Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supplementary Information

Flow-Facilitated Ring Opening Metathesis Polymerization (ROMP) and Post-Polymerization Modification Reactions

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Contents:

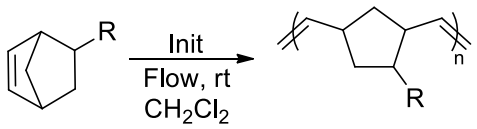
General Considerations and Materials:

All reagents and chemicals were purchased and used as received from commercial sources (Alfa Assar Chemicals, Sigma Aldridge, TCI Chemicals). Pure *exo*-norbornene carboxylic acid was either purchased or prepared according to literature procedures[1] and was utilized to synthesize *exo* isomers of monomers **3**[2], **4**[3], **5**[4] and **6**[2] following previously reported literature methods. Initiator **1** was synthesized according to literature procedures from the commercially-available Grubbs 2nd Generation initiator.[5]

Continuous flow was performed using a dual syringe pump (Harvard Apparatus Model 22) for synthesis of the homopolymers. A monosyringe pump (Cellpoint Scientific Inc.) was utilized in addition to the dual syringe pump to polymerize the block co-polymers and to perform the thio-bromo click reactions under flow conditions. Plastic (laboratory-grade polypropylene and polyethylene) syringes (13 mm diameter) with tubular reaction of 92 cm length polymer tubing (1/16 x 0.04, IDEX Health and Science) were connected to a T-mixer (1/16 in PEEK .040 thru, IDEX Health and Science). Two segments of inlet tubing of 14 cm length was connected to the T-mixer on one end, and the plastic syringes on the other (Figure 1).

^{1}H NMR spectra were recorded on an Oxford NMR 300 instrument, operating at 300 MHz, respectively. Gel Permeation Chromatography (GPC) analysis was conducted on a Viscotek VE 1122 solvent delivery system and VE 3580 RI detector with LT4000L mixed column and molecular weight data were calculated relative to polystyrene standards.

Experimental Procedures:



General Procedure for Continuous Flow Homopolymerizations

To a 6 mL, plastic (laboratory-grade polypropylene and polyethylene) syringe was loaded a solution of monomer (1.5 mmol) in CH_2Cl_2 (4 mL). Another 6 mL syringe was loaded with a solution of **1** (0.0066 mmol) in CH_2Cl_2 (4 mL). The two syringes were then connected to the reaction loop and placed in the syringe pump and subsequently pumped through the reaction loop at either 2 or 6 mL/min, corresponding to a specific residence time (22.5 or 7.5 s, respectively). For experiments performed at 0 ^{o}C, the mixer and reaction tube reactor was submerged in an ice water bath. The product solution was collected in a vial of stirring ethyl vinyl ether (1 mL) and was allowed to stir for a few minutes. % conversions were determined through comparison the integration values of polymeric olefinic signals with those of the monomers in the ^{1}H NMR spectra. Pure product was obtained through solvent precipitation into methanol followed by characterization by ^{1}H NMR and GPC.

*Polymerization of **2**.* Monomer **2** was polymerized according to the general procedure outlined above. Product was isolated in 76 % yield for 7.5 s. Product was isolated in 83 % yield for t_R = 22.5 at 0 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.35-5.25 (m, 1H), 5.2-5.15 (d, 2H), 2.85-2.7 (bs, 2H), 2.5-2.35 (bs, 1H), 1.9-1.7 (bs, 5H), 1.6-1.15 (m, 12H), 1.1-0.9 (bs, 2H). GPC analysis showed M_n = 44,200 g/mol and $Đ$ = 1.18 for t_R = 22.5 s, M_n = 32,000 g/mol and $Đ$ = 1.14 for t_R = 22.5 s at 0 °C, and M_n = 36,500 g/mol and $Đ$ = 1.07 for t_R = 7.5 s.

*Polymerization of **3_{exo}**.* Monomer ***3_{exo}*** was polymerized according to the general procedure outlined above. Product was isolated in 77 % yield for t_R = 7.5 s. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.4-5.1 (m, 2H), 3.7-3.6 (bs, 3H), 3.2-2.9 (m, 1H), 2.8-2.4 (m, 2H), 2.2-1.8 (m, 2H), 1.75-1.43 (bs, 2H), 1.4-1.1 (bs, 2H). GPC analysis showed M_n = 43,400 g/mol and $Đ$ = 1.30 for t_R = 22.5 and M_n = 34,900 g/mol and $Đ$ = 1.11 for t_R = 7.5 s.

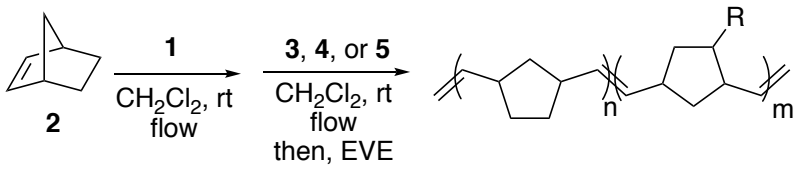
*Polymerization of **$3_{(endo/exo)}$**.* Monomer ***$3_{(endo/exo)}$*** was polymerized according to the general procedure outlined above. Product was isolated in 40 % yield for t_R = 22.5 s. Product was isolated in 45 % yield for t_R = 7.5 s. GPC analysis showed M_n = 11,000 g/mol and $Đ$ = 1.67 for t_R = 22.5 and M_n = 22,000 g/mol and $Đ$ = 1.57 for t_R = 7.5 s.

*Polymerization of **4**.* Monomer **4** was polymerized according to the general procedure outlined above. Product was isolated in 86 % yield for t_R = 7.5 s ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38-5.05 (m, 5H), 3.8-3.3 (m, 12H), 2.9-2.65 (bs, 2H), 2.6-2.3 (bs, 2H), 2.25-2.1 (bs, 1H), 1.95-1.65 (bs, 6H), 1.6-1.35 (bs, 10H), 1.3-1.2 (m, 1H). GPC analysis showed M_n =54,000 g/mol and $Đ$ = 1.16 for t_R = 22.5 and M_n = 68,300 g/mol and $Đ$ = 1.18 for t_R = 7.5 s.

*Polymerization of **5**.* Monomer **5** was polymerized according to the general procedure outlined above. Product was isolated in 93 % yield for t_R = 7.5 s. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.4-5.1 (bs, 2H), 4.45-4.3 (m, 1H), 4.25-3.9 (m, 2H), 3.0-2.8 (bs, 1H), 2.65-2.4 (m, 1H), 2.1-1.8 (m, 4H), 1.4-1.05 (m, 3H). GPC analysis showed M_n = 44,000 g/mol and $Đ$ = 1.33 for t_R = 22.5 and M_n = 45,200 g/mol and $Đ$ = 1.12 for t_R = 7.5 s.

*Polymerization of **6**.* Monomer **6** was polymerized according to the general procedure outlined above. Product was isolated in 76 % yield for t_R = 450 s. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.65-5.5 (bs, 2H), 5.23 (m, 1H), 5.15-5.0 (s, 2H), 4.7 (s, 1H), 3.8-3.6 (s, 10H), 3.5-3.0 (s, 3H), 1.7-1.5 (s, 7H), 1.4-1.25 (bs, 1H). GPC analysis showed and M_n = 52,000g/mol and $Đ$ = 1.24 for t_R = 450 s.

General Procedure for Continuous Flow Copolymerizations



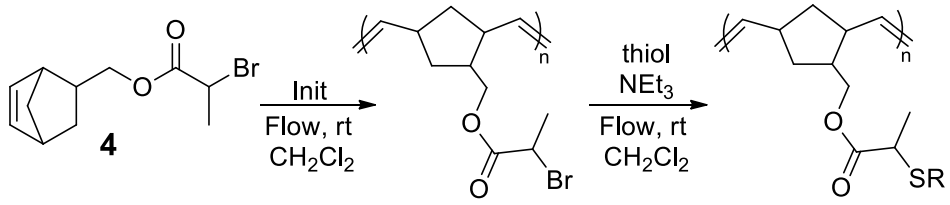
To a 6 mL plastic (laboratory-grade polypropylene and polyethylene) syringe was loaded a solution of norbornene (**2**) (0.66 mmol) in CH_2Cl_2 (2 mL). Another 6 mL syringe was loaded with a solution of **1** (0.0066 mmol) in CH_2Cl_2 (2 mL). Those two syringes were then connected to the first segment of reaction loop. A third 6 mL syringe was loaded with a solution of **3**, **4**, or **5** (0.66 mmol) and connected to the inlet tubing of the second segment of reaction loop and placed in the monosyringe pump. The reaction solution of **1** and **2** was pumped through the first segment of reaction loop at 2 mL/ min until the solution reached the second T-mixer, at which point the monosyringe pump was turned on at a rate of 2 mL/min. The product solution was collected in a vial of stirring ethyl vinyl ether (1 mL) and was allowed to stir for a few minutes. % conversions were determined through comparison the integration values of polymeric olefinic signals with those of both monomers in the ^{1}H NMR spectra. Pure product was obtained through solvent precipitation into methanol followed by characterization by ^{1}H NMR and GPC.

*Copolymerization of norbornene and **3***. Monomer **3** and norbornene were polymerized according to the general procedure outlined above. Product was isolated in 78 % yield for t_R = 22.5 for each loop. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.4-5.05 (m, 2H), 3.7-.55 (bs, 2H), 3.2-2.9 (bs, 1H), 2.9-2.3 (m, 2H), 2.1-1.45 (m, 4H), 1.4-0.8 (m, 3H). GPC analysis showed M_n = 35,600 g/mol and $Đ$ = 1.21.

*Copolymerization of norbornene and **4*** Monomer **4** and norbornene were polymerized according to the general procedure outlined above. Product was isolated in 71 % yield for t_R = 22.5 for each loop. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.4-5.1 (m, 2H), 3.8-3.35 (m, 1H), 2.9-2.7 (bs, 1H), 2.65-2.1 (m, 1H), 2.0-1.65 (bs, 3H), 1.6-1.2 (m, 2H). GPC analysis showed M_n = 44,500 g/mol and $Đ$ = 1.25.

*Copolymerization of norbornene and **5***. Monomer **5** and norbornene were polymerized according to the general procedure outlined above. Product was isolated in 80 % yield for t_R = 22.5 for each loop. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.4-5.15 (m, 2H), 4.5-4.3 (m, 2H), 4.25-4.15 (m, 2H), 2.9-2.7 (bs, 2H), 2.6-2.3 (bs, 1H), 2.1-1.5 (bs, 18 H), 1.4-1.1 (m, 7H). GPC analysis showed M_n = 43,600 g/mol and $Đ$ = 1.27.

General Procedure for Continuous Flow ROMP and Thio-Bromo Click Reactions



To a 6 mL plastic (laboratory-grade polypropylene and polyethylene) syringe was loaded a solution of monomer **5** (1.5 mmol) in CH_2Cl_2 (2 mL). Another 6 mL syringe was loaded with a solution of **1** (0.0066 mmol) in CH_2Cl_2 (2 mL). Those two syringes were then connected to the first segment of reaction loop. A third 6 mL syringe was loaded with a solution of thiol (4.5 mmol) and triethylamine (4.5 mmol) in sufficient THF to create a total 2 mL volume (0.66 mmol) that was then connected to the inlet tubing of the second segment of reaction loop and placed in the monosyringe pump. The Monomer **5** and **1** solution were pumped through the first segment of reaction loop at 2 mL/ min until the solution reached the second T-mixer at which point the monosyringe pump was turned on at a rate of 2 mL/min. The product solution was collected in a vial of stirring ethyl vinyl ether (1 mL) and was allowed to stir for a few minutes. % conversions were determined through comparison the integration values of polymeric olefinic signals with those of the monomers as well as the signal associated with the bromo ester (Figure S3) in the ^{1}H NMR spectra. Pure product was obtained through solvent precipitation into methanol followed by characterization by ^{1}H NMR and GPC. The product solution was collected in a vial. % conversions were determined through comparison the integration values of polymeric olefinic signals with those of the monomers in the ^{1}H NMR spectra. Pure product was obtained through solvent precipitation into methanol followed by characterization by ^{1}H NMR and GPC.

Thio-Bromo Click reaction of **7**. Monomer **5** was polymerized according to the general procedure outlined above, then reacted with thiol **7**. Product was isolated in 78 % yield for t_R = 22.5. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.5–7.3 (d, J 5 6.07 Hz, 1H), 7.3–7.18 (s, 2H), 5.5–5.0 (m, 2H), 4.42– 4.27 (t, J 5 71.79 Hz, 1H), 3.6–3.4 (s, 2H), 3.03–2.16 (m, 1H), 2.04–0.9 (m 5H). GPC analysis showed M_n = 43,200 g/mol and $Đ$ = 1.21.

Thio-Bromo Click reaction of ***8***. Monomer **5** was polymerized according to the general procedure outlined above, then reacted with thiol **8**. Product was isolated in 82 % yield for t_R = 22.5. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48–7.3 (d, J 5 22.18 Hz, 1H), 7.2–7.0 (s, 1H), 5.38–5.08 (m, 1H), 4.13–3.71 (d, J 5 36.03Hz 1H), 3.78–3.6 (s, 1H), 3.58–3.42 (s, 4H), 3.02–2.5 (m, 3H), 2.08–0.91 (m, 7H). GPC analysis showed M_n = 48,100 g/mol and $Đ$ = 1.22.

Thio-Bromo Click reaction of ***9***. Monomer **5** was polymerized according to the general procedure outlined above, then reacted with thiol **9**. Product was isolated in 74 % yield for t_R = 22.5. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.5–7.3 (s, 1H), 5.49–5.1 (m, 9H), 4.3–3.8 (m, 13H), 3.6–3.57 (m, 3H), 3.5–3.414 (m, 13H), 3.37-3.239 (m, 3H), 3.13–2.69 (m, 5H), 2.6–

2.24 (m, 4H), 2.10–1.53 (m, 12H), 1.52–1.38 (m, 9H), 1.36–1.04 (m, 18H). GPC analysis showed M_n = 40,000 g/mol and $Đ$ = 1.21.

Control experiment for thio-bromo click modifications. As observed in Table 4, M_n values for polymers **7**-**9** were much lower than expected. Initially, it was thought that this may have arisen as an effect that either thiol, triethylamine, or THF (or a combination of these) may have on the polymerization of the unreacted monomer remaining after reactor 1. To investigate this, a control reaction was performed. This involved the preparation and isolation of **5** (according to the ***General Procedure for Continuous Flow Homopolymerizations*** *using a t_R of 22.5 s*) prior to the click modification. This polymer was quenched, isolated, and analyzed by GPC (M_n = 48,000 Da, $Đ$ = 1.30). Then, a CH_2Cl_2 solution (1 mL) of **5** (0.198 g, 0.76 mmol) was then loaded into a 6-mL plastic syringe. Another 6 mL syringe was loaded with a THF solution (1 mL) of thiocresol (0.29 g, 2.29 mmol) and triethylamine (0.32 mL, 2.29 mmol). The two syringes were then connected to the reaction loop and placed in the syringe pump and subsequently pumped through the reaction loop at 2 mL/min, corresponding to a residence time of 22.5 s. The product solution was collected in a vial. % conversions were determined through comparison the integration values of polymeric olefinic signals with those of the monomers in the ^{1}H NMR spectra. Pure product was obtained through solvent precipitation into methanol followed by characterization by ^{1}H NMR and GPC. GPC analysis found this polymer to exhibit M_n and $Đ$ values of 44,000 Da and 1.25; a shift to a higher-molecular weight species is not apparent in this case. So, GPC cannot be used as an accurate analytical technique to quantify the extent of modification in this case. This could possibly result from differences in the hydrodynamic radii of the polymers as well as the limits to the sensitivity of the GPC instrument available to us. This deviation from expectations is not an uncommon problem when differentiating between materials with only slight differences in molecular weights, especially in post-polymerization modifications.[6-8] However, confirmation of successful reaction was ascertained by ^{1}H NMR.

Tables/Figures:

Figure S1*. Experimental set-up for continuous flow reactions.*

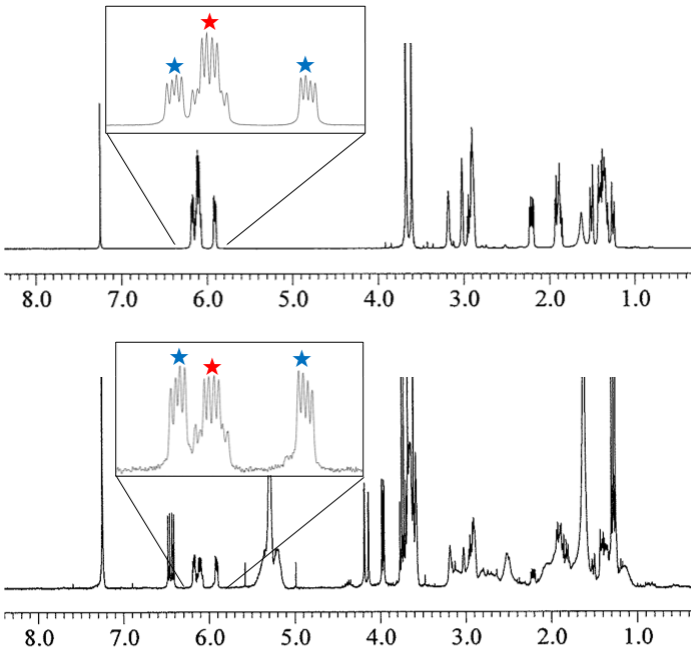


Figure S2*. Photograph showing partial ^{1}H NMR spectra of the commercially-available exo/endo monomer **3** (top) and the crude spectrum after polymerization (bottom). The olefin regions have been blown up and labeled to show changes in exo (red star) and endo (blue stars) signals.*

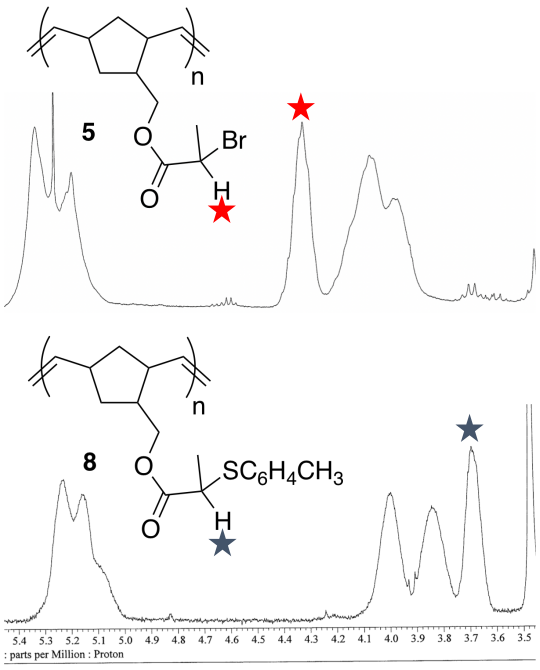


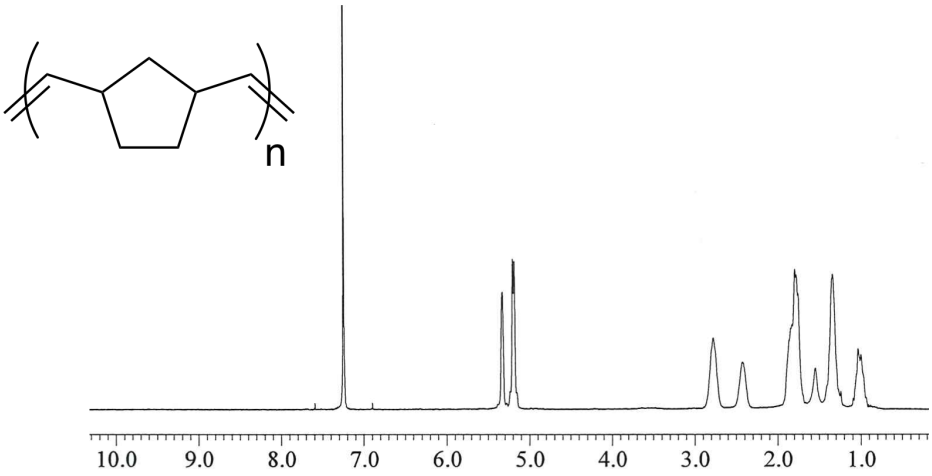
Figure S3. *Photograph showing partial ^{1}H NMR spectra of polymer **5** before and after thio-bromo click modification.*

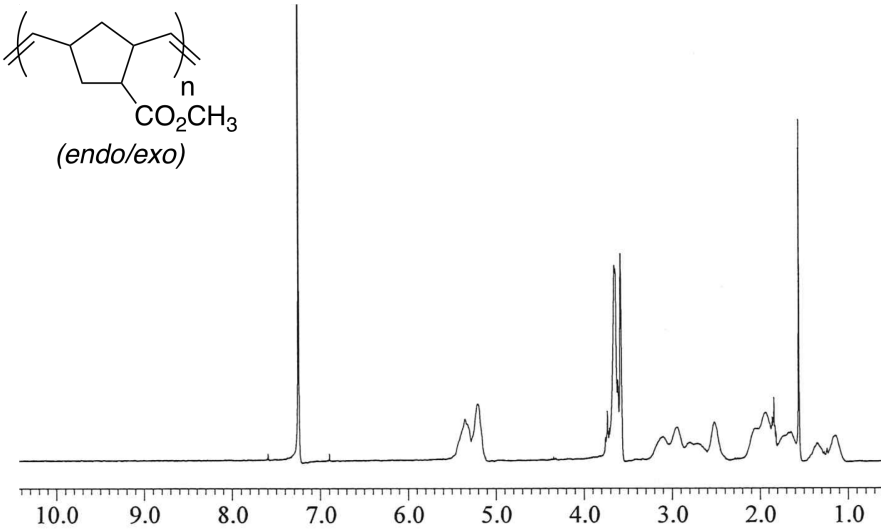
Table S1. *Homopolymerizations of exo monomers **3**-**5** at 0 °C.*

Entry[a]	*Mon.*	*Conv. (%)*[b]	$M_{n(theor.)}$ *(Da)*	M_n *(Da)*[c]	$Đ$ [c]
1	***3***	*89*	*34,547*	*19,400*	*1.65*
2	***4***	*87*	*63,678*	*22,100*	*1.77*
3	***5***	*70*	*58,825*	*28,800*	*1.61*

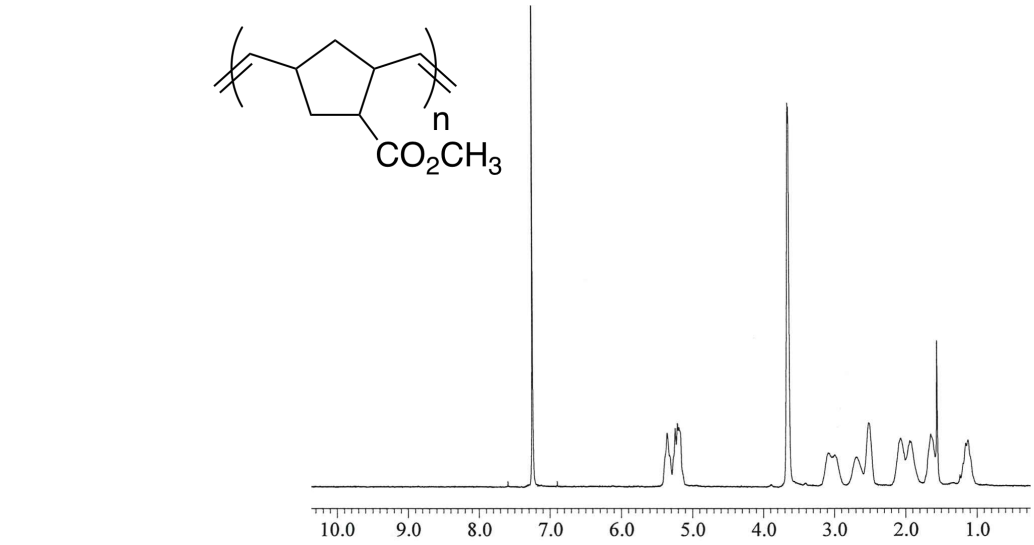
[a]*Conditions: M:**1** = 227:1, $[M]_o$ = 0.38 M, $[\mathbf{1}]_o$ = 0.0017 M, t_R = 22.5 s, tubular path length = 92 cm.*
[b]*Determined by ^{1}H NMR.* [c] *Determined by GPC.*

^{1}H NMR spectra:





(endo/exo)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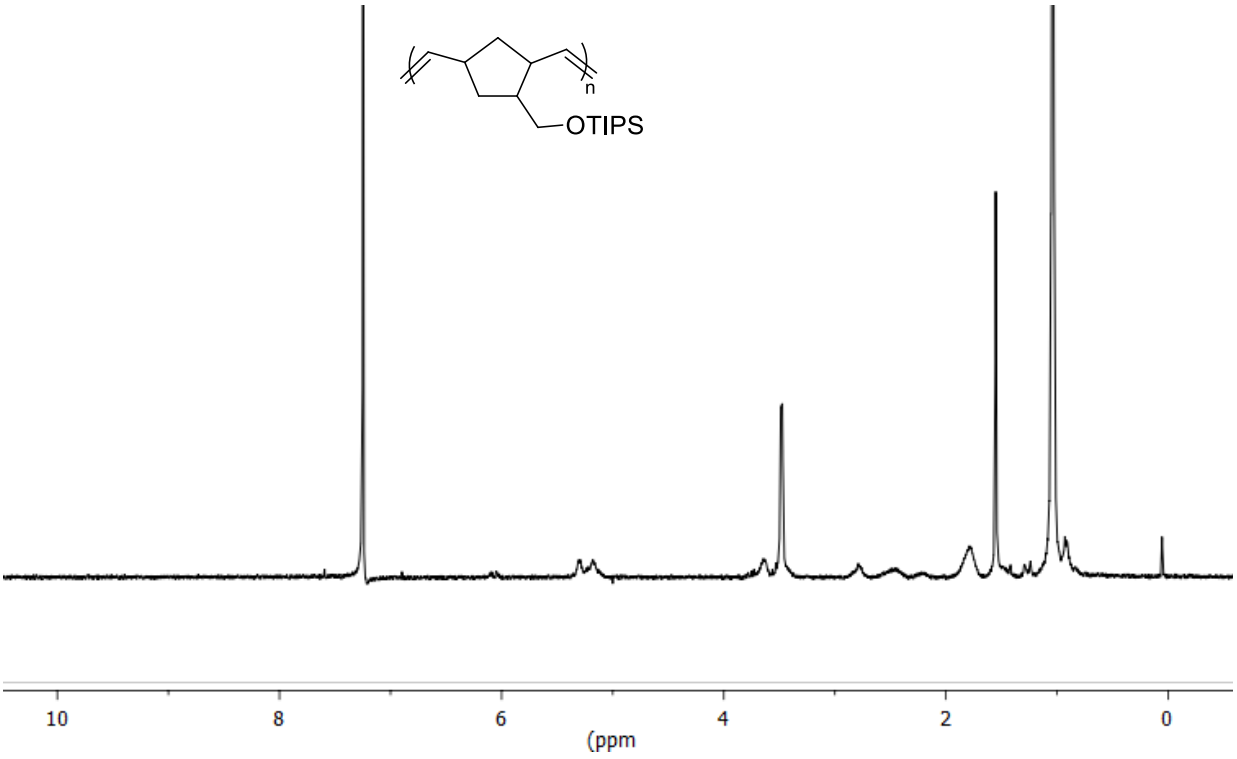
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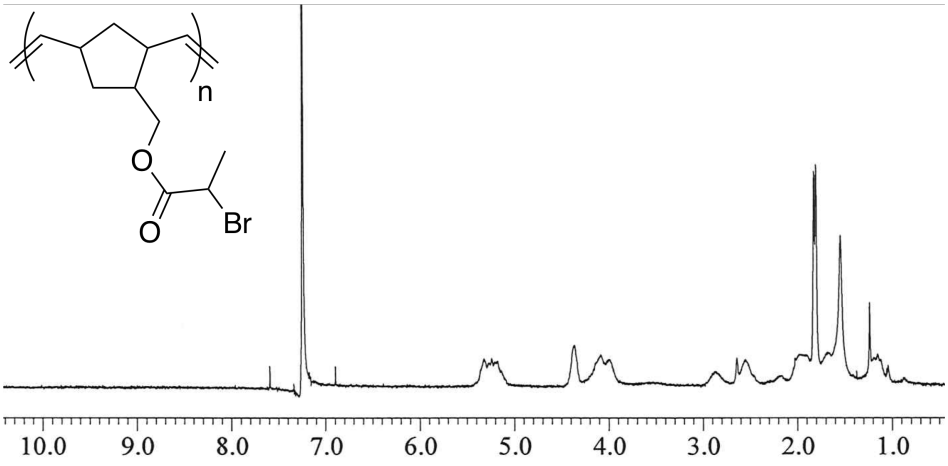
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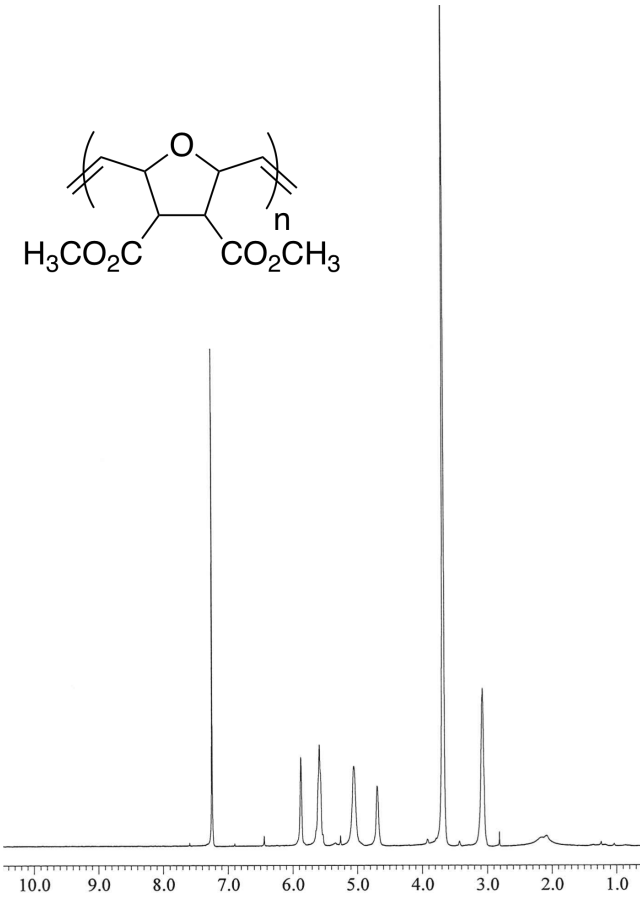
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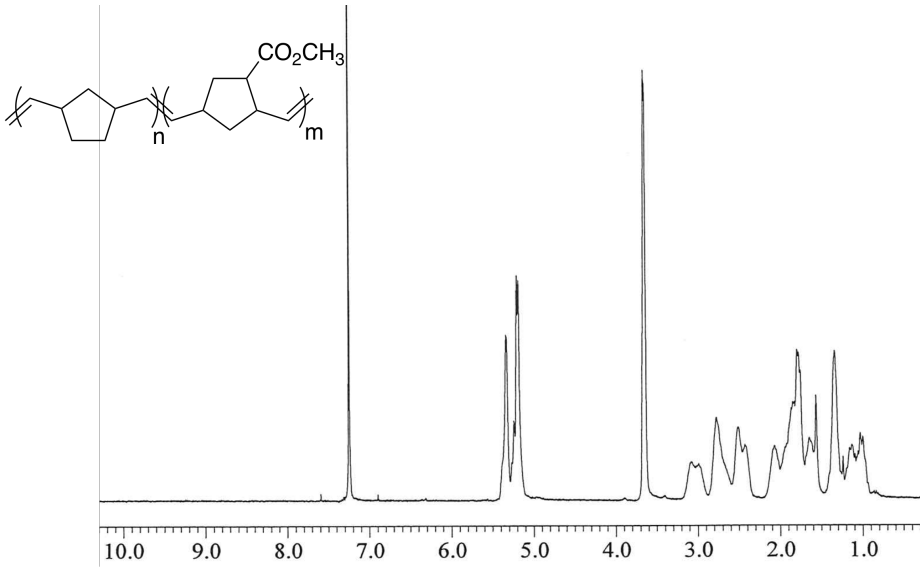
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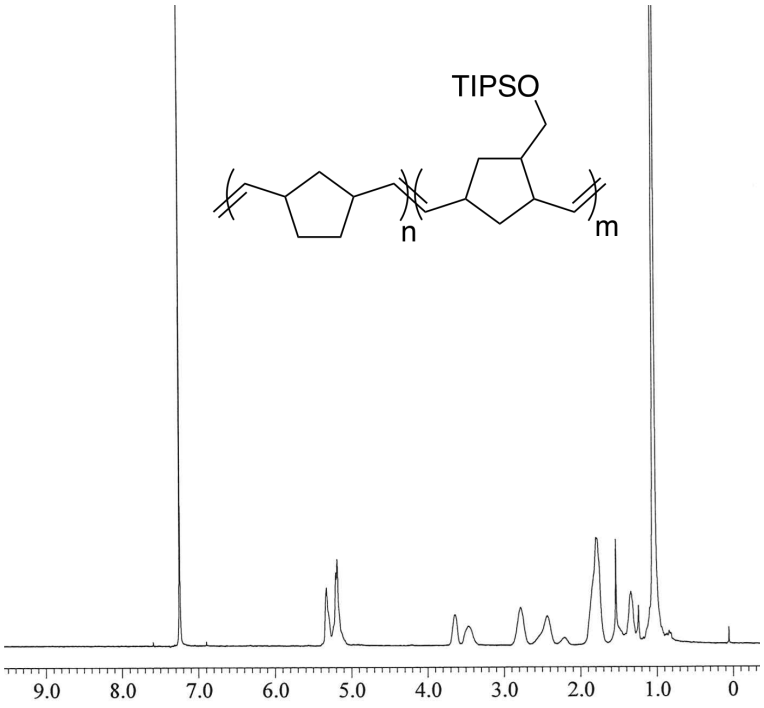
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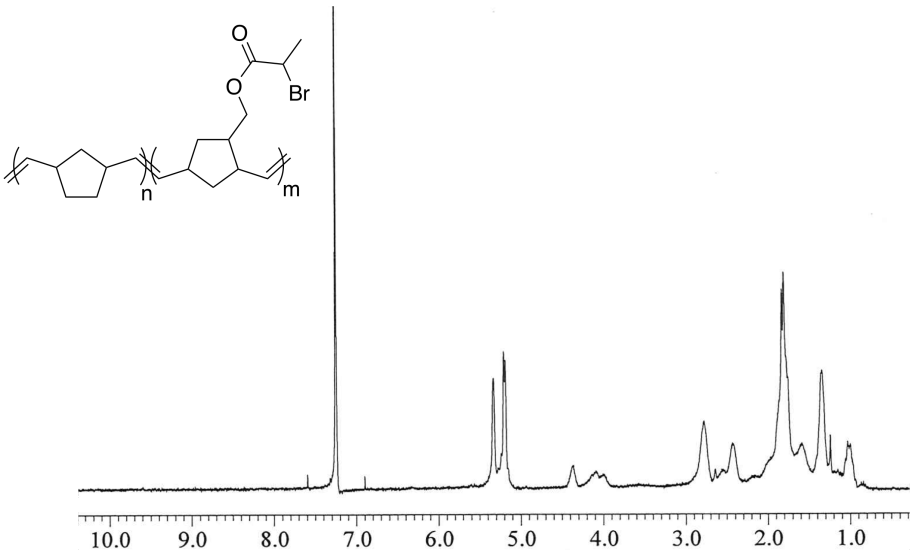
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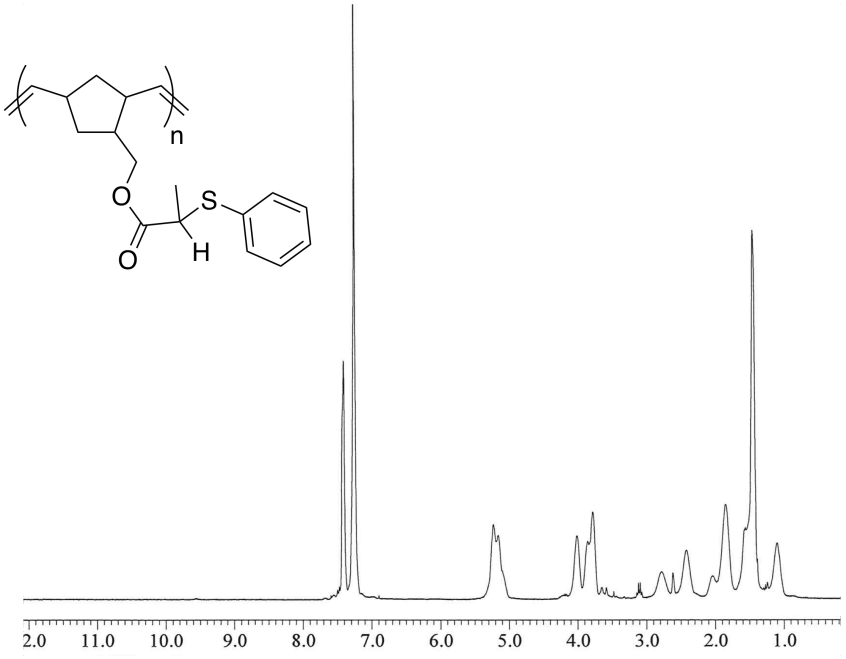
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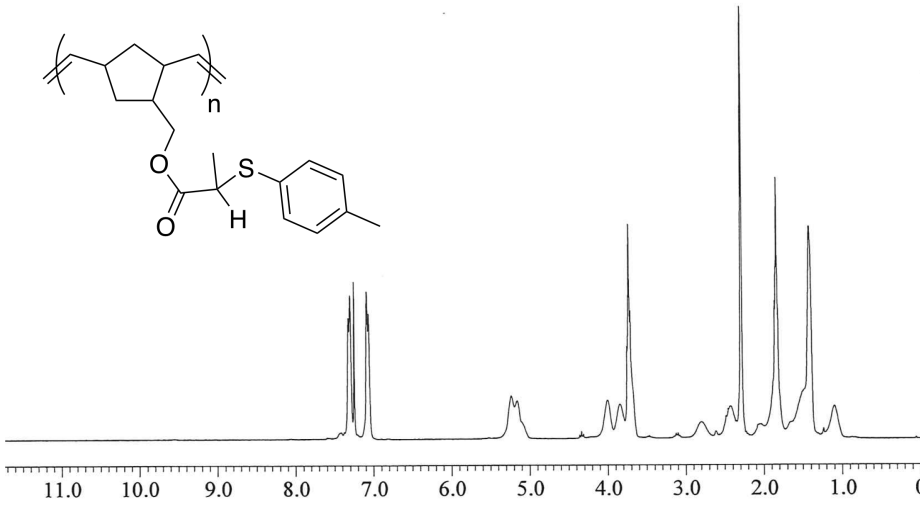
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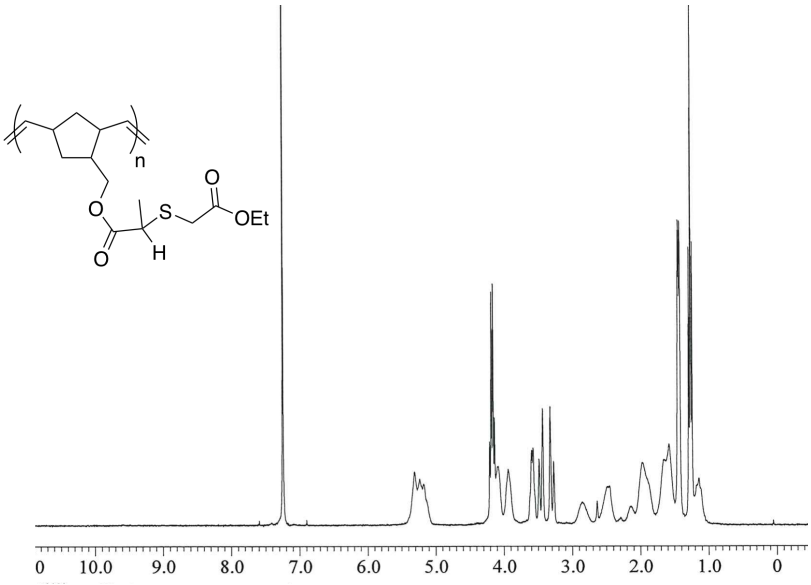
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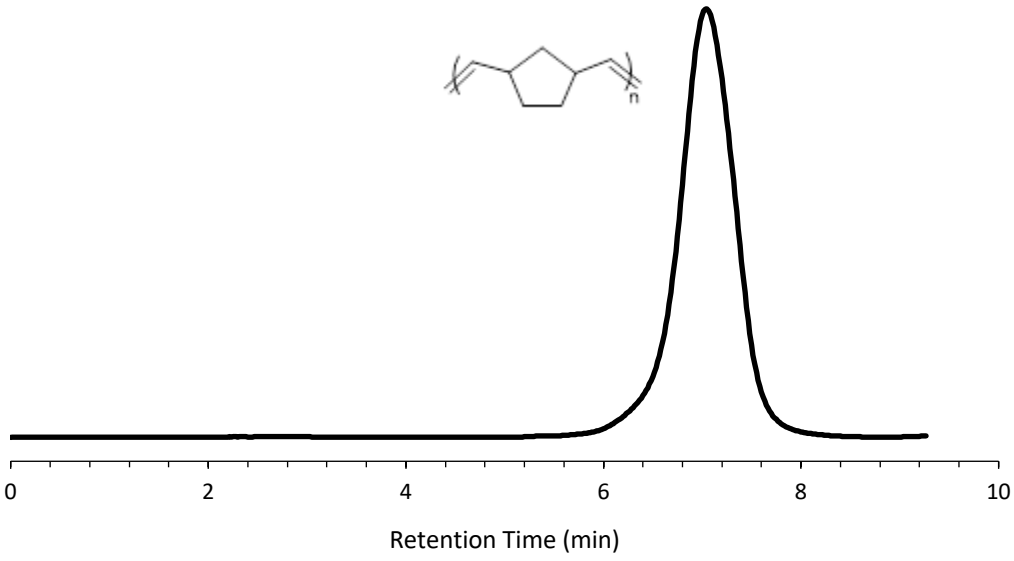
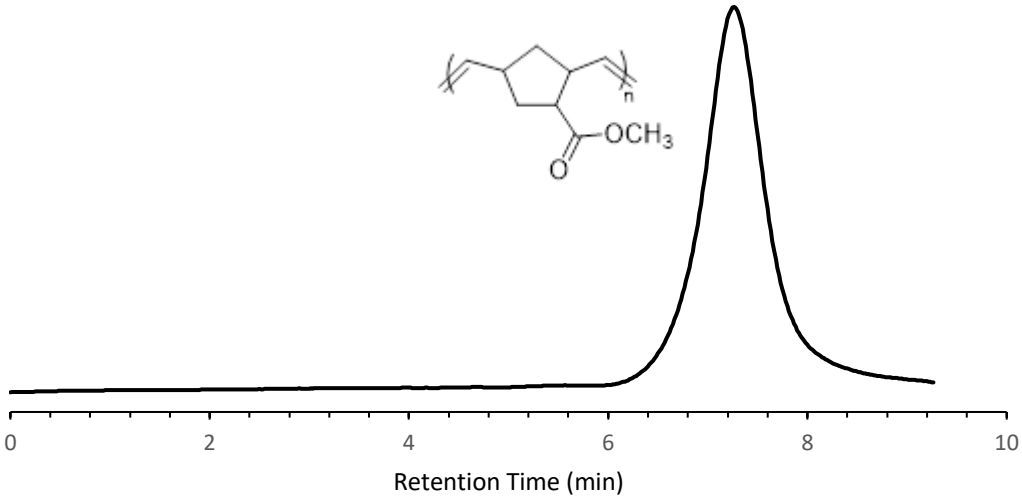
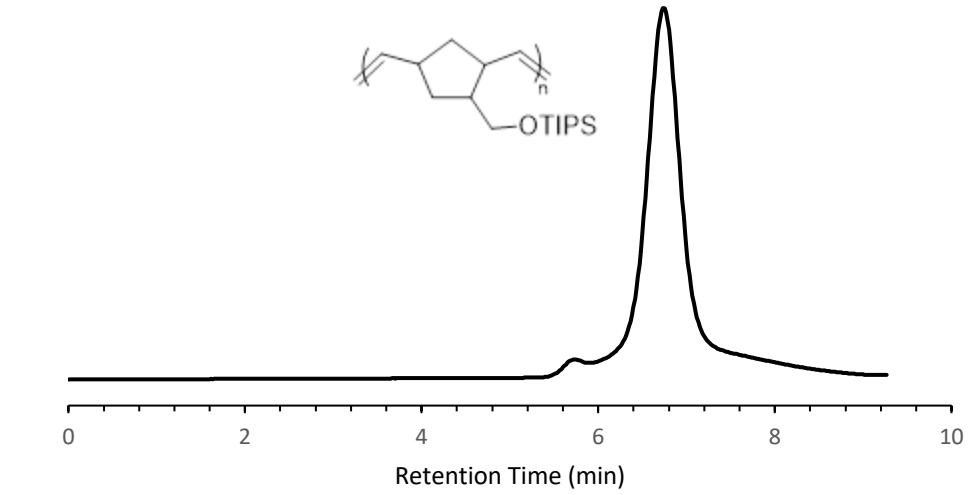
GPC traces for homopolymers:



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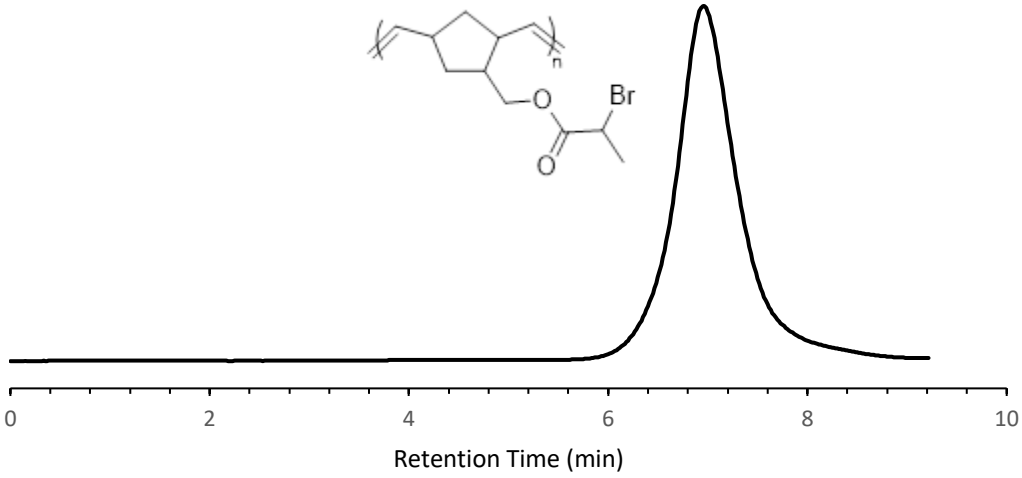
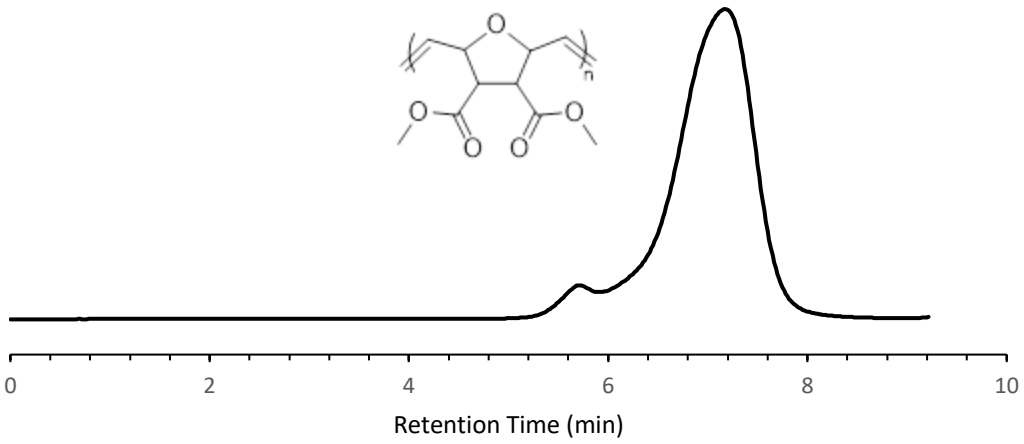
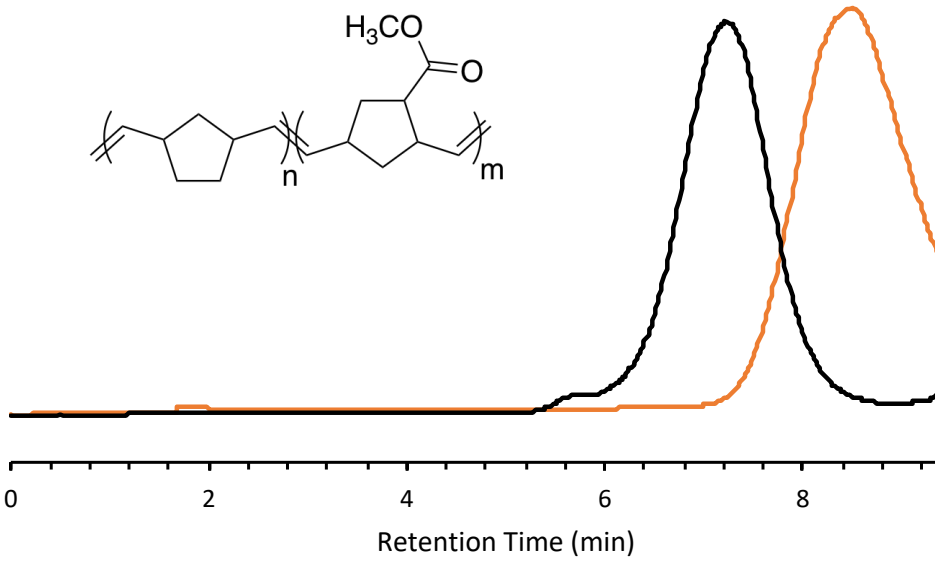
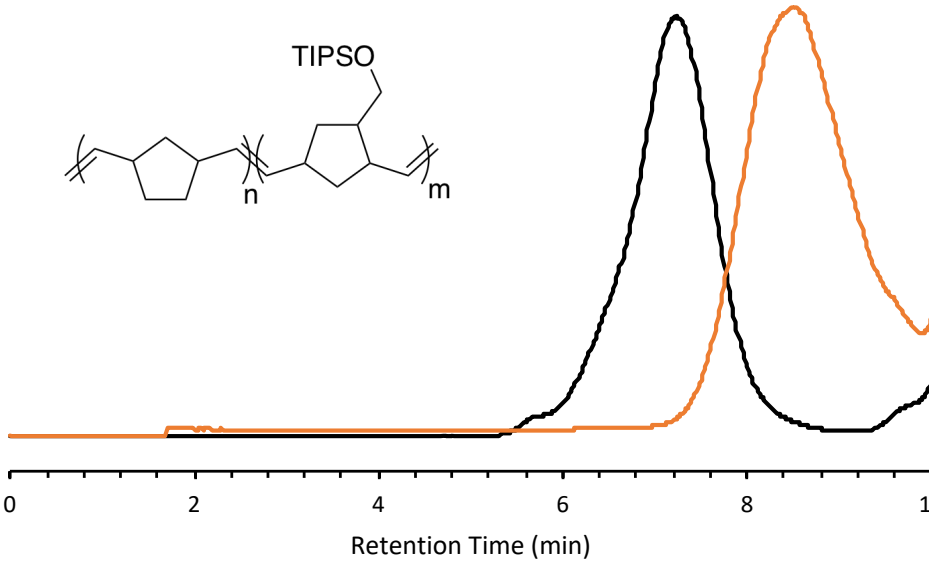
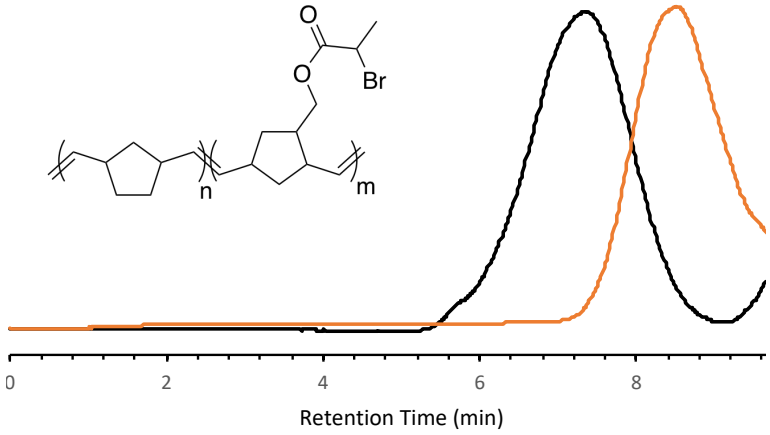

Br
O
O
n
0
2
4
6
8
10
Retention Time (min)



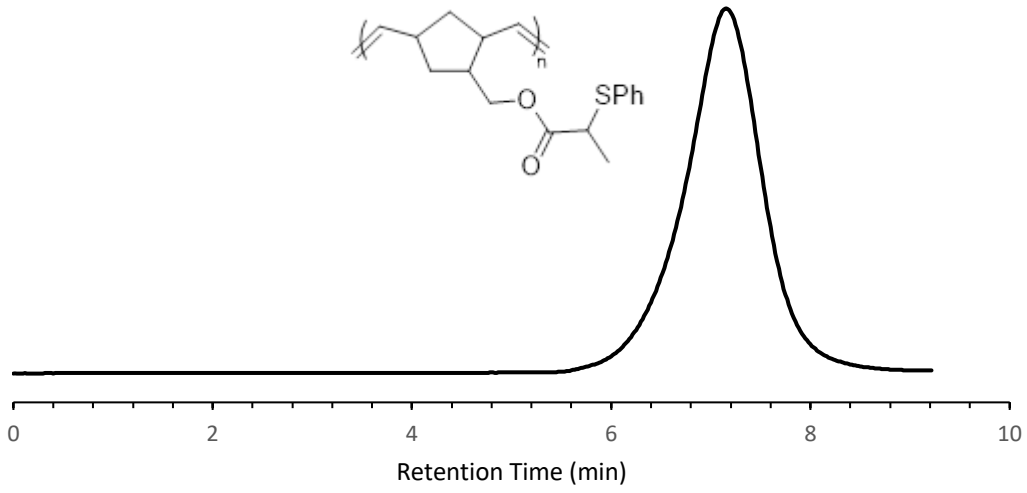
GPC traces before (orange trace) and after (black trace) chain extension:

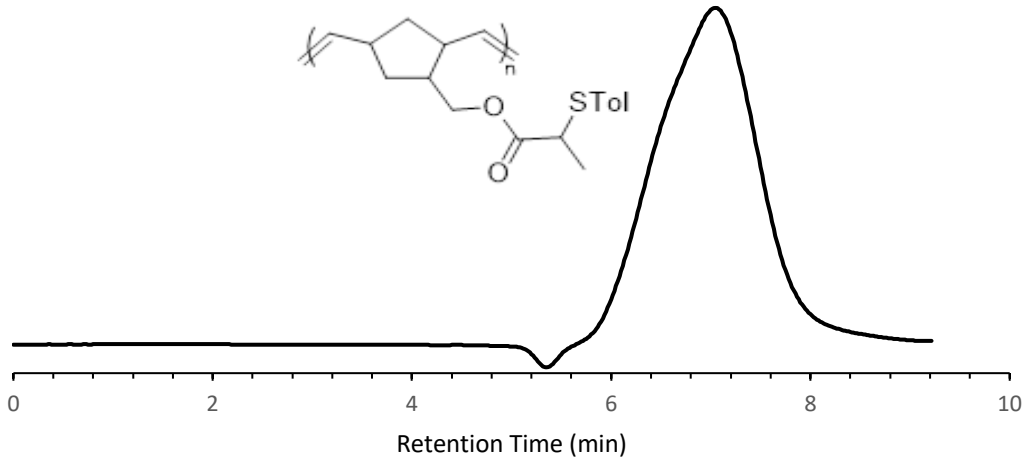


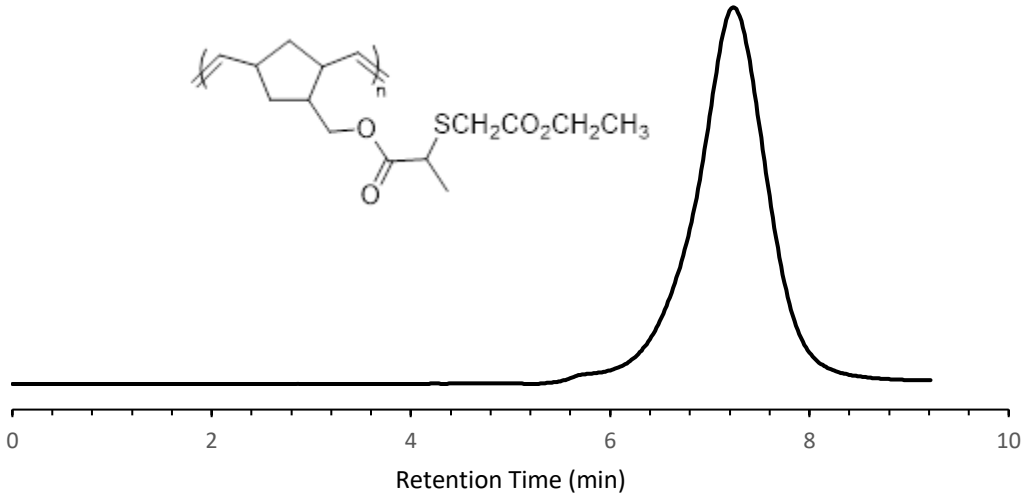

TIPSO
n
m
0
2
4
6
8
1
Retention Time (min)


O
O
Br
n
m
0
2
4
6
8
Retention Time (min)

GPC Traces of thio-bromo click products:







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