The Role of the CAI-1 Fatty Acid Tail in the *Vibrio cholerae* Quorum Sensing Response

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Supporting Information

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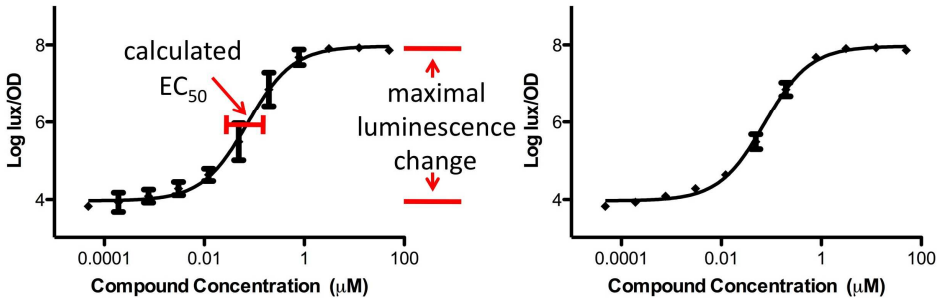
A. Primary bioassay data for all new compounds.

A.1. *Vibrio cholerae* Agonism Bioassay.

Reporter strain MM920 (*V. cholerae* Δ*cqsA* Δ*luxQ* carrying pBB1 cosmid, which contains the *V. harveyi luxCDABE* luciferase operon) was used to assay agonist activity of each synthetic compound. This strain was grown in LB medium containing 10 μg/mL tetracycline at 30 °C for >16 hours and diluted 20-fold with the same medium. Two μL of each synthetic compound dissolved in DMSO in various concentrations was added to 200 μL of the diluted reporter strain in triplicate in a 96-well plate. Bioluminescence and OD_{600} were measured in a PerkinElmer EnVision Multilabel Reader following 4-hour incubation at 30 °C with shaking. DMSO was used as the negative control.

A.1.1. Primary data for Table 1: Dose-response curves for compounds **1** and **6-12**.



Above is an example of typical dose response curve highlighting the data that is represented in the Tables presented in the manuscript. Both of the above dose-response curves were generated using GraphPad Prism 5 from the identical primary luminescence measurements.

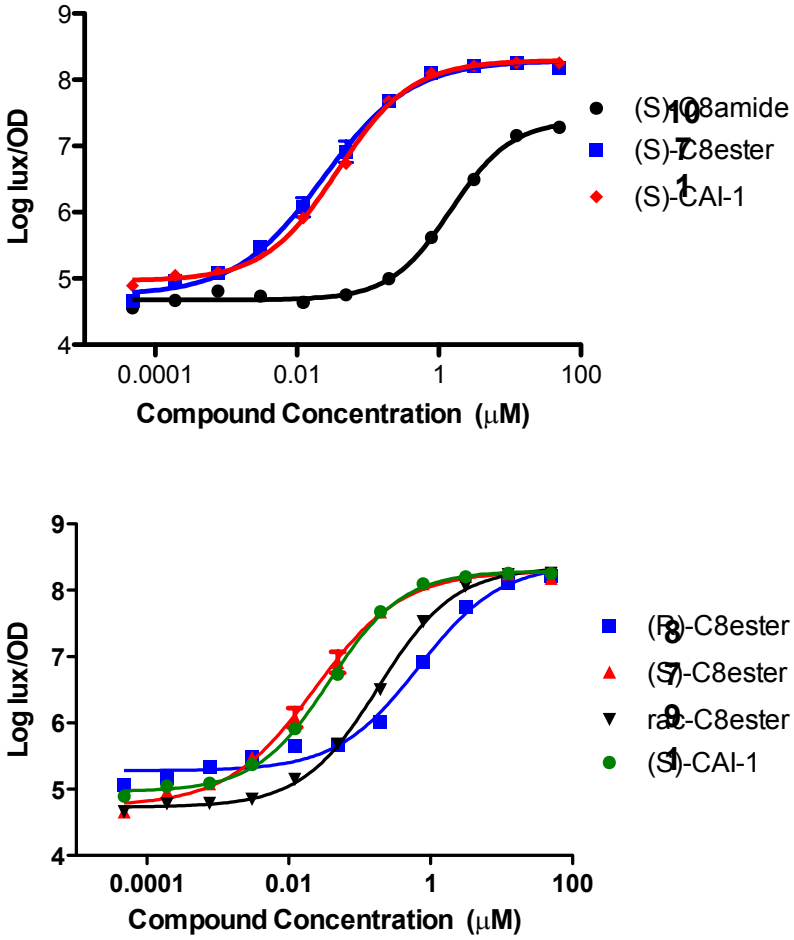
The dose-response curve on the left displays error bars that represent the 95% confidence intervals for each of the luminescence measurements. The curve on the right displays the standard deviation of the data.

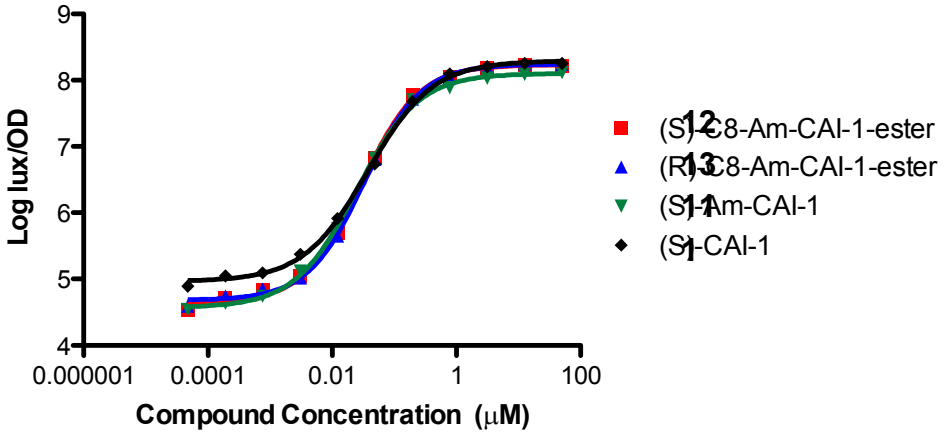
EC_{50} values were calculated by Prism 5 using standard settings and are described in the Tables and text in the manuscript with the error representing the 95% confidence interval for the calculated EC_{50} value.

The values for % response described in the Tables and text in the manuscript describe the maximal luminescence change for each of the analogs as a percent of CAI-1 (set at 100%) which was included as an standard of activity for each of the assays. The error described within the tables represents the 95% confidence intervals for this data expressed as a percentage. These values were calculated using standard methods for the propagation of error and include the 95% confidence interval for both the standard compound (CAI-1) as well as the 95% confidence interval for the response of the ester analog described. We note that while there is typically little variation in the maximal luminescence at saturation, there is some noise at low concentrations, compare for

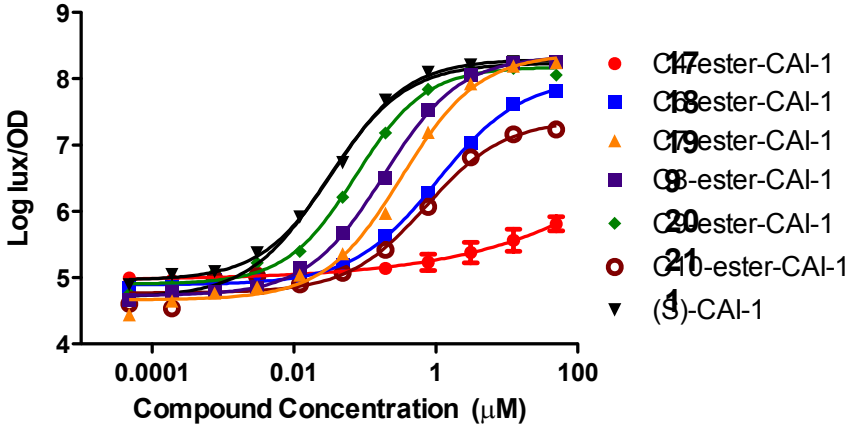
example the 95% confidence intervals for the points of low compound concentration and the points of high concentration on the left.

A.1.2. Primary data for Table 2: Dose-response curves for compounds **7-13**.

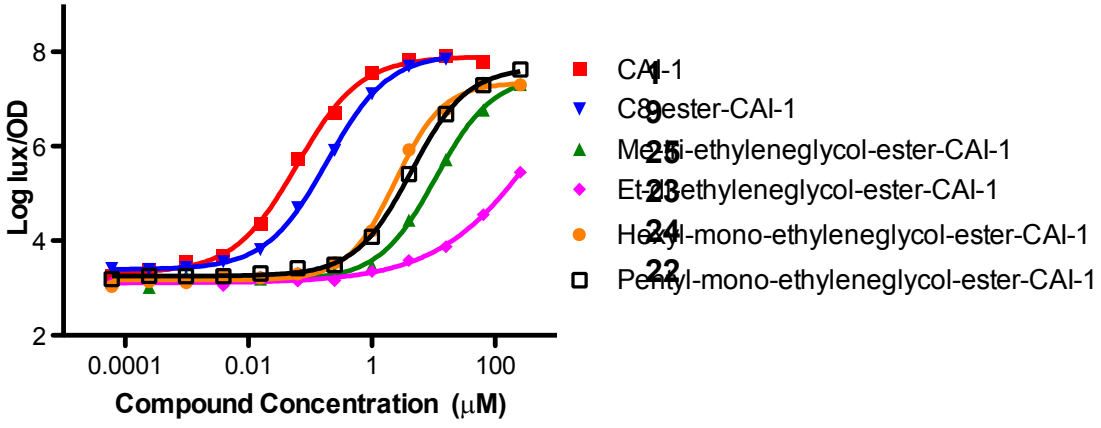




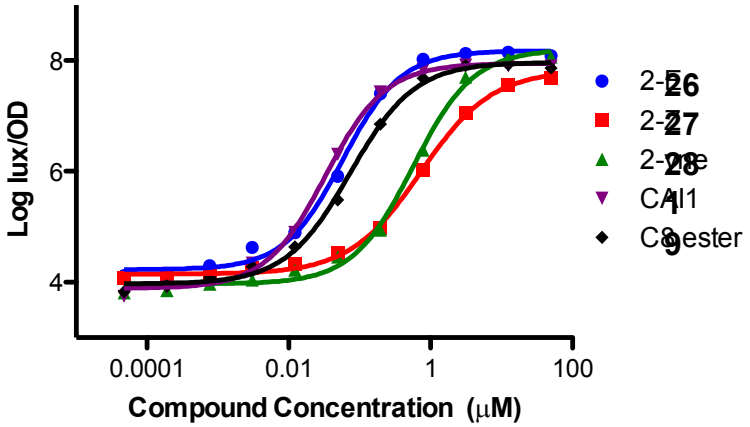
A.1.3. Primary data for Table 3: Dose-response curves for compounds **17-21**.

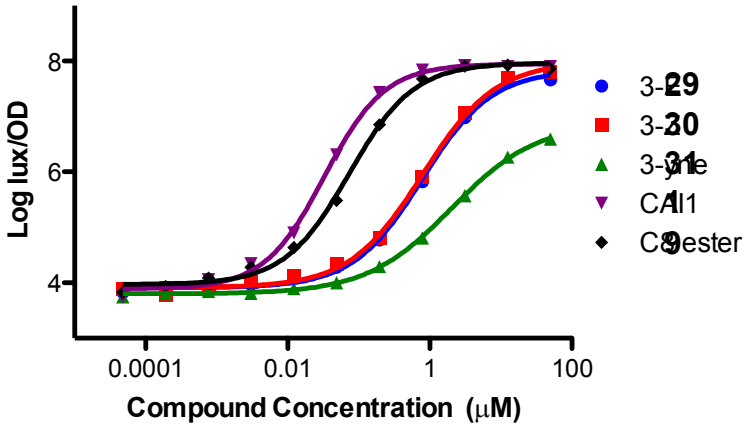


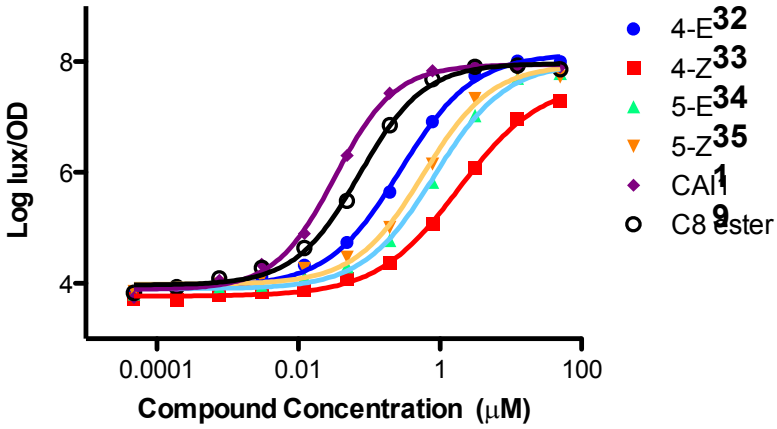
A.1.3. Primary data for Table 4: Dose-response curves for compounds **22-25**.



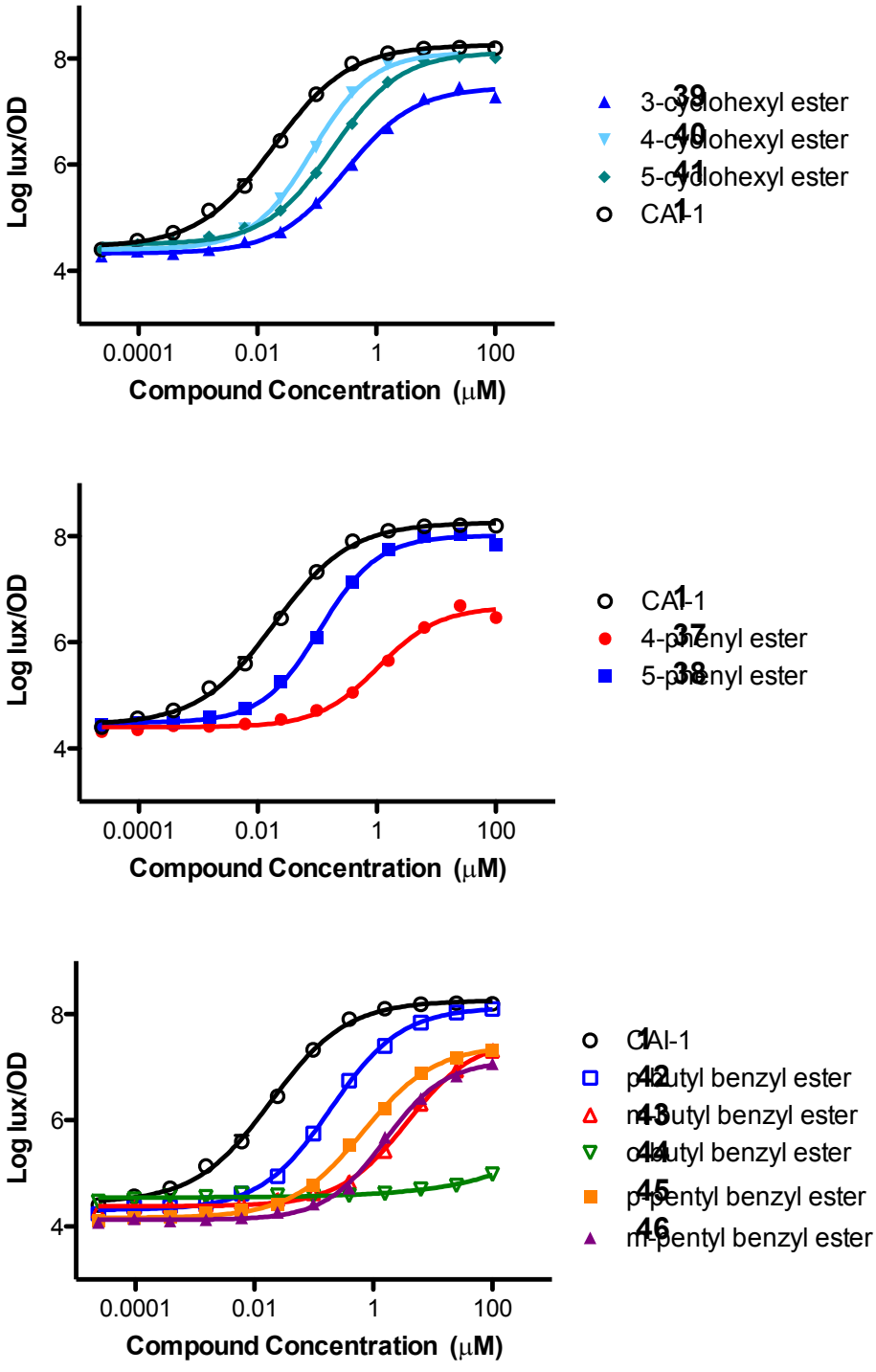
A.1.3. Primary data for Table 4: Dose-response curves for compounds **26-35**.

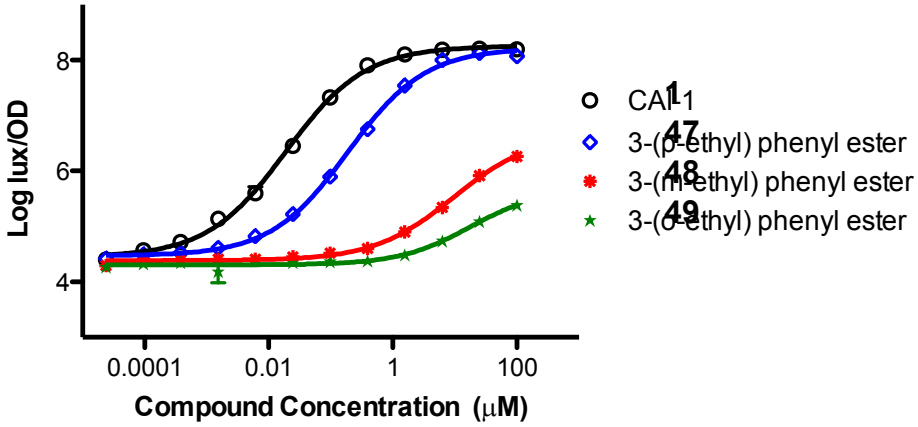






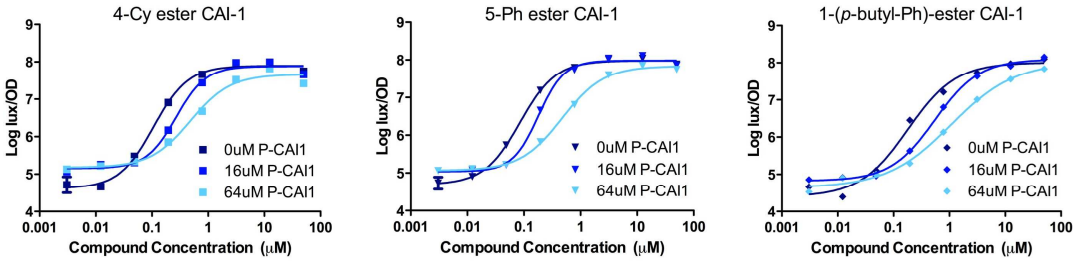
A.1.3. Primary data for Table 4: Dose-response curves for compounds **37-49**.





B. The CAI-1 ester analogs are competitive agonists of CqsS.

We previously described P-CAI-1 as a competitive antagonist of CAI-1.[1] Here we show that P-CAI-1 is similarly a competitive antagonist of selected CAI-1 ester analogs: 5-Ph-ester-CAI-1, **35**; 4-Cy-ester-CAI-1, **37**, and 1-(*p*-butyl-Ph)-ester-CAI-1, **39**. Increasing concentrations of P-CAI-1 increase the EC_{50} values of the CAI-1 esters for *luxCDABE* expression, while increasing concentrations of the CAI-1 ester analogs alleviate antagonism.



P-CAI-1 added (μM)	4-Cy ester CAI-1, **40** EC_{50} (μM)	5-Ph ester CAI-1, **38** EC_{50} (μM)	1(*p*-butyl-Ph) ester CAI-1, **42** EC_{50} (μM)
0	0.11±0.020	0.085±0.12	0.18±0.044
16	0.27±0.041	0.18±0.019	0.55±0.052
64	0.48±0.12	0.47±0.24	1.1±0.66

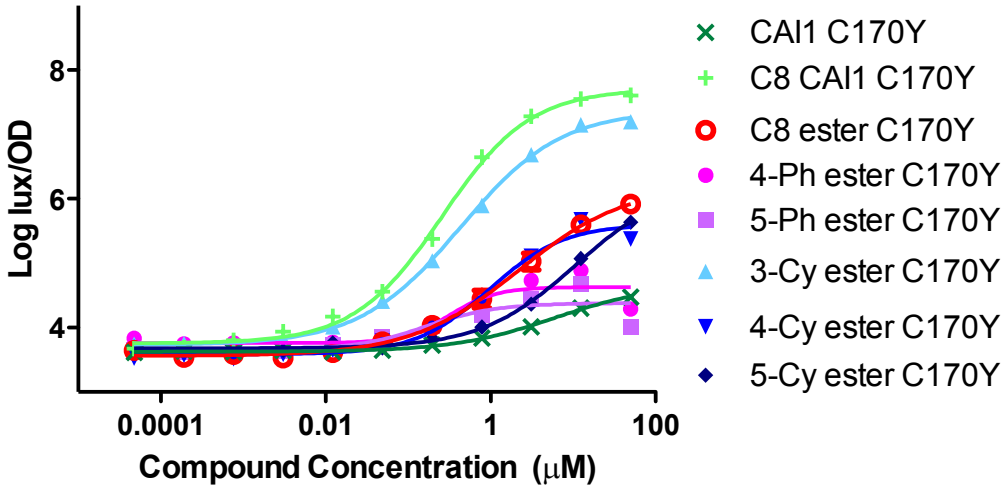
C. Bioassay with mutant CqsS receptors.

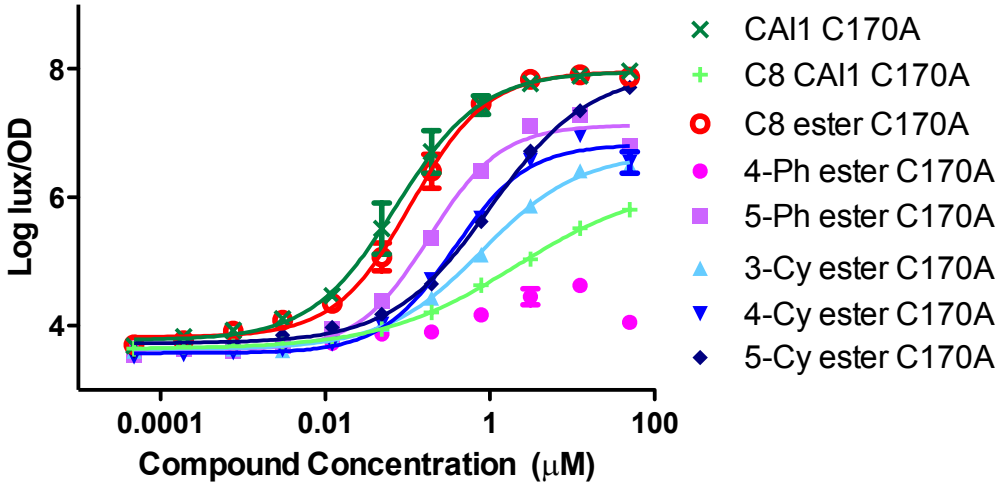
C.1. Bacterial strains and media.

Construction of CqsS C170Y and CqsS C170A mutants

The *cqsS*^{C170Y} and *cqsS*^{C170A} mutations were first reported in [2,3] that alter the *Vibrio cholerae* CqsS receptor specificity to CAI-1 type ligands. To introduce these mutations to the genome of *Vibrio cholerae*, these two *cqsS* alleles were first cloned into the suicide vector pKAS32 [4] resulting in plasmids WN1957 (C170Y) and WN1961 (C170A), respectively. These two *cqsS* mutations were subsequently introduced into the genome of the *V. cholerae* strain WN1170 (Δ*cqsA* Δ*luxQ*) as described previously [4], resulting in WN1977 (Δ*cqsA* Δ*luxQ cqsS*^{C170Y}) and WN1982 (Δ*cqsA* Δ*luxQ cqsS*^{C170A}). The presence of the desired *cqsS* mutation was confirmed by sequencing. The *luxCDABE* operon from *Vibrio harveyi* carried on cosmid pBB1 was introduced into WN1977 and WN1982 by conjugation, yielding strain WN1989 andWN1994, respectively. Quorum-sensing dependent response from these *V. cholerae* strains was monitored by measuring bioluminescence in the presence of different ligands.

C.2. Primary data for Table 6: Dose response curves for CAI-1, C8-CAI-1 and CAI-1 ester analogs in CqsS mutants C170Y CqsS and C170A CqsS.





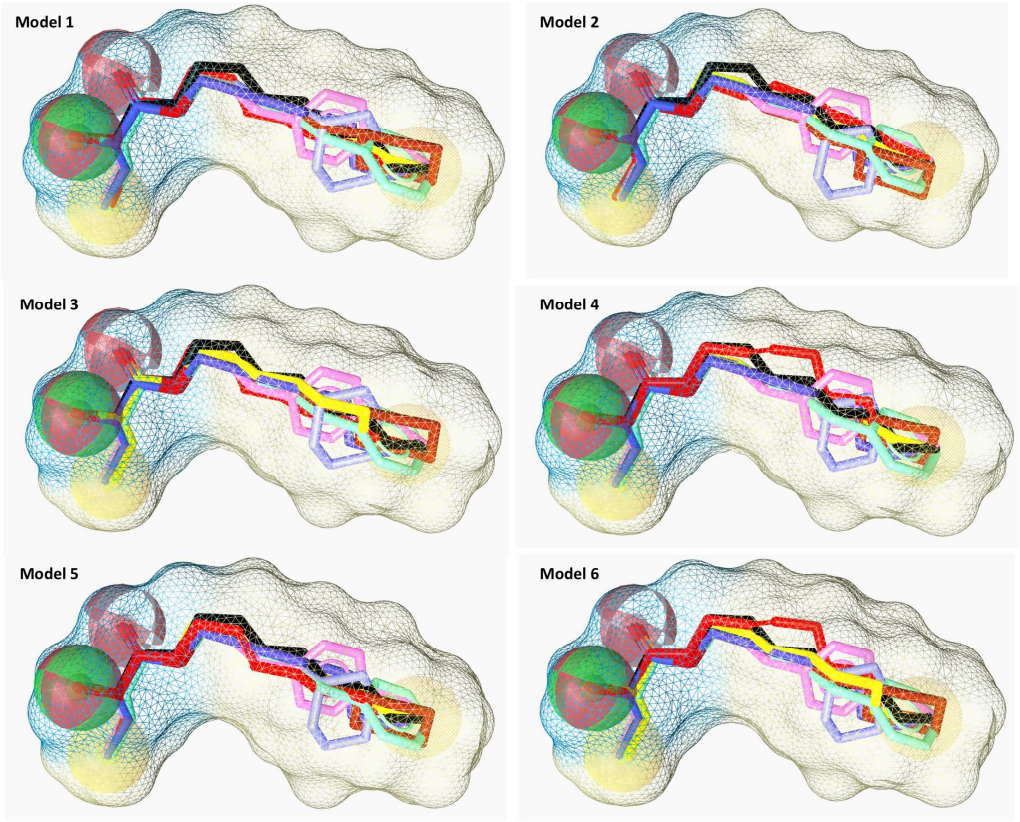
D. Development of a Pharmacophore Model.

Pharmacophore model generation was carried out using the software Ligand Scout. Ligand Scout version 3.03b (inteligand.com) was used. Ligand Scout generates ligand based as well as structure-based Pharmacophore models based on sophisticated algorithms for performing alignments and interpreting ligand–macromolecule interactions. It generates customized and highly specific 2D as well as 3D pharmacophore models and number of successful applications have been published. [5 6 7]

The "Training Set" consisting of eight CAI-1 ester analogs that we had identified during our SAR studies. The compounds selected all displayed EC_{50} values of less then 0.2 μM and were capable of activating greater than 92% of the maximal quorum sensing response. A ligand-based pharmacophore was generated for the selected data. For pharmacophore generation, the sdf files of the data set, all as the (*S*)-stereoisomer, were provided as an input. Sdf files of the data set were obtained from ChemDraw Ultra using iBabel for file conversion. The sdf files were imported into Ligand Scout and an unbiased pharmacophore model was generated using the default "BEST" settings, generating 500 unique conformers of each of the ligands and a aligning each pharmacophore conformer to provide 10 best fit models which served as the pharmacophore model.

The use of fewer analogs in pharmacophore model generation or the use of the "FAST" setting, only generating 25 conformers of each of the analogs, provided a series of "best fit" pharmacophore models that were structurally distinct from each other. This feature likely arises from the broad range of possible tail conformations that are accessible to the molecules within this series. Using the settings described above, however, resulted in the generation of a consensus pharmacophore model which we describe in the manuscript and employed for all further modeling. Notably among the 10 "best fit" models only subtle structural variations are observed between the conformations of the biologically active analogs used to generate the pharmacophore model and the overall molecular topology is highly similar (Figure S1).

Subsequent modeling of inactive analogs ("Test Set" Compounds) was achieved using the pharmacophore model generated above and including a series of analogs displaying lower biological activity as "Test Set" analogs. It is notable that clear deviation from the consensus pharmacophore model is observed in many of these cases providing rational for the lower activity observed with certain compounds. Examples of the "best fit" models for the compounds with lower biological activity are provided.



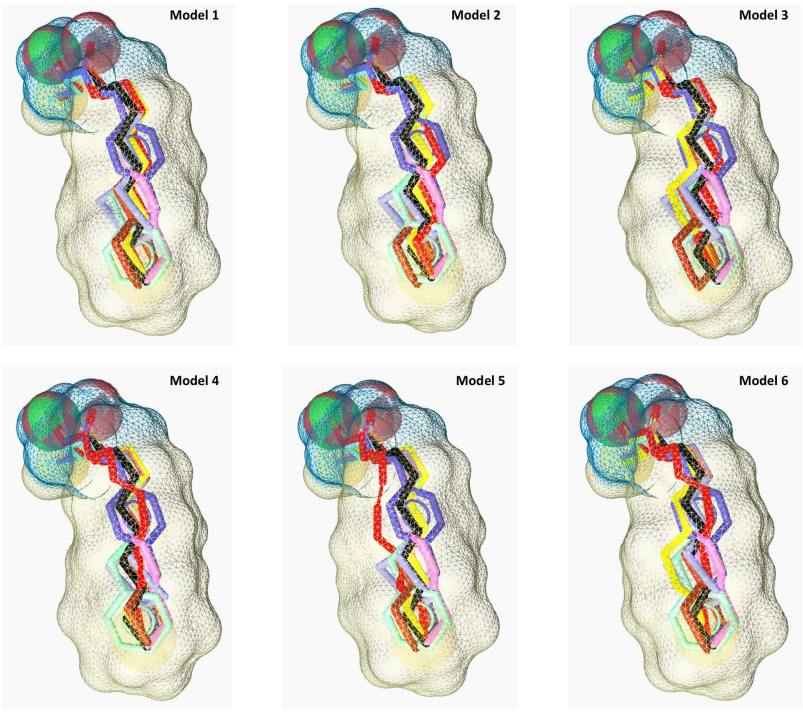


Figure S1. Two views of the top 6 "best fit" pharmacophore models for the biologically active analogs.

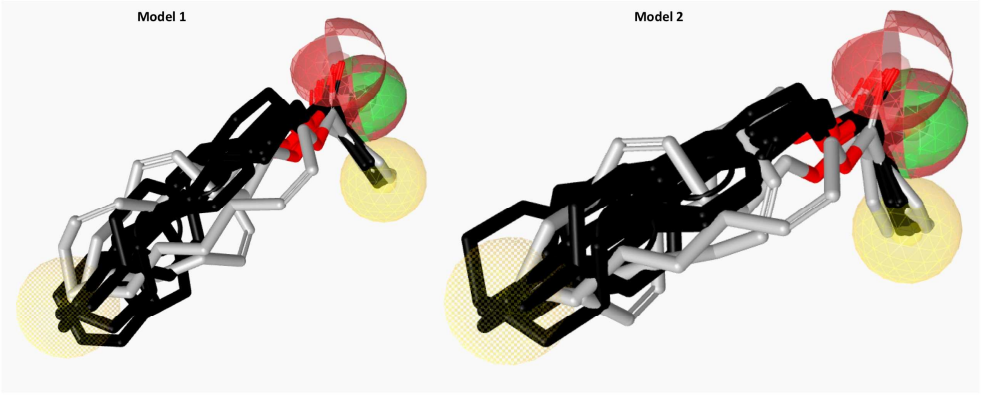


Figure S2. Two "best fit" models showing the deviation of the Z-olefin containing analogs (**27**, **30**, **33**, and **35**; shown in grey**)** from the pharmacophore model of the active compounds (shown in black).

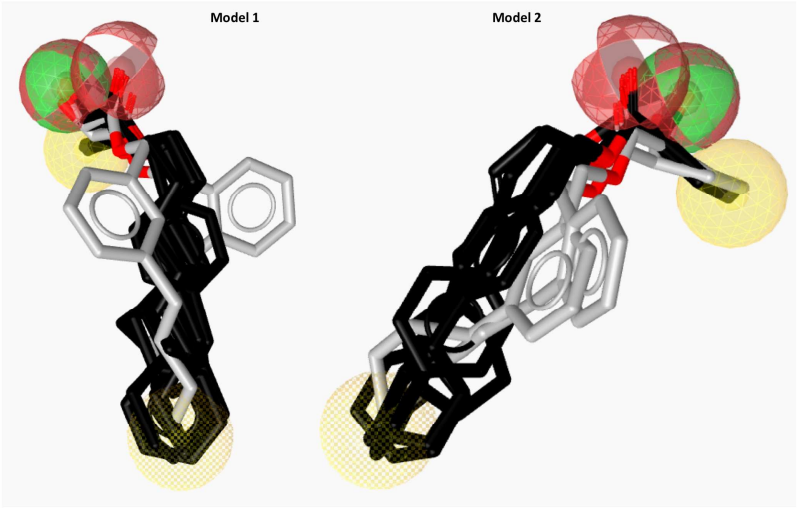


Figure S3. Two "best fit" models showing the deviation of the butyl-substituted benzyl containing analogs (**43** and **44**; shown in grey**)** from the pharmacophore model of the active compounds (shown in black).

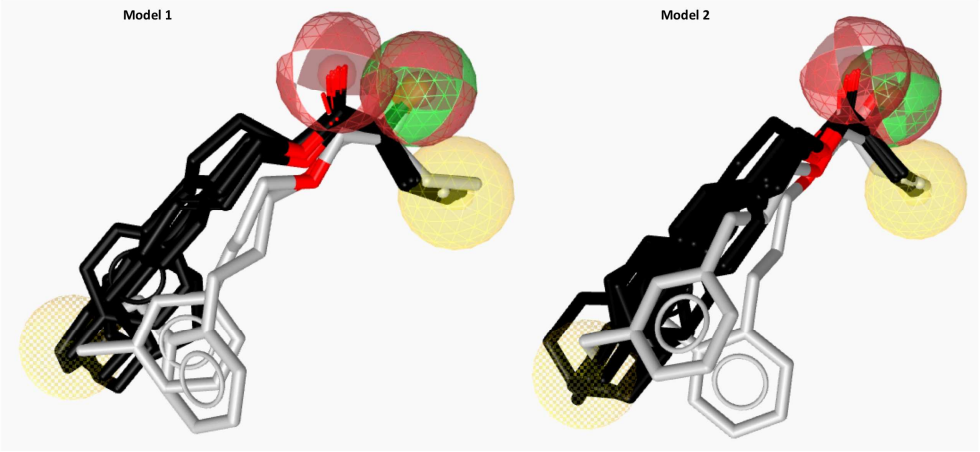


Figure S4. Two "best fit" models showing the deviation of the ethyl-substituted phenyl containing analogs (**48** and **49**; shown in grey**)** from the pharmacophore model of the active compounds (shown in black).

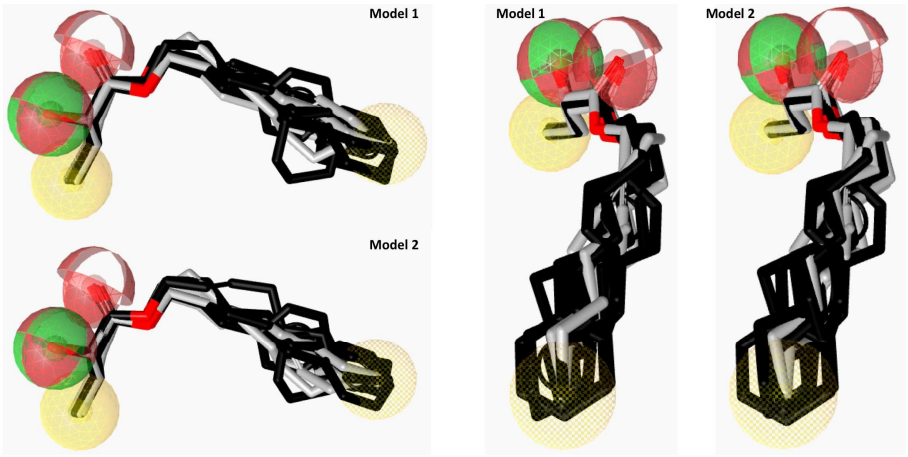


Figure S5. Two "best fit" models showing no apparent deviation of the E-olefin containing analogs (**29**, **32**, and **34**; shown in grey**)** from the pharmacophore model of the active compounds (shown in black).

E. Compound synthesis and tabulated compound data

E.1. General Experimental.

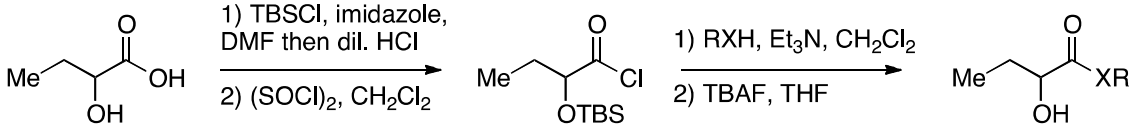
Unless otherwise noted, all reactions were performed in flame-dried glassware under an atmosphere of nitrogen or argon using dried reagents and solvents. All chemicals were purchased from commercial vendors and used without further purification. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were dried by distillation from sodium benzophenone ketyl under argon. Dichloromethane (DCM) was distilled from calcium hydride (CaH_2) under argon. Other anhydrous solvents were purchased from commercial vendors.

Flash chromatography was performed using standard grade silica gel 60 230-400 mesh from SORBENT Technologies. Silica gel was loaded into glass columns as a slurry. Analytical thin-layer chromatography was carried out using Silica G TLC plates, 200 µm with UV_{254} fluorescent indicator (SORBENT Technologies), and visualization was performed by staining and/or by absorbance of UV light. Preparative thin-layer chromatography was carried out using SIL G-200 pre-coated glass TLC plates, 2.0 mm with UV_{254} fluorescent indicator (Macherey-Nagel).

NMR spectra were recorded using a Bruker Avance II (500 MHz for ^{1}H; 125 MHz for ^{13}C) spectrometer fitted with either a ^{1}H-optimized TCI (H/C/N) cryoprobe or a ^{13}C-optimized dual C/H cryoprobe. Chemical shifts are reported in parts per million (ppm) and were calibrated according to residual protonated solvent. High-resolution mass spectral analysis was performed using an Agilent 1200-series electrospray ionization – time-of-flight (ESI-TOF) mass spectrometer in the positive ESI mode.

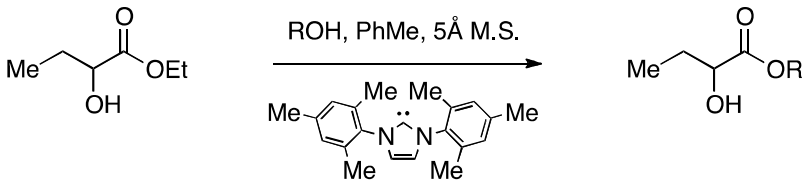
D.2. Compound Synthesis.

Typical procedure for the synthesis of CAI-1 analogs **9**, **10** and **22-25** (for specific details see below).

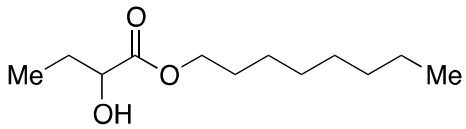


To a solution of the α-hydroxy acid (1.0 eq) in DMF (1.5M) at room temperature was added imidazole (3.0 eq) and *tert*-butyldimethylsilyl chloride (3.0 eq). The mixture was stirred at room temperature overnight. The reaction was quenched with hydrochloric acid (1N), was extracted with ethyl acetate (EtOAc), washed with H_2O and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was treated with $SOCl_2$ (6.6 eq) and heated to reflux overnight. Excess $SOCl_2$ was removed *in vacuo*, and the product was used for the next reaction step without further purification. To a solution of octanol (1.0 eq) and DMAP (1.1 eq) in THF (0.13M) at room temperature was added the acid chloride obtained in the previous step (1.1 eq), dropwise. The mixture was allowed to stir overnight at room temperature and was concentrated *in vacuo* to form a slurry which was purified by silica gel chromatography. The purified TBS-protected intermediate in THF (1M) was treated with TBAF (3 eq) and the mixture was allowed to stir overnight before direct concentration and purification by silica gel chromatography.

Typical procedure for the synthesis of CAI-1 ester analogs **7**, **8**, **17-21** and **26-49** (for specific details see below).



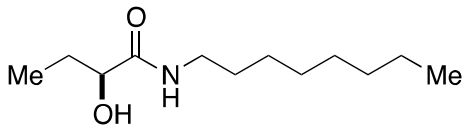
Molecular sieves (5Å powdered, 0.5 g/mmol of ester) and the carbene catalyst (0.1 eq) were added to a screw-top vial equipped with a stir bar. The vial was evacuated and purged to N_2 three times before being placed under nitrogen. To the vial was added PhMe (0.5M), ethyl 2-hydroxybutyrate (1 eq) and the primary alcohol (2 eq). The reaction mixture was stirred overnight at room temperature, was directly concentrated and the residue was purified by silica gel chromatography.



Octyl 2-hydroxybutanoate, 9. To a solution of 2-hydroxybutyric acid (540 mg, 4.27 mmol) in DMF (2.7 mL) at room temperature was

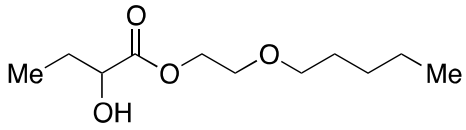
added imidazole (865 mg, 12.9 mmol) and *tert*-butyldimethylsilyl chloride (1.94 g, 12.9 mmol), sequentially. The mixture was allowed to stir overnight at room temperature and was quenched with 1N HCl, bringing the pH of the mixture to pH~2. The resulting mixture was extracted with EtOAc (2 x 25 mL), washed with H_2O (4 x 25 mL) and brine (2 x 25 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide a clear colorless oil that was directly treated with SO_2Cl_2 (2.0 mL, 28.3 mmol) dropwise at room temperature. The mixture was heated to reflux and allowed to react overnight. Excess SO_2Cl_2 was removed *in vacuo* and the crude residue was used without further purification in the subsequent transformation. To a solution of octanol (610 μL, 3.87 mmol) and DMAP (518 mg, 4.24 mmol) in THF (30 mL) at room temperature was added dropwise the crude acid chloride obtained from the previous step as a solution in THF (4.3 mL). The mixture was allowed to stir overnight at room temperature and was concentrated *in vacuo* to provide a slurry that was directly purified using silica gel chromatography, eluting with a gradient from hexanes to 60% EtOAc/hexanes to provide 2-(*tert*-butyldimethylsilyloxy)octylbutanoate as a clear colorless oil (473 mg, 37%, three steps). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.14-4.03 (m, 3H), 1.77-1.52 (m, 4H), 1.36-1.17 (m, 10H), 0.96-0.79 (m, 15H), 0.06 (s, 3H), 0.03 (s, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 174.0, 73.4, 64.8, 31.8, 29.2, 28.6, 28.4, 25.9, 25.7, 22.6, 18.4, 14.1, 9.7, -4.9, -5.3.

To 2-(*tert*-butyldimethylsilyloxy)octylbutanoate (50 mg, 0.142 mmol, 1.0 eq) in THF (1.4 mL) was added 1M tetra-*n*-butylammonium fluoride in THF (0.43 mL, 0.43 mmol). The mixture was allowed to stir at room temperature overnight. Silica was added directly to the flask and concentrated *in vacuo*. The resulting slurry was added to a silica gel column for purification, eluting with a gradient from hexanes to 60% EtOAc/hexanes, to provide octyl 2-hydroxybutanoate (20 mg, 65% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.23-4.09 (m, 3H), 2.73 (d, J = 5.7 Hz, 1H), 1.88-1.76 (m, 1H), 1.74-1.59 (m, 3H), 1.38-1.18 (m, 10H), 0.96 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 175.4, 71.4, 65.8, 31.8, 29.1, 29.1, 28.6, 27.5, 25.8, 22.6, 14.1, 8.9. HRMS (ESI-TOF) calculated for $C_{12}H_{25}O_3$, 217.1798; found 217.1800 $[M+H]^+$.



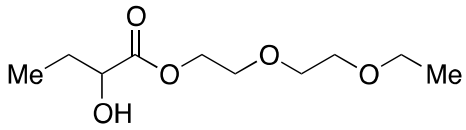
***(S)*-2-Hydroxy-N-octylbutanamide, 10.** Prepared following the procedure for the synthesis of octyl 2-hydroxybutanoate (**8**) using *(S)*-2-hydroxybutyric acid as a starting material and octylamine in place of octanol. The resulting mixture was purified with silica gel chromatography, eluting with double column volumes of hexanes, 10% and 20% EtOAc/Hex mixtures. The desired fractions were concentrated *in vacuo*, giving *(S)*-2-(*tert*-butyldimethylsilyloxy)-N-octylbutanamide (127 mg, 66% yield, three steps). ^{1}H-NMR (500MHz, $CDCl_3$) δ 6.68-6.51 (brs, 1H), 4.09 (t, J = 4.8 Hz, 1H), 3.34-3.22 (m, 1H), 3.22-3.11 (m, 1H), 1.83-1.64 (m, 2H), 1.53-1.41 (m, 2H), 1.34-1.11 (m, 10H), 0.99-0.76 (m, 15H), 0.07 (s, 3H), 0.05 (s, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 173.5, 74.2, 38.8, 31.8, 29.7, 29.2, 28.1, 26.9, 25.8, 22.6, 18.1, 14.1, 8.4, -4.8, -5.3.

To the above prepared amide (84 mg, 0.255 mmol, 1.0 eq) in THF (2.55 mL, 0.1M) was added 1M tetra-*n*-butylammonium fluoride in THF (0.765 mL, 0.765 mmol). The mixture was allowed to stir at room temperature overnight. Silica was added directly to the flask and concentrated *in vacuo*. The resulting slurry was added to a silica gel column for purification, eluting with a gradient from hexanes to 20% EtOAc/hexanes, providing *(S)*-2-hydroxy-N-octylbutanamide (44 mg, 80% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 6.69-6.57 (brs, 1H), 4.02 (dd, *J* = 3.8, 7.0 Hz, 1H), 3.38-3.13 (m, 3H), 1.89-1.76 (m, 1H), 1.71-1.58 (m, 1H), 1.54-1.43 (m, 2H), 1.35-1.14 (m, 10H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.83 (t, *J* = 6.7 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 173.8, 73.0, 39.1, 31.8, 29.6, 29.3, 29.2, 27.9, 26.9, 22.7, 14.1, 9.1. HRMS (ESI-TOF) calculated for $C_{12}H_{26}NO_2$, 216.1958; found 216.1974 $[M+H]^+$.



2-(Pentyloxy)ethyl 2-hydroxybutanoate, 22. Prepared following the procedure for the synthesis of octyl 2-hydroxybutanoate (**8**) using 2-(pentyloxy)ethanol (1.0 eq) was used in place of octanol. The resulting mixture was purified by silica gel chromatography, eluting with a gradient from hexanes to 60% EtOAc/hexanes, providing 2-(*tert*-butyldimethylsilyloxy)-2-(pentyloxy)ethylbutanoate (0.197 g, 55% yield, three steps). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.32-4.19 (m, 2H), 4.14 (dd, *J* = 4.6, 7.4Hz, 1H), 3.65-3.56 (m 2H), 3.49-3.34 (m, 2H), 1.81-1.66 (m, 2H), 1.61-1.49 (m, 2H), 1.33-1.23 (m, 4H), 1.02-0.78 (m, 15H), 0.05 (s, 3H), 0.03 (s, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 173.8, 73.2, 71.5, 68.4, 63.7, 29.3, 28.3, 28.2, 25.7, 22.5, 18.2, 14.0, 9.6, -4.9, -5.3.

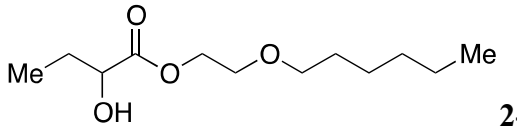
To the above prepared ester (0.197 g, 0.593 mmol) in THF (6 mL) was added 1M TBAF in THF (1.8 mL, 1.8 mmol). The mixture was allowed to stir at room temperature overnight. Silica was added directly to the flask and concentrated *in vacuo*. The resulting slurry was added to a silica gel column for purification, eluting with a rapid gradient from hexanes to 80% EtOAc/hexanes. Desired fractions were concentrated *in vacuo*, giving 2-(pentyloxy)ethyl 2-hydroxybutanoate (77.8 mg, 40% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.37-4.26 (m, 2H), 4.18 (dd, *J* = 5.1, 10.5 Hz, 1H), 3.63 (t, *J* = 4.7 Hz, 2H), 3.43 (t, *J* = 6.7 Hz, 2H), 2.73 (d, *J* = 5.4 Hz, 1H), 1.88-1.79 (m, 1H), 1.73-1.64 (m, 1H), 1.61-1.52 (m, 2H), 1.32-1.26 (m, 4H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 175.3, 71.5, 71.4, 68.3, 64.6, 29.3, 28.2, 27.5, 22.5, 14.1, 8.9. HRMS (ESI-TOF) calculated for $C_{11}H_{23}O_4$, 219.1591; found 219.1592 [M+H].



2-Hydroxy-2-(2-ethoxyethoxy)ethylbutanoate, 23. Prepared following the procedure for the synthesis of octyl 2-hydroxybutanoate (**8**) using 2-(2-ethoxyethoxy)ethanol in place of octanol. The resulting mixture was purified by

silica gel chromatography, eluting with a gradient from hexanes to 60% EtOAc/hexanes, providing 2-(*tert*-butyldimethylsilyloxy)-2-(2-ethoxyethoxy)ethylbutanoate (790 mg, 99% yield, three steps). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.32-4.20 (m, 2H), 4.13 (dd, *J* = 4.6, 7.4 Hz, 1H), 3.67 (t, *J* = 4.9 Hz, 2H), 3.62-3.57 (m, 2H), 3.57-3.53 (m, 2H), 3.49 (q, *J* = 7.0 Hz, 2H), 1.64-1.80 (m, 2H), 1.18 (t, *J* = 7.0Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.84-0.89 (m, 9H), 0.06 (s, 3H), 0.02 (s, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 173.8, 73.2, 70.6, 69.8, 69.1, 66.7, 63.6, 28.4, 25.7, 18.4, 15.2, 9.7, -4.9, -5.4.

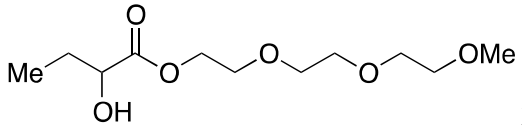
To the above prepared ester (570 mg, 1.61 mmol) in THF (16.1mL) was added 1M TBAF in THF (4.8 mL, 4.8 mmol). The mixture was allowed to stir at room temperature overnight. Silica was added directly to the flask and concentrated *in vacuo*. The resulting slurry was added to a silica gel column for purification, eluting with a rapid gradient from hexanes to 80% EtOAc/hexanes. Desired fractions were concentrated *in vacuo*, giving 2-hydroxy-2-(2-ethoxyethoxy)ethylbutanoate (0.349 g, 61% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.39-4.26 (m, 2H), 4.17 (dd, *J* = 5.7, 10.9 Hz, 1H), 3.72 (t, *J* = 4.7 Hz, 2H), 3.65-3.61 (m, 2H), 3.59-3.56 (m, 2H), 3.50 (dd, *J* = 7.0, 14.0 Hz, 2H), 2.74 (d, *J* = 5.7 Hz, 1H), 1.88-1.79 (m, 1H), 1.74-1.63 (m, 1H), 1.20 (t, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 175.4, 71.4, 70.7, 69.8, 68.9, 66.8, 64.5, 27.5, 15.2, 8.9. HRMS (ESI-TOF) calculated for $C_{10}H_{21}O_5$, 221.1384; found 221.1389 $[M+H]^+$.



2-(Hexyloxy)ethyl 2-hydroxybutanoate, 24. Prepared following the procedure for the synthesis of octyl 2-hydroxybutanoate (**8**) using 2-(hexyloxy)ethanol in place of octanol. The resulting mixture was purified by silica gel chromatography, eluting with a gradient from hexanes to 60% EtOAc/hexanes, providing 2-(*tert*-butyldimethylsilyloxy)-2-(hexyloxy)ethylbutanoate (0.834g, 99% yield, three steps). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.30-4.17 (m, 2H), 4.15 (dd, *J* = 4.6, 7.4 Hz, 1H), 3.60 (t, *J* = 4.9 Hz, 2H), 3.40 (t, *J* = 6.8 Hz, 2H), 1.80-1.63 (m, 2H), 1.57-1.49 (m, 2H), 1.34-1.20 (m, 6H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.90-0.80 (m, 12H), 0.06 (s, 3H), 0.04 (s, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 174.0, 73.2, 72.2, 71.4, 68.5, 63.8, 31.7, 29.6, 28.4, 25.8, 25.8, 22.7, 14.1, 9.7, -4.9, -5.4.

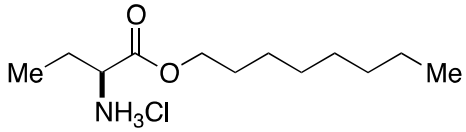
To the above prepared ester (0.834 g, 2.28 mmol) in THF (23 mL) was added 1M TBAF in THF (6.8 mL, 6.8 mmol). The mixture was allowed to stir at room temperature overnight. Silica was added directly to the flask and concentrated *in vacuo*. The resulting slurry was added to a silica gel column for purification, eluting with a rapid gradient from hexanes to 50% EtOAc/hexanes. Desired fractions were concentrated *in vacuo*, giving 2-(hexyloxy)ethyl 2-hydroxybutanoate (0.163g, 20% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.34-4.21 (m, 2H), 4.13 (dd, 1H, *J* = 4.2, 8.8 Hz), 3.58 (t, 2H, *J* = 4.7 Hz), 3.38 (t, 2H, *J* = 6.7 Hz), 2.67 (d, 1H, *J* = 5.8 Hz), 1.86-1.74 (m, 1H), 1.69-1.57 (m, 1H), 1.51-1.46 (m, 2H), 1.31-1.16 (m, 6H), 0.92-0.88 (m, 3H), 0.82 (t, 3H, *J* = 6.9 Hz). ^{13}C-NMR (125MHz,

$CDCl_3$) δ 175.4, 71.5, 71.4, 68.3, 64.7, 31.7, 29.6, 27.5, 25.8, 22.7, 14.1, 8.9. HRMS (ESI-TOF) calculated for $C_{12}H_{25}O_4$, 233.1747; found 233.1752 [M+H].

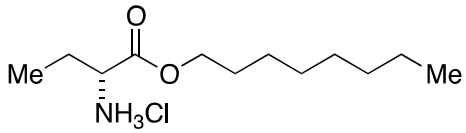


2-Hydroxy-2-(2-(2-methoxyethoxy)ethoxy)ethylbutanoate, 25. Prepared following the procedure for the synthesis of octyl 2-hydroxybutanoate (**8**) using 2-(2-(2-methoxyethoxy)ethoxy)ethanol in place of octanol. The resulting mixture was purified with silica gel chromatography eluting with a gradient from hexanes to 60% EtOAc/hexanes, providing 2-(*tert*-butyldimethylsilyloxy)-2-(2-(2-methoxyethoxy)ethoxy)ethylbutanoate (0.737 g, 99% yield, three steps). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.30-4.19 (m, 2H), 4.13 (dd, *J* = 4.6, 7.4 Hz, 1H), 3.66 (t, *J* = 4.9 Hz, 2H), 3.60-3.63 (m, 6H), 3.50-3.54 (m, 2H), 3.35 (s, 3H), 1.66-1.75 (m, 2H), 0.90-0.94 (m, 3H), 0.80-0.89 (m, 9H), 0.06 (s, 3H), 0.03 (s, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 173.8, 73.2, 71.9, 70.6, 70.6, 69.1, 63.6, 59.1, 28.4, 25.7, 18.3, 9.6, -4.9, -5.3.

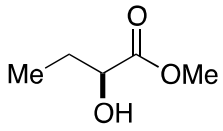
To the above prepared ester (737 mg, 1.94 mmol) in THF (19.4 mL) was added 1M TBAF in THF (5.83 mL, 5.83 mmol). The mixture was allowed to stir at room temperature overnight. Silica was added directly to the flask and concentrated *in vacuo.* The resulting slurry was added to a silica gel column for purification, eluting with a rapid gradient from hexanes to 80% EtOAc/hexanes. Desired fractions were concentrated *in vacuo*, giving 2-hydroxy-2-(2-(2-methoxyethoxy)ethoxy)ethylbutanoate **(**412 mg, 55% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.37-4.29 (m, 2H), 4.19-4.15 (m, 1H), 3.70 (t, *J* = 4.7 Hz, 2H), 3.66-3.60 (m, 4H), 3.55-3.51 (m, 2H), 3.36 (s, 2H), 2.90 (d, *J* = 5.8 Hz, 1H), 1.88-1.78 (m, 1H), 1.73-1.64 (m, 1H), 1.62 (s, 3H), 0.98-0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 175.2, 71.9, 71.5, 70.6, 70.6, 70.6, 68.9, 64.5, 59.1, 27.5, 9.0. HRMS (ESI-TOF) calculated for $C_{11}H_{22}O_6Na$, 273.1309; found 273.1316 $[M+Na]^+$.



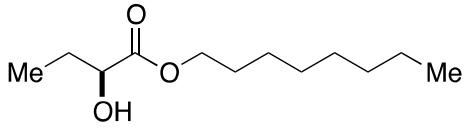
***(S)*-2-aminooctylbutanoate hydrochloride, 12.** To L-aminobutyric acid (500 mg, 4.83 mmol) was added octanol (40.3 mL) and 2M HCl/ether (7.0 mL). The mixture was heated to reflux (150°C) for 24 hours and was concentrated *in vacuo*. Upon cooling, a solid was formed which was dissolved in ethyl acetate with warming. The solution was left overnight to form crystals which were subsequently filtered and air-dried, giving *(S)*-2-aminooctylbutanoate hydrochloride (0.611g, 50% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 8.97-8.83 (brs, 2H), 4.31-4.16 (m, 2H), 4.06 (t, *J* = 5.8 Hz, 1H), 2.22-2.06 (m, 2H), 1.76-1.64 (m, 2H), 1.42-1.23 (m, 10H), 1.15 (t, *J* = 7.5 Hz, 3H), 0.91 (t, *J* = 6.9 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 169.2, 66.8, 54.5, 32.0, 29.4, 29.3, 28.6, 25.9, 24.1, 22.8, 14.3, 9.7. HRMS (ESI-TOF) calculated for $C_{12}H_{26}NO_2$, 216.1958; found 216.1959 [M+H].



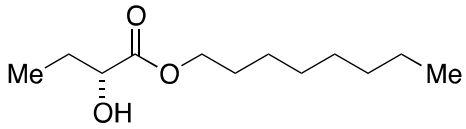
***(R)*-2-aminooctylbutanoate hydrochloride, 13.** Prepared following the procedure for the synthesis of octyl 2-hydroxybutanoate (**12**) from D-aminobutyric acid. ^{1}H-NMR (500MHz, $CDCl_3$) δ 8.96-8.84 (brs, 2H), 4.30-4.14 (m, 2H), 4.07 (t, J = 5.8, 1H), 2.20-2.08 (m, 2H), 1.75-1.64 (m, 2H), 1.39-1.24 (m, 10H), 1.14 (t, J = 7.5 Hz, 3H), 0.91 (t, J = 6.9 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 169.1, 66.7, 54.3, 31.8, 29.2, 29.2, 28.4, 25.8, 24.0, 22.7, 14.2, 9.5. HRMS (ESI-TOF) calculated for $C_{12}H_{26}NO_2$, 216.1958; found 216.1965 [M+H].



(*S*)-methyl 2-hydroxybutanoate. To a solution of (*S*)-2-hydroxybutyric acid (3.0 g, 28.8 mmol) in MeOH (64 mL) at room temperature was added H_3BO_3 and the mixture was allowed to stir overnight. The volatiles were removed *in vacuo* and the residue was distilled (bp = 60-62°C, 10 mmHg) to provide (*S*)-methyl 2-hydroxybutanoate as a clear colorless oil (1.97 g, 57%). The spectroscopic data for this compound was consistent with previously reported data.[8]

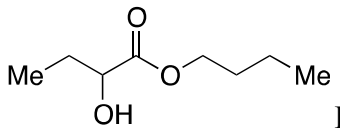


(*S*)-Octyl 2-hydroxybutanoate, 7. Oven dried 4Å molecular sieves (322 mg) and 1,3-Bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (19.6 mg, 0.064 mmol) were added to a screw-top vial which was evacuated and purged to N_2 three times before adding (*S*)-methyl 2-hydroxybutanoate (76.1 mg, 0.644 mmol) as a solution in THF (645 μL). The mixture was treated with octanol (100 μL, 0.644 mmol) and was allowed to stir overnight, was concentrated *in vacuo* and the residue was purified by silica gel chromatography to provide (*S*)-Octyl 2-hydroxybutanoate as a clear colorless oil (55 mg, 40%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.17-4.11 (m, 3H), 2.74 (d, J = 5.5 Hz, 1H), 1.88-1.77 (m, 1H), 1.72-1.59 (m, 3H), 1.38-1.19 (m, 10H), 0.94 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 77.5, 77.2, 77.0, 66.0, 32.0, 29.4, 29.3, 28.7, 27.7, 26.0, 22.8; HRMS (ESI-TOF) calculated for $C_{12}H_{25}O_3$, 217.1804; observed, 217.1794 $[M+H]^+$.

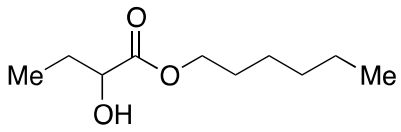


(*R*)-Octyl 2-hydroxybutanoate, 8. Prepared in an analogous manner to (*S*)-Octyl 2-hydroxybutanoate, **6** from (*R*)-methyl 2-

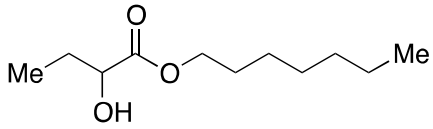
hydroxybutanoate and octanol. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.17-4.11 (m, 3H), 2.73 (d, J = 5.7 Hz, 1H), 1.87-1.77 (m, 1H), 1.72-1.54 (m, 3H), 1.38-1.19 (m, 10H), 0.94 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 77.5, 77.2, 77.0, 66.0, 32.0, 29.4, 29.3, 28.7, 27.7, 26.0, 22.8; HRMS (ESI-TOF) calculated for $C_{12}H_{25}O_3$, 217.1804; observed, 217.1793 $[M+H]^+$.



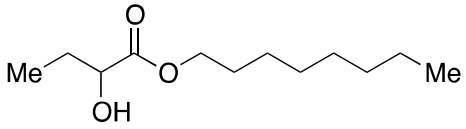
Butyl 2-hydroxybutanoate, 17. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1.0 mmol) and 1-butanol (180 μL, 2.0 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide butyl 2-hydroxybutanoate (29 mg, 20% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.22-4.04 (m, 3H), 2.88 (bs, 1H), 1.86-1.74 (m, 1H), 1.68-1.56 (m, 3H), 1.38-1.30 (m, 2H), 0.92 (t, J = 7.5 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 71.5, 65.6, 30.7, 27.7, 19.2, 13.8, 9.1; HRMS (ESI-TOF) calculated for $C_8H_{17}O_3Na$, 183.0997; observed, 183.0992 $[M+Na]^+$.



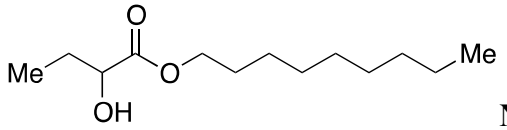
Hexyl 2-hydroxybutanoate, 18. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1.0 mmol) and 1-hexanol (250 μL, 2.0 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide hexyl 2-hydroxybutanoate (105 mg, 56% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.22-4.10 (m, 3H), 2.75 (d, J = 5.7 Hz, 1H), 1.87-1.77 (m, 1H), 1.70-1.59 (m, 3H), 1.38-1.22 (m, 6H), 0.94 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 71.5, 66.0, 31.5, 28.7, 27.7, 25.7, 22.7, 14.2, 9.1; HRMS (ESI-TOF) calculated for $C_{10}H_{21}O_3$, 189.1491; observed, 189.1500 $[M+H]^+$.



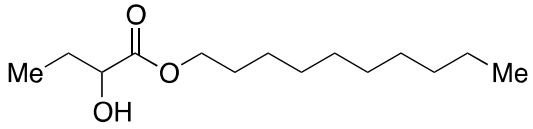
Heptyl 2-hydroxybutanoate, 19. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1.0 mmol) and 1-heptanol (285 μL, 2.0 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide heptyl 2-hydroxybutanoate (60 mg, 30% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.21-4.10 (m, 3H), 2.75 (d, *J* = 5.7 Hz, 1H), 1.87-1.76 (m, 1H), 1.70-1.59 (m, 3H), 1.37-1.20 (m, 8H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 175.6, 71.5, 66.0, 31.9, 29.1, 28.7, 27.7, 26.0, 22.8, 14.3, 9.1. HRMS (ESI-TOF) calculated for $C_{11}H_{23}O_3$, 203.1647; observed, 203.1650 $[M+H]^+$.



Octyl 2-hydroxybutanoate, 9. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1.0 mmol) and 1-octanol (160 μL, 1.0 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide octyl 2-hydroxybutanoate (86 mg, 40% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.22-4.09 (m, 3H), 2.74 (d, *J* = 5.5 Hz, 1H), 1.87-1.77 (m, 1H), 1.72-1.59 (m, 3H), 1.37-1.18 (m, 10H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 77.5, 77.2, 77.0, 66.0, 32.0, 29.4, 29.3, 28.7, 27.7, 26.0, 22.8; HRMS (ESI-TOF) calculated for $C_{12}H_{25}O_3$, 217.1804; observed, 217.1794 $[M+H]^+$.

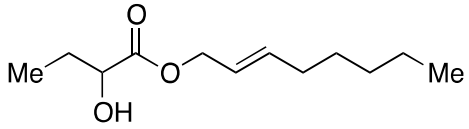


Nonyl 2-hydroxybutanoate, 20. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1.0 mmol) and 1-nonanol (350 μL, 2.0 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide nonyl 2-hydroxybutanoate (143 mg, 62% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.23-4.09 (m, 3H), 2.77 (d, *J* = 5.2 Hz, 1H), 1.87-1.76 (m, 1H), 1.70-1.56 (m, 3H), 1.38-1.16 (m, 12H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.85 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 71.5, 66.0, 32.0, 29.6, 29.4, 29.4, 28.7, 27.7, 26.0, 22.9, 14.3, 9.1; HRMS (ESI-TOF) calculated for $C_{13}H_{27}O_3$, 231.1960; observed, 231.1961 $[M+H]^+$.



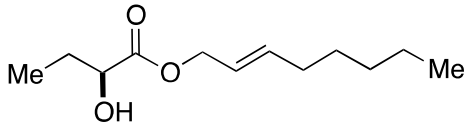
Decyl 2-hydroxybutanoate, 21. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7**

using ethyl 2-hydroxybutyrate (130 μL, 1.0 mmol) and 1-decanol (380 μL, 2.0 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide decyl 2-hydroxybutanoate (158 mg, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.22-4.09 (m, 3H), 2.75 (d, J = 5.5 Hz, 1H), 1.87-1.76 (m, 1H), 1.70-1.59 (m, 3H), 1.37-1.17 (m, 14H), 0.94 (t, J = 7.4 Hz, 3H), 0.85 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 71.3, 65.9, 31.9, 29.5, 29.5, 29.3, 29.2, 28.6, 27.5, 25.8, 22.7, 14.2, 8.9; HRMS (ESI-TOF) calculated for $C_{14}H_{29}O_3$, 245.2117; observed, 245.2122 $[M+H]^+$.



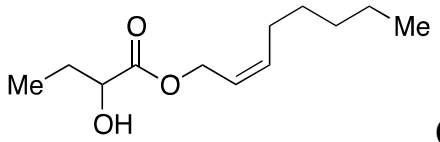
(*E*)-Oct-2-en-1-yl 2-hydroxybutanoate, 26

Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1.0 mmol) and (E)-2-octen-1-ol (300 μL, 2.0 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*E*)-oct-2-en-1-yl 2-hydroxybutanoate (134 mg, 63% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83-5.74 (m, 1H), 5.59-5.49 (m, 1H), 4.65-4.55 (m, 2H), 4.14 (dd, J = 6.2, 4.7 Hz, 1H), 2.73 (bs, 1H), 2.03 (q, J = 7.1 Hz, 2H), 1.87-1.77 (m, 1H), 1.71-1.61 (m, 1H), 1.40-1.31 (m, 2H), 1.31-1.21 (m, 4H), 0.94 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 138.0, 123.2, 71.6, 66.6, 32.4, 31.5, 28.7, 27.7, 22.7, 14.3, 9.1; HRMS (ESI-TOF) calculated for $C_{12}H_{22}O_3Na$, 237.1466; observed, 237.1470 $[M+Na]^+$.

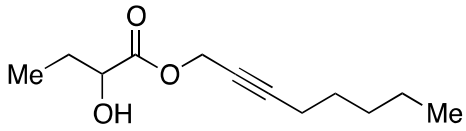


(*S*)-(*E*)-Oct-2-en-1-yl 2-hydroxybutanoate, (*S*)-26

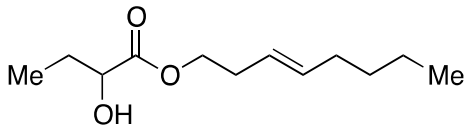
Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using (*S*)-methyl 2-hydroxybutanoate and (E)-2-octen-1-ol. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*S*)-(*E*)-oct-2-en-1-yl 2-hydroxybutanoate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83-5.74 (m, 1H), 5.59-5.49 (m, 1H), 4.65-4.55 (m, 2H), 4.14 (dd, J = 6.2, 4.7 Hz, 1H), 2.73 (bs, 1H), 2.03 (q, J = 7.1 Hz, 2H), 1.87-1.77 (m, 1H), 1.71-1.61 (m, 1H), 1.40-1.31 (m, 2H), 1.31-1.21 (m, 4H), 0.94 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 138.0, 123.2, 71.6, 66.6, 32.4, 31.5, 28.7, 27.7, 22.7, 14.3, 9.1; HRMS (ESI-TOF) calculated for $C_{12}H_{22}O_3Na$, 237.1466; observed, 237.1468 $[M+Na]^+$.



(*Z*)-Oct-2-en-1-yl 2-hydroxybutanoate, 27 0.5 g of 5Å molecular sieves (0.5 g for each mmol of ethyl-2 hydroxybutyrate) and 1,3-bis (2,4,6-trimethylphenyl) imidazol-2-ylidene (30.4 mg, 0.1 mmol) were added to a round-bottom flask equipped with a stir bar. The vial was brought to vacuum and subsequently placed under N_2 three times. To the reaction flask was added 1 mL toluene, followed by ethyl 2-hydroxybutyrate (130 μL, 1mmol). (*Z*)-2-octen-1-ol (300 μL, 2 mmol) was subsequently added, and the reaction mixture was stirred for 1 hour. Once the reaction was complete, the mixture was transferred to a round-bottom flask, using ether to facilitate the transfer through a cotton-celite filter, to remove residues of the molecular sieves and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*Z*)-oct-2-en-1-yl 2-hydroxybutanoate (180 mg, 84% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.71-5.62 (m, 1H), 5.55-5.46 (m, 1H), 4.77-4.65 (m, 2H), 4.14 (s, 1H), 2.74 (s, 1H), 2.08 (q, *J* = 7.3 Hz, 2H), 1.87-1.76 (m, 1H), 1.73-1.60 (m, 1H), 1.40-1.21 (m, 6H), 0.93 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 136.7, 122.6, 71.6, 61.6, 31.6, 29.2, 27.7, 27.7, 22.7, 14.3, 9.1; HRMS (ESI-TOF) calculated for $C_{12}H_{22}O_3Na$, 237.1466; observed, 237.1471 $[M+Na]^+$.

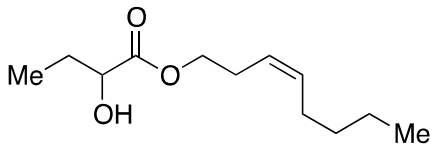


Oct-2-yn-1-yl 2-hydroxybutanoate, 28 Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1 mmol) and 2-octyn-1-ol (290 μL, 2 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide oct-2-yn-1-yl 2-hydroxybutanoate (102 mg, 48% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.80-4.70 (m, 2H), 4.19 (dd, *J* = 6.3, 4.4 Hz, 1H), 2.67 (s, 1H), 2.22-2.15 (m, 2H), 1.89-1.79 (m, 1H), 1.76-1.65 (m, 1H), 1.53-1.44 (m, 2H), 1.37-1.24 (m, 4H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 88.7, 73.4, 71.5, 54.1, 31.2, 28.2, 27.6, 22.4, 18.9, 14.2, 9.0; HRMS (ESI-TOF) calculated for $C_{12}H_{20}O_3Na$, 235.1310; observed, 235.1310 m/z $[M+Na]^+$.

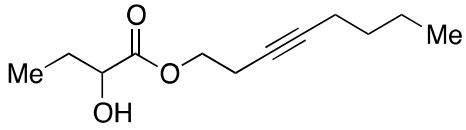


(*E*)-Oct-3-en-1-yl 2-hydroxybutanoate, 29 Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (55 μL, 0.42 mmol) and (*E*)-3-octen-1-ol (106.1 mg, 0.84 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*E*)-oct-3-en-1-yl 2-hydroxybutanoate (88 mg, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ

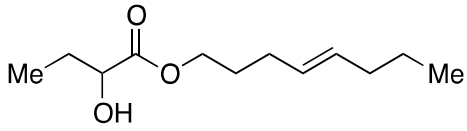
5.54-5.44 (m, 1H), 5.36-5.26 (m, 1H), 4.23-4.07 (m, 3H), 2.79 (s, 1H), 2.32 (q, J = 6.7 Hz, 2H), 2.00-1.90 (m, 2H), 1.84-1.74 (m, 1H), 1.70-1.58 (m, 1H), 1.34-1.19 (m, 4H), 0.93 (t, J = 7.4 Hz, 3H), 0.85 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 134.2, 124.7, 71.5, 65.4, 32.5, 32.1, 31.7, 27.7, 22.3, 14.1, 9.1; HRMS (ESI-TOF) calculated for $C_{12}H_{22}O_3Na$, 237.1466; observed, 237.1475 $[M+Na]^+$.



(*Z*)-Oct-3-en-1-yl 2-hydroxybutanoate, 30 Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1 mmol) and (*Z*)-3-octen-1-ol (300μL, 2 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*Z*)-oct-3-en-1-yl 2-hydroxybutanoate (60 mg, 30% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.55-5.43 (m, 1H), 5.34-5.23 (m, 1H), 4.21-4.08 (m, 3H), 2.79 (d, J = 3.4 Hz, 1H), 2.38 (q, J = 7.0 Hz, 2H), 2.08-1.95 (m, 1H), 1.84-1.74 (m, 1H), 1.69-1.59 (m, 1H), 1.34-1.24 (m, 4H), 0.93 (t, J = 7.5 Hz, 3H), 0.87 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 133.5, 123.9, 71.6, 65.2, 31.9, 27.7, 27.2, 27.0, 22.5, 14.1, 9.1; HRMS (ESI-TOF) calculated for $C_{12}H_{22}O_3Na$, 237.1466; observed, 237.1475 $[M+Na]^+$.

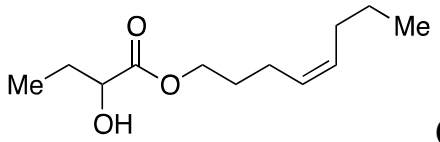


Oct-3-yn-1-yl 2-hydroxybutanoate, 31 Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (130 μL, 1 mmol) and 3-octyn-1-ol (290 μL, 2 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide oct-3-yn-1-yl 2-hydroxybutanoate (110 mg, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.29-4.13 (m, 3H), 2.70 (s, 1H), 2.54-2.46 (m, 2H) 2.14-2.07 (m, 2H), 1.88-1.77 (m, 1H), 1.74-1.62 (m, 1H), 1.47-1.31 (m, 4H), 0.95 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 82.5, 75.2, 71.5, 64.1, 31.1, 27.7, 22.1, 19.5, 18.5, 13.8, 9.1; HRMS (ESI-TOF) calculated for $C_{12}H_{20}O_3Na$, 235.1310; observed, 235.1313 $[M+Na]^+$.

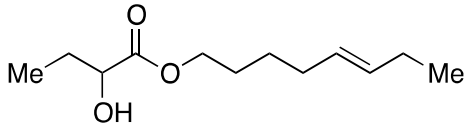


(*E*)-Oct-4-enyl 2-hydroxybutanoate, 32. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (115 μL, 0.875 mmol) and (*E*)-4-octyn-1-ol (56.1 mg, 0.437 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*E*)-oct-4-enyl 2-

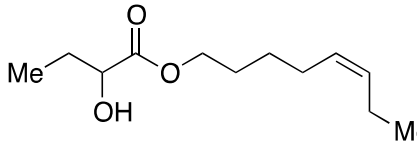
hydroxybutanoate (69.9 mg, 75% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 5.46-5.29 (m, 2H), 4.22-4.09 (m, 3H), 2.75 (s, 1H), 2.04 (q, *J* = 7.0 Hz, 2H), 1.93 (q, *J* = 6.9 Hz, 2H), 1.87-1.77 (m, 1H), 1.74-1.62 (m, 3H), 1.39-1.29 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.4 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 175.6, 131.9, 128.7, 71.5, 65.3, 34.8, 28.9, 28.6, 27.7, 22.8, 13.9, 9.1. HRMS (ESI-TOF) calculated for $C_{12}H_{23}O_3$, 215.1647; observed, 215.1644 $[M+H]^+$.



(*Z*)-Oct-4-enyl 2-hydroxybutanoate, 33. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (94 μL, 0.722 mmol) and (*Z*)-4-octyn-1-ol (46.3 mg, 0.361 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*Z*)-oct-4-enyl 2-hydroxybutanoate (42.7 mg, 55% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 5.45-5.27 (m, 2H), 4.23-4.09 (m, 3H), 2.76 (d, *J* = 5.7 Hz, 1H), 2.09 (q, *J* = 7.3 Hz, 2H), 1.97 (q, *J* = 7.3 Hz, 2H), 1.88-1.77 (m, 1H), 1.76-1.62 (m, 3H), 1.39-1.28 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 175.5, 131.4, 128.2, 71.5, 65.4, 29.5, 28.7, 27.7, 23.6, 23.0, 14.0, 9.1. HRMS (ESI-TOF) calculated for $C_{12}H_{23}O_3$, 215.1647; observed, 215.1646 $[M+H]^+$.

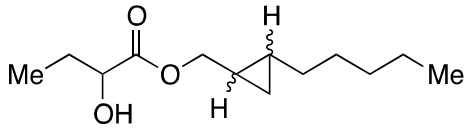


(*E*)-Oct-5-enyl 2-hydroxybutanoate, 34. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using ethyl 2-hydroxybutyrate (78 μL, 0.593 mmol) and (*E*)-5-octyn-1-ol (38 mg, 0.296 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*E*)-oct-5-enyl 2-hydroxybutanoate (41.3 mg, 65% yield). ^{1}H-NMR (500MHz, $CDCl_3$) δ 5.49-5.29 (m, 2H), 4.23-4.09 (m, 3H), 2.74 (d, *J* = 5.7 Hz, 1H), 2.04-1.93 (m, 4H), 1.86-1.78 (m, 1H), 1.71-1.59 (m, 3H), 1.44-1.35 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 6H). ^{13}C-NMR (125MHz, $CDCl_3$) δ 175.6, 133.0, 128.5, 71.5, 65.8, 32.2, 28.2, 27.7, 25.9, 25.8, 14.2, 9.1. HRMS (ESI-TOF) calculated for $C_{12}H_{23}O_3$, 215.1647; observed, 215.1642 $[M+H]^+$.

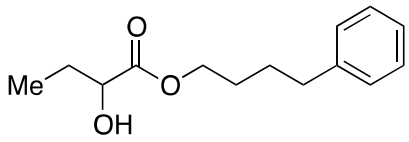


(*Z*)-Oct-5-en-1-yl 2-hydroxybutanoate, 35. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7**

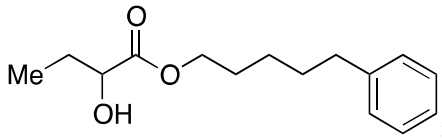
using ethyl 2-hydroxybutyrate (90 μL, 0.7 mmol) and (*Z*)-5-octen-1-ol (210 μL, 1.4 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*Z*)-oct-5-en-1-yl 2-hydroxybutanoate (116 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.42-5.34 (m, 1H), 5.32-5.23 (m, 1H), 4.23-4.09 (m, 3H), 2.09-1.96 (m, 4H), 1.86-1.77 (m, 1H), 1.70-1.61 (m, 3H), 1.45-1.35 (m, 2H), 0.99-0.88 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 132.6, 128.4, 71.5, 65.8, 28.3, 27.7, 26.7, 26.1, 20.7, 14.6, 9.1; HRMS (ESI-TOF) calculated for $C_{12}H_{22}O_3Na$, 237.1466; observed, 237.1472 $[M+Na]^+$.



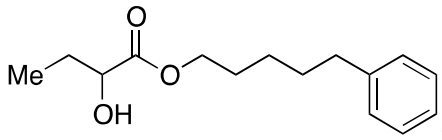
(2-Pentylcyclopropyl)methyl 2-hydroxybutanoate, 36. The ester was prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using (*S*)-methyl 2-hydroxybutyrate (20.4 mg, 0.17 mmol) and (2-pentylcyclopropyl)methanol (27 mg, 0.19 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (2-pentylcyclopropyl)methyl 2-hydroxybutanoate as a mixture of stereoisomers (23.7 mg, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.17-4.11 (m, 1H), 4.10-3.90 (m, 2H), 2.76 (d, *J* = 5.6 Hz, 1H), 1.89-1.78 (m, 1H), 1.73-1.62 (m, 1H), 1.39-1.20 (m, 7H), 1.18-1.08 (m, 1H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 6.9 Hz, 3H), 0.70-0.61 (m, 1H), 0.45-0.38 (m, 1H), 0.38-0.31 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.63, 71.6, 71.5, 70.4, 70.3, 33.6, 31.8, 29.3, 29.3, 27.7, 22.9, 18.1, 18.0, 17.3, 17.3, 14.3, 10.7, 10.7, 9.1, 9.1. HRMS (ESI-TOF) calculated for $C_{13}H_{25}O_3$, 229.1804; observed, 229.1810 $[M+H]^+$.



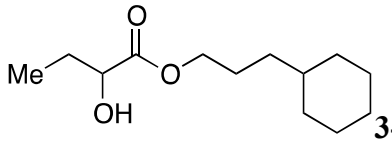
4-Phenylbutyl 2-hydroxybutyrate, 37. 0.5 g of 5Å molecular sieves (0.5 g for each mmol of ethyl-2 hydroxybutyrate) and 1,3-bis (2,4,6-trimethylphenyl) imidazol-2-ylidene (30.4mg, 0.1 mmol) were added to a round-bottom flask equipped with a stir bar. The vial was brought to vacuum and subsequently placed under N_2 three times. To the reaction flask was added 1mL toluene, followed by ethyl 2-hydroxybutyrate (130 μL, 1mmol). 4-phenyl-1-butanol (305 μL, 2 mmol) was subsequently added, and the reaction mixture was stirred overnight. Once the reaction was complete, the mixture was transferred to a round-bottom flask, using ether to facilitate the transfer through a cotton-celite filter, to remove residues of the molecular sieves. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 4-phenylbutyl 2-hydroxybutyrate (200 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.22 (m, 2H), 7.21-7.13 (m, 3H), 4.25-4.14 (m, 2H), 4.13 (dd, *J* = 6.6, 4.4 Hz, 1H), 2.70 (s, 1H), 2.67-2.57 (m, 2H), 1.87-1.76 (m, 1H), 1.73-1.61 (m, 5H), 0.94 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 141.8, 128.4, 128.4 125.9, 71.4, 65.5, 35.4, 28.2, 27.6, 27.5, 8.9. HRMS (ESI-TOF) calculated for $C_{14}H_{21}O_3$, 237.1491; observed, 237.1494 $[M+H]^+$.



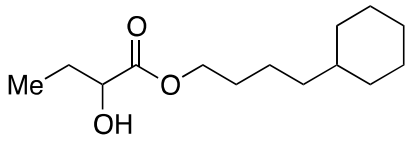
5-Phenylpentyl 2-hydroxybutyrate, 38 Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (129 μL, 1 mmol) and 5-phenyl pentan-1-ol (340 μL, 2 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 5-phenylpentyl 2-hydroxybutyrate (220 mg, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.11 (m, 2H), 7.19-7.12 (m, 3H), 4.22-4.07 (m, 3H), 2.71 (d, *J* = 5.7 Hz, 1H), 2.60 (t, *J* = 7.7 Hz, 2H), 1.84-1.76 (m, 1H), 1.71-1.58 (m, 5H), 1.43-1.33 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 142.4, 128.6, 128.5, 126.0, 71.5, 65.8, 35.9, 31.2, 28.6, 27.7, 25.6, 9.1. HRMS (ESI-TOF) calculated for $C_{15}H_{23}O_3$ 251.1647; observed, 251.1655 $[M+H]^+$.



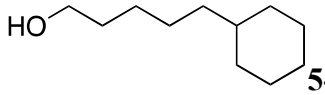
(*S*)-5-Phenylpentyl 2-hydroxybutyrate, (*S*)-38 Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using (*S*)-methyl 2-hydroxybutanoate and and 5-phenyl pentan-1-ol. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*S*)-5-phenylpentyl 2-hydroxybutyrate. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.11 (m, 2H), 7.19-7.12 (m, 3H), 4.22-4.07 (m, 3H), 2.71 (d, *J* = 5.7 Hz, 1H), 2.60 (t, *J* = 7.7 Hz, 2H), 1.84-1.76 (m, 1H), 1.71-1.58 (m, 5H), 1.43-1.33 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 142.4, 128.6, 128.5, 126.0, 71.5, 65.8, 35.9, 31.2, 28.6, 27.7, 25.6, 9.1. HRMS (ESI-TOF) calculated for $C_{15}H_{23}O_3$ 251.1647; observed, 251.1653 $[M+H]^+$.



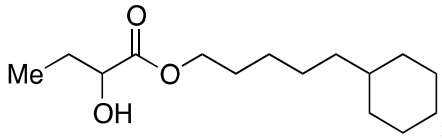
3-Cyclohexylpropyl 2-hydroxybutyrate, 39 Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (129 μL, 1 mmol) and 3-cyclohexyl-1-propanol (300 μL, 2 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 3-cyclohexylpropyl 2-hydroxybutyrate (218 mg, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.21-4.08 (m, 3H), 2.72 (s, 1H), 1.87-1.77 (m, 1H), 1.73-1.58 (m, 8H), 1.25-1.05 (m, 6H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.90-0.78 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 71.6, 66.3, 37.5, 33.6, 33.5, 27.7, 26.8, 26.5, 26.2, 9.1. HRMS (ESI-TOF) calculated for $C_{13}H_{25}O_3$, 229.1804; observed, 229.1809 m/z $[M+H]^+$.



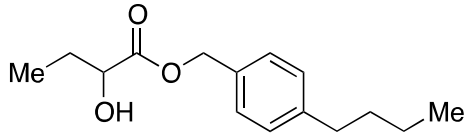
4-Cyclohexylbutyl 2-hydroxybutyrate, 40 Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (90 μL, 1 mmol) and 4-cyclohexyl-1-butanol (350 μL, 2 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 4-cyclohexylbutyl 2-hydroxybutyrate (225 mg, 93% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.22-4.09 (m, 3H), 2.78 (s, 1H), 1.87-1.76 (m, 1H), 1.70-1.56 (m, 8H), 1.37-1.28 (m, 2H), 1.24-1.03 (m, 6H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.89-0.76 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 71.5, 66.0, 37.7, 37.2, 33.5, 29.0, 27.7, 26.9, 26.6, 23.2, 9.1. HRMS (ESI-TOF) calculated for $C_{14}H_{27}O_3$ 243.1960; observed, 243.1962 $[M+H]^+$.



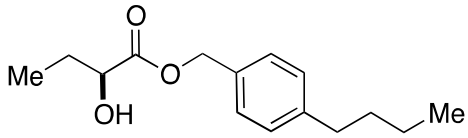
5-Cyclohexyl-1-pentanol. To lithium aluminum hydride (xx mL, 15.6 mmol, 1.0M in THF) at 0°C was added dropwise a 0.1 M solution of 5-cyclohexylpentanoic acid (2.6 mmol) in THF. The mixture was allowed to warm to room temperature and was stirred for 1 hour. The reaction mixture was then quenched by a minimum amount of water, dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 5-cyclohexyl-1-pentanol (445 mg, 99% yield). Spectral data for this compound was consistent with previously reported data [Liutkus,M. *et. al.* Journal of Enzyme Inhibition and Medicinal Chemistry, **2010**, 25(5), 653-672]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (s, 1H), 3.62 (dd, *J* = 11.3, 6.3 Hz, 2H), 1.59 (ddd, *J* = 20.7, 12.9, 6.3 Hz, 8H), 1.36-1.24 (m, 4H), 1.24-1.05 (m, 7H), 0.83 (dd, *J* = 21.2, 10.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 63.3, 63.1, 37.8, 37.7, 33.6, 33.0, 30.1, 27.0, 26.9, 26.7, 26.2.



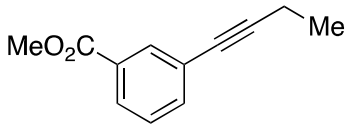
5-Cyclohexylpentyl 2-hydroxybutyrate, 41 Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (96 μL, 0.73 mmol) and 5-cyclohexyl-1-butanol (250 mg, 1.47 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 5-cyclohexylpentyl 2-hydroxybutyrate (151 mg, 59% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.21-4.10 (m, 3H), 2.73 (d, *J* = 5.7 Hz, 1H), 1.87-1.76 (m, 1H), 1.70-1.57 (m, 8H), 1.35-1.25 (m, 4H), 1.23-1.06 (m, 6H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.88-0.76 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 71.5, 66.0, 37.8, 37.5, 33.6, 28.8, 27.7, 26.9, 26.6, 26.6, 26.3, 9.1. HRMS (ESI-TOF) calculated for $C_{15}H_{29}O_3$ 257.2117; observed, 257.2120 $[M+H]^+$.



(1-(*p*-Butyl-phenyl)methyl 2-hydroxybutyrate), 42. Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (129 μL, 1 mmol) and (4-butylphenyl)methanol (342 μL, 2 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to **(**1-(*p*-butyl-phenyl)methyl 2-hydroxybutyrate) (193 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.1 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.16 (s, 2H), 4.17 (dd, *J* = 6.7, 4.3 Hz, 1H), 2.59 (dd, *J* = 7.8, 7.8 Hz, 2H), 1.88-1.78 (m, 1H), 1.72-1.62 (m, 1H), 1.61-1.52 (m, 2H), 1.38-1.28 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 143.7, 132.5, 128.9, 128.7, 71.6, 67.6, 35.6, 33.8, 27.7, 22.5, 14.2, 9.1; HRMS (ESI-TOF) calculated for $C_{15}H_{22}O_3Na$, 237.1466; observed, 273.14715 $[M+Na]^+$.

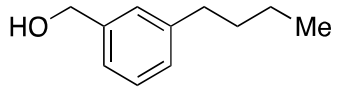


(*S*)-(1-(*p*-Butyl-phenyl)methyl 2-hydroxybutyrate), (*S*)-42. Prepared according to the procedure given for the preparation of (*S*)-Octyl 2-hydroxybutanoate, **7** using (*S*)-methyl 2-hydroxybutanoate and (4-butylphenyl)methanol. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (*S*)-**(**1-(*p*-butyl-phenyl)methyl 2-hydroxybutyrate). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.1 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.16 (s, 2H), 4.17 (dd, *J* = 6.7, 4.3 Hz, 1H), 2.59 (dd, *J* = 7.8, 7.8 Hz, 2H), 1.88-1.78 (m, 1H), 1.72-1.62 (m, 1H), 1.61-1.52 (m, 2H), 1.38-1.28 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 143.7, 132.5, 128.9, 128.7, 71.6, 67.6, 35.6, 33.8, 27.7, 22.5, 14.2, 9.1; HRMS (ESI-TOF) calculated for $C_{15}H_{22}O_3Na$, 237.1466; observed, 273.1473 $[M+Na]^+$.

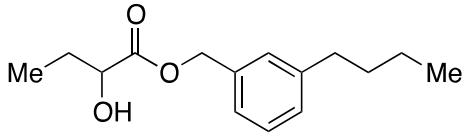


Methyl 3-(but-1-yn-1-yl)benzoate. Methyl 3-bromobenzoate (2.0 g, 9.3 mmol), Bis(triphenylphosphine)palladiumchloride (0.53 g, 0.78 mmol) and copper iodide (0.07 g, 0.4 mmol) were added to a 250 mL Schlenk flask which was subsequently evacuated and purged to N_2 three times. Benzene (26 mL) and Et_3N (5.2 mL) were added and 1-butyne was subsequently bubbled through the mixture for at least 5 minutes and the flask was sealed. The mixture was then warmed to 80°C and allowed to react for 1 hour before subsequent addition of additional 1-butyne. Based on the volume of the flask, 1-butyne was added into the reaction mixture 5 times in order to introduce approximately 2 equivalents of the alkyne. The crude reaction mixture was filtered through a plug of SiO_2, washing with EtOAc and was concentrated *in vacuo*. The residue

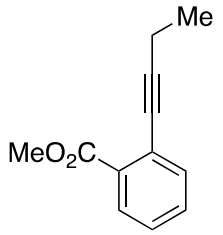
was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide methyl 3-(but-1-yn-1-yl)benzoate (0.68 g, 40% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.91 (d, J = 7.84 Hz, 1H), 7.54 (d, J = 7.7 Hz, 1H), 7.34 (t, J = 7.8 Hz, 1H), 3.89 (s, 3H), 2.41 (q, J = 7.5 Hz, 2H), 1.22 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 143.4, 133.3, 129.7, 128.5, 127.1, 52.3, 35.6, 33.8, 22.5, 14.2.



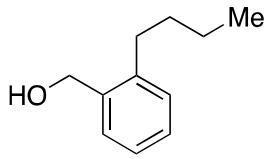
(3-Butylphenyl)methanol. To a solution of methyl 3-(but-1-yn-1-yl)benzoate (95 mg, 0.49 mmol) in EtOH (1 mL) was added 10% Pd/C (68 mg) and the mixture was stirred vigorously under an atmosphere of H_2 (1 atm) overnight. The mixture was filtered through a plug of Celite, was concentrated *in vacuo* and was used without further purification. The residue was dissolved in THF (1 mL) and was treated with $LiAlH_4$ (65 mg, 1.72 mmol) at 0^{o}C. The resulting mixture was allowed to warm to room temperature overnight, was quenched with a minimal amount of H_2O, was dried over $MgSO_4$ and was concentrated *in vacuo*. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (3-butylphenyl)methanol (75.3 mg, 93%, two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.79 (m, 2H), 7.38-7.28 (m, 2H), 3.89 (s, 3H), 2.66-2.61 (m, 2H), 1.63-1.56 (m, 2H), 1.36-1.28 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 143.4, 133.3, 130.2, 129.7, 128.5, 127.1, 52.3, 35.6, 33.8, 22.5, 14.2.



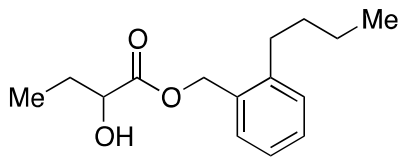
1-(*m*-Butyl-phenyl)methyl 2-hydroxybutyrate), 43. Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (35 μL, 0.25 mmol) and (3-butylphenyl)methanol (75 mg, 0.42 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 1-(*m*-butyl-phenyl)methyl 2-hydroxybutyrate) (29 mg, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.22 (m, 1H), 7.18-7.12 (m, 3H), 5.19 (A of AB, J = 12.1 Hz, 1H), 5.15 (B of AB, J = 12.1 Hz, 1H), 4.19 (dd, J = 10.8, 5.9 Hz, 1H), 2.72 (d, J = 5.8 Hz, 1H), 2.60 (dd, J = 7.7, 7.7 Hz, 2H), 1.89-1.78 (m, 1H), 1.73-1.62 (m, 1H), 1.61-1.51 (m, 2H), 1.39-1.28 (m, 2H), 0.95-0.87 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 143.7, 135.2, 128.9, 128.8, 128.7, 125.8, 71.6, 67.7, 35.7, 33.8, 27.7, 22.6, 14.2, 9.1. HRMS (ESI-TOF) calculated for $C_{15}H_{22}O_3Na$, 273.1467; observed, 273.1478 $[M+Na]^+$.



Methyl 2-(but-1-yn-1-yl)benzoate Prepared according to the procedure given for the preparation of methyl 3-(but-1-yn-1-yl)benzoate (see Supporting Information, page 22), using methyl 2-bromobenzoate (2.0 g, 9.3 mmol), Bis(triphenylphosphine)palladiumchloride (0.53 g, 0.78 mmol), copper iodide (0.07 g, 0.4 mmol), and 1-butyne. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide methyl 2-(but-1-yn-1-yl)benzoate (1.13 g, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 7.3 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.40 (dt, J = 7.6, 1.0 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 3.90 (s, 3H), 2.47 (q, J = 7.5 Hz, 2H), 1.25 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 134.4, 132.0, 131.8, 130.4, 127.4, 124.6, 97.4, 78.8, 52.3, 14.0, 13.7.

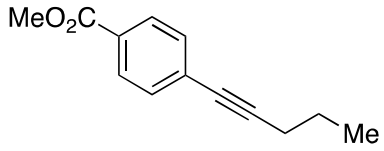


(2-Butylphenyl)methanol Prepared according to the procedure given for the preparation of (3-butylphenyl)methanol (see Supporting Information, page 22), using methyl 2-(but-1-yne)benzoate (113 mg, 0.6 mmol), 10% Pd/C (39 mg) and $LiAlH_4$ (33 mg, 0.9 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (2-butylphenyl)methanol (59.0 mg, 60%, two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 7.2 Hz, 1H), 7.27-7.15 (m, 3H), 4.71 (s, 2H), 2.66 (dd, J = 7.9, 7.9 Hz, 2H), 1.63-1.48 (m, 2H), 1.44-1.31 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.2, 138.4, 129.6, 128.3, 128.1, 126.3, 63.3, 33.7, 32.3, 23.0, 14.2.

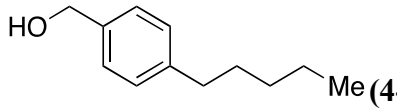


(1-(*o*-Butyl-phenyl)methyl 2-hydroxybutyrate), 44 Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (76 μL, 0.59 mmol) and (2-butylphenyl)methanol (192 mg, 1.17 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 1-(*o*-butyl-phenyl)methyl 2-hydroxybutyrate) (55 mg, 40% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.26 (m, 2H), 7.22-7.16 (m, 2H), 5.23 (s, 2H), 4.17 (dd, J = 10.6, 6.1 Hz, 1H), 2.72 (d, J = 5.7 Hz, 1H), 2.63 (dd, J = 7.8, 7.8 Hz, 2H), 1.88-1.78 (m, 1H), 1.72-1.62 (m, 1H), 1.59-1.50 (m, 2H), 1.42-1.33 (m, 2H), 0.92 (t, J = 7.4 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 142.1, 132.7, 130.1, 129.8, 129.2, 126.3, 71.6, 65.7, 33.7,

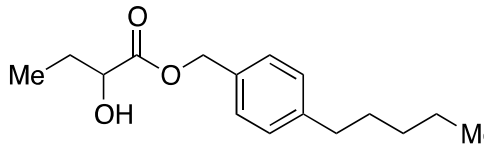
32.5, 27.7, 23.0, 14.2, 9.1. HRMS (ESI-TOF) calculated for $C_{15}H_{22}O_3Na$, 273.1467; observed, 273.1465 $[M+Na]^+$.



Methyl 4-(pent-1-yn-1-yl)benzoate. Prepared according to the procedure given for the preparation of methyl 3-(but-1-yn-1-yl)benzoate (see Supporting Information, page 22), using methyl 4-bromobenzoate (2.15 g, 10 mmol), Bis(triphenylphosphine)palladiumchloride (0.56 g, 0.8 mmol), copper iodide (0.07 g, 0.4 mmol), and 1-pentyne. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide methyl 4-(pent-1-yn-1-yl)benzoate (1.92 g, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 3.89 (s, 3H), 2.39 (t, J = 7.0 Hz, 2H), 1.61 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 131.7, 129.6, 129.1, 128.9, 94.0, 80.4, 52.4, 22.3, 21.7, 13.8.

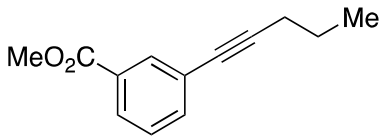


(4-Pentylphenyl)methanol Prepared according to the procedure given for the preparation of (3-butylphenyl)methanol (see Supporting Information, page 22), using methyl 4-(pent-1-yn-1-yl)benzoate (1.9 g, 9.39 mmol), 10% Pd/C (500 mg) and $LiAlH_4$ (713 mg, 18.8 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (4-pentylphenyl)methanol (0.72 g, 43%, two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, J = 7.8 Hz, 2H), 7.16 (d, J = 7.8 Hz, 2H), 4.64 (d, J = 5.4 Hz, 1H), 2.58 (t, J = 7.7 Hz, 2H), 1.64-1.50 (m, 4H), 1.37-1.24 (m, 4H), 0.87 (t, J = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.8, 138.3, 128.9, 127.3, 65.6, 35.8, 31.7, 31.5, 22.8, 14.3.

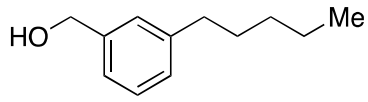


(1-(*p*-Pentyl-phenyl)methyl 2-hydroxybutyrate), 45. Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (83 μL, 0.64 mmol) and (4-pentylphenyl)methanol (229 mg, 1.28 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (1-(*p*-pentyl-phenyl)methyl 2-hydroxybutyrate) (124 mg, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 7.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 5.16 (s, 2H), 4.17 (dd, J = 10.8, 6.0 Hz, 1H), 2.72 (d, J = 5.7 Hz, 1H), 2.58 (dd, J = 7.7 Hz, 2H), 1.87-1.77 (m, 1H), 1.72-1.62 (m, 1H), 1.62-1.54 (m, 2H), 1.35-1.25 (m, 4H), 0.91 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 143.8, 132.5, 128.9,

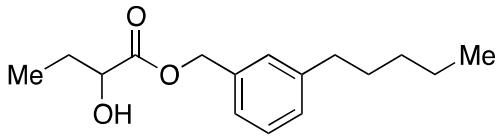
128.7, 71.6, 67.6, 35.9, 31.7, 31.3, 27.7, 22.7, 14.3, 9.1. HRMS (ESI-TOF) calculated for $C_{16}H_{24}O_3Na$, 287.1623; observed, 287.1631 $[M+Na]^+$.



Methyl 3-(pent-1-yn-1-yl)benzoate. Prepared according to the procedure given for the preparation of methyl 3-(but-1-yn-1-yl)benzoate (see Supporting Information, page 22), using methyl bromobenzoate (3.85 g, 17.9 mmol), Bis-(triphenylphosphine)-palladiumchloride (0.95 g, 1.35 mmol), copper iodide (70 mg, 0.35 mmol) and 1-pentyne. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide methyl 3-(pent-1-yn-1-yl)benzoate (1.7 g, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 7.7 Hz, 1H), 7.34 (t, J = 7.8 Hz, 1H), 3.89 (s, 3H), 2.37 (t, J = 7.0 Hz, 2H), 1.67-1.57 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 136.0, 132.9, 130.4, 128.7, 128.5, 124.7, 91.6, 80.0, 52.5, 22.3, 21.6, 13.8.

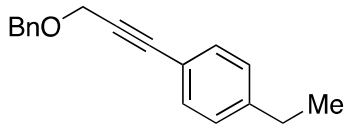


(3-Pentylphenyl)methanol. Prepared according to the procedure given for the preparation of (3-butylphenyl)methanol (see Supporting Information, page 22), using methyl 3-(pent-1-yn-1-yl)benzoate (1.1 g, 5.42 mmol), 10% Pd/C (170 mg) and $LiAlH_4$ (410 mg, 10.8 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (3-pentylphenyl)methanol (0.30 g, 31% yield, two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.24 (m, 1H), 7.19-7.08 (m, 3H), 5.27 (s, 1H), 4.60 (d, J = 5.1 Hz, 2H), 2.66-2.55 (m, 2H), 1.70-1.57 (m, 2H), 1.40-1.27 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 140.9, 128.5, 127.8, 127.2, 124.4, 65.3, 36.0, 31.7, 31.4, 22.7, 14.2.

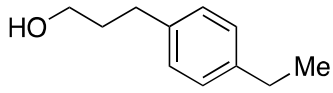


(1-(*m*-Pentyl-phenyl)methyl 2-hydroxybutyrate), 46. Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (100 μL, 0.8 mmol) and (3-pentylphenyl)methanol (282 mg, 1.58 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (1-(*m*-pentyl-phenyl)methyl 2-hydroxybutyrate) (170 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.22 (m, 1H), 7.19-7.10 (m, 3H), 5.19 (A of AB, J = 12.1 Hz, 1H), 5.16 (B of AB, J = 12.1 Hz, 1H), 4.19 (dd, J = 10.6, 6.1 Hz, 1H), 2.72 (d, J = 5.7 Hz, 1H), 2.59 (dd, J = 7.7, 7.7 Hz, 2H), 1.89-1.78 (m, 1H), 1.74-1.64 (m, 1H), 1.64-1.53

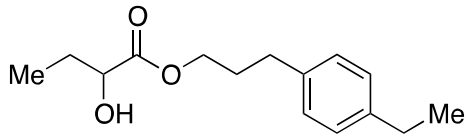
(m, 2H), 1.37-1.24 (m, 4H), 0.92 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 143.7, 135.2, 128.9, 128.8, 128.6, 125.9, 71.6, 67.7, 36.0, 31.7, 31.4, 27.7, 22.7, 14.3, 9.1. HRMS (ESI-TOF) calculated for $C_{16}H_{24}O_3Na$, 287.1623; observed, 287.1631 $[M+Na]^+$.



1-(3-(Benzyloxy)prop-1-yn-1-yl)-4-ethylbenzene. 1-bromo-2-ethylbenzene (0.75 mL, 5.5 mmol), Bis-(triphenylphosphine)-palladium chloride (0.31 g, 0.44 mmol), and copper iodide (42 mg, 0.22 mmol) were added to a 250 ml round bottom flask equipped with a reflux condenser. The flask was brought to vacuum and put under nitrogen gas three times. Benzene (22 mL) and Et_3N (5 mL) were added followed by ((prop-2-yn-1-yloxy)methyl)benzene (1.61 g, 11 mmol). The reaction mixture was warmed to 80°C and stirred for 48 hours. The mixture was passed through a silica pad and washed with EtOAc and was concentrated *in vacuo*. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 1-(3-(benzyloxy)prop-1-yn-1-yl)-4-ethylbenzene (0.35 g, 26% yield).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.29 (m, 7H), 7.13 (d, J = 8.1 Hz, 2H), 4.66 (s, 2H), 4.38 (s, 2H), 2.63 (q, J = 7.6 Hz, 2H), 1.21 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.1, 137.7, 134.8, 132.0, 128.7, 128.4, 128.1, 122.9, 120.0, 86.8, 84.5, 72.1, 71.8, 60.6, 58.2, 29.0, 15.6, 14.4.

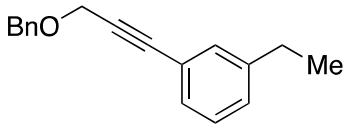


3-(4-Ethylphenyl)propan-1-ol. 1-(3-(benzyloxy)prop-1-yn-1-yl)-4-ethylbenzene (0.35 g, 1.4 mmol) and 10% by wt. palladium on carbon (100 mg) in 7 mL ethanol was allowed to react under a H_2 atmosphere (1 atm) at room temperature overnight. The reaction mixture was filtered through a Celite pad and concentrated *in vacuo*. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 3-(4-ethylphenyl)propan-1-ol (135 mg, 59% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (s, 4H), 3.66 (t, J = 6.4 Hz, 2H), 2.69-2.56 (m, 4H), 1.91-1.83 (m, 2H), 1.20 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.0, 139.1, 128.6, 128.1, 62.6, 34.5, 31.8, 28.6, 15.9.

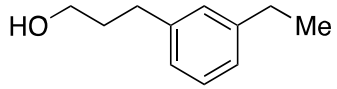


3-(*p*-ethyl-phenyl)propyl 2-hydroxybutyrate, 47 Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (25 μL, 0.18 mmol) and (3-(4-ethylphenyl)propan-1-ol (56 mg, 0.35 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 3-

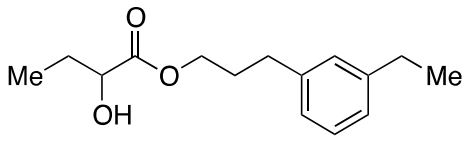
(*p*-ethyl-phenyl)propyl 2-hydroxybutyrate (39 mg, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 7.8 Hz, 2H), 7.07 (d, *J* = 7.8 Hz, 2H), 4.24-4.10 (m, 3H), 2.70 (d, *J* = 5.6 Hz, 1H), 2.68-2.55 (m, 4H), 2.01-1.91 (m, 2H), 1.87-1.77 (m, 1H), 1.73-1.61 (m, 1H), 1.20 (t, *J* = 7.6 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 148.3, 138.2, 128.5, 128.2, 71.5, 65.2, 31.8, 30.4, 28.6, 27.7, 15.9, 9.2. HRMS (ESI-TOF) calculated for $C_{15}H_{23}O_3$ 251.1647; observed, 251.1660 $[M+H]^+$.



1-(3-(Benzyloxy)prop-1-yn-1-yl)-3-ethylbenzene Prepared according to the procedure given for the preparation of 1-(3-(benzyloxy)prop-1-yn-1-yl)-4-ethylbenzene, using 1-bromo-3-ethylbenzene (1.38 g, 10 mmol), Bis(triphenylphosphine)palladiumchloride (0.56 g, 0.80 mmol), copper iodide (0.07 g, 0.4 mmol), and ((prop-2-yn-1-yloxy)methyl)benzene (20 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 1-(3-(benzyloxy)prop-1-yn-1-yl)-3-ethylbenzene (1.08 g, 43% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.13 (m, 8H), 7.10 (d, *J* = 7.5 Hz, 1H), 4.61 (s, 2H), 4.33 (s, 2H), 2.56 (q, *J* = 7.6 Hz, 2H), 1.16 (dd, *J* = 9.5, 5.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.5, 137.7, 131.4, 129.3, 128.7, 128.5, 128.5, 128.4, 128.1, 122.6, 86.9, 84.8, 71.8, 58.1, 28.8, 15.7.

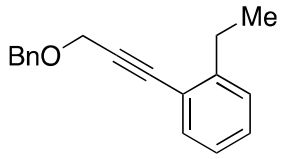


3-(3-Ethylphenyl)propan-1-ol Prepared according to the procedure given for the preparation of 3-(4-ethylphenyl)propan-1-ol, using 1-(3-(benzyloxy)prop-1-yn-1-yl)-3-ethylbenzene (1.08 g, 4.3 mmol), and 0.18 g 10% Pd/C. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (0.65 g, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.8 Hz, 1H), 7.04-6.99 (m, 3H), 3.67 (dd, *J* = 11.1, 6.0 Hz, 2H), 2.72-2.56 (m, 4H), 1.93-1.82 (m, 2H), 1.21 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.4, 141.8, 128.4, 128.1, 125.7, 125.4, 62.5, 34.3, 32.1, 28.9, 15.7.

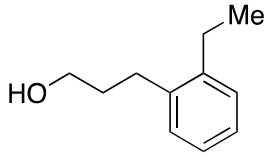


3-(*m*-Ethyl-phenyl)propyl 2-hydroxybutyrate, 48 Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (129 μL, 1.0 mmol) and (3-(3-ethylphenyl)propan-1-ol (328 mg, 2.0 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 3-(*p*-ethyl-phenyl)propyl 2-hydroxybutyrate (231 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 7.01-6.95 (m, 2H), 4.23-4.11

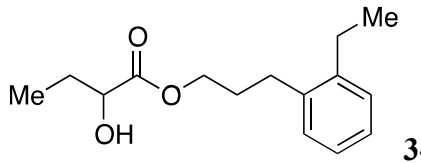
(m, 3H), 2.70 (d, J = 5.7 Hz, 1H), 2.68-2.57 (m, 4H), 2.03-1.93 (m, 2H), 1.89-1.78 (m, 1H), 1.72-1.62 (m, 1H), 1.21 (t, J = 7.6 Hz, 3H), 0.96 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 144.7, 141.0, 128.7, 128.2, 125.9, 125.8, 71.6, 65.3, 32.3, 30.4, 29.0, 27.7, 15.8, 9.2. HRMS (ESI-TOF) calculated for $C_{15}H_{23}O_3$, 251.1647; observed, 251.1653 $[M+H]^+$.



1-(3-(Benzyloxy)prop-1-yn-1-yl)-2-ethylbenzene Prepared according to the procedure given for the preparation of 1-(3-(benzyloxy)prop-1-yn-1-yl)-4-ethylbenzene, using 1-bromo-2-ethylbenzene (1.38 g, 10 mmol), Bis(triphenylphosphine)palladium chloride (0.56 g, 0.80 mmol), copper iodide (0.07 g, 0.4 mmol), and ((prop-2-yn-1-yloxy)methyl)benzene (2.9 g, 20 mmol). The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 1-(3-(benzyloxy)prop-1-yn-1-yl)-3-ethylbenzene (0.42 g, 19% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 7.6 Hz, 1H), 7.40-7.19 (m, 7H), 7.14 (t, J = 7.5 Hz, 1H), 4.68 (s, 2H), 4.43 (s, 2H), 2.82 (q, J = 7.6 Hz, 2H), 1.25 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.5, 137.7, 132.7, 128.9, 128.7, 128.4, 128.2, 128.0, 125.8, 88.6, 85.4, 71.6, 58.1, 27.9, 15.2, 15.1.



3-(2-Ethylphenyl)propan-1-ol Prepared according to the procedure given for the preparation of 3-(4-ethylphenyl)propan-1-ol, using 1-(3-(benzyloxy)prop-1-yn-1-yl)-2-ethylbenzene (0.42 g, 1.7 mmol), and 70 mg 10% Pd/C. The crude product was purified by silica gel chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide (0.16 g, 59% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19-7.09 (m, 4H), 3.70 (s, 2H), 2.74-2.60 (m, 4H), 1.89-1.81 (m, 2H), 1.30 (s, 1H), 1.21 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.1, 139.5, 129.3, 128.7, 126.4, 126.1, 62.9, 34.1, 29.0, 25.7, 15.6.



3-(*o*-Ethyl-phenyl)propyl 2-hydroxybutyrate, 49 Prepared according to the procedure given for the preparation of 4-phenylbutyl 2-hydroxybutyrate, **37** using ethyl 2-hydroxybutyrate (26 μL, 0.2 mmol) and (3-(2-ethylphenyl)propan-1-ol (65 mg, 0.4 mmol). The crude product was purified by silica gel

chromatography using a gradient from hexanes to 20% EtOAc/hexanes to provide 3-(*o*-ethyl-phenyl)propyl 2-hydroxybutyrate (37 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19-7.09 (m, 4H), 4.30-4.07 (m, 4H), 2.76-2.58 (m, 4H), 1.99-1.90 (m, 2H), 1.89-1.78 (m, 1H), 1.73-1.63 (m, 1H), 1.20 (t, *J* = 7.6 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 175.5, 142.1, 138.6, 129.3, 128.8, 126.7, 126.2, 71.6, 65.5, 30.1, 29.0, 27.7, 25.7, 15.6, 9.2. HRMS (ESI-TOF) calculated for $C_{15}H_{23}O_3$, 251.1647; observed, 251.1652 $[M+H]^+$.

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(1) Ng, W.-L.; Wei, Y.; Perez, L. J.; Cong, J.; Long, T.; Koch, M.; Semmelhack, M. F.; Wingreen, N. S.; Bassler, B. L. *Proceedings of the National Academy of Sciences of the United States of America* **2010**, *107*, 5575.

(2) Ng, W. L.; Perez, L. J.; Wei, Y.; Kraml, C.; Semmelhack, M. F.; Bassler, B. L. *Mol Microbiol* **2011**, *79*, 1407.

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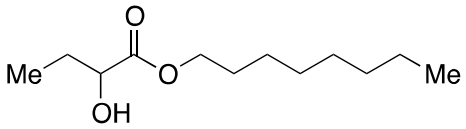
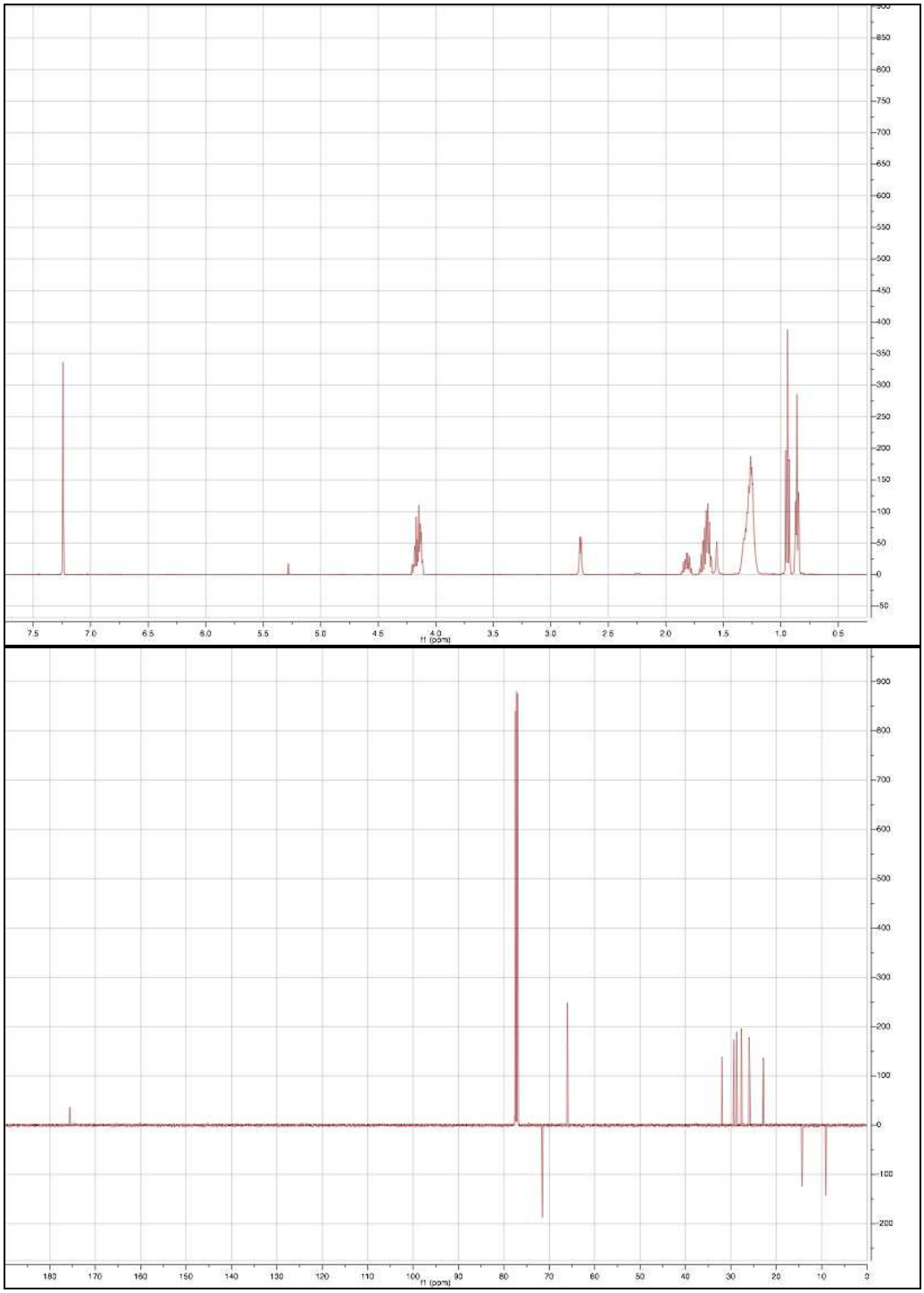
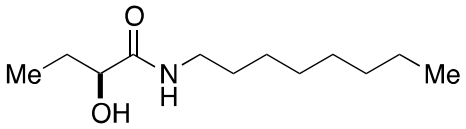
F. ^{1}H-NMR and ^{13}C-NMR spectra for all new compounds

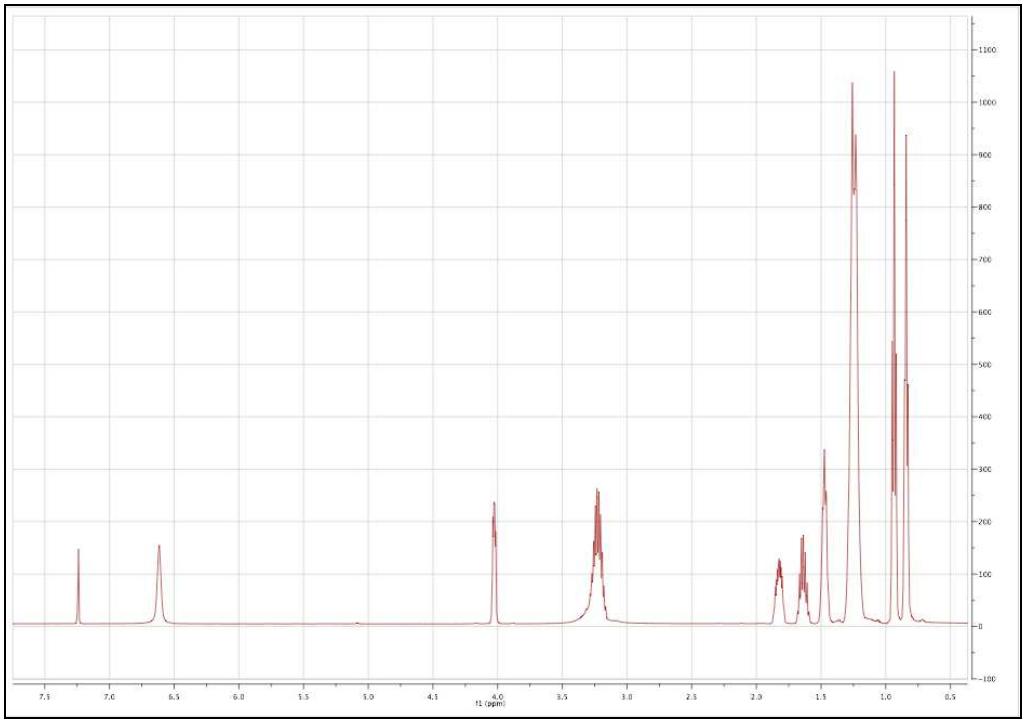


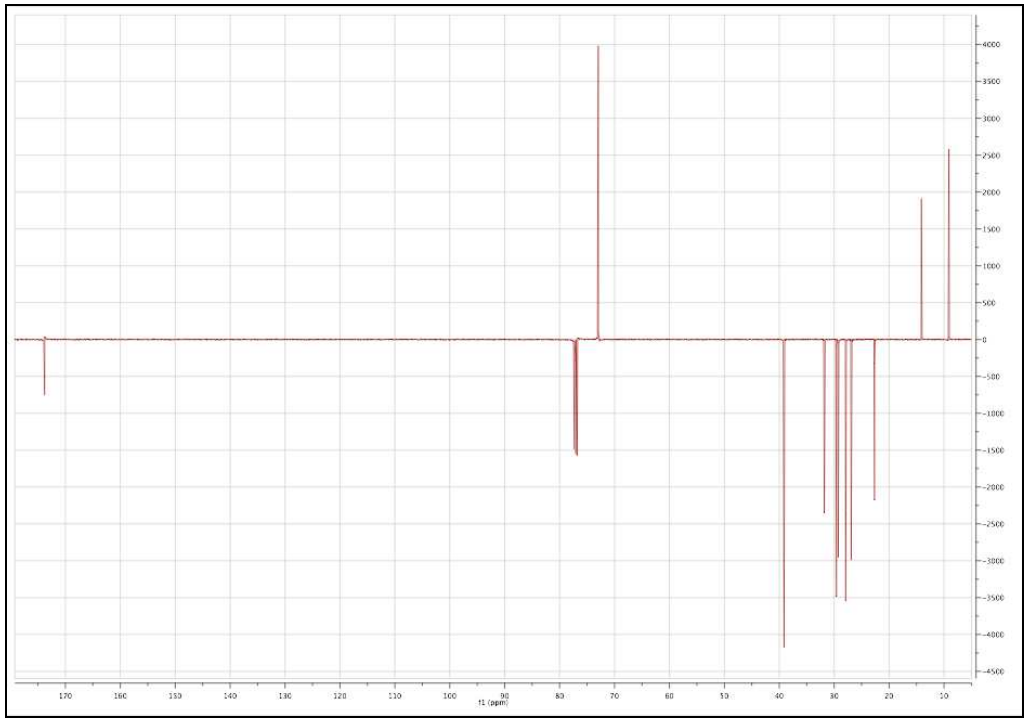
Octyl 2-hydroxybutanoate, 9.

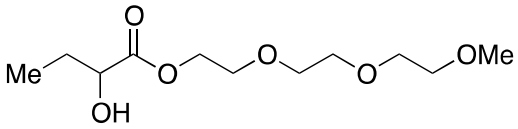




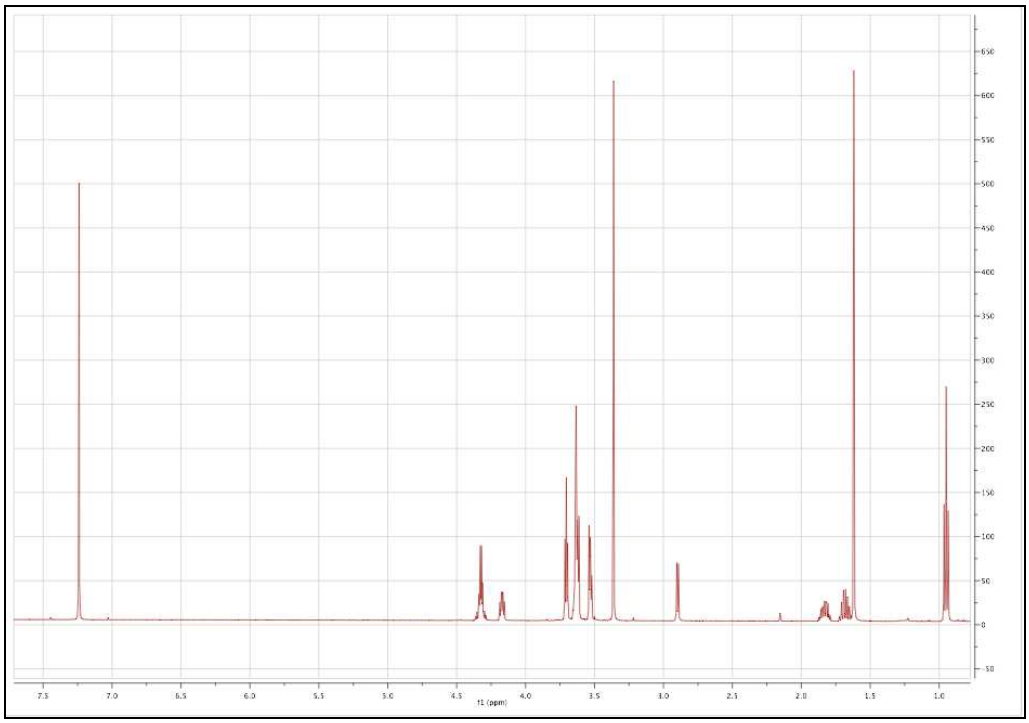
***(S)*-2-Hydroxy-N-octylbutanamide, 9.**

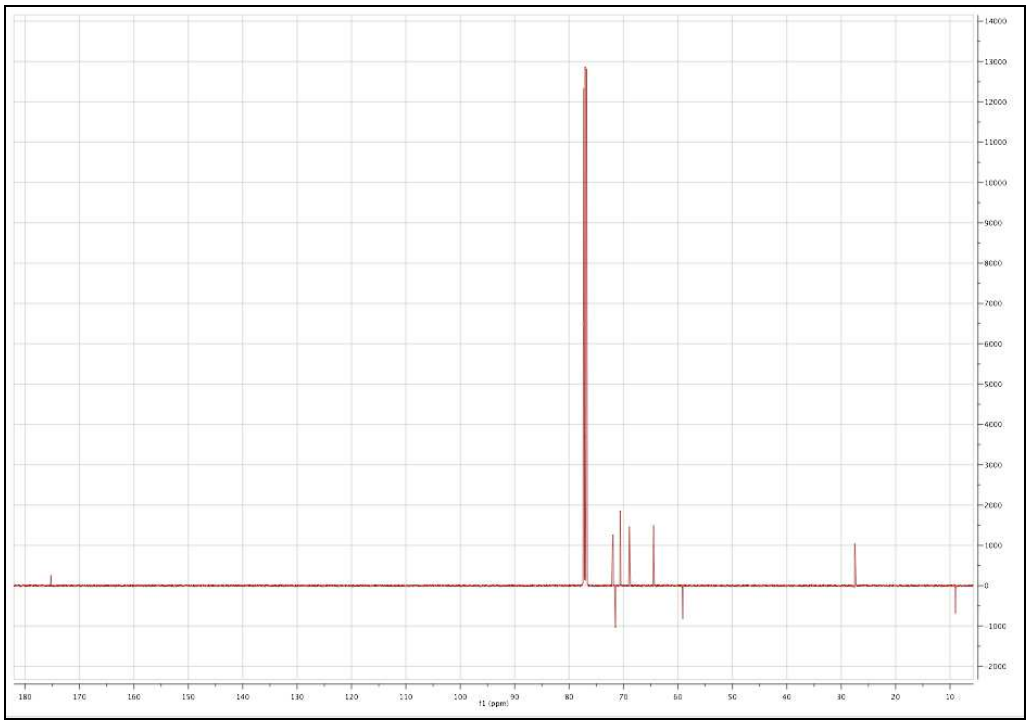


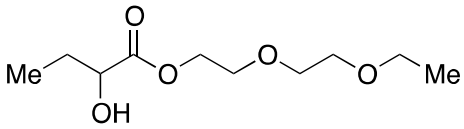




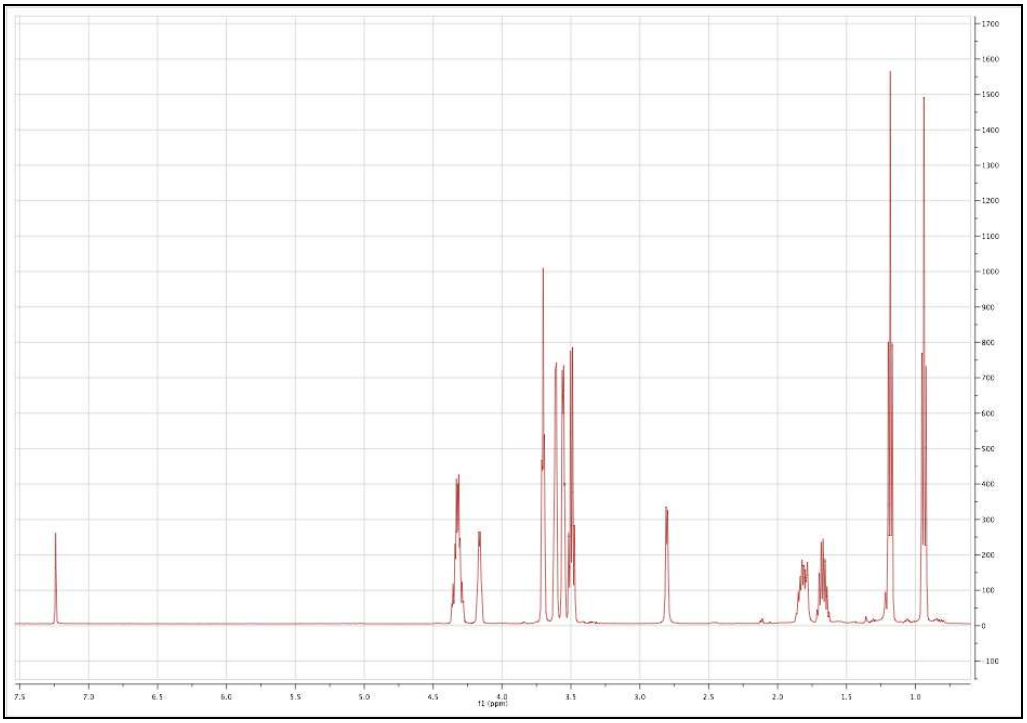
2-Hydroxy-2-(2-(2-methoxyethoxy)ethoxy)ethylbutanoate, 25.

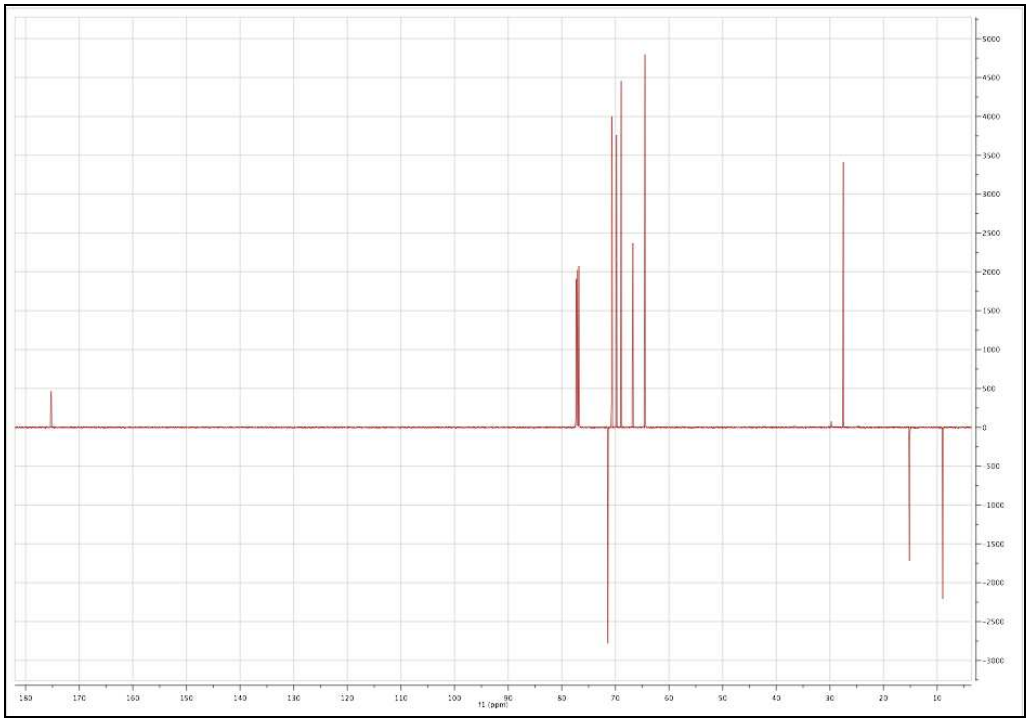


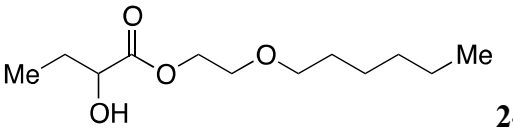




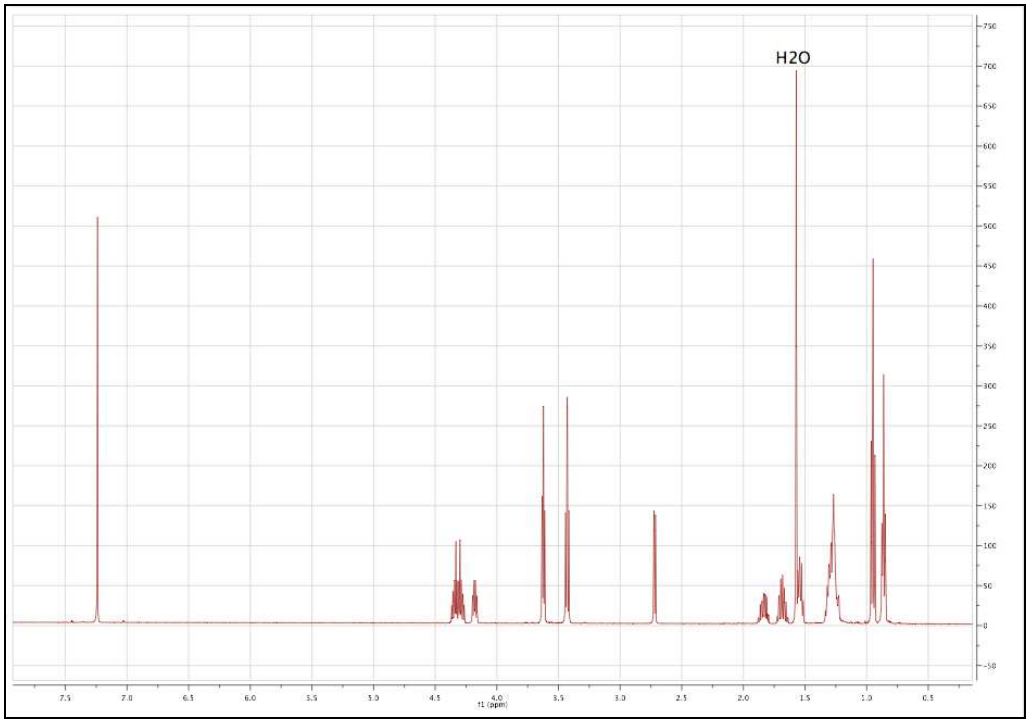
2-Hydroxy-2-(2-ethoxyethoxy)ethylbutanoate, 23.

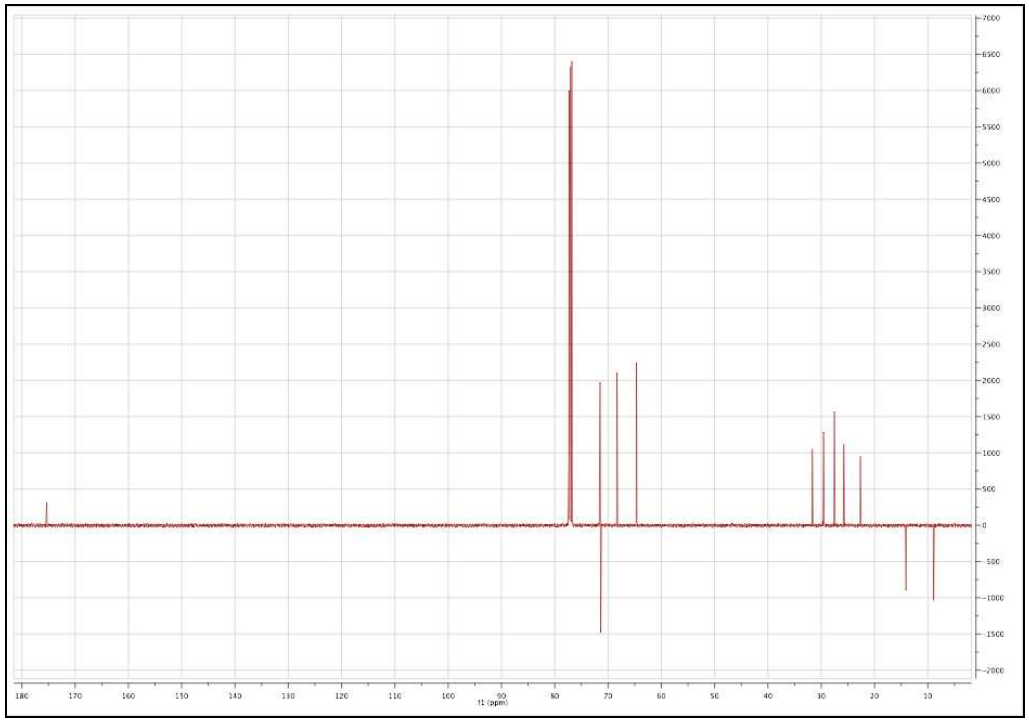


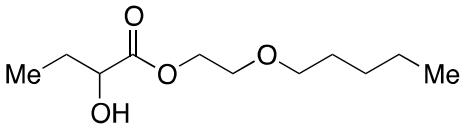




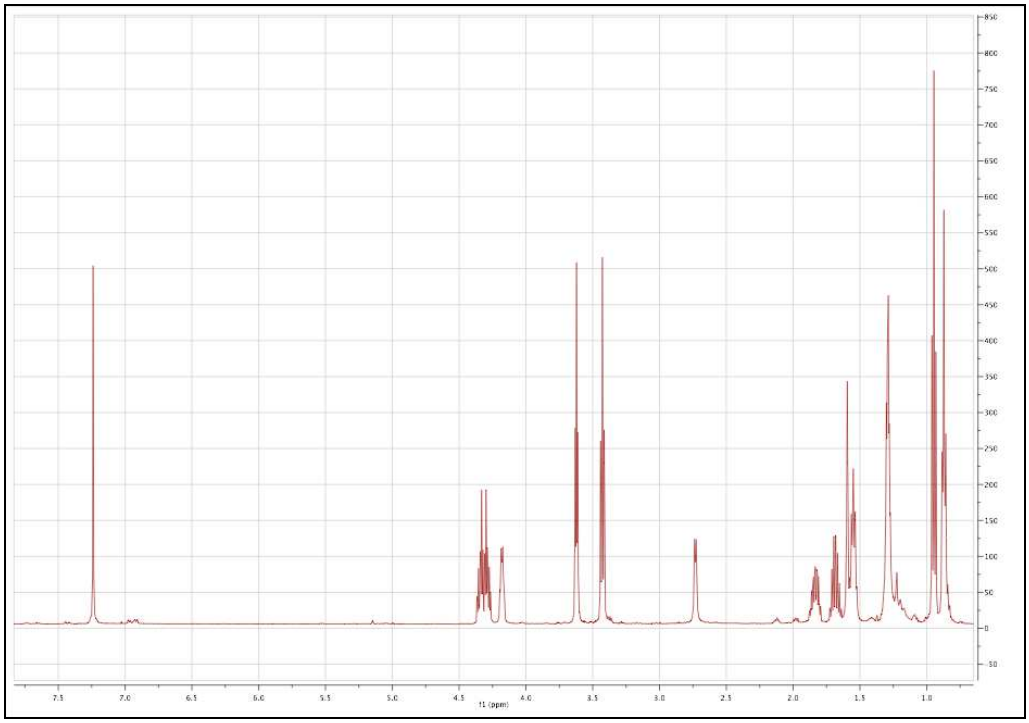
2-(Hexyloxy)ethyl 2-hydroxybutanoate, 24.

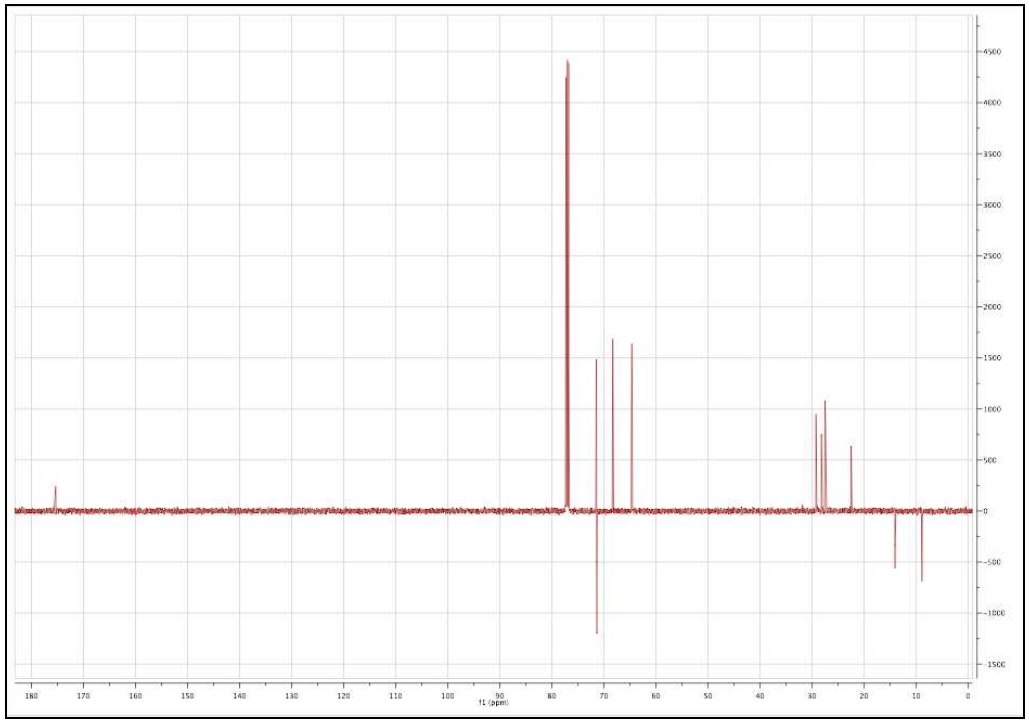


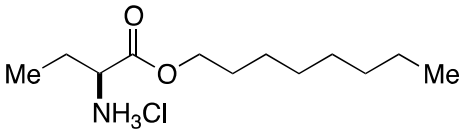




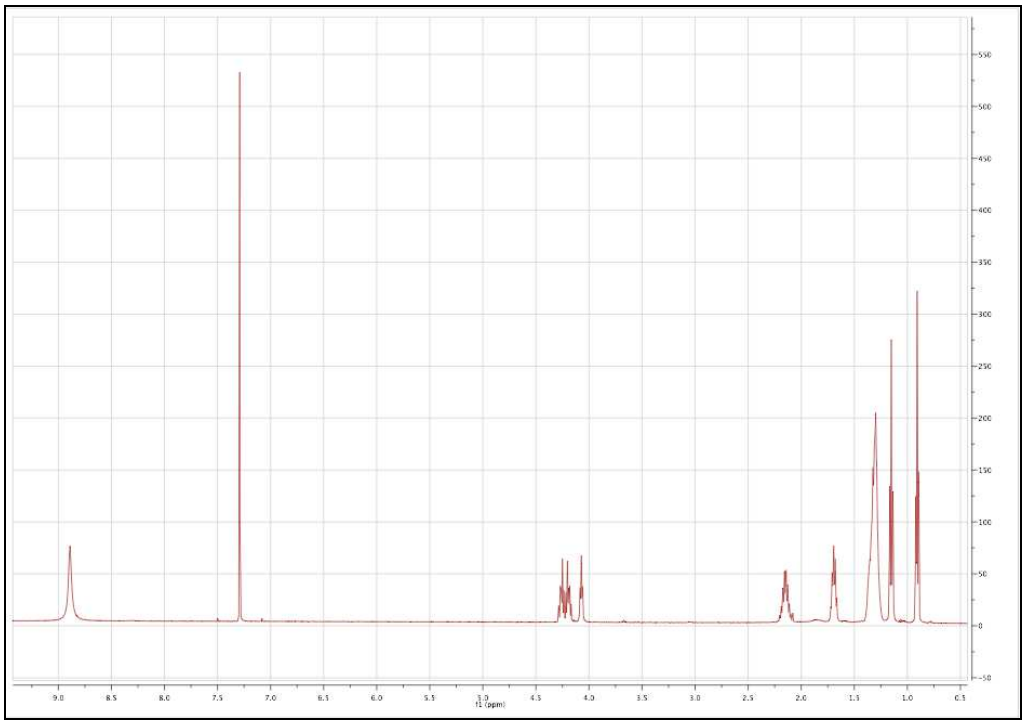
2-(Pentyloxy)ethyl 2-hydroxybutanoate, 25.

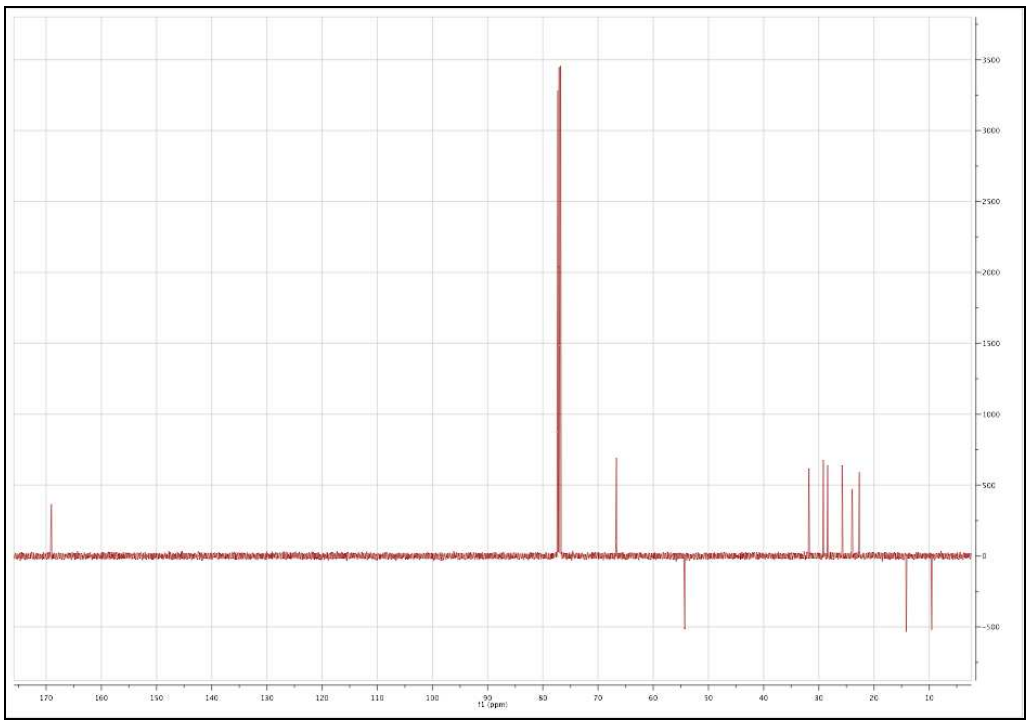


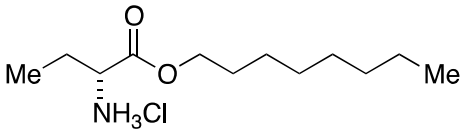




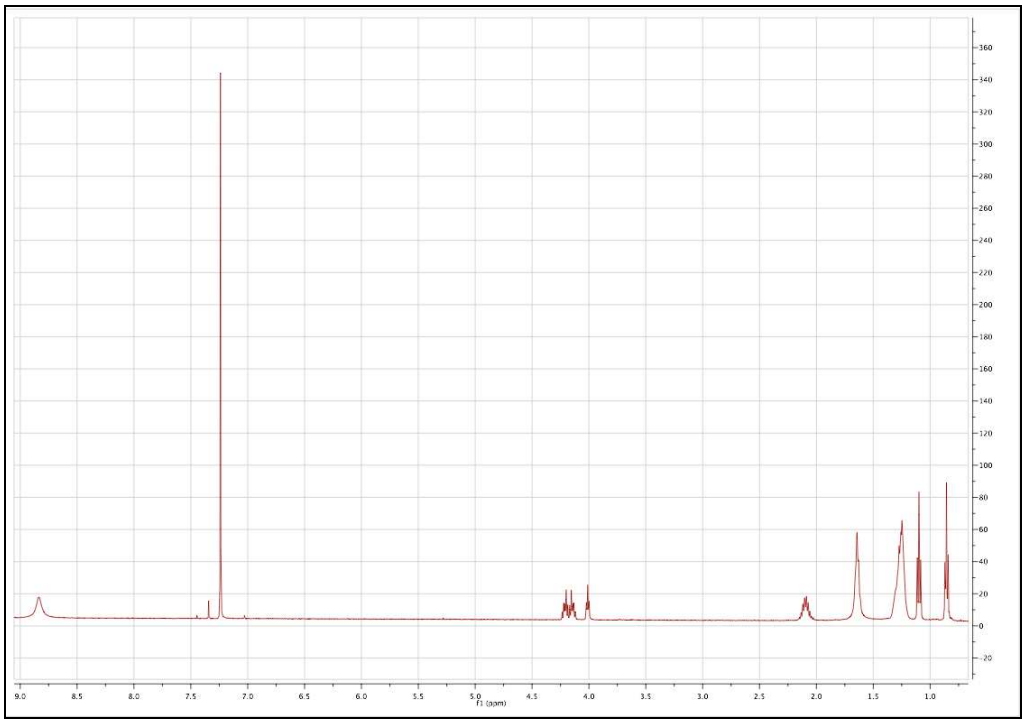
***(S)*-2-aminooctylbutanoate hydrochloride, 12.**

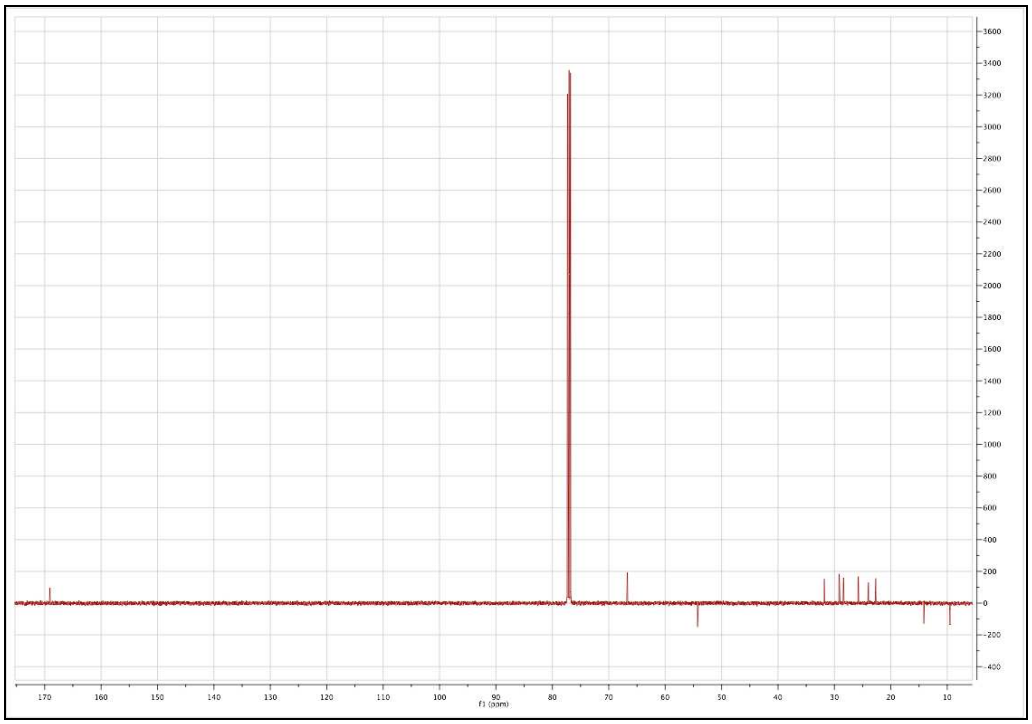


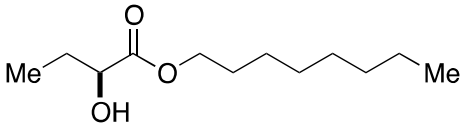




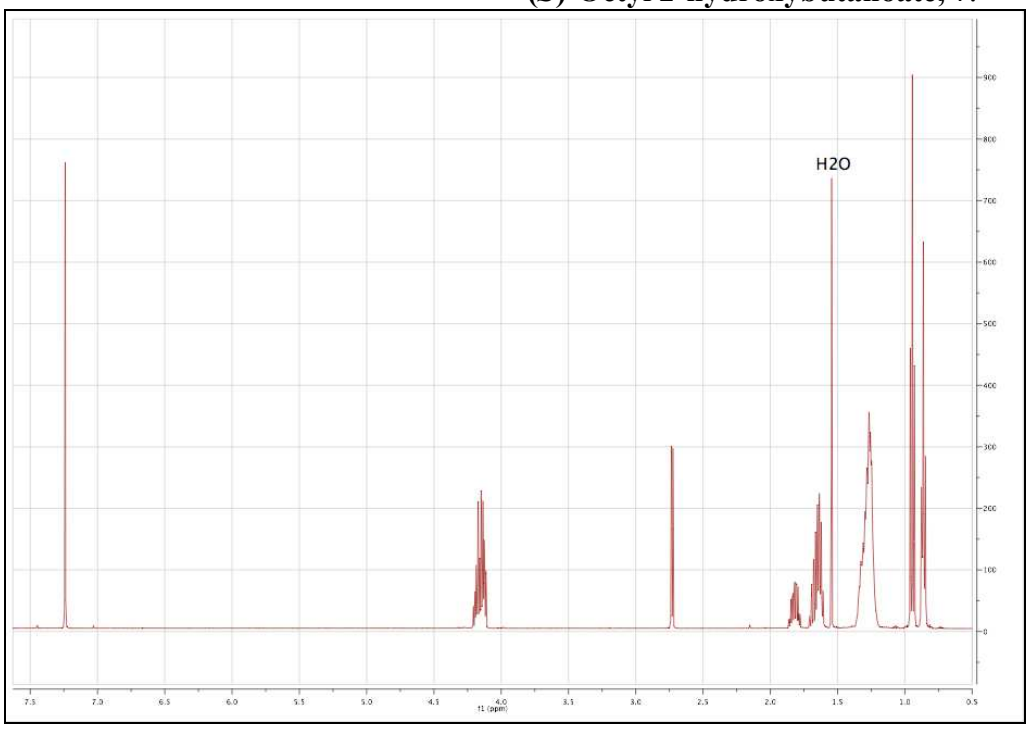
***(R)*-2-aminooctylbutanoate hydrochloride, 13.**

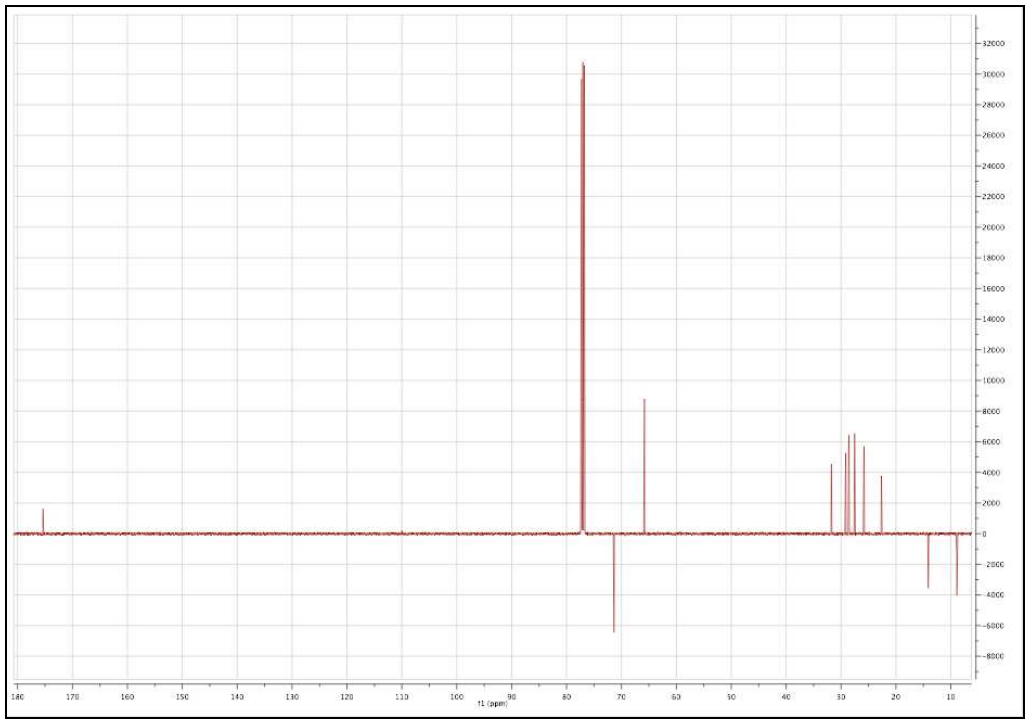


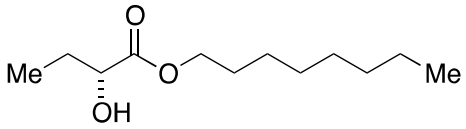




(*S*)-Octyl 2-hydroxybutanoate, 7.







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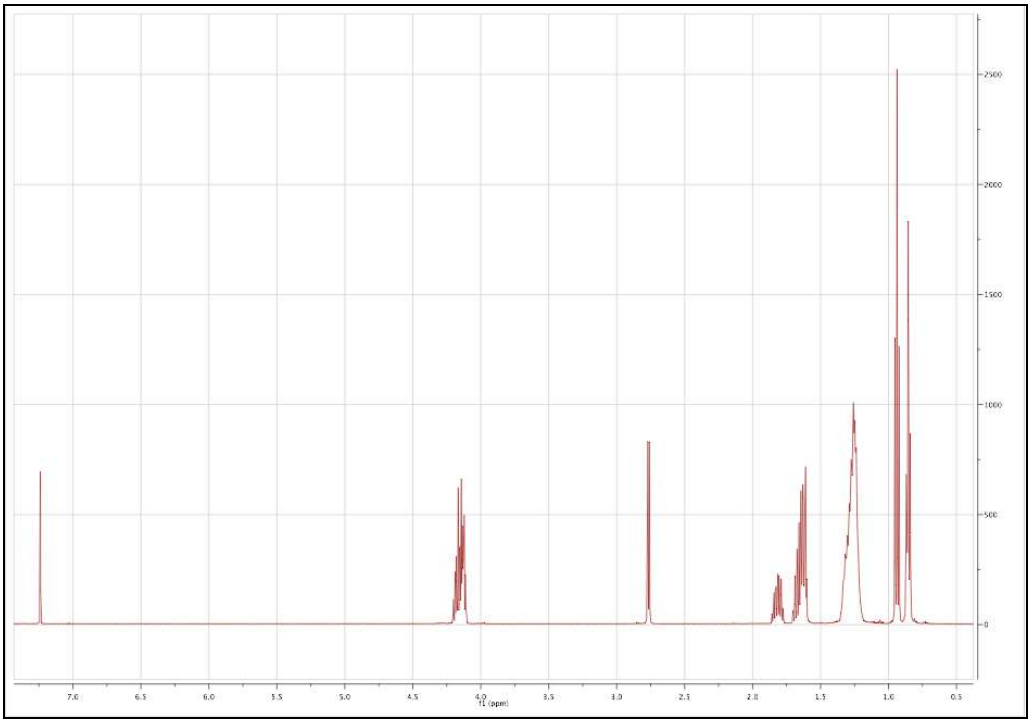
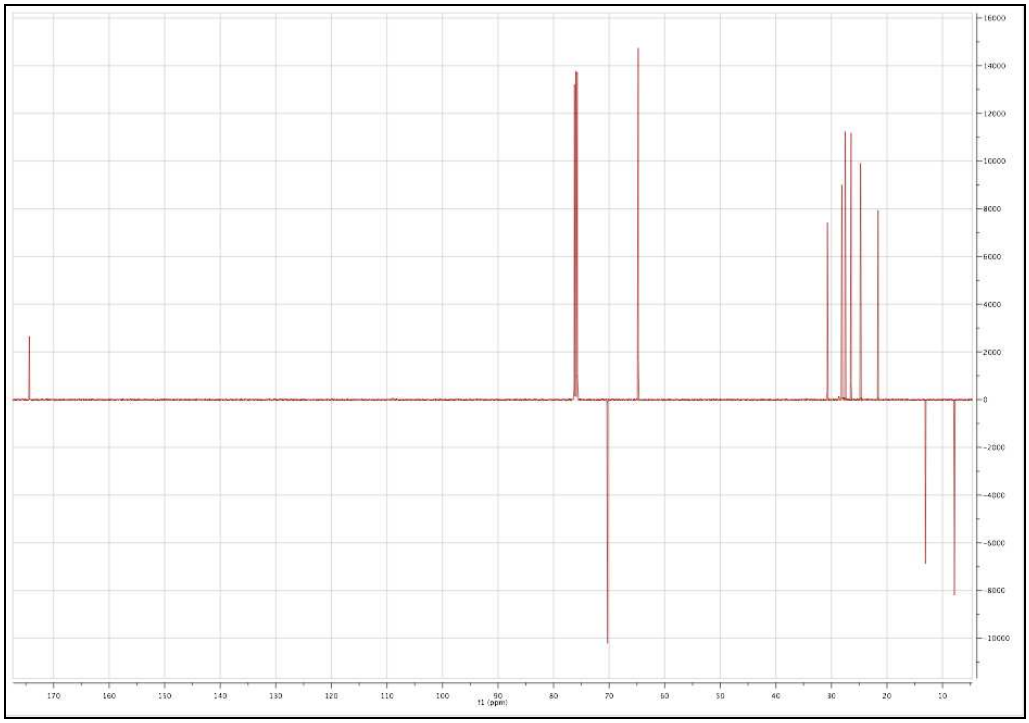
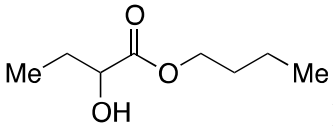
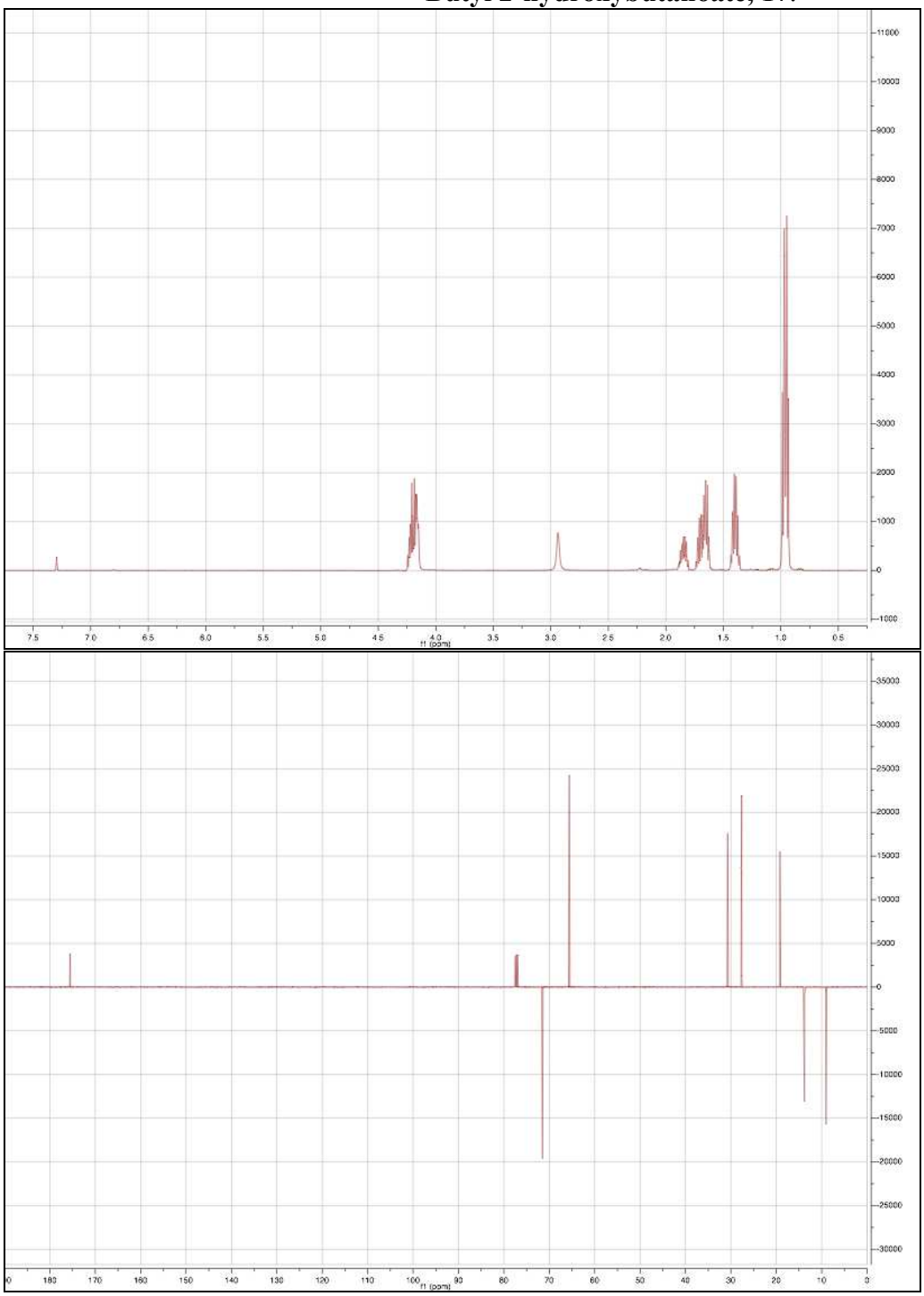
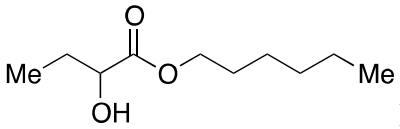




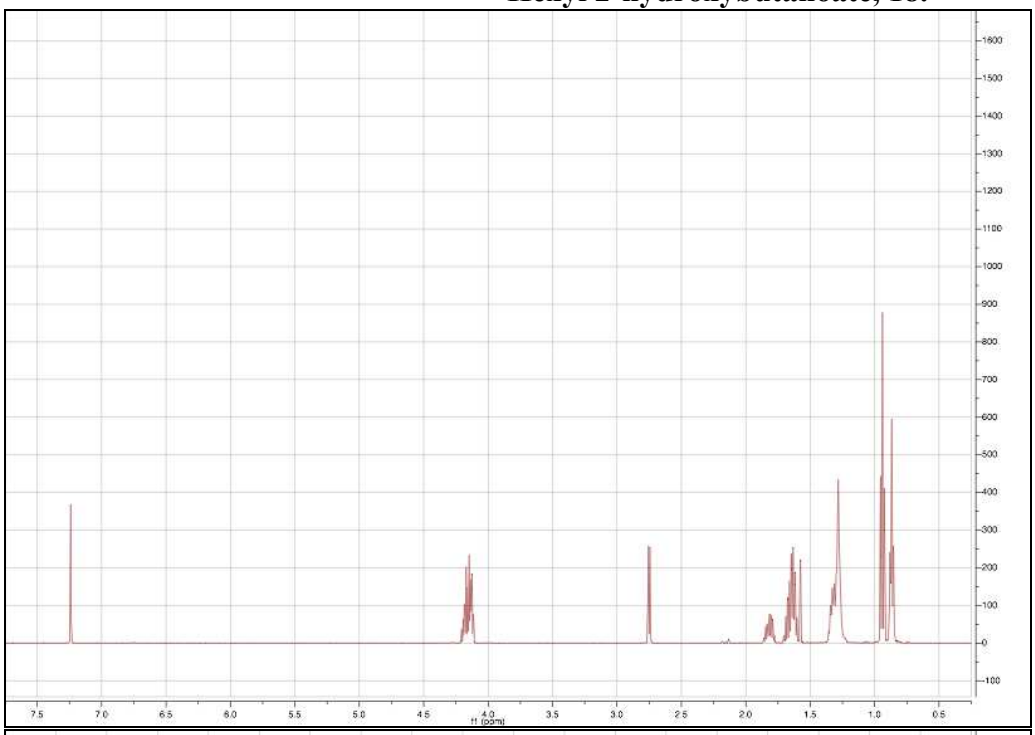


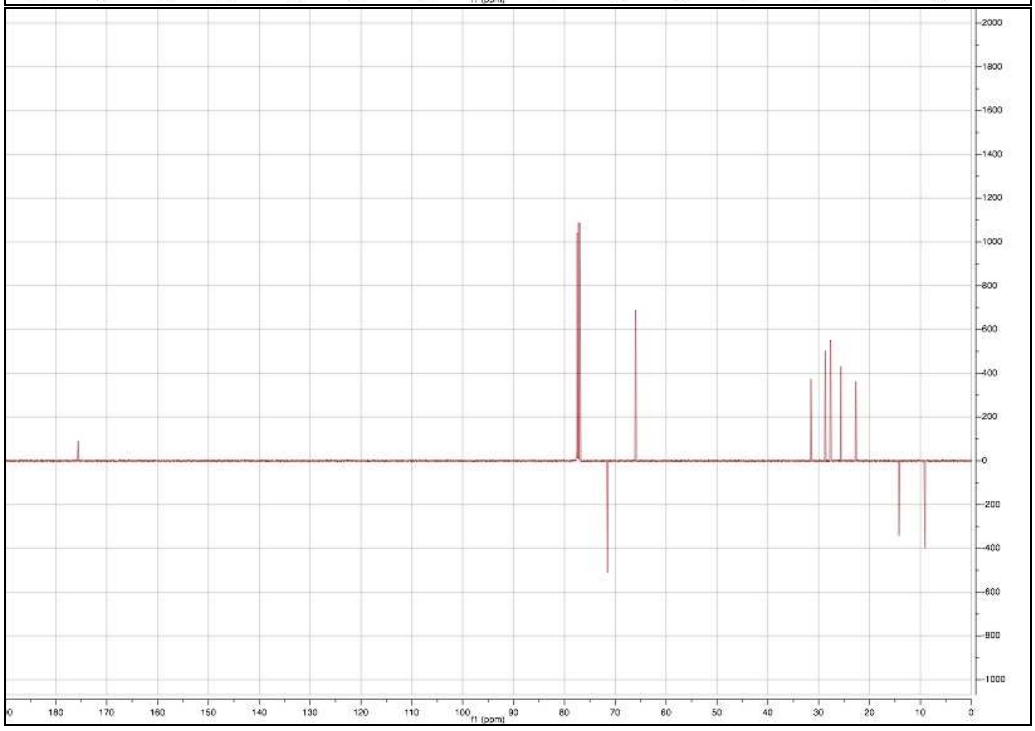
Butyl 2-hydroxybutanoate, 17.

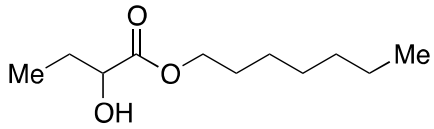




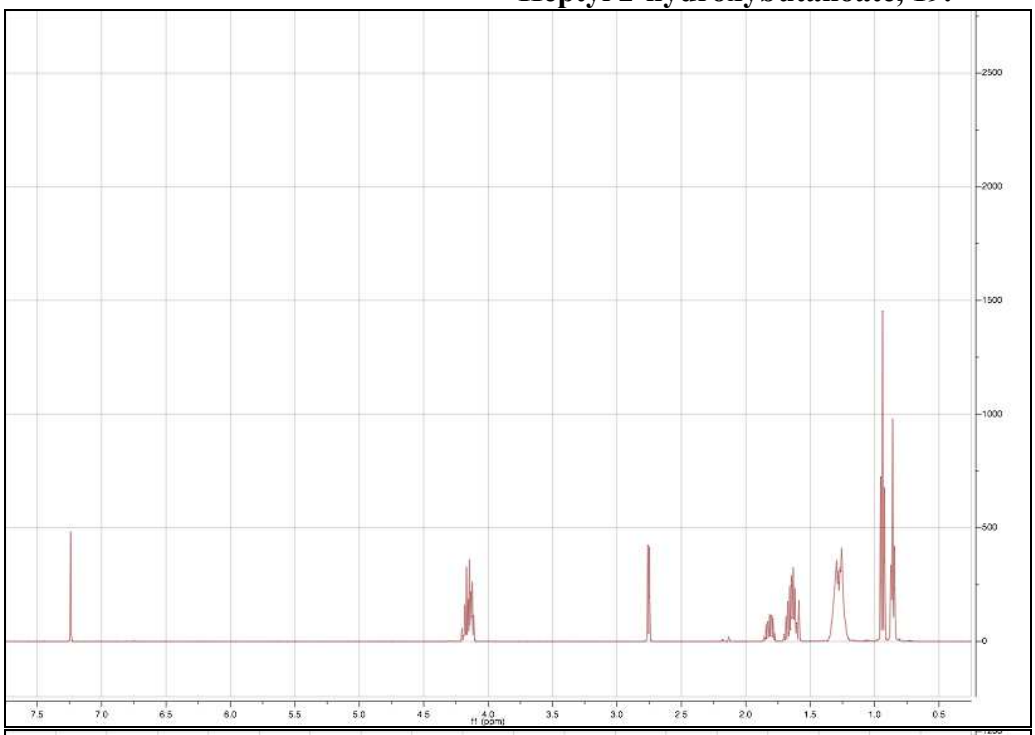
Hexyl 2-hydroxybutanoate, 18.

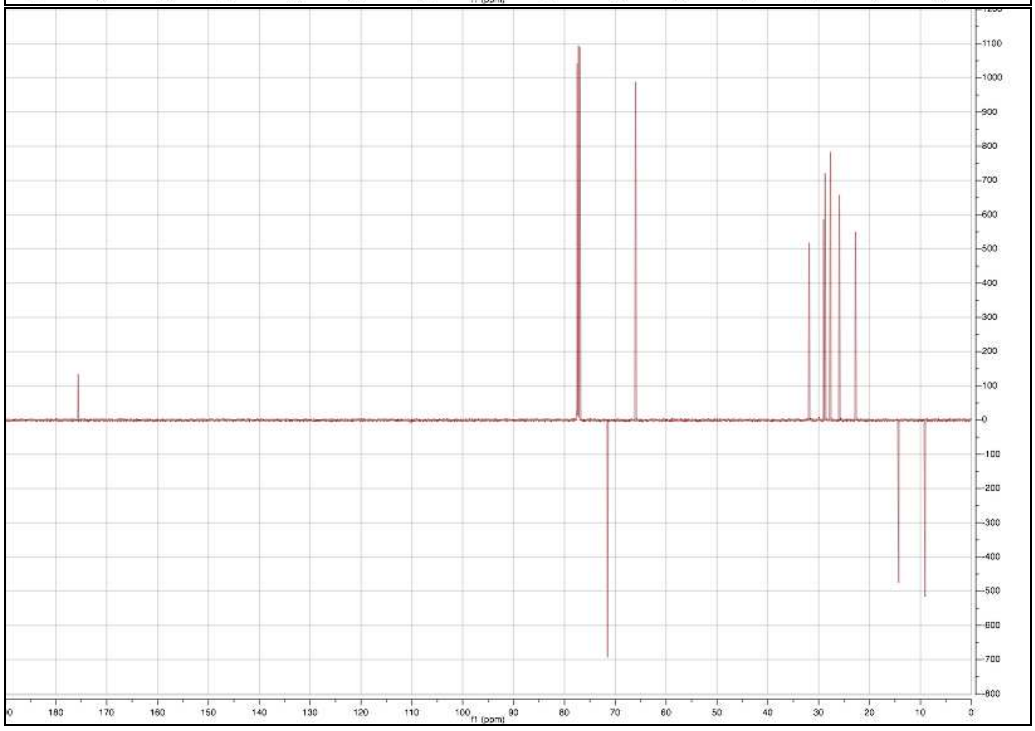


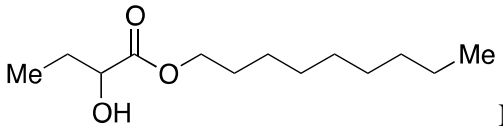




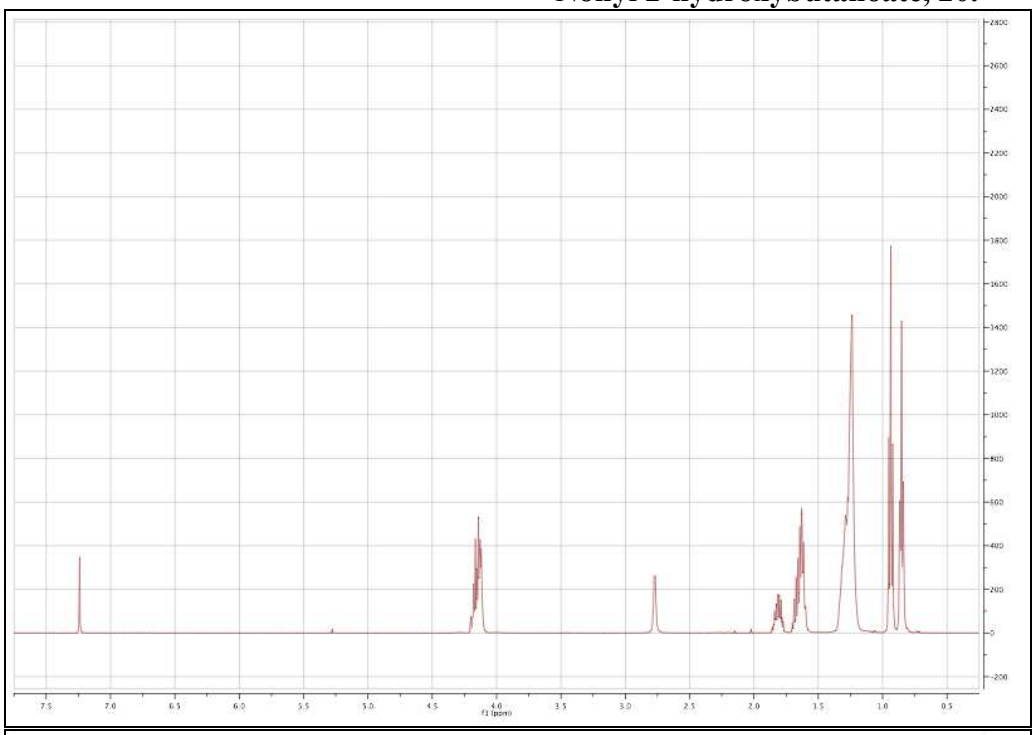
Heptyl 2-hydroxybutanoate, 19.

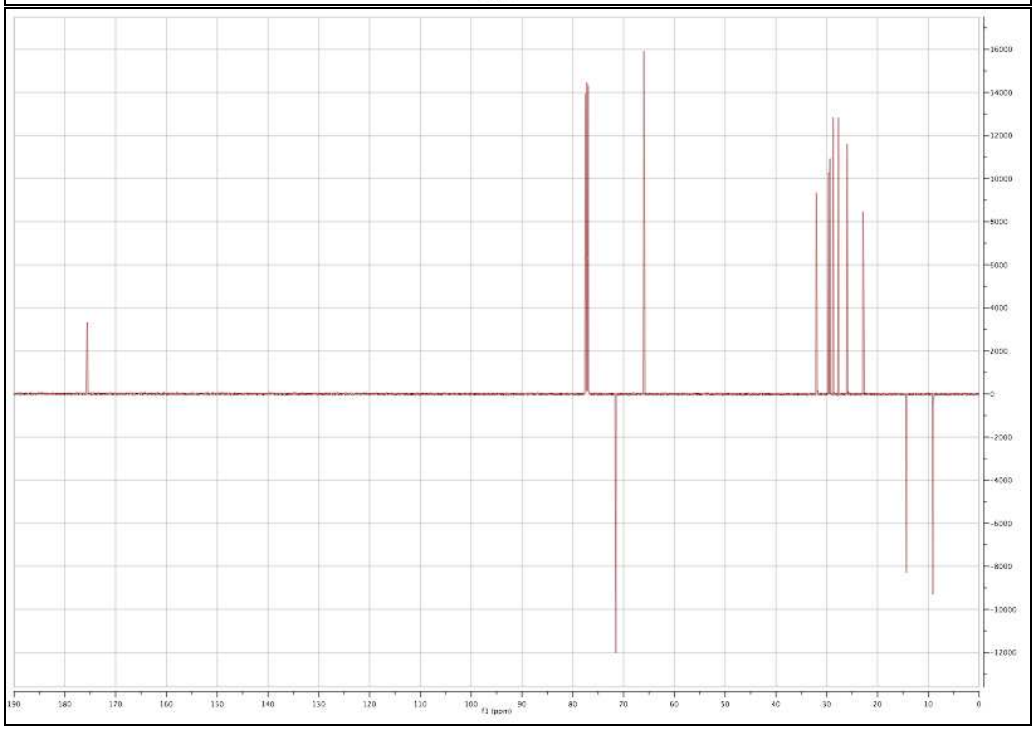


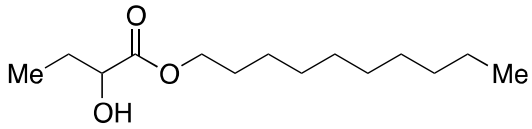




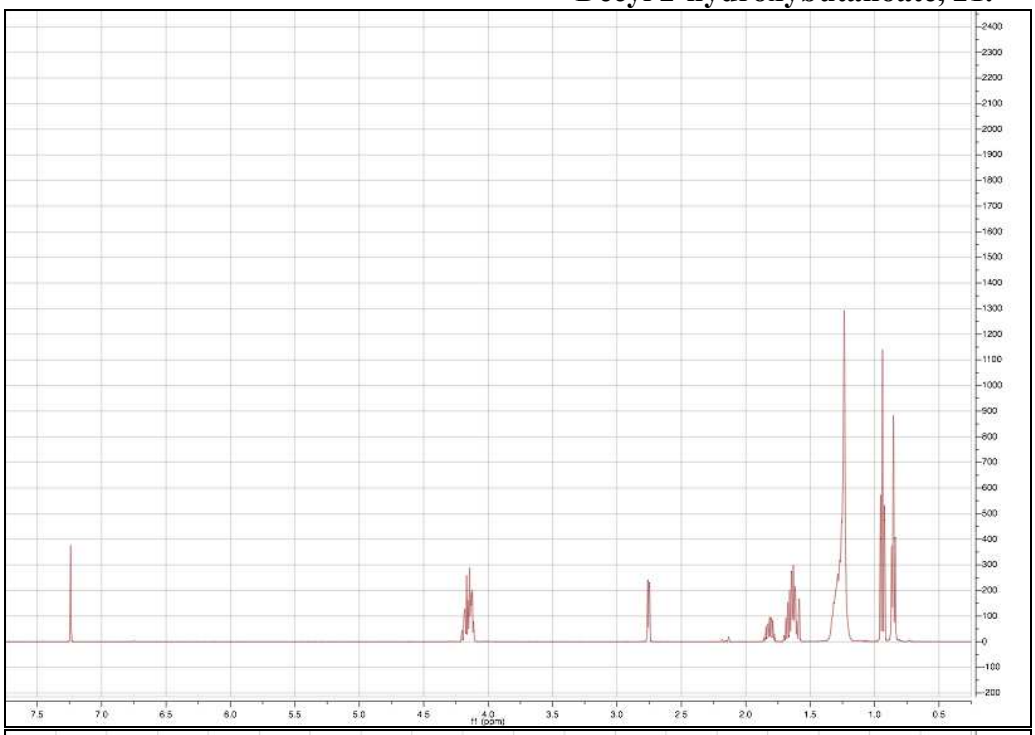
Nonyl 2-hydroxybutanoate, 20.

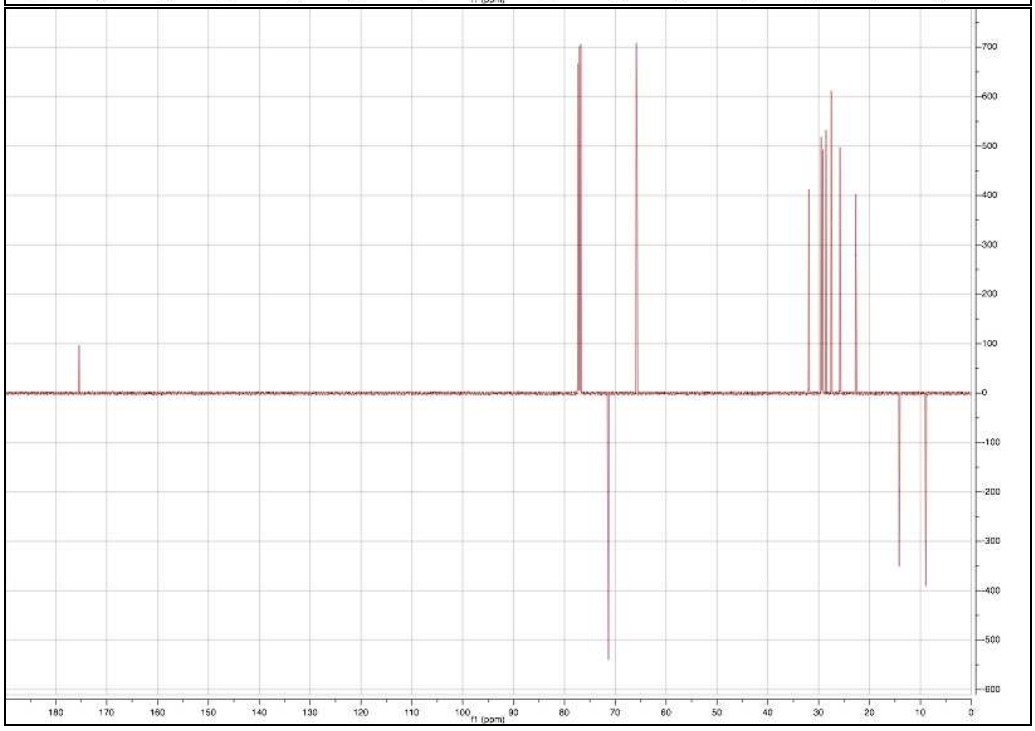


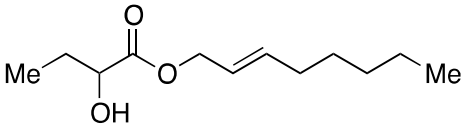




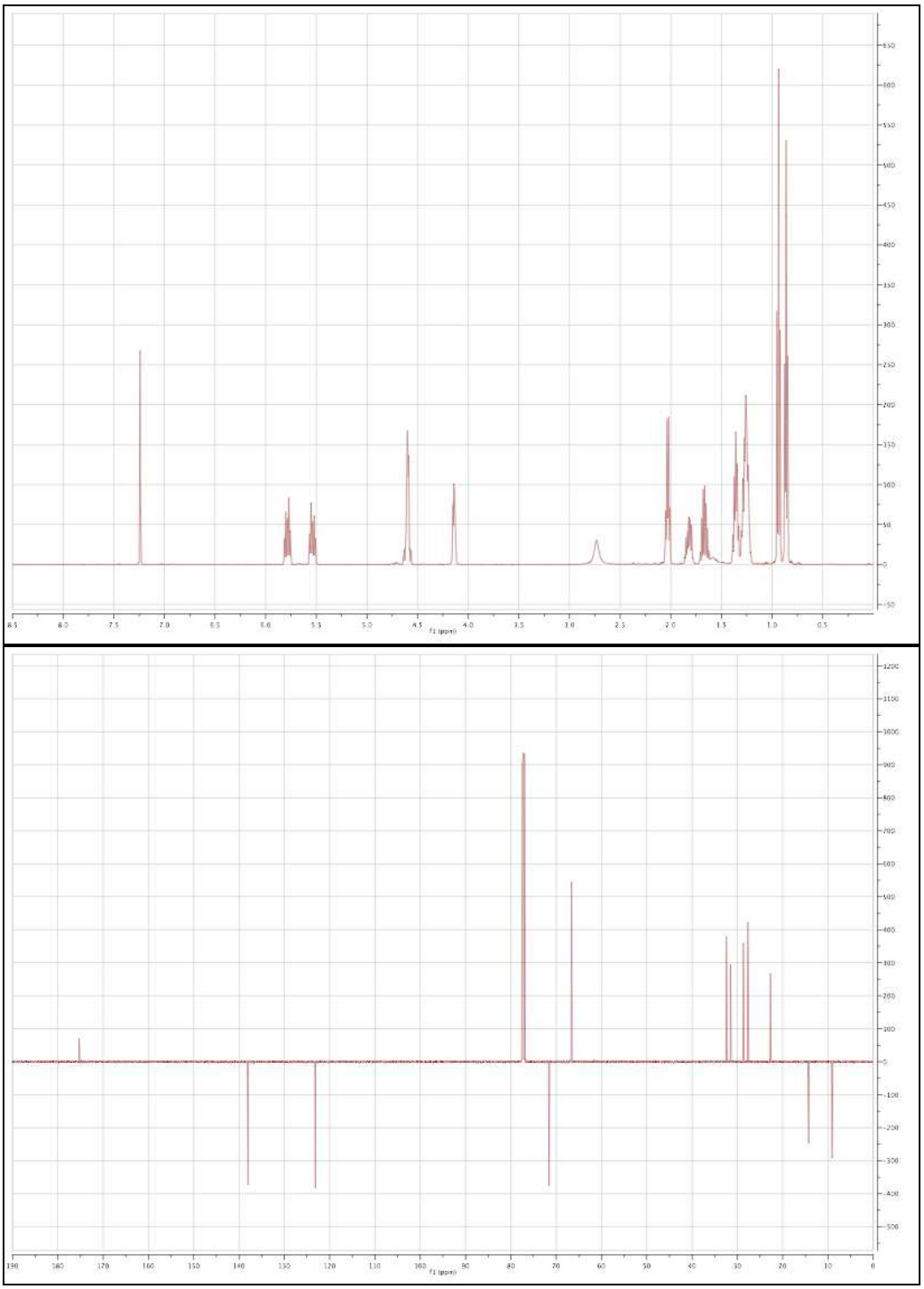
Decyl 2-hydroxybutanoate, 21.

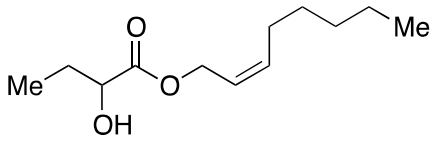




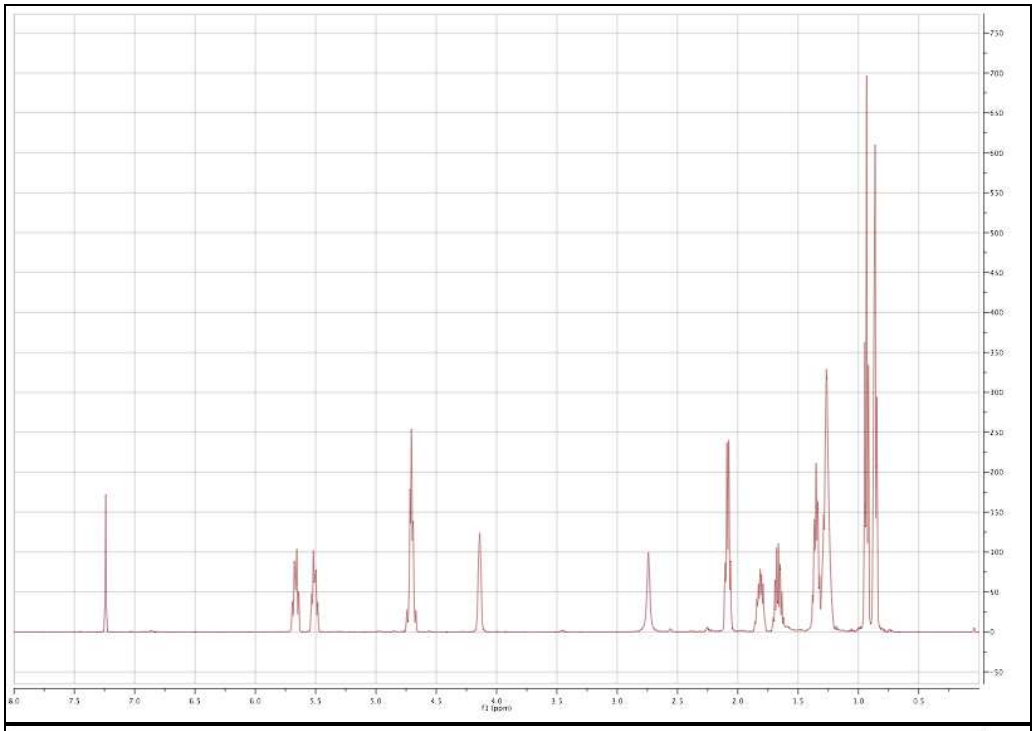


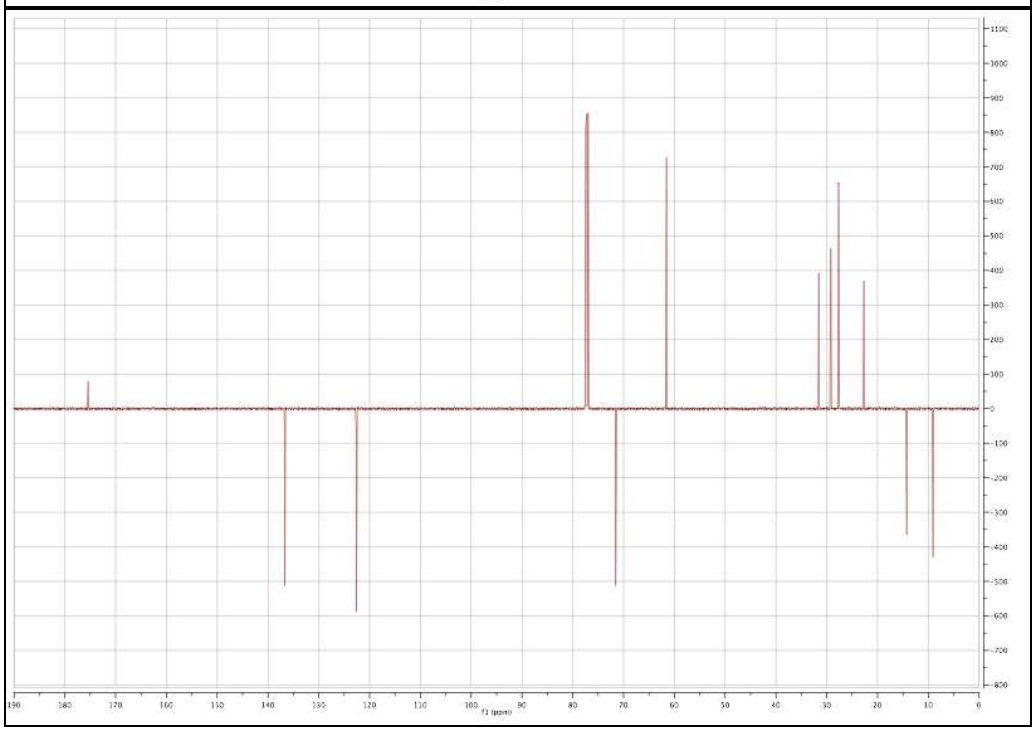
(*E*)-Oct-2-en-1-yl 2-hydroxybutanoate, 26

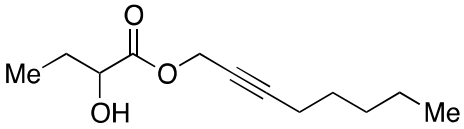




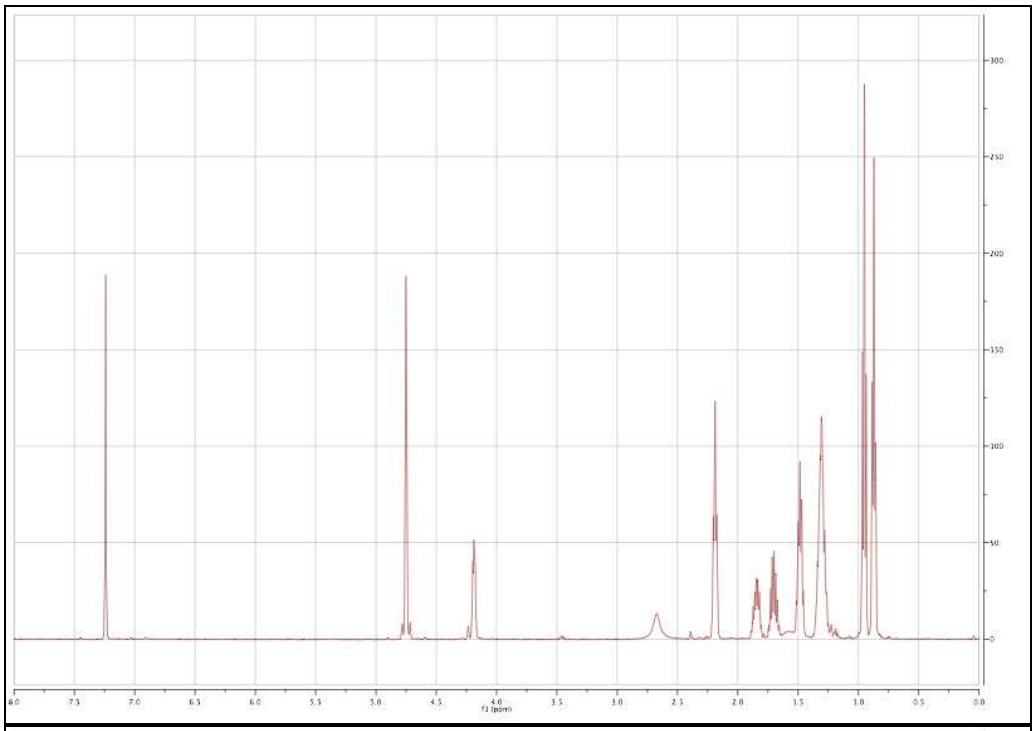
(*Z*)-Oct-2-en-1-yl 2-hydroxybutanoate, 27

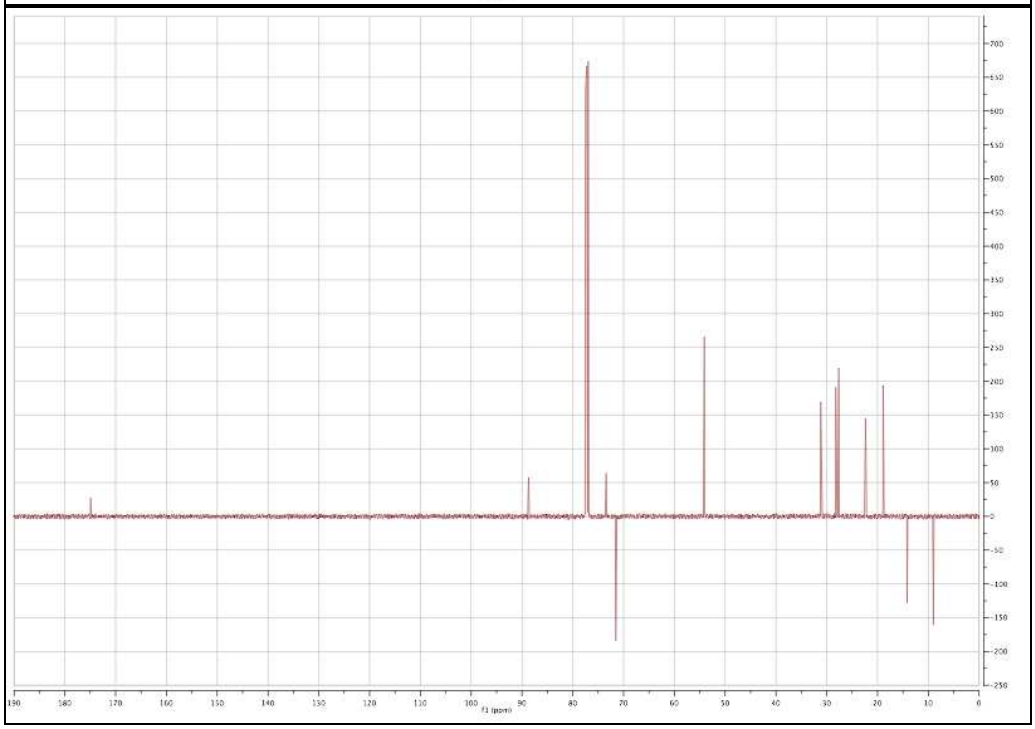


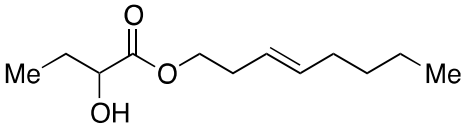




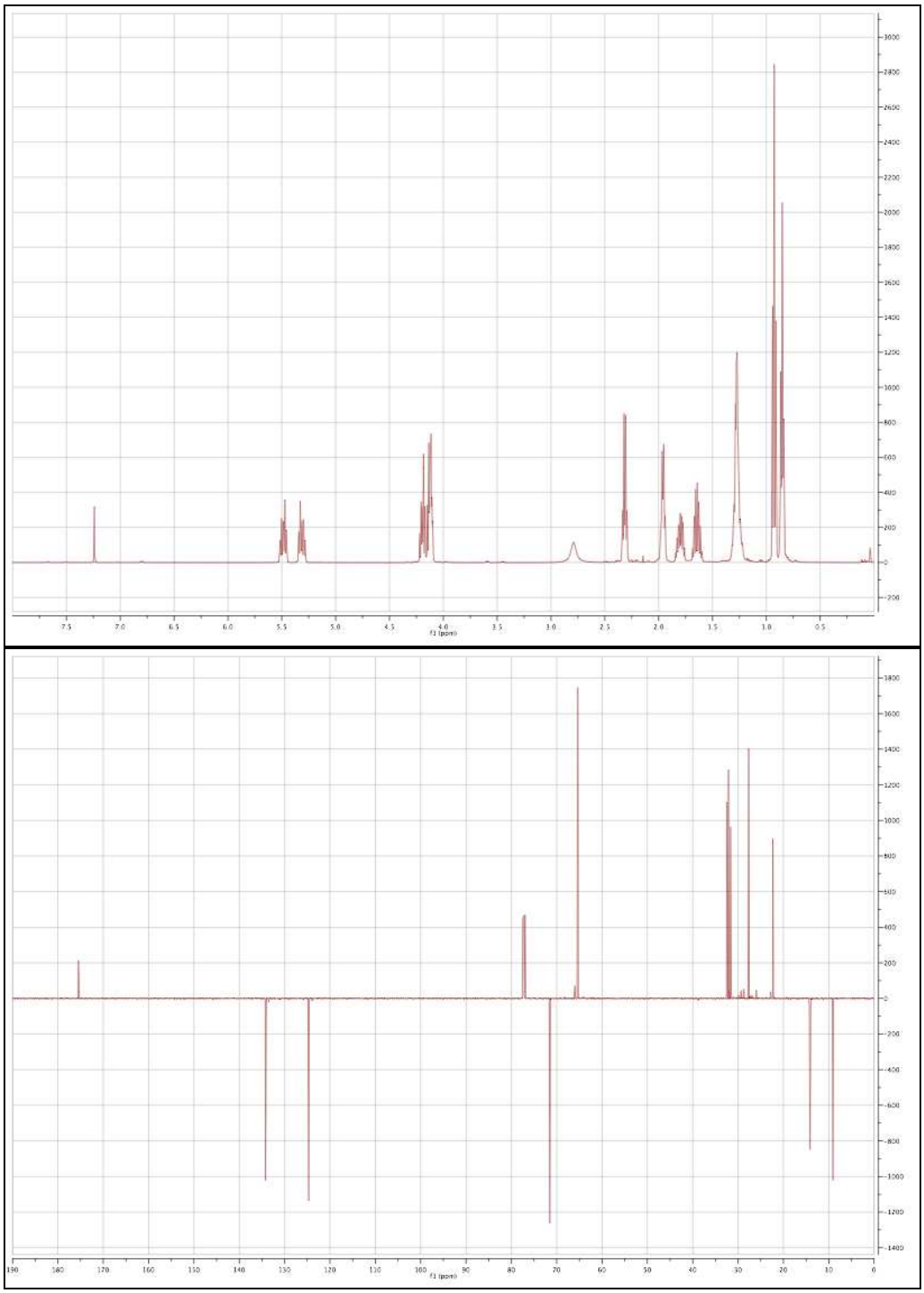
Oct-2-yn-1-yl 2-hydroxybutanoate, 28

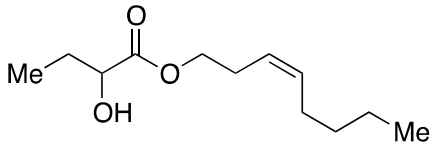




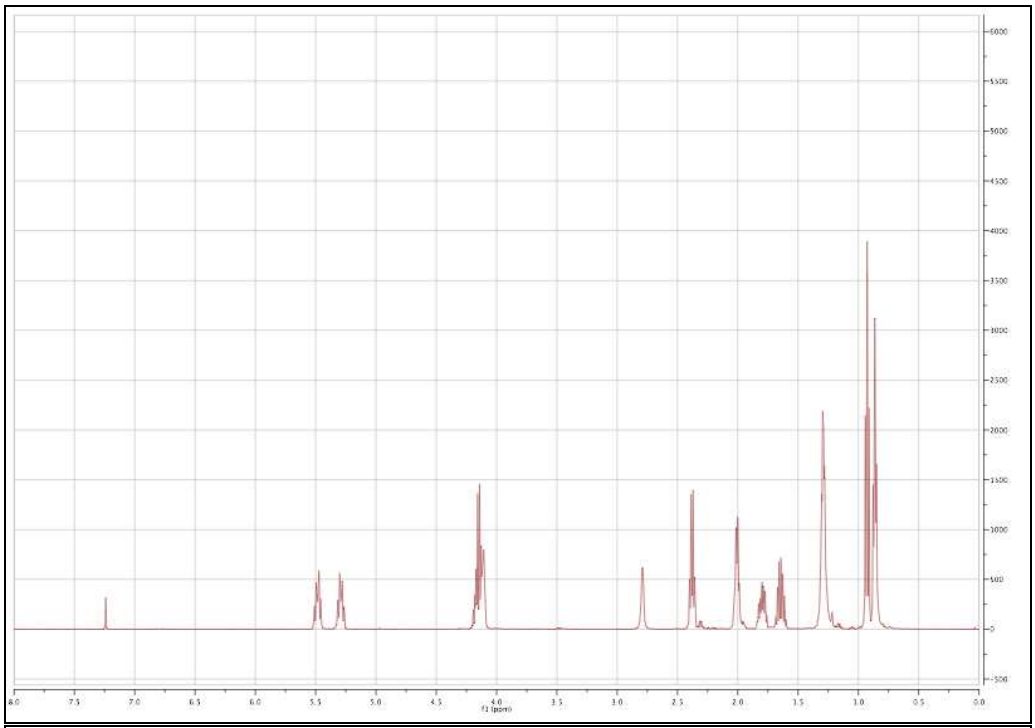


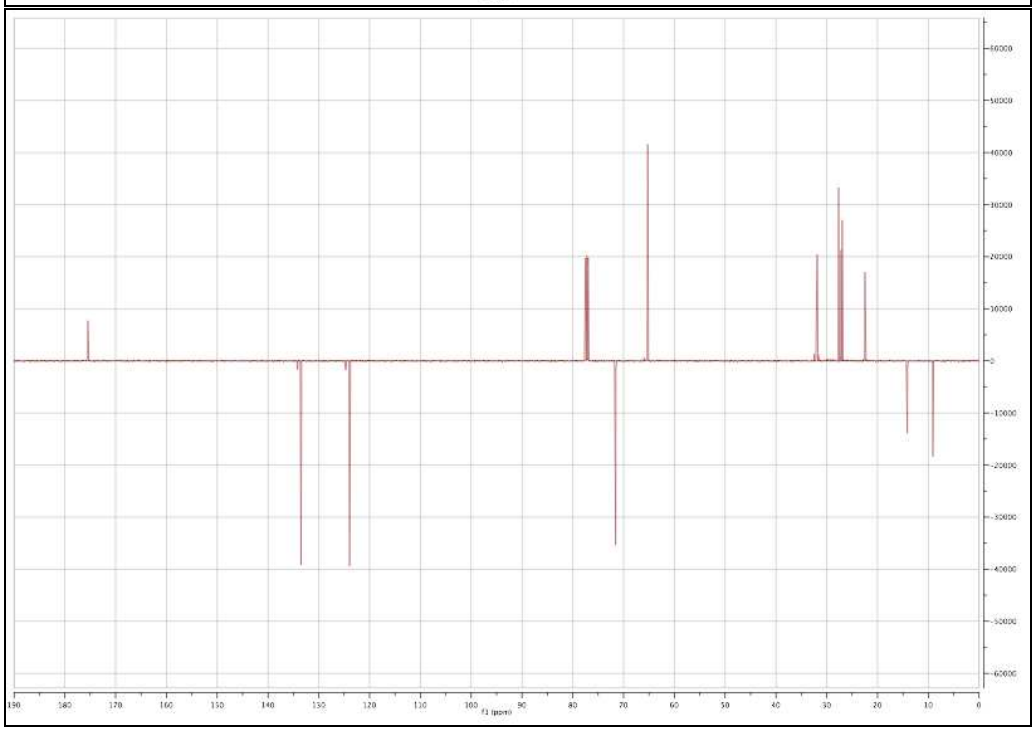
(*E*)-Oct-3-en-1-yl 2-hydroxybutanoate, 29

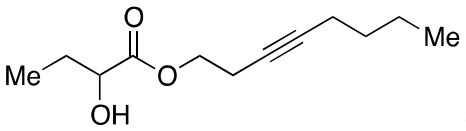




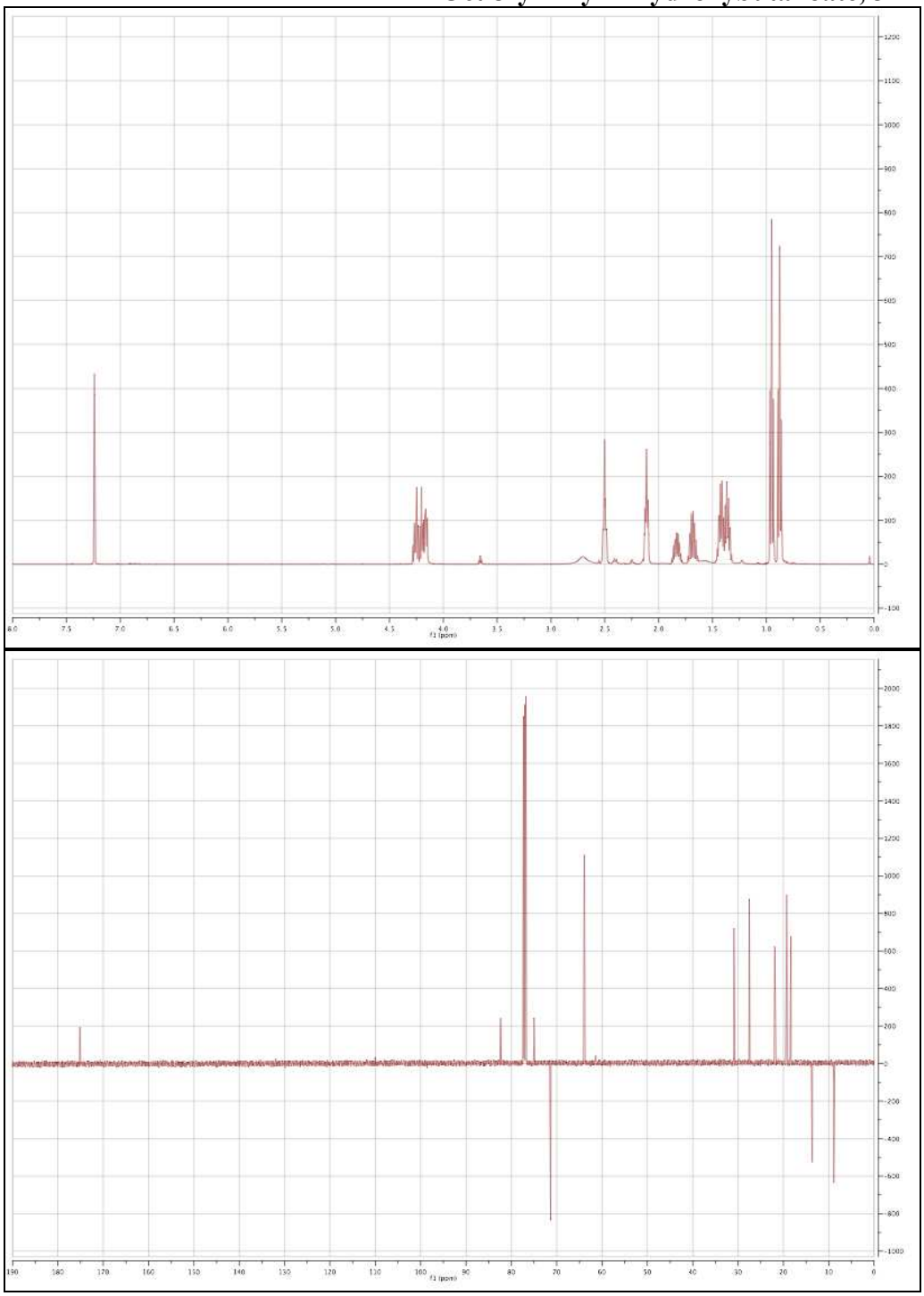
(*Z*)-Oct-3-en-1-yl 2-hydroxybutanoate, 30

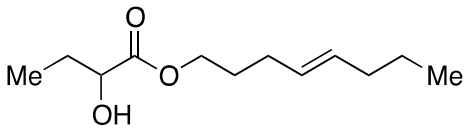




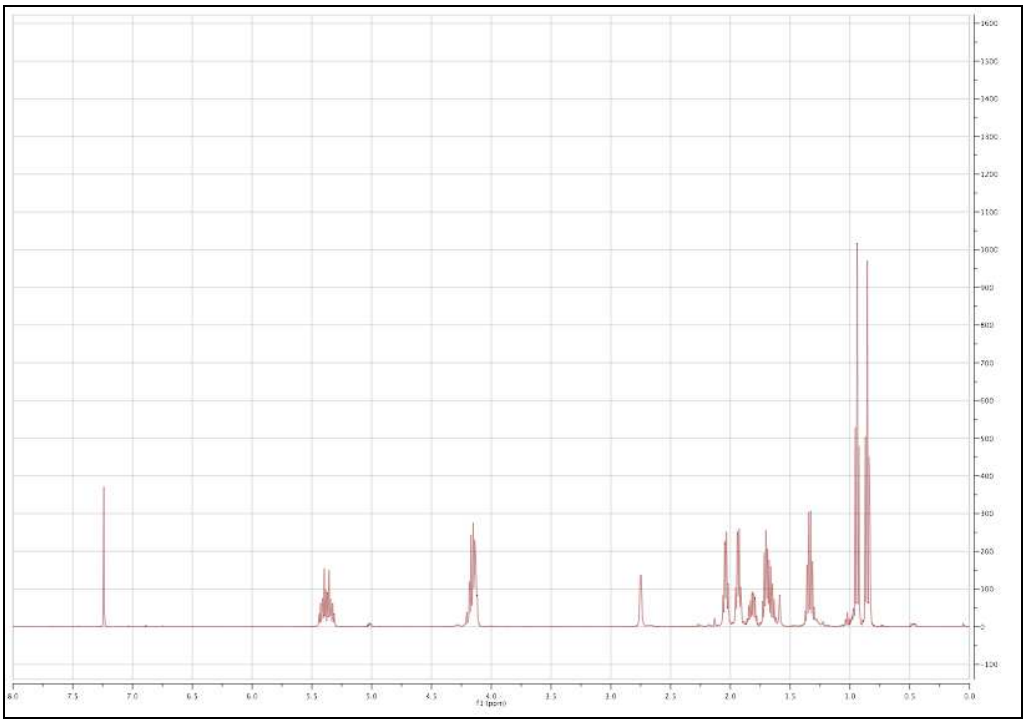


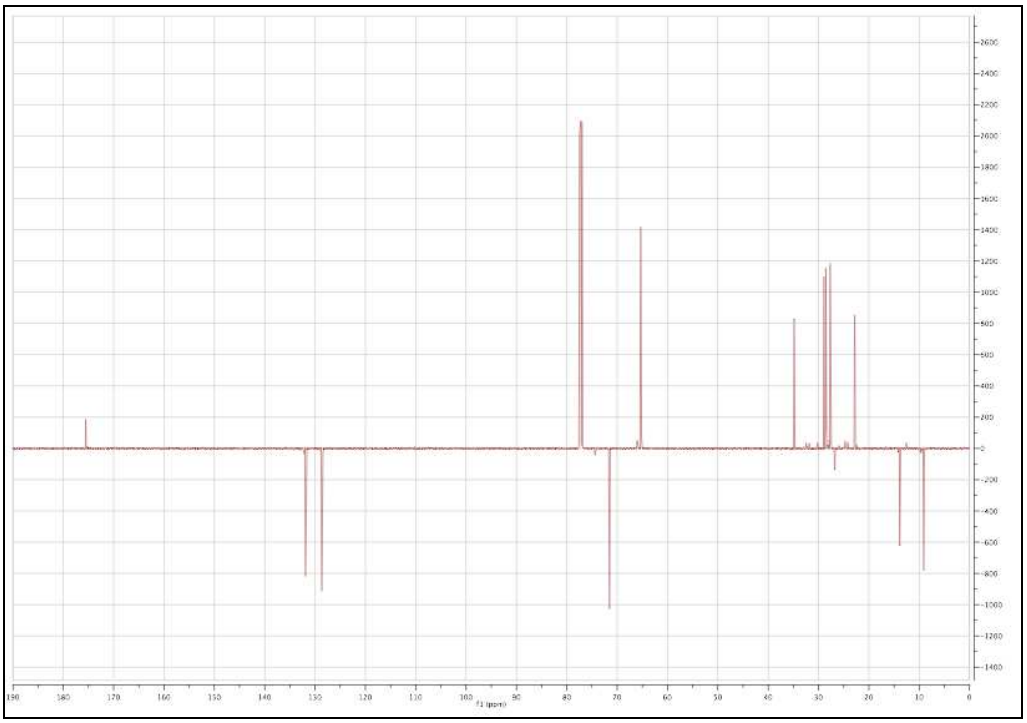
Oct-3-yn-1-yl 2-hydroxybutanoate, 31

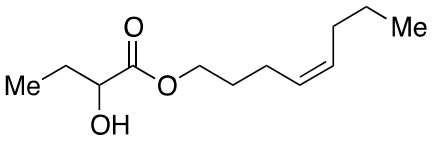




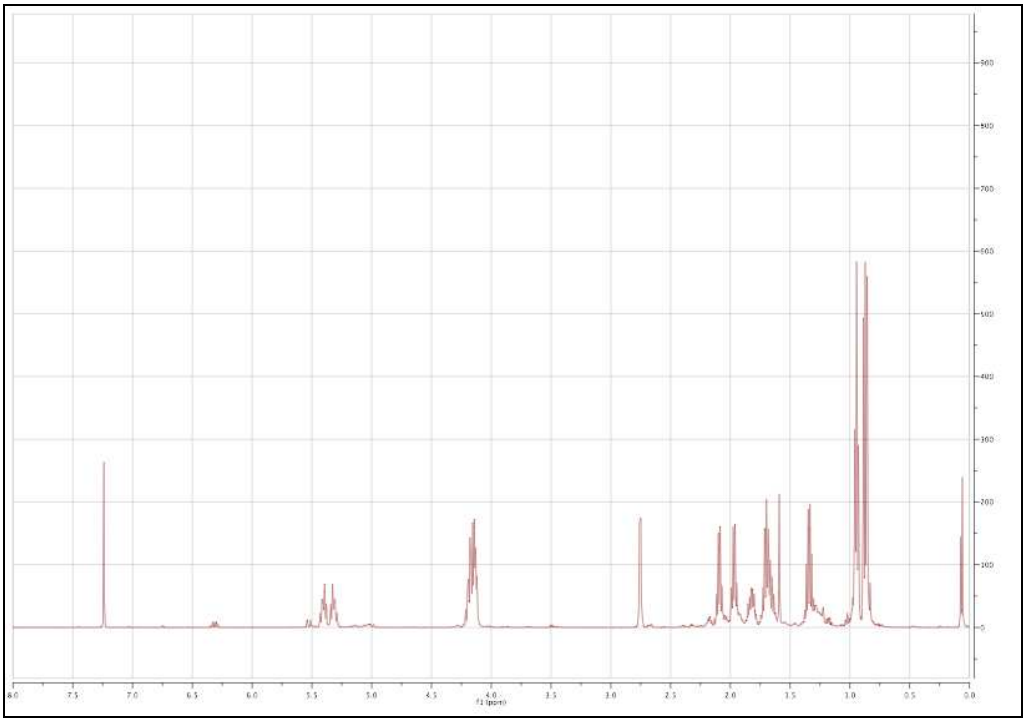
(*E*)-Oct-4-enyl 2-hydroxybutanoate, 32.

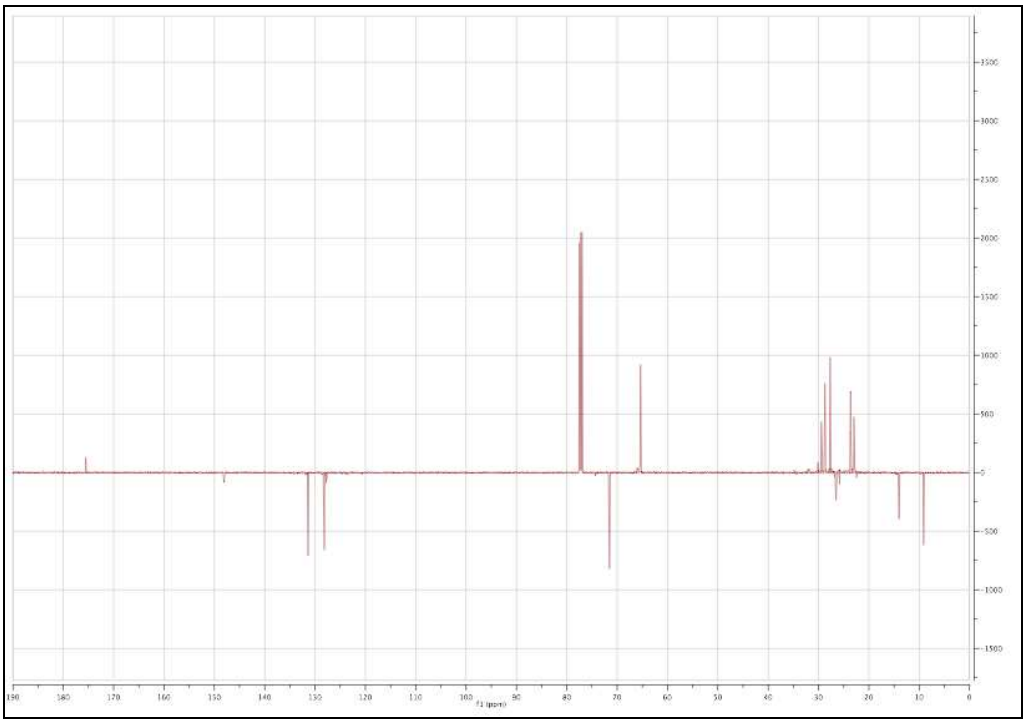


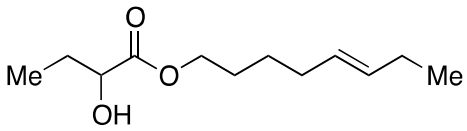




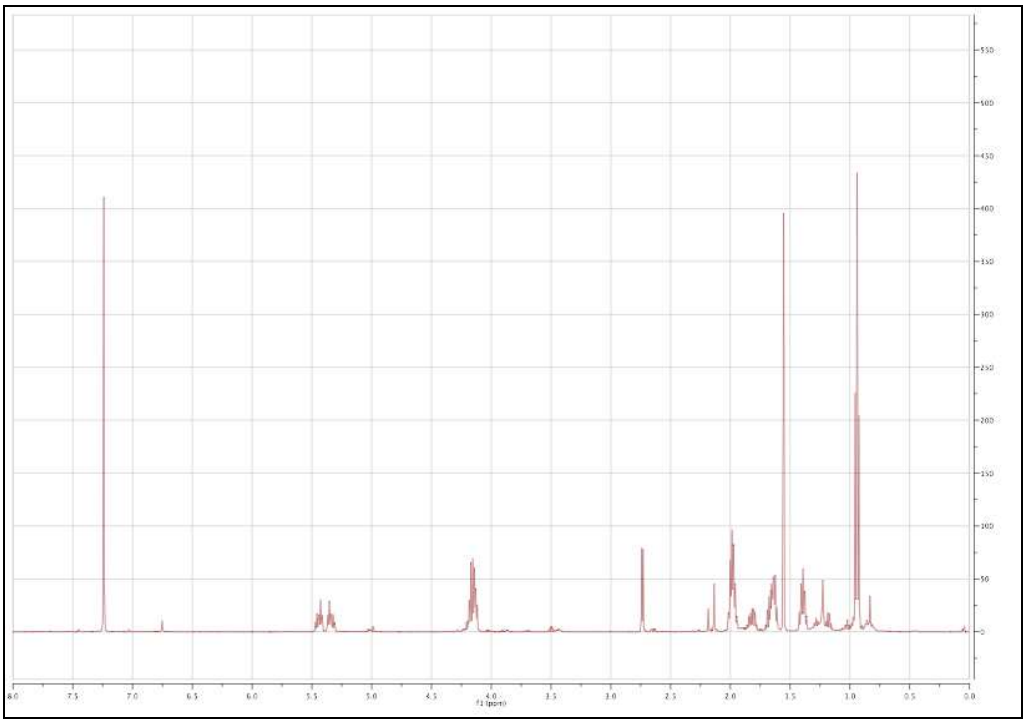
(*Z*)-Oct-4-enyl 2-hydroxybutanoate, 33.

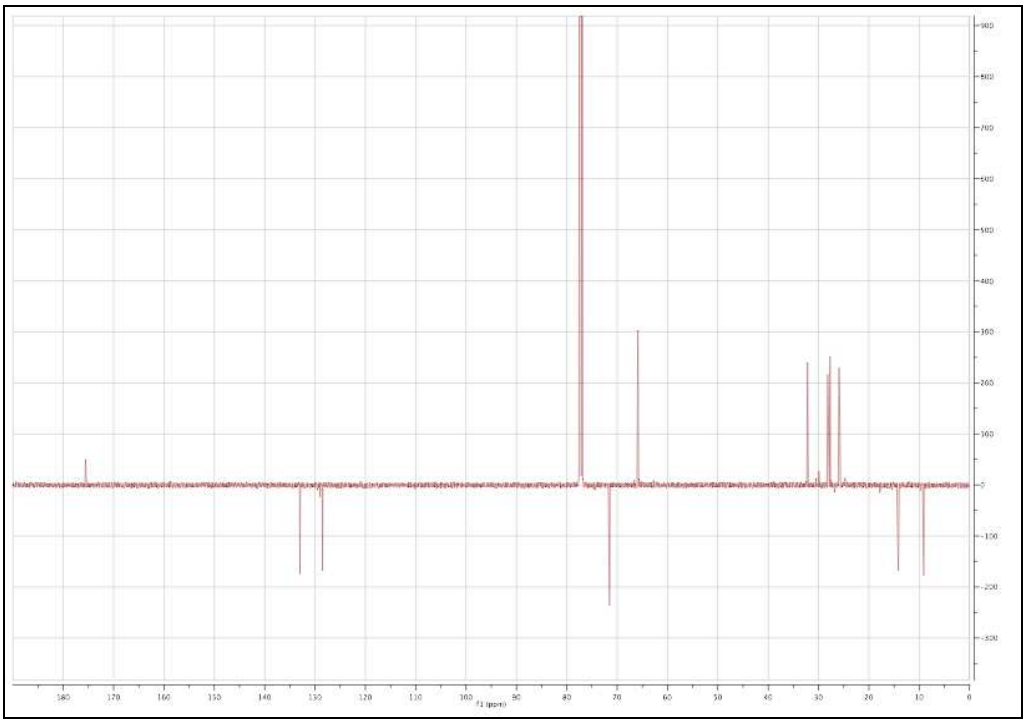


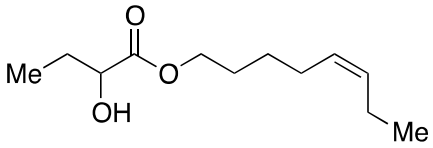




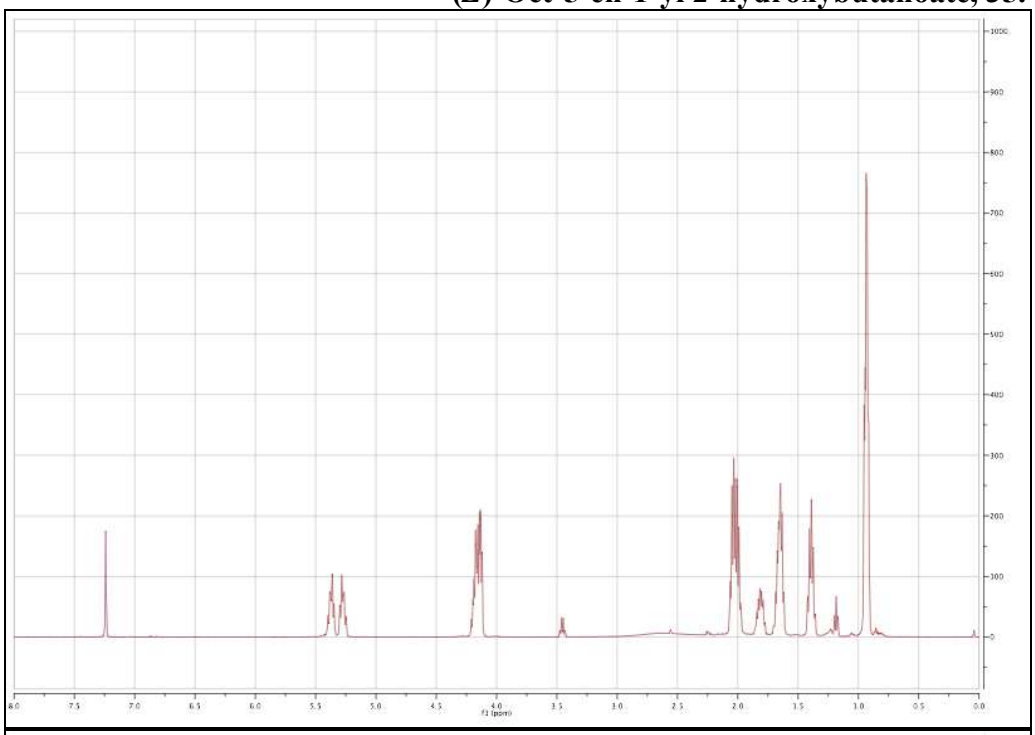
(*E*)-Oct-5-enyl 2-hydroxybutanoate, 34.

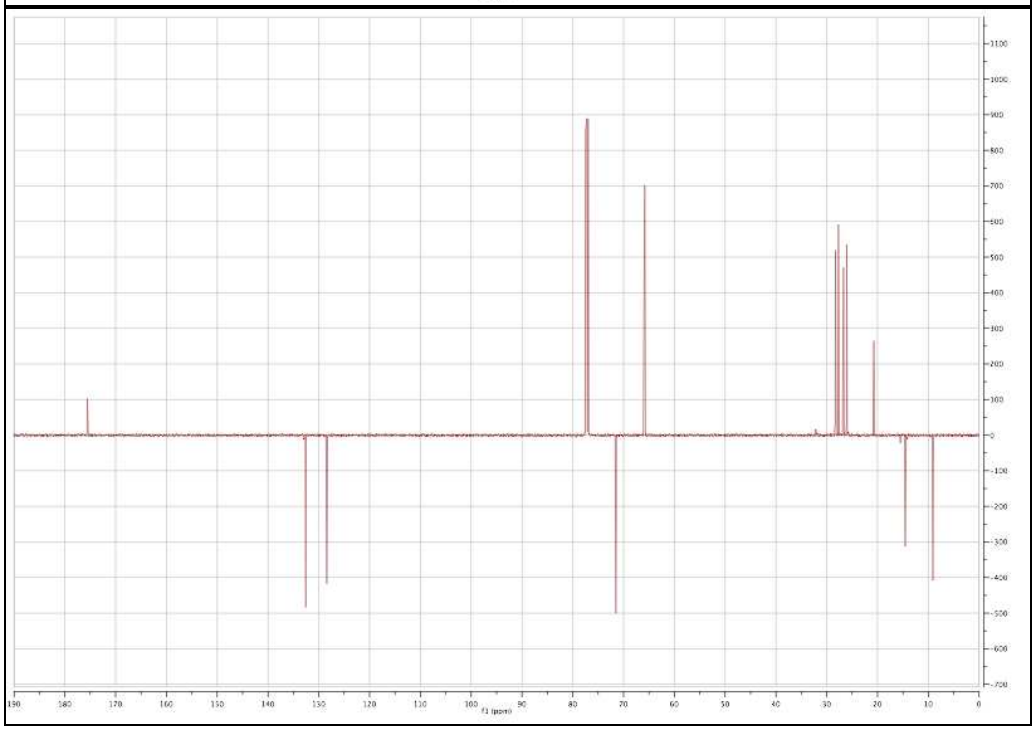


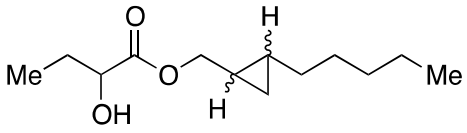




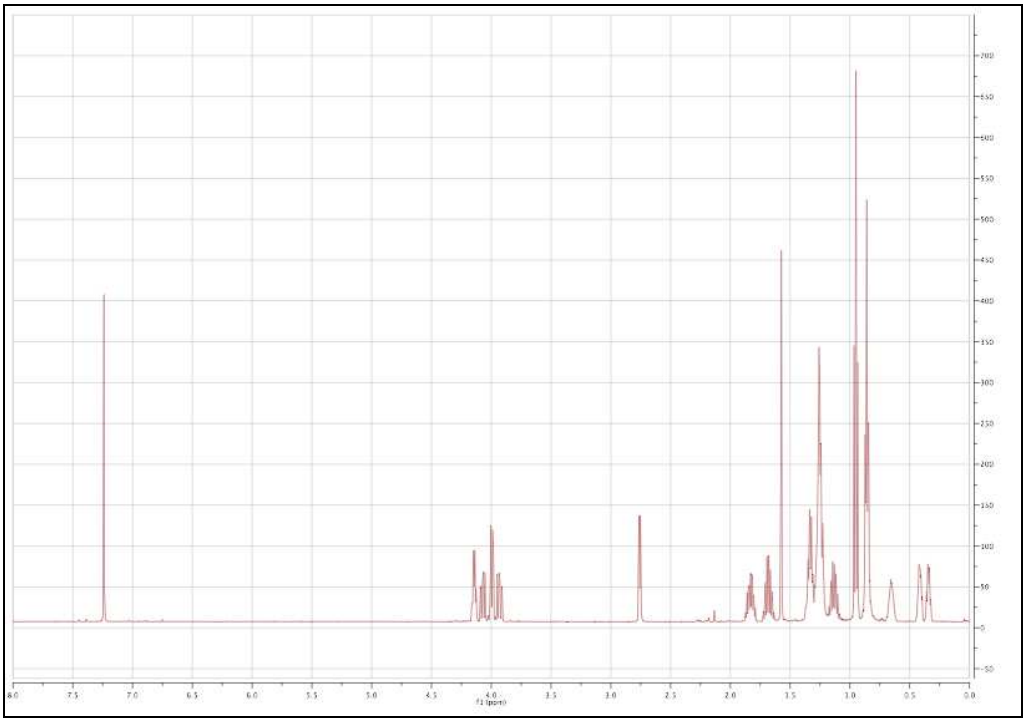
(*Z*)-Oct-5-en-1-yl 2-hydroxybutanoate, 35.

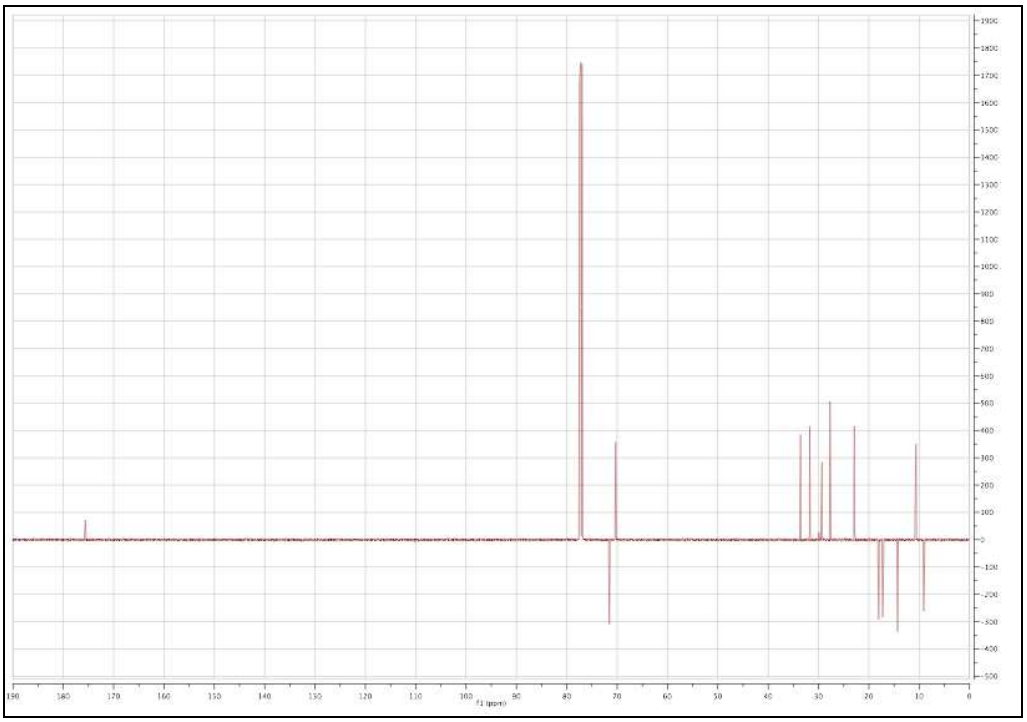


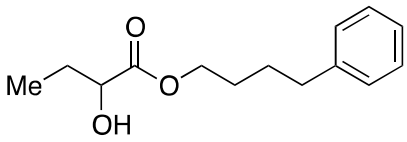




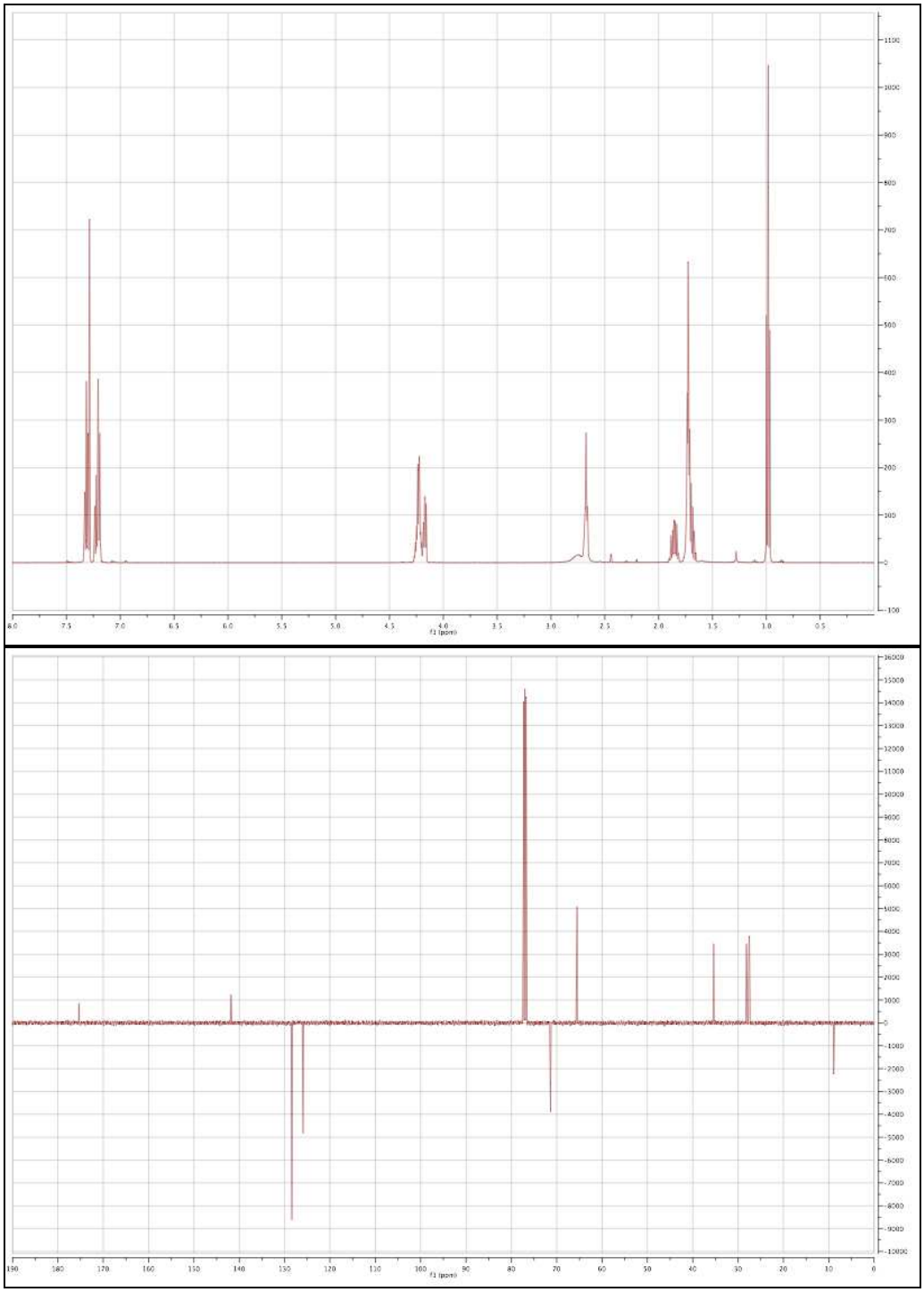
(2-pentylcyclopropyl)methyl 2-hydroxybutanoate, 36.

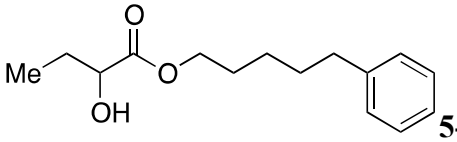




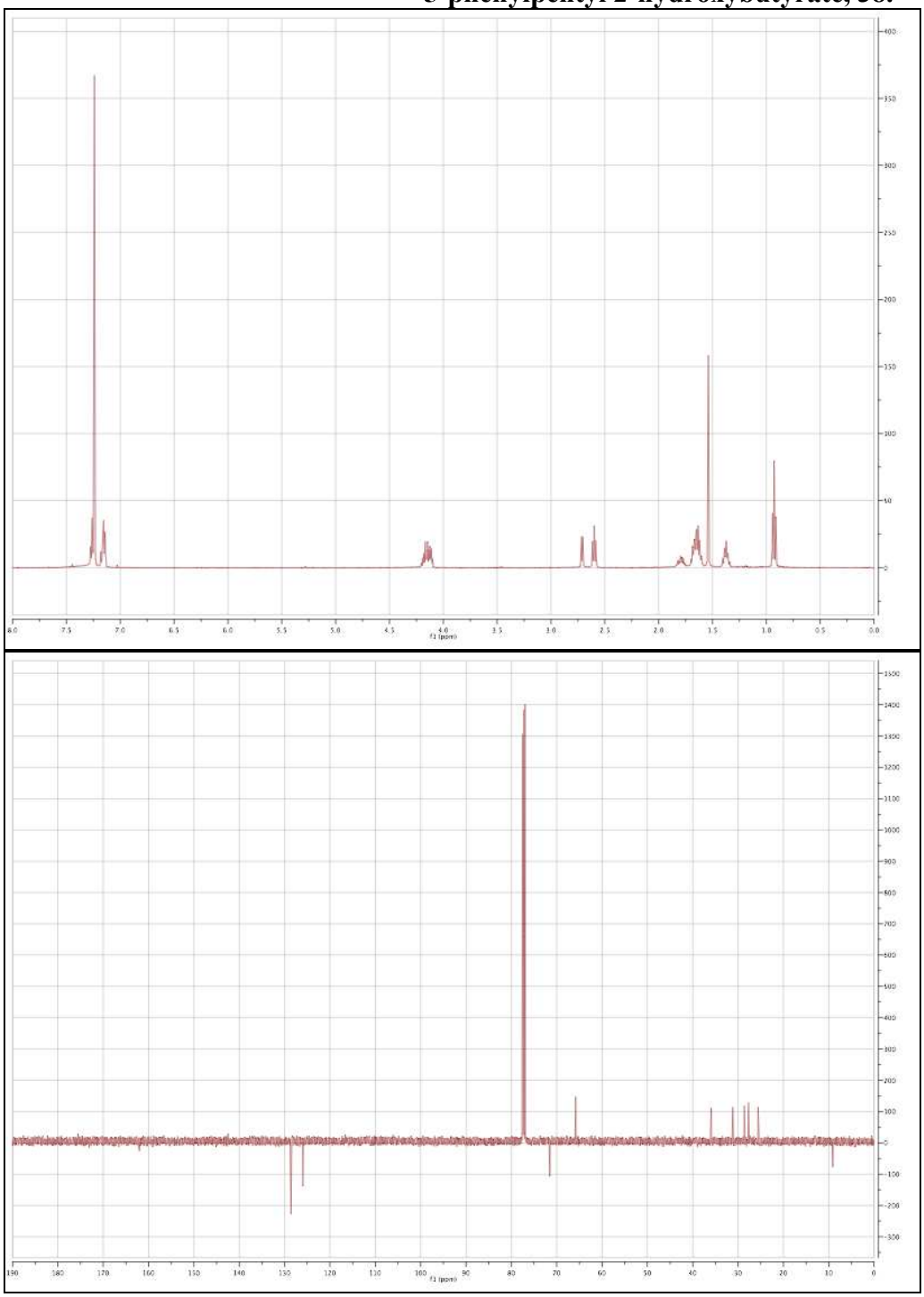


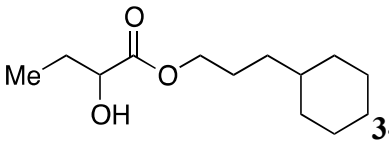
4-phenylbutyl 2-hydroxybutyrate, 37



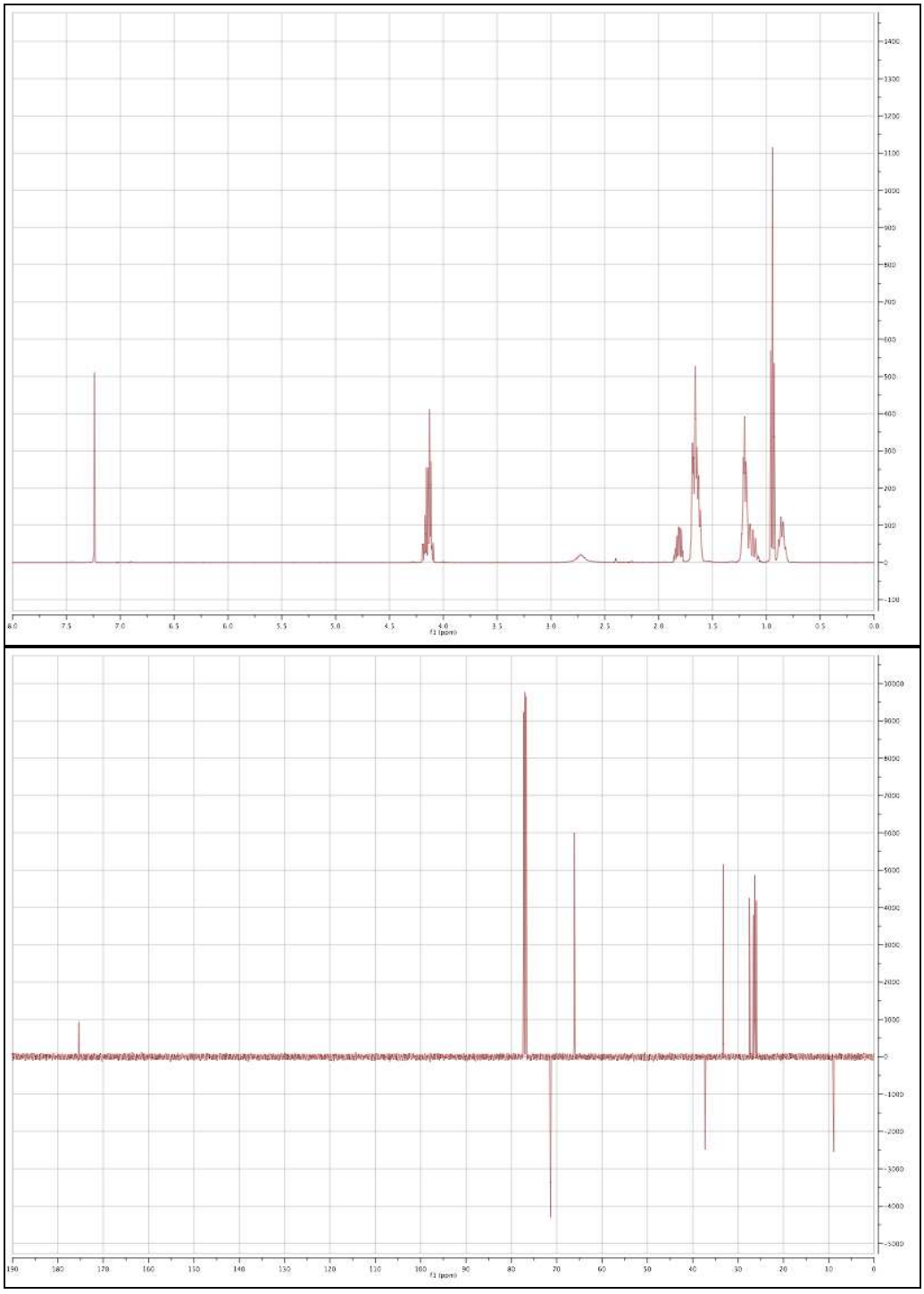


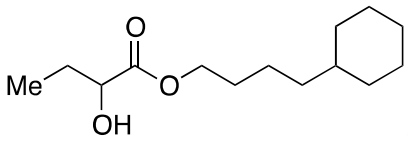
5-phenylpentyl 2-hydroxybutyrate, 38.



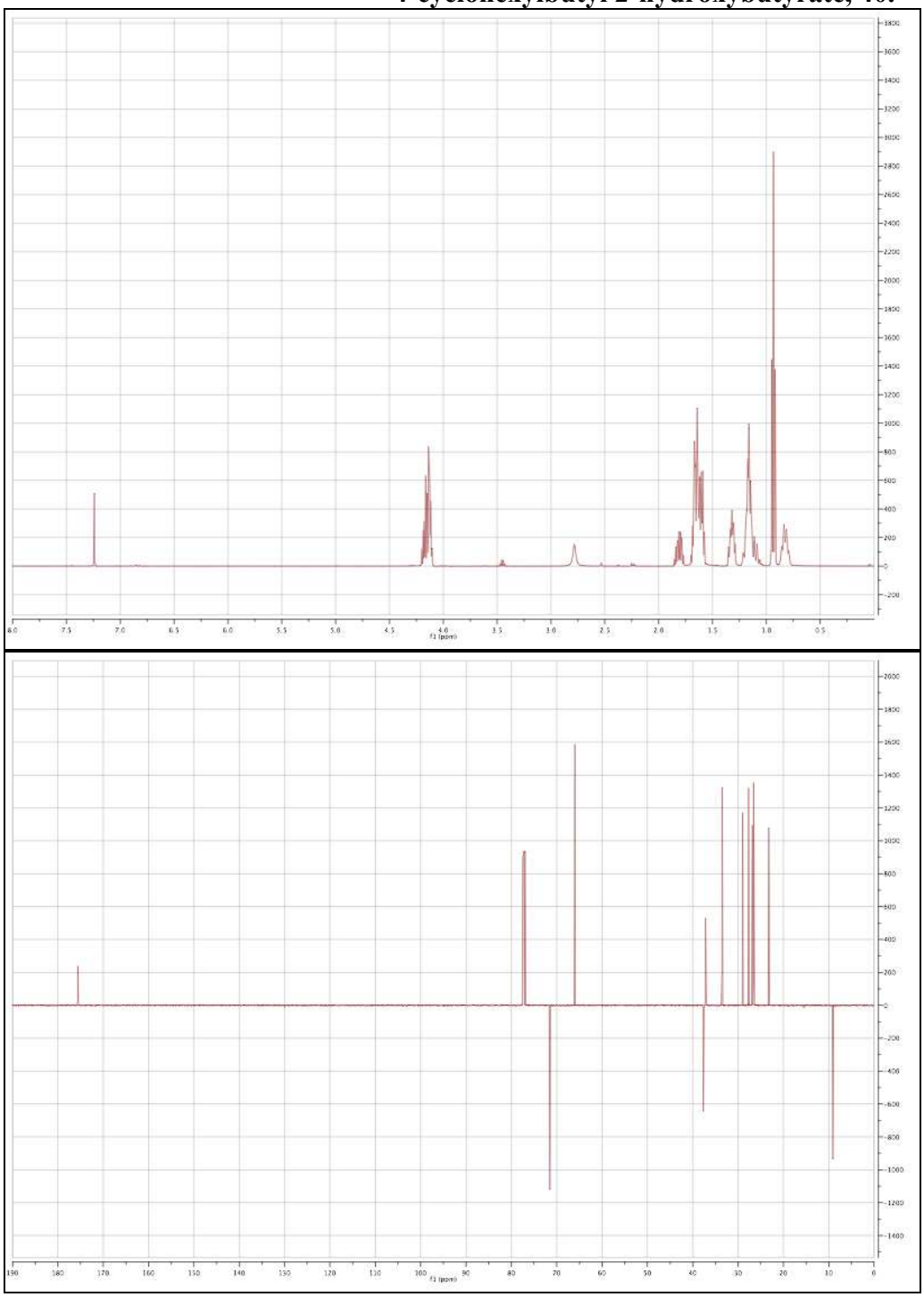


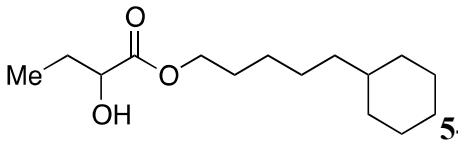
3-cyclohexylpropyl 2-hydroxybutyrate, 39



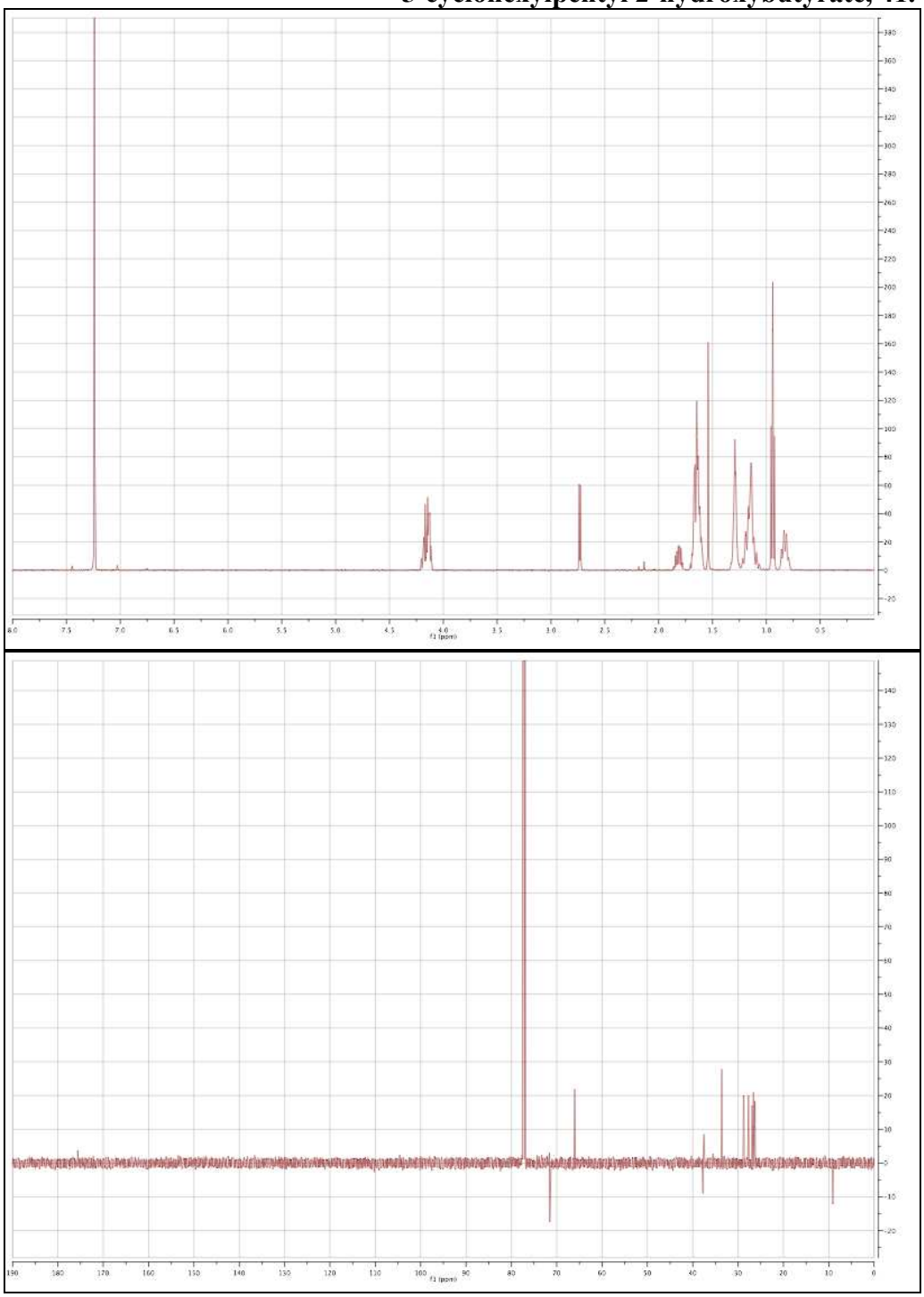


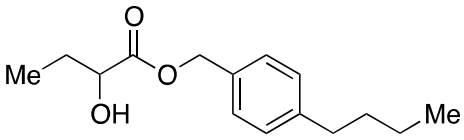
4-cyclohexylbutyl 2-hydroxybutyrate, 40.



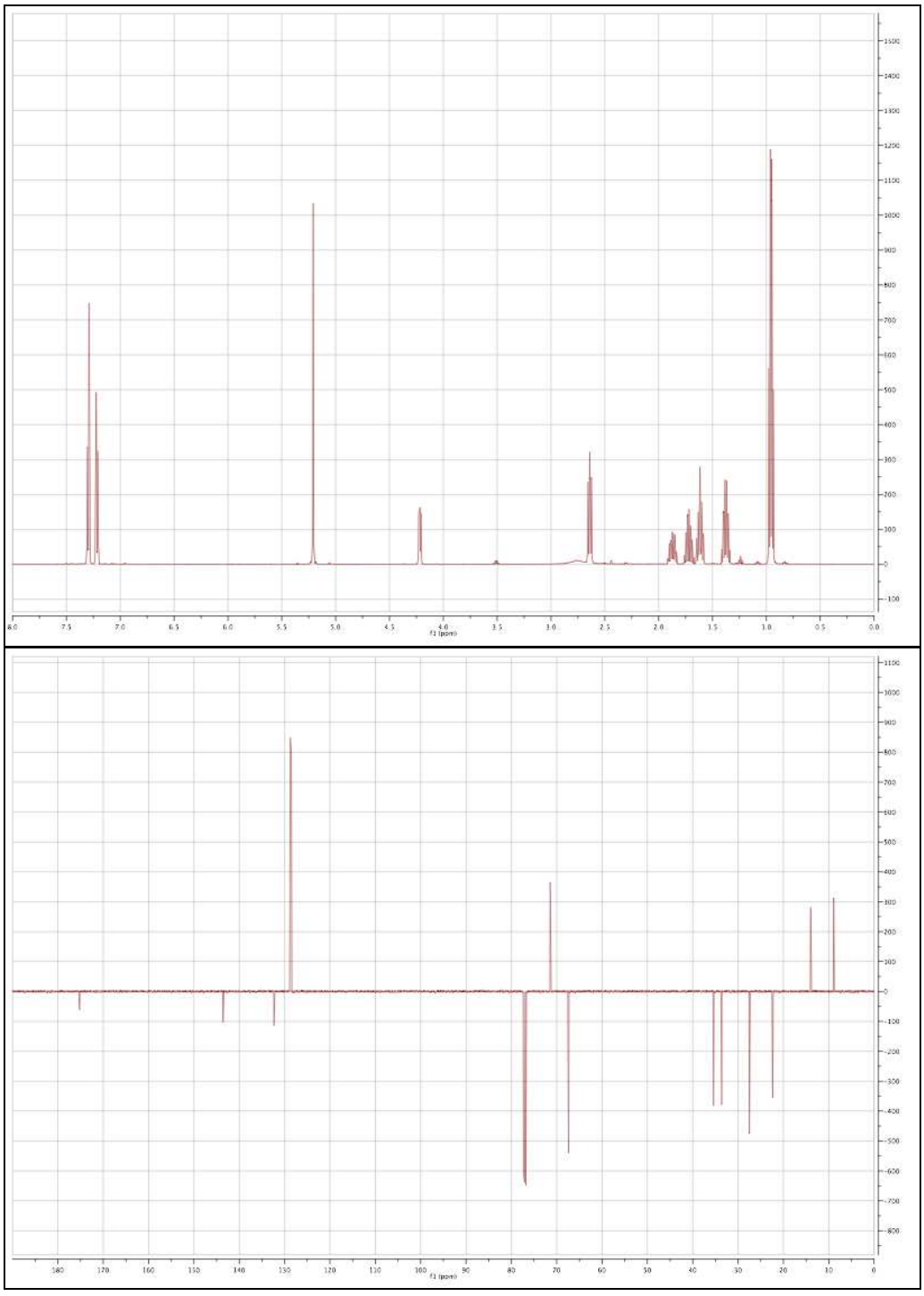


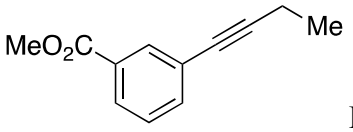
5-cyclohexylpentyl 2-hydroxybutyrate, 41.



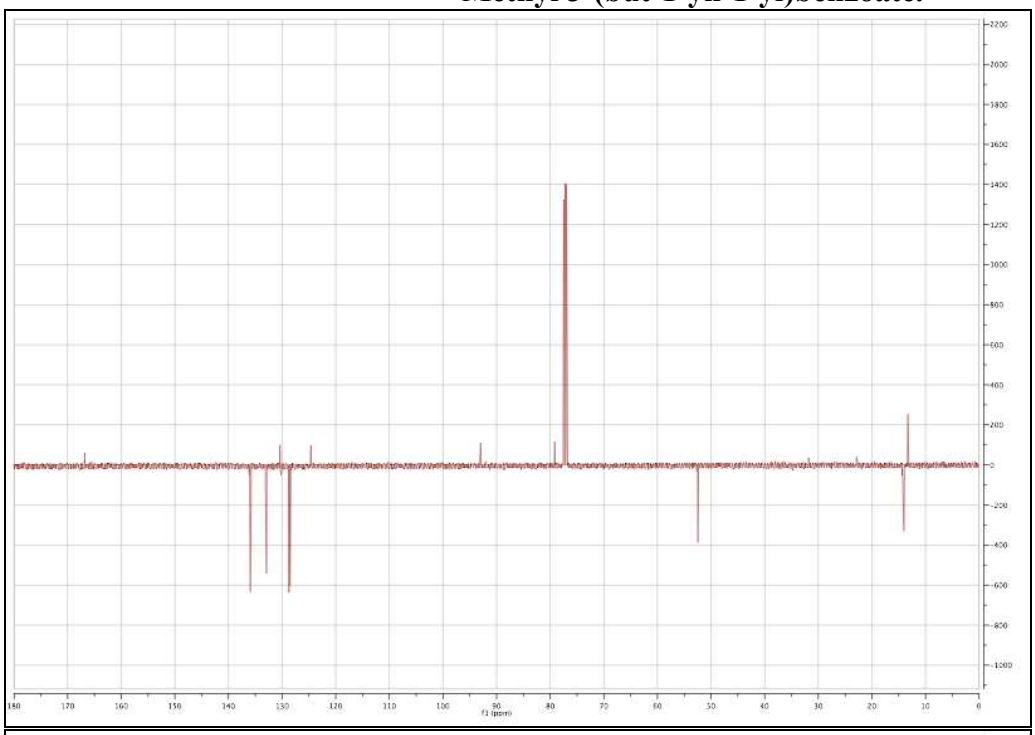


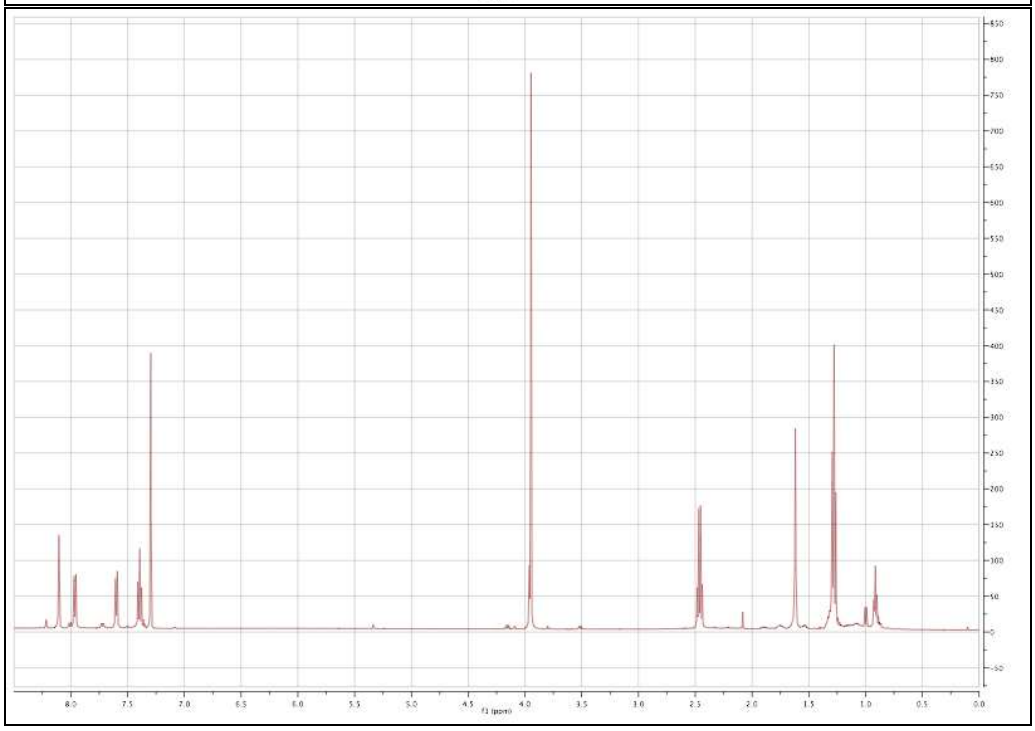
(1-(*p*-butyl-phenyl)methyl 2-hydroxybutyrate), 42.

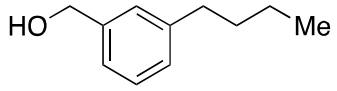




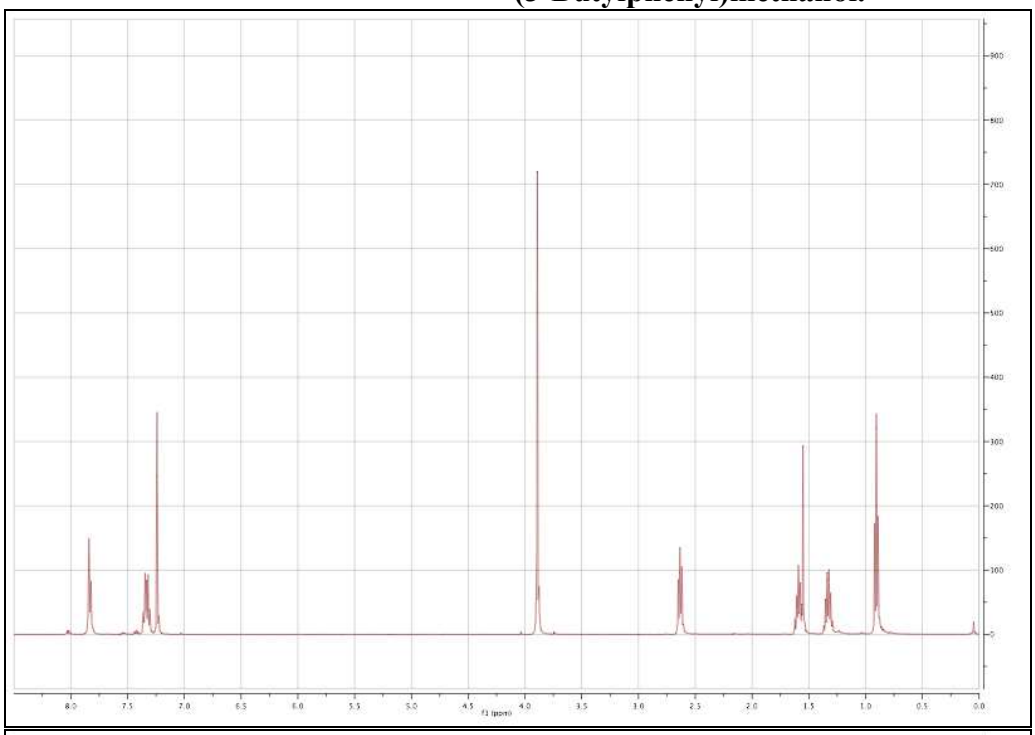
Methyl 3-(but-1-yn-1-yl)benzoate.

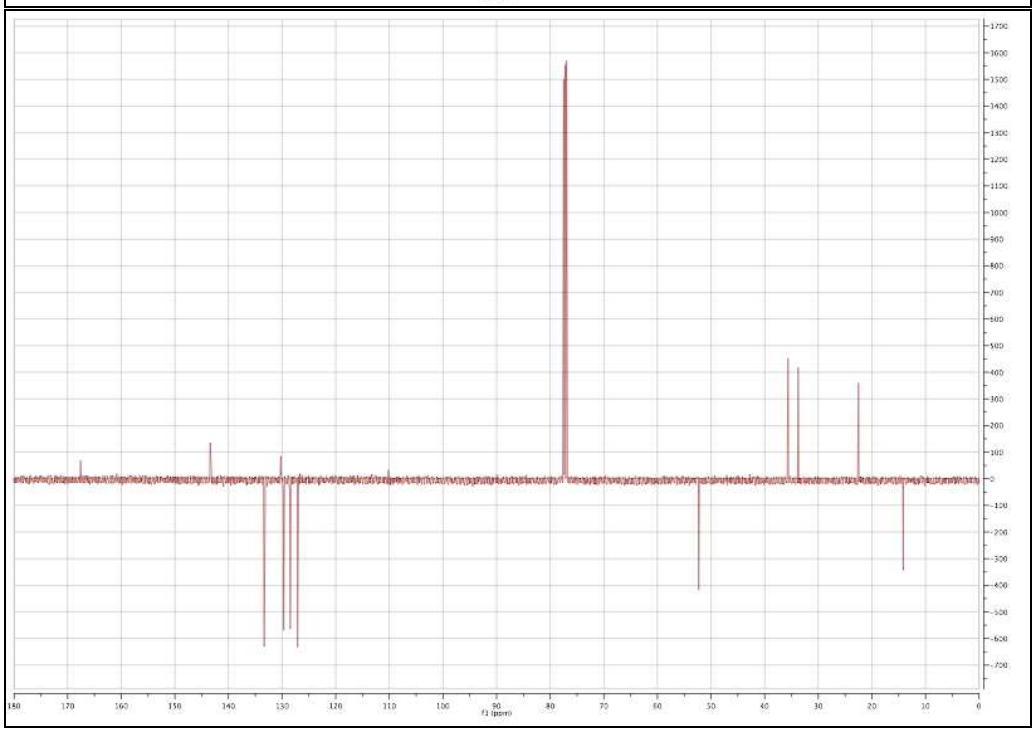


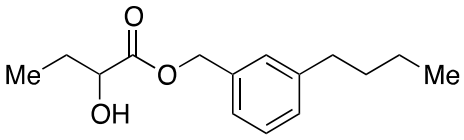




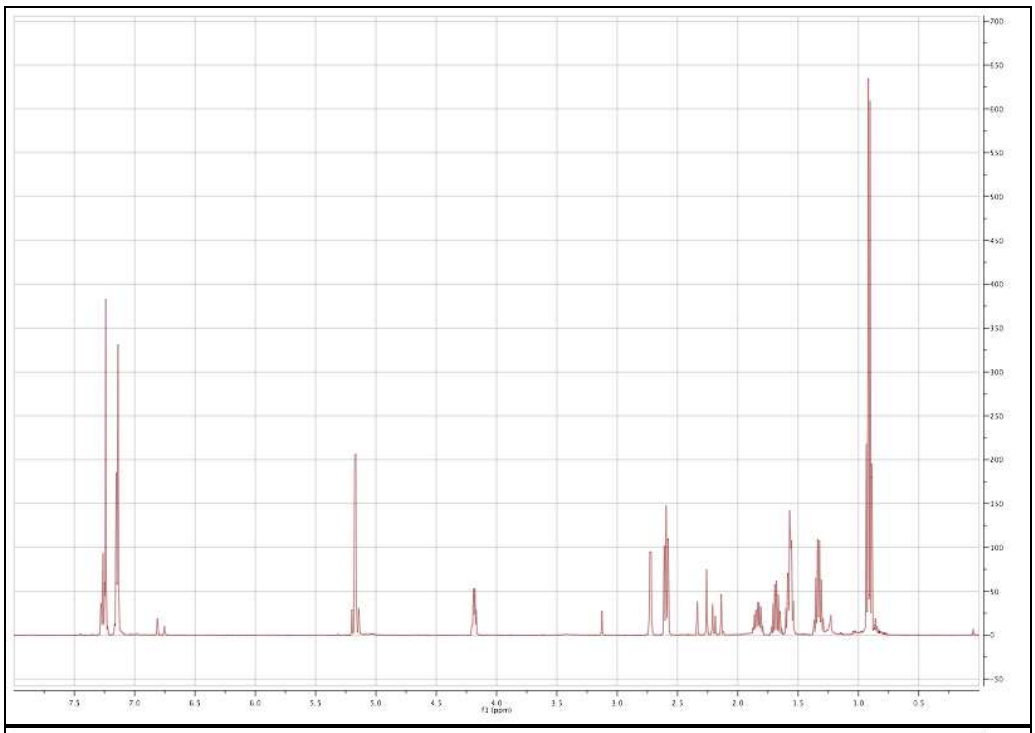
(3-Butylphenyl)methanol.

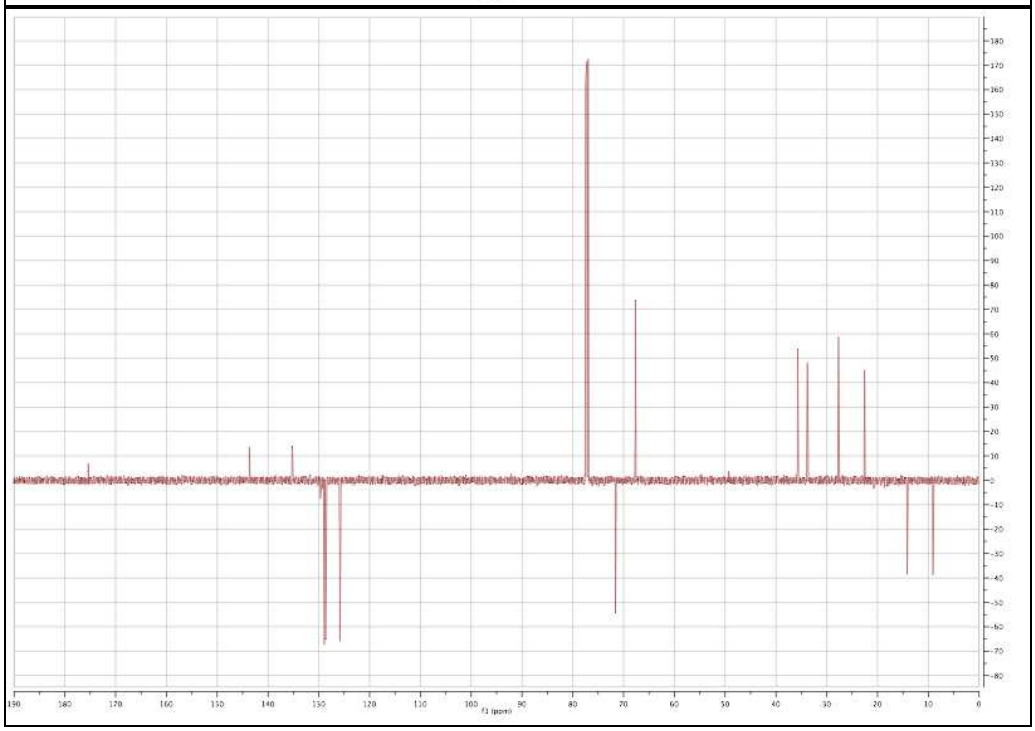


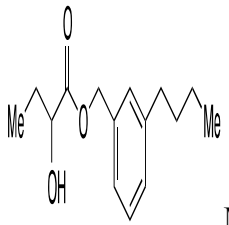




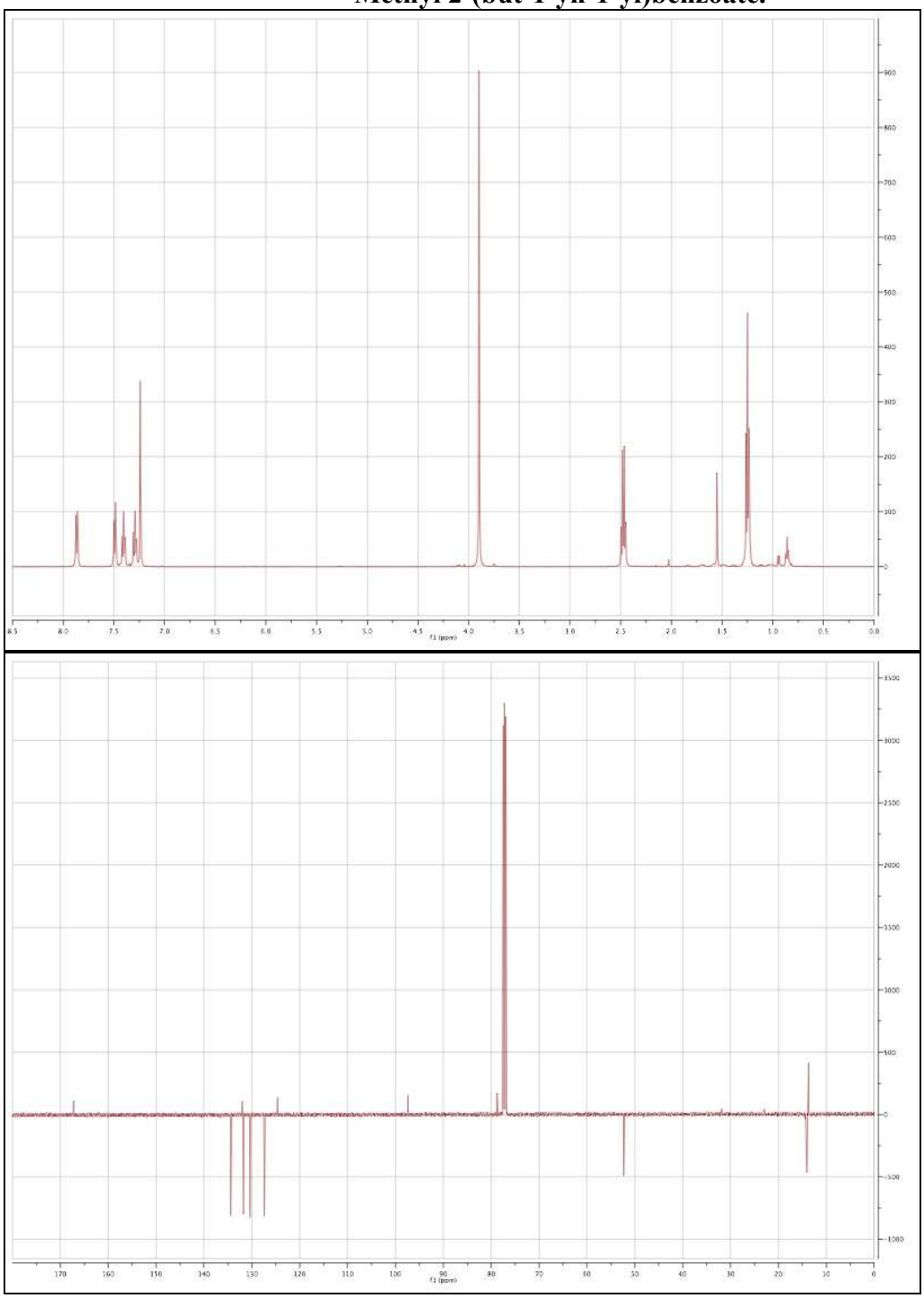
1-(*m*-Butyl-phenyl)methyl 2-hydroxybutyrate), 43.

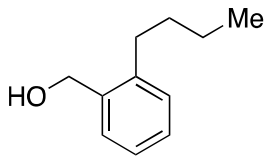




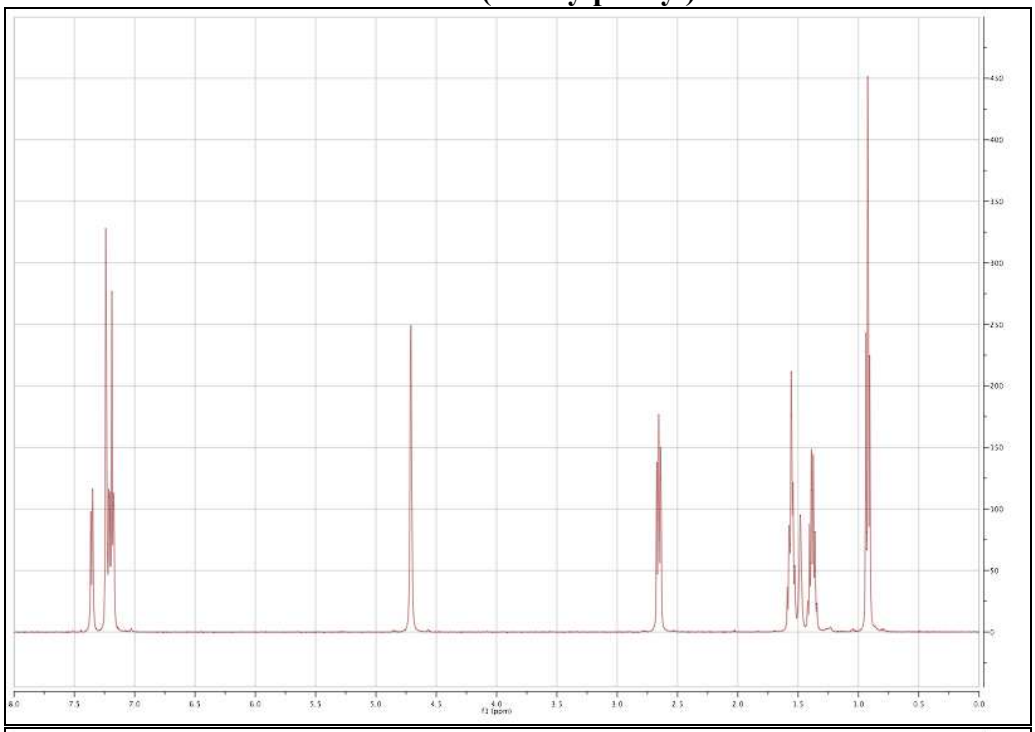


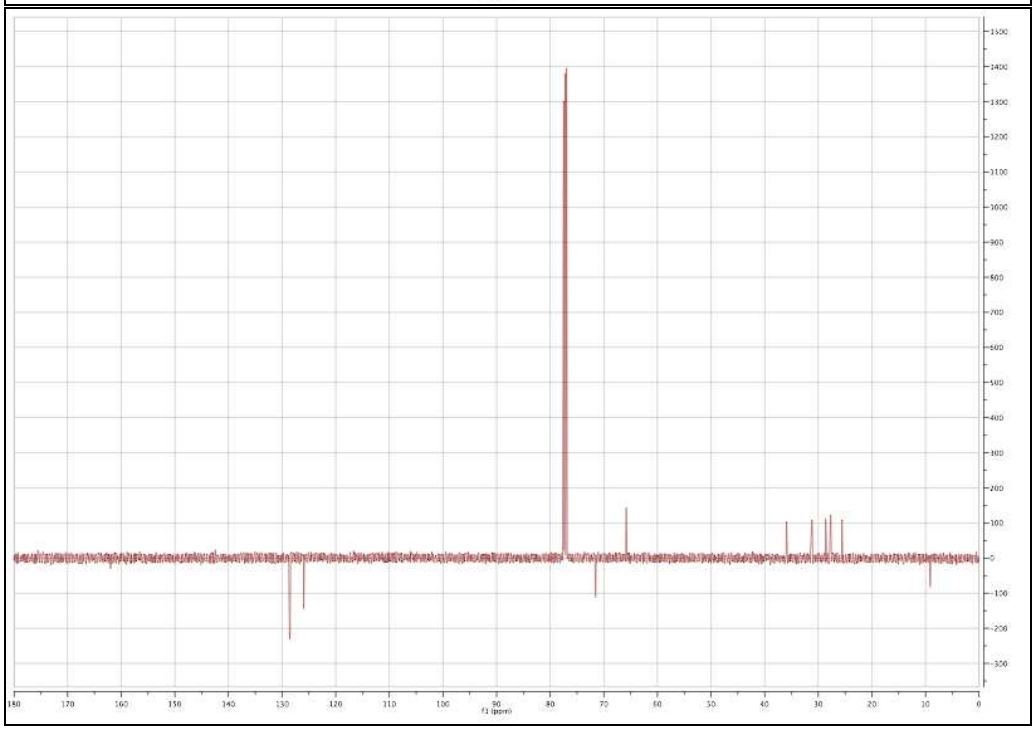
Methyl 2-(but-1-yn-1-yl)benzoate.

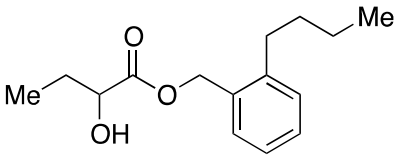




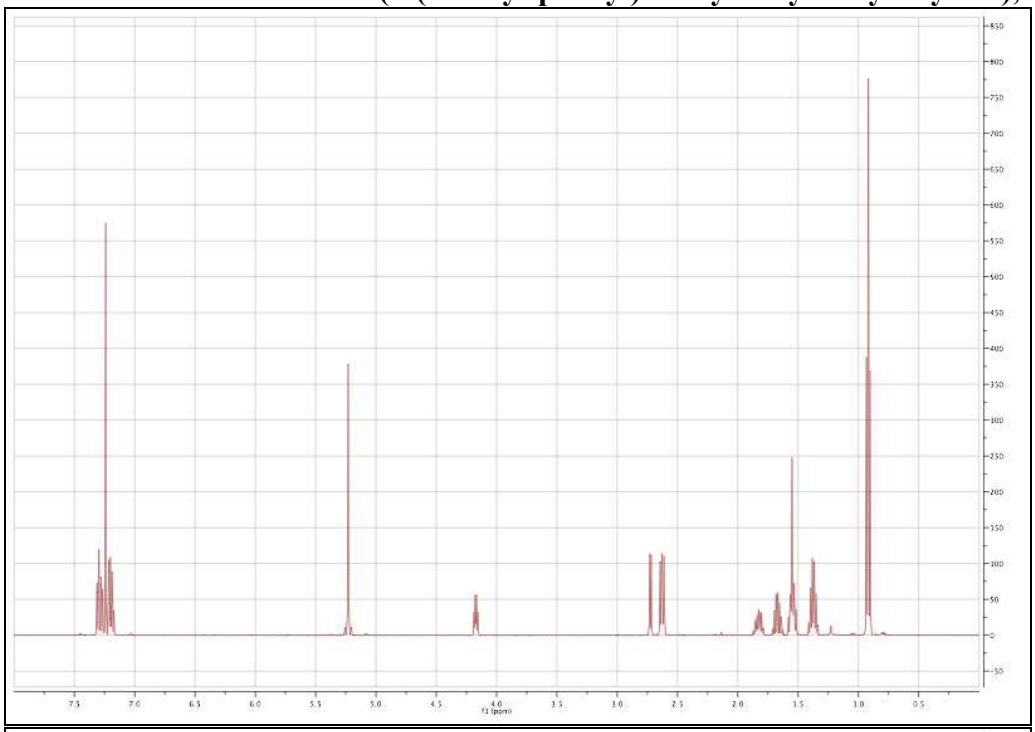
(2-Butylphenyl)methanol.

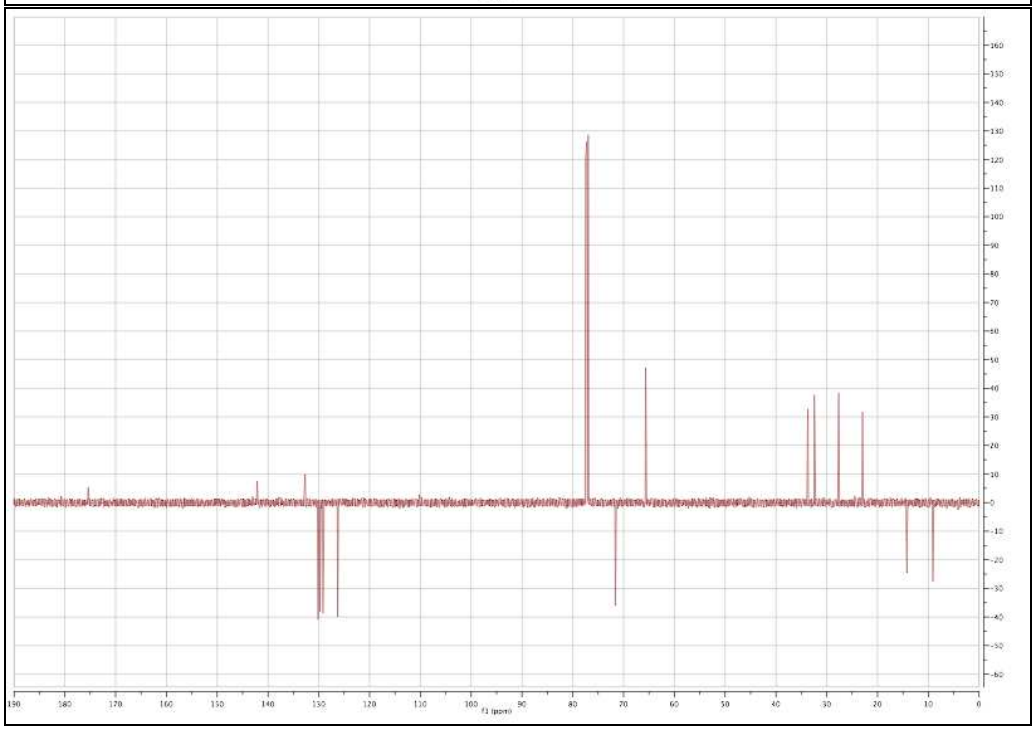


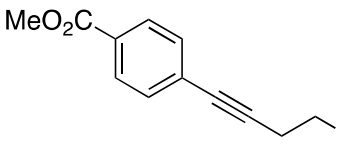




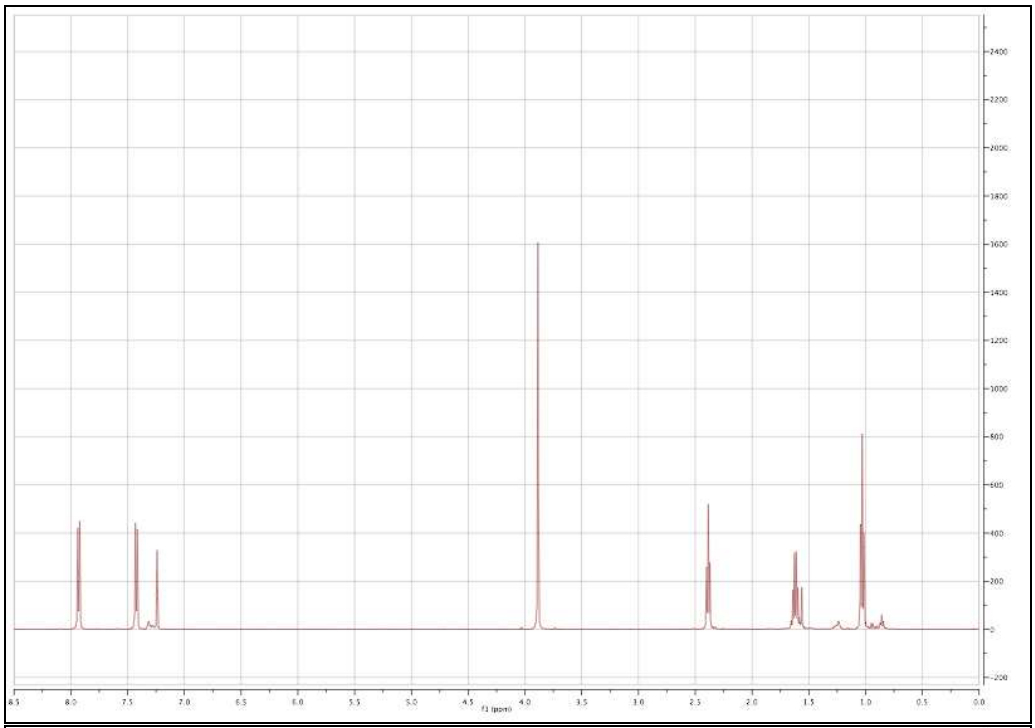
(1-(*o*-Butyl-phenyl)methyl 2-hydroxybutyrate), 44.

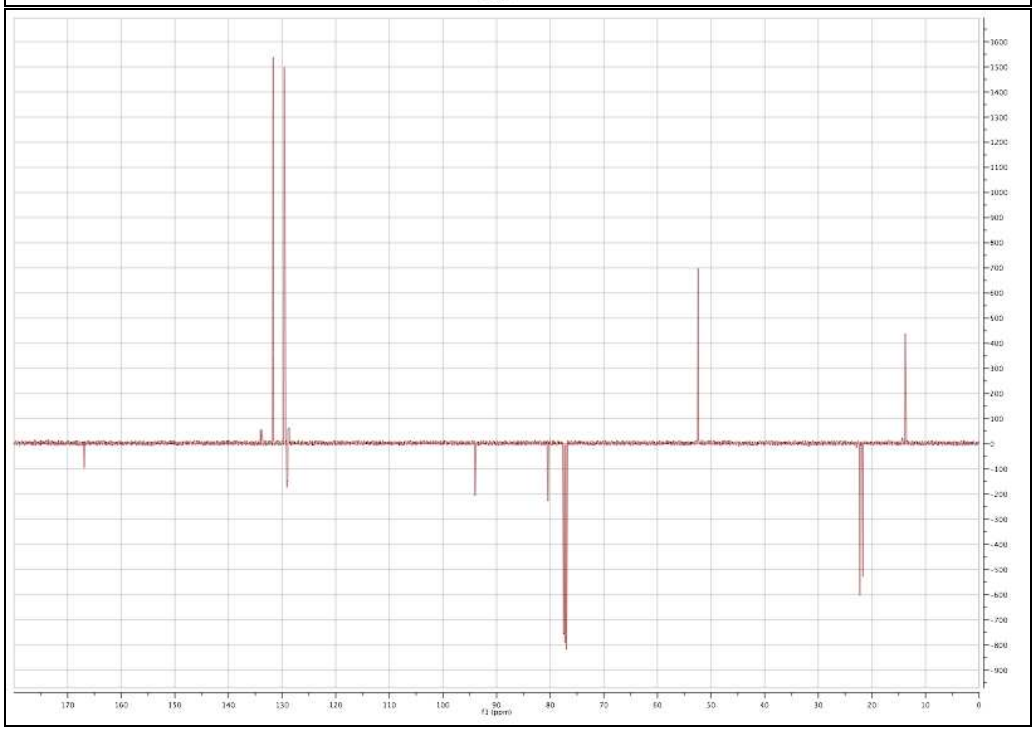


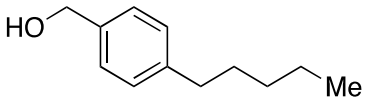




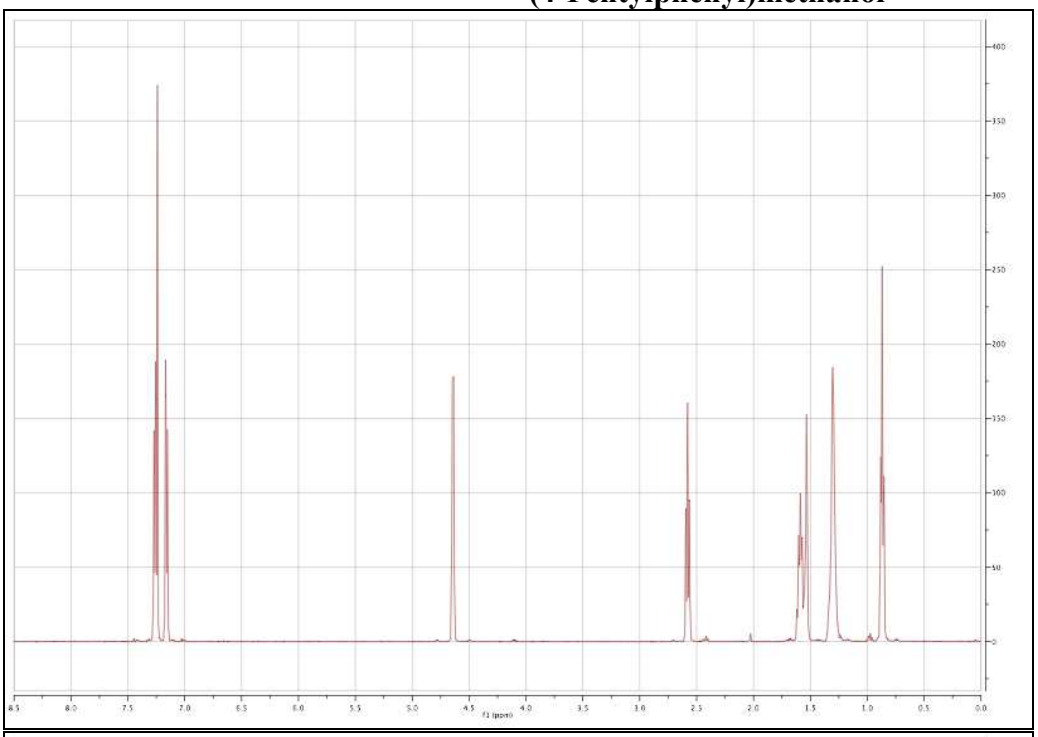
Methyl 4-(pent-1-yn-1-yl)benzoate.

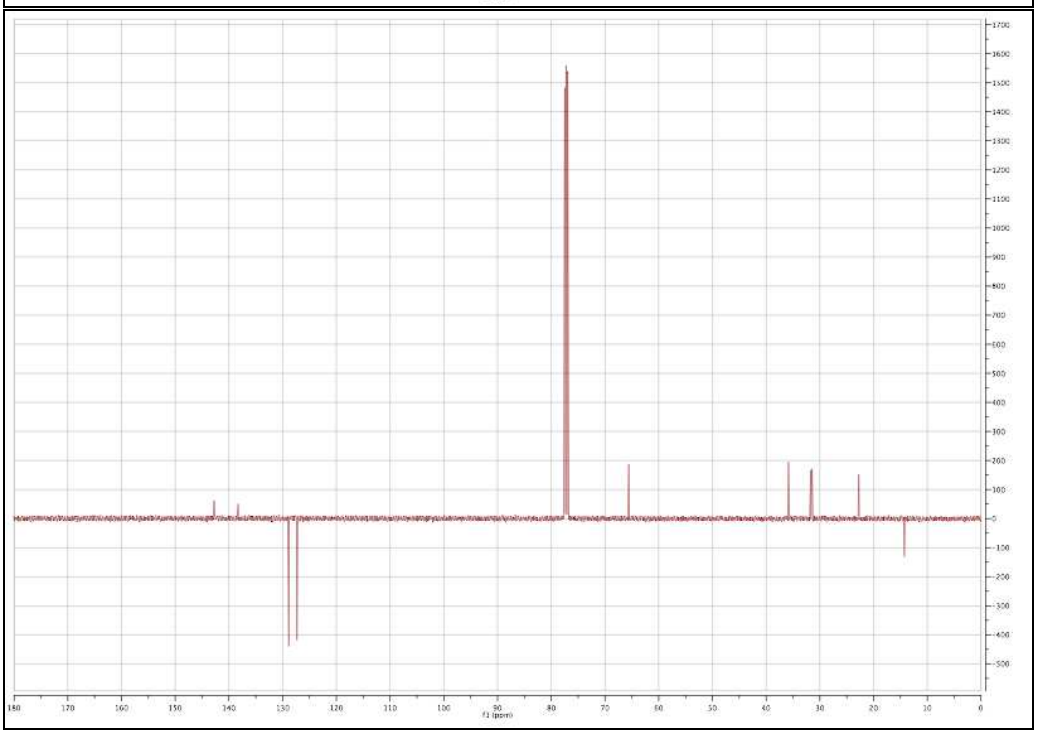


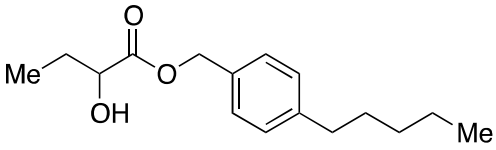




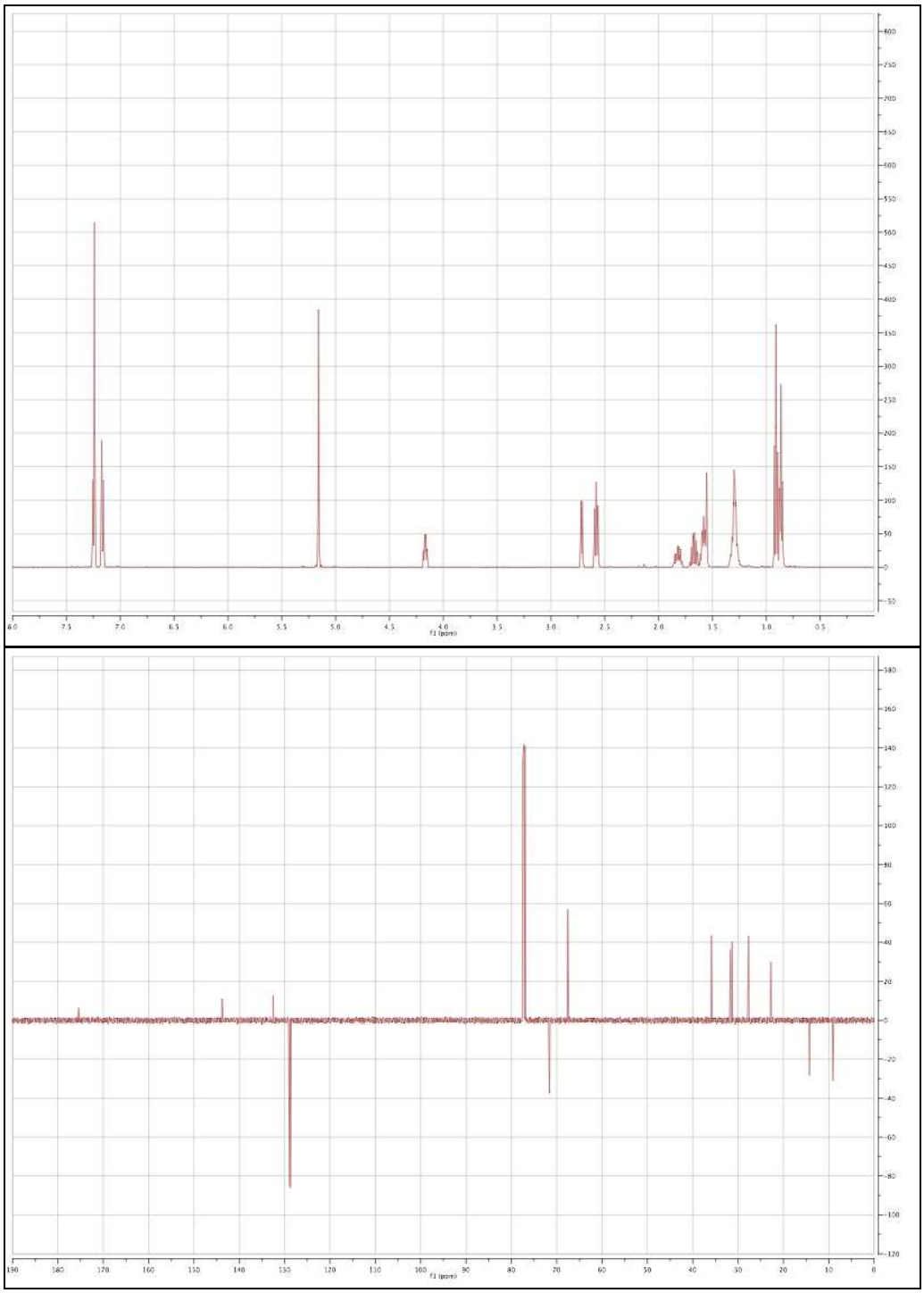
(4-Pentylphenyl)methanol

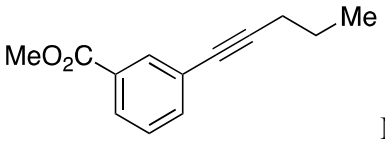




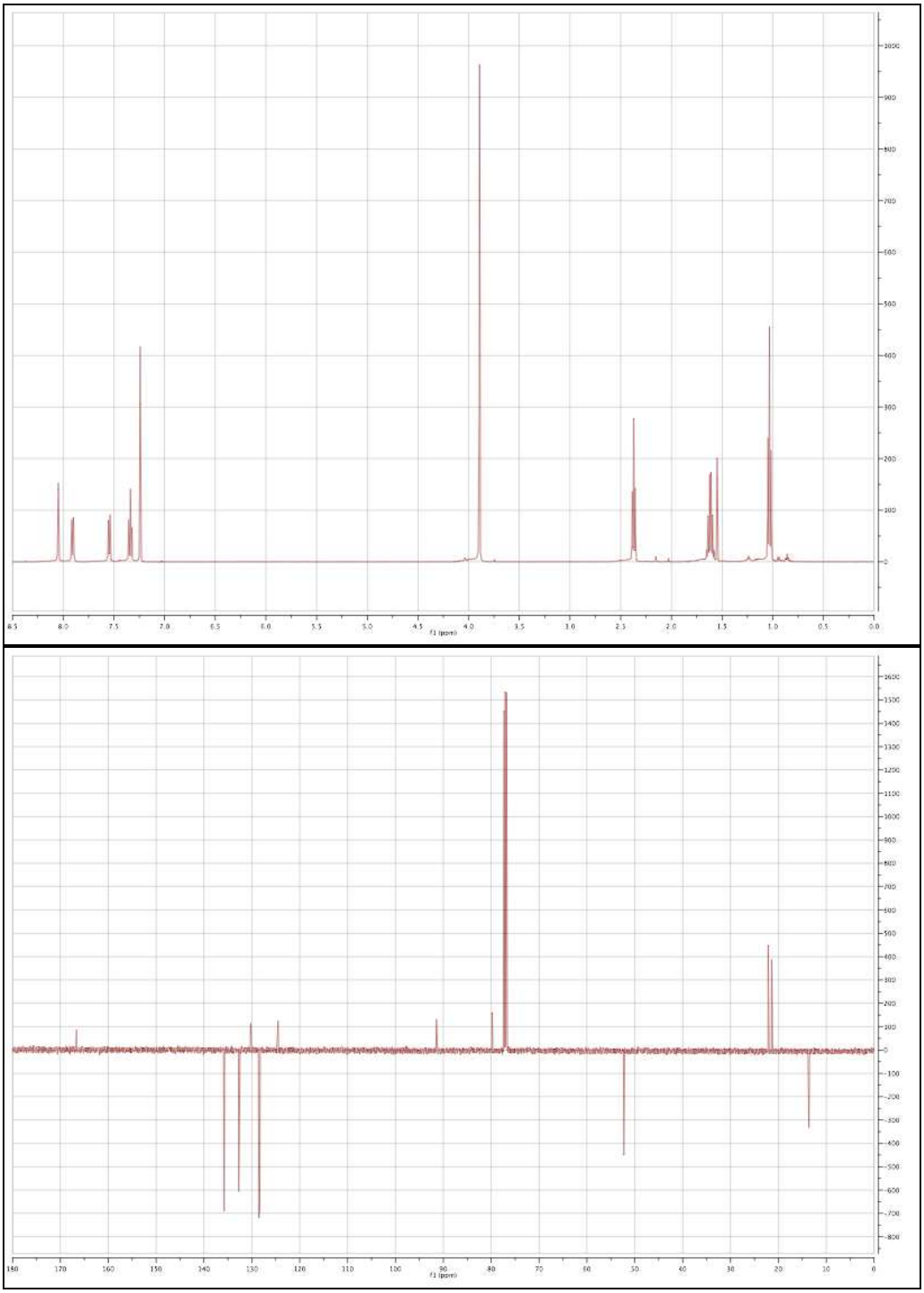


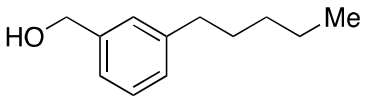
(1-(*p*-Pentyl-phenyl)methyl 2-hydroxybutyrate), 45.



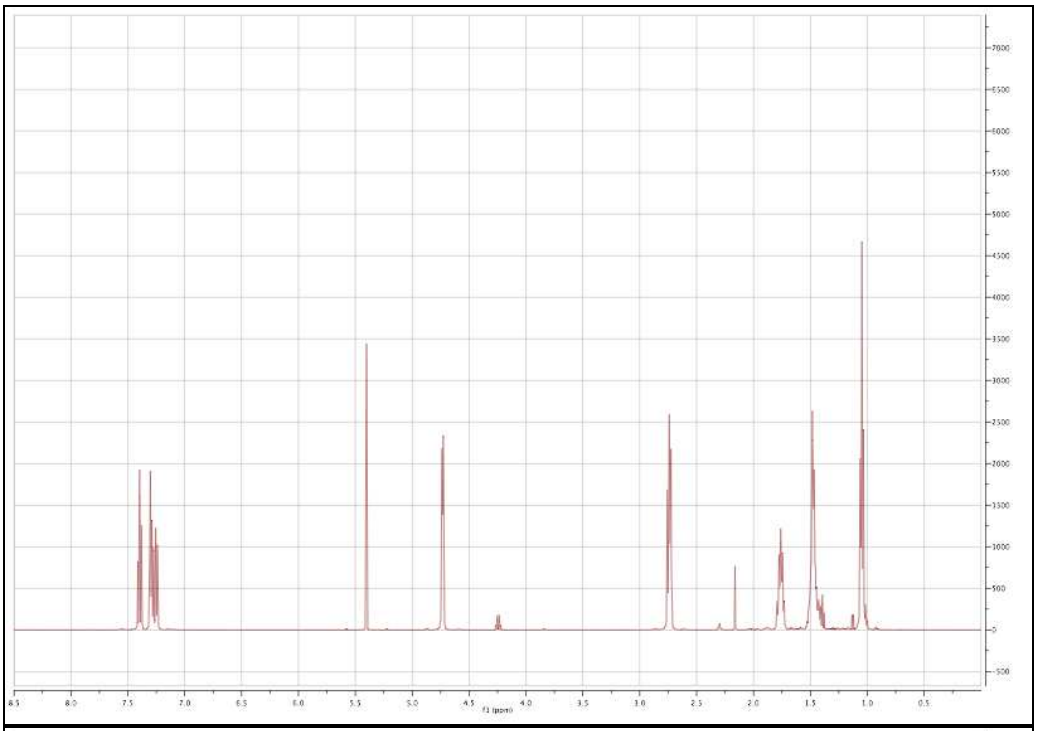


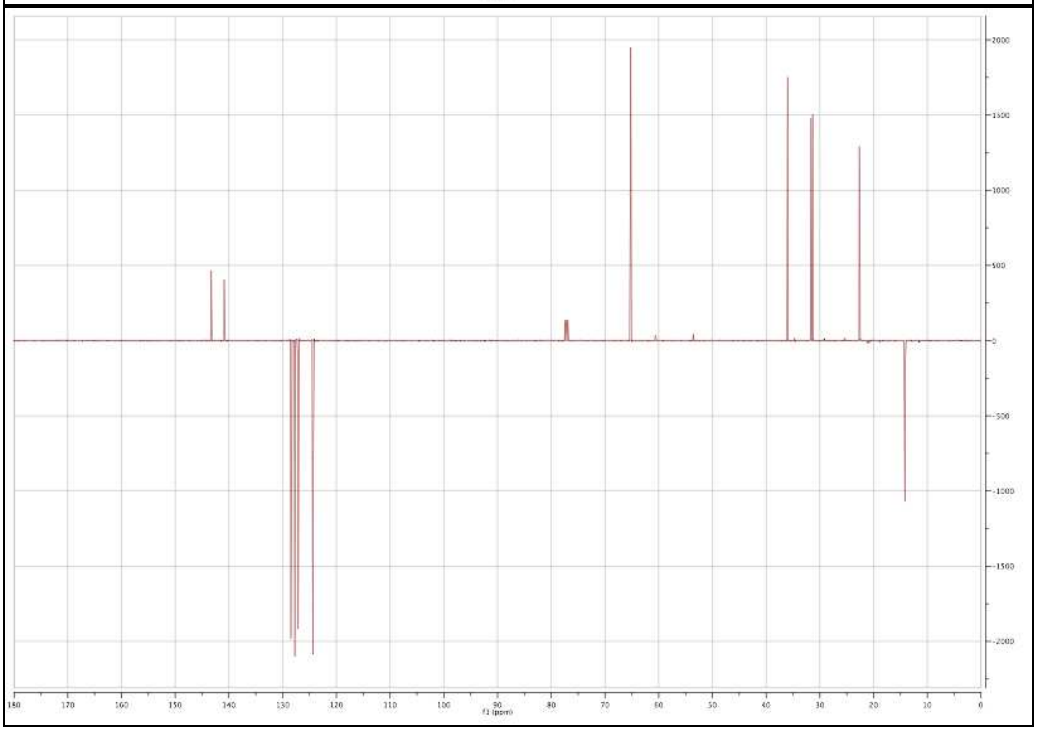
Methyl 3-(pent-1-yn-1-yl)benzoate.

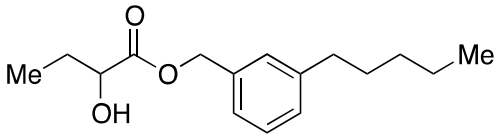




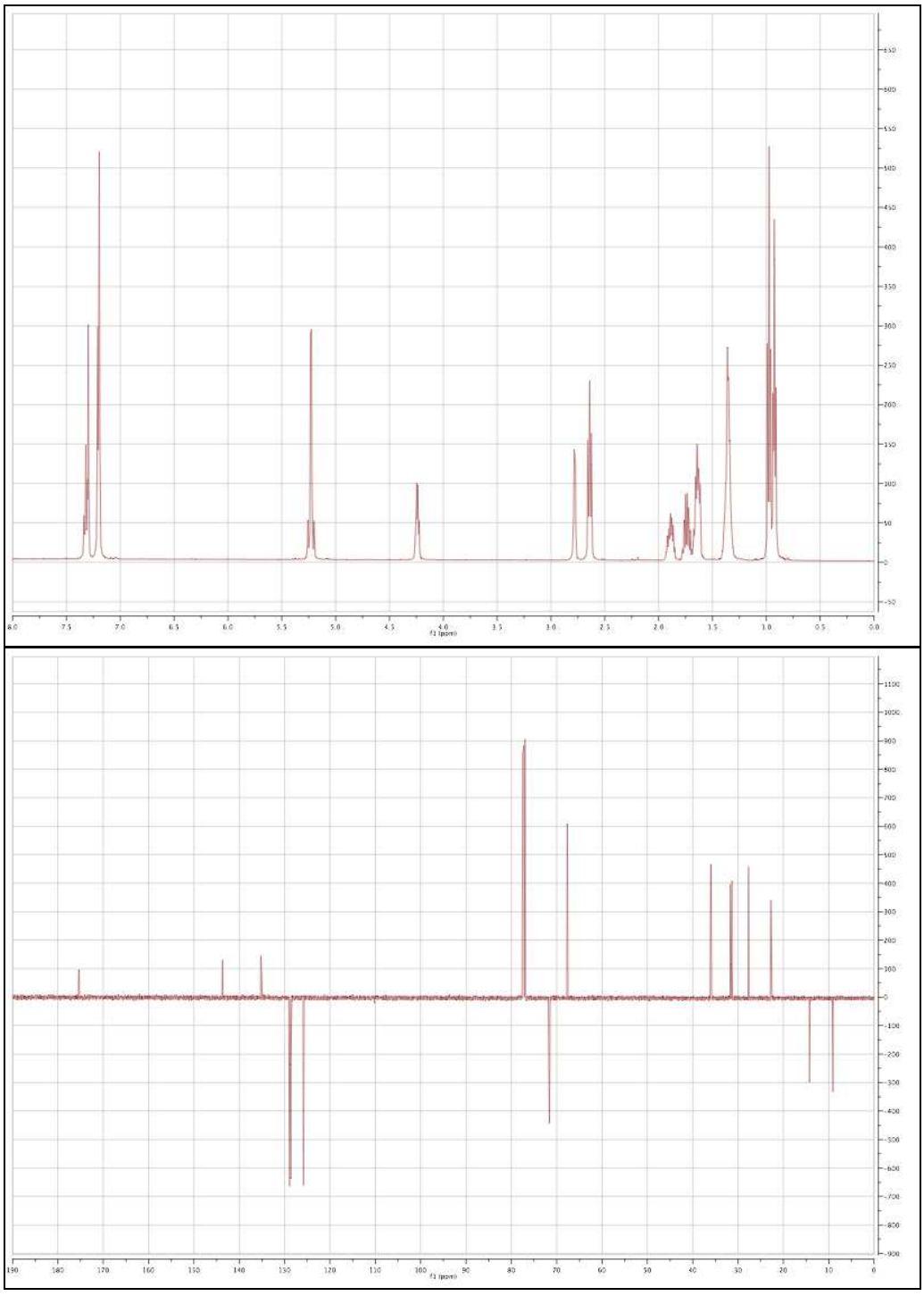
(3-Pentylphenyl)methanol.

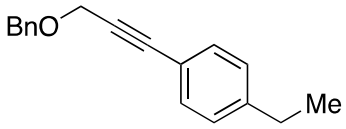




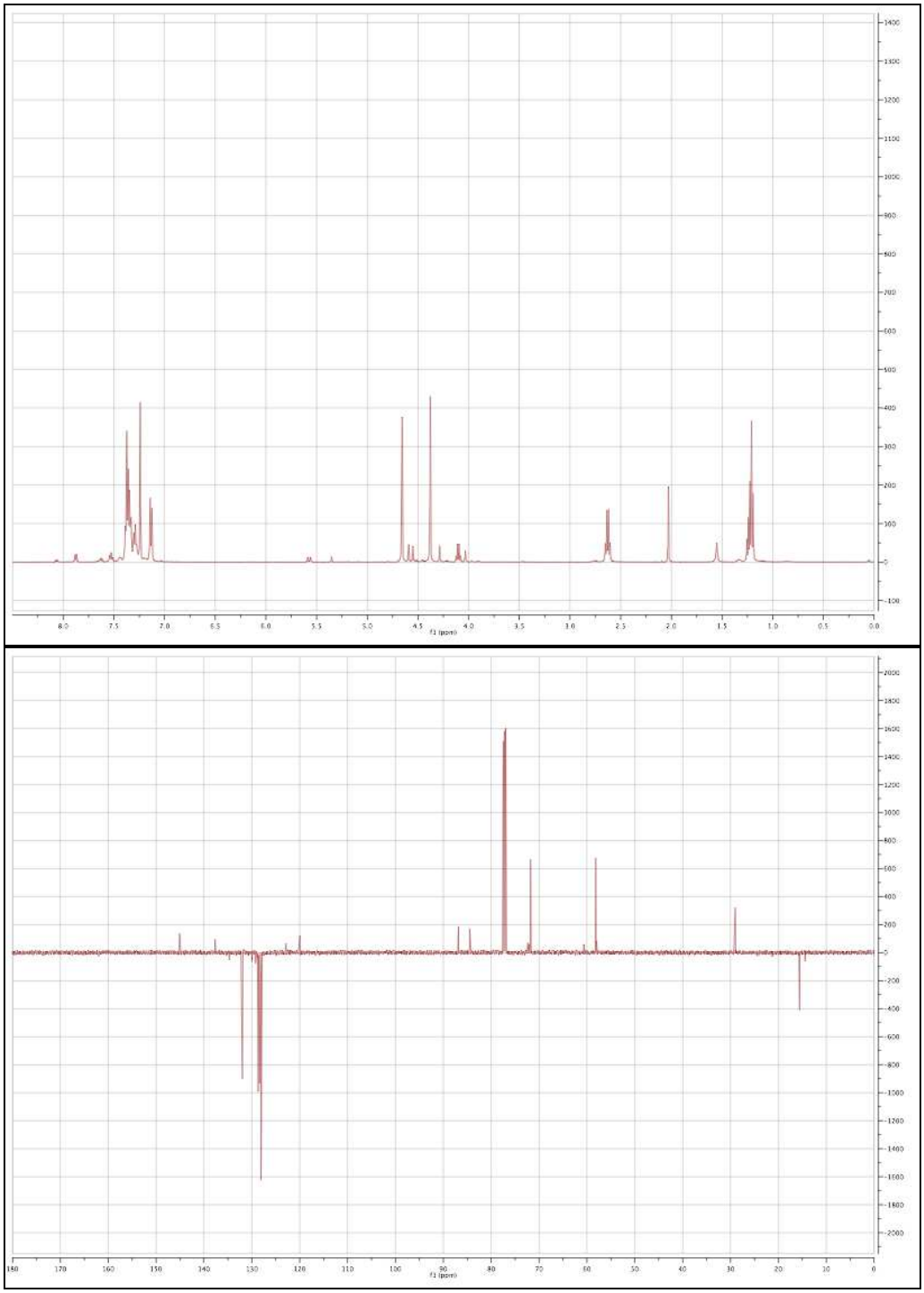


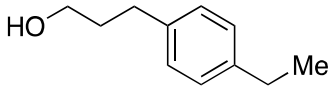
(1-(*m*-Pentyl-phenyl)methyl 2-hydroxybutyrate), 46.



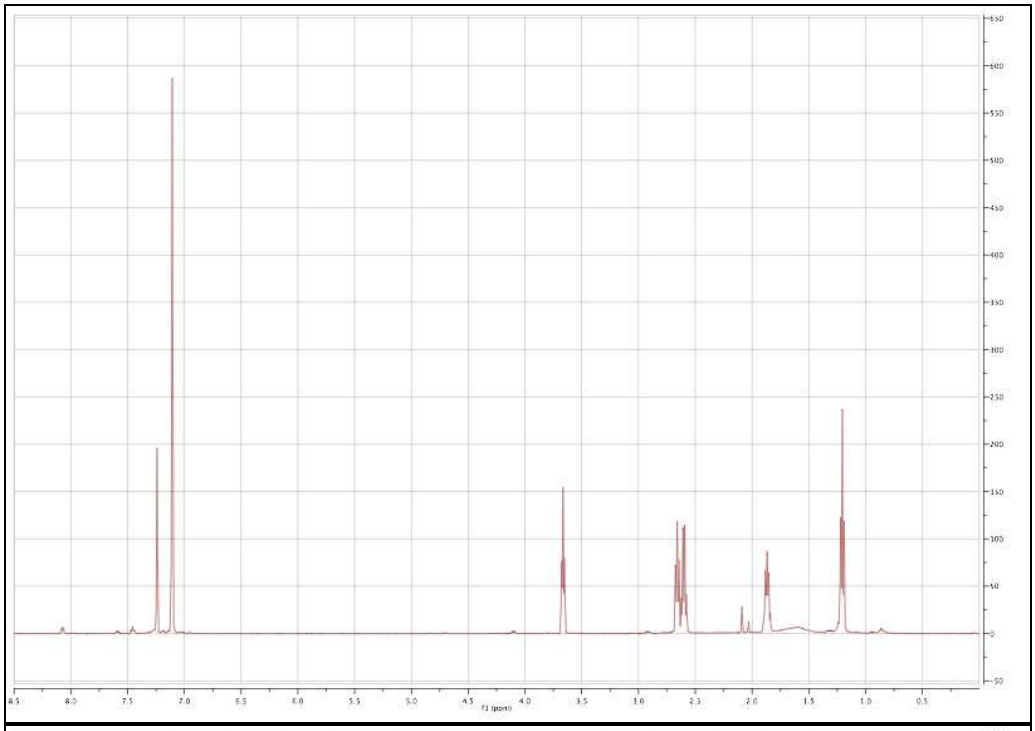


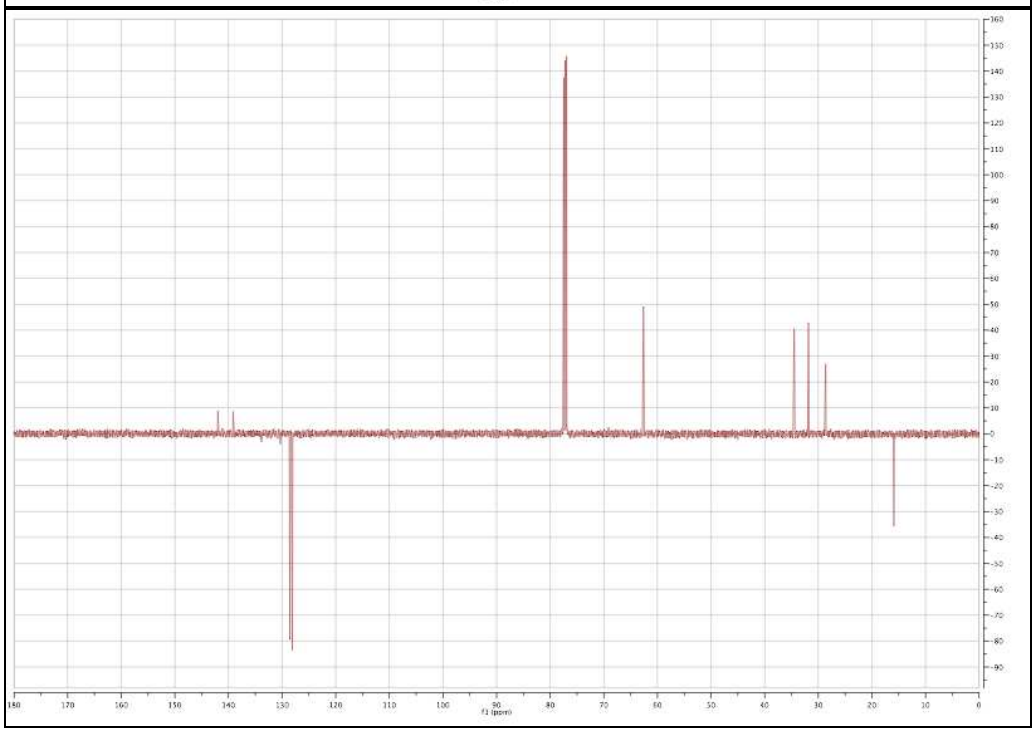
1-(3-(Benzyloxy)prop-1-yn-1-yl)-4-ethylbenzene.

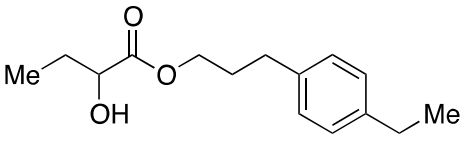




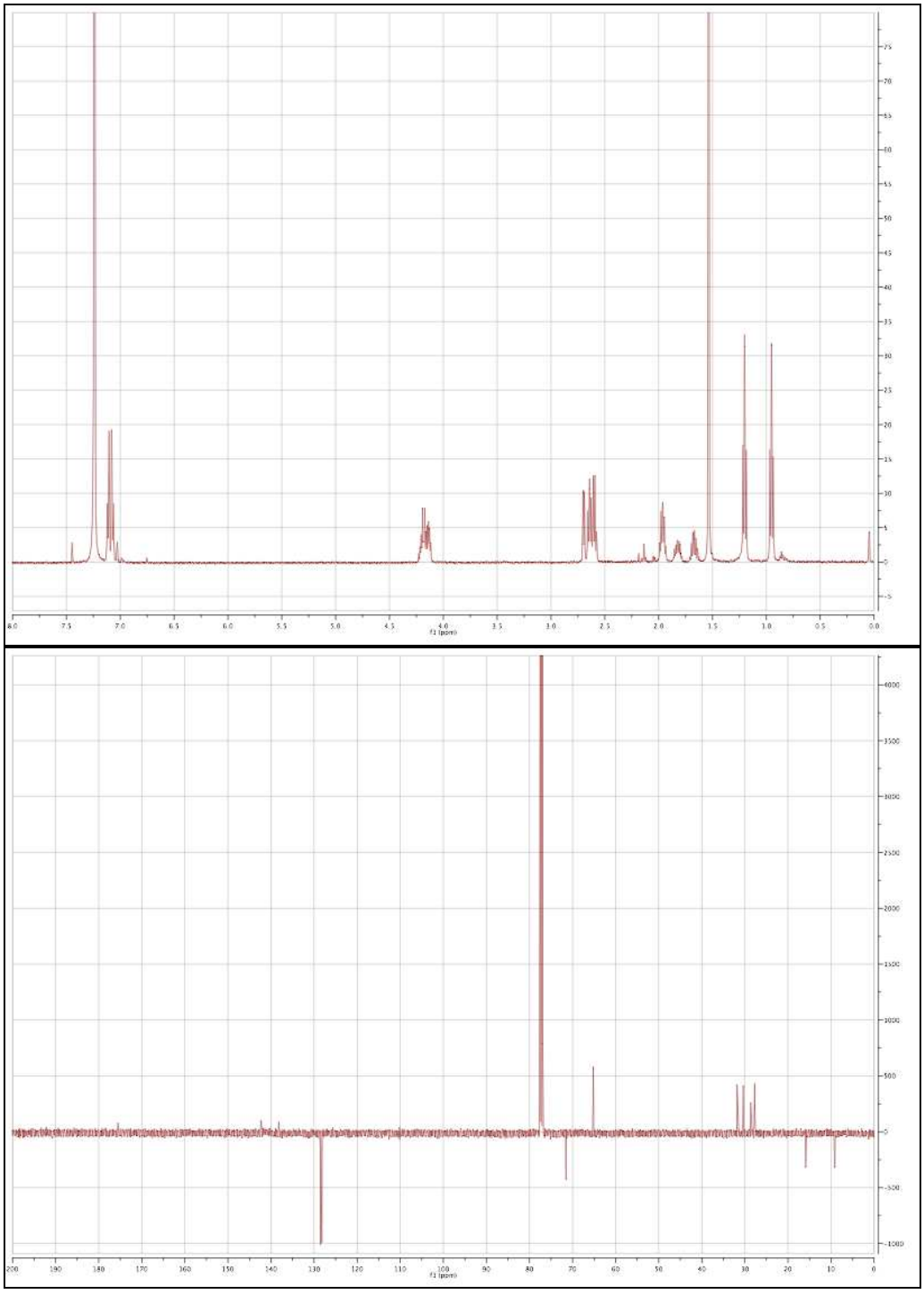
3-(4-Ethylphenyl)propan-1-ol.

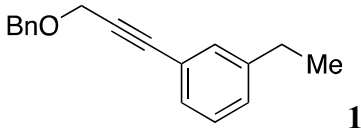




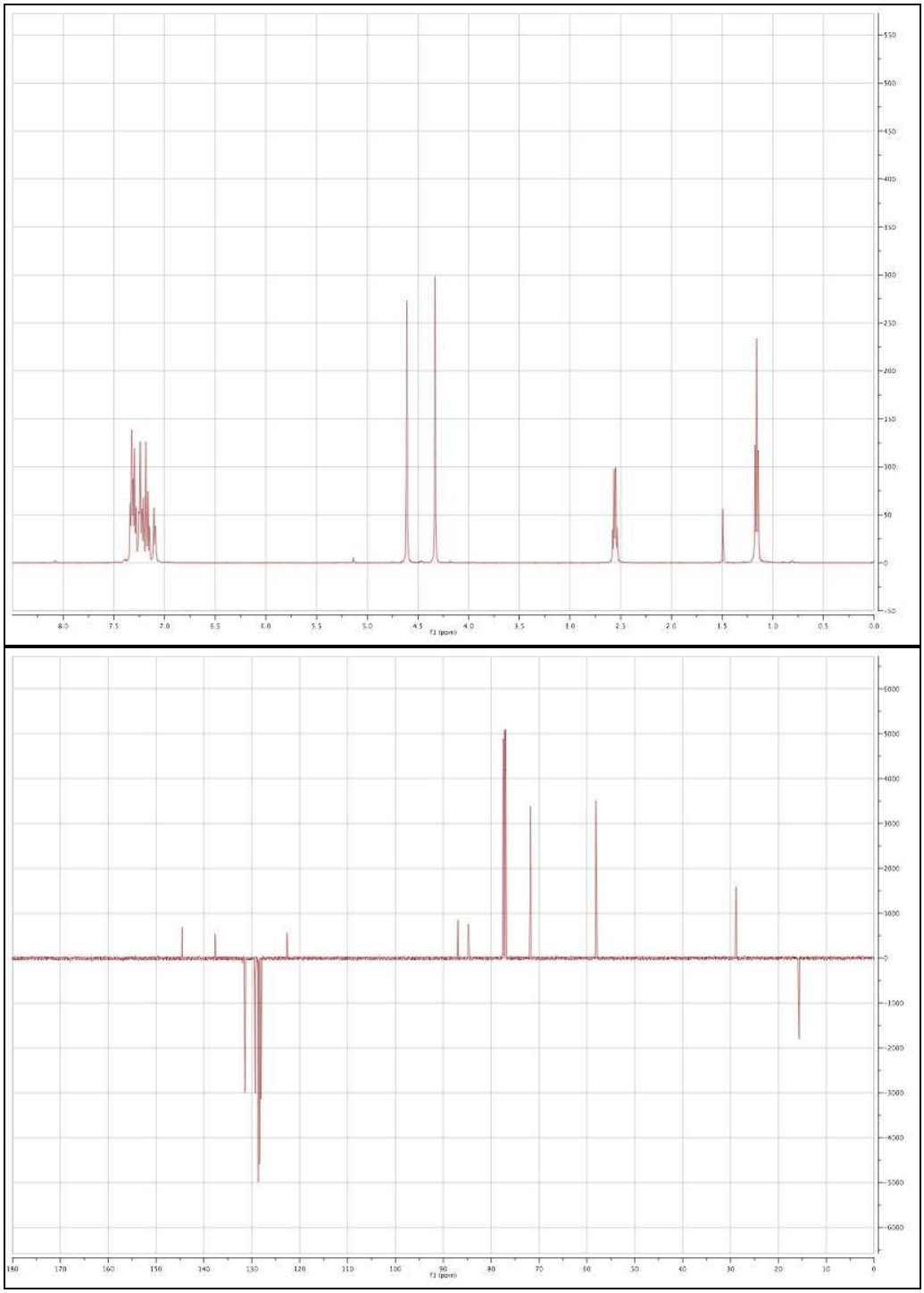


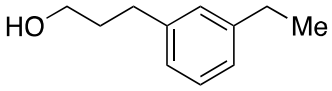
3-(*p*-ethyl-phenyl)propyl 2-hydroxybutyrate, 47.



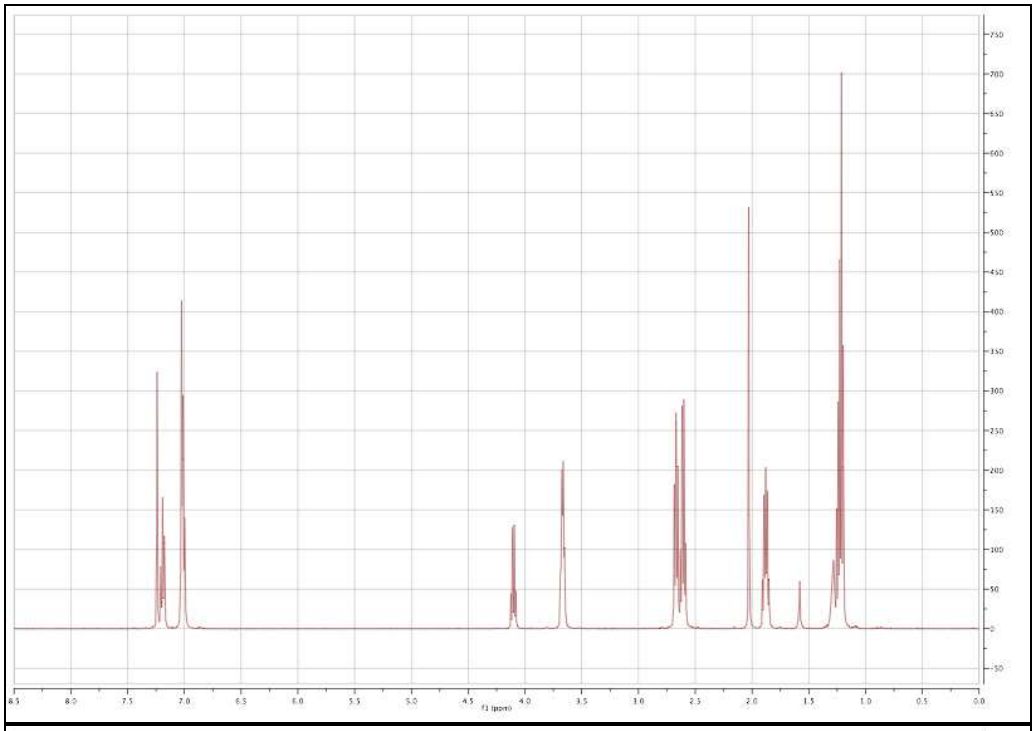


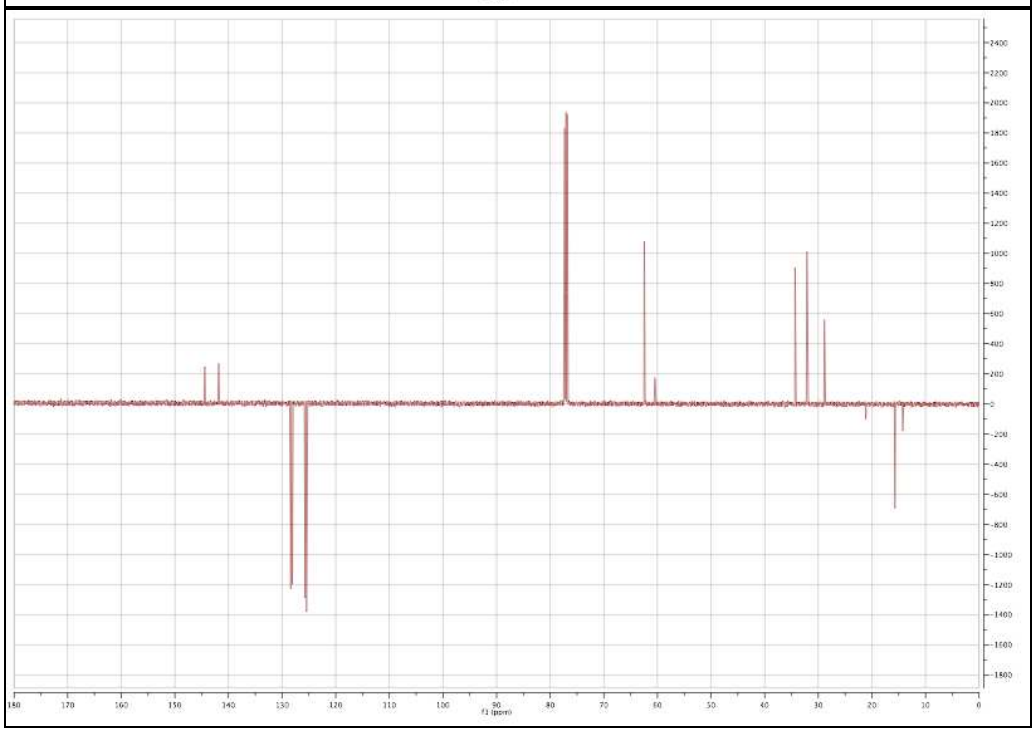
1-(3-(Benzyloxy)prop-1-yn-1-yl)-3-ethylbenzene.

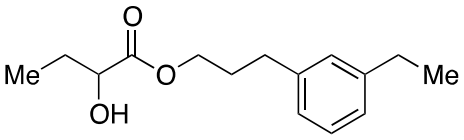




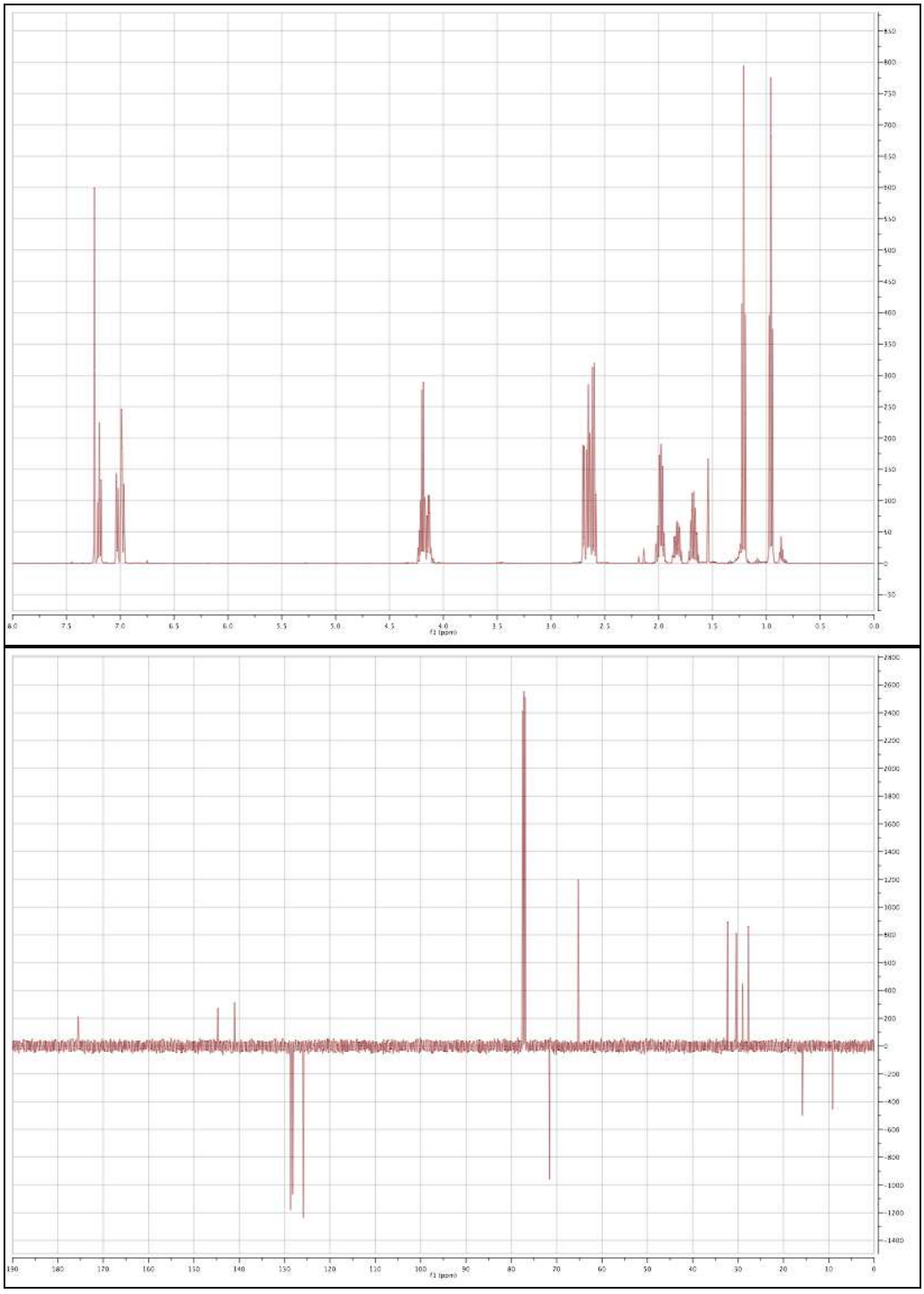
3-(3-Ethylphenyl)propan-1-ol.

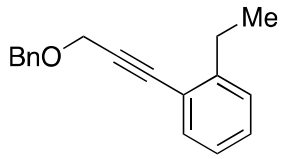




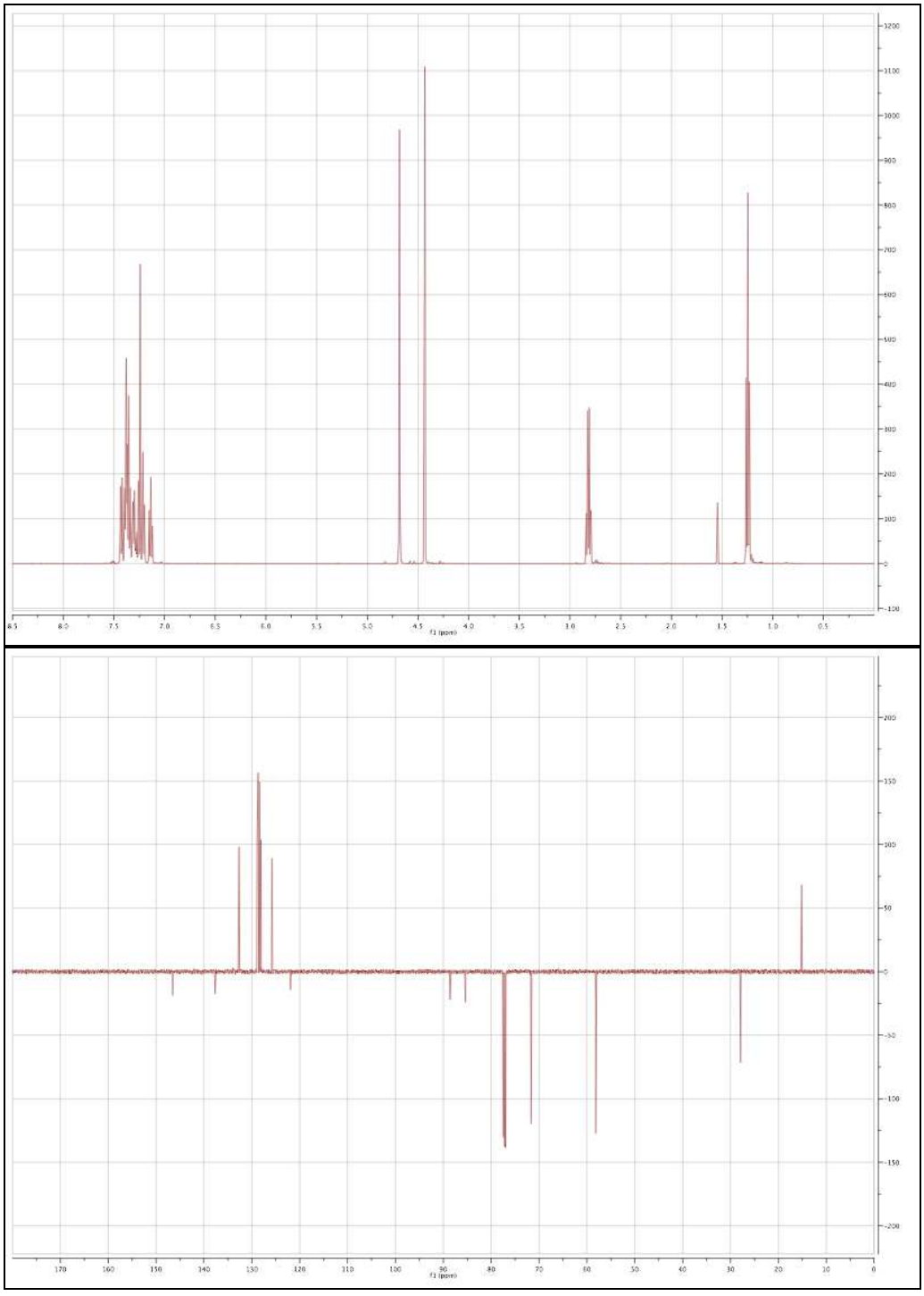


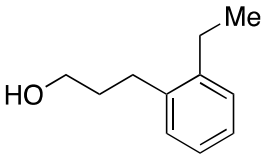
3-(*m*-Ethyl-phenyl)propyl 2-hydroxybutyrate, 48.



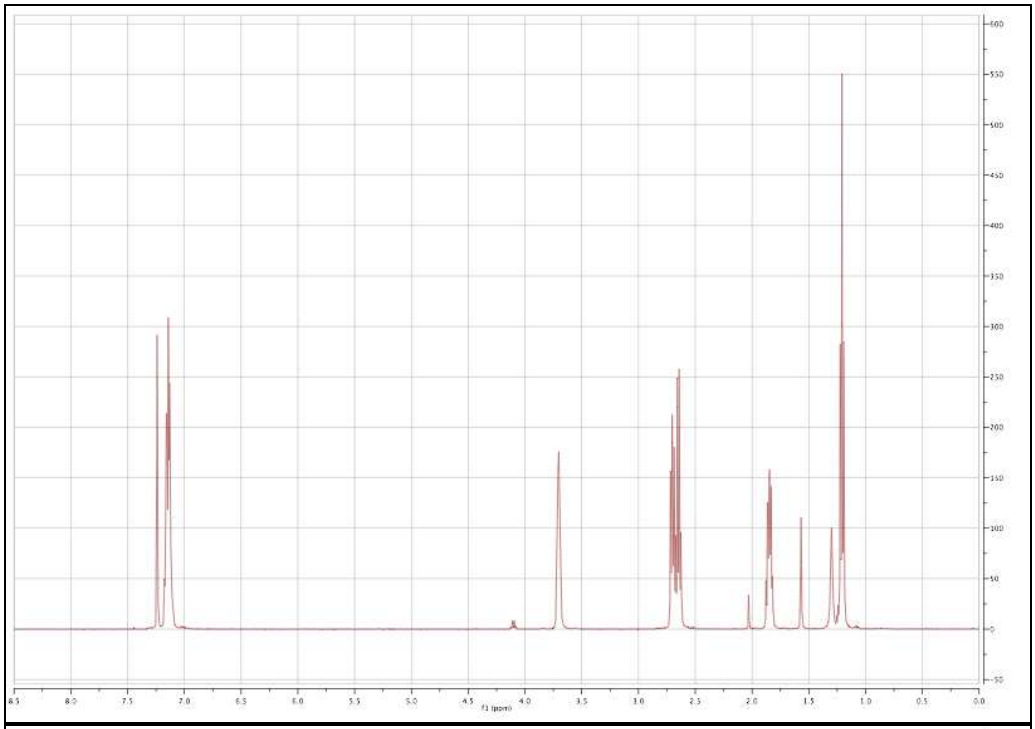


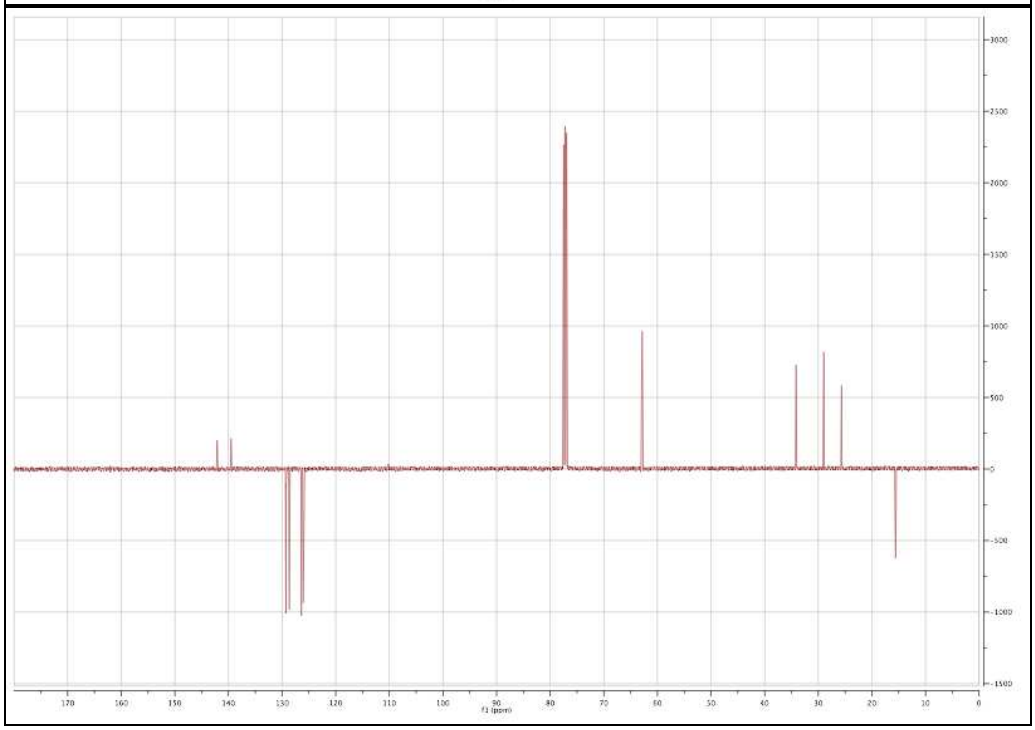
1-(3-(Benzyloxy)prop-1-yn-1-yl)-2-ethylbenzene.

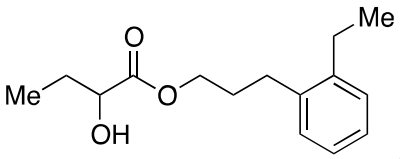




3-(2-Ethylphenyl)propan-1-ol.







3-(*o*-Ethyl-phenyl)propyl 2-hydroxybutyrate, 49.