

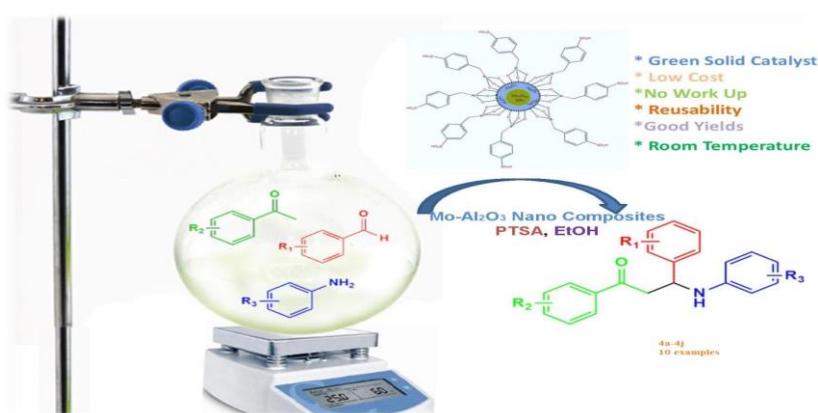
Full Paper | <http://dx.doi.org/10.17807/orbital.v14i4.16358>

A Heterogeneous, Highly Efficient, and Reusable Mo-Al₂O₃ Composites Based Organocatalyst for One Pot Three-Component Mannich Reaction for the Synthesis of β-aminocarbonyl Compounds

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We have successfully developed a new Mo-Al₂O₃/p-TSA organocatalyst which has improved the yield of the Mannich reaction. This protocol has the advantage of mild conditions, high yield, easy work-up, environmentally friendly procedure, and the solid catalyst was recycled. The catalyst was analysed by XRD, SEM, and EDS techniques. The synthesized Mo-Al₂O₃ composites were used in the presence of *p*-toluenesulfonic acid (*p*-TSA) conducts the one-pot three-component Mannich reaction and various β-amino ketones prepared with good yields and characterized by IR, ¹H, and ¹³C NMR Techniques.

Graphical abstract



1. Introduction

In synthetic organic chemistry, the Mannich reaction is a well-known reaction for forming carbon–carbon bonds, and this is the simple method for synthesizing β-amino carbonyl compounds, which are essential organic molecules in the production of numerous nitrogen-containing natural products and pharmacophore agents [1]. Three-component reactions have proven themselves to be an almost useful synthetic approach in combination with three reactants to generate new

products in a single step, in mild and economically valid procedures. The synthesized complex products along with the added advantages of atom efficiency and time-saving procedure. For these reasons, three-component approaches to Mannich reactions carried out in the presence of various catalysts and imines formed *in situ* have gained considerable importance [2].

A variety of catalysts have been used for this reaction

Keywords

β-amino ketones
Mannich Reaction
Mo-Al₂O₃ composites
FT-IR
NMR spectra
SEM

Article history

Received 21 Aug 2022
Revised 02 Dec 2022
Accepted 03 Dec 2022
Available online 02 Jan 2023

Handling Editor: Jamal Rafique

including Bronsted [3] and Lewis's acids [4] (organic or mineral), Lewis bases [5], ionic liquids [11], and others. However, catalysts that allow the reaction to be carried out under mild and green conditions are desired. For this reason, some Lewis's acids such as metal triflates [4b, 4i], chlorides [4c, 4f] and Bronsted [4d] and heteropoly acids [4g, 4h] were investigated in the catalysis of Mannich reaction. Bronsted and Lewis acids required long reaction times and are, therefore not effective catalysts, because they cause environmental pollution, corrosion of equipment, and other problems.

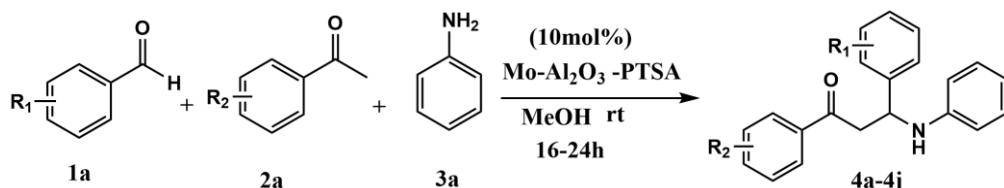
Recently, a lot of reports with solid supported [6], various acid and base catalysts [7-10] and transition metal salts [12-20], and rare earth metal salts [21-24] were used in the three component Mannich reaction successfully with different yields.

Considering above mentioned problematic and the necessity for a deeper investigation and development in Mannich reactions, the authors, describe a mild, convenient, green, and simple procedure for effective one-pot, three-component Mannich reaction of aniline with various benzaldehydes and acetophenones for the preparation of β -amino ketones using Mo-Al₂O₃ composites in *p*-toluenesulfonic acid as a catalyst.

2. Material and Methods

2.1 General

All reactions were performed at room temperature. High-speed stirring was carried out with magnetic force. All the chemicals used in this investigation were purchased from the Sigma-Aldrich, Alfa Aesar, and E. Merck chemical companies. Analytical thin-layer chromatography was performed with E. Merck silica gel 60F₂₅₄TLC plates. Visualization of the developed chromatogram was performed by UV light (254 nm). Column chromatography was performed on silica gel 200–300 mesh. Melting points of all β -amino ketones have been determined in open glass capillaries on the Mettler FP51 melting point apparatus. Infrared spectra (KBr, 4000–400 cm⁻¹) were recorded on OMNIC Fourier transform spectrophotometer. Bruker AV400 & 500 NMR spectrometer operating at 500 MHz & 100 MHz was used to record ¹H, ¹³C NMR spectra in CDCl₃ solvent, using TMS as internal standard.



Scheme 1. One pot synthesis of Mannich bases catalysed by Mo-Al₂O₃ composites in *p*-TSA.

Table 1. Table describing different examples of synthesized Mannich bases.

Entry	Aldehyde R ₁	Ketone R ₂	Amine R ₃	Product	Time(h)	Yield (%)
1					16	99

The SEM images of the catalysts were recorded on the Ametex SEM instrument. The Bruker AXS D8 Advance X-ray diffractometer was used to record the powder XRD pattern of the catalyst.

2.2 Preparation of Mo-Al₂O₃ composites

About 20 mL of ethanol was taken in a conical flask in which (5 mmol, 0.98 g) (NH₄)₂MoO₃ was added and sonicated up to a colloidal suspension. In another conical flask 20 mL of ethanol which contains (5 mmol, 0.51 g) basic alumina (Al₂O₃) added and sonicated up to the colloidal suspension, then the two solutions were added dropwise using a separatory funnel and stirred up to a homogeneous mixture using a magnetic stirrer for 24 h. After the Mo-Al₂O₃ composites were formed then, the mixture was sonicated to get a fine powder. The resulting solution was stirred for 4 h at room temperature. The solution was filtered with a Buckner funnel using Whatman filter paper at room temperature. The obtained solid was dried at 110 °C for 5 h in an oven and grind with a pestle and mortar to afford the Mo-Al₂O₃ composites as a fine powder. This catalyst was calcined at 400 °C for 2 h using a muffle furnace. The obtained Mo-Al₂O₃ composites were characterized by the powder XRD (X-Ray Diffraction), SEM (Scanning Electron Microscopy), and EDS (Energy Dispersive X-ray Spectroscopy) analysis.

2.3 Procedure for preparation of β -amino carbonyl compound

In the round bottom flask, 5 mL of methanol was taken as a solvent in that flask aniline (0.46 g, 5 mmol), benzaldehyde (0.53 g, 5 mmol), and acetophenone (0.6 g, 5 mmol) were added and stirred for 2 minutes then to the flask (0.5 mmol, 0.23 g) Mo-Al₂O₃-PTSA (10 mol%) (10% with respect to the weight of benzaldehyde) and *p*-Toluene sulphonic acid (5 mmol, 0.861 g) was added into the reaction mass. The reaction mixture was maintained with constant stirring at room temperature (30 °C) for 16–24 h (Scheme 1). At the end of the reaction, 20 mL of ethyl acetate was added to the reaction mixture and the catalyst was recovered from the reaction mass by filtration. The ethyl acetate layer was collected and coated with silica and did hexane/ethyl acetate column chromatography to get the pure product (Table 1).

2					16	98
3					16	91
4					24	95
5					20	98
6					20	90
7					24	98
8					24	98
9					24	91
10					24	95

The yield, physical constants, and complete spectroscopic characterization data of synthesized Mannich bases are summarized below.

1, 3-diphenyl-3-(phenyl amino) propane-1-one (4a): Yield, 99%; white solid; m.p. 162–163 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.96–7.89 (d, 2H), 7.60–7.53 (t, 1H), 7.50–7.40 (m, 4H), 7.35–7.30 (t, 2H), 7.25–7.20 (t, 1H), 7.15–7.06 (t, 2H), 6.73–6.64 (t,

1H), 6.61-6.55 (d, 2H), 5.00(t, 1H) 3.60-3.40(m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 198.28, 146.98, 142.97, 136.69, 133.44, 129.11, 128.83, 128.71, 128.22, 127.36, 126.37, 117.78, 113.81, 54.80, 46.32. IR (KBr): ν 3383, 3052, 2916, 1667, 1595, 1509, 1448, 1414, 1310, 1219, 1026, 988, 856, 767, 683 cm⁻¹.

3-(4-chlorophenyl)-1-phenyl-3-(phenyl amino) propan-1-one (4b): Yield, 98%; white solid; m.p. 115–116 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.93-7.91 (d, 2H), 7.60-7.53 (t, 1H), 7.50-7.40 (m, 4H), 7.35-7.30 (t, 2H), 7.21-7.10 (t, 2H), 6.80-6.73 (t, 1H), 6.53-6.42 (t, 2H), 5.00(t, 1H) 3.50-3.40(m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 197.90, 146.74, 141.56, 136.65, 133.54, 132.99, 129.17, 128.97, 128.75, 128.17, 118.09, 113.90, 54.23, 46.10. IR (KBr): ν 3394, 3051, 2921, 1677, 1599, 1510, 1487, 1448, 1316, 1217, 1013, 992, 862, 746, 689 cm⁻¹.

3-(4-fluorophenyl)-1-phenyl-3-(phenyl amino) propan-1-one (4c): Yield, 91%; light yellow solid; m.p. 110–112 °C; A white solid; ¹H NMR (500 MHz, CDCl₃) δ 8.10-7.85 (m, 5H), 7.83-7.71 (d, 2H), 7.70-7.60 (m, 3H), 7.55-7.40 (t, 2H), 7.11-7.05 (t, 1H), 6.80-6.53 (d, 1H), 6.53-6.42 (t, 2H), 5.00(t, 1H) 3.60-3.10(m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 197.55, 143.54, 138.17, 132.89, 131.20, 128.69, 128.52, 121.82, 116.28, 116.06, 115.78, 56.83, 47.12. IR (KBr): ν 3394, 3058, 2922, 1661, 1598, 1507, 1447, 1404, 1313, 1214, 1014, 979, 824, 750, 681 cm⁻¹.

3-(4-methoxyphenyl)-1-phenyl-3-(phenyl amino) propan-1-one (4d): Yield, 95%; colourless solid; m.p. 76–77 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.96-7.90 (d, 2H), 7.60-7.53 (t, 1H), 7.50-7.35 (m, 4H), 7.20-7.05 (t, 2H), 7.01-6.85 (t, 2H), 6.81-6.65 (t, 1H), 6.63-6.52 (t, 2H), 5.00(t, 1H) 3.81-3.7 (s, 3H), 3.56-3.35(m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 198.44, 158.78, 147.03, 136.74, 134.94, 133.41, 129.11, 128.70, 128.22, 127.47, 117.73, 114.19, 113.82, 55.26, 54.21, 46.35. IR (KBr): ν 3374, 3058, 2956, 1663, 1600, 1508, 1461, 1446, 1344, 1218, 1068, 944, 867, 746, 683 cm⁻¹.

1-phenyl-3-(phenyl amino)-3-(p-tolyl) propan-1-one (4e): Yield, 98%; light yellow solid; m.p. 140–142 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.93-7.81 (d, 2H), 7.56-7.43 (t, 1H), 7.40-7.31 (d, 2H), 7.30-7.20 (t, 2H), 7.05-6.99 (m, 4H), 6.58-6.55 (t, 1H), 6.49-6.47 (t, 2H), 5.00(t, 1H) 3.43-3.33(m, 2H), 2.30-2.20 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 198.36, 147.08, 139.98, 136.96, 133.38, 129.51, 129.11, 128.69, 128.22, 126.28, 117.72, 113.83, 54.53, 46.37, 21.07. IR (KBr): ν 3386, 3034, 2921, 1664, 1600, 1509, 1443, 1399, 1317, 1284, 1069, 989, 813, 743, 680 cm⁻¹.

3-(4-nitrophenyl)-1-phenyl-3-(phenyl amino) propan-1-one (4f): Yield, 90%; yellow solid; m.p. 160–162 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.30-8.17 (d, 2H), 8.07-8.05 (t, 1H), 7.93-7.54 (m, 4H), 7.49-7.45 (t, 2H), 7.14-7.11 (t, 2H), 6.74-6.71 (t, 1H), 6.56-6.52 (t, 2H), 5.00(t, 1H) 3.50-3.40(m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 197.19, 141.51, 141.08, 137.58, 136.35, 129.30, 128.94, 128.61, 128.14, 127.56, 125.80, 124.23, 124.08, 114.18, 54.53, 45.56. IR (KBr): ν 3400, 3049, 2927, 1671, 1597, 1509, 1445, 1405, 1339, 1287, 1099, 983, 848, 743, 684 cm⁻¹.

3-(4-tolyl)-3-(phenyl amino)-1-(4-chloro phenyl) propan-1-one (4g): Yield, 98%; white solid; m.p. 166–168 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.88-7.86 (d, 2H), 7.74-7.70 (t, 1H), 7.47-7.40 (d, 2H), 7.38-7.34 (t, 2H), 7.15-6.99 (m, 4H), 6.65-6.53 (t, 1H), 6.53-6.42 (t, 2H), 5.00(t, 1H) 3.50-3.40(m, 2H), 2.21-2.15

(s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 197.00, 141.40, 139.12, 136.69, 129.57, 128.95, 128.61, 126.37, 120.52, 118.20, 114.15, 54.76, 46.10, 21.11. IR (KBr): ν 3380, 3055, 2917, 1655, 1585, 1508, 1485, 1438, 1366, 1283, 1088, 984, 805, 738, 689 cm⁻¹.

1-(4-tolyl)-3-(phenyl amino)-3-(4-chloro phenyl) propan-1-one (4h): Yield, 98%; yellow solid; m.p. 165–166 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.86-7.85 (d, 2H), 7.75-7.63 (d, 2H), 7.55-7.40 (m, 4H), 7.35-7.28 (t, 2H), 7.25-7.20 (t, 2H), 7.18-7.13 (t, 1H), 5.00(t, 1H) 3.50-3.40(m, 2H) 2.34-2.32 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 189.76, 143.89, 142.92, 135.49, 129.59, 129.43, 129.26, 128.69, 122.53, 118.77, 54.23, 46.10, 21.74. IR (KBr): ν 3388, 3087, 2920, 1658, 1600, 1509, 1488, 1404, 1370, 1285, 1180, 1088, 984, 807, 747, 691 cm⁻¹.

3-(4-chlorophenyl)-1-(4-methoxyphenyl)-3-(phenylamino)propan-1-one (4i): Yield, 91%; light yellow solid; m.p. 115–116 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.96-7.91 (d, 2H), 7.68-7.65 (d, 2H), 7.50-7.48 (m, 3H), 7.45-7.30 (m, 3H), 7.01-6.73 (m, 3H), 5.00(t, 1H) 3.78-3.56(s, 3H), 3.50-3.40 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 188.45, 142.58, 136.22, 133.61, 130.88, 130.61, 129.55, 129.24, 129.00, 122.31, 113.94, 54.23, 46.10, 29.74. IR (KBr): ν 3386, 3015, 2921, 1655, 1595, 1509, 1488, 1405, 1311, 1252, 1162, 1012, 980, 814, 746, 691 cm⁻¹.

3-(4-chlorophenyl)-1-(4-chloroxyphenyl)-3-(phenylamino)propan-1-one (4j): Yield, 95%; light yellow solid; m.p. 120–122 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.96-7.91 (d, 2H), 7.68-7.65 (d, 2H), 7.60-7.58 (d, 2H), 7.54-7.50 (d, 2H), 7.31-7.28 (s, 1H), 7.15-7.05 (d, 2H), 6.83-6.80(s, 1H), 6.70-6.60 (d, 2H), 5.00(t, 1H) 3.50-3.40 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 196.69, 146.58, 143.83, 141.31, 134.90, 133.10, 129.91, 129.41, 129.20, 129.02, 127.81, 121.91, 118.18, 113.88, 54.09, 46.01. IR (KBr): ν 3382, 3058, 2924, 1669, 1585, 1486, 1399, 1281, 1215, 1177, 1090, 1010, 813, 745, 690 cm⁻¹.

3. Results and Discussion

3.1 Catalyst characterizations

The synthesized Mo-Al₂O₃ composites were characterized by FT-IR, SEM, Powder XRD, and EDS Analysis.

3.1.1 FT-IR Analysis

The functional group assessment of the synthesized catalyst was characterized by FT-IR spectra. (Fig. 1) shows the FT-IR spectra of the synthesized Mo-Al₂O₃ composites. From the FT-IR spectrum, it could be determined that the absorption peak at 985 cm⁻¹ was the stretching vibration of the 'O' double bond, and the peaks at 878 cm⁻¹, 814 cm⁻¹, and 673 cm⁻¹ are due to the stretching vibrations of the Mo—O—Mo bond. The stretching vibration peak of the Al—O bond of the alumina was observed at 867 cm⁻¹ and the bending vibrations of the bond were observed near 650 cm⁻¹. These observations indicate that Mo was well dispersed on the surface of the Al₂O₃ and metal-oxygen first-overtones were observed in the region of (2150-1850 cm⁻¹). Within these observations, the FT-IR results were in great agreement with XRD.

3.1.2 XRD analysis

Fig. 2 shows the Powder XRD pattern of synthesized composites. The phase and crystalline nature of the prepared material were scrutinized by XRD analysis. From the XRD

spectra, the diffraction peaks at $2\theta = 26.90^\circ$, 38.40° , and 54.80° are corresponding to the Al_2O_3 . They are nearly the same as the characteristic diffraction peaks of hierarchically structured Mo- Al_2O_3 catalyst. Moreover, the diffraction peaks appeared in a well-intense form indicating the crystalline nature of the sample. In addition, the characteristic peaks of molybdenum oxide were not obvious, indicating that molybdenum was uniformly dispersed inside and, on the alumina, and no agglomeration of oxides was formed, which coming from the synthesis of hierarchically macro-mesoporous Al_2O_3 supports. These composites were previously reported by R. Torrecillas [25] at 450°C . The XRD closely matches the literature.



Fig.1. FT-IR spectra of Mo- Al_2O_3 composites.

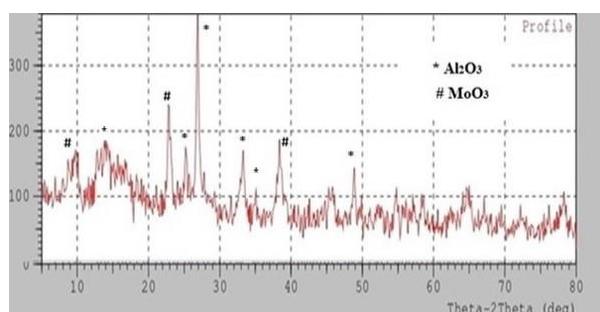


Fig. 2. PXRD pattern of Mo- Al_2O_3 composites: (a) Mo- Al_2O_3 composites.

3.1.3 SEM and EDX Analysis

The SEM images of the Mo- Al_2O_3 composites in Fig. 3. (a-b) display the surfaces of the catalyst particles. The Surface texture of the synthesized Mo- Al_2O_3 composite was analysed by SEM analysis. Fig. 3a shows the low-magnification SEM image of the catalyst, it shows the spherical shape of the prepared sample. Besides, the high magnification image (3b) of the prepared catalyst shows most of the particles appeared in the form of a flakes structure. Moreover, the catalyst shows less agglomeration, which is related to better catalyst performance. In Energy Dispersion X-ray (EDS) analysis was performed for the Mo- Al_2O_3 composites which confirmed the presence of Mo, Al, and O respective metal ions as shown in Fig. 3c.

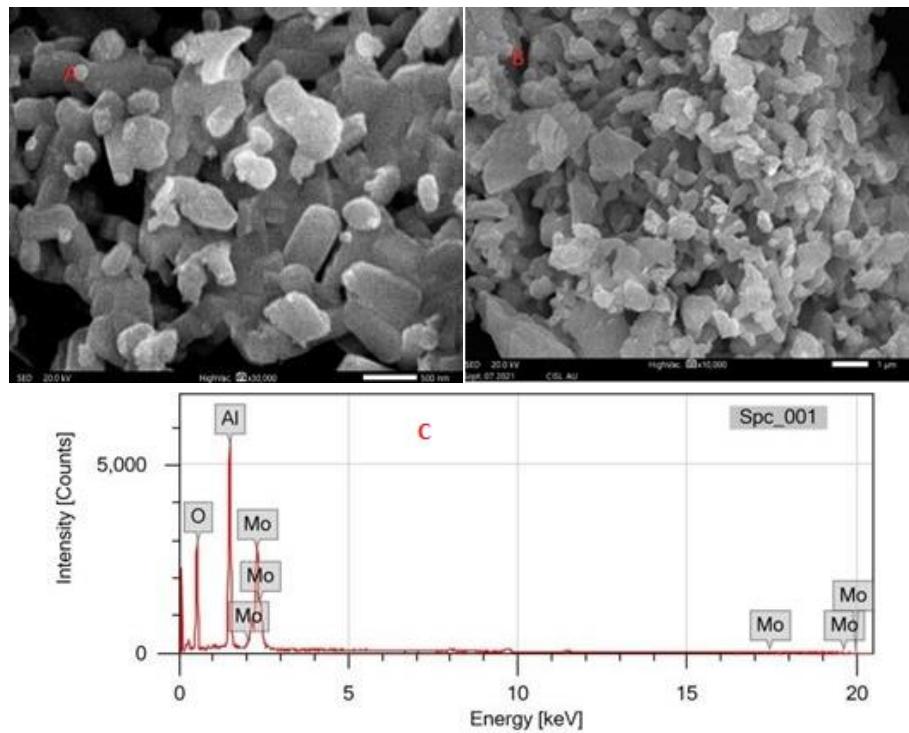


Fig. 3. SEM (a) 500nm and (b) 1μm images of Mo- Al_2O_3 composites (c) EDX images of Mo- Al_2O_3 composites.

3.2 Optimization of the catalyst

To start with our study, benzaldehyde was reacted with acetophenone, and aniline at different temperatures and times using various catalysts affording 1,3-diphenyl-3-(phenyl amino) propane-1-one (**4a**) as a reference reaction. For optimizing the solvent conditions, we tried different solvents like CH_2Cl_2 , DMF, toluene, methanol, DMSO, and THF. We found that the reaction of benzaldehyde (**1a**), acetophenone

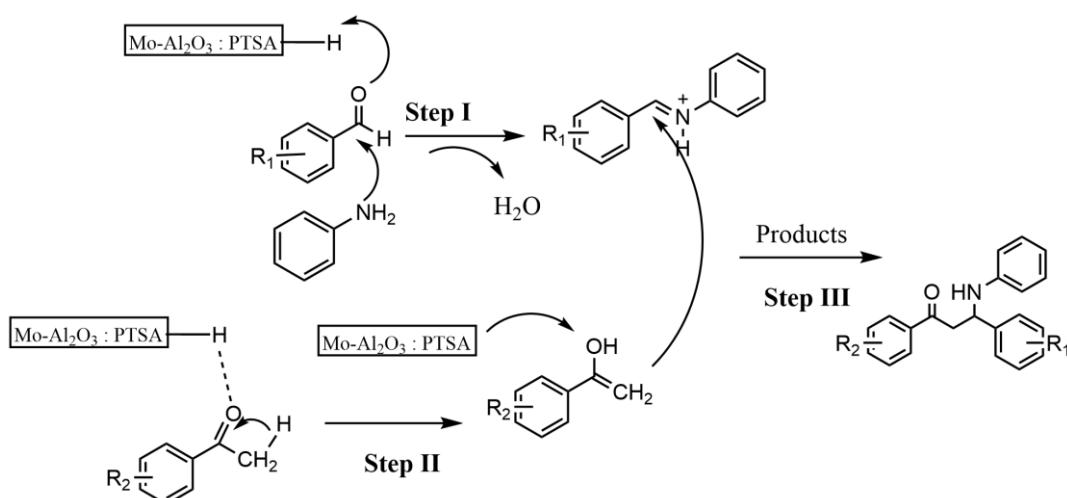
(**2a**) with aniline (**3a**) at room temperature (30°C) in the presence of Mo- Al_2O_3 composites in *p*-TSA in Methanol (Table 1, entry 9) as the solvent afforded 1,3-diphenyl-3-(phenyl amino) propane-1-one (**4a**) in optimal yields (Table 1, entry 9). No reaction was observed in the absence of a catalyst and the starting materials were recovered and unchanged (Table 1, entry 1). The results are summarized in Table 2.

Table 2. Optimization of catalyst.

Entry	Catalyst	Solvent	Temp(°C)	Time (h)	Yield (%)
1	no catalyst added	Methanol	rt	24h	nr
2	H ₂ SO ₄	H ₂ O	rt	24h	nr
3	ZnCl ₂	THF	80°C	24h	nr
4	CuCl ₂	Toluene	100°C	24h	nr
5	Al ₂ O ₃	CH ₂ Cl ₂	rt	24h	nr
6	(NH ₄) ₂ MoO ₃ +Al ₂ O ₃	CH ₂ Cl ₂	rt	24h	nr
7	p-TSA	CH ₂ Cl ₂	rt	24h	2
8	Al ₂ O ₃ /p-TSA	Methanol	rt	24h	5
9	Mo-Al₂O₃: PTSA	Methanol	rt	24h	99

This reaction was preceded with acid catalysed nucleophilic addition and elimination of water. The first step consists of the protonation of aldehydic carbonyl oxygen, carbon gets a positive charge. The second step consists of amine added to the aldehydic carbon to form iminium cation.

The third step is the aryl ketone undergoes enolization by the catalyst and it adds to iminium ion and proton transfer to iminium carbon followed by saturation given the Mannich bases. The proposed mechanistic pathway is shown in (Scheme 2).

**Scheme 2.** Proposed reaction pathway for Mannich reaction catalysed by Mo-Al₂O₃ composites in *p*-TSA.

3.3 Optimization of the solvent

The direct Mannich reaction catalysed by 10 mol% Mo-Al₂O₃ composites in the *p*-TSA catalyst in different solvents was observed and (Table 3) gives the best solvent for the reaction.

Table 3. Optimization of solvent.

Entry	Solvent	Time (h)	Yield (%)
1	no solvent added	24	65
2	CH ₂ Cl ₂	24	62
3	CHCl ₃	24	73
4	Toluene	24	42
5	THF	24	35
6	EtOH	24	86
7	MeOH	24	99
8	H ₂ O	24	nr
9	DMSO	24	nr
10	DMF	24	nr

3.4 Loading of the catalyst

The reaction was conducted with different mol% of the catalyst and the results were reported in Table 4. For preparation of Mo-Al₂O₃nano composites we have taken (NH₄)₂MoO₃and Al₂O₃in 1:2 ratios in methanol. Lower ratios (0.5:1, 0.1:1, etc.) are not successful to conduct one-pot three-component Mannich reaction. The below table gives the yields of the reaction with different mol% of catalyst.

3.5 Reusability of the catalyst

The reusability of the catalyst was checked by the reaction of aniline, benzaldehyde, and acetophenone with 10.0% of the Mo-Al₂O₃/*p*-TSA composites for 24 h at room temperature. The Mo-Al₂O₃/*p*-TSA catalyst was recovered and reused for a further five consecutive reactions, which gave the product 70–75% yield and the graphical representation as illustrated in Figure 4. The recovered catalyst was subjected to FT-IR and XRD analysis. A similar infrared and XRD pattern was observed for the Mo-Al₂O₃/*p*-TSA catalyst before and after the catalytic reaction. These results indicate that Mo-Al₂O₃/*p*-TSA composites do not lose their activity and can be reused.

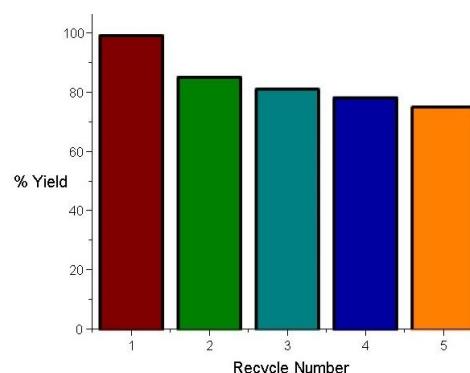
**Fig. 4.** Recycling of catalyst: Catalyst recycling of Mo-Al₂O₃/*p*-TSA catalyst for Mannich reaction. Reaction condition: benzaldehyde: aniline: acetophenone, 1:1:1 (5 mmole ratio), Mo-Al₂O₃/*p*-TSA (0.5 mmol, 0.23 g) at room temperature (30 °C).

Table 4. Effect of loading of catalyst.

Entry	Catalyst mol (%)	Temperature(T)	Time (h)	Yield ^a (%)
1	1.0	rt	24h	40
2	2.0	rt	24h	42
3	5.0	rt	24h	56
4	8.0	rt	24h	75
5	10.0	rt	24h	99
6	10.0	80 °C	8h	62
7	12.0	rt	24h	82

Reaction condition: benzaldehyde: aniline: acetophenone, 1:1:1 (5 mmole ratio), solvent (methanol). ^aYield of the isolated product determined by column chromatography separation.

4. Conclusions

In conclusion, a three-component Mannich-type reaction of aniline, and various benzaldehydes with acetophenones were efficiently catalysed by Mo-Al₂O₃/p-TSA catalyst in methanol. The noteworthy features of the reported protocol include (a) simple procedure; (b) air-stable and solid catalyst; (c) cheap and non-toxic solvent; (d) the reuse of the catalytic system. Furthermore, this protocol is adaptive for the synthesis of a diverse set of β-amino ketones.

Supporting Information

Experimental and analytical data are provided in the Supporting Information.

Acknowledgments

The authors are thankful to Prof. R. Balamurugan, University of Hyderabad for providing laboratory facilities to carry out this work. A.K.R. is thankful to UGC-NRC, University of Hyderabad for providing instrumentation and our sincere thanks to Annamalai University for NMR, SEM, EDX, PXRD instrumentation facility and thanks to UGC, India.

Author Contributions

Kotiswara Rao Anam: Investigation, Analysis, resources and writing. Ganesamoorthy Thirunarayanan: methodology, review, investigation, and supervision.

References and Notes

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How to cite this article

Anam, K. R.; Thirunarayanan, G. *Orbital: Electron. J. Chem.* **2022**, 14, 234. DOI: <http://dx.doi.org/10.17807/orbital.v14i4.16358>