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ELECTRONIC SUPPORTING INFORMATION

One-pot Synthesis of Amphiphilic Multiblock Poly(2-oxazolines) via *para*-Fluoro-Thiol Click Reaction

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1. Experimental Section

Materials 2,3,4,5,6-Pentafluorobenzyl bromide (PFBB) (Aldrich, 99%), 2-ethyl-2-oxazoline (Aldrich, 99%), 2-methyl-2-oxazoline (Aldrich, 99%), 4,4′-Thiobisbenzenethiol (Aldrich, 98%), 2,2′-(Ethylenedioxy)diethanethiol (Aldrich, 95%), 1,2-ethanedithiol (Aldrich, ≥98.0% (GC), Pentaerythritol tetrakis(3-mercaptopropionate) (Aldrich, 95%) and Trimethylolpropane tris(3-mercaptopropionate) (Aldrich, 95%) were selected as initiators and starting materials of preparation of clickable polyoxazolines and subsequent block and star polymer synthesis. Triethylamine (Aldrich, ≥99.5%), were used to activate PFTR click reactions. *N,N*-Dimethylformamide (DMF, Aldrich, for molecular biology, ≥99%), chloroform (Aldrich, >99.9%, HPLC grade), tetrahydrofuran (THF, Aldrich, inhibitor-free, suitable for HPLC, ≥99.9%), diethyl ether (Aldrich, suitable for HPLC, ≥99.9%, inhibitor-free) and anhydrous acetonitrile (Aldrich, 99.8%) were used as the solvent for polymerization, click reaction and polymer precipitation. Dimethylphenylphosphine (Aldrich, 99%) was used as to prevent the disulfide bond formation.

Instrumentation Nuclear Magnetic Resonance (NMR) spectroscopic measurements were performed on 300 or 400 MHz Bruker instruments in 5 mm NMR tubes. Residual solvent signals of $CHCl_3$ (δH = 7.26 ppm, δC =77.2 ppm) was used as reference. Gel permeation chromatography (GPC) measurements were conducted on an Agilent 1260 infinity system operating in THF with 2% TEA 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 PMMA standard calibration kits from Agilent with nominal M_p ranging from 500 to 300000 Da. All samples were filtered through 0.2 μm PTFE filters before analysis. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI TOF MS) was performed

on a Bruker Autoflex Speed mass spectrometer using a nitrogen laser delivering 2 ns pulses at 337 nm with positive ion ToF detection performed using an accelerating voltage of 25 kV. The matrix used was trans-2-[3-(4-tertbutylphenyl)-2-methyl-2-propylidene]malonitrile (DCTB) dissolved in THF. Sodium trifluoroacetate used as a cationic agent (solution in acetonitrile). The compound (diluted in THF) was applied after separate loadings of DCTB and sodium trifluoroacetate. Samples were measured in reflective or linear mode and calibrated against poly(methyl methacrylate) standards. The morphologies of the self-assembled structures were analysed by Transmission Electron Microscopy (TEM), using a JEOL 2100 instrument operating at an acceleration voltage of 200 kV and equipped with a CCD camera from Gatan. Each TEM sample was prepared by dropping 20 μL of the nanoparticle aqueous solution on a Fresh glow-discharged carbon-coated copper grid for 1 min. The residue of aqueous solution was blotted away with a strip of filter paper and then the grid was dried under vacuum and stored at room temperature until imaging. The transmittance measurements were performed on a Cary 100 Uv-Vis spectrometer which has good photometric performance in the 175-900 nm range.

General procedure of cationic ring opening polymerisation of oxazoline monomer with 2,3,4,5,6 pentafluoro benzyl bromide (PFBB). An oven dried clean microwave vial was loaded with a dried magnetic follower, sealed and connected to vacuum line for 10 minutes before switch to nitrogen flow. PFBB (1 equiv) that distilled and stored over molecular sieves were transferred to the sealed microwave vial under inert conditions with purged syringes. Anhydrous acetonitrile was transferred to the sealed microwave vial under inert conditions with purged syringes, the amount of anhydrous acetonitrile used were calculated to give a 4.0 M solution of the selected oxazoline monomer. Distilled and stored over molecular sieves oxazoline monomer (equiv depends on required degree of polymerization) were then transferred to the sealed microwave vial under inert conditions with purged syringes. The

reaction mixture was then transferred to a microwave reactor and heated at determined temperature for determined reaction time. Subsequent termination step was done by injecting NaOH/MeOH solution to give a hydroxyl chain end or a solution of selected dithiol in dry DMF to allow the step-growth polymerization to happen.

General procedure of block polymer and star polymer synthesis via PFTR click reaction of PFBB initiated clickable polyoxazoline and thiols. To a clean reaction vial charged with one clean magnetic follower was added the solution of selected clickable polyoxazoline with 1 equivalent of pentafluoro end group in least amount of DMF that allows full dissolution of polymer. Selected dithiol or multithiol compound was then added to the solution, 0.5 equivalent, 0.33 equivalent and 0.25 equivalent were used for dithiol, trithiol and tetrathiol, respectively. 0.5 mol% DMPP was added to the reaction vial to avoid disulfide bridge formation and then 1.05 equivalent of TEA was added to the reaction mixture to mediate the PFTR click reaction and act as the fluorine scavenger. The reaction mixture was then allowed to stir under room temperature, GPC samples were taken to deteremine the end of the reaction. The procedure could be directly done in a one-pot manner following the polymerisation of oxazoline monomers with PFBB by injecting 1.0M dithiol solution in DMF, 0.5mol% DMPP and TEA directly into the polymerisation mixture.

One-pot synthesis of multiblock polyoxazoline via PFTR click reaction and the direct termination of polyoxazoline living chain ends. After PFBB initiated polymerisation of oxazoline monomers shown previously, instead of terminating the chain with a NaOH/MeOH solvent mixture, a degassed and well-stirred solution of selected dithiol, DMPP and dry TEA in dry DMF was injected into the reaction vial containing the polyoxazoline crude solution for step-growth polymerisation via PFTR click reaction and direct termination of polyoxazoline living chain end. The reaction mixture was then transferred to a microwave reactor and heated

at 70℃ for 3 minutes. White precipitation was observed in the reaction vial which indicates the generation of fluorine salt of TEA.

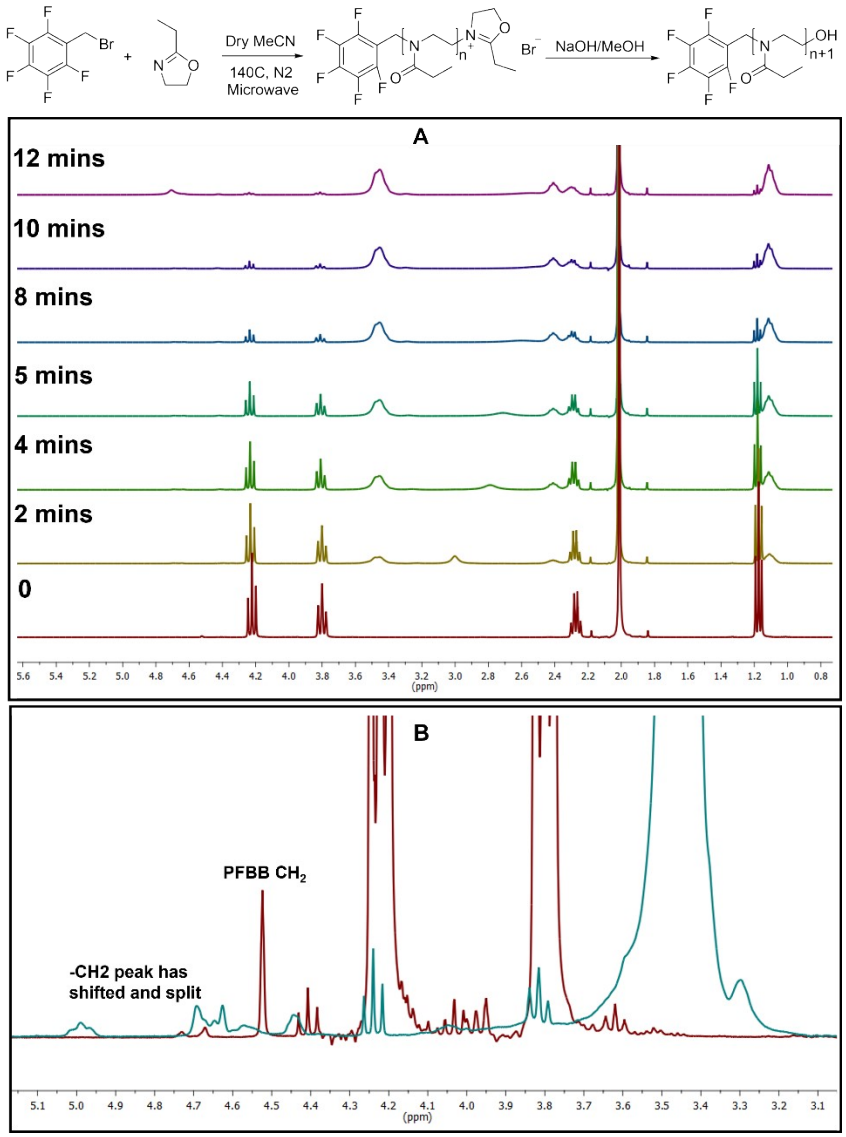


Figure S1. ^{1}H NMR kinetics of PEtOx polymerization with pentafluoro benzyl bromide as the initiator.

The ^{1}H NMR kinetic shows the elimination of monomers and the shift and split of methylene group from pentafluoro benzyl bromide. The kinetics plot (A) shown the appearance of polymer backbone broad peaks (1.0-1.2 ppm, 2.2-2.4 ppm and 3.3-3.5 ppm). The overlapped t_0(red) and t(2mins) (green) shown that the methylene group from pentafluoro benzyl bromide has shifted from 4.5 ppm to 5.0 ppm.

Calculation of apparent polymerization rate

eq 1, in presence of the assumption that the concentration of active chains [P*] is equal to the concentration of initiator $[I]_0$:

$$-\frac{d[M]}{dt} = k_{app}[P^*][M] \#(Equation\ S1)$$

Integration of eq 1 with substitution of [P*] with [I] give rise to eq 2

$$ln\frac{[M]_0}{[M]_t} = k_{app}[I]_0 t \#(Equation\ S2)$$

General procedure of MALDI-ToF sample preparation

20 mg/ml *trans*-2-[3-(4-*tert*-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) solution, 0.5 mg/ml polymer solution and 1mg/ml sodium trifluoroacetate solution were prepared fresh. 0.5 µl of each solution were mixed and 0.5 µl of mixed solution was taken to prepare one MALDI spot.

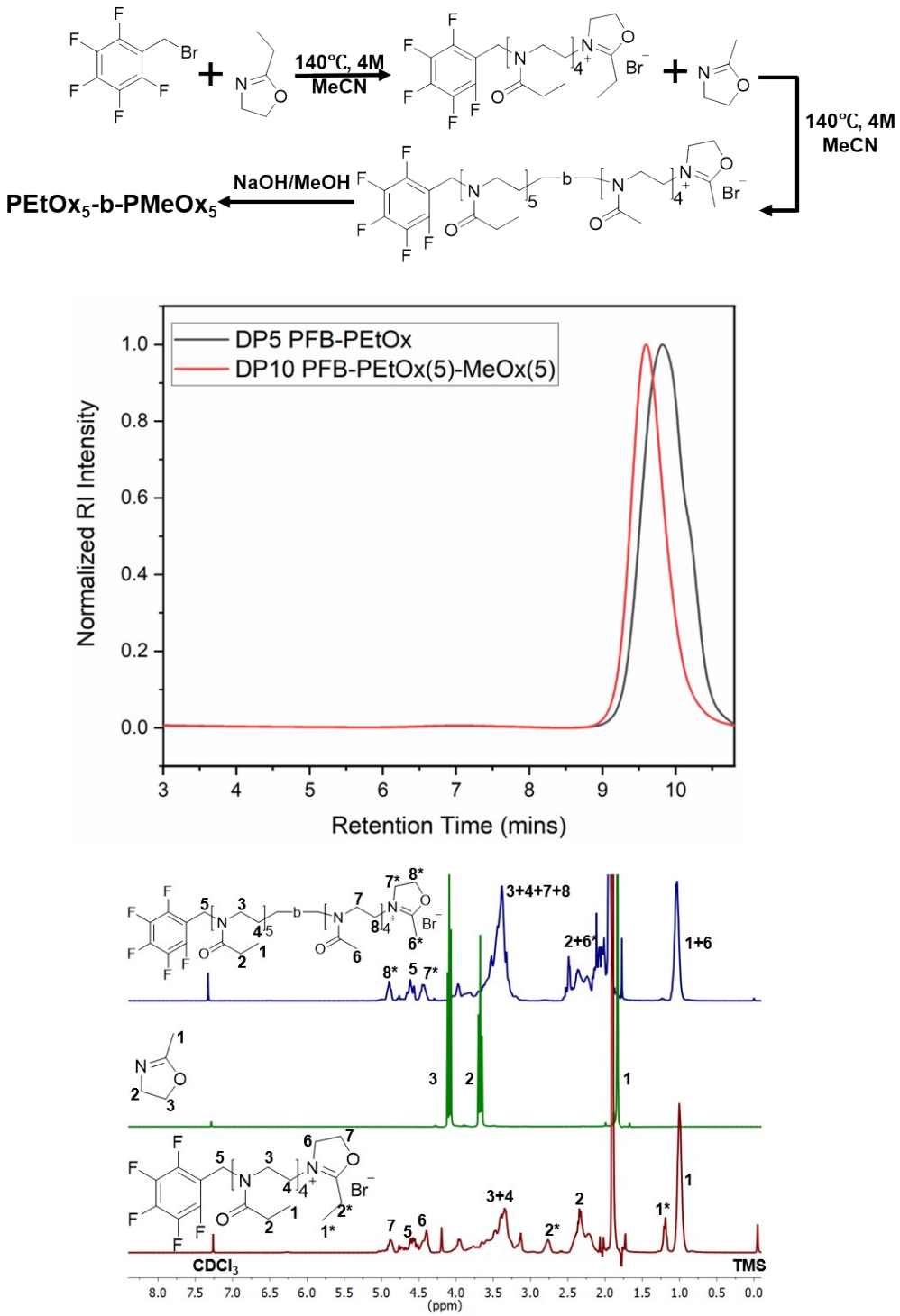
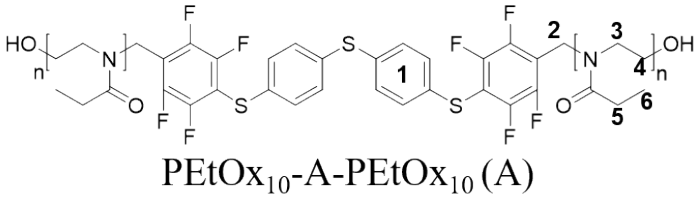
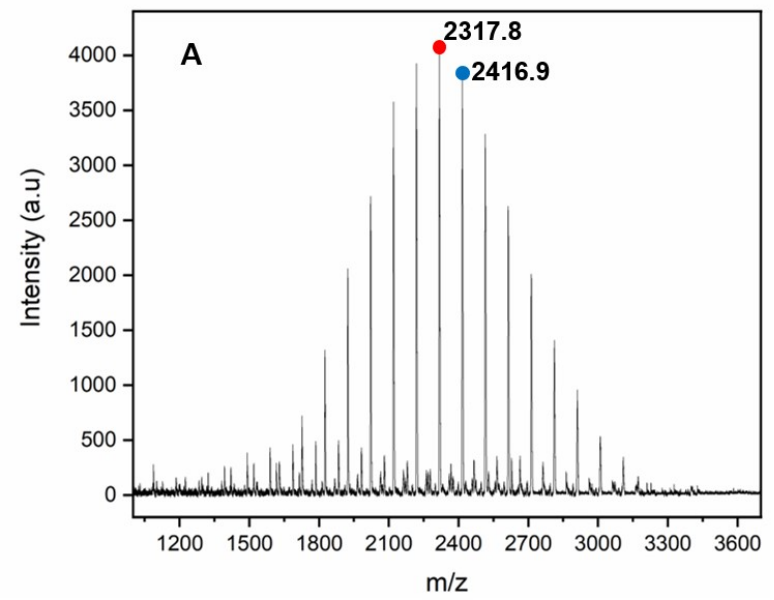


Figure S2. THF GPC and ^{1}H NMR characterization of P(EtOx)$_5$-b-P(MeOx)$_5$ using PFBB as the initiator.

THF GPC traces shown a hydrodynamic volume change while ^{1}H NMR shows the presence of desired polymer, and the consumption of MeOx monomer.



$PEtOx_{10}$-A-$PEtOx_{10}$ (A)



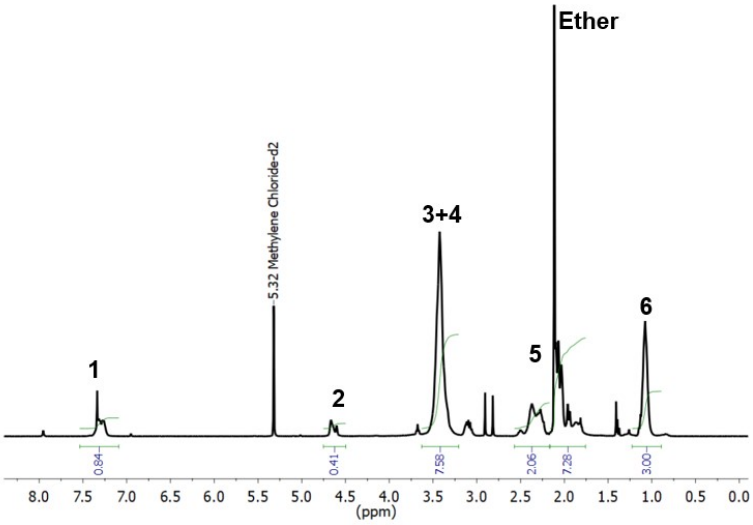
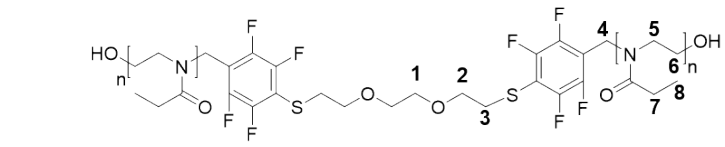
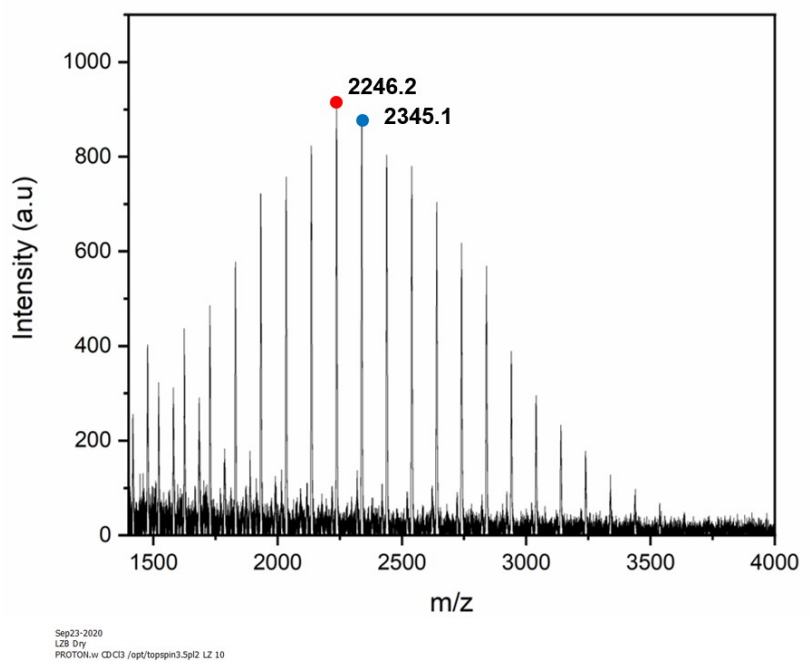


Figure S3. MALDI-ToF and ^{1}H NMR characterization of $PEtOx_{10}$-A-$PEtOx_{10}$ (P2)

^{1}H NMR has shown peaks of desired structure, while the MALDI-ToF results shown a major distribution of desired structure. For example, peak at 2317.8 Da was close to the theoretical value, 2314.1 Da of a diblock polymer with 17 EtOx units, two hydroxyl end groups, dithiol A as the connection unit and flying in the formation of sodium salt, while the difference between peaks was 99.1 Da that corresponds to a EtOx unit.



$PEtOx_{10}$-B-$PEtOx_{10}$ (B)



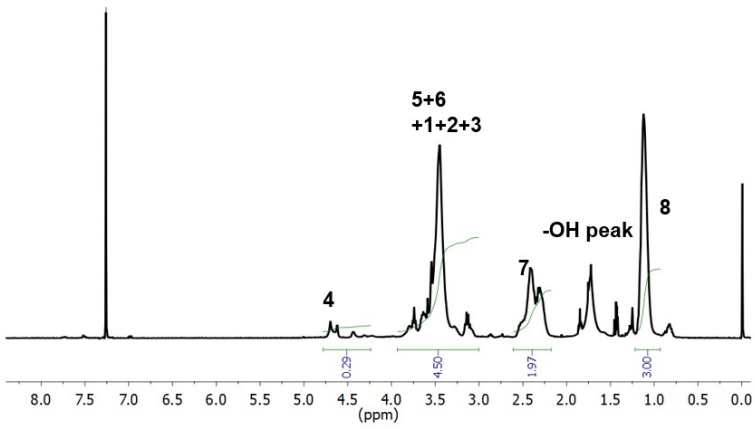


Figure S4. MALDI-ToF and ^{1}H NMR characterization of $PEtOx_{10}$-B-$PEtOx_{10}$ (P3)

^{1}H NMR has shown peaks of desired structure, while the MALDI-ToF results shown a major distribution of desired structure. For example, peak at 2248.2 Da was close to the theoretical value, 2246.2 Da, of a diblock polymer with 17 EtOx units, two hydroxyl end groups, dithiol A as the connection unit and flying in the formation of sodium salt. The difference between peaks was 99 Da that corresponds to a EtOx unit.

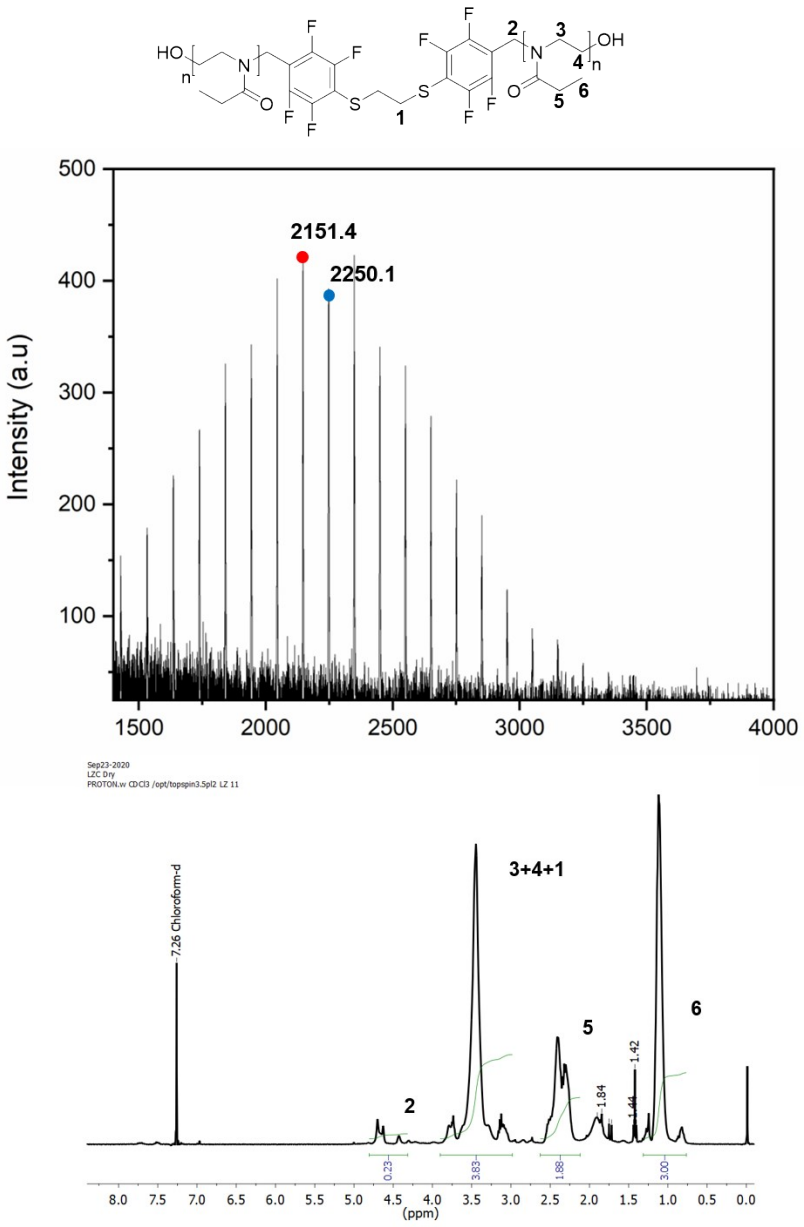


Figure S5. MALDI-ToF and ^{1}H NMR characterization of PEtOx$_{10}$-C-PEtOx$_{10}$ (P4)

^{1}H NMR has shown peaks of desired structure, while the MALDI-ToF results shown a major distribution with the difference between peaks was 98.7 Da that corresponds to a EtOx unit. The peak at 2151.4 Da was deviated from the theoretical value, 2158.1, of a diblock polymer with 17 EtOx units, two hydroxyl end groups, dithiol C as the connection unit and flying in the formation of sodium salt. As ^{1}H NMR and SEC reveals the reaction did happen, this significant deviation indicates the PMMA 2000 calibration standard used here might not be the most appropriate one, and the MALDI-ToF matrix-solvent-salt system used could be improved.

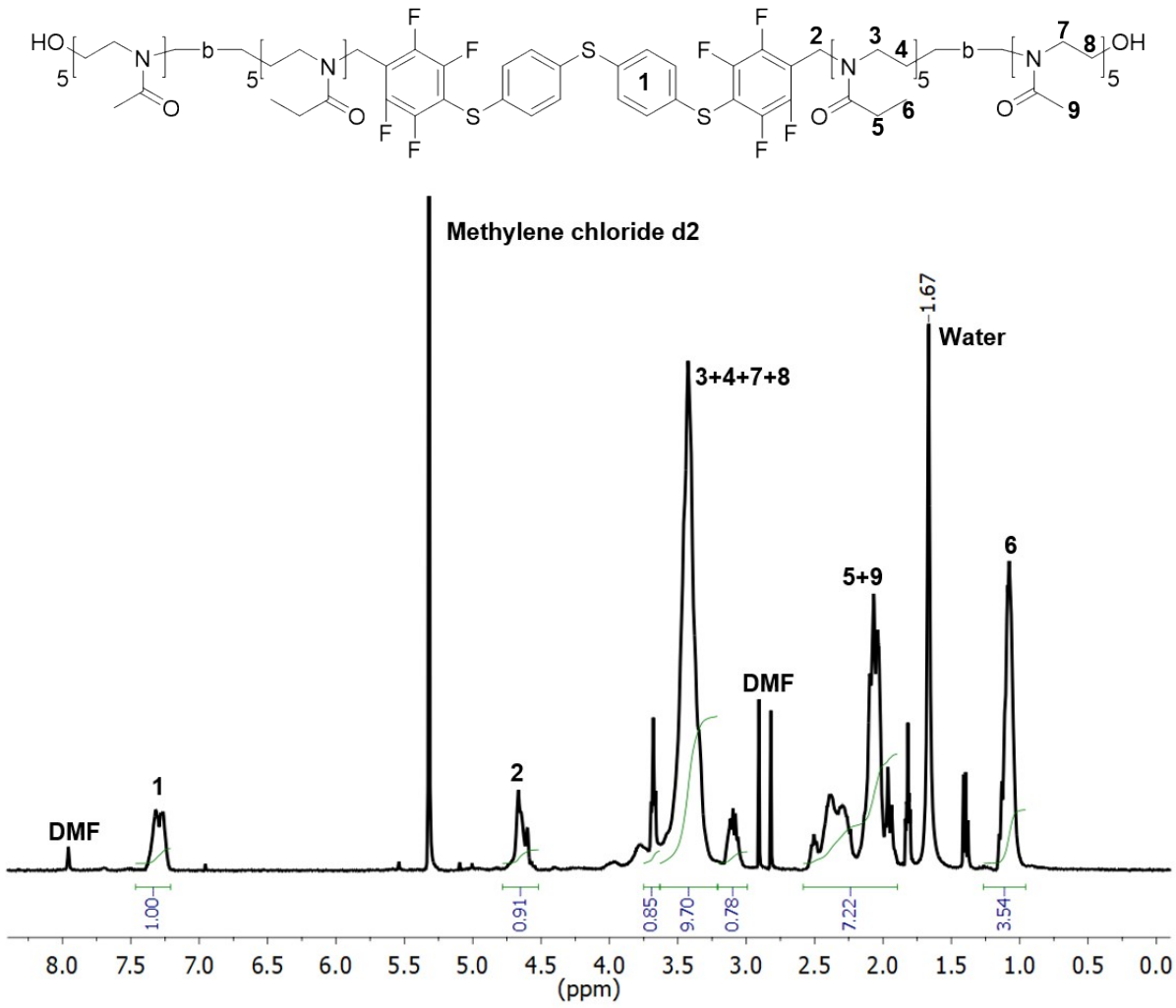


Figure S6. ^{1}H NMR characterization of tetrablock polymer P(EtOx$_5$-MeOx$_5$)$_2$-A (P7)

^{1}H NMR characterization has shown the formation of desired polymer structure, however, the rather distorted ratio of peaks suggesting the final product is a mixture of tetrablock polymer and diblock polymer, which shown by the ratio between aromatic peak **1** and -CH_2 peak **2**. Reason might be possible chain transfer in block polymer formation results in reduced chain end fidelity.

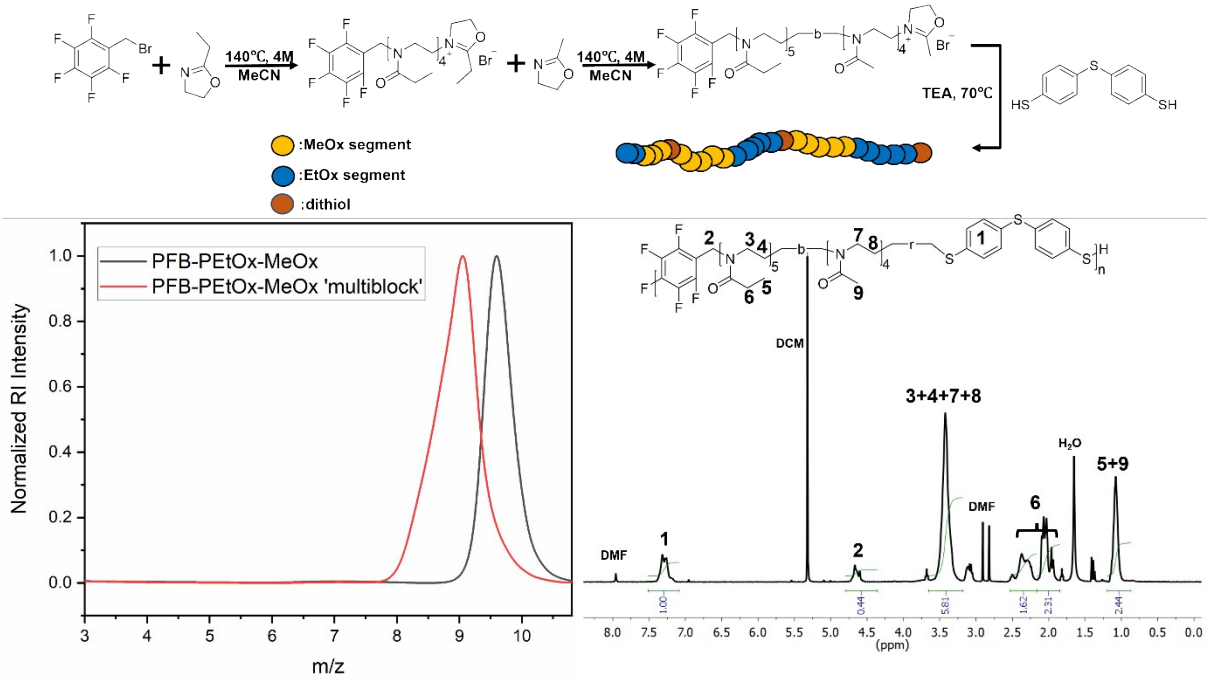


Figure S7. THF GPC traces and ^{1}H NMR characterization of multiblock P(EtOx-MeOx) (P10)

The THF GPC trace has shown a significant hydrodynamic volume change while in the ^{1}H NMR, although the specific peaks have been observed, the distorted ratio between peaks were suggesting that leftover of diblock PEtOx-MeOx existing in the final product. The reason could be the living chain end fidelity was affected during synthesis of block copolymer and the chain transfer during polymerization results in missing α-end functional groups.