ELECTRONIC SUPPORTING INFORMATION

Direct Polymerization of Levulinic Acid via Ugi Multicomponent Reaction

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Experimental Section:

1. Materials

The following chemicals were used as received: levulinic acid **1** 98% (Sigma Aldrich), ethylenediamine **2** >99% (Sigma Aldrich), 1,6-diisoncyanohexane **3** 98% (Sigma Aldrich), hexamethylenediamine **4** 98% (Sigma Aldrich), 1,12-diaminododecane 98% **5** (Sigma Aldrich), spermine **6** ≥97.0% (Sigma), *p*-phenylenendiamine (Sigma Aldrich), tris(2-aminoethyl)amine 96% (Sigma Aldrich), poly(ethylene glycol) bis(3-amino propyl) terminated M_n ~ 1500 Da (Sigma Aldrich), chloroform-d 99.8 atom% D (Sigma Aldrich). All solvents were used without further purification, unless otherwise noted.

2. Characterization

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AV-III 400 for ^{1}H- and at 101 MHz for ^{13}C NMR measurements. $CDCl_3$ was used as solvent and the resonance signal at 7.26 ppm (^{1}H) and 77.16 ppm (^{13}C) served as reference for the chemical shift δ.

Gel permeation chromatography (GPC) measurements were conducted on an Agilent 1260 infinity system operating in DMF with 5 mM $NH_4BF_4$and equipped with refractive index detector and variable wavelength detector, 2 PLgel 5 µm mixed-C columns (300 × 7.5 mm), a PLgel 5 mm guard column (50 × 7.5 mm) and an autosampler. The instrument was calibrated with linear narrow poly(methyl methacrylate) standards in range of 550 to 46 890 g·mol. All samples were filtered with a 0.2 µm Nylon 66 before analysis.

Matrix assisted laser desorption/ionisation – time of flight mass spectroscopy (MALDI-ToF MS) was performed using a Bruker Daltonics AuToFlex MALDI-ToF mass spectrometer, equipped with a nitrogen laser at 337 nm with positive ion ToF detection. Polymer samples were measured as follows; solutions in methanol of dithranol (≥98%, Sigma Aldrich) as matrix (30 mg·mL^{-1}), potassium trifluoroacetate (KTFA) or silver trifluoroacetate (AgTFA) as cationization agent (10 mg·mL^{-1}) and sample (10 mg·mL^{-1}) were mixed together in a 9:1:1 volume ratio for a total volume of 75 µL. 2 µL of the mixture was applied to the target plate. Spectra were recorded in reflectron mode and the mass spectrometer was calibrated with a peptide mixture up to 6000 Da.

Differential scanning calorimetry (DSC) was conducted with a *Thorn Scientific* STA 1500 system operating under nitrogen atmosphere using 7 – 13 mg of the respective sample for the analysis. Method settings: heating from 25 to 200 °C with a heating rate of 10 °C/min, then cooling from 200 to 25 °C with a cooling rate of 10 °C/min, the second cyle starts at 25 to 200 °C with a heating rate of 10 °C/min.

Thermal gravimetric analysis (TGA) was conducted with a *TA Instruments* TGA Q500 under nitrogen atmosphere using 7 – 13 mg of the respective sample for the analysis. Method settings: heating from 25 to 200 °C with a heating rate of 10 °C/min, then cooling from 200 to 25 °C with a cooling rate of 10 °C/min, the second cycle starts at 25 to 600 °C with a heating rate of 10 °C/min.

3. General procedures

General procedure for the Ugi-4C8C-polymerization on bench top

A flask was charged with levulinic acid (159 mg, 1.37 mmol), methanol (600 µL, if required), 1,6-diisocyanohexane (93.2 mg, 685 µmol), and the ethylenediamine (46 µl, 685 µmol). The reaction mixture was stirred under the respective conditions for a designated period of time. After the reaction the crude mixture was, if necessary, diluted with methanol to 1 mL and added dropwise into 10.0 mL cold diethylether (or cold aceton for the reactions carried out in water). The resulting precipitate was filtered or decanted off and dried, diluted with methanol to 1.00 mL, precipitated in cold diethylether again, and dried under vacuum to obtain the Ugi-polymer as typically pale yellow powder.

General Procedure for the Microwave Assisted Ugi-4C8C-Polymerization

A microwave vial was charged with levulinic acid (159 mg, 1.37 mmol), the respective amount of solvent (if required), 1,6-diisocyanohexane (93.2 mg, 685 µmol), and the diamine (685 µmol). The reaction mixture was stirred under the respective conditions for a designated period of time. After the reaction the crude mixture was, if necessary, diluted with methanol to 1 mL and added dropwise into 10.0 mL cold diethylether (or cold aceton for the reactions carried out in water). The resulting precipitate was filtered or decanted off and dried, diluted with methanol to 1.00 mL, precipitated in cold diethylether again, and dried under vacuum to obtain the Ugi-polymer as typically pale yellow powder.

4. Results obtained in the initial experiments

Table S1. Initial results of the UGI-polymerization.

Entry	Conditions	M_n [g·mol^{-1}]	$Đ$[a]	Yield [%][b]
PS1	bulk, µw, 100 °C, 10 min	4310	2.48	n.d.
PS2	bulk, µw, 220 °C, 10 min	6350	4.59	>99
PS3	2.28 M in MeOH, µw, 100 °C, 30 min	7110	1.41	>99
PS4	2.28 M in MeOH, µw, 100 °C, 5 min	3910	1.86	79
PS5	2.28 M in MeOH, rt, 1 d	6560	1.51	*n.d.*
PS6	2.28 M in MeOH, rt, 3 d	7620	1.60	*n.d.*
PS7	2.28 M in MeOH, rt, 4 d	7390	1.61	*n.d.*
PS8	2.28 M in MeOH, 100 °C, 30 min	6110	2.06	94
PS9	bulk, rt, 30 min	3670	1.26	20

[a] Determined by GPC at 50 °C using DMF as the eluent against PMMA standards. [b] Isolated yield after second precipitation.

5. Results obtained for the optimization of the Ugi-4C8C-polymerization

Table S2. Influence of the dilution. μw, 100 °C, 30 min, 2.28 M in MeOH.

Entry	Diamine	M_n [g·mol^{-1}]	$Đ$[a]	Yield [%][b]
P3	$H_2N(CH_2)_2NH_2$	7530	1.42	97
P16	$H_2N(CH_2)_6NH_2$	12 320	1.66	93
P17	$H_2N(CH_2)_{12}NH_2$	11 760	1.63	95
P18	Spermine	5230	1.36	87
P19	$N((CH_2)_2NH_2)_3$	-	-	96
P20	$H_2N(p\text{-Ph})NH_2$	6540/1840	1.09/1.15	89
P21	PEG-diamine	10 300	1.78	89

[a] Determined by GPC at 50 °C using DMF as the eluent against PMMA standards. [b] Isolated yield after second precipitation.

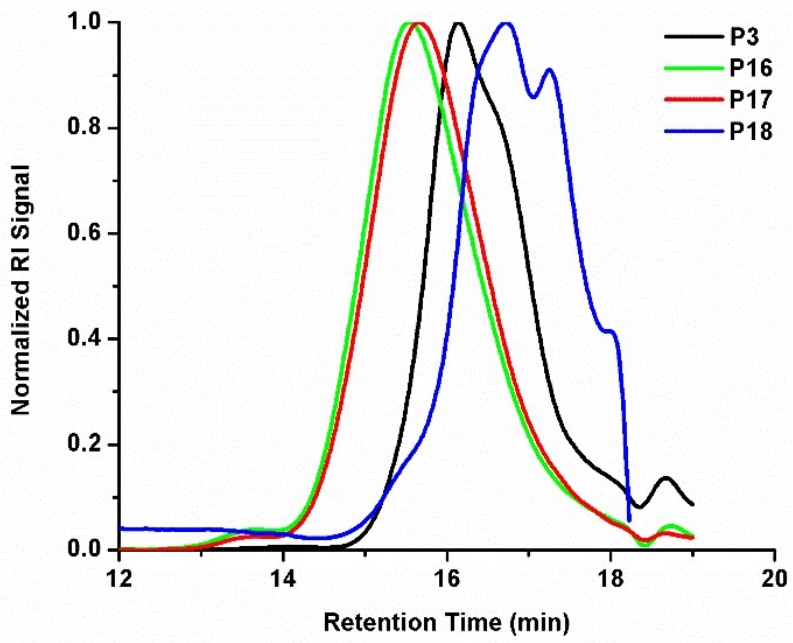

Figure S1. GPC traces of polymer **P3, P16,** and **P17**.

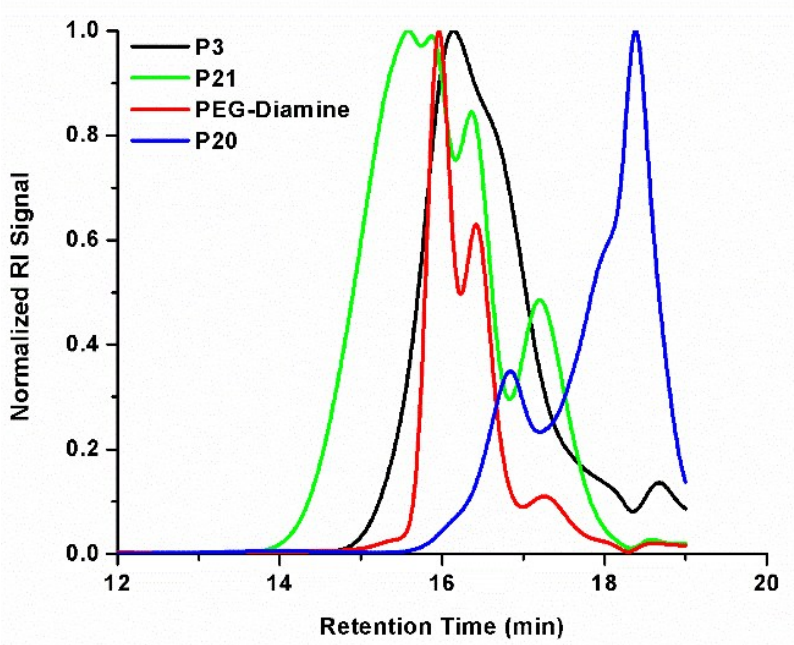

Figure S2. GPC traces of polymers obtained using benzene-1,4-diamine and PEG-diamine as starting material, as well as PEG-diamine as reference.

6. Ugi Multicomponent reactions using water as a solvent

Table S3. Influence of the reaction time. μw, 2.28 M in water .

Entry	Time [min]	Temp [°C]	M_n [g·mol^{-1}]	$Đ$[a]	Yield [%][b]
1	30	100	4280	1.64	>99
2	30	130	3030	1.73	*n.d.*
3	60	100	2680	2.00	*n.d.*

[a] Determined by GPC at 50 °C using DMF as the eluent against PMMA standards. [b] Isolated yield after first precipitation.

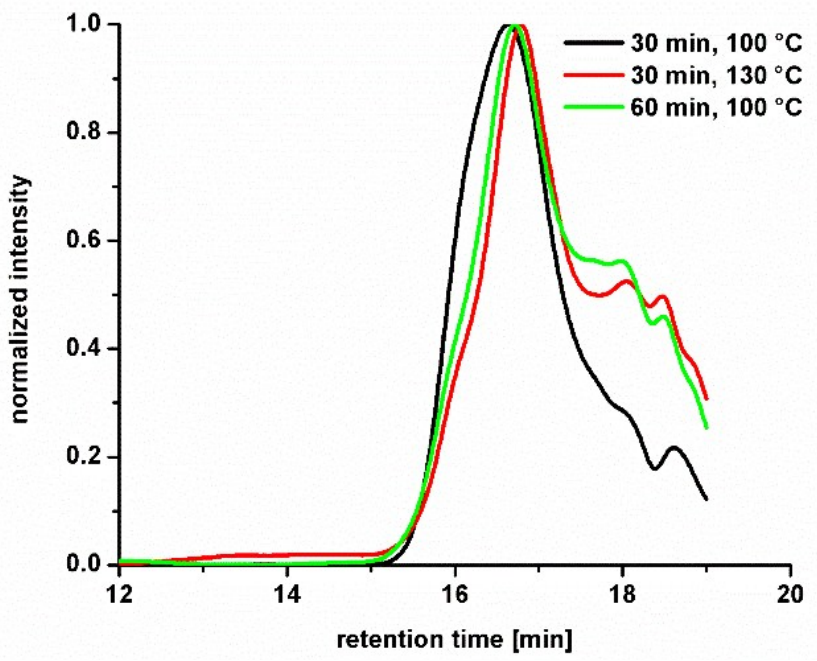

Figure S3. SEC traces of the polymers obtained by reaction in water under different conditions.

7. Comparison of reactions performed via conventional or microwave heating

Table S4. Bench top vs microwave reactionse. 100 °C, 30 min, 2.28 M in MeOH.

Entry	Time [min]; temp [°C]	M_n [g·mol^{-1}]	$Đ$[a]	Yield [%][b]
1	conventional	5460	1.95	>99
2	microwave	7530	1.42	>99

[a] Determined by GPC at 50 °C using DMF as the eluent against PMMA standards. [b] Isolated yield after first precipitation.

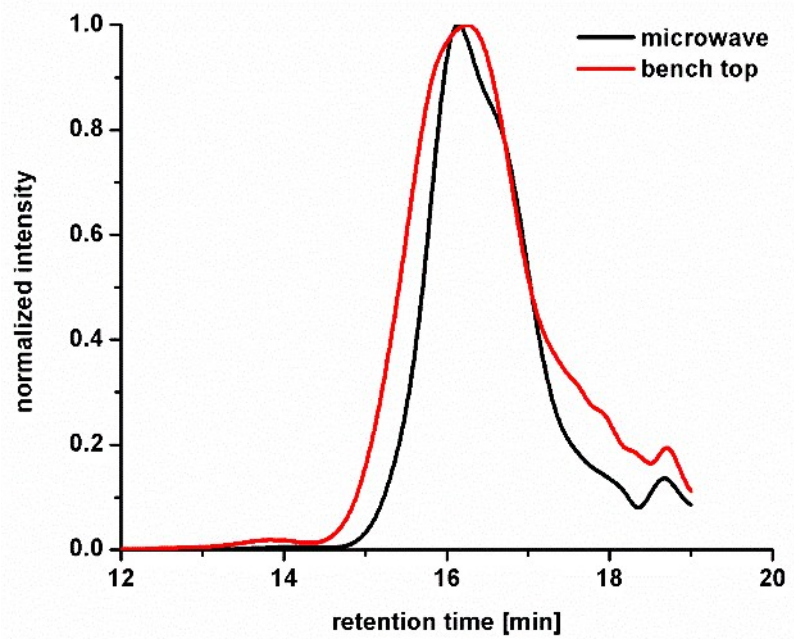

Figure S4. SEC traces of the polymers obtained by reaction under microwave irradiation and in bench top.

8. The effect of diamine concentration

Table S5. Influence of the reaction time. μw, 100 °C, 30 min, 2.28 M in MeOH.

Entry	Diamine [eq]	M_n [g·mol^{-1}]	$Đ$[a]	Yield [%][b]
1	1.00	7530	1.42	>99
2	1.20	8110	1.48	98
3	1.50	5070	1.39	>99

[a] Determined by GPC at 50 °C using DMF as the eluent against PMMA standards. [b] Isolated yield after first precipitation.

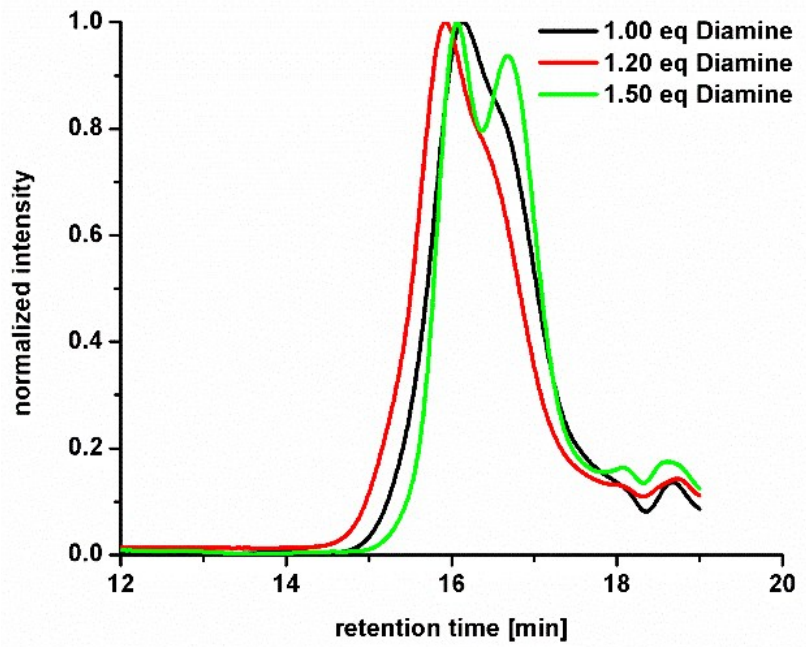

Figure S5. SEC traces of the polymers obtained by use of different loading of ethylenediamine.

9. Reaction kinetics

After 5 min under microwave irradiation at 100 °C, 97% conversion of levulinic acid, >99% ethylenediamine and 98% 1,6-diisocyanohexane were observed by GC. Thus, a further study at room temperature was carried out. As expected from the mechanistic proposal, the conversions of the diisocyanide are shifted slightly after the levulinic acid and ethylenediamine, whereas the conversion of those are almost identical. The molecular weight is increasing to t = 15 min. After, the molecular weight drops slightly and stays constant.

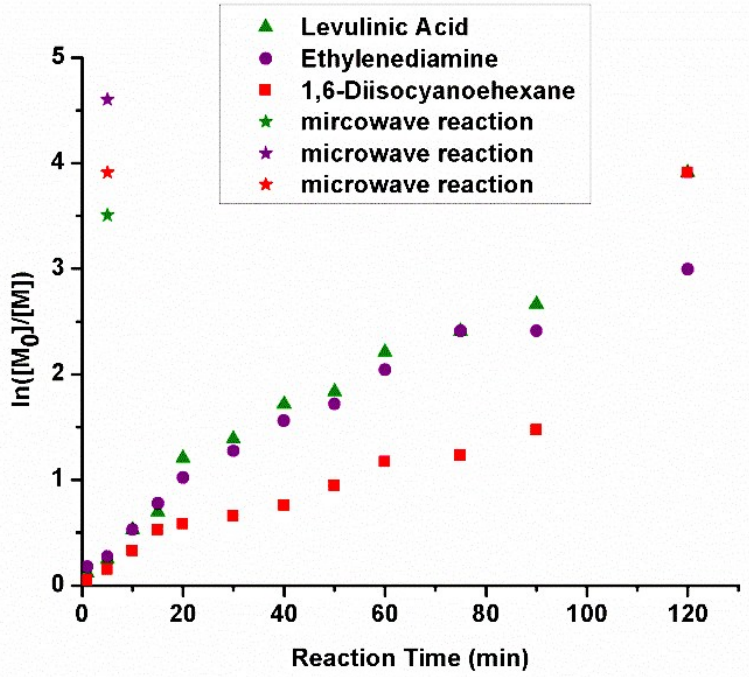

Figure S6. Conversions of levulinic acid, ethylenediamine, and 1,6-diisocyano-hexane at room temperature.

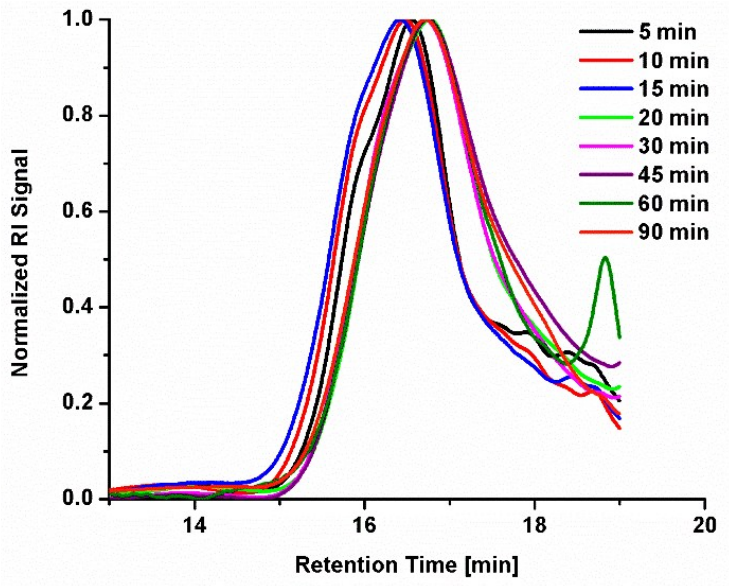

Figure S7. SEC traces of polymers after designated periods of time.

10. TGA Analysis

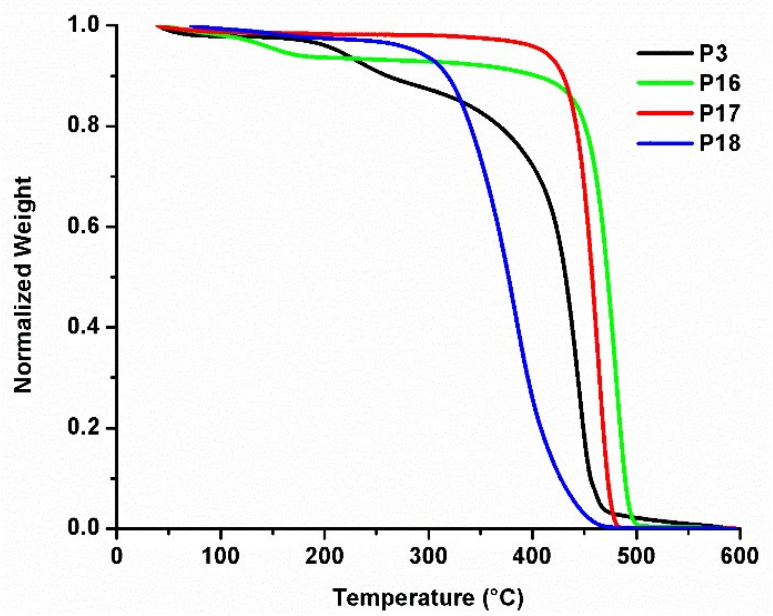

Figure S8. TGA analysis data (second cycle) of the polymers **P3**, **P16** - **P18**.

11. DSC Analysis

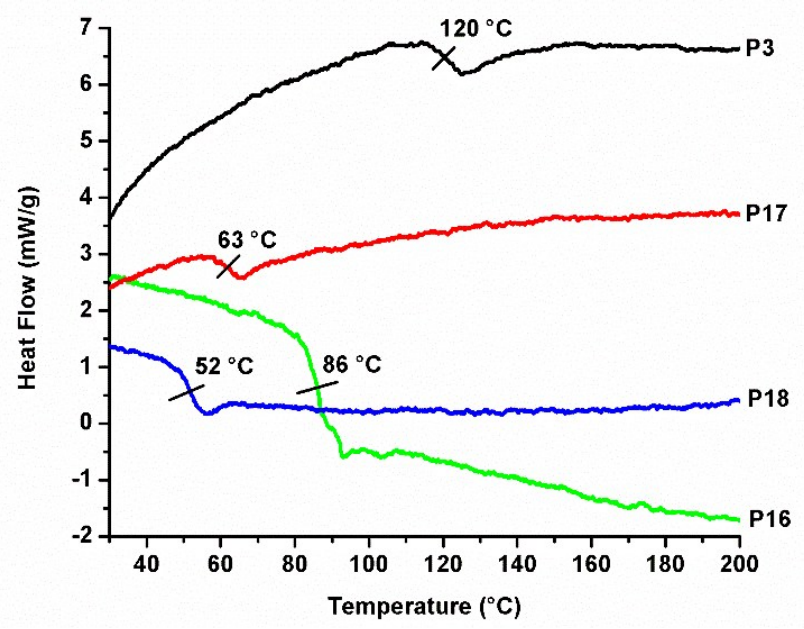

Figure S9. DSC analysis data (second cycle) of the polymers **P3**, **P16** - **P18**.

12. MALDI-TOF Analysis

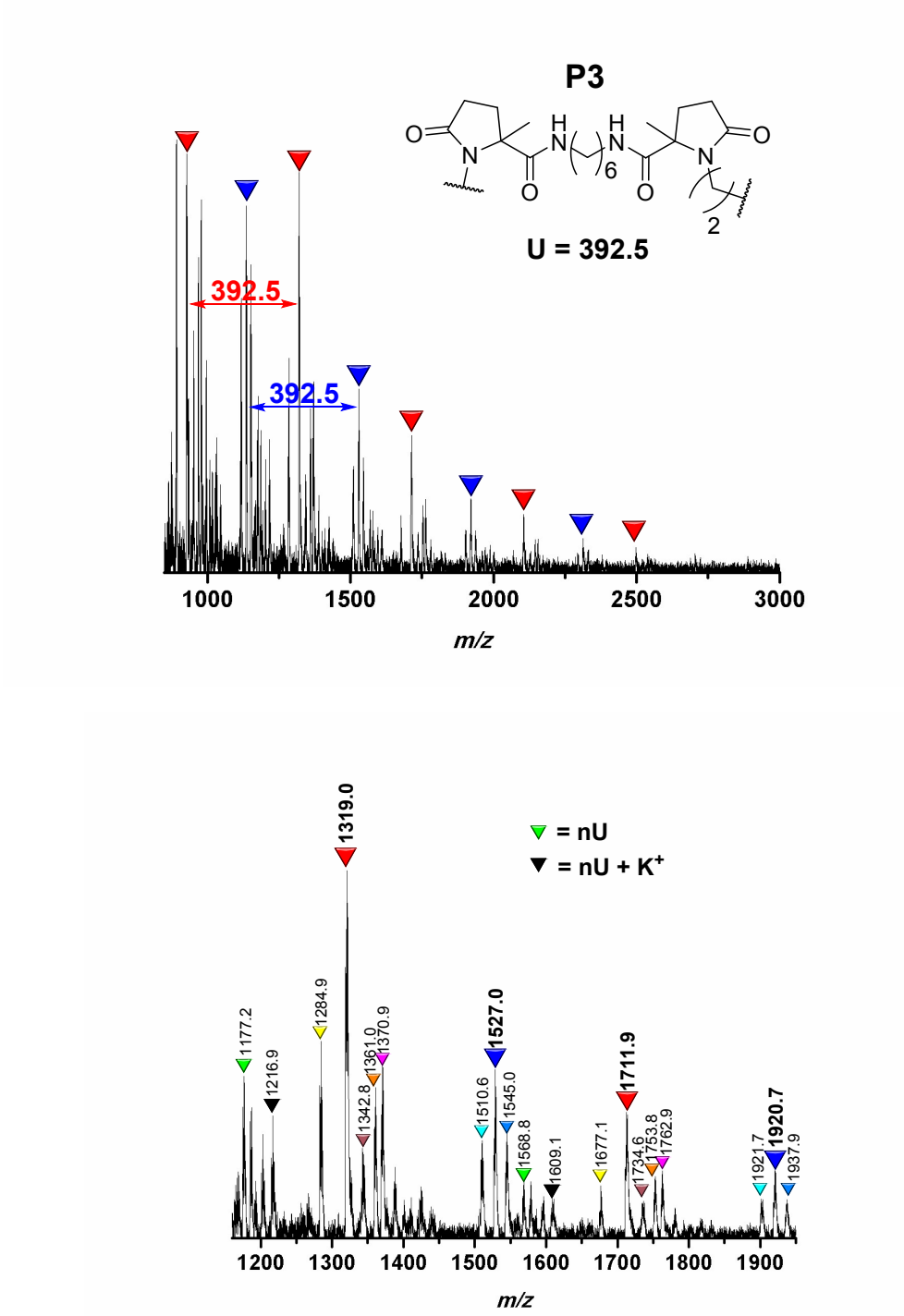

Figure S10. MALDI-TOF analysis data of **P3**: AgTFA/Dithranol/**P3** (1/9/1) in MeOH**.** Top: full spectrum, displaying two main distributions (red and dark blue) with Δ(*m/z*) = 392.5 Da. Bottom:zoom, displaying the two main distribution (red, dark blue) and six minor distributions (yellow, dark red, orange, pink, light blue, and blue) with each Δ(*m/z*) = 392.5 Da. Furthermore, distributions for macrocycles (green and black) with n repetition units U are displayed.

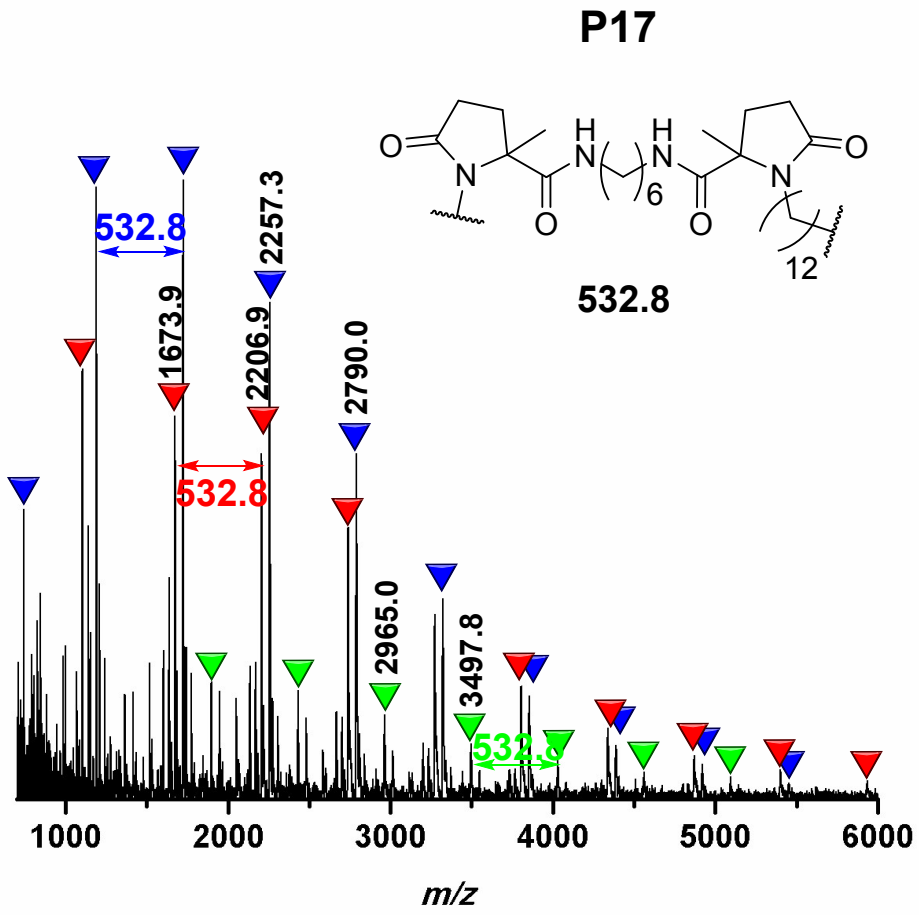

Figure S11. MALDI-TOF analysis data of **P17**: AgTFA/Dithranol/**P17** (1/9/1) in MeOH**.** The spectrum, displays three distributions with Δ(*m/z*) = 532.8 Da.

13. NMR Analysis

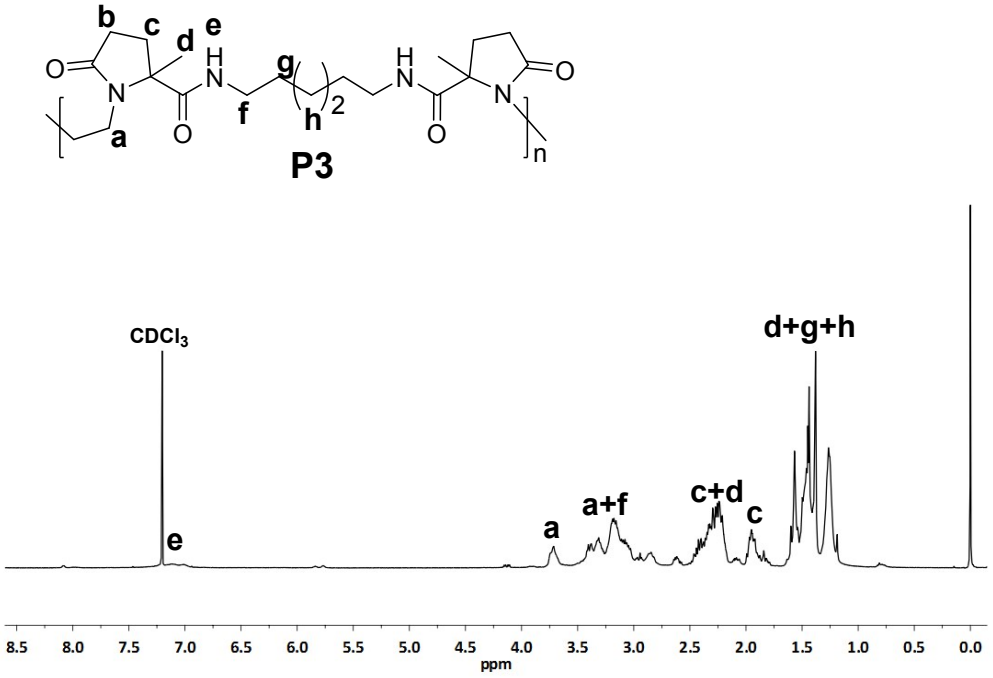

Figure S12. Representative **^{1}H NMR** spectrum of **P3** ($CDCl_3$, 400 MHz) δ = 7.13 (br-s, H^{e}), 3.83 – 3.72 (br-m, $H^{a/2}$), 3.51 – 2.84 (m, $H^{(a/)2+f}$), 2.54 – 2.21 (m, $H^{(c/2)+d}$), 2.09 – 1.92 (m, $H^{c/2}$), 1.69 – 1.22 (m, H^{d+g+h}).

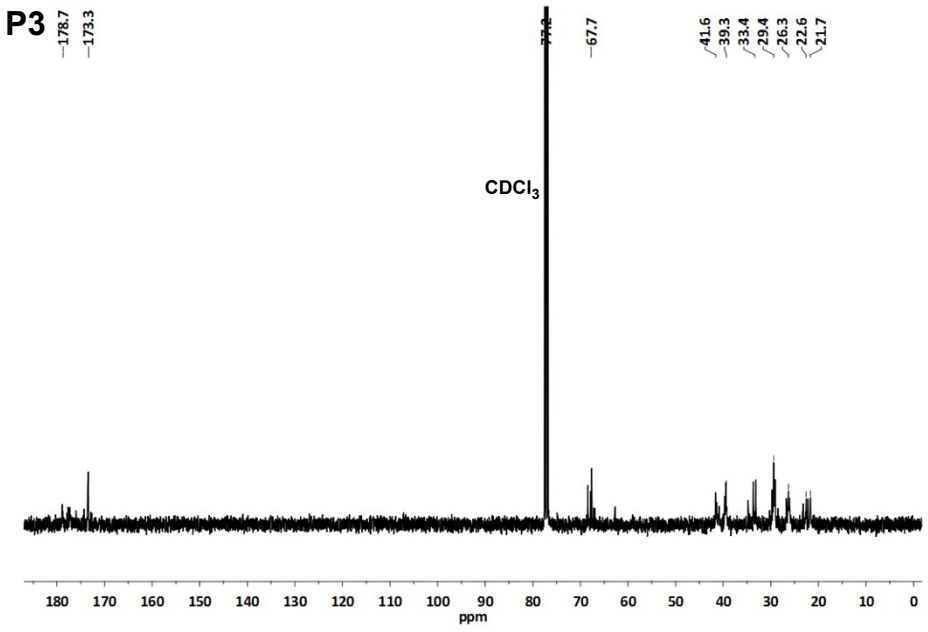

Figure S13. ^{13}C NMR spectrum of **P3** ($CDCl_3$, 101 MHz) δ = 178.6 (N*C*=O^{lactam}), 173.3 (N*C*=O^{amid}), 67.7 (*C*^{quat}), 41.6, 39.3, 33.7, 29.4, 26.3, 22.6, 21.7 (C*C*H_3).

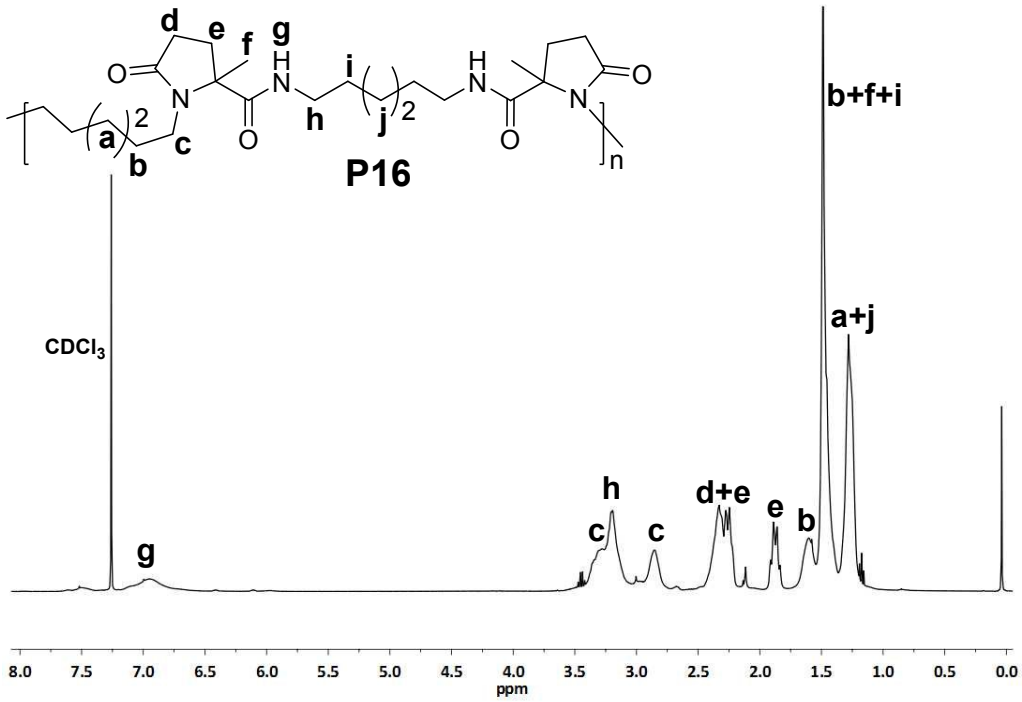

Figure S14. **^{1}H NMR** spectrum of **P16** ($CDCl_3$, 400 MHz) δ = 6.97 (br-s, H^{e}), 3.41 – 3.07 (br-m $H^{(c/2)+h}$), 2.88 (br-s, $H^{c/2}$), 2.45 – 2.19 (m, $H^{d+(e/2)}$), 1.86 (dd, J = 21.0, 9.6 Hz, $H^{e/2}$), 1.69 – 1.55 (m, $H^{(b/2)}$), 1.55 – 1.36 (m, $H^{(b/2)+f+i}$), 1.35 – 1.20 (br-m, H^{a+j}).

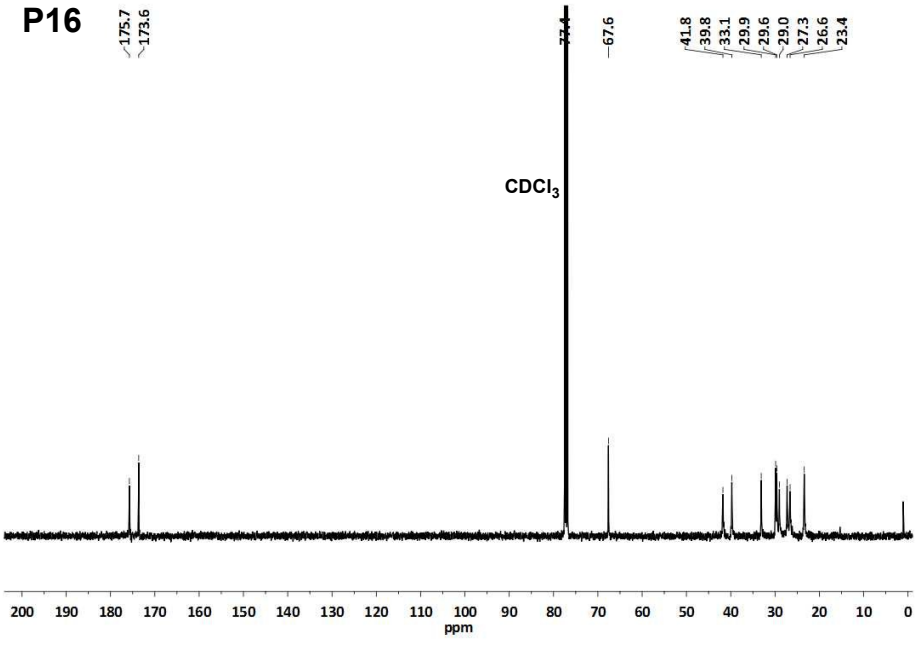

Figure S15. **^{13}C NMR** spectrum of **P16** ($CDCl_3$, 101 MHz) δ = 175.7 (N*C*=O^{lactam}), 173.6 (N*C*=O^{amid}), 67.6 (*C*^{quat}), 41.8 (*C*H_2^{lactam}), 39.8 (*C*H_2^{lactam}), 33.1, 29.9, 29.6 (m), 29.0 , 27.3, 26.6, 23.4 (C*C*H_3).

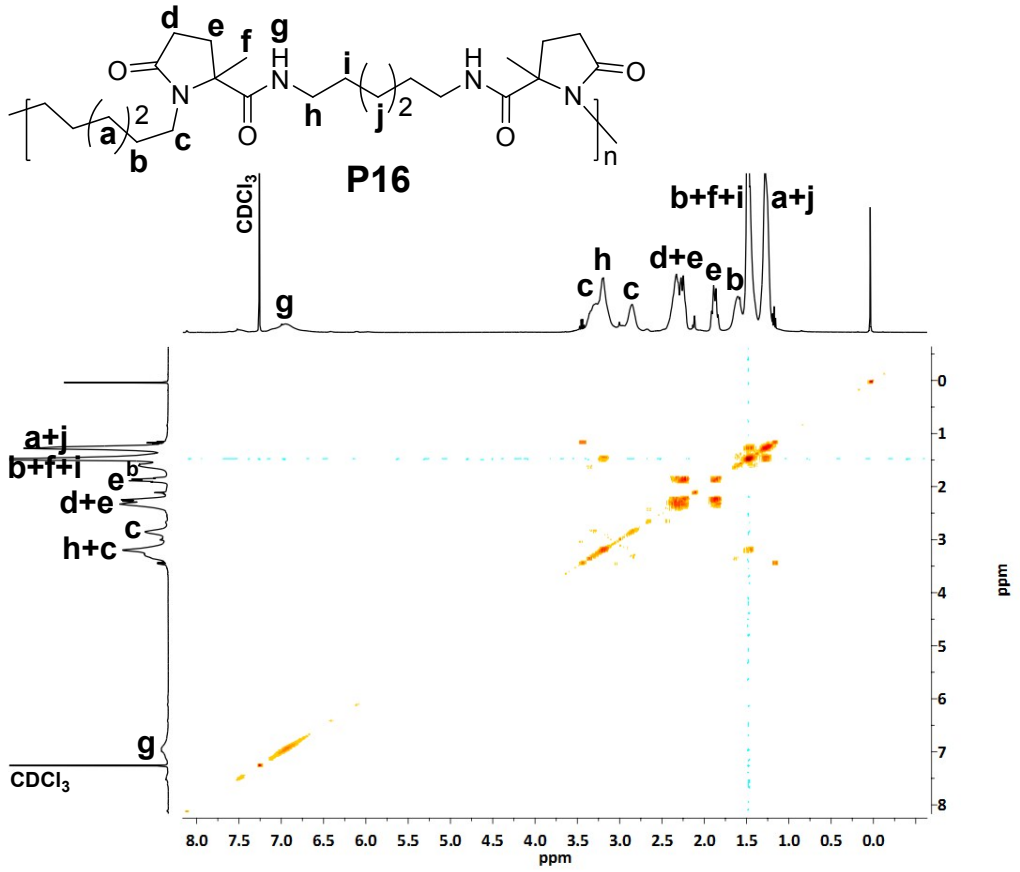

Figure S16. COSY NMR spectrum of **P16** ($CDCl_3$, 400 MHz).

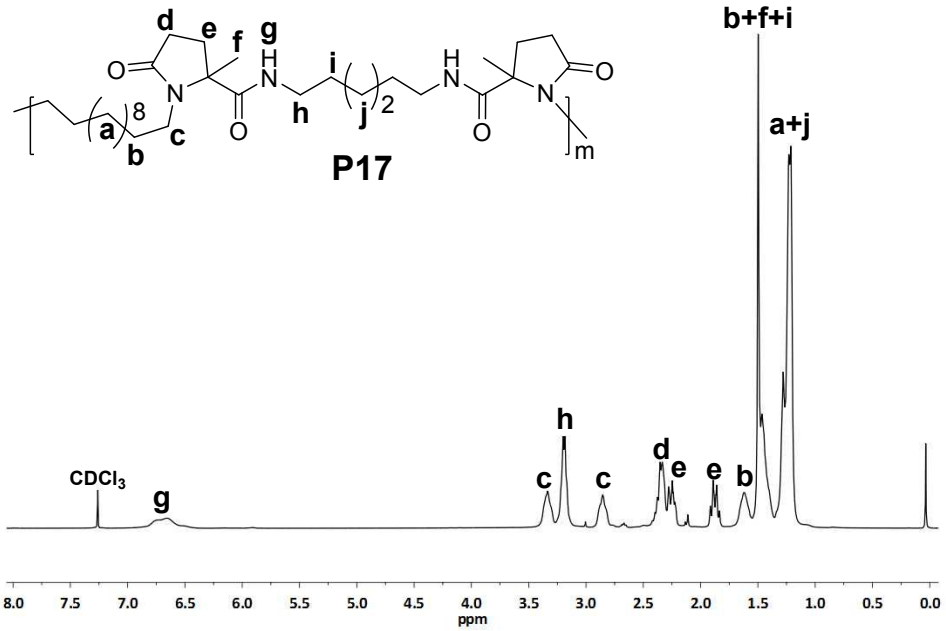

Figure S17. ^{1}H NMR spectrum of **P17** ($CDCl_3$, 400 MHz) δ = 6.83 – 6.55 (br-s, H^g), 3.37 – 3.31 (br-m, $H^{c/2}$), 3.19 (br-d, J = 6.3 Hz, H^h), 2.90 – 2.81 (m, $H^{c/2}$), 2.44 – 2.30 (m, H^d), 2.25 (br-m, $H^{e/2}$), 1.87 (dd, J = 22.1, 9.4 Hz, $H^{e/2}$), 1.69 – 1.55 (br-m, H^b), 1.53 – 1.37 (m H^{b+f+i}), 1.35 – 1.12 (br-m, H^{a+j}).

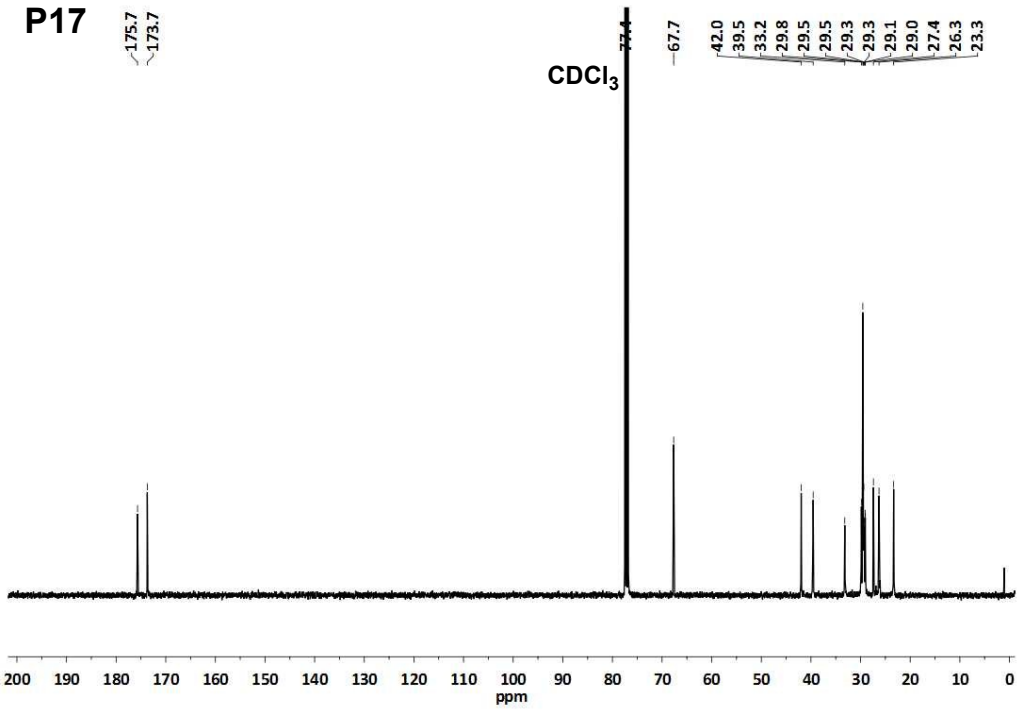

Figure S18. ^{13}C NMR spectrum of **P17** ($CDCl_3$, 101 MHz) δ = 175.7 ($NC{=}O^{lactam}$), 173.7 ($NC{=}O^{amid}$), 67.7 (C^{quat}), 42.0 (CH_2^{lactam}), 39.6 (CH_2^{lactam}), 33.2, 29.8, 29.5, 29.4 (d), 29.3, 29.1 (d), 27.4, 26.3, 23.3 (CCH_3).

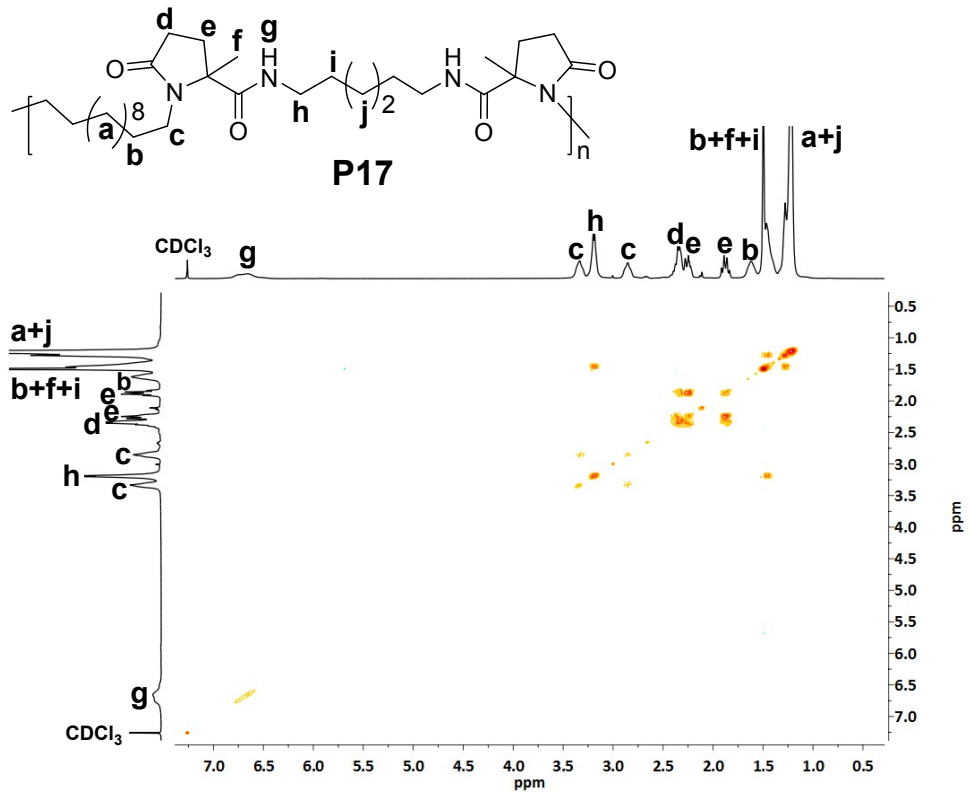

Figure S19. COSY NMR spectrum of **P17** ($CDCl_3$, 400 MHz).

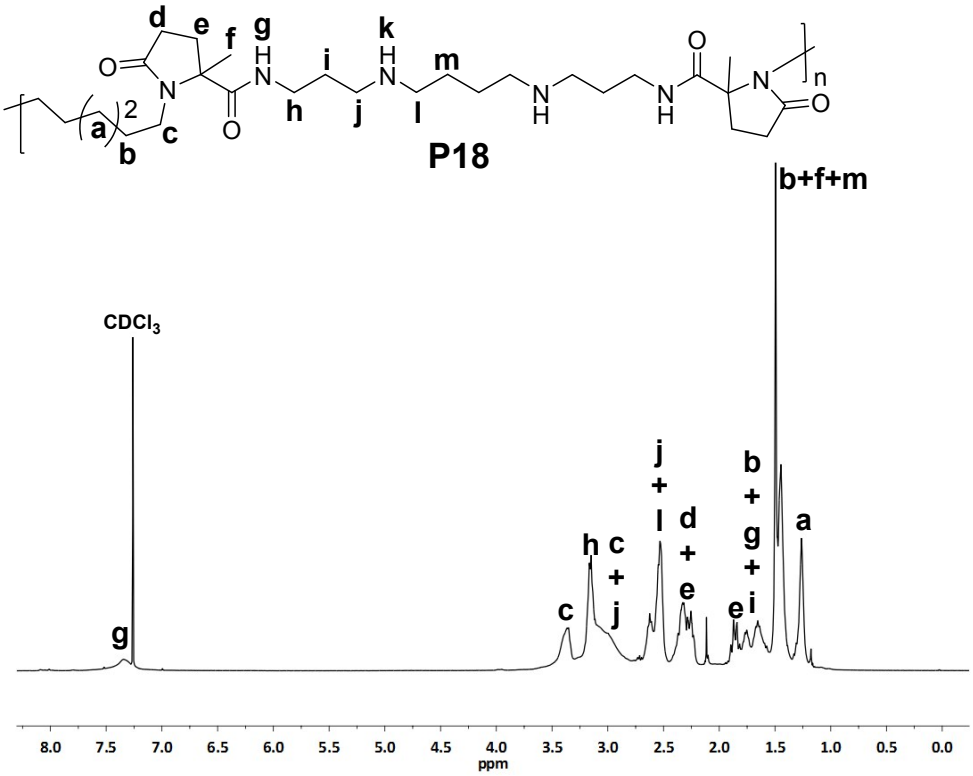

Figure S20. **^{1}H NMR** spectrum of **P18** ($CDCl_3$, 400 MHz) δ = 7.31 (br-s, H^{g}), 3.36 (br-m, $H^{c/2}$), 3.22 – 2.85 (m, $H^{(c/2)+h+(j/2)}$), 2.68 – 2.45 (br-m, $H^{(j/2)+l}$), 2.43 – 2.20 (br-m, $H^{d+(e/2)}$), 1.86 (dd, J = 12.3, 9.5 Hz, $H^{e/2}$), 1.80 – 1.55 br-(m, $H^{(b/2)+g+i}$), 1.55 – 1.35 (m, $H^{(b/2)+f+m}$), 1.34 – 1.20 (m, H^{a}).

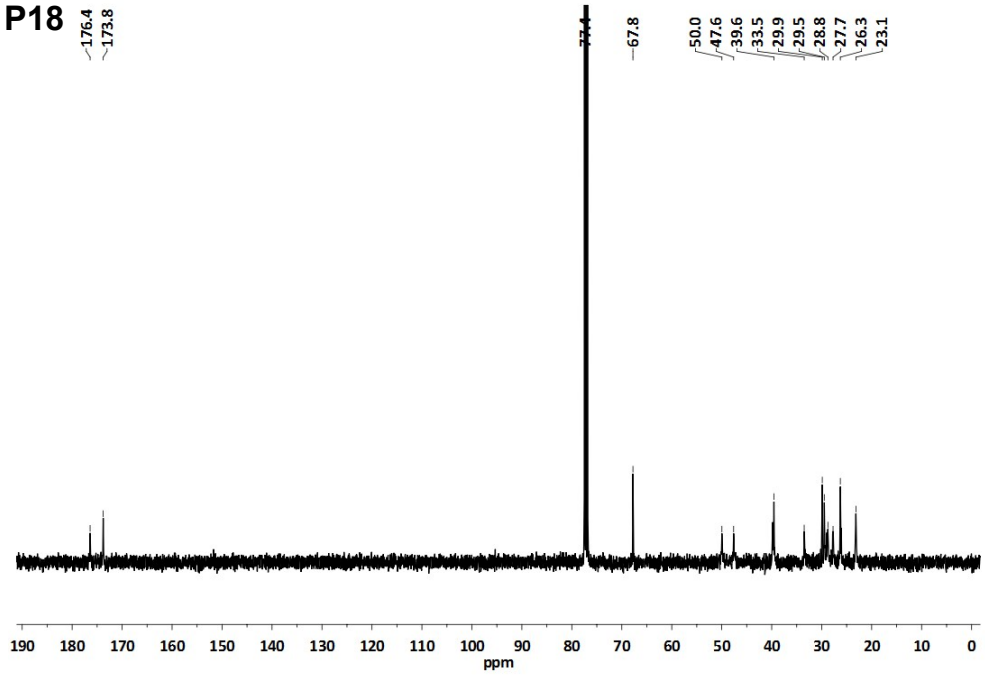

Figure S21. **^{13}C NMR** spectrum of **P18** ($CDCl_3$, 101 MHz) δ = 176.4 ($NC{=}O^{lactam}$), 173.8 ($NC{=}O^{amid}$), 67.8 (C^{quat}), 50.0 (CH_2^{lactam}), 47.6 (CH_2^{lactam}), 39.8 (d), 33.5, 29.9, 29.5, 28.8, 27.7, 26.3 (m), 23.1 (CCH_3).