Master's Thesis Engineering Technology

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Synthesis of sequence-defined nucleobase acrylate oligomers via RAFT polymerization

Optimization of the first monomer insertion

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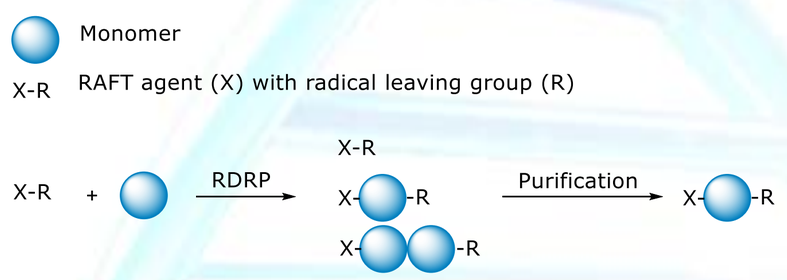
Introduction

The interest in DNA mimics has increased the last decade. The PRD research group has an ongoing project on the development of a method to facilitate the easier synthesis of sequence-defined nucleobase acrylate oligomers. These oligomers could have a function as DNA mimic, tag or chemical data unit. To be able to develop this easier synthesis method, first, sequence defined nucleobase acrylate oligomers must be synthesized with the single unit monomer insertion (SUMI) procedure. The master's thesis focusses on the insertion of the first monomer.

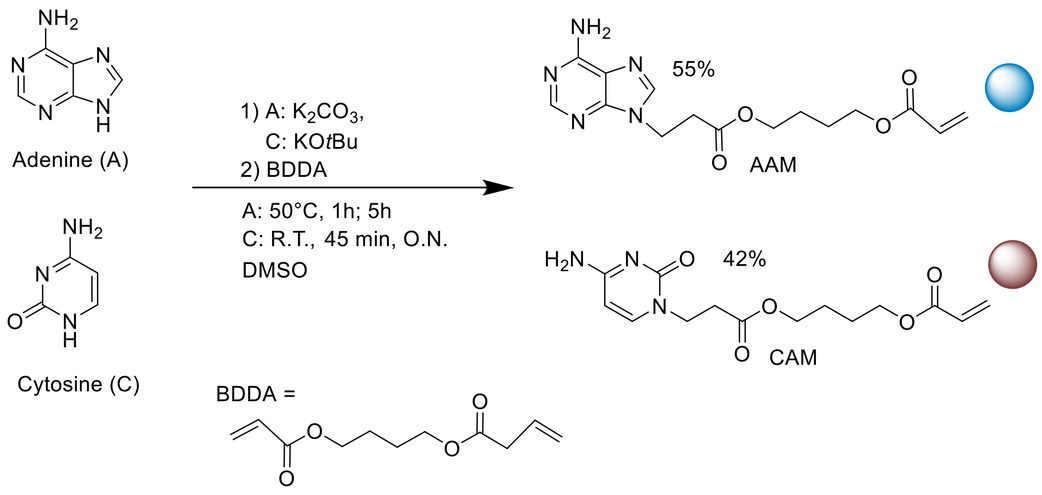
Goals

- ☐ The synthesis of nucleobase acrylate monomers. The synthesis procedures of adenine-, cytosine- and thymine acrylate monomers are already known but further optimization of these procedures as synthesis on a larger scale or easier purification of the products would be desirable.
- ☐ The synthesis and optimisation of the first nucleobase SUMI. This features the optimisation of the reaction parameters reaction time, RAFT agent, concentration, solvent and starting product equivalents for the first monomer insertion.

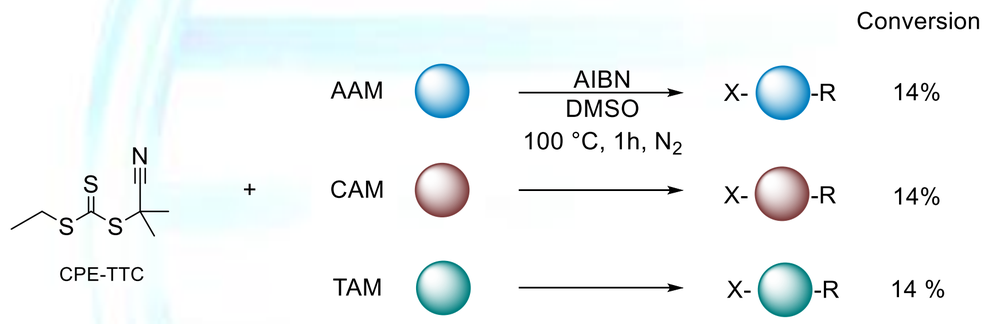
General SUMI procedure for the first insertion



Adenine and Cytosine Acrylate Monomer synthesis[1]

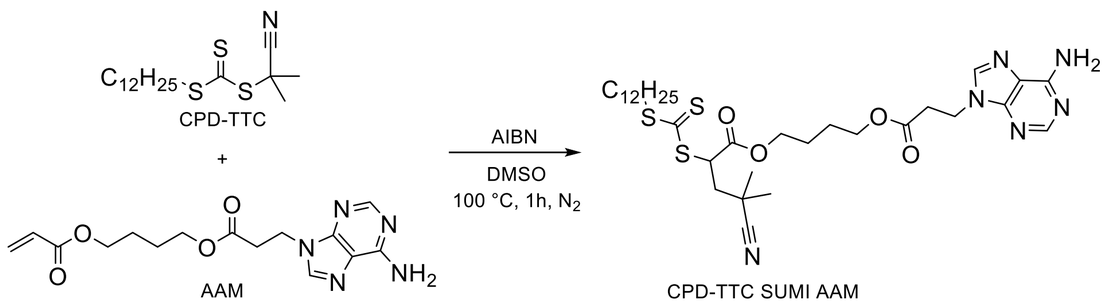


Influence of different monomers in SUMI on CPE-TTC

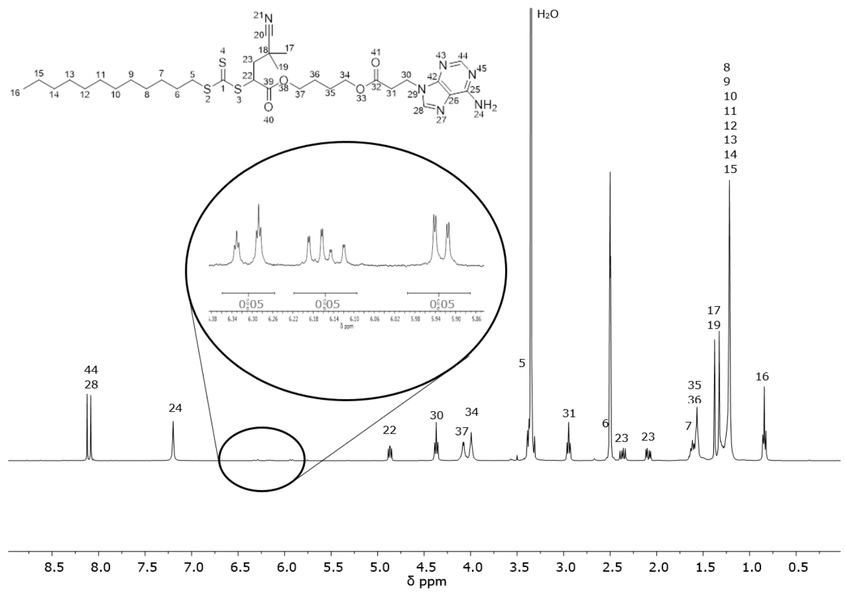


The conversion of adenine-, cytosine- and thymine acrylate monomers was tested. All three monomers showed the same conversion of 14%. Therefore, it is likely that all experiments performed with AAM would function with CAM and TAM,

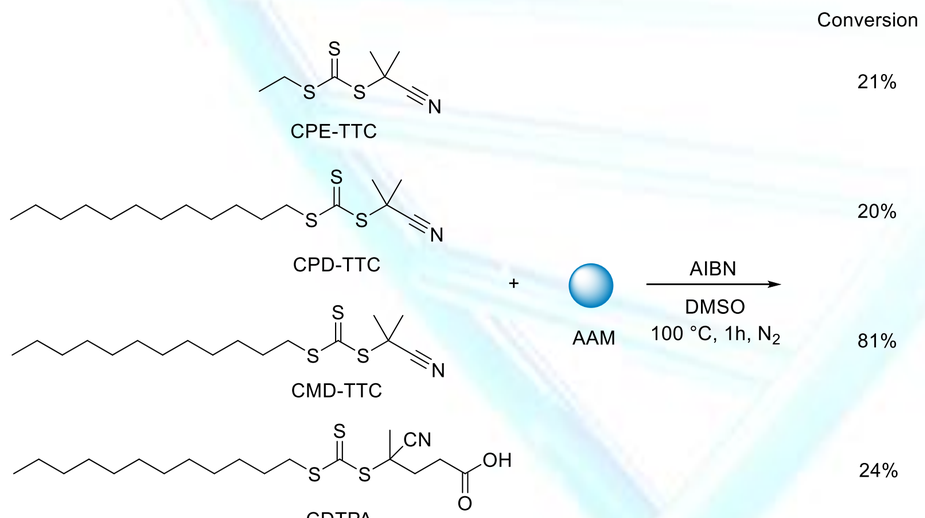
Optimization of CPD-TTC AAM SUMI synthesis



The ideal reaction equivalents are monomer:RAFT:initiator (5:1:0.05) when using AAM as monomer, CPD-TTC as RAFT agent and AIBN as initiator in DMSO when reacting 1h. at 100 °C. Purification is performed with flash chromatography when using MeOH:DCM (7:93) as mobile phase. A purity of 95% was achieved and confirmed with ^{1}H-NMR analysis



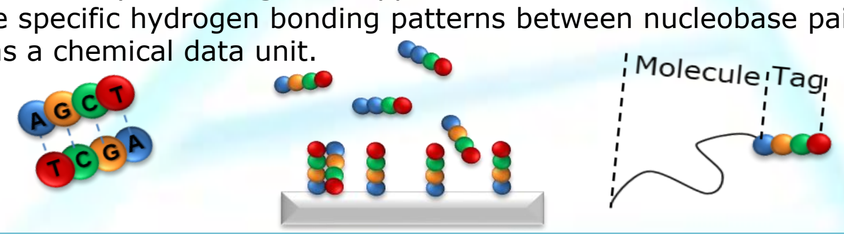
Influence of different RAFT agents with AAM insertion



CPE-TTC and CPD-TTC show approximately the same conversion and these products are used further for the optimization of the purification process. The reactivity of CMD-TTC is too high in these conditions. CDTPA has also an interesting conversion but is unusable for purification with flash chromatography.

Conclusion and future perspectives

- ☐ The first SUMI of nucleobase functionalized acrylates was performed. With this a strong foundation is laid for the synthesis of monodisperse nucleobase functionalised oligomers. As development of multiple insertions is only a matter of time, can already be thought of applications as molecular structure recognition using the specific hydrogen bonding patterns between nucleobase pairs, molecular tags or as a chemical data unit.



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References:

[1] S. Cheng, M. Zhang, N. Dixit, R. B. Moore, and T. E. Long, "Nucleobase Self-Assembly in Supramolecular Adhesives," *Macromolecules,* vol. 45, no. 2, pp. 805-812, 2012.

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