

Electronic Supplementary Information

A Green and Sustainable Phosphine-Free NHC-Ruthenium Catalyst for Selective Oxidation of Alcohols to Carboxylic Acids in Water

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1. Experimental Section:

1.1 Materials

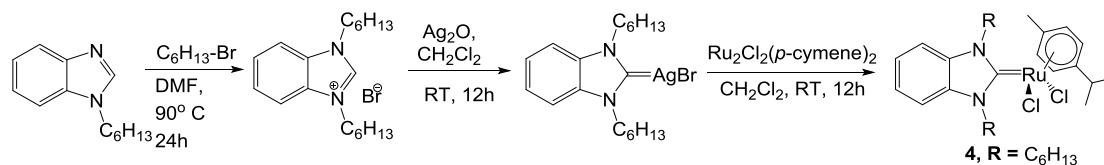
Benzimidazole (99%, Sigma Aldrich), 1-bromohexane (99%, Acros Organics), silver oxide (99.9%, Sigma Aldrich), [Ru(p-cymene)Cl₂]₂ (99.9%, Sigma Aldrich), glycidol (96%, Sigma-Aldrich), ethyl vinyl ether (99%, Sigma-Aldrich), 9-decan-1-ol (99%, Sigma-Aldrich), tetrabutylammonium bromide (NBu₄Br) (98%, Aldrich), triisobutylaluminum (Al(*i*-Bu)₃) (1mol/L in toluene, Aldrich), ¹⁸OH₂ (97%, ABCR), were used without further purification. Unless otherwise indicated, all solvents were purchased from commercial sources and were used without further purification. All polymerization reactions were performed under inert gas atmosphere. All functional transformations were performed in air, unless otherwise noted. Polyglycidols was prepared according to literature method.^[S1]

1.2 Measurements

¹H and ¹³C NMR spectra were recorded on a Bruker DPX-400 FT NMR spectrometer (400, 600 MHz and 100, 150 MHz, respectively) and are reported as follows: chemical shift δ (ppm) (multiplicity, coupling constant *J* (Hz), number of protons, assignment). Chemical shifts are reported in ppm to the nearest 0.01 ppm for ¹H and the nearest 0.1 ppm for ¹³C. Mass spectra were recorded on a Finnigan SSQ 7000 spectrometer and HRMS spectra on a Thermo Scientific LTQ Orbitrap XL spectrometer. Infrared spectra were carried out on a ThermoNicolet FT-IR Nexus spectrometer and are recorded by using an ATR unit (ThermoNicolet, Smart SplitPEA). Transmission maxima are reported in wavenumbers (cm⁻¹) and only selected intensities are reported. SEC with THF (HPLC grade, Carl Roth) as eluent was performed using a HPLC pump (PU-2080plus, Jasco) equipped with a refractive index detector (RI-2031plus, Jasco). The sample solvent contained 250 mg·mL⁻¹ 3,5-di-tert-4-butylhydroxytoluene (BHT, $\geq 99\%$, Fluka) as internal standard. One pre-column (8x50 mm) and four SDplus gel columns (8x300 mm, SDplus, MZ Analysentechnik) were applied at a flow rate of 1.0 mL·min⁻¹ at 20 °C. The diameter of the gel particles measured 5 μ m, the nominal pore widths were 50, 10², 10³ and 10⁴ Å. Calibration was achieved using narrow distributed poly(methyl methacrylate) standards. The number-average

molecular weight M_n , the weight-average molecular weight M_w , and the dispersity $D_w = M_w/M_n$ were calculated by the program PSS WinGPC UniChrom software (Version 8.1.1).

1.3 Synthesis of NHC-Ruthenium complex **4**^[S2]



1.4 General procedure for synthesis of carboxylic acids from primary alcohols

An oven-dried Schlenk tube was charged with complex **4** (5.9 mg, 0.01 mmol), NaOH (60 mg, 1.5 mmol), alcohol (1 mmol) and water (1 mL). The reaction mixture was heated to reflux for 24h and cooled to room temperature. The reaction mixture was washed with diethyl ether to extract the catalyst and alcohol residues. The aqueous layer was acidified with 3N HCl and extracted with ethyl acetate. The organic layer was dried over Na₂SO₄, the solution was filtered and the solvent was removed under reduced pressure to obtain the carboxylic acid. All carboxylic acids were identified by comparison of their NMR spectra with literature data.

2-Phenylacetic acid (5f): ¹H NMR (400 MHz, DMSO, 298 K) δ = 12.37 (s, 1H), 7.29-7.33 (m, 2H), 7.25 (d, J = 7.2, 3H), 3.56 (s, 2H). ¹³C NMR (DMSO, 100 MHz): δ = 172.67, 134.98, 129.33, 128.20, 126.54, 40.64. Yield = 90%.

3-Phenylpropanoic acid (5g): ¹H NMR (400 MHz, DMSO, 298 K) δ = 12.14 (s, 1H), 7.28 (m, 2H), 7.18-7.24 (m, 3H), 2.82 (t, J = 7.7, 2H), 2.53 (m, 2H). ¹³C NMR (DMSO, 100 MHz, 298 K): δ = 173.73, 140.84, 128.25, 128.19, 125.93, 35.19, 30.3. Yield = 87%.

3,4-Dimethoxybenzoic acid (5k): ¹H NMR (400 MHz, DMSO, 298 K) δ = 12.67 (s, 1H), 7.56 (dd, J = 8.5, J = 2.0, 1H), 7.44 (d, J = 2.2, 1H), 7.04 (d, J = 8.4, 1H), 3.82 (s, 3H), 3.79 (s, 3H). ¹³C NMR (DMSO, 100 MHz, 298 K): δ = 167.08, 152.55, 148.25, 123.13, 122.88, 111.8, 110.92, 55.6, 55.38. Yield = 84%.

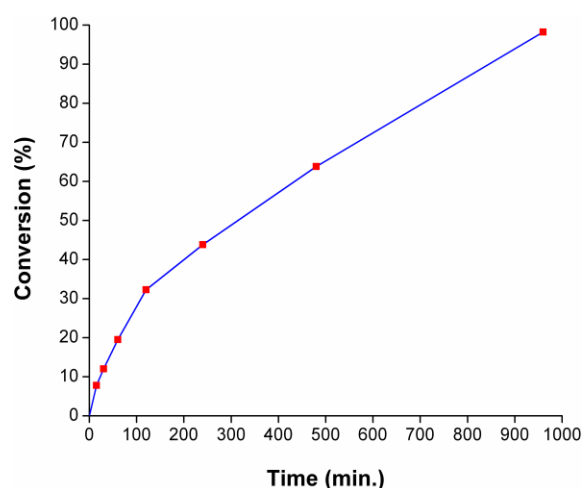
3-chlorobenzoic acid (5j): ¹H NMR (400 MHz, DMSO, 298 K) δ = 13.33 (s, 1H), 7.85-7.92 (m, 2H), 7.64-7.72 (m, 1H), 7.53 (td, J = 8.0, J = 1.7, 1H). ¹³C NMR (DMSO, 100 MHz, 298 K): δ = 166.04, 133.30, 132.85, 132.67, 130.6, 128.79, 127.87. Yield = 79%.

Compound 6: ¹H NMR (400 MHz, DMSO, 298 K) δ = 5.53 (d, J = 5.0 Hz, 1H), 4.65 (dd, J = 7.7, J = 2.5, 1H), 4.51 (dd, J = 7.7, J = 2.3, 1H), 4.40 (dd, J = 5.0, J = 2.6, 1H), 4.18 (d, J = 2.2 Hz, 1H), 1.43 (s, 3H), 1.32 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H). ¹³C NMR (DMSO, 100 MHz, 298 K): δ = 168.85, 108.68, 108.05, 95.73, 71.42, 70.01, 69.49, 67.20, 25.79, 25.64, 24.63, 24.38. Yield = 22%.

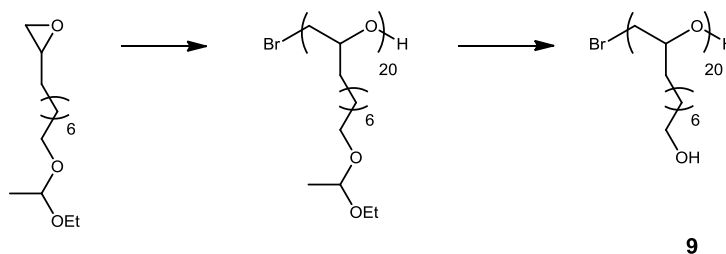
Compound 7: ^1H NMR (400 MHz, DMSO, 298 K) δ = 1.26 (s, 3 H), 1.38 (s, 3H), 3.28 (s, 3H), 4.51 (d, J = 5.9, 1H), 4.54 (s, 1H), 4.98 (s, 1H), 5.10 (d, J = 5.9 Hz, 1H), 12.83 (s, 1H). ^{13}C NMR (DMSO, 100 MHz, 298 K): δ = 171.29, 111.56, 108.16, 83.67, 82.68, 81.65, 54.58, 26.15, 24.61. Yield = 28%.

1.5 Time dependence of the catalytic dehydrogenation of n-hexanol to hexanoate.

An oven-dried Schlenk tube was charged with catalyst **4** (35.5 mg, 0.06 mmol), NaOH (120 mg, 3 mmol), 1-hexanol (2 mmol), internal standard 1,3,5-trioxane (0.66 mmol), and D_2O (3 mL). The reaction mixture was heated to reflux. The progress of the reaction was monitored by NMR spectroscopy.



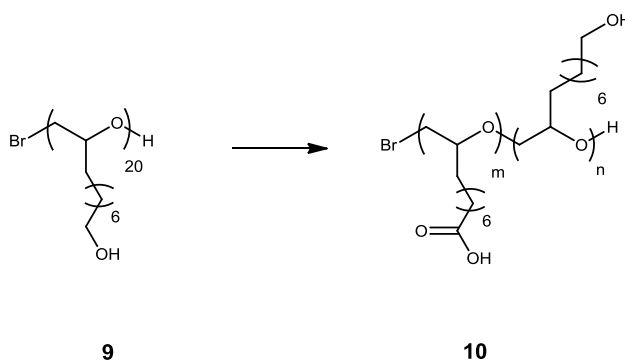
1.6 Synthesis of Poly (1,2- oxiranyl-8-octanol) **9**:



An oven-dried Schlenk tube was charged with (1-(8-(2-oxiranyl)octyloxy)-1-ethoxyethane)^[S3] (2.443 g, 5 mmol) and dissolved in dry toluene (10 mL). After the addition of NBu_4Br (0.166 g, 0.5 mmol) the reaction mixture was cooled to 0 °C in an ice bath and a 1.1M toluene solution of $\text{Al}(i\text{-Bu})_3$ (1 mL, 1 mmol) was added. The mixture was stirred at room temperature for 12h after which it was quenched with ethanol (1mL). For work-up the solvents were removed in vacuo, the residue was redissolved in dichloromethane (50mL) and washed with 20% aqueous NaOH (50mL x 3). The organic phase was dried over Na_2SO_4 and concentrated in vacuo to give the acetal protected polymer as a viscous oil. Yield: 2.3 g (98%). ^1H NMR (CDCl_3 , 400 MHz, 298 K): δ = 4.6 (q, J = 5.3, 1H), 3.31-3.68 (m, 7H), 1.47-1.50 (m, 2H), 1.21-1.28 (m, 15H). 1.13 (t, J = 7.1, 3H). ^{13}C NMR (CDCl_3 , 100 MHz, 298 K): δ = 99.5, 65.26, 60.61, 32.16, 29.96, 29.91, 29.73, 29.61, 29.49, 26.32, 26.28, 19.88, 15.34. M_n = 4,600 g/mol, M_w/M_n = 1.22. The obtained acetal protected polymer was dissolved in dry THF (50 mL) and treated with 0.5 mL of aqueous HCl (32%). The reaction was stirred for 30 min at room temperature, and the

polymer **9** was obtained as a white solid. The solvent was decanted, and the residue was washed twice with THF. After being dried in a vacuum at 40 °C overnight, the polymer **9** was isolated in a yield of 1.53 g (81%). ¹H NMR (DMSO, 400 MHz, 298 K): δ = 4.32 (t, J = 5.0, 1H), 3.5 (bm, 1H), 3.28-3.38 (m, 4H), 1.37-1.39 (m, 4H), 1.23 (bs, 10H). ¹³C NMR (DMSO, 100 MHz, 298 K): δ = 78.68, 78.54, 60.73, 32.61, 31.57, 29.34, 29.14, 25.61, 24.90. IR (cm⁻¹) = 3322, 2923, 2851, 1466, 1135, 1059. M_n = 4,200 g/mol, M_w/M_n = 1.16.

1.7 Synthesis of poly (1,2-oxiranyl-8-octanol- ω -1,2-oxiranyl- ω -carboxylic acid) **10**:



An oven-dried Schlenk tube was charged with polymer **9** (0.172 g, 1 mmol repeating unit), NaOH (60 mg, 1.5 mmol), complex **4** (14.6 mg, 0.03 mmol) and DMSO (1 mL). After complete dissolution of the reaction mixture water (1 mL) was added. The reaction mixture was heated to 120 °C for 48h and cooled to room temperature. All the volatiles were removed under vacuum and the product obtained was washed with diethyl ether leading to the carboxylic acid salts in quantitative yields. The carboxylic acid salts were further neutralized with 3N HCl and converted to the carboxylic acid **10**. Yield: 0.158 g (92%). ¹H NMR (DMSO, 600 MHz, 298 K): δ = 11.93 (s, 1H), 3.50 (bs, 2H), 3.34 (bs, 1H), 2.12 (t, J = 7.1, 1H), 1.46 (m, 2H), 1.38 (m, 2H), 1.23-1.35 (bs, 8H). ¹³C NMR (DMSO, 100 MHz, 298 K): δ = 174.82, 79.09, 61.22, 34.13, 33.07, 32.02, 29.70, 29.17, 26.07, 25.36, 25.01. IR (cm⁻¹) = 3301, 2923, 2851, 1708, 1463, 1102, 1057. GPC was not obtained due to the limited solubility of the polymer.

1.8 Mercury Poisoning Test:

An oven-dried Schlenk tube was charged catalyst **4**, (35.5 mg, 0.06 mmol), NaOH (120 mg, 3 mmol), 1-hexanol (204 mg, 2 mmol), internal standard 1,3,5-trioxane (59.9 mg, 0.66 mmol), mercury (6g, 30 mmol, 500 equivalents with respect to the ruthenium complex), and D₂O (3 mL). The reaction mixture was heated to reflux for 18h. The formation of hexanoate was determined by NMR spectroscopy. A 56% conversion of 1-hexanol was observed after 18h.

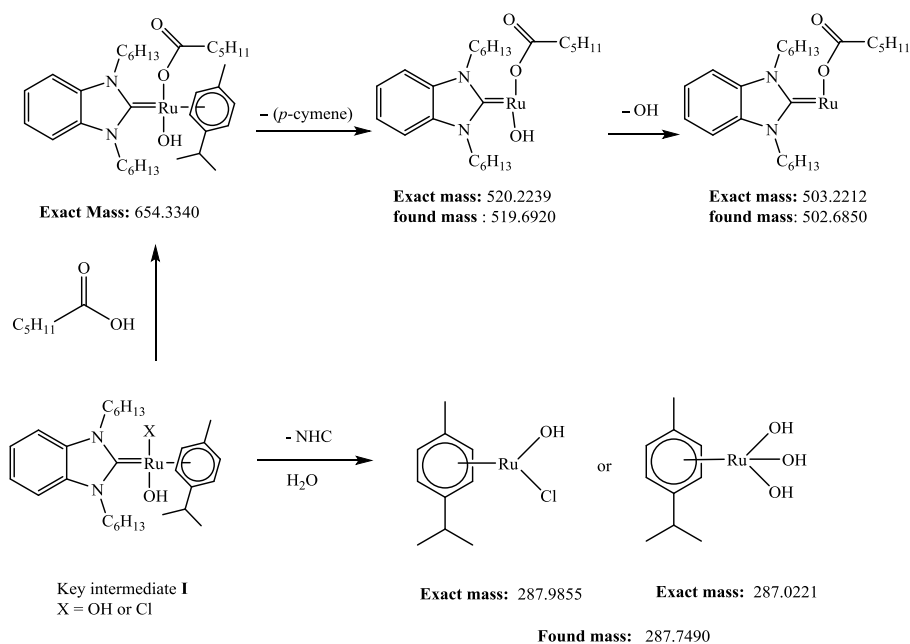
1.9 Detection of molecular hydrogen:

In order to detect the molecular hydrogen formed during reaction the following experiment was performed: A Schlenk tube was charged with catalyst **4** (592.6 mg, 1 mmol), NaOH (600mg, 15 mmol), 1-hexanol (2.02 g, 10 mmol), and water (15 mL). A second Schlenk tube was charged with 1 mol% of catalyst **4** (5.9 mg, 0.01 mmol), KO^tBu (10 mg, 0.09 mmo), 1-(chloromethyl)-4-vinylbenzene (152mg, 1 mmol), and dry toluene (2 mL). The gas

phases of the two Schlenk tubes were connected through a cannula. Then the first Schlenk tube was heated to 100°C, the second to 110 °C. During the catalytic cycle the molecular hydrogen generated in the first tube was transferred to the second Schlenk tube via the cannula. In the presence of hydrogen, the double bond of the substrate was hydrogenated leading to 1-(chloromethyl)-4-ethylbenzene. The obtained hydrogenated product was identified by NMR and GC-MS spectroscopy. From these results the formation of molecular hydrogen during the dehydrogenation of alcohols was proven. (In a blind experiment we could show that no 1-(chloromethyl)-4-ethylbenzene is formed if tube 1 and tube 2 are not connected.)

2.0 Reactivity of complex **4** with 1-hexanol under catalytic conditions without base:

In order to investigate the key intermediates, catalyst **4** (296 mg, 0.5 mmol), was added to a Schlenk flask and 2 mL of H₂O and hexanol (101 mg, 0.5 mmol) were subsequently introduced. The reaction flask was sealed under nitrogen and the contents were refluxed for 24 hrs. Then the reaction mixture was analyzed by ESI-MS spectroscopy. According to the ESI-MS spectrum the main peak belongs to [Ru-(*p*-cymene)(OH)(Cl)] or [Ru-(*p*-cymene)(OH)₃] which results from the key intermediate I. On the other hand key intermediate I could react with the resulting acid yielding [NHC-Ru-(*p*-cymene)(OH)(C₅H₁₁COO)], which in the ESI-MS loses the *p*-cymene ligand yielding [NHC-Ru-(OH)(C₅H₁₁COO)], with a mass of 519.692. This loses the hydroxide ligand yielding [NHC-Ru-(C₅H₁₁COO)], with a mass of 502.685.



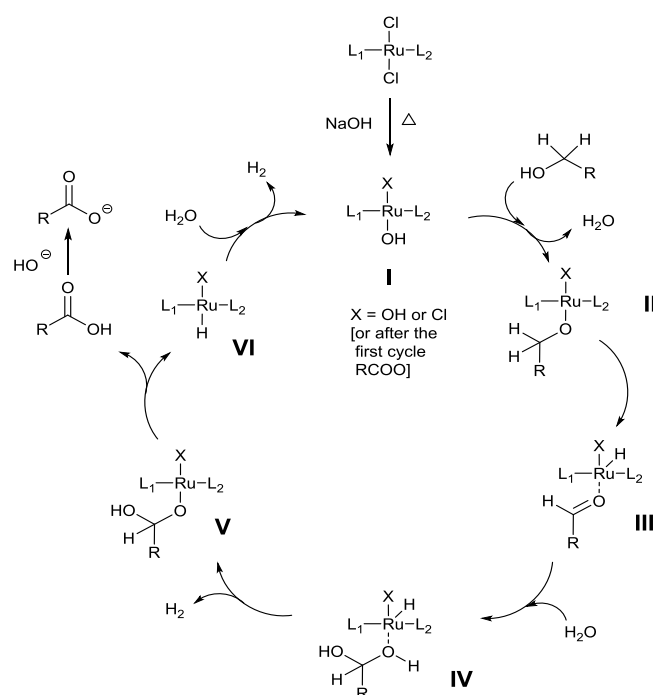
2.1 Dehydrogenative oxidation experiment using ¹⁸O₂:

An oven-dried Schlenk tube was charged with complex **4** (14.8 mg, 0.025 mmol), Na¹⁶OH (30 mg, 0.75 mmol), 3-phenylproanol (68 mg, 0.5 mmol) and ¹⁸O-water (0.9 mL). The reaction mixture was subjected to three times freeze-pump-thaw cycles and filled with nitrogen. The resultant reaction mixture was heated to reflux for 24h and cooled to room temperature. The reaction mixture was washed with diethyl ether to extract the catalyst and alcohol residues. The solvent was distilled off under reduce temperature and dried

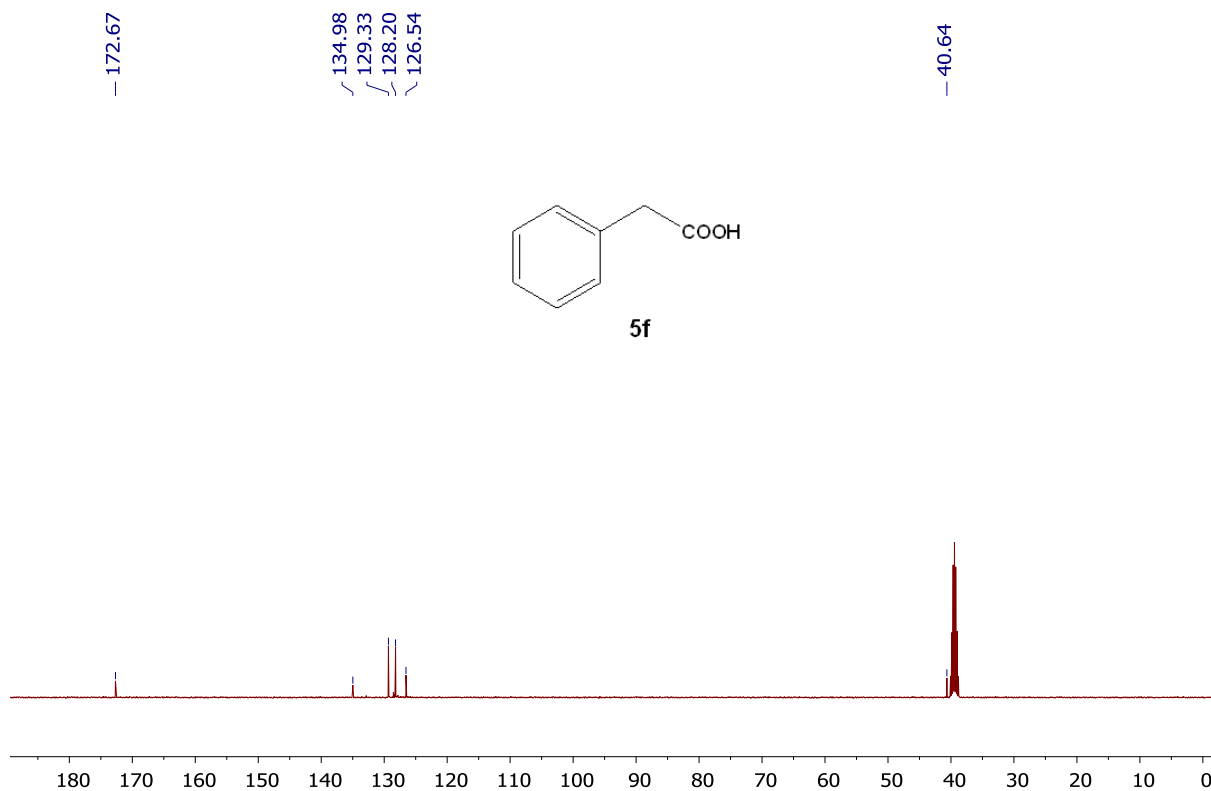
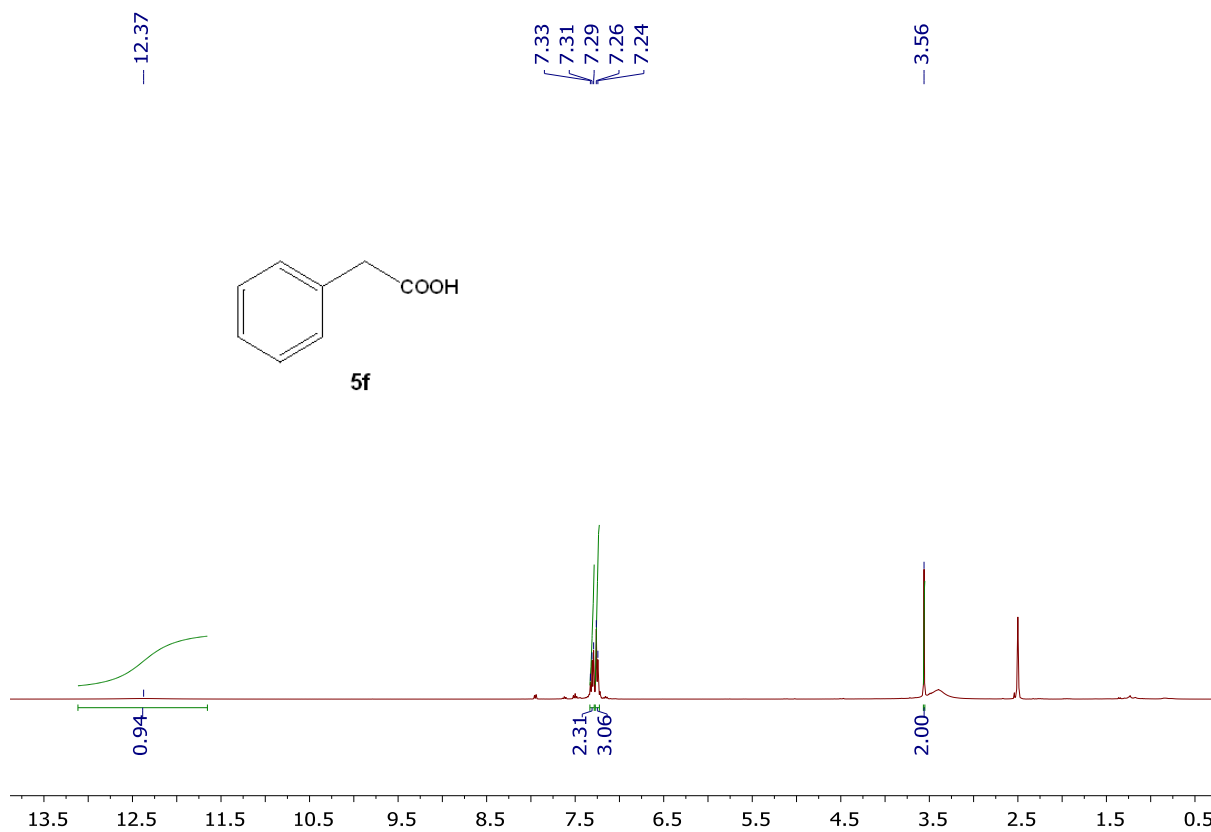
under vacuum. The crude reaction mixture was taken for analysis directly without any further workup. ^1H NMR (D_2O , 600 MHz, 298 K): $\delta = 7.36$ (t, $J = 7.6$, 2H), 7.30 (d, $J = 7.3$, 2H), 7.26 (t, $J = 7.2$, 1H), 2.88 (t, $J = 7.8$, 2H), 2.48 (t, $J = 7.8$, 2H). ^{13}C NMR (D_2O , 150 MHz, 298 K): $\delta = 182.597$, 142.093, 128.640, 128.309, 126.089, 39.210, 31.939. IR (cm^{-1}) = 3032, 2946, 1537, 1403, 961. ESI/MS: $\text{PhCH}_2\text{CH}_2\text{COO}(\text{Na})_2$ (MW 199). ^1H NMR, ^{13}C NMR, IR and ESI Mass Spectra of unlabeled and ^{18}O -labeled 3-phenyl propionic acid see chapter 2.3.

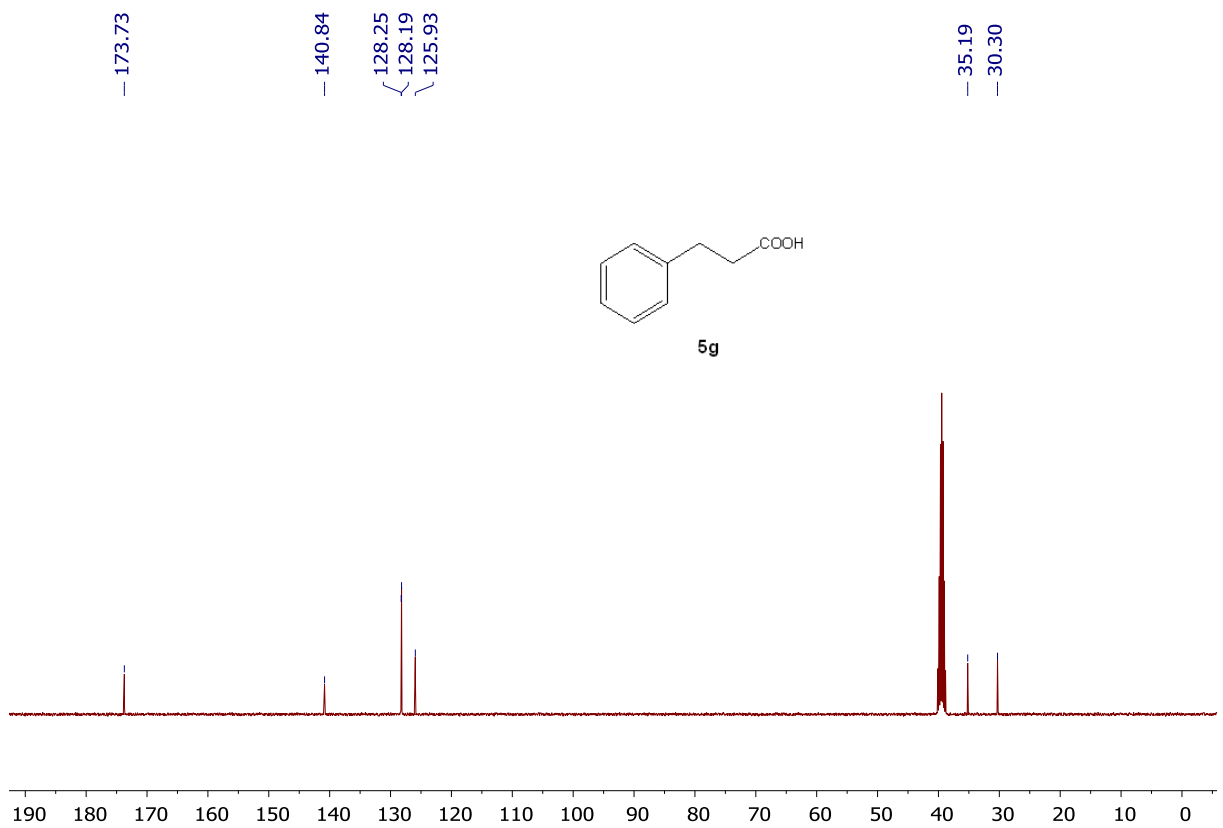
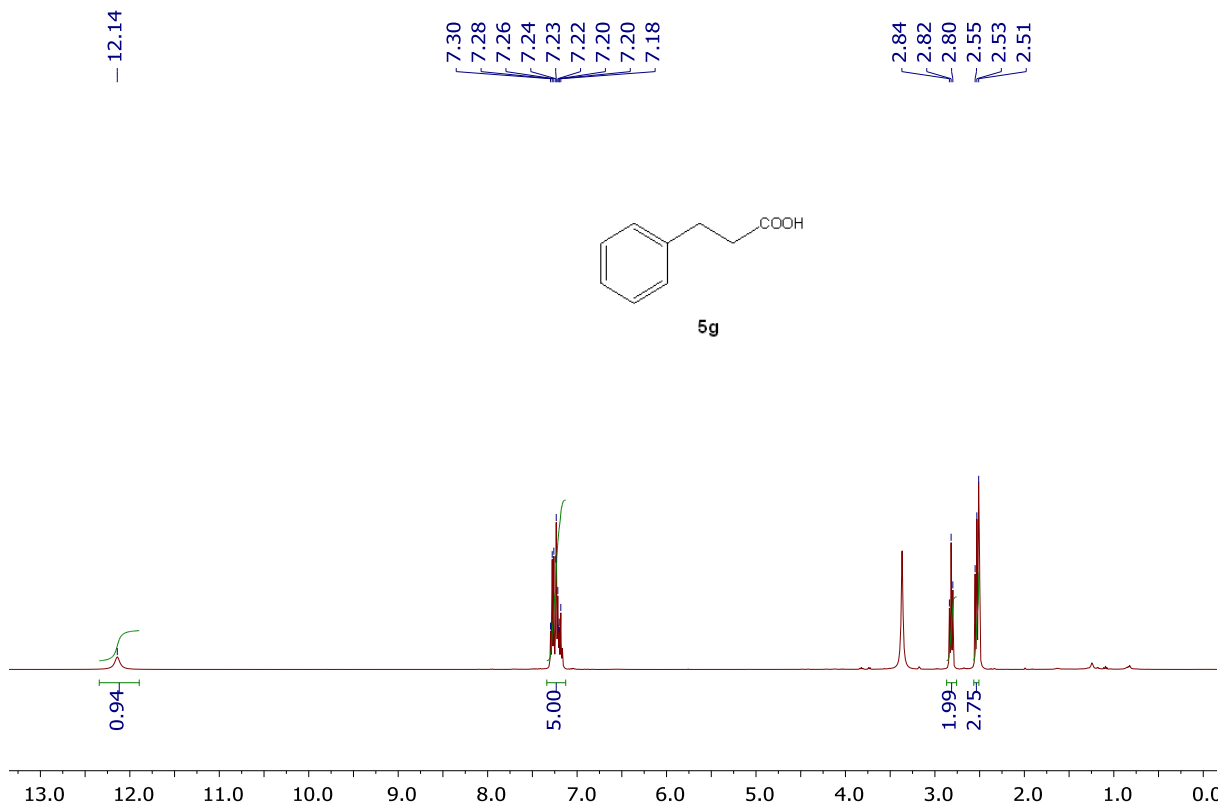
2.2 Proposed reaction mechanism.

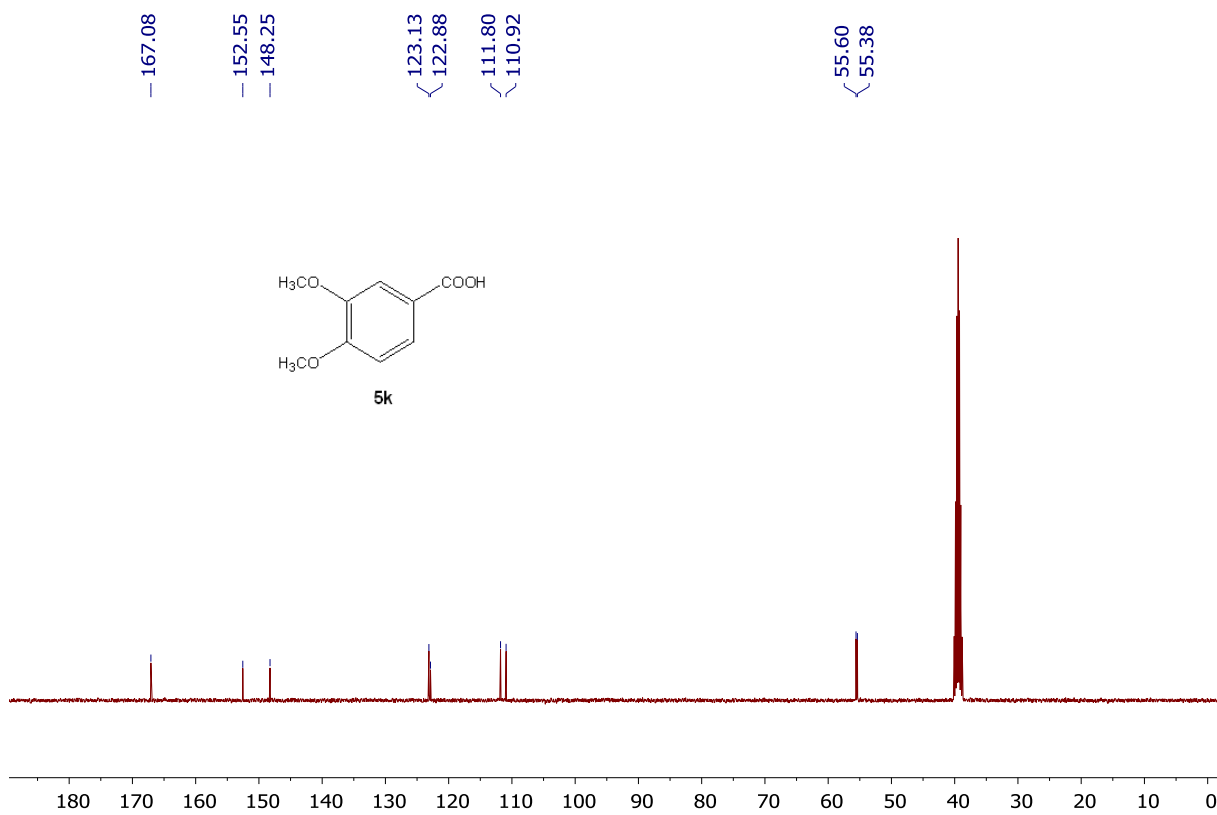
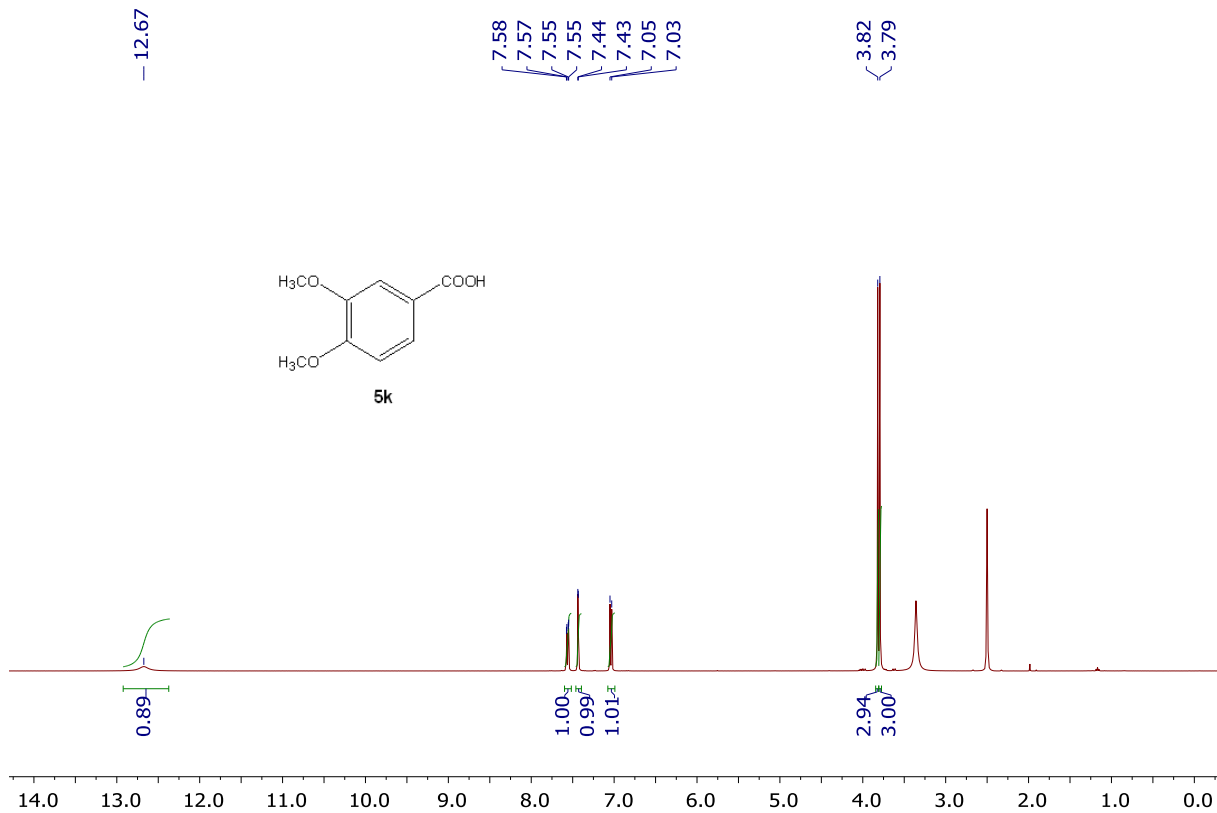
In the first step catalyst **4** is activated by replacement of the chloride ligand with hydroxide nucleophile. We are expecting that the ruthenium hydroxide complex **I** (NHC and *p*-cymene ligands are denoted as L_1 , L_2)²⁴ is the catalytically active species. The active catalyst further coordinates alcohol and liberates water generating complex **II**. Subsequently, transfer of hydride from the coordinated RCH_2O^- to the ruthenium occurs by β -hydride elimination and formation of an aldehyde complex **III**. The intermediate aldehyde complex **III** reacts with water to give a coordinated geminal-diolate complex **IV**. Combination of a proton with a hydride liberates molecular hydrogen with formation of complex **V**, from which by β -hydride transfer the ruthenium hydride complex **VI** is formed and the carboxylic acid is released. The hydride ruthenium complex **VI** reacts with water regenerating the active catalyst **I** and liberating second molecule of hydrogen. In this stage the formed acid can replace the ligand *x* by nucleophilic substitution. In non basic conditions this key intermediate was identified by ESI-MS (see SI chapter 2.0). Under alkaline conditions the carboxylate salt is formed.

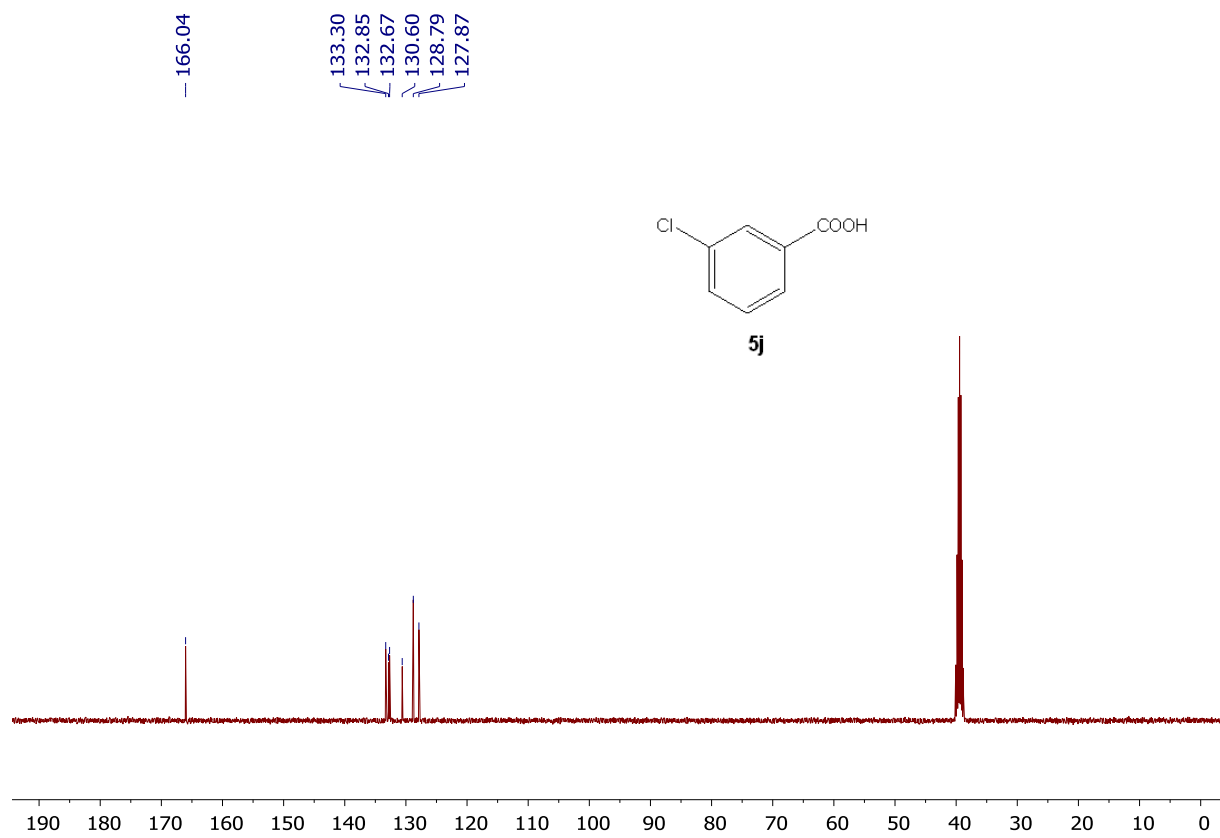
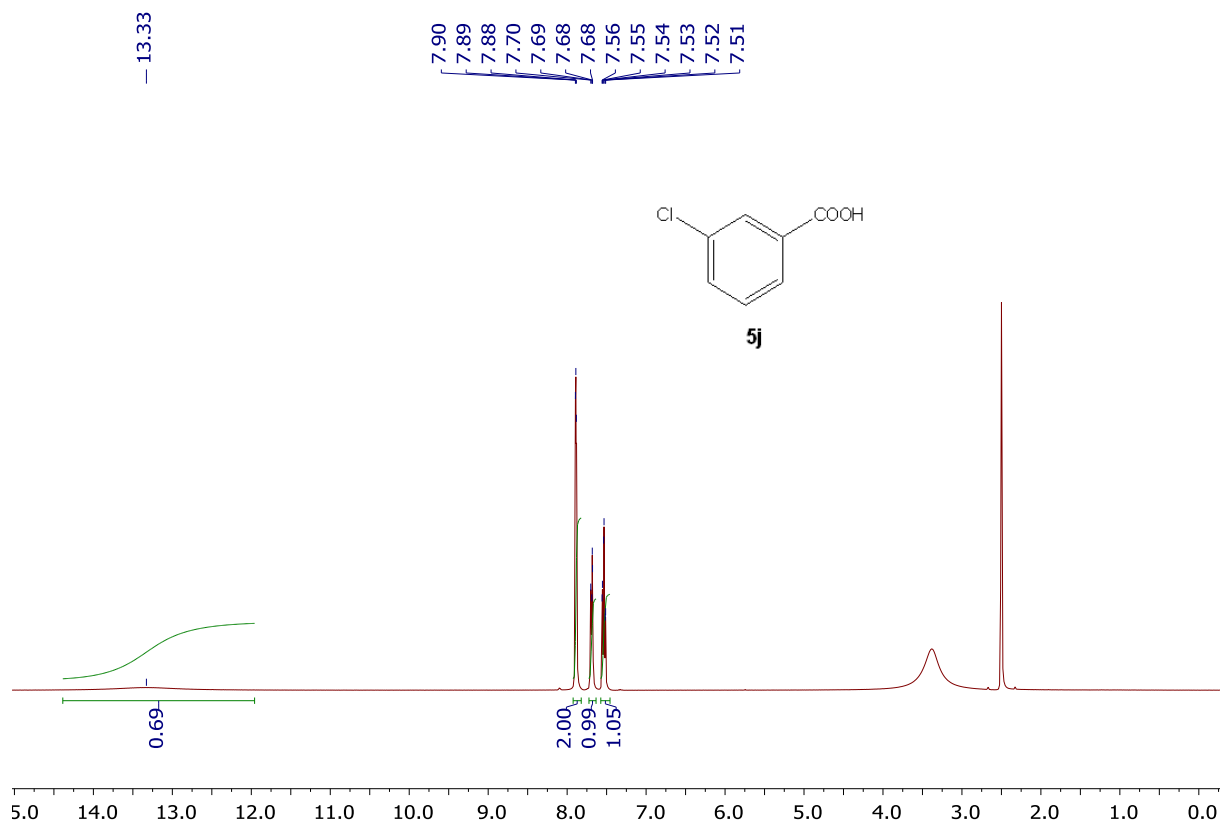


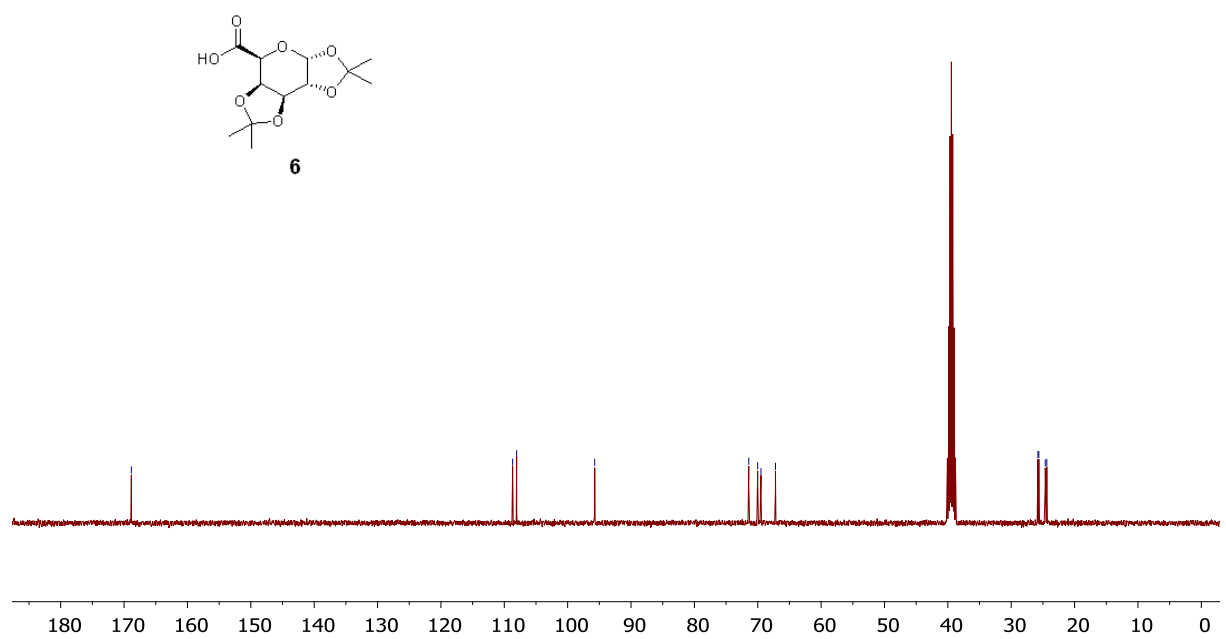
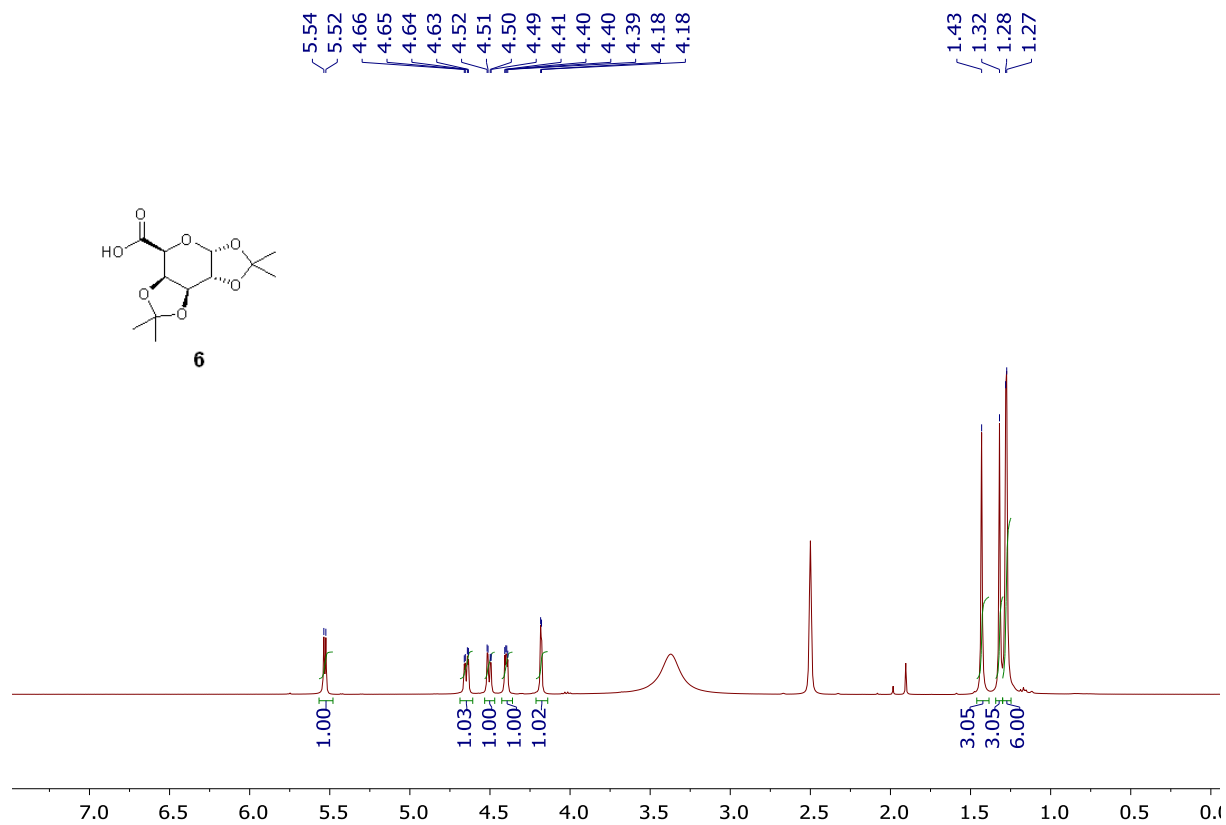
2.3 ^1H , ^{13}C NMR and IR Spectra of selected compounds prepared

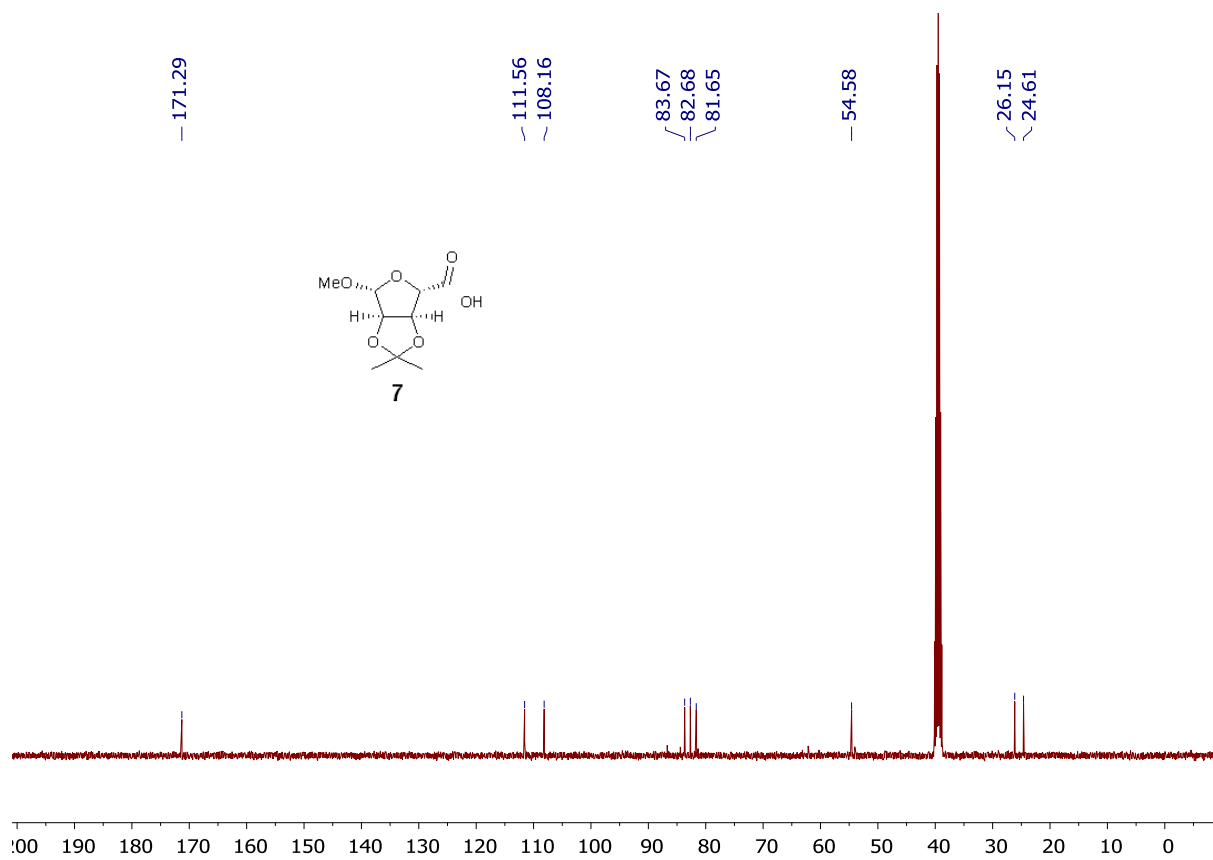
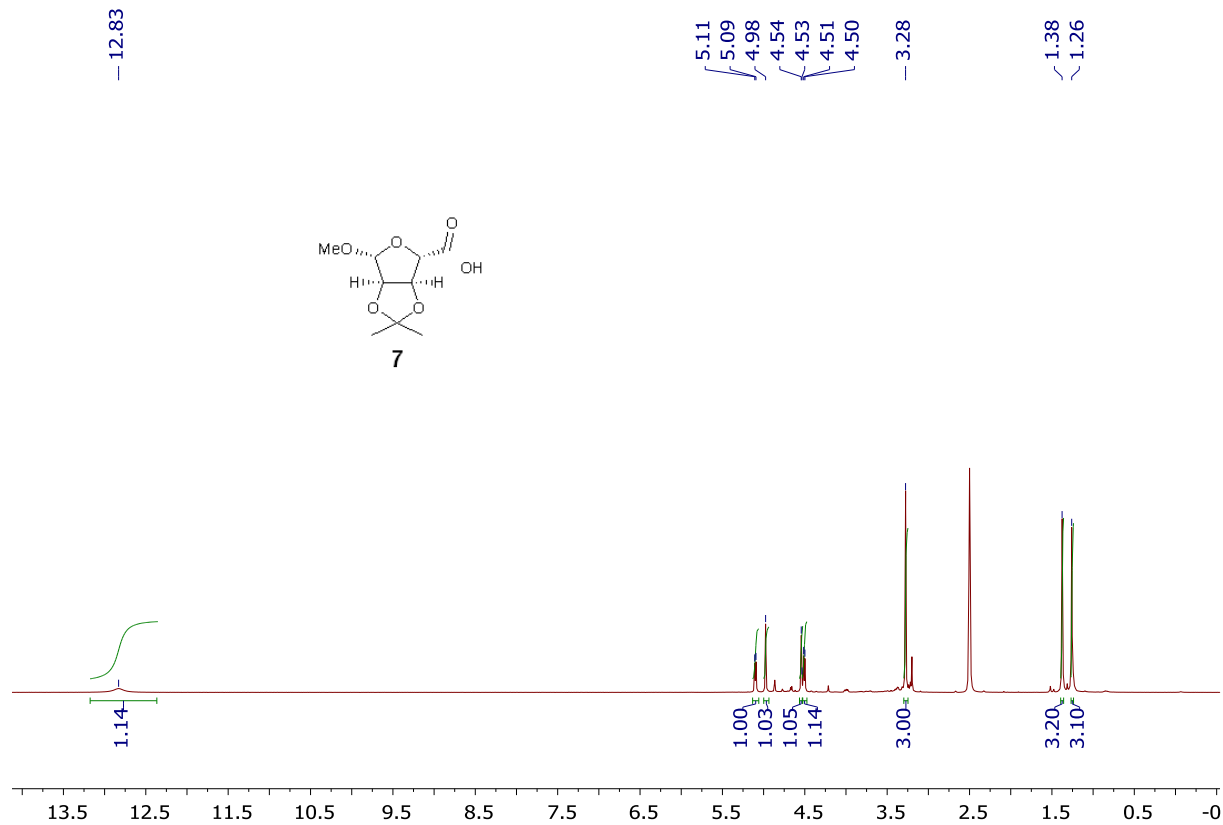


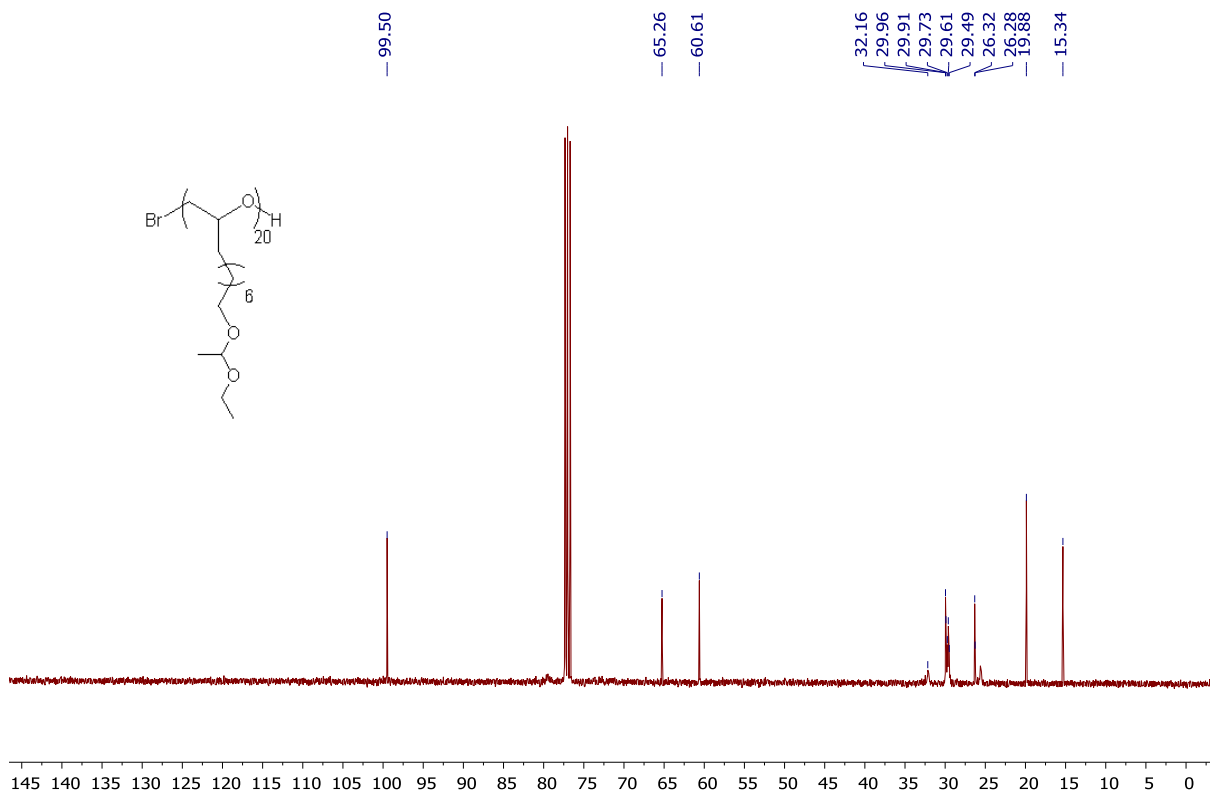
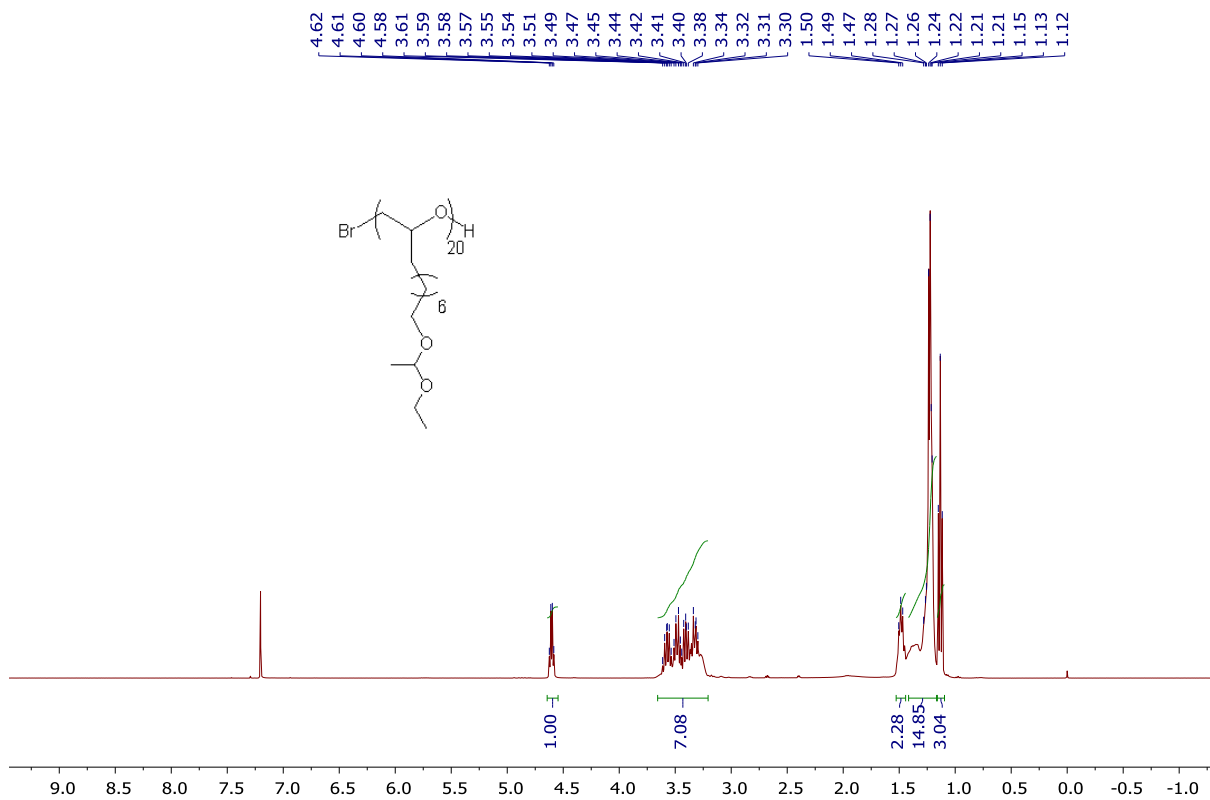


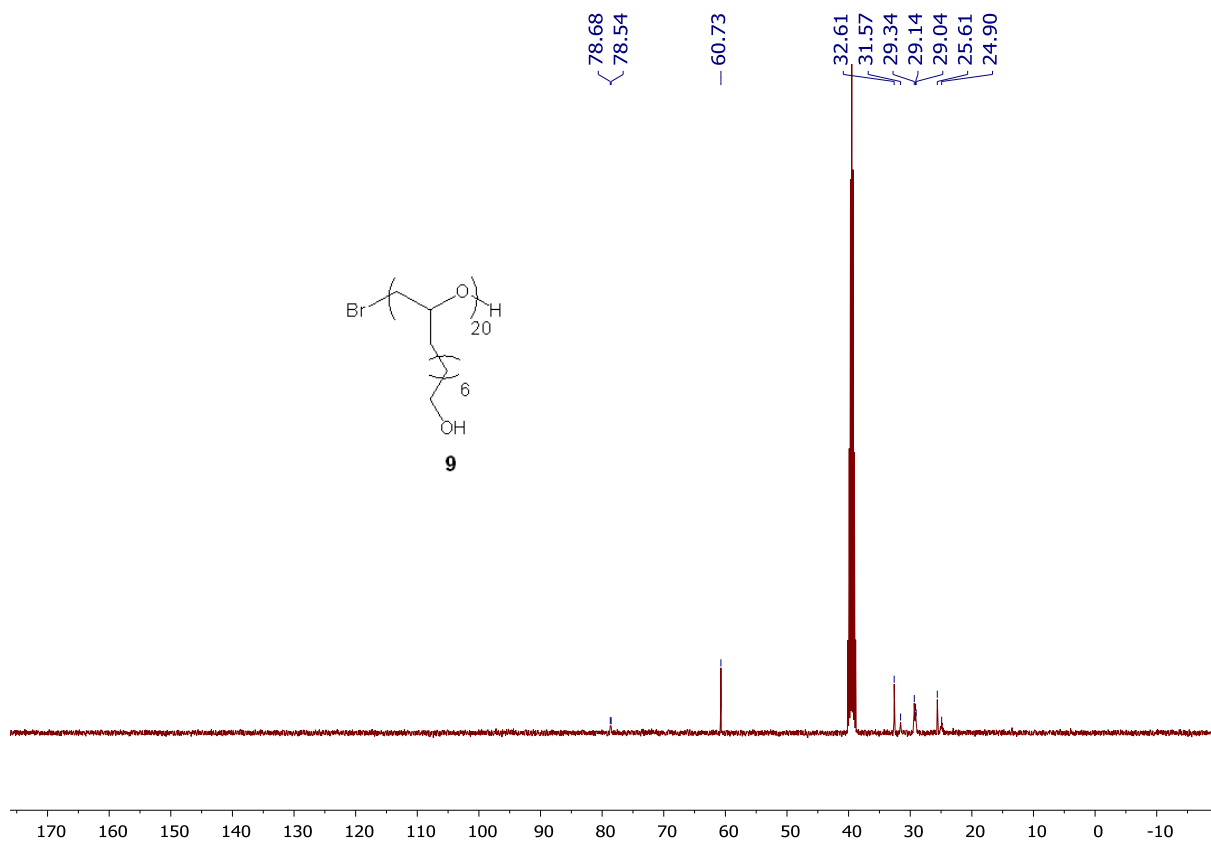
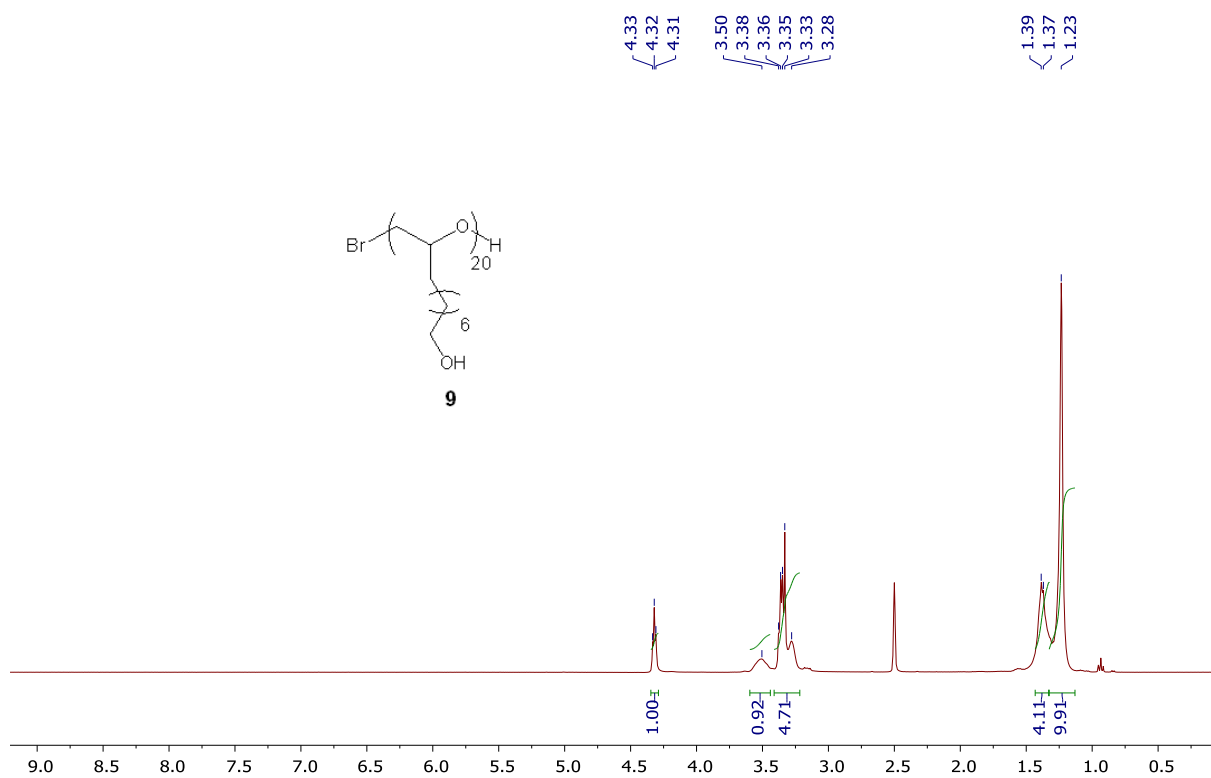


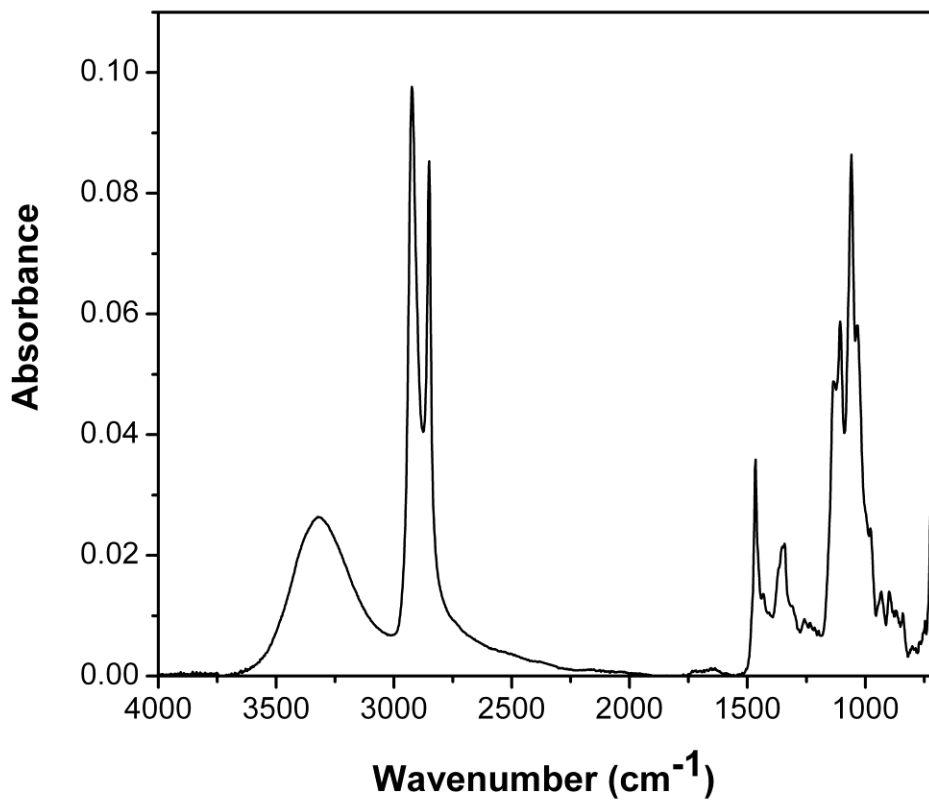




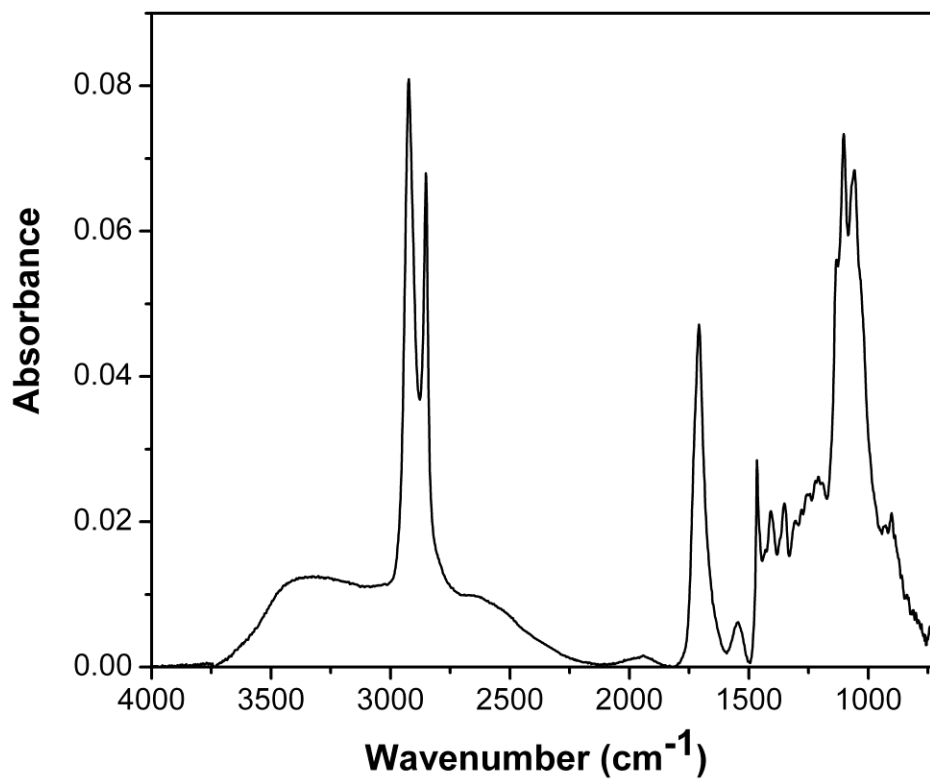






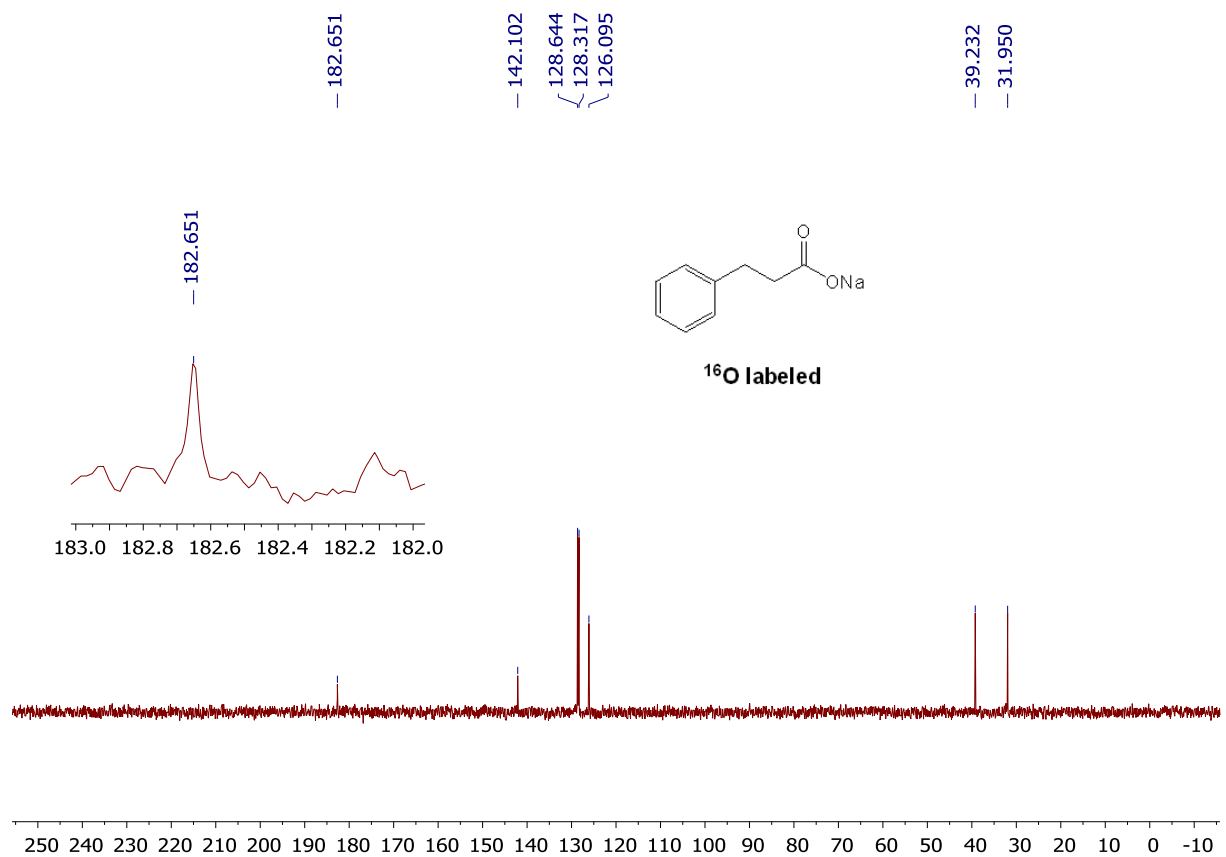
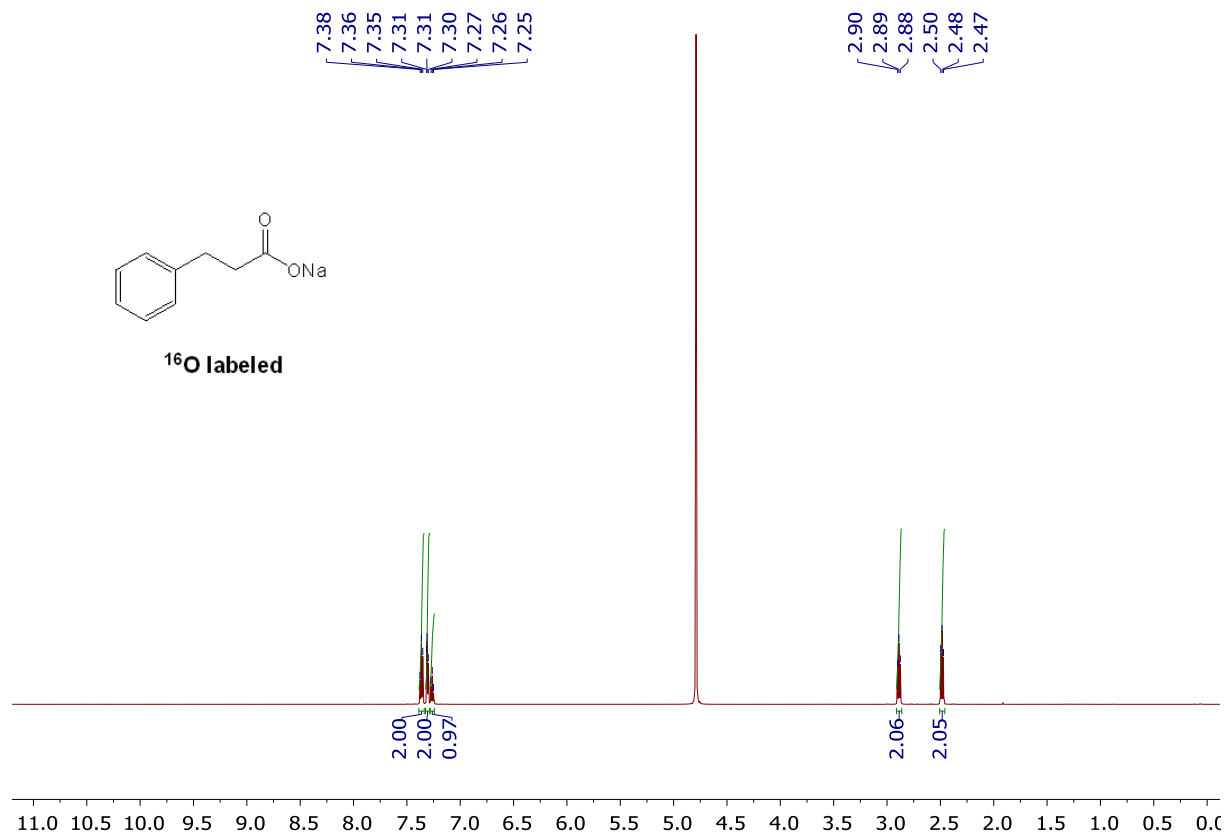


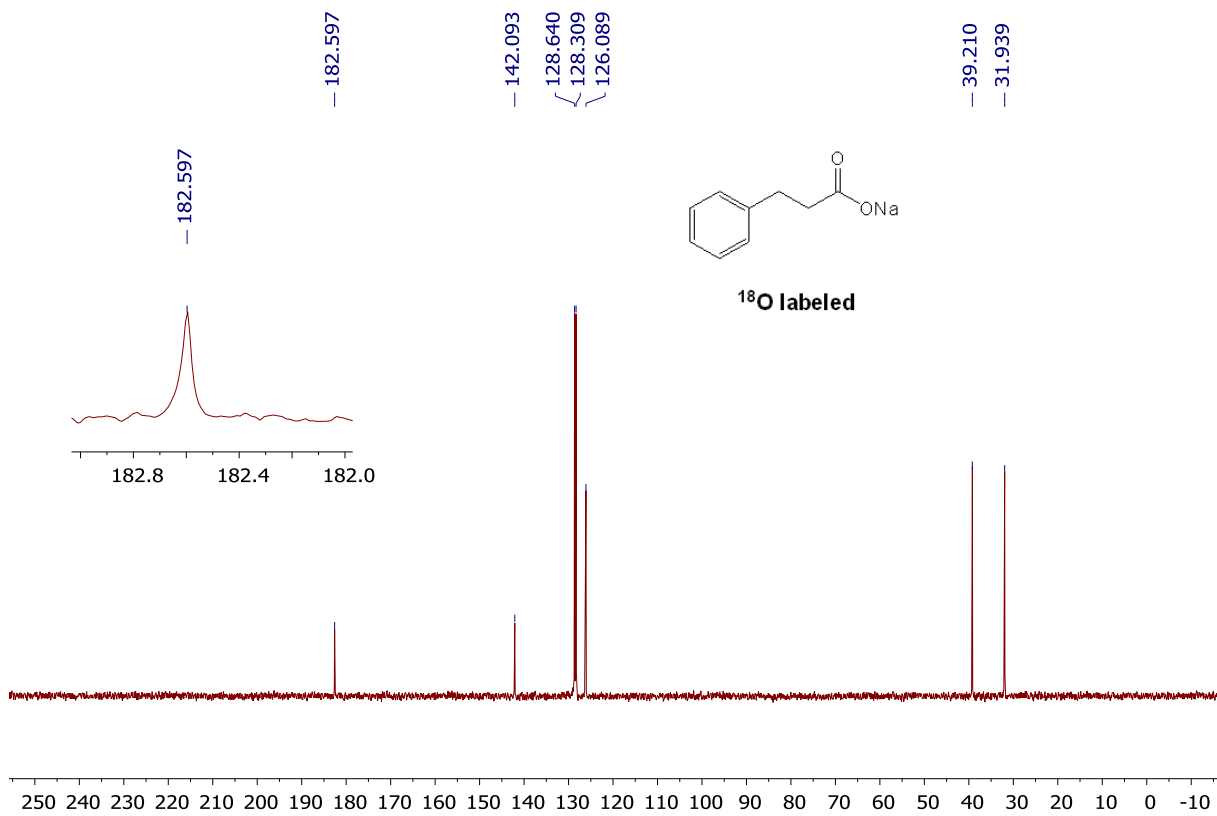
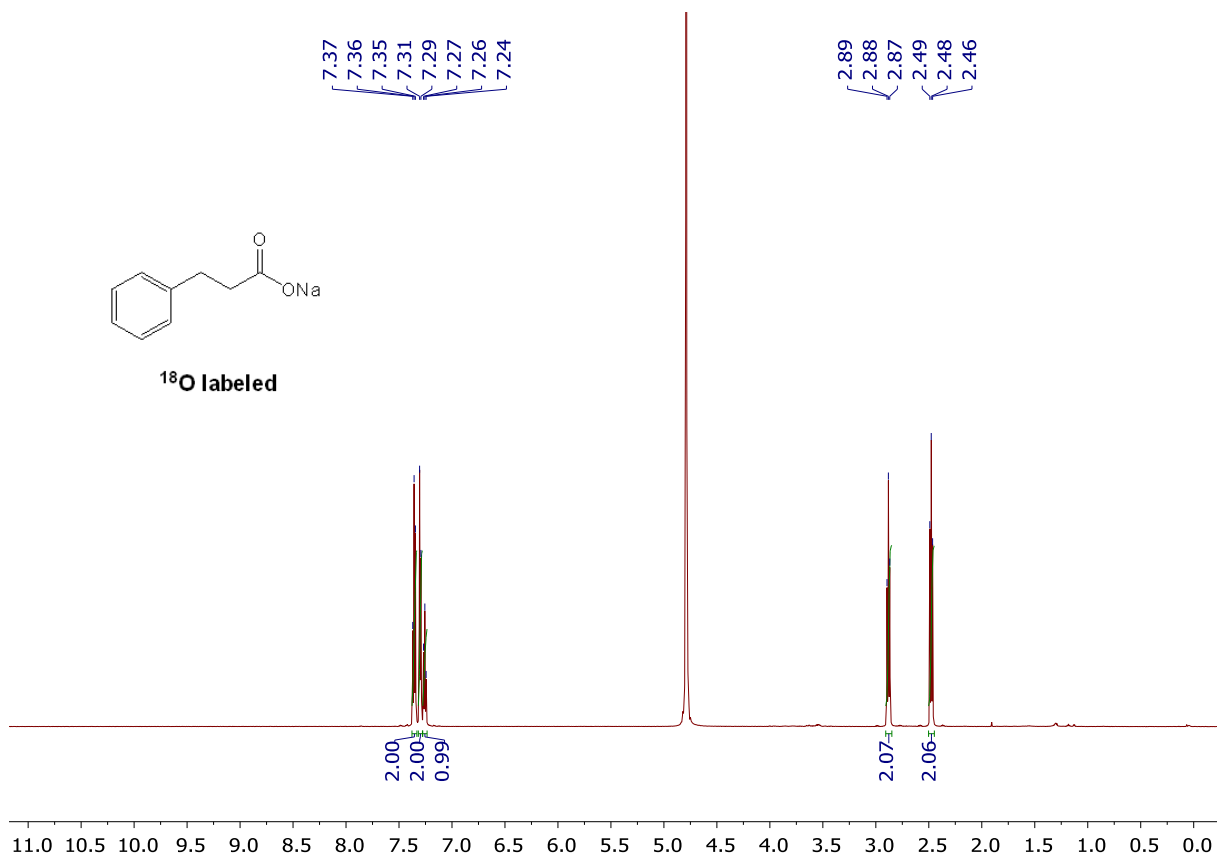
IR spectrum of Polymer **9**

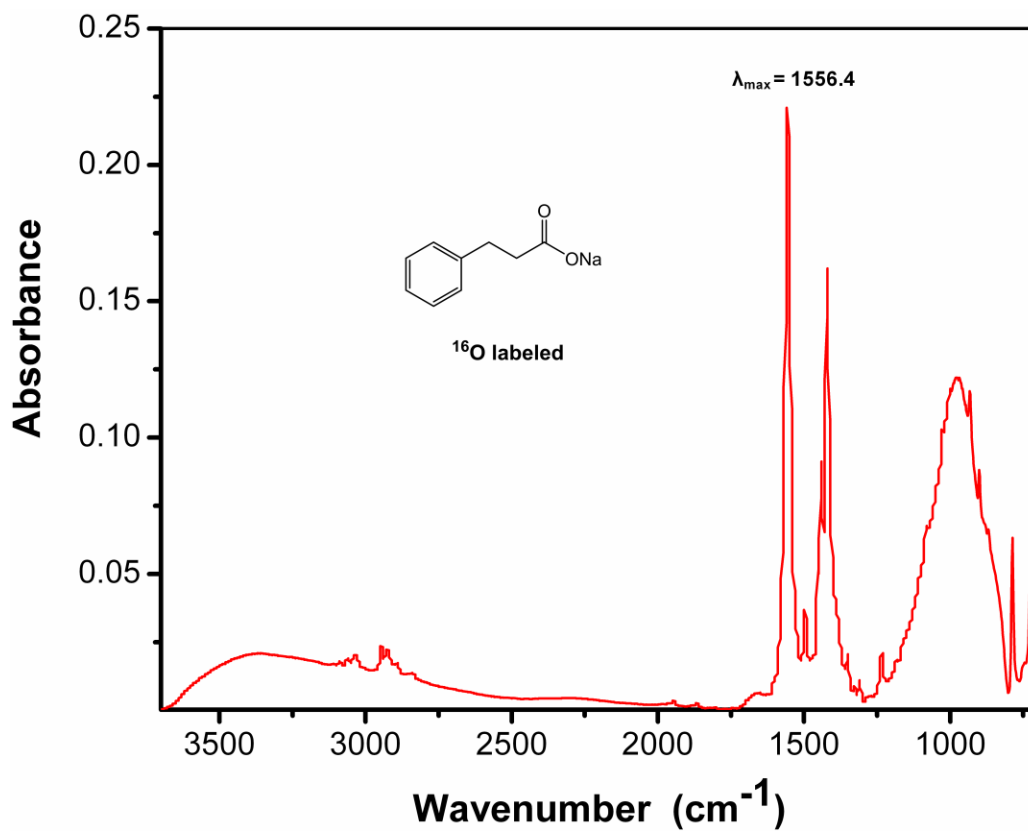


IR spectrum of Polymer **10**

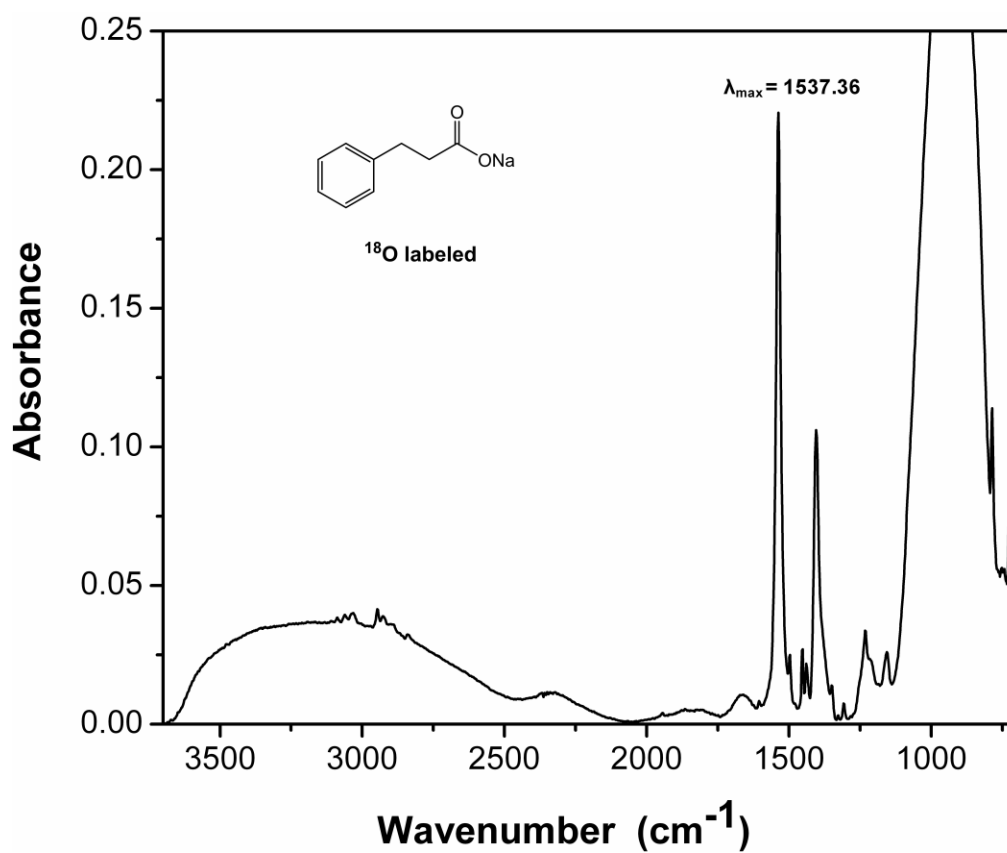
2.3 ^1H , ^{13}C NMR, IR and ESI Mass Spectra's of unlabeled and ^{18}O -labeled 3-phenyl propionic acid







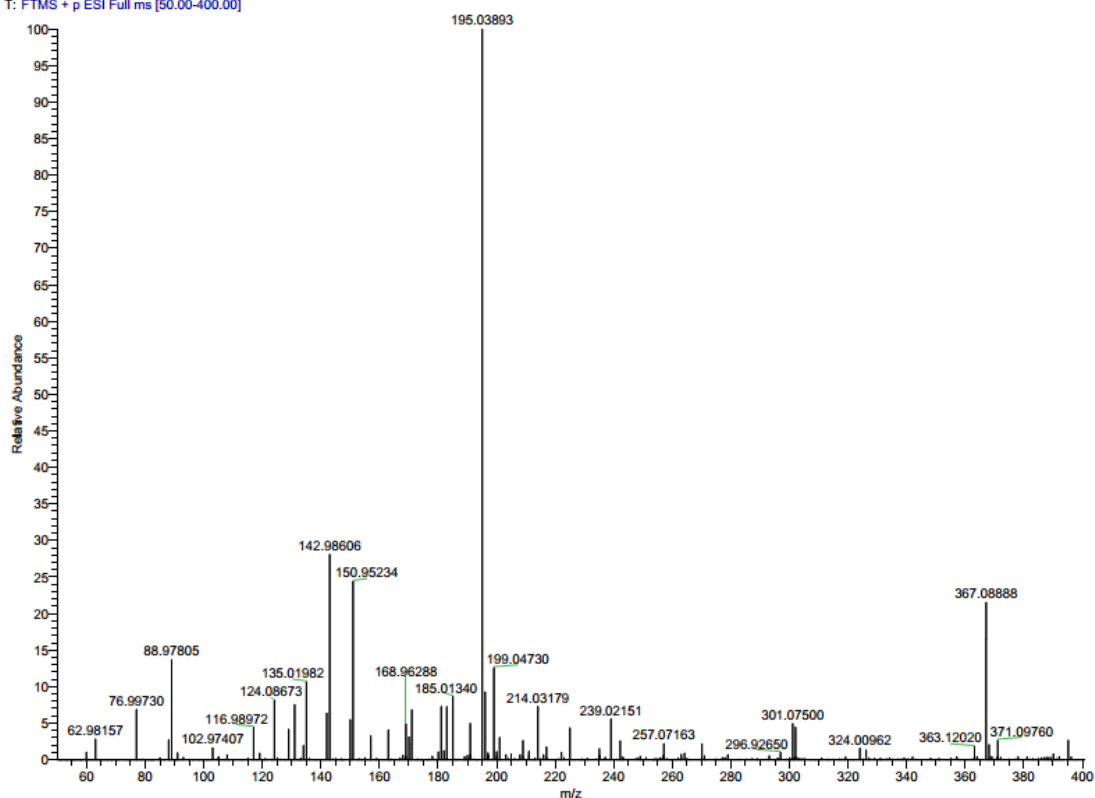
IR spectrum of unlabeled sodium salts of 3-phenylpropionic acid.



IR spectrum of ¹⁸O-labeled sodium salts of 3-phenylpropionic acid

LTO Orbitrap XL ke-ppa-16_150323114854

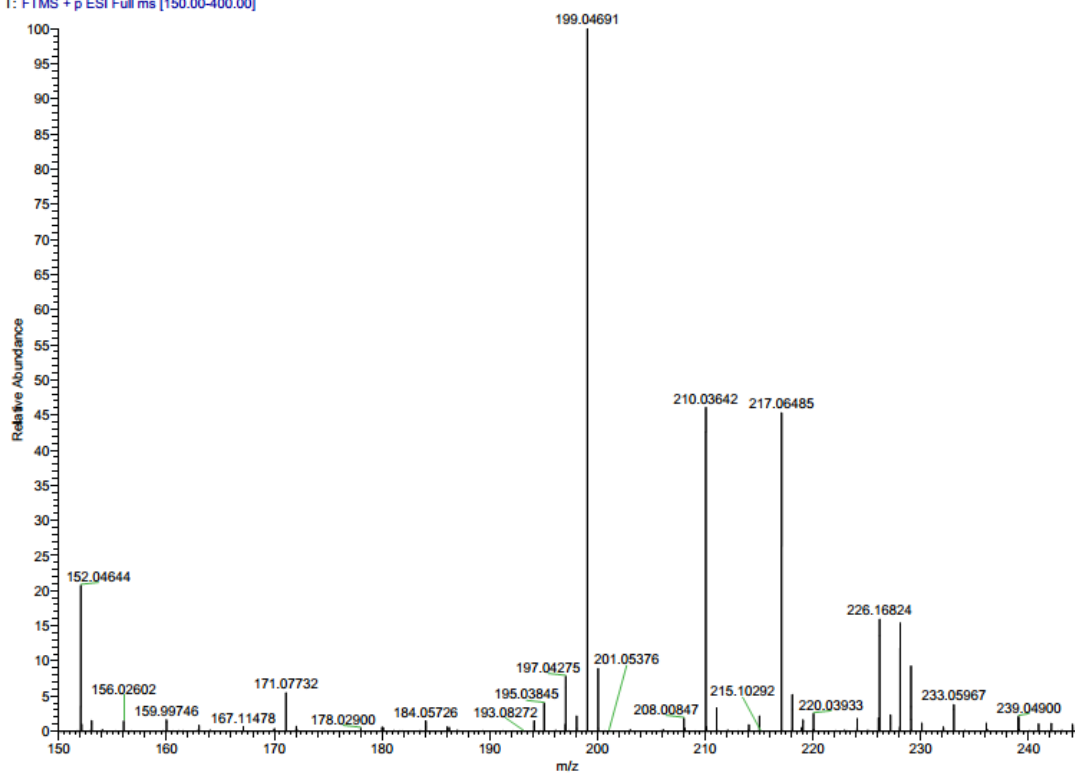
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ESI-MS spectra of unlabeled sodium salts of 3-phenylprionic acid.

LTO Orbitrap XL es ppa-18_150325113404

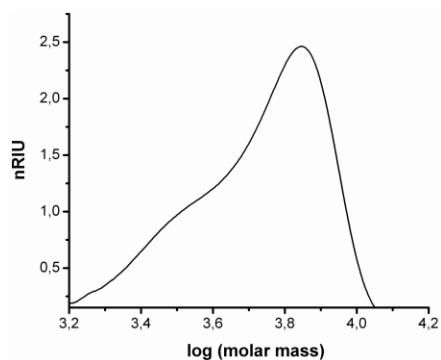
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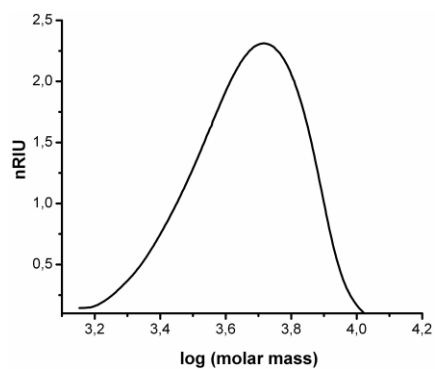
MS spectra of ¹⁸O-labeled sodium salts of 3-phenylprionic acid.

ESI-

3.0 Representative GPC traces of Polymers



Acetal protected polymer



Polymer 9

4.0 References

- [S1]. M. Gervais, A.-L. Brocas, G. Cendejas, A. Deffieux and S. Carlotti, *Macromolecules*, 2010, **43**, 1778.
- [S2]. J. Malineni, C. Merkens, H. Keul and M. Möller, *Catal. Commun.*, 2013, **40**, 80.
- [S3]. Y. Deng, R. G. Salomon, *J. Org. Chem.*, 2000, **65**, 6660.