Synthesis of the Chiral Cyclic Amines 1-aminooindan and 1,2,3,4-tetrahydronaphthalen-1-amine by Reduction of Imine Precursors with Activated Metal Borohydrides

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Introduction
Chirality is a crucial aspect of chemicals used in an array of applications from pharmaceuticals to foods. The same molecule with different chirality may have completely different properties. The goal of this experiment was to find safe and more effective ways to stereoselectively reduce the two diphenylphosphinic protected imines of 1-aminooindan oxime and 3,4-dihydronaphthalen-1(2H)-one oxime using various metal borohydride complexes.

Methods
The first successful reduction was made using Zr(BH$_4$)$_4$ in THF. ZrCl$_4$ and NaBH$_4$ were allowed to react in THF and left to stir for 24 hours under nitrogen in a glove box to synthesize Zr(BH$_4$)$_4$. 100 mg of diphenylphosphinic protected imine 1-aminooindan oxime were then added and the solution was left to stir for another 24 hours. This procedure was repeated for the diphenylphosphinic protected imine of 3,4-dihydronaphthalen-1(2H)-one oxime, with two trials for each imine for a total of four vials.

A washing procedure using HCl, NaOH, and brine was used to isolate the organic layer, which was dried with magnesium sulfate. In hopes of synthesizing enantiomerically rich products, this procedure was amended by adding (R) and (S) BINOL.

Future Work
Future work will continue with examining effects of BINOL on the stereoselectivity of the reduction with the ultimate goal of creating enantiomeric excess within the amine product.

Results
Simple borohydrides are ineffective at reducing the deactivated imines. Trials were performed using NaBH$_4$, [(C$_6$H$_5$)$_3$P]$_2$CuBH$_4$, and (C$_2$H$_5$)$_4$N(BH$_4$) as reducing agents in a variety of solvents, and none yielded amine products. Zr(BH$_4$)$_4$ in THF acted as an effective reducing agent for the deactivated imines. (R) and (S) isomers of BINOL were introduced to the reaction in order to yield enantiomerically enriched products. NMR shift studies point to enriched amine products, but further study needs to be done in order to determine the effectiveness of this method.

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**Figure 2.** GC-MS Spectra of pure amine purchased from Sigma Aldrich showing that the retention time of pure 1-aminooindan is 7.10 minutes.

**Figure 3.** NMR spectra of (S) isomer 1-aminooindan (right) and racemic 1-aminooindan spiked with binol (left).

The NMR shift for the hydrogen indicated on the left is different depending on the chirality of the amine as it interacts with BINOL, so integrating its peak could be used to determine e.e.

**Figure 4.** GC-MS spectra of product from Zr(BH$_4$)$_4$ reduction, showing presence of amine product.