Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

An electrochemical Hofmann rearrangement on acrylamide copolymers

Muzhao Wang and Paul Wilson*

University of Warwick, Department of Chemistry, Library Road, Coventry, UK.

E-mail: p.wilson.1@warwick.ac.uk

Experimental

1. Materials

Chloroform-d (Sigma-Aldrich, 99.8% atom % D, contains 0.03% (v/v) TMS), deuterium oxide (99.9 atom % D), sodium bromide (Alfa Aesar, 99+% (dry wt.), water <1.0%), benzamide (Sigma-Aldrich, 99%), butyramide (Sigma-Aldrich, ≥98.0% (T)), water (Sigma-Aldrich, HPLC Plus), methanol (Fisher Chemical, ≥99.8%, HPLC grade), acetonitrile (Fisher Chemical, ≥99.9%, HPLC Gradient grade), acetone (Sigma-Aldrich, puriss. P.a., ACS reagent, reag. ISO, reag. Ph. Eur., ≥99.5% (GC)), acrylamide (Sigma-Aldrich, suitable for electrophoresis, ≥99%), *N*,*N*-Dimethylacrylamide (Sigma-Aldrich, 99%, contains 500 ppm monomethyl ether hydroquinone as inhibitor), 2,2'-Azobis(2-methyl-propionitrile) (Sigma-Aldrich, 98%), chloroform (Sigma-Aldrich, puriss. P.a., reag. ISO, reag. Ph. Eur., 99.0-99.4% (GC)), diethylene glycol monomethyl ether (Sigma-Aldrich, ≥99%) and hexane fraction from petroleum (Fisher Chemical, Laboratory reagent grade) were used as received.

2. Instruments

Size exclusion chromatography (SEC). DMF SEC was performed using an Agilent Infinity II MDS instrument equipped with differential refractive index (DRI), viscometry (VS), dual angle light scatter (LS) and variable wavelength UV detectors. The system was equipped with 2 x PLgel Mixed D columns (300 x 7.5 mm) and a PLgel 5 µm guard column. The eluent was DMF with 5 mmol NH_4BF_4 additive. Samples were run at 1ml/min at 50 °C. Poly(methyl

methacrylate) standards (Agilent EasyVials) were used for calibration between 955,000 – 550 $g.mol^{-1}$. Analyte samples were filtered through a nylon membrane with 0.22 μm pore size before injection. Respectively, experimental molar mass ($M_{n,SEC}$) and dispersity ($Đ_m$) values of synthesized polymers were determined by conventional calibration using Agilent GPC/SEC software.

Aqueous SEC was performed using an Agilent PL50 instrument equipped with differential refractive index (DRI) detector. The system was equipped with 2 x Aquagel H columns (300 x 7.5 mm) and an Aquagel 5 µm guard column. 80:20 0.1 M $NaNO_{3(aq)}$:methanol. Samples were run at 1ml/min at 35 ^oC. Poly(ethylene oxide) standards (Agilent EasyVials) were used for calibration. Analyte samples were filtered through a membrane with 0.45 μm pore size before injection. Respectively, experimental molar mass ($M_{n,SEC}$) and dispersity ($Đ$) values of synthesized polymers were determined by conventional calibration using Agilent GPC/SEC software.

Nuclear magnetic resonance (NMR). ^1H NMR Spectra were recorded in $CDCl_3$ or in D_2O either on a Bruker Avance III HD 500 operating at 500.13 MHz, Bruker Avance III ^{TM} HD 400 operating at 400.13 MHz or on a Bruker Avance III ^{TM} HD 300 operating at 300.13 MHz. ACDLABS 12.0 with 1D NMR Processor was used to conduct the integration.

Fourier-transform infrared spectroscopy (FT-IR). FT-IR Spectra were recorded on a Bruker ALPHA PLATINUM-ATR. Background was measured before samples were placed. The anvil was pulled down to apply pressure on the sample before sample measurements.

Thermal gravimetric analysis (TGA).

TGA trace was recorded on Mettler-Toledo TGA with autosampler. Alumina 90 µL pan was applied to load samples. Air was chosen to conduct cooling cycle; temperature range was set as room temperature to 600 ^oC with heating rate 10 ^oC per min. 5 min isothermal run was applied before start heating process.

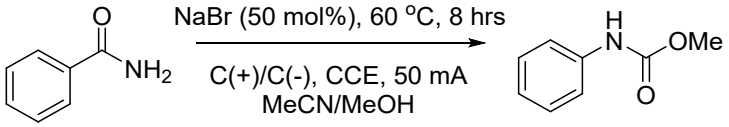
Differential scanning calorimetry (DSC).

DSC trace was recorded on Mettler-Toledo DSC1 with autosampler. Tzero Pan and Tzero Hermetic Lid were applied to load samples. Nitrogen was chosen to conduct cooling cycle; temperature range was set as -100 ^{o}C to 200 ^{o}C with heating rate 10 ^{o}C per min. 10 min isothermal run was applied between heating and cooling cycle.

Cyclic voltammetry (CV). Cyclic voltammetry was conducted on a CH-Instruments 600 E potentiostat using a 3 mm glassy carbon disc electrode which was polished with 0.05 µm alumina powder, rinsed sequentially with acetone, ethanol and MilliQ water prior to each use. The counter electrode was a platinum wire coil. The reference electrode was Ag/AgCl, the silver wire was polished and rinsed sequentially with acetone, ethanol and MilliQ water the wire was then placed into a glass capillary tube fitted with a vycor frit and filled 1 M KCl solution. Before CVs, the reaction cell was purged with N_2 for 15 mins. A background CV was recorded to confirm the absence of impurities and oxygen.

3. Experimental procedures

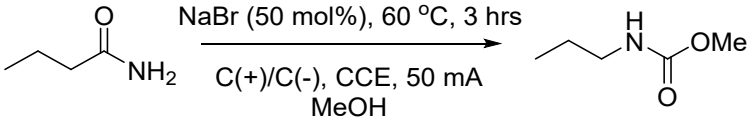
Synthesis of methyl phenylcarbamate



Benzamide (121 mg, 1 mmol, 1 Eq.) and sodium bromide (50 mg, 0.5 mmol, 0.5 Eq.) were added into the reaction vial, followed by acetonitrile (8 mL) and then methanol (2 mL). The solution vial was then attached to the cap from IKA ElectraSyn 2.0 GoGo module and placed on a Heidolph MR Hei-Standard hot-plate stirrer to stir (800 rpm) at under room temperature until a colourless, homogenous solution was achieved. The cap was removed and affixed with two graphite working and counter electrodes (5.2 x 0.7 x 0.1 cm^3; IKA ElectraSyn 2.0 accessory) before being reattached to the vial containing the reaction solution. The vial was transferred into the oil bath with set temperature 60 ^{o}C with stirring (500 rpm) for 8 hrs. Electroylsis was performed in constant current mode (I_{app} = 50mA). The reaction was sampled periodically for reaction monitoring by ^{1}H NMR (Fig. S2). Upon completion, the solvent was removed in vacuo to yield a brown residue which was dissolved in chloroform (100 mL) and washed with water (3 × 100 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo to give the crude reaction production as a brown oil like product. ^{1}H

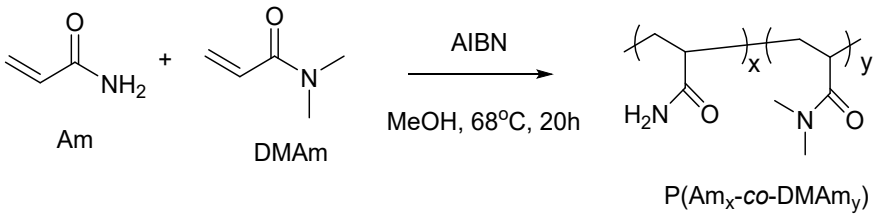
NMR (400MHz, $CDCl_3$): δ_H (ppm) 3.80 (s, 3H, -OCH_3), 7.10 (t, 1H, aromatic ring), 7.33 (t, 2H, aromatic ring), 7.40 (d, 2H, aromatic ring). ^{13}C NMR (100MHz, $CDCl_3$): δ_C (ppm) 52, 123, 127, 129, 133, 154.

Preparation of methyl propylcarbamate



Butyramide (87 mg, 1 mmol, 1 Eq.) and then sodium bromide (50 mg, 0.5 mmol, 0.5 Eq.) were added into the vial, followed by methanol (10 mL) The solution vial was then attached to the cap from IKA ElectraSyn 2.0 GoGo module and placed on a Heidolph MR Hei-Standard hot-plate stirrer to stir (800 rpm) at under room temperature until a colourless, homogenous solution was achieved. The cap was removed and affixed with two graphite working and counter electrodes (5.2 x 0.7 x 0.1 cm^3; IKA ElectraSyn 2.0 accessory) before being reattached to the vial containing the reaction solution. The vial was transferred into the oil bath with set temperature 60 °C with stirring (500 rpm) for 3 hrs. Electroylsis was performed in constant current mode (I_{app} = 50mA). The reaction was sampled periodically for reaction monitoring by ^1H NMR (Fig. S3). Upon completion, the solvent was removed in vacuo to yield a brown residue which was dissolved in chloroform (100 mL) and washed with water (3 × 100 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo to give the crude reaction product as a white solid. ^1H NMR (400MHz, $CDCl_3$): δ_H (ppm) 0.90 (t, 3H, -CH_2CH_3), 1.50 (m, 2H, -CH_2CH_3), 3.12 (q, 2H, -$NHCH_2$), 3.65 (s, 3H, -OCH_3). ^{13}C NMR (100MHz, $CDCl_3$): δ_C (ppm) 11, 23, 44, 53, 157.

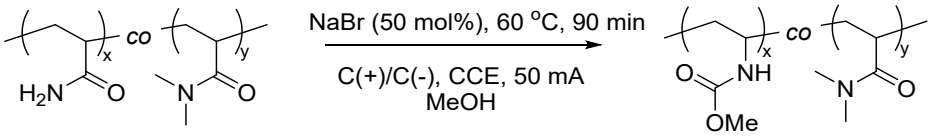
General procedure for the synthesis of P(Am_x-*co*-$DMAm_y$) scaffolds



For x = 0.2, y = 0.8 (targeting 20 mol% Am). Acrylamide (710 mg, 10 mmol), *N*,*N*-Dimethylacrylamide (3965 mg, 40 mmol) and 2,2'-Azobis(2-methyl-propionitrile) (82 mg, 0.5 mmol) were dissolved in MeOH (25 mL). The solution was stirred to give clear colourless

solution and then deoxygenated by bubbling with nitrogen for 20 min. Then the reaction flask was then transferred into an oil bath at 68 °C and stirred (500 rpm) for 20 h as a colourless solution. Upon completion the reaction mixture was allowed to cool to room temperature and then precipitated in cold diethyl ether (1 L), collected by filtrate and dried in a vacuum oven to yield the pure copolymer as a white solid. ^{1}H NMR (400MHz, D_2O): δ_H (ppm) 1,25-1.75 (polymer backbone), 1.75-2.75 (-NH_2 in polyAA), 2.75-3.10 (-CH_3 in polyDMA). ^{13}C NMR (125MHz, D_2O): δ_C (ppm) 36, 37, 41, 176, 179. ν_{max}/cm^{-1} 3413, 2927, 1674, 1617, 1495, 1399, 1352, 1256, 1140, 1095, 1056 and 623.

General procedure for the eHofmann rearrangement on P(Am$_x$-*co*-DMAm$_y$) scaffolds



For x = 0.2, y = 0.8 (i.e. 20 mol% Am). P(Am$_x$-co-DMAm$_y$) (467.6 mg, 1 mmol w.r.t Am) and then sodium bromide (50 mg, 0.5 mmol, 1 Eq.) were added into the reaction vial and dissolved in MeOH (10 mL). The solution vial was then attached to the cap from IKA ElectraSyn 2.0 GoGo module and placed on a Heidolph MR Hei-Standard hot-plate stirrer to stir (800 rpm) at under room temperature until a colourless, homogenous solution was achieved. The cap was removed and affixed with two graphite working and counter electrodes (5.2 x 0.7 x 0.1 cm^3; IKA ElectraSyn 2.0 accessory) before being reattached to the vial containing the reaction solution. The vial was transferred into the oil bath with set temperature 60 °C with stirring (500 rpm) for 3 hrs. Electroylsis was performed in constant current mode (I_{app} = 50mA). The reaction was sampled periodically for reaction monitoring by ^{1}H NMR (Fig. 2, manuscript). The solvent was removed to give yellow oil which was dissolved in choloroform (3 mL) and precipitated by dropwise addition to cold hexane (100 mL) to give the crude polymer scaffold as a light yellow powder. The crude polymer was purified (to remove sodium bromide) by dialysis against MilliQ water for 3 days. The pure polymer was isolated by lyophilisation to yield the pure *O*-methyl carbamate functionalised polymer scaffold as a white solid. ^{1}H NMR (500MHz, D_2O): δ (ppm) 1.50-2.00 (polymer backbone), 2.90-3.10 (-CH_3 in polyDMA), 3.50-3.70 (-CH_3 in carbamate structure). ^{13}C NMR (125MHz, D_2O): δ_C (ppm) 36, 37, 48, 52, 158, 176. ν_{max}/cm^{-1} 3247, 2921, 1708, 1617, 1497, 1446, 1399, 1352, 1252, 1139 and 1056.

Supporting Figures

Fig. S1 IKA ElectraSyn 2.0 device configuration for the eHoffman reaction. A and B) IKA head/cap; C) IKA graphite electrodes; D) fully assembled reaction using the IKA ElectraSyn GoGo module to enabled the reaction to be heated in an oil bath. Direction for setting up the reaction using the ElectraSyn interface includes E) select new experiment; F) choose constant current electrolysis (CCE); G) use the dial to set I_{app} (50 mA in our hands); H) press 'no' if no reference electrode is required (which is the case for CCE); I) select the 'Time'; J) use the dial to set the reaction time (1 h 30 min 00 sec in this case); K) use the dial to set the substrate concentration (1 mmol in this case); L) select 'no' to alternating polarity; M) choose whether to save the data or not; N) press start.

Table S1 Reaction monitoring of the eHofmann reaction of benzamide (1 mmol) in the presence of NaBr (50 mol%) in a MeCN/MeOH (8 : 2 v/v) at 60 °C under constant current electrolysis (CCE) at 50 mA with graphite working and counter electrodes. Conversion calculated by ^{1}H NMR (Fig. S2).

Time (h)	Conversion (%)
0	0
1	11
3	34
4	53
5	65
6	81
6.5	94
8	~99

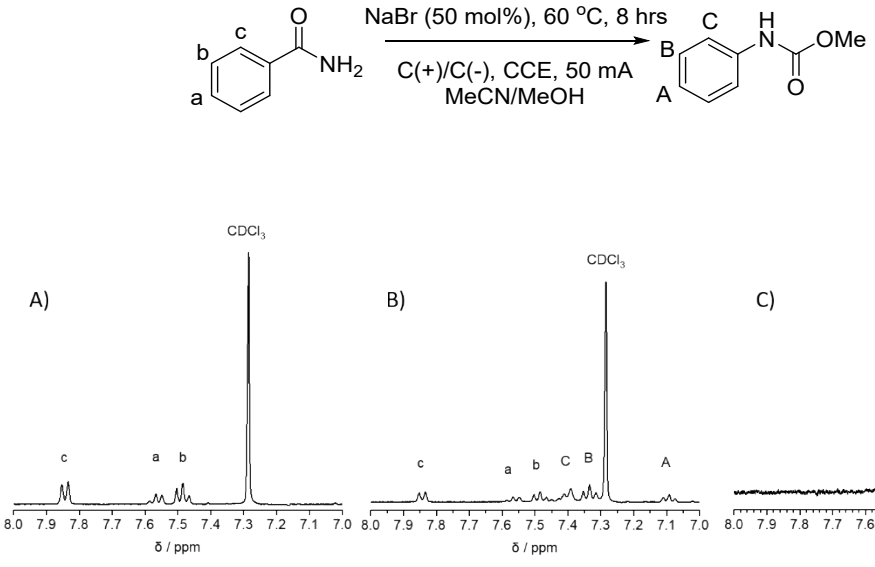


Fig. S2 ^{1}H NMR reaction monitoring of the eHofmann reaction of benzamide (1 mmol) at A) t = 0; B) t = 4 hrs; C) t = 8 hrs. Reaction performed in the presence of NaBr (50 mol%) in a MeCN/MeOH (8 : 2 v/v) at 60 °C under constant current electrolysis (CCE) at 50 mA with graphite working and counter electrodes. Conversion calculated through comparison of the integrals of H_a in benzamide and H_A in the carbamate product.

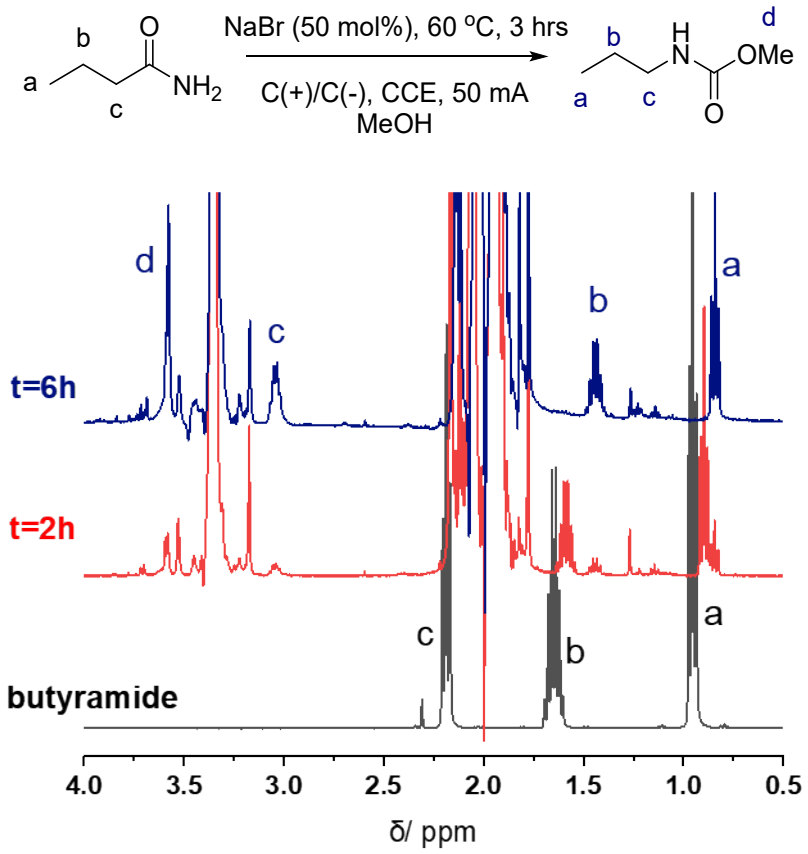


Fig. S3 ^{1}H NMR reaction monitoring of the eHofmann reaction of butyramide (1 mmol) at t = 2 h (red) and t = 6 hrs (blue). Reaction performed in the presence of NaBr (50 mol%) in a MeCN/MeOH (8 : 2 v/v) at 60 °C under constant current electrolysis (CCE) at 50 mA with graphite working and counter electrodes.

Table S2 Reaction conditions for the FRP (co)polymerisation of Am and DMAm in MeOH

Entry	Am (%)	Am (mmol)	DMAm (mmol)	Am (mg)	DMAm (mg)
1	0	0	50	0	4956.5
2	10	5	45	355.4	4460.85
3	20	10	40	710.8	3965.2
4	30	15	35	1066.2	3469.55
5	40	20	30	1421.6	2973.9
6	50	25	25	1777	2478.25
7	100	50	0	3554	0

0.05mol% AIBN (82mg) used in each reaction.
V_{MeOH} = 25 mL
T = 68 °C

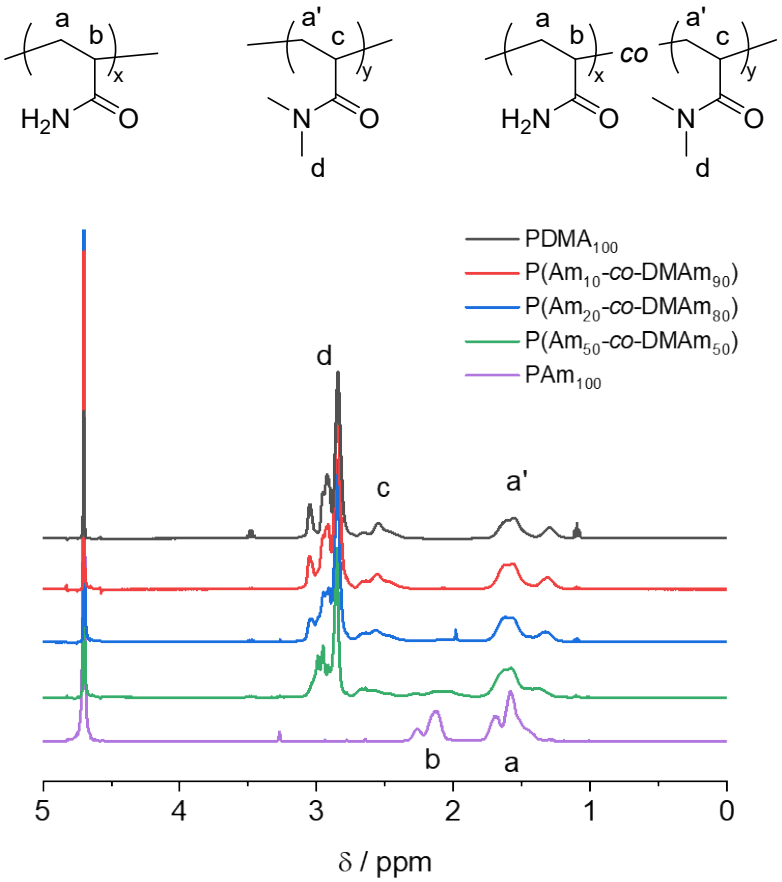


Fig. S4 ^{1}H NMR overlay of PAm, PDMAm and P(Am_x-*co*-$DMAm_y$) scaffolds synthesised by FRP. Compositional ratio's (Table S4) calculated by integration of *N,N*-dimethyl group of the DMAm side chain (H_d), against the entire copolymer backbone (H_a, H_b, $H_{a'}$, H_c) with correction for the contribution to the backbone from DMAm ($H_{a'}$, H_c).

Table S3 Compositional analysis from ^{1}H NMR (Fig S4) and molecular weight data from aqueous SEC (Fig. S7) for the P(Am_x-*co*-$DMAm_y$) scaffolds synthesised by FRP.

Entry	Am_{feed} (mol%)	$DMAm_{feed}$ (mol%)	Am_{NMR} (mol%)	$DMAm_{NMR}$ (mol%)	$M_{n,SEC}$ (g.mol^{-1})	$M_{w,SEC}$ (g.mol^{-1})	$Đ_m$
1	0	100	0	100	21400	72700	3.4
2	10	90	7	93	20000	74900	3.7
3	20	80	17	83	19500	78800	4.0
4	50	50	50	50	13700	76000	5.6
5	100	0	100	0	7800	38000	4.9

0.05 mol% AIBN (82mg) used in each reaction.
V_{MeOH} = 25 mL
T = 68 °C

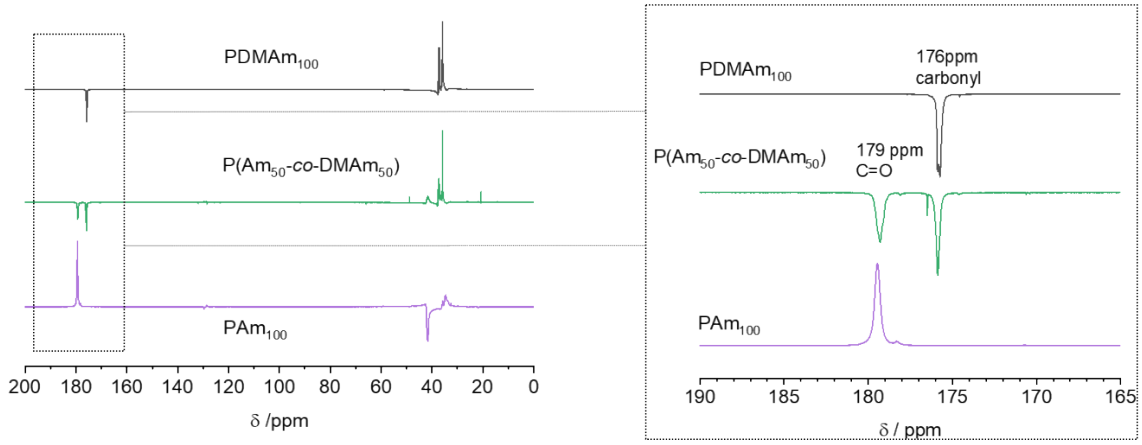


Fig. S5 ^{13}C NMR overlay of PAm, PDMAm and P(Am_x-*co*-$DMAm_y$) scaffolds synthesised by FRP.

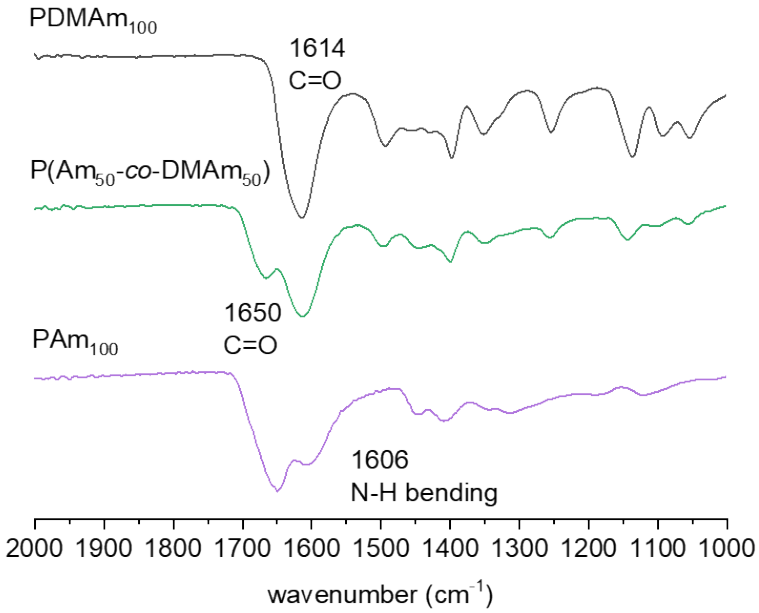


Fig. S6 FTIR overlay of PAm, PDMAm and P(Am_x-*co*-$DMAm_y$) scaffolds synthesised by FRP.

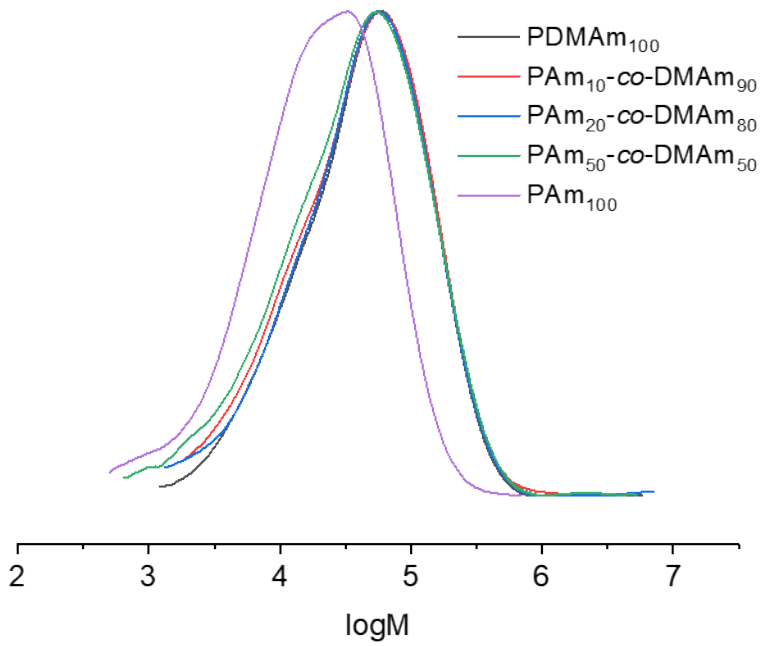


Fig. S7 Aqueous SEC analysis of PAm, PDMAm and P(Am_x-*co*-$DMAm_y$) scaffolds synthesised by FRP. See Table S3 for molecular weight data.

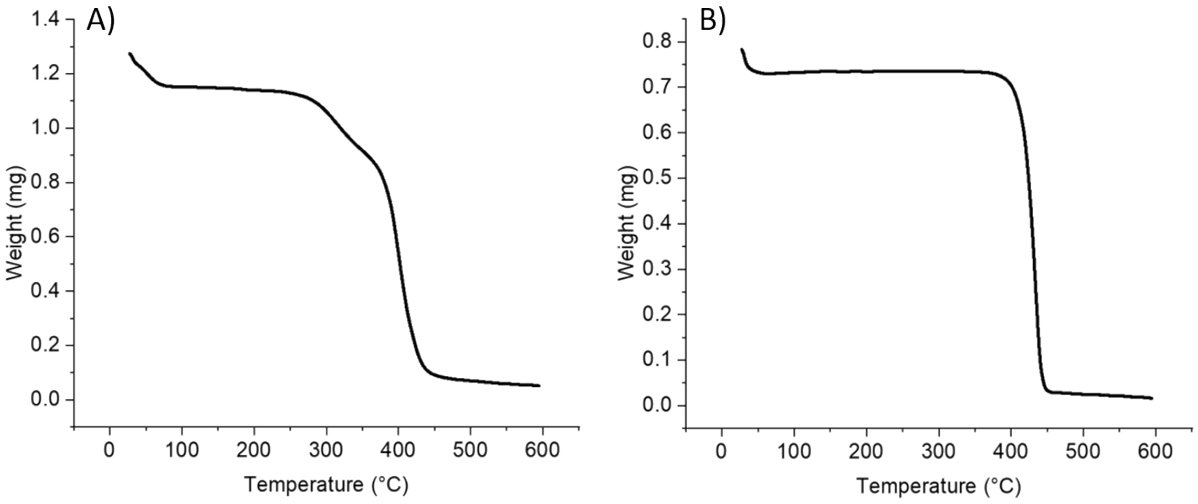


Fig. S8 TGA of PAm (Table S3, entry 5) and PDMAm (Table S3, entry 1) synthesized via FRP.

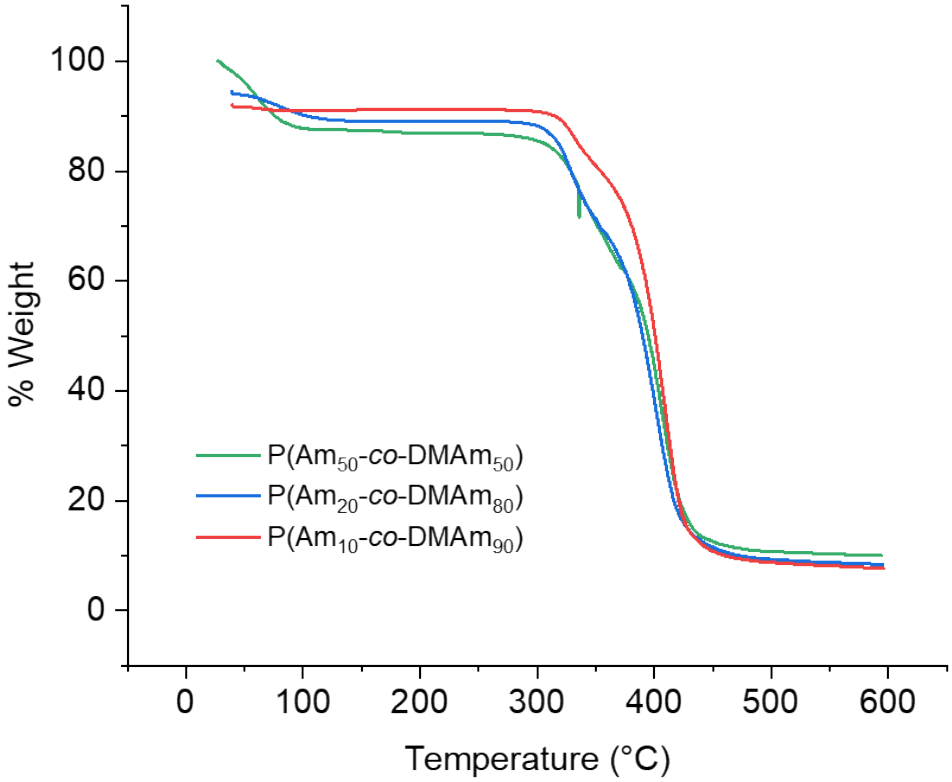


Fig. S9 TGA of P(Am_x-*co*-$DMAm_y$) scaffolds synthesized via FRP (Table S3, entry 2-4).

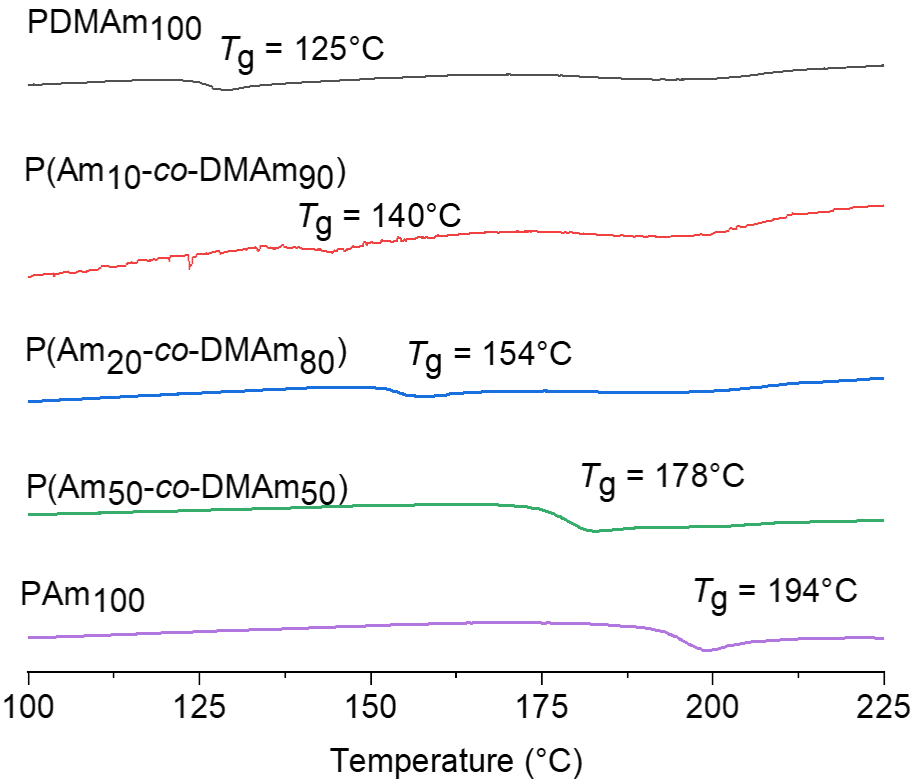


Fig. S10 DSC analysis of PAm (Table S3, entry 5), PDMAm (Table S3, entry 1) and P(Am_x-*co*-$DMAm_y$) (Table S3, entry 2-4) scaffolds synthesized via FRP.

Table S4 Molecular weight data from aqueous SEC (Fig. S11) for the P(Am_x-*co*-$DMAm_y$) scaffolds synthesised by FRP.

Am (mol%)	$M_{n,SEC}$ (g.mol)	$M_{w,SEC}$ (g.mol)	$Đ_m$
7	15500	65200	4.2
17	15600	63400	4.1
50	10900	54800	5.0

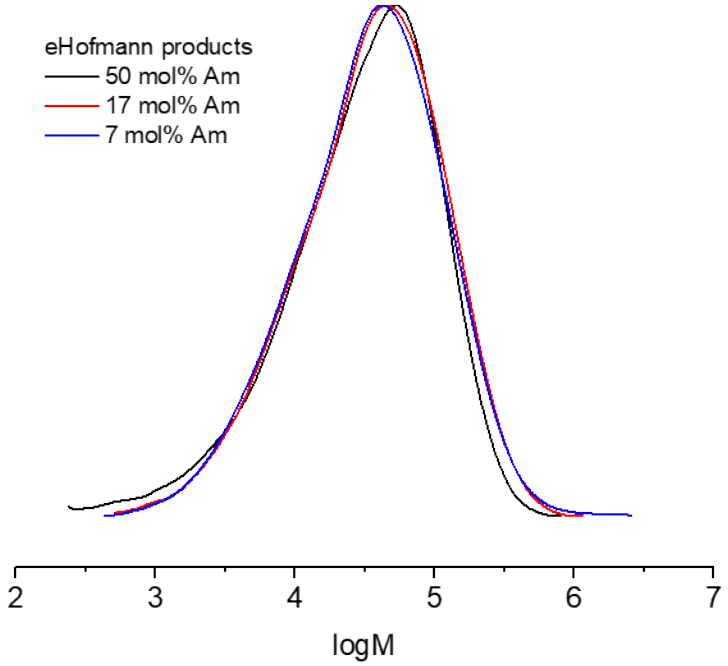


Fig. S11 Molecular weight distributions from aqueous SEC of the *O*-methyl carbamate functionalised polymer products formed via eHofmann rearrangement (Table S4).

Table S5 Comparison of the thermal stability and properties of the P(Am-*co*-DMAm) scaffold and *O*-methyl carbamate functionalised polymer products formed *via* eHofmann rearrangement.

	P(Am-*co*-DMAm)		eHofmann product	
Am (mol%)	$T_{d,onset}$ °C	T_g °C	$T_{d,onset}$ °C	T_g °C
7	308	140	250	132
17	290	154	235	137
50	270	178	205	152

$T_{d,onset}$ from TGA analysis
T_g from DSC analysis

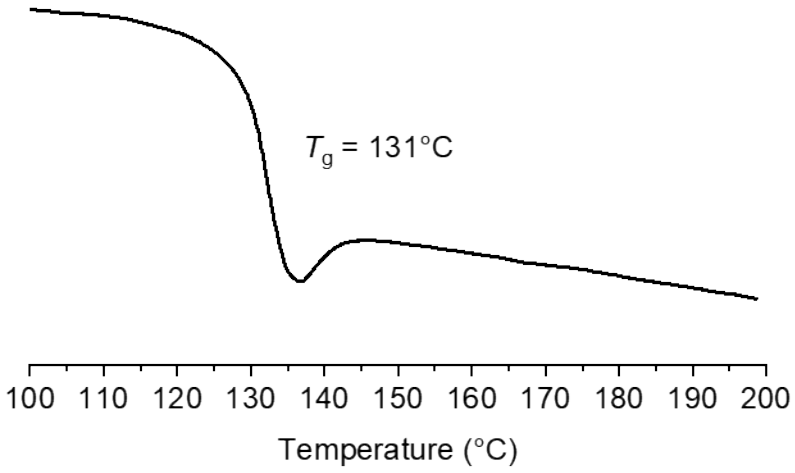


Fig. S12 DSC analysis of the *O*-methyl carbamate functionalised polymer derived from P(Am-*co*-DMAm) containing 7 mol% Am.

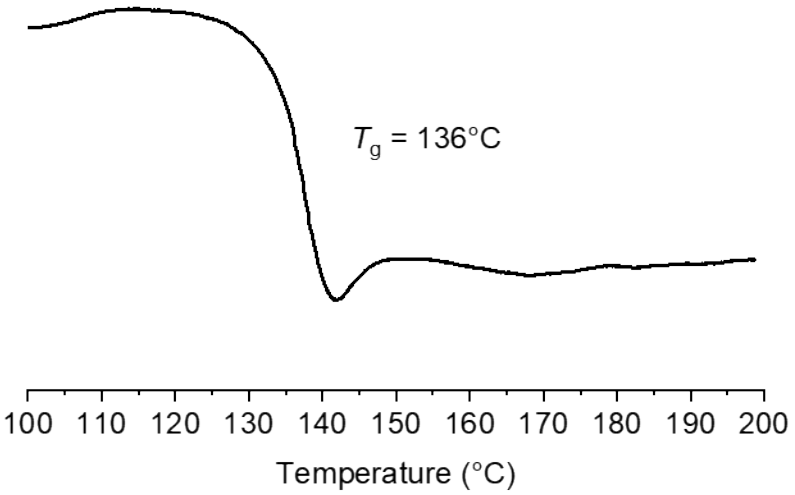


Fig. S13 DSC analysis of the *O*-methyl carbamate functionalised polymer derived from P(Am-*co*-DMAm) containing 17 mol% Am.

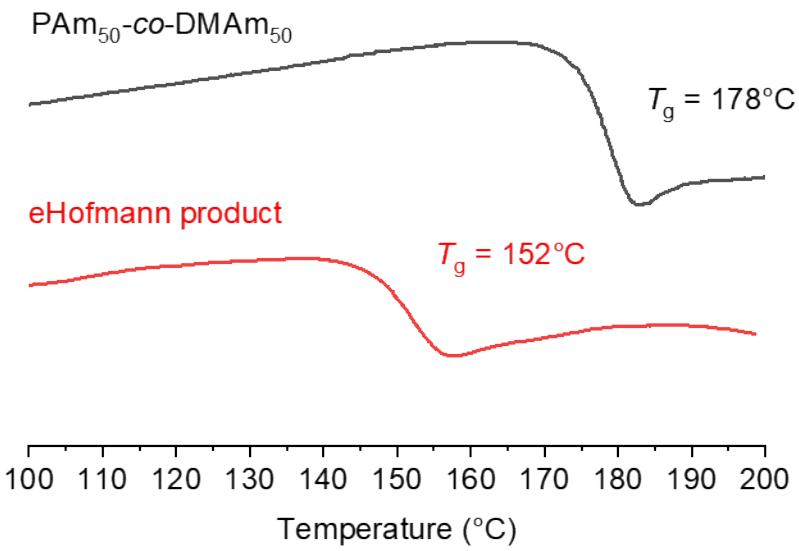


Fig. S14 DSC overlay demonstrating the change in T_g following the eHofmann rearrangement of the P(Am-*co*-DMAm) scaffold contain 50 mol% Am (black) to form the *O*-methyl carbamate functionalised product (red).

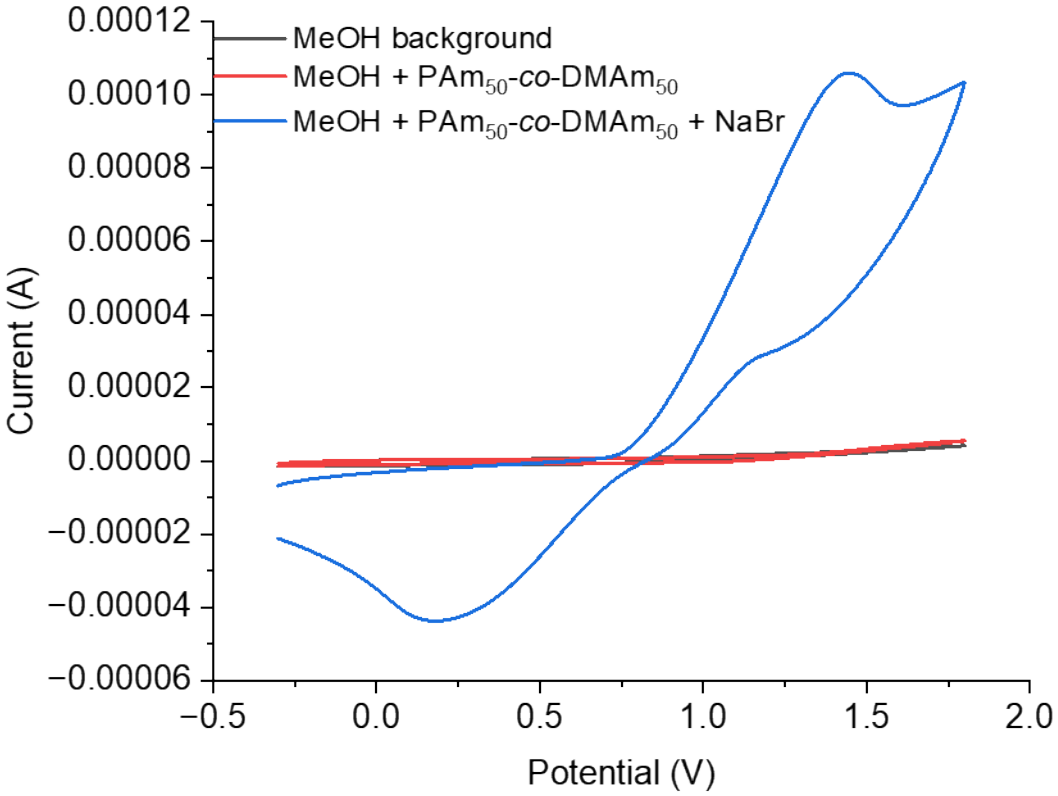


Fig. S15 Cyclic voltammograms of MeOH background (black), MeOH and P(Am-*co*-DMAm) (50 mol % Am, 0.05 mmol w.r.t. Am; red) and MeOH, P(Am-*co*-DMAm) (50 mol % Am, 0.05 mmol w.r.t. Am) and NaBr (0.05 mmol; blue). Ag/AgCl reference electrode applied with 1M KCl inside; glassy carbon disc electrode as working electrode and platinum wire coil as counter electrode. Scan rate was set with 0.1V/s.

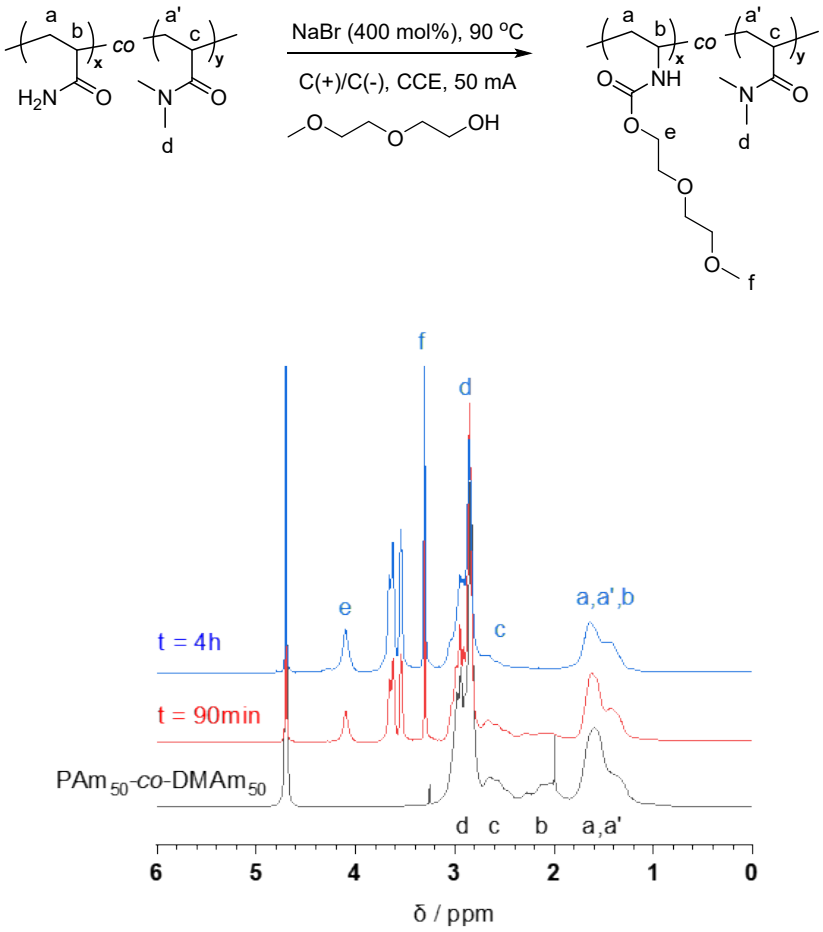


Fig. S16 ^{1}H NMR analysis monitoring reaction conversion during the eHofmann rearrangement of P(Am-*co*-DMAm) (50 mol % Am) in DEGME using NaBr (400 mol %).

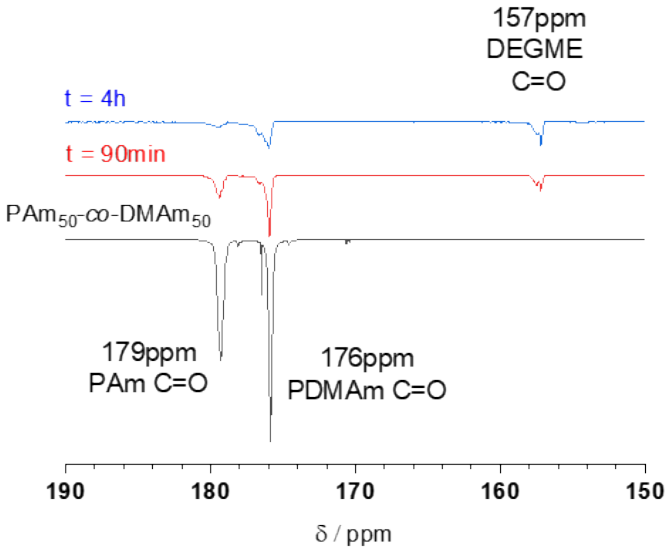


Fig. S17 ^{13}C NMR analysis monitoring reaction conversion during the eHofmann rearrangement of P(Am-*co*-DMAm) (50 mol % Am) in DEGME using NaBr (400 mol %).

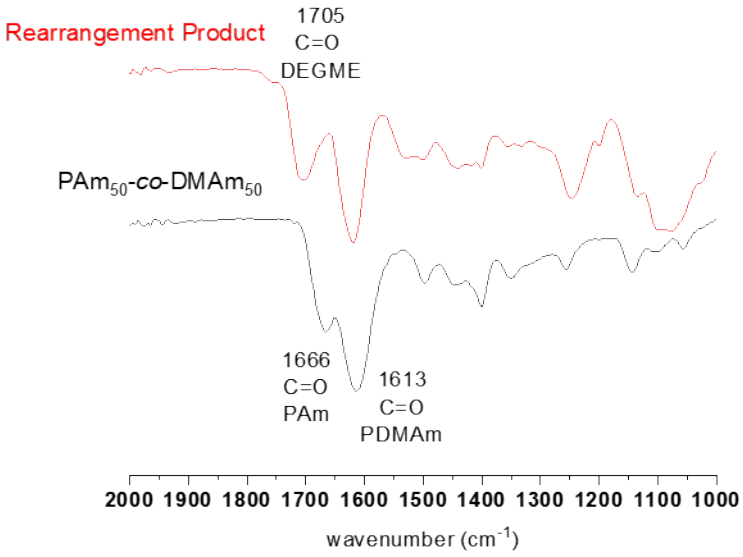


Fig. S18 FTIR overlay of the P(Am-*co*-DMAm) scaffold containing 50 mol% Am and the product formed eHofmann rearrangement of P(Am-*co*-DMAm) (50 mol % Am) in DEGME using NaBr (400 mol %).

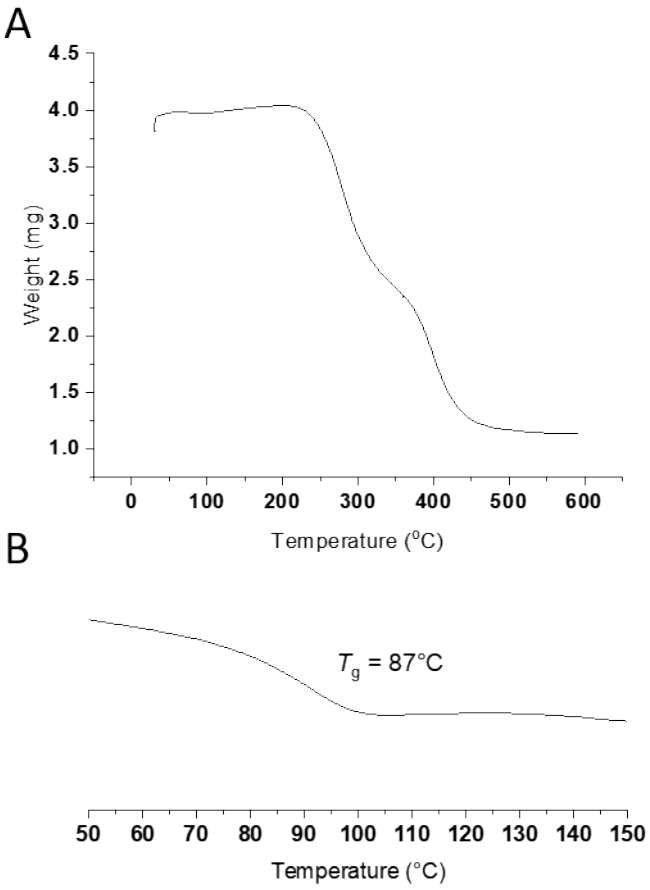


Fig. S19 For the *O*-DEGME carbamate functionalised polymer product derived from P(Am-*co*-DMAm) containing 50 mol% Am; (A) TGA analysis showing two thermal events with the first occurring at $T_{d,onset}$ = 225 °C; (B) DSC analysis showing that T_g = 87 °C, decreasing from 178 °C following eHofmann rearrangement (Fig. S10)**.**