SYNOPSIS

Oleochemicals based L-proline Derivatives as Organocatalysts: Their Synthesis, Characterization and Applications in Asymmetric Organic Transformations

Submitted to

The Maharaja Sayajirao University of Baroda

For the degree of

Doctor of Philosophy

In

Chemistry

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Chapter 1

Introduction: L-Proline and Oleochemicals – An Important Renewable Feedstock

Globally there are challenges to face shortage of the raw materials from petroleum-based products due to depletion of non-renewable sources and its adverse effect on the environment as well. Now most of the research focused on sustainable approaches. In alignment of that, we tried to develop some catalysts from renewable sources. L-Proline is the versatile green sourced organocatalyst, but it needs to modify for heterogeneous system, especially for aqueous reaction conditions. Commonly, it modified with the petroleum based organic bulky reagents by multistep processes to achieve steric environment in the catalytic molecule. Our strategy is to replace this petroleum based organic reagents with the sustainable solutions (like oleochemicals) with fulfilling the purpose of heterogeneity for aqueous condition as well as steric environment for better enantio-selectivity. For sustainable solution, biomass is one of the sustainable sources for chemicals and fuels. Oleochemicals (fatty acids, fatty alcohols, fatty amines, fatty esters, glycerine etc.) derived from plants and animals. They are sustainable building blocks for a large variety of chemicals that can applied as high value starting materials in various industrial fields such as food, pharmaceuticals, cosmetics, bio-refineries, plastics, and many others.

Chapter 2

FA-L-proline catalyzed Asymmetric Direct Aldol reaction in aqueous system: Molecular Conformations Affect Chiral Induction

We have demonstrated that chiral induction in the Aldol product is possible by generating an enzyme-like cavity in molecular framework of the amphiphilic catalyst. The esters of *trans*-4-hydroxy-L-proline and long chain fatty acids have been synthesized by *O*-acylation. Synthesized molecules used as organocatalysts for asymmetric direct Aldol reaction between 4-nitrobenzaldehyde and cyclohexanone. The molecular framework of the catalyst not only induces the amphiphilicity but also acquires specific conformation leads to formation of catalytic cavity facilitating stereo-induction in the model Aldol product. Systematic addition of olefinic bonds in the long hydrocarbon chain makes this cavity more robust stabilizing transition state of the Aldol product. By proper tuning of the water content and % loading of the catalyst in Aldol reaction, o/w or w/o type emulsion was formed due to aggregation of catalyst molecules. Performance based evaluation of catalytic activity suggests that Aldol reaction proceeds with ~ 99% yield, 84% dr and 98% ee in presence of 10 mole% catalyst (having three π bonds), in an o/w emulsion (85 equiv. of water) within 12 h. The stereoselectivity of the catalyst is maintained up to 2.5 mole% loading. The high stereoselectivity of the Aldol reaction maintained even on increasing the amount of water to 300 equiv. A plausible reason has been proposed for retaining the high stereoselectivity and corroborated by computational analysis.

Chapter 3

FA-L-Proline catalyzed One-pot Asymmetric Direct Mannich reaction: Emulsion droplet as a Micro-reactor

We have demonstrated in this study that chiral induction in the one-pot direct three-component Mannich reaction is possible by generating an enzyme-like cavity in molecular framework of the amphiphilic organocatalyst. The esters of *trans*-4-hydroxy-L-proline and long chain fatty acids have been synthesized by *O*-acylation (A series). Synthesized molecules used as organocatalysts for one-pot asymmetric direct Mannich reaction among cyclohexanone, 4-nitrobenzaldehyde and aniline. The molecular framework of the catalyst not only induces the amphiphilicity but also acquires specific conformation leads to formation of catalytic cavity facilitating stereo-induction in the Mannich product. The catalytic efficiency of the as-synthesized proline based molecular framework evaluated by systematic addition of olefinic bonds in the long hydrocarbon chain that makes the cavity more robust with decreasing in size. However, the cavity possessing single cis-π bond is more efficient stabilizing the transition state of the Mannich product with more % yield and selectivity. To trace the origin of stereoselectivity and the role of H-bond towards the given stereochemical outcome, two new series of organocatalysts having –$COOCH_3$ and –H group in place of –COOH group in the basic proline molecular framework have been synthesized (**B** and **C** series, respectively) and evaluated as catalyst for the same reaction. Performance based evaluation of catalytic activity suggests that Mannich reaction proceeds with ~ 99% yield, 84% dr and 98% er in presence of 10 mole% catalyst (having three π bonds), in an o/w emulsion (85 equiv. of water) within 12 h. The stereoselectivity of the catalysts from all these series maintained for *anti*-Mannich product, however, the opposite stereoisomer of the *anti*-configuration *(2S, R)* was favoured in the case of catalysts from **C** series. A plausible reason has been proposed for the high stereoselectivity and opposite configuration of stereo-centres corroborated by computational analysis.

Chapter 4

L-proline based Sustainable Material for Continuous Flow Processes: A case of Asymmetric Aldol Reaction

Nowadays, industrial vision towards sustainability and green processes preferred in alignment with fourth industrial revolution. Continuous flow technologies have many benefits, Organocatalysts rarely reported for continuous flow system due to challenge of gel formation with most of solvents. It is very technically challenged task for using gel for continuous flow methods. Our strategy was to design immobilized-L-proline on cross-linked polymeric material PMHC18-L-pro-CL and blended with a stable and inert material to overcome the gel formation for continuous flow techniques for organocatalyst. Polymer based immobilized L-Proline with cross-linking strategy (PMHC18-L-pro-CL) effectively works for the model Aldol reaction. Aqueous DMSO (DMSO: water; 90:10) was observed as the most suitable solvent for PMHC18-L-Pro-CL catalyzed Aldol process. Strategy regarding the blending of sawdust with PMHC18-L-pro-CL for continuous flow system, found successful for the model Aldol reaction of 4-nitrobenzaldehyde and cyclohexanone. We observed 92% ee and 97% dr with 99% conversion by using PMHC18-L-pro-CL:sawdust in a 50:50 composition in continuous flow method. Continuous flow process shows better results in terms of stereoselectivity and %conversion than the corresponding batch process. Recyclability and effectiveness of the catalyst was validated for five times. This process has a potential to explore the synthesis of APIs like Norephedrine etc and their industrial scale production keeping sustainability point of views.

Chapter 5

Unusual Fluorescence compound from Oleylamine: Fluorescence and its Potential Applications

New fluorescent materials with special photo- and/or bioactive features are very attractive for both scientific and applicative reasons. For fluorescent organic compounds, existence of some units with large π-conjugated systems and rigid planar structures is a prerequisite according to the classical theory. In recent years, strong blue fluorescence from several types of amine-containing polymers without having conventional fluorophores was observed and also applied for biological imaging. In this study, the aliphatic fluorescent viscous liquid and gel in the form of amide salt was made from the naturally occurring and non-toxic compounds like oleylamine and maleic anhydride. The compound OM-1 was soluble in solvents having dielectric constant in the range of 5-20. It showed fluorescence emission at 465 nm on 355 nm excitation. The quantum yield of OM-1 was found to be 5.3%. It was characterized by spectroscopic, thermogravimetric, rheological and chromatographic analysis. OM-1 proved as a non-toxic material and it was applied as a drug carrier for azithromycin/ erythromycin antibiotics. It increased the efficacy of the drug 5 times. OM-1 can be explored with other costly drugs. OM-1 fluorescence was found very sensitive to the presence of Cu^{+2}, Fe^{+2} and Fe^{+3} metal ions in aqueous solution. The specialty of OM-1 is, it can distinguish Cu^{+1} and Cu^{+2} metal ions. Hence, it has a potential to apply as a metal sensor.