Strategic Design of Silica-supported Enantioselective Organocatalyst for Asymmetric Aldol Reaction: An Economical and Sustainable Approach

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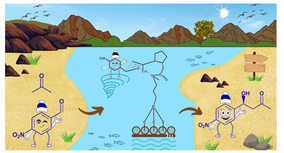
Abstract To graft proline on a silica support, a single-step reaction was carried out between L-proline methyl ester and N-methylaminopropyl silica. This procedure was carried out without the use of any protective groups for the proline amine functional group and any pricey organic substrate. The resulting catalyst was characterized by ^{13}C CP MAS NMR, X-ray diffraction, High-resolution transmission electron microscopy, BET analysis, elemental analysis, and FTIR spectra. The characterization results show that organic amine is efficiently attached to the mesoporous silica surface without affecting the support structure. The catalyst was tested for the asymmetric aldol reaction, which achieved conversions of up to 100% and enantioselectivity (ee)>99%. Filtration is used to effortlessly separate the prepared catalyst from the reaction mixture. For seven runs, no drop of catalytic activity was found, indicating excellent reusability and recyclability. In catalytic investigations, no extra organic solvent was used, making the total catalytic studies cost-effective and environmentally friendly.

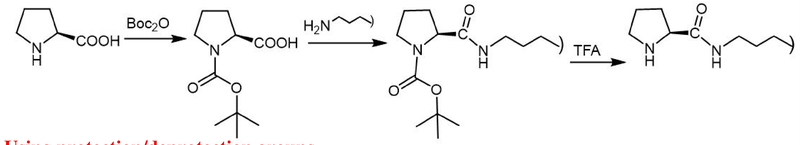


Keywords Organocatalysis; Silica-supported L-proline; Asymmetric aldol reaction; Mesoporous silica.

Synthesis of catalyst

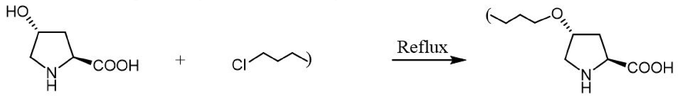
Previous works :

I) This method reported by Z. An et al.



- **Using protection/deprotection groups**

II) This nethod reported by A. A. Elmekawy et al.



- **Using very expensive organic substrate**

Present work :

- **Without use of protection/deprotection groups**
- **No use of pricey organic substrate**

Characterization

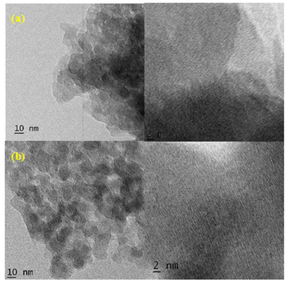


Fig. 1. HR-TEM image (a) pure silica (b) L-proline-(3°amine)-*f*-SiO_2

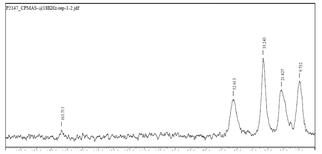


Fig. 4. 13C CP MAS NMR spectra of L-proline-(3°amine)-*f*-SiO_2

Sample	Surface area/m^2 g^{-1}	Pore volume/cm^3 g^{-1}	Average pore diameter/nm
Pure silica	355.49	0.66	6.0
CH_3NH-*f*-SiO_2	197.03	0.30	4.7
L-proline-(3°amine)-*f*-SiO_2	184.12	0.30	5.6

Table 1. Textural Parameters of catalysts

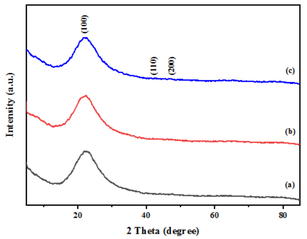


Fig. 2. XRD patterns (a) pure silica (b) CH_3NH-*f*-SiO_2 (c) L-proline-(3°amine)-*f*-SiO_2.

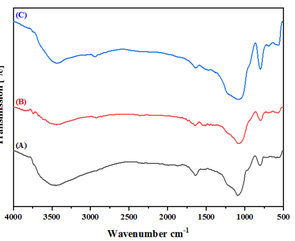


Fig. 3. FTIR spectra of (A) pure silica (B) CH_3NH-*f*-SiO_2 (C) L-proline-(3°amine)-*f*-SiO_2.

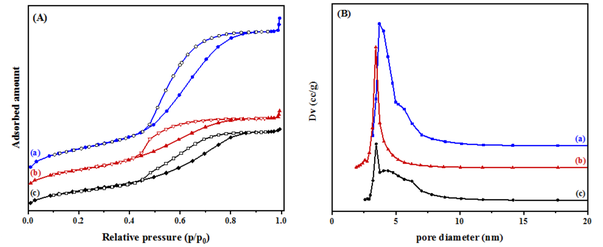
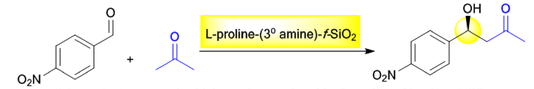


Fig. 5. (A) N_2 adsorption–desorption isotherms of (a) pure silica (b) CH_3NH-*f*-SiO_2(c) L-proline-(3°amine)-*f*-SiO_2 (B) BJH pore size distributions of (a) pure silica (b) CH_3NH-*f*-SiO_2 (c) L-proline-(3°amine)-*f*-SiO_2.

Catalytic Activity



Scheme 1 : Asymmetric aldol reaction catalyzed by L-proline-(3°amine)-*f*-SiO_2.

Table 2. Effect of temperature on asymmetric aldol reaction.

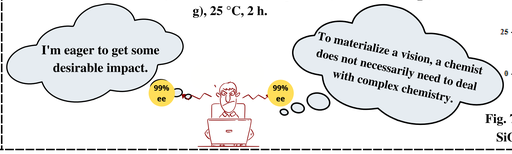
Entry	Temperature/°C	Conversion (%) [a]	ee (%) [b]
1	0°C	100	97.48
2	25°C	100	99.10
3	RT (33°C)	100	95.56
4	50°C	100	89.11

a) Conversion determined by normal HPLC analysis, b ee determined by chiral-phase HPLC analysis (Chiralpak OJ-H).

Table 3. Recyclability data of the direct asymmetric aldol reaction.

Entry	Conversion (%) [a]	ee (%) [b]
0	100	99.10
1	100	98.45
2	100	98.39
3	100	97.92
4	100	97.73
5	100	97.52
6	100	97.26
7	96.48	95.97
8	95.88	95.34
9	95.39	94.85

a) Conversion Determined by normal HPLC analysis. b ee Determined by chiral-phase HPLC analysis (Chiralpak OJ-H); Reaction condition: 4-nitrobenzaldehyde (1 mmol), acetone (10 mL), L-proline-(3°amine)-*f*-SiO_2 (0.5 g), 25 °C, 2 h.



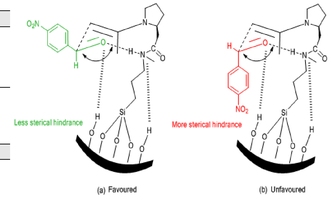


Fig. 6. A plausible reaction pathway for the asymmetric aldol reaction using L-proline-(3°amine)-*f*-SiO_2.

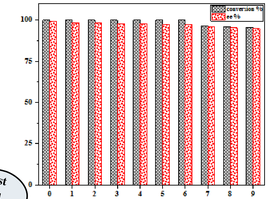


Fig. 7. Recyclability test of L-proline-(3°amine)-*f*-SiO_2 catalyst over asymmetric aldol reaction.

Conclusion

In the concluding remark, for the first time, we have executed a ground-breaking strategy in the development of an inexpensive route for the synthesis of L-proline chiral scaffold tethered onto the silica matrix avoiding the protecting/ deprotecting steps. The as-synthesized catalyst was weigh-up against the asymmetric aldol reaction with no use of redundant organic solvent, showing unprecedented activity with 100% conversion and (ee) > 99% enantioselectivity. Moreover, the as-synthesized catalyst was effortlessly recycled seven consecutive times with absolutely zero loss of activity as well.

Acknowledgments

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References

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2. An, Z., Guo, Y., Zhao, L., Li, Z. & He, J. - Proline-grafted mesoporous silica with alternating hydrophobic and hydrophilic blocks to promote direct asymmetric aldol and Knoevenagel–Michael cascade reactions. ACS Catal. 4, 2566–2576 (2014).