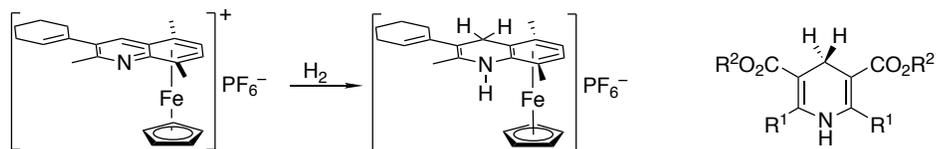


PRF#57670

Iron-Based Catalysts for Asymmetric Hydrogenations Containing Planar Chirality
Aaron Odom, Michigan State University

The proposed work under this New Directions grant is to find new iron-based catalysts for organic synthesis. The hope is to generate new catalytic systems for the most Earth-abundant transition metal, iron. As part of this research, we began with understanding the synthesis of Group-8 quinoline structures with possible applications to asymmetric hydrogenation of heterocycles, imines, and related systems. As an extension of the work, we have also examined Group-8 imido complexes and their reactivity and properties.

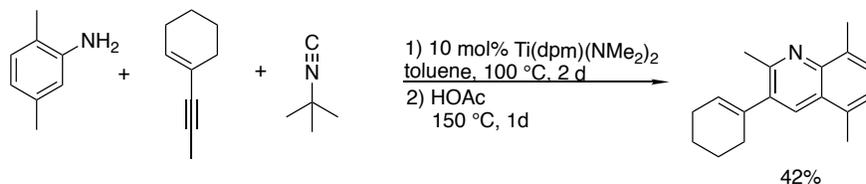
One of the proposals for new Group-8 catalysis is to generate metal quinoline complexes of the type shown below. These complexes are modeled after the Hantzsch ester shown on the right. Hantzsch esters are used in a variety of different organic transformations as surrogates for dihydrogen. The 1,4-dihydropyridine moiety can give up the equivalent of H₂ to hydrogenate a substrate (*vide infra*). The disadvantage of these Hantzsch reagents is that it *only* acts as an H₂ donor in the reactions and the rest of the pyridine is a byproduct. The goal of the project here, is to generate complex like those shown on the left to act as recyclable surrogates for the Hantzsch reagent. The iron-cyclopentadienyl group will reside on the aryl-side of the quinoline in the ground state, which gives a structure isoelectronic with ferrocene. On addition of dihydrogen, it is hoped that the iron center will enable hydrogenation of the pyridine ring in a 1,4-fashion. The substituents on the quinoline in the 2,3-positions are there to encourage this 1,4-hydrogenation of the quinoline ring. The product of this hydrogenation is a 1,4-dihydroquinoline with a pendant iron center.



One attractive feature of the system above is that it is chiral and could potentially be used to control chirality in the product. As a result, the catalytic system above could be used with an achiral cocatalyst such as a phosphoric acid to hydrogenate imines, for example.

Ruthenium could potentially be used in the system as well and is better known as a hydrogenation catalyst. Further, haptotropic shifts like the one in the hydrogenation mechanism shown below are required if the metal center is to activate the H₂ to give the desired 1,4-dihydroquinoline. After experiencing some difficulty with the iron systems, we decided to work with ruthenium systems some as these may be easier to produce. Iron, of course, would be better from an Earth abundance standpoint if we can get it working. Once we know how to produce and optimize the ruthenium system, the iron system would be reexamined.

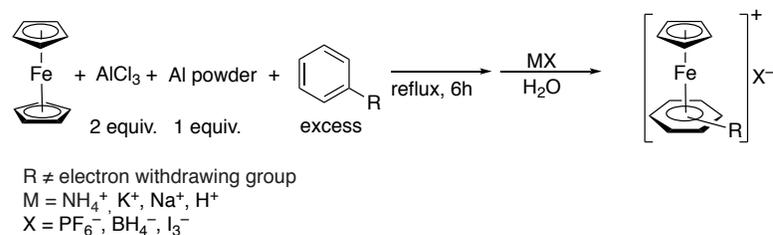
The substituents on the quinoline were chosen based on computational models, and the heterocycle was previously unknown. As a result, we first had to produce the quinoline shown, which was done using the procedure shown below in 42% overall yield (2 steps, 1 pot).



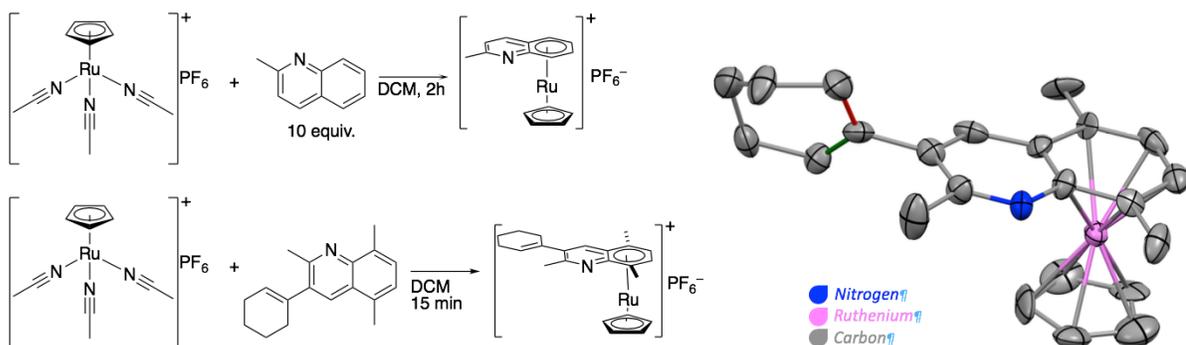
Only two metal-quinoline complexes have been structurally characterized, and these are isomers of the same complex. The two complexes were prepared by the Parkin group, and the metal center was molybdenum. There are very few quinoline complexes reported with any metal center, it seems. As a result, we began exploring different synthetic protocols for their production.

The typical procedure for placing an arene on iron is shown below, which involves reaction of ferrocene with AlCl₃, Al powder, and excess arene. Following this, a salt is added to give the CpFe(arene)⁺ product. Attempts to use the quinoline as the arene in this synthesis are complicated, in all likelihood, by the basic nitrogen on the quinoline. Several different sets of conditions were attempted with different salts at the end. The only quinoline-based product observed was due to simple protonation of the quinoline by acid. Several related reactions were attempted such as

replacement of benzene in $\text{FeCp}(\text{benzene})^+$ with quinoline under thermal and photochemical conditions. In addition, replacement of bromide in $\text{FeCp}(\text{CO})_2\text{Br}$ with quinoline in the presence of AgSbF_6 was attempted with the presumption that the carbonyls in $\text{FeCp}(\text{CO})_2(\text{quinoline})^+$ might be removed by photolysis. However, none of these attempts were successful in placing the quinoline on iron.



A couple of ruthenium quinoline complexes had been prepared; although none had been structurally characterized. As a result, we decided to try ruthenium systems in hopes that these would provide insight into how the iron complexes might be accessed and to give the young students some success in the synthesis of these complexes. In the top part of the figure below is the Fish and coworkers 1991 synthesis of $\text{CpRu}(2\text{-Me-quinoline})^+$ complex, and below this is the successful synthesis of the ruthenium complex with our desired quinoline.



Again, the ruthenium quinoline structure above is the first of its kind for this class of molecules and very encouraging. We plan to examine hydrogenation of the pyridine in this complex and examine the compound for the desired activity.

Unfortunately, it does not appear that the relevant iron starting material, $\text{FeCp}(\text{NCMe})_3^+$, is readily available; however, we will attempt to generate it in situ to duplicate the ruthenium synthesis above. Hopefully, this will allow expansion of this chemistry back to iron.

In other work, we discovered that iron(II) imido complexes could be readily prepared, such as $\text{Fe}(\text{NAr})(\text{PMe}_3)_3$. These complexes were thought to provide inroads to new C–N bond forming reactions. In addition to this, however, they have unusual properties and reaction chemistry in general, which we have been exploring. The similar ruthenium complexes have been generated as well.

The funding in this first year went to several students who worked on various aspects of the chemistry described above. One student was working on generating quinoline species. Another explored the synthesis of iron and ruthenium quinoline complexes. Yet another student worked on iron imido complexes. Most of these students were supported in the Summer session on the grant, but materials were supplied for the work year-round. Finally, a student considering joining the group was able to work with us over the Summer before starting his first year of graduate school. (I named him as an undergraduate in the personnel report, but he was about to start graduate school.) The funding provided the PI the flexibility to support several different students working on different aspects of the science in a time when funding is only available from sources outside the department. For this time the students were able to focus on research and make significant progress towards degrees. In addition, the support gave the PI the opportunity to attempt to recruit new students towards the science.