Synthesis of UV-Cleavable, Drug-Containing ROMP Monomers Towards the Generation of Nanomaterials for Targeted Cancer Therapy

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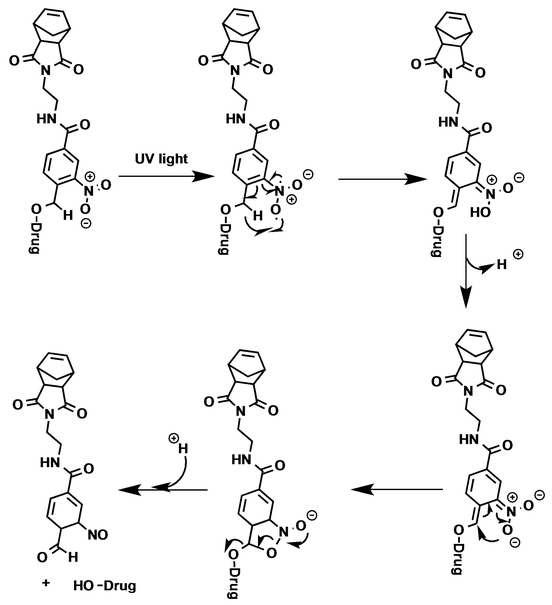
ABSTRACT

Recently, the Gianneschi Lab demonstrated the capability of enzyme-responsive nanomaterials to selectively accumulate in tumor tissue and release a payload of drug that is capable of slowing the progression of tumor growth[1]. In this system, generated through Ring Opening Metathesis Polymerization (ROMP), the cancer drug was trapped in the core of the nanoparticle through an ester bond. This bond slowly hydrolyzed after nanoparticle accumulation in tumor tissue to release the drug in a time-dependent manner.

Herein, we describe synthetic steps towards a novel drug-containing ROMP monomer that seeks to improve upon the system described above. By attaching the cancer drug to the polymer backbone through a UV-sensitive bond, rather than a water-sensitive ester bond, we hypothesize that nanoparticles formed from polymers made with these UV-sensitive monomers will be more efficient at releasing their drug cargo after accumulation than their ester predecessors, if the system is first irradiated with UV-light.

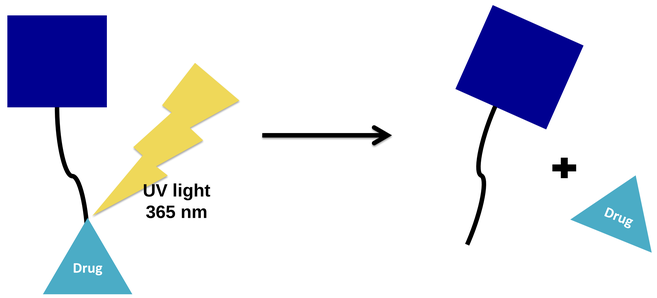
[1]Callmann, C. E., Barback, C. V., Thompson, M. P., Hall, D. J., Mattrey, R. F., & Gianneschi, N. C. (2015). Therapeutic Enzyme-Responsive Nanoparticles for Targeted Delivery and Accumulation in Tumors. Advanced Materials. doi: 10.1002/adma.201501803

MECHANISM OF UV-CLEAVAGE

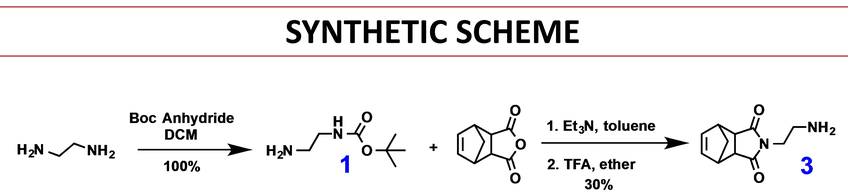


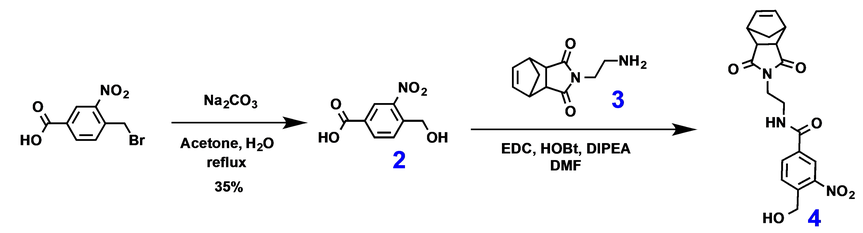
HYPOTHESIS

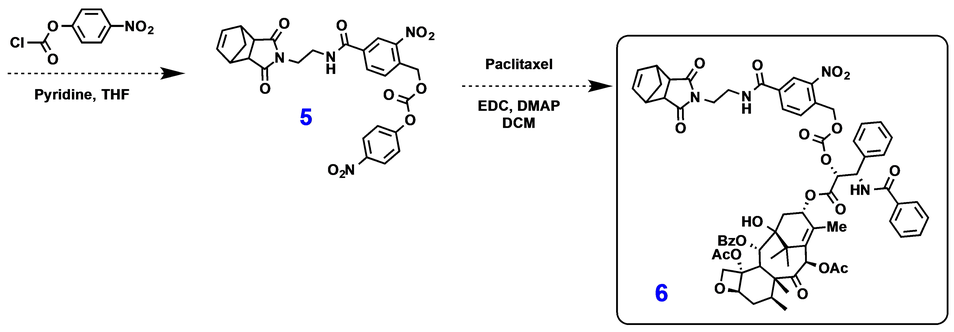
Attaching cancer drugs to ROMP monomers through UV-sensitive covalent bonds should allow for the generation of drug-containing polymers and nanoparticles that should can release their drug cargo “on demand” after UV-irradiation at 365 nm.



SYNTHETIC SCHEME







ANALYSIS

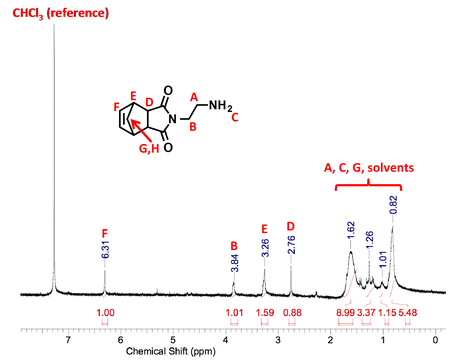


Figure 1. NMR Spectrum of Compound **3**.

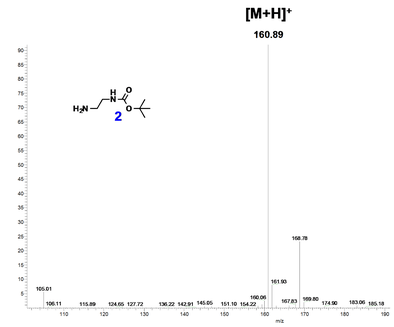


Figure 2. MS Spectrum of Compound **2**.

CONCLUSIONS

We have synthesized compounds **1**, **2**, **3** and **4** in the synthetic scheme. Using NMR, TLC, and Mass spectrometry, we were able to determine the success of each compound. We purified compounds through liquid-liquid extraction by using a separatory funnel. After purifying each compound, it was isolated with a rotary evaporator.

FUTURE DIRECTIONS

Compounds **5** and **6** will need to be synthesized in the future in order to continue the experiment. After synthesizing the compounds, we will cleave them with UV light. Then make polymers and nanoparticles and test them under UV light as well.