Research Article

One Pot Multicomponent Reactions Using Cu^{2+} Immobilized Coconut Coir: An Efficient and Reusable Heterogeneous Catalyst for Green Synthesis of Imidazoles, β-Acetamidoketones and β-Hydroxyketones

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Abstract

A facile procedure was developed for the green synthesis of imidazoles, β-acetamidoketones and β-hydroxyketones using Cu^{2+} immobilized coconut coir (Cu^{2+}-CC). Coconut coir is a natural adsorbent and Cu^{2+} metal ions were immobilized on coconut coir to generate highly efficient, economical and environmentally benign heterogeneous catalyst. Development of Cu^{2+}-CC was characterized using scanning electron microscope (SEM). Multicomponent reactions (MCRs) using Cu^{2+}-CC afforded imidazoles, β-acetamidoketones and β-hydroxyketones in excellent yields under mild conditions. Cu^{2+}-CC heterogeneous catalyst was recoverable and found to be efficient for 3 consecutive cycles providing compounds in constant good yield.

Keywords: green synthesis, imidazoles, β-acetamidoketones, β-hydroxyketones, coconut coir, heterogeneous catalyst

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Introduction

There is great demand for environmentally benign, economical and easily available catalysts in synthesis, since these catalysts do not produce any pollutant. Also, in recent years multicomponent reactions (MCRs) have proved to be powerful tools to access combinatorial libraries of organic molecules for finding efficient lead structure in drug discovery programmes [1, 2]. MCRs generate products in a single synthetic operation thus saving energy and time [3]. Development of new MCRs [4] and improvement of existing ones are the areas of considerable interest for synthetic chemists. Multicomponent synthesis of imidazoles, β-acetamidoketones and β-hydroxyketones are of great interest in the field of organic synthesis because of their broad spectrum of applications. Their applications as enzyme inhibitors, antibiotics, peptide mimics, herbicides, pharmacological agents and many other utilities are well documented [5-11]. Imidazoles, β-acetamidoketones and β-hydroxyketones being important biological active compounds have been synthesized by a diverse number of synthetic approaches. Various synthetic methods for their preparation through the multicomponent condensation have been reported in presence of various catalysts such as silica gel or HY zeolite [12] silica gel/$NaHSO_4$ [13] $K_5CoW_{12}O_{40}.3H_2O$ [14], molecular iodine [15], $HClO_4$-SiO_2 [16], $In(OTf)_3$ [17], $Al(HSO_4)_3$ [18], $CuCl_2.2H_2O$/$CuSO_4.5H_2O$ [19], $FeCl_3.6H_2O$/TMSCl [20], $MgCl_2.6H_2O$ [21], $SnCl_2.2H_2O$ [22], $Ce(NO_3)_3.6H_2O$ [23], $Zn(NO_3)_2$ [24], $Yb(NTf_2)_3$ [25], $CuBr_2$ [26], VCl_3 [27]. However, most of the reported synthetic methods have limitation like harsh reaction conditions, use of hazardous catalysts and solvents, and thus their disposal pollutes the environment. Consequently, there is a scope to develop new methods which are simple, efficient, clean, high yielding and environmentally benign.

In continuation of our research programme to develop green, economical catalysts and synthetic methods [28-32] for the synthesis of various classes of compounds, we report herein, Cu^{2+} immobilized coconut coir (Cu^{2+}-CC) as a new heterogeneous catalyst for the synthesis of imidazoles, β-acetamidoketones and β-hydroxyketones.

Experimental

General Procedure for Synthesis of Cu^{2+} Immobilized Coconut Coir (Cu^{2+}-CC)

5 g of powdered coconut coir was treated with 1g aqueous solution of $CuSO_4$. Mixture was then stirred for 6 hours on a mechanical shaker. Finally, mixture was washed with distilled water and dried under vacuum to give Cu^{2+} immobilized coconut coir (Cu^{2+}-CC).

General Procedure for Synthesis of Tetrasubstituted Imidazoles

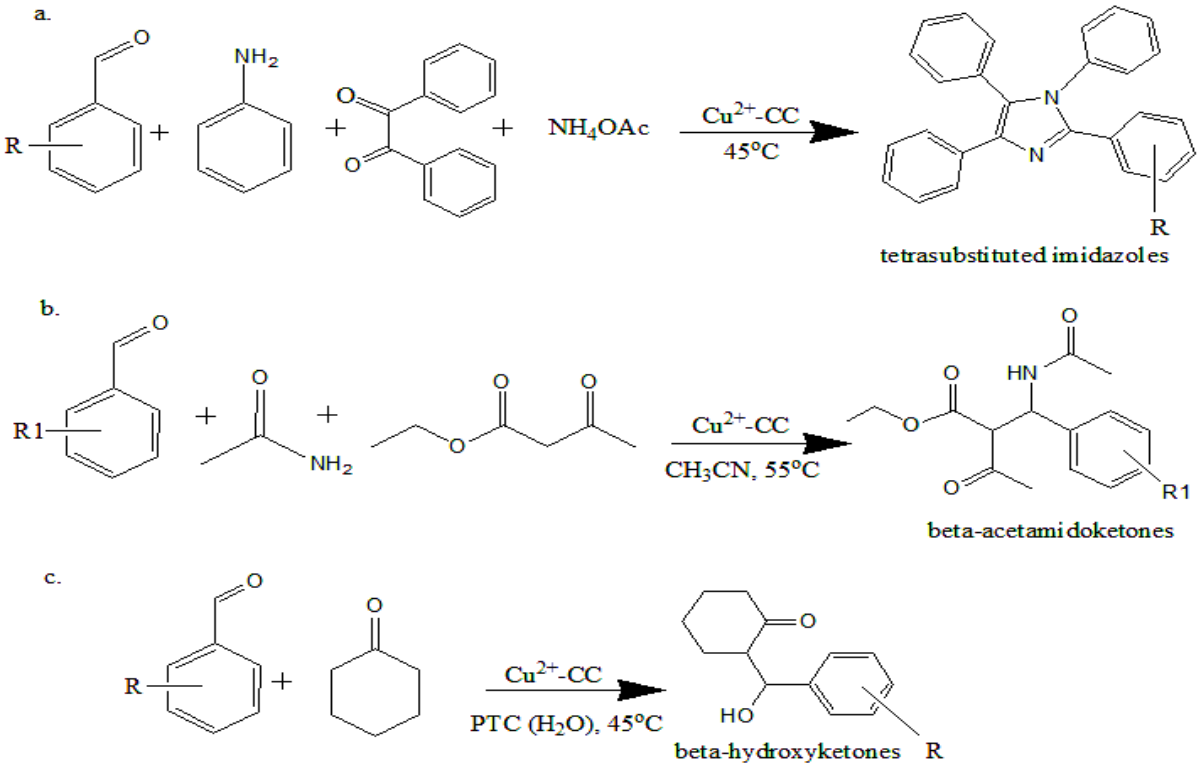
To the 100 mL round bottom flask, a mixture of aromatic aldehyde (5 mmol), aniline (5 mmol), benzil (5 mmol), ammonium acetate (5 mmol) and Cu^{2+}-CC (0.5 mmol) was taken and heated at 45°C under solventless condition (**Scheme 1a**). The reaction progress was monitored over silica gel TLC Plates. After completion of the reaction, ice cold water was added to the mixture to obtain solid product, which was further filtered and washed with cold water. The crude product was crystallized using ethyl alcohol.

General Procedure for Synthesis of β-Acetamidoketones

Aromatic aldehyde (1 mmol), acetamide (1.5 mmol), ethylacetoacetate (1.5 mmol) along with catalyst, Cu^{2+}-CC (0.5 mmol) were taken with acetonitrile (5 mL) into a 500 mL two necked round bottom flask equipped with reflux condenser and thermometer. The reaction mixture was refluxed at 55°C on heating mantle (Scheme 1b). The completion of reaction was confirmed by TLC. The solid product formed was washed with chloroform. Recrystallization was done from acetone to get the pure product.

General Procedure for Synthesis of β-Hydroxyketones

Into 250 mL two necked round bottom flask equipped with reflux condenser and thermometer, aromatic aldehyde (2 mmol), cyclohexanone (2 mmol) and Cu^{2+}-CC (0.5 mmol) were taken in the solution of water (8 mL) containing 0.04 mmol benzyltriethyl ammonium chloride as a phase transfer catalyst. The reaction mixture was refluxed at 45°C on heating mantle (Scheme 1c). The completion of reaction was confirmed by TLC. The water was disposed off and the crude product was recrystallized from chloroform to obtain pure product.



Scheme 1 Synthesis of a). imidazoles, b). β-acetamidoketones, c). β-hydroxyketones using Cu^{2+} immobilized coconut coir (Cu^{2+}-CC)

Results and Discussions

As part of our ongoing research programme to the development of environmentally benign catalysts, we studied the synthesis of imidazoles, β-acetamidoketones and β-hydroxyketones. It has been found that the compounds were prepared in good to excellent yields. Perusal of **Table 1-3** showed the efficiency of Cu^{2+} immobilized coconut coir (Cu^{2+}-CC) as a heterogeneous catalyst for multicomponent reaction of imidazoles, β-acetamidoketones and β-hydroxyketones. Reusability and recyclability of Cu^{2+}-CC was determined for the synthesis of 2-(4-chlorophenyl)-1,4,5-triphenyl-1*H*-imidazole, ethyl 2-(acetamido(4-chlorophenyl)methyl)-3-oxobutanoate and 2-((4-chlorophenyl)

(hydroxy)methyl) cyclohexanone and is shown in **Figure 1**. Cu^{2+}-CC even after 3 consecutive cycles gave compounds in constant good yield. Also, Cu^{2+}-CC has wide substrate scope as it worked well with both types of aromatic aldehydes having electron donating and withdrawing groups on benzene ring.

Table 1 Synthesized tetrasubstituted imidazoles in the presence of Cu^{2+} immobilized coconut coir (Cu^{2+}-CC)

Entry	Name of synthesized compound	Yield %	Time (hour)	Melting point
1	2-(4-nitrophenyl)-1,4,5-triphenyl-1*H*-imidazole	79	1.5	56^0C
2	2-(3-methoxyphenyl)-1,4,5-triphenyl-1*H*-imidazole	81	2	59^0C
3	2-(4-chlorophenyl)-1,4,5-triphenyl-1*H*-imidazole	83	1.5	52^0C
4	2-(4-fluorophenyl)-1,4,5-triphenyl-1*H*-imidazole	79	1.5	54^0C
5	2-(4-methylphenyl)-1,4,5-triphenyl-1*H*-imidazole	78	2	60^0C

Table 2 Synthesized β-acetamidoketones in the presence of Cu^{2+} immobilized coconut coir (Cu^{2+}-CC)

Entry	Name of synthesized compound	Yield %	Time (hour)	Melting point
6	Ethyl 2-(acetamido(4-fluorophenyl)methyl)-3-oxobutanoate	81	4	105^0C
7	Ethyl 2-(acetamido(4-chlorophenyl)methyl)-3-oxobutanoate	76	3.5	111^0C
8	Ethyl 2-(acetamido(3-chlorophenyl)methyl)-3-oxobutanoate	82	2.5	115^0C
9	Ethyl 2-(acetamido(3-methoxyphenyl)methyl)-3-oxobutanoate	85	5	109^0C
10	Ethyl 2-(acetamido(4-methylphenyl)methyl)-3-oxobutanoate	79	2.5	100^0C

Table 3 Synthesized β-hydroxyketones in the presence of Cu^{2+} immobilized coconut coir (Cu^{2+}-CC)

Entry	Name of synthesized compound	Yield %	Time (hour)	Melting point
11	2-(hydroxy(4-nitrophenyl)methyl) cyclohexanone	82	1	99^0C
12	2-((4-chlorophenyl)(hydroxy)methyl) cyclohexanone	79	1	97^0C
13	2-((4-fluorophenyl)(hydroxy)methyl) cyclohexanone	85	1.5	100^0C
14	2-((4-bromophenyl)(hydroxy)methyl) cyclohexanone	81	1	99^0C
15	2-(hydroxy(4-methylphenyl)methyl) cyclohexanone	83	2	100^0C

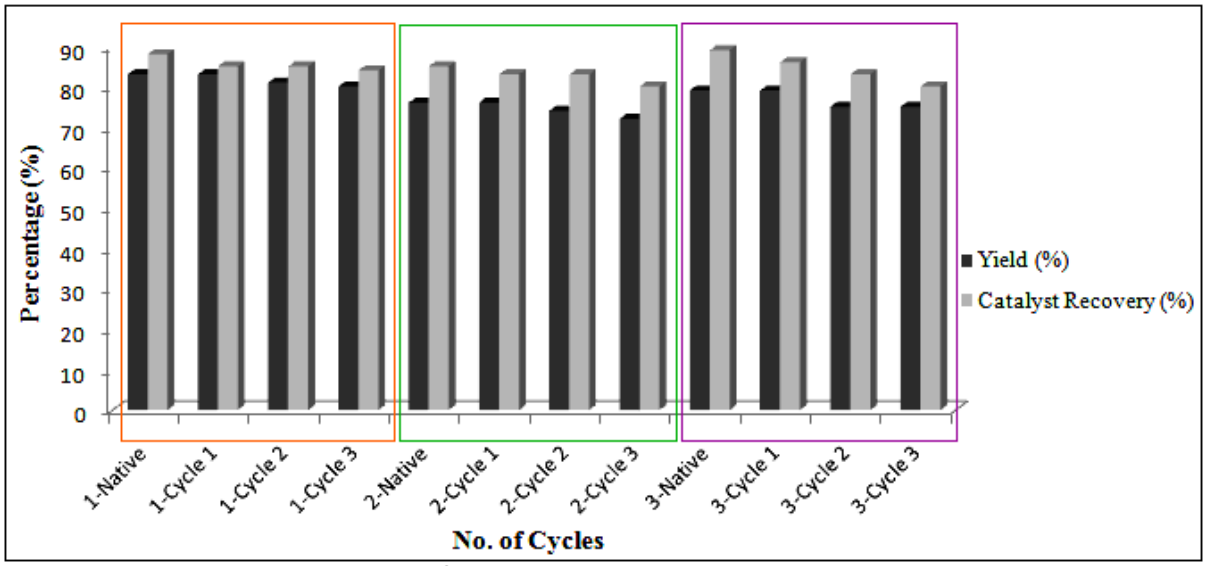


Figure 1 Reusability and recyclability of (Cu^{2+}-CC) for 2-(4-chlorophenyl)-1,4,5-triphenyl-1*H*-imidazole (1-Native to 1-Cycle 3), ethyl 2-(acetamido(4-chlorophenyl)methyl)-3-oxobutanoate (2-Native to 2-Cycle 3)and 2-((4-chlorophenyl)(hydroxy)methyl) cyclohexanone (3-Native to 3-Cycle 3)

Characterization of Heterogeneous Catalyst- Cu^{2+} Immobilized Coconut Coir (Cu^{2+}-CC)

SEM Analysis

Morphological changes of coconut coir before and after Cu^{2+} immobilization were observed using scanning electron microscope (SEM). SEM micrograph of raw coconut coir clearly indicates the presence of open tubular surface with intervening pores containing void space (**Figure 2a**) [33]. The Cu^{2+} immobilized coconut coir exhibit closed tubules

with partially shrunken pores (Figure 2b). These surface modifications indicated the development of Cu^{2+} immobilized coconut coir (Cu^{2+}-CC).

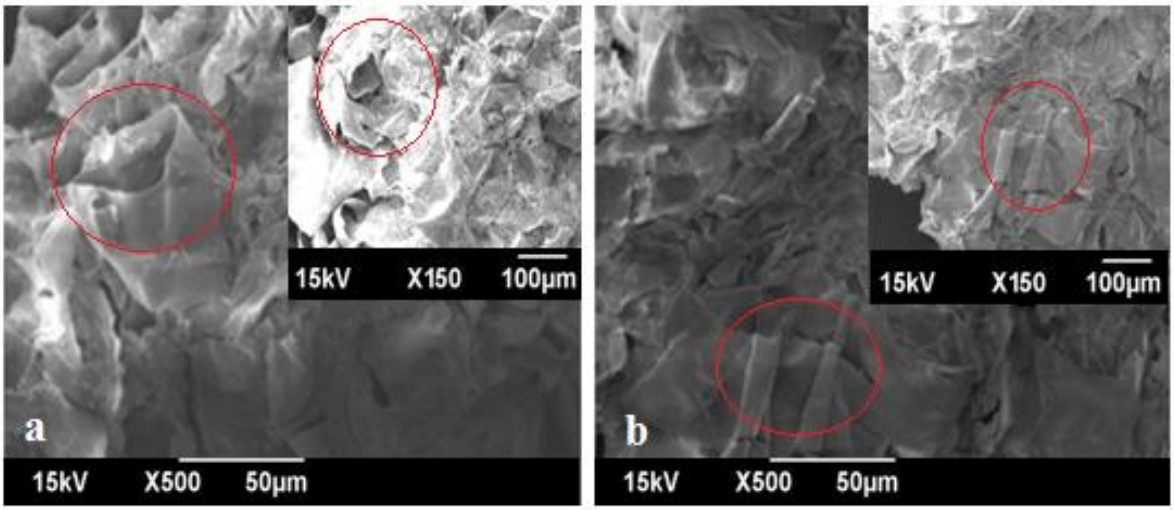


Figure 2 (a) SEM micrograph of untreated coconut coir, (b) SEM micrograph of Cu^{2+} immobilized coconut coir (Cu^{2+}-CC)

Characterization of Synthesized Compounds

IR spectra were recorded on Brucker FT-IR spectrophotometer using KBr pellets. ^{1}H NMR spectra were recorded on Brucker AVANCE II 400 MHz instrument using $CDCl_3$ with TMS as internal standard.^{1}H NMR and IR spectra of synthesized compounds are as follows:

Table 1, Entry 1: 2-(4-nitrophenyl)-1,4,5-triphenyl-1*H*-imidazole
IR (KBr), 3104, 1590, 1367, 831 cm^{-1}.
^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 7.1- 7.9 (m, 19H, Ar-H).

Table 1, Entry 2: 2-(3-methoxyphenyl)-1,4,5-triphenyl-1*H*-imidazole
IR (KBr), 3245, 1572, 1456, 843 cm^{-1}.
^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 3.1 (s, 3H, $-OCH_3$), 7.2-8.1 (m, 19H, Ar-H).

Table 1, Entry 3: 2-(4-chlorophenyl)-1,4,5-triphenyl-1*H*-imidazole
IR (KBr), 3124, 1584, 1435, 833 cm^{-1}.
^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 7.2- 8.3 (m, 19H, Ar-H).

Table 1, Entry 4: 2-(4-fluorophenyl)-1,4,5-triphenyl-1*H*-imidazole
IR (KBr), 3059, 1516, 1424, 865 cm^{-1}.
^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 7.4- 8.3 (m, 19H, Ar-H).

Table 1, Entry 5: 2-(4-methylphenyl)-1,4,5-triphenyl-1*H*-imidazole
IR (KBr), 3145, 1603, 1374, 857 cm^{-1}.
^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 2.7 (s, 3H, $-CH_3$), 7.1- 8.2 (m, 19H, Ar-H).

Table 2, Entry 6: Ethyl 2-(acetamido(4-fluorophenyl)methyl)-3-oxobutanoate
IR (KBr) 3327, 2906, 1721, 1659, 1536, 1484, 1387 cm^{-1}.
^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.3 (t, 3H, $-O-CH_2-CH_3$), 2.2 (s, 3H, $-NH-CO-CH_3$), 2.35 (s, 3H, $-CO-CH_3$), 2.6 (q, 2H, $-CO-CH_2-$), 3.4 (d, 1H, -CO-CH-CO-), 4.2 (d, 1H, Ar-CH-NH-), 7.25-7.8 (m, 4H, Ar-H), 8.3 (s, 1H, -NH-CO-).

Table 2, Entry 7: Ethyl 2-(acetamido(4-chlorophenyl)methyl)-3-oxobutanoate
IR (KBr) 3280, 3024, 1722, 1661, 1524, 1489, 1353 cm^{-1}.
^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.5 (t, 3H, $-O-CH_2-CH_3$), 2.45 (s, 3H, $-NH-CO-CH_3$), 2.7 (s, 3H, $-CO-CH_3$), 3.1 (q, 2H, $-CO-CH_2-$), 3.6 (d, 1H, -CO-CH-CO-), 4.3 (d, 1H, Ar-CH-NH-), 7.1-7.85 (m, 4H, Ar-H), 8.25 (s, 1H, -NH-CO-).

Table 2, Entry 8: Ethyl 2-(acetamido(3-chlorophenyl)methyl)-3-oxobutanoate
IR (KBr) 3305, 2043, 1814, 1704, 1524, 1473, 1391 cm^{-1}.
^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.35 (t, 3H, $-O-CH_2-CH_3$), 2.05 (s, 3H, $-NH-CO-CH_3$), 2.2 (s, 3H, $-CO-CH_3$), 2.4 (q, 2H, $-CO-CH_2-$), 3.15 (d, 1H, -CO-CH-CO-), 3.9 (d, 1H, Ar-CH-NH-), 7.1-7.7 (m, 4H, Ar-H), 8.1 (s, 1H, -NH-CO-).

Table 2, Entry 9: Ethyl 2-(acetamido(3-methoxyphenyl)methyl)-3-oxobutanoate

IR (KBr) 3172, 2961, 1824, 1680, 1527, 1534, 1411 cm^{-1}.

^1H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.4 (t, 3H, -O-CH_2-CH_3), 1.8 (s, 3H, -OCH_3), 2.4 (s, 3H, -NH-CO-CH_3), 2.6 (s, 3H, -CO-CH_3), 2.8 (q, 2H, -CO-CH_2-), 3.25 (d, 1H, -CO-CH-CO-), 4.5 (d, 1H, Ar-CH-NH-), 7.05-7.85 (m, 4H, Ar-H), 8.05 (s, 1H, -NH-CO-).

Table 2, Entry 10: Ethyl 2-(acetamido(4-methylphenyl)methyl)-3-oxobutanoate

IR (KBr) 3273, 1735, 1701, 1538, 1475, 1430 cm^{-1}.

^1H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.6 (t, 3H, -O-CH_2-CH_3), 2.1 (s, 3H, -CH_3), 2.65 (s, 3H, -NH-CO-CH_3), 2.85 (s, 3H, -CO-CH_3), 3.2 (q, 2H, -CO-CH_2-), 3.75 (d, 1H, -CO-CH-CO-), 4.35 (d, 1H, Ar-CH-NH-), 7.1-7.7 (m, 4H, Ar-H), 8.2 (s, 1H, -NH-CO-).

Table 3, Entry 11: 2-(hydroxy(4-nitrophenyl)methyl) cyclohexanone

IR (KBr) 3014, 1698, 1587, 1412, 798 cm^{-1}.

^1H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.5-2.2 (m, 6H), 2.4-2.65 (m, 2H), 2.9-3.2 (m, 1H), 4.6 (d, 1H), 7.4 (d, 2H), 8.2 (d, 2H).

Table 3, Entry 12: 2-((4-chlorophenyl)(hydroxy)methyl) cyclohexanone

IR (KBr) 2965, 1712, 1625, 1421, 814 cm^{-1}.

^1H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.65-2.3 (m, 6H), 2.5-2.75 (m, 2H), 3.1-3.35 (m, 1H), 4.85 (d, 1H), 7.15 (d, 2H), 8.1 (d, 2H).

Table 3, Entry 13: 2-((4-fluorophenyl)(hydroxy)methyl) cyclohexanone

IR (KBr) 2935, 1689, 1617, 1408, 805 cm^{-1}.

^1H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.8-2.35 (m, 6H), 2.6-2.75 (m, 2H), 3.2-3.45 (m, 1H), 4.55 (d, 1H), 7.45 (d, 2H), 7.9 (d, 2H).

Table 3, Entry 14: 2-((4-bromophenyl)(hydroxy)methyl) cyclohexanone

IR (KBr) 2953, 1724, 1642, 1388, 855 cm^{-1}.

^1H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 2.1-2.55 (m, 6H), 2.8-2.95 (m, 2H), 3.15-3.45 (m, 1H), 4.45 (d, 1H), 7.2 (d, 2H), 8.15 (d, 2H).

Table 3, Entry 15: 2-(hydroxy(4-methylphenyl)methyl) cyclohexanone

IR (KBr) 3042, 1681, 1633, 1424, 763 cm^{-1}.

^1H NMR ($CDCl_3$, TMS, 400 MHz): δ (ppm) 1.55-2.1 (m, 6H), 2.1-2.3 (m, 2H), 2.6-2.85 (m, 1H), 3.45-3.7 (s, 3H), 4.3 (d, 1H), 7.2-8.25 (d, 4H).

Conclusion

In conclusion, an efficient, mild and environmentally benign approach for the synthesis of tetrasubstituted imidazoles, β-acetamidoketones and β-hydroxyketones has been developed using Cu^{2+} immobilized coconut coir (Cu^{2+}-CC) as green heterogeneous catalyst via multicomponent reaction. Cu^{2+}-CC also showed its efficacy towards MCRs in terms of its reusability and recyclability. Easy work up, high yields and environmentally benign are the key features of the procedure.

Acknowledgement

Authors are sincerely thankful to DST, New Delhi for the award of DST-INSPIRE Fellowship to conduct the research work. Indian Institute of Chemical Technology, Hyderabad and Punjab University, Chandigarh, India are also gratefully acknowledged for providing spectral analysis.

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Publication History
Received 10th Apr 2018
Revised 28th Apr 2018
Accepted 06th May 2018
Online 30th May 2018