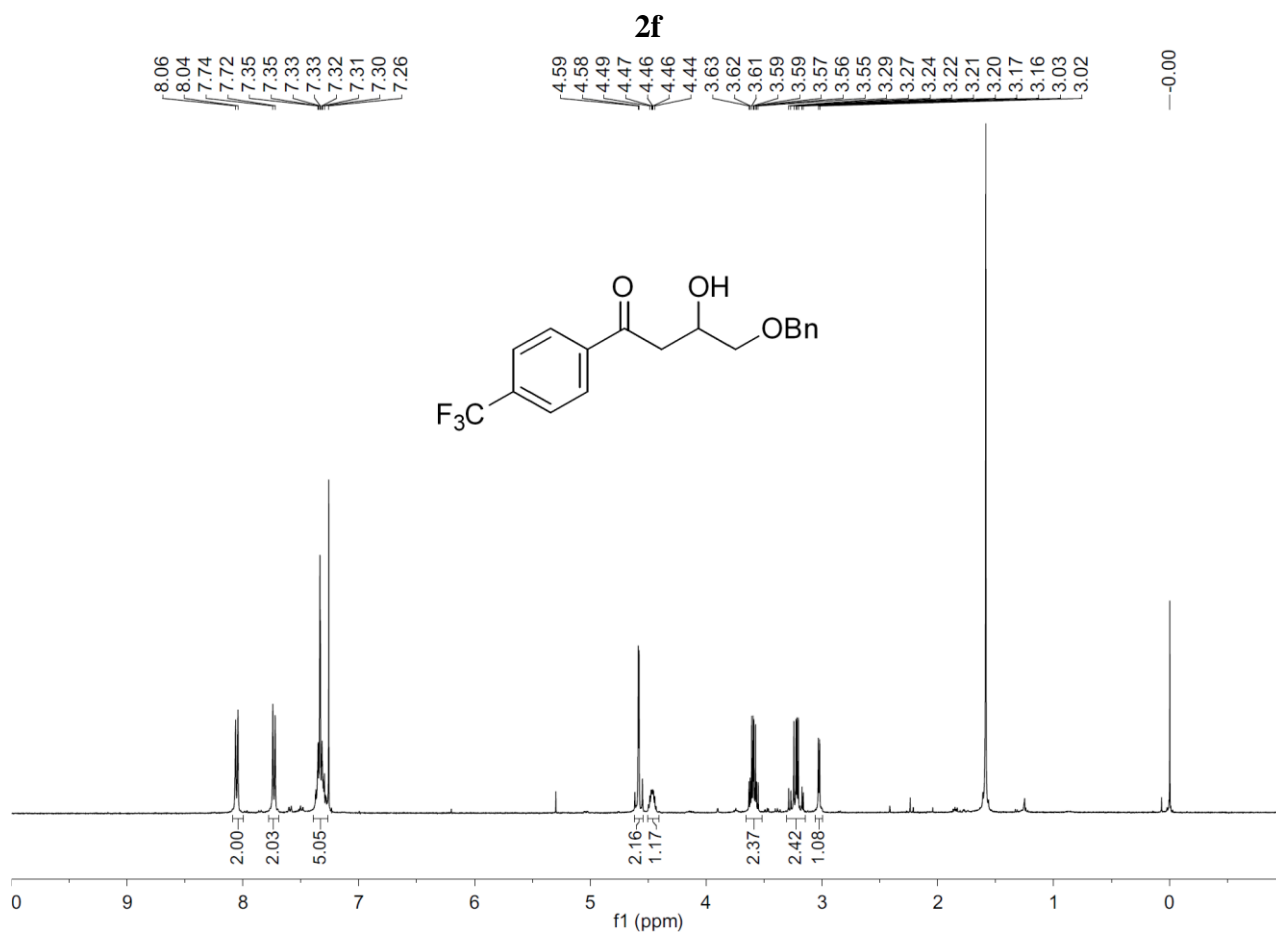


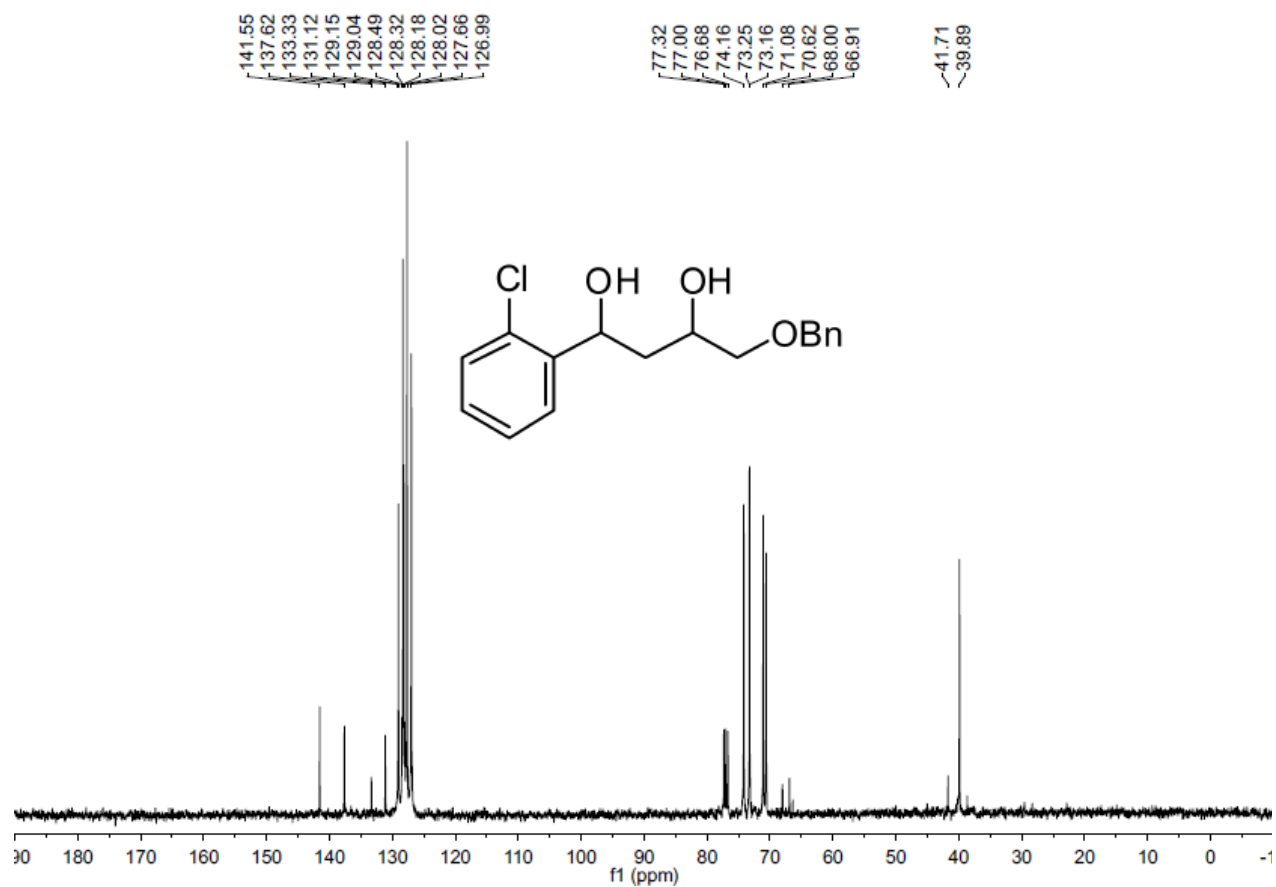
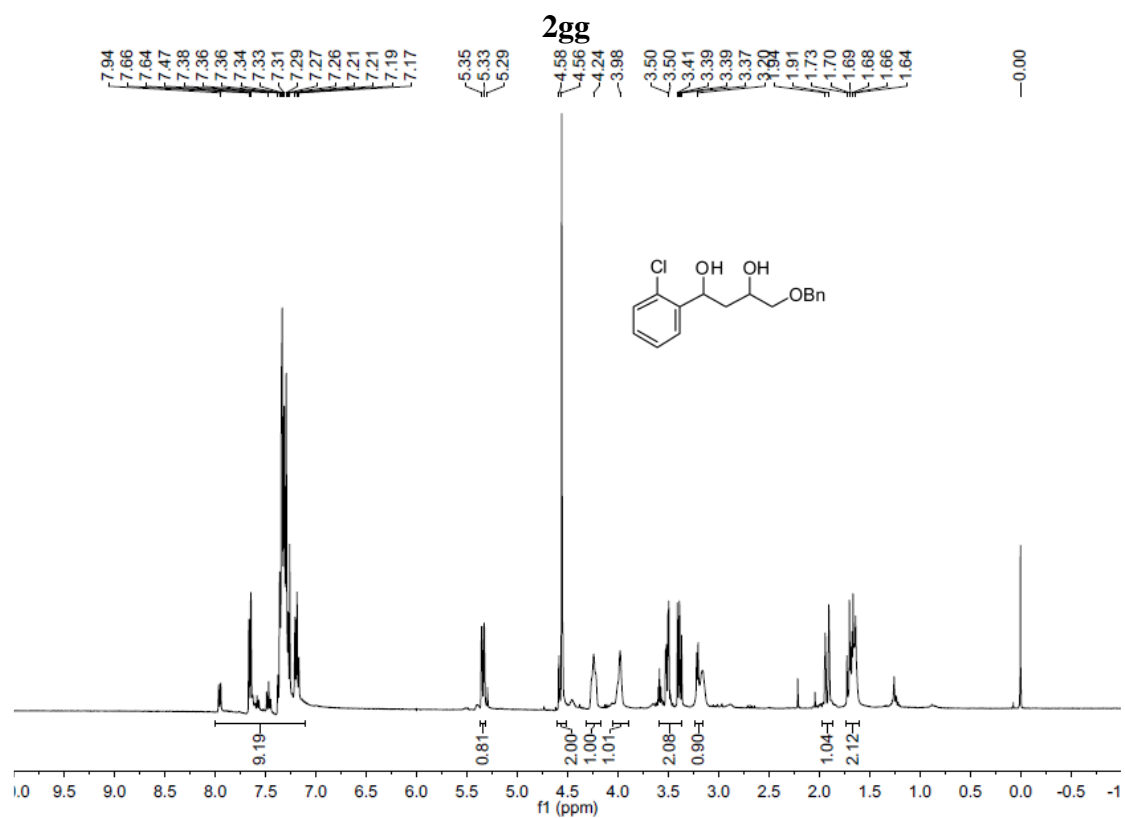


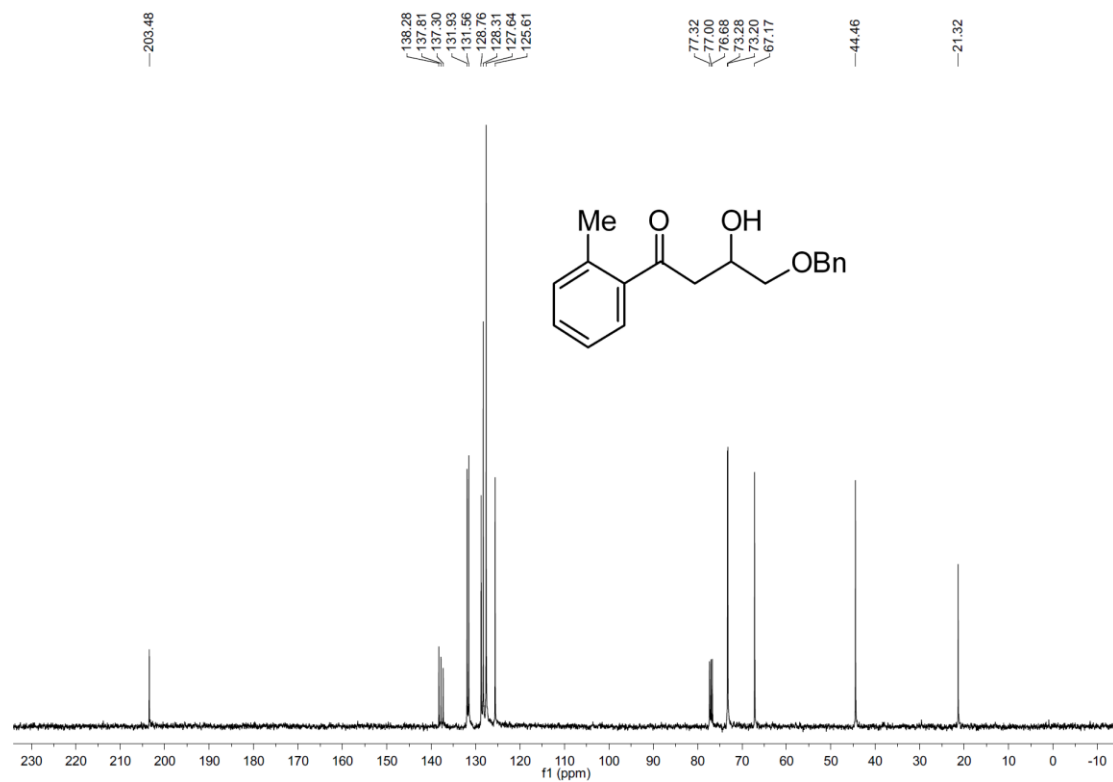
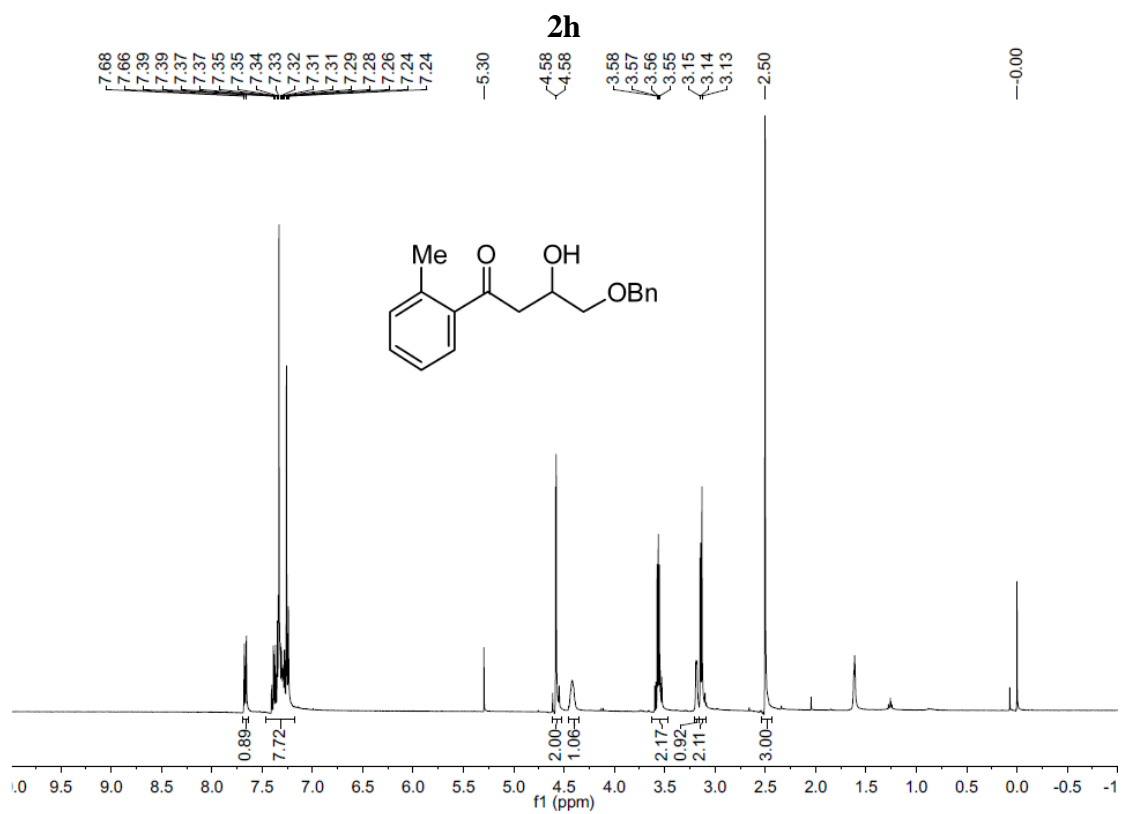


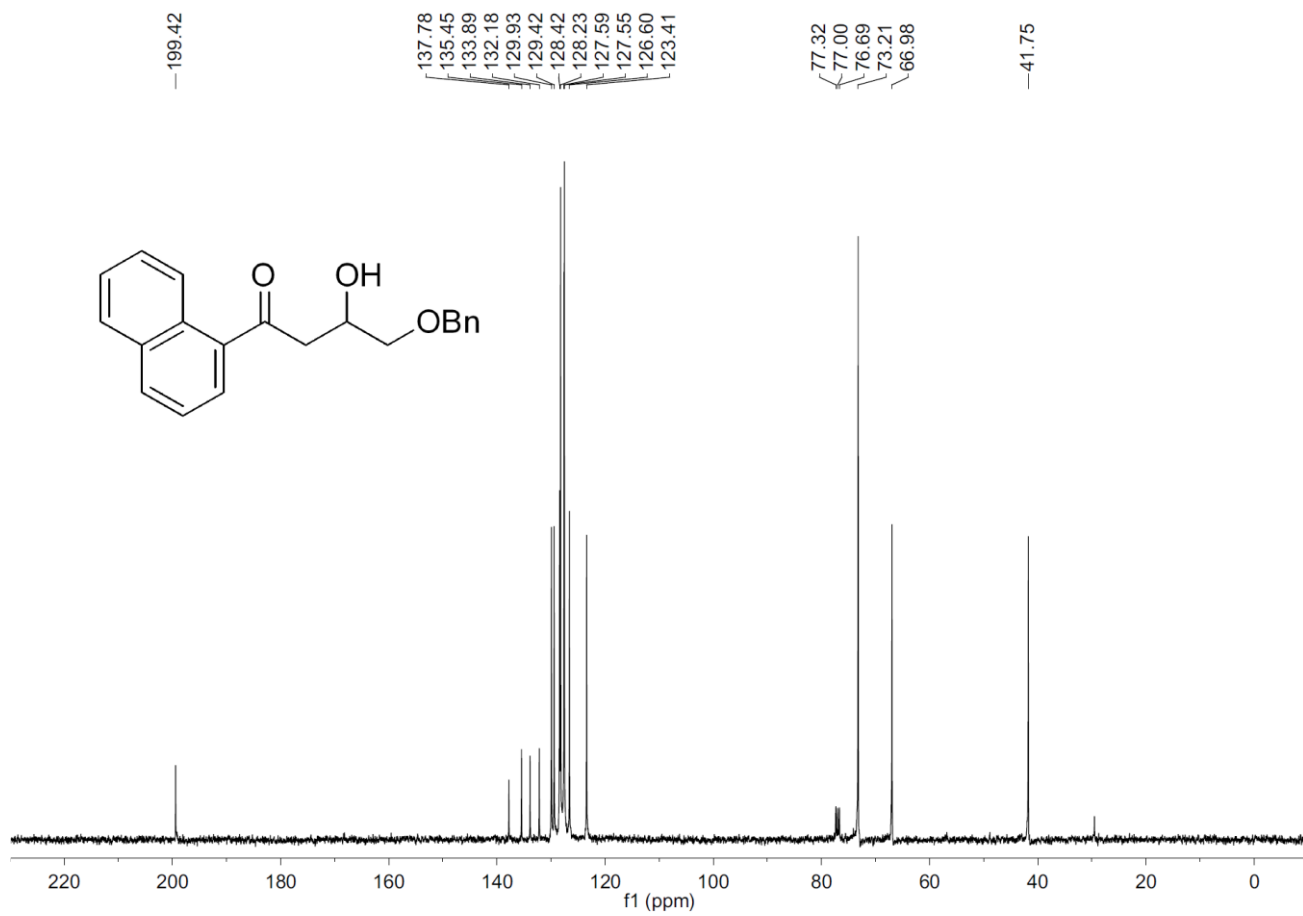
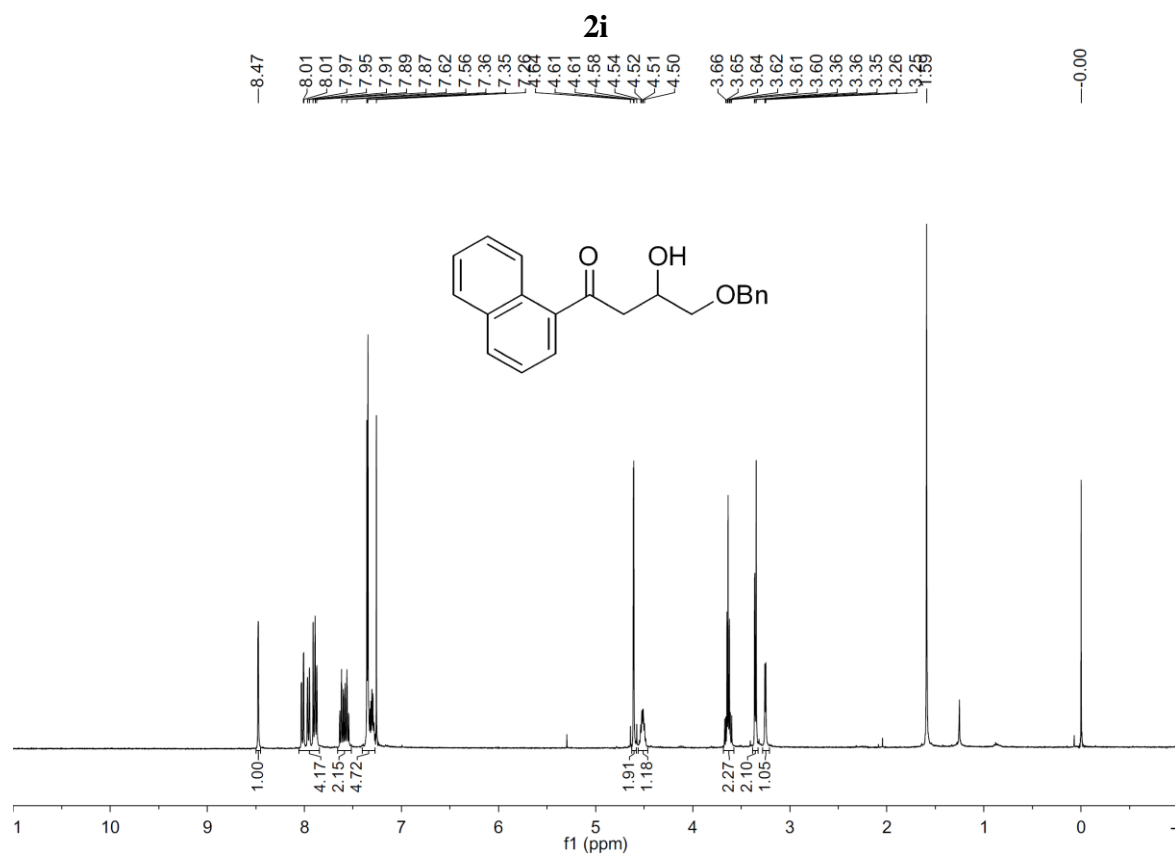


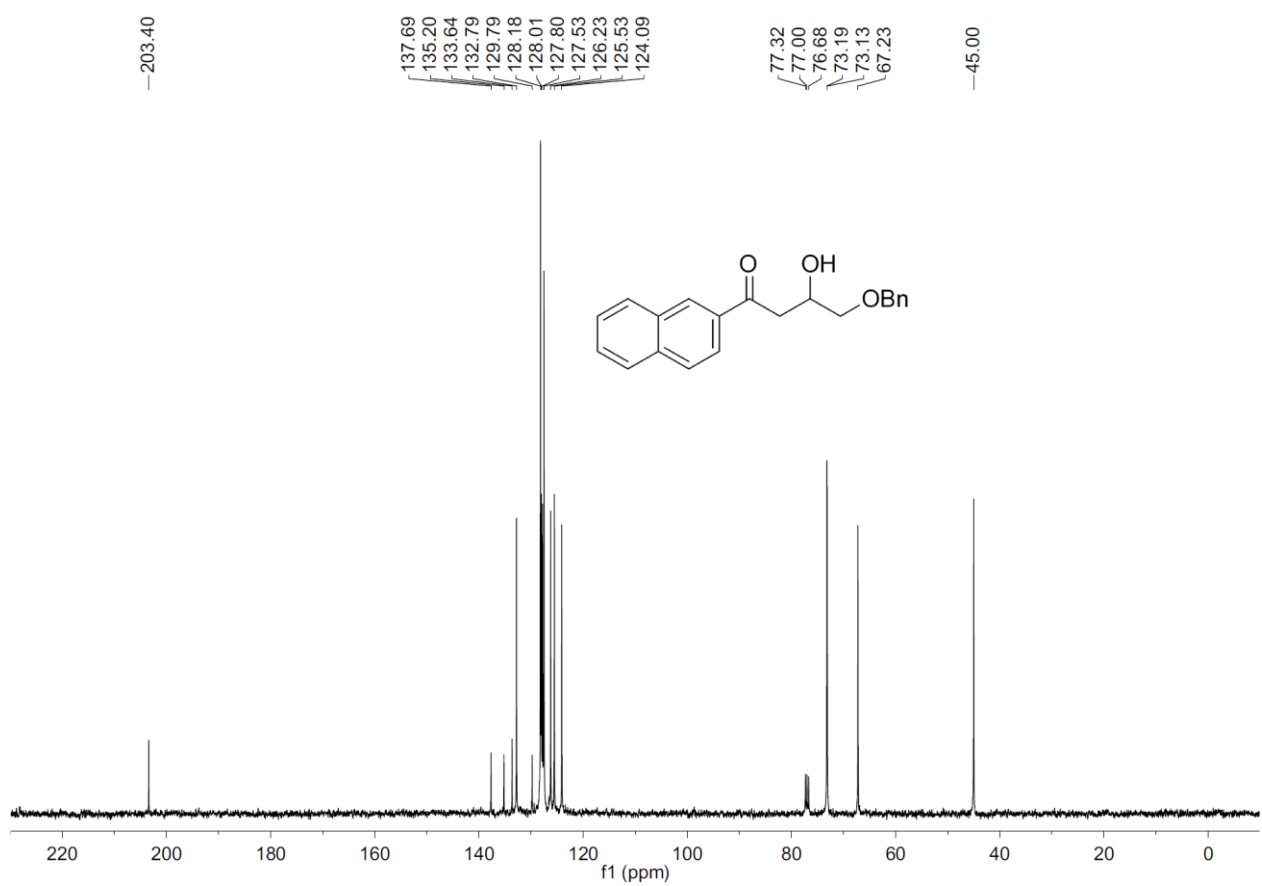
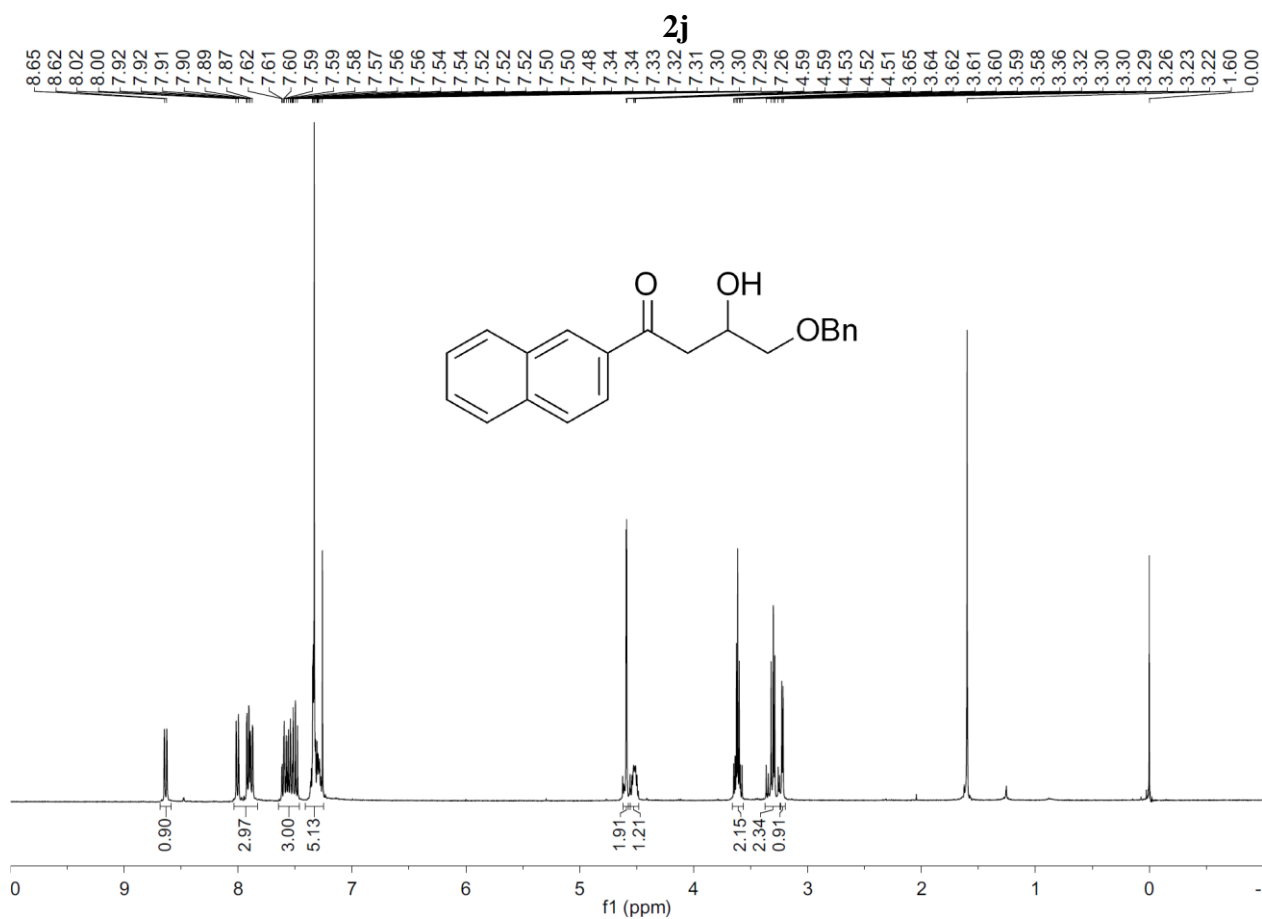


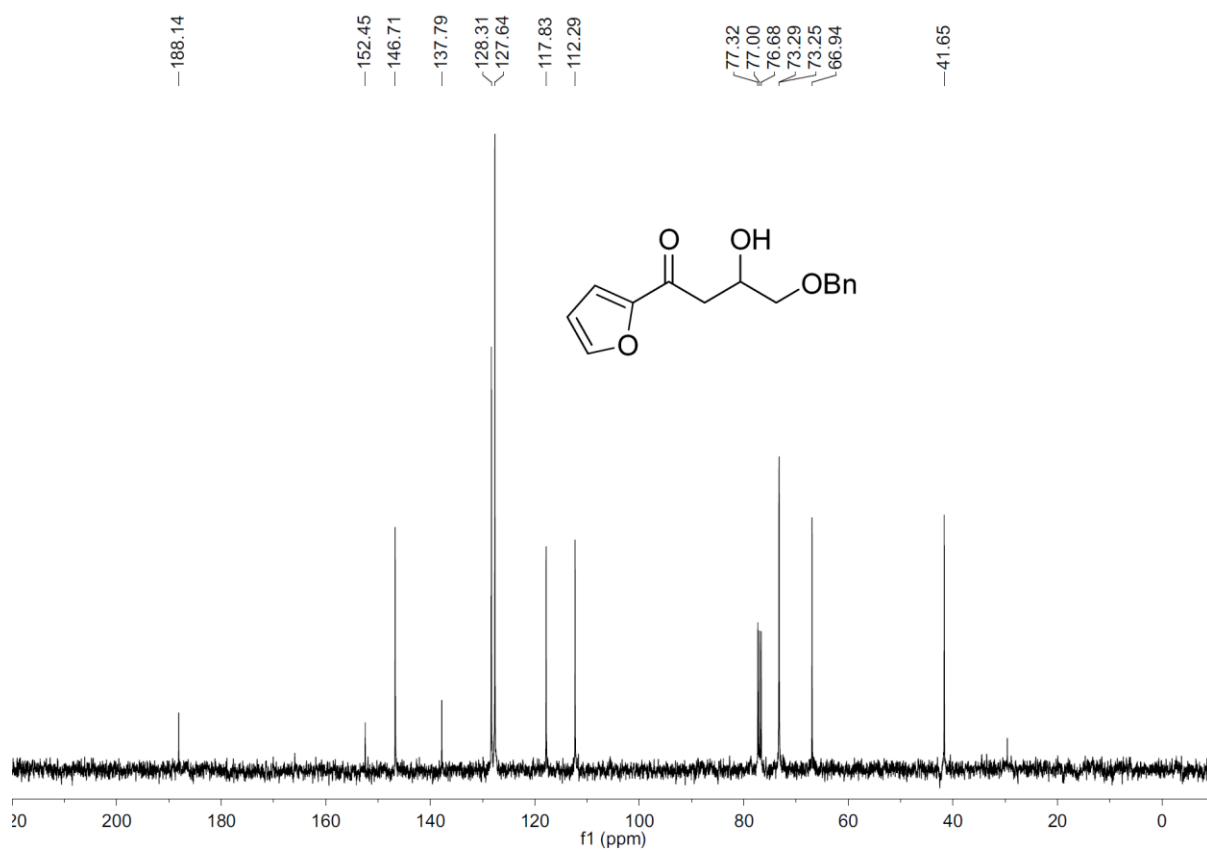
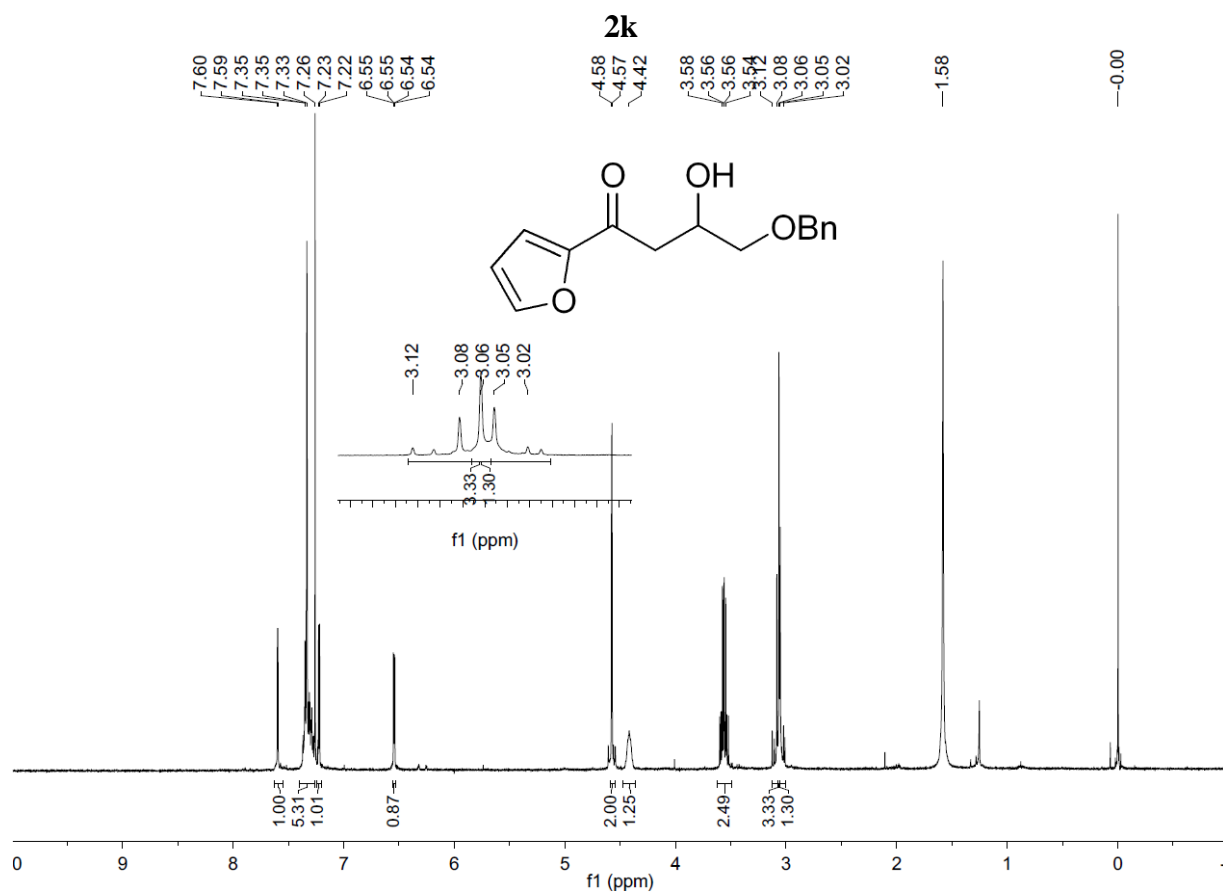




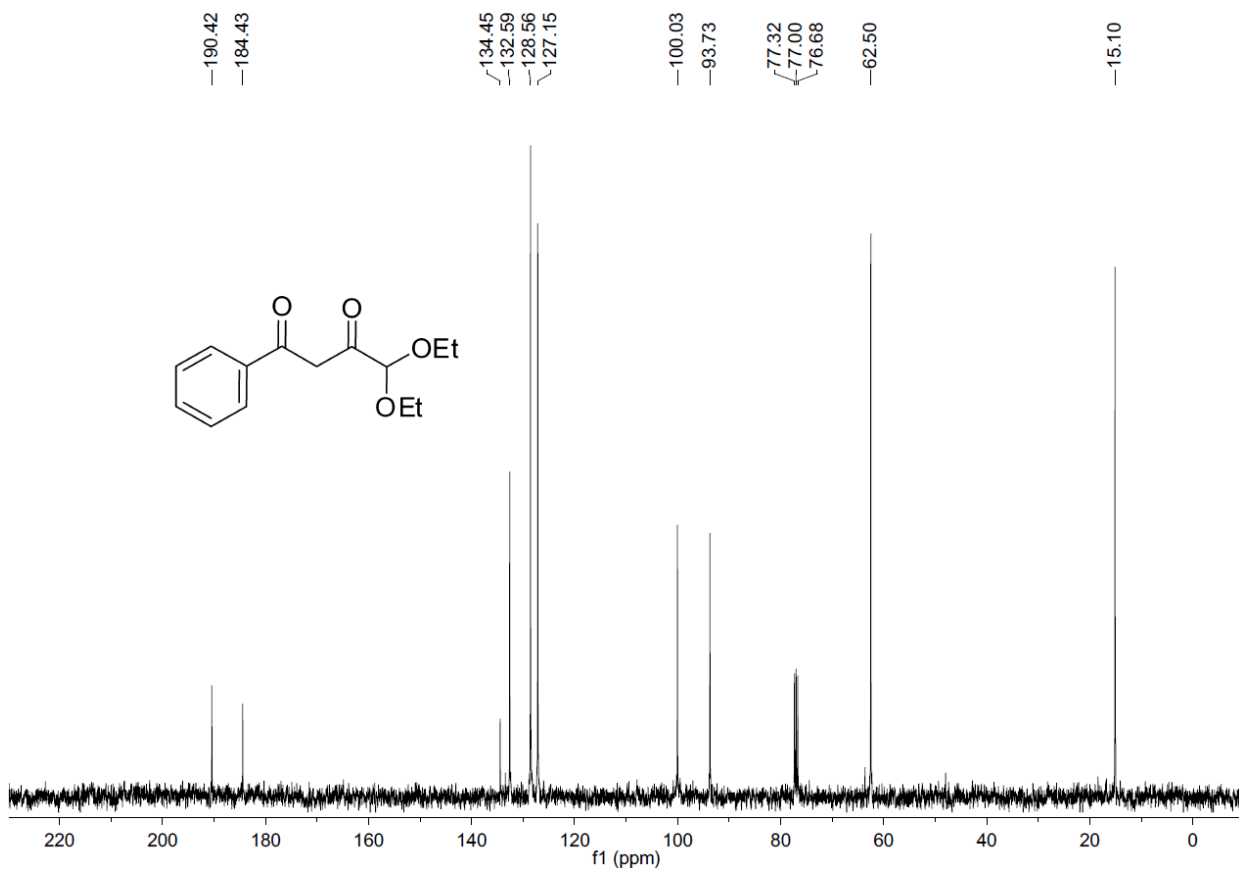
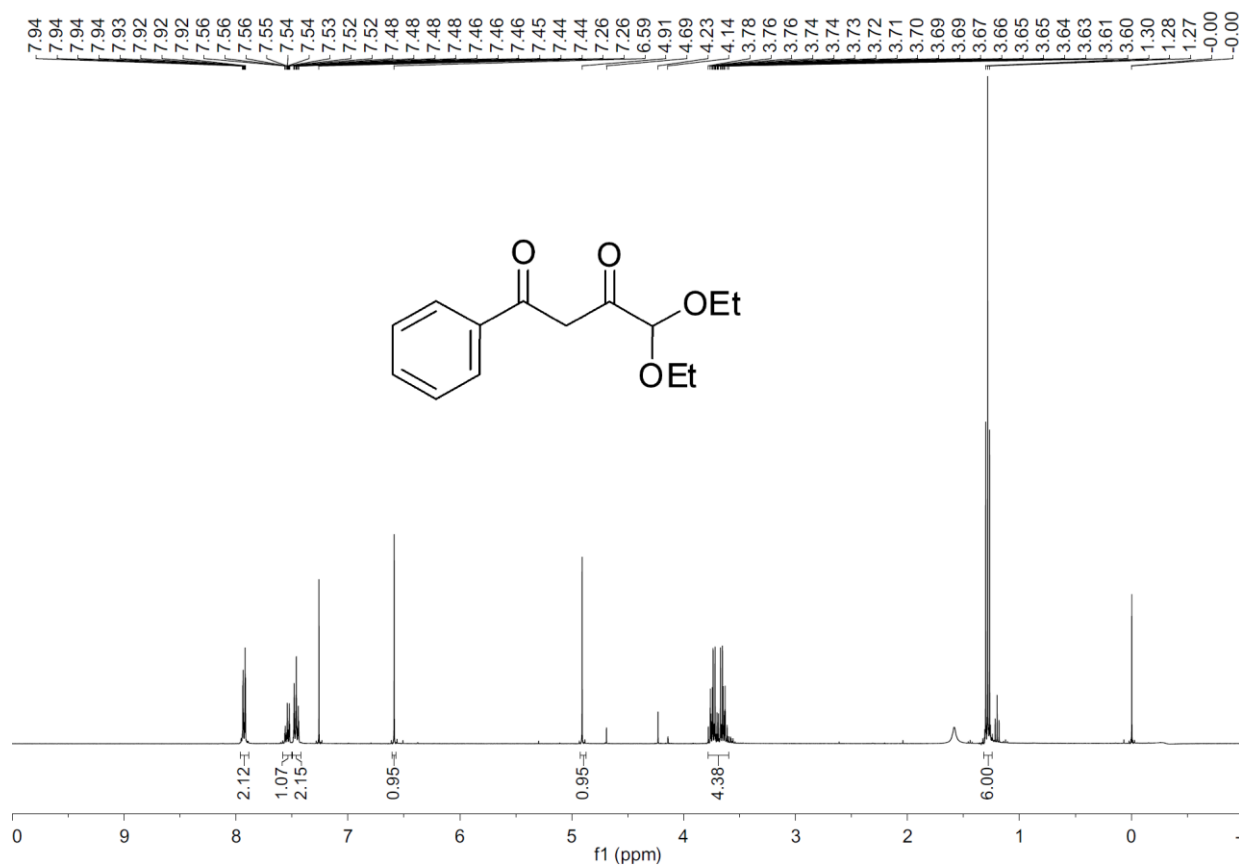


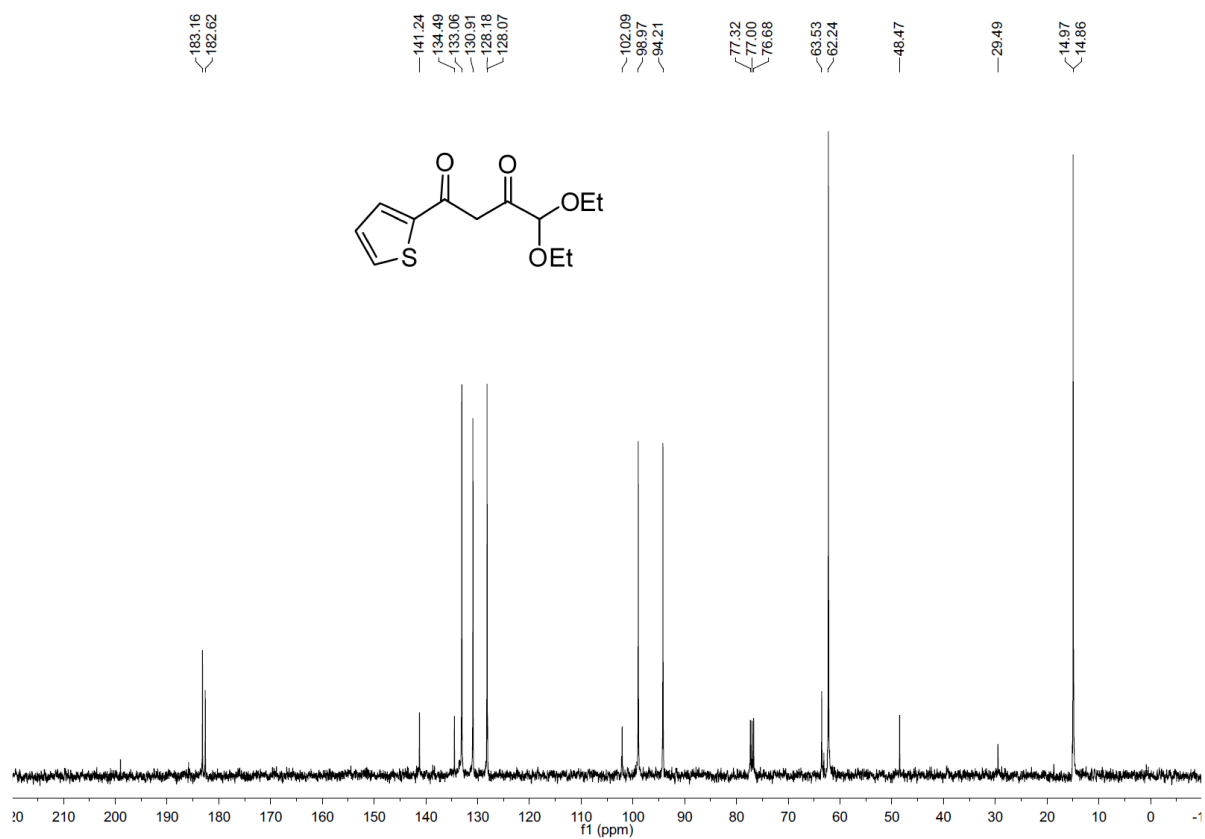
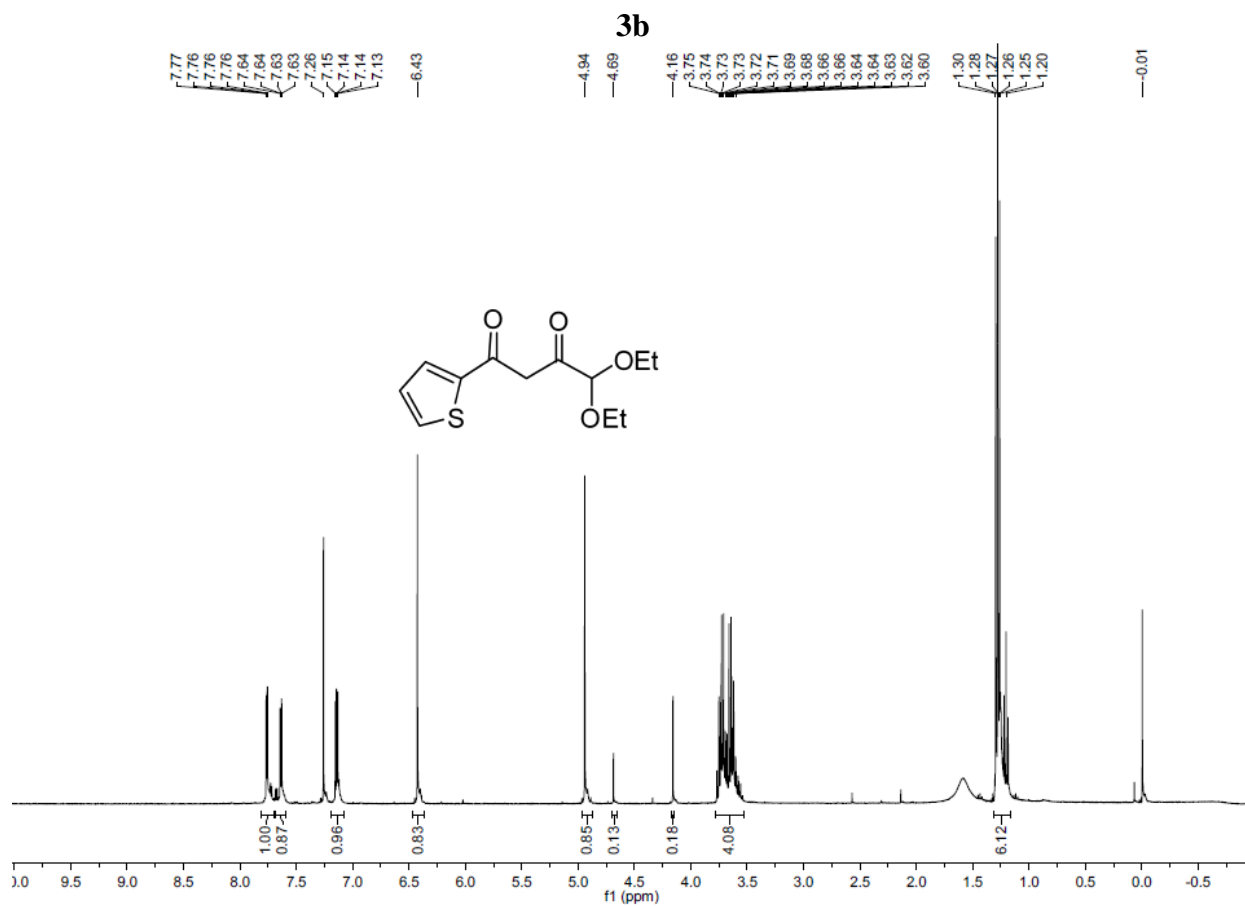


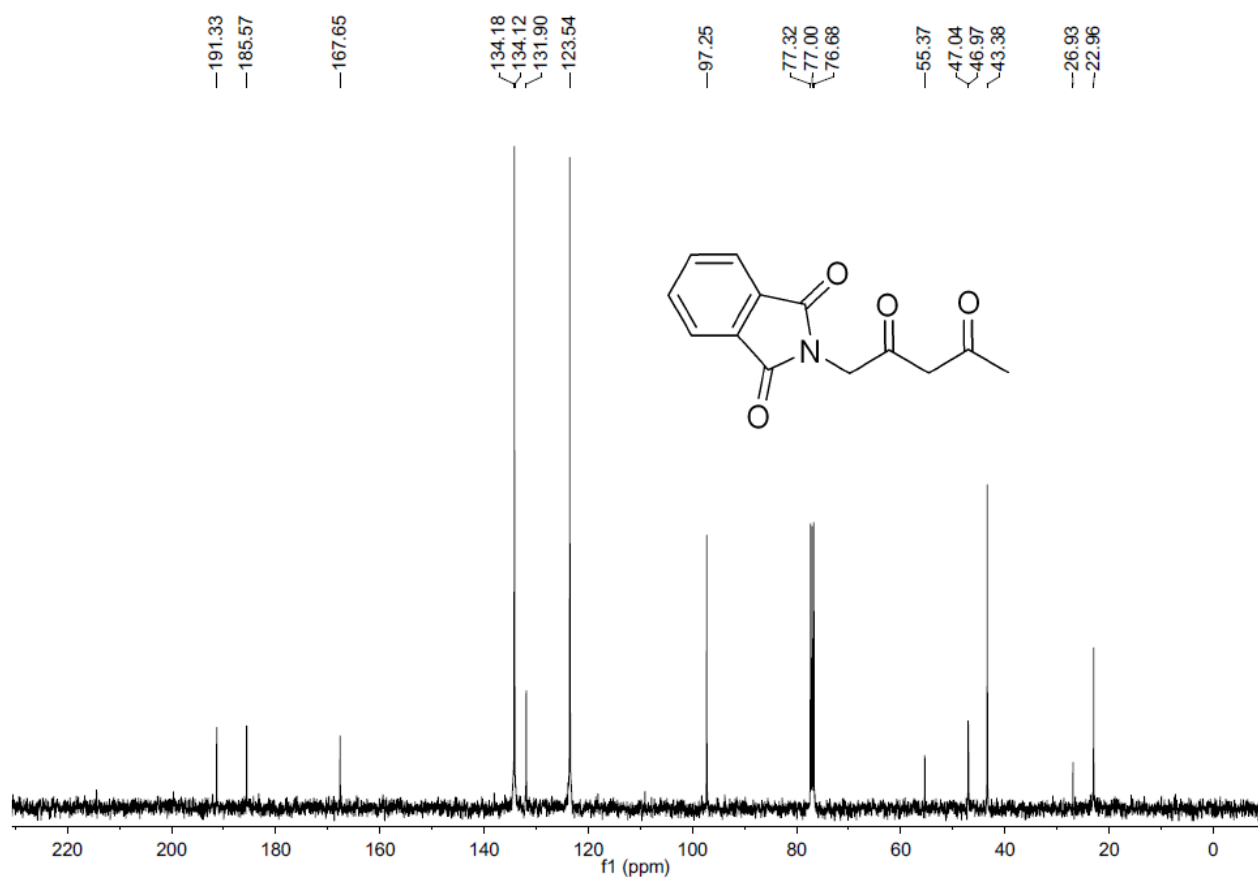
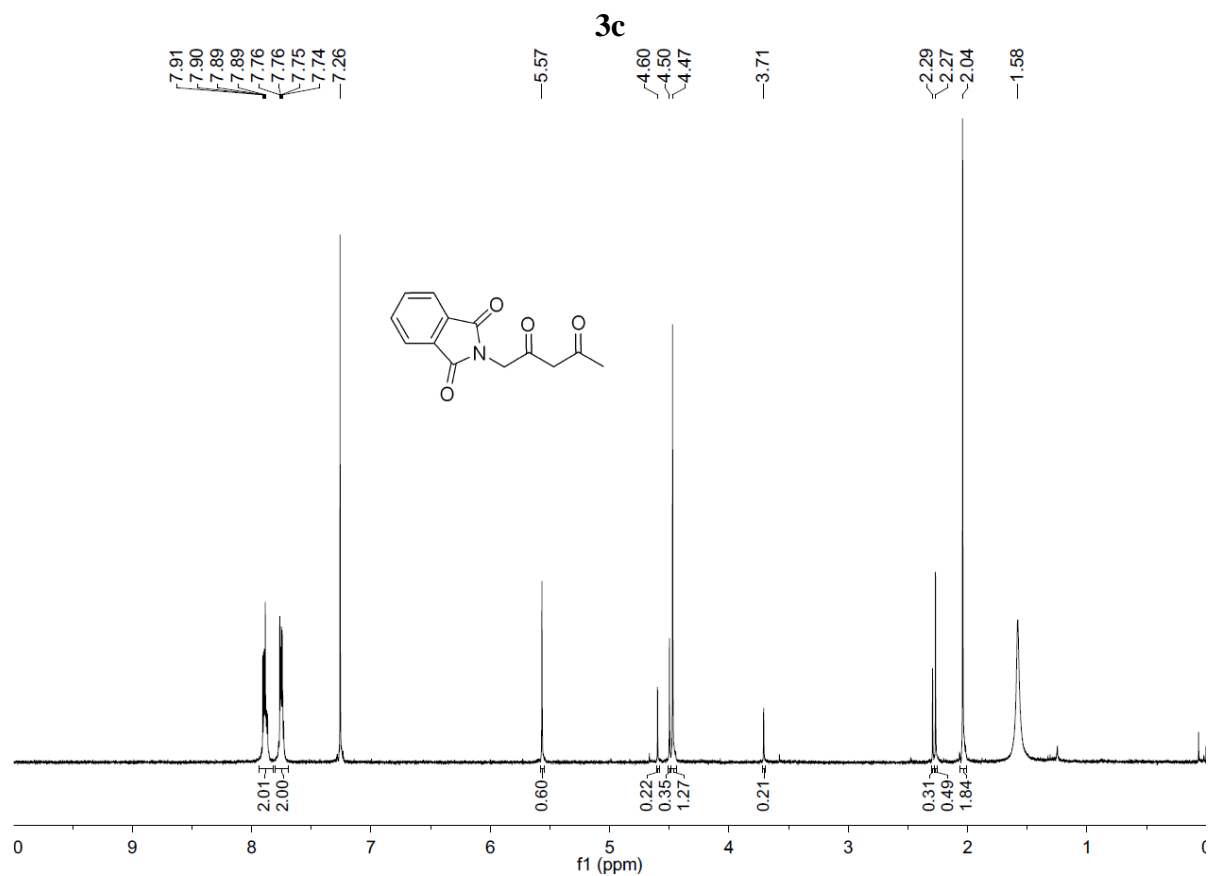


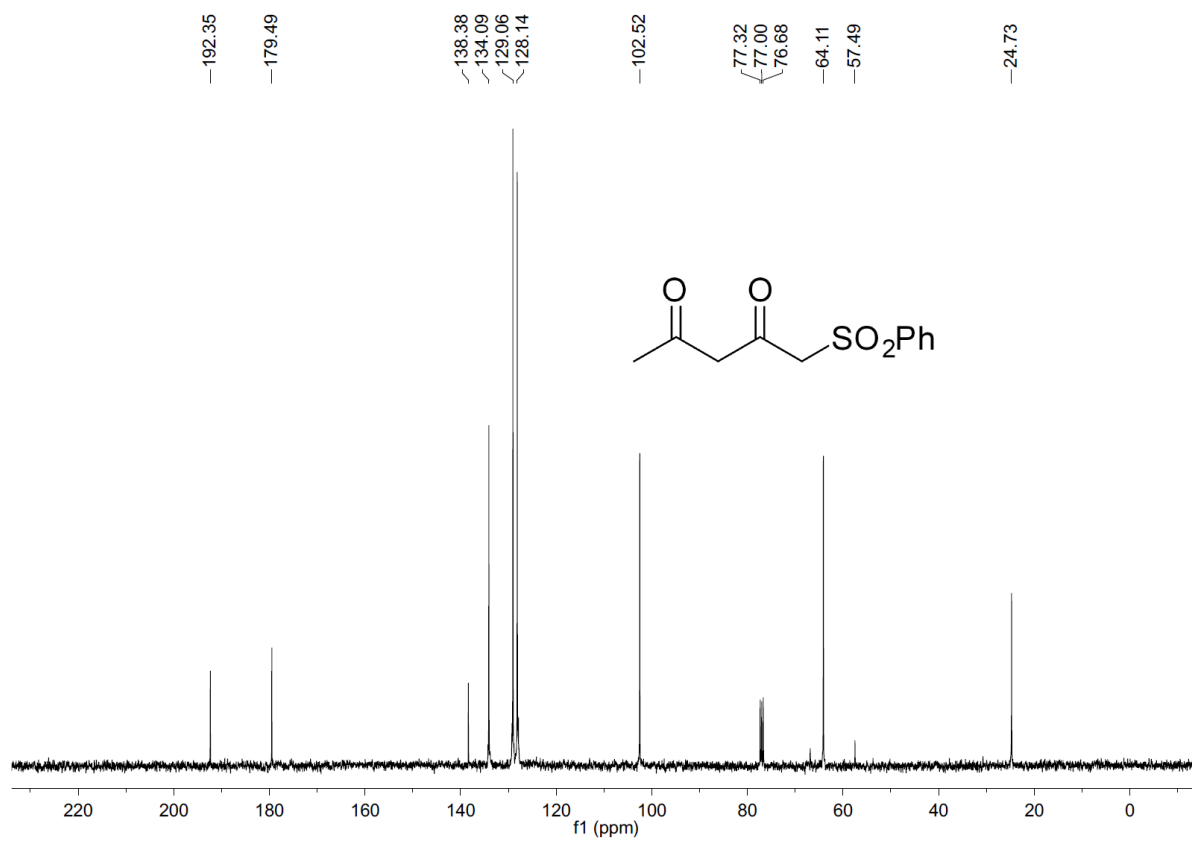
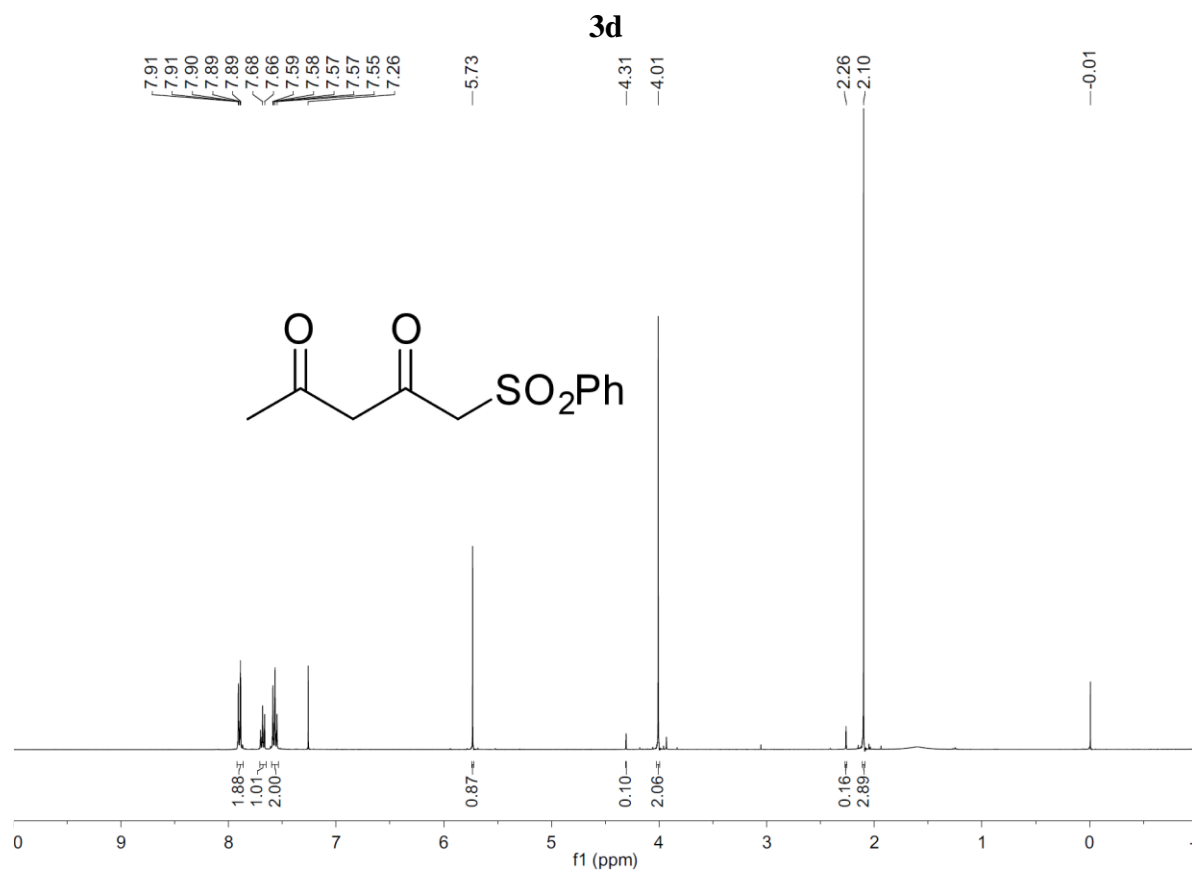


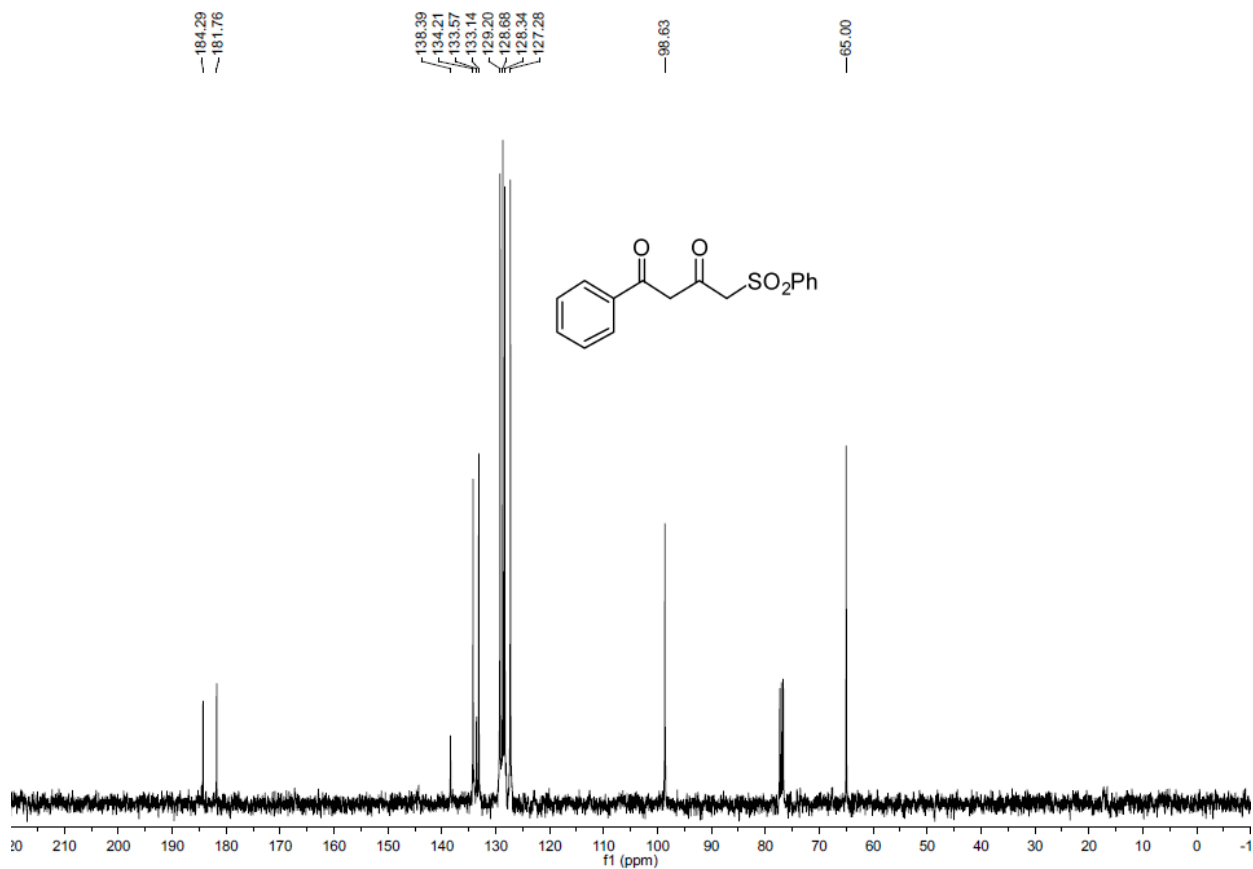
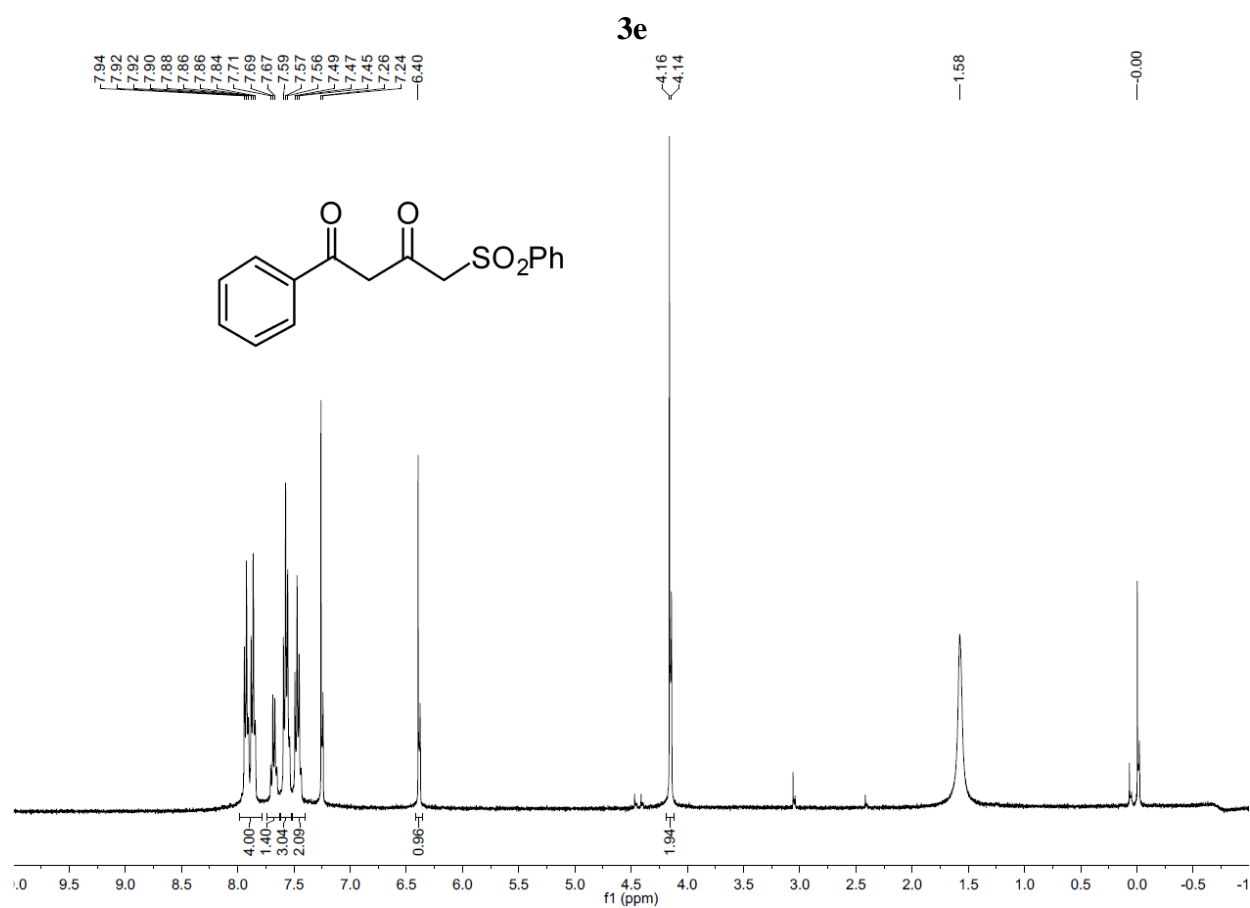
3a



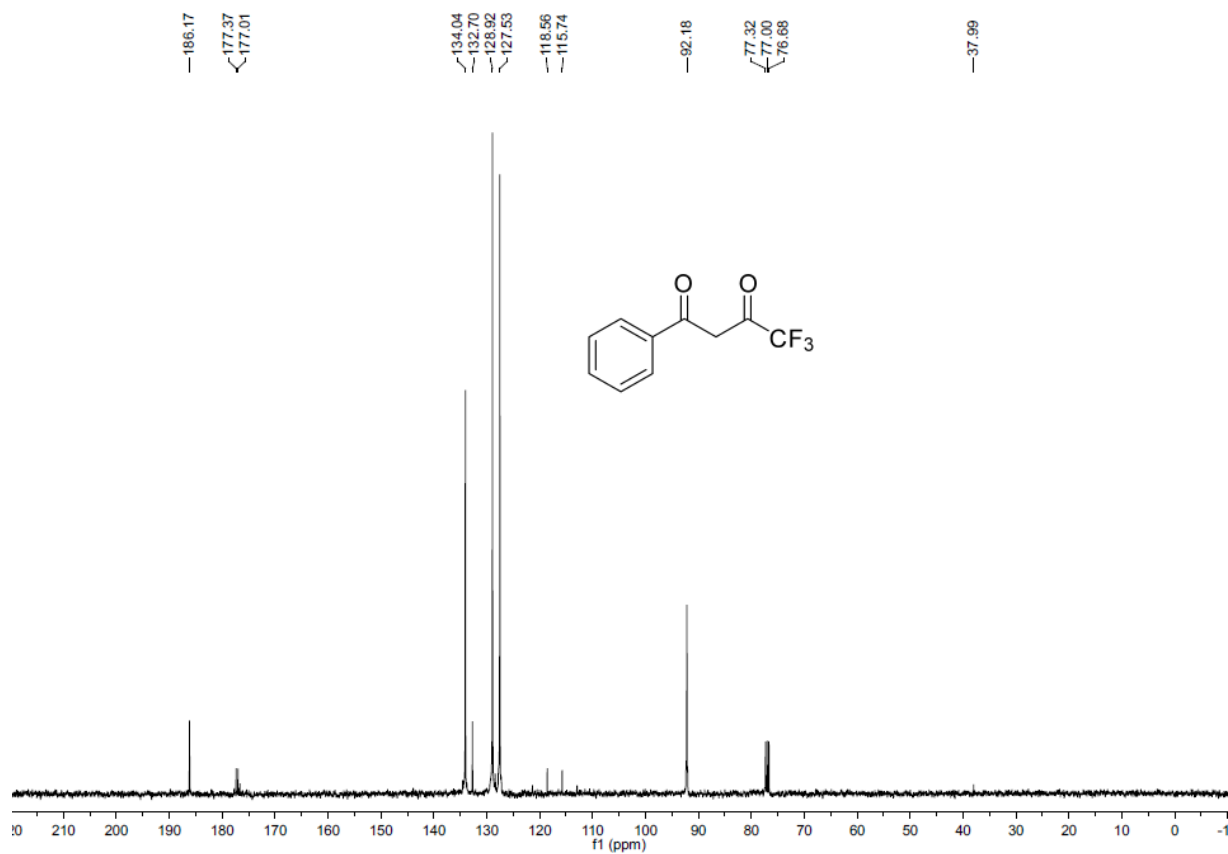
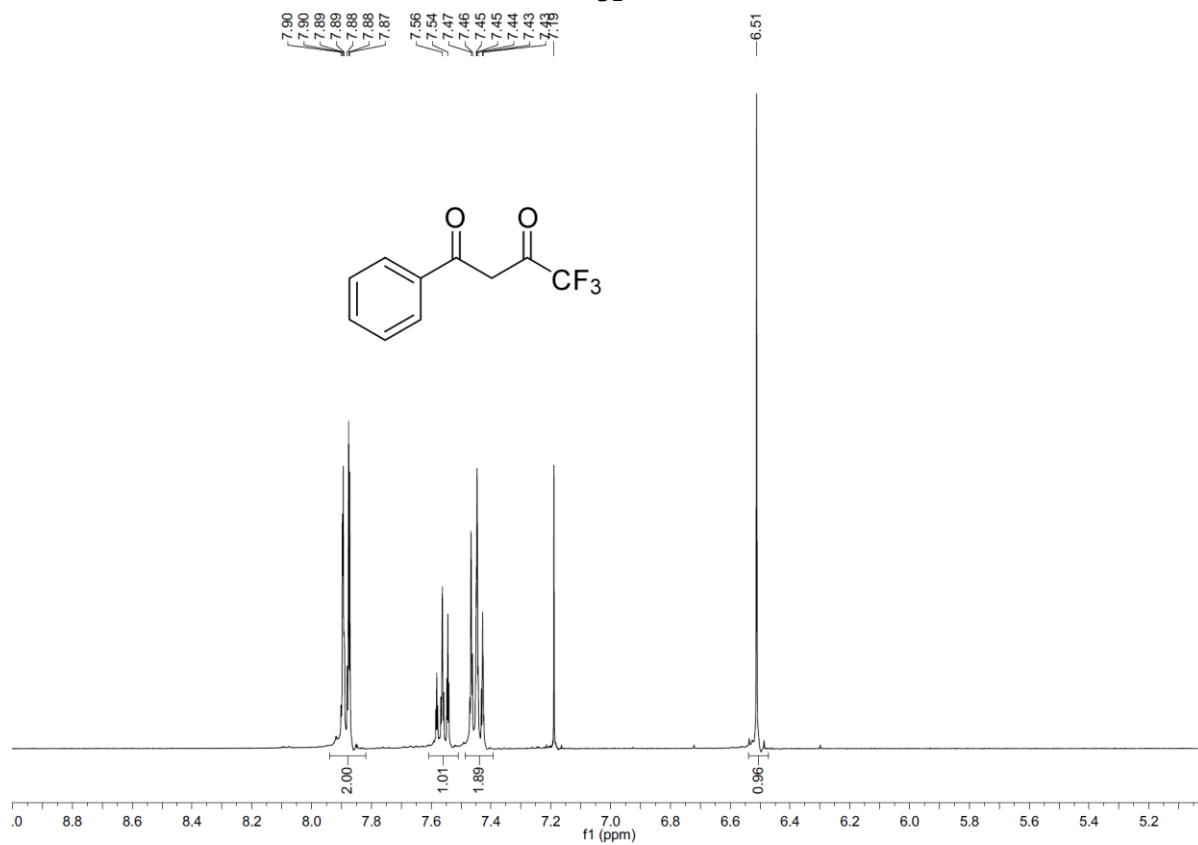


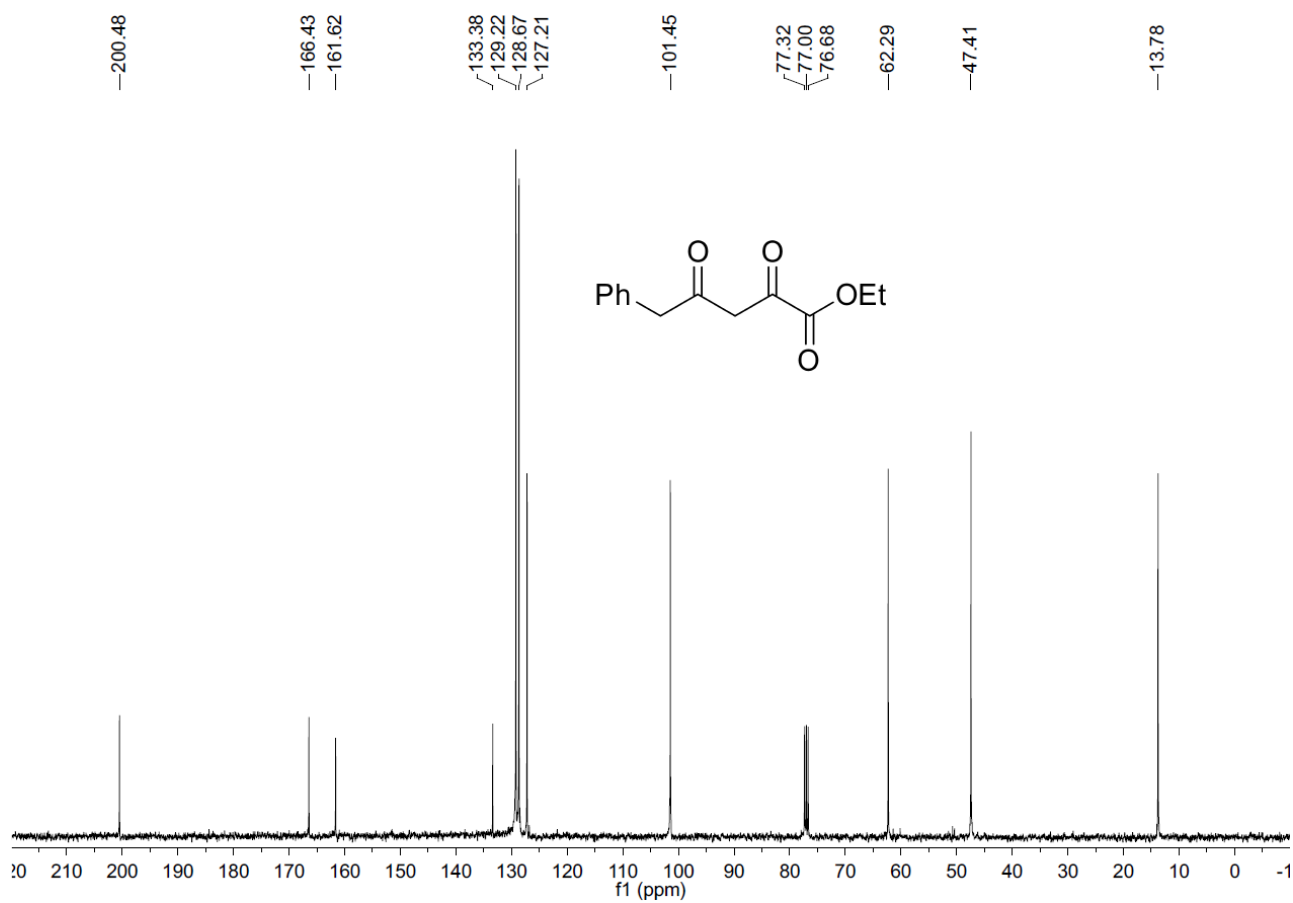
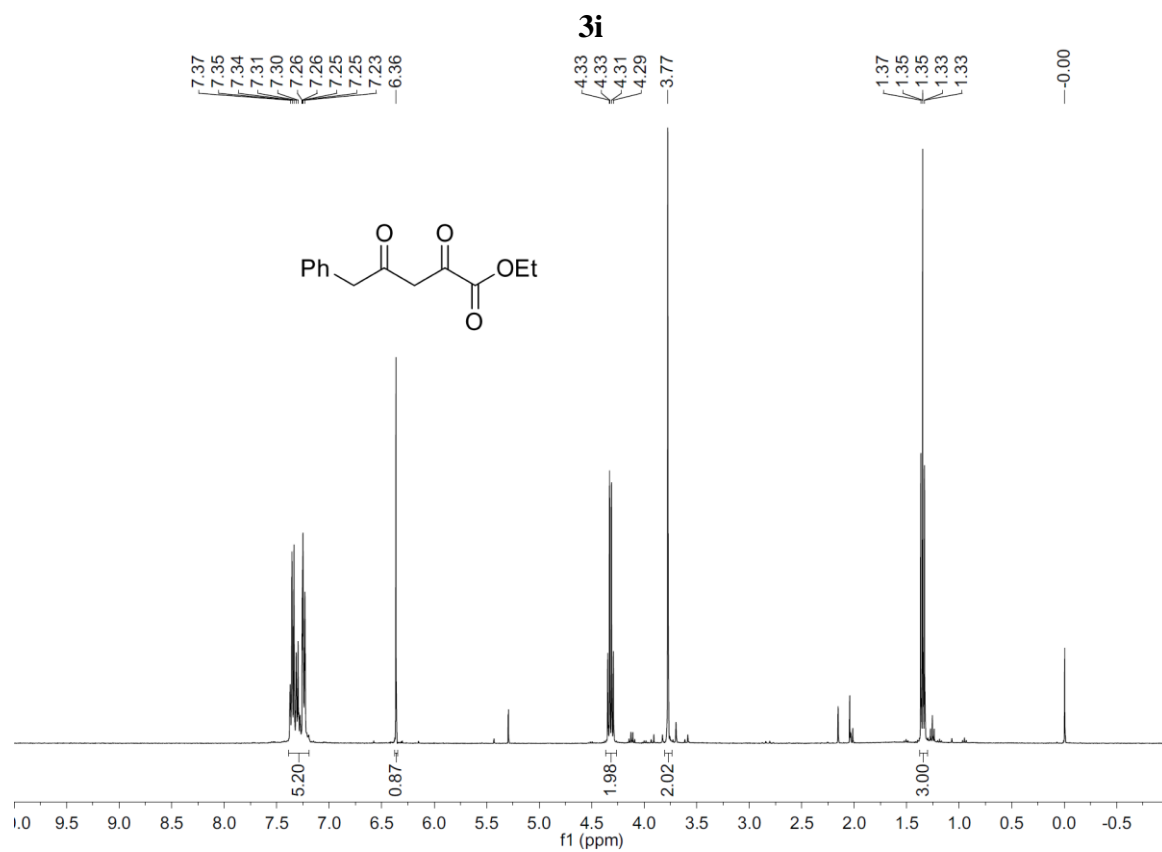


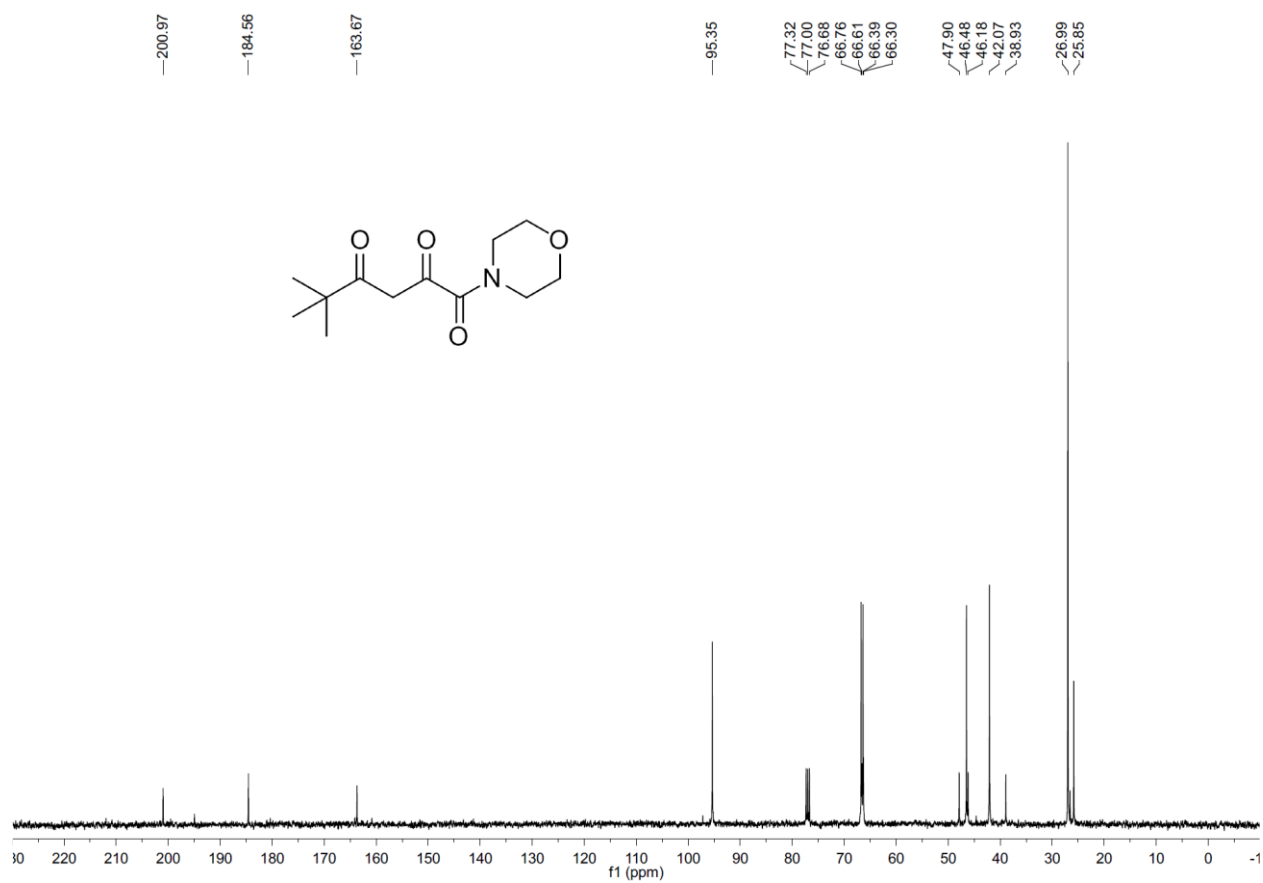
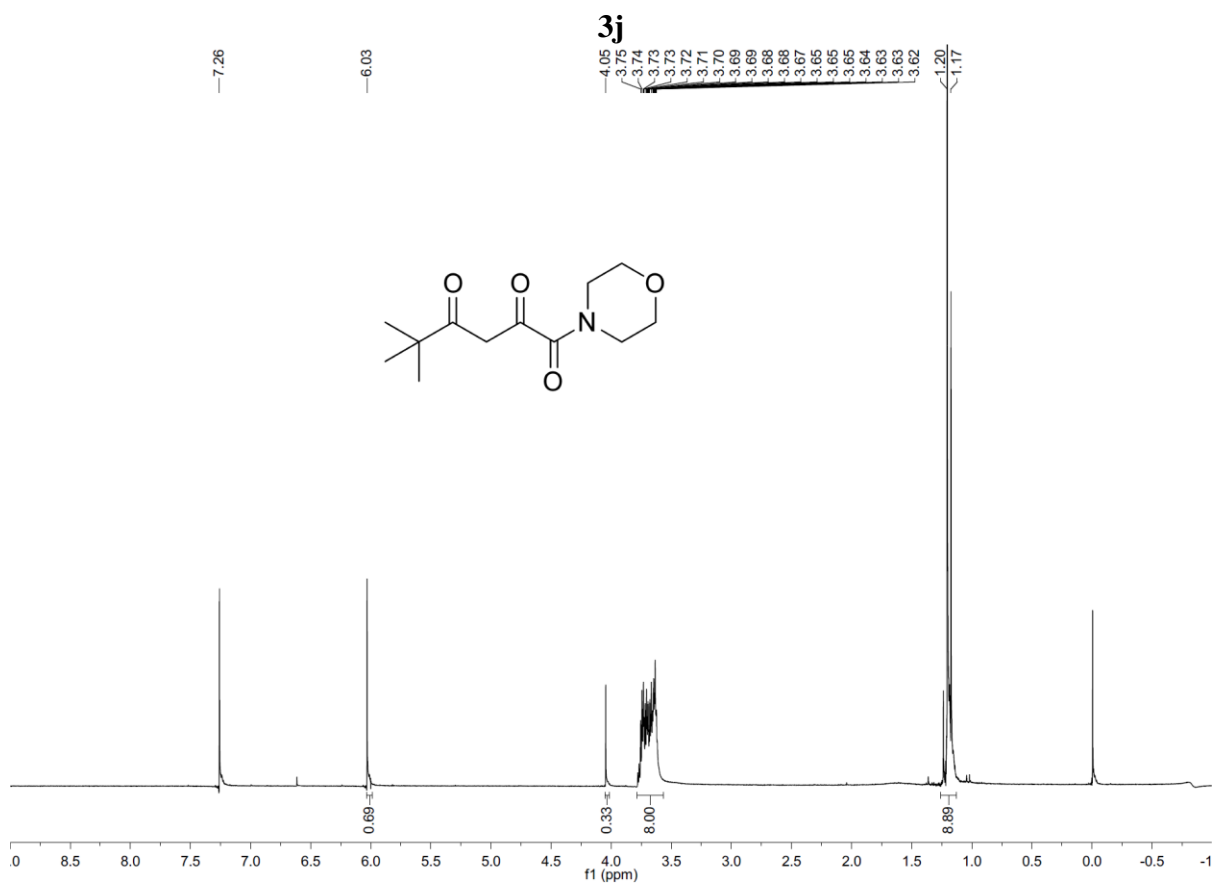


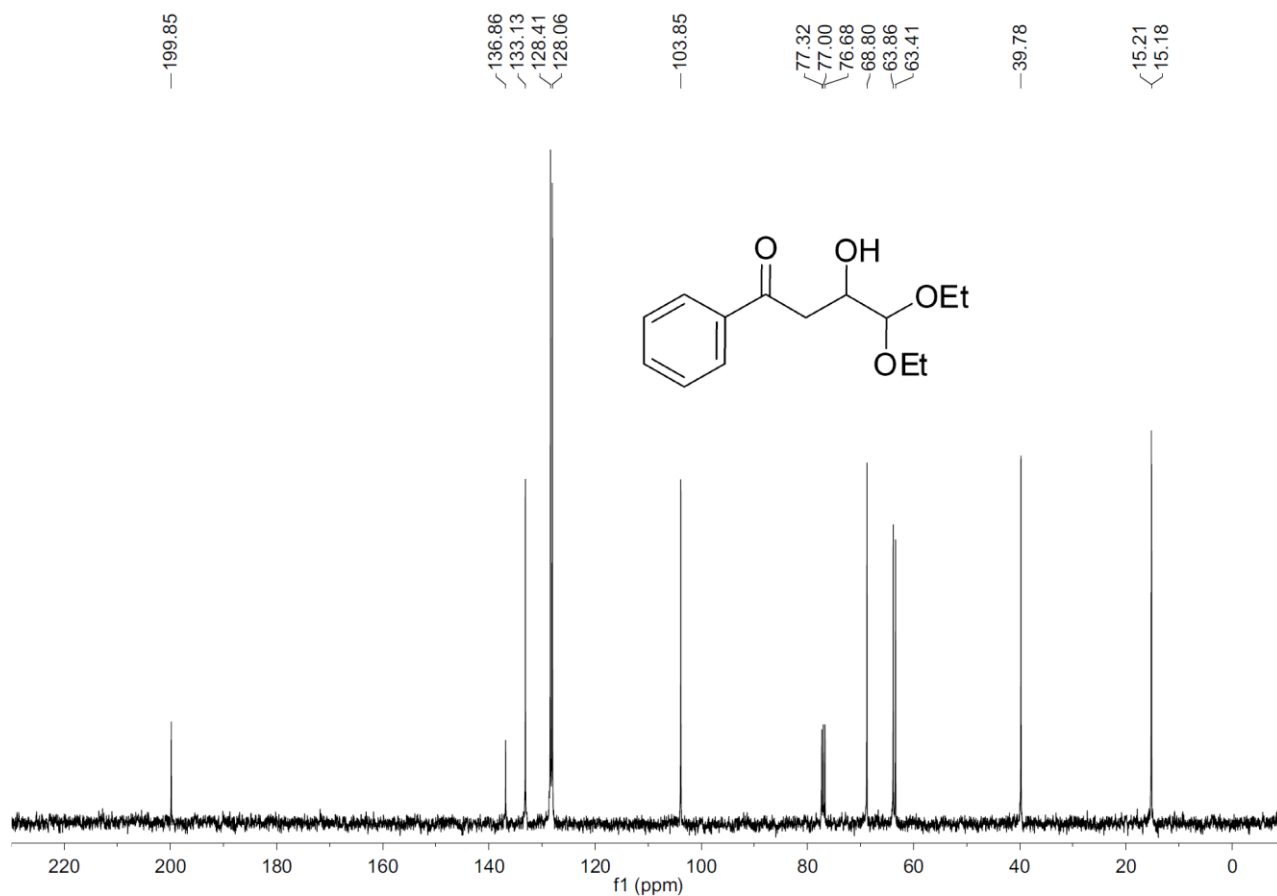
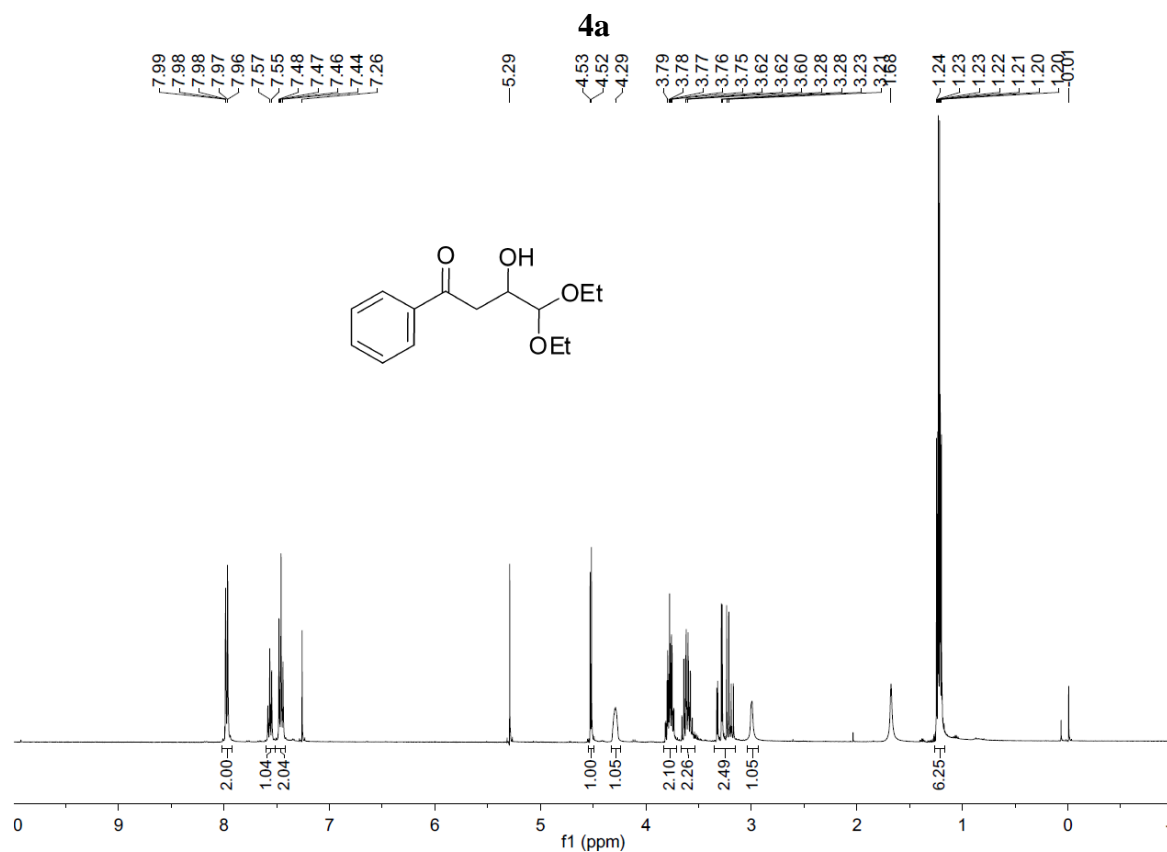


3f

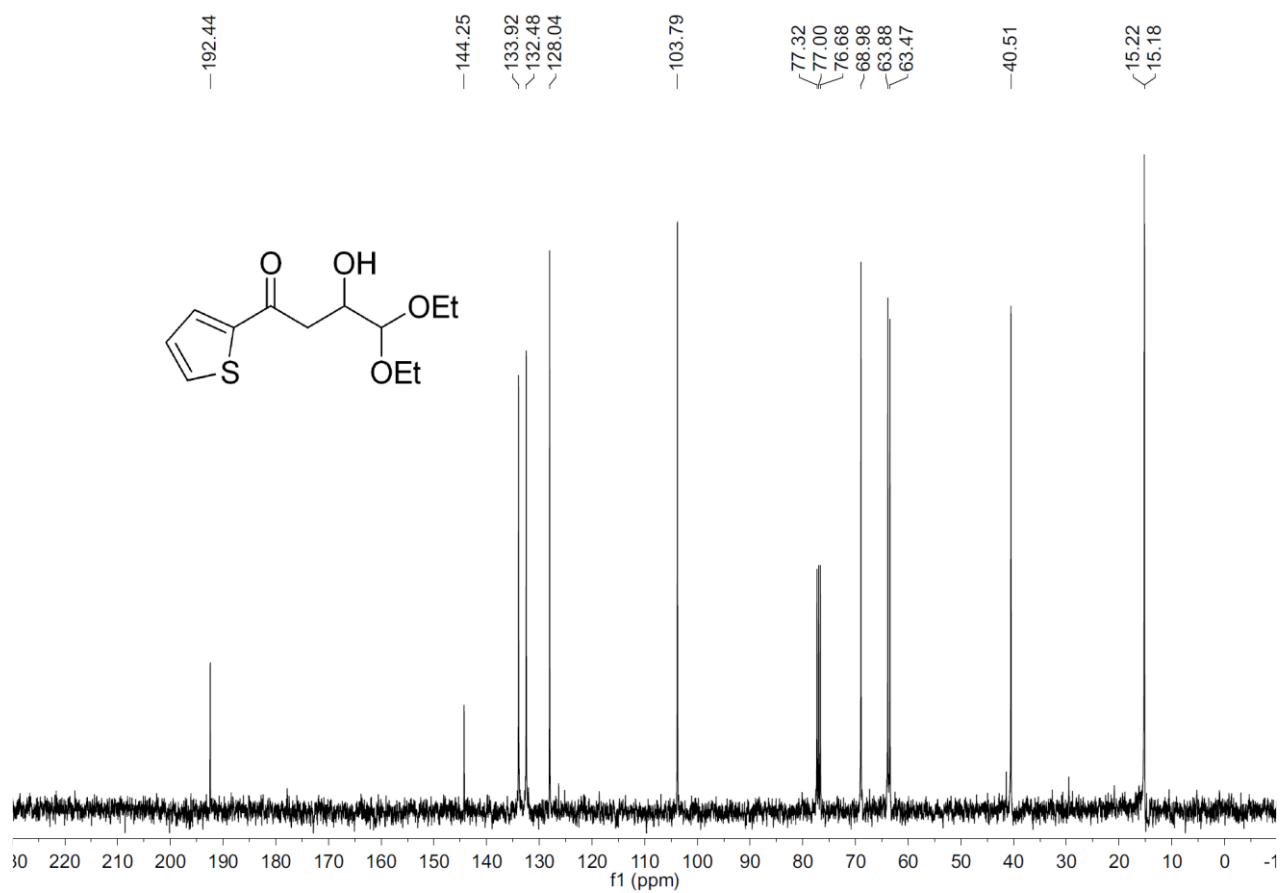
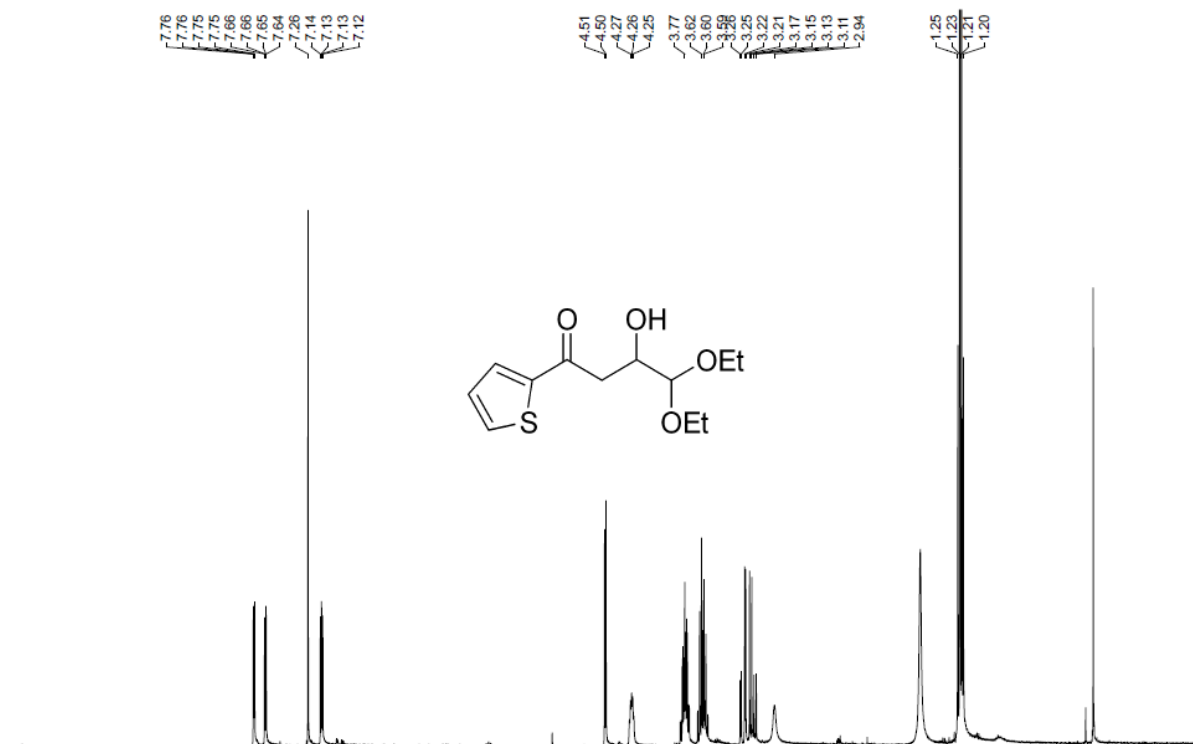




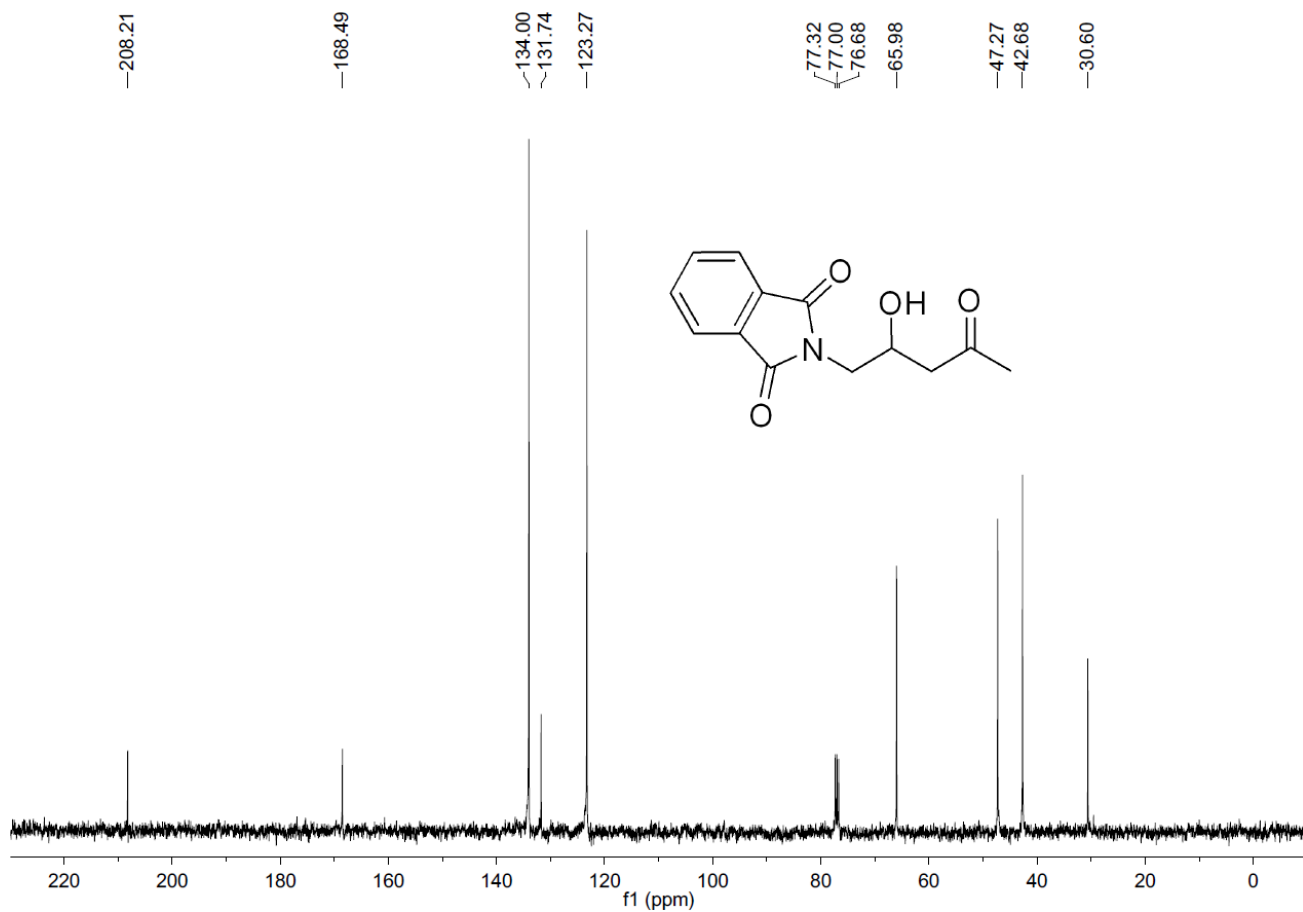
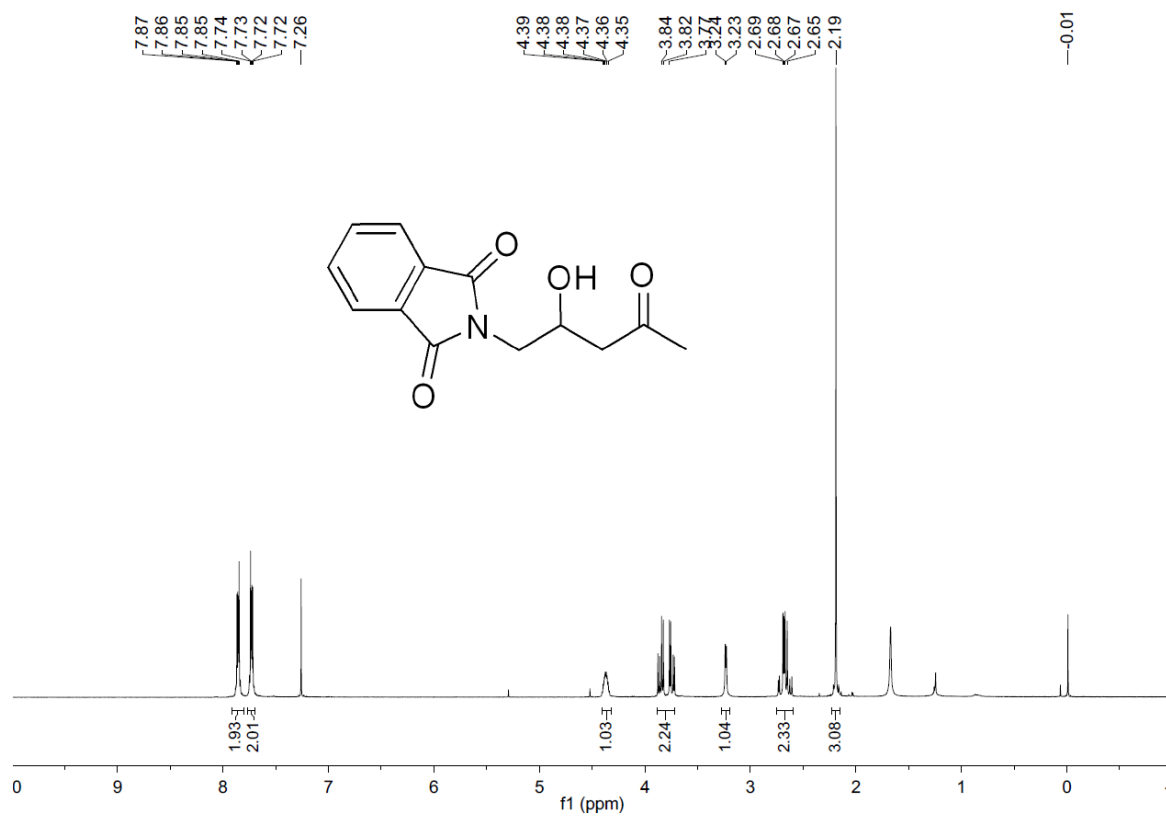


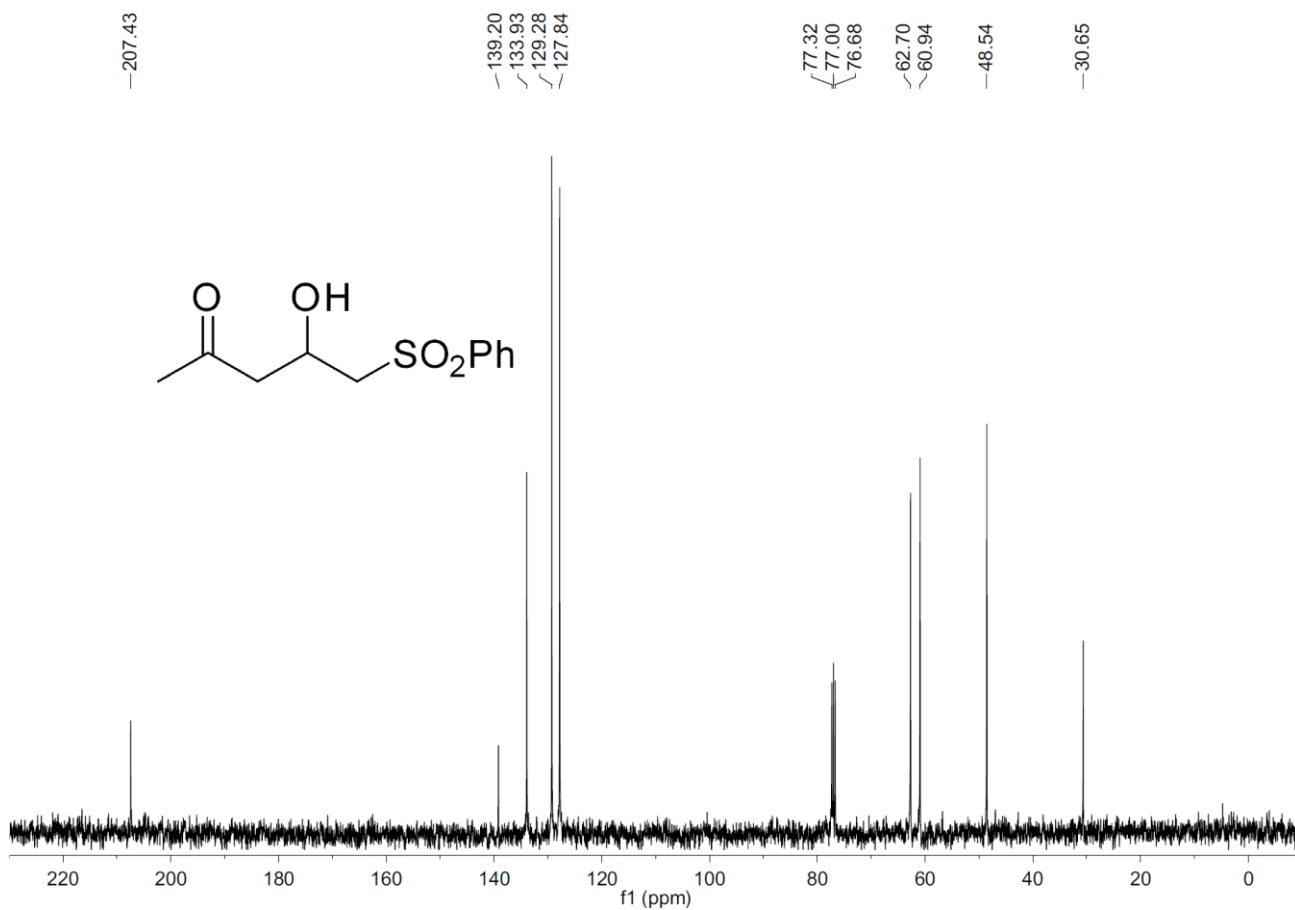
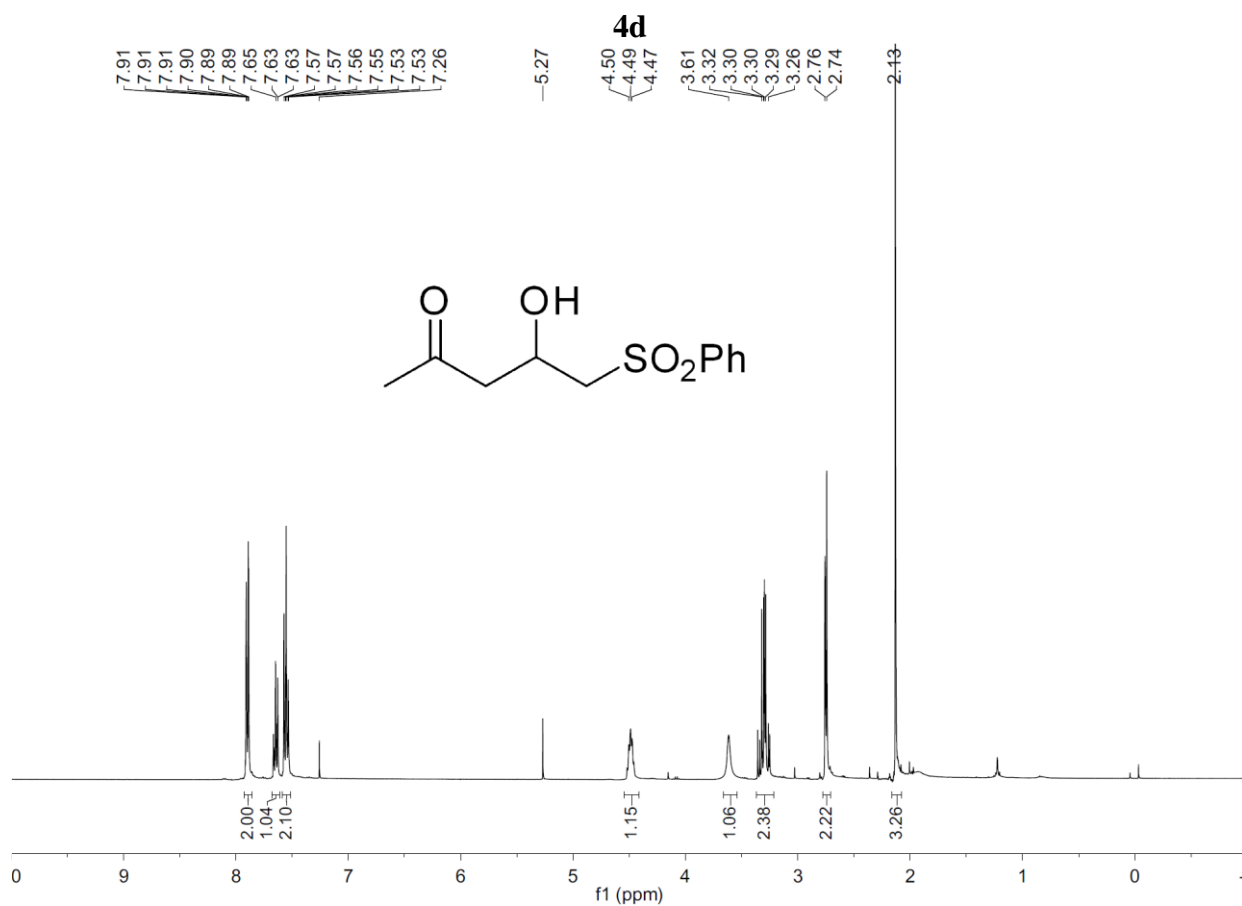


4b

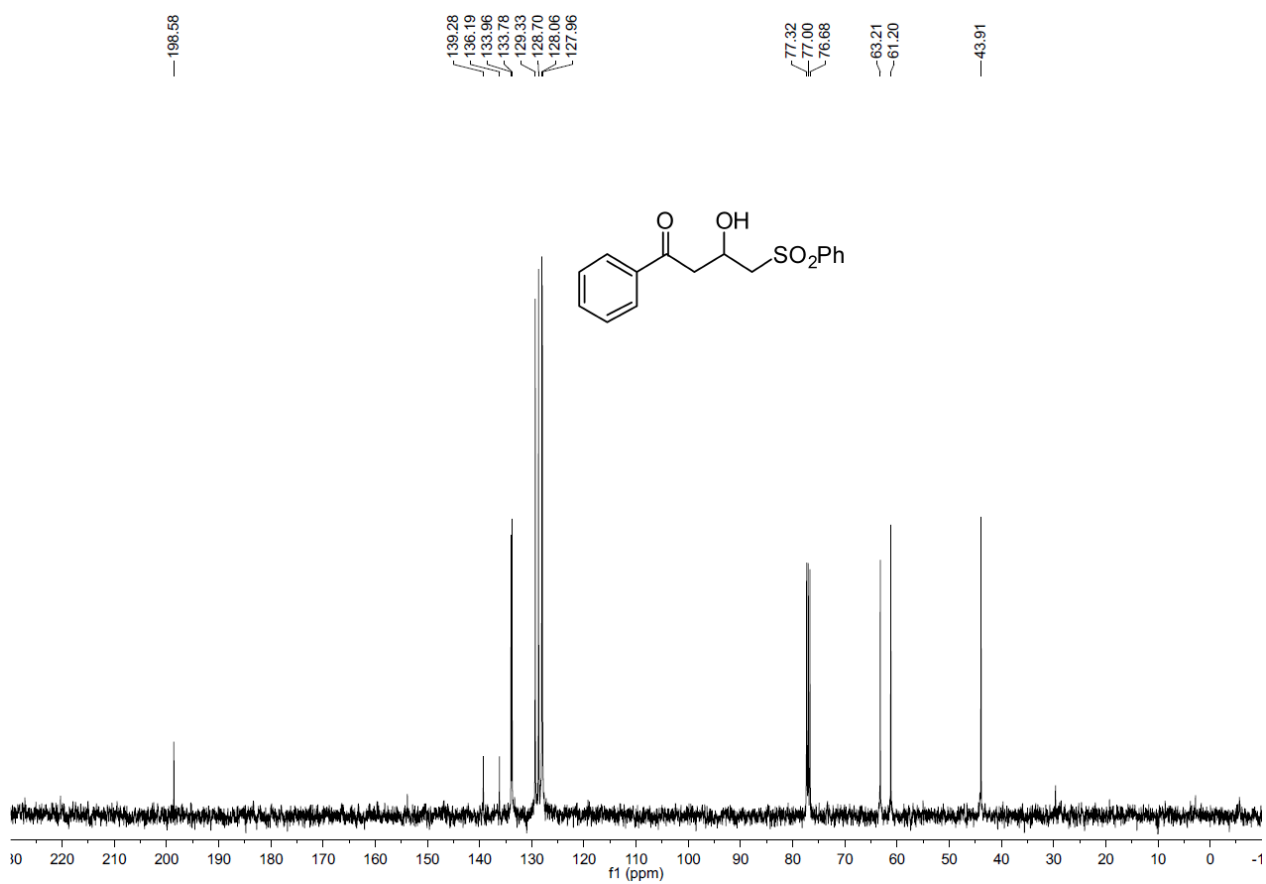
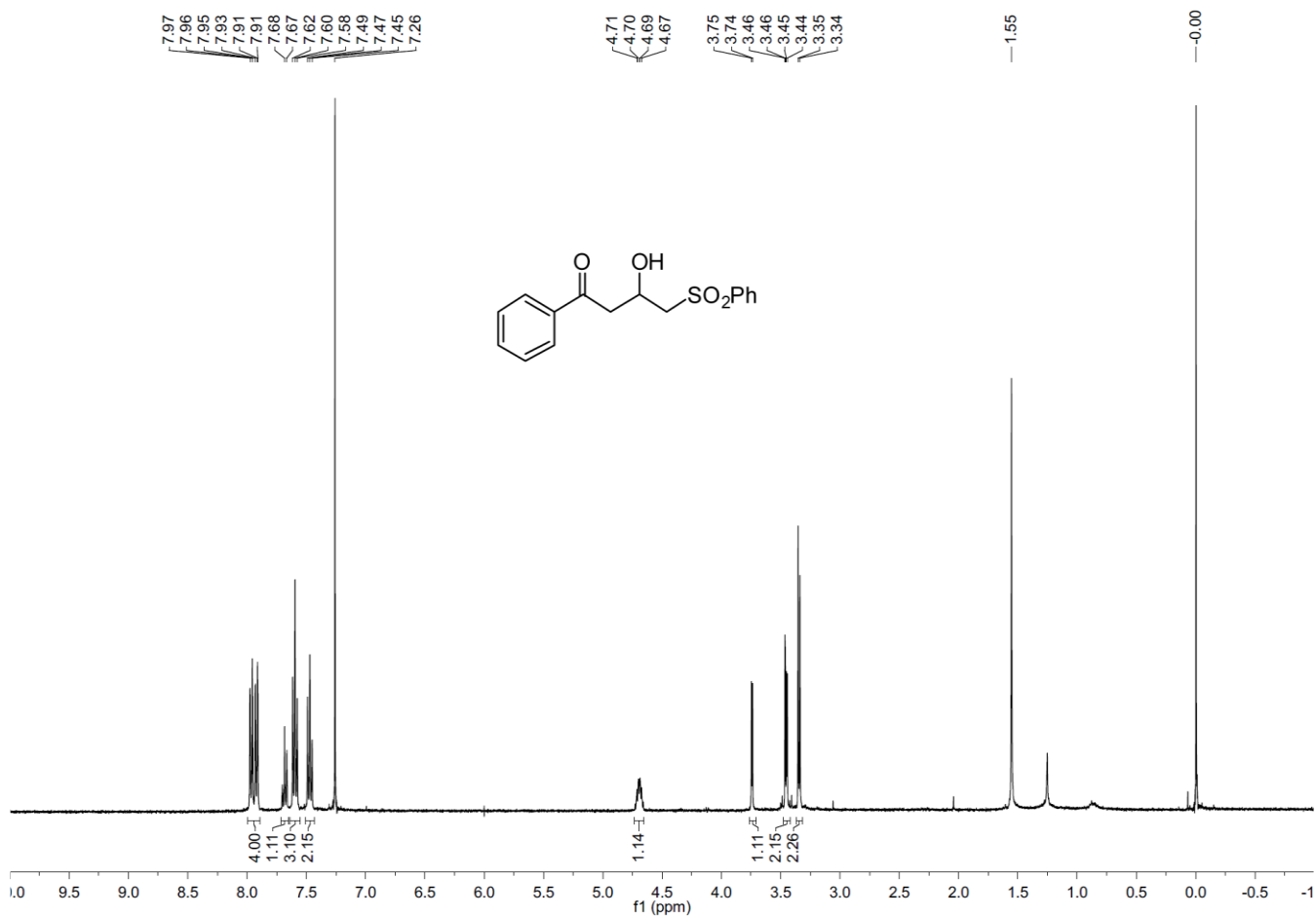


4c



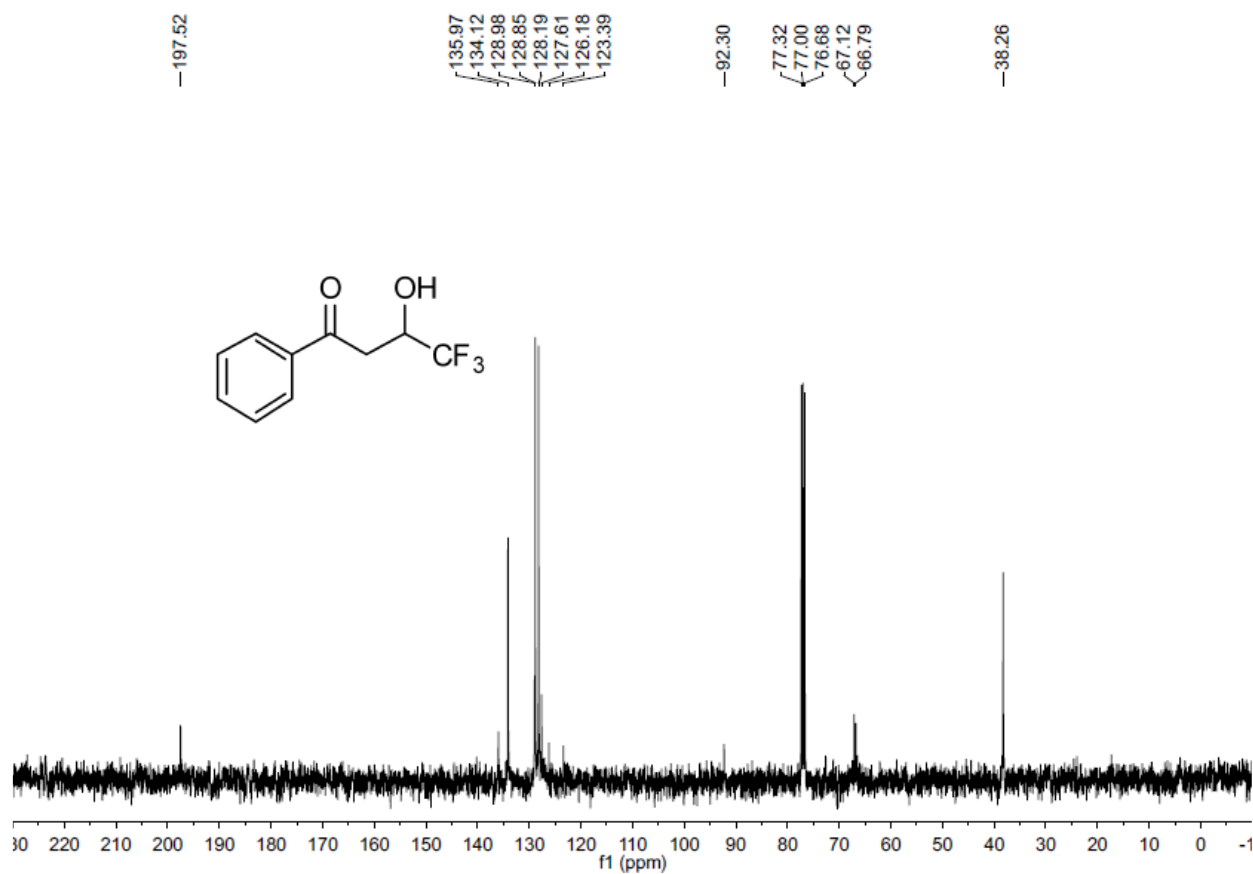
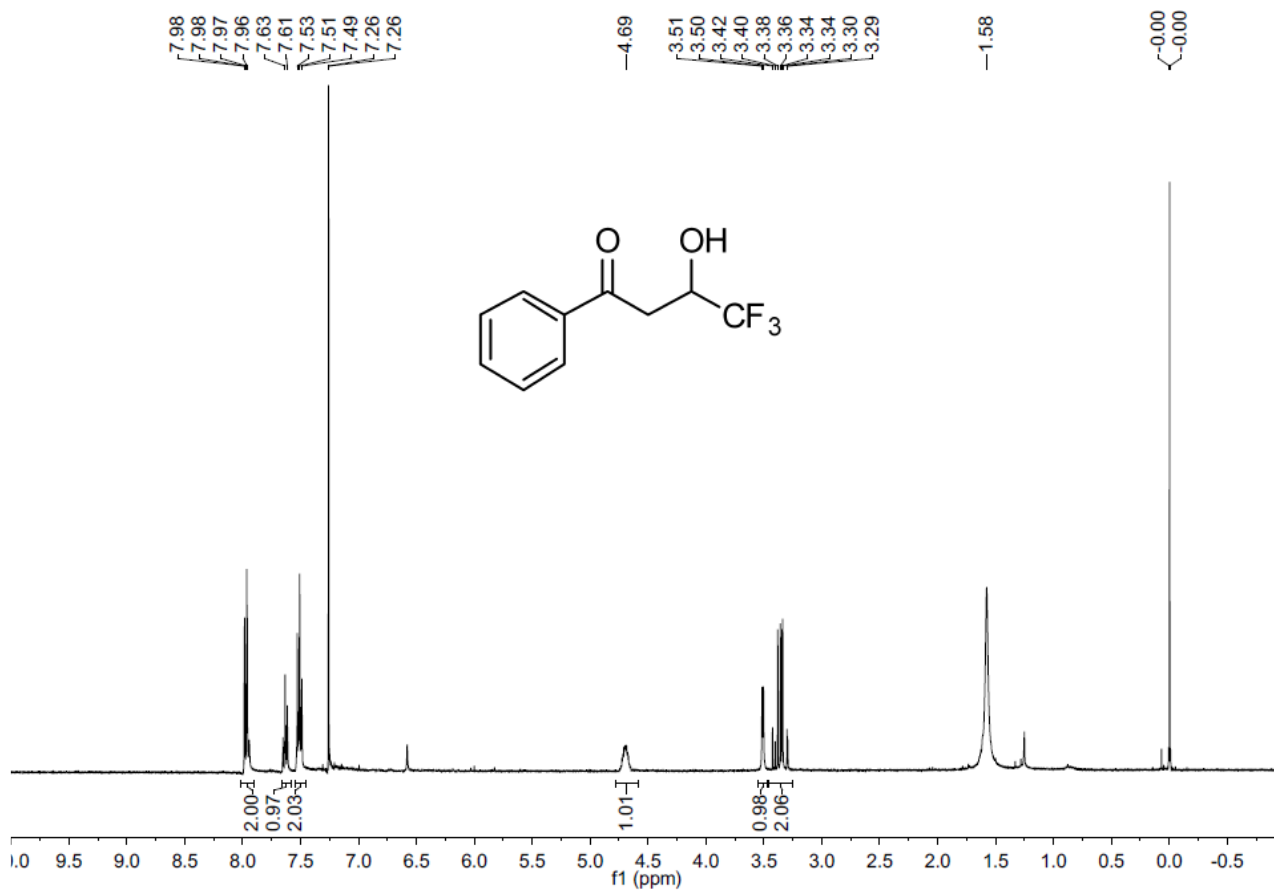


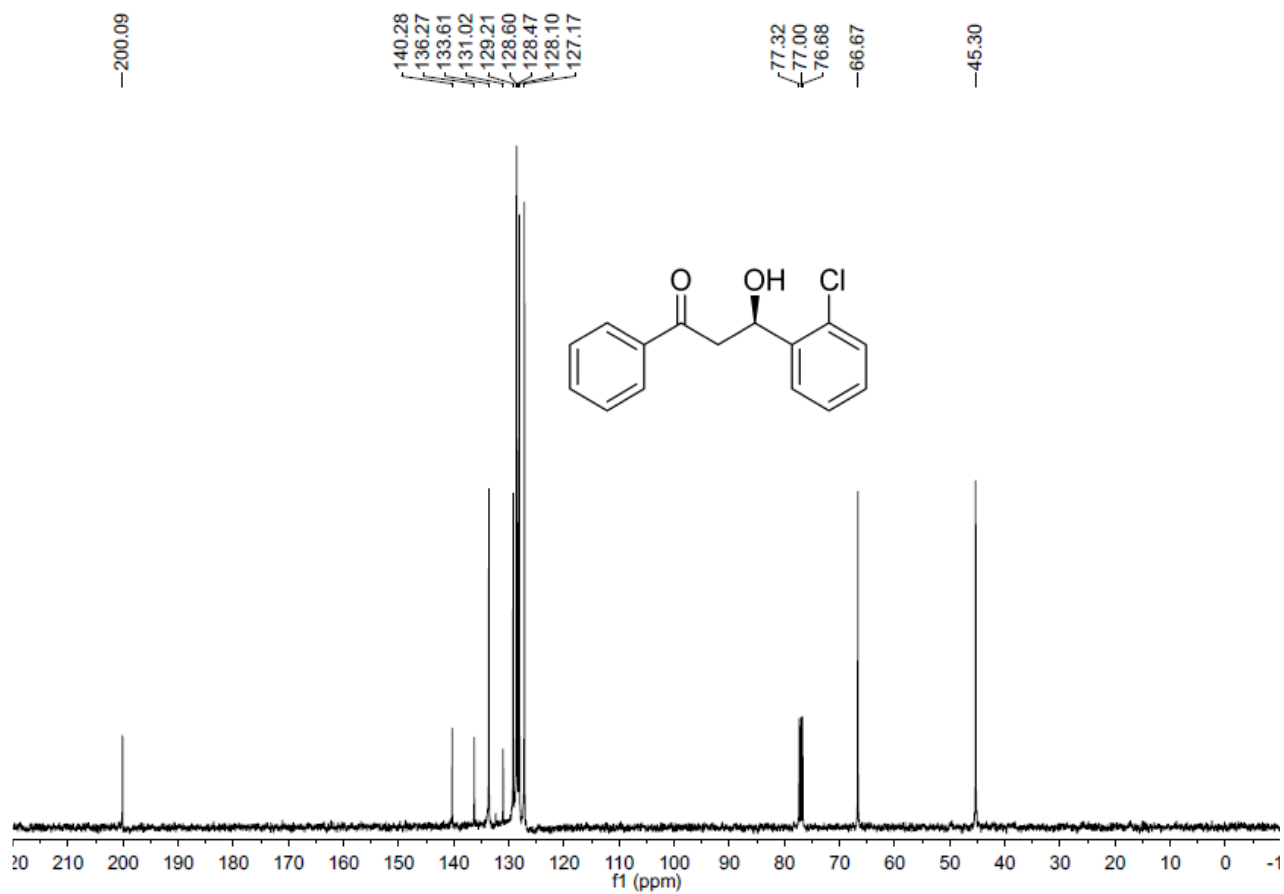
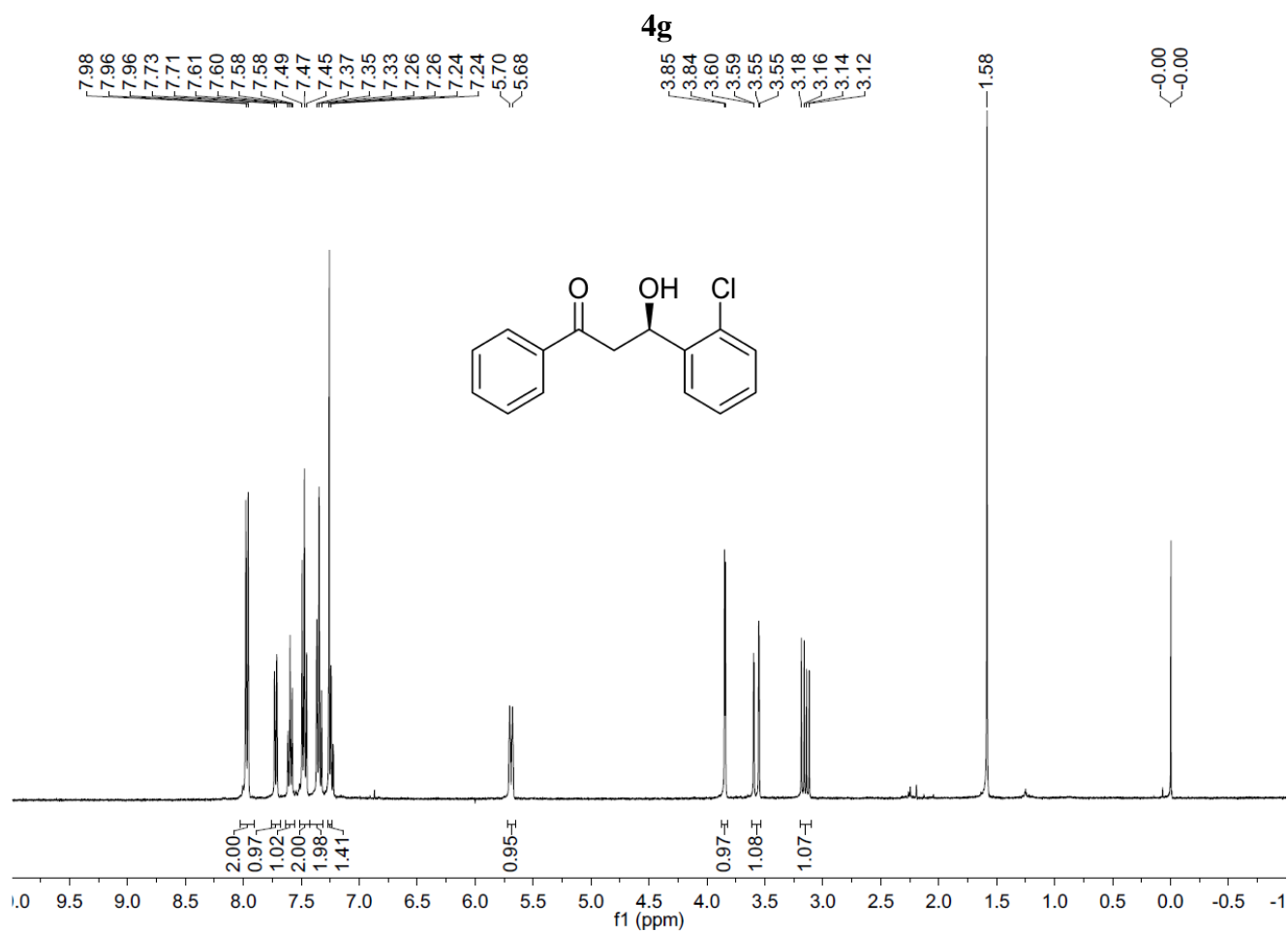
4e



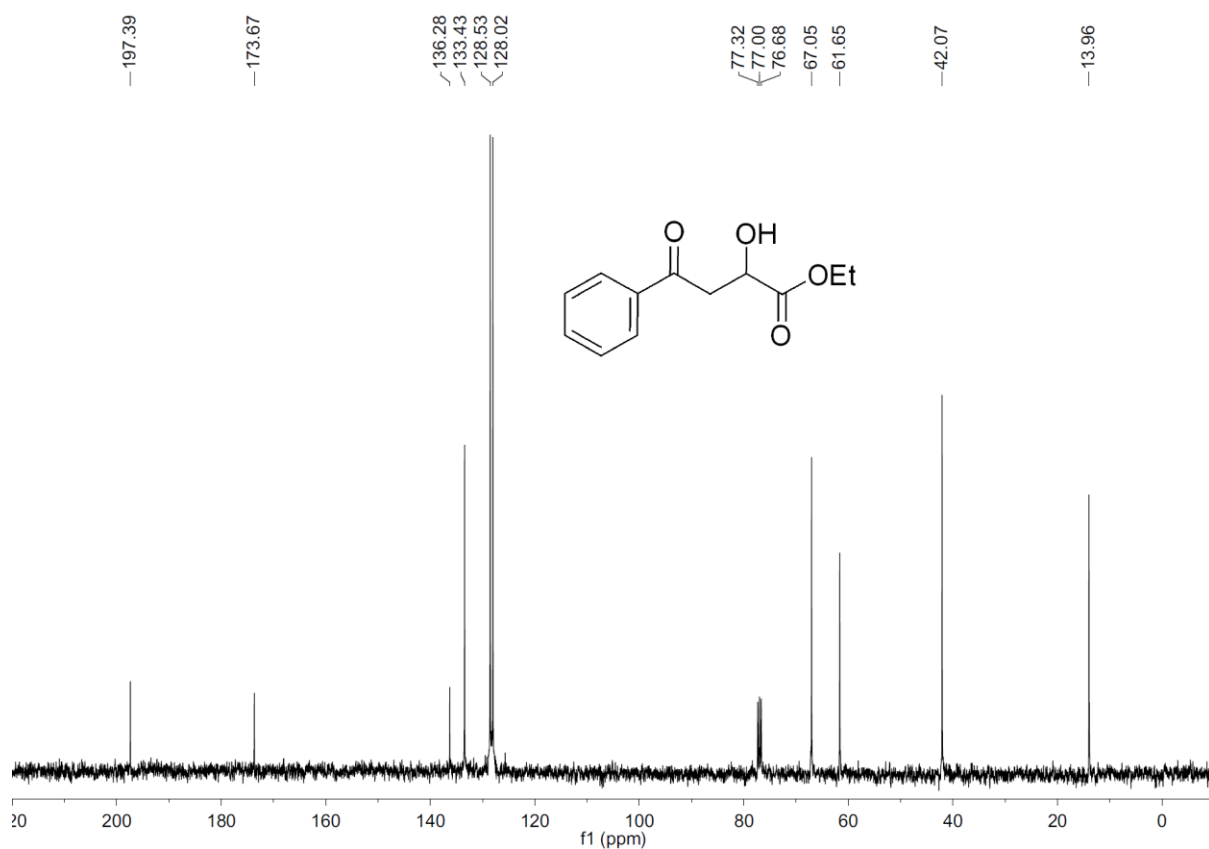
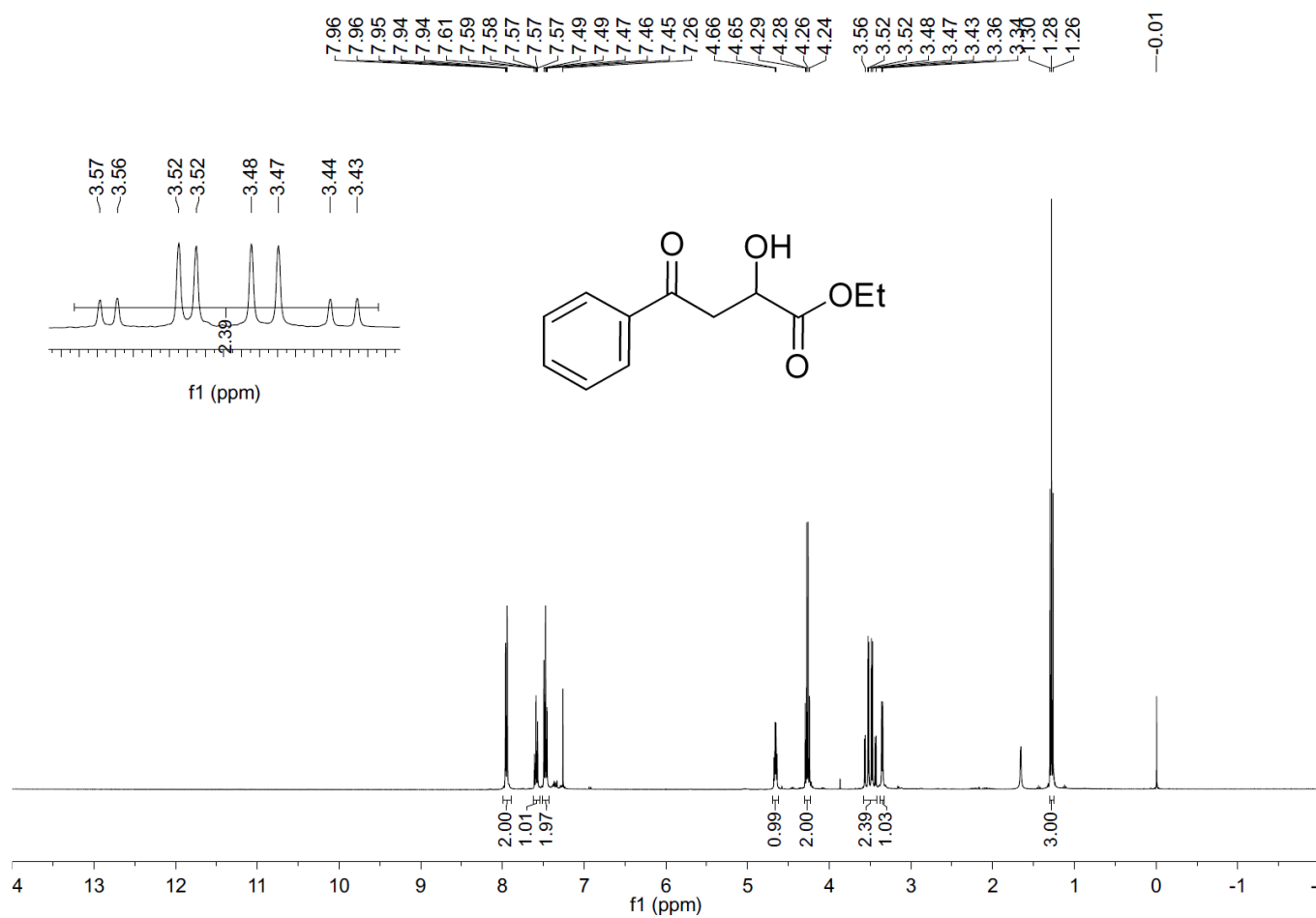
55

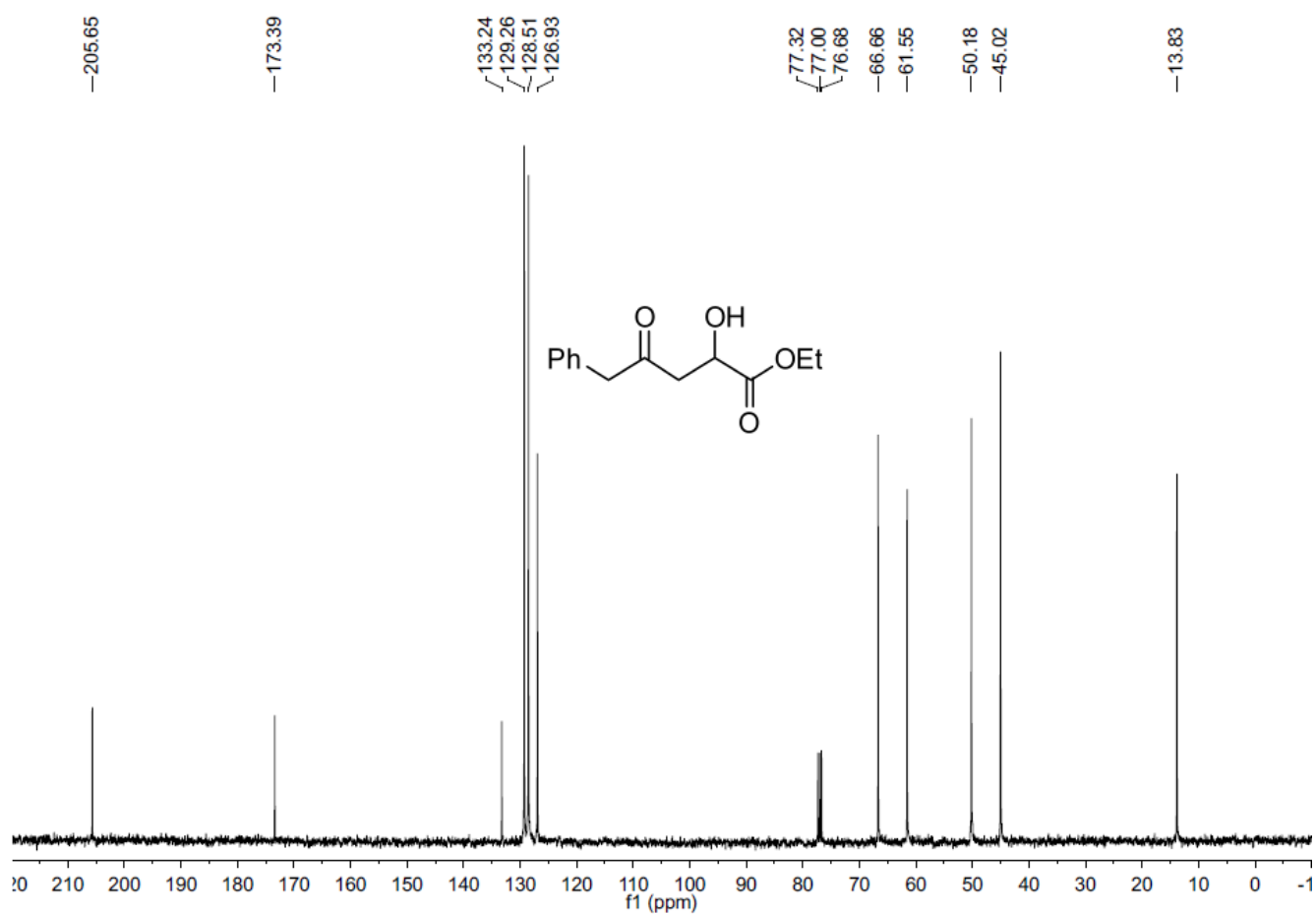
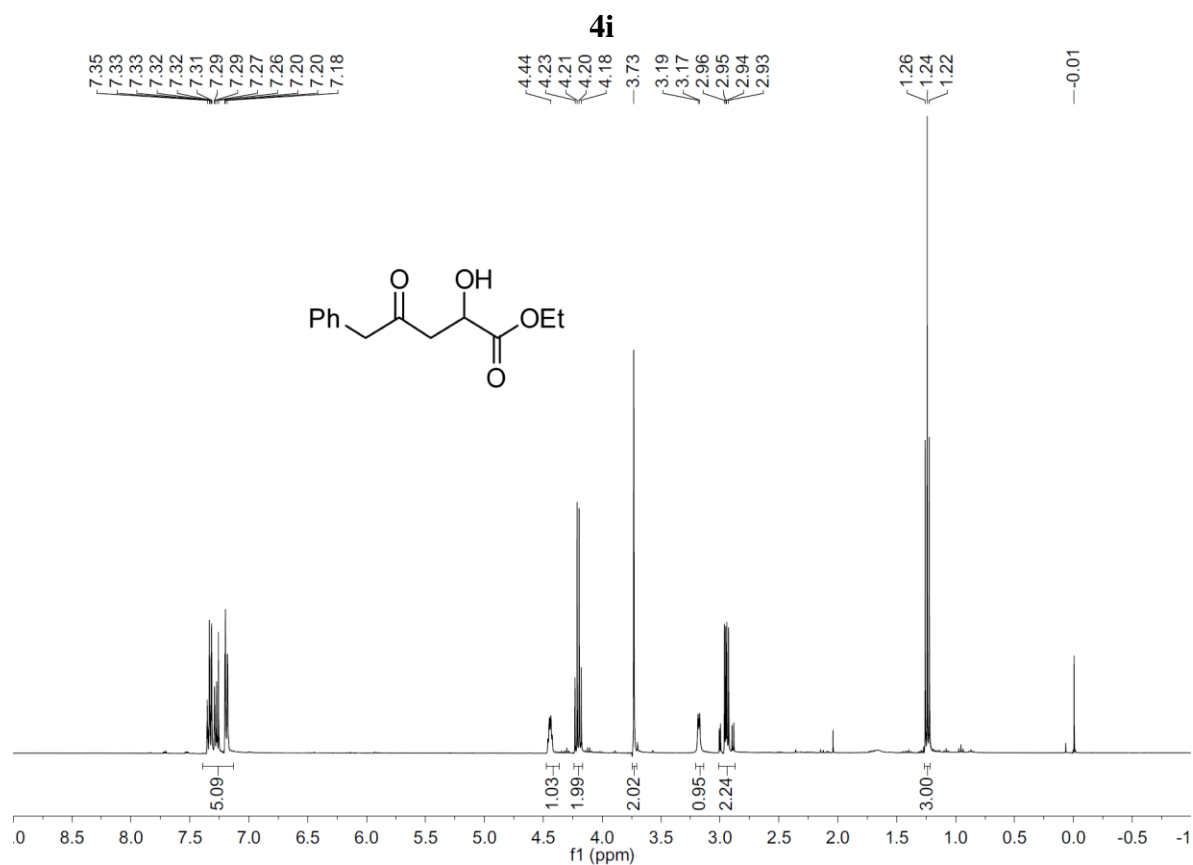
4f



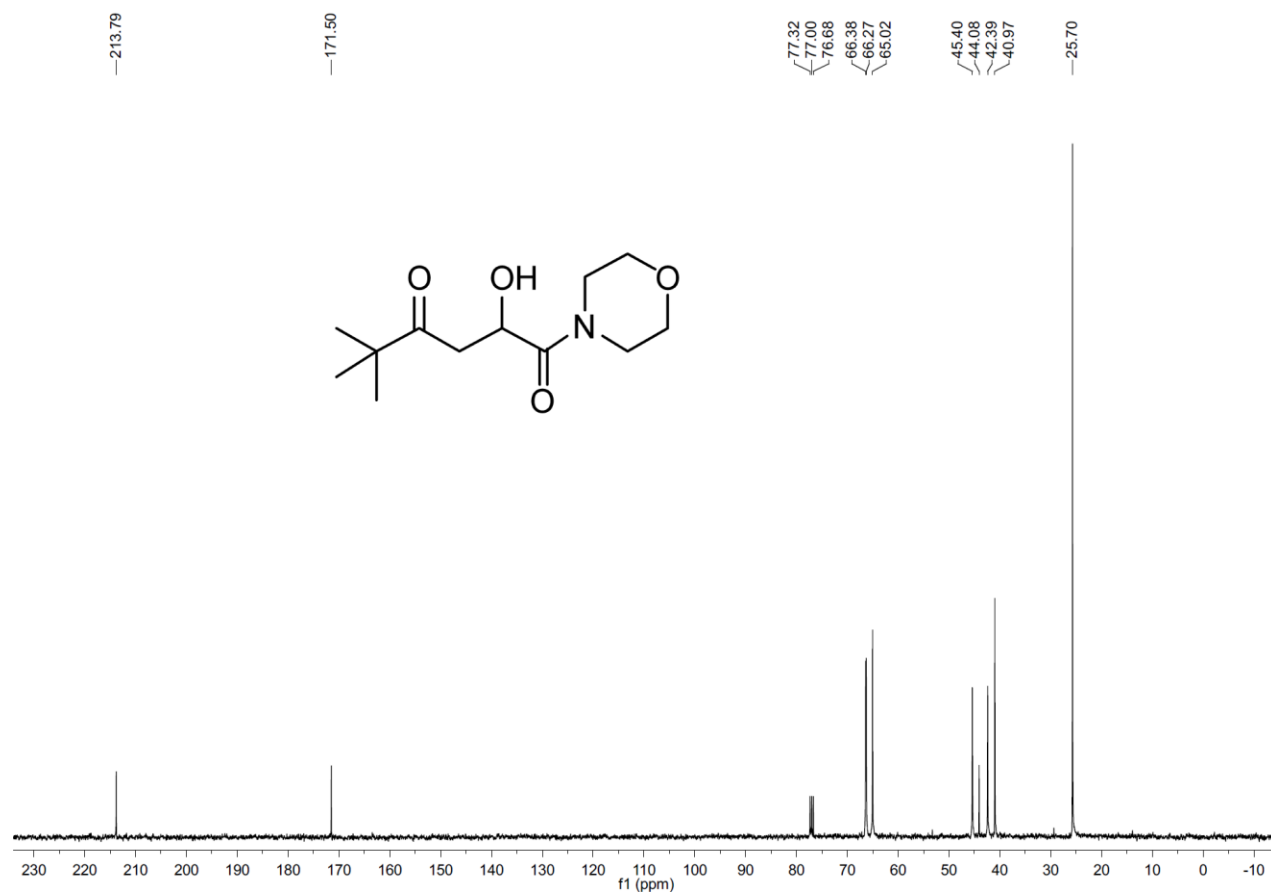


4h





60



8. HPLC diagram of chiral products

(2a) Table 1, racemate of 2a

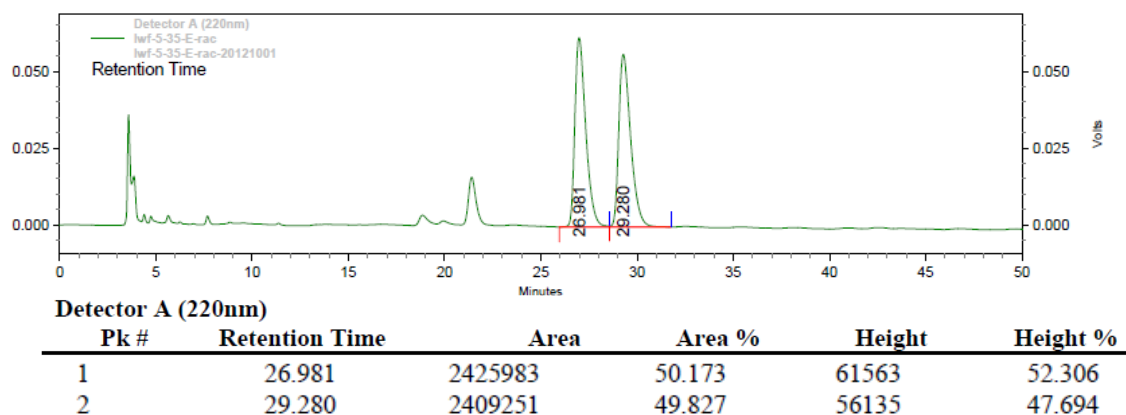


Table 1, entry 1: Ru-(*S*)-SunPhos, 50 °C, 10 bar H₂

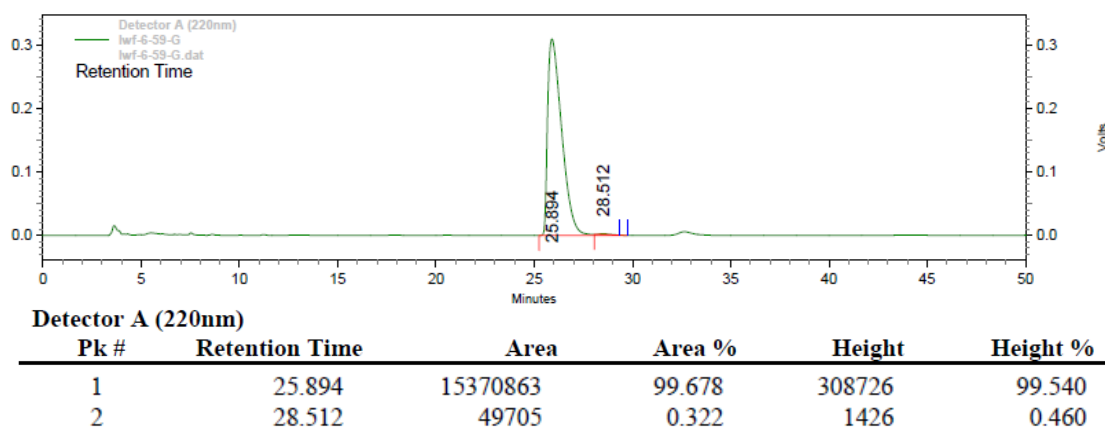


Table 1, entry 2 : Ru-(*S*)-SunPhos, 50 °C, 20 bar H₂

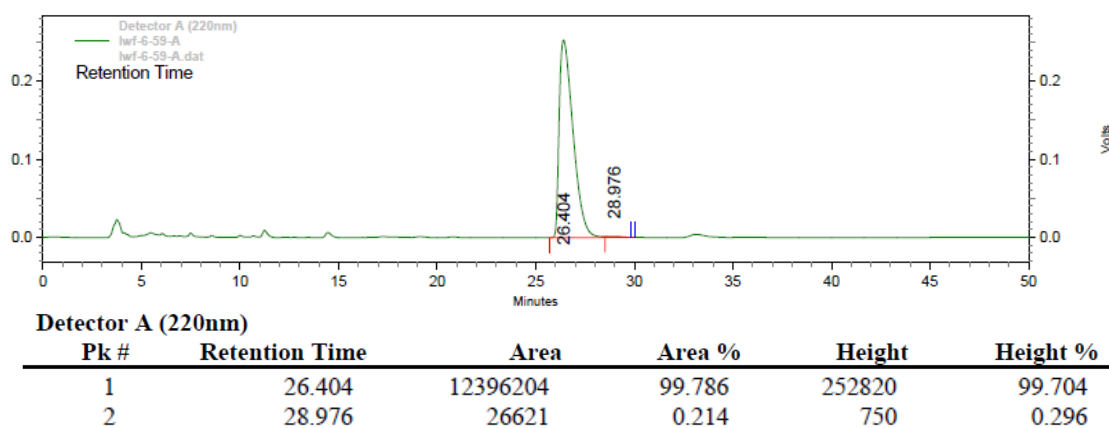


Table 1, entry 3 : Ru-(*S*)-SunPhos, 70 °C, 20 bar H₂

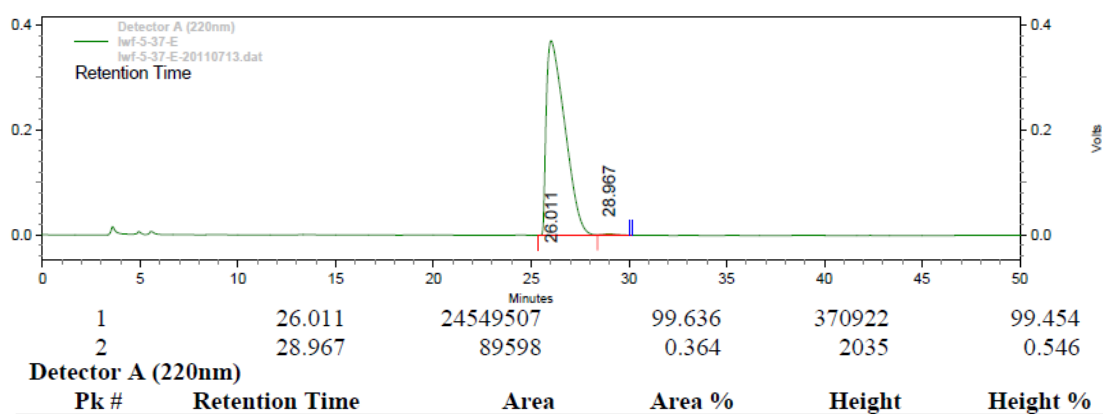


Table 1, entry 4: Ru-(*S*)-SunPhos, 90 °C, 20 bar H₂

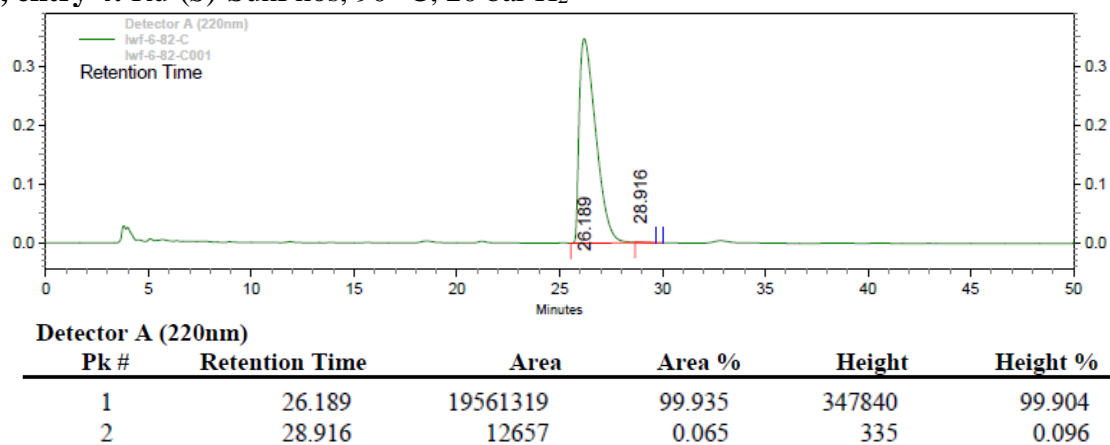


Table 1, entry 5: Ru-(*S*)-SegPhos , 70 °C, 20 bar H₂

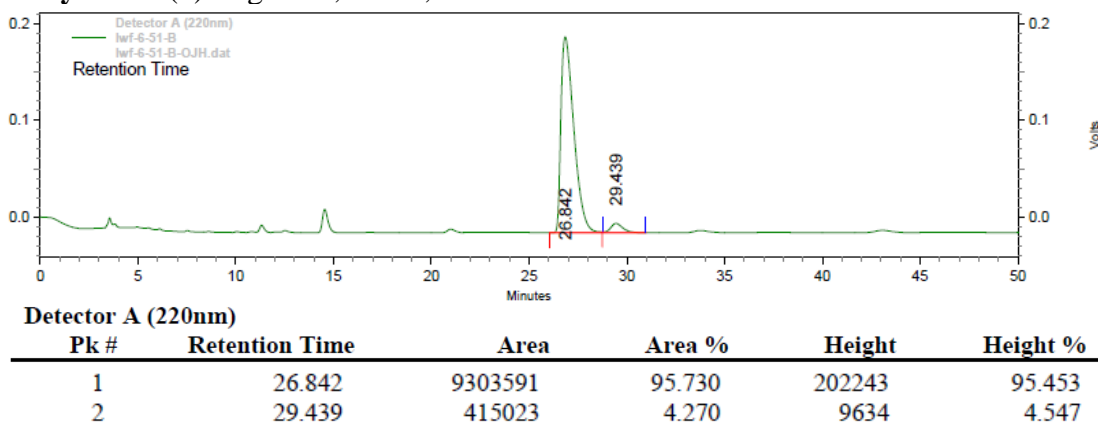


Table 1, entry 6: Ru-(*R*)-Binap , 70 °C, 20 bar H₂

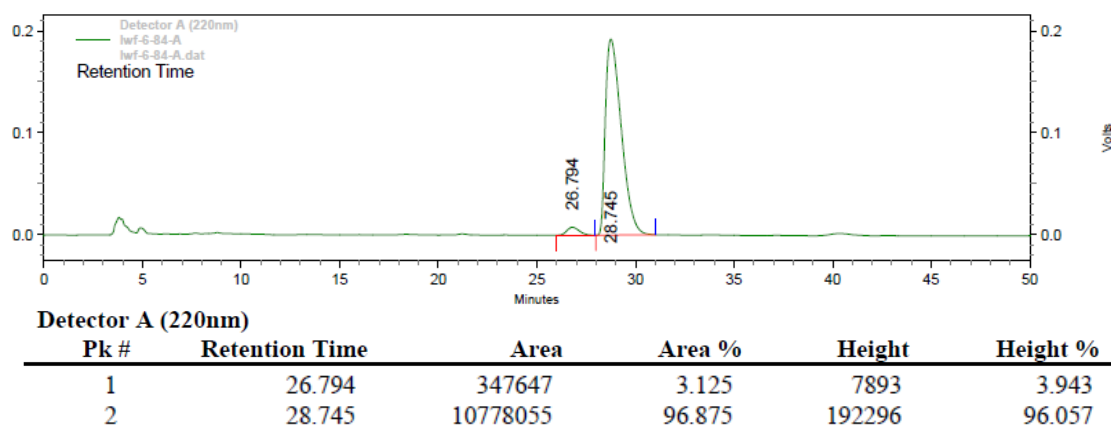


Table S1, entry 3: Ru-(*S*)-SunPhos, 1,4-dioxane, 70 °C, 20 bar H₂

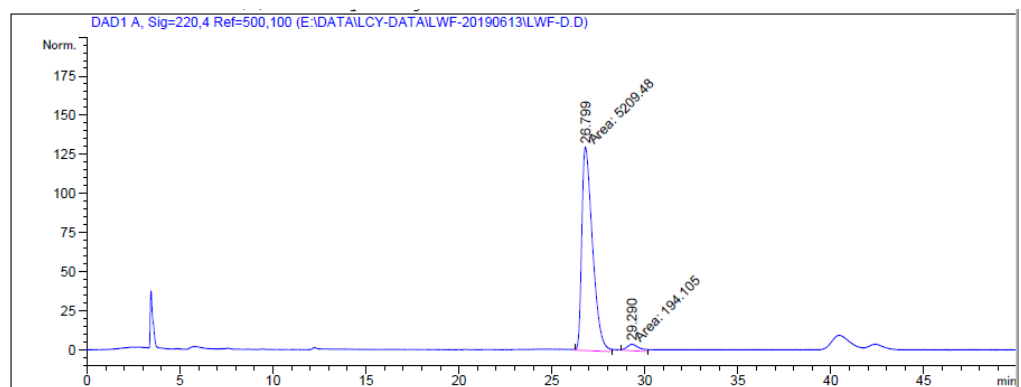
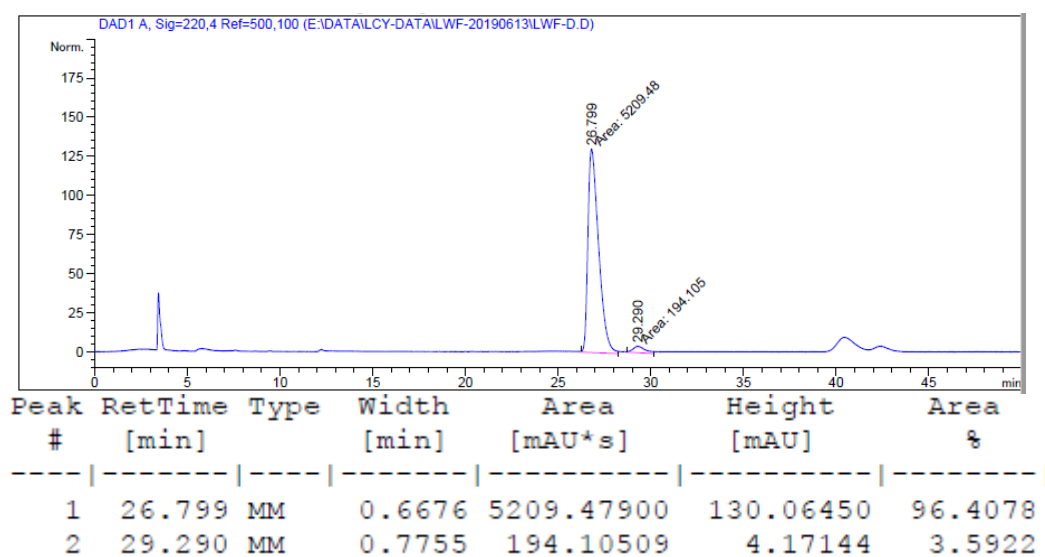
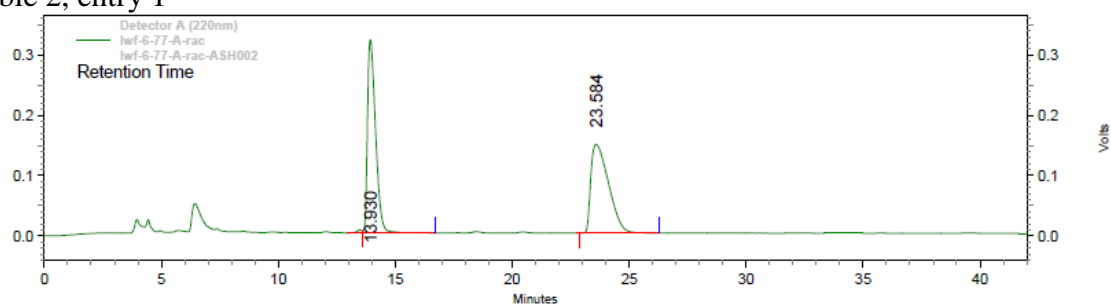


Table S1, entry 4: Ru-(*S*)-SunPhos, EtOAc, 70 °C, 20 bar H₂

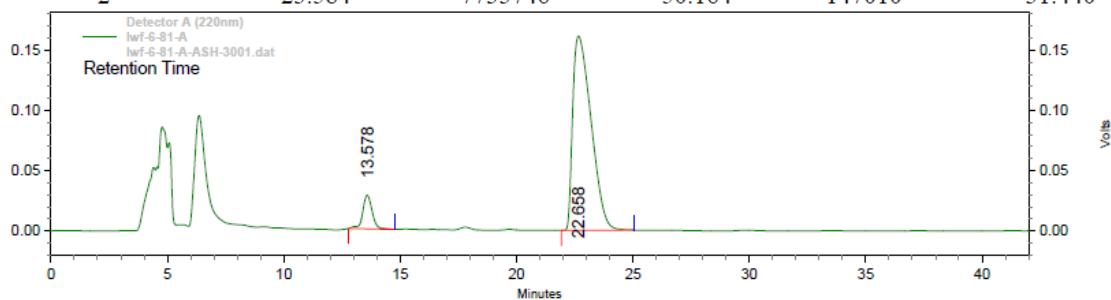


(2b) Table 2, entry 1



Detector A (220nm)

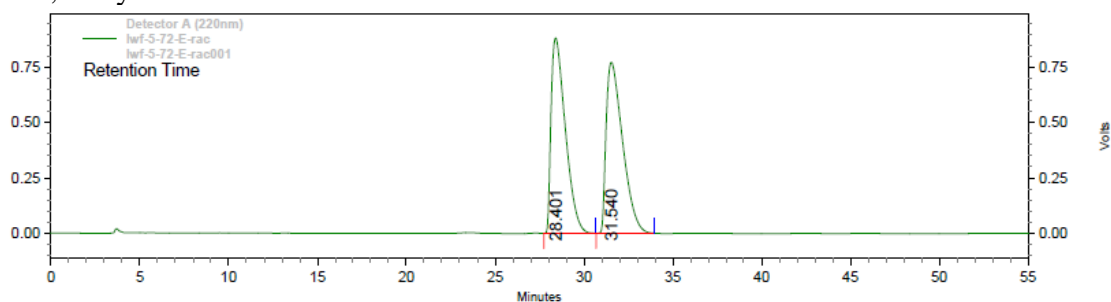
Pk #	Retention Time	Area	Area %	Height	Height %
1	13.930	7683030	49.836	320574	68.560
2	23.584	7733746	50.164	147010	31.440



Detector A (220nm)

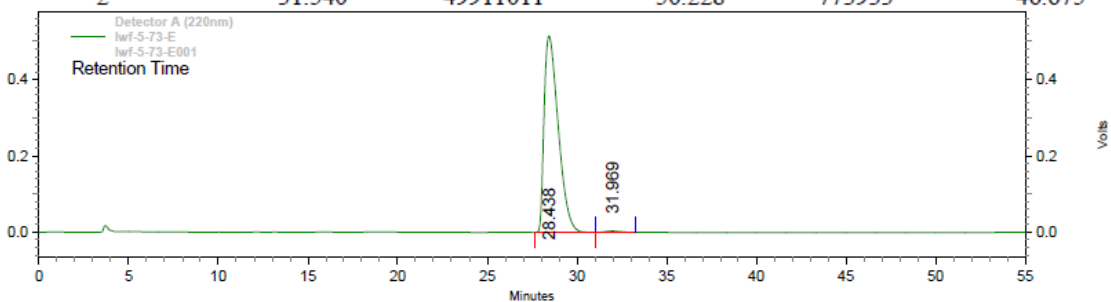
Pk #	Retention Time	Area	Area %	Height	Height %
1	13.578	784542	8.134	27910	14.742
2	22.658	8860720	91.866	161414	85.258

(2c) Table 2, entry 2



Detector A (220nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	28.401	49457136	49.772	884200	53.325
2	31.540	49911011	50.228	773933	46.675

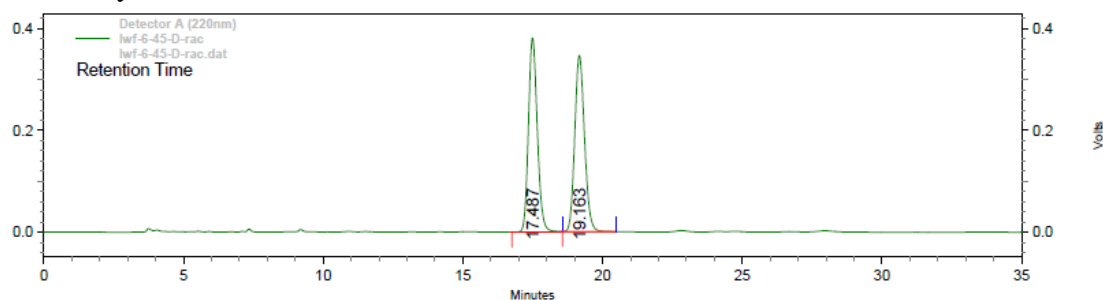


Detector A (220nm)

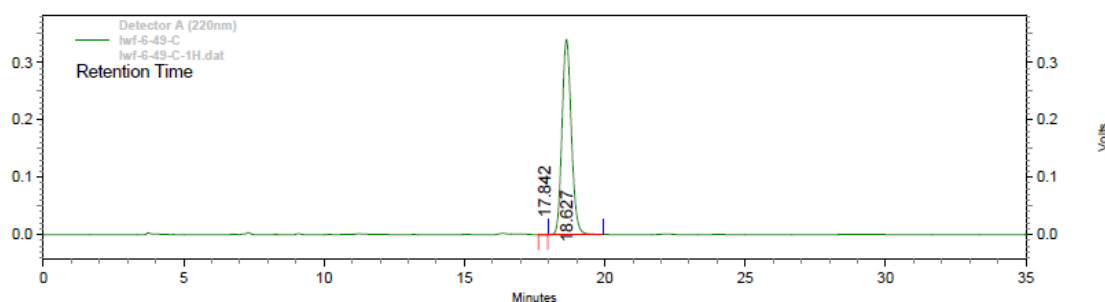
Pk #	Retention Time	Area	Area %	Height	Height %
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1	28.438	28198335	99.295	514823	99.324
2	31.969	200074	0.705	3504	0.676

(2d) Table 2, entry 3

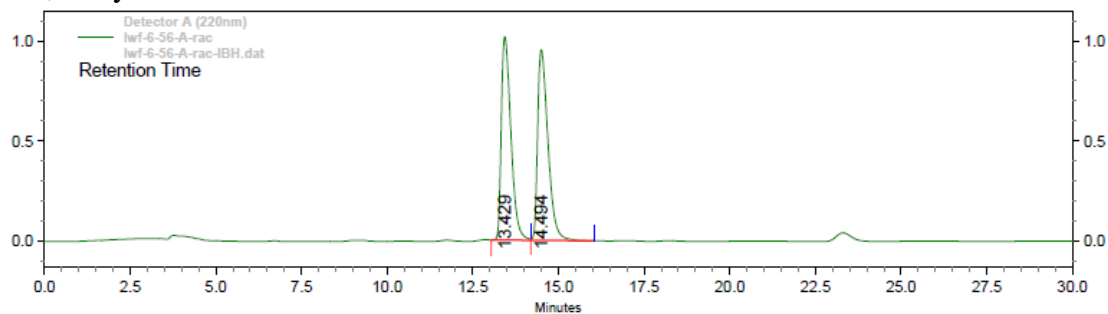


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	17.487	8446290	49.937	381894	52.395
2	19.163	8467723	50.063	346982	47.605

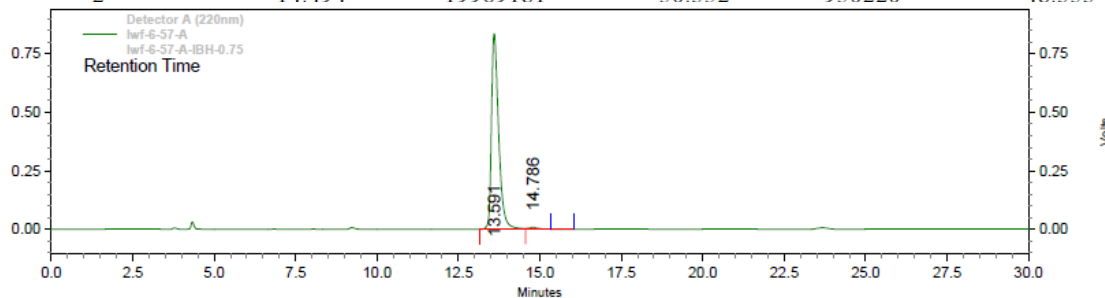


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	17.842	623	0.008	43	0.013
2	18.627	7875929	99.992	340048	99.987

(2e) Table 2, entry 4



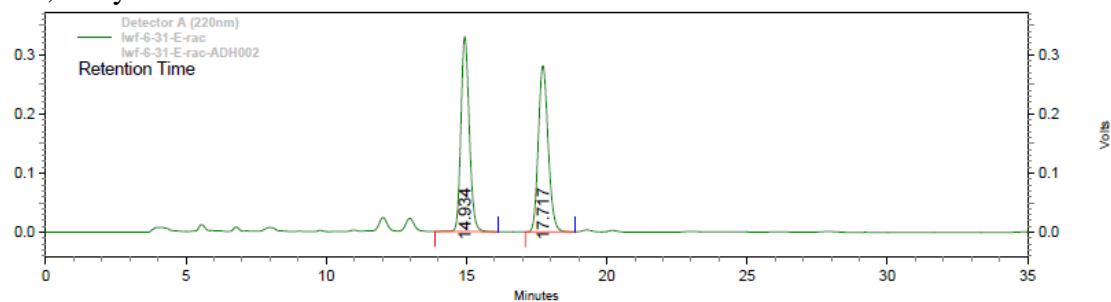
Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	13.429	19690326	49.648	1014973	51.647
2	14.494	19969181	50.352	950220	48.353



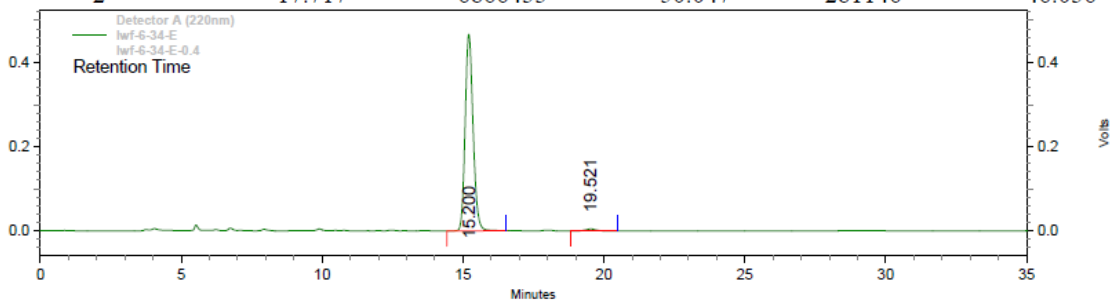
Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %

1	13.591	12956197	99.353	836015	99.299
2	14.786	84348	0.647	5901	0.701

(2f) Table 2, entry 5

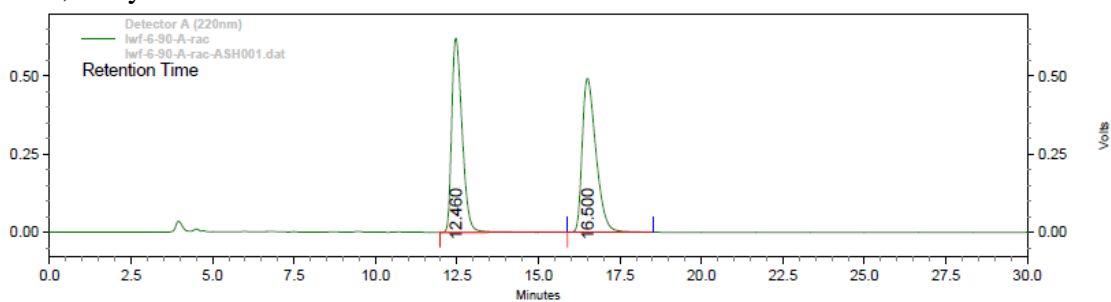


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	14.934	6853461	49.953	329564	53.964
2	17.717	6866433	50.047	281146	46.036

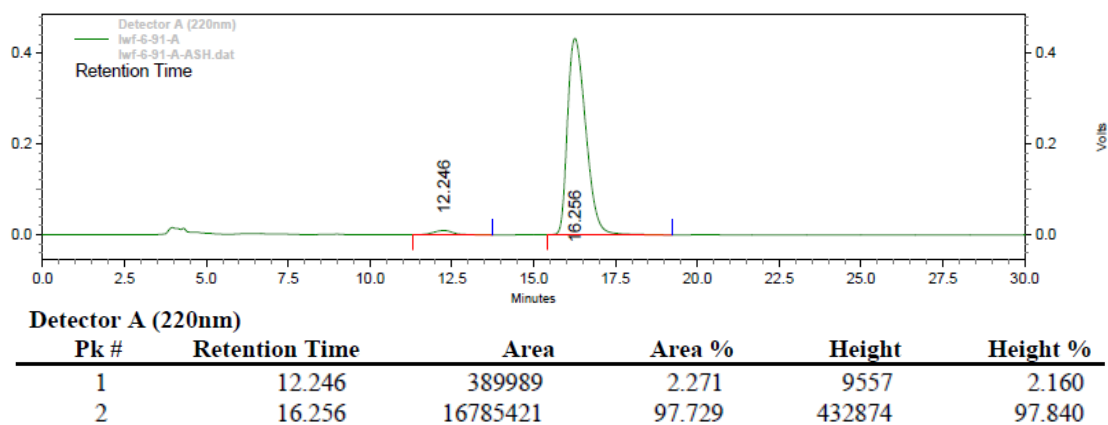


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	15.200	9149099	98.711	467019	99.014
2	19.521	119451	1.289	4651	0.986

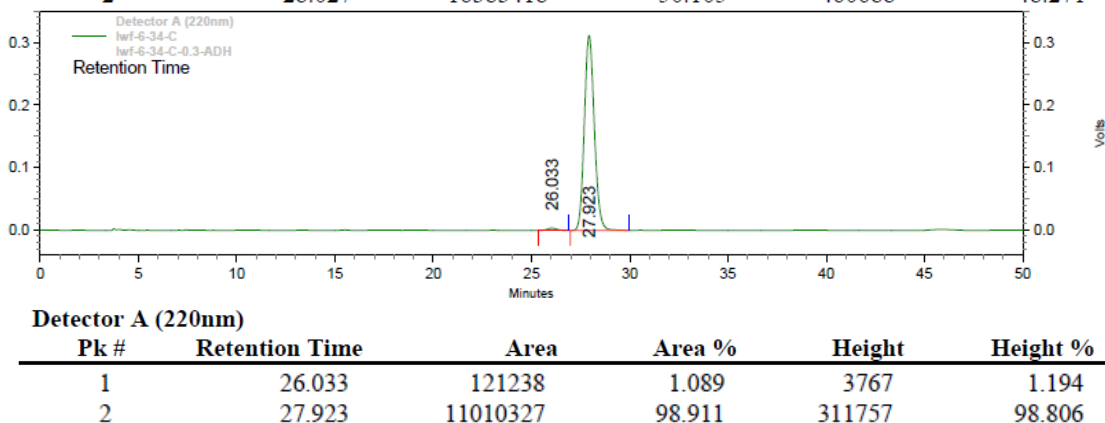
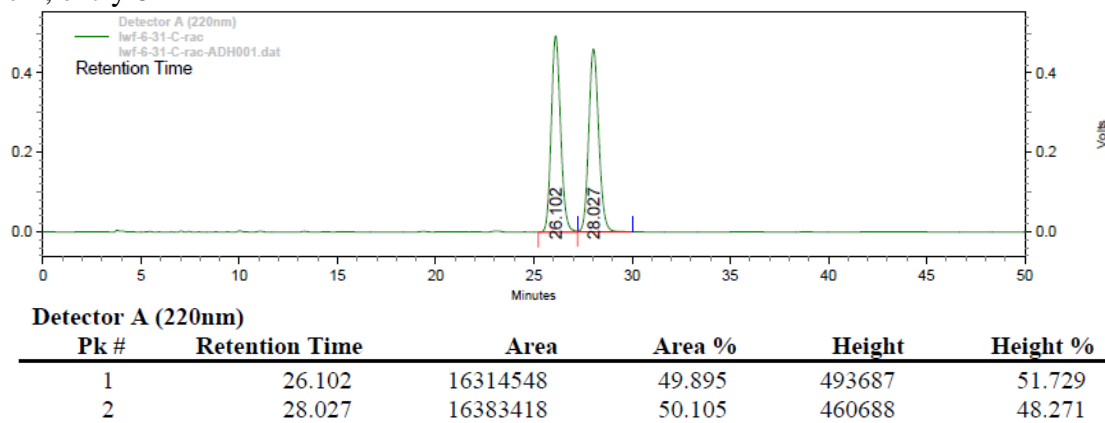
(2h) Table 2, entry 7



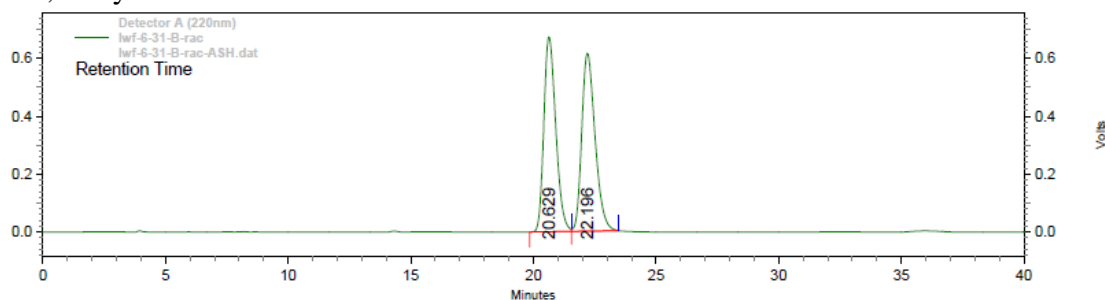
Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	12.460	13807978	48.863	622017	55.808
2	16.500	14450430	51.137	492544	44.192



(2i) Table 2, entry 8

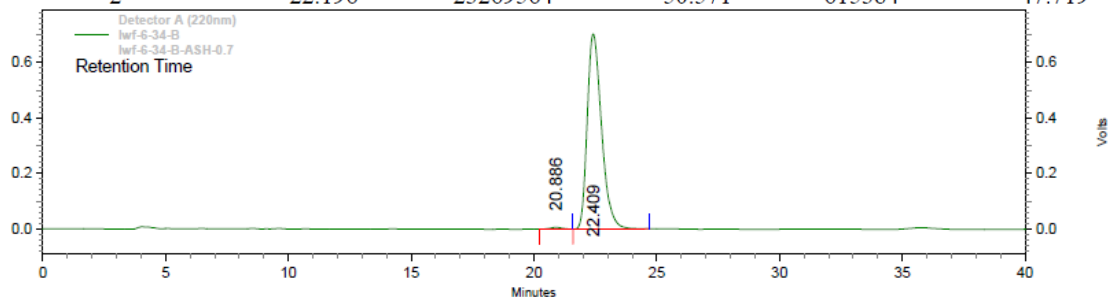


(2j) Table 2, entry 9



Detector A (220nm)

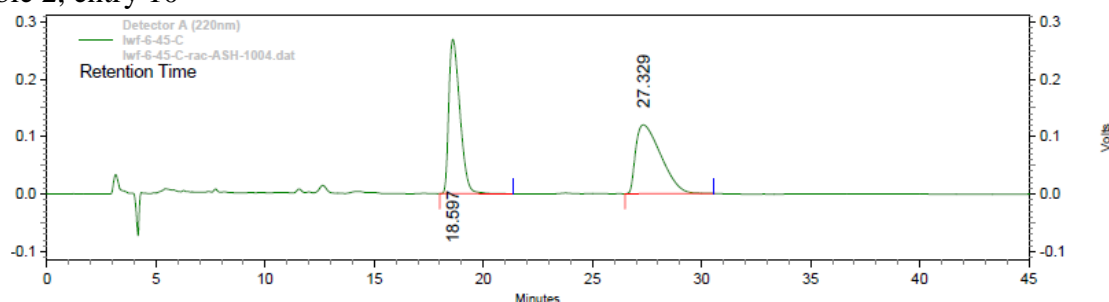
Pk #	Retention Time	Area	Area %	Height	Height %
1	20.629	22744132	49.429	674214	52.281
2	22.196	23269564	50.571	615384	47.719



Detector A (220nm)

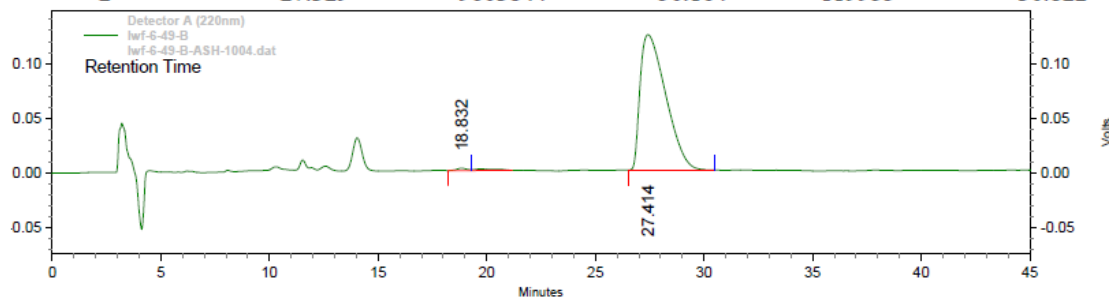
Pk #	Retention Time	Area	Area %	Height	Height %
1	20.886	215658	0.750	6391	0.900
2	22.409	28542536	99.250	703707	99.100

(2k) Table 2, entry 10



Detector A (220nm)

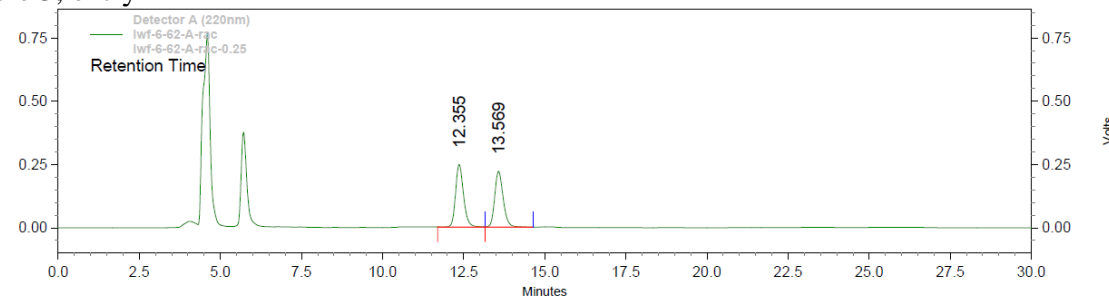
Pk #	Retention Time	Area	Area %	Height	Height %
1	18.597	9540886	49.836	269238	69.178
2	27.329	9603844	50.164	119955	30.822



Detector A (220nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	18.832	69387	0.681	2057	1.640
2	27.414	10118010	99.319	123333	98.360

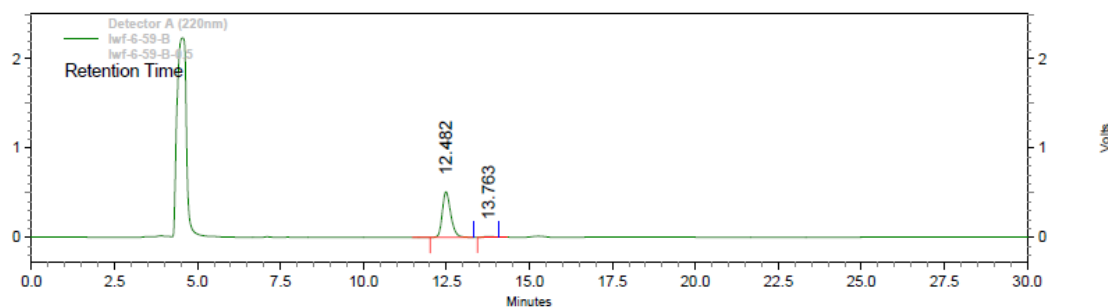
(4a) Table 3, entry 1



Detector A (220nm)

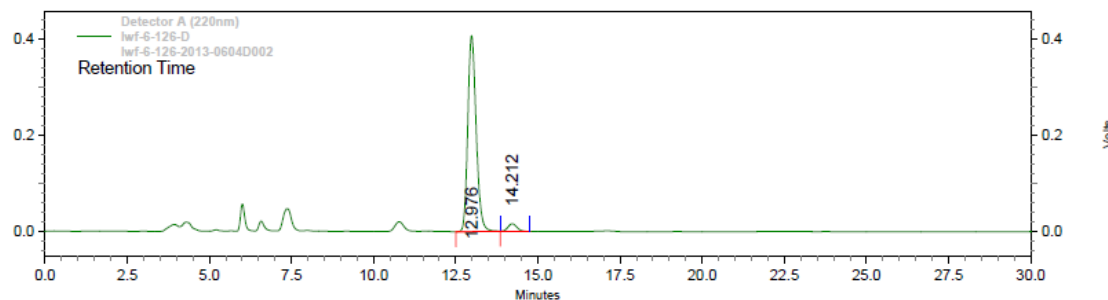
Pk #	Retention Time	Area	Area %	Height	Height %
1	12.355	4229901	51.223	246749	52.795
2	13.569	4027851	48.777	220625	47.205

50 °C



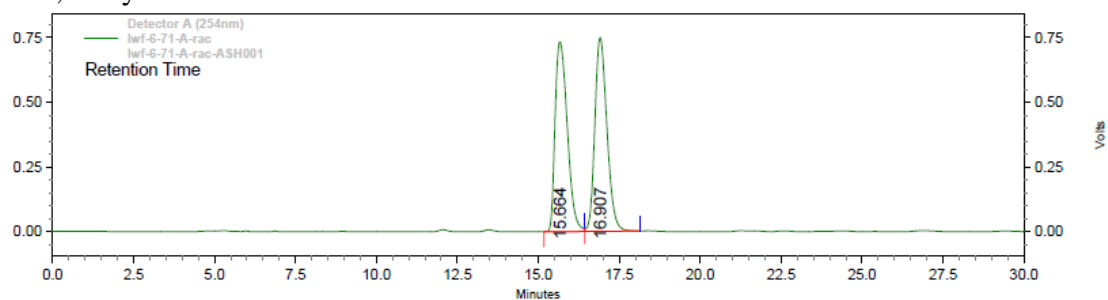
Detector A (220nm)						
Pk #	Retention Time	Area	Area %	Height	Height %	
1	12.482	8979284	98.729	509884	98.754	
2	13.763	115576	1.271	6432	1.246	

70 °C, 0.05 mmol CaCO₃ was added:

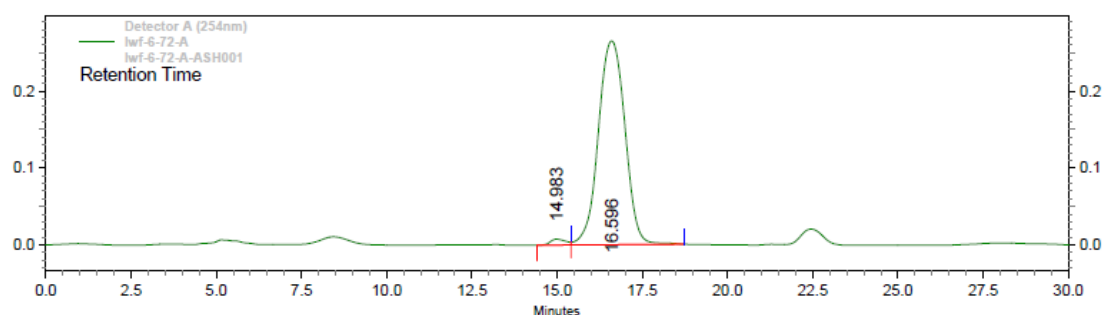


Detector A (220nm)						
Pk #	Retention Time	Area	Area %	Height	Height %	
1	12.976	7255379	95.807	407740	96.157	
2	14.212	317555	4.193	16297	3.843	

(4b) Table 3, entry 2

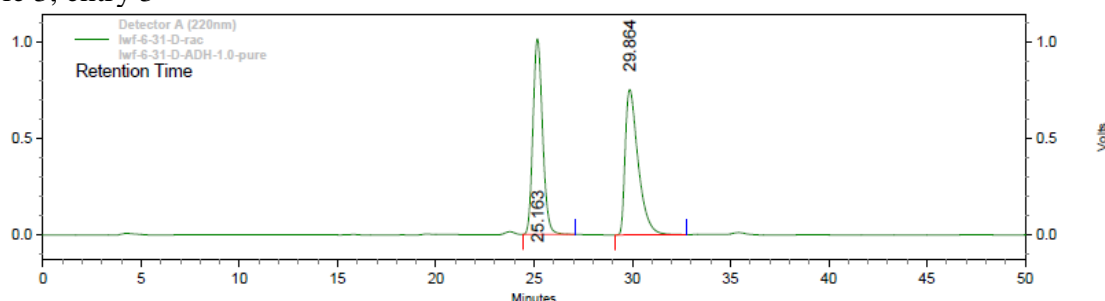


Detector A (220nm)						
Pk #	Retention Time	Area	Area %	Height	Height %	
1	15.664	19172409	49.691	733136	49.500	
2	16.907	19410483	50.309	747941	50.500	

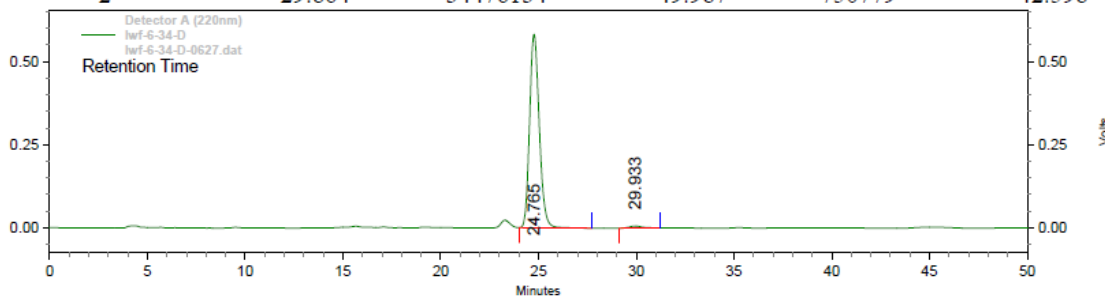


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	14.983	238748	1.630	7589	2.783
2	16.596	14405608	98.370	265071	97.217

(4c) Table 3, entry 3

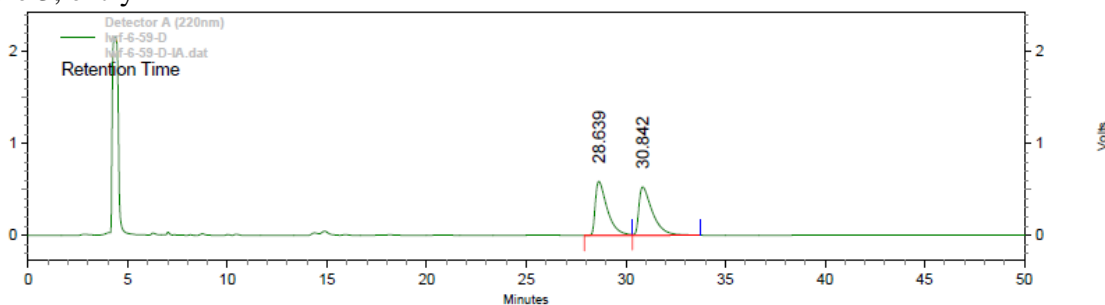


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	25.163	34493751	50.013	1011693	57.402
2	29.864	34476134	49.987	750779	42.598

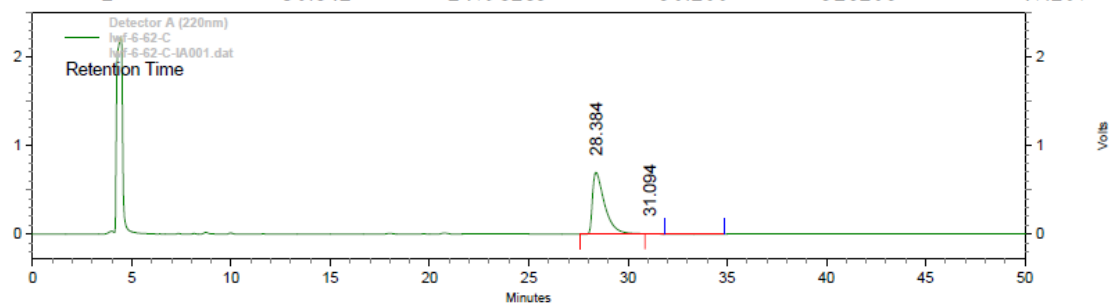


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	24.765	20078245	98.789	582999	99.003
2	29.933	246128	1.211	5874	0.997

(4d) Table 3, entry 4

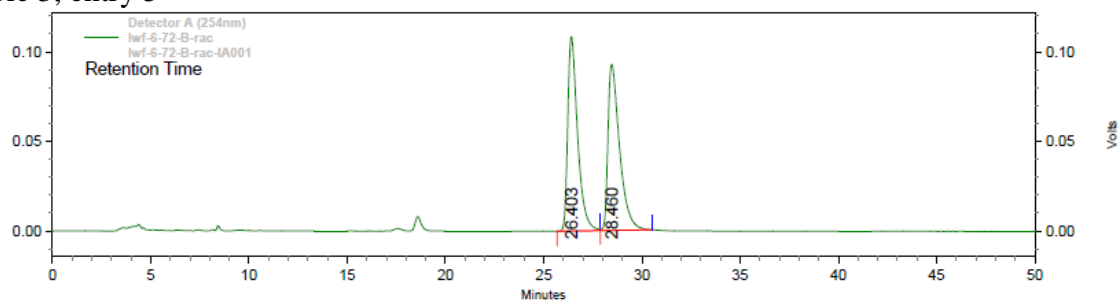


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	28.639	24601102	49.800	588481	52.793
2	30.842	24798285	50.200	526206	47.207

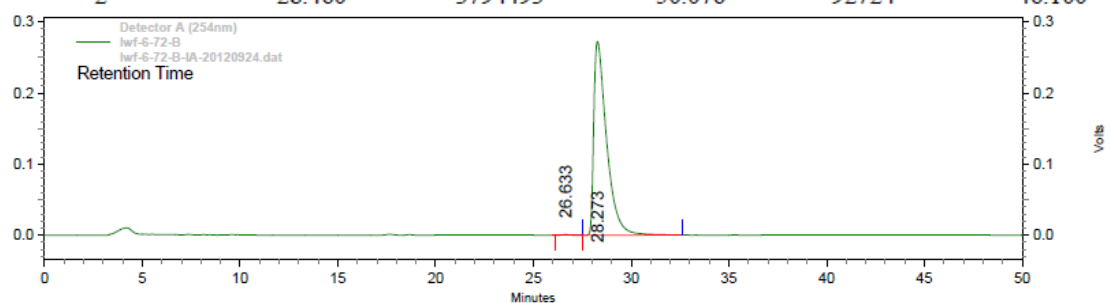


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	28.384	30165308	99.892	697743	99.865
2	31.094	32540	0.108	942	0.135

(4e) Table 3, entry 5

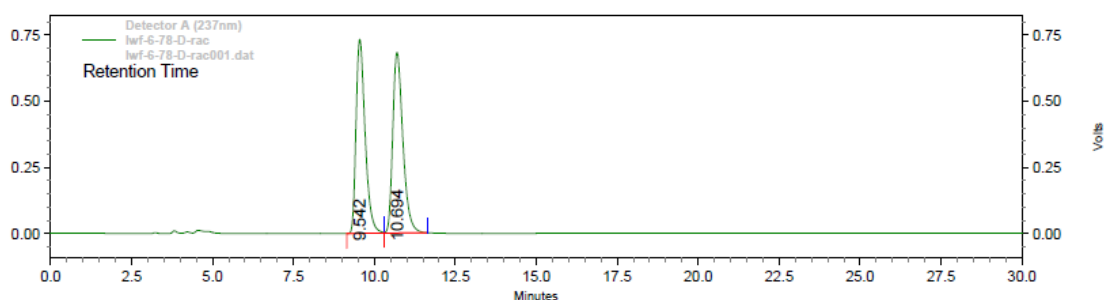


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	26.403	3782977	49.924	108412	53.900
2	28.460	3794493	50.076	92724	46.100



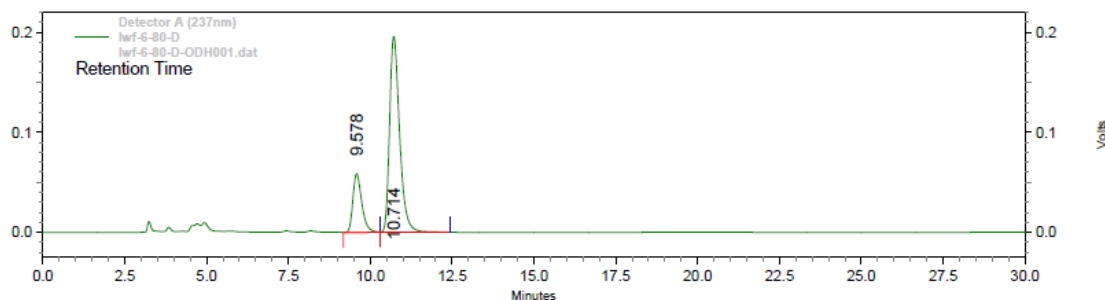
Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	26.633	24165	0.194	704	0.258
2	28.273	12419566	99.806	272534	99.742

(4f) Table 3, entry 6



Detector A (220nm)

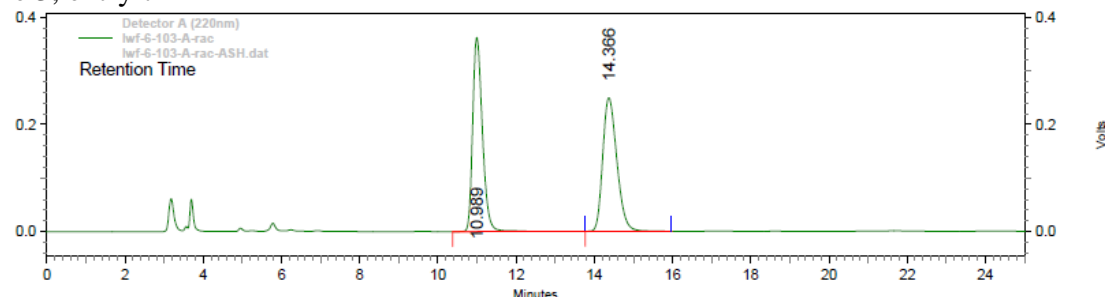
Pk #	Retention Time	Area	Area %	Height	Height %
1	9.542	14309517	49.038	733398	51.789
2	10.694	14871114	50.962	682729	48.211



Detector A (220nm)

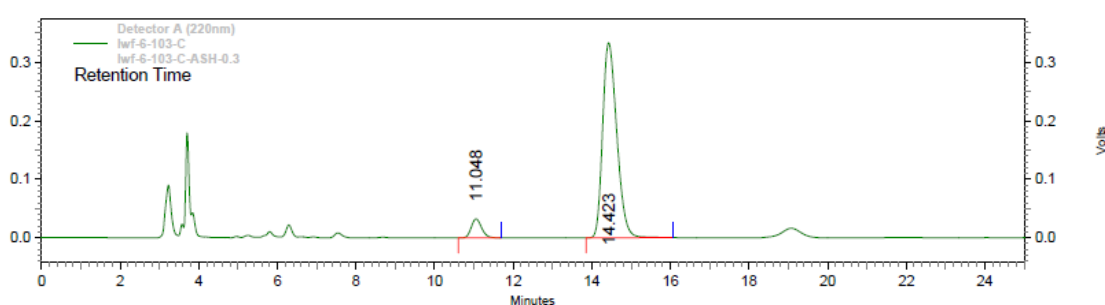
Pk #	Retention Time	Area	Area %	Height	Height %
1	9.578	1106037	20.994	58660	23.038
2	10.714	4162373	79.006	195966	76.962

(4g) Table 3, entry 7



Detector A (220nm)

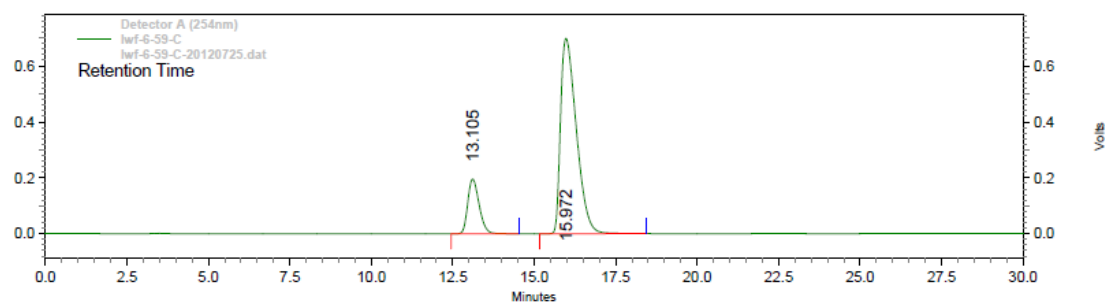
Pk #	Retention Time	Area	Area %	Height	Height %
1	10.989	6265651	50.011	361903	59.236
2	14.366	6262895	49.989	249052	40.764



Detector A (220nm)

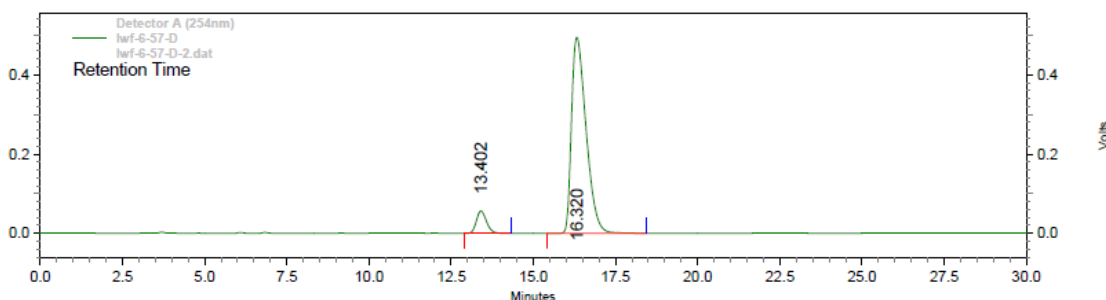
Pk #	Retention Time	Area	Area %	Height	Height %
1	11.048	594762	6.648	32455	8.870
2	14.423	8351708	93.352	333456	91.130

(4h) Table 3, entry 8



Detector A (220nm)

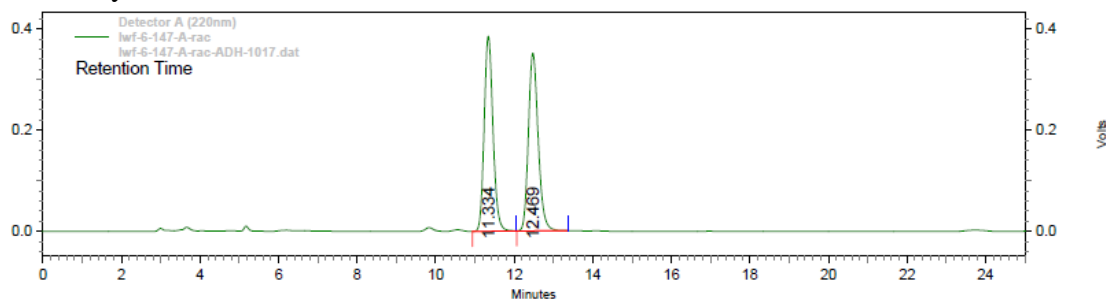
Pk #	Retention Time	Area	Area %	Height	Height %
1	13.105	4742732	16.825	195375	21.880
2	15.972	23445426	83.175	697563	78.120



Detector A (220nm)

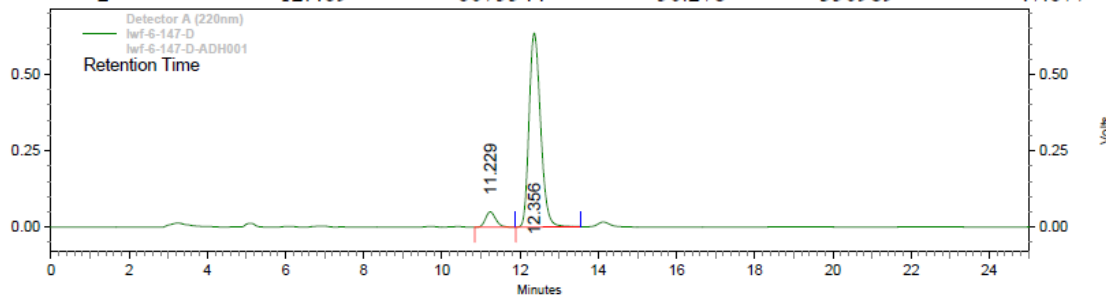
Pk #	Retention Time	Area	Area %	Height	Height %
1	13.402	1209300	7.348	56477	10.248
2	16.320	15248424	92.652	494607	89.752

(4i) Table 3, entry 9



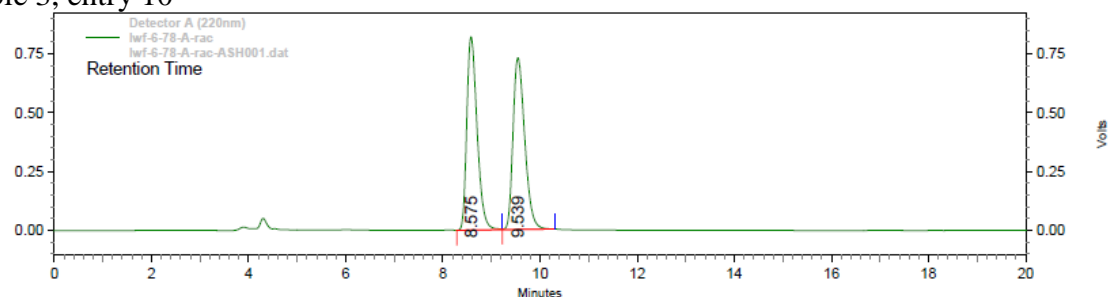
Detector A (220nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	11.334	6008279	49.722	385187	52.323
2	12.469	6075544	50.278	350989	47.677

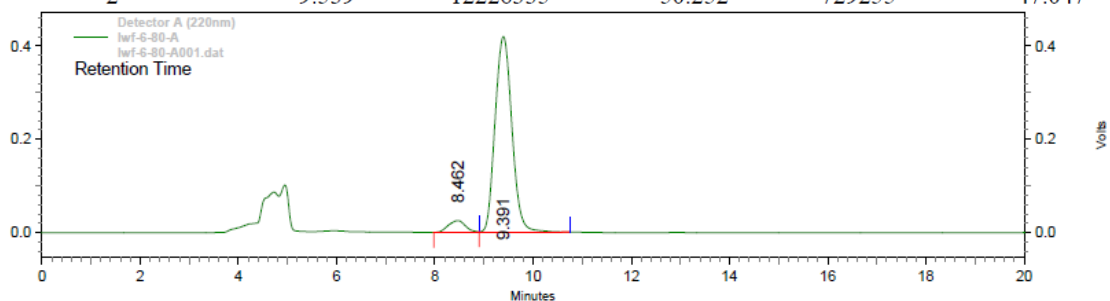


Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	11.229	912839	6.550	50105	7.302
2	12.356	13022587	93.450	636064	92.698

(4j) Table 3, entry 10



Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	8.575	12103533	49.748	820800	52.953
2	9.539	12226335	50.252	729255	47.047



Detector A (220nm)					
Pk #	Retention Time	Area	Area %	Height	Height %
1	8.462	618778	5.819	25420	5.713
2	9.391	10014896	94.181	419502	94.287