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ARTICLE TYPE

L-proline-modified magnetic nanoparticles (LPMNP): A novel magnetically separable organocatalyst

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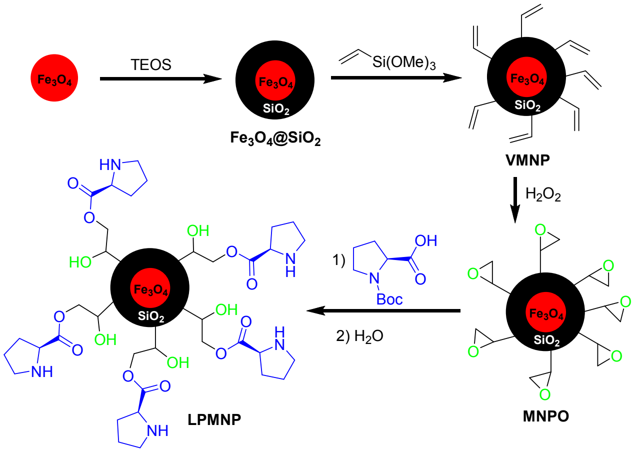
This study offers a new and efficient method for the stabilization of L-proline moieties on magnetic nanoparticles in order to prepare a novel magnetic recyclable organocatalyst for application in organic transformations. The catalytic activity of this heterogeneous organocatalyst was evaluated in the condensation reaction of indoles and aldehydes for the synthesis of bis(indolyl)methanes in water.

Organocatalysis has become a very considerable area of research, because it has emerged as a powerful methodology in organic synthesis.[1] As well, organocatalysis is essentially important since it affords a sustainable way to convert materials into precious chemicals in a cost-effective, proficient, and environmentally benign methods.[2] Moreover, a range of important reactions have been performed using organocatalyst systems.[3] This environmentally benign methodology has been made even greener by immobilization of the organocatalysts onto solid supports.[4] However, due to the decreasing in reactant diffusion rate to the surface of catalyst, the reactivity and selectivity of immobilized organocatalyst on a solid support are frequently decreased.[5] Fortunately, the aforementioned problem can be resolved to some extent by selecting the very small size ranges of the support. Thus, the resulted reactivity due to the homogeneous catalyst can be effective in the reaction progress.[6] Accordingly, because of nanometer size-range of nanoparticles which allow their surface areas to increase dramatically, these materials are reasonable potential candidate supports. Also, nanoparticles can disperse in solution to form emulsion and this action increases the diffusion rate of reactant to the surface of catalyst. Furthermore, reactants in solution have easy access to the active sites on the surface of nanoparticles because of their large surface-to-volume ratio.[7] Nevertheless, when the size of support is decreased to nanometer scale, a simple filtration method cannot overcome the big obstacle of catalyst separation from the reaction media.[8] Trying to find a solution to this problem, the efforts have been focused on magnetic recyclable supports.[9] Due to the magnetic nature of the catalyst, it could be recovered within a few seconds using an external magnetic field. Most importantly, the isolation of the final product can be possible by a simple decantation. In addition to these advantages, such catalysts also showed better selectivity, and superior stability when compared to their other supported and unsupported counterparts. There are various reported magnetically separable nano-organocatalysts for application in organic transformations.[10] On the other hand, L-proline and its derivatives have shown considerable catalytic efficiency in different organic transformations.[11] There are widespread interest to the development of new heterogeneous organocatalysts based on L-proline.[12] In this communication, in continuing of our previous works on L-proline-catalyzed reactions[13,14] we would like to report a new and easy access to a new magnetic nanoparticle-supported organocatalyst based on L-proline. Our strategy for the synthesis of L-proline-modified magnetic nanoparticles (LPMNPs) is shown in Scheme 1.



Scheme 1 Synthetic route for the preparation of LPMNP catalyst.

In this study, MNPs were prepared by co-deposition method using a procedure in the literature.[15] The synthesized MNPs, were coated by silica using a sol-gel process to obtain core-shell MNPs ($Fe_3O_4@SiO_2$).[16] The SiO_2 layer can prevent Fe_3O_4 core from aggregation, lead to simple surface functionalization. Anchoring the SiO_2 layer to the surfaces of Fe_3O_4 could provide Si-OH groups for fine chemical modification using available alkoxy silane materials [$(R_n\text{-}Si(OR)_{3-n}$]. Afterward, the $Fe_3O_4@SiO_2$ substrate was treated with trimethoxy(vinyl)silane to produce a vinyl MNP (VMNP) substrate. Subsequently, VMNP was oxidized using H_2O_2 to generate the MNP-oxiran (MNPO) material. The VMNP and MNPO materials are the key intermediates in our strategy. We believed that these materials (especially MNPO)

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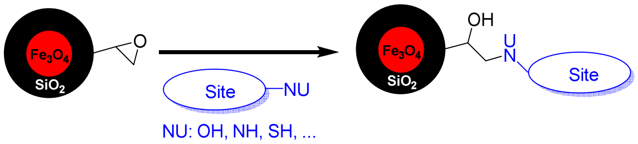
can open up a new direction in the synthesis of various heterogeneous catalysis and adsorption materials (Scheme 2).[14]



Scheme 2 Generation of catalytic sites on the MNPs surface using MNPO substrate

Ring-opening of oxiranes in the MNPO substrate with L-proline (in this study), was resulted the production of LPMNP catalyst. After preparation of the LPMNP catalyst, it was characterized using various techniques such as FT-IR, TGA, XRD, TEM, SEM, EDX, VSM and elemental analysis. Comparison between the FT-IR spectra of Fe_3O_4, $Fe_3O_4@SiO_2$, VMNP, MNPO, *N*-Boc-protected L-proline and the LPMNP catalyst, reveals some absorption bands which confirm the presence of L-proline moieties in the structure of the catalyst (ESI†, Fig. 1S). The TEM and SEM images of the synthesized catalyst were recorded and represented in Fig. 1a and 1b, respectively. According to TEM image and histogram (Fig. 1d), the average diameter of the synthesized LPMNPs based on the proposed procedure is estimated to be about 50 nm. Considering the SEM image (Fig. 1c), it is clear that the LPMNPs are regular in shape and approved in an approximately good arranged mode. These images also established this point that the LPMNPs are created with near sphere-shaped morphology. The histogram was anticipated according to the results obtained from the TEM and SEM images (Fig. 1d).

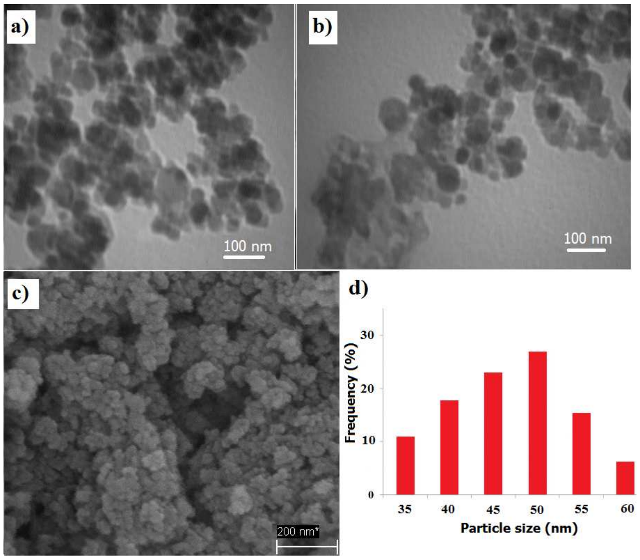


Fig. 1 A TEM images of two different positions of LPMNP catalyst particles (a & b). A SEM image of the LPMNP catalyst (c). A histogram which representing the size distribution of the LPMNP catalyst

The TGA curve of LPMNP catalyst (Fig. 2a) shows three main weight losses. The first one is accounted for adsorbed water in the structure of the catalyst (~4%). The seconded one which is occurred at ~150–280 °C is related to the decomposition of grafted L-proline from the silica substrate. This part of the thermogram reveals the amounts of supported L-proline on silica which is estimated to be ~6% (w/w). The reduction in the weight percentage of the catalyst at ~300–360 °C is related to decomposition of carbon chain from the surface of MNPs. So, the elevated temperature for grafted organic group removal indicates the high thermal stability for LPMNP catalyst which establishes the covalent bonding of these groups to the surface of MNPs. The amount of N percent in elemental analysis was 0.7, which demonstrates there is ~5 mol% of L-proline in the structure of LPMNP catalyst.

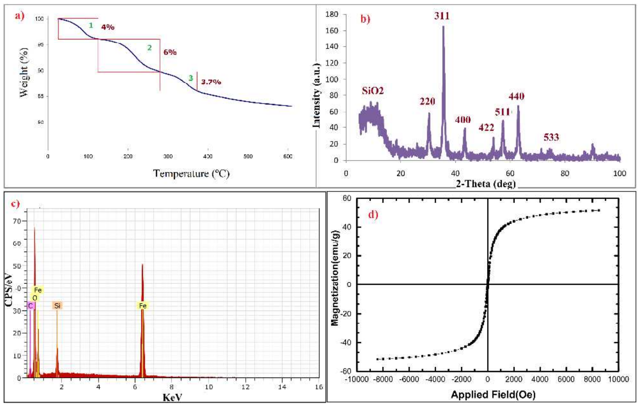
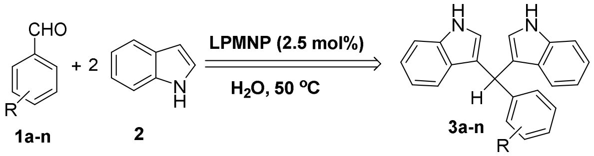


Fig. 2 A typical TGA curve from LPMNP catalyst (a). The XRD pattern of LPMNP catalyst (b). The EDX analysis of the LPMNP catalyst (c). The vibrating sample magnetometer (VSM) of the LPMNP catalyst (d).

According to the XRD patterns of LPMNP catalyst (Fig. 2b), the strongest peaks of the XRD pattern correspond to SiO_2, demonstrating that the core-shell structure of material. The peaks are indexed as the (220), (311), (400), (422), (511), (440), and (533) planes of the Fe_3O_4 nanoparticle.[17] The EDX from the obtained LPMNP catalyst (Fig. 2c) presented the presence of the expected elements in the structure of the catalyst. The magnetic properties of the catalyst was explored at room temperature using a vibrating sample magnetometer (VSM) (Fig. 2d). Based on magnetization curve, the magnetization is saturated up to 50 emu g^{-1} at an applied field of 8300 Oe, with an almost unimportant coercivity.

After preparation and characterization of the LPMNP catalyst, its catalytic activity was evaluated in a condensation reaction between 1*H*-indole and aldehydes for the preparation of bis(indol-3-yl)methanes[18] under green conditions. To achieve appropriate conditions for the synthesis of bis(indol-3-yl)methane derivatives using LPMNP catalyst, we tested the reaction of benzaldehyde and indole as a simple model substrate in various conditions (ESI†, Table. 1S). Thus, a simple system including LPMNP (2.5 mol%) and H_2O at 50 °C was chosen as the optimized reaction conditions (Scheme 2).



Scheme 2 General strategy for the synthesis of bis(indol-3-yl)methanes in the presence of LPMNP catalyst

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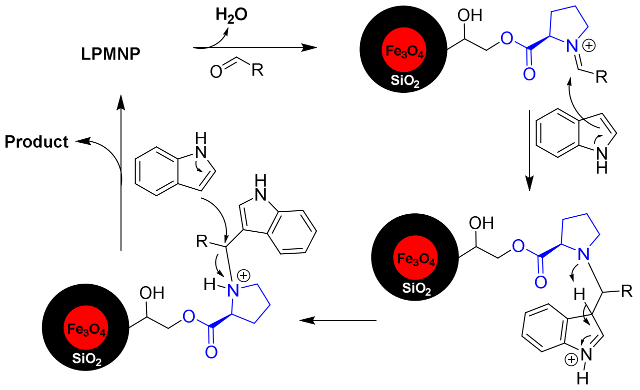
It is established that condensation between different aldehydes and 1*H*-indole (2) in water at 50 °C (Table 1) produces bis(indol-3-yl)methanes in good to excellent yields over LPMNP catalyst. The obtained products are characterized by ^{1}H, ^{13}C NMR, mass and elemental analysis and the data are given in ESI.

Table 1. Synthesis of bis(indol-3-yl)methanes using LPMNP catalyst[a]

Entry	R	Product	Time (min)	Yield (%)[b]
1	C_6H_5	**3a**	60	94
2	2-OH-C_6H_4	**3b**	90	80
3	4-OH-C_6H_4	**3c**	90	83
4	3-OH-C_6H_4	**3d**	90	85
5	4-OMe-C_6H_4	**3e**	60	92
6	4-OMe-3-OH-C_6H_3	**3f**	60	81
7	4-Me-C_6H_4	**3g**	60	92
8	3,4-F-C_6H_3	**3h**	75	93
9	3-CN-C_6H_4	**3i**	75	91
10	3-NO_2-C_6H_4	**3j**	90	90
11	4-NO_2-C_6H_4	**3k**	90	95
12	2-NO_2-C_6H_4	**3l**	90	90
13	2-Cl-C_6H_4	**3m**	75	88
14	4-Cl-C_6H_4	**3n**	75	89

[a] Reaction conditions: LPMNP (0.05 g, 2.5 mol%), H_2O (2 mL), aldehyde (1.0 mmol) and indole (2.1 mmol). [b] Isolated yield.

In view point of mechanism, activation of the aldehyde can be achieved by grafted L-proline on the surface of MNPs via the iminium formation (Scheme 3).



Scheme 3 Proposed reaction mechanism for the preparation of bis(indol-3-yl)methanes in the presence of LPMNP catalyst via iminium formation

For practical applications of this heterogeneous organocatalyst, the level of reusability was also evaluated. The catalyst could be reused for at least 8 times without any treatment (ESI†, Table. 2S). The elemental analysis of the catalyst after 8 cycles of reusability has shown that only a very small amount (~ 0.5%) of the L-proline moiety was removed from the magnetic substrate. To confirm the integrity in morphology of the particles after recycling runs, the recovered catalysts was also characterized using TEM (ESI†, Fig. 2S). The TEM image of the catalyst showed that the morphology and size of the catalyst after recycling 8 times does not change significantly. The results confirmed that the supported L-proline on the MNP substrate provides the high catalytic activity without leaching of a significant quantity of L-proline in the reaction media.

In conclusion, a simple and practical synthetic strategy for the synthesis of a novel MNP-supported organocatalyst based on L-proline has been developed. The catalytic usefulness of this magnetic recyclable organocatalyst was evaluated in the condensation reaction of aldehydes and 1*H*-indole for efficient synthesis of bis(indolyl)methanes in water. This is the first example of magnetic recyclable organocatalyst based on L-proline which prepared using the reaction of L-proline with MNP-oxiran. We anticipate that the MNP-oxiran material opens up a new direction for the development of new magnetic recyclable organocatalysts. Also, the LPMNP catalyst provides great promise toward further useful applications in other organic transformations in the future.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental procedures, recycling tests of LPMNP, and copy of ^{1}Hand ^{13}C NMR data for the synthesized products along with the spectral data. See DOI: 10.1039/b000000x/

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