

Pericàs Research Group



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Abstract

Over the last years, the Pericàs laboratory at ICIQ has been engaged in a broad research program aimed at developing a complete toolkit of polymer-supported and (to a lesser extent) magnetic nanoparticle-immobilized catalysts, with optimized characteristics of catalytic activity,

high induced stereoselectivity and extended life cycle.

The ultimate goal of this research has been the development of single-pass, catalytic and enantioselective flow versions of the most relevant processes for organic synthesis, contributing in this manner to a more sustainable practice of chemical synthesis. Our laboratory at ICIQ has been pioneer in this effort, being recognized as one of the leaders in the field.

Supported catalysts and flow processes

We have reported the first example of a chiral squaramide organocatalyst covalently immobilized onto a polystyrene resin. This bifunctional catalyst promotes fast Michael addition of 2-hydroxy-1,4-naphthoquinone to nitroalkenes with very high enantioselectivities at low catalyst loadings. The polystyrene (PS)-supported squaramide can be recycled without any decrease in enantioselectivity and adapted to continuous flow operation. A single flow experiment involving six different nitroalkenes in a sequential manner highlights the applicability of this methodology for rapid access to chemical diversity.

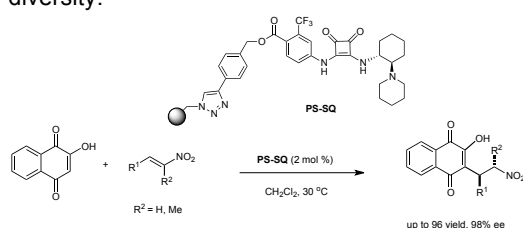


Fig. 1 – Continuous Flow, Highly Enantioselective Michael Additions Catalyzed by a PS-Supported Squaramide.

After the development of a family of enantiopure 3-aminopyrrolidines with very high catalytic activity and enantioselectivity in *anti*-selective Mannich reactions, last year we have presented a PS-supported version of the best organocatalyst demonstrating its effective recyclability and further improve its activity under batch and continuous flow applications. The very robust, immobilized catalyst has been successfully used in the implementation of a continuous flow process with short residence times (down to 6 min) for the production of highly enantioenriched *anti*-type Mannich adducts at the preparative scale.

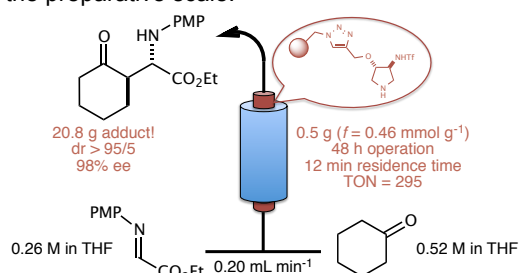


Fig. 2 – Asymmetric *anti*-Mannich Reactions in Continuous Flow.

A polystyrene (PS)-supported BINOL-derived phosphoric acid has been synthesized and applied in the enantioselective Friedel–Crafts reaction of indoles and sulfonylimines. The immobilized catalyst was highly active and selective, and gave rise to a broad range of 3-

indolylmethanamines in high yields and excellent enantioselectivities after short reaction times under very convenient reaction conditions. Moreover, the applicability of the system was further confirmed by rapid access to a library of compounds with three points of diversity in a single continuous-flow experiment that involved sequential pumping of different substrate combinations. A patent application to protect this discovery was presented in Dec 2013: “Polymer supported phosphoric acids and use thereof as catalysts in the preparation of 3-indolylmethanamines” Pericàs, M. A.; Rodríguez Escrich, C.; Osorio Planes, L. EP13382508.

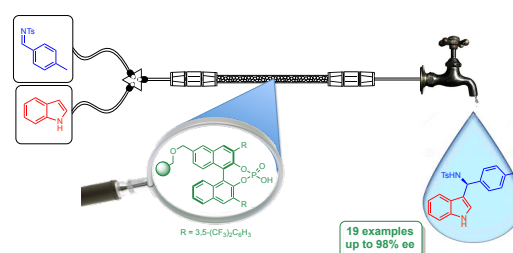


Fig. 3 – Enantioselective Continuous-Flow Production of 3-Indolylmethanamines Mediated by an Immobilized Phosphoric Acid Catalyst

Development of smart catalytic systems

By taking advantage of the properties inherent to immobilized species, we have been able to combine two otherwise incompatible catalysts, such as diarylprolinol silyl ether and an arylsulfonic acid. This application of the site-isolation principle has allowed us to use paraldehyde as a precursor of acetaldehyde, which results in much more convenient and easy-to-reproduce experimental procedures. These conditions have proven successful in promoting a one-pot, two-step procedure that gives rise to acetaldehyde Michael adducts in good yields with excellent enantioselectivities.

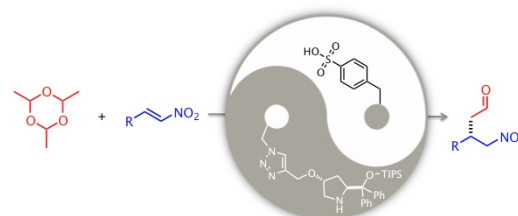


Fig. 4 – Paraldehyde as an Acetaldehyde Precursor in Asymmetric Michael Reactions Promoted by Site-Isolated Incompatible Catalysts

The application of the dual catalysis under site isolation to other reactions involving acetaldehyde, as well as studies concerning the recyclability of this dual catalytic system are currently underway in our laboratories.

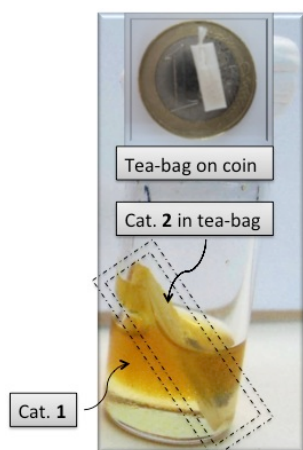


Fig. 5 – Picture illustrating the practical setup for site-isolation

During the last years we have explored different alternatives for anchoring catalysts onto supports through non-covalent bonding. A carboxylic acid containing a pyrrolidine substituent has been efficiently loaded onto KF through strong hydrogen bond (SHB) formation, affording a recyclable KF-supported catalyst for the direct asymmetric Michael addition of carbonyl compounds to *trans*- β -nitrostyrenes. Potassium fluoride has proven to be a practical and cheap non-covalent solid support for conveniently functionalized catalytic species.

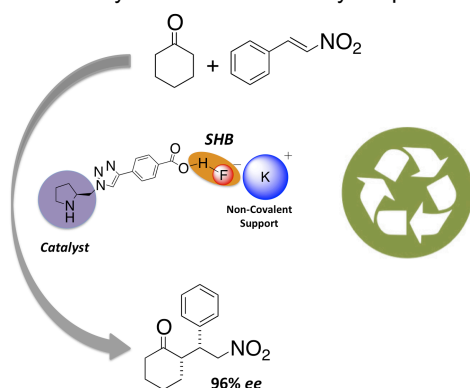


Fig. 6 – Potassium fluoride: A convenient, non-covalent support for the immobilization of organocatalysts through strong hydrogen bonds.

The copper catalyzed alkyne azide cycloaddition (CuAAC) reaction has been mostly used as a supporting strategy to connect the catalytic species with the corresponding supports. Along these studies, we observed that 1,2,3-triazole linkers placed near the catalytic unit exhibit remarkable cooperative catalytic effects. As a continuation of these studies, we have presented a polyfluoroalkyl derivative of 4-hydroxyproline, assembled through a 1,2,3-triazole linker, which displays high catalytic activity and enantioselectivity in aldol reactions

of acetone with aromatic aldehydes. The presence of the fluorinated tag allows the aldol reactions to be performed in a perfluorohexane/acetone biphasic system. In this way, both the catalyst and the perfluorinated solvent can be easily recycled and reused.

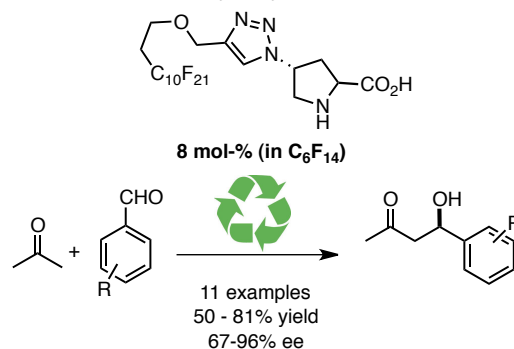


Fig. 7 – A Fluorous Proline Organocatalyst with Acetone-Dependent Aldolase Behavior.

Over the last years our research group has played the role of technology provider in the field of CuAAC reactions. For example, novel quantum dot capping ligands based on fullerene derivatives have been attached through click-chemistry to the surface of semiconductor CdSe nanocrystals (C70-CdSe). When this material was blended with the polymer poly-3-hexyl thiophene (P3HT) to fabricate bulkheterojunction solar cells, P3HT/C70-CdSe devices doubled the light-to-energy conversion efficiency when compared to P3HT/Py-CdSe reference devices prepared using pyridine as the capping agent.



Fig. 8 – Improving CdSe Quantum Dot/Polymer Solar Cell Efficiency Through the Covalent Functionalization of Quantum Dots: Implications in the Device Recombination Kinetic.

Superparamagnetic nanoparticles

Two new Ru-aqua complexes have been anchored onto magnetic nanoparticles (MNPs) and used for the exoxidation of olefins. These catalytic systems represent a very successful example of using anchored catalysts in MNPs that behave exactly like the homogeneous phase but that can benefit from the easy separation of MNPs using a simple magnet. The

combination of all these well-behaved properties enables the present system to be used in multiple recycling experiments without significant degradation.

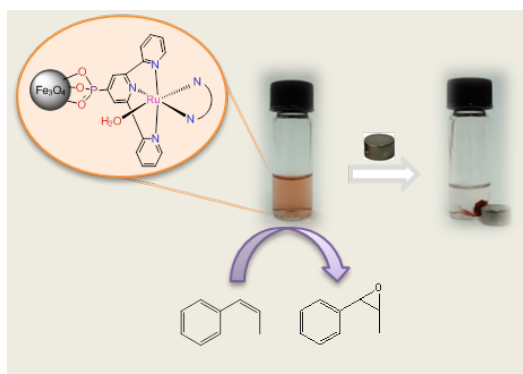


Fig. 9 – Molecular ruthenium complexes anchored on magnetic nanoparticles that act as powerful and magnetically recyclable stereospecific epoxidation catalysts.

Articles

“Molecular ruthenium complexes anchored on magnetic nanoparticles that act as powerful and magnetically recyclable stereospecific epoxidation catalysts”

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“Paraldehyde as an Acetaldehyde Precursor in Asymmetric Michael Reactions Promoted by Site-Isolated Incompatible Catalysts”

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