Electronic Supplementary Information: Continuous Dimethyldioxirane Generation for Polymer Epoxidation

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Contents

1 General Considerations

1.1 Safety

CAUTION: DMDO is a volatile organic peroxide and should be handled accordingly. All manipulations should be carried out in a functioning fume hood, and reaction mixtures should be quenched properly before concentration or isolation of products.

1.2 Materials

Polymers, reagents, and solvents were purchased from Millipore Sigma and used as received. "Low molecular weight (MW) PBD" refers to *cis*-polybutadiene, catalog number 434779, average M_n 1,530-2,070 by VPO. "High MW PBD" refers to *cis*-polybutadiene, catalog number 181382, average M_w 200,000. "Polyisoprene" refers to *cis*-polyisoprene, catalog number 431265, average M_w $\sim$35,000 by GPC, made from synthetic rubber.

Deionized water was obtained from an in-house supply. High purity PFA tubing, PEEK mixers and unions, and ferrules were purchased from IDEX Scientific. Teflon tape and grade 415 filter paper was purchased from VWR. Variable back-pressure regulators were purchased from Zaiput. Syringe pumps were Harvard PhD Ultra syringe pumps with 8 mL stainless steel Harvard syringes. Peristaltic pumps were VapourTec SF-10 or easyMedChem pumps equipped with blue tubing inserts.

1.3 Analysis

Nuclear magnetic resonance (NMR) spectra were recorded on Bruker Avance III spectrometers at 400/100, 500/125, or 600/150 MHz for $^1H/^{13}C$ respectively. NMR samples were taken in deuterated chloroform (Cambridge Isotope Laboratories). Chemical shifts for ^1H NMR are expressed in parts per million (ppm) relative to residual $CDCl_3$ solvent protons (δ 7.26 ppm). Chemical shifts for ^{13}C NMR are expressed in ppm relative to $CDCl_3$ (δ 77.16 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, m = multiplet). Infrared (IR) spectra were recorded for neat polymers using an Agilent Cary 630 spectrometer equipped with a diamond ATR attachment. Data are reported as follows: peak in wavenumbers (assignment). Gel permeation chromatography (GPC) was performed using a chloroform mobile phase and a Tosoh EcoSEC HLC-8320 instrument with dual TSKgel SuperH3000 columns. Calculated molecular weight and dispersity are based off a polystyrene standard curve.

2 Flow Reactor Construction

2.1 Construction of Initial Plug Flow Reactor

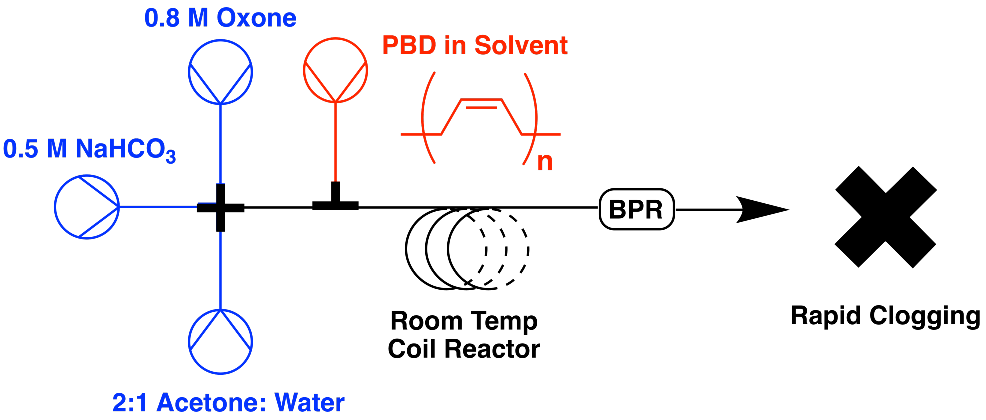


Figure S1 Initial design for plug flow reactor.

The following solutions were prepared: 0.8 M Oxone in DI water (A), 0.5 M NaHCO$_3$ in DI water (B), 2:1 acetone:DI water (C), and 10 g/L low MW PBD in ethyl acetate (D). A plug-flow reactor was constructed from 88 cm 0.03" ID PFA tubing (reactor volume 400 μL). Each solution was pumped at a flow rate of 100 μL/min and the solutions combined at a cross mixer (0.06" ID) and then entered the plug flow reactor, yielding a total flow rate of 400 μL and residence time of one minute. The reaction mixture exited through a BPR set to 3 bar and was collected in a flask containing saturated aqueous Na$_2$S$_2$O$_3$. When run, visible solid precipitation occurred within one minute, and the solid accumulation later clogged the reactor.

2.2 Construction of CSTR-Based System

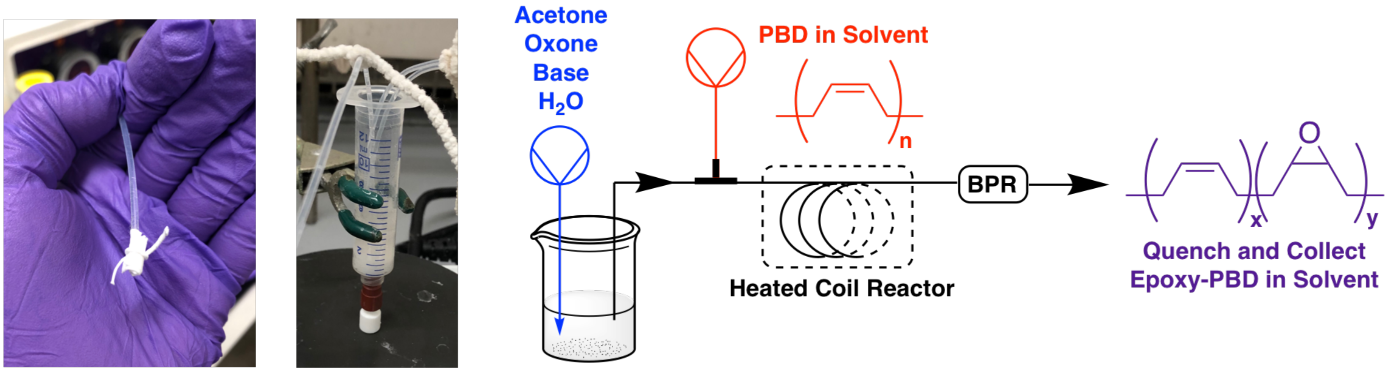


Figure S2 From left to right: Teflon tape and filter paper assembled into a simple imput filter, CSTR constructed from a stoppered Luer syringe, schematic of reactor design for DMDO epoxidation using a CSTR.

A plug-flow reactor was constructed from 88 cm 0.03" ID PFA tubing (reactor volume 400 μL). Oxone (0.8 M in DI water) and base/acetone (0.5 M K$_3$PO$_4$ in DI water and 2:1 acetone: DI water or 0.33 M K$_3$PO$_4$ in 70:30 water: acetone) were pumped using syringe pumps at a flow rate of 100 μL/min and combined in the barrel of a stoppered 10 mL plastic Luer-tipped syringe (see photo). The CSTR was stirred slowly with a magnetic stir bar, allowing solid precipitates to settle towards the bottom while still stirring the incoming reactants. The residence time in the CSTR was approximately 10 minutes (3 mL, 300 μL/min). The solution was pumped forward through a piece of filter paper tied on to the tubing with Teflon tape (see photo). Using a peristaltic pump at 300 μL/min, the combined solutions were pumped forward to meet the polymer solution, pumped at 100 μL/min, in a T-mixer. The biphasic mixture then entered the plug flow reactor, yielding a total flow rate of 400 μL/min and a residence time of one minute. The reaction mixture exited through a

BPR set to 3 bar and was collected in a flask containing saturated aqueous $Na_2S_2O_3$. No solid precipitation was observed outside of the CSTR.

2.3 Construction of Large-Scale Flow Reactor

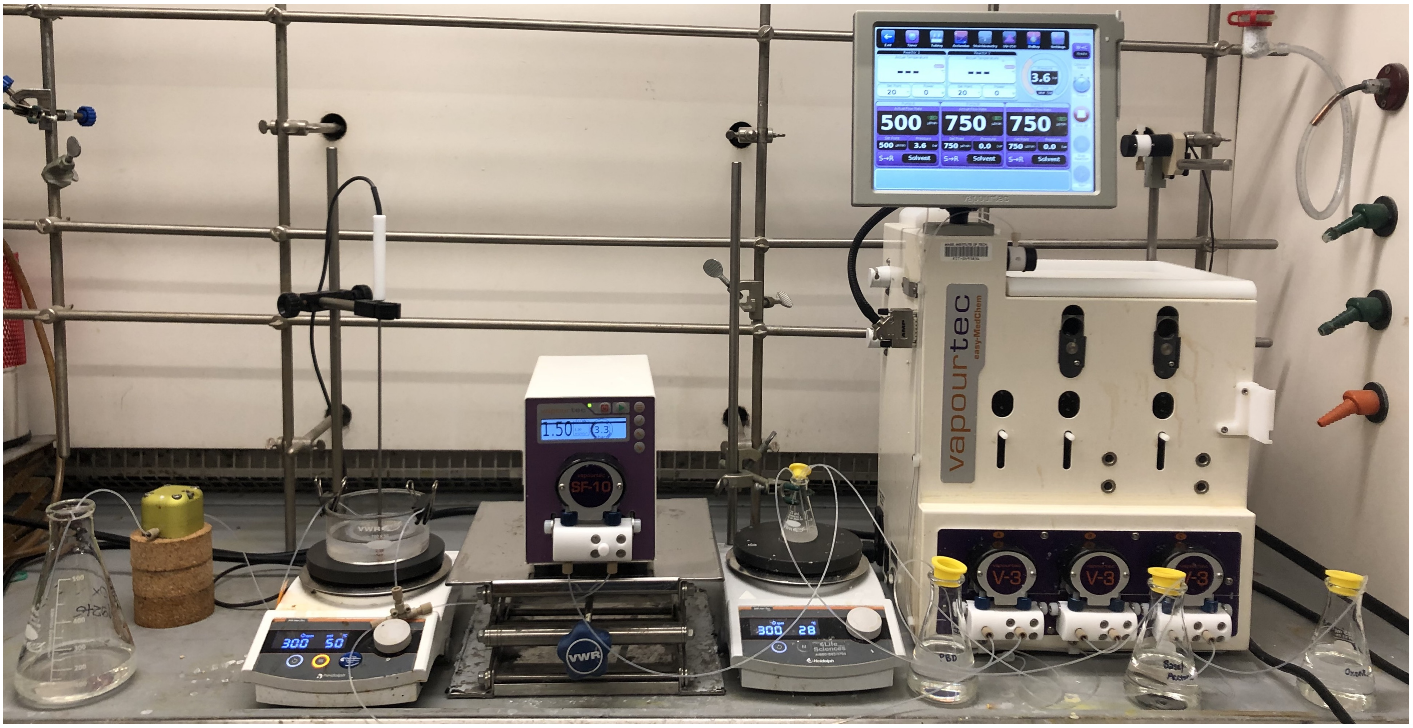


Figure S3 Photograph of large-scale flow reactor setup.

A plug-flow reactor was constructed from 439 cm 0.03" ID PFA tubing (reactor volume 2 mL). Oxone (0.8 M in DI water) and base/acetone (0.33 M K_3PO_4 in 70:30 water: acetone) were pumped using VapourTec peristaltic pumps at a flow rate of 750 μL/min and combined in a 25 mL Erlenmeyer flask. The CSTR was stirred slowly with a magnetic stir bar, allowing solid precipitates to settle towards the bottom while still stirring the incoming reactants. The residence time in the CSTR was approximately 10 minutes (15 mL, 1.5 mL/min). The solution was pumped forward through a piece of filter paper tied on to the tubing with Teflon tape. Using a peristaltic pump at 1.5 mL/min, the combined solutions were pumped forward to meet the polymer solution, pumped with a peristaltic pump at 500 μL/min, in a T-mixer. The biphasic mixture then entered the plug flow reactor, yielding a total flow rate of 2 mL/min and a residence time of one minute. The reaction mixture exited through a BPR set to 3 bar and was collected in a flask containing saturated aqueous Na_2SO_3.

3 General Procedures

3.1 Determination of Epoxide Incorporation by NMR

Epoxide incorporation was determined by ^{1}H NMR integration using the procedure of Durbetaki and Miles.[1] Polymers were dissolved in $CDCl_3$ and ^{1}H NMR spectra were taken using a relaxation delay of 30 seconds. The ratio of alkene protons (δ5.0-5.5 ppm depending on polymer) and epoxide protons (δ2.7-2.9 ppm depending on polymer) were compared via integration. The percentage of epoxide incorporation was calculated using the following formula:

$$Epoxide\,Incorporation = \frac{\int Epoxide\,Protons}{\int Epoxide\,Protons + \int Alkene\,Protons} * 100\% \tag{1}$$

Values are rounded to the nearest percent.

3.2 Polymer Epoxidation

Polymers were epoxidized using the flow setup described in Section 2.2, varying reactor volumes, solvents, concentrations, flow rates, and temperatures as desired for optimization. After collection into the quench, the polymers were isolated by extracting the aqueous layer one to five times using the organic reaction solvent. The combined organic layers were washed with deionized water and saturated aqueous sodium chloride, dried over $MgSO_4$,and then concentrated by rotary evaporation and fully dried under high vacuum. No purification was performed.

4 Further Reaction Data

4.1 Reaction Screening Data

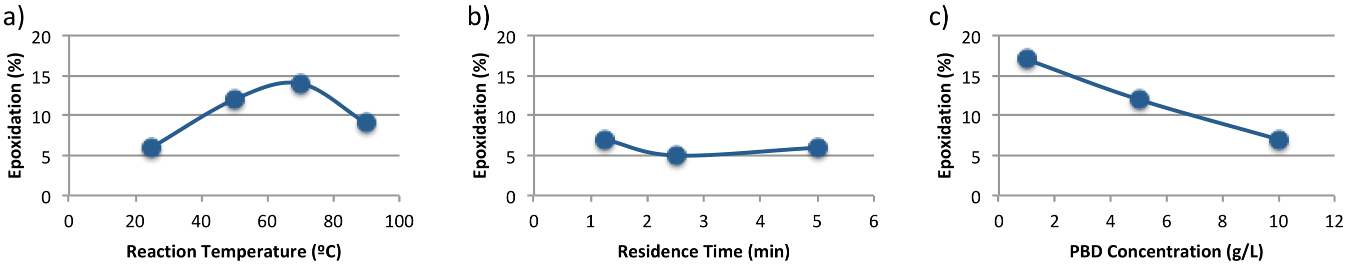


Figure S4 Main text Figure 3, reproduced for convenience. Effect of a) temperature, b) residence time, and c) polymer concentration on epoxide incorporation. Unless otherwise noted, conditions are 25 °C, 5 min t_R, and 10 g/L PBD in EtOAc. Epoxide incorporation calculated by NMR, see Section S3.1 for further experimental details.

Table 1 Full reaction screening data captured in main text Figure 3

Entry	[PBD] (g PBD/L EtOAc)	t_R (min)	Temp (°C)	Epox. (%)
1	10	5	25	6
2	10	5	50	12
3	10	5	70	14
4	10	5	90	9
5	10	2.5	25	5
6	10	1.25	25	7
7	5	1.25	25	12
8	1	1.25	25	17

4.2 Reproducibility

Table 2 Reproducibility data for repeated experiments. Conditions are 70 °C and 10 g/L PBD in EtOAc

Entry	t_R (min)	Epox. (%)
1	5	14
2	5	15
3	5	14
4	10	14

These reactions were run on three separate days using different batches of stock solution. The average epoxidation result is 14±1%.

5 Sample Procedures

5.1 Sample Procedure: Low MW PBD

Low MW PBD was epoxidized as described in section 3.2 using a polymer concentration of 10 g/L LMW PBD in ethyl acetate, a total flow rate of 1 mL/min, a 3:1 ratio of DMDO to polymer solution flow rates, a temperature of 50 °C, a reactor volume of 1 mL, and a residence time of 1 min. Collection for 20 mins (theoretical yield 0.05 g) yielded 0.0445 g (89%) of isolated epoxy-PBD. The polymer was 4% epoxidized, as determined using the procedure from Section 3.1. Spectral and polymer characterization data for this sample can be found in Section 6.1.

5.2 Sample Procedure: High MW PBD

High MW PBD was epoxidized as described in section 3.2 using a polymer concentration of 10 g/L HMW PBD in toluene, a total flow rate of 1 mL/min, a 3:1 ratio of DMDO to polymer solution flow rates, a temperature of 50 °C, a reactor volume of 1 mL, and a residence time of 1 min. Collection for 20 mins (theoretical yield 0.05 g) yielded 0.0404 g (81%) of isolated epoxy-PBD. The polymer was 6% epoxidized, as determined using the procedure from Section 3.1. Spectral and polymer characterization data for this sample can be found in Section 6.2.

5.3 Sample Procedure: PIP

PIP was epoxidized as described in section 3.2 using a polymer concentration of 10 g/L PIP in toluene, a total flow rate of 1 mL, a 3:1 ratio of DMDO to polymer solution flow rates, a temperature of 50 °C, a reactor volume of 1 mL, and a residence time of 1 min. Collection for 20 mins (theoretical yield 0.05 g) yielded 0.0418 g (84%) of isolated epoxy-PIP. The polymer was 7% epoxidized, as determined using the procedure from Section 3.1. Spectral and polymer characterization data for this sample can be found in Section 6.3.

5.4 Sample Procedure: Gram Scale Epoxidation of Low MW PBD

Low MW PBD was epoxidized as described in section 3.2 using the system described in section 2.3 with a polymer concentration of 30 g/L LMW PBD in toluene, a total flow rate of 2 mL/min, a 3:1 ratio of DMDO to polymer solution flow rates, a temperature of 50 °C, a reactor volume of 2 mL, and a residence time of 1 min. Collection for 90 mins (theoretical yield 1.35 g) yielded 1.287 g (95%) of isolated epoxy-PBD. The polymer was 1% epoxidized, as determined using the procedure from Section 3.1.

6 Spectral Data

6.1 Low MW PBD

The sample was prepared as described in Section 5.1. Characterization data matched reported literature values.[1] δ^{1}H(600 MHz, $CDCl_3$): 1.26 (s), 1.42 (br), 1.64 (s), 1.86-2.29 (m), 2.73 (m), 2.93 (s), 5.12-5.67 (m). δ^{13}C(150 MHz, $CDCl_3$): 18.1, 24.3, 27.5, 32.9, 57.0, 129.8. IR ν_{max}/cm^{-1}: 3006, 2923, 2855 (CH); 1717 (C=C). GPC: calculated M_n 4,778 g/mol, M_w 8,766 g/mol, D 1.835.

6.2 High MW PBD

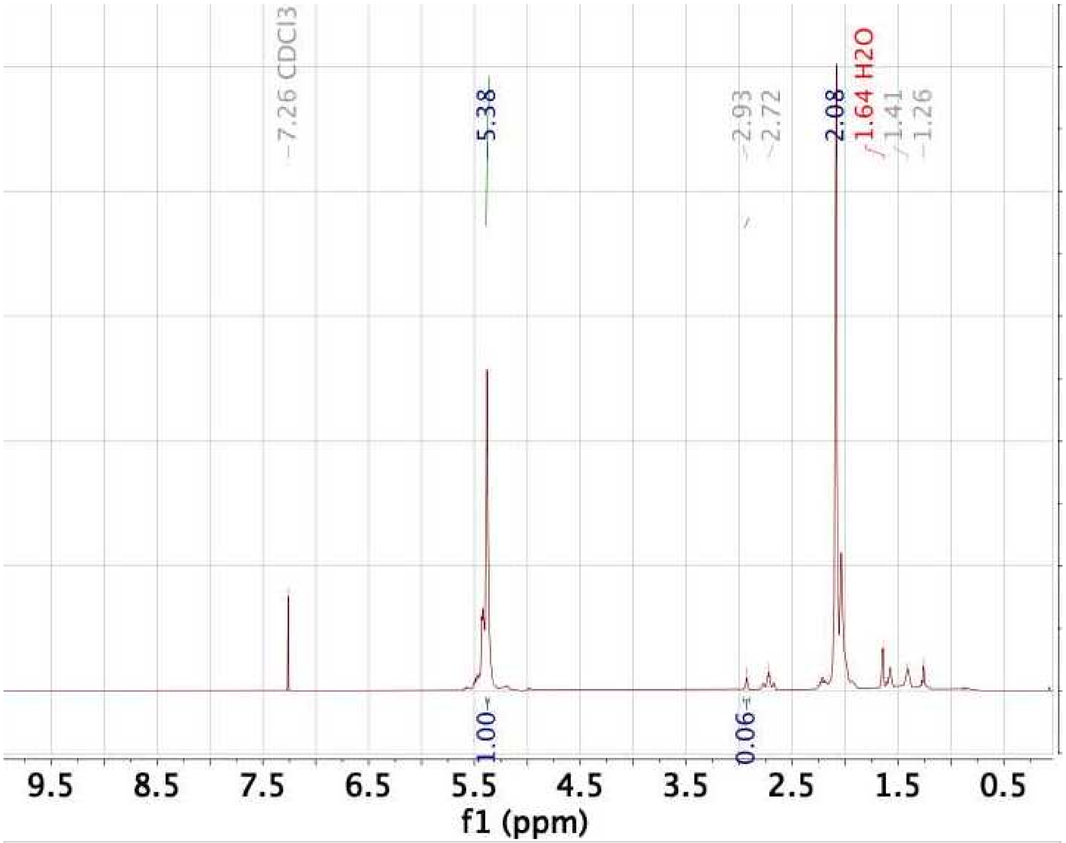
The sample was prepared as described in Section 5.2. Characterization data matched reported literature values.[1] δ^{1}H(600 MHz, $CDCl_3$: 1.25 (s), 1.55 (m), 1.97-2.17 (m), 2.93 (m), 5.24-5.50 (m). δ^{13}C(150 MHz, $CDCl_3$): 27.8, 57.8, 129.9. IR ν_{max}/cm^{-1}: 3006, 2935, 2852 (CH); 1654 (C=C). GPC: calculated M_n 155,562 g/mol, M_w 482,220 g/mol, D 3.100.

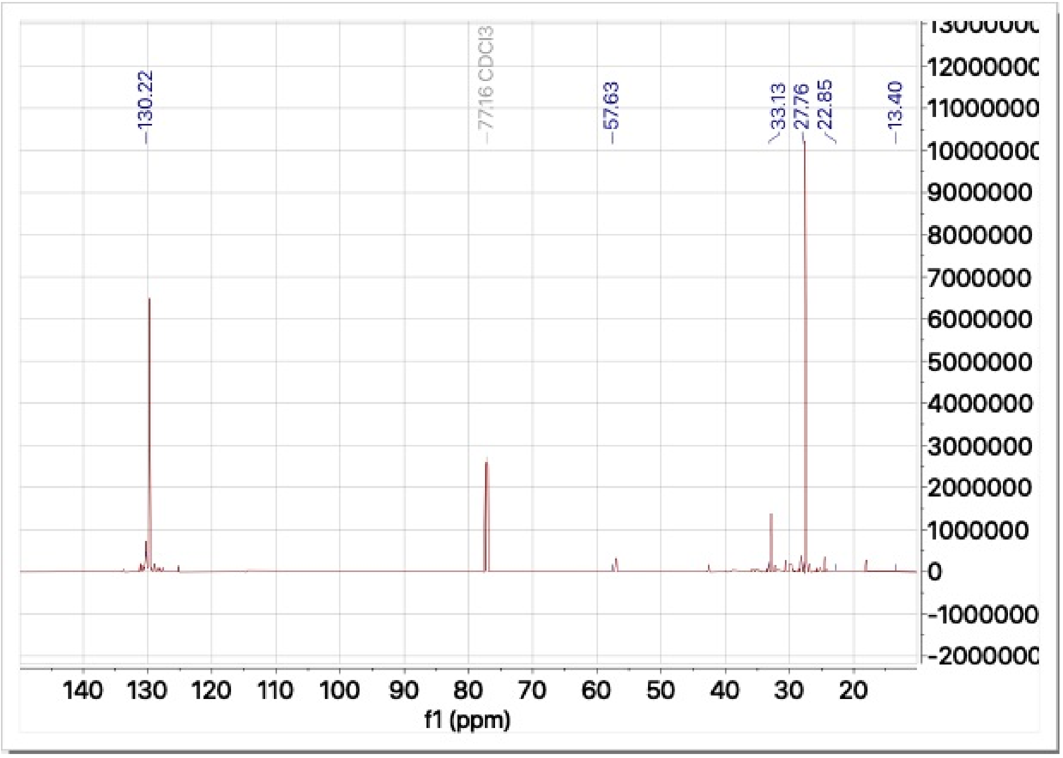
6.3 PIP

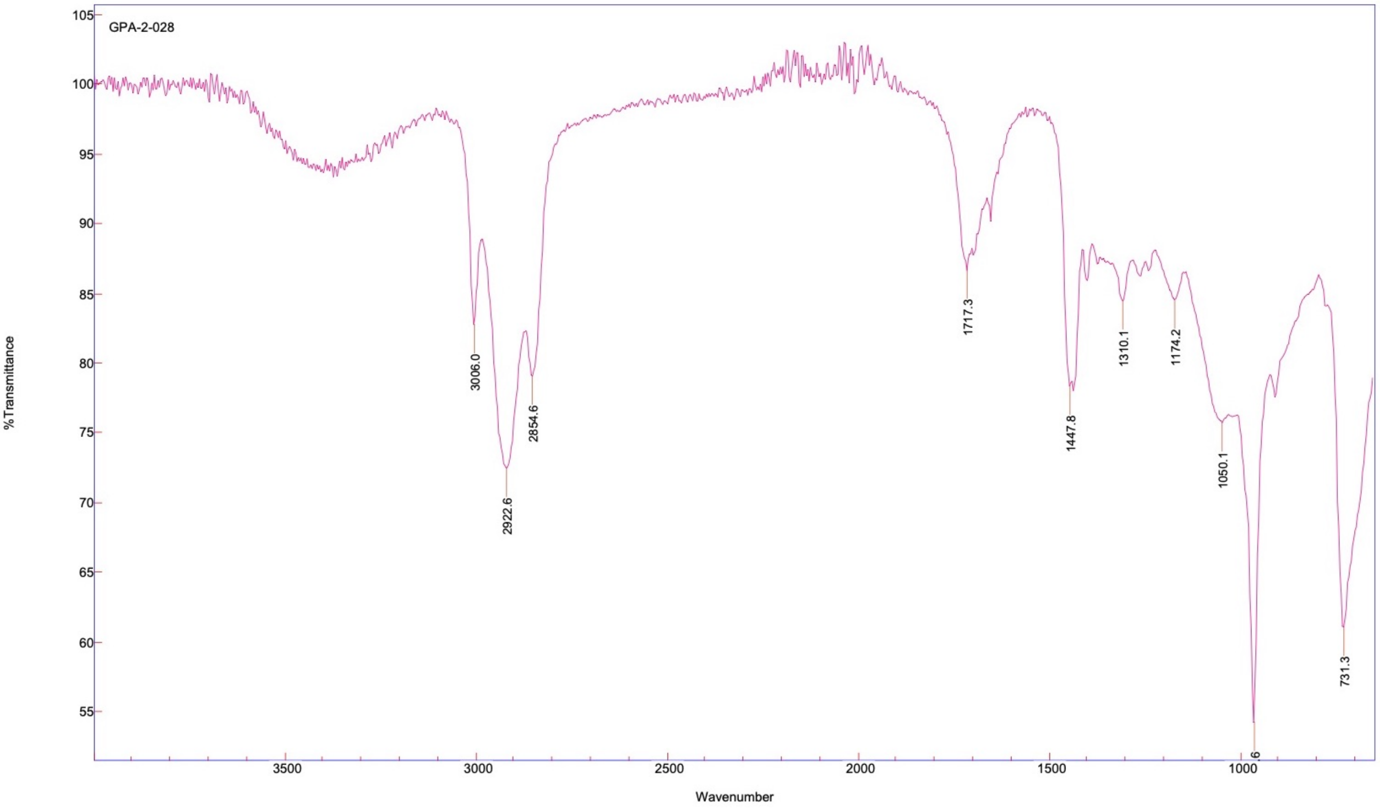
The sample was prepared as described in Section 5.3. Characterization data matched reported literature values.[2] δ^{1}H(600 MHz, $CDCl_3$: 1.26-1.30 (m), 1.50-1.80 (m), 1.84-2.25 (m), 2.70 (m), 4.68 (s), 4.77 (s), 5.04-5.24 (m). δ^{13}C(150 MHz, $CDCl_3$): 23.7, 26.8, 32.5, 65.6, 125.3, 135.4. IR ν_{max}/cm^{-1}: 2961, 2916, 2854 (CH); 1663, 1658 (C=C). GPC: calculated M_n 34,647 g/mol, M_w 52,214 g/mol, D 1.507.

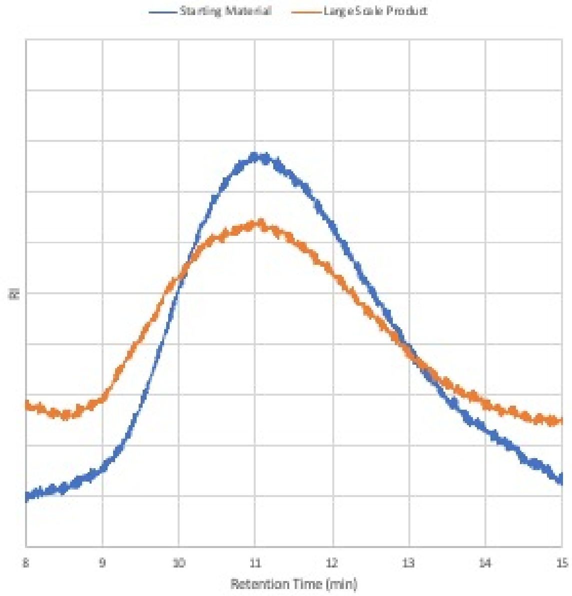
7 Spectra

7.1 Low MW PBD



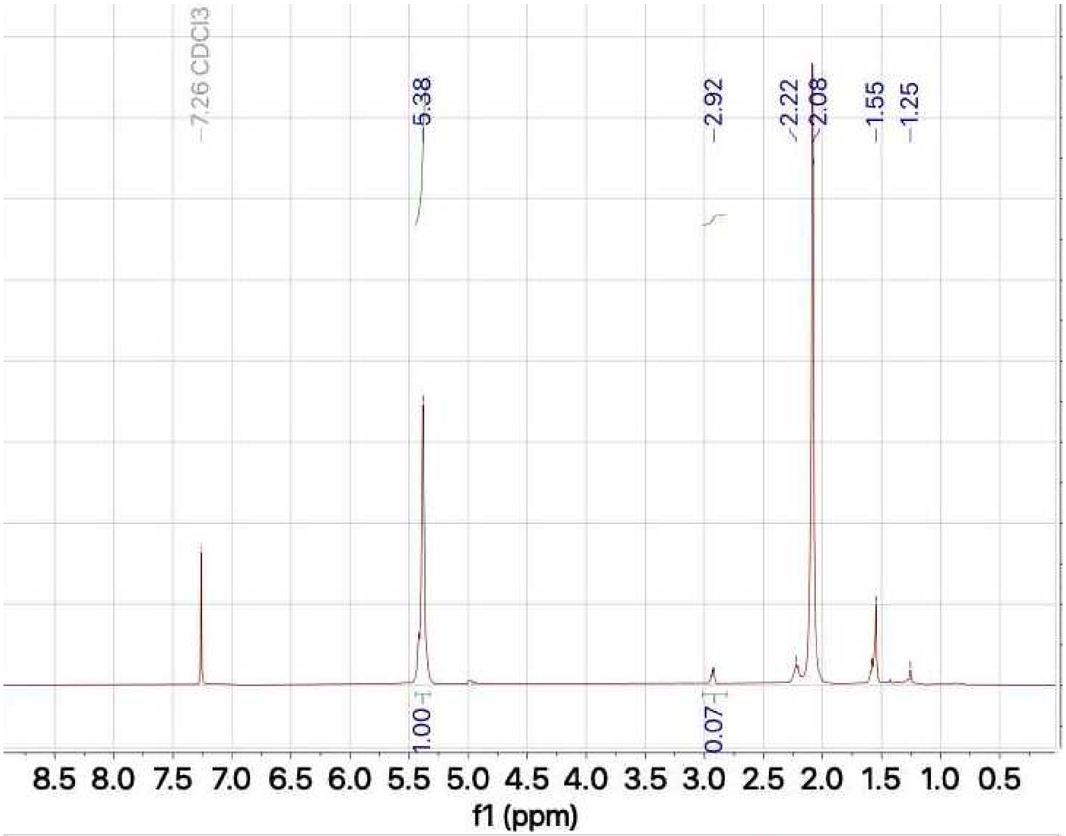


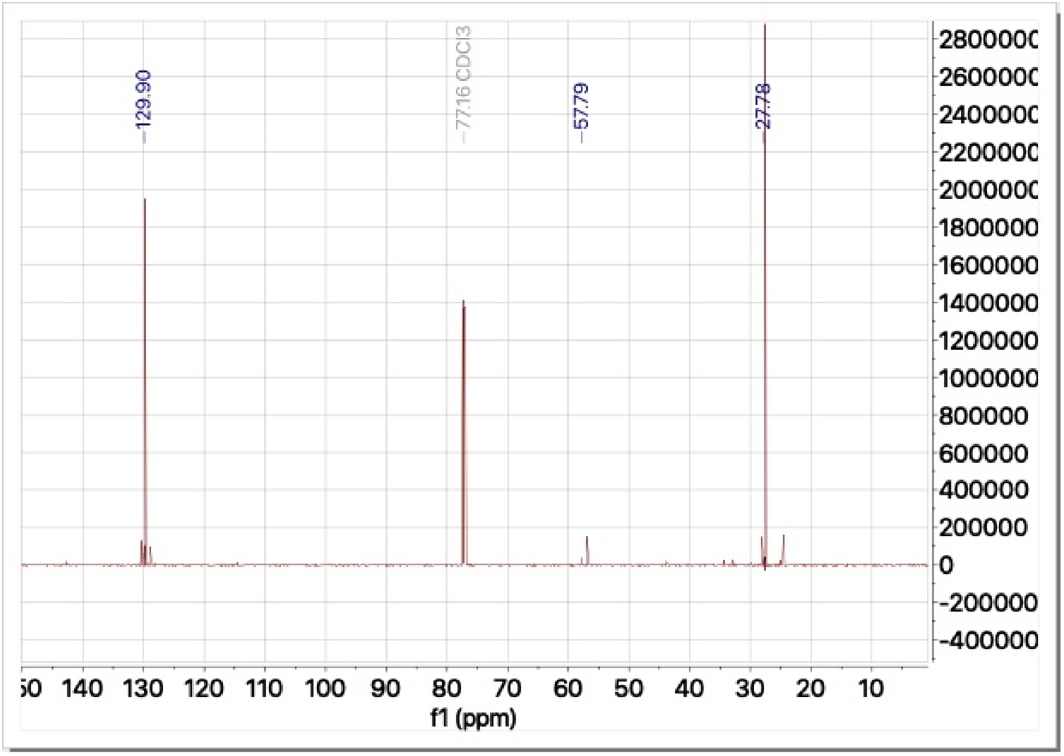


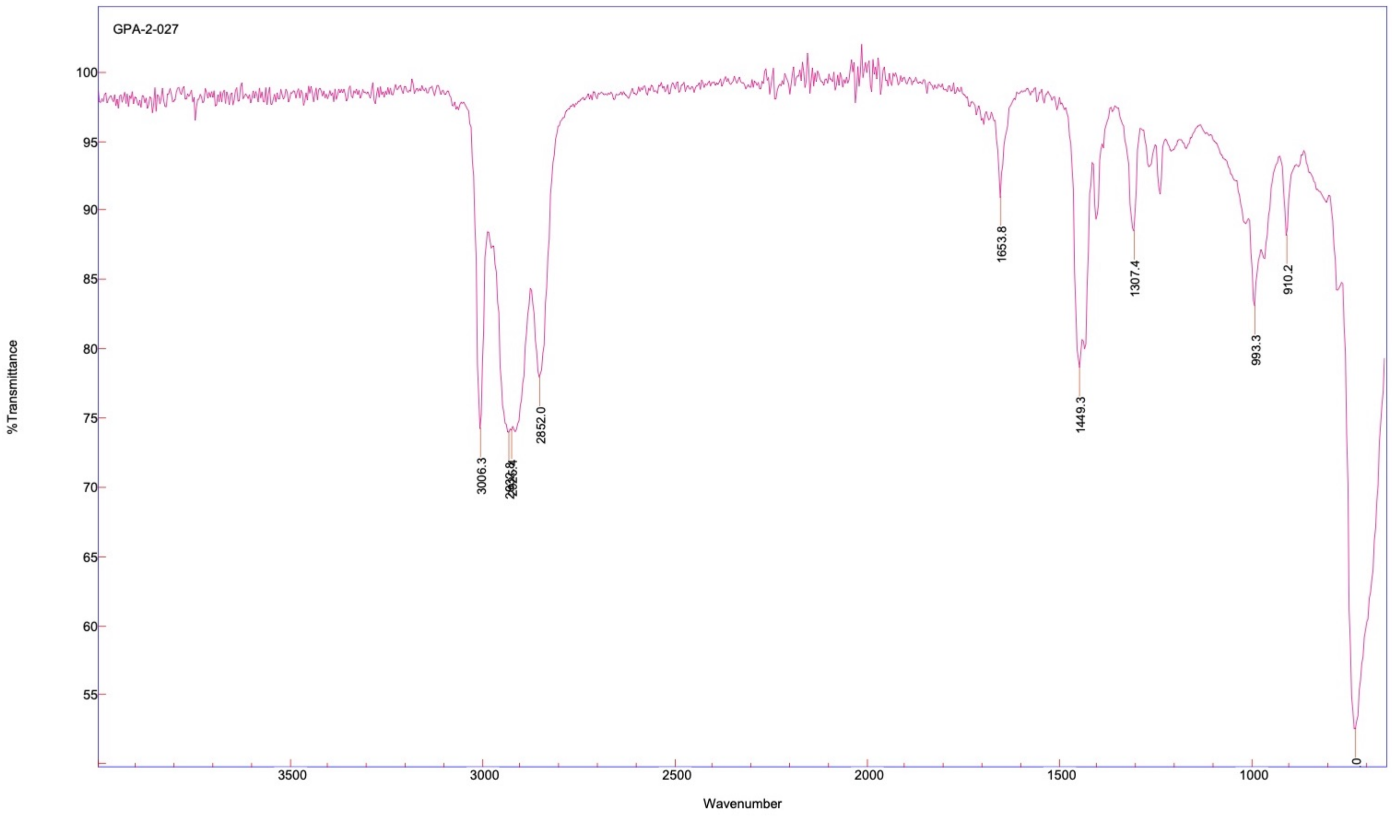


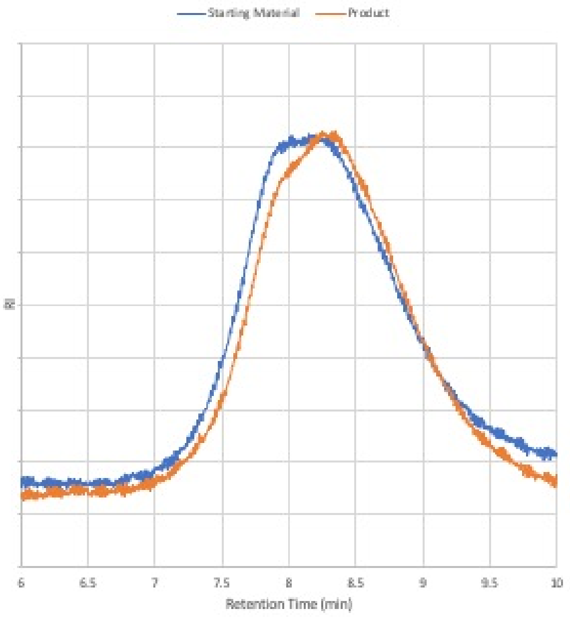
Sample	M_n (g/mol)	M_w (g/mol)	Đ
LMW PBD	3,354	8,708	2.596
Epoxy-LMW PBD	4,778	8,766	1.835

7.2 High MW PBD



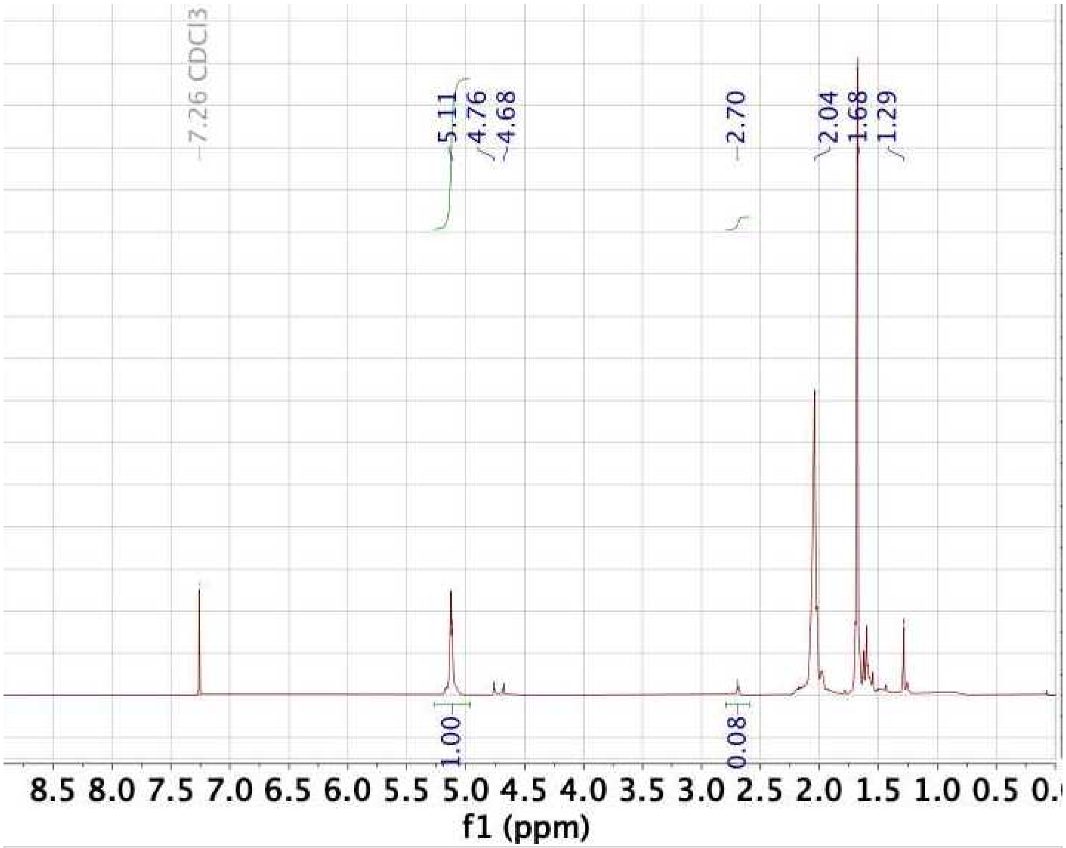




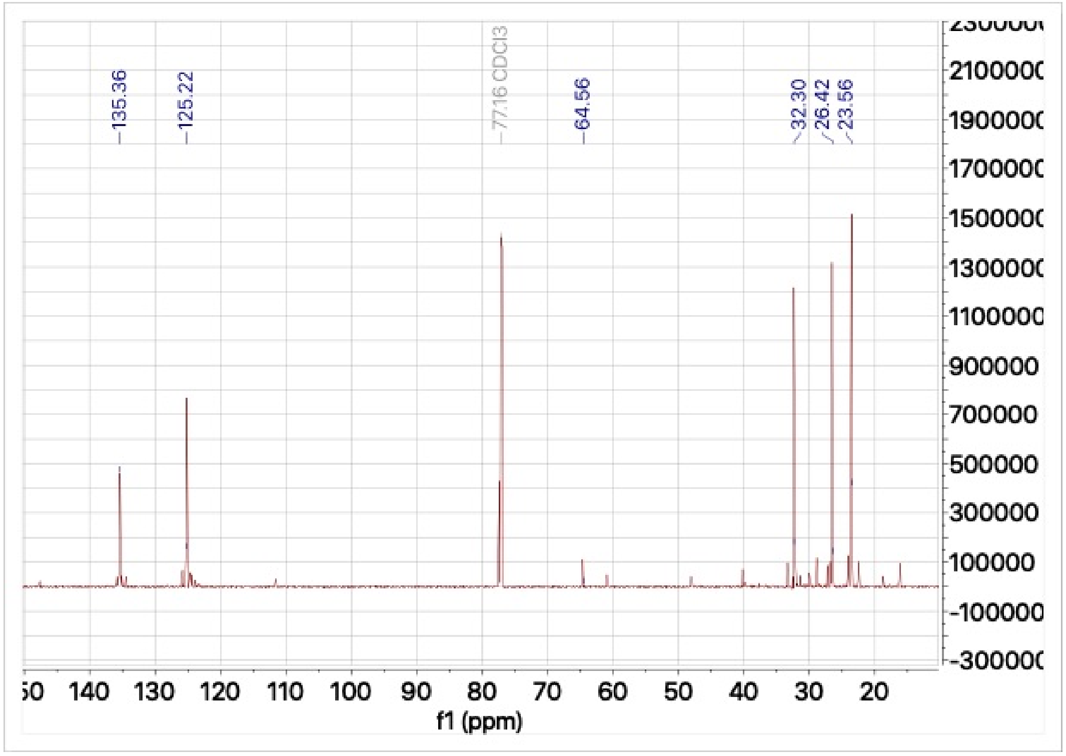


Sample	M_n (g/mol)	M_w (g/mol)	Đ
HMW PBD	181,965	736,887	4.05
Epoxy-HMW PBD	155,562	482,220	3.1

7.3 PIP



7.26 CDCl3
5.11
4.76
4.68
2.70
2.04
1.68
1.29
1.00
0.08
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)



135.36
125.22
77.16 CDCl3
64.56
32.30
26.42
23.56
2100000
1900000
1700000
1500000
1300000
1100000
900000
700000
500000
300000
100000
-100000
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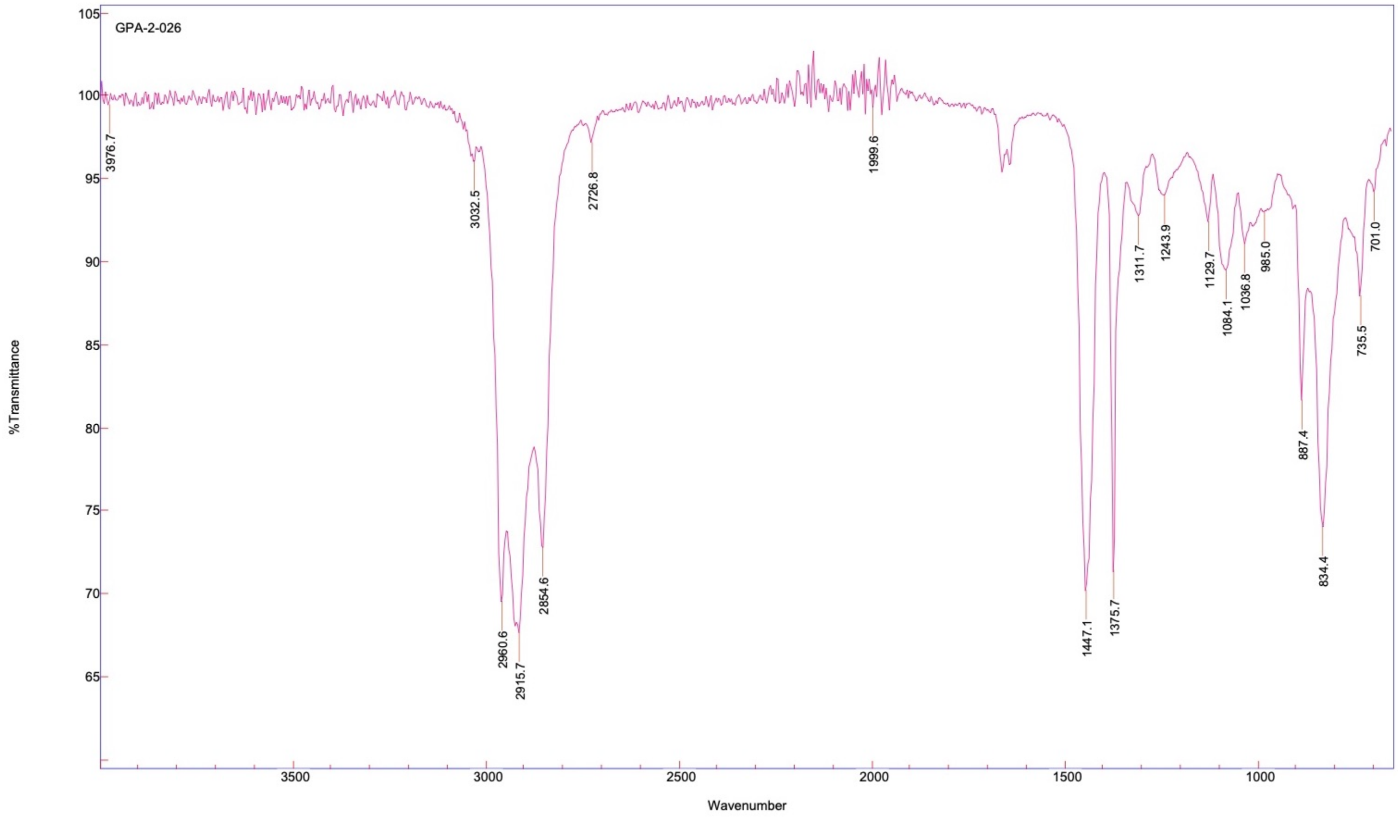
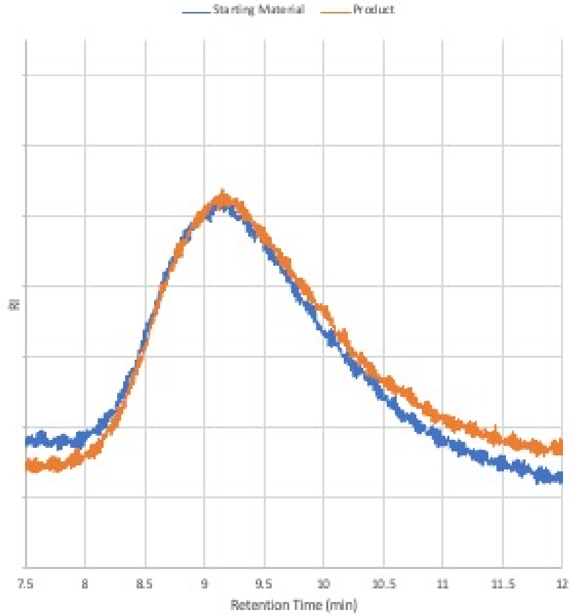
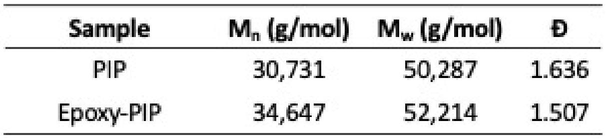
140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)







Sample	M_n (g/mol)	M_w (g/mol)	Đ
PIP	30,731	50,287	1.636
Epoxy-PIP	34,647	52,214	1.507

8 References

1 A. J. Durbetaki and C. M. Miles, *Anal. Chem.*, 1965, **37**, 1231–1235.

2 J. H. Bradbury and M. C. S. Perera, *J. Appl. Polym. Sci.*, 1985, **30**, 3347–3364.