Synthesis of novel Levulinic Acid based Poly(amine-*co*-ester)s

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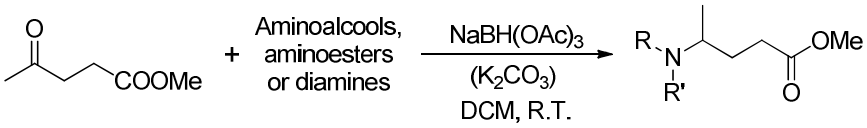
1. General information

Chemicals used in this study have been purchased from Acros Organics and Sigma Aldrich. Solvents were dried by using an MBRAUN Solvent Purification Systems (MB-SPS-800). All reactions were monitored by GC analysis on a Shimadzu GC-2014 equipped with an FID detector. Analytical thin layer chromatography (TLC) was performed on commercial silica gel 60 with fluorescent indicator UV absorbance 254 (Merck). Detection was accomplished by treatment of the plate with dying reagents (potassium permanganate, vanillin or anisaldehyde). Chromatographic purifications were realized on silica gel columns (silica 60 A, 40–63 μm) with a dichloromethane/methanol eluent system. Distillations were conducted with a Kugelrohr apparatus. Polymerisation reactions were performed with a Kugelrohr apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 300 spectrometer. Chemical shift data are reported in units of δ (ppm) using $CHCl_3$ (δ = 7.26 for ^{1}H NMR spectra and δ = 77.36 for ^{13}C NMR spectra) as internal standard. Multiplicities are given as s (singlet), d (double), t (triplet), m (multiplet). Coupling constants, *J*, are reported in Hz. Spectra were fully attributed using -if needed- 2D-NMR (COSY, HSQC, HMBC) spectroscopy. High resolution mass spectra (HRMS) were measured on a Waters Synapt G2-Si (mode ESI(+)) at the Organis Synthesis & Mass Spectrometry Laboratory (S2MOs), University of Mons, Belgium using $(NaI)_nNa^+$ cluster ions as the external reference ions. The referent ions are generated upon ESI(+) of a NaI solution (200 mg/100 mL in water/isopropanol 1/1.

2. Additional reductive amination.



	Aminoalcohols, aminoesters or diamines	Conditions Eq. $NaBH(OAc)_3$	Eq. K_2CO_3	t (h)	GC ratio [a] (LevOMe/Product)	Isolated yields (%)
1	*N-methylamino ethanol*	2.1	0	72	25/75	72
2	*N-ethylamino ethanol*	3.6	0	96	80/20	non isolated
3	*L-prolinol*	1.5	0	48	5/95	86
4	*Sarcosine methyl ester .HCl*	2.1	1.5	72	35/65	56
5	*L-proline methyl ester .HCl*	1.5	1.5	48	5/95	90
6	*N-pipecolic methyl ester .HCl*	3.6	1.5	96	100/0	non isolated
7	*N,N'-dimethylethylene diamine*	4.2	0	144	10/40/50[b]	39
8	*Piperazine*	4.2	0	144	90/10	non isolated

Table S1. Structure, experimental conditions, GC ratio and isolated yields for the synthesis of product of reductive amination between methyl levulinate (**LevOMe**) and amino-alcohol/esters or diamines.

[a]GC ratio is the percentage of the area of the peak of the starting material (LevOMe) / the alkylated product compare to the total area (LevOMe + Product).

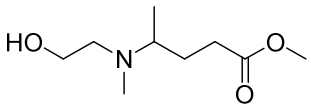
[b]two products (so to peaks) are observed, *i.e.* the product of mono-alkylation and the product of dialkylation.

3. General procedure for the synthesis of monomers

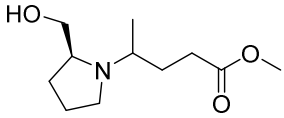
A 250 mL two-necked round-bottom flask was conditioned under argon atmosphere and charged with anhydrous dichloromethane (100 mL). Then, methyl levulinate (3 mL, 24.2 mmol) and the appropriate amino-alcohol/amino-ester (36.3 mmol) were introduced into the flask, followed by potassium carbonate (for compounds **1c** and **1d**) and sodium triacetoxyborohydride (10.8 g, 50.9 mmol). The reaction mixture was stirred under argon atmosphere at room temperature and monitored by GC analysis. When the conversion remains unchanged (48-72 h), 100 mL of 1 M aqueous solution of NaOH were added to the reaction, and the two layers were separated. The aqueous layer was further extracted twice with 50 mL of dichloromethane, and the combined organic layers were dried with magnesium sulfate and concentrated under reduced pressure. The product was directly

purified by distillation under a short-path vacuum distillation apparatus (Kugelrohr apparatus) and obtained as a colourless liquid.

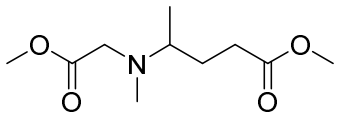
4. Characterization data of monomers.



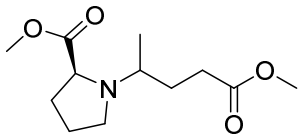
Methyl 4-(*N*-(2-hydroxyethyl)-*N*-methylamino)pentanoate (**2a**).The product (77% yield) was purified by distillation. Colorless liquid. Bp: 80°C (0.25 mBar). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (d, ^{3}J = 6.6 Hz, 3H, -CH-C***H***$_3$), 1.48-1.60 (m, 1H, -CH-C***H***$_2$-), 1.69-1.81 (m, 1H, -CH-C***H***$_2$-), 2.05 (s, 3H, -N-C***H***$_3$), 2.26-2.32 (m, 2H, -C***H***$_2$-CO-), 2.45-2.49 (m, 2H, -C***H***$_2$-N(CH_3)-), 2.55-2.63 (m, 1H, -N-C***H***-CH_3), 2.93 (s, 1H, -O***H***), 3.46 (t, ^{3}J= 5.3 Hz, 2H, -C***H***$_2$-OH), 3.58 (s, 3H, -O-C***H***$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.0 (-CH-***C***H_3), 29.2 (-CH-***C***H_2-), 31.8 (-***C***H_2-CO-), 34.5 (-N-***C***H_3), 51.5 (-O-***C***H_3), 55.7 (-***C***H_2-N(CH_3)-), 58.1 (-***C***H-), 58.5 (-***C***H_2-OH), 174.4 (-***C***=O). HRMS m/z calcd. for $C_9H_{20}NO_3$: 190.1443 $[M+H]^+$; found: 190.1442.



Methyl 4-((*S*)-2-(hydroxymethyl)pyrrolidin-1-yl)pentanoate (**2b**). The product (50% yield) was purified by distillation as a mixture of diastereomers (Major (*M*)/minor (*m*), 70:30). Colorless liquid. Bp: 100°C (0.20 mBar). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (d, ^{3}J = 6.4 Hz, 0.89H, -CH-C***H***$_3$ (*m*)), 1.03 (d, ^{3}J = 6.7 Hz, 2.11H, -CH-C***H***$_3$ (*M*)), 1.50-1.85 (m, 6H, -C***H***$_2$-), 2.19-2.97 (m, 6.70H, -C***H***$_2$- and -C***H***- and -O***H***), 3.21-3.28 (m, 1H, -C***H***$_2$-OH), 3.38-3.51 (m, 1.30H, -C***H***$_2$-OH and -C***H***-), 3.60 (2x s, -O-C***H***$_3$, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.4 (-CH-***C***H_3 (*m*)), 18.5 (-CH-***C***H_3 (*M*)), 24.2 (-***C***H_2- (*m*)), 24.3 (-***C***H_2- (*M*)), 27.8 (-***C***H_2- (*M*)), 28.0 (-***C***H_2- (*m*)), 29.2 (-***C***H_2- (*M*)), 31.2 (-***C***H_2- (*M*)), 31.3 (-***C***H_2- (*m*)), 32.2 (-***C***H_2- (*m*)), 44.3 (-***C***H_2- (*m*)), 48.9 (-***C***H_2- (*M*)), 51.5 (-O-***C***H_3 (*m*)), 51.6 (-O-***C***H_3 (*M*)), 52.3 (-***C***H- (*m*)), 54.1 (-***C***H- (*M*)), 59.4 (-***C***H- (*M*)), 60.4 (-***C***H- (*m*)), 62.3 (-***C***H_2- (*m*), 63.6 (-***C***H_2- (*M*)), 174.1 (-***C***=O (*M*)), 174.5 (-***C***=O (*m*)). HRMS m/z calcd. for $C_{11}H_{22}NO_3$: 216.1600 $[M+H]^+$; found: 216.1605.



Methyl 4-(*N*-(2-methoxy-2-oxoethyl)(*N*-methylamino)pentanoate (**2c**). The product (56% yield) was purified by distillation. Colorless liquid. Bp: 90°C (0.3 mBar). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (d, ^{3}J = 6.6 Hz, 3H, -CH-C***H***$_3$), 1.46-1.59 (m, 1H, -CH-C***H***$_2$-), 1.66-1.78 (m, 1H, -CH-C***H***$_2$-), 2.22 (s, 3H, -N-C***H***$_3$), 2.30-2.39 (m, 2H, -CH_2-C***H***$_2$-CO-), 2.59-2.70 (m, 1H, -N-C***H***-CH_3), 3.07-3.22 (m, 2H, -N-C***H***$_2$-CO-), 3.59 (s, 3H, -O-C***H***$_3$), 3.63 (s, 3H, -O-C***H***$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8 (-CH-C***H***$_3$), 28.9 (-CH-***C***H_2-), 31.1 (-CH_2-***C***H_2-CO-), 37.7 (-N-***C***H_3), 51.4 (-O-***C***H_3), 51.6 (-O-***C***H_3), 54.8 (-N-***C***H_2-CO-), 57.5 (-***C***H-), 172.1 (-***C***=O), 174.4 (-***C***=O). HRMS m/z calcd. for $C_{10}H_{20}NO_4$: 218.1392 $[M+H]^+$; found: 218.1393.



Methyl (5-methoxy-5-oxopentan-2-yl)-L-prolinate (**2d**). The product (90% yield) was purified by distillation as a mixture of diastereomers (Major (*M*)/minor (*m*), 71:29). Colorless liquid. Bp: 110°C (0.12 mBar). The compound is obtained ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (d, ^{3}J = 6.5 Hz, 0.87H, -CH-C***H***$_3$ (*m*)), 1.00 (d, ^{3}J = 6.5 Hz, 2.13H, -CH-C***H***$_3$ (*M*)), 1.53-2.05 (m, 6H, -C***H***$_2$-), 2.23-2.44 (m, 4H, -C***H***$_2$-), 2.50-2.88 (m, 2.29H, -C***H***$_2$- and CH_3-C***H***-N-), 2.99-3.08 (m, 0.71H, CH_3-C***H***-N- (*M*)), 3.39 (dd, ^{3}J = 8.6 Hz, 5.0 Hz, 0.29H, -C***H***-CO_2Me (*m*)), 3.46 (dd, ^{3}J = 8.6 Hz, 3.9Hz, 0.71H, -C***H***-CO_2Me (*M*)), 3.60, 3.61, 3.64, 3.65 (4s, 6H, -O-C*H*$_3$).^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (-CH-***C***H_3 (*m*)), 16.9 (-CH-***C***H_3 (*M*)), 23.8 (-***C***H_2- (*M*)), 24.0 (-***C***H_2- (*m*), 29.4 (-***C***H_2- (*M*)), 29.8 (-***C***H_2- (*m*), 30.4 (-***C***H_2- (*M*)), 30.5 (-***C***H_2- (*m*)), 30.7 (-***C***H_2- (*M*)), 30.8 (-***C***H_2- (*m*)), 46.0 (-***C***H_2- (*m*)), 50.0 (-***C***H_2- (*M*)), 51.4 (-***C***H- (*m*)), 51.5 (-***C***H- (*M*)), 51.6 (-***C***H- (*m*)), 51.7 (-***C***H- (*M*)), 54.0 (-O-***C***H_3 (*m*)), 55.3 (-O-***C***H_3 (*M*)), 61.2 (-O-***C***H_3 (*M*)), 62.4 (-O-***C***H_3 (*m*)), 174.3 (-***C***=O (*M*)), 174.6 (-***C***=O (*m*)), 175.5 (-***C***=O (*m*)), 176.0 (-***C***=O (*M*)). HRMS m/z calcd. for $C_{12}H_{22}NO_4$: 244.1549 $[M+H]^+$; found: 244.1553.

5. ^{1}H and ^{13}C NMR spectra and GC chromatogram of monomers

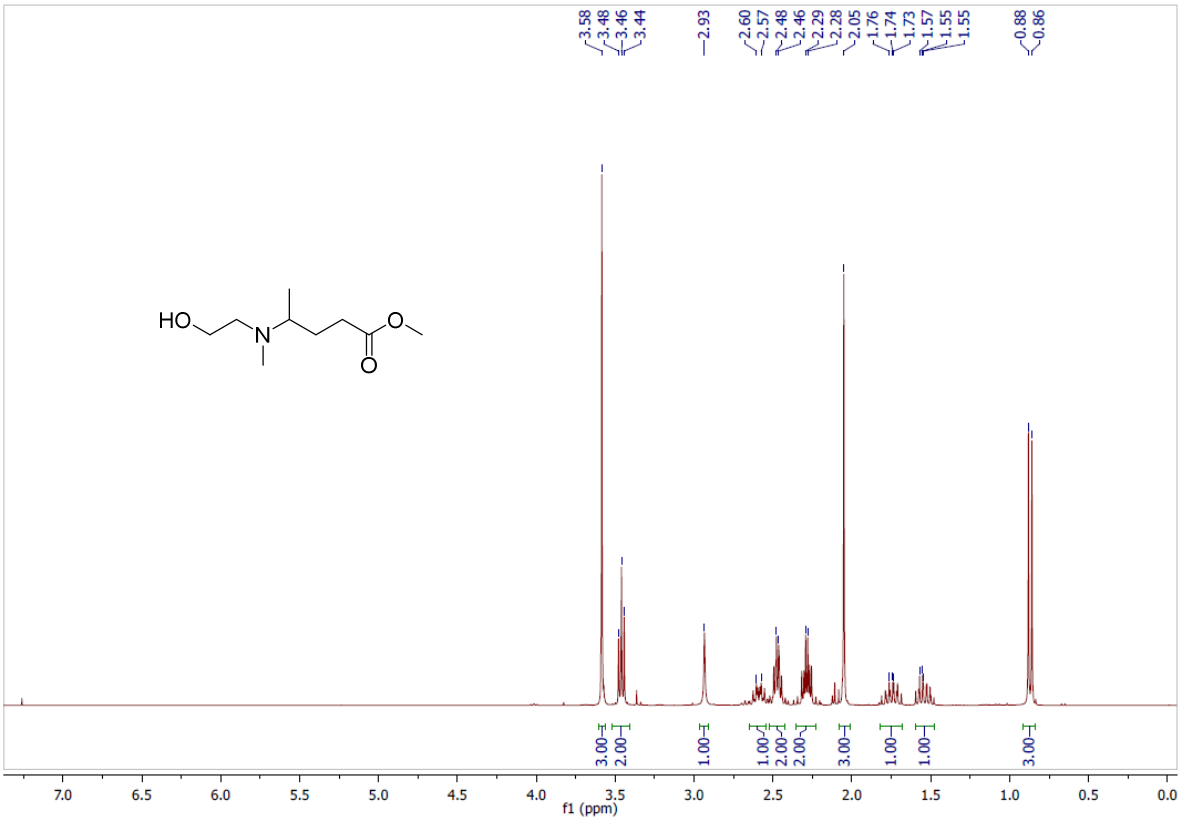


Figure S1. ^{1}H NMR Spectrum of **2a** ($CDCl_3$, 300 MHz)

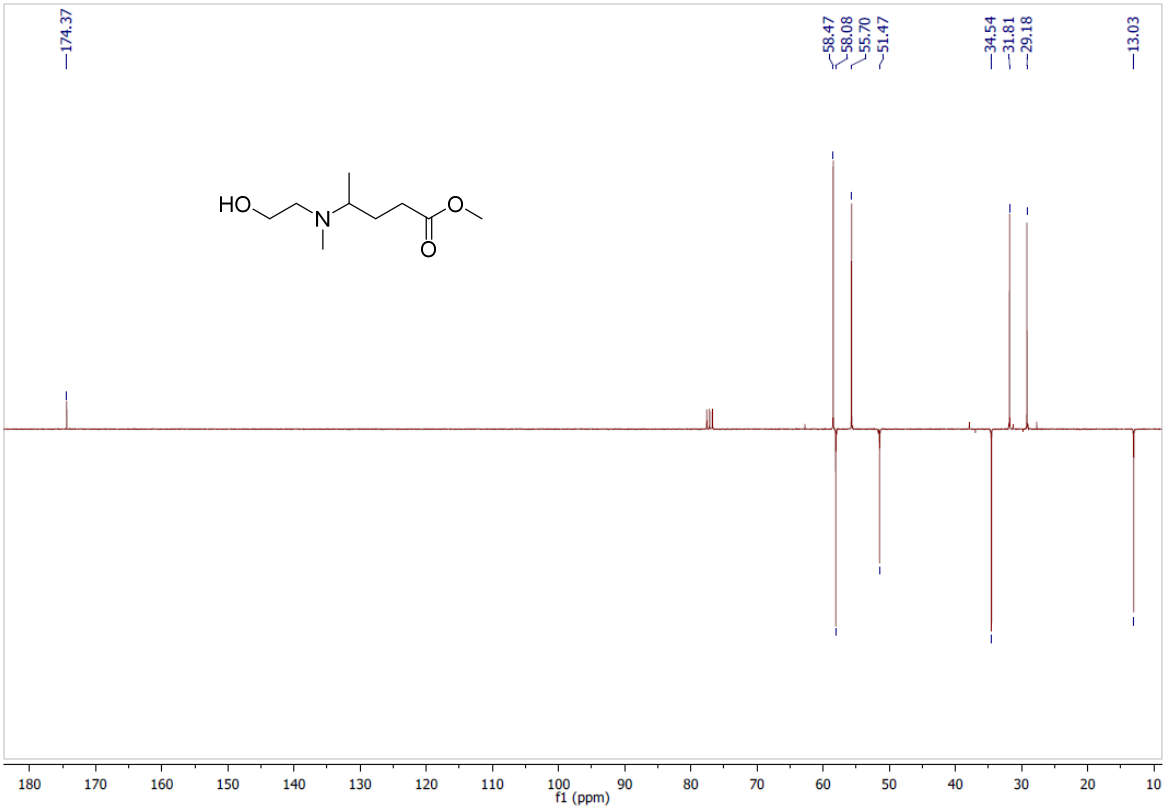


Figure S2. ^{13}C NMR Spectrum of **2a** ($CDCl_3$, 75 MHz)

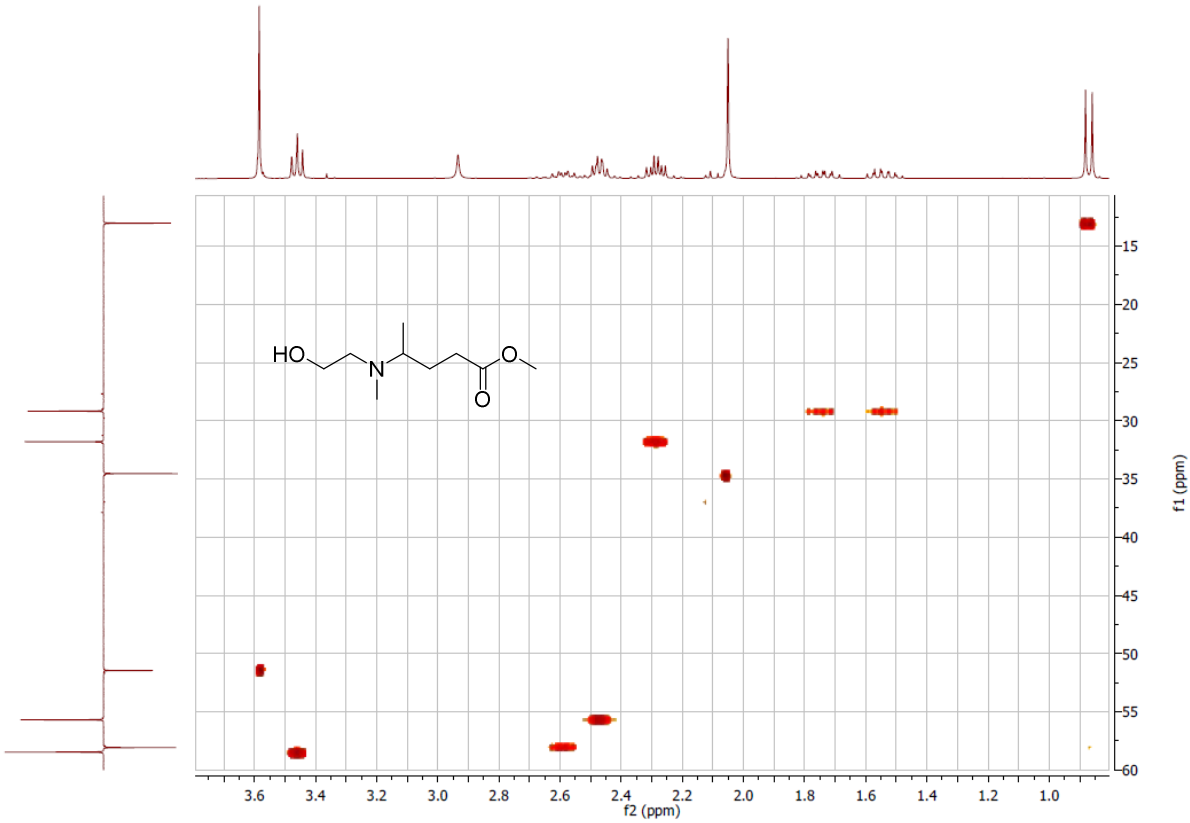


Figure S3. 2D HSQC NMR Spectrum of **2a** ($CDCl_3$, 300/75 MHz)

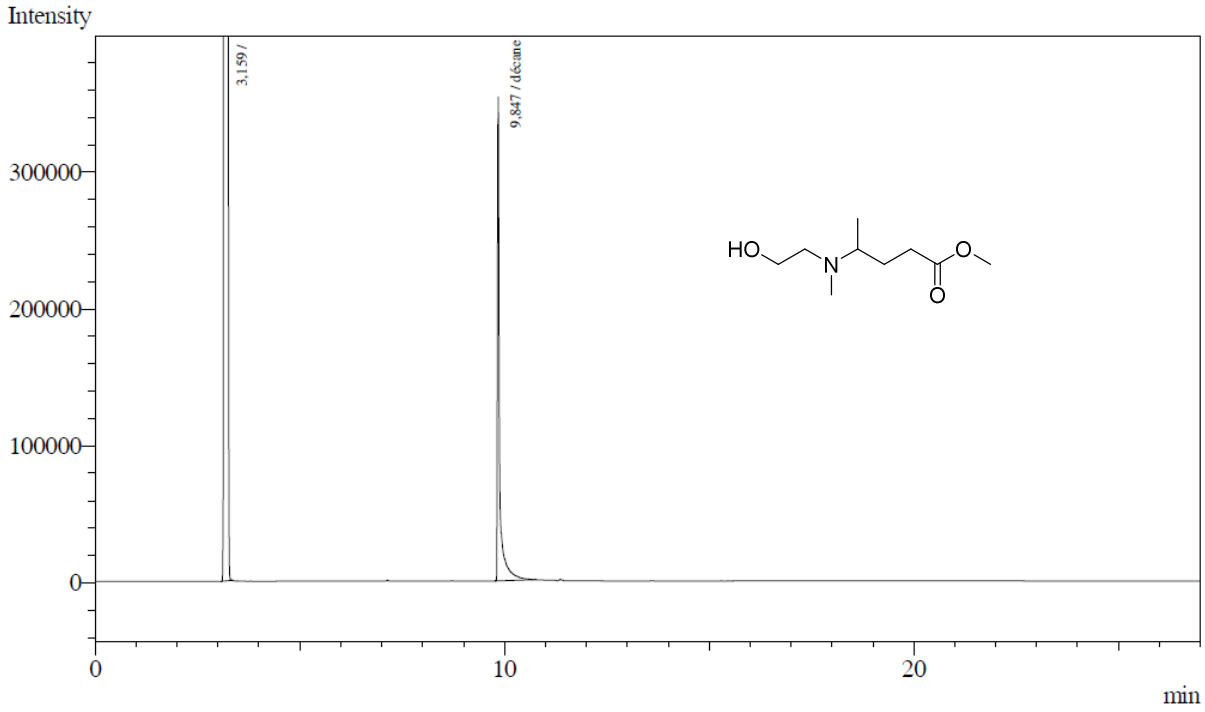


Figure S4. GC chromatogram of **2a**

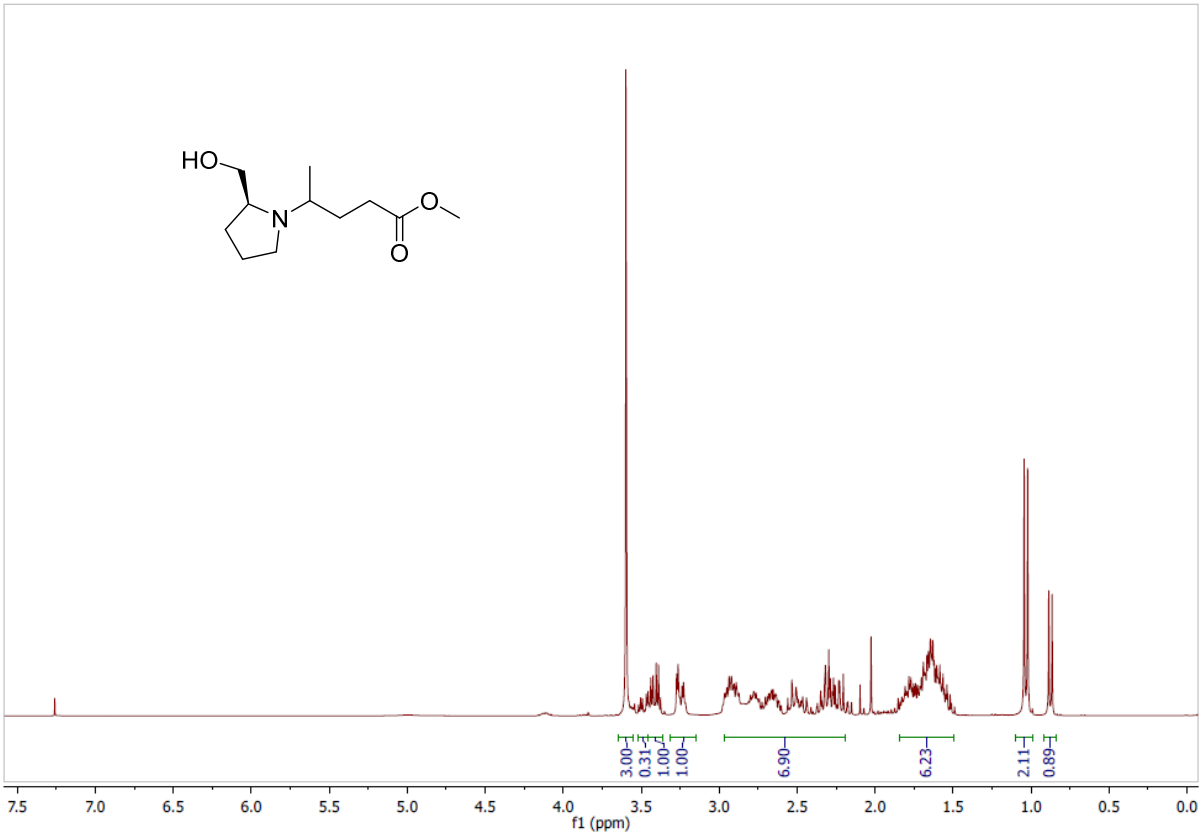


Figure S5. ^{1}H NMR Spectrum of **2b** ($CDCl_3$, 300 MHz)

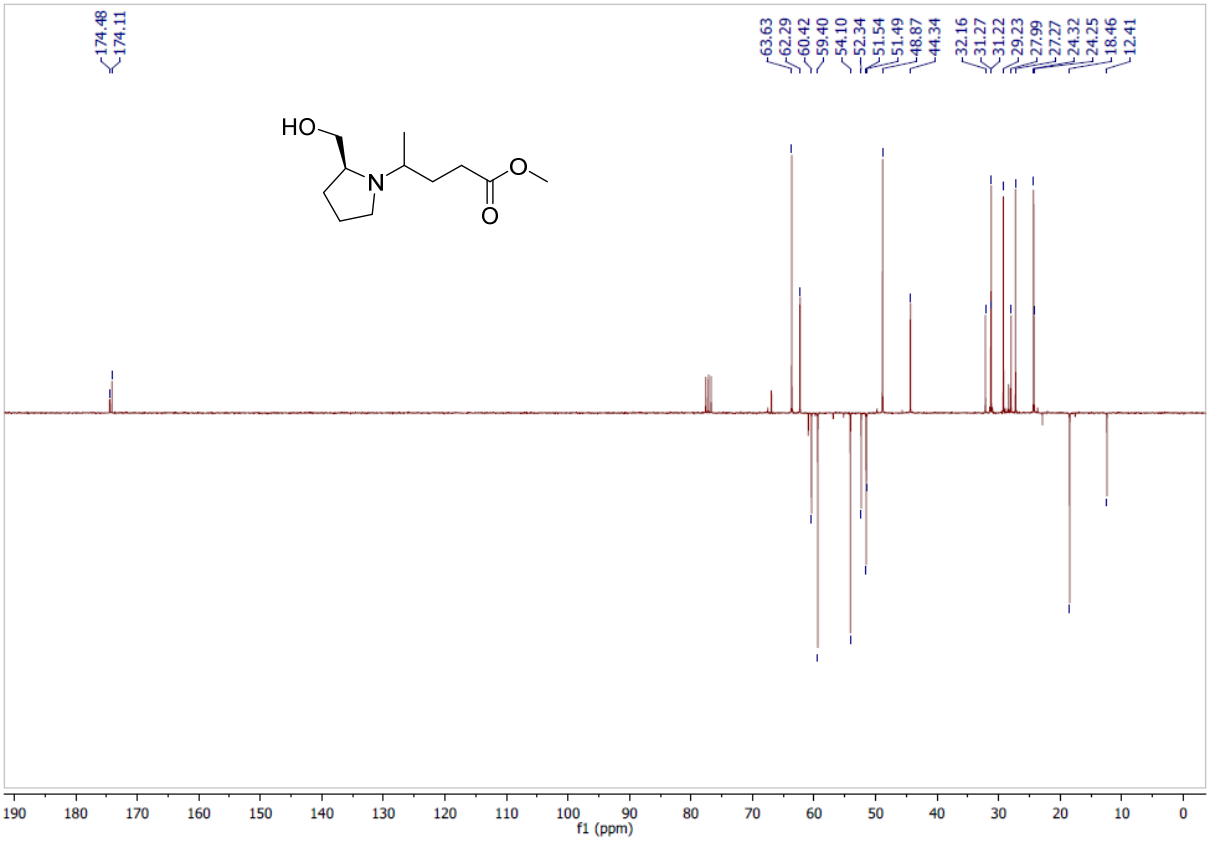


Figure S6. ^{13}C NMR Spectrum of **2b** ($CDCl_3$, 75 MHz)

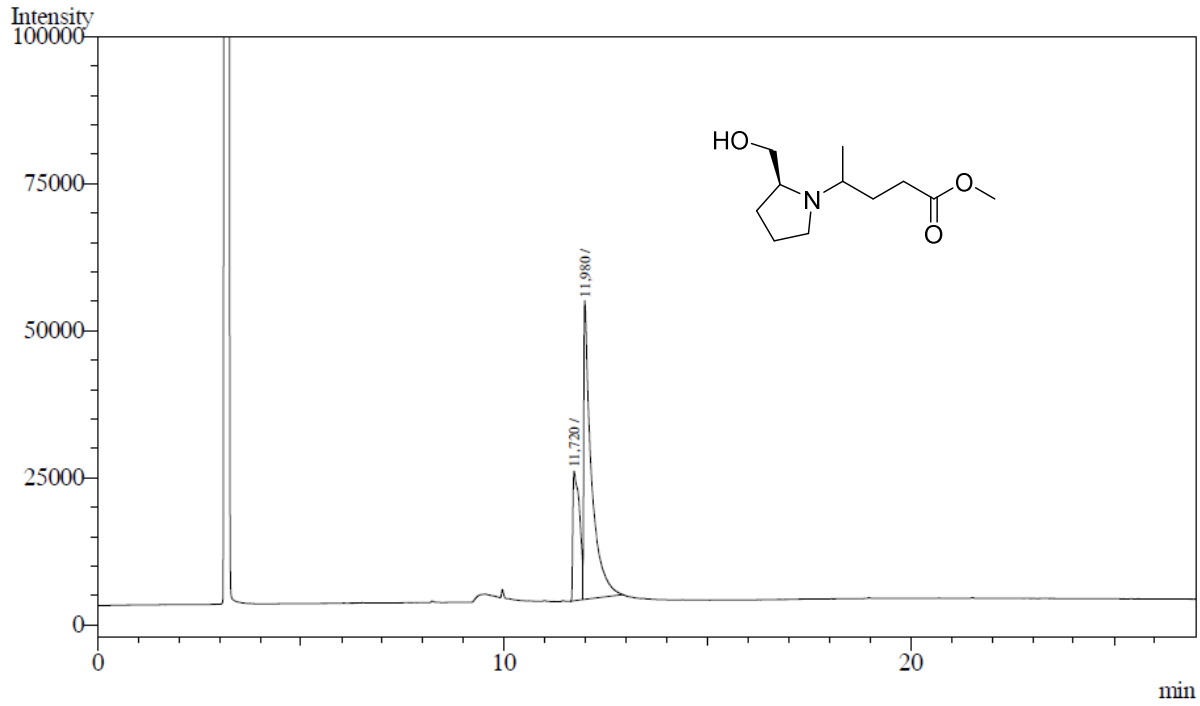


Figure S7. GC chromatogram of **2b**

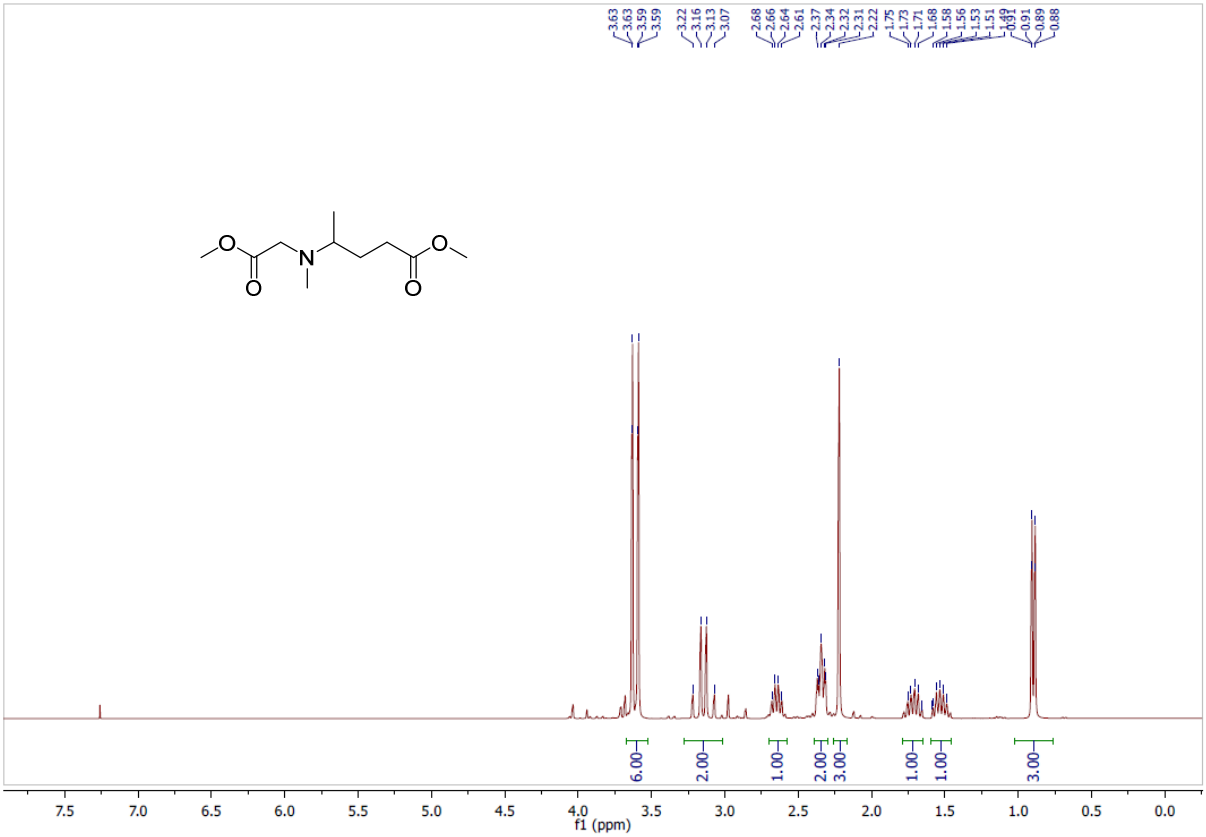


Figure S8. ^{1}H NMR Spectrum of **2c** ($CDCl_3$, 300 MHz)

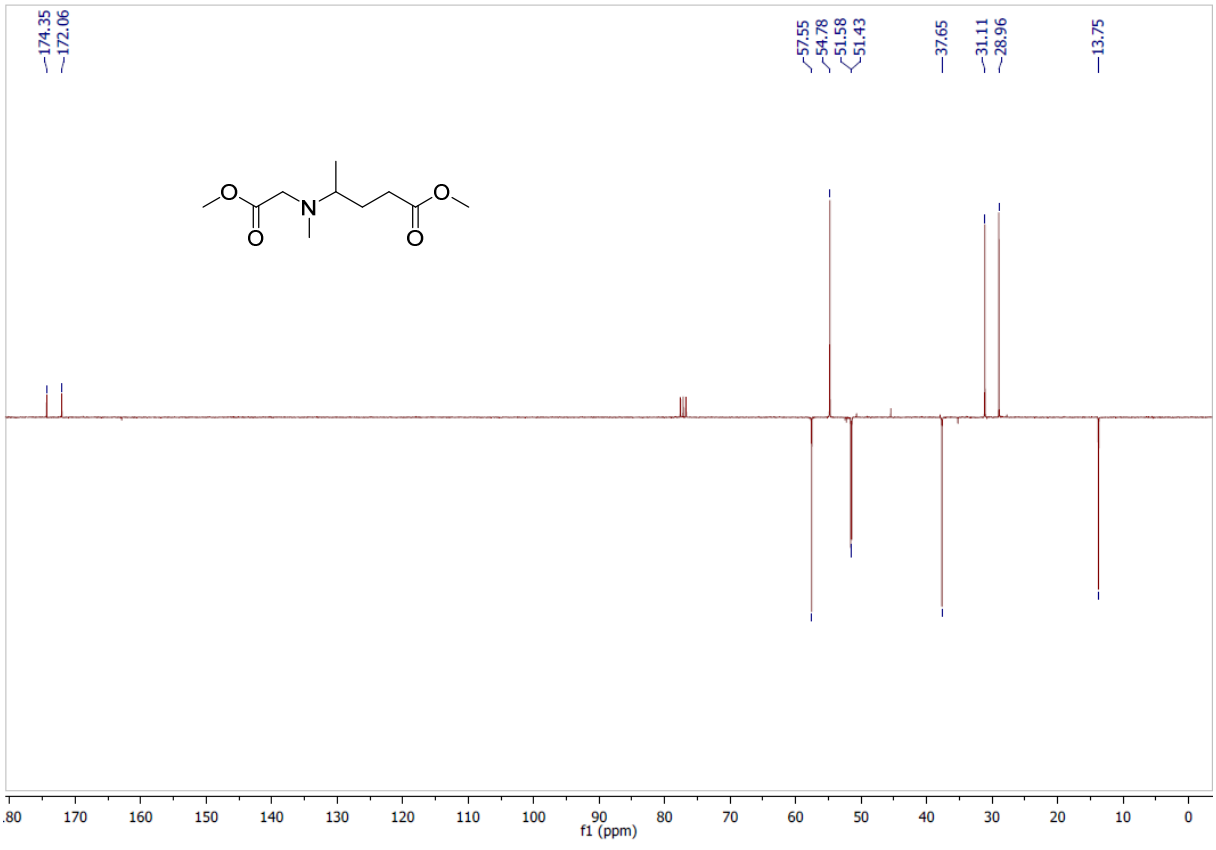


Figure S9. ^{13}C NMR Spectrum of **2c** ($CDCl_3$, 75 MHz)

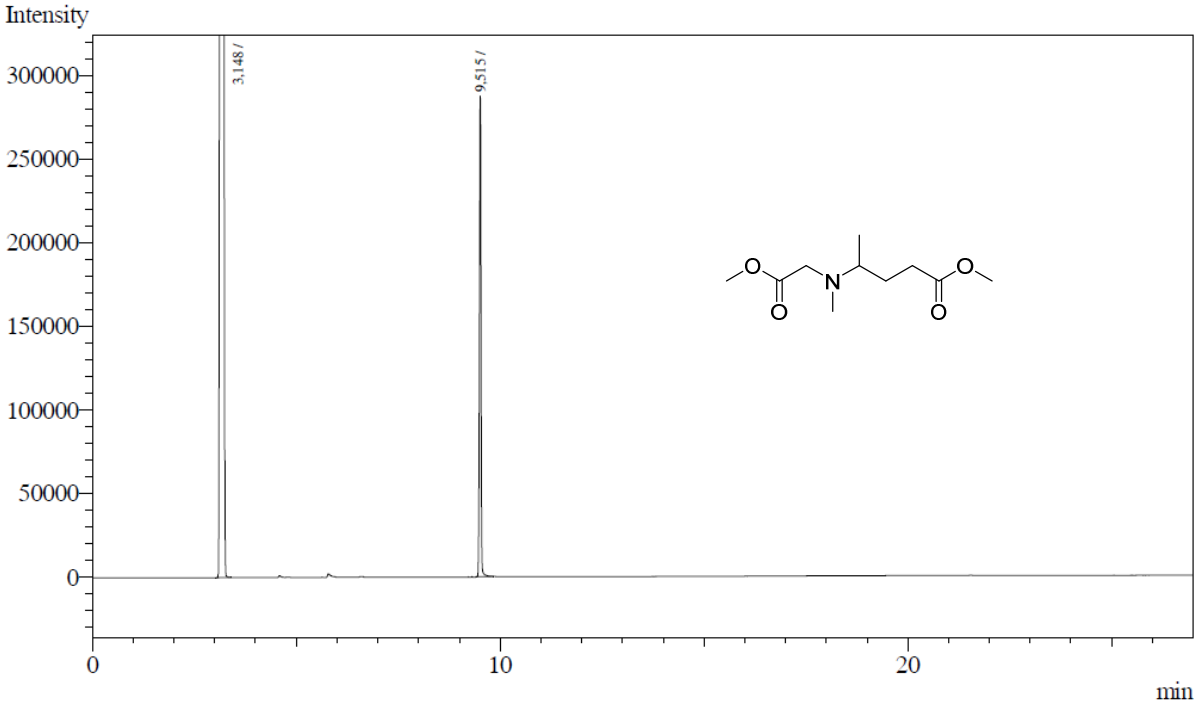


Figure S10. GC chromatogram of **2c**

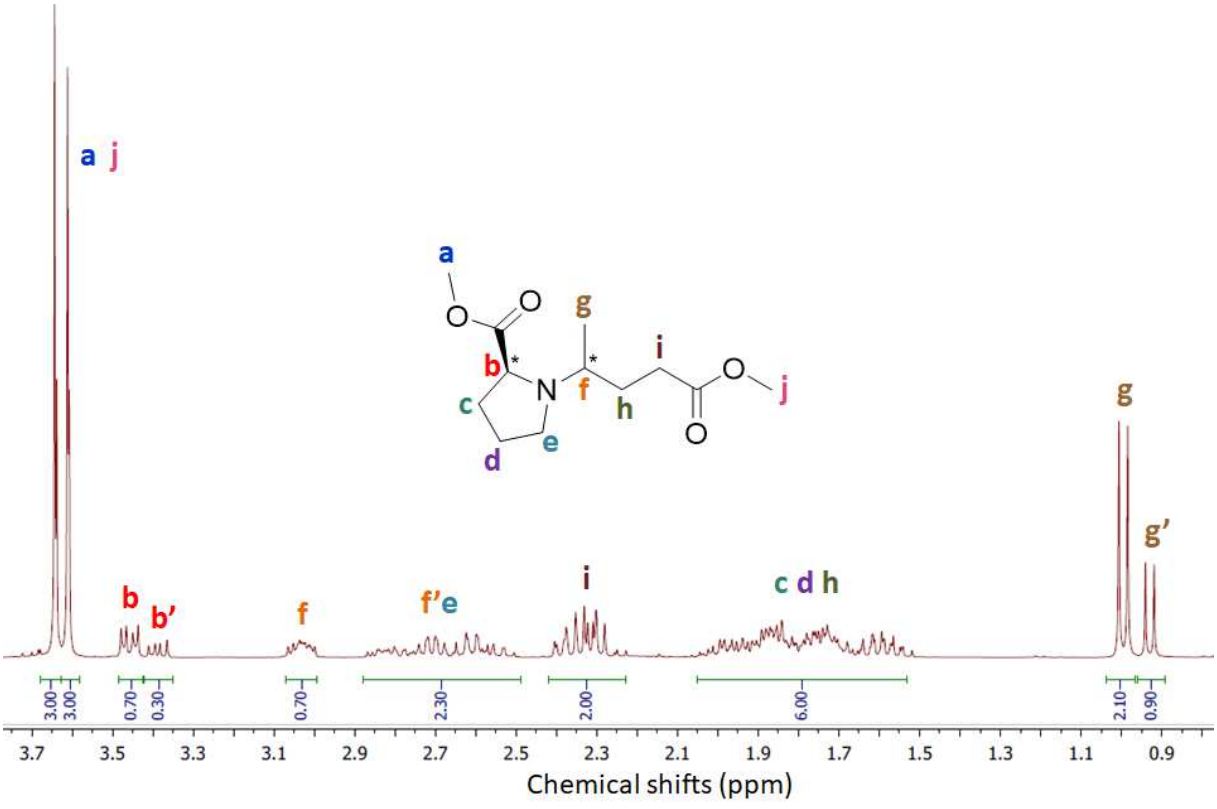


Figure S11. ^{1}H NMR Spectrum of **2d** ($CDCl_3$, 300 MHz)

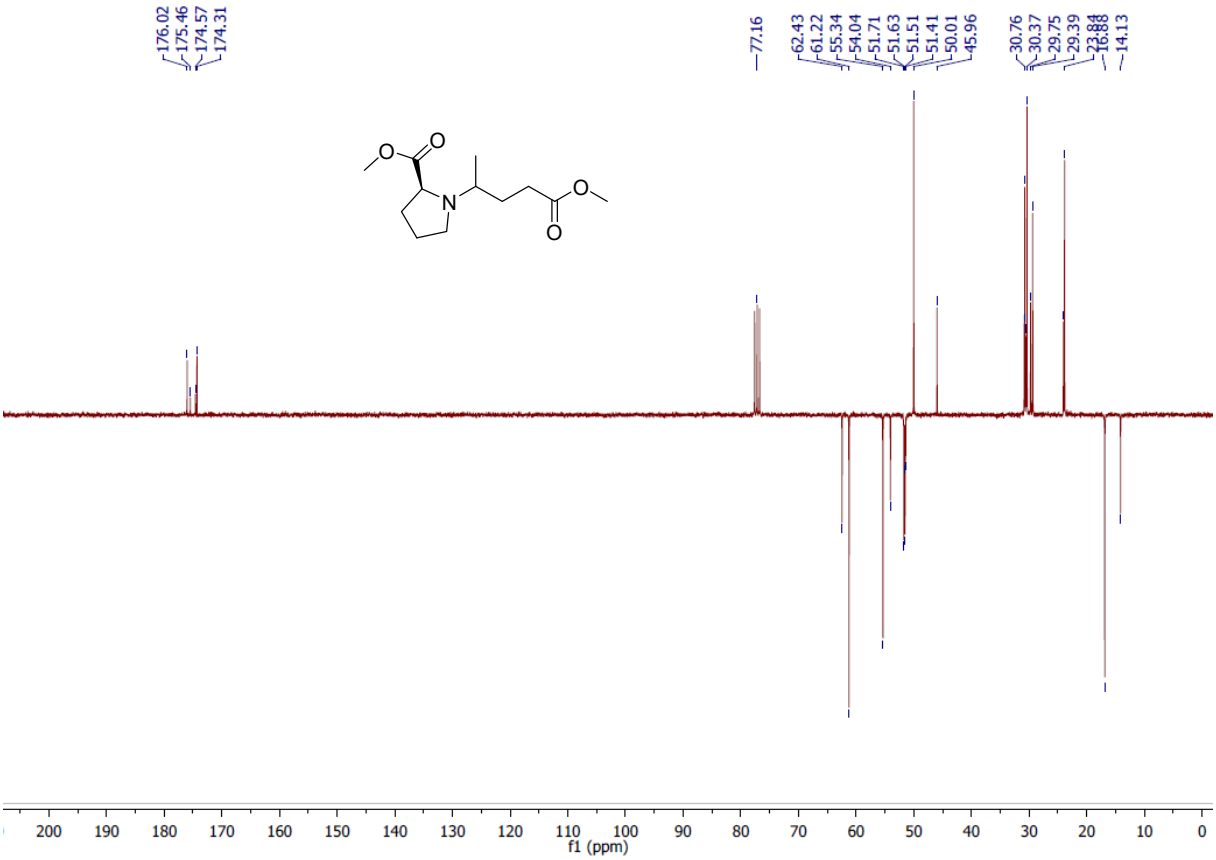


Figure S12. ^{13}C NMR Spectrum of **2d** ($CDCl_3$, 75 MHz)

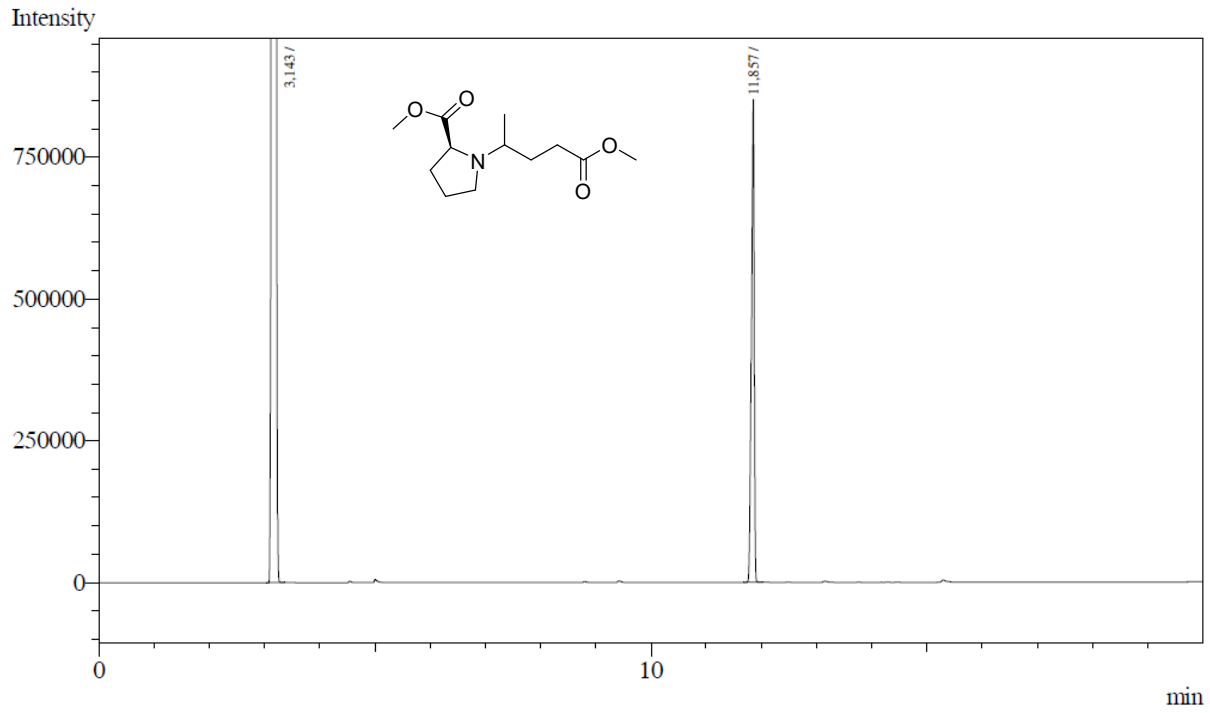


Figure S13. GC chromatogram of **2d**

6. NMR Spectra, SEC curves and DSC curves of polymers

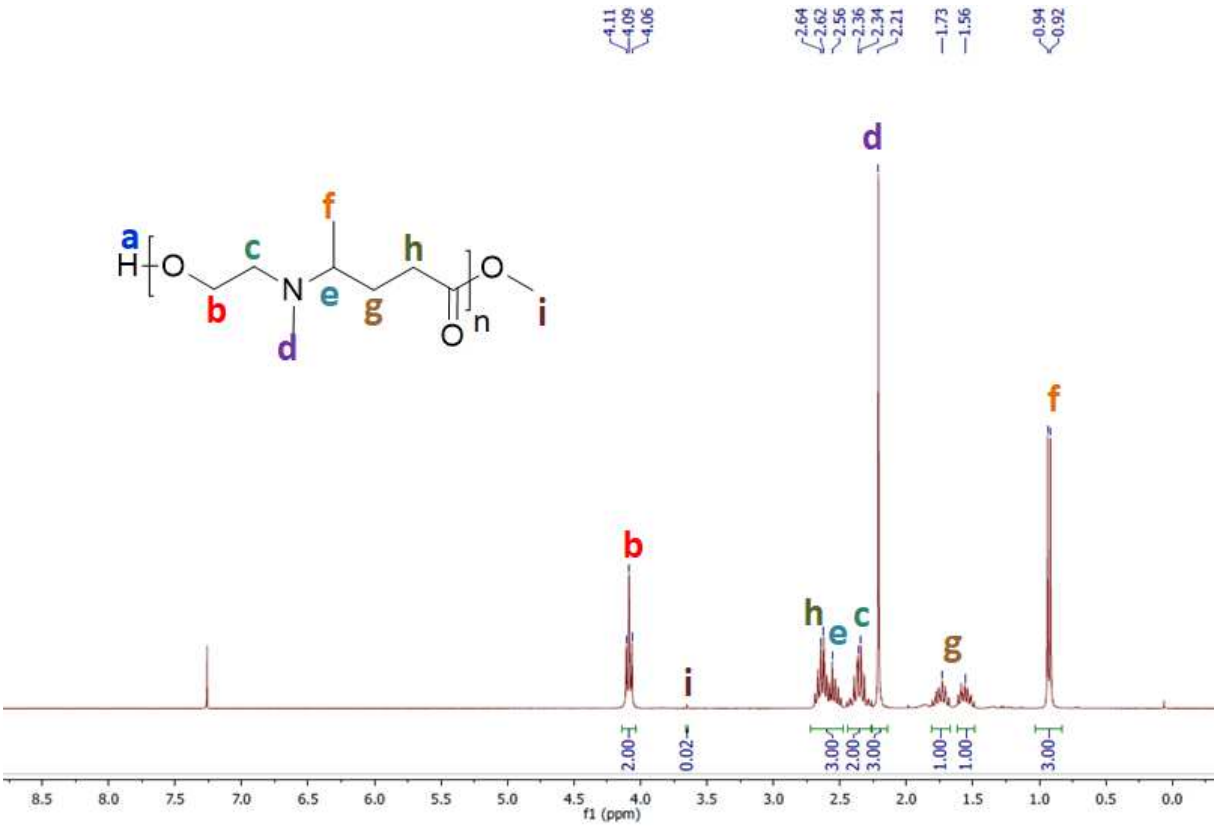


Figure S14. ^{1}H NMR Spectrum of **PEA-I** ($CDCl_3$, 300 MHz)

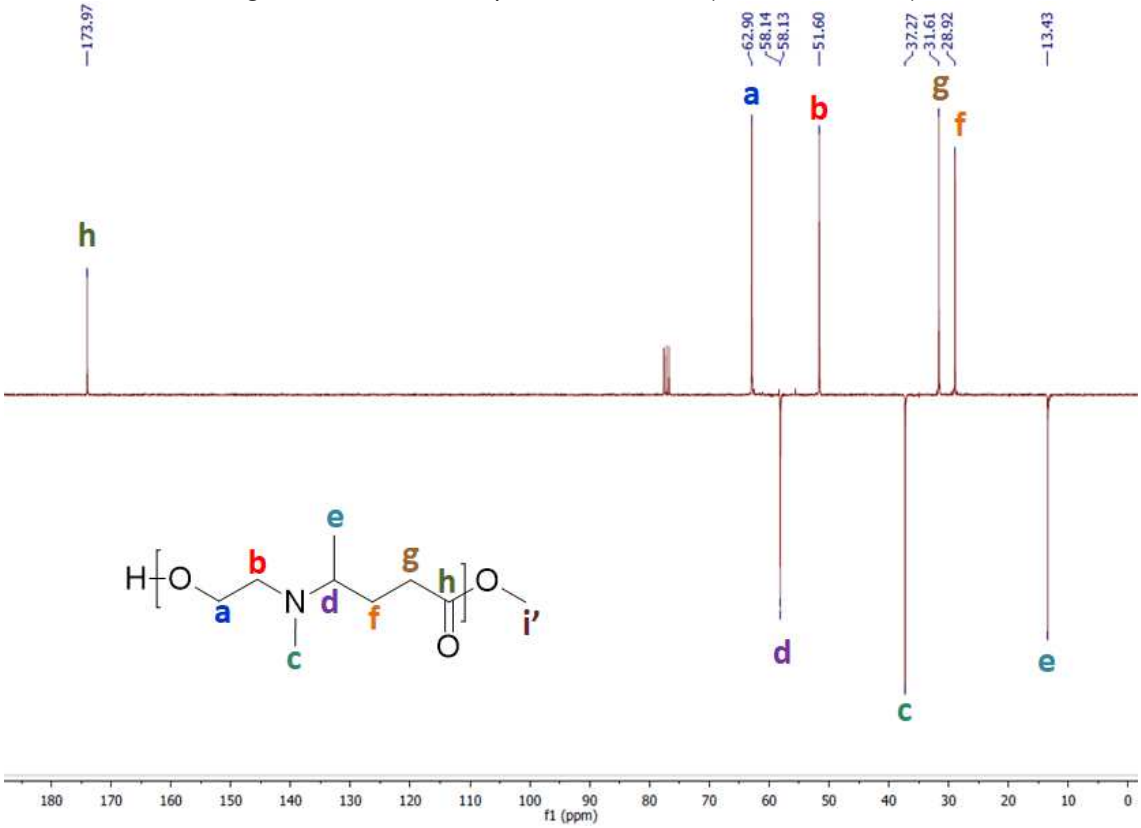


Figure S15. ^{13}C NMR Spectrum of **PEA-I** ($CDCl_3$, 75 MHz)

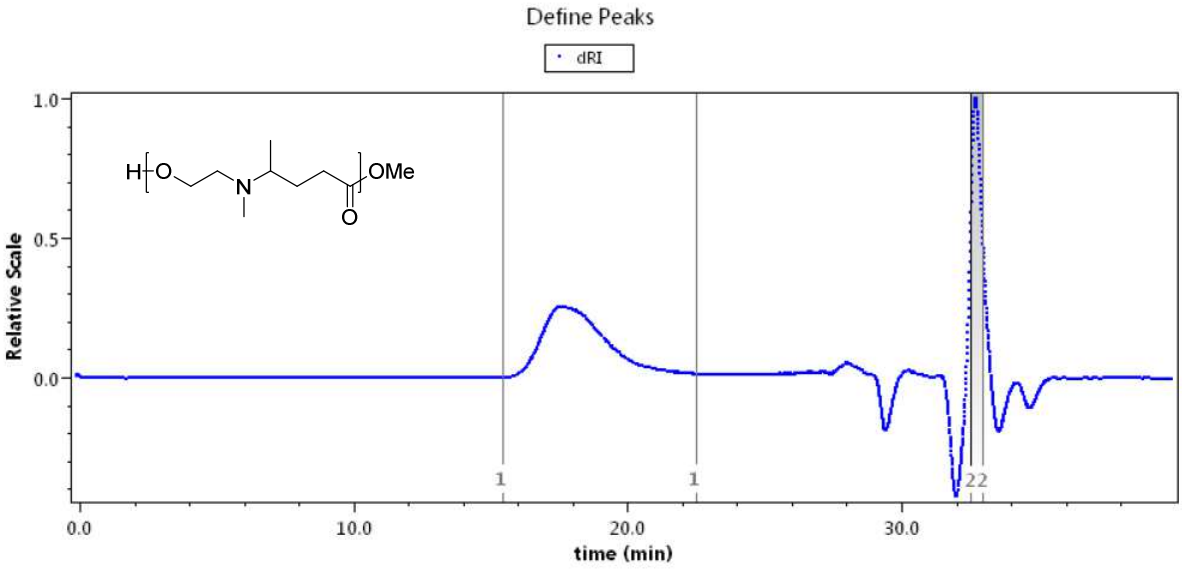


Figure S16. GPC curve and datas of **PEA-I** (THF, PS as standart)

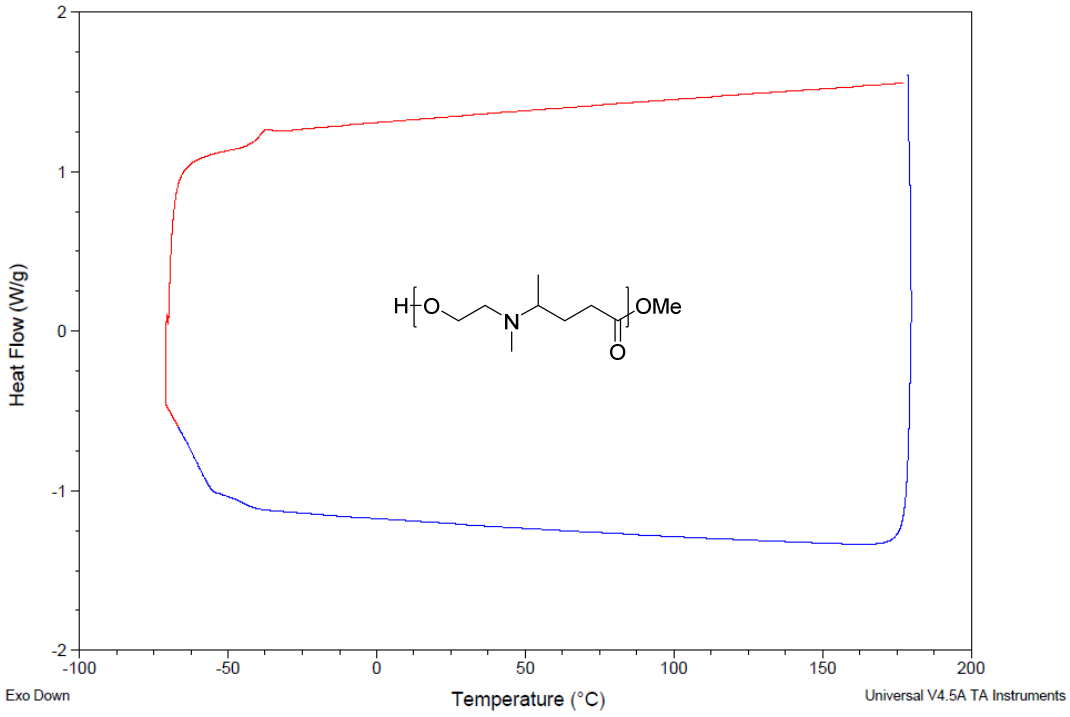


Figure S17. Second heating and cool down DSC curves of **PEA-I** (10°C/min, exo down)

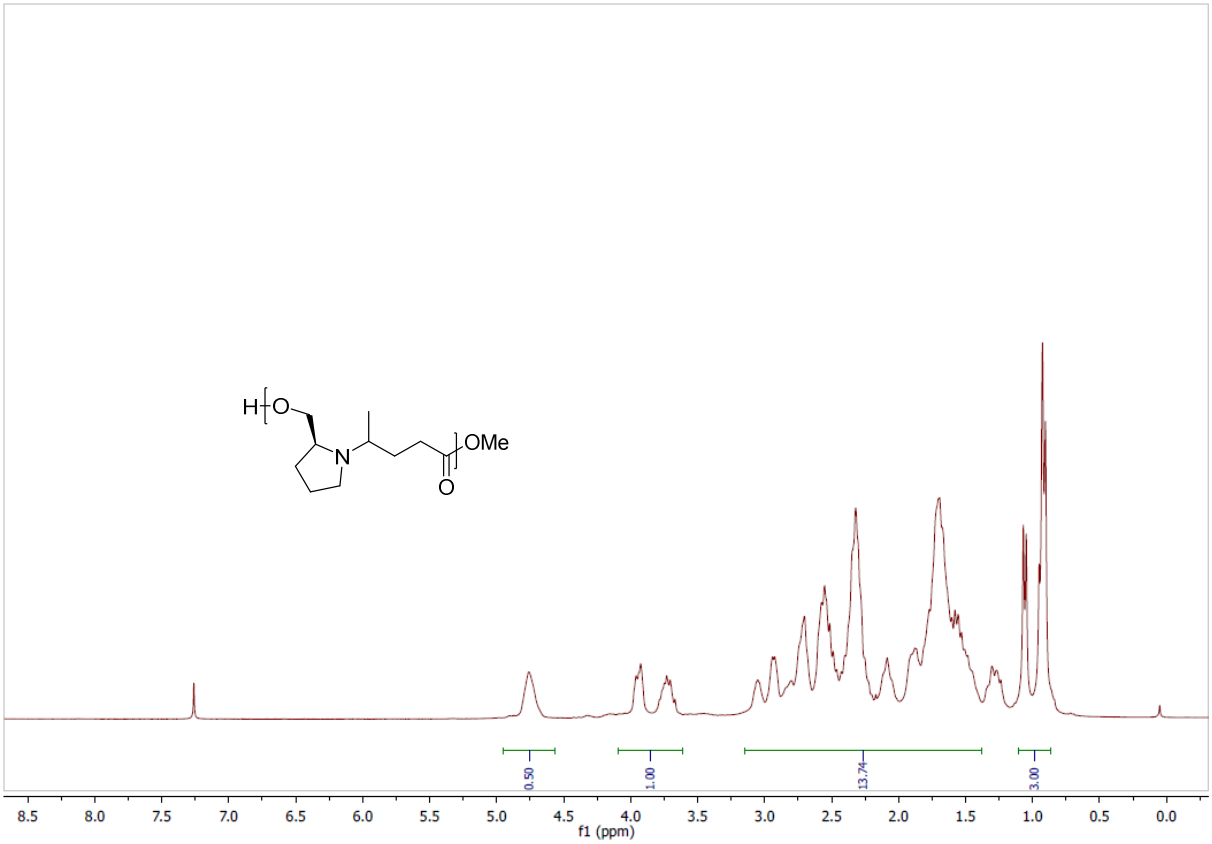


Figure S18. ^{1}H NMR Spectrum of **PEA-II** ($CDCl_3$, 300 MHz)

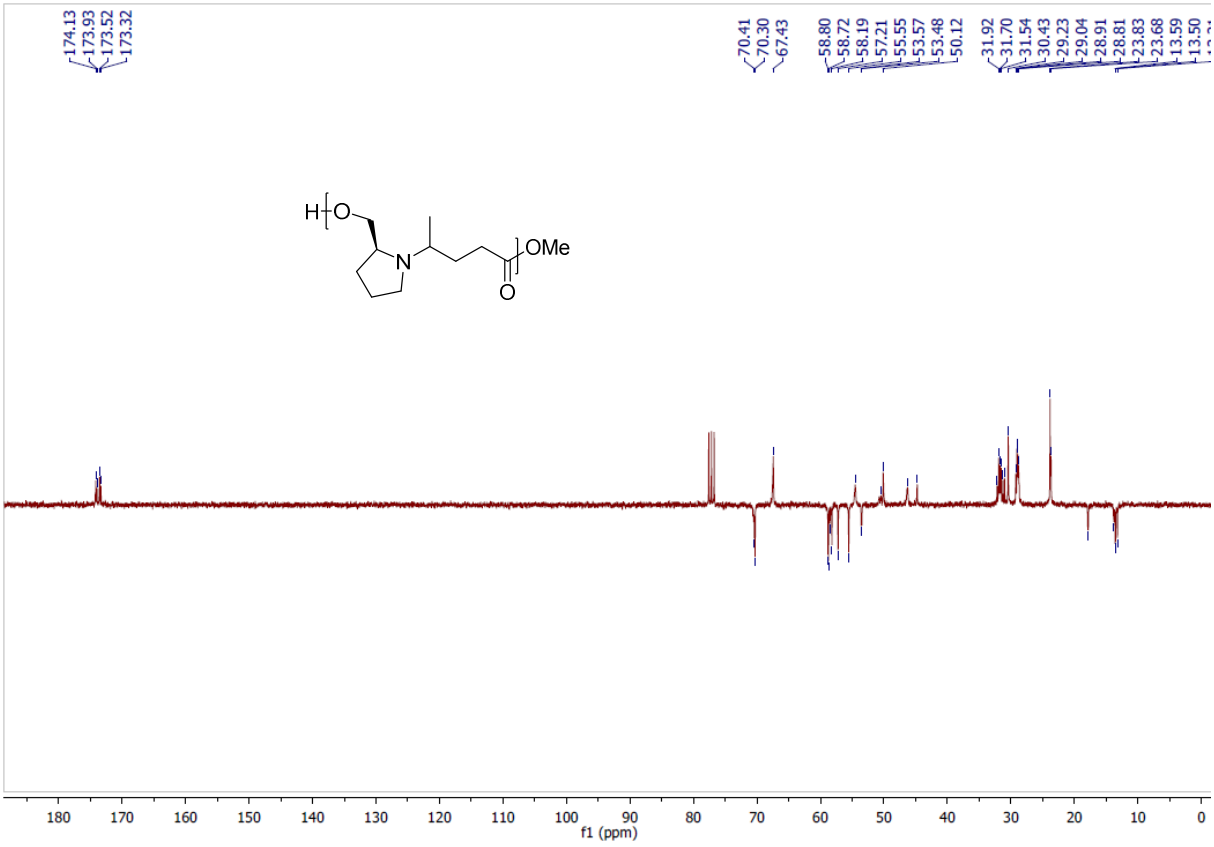


Figure S19. ^{13}C NMR Spectrum of **PEA-II** ($CDCl_3$, 75 MHz, 300 K)

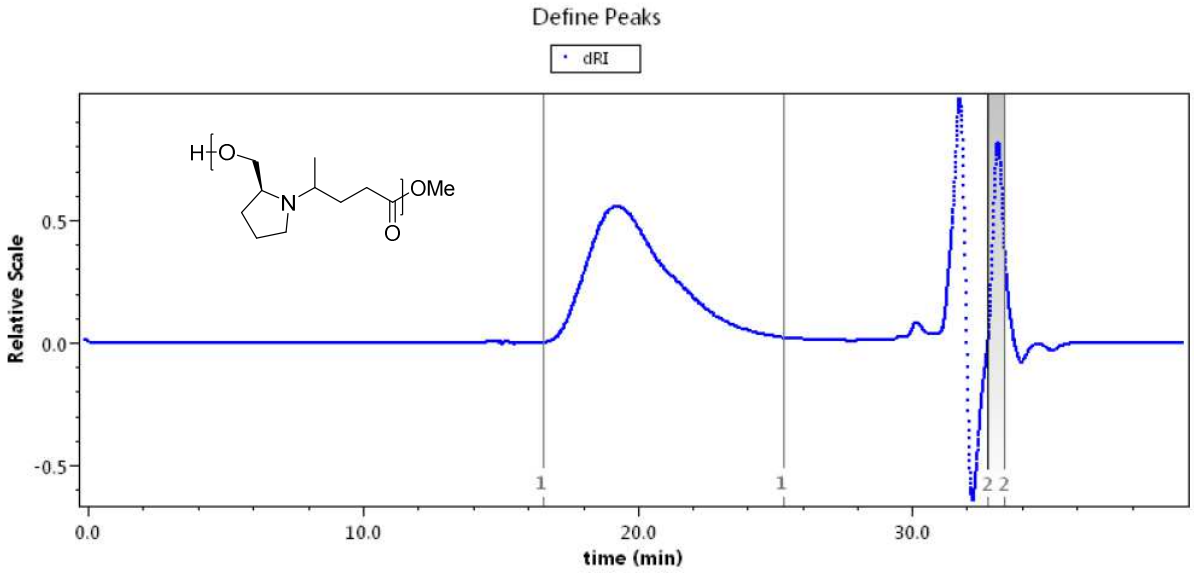


Figure S20. GPC curve and datas of **PEA-II** (THF, PS as standart)

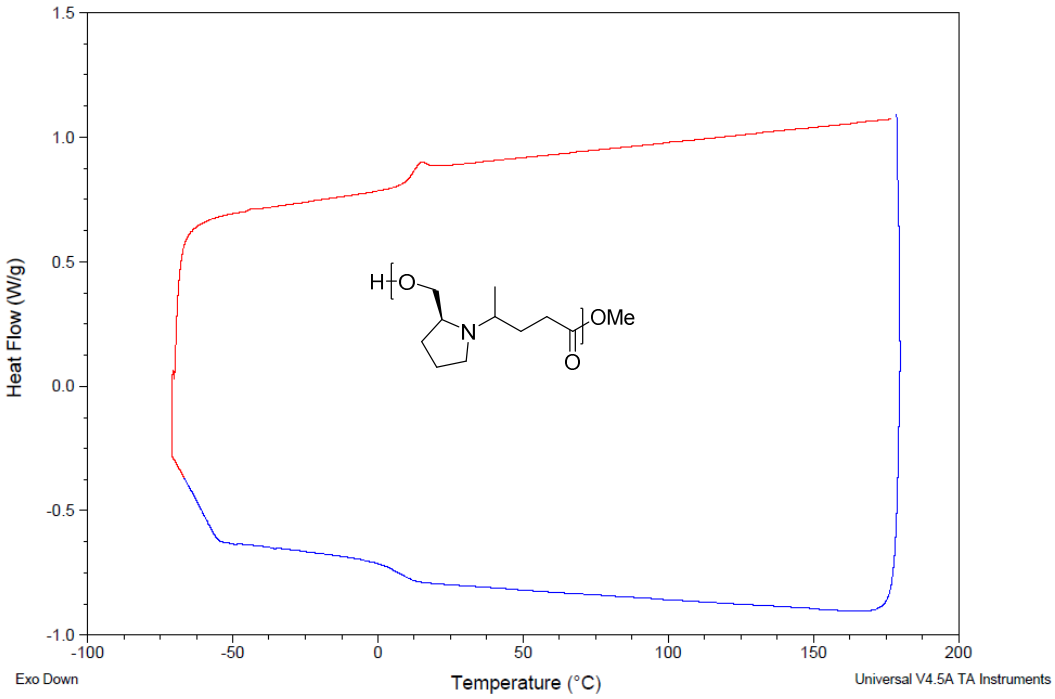


Figure S21. Second heating and cool down DSC curves of **PEA-II** (10°C/min, exo down)

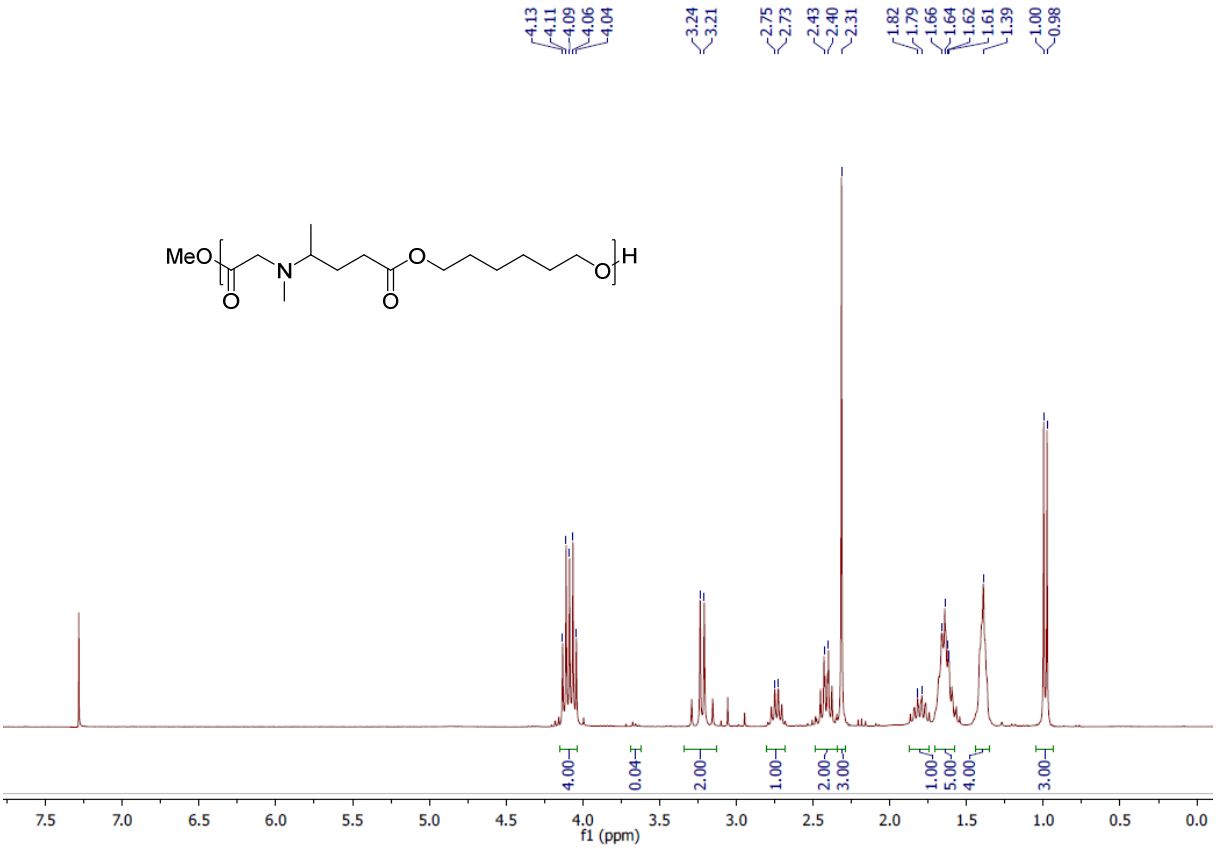


Figure S22. ^{1}H NMR Spectrum of **PEA-III** ($CDCl_3$, 300 MHz)

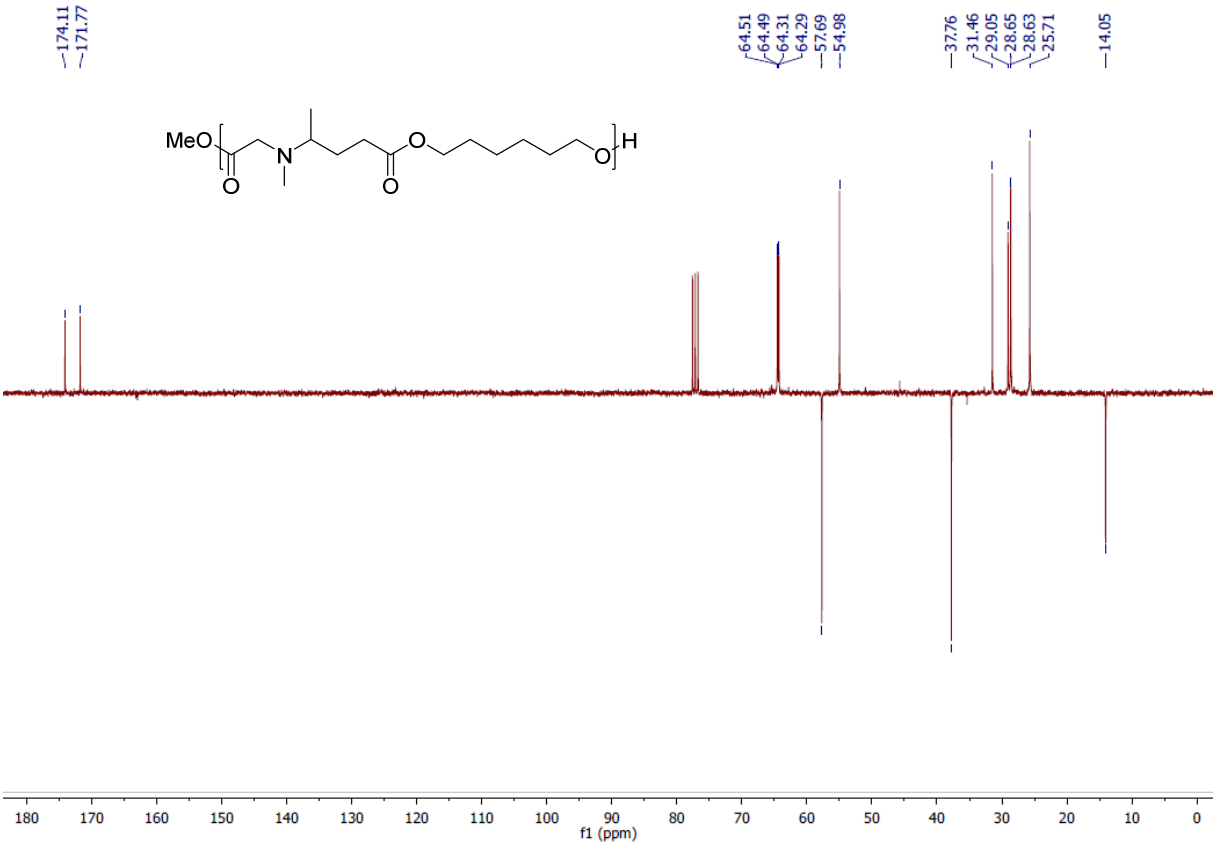


Figure S23. ^{13}C NMR Spectrum of **PEA-III** ($CDCl_3$, 75 MHz)

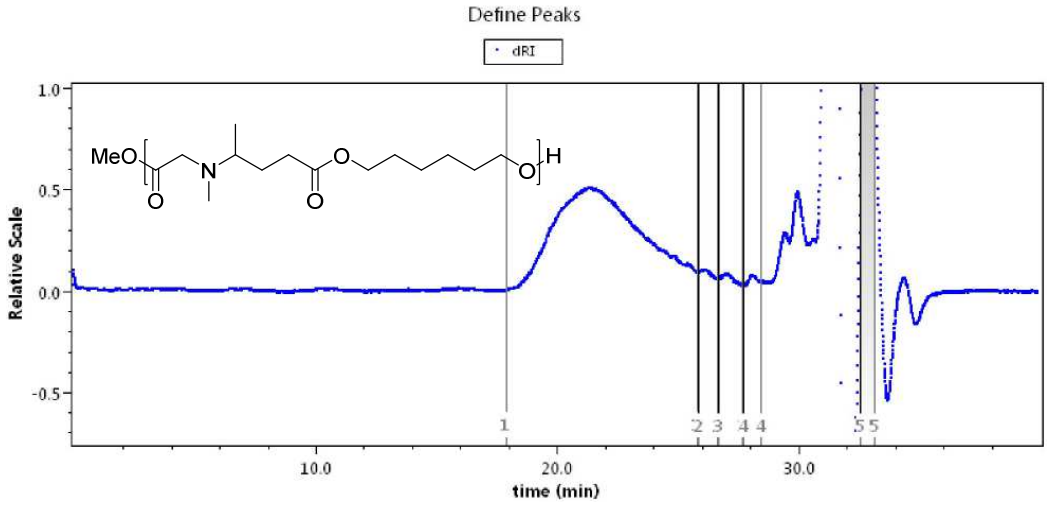


Figure S24. GPC curve and datas of **PEA-III** (THF, PS as standart)

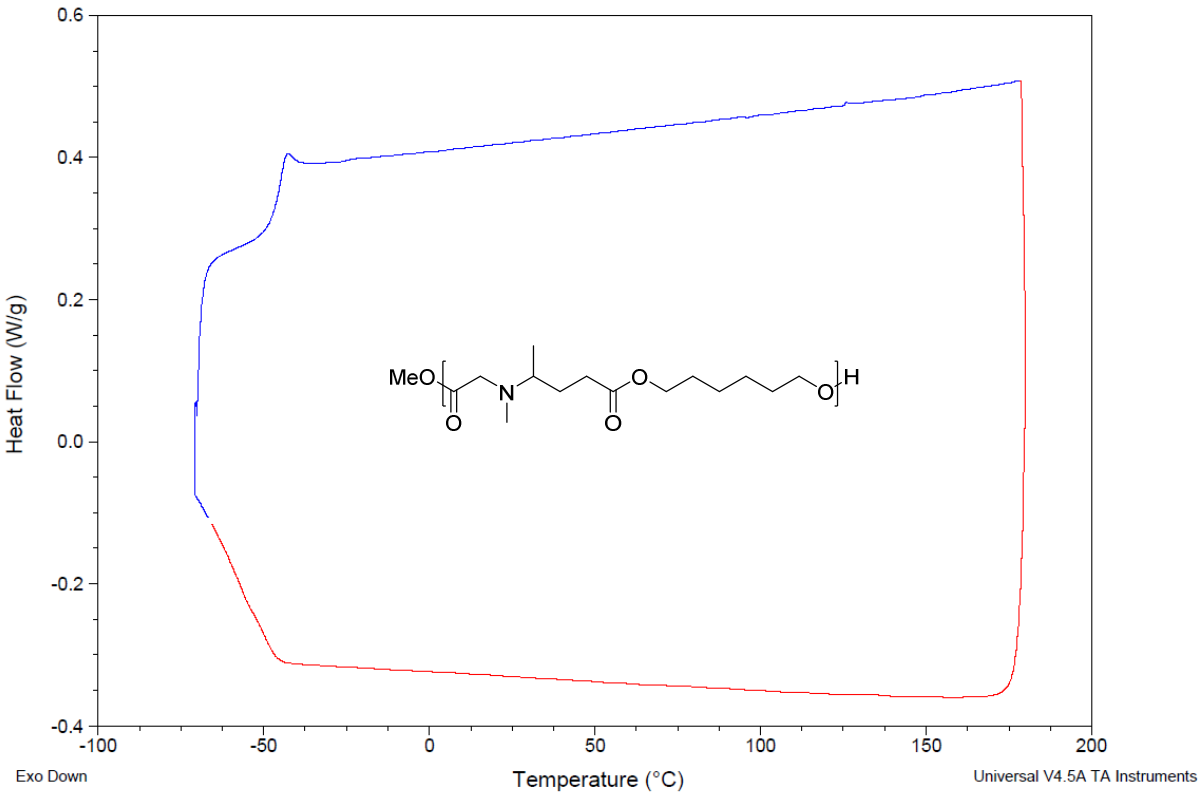


Figure S25. Second heating and cool down DSC curves of **PEA-III** (10°C/min, exo down)

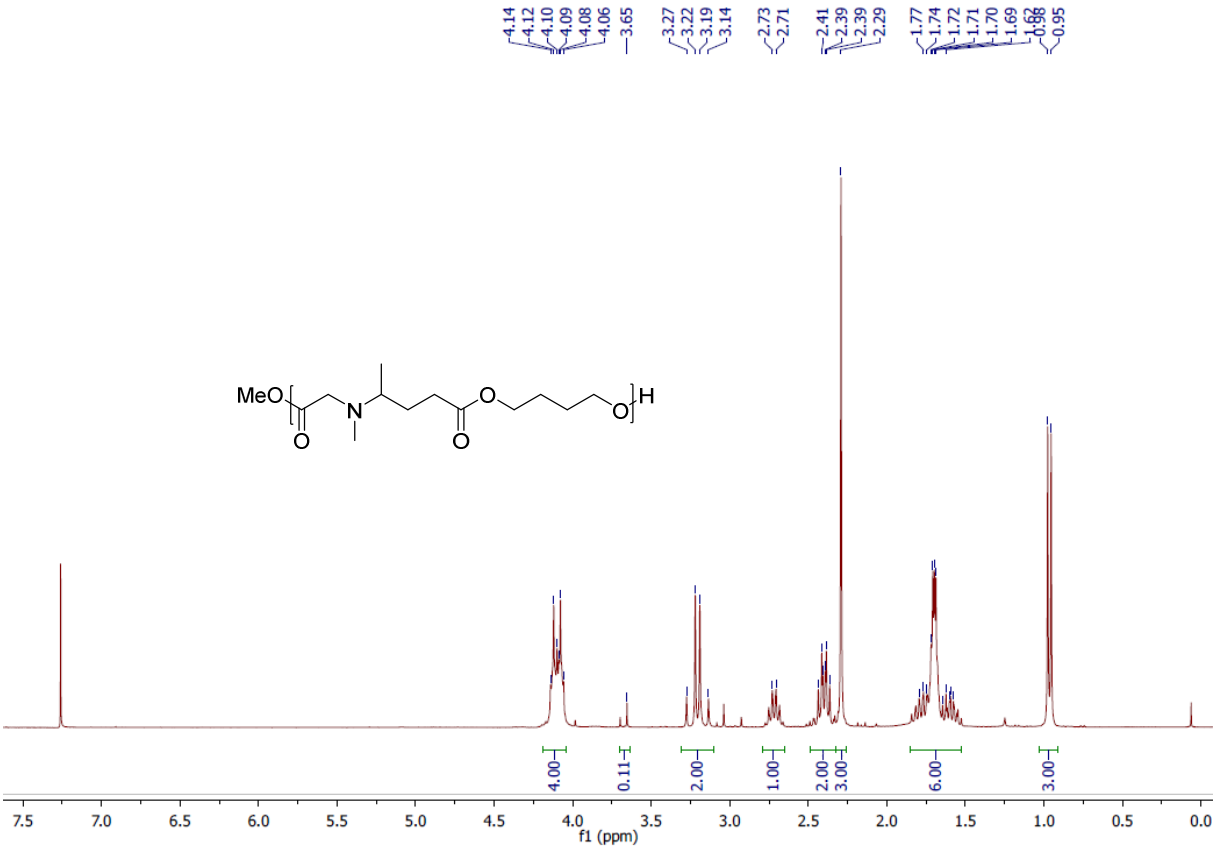


Figure S26. ^{1}H NMR Spectrum of **PEA-IV** ($CDCl_3$, 300 MHz)

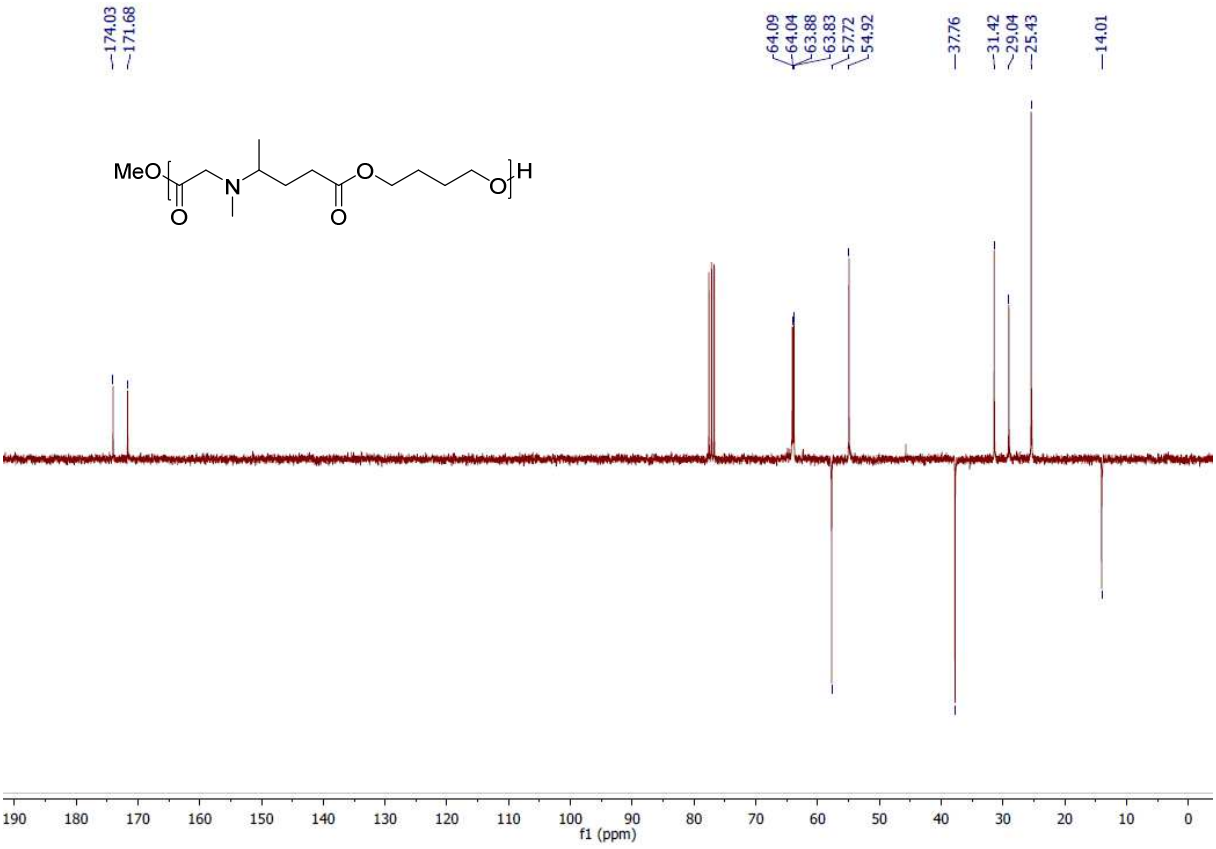


Figure S27. ^{13}C NMR Spectrum of **PEA-IV** ($CDCl_3$, 75 MHz)

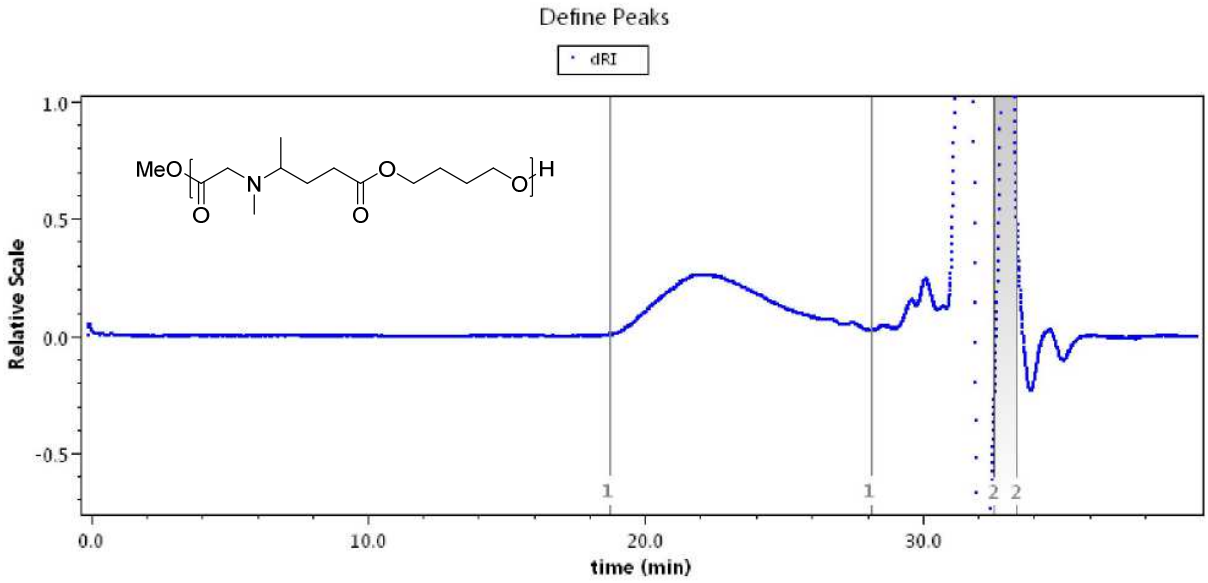


Figure S28. GPC curve and datas of **PEA-IV** (THF, PS as standart)

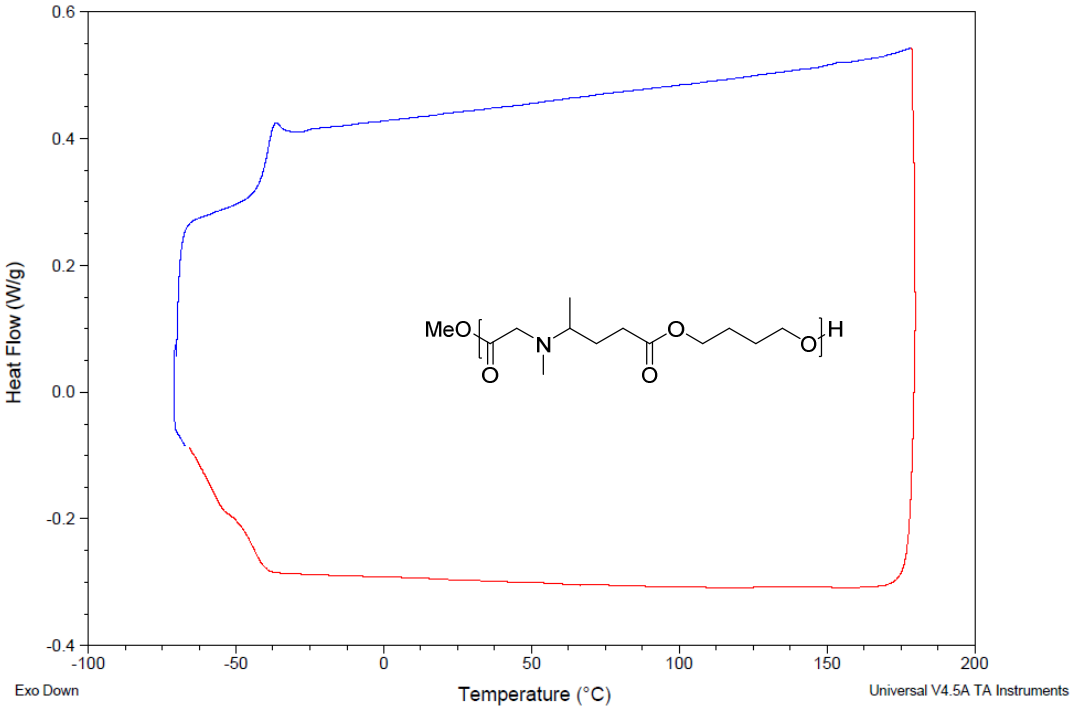


Figure S29. Second heating and cool down DSC curves of **PEA-IV** (10°C/min, exo down)

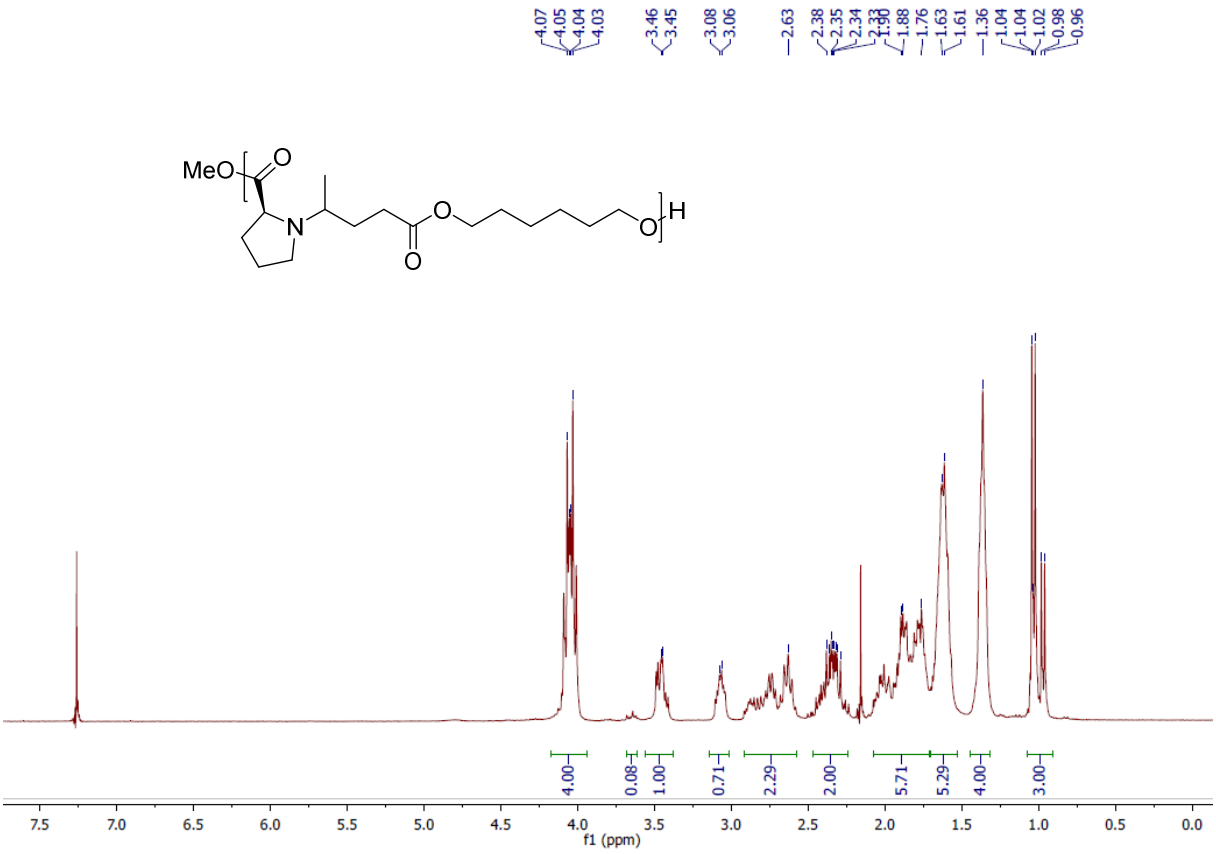


Figure S30. ^{1}H NMR Spectrum of **PEA-V** ($CDCl_3$, 300 MHz)

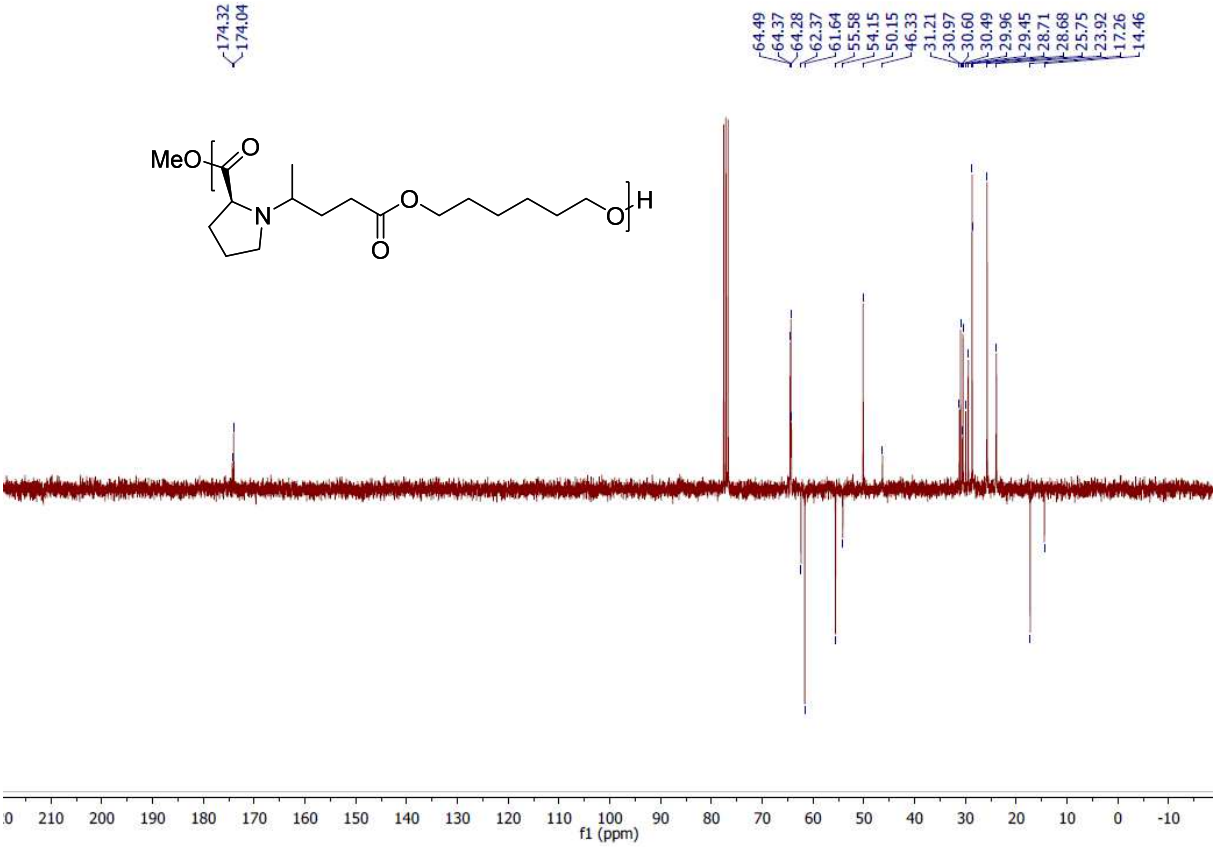


Figure S31. ^{13}C NMR Spectrum of **PEA-V** ($CDCl_3$, 75 MHz)

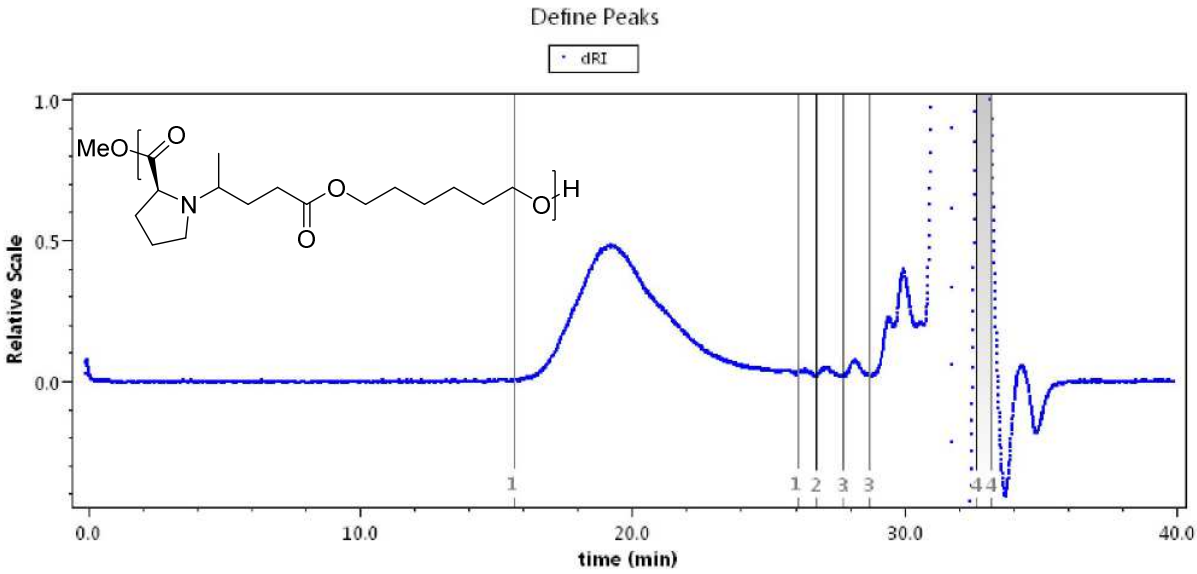


Figure S32. GPC curve and datas of **PEA-V** (THF, PS as standart)

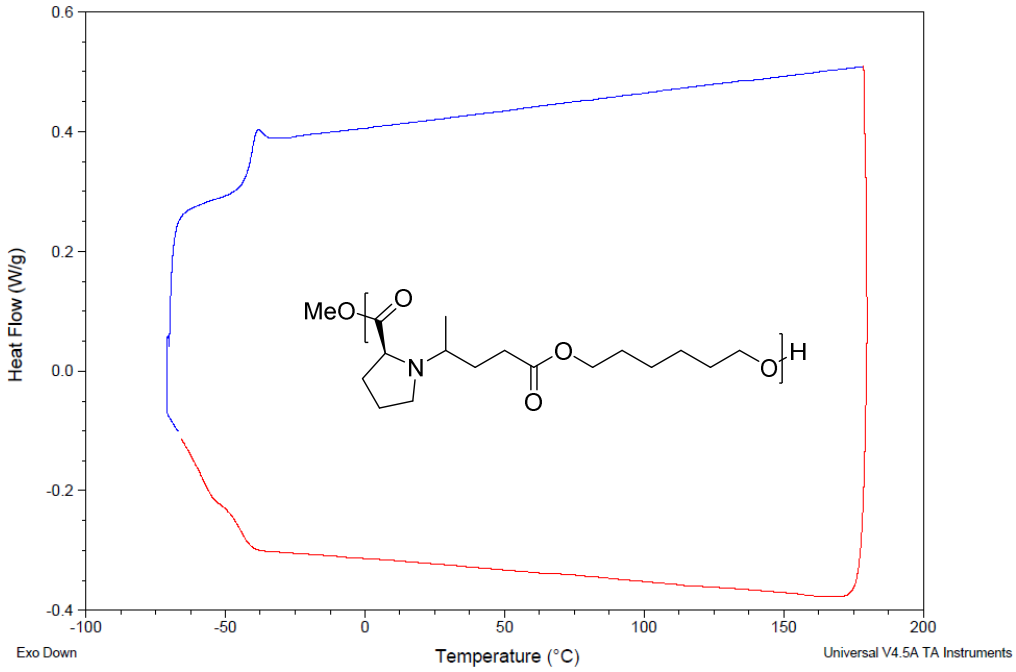


Figure S33. Second heating and cool down DSC curves of **PEA-V** (10°C/min, exo down)

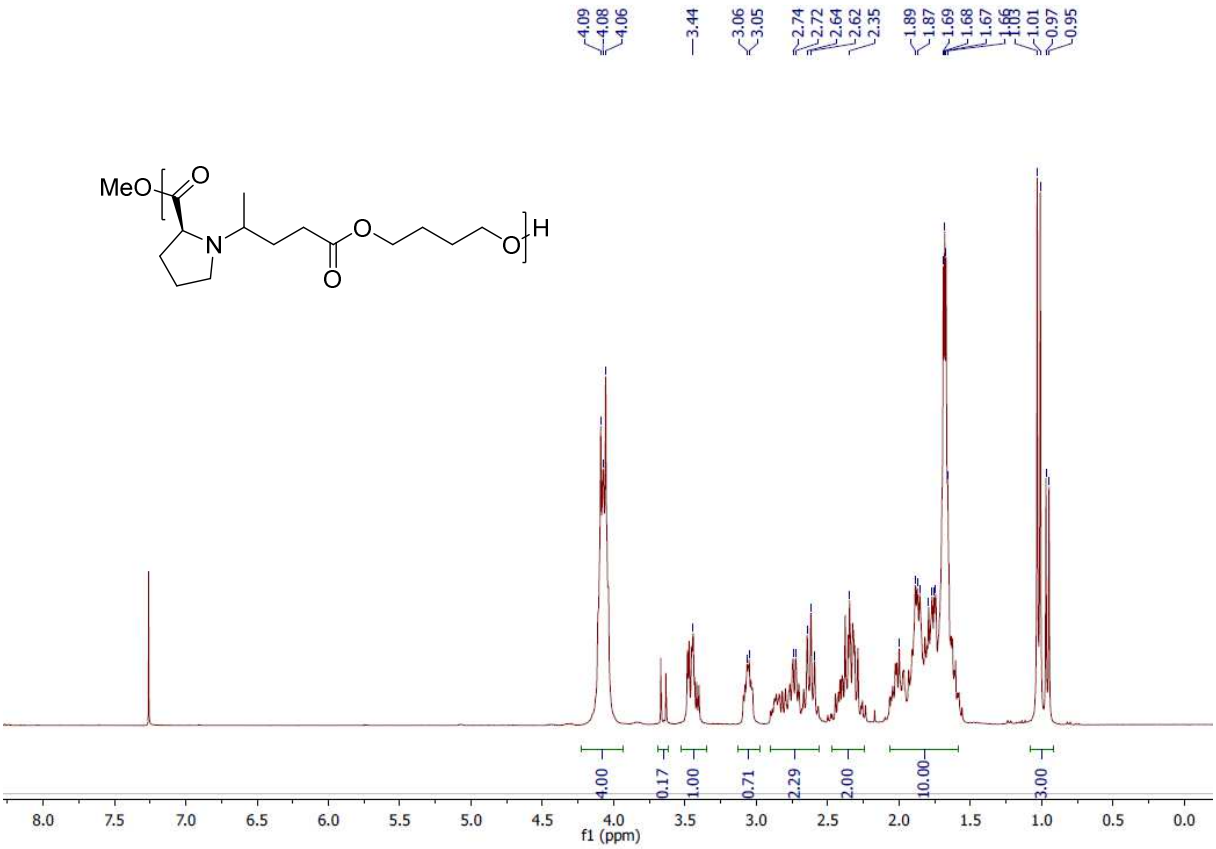


Figure S34. ^{1}H NMR Spectrum of **PEA-VI** ($CDCl_3$, 300 MHz)

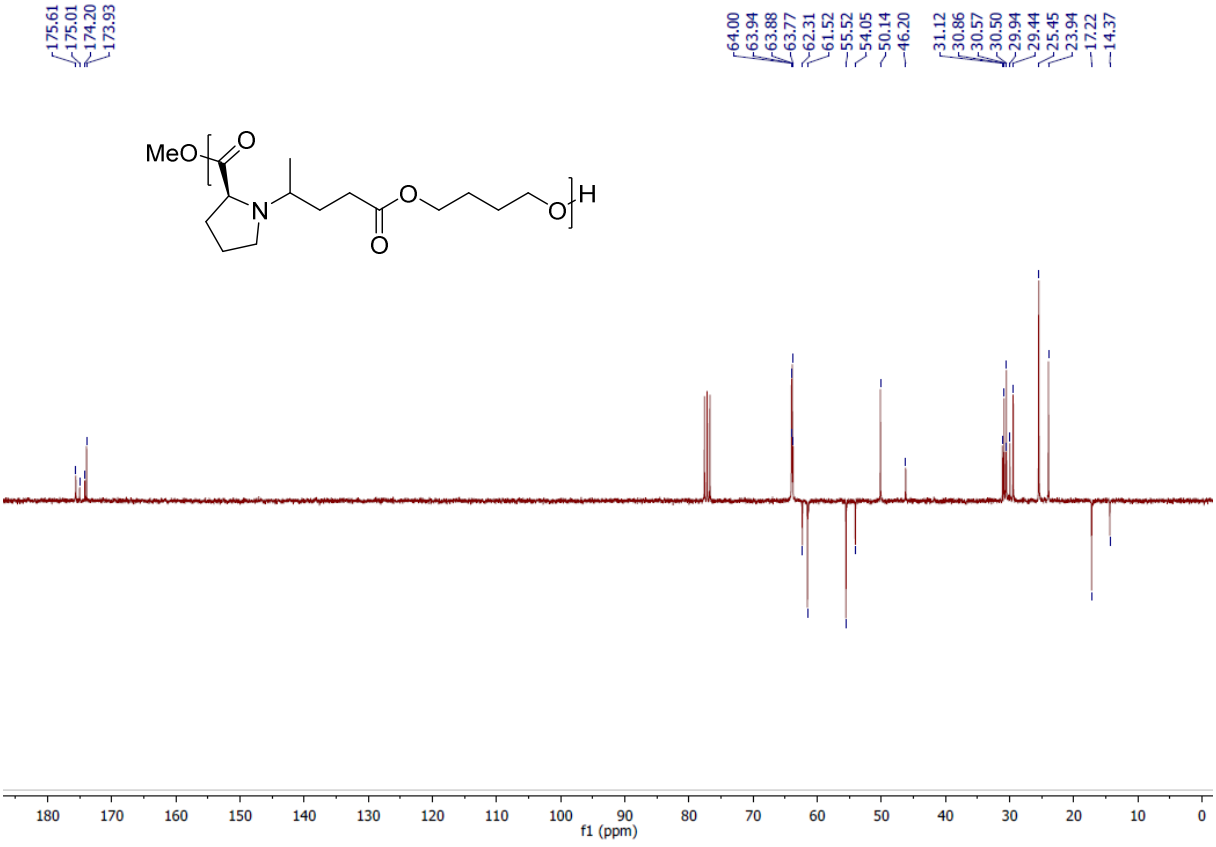


Figure S35. ^{13}C NMR Spectrum of **PEA-VI** ($CDCl_3$, 75 MHz)

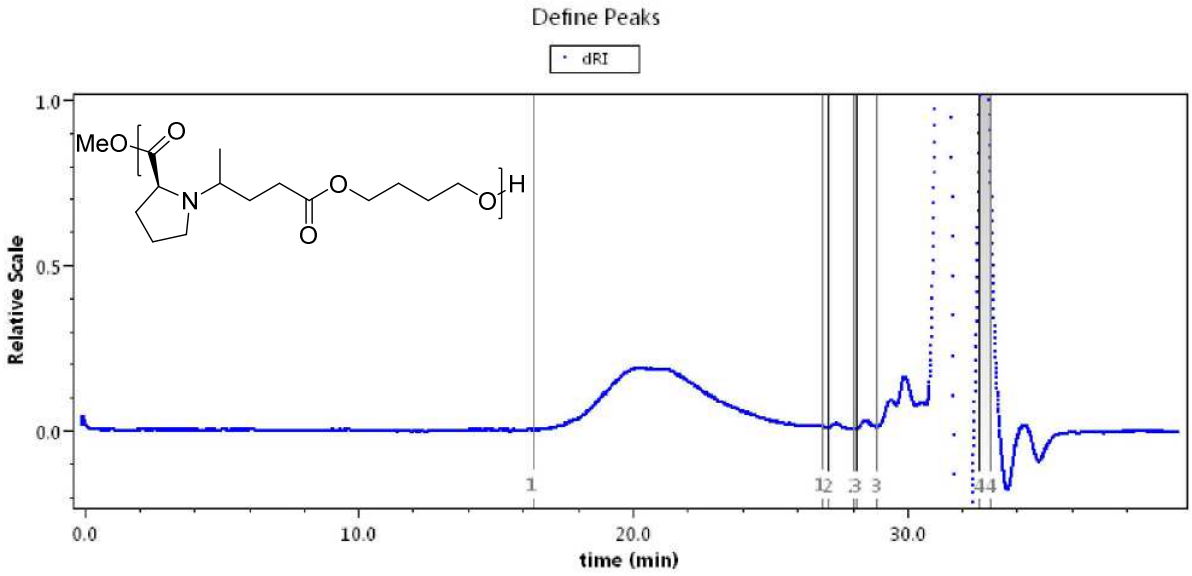


Figure S36. GPC curve and datas of **PEA-VI** (THF, PS as standart)

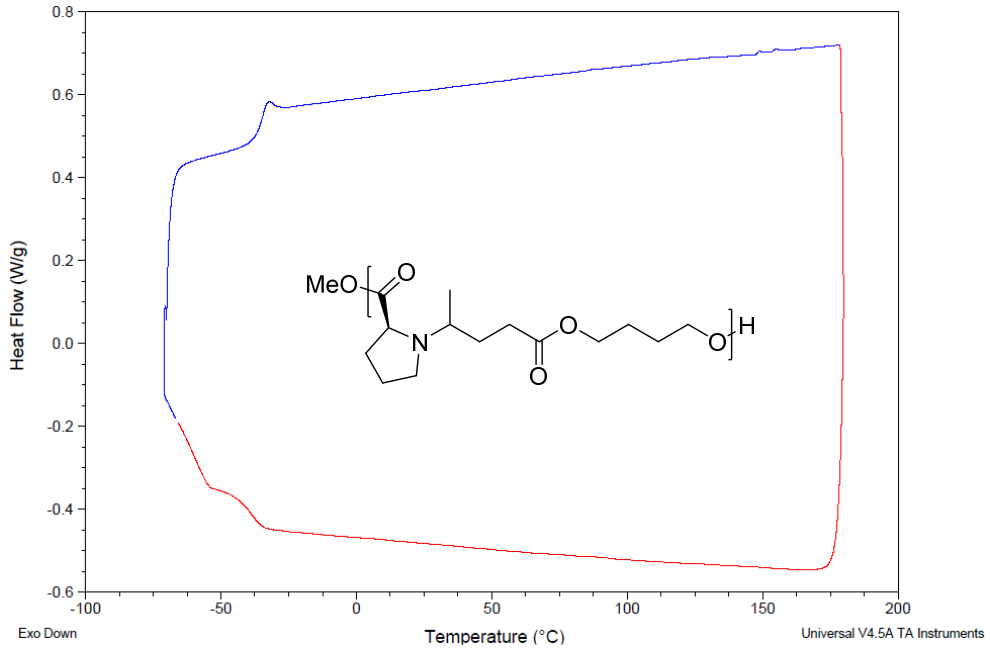


Figure S37. Second heating and cool down DSC curves of **PEA-VI** (10°C/min, exo down)

7. NMR spectrum of protonated polymer PEA-I-H$^+$

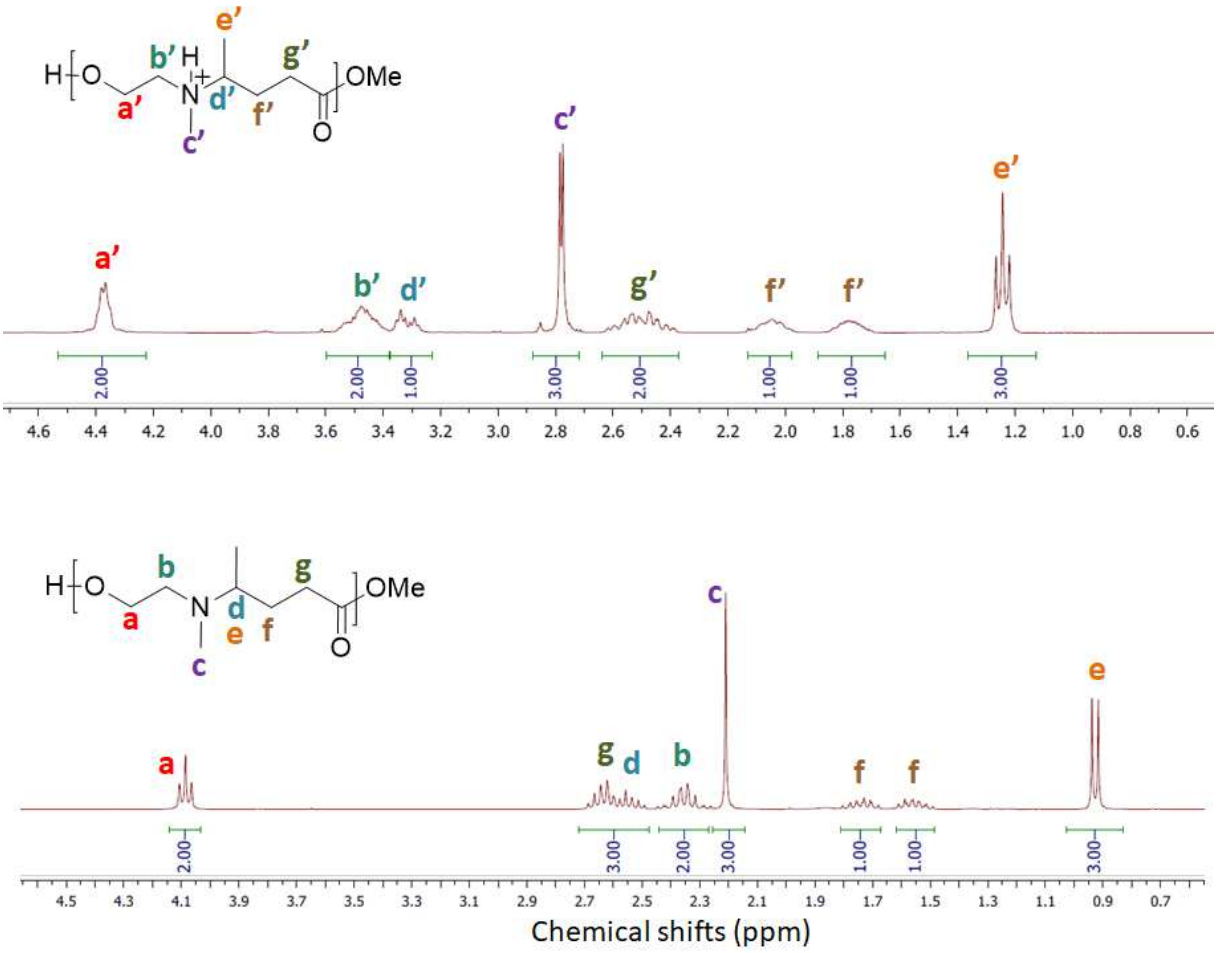


Figure S38. ^{1}H NMR Spectra of **PEA-I** in $CDCl_3$(bottom) and in D_2O containing 5% of deuterated trifluoroacetic acid (TFA-d) (top) (300 MHz).