

## Drew Rutherford



Drew Rutherford joined the faculty at Concordia College in 1998 after receiving his Ph.D. in inorganic chemistry in 1996 from North Dakota State University under the direction of D.A. Atwood. Prior to that, he earned a M.S. in organic chemistry from North Dakota State University in 1994 under M.P. Sibi and a B.A. in biology and chemistry from the University of Minnesota-Morris in 1991. From 1997 to 1998, he held a post-doctoral position at the University of Utah with J.A. Gladysz. Drew Rutherford has been named the Carl L. Bailey Centennial Research Scholar (2001), a Council on Undergraduate Summer Research Awardee (2001), and an Individual USDA Grant Recipient (2001).

**Research Interests:** My interests center around the synthesis of interesting materials, specifically biologically active organic molecules and organometallic catalysts. Several projects in my laboratory involve collaborative work with scientists at the USDA-Biosciences Research Laboratory (BRL) to synthesize bioactive molecules. The BRL is located in Fargo, ND and specializes in investigating how animals metabolize foreign materials within their bodies and excrete or retain (bioaccumulate) the byproducts in their tissues. One of the keys to undertaking these studies is the ability to synthesize the contaminant of interest in a radioactive form (radiolabeled). The radioactivity of the sample allows scientists to track it within the body or when excreted.

A new liquid phase was recently reported in which all of the hydrogens of ordinary organic liquids were replaced by fluorines. The term “fluorous” was coined as the analogue to aqueous in classifying these new perfluorinated liquids. Perfluorinated alkanes exhibit unique physical properties of which temperature-dependent miscibilities with many organic liquids are the most relevant for this work. The temperature-dependence of fluorous/organic miscibilities creates an opportunity to use catalysts and reagents that possess high affinities for fluorous solvents in chemical transformations in either homogeneous or heterogeneous regimes. The ability to use a catalyst to affect a reaction in the homogeneous state while maintaining the advantages of heterogeneous product/catalyst separation by a simple change in reaction temperature is the main driving force to this diverse project.

### Selected Publications:

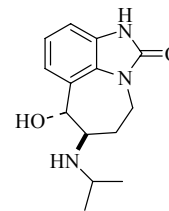
- D. Rutherford and D.A. Atwood “Unusual Alkylaluminum Amides, Adducts, and Aluminates Containing Lithium” *J. Am. Chem. Soc.* **118**, 11535 (1996).
- J.J.J. Juliette, D. Rutherford, I.T. Horváth and J.A. Gladysz “Transition Metal Catalysis in Fluorous Media: Practical Application of a New Immobilization Principle to Rhodium-Catalyzed Hydroboration of Alkenes and Alkynes” *J. Am. Chem. Soc.* **121**, 2696 (1999).
- M.P. Sibi, D. Rutherford, P.A. Renhowe and B. Li “Investigations of a Nucleophilic Alaninol Synthon Derived from Serine” *J. Am. Chem. Soc.* **121**, 7509 (1999).
- T. Soós, B.L. Bennett, D. Rutherford, L.P. Barthel-Rosa and J.A. Gladysz “Synthesis, Reactivity, and Metal Complexes of Fluorous Triarylphosphines of the Formula  $P(p\text{-C}_6\text{H}_4(\text{CH}_2)_3(\text{CF}_2)_{n-1}\text{CF}_3)_3$  ( $n = 6, 8, 10$ )” *Organometallics* **20**, 3079 (2001).



## Research Projects

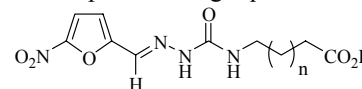
**Radiolabeled Synthesis of Zilpaterol:** The USDA Agricultural Research Service-Biosciences Research Laboratory-Animal Metabolism Unit (BRL) located in Fargo specializes in investigating how animals metabolize foreign materials (natural toxins, environmental pollutants, antibiotics, pesticides or feed additives) within their bodies and excrete or retain (bioaccumulate) the byproducts in their tissues. One of the keys to undertaking these studies is the ability to synthesize the contaminant of interest in a radioactive form (radiolabeled). The radioactivity of the sample allows scientists to track it within the body or when excreted. Additionally, if the original sample is metabolized into something slightly different, the radioactivity “tags” the metabolite as a “descendant” of the original sample.

Zilpaterol is a surprisingly simple molecule and its synthesis is perfectly suited for an undergraduate summer project. The agricultural food additive Zilmax, marketed by Hoechst, contains zilpaterol as the active ingredient. Zilpaterol is a pharmacologically active  $\beta_2$ -adrenergic agonist and is capable of redirecting cellular metabolism in favor of protein synthesis while promoting lipolysis in adipose tissues. Zilpaterol is used as a “repartitioning agent” in cattle feed to enhance weight gain, feed efficiency and carcass yield. While this product is used legally in Mexico and South Africa, zilpaterol is not currently approved for use in the United States. The United States Department of Agriculture is interested in determining how this compound is metabolized and identifying the products of the metabolism and where each of them bioaccumulates. The work in my laboratory at Concordia is to work closely with scientists at the USDA lab to develop a high-yielding, cost-effective methodology for the synthesis of radiolabelled Zilpaterol.



Zilpaterol

**Immunochemistry - “Tethered”-nitrofurazone:** Another area where the Biosciences Research Laboratory is concentrating effort is immunoaffinity quantitation of molecules. This is a highly selective method of quantifying very dilute amounts of a target molecule directly from a complex mixture. In this process, antibodies to the molecule of interest (the antigen) are attached to a support material and packed into a column. A heterogeneous, potentially non-manipulated, sample mixture is passed through the column containing the antibodies. When the antigen encounters the antibody engineered to bind to it, it is selectively removed from the mixture, adsorbing to the stationary support. Once the sample (sans antigen) has eluted from the column, the column is washed in a manner that allows the antigen to be released from the support. It is then quantified. Unfortunately, the molecules of interest that the BRL studies are too small to elicit an immune response directly. Rather, the molecule is “tethered” to a larger protein that is capable of eliciting an immune response. When an animal (often a rabbit) mass-produces antibodies to the molecule-protein complex, specific B-cells are involved. The activated B-cells can be isolated and made “immortal” through fusion with a cancer cell line and related cell biology techniques, resulting in an unlimited supply of antigen-specific, antibody-producing cells. These cells are then stimulated to produce large quantities of the antibody necessary for the immunoaffinity column.



“Tethered” Nitrofurazone

The chemist's role in this process is to modify the molecule of interest with a long (at least 4-carbon), aliphatic carboxylic acid-terminated “tether”. The tether is used to link the molecule to the protein, forming the immunoactive molecule-protein complex.

Nitrofurazone is used as an agricultural antibiotic. The USDA is interested in developing an immunochemical assay for foods exposed to this compound. This project centers around developing a synthesis of the “tether”-modified nitrofurazone.

**Fluorous Chemistry:** A new liquid phase was recently reported in which all of the hydrogens of ordinary organic liquids were replaced by fluorines. The term “fluorous” was coined as the analogue to aqueous in classifying these new perfluorinated liquids. Perfluorinated alkanes (ethers or amines) exhibit unique physical properties of which temperature-dependent miscibilities with many organic liquids are the most relevant for this work. The temperature-dependence of fluorous/organic miscibilities creates an opportunity to use catalysts and reagents that possess high affinities for fluorous solvents in chemical transformations in either homogeneous or heterogeneous regimes. The ability to use a catalyst to affect a reaction in the homogeneous state while maintaining the advantages of heterogeneous product/catalyst separation by a simple change in reaction temperature is the main driving force to this project. In particular, I am interested in synthesizing chiral, fluorous derivatives of binaphthol, salen and bis(oxazoline) ligand systems. Non-fluorous ligand systems of this type have found success in enantioselective catalytic reactions including hydrogenations, epoxidations and cyclopropanations of alkenes and enantioselective conjugate additions of radicals. The prospect of extending this type of chemistry into the fluorous realm is extremely exciting.

**Enantioselective Catalysis in Supercritical CO<sub>2</sub>:** Supercritical carbon dioxide has gained widespread attention in synthetic chemistry for its potential to replace traditional organic solvents. Supercritical CO<sub>2</sub> can be envisaged as an environmentally benign or “green” solvent due to its low toxicity as compared to other organic solvents. While seemingly the perfect solvent choice for any organic reaction – cheap, abundant, non-toxic, volatile and easily scrubbed of moisture - one decidedly negative attribute of supercritical CO<sub>2</sub> as a solvent is the difficulty in solubilizing catalysts in this nonpolar medium.

The focus of this project will be to attempt to remedy the insolubility of catalysts in supercritical CO<sub>2</sub> and bring an arsenal of organic transformations and catalysts into this area of chemistry. In fact, this project is an extension of the fluorous project, in that the same modifications made to ligands that promote high fluorous-phase affinities also impart increased solubility of these ligands (and theoretically the metals they are attached to) into supercritical CO<sub>2</sub>. Thus, we can get twice the bang-for-the-buck when fluorous-soluble catalysts are developed; we can explore the chemistry of the catalysts in both fluorous and supercritical CO<sub>2</sub> solvents.