Statement of Research Interest

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Introduction

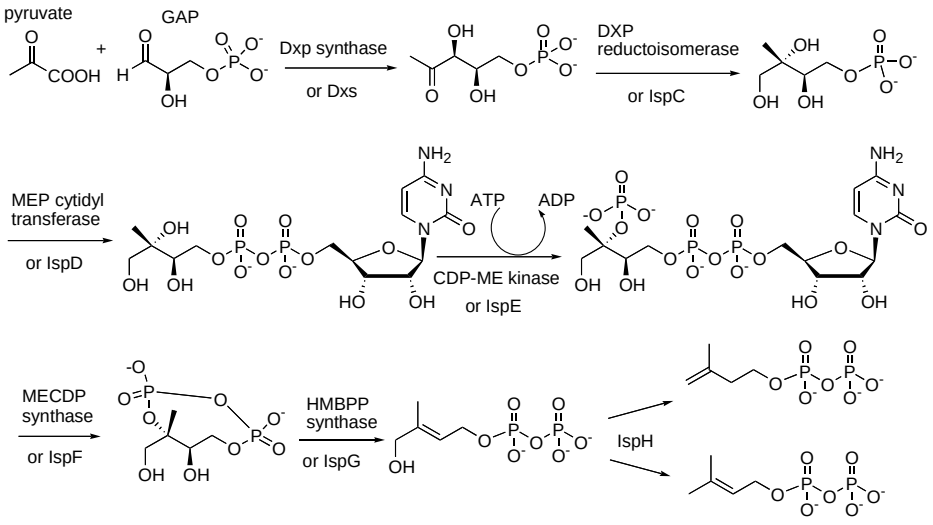
Research and education goes together for better future. Today we are in good condition because of good research in past and present. Similarly for to have better future we need to do outstanding research. For this research I do things systematically as follows

1. Planning the research project, writing proposals, creating funding, training manpower, earning facilities, etc.,
2. Executing the project, facing the problems, solving it, standby solutions, working towards the target and gaining experience.
3. After getting results publishing, patenting, implying in industry which all leads to humanity development.
4. Doing research, sharing the knowledge with others, training students and motivating them for great future are the important things, which I enjoy with everybody.

Drug discovery is an important area of research in present days because of its influence in medicinal chemistry and daily basis of human life. So I selected this as my research topic.

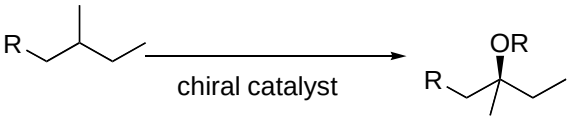
Drug discovery and designing for infectious diseases –Tuberculosis including broad spectrum antibiotics

Colorado state university is the first in the world in the area of research in infectious diseases. They offered me a job as medicinal chemist for drug designing and drug discovery for infectious diseases. Here I got an opportunity to learn this process, which I certainly want to use in my future research. I like to design new enzyme inhibitors for infectious diseases and discover new mimicks for active species in nucleic acids. Which includes library synthesis of MraY, Menaquinone and MEP pathway inhibitors.



Small molecules for drug discovery by new reactions in solution and solid phase

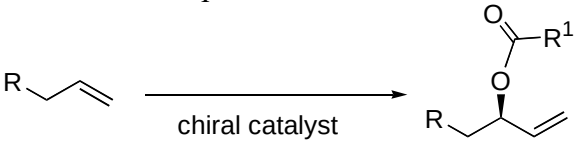
In my Ph. D work I First developed asymmetric inverse electron demand Diels-Alder reaction using chiral catalyst for synthesis of chiral quinone derivatives. Then I used the same ligand for making heterobimetalic chiral catalyst for Michael addition reaction, forming C-C, C-N, C-S bonds, leading to good yield and high to moderate enantiomeric excess. To enhance the yield and enantiomeric excess, reduce the workup procedure and wastage I designed a polymer anchored chiral catalyst and I have also done solid phase synthesis of hydrazines. In NDSU I also discovered that metal geometry is mainly responsible for difference in asymmetric induction in the transition state. With the help of chiral relay technique in asymmetric induction I described these results. All these techniques can be used for synthesizing new small molecules and new organic reaction. Which can lead to potentially, biologically important small molecules (eg. antiviral drugs)



Though I did varies asymmetric induction I did not get a chance to do pi-allylic asymmetric induction.

Stereoselective synthesis of PKC inhibitor, Hepatitis C inhibitor

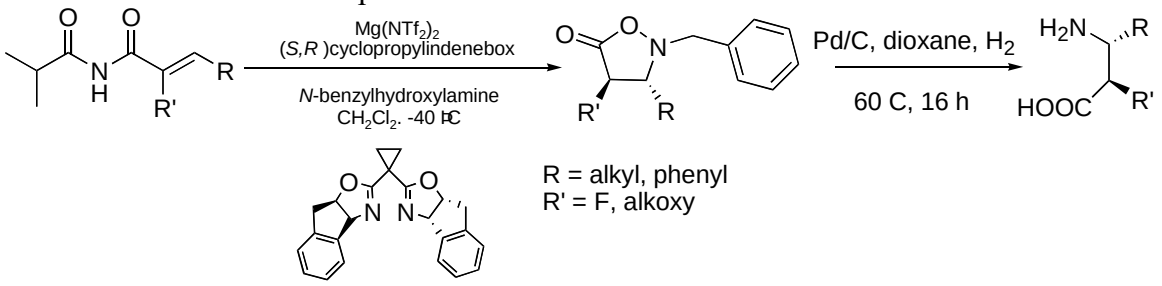
Harvard University offered me a postdoc position to work on pi-allylic asymmetric induction. It is one of the greatest challenges in the present scientific community. I was happy to work on it and able to get moderate enantioselectivity for the first time. In my future research plan I like to work on the same area and improve the enantioselectivity.



Similar modern technique can be used to make different asymmetric macrolactones and macrolactams in near future for PKC inhibitor.

Drug discovery for MMP inhibitor

Since, I want to develop my experience in drug discovery, I also worked in Prof. Mukund Sibi's lab at NDSU, fargo. There I developed a new and novel methodology for the synthesis of α,β-disubstituted β-amino acids, which are showing considerable attention in recent years. A novel catalytic method for the preparation of α,β-disubstituted β-amino acids has been developed in our laboratory (*J. Am. Chem. Soc.*, **2003,** 125, 11796-11797). We surmised that rotomer control for the substrate combined with concerted addition of N-benzylhydroxylamine to α,β-disubstituted and unsaturated imides in the presence of a chiral Lewis acids (prepared from $Mg(NTf_2)_2$ and bisoxazoline) provided 70-95 % yield, 90-95 % de and 80-95 % ee. We are also able to alkylate the α-position to obtain α-quaternary centered β-amino acids. I have patented this methodology, and all the intermediates and final compounds.



Using this method we are able to synthesize, α-fluoro (halo) substituted β-amino acids and α-alkoxy substituted β-amino acids in good yield and moderate MMP inhibitors. In future I would like to work on this project to improve the designing and drug discovery for MMP inhibitors.

Drug discovery for HIV

Discovering an anti-HIV drug is also one of my long time goal. The process of reverse transcription of genomic RNA into double stranded DNA by the enzyme reverse transcriptase is central to the replication of HIV. Therefore the inhibitor of this key biochemical event in the viral life cycle provides the most attractive target for anti-HIV drug development. Non-nucleosides have been found to interact noncompetitively with an allosteric site leading to inactivation of the enzyme. I will be designing and discovering RT inhibitors.

The cleavage of large polypeptide precursors into smaller, funtional protein fragments required for packaging and infectivity og budding virons needs HIV protease. This is a viral encoded homodimeric aspartyl protease with C2- symmetry. The inhibitor of this enzyme invitro results in the production of progens virions that are immature and non-infectious. So, I will be designing and discovering protease inhibitor also.

Professional development

I hope to continue to expand on these research streams in the future. I believe my work in drug discovery will provide many prospects for interesting, cutting edge study in the field of medicinal chemistry that is relatively new. I constantly sharpen my skills through self-reflection, updates from academic and literature, seminars and my interactions with faculty, peers, students and practitioners. Furthermore, I hope to advance the traditional drug discovery field with new questions and pertinant issues of twentyfirst century.