Supporting Information

Sequence-coded ATRP Macroinitiators

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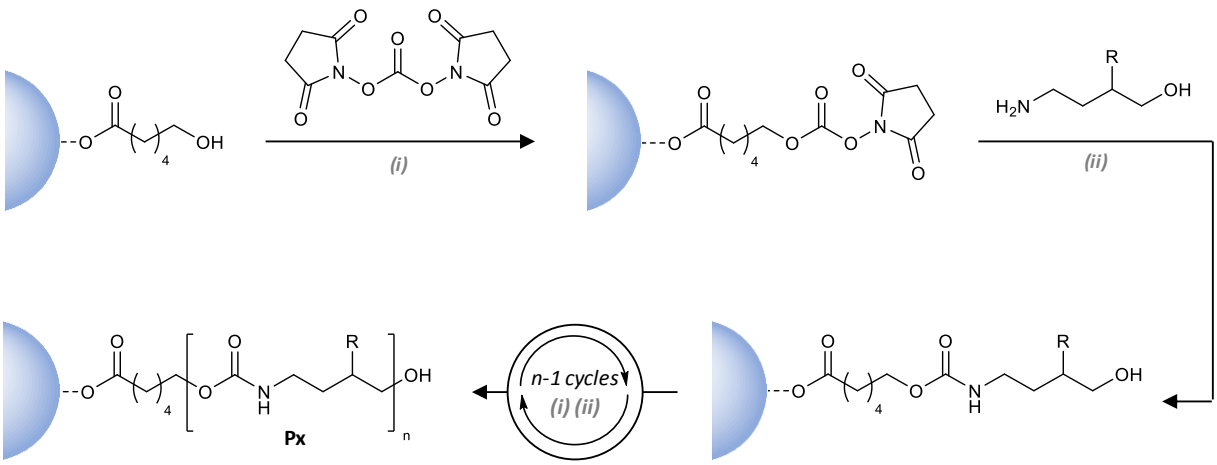
A. Materials

The following compounds were purchased from Sigma-Aldrich and used as received: p-toluenesulfonic acid monohydrate (PTSA, 98.5%), trifluoroacetic acid (TFA, 99%), 4-(dimethylamino)pyridine (DMAP, 99%), anhydrous pyridine (99.8%), DCM (99.9%), anhydrous acetonitrile (dry ACN, 99.8%), anhydrous N,N-dimethylformamide (dry DMF, 99.8%), DMF (99%), and tetrahydrofuran (THF, 99%, stabilized with 2,6-di-*tert*-butyl-4-methylphenol). Styrene (Aldrich, 99%) was distillated over CaH_2 and then degassed by bubbling argon through it. 2-bromoisobutyric acid, 98% (98%) and copper(I) bromide (CuBr, 98%) were obtained from Alfa Aesar. CuBr was purified by stirring in acetic acid and rinsing with ethanol and diethyl ether and then dried. The 4-amino-1-butanol (98%), 4-amino-2-methyl-1-butanol (98%), 4,4'-di-n-nonyl-2,2'-bipyridine (dNbpy, >98%) and N,N-disuccinimidyl carbonate (DSC, >98.0%) were purchased from TCI and used as received. Ethanol absolute (99.9%) was obtained by VWR. Diethyl ether and methanol were delivered by Carlo Erba and triethylamine (TEA, >97%) by Merck. The polystyrene solid support (Wang resin 100–200 mesh, 0.94 mmol/g and 1.8 mmol/g resin were used from Iris Biotech) was modified with a cleavable hydroxy-functional linker as previously reported.[1] 2-bromoisobutiric anhydride was synthesized according to a reported procedure.[2] A Monowave 300 (Anton Paar) microwave reactor was used for step *(i)* of the oligourethane synthesis. Solid phase chemistry was conducted in solid-phase extraction (SPE) tubes using a KS 130 basic (IKA) shaker.

B. Experimental procedure

B.1. Synthesis of P1-P4 by iterative solid phase chemistry

The sequence-coded oligourethanes **P1**-**P4** were synthesized using a recently described orthogonal iterative protocol.[1] In brief, this procedure involves two successive orthogonal coupling steps (Scheme S1). In a first step (step *(i)* in Scheme S1), the Wang resin (1 molar equiv) was reacted with N,N-disuccinimidyl carbonate (6 molar equiv) in the presence of TEA in dry ACN under microwave irradiation for 1 h at 60°C. Afterward, the resin was washed 10 times with DMF in a SPE tube. In a second step (step *(ii)* in Scheme S1), the resin was reacted with an excess amino-alcohol (either 4-amino-1-butanol (0) or 4-amino-2-methyl-1-butanol (1), 10 molar equiv) in the presence of TEA in dry DMF for 30 min at room temperature. Then, the resin was washed 10 times with DMF, diethyl ether, and transferred back to a microwave tube. These two coupling steps were repeated successively to reach a desired sequence and chain-length. The final oligourethanes were kept on the solid support for further modification steps (*vide infra*). However, a small fraction was cleaved from the resin for characterization. Cleavage was performed using a TFA/DCM mixture (1:1 v/v). After filtering-off the resin, solvent was evaporated under reduced pressure to afford the oligourethanes **P1**-**P4** as white solids.



Scheme S1. Solid-phase iterative orthogonal strategy used for the synthesis of the sequence–coded oligourethanes.

B.2. Synthesis of P1'-P4' by ω-chain-end modification on the solid support

The modified oligourethanes **P1'-P4'** were obtained by esterification of their ω-alcohol terminus (step *(iii)* in Scheme 1, main text). To an 8 mL SPE tube containing the resin-immobilized oligourethane **P3** (1 molar equiv) was added dry pyridine (2 mL), DMAP (2 molar equiv) and 2-bromoisobutiric anhydride (8 molar equiv). The mixture was put under argon atmosphere, sealed with a septum and shaken for 24 h at RT. After the reaction, the resin was washed 5 times with THF, 5 times with DMF and twice with diethyl ether.

B.3. Cleavage of P1'-P4' from the solid support

The cleavage of **P1'-P4'** (step *(iv)* in Scheme 1, main text) was performed using a mixture of TFA and DCM (1:1 v/v). The vial was sealed and the reaction was conducted for 2 h at RT. Afterwards, the resin was filtered off, washed several times with DCM, and the filtrate was collected. Solvent and DCM were removed under reduced pressure affording **P1'-P4'** as pale yellow oil. Yield (**P3'**): 150 mg (94%).

B.4. Synthesis of P1"-P4" by α-chain end modification in solution

The modified oligourethanes **P1"-P4"** were obtained by esterification of their α-COOH terminus (step *(v)* in Scheme 1, main text). The following example corresponds to oligomer **P3"** (Table 1). PTSA (12 mg, 0.07 mmol, 0.4 molar equiv) was added to a 25 mL round bottom flask containing a stirred solution of **P3'** (150 mg, 0.16 mmol, 1 molar equiv) in ethanol absolute (10 mL). The flask was then equipped with a condenser and the reaction mixture was stirred at 65°C for 16 h and afterwards at RT. until the formation of a white precipitate. The mixture was filtrated and the filtrates were collected. Solvents were evaporated under reduced pressure, affording **P3"** as a pale yellow powder. Yield: 114 mg (73%).

B.5. Example of styrene ATRP in presence of a macroinitiator

Macroinitiator **P3"** (114 mg, 0.125 mmol, 1 molar equiv), dNbpy (98 mg, 0.250 mmol, 2 molar equiv) and CuBr (17 mg, 0.125 mmol, 1 molar equiv) were added to a small dried flask containing a stir bar. The mixture was degassed and put under argon atmosphere before being sealed with a septum. Styrene (2.6 g, 25 mmol, 200 molar equiv) was then added to the flask, the solution was degassed by 3 freeze-pump-thaw cycles and put under argon. The flask was then immersed in an oil bath thermostated at 110°C. Samples were withdrawn periodically during the polymerization and were analyzed by ^{1}H NMR spectroscopy, in order to follow styrene conversion. The polymer was precipitated into cold methanol. The precipitate was collected by filtration, washed with methanol and dried overnight at room temperature.

C. Characterization

C.1. NMR

^{1}H NMR spectra were recorded using a Bruker Avance 400 MHz spectrometer equipped with an Ultrashield magnet in $CDCl_3$ at 298 K. Conversion of styrene were determined by comparing the integration of two vinyl protons of the styrene monomer at 5.18 and 5.69 ppm to the integration of protons in the region 6.25-7.25 ppm which contains five aromatic protons of the formed polymer.

C.2. Size Exclusion Chromatography

Number average molecular weight and dispersity were determined by size exclusion chromatography (SEC) analysis. SEC analysis was performed in tetrahydrofuran (flow rate: 1 mL min^{-1}) using a Shimadzu LC20AD pump. The set-up was equipped with four PLGel Mixed C columns (5 mm, 30 cm, diameter = 7.5 mm), a Wyatt Viscostar-II viscometer, a Wyatt TREOS light scattering detector, a Shimadzu SPD-M20A diode array UV detector, and a Wyatt Optilab T-rEX refractometer. The calibration was done with 15 linear polystyrene (PS) standards from Agilent (Polymer Laboratories) within a range of 1 350-1 950 000 g.mol^{-1}.

C.3. Mass spectrometry

High resolution MS and MS/MS experiments were performed using a QqTOF mass spectrometer (QStar Elite, Applied Biosystems SCIEX, Concord, ON, Canada) equipped with an ESI source operated in the negative ion mode (capillary voltage: -4200 V; cone voltage: -75 V) for **Px** and **Px'** oligomers (that contain a deprotonable α termination), and in the positive ion mode (capillary voltage: +5500 V; cone voltage: +75 V) for **Px"** samples. Accurate mass measurements in the MS mode were all performed in the positive ion mode due to the limited availability of standards that can be used for proper internal calibration, in the negative mode, of the orthogonal acceleration time-of-flight (oa-TOF) mass analyzer. Typical cations used for calibrations were PEG or PMMA oligomers adducted with ammonium. MS/MS experiments were conducted in collision-induced dissociation conditions, where precursor ions were selected in a quadrupole mass analyzer prior entering a collision cell filled with nitrogen, and products ions were measured in the oa-TOF. In this instrument, air was used as nebulizing gas (10 psi) while nitrogen was used as curtain gas (20 psi). Instrument control, data acquisition and data processing were achieved using Analyst software (QS 2.0) provided by Applied Biosystems. Oligomers (1-2 mg) were dissolved in methanol (300 µL) in an ultrasonic bath (15 min). Samples were further diluted ($1/10^2$ to $1/10^4$, v/v) in a methanolic solution of ammonium acetate (3 mM), and injected in the ESI source at a 10 µL min^{-1} flow rate using a syringe pump.

D. Supplementary figures

MS/MS sequencing – Activation of deprotonated oligourethanes generated in the negative ion mode ESI induces cleavage of all O–(CO) carbamate bonds in a competitive manner, leading to the formation of a series of fragments spaced by the mass of one or the other co-monomer, that is, m(0) = 115.0 Da and m(1) = 129.0 Da.[1] Sequence of any information-coded oligourethanes can hence readily be established by MS/MS.

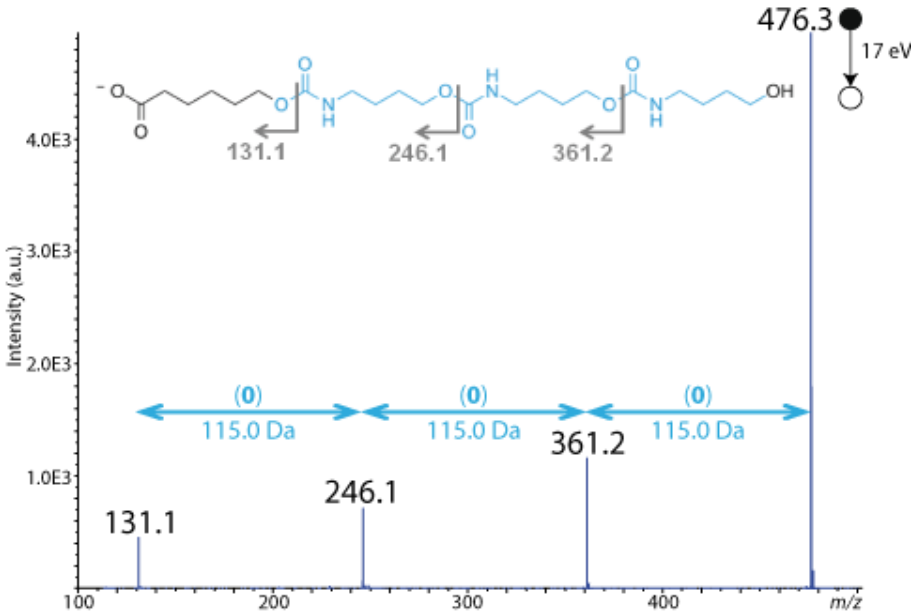


Figure S1. MS/MS spectrum of [**P1** – H]$^-$ at *m/z* 476.3, validating the 000 sequence in **P1** (see fragmentation scheme). Collision energy is indicated in the laboratory frame.

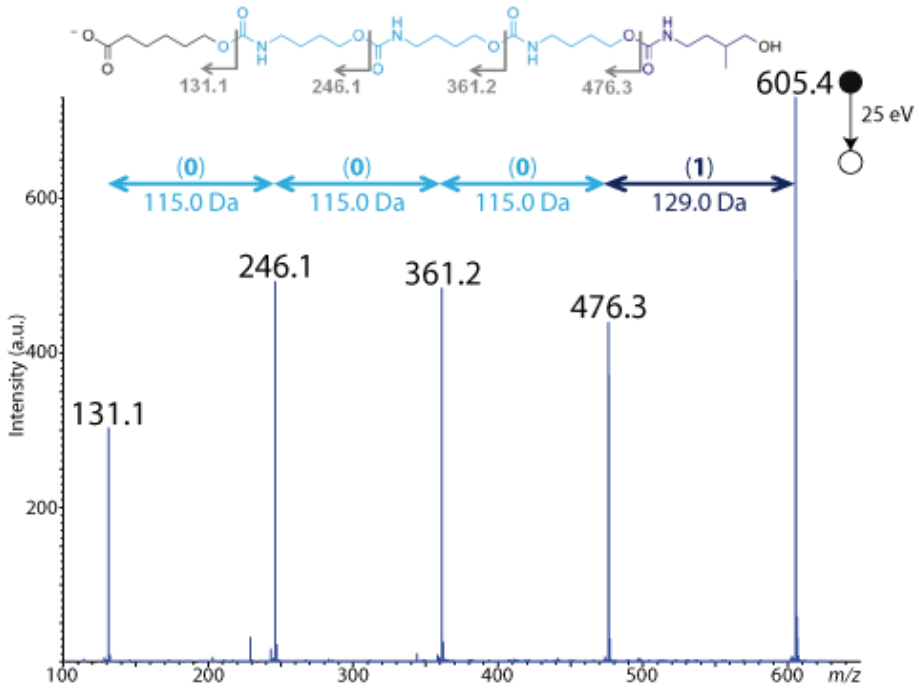


Figure S2. MS/MS spectrum of [**P2** – H]$^-$ at *m/z* 605.4, validating the 0001 sequence in **P2** (see fragmentation scheme). Collision energy is indicated in the laboratory frame.

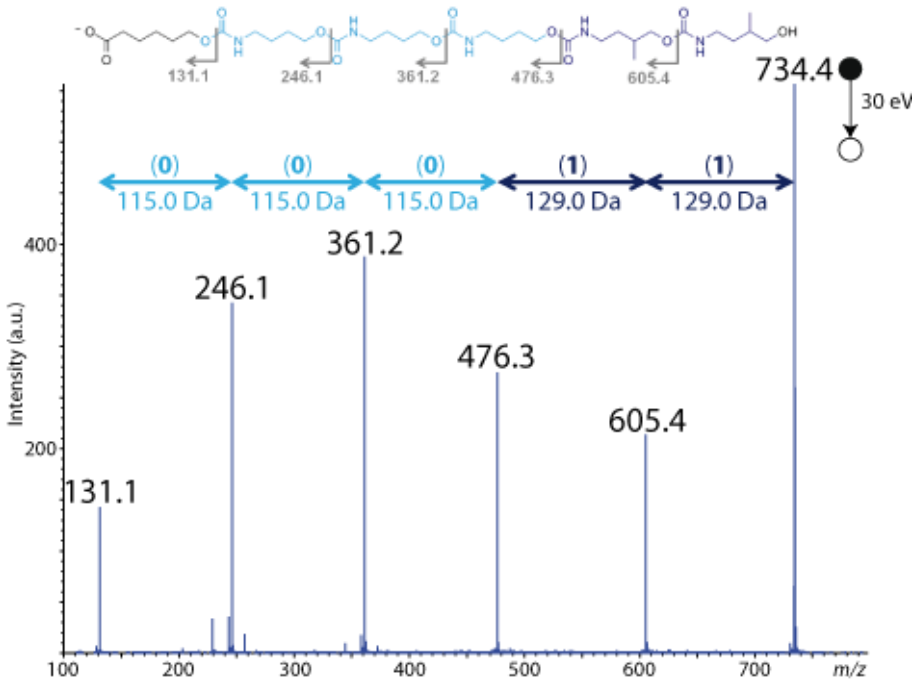


Figure S3. MS/MS spectrum of [**P3** – H]$^-$ at *m/z* 734.4, validating the 00011 sequence in **P3** (see fragmentation scheme). Collision energy is indicated in the laboratory frame.

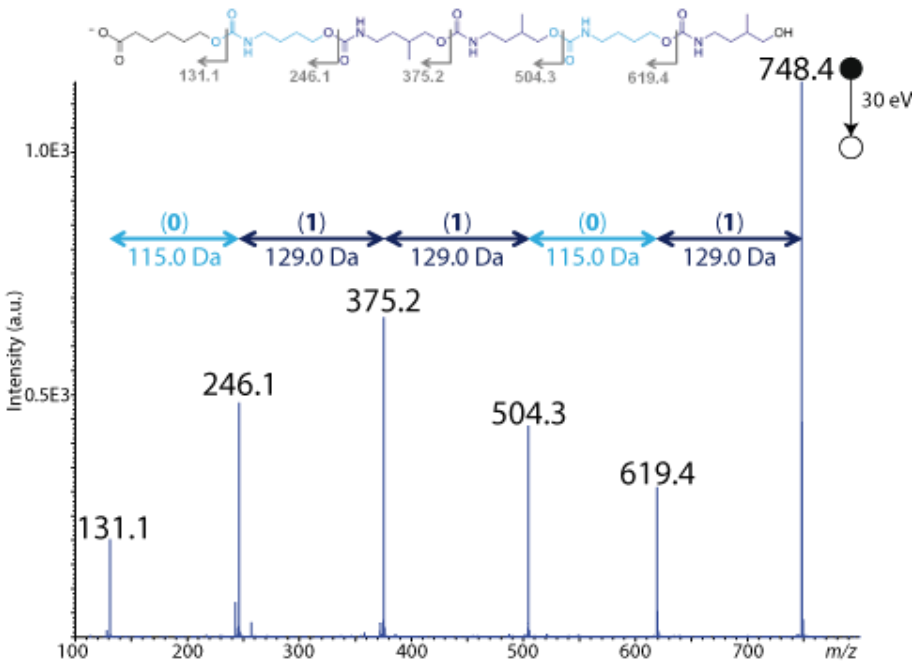


Figure S4. MS/MS spectrum of [**P4** – H]$^-$ at *m/z* 748.4, validating the 01101 sequence in **P4** (see fragmentation scheme). Collision energy is indicated in the laboratory frame.

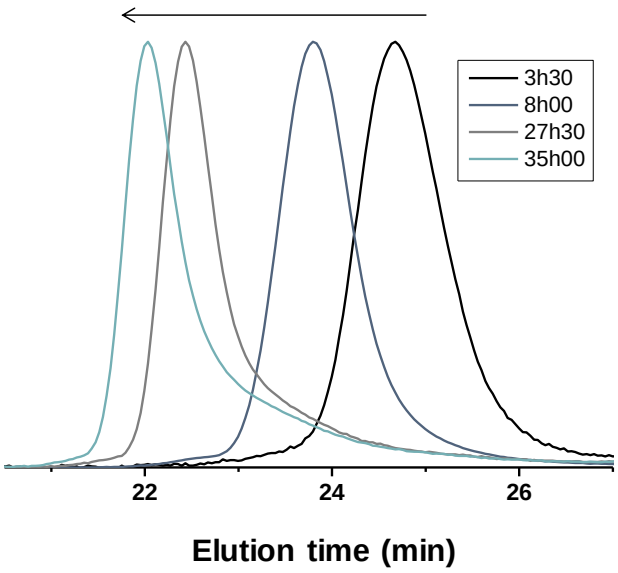


Figure S5. SEC chromatograms recorded in THF for a styrene ATRP initiated by **P3"** (see Table 2, Entry 6 in the main text for experimental conditions).

E. References

1. U. S. Gunay, B. E. Petit, D. Karamessini, A. Al Ouahabi, J.-A. Amalian, C. Chendo, M. Bouquey, D. Gigmes, L. Charles and J.-F. Lutz, *Chem*, 2016, **1**, 114-126.

2. E. Östmark, S. Harrisson, K. L. Wooley and E. E. Malmström, *Biomacromolecules*, 2007, **8**, 1138-1148.