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Master of Science HES-SO in Life Sciences

Optimization of Gold Catalyzed Reactions by application of a Porous Organic Cage (POC) in a Micellar System

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CHEMICAL DEVELOPMENT & PRODUCTION

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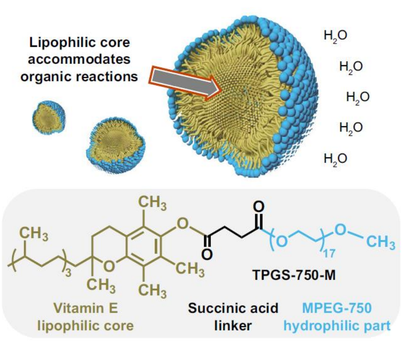
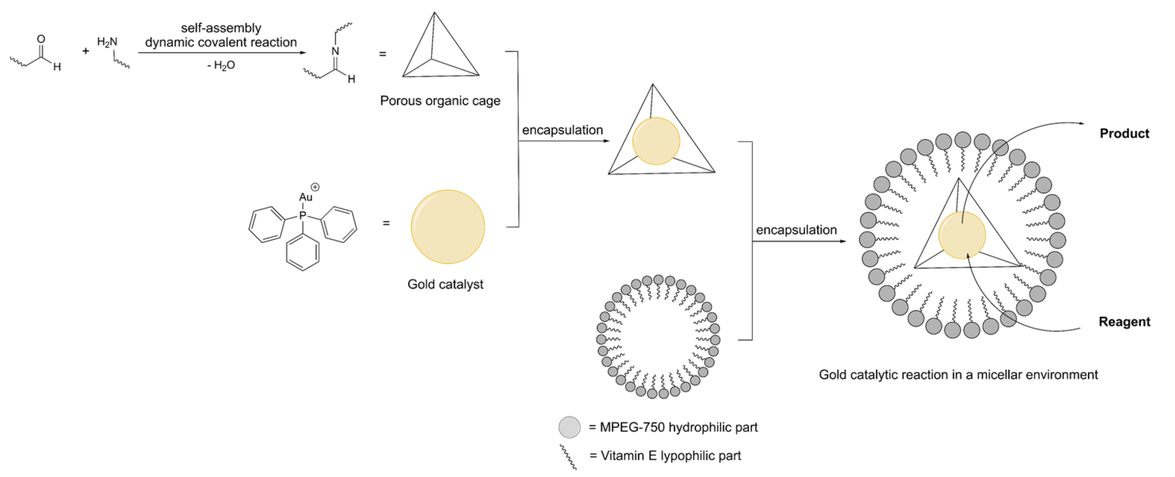
DESCRIPTION

Solvents are the biggest challenge for the green chemistry today, it represents 60% of all waste from the chemical and pharmaceutical industry. The group of Lipshutz revived in 2008 the use of surfactants in water to replace these solvents. The most studied one is called TPGS-750-M. Suzuki-Myiaura reactions have already been optimized in such conditions. The lipophilic core of the micelle enables the reaction to take place inside this “nanoreactor”.



A second challenge of todays green chemistry is the field of catalysis. Most metals used in catalysis will reach a critical minimum within the 5 to 50 years. Especially gold is problematic because of the high loading required for the reaction, up to 5 mol%. This led to the choice of optimizing gold catalyzed reactions in a micellar environment.



The method chosen to decrease the catalyst loading is called molecular encapsulation. The gold catalyst (guest) is encapsulated in a porous organic cage (host) which increases the local concentration and leads to a unique reactivity. The build complex is then inserted in the micellar environment where the reaction takes place

OBJECTIVES

The aim of this master thesis is to optimize gold catalyzed reactions by encapsulation of the catalyst in a porous organic cage. The second goal is to apply the complex in a micellar environment with TPGS-750-M as surfactant. Different objectives have been fixed:

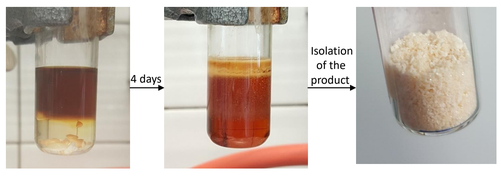
- Synthesis of different porous organic cages
- Optimize the encapsulation of gold catalysts with the different cages
- Apply the micellar and cage system to different gold catalyzed reactions and optimize these reactions
- Standardization of the characterization methods for the important steps
- Proof of concept of the system
- Selection of a final reaction
- Optimization and scale-up of the final reaction

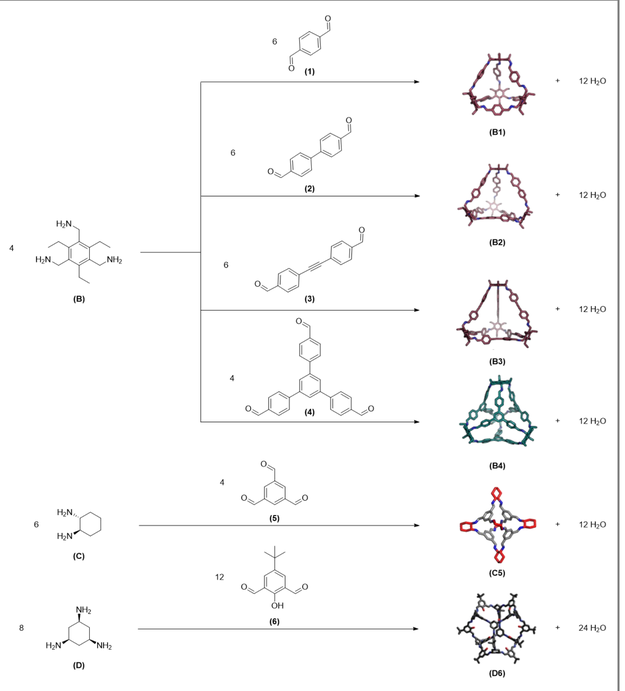
RESULTS

Synthesis of POCs

A typical imine condensation occurs between a di- or trialdehyde and a di- or triamine to build a porous organic cage.
The dynamic covalent reaction is a thermodynamically controlled process. Different strategies are known to control the reaction:

- High dilution – 4.6mM solution to respect of amine
- Solubility control of one of the reagents
- Slow addition of one of the reagents (over 24 hours)





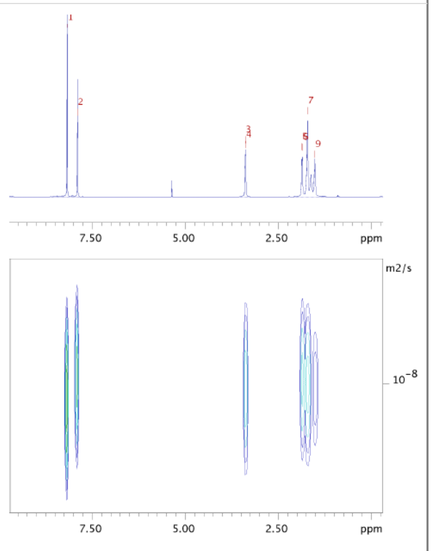
Six POCs have been chosen because they are ideal hosts for a gold catalyst and an ideal guest for the surfactant. They have been synthesized with moderate to good yields depending on the cage (31-91%).

Scheme for the synthesis of porous organic cages

Proof of encapsulation

The encapsulation was determined by various NMR methods; ^{1}H, ^{31}P and DOSY. A molecule doesn’t have the same chemical shift if it is free or encapsulated because the complex built during this process acts as a single species. This property changed the relaxation time of the molecule and was visible on NMR. The two relaxation times, longitudinal relaxation (T_1) and spin-spin relaxation (T_2) have been determined and the results prove the encapsulation by formation of a complex.

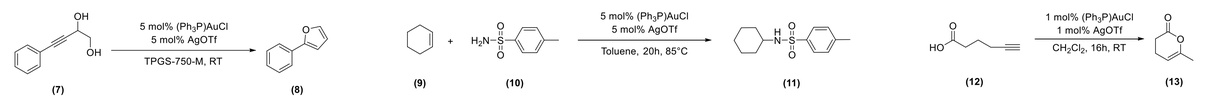
	Non-activated Catalyst	Activated Catalyst	Cage C5	Complex cage-catalyst	
				Peak 1	Peak 2
T1	4.7 s	4.7 s	1.38 s	3 s	0.69 s
T2	4.3 s	2.7 s	-	0.27 s	9 ms



DOSY of the cage C5

Gold catalysis

The complex cage-catalyst has been applied on three different gold catalyzed reactions. It wasn’t possible to decrease the catalyst loading with this method. The encapsulation process isolates the catalyst from the reaction mixture and decreases the conversion. Moreover, the reagents are probably reacting with the cage or activate the degradation process in presence of water.



CONCLUSION

Different porous organic cages have been synthesized with different affinities to enable the encapsulation. These POCs have been characterized and used as hosts for the encapsulation of the gold catalyst chloro(triphenylphsophine)gold(I). The molecular encapsulation has been proved by various NMR methods (^{1}H, ^{31}P, DOSY, T_1 and T_2). These values enabled the study of the properties of such a unique complex. Nevertheless, the application in gold catalyzed reaction wasn’t succesfull. Instead of increasing the local concentration in the reaction mixture, the catalyst might be isolated from it. This prevents the reagents from accessing the catalyst because of steric hindrance or because the reagents react directly with the cage.

The application of a porous organic cage to optimize gold catalyzed reactions should be further tested with different reactions which match the needed specifications without affecting the stability of the cage or without reacting with the imine bonds. Ideally, an intramolecular reaction which involves a rather small molecule.

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