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Supporting Information

Glycidyl Tosylate: Polymerization of a "Non-Polymerizable" Monomer permits Universal Post-Functionalization of Polyethers

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SUPPORTING INFORMATION

Table of Contents

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SUPPORTING INFORMATION

Results and Discussion

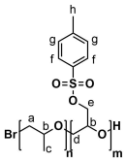
A) Experimental procedures and additional discussion

Materials. All solvents and reagents were purchased from Sigma-Aldrich, Acros Organics or TCI and used as received, unless otherwise described. Chloroform-d_1 was purchased from Deutero GmbH.

Instrumentation. ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were recorded using a Bruker Avance III HD 400 spectrometer equipped with a 5 mm BBFO-SmartProbe (Z-gradient probe) and an ATM as well as a SampleXPress 60 auto sampler. All spectra are referenced internally to residual proton signals of the deuterated solvent ($CDCl_3$). SEC measurements were performed in DMF (containing 0.25 g L^{-1} lithium bromide as an additive) at 50 °C. An Agilent 1100 Series was used as an integrated instrument, including a PSS HEMA column (300/100/40 · 10-10 porosity) as well as a UV (Agilent G1314A) and a RI (Agilent 61362A) detector. All calibrations were carried out using poly(ethylene glycol) standards with molecular weights between 106 g/mol and 42700 g/mol purchased from Polymer Standards Service. Sample concentration is 3 mg ml^{-1}. DSC measurements were performed under a nitrogen atmosphere using a PerkinElmer DSC 8500 with PerkinElmer CLN2 in the temperature range from −100 to 100 °C at heating rates of 20 and 10 K min^{-1} for the first and the second heating run, respectively.

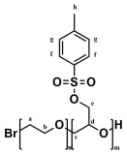
Preparation of Glycidyl tosylate (GlyTs). In a round bottom flask dry glycidol (8 g, 0.05 mol, 1eq) is dissolved in dry dichloromethane (100 mL). After addition of triethylamine (21.8 g, 0.1 mol, 2eq) and N,N-Dimethylaminopyridine (0.06 g, 0.003 mol, 0,1 eq) under Ar-atmosphere p-Toluenesulfonic acid (19.5 g, 0.05 mol, 1 eq) is slowly added. The mixture is stirred at 0 °C for 2h and then allowed to heat up to room temperature. The reaction mixture is washed with 1M HCl and purified via column chromatography (ethylacetate 2:1 cyclohexane). Yield: 60% (6.95 g).
^{1}H-NMR ($CDCl_3$, 400 MHz) GlyTs: δ = 7.80 (d, 2H, aromatic), 7.35 (d, 2H, aromatic), 4.22–4.28 (dd, 1H, CHHOS), 3.91–3.96 (dd,1H, CHHOS), 3.16–3.21 (m, 1H, CH), 2.79 (t,1H, CHHoxirane), 2.56–2.58 (dd, 1H, CHH oxirane), 2.43 (s, 3H, CH_3) ppm.

Preparation of P(PO-*co*-GlyTs).
To prepare P(PO-co-GlyTs), in a Schlenk-flask, $N(Oct)_4Br$ (0,05 g, 1.1x10-4 mol, 1 eq) and GlyTs (0.130 g, 5.7x10-4 mol, 5 eq) are dried with benzene in vacuo overnight. Dry toluene (5 mL) and freshly over CaH_2 distilled PO (0.33 g, 5.7x10-3 mol, 50 eq) are added under argon atmosphere. The mixture was cooled to -78 °C. Addition of the catalyst triisobutyl aluminum (0.31 mL, 3.4x10-4 mol, 3 eq) in toluene (1.1 M) initiated the reaction. The polymerization was allowed to slowly raise to 25 °C. After 1 d, ethanol was added to quench the reaction. The crude product was dialyzed against dichloromethane for 12 h, the formed aluminum oxides were removed by filtration, and the solvent evaporated. This resulted in a colorless, highly viscous product (0.44 g, 95%). The copolymer composition was determined via ^{1}H-NMR using the ratio of the methylgroup at 0.90 – 1.20 ppm versus the methylgroup of the tosylate moiety at 2.20 – 2.46 ppm.



^{1}H-NMR ($CDCl_3$, 400 MHz) P($PO_{0.92}$-co-$GlyTs_{0.08}$): δ = 7.79 – 7.77 (d, 0.5H, H_f), 7.39 – 7.29 (d, 0.5H, H_g), 3.74 – 3.25 (m, 3.38H, polyether backbone), 2.49 –2.40 (s,0.26H, H_h), 1.12 – 0.98 (m, 3H, H_c) ppm.
^{13}C-NMR, HSQC ($CDCl_3$, 100 MHz) P($PO_{0.92}$-co-$GlyTs_{0.08}$): δ = 129.82 (C_g), 127.98 (C_f), 75.53-72.83 (polyether backbone), 21.65 (C_h), 17.27 (C_c) ppm.

Preparation of P(EO-*co*-GlyTs). P(EO-*co*-GlyTs) was synthesized in a similar manner. After drying of $N(Oct)_4Br$ (0,18 g, $3.3x10^{-4}$ mol, 1 eq) and GlyTs (0,50 g, $2.2x10^{-3}$ mol, 7 eq), EO (0,90 g, 2.0x10-2 mol, 62 eq) was condensed at -60 °C and triisobutyl aluminum (0.89 mL, $9.9x10^{-4}$ mol, 3 eq) was added. After 16 h the reaction was quenched with ethanol and the product dialyzed against dichloromethane for 12 h. Yield: 1.3g (95%).



^{1}H-NMR ($CDCl_3$, 400 MHz) P($EO_{0.92}$-co-$GlyTs_{0.08}$): δ = 7.80 – 7.77 (d, 2H, H_f), 7.38 – 7.30 (d, 2H, H_g), 3.75 – 3.40 (m, 54H, polyether backbone), 2.49 – 2.40 (s, 3H, H_h) ppm.
^{13}C-NMR, HSQC ($CDCl_3$, 100 MHz) P($EO_{0.92}$-co-$GlyTs_{0.08}$): δ = 129.94 (C_g), 128.09 (C_f), 70.97 – 69.71 (polyether backbone), 21.75 (C_h) ppm.

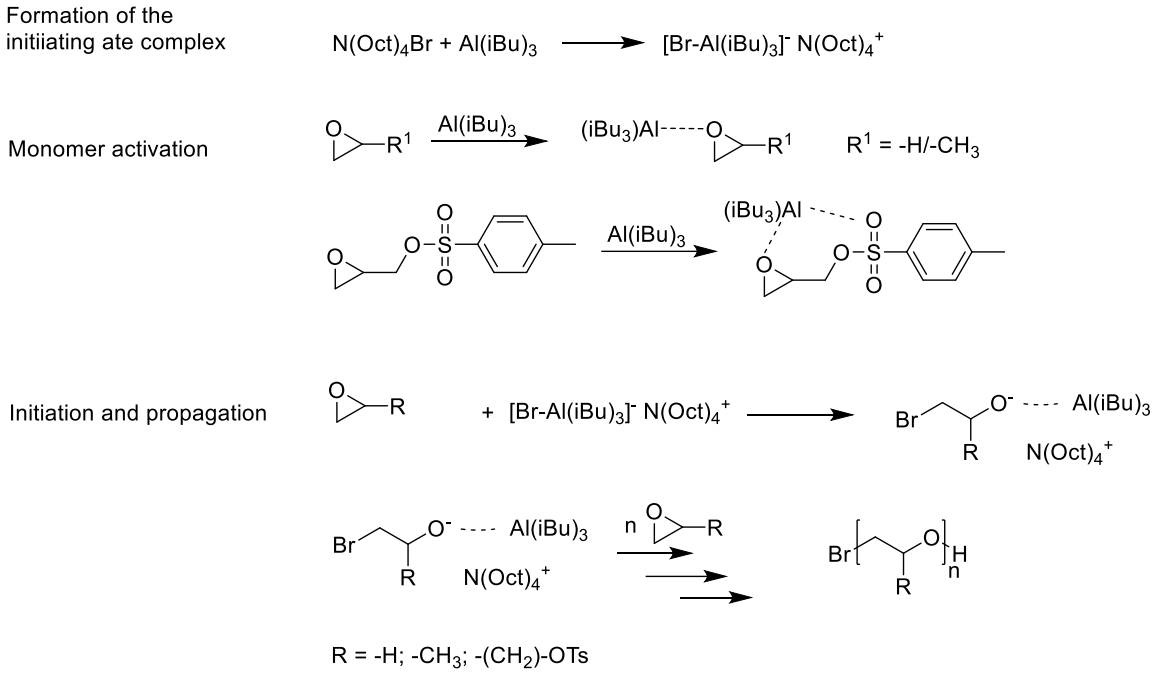
Preparation of P(PO-*co*-DMGA). In a round bottom flask, P($PO_{0.92}$-co-$GlyTs_{0.08}$) (200 mg) is dissolved in acetonitrile (3 mL) and dimethylamine solution (40 wt.% in water, 2 mL) is added. The mixture is heated to 80 °C over night. After cooling to room temperature, the reaction solution is dialyzed against methanol for 16 h. After freeze drying, a slightly yellow, highly viscous liquid remains. Yield: quant.
^{1}H-NMR ($CDCl_3$, 400 MHz) P($PO_{0.92}$-co-$DMGAs_{0.08}$): δ = 3.75 – 3.40 (m, 54H, polyether backbone), 2.27 (s, 0.27H, -N(CH_3)$_2$), 1.20 – 1.108 (m, 3H, -CH_3) ppm.
^{13}C-NMR, HSQC ($CDCl_3$, 100 MHz) P($PO_{0.92}$-co-$DMGAs_{0.08}$): δ =75.53-72.83 (polyether backbone), 21.67 (-N-CH_3), 17.27 (-CH_3) ppm.

Preparation of P(PO-*g*-mPEG). In a dry schlenk flask, $mPEG_{500}$ (33 mg, $9.7x10^{-5}$ mol, 1 eq) is dissolved in in benzene (3 mL) and potassium tert-butoxide (0.03g, $2.7x10^{-4}$ mol, 3 eq) is added. After stirring for 30 min, the solvent is removed under reduced pressure. P($PO_{0.92}$-*co*-$GlyTs_{0.08}$) (400 mg, $9.7x10^{-5}$ mol, 1 eq) is dried in vacuo, dissolved in dry acetonitrile and added under Ar via syringe. The reaction mixture is heated to 80 °C for 16 h. After cooling to room temperature, the reaction solution is added dropwise to cold diethyl ether. Excess mPEG precipitates, the desired functional polymer remains in solution and can therefore be separated easily. After removal of the solvent under reduced pressure, a slightly yellow, highly viscous liquid remains. Yield: quant.
^{1}H-NMR ($CDCl_3$, 400 MHz) P($PO_{0.92}$-g-$mPEG_{0.08}$): δ = 3.81 – 3.36 (m, 6H, polyether backbone), 1.20 – 1.04 (m, 3H, -CH_3) ppm.
^{13}C-NMR, HSQC ($CDCl_3$, 100 MHz) P($PO_{0.92}$-g-$mPEG_{0.08}$): δ = 75.50 – 70.50 (polyether backbone), 17.47 (-CH_3) ppm.

Preparation of P(PO-*co*-GA). In a Schlenk flask, P($PO_{0.92}$-*co*-$GlyTs_{0.08}$) (500 mg, $1.4x10^{-4}$ mol, 1 eq) and NaN3 (0.014 g, $2,1x10^{-4}$ mol, 1.5 eq) are dried with benzene in vacuo. Dry dimethylformamide (5 mL) is added via syringe and the reaction mixture is heated to 120 °C for 16 h. After cooling to room temperature, the solution is filtered and dialyzed against methanol for 16 h. After removal of the solvent under reduced pressure, a highly viscous, slightly orange liquid remains. Yield: quant.
^{1}H-NMR ($CDCl_3$, 400 MHz) P($PO_{0.92}$-*co*-$GA_{0.08}$): δ = 3.75 – 3.29 (m, 4H, polyether backbone), 1.31 – 1.04 (m, 3H, -CH_3) ppm.
^{13}C-NMR, HSQC ($CDCl_3$, 100 MHz) P($PO_{0.92}$-*co*-$GA_{0.08}$): δ = 75.54 – 72.83 (polyether backbone), 52.14 (-CH_2-N_3), 17.48 (-CH_3) ppm.

^{1}H NMR kinetic studies. For ^{1}H NMR kinetic studies, a pre-dried NMR tube was prepared. Under Ar, dry GlyTs, PO/EO and the initiator were added according to the general procedure described above. After cooling to -78 °C, triisobutyl aluminum and $CDCl_3$ (0.2 mL) were added. The tube was directly sealed with a Teflon stop-cock and placed into a tempered NMR (20 °C), which performed measurements every 30s. The gathered spectra were analyzed using Mestrenova and Matlab.

SUPPORTING INFORMATION



Scheme S1: Reaction scheme for the proposed monomer activated ROP of GlyTs and PO/EO as presented in this work.

The above scheme depicts the mechanism of polymerization as shown in literature. As we showed in Table 1, we focused on copolymers containing 10 – 25% of tosylate moieties to maintain the characteristic properties of PEG/PPO. However, it is possible to incorporate more than 25% of tosylate moieties. While theoretical and experimental amounts of incorporated GlyTs are in good agreement, total monomer conversion and molecular weights decrease with increasing amount of GlyTs. We tentatively propose that the Lewis acid interacts with the tosylate moiety and therefore increasing amounts of tosylate in the polymer backbone may inhibit propagation by decreasing the concentration of free Lewis acid.

Table S1: Overview of the synthesized copolymers with ≥ 25% GlyTs. Yields and molecular weights were determined after dialysis ($M_{w,\ cutoff}$ = 1000 g/mol) against methanol/dichloromethane.

Structure	%GlyTs (theo)	%GlyTs	yield	M_n (g/mol)	Đ
P($PO_{0,75}$-*co*-$GlyTs_{0,25}$)	25	25	88 %	3000	2.1
P($PO_{0,68}$-*co*-$GlyTs_{0,32}$)	35	32	60 %	2800	2.0
P($PO_{0,52}$-*co*-$GlyTs_{0,58}$)	50	48	30 %	2200	1.5

B) SEC of the presented P(PO-*co*-GlyTs) and P(EO-*co*-GlyTs) copolymers.

All polymers show monomodal distributions, UV and RI traces match perfectly. The presence of a UV trace indicates that the tosylate moieties are incorporated in the polymer chains because PEG/PPO on their own show no UV activity. The samples listed in Table 1 with up to 25% of tosylate moieties are shown.

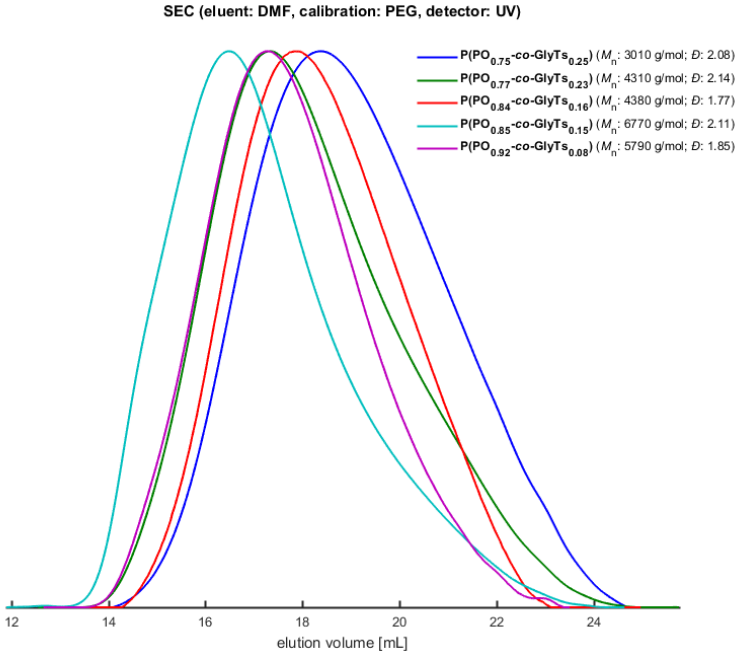


Figure S1. SEC elugrams (DMF, Detector: UV, PEG-standards) of P(PO-*co*-GlyTs) copolymers.

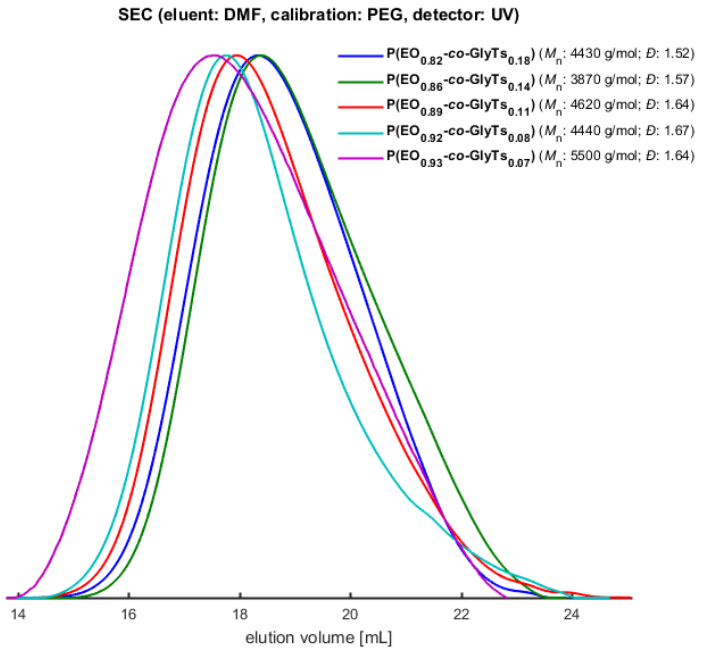


Figure S2. SEC elugrams (DMF, Detector: UV, PEG-standards) of P(EO-*co*-GlyTs) copolymers.

C) ^{1}H-NMR/^{13}C-NMR spectra of the P(PO-*co*-GlyTs) and P(EO-*co*-GlyTs) copolymers.

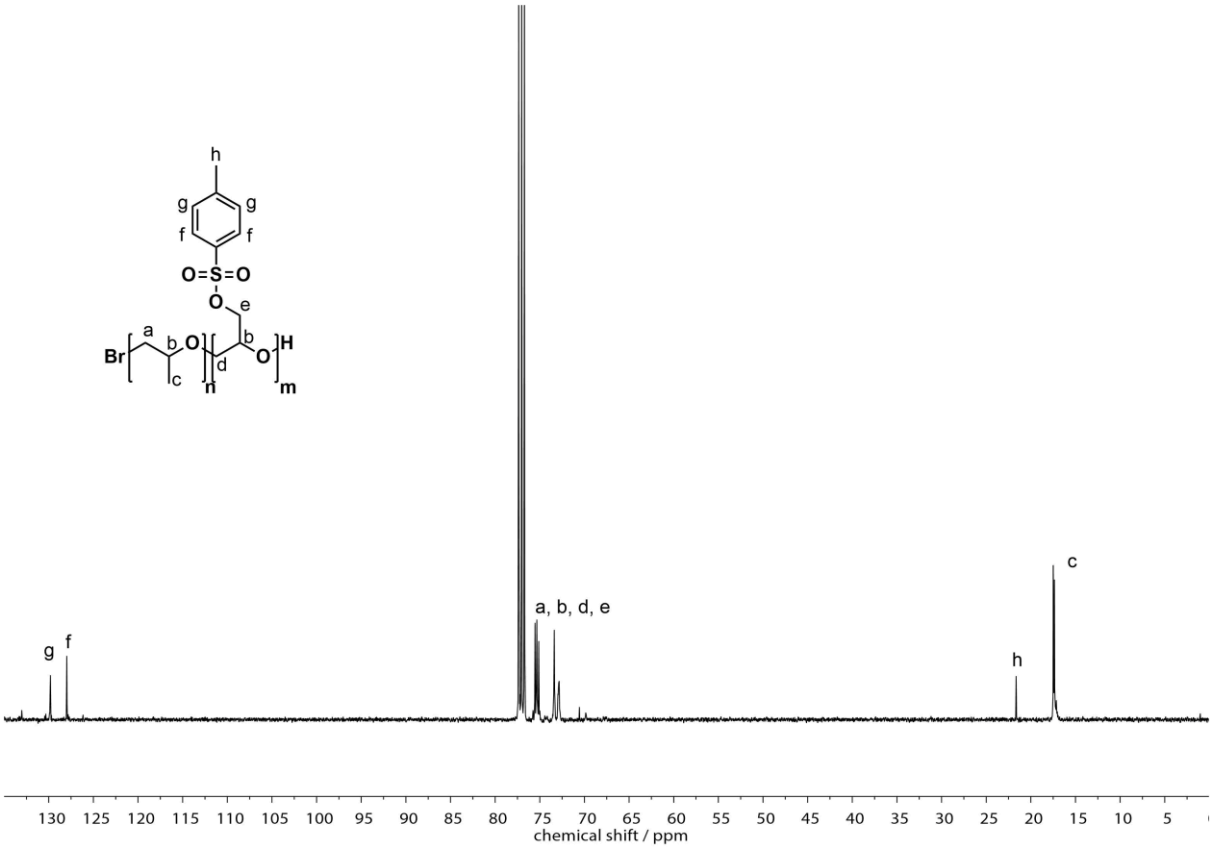


Figure S3. ^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of P($PO_{0.92}$-co-$GlyTs_{0.08}$).

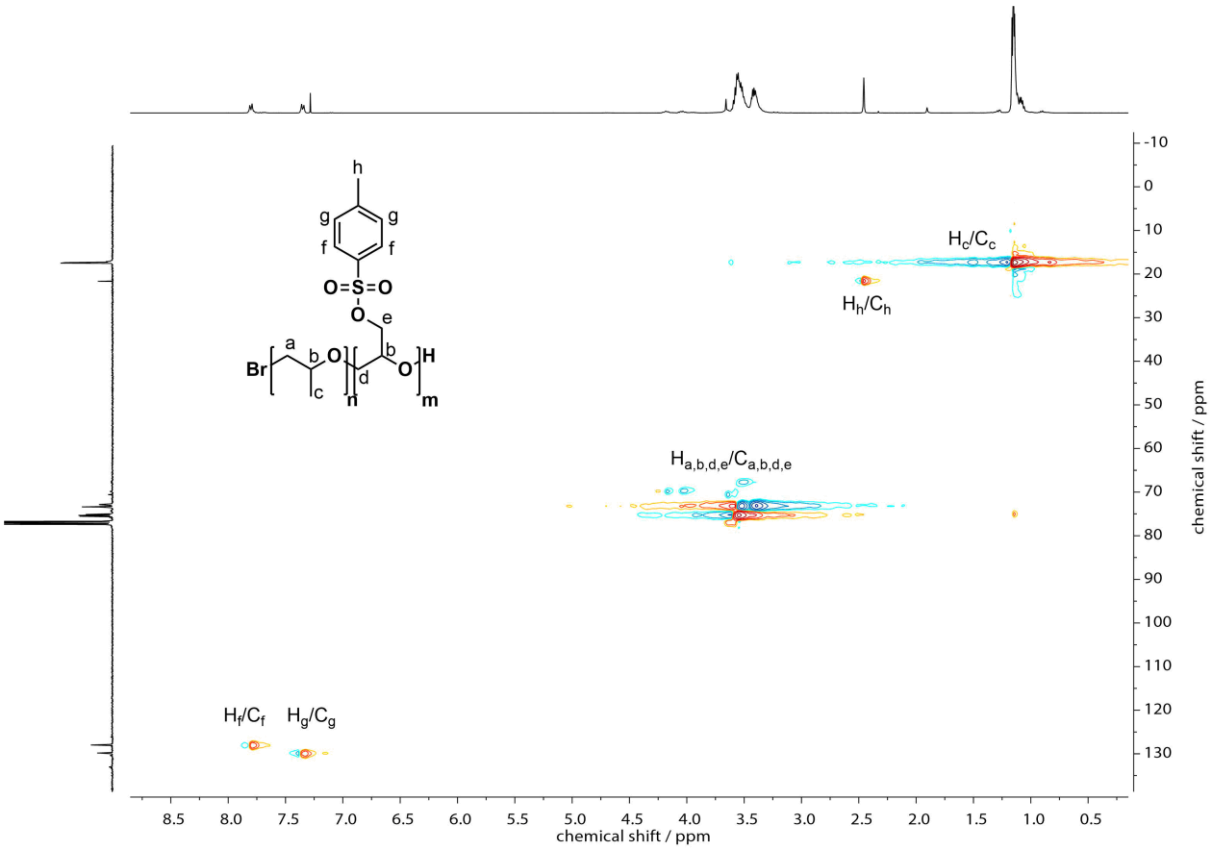


Figure S4. HSQC NMR spectrum ($CDCl_3$) of P($PO_{0.92}$-co-$GlyTs_{0.08}$).

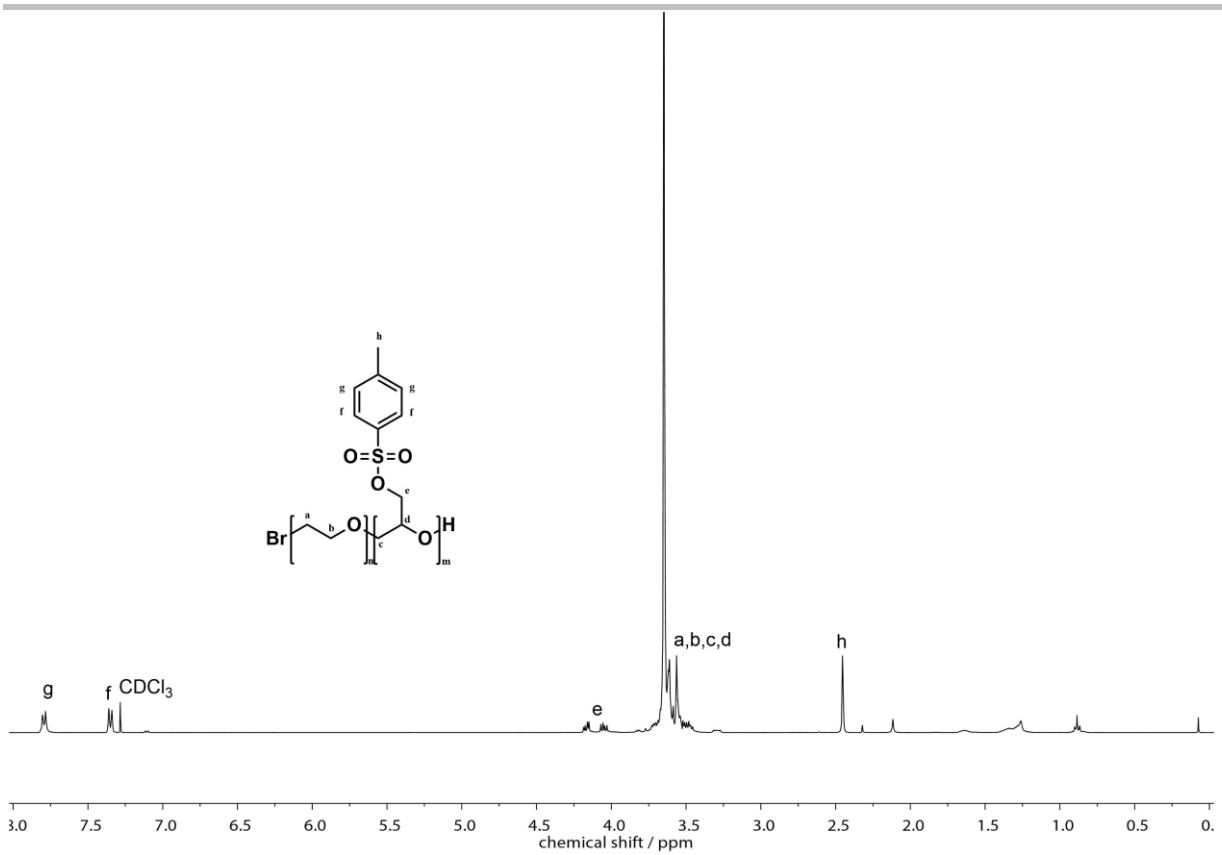


Figure S5. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of P($EO_{0.92}$-co-$GlyTs_{0.08}$).

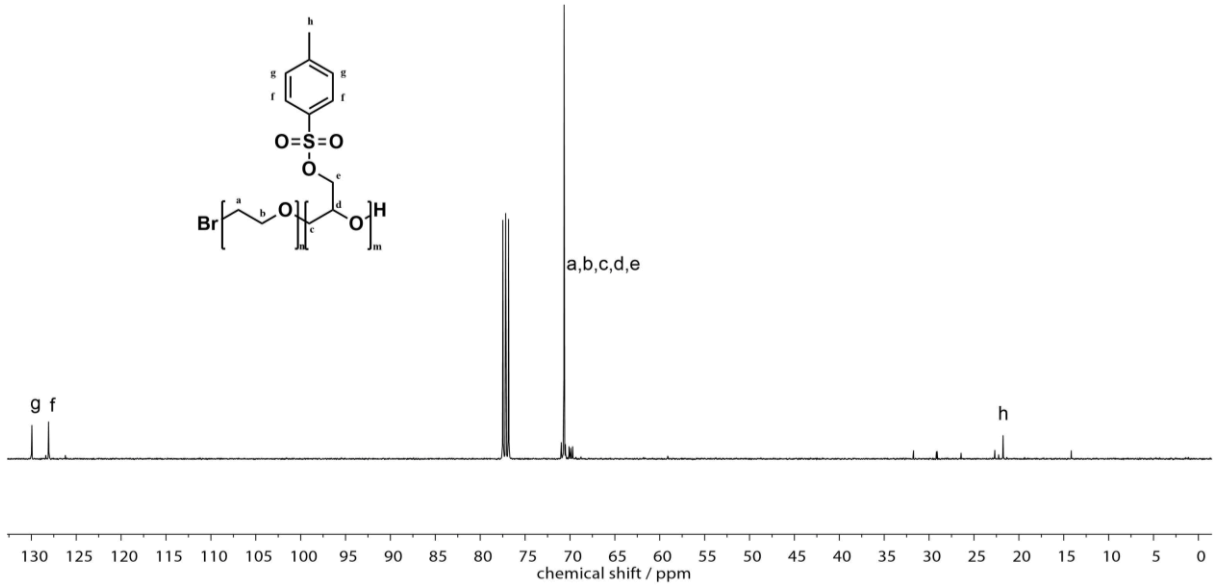


Figure S6. ^{13}C-NMR (100 MHz, $CDCl_3$) of P($EO_{0.92}$-co-$GlyTs_{0.08}$).

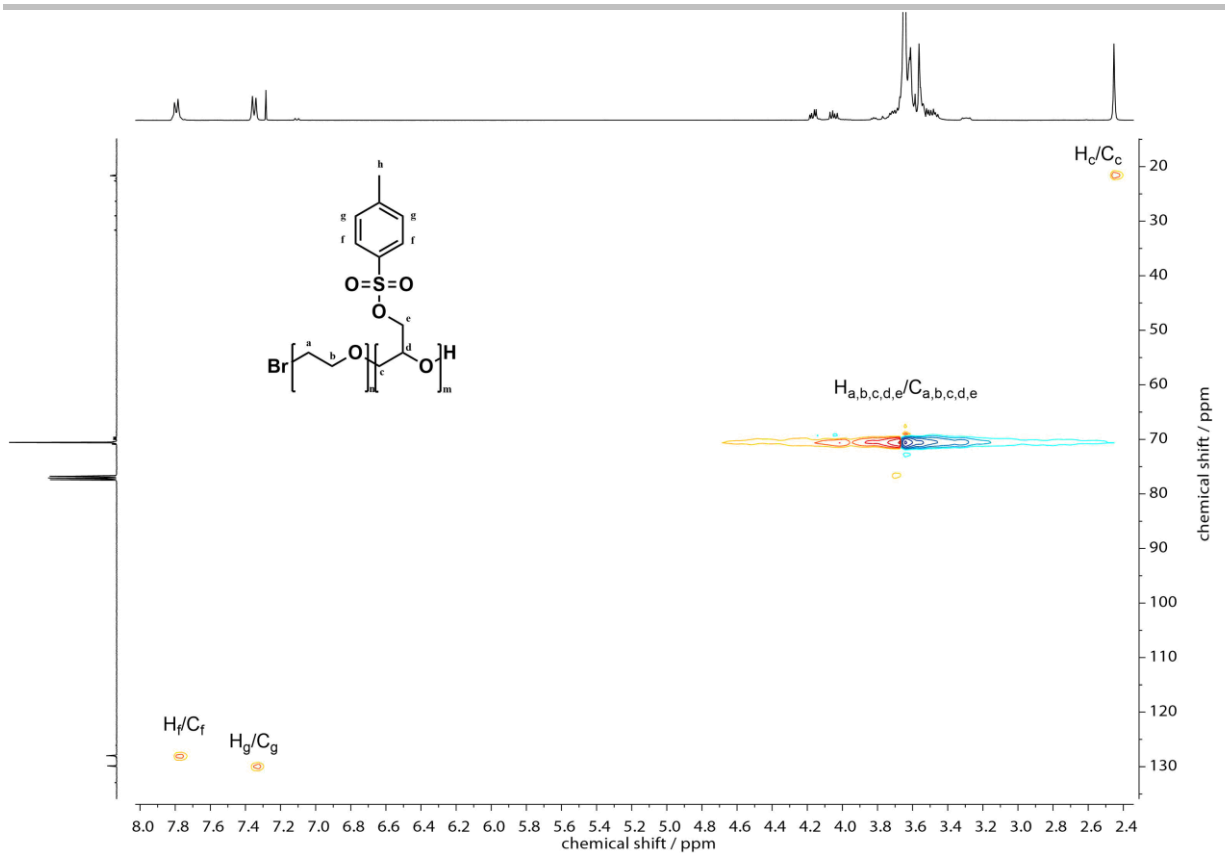


Figure S7. HSQC NMR spectrum ($CDCl_3$) of $P(EO_{0.92}$-co-$GlyTs_{0.08})$.

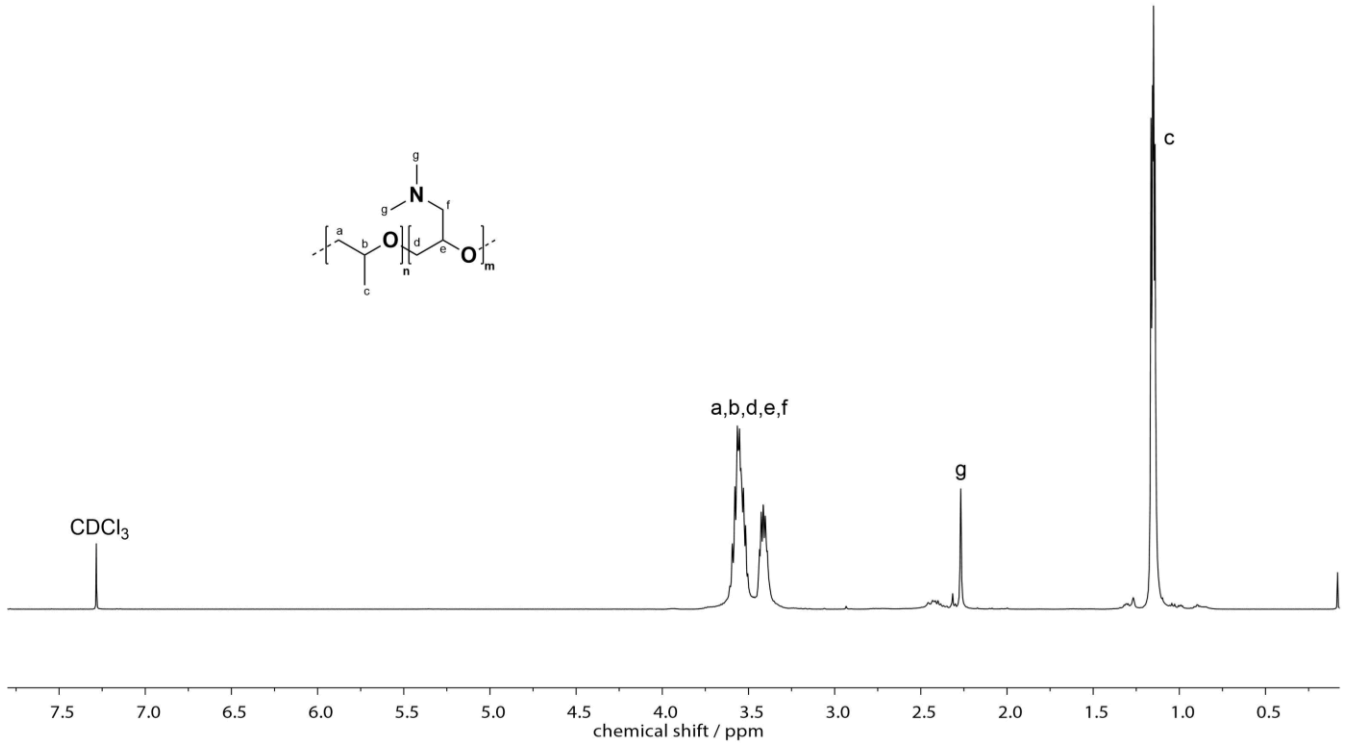


Figure S8. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of dimethylamine substituted $P(PO_{0.92}$-co-$GlyTs_{0.08})$. The signals assigned to the tosylate-moiety have disappeared, and the protons of the dimethylamine-moiety can be observed.

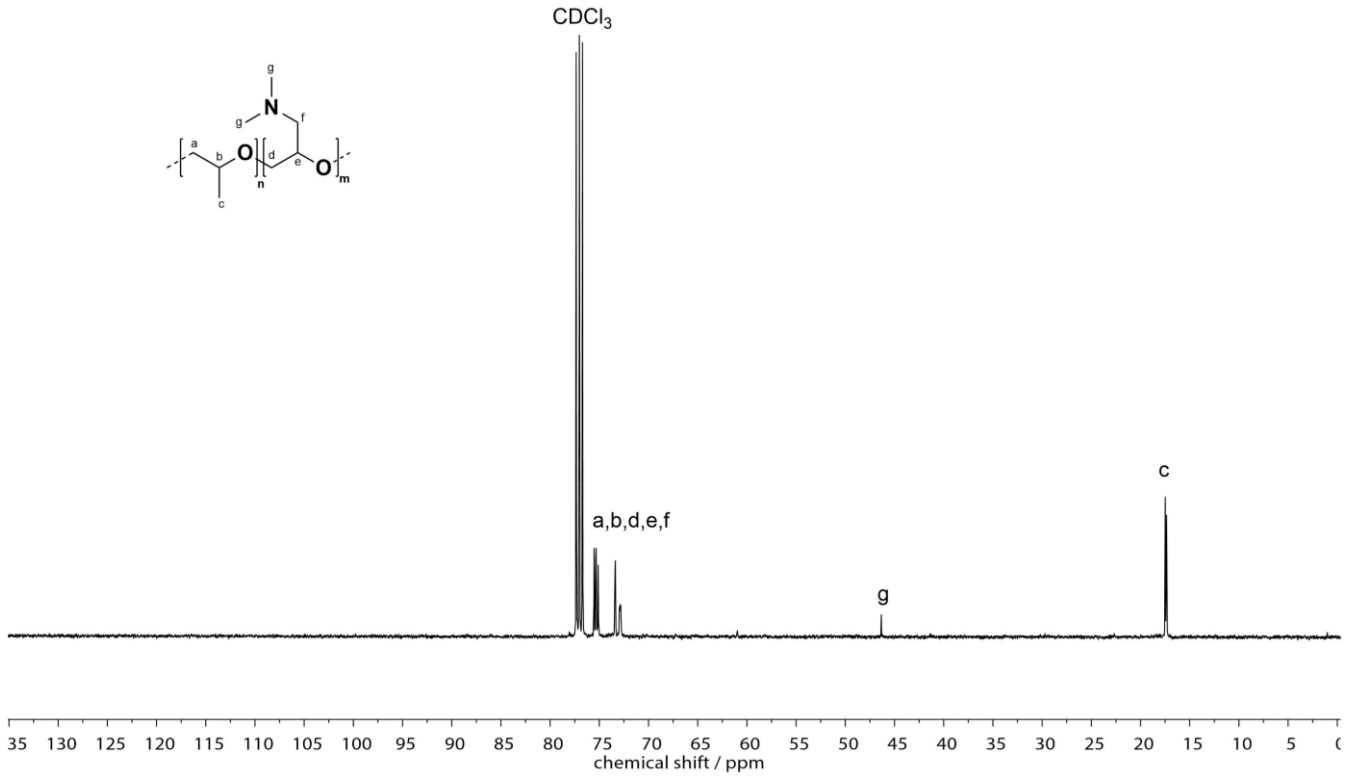


Figure S9. ^{13}C-NMR (100 MHz, $CDCl_3$) of $P(PO_{0.92}\text{-co-}GlyTs_{0.08})$ after quantitative functionalization with dimethylamine.

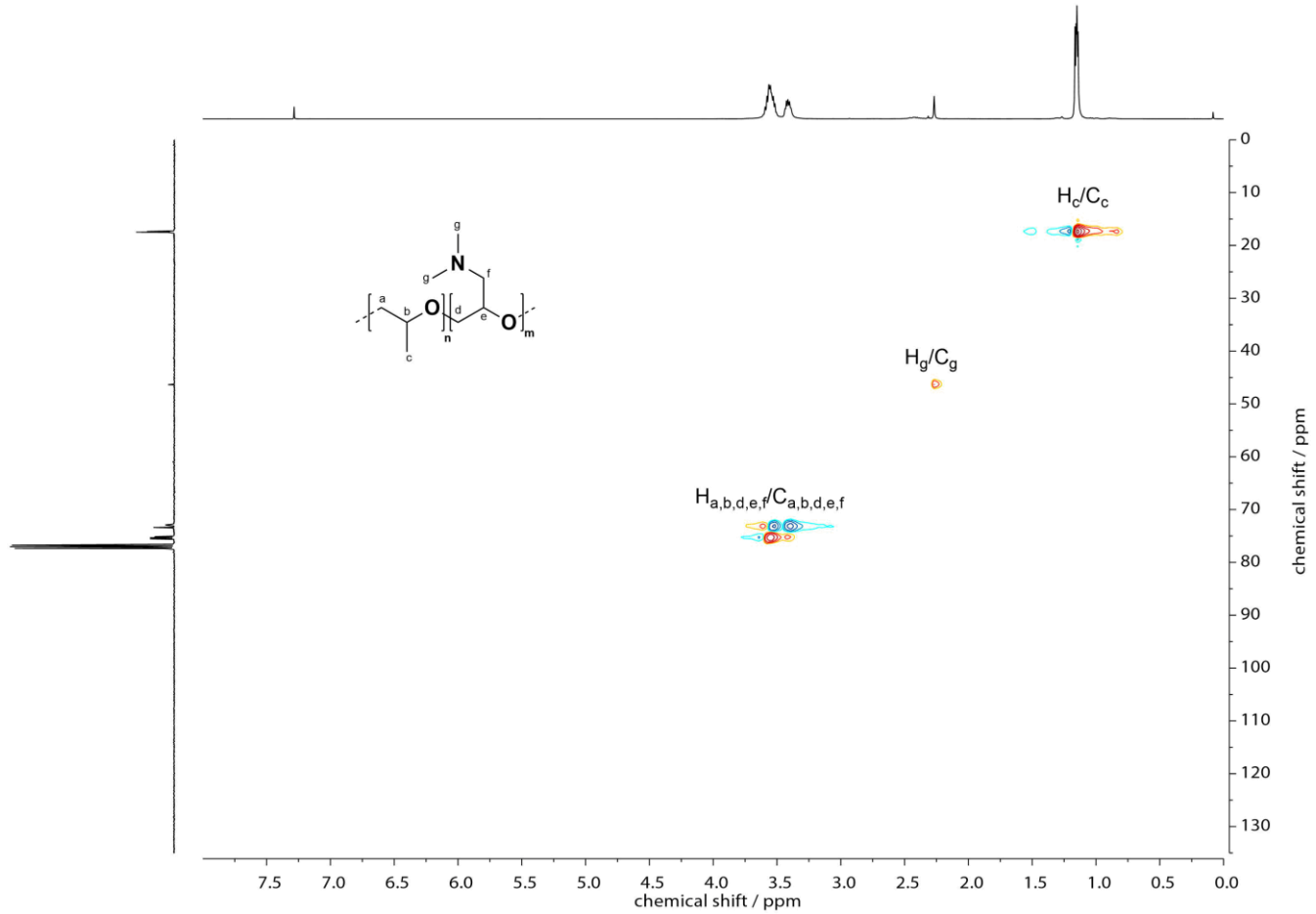


Figure S10. HSQC NMR spectrum ($CDCl_3$) of $P(PO_{0.92}\text{-co-}GlyTs_{0.08})$ after quantitative functionalization with dimethylamine.

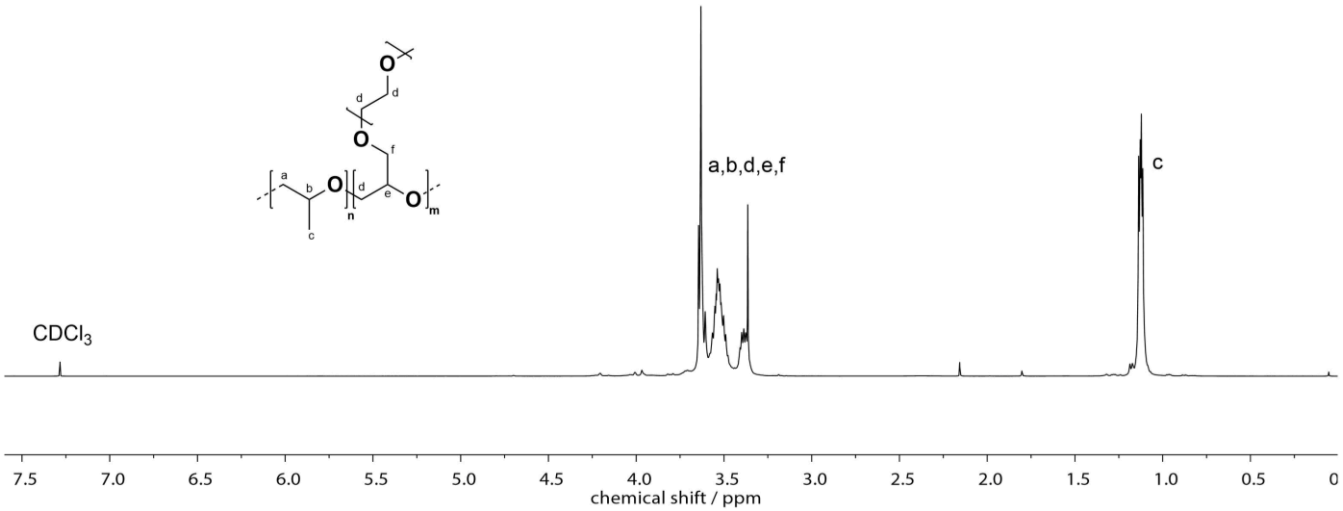


Figure S11. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of $P(PO_{0.92}\text{-co-}GlyTs_{0.08})$ obtained after quantitative functionalization with $mPEG_{500}$-OK.

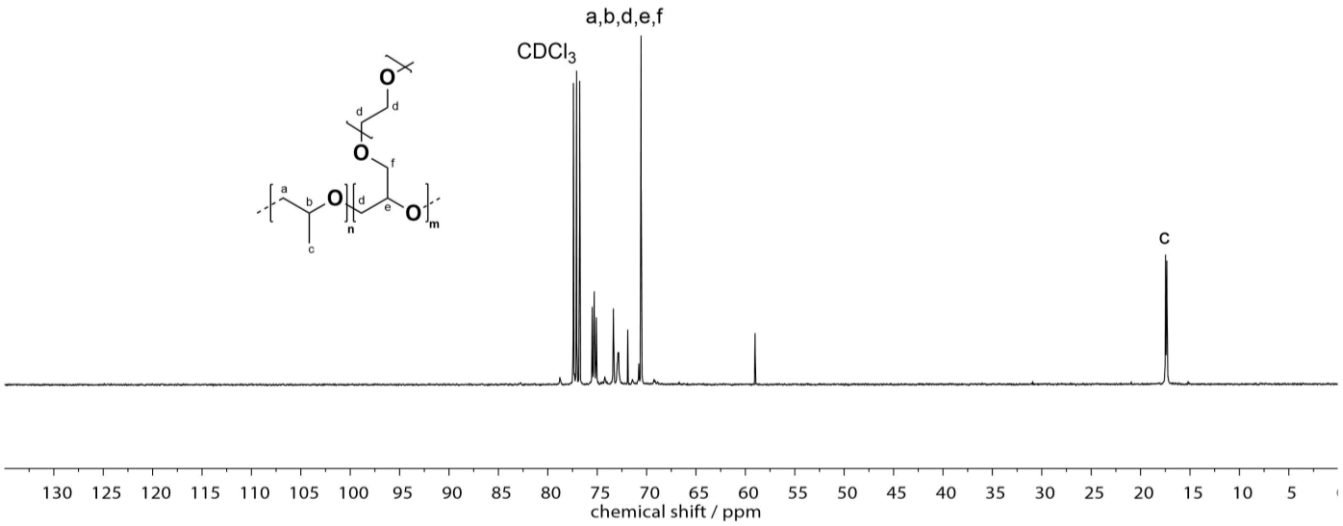


Figure S12. ^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of $P(PO_{0.92}\text{-co-}GlyTs_{0.08})$ after quantitative functionalization with $mPEG_{500}$-OK.

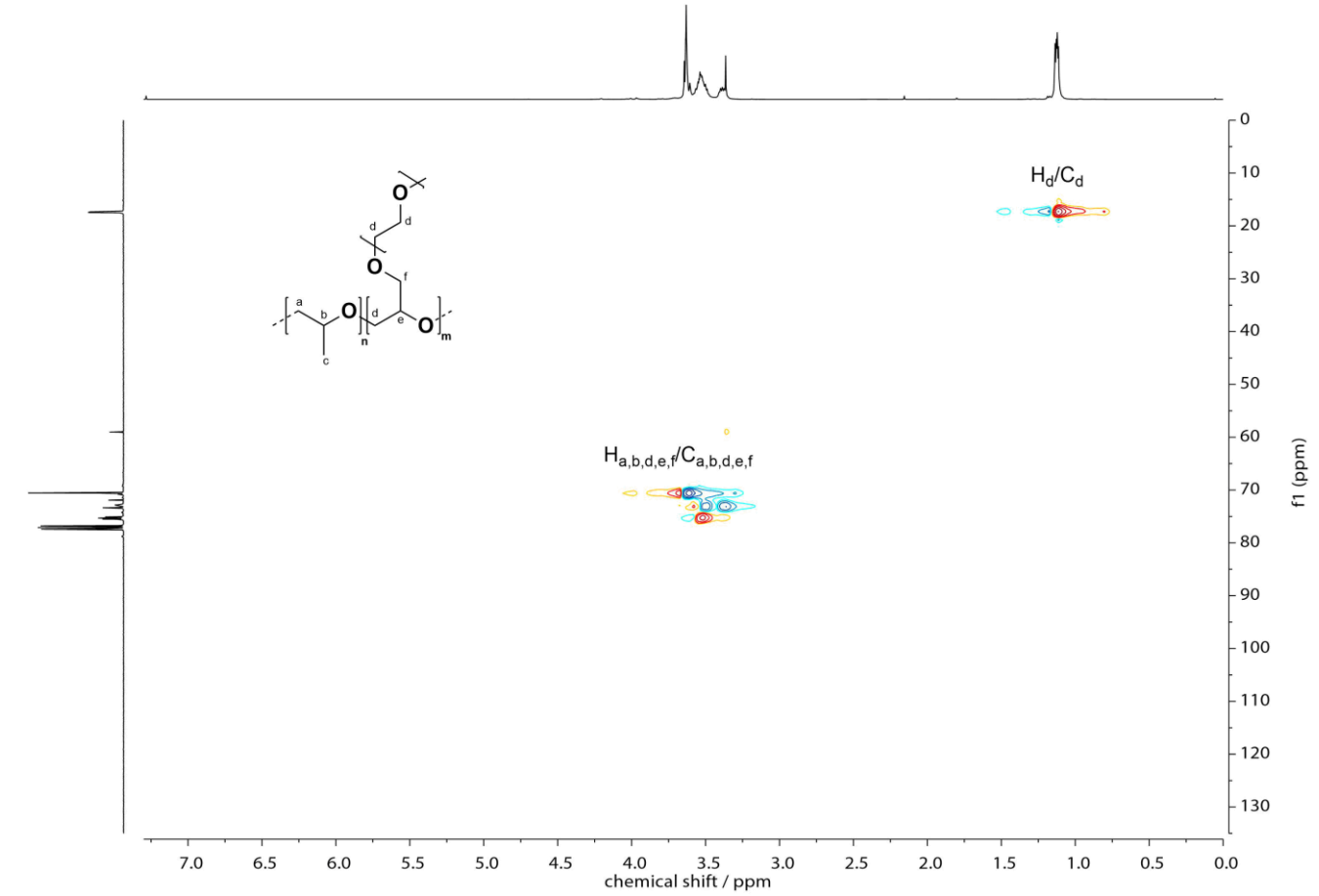


Figure S13. HSQC NMR spectrum ($CDCl_3$) of $P(PO_{0.92}$-co-$GlyTs_{0.08})$ after quantitative functionalization with $mPEG_{500}$-OK.

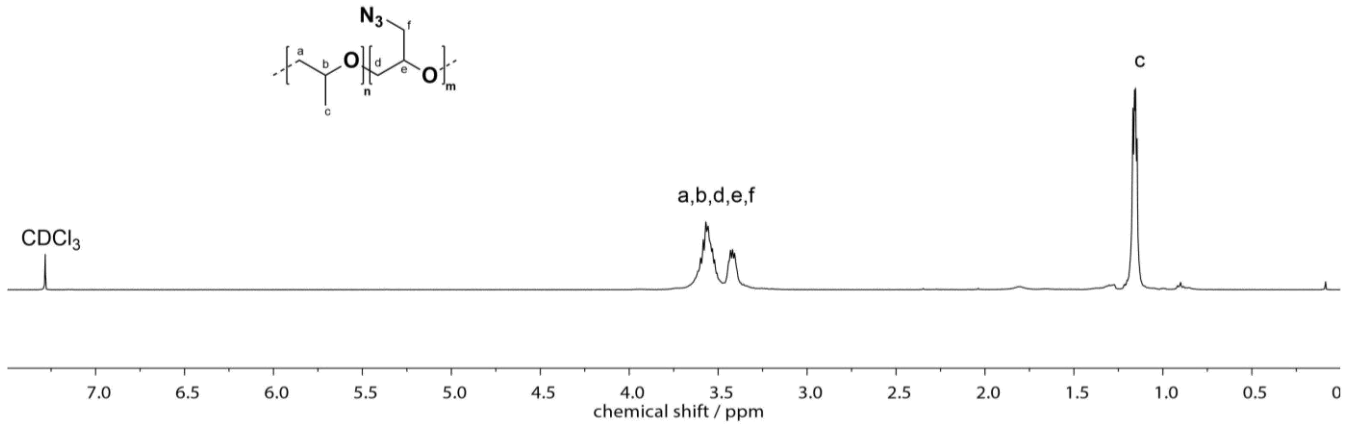


Figure S14. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of $P(PO_{0,92}$-co-$GlyTs_{0.08})$ after quantitative functionalization with NaN_3.

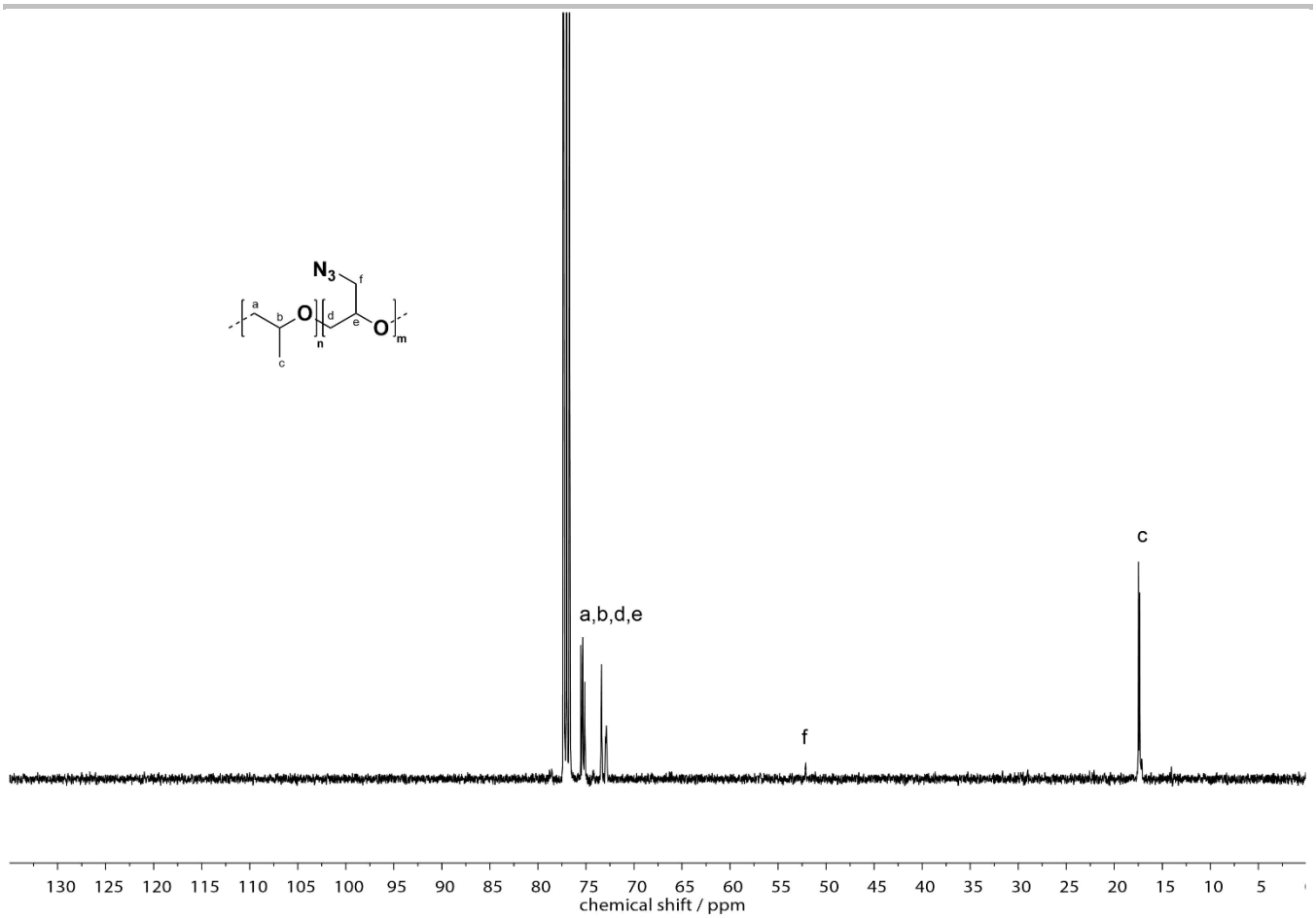


Figure S15. ^{13}C-NMR (100 MHz, $CDCl_3$) of P($PO_{0.92}$-co-Gly$Ts_{0.08}$) after quantitative functionalization with NaN_3.

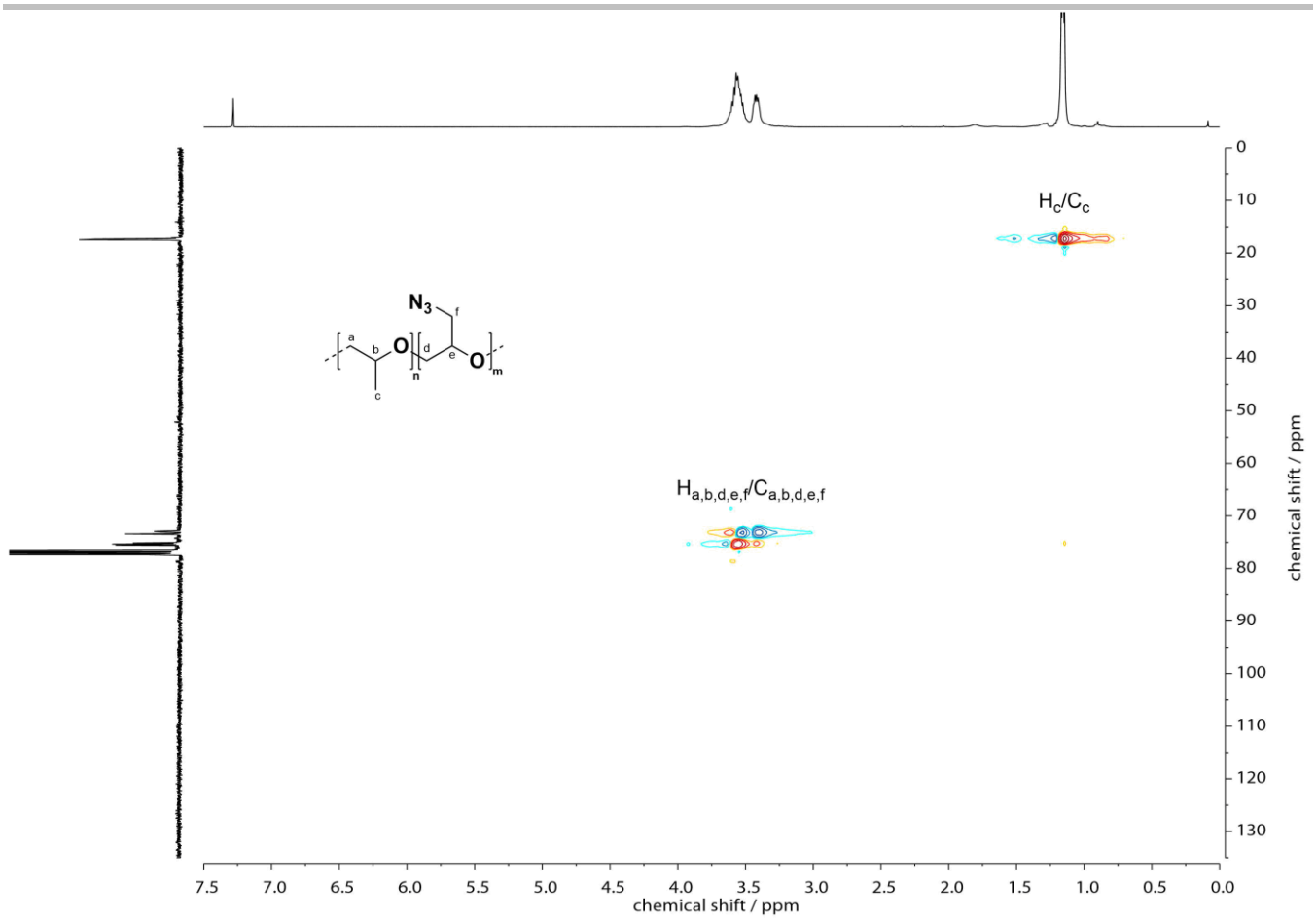


Figure S16. HSQC NMR spectrum ($CDCl_3$) of $P(PO_{0.92}$-co-$GlyTs_{0.08})$ after quantitative functionalization with NaN_3.

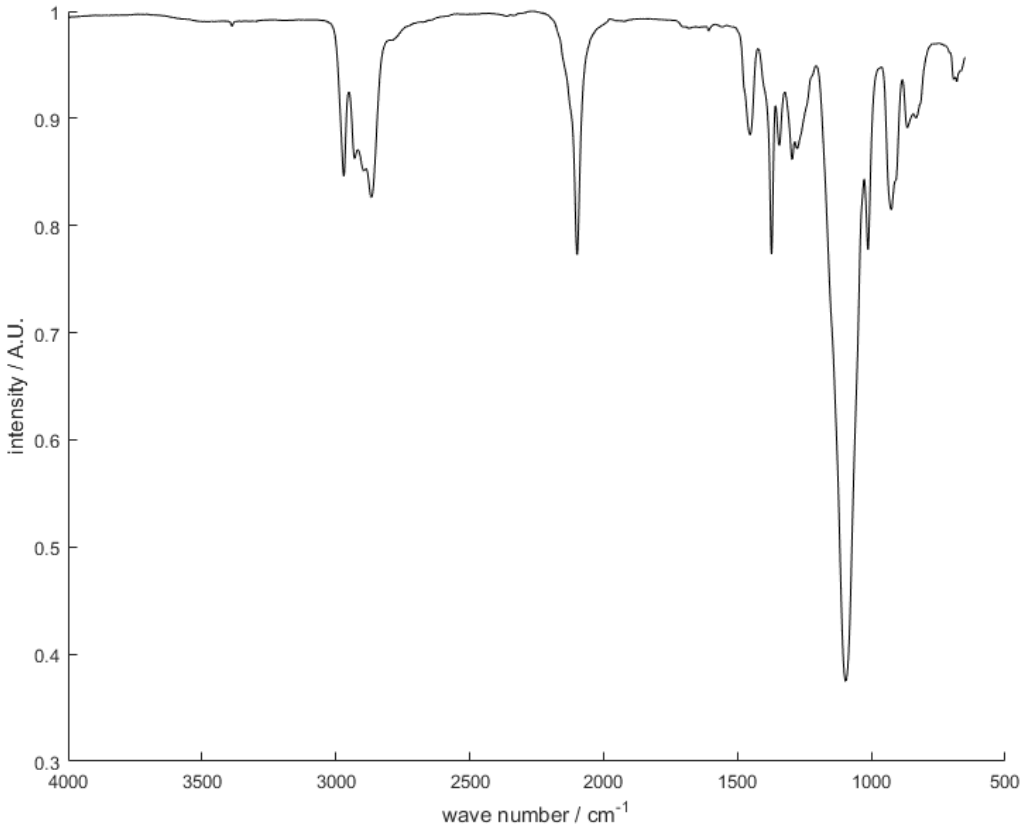


Figure S17. IR spectrum (ATR) of P($PO_{0.92}$-co-$GlyTs_{0.08}$) after quantitative functionalization with NaN_3. The characteristic azide peak is clearly visible (2100 cm^{-1}).

D) ^{1}H-NMR kinetics: Fits and further information

Further details on the way reactivity ratios were determined are given in a work of Blankenburg *et al*[1]. The data was gathered from the online ^{1}H NMR kinetic studies described previously.

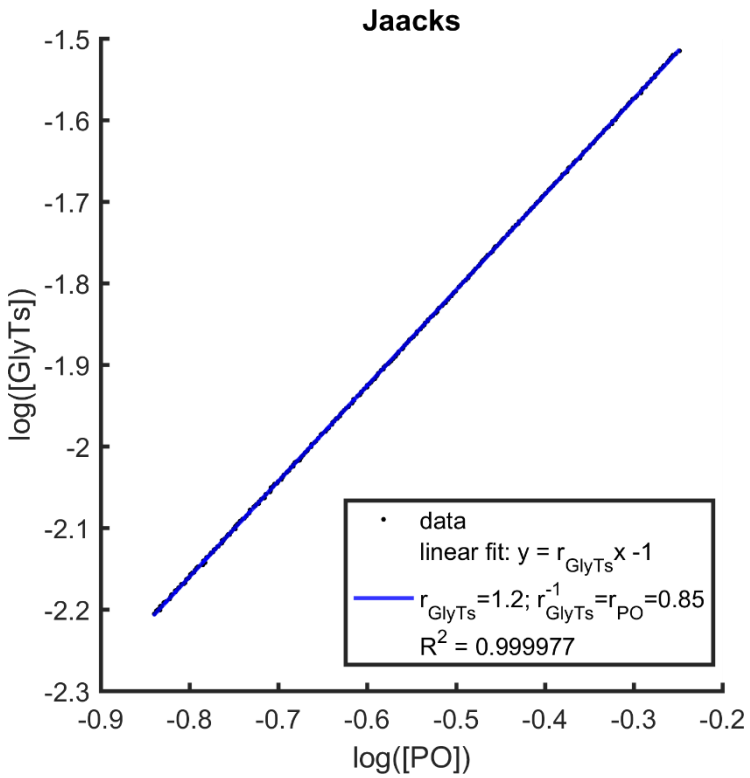


Figure S18. Jaacks fit of in-situ NMR data for an assumed ideal copolymerization of PO and GlyTs[2].

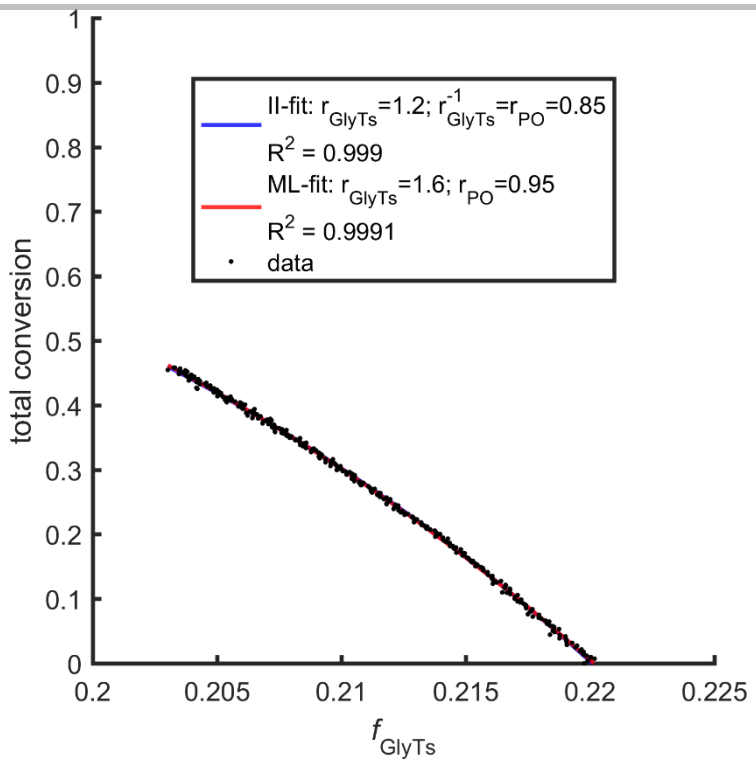


Figure S19. Comparison of the Ideal-Integrated (II) fit with the Meyer-Lowry (ML) fit for the in-situ NMR data of copolymerization of PO and GlyTs[1].

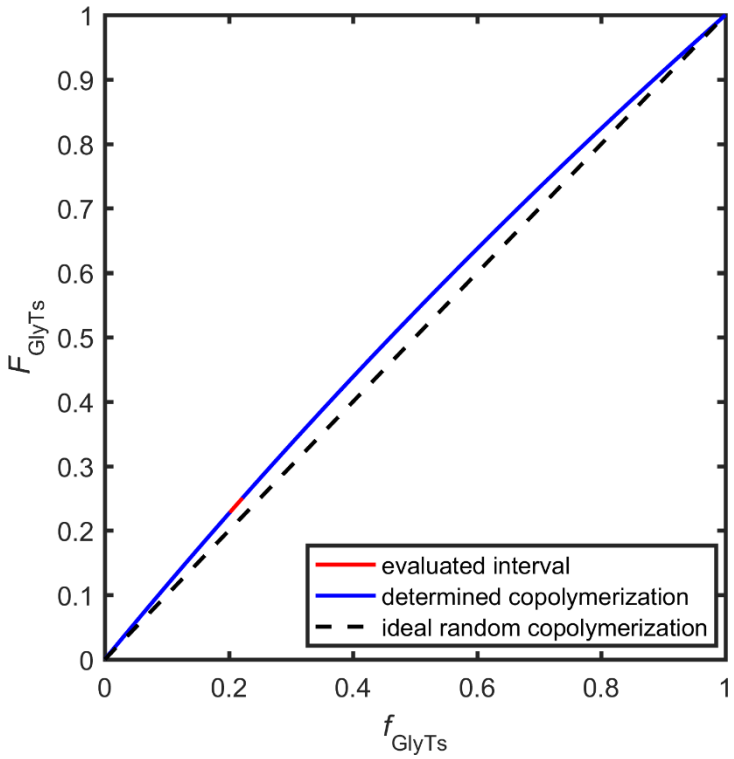


Figure S20: Copolymerization diagram of PO and GlyTs.

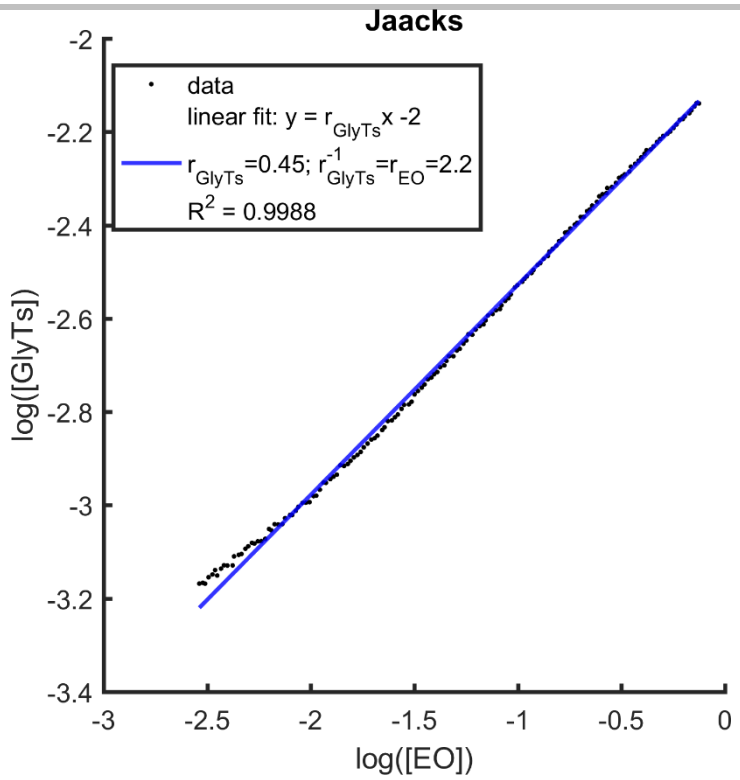


Figure S21. Jaacks fit of in-situ NMR data for an assumed ideal copolymerization of EO and GlyTs[2].

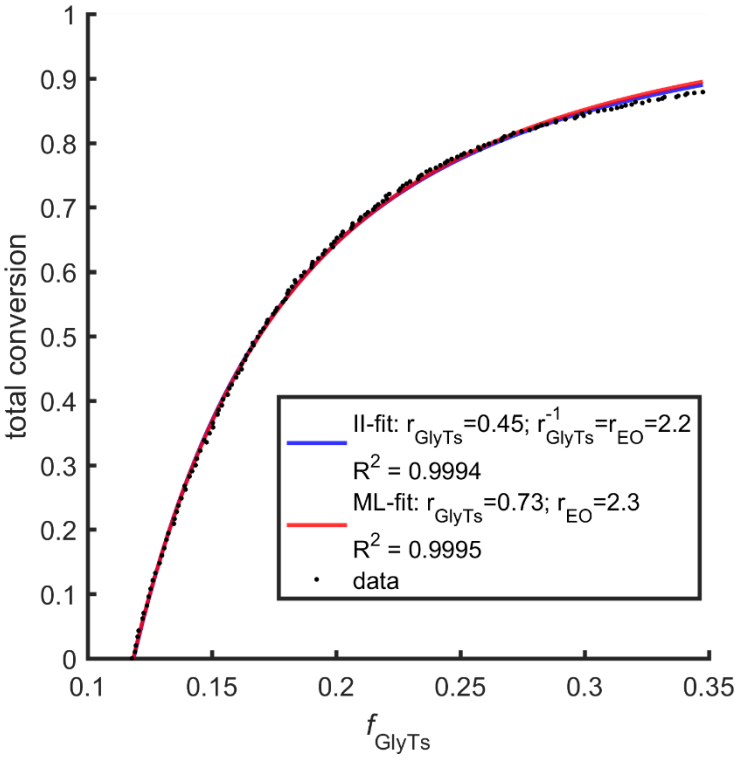


Figure S22. Comparison of the Ideal-Integrated (II) fit with the Meyer-Lowry (ML) fit for the in-situ NMR data for the copolymerization of EO and GlyTs[1][3].

E) Maldi-ToF spectrometry

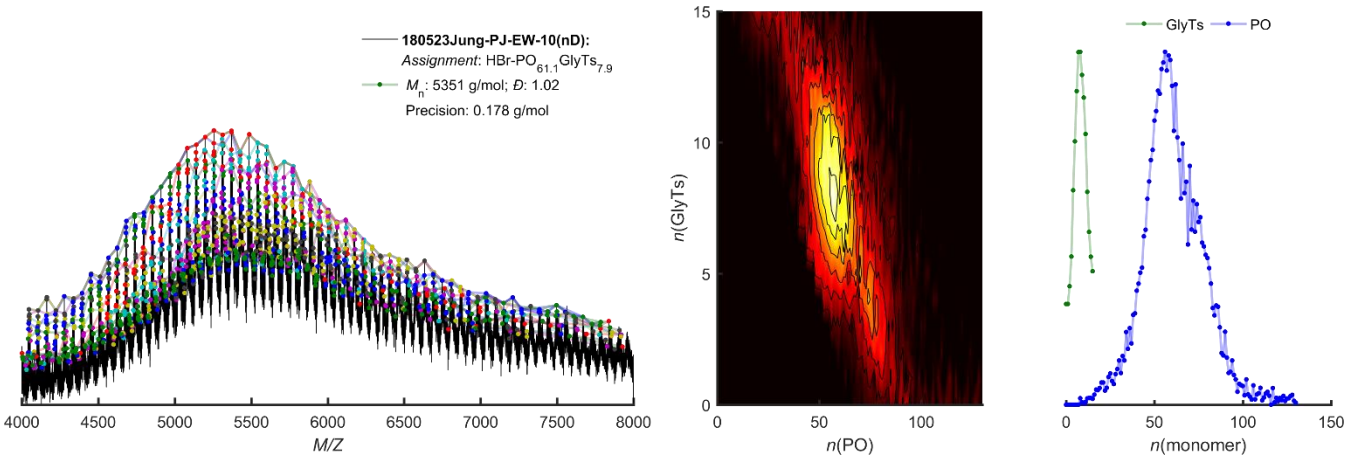


Figure S23. Maldi-ToF spectra of P(PO-*co*-GlyTs) with assignment of the copolymer chains.

References

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Author Contributions

Philipp Jung (lead) developed and investigated the copolymerization of GlyTs with EO or PO, respectively, gathered the analytical data, performed the post functionalizations and wrote the original draft. Arthur D. Ziegler (supporting) provided the monomer and was involved in developing the project. Jan Blankenburg (supporting) evaluated the data gathered from the ^{1}H-NMR kinetic studies, determined the reactivity ratios of the monomers and calculated the corresponding copolymer structure. Holger Frey was responsible for project administration, funding acquisition and writing of the original draft.