

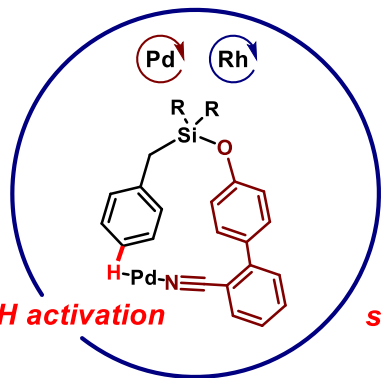
Unlocking new chemical space via selective catalysis



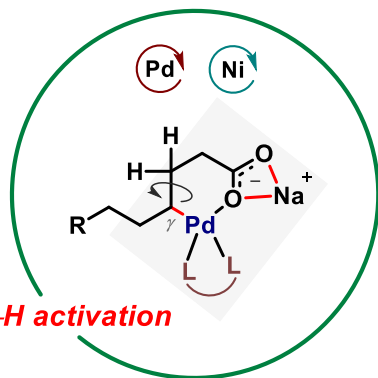
Debabrata Maiti
IIT Bombay, Mumbai, India
www.dmaiti.com

dmaiti@iitb.ac.in
+91-9820907155

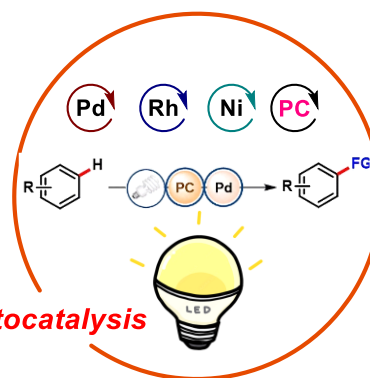
Key Research Areas



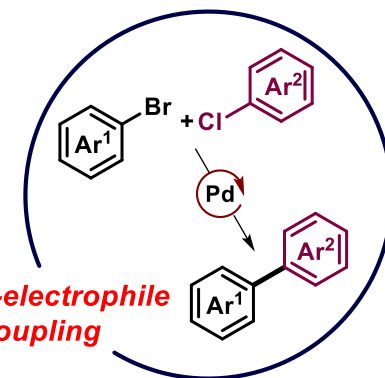
sp^2 C-H activation



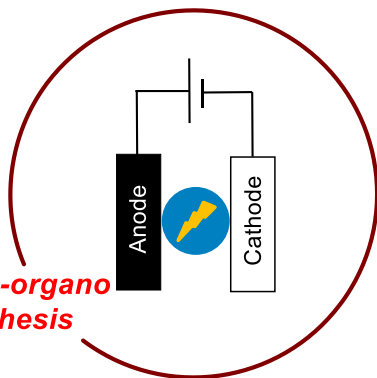
sp^3 C-H activation



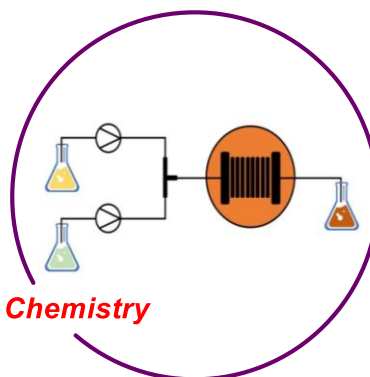
Photocatalysis



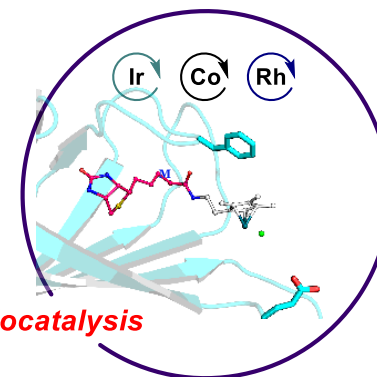
Cross-electrophile coupling



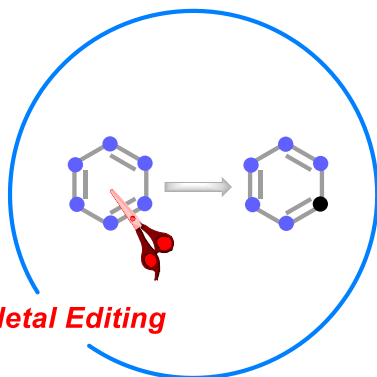
Electro-organo synthesis



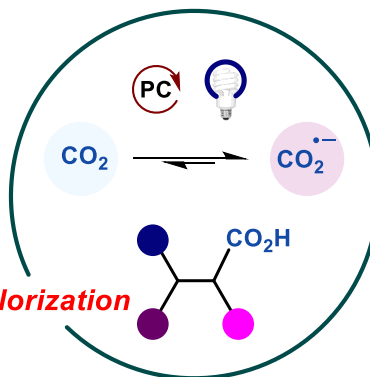
Flow Chemistry



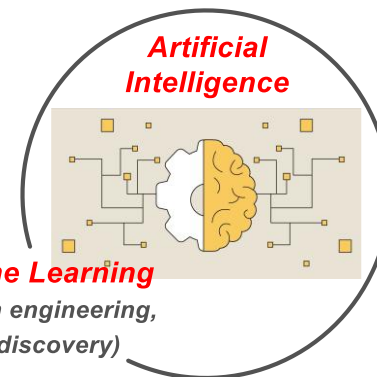
Biocatalysis



Skeletal Editing



CO₂ valorization

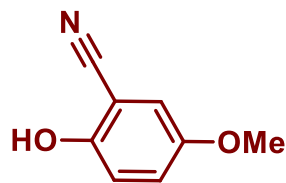
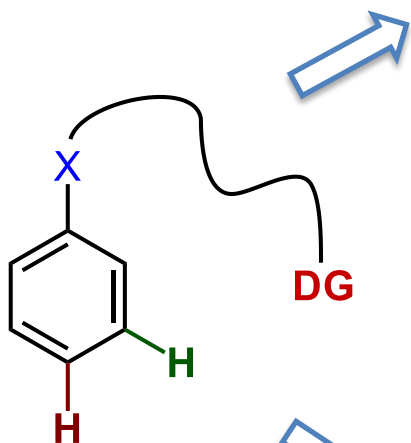


Artificial Intelligence

Machine Learning
(reaction engineering,
drug discovery)

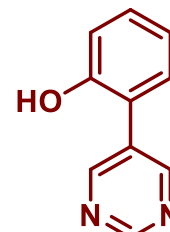
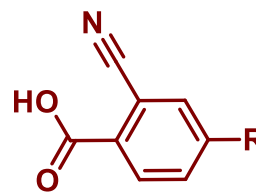
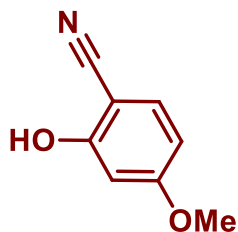
Directing scaffolds controls LSF

meta-C-H functionalization



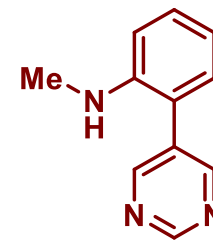
SIGMA-ALDRICH

Maiti-Bera-Modak Auxiliary
Catalogue number 798193

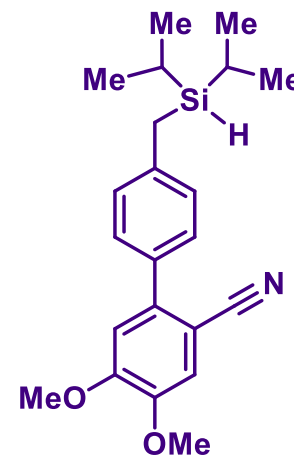
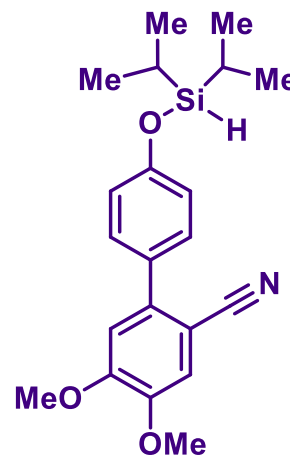
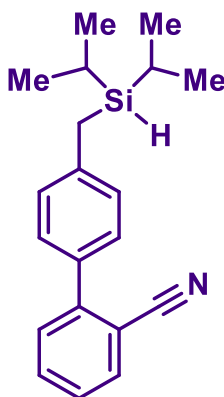
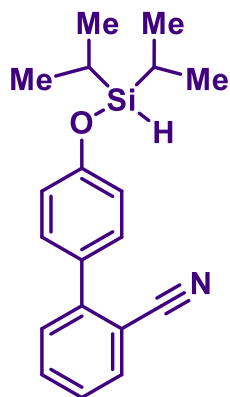


SIGMA-ALDRICH

Maiti-Bag-Dutta Auxiliary
Catalogue number 930083

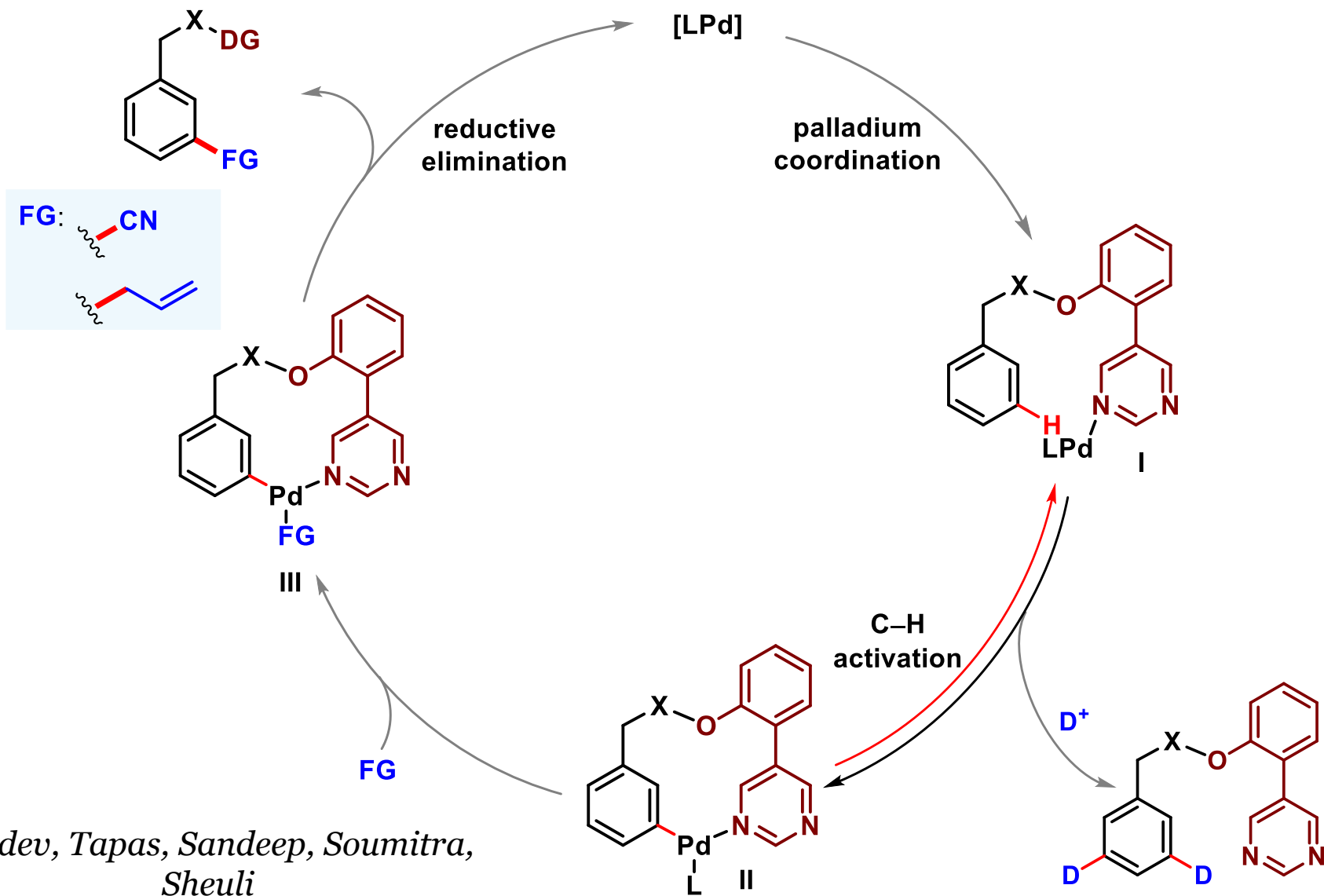


para-C-H functionalization

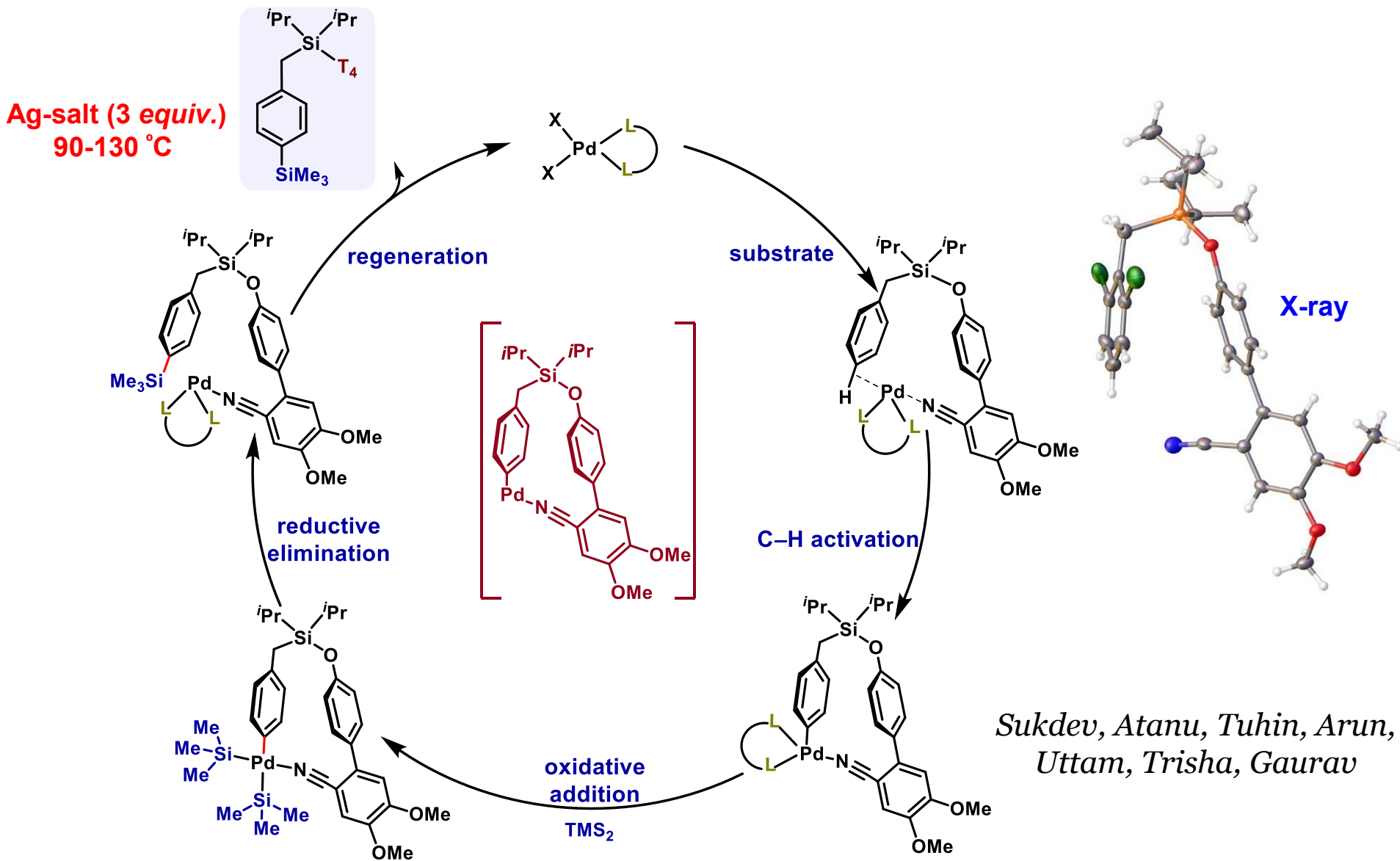


Maiti-Patra-Bag Auxiliary
TCI

Low energetic C–H activation step: **Reversible?**



Mechanism of *para*-C–H functionalisation



Evolution of transient approach

Covalent DG Approach



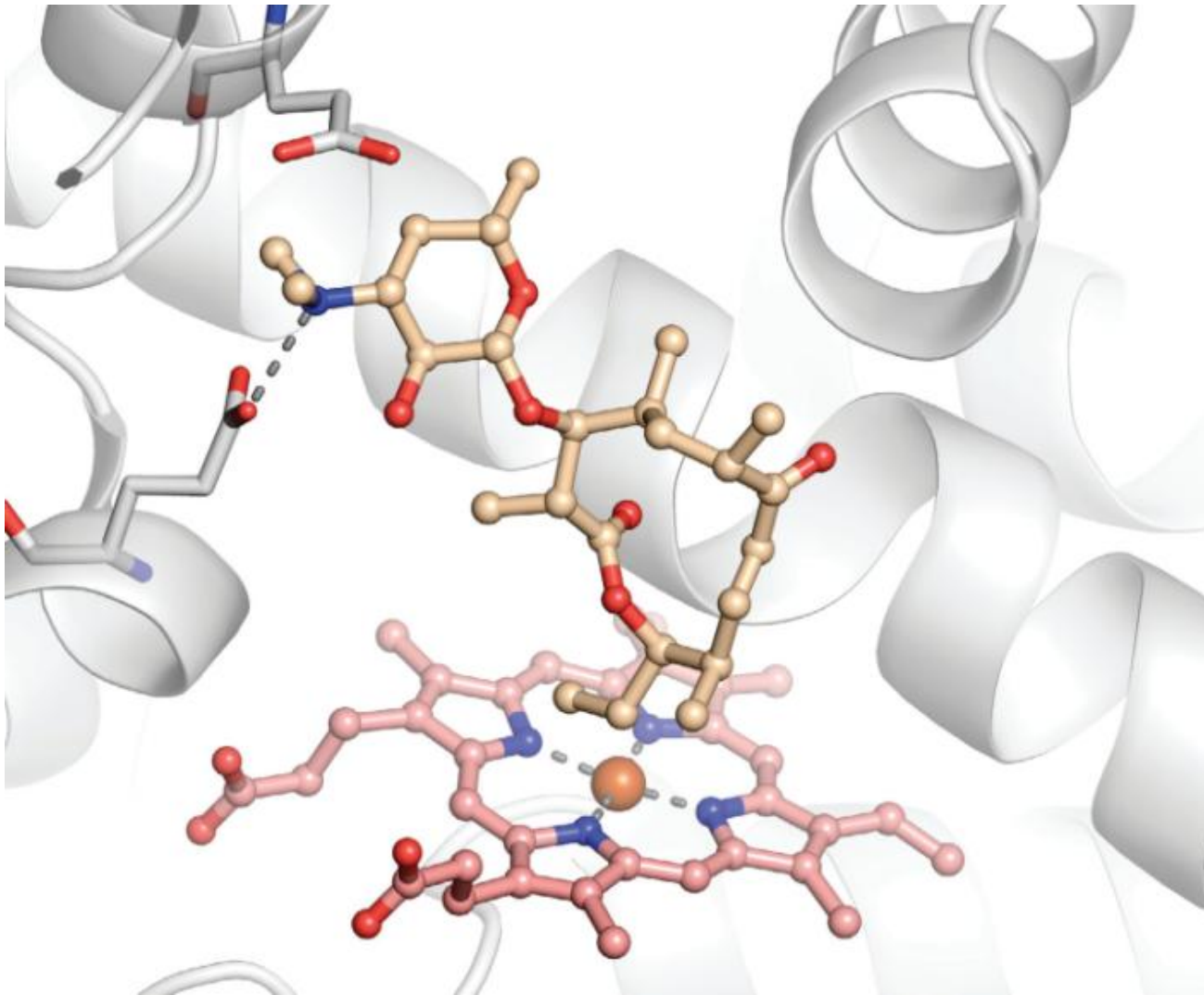
- Rigid backbone to maintain distance and geometry
- Extra steps for installation and removal of DG
- High molecular weight scaffold

Transient DG Approach



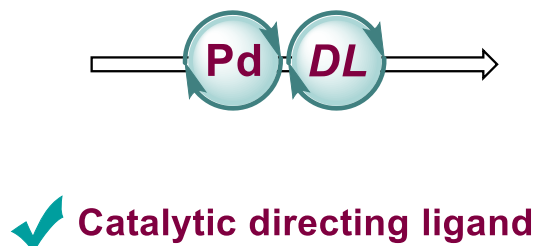
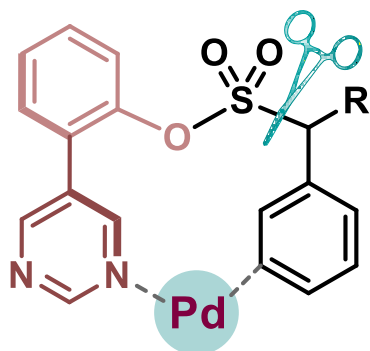
- Reversibly attachable-and-detachable DG
- One pot synthesis

Cytochrome P450 mediated hydroxylation

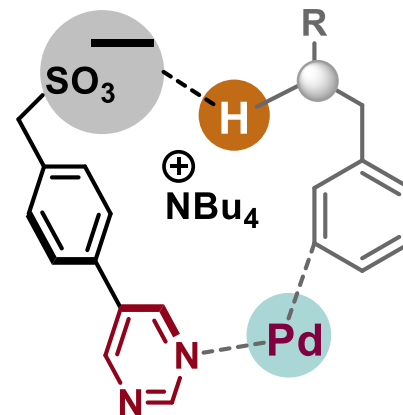


Introducing catalytic anionic ligand

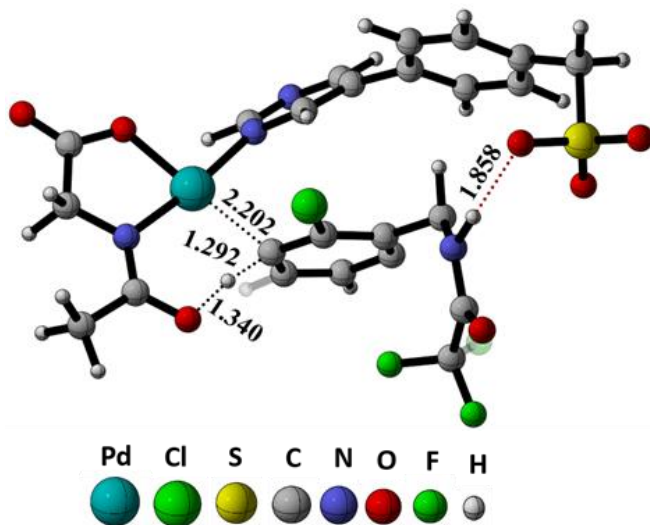
Previous approach
with covalent DG



Non-covalent approach
with organic salts



- ✓ Anionic ligand directed distal activation
- ✓ Pd-catalysed *meta*-olefination of amines
- ✓ Non-covalent interaction assisted *meta*-olefination

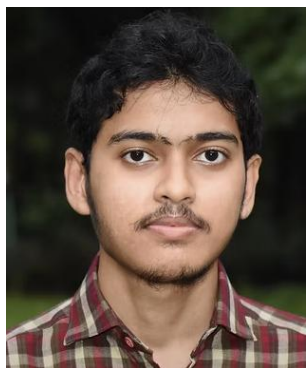
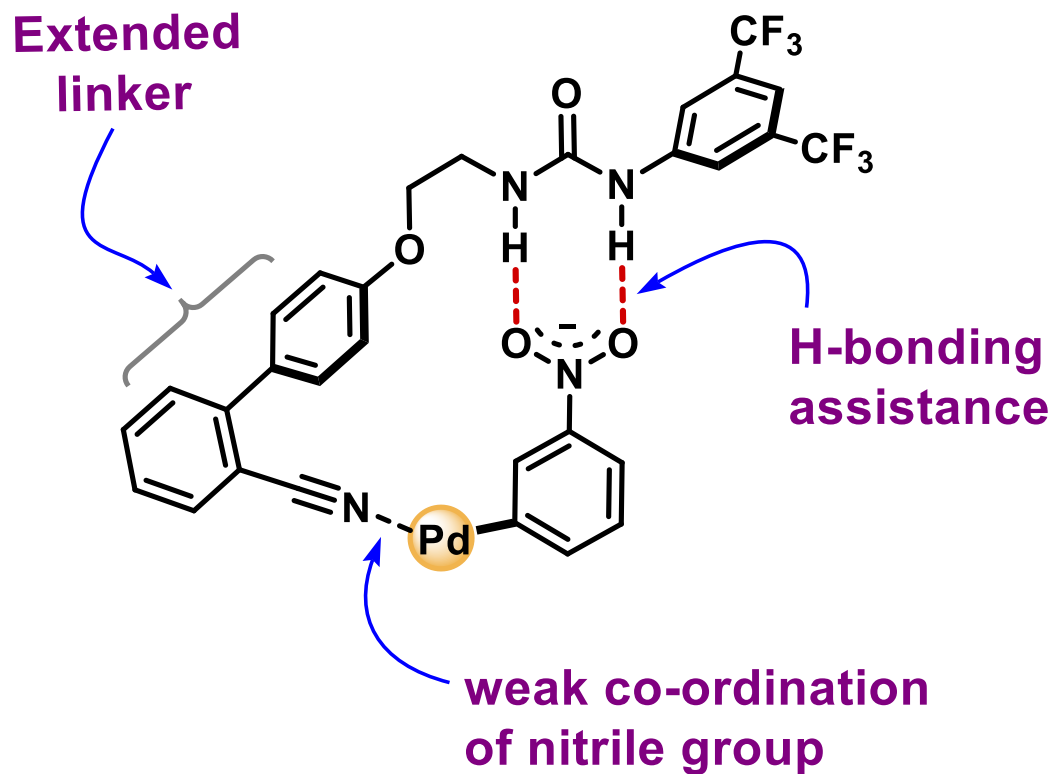


Nupur



Soumya

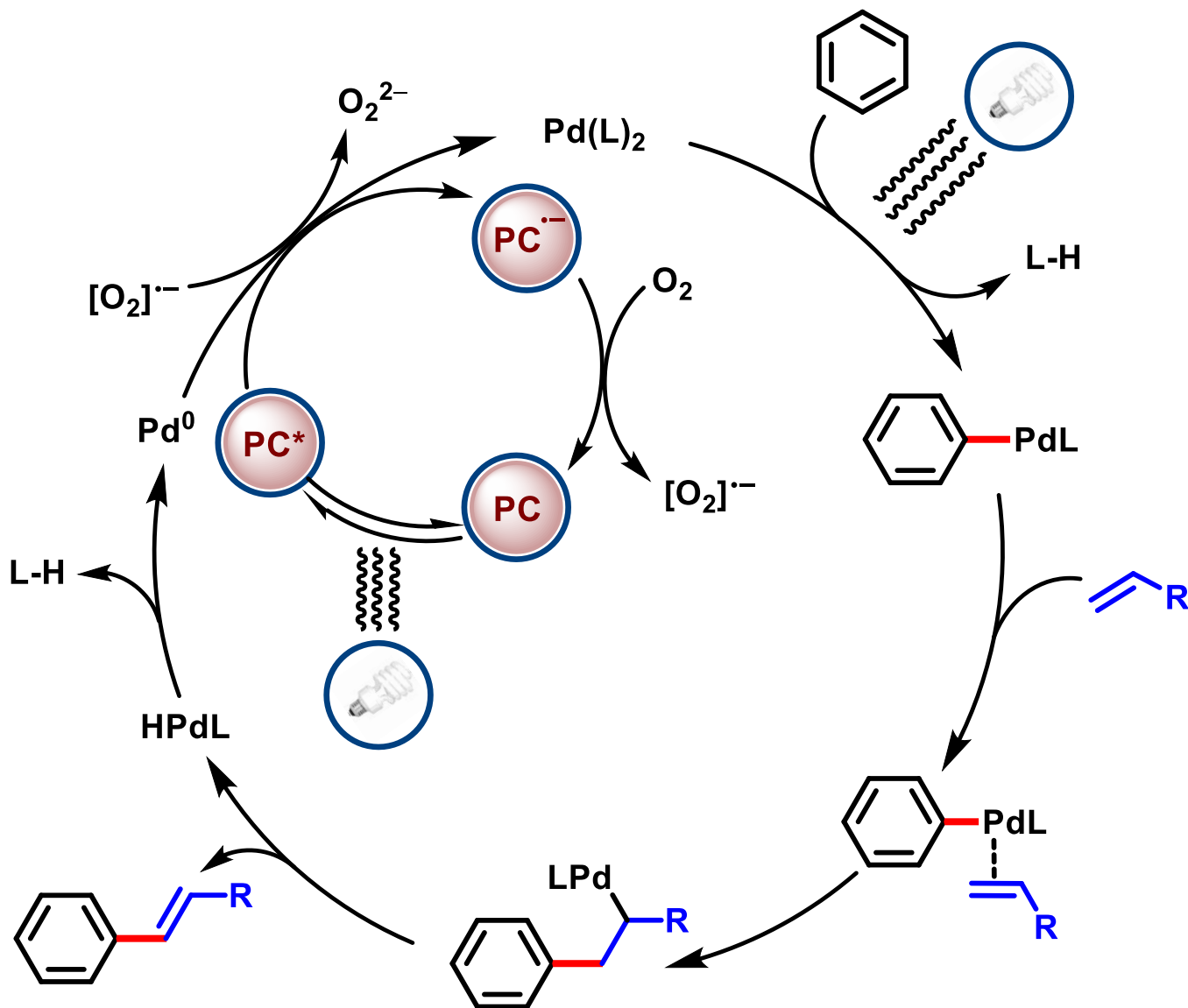
Substrate-ligand two fold **H-bonding** interaction



Bishal

- ✓ *H-bonding interaction guides regioselectivity*
- ✓ *Meta-C-H activation of nitroarenes*

Photocatalysis with Pd @ RT, oxidant free



Superior photocatalytic performances

Thermal approach

Our Photocatalytic approach

Thermal approach

Our Photocatalytic approach

AgOAc (2 equiv.)

No external oxidant

100 °C

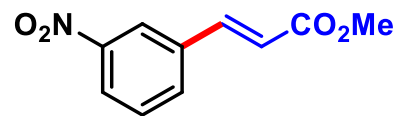
RT

Yu and coworkers
Nature **2017**, 551, 490

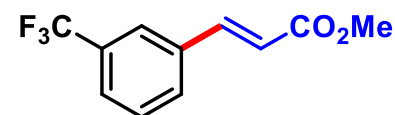


Argha

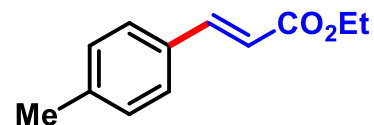
Srimanta



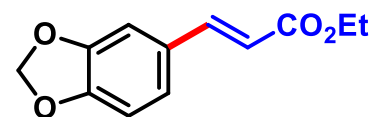
(*m/p* = 14.1/1.0)



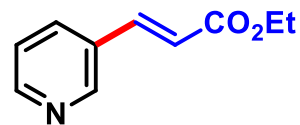
69%, (*m/p* = 3.3/1.0)



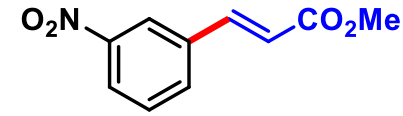
(*o/m/p* = 1.0/12.2/13.8)



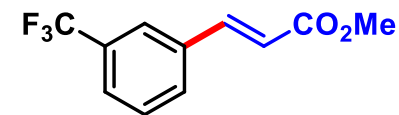
(β/α = 1.8/1.0)



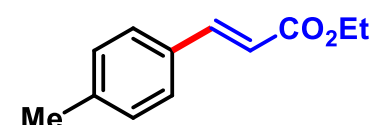
(*C-3/C-2/C-4* = 12/1/1)



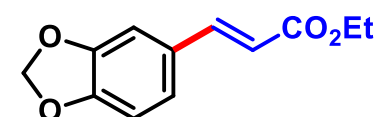
exclusive



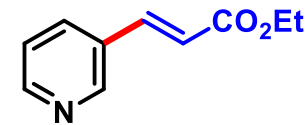
exclusive



exclusive

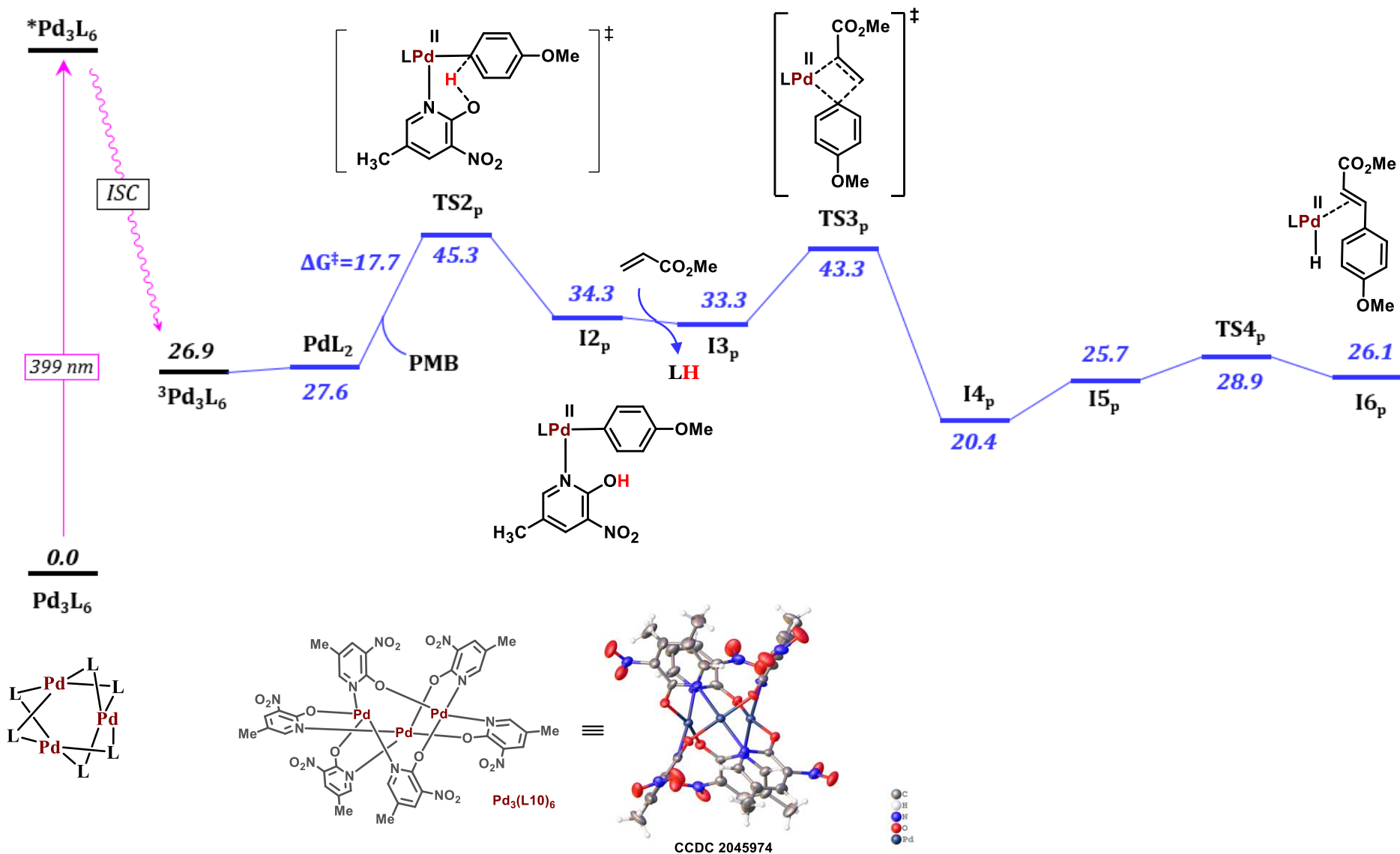


exclusive

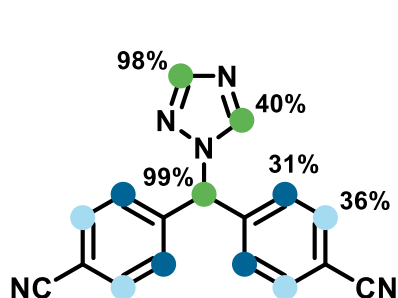


exclusive

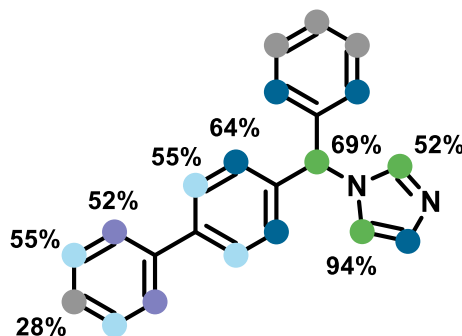
Theory corroborates with experimental data



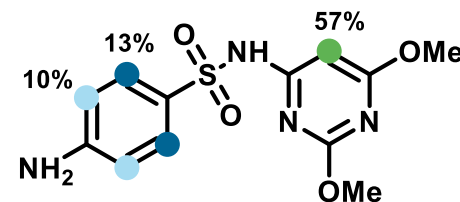
Deuteration and Tritiation of Pharmaceuticals



6[²H], 78%
Letrozole
- D/molecule

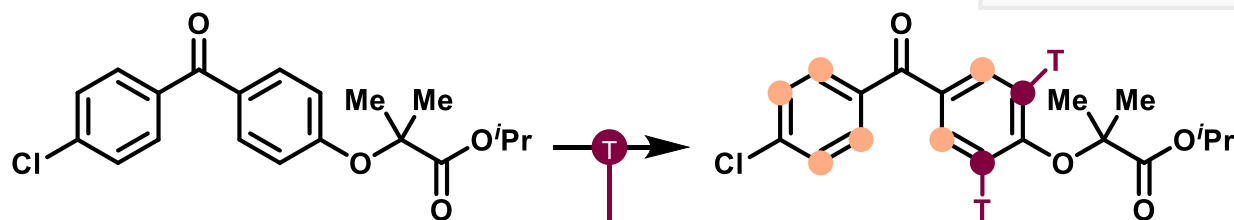


7[²H], 88%
Bifonazole
9.71 D/molecule



8[²H], 73%
Sulfadimethoxine
1.03 D/molecule

Tritium labelling



Fenofibrate 14

T-Fenofibrate, 14[³H]

Tritiation by HTO

molar activity
259 GBq mol⁻¹

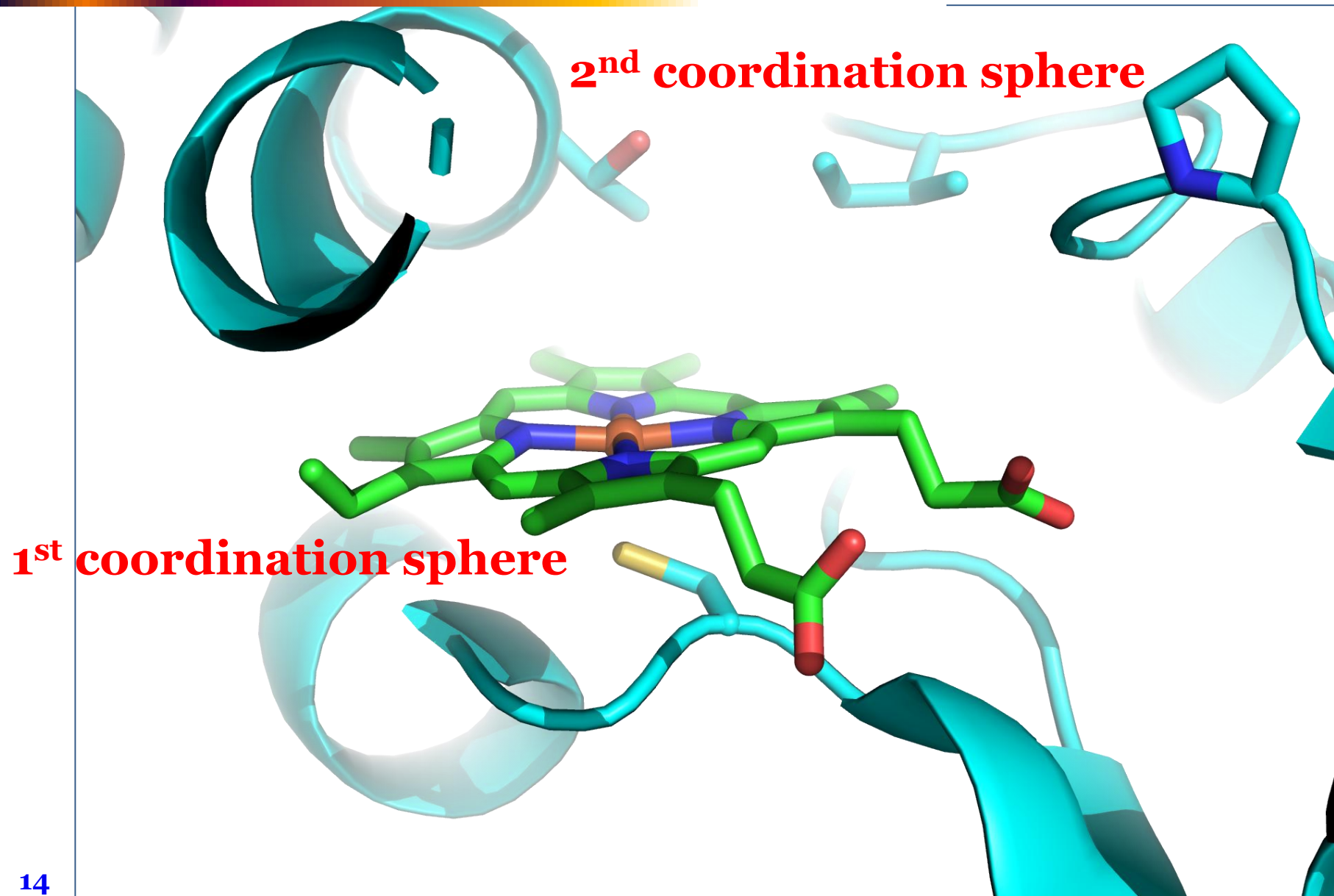
radiochemical purity
>98%

in situ preparation of HTO (~ 4 Ci) by reduction of Pt₂O in TFT/Dioxane



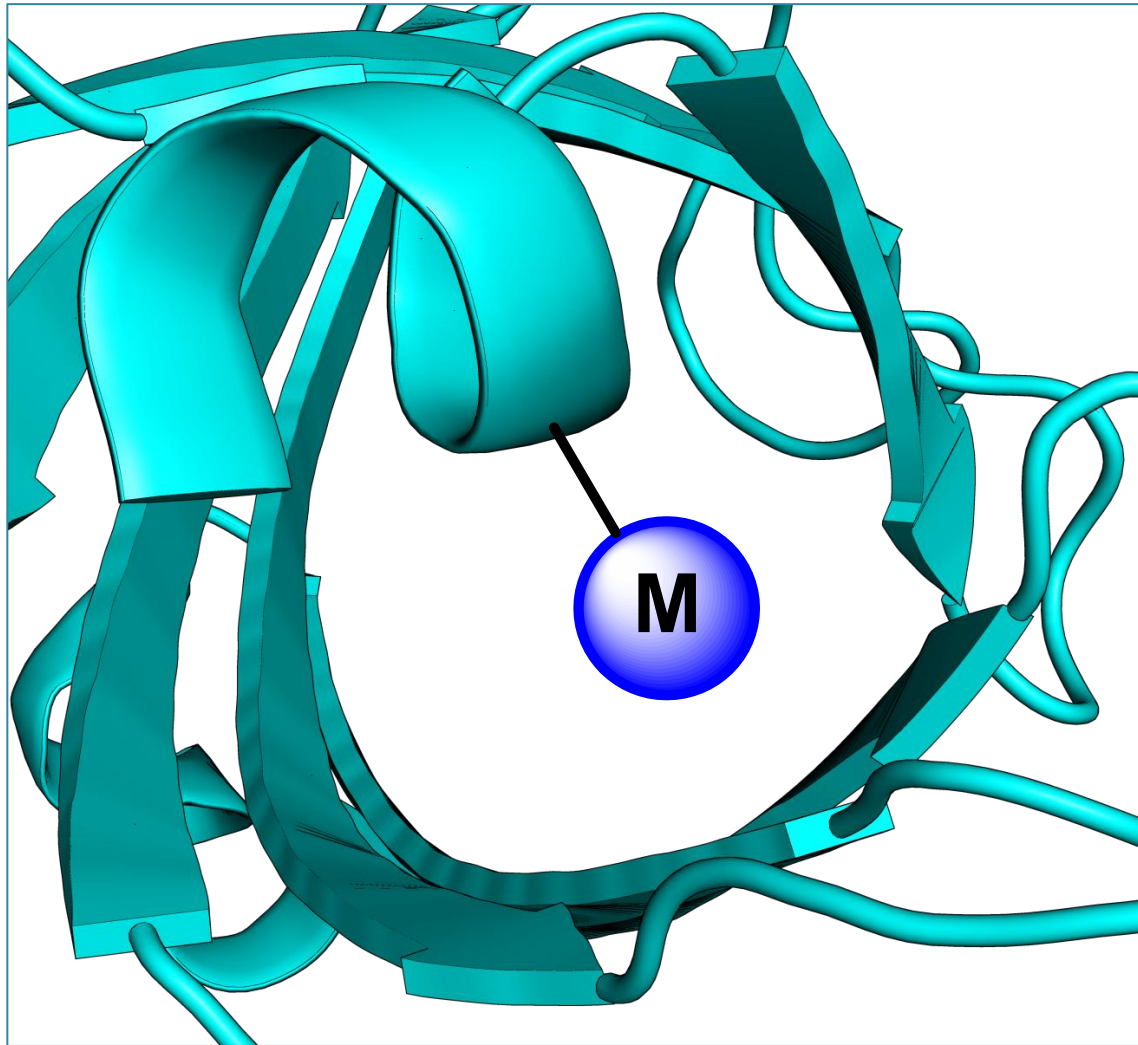
Dr. Grégory Pieters
CEA Paris-Saclay, France

Achiral metal, *chiral* cavity



Metalloenzyme's active site

Artificial metalloenzyme (*hybrid platform*)



Mutation is the *way forward*



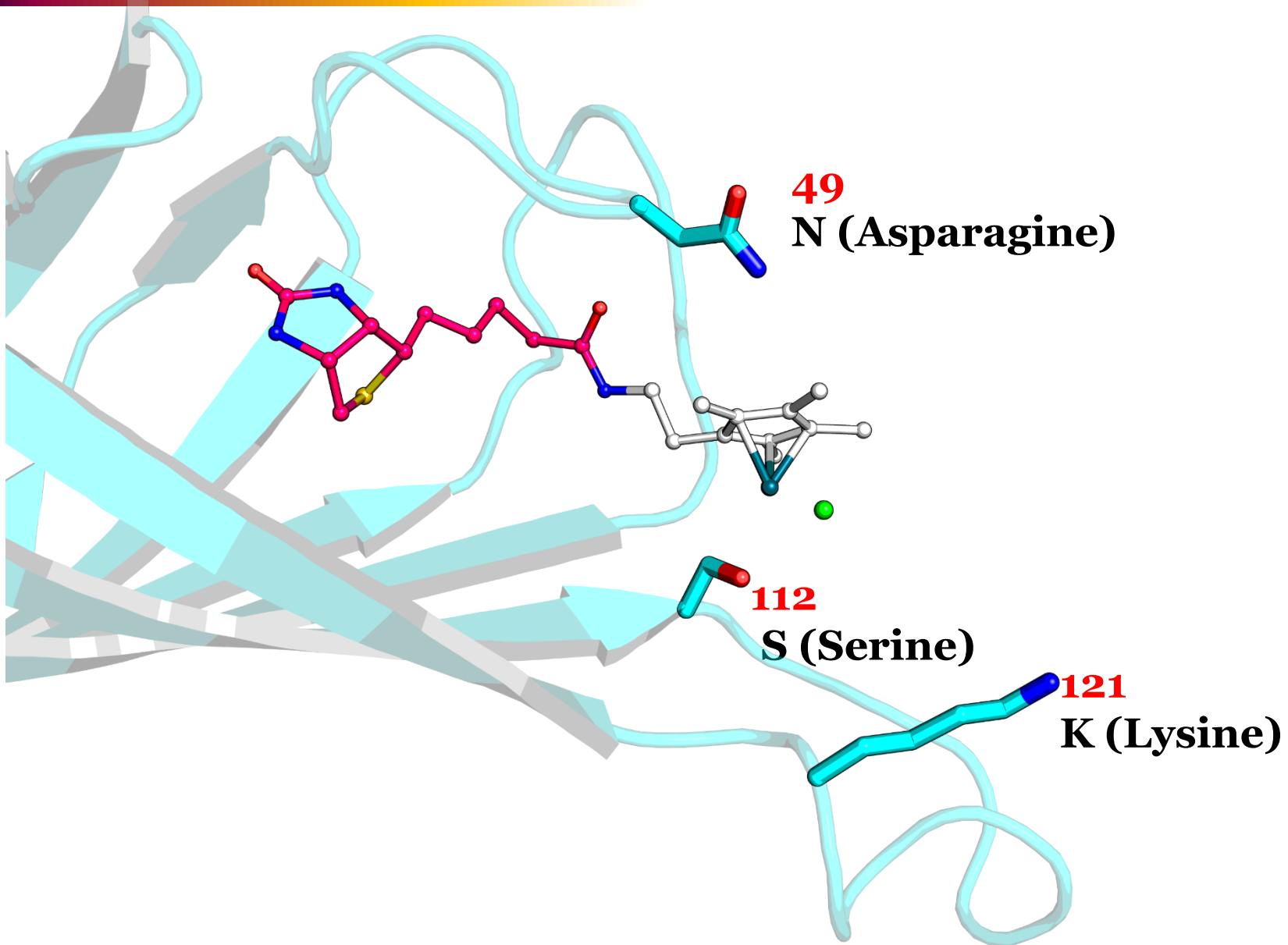
Prasun



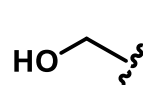
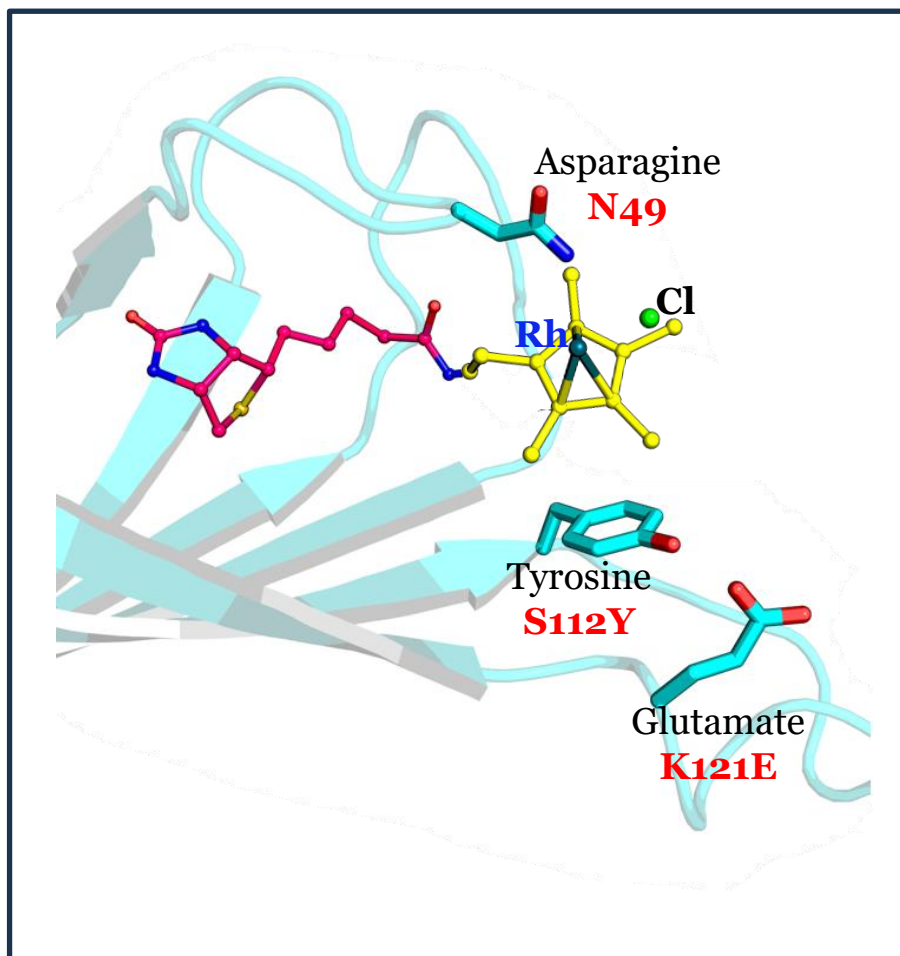
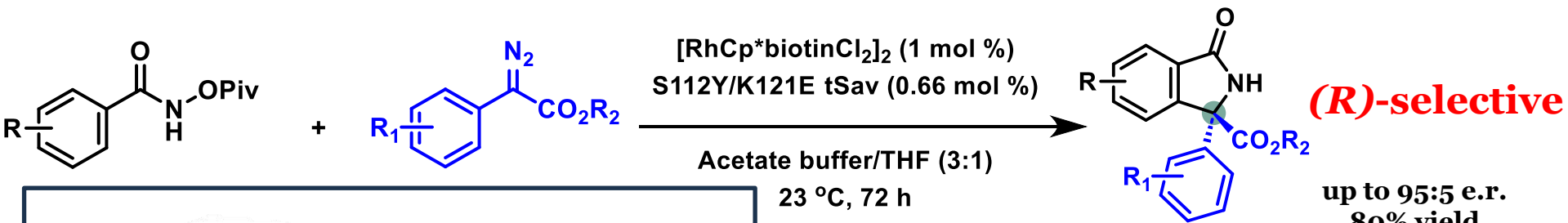
Hirak



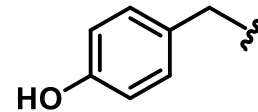
Nandita



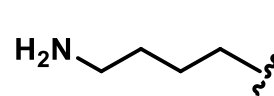
(R)-Selectivity by site directed mutagenesis



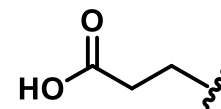
Serine (S112)



Tyrosine (S112Y)



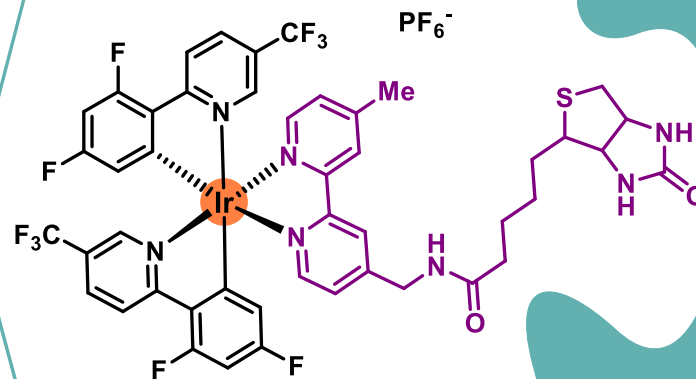
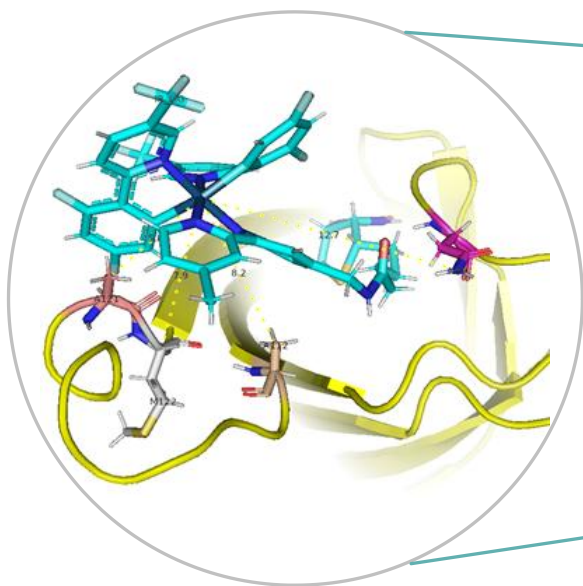
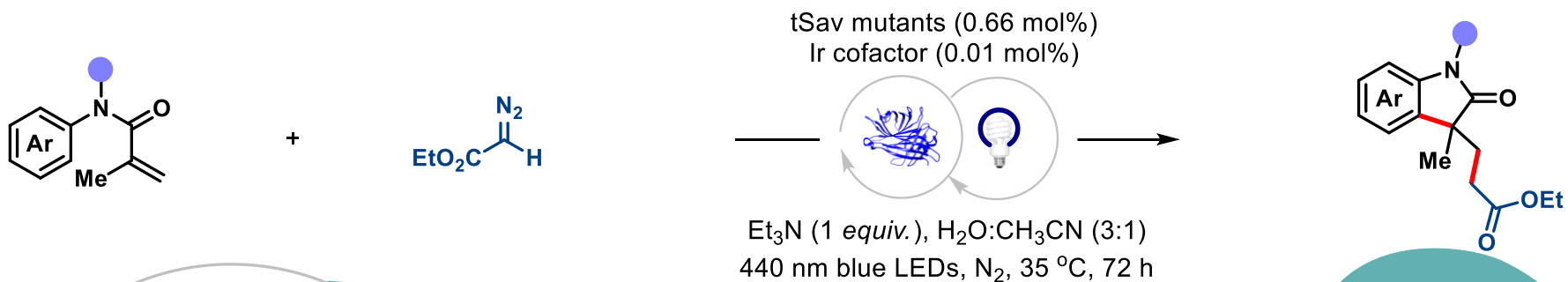
Lysine (K121)



**Glutamic acid
(K121E)**

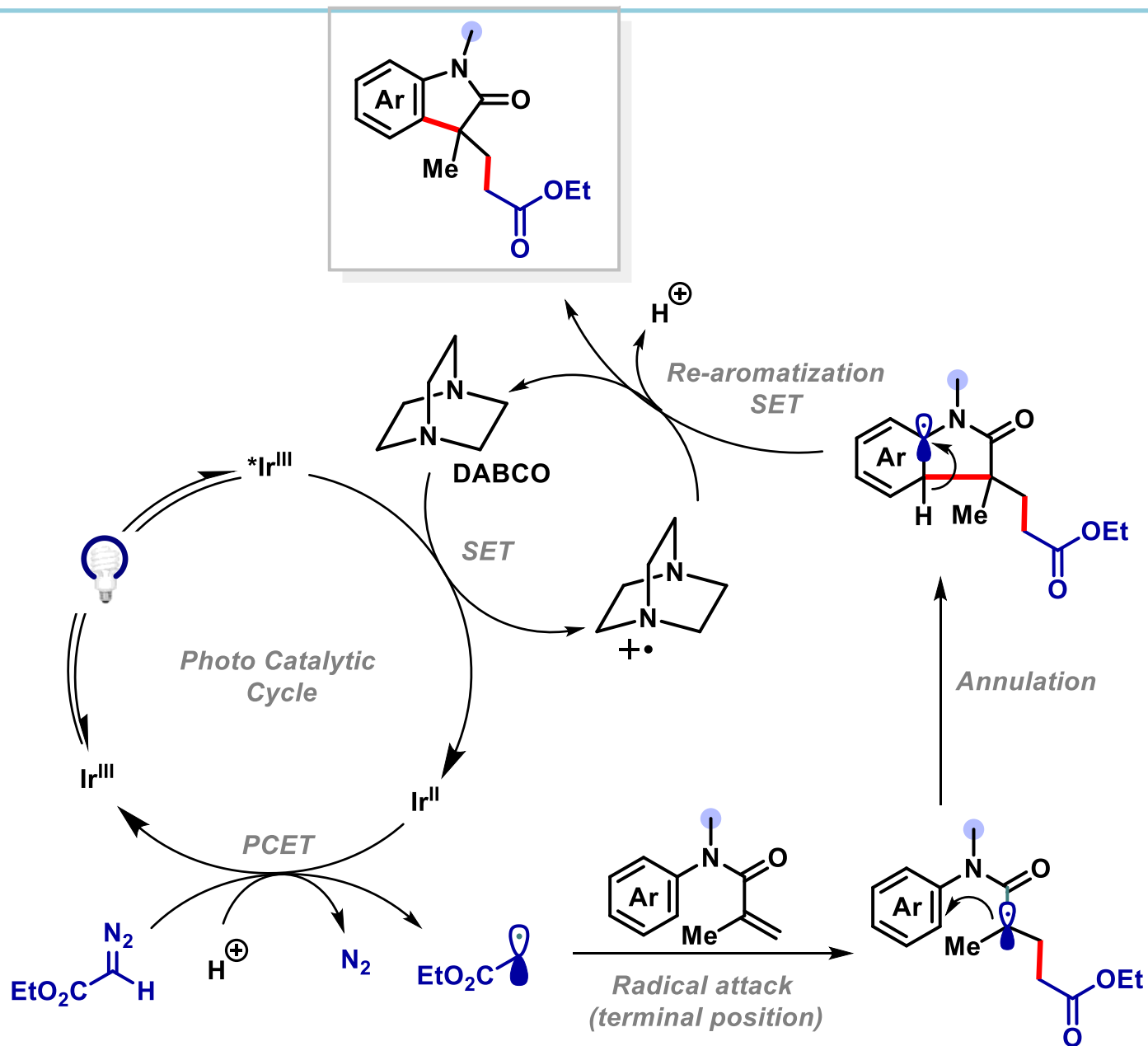
ArMs catalyzed Photo redox reactions

Photoinduced iridium artificial metalloenzymes mediated indolone synthesis

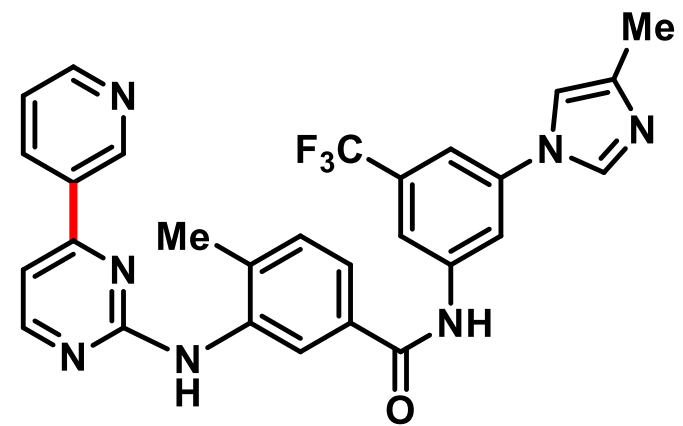
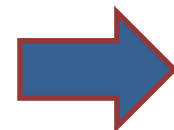
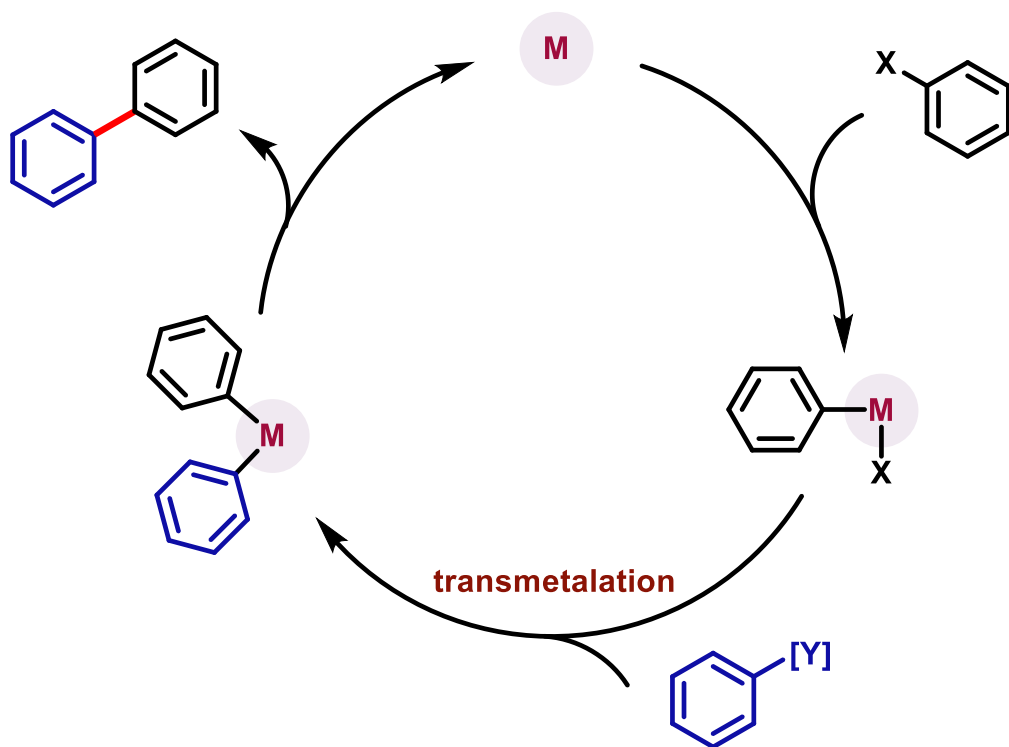
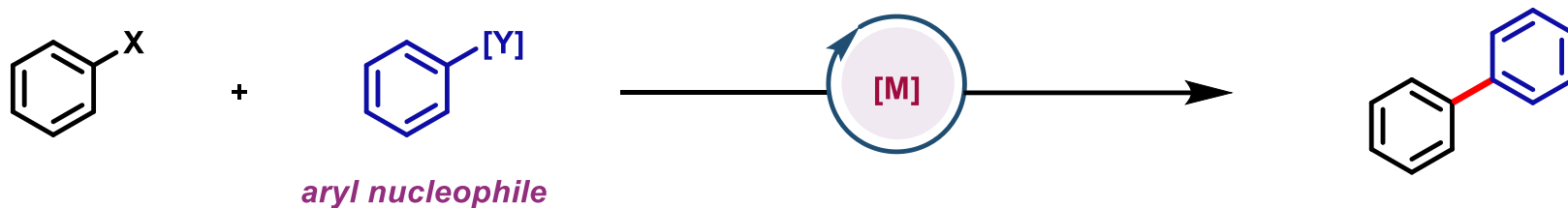


Biotinylated iridium co-factor into streptavidin

ArMs catalyzed Photo redox reactions

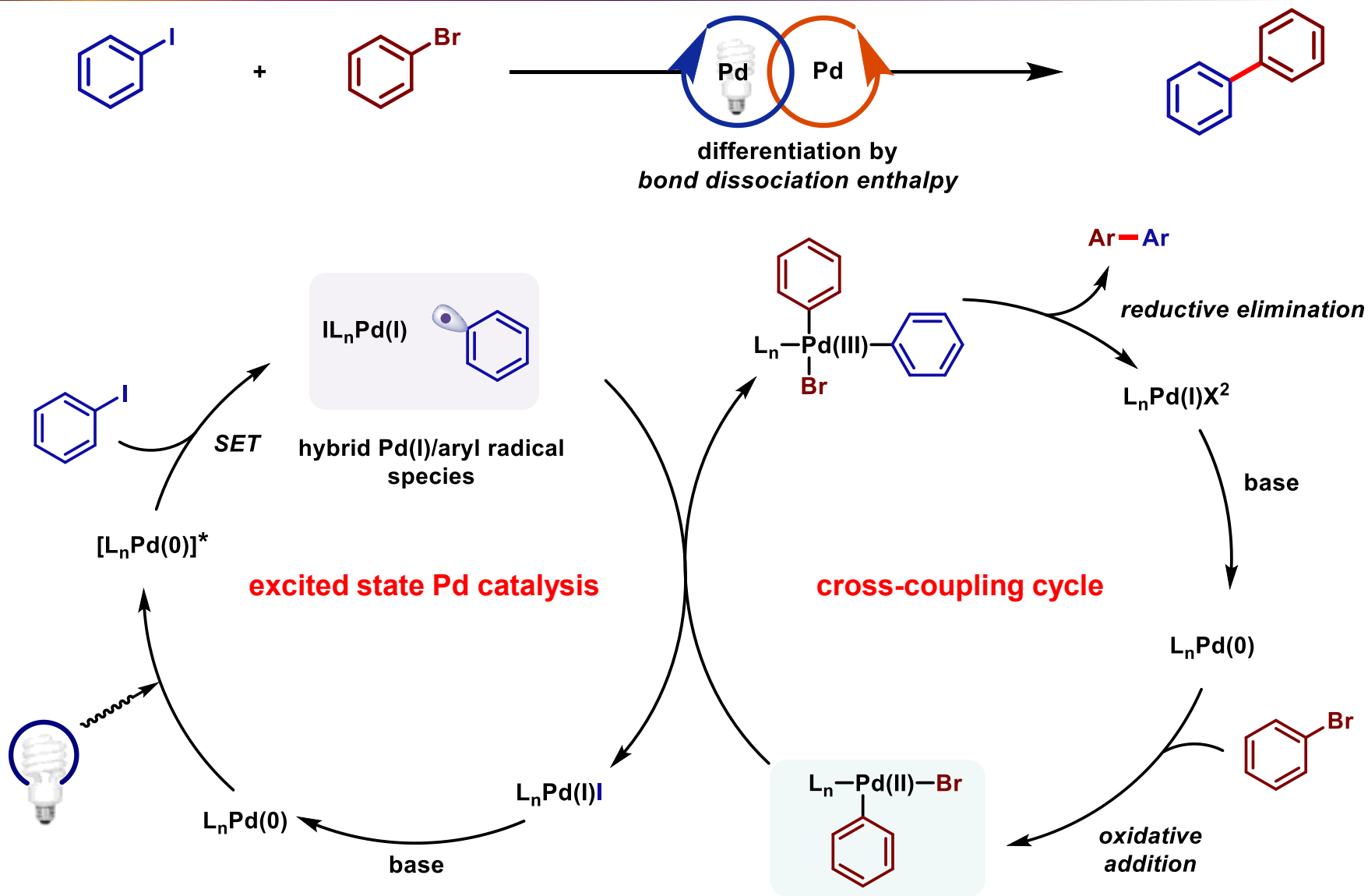


Cross-coupling leads the way...

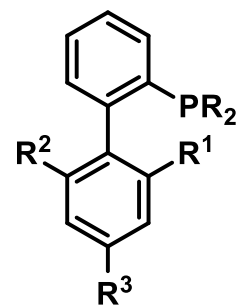


Tasigna
\$1.923 Billion
Hematology

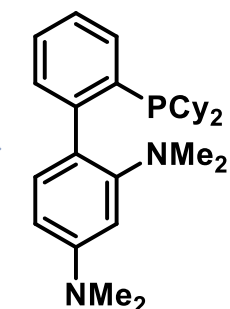
Breaking barriers in cross-electrophile coupling



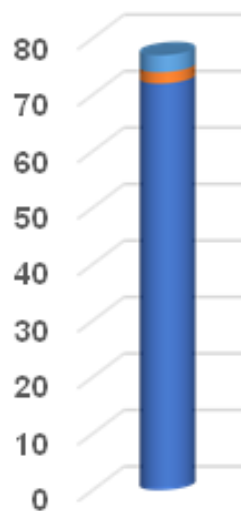
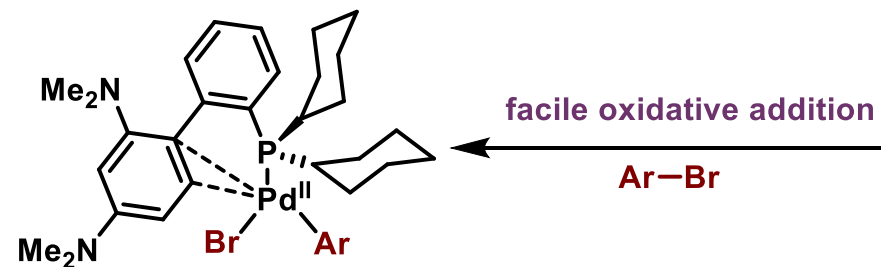
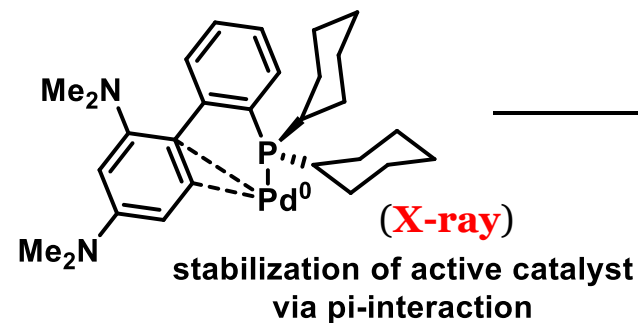
2,4-di-NMe₂ stabilises Pd⁰



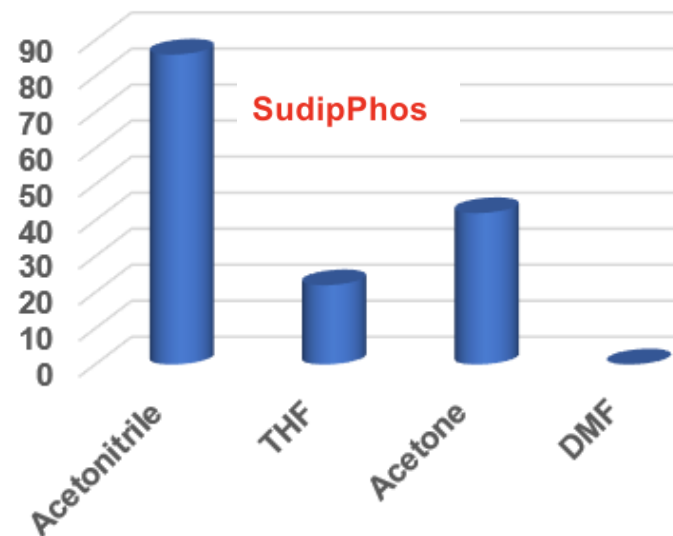
stereoelectronic modulation



SudipPhos

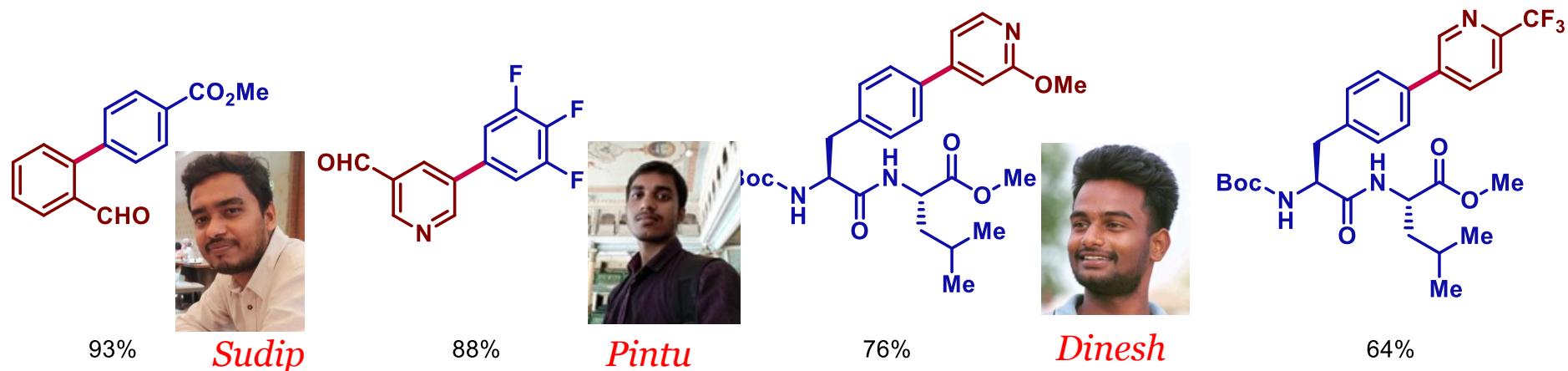
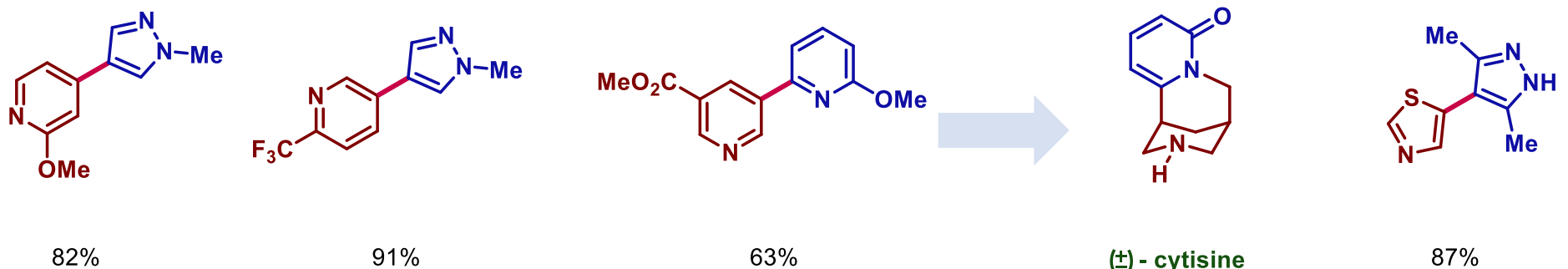
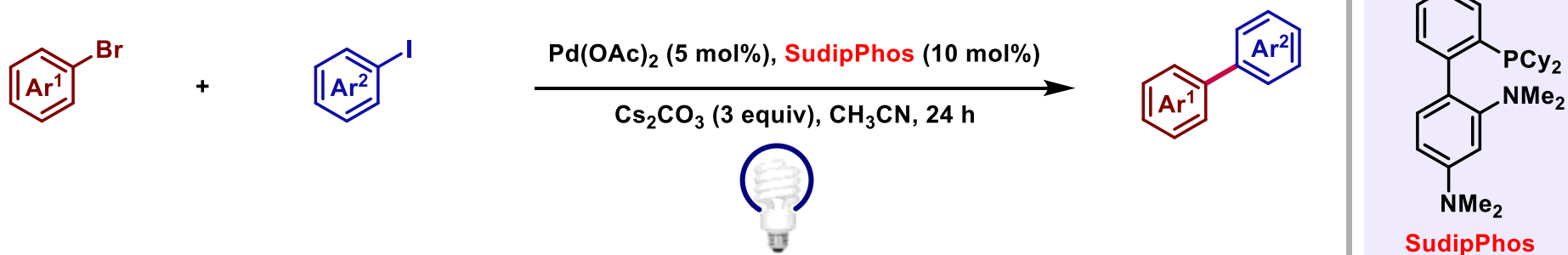


SudipPhos

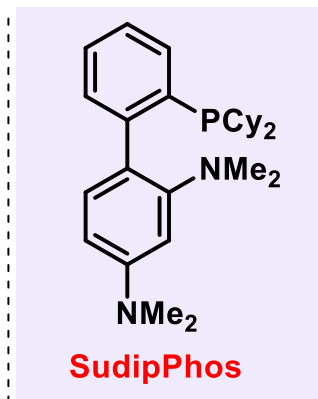
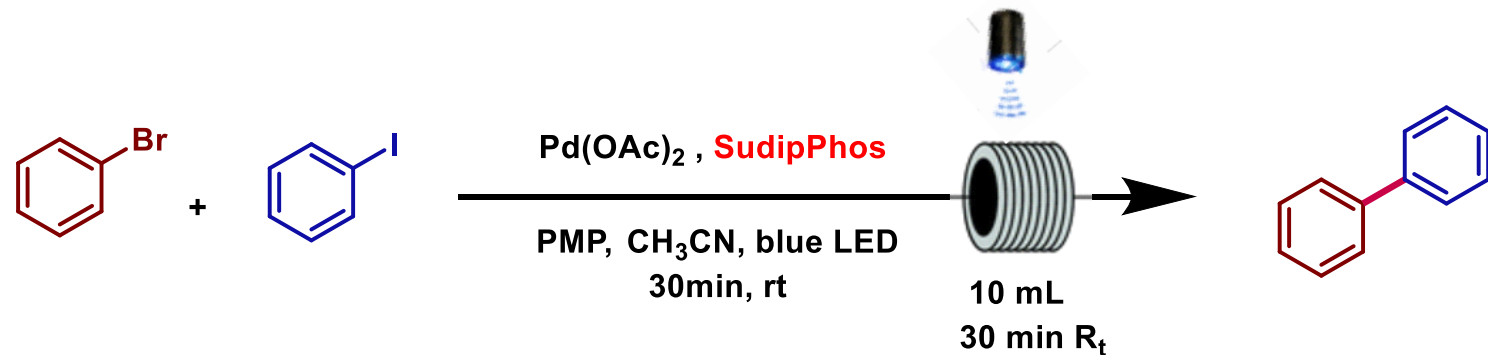


SudipPhos

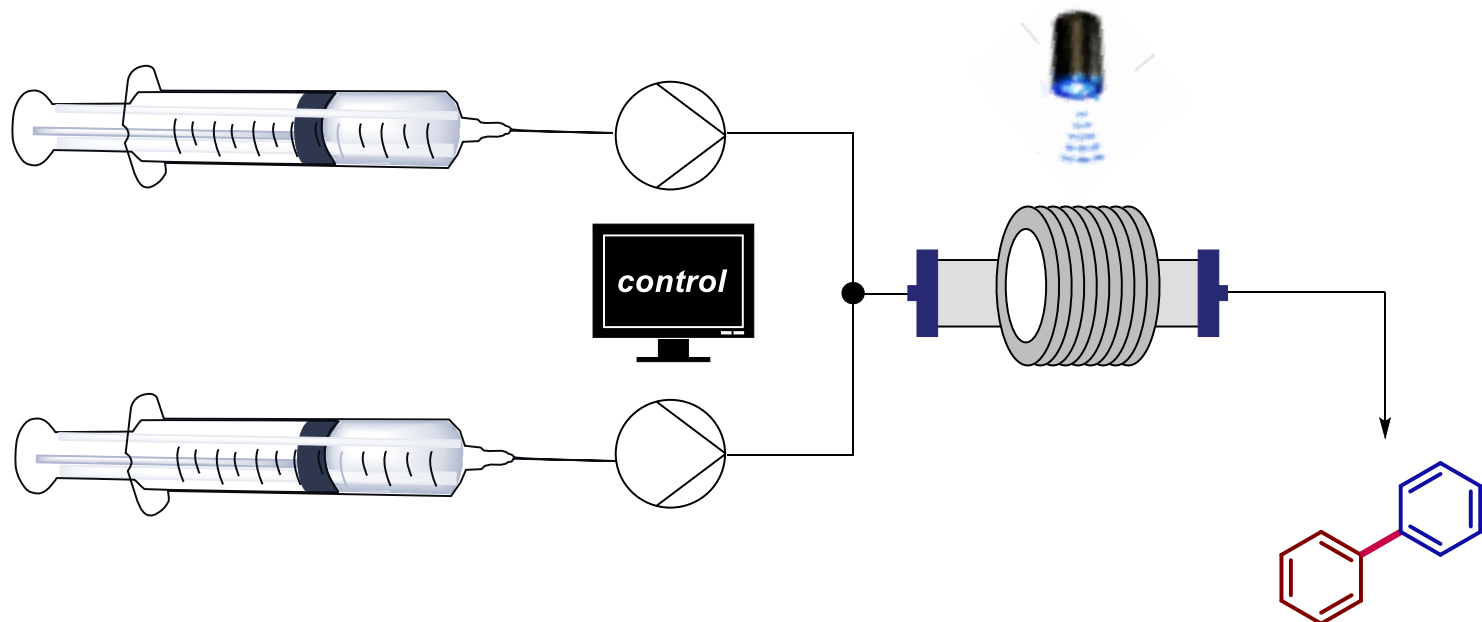
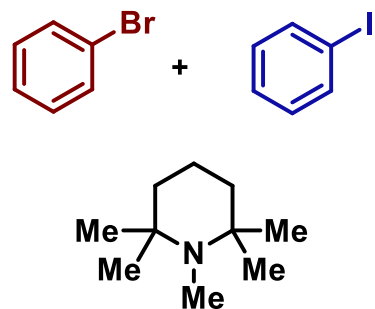
Replacing expensive boronic acids by halides



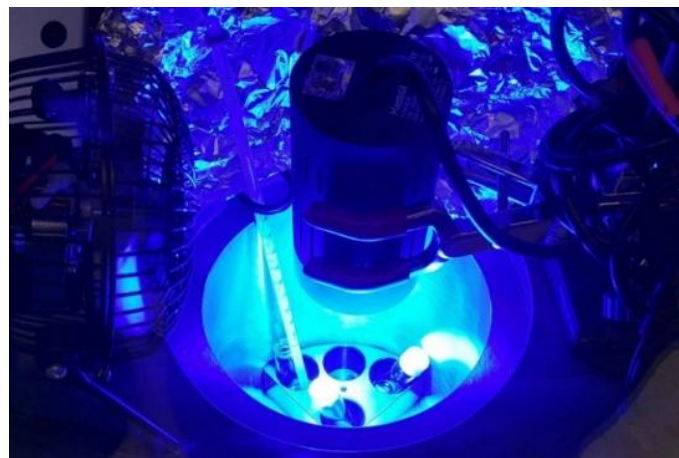
XEC reaction *via* continuous photo-flow



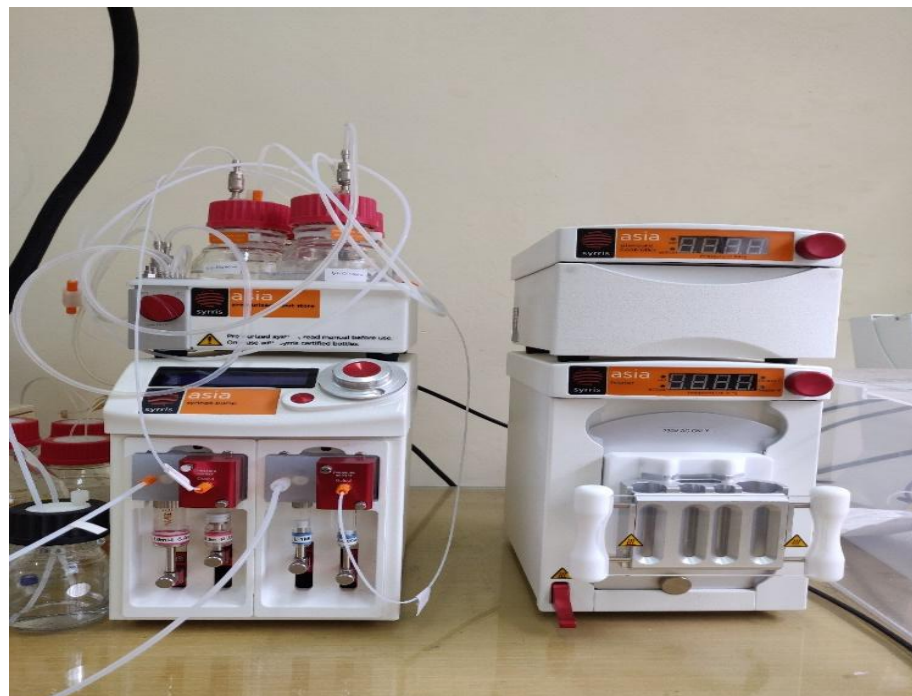
Pd(OAc)_2
SudipPhos



Industrial scale application



Light set-up in laboratory
440 nm, 34 W LEDs (for trial on 1 kg scale)



Thank You @ICOPP

Funding Agencies – BARC, DST, ANRF, CSIR, DRDO, ISRO,
ACTREC, Industry Partners

Collaborators, students



Unlocking new chemical space via selective catalysis



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dmaiti@iitb.ac.in

+91-9820907155

Use of industrial waste **carbon dioxide** and **olefins**



CO₂

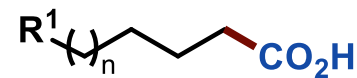
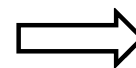
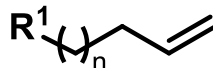


*Development of strategies for fixing CO₂
in unsaturated hydrocarbon*

AXILOR
WHERE INNOVATION MEETS EXECUTION

CO₂

+



oil industry (mainly from fume)

petroleum waste olefin

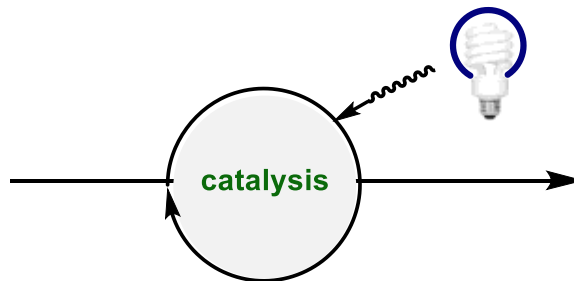
Kilogram scale

Terminal carboxylic acid containing **pharmaceuticals**

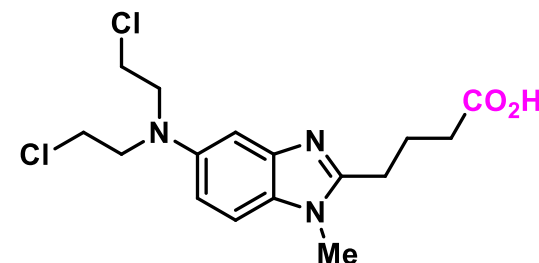
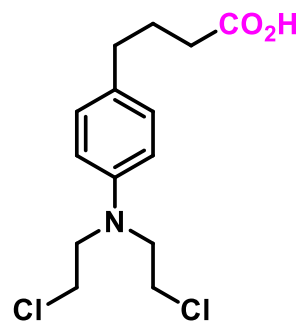
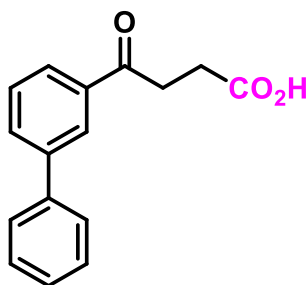
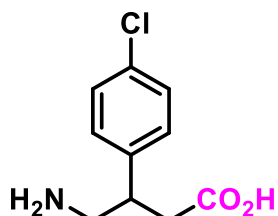
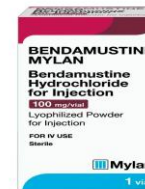


+

Olefin



Medicines



Baclofen

relaxes muscles

Fenbufen

nonsteroidal
anti-inflammatory drug

Chlorambucil

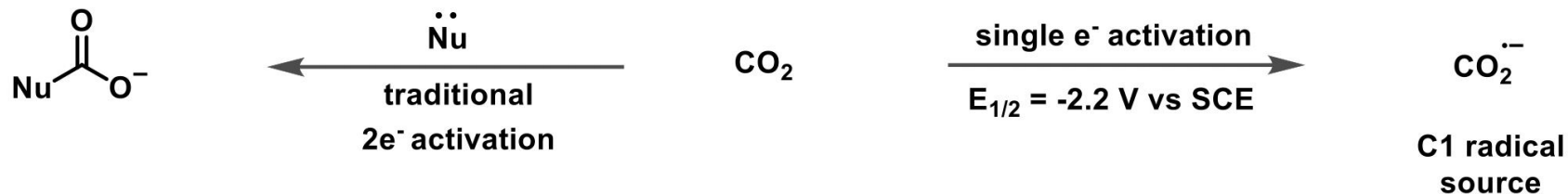
chronic lymphocytic
leukemia

Bendamustine

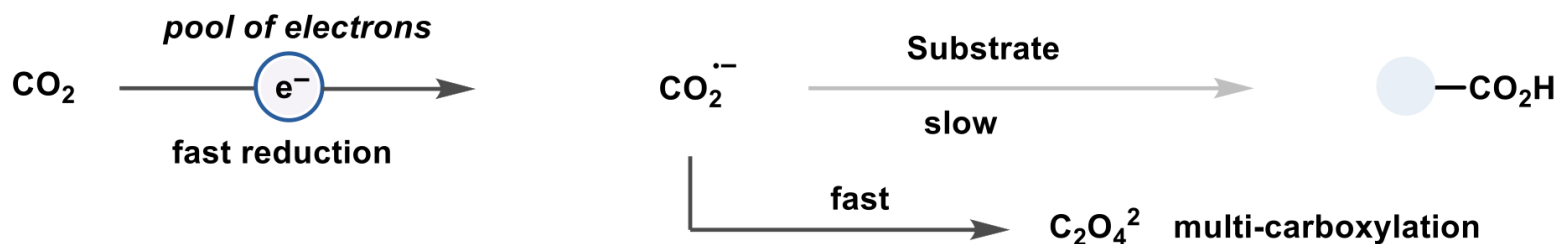
chronic lymphocytic leukemia

Challenges of hydrocarboxylation reaction

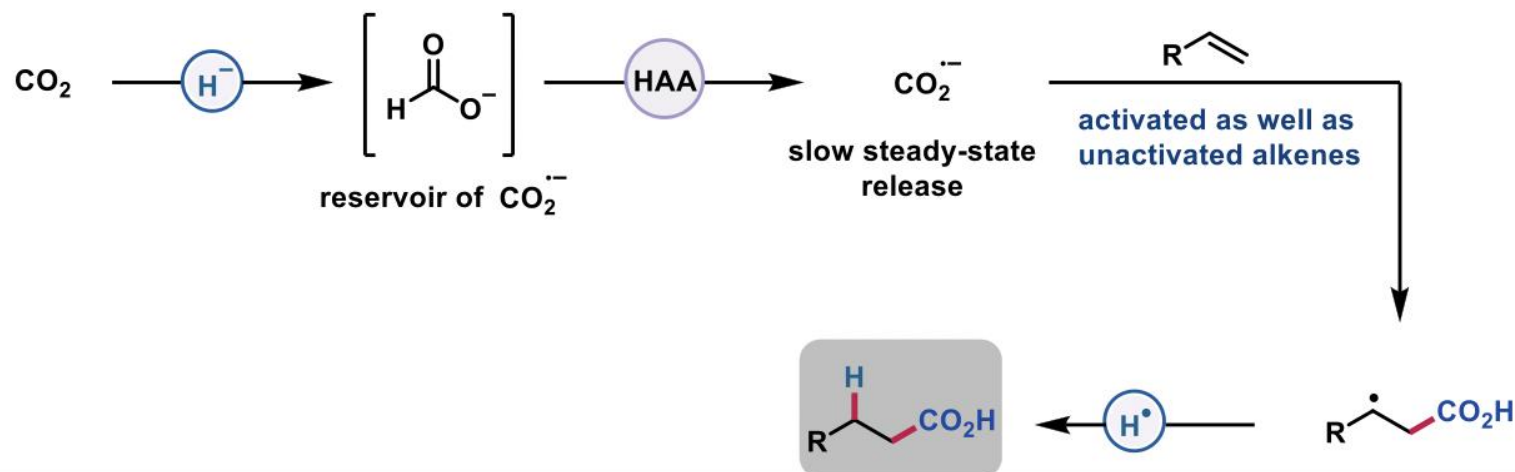
- challenges associated with single electron reduction of CO_2



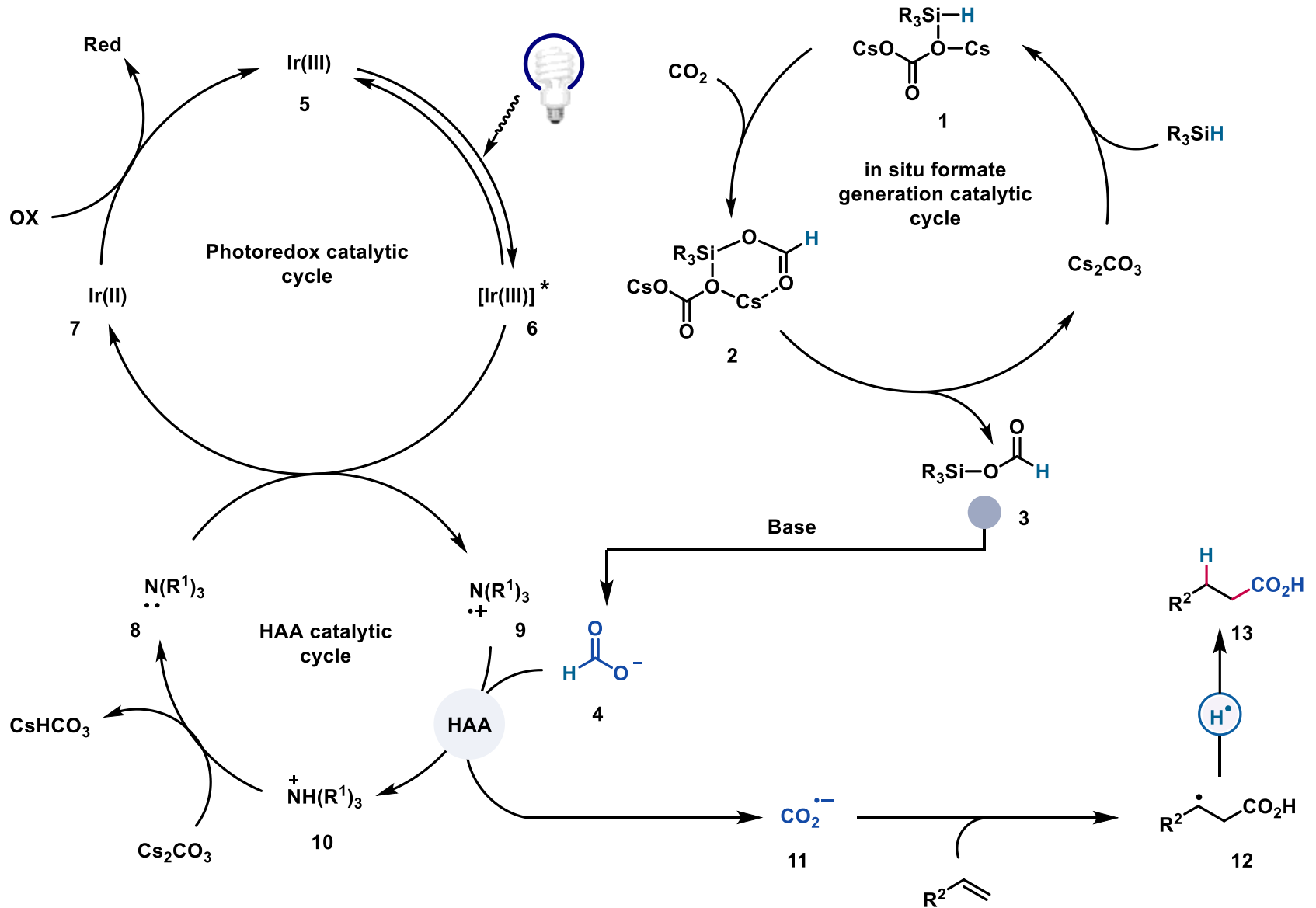
- difficulties of valorization of $\text{CO}_2^{\cdot-}$



- our approach: A H^- and H^\cdot atom transfer synergy for selective carboxylation



Taming $\text{CO}_2^{\bullet-}$



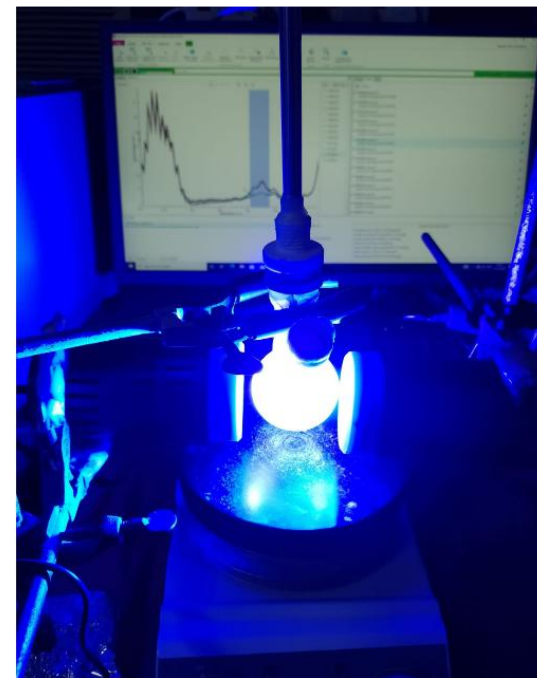
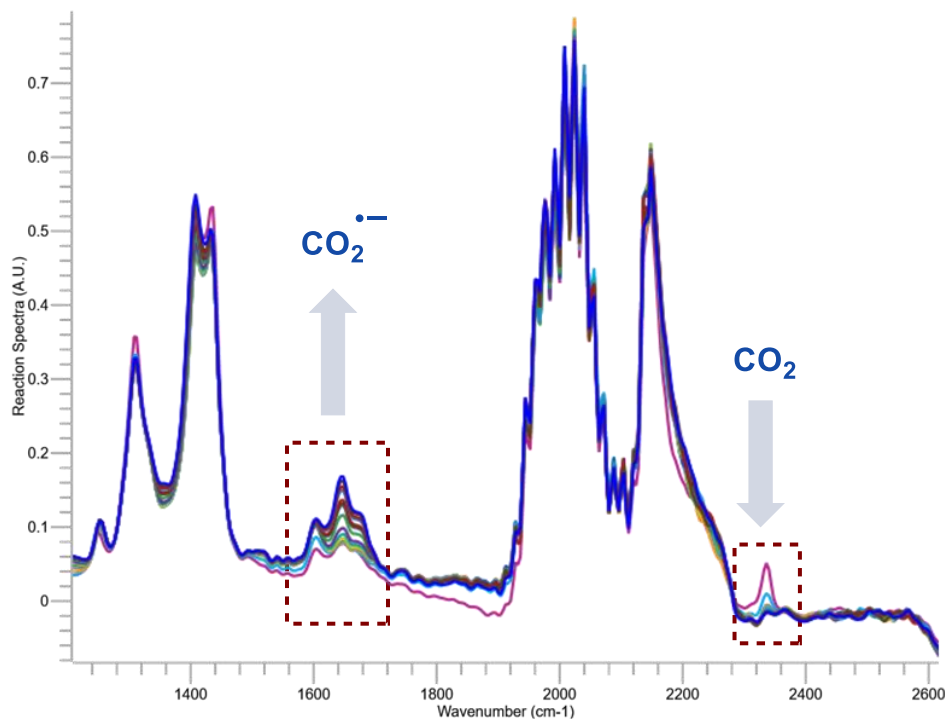
CO₂^{•-} generation

CO₂

Ir-PC (1 mol%), TTMSS (2 equiv.), DABCO (1 equiv.)

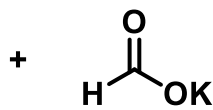
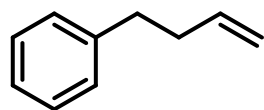
Cs₂CO₃ (3 equiv.), DMSO, blue LEDs

CO₂^{•-}



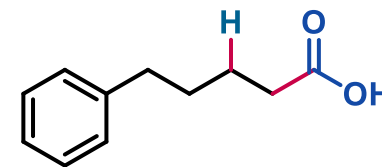
ReactIR FTIR setup

● Probing CO₂^{•-} generation from formate



standard reaction conditions

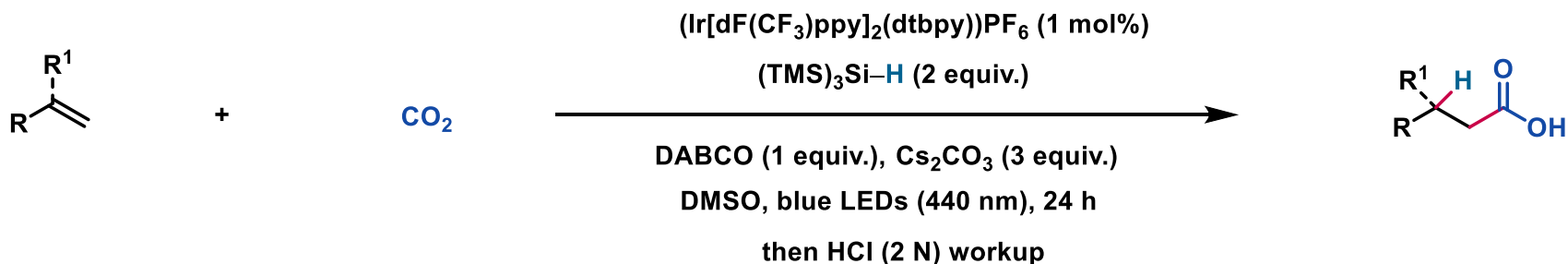
CO₂ radical anion generates from formate



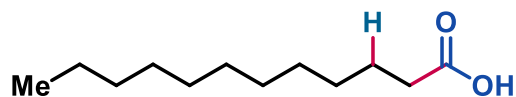
20%

32

Radiolabeling during olefin hydrocarboxylation

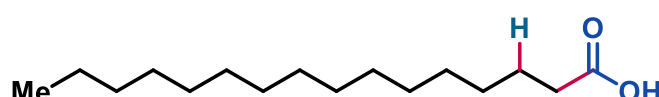


Long chain aliphatic alkene scope



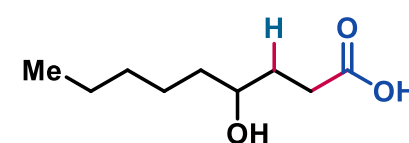
Lauric acid

17, 75%



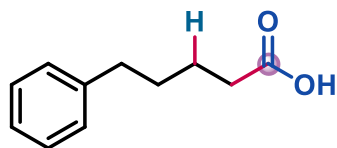
Palmitic acid

18, 71%

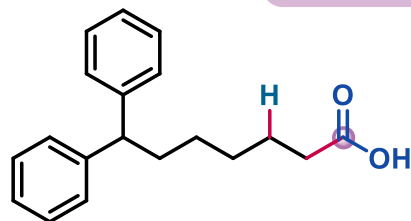


20, 67%

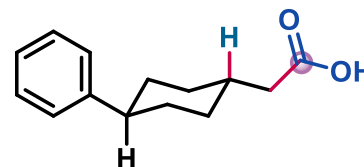
Carbon-13/14 radiolabelling



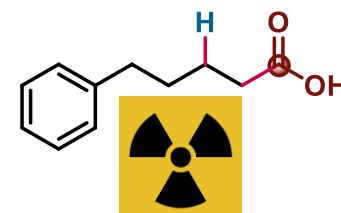
[¹³C]24, (45%), 32%



[¹³C]25, (47%), 28%



[¹³C]26, (54%), 29%



[¹⁴C]27, (39%), 38%
A_m = 0.877 GBq.mmol⁻¹

Thank You @ICOPP@Prof. Aftab Alam

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ACTREC, Industry Partners

Collaborators, students



Unlocking new chemical space via selective catalysis



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