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Self-Immolative Phenylcarbonates for Nucleic Acid Templated Reactions

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Nucleic acid templated reactions exploit the high level of pre-organisation offered by the hybridisation of complementary nucleic acid sequences, which allows chemical reactions between reacting partners attached to oligonucleotides to occur at low concentrations. At those very low concentrations, classical, non-templated bimolecular reactions can hardly occur. Due to that, those templated reactions are highly selective, as a suitable complementary sequence to the reacting probes needs to be present in the reaction medium. This allows for the sensing and recognition of a complementary genetic sequence in a sample.

We have recently reported on a DNA templated reaction between a *p*-nitrophenylcarbonate and an amine. Both reacting partners are each attached to a DNA oligonucleotide. The reaction releases a coloured reporter, which can be used to assess of the success of the reaction. The whole system can be assembled from commercially available oligonucleotides with click chemistry

This thesis describes our investigations to improve on our original *p*-nitrophenylcarbonate templated reaction on different aspects. To do so, a new generation of different self-immolative carbonates were synthesized. Improvements such as the release of a more easily detectable fluorescent reporter, faster reaction rates and a diminution of the background noise could be achieved. This new family of carbonate also allowed us to tune the reaction kinetics through easy structural modifications of the carbonate and linker.

A series of nucleophiles to be used with those carbonates were also synthesized and tested. Finally, a proof-of-concept work that uses a FRET-based readout instead of the release of a reporter was investigated.

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