

# THE APPLICATION OF NANOPARTICLES SUPPORTED CHIRAL ORGANOCATALYSTS IN ASYMMETRIC ALDOL REACTIONS: A STUDY ON THE RECENT ADVANCEMENT

## Abstract

The nanotechnology witnessed a tremendous growth over the last two decades. Various types of nanomaterials were invented and were applied in diverse field. They have also been utilized as supporting agents to immobilize or graft various catalysts to improve their catalytic activity, stabilization, recycling ability etc. Recently nanoparticles have been extensively used as a supporting agent to prepare nano-particles-supported chiral organo-catalysts (NPSCOCs) and evaluated their catalytic activity in various asymmetric organic transformations. Nanoparticles supported chiral catalysts have high stability and generally provide better selectivity. The most importantly, the supported catalysts can easily be recovered and recycled several times. Thus, this improves the catalytic efficiency and turnover number of the catalyst. Besides, the NPSCOCs can work in eco-friendly solvent like water. This article will focus on the application of NPSCOCs in asymmetric aldol reaction in eco-friendly conditions.

**Keywords:** Functionalised nanoparticles, Immobilization, Supported chiral organo-catalyst, Green Chemistry, asymmetric aldol reaction.

## Authors

**Joydeb Das**

Department of Chemistry  
Sreegopal Banerjee College (University of  
Burdwan)  
Bagati, Mogra, Hooghly,  
West Bengal, India

## I. INTRODUCTION

The development of environmentally benign together with economically favourable chemical method is highly challenging task in synthetic organic chemistry. In this aspect, catalysis is most popular choice as it leads to highly efficient green process producing least amount of waste with accelerated reaction rate. Among the various catalysis the most favoured one is organocatalysis for its unique characteristics like being devoid of heavy metals, easy to prepare or available in the nature, least or no sensitivity towards oxygen and moisture, cost effective, availability of diverse structural feature, etc [1-3]. The incredible potential of asymmetric catalysis for making enantio-enrich organic compounds is well-known. Now-a-days, asymmetric organocatalysis turns into integral part of asymmetric synthesis [4-6]. However, non-recyclability of homogenous organocatalysts and high catalyst loading are major drawbacks [7-9]. These limitations were partly overcome by the invention of various types of supporting agents like polymers, hybrid silica gel, fluorinated tags, nanoparticles (NPs), ionic liquids for the synthesis of recoverable supported organocatalysts [10-14]. With the fast advancement of nanotechnology various types of functionalized nanoparticles have been developed and used as supporting agent for diverse types of catalysts [15-23]. The retrievable nano-particles supported organocatalysis becomes one of the most widely used process in the various asymmetric transformations due to its simple recoverability and recyclability [24, 25].

Asymmetric Aldol reaction has been extensively studied reaction in diverse unsupported organocatalysis [26, 27]. The chiral organocatalysts that were active in asymmetric aldol reactions were also immobilized using nano-particles and the NPSCOCs were evaluated in asymmetric aldol reaction to find out their recoverability, efficiency as well as to develop eco-friendly better catalytic conditions [28-32]. Several review articles are present in the literature with emphasising the detailed discussion on the preparation of various types of supported nanoparticles, their characterization, chemical properties, etc. [14-17]. This article is going to emphasis on the recent application of retrievable NPSCOCs on asymmetric aldol reactions.

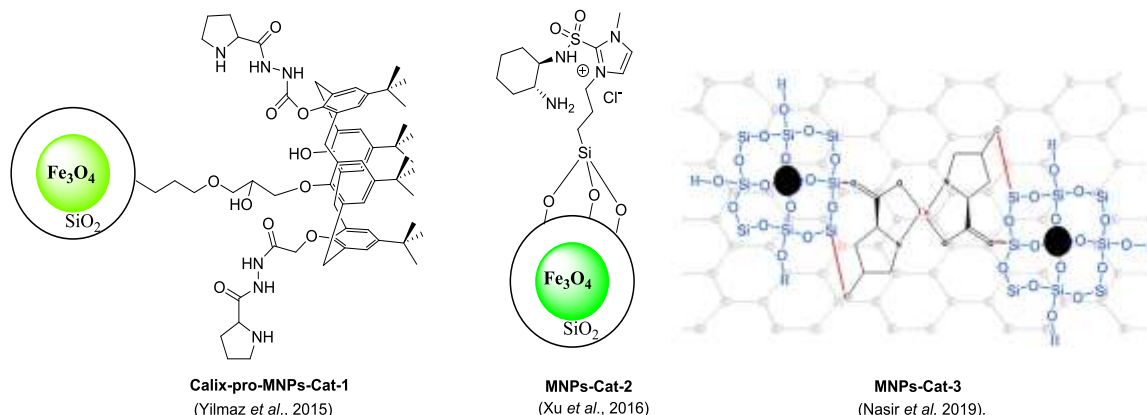
## II. DISCUSSION

**1. Magnetic Nanoparticles (MNPs) as Supporting Agent:** Among the various nanoparticles used as supporting agents for organocatalyst, MNPs were the most popular choices for chemist. Because the MNPs supported catalysts are cost effective, easy to prepare, highly active like their homogeneous counterparts, etc. [33, 34] Besides these, it can easily be separated using external magnet avoiding monotonous filtration or centrifugation process and can be reused for several times. The quasi-homogeneous nature and high stability of the MNPSCOC plays crucial role to provide highly pure enantio-enrich organic products in environmentally friendly solvents like water [35-40].

There are several brilliant reviews present in literature discussing about the preparation, characterisation and properties of the magnetic nanoparticles supported chiral organo-catalysts (MNPSCOC) [41-43]. This article will focus only on the recent application of MNPSCOC in asymmetric aldol reaction.

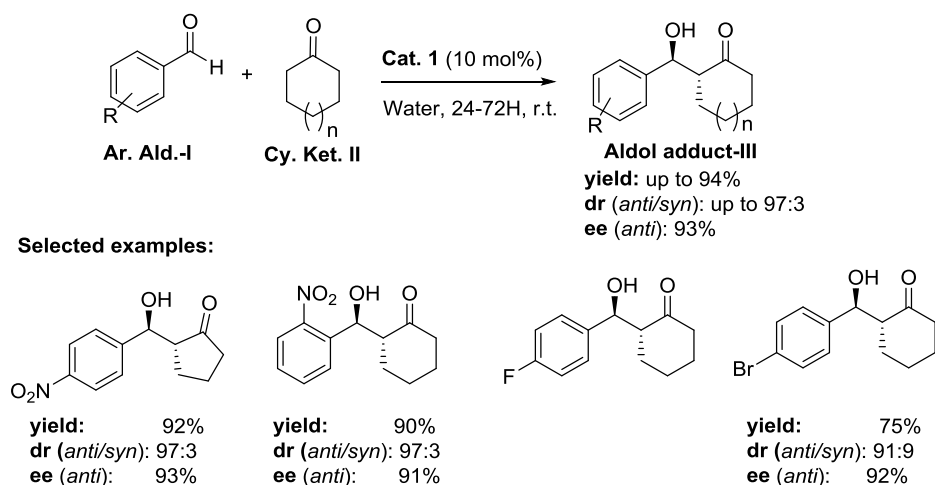
## 2. Magnetic Nanoparticle Supported Organocatalysts in Asymmetric Aldol Reaction:

In 2015, Yilmaz *et al.* successfully developed a simple methodology to prepare a new type of MNP-supported chiral organocatalysts MNPs-Cat-1 from calixarene-containing proline (Fig. 1) for the first time [44].



**Figure 1:** MNPSCOCs Developed and Evaluated in ADA Reaction by Various Groups

The catalyst MNPs-Cat-1 having spherical dimension was evaluated on asymmetric direct aldol (ADA) reactions between aromatic aldehydes (acceptor **I**) and cyclohexanone (donor **II**) and was found very efficient in affording aldol adduct **III** with good to excellent selectivities [dr (*anti:syn*): up to 97:3 and ee (*anti*): up to 93%] with high yield (Fig. 2).



**Figure 2:** Catalytic Performances of MNPs-Cat-1 in ADA Reaction, Yilmaz *et al.*, 2015, [44].

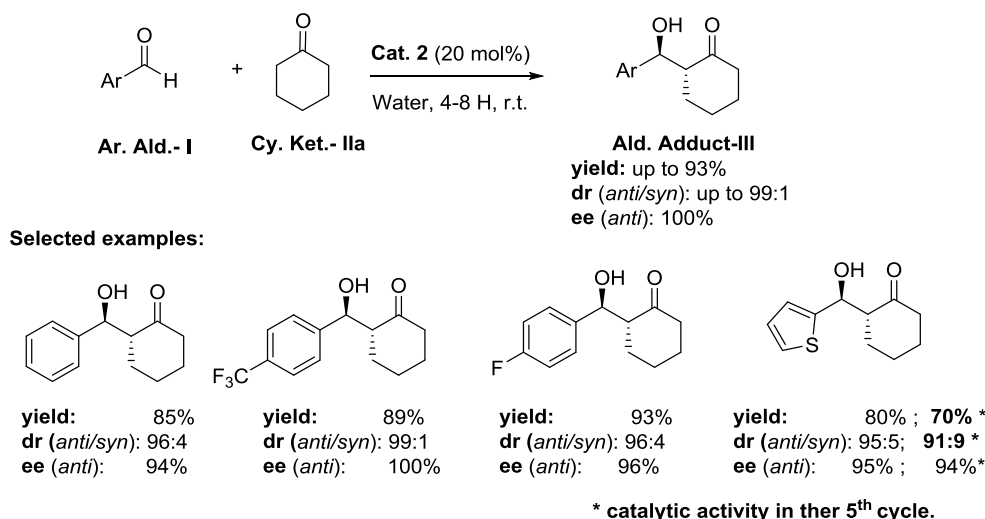
The authors also performed recycling experiment of the Calix-pro-MNPs-Cat-1 and observed no significant loss of activities and selectivities up to five cycles, but, thereafter, it started to drastically loss both the activities and selectivities (Table 1).

**Table 1: Calix-Pro-MNPs-Cat-1 in Recycling Experiment in ADA Reaction (Donor: Cyclohexanone, Acceptor: 4-Nitrobenzaldehyde), Yilmaz *et al.*, 2015, [44].**

Cycle	Yield (%)	dr ( <i>anti:syn</i> )	ee ( <i>anti</i> )(%)
1	92	97:3	93
3	90	89:11	87
6	82	84:16	79
8	68	73:27	64

In 2016, Xu *et al.* prepared a magnetic nanoparticles-supported chiral aminocyclohexane MNPs-Cat-2 (Fig. 1) containing an imidazolium ionic liquid moiety. The incorporation of ionic liquid in the MNPs-Cat-2 will provide several advantages like better stability, higher quasi-homogeneity leading to superior catalytic activity, higher recyclability, etc.

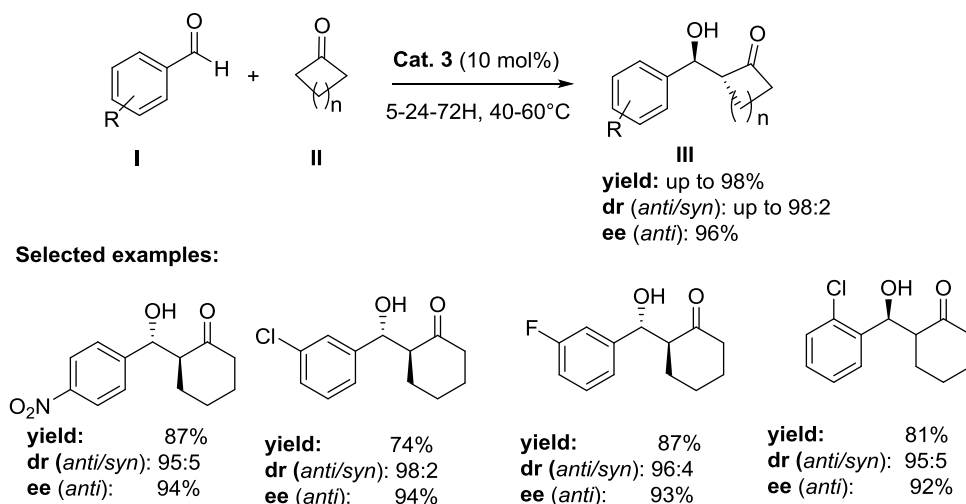
The ionic liquid tagged MNPs-Cat-2 was successfully evaluated in the ADA reactions between cyclohexanone **II** and aromatic & heteroaromatic aldehydes **I** under a green procedure in water. The synthesized catalyst demonstrated good to high catalytic activity yielding 70–94% aldol addition adduct **III** and excellent stereoselectivity (ee: 92–100%, dr: 91:9–99:1) (Fig. 3). The excellent performance of the catalyst can be explained by the vital role played by the ionic liquid moiety through facilitating the link among reactants and catalytic sites in water medium. The MNPs-Cat-2 was readily recovered from the reaction medium by applying an external permanent magnet and recycled for five times without any significant loss of catalytic efficiency [45].



**Figure 3: ADA Reaction Catalyzed by MNPs-Cat-2, Xu *et al.*, 2016 [45].**

In 2019, Nasir *et al.* developed a noble catalyst via immobilization of Cu(proline)<sub>2</sub> complex onto the surface of magnetic grapheme, G/MF@SiO<sub>2</sub>@Cu(proline)<sub>2</sub>, MNPs-Cat-3 (Fig. 1). The authors successfully developed a greener catalytic procedure for ADA reaction using the grapheme based MNPs-Cat-3 under solvent free condition. The prepared nanocatalyst MNPs-Cat-3 afforded all aldol

products in good to excellent yield (up to 98%) with outstanding enantiomeric excess (> 90%) (Fig. 4) [46].



**Figure 4:** ADA Reaction Catalyzed by MNPs-Cat-3 Under Solvent-Free Condition, Nasir *et al.*, 2019 [46].

The authors also executed a separate experiment of the ADA reaction using various components as catalyst that was used in the synthesised MNPs-Cat-3 to find out the active components of the designed catalyst and they found that only proline,  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ , and  $\text{Cu}(\text{proline})_2$  complex afforded the aldol adduct with lower yield compared with the synthesised catalyst  $\text{G/MF@SiO}_2\text{@Cu}(\text{proline})_2$ , Cat-3 (Table 3). These experiments imply that the catalytic activity of the copper complex,  $\text{Cu}(\text{proline})_2$  and proline were improved many fold after immobilization onto the surface of magnetic Graphene ( $\text{G/MFe@SiO}_2$ ) composite.,

**Table 4:** Comparative Study of Various Materials in Aldol Reaction, Nasir *et al.*, 2019 [46].

Entry	Nanocatalyst	Yield (%)
1	Graphene	Trace
2	$\text{MnFe}_2\text{O}_3$	Trace
3	G/MF*	Trace
4	$\text{G/MF@SiO}_2$	Trace
5	Proline	59
6	$\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$	60
7	$\text{Cu}(\text{Proline})_2$	65
8	MNPs-Cat-3	98

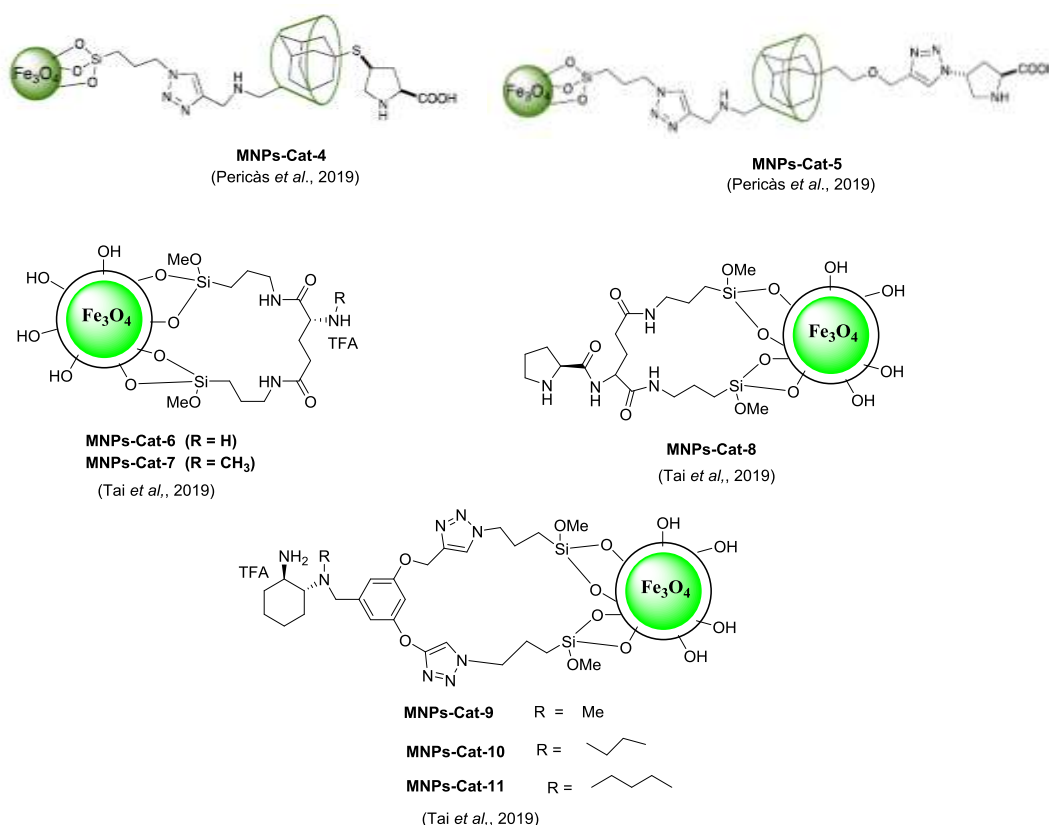
\* G: Graphene; MF:  $\text{MnFe}_2\text{O}_3$

As like other MNPs supported catalysts, it can be easily recovered with an external magnet and recycled up to five cycles without any substantial loss of activity with extremely small leaching of the catalyst (Table 3) [46].

**Table 3: Recycling Experiments of MNPs-Cat-3 in ADA Reaction, Nasir *et al.*, 2019 [46].**

Cycle*	Yield (%)	dr ( <i>anti/syn</i> )	ee ( <i>anti</i> ) (%)
1	98	73:27	89%
2	96	73:27	89%
3	95	73:27	89%
4	93	73:27	89%
5	90	73:27	89%
* Donor: Cyclohexanone, Acceptor: <i>p</i> -nitrobenzaldehyde			

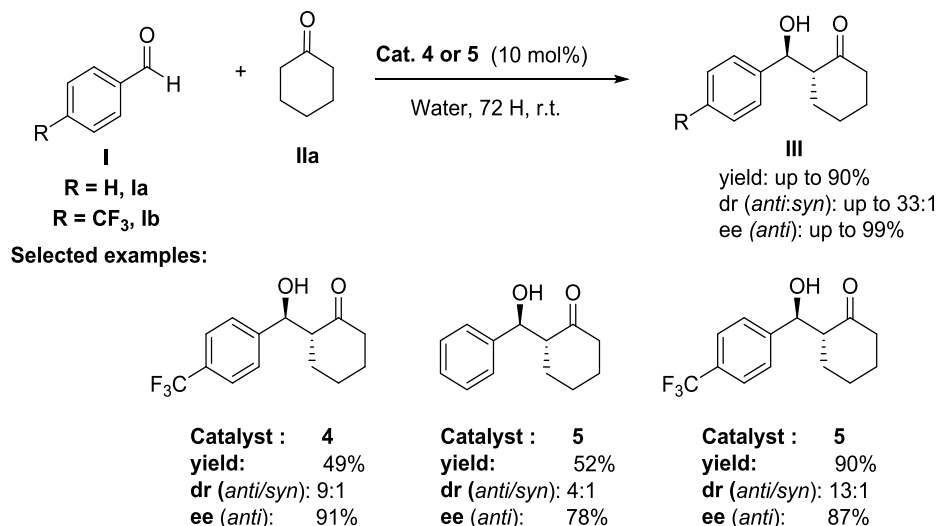
In 2019, Pericàs *et al.* reported very interesting noble type of MNPs supported a supramolecular motif based adamantly substituted proline organocatalysts MNPs-Cat-4 and MNPs-Cat-5 (Fig. 5). The designed catalyst can acts as magnetic shuttle where the supramolecular motif containing  $\beta$ -CD acts as a reversible connector between the MNPs and the organocatalyst molecule [47].



**Figure 5: Catalysts Developed by Pericàs *et al.*, 2019 for ADA Reaction.**

The authors used the adamantyl-decorated MNPs-COCs with proline as active site, MNPs-Cat-4 & 5 as modular, magnetically recyclable catalysts to develop an environmentally benign procedure on ADA reaction between aromatic aldehydes (acceptor-**I**) and cyclohexanone (donor **IIa**) in water ( dr: up to 33:1; ee: up to 99 %) (Fig.- 6) [47].

THE APPLICATION OF NANOPARTICLES SUPPORTED CHIRAL ORGANOCATALYSTS  
IN ASYMMETRIC ALDOL REACTIONS: A STUDY ON THE RECENT ADVANCEMENT



**Figure 6:** Catalytic Activity of MNPs-Cat-4 & 5 in ADA Reaction by Pericàs *et al.*, 2019 [47].

Interestingly, the catalytic assemblies can be readily disassembled in organic media, and the authors used recovered nanoparticles as chemical shuttles to re-complex with another substituted catalytic unit. The both catalysts were also recyclable but the catalyst **5** found to be more stable under the reaction as well as work up conditions and remained active up to 3 consecutive cycles without any significant loss of enantioselectivity. (Table 4) [47].

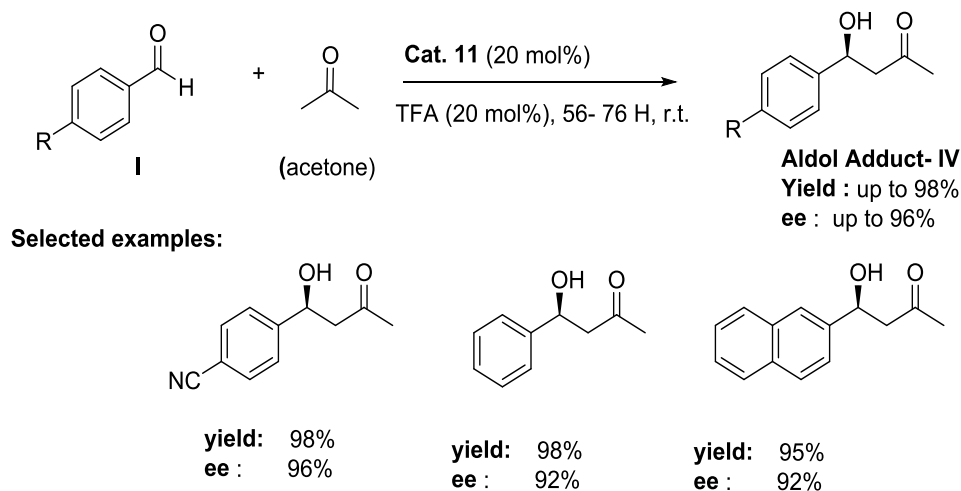
**Table 4: Recycling of the Catalysts 4 and 5 in the ADA Reaction of Ib with IIa [47].**

Catalyst	Cycle	Yield (%)	dr ( <i>anti:syn</i> )	ee ( <i>anti</i> ) (%)
<b>4</b>	1	32	9:1	92
	2	17	9:1	93
	3	traces	6:1	91
	4	traces	6:1	92
<b>5</b>	1	89	14:1	89
	2	57	10:1	87
	3	35	5:1	85

In 2019, Tai *et al.* prepared several silica-coated MNPSCOCs, MNPs-Cat-**6** to **11**, from the derivatives of chiral amine, Pro-Glu or cyclohexyl-1,2-diamine (Fig. 5) and their bifunctional enamine activities were examined in the ADA reaction [48].

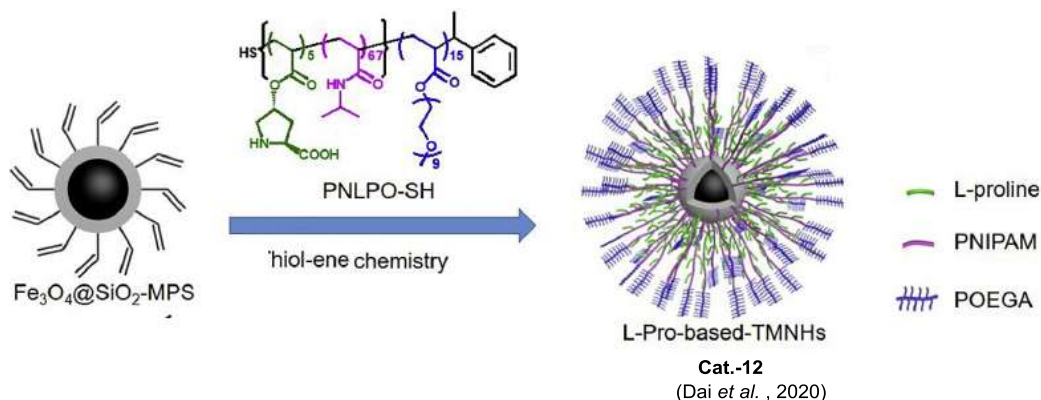
They observed that MNPs-Cat-**11** with the largest macrocyclic ring and the longest aliphatic chain provided best selectivities (up to 96% ee) (Fig. 7). The authors explained the results with '*macrocyclic effect*'. The MNPs-Cat-**11** was also found to recyclable up to 3 runs [48].

THE APPLICATION OF NANOPARTICLES SUPPORTED CHIRAL ORGANOCATALYSTS  
IN ASYMMETRIC ALDOL REACTIONS: A STUDY ON THE RECENT ADVANCEMENT



**Figure 7:** Catalytic Performance of MNPs-Cat-11 in ADA Reaction, Tai *et al.*, 2019, [48].

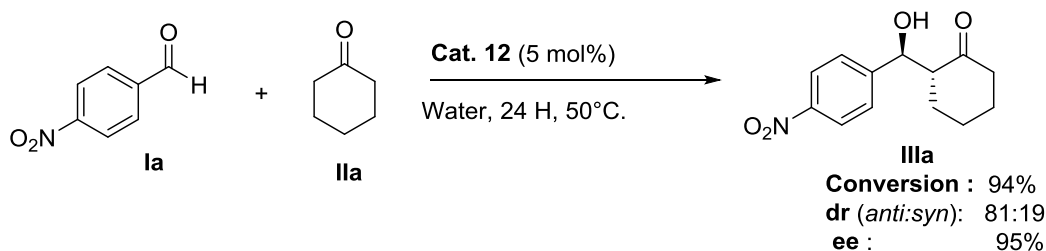
In 2020, Dai *et al.* made L-Pro-based thermal and magnetic dual-responsive nano-hybrids supported MNPs-Cat-12. The catalyst **12** was synthesised by thiol-ene click chemistry [49]. A synthetic diagram for the preparation of catalyst is represented in Figure 8.



**Figure 8:** Schematic Representation of the Synthesis MNPs.Cat.-12 in ADA Reaction.[49]

The catalytic activity of the synthesized catalyst was successfully evaluated in ADA reaction between cyclohexanone and 4-nitrobenzaldehyde in aqueous medium. Thermal-responsive L-Pro-based-TMNHs-**cat.-12** shown good catalytic activity and selectivity above LCST (lower critical solution temperature), which was explained by the shaping of hydrophobic aggregates to collect organic reactants and forming a hydrophobic micro-environment for specific organic synthesis [50, 51].



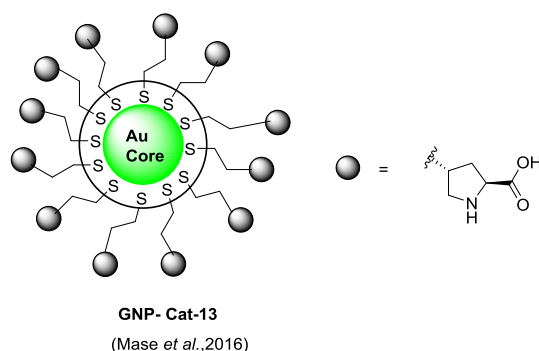


**Figure 9:** Catalytic Performance of the MNPs-Cat-12 in ADA Reaction, Dai *et al.* 2020 [49].

The Magnetic responsive L-Pro-based-TMNHs- Cat-12 was found very efficient even after ten recycling run [52].

- 3. Gold Nanoparticles Supported Chiral Organocatalysts (GnpSCOCs) in Asymmetric Aldol Reaction:** Gold nanoparticles have also been attracted the attention of many chemists for their remarkably efficient catalytic properties [53-56]. It can also be used as supporting agent to prepared various recoverable and recyclable organo-catalyst. There are many examples of the application of GNPSOCs in diverse organic reactions [57]. These articles will focus only on the recent application of GNPSOCs in asymmetric aldol reaction.

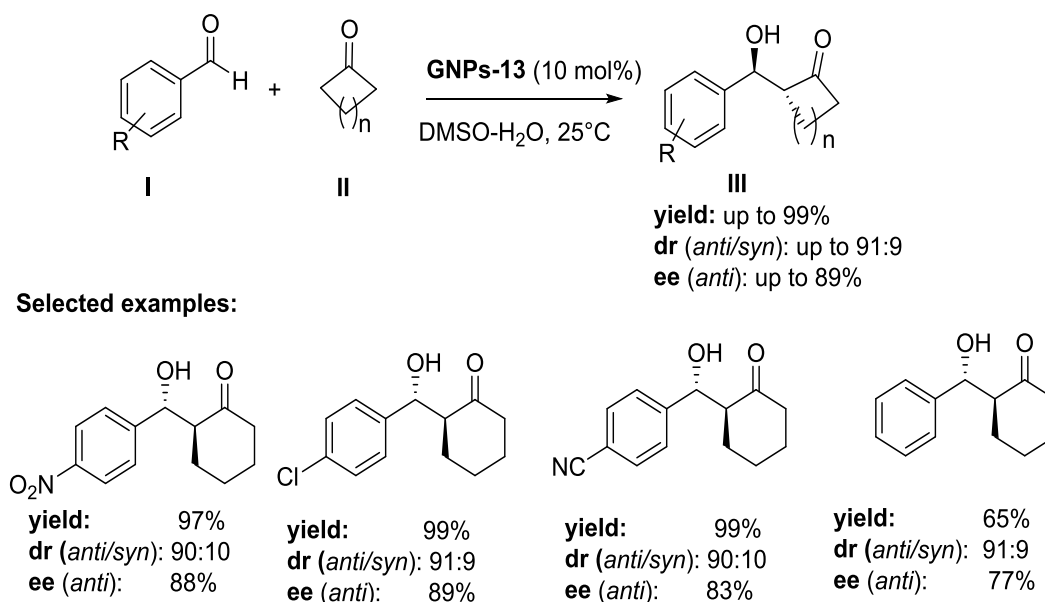
In 2016, Mase *et al.* prepared a self-assembling gold nanoparticle (GNPs)-supported L-proline derivative **GNPs-Cat-13** through one-phase modified Brust-Schiffrin method from chloroauric acid and 4-hydroxy-L-proline (Fig.10) [58].



**Figure 10:** GNP-Supported L-Proline Cat-13 as Organocatalysts by Mase *et al.*, 2016 [58].

Catalytic activity of **GNPs-Cat-13** was successfully evaluated in ADA reaction. The catalyst demonstrated high catalytic activity and in most cases, it was observed that the reactions afforded the *anti*-aldol products with high to excellent diastereo- and enantioselectivities. (Yields: up to 99%, dr (*anti:syn*): 91:9 & ee (*anti*): up to 89 (Fig. 11) [58].

THE APPLICATION OF NANOPARTICLES SUPPORTED CHIRAL ORGANOCATALYSTS  
IN ASYMMETRIC ALDOL REACTIONS: A STUDY ON THE RECENT ADVANCEMENT



**Figure 11:** GNPs-Cat-13 Catalyzed ADA Reaction Reported by Mase *et al.*, 2016 [58].

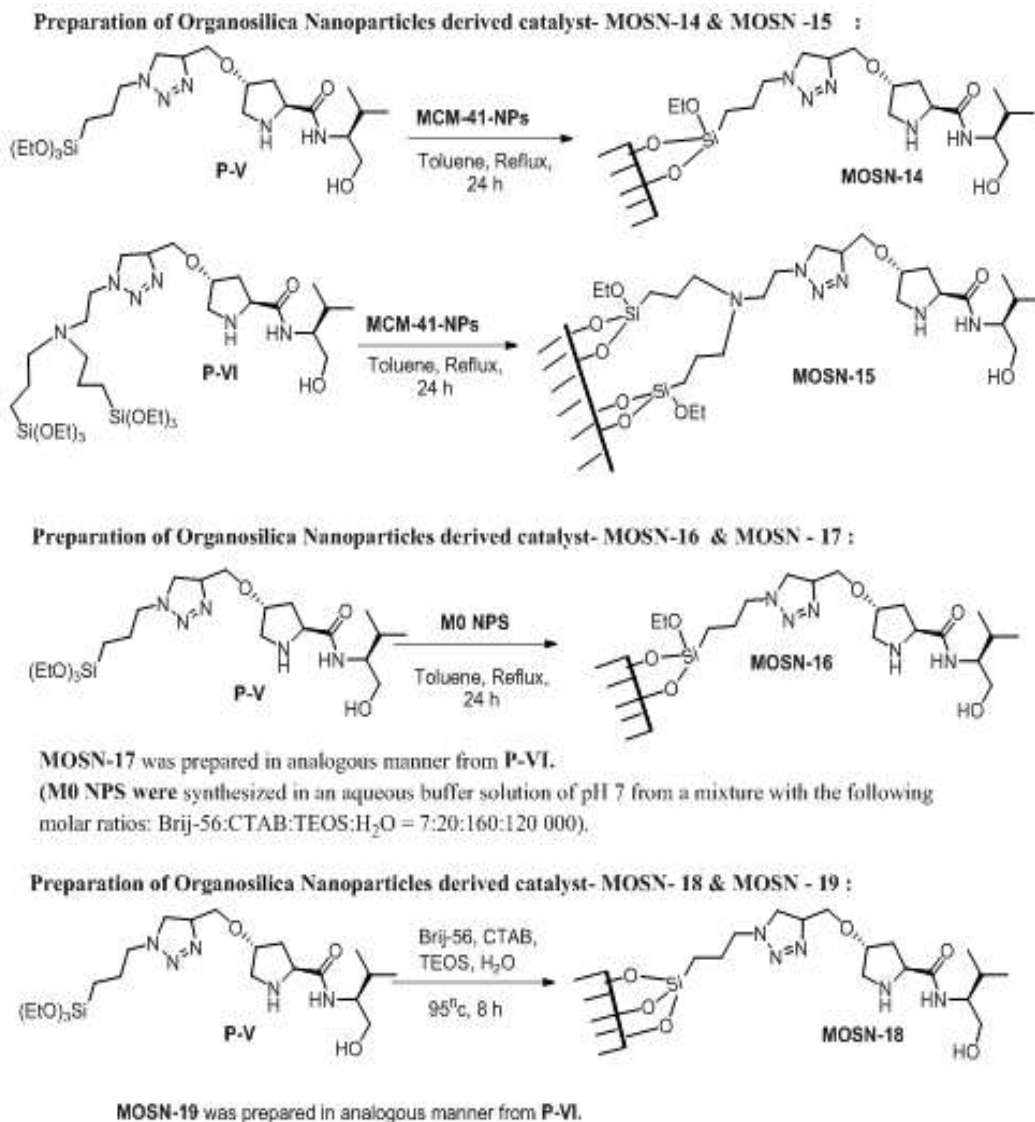
This catalyst, **GNPs-Cat-13** was recycled up to five consecutive cycles maintaining outstanding activity and selectivity. The GNPs catalyst having colloidal properties aggregates on change in dielectric constant of the reaction medium and the reaction mixture turns into heterogeneous. The **GNPs-Cat-13** was easily recovered from the reaction mixture by centrifugation followed by decantation after adding EtOAc in the reaction mixture (Table 5).

**Table 5:** Recycling of GNPs-Cat-13 in ADA reaction of p-NBA & Cyclohexanone [58].

Cycle	Yield (%)	dr (anti/syn)	ee (anti) (%)	Recovery (%)
1	97	90:10	88	>99
2	98	91:9	88	>99
3	98	91:9	88	>99
4	98	92:8	88	>99
5	98	92:8	88	>99

- 4. Mesoporous Organosilica Nanoparticles Supported Chiral Organocatalysts in Ada Reaction:** In 2019, Pleixats *et al.* prepared several eco-friendly mesoporous organosilica nanoparticles supported chiral organocatalysts **MOSN-14 - MOSN-19** from mono- and bis-silylated proline-valinol amides (Fig.-12) [59].

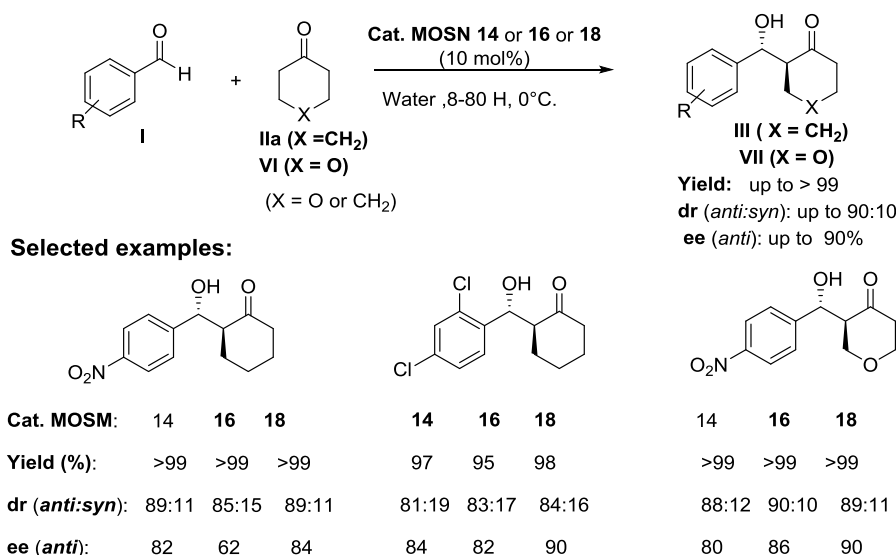
THE APPLICATION OF NANOPARTICLES SUPPORTED CHIRAL ORGANOCATALYSTS  
IN ASYMMETRIC ALDOL REACTIONS: A STUDY ON THE RECENT ADVANCEMENT



**Figure 12:** Schematic Preparation of MOSN-14- MOSN-19 Reported by Pleixats *et al.*[59].

The authors examined the catalytic activity of these silica supported nanocatalysts **MOSN-14 to MOSN -19** in the ADA reaction. They found that the organo-nanocatalysts derived from mono silylated precursors were more active than that of bis-silylated one. According to the authors, the chiral moiety present in the bis-silylated derived catalysts **MOSN-15, MOSN-17 and MOSN-19** have less flexibility which limits their catalytic activity and selectivity. The mono silylated precursor derived catalyst **MOSN-14 and MOSN-18** were found most active in ADA reaction leading to excellent yield and selectivity. Comparative results were summarized in the figure below (Fig. 13).

THE APPLICATION OF NANOPARTICLES SUPPORTED CHIRAL ORGANOCATALYSTS  
IN ASYMMETRIC ALDOL REACTIONS: A STUDY ON THE RECENT ADVANCEMENT



**Figure 13:** Catalytic Performances of the Catalysts MOSN-14, MOSN-16, and MOSN-18 [59].

The **MOSN** catalysts could easily be separated by decantation after centrifugation. The recovered catalysts also showed excellent performances in the ADA reaction between cyclohexanone and *p*-nitrobenzaldehyde up to five recycles (Table 6) [59].

**Table 6:** Recycling of MOSN 14 in ADA Reaction Between *p*-NBA and Cyclohexanone [59].

Cycle	Yield (%)	dr ( <i>anti/syn</i> )	ee ( <i>anti</i> ) (%)
1	>99	89/11	82
2	>99	88/12	78
3	>99	89/11	80
4	>99	89/11	82
5	>99	89/11	82

### III. CONCLUSION

The application of nanoparticles supported chiral organocatalysts (NPSCOCs) in asymmetric aldol reaction were discussed throughout the article, In all cases moderate to excellent yields, diastereo-selectivities and enantioselectivities were obtained during the catalytic activity evaluation test of the supported catalyst in ADA reaction. The catalysts were easily separated from the reaction mixture and recycled several times without any major loss in activity or selectivity as well as catalytic efficiency. In some cases, immobilization or grafting of chiral organocatalyst on nanoparticles led to improve catalytic activity. Interestingly, in most cases, a significantly improved eco-friendly procedure was developed. But, there are lots to progress in this field. More vigorous studies are required to develop more competent protocols that can be used in pharmaceutical industry.

## REFERENCES

- [1] P.T. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press:, London, 1998.
- [2] P. T. Anastas and J. B. Zimmerman, "Through the 12 Principles Green Engineering" *Environ. Sci. Technol.*, vol. 37, pp. 94A–101A, 2003.
- [3] P.T. Anastas and E. S. Beach, "Green chemistry: the emergence of a transformative framework," *Green Chem. Lett. Rev.*, vol. 1, pp. 9–24, 2007.
- [4] B. Han, X.-H. He, Y.-Q. Liu, G. He, C. Peng and J.-L. Li, "Asymmetric organocatalysis: an enabling technology for medicinal chemistry," *Chem. Soc. Rev.*, vol. 50, pp. 1522-1586, 2021.
- [5] D. L. Hughes, "Highlights of the Recent Patent Literature: Focus on Asymmetric Organocatalysis," *Org. Process Res. Dev.*, vol. 26, pp. 2224–2239, 2022.
- [6] N. Wang, Z. Wu, J. Wang, N. Ullah, and Lu, Y., "Recent applications of asymmetric organocatalytic annulation reactions in natural product synthesis," *Chemical Society Reviews*, vol. 50(17), pp. 9766–9793, 2021.
- [7] M. Benaglia, *Recoverable and Recyclable Catalysts*, Wiley, 2009.
- [8] K. Ding and Y. Uozumi, *Handbook of Asymmetric Heterogeneous Catalysis*, Wiley-VCH Verlag GmbH & Co. KGaA, 2008.
- [9] G. Rothenberg, *Catalysis: Concepts and Green Applications*, Wiley- VCH Verlag GmbH & Co. KGaA, 2008.
- [10] D. C. Sherrington and A. P. Kybett (Editors), *Supported Catalysts and Their Applications*, Royal Society of Chemistry (Great Britain), London, 2001.
- [11] W. Miao and T. H. Chan, "Ionic-Liquid-Supported Synthesis: A Novel Liquid-Phase Strategy for Organic Synthesis," *Acc. Chem. Res.*, vol. 39, pp. 897–908, 2006.
- [12] J. A. Gladysz, D. P. Curran and I. T. Horvath (Editors), *Handbook of Fluorous Chemistry*, Wiley-VCH, Weinheim, 2004.
- [13] T. Arai , T. Sato, H. Kanoh, K. Kaneko, K. Oguma and A. Yanagisawa, "Organic–Inorganic Hybrid Polymer-Encapsulated Magnetic Nanobead Catalysts," *Chem. Eur. J.*, vol. 14, pp. 882–885, 2008.
- [14] R.B. Nasir Baig and R.S. Varma, "Organic synthesis *via* magnetic attraction: benign and sustainable protocols using magnetic nanoferrites," *Green Chem.*, vol. 15, pp. 398–417, 2013.
- [15] V. Polshettiwar, R. Luque, A. Fihri, H. Zhu, and M. Bouhrara, J. M. Basset, "Magnetically Recoverable Nanocatalysts" *Chem. Rev.*, vol. 111, pp. 3036–3075, 2011.
- [16] M. B. Gawande, P. S. Branco and R. S. Varma, "Nano-magnetite (Fe<sub>3</sub>O<sub>4</sub>) as a support for recyclable catalysts in the development of sustainable methodologies" *Chem. Soc. Rev.*, 42, pp. 3371–3393, 2013.
- [17] R. B. Nasir Baig and R. S. Varma, "Magnetically retrievable catalysts for organic synthesis," *Chem. Commun* , vol. 49, pp. 752–770, 2013.
- [18] F. Shi, M. K. Tse, S. Zhou, M. –M. Pohl, J. Radnik, S. Hubner, K. Jahnisch, A. Bruckner and M. J. Beller, "Green and Efficient Synthesis of Sulfonamides Catalyzed by Nano-Ru/Fe<sub>3</sub>O<sub>4</sub>" *J. Am. Chem. Soc.*, vol. 131, pp. 1775–1779, 2009.
- [19] G. Hu, G. T. Yee and W. Lin, "Magnetically Recoverable Chiral Catalysts Immobilized on Magnetite Nanoparticles for Asymmetric Hydrogenation of Aromatic Ketones," *J. Am. Chem. Soc.*, vol. 127, pp. 12486–12487, 2005.
- [20] Kaboudin, R. Mostafalu and T. Yokomatsu, "Fe<sub>3</sub>O<sub>4</sub>nanoparticle-supported Cu(ii)-β-cyclodextrin complex as a magnetically recoverable and reusable catalyst for the synthesis of symmetrical biaryls and 1,2,3-triazoles from aryl boronic acids," *Green Chem.*, vol. 15, pp. 2266–2274, 2013.
- [21] Wang, L. Salmon, J. Ruiz and D. Astruc, "A recyclable ruthenium(ii) complex supported on magnetic nanoparticles: a regioselective catalyst for alkyne–azide cycloaddition," *Chem. Commun.*, vol. 49, pp. 6956–6958, 2013.
- [22] Q. Zhang, H. Su, J. Luo and Y. Wei, ""Click" magnetic nanoparticle-supported palladium catalyst: a phosphine-free, highly efficient and magnetically recoverable catalyst for Suzuki–Miyaura coupling reactions" *Catal. Sci. Technol.*, vol. 3, pp. 235–243, 2013.
- [23] C. Ó. Dálaigh, S. A. Corr, Y. Gunko and S. J. Connon, "A Magnetic-Nanoparticle-Supported 4-*N,N*-Dialkylaminopyridine Catalyst: Excellent Reactivity Combined with Facile Catalyst Recovery and Recyclability," *Angew. Chem. Int. Ed.* vol. 46, pp. 4329–4332, 2007.
- [24] Z. D. Susam and C. Tanyeli, "Recyclable Organocatalysts in Asymmetric Synthesis," *Asian J. Org. Chem.*, vol. 10, pp. 1251-1266, 2021.

THE APPLICATION OF NANOPARTICLES SUPPORTED CHIRAL ORGANOCATALYSTS  
IN ASYMMETRIC ALDOL REACTIONS: A STUDY ON THE RECENT ADVANCEMENT

- [25] N. Amirmahani, N.t O. Mahmoodi, M. Bahramnejad and N. Seyedi, "Recent developments of metallic nanoparticles and their catalytic activity in organic reactions," *J. Chin. Chem. Soc.*, vol. 67, pp. 1326-1337, 2020.
- [26] J. Das, "Recent Developments on Brønsted Acid Catalyzed Asymmetric Aldol Reactions and the Fate of the Catalysts," *J. Sci. Res.*, vol. 15, pp. 285-300, 2023.
- [27] C. G. Jacoby, P. H. V. Vontobel, M. F. Bach, and P. H. Schneider, "Highly efficient organocatalysts for the asymmetric aldol reaction," *N. J. Chem.*, vol. 42, pp. 7416-7421, 2018.
- [28] S. Luo, X. Zheng and J. -P. Cheng, "Asymmetric bifunctional primary aminocatalysis on magnetic nanoparticles" *Chem. Commun.*, pp. 5719-5721, 2008.
- [29] P. Agrigento, M. J. Beier, J. T. N. Knijnenburg, A. Baiker and M. Gruttadauria, "Highly cross-linked imidazolium salt entrapped magnetic particles – preparation and applications," *J. Mat. Chem.*, vol. 22, pp. 20728-20735, 2012.
- [30] Z. Yacob, A. Nan and J. Liebscher, "Proline-Functionalized Magnetic Core-Shell Nanoparticles as Efficient and Recyclable Organocatalysts for Aldol Reactions," *Adv. Synth. Catal.*, vol. 354, pp. 3259-3264, 2012.
- [31] H. Yang, S. Li, X. Wang, F. Zhang, X. Zhong, Z. Dong and J. Ma, "Core-shell silica magnetic microspheres supported proline as a recyclable organocatalyst for the asymmetric aldol reaction," *J. Mol. Catal. A: Chem.*, vol. 363-364, pp. 404-410, 2012.
- [32] Y. Kong, R. Tan, L. Zhao and D. Yin, "l-Proline supported on ionic liquid-modified magnetic nanoparticles as a highly efficient and reusable organocatalyst for direct asymmetric aldol reaction in water," *Green Chem.*, vol. 15, pp. 2422- 2433, 2013.
- [33] T. Arai, T. Sato, H. Kanoh, K. Kaneko, K. Oguma and A. Yanagisawa, "Organic-inorganic Hybrid Polymer-encapsulated Nano Beads Catalysts," *Chem. Eur. J.*, vol. 14, pp. 882 – 885, 2008.
- [34] R. B. Nasir Baig and R. S. Varma, "Organic Synthesis via Magnetic Attraction: Benign and Sustainable Protocols Using Magnetic Nano Ferrites," *Green Chem.*, vol. 15, pp. 398 – 417, 2013.
- [35] D. Astruc, F. Lu and J. R. Aranzas, "Nanoparticles as Recyclable Catalyst: The Frontier between Homogeneous and Heterogeneous Catalysis," *Angew. Chem. Int. Ed.*, vol. 44, pp. 7852 – 7872, 2005.
- [36] D. Astruc, *Nanoparticles and Catalysis (Wiley-VCH Verlag GmbH & Co. KGaA, 2008.)* pp. 1 - 48.
- [37] N. Yan, C. Xiao and Y. Kou, "Transition Metal Nanoparticles Catalysis in Green Solvents," *Coord. Chem. Rev.*, vol. 254, pp. 1179 – 1218, 2010.
- [38] H. Cong and J. A. Porco, "Chemical Synthesis of Complex Molecules Using Nanoparticles Catalysis," *ACS Catalysis*, vol. 2, pp. 65 - 70, 2012.
- [39] R. B. N. Baig and R. S. Varma, "Magnetically Retrievable Catalyst for Organic Synthesis," *Chem. Commun.*, vol. 49, pp. 752 – 770, 2013.
- [40] R. Hudson, Y. T. Feng, R. S. Varma and A. Moores, "Bare Magnetic Nanoparticles: Sustainable Synthesis and Application in Catalytic Organic Transformation," *Green Chem.*, vol. 16, 4493 – 4505, 2014.
- [41] V. Polshettiwar, R. Luque, A. Fihri, H. Zhu, M. Bouhrara and J. M. Basset, "Magnetically Recoverable Nanocatalysts," *Chem. Rev.*, vol. 111, 3036 – 3075, 2011.
- [42] M. B. Gawande, P. S. Branco and R. S. Varma, "Nano-magnetite (Fe<sub>3</sub>O<sub>4</sub>) as a Support for Recyclable Catalysts in the Development of Sustainable Methodologies," *Chem. Soc. Rev.*, vol. 42, pp. 3371 – 3393, 2013.
- [43] F. Shi, M. K. Tse, S. Zhou, M. -M. Pohl, J. Radnik, S. Hubner, K. Jahnisch, A. Bruckner, and M. Beller, "Green and Efficient Synthesis of Sulfonamides Catalyzed by Nano-Ru/Fe<sub>3</sub>O<sub>4</sub>," *J. Am. Chem. Soc.*, vol. 131, pp. 1775 – 1779, 2009.
- [44] E. Akceylan, A. Uyanik, S. Eymur, O. Sahin, and M. Yilmaz, "Calixarene-proline modified iron oxide magnetite nanoparticles (Calix-Pro-MN): An efficient recyclable organocatalysts for asymmetric aldol reaction in water," *Appl. catal. A: Gen.*, vol. 499, pp. 205 - 212, 2015.
- [45] Ying, S. Liu, Z. Li, G. Chen, J. Yang, H. Yan, and S. Xu. "Magnetic Nanoparticles-Supported Chiral Catalyst with an Imidazolium Ionic Moiety: An Efficient and Recyclable Catalyst for Asymmetric Michael and Aldol Reactions," *Adv. Synth. Catal.*, vol. 358, pp. 2116 – 2125, 2016.
- [46] M. Kooti, F. Kooshki and E. Nasiri, "Preparation and Characterization of Magnetic Graphene Nanocomposite Containing Cu(Proline)<sub>2</sub> as Catalyst for Asymmetric Aldol Reaction," *Res. Chem. Intermed.*, vol. 45, pp. 2641 – 2656, 2019.
- [47] C. Mendoza, A.d. I. Croix, P. Riente, L. Llorens, J. d. Mendoza and M. A. Pericàs, "Reuseable Shuttles For Exchangeable Functional Cargos: Reversibly Assembled, Magnetically Powered Organocatalysts for Asymmetric Aldol Reaction," *Tetrahedron*, vol. 75, pp. 130592, 2019.

THE APPLICATION OF NANOPARTICLES SUPPORTED CHIRAL ORGANOCATALYSTS  
IN ASYMMETRIC ALDOL REACTIONS: A STUDY ON THE RECENT ADVANCEMENT

- [48] V. Angamuthu and D.-F. Tai, "Chiral Amine and Macrocyclic Fabricated Magnetic Nanoparticle Asymmetrically Catalyzed Direct Aldol Reaction," *Sustain. Chem. Pharm.*, vol. 13, pp. 100152, 2019.
- [49] R. R. Liu, P. Zhang and H. L. Dai, "Synthesis of Magnetic Particles with Well-Defined Living Polymeric Chains via Combination of RAFT Polymerization and Thiol-Ene Click Chemistry," *J. Polym. Res.*, vol. 23, pp. 218, 2016.
- [50] K. Liu, W. W. Xu, Q. Y. Wang, Y. Tang, W. B. Sheng, Y. H. Shen and L. J. Shi, "Self-Assembly of L-Proline Functional Thermo-Responsive Double Hydrophilic Block Copolymers for Aldol Reaction in Water: The Influence of POEGA Block Content," *Colloid Polym. Sci.* vol. 296, pp. 1109 – 1117, 2018.
- [51] H.A. Zayas, A. Lu, D. Valade, F. Amir, Z.F. Jia, R.K. O'Reilly and M.J. Monteiro, "Thermo Responsive Polymer-Supported L-Proline Micelle Catalysts for the Direct Asymmetric Aldol Reaction in Water," *ACS Macro Lett.*, vol. 2, pp. 327 – 331, 2013.
- [52] Q. Wang, Y. Tang, L. Wu, W. Xu, Y. Shen, L. Shi and S. Dai, "Thermal and Magnetic Dual-Responsive L-Proline Nanohybrids for Aqueous Asymmetric Aldol Reaction," *React. Funct. Polym.*, vol. 149, pp. 104508, 2020.
- [53] M. Haruta, T. Kobatashi, H. Sano and N. Yamada, "Novel Gold Catalysts for the Oxidation of Carbon Monoxide at a Temperature far Below 0°C," *Chem. Lett.*, vol. 16, pp. 405 – 408, 1987.
- [54] M. Y. Kuo, C. F. Hsiao, Y. H. Chiu, T. H. Lai, M. J. Fang, J. Y. Wu, J. W. Chen, C. L. Wu, K. H. Wei, H. C. Lin and Y. J. Hsu, "Au@Cu<sub>2</sub>O Core@Shell Nanocrystals as Dual-Functional Catalysts for Sustainable Environmental Applications," *Appl. Catal. B: Environ.* vol. 242, pp. 499 – 506, 2019.
- [55] Y. Liu, Y. Y. Zhang, Q. W. Kou, D. D. Wang, D. L. Han, Z. Y. Lu, Y. Chen, L. Chen, Y. X. Wang, Y. J. Zhang, J. H. Yang, and S. Xing, "Fe<sub>3</sub>O<sub>4</sub>/Au Binary Nanocrystals: Facile Synthesis with Diverse Structure Evolution and Highly Efficient Catalytic Reduction with Cyclability Characteristics in 4-Nitrophenol," *Powder Technol.*, vol. 338, pp. 26 – 35, 2018.
- [56] K. M. Mayer and J. H. Hafner, "Localized Surface Plasmon Resonance Sensors," *Chem. Rev.*, vol. 111, pp. 3828 – 3857, 2011.
- [57] S. Roy and M. A. Pericàs, "Functionalized nanoparticles as catalysts for enantioselective processes," *Org. Biomol. Chem.*, vol. 7, pp. 2669 – 2677, 2009.
- [58] P. L. Soti, H. Yamashita, K. Sato, T. Narumi, M. Toda, N. Watanabe, G. Marosi and N. Mase, "Synthesis of Self-Assembling Gold Nanoparticle-Supported Organocatalyst for Enamine-Based Asymmetric Aldol Reaction," *Tetrahedron*, vol. 72, pp. 1984 – 1990, 2016.
- [59] H. Li, M. Pérez-Trujillo, X. Cattoe and R. Pleixats, "Recyclable Mesoporous Organosilica Nanoparticles Derived from Proline-Valinol Amides for Asymmetric Organocatalysis," *ACS Sustain. Chem. Eng.*, vol. 7, pp. 14815 – 14828, 2019.