

# Synthesis of single-chain nanoparticles *via* atom-transfer radical coupling

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## Introduction

The production of well-defined single-chain nanoparticles (SCNPs) has proven challenging with respect to finding synthetic routes that are scalable and do not require harsh reaction conditions. In order to combat these challenges, a route that utilizes atom-transfer radical coupling (ATRC) to collapse linear polymer chains through pendant functional groups has been tested.<sup>1</sup> Our process uses a minimal number of synthetic steps, beginning with a one-step synthesis of an ATRC functionalized monomer, which is then polymerized in 10, 20, and 50% incorporations with methyl methacrylate (MMA) through reversible addition-fragmentation chain transfer (RAFT).<sup>2</sup> An irreversible cross-link is then accomplished by ATRC to collapse the parent polymers into SCNPs. Successful collapse of parent polymers can be seen by gel permeation chromatography (GPC) where SCNPs display a shift to longer retention times.

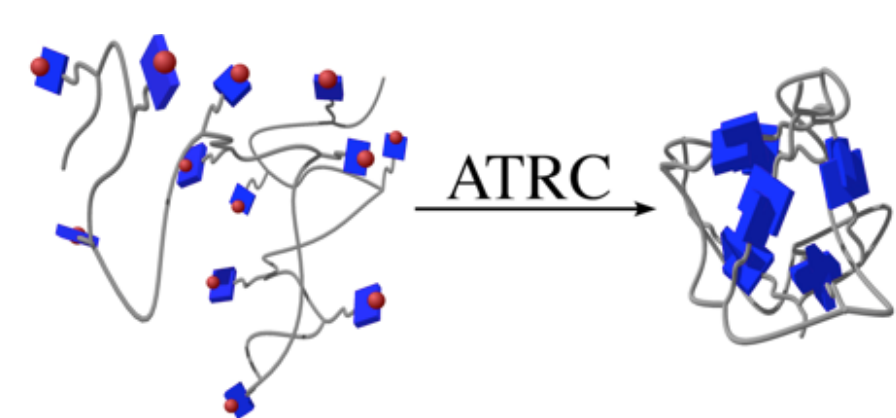
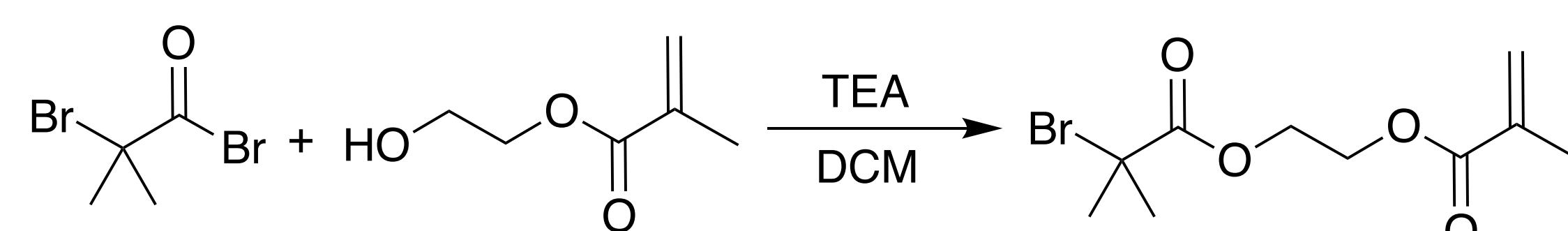
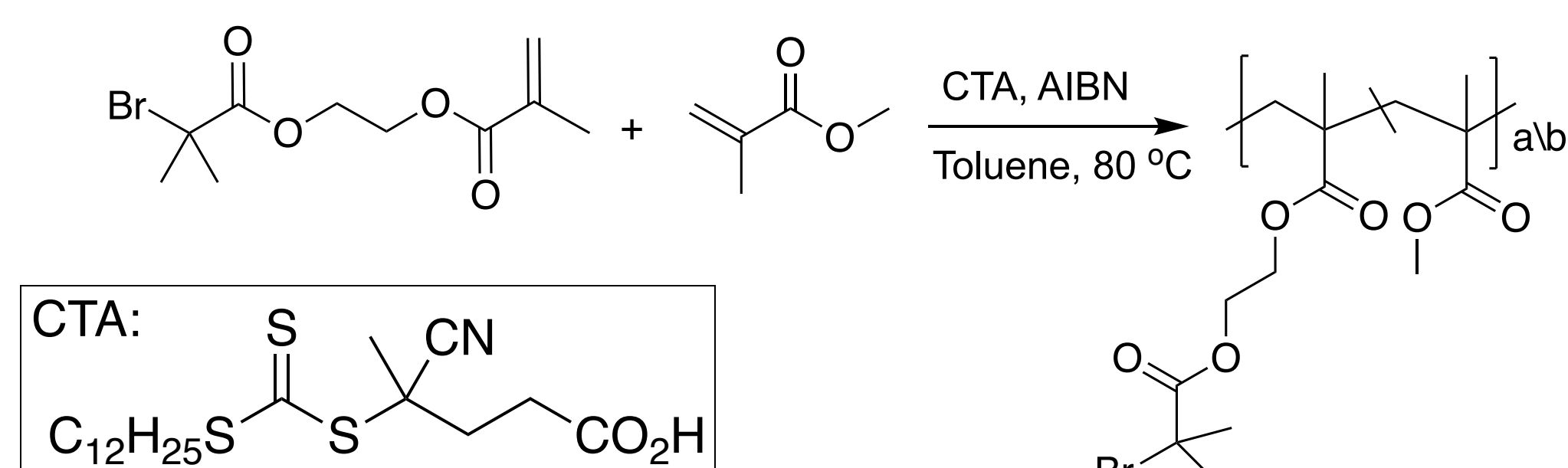


Figure 1. General collapse of parent polymer to SCNP<sup>3</sup>.

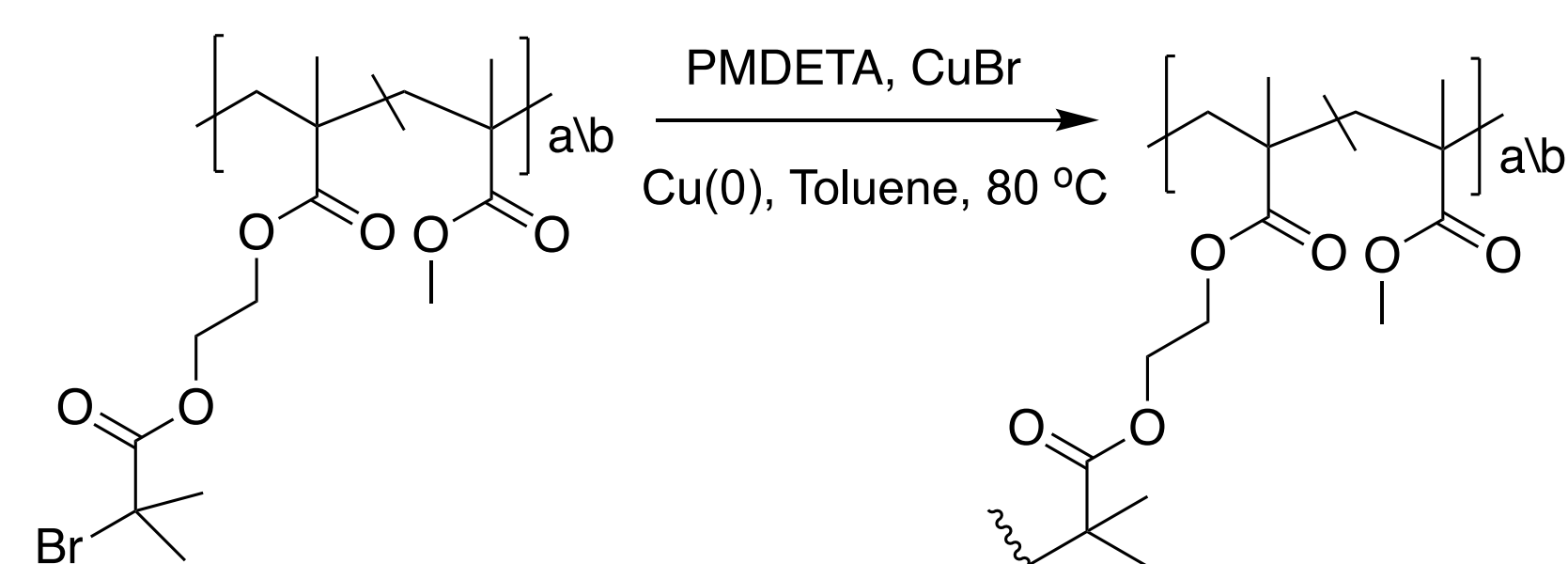
## Experimental Design



Scheme 1. Synthesis of dimethylbromoethyl methacrylate (Me<sub>2</sub>Brema).



Scheme 2. Synthesis of poly(Me<sub>2</sub>Brema-co-MMA) parent polymers.



Scheme 3. Synthesis of SCNPs by ATRC collapse through pendant functionality.

The ATRC active Me<sub>2</sub>Brema monomer was synthesized in one step from commercially available starting materials (Scheme 1). Parent polymers were synthesized by RAFT to obtain linear polymer chains with low molecular weight dispersity (Scheme 2). SCNP were achieved through the cross-linking of the ATRC active sites on the pendant monomers (Scheme 3).

## Characterization

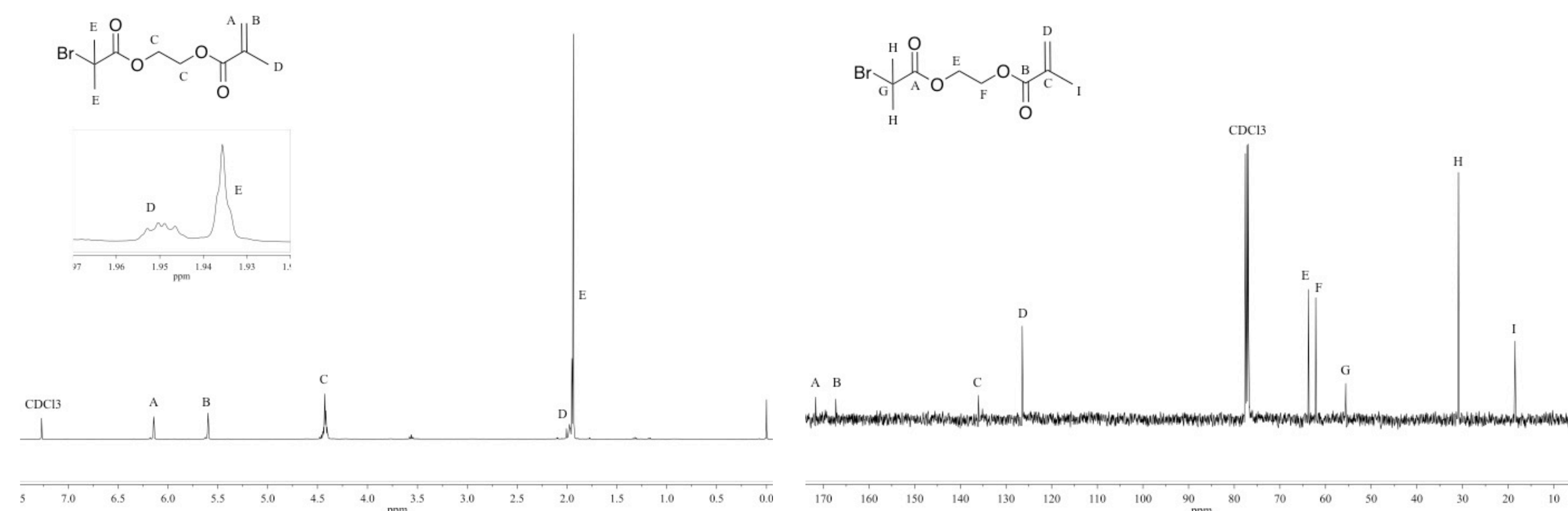


Figure 2. <sup>1</sup>H NMR of Me<sub>2</sub>Brema.

Figure 3. <sup>13</sup>C NMR of Me<sub>2</sub>Brema.

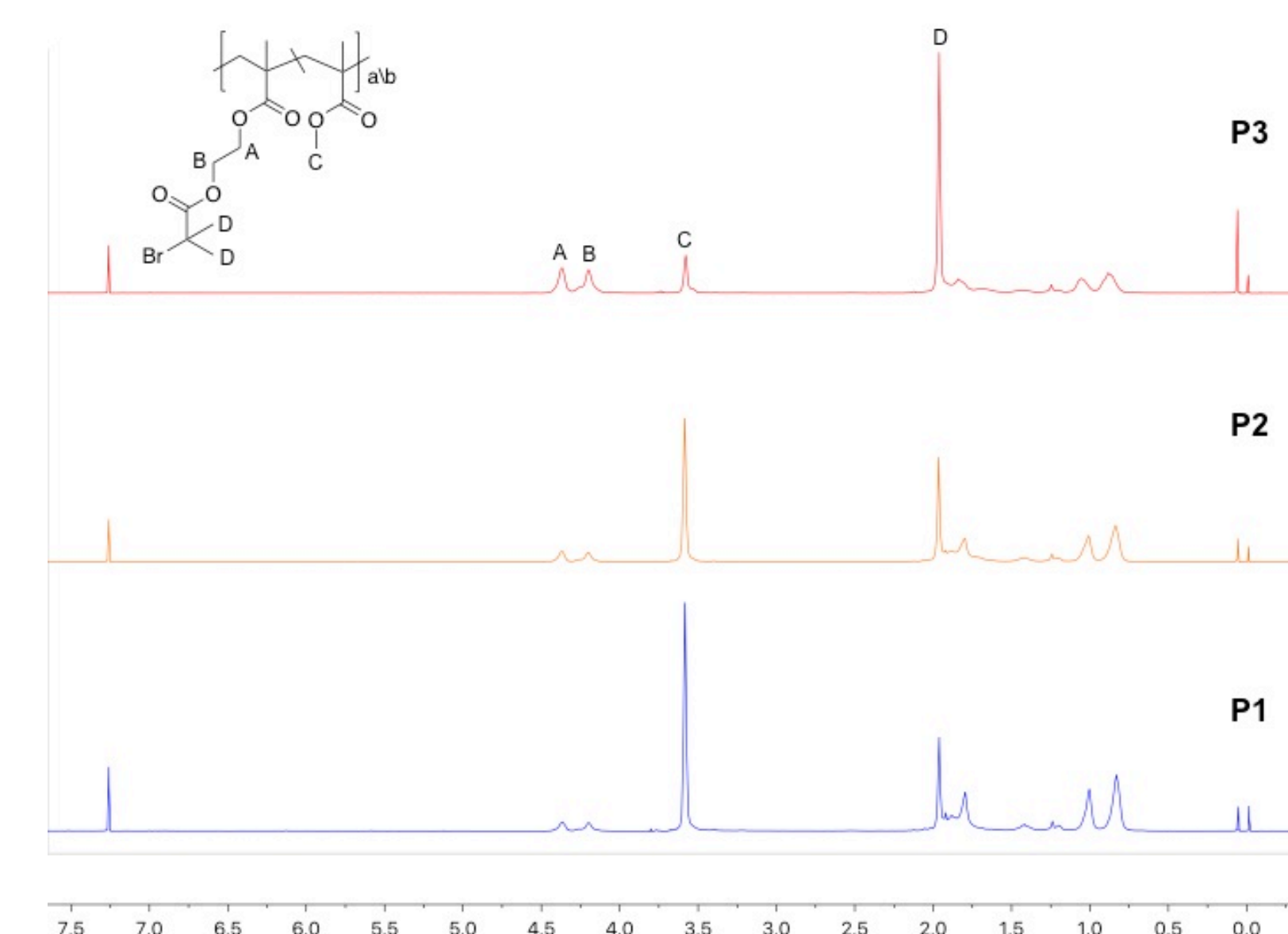


Figure 4. Stacked <sup>1</sup>H NMR spectra of P1, P2 and P3.

Table 1. Percent incorporation calculated by <sup>1</sup>H NMR, molecular weight and poly-dispersity index data found by GPC for polymers P1, P2 and P3.

Polymer	Target Incorp.	Actual Incorp.	M <sub>n</sub>	M <sub>w</sub>	PDI
P1	10	13.4	1.39x10 <sup>4</sup>	1.47x10 <sup>4</sup>	1.08
P2	20	20.2	1.36x10 <sup>4</sup>	1.51x10 <sup>4</sup>	1.11
P3	50	65.8	2.59x10 <sup>4</sup>	3.25x10 <sup>4</sup>	1.26

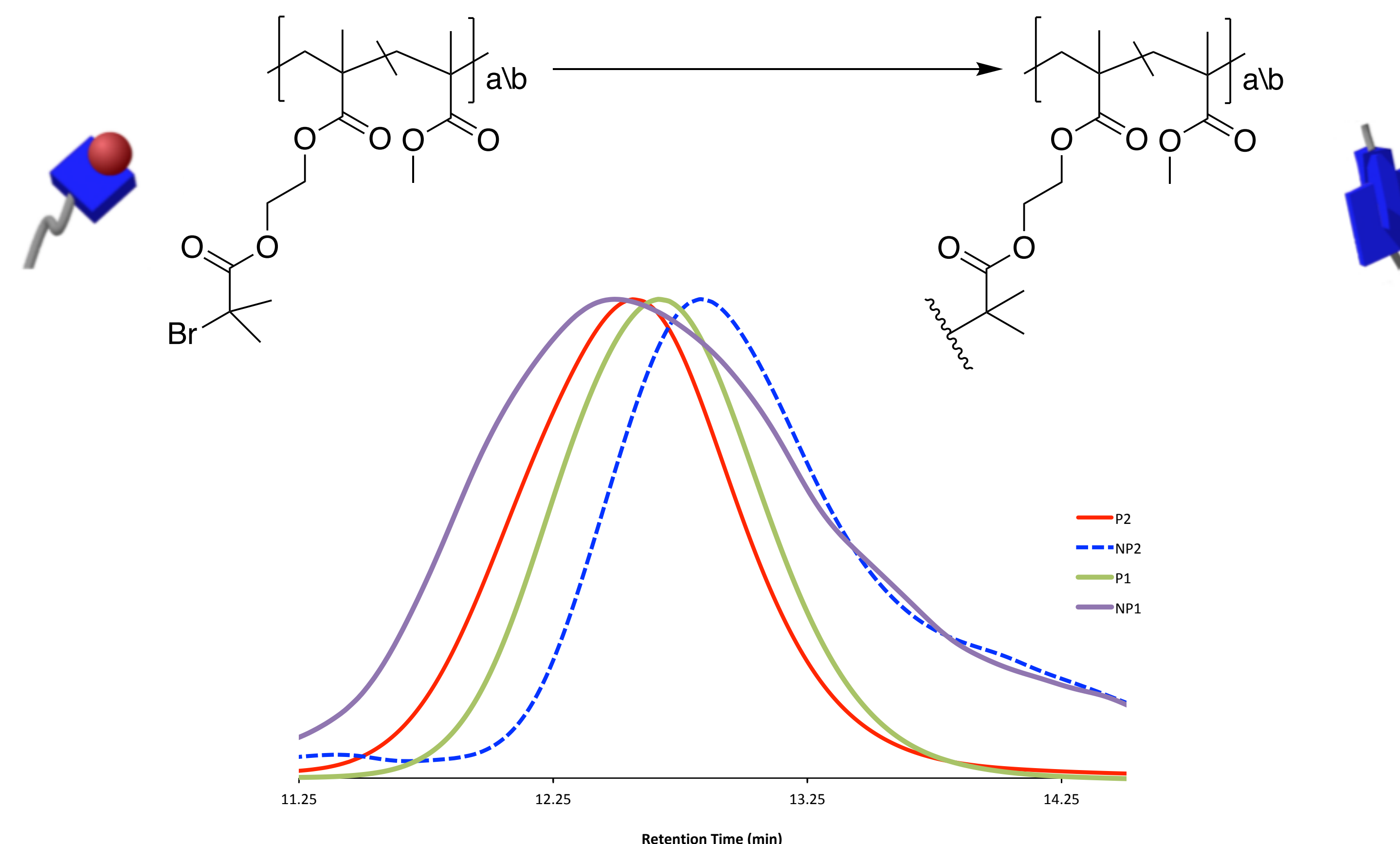


Figure 5. GPC MALS trace of P1-P2 and NP1-NP2.

## Discussion

Carbon and proton NMR were used to track the successful synthesis of the Me<sub>2</sub>Brema monomer (Figures 2-3), which obtained a yield of 84%. In Figure 3, integration of peaks A or B and C were used to calculate the percent incorporation of MMA and Me<sub>2</sub>Brema in the copolymer sequence. The disappearance of peak C and growth of peaks A and B from P1 to P3 show the successful increase in Me<sub>2</sub>Brema in the backbone of the parent polymers. The copper-mediated ATRC coupling of pendant Me<sub>2</sub>Brema can be seen in Figure 5. A shift in retention time on the GPC MALS trace shows formation of SCNPs. Unfortunately, some peaks show broadening after collapse due to disproportionation events.

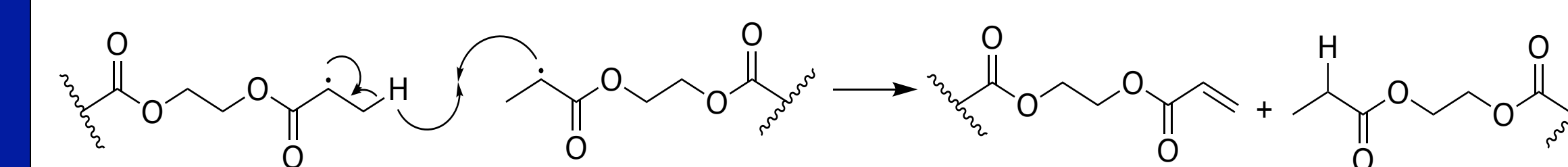
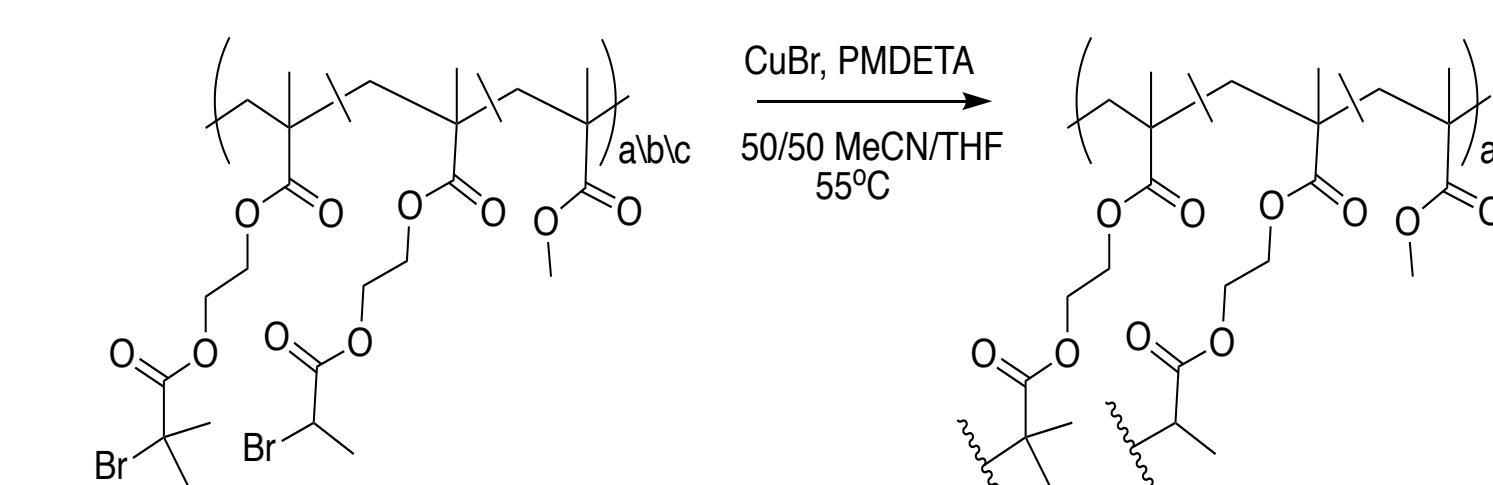


Figure 6. Disproportionation, where a hydrogen abstraction occurs instead of coupling of pendant groups.

Disproportionation has a high probability of occurrence on the pendant Me<sub>2</sub>Brema because it has six available hydrogen atoms that could participate in an abstraction.

## Conclusions and Future Work

Monomer and parent polymer synthesis was successful. SCNPs were formed, however the broadening of the GPC trace (Figure 5) from parent polymer to SCNP was not ideal. Broadening of the GPC trace was likely due to disproportionation. Optimization of the ATRC process will be important for future SCNP formation.



Scheme 4. Collapse of terpolymer into SCNP by optimized ATRC conditions.

## Acknowledgements

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## References

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