A

Synopsis Submitted to

The Maharaja Sayajirao University of Baroda

For the Degree of

Doctor of Philosophy

in

Applied Chemistry

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Subject	**:**	**Applied Chemistry**
Faculty	**:**	**Technology & Engineering**
Title of Thesis	**:**	**Silica-based Porous Solid Supports: Towards the Development of Enantioselective Chiral Catalysts**
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Registration Number	**:**	**FOTE/1034**
Date of Registration	**:**	**30/12/2020**
Place of the Work	**:**	**Applied Chemistry Department** **Faculty of Technology & Engineering,** **The M. S. University of Baroda** **Vadodara – 390001, Gujarat (India)**

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Introduction

The demand for nonracemic chiral compounds has significant value in the development of effective methods to produce enantiomerically enriched products, benefiting both industry and academia. Catalysis, an essential aspect of Green Chemistry, has replaced traditional stoichiometric techniques with environmentally friendly alternatives.[1] Asymmetric catalysis, known for its chiral selectivity and ecological considerations, enables complete conversion of reactants to products under mild conditions. Homogeneous catalysts are highly valued for their reactivity, selectivity, and low loading requirements. However, they suffer from metal contamination and limited reusability, causing economic losses and environmental issues.[2] Nevertheless, the availability of recyclable chiral catalysts remains a critical concern, especially for large-scale reactions. The loss of precious metal catalysts in homogeneous systems poses economic burdens due to the difficulty in recovery. Metal leaching further hampers the production of fine chemicals and pharmaceuticals.[3] To overcome these challenges, significant progress has been made in homogenous chiral catalysis, leading to the development of various chiral ligands and metal coordination compounds for organic transformations.[4,5]

Heterogeneous asymmetric catalysis has emerged as a promising solution. It utilizes specially designed heterogeneous metal catalysts and immobilized homogeneous asymmetric catalysts.[6-8] Immobilizing a homogeneous catalyst into a heterogeneous form presents challenges, such as reduced activity and enantioselectivity due to limited access to active sites and interactions with the support.[9] To address these issues, an appropriate linker length allows the scaffold to move freely between the liquid reaction phase and the surface. Recoverable catalysts require robust support surface layers and active channels to maintain catalytic properties during reuse. Compatibility and stability of the catalytic scaffold, linker, and support with the solvent are crucial to prevent metal and/or scaffold leaching.[10-12] Additionally, chemical, thermal, and mechanical stabilities of the linker and support materials are necessary for enduring process parameters. The choice of a suitable heterogeneous support material is crucial, necessitating physical, chemical, and thermal resistance, synthetic durability, and uniform behaviour. Simple recovery methods, such as filtering or extraction, are desirable. Common supports include cross-linked polymers, ordered silicas, and clays, while immobilization techniques involve metal coordination, ligand grafting, electrostatic interactions, microencapsulation, and ion exchange.[13,14]

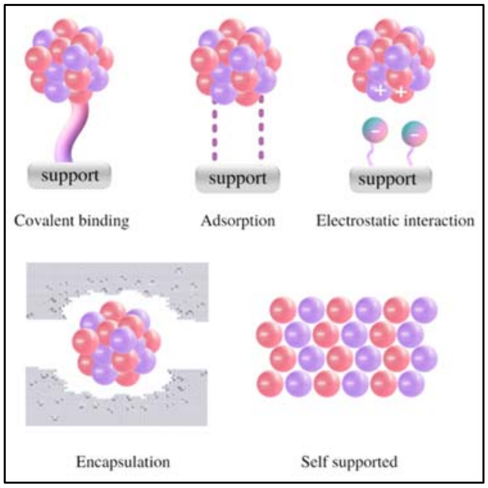

Figure 1 Various strategies for the confinement of homogeneous chiral catalysts

Scope of the research study

In the present era, the field of supported heterogeneous catalysis has attracted substantial interest in cutting-edge scientific and technological research. This field presents diverse applications in various industrially significant catalytic reactions, leading to enhanced outcomes, improved stability, high conversion rates, and desired selectivity. Literature scanning reveals the existence of various entrenched heterogeneous systems, including mesoporous titanosilicate, superparamagnetic mesoporous bimetallic oxides, graphene oxide, nanocrystalline, acrylic resin immobilized lipase, chitosan hydrogel, ceria-zirconia, and ZIF-8. [15,16] However, these solid catalysts suffer from several drawbacks, including low selectivity, high operating temperatures, long reaction times, and labor-intensive work-up methods. Many heterogeneous catalysts exhibit both high selectivity and activity, enabling the production of valuable chemicals from simple and cost-effective substrates. These catalysts operate with a high atom economy, ensuring minimal generation of residues and reducing the environmental impact. The primary goal of this research is to develop a range of chiral scaffolds that are anchored onto silica-based supports. These scaffolds will be utilized in sustainable chemical processes, promoting environmentally friendly practices. The present work focuses on synthesizing and characterizing innovative scaffold structures, such as proline, binol, salen, and thiourea, embedded onto silica-based supports, namely L-proline-(3°amine)-*f*-SiO_2 and Ru-BINOL-AP@MSNs. The synthesized catalysts were validated using a range of physicochemical techniques, including elemental analysis, ICP-AES, (^{13}C CP MAS NMR, FT-IR, Raman) spectral studies, HRTEMs, FE-SEMs, BET, XPS, thermal analysis, and XRD patterns. These techniques provided valuable insights into the structural and chemical properties of the catalysts. In order to accomplish our research objectives, we assessed the catalytic performance of the synthesized catalysts in industrially significant organic transformations. These include asymmetric aldol, asymmetric hydrogenation, Biginelli coupling, and Strecker reactions. We optimized various parameters such as catalyst loading, reaction time, temperature, and solvent choice to enhance efficiency. By fine-tuning these factors, we achieved improved yields and selectivity in the desired reactions. Notably, the organic products formed in these catalytic reactions play a crucial role as intermediates in the pharmaceutical industry. They serve as building blocks for synthesizing complex pharmaceutical compounds, making a significant impact on the production of valuable drugs and contributing to advancements in medicine and healthcare.

Summary of Research Findings

The thesis comprises seven chapters, which are outlined as follows:

Chapter 1: Introduction; Chapter 2: Preparation, characterization, and catalytic performance of L-proline-(3°amine)-*f*-SiO_2 in asymmetric aldol reaction; Chapter 3: Preparation, characterization, and catalytic performance of Ru-BINOL-AP@MSNs in asymmetric hydrogenation reaction; Chapter 4: Preparation, characterization, and catalytic performance of encapsulated chiral Cu(II) salen complex in asymmetric Biginelli reaction; Chapter 5: Preparation, characterization, and catalytic performance of encapsulated chiral Zn(II) salen complex in asymmetric Mannich reaction; Chapter 6: Preparation, characterization, and catalytic performance of MMT-silica-GO-CTU (where MMT = montmorillonite, GO = graphene oxide, CTU = chiral thiourea-based moiety) in asymmetric Strecker reaction; Chapter 7: Summary and Conclusions.

Chapter 1

This chapter in the thesis offers a comprehensive overview that includes a general introduction, a brief historical background, fundamental aspects, and the current state of asymmetric catalysts. It provides insights into various types of catalysts, emphasizing their advantages, disadvantages, and the emergence of new materials in the context of industrial applications. The heterogenization of homogeneous catalysts using various solid supports is explored, with a specific focus on the chosen silica-based support for this work.

Chapter 2

This chapter describes a ground-breaking strategy in the synthesis of *L*-proline chiral scaffold tethered onto the silica matrix i.e., *L*-proline-(3°amine)-*f*-SiO_2 via the reaction between *L*- proline methyl ester and N-methyl aminopropyl silica with absolutely no use of protecting/ deprotecting groups. The as-synthesized catalyst was well corroborated through various physicochemical techniques such as ^{13}C CP MAS NMR, X-ray diffraction (XRD), HRTEM, N_2 adsorption− desorption isotherms, elemental analysis and FT-IR spectral studies. Emphatically, *L*-proline-(3°amine)-*f*-SiO_2 significantly promoted an asymmetric aldol reaction under ambient conditions with no use of redundant organic solvent, bestowing unprecedented activity with good conversion and excellent enantioselectivity (ee) of *S*-isomer. Moreover, the as synthesized catalyst was effortlessly recycled seven times with absolutely zero loss of activity as well.

Chapter 3

The details concerning greener protocol for a Cu(II)–salen complex encapsulated in MWW-framework as an efficient chiral organocatalyst was developed for the synthesis of 3,4-dihydropyrimidin-2-(1*H*)-one (DHPMs) derivatives via an asymmetric pathway. In order to confirm its structural properties, single-crystal X-ray diffraction, powder XRD, BET, XPS, FE-SEM, EDX, UV-Vis, and FTIR spectra were used. Using computer-assisted DFT calculations, the Cu(II)–salen complex has been fine-tuned to fit into the pocket of the porous MWW support while keeping its chirality. This organocatalyst was shown to be a potent catalyst for the formation of the desired DHPMs product under short reaction times. Furthermore, this green protocol allows rapid and simple isolation of active MWW-trapped Cu(II)–salen scaffolds and its reusability good numbers of runs without losing much of its activity have examined and derivative are included in this chapter.

Chapter 4

The chapter describes an unprecedented blueprint for the chiral (*S*)-1,1-Bi-2-naphthol ligand (BINOL) immobilized on amine functionalized mesoporous silica nanoparticles (MSNs) via a linker, which is then converted into a ruthenium complex, i.e., Ru-BINOL-AP@MSNs (where AP = (3-aminopropyl)trimethoxysilane), without the use of deprotecting or protecting groups. Using a variety of techniques, such as FTIR, N_2 adsorption–desorption isotherms, solid-state ^{13}C CP MAS NMR, powder XRD, FESEM, HRTEM, XPS, and thermogravimetric analysis, the as-synthesized catalyst was persuasively verified. Asymmetric transformations of enantiomerically enriched chiral alcohols can be achieved with the aforesaid active catalytic precursors, making the proposed method even more appealing. During the asymmetric hydrogenation reaction, the Ru-BINOL-AP@MSNs catalyst proved to be catalytically competent, leading to a good conversion with an excellent enantioselectivity of the *R*-isomer. Furthermore, the synthesized catalyst was capable of being recycled and only a minute loss of its effectiveness, thereby reducing solvent waste and precious metal or ligand losses.

Chapter 5

The chapter deals with a greener decorum for synthesizing distinctive Zn(II)-Salen ligand encapsulated in MWW host as a heterogeneous chiral catalyst, i.e., Zn(II)-Salen@MWW. A variety of techniques were used to substantiate the chiral Zn(II) ligand encapsulation, including FTIR, FESEM, EDX, XRD, BET, and XPS. Using an unpretentious ultrasonic approach, the synthesized catalyst could effectively generate chiral β-amino carbonyl compounds at room temperature under solvent-free condition. There are multiple advantages to use this protocol, including a green and efficient catalyst, a simple set-up procedure, effortless separation, and the ability to reprocess up to five runs of the chiral Zn(II)-Salen@MWW catalyst.

Chapter 6

This chapter delineates fabrication of a novel composite material consisting of montmorillonite, silica and graphene oxide (MMT-silica-GO), encapsulated with chiral thiourea-based moiety (CTU), was synthesized via a sol-gel method. The resulting composite material was characterized using various techniques, including such as (FT-IR and Raman) spectral studies, BET, SAXS, thermogravimetric analysis, XPS, HRTEM and XRD patterns are included in this chapter. The catalytic performance of the composite material was evaluated for the Strecker reaction and monitored recyclability of the as-prepared catalyst as well.

Chapter 7

This chapter offers a comprehensive summary of our systematic investigation into the development and optimization of chiral catalysts for relevant catalytic reactions. It presents a synthesis of our findings, including key outcomes, and concludes with a brief discussion on potential future research directions for further exploration in related areas.

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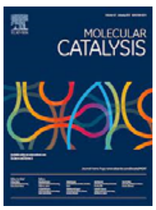
List of Patents & Publications (Related to Thesis)

1	INTELLECTUAL PROPERTY INDIA PATENTS | DESIGNS | TRADE MARKS GEOGRAPHICAL INDICATIONS	METHOD FOR SYNTHESIS OF *L*-PROLINE GRAFTED ON SILICA SUPPORTED CATALYST AND ITS USE IN ASYMMETRIC ALDOL REACTION **Pratikkumar Lakhani**, Chetan K. Modi **Application number:** 202121048846 **Publication date:** 07/01/2022

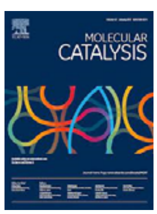
2		BINOL-RU GRAFTED ONTO A SILICA SUPPORTED CATALYST: METHOD OF SYNTHESIS AND ITS USE IN ASYMMETRIC HYDROGENATION REACTION **Pratikkumar Lakhani**, Chetan K. Modi **Application number:** 202221051932 **Publication date:** 07/10/2022
3		A TAILORED MONTMORILLONITE-SILICA-GRAPHENE OXIDE-BASED COMPOSITE FOR ENHANCING CHIRAL CATALYTIC APPLICATION **Pratikkumar Lakhani**, Chetan K. Modi **Application number:** 202321041553 **Filed date:** 19/06/2023
4		Spick-and-span protocol for designing of silica-supported enantioselective organocatalyst for the asymmetric aldol reaction **Pratikkumar Lakhani**, Chetan K. Modis ***Mol. Catal.*** *2022, 525, 112359* **DOI: 10.1016/j.mcat.2022.112359**
5		Asymmetric Hydrogenation using Covalently Immobilized Ru-BINOL-AP@MSNs Catalyst **Pratikkumar Lakhani**, Chetan K. Modi ***New J. Chem.*** *2023, 47, 8767-8775* **DOI: 10.1039/D3NJ00495C**
6		DFT stimulation and experimental insights of chiral Cu(II)-salen scaffold within the pocket of MWW-zeolite and its catalytic study **Pratikkumar Lakhani**, Darshil Chodvadiya, Prafulla K. Jha, Vivek Kumar Gupta, Damian Trzybiński, Krzysztof Wozniak, Krzysztof Kurzydłowski, U. K. Goutam, Himanshu Srivastava, Chetan K. Modi ***Phys. Chem. Chem. Phys.*** *2023, 25, 14374-14386* **DOI: 10.1039/D3CP00857F**

7		Sustainable approach for the synthesis of Chiral β-aminoketones using Encapsulated Chiral Zn(II)-Salen complex **Pratikkumar Lakhani**, Sanjeev Kane, Himanshu Srivastava, U. K. Goutam, Chetan K. Modi ***RSC Sustain.*** (Under Communication)

Publication (Non-related to Thesis)

	Harnessing Bimetallic Nanoparticles on Ionic Liquid Functionalized Silica for Enhanced Catalytic Performance Rithik Parmar, **Pratikkumar Lakhani,** Dhavalkumar Bhanderi, Sanjeev Kane, U.K. Goutam, Chetan Modi ***New J. Chem.*** (Under Communication)

Review Article

	Shaping Enantiochemistry: Recent Advances in Enantioselective Reactions via Heterogeneous Chiral Catalysis **Pratikkumar Lakhani**, Chetan K. Modi* ***Mol. Catal.*** *2023, Accepted (In press)*

Work presented in Conferences/ Seminars/ Workshops

1		Economical and sustainable approach for the synthesis of supported L-proline catalyst for asymmetric aldol reaction **Pratikkumar Lakhani**, Chetan K. Modi* **National Conference** of Chemical Research Society of India 28th National Symposium in Chemistry (CRSI NSC-28), 25-27th March 2022 at IIT Guwahati. **Presented Session: POSTER**

2		Catalytic Behaviour of Alkali Treated Meso- and Microporous Silica-based Materials **Pratikkumar Lakhani**, Niraj V. Rana, Chetan K. Modi* **National Conference** of DAE-BRNS 9th Interdisciplinary Symposium on Materials Chemistry (ISMC-2022) Chemistry Division, Bhabha Atomic Research Centre, and Society for Materials Chemistry, 7-10th December 2022 at Mumbai. **Presented Session: POSTER**
3		Development of BINOL-Ru Catalyst Covalently Immobilized on MSNs and Their Application in Asymmetric Hydrogenation **Pratikkumar Lakhani**, Chetan K. Modi* **National conference** of Chemical Research Society of India 30th National Symposium in Chemistry (CRSI NSC-30), 2-5th February 2023 at JNU New Delhi. **Presented Session: POSTER**
4		Strategic Design of Silica-supported Enantioselective Organocatalyst for Asymmetric Aldol Reaction: An Economical and Sustainable Approach **Pratikkumar Lakhani**, Chetan K. Modi* **International conference** of 3rd Commonwealth Chemistry Posters. Royal Society of Chemistry, 28-29th September 2022 **Presented Session: POSTER**
5		Biologically Potent 3,4-dihydropyrimidine-2-(1*H*)-one Derivatives Synthesized Through Chiral Cu(II)-salen Encapsulated in MWW **Pratikkumar Lakhani**, Chetan K. Modi* **International conference** on 7th International Conference on Nanoscience and Nanotechnology – ICONN 2023 (Virtual Conference) Organised by SRM Institute of Science & Technology, Kattankulathur, Tamil Nadu. **Presented Session: POSTER**

Achievement:

Received **Best Poster Presentation Award** at the **7th International Conference on Advanced Nanoscience and Nanotechnology – (ICONN 2023)**, SRM Institute of Science & Technology, Kattankulathur, Tamil Nadu, India on 27-29th March 2023.

Participated:		
6		Training Program for Developing Skills on **“Advancing Knowledge from Quantum mechanical Perspectives in materials science”** Attended one-day workshop organised on April 15th,2023 at Department of Physics, The Maharaja Sayajirao University of Baroda, Vadodara.
7		STEM Early Researchers by a Ph.D. student of Inspiring India in Research, Innovation, and STEM Education (iRISE) on the theme **“IP and Knowledge Management”** on 28th September 2022 at IISER Pune.
8		Synergistic Training Program Utilizing the Scientific and Technological Infrastructure (STUTI-21), A One-Week Training Program on R&D Equipment on the theme “Modern Spectroscopic, Thermal and Microscopic Techniques" on 21-27th September 2022 at Defence Institute of Advanced Technology, Pune, MH.
9		Synergistic Training Program Utilizing the Scientific and Technological Infrastructure (STUTI-21), A One-Week Training Program on R&D Equipment on the theme “ADVANCES IN CHARACTERIZATION OF MATERIALS" on 12-18th September 2022 at Applied Physics Department, The Maharaja Sayajirao University of Baroda, Vadodara, Gujarat.
10		1st International Conference on Emerging Porous Materials (ePorMat-2021) A Virtual Conference held on 29-30th July, 2021 NISER Bhubaneswar in association with VIT Vellore and IIT Jammu, India.

Pratikkumar C. Lakhani
(Research Scholar)

Dr. Chetan K. Modi
Guide