# Photoregulated Organocatalysis- from Caged Catalysis to Photoswitchable Catalytic Systems

Final Publishable Summary Report

Clément Padié, Kirsten Zeitler

## Project's objectives

The purpose of our project was the development of a controllable catalytic system with influence of light. We based our work on the amino acid organocatalytic system that allows for the formation of the reactive enamine species with enolisable aldehydes or ketones. Mainly, two approaches were proposed. The first one is based on the introduction of orthogonal photolabile protecting groups (deprotection by irradiation at different wavelengths) to provide for selective activation of a bifunctional catalyst (figure 1) and its corresponding different reactivity. The second approach deals with a photoswitch and concerns the inactivation of the free catalyst by complexation with the "open" merocyanine (MC) that can be obtain after irradiation of its closed spiropyran form (SP).

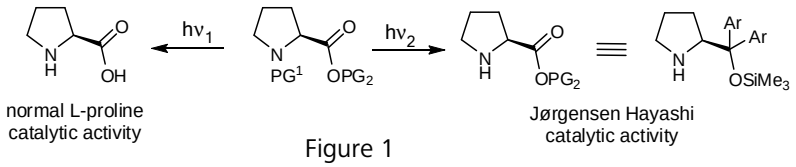


Figure 1

## Main results

### *Caged organocatalysts*

In order to simplify and validate our proposed system, we first developed a system based on known protecting groups that can be removed chemically. We also simplified the secondary amine catalyst for the intended enamine catalysis. Thus, we chose TEOC protected pyrrolidine that can be readily deprotected in the presence of fluoride as a trigger to provide the free amine prone to form enamines with aldehydes or ketones. This system proved to be an applicable test system as the reaction upon addition of acetone to nitrobenzaldehyde could be followed by $^1$H NMR (figure 2). This system can be considered as a good fluoride sensing test as the amplification by the initiation of catalysis by the fluoride allows for a high sensitivity. To improve our method, an easier method of visualization of the reaction evolution was needed. For this purpose we developed and tested a number of different fluorochromic substrates for the reaction described above. However, we observed that maleimide based fluorochromic molecules themselves reacted with fluoride and hence the use of these fluorochromes allows for a direct fluoride detection and quantification. We proved that fluoride induces a polymerization reaction of the maleimide by a Baylis-Hillman type reaction mechanism. This reaction constitutes a new qualitative and quantitative test for fluoride (figure 3). These results were already published in *New Journal of Chemistry* in early 2011. The article was among the three most accessed articles in March, April and May 2011.

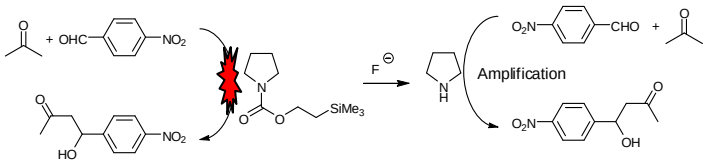


Figure 2

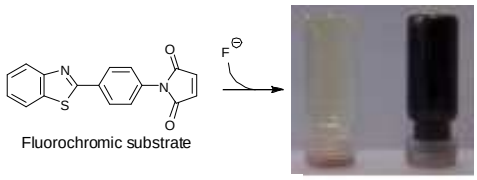


Figure 3

We also proved that it was possible to activate a pyrrolidine-based catalyst bearing a 2-nitrobenzyloxy-carbonyl group by a simple light irradiation. The free catalyst undergoes the addition of acetone onto the already described fluorogenic maleimide.

In order to get closer from our purpose and being able to switch the selectivity of the catalyzed reactions, the desired type **1** catalysts were synthesized in good yields.

However, a detailed study on the irradiation of the molecule in solution with different wavelengths and different light sources showed that it was not possible to get an efficient and selective general method for the needed deprotection leading to the desired active catalyst.

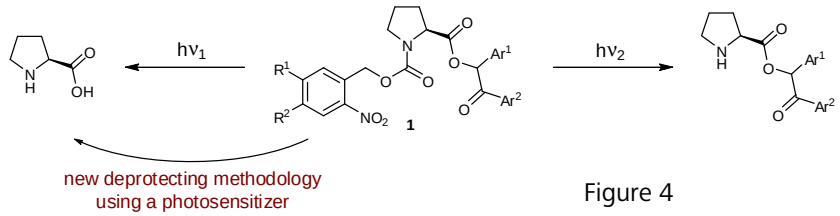


Figure 4

In order to get a selective deprotection we had to develop a new method. Introduction of a photosensitizer permits to initiate the radical formation with suitable irradiation and a quencher allows for the intermediately formed desyl radical (figure 4). This novel methodology proves to be broadly applicable and will be published in due course.

*ON/OFF induction of organocatalysts by interaction with immobilized spiropyranes*

As known from literature MC forms can be stabilized by immobilization of the molecule onto polymers. We used an azide/alkyne "click" chemistry approach for the synthesis of the desired functionalized polymers in order to allow for facile variation of the support and to study the influence of the polarity of the polymer on an expected proline/MC interaction.

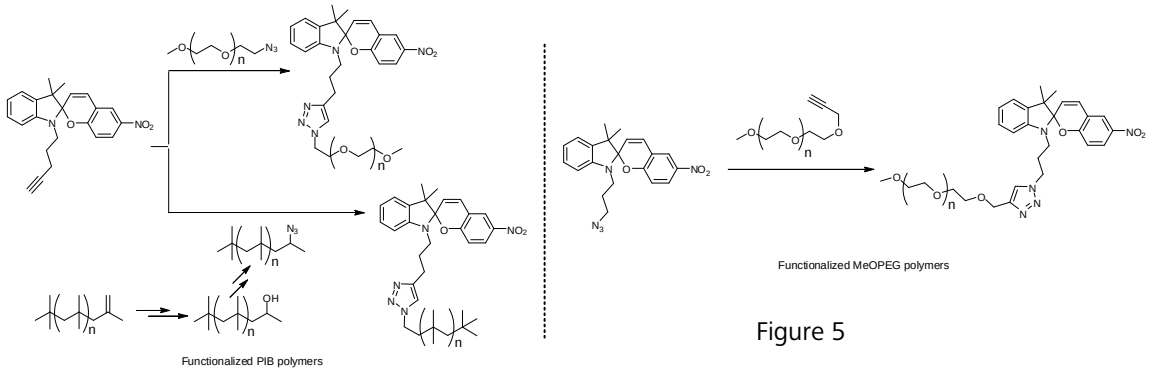


Figure 5

We succeeded in synthesizing the desired alkyne and azid functionalized SP and the reaction with the corresponding azide or alkyne MeOPEG was efficiently conducted. The less polar polymer PIB was chosen for comparison. In this context a new improved methodology for the introduction of a hydroxyl terminated PIB was developed. The obtained OH group allows for versatile further transformations and such as transformation into an azide that was subsequently "clicked" with the alkyne-SP. The first measurements of the complexation ability of MeOPEG-SP under light irradiation with proline are encouraging for further investigation and its use as an ON/OFF switchable organocatalytic system. However, due to the lack of time further studies could not been performed.

## Potential impact / Conclusion

We have been able to introduce a new concept in organocatalysis and proved its feasibility. During the course of this study, different questions and problems emerged from the initial project leading to interesting results bringing answers to other issues touching the community:

- Fluoride is one of the major biological active ions present in drinking water. WHO recommends controlling the concentration of fluoride in drinking water supplies and we provided a new, easy, convenient and economical visual test for this purpose.
- We discovered that fluoride might be of a special interest in organic synthesis as a potent nucleophilic catalyst
- PIB post synthesis functionalization is of great interest regarding the applications of this polymer towards different applications such as a biocompatible polymer.
- Spiropyrans offer a widespread variety of applications in adaptable materials. Our new, versatile synthetic methodology allows for a general immobilization approach of SP onto already reported azido materials.