Functionalized Polymers and Conjugation Efficiency

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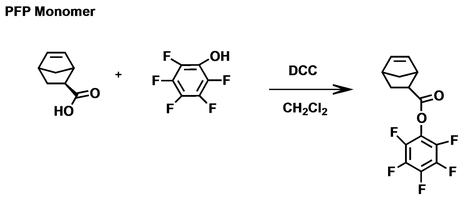
Introduction

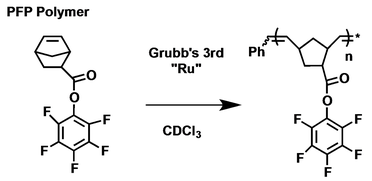
Synthesizing functionalized polymers has a variety of uses in the field of nanotechnology and biotechnology. The method consists of polymerizing specific monomers via ring-opening metathesis polymerization (ROMP). Grubb's 3rd generation catalyst is a fast-initiating catalyst that has been found to be particularly effective for polymerization due to its ability to work with an array of functional groups. Pentafluorophenol (PFP) is useful in peptide synthesis, soluble in many organic solvents; meanwhile N-Hydroxysuccinimide (NHS) is used as an activating agent for carboxylic acids. Once polymers are synthesized, dialysis may be performed to produce amphiphilic micelles of ranging morphologies and functions which may be useful in aiding biological functions. Also, the efficiency of the conjugation of amines on to the polymer is important for peptide synthesis and its effect in a living organism.

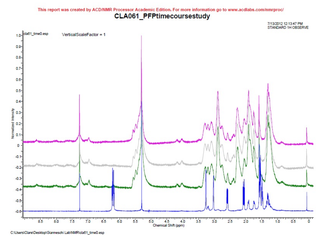
PFP Monomer



Norbornene carboxylic acid , pentafluorophenol, and dicyclohexanecarbodiimide (coupling reagent)were dissolved in dichloromethane and reacted 24 hours to form the pentafluorophenol monomer.

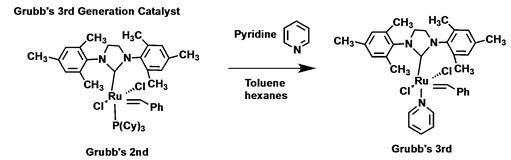
PFP Polymerization with Grubb's 3rd Generation Catalyst





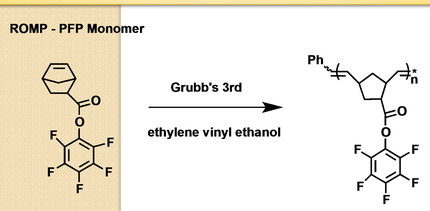
To test the polymerization of the PFP monomer,, a time course NMR study was taken. At time t=0 only the monomer was present. The Grubb's catalyst solution was added to the monomer solution causing a color change from bright green to brown, indicating polymerization. The monomer fully polymerized in 12 minutes.

Grubb's 3rd Generation Catalyst



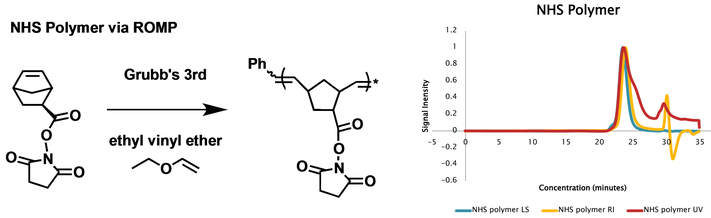
In dried schlenk flask under Nitrogen, added 2ND generation catalyst (red). Added ~8mL of dry toluene. Stirred to dissolve. Added anhydrous pyridine to solution, which changed to dark green. Let stir for 15minutes, then add slowly and portion-wise to cold hexanes to precipitate out. Wash 3-4 more times with cold hexanes. Dry under vacuum for about an hour.

PFP Polymer via ROMP



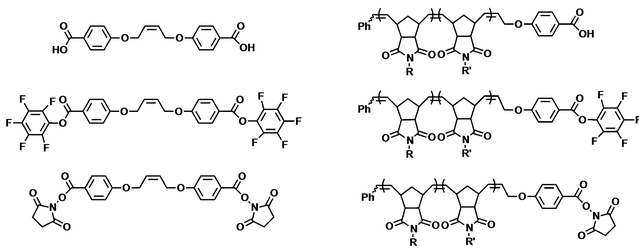
300mg of PFP monomer were dissolved in 2mL of dry DCM. Then 1mL (150mg) of the monomer solution was added. It took 15 minutes to polymerize, and there was a color change from bright green to pale brown. The reaction was terminated with 40 μ L of ethyl vinyl ether, then precipitated in ether and centrifuged for 20mins, forming a white pellet.

NHS Polymer via ROMP



93mg of NHS monomer were dissolved in dry DCM, then 1mL of the solution was added to the stirring catalyst. After 15 minutes the reaction was terminated with 40 μ L of ethyl vinyl ether, then precipitated in ether and centrifuged for 20 minutes.

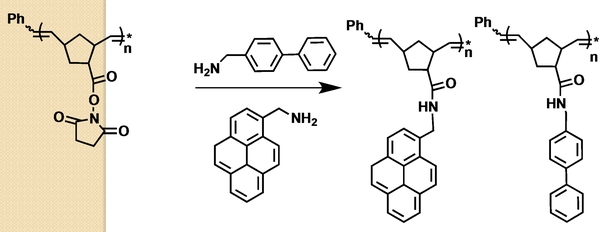
Future Directions

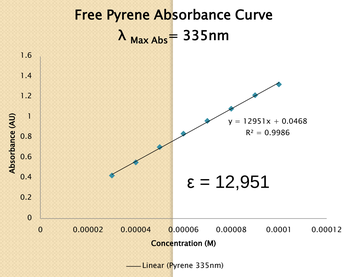


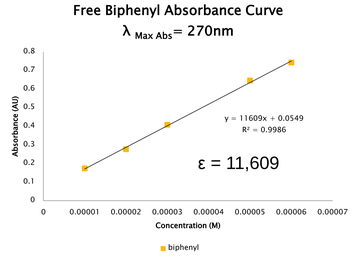
The purpose of synthesizing terminating agents is to allow amines to be conjugated on different locations of the polymers as seen above. The NHS and PFP esters are on the ends of the functionalized polymers.

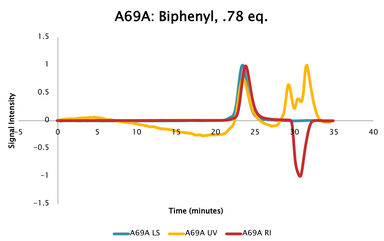
Conjugation of Biphenyl and Pyrene Amines on NHS Polymer

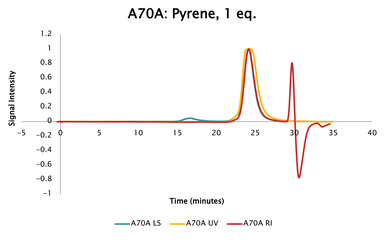
NHS Polymer with Conjugated Amine

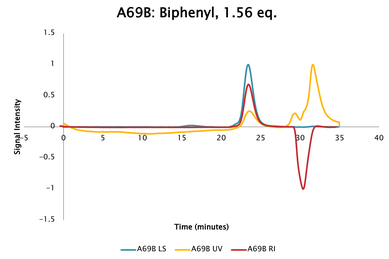


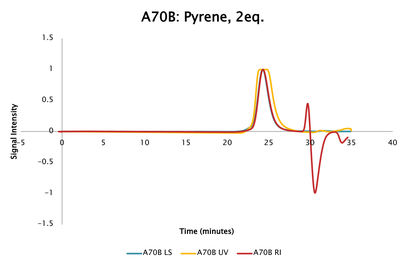








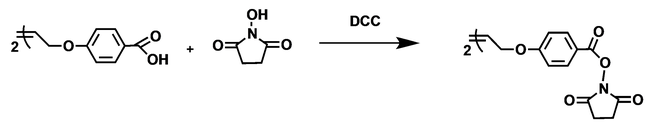




20mg of NHS polymer were dissolved in 2mL of dry DMF, then half of the solution was put in a separate flask. 6mg (0.78eq.) of biphenyl amine were dissolved in 0.5mL of dry DMF and added to the NHS solution. 12mg (1.56 eq.) of biphenyl amine were then dissolved in 1mL of dry DMF and added to the other NHS solution. The same procedure was followed for pyrene conjugation to the NHS polymer.

The above are SLS traces of amine conjugation to the NHS polymers. In all cases, a peak shift shows a quantitative conjugation of the amine to the polymer. However exact molecular weights of the polymers could not be determined, so quantitative analysis could not be performed. Pure polymers were difficult to isolate, so efficiency of conjugation could not be confidently determined.

NHS Terminating Agent



An experiment was performed to produce an NHS Terminating Agent by reacting the NHS monomer in DCC and carboxylic acid in dry DMF under nitrogen. After an hour, promising results were yielded. There was a color change from dark yellow to bright yellow.

Conclusions

Using Light Scattering Data from the Original NHS Polymer, a comparison could be made to the conjugated polymer in order to understand the efficiency of the Biphenyl and Pyrene amines to conjugate on to the NHS polymer. LS data provides insight about the molecular weight of the polymer and its polydispersity by the sample's ability to absorb light, so the more dense conjugated polymer should produce a peak earlier than the less dense NHS Polymer. The NHS Polymer reaches its absolute max height of 1 AU at time 23.47 minutes, while the polymer with the conjugated biphenyl amine reaches its peak at 23. 41 minutes. Also, the molecular weight data shows a definite increase from the original NHS Polymer to the conjugated polymer. Knowing the amine conjugation efficiency and optimized conditions will allow us to apply that knowledge to more complex systems, such as conjugating peptides to polymers.