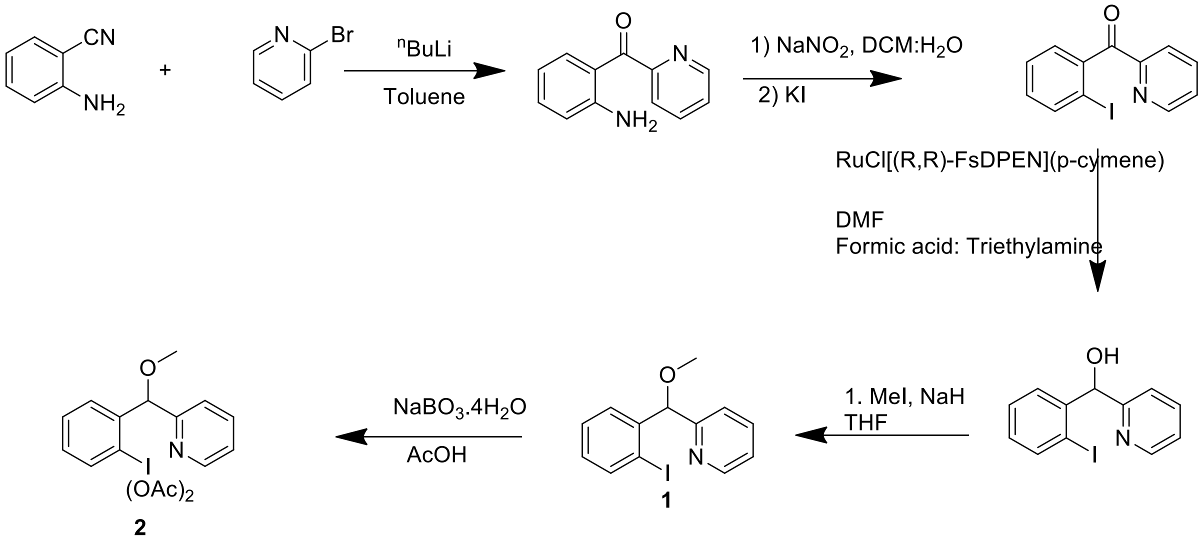
Introduction.

Hypervalent iodine reagents have found broad application in organic chemistry and are nowadays frequently used in synthesis. It is of great interest to investigate their ability as highly selective oxidants, electrophilic reagents and to develop new reactions using hypervalent iodine compounds. Because these are non-metallic oxidation reagents, they avoid the issues of toxicity of many transition metals commonly involved in such processes. Hypervalent iodine compounds bear a high potential for the improvement of known reactions not only from the environmental point of view, they are also interesting reagents for the development of completely new synthetic transformations.

Results and Discussions

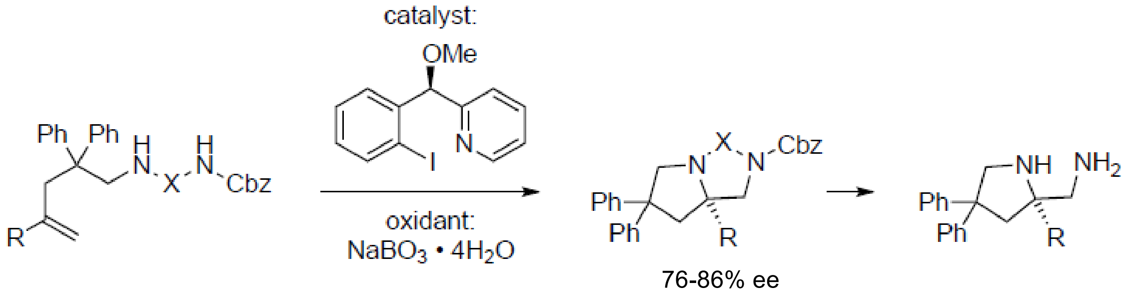
The enantioselective synthesis of diamines from alkenes using catalytic amounts of an enantiomerically pure iodine catalyst and an oxidant was the ultimate goal of this project. The possibility of directly introducing nitrogen nucleophiles to alkenes was very promising as this would provide access to a huge and highly interesting range of building blocks for target synthesis. During the course of the project we were able to develop an efficient metal-free, highly stereoselective intramolecular diamination using a novel chiral hypervalent iodine reagent together with its application as an efficient catalyst for the synthesis of diamines.

We designed and synthesized a novel hypervalent reagent with a pyridine moiety attached to a chiral benzylic center, which should allow an efficient coordination of the pyridine nitrogen to the iodine atom. It is well known that pyridines are good ligands for iodine(III), the close proximity to the stereogenic center should allow high selectivities to be obtained (Scheme 1).



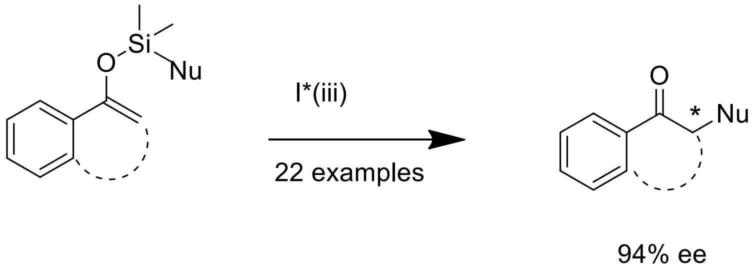
Scheme 1

This reagent **2** served as an efficient reagent obtaining diaminated product in good enantiomeric access when used in stoichiometric amount. We then investigated the possibility of an in situ formation of the hypervalent iodine species by using the iodine(I) catalyst **1** together with stoichiometric amounts of an oxidant. The reaction occurred when 20 mol% of the iodine(I) catalyst **1** was used together with 2.2 equivalents meta-chloroperbenzoic acid (mCPBA) at –48 ºC in acetonitrile. However, the yield was low and the enantioselectivity only moderate. Upon changing the oxidant to sodium perborate and after addition of 3 equivalents acetic acid at room temperature, much higher yields and selectivities were obtained (Scheme 2).



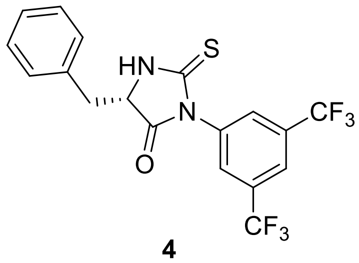
Scheme 2

During the course of our research we developed a novel methodology for flexible functionalisations of carbonyl compounds through umpolung using hypervalent iodine reagents. Through polarity reversal, or ‘Umpolung’, we showed that typical nucleophiles such as oxygen or nitrogen and even carbon nucleophiles can be used for addition reactions after tethering them to enol ethers. Our findings allow novel retrosynthetic planning and rapid assembly of enantiomericaly pure structures previously accessible only by multistep sequences. Enolates and their derivatives such as enol ethers are almost exclusively being used as nucleophiles for reactions with electrophilic compounds. We made use of the high electrophilicity as well as the high nucleofugality of hypervalent iodine reagents for the additions of nucleophiles to the α – position of carbonyl compounds using the umplong strategy (Scheme 3).



I*(iii): Chiral Hypervalent iodine reagent

In addition to use of hypervalent iodine reaction we further expanded our research areas to other form of metal free catalyst i.e Organocatalyst. We developed a novel organo catalyst **4** and a methodology for the stereoselective iodoamination of alkenes. Additional investigations have been performed to control the regioselectivity of such iodoaminations. (Scheme 4)



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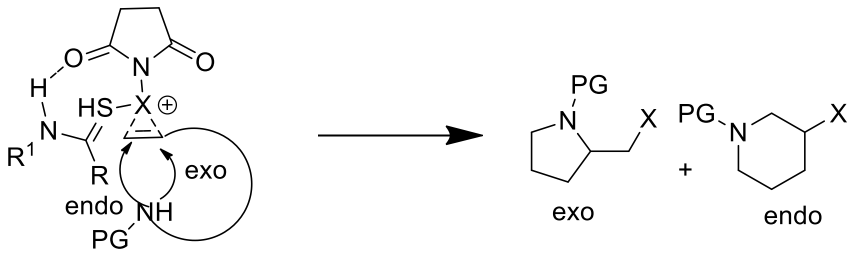

Scheme 4

Conclusion:

1. We have established a highly stereoselective intramolecular diamination using a novel chiral hypervalent iodine.
2. In addition we have developed a methodology for flexible stereoselective functionalizations of ketones through umpolung with hypervalent Iodine reagents
3. Lastly the work was further extended to other green approach towards organic synthesis by development of a organocatalytic stereoselective Iodoamination of alkenes