# RESEARCH INTERESTS
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## Introduction

My laboratory conducts research in organic chemistry directed at implementing more sustainable and efficient chemical processes. The main themes are green chemistry and homogeneous catalysis. Green chemistry is concerned with the development of more efficient, safer and less wasteful chemical processes. Key contributors to implementing greener processes are catalysts, which are substances that can increase the efficiency and decrease the amount of waste generated in chemical transformations. The emphasis is on sustainable technologies and catalytic processes promoted by organic and main group compounds and by transition metal complexes, with a particular interest in potential industrial and biological applications. The current projects are concerned with two principal research areas:

(1) development of synthetic methodologies related to medicinal chemistry;

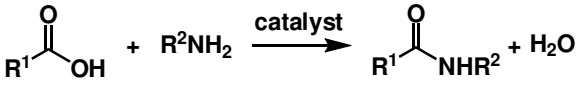
(2) development of transformations to facilitate the synthesis of complex organic molecules.

Research involves the synthesis of organic, main group and organometallic catalysts through the use of the traditional techniques and instrumentation of organic and organometallic chemistry. In particular, air-free techniques (Schlenk and high-vacuum lines, inert atmosphere glovebox) are often necessary to synthesize metal catalysts. In addition, significant efforts are devoted to the synthesis of the substrates on which to test for a desired reactivity. A typical project may involve the synthesis of potential catalysts (often requiring the prior synthesis of organic ligands) and model substrates, followed by the examination of catalytic activity and optimization of catalysts structure and reaction conditions. Students more interested in synthesis than in the testing of catalysts are offered the possibility to synthesize more densely functionalized substrates or compounds of industrial or pharmaceutical interest that will be used to demonstrate the effectiveness of the catalysts. Students thus become familiar with a variety of synthetic, spectroscopic and analytical techniques, with NMR spectroscopy playing a predominant role.

1. Development of catalysts for the formation of amides from carboxylic acids and amines

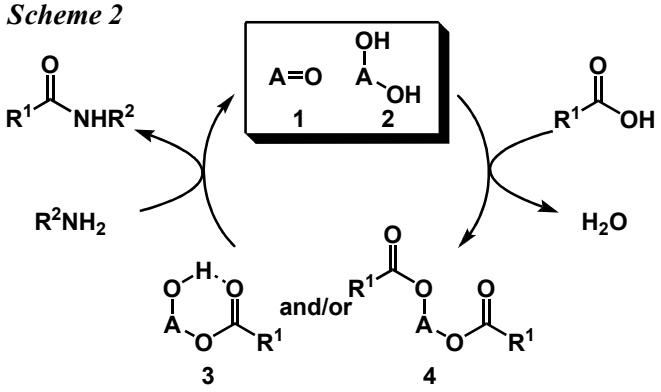
***Objectives of the research.*** The objective of this research is to develop catalysts for the production of amides from carboxylic acids and amines. A 2006 survey on the reactions used at GlaxoSmithKline, AstraZeneca and Pfizer concluded that "there is still a pressing need for the development of catalytic, environmentally friendly acylation processes" for the synthesis of amides (Scheme 1).[1] In fact, a 2007 panel of six pharmaceutical companies unanimously identified the atom-economical formation of amides as a top priority research area.[2] Our research is aimed at filling this pressing need. Such green catalytic transformations (water is the only by-product) could dramatically increase the efficiency of amidations and could replace the more traditional methods of synthesizing amides that typically use toxic reagents, generate large amounts of waste, necessitate the use of protecting groups and can be prohibitively expensive to conduct on large scale.

*Scheme 1*




***Research.*** We initially studied catalysts based on arsenic (A = As) and antimony (A = Sb) oxides that can be represented by structures **1** or **2** (Scheme 2). As shown in this general catalytic cycle, the main mode of activation of these catalysts was expected to be by transformation of the OH group of the carboxylic acid into a better leaving group. We have discovered what constitutes, to our knowledge, the first instance of an

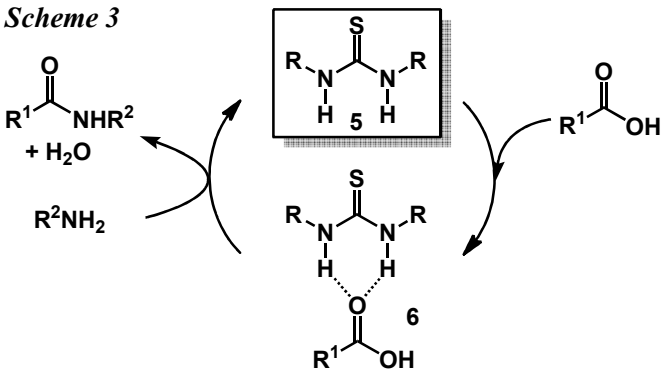
*Scheme 2*



As-catalyzed amidation reaction. Unfortunately, even after extensive studies the activity of the catalysts could not be brought up to the level necessary for the catalysts to be broadly useful.

So we have just started a new approach based on the use of thioureas **5** as strong hydrogen bonding catalysts (Scheme 3). In this new approach, a completely new activation mode is targeted in which the thiourea activates the carboxylic acid through strong hydrogen bonding, making it a better electrophile for reaction with the nucleophilic amine.

***Scheme 3***



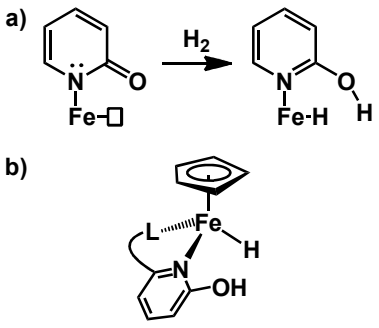

2. Development of iron-based catalysts for the homogeneous hydrogenation of C=X and C≡X bonds

***Objectives of the research.*** The main objective of this project is to develop iron-based catalysts for the homogeneous hydrogenation of C=X and C≡X bonds. Homogeneous hydrogenation technologies have been widely embraced by industry, with particularly impressive applications in medicinal chemistry. However, several serious limitations remain. Chief among them is that the metals traditionally used in homogeneous hydrogenation are very expensive (about 200-4000 $/mol for Ru, Ir and Rh). Their replacement with metals like iron, for which worldwide prices are usually below 0.20 $/mol, has therefore received considerable attention in recent years. In addition, Ru, Rh and Ir residues are usually toxic; Fe residues usually display lower toxicity and are more environmentally acceptable.

While hundreds of Ru, Rh and Ir complexes have been used in homogeneous hydrogenation reactions, the number of known iron-based catalysts is much smaller.[3]

***Research.*** In our current research, the key ligands incorporate a 2-hydroxypyridine unit that will potentially allow them to participate in a ligand-assisted heterolytic cleavage of dihydrogen (Scheme 4a). Recent reports of the use of this type of strategy with Ru and Ir complexes suggest that this mode of activation of $H_2$ is particularly effective in hydrogenation reactions.

***Scheme 4***




Work in lab is in three steps: (1) we need to synthesize the organic ligands that (2) are then attached to iron to form potential catalysts that (3) are then tested for catalytic activity. The iron complexes that we currently target are piano stool complexes as shown in Scheme 4b.

The use of Fe complexes in catalytic transformations is still in its infancy and there is a tremendous opportunity to develop new catalysts and discover new types of reactivity. Clearly, the discovery of efficient iron catalysts for homogeneous hydrogenation could have a major effect on the fields of homogeneous catalysis and green chemistry and on the industrial practice of hydrogenation processes.

## References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2. Constable, D. J. C.; Dunn, P. J.; Hayler, J. D.; Humphrey, G. R.; Leazer, J. L., Jr.; Linderman, R. J.; Lorenz, K.; Manley, J.; Pearlman, B. A.; Wells, A.; Zaks, A.; Zhang, T. Y. "Key green chemistry research areas - A perspective from pharmaceutical manufacturers" *Green Chem.* **2007**, *9*, 411-420.

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