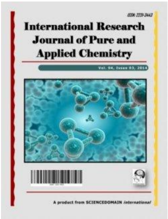

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Fe^{3+}-Montmorillonite K10 as an Efficient, Green and Reusable Heterogeneous Catalyst for Synthesis of Mannich Type Reaction under Solvent-free Condition

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Authors' contributions

This work was carried out in collaboration between both authors. Author SB designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author VK read and approved the final manuscript.

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ABSTRACT

A simple and efficient one-pot three-component synthesis of Mannich type reaction has been developed using recyclable Fe^{+3}-montmorillonite K10 (Fe^{+3}@K10) under solvent-free condition. The reaction of aromatic aldehydes, aromatic anilines and aryl ketones produced β-amino carbonyl derivatives in good to excellent yields. The developed method making use of a recyclable catalyst is economical and eco-friendly and affords good yields under mild reaction conditions.

Keywords: Fe^{+3}-montmorillonite K10; Mannich reaction; heterogeneous; recyclable; solvent free.

1. INTRODUCTION

A Mannich reaction is an important tool for carbon-carbon bond forming in organic synthesis [1]. The Mannich products are mainly β-amino carbonyl compounds and their derivatives. The β-amino carbonyl compounds are important building blocks in the synthesis of

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pharmaceutical and natural products [2,3]. The synthesis of β-amino carbonyl compound derivatives has been extensively explored in recent years as these compounds are the important precursor for pharmaceuticals, natural products. The β-amino carbonyl compounds are not only active biologically but also serve as key intermediates for the synthesis of important nitrogen-containing compounds such as β-amino acids, β-lactams and β- amino alcohols [4-8]. The Mannich bases exhibit anticonvulsant [9,10], antitubercular [11], antimalarial [12], anti-HIV [13], anti-viral [14], and anti-cancer [15] activities.

Numerous recent methods for direct one-pot three-component synthesis of β-amino carbonyls derivatives using various catalytic systems such as proline [16,17], I_2 [18], Lewis acids [19], ionic-liquids [20-23], and nanoparticles [24-26] have been reported. The reported methods are associated with a number of limitations and drawbacks such as harsh reaction conditions, prolonged reaction time, low yield, use of expensive reagents, hazardous solvents and tedious workup. Hence, the development of the novel method for the synthesis of β-amino carbonyl compounds is of high significance. To overcome the drawbacks and keeping in view the growing environmental concern, solid acids have gained significant importance in recent years.

It is well known that one pot multicomponent reactions are always better than multi-steps synthesis [27] as they require minimal workup and desired products and can be obtained in one pot often in quantitative yields. The need to reduce the amount of toxic waste and by-products arising from chemical processes requires increasing emphasis on the use of less toxic and more environmentally compatible materials in the design of new synthetic methods [28].

Fe^{+3}–montmorillonite K10 catalyst was insensitive to moisture and excellent reusability, while anhydrous iron (III) chloride is deliquescent, besides reusability of $FeCl_3$ is a tedious process. Therefore, to overcome this problem, $FeCl_3$ is loaded on support material for easy utilization and handling. Among the supports used, montmorillonite K10 gave the more effective catalysts, as the clay itself has its own activity [29]. The use of clay as catalyst or catalyst support has received considerable attention due to their high chemical and thermal stability. Metal cations can be introduced readily into the expandable interlayer spaces, thus making it possible to alter the acidic nature of the material by simple ion-exchanged with clay. Introduction of metal ion in montmorillonite K10 enhances the Lewis acidity of the catalyst with increasing charge-to-radius ratio of cation. Therefore, the Fe^{+3}–montmorillonite K10 is the most superior catalyst compared to another clay catalyst in this reaction [30-32]. In recent years, the catalytic activity of Fe^{+3}-montmorillonite clay has been explored for the modification of heterogeneous solid acid catalysts in organic synthesis [33-38].

We hereby report a novel green method for the synthesis of β-amino carbonyl compounds using Fe^{+3}-montmorillonite K10 as an environmentally benign and efficient recyclable catalytic system under solvent-free condition. The catalyst offers easy in handling, low cost and recovery affording five cycles without significant loss in activity. To the best of our knowledge, we are first to report the use of the Fe^{+3}@K10 catalyst for the synthesis of β-amino carbonyl derivatives.

2. MATERIALS AND METHODS

2.1 General Information

Reactions were monitored by thin-layer chromatography (TLC). FT-IR spectra were recorded using KBr disks on a Bruker model Alpha (SN: 200855) spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with JNM-ECS 400 spectrometer as $CDCl_3$ solutions, and the chemical shifts are expressed as δ units with Me_4Si as the internal standard. The crystallographic structure of the powder was investigated using a Rigaku Smart Lab powder X-ray diffractometer using Cu Kα radiation. All chemicals and reagents were purchased from Hi-Media, SDS and used without further purification.

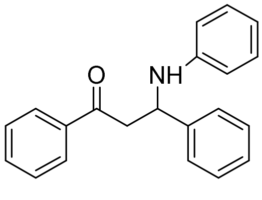
2.2 Catalyst Preparation

To anhydrous $FeCl_3$ (15 g), dissolved in demineralized water (60 ml), montmorillonite K10 (10 g) was added over a period of 10 min and the resulting slurry was stirred at RT for 5 hr. The clay catalyst was filtered and washed with demineralized water until disappearance of chloride ions from the discarded H_2O. The clay catalyst after drying overnight in an oven at 120°C were preserved in a vacuum desiccator and used when necessary [28,39].

2.3 General Procedure

A mixture of aromatic acetophenone (6 mmol), benzaldehyde (5 mmol) and aryl amines (5 mmol) was taken in a round bottom flask and to it, Fe^{+3}@K10 (0.15 g) was added. The reaction mixture was stirred at room temperature. The progress of the reaction was checked by TLC in solvent system of ethyl acetate: n-hexane (5:95). After completion of the reaction, the mixture was extracted with ethyl acetate, dried over anhydrous sodium sulfate and excess solvent was removed by rotavapor to afford crude product. Recrystallization of crude products from ethyl acetate: hexane yielded pure product. The identity and purity of products were confirmed by melting point and spectral data with those reported in the literature.

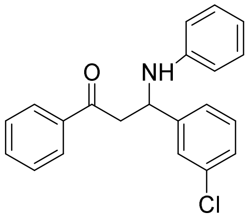
2.4 Spectral Analysis



Chemical formula: $C_{21}H_{19}NO$

1, 3-diphenyl-3-(phenyl amino) propan-1-one (4a)

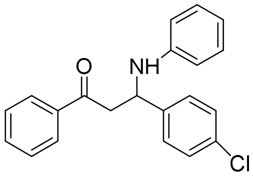
Colourless solid; 89 % yield; mp 167-168 ^{0}C (lit.[1] 169-170 ^{0}C); IR ($CHCl_3$): *υ* 3379, 2383, 1665, 1549, 1509, 1451, 1367, 1287, 1216, 1070, 992, 857, 743, 688 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 3.41 (dd, *J* = 7.3, *J* =15.9 *Hz*, 1H), 3.51 (dd, *J* = 5.5, *J* = 16.5 Hz, 1H), 4.55 (br, 1H), 4.99-5.02 (m, 1H), 6.55.6.57 (m, 2H, ArH), 6.66 (t, 1H, *J* = 7.3 Hz, ArH), 7.06-7.10 (m, 2H, ArH), 7.21-7.25 (m, 1H, ArH), 7.30-7.34 (m, 2H, ArH), 7.42-7.46 (m, 4H, ArH), 7.56 (m, 1H,ArH), 7.90-7.91 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 46.4, 54.8, 113.9, 117.8, 126.5, 127.5, 128.3, 128.8, 128.9, 129.2, 133.6, 136.7, 143.1, 147.1, 198.4.



Chemical formula: $C_{21}H_{18}ClNO$

3-(3-chlorophenyl)-1-phenyl-3-(phenyl amino) propan-1-one (4b)

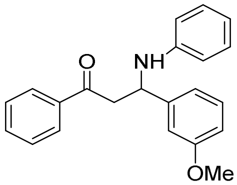
Colourless solid; 90% yield; mp 141-142 ^{0}C (lit.[45] 140-141°C); IR ($CHCl_3$): *υ* 3388, 3020, 2378, 1695, 1595, 1513, 1468, 1427, 1217, 1070, 989, 831, 745, 683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 3.39-3.465 (m, 2H), 4.55 (br, 1H), 4.94-4.96 (m, 1H), 6.52-6.54 (m, 2H, ArH), 6.68 (t, 1H, *J* = 7.4 Hz, ArH), 7.07-7.11 (m, 2H, ArH), 7.20-7.22 (m, 1H, ArH), 7.33 (d, 1H, *J* = 7.3 Hz, ArH), 7.43-7.47 (m, 3H, ArH), 7.55-7.59 (m, 1H, ArH), 7.89-7.91 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 46.2, 54.4, 113.9, 118.2, 124.7, 126.6, 127.7, 128.3, 128.9, 129.3, 130.2, 133.7, 145.4, 146.8, 197.9.



Chemical formula: $C_{21}H_{18}ClNO$

3-(4-chlorophenyl)-1-phenyl-3-(phenylamino)propan-1-one (4c)

Colourless solid; 92 % yield; mp 117-118 ^{0}C (lit.[1] 115-116 ^{0}C); IR ($CHCl_3$): *υ* 3380, 3020, 2370, 1675, 1596, 1511, 1404, 1289, 1089, 991, 825, 746, 687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 3.37-3.46 (m, 2H), 4.57 (br, 1H), 4.95-4.97 (m, 1H), 6.52 (d, 2H, *J* = 7.3 Hz, ArH), 6.67 (t, 1H, *J* = 7.3 Hz, ArH), 7.06-7.10 (m, 2H, ArH), 7.25-7.28 (m, 2H, ArH), 7.36-7.38 (m, 2H, ArH), 7.42-7.46 (m, 2H, ArH), 7.55-7.58 (m, 1H, ArH), 7.88-7.90 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 46.2, 54.2, 113.9, 118.1, 127.9, 128.3, 128.6, 128.9, 129.1, 129.3, 133.7, 136.6, 141.6, 146.8, 198.0.

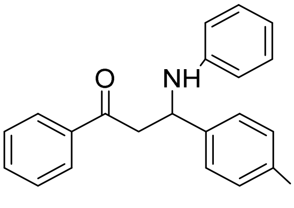


Chemical formula: $C_{22}H_{21}NO_2$

3-(3-methoxyphenyl)-1-phenyl-3-(phenylamino)propan-1-one (4d)

Colourless solid; 84 % yield; mp 103-104 ^{0}C (lit.[1] 106-107 ^{0}C); IR ($CHCl_3$): *υ* 3378, 3020, 2370, 1660, 1597, 1510, 1485, 1405, 1283, 1048, 863, 746, 689 cm^{-1}; ^{1}H NMR (400 MHz,

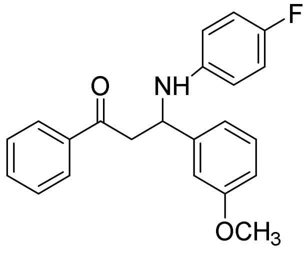
$CDCl_3$): δ 3.39 (dd, 1H, *J* = 7.3, *J* = 16.5 Hz), 3.49 (dd, 1H, *J* = 4.9, *J* = 15.9 Hz), 3.76 (s, 3H, -OCH_3), 4.53 (br, 1H), 4.93-4.95 (m, 1H), 6.55 (d, 2H, *J* = 7.9 Hz, ArH), 6.65 (t, 1H, *J* = 7.3 Hz, ArH), 6.76 (d, 1H, *J* = 5.6 Hz, ArH), 6.98-6.99 (m, 1H, ArH), 7.03 (m, 1H, ArH), 7.06-7.09 (m, 2H, ArH), 7.21-7.23 (m, 1H, ArH), 7.42-7.46 (m, 2H, ArH), 7.54-7.57 (m, 1H, ArH), 7.89-7.91 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.4, 54.9, 55.3, 112.6, 117.9, 118.7, 128.3, 128.8, 129.2, 130.0, 133.6, 136.7, 145.0, 147.1, 160.1, 198.3.



Chemical formula: $C_{21}H_{18}FNO$

3-(4-fluorophenyl)-1-phenyl-3-(phenylamino)propan-1-one (4e)

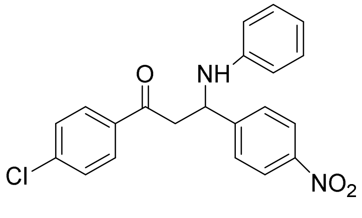
Colourless solid; 88 % yield; mp 104-105 ^{0}C; IR ($CHCl_3$): υ 3380, 3020, 2312, 1672, 1600, 1548, 1507, 1425, 1167, 1102, 1062, 826, 746, 684 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.40-3.49 (m, 2H), 4.55 (br, 1H), 4.97 (t, 1H, J = 7.3 Hz), 6.52-6.54 (m, 2H, ArH), 6.67 (t, 1H, *J* = 7.4 Hz, ArH), 6.97-7.01 (m, 2H, ArH), 7.07-7.11 (m, 2H, ArH), 7.38-7.46 (m, 4H, ArH), 7.54-7.56 (m, 1H, ArH), 7.88-7.90 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.3, 54.2, 113.9, 115.6, 115.9, 118.1, 128.0, 128.1, 128.3, 128.8, 129.2, 133.7, 146.8, 163.3, 198.2.



Chemical formula: $C_{22}H_{20}FNO_2$

3-((4-fluorophenyl)amino)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (4f)

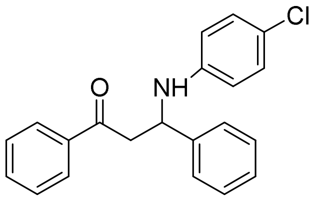
Colourless solid; 83 % yield; mp 120-121 ^{0}C; IR ($CHCl_3$): υ 3362, 3010, 2317, 1660, 1574, 1502, 1433, 1252, 1108, 1073, 1037, 809, 751, 679 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.40-3.49 (m, 2H), 3.76 (s, 1H, OCH_3), 4.44 (br, 1H), 4.85-4.87 (m, 1H), 6.46-6.49 (m, 2H, ArH), 6.75-6.80 (m, 3H, ArH), 6.96-6.97 (m, 1H, ArH), 7.00 (d, 1H, *J* = 7.3 Hz, ArH), 7.24-7.25 (m, 1H, ArH), 7.42-7.46 (m, 2H, ArH), 7.54-7.56 (m, 1H, ArH), 7.89-7.91 (m, 2H, ArH), 7.89-7.91 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.5, 55.3, 55.5, 112.2, 114.9, 115.5, 115.7, 118.7, 128.3, 128.8, 130.0, 133.6, 136.7, 144.8, 160.1, 198.3.



Chemical formula: $C_{21}H_{17}ClN_2O_3$

1-(4-chlorophenyl)-3-(4-nitrophenyl)-3-(phenylamino)propan-1-one (4g)

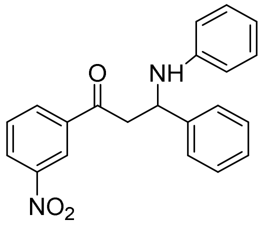
Yellow solid; 80 % yield; mp 141-142 ^{0}C; IR ($CHCl_3$): υ 3399, 3020, 2310, 1669, 1590, 1510, 1400, 1340, 1093, 1049, 845, 745, 689 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (dd, 2H, *J* = 5.5, *J* = 11.0 Hz), 4.62 (br, 1H), 5.10 (t, 1H, *J* = 6.1 Hz), 6.52 (d, 2H, *J* = 7.9 Hz, ArH), 6.72 (t, 1H, *J* = 7.4 Hz, ArH), 7.09-7.13 (m, 2H, ArH), 7.42-7.45 (m, 2H, ArH), 7.62-7.64 (m, 2H, ArH), 7.82-7.85 (m, 1H, ArH), 8.08-8.10 (m, 1H, ArH), 8.17-8.20 (m, 1H, ArH), 8.33-8.35 (m, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.7, 54.1, 113.9, 118.7, 124.1, 127.6, 129.1, 129.3, 129.6, 134.7, 140.5, 146.3, 150.7, 157.5, 196.1.



Chemical formula: $C_{21}H_{18}ClNO$

3-((4-chlorophenyl)amino)-1,3-diphenylpropan-1-one (4h)

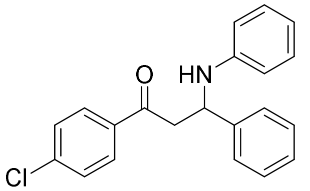
Light yellow solid; 76 % yield; mp 167-168 ^{0}C (lit.[46] 166-168 ^{0}C); IR ($CHCl_3$): υ 3369, 3010, 2320, 1661, 1594, 1490, 1448, 1405, 1280, 851, 745, 681 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.41-3.50 (m, 2H), 4.65 (br, 1H), 4.92-4.94 (m, 1H), 6.45-6.47 (m, 2H, ArH), 7.00-7.02 (m, 2H, ArH), 7.21-7.24 (m, 1H, ArH), 7.30-7.33 (m, 2H, ArH), 7.39-7.46 (m, 4H, ArH), 7.54- 7.58 (m, 1H, ArH), 7.88-7.90 (m, 2H, ArH); ^{13}C NMR (100 MHz, CDCl$_3$): δ 46.3, 55.0, 115.0, 122.5, 126.4, 127.6, 128.3, 128.8, 129.0, 129.1, 133.6, 136.6, 142.6, 145.6, 198.3.



Chemical formula: $C_{21}H_{18}N_2O_3$

1-(3-nitrophenyl)-3-phenyl-3-(phenylamino)propan-1-one (4i)

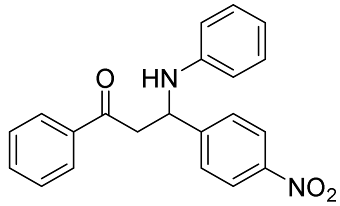
Colourless solid; 53 % yield; mp 171-172 ^{0}C (lit.[46] 169-171 ^{0}C); IR (CHCl$_3$): υ 3389, 3010, 2320, 1678, 1617, 1519, 1450, 1417, 1305, 1219, 1187, 1077, 990, 735, 698, 684 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.50 (d, 2H, J = 6.7 Hz), 4.70 (br, 1H), 5.06 (t, 1H, J = 6.7 Hz), 6.51-6.57 (m, 2H, ArH), 6.82 (t, 1H, J =7.3 Hz, ArH), 6.91-6.96 (m, 1H, ArH), 7.21-7.25 (m, 1H, ArH), 7.30-7.34 (m, 2H, ArH), 7.42-7.46 (m, 4H, ArH), 7.54-57 (m, 1H, ArH), 7.90-7.92 (m, 2H, ArH); ^{13}C NMR (100 MHz, CDCl$_3$): δ 46.1, 53.4, 113.0, 113.9, 114.1, 116.2, 124.2, 126.2, 127.0, 128.4, 133.1, 142.8, 150.0, 152.4, 197.3.



Chemical formula: $C_{21}H_{18}ClNO$

1-(4-chlorophenyl)-3-phenyl-3-(phenylamino)propan-1-one (4j)

Colourless solid; 74% yield; mp 117-118 ^{0}C (lit.[1] 120-121°C); IR (CHCl$_3$): υ 3371, 3021, 2877, 1664, 1579, 1486, 1447, 1277, 1084, 985, 820, 746, 687 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.40-3.52 (m, 2H), 4.53 (br, 1H, -NH), 5.02 (t, 1H, J = 8.0 Hz), 6.59 (d, 2H, J = 10.6 Hz, ArH), 6.70 (t, 1H, J = 9.3 Hz, ArH), 7.10-7.14 (m, 2H, ArH), 7.24-7.28 (m, 1H,ArH), 7.32-7.36 (m, 2H, ArH), 7.42-7.45 (m, 4H, ArH), 7.85 (d, 2H, J = 10.6 Hz); ^{13}C NMR (100 MHz, CDCl$_3$): δ 46.2, 54.8, 113.9, 117.9, 126.4, 127.5, 128.9, 129.0, 129.2, 129.6, 135.1, 139.9, 142.8, 146.9, 197.1.



Chemical formula: $C_{21}H_{18}N_2O_3$

3-(4-nitrophenyl)-1-phenyl-3-(phenylamino)propan-1-one (4k)

Yellow solid; 87% yield; mp 106-107 ^{0}C (lit.[47] 102-104°C); IR (CHCl$_3$): υ 3398, 3010, 1672, 1599, 1510, 1340, 1288, 1215, 1181, 986, 851, 744, 687 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 3.54 (d, 2H, J = 6.2 Hz), 4.70 (br, 1H-NH), 5.13 (t, 1H, J = 6.5 Hz), 6.55 (d, 2H, J = 8.8 Hz, ArH), 6.73 (t, 1H, J = 7.4 Hz, ArH), 7.11-7.15 (m, 2H, ArH), 7.47-7.51 (m, 2H, ArH), 7.60-7.63 (m, 1H, ArH), 7.65-7.67 (m, 2H, ArH), 7.91-7.94 (m, 2H, ArH), 8.20 (d, 2H, J = 9.1 Hz, ArH); ^{13}C NMR (100 MHz, CDCl$_3$): δ 45.7, 54.3, 113.9, 118.5, 124.1, 127.5, 128.2, 128.9, 129.3, 133.8, 136.4, 146.3, 147.3, 150.8, 197.3.

3. RESULTS AND DISCUSSION

The catalyst Fe^{+3}@K10 was prepared by the reported methods [28,39] and it was characterized by powder X-ray diffraction (XRD) and FT-IR spectroscopy. The powder X-ray diffraction (XRD) pattern of parent montmorillonite K-10 and Fe^{+3}-montmorillonite K10 are shown in Fig. 1. The diffraction peaks at 19.8°, 26.0°, 35.1° and 45.5^{0} correspond to montmorillonite (Fig. 1a). The decrease in diffraction peak intensities of Fe^{+3}-montmorillonite K10 at 19.8°, 35.1° and 45.5° is attributed to the fact that the metal ions in the framework on the surface of montmorillonite K10 are inserted [40]. (Fig. 1b). The disappearance of some low-intensity peaks confirms the incorporation of metal ions in the surface of montmorillonite K10.

The FT-IR spectroscopic measurements of montmorillonite-K10 clay and Fe^{+3}@K10 catalyst were carried out using KBr disks on a Bruker model Alpha (SN: 200855) FT-IR spectrophotometer. Fig. 4.10a-b shows the FT-IR spectrum of montmorillonite-K10 clay and Fe^{+3}@K10. Absorption bands at 596 and 586 cm-1 are due to bending vibration of Si-O-Mg and Si-O-Fe in Montmorillonite-K10 clay and Fe^{+3}@K10 respectively [48]. The absorption peak at 796 cm^{-1} is due to asymmetric vibration of Al+4 tetrahedral found in all three spectra.[49] The broad peaks in the range 3200-3530 cm^{-1} are due to an octahedral layer of Al-OH-Al group. The broad peaks at 3497 (clay), 3478 (Fe^{+3}@K10) and 1640 cm^{-1} are due to bending and stretching vibrations of the water molecule. The absorption peaks at 1030 (clay) and 1040 (Fe^{+3}@K10) are due to asymmetric vibration SiO2 tetrahedral. The slight decrease in peak intensity at 1640 cm^{-1} due to the incorporation of metal ion on the montmorillonite-K10 clay surface. Fig. 4.10c shows the FT-IR spectrum of recovered Fe^{+3}@K10catalyst, which shows peaks similarity with FT-IR spectrum of fresh Fe^{+3}@K10catalyst (Fig. 4.1b).

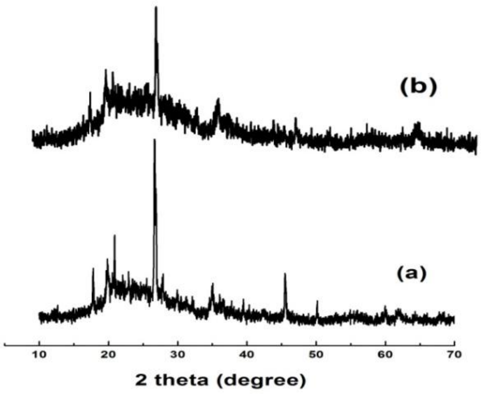


Fig. 1. XRD pattern of (a) Montmorillonite-K10 clay (b) Fe^{+3}@K10

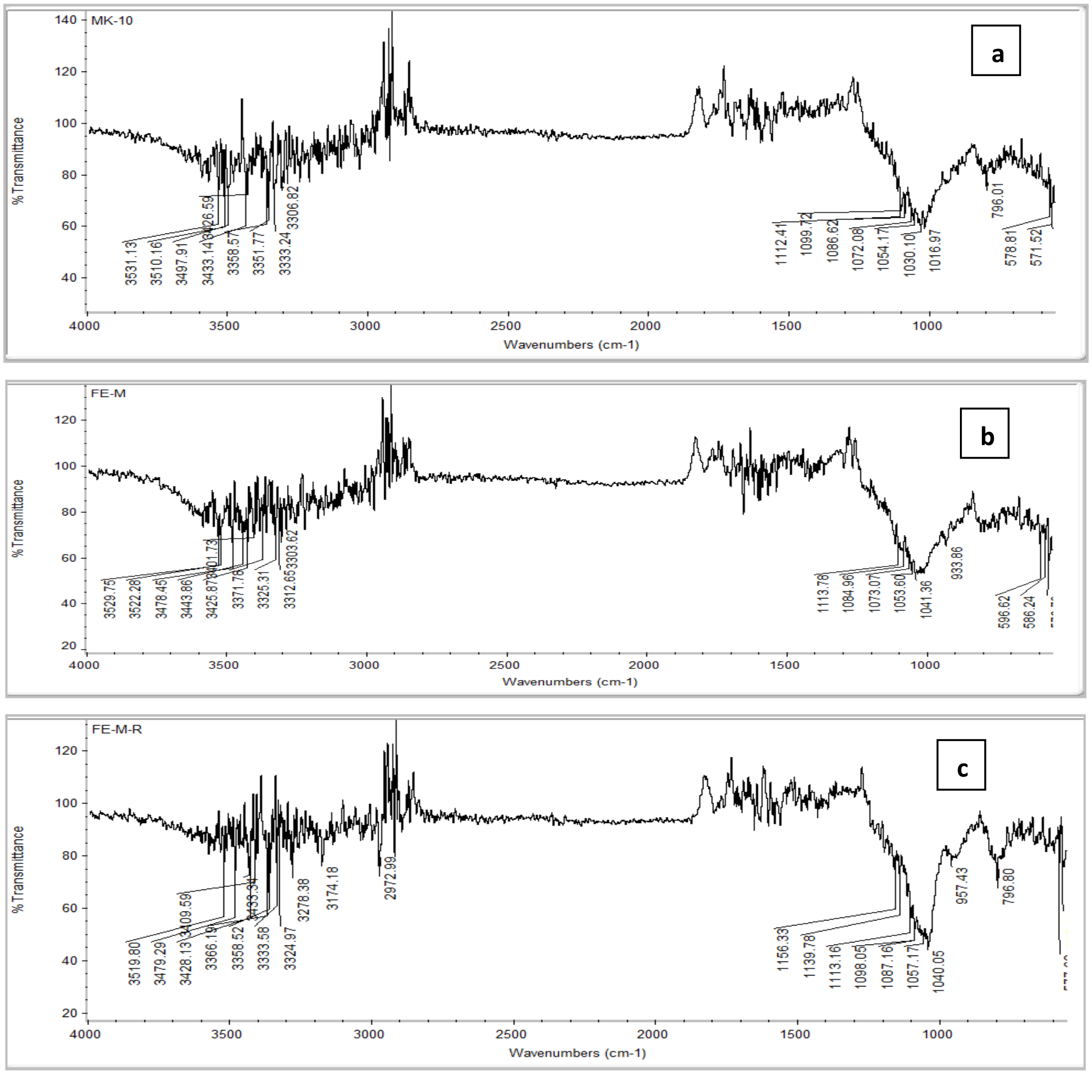
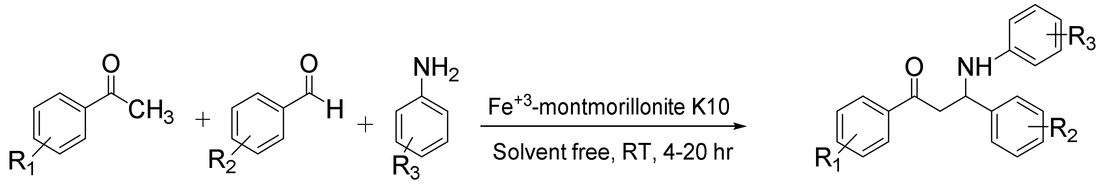


Fig. 2. FT-IR spectra of (a) Montmorillonite K10 (b) Fe^{+3}-montmorillonite K10 (c) recovered the catalyst

The reaction conditions were optimized by taking acetophenone (1a), benzaldehyde (2a), and aniline (3a) as reactants in the presence of various amounts (10, 20, 30 and 40 mg) of Fe^{+3}@K10 catalyst (Scheme 1) affording yield 30% 65%, 89% and 90% respectively (Table 1). This indicates that on increasing the amount of catalyst beyond 30 mg, there is no significant improvement in the yield. It is noteworthy that in the absence of a catalyst, the reaction failed to give the product within 24 hr. The model reaction was also carried out in several solvents (ethanol, methanol, acetonitrile, and water), and it was found that maximum yield of product was obtained under solvent-free condition within 4 hr. So, the reaction under solvent-free condition was selected as the optimal condition, at room temperature and in the presence of 30 mg of catalyst.

With the optimized reaction conditions, we began to explore the substrate scope by using acetophenones, aldehydes and amines having electron withdrawing as well as electron donating substituents groups on their benzene rings. The reaction afforded good to excellent yield for various aromatic aldehydes, aromatic amines and aromatic acetophenones indicating wide substrates scope of the reaction (Table 1). Though, electron-withdrawing substituents in



a: R_1 = H
b: R_1 = 4-Cl
c: R_1 = 3-No$_2$

a: R_2 = H
b: R_2 = 3-Cl
c: R_2 = 4-Cl
d: R_2 = 3-OMe
e: R_2 = 4-F
f: R_2 = 4-No$_2$
g: R_2 = 4-OMe

a: R_3 = H
b: R_3 = 4-F
c: R_3 = 4-Cl
d: R_3 = 4-No$_2$

a: R_1 = R_2 = R_3 = H
b: R_1 = R_3 =H; R_2 = 3-Cl
c: R_1 = R_3 =H; R_2 = 4-Cl
d: R_1 = R_3 =H; R_2 = 3-OMe
e: R_1 = R_3 =H; R_2 = 4-F
f: R_1 = H; R_2 =4-OMe; R_3 =4-F
g: R_1 = 4-Cl; R_2 = 4-NO$_2$; R_3 =H
h: R_1 = R_2 = H; R_3 =4-Cl
i: R_1 = 3-NO$_2$; R_2 = R_3 = H
j: R_1 = 4-Cl; R_2 = R_3 = H
k: R_1 = R_3 =H; R_2 = 4-NO$_2$

Scheme 1. Fe^{+3}@K10 catalyzed the multicomponent one-pot synthesis of β-amino ketone derivatives

Table 1. Fe^{+3}@K10- catalyzed the direct Mannich reaction of various aromatic acetophenones and aromatic aldehydes with aromatic amines[a]

Entry	R_1	R_2	R_3	Time (hr)	Product	Yield (%)[b]
1	H	H	H	4	4a	89
2	H	3-Cl	H	6	4b	90
3	H	4-Cl	H	6	4c	92
4	H	3-OMe	H	9	4d	84
5	H	4-F	H	8	4e	88
6	H	4-OMe	4-F	12	4f	83
7	4-Cl	4-NO$_2$	H	15	4g	80
8	H	H	4-Cl	12	4h	76
9	3-NO$_2$	H	H	20	4i	53
10	4-Cl	H	H	18	4j	74
11	H	4-NO$_2$	H	10	4k	87

[a]reaction conditions: aromatic acetophenone (1.2 mmol), aromatic aldehydes (1 mmol) and aromatic amines (1 mmol), all of the reactions were carried out with 40 mg of Fe^{+3}@K10 at room temperature. [b]Isolated yields.

aldehydes and electron donating substituents in amines afforded slightly increased yield of products. The reaction time increased for substituted acetophenone having electron withdrawing groups on the benzene ring.

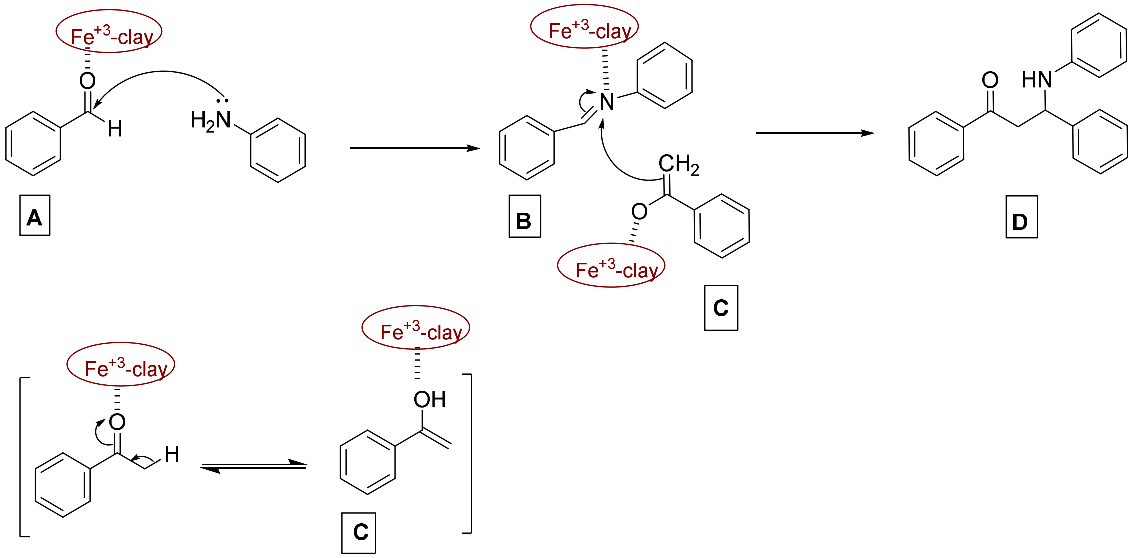
Reported methods for the Mannich reaction of acetophenone with benzaldehyde and aniline are summarized in Table 2 for comparison with the method developed by us. In comparison with the other catalysts used in literature, Fe^{+3}@K10 catalyst showed efficiently high catalytic activity in terms of recycling and reaction time.

The plausible reaction mechanism for the synthesis of β-amino ketones initiated by Fe^{+3}@K10 is outlined in Scheme 2. The mechanism is in accordance with earlier reported mechanisms in literature [50]. The aldehydes are activated by Fe^{+3}@K10 catalyst to form complex A. Then, amine attacks the carbonyl group of the activated aldehydes and leads to the formation of an iminium ion as the intermediate B. The complex C acts as enolate which is generated in situ by ketone activated by Fe^{+3}@K10 catalyst. Then, complex C attacks on B to affords the expected β-amino ketone D.

The reusability performance of Fe+3@K10 catalyst was also investigated for optimized model reaction. The catalyst was simply filtered after each run, washed with deionized water and activated at 1200 C. The comparison of FT-IR spectra of fresh and recovered catalyst, reveals that spectra are resembling very large extent indicating clearly that the structure of catalytic system remains intact after five cycles (Fig. 2). The results of runs of catalyst are shown in Fig. 3. The perusal of Fig. 3 clearly reveals that there is no significant decrease in yield up to five successive runs.

Table 2. Comparison of Fe^{+3}@K10 catalyst with other catalysts reported in the literature for the Mannich reaction of acetophenone and benzaldehyde with aniline

Entry	Catalyst, Condition	Time (h)	Yield (%)	Ref.
1	$[C_3SO_3Hnhm]HSO_3$, rt, EtOH	6	86	[41]
2	$HClO_4$-SiO_2, rt, EtOH	12	95	[42]
3	Ph-$B(OH)_2$, rt, CH_3CN	8	90	[43]
4	$BiCl_3$, rt, solvent-free	4	69	[44]
5	$NbCl_5$, rt, solvent-free	4	50	[45]
6	**Fe^{+3}@K10, rt, solvent-free**	**4**	**89**	**This work**



Scheme 2. The plausible mechanism for synthesis of β-amino carbonyl derivatives using Fe^{+3}@K10 as catalyst

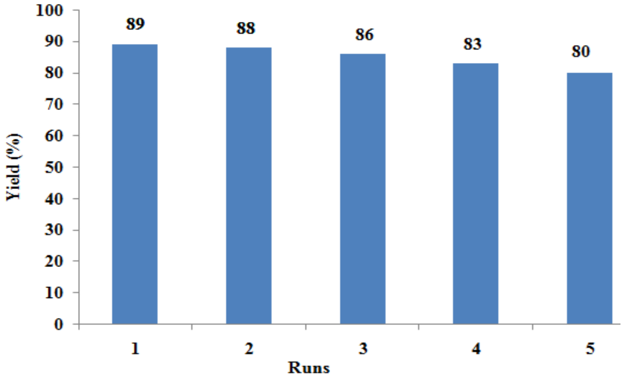


Fig. 3. Reusability of Fe^{+3}@K10 catalyst. Reaction conditions: acetophenone 1.2 mmol, benzaldehyde, 1.0 mmol, and aniline 1.0 mmol under solvent-free conditions, 4 hr.

4. CONCLUSION

We have developed the facile and eco-friendly one-pot three component protocol for the synthesis of β-amino carbonyl derivatives via Mannich type reaction using Fe^{3+}-montmorillonite K10 as reusable, efficient heterogeneous catalyst. The usefulness of this methods is mild reaction conditions, regeneration of catalyst, low cost, simple work-up procedure and improved product yield. The advantage of reusability of Fe^{3+}-montmorillonite K10 makes this protocol green and attractive procedure in comparison to earlier reported methods.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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