Discrete, Self-immolative *N*-substituted Oligourethanes and their use as Molecular Tags

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Content

1 Materials

All chemicals were used as supplied, unless otherwise stated. Deionised water was used in the procedures. DMSO-d_6 and CD_2Cl_2 (≥99.8%) were purchased from Eurisotop. Magnesium sulphate (dried ≥99%), sodium hydrogen carbonate (99%) and sodium chloride (99%) were purchased from Carl Roth. Hydrochloric acid (36 wt%) was purchased from Chem Lab NV. Dichloromethane (HPLC grade, 99.5%), anhydrous chloroform (99.8%), Pyridine (99%), *N,N'*-dimethylformamide (HPLC grade, 99.8%) and triethylamine (99%) were purchased from Acros Organics. *N*-methyl ethanolamine (98%), Ethyl acetate (HPLC grade, 99.7%), 2-Methoxy-N-methyl ethanolamine (97%), 2-phenylethanol (98%), N-benzyl ethanolamine (95%), N-phenyl ethanolamine (95%), acetyl chloride (99%), sodium carbonate (99.5%), Dibutyltindilaurate (95%), and chloroform (HPLC grade, 99.9%) were purchased from Sigma Aldrich. Acetone (HPLC grade, 99.5%), acetonitrile (HPLC grade, 99.9%), and *N,N'*-dimethylformamide (HPLC grade, 99.7%) were purchased from Fischer Scientific. *N*-ethyl ethanolamine (98%), 4-(hydroxymethyl)benzoate (98%) and *N*-butyl ethanolamine (98%) were purchased from TCI Europe**.** DL-Prolinol (98%), 1,1'-carbonyldiimidazole (98%), 2-piperidinemethanol (97%), citric acid (99%) and N,N'-Disuccinimidyl carbonate (98%) were purchased from ABCR. Desmodur N3600 was kindly provided by Covestro and Pripol 2033 was kindly provided by Croda.

2 Instrumentation

2.1 Nuclear magnetic resonance (NMR) spectroscopy

All ^{1}H and ^{13}C spectra were recorded in DMSO-d_6 or $CDCl_3$, with a Bruker Avance 300 (300 MHz) or a Bruker Avance 400 (400 MHz) device. The assignment of the obtained spectra was aided by 2D NMR.

2.2 Liquid Chromatography Mass Spectrometry (LC-MS)

An Agilent technologies 1100 series LC/MSD system equipped with a diode array detector and single quad MS detector (VL) with an electrospray source (ESI-MS) was used for classic reversed phase LC-MS and MS analysis. Analytic reversed phase HPLC (high-performance liquid chromatography) was performed with a Phenomenex Kmetex C18 (2) column with a solid core at 35°C and a flow rate of 1.5 mL min-1 (5 µm, 250 × 4.6 mm) using a solvent gradient (0 → 100 %) acetonitrile in H_2O over 6 min, unless otherwise stated. The eluting compounds were detected via UV-detection (λ = 214 nm).

2.3 Infrared (IR)

All measurements were recorded on a Perkin Elmer FTIR SPECTRUM 1000 spectrometer with Attenuated Total Reflection (ATR) with a PIKE Miracle ATR unit in a frequency range from 4000 to 600 cm^{-1} .

2.4 Thermogravimetric analysis (TGA)

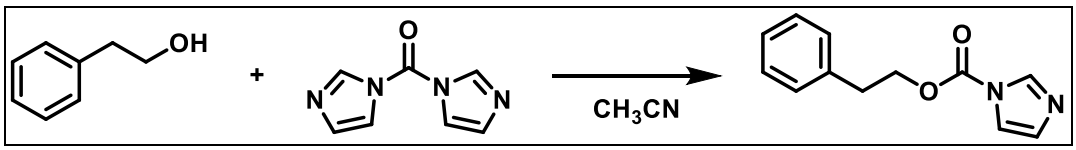
TGA analyses were performed with a Mettler Toledo TGA/ SDTA851e instrument under nitrogen atmosphere at a heating rate of 10 $K.min^{-1}$ from 25 °C to 800 °C.

2.5 Differential scanning calorimetry (DSC)

DSC analyses were performed with a Mettler Toledo instrument 1/700 under nitrogen atmosphere at a heating and cooling rate of 10 $K.min^{-1}$. Measurements were performed from -50 to 150 °C.

3 Synthetic procedures

3.1 Activation of 2-phenylethanol with CDI (1)



1,1'-Carbonyldiimidazole (CDI, 3.98 g, 23.6 mmol, 1.5 eq.) was placed in a 50 mL 2-neck flask and solubilised in 15 mL acetonitrile. The reaction was flushed with nitrogen, followed by the dropwise addition of a solution of 2-phenylethanol (2 g, 16.4 mmol, 1 eq.) in 5 mL acetonitrile. The reaction was stirred vigorously for 1 hour, after which TLC analysis indicated complete consumption of the starting material. The majority of the solvent was removed in vacuo, followed by resolubilisation of the reaction mixture in ethyl acetate. The organic phase was then washed with water (3 x 20 mL) and brine (1 x 20 mL). The organic phase was dried with $MgSO_4$, filtered and concentrated in vacuo, yielding an off-white solid (**1**, 2.47g, 70%).

^{1}H-NMR (300 MHz, DMSO-d_6, δ): 8.20 (br, 1H, CH), 7.52 (br, 1H, CH), 7.30 (m, 5H, 5xCH), 7.06 (br, 1H, CH), 4.56 (t, 2H, CH_2), 3.05 (t, 2H, CH_2).
IR (ATR platinum diamond): ν [cm^{-1}] = 3031 (C_{ar}-H), 2917 (C-H), 1750 (C=O), 1282 (C-N), 1061 (C-O), 748 (C-H).

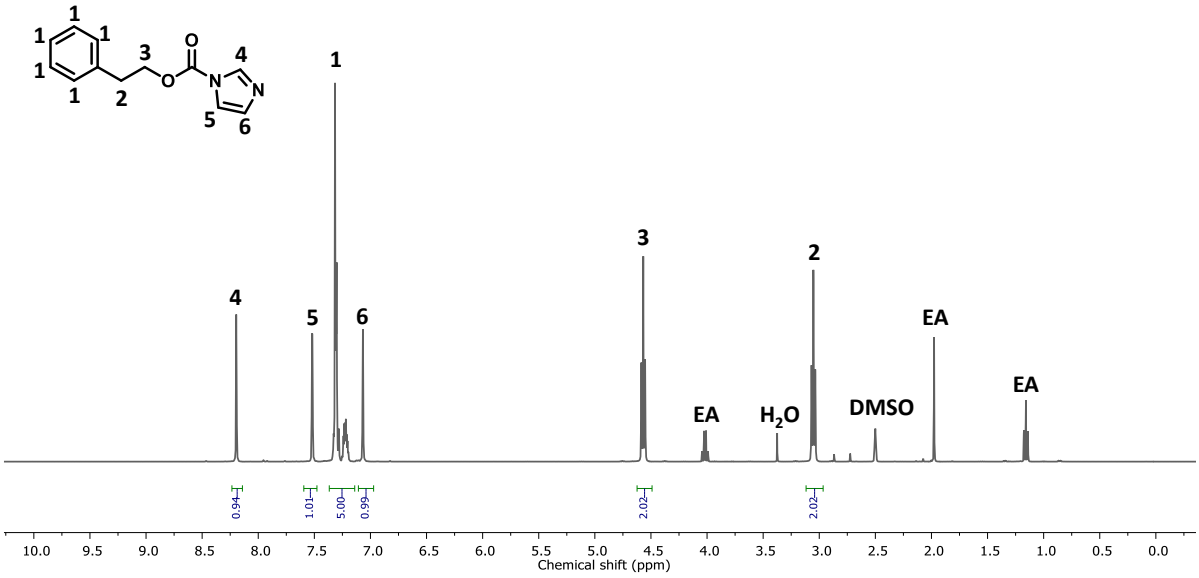
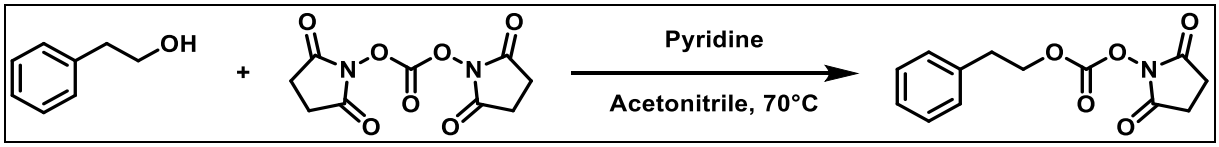


Figure S1: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of activated 2-phenylethanol (**1**). EA = ethyl acetate.

3.2 Activation of 2-phenylethanol with DSC (2)



N,*N*'-Disuccinimidyl Carbonate (DSC, 12.6 g, 49.1 mmol, 1.2 eq.) was placed in a 100 mL 2-neck flask and suspended in 40 mL acetonitrile, followed by the addition of pyridine (4.95 mL, 61.4 mmol, 1.5 eq.). Next, 2-phenylethanol (4.90 mL, 41 mmol, 1 eq.) was added dropwise to the reaction mixture, after which it was flushed with nitrogen and placed in a pre-heated oil bath at 70°C. The reaction was stirred vigorously for 15 minutes, after which TLC analysis indicated complete consumption of the starting material. The reaction mixture was concentrated in vacuo to remove the majority of the acetonitrile and diluted with ethyl acetate (50 mL). The organic phase was then washed with a citric acid solution (3 x 50 mL), saturated bicarbonate solution (3 x 50 mL) and brine (1 x 50 mL). The organic phase was dried with $MgSO_4$ and concentrated in vacuo, yielding a viscous liquid that solidified upon further drying (**2**, 9.87 g, 92%).

^{1}H-NMR (300 MHz, DMSO-d_6, δ): 7.30 (m, 5H, 5xCH), 4.56 (t, 2H, CH_2), 3.02 (t, 2H, CH_2), 2.8 (s, 4H, 2xCH_2).
^{13}C-NMR (75 MHz, DMSO-d_6, δ): 169.8 (C), 151.1 (C), 136.4 (C), 128.2 (CH), 125.8 (CH), 71.1 (CH_2), 33.3 (CH_2), 25.5 (CH_2).
IR (ATR platinum diamond): *v* [cm^{-1}] = 3033 (C_{ar}-H), 2968 (C-H), 1808 (C=O), 1776 (C=O), 1667 (C-O), 1287 (C-N), 1046 (C-O), 770 (C-H).

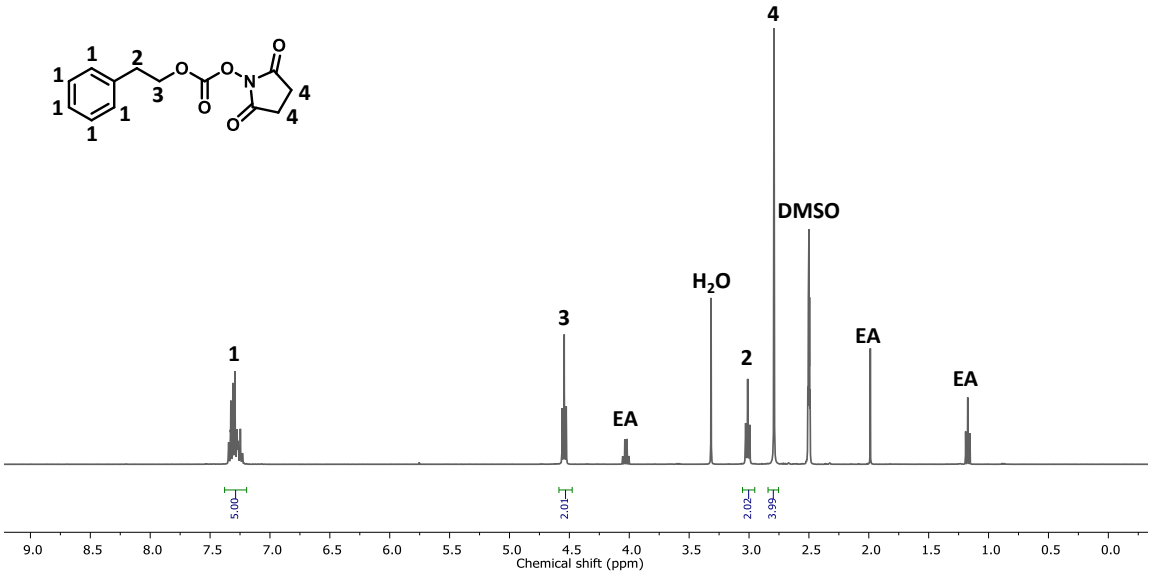


Figure S2: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of activated 2-phenylethanol (**2**). EA = ethyl acetate.

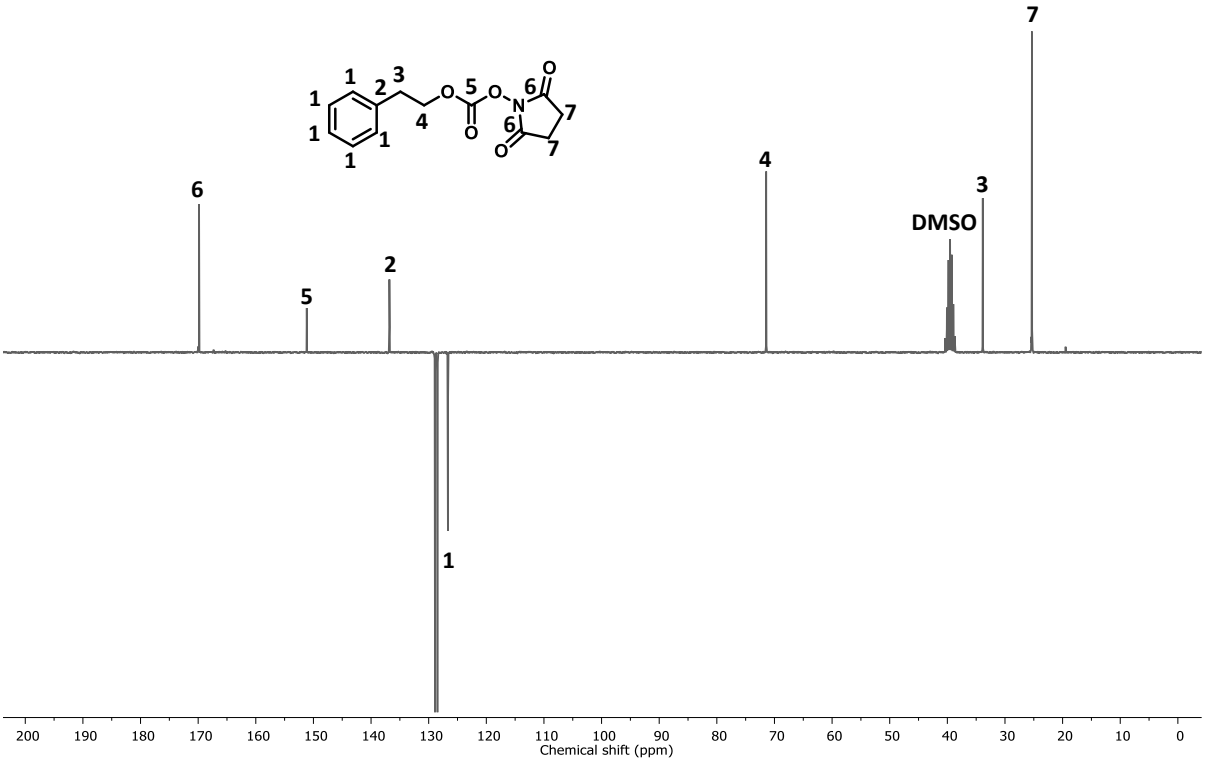
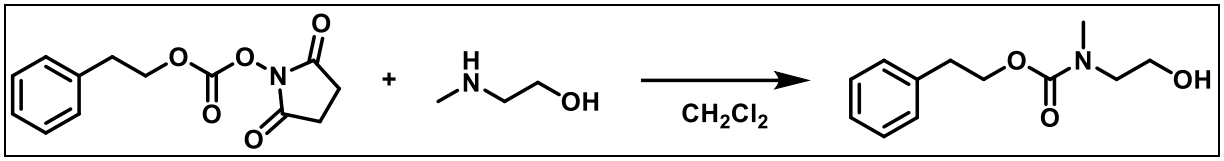


Figure S3: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **2**.

3.3 N-methyl β-hydroxy carbamate model compound (3)



General procedure for substitution reactions: **2** (300 mg, 1.14 mmol, 1 eq.) was solubilised in 1 mL dichloromethane and added dropwise to a solution of N-methyl ethanolamine (0.23 mL, 2.85 mmol, 2.5 eq.) in 5 mL dichloromethane. The reaction was stirred vigorously for 5 minutes, after which TLC analysis indicated complete consumption of the starting material. The reaction mixture was then diluted with 25 mL dichloromethane and washed with 1M HCl (3 x 25 mL), a saturated bicarbonate solution (3 x 25 mL) and brine (25 mL). The organic phase was dried with $MgSO_4$, filtered and concentrated in vacuo to yield a transparent oil (**3**, 223 mg, 87%).

^{1}H-NMR (300 MHz, DMSO-d_6, δ): 7.30 (m, 5H, 5xCH), 4.64 (t, 1H, OH), 4.16 (t, 2H, CH_2), 3.42 (m, 2H, CH_2), 3.21 (m, 2H, CH_2), 2.84 (m, 5H, CH_2 + CH_3).
^{13}C-NMR (75 MHz, DMSO-d_6, δ): 155.1 (C), 137.1 (C), 128.2 (CH), 125.8 (CH), 64.9 (CH_2), 58.5 (CH_2), 50.5 (CH_2), 35.1 + 34.2(CH_3), 34.4 (CH_2).
IR (ATR platinum diamond): *ν* [cm^{-1}] = 3425 (O-H), 3029 (C_{ar}-H), 2941 (C-H), 1673 (C=O), 1454 (C-H), 1213 (C-N), 1052 (C-O), 767 (C-H).

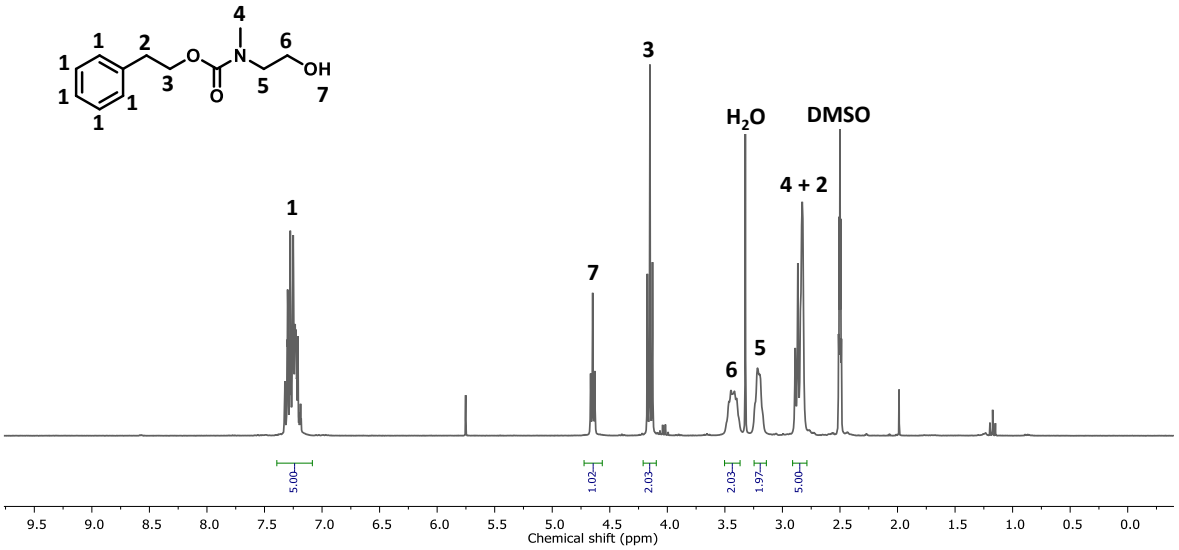


Figure S4: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of **3**.

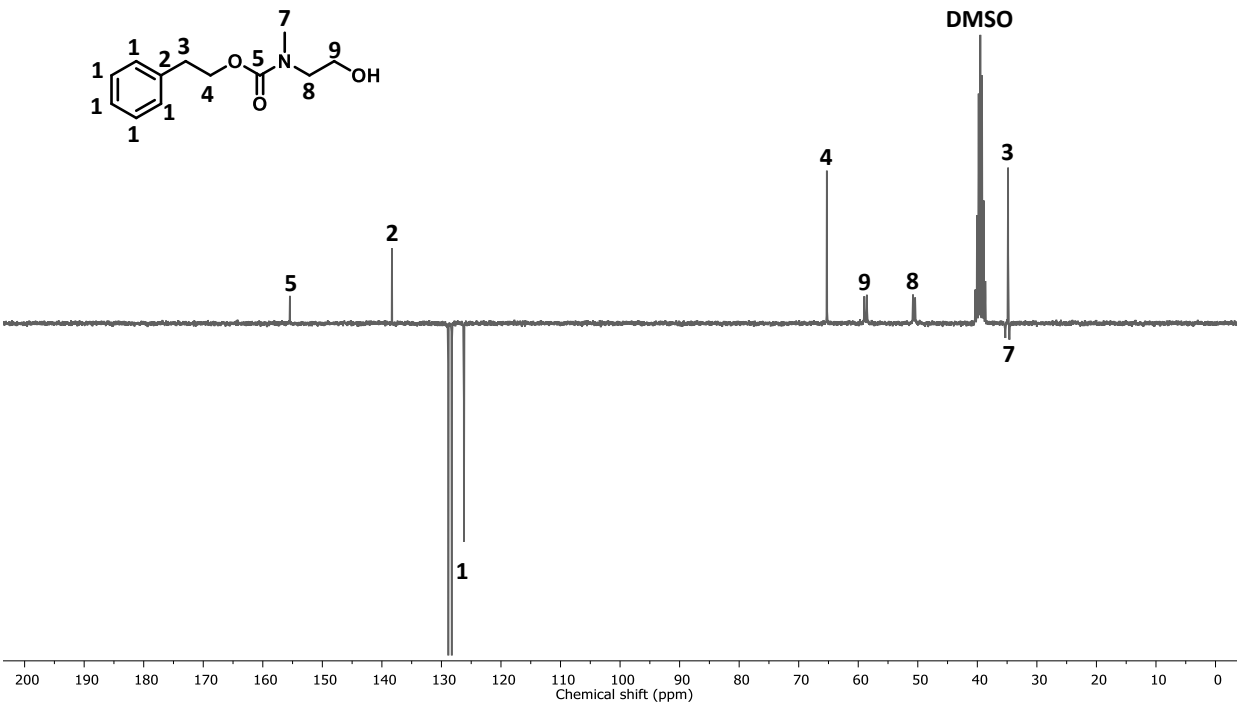


Figure S5: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **3**.

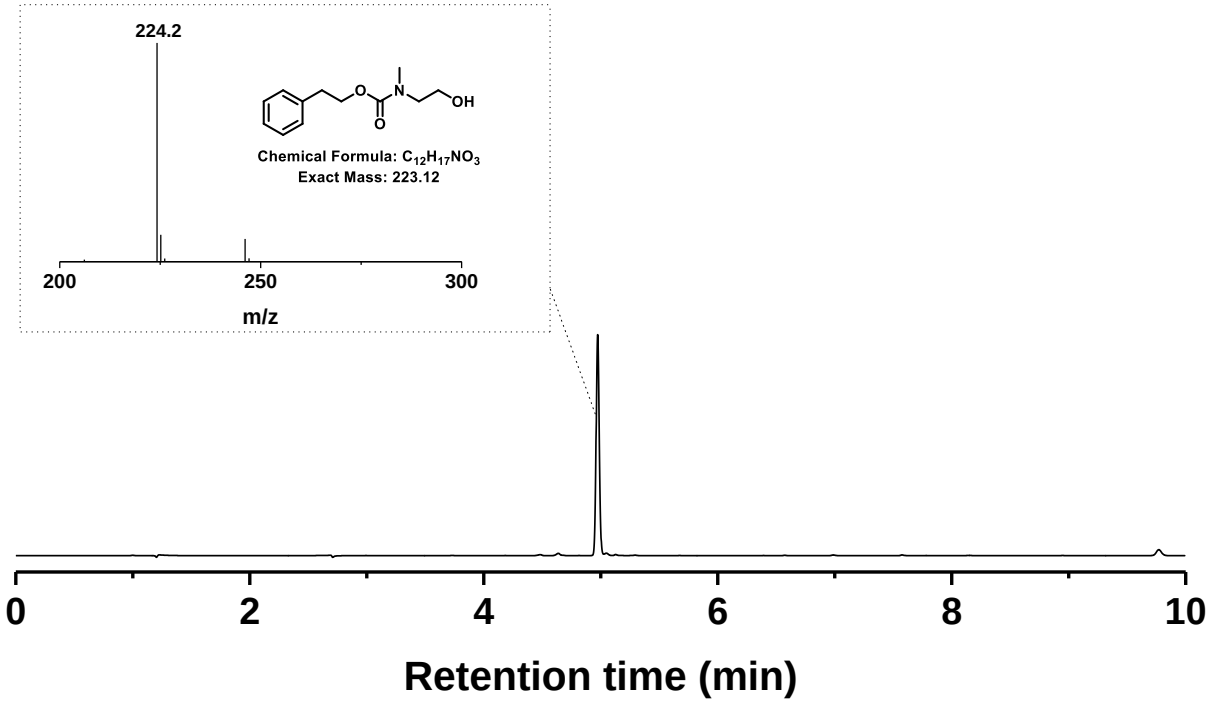


Figure S6: LC-MS trace (λ = 214 nm) of **3**. The product is observed as $[M+H]^+$, t = 4.94 min.

3.4 Synthesis of M1

All macromolecules were synthesized according to the general procedure (see 3.2 and 3.3)

3.4.1 Dimer

The dimer was obtained by activation of **3** and subsequent substitution with N-ethyl ethanolamine according to the general procedure. Obtained as a clear viscous oil (0.73 g, 87%).

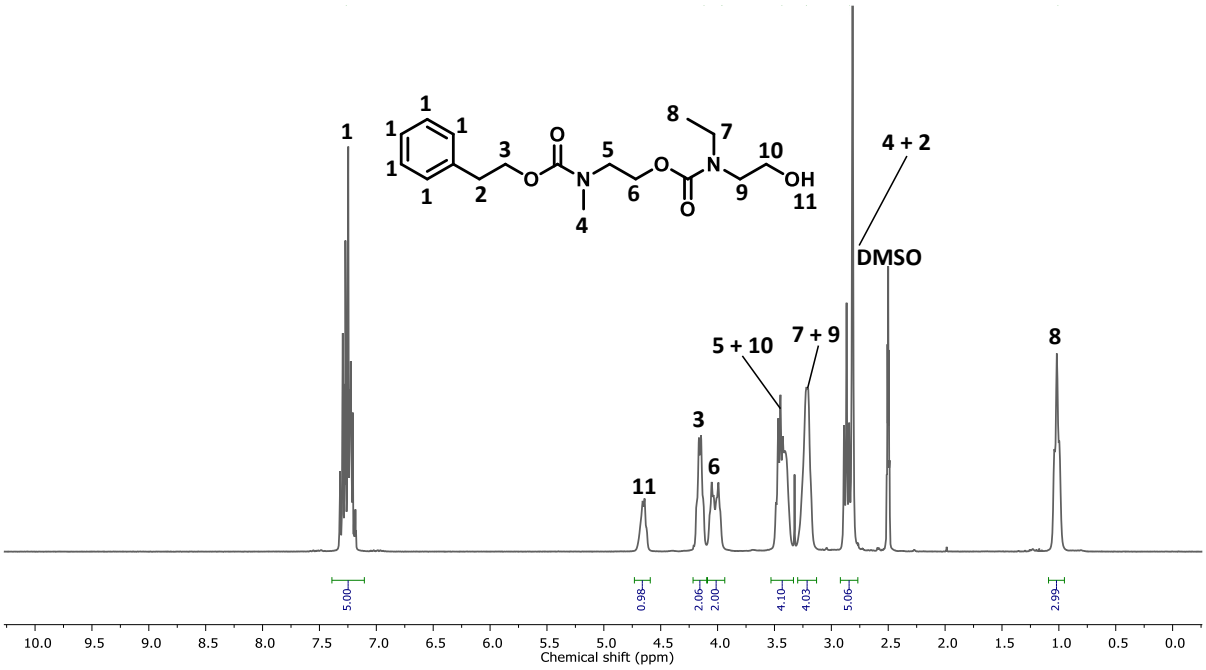


Figure S7: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of the dimer intermediate during the synthesis of **M1**.

3.4.2 Trimer

The trimer was obtained by activation of dimer (3.4.1) and subsequent substitution with N-methyl ethanolamine according to the general procedure. Obtained as a clear viscous oil (0.66 g, 80%).

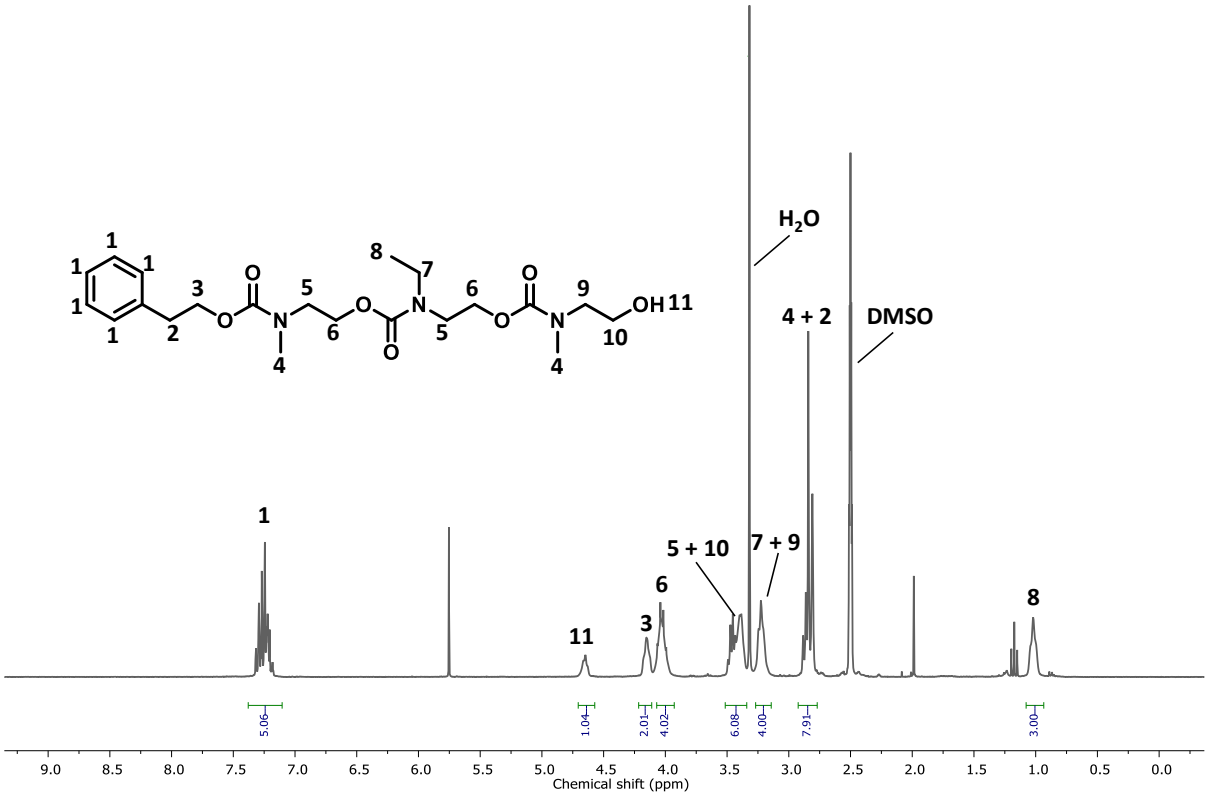


Figure S8: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of the trimer intermediate during the synthesis of **M1**.

3.4.3 Tetramer M1

Tetramer M1 was obtained by activation of trimer (3.4.2) and subsequent substitution with N-ethyl ethanolamine according to the general procedure. Obtained as a clear viscous oil (0.54 g, 78%).

IR (ATR platinum diamond): *v* [cm^{-1}] = 3456 (O-H), 2927 (C-H), 1689 (C=O), 1455 + 1476 (C-H), 1271 (C-N), 1070 (C-O), 767 (C-H).

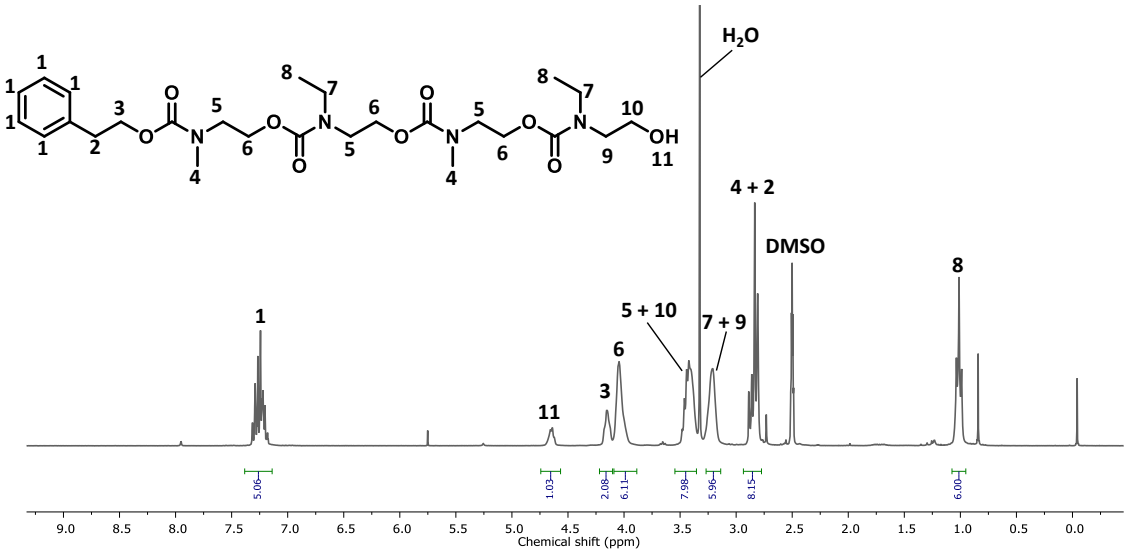


Figure S9: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of **M1**.

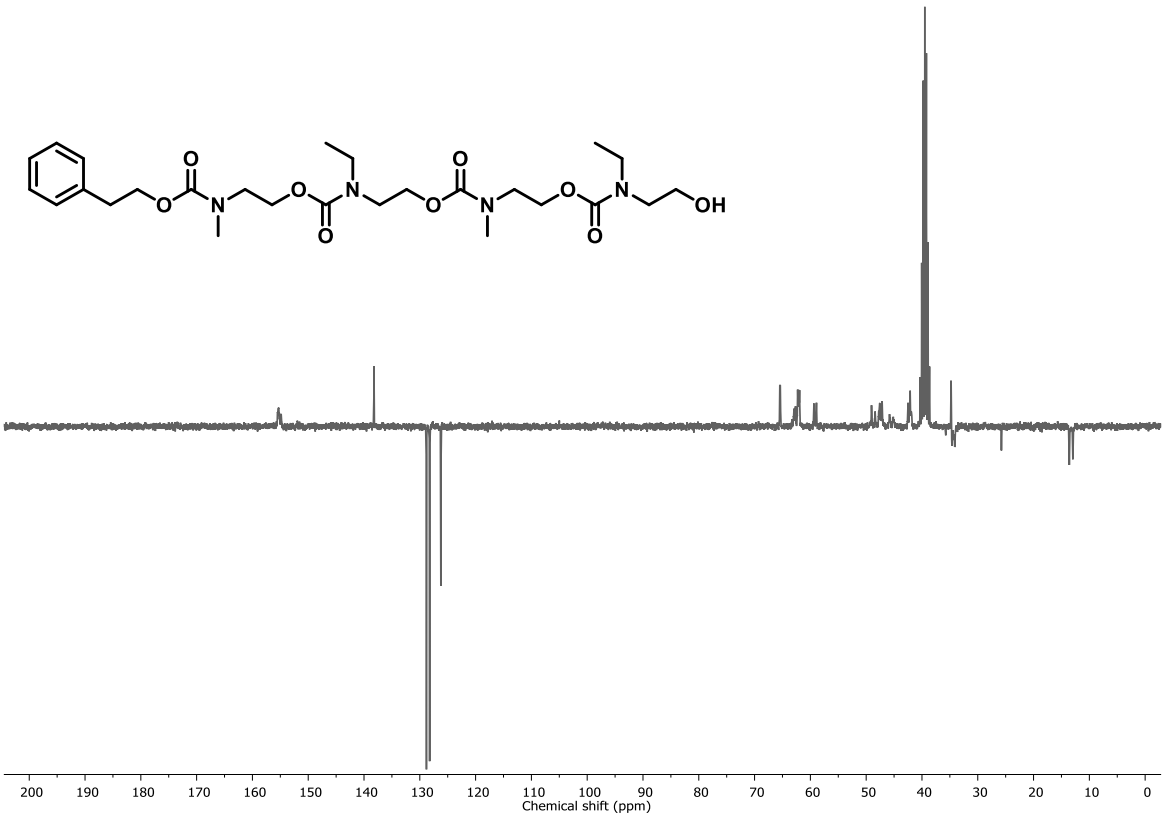


Figure S10: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **M1**.

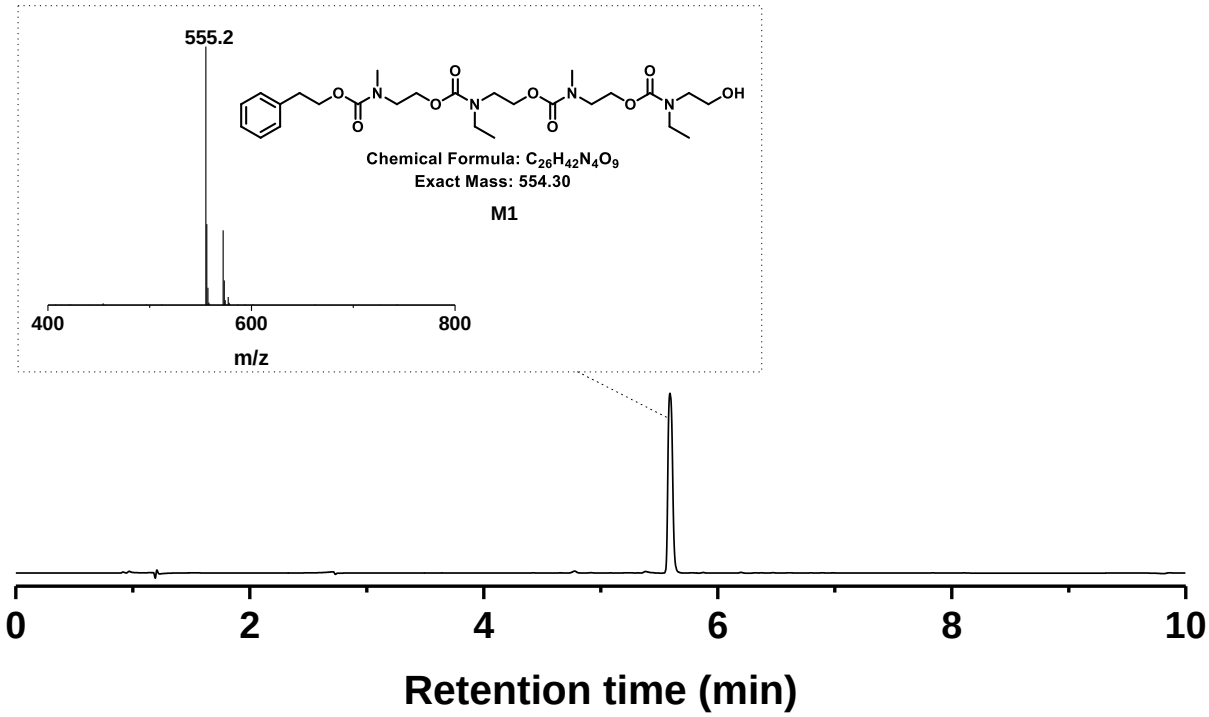
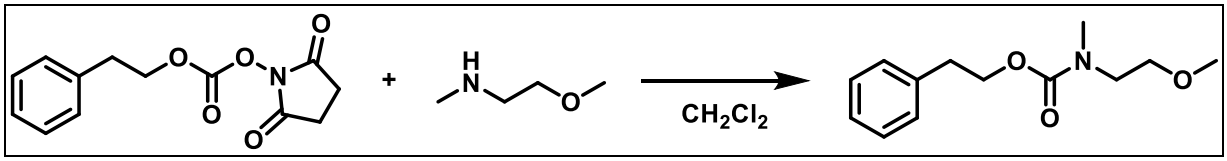


Figure S11: LC-MS trace (λ = 214 nm) of **M1**. The product is observed as $[M+H]^+$, t = 5.57 min.

3.5 N-methyl β-methoxy carbamate model compound (4)



Model compound 4 was synthesized according to the general procedure (200 mg starting material **2**), yielding a transparent oil (168 mg, 93%).

^{1}H-NMR (300 MHz, DMSO-d_6, δ): 7.30 (m, 5H, 5xCH), 4.16 (t, 2H, CH_2), 3.35 (m, 4H, 2xCH_2), 3.21 (m, 3H, CH_3), 2.84 (s, 3H, CH_3).
^{13}C-NMR (75 MHz, DMSO-d_6, δ): 155.1 (C), 137.1 (C), 128.2 (CH), 125.8 (CH), 69.4 (CH_2) 64.9 (CH_2), 57.5 (CH_3), 47.3 (CH_2), 35.0 (CH_2), 35.1 + 34.2(CH_3).
IR (ATR platinum diamond): *ν* [cm^{-1}] = 3027 (C_{ar}-H), 2927 (C-H), 1680 (C=O), 1447 (C-H), 1222 (C-N), 1108(C-O), 1050 (C-O), 767 (C-H).

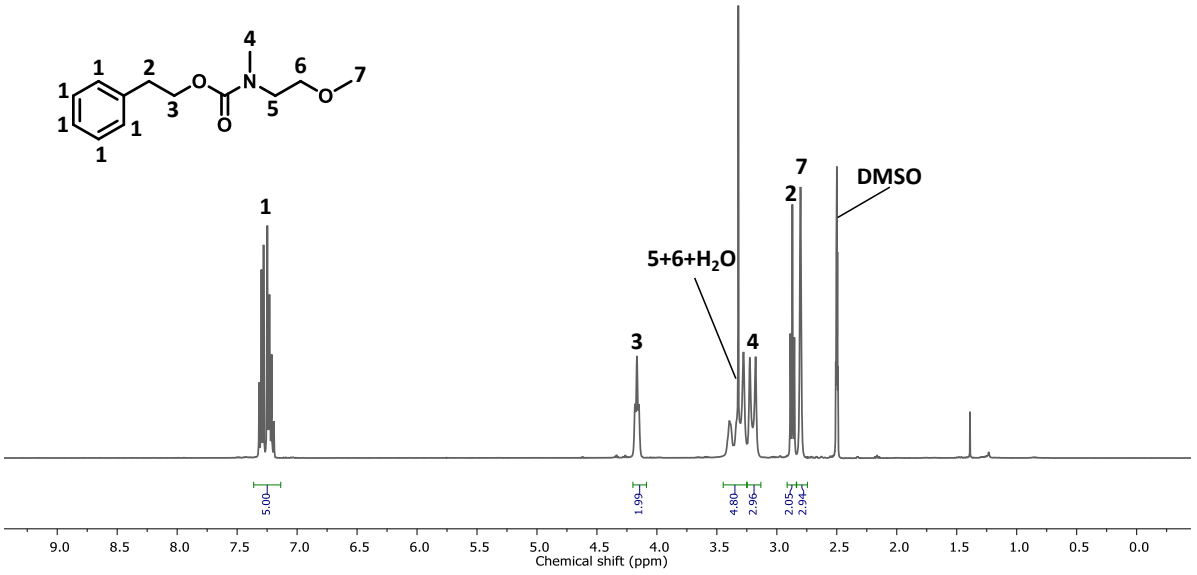


Figure S12: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of **4**.

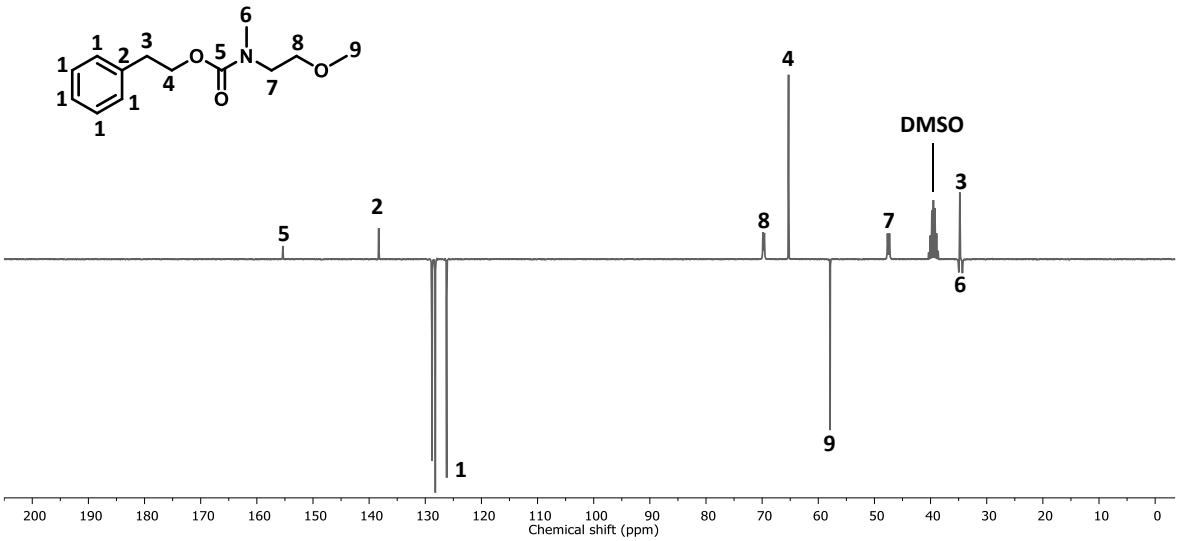


Figure S13: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **4**.

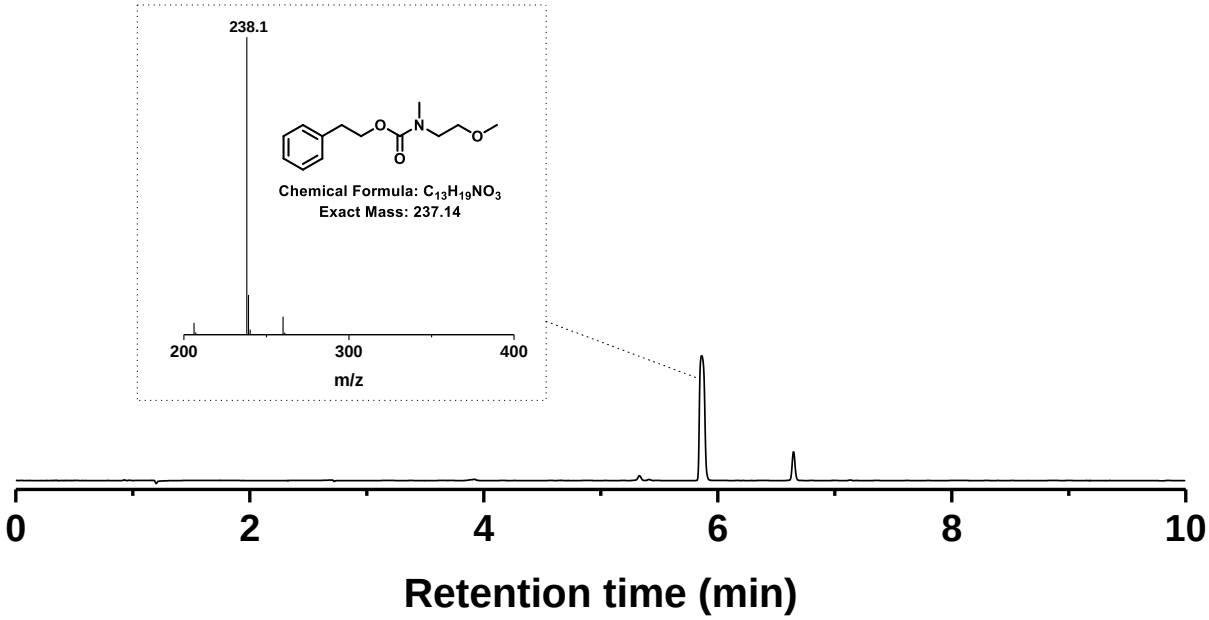
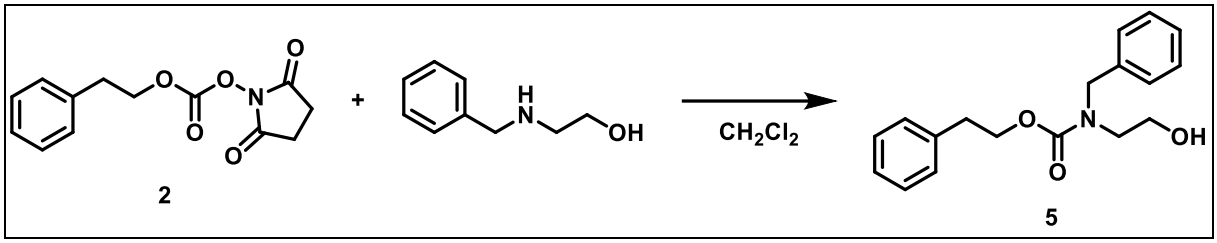


Figure S14: LC-MS trace (λ = 214 nm) of **4**. The product is observed as $[M+H]^+$, t = 5.89 min.

3.6 N-benzyl β-hydroxy carbamate model compound (5)



Model compound **5** was synthesized according to the general procedure (200 mg starting material **2**), yielding a transparent oil (204 mg, 90%).

^{1}H-NMR (300 MHz, DMSO-d_6, δ): 7.25 (m, 10H, 10xCH), 4.64 (t, 1H, OH), 4.44 (double singlet, cis/trans rotamers 2H, CH_2), 4.22 (t, 2H, CH_2), 3.42 (m, 2H, CH_2), 3.21 (m, 2H, CH_2), 2.84 (m, 2H, CH_2).
^{13}C-NMR (75 MHz, DMSO-d_6, δ): 155.1 (C), 138.12 (C), 128.2 (CH), 64.9 (CH_2), 58.2 (CH_2), 52.5 (CH_2), 34.4 (CH_2).
IR (ATR platinum diamond): *ν* [cm^{-1}] = 3415 (O-H), 3030 (C_{ar}-H), 2940 (C-H), 1673 (C=O), 1453 (C-H), 1228 (C-N), 1053 (C-O), 766 (C-H).

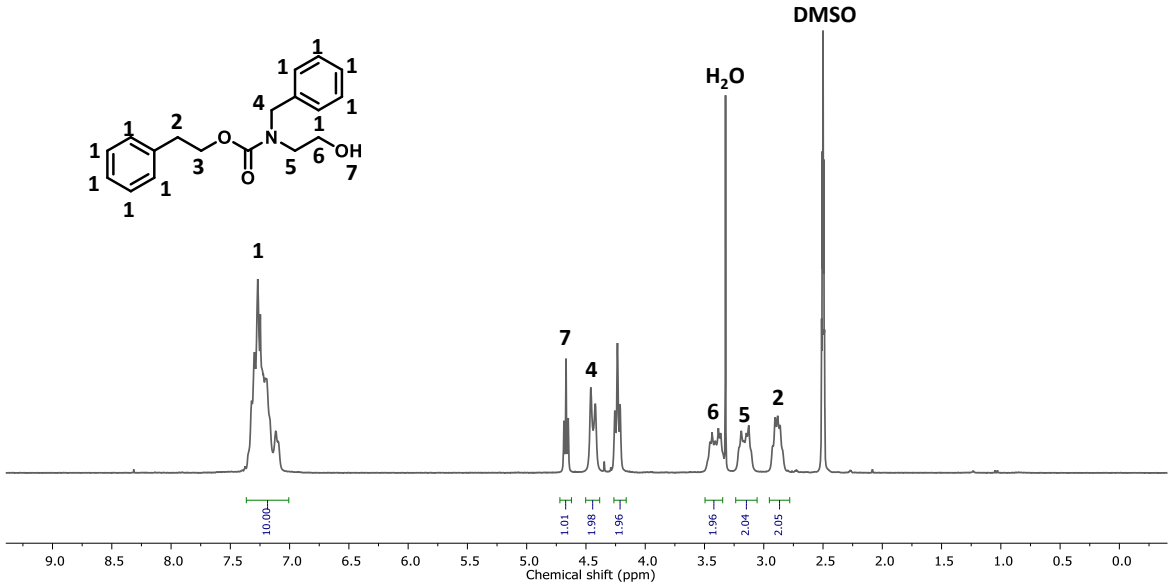


Figure S15: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of **5**.

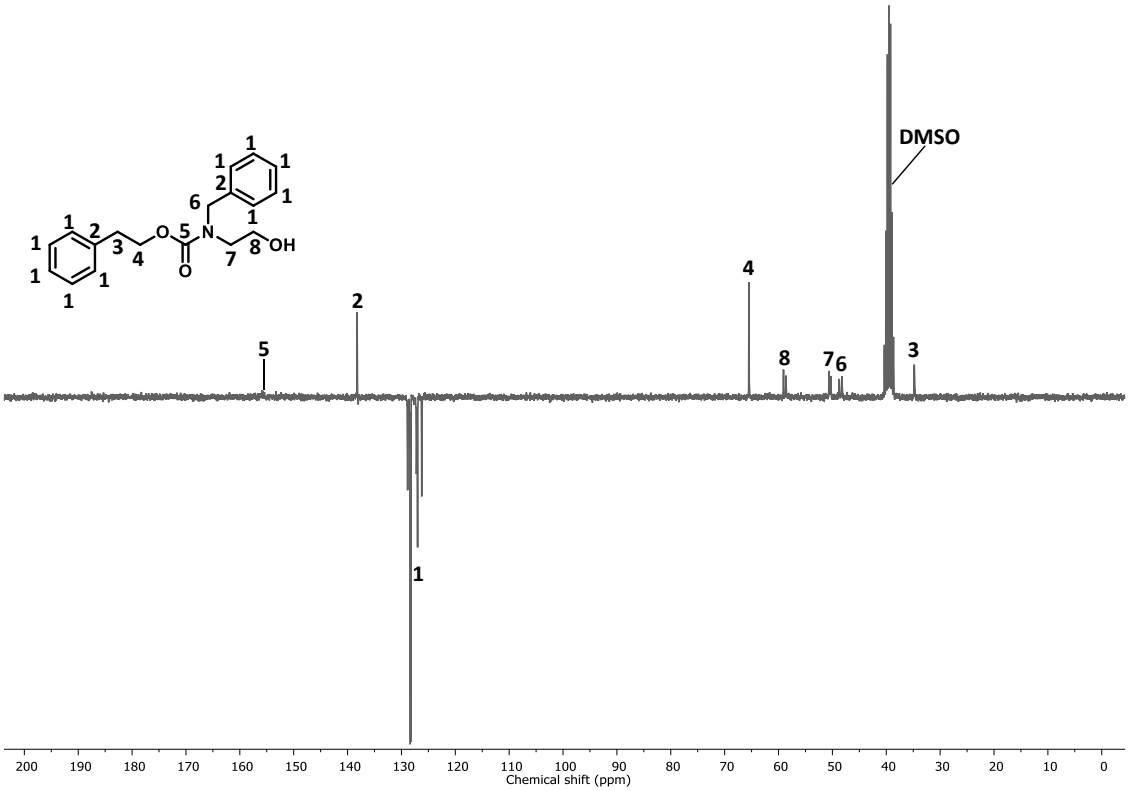


Figure S16: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **5**.

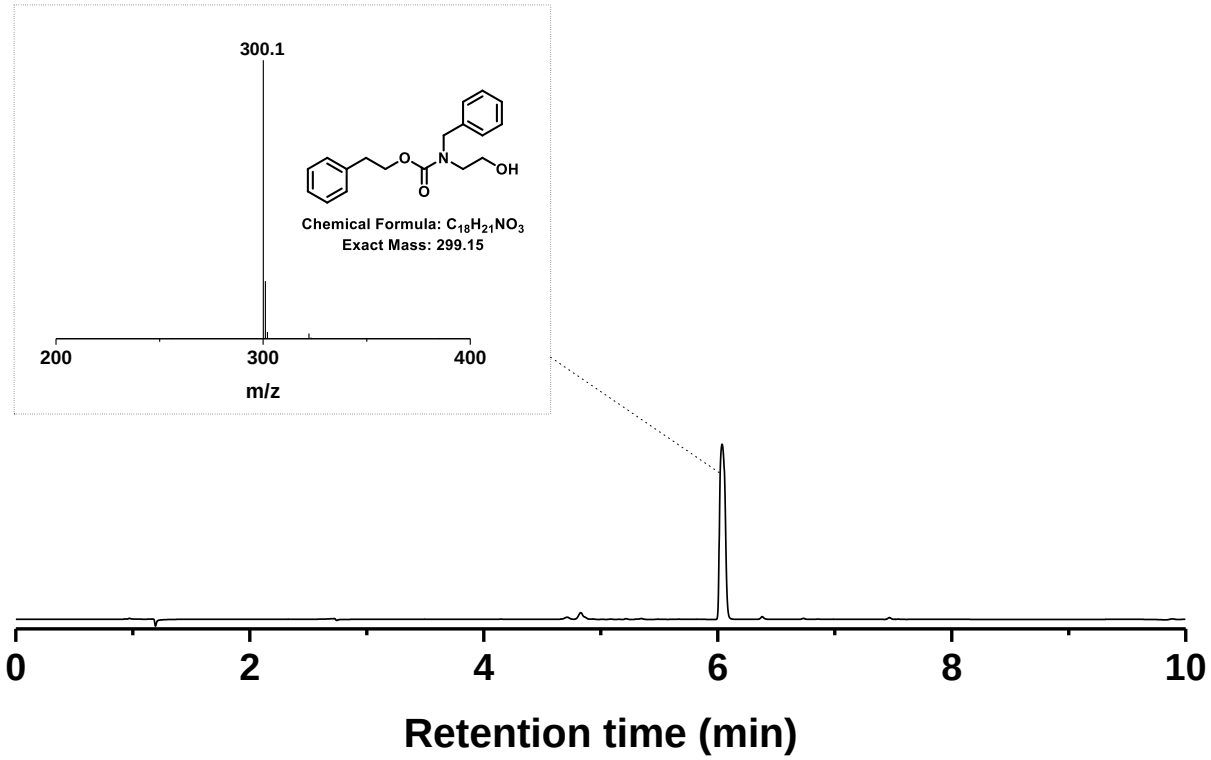
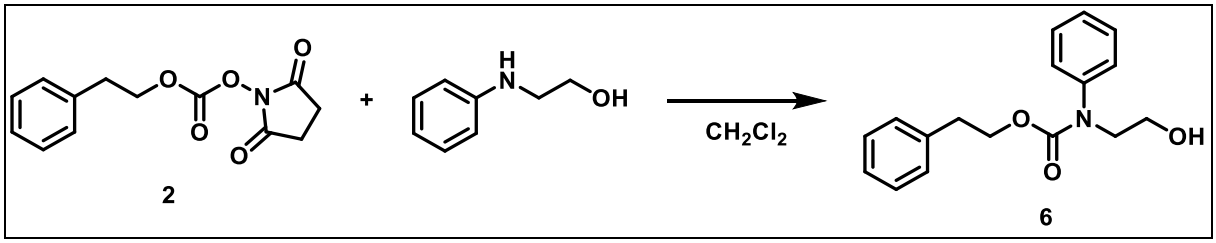


Figure S17: LC-MS trace (λ = 214 nm) of **5**. The product is observed as $[M+H]^+$, t = 6.05 min.

3.7 N-phenyl β-hydroxy carbamate model compound (6)



Model compound **6** was synthesized according to the general procedure, but the reaction was left to stir overnight (200 mg starting material **2**), yielding a viscous oil (186 mg, 86%).

^{1}H-NMR (300 MHz, DMSO-d_6, δ): 7.27 (m, 10H, 10xCH), 4.68 (t, 1H, OH), 4.17 (t, 2H, CH_2), 3.60 (m, 2H, CH_2), 3.43 (m, 2H, CH_2), 2.84 (m, 2H, CH_2).
^{13}C-NMR (75 MHz, DMSO-d_6, δ): 155.1 (C), 138.1 (C), 128.2 (CH), 64.9 (CH_2), 58.2 (CH_2), 52.5 (CH_2), 34.4 (CH_2).
IR (ATR platinum diamond): *v* [cm^{-1}] = 3423 (O-H), 3029 (C_{ar}-H), 2942 (C-H), 1676 (C=O), 1450 (C-H), 1228 (C-N), 1053 (C-O), 767 (C-H).

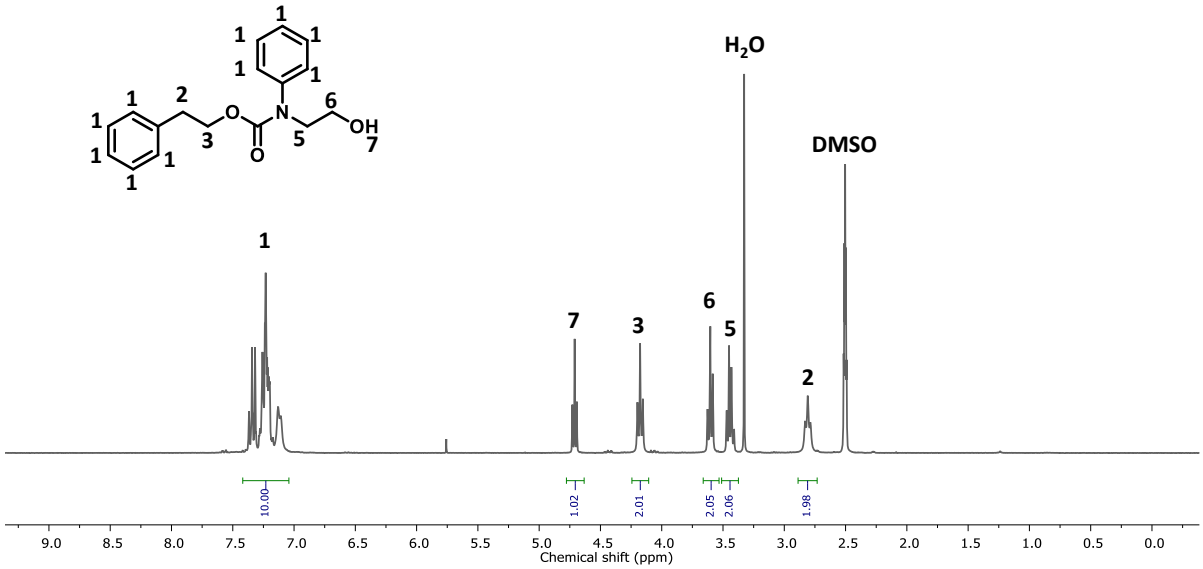


Figure S18: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of **6**.

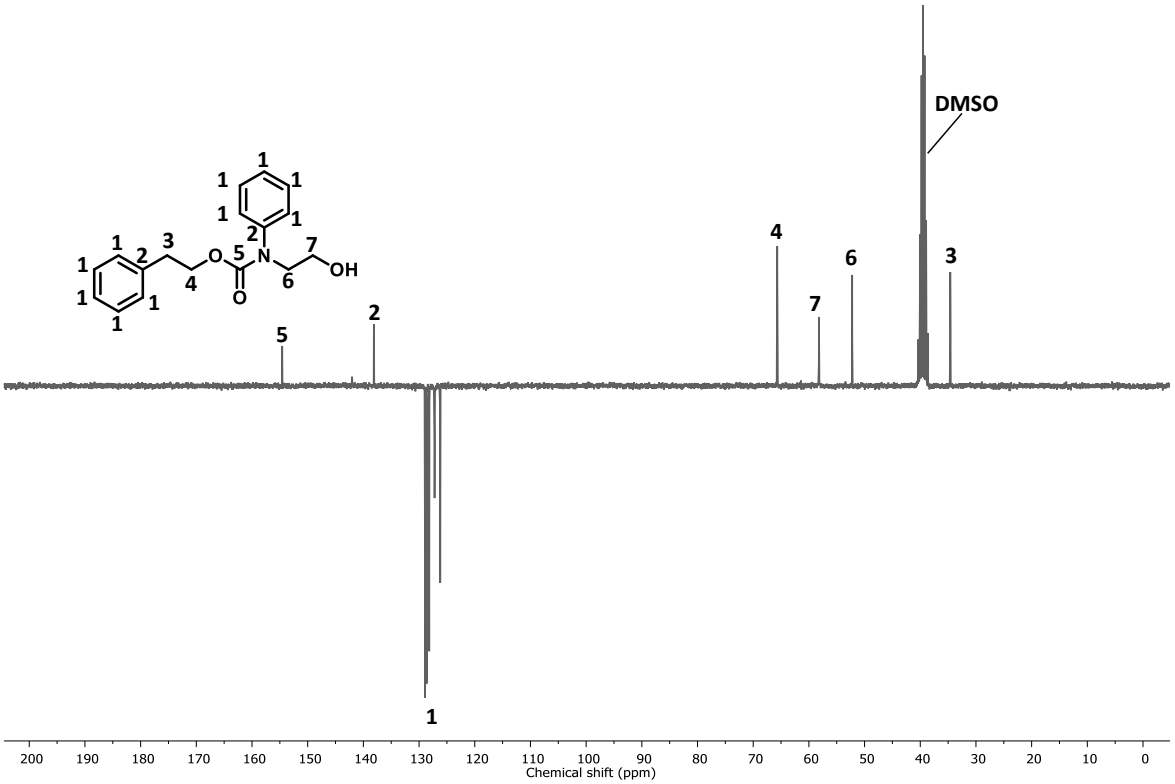


Figure S19: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **6**.

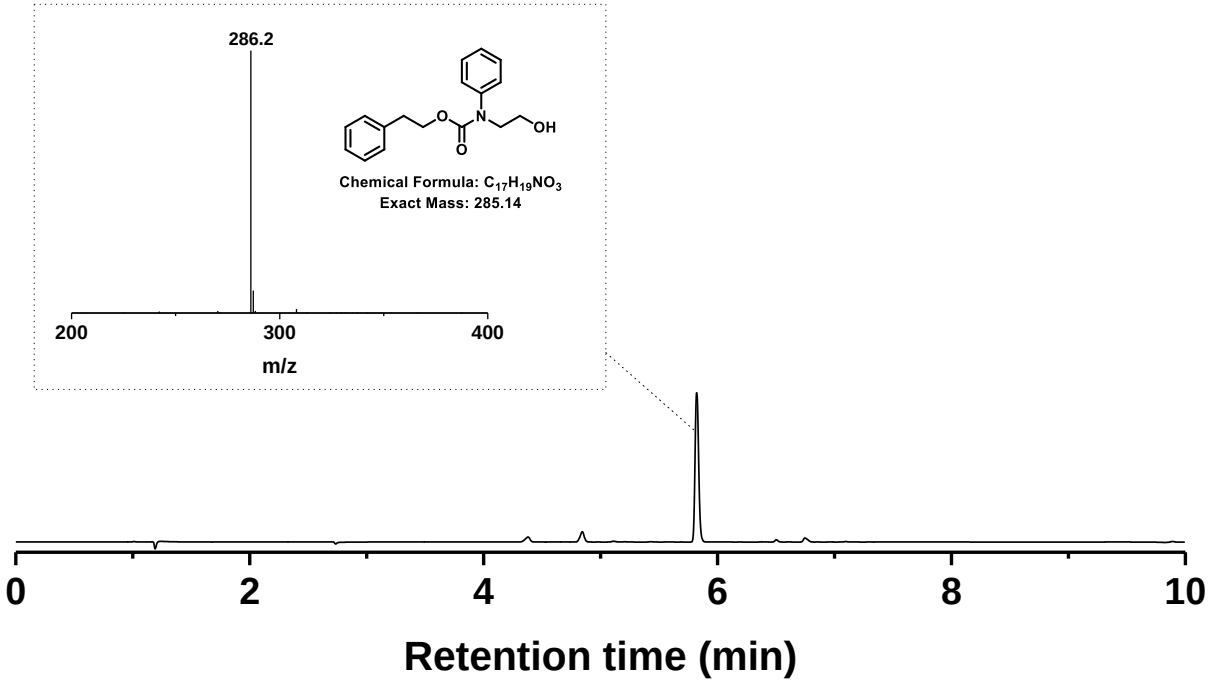
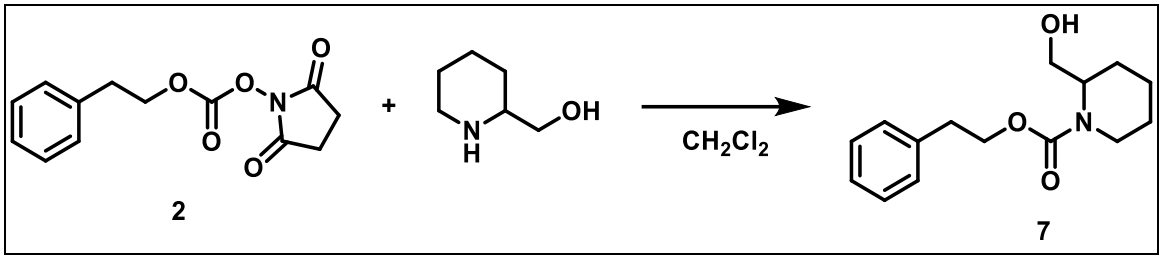


Figure S20: LC-MS trace (λ = 214 nm) of **6**. The product is observed as $[M+H]^+$, t = 5.83 min.

3.8 2-piperidinemethanol-based model compound (7)



Model compound **7** was synthesized according to the general procedure (200 mg starting material **2**), yielding a transparent oil (192 mg, 96%).

^{1}H-NMR (300 MHz, DMSO-d_6, δ): 7.27 (m, 5H, 5xCH), 4.66 (t, 1H, OH), 4.17 (t, 2H, CH_2), 4.05 (m, 1H, CH), 3.84 (m, 1H, CH_2), 3.44 (m, 2H, CH_2), 2.84 (m, 2H, CH_2), 2.76 (m, 1H, CH_2), 1.74 (m, 1H, CH_2), 1.47 (m, 4H, 2xCH_2), 1.23 (m, 1H, CH_2).
^{13}C-NMR (75 MHz, DMSO-d_6, δ): 155.1 (C), 138.1 (C), 128.2 (CH), 64.9 (CH_2), 58.2 (CH_2), 51.4 (CH), 39.5 (CH_2), 34.9 (CH_2), 24.9 (CH_2), 23.8 (CH_2), 18.4 (CH_2).
IR (ATR platinum diamond): *v* [cm^{-1}] = 3418 (O-H), 3026 (C_{ar}-H), 2928 (C-H), 1664 (C=O), 1425 (C-H), 1261 (C-N), 1048 (C-O), 765 (C-H).

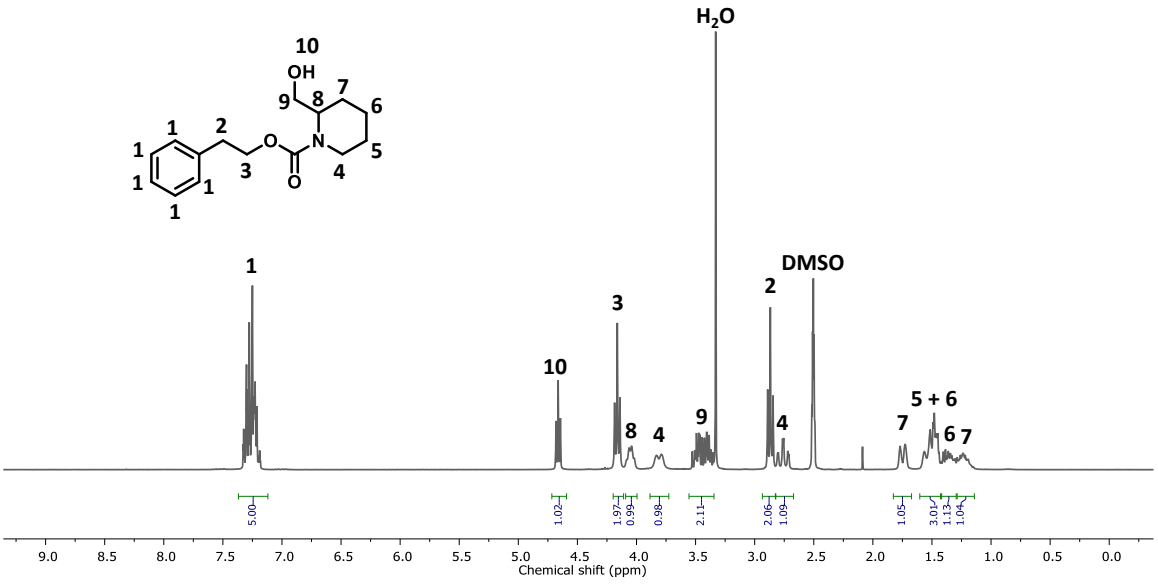


Figure S21: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of **7**.

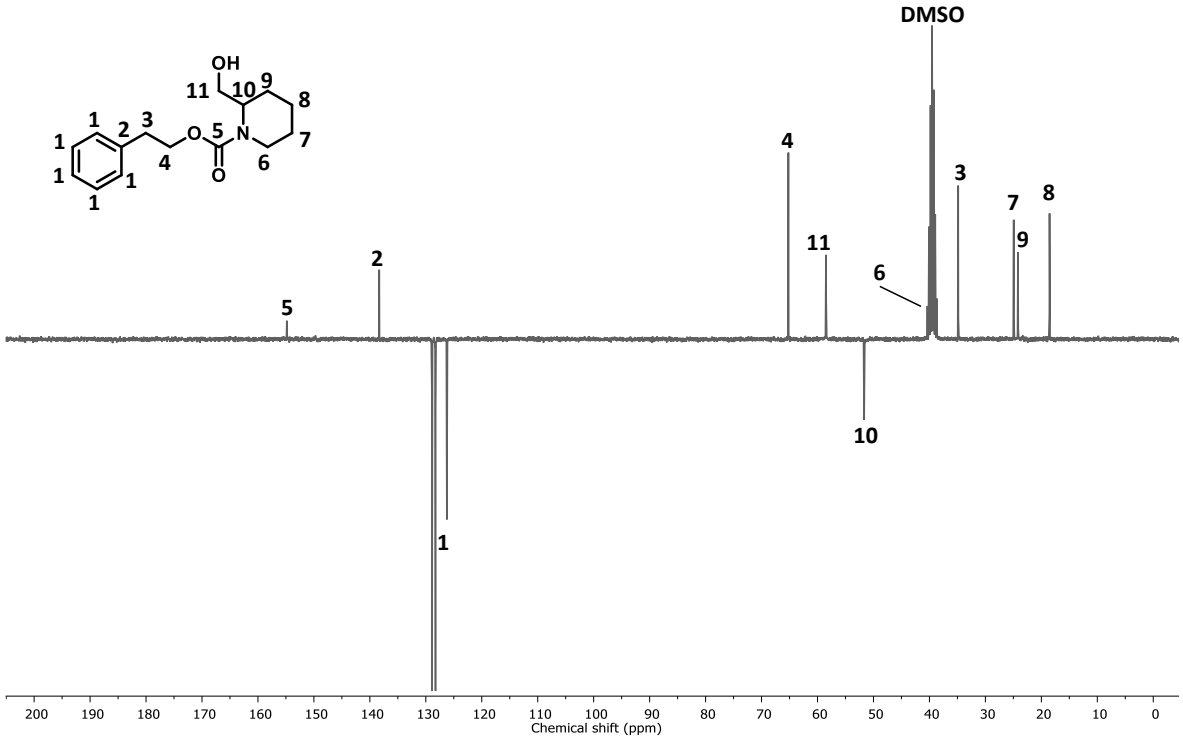


Figure S22: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **7**.

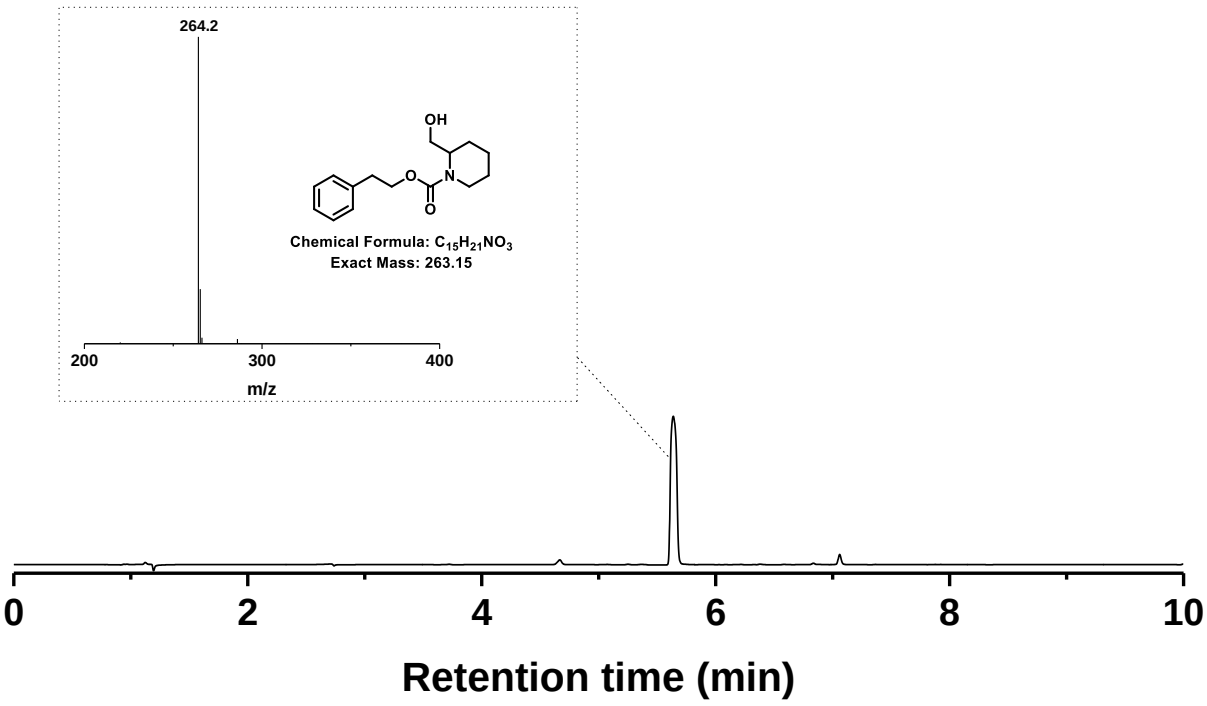
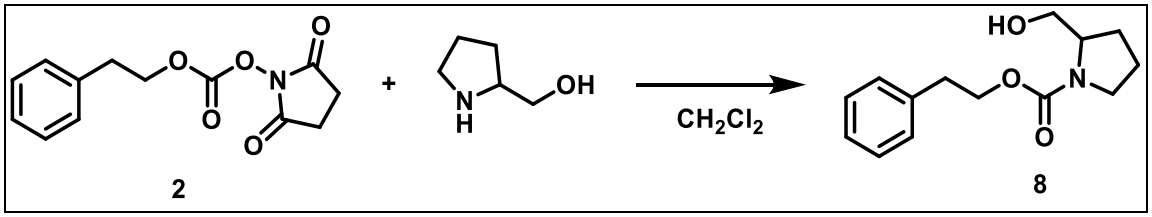


Figure S23: LC-MS trace (λ = 214 nm) of **7**. The product is observed as $[M+H]^+$, t = 5.65 min.

3.9 *DL*-prolinol based model compound (8)



Model compound **8** was synthesized according to the general procedure (200 mg starting material **2**), yielding a transparent oil (155 mg, 82%).

^{1}H-NMR (300 MHz, DMSO-d_6, δ): 7.27 (m, 5H, 5xCH), 4.68 (br, 1H, OH), 4.17 (t, 2H, CH_2), 4.05 (m, 1H, CH), 3.68 (br, 1H, CH), 3.45 (m, 1H, CH_2), 3.22 (m, 3H, CH_2 and 1H from CH_2), 2.84 (m, 2H, CH_2), 1.83 (m, 4H, 2 x CH_2).
^{13}C-NMR (75 MHz, DMSO-d_6, δ): 155.1 (C), 138.1 (C), 128.2 (CH), 64.9 (CH_2), 61.4 (CH_2), 58.2 (CH), 46.3 (CH_2), 34.9 (CH_2), 27.5 (CH_2), 22.8 (CH_2).
IR (ATR platinum diamond): *v* [cm^{-1}] = 3396 (O-H), 3030 (C_{ar}-H), 2955 (C-H), 1670 (C=O), 1417 (C-H), 1250 (C-N), 1046 (C-O), 768 (C-H).

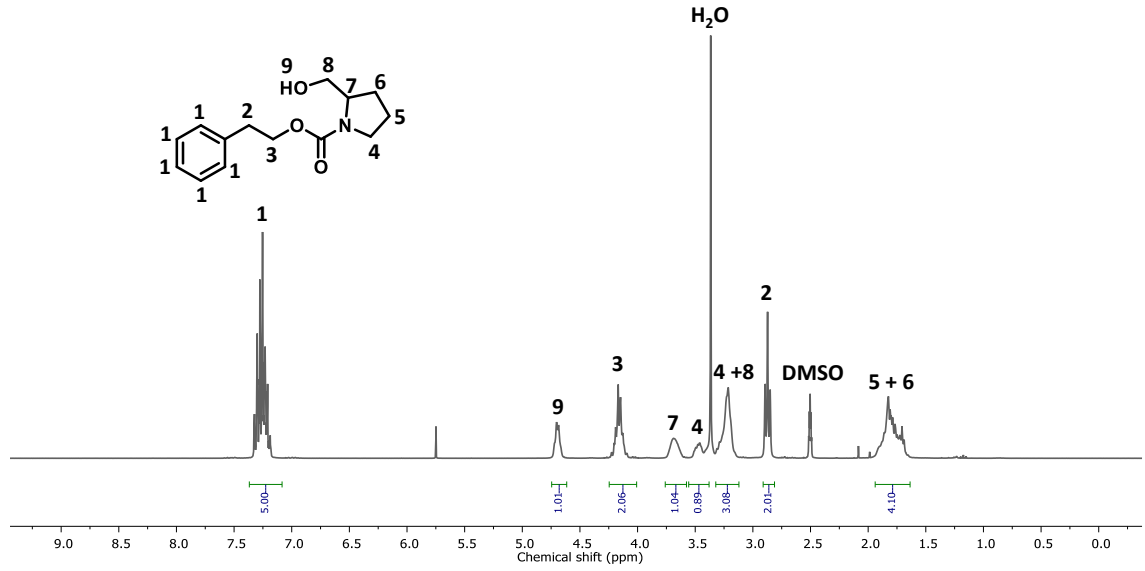


Figure S24: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of **8**.

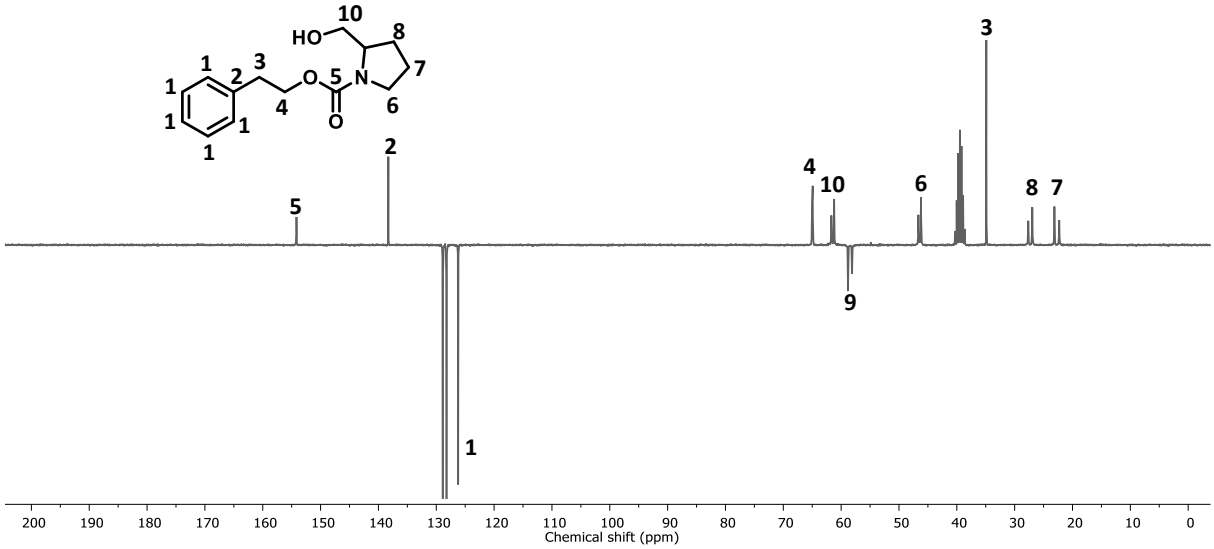


Figure S25: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **8**.

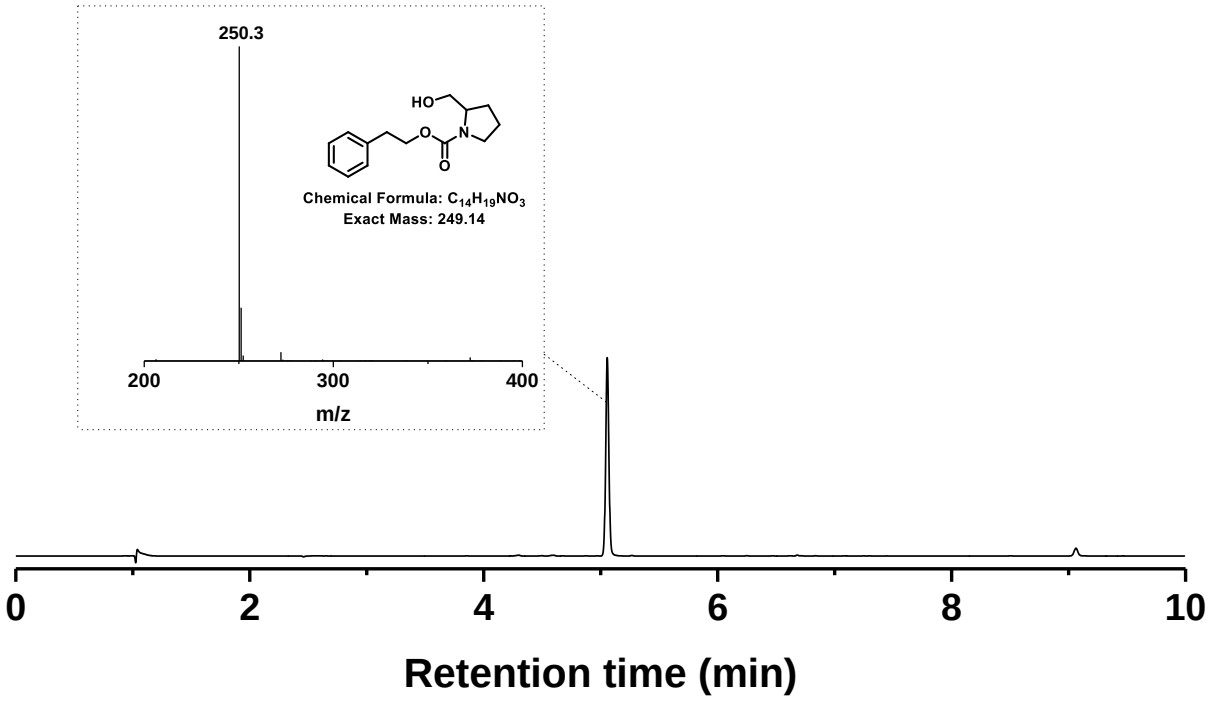


Figure S26: LC-MS trace (λ = 214 nm) of **8**. The product is observed as $[M+H]^+$, t = 5.05 min.

3.10 Synthesis of M2

The 1-mer was obtained by activation of 4-(hydroxymethyl)benzoate (1.5 g) and subsequent substitution with N-methyl ethanolamine according to the general procedure. Obtained as a viscous oil (2.11 g, 87%).

3.10.1 1-mer

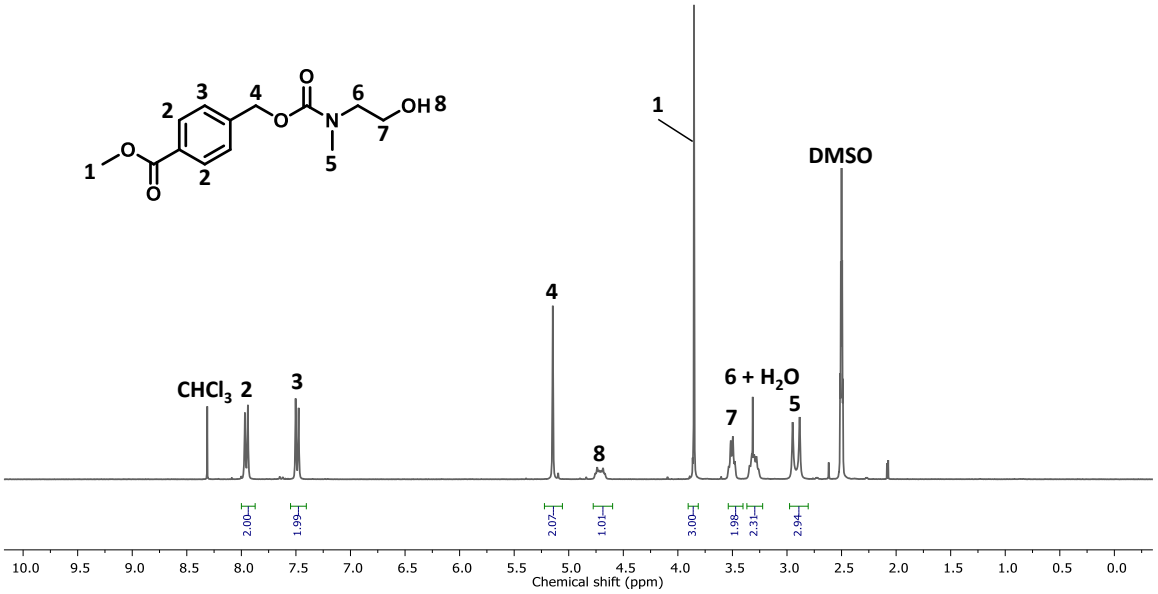


Figure S27: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of the first intermediate during the synthesis of **M2**.

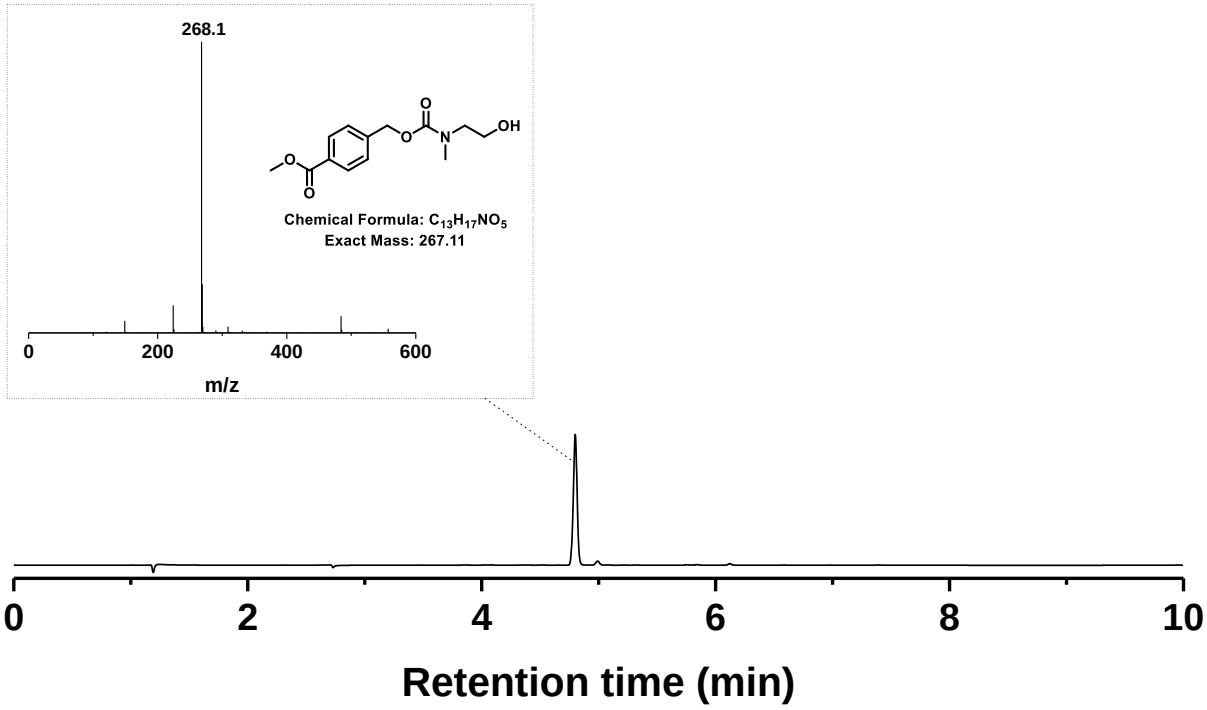


Figure S28: LC-MS trace (λ = 214 nm) of the first intermediate during the synthesis of **M2**. The product is observed as $[M+H]^+$, t = 4.82 min.

3.10.2 Dimer

The dimer was obtained by activation of the 1-mer (3.10.1) and subsequent substitution with N-ethyl ethanolamine according to the general procedure. Obtained as a viscous oil (2.52 g, 85%).

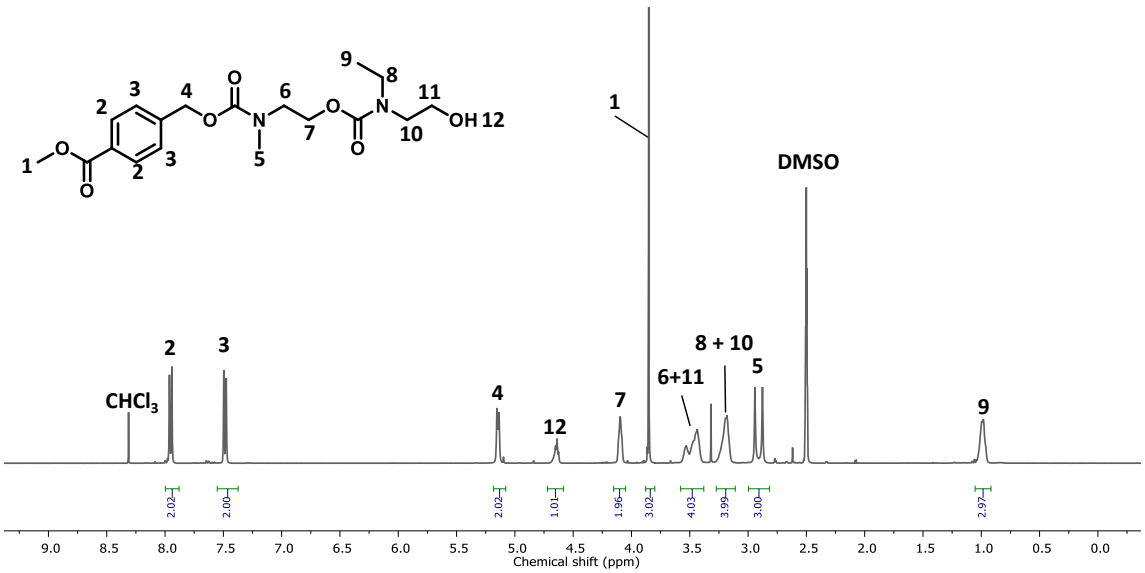


Figure S29: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of the dimer intermediate during the synthesis of **M2**.

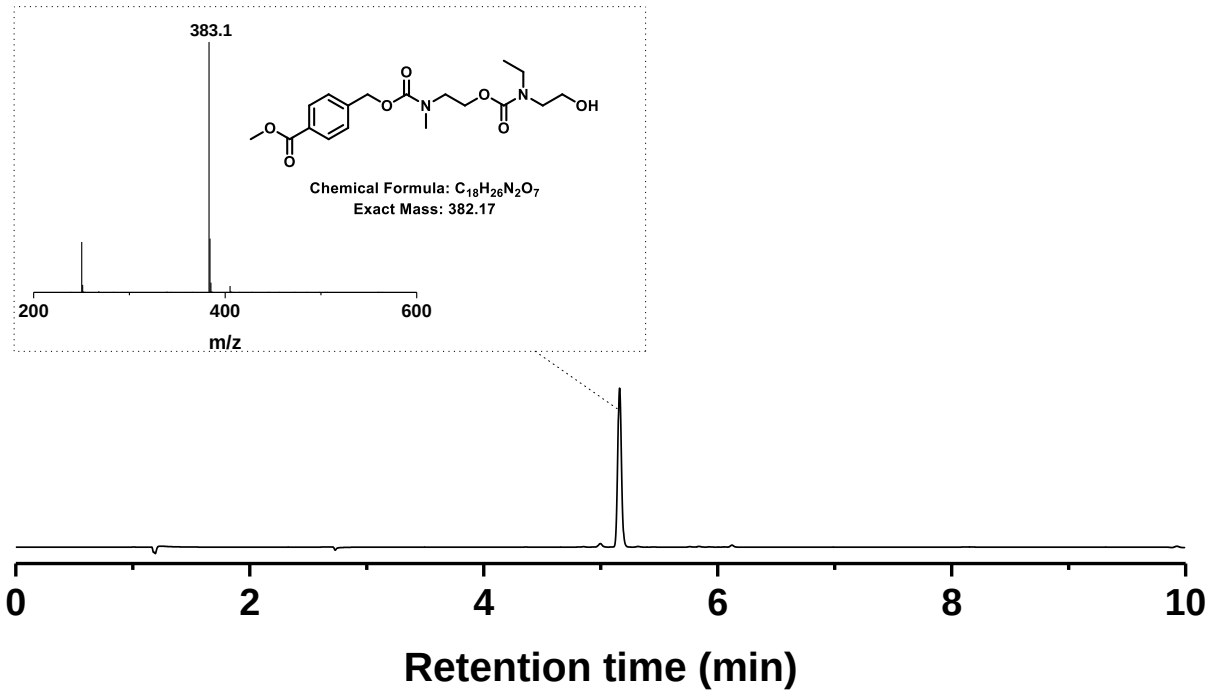


Figure S30: LC-MS trace (λ = 214 nm) of the dimer intermediate during the synthesis of **M2**. The product is observed as $[M+H]^+$, t = 5.17 min.

3.10.3 Trimer

The trimer was obtained by activation of the dimer (3.10.2) and subsequent substitution with N-methyl ethanolamine according to the general procedure. Obtained as a viscous oil (2.57 g, 89%).

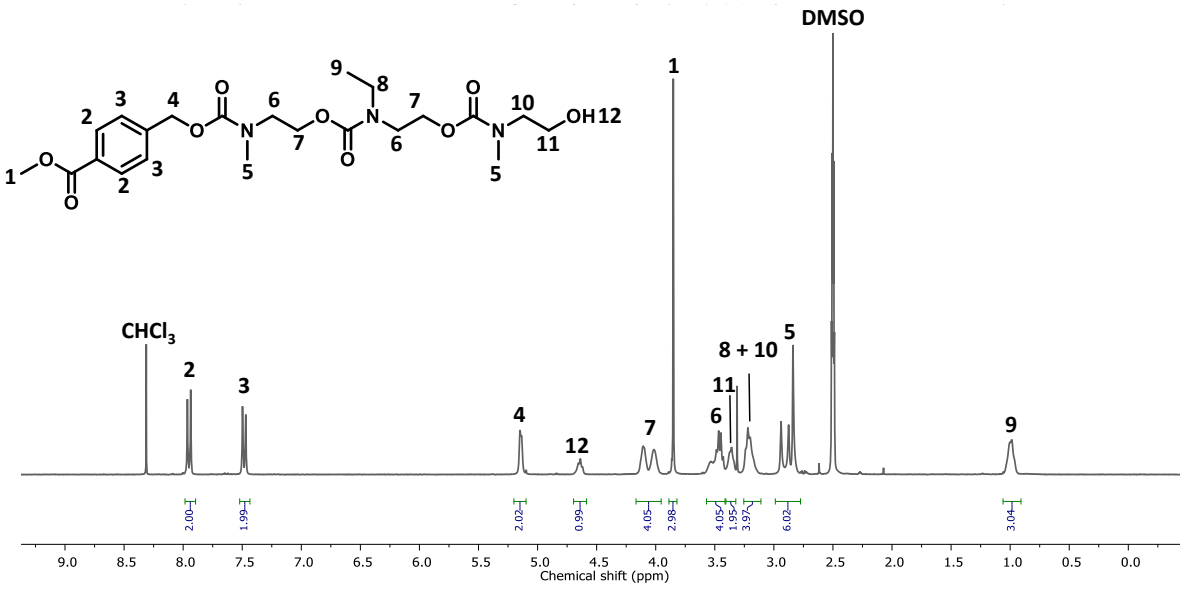


Figure S31: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of the trimer intermediate during the synthesis of **M2**.

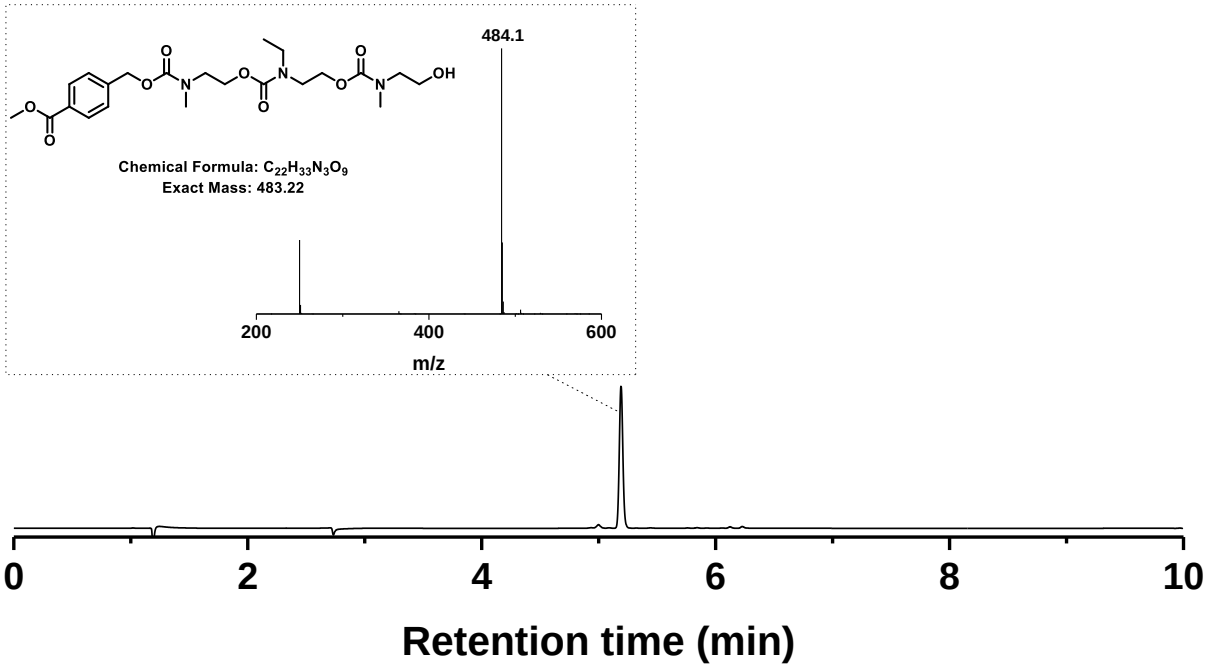


Figure S32: LC-MS trace (λ = 214 nm) of the trimer intermediate during the synthesis of **M2**. The product is observed as $[M+H]^+$, t = 5.24 min.

3.10.4 Tetramer

The tetramer was obtained by activation of the trimer (3.10.3) and subsequent substitution with N-methyl ethanolamine according to the general procedure. Obtained as a viscous oil (2.29 g, 88%).

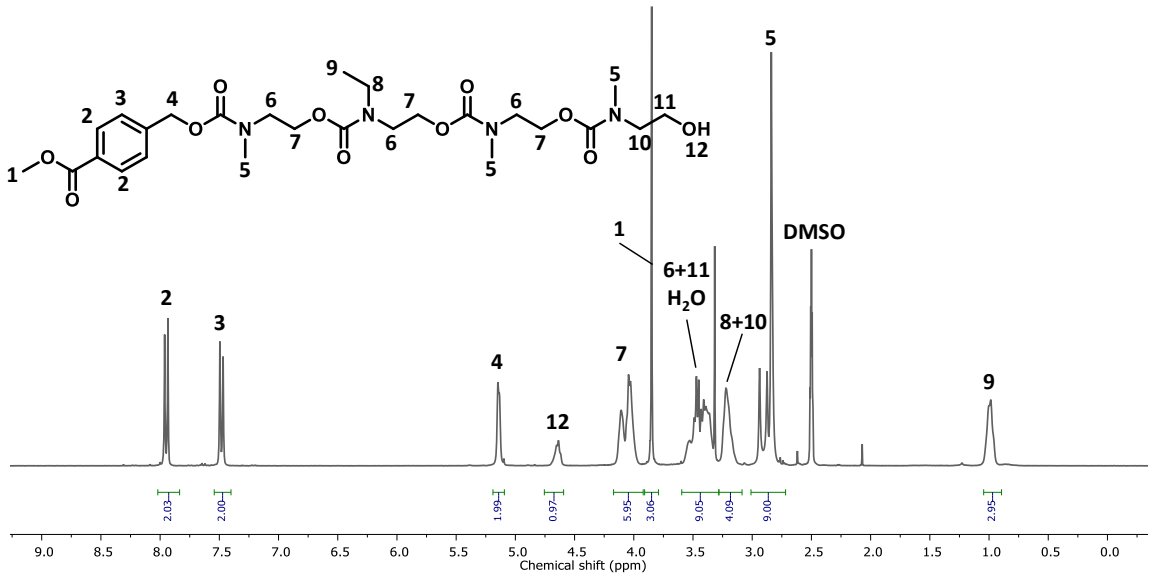


Figure S33: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of the tetramer intermediate during the synthesis of **M2**.

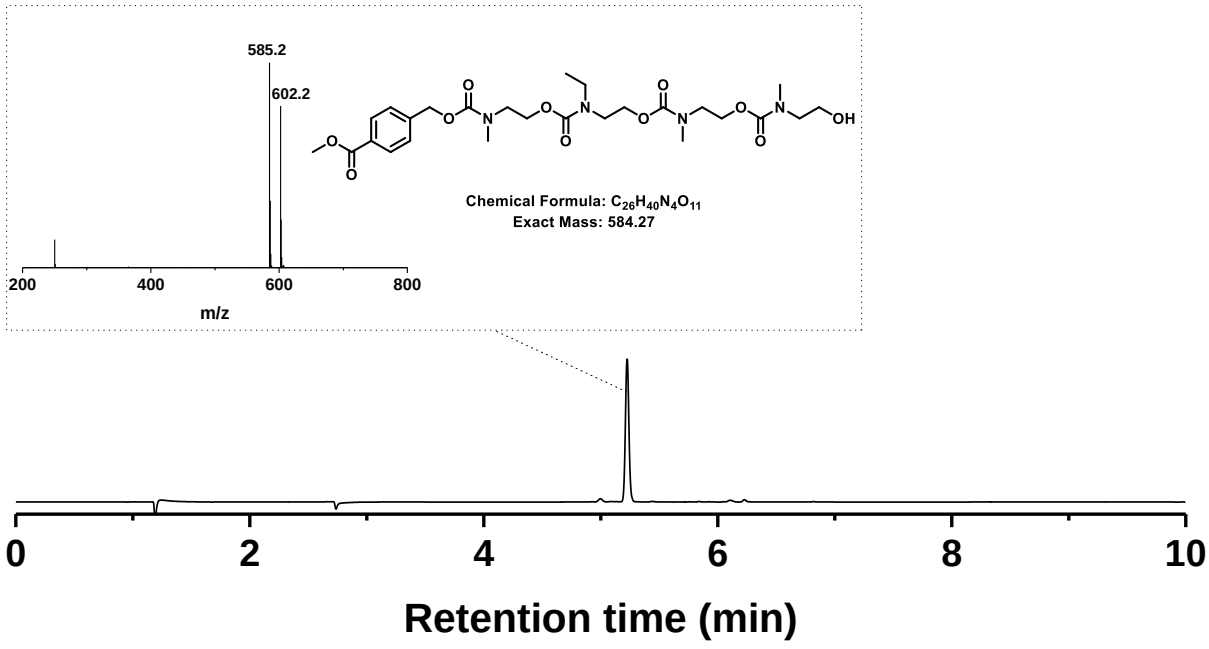


Figure S34: LC-MS trace (λ = 214 nm) of the tetramer intermediate during the synthesis of **M2**. The product is observed as $[M+H]^+$and $[M+NH_4]^+$ t = 5.21 min.

3.10.5 Pentamer

The pentamer was obtained by activation of the tetramer (3.10.4) and subsequent substitution with N-ethyl ethanolamine according to the general procedure. Obtained as a viscous oil (1.98 g, 83%).

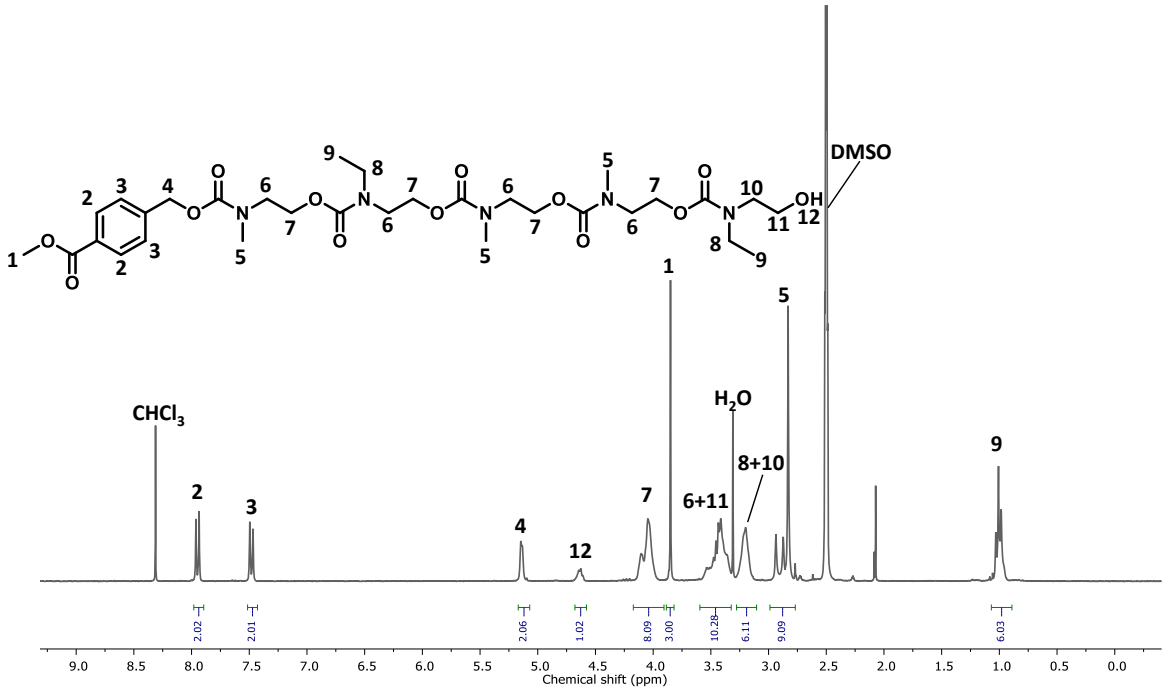


Figure S35: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of the pentamer intermediate during the synthesis of **M2**.

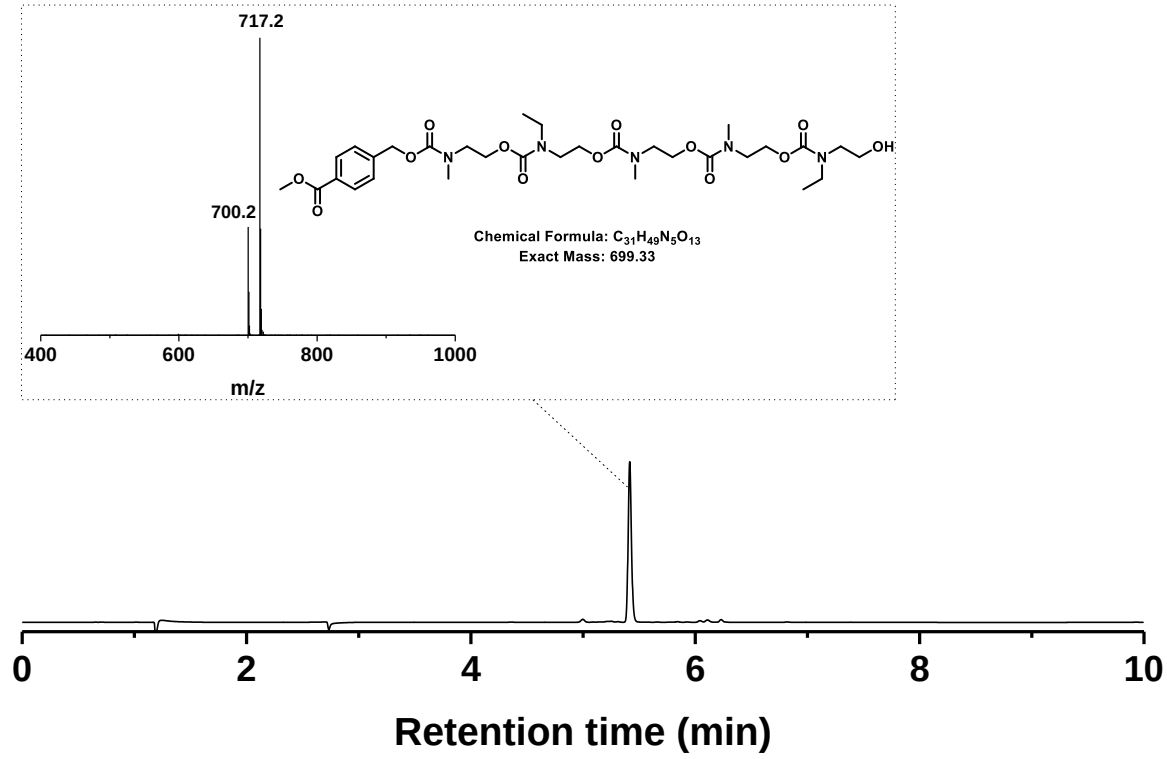


Figure S36: LC-MS trace (λ = 214 nm) of the pentamer intermediate during the synthesis of **M2**. The product is observed as $[M+H]^+$and $[M+NH_4]^+$, t = 5.41 min.

3.10.6 Hexamer M2

Hexamer **M2** was obtained by activation of the pentamer (3.10.5) and subsequent substitution with N-methyl ethanolamine according to the general procedure. Obtained as a viscous oil (1.89 g, 85%).

IR (ATR platinum diamond): *v* [cm^{-1}] = 3467 (O-H), 2952 (C-H), 1689 (C=O), 1455 + 1476 (C-H), 1275 (C-N), 1066 (C-O), 753 (C-H).

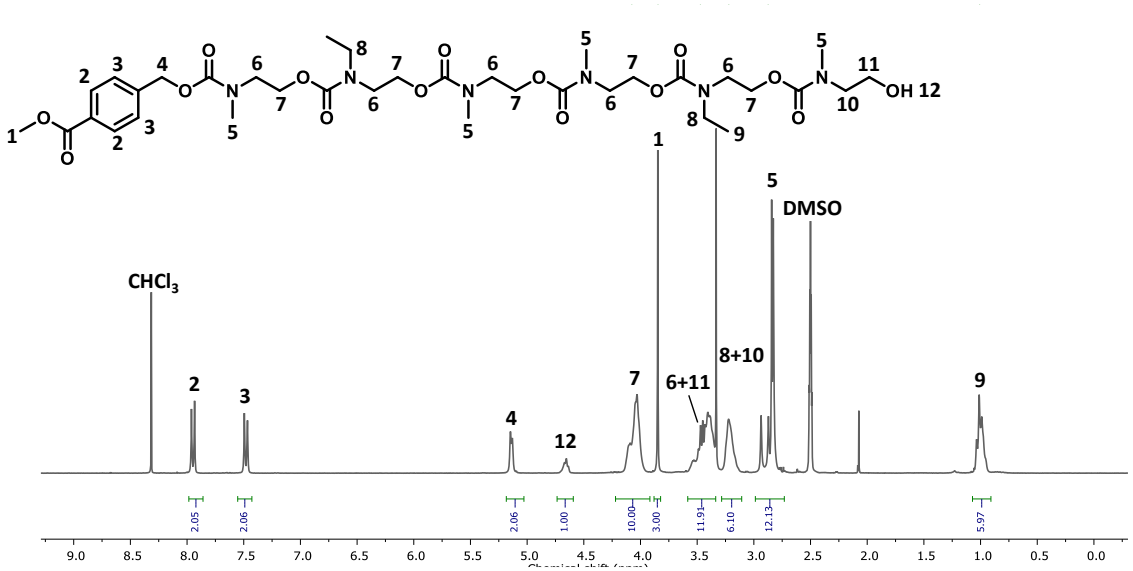


Figure S37: ^{1}H NMR analysis (300 MHz, DMSO-d_6) of **M2**.

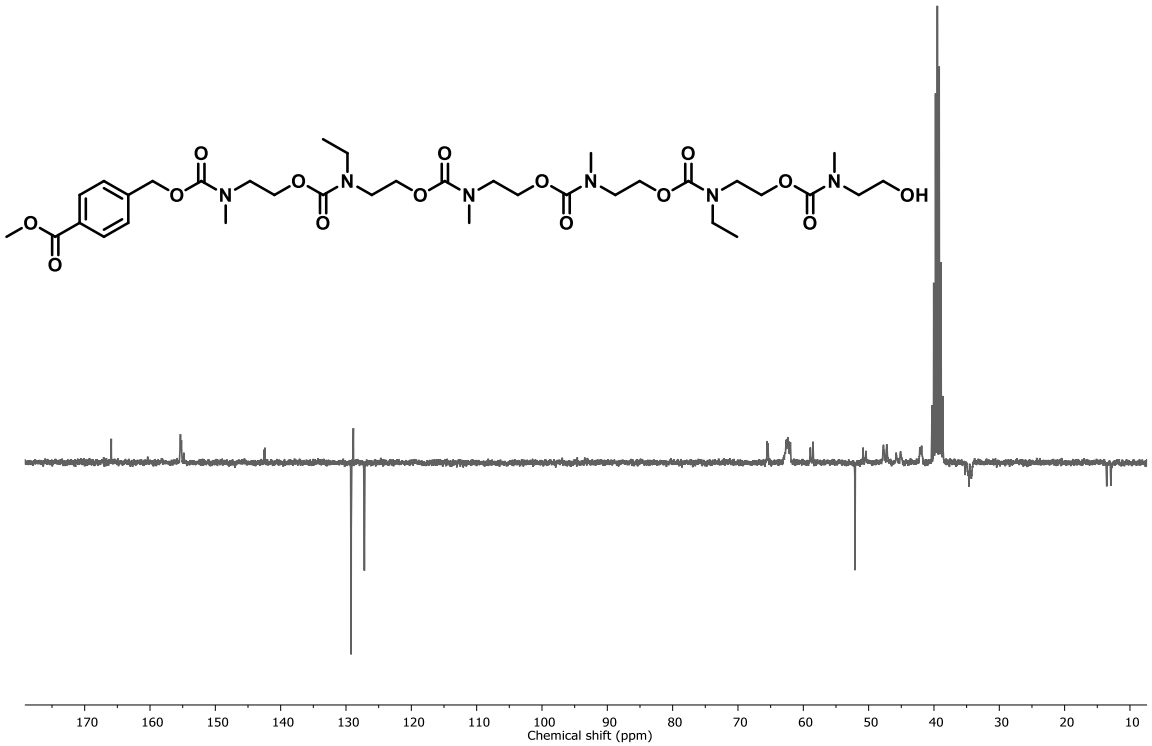


Figure S38: ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of **M2.**

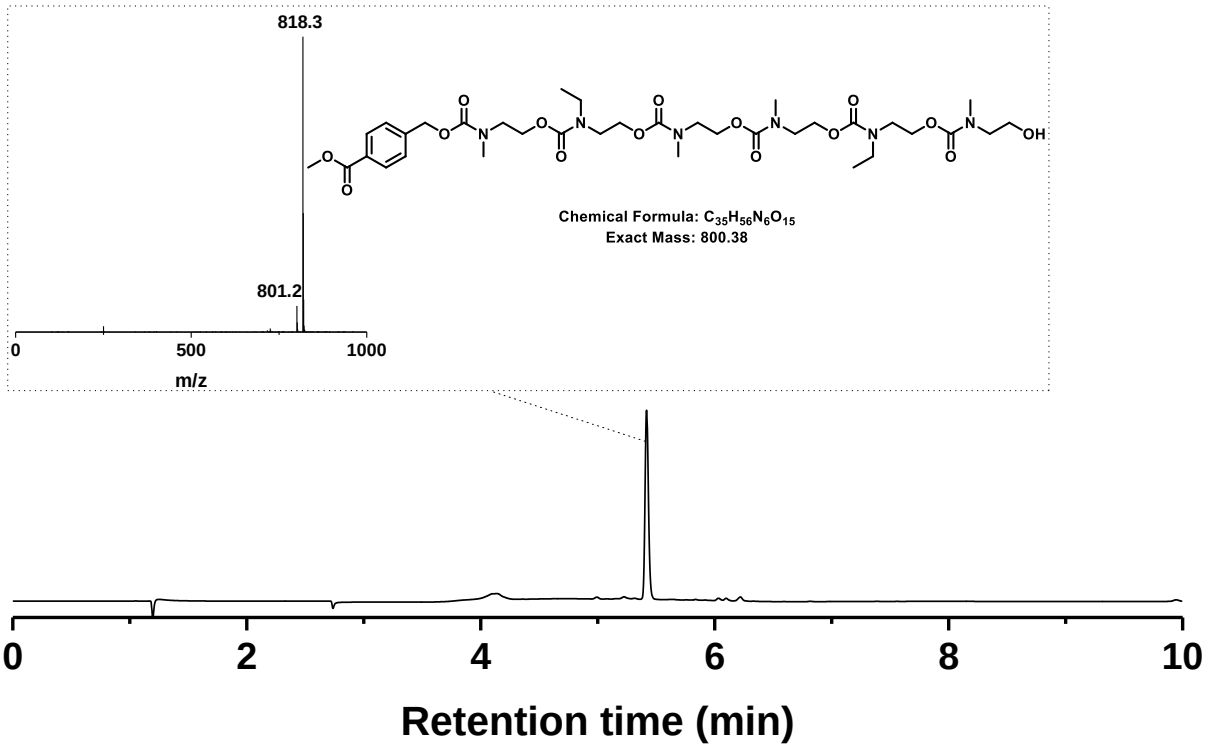
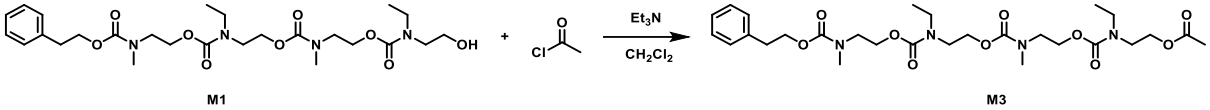


Figure S39: LC-MS trace (λ = 214 nm) of **M2**. The product is observed as $[M+H]^+$and $[M+NH_4]^+$, t = 5.41 min.

3.11 Synthesis of M3



A solution of **M1** (50 mg, 90µmol, 1 eq.) in 3 mL dichloromethane was treated with triethylamine (25 µL, 180 µmol, 2 eq.) and cooled to 0°C. Next, a solution of acryloyl chloride (9 µL, 135 µmol, 1.5 eq.) in 1 mL dichloromethane was added dropwise, and the reaction mixture was flushed with nitrogen. The reaction was then allowed to warm to room temperature, after which it was vigorously stirred for 5 hours. The mixture was further diluted with dichloromethane (10 mL) and washed with a 1M HCl solution (2 x 20 mL), saturated bicarbonate (2 x 20 mL) and brine (1 x 20 mL). The organic phase was dried with $MgSO_4$, filtered and concentrated in vacuo to yield **M3** as a clear viscous oil (51 mg, 95%).

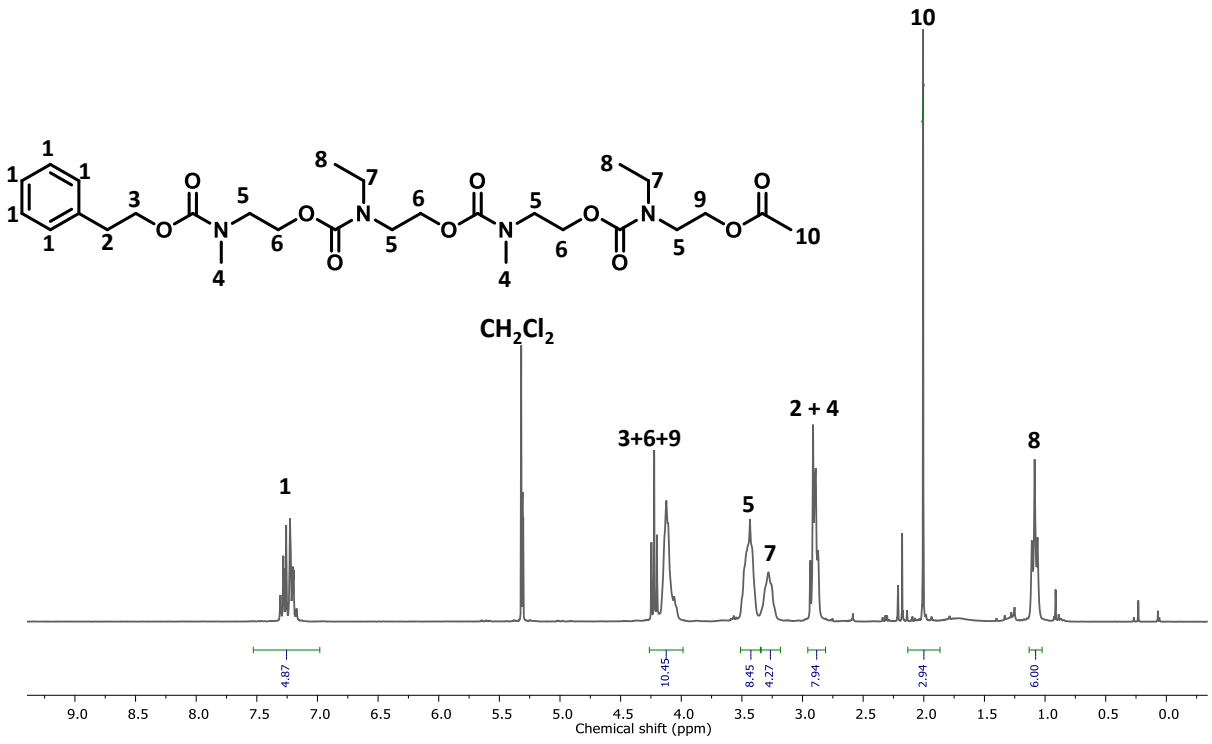


Figure S40: ^{1}H NMR analysis (300 MHz, CD_2Cl_2) of **M3**.

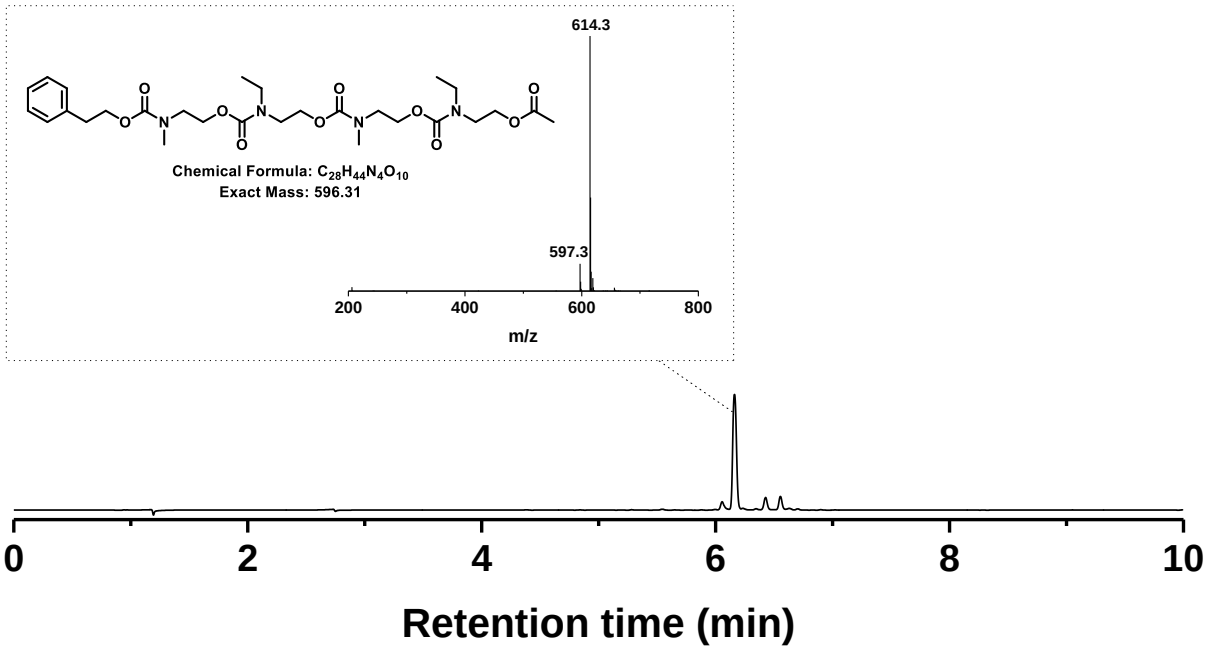


Figure S41: LC-MS trace (λ = 214 nm) of **M3**. The product is observed as $[M+H]^+$and $[M+NH_4]^+$, t = 6.15 min.

3.12 Synthesis and tagging of polyurethane (PU) material

3.12.1 Synthesis of PU-disk

A mixture of desmodur N3300A (1.5 g), pripol 2033 (2.2 g) and dibutyltin dilaurate (DBTL, 24 µL) was put in a plastic cup. This cup was placed in the speed mixer for 2 minutes (3000 rpm), after which it was further cured overnight at 50°C.

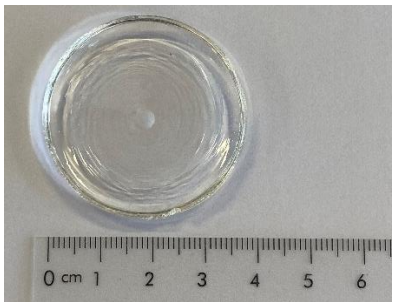


Figure S42: Non-labelled PU-disk.

Soluble fraction (%, after swelling in THF for 24h at 25°C): 0.8 ± 0.4

Swelling ratio (%, after swelling in THF for 24h at 25°C): 128 ± 0.3

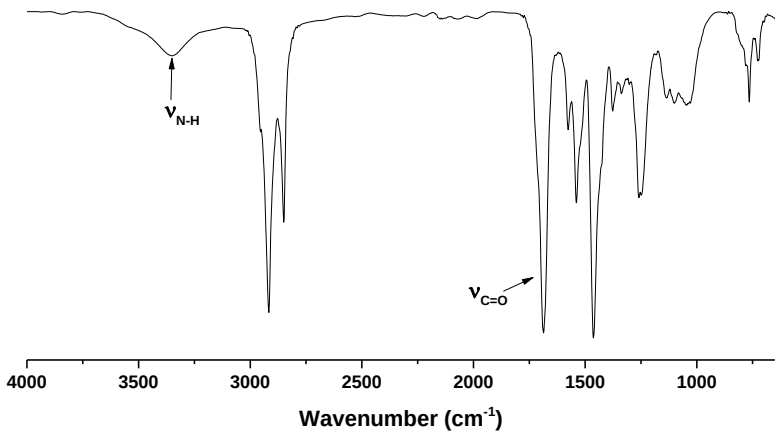


Figure S43: FT-IR spectra in transmission mode of the obtained polyurethane disk, indicating complete consumption of the isocyanate moieties.

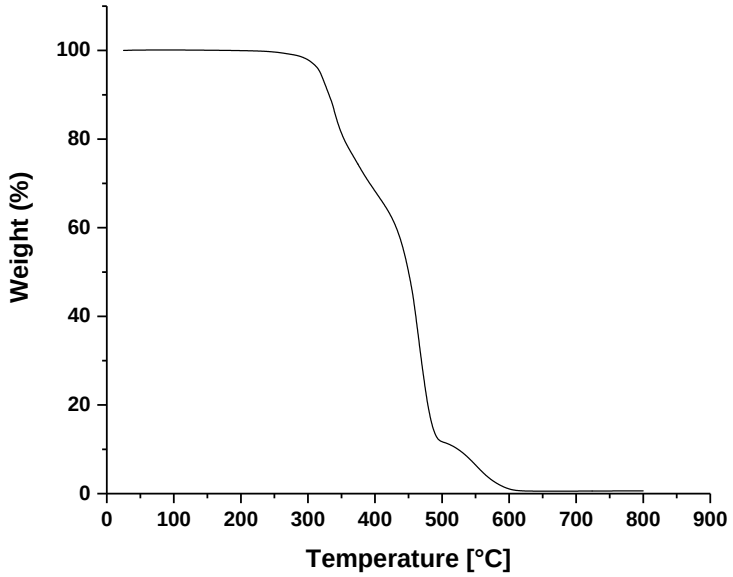


Figure S44: TGA analysis under N_2 atmosphere of the PU-disk with a temperature ramp from 25-800 °C and a heating rate of 10 °C.min^{-1}. $T_{d2\%}$ = 297°C.

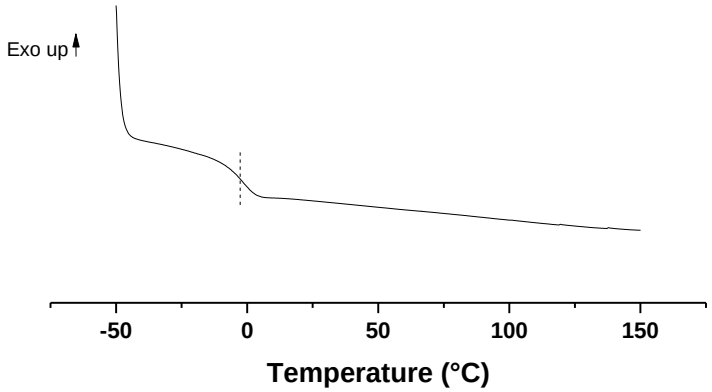


Figure S45: DSC thermogram of the second heating step of the PU measured at a heating rate of 10 °C.min^{-1}.

3.12.2 Post-synthesis addition of M1

A small part of the PU-disk was cut out and placed in a glass vial and swollen in 1 mL THF. Next, a solution of **M1** in THF (1 mL) was added to the glass vial, after which the solvent was allowed to slowly evaporate overnight at room temperature to yield the tagged PU-material.

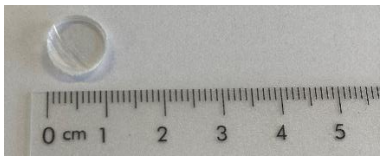


Figure S46: Part of the PU-disk that was cut out and used for the addition of **M1** as macromolecular tag.

3.12.3 Synthesis of PU-disk with M3 as molecular tag

A mixture of desmodur N3300A (1.5 g), pripol 2033 (2.2 g), **M3** (50mg) and dibutyltin dilaurate (DBTL, 24 µL) was put in a plastic cup. This cup was placed in the speed mixer for 2 minutes, after which it was further cured overnight at 50°C.

Soluble fraction (%, after swelling in THF for 24h at 25°C): 3.2 ± 0.4

Swelling ratio (%, after swelling in THF for 24h at 25°C): 120 ± 2.5

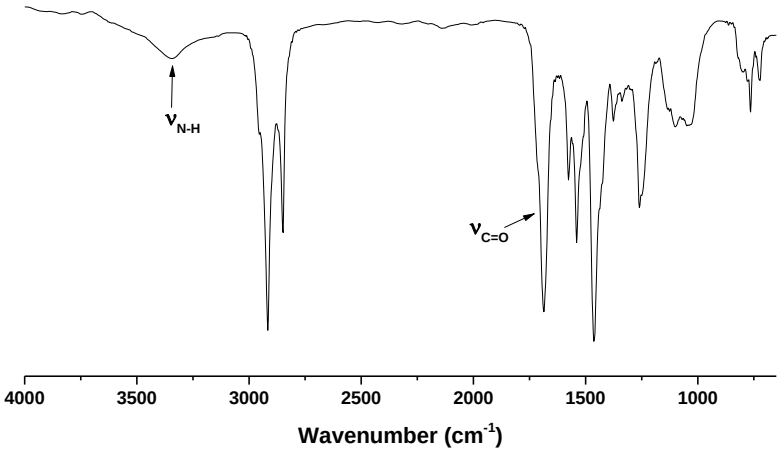


Figure S47: FT-IR spectra in transmission mode of the obtained labelled polyurethane disk, indicating complete consumption of the isocyanate moieties.

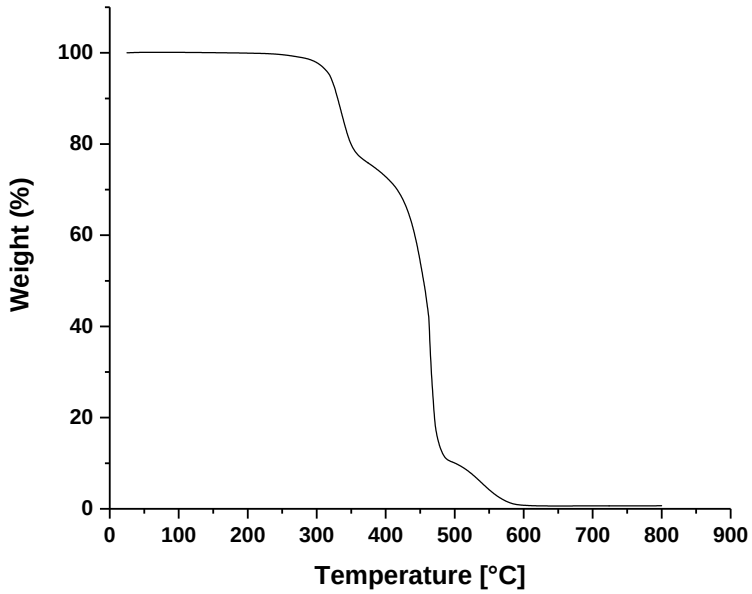


Figure S48: TGA analysis under N_2 atmosphere of the labelled PU-disk with a temperature ramp from 25-800 °C and a heating rate of 10 °C.min^{-1}. $T_{d2\%}$ = 299°C.

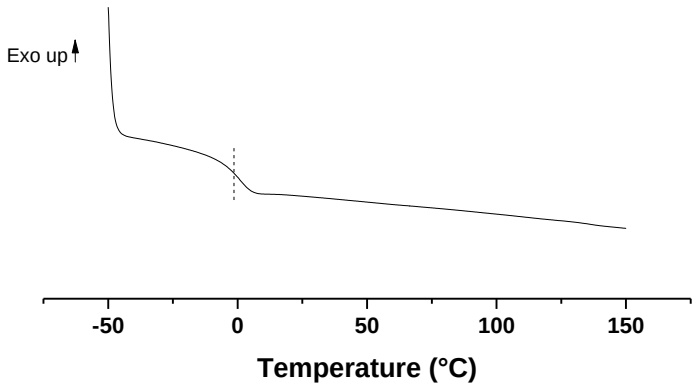


Figure S49: DSC thermogram of the second heating step of the labelled PU disk measured at a heating rate of 10 °C.min^{-1}.

3.12.4 Removal of molecular tag and subsequent sequencing

A small part of the PU-disk was cut out and placed in a glass vial and swollen in THF (2 mL) 30 minutes. The solvent was then transferred to a separate vial, where the THF was removed by means of a gentle flow of N_2 gas. Following solvent removal, a portion of the obtained crude was subjected to the chemical sequencing conditions (5 mg in 1 mL ACN:H_2O 1:1 in the presence of NaOH (5 eq.)).

Figure S50: A small PU-disk was cut out and placed in a vial containing 1 mL THF to remove the molecular tag.

4 Model studies

4.1 Parameter influence on the rate of cyclization

General procedure: the model compound (5 mg, 1 eq.) was solubilised in 0.8 mL of the desired solvent mixture in a 1.5 mL glass vial. The mixture was heated to the temperature of choice, followed by the addition of a stock solution that contained the chosen base (0.2 mL, 5 eq. of base in total). The mixture was continued to be heated at the desired temperature and aliquots were taken at specified time intervals. For this, 200 microliter of the mixture was removed and placed in a 1.5 mL glass vial, quenched with acetic acid (5 eq.) and diluted with acetonitrile until a total volume of 1 mL was reached. This crude mixture was then directly analysed by LC-MS without further sample preparation or purification. Conversions were calculated by integration of the product peak and the formed 2-phenylethanol in the LC-trace at 214 nm.

4.1.1 Base

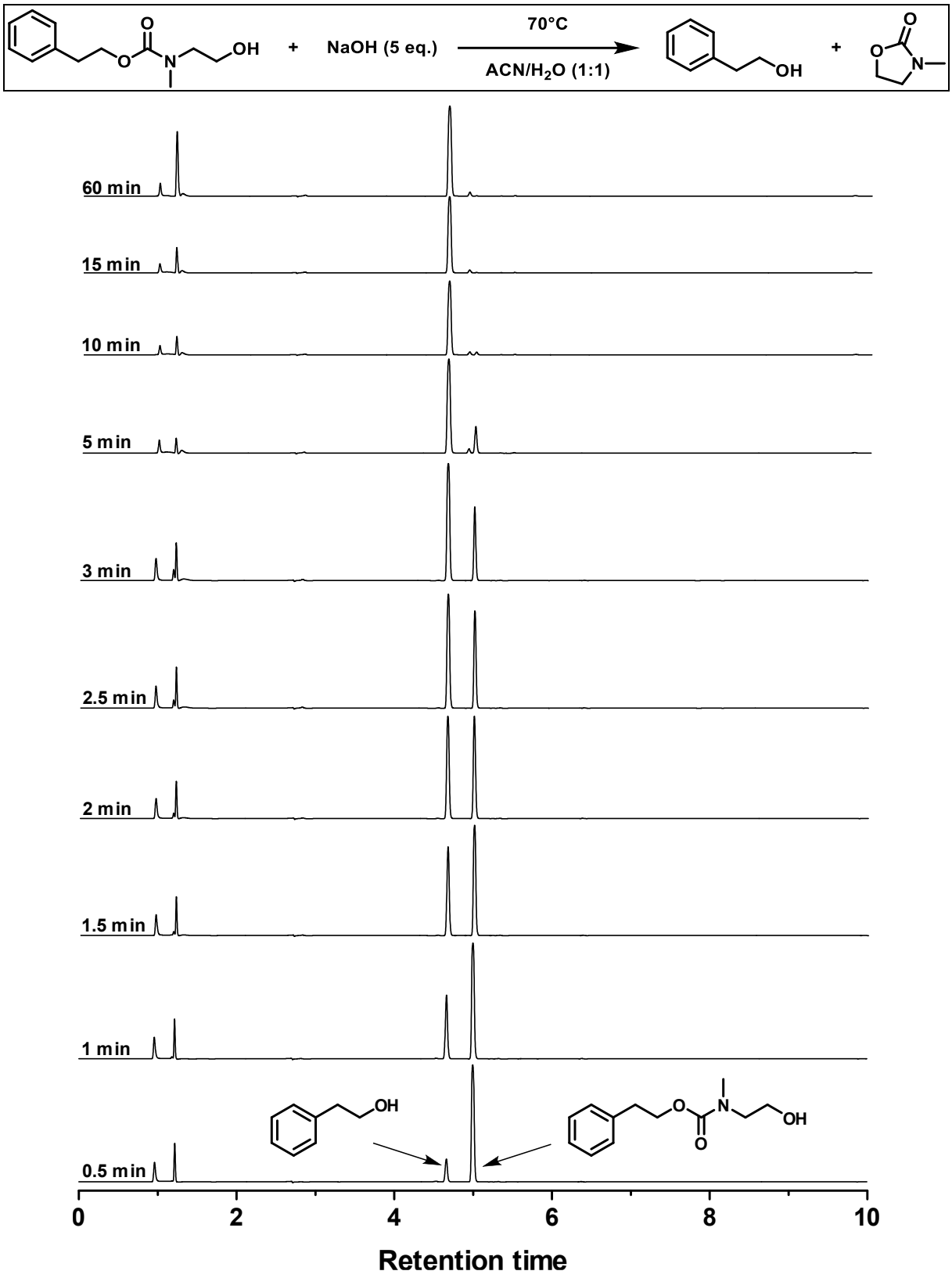


Figure S51: LC trace (λ = 214 nm) of the reaction between **3** and NaOH (5 eq.) at 70°C in ACN:H_2O (1:1) as a function of time.

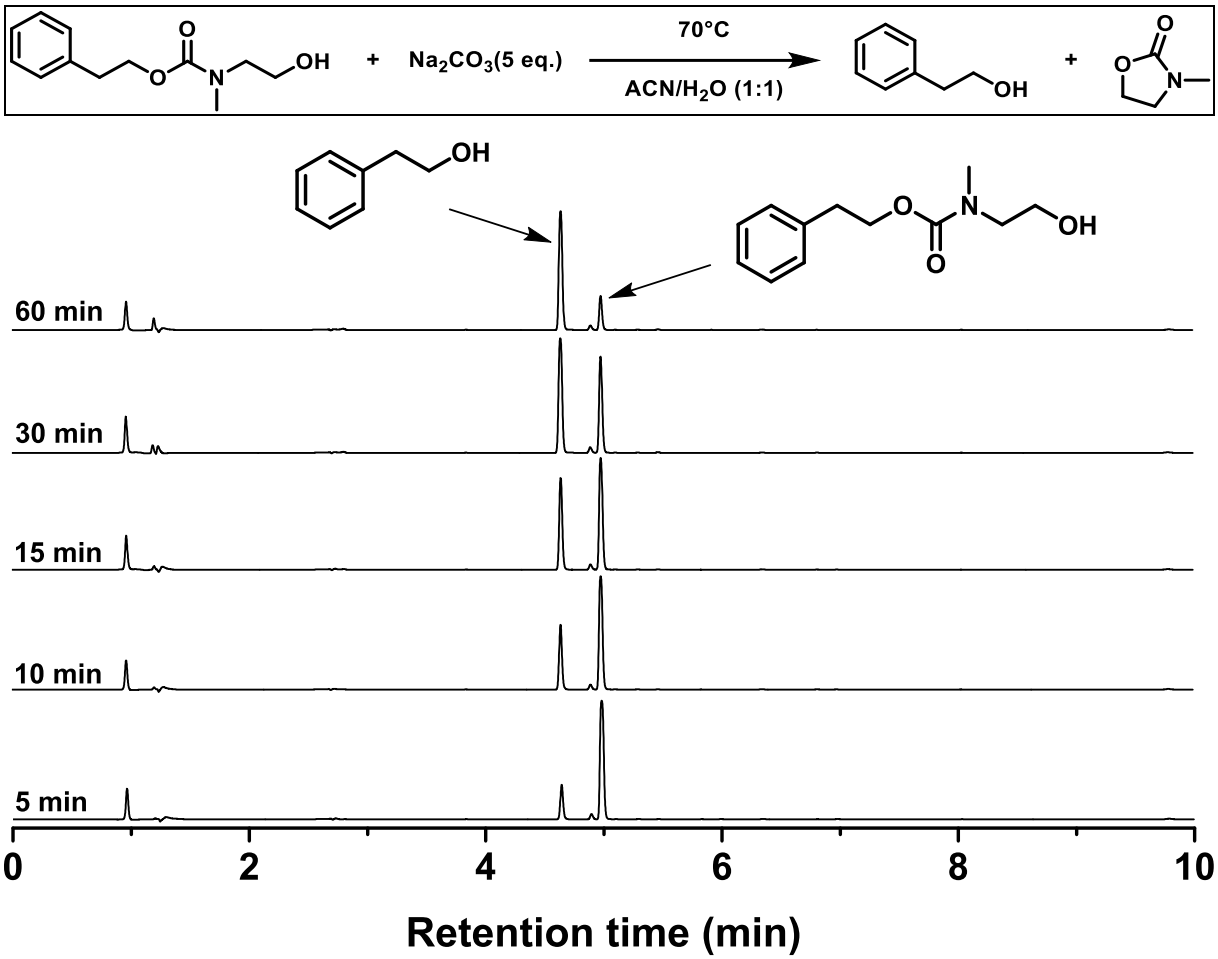


Figure S52: LC trace (λ = 214 nm) of the reaction between **3** and Na_2CO_3 (5 eq.) at 70°C in ACN:H_2O (1:1) as a function of time.

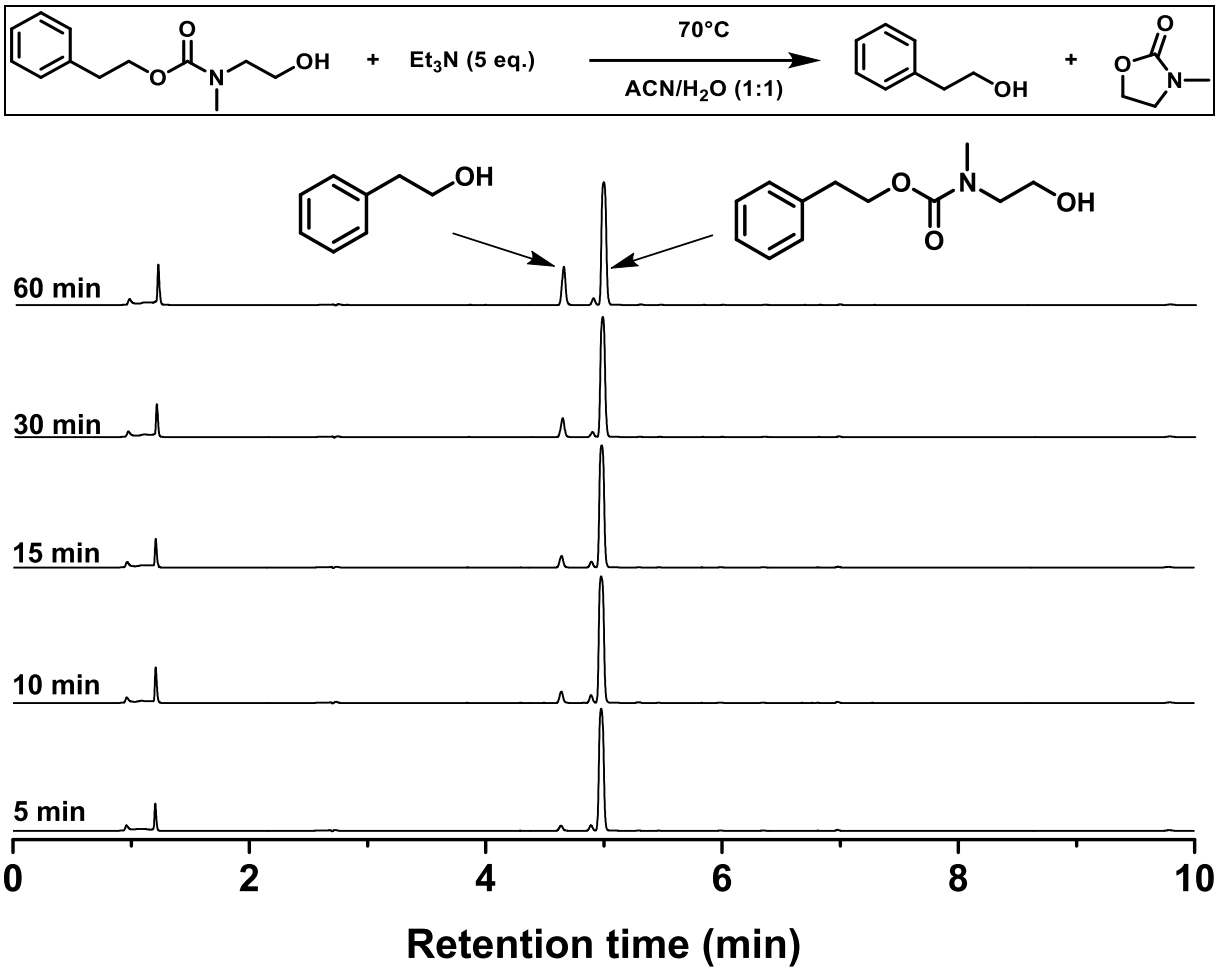


Figure S53: LC trace (λ = 214 nm) of the reaction between **3** and Et_3N(5 eq.) at 70°C in ACN:H_2O (1:1) as a function of time.

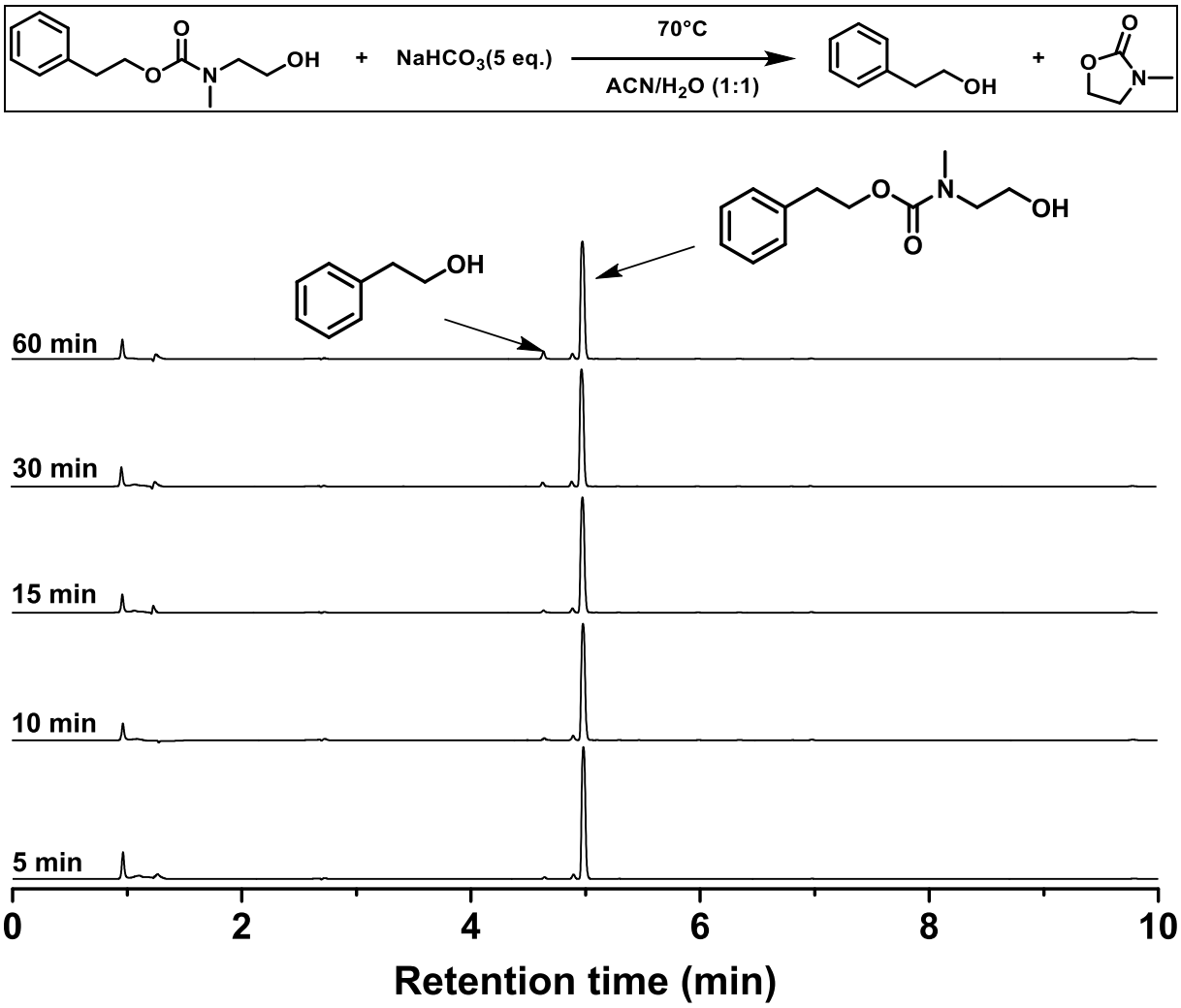


Figure S54: LC trace (λ = 214 nm) of the reaction between **3** and $NaHCO_3$ (5 eq.) at 70°C in ACN:H_2O (1:1) as a function of time.

4.1.2 Temperature

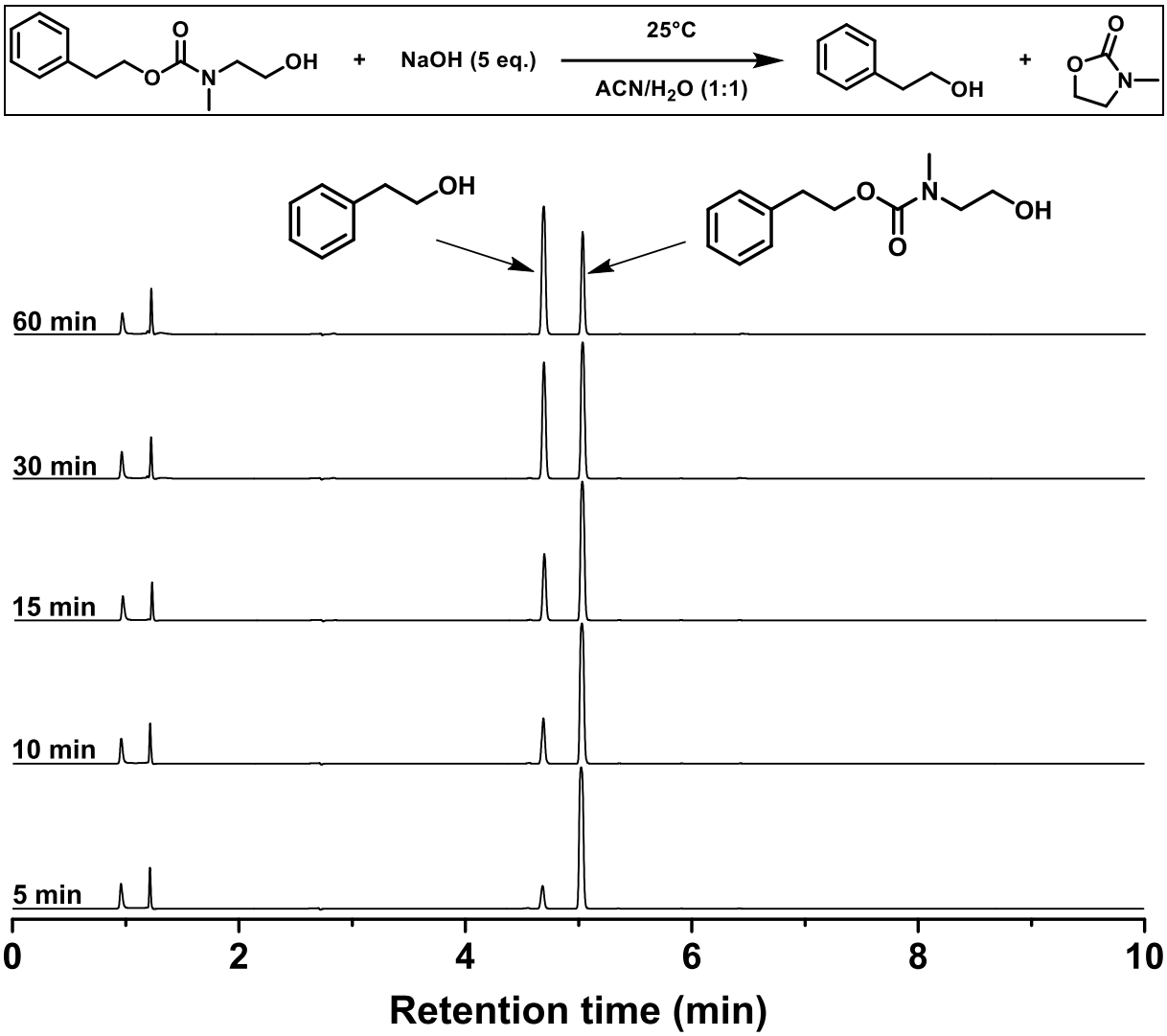


Figure S55: LC trace (λ = 214 nm) of the reaction between **3** and NaOH (5 eq.) at 25°C in ACN:H_2O (1:1) as a function of time.

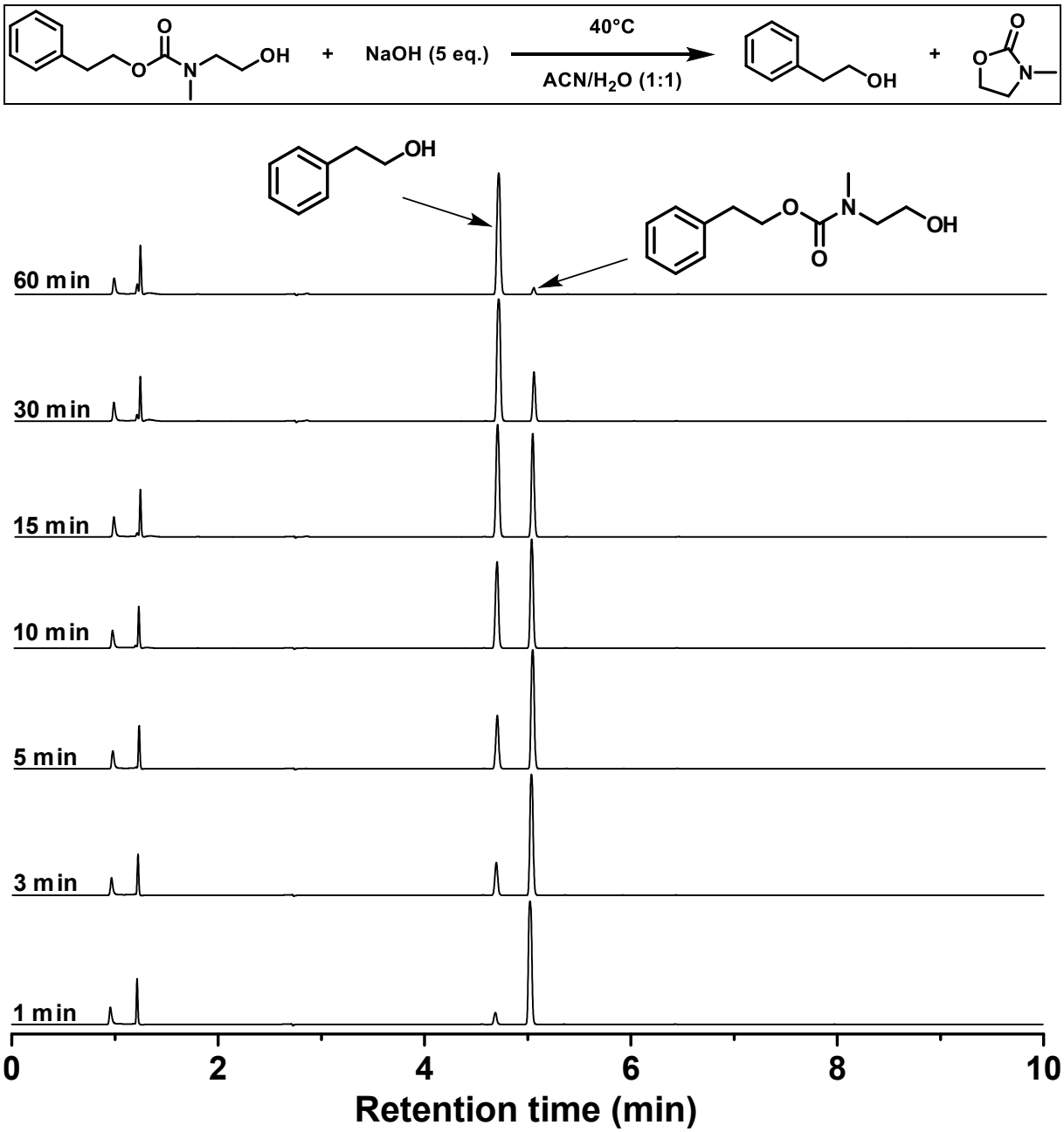


Figure S56: LC trace (λ = 214 nm) of the reaction between **3** and NaOH (5 eq.) at 40°C in ACN:H_2O (1:1) as a function of time.

4.1.3 Solvent

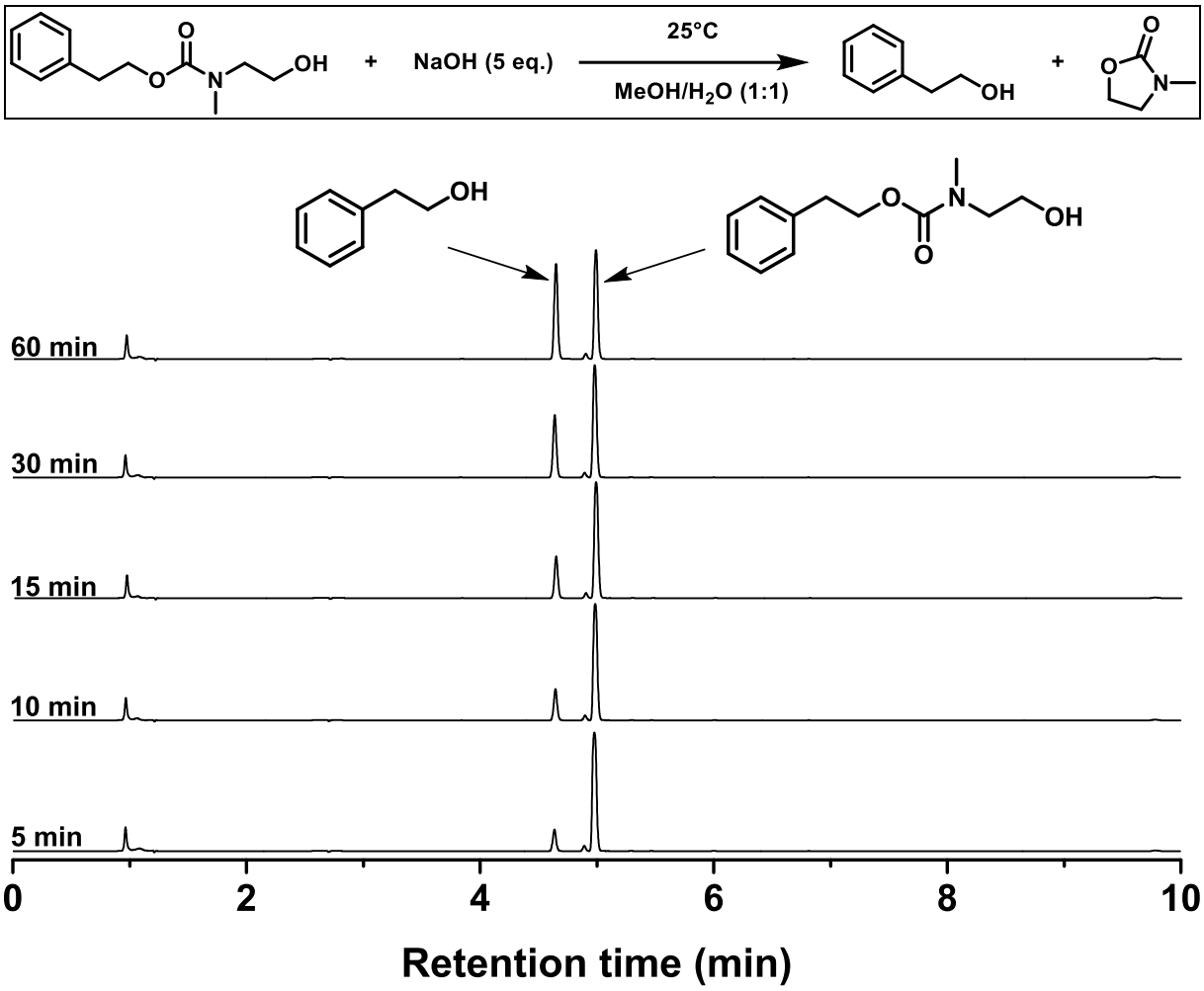


Figure S57: LC trace (λ = 214 nm) of the reaction between **3** and NaOH (5 eq.) at 25°C in MeOH:H_2O (1:1) as a function of time.

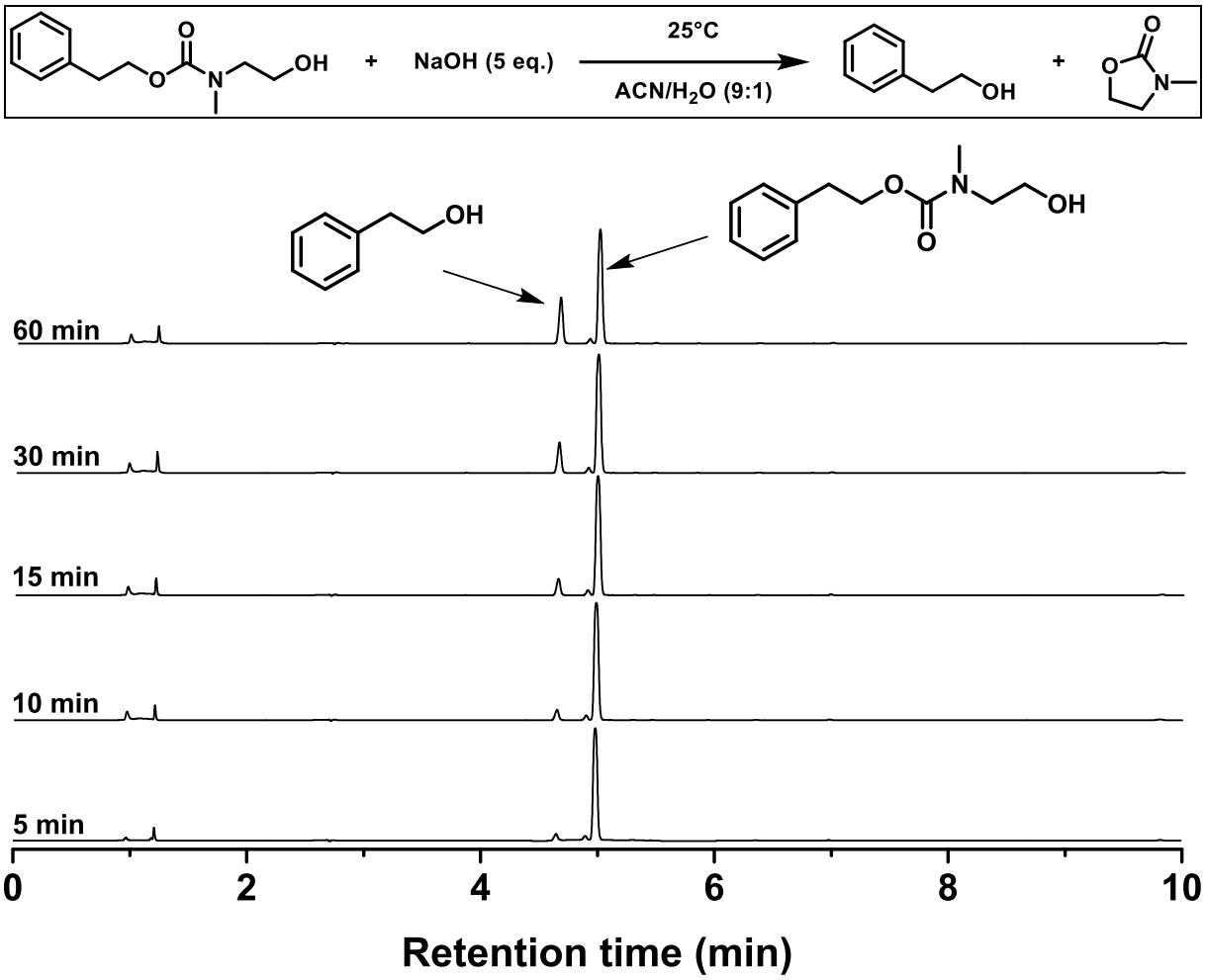
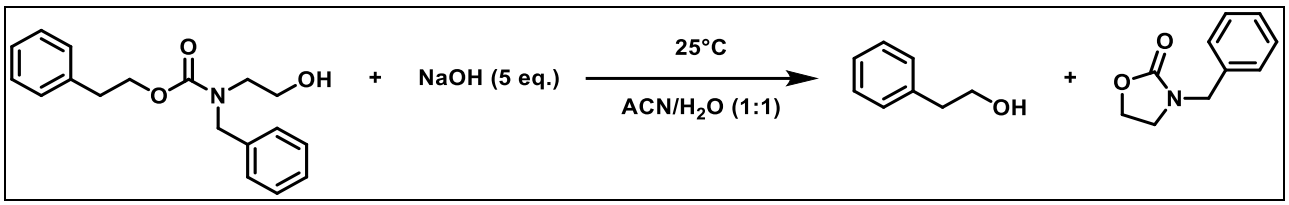


Figure S58: LC trace (λ = 214 nm) of the reaction between **3** and NaOH (5 eq.) at 25°C in ACN:H_2O (9:1) as a function of time.

4.1.4 Substitution pattern



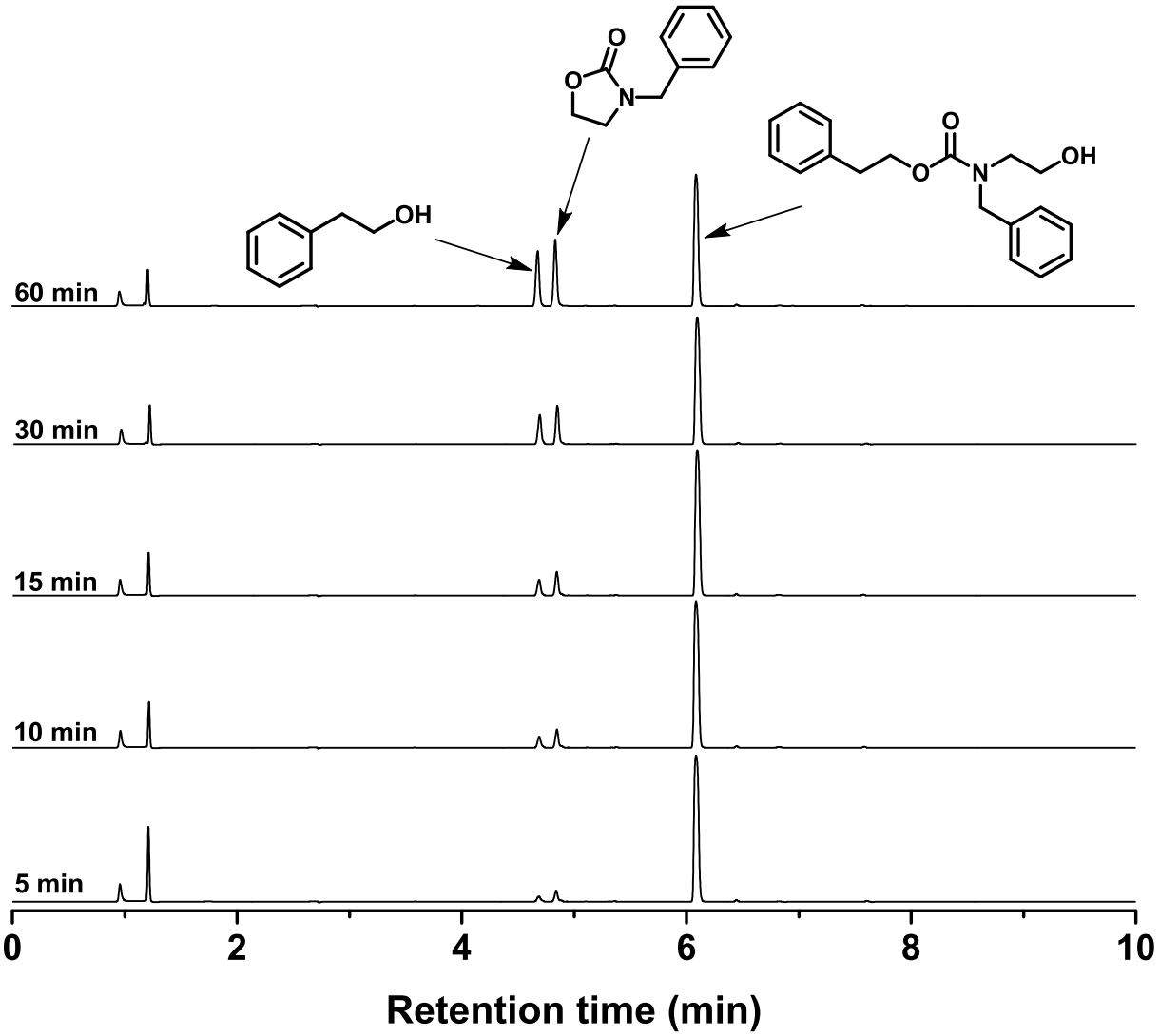


Figure S59: LC trace (λ = 214 nm) of the reaction between **5** and NaOH (5 eq.) at 25°C in ACN:H_2O (1:1) as a function of time.

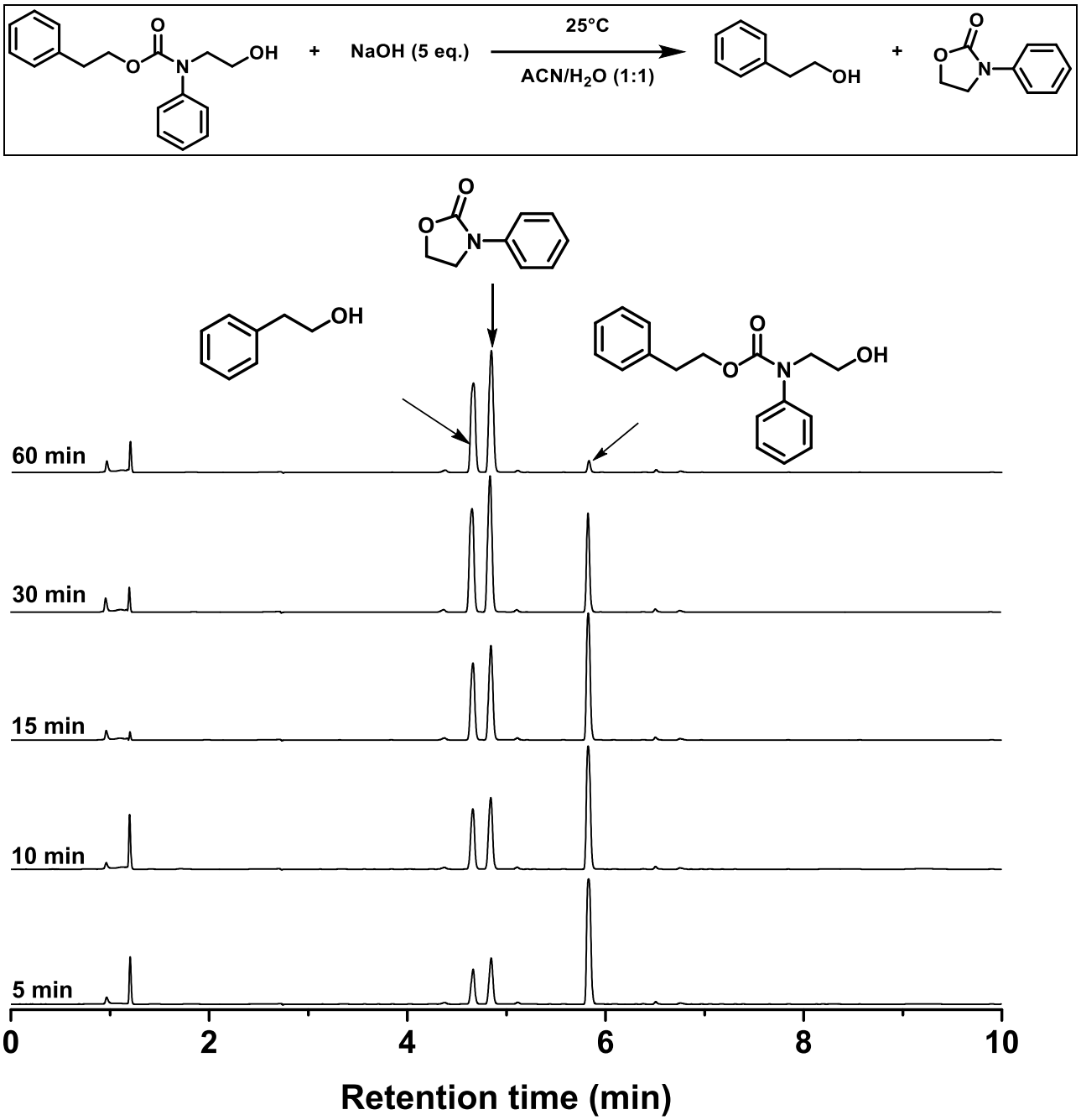


Figure S60: LC trace (λ = 214 nm) of the reaction between **6** and NaOH (5 eq.) at 25°C in ACN:H_2O (1:1) as a function of time.

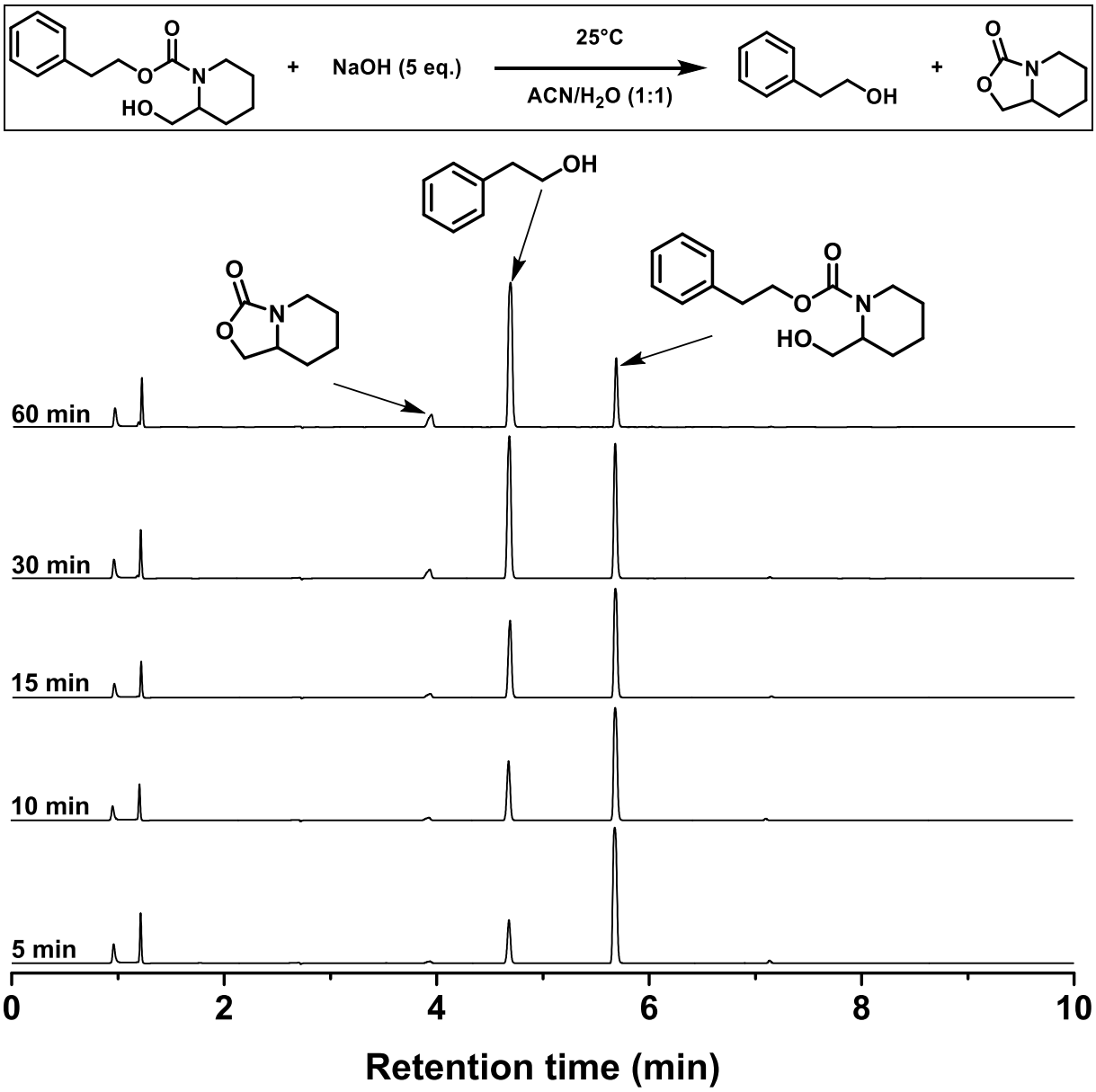


Figure S61: LC trace (λ = 214 nm) of the reaction between **7** and NaOH (5 eq.) at 25°C in ACN:H_2O (1:1) as a function of time.

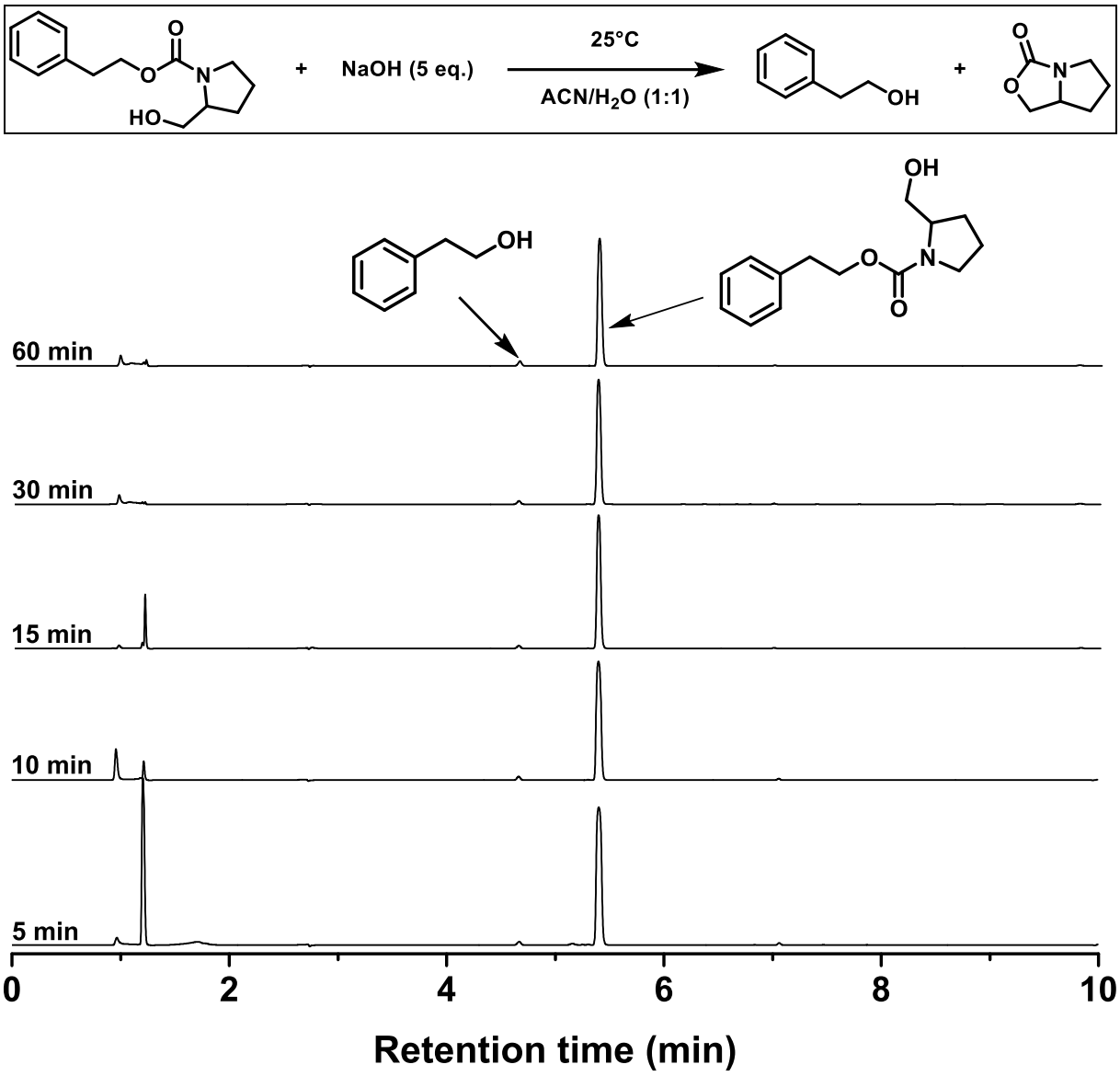
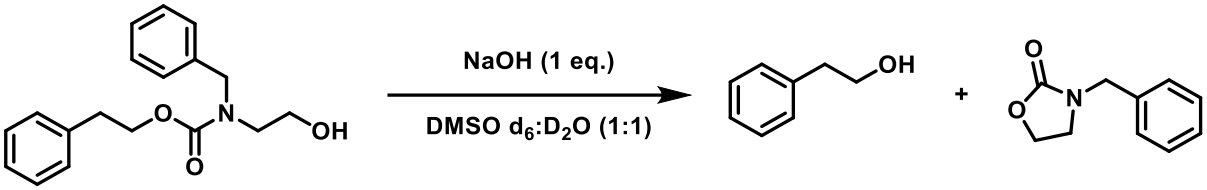


Figure S62: LC trace (λ = 214 nm) of the reaction between **7** and NaOH (5 eq.) at 25°C in ACN:H_2O (1:1) as a function of time.

4.2 Oxazolidinone formation via NMR



A solution of **5** (10 mg, 33µmol, 1 eq.) in 0.3 mL DMSO-d_6 was placed in an NMR tube, followed by the addition of a solution of NaOH (1.34 mg, 33µmol, 1 eq.) in D_2O (0.3 mL). The NMR tube was left to stand at room temperature without any form of spinning, and NMR analysis was performed at different time intervals. These indicated the clean formation of the oxazolidinone species as a function of time.

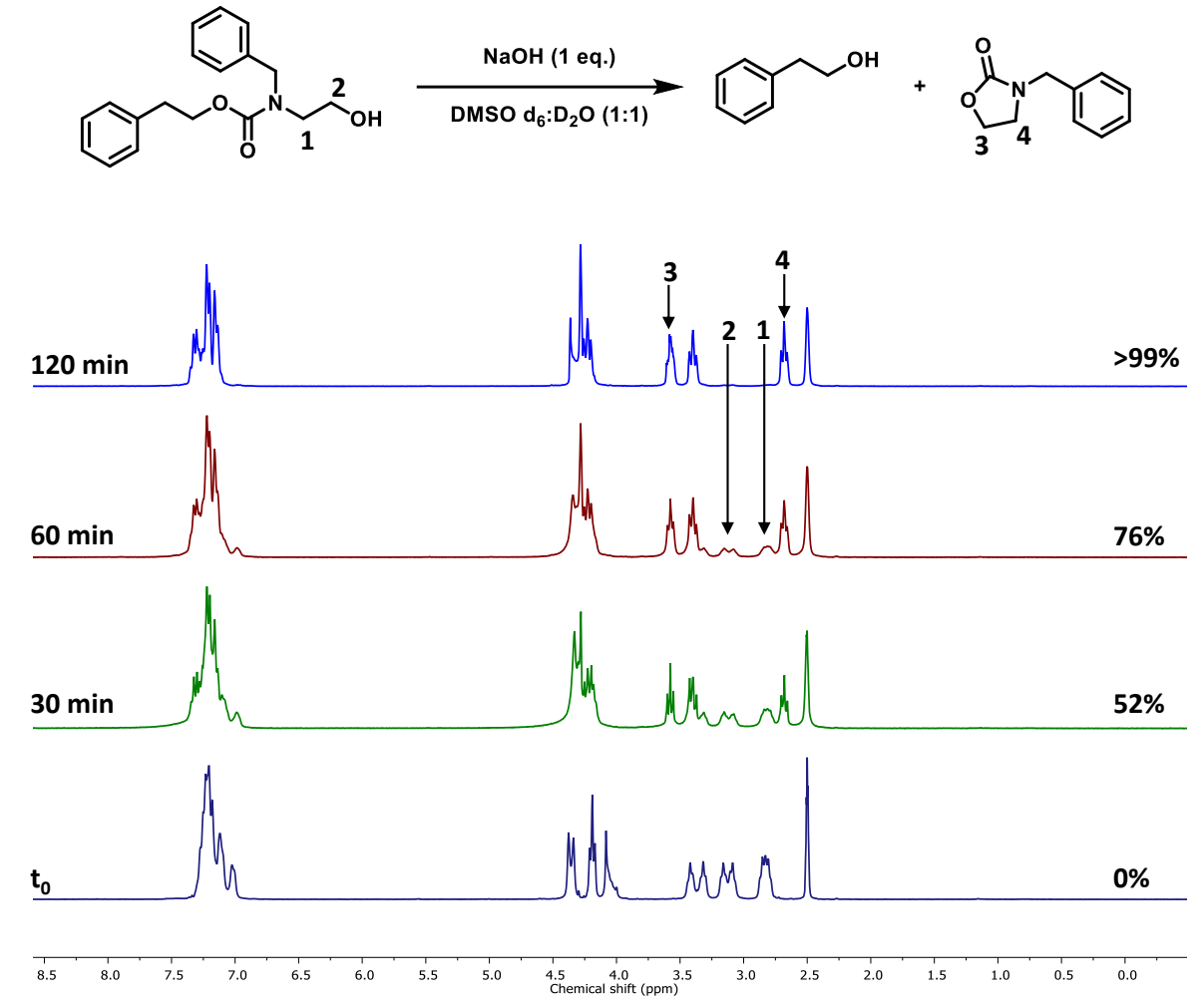


Figure S63: Overlay of ^{1}H NMR analysis (300 MHz, DMSO-d_6/D_2O) of **5** in the presence of NaOH. NMR analysis at different time intervals showcases the clean formation of the oxazolidinone product.

4.3 Hydrolysis of 4

Methoxy-containing model compound **4** (5 mg, 21 µmol, 1 eq.) was solubilised in 1 mL of an ACN:H_2O (1:1) solution, followed by the addition of NaOH (4.2 mg, 105 µmmol, 5 eq.). The solution was heated to 70°C for 2 hours, after which the reaction was quenched via the addition of acetic acid. The crude reaction mixture was then analysed by LC-MS, indicating no significant degradation of the carbamate moiety.

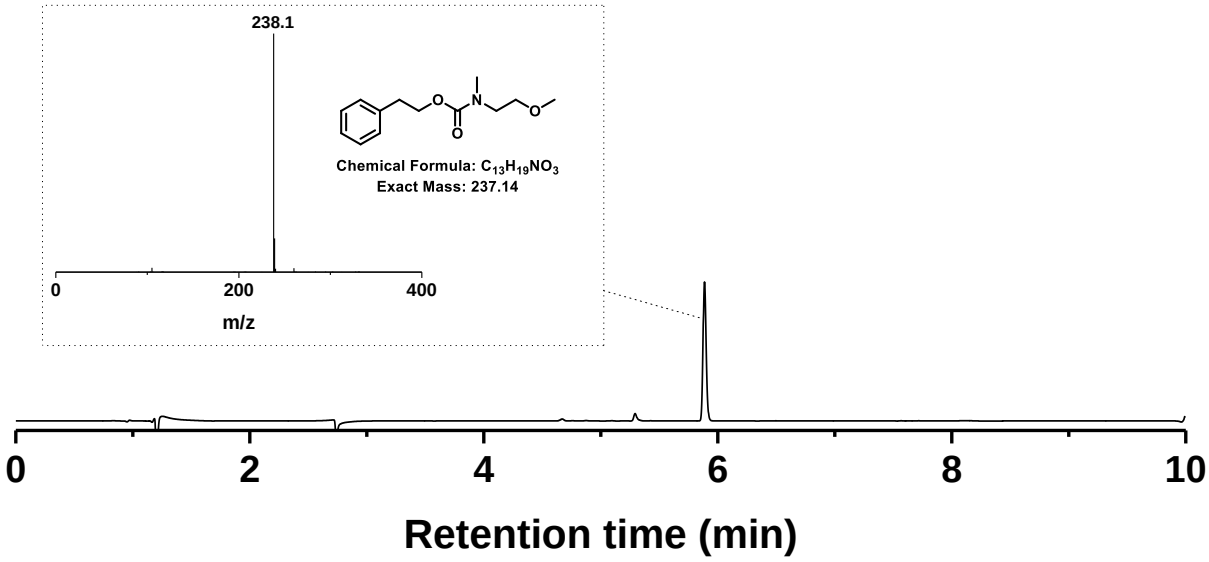
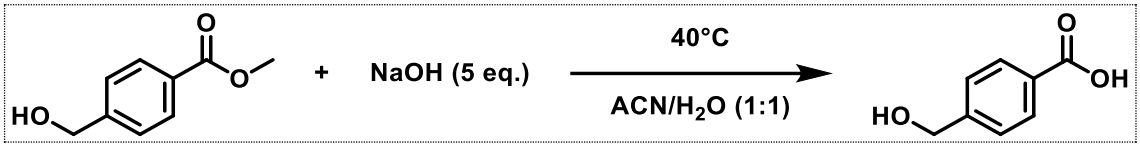


Figure S64: LC trace (λ = 214 nm) of the reaction between **4** and NaOH (5 eq.) at 70°C in ACN:H_2O (1:1) after 2 hours.

4.4 Hydrolysis of methyl 4-(hydroxymethyl)benzoate



Methyl 4-(hydroxymethyl)benzoate (1 mg, 6 µmol, 1 eq.) was solubilised in 1 mL of an ACN:H_2O (1:1) solution, followed by the addition of NaOH (1.2 mg, 30 µmmol, 5 eq.). The solution was heated to 40°C for 2 hours, after which the reaction was quenched via the addition of acetic acid. The crude reaction mixture was then analysed by LC-MS, indicating complete conversion of the starting material to the hydrolysed product.

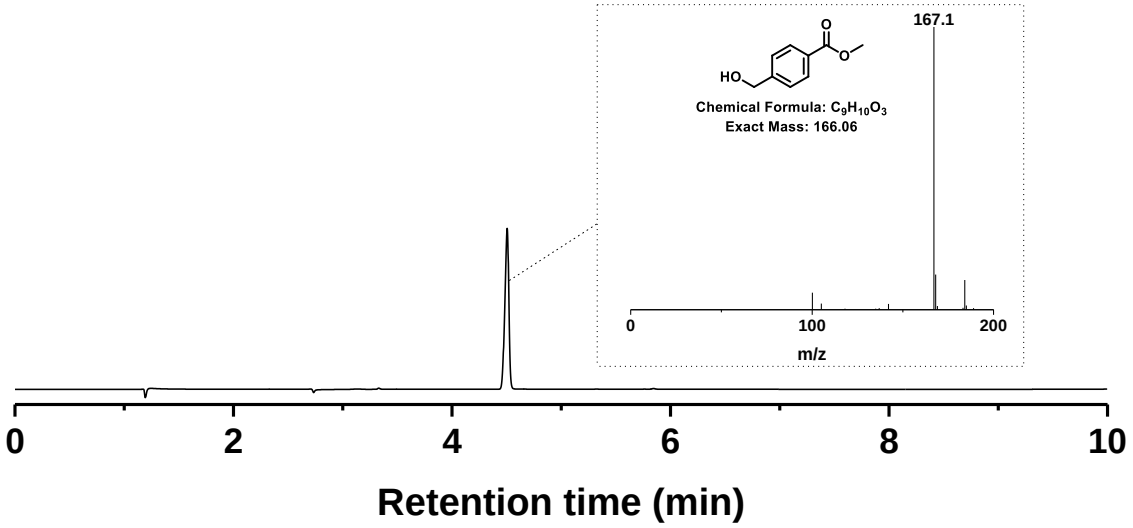


Figure S65: LC trace (λ = 214 nm) of methyl 4 (hydroxymethyl)benzoate.

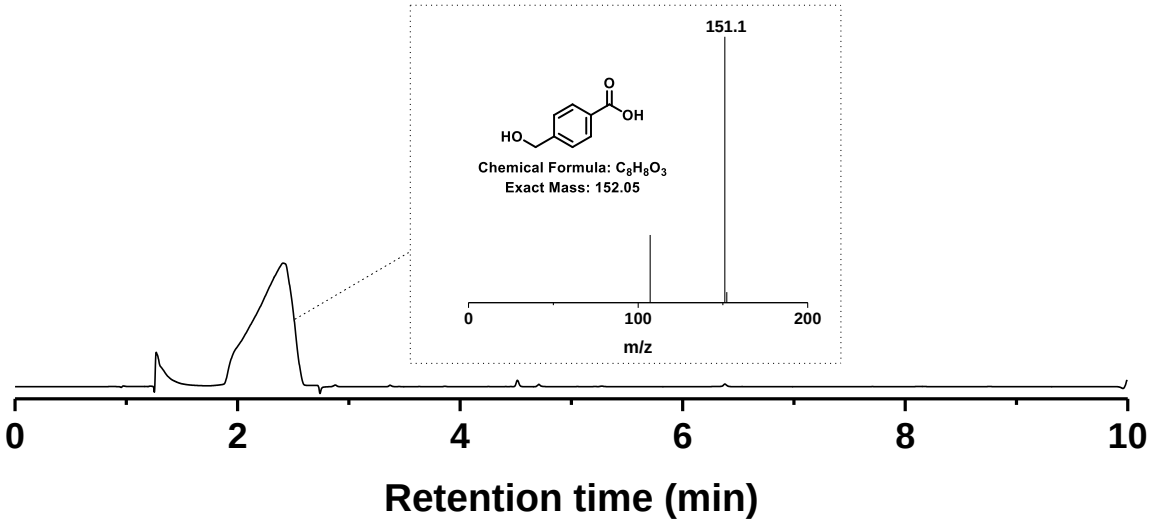


Figure S66: LC trace (λ = 214 nm) of the reaction between methyl 4 (hydroxymethyl)benzoate and NaOH (5 eq.) at 40°C in ACN:H_2O (1:1) after two hours.

5 Macromolecular sequencing

General procedure: the oligomer (5 mg) was solubilised in 1 mL of an ACN:H_2O (1:1) solution that contained 5 eq. sodium hydroxide. The solution was stirred vigorously and aliquots were taken at specified time intervals. For this, 0.2 mL of the crude reaction mixture was removed, quenched with acetic acid and diluted further with acetonitrile until a total volume of 1 mL was obtained. This solution was then directly analysed by either LC- or ESI-MS.

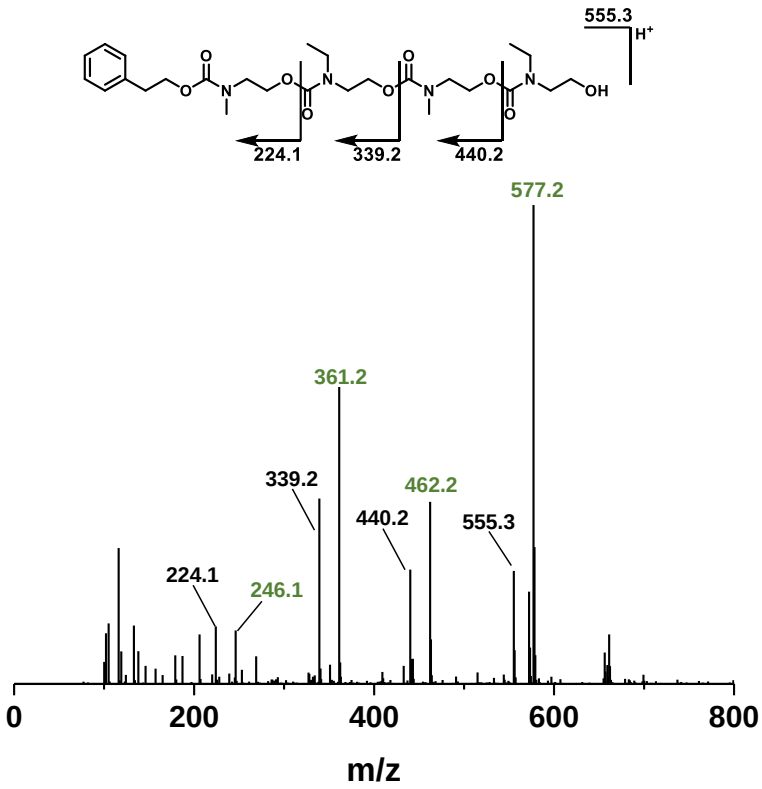


Figure S67: ESI-MS analysis of the crude reaction mixture of the sequencing of **M1** according to the general procedure after 60 minutes. Fragments observed as $[M+H]^+$ are depicted in black, fragments observed as $[M+Na]^+$ are shown in green.

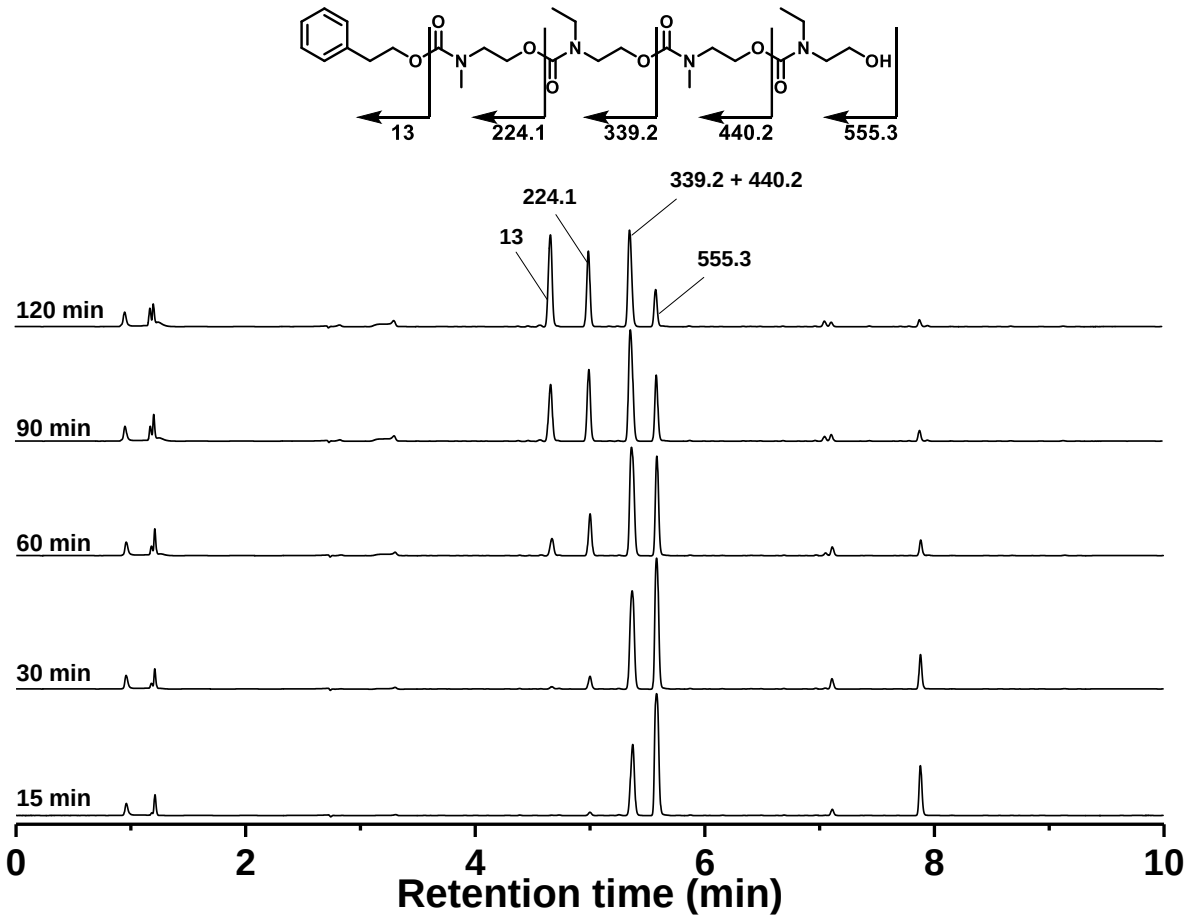


Figure S68: Sequencing via LC-MS (λ = 214 nm) of **M1** using the general conditions after its removal from the PU-disk. Note that minor impurities can be associated with the soluble fraction of the PU-disk.

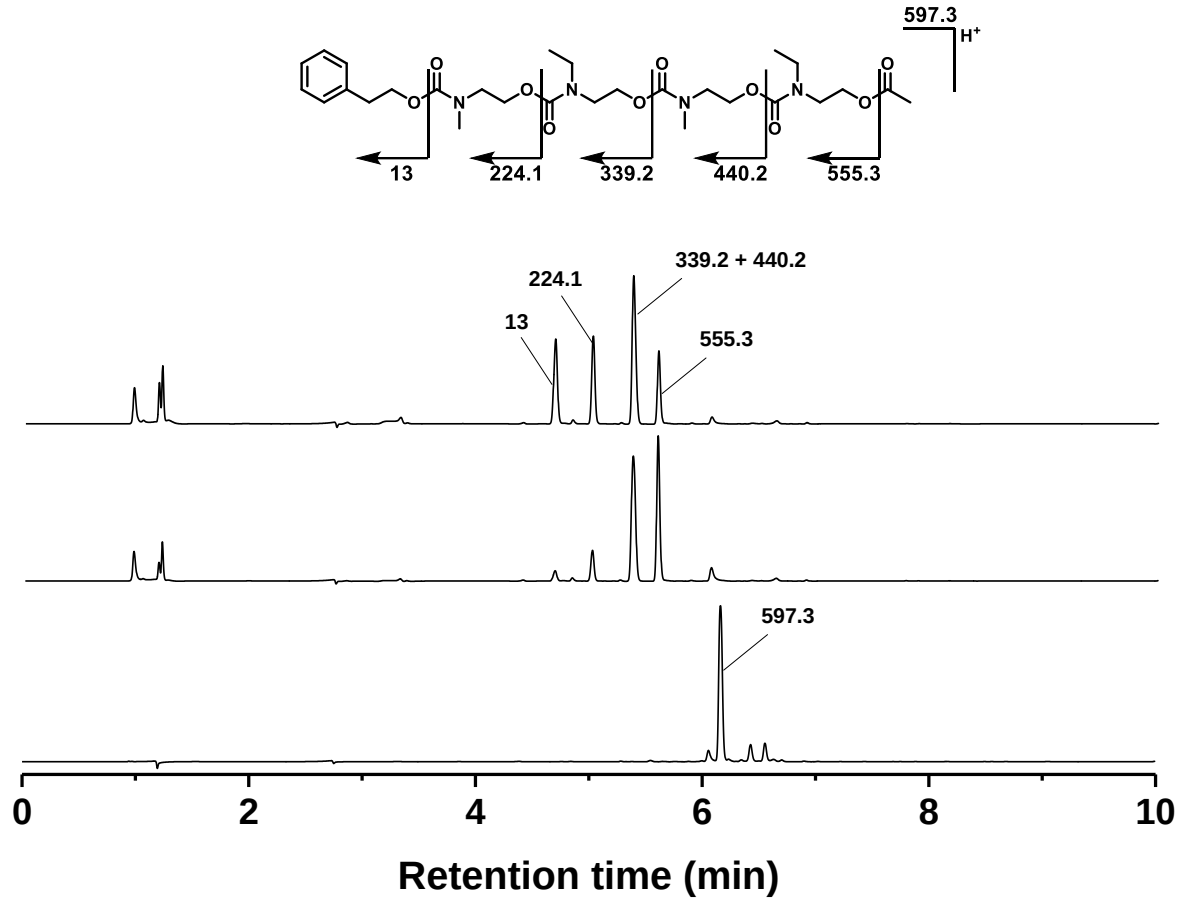


Figure S69: LC trace (λ = 214 nm) of the sequencing of **M3** according to the general procedure as a function of time.

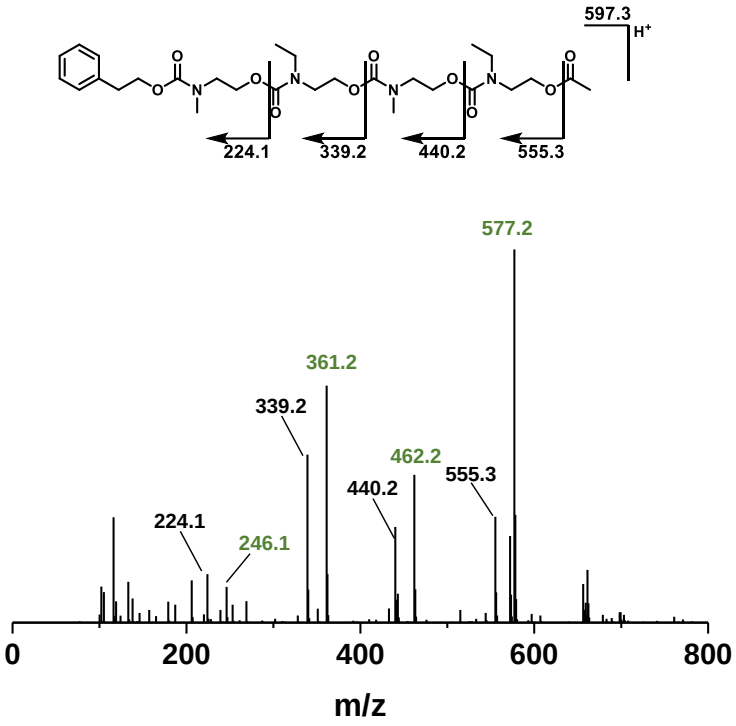


Figure S70: ESI-MS analysis of the crude reaction mixture of the sequencing of **M3** according to the general procedure after 60 minutes. All characteristic fragments that are necessary for an accurate structure elucidation can be observed. Fragments observed as $[M+H]^+$ are depicted in black, fragments observed as $[M+Na]^+$ are shown in green.

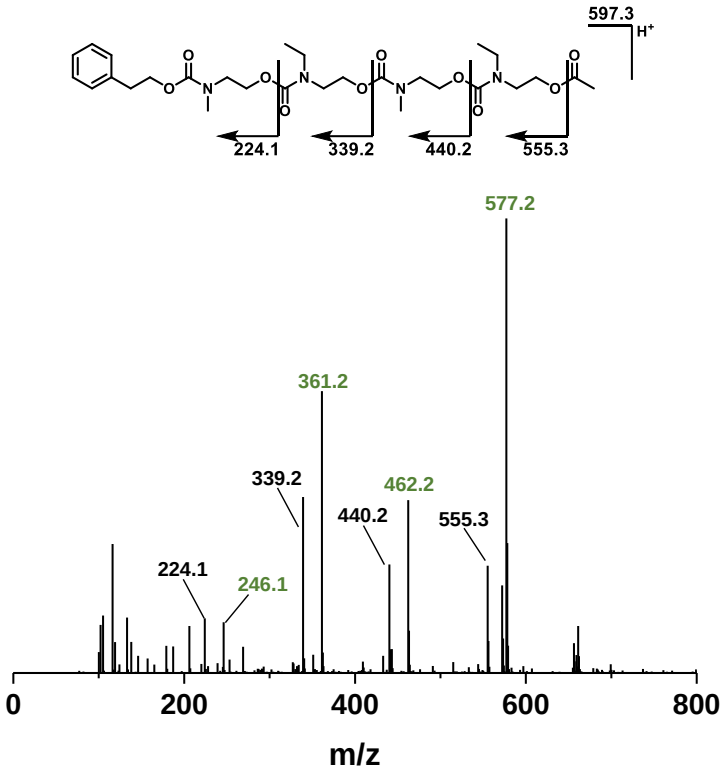


Figure S71: ESI-MS analysis of the crude reaction mixture of the sequencing of **M3** following its removal from the PU-disk after 60 minutes. All characteristic fragments that are necessary for an accurate structure elucidation can be observed. Fragments observed as $[M+H]^+$ are depicted in black, fragments observed as $[M+Na]^+$ are shown in green. Note that this ESI-MS spectrum is almost identical to the one obtained following sequencing of **M3** without its use as molecular tag (see **Figure S70**), demonstrating the robustness of the use of these molecules in the area of anti-counterfeiting.

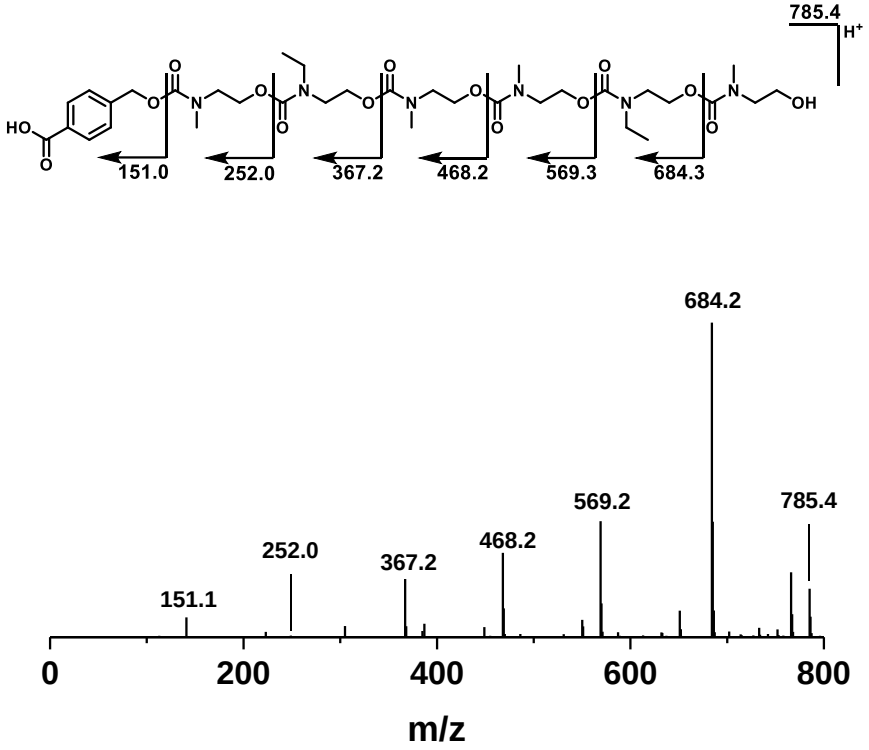


Figure S72: ESI-MS analysis of the crude reaction mixture of the sequencing of **M2** according to the general procedure after 60 minutes. All characteristic fragments that are necessary for an accurate structure elucidation can be observed. Fragments are observed as $[M-H]^-$.