A SYNOPSIS

of the thesis entitled

Synthesis of some metallopolymers and nanoreactors for catalyzing solitary and cascade organic transformations

to be submitted

as a partial fulfillment for the award of the degree of

DOCTOR OF PHILOSOPHY

in

CHEMISTRY

by

Falguni Shukla

under the supervision of

Dr. SONAL THAKORE, Associate Professor

Department of Chemistry
Faculty of Science
The Maharaja Sayajirao University of
BarodaVadodara 390 002, Gujarat
(INDIA)

June 2023

SYNOPSIS OF THE THESIS

to be submitted to
THE MAHARAJA SAYAJIRAO UNIVERSITY OF BARODA
for the award of the degree of **DOCTOR OF PHILOSOPHY** in
CHEMISTRY

Research Student – **Falguni Shukla**

Title of Thesis – **Synthesis of some metallopolymers and nanoreactors for catalyzing solitary and cascade organic transformations**

Supervisor – **Dr. Sonal Thakore,** Associate Professor

Department – CHEMISTRY

Faculty – Faculty of Science
The Maharaja Sayajirao University of Baroda

Registration No. – **FOS/2238**

Date of Registration – **January 13, 2021**

Shukla

Falguni Shukla
Research Student

Dr. Sonal Thakore
Research Supervisor

Dr. S[illegible] Thakore
Associate Professor
Department of Chemistry
Faculty of Science
The M.S.University of Baroda
Vad[illegible]

Prof. Ashutosh V. Bedekar
Offg. Head
Department of Chemistry

HEAD
Department of Chemistry
Faculty of Science
The Maharaja Sayajirao University of Baroda
Vadodara - 390002. Gujarat - INDIA

The thesis will be presented in the form of the following chapters-

Chapter 1
Introduction

Chapter 2
α-Hydroxy acids modified β-cyclodextrin capped iron nanocatalyst for rapid reduction of nitroaromatics: A sonochemical approach

Chapter 3
Palladium nanoparticles-confined pore-engineered urethane-linked thiol-functionalized covalent organic frameworks: a high-performance catalyst for the Suzuki Miyaura cross-coupling reaction

Chapter 4
Copper nanoparticles loaded polymer vesicles as environmentally amicable nanoreactors: A sustainable approach for cascading synthesis of benzimidazole

Chapter 5
***Candida antarctica* Lipase B and nZVI co-loaded bioinspired nanomicelles: A sustainable catalytic nanoreactor for cascade synthesis of p-aminophenol**

Chapter 1:

INTRODUCTION

Nanocatalytic systems play an important role in academic as well as industrial research and development. Metal nanoparticles (NPs) have emerged as a promising candidate for catalyzing various organic processes. But the main problem with metal nanoparticles as a catalyst is aggregation. Several capping agents and supports have been employed to solve the issue of aggregation. Among them, polymers are the traditional capping agents for metal nanoparticles because they can control the morphology and size of NPs, passivate the NPs surface, provide stability, and imparts valuable properties such as flexibility and robustness.

Additional advantages

Serve as support thus eliminating the need for additional organic or inorganic supports

Imparts valuable properties such as flexibility and robustness

Figure 1: Various polymers as capping agents for metal nanoparticles

With suitable functionalities polymers can also support metal nanoparticles resulting in metallopolymers that can aid to adopt an approach where reactions can be performed under relatively mild conditions. This spatial confinement within the metallopolymer provides longevity of the catalytic activities by protecting the encapsulated catalysts from contamination or hydrolytic degradation.

Heterogeneous catalysis is preferred in the industry as it facilitates ease of separation and recovery of the catalyst. However, homogeneous catalysis displays the advantage of usually being much more selective. The use of hybrids as supports to heterogenise homogeneous catalysts has been an intense field of research. By incorporating binding sites in individual polymers, these hybrid catalysts can be endowed with a variety of unexpected functionalities. The challenge of combining the better selectivity of homogeneous catalysis with the recoverability and reusability factor of heterogeneous catalysis puts forward the need of developing innovative and smart materials that smartly address the demands of green catalysis. Nanoreactors have combined the advantages of both heterogeneous and homogenous catalysts as well as it allows rapid, selective chemical transformation with excellent product yield.

They aid to heterogenise homogeneous catalysts. Various types of nanoreactors are reported such as micelles, vesicles, dendrimers, nanogels etc.

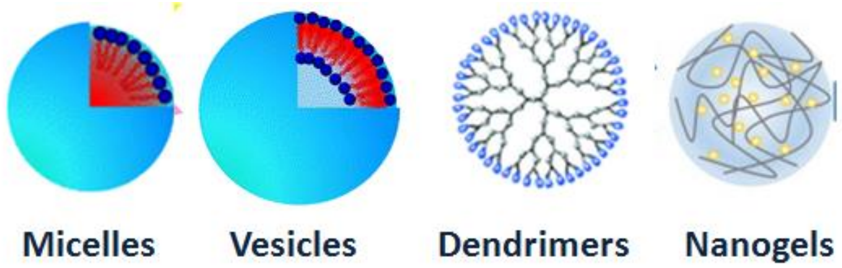


Figure 1: Various morphologies of self-assembled nanoassemblies

Thus, the fabrication of metallopolymers and nanoreactors with appropriate rationale can turn out to bring a new advent in sustainable chemistry due to their ubiquitous assistance in the synthesis of commercially important compounds.

The classical approach of synthesis suffers from various limitations such as the use of expensive catalysts, harsh reaction conditions (bases and toxic solvents), formation of undesirable and hazardous by-products. Low yields, difficulties in product separation, and lack of catalyst recyclability are also identified as key limitations.

Based on these earlier reports we have planned to prepare some novel metallopolymers and nanoreactors which can be employed as a good catalyst for carrying out different sets of solitary and cascade organic reactions under ambient conditions.

Aims and Objectives:

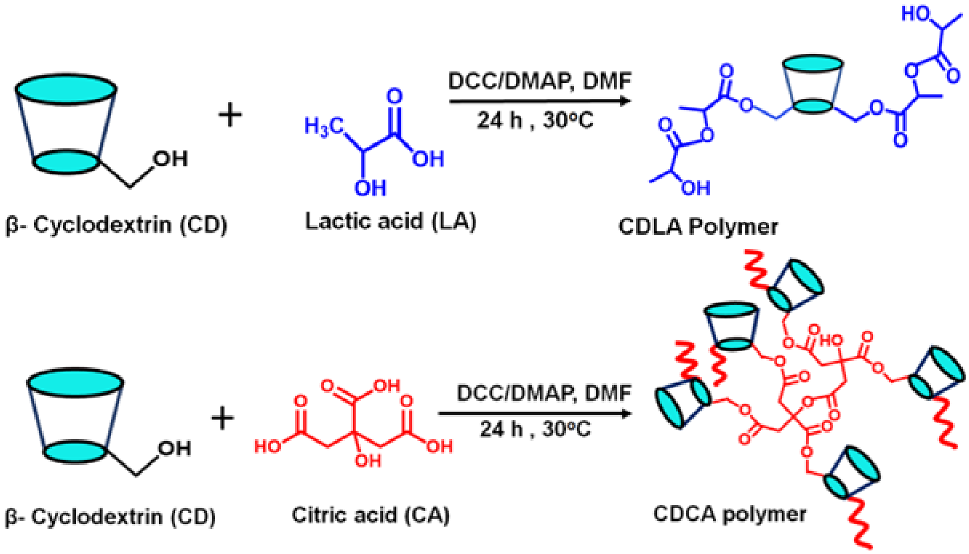
1. Synthesis of some polymers decorated with metal nanoparticles to obtain metallopolymers and nanoreactors.
2. Characterization and structural evaluation of metallopolymers and nanoreactors.
3. Assessment of the catalytic potential of metallopolymers and nanoreactors for the synthesis of industrially important compounds by solitary and cascade routes.
4. Investigation of reaction parameters, kinetics, mechanism, substrate scope, and recycling efficiency of the catalytic process.

Chapter 1 will cover an introduction to metal nanoparticles, metallopolymers, and nanoreactors. The role of metallopolymers and nanoreactors in catalytic application will be elaborated. Synthesis and application of metallopolymer and nanoreactors will also be covered.

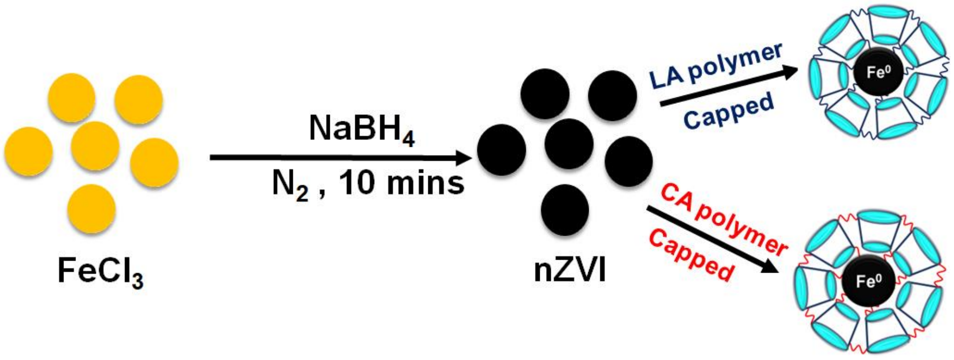
Chapter 2:

α-Hydroxy acids modified β-cyclodextrin capped iron nanocatalyst for rapid reduction of nitroaromatics: A sonochemical approach

This chapter discusses the synthesis of sustainable citric acid and lactic acid crosslinked cyclodextrin polymers via a simple one-pot esterification reaction for capping for zerovalent iron nanoparticles via the ultrasonication method (s**hown in Scheme 1 & Scheme 2**).



Scheme 1: Synthetic route for preparing lactic acid modified β-Cyclodextrin and citric acid modified β-Cyclodextrin derived crosslinked polymers.

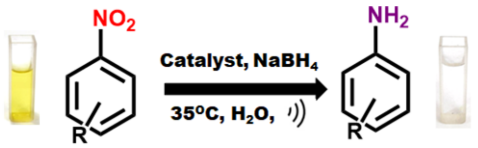


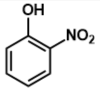
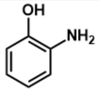
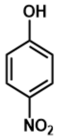
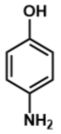
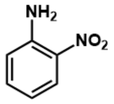
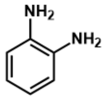
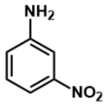
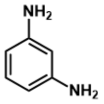
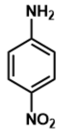
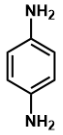
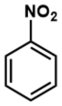
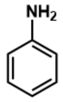
Scheme 2: Synthetic route for preparing β-Cyclodextrin derived cross-linked polymers capped zerovalent iron nanoparticles via ultrasonication method.

The polymers and the catalysts were characterized by NMR, FTIR, HRTEM, DLS, Zeta potential, FESEM, EDAX, VSM, XRD, XPS, and TGA analysis. The sonochemical approach imparted good control over the morphology, nano size, and dispersibility of the prepared FeNPs.

The synthesized polymer capped nZVI catalyzed the sonochemical conversion of 4-nitrophenol to 4-aminophenol in a very short time in an aqueous medium. Application of the ultrasonication to the reaction system increases the temperature and reduced the reaction time.

Table 1: Reduction of some nitro aromatic compounds to corresponding aromatic amines using LA@nZVI and CA@nZVI at optimized conditions



Sr. No.	Substrate	Product	Time ^{a} (s)	Time ^{b} (s)
1.			50	165
2.			70	210
3.			35	89
4.			14	50
5.			61	114
6.			35	100

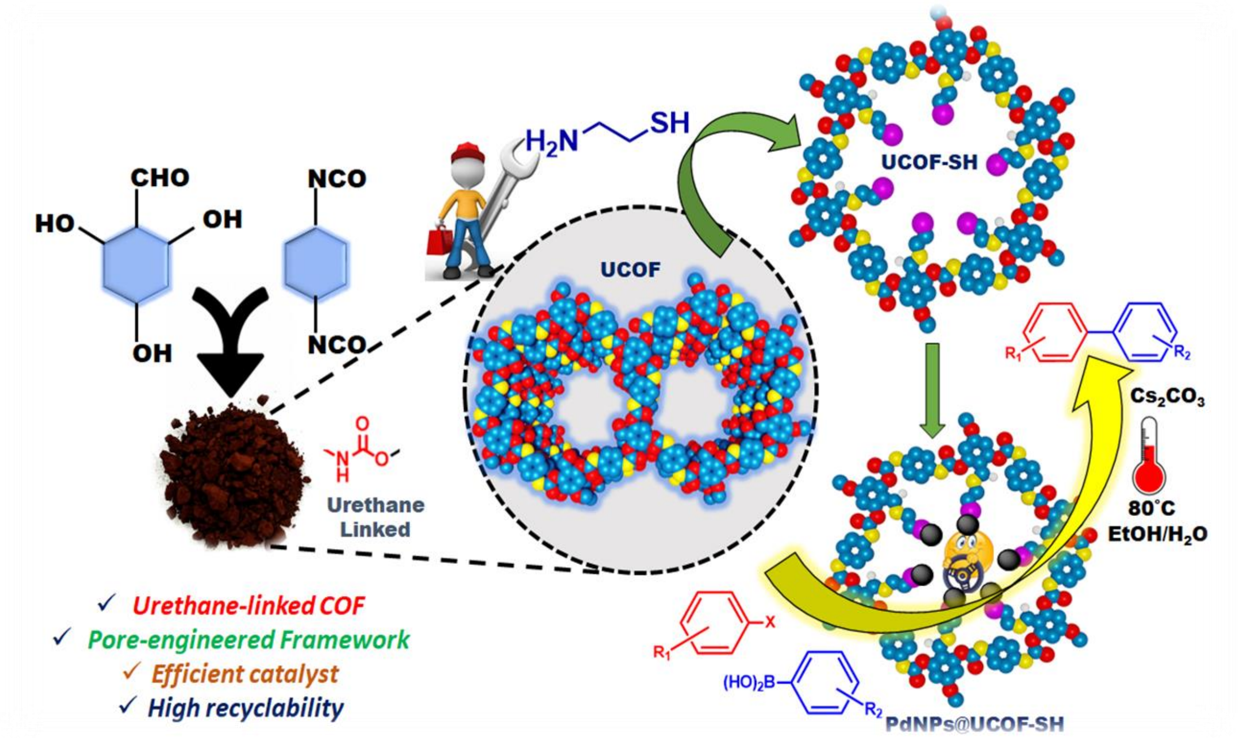
Reaction conditions: All reactions carried out at room temperature (35°C),1.5 mL of substrate (0.24 mM), catalyst 10 mg, 1.5 mL $NaBH_4$ (2.16 mM).

In addition, the surface area of nZVI was increased. Several other nitroaromatic compounds could be reduced with excellent isolated yield (89–95%), as well as high TON and TOF. The recycling studies especially revealed the robust nature of the polymer-capped nZVI. The rate constant values obtained from kinetic studies suggested that the catalytic activity of nZVI is comparable to the commonly used noble metal catalysts.

Chapter 3:

Palladium nanoparticles-confined pore-engineered urethane-linked thiol-functionalized covalent organic frameworks: a high-performance catalyst for the Suzuki Miyaura cross-coupling reaction

This chapter discusses the synthesis and functionalization of a novel urethane-linked covalent organic framework for the first time. The pendant formyl group of the UCOF was rationally functionalized using cysteamine to obtain a thiol-decorated COF which can assist in the size-controlled synthesis of stable and highly dispersed ultrafine palladium NPs.



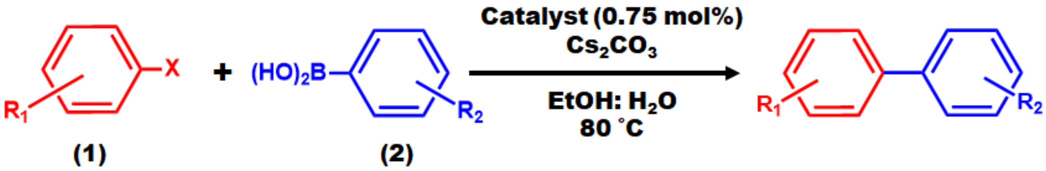
Scheme 3: Synthetic representation of palladium nanoparticles loaded thiol functionalized urethane linked covalent organic framework for Suzuki Miyuara Coupling reaction.

Beside synthesis, we also made an effort to thoroughly characterize COFs and Pd catalyst using various analytical techniques such as CP-MAS NMR, FTIR, PXRD, BET, FEG-SEM, HRTEM, XPS, TGA, and ICP-AES.

With the assistance of equally spaced thiol groups in the ordered framework, Pd NPs of small size (4–6 nm) dispersion were acquired successfully. The UCOF-SH stabilized Pd NPs showed excellent catalytic activity in terms of low catalyst loading, high yield, and milder reaction conditions toward the Suzuki cross-coupling reaction.

The reaction parameters such as base additives, temperature, solvents, catalyst dosage, and solvent ratio were studied. The optimized reaction conditions were cesium carbonate as a base additive, 10 mg catalyst, 80 ˚C, and Water: Ethanol (5:5) mixture as solvent. The scope was extended to various aryl boronic acids and aryl halides (I, Br, and Cl).

Table 2: Optimization of reaction conditions for Suzuki Miyuara Cross-Coupling reaction



Sr. No.	Aryl halide (1)	Aryl halide	Aryl boronic acid (2)	Time (h)	%Yield
1	R1=H	X=I	R2=H	**1**	**99**
2	R1=H	X=I	R2=OCH_3	**0.5**	**98**
3	R1=H	X=Br	R2=H	**2**	**99**
4	R1=OCH_3	X=Br	R2=H	**3**	**97**
5	R1=OCH_3	X=Br	R2=OCH_3	**2**	**97**
6	R1=$COCH_3$	X=Br	R2=H	**5**	**89**
7	R1=PhCN	X=Br	R2=F	**6**	**50**
8	R1=(NO_2)	X=Br, F	R2=F	**8**	**68**
9	R1=CH_3	X=Cl	R2=H	**7**	**80**
10	R1=CH_3	X=Cl	R2=F	**10**	**72**

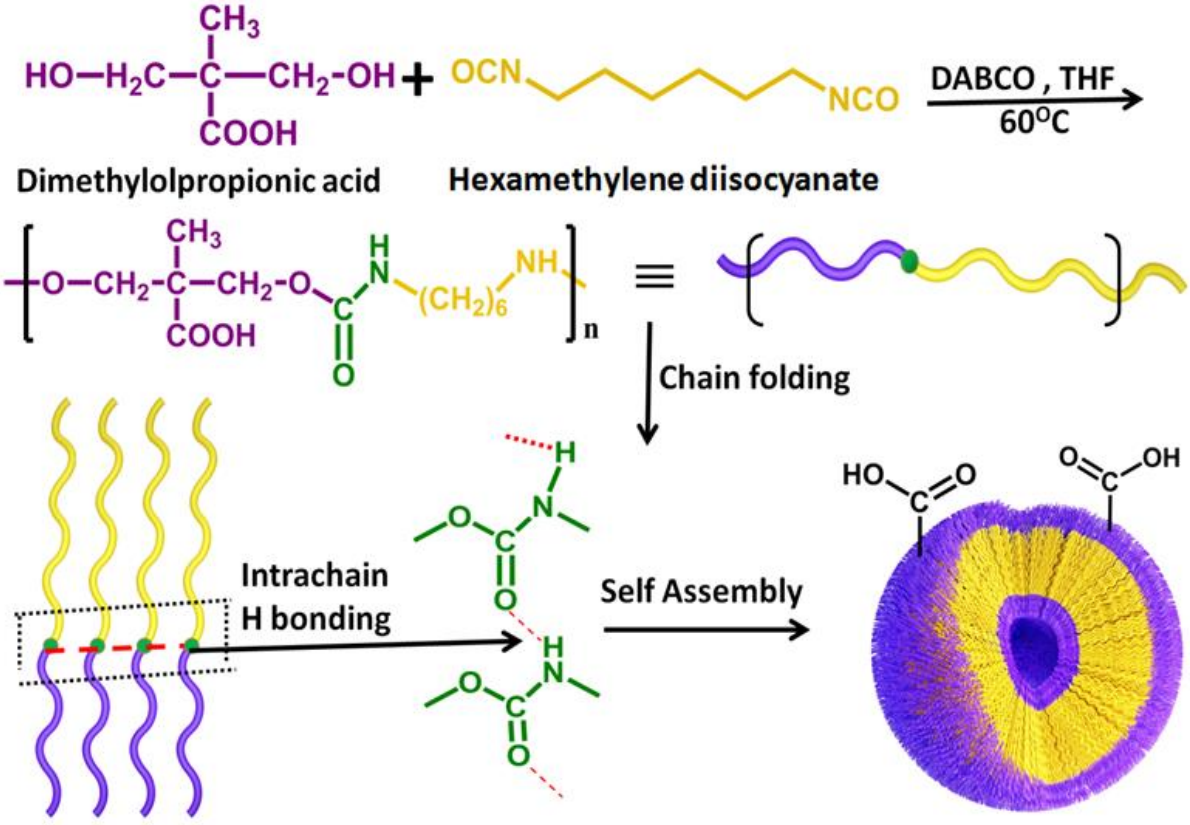
Reaction Conditions: Aryl halide (0.5 mmol), arylboronic acid (0.75 mmol), 1.0 mmol of Cs_2CO_3, 0.75 mol % of PdNPs@UCOF-SH, and solvent EtOH: H_2O (1:1) 5 mL. ^{a}Isolated Yield.

The halo-substituted and non-halo biaryl derivatives were obtained in good to excellent yields, within a shorter reaction time, avoiding the homocoupling of aryl boronic acid. Additionally, the catalyst is extremely stable, easily recyclable, and reusable. The pore-engineered COF-derived catalyst is selective and easily recycled up to 10 runs without significant loss of catalytic activity. This reveals the robust nature of the PdNPs@UCOF-SH catalyst and the sustainability of the process which opens a new frontier for several catalytic applications.

Chapter 4:

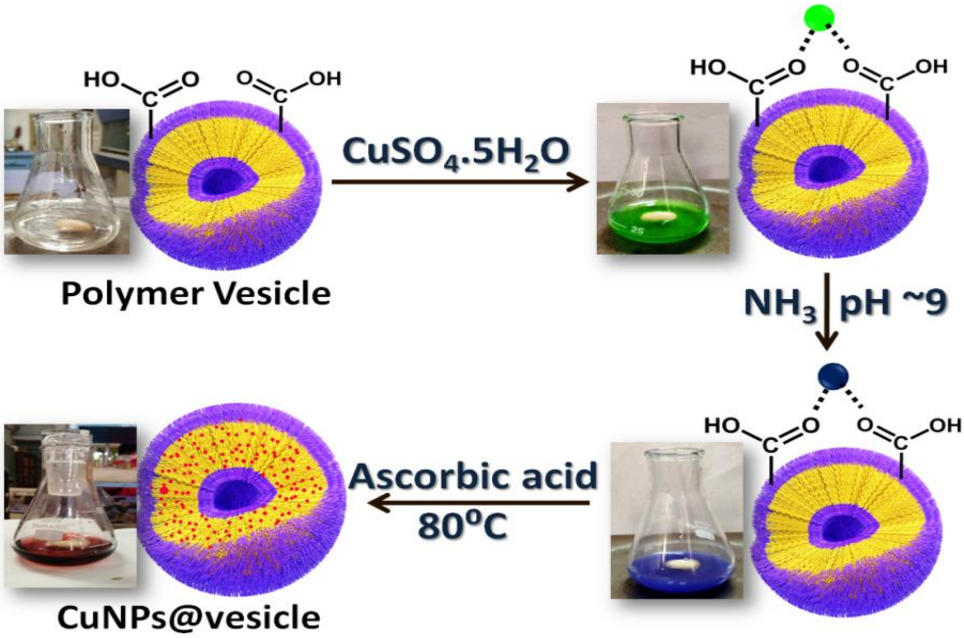
Copper nanoparticles loaded polymer vesicles as environmentally amicable nanoreactors: A sustainable approach for cascading synthesis of benzimidazole

This chapters discusses the synthesis of synthesis and characterization of Cu nanoparticle-loaded, surfactant-free metallovesicles (CuNPs@vesicles) as nanoreactors to produce benzimidazoles via cascade reaction.



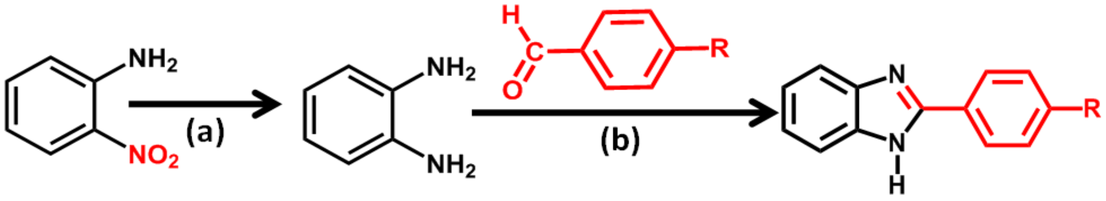
Scheme 4: Synthesis of amphiphilic DMPA-HMDI co-polymer and subsequent self-assembly into vesicle .

The vesicles exhibited uniform size distribution, spherical morphology, excellent stability, and efficient Cu loading. After synthesizing the polymer vesicles our efforts were directed towards loaded copper metal into polymer vesicles and subsequently reduce them inside the vesicles to metal nanoparticles to act as metallovesicle. The prepared metallovesicle was utilized as catalyst for the cascade reaction.



Scheme 5: Visual changes observed in the process of CuNPs@vesicles formation(i) bare vesicles (ii) binding of Cu^{2+} ions with vesicles (iii) Color change upon pH adjustment of the metal encapsulated vesicles (iv) reduction and formation of Cu Nanoparticles.

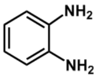
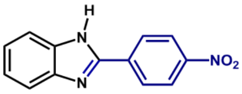
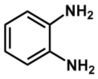
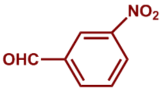
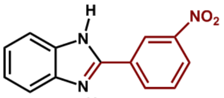
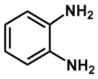
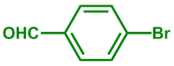
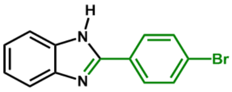
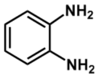
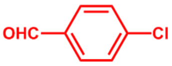
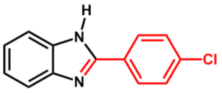
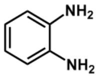
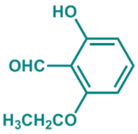
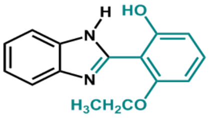
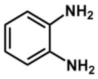
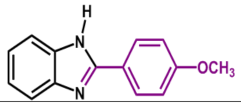
This strategy is unique for the fact that environmental contaminants like nitroaniline have been utilized as precursors and converted into fine chemicals of commercial significance via non-toxic intermediates. CuNPs@vesicles reduces 2-nitroaniline to o-phenylenediamine which further acts as a precursor for benzimidazole synthesis.



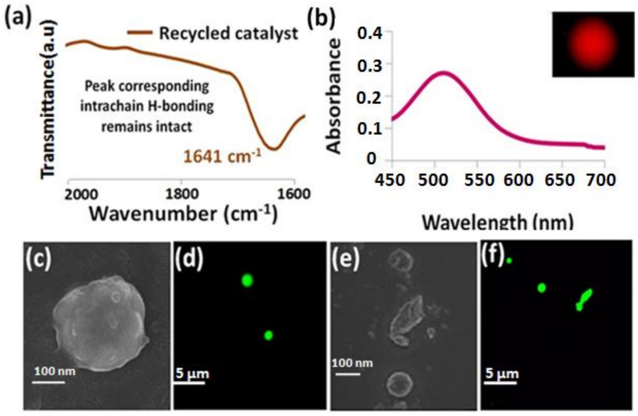
Scheme 6: CuNPs@vesicles catalyzed reactions for synthesis of benzimidazoles via cascading pathway. [Reaction conditions (a) catalyst 5 ml, $NaBH_4$, H_2O, 30 °C (b) catalyst 5 ml, H_2O, 30 °C]

Thus, the reaction occurs via a two-step cascade pathway comprising reduction and cross-coupling reactions in water. The preliminary studies suggest encouraging results for performing dehydrogenative coupling under relatively mild conditions using CuNPs@vesicles as a catalyst. All the products are obtained in good to excellent yield with facile catalyst regeneration and recyclability up to 5 cascading cycles.

Table 3: Substrate scope of reaction as per scheme 3 by using o-PDA and substituted aromatic aldehydes via reduction of 2-Nitroaniline

Sr.no	Diamine	Aromatic aldehyde	Product	Catalyst (ml)	Time (mins)	Yield[b] (%)	E-factor
1				5	30	90	0.11
2				5	40	86	0.16
3				5	60	88	0.14
4				5	45	85	0.18
5				5	70	84	0.18
6				5	60	84	0.19

Reaction conditions: o-phenylenediamine (1.0 mmol), aromatic aldehyde (1.0 mmol), CuNPs@vesicles (5 ml, 1440 ppm), water (15 ml), room temperature (30 ºC). [a] Isolated yield. Thus, the approach is environmentally benign, as the entire cascade of reactions proceeds in aqueous medium at ambient conditions.



Scheme 7: Characterization of the recycled catalyst (A) FT-IR, (B) UV-Visible, (C & E) FEG-SEM of 1st and 5th cycle, (D& F) florescence imaging of 1st and 5th cycle

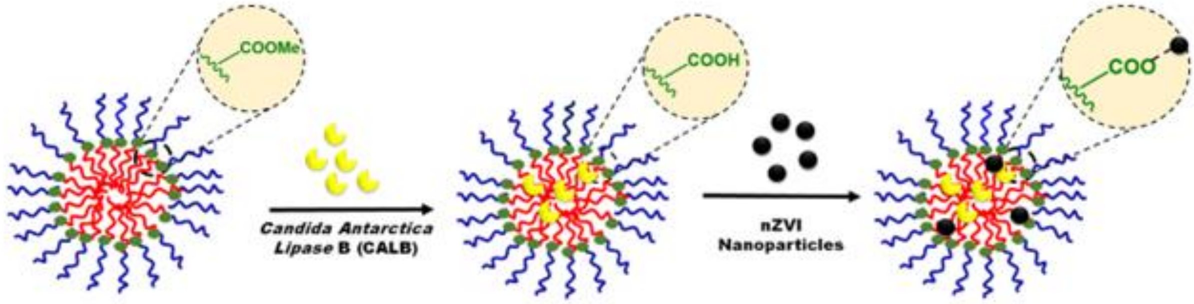
The important feature of regeneration and recyclability (upto 5 cascade cycles) can be attributed to the robust nature and stability of vesicular nanostructures.

Chapter 5:

Candida antarctica Lipase B and nZVI co-loaded bioinspired nanomicelles: A sustainable catalytic nanoreactor for cascade synthesis of p-aminophenol

This work reports a synthesis of a novel amphiphilic polymer by functionalizing tyrosine with polyethylene glycol and undecanoic acid.

The latter successfully self-assembled to nanomicelles with a low CMC value of 0.97 mg/L, which indicated the high stability of nanomicelles. These nanomicelles were employed for stabilizing the CALB enzyme and nZVI nanoparticles at a single platform in the hydrophobic core, to obtain catalytic nanoreactors.

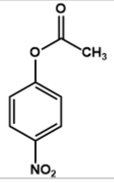
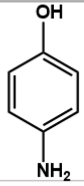
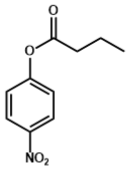
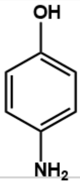
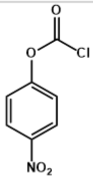
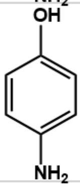
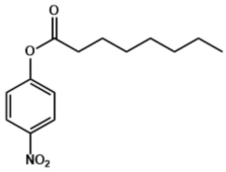
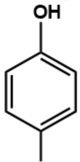
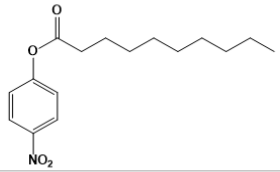
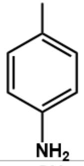
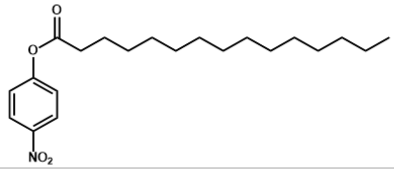
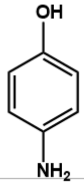


Scheme 8: Schematic representation of preparation of catalytic nanoreactors by loaded the *Candida antarctica* Lipase B enzyme and zerovalent iron nanoparticles in the nanomicelles derived from tyrosine derives amphiphilic polymer.

Inspired by the nanobiohybrid concept by Palomo *et.al*, we have prepared catalytic nanoreactors for the chemoenzymatic cascade reaction of p-nitrophenylesters to p-aminophenol using the rationally designed catalytic nanoreactors in water at ambient reaction conditions. To demonstrate the robust nature of the nanoreactors a series of p-nitrophenyl ester derivatives were employed as reactants for the cascade reactions. The corresponding p-aminophenol was obtained as a desired product under mild reaction conditions in reasonable reaction time.

Finally, the operational recyclability showed no significant loss in activity up to 5 consecutive cascade cycles of use at 35˚C. The easy magnetic recovery and reusability of the catalytic nanoreactors is critical for their application in scale-up processes.

Table 4: Substrate scope of the reaction under the optimized condition using nZVI-CALB@NM.

Sr.No.	Substrate	Product	Time (min)	%Conversion
1.			20	98
2.			22	96
3.			35	95
4.			43	96
5.			45	98
6.			50	99

Reaction conditions: Substrates (1 mM) Catalyst (2 mL, contains nZVI (18 wt%)), $NaBH_4$ (1.4 mM) at 35˚, % Conversion was calculated for the hydrogenation step using UV-Visible Spectrophotometry.

From this work, we envisage the enzymatic and heterogeneous catalysis can be combined in nanomicelles to create novel cascade industrial manufacturing processes. These findings also imply that similar results can be anticipated for other enzymatic processes and sequential cascade catalysis.

References-

1. W. Teng, J. Fan, W. Wang, N. Bai, R. Liu, Y. Liu, Y. Deng, B. Kong, J. Yang, D. Zhao, W. xian Zhang, *J. Mater. Chem. A*,2017,5, 4478–4485.
2. M. Sundarapandi, P. Viswanathan, S. Sivakumar, R. Ramaraj, *Langmuir*,2018,34,13897–13904.
3. T. Niwa, Y. Uetake, M. Isoda, T. Takimoto, M. Nakaoka, D. Hashizume, H. Sakurai and T. Hosoya, *Nat. Catal.*, 2021, **4**, 1080–1088.
4. K. Geng, T. He, R. Liu, S. Dalapati, K. T. Tan, Z. Li, S. Tao, Y. Gong, Q. Jiang and D. Jiang, *Chem. Rev.*, 2020, **120**, 8814–8933.
5. C. Xiong, H. Ning, G. Jia, X. Hong, X. Fei and J. Donglin, *Chem. Commun.*, 2014, **50**, 6161–6163.
6. T. Kundu, J. Wang, Y. Cheng, Y. Du, Y. Qian, G. Liu and D. Zhao, *Dalt. Trans.*, 2018, **47**, 13824–13829.
7. R. L. Wang, D. P. Li, L. J. Wang, X. Zhang, Z. Y. Zhou, J. L. Mu and Z. M. Su, *Dalt. Trans.*, 2019, **48**, 1051–1059.
8. Y. Jiang, C. Liu and A. Huang, *ACS Appl. Mater. Interfaces*, 2019, **11**, 32186–32191.
9. H. Sun, J. Jiang, Y. Xiao, J. Du, *ACS Appl. Mater. Interfaces* **10** (2018) 713–722.
10. Y. Zhu, L. Fan, B. Yang, J. Du, *ACS Nano* **8** (2014) 5022–5031.
11. Q. Guan, Q. Sun, L. Wen, Z. Zha, Y. Yang, Z. Wang, *Org. Biomol. Chem.* **16** (2018) 2088–2096.
12. N. Kaur, S. Kaur, G. Kaur, A. Bhalla, S. Srinivasan, G.R. Chaudhary, *J. Mater. Chem. A* **7** (2019) 17306–17314.
13. R.R. Thakore, B.S. Takale, G. Casotti, E.S. Gao, H.S. Jin, B.H. Lipshutz, *Org. Lett.* **22** (2020) 6324–6329.
14. P.S. Rathore, R. Patidar, T. Shripathi, S. Thakore, *Catal. Sci. Technol.* **5** (2015) 286–295.
15. Kozma, G.; Rónavári, A.; Kónya, Z.; Kukovecz, Á. *ACS Sustain. Chem. Eng.* 2016, ***4*** (1), 291–297.
16. Benavente, R.; Lopez-Tejedor, D.; Palomo, J. M. *Chem. Commun.* 2018, ***54*** (49), 6256–6259.
17. Lawin, L. R.; Fife, W. K.; Tian, C. X. *Langmuir* 2000, ***16*** (8), 3583–3587.
18. Tao, R.; Gao, M.; Liu, F.; Guo, X.; Fan, A.; Ding, D.; Kong, D.; Wang, Z.; Zhao, Y. *ACS Appl. Mater. Interfaces.* 2018, ***10*** (26), 21836–21846.
19. Imai, S.; Takenaka, M.; Sawamoto, M.; Terashima, T. *J. Am. Chem. Soc.* 2019, ***141*** (1), 511–519.
20. Aluri, R.; Saxena, S.; Joshi, D. C.; Jayakannan, *Biomacromolecules* **2018**, *19* (6), 2166–2181.

Falguni Shukla
Research Student

Dr. Sonal Thakore
Research Supervisor