Maleimide functionalized monomer for synthesis of single-chain nanoparticles

Jennifer Chouinard, Holly Guevara, Alka Prasher
jmr386@wildcats.unh.edu; Parsons Hall, 23 Academic Way, Durham NH 03824

Introduction

This was a synthetic approach to produce a monomer **3,** which will copolymerize with a furan based monomer **6** and methyl methacrylate (MMA) **7,** to synthesize various polymers **8** using ATRP. These polymers will then undergo reversible cross-linking to form single chain nanoparticles under dilute conditions. The folding of a polymer chain into a well-defined structure is a developing technology in polymer science. This single-chain folding can be considered a mimic of biomacromolecules such as proteins which then can potentially be used for drug and DNA delivering systems in nanotechnology applications[1].

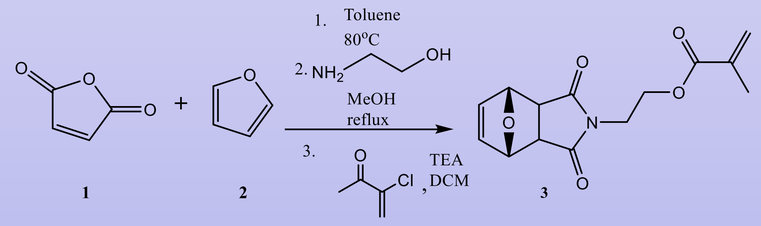


Figure 1. Synthetic route for 2-Propenoic acid, 2-methyl-, 2-(1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-epoxy-2*H*-isoindol-2-yl)ethyl ester

Experimental

A multistep synthesis was performed, starting with a Diels-Alder reaction of maleic anhydride **1** with furan **2** to yield purified *exo* 10-dioxatricyclo[5.2.1.02,6]dec-8-ene-3,5-dione **3**[2], which was then reacted with anhydrous methanol and ethanolamine to synthesize 3-acetyl-N-(2-hydroxyethyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxamide **4**. This product then underwent alcoholysis of methacryloyl chloride[3] with triethylamine to produce 2-propenoic acid, 2-methyl-, 2-(1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-epoxy-2*H*-isoindol-2-yl)ethyl ester **5**. Each step was analyzed using ^{1}H NMR and melting point to verify the purity of the products.

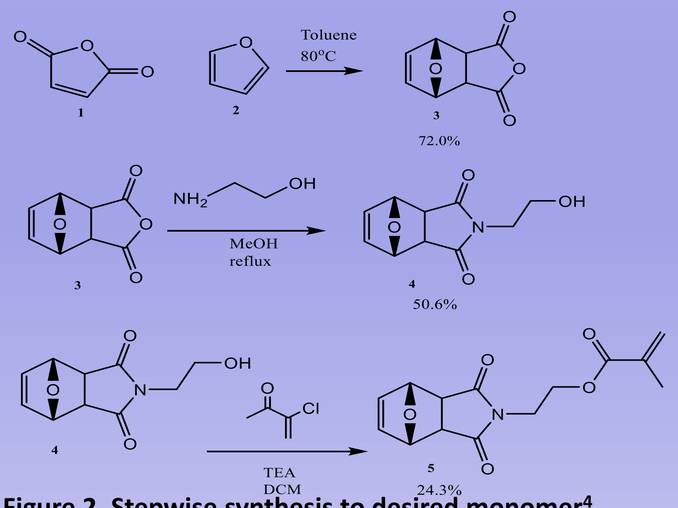


Figure 2. Stepwise synthesis to desired monomer[4]

Results and Discussion

The Diels-Alder reaction of maleic anhydride **1** with furan **2** was successful in producing *exo* maleimide-furan cycloadduct **3**. This adduct reacted with ethanolamine to produce the protected maleimide alcohol **4** which then reacted with trimethylamine and methacryloyl chloride to produce the desired monomer **5**. To enhance the results, the last step in the synthesis of the monomer should be left to react for approximately 24 hours per 5.00 g of the protected maleimide alcohol.

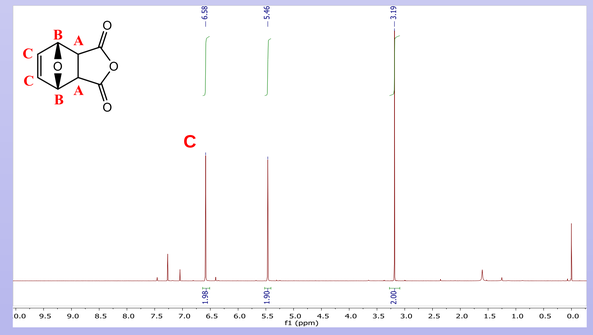


Figure 3. ^{1}H NMR of purified 3

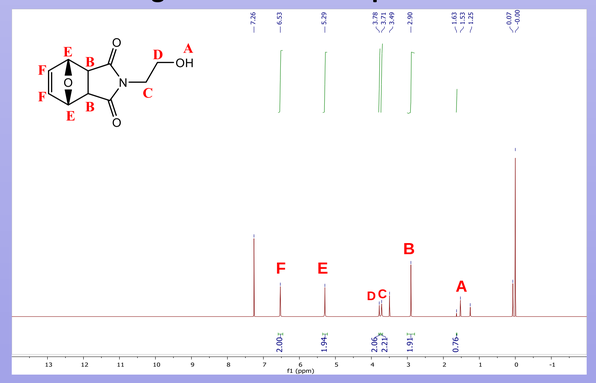


Figure 4. ^{1}H NMR of purified 4

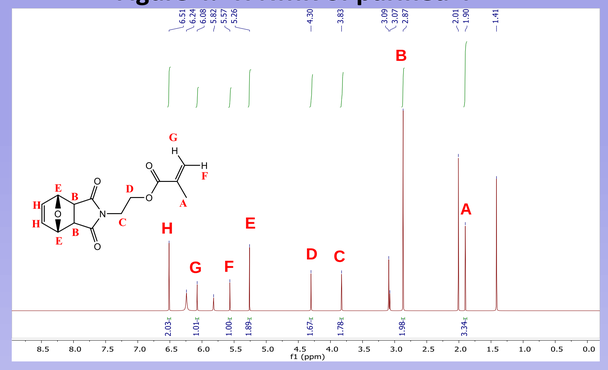
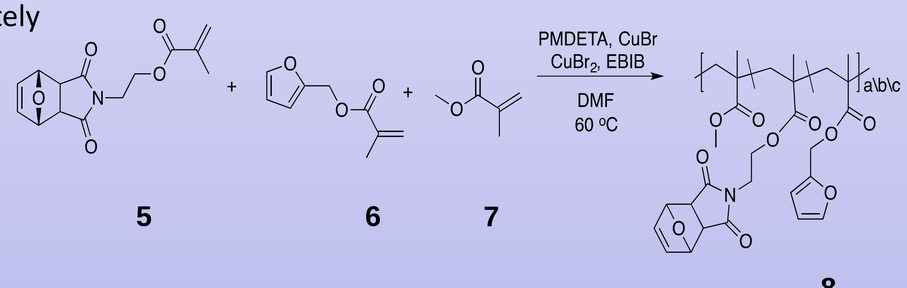


Figure 5. ^{1}H NMR of purified 5

Future Work

The monomer **5** that was synthesized will be used in Dr. Berda's research group by PhD student Ashley Hanlon. It will be used to reversibly cross-link as a single chain nano particle. A furan based monomer **6** and MMA **7** will be used to form a polymer **8** and thermally driving off the furan with a retro Diels-Alder reaction to leave the maleimide and furan group to intramolecularly cross-link via Diels-Alder reaction[1,5].



5 **6** **7** **8**

Conclusions

The organic synthesis of the monomer 2-Propenoic acid, 2-methyl-, 2-(1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-epoxy-2*H*-isoindol-2-yl)ethyl ester was successful as proven by ^{1}H NMR . This means that the monomer can now be polymerized in further experiment. The yields are relatively high and can be further improved by running the experiment again. Allowing proper reaction time for the last step will also increase the yield of the monomer.

Acknowledgments

I would like to thank the Berda research group for their support as well as the UNH Department of Chemistry for their funding.

References

(1) Altinas, O; Gliemann, H; Kowollik, C.B.; Oehlenschlaeger, K.; Sidenstein, P.K.; Willenbacher, J.; Wuest, K. *A Mild and Efficient Approach to Functional Single-Chain Polymeric Nanoparticles via Photoinduced Diels–Alder Ligation. J.* Am. Chem. Soc.46. 8092 (2013).

(2) M. W. Lee, W.C. Herndon, *Stereochemistry of the Furan-Maleic Anhydride Cycloaddition*. J. Org. Chem. 43, 518 (1978).

(3) Schmidt, Friedrich Georg; Hilf, Stefan; Barner-Kowollik, Christopher; Guimard, Nathalie; Oehlenschlaeger, Kim Klaus; Mueller, Jan Assignee Evonik Industries AG, Germany; Karlsruher Institut fuer Technologie (2013).

(4) Hart-Smith, G.; Jiang, Y.; Liang, M.; Lu, S.; Scarano, W.; Stenzel, M.; Sveikar, D. *Albumin-Micelles via an one-pot Technology Platform for the Delivery of Drugs Contents.* Royal Society for Chemistry. 2014.

(5) Kell, A.; Workentin, M.; Zhu, J. J. Am. Chem. Soc. 8. 4993-4996 (2006).