Supporting information

Poly(2-isopropenyl-2-oxazoline) - A Structural Analogue to Poly(vinyl azlactone) with Orthogonal Reactivity

Meike N. Leiske,[a,†] *Ayaat M. Mahmoud,*[a,†] *Nicole Warne,*[a] *Jeroen A. C. M. Goos,*[a,b] *Sagrario Pascual,*[c] *Véronique Montembault,*[c] *Laurent Fontaine,*[c] *Thomas P. Davis,*[a,d] *Michael R. Whittaker,*[a] *and Kristian Kempe*[a,e,*]

[a]ARC Centre of Excellence in Convergent Bio-Nano Science & Technology, and Drug Delivery, Disposition and Dynamics, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, VIC 3052, Australia

[b]Departments of Clinical Neuroscience, Radiopharmacy and Oncology & Pathology, Karolinska Institute, Stockholm, Sweden
MedTechLabs, Stockholm, Sweden

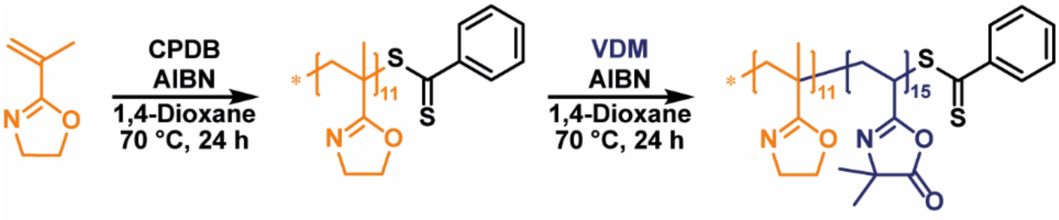
[c]Institut des Molécules et Matériaux du Mans (IMMM), UMR 6283 CNRS – Le Mans Université, Av. O. Messiaen, 72085 Le Mans Cedex 9, France

[d]Centre for Advanced Imaging (CAI) and Australian Institute for Bioengineering and Nanotechnology, ARC Centre of Excellence in Convergent Bio-Nano Science and Technology and ARC Training Centre for Innovation in Biomedical Imaging Technology, The University of Queensland, St. Lucia, QLD 4072, Australia

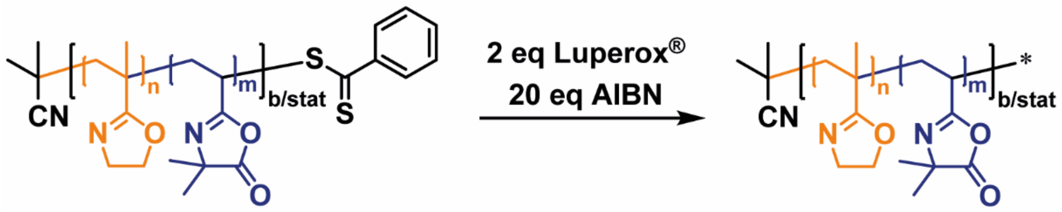
[e]Materials Science and Engineering, Monash University, Clayton, VIC 3800, Australia

†M. N. L. and A. M. M. contributed equally to this study.

*Correspondence to: kristian.kempe@monash.edu



Scheme S1. Preparation of block copolymers.



Scheme S2. Reaction conditions used for complete CTA removal. Polymers were reacted with 2 eq. Luperox® and 20 eq. AIBN in toluene at 80 °C for 2.5 h.

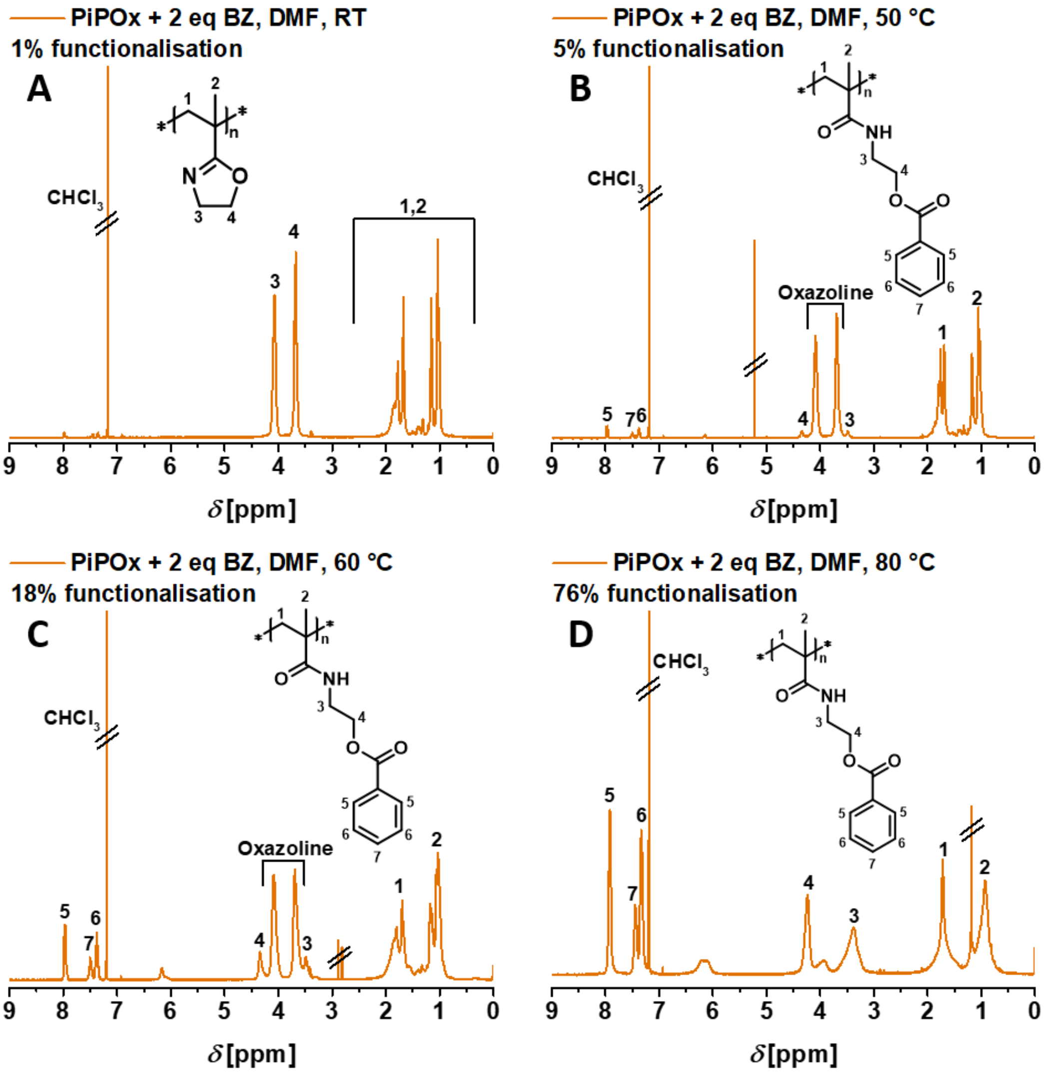


Figure S1. Characterisation of BZ-functionalised PiPOx homopolymers by ^{1}H NMR (400 MHz) in $CDCl_3$. Polymers were reacted in DMF for 24 h with 2 eq. BZ at various temperatures. (A) RT. (B) 50 °C. (C) 60 °C. (D) 80 °C.

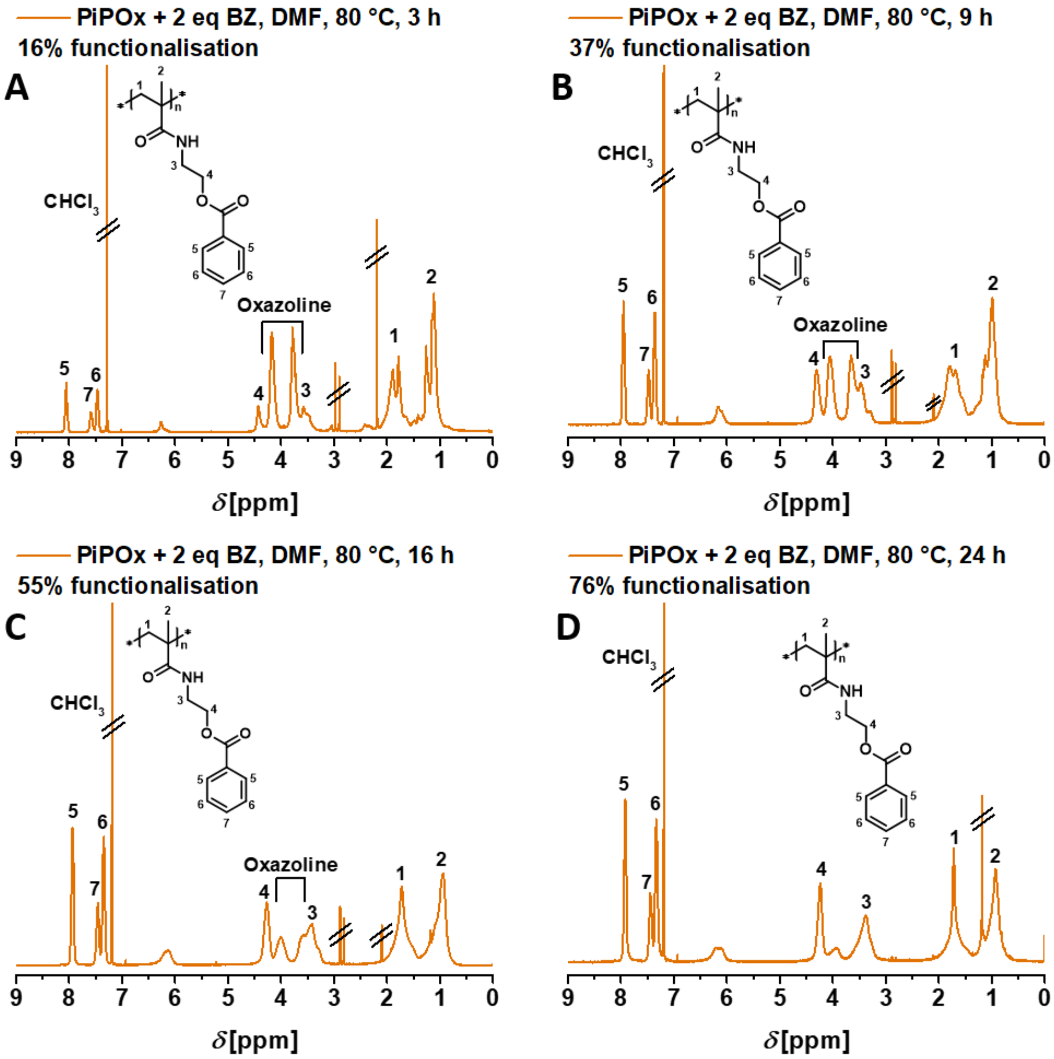


Figure S2. Characterisation of BZ-functionalised PiPOx homopolymers by ^{1}H NMR (400 MHz) in $CDCl_3$. Polymers were reacted at 80 °C in DMF with 2 eq. BZ for indicated times. (A) 3 h. (B) 9 h. (C) 16 h. (D) 24 h.

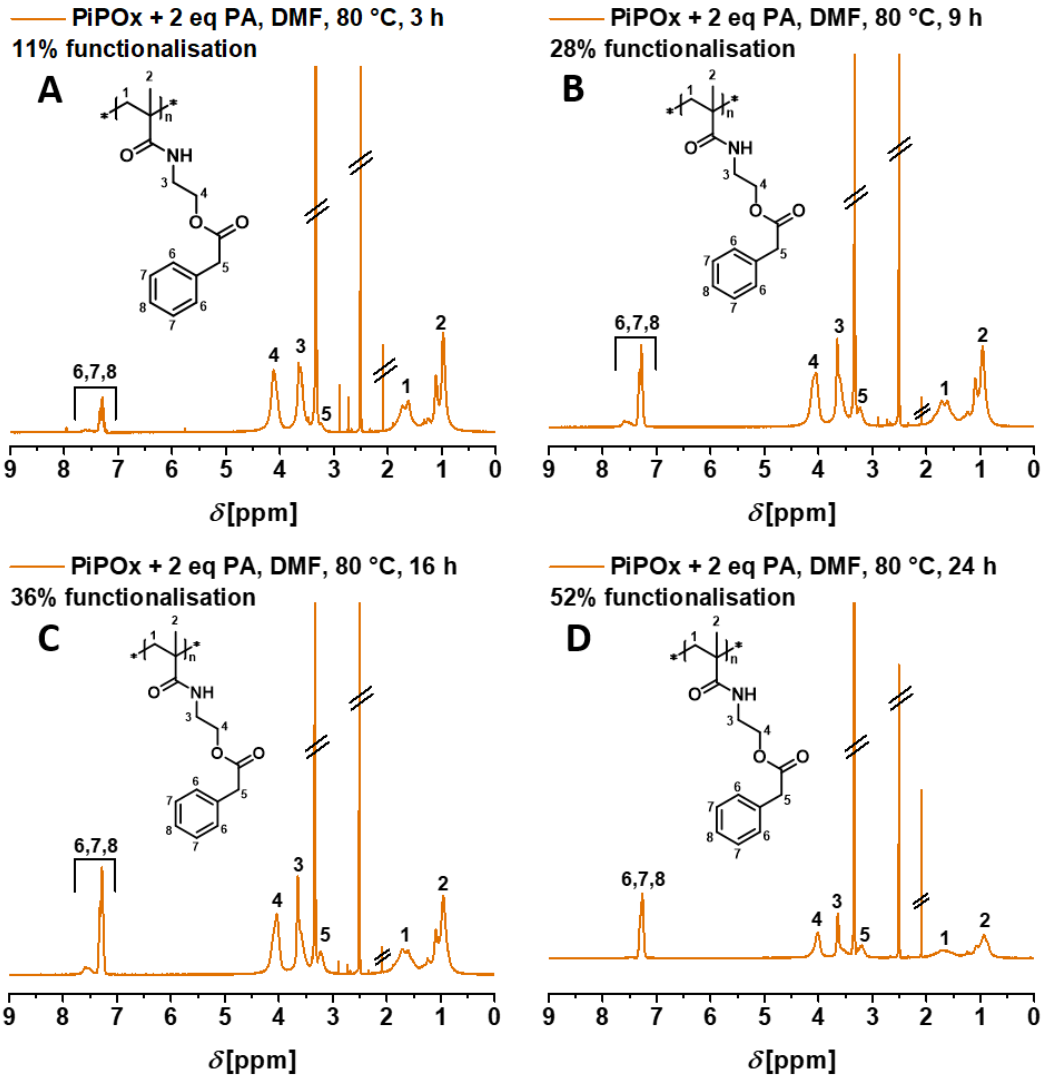


Figure S3. Characterisation of PA-functionalised PiPOx homopolymers by ^{1}H NMR (400 MHz) in DMSO-d_6. Polymers were reacted at 80 °C in DMF with 2 eq. PA for indicated times. (A) 3 h. (B) 9 h. (C) 16 h. (D) 24 h.

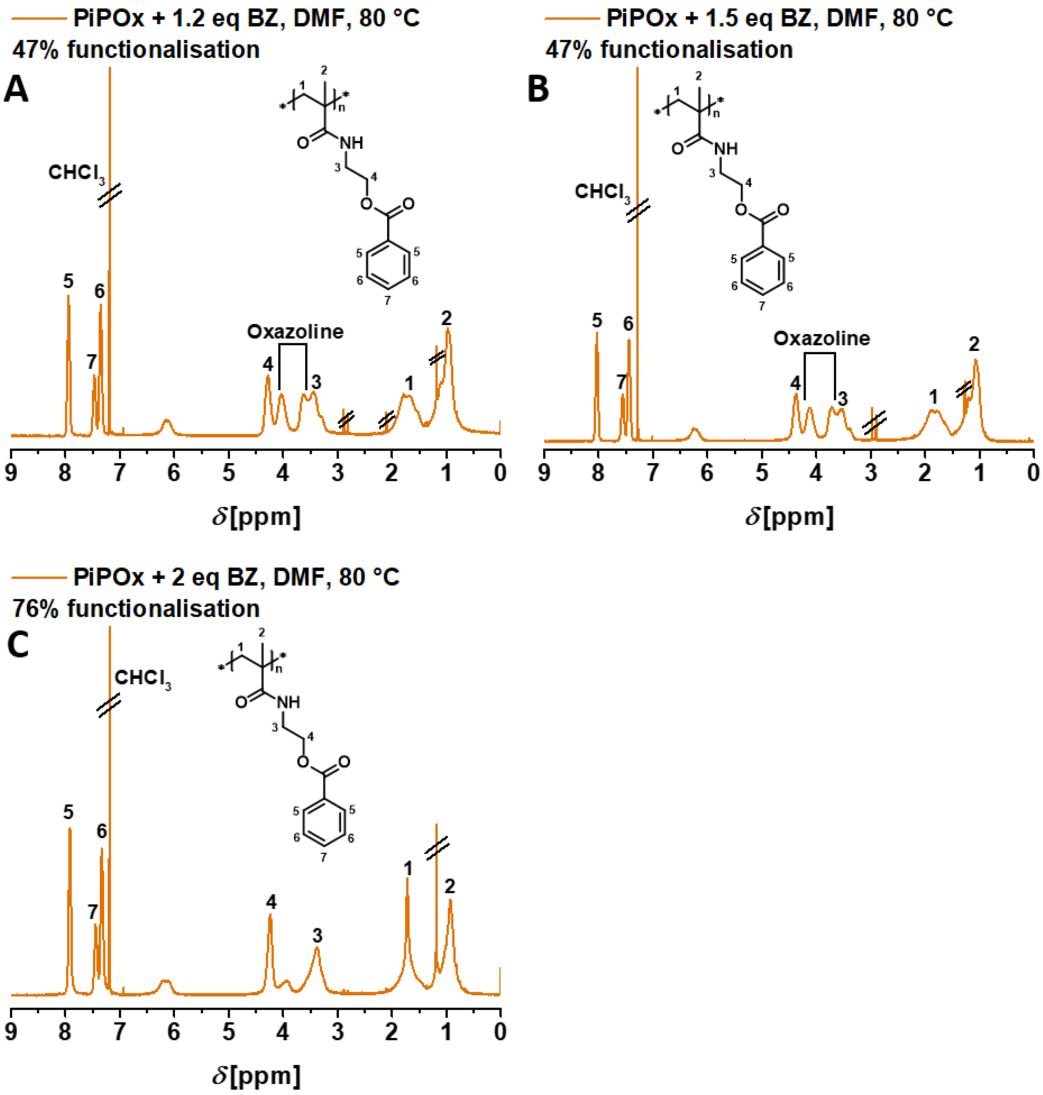


Figure S4. Characterisation of BZ-functionalised PiPOx homopolymers by ^{1}H NMR (400 MHz) in $CDCl_3$. Polymers were reacted at 80 °C in DMF for 24 h with indicated amounts of BZ. (A) 1.2 eq. (B) 1.5 eq. (C) 2.0 eq.

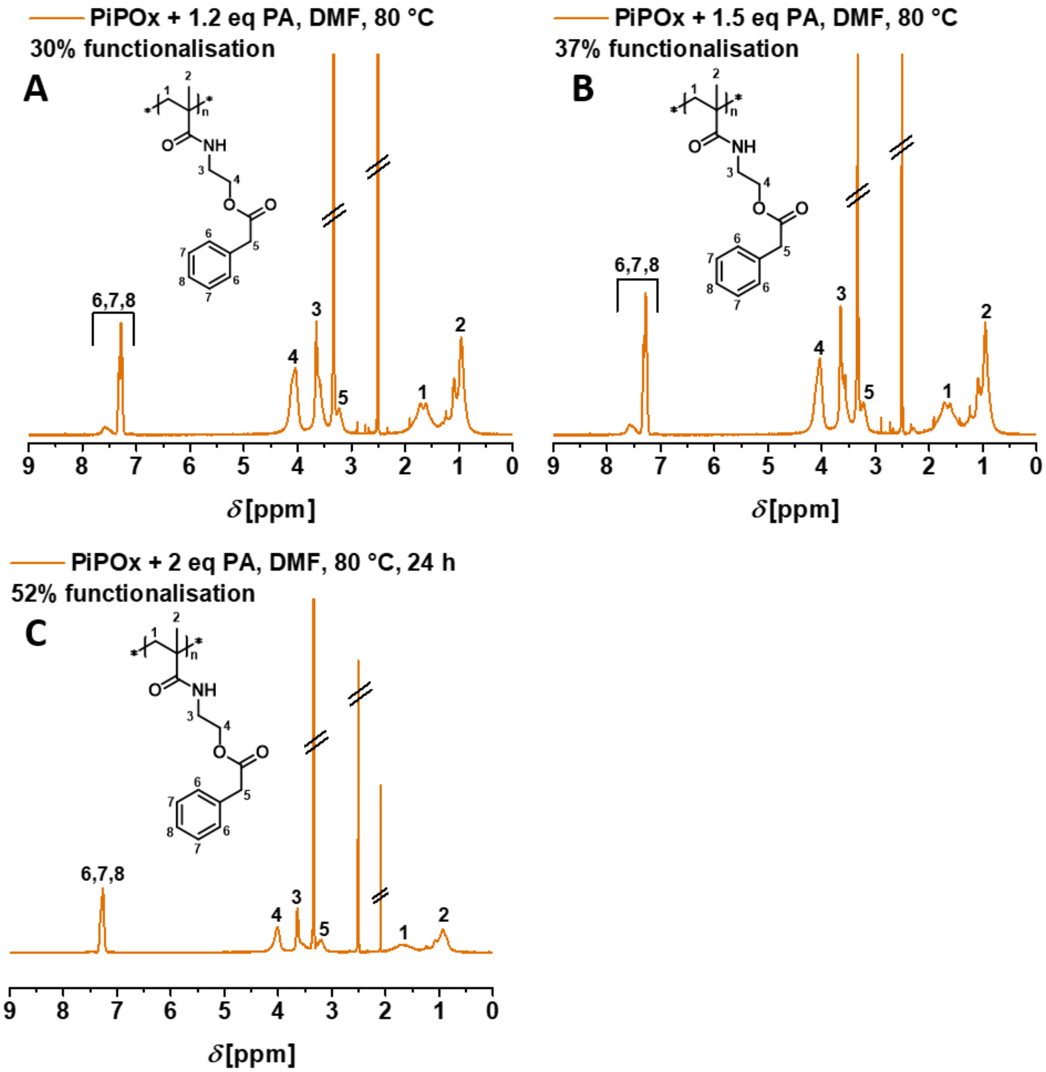


Figure S5. Characterisation of PA-functionalised PiPOx homopolymers by ^{1}H NMR (400 MHz) in DMSO-d_6. Polymers were reacted at 80 °C in DMF for 24 h with indicated amounts of PA. (A) 1.2 eq. (B) 1.5 eq. (C) 2.0 eq.

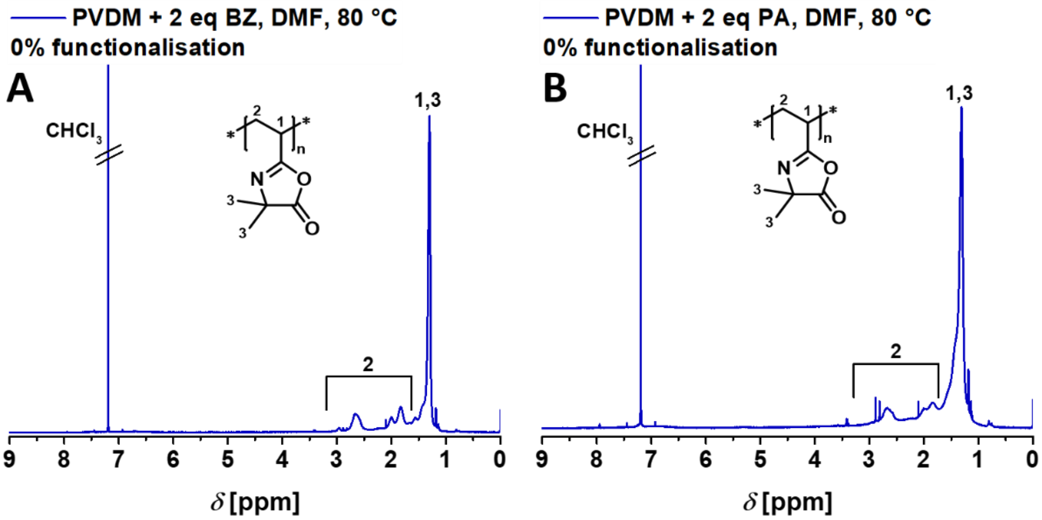


Figure S6. Characterisation of the reaction of PVDM homopolymers with BZ by ^{1}H NMR (400 MHz) in $CDCl_3$. Polymers were reacted in DMF for 24 h with 2 eq. BZ (A) or PA (B) at 80 °C.

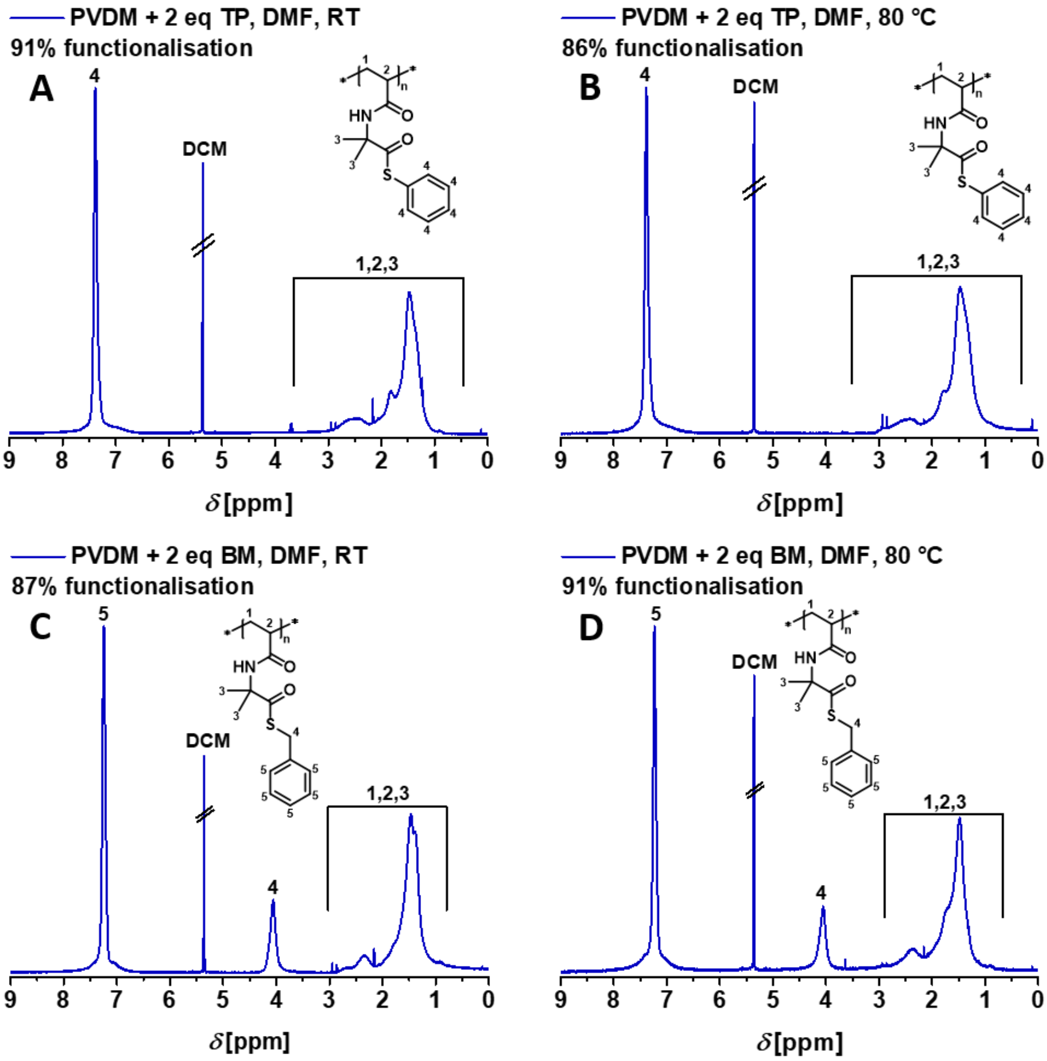


Figure S7. Characterisation of BM- and TP-functionalised PVDM homopolymers by ^{1}H NMR (400 MHz) in CD_2Cl_2. Polymers were reacted in DMF for 24 h with 2 eq. BM or TP at indicated temperature. (A) TP, RT. (B) TP, 80 °C. (C) BM, RT. (D) BM, 80 °C.

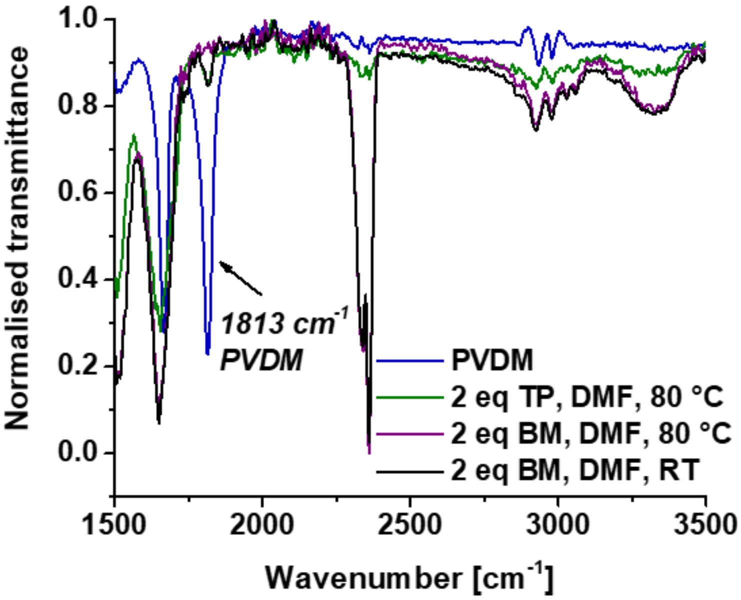


Figure S8. Characterisation of the reaction of PVDM homopolymers with the thiolated aromatic compounds TP and BM by FT-IR. Polymers were reacted in DMF for 24 h with 2 eq. BM or TP at indicated temperatures.

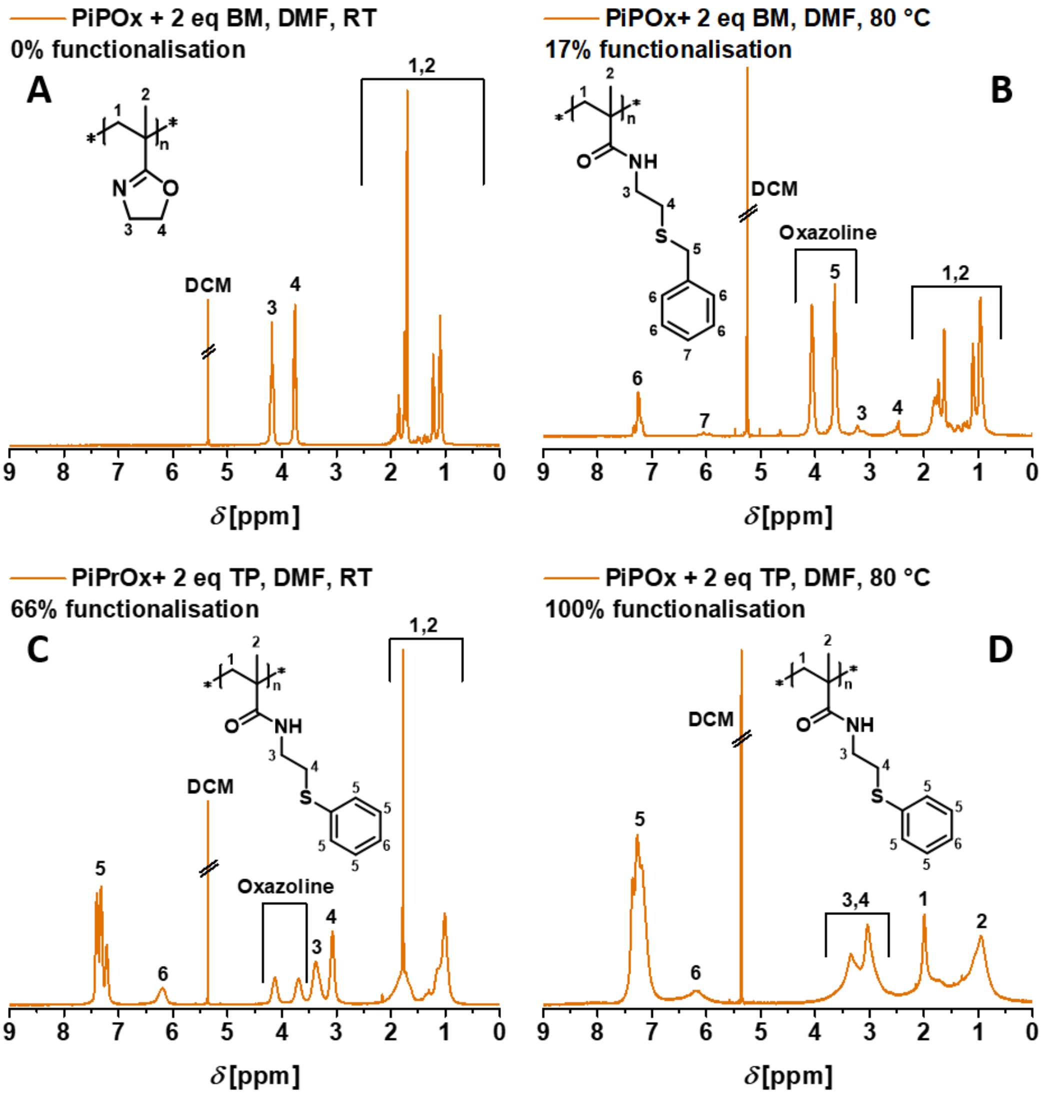


Figure S9. Characterisation of BM- and TP-functionalised PiPOx homopolymers by ^{1}H NMR (400 MHz) in CD$_2$Cl$_2$. Polymers were reacted in DMF for 24 h with 2 eq. BM or TP at indicated temperature. (A) BM, RT. (B) BM, 80 °C. (C) TP, RT. (D) TP, 80 °C.

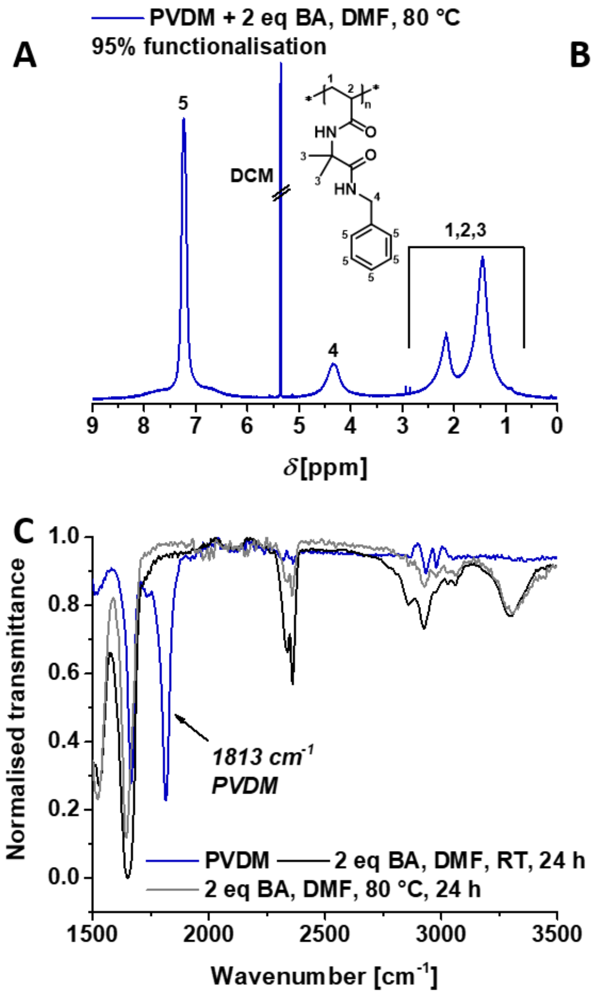


Figure S10. Characterisation of BA-functionalised PVDM homopolymers. Polymers were reacted in DMF for 24 h with 2 eq. BA at indicated temperatures. (A) and (B) ^{1}H NMR (400 MHz) in CD_2Cl_2. (C) FT-IR.

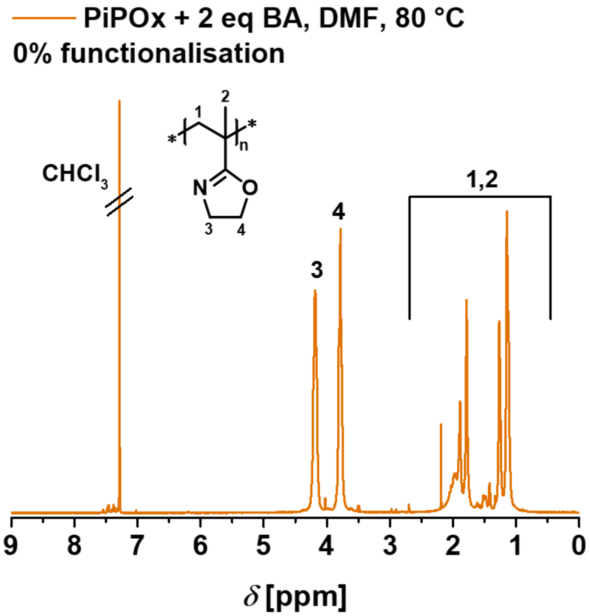


Figure S11. Characterisation of the reaction of PiPOx homopolymers with BA by ^{1}H NMR (400 MHz) in $CDCl_3$. Polymers were reacted in DMF for 24 h with 2 eq. BA at 80 °C.

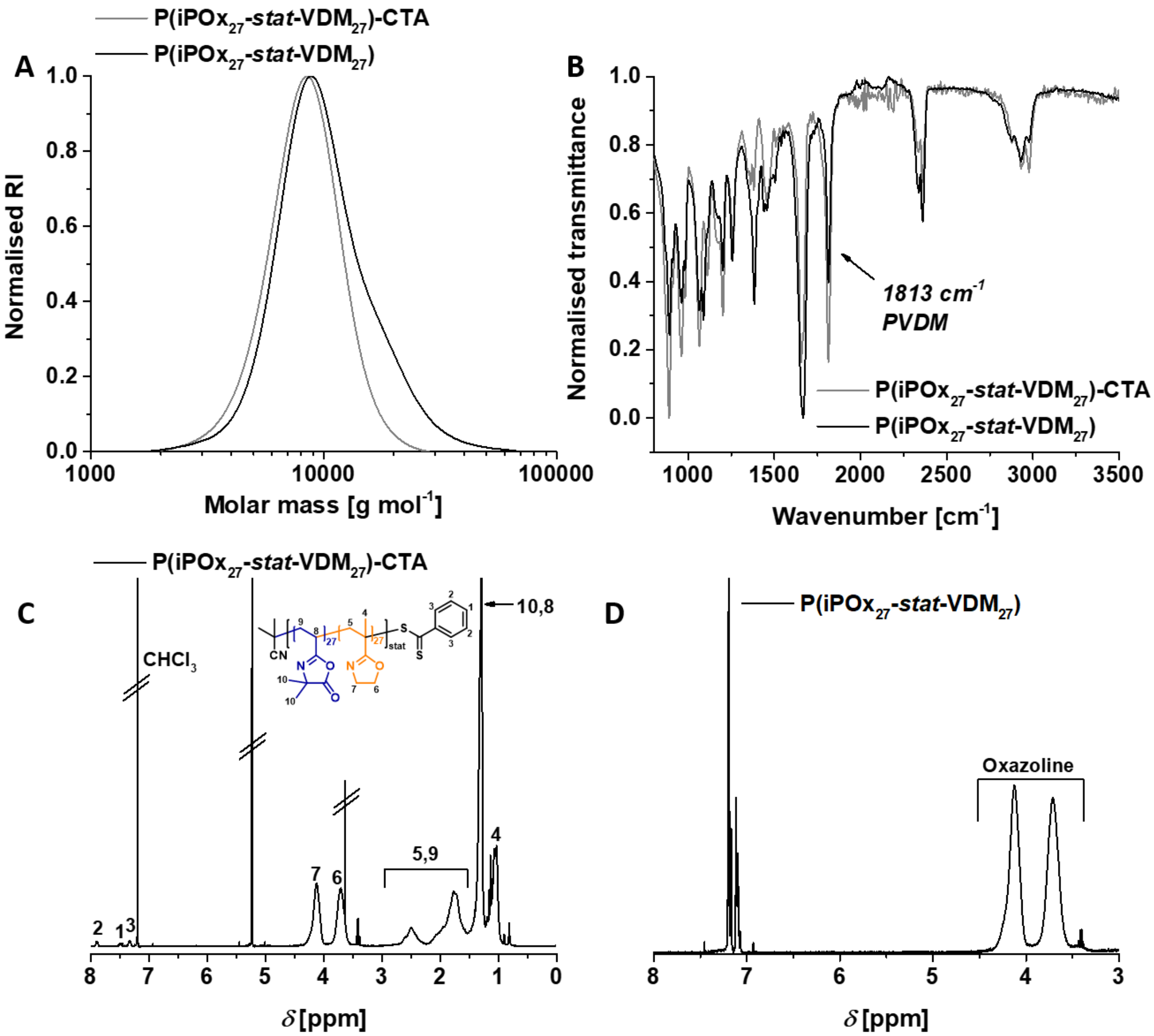


Figure S12. Characterisation of P(iPOx$_{27}$-*stat*-VDM$_{27}$) before and after end-group removal. (A) SEC (DMAc, PS-cal.). (B) FT-IR. (C) and (D) ^{1}H NMR (400 MHz) in CDCl$_3$.

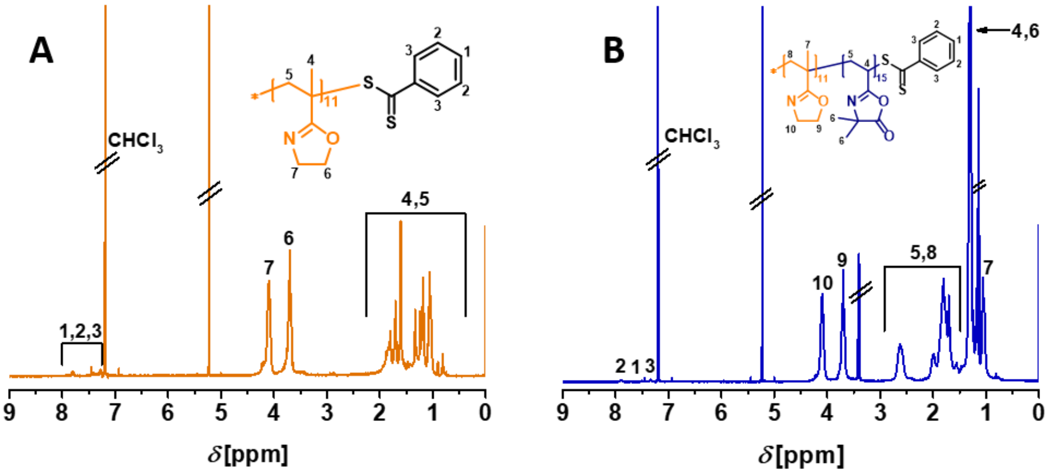


Figure S13. Characterisation of block copolymer synthesis by ^{1}H NMR (400 MHz) in $CDCl_3$. (A) PiPOx$_{11}$-CTA. (B) P(iPOx$_{11}$-*b*-VDM$_{15}$)-CTA.

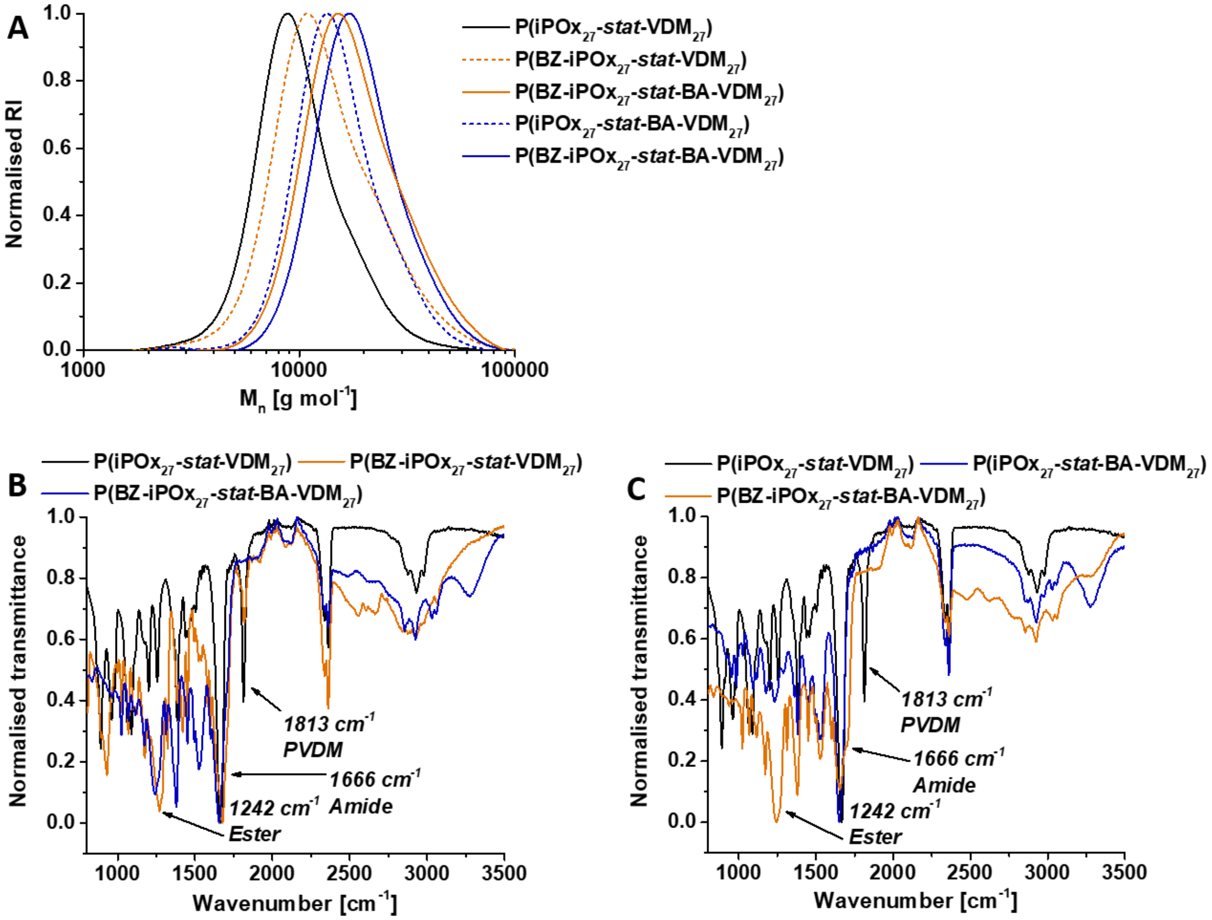


Figure S14. Characterisation of the PPM of P(iPOx$_{27}$-*stat*-VDM$_{27}$) with BA and BZ. Polymers were modified in a two-step reaction and not purified in-between. Samples were taken for characterisation by SEC to show the evolution of the molar mass and FT-IR to prove the integrity of the VDM group. (A) SEC in DMAc (PS-cal.). First reaction depicted in dashed lines, second reaction shown in solid lines. (B) and (C) FT-IR. (B) P(iPOx$_{27}$-*stat*-VDM$_{27}$) was modified with BZ in a first reaction and with BA in a second reaction. (C) P(iPOx$_{27}$-*stat*-VDM$_{27}$) was modified with BA in a first reaction and with BZ in a second reaction.

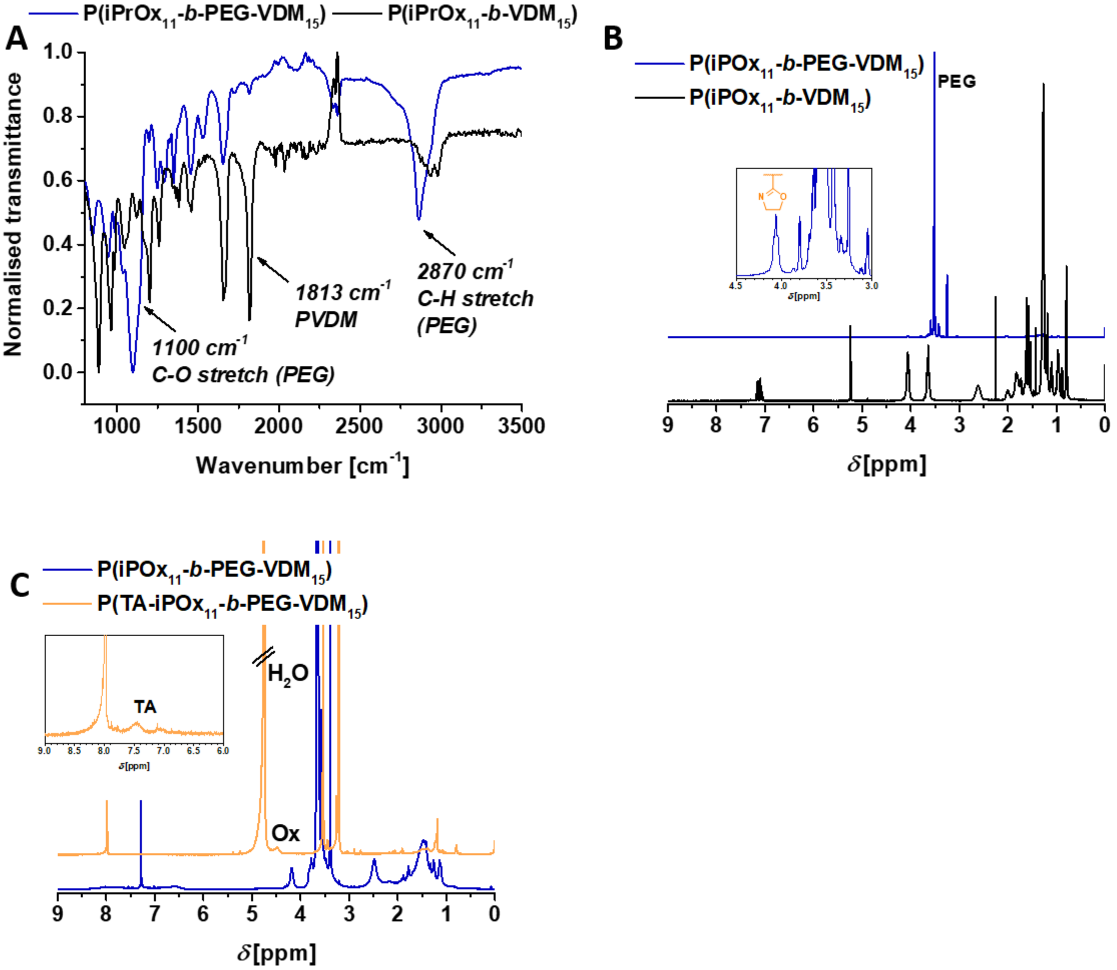


Figure S15. Characterisation of the two-step PPM of block copolymers with PEG and TA. Polymers were reacted in DMF at 80 °C for 24 h with 2 eq. PEG-NH$_2$ and TA per repeating unit. Polymers were purified in-between steps. (A) FT-IR. (B) ^{1}H NMR (400 MHz) in $CDCl_3$ (top) and CD_2Cl_2 (bottom). (C) ^{1}H NMR (400 MHz) in MeOD (top) and $CDCl_3$ (bottom).

Figure S16. Reaction of PiPOx with different amounts of TA. (A) 2 eq (4 eq). (B) 1 eq (2eq). (C) 0.5 eq (1 eq). Numbers in brackets correspond to the molar ratio of carboxylic acid to iPOx applied during the reaction.

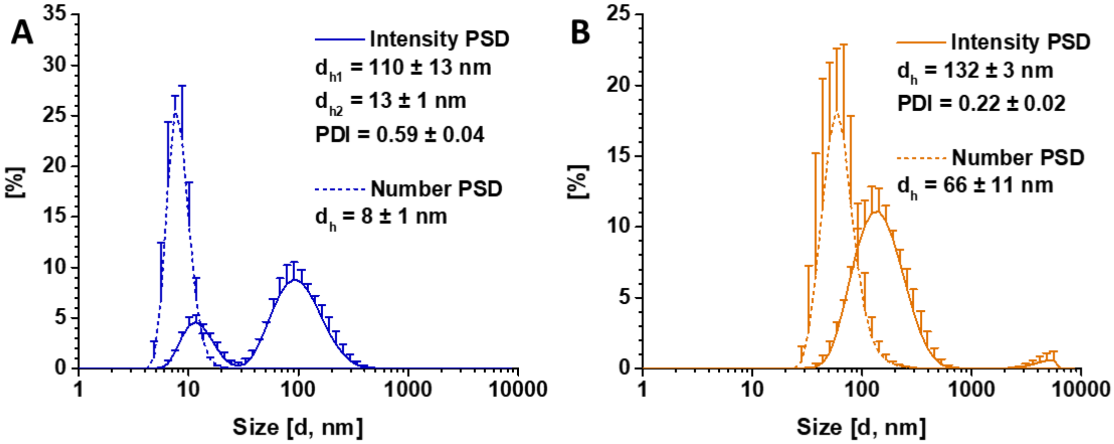


Figure S17. Characterisation of block copolymer derived nanostructures in PBS by DLS. 5 measurements with 3 runs each. Values represent the mean and SD. (A) P(iPOx$_{11}$-*b*-PEG-VDM$_{15}$). (B) P(TA-iPOx$_{11}$-*b*-PEG-VDM$_{15}$).

Table S1. Reactants used for the PPM of PiPOx and PVDM homopolymers with 2.0 eq functionalisation agent. For other molar ratios, the amount of functionalisation agent was varied, while the polymer mass and the solvent volume were kept constant. Reactions were performed at indicated temperatures for the described times as reported in the figures.

Polymer				**Functionalisation agent**					**DMF**
Name	*Eq*	*n [mmol]*	*m [mg]*	*Name*	*Eq*	*n [mmol]*	*m [mg]*	*V [µL]*	*V [mL]*
PiPOx	1.0	0.225	25.0	BZ	2.0	0.45	55.0		0.75
				PA			61.3		0.75
				BA			48.2	49.0	0.75
				BM			55.9	53.0	0.75
				TP			49.6	49.9	0.75
PVDM	1.0	0.179	25.0	BZ	2.0	0.359	43.9		0.75
				PA			48.9		0.75
				BA			38.5	39.0	0.75
				BM			44.7	42.2	0.75
				TP			39.6	36.7	0.75

BA: Benzylamine. BM: Benzyl mercaptan. BZ: Benzoic acid. PA: Phenylacetic acid. TP: Thiophenol.

Table S2. Characterisation of purified copolymers prepared by RAFT polymerisation. [a]SEC in DMAc (PS-cal.). [b] ^{1}H NMR (400 MHz) in $CDCl_3$. [c]Degree of polymerisation (DP) was calculated from monomer conversion as determined by ^{1}H NMR from reaction mixture. [d]M_n was calculated from DP.

	SEC[a]			**^{1}H NMR[b]**	
Polymer name	M_n *[g mol^{-1}]*	M_w *[g mol^{-1}]*	*Đ*	*DP[c]*	M_n *[g mol^{-1}][d]*
P(iPOx)$_{11}$-CTA	2,000	2,500	1.25	11	1,400
P(iPOx$_{11}$-*b*-VDM$_{15}$)-CTA	14,800	19,100	1.29	26	3,500
P(iPOx$_{11}$-*b*-VDM$_{15}$)	15,600	20,400	1.31	26	3,300
P(iPOx$_{27}$-*stat*-VDM$_{27}$)-CTA	7,600	8,700	1.15	54	7,000
P(iPOx$_{27}$-*stat*-VDM$_{27}$)	8,900	11,100	1.25	54	6,800

Table S3. Characterisation of functionalised copolymers. ^{a}SEC in DMAc (PS-cal.). ^{b} ^{1}H NMR (400 MHz) in CD_2Cl_2. ^{c}Reactions were conducted in a "one-pot" approach, reacting the functionalisation agents consecutively, however, omitting the purification of the crude products. n. d. not determinable due to peak overlap. n. a. not available.

			SEC^{a}			**^{1}H NMR^{b}**	
Run	*Polymer name*	*Functionalisation order*	M_n *[g mol^{-1}]*	M_w *[g mol^{-1}]*	*Đ*	*% BA*	*% BZ*
1a	P(iPOx$_{27}$-*stat*-VDM$_{27}$)	BA^{c}	13,500	16,700	1.23	n. d.	n. d.
1b		BZ^{c}	16,900	20,600	1.22	n. d.	n. d.
2a	P(iPOx$_{27}$-*stat*-VDM$_{27}$)	BZ^{c}	11,300	15,300	1.35	n. d.	n. d.
2b		BA^{c}	15,700	20,100	1.28	n. d.	n. d.
3a	P(iPOx$_{27}$-*stat*-VDM$_{27}$)	BA	12,300	15,000	1.22	100	n. a.
3b		BZ	16,300	22,000	1.35	100	100
4	P(iPOx$_{27}$-*stat*-VDM$_{27}$)	BZ	12,600	23,000	1.83	n. a.	n. d.
5a	P(iPOx$_{11}$-*b*-VDM$_{15}$)	BA	22,800	30,200	1.32	100	n. a.
5b		BZ	24,900	31,900	1.28	100	60
6a	P(iPOx$_{11}$-*b*-VDM$_{15}$)	BZ	16,500	27,100	1.64	n. a.	28
6b		BA	20,400	33,200	1.63	100	28

BA: Benzylamine. BZ: Benzoic acid.

Table S4. Characterisation of functionalised copolymers. ^{a}SEC in DMAc (PS-cal.). ^{b} ^{1}H NMR (400 MHz) in CD_2Cl_2. n. d. not determinable due to peak overlap. n. a. not available.

			SEC^{a}			**^{1}H NMR^{b}**	
Run	*Polymer name*	*Functionalisation order*	M_n *[g mol^{-1}]*	M_w *[g mol^{-1}]*	*Đ*	*% BA*	*% BZ*
7a	P(iPOx$_{11}$-*b*-VDM$_{15}$)	PEG-NH_2	39,800	47,400	1.19	100 (PEG)	n. a. (TA)
7b		TA	42,400	52,000	1.23	100 (PEG)	n. d. (TA)

PEG: Poly(ethylene glycol). TA: Terephthalic acid.