

Renewable Pyridinium ionic Liquids from the continuous hydrothermal Decarboxylation of Furfural-Amino Acid derived Pyridinium Zwitterions

Sarah Kirchhecker^a, Steffen Tröger-Müller^a, Sebastian Bake^b, Markus Antonietti^a, Andreas Taubert^b and Davide Esposito^{*a}

^a: Max-Planck-Institute of Colloids and Interfaces, 14424 Potsdam, Germany

^b: University of Potsdam, Institute of Chemistry, D-14469 Potsdam, Germany

*Corresponding Author

E-Mail: davide.esposito@mpikg.mpg.de

Materials and Methods

All chemicals were used as supplied. The PMMA used had a MW of about 120,000 g/mol. ¹H- and ¹³C-NMR spectra were recorded on a Bruker Spectrospin 400 MHz Ultrashield Spectrometer in deuterated solvents, with chemical shifts referenced to the residual solvent signals unless otherwise stated. ESI - Mass Spectra were recorded on a Thermo Scientific Velos Pro LC-MS (linear ion trap). Infrared spectra of the synthesised compounds were recorded on a ThermoScientific Nicolet iS5 FT-IR spectrometer with an ATR attachment at a resolution of 4 cm⁻¹ and 16 scans. Differential scanning calorimetry of the ionic liquids was performed on a Mettler-Toledo DSC1 Stare System. The samples were preheated at 130 °C for 2h to evaporate off possible residual water, then cooled to -80 °C and heated to 100 °C at a rate of 10 K/min twice. Glass transition temperatures were determined as inflection points using Mettler Toledo STARe software V9.30. GC-MS analysis was performed using an Agilent Technologies 5975 gas chromatograph equipped with a MS detector and a capillary column (HP-5MS, 30 m, 0.25 mm, 0.25 micron). The temperature program started with an isothermal step at 50 °C for 2 min, the temperature was then increased to 300 °C with a rate of 30 °C/min and maintained for 1 min. Qualitative analysis was performed with MS library NIST 08 database with a retention index allowance of ± 100. Hydrothermal decarboxylation was performed on a ThalesNano X-Cube Flash flow reactor equipped with a Hastelloy reaction coil of 4 mL. DSC experiments on the ionogels were performed on a NDSC Netzsch 204 F1 Phoenix. Samples of about 10 mg were placed in aluminium pans with pierced lids. The samples were then cooled to -100 °C and heated to 150 °C at a rate of 10 K/min twice. Isothermal times were 20 min. IR spectra of ionogels were recorded on a Thermo Nicolet FT-IR Nexus 470 with an ATR attachment. Static contact angles were determined with a Cam100 contact angle meter (KSV Instruments Ltd., Finland) using 3.56 µL (3.56 ± 0.26 mg) of de-ionised water (Millipore®, resistance 18.2 mΩ, TOC 2 mg L⁻¹). Three samples were investigated using 4-5 repeats on every sample for both the ionogel and the PMMA films.

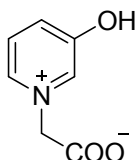
General procedure for the synthesis of the pyridinium zwitterions

The amino acid (40 mmol) was suspended in MeOH (30 mL) under stirring, and a solution of NaOH (1.6 g, 40 mmol) in MeOH (40 mL) was added slowly. The solvent was removed under reduced pressure and the residue was dissolved in a EtOH/ H₂O mixture (100 mL/ 4 mL). Furfural (3.412 mL, 40 mmol) was added and the solvent was slowly removed under reduced pressure at 50 °C using a rotary evaporator. The residue was freeze-dried to remove the residual water. All imines formed quantitatively as assessed by NMR of the residue after freeze-drying. The residue was dissolved in MeOH (80 mL). NaBH₄ (1.05 eq, 1.51 g) was slowly added under stirring at 0 °C. An aliquot was taken

and the yield of amine formation was determined by NMR using 2-methyl imidazole as the internal standard. After completion of the reduction, MeOH was removed under reduced pressure and the residue was redissolved in 3 M HCl (50 mL). Hydrogen peroxide (8 mL of 30 % aqueous solution, 2 eq) was added and the solution was stirred at 100 °C for 30 min using a reflux condenser. Then the solution was allowed to cool to room temperature. An aliquot was taken and the yield of pyridinium zwitterion was determined by NMR, again using 2-methyl imidazole as the internal standard. The acid was neutralised using concentrated NH₄OH and the reaction mixture was freeze-dried. The residue was dissolved in EtOH or alternatively acetic acid and filtered to yield the crude product. The pyridinium zwitterions were recrystallised from hot EtOH unless otherwise stated. Compounds with crystallisation yield below 40 % were recrystallised several times in order to accumulate products to be used during the hydrothermal decarboxylation

Pyridinium zwitterions

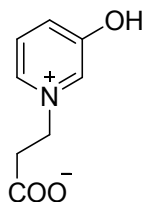
(3-pyridinol-1-ium)-acetate (1)



Yield amine (NMR): 98.0 %, yield pyridinium (NMR): 78.0 %

¹H NMR (400 MHz, D₂O) δ 8.30 (s, 1H) 8.25 (d, *J* = 5.9 Hz, 1H), 7.98 – 7.94 (m, 1H), 7.86 (m, 1H), 5.12 (s, 2H); ¹³C NMR (101 MHz, d₂o) δ 170.75, 156.34, 136.57, 133.43, 131.85, 128.07, 63.11; ESI-MS (*m/z*): [M+H]⁺ calcd. for C₇H₇NO₃: 154.05, found, 154.14; IR *v*_{max}/cm⁻¹ = 3027 (C-H), 1627 (C=O), 1489 (C=C ar), 1317 (C-O), 1210; Elemental analysis: (calcd., found for C₇H₇NO₃): C, 54.90, 54.46; H, 4.61, 4.53; N, 9.15, 8.95

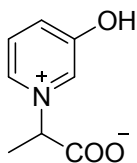
3-(3-pyridinol-1-ium)-propanoate (2)



Yield amine (NMR) = 93.0 %, yield pyridinium (NMR) 71.9 %

¹H NMR (400 MHz, D₂O) δ 8.35 – 8.29 (m, 2H), 7.90 – 7.77 (m, 2H), 4.70 (t, *J* = 6.6 Hz, 2H), 2.91 (t, *J* = 6.6 Hz, 2H); ¹³C NMR (101 MHz, D₂O) δ 176.67, 157.76, 134.85, 132.72, 132.17, 128.24, 58.39, 37.72; ESI-MS (*m/z*): [M+H]⁺ calcd. for C₈H₉NO₃: 168.07, found, 168.14; IR *v*_{max}/cm⁻¹ = 3073 (C-H), 1729 (C=O), 1585 (C=C ar), 1313 (C-O), 1035; Elemental analysis: (calcd., found for C₈H₉NO₃): C, 57.48, 55.11; H, 5.43, 5.23; N, 8.38, 7.84

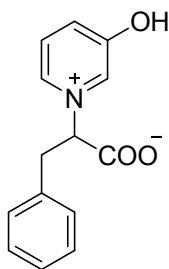
2-(3-pyridinol-1-ium)-propanoate (3)



Yield amine (NMR): 98.5 %, yield pyridinium (NMR): 93.8 %

^1H NMR (400 MHz, D_2O) δ 7.82 (td, $J = 4.7, 1.7$ Hz, 2H), 7.57 – 7.45 (m, 2H), 5.05 (q, $J = 7.3$ Hz, 1H), 1.77 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR (101 MHz, D_2O) δ 174.37, 164.43, 133.58, 133.13, 128.91, 127.30, 70.20, 17.75; ESI-MS (m/z): $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_8\text{H}_9\text{NO}_3$: 168.07, found, 168.16; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3061$ (C-H), 1615 (C=O), 1569 (C=C ar), 1489, 1322 (C-O); Elemental analysis: (calcd., found for $\text{C}_8\text{H}_9\text{NO}_3$): C, 57.48, 56.99; H, 5.43, 5.24; N, 8.38, 8.20

3-phenyl-2-(3-pyridinol-1-ium)-propanoate (4)

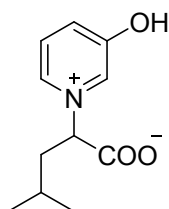


Yield amine (NMR): 58.5 %, pyridinium (NMR): 55.4 %, isolated yield: 47.7 %

Note: Upon addition of furfural to the phenylalanine salt formation of a foam is observed, which hinders homogeneous mixing. The crude pyridinium zwitterion was washed with a small amount of water, which afforded pure **4** as a white solid.

^1H NMR (400 MHz, D_2O) δ 8.14 – 8.10 (m, 2H), 7.77 – 7.74 (m, 1H), 7.65 (dd, $J = 8.9, 6.0$ Hz, 1H), 7.24 (td, $J = 6.3, 5.4, 3.1$ Hz, 3H), 7.13 – 7.10 (m, 2H), 5.35 (dd, $J = 11.5, 4.6$ Hz, 1H), 3.78 (dd, $J = 14.9, 4.5$ Hz, 1H), 3.42 – 3.36 (m, 1H); ^{13}C NMR (101 MHz, D_2O) δ 171.83, 156.72, 135.53, 135.41, 132.51, 132.30, 128.94, 128.59, 127.92, 127.38, 77.00, 38.73; ESI-MS (m/z): $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_3$: 244.10, found, 244.22; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3038$ (C-H), 1639 (C=O), 1600 (C=C ar), 1488, 1299 (C-O); Elemental analysis: (calcd., found for $\text{C}_{14}\text{H}_{13}\text{NO}_3$): C, 69.12, 69.04; H, 5.39, 5.30; N, 5.76, 5.77.

4-methyl-2-(3-pyridinol-1-ium)-pentanoate (5)



Yield amine (NMR) 100 %, yield pyridinium (NMR): 100 %, crystallisation yield: 41.3 %

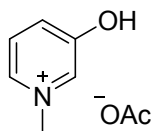
^1H NMR (400 MHz, D_2O) δ 8.32 – 8.27 (m, 2H), 7.77 – 7.70 (m, 2H), 5.02 (dd, $J = 10.4, 5.2$ Hz, 1H), 2.21 – 2.06 (m, 2H), 1.31 – 1.22 (m, 1H), 0.93 (d, $J = 6.6$ Hz, 3H), 0.87 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (101 MHz, D_2O) δ 173.38, 157.86, 134.63, 132.58, 132.51, 128.17, 74.10, 40.66, 24.32, 22.19, 20.39; ESI-MS (m/z): $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{11}\text{H}_{15}\text{NO}_3$: 210.11, found, 210.10; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3069$ (C-H), 2962 (C-H), 1632 (C=O), 1498 (C=C ar), 1260 (C-O); Elemental analysis: (calcd., found for $\text{C}_{11}\text{H}_{15}\text{NO}_3$): C, 63.14, 62.23; H, 7.23, 7.35; N, 6.69, 6.44.

Pyridinium ILS

General procedure for the hydrothermal decarboxylation

An aqueous solutions of pyridinium zwitterions (5 mL, 0.1 M) containing acetic acid (2 eq) was injected into the X-cube Flash reactor (Thales Nano) and allowed to react at the optimised settings of 250 °C and 120 bar pressure for 4 min. The eluate was collected and diluted with water and washed 3 x with diethyl ether. The water phase was freeze-dried to yield the pure ionic liquids.

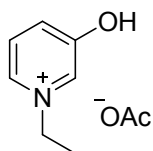
1-Methyl-3-hydroxy pyridinium acetate (6)



Yield: 68.8 %

^1H NMR (400 MHz, D_2O) δ 7.88 – 7.85 (m, 2H), 7.59 – 7.49 (m, 2H), 4.13 (s, 3H), 1.88 (s, 3H); ^{13}C NMR (101 MHz, D_2O) δ 179.75, 160.96, 134.03, 133.14, 132.32, 127.84, 47.63, 22.24; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3398$ (O-H), 3066 (C-H), 1691 (C=O), 1562 (C=C ar), 1025; Tg (DSC) = -13.0 °C.

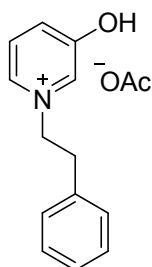
1-Ethyl-3-hydroxy-pyridinium acetate (7)



Yield: 91.0 %

^1H NMR (400 MHz, D_2O) δ 8.11 – 7.95 (m, 2H), 7.72 – 7.54 (m, 2H), 4.43 – 4.37 (m, 2H), 1.90 (s, 3H), 1.52 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (101 MHz, D_2O) δ 179.83, 161.13, 132.78, 132.44, 131.91, 128.07, 56.85, 22.36, 15.68; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3398$ (O-H), 3072 (C-H), 1700 (C=O), 1563 (C=C ar), 1249; Tg (DSC) = -18.9 °C

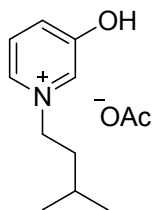
1-(2-phenyl-ethyl)-3-hydroxy-pyridinium acetate (8)



Yield: 81.0 %

^1H NMR (400 MHz, D_2O) δ 7.68 (dd, $J = 5.8, 3.9$ Hz, 2H), 7.53 – 7.43 (m, 2H), 7.29 – 7.22 (m, 3H), 7.04 (d, $J = 2.5$ Hz, 2H), 4.57 (t, $J = 6.6$ Hz, 2H), 3.18 (t, $J = 6.7$ Hz, 2H), 1.92 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 172.60, 167.83, 136.83, 133.80, 132.52, 128.81, 128.51, 126.87, 123.02, 60.46, 36.60, 21.73; ESI-MS (m/z): $[\text{M}]^+$ calcd. for $\text{C}_{13}\text{H}_{14}\text{NO}^+$: 200.11, found, 200.15; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3064$ (C-H), 1669 (C=O), 1507, 1163, 683; Elemental analysis: (calcd., found for $\text{C}_{15}\text{H}_{17}\text{NO}_3$): C, 69.48, 69.01; H, 6.61, 6.18; N, 5.40, 5.91; Tg (DSC) = -7.55 °C

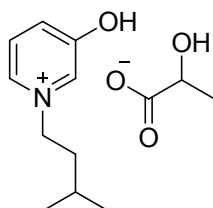
1-(3-methyl-butyl)-3-hydroxy-pyridinium acetate (9)



Yield: 80.7 %

^1H NMR (400 MHz, D_2O) δ 8.14 – 7.92 (m, 2H), 7.76 – 7.56 (m, 2H), 4.43 (t, $J = 7.7$ Hz, 2H), 1.95 (s, 3H), 1.86 (q, $J = 7.4$ Hz, 2H), 1.61 (dt, $J = 13.4, 6.7$ Hz, 1H), 0.95 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (101 MHz, D_2O) δ 179.48, 160.78, 133.09, 132.55, 132.38, 128.01, 60.04, 39.35, 24.85, 22.04, 21.29; ESI-MS (m/z): $[\text{M}]^+$ calcd. for $\text{C}_{12}\text{H}_{12}\text{NO}^+$: 166.12, found, 166.21; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3407$ (O-H), 3075 (C-H), 2961 (C-H), 1709 (C=O), 1562 (C=C ar), 1152; Elemental analysis: (calcd., found for $\text{C}_{12}\text{H}_{19}\text{NO}_3$): C, 63.98, 63.05; H, 8.50, 8.22; N, 6.22, 6.94; Tg (DSC) = -32.04 °C

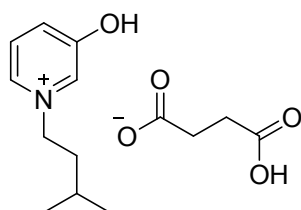
1-(3-methyl-butyl)-3-hydroxy-pyridinium lactate (10)



Yield: 84.0 %

^1H NMR (400 MHz, D_2O) δ 8.28 – 8.22 (m, 2H), 7.84 – 7.73 (m, 2H), 4.48 (t, $J = 7.7$ Hz, 2H), 4.15 (q, $J = 6.9$ Hz, 1H), 1.85 (q, $J = 7.4$ Hz, 2H), 1.59 (dt, $J = 13.5, 6.7$ Hz, 1H), 1.32 (d, $J = 6.9$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (101 MHz, D_2O) δ 180.29, 157.02, 135.34, 132.52, 131.61, 128.38, 67.29, 60.39, 39.33, 24.86, 21.28, 21.26, 19.57; ESI-MS (m/z): $[\text{M}]^+$ calcd. for $\text{C}_{12}\text{H}_{12}\text{NO}^+$: 166.12, found, 166.17; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3468$ (O-H), 3081 (C-H), 2965 (C-H), 1733 (C=O), 1493 (C=C ar), 1277; Elemental analysis: (calcd., found for $\text{C}_{13}\text{H}_{21}\text{NO}_4$): C, 61.16, 60.28; H, 8.29, 8.042; N, 5.49, 5.62; Tg (DSC) = -6.0 °C

1-(3-methyl-butyl)-3-hydroxy-pyridinium succinate (11)



Yield: 82.4 %

^1H NMR (400 MHz, D_2O) δ 8.43 – 8.03 (m, 2H), 7.95 – 7.62 (m, 2H), 4.46 (t, $J = 7.7$ Hz, 2H), 2.53 (s, 4H), 1.84 (q, $J = 7.1$ Hz, 2H), 1.58 (dt, $J = 13.0, 6.5$ Hz, 1H), 0.92 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (101 MHz, D_2O) δ 179.08, 158.79, 134.04, 132.79, 131.98, 128.21, 60.23, 39.35, 30.72, 24.87, 21.29; ESI-MS (m/z): $[\text{M}]^+$ calcd. for $\text{C}_{12}\text{H}_{12}\text{NO}^+$: 166.12, found, 166.23; IR $\nu_{\text{max}}/\text{cm}^{-1} = 3493$ (O-H), 3073 (C-H), 2962 (C-H), 1717 (C=O), 1568 (C=C ar), 1496; Elemental analysis: (calcd., found for $\text{C}_{14}\text{H}_{21}\text{NO}_5$): C, 59.35, 59.20; H, 7.47, 7.20; N, 4.94, 5.09; Tg (DSC) = -11.7 °C

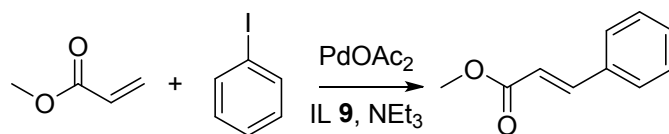
PMMA and ionogel films

PMMA films were made by dissolving 1 g of PMMA in 10 mL of acetone. The mixture was shaken for 90 min at room temperature in a sealed vial. The clear solution was then transferred to a petri dish and the acetone was allowed to evaporate for 48 h. Ionogels were made by dissolving 0.8 g of PMMA and 0.2 g of IL **9** in 10 mL of acetone, followed by the same casting and drying procedure.

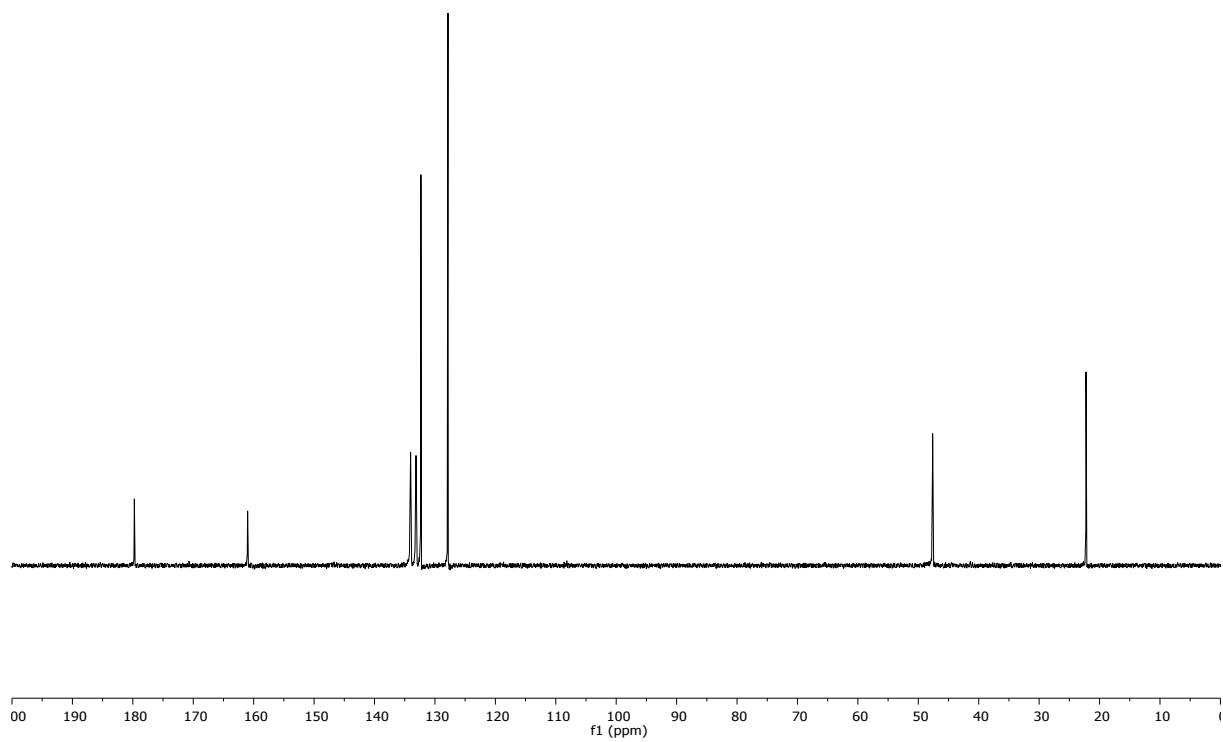
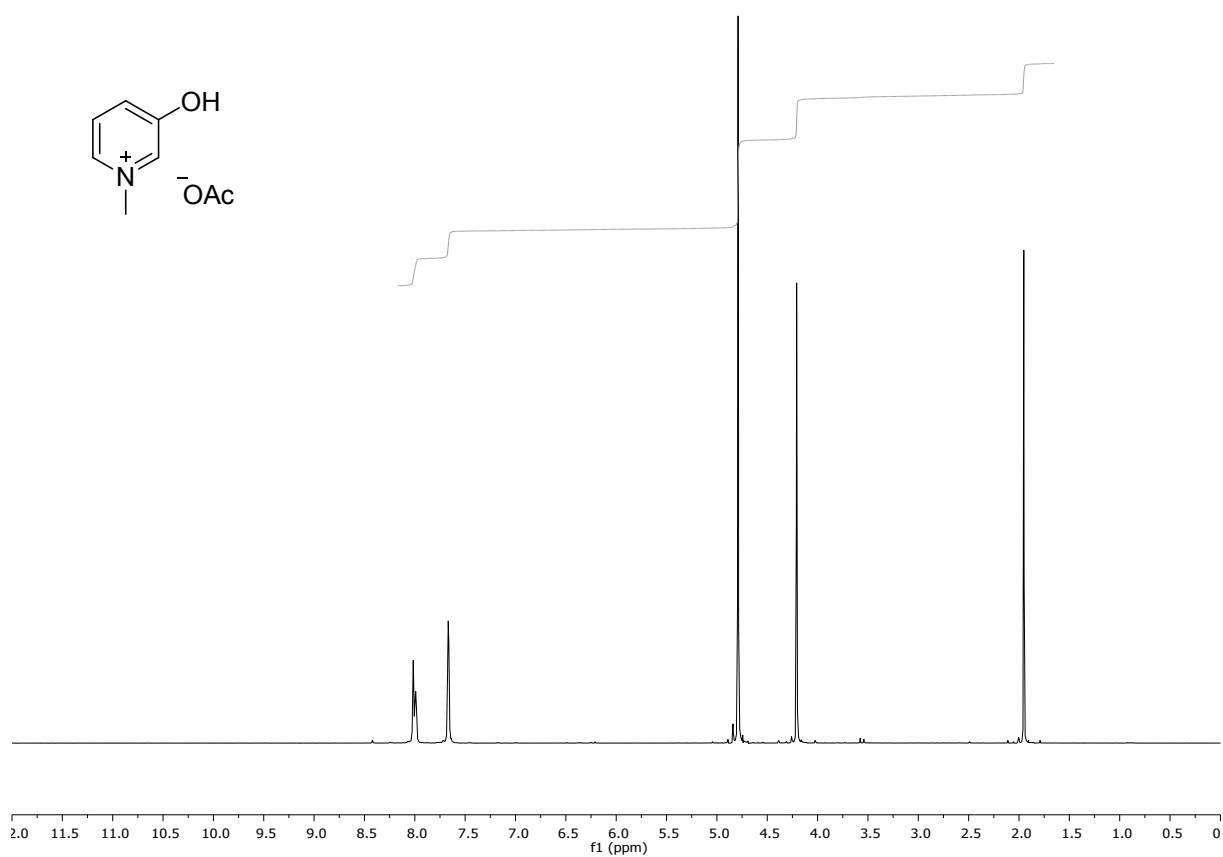
Heck reaction

An aliquot of **9** was dissolved in a small amount of water and an aqueous solution of Li bistrifluoromethanesulfonylimide (TFSI, 1.5 eq) was added under stirring. The newly formed 1-(3-methyl-butyl)-3-hydroxy-pyridinium TFSI ionic liquid separated from the aqueous phase and was washed with water 5 times before drying in a vacuum oven overnight. The successful occurrence of the metathesis was confirmed by the absence of the acetate peak in the NMR [^1H NMR (400 MHz, DMSO) δ 8.49 – 8.14 (m, 2H), 7.73 (ddd, $J = 34.9, 8.7, 4.1$ Hz, 2H), 4.55 – 4.34 (t, 2H), 1.77 (q, $J = 7.0$ Hz, 2H), 1.63 – 1.41 (m, 1H), 0.93 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (101 MHz, DMSO) δ 160.51, 160.39, 133.12, 131.98, 131.43, 128.10, 124.25, 121.05, 117.85, 114.65, 58.97, 39.63, 25.08, 22.03.]. Thus, $\text{Pd}(\text{OAc})_2$ (1.5 mg, $7 \mu\text{mol}$) was dissolved in 1.5 mL of freshly prepared TFSI ionic liquid and the

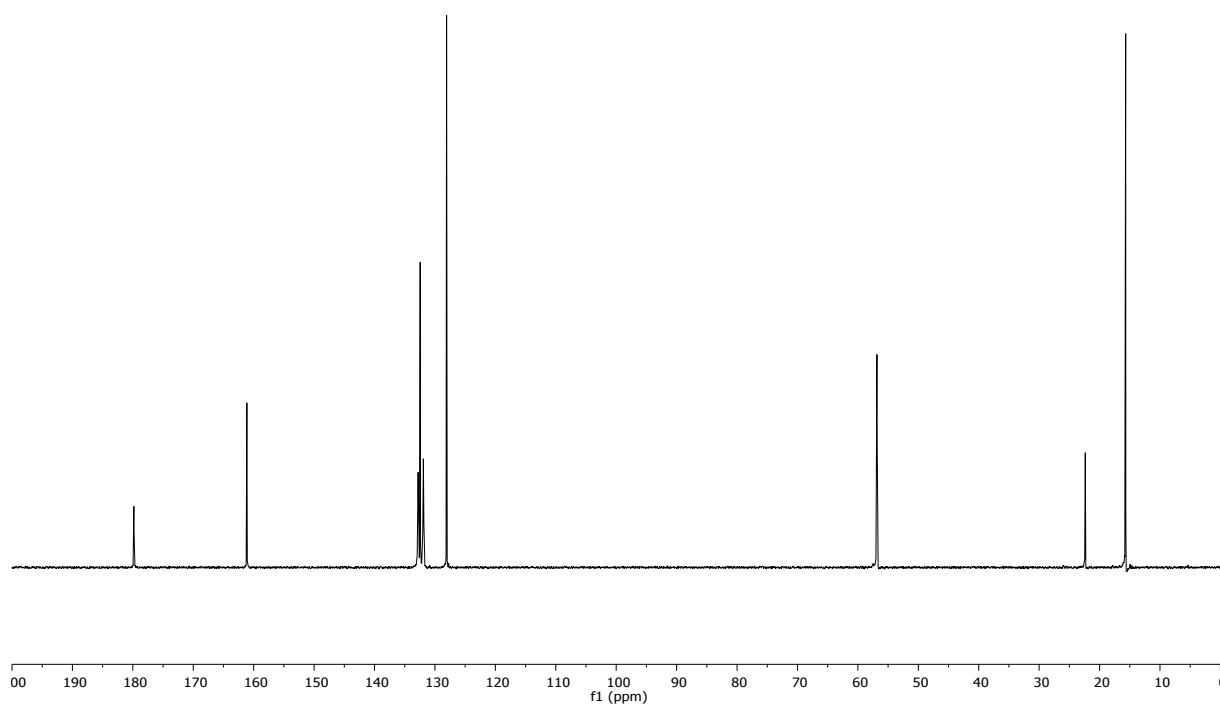
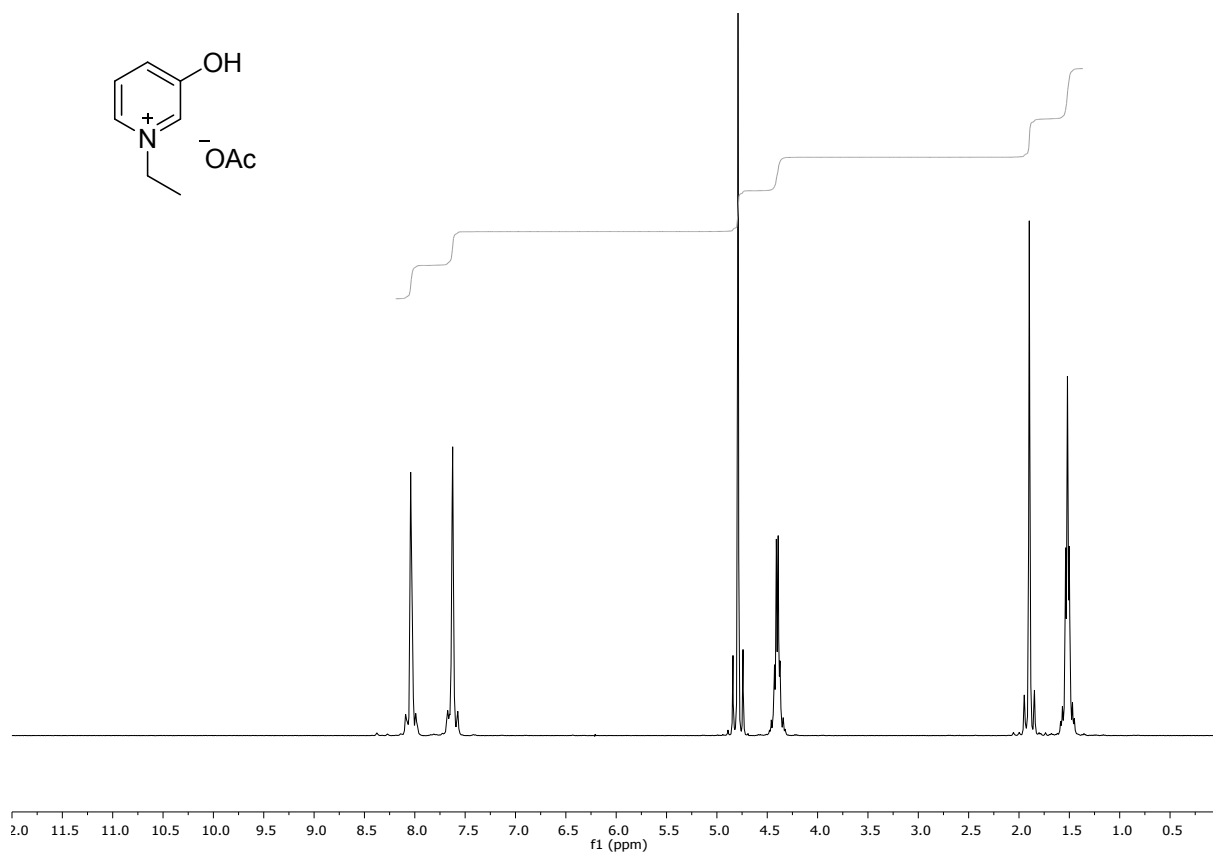
mixture was stirred at 80 °C for 30 min. The flask was conditioned with argon and triethylamine (0.5 mL, 3.58 mmol), iodobenzene (0.3 mL, 2.65 mmol) and methyl acrylate (0.3 mL, 3.32 mmol) were added. The solution was stirred for 1 h at 80 °C followed by 3 h at 100 °C. Completion of the reaction was verified by GC-MS and the ionic liquid was extracted with toluene five times. The organic layers were combined and concentrated under reduced pressure, yielding the desired product in 98% yield (420 mg, 2.59 mmol).



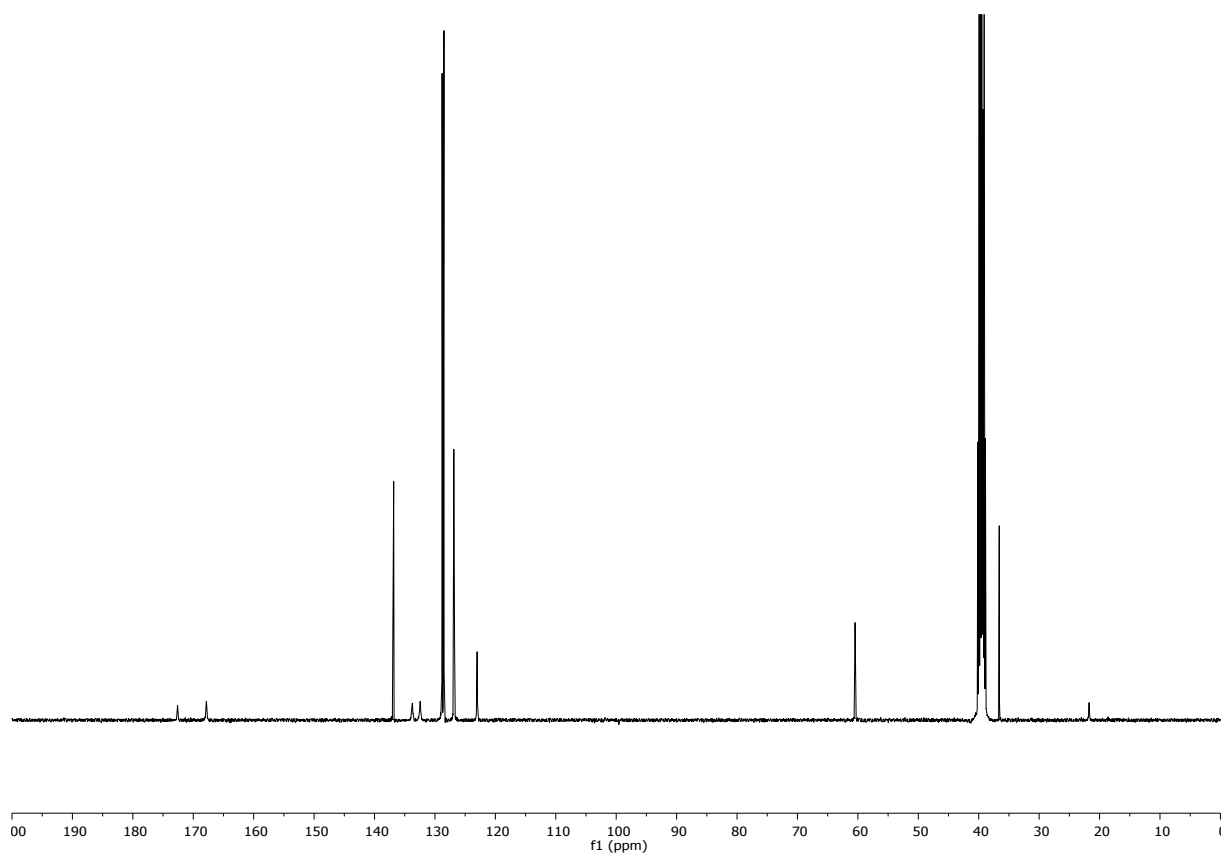
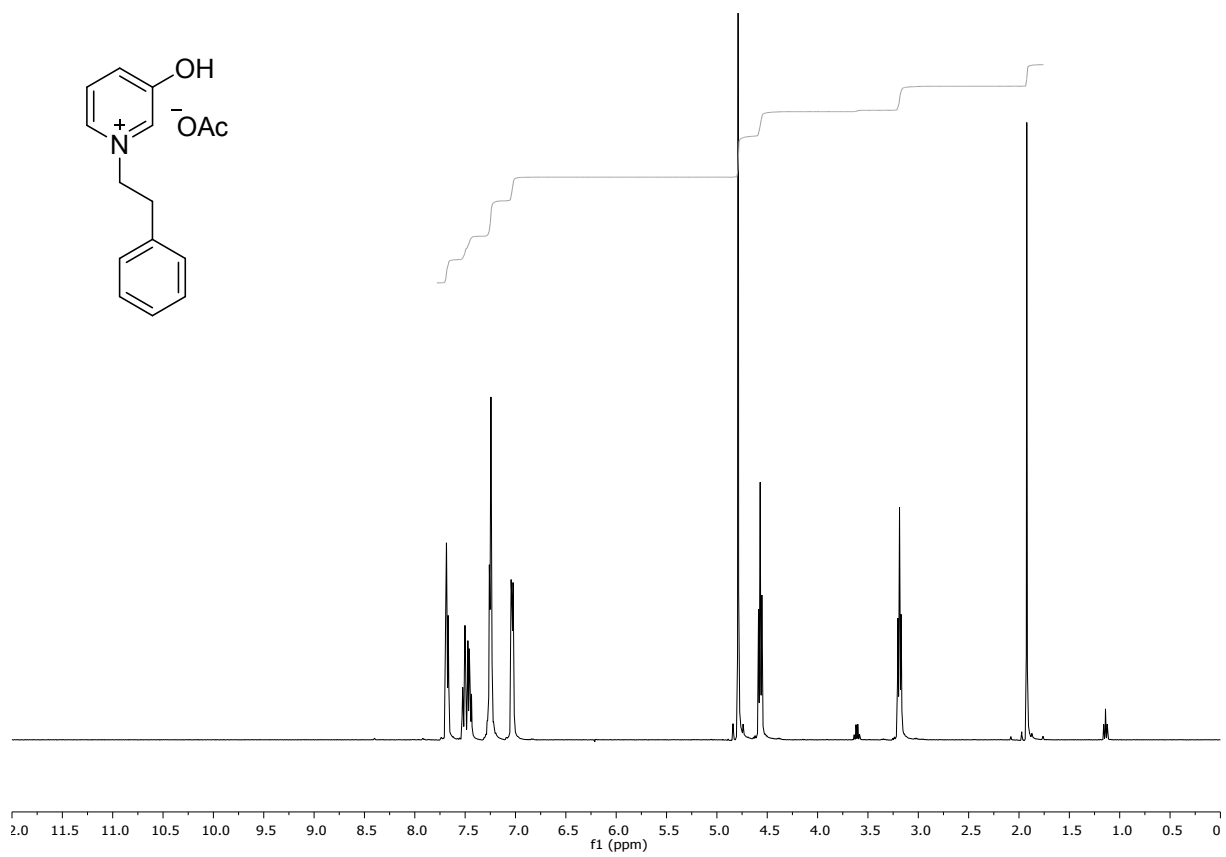
Pyridinium ILs NMR spectra



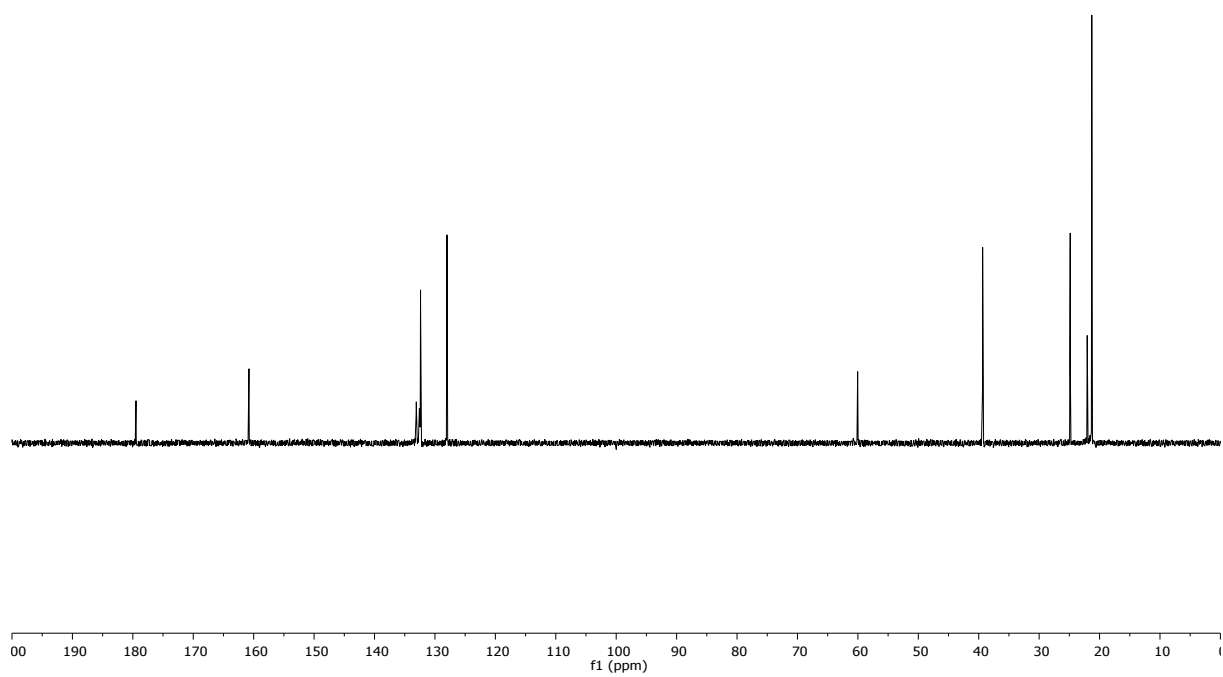
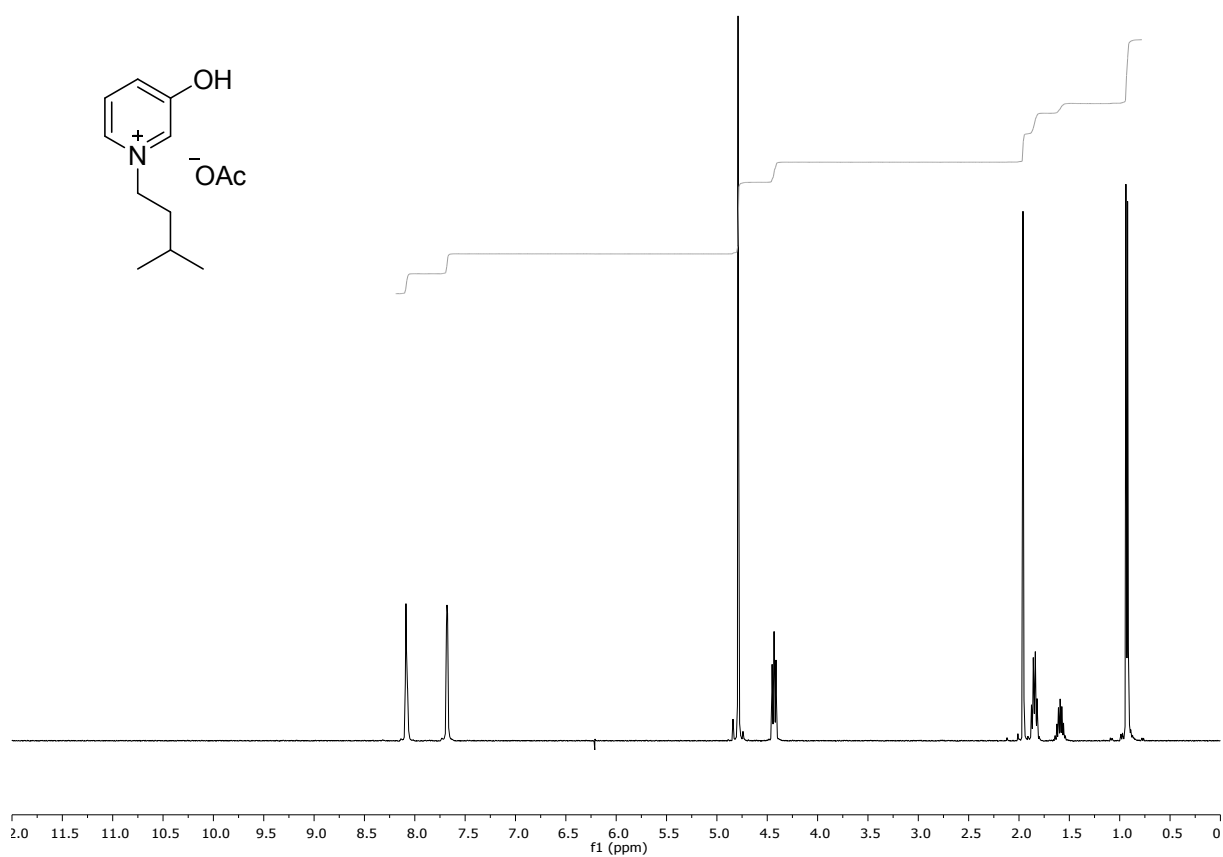
¹H- and ¹³C- NMR spectra of **6**



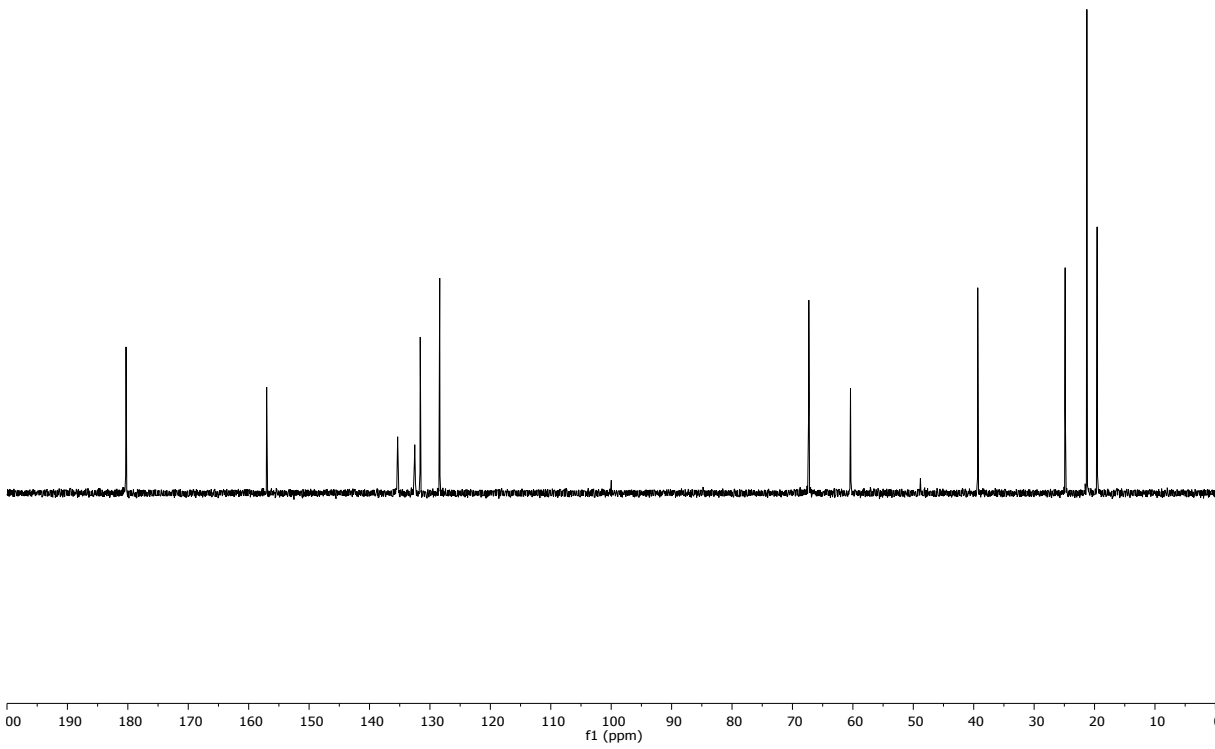
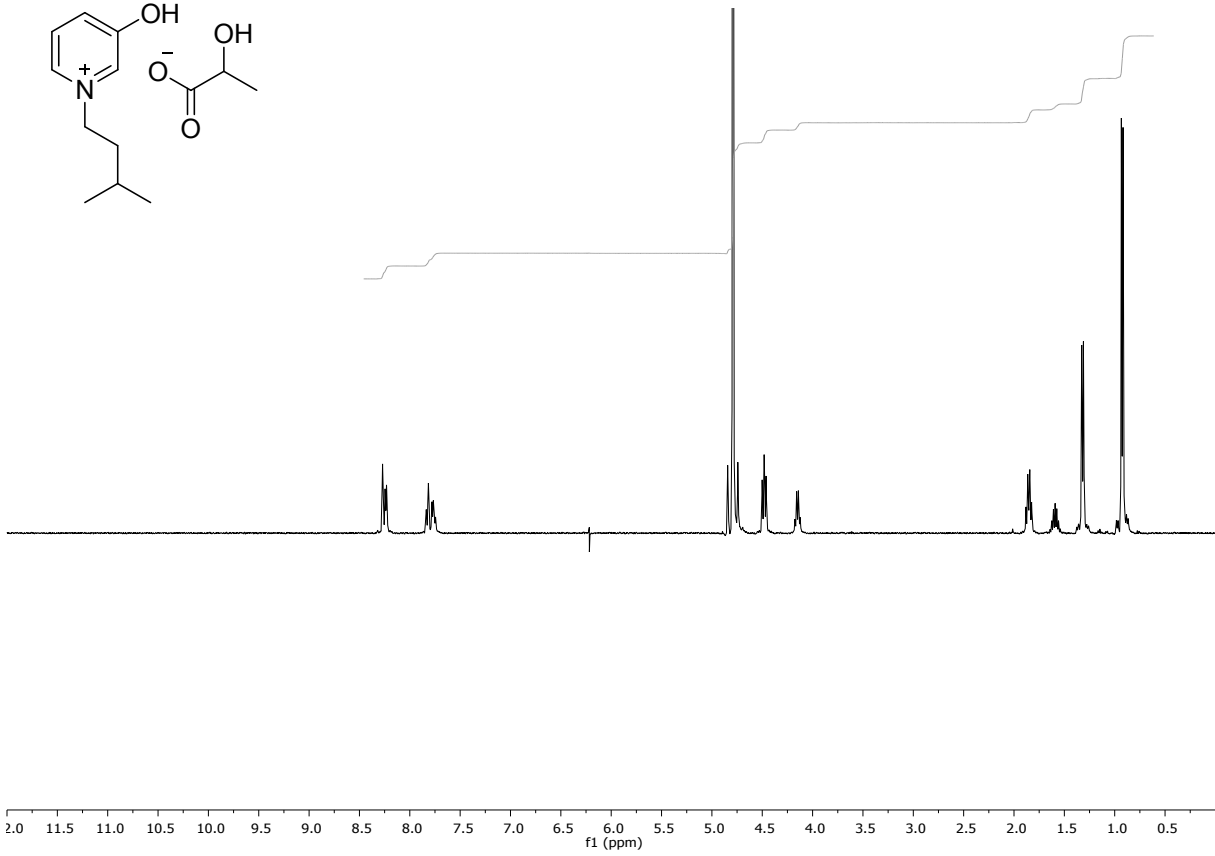
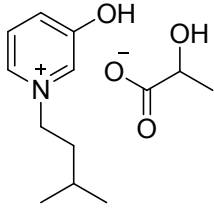
^1H - and ^{13}C - NMR spectra of **7**



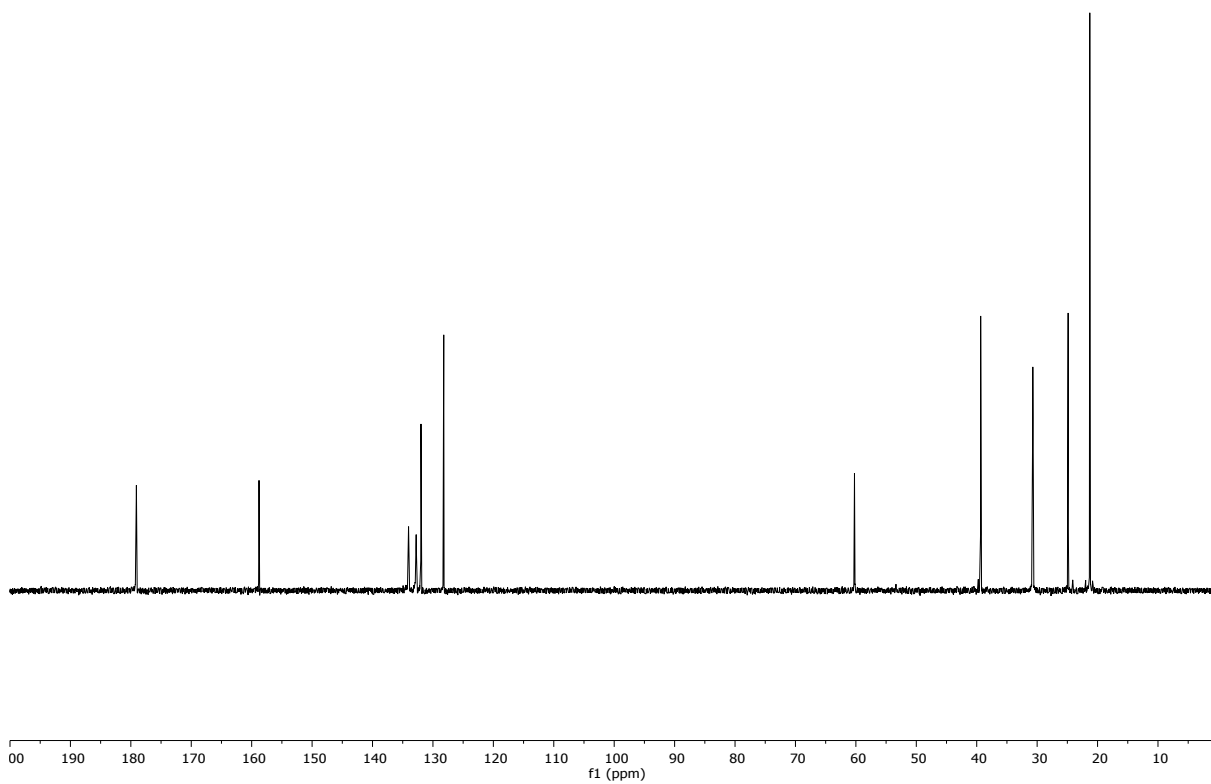
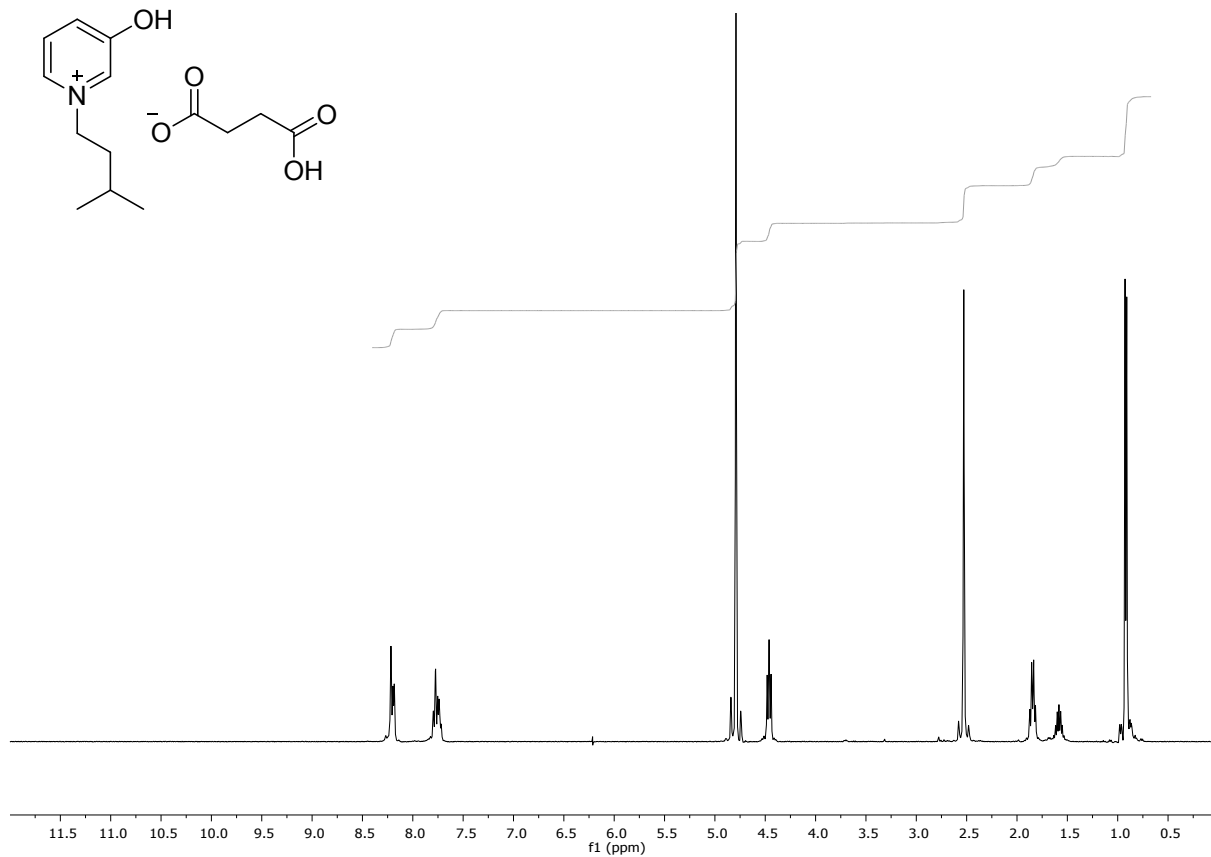
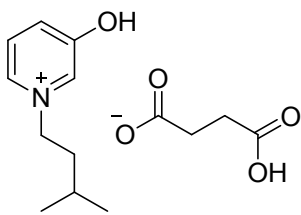
^1H - and ^{13}C - NMR spectra of **8**



¹H- and ¹³C- NMR spectra of **9**

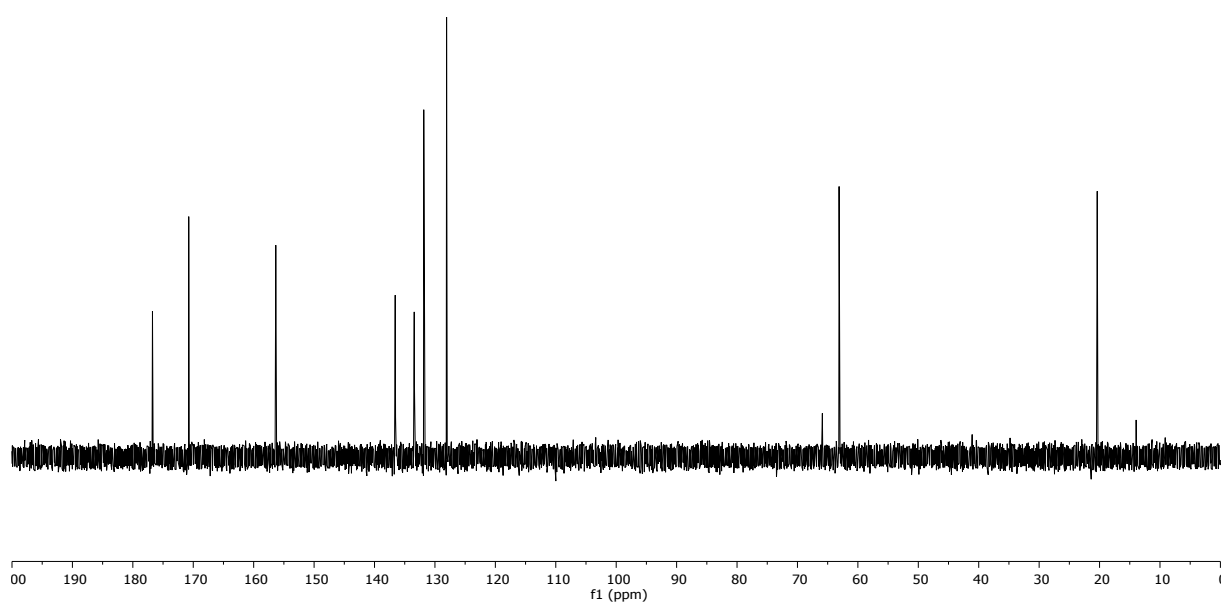
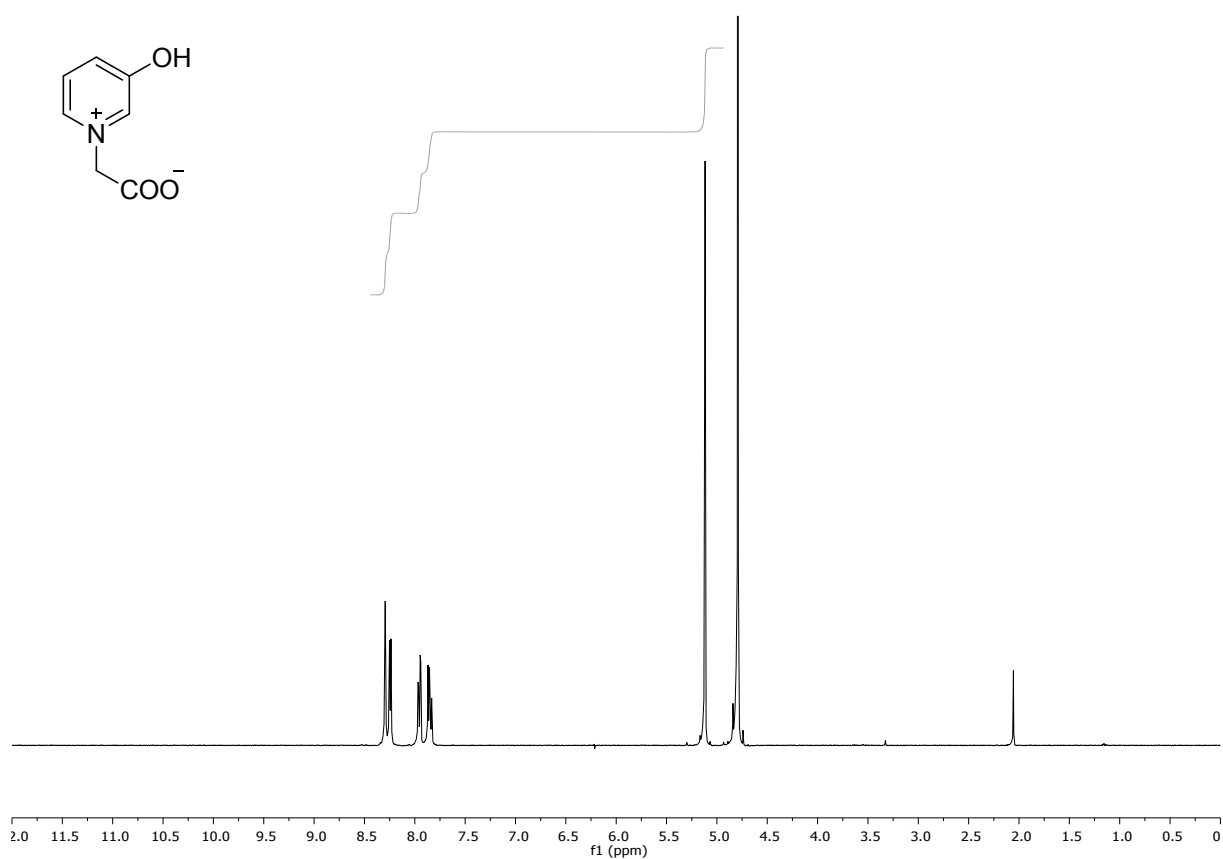


^1H - and ^{13}C - NMR spectra of **10**

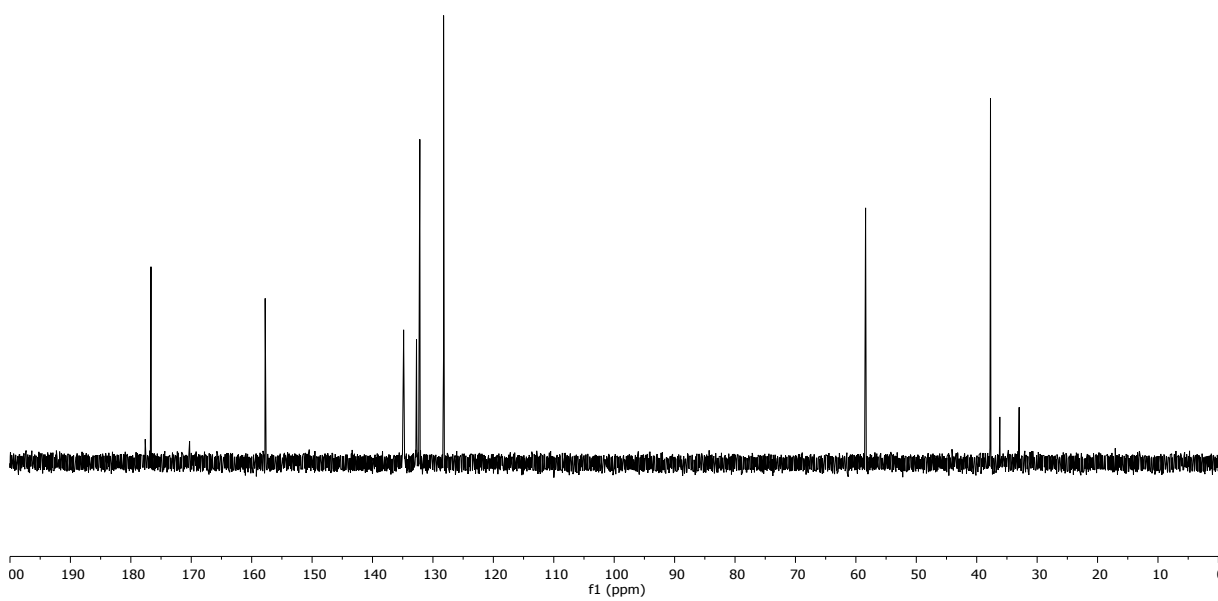
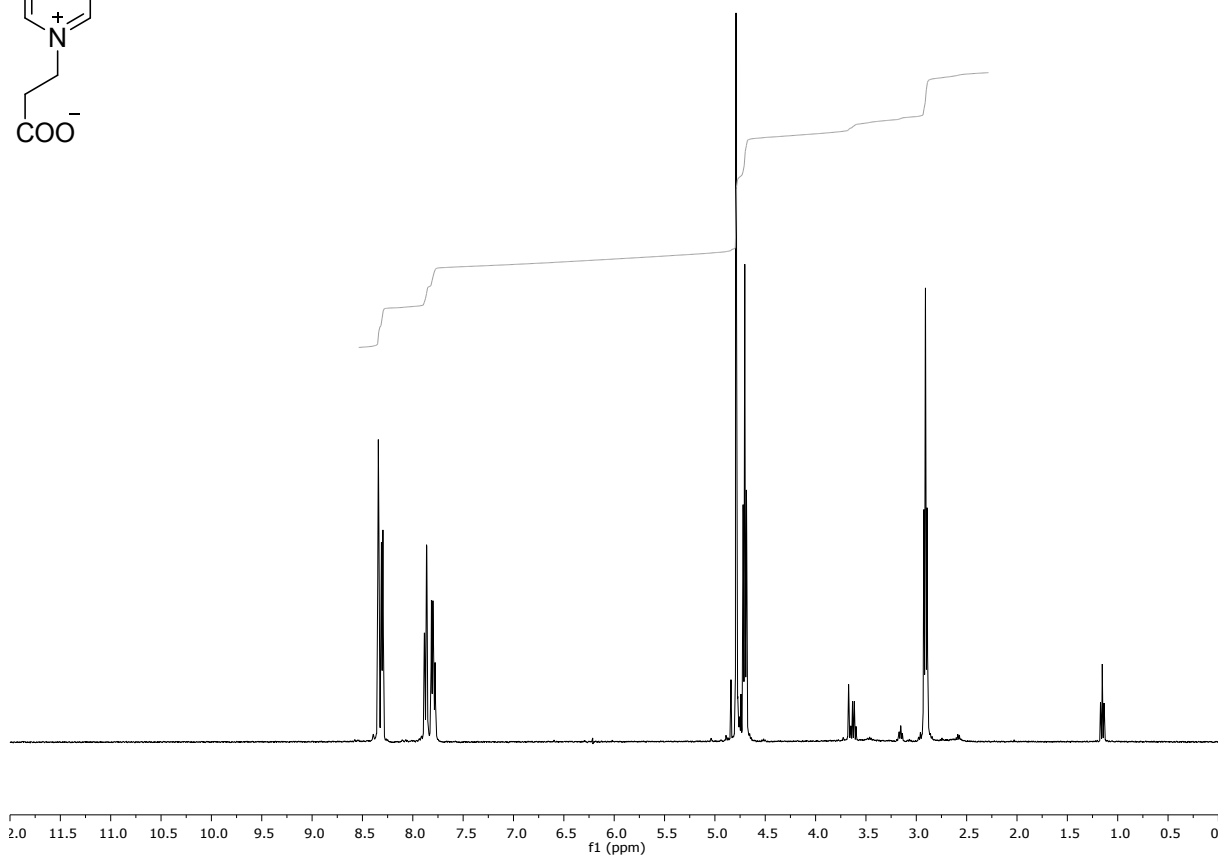
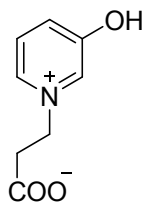


^1H - and ^{13}C - NMR spectra of **11**

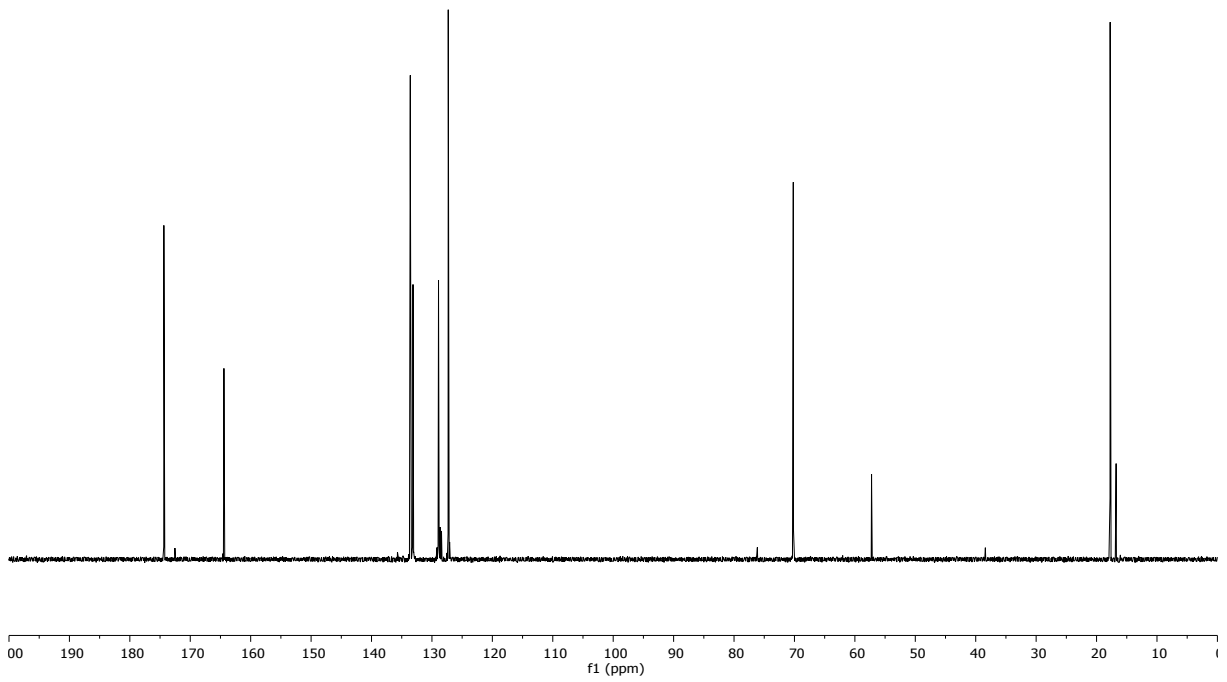
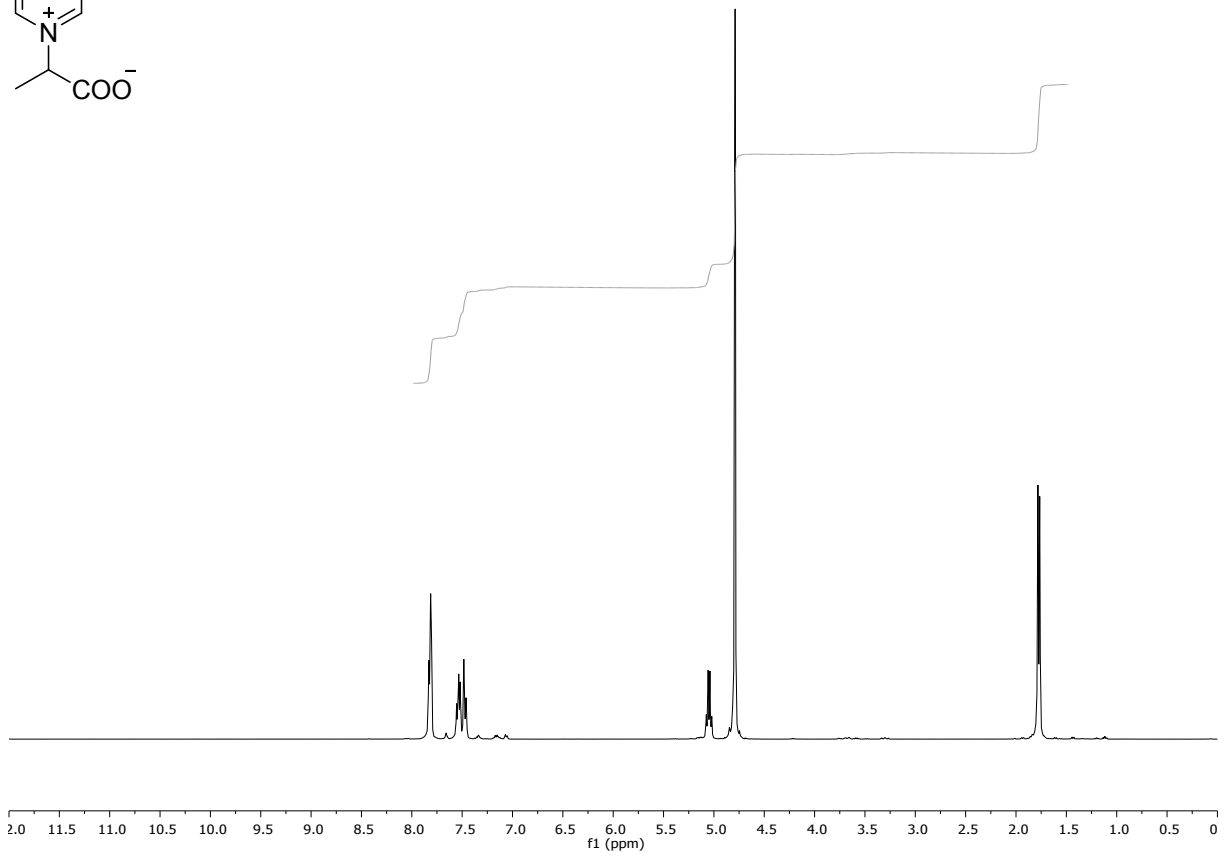
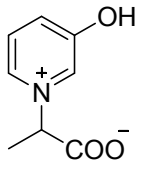
Pyridinium zwitterions NMR spectra



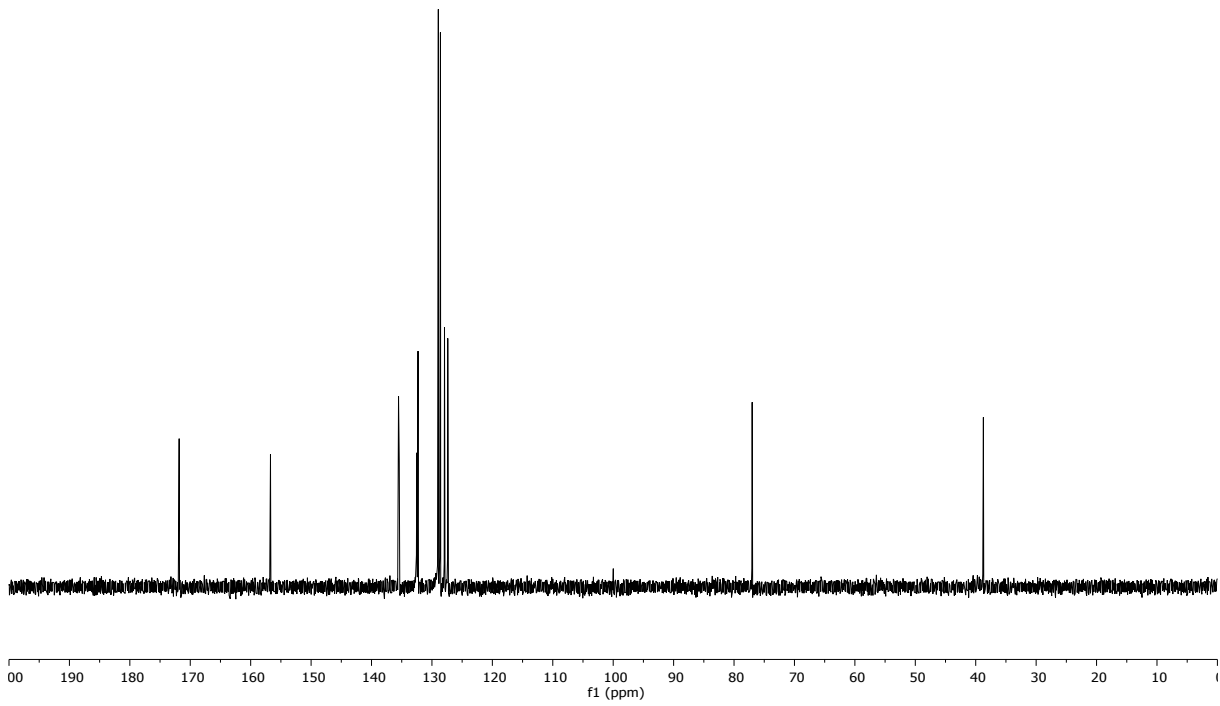
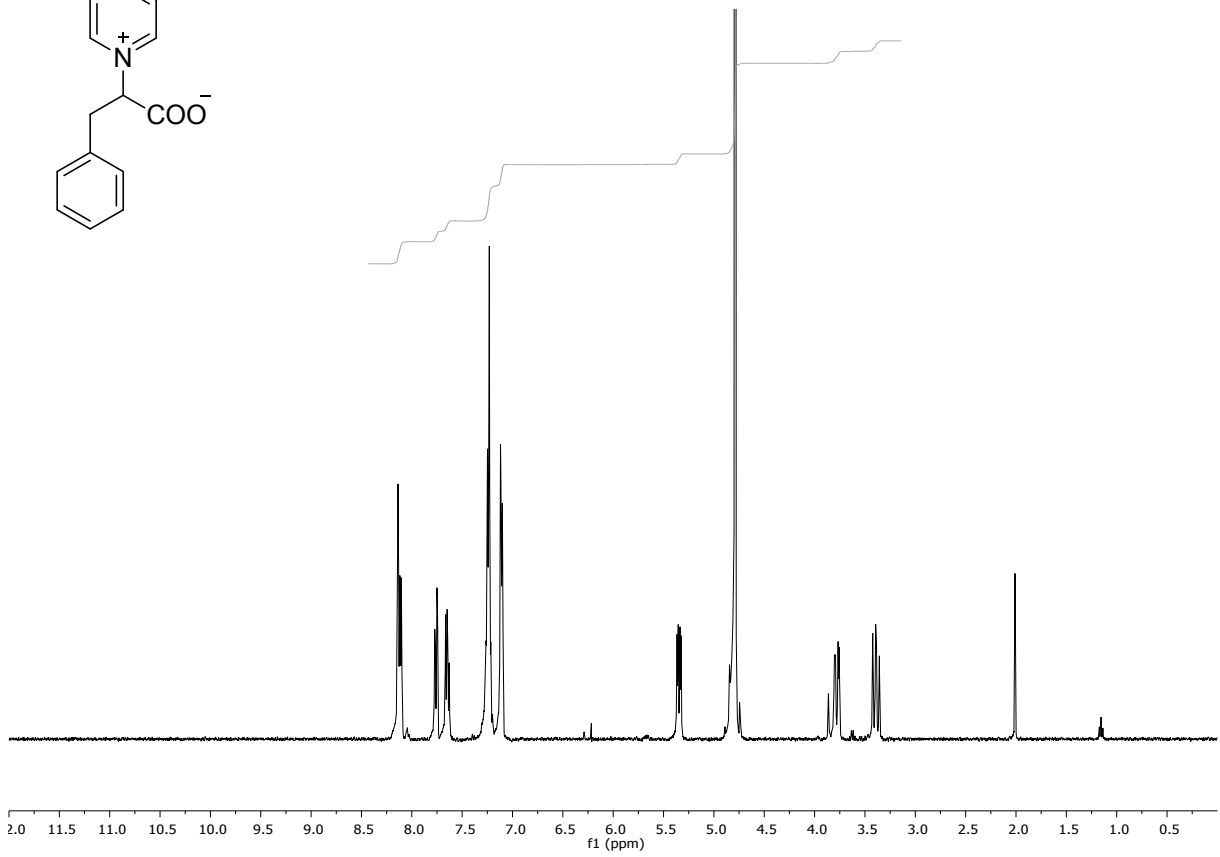
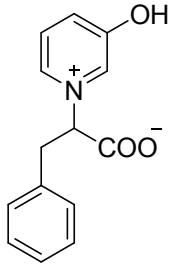
¹H- and ¹³C- NMR spectra of **1**



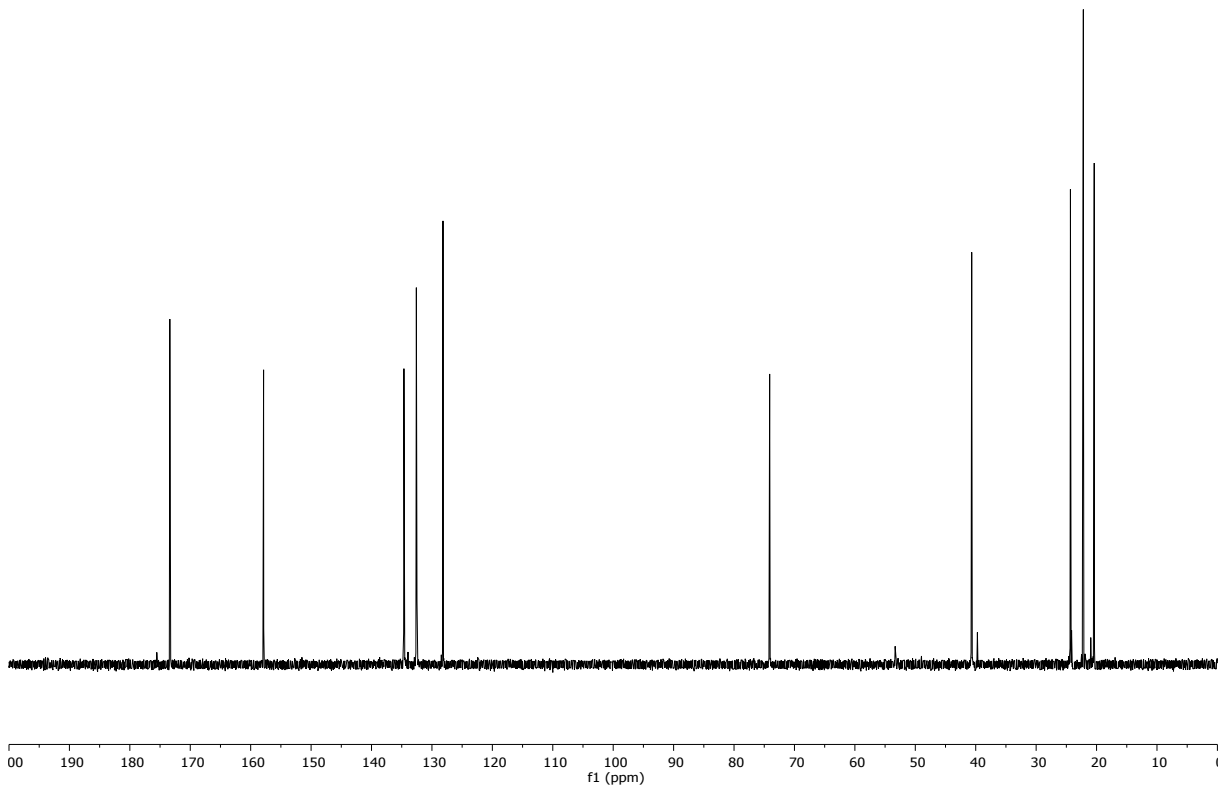
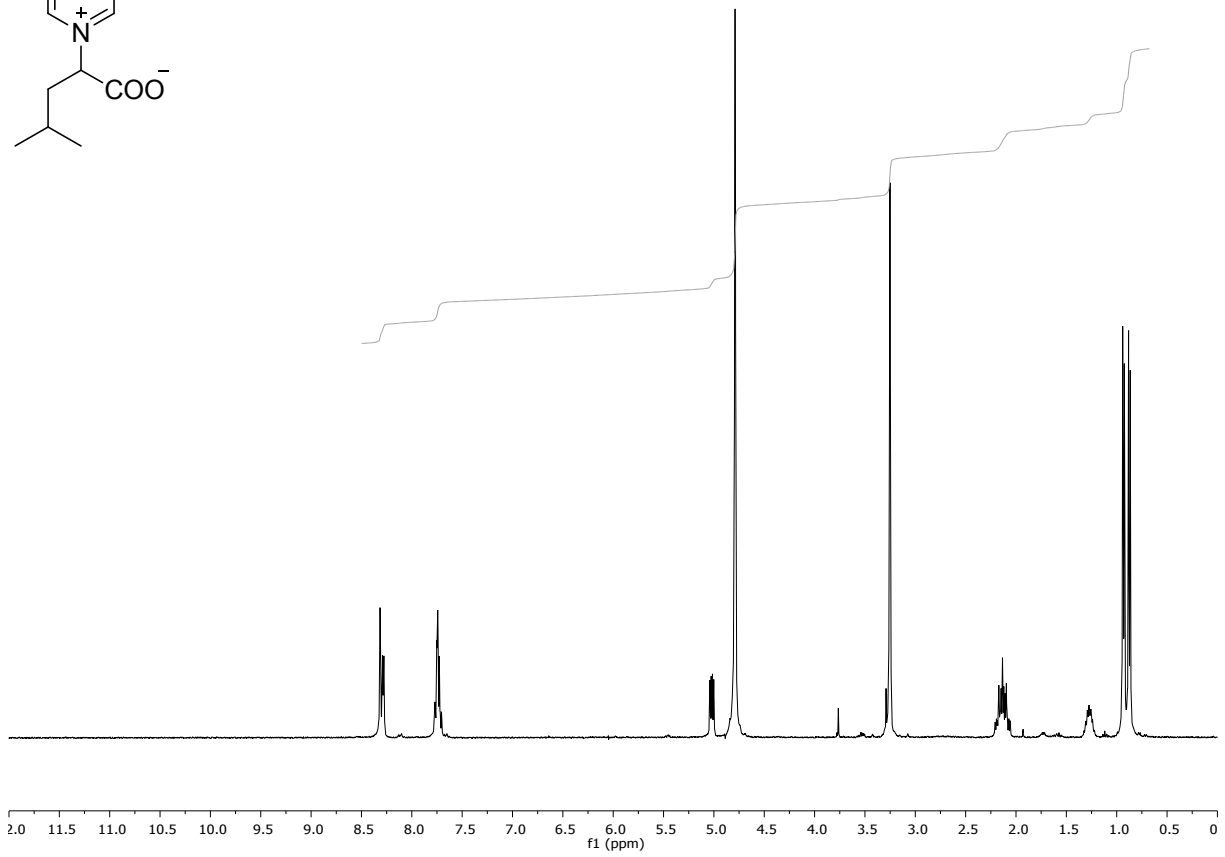
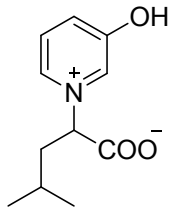
$^1\text{H-}$ and $^{13}\text{C-}$ NMR spectra of **2**



¹H- and ¹³C- NMR spectra of **3**



¹H- and ¹³C- NMR spectra of **4**



¹H- and ¹³C- NMR spectra of 5