Investigation into the Synthetic Route and Characterization of 2,3-Dimethylmaleimide Functionalized Monomer for Photo-cross-linking

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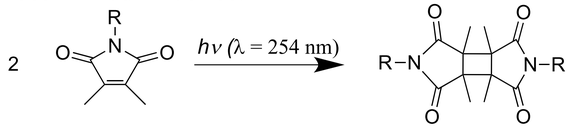
Introduction

2,3-dimethylmaleimide has been reported to undergo a [2+2] cycloaddition (**Scheme 1**) when irradiated with UV light (λ = 254 nm).[1] Recently, Sumerlin *et al* reported a system that utilized an acrylamide functionalized with 2,3-dimethylmaleimide cross-linker to yield core cross-linked micelles.[1]



Scheme 1: Photodimerization of 2,3-dimethylmaleimide

This experiment focuses on the method of the synthesis of the 2,3-dimethylmaleimide functionalized monomer (**Fig. 1**) as proposed by Roy and Sumerlin[2].

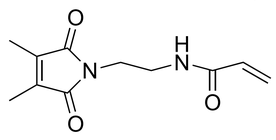
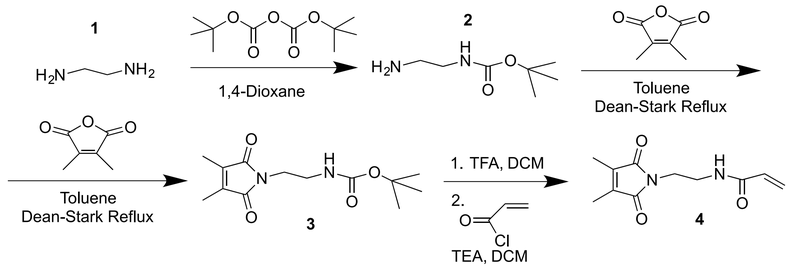


Figure 1: Target 2,3-dimethylmaleimide functionalized monomer

The successful synthesis of this dimethylmaleimide-functionalized monomer grants access to form single-chain nanoparticles (SCNP) when polymerized with a comonomer spacer. Following functionalization with a diiron cluster and the collapse of the polymer to form the SCNP, the polymer scaffold can mimic a secondary protein structure environment of hydrogenase. This creates a suitable environment of the protein active site to enhance hydrogen gas production during electrocatalysis in an acidic solution[3]. The long-term goal of this research is to progress toward a more efficient form of hydrogen production for a clean energy alternative.

Experimental Design

The addition of di-tert-butyl dicarbonate to ethylenediamine (**1**) yielded *tert*-butyl-N-(2-aminoethyl)carbamate (**2**). When heated with dimethyl maleic anhydride, the carbamate formed N-[2-(3,4-dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-aminoethyl]-tertbutyl-carbamate (**3**). The final product, N-[2-(3,4-dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-ethyl]-acrylamide (**4**), was afforded by the addition of trifluroacetic acid to reform the amine, followed by the addition of acrloyl chloride.



Scheme 2: Proposed synthetic route to the 2,3-dimethylmaleimide functionalized monomer

Results & Discussion

Step 1: The boc-protection of ethylenediamine resulted in an 89% crude yield. The addition of boc-anhydride was done slowly to assure that only one of the amines were protected, leaving the other available to react in the proceeding step. The product was characterized by ^{1}H NMR (**Fig. 2**) and ^{13}C NMR for product confirmation and purity. No thorough purification was performed before moving forward to the next synthetic step.

Step 2: The resulting carbamate synthesized in step 1 was refluxed with 2,3-dimethylmaleic anhydride. This formed the functionalized malimide opposite the boc-protected amine (90% yield). Characterization via ^{1}H NMR (**Fig. 3**), as well as TLC was used to confirmed the product and to check for purity. No thorough purification was performed before moving forward to the next synthetic step.

Step 3: With the addition of trifluoroacetic acid, the protection group was removed to reform the amine. In the presence of triethylamine, acryloyl chloride was reacted with the amine, affording the acrylamide final product.

The work-up and purification of the final product is ongoing in a meticulous manner to ensure high purity before polymerization.

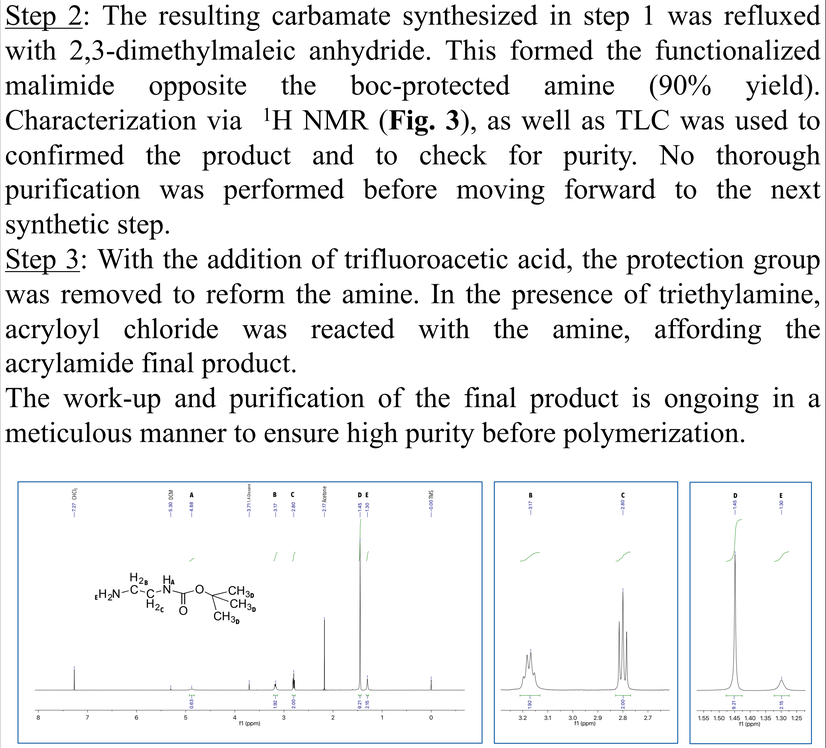


Figure 2: ^{1}H NMR of *tert*-butyl-N-(2-aminoethyl)carbonate

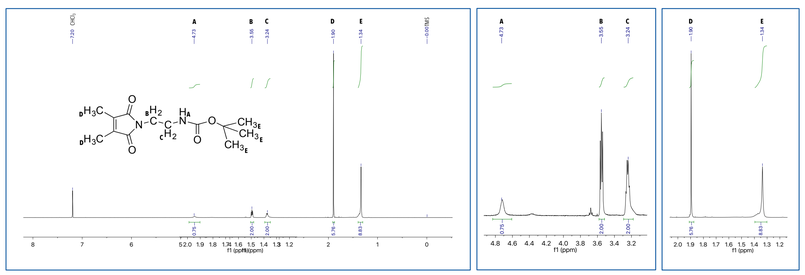


Figure 3: ^{1}H NMR of N-[2-(3,4-dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-aminoethyl]-*tert*-butyl-carbamate

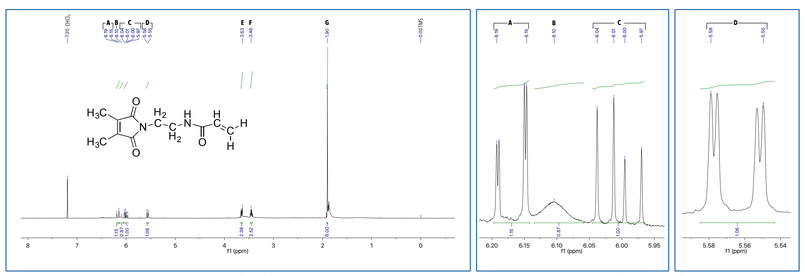


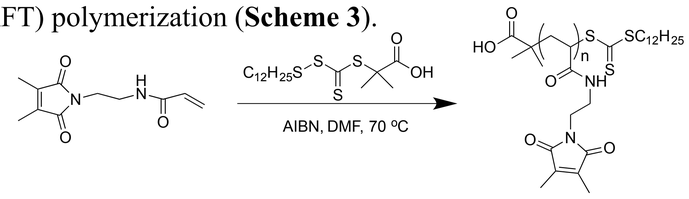
Figure 4: ^{1}H NMR of N-[2-(3,4-dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-ethyl]-acrylamide

Conclusion

The proposed synthetic route to produce N-[2-(3,4-dimethyl-2,5-dioxo-2,5-dihydro-pyrrol-1-yl)-ethyl]-acrylamide proved to be a successful path. By ^{1}H NMR spectroscopy, the product was confirmed to match the previously known literature results. Overall the reaction scheme has shown to be both efficient and practical. Increased yields may be possible by allowing more time for reactions, improved techniques to limit mechanical loses, and an optimization of reaction conditions. The work-up and purification of the final product revealed itself to be both excessive and time consuming, revealing an area for potential improvement in efficiency.

Future Work

The future progress if this project is to incorporate the synthesized 2,3-dimethylmaleimide functionalized monomer into a polymer compound via reversible addition fragmentation chain-transfer (RAFT) polymerization (**Scheme 3**).



Scheme 3: RAFT polymerization of the 2,3-dimethylmaleimide functionalized monomer

Once polymerized, the 2,3-dimethylmaleimide can undergo a [2+2] cycloaddition, creating a SCNP. When functinoalized with a suitable sulfur-diiron complex (**Fig. 4**), the SNCP adopts synthetic structure similar to the secondary folding of proteins.

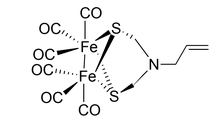


Figure 4: Proposed synthetic diiron cluster for the hydrogenase active site

In an acidic medium, the polymer scaffold in combination with the synthetic active site of sulfur-diiron cluster and a reducing agent can replicate the same sort of hydrogen production seen in hydrogenase enzymes.

Exploring various polymer frameworks (e.g., amides, methacrylates, styrenes, etc.) to find the optimal secondary coordination sphere environment to optimize H_2 production will reduce the cost of their production on an industrial. The broad impact of this research is to progress toward clean and reliable source for hydrogen production, to decrease the dependence on fossil fuels.

References

1. Seiffert, S.; Oppermann, W.; Saalwaechter, K. *Polymer,* **2007,** *48*, 5599.
2. Roy, D.; Sumerlin, B.S. *Macromol. Rapid Commun.* **2013,** *35*, 174-179.
3. Tooley, C.A.; Pazicni, S; Berda, E.B. *Polymer Chemistry.* **2015,** *6*, 7646-7651.
4. R. Cammack, Nature, **1999**, 397, 214–215.