Supporting Information

Acid-Labile δ-Ketal-β-Hydroxy Esters by Asymmetric Hydrogenation of Corresponding δ-Ketal-β-Keto Esters in the Presence of $CaCO_3$†

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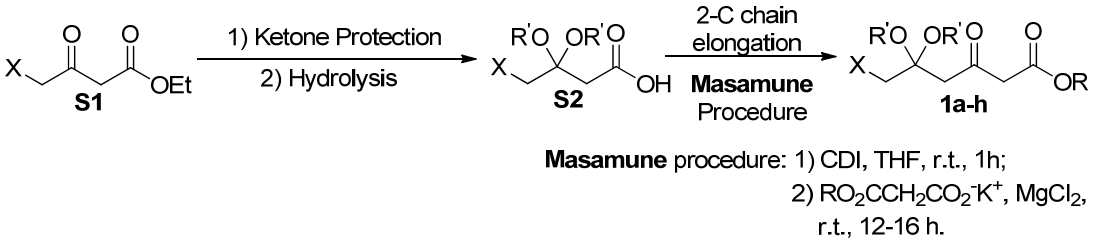
1. General method:

All reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques or in a nitrogen-filled glove box, unless otherwise noted. Commercially available reagents were used throughout without further purification other than those detailed below. Anhydrous MeOH and EtOH were freshly distilled from Mg. Anhydrous i-PrOH and CH_2Cl_2 were freshly distilled from calcium hydride. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. The chemical shifts for ^{1}H NMR were recorded in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. The chemical shifts for ^{13}C NMR were recorded in ppm downfield using the central peak of deuterochloroform (77.00 ppm) as the internal standard. Coupling constants (J) are reported in Hz and refer to apparent peak multiplications. HRMS were recorded on APEXII and ZAB-HS spectrometer. Flash column chromatography was performed on silica gel (300-400 mesh). $[\alpha]_D$ values are given in deg cm^2 g^{-1} and were recorded at the $_D$ line of sodium (589 nm) in a 0.05 dm cell.

2. Preparation of ε-substituted δ-ketal-β-keto esters:[1-2]

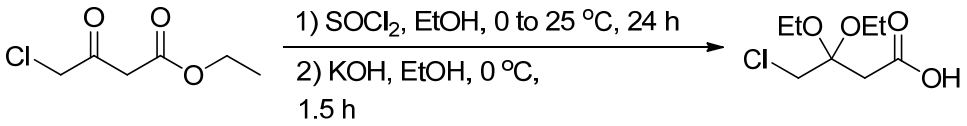
2.1 Synthesis of ε-substituted δ-ketal-β-keto esters 1a-h.



The synthesis of ε-substituted δ-ketal-β-keto esters **1a-h** was accomplished via a three-step sequence as shown above. Protection of carbonyl groups of β-keto esters **S1** with ethylene alcohol, methanol or ethanol in the presence of an acid as the catalyst produced different β-ketal esters,[3-4] which were hydrolyzed into their corresponding acids **S2**. The acids **S2** were further converted to ε-substituted δ-ketal-β-keto esters **1a-h** by Masamune procedure.

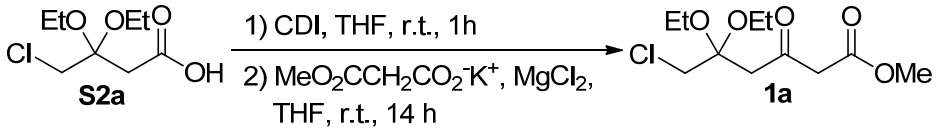
2.1.2 Typical synthetic procedures for preparation of methyl 6-chloro-5,5-diethoxy-3-oxohexanoate 1a

A. Synthesis of 4-chloro-3,3-diethoxybutanoic acid S2a



Under N_2 at 0 °C, $SOCl_2$ (15.2 g, 128 mmol) was dropwise added to anhydrous EtOH (30 mL) over 20 min, followed by ethyl 4-chloroacetoacetate (20.0 g, 122 mmol). The mixture was allowed to warm to RT and stirred for 24 h. After the removal of volatile materials under reduced pressure, 91 mL of 2 M potassium hydroxide (aq.) was added to the solution of the residue in EtOH (100 mL) at 0 °C and the mixture was stirred for 1.5 h at RT. The resultant reaction mixture was concentrated under reduced pressure, and the aqueous phase was washed with diethyl ether (30 mL x 2). The aqueous phase was acidified to pH = 3 with 2 M HCl (aq.), followed by extraction with CH_2Cl_2 (50 mL x 3). The combined organic phase was washed with saturated NaCl (aq.) (30 ml) and dried over Na_2SO_4, concentrated in vacuo to give crude 4-chloro-3,3-dimethoxybutanoic acid **S2a**, which was directly used in the subsequent reaction without further purification.

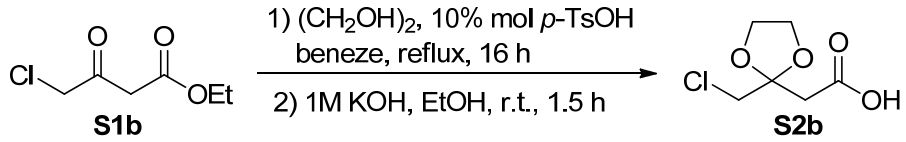
B. Preparation of methyl 6-Chloro-5,5-diethoxy-3-oxohexanoate 1a



To a solution of crude 4-chloro-3,3-diethoxybutanoic acid **S2a** (20.6 g, 98 mmol) in THF (100 mL)was added *N,N'*-carbonyldiimidazole (19.1 g, 118 mmol) and the resulting solution was stirred at RT for 1 h. Treatment of potassium monoethyl malonate (18.4 g, 118 mmol) with magnesium chloride (14.0 g, 147 mmol) at RT for 30 min, generated the dianion as its magnesium chelate. To this solution was added the imidazolide solution, and a gummy precipitate began to form immediately. After the resulting mixture was stirred at RT for 14 h, the reaction was poured into ice-cold 1 M HCl. Extraction with EtOAc (100 mL x 2) followed by washing the combined organics with saturated $NaHCO_3$ (50 mL x 2) and brine (50 mL) and drying over $MgSO_4$. Evaporation of the solvent gave the crude product, which was further purified by silica-gel column chromatography with petroleum ether and ethyl acetate (6:1) as eluent. Likewise, **1e** and **1f** were synthesized using the same procedure.

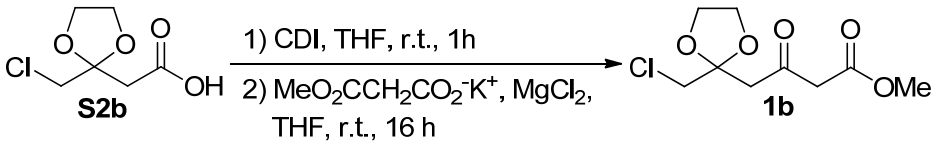
2.1.2 Typical synthetic procedures for preparation of methyl 4-(2-(chloromethyl)-1,3-dioxolan-2-yl)-3-oxobutanoate 1b

A. Preparation of 2-(2-(chloromethyl)-1,3-dioxolan-2-yl)acetic acid S2b



A mixture of ethyl 4-chloroacetoacetate (20.0 g, 122 mmol), ethylene glycol (11.3 g, 182 mmol) and tosylic acid (1.2 g, 6 mmol) in benzene (80 mL) was heated under reflux with a Dean-Stark apparatus for 16 hours to remove water. After the ethyl 4-chloroacetoacetate was completely consumed, benzene was evaporated under vacumm, followed by addition of saturated aqueous $NaHCO_3$ solution (30 mL), and then the reaction mixture was extracted with ethyl acetate (50 mL x 2). The ethyl acetate layer was washed with saturated aqueous solution of sodium chloride (30 mL), dried over anhydrous $MgSO_4$, concentrated in vacuum to give the crude product, which was dissolved in EtOH (100 mL), and to the solution was dropwise added 91 mL of 2 M potassium hydroxide (aq.). After stirring for 1.5 h at RT, the resultant reaction mixture was concentrated under reduced pressure, and the aqueous phase was washed with dimethyl ether (30 mL x 2). The aqueous phase was acidified to pH = 3 with 2 M HCl (aq.), followed by extraction with CH_2Cl_2 (50 mL x 3). The combined organic phase was washed with saturated NaCl (aq.) (30 ml) and dried over Na_2SO_4, concentrated in vacuo to give the 2-(2-(chloromethyl)-1,3-dioxolan-2-yl)acetic acid **S2b**, which was directly used in the subsequent reaction without further purification.

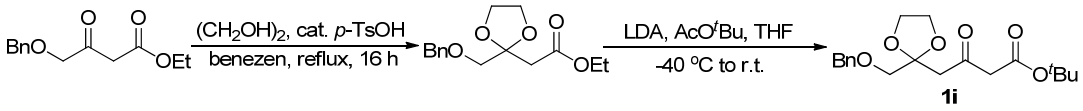
B. Preparation of methyl 4-(2-(chloromethyl)-1,3-dioxolan-2-yl)-3-oxobutanoate 1b



To a solution of crude 2-(2-(chloromethyl)-1,3-dioxolan-2-yl)acetic acid **S2b** (17.6 g, 97 mmol) in THF (80 mL)was added *N,N'*-carbonyldiimidazole (19.0 g, 117 mmol) and the resulting solution was stirred at RT for 1 h. Treatment of potassium monoethyl malonate (18.3 g, 117 mmol) with magnesium chloride (13.9 g, 146 mmol) at RT for 30 min, generated the dianion as its magnesium chelate. To this solution was added the imidazolide solution, and a gummy precipitate began to form immediately. After the resulting mixture was stirred at RT for 16 h, the reaction was poured into ice-cold 1 M HCl. Extraction with EtOAc (100 mL x 2) followed by washing the combined organics with saturated $NaHCO_3$ (50 mL x 2) and brine (50 mL) and drying over $MgSO_4$. Evaporation of the solvent gave the crude product, which was purified by silica-gel column chromatography using petroleum ether and ethyl acetate (10/1 - 5/1) as the eluent.

Likewise, **1c**, **1d** and **1g-1i** were synthesized as the same procedure.

2.1.3 Preparation of *tert*-butyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-oxobutanoate 1i[1]



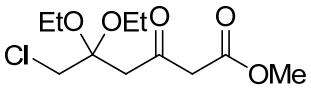
A. Synthesis of ethyl 2-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)acetate

A mixture of ethyl 4-(benzyloxy)-3-oxobutanoate (5.0 g, 21 mmol), ethylene glycol (2.0 g, 32 mmol) and tosylic acid (182 mg, 1 mmol) in benzene (50 mL) was heated under reflux under Dean-Stark apparatus for 16 hours. After the ethyl 4-(benzyloxy)-3-oxobutanoate was completely consumed, benzene was evaporated under vacumm, followed by addition of saturated aqueous $NaHCO_3$ solution (20 mL), and then the reaction mixture was extracted with ethyl acetate (50 mL x 2). The ethyl acetate layer was washed with saturated aqueous solution of sodium chloride (30 mL), dried over anhydrous $MgSO_4$, concentrated in vacuum to give the crude ethyl 2-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)acetate, which was directly used in the subsequent reaction without further purification.

B. Synthesis of *tert*-butyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-oxobutanoate 1i

A 2.4 M solution of *n*-BuLi (30 mL, 71 mmol) was added at –10 °C within 10 min to a solution of *i*Pr_2NH (7.4 g, 73 mmol) in THF (100 mL). The resulting mixture was stirred 10 min at 0 °C, and *tert*-butyl acetate (7.1 g, 61 mmol) was added dropwise within 20 min at –40 °C. A solution of crude ethyl 2-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)acetate (5.7 g, 20 mmol) in THF (30 mL) was added dropwise within 20 min at –40 °C, and the mixture was stirred for 40 min at –40 °C. After completion of the reaction, saturated NH_4Cl (aq.) (50 mL) was added to the reaction mixture (without cooling) within 10 min, leading to an inner temperature of 0 °C. The mixture was concentrated via rotary evaporation and diluted with EtOAc (50 mL), the layers were separated and the aqueous layer was extracted with EtOAc (40 mL x 2) and the combined organic layers were washed with sat. NaCl (aq.) (80 mL) and dried over anhydrous Na_2SO_4, followed concentrated *in vacuo*. The residue was purified by silica gel chromatography with petroleum ether and ethyl acetate (7:1) as eluent.

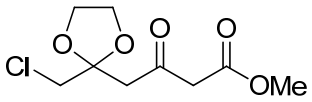
Methyl 6-chloro-5,5-diethoxy-3-oxohexanoate, 1a



White solid, 62% yield (from ethyl 4-chloroacetoacetate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.08 (s, 0.70H), 5.16 (s, 0.81H), 3.74 (s, 3H), 3.65 (s, 2H),

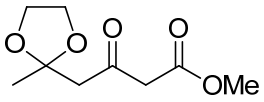
3.63 – 3.50 (m, 4H), 2.74 (s, 2H), 1.20 (t, J = 7.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 173.0, 172.7, 167.4, 100.4, 99.9, 91.7, 56.4, 52.1, 51.1, 49.9, 45.4, 44.2, 43.5, 37.8, 14.84, 14.78. HRMS-ESI (m/z): Calculated for $[C_{11}H_{19}ClO_5Na]^+$: 289.0813, found: 289.0823.

Methyl 4-(2-(chloromethyl)-1,3-dioxolan-2-yl)-3-oxobutanoate, 1b



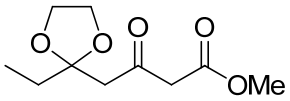
Colorless oil, 63% yield (from ethyl 4-chloroacetoacetate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.08 (s, 0.12H), 5.15 (s, 0.15H), 4.08 – 4.04 (m, 4H), 3.75 (s, 3H), 3.62 (s, 2H), 3.56 (s, 2H), 3.08 (s, 2H), 2.70 (s, 0.36H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 167.2, 107.4, 92.3, 65.8, 65.6, 52.2, 51.1, 50.3, 47.4, 46.9, 46.6, 41.4. HRMS-ESI (M/Z)-ESI (m/z): Calculated for $[C_9H_{13}ClO_5Na]^+$: 259.0344, found: 259.0356.

Ethyl 4-(2-Methyl 4-(2-methyl-1,3-dioxolan-2-yl)-3-oxobutanoate, 1c



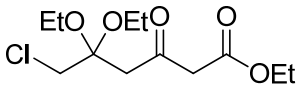
Colorless oil, 48% yield (from methyl 3-oxobutanoate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.05 (s, 0.11H), 5.11 (s, 0.10H), 3.99 – 3.97 (m, 4H), 3.74 (s, 3H), 3.58 (s, 2H), 2.89 (s, 2H), 2.53 (s, 0.28H), 1.44 (s, 0.54H), 1.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 173.3, 167.6, 107.6, 91.7, 64.7, 64.5, 52.2, 51.6, 51.1, 50.0, 44.5, 24.4, 24.2. HRMS-ESI (m/z): Calculated for $[C_9H_{14}O_5Na]^+$: 225.0733, found: 225.0744.

Methyl 4-(2-ethyl-1,3-dioxolan-2-yl)-3-oxobutanoate, 1d



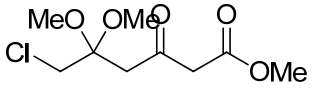
Pale yellow oil, 48% yield (from methyl 3-oxobutanoate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.05 (s, 0.11H), 5.10 (s, 0.10H), 4.02 – 3.94 (m, 4H), 3.73 (s, 2H), 3.59 (s, 2H), 2.86 (s, 2H), 2.51 (s, 0.28H), 1.71 (q, J = 7.4 Hz, 2H), 0.92 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 167.5, 110.1, 109.7, 91.5, 65.0, 64.8, 52.0, 50.9, 49.9, 49.4, 42.5, 30.6, 30.3, 7.6. HRMS-ESI (m/z): Calculated for $[C_{17}H_{22}O_6Na]^+$: 239.0895, found: 239.0875.

Ethyl 6-chloro-5,5-diethoxy-3-oxohexanoate, 1e



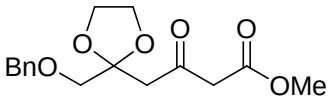
White solid, 60% yield (from ethyl 4-chloroacetoacetate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.18 (s, 0.27H), 5.15 (s, 0.27H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.72 (s, 1.46H), 3.65 (s, 0.62H), 3.64 – 3.56 (m, 1H), 3.55 – 3.47 (m, 5H), 3.09 (s, 1.50H), 2.73 (s, 0.62H), 1.31 – 1.27 (m, 3H), 1.22 – 1.18 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 172.9, 172.4, 167.0, 100.5, 99.9, 92.1, 61.3, 60.1, 56.4, 50.3, 45.4, 44.3, 43.5, 37.8, 14.92, 14.87, 14.1, 14.0. HRMS-ESI (m/z): Calculated for $[C_{12}H_{21}ClO_5Na]^+$: 303.0970, found: 303.0981.

Methyl 6-chloro-5,5-dimethoxy-3-oxohexanoate, 1f



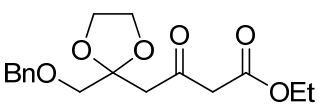
Colorless oil, 56% yield (from ethyl 4-chloroacetoacetate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.10 (s, 0.16H), 5.17 (s, 0.17H), 3.74 (s, 3H), 3.72 (s, 1.58H), 3.64 (s, 0.44H), 3.55 (s, 1.42H), 3.29 (s, 1.35H), 3.25 (s, 4.64H), 3.07 (s, 1.59H), 2.72 (s, .43H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 172.7, 167.4, 100.3, 92.0, 52.3, 51.2, 50.1, 48.7, 48.6, 44.4, 43.4, 42.8, 37.1. HRMS-ESI (M/Z): Calculated for $[C_9H_{15}ClO_5Na]^+$: 261.0500, found: 261.0509.

Methyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-oxobutanoate, 1g



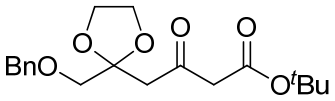
Colorless oil, 54% yield (from ethyl 4-(benzyloxy)-3-oxobutanoate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.05 (s, 0.09H), 7.36 – 7.26 (m, 5H), 5.12 (s, 0.12H), 4.61 (s, 0.37H), 4.57 (s, 2H), 4.03 – 3.96 (m, 4H), 3.73 (s, 0.38H), 3.72 (s, 3H), 3.67 (s, 0.10H), 3.58 (s, 2H), 3.50 (s, 0.29H), 3.47 (s, 2H), 2.98 (s, 2H), 2.66 (s, 0.29H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 167.6, 137.6, 128.3, 127.6 (2C), 108.4, 107.9, 91.9, 73.5, 72.1, 72.0, 65.4, 65.2, 52.1, 51.1, 50.2, 48.1, 40.8. HRMS-ESI (m/z): Calculated for $[C_{16}H_{20}O_6Na]^+$: 331.1158, found: 331.1131.

Ethyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-oxobutanoate, 1h



Colorless oil, 57% yield (from ethyl 4-(benzyloxy)-3-oxobutanoate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.14 (s, 0.09H), 7.66 – 7.27 (m, 5H), 5.10 (s, 0.10H), 4.61 (d, *J* = 2.7 Hz, 0.42H), 4.57 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.03 – 3.96 (m, 4H), 3.58 (s, 0.17H), 3.56 (s, 1.39H), 3.50 (s, 0.26H), 3.47 (s, 1.58H), 2.98 (s, 1.56H), 2.80 (s, 0.15H), 2.65 (s, 0.24H), 1.26 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.7, 167.3, 137.7, 128.3, 127.7 (2C), 108.0, 92.3, 73.5, 72.2, 72.0, 65.4, 65.2, 61.2, 50.5, 48.1, 40.9, 14.1. HRMS-ESI (m/z): Calculated for $[C_{17}H_{22}O_6Na]^+$: 345.1314, found: 345.1303.

***tert*-Butyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-oxobutanoate, 1i**

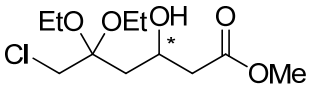


Pale yellow oil, 86% yield (from ethyl 4-(benzyloxy)-3-oxobutanoate). Mixture of keto and enol forms: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.27 (s, 0.08H), 7.37 – 7.27 (m, 5H), 5.00 (s, 0.08H), 4.61 (s, 0.23H), 4.57 (s, 2H), 4.01 – 3.98 (m, 4H), 3.48 (s, 2H), 3.46 (s, 2H), 2.97 (s, 2H), 2.61 (s, 0.18H), 1.49 (s, 0.85H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 166.4, 137.6, 128.2, 127.6 (2C), 107.9, 93.6, 81.6, 73.4, 72.0, 65.3, 65.1, 51.7, 47.7, 40.9, 28.1, 27.8. HRMS-ESI (m/z): Calculated for $[C_{19}H_{26}O_6Na]^+$: 373.1622, found: 373.1636.

3. Typical procedure for asymmetric hydrogenation

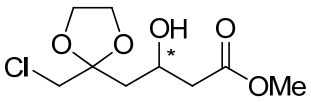
General procedure (substrate/catalyst = 250/1): To a 20 mL Schlenk tube were added $[Ru(benzene)Cl_2]_2$ (10 mg, 0.020 mmol) and (*S*)-SunPhos (30 mg, 0.044 mmol). The tube was vacuumed and purged with nitrogen three times before addition of freshly distilled and degassed EtOH / DCM (3 mL / 3 mL). The resulting mixture was heated at 50 °C for 1 h and then cooled to RT. The solvent was removed under vacuum to give the catalyst. This catalyst was dissolved in degassed ethanol (10 mL), and distributed equally to four vials. The β-keto esters (1.25 mmol) and $CaCO_3$ (12 mg) were added to these vials, respectively, and were transferred to an autoclave. The autoclave was purged with H_2 three times, and the pressure of H_2 was set to 60 bar. Then the autoclave was stirred for 4.5 h, and the autoclave was then cooled to RT and the H_2 was carefully released. The autoclave was opened and the ethanol was evaporated. The enantiomeric excess was determined by HPLC after passing the residue through a short pad of silica gel column with petroleum ether and ethyl acetate.

Methyl 6-chloro-5,5-diethoxy-3-hydroxyhexanoate, 2a



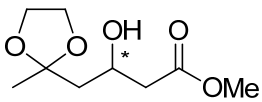
Colorless oil, 97% yield, 99.2% ee, $[\alpha]_D^{20}$ = +11.3 (*c* = 0.97 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.33 – 4.26 (m, 1H), 3.78 (d, *J* = 11.8 Hz, 1H), 3.72 (s, 3H), 3.62 – 3.47 (m, 6H), 2.57 – 2.45 (m, 2H), 2.09 (dd, *J* = 14.9, 9.9 Hz, 1H), 1.93 (dd, *J* = 14.9, 2.1 Hz, 1H), 1.22 – 1.18 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 101.3, 64.5, 56.3, 56.2, 51.6, 44.6, 41.8, 38.6, 15.0. HRMS-ESI (m/z): Calculated for $[C_{11}H_{21}O_5ClNa]^+$: 291.0975, found: 291.0956. The enantiomeric excess was determined via its corresponding 4-chlorobenezenthiol substituted derivative **4a** (deprotection of **2a** and then substituted with 4-chlorobenezethiol) by HPLC on chiralcel OB-H column, hexane: isopropanol = 60:40, flow rate = 0.7 mL/min, UV detection at 254 nm, t_R = 23.9 min (minor), 26.1 min (major).

Methyl 4-(2-(chloromethyl)-1,3-dioxolan-2-yl)-3-hydroxybutanoate, 2b



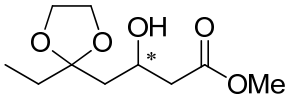
Colorless oil, 95% yield, 99.7% *ee*, $[\alpha]_D^{20}$ = +2.1 (*c* = 0.77 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.37 – 4.30 (m, 1H), 4.11 – 4.07 (m, 4H), 3.71 (s, 3H), 3.57 (d, *J* = 1.6 Hz, 2H), 3.36 (d, *J* = 2.3 Hz, 1H), 2.57 – 2.46 (m, 2H), 2.04 – 2.03 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 108.9, 65.5, 65.3, 64.2, 51.6, 46.5, 41.5, 40.8. HRMS-ESI (m/z): Calculated for $[C_9H_{16}O_5ClNa]^+$: 239.0686, found: 239.0683. The enantiomeric excess was determined via its corresponding 4-nitrobenzoate **3b** by HPLC on chiralcel AD-H column, hexane: isopropanol = 75:25, flow rate = 0.6 mL/min, UV detection at 254 nm, t_R = 42.5 min (major), 46.3 min (minor).

Methyl 3-hydroxy-4-(2-methyl-1,3-dioxolan-2-yl)butanoate, 2c



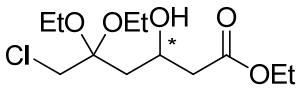
Colorless oil, 79% yield, 99.3% ee, $[\alpha]_D^{20}$ = +4.4 (*c* = 1.08 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): 4.38 – 4.34 (m, 1H), 4.03 – 3.98 (m, 4H), 3.78 – 3.66 (m, 4H), 2.57 – 2.43 (m, 2H), 1.92 – 1.85 (m, 2H), 1.43 – 1.36 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 172.0, 109.6, 64.8, 64.4, 64.1, 51.5, 44.2, 41.6, 23.9. HRMS-ESI (m/z): Calculated for $[C_9H_{16}O_5ClNa]^+$: 227.0895, found: 227.0879. The enantiomeric excess was determined via its corresponding *p*-nitrobenzoate **4c** by HPLC on chiralcel OD-H column, hexane: isopropanol = 85:15, flow rate = 0.6 mL/min, UV detection at 254 nm, t_R = 32.7 min (minor), 36.2 min (major).

Methyl 4-(2-ethyl-1,3-dioxolan-2-yl)-3-hydroxybutanoate, 2d



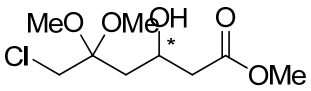
Colorless oil, 81% yield, 99.5% ee, $[\alpha]_D^{20}$ = +5.2 (*c* = 1.19 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.36 – 4.29 (m, 1H), 4.04 – 3.95 (m, 4H), 3.73 (s, 1H), 3.71 (s, 3H), 2.56 – 2.42 (m, 2H), 1.90 – 1.79 (m, 2H), 1.73 – 1.66 (m, 2H), 0.92 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 111.7, 64.6, 64.4, 51.4, 41.7, 41.5, 29.8, 7.8. HRMS-ESI (m/z): Calculated for $[C_{10}H_{18}O_5ClNa]^+$: 241.1052, found: 241.1022. The enantiomeric excess was determined via its corresponding *p*-nitrobenzoate **4d** by HPLC on chiralcel AS-H column, hexane: isopropanol = 80:20, flow rate = 0.55 mL/min, UV detection at 254 nm, t_R = 23.8 min (major), 26.5 min (minor).

Ethyl 6-chloro-5,5-diethoxy-3-hydroxyhexanoate, 2e



Colorless oil, 95% yield, 99.4% ee, $[\alpha]_D^{20}$ = +10.0 (*c* = 1.16 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.31 – 4.25 (m, 1H), 4.21 – 4.13 (m, 2H), 3.80 (d, *J* = 11.9 Hz, 1H), 3.63 – 3.46 (m, 6H), 2.56 – 2.43 (m, 2H), 2.09 (dd, *J* = 15.0, 9.9 Hz, 1H), 1.92 (dd, *J* = 15.0, 2.2 Hz, 1H), 1.29 – 1.18 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 101.2, 64.5, 60.5, 56.3, 56.2, 44.6, 42.1, 38.6, 15.0, 14.0. HRMS-ESI (m/z): Calculated for $[C_{12}H_{23}O_5ClNa]^+$: 305.1132, found: 305.1095. The enantiomeric excess was determined via its corresponding 4-chlorobenezenthiol substituted derivative **4e** (deprotection of **2e** and then substituted with 4-chlorobenezethiol) by HPLC on chiralcel OB-H column, hexane: isopropanol = 65:35, flow rate = 0.6 mL/min, UV detection at 254 nm, t_R = 19.8 min (minor), 23.4 min (major).

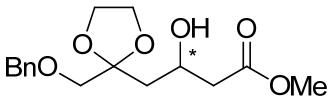
Methyl 6-chloro-3-hydroxy-5,5-dimethoxyhexanoate, 2f



Colorless oil, 91% yield, 99.2% ee, $[\alpha]_D^{20}$ = +11.6 (*c* = 1.02 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (m, 1H), 3.79 (d, *J* = 12.0 Hz, 1H), 3.72 (s, 3H), 3.59 (d, *J* = 12.0 Hz, 1H), 3.30 (d, *J* = 2.9 Hz, 1H), 3.28 (s, 3H), 3.25 (s, 3H), 2.58 – 2.46 (m, 2H), 2.08 (dd, *J* = 15.1, 9.9 Hz, 1H), 1.90 (dd, *J* = 15.1, 2.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 101.4, 64.3, 51.6, 48.4, 43.7, 41.8, 37.6. HRMS-ESI (m/z): Calculated for $[C_9H_{17}O_5ClNa]^+$: 263.0662, found: 263.0638. The enantiomeric excess was determined via its corresponding 4-

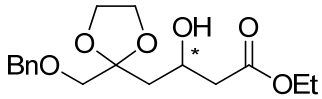
chlorobenezenthiol substituted derivative **4f** (deprotection of **2f** and then substituted with 4-chlorobenezethiol) by HPLC on chiralcel OB-H column, hexane: isopropanol = 60:40, flow rate = 0.7 mL/min, UV detection at 254 nm, t_R = 21.7 min (minor), 25.0 min (major).

Methyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-hydroxybutanoate, 2g



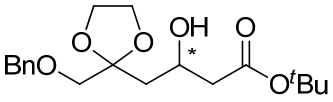
Colorless oil, 93% yield, 99.2% ee, $[\alpha]_D^{20}$ = +0.7 (*c* = 1.07 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.25 (m, 5H), 4.63 – 4.56 (m, 2H), 4.38 – 4.32 (m, 1H), 4.05 – 4.00 (m, 1H), 3.70 (s, 3H), 3.59 (d, *J* = 1.5 Hz, 1H), 3.48 – 3.41 (m, 2H), 2.56 – 2.48 (m, 2H), 2.02 – 1.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 137.7, 128.3, 127.7, 127.6, 109.6, 73.5, 71.9, 65.3, 65.0, 64.5, 51.6, 41.9, 40.9. HRMS-ESI (m/z): Calculated for $[C_{16}H_{22}O_6ClNa]^+$: 333.1314, found: 333.1292. The enantiomeric excess was determined by HPLC on chiralpak IB-3 column, hexane: isopropanol = 80:20, flow rate = 0.5 mL/min, UV detection at 215 nm, t_R = 21.6 min (minor), 23.5 min (major).

Ethyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-hydroxybutanoate, 2h



Colorless oil, 91% yield, 99.2% ee, $[\alpha]_D^{20}$ = +1.2 (*c* = 0.57 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H), 4.63 – 4.56 (m, 2H), 4.38 – 4.31 (m, 1H), 4.16 (qd, *J* = 7.1, 1.4 Hz, 2H), 4.05 – 4.01 (m, 4H), 3.59 (d, *J* = 1.8 Hz, 1H), 3.48 – 3.42 (m, 2H), 2.54 – 2.42 (m, 2H), 2.02 – 1.92 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 137.7, 128.3, 127.7, 127.6, 109.6, 73.5, 72.0, 65.3, 65.1, 64.5, 60.5, 42.1, 40.9, 14.1. HRMS-ESI (m/z): Calculated for $[C_{17}H_{24}O_6ClNa]^+$: 347.1471, found: 347.1464. The enantiomeric excess was determined by HPLC on chiralpak IB-3 column, hexane: isopropanol = 90:10, flow rate = 0.5 mL/min, UV detection at 215 nm, t_R = 34.5 min (minor), 37.8 min (major).

***tert*-Butyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-hydroxybutanoate, 2i**

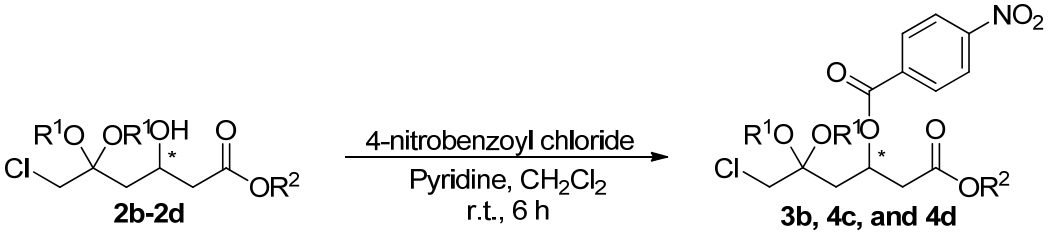


Colorless oil, 95% yield, 99.6% ee, $[\alpha]_D^{20}$ = +1.6 (*c* = 0.94 CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 4.63 – 4.56 (m, 2H), 4.29 – 4.26 (m, 1H), 4.05 – 4.00 (m, 4H), 3.57 (d, *J* = 1.8 Hz, 1H), 3.46 (q, *J* = 10.6 Hz, 2H), 2.47 – 2.33 (m, 2H), 1.99 – 1.90 (m, 2H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 137.8, 128.3, 127.6, 127.6, 109.6, 80.7,

73.5, 72.1, 65.3, 65.1, 64.6, 43.1, 40.9, 28.0. HRMS-ESI (m/z): Calculated for $[C_9H_{28}O_6ClNa]^+$: 375.1784, found: 375.1761. The enantiomeric excess was determined by HPLC on chiralcel OJ-H column, hexane: isopropanol = 95:5, flow rate = 0.6 mL/min, UV detection at 215 nm, t_R = 54.4 min (major), 64.8 min (minor).

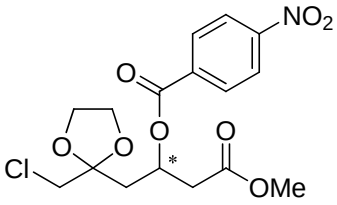
4. Preparation of the Corresponding Derivatives of 2a-f

4.2 Typical procedure for the preparation of the *p*-nitrobenzoates 3b, 4c, and 4d



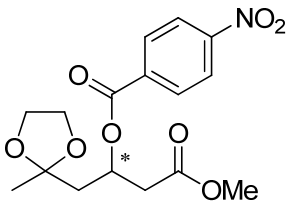
A 25 mL round flask was charged with **2b** (1 mmol), pyridine (0.4 mL, 5 mmol), 4-nitrobenzoyl chloride (278 mg, 1.5 mmol), DMAP (6 mg) and CH_2Cl_2 (10 mL). The mixture was stirred at 25-30 °C for 6 hours, saturated aqueous $NaHCO_3$ solution (5 mL) was added and the organic layer was separated. The organic layer was washed with 1M aqueous hydrochloric acid, saturated aqueous $NaHCO_3$ solution and brine. The washed organic solution was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to obtain the crude product, which was purified by column chromatography with petroleum ether and ethyl acetate (3:1) as eluent.

1-(2-(Chloromethyl)-1,3-dioxolan-2-yl)-4-methoxy-4-oxobutan-2-yl 4-nitrobenzoate, 3b



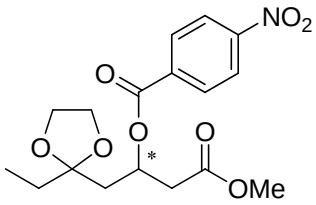
Yellow oil, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 – 8.18 (m, 4H), 5.77 – 5.71 (m, 1H), 4.07 – 3.96 (m, 4H), 3.68 (s, 3H), 3.51 (q, *J* = 11.8 Hz, 2H), 2.88 – 2.77 (m, 2H), 2.48 (dd, *J* = 15.2, 7.4 Hz, 1H), 2.29 (dd, *J* = 15.2, 4.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 163.8, 150.5, 135.5, 130.7, 123.5, 108.1, 67.8, 65.50, 65.46, 51.9, 46.4, 39.6, 38.4. HRMS-ESI (m/z): Calculated for $[C_{16}H_{18}NO_8ClNa]^+$: 410.0619, found: 410.0615.

4-Methoxy-1-(2-methyl-1,3-dioxolan-2-yl)-4-oxobutan-2-yl 4-nitrobenzoate, 4c



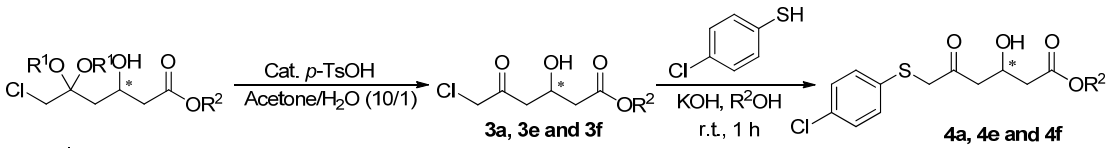
Yellow oil, 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 – 8.18 (m, 4H), 5.75 – 5.69 (m, 1H), 3.97 – 3.89 (m, 4H), 3.67 (s, 3H), 2.88 (dd, *J* = 15.8, 5.1 Hz, 1H), 2.78 (dd, *J* = 15.8, 7.4 Hz, 1H), 2.27 (dd, *J* = 14.8, 6.8 Hz, 1H), 2.11 (dd, *J* = 14.8, 5.2 Hz, 1H), 1.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 163.7, 150.3, 135.6, 130.6, 123.4, 108.1, 68.6, 64.3, 51.7, 42.0, 39.4, 24.1. HRMS-ESI (m/z): Calculated for $[C_{16}H_{19}NO_8Na]^+$: 376.1008, found: 376.1014.

1-(2-Ethyl-1,3-dioxolan-2-yl)-4-methoxy-4-oxobutan-2-yl 4-nitrobenzoate , 4d



Yellow oil, 68% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.17 (m, 4H), 5.72 – 5.65 (m, 1H), 3.99 – 3.89 (m, 4H), 3.67 (s, 3H), 2.89 (dd, *J* = 15.8, 5.0 Hz, 1H), 2.77 (dd, *J* = 15.8, 7.4 Hz, 1H), 2.24 (dd, *J* = 14.8, 6.6 Hz, 1H), 2.07 (dd, *J* = 14.8, 5.5 Hz, 1H), 1.69 (q, *J* = 7.5 Hz, 2H), 0.93 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 163.8, 150.5, 135.8, 130.7, 123.5, 110.4, 68.8, 64.85, 64.80, 51.8, 39.8, 39.6, 30.3, 8.0. HRMS-ESI (m/z): Calculated for $[C_{17}H_{21}NO_8Na]^+$: 390.1165, found: 390.1140.

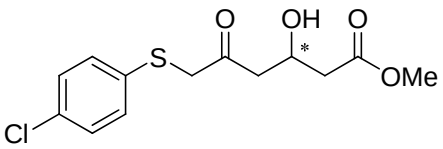
4.2 Typical procedure for the preparation of 4-chlorobenezethiol substited derivatives 4a, 4e and 4f



2a, R' = Et, R = Me
2e, R' = Et, R = Et
2f, R' = R = Me

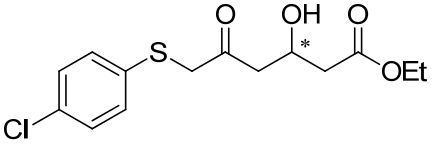
To the solution of **2a** (0.5 mmol) in acetone (2.0 mL) and H_2O (0.2 mL) was added 10% mol of *p*-TsOH, and the resulting solution was stirred for 2 h at 35°C. After **2a** was completely consumed, $NaHCO_3$ (0.1 mmol) was added and the mixture was stirred for 10 min at RT. The resultant was concentrated under reduced pressure and the residue was dissolved in MeOH (10 mL), and then 4-chlorobenezethiol (0.6 mmol) and potassium hydroxide (0.5 mmol) were added. The resulting mixture was stirred for 1 h at RT. After completion of the reaction, MeOH was removed under reduced pressure to give the crude product **4a**, which was purified by column chromatography with petroleum ether and ethyl acetate (2:1) as eluent.

Methyl 6-((4-chlorophenyl)thio)-3-hydroxy-5-oxohexanoate, 4a and 4f



Colorless oil, 86% yield from **2a** and **2e**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 4H), 4.49 – 4.42 (m, 1H), 3.71 (s, 3H), 3.69 (d, *J* = 1.5 Hz, 2H), 3.28 (d, *J* = 3.9 Hz, 1H), 2.90 – 2.76 (m, 2H), 2.51 (d, *J* = 6.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 172.2, 133.1, 132.7, 131.1, 129.3, 64.4, 51.8, 46.1, 44.5, 40.3. HRMS-ESI (m/z): Calculated for $[C_{13}H_{15}SO_4ClNa]^+$: 325.0277, found: 325.0262.

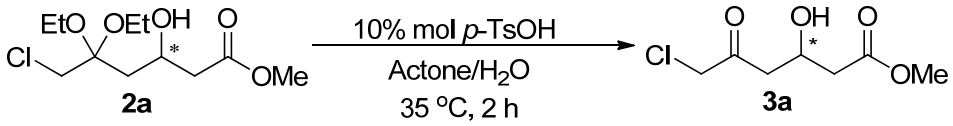
Ethyl 6-((4-chlorophenyl)thio)-3-hydroxy-5-oxohexanoate, 4e:



White solid, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.25 (m, 4H), 4.49 – 4.42 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.73 – 3.65 (m, 2H), 3.35 (d, *J* = 3.9 Hz, 1H), 2.90 – 2.76 (m, 2H), 2.49 (d, *J* = 6.3 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.1, 171.8, 133.0, 132.7, 131.0, 129.2, 64.4, 60.7, 46.2, 44.5, 40.5, 14.0. HRMS-ESI (m/z): Calculated for $[C_{14}H_{17}SO_4ClNa]^+$: 339.0434, found: 339.0414.

5. Synthesis of δ-keto-β-hydroxy esters

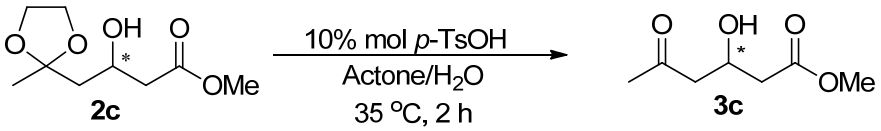
5.1 Synthesis of 6-chloro-3-hydroxy-5-oxohexanoate 3a



To the solution of methyl 6-chloro-5,5-diethoxy-3-hydroxyhexanoate (500 mg, 1.9 mmol) in acetone (3.0 mL) and H_2O (0.3 mL) was added 10% mol *p*-TsOH (32 mg), and the resulting solution was stirred for 2 h at 35 °C. After methyl 6-chloro-5,5-diethoxy-3-hydroxyhexanoate was completely consumed, $NaHCO_3$ (32 mg) was added and the mixture was stirred for 10 min at RT. The resultant was concentrated under reduced pressure and the residue was diluted with ethyl acetate (20 mL) and water (5 mL), the aqueous was extracted with ethyl acetate (10 mL x 3) and the combined organic phase was dried over anhydrous $MgSO_4$, concentrated in vacumm. The residue was purified by silica-gel column chromatography with petroleum ether and ethyl acetate (2:1) as eluent to give methyl 6-chloro-3-hydroxy-5-oxohexanoate **3a** (349 mg, 96%) as white solid. $[\alpha]_D^{20}$ = –11.1 (*c* = 0.93

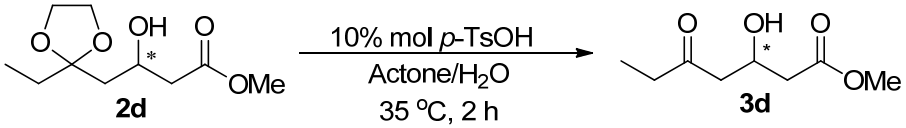
CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.55 – 4.48 (m, 1H), 4.15 (s, 2H), 3.73 (s, 3H), 3.31 (d, *J* = 4.0 Hz, 1H), 2.89 – 2.76 (m, 2H), 2.60 – 2.51 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5, 172.1, 64.1, 51.8, 48.8, 45.6, 40.4. HRMS-ESI (m/z): Calculated for $[C_7H_{11}O_4ClNa]^+$: 217.0244, found: 217.0245.

5.2 Synthesis of methyl 3-hydroxy-5-oxohexanoate 3c[5]



The methyl 3-hydroxy-5-oxohexanoate **3c** was prepared as synthetic procedure for **3a**. Colorless oil, 93% yield. $[\alpha]_D^{20}$ = –16.6 (*c* = 1.04 in $CHCl_3$) ($[\alpha]_D^{20}$ = –10.0 (*c* = 1.1 in $CHCl_3$), 75% *ee* (*S*)[6]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52 – 4.45 (m, 1H), 3.72 (s, 3H), 3.43 (d, *J* = 3.6 Hz, 1H), 2.70 – 2.69 (m, 2H), 2.54 – 2.52 (m, 2H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1, 172.0, 64.0, 51.6, 48.9, 40.3, 30.5.

5.3 Synthesis of methyl 3-hydroxy-5-oxoheptanoate 3d[7]



The methyl 3-hydroxy-5-oxoheptanoate **3d** was prepared as synthetic procedure for **3a**. Colorless oil, 93% yield. $[\alpha]_D^{20}$ = –12.8 (*c* = 1.19 in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52 – 4.46 (m, 1H), 3.72 (s, 3H), 3.47 (d, *J* = 3.4 Hz, 1H), 2.67 – 2.66 (m, 2H), 2.53 (dd, *J* = 6.4, 2.1 Hz, 2H), 2.48 (q, *J* = 7.3 Hz, 2H), 1.07 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.0, 172.1, 64.3, 51.7, 47.7, 40.4, 36.6, 7.4.

Reference

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[4] S. -Y. Chou, *Heterocycles*, 2003, **60**, 1095.

[5] (a) C. L. Sann, T. J. Simpson, D. I. Smith, P. Watts, C. L. Willis, *Tetrahedron Lett.,* 1999, **40**, 4093; (b) K. –M. Cheung, S. J. Coles, M. B. Hursthouse, N. I. Johnson, P. M. Shoolingin-Jordan, *Angew. Chem. Int. Ed.,* 2002, **41**, 1198.

[6] V. Blandin, J. F. Carpentier, A. Mortreux, *Eur. J. Org. Chem.*, 1999, 3421.

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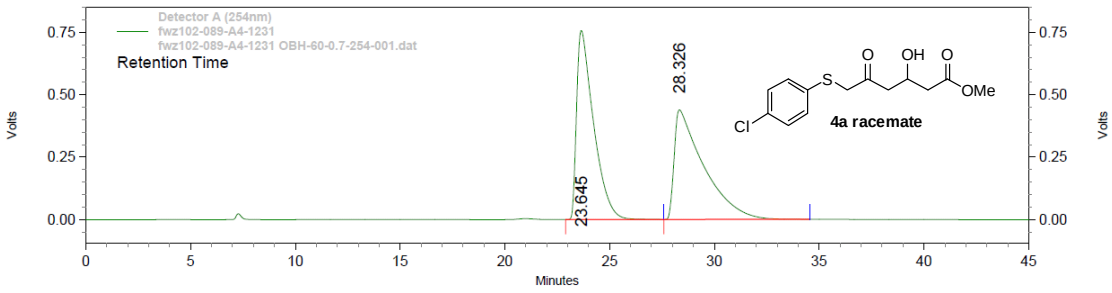
6. HPLC Chromatography of the Hydrogenation Products

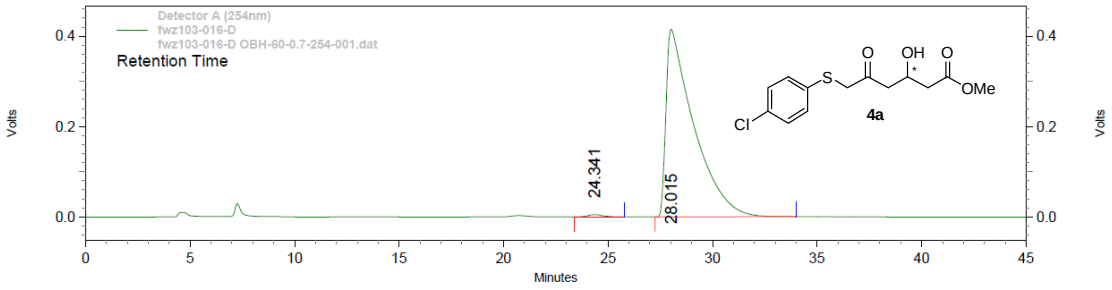
Scheme 1

The enantiomeric excess of methyl 6-chloro-5,5-diethoxy-3-hydroxyhexanoate **2a** was determined via its corresponding 4-chlorobenezenthiol substituted derivative **4a** (deprotection of **2a** and then substituted with 4-chlorobenezethiol) by HPLC on chiralcel OB-H column.



Detector A (254nm)

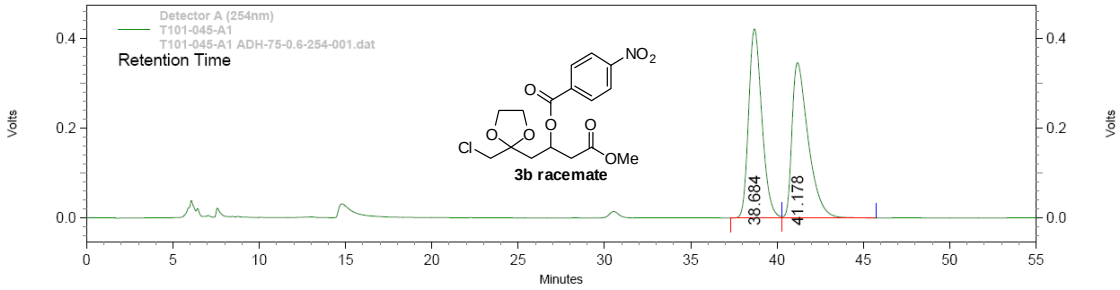
Pk #	Retention Time	Area	Area %	Height	Height %
1	23.645	42638851	49.915	757083	63.304
2	28.326	42783785	50.085	438866	36.696
Totals		85422637	100.000	1195948	100.000



Detector A (254nm)

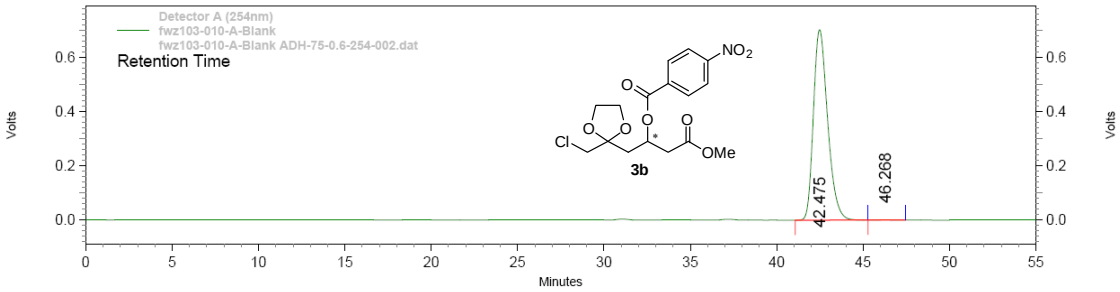
Pk #	Retention Time	Area	Area %	Height	Height %
1	24.341	226751	0.589	4705	1.120
2	28.015	38267248	99.411	415257	98.880
Totals		38493999	100.000	419962	100.000

The enantiomeric excess of methyl 4-(2-(chloromethyl)-1,3-dioxolan-2-yl)-3-hydroxybutanoate **2b** was determined via its corresponding 4-nitrobenzoate **3b** by HPLC on chiralcel AD-H column.



Detector A (254nm)

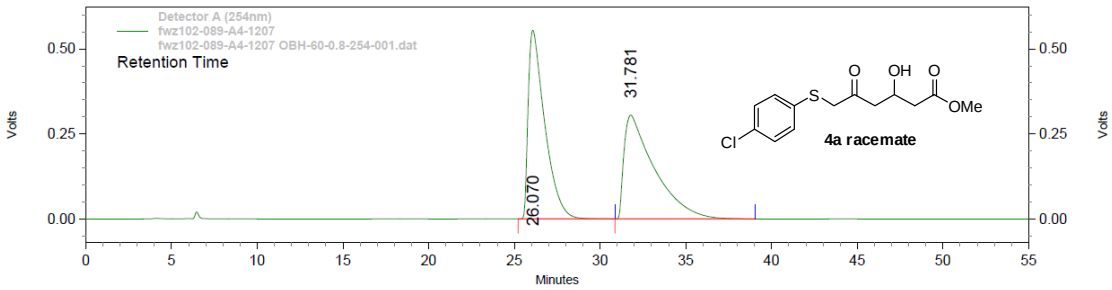
Pk #	Retention Time	Area	Area %	Height	Height %
1	38.684	22477638	49.933	421091	54.911
2	41.178	22538065	50.067	345768	45.089
Totals		45015703	100.000	766859	100.000



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	42.475	40247820	99.829	702977	99.852
2	46.268	68799	0.171	1044	0.148
Totals		40316618	100.000	704021	100.000

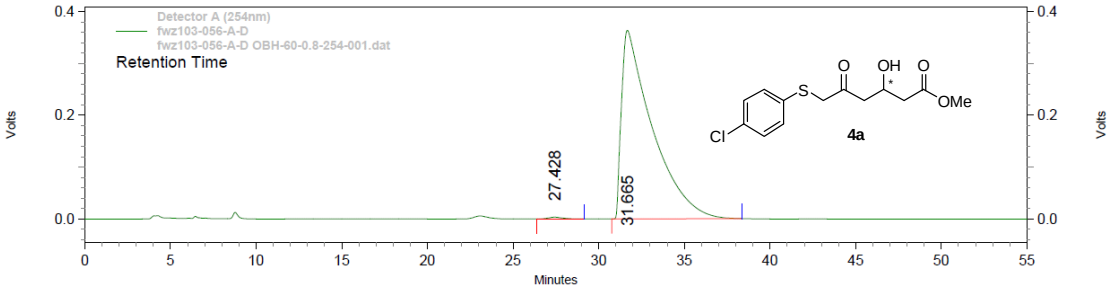
HPLC of 4a racemate:



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	26.070	37221572	49.806	554793	64.515
2	31.781	37511718	50.194	305153	35.485
Totals		74733290	100.000	859946	100.000

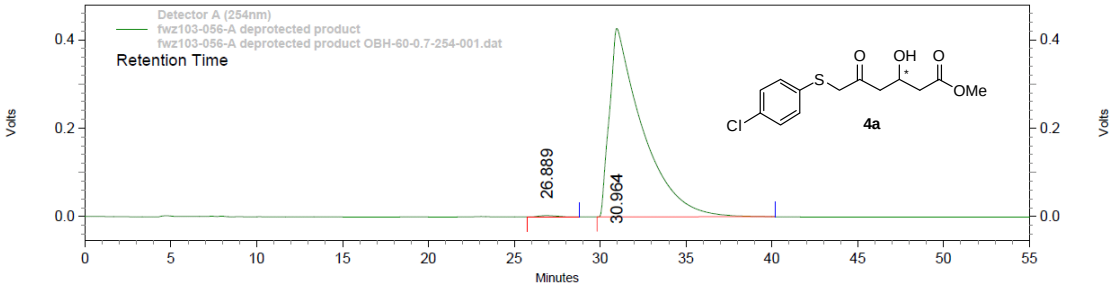
Table 1, entry 1: no additive



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	27.428	180433	0.397	3222	0.877
2	31.665	45321190	99.603	364105	99.123
Totals		45501622	100.000	367327	100.000

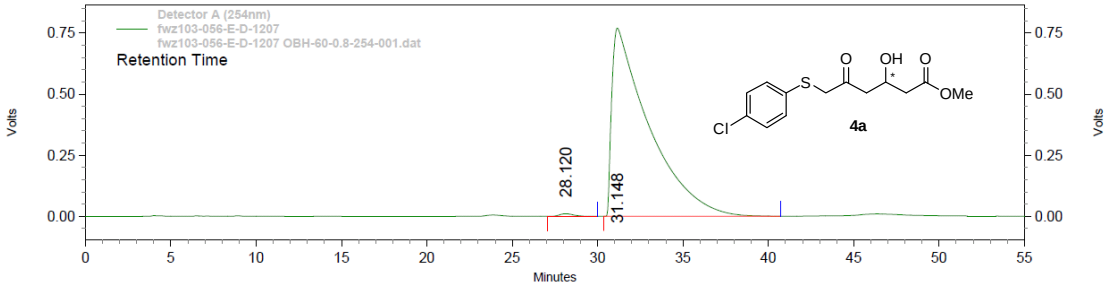
***ee* of 3a:** enantiomeric excess of **3a** was determined via its corresponding 4-chlorobenezethiol substituted derivative



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	26.889	217551	0.382	3084	0.718
2	30.964	56763272	99.618	426441	99.282
Totals		56980822	100.000	429525	100.000

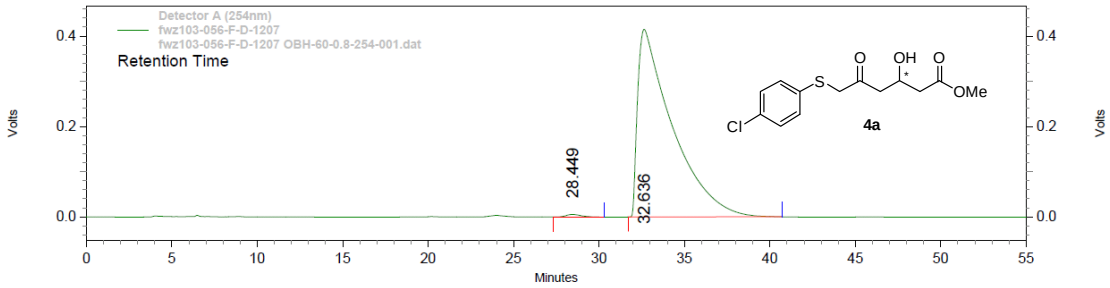
Table 1, entry 2: Et_3N as additive



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	28.120	584244	0.498	10784	1.381
2	31.148	116849239	99.502	770078	98.619
Totals		117433483	100.000	780862	100.000

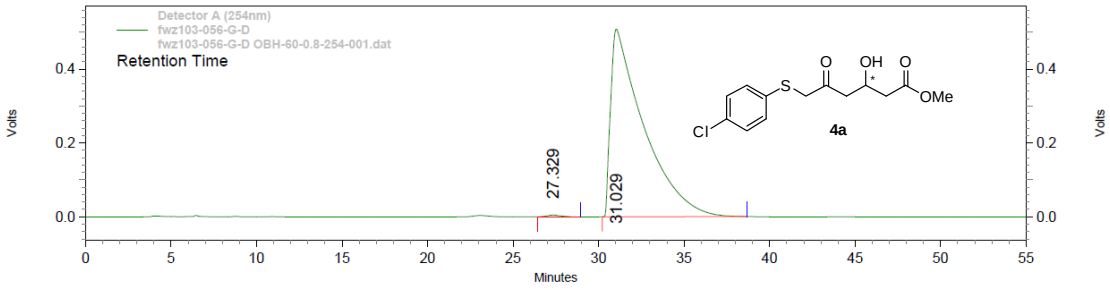
Table 1, entry 3: *i*Pr$_2$NEt as additive



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	28.449	328136	0.556	5616	1.334
2	32.636	58697457	99.444	415462	98.666
Totals		59025593	100.000	421078	100.000

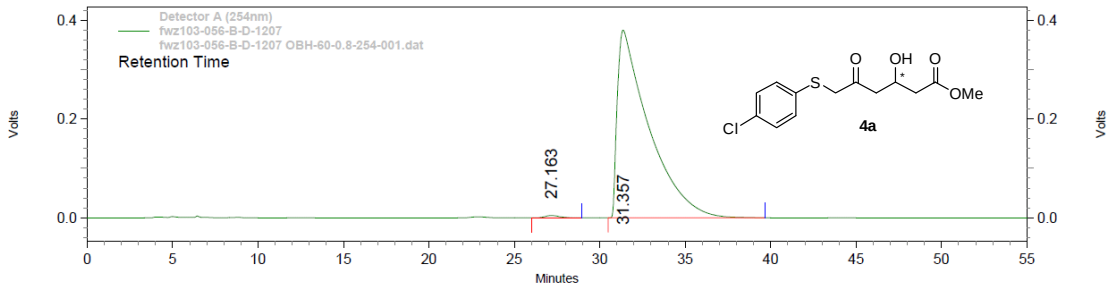
Table 1, entry 4: Imidazole as additive



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	27.329	235493	0.343	4348	0.849
2	31.029	68354212	99.657	507972	99.151
Totals		68589705	100.000	512320	100.000

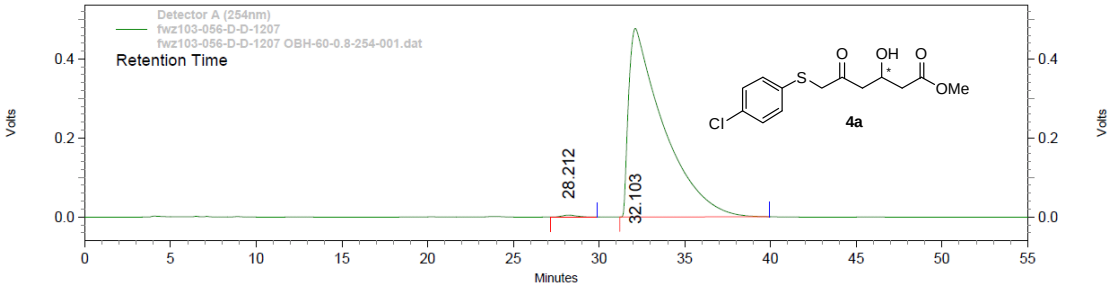
Table 1, entry 5: AcONa as additive



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	27.163	256373	0.523	4650	1.210
2	31.357	48748410	99.477	379601	98.790
Totals		49004783	100.000	384251	100.000

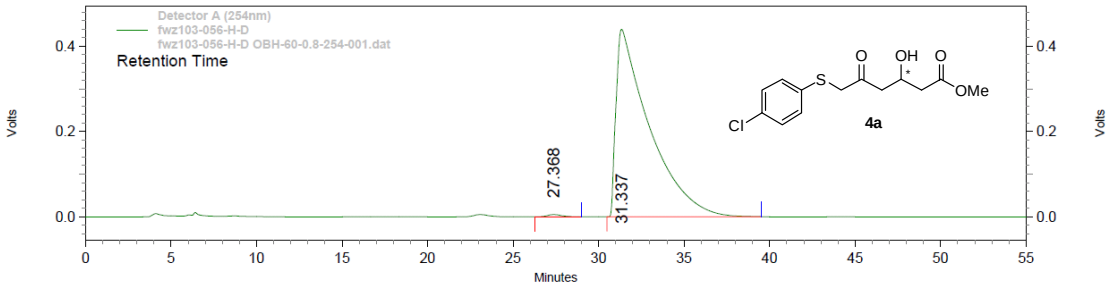
Table 1, entry 7: 4 mg $CaCO_3$ as additive



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	28.212	265404	0.391	4673	0.970
2	32.103	67607751	99.609	477364	99.030
Totals		67873156	100.000	482037	100.000

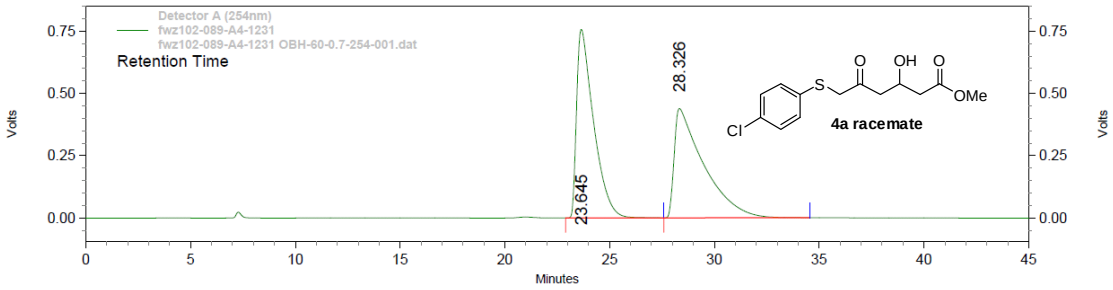
Table 1, entry 8: Basic Al_2O_3 as additive



Detector A (254nm)

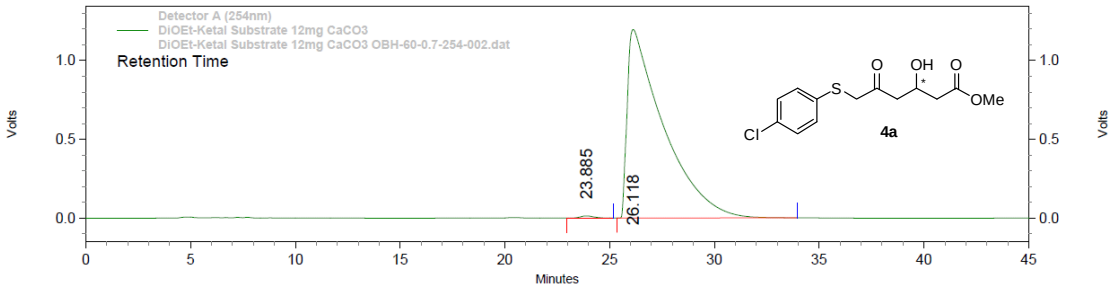
Pk #	Retention Time	Area	Area %	Height	Height %
1	27.368	285311	0.477	5171	1.162
2	31.337	59507447	99.523	440003	98.838
Totals		59792758	100.000	445174	100.000

Table 1, entry 9: 12 mg $CaCO_3$ was added as additive



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.645	42638851	49.915	757083	63.304
2	28.326	42783785	50.085	438866	36.696
Totals		85422637	100.000	1195948	100.000

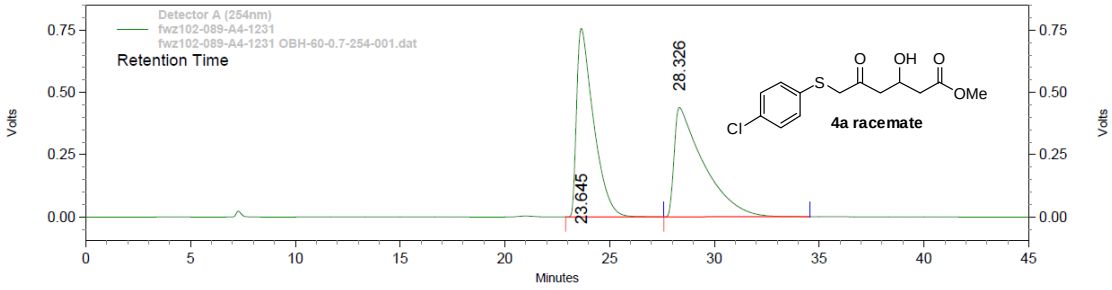


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.885	574315	0.397	13387	1.106
2	26.118	144055084	99.603	1196612	98.894
Totals		144629400	100.000	1209999	100.000

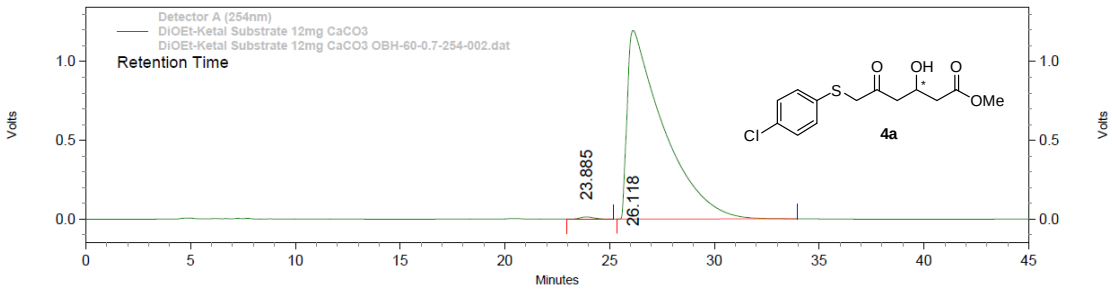
Table 2, entry 1:

The enantiomeric excess of methyl 6-chloro-5,5-diethoxy-3-hydroxyhexanoate **2a** was determined via its corresponding 4-chlorobenezenthiol substituted derivative **4a** (deprotection of **2a** and then substituted with 4-chlorobenezethiol) by HPLC on chiralcel OB-H column.



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.645	42638851	49.915	757083	63.304
2	28.326	42783785	50.085	438866	36.696
Totals		85422637	100.000	1195948	100.000

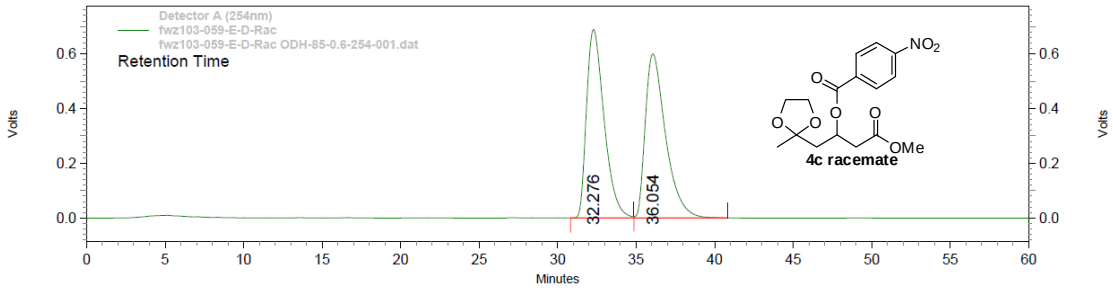


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.885	574315	0.397	13387	1.106
2	26.118	144055084	99.603	1196612	98.894
Totals		144629400	100.000	1209999	100.000

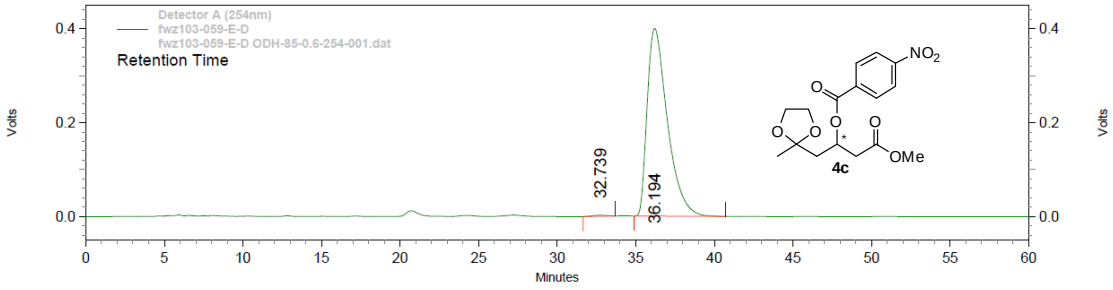
Table 2, entry 2:

The enantiomeric excess of methyl 3-hydroxy-4-(2-methyl-1,3-dioxolan-2-yl)butanoate **2c** was determined via its corresponding 4-nitrobenzoate **4c** by HPLC on chiralcel OD-H column.



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	32.276	53574116	49.860	689264	53.485
2	36.054	53875386	50.140	599448	46.515
Totals		107449501	100.000	1288712	100.000

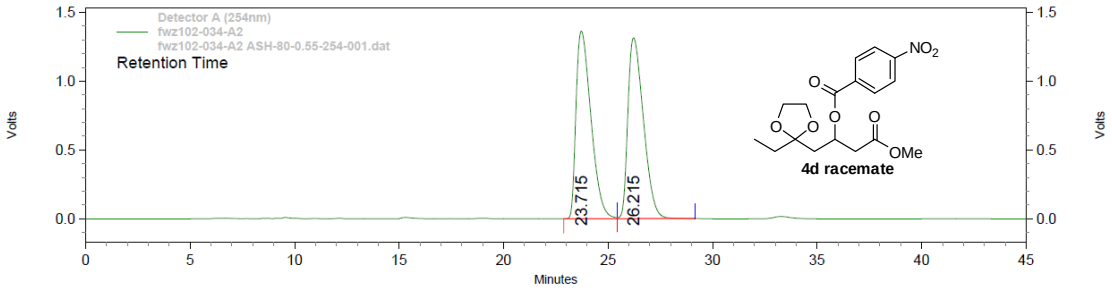


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	32.739	125507	0.349	2186	0.543
2	36.194	35817876	99.651	400467	99.457
Totals		35943383	100.000	402653	100.000

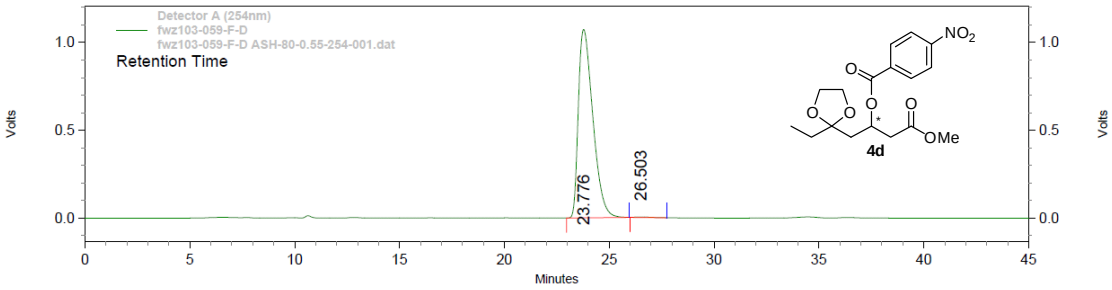
Table 2, entry 3:

The enantiomeric excess of methyl 4-(2-ethyl-1,3-dioxolan-2-yl)-3-hydroxybutanoate **2d** was determined via its corresponding 4-nitrobenzoate **4d** by HPLC on chiralcel AS-H column.



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.715	67655821	49.934	1363066	50.925
2	26.215	67835749	50.066	1313543	49.075
Totals		135491570	100.000	2676610	100.000

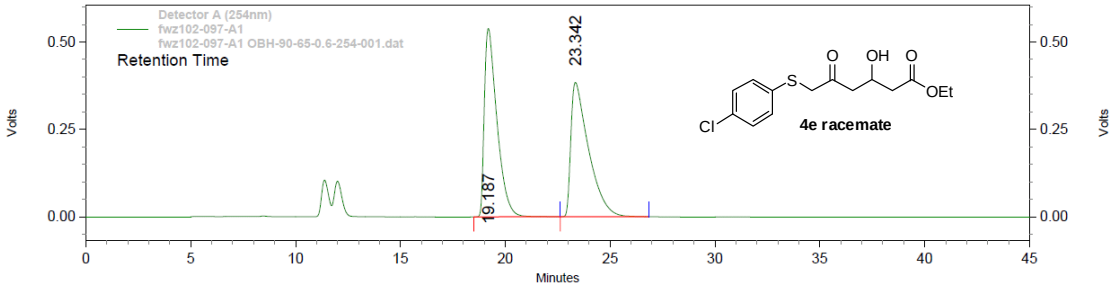


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.776	51619859	99.745	1073978	99.716
2	26.503	132160	0.255	3061	0.284
Totals		51752019	100.000	1077039	100.000

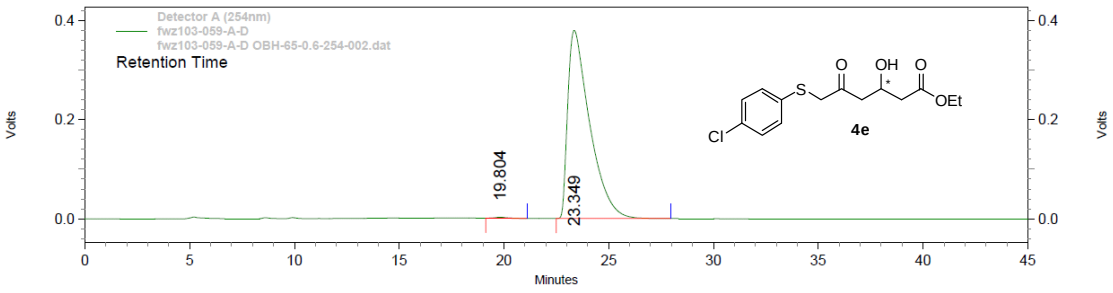
Table 2, entry 4:

The enantiomeric excess of ethyl 6-chloro-5,5-diethoxy-3-hydroxyhexanoate **2e** was determined via its corresponding 4-chlorobenezenthiol substituted derivative **4e** (deprotection of **2e** and then substituted with 4-chlorobenezethiol) by HPLC on chiralcel OB-H column.



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.187	22534210	49.922	539446	58.380
2	23.342	22605019	50.078	384579	41.620
Totals		45139229	100.000	924025	100.000

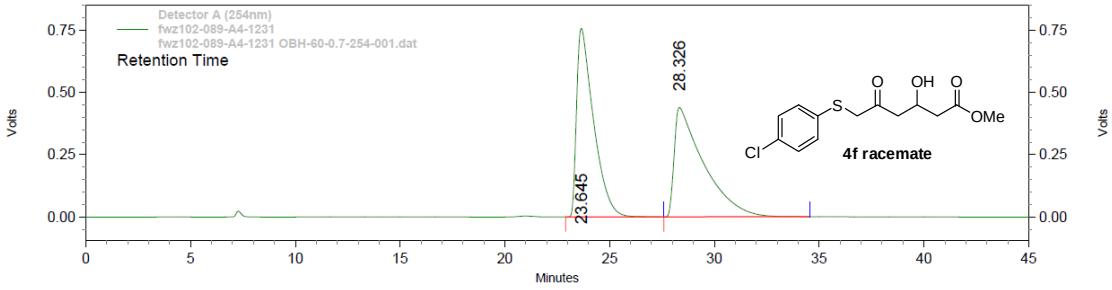


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	19.804	80305	0.290	1805	0.474
2	23.349	27638756	99.710	378898	99.526
Totals		27719061	100.000	380703	100.000

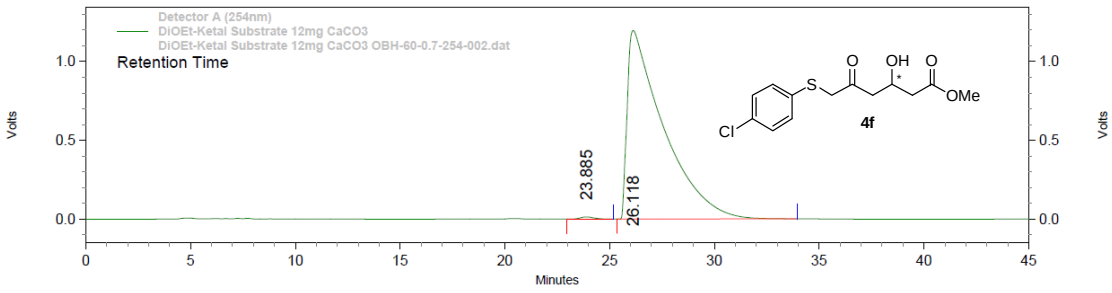
Table 2, entry 5:

The enantiomeric excess of methyl 6-chloro-5,5-diethoxy-3-hydroxyhexanoate **2f** was determined via its corresponding 4-chlorobenezenthiol substituted derivative **4f** (deprotection of **2f** and then substituted with 4-chlorobenezethiol) by HPLC on chiralcel OB-H column.



Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.645	42638851	49.915	757083	63.304
2	28.326	42783785	50.085	438866	36.696
Totals		85422637	100.000	1195948	100.000

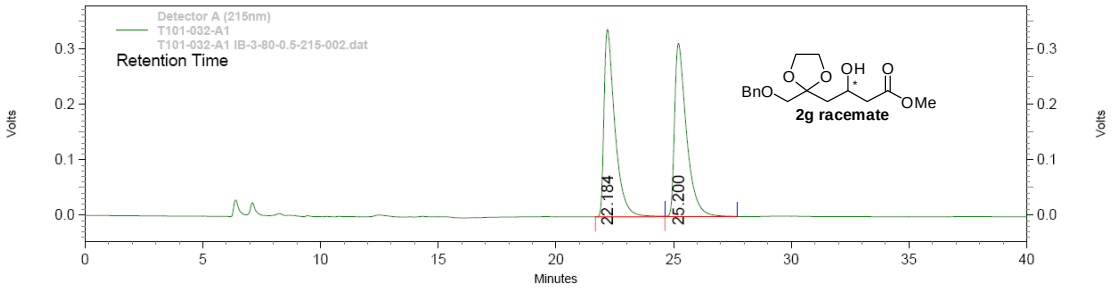


Detector A (254nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	23.885	574315	0.397	13387	1.106
2	26.118	144055084	99.603	1196612	98.894
Totals		144629400	100.000	1209999	100.000

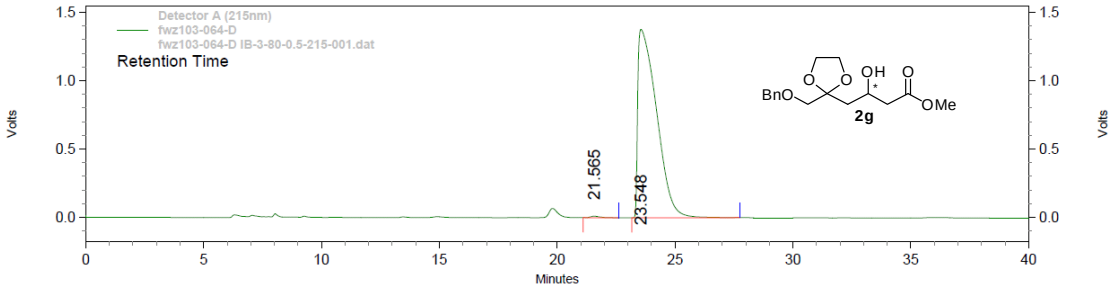
Table 2, entry 6:

The enantiomeric excess of methyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-hydroxybutanoate **2g** was determined by HPLC on chiralpak IB-3 column.



Detector A (215nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	22.184	10872390	49.843	337144	51.959
2	25.200	10940836	50.157	311717	48.041
Totals		21813227	100.000	648861	100.000

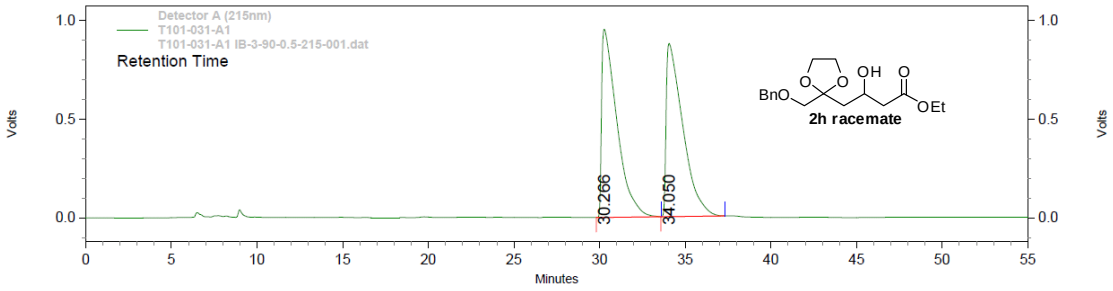


Detector A (215nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	21.565	293563	0.384	10908	0.785
2	23.548	76203811	99.616	1378286	99.215
Totals		76497374	100.000	1389194	100.000

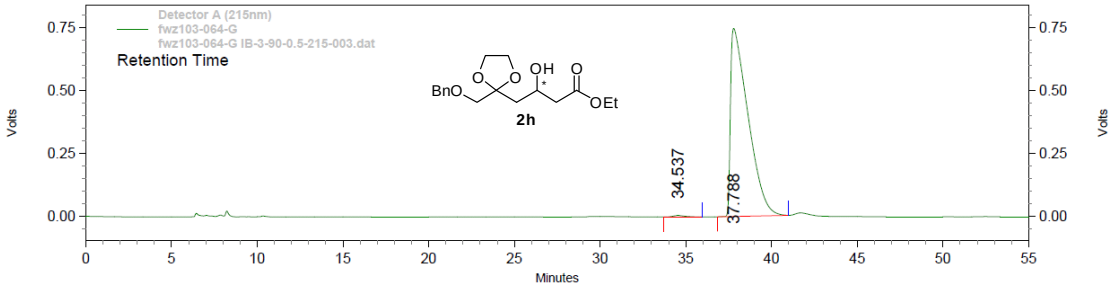
Table 2, entry 7:

The enantiomeric excess of ethyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-hydroxybutanoate **2h** was determined by HPLC on chiralpak IB-3 column.



Detector A (215nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	30.266	59101912	49.945	955375	52.087
2	34.050	59231129	50.055	878807	47.913
Totals		118333040	100.000	1834182	100.000

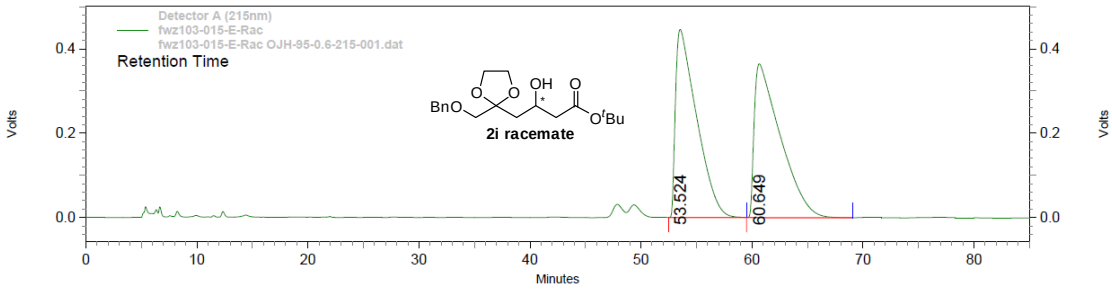


Detector A (215nm)

Pk #	Retention Time	Area	Area %	Height	Height %
1	34.537	227091	0.426	5487	0.727
2	37.788	53069536	99.574	748809	99.273
Totals		53296627	100.000	754296	100.000

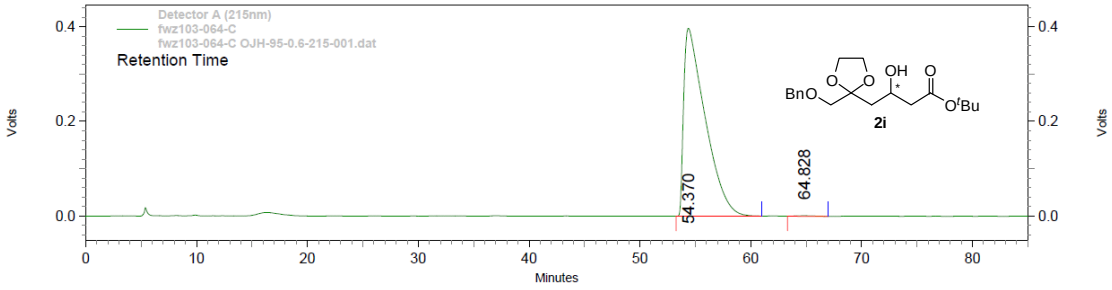
Table 2, entry 8:

The enantiomeric excess of *tert*-butyl 4-(2-((benzyloxy)methyl)-1,3-dioxolan-2-yl)-3-hydroxybutanoate **2i** was determined by HPLC on chiralcel OJ-H column.



Detector A (215nm)

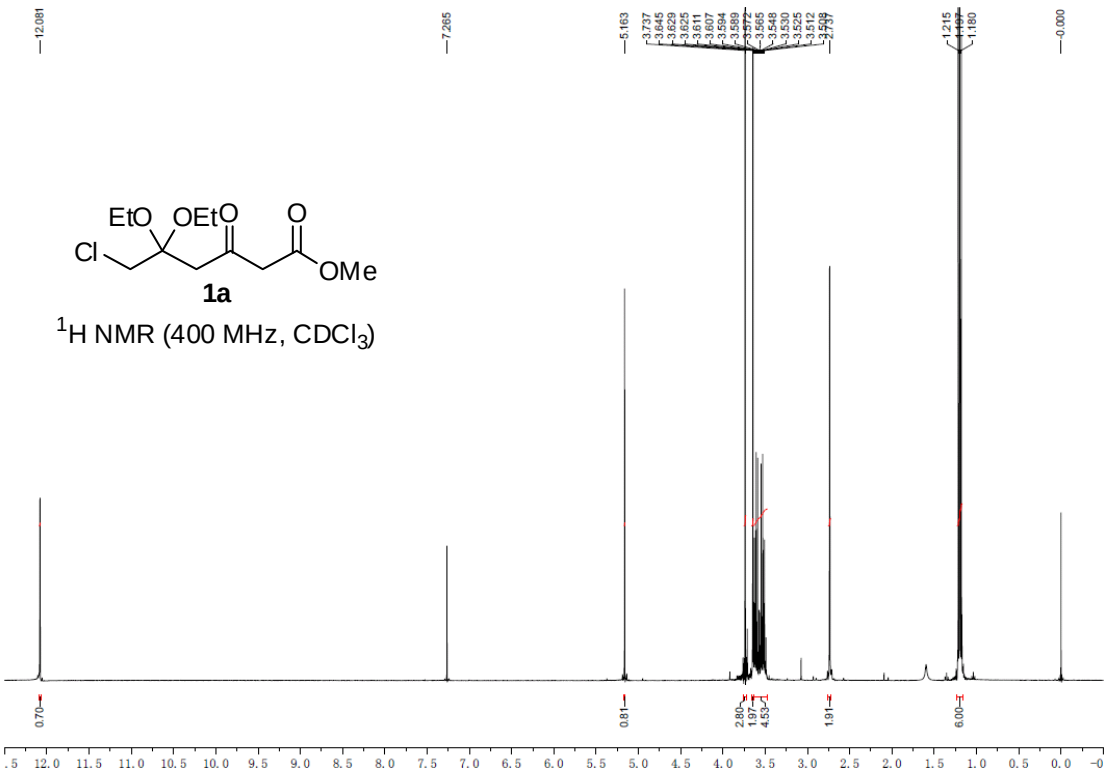
Pk #	Retention Time	Area	Area %	Height	Height %
1	53.524	58974003	49.698	446389	55.019
2	60.649	59689772	50.302	364952	44.981
Totals		118663775	100.000	811342	100.000



Detector A (215nm)

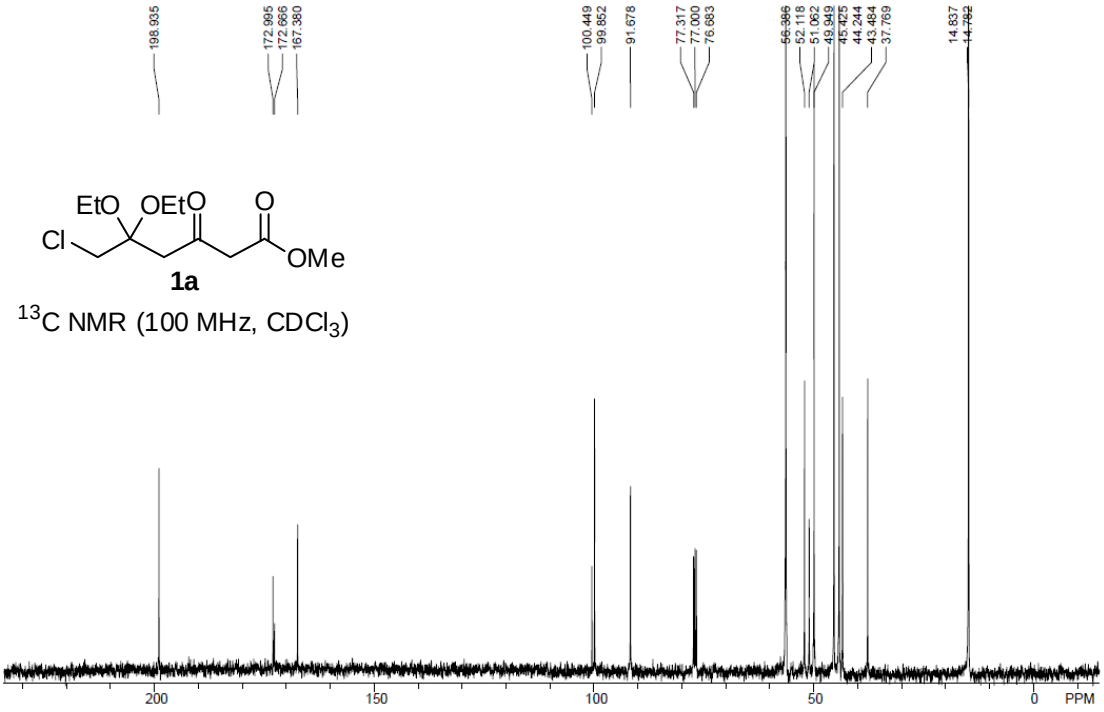
Pk #	Retention Time	Area	Area %	Height	Height %
1	54.370	53397794	99.792	397042	99.720
2	64.828	111302	0.208	1116	0.280
Totals		53509096	100.000	398157	100.000

7. NMR spectra of the products



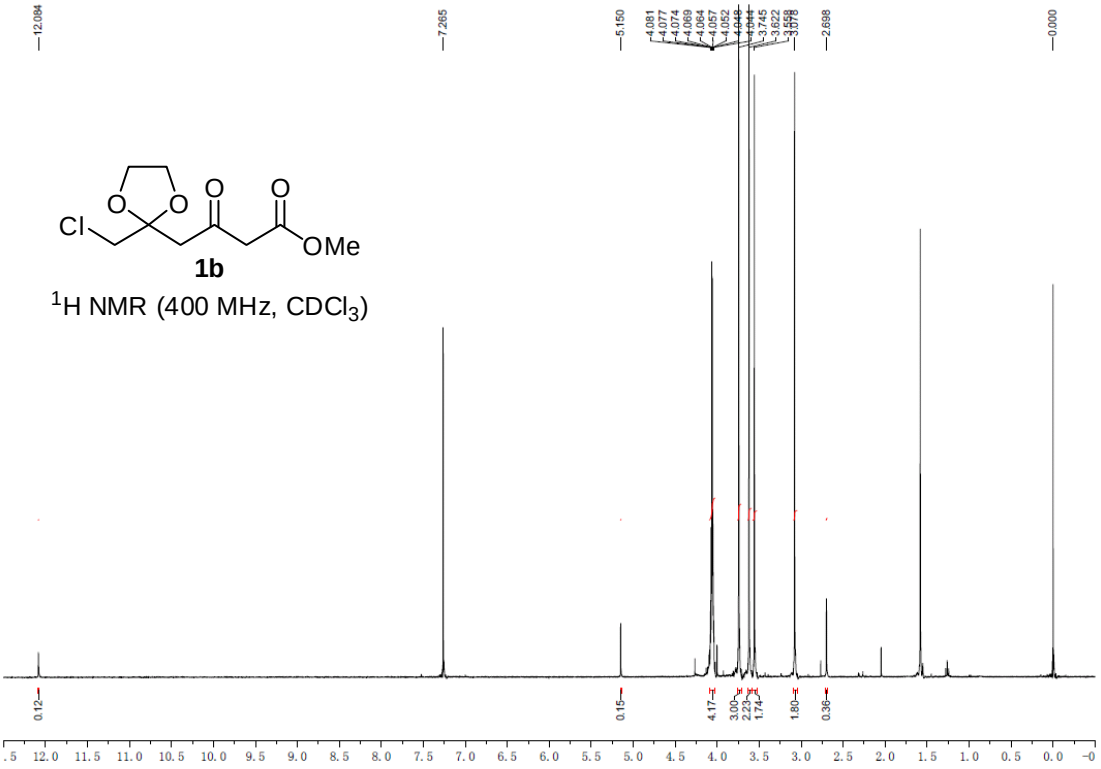
1a

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



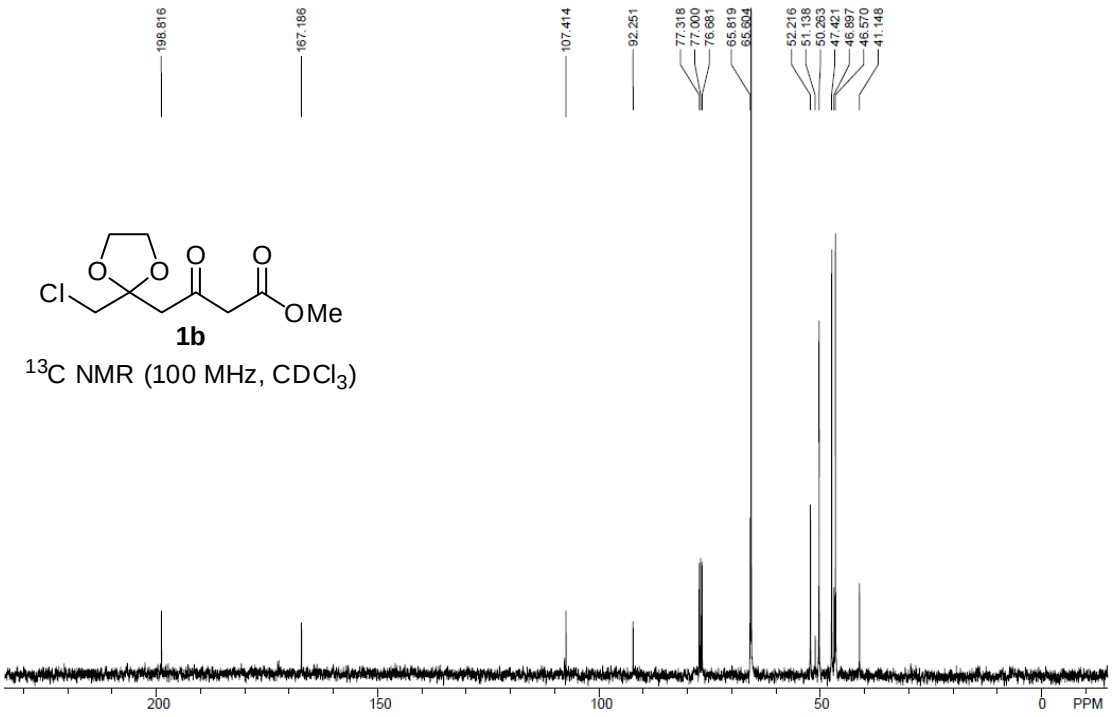
1a

^{13}C NMR (100 MHz, $CDCl_3$)



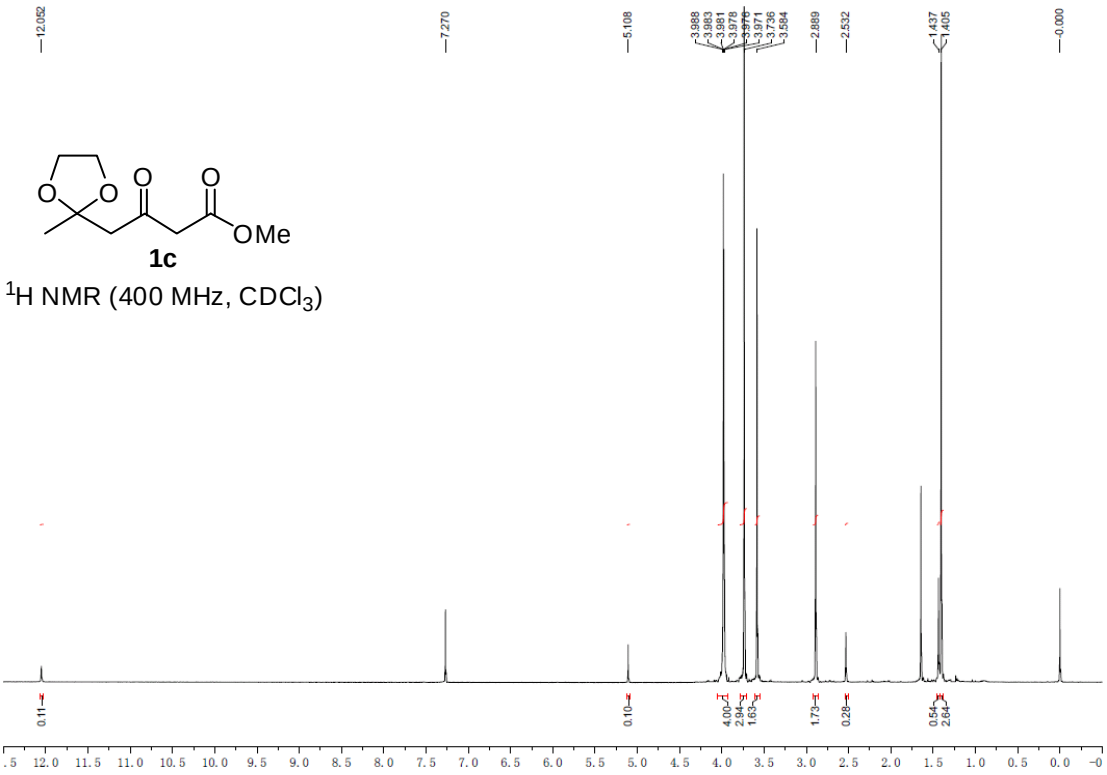
1b

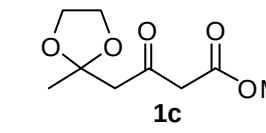
^{1}H NMR (400 MHz, $CDCl_3$)



1b

^{13}C NMR (100 MHz, $CDCl_3$)



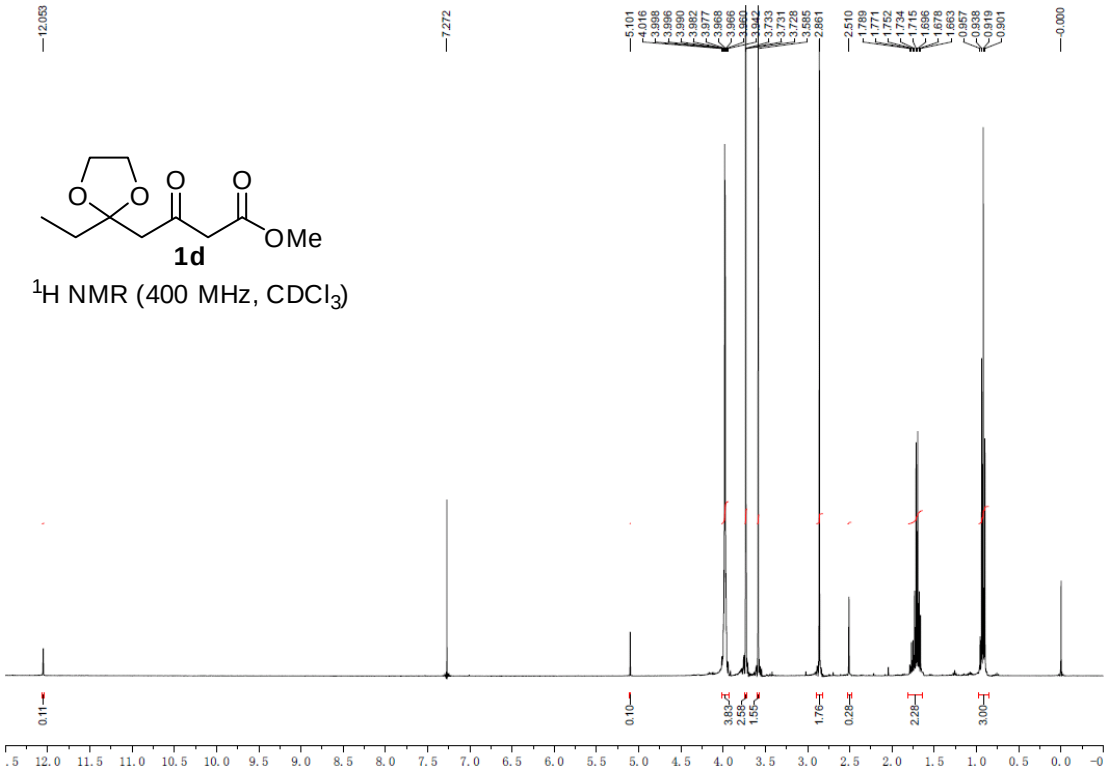


1c

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

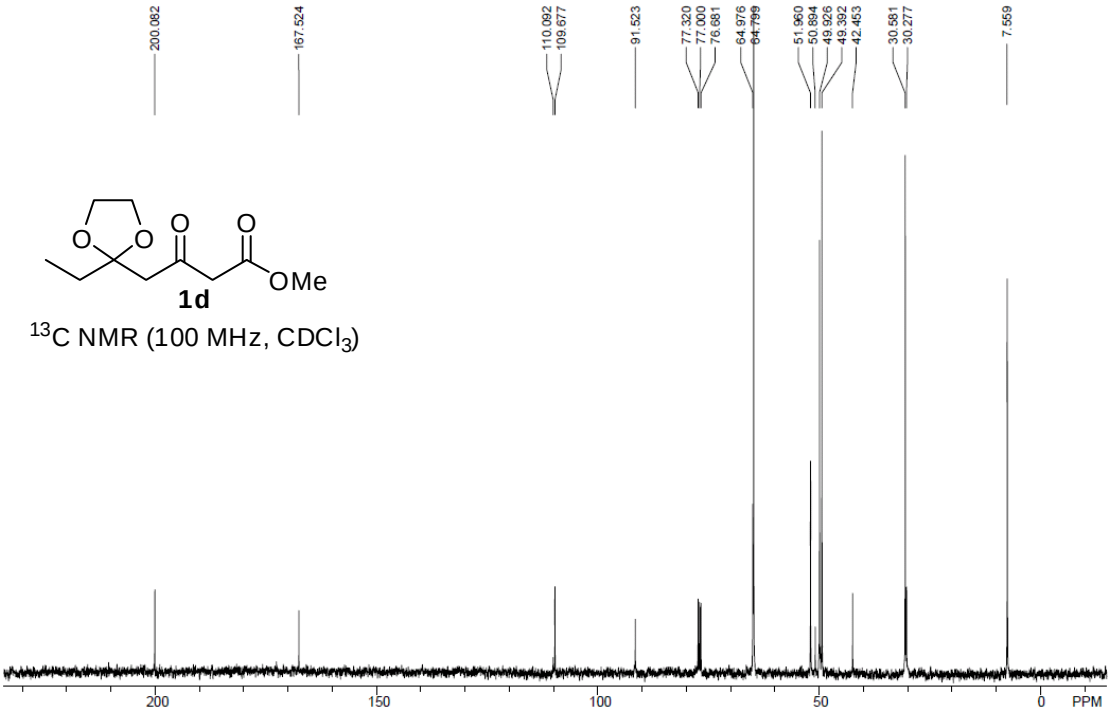
1c

^{13}C NMR (100 MHz, $CDCl_3$)



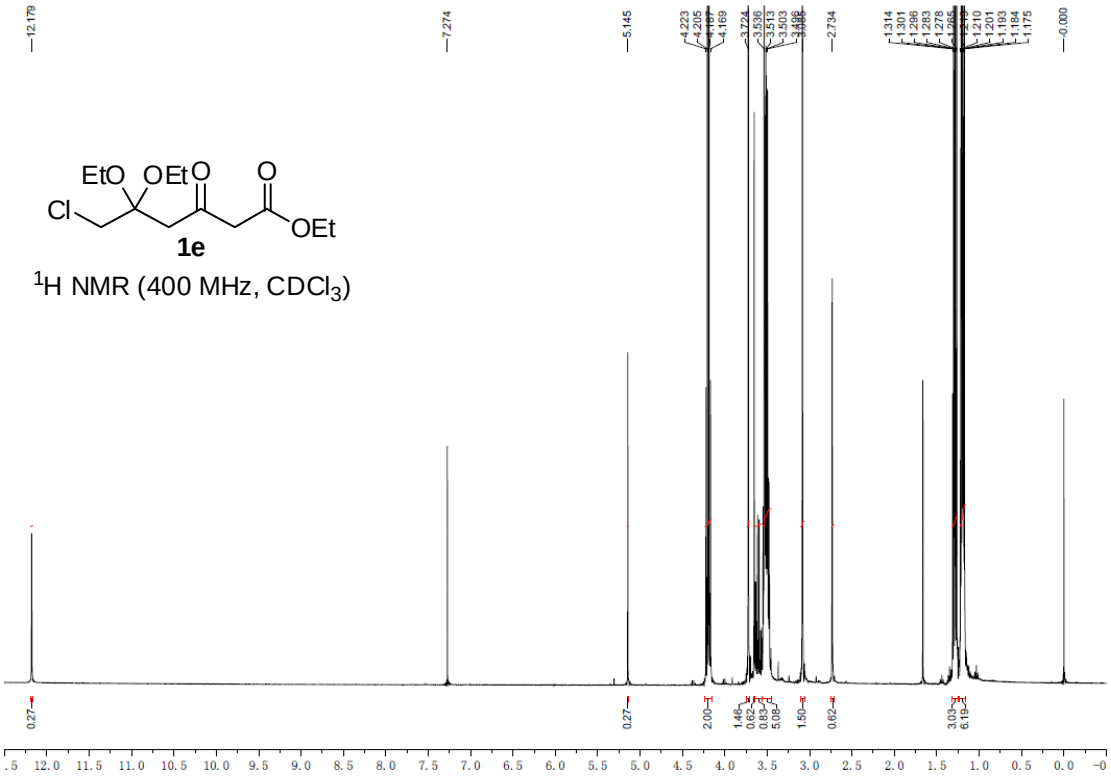
1d

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

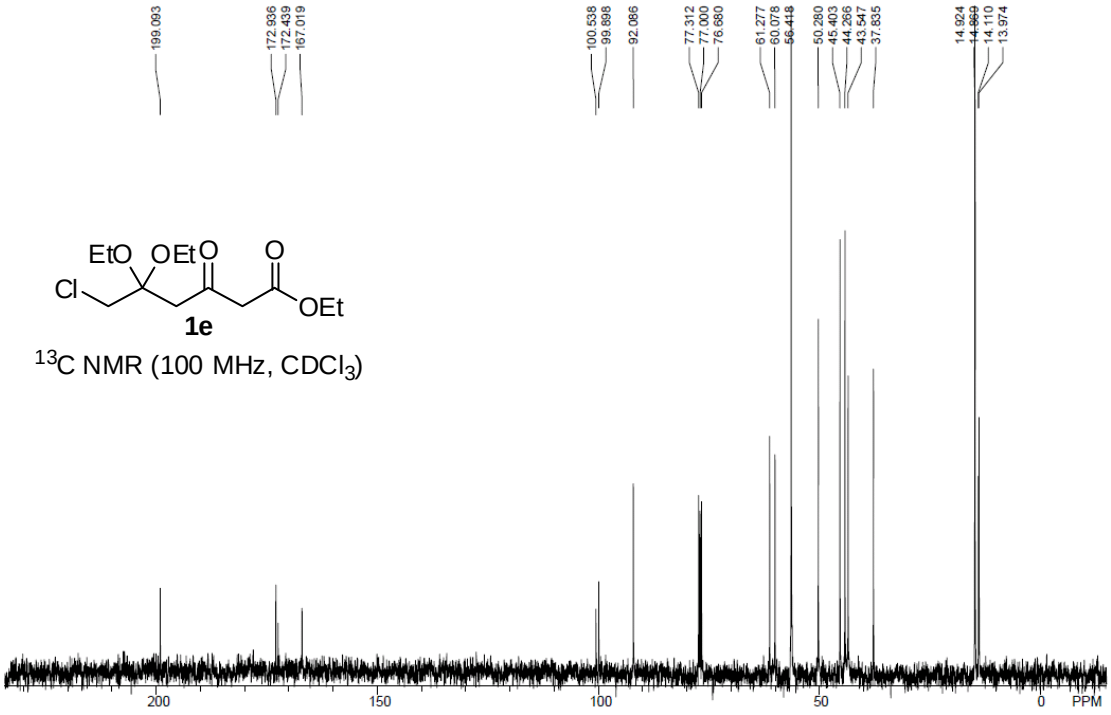


1d

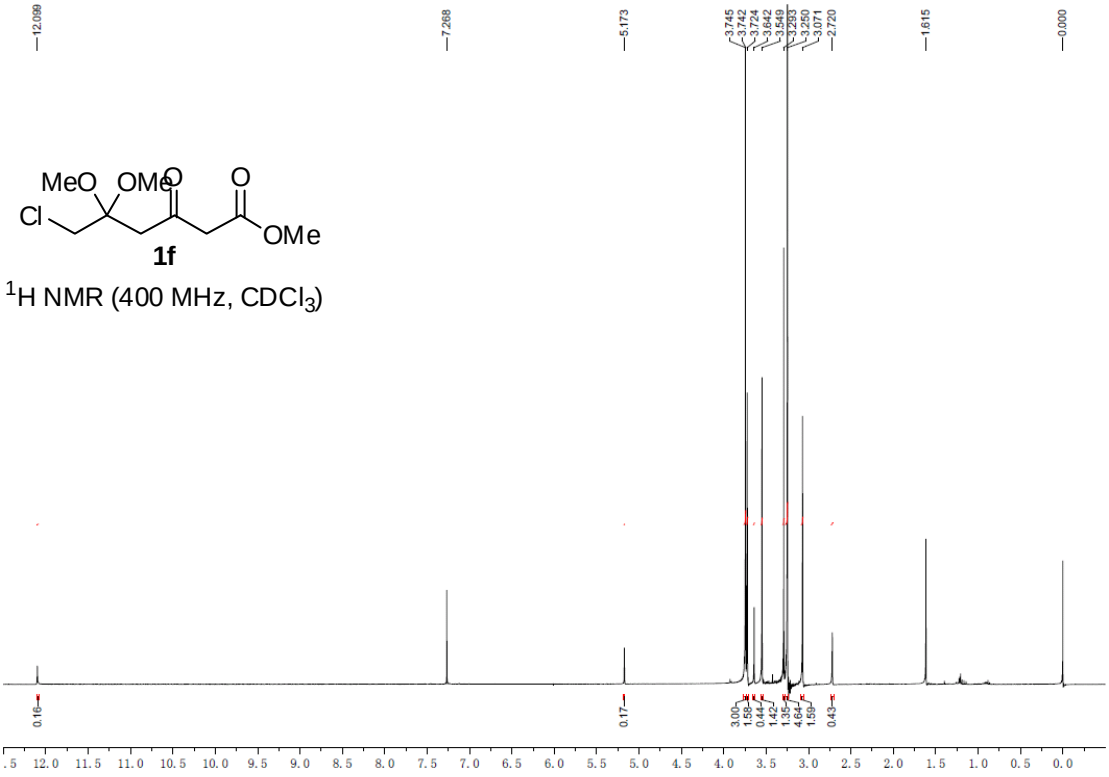
^{13}C NMR (100 MHz, $CDCl_3$)



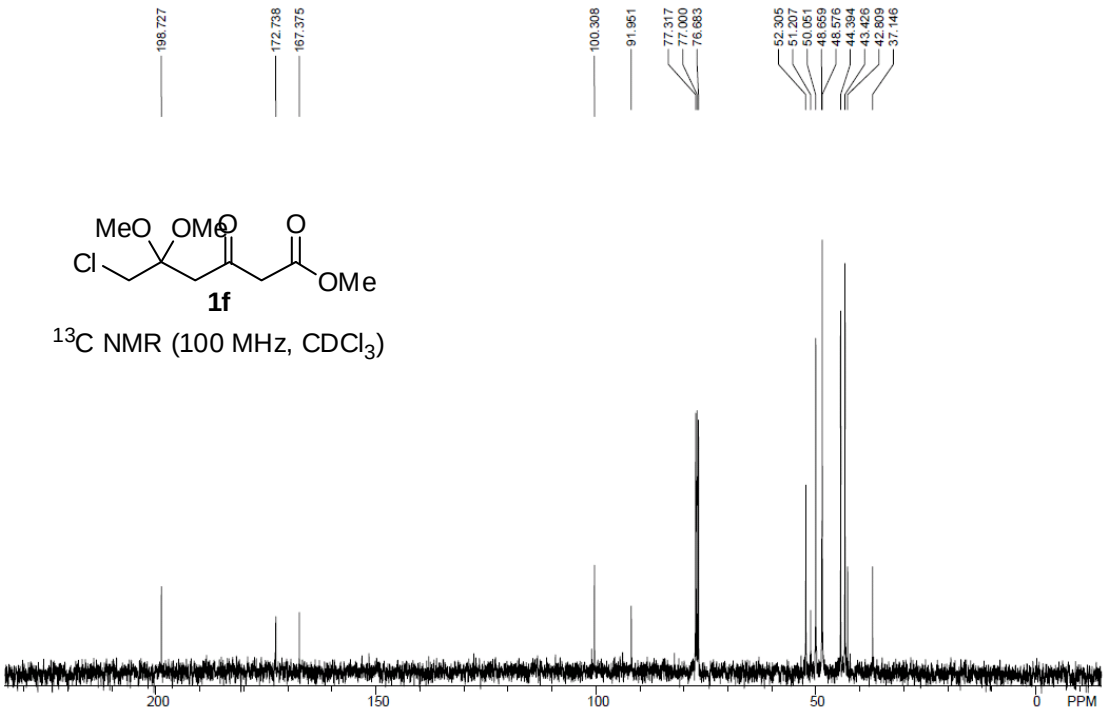
^{1}H NMR (400 MHz, $CDCl_3$)



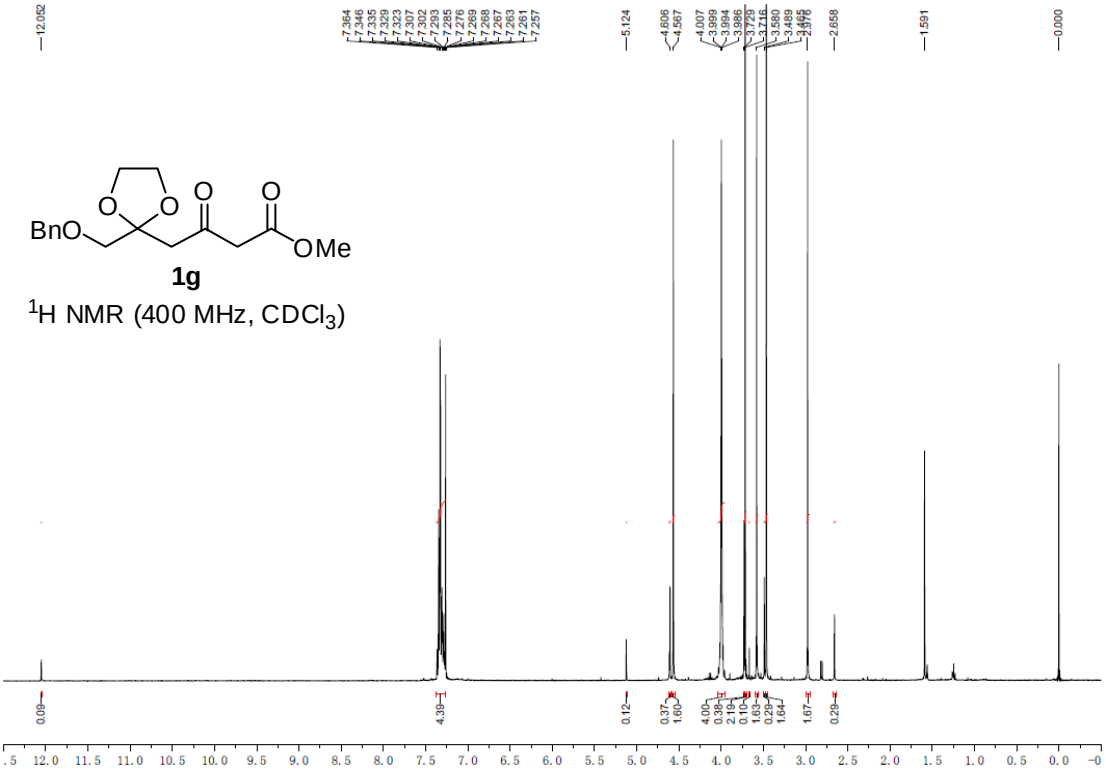
^{13}C NMR (100 MHz, $CDCl_3$)



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

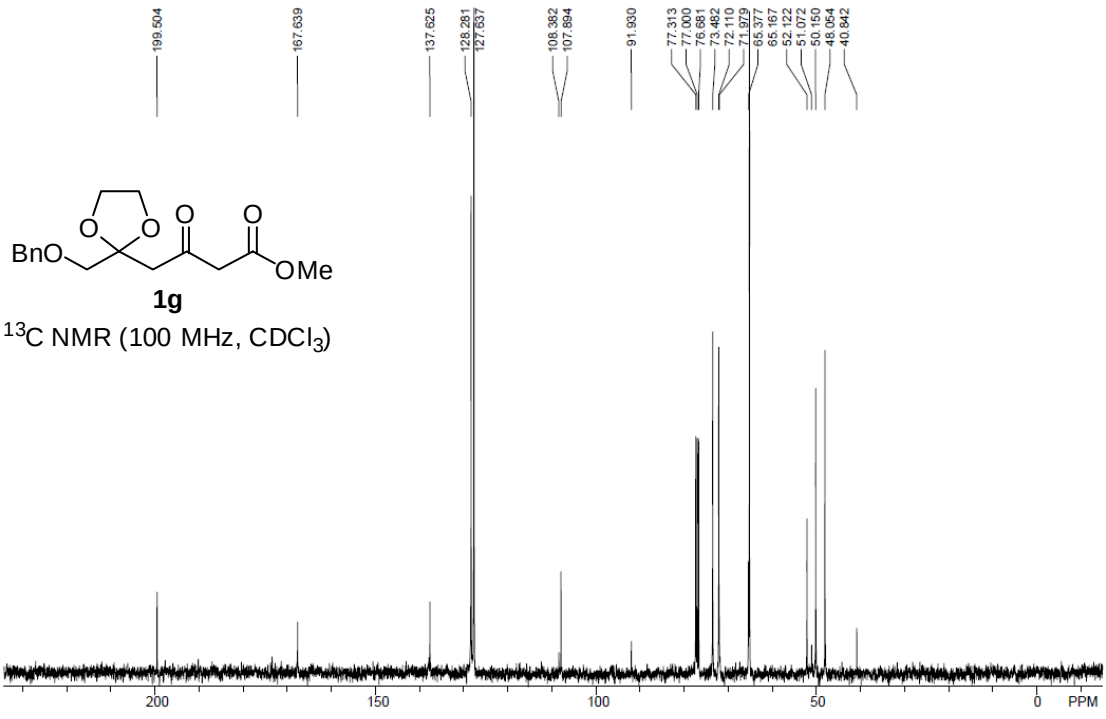


^{13}C NMR (100 MHz, $CDCl_3$)



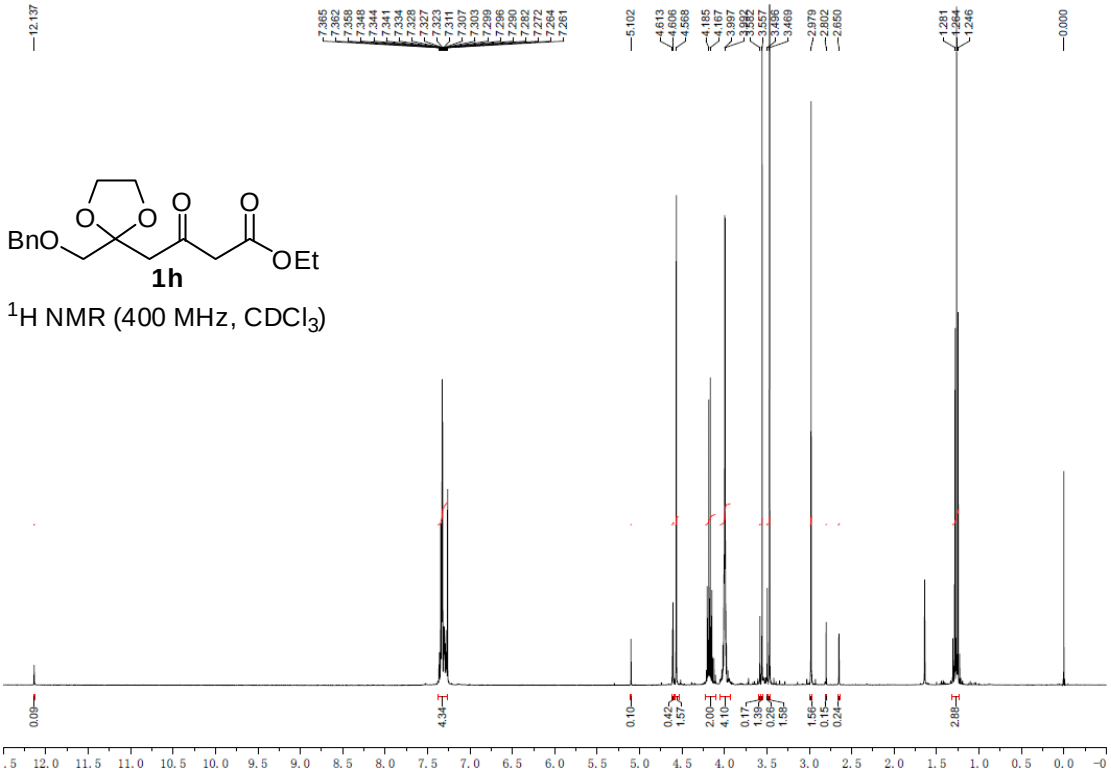
1g

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

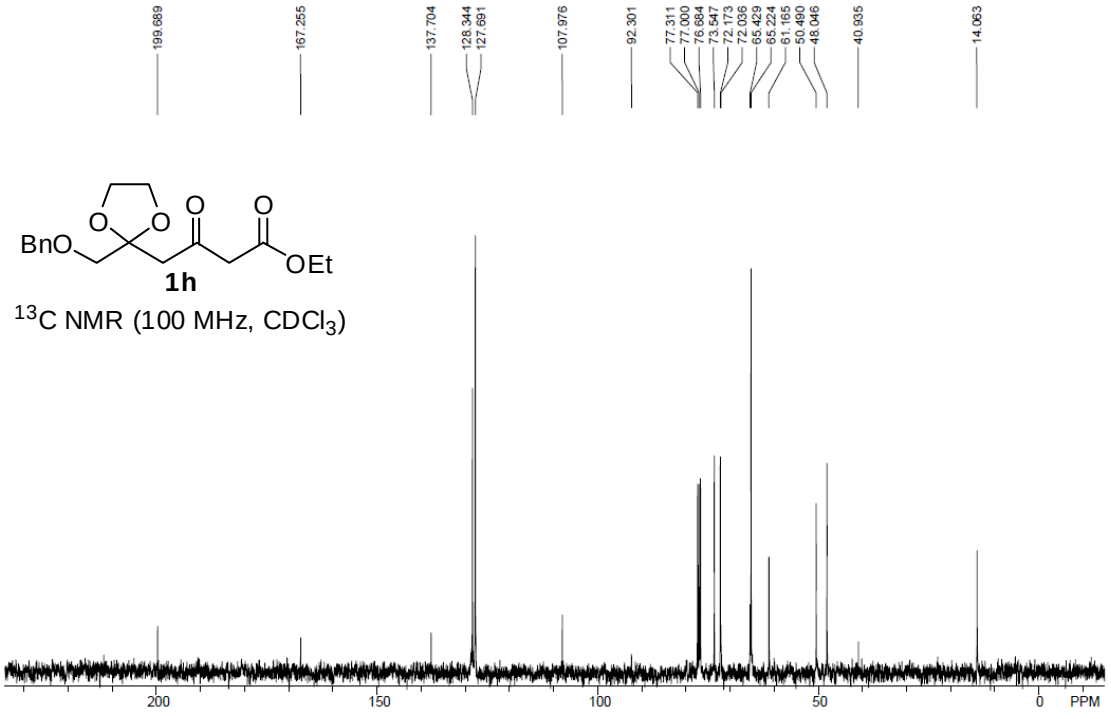


1g

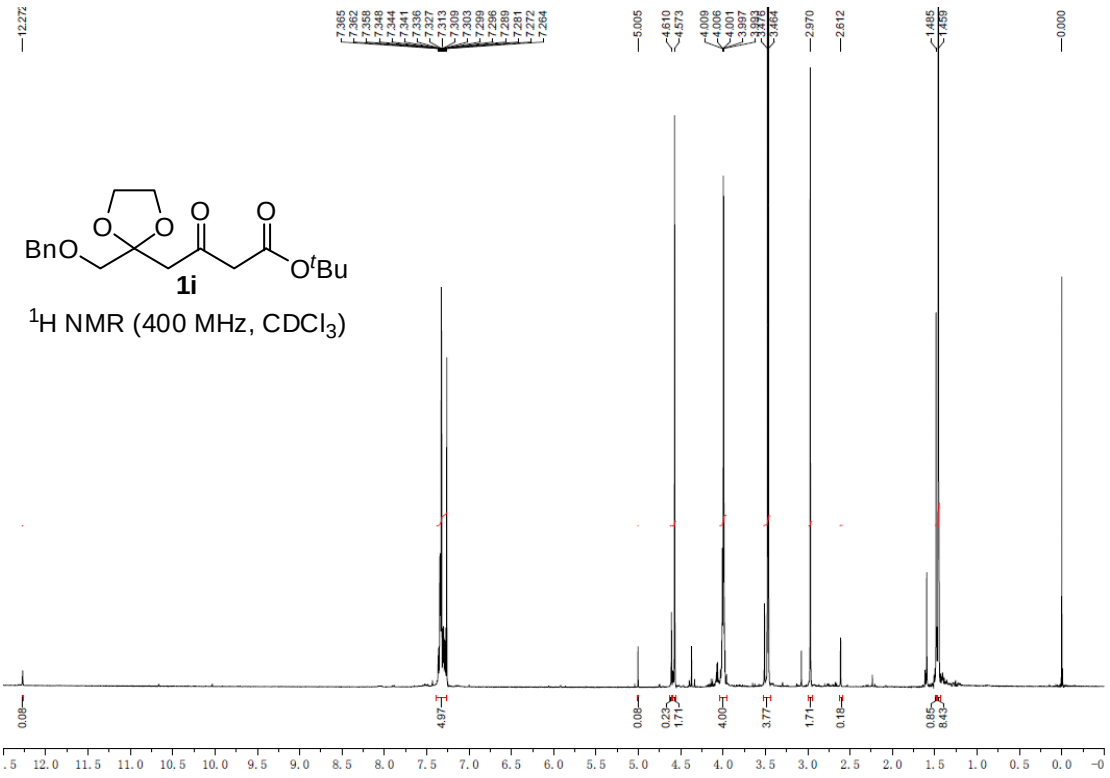
^{13}C NMR (100 MHz, $CDCl_3$)



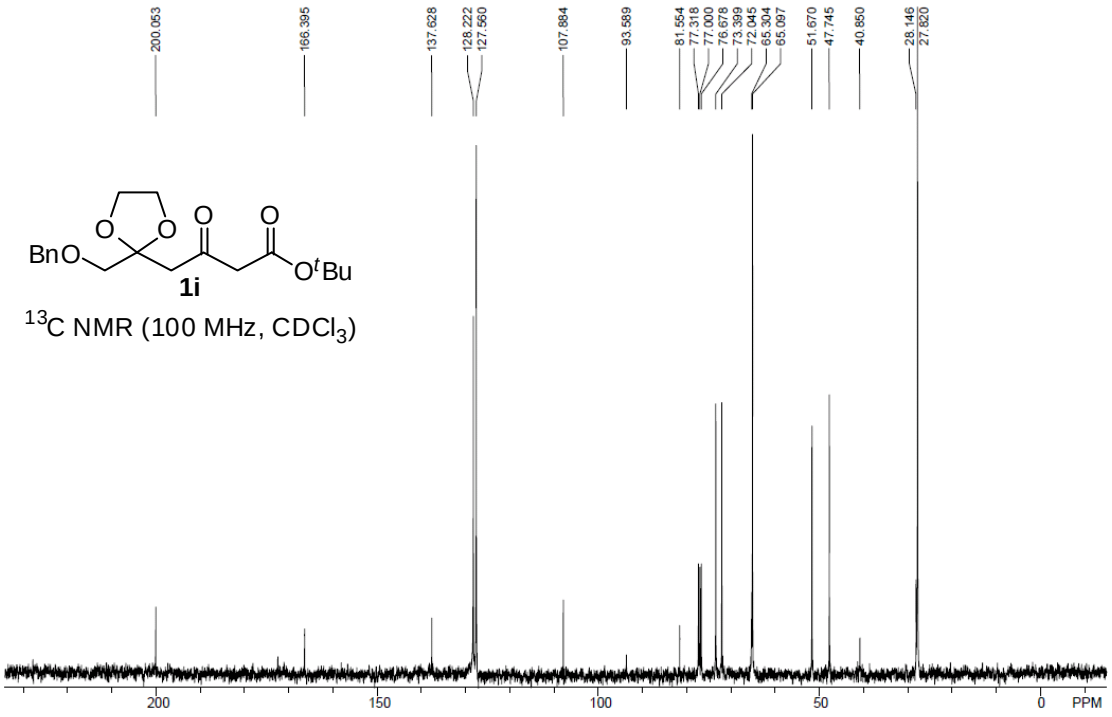
^{1}H NMR (400 MHz, $CDCl_3$)



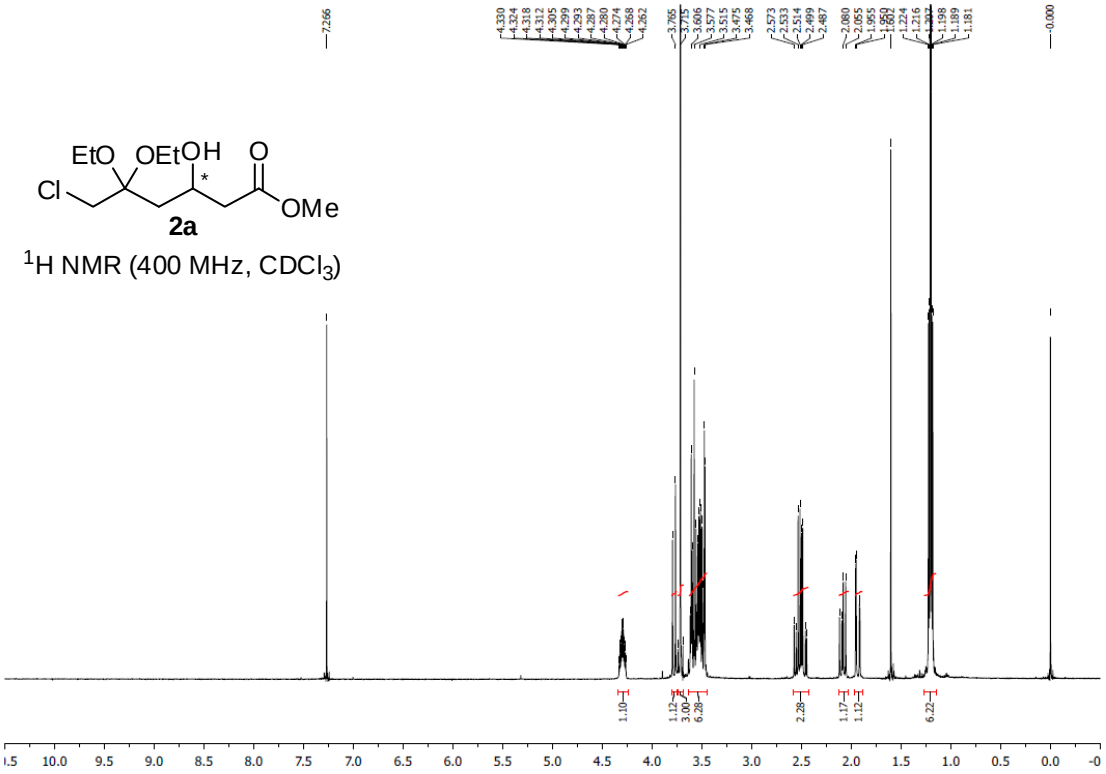
^{13}C NMR (100 MHz, $CDCl_3$)



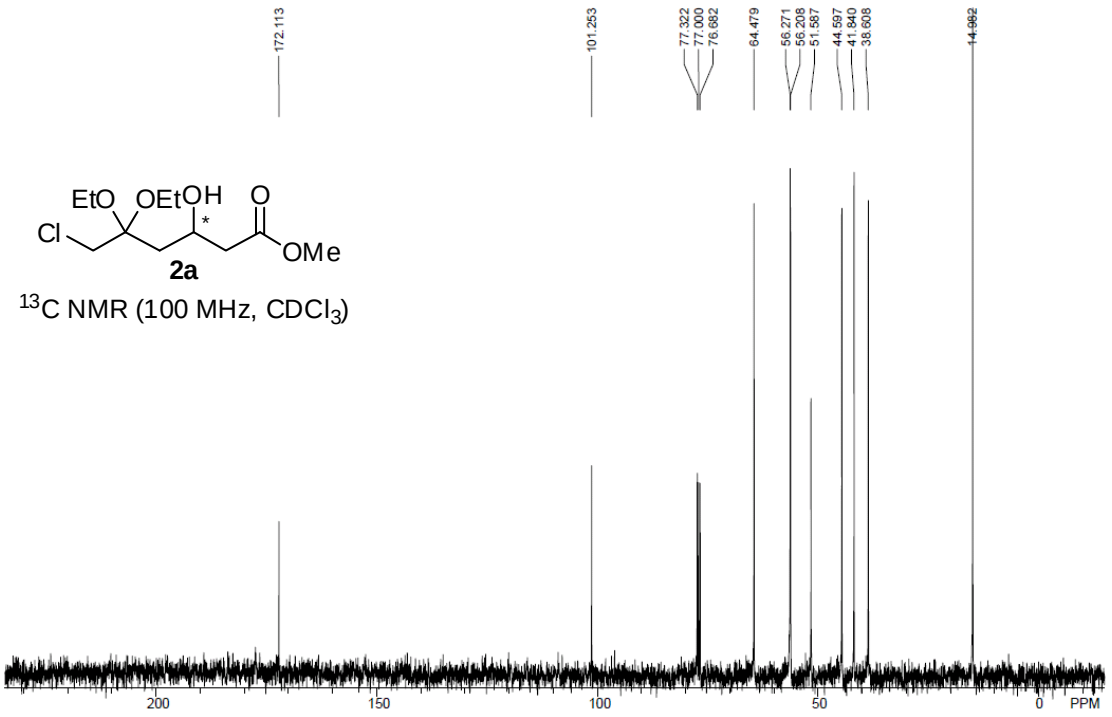
^{1}H NMR (400 MHz, $CDCl_3$)



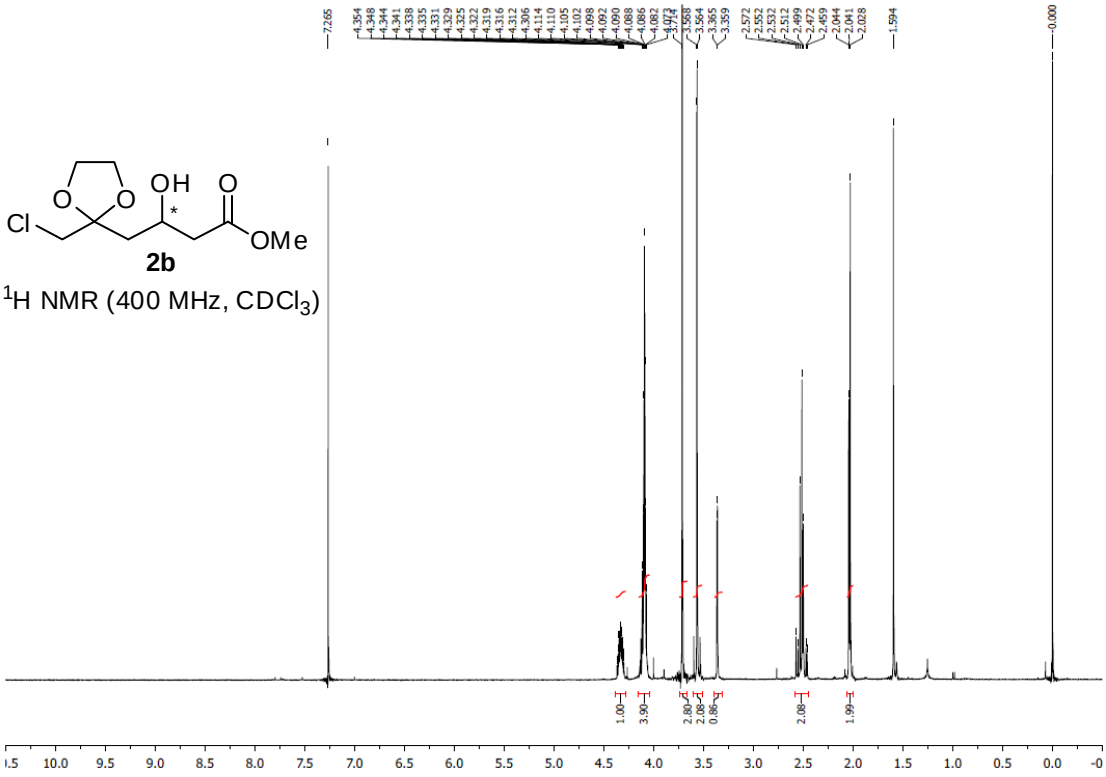
^{13}C NMR (100 MHz, $CDCl_3$)



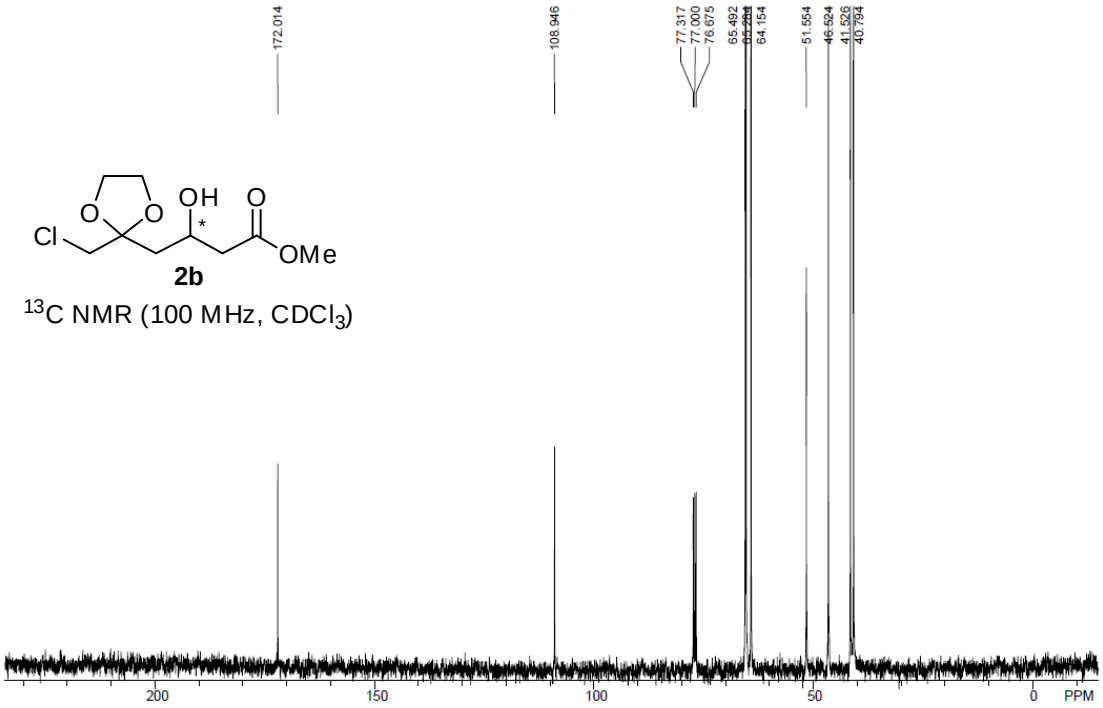
^{1}H NMR (400 MHz, $CDCl_3$)



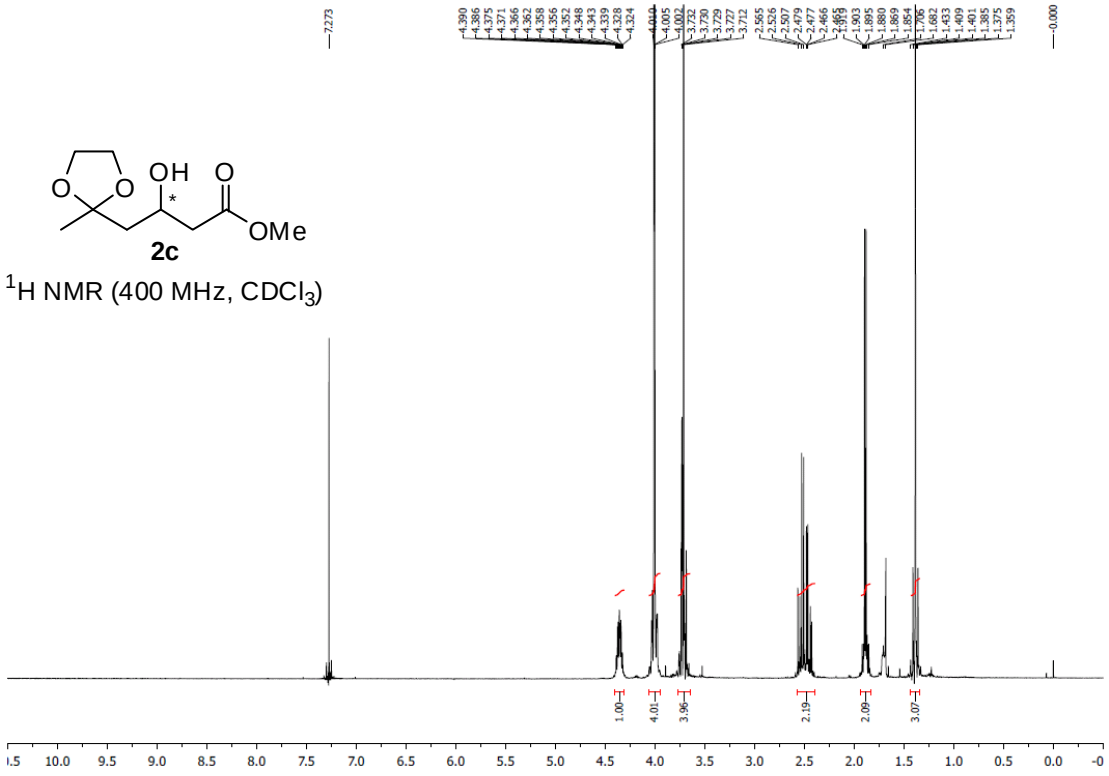
^{13}C NMR (100 MHz, $CDCl_3$)



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

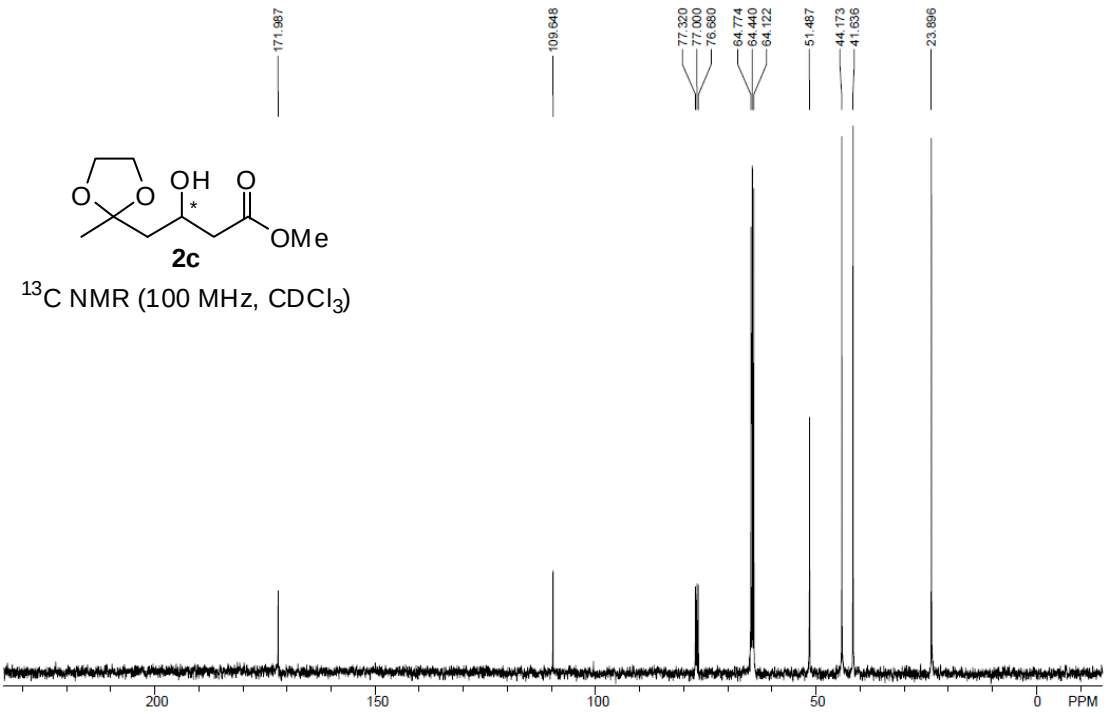


^{13}C NMR (100 MHz, $CDCl_3$)



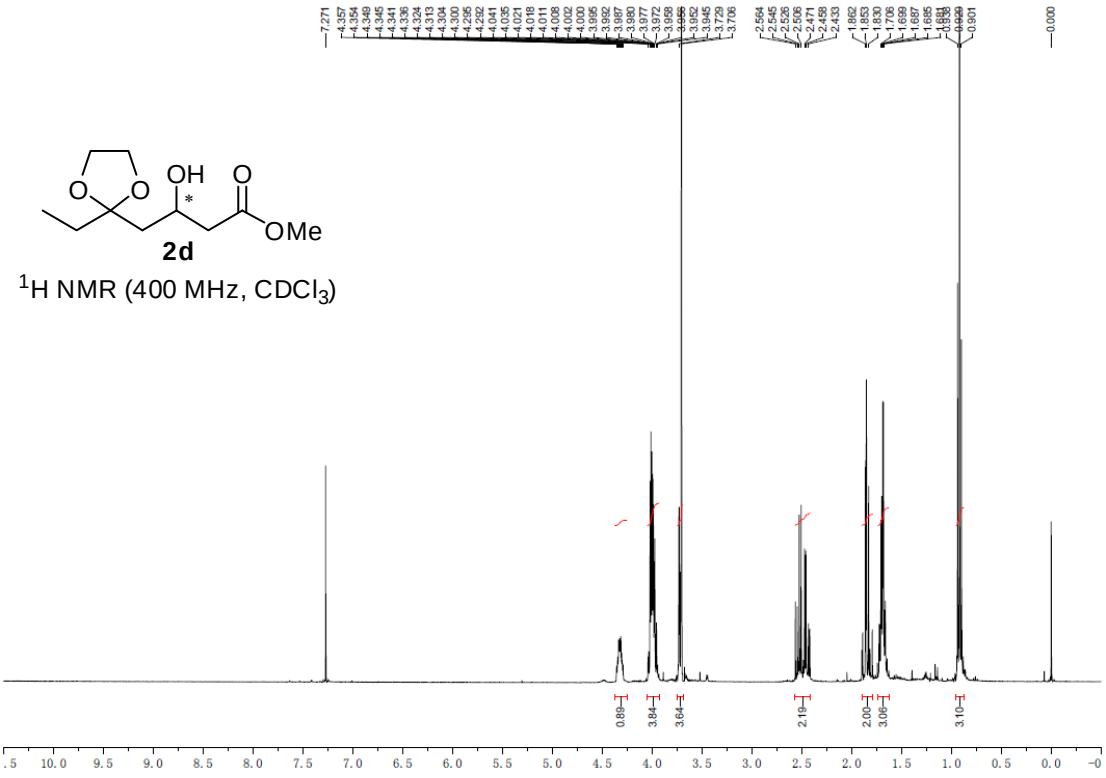
2c

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

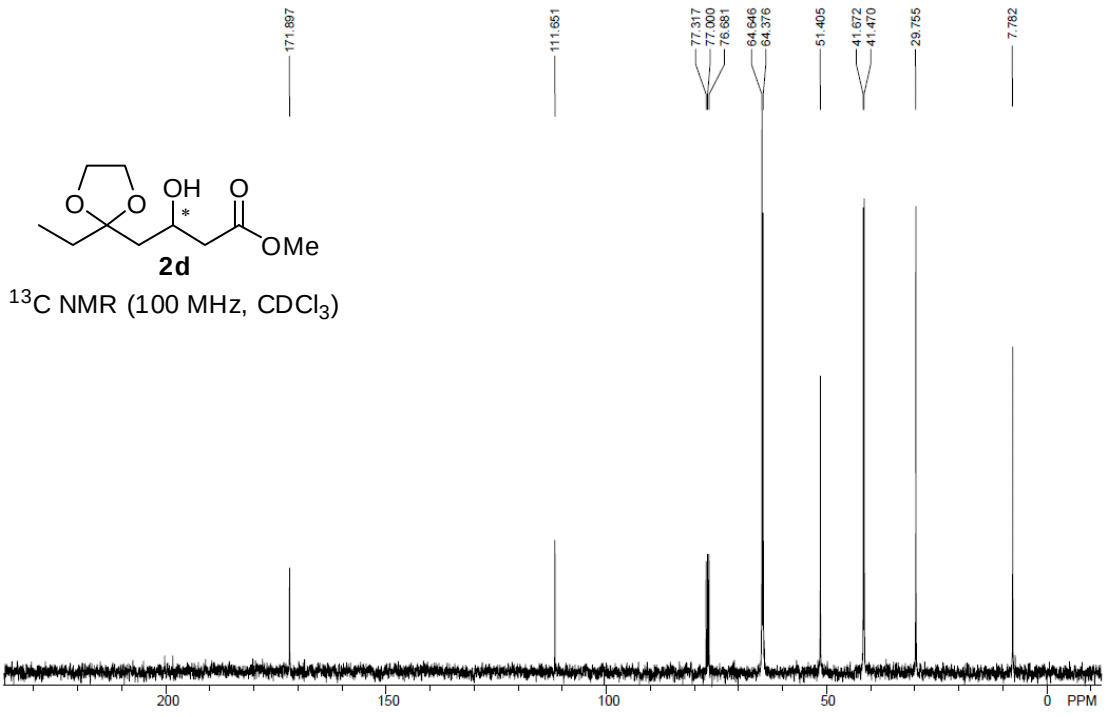


2c

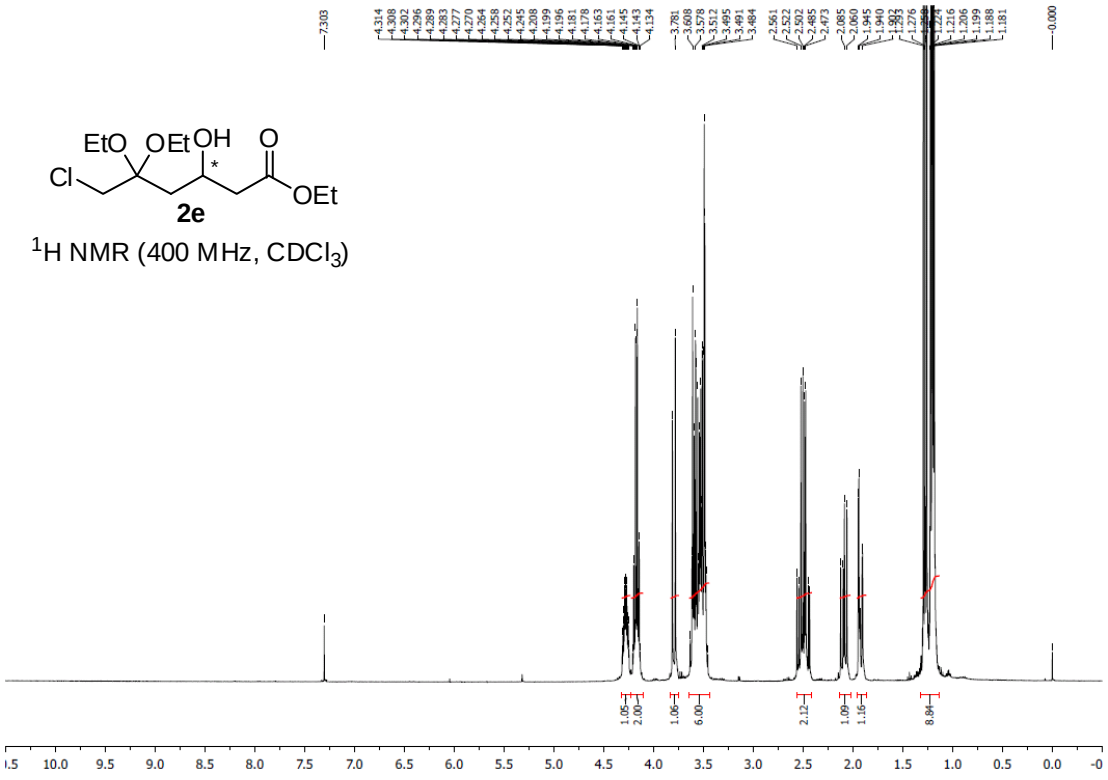
^{13}C NMR (100 MHz, $CDCl_3$)



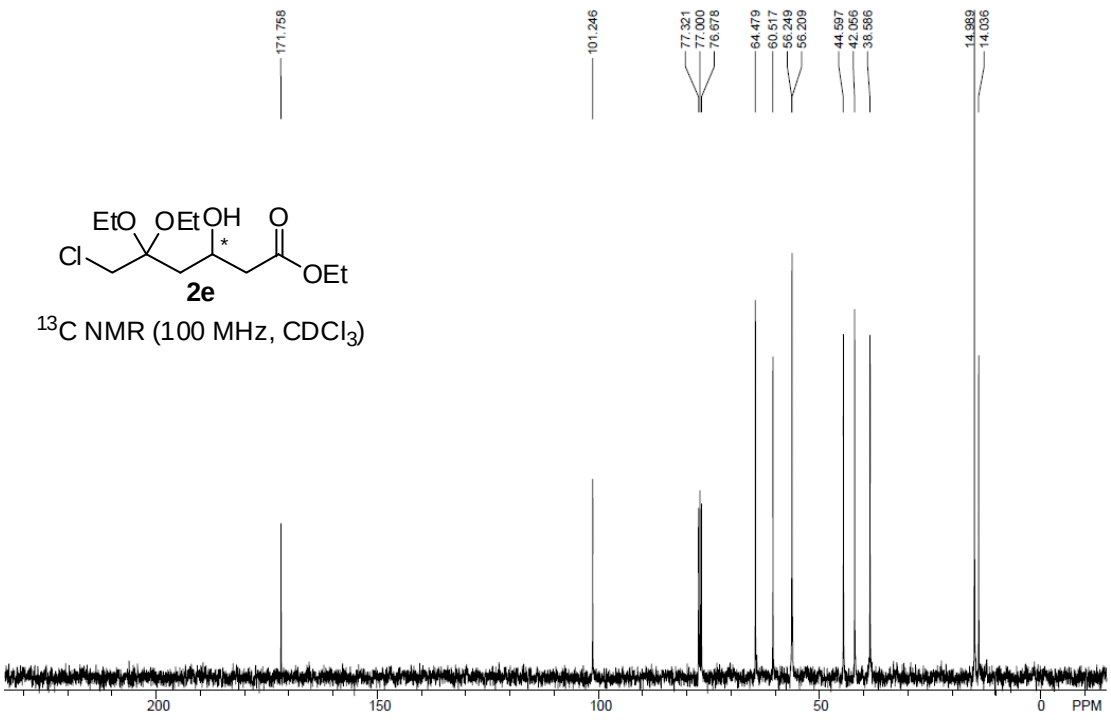
^{1}H NMR (400 MHz, $CDCl_3$)



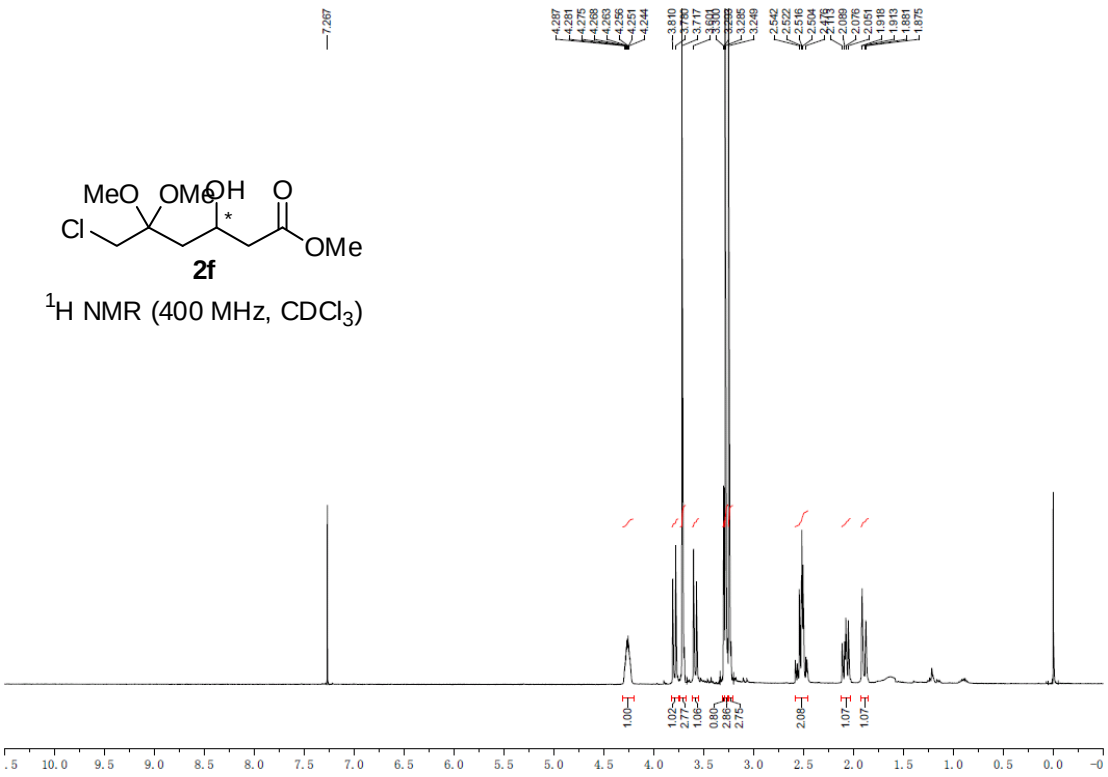
^{13}C NMR (100 MHz, $CDCl_3$)



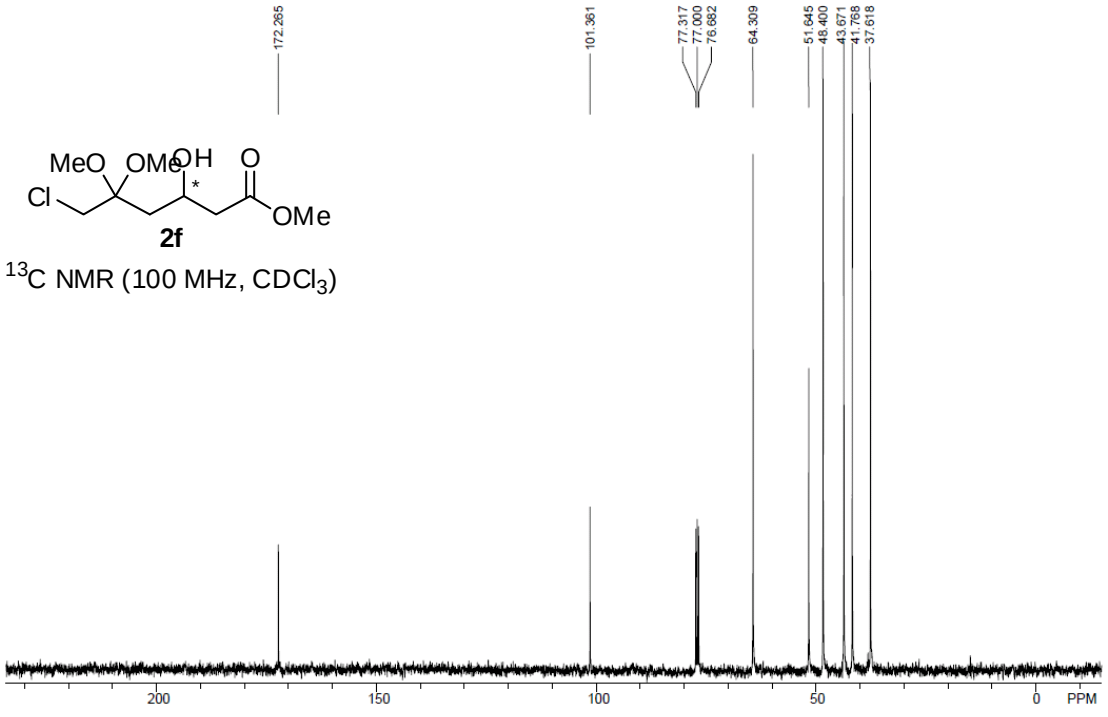
^{1}H NMR (400 MHz, $CDCl_3$)



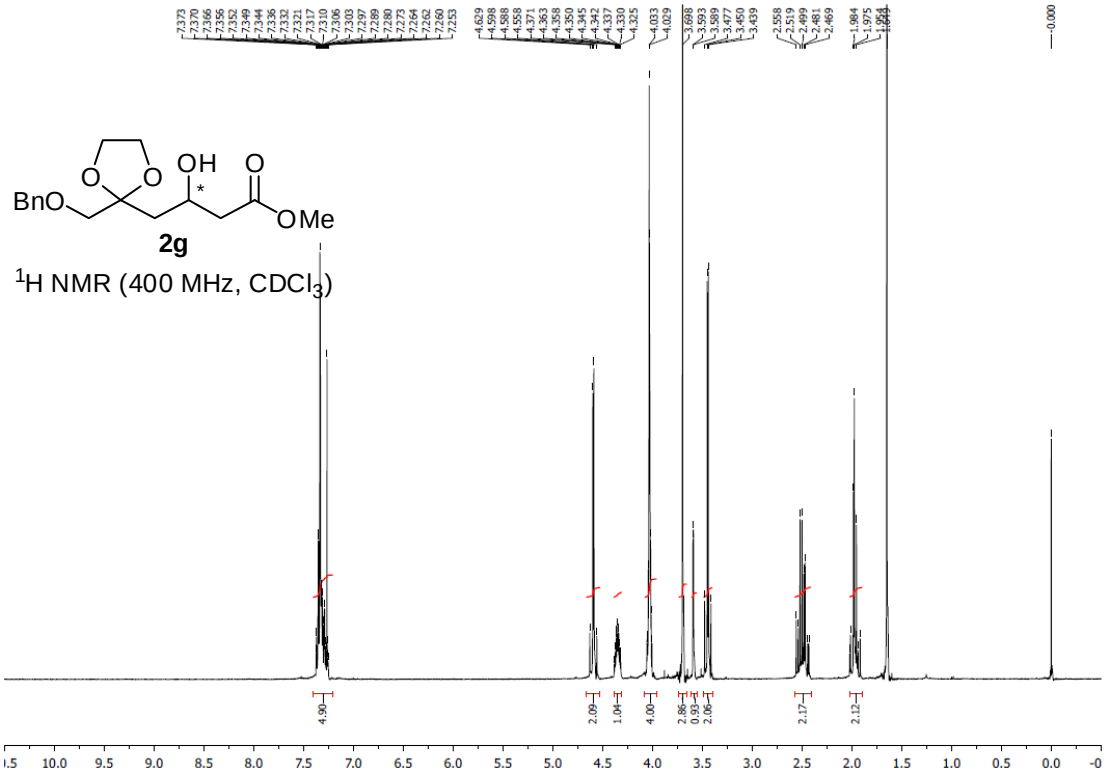
^{13}C NMR (100 MHz, $CDCl_3$)



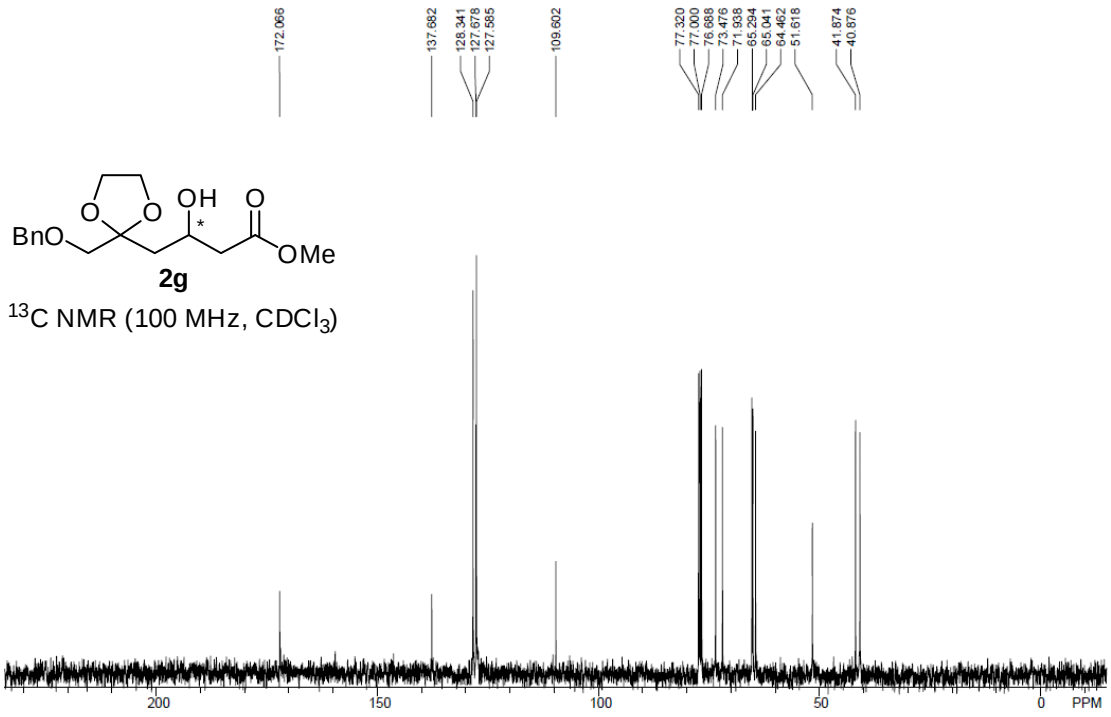
^{1}H NMR (400 MHz, $CDCl_3$)



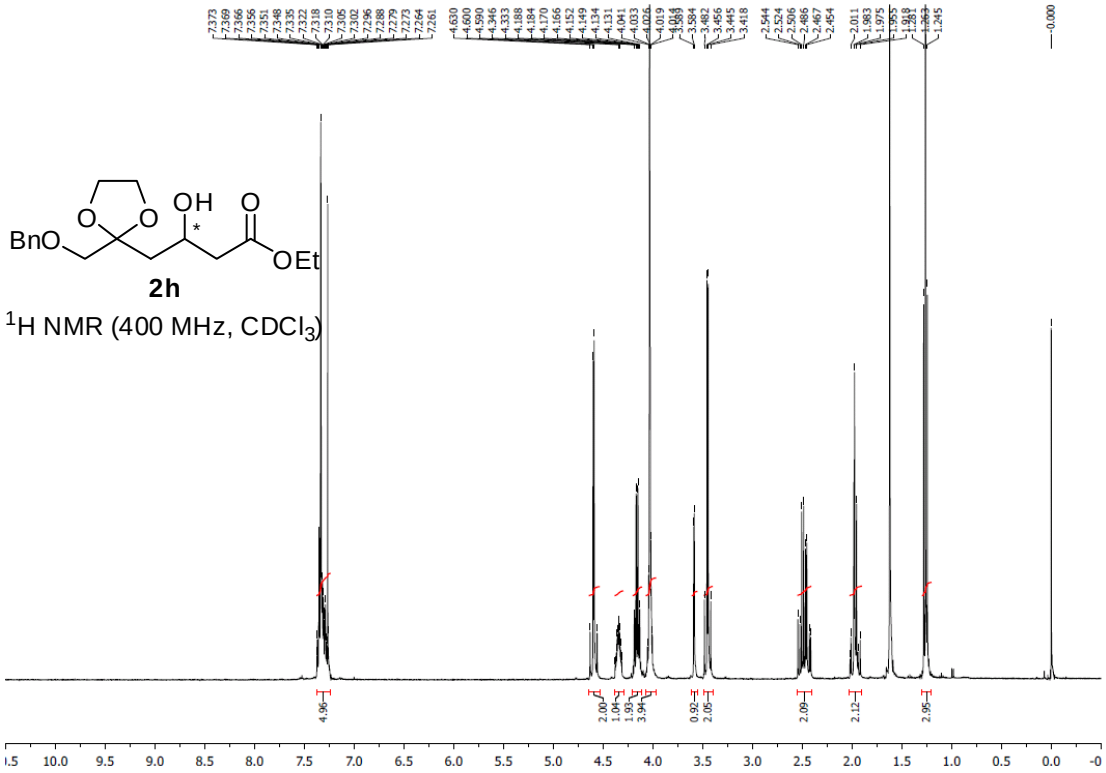
^{13}C NMR (100 MHz, $CDCl_3$)

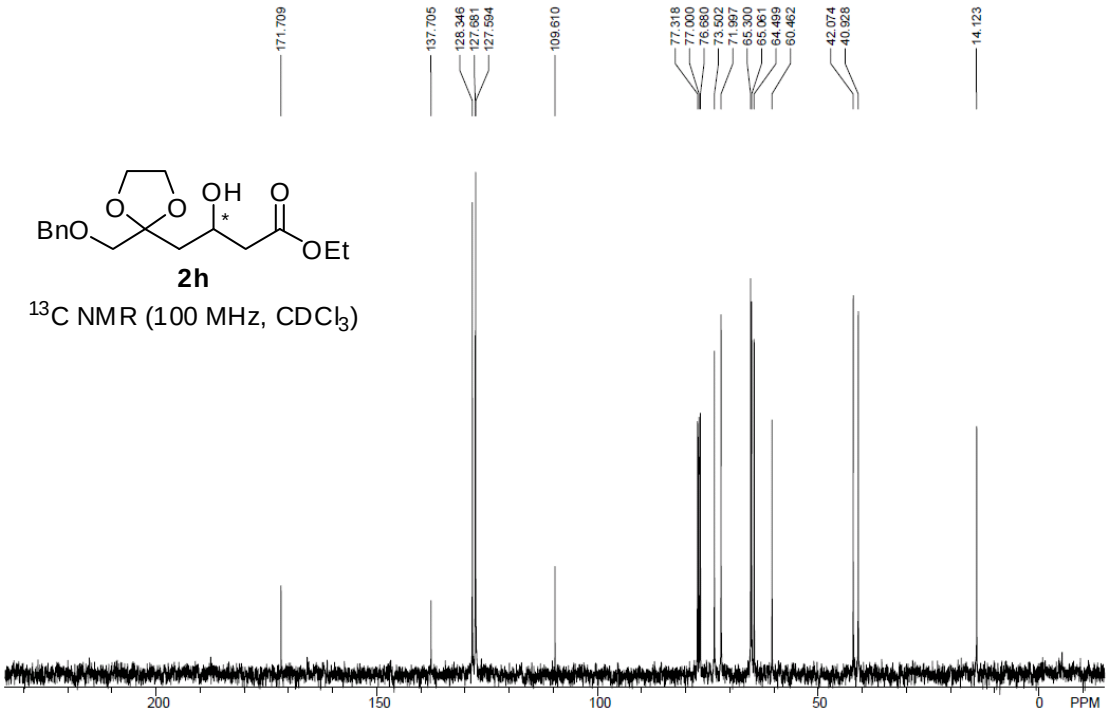


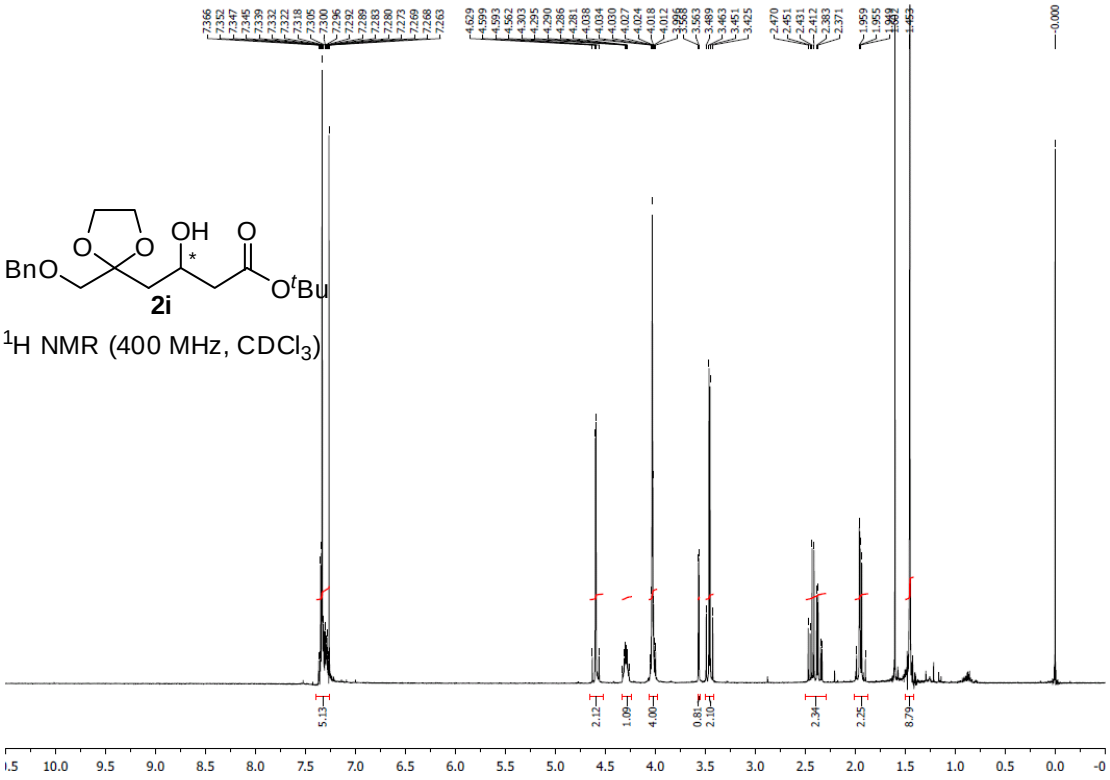
^{1}H NMR (400 MHz, $CDCl_3$)



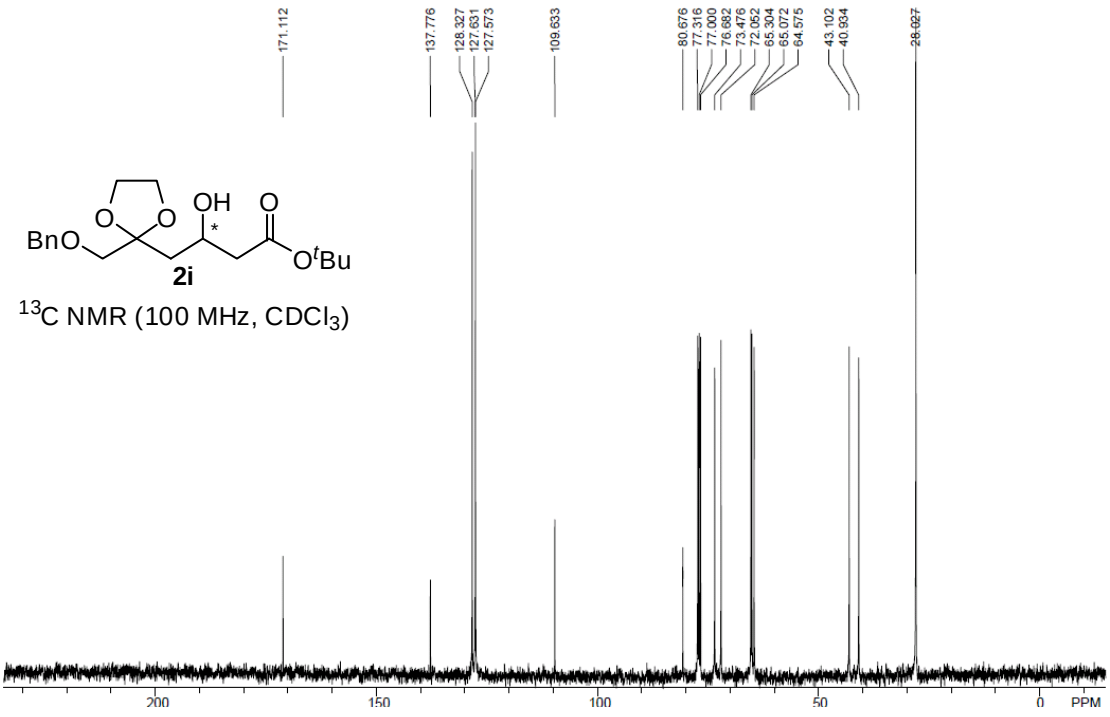
^{13}C NMR (100 MHz, $CDCl_3$)


BnO
OH
O
OEt
*
2h
1H NMR (400 MHz, CDCl3)

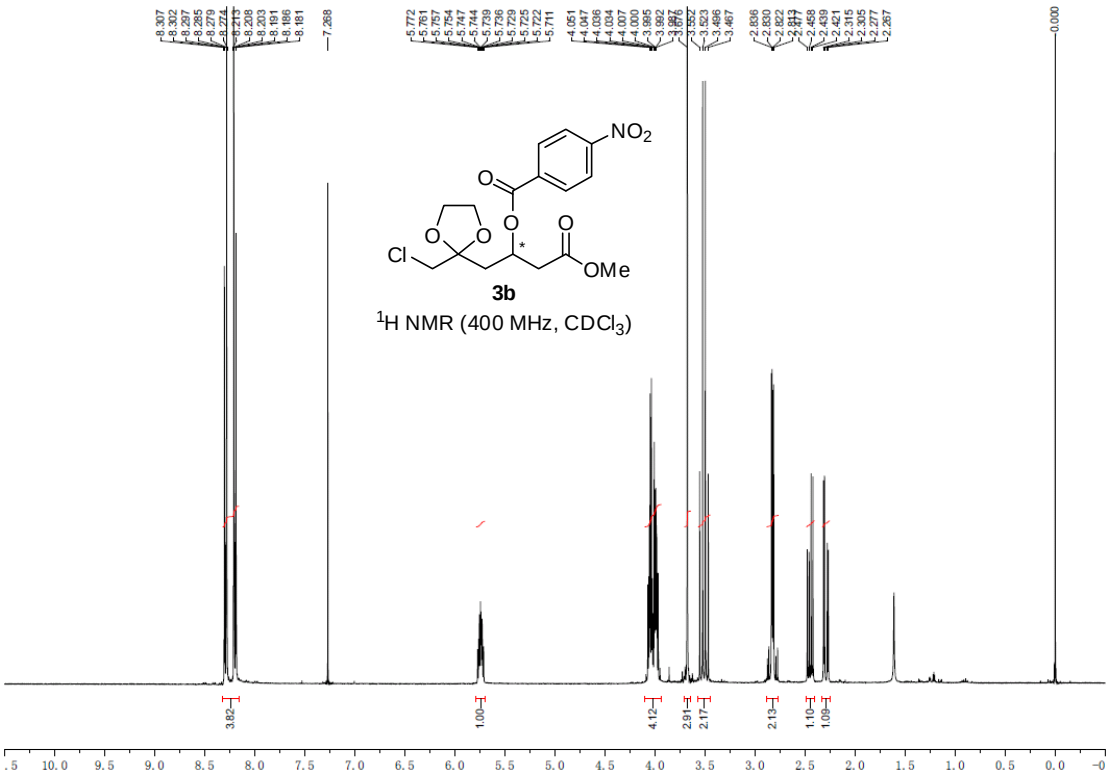

BnO
OH
O
OEt
*
2h
13C NMR (100 MHz, CDCl3)
PPM



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

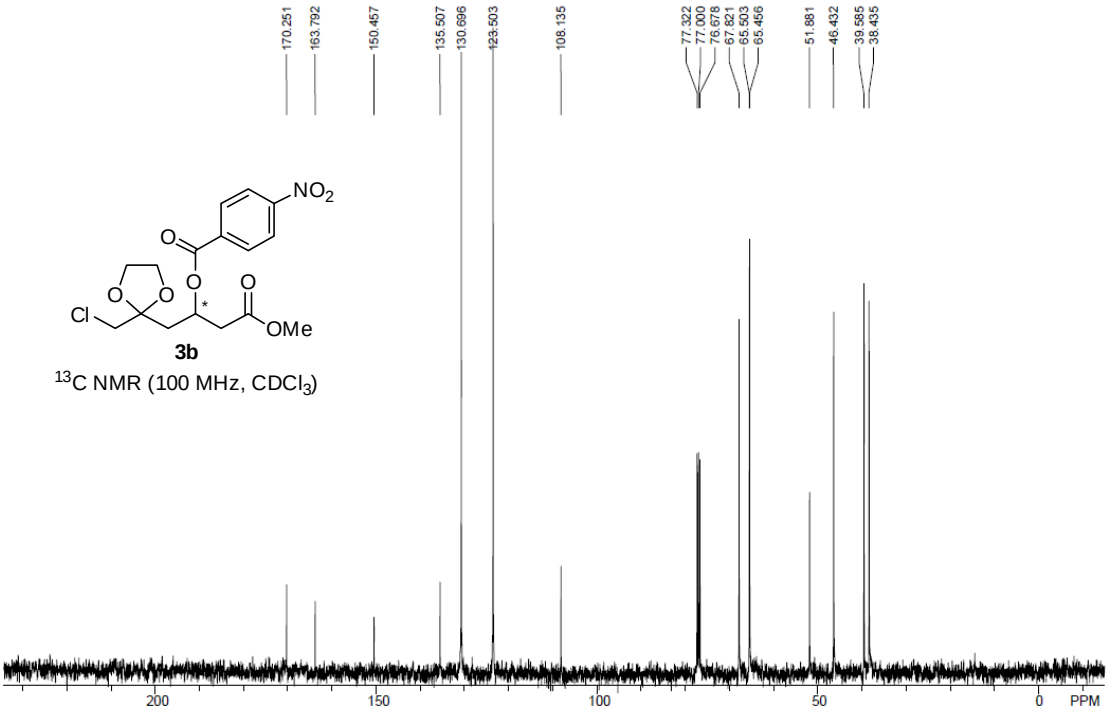


^{13}C NMR (100 MHz, $CDCl_3$)



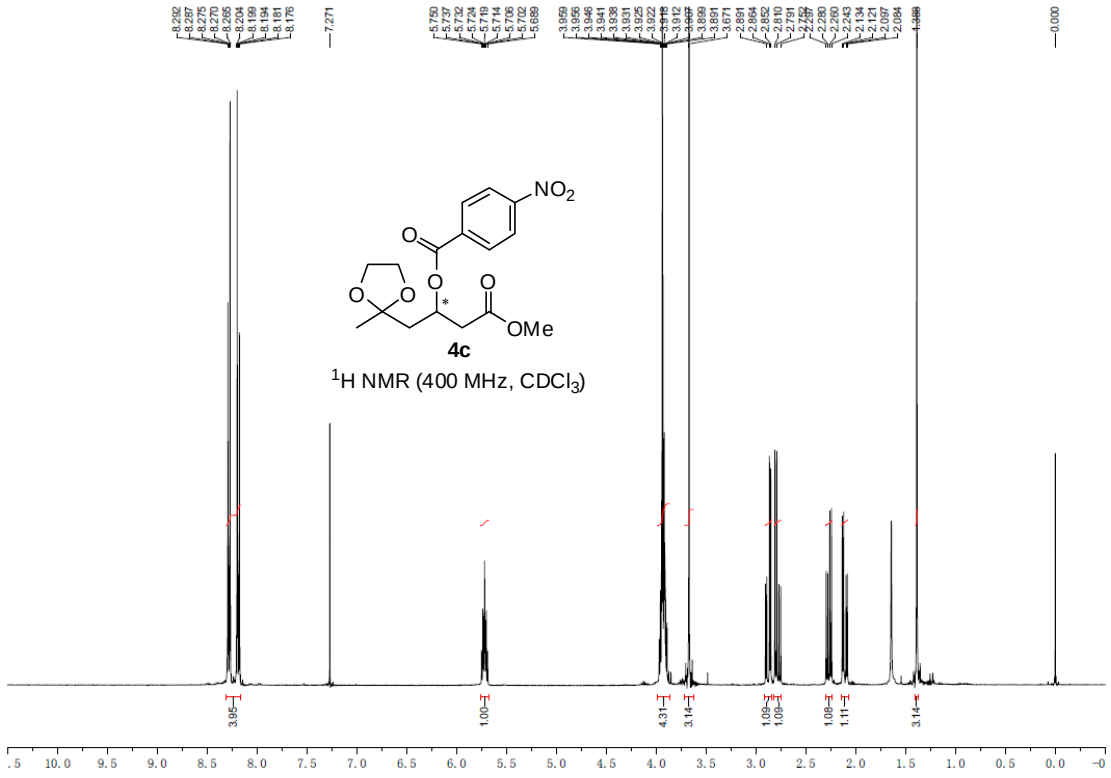
3b

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



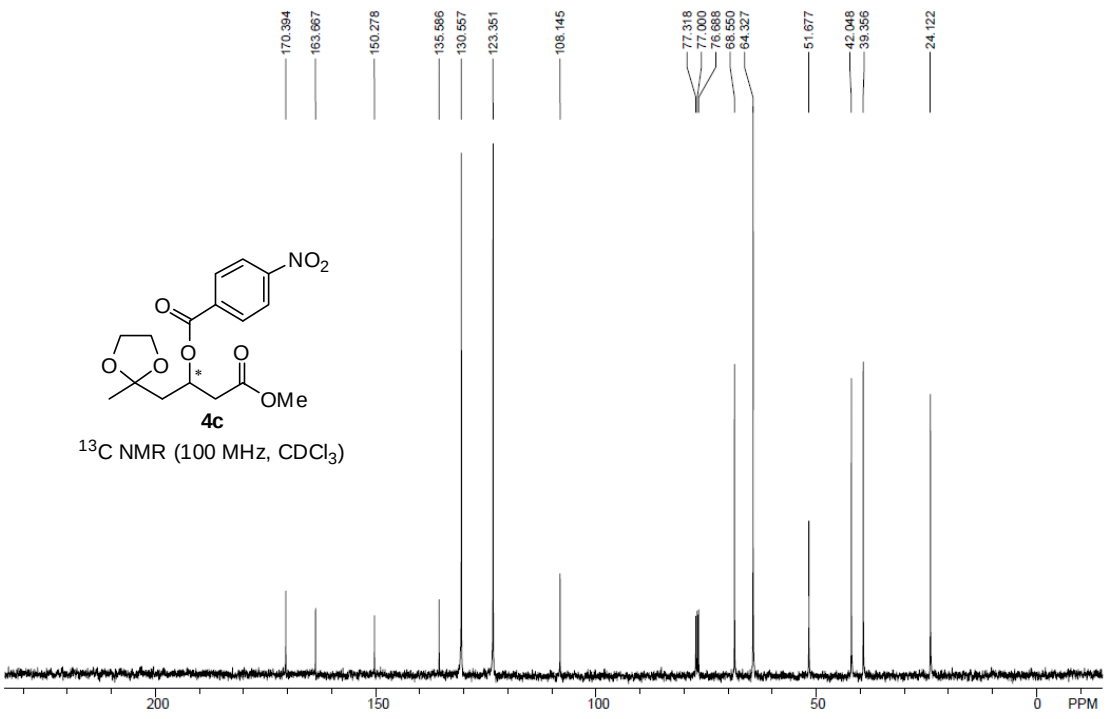
3b

^{13}C NMR (100 MHz, $CDCl_3$)



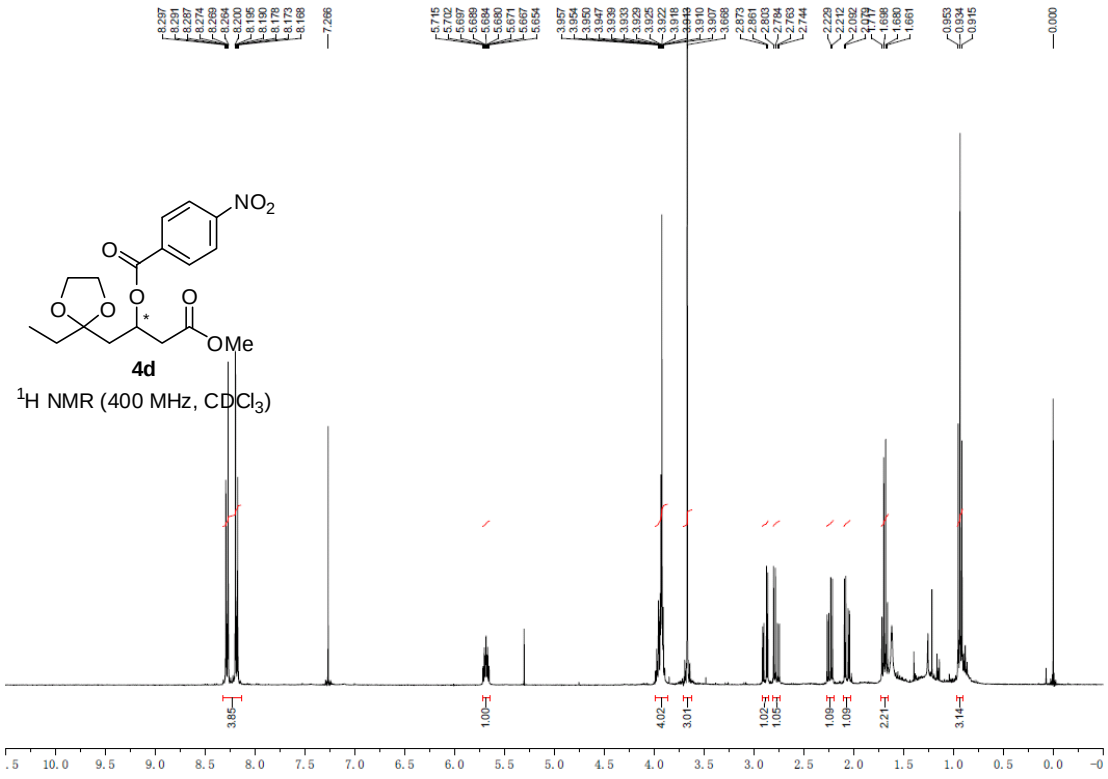
4c

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

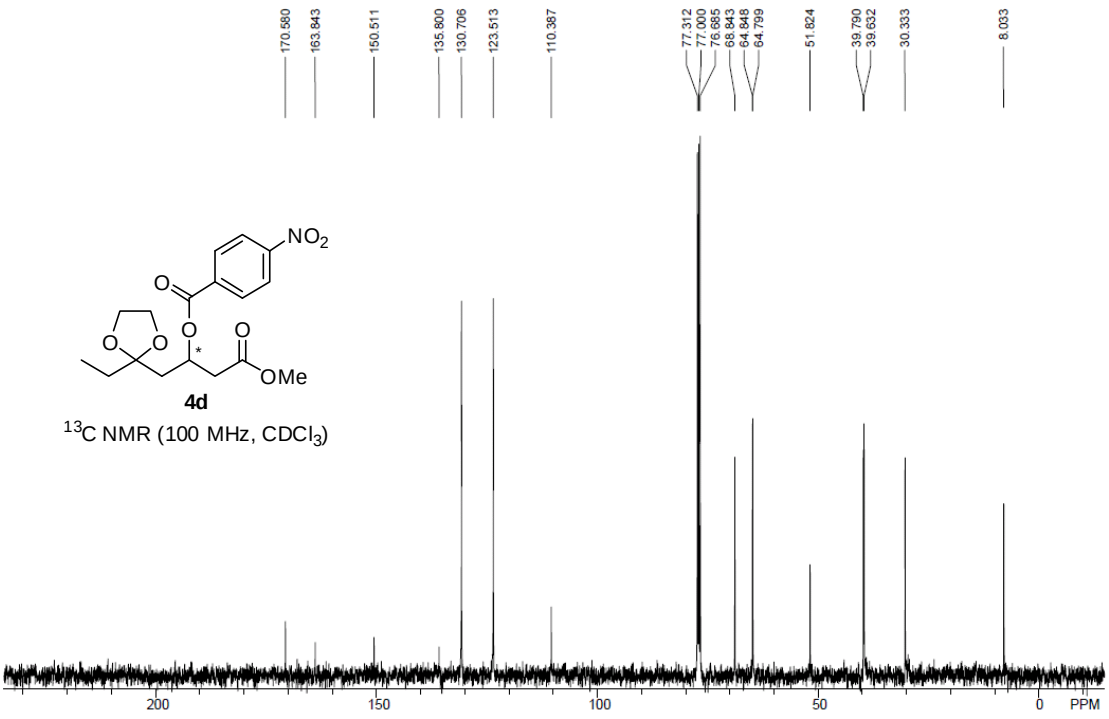


4c

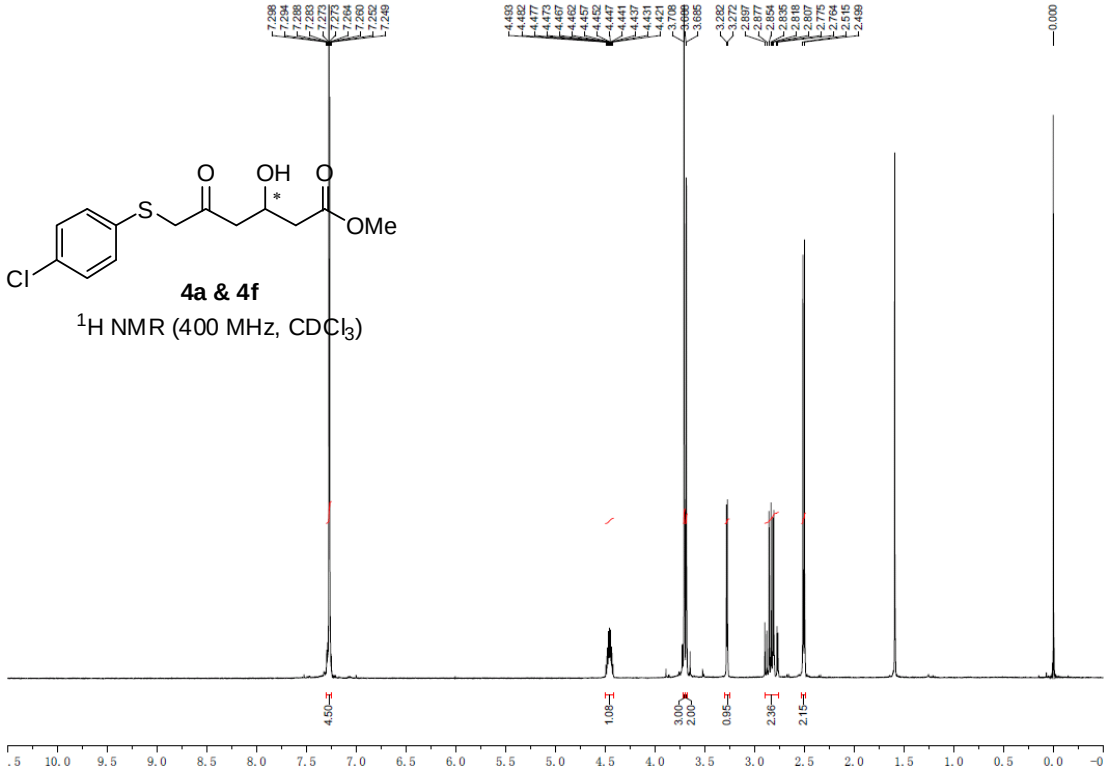
^{13}C NMR (100 MHz, $CDCl_3$)



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

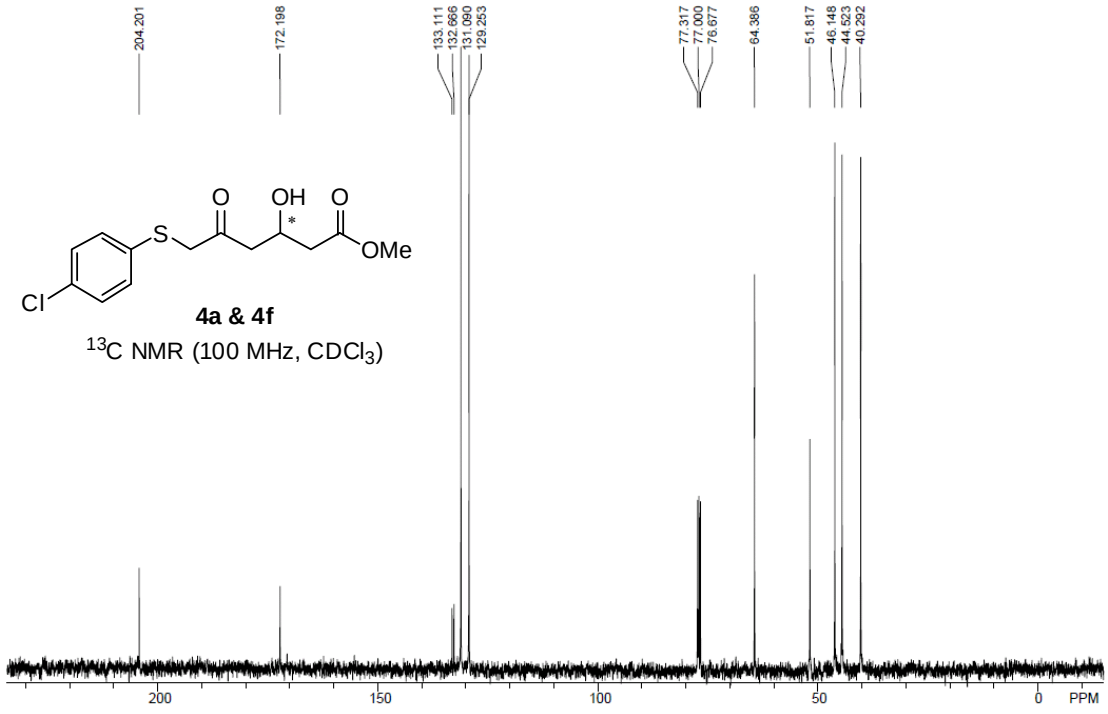


^{13}C NMR (100 MHz, $CDCl_3$)



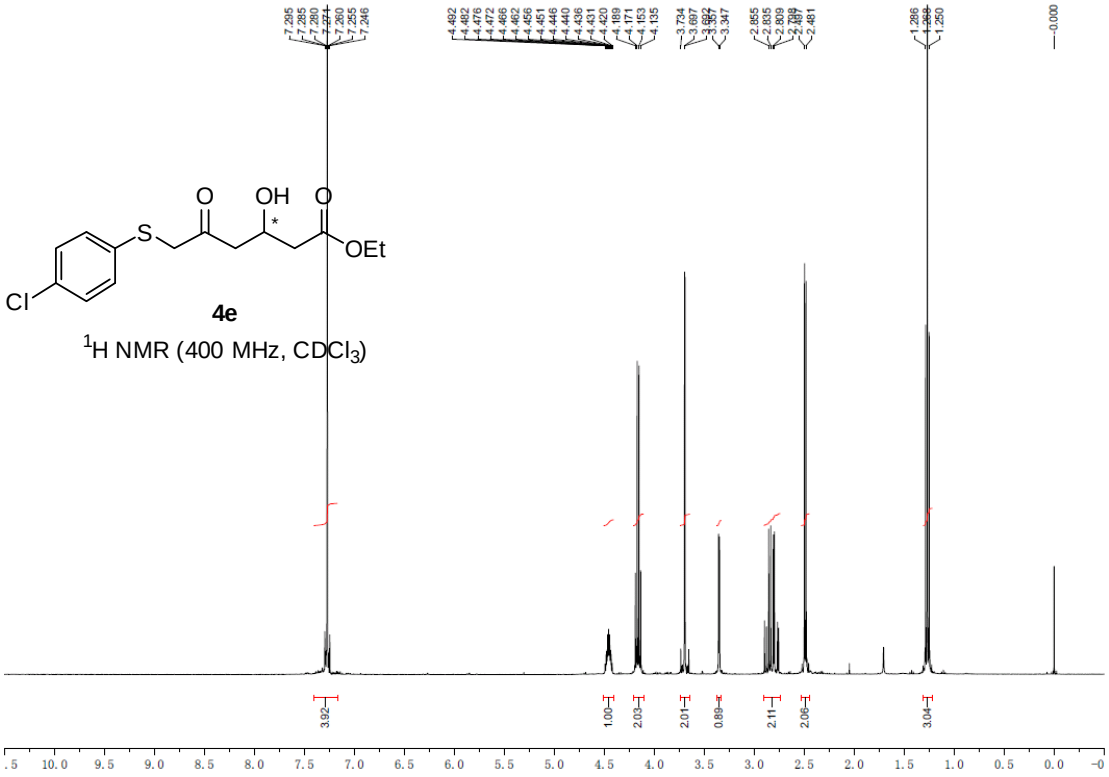
4a & 4f

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



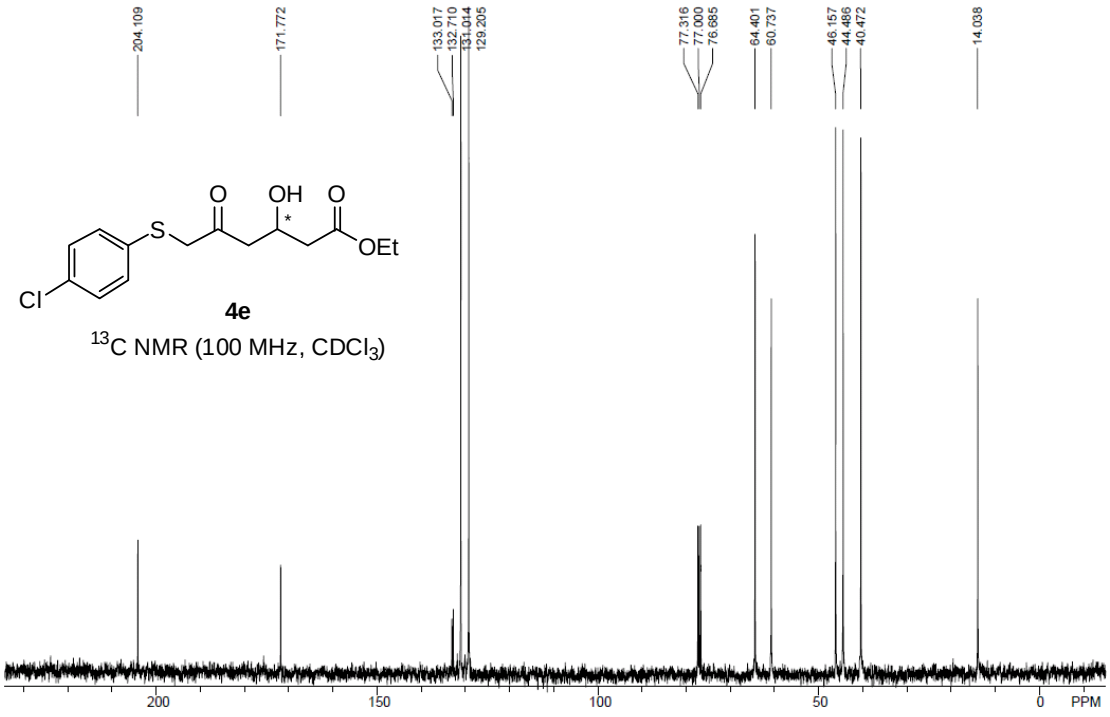
4a & 4f

^{13}C NMR (100 MHz, $CDCl_3$)



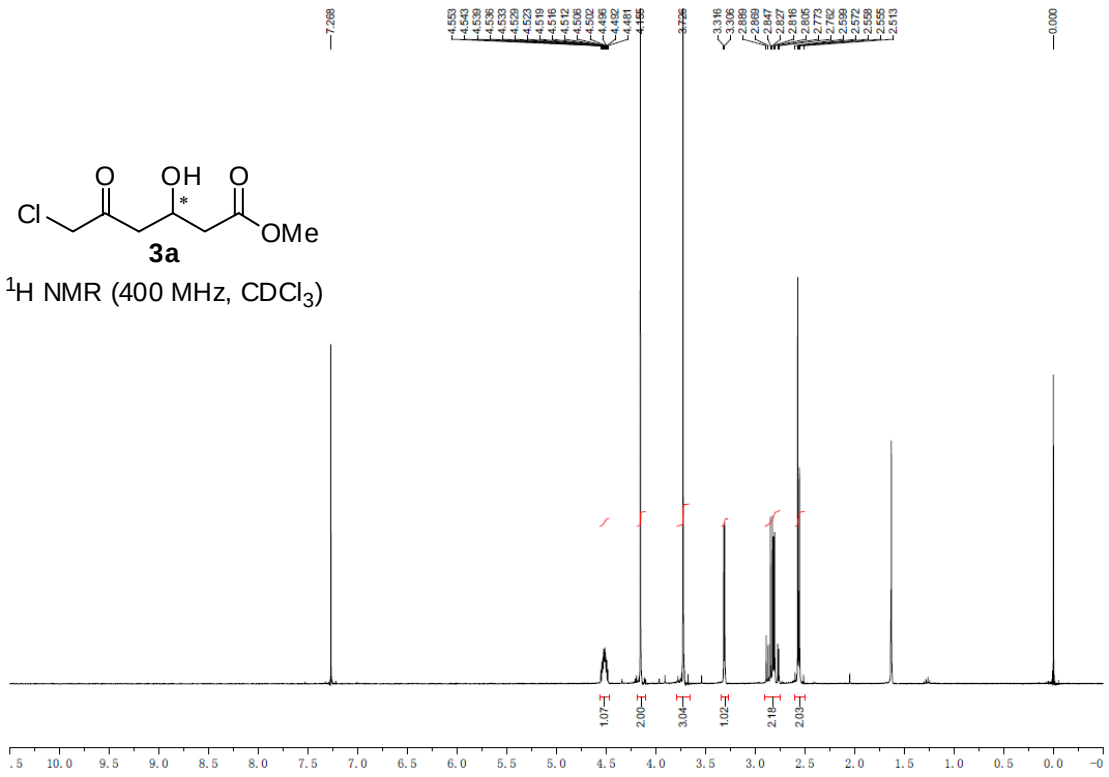
4e

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



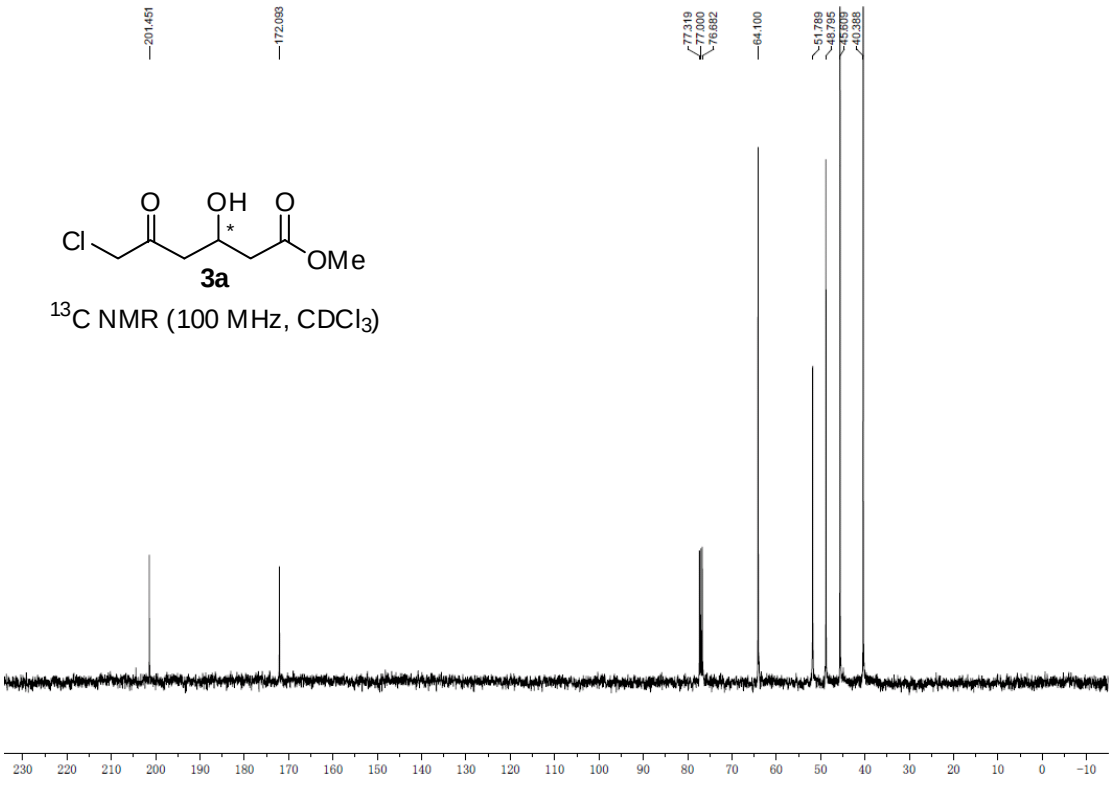
4e

^{13}C NMR (100 MHz, $CDCl_3$)



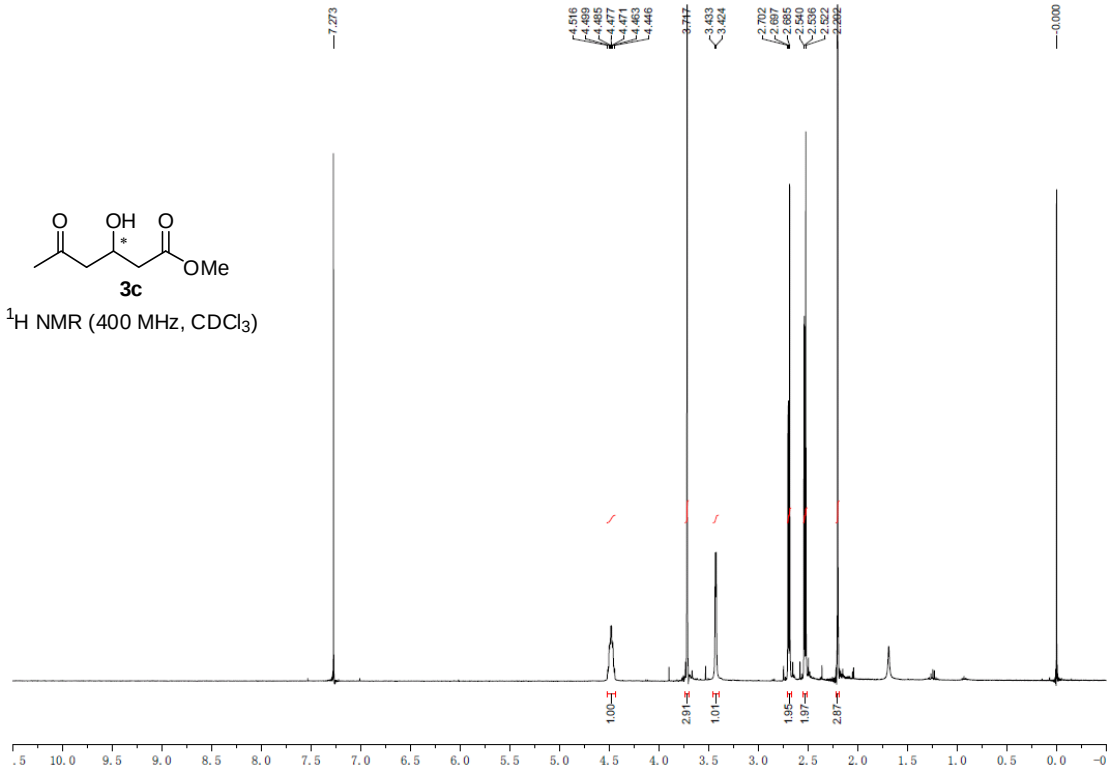
3a

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



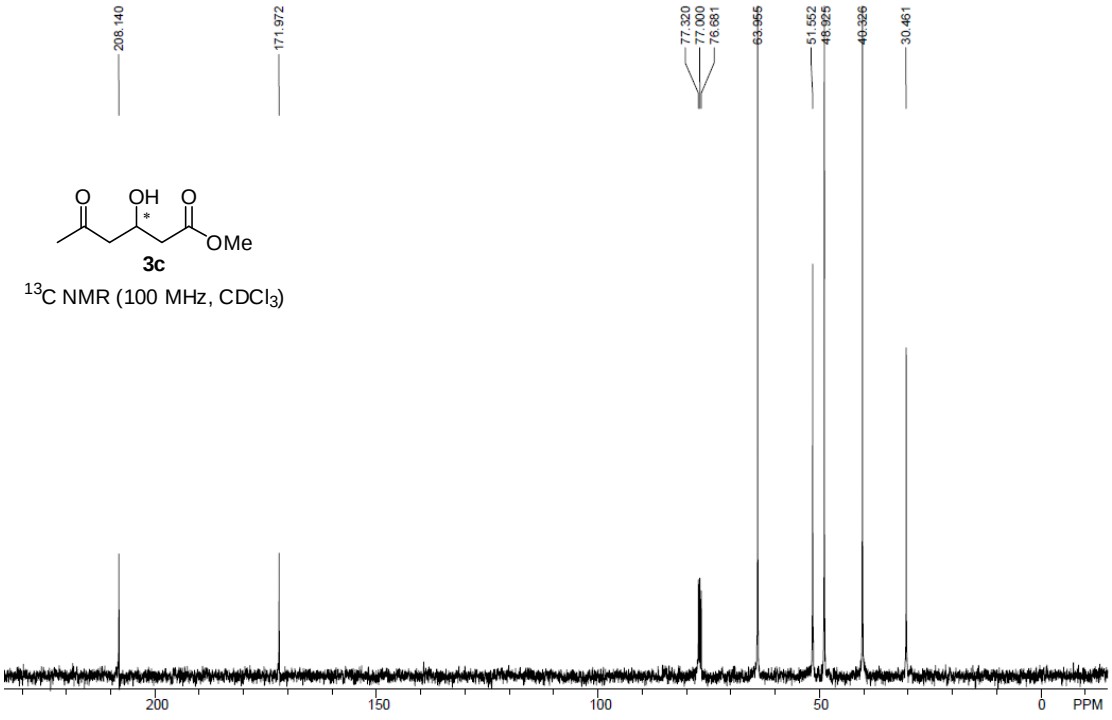
3a

^{13}C NMR (100 MHz, $CDCl_3$)



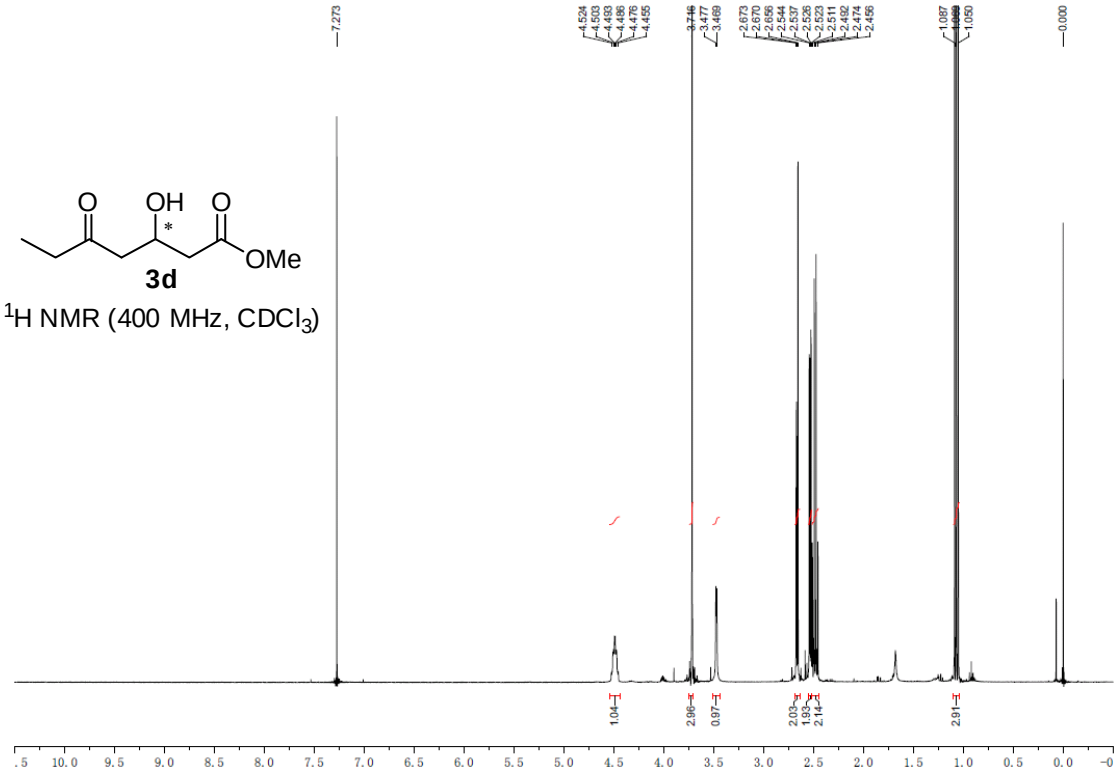
3c

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

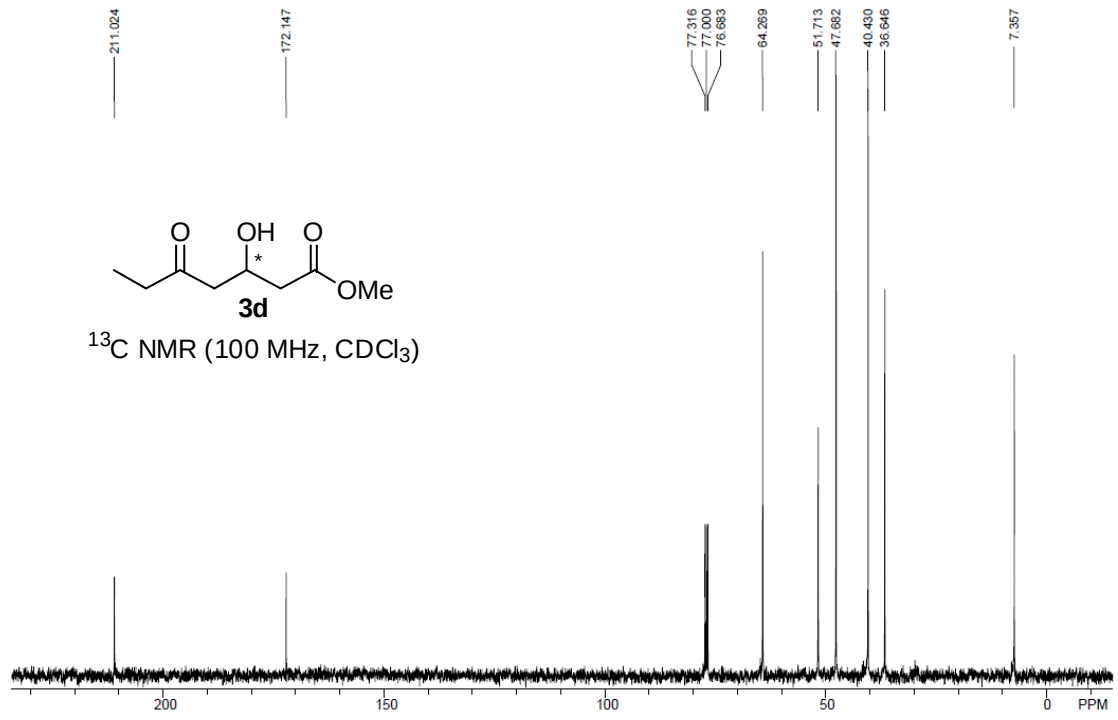


3c

^{13}C NMR (100 MHz, $CDCl_3$)



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



^{13}C NMR (100 MHz, $CDCl_3$)