IITB-Monash Research Academy

An Indian-Australian research partnership

Indian Institute of Technology Bombay | MONASH University

Project Title:	**Asymmetric palladium catalyzed C−H functionalization of benzyl acetic acid derivatives *via* photocatalysis.**	
Project Number	**IMURA1072**	
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IITB Department:	Department of Chemistry	

Research Clusters:

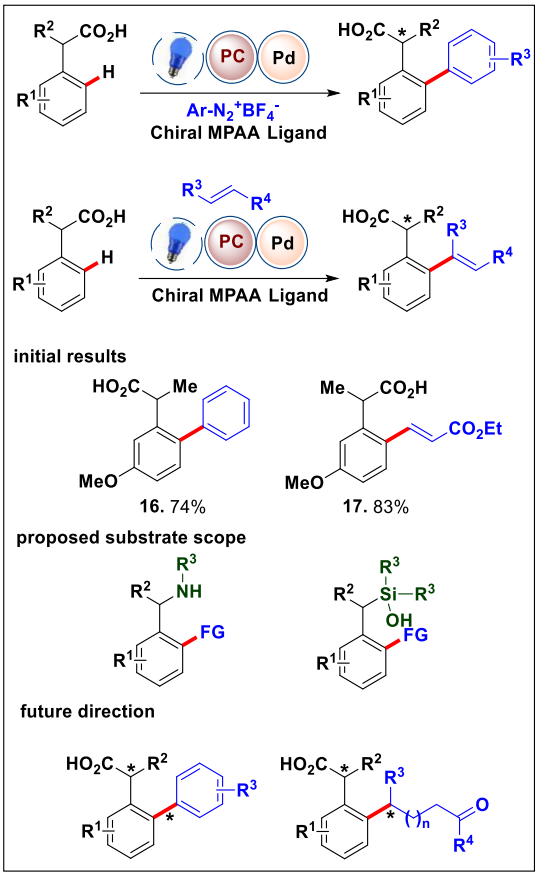
	Highlight which of the Academy's CLUSTERS this project will address? *(Please nominate JUST **one.** For more information, see www.iitbmonash.org)*
1	*Material Science/Engineering (including Nano, Metallurgy)*
2	*Energy, Green Chem, Chemistry, Catalysis, Reaction Eng*
3	*Math, CFD, Modelling, Manufacturing*
4	*CSE, IT, Optimisation, Data, Sensors, Systems, Signal Processing, Control*
5	*Earth Sciences and Civil Engineering (Geo, Water, Climate)*
6	*Bio, Stem Cells, Bio Chem, Pharma, Food*
7	*Semi-Conductors, Optics, Photonics, Networks, Telecomm, Power Eng*
8	*HSS, Design, Management*

Research Themes:

	Highlight which of the Academy's Theme(s) this project will address? *(Feel free to nominate more than one. For more information, see www.iitbmonash.org)*
1	*Artificial Intelligence and Advanced Computational Modelling*
2	*Circular Economy*
3	***Clean Energy***
4	***Health Sciences***
5	*Smart Materials*
6	*Sustainable Societies*
7	*Infrastructure*

The research problem

Kinetic resolution of achiral compounds is an important means to obtaining enantioenriched materials.[89-91] Encouraged by the effectiveness of Pd photocatalyzed *ortho* olefination as indicated by our initial result using benzyl acetic acid as a DG, and as demonstrated by our olefination protocol, in which benzyl amines and benzyl silanols were used as effective DGs, we envisioned that the addition of a substituent on the benzylic position of these starting material and using them in racemic mixtures could realize kinetic resolution in the presence of a chiral MPAA ligand (Scheme 1). Our design extends to the single-step synthesis of compounds containing multiple chiral motifs starting from racemic mixtures. A tandem kinetic resolution and atroposelective arylation using *ortho* substituted aryl coupling partners would yield centrally as well as axially chiral biphenyls, whereas the use of olefins subject to double bond migration might lead to the formation of compounds with doubly chiral benzylic centers.



Scheme 1. Proposed Kinetic Resolution of Simple Benzyls via Pd Photocatalyzed C−H Functionalization.

Although it may seem very challenging to carry out such reactions while controlling the stereochemistry of the multiple chiral environments generated simultaneously, we will present an example later in this proposal in which we are able to accomplish just that, albeit in a reaction system run under thermal rather than photocatalytic conditions.

Project aims

In current project we aim to enrich the field of asymmetric palladium catalyzed C−H functionalization specifically *via* photocatalysis. We have found that photoinduced C−H functionalization is an effective and practical alternative to thermally catalysed reactions. We hypothesize that the additional control over the stereoselectivity of photoinduced Pd-catalyzed C−H functionalization reactions would enable us to synthesize enantioenriched derivatives of pharmaceutically important molecules. Since these medicinal compounds typically function in highly chiral environments, the introduction of controlled new chiral motifs could be key in exploring and developing their functionalities.

How skills/experience of the IITB and the Monash supervisor(s) support the proposed project

Both supervisors and their research groups have expertise in the field of asymmetric catalysis and C-H activation. Over the years, both the group individually as well as collaboratively contributed significantly in this domain. Some of their work can be highlighted as follows :

1. Photoinduced Regioselective Olefination of Arenes at Proximal and Distal Sites Saha, A.;† Guin, S.;† Ali, W.; Bhattacharya, T.; Sasmal, S.; Goswami, N.; Prakash, G.; Sinha, S. K.; Chandrashekar, H. B.; Panda, S.; Anjana, S. S.; Maiti, D. *J. Am. Chem. Soc.*, 2022, *144*, 1929

2. Substrate-Rhodium Cooperativity in Photoinduced ortho-Alkynylation of Arenes Saha, A.; Ghosh, A.; Guin, S.; Panda, S.; Mal, D. K.; Majumdar, A.; Akita, M.; Maiti, D. *Angew. Chem. Int. Ed.*,2022,*61*,e202210492

3. Photo-Excited Nickel-Catalyzed Silyl-Radical-Mediated Direct Activation of Carbamoyl Chlorides To Access (Hetero)aryl Carbamides
Maiti, S.;† Roy, S.;† Ghosh, P.; Kasera, A.; Maiti,D. *Angew.Chem.Int.Ed.*,2022 61,e2022074

4. Enantioselective Synthesis of Pyrrolidines by a Phosphine-Catalyzed γ-Umpolung/β-Umpolung Cascade.
Jeremy T Maddigan-Wyatt, Jing Cao, Jhi Ametovski, Joel F Hooper, David W Lupton*
Org. Lett. **2022**, *24*, 2847

What is expected of the student when at IITB and when at Monash?

The student is expected to learn how to set up optimisation reactions under photo conditions, designing new asymmetric ligands and photocatalysts, acquire and analyse HPLC data on a regular basis.

Expected outcomes

a) Method will be optimized and scope will be evaluated.
b) Further evaluation of existing methodology in the context of our finding.
c) Development of palladium photocatalysis and utilizing it in enantioselective functionalization.
d) Utilization of palladium catalysis in introducing and controlling complex stereochemistry in single step transformations.
The proposed will have a positive impact on many fields of research, industry, as well as medicine since the design and synthesis of chiral small organic molecules.
e) Results will be published in peer-reviewed journals.
f) Effective catalysts may be patented following the guidelines.
g) Application of catalyst in industrial and academic settings.

How will the project address the Goals of the above Themes?

Chiral centres are ubiquitous in various bioactive molecules and potential drug candidates. The current project proposed aims to generate axially chiral products which might be useful for creating various structural motifs of biologically and pharmacologically important products. Also axially chiral motifs are present in various ligands employed for asymmetric synthesis and hence our protocol can prove useful to provide alternate strategies for chiral ligand design. These ligands may find application in fuel grade alkane synthesis and thus provide solution to the current clean energy crisis.

Potential RPCs from IITB and Monash

Provide names of the potential research progress committee members (RPCs) and describe why they are most suited for the proposed project

Capabilities and Degrees Required

M. Sc. (Chemistry) with a good knowledge of reaction kinetics and organic chemistry
B.Sc(Chemistry)

Necessary Courses

1. Organometallic Chemistry
2. Organic Spectroscopy
3. Physical Organic Chemistry

Select up to **(4)** keywords from the Academy's approved keyword list **(available at http://www.iitbmonash.org/becoming-a-research-supervisor/)** relating to this project to make it easier for the students to apply.

Aliphatic and aromatic compounds, Photocatalysis, Asymmetric C-H activation, Transition metal catalysis.