

Final Report  
National Science Foundation  
Grant CHE-0414325

Cleavage and Formation of C–S and C–N Bonds in Heterocyclic Compounds by  
Homogeneous Transition Metal Complexes

William D. Jones, P.I.  
Department of Chemistry, University of Rochester, Rochester, NY 14627

Three years - July 1, 2004-June 30, 2007

The goal of this project is to advance our understanding of the basic chemistry of and develop new synthetic applications for the cleavage and formation of C-S and C-N bonds in thiophenes and heterocyclic nitrogen containing compounds with transition metal fragments. The studies with sulfur have applications in deep hydrodesulfurization (deep HDS), whereas the work with nitrogen will focus on the use of allylamines for heterocycle synthesis. The work has the following objectives: (1) provide basic information about the requirements for the cleavage of these strong and/or hindered C-X bonds (X = S, N), (2) provide information about the mechanism(s) for C-X bond cleavage, (3) examine structural motifs for the binding of sulfur- and nitrogen-containing organic compounds to metals, (4) understand the chemistry of metal sulfhydryl and sulfido compounds, their interconversion, and their lability, and (5) developing catalytic systems for manipulation of C-S and C-N bonds. New concepts to be explored include the determination of electronic effects on bond cleavage and the use of supported systems for catalysis.

### Intellectual Merits of Proposed Study:

This project has advanced our understanding of the basic chemistry of the cleavage and formation of C-S and C-N bonds in thiophenes and heterocyclic nitrogen containing compounds using transition metal fragments. The studies with sulfur serve as models for hydrodesulfurization, whereas the work with nitrogen has focused on the use of allylamines for heterocycle synthesis. The work has (1) investigated the requirements for the cleavage of hindered C-S bonds, (2) provided information about the mechanism for C-N bond cleavage, (3) examined structural motifs for the binding of sulfur- and nitrogen-containing organic compounds to metals, and (4) developed catalytic systems for manipulation of C-S and C-N bonds.

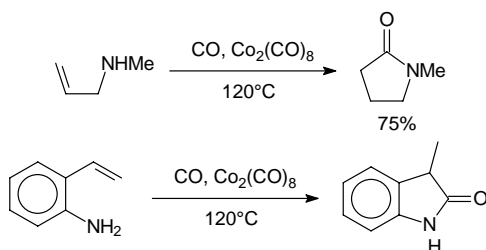
### Broader Impacts of Proposed Study:

In the process of these studies, both undergraduate and graduate students were trained at an advanced level to use the concepts of inorganic, organic, analytical, and physical chemistry for the solution of difficult technical problems. We have been active in the NSF REU and RET programs, and have had undergraduates and high school teachers to the University for summer research activities in our laboratory.

The success of the scientific work presented in this proposal will lead to a better understanding of how to desulfurize the most resistant thiophenes still found in hydrocarbon fuels. This knowledge will contribute to meeting the new EPA standards for low sulfur emissions from fuels. The EPA ruling requires that most refiners and importers meet a corporate average gasoline sulfur standard of 80 ppm and most refineries must produce gasoline averaging no more than 30 ppm sulfur. Current technology in refineries is not capable of meeting this target, so that major problems can be anticipated. Another impact of the work has been to discover new synthetic routes to nitrogen-containing heterocycles, a fundamental building block in many biologically important compounds. New routes to these species involving C-N cleavage and reformation, combined with intramolecular C-H activation, have been discovered and their mechanism investigated. These catalysts can have an impact on new processes for routes to intermediates of pharmaceutical importance.

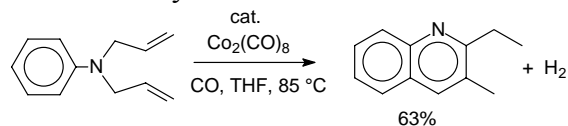
### Findings: Nitrogen Containing Heterocycles

Specific examples of accomplishments include the formation of lactams by carbonylative cyclization. Both simple and fused heterocycles have been produced catalytically using cobalt carbonyl as catalyst.

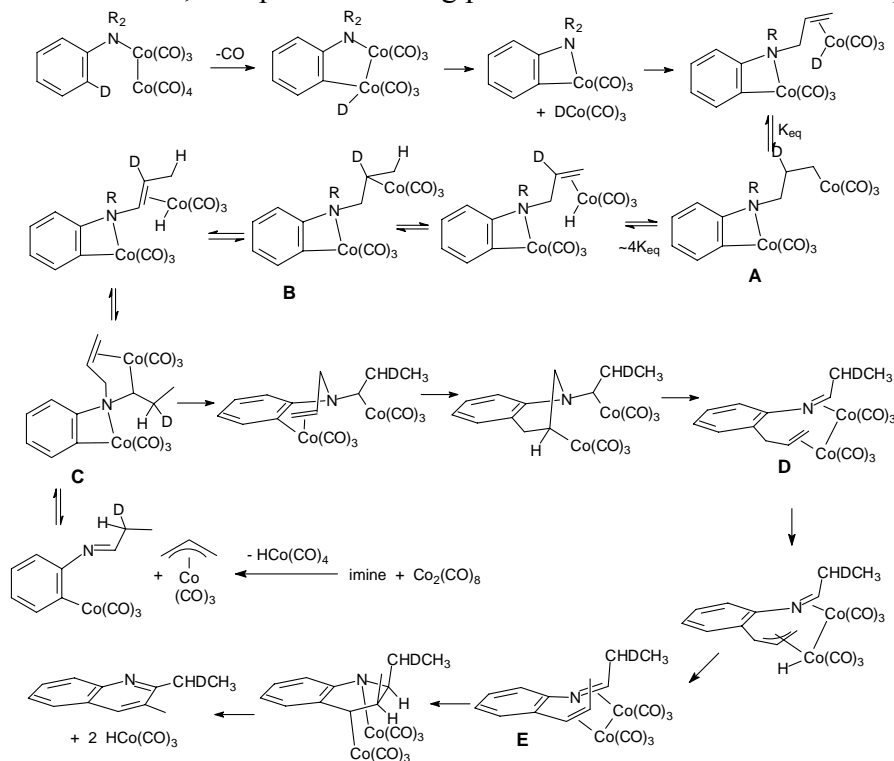


We have also discovered a new route to quinolines. The reaction conditions are the same as above, but no carbon monoxide is incorporated into the product. Instead, allylanilines are used to complete the formation of the heterocycle. The scope of this reaction has been broadened to include a wide variety of substituted anilines, with both steric and electronic effects being

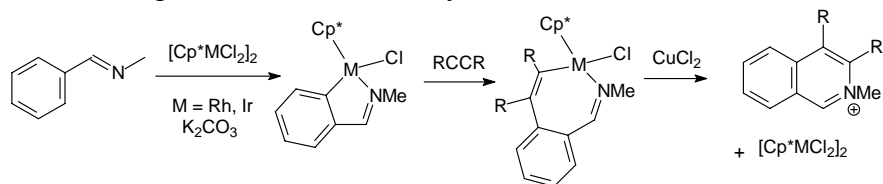
studies. In general, our findings show tolerance of a wide variety of groups although ortho substitution clearly interferes with the cyclization.



Additional studies have been performed to determine the mechanism of the reaction. Use of deuterium labeled anilines has permitted the pathway for the cyclization to be determined. Our findings show that one allyl group is cleaved to give allylcobalttricarbonyl and an imine, which then combine to give a vinyl-imine that undergoes oxidative coupling followed by a double  $\beta$ -elimination. In this manner, the specific labeling pattern that we observe can be explained.

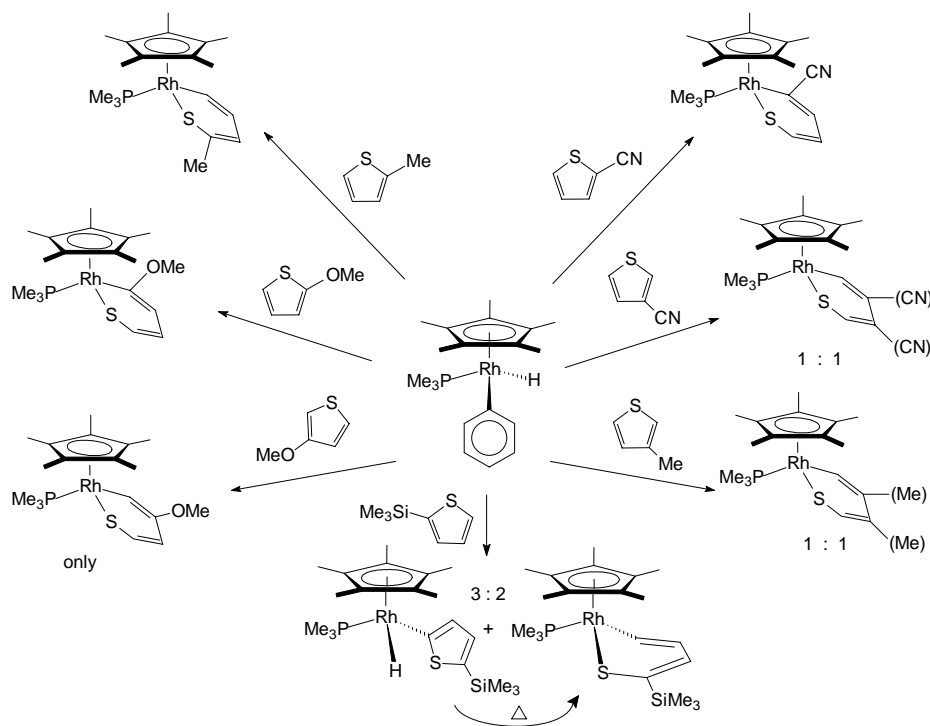


In addition to these quinoline studies, we have also discovered a new route to isoquinolines. This recent discovery is the subject of ongoing studies under the continuation of this NSF-funded project. The new route involves orthometallation of imines using potassium carbonate, which then undergo insertion reactions with acetylenes followed by oxidative coupling to give the isoquinoline products. The reactions are not yet catalytic, but the original metal complex is isolated as the final metal product and can be recycled.



## Findings: Thiophene C-S Cleavage and Formation

Our studies have also expanded our understanding of C-S bond cleavage and formation in a variety of thiophenes. With the fragment  $[\text{Cp}^*\text{Rh}(\text{PMe}_3)]$ , we have determined the selectivity with a variety of substituted thiophenes as shown below. It is interesting to note that 2-substitution sterically disfavors C-S cleavage, but that electronic effects can override this steric influence and give rise to exclusive cleavage adjacent to the functional group.



In order to understand these selectivities, we have undertaken DFT studies of the cleavage reaction. As our first foray into this area, we first attempted to repeat the earlier calculations published by Sargent and Lledos on this system ( $\text{Cp}^*\text{Rh}(\text{PMe}_3) + \text{thiophene}$ ) to make sure we could properly do calculations. We found that we could not reproduce the optimization of the reported transition state for C-S cleavage – or rather – the reported transition state for C-S cleavage was not the transition state for this process, but rather for migration from an  $\eta^2\text{-C,C}$  complex to an  $\eta^2\text{-C,S}$  complex. We fully investigated this system via DFT and discovered another transition state for C-S cleavage joined to the  $\eta^2\text{-C,S}$  complex. A separate transition state was located for migration to the sulfur ( $\eta^1\text{-bound}$ ). We also included solvation effects, which were shown to have a dramatic effect on the energetics of the reaction. Also, there are two sets of intermediates and transition states that we discovered, one with the thiophene pointing towards the  $\text{Cp}^*$  (lower E) and one with the thiophene pointing towards the  $\text{PMe}_3$  (higher E).

### Impact of the Proposed Work.

This project will meet several of the NSF Criterion for Broader Impact, as summarized below.

- (1) **Benefits to Society:** HDS is a mature technology that allows fuels and hydrocarbon products to be produced with sulfur levels on the order of a few hundred ppm. While this level may have been acceptable in the previous century, modern chemical industry must focus on doing better. There is substantial public pressure to decrease environmental emissions by the chemical industry. The studies presented here allow us to better design systems capable of reducing sulfur to the 10's of ppm in petroleum products. Some of our test compounds have been examined by catalyst engineers at Grace Davison in supported catalysts. It is possible that the type of chemistry developed here could be used to chemisorb the thiophenes, which would be feasible because one is only removing the last few ppm of sulfur from the hydrocarbon. The discovery of a complex that could remove the last traces of sulfur from petroleum would contribute to improved air quality for the public.
- (2) **Broaden the Participation of Underrepresented Groups:** A portion of the work on the planar vs. bent structures of C-S cleavage products involves a collaboration with Prof. Juventino Garcia at UNAM, with which we exchange graduate students. The University also has an active McNair Scholars Program which brings minorities to the University, and specifically has brought individuals to our laboratory to do research (Brian Warsop, '04).
- (3) **Enhance Infrastructure of Research and Education:** In addition to the obvious benefit to chemistry by training graduate students, our program helps faculty at surrounding small colleges by providing access to modern research facilities and equipment. For example, we have a policy of providing gratis X-ray structures for educators at 4-year colleges in the area to enhance their own research projects with their undergraduate students. High-field NMR service is also provided to these people. While the service is used only a few times a year, it offers a tremendous benefit to these educators. Our department also has invited student groups from local Community Colleges to visit and participate in some experimental work with our advanced instrumentation. During the visits, we have workshops on solving X-ray structures, computer modeling, and other topics of interest not available routinely to this group of students. My research group and I are active leaders in this activity, and we assist in the spectroscopic measurements and X-ray structure determinations.
- (4) **Enhance Infrastructure for Research and Education:** Our group has enlisted the participation of summer high school teachers through the NSF RET program. We have had and will continue to have high school teachers work on these projects (Roger Skugrud, '02; Colleen Cavalier, '01). Several of our graduate students have gone on to become high school teachers after attaining a research-based M.S. degree in my group (Rich Ognibene, '87; Karlyn Skugrud, '03). Several Ph.D. students from my group went on to faculty positions in research universities or 4-year colleges (Frank Feher, '84; Martin Chin, '94; Dave Wick, '96; Dave Vicic, '99; Brad Kraft, '03; Steve Oster, '03; Brian Edelbach, '03).
- (5) **Broad Dissemination to Enhance Scientific and Technological Understanding:** We are fortunate to have close relations with a member of the scientific staff at the Rochester Museum & Science Center, Dr. Calvin Uzelmeier. Dr. Uzelmeier was a staff member in charge of Education and Outreach at the University of Rochester in the NSF STC for Photoinduced Charge Transfer until 2000, when he move to the RMSC. Calvin now

coordinates activities with individuals in the department, such as hands on participation in National Chemistry Week, events for our Undergraduate Chemistry Council, local ACS section travel grants for undergraduates, and occasional demonstrations at the museum. Members of my group have assisted in several of these activities in the past, and we will continue to be active in supporting these activities in the future. The P.I. has also taught a short course (4 days) at Kodak.