

Sulfonated polystyrene/montmorillonite nanocomposite as a new and efficient catalyst for the solvent-free Mannich reaction

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ABSTRACT

Sulfonated polystyrene/montmorillonite nanocomposite (OMMT/PS-SO₃H) was prepared and used as a novel, efficient and inexpensive heterogeneous acid catalyst in the one-pot reaction three-component Mannich reaction of ketones, aromatic aldehydes and amines under solvent-free conditions. The catalyst was characterized by XRD, SEM, TG, BET and FT-IR techniques. This method has advantages of high yield, moderate to excellent diastereoselectivity, mild condition, catalyst recyclability, and simple work-up procedure.

Keywords: Mannich reaction, β -amino carbonyl compound, OMMT/PS-SO₃H, Nano composite, Solvent-free.

1. Introduction

The Mannich reaction is an important carbon-carbon bond forming reaction in organic synthesis and one of the most widely utilized chemical transformations for constructing β -amino ketones and other β -amino carbonyl compounds, which in turn are important synthetic intermediates for various pharmaceuticals and natural products [1]. Mannich reactions using electrophilics, such as imines and stable nucleophiles, such as enolates, enol ethers and enamines, have been developed [2]. One of the efficient routes is to conduct a one-pot three-component approach that allowed a wide range of structural variations in the reactants aldehydes, anilines, and ketones to give Mannich products using an appropriate catalyst such as protic acids[3-5], Lewis acids [6-8] and organo-catalyst [9-11] in hazardous solvents. Trogers [12], ionic liquids [13], Fe(Cp)₂PF₆ [14] and Cu-nanoparticles [15] have also been found to catalyze this reaction.

Recently, nanocomposites composed of polymers and layered silicates (PLSN) have attracted considerable attention from both basic research and commercial applications. The *in-situ* polymerization is the most powerful technique to produce polymer nanocomposites with good distribution and dispersion of the fillers inside polymer matrix [16]. Two types of PLSN are known:

intercalative and exfoliated. In the former case the polymer chains are inserted between the silicates layers. In the exfoliated case the silicate layers are uniformly dispersed over the polymer matrix and the stacks of the original clay structure are delaminated [17]. The most commonly used clay to prepare nanocomposite is from the smectite group such as montmorillonite (MMT) [18]. As a representative clay mineral is a sheet like clay, the main part of which is mineral Montmorillonite, a 2:1 type of aluminosilicate. The isomorphous substitutions require cations, denominated exchange cations, to compensate the negative charges in their laminar edges [19]. Organo Montmorillonite (OMMT) is produced by the exchange of organic cations for inorganic ions (e.g., K⁺, Na⁺, and Ca⁺²) on the layer surfaces of MMT. As a result, (OMMT) are powerful sorbents for non-ionic organic pollutants relative to natural Montmorillonite and other clays [20].

A variety of sulfonated polymers, such as sulfonated polystyrene [21], sulfonated polyphosphazene [22], sulfonated polyarylene ether sulfone [23] and sulfonated polyether ketone [24] have been utilized as catalyst in organic reactions. Some of disadvantages of these catalysts are low surface area, none complete heterogeneous characterization and probably leaching with organic solvents. In continuation of our research on the synthesis and application of solid acid catalyst [25] especially in solvent-free conditions [26] and also preparation and application of polymer-inorganic hybrid materials [27], we report in the present study the preparation and characterization of OMMT/Polystyrene-SO₃H nano-

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composite and its use in diastereo-controlled Mannich reactions as a novel and efficient solid acid catalyst under solvent-free conditions.

2. Experimental method

2.1. General

All chemicals were obtained from Sigma–Aldrich, Merck and were used without further purification. The used clay in this work is sodium Montmorillonite because of its natural abundance and low cost. The catalyst was characterized by X-ray diffraction (Bruker D8ADVANCE, Cu K_{α} radiation), FT-IR spectroscopy (Nicolet 400D in KBr matrix in the range of 4000–400 cm^{-1}), BET specific surface areas and BJH pore size distribution (Series BEL SORP MINI II), Thermal analyzer TGA (STA.TG Type 503; in a temperature range of 30–700°C and heating rate of 10°C/min in N_2 atmosphere) and SEM (Philips, XL20, SE detector). The products were characterized by ^1H and ^{13}C NMR spectra (Bruker DRX-500 Avance spectrometer), Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. All the products are known compounds and physical properties were compared satisfactorily with those reported in the literature.

2.2. Catalyst preparation

2.2.1. Preparation of the organomontmorillonite

For preparation of organomontmorillonite (OMMT), 0.2 g sodium montmorillonite (Na-MMT) with a cation exchange capacity (CEC) of 70 meq/100 was dispersed in 20 mL CTAB solution (2.36×10^{-3} mol. dm^{-3}) and the mixture was shaken for 24 h at room temperature. The organo modified clay was filtered, and dried at 100 °C in a vacuum oven. This organically modified MMT is denoted as OMMT.

2.2.2. Preparation of OMMT/polystyrene nanocomposite

The OMMT/polystyrene nanocomposite was obtained by in situ radical polymerization of styrene in the presence of OMMT. Styrene (1 mL) and OMMT (1 g) in 14 mL acetonitrile were placed in a round bottom flask. Benzoyl peroxide (0.16 g) was added and the mixture was heated at 80°C for 6 h while being stirred under N_2 gas. OMMT/polystyrene nanocomposite (OMMT/PS) was precipitated in ethanol/water (40:10), then filtered and washed with ethanol to remove residual monomers and dried at 80°C overnight.

2.2.3. Preparation of OMMT/polystyrene sulfonated nanocomposite

OMMT/Polystyrene was sulfonated using chlorosulfonic acid as a sulfonating agent. For this purpose, the OMMT/PS nanocomposites (1 g) were dispersed in 10 mL of acetonitrile in a 25 mL three-necked round-bottomed flask. Chlorosulfonic acid (11.0 mmol, 0.66 mL) was added dropwise into the mixture. The mixture was stirred for 24 h under N_2 atmosphere at room temperature. The sulfonated

OMMT/PS (OMMT/PS- SO_3H) was precipitated by the addition of the colloidal suspension to deionized water and stirred for 2 h. Then it was filtered and dried in an oven at 60 °C.

The acid site content of OMMT/PS- SO_3H nanocomposite was estimated by back titration using HCl (0.337 N). 10 mL of NaOH (0.130 N) was added to 0.1 g of this composite and stirred for 30 min. The catalysts were separated, washed with deionized water. The excess amount of NaOH was titrated with HCl (0.337 N) in the presence of phenolphthalein as indicator. The acid site content was 7.3 mmol g^{-1} .

2.4. General procedure for Mannich reaction

To a vigorously stirred mixture of benzaldehyde (1 mmol, 0.1 mL), aniline (1 mmol, 0.12 mL) and catalyst, OMMT/PS- SO_3H (0.06g) cyclohexanone (2.5 mmol, 0.26 mL) was added at room temperature under solvent-free conditions. The progress of the reaction was monitored by TLC. After completion of the reaction (45 min), ethyl acetate (20 mL) was added and the catalyst removed by filtration. After evaporation of the solvent, the crude product was purified by recrystallization in ethyl acetate: n-hexane mixed solvent or ethanol.

Selected Spectral data

(S)-2-((R)-(2-(phenyl (phenylamino)methyl) cyclohexanone mp: 128-129°C, IR (KBr, cm^{-1}): 1451 (CN), 3327(NH), 1597(ArH), 1703 (CO), ^1H NMR (500 MHz, CDCl_3 , ppm) δ : 7.4 (d, 2H, $J = 7.5$ Hz, ArH), 7.34 (t, 2H, $J = 7.5$ Hz, ArH), 7.2 (t, 1H, $J = 7.5$ Hz, ArH), 7.1 (t, 2H, $J = 7.5$ Hz, ArN), 6.6 (t, 1H, $J = 7.5$ Hz, ArN), 6.57 (d, 2H, $J = 8.5$ Hz, ArN), 4.77 (s, 1H, br), 4.68 (d, 1H, $J = 7.0$ Hz, CHNH), 2.78-2.82 (m, 1H, CH), 2.37-2.51 (m, 2H, CH_2), 1.7-1.9 (m, 6H, CH_2); ^{13}C NMR (125 MHz, CDCl_3 , ppm) δ : 213.3 (C=O), 147.6 (C- ArH), 142.1 (C, ArN), 129.4 (CH, m-ArH), 128.9 (CH, m-ArN), 127.7 (CH, p-ArH), 127.6 (CH, p-ArN), 117.9 (CH, ArN), 114.0 (CH, ArH), 58.4 (CH, CH-NH), 57.9 (C, C-C=O), 51.2 (CH), 42.1 (CH_2), 31.7 (CH_2), 28.3 (CH_2), 24.1 (CH_2).

(S)-2-((R)-(2-chlorophenyl) (phenylamino) methyl) cyclohexanone: mp: 136-137°C, IR (KBr, cm^{-1}): 3392 (NH), 1604 (ArH), 1696 (CO), 1437 (CN), ^1H NMR (500 MHz, CDCl_3 , ppm) δ : 7.62 (m, 1H, ArH), 7.33 (m, 1H, ArH), 7.10-7.25 (m, 4H, ArH, ArN), 6.69 (t, 1H, $J = 7.5$ Hz, ArN), 6.56 (d, 2H, $J = 8.0$ Hz, ArN), 5.04 (s, 1H, br), 4.95 (d, 1H, $J = 5.0$ Hz, CH), 2.94-3.0 (m, 1H, CH), 2.32-2.45 (m, 2H, CH_2), 1.71 - 2.19 (m, 6H, CH_2); ^{13}C NMR (125 MHz, CDCl_3 , ppm) δ : 213.7 (C=O), 146.5 (C, ArN), 141.5 (C- ArH), 129.2 (C, Ar-Cl), 128.9 (CH, p- ArH), 127.7 (CH, m-ArH), 127.6 (CH, m-ArH), 115.6 (CH, m-ArH), 115.2 (CH, p-ArN), 114 (CH, o-ArN), 58.6 (C, C-NH), 57.7 (C, C-C=O), 42.1 (CH_2), 31.7 (CH_2), 28.3 (CH_2), 24 (CH_2).

(S)-2-((R)-(4-bromophenylamino)(4-nitrophenyl) methyl) cyclohexanone: mp: 134-135°C, IR (KBr, cm^{-1}): 3321 (NH),

1497 (CN), 1700 (CO), 1602 (ArH); ^1H NMR (500 MHz, CDCl_3 , ppm) δ : 8.17 (d, 2H, $J = 10.0$ Hz, ArH), 7.59 (d, 2H, $J = 10.0$ Hz, ArH), 6.93 (d, 2H, $J = 8.5$ Hz, ArN), 6.45 (d, 2H, $J = 8.5$ Hz, ArN), 4.85 (s, 1H, br), 4.72 (d, 1H, $J = 5.5$ Hz CH), 2.58-2.80, (m, 1H, CH), 2.3-2.4 (m, 2H, CH_2), 1.77 - 2.04 (m, 6H, CH_2)

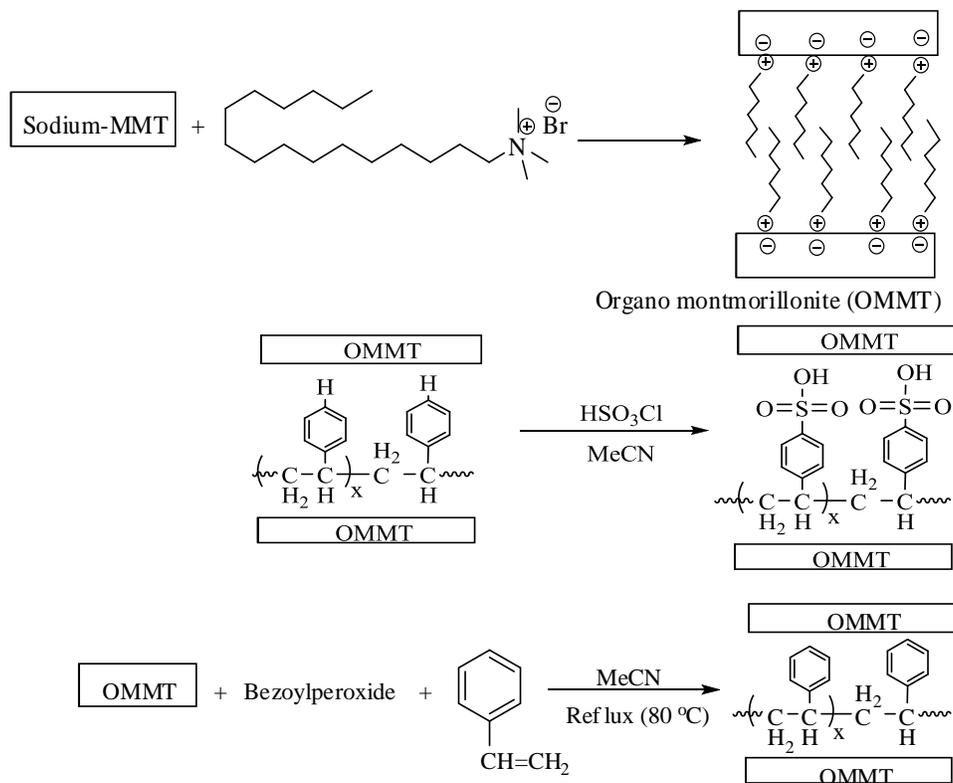
(S)-2-((R)-(4-bromophenylamino)(4-methoxyphenyl) methyl) cyclohexanone: mp = 132-133°C, IR (KBr, cm^{-1}): 3327 (NH), 1604 (ArH), 1703 (CO), 1494 (CN); ^1H NMR (500 MHz, CDCl_3 , ppm) δ : 7.30 (d, 2H, $J = 8.5$ Hz, ArH), 7.16 (d, 2H, $J = 8.0$ Hz, ArN), 6.87 (d, 2H, $J = 8.5$ Hz, ArH), 6.43 (d, 2H, $J = 7.5$ Hz, ArN), 4.59 (s, 1H, br), 4.53 (d, 1H, $J = 7.0$ Hz, CH) 3.80(s, 3H, CH_3), 2.70 (m, 1H, CH), 2.32-2.46 (m, 2H, CH_2), 1.71-1.92 (m, 6H, CH_2).

(S)-2-((R)-(4-bromophenyl)(4-chlorophenylamino) methyl) cyclohexanone: mp: 136-137°C, IR (KBr, cm^{-1}): 3321 (NH), 1602 (ArH), 1700 (CO), 1497 (CN); ^1H NMR (500 MHz, CDCl_3 , ppm) δ : 8.21 (d, 2H, $J = 8.5$ Hz, ArH), 7.65 (d, 2H, J

= 8.5 Hz, ArH), 7.21 (m, 2H, ArN), 6.44 (m, 2H, ArN), 4.83 (d, 1H, $J = 7.0$ Hz, CH), 4.59 (s, 1H, br), 2.8 (m, 1H, CH), 2.31-2.53 (m, 2H, CH_2), 1.57-2.01 (m, 6H, CH_2)

(S)-2-((R)-(2-methoxyphenylamino) (phenyl)methyl) cyclohexanone: mp: 136-137°C, IR (KBr, cm^{-1}): 3389 (N H), 1493 (CN), 1701(CO), 1604 (ArH); ^1H NMR (500 MHz, CDCl_3 , ppm) δ : 7.20-7.41 (m, 5H, ArH), 6.40-6.68 (m, 4H ArN), 5.1 (s, 1H, br), 4.92 (d, 0.43H, $J = 5.5$, CH syn), 4.75 (d, 0.57H, $J = 7.0$ Hz, CH anti), 3.9 (s, 3H, CH_3) 2.85-2.93 (m, 1H, CH), 2.35-2.59 (m, 2H, CH_2), 1.69-2.01 (m, 6H.)

(S)-2-((R)-(4-chlorophenylamino) (phenyl)methyl) cyclohexanone: mp: 117-119°C, IR (KBr, cm^{-1}): 3383 (NH), 1604 (ArH), 1701 (CO), 1493 (CN); ^1H NMR (500 MHz, CDCl_3 , ppm) δ : 7.20-7.38 (m, 5H, ArH), 6.90-7.05 (m, 2H, ArN), 6.40-6.49 (m, 2H), 4.89 (s, 1H, br), 4.77 (d, 0.44H, $J = 4.5$ Hz, CH syn), 4.57 (d, 0.56H, $J = 6.5$ Hz, CH anti), 2.30-2.41 (m, 3H), 1.80-2.04 (m, 4H, CH_2), 1.51-1.63 (m, 2H, CH_2)



Scheme 1.

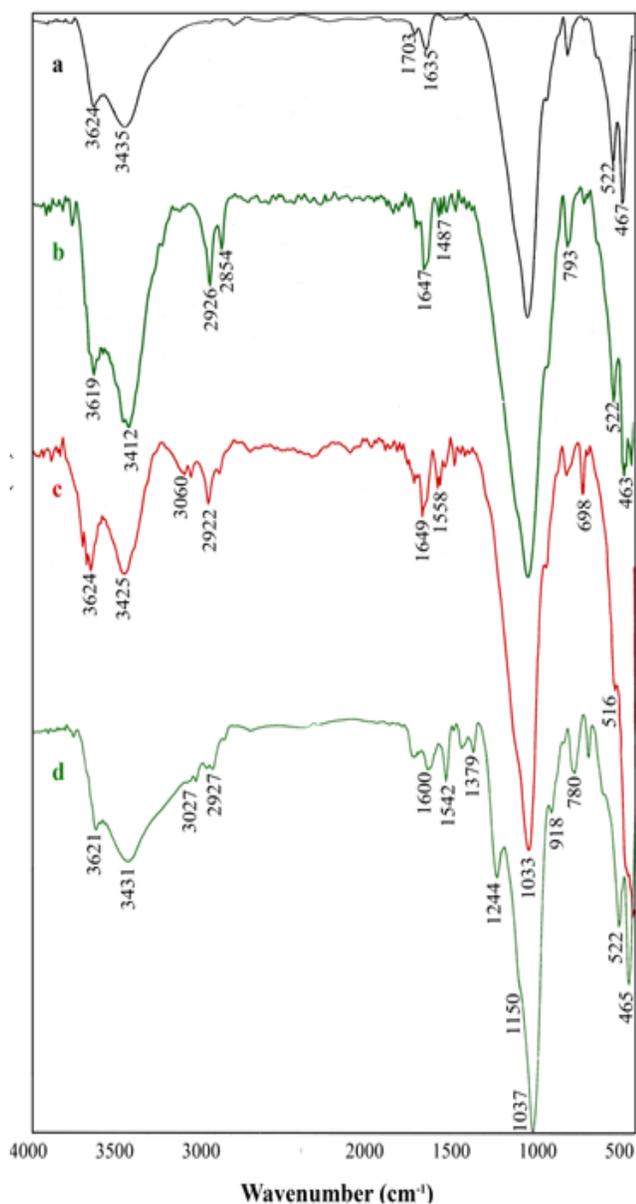


Fig. 1. FT-IR spectra for (a) MMT, (b) OMMT (c) OMMT/PS and (d) OMMT/PS-SO₃H.

3. Results and discussion

OMMT/PS-SO₃H nanocomposite was prepared in two steps: in the first step, OMMT/PS nanocomposite was prepared by in situ polymerization of styrene between organo montmorillonite layers and then in the second step, OMMT/PS-SO₃H was prepared via sulfonation of OMMT/PS with chlorosulfonic acid. The procedure to prepare sulfonated polystyrene organomontmorillonite is given in Scheme 1.

3.1. Characterization of the catalyst

Fig. 1 shows the FT-IR spectra of MMT (a), OMMT (b), OMMT/PS (c) and OMMT/PS-SO₃H (d) samples. Similar

to MMT, OMMT, OMMT/PS and OMMT/PS-SO₃H samples show a distinct absorption band around 1030 cm⁻¹ due to the Si-O stretching vibration in Si-O-Al (Fig. 1a,b,c,d). The presence of peaks at around 2800-3050 cm⁻¹ corresponds to the aliphatic and aromatic C-H stretching in OMMT/PS and OMMT/PS-SO₃H samples (Fig. 1c,d). Moreover, in the OMMT/PS-SO₃H spectrum the bands at 1150 and 1244 cm⁻¹ are related to grafted sulfonic acid groups on rings, which show the symmetric and asymmetric vibrations from S=O group (Fig. 1d) [28] (Ganguly, and Bhowmick, 2008).

Fig. 2 shows the powder XRD patterns of MMT (a), OMMT (b), OMMT/PS (c), and OMMT/PS-SO₃H (d) samples. All the samples show a reflection in the region $2\theta = 7^\circ$ to 9° . Furthermore, the prominent peak of OMMT, OMMT/PS and OMMT/PS-SO₃H samples shifts to lower angles compared to MMT, which is attributed to entering the organic compounds into the interlayer of MMT. The interlayer distance between silicate layers can be obtained from the basal reflection of the X-ray diffraction pattern (Table 1). As it can be seen, after modification of MMT with CTAB, the basal spacing is increased, which can be related to the incorporation of organic chains into the interlayer of MMT. Moreover, after in situ polymerization of PS in the presence of OMMT, the basal spacing is increased further. The spacing indicates that styrene can enter the interlayer space (Table 1, entries 2,3). Thus, the monomer can be polymerized between silicate layers and enlarge the basal spacing further.

The N₂ adsorption-desorption isotherm of pure MMT, OMMT, MMT/PS and MMT/PS-SO₃H samples are shown in Fig. 3. The isotherm is similar to the Type IV isotherm with H1-type hysteresis loops at high relative pressure according to the IUPAC classification, characteristic of materials with highly uniform size distributions. The specific surface areas were calculated using Brunauer-Emmett-Teller (BET) methods. Structural data of all these materials (BET surface area and total pore volume) were summarized in Table. 2. It is clear that OMMT/PS and OMMT/PS-SO₃H samples show lower specific surface areas and pore volumes in comparison with those of MMT and OMMT which can be related to the presence of polymer chain on the surface of the OMMT/PS and OMMT/PS-SO₃H. Although there are significant decreases in the surface area, OMMT/PS-SO₃H surfaces were not blocked by deposition of polymers (Table 2). Hence, OMMT/PS-SO₃H is suitable to act as a catalyst.

Table 1. d-Spacing.

Entry	Sample	d-Spacing(nm)
1	MMT	98
2	OMMT	120
3	OMMT/PS	125
4	OMMT/PS-SO ₃ H	130

Table 2. Porosity data of OMMT/PS-SO₃H (d).

Sample	BET. surface area (m ² g ⁻¹)	V _p (cm ³ g ⁻¹)	D _p (nm)
MMT	26.86	0.106	15.83
OMMT	30.94	0.114	14.78
OMMT-PS	0.54	0.0055	40.85
OMMT/PS-SO ₃ H	12.46	0.133	42.78

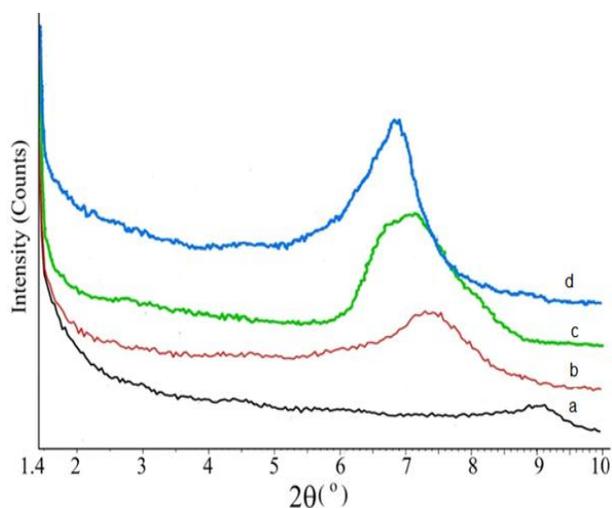
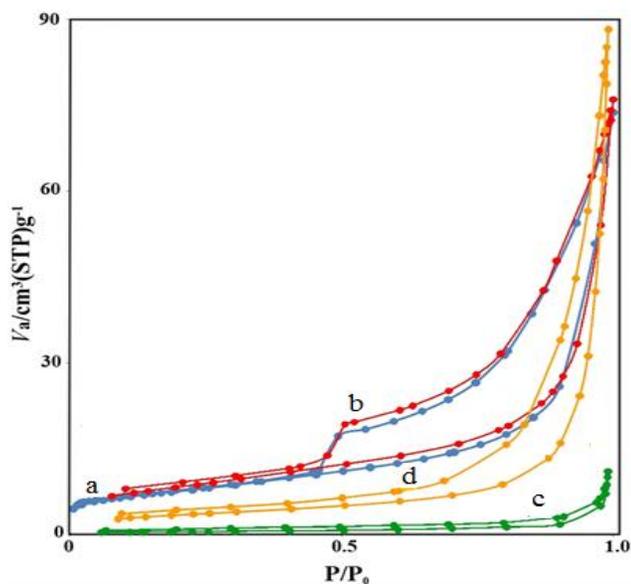
**Fig. 2.** Powder XRD patterns of (a) MMT, (b) OMMT, (c) OMMT/PS and (d) OMMT/PS-SO₃H.**Fig. 3.** Nitrogen adsorption/desorption isotherms for (a) MMT, (b) OMMT, (c) OMMT/PS and (d) OMMT/PS-SO₃H.

Fig. 4 gives the scanning electron microscopy (SEM) photographs of MMT, OMMT, OMMT/PS, and OMMT/PS-

SO₃H nanocomposite. It is obvious that before polymerization of styrene on the surface of MMT, it has lamellar and irregular plate-like shapes of hundreds of micrometers were very smooth with fluffy appearance, whereas after modification with CTAB and polymerization with styrene, it shows foliated structure and gain more rough surface (Fig. 4b,c). However, it can be seen that OMMT/PS nanocomposite has a globular pattern with non-uniform particle distribution. Nevertheless, although we can see some changes in the morphology of OMMT/PS-SO₃H, but these changes are minor and foliated structure of composite is preserved.

Fig. 5 presents the TGA curves of MMT, OMMT/PS, and OMMT/PS-SO₃H under N₂ atmosphere. The mass loss at temperature <150 °C (around 3.5%, w/w) is attributed to desorption of water present in the surfaces of MMT (Fig. 5a). Thermo analysis of OMMT/PS shows one step of mass loss (around 35%, w/w) which appeared at 350 °C which is attributed to degradation of the polymer and the degradation ended at 450 °C (Fig. 5c). However, for OMMT/PS-SO₃H nanocomposite, one weight loss step (around 18%, w/w) can be seen which is related to the degradation of the polymer (Fig. 5d). By comparing OMMT/PS and OMMT/PS-SO₃H curves, one can find that the weight loss of OMMT/PS-SO₃H has slower degradation rate than OMMT/PS (Fig. 5c,d).

3.2. Application of OMMT/PS-SO₃H for the synthesis of various β -amino carbonyl esters

The effect of different parameters on Mannich reaction was investigated. A summary of the optimization reactions is provided in Table 3. In our initial study, the reaction of benzaldehyde, aniline and cyclohexanone as a reaction model was investigated in different solvents. The reaction proceeded smoothly in polar organic solvents such as EtOH and CH₃CN which afforded higher yields than THF, CH₂Cl₂ (Table 3. entries 1-4). To improve the eco-friendliness of the reaction conditions, the same reaction was performed in water as solvent, but unfortunately only 40 % of product was obtained after 4 hrs (Table 3. entry 5). Finally the reaction was carried out under solvent-free conditions at room temperature; interestingly, it was completed in 45 min and afforded the desired product in 95% yield (Table 3. entry 6). The acceleration effect was probably attributed to a

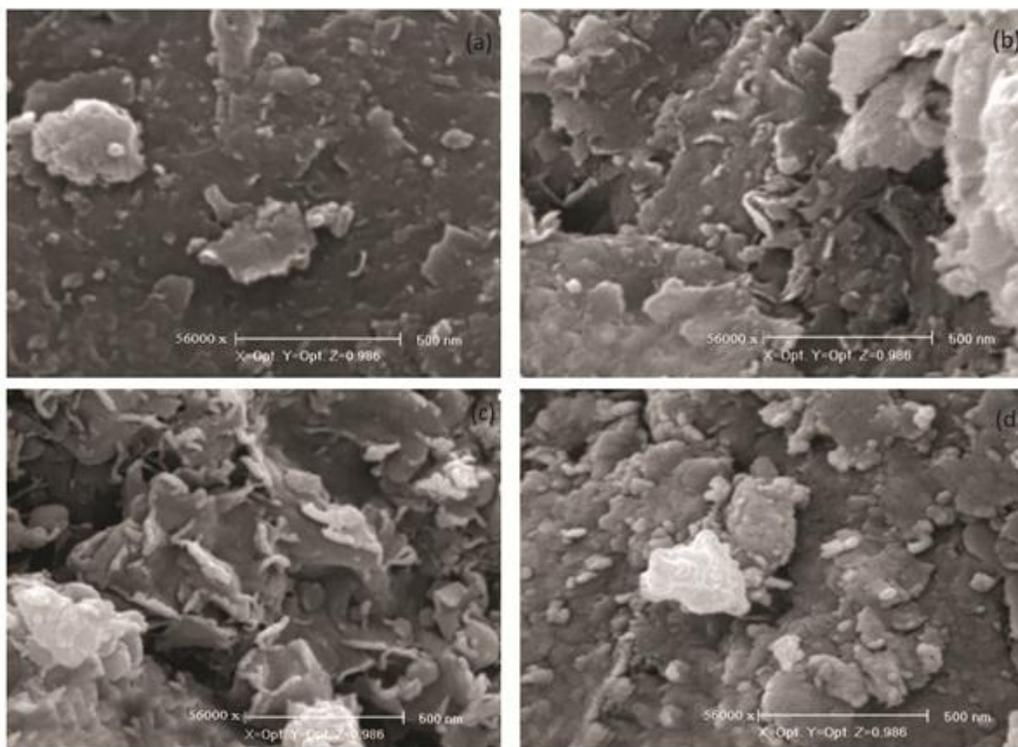


Fig. 4. SEM images of (a) MMT, (b) OMMT, (c) OMMT/PS and (d) OMMT/PS-SO₃H.

higher concentration of local reaction sites. Thereafter the reaction was carried out by varying the amount of reactants (Table 3. entries 6-8). The best result was obtained when the ratio of benzaldehyde, aniline and cyclohexanone was 1.0:1.0:2.5.

The variation of catalytic activity with the amount of catalyst on Mannich reaction was investigated using 0.02–0.1 g of the catalyst under solvent-free conditions (Table 3. entries 6 and 9-11). There was an upward trend of product

yield by raising catalyst amounts from 0.02 to 0.06 g. Higher amounts of the catalyst did not improve the yields to greater extent. The reaction was also studied in the absence of the catalyst. No formation of product was observed in this case. Effect of reaction temperature on the Mannich reaction was studied in the range of 25–80°C under solvent-free conditions. Increasing the temperature not only did not increase the yield, but also decreased the yield of desired product due to side reactions.

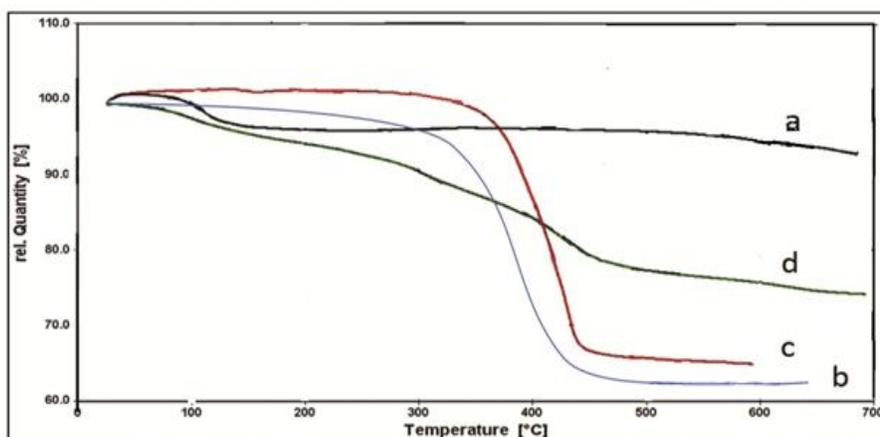


Fig. 5. TGA curve for (a) MMT, (b) PS, (c) OMMT/PS and (d) OMMT/PS-SO₃H.

Table 3. Mannich reactions of benzaldehyde (1 mmol), aniline (1 mmol) and cyclohexanone under different conditions.

Entry	Solvent	OMMT/PS-SO ₃ H (g)	Cyclohexanone (mmol)	Time (min)	Yield (%) ^a
1	EtOH	0.06	2.5	240	90
2	CH ₃ CN	0.06	2.5	240	87
3	CH ₂ Cl ₂	0.06	2.5	240	61
4	THF	0.06	2.5	240	65
5	H ₂ O	0.06	2.5	240	40
6	Solvent-free	0.06	2.5	45	95
7	Solvent-free	0.06	1.5	100	75
8	Solvent-free	0.06	2.0	100	85
9	Solvent-free	0.04	2.5	45	90
10	Solvent-free	0.02	2.5	45	75
11	Solvent-free	-	2.5	240	0

^aIsolated yield

With the optimized conditions in hand, the catalytic activity of OMMT/PS-SO₃H was investigated for the three component Mannich reactions of various aromatic aldehydes and amines to ascertain the generality and scope of this method (Scheme 2). The results are summarized in Table 4. It could be seen from Table 4 that the solvent-free Mannich reaction were proceeded smoothly at room temperature in the presence of OMMT/PS-SO₃H and the reactions were completed for periods ranging from 45 to 125 min to provide good to excellent yields (85–95%) of β-amino ketones. Compared with the other method and catalyst, the separation procedure of products and catalyst from the reaction mixture was easier. As can also be known from Table 4, aldehydes and amines with both electron-donating and electron-withdrawing substituents undergo the reaction with good to excellent yields and the anti-products were always formed as only or in a major scale, independent of the nature of substituent. The anti and syn isomers were identified by the coupling constants (*J*) of the vicinal protons adjacent to C=O and NH in their ¹H NMR spectra. *J* signal of anti isomer is higher than that of the syn one. The anti/syn ratio was determined by ¹H NMR judged by the intensity of the H₁ (Scheme 2).

A comparative study was done for the use of OMMT/PS-SO₃H with some of the reported methods for the Mannich reaction (Table 4). It is noteworthy to mention that this new method eliminates the use of organic solvents and the products were obtained after a simple work-up in relatively short reaction time.

3.3. Study of the reusability of the catalyst

Finally, we were interested in studying the reusability of the catalysts due to economical and environmental aspects. For this purpose the recovered catalyst from the experiment was washed with water (10 mL) and acetone (3×5 mL), then was dried in oven at 60°C and used in the Mannich reaction. The results show that the catalyst can be reused 3 times without any modification and no significant loss of activity/selectivity performance was observed.

4. Conclusion

In conclusion, we have found OMMT/PS-SO₃H nanocomposite as a noble organic-inorganic hybrid acid

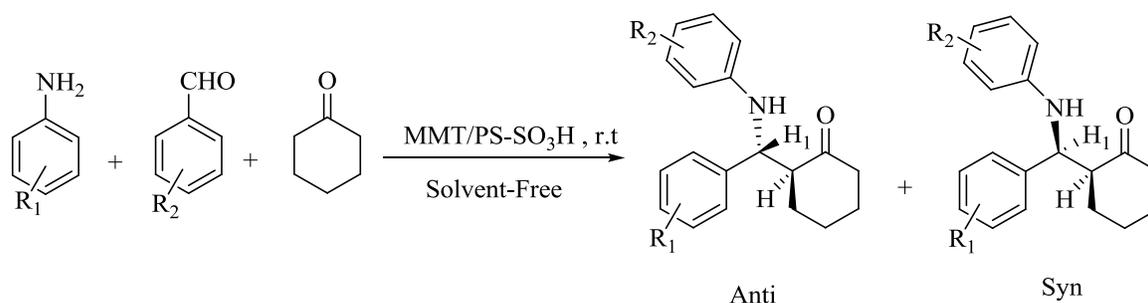
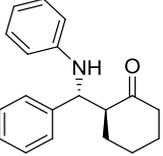
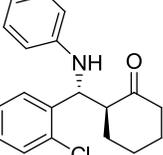
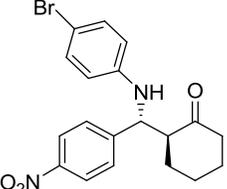
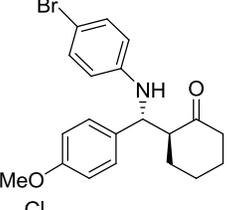
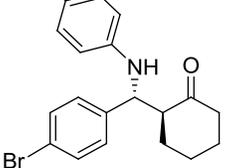
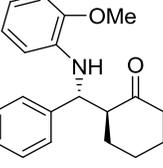
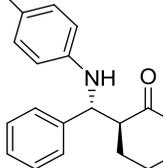
**Scheme 2.** Direct Mannich reactions of aromatic aldehydes, anilines, and cyclohexanone.

Table 4. Direct Mannich –type reaction of aromatic aldehydes, aniline and cyclohexanone catalyzed by OMMT/PS-SO₃H catalyzed.

Entry	R ¹	R ²	Product	Time (min)	Yield (%)	m.p./°C (Lit)	Anti/Syn
1	H	H		45	95	128-129 (129 ⁸)	100:0
2	2-Cl	H		70	95	136-137 (139 ²¹)	100:0
3	4-NO ₂	4-Br		75	85	134-135	100:0
4	4-OMe	4-Br		80	95	132-133 (131 ^{3f})	100:0
5	4-Br	4-Cl		80	95	136-137 (138 ⁸)	100:0
6	H	2-OMe		125	85	136-137 (137 ¹⁴)	57:43
7	H	4-Br		105	90	98-99 (98 ^{3f})	56:44

^aReaction conditions: benzaldehyde (1mmol), aniline (1mmol), cyclohexanone (2.5mmol), catalyst (0.06 g), room temperature, solvent-free.

catalyst for the synthesis of β -amino carbonyl compound under solvent-free conditions. Low cost, easy preparation, high thermal stability, high catalyst activity, good reusability and environmentally friendly are some of the catalyst advantages. Also, this procedure offers several advantages for the Mannich reaction such as low loading of catalyst,

mild conditions, high yields, clean reactions, which make it a useful and attractive methodology for organic synthesis. Furthermore, the existence of both organic and inorganic phase in this composite has had the critical effect on the catalytic activity. Further applications of this catalyst to other transformations are currently under investigation.

Table 5. Comparison of some reported Mannich reaction between aniline, benzaldehyde and cyclohexanone in the presence of different catalyst.

Entry	Catalyst	Solvent	Time (min)	Yield (%)	ref.
1	Silica Sulfuric Acid	C ₂ H ₅ OH	180	96	4
2	HClO ₄ -SiO ₂	C ₂ H ₅ OH	120	98	5
3	Troger Reagent	H ₂ O	120	98	12
4	Cu (Nono Particle)	CH ₃ OH	540	88	15
5	Zn(OTf) ₂	CH ₂ Cl ₂	240	93	29
6	Adenine-H ₂ O ₂	H ₂ O	360	95	30
7	OMMT/PS-SO ₃ H	Solvent-Free	45	95	This Work

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