

Pericàs Research Group



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Laboratory Engineer: Patricia Llanes

Visiting Students: Christian Hempel (Feb-Jul and Oct-Dec) / Corina Eichenseer (April-June) / José Luis Capdevila (Summer Fellow) / Zachary Bryan (June-Aug)

Administrative Support: Núria Mas / Sara Garcia

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 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

A series of primary amino acids covalently supported onto polystyrene through a click strategy have been synthesized and evaluated as catalysts in asymmetric aldol-type reactions. We have reported the first example of three-component Mannich reactions in flow using a threonine derivative anchored to polystyrene. We have also shown that this flow system can be applied to the diastereo- and enantioselective medium-scale preparation of a diverse library of *anti*-Mannich adducts in a sequential manner.



Fig. 1 – Continuous Flow Enantioselective Three-Component *anti*-Mannich Reactions Catalyzed by a Polymer-Supported Threonine Derivative.

The enantioselective Friedel–Crafts reaction of indoles and sulfonylimines mediated by a polystyrene-supported (PS) BINOL-derived phosphoric acid allows the synthesis 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. This discovery has been protected by a patent application.

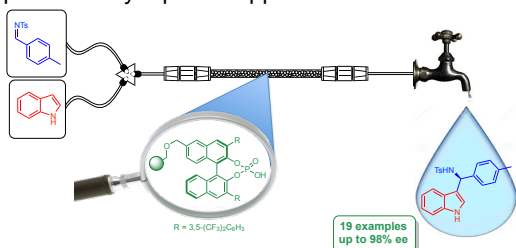


Fig. 2 – Enantioselective Continuous-Flow Production of 3-Indolylmethanamines Mediated by an Immobilized Phosphoric Acid Catalyst

During the last years we have explored different alternatives for anchoring catalysts onto supports through non-covalent bonding. Significant improvement has been achieved in this field, mainly in the framework of a collaborative research with the groups of Profs. Patrick Walsh and Eric J. Schelter at the Univ. of

Pennsylvania. We have reported a novel non-covalent binding strategy for Shibasaki's REMB framework {RE=rare earth metal; M=Li, Na, K; B=BINOL; RE:M:B=1:3:3, [M₃(sol)_n][(BINOLate)₃RE]} and explored the reactivity of the supported catalysts in several asymmetric transformations.

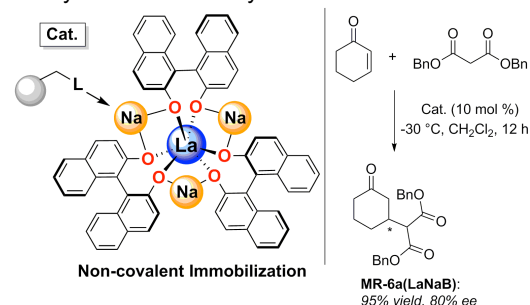


Fig. 3 – Non-covalent Immobilization of Rare Earth Heterobimetallic Frameworks and their Reactivity in an Asymmetric Michael Addition.

Development of smart catalytic systems

Unwanted acid-base neutralization is not a problem anymore! Under the site-isolation concept, PS-acidic and PS-basic catalysts worked compatibly as a “wolf-and-lamb” system for the cascade deoligomerization of paraldehyde and subsequent enantioselective cross aldol reaction with benzaldehydes. This site isolated, dual catalytic system can be reused at least ten times. The suitability of the crude cross-aldol products for the straightforward preparation of enantiopure drug analogues highlights the potential of the present methodology in medicinal chemistry.

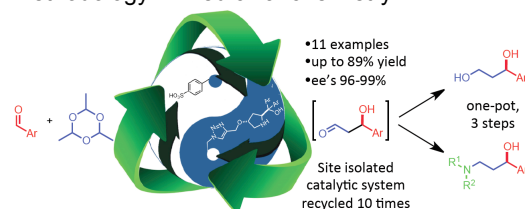


Fig. 4 – Highly Enantioselective Cross-Aldol Reactions of Acetaldehyde Mediated by a Dual Catalytic System Operating under Site Isolation

Now it's bismuth time! The asymmetric intermolecular α -alkylation of aldehydes with α -bromocarbonyl compounds can be achieved under visible-light irradiation by combining the second-generation MacMillan catalyst and an inexpensive, nontoxic, and commercially available Bi₂O₃ powder. This reaction also proceeded with high efficiency when the reaction vial was exposed to the morning sunlight in Tarragona.

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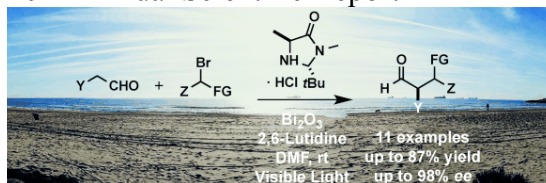


Fig. 5 – Light-Driven Organo catalysis Using Inexpensive, Nontoxic Bi_2O_3 as Photocatalyst.

A series of azobenzene-based thiourea catalysts have been developed with the aim of achieving control over the catalytic activity by the use of light. The conceptual design of these systems relies on the inactivation by means of intramolecular hydrogen bonding, only likely to take place in one of their isomeric forms. After fine structure modulation of the catalyst a substantial difference in activity has been observed between the irradiated and the nonirradiated reaction. Furthermore, the system allowed in situ manipulation of the catalyst activity during the course of a given experiment.

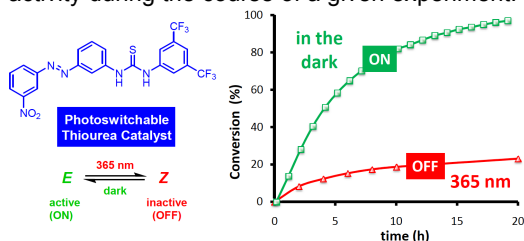


Fig. 6 – Photoswitchable Thioureas for the External Manipulation of Catalytic Activity.

In collaboration with Prof. Kleij's research group at ICIQ, we have developed a heterogeneous one-component bifunctional catalyst system able to promote the conversion of carbon dioxide and oxiranes to organic cyclic carbonates at low temperature ($45\text{ }^\circ\text{C}$). The bifunctional system can be easily recycled and reactivated when required. When compared with other heterogeneous organocatalysts for the same transformation, the reported catalyst is active at much milder temperatures, thus emphasising the optimal sustainability profile of the new catalytic system.

Articles

“Light-Driven Organocatalysis Using Inexpensive, Nontoxic Bi_2O_3 as the Photocatalyst”

Angew. Chem. Int. Ed. **2014**, *53*, 9613-9616
*Hot paper

*Highlighted in *Synfacts 2014*, issue 10, 1085

P. Riente, A. Mata Adams, J. Albero, E. Palomares, M. A. Pericàs

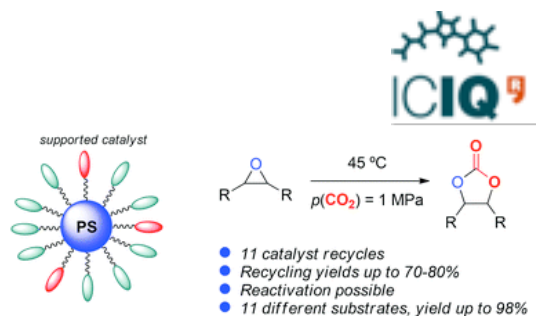


Fig. 7 – Conversion of oxiranes and CO_2 to organic cyclic carbonates using a recyclable, bifunctional polystyrene-supported organocatalyst.

Superparamagnetic nanoparticles

The development of functional magnetic Fe_3O_4 nanoparticles (MNPs) as the core of general-purpose platforms for the covalent supporting of ligands and catalysts is an active topic of research in the Group and particularly in the framework of the Mag(net)icFun project (PITN-GA-2012-290248).

This year we have reported two hybrid magnetic materials prepared from κ -carrageenan and Fe_3O_4 nanoparticles that have been tested as catalysts for the Michael addition of aldehydes to nitroalkenes. Remarkably, the material prepared from non modified κ -carrageenan showed catalytic activity in the reaction of choice, while the individual components were inactive. This points out to a synergistic effect between the MNPs and κ -carrageenan. The second catalyst, bearing a diphenylprolinol silyl ether moiety, was also shown to promote the reaction, giving rise to the corresponding adducts in excellent ee's. After the reaction is complete, the catalysts can be conveniently retrieved by simple magnetic decantation.

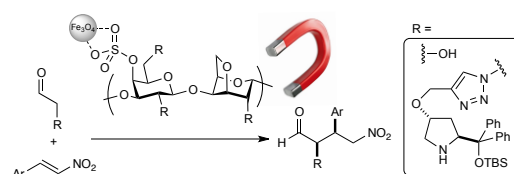


Fig. 8 – Hybrid magnetic materials (Fe_3O_4 - κ -carrageenan) as catalysts for the Michael addition of aldehydes to nitroalkenes.

“Continuous Flow Enantioselective Three-Component anti-Mannich Reactions Catalyzed by a Polymer-Supported Threonine Derivative”
ACS Catal. **2014**, *4*, 3027-3033

C. Ayats, A. H. Henseler, E. Dibello, M. A. Pericàs

"Highly Enantioselective Cross-Aldol Reactions of Acetaldehyde Mediated by a Dual Catalytic System Operating under Site Isolation"
Chem. Eur. J. **2014**, *20*, 13089-13093
X. Fan, C. Rodríguez-Escrich, S. Wang, S. Sayalero, M. A. Pericàs

"Reversible photocontrolled disintegration of a dimeric tetraurea-calix[4]pyrrole capsule with all-trans appended azobenzene units"
Chem. Sci. **2014**, *5*, 4260-4264
L. Osorio-Planes, M. Espelt, M. A. Pericàs, P. Ballester

"A Theoretically-Guided Optimization of a New Family of Modular P, S-Ligands for Iridium-Catalyzed Hydrogenation of Minimally Functionalized Olefins"
Chem. Eur. J. **2014**, *20*, 12201-12214
J. Margalef, X. Caldentey, E. A. Karlsson, M. Coll, J. Mazuela, O. Pàmies, M. Diéguez, M. A. Pericàs

"Hybrid magnetic materials (Fe₃O₄-k-carrageenan) as catalysts for the Michael addition of aldehydes to nitroalkenes"
Tetrahedron **2014**, *70*, 6169-6173
**Highlighted in Synfacts 2014, issue 11, 1229*
C. A. Mak, S. Ranjbar, P. Riente, C. Rodríguez-Escrich, M. A. Pericàs

"An Enantioselective Recyclable Polystyrene-Supported Threonine-Derived Organocatalyst for Aldol Reactions"
Adv. Synth. Catal. **2014**, *356*, 1795-1802
**Highlighted in Synfacts 2014, issue 8, 889*
A. H. Henseler, C. Ayats, M. A. Pericàs

"Air- and Water-Tolerant Rare Earth Guanidinium BINOLate Complexes as Practical Precatalysts in Multifunctional Asymmetric Catalysis"
J. Am. Chem. Soc. **2014**, *136*, 8034-8041
J. R. Robinson, X. Fan, J. Yadav, P. J. Carroll, A. J. Wooten, M. A. Pericàs, E. J. Schelter, P. J. Walsh

"Asymmetric Allylation of Ketones and Subsequent Tandem Reactions Catalyzed by a Novel Polymer-Supported Titanium-BINOLate Complex"
Chem. Eur. J. **2014**, *20*, 7122-7127
**Highlighted in Synfacts 2014, issue 8, 883*
J. Yadav, G. R. Stanton, X. Fan, J. R. Robinson, E. J. Schelter, P. J. Walsh, M. A. Pericàs

"Non-Covalent Immobilization of Rare Earth Heterobimetallic Frameworks and their Reactivity in an Asymmetric Michael Addition"

Adv. Synth. Catal. **2014**, *356*, 1243-1254
COVER
J. R. Robinson, J. Yadav, X. Fan, G. R. Stanton, E. J. Schelter, M. A. Pericàs, P. J. Walsh

"Photoswitchable Thioureas for the External Manipulation of Catalytic Activity"
Org. Lett. **2014**, *16*, 1704-1707
L. Osorio-Planes, C. Rodríguez-Escrich, M. A. Pericàs

"A Bis(Triazolecarboxamido) Ligand for Enantio- and Regioselective Molybdenum-Catalyzed Asymmetric Allylic Alkylation Reactions"
Adv. Synth. Catal. **2014**, *356*, 711-717
**This paper has been selected by the Editorial Board of SYNFACTS for its important insights: Synfacts 2014, 7, 607*
E. Ozkal, M. A. Pericàs

"Reaction of Alkynes and Azides: Not Triazoles Through Copper-Acetylides but Oxazoles Through Copper-Nitrene Intermediates"
Chem. Eur. J. **2014**, *20*, 3463-3474
E. Haldón, M. Besora, I. Cano, X. C. Cambeiro, M. A. Pericàs, F. Maseras, M. C. Nicasio, P. J. Pérez

"Fine-Tunable Tris(triazolyl)methane Ligands for Copper(I)-Catalyzed Azide-Alkyne Cycloaddition Reactions"
Adv. Synth. Catal. **2014**, *356*, 857-869
E. Ozkal, P. Llanes, F. Bravo, A. Ferrali, M. A. Pericàs

"Conversion of oxiranes and CO₂ to organic cyclic carbonates using a recyclable, bifunctional polystyrene-supported organocatalyst"
Green Chem. **2014**, *16*, 1552-1559
C. J. Whiteoak, A. H. Henseler, C. Ayats, A. W. Kleij, M. A. Pericàs

"Enantioselective Continuous-Flow Production of 3-Indolylmethanamines Mediated by an Immobilized Phosphoric Acid Catalyst"
Chem. Eur. J. **2014**, *20*, 2367-2372
**Highlighted in Organic Process Research & Development, 2014, 18, 461-467*
**Highlighted in Synfacts, 2014, issue 5, 546*
L. Osorio-Planes, C. Rodríguez-Escrich, M. A. Pericàs

"Optical Control of Enzyme Enantioselectivity in Solid Phase"
ACS Catal. **2014**, *4*, 1004-1009
A. Bautista-Barrufet, F. López-Gallego, V. Rojas-Cervellera, C. Rovira, M. A. Pericàs, J. M. Guisán, P. Gorostiza