Executive Summary of the Ph.D. thesis Entitled

“Silica-based Porous Solid Supports: Towards the Development of Enantioselective Chiral Catalysts”

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Chapter 6 ***Enhanced Thermal Stability and Catalytic Performance of Montmorillonite-Silica-Graphene Oxide Composite Incorporating with Chiral Thiourea for the Strecker Reaction*** **127-159**

In the realm of modern organic chemistry, the art of crafting complex molecules with precision and expertise has garnered profound attention. Asymmetric synthesis, a captivating and intricate facet of chemical synthesis, holds the key to manipulating molecules in a profoundly selective manner, bestowing upon them unique three-dimensional structures and, consequently, distinct properties. This profound scientific discipline, sometimes referred to as enantioselective synthesis, stands as a testament to the astonishing intricacies that govern the interactions between matter on a molecular scale.[1,2] At its core, asymmetric synthesis is a branch of chemical synthesis that is dedicated to the construction of molecules possessing chirality – a property intrinsic to many organic compounds that results in their mirror-image isomers, known as enantiomers (*Figure 1*).

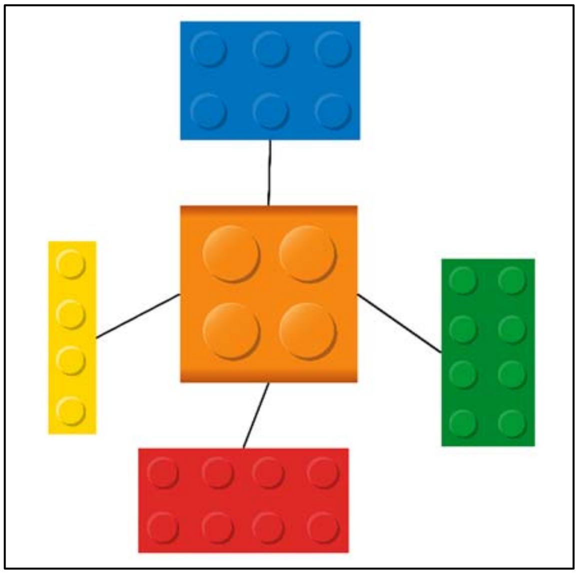

Figure 1 How does a chiral molecule function?

At the heart of asymmetric catalysis lies a quest to harness chirality's exquisite intricacies to create molecules of distinct handedness, where a single enantiomer takes center stage, while its mirror image counterpart languishes in the wings. This pursuit is fueled by the realization that these enantiomers, though near-identical in composition, can possess dramatically different chemical, physical, and biological properties. Asymmetric catalysis elevates this endeavor to new heights, employing catalysts as chemical conductors that guide reactions toward a preferred enantiomer, akin to a maestro skillfully directing an orchestra.[3,4] The virtuosity of asymmetric catalysis is elegantly showcased through the utilization of privileged chiral ligands.

Privileged chiral ligands possess a unique blend of structural features that render them exceptionally adept at steering reactions towards desired enantiomers, effectively serving as guiding stars in the constellation of asymmetric catalysis.[5] Within the realm of privileged chiral ligands, diverse structural motifs have emerged as focal points of exploration. From the salen and bi-2-naphthol-based ligands, which have orchestrated transformations through transition metal catalysts with unparalleled finesse, to the proline and thiourea-based ligands, which have conducted symphonies of organocatalysis with exquisite control, these privileged architectures exemplify the marriage of creativity and functionality.

At its core, asymmetric homogeneous catalysis employs both transition metal complexes and organocatalysts as the catalysts of choice. These chiral agents interact harmoniously with reactants, choreographing a precise dance of molecular interactions that guides the synthesis of specific mirror-image molecules. Transition metal complexes, often adorned with intricate chiral ligands, play the role of conductors in this intricate symphony. These ligands meticulously orchestrate the trajectory of reactants, ensuring that they align in a manner that leads to the desired enantiomeric outcome. On the other hand, organocatalysts wield their chiral influence through non-covalent interactions like hydrogen bonding, enacting their role as artistic directors of diverse chemical transformations.[6]

While the elegance of asymmetric homogeneous catalysis is undeniable, challenges abound. Catalyst stability and selectivity form a dynamic duet, each influencing the other. Ensuring the recovery and recycling of precious catalysts presents logistical intricacies. Moreover, orchestrating a harmonious interplay of catalysts, ligands, and reactants can be akin to conducting a complex symphony, requiring meticulous coordination.[7–10]

Asymmetric heterogeneous catalysis stands as a captivating branch of modern chemistry, offering a distinctive approach to crafting chiral molecules with precise three-dimensional arrangements. This field harnesses solid catalysts, each possessing a carefully designed chiral environment, to orchestrate enantioselective transformations. In contrast to its homogeneous counterpart, asymmetric heterogeneous catalysis involves catalysts existing as solids while the reactants remain in liquid or gaseous phases. These solid catalysts, often derived from modified or immobilized chiral homogeneous catalysts, interact with substrates at their surface, guiding reactions towards producing specific enantiomers. Solid catalysts in asymmetric heterogeneous catalysis showcase a fascinating array of surface properties that facilitate chirality-induced selectivity. Immobilized chiral ligands on the catalyst surface establish a platform for strategic interactions with reactants, enabling the creation of chiral transition states that favor desired enantiomeric outcomes.[11–15]

This thesis embarks on an exploration of the captivating work of asymmetric heterogeneous catalysis, delving into the arrangement of chiral surfaces, the intricacies of catalyst design, and the mechanistic tones that underscore enantioselective transformations.

Brief Research Methodologies

In this, it is noted that the challenging task of separating the catalyst from the reaction medium in a way that is both simple and affordable is a significant barrier to the commercial utilization of chiral homogeneous catalysis. One of the most methodical solutions to this problem is the confinement of the catalyst-active substance on a hard support.[16] Many researchers have offered alternative techniques for immobilizing chiral compounds. Based on the catalyst-solid support interaction, covalent binding, electrostatic interaction, adsorption, and encapsulation are four key methods for immobilizing homogeneous catalysts as depicted in *Figure 2*

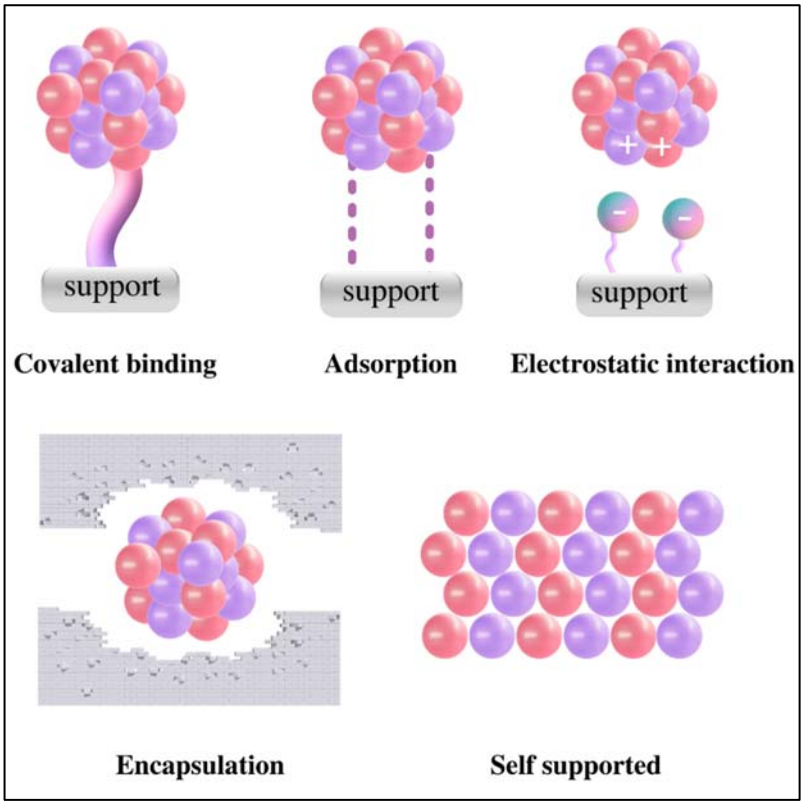

Figure 2 Various tactics for the confinement of homogeneous chiral catalysts.

In the wide-ranging field of heterogeneous asymmetric catalysis research, the use of inorganic support in the sketching of entrapped catalysts favored reusability, and the potential application of this strategy is growing. In enabling easy catalyst reuse, the heterogenization of chiral catalysts onto inorganic materials also significantly improves the catalytic performances (activity, stability, and enantioselectivity), mostly as a result of site isolation and confinement effects.

In the realm of catalysis, where molecular transformations are orchestrated with finesse, catalyst supports play an instrumental role in shaping the performance and efficacy of catalytic systems. Among these, porous silica materials stand as architecturally exquisite platforms, poised at the intersection of structural versatility and catalytic prowess. This thesis embarks on a profound exploration into the multifaceted realm of porous silica materials as catalyst supports, delving into their design, impact on catalytic efficiency, and their role in tailoring selectivity across diverse reactions. At the heart of porous silica materials lies a complex network of interconnected pores and channels, akin to a scaffold that cradles catalytic species. This structural intricacy, reminiscent of an artful framework, provides a high surface area and a three-dimensional milieu for the deposition and immobilization of catalytically active species. The porous domains not only serve as repositories for active counterparts but also influence the accessibility of reactants to the catalytic sites, thereby orchestrating a delicate balance between reactivity and selectivity.[17–19]

This thesis presents an innovative approach to address these challenges by developing a range of chiral scaffold structures anchored onto silica-based supports. These chiral scaffolds, including *L*-Proline, *S*-BINOL, Salen, and Thiourea, were synthesized and characterized extensively, utilizing various physicochemical techniques. These techniques provided invaluable insights into the structural and chemical properties of the catalysts. The primary objective of this research was to assess the catalytic performance of the synthesized catalysts in industrially significant organic transformations, including asymmetric aldol, asymmetric hydrogenation, Biginelli coupling, chiral β-aminoketones synthesis and Strecker reactions. Parameters such as catalyst loading, reaction time, and temperature were optimized to enhance catalytic efficiency, resulting in improved yields and selectivity. Importantly, the organic products generated in these reactions have a crucial role in pharmaceutical intermediate synthesis, contributing significantly to the production of valuable drugs and advancements in the field of medicine and healthcare. This research covers the way for more sustainable and environmentally friendly practices in the field of heterogeneous catalysis. The thesis comprises seven chapters, which are outlined as follows:

1) Provides a foundational introduction to the field of asymmetric catalysts in **Chapter 1**. It outlines the historical context, fundamental aspects, and the current state of these catalysts, emphasizing their types, advantages, disadvantages, and their applications in industrial contexts. It also delves into the heterogenization of homogeneous catalysts using solid supports, with a specific focus on silica-based supports.

2) In **Chapter 2** presents a pioneering approach for synthesizing L-proline chiral scaffolds tethered onto silica, *L*-proline-(3°amine)-*f*-SiO_2, without the use of protecting/deprotecting groups. The chapter includes the characterization of the catalyst through various physicochemical techniques and highlights its exceptional performance in promoting an asymmetric aldol reaction under ambient conditions, along with remarkable recyclability.

3) In **Chapter 3** shown the development of a greener protocol for a Cu(II)-salen complex encapsulated in an MWW-framework for asymmetric synthesis of 3,4-dihydropyrimidin-2-(1*H*)-one (DHPMs) derivatives. The structural properties are confirmed through various techniques, and the chapter explores the catalyst's efficiency, reusability, and examination of derivatives.

4) In **Chapter 4** introduces a novel approach for immobilizing the (*S*)-1,1-Bi-2-naphthol ligand (BINOL) on amine-functionalized mesoporous silica nanoparticles (MSNs), forming Ru-BINOL-AP@MSNs. The chapter includes extensive characterization of the catalyst and demonstrates its effectiveness in asymmetric transformations of chiral alcohols, specifically in asymmetric hydrogenation, with high enantioselectivity and recyclability.

5) In **Chapter 5** discusses the synthesis of a Zn(II)-Salen ligand encapsulated in an MWW host, Zn(II)-Salen@MWW, as a heterogeneous chiral catalyst. The chapter examines the catalyst's character through various techniques and highlights its ability to generate chiral β-amino carbonyl compounds under green, solvent-free conditions, with several runs of reusability.

6) In **Chapter 6** present the fabrication of a composite material, MMT-silica-GO, encapsulated with a chiral thiourea-based moiety (CTU). Characterization techniques are used to verify the composite material, and its catalytic performance is evaluated for the Strecker reaction, including the recyclability of the catalyst.

7) In **Chapter 7** provides a comprehensive summary of the research, highlighting key findings and outcomes from the systematic investigation of chiral catalysts. It concludes by

discussing potential future research directions in related areas, offering insights into the possibilities for further exploration.

Key Findings:

The chiral scaffold structures anchored onto silica-based supports is successfully used for the catalytic activity and for future applications is provided. The thesis proposes innovative approach to address these challenges by developing a range of chiral scaffold structures to obtain desired catalyst for specific catalytic applications.

Conclusion:

In the pursuit of unraveling the intricate world of porous silica materials as catalyst supports, this thesis has embarked on a comprehensive journey through seven illuminating chapters. The work of catalysis conducted on these architecturally diverse platforms has been explored, shedding light on their structural nuances, synthesis strategies, and catalytic prowess, showcasing their far-reaching impacts from fine chemical synthesis to industrial processes. Each chapter paints a vivid panorama of their catalytic innovation and role in sustainable chemical transformations. These materials are clearly pivotal in ushering in an era of selective and sustainable chemistry.

Recommendation and Suggestions:

This summary indicates the potential of heterogeneous chiral catalysis to greatly influence the academia and industrial research on chiral compounds. Several noteworthy instances have showcased the importance of solid support surfaces and pores. However, there remains a considerable need to enhance the enantioselectivity, activity, and stability of most heterogeneous chiral catalysts before their extensive integration into the industrial production of chiral compounds.

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