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Synthesis of Ligands for Studies on Iron-Based Hydrogenation Catalysts

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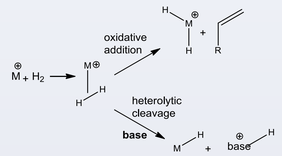
Introduction

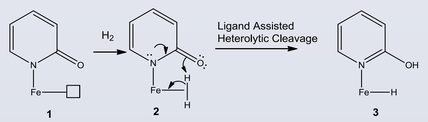
- Catalysis is fundamental to industrial level hydrogenation reactions. Traditional hydrogenation mechanisms begin with oxidative addition of H_2 onto a metal center to form a metal dihydride complex. Alternatively a metal hydride can be formed by deprotonation of the dihydrogen complex (Scheme 1).

Scheme 1



- Current catalysis in industrial level hydrogenation reactions uses very efficient, yet expensive and toxic metal based catalysts: rhodium, iridium, and ruthenium.[1] Our research offers a similar type of catalyst that is based on iron which is less toxic and less expensive.
- The catalysts works through ligand assisted heterolytic cleavage to perform the hydrogenation (Scheme 2). This type of pyridone-based system has been recently proven to have high reactivity in hydrogenation reactions with iridium complexes.[2]

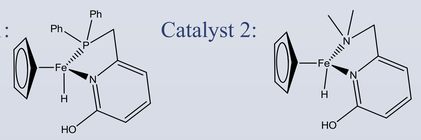
Scheme 2



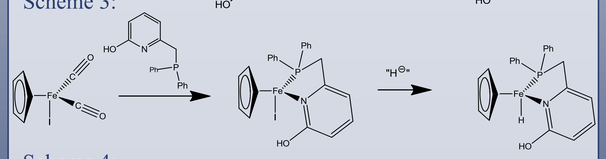
Objectives

- Synthesize ligand A and ligand B, attach them to the iron centers (Scheme 3 and 4), and test catalysts formed.
- Test the efficacy of these catalysts in hydrogenation reactions.

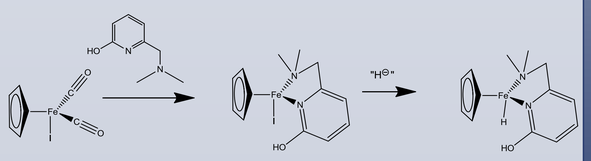
Catalyst 1: Catalyst 2:



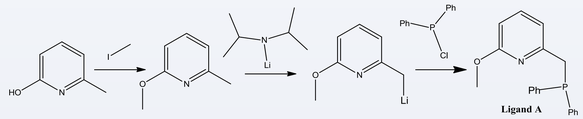
Scheme 3:



Scheme 4:



Ligand A Synthesis and Results

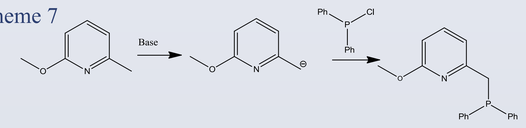


- Step 1: Success observed in singlet at 3.90 ppm (added methyl group) in ^{1}H NMR.
- Literature uses 10 equivalents of methyl iodide, we use only 2 equivalents of this expensive, toxic reagent (Scheme 6).[3]

Scheme 6

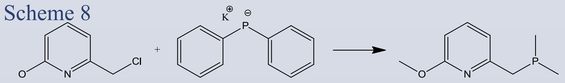
- Step 2: In Scheme 7 deprotonating starting material yields strongly nucleophilic intermediate which attacks electrophilic chlorodiphenylphosphine displacing the chlorine and achieving Ligand A.
- Results using LDA unsuccessful (performed twice).
- LiHMDS substituted for LDA with similar results
- Tert-butoxide in conjunction with n-butyl lithium used, deprotonation was again unsuccessful

Scheme 7

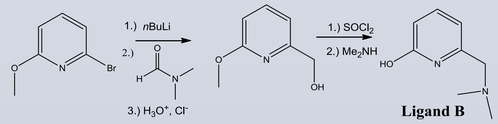


- Scheme 8 represents an alternative synthesis of ligand A.
- Chloride electrophile is attacked with potassium diphenylphosphide nucleophile.
- Under similar conditions to literature, there was no initial success. [4]
- A catalytic amount of sodium iodide was added to provide the sodium counter ion that was used in the literature, yet unsuccessful.
- Triethylamine added with still no affect
- A 1:1 equivalent of DMF to THF solvent was added with no affect (Scheme 8)

Scheme 8

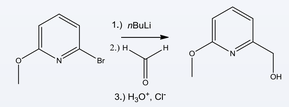


Ligand B Synthesis and Results



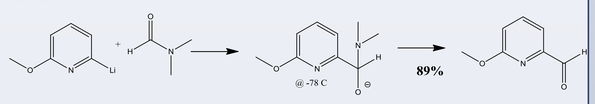
- Step 1: Results unsuccessful shown through messy ^{1}H NMR spectra (Scheme 10).
- Condition changes: anhydrous conditions emphasized through new THF (methoxy pyridine and unreacted paraformaldehyde impurities), results unchanged

Scheme 10



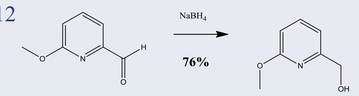
- Alternative synthesis of the alcohol using dimethylformamide as the electrophile in the reaction (Scheme 11).
- Success of this reaction was clearly observed with aldehyde peak at 9.94 ppm, consistent with literature data.[5]

Scheme 11



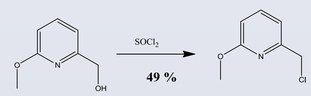
- Aldehyde reduced to an alcohol (Scheme 12)
- Chromatotron effectively removed bromomethoxypyridine, methoxypyridine, and other impurities.

Scheme 12



- Step 2: Alkyl chloride replaces alcohol (Scheme 13).
- Achieved in excellent purity; chlorine leaving group facilitates S_N2 reaction in the next synthetic step

Scheme 13

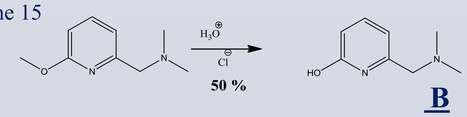


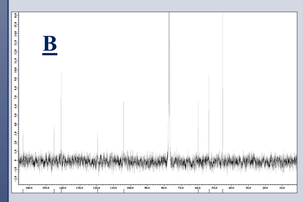
- Step 3: Dimethylamine displaces chloride yielding methoxy protected ligand B (Scheme 14).
- Purity confirmed by GC/MS which indicated that the product was 91 % product and only 9 % impurities.

Scheme 14.

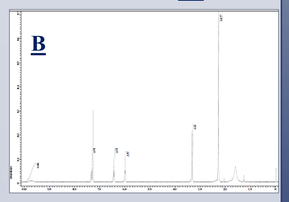
- Step 4: Deprotection of the methoxy group (Scheme 15).
- ^{1}H NMR spectrum indicates disappearance of the methoxy peak previously observed at 3.9 ppm and appearance of OH at 10.0 ppm.
- ^{13}C NMR spectrum: disappearance of previous methoxy signal observed

Scheme 15





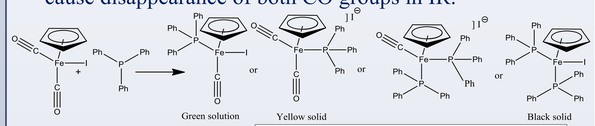
^{13}C NMR ($CDCl_3$)



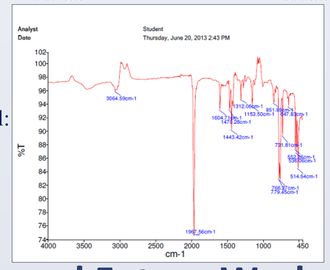
^{1}H NMR ($CDCl_3$)

Iron Testing Results

- Iron testing objective: displace both CO groups to model future potential for ligand displacements.
- Literature examples of displacement of one CO characterized by a green solid, one iodide as a yellow solid, and both CO and iodide as a black solid.
- Displacement of one CO common with simple addition of triphenylphosphine.
- Combination of triphenylphosphine and n-trimethylamine cause disappearance of both CO groups in IR.



- IR spectrum of iron complex starting material:



Conclusions and Future Work

- Ligand B can be synthesized in good yield and purity.
- Ligand A's first synthetic step has been optimized .
- Displacement of both iron CO groups is possible.
- Progress is contingent on finding a method to displace both CO groups that will not interfere with attaching ligands
- Ligand A, synthetic step 2 should be attempted again through deprotonation mechanism.
- Ligand B synthesis yields leave room for optimization.

Acknowledgements/References

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