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PAPER

An efficient biomaterial supported bifunctional organocatalyst (ES-SO_3^- $C_5H_5NH^+$) for the synthesis of β-amino carbonyls

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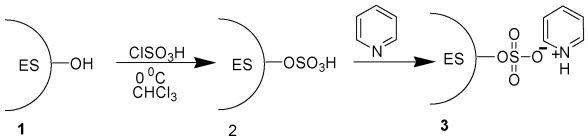
A biomaterial supported organocatalyst, readily synthesized by the reaction of chemically modified sulfonic group containing expanded corn starch with pyridine exhibited excellent catalytic activity for the synthesis of β-amino carbonyls in excellent yields *via* aza-Michael addition of amines to electron deficient alkenes. A remarkable enhancement in the reaction rates was observed with the prepared bifunctional organocatalyst in comparison to the either starch grafted sulfonic acid or the corresponding homogeneous pyridinium *p*-toluenesulfonate.

Introduction

Our future challenges in resources, environmental and economical sustainability need the development of more efficient and atom economic technologies in chemical industry. Presently, the considerable depletion in the availability of non-renewable organic feedstocks is continuously focusing our attention towards the utilization of renewable resources for the sustainable development of our society.[1] Expanded corn starches due to their high surface area and pore volumes have emerged to be promising materials and their uses in catalysis is a key enabling area for the development of new and improved processes for chemical reactions.[2] Organocatalysis, which involves the use of small organic molecules to catalyze organic reactions, is another step forward towards developing the green chemical synthesis.[3] In contrast to the conventional catalysts, these organic catalysts are easily available, more stable to air and water, easy to handle, less toxic, and can promote an organic reaction by several activation modes. On the other hand, immobilization of these organic molecules, which allows the advantages of being their facile recovery and their repeated use with retaining their catalytic activity, is gaining ever increasing interest in current years.[4] In this context, a variety of organic and inorganic materials have been widely used as supports for the immobilization,[5] whereas, to the best of our knowledge there is no report on the use of biomaterial supported organocatalysts for organic transformations. Among the known reactions, the formation of new carbon-heteroatom bonds *via* aza-Michael addition is one of the important transformations in organic chemistry. These aza-Michael adducts are versatile synthetic intermediates and have been widely used in the synthesis of a variety of biologically active natural products, chiral auxiliaries, antibiotics, and other nitrogen containing molecules.[6] In contrast to the many improved protocols using metal based Lewis acids,[7] boric acid/H_2O,[8] ionic liquids either alone[9] or in conjunction with $Cu(acac)_2$,[10] quaternary ammonium salt,[11] β-cyclodextrin in H_2O,[12] PEG[13] and H_2O,[14] the organocatalytic version of this reaction are relatively less explored. Since, most of the known organocatalysts are based on the secondary amines, resembling to the nucleophiles in the aza-Michael addition and therefore make the reaction of less synthetic importance. Recently, few reports dealing with the use of tributylphosphine,[15] nano-organocatalysts,[16] bifunctional thioureas[17] have been reported for this reaction. However, the major limitations of these methods such as homogeneous nature, longer reaction times and moderate yield of the products, leaving the scope for further development in this area. Therefore we decided to develop an environmentally benign, economical, easily recoverable, and reusable bifunctional organocatalyst to further extend the area of organocatalytic aza-Michael reactions.

In the present paper we report a cost effective, environmentally benign, easily accessible, recyclable and highly efficient pyridinium-based organocatalyst grafted to the chemically modified expanded starch (Scheme 1) for the synthesis of β-aminocarbonyls by aza-Michael reaction of amines to electron deficient alkenes under mild reaction conditions (Scheme 2). A remarkable enhancement in the reaction rates could be observed than the corresponding pyridinium-based homogeneous pyridinium *p*-toluenesulfonate



Scheme 1 Synthetic approach of organocatalyst **3**.

Results and discussion

Initially, we synthesized the expanded starch by following a literature procedure with some modifications.[2a] For the

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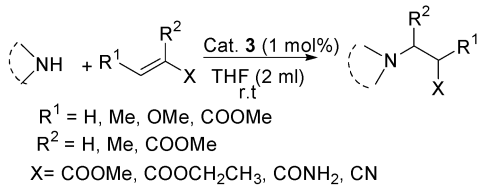


Scheme 2 Organocatalytic aza-Michael addition.

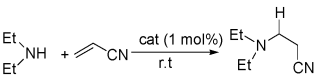
expansion process, normal corn starch was initially heated in water under reflux for 5–6 h followed by continuing the stirring at room temperature overnight. The resulting gel was separated by centrifugation and washed several times with ethanol. Finally, the obtained solid was stirred at room temperature in ethanol for 5–6 h. The white solid was filtered off and dried at room temperature. The surface area of the expanded material was found to be 105 m^2 g^{-1}. The resulting expanded starch (ES) was utilized for further chemical modifications to synthesize the desired starch supported pyridinium-based organocatalyst as shown in Scheme 1.

The drop-wise addition of chlorosulfonic acid into the stirred suspension of expanded starch (ES) **1** in at 0 °C, resulting in the formation of the sulfonated starch material (ES-SO_3H) **2**. The presence of sulfonic acid group was confirmed by the IR spectroscopy as it revealed characteristic bands at 3420–3242 (b, OH) and 1096 cm^{-1} (S═O). Further the remarkable decrease in the values of BET surface area from 105 m^2 g^{-1} to 30 m^2 g^{-1}, established the high loading of the sulfonic acid groups to the support. The loading of the acidic H^+ was determined by acid–base titration and was found to be 0.89 mmol g^{-1}. In the next step, the obtained support **2** was treated with pyridine in dry THF to obtain the desired bifunctional organocatalyst **3**. The presence of characteristic bands such as (3384; NH), 1641, 1520, 1491 (aromatic C–C), 1154, 1081 (S═O) cm^{-1} in the IR spectrum revealed the successful formation of the catalyst **3**. Further, the loading of the organanocatalyst was found to be 0.82 mmol g^{-1} as determined by the value of nitrogen content in elemental analysis. The thermal stability of the prepared organocatalyst **3** was found to be good and it did not show any decomposition up to 250 °C in TGA analysis.

Thecatalytic potential of the prepared catalyst **3** was tested for aza-Michael addition reaction as shown in Scheme 2.

In a typical experimental procedure, a mixture containing dibenzyl amine (1 mmol), acrylonitrile (1.2 mmol) and 3 (1 mol%) in dry THF (2 ml) was stirred for 20 min at room temperature. After completion, the catalyst was recovered by decantation, washed with THF, dried at room temperature and reused as such for subsequent runs. The combined organic layer was concentrated and the obtained crude product was purified by column chromatography. Next we compared the catalytic efficiency of the supported catalyst **3** with its corresponding mono-functional biomaterial supported sulfonic acid, pyridine and also with the homogeneous bifunctional catalyst pyridinium *p*-toluenesulfonate (PTTS) under similar reaction conditions. The results of these experiments are presented in Table 1. In the absence of catalyst, no reaction occurred under the described reaction conditions (Table 1, entry 1). It is worthy to mention that in the presence of either sulfonated expanded starch (ES-SO_3H) or pyridine alone, the reaction between dibenzyl amine and acrylonitrile was found to be very slow and did not reach completion as

Table 1 Results of various optimization experiments[a]



Entry	Reaction time (min)	Yields (%)[b]
1	60	—[c]
2	35	65[d]
3	50	35[e]
4	35	72[f]
5	35	84[f]
6	30	85[f]
7	25	92[f]
8	20	96[g]
9	35	68[h]

[a] Conditions: substrate (1 mmol), nucleophile (1.2 mmol), catalyst (1 mol%). [b] Isolated yields. [c] Without catalyst. [d] Using expanded starch supported SO_3H as catalyst (10 mol%). [e] By using pyridine as catalyst. [f] Catalyst was prepared by varying the concentration of pyridine from 10, 20, 40, 60% to SO_3H. [g] By using **3** (1 mol%) as catalyst. [h] By using homogeneous pyridinium-*p*-toluenesulfonate as catalyst.

shown in the Table 1, entry 2–3. Further, to see the effect of the pyridine in accelerating the reaction rates, we prepared a series of organocatalysts by varying the amount of pyridine from 10%, 20%, 40%, 60% relative to the SO_3H group in the reaction mixture containing supported sulfonated expanded starch (ES-SO_3H). We then studied the catalytic efficiency of the prepared catalysts for the reaction between dibenzyl amine and acrylonitrile under similar reaction conditions. Results of these experiments are summarized in Table 1 (entries 4–7). The rate of the reaction was found to increase as the amount of the pyridine increases, the use of 1 : 1 molar ratio of SO_3H and pyridine provided best results (Table 1, entry 8), however, excess use of pyridine did not improve the reaction to any significant extend. Similarly, in case of the homogeneous pyridinium salt of *p*-toluenesulfonic acid (PTTS), the reaction proceeded slowly and provided moderate yield of the desired product (Table 1, entry 9).

Next, we extended the scope of the reaction by using a variety of primary and secondary amines with various α,β-unsaturated compounds such as acrylamide, methyl acrylate, acrylonitrile *etc.* under the described reaction condition to afford corresponding β-amino carbonyl compounds. These results are presented in Table 2. All the reactants were efficiently converted to the corresponding β-amino carbonyl in excellent yields within 20–35 min. The method also worked well with substituted olefins such as methyl methacrylate, ethyl 2-methylacrylate, methyl 3-methoxyacrylate (Table 2, entries 4–6) and dimethyl fumerate (Table 2, entry 7) and afforded high product yields under described reaction conditions. However, the reaction was found to be very slow in case of trimethylsilyl 3,3-dimethylacrylate (Table 2, entry 8) and gave trace amount of the corresponding addition product, perhaps the steric factors are responsible for this reactivity. Among the various amines studied, secondary amines in general were found to be more reactive than primary amines. However, primary amines yielded mono-addition products selectively without any evidence for the formation of bis products as mentioned in several existing procedures. Aromatic amines such as aniline and *p*-anisidine were found to be less reactive and afforded poor product yield in longer reaction times (Table 2, entries 26–27). All the products were

Table 2 Aza-Michael addition of amines to α, β-unsaturated compounds[a]

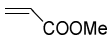
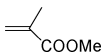
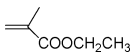
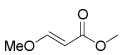
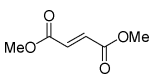
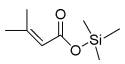
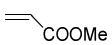
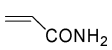
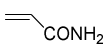
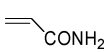
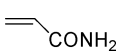
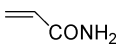
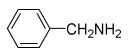
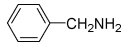
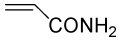
Entry	Amine	Michael acceptor	Reaction time (min)	Yields (%)[b]
1			20	96
2			30	95
3			30	92
4			60	90
5			60	87
6			45	92
7			20	96
8			90	trace
9			25	94
10			35	95
11			30	94
12			25	92
13			35	94
14	$nBuNH_2$		30	96
15	$nBuNH_2$		35	90
16			30	89
17			35	86
18			25	95
19			35	87
20			25	95
21			30	82
22			20	96

Table 2 *(Contd.)*

Entry	Amine	Michael acceptor	Reaction time (min)	Yields (%)[b]
23			25	95
24			30	91
25			35	92
26			180	65
27			160	70

[a] Conditions: amine (1 mmol), α,β-unsaturated compound (1.2 mmol), catalyst (1 mol%), THF (2 ml) at room temperature. [b] Isolated yields.

analyzed by GCMS and characterized by comparing their physical and spectral data (IR & ^{1}H NMR) with authentic compounds.

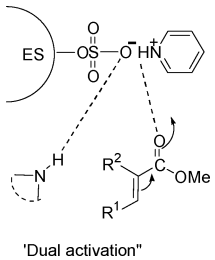
To check the recycling of the prepared material **3**, we studied the reaction of dibenzyl amine and acrylonitrile under described reaction conditions. After completion of the reaction, the catalyst could easily be recovered by decantation, washed successively with THF and dried. The recovered catalyst was used for the subsequent experiments (6 runs). The results of these experiments are shown in the Table 3. As shown in the results, no significant difference was obtained in the yield of the product and reaction time, establishing the efficient recycling of the synthesized catalyst. As suggested by one of the Referees, we repeated the recycling experiments by stopping the reactions after 5 min and recovered the catalyst by filtration. The conversion was determined by GCMS, these results are summarized in Table 3. In all cases we obtained 50–60% conversion in five minutes, indicating the consistent catalytic efficiency of the catalyst during recycling. Similarly, to check the leaching of the active sites from the catalyst support, we stirred the catalyst **3** for 5–6 h in dichloromethane and then catalyst was filtered off. The filtrate was charged with substrates and allowed the reaction under described reaction conditions. The reaction did not occur clearly indicating that there was no leaching occurred and the reaction is truly heterogeneous in nature.

Table 3 Results of recycling experiments using dibenzyl amine and acrylonitrile as substrates[a]

Run	Time (min)	Yield (%)[b]	Conv. (%)[c]
1	20	96	60
2	20	96	60
3	20	95	52
4	20	95	52
5	20	95	55
6	20	95	50

[a] Conditions as mentioned in the text. [b] Isolated yield. [c] Conversion was determined by GCMS after stopping the reaction in 5 min.

The exact mechanism of the reaction is not clear; we assume that the probable mechanism of the reaction may involving the activation of both α,β-unsaturated carbonyl compound and amine *via* hydrogen bonding with acidic site and basic site of the catalyst respectively.[18] This activation increases the electrophilic character of the β-carbon, which is subsequently attacked by the nucleophilic amine. The dual activation, resulting through the interaction of unsaturated carbonyl compound and amine with acidic and basic sites of the catalyst may be facilitating the reaction and enhancing the reaction rates (Scheme 3).



Scheme 3 The proposed role of catalyst *via* dual activation.

Conclusions

In summary, we have developed for the first time a cost effective, environmentally benign, biodegradable, highly efficient and recyclable biomaterial grafted pyridinium-based organocatalyst in a very simple manner for the synthesis of β-amino carbonyl compounds *via* aza-Michael reaction. The immobilized catalyst is found to be efficient with remarkable enhancement in reaction rates than the corresponding homogeneous pyridinium salt as well as starch immobilized monofunctional catalyst. Further, the biodegradable nature of the support, the recycling/reusability of the catalyst and the faster reaction rates make the method more environmentally friendly and will open a wide scope in developing sustainable chemistry.

Experimental section

General Experimental

All the solvents were commercially available and used as obtained. All the substrates were purchased from Aldrich and used as received. Chlorosulfonic acid was purchased from Acros Chemicals and used the fresh sample. Dichloromethane was distilled and dried before use. Pyridine was distilled and dried over KOH pellets before use. Pyridinium *p*-toulenesulfonate (PPTS) was purchased from Acros chemicals. The ^{1}H NMR Spectra were recorded on Bruker 300 MHz spectrometer. The IR spectra were recorded on a Perkin Elmer FTIR X 1760 instrument. Elemental analysis was done by using ASTM D-3828 (Kjeldhal method). GCMS analysis were done by high resolution GCMSD, EI, quadrapole mass analyzer, EM detector.

Synthesis of expanded starch supported organocatalyst 3

To a stirred mixture of expanded starch (5.00 gm) in dry dichloromethane chlorosulfonic acid (1.2 g, 10 mmol) was added dropwise at 0 °C during 3 h. After completion, the mixture was stirred for 3–4 h at room temperature. The obtained solid was filtered off and thoroughly washed with dichloromethane (3 × 30 ml) and dried at room temperature to obtain sulfonated expanded starch **2** as a white powder (5.2 g). The loading of the sulfonic acid groups or H^+ sites were determined by acid–base titration and was found to be 0.89 mmol g^{-1}. In the next step, the suspended mixture containing sulfonated expanded starch (ES-SO_3H) (5 g) in dry THF (20 ml) with dry pyridine (0.39 g, 5 mmol) and the resulting mixture was stirred for 2 h. The solid thus obtained was separated by filtration, washed with THF and dried first at room temperature and then under vacuum. The expanded starch supported (ES-$SO_3^-\cdot C_5H_5NH^+$) bifunctional catalyst **3** was obtained as a white solid in yield (94%, 4.3 g). The loading of the organic moiety to the support was calculated by nitrogen content as determined in elemental analysis and was found to be 0.82 mmol g^{-1}. IR (cm^{-1}): 3384, 2925, 1641, 1419, 1154, 1081, 931

Representative experimental procedure for aza-Michael addition

A reaction mixture containing amine (1 mmol), α,β unsaturated compound (1.2 mmol) and catalyst **3** (1 mol%) in dry THF (2 ml) was stirred at room temperature for the time as given in Table 2. The completion of the reaction was monitored by TLC (SiO_2). After completion, the catalyst was separated by filtration, thoroughly washed with THF, dried and reused for recycling experiments. The combined organic layer was concentrated under reduced pressure and the obtained crude product was purified by column chromatography using ethyl acetate/hexane (6 : 4) as eluent.

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