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MICROENCAPSULATED COPPER (II) ACETYLACETONATE: AN EFFICIENT, ENVIRONMENTAL BENIGN AND RECYCLABLE CATALYST FOR MICROWAVE-PROMOTED SYNTHESIS OF AMIDOALKYL NAPHTHOL

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ABSTRACT

Microwave assisted Microencapsulated-Cu(acac)$_2$ [MC-Cu(acac)$_2$] is found an efficient, environmentally benign catalyst for the one pot multicomponent condensation reaction of aromatic aldehyde, β-naphthol and amide to form the amidoalkyl naphthols in good yield. Additionally, the catalyst could be reused upto four times without the significant loss in yield and selectivity of the product. The notable features of this multicomponent one pot C-C and C-N bond forming reaction procedure are high conversations, economically cheap, operationally simple, and eco-friendly method.

KEYWORDS: Microwave, MC-Cu (acac)$_2$, Multicomponent reaction, Heterogeneous catalysis.

INTRODUCTION

In recent years, one-pot multicomponent reactions have attracted significant attention. MCRs are gave the desired product in a single operation without need to separate any intermediates throughout the processes. This type of techniques decreases the reaction time significantly increase the yield of the desired products as compaired with normal multi-step process, save an energy input.[1-3] They have advantages over two components reaction in numerous features involving the ease of a one pot procedures, good yield, possible structural variation and building up complex molecules.[4-6] In addition the implementation of several conversions in a single operation is highly compatible with the goals of sustainable and green chemistry.

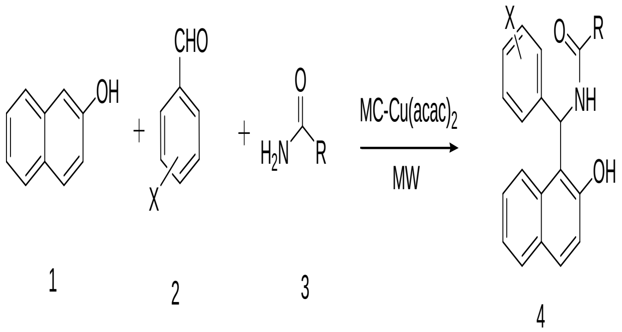
Compounds having 1,3-amino-oxygenated functional groups are widely used in many biologically important natural products, potent drugs including a number of nucleoside antibiotics and HIV protease inhibitors such as ritonavir and lipinavir.[7,8] It is important that 1-amidoalkyl-2-naphthol can be simply hydrolyzed to significant biologically active 1-aminoalkyl-2-naphthol derivatives and shows biological activities like hypotensive and bradycardic effects.[9-11]

Conventionally, these compounds have been synthesized by one-pot multicomponent condensation reaction of β-naphthol, aryl-aldehyde and amide in presence of different acid catalysts. such as TMSCl/NaI[12], P_2O_5[13], Iodine[14,15], Bi(OTf)$_3$[16], Bi(NO$_3$)$_3$.5H$_2$O[17], ZrOCl$_2$.8H$_2$O[18], Ce(SO$_4$)$_2$,[19] Fe(HSO$_4$)$_3$[20],Sr(OTf)$_2$[21], Yb(OTf)$_3$[22], InCl$_3$[23], *p*-TSA[24], Montmorillonite K-10.[25] But all of these procedures have suffers from the some drawbacks of green chemistry such as long reaction time, low yield, high reaction temperature, reusability of catalysts etc. The recovery and reusability of the catalyst is also a major problem. Therefore, the demand for green and eco-friendly procedure that uses reusable catalyst needed us to improve an alternative method for the synthesis of amidoalkyl naphthol.

Heterogeneous catalysts have gained much importance in recent years due to economic and environmental considerations.[26,27] These catalysts are usually cheap, highly reactive, environmentally benign, easy to handle, decrease reaction time, simple work up and reusability of the catalyst.

Immobilized heterogeneous catalyst has been of great interest due to several advantages, such as ease of products separation and reuse of the catalyst.[28,29] Recently Kobayashi et. Al[30-33] and Kantam et. al.[34] has reported the use of microencapsulation as a technique for immobilizing metal complexes. Microencapsulation is a reasonably new method for immobilizing transition metal catalysts into polymers. This allows interactions between the π-bond electrons of benzene rings of the polystyrene-based polymers and vacant orbitals of the transition metal compound rendering the catalysts system more efficient. This microencapsulation technique has been used in a variety of reactions such as [MC-Sc(OTf)$_3$] is Lewis acid catalysts in several reactions.[30,35,36] [MC-Pd(PPh$_3$)] for allylic substitution, Suzukicoupling and Mizoroki Heck reactions.[32] Kantam et. al. have synthesized [MC-Cu(acac)$_2$] catalyst and used for the aziridination of olefins with [N-(p-tolylsulfonyl)imino]phenyliodinane as the nitrogen source.[34]

Many chemists have made a great deal of an efforts to design environmental benign and clean synthetic procedures to replace the classical synthetic methods. Microwave heating is an eco-friendly methodology and a valuable tool for synthetic chemists because it is possible to increase the reaction rate and product yields as well as exploits a variety of factors such as milder and more efficient environments, shorter reaction times, energy conservation, formation of purer products and waste minimization.[37] There is a considerable increase of interest in this promising technique for promoting reactions.



Scheme. 1: Synthesis of 1-amidoalkyl-2-naphthols.

In our continuous work on the development of C-C and C-N bond forming reactions[38-40] by using an efficient and environmental benign catalyst herein, we are reporting the microwave assisted one pot three omponent reaction of β-naphthol, aromatic aldehyde and amide using MC-Cu(acac)$_2$ as catalyst for the preparation of amidoalkyl naphthol in good to excellent yield (**Scheme 1**). It has various advantages due to low toxicity, low price and experimental simplicity.

RESULTS AND DISCUSSION

Microencapsulated-Cu(acac)$_2$ catalyst is prepared according to the procedure reported by Kobayashi et. al. and Kantam et. al. The synthesized MC-Cu(acac)$_2$ catalyst was characterized by FT-IR spectroscopy (figure 1). The IR spectrum of catalyst has peaks at 3062, 3024 and 2922 cm^{-1} assigned to C-H bond stretching. The peaks at 1942, 1872, 1805 cm^{-1} shows that the aromatic benzene ring presents in polystyrene.[30] The peak at 1577 and 1529 cm^{-1} band assigned to ν(C=C) coupled with ν(C=O), and ν(C=O) coupled with ν(C=C) respectively.[41] Peak at 1446 cm^{-1} shows ν(C=C) and the peak at 451cm^{-1} for ν(Cu-O)stretching.

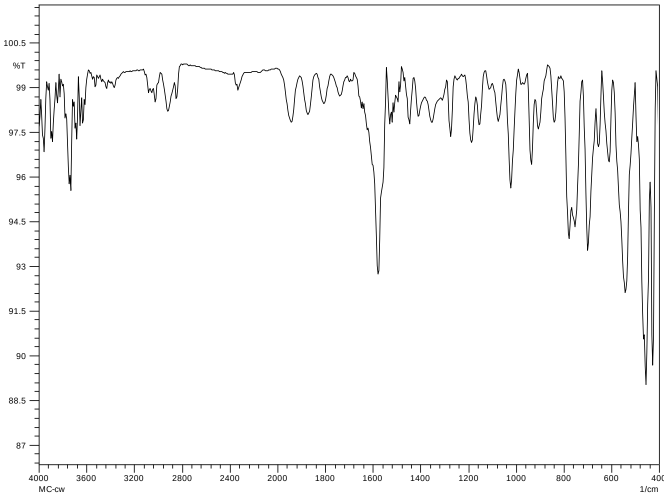


Figure. 1: FT-IR spectra of [MC-Cu(acac)$_2$].

Table. 1: Effects of various parameters on synthesis of 1-amidoalkyl-2-naphthols[a].

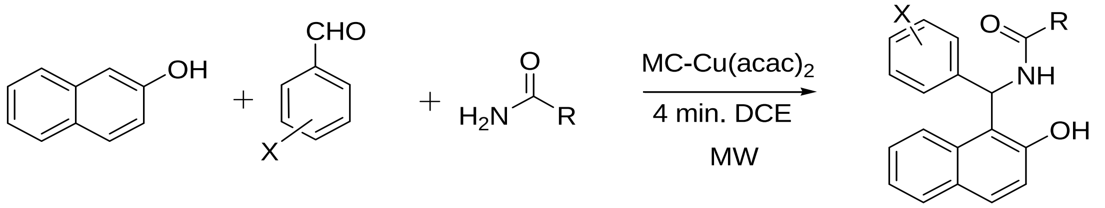
Entry	Catalyst	Catalyst loading (mg)	Time (min.)	Yield (%)[b]
1	--	--	5	34
2	MC-Cu(acac)$_2$	30	5	76
3	MC-Cu(acac)$_2$	40	5	94
4	MC-Cu(acac)$_2$	50	5	94
5	MC-Cu(acac)$_2$	40	4	82
6	MC-Cu(acac)$_2$	40	6	94
7[c]	MC-Cu(acac)$_2$	40	1080	91

[a]Reaction conditions: β-naphthol (1 mmol), Benzaldehyde (1 mmol), acetamide (1.1 mmol), DCE (3 mL), Microwave Irradiation.[b]Isolated yield, [c]By thermal method.

At the onset of the research, we have made a conscious effort to develop a catalytic system that would address the limitations of the previously reported reactions. During preliminary studies benzaldehyde and acetamide was chosen as a model system for the reaction with β-naphthol, benzaldehyde was treated with equimolar amount of β-naphthol and acetamide in the presence of MC-Cu(acac)$_2$ in microwave irradiation to afford amidoalkyl naphthols. A series of experiments were performed to optimize various reaction parameters, such as the effect of MC-Cu(acac)$_2$ catalyst loading and time for the present multicomponant reaction. Westudied catalyst loding from 30 mg to 50 mg. The yield improved as the loading of MC-Cu(acac)$_2$ catalyst increased from 30 to 40 mg and became almost steady when the amount of catalyst was further increased beyond this. (Table 1, entry-1, 1-4). We have studied the effect of irradiation time on the model reaction and give good yield of desired products in 5 min. (Table 1 entries 3, 5,6).

Having optimized the reaction condition in hand we next set out to explore the substrate scope of Mc-Cu(acac)$_2$ catalysts for amidoalkyl naphthols. Most importantly aromatics aldehydes carrying either electron donating or withdrawing substituent afforded to good yield of products; a variety of common functional groups, such as alkyl, ether, halo and nitro were tolerated, regardless of the meta- or para- position, however ortho- substituted aryl aldehyde gave lower yields, maybe due to steric hindrance. The outcomes of these reactions are summarized in **Table 2**. Moreover, we also explored the reusability study of the catalytic system on the benchmark reaction and the results are presented in the **scheme 2**. Subsequently completion of the reaction according to TLC, the reaction mixture was diluted with ethyl acetate and catalyst was separated by simple filtration. The catalyst was washed with acetonitrile (3×10 ml), then used directly in the reusability studies.

Table. 2: MC-Cu(acac)$_2$ catalysed one-pot multicomponent synthesis of substituted amidoalkyl naphthols.[a]

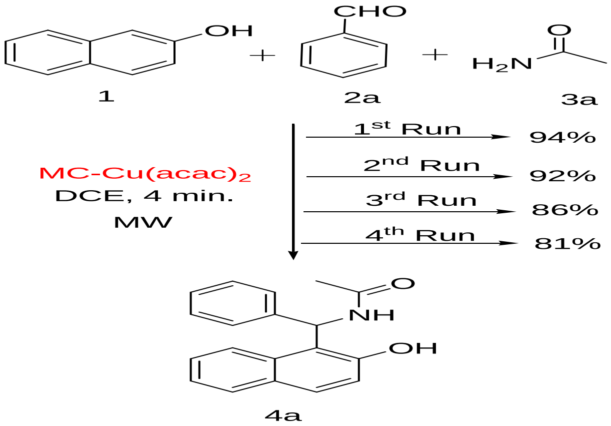


1 2(a-g) 3(a,b) 4(a-m)

Entry	X	R	Product	Yield (%)[b]	M. P. (°C), (Reported)[Ref.]
1	H	$-CH_3$	4a	94	240-242 (241-243)[19]
2	4-Cl	$-CH_3$	4b	93	238-240 (237-238) [13]
3	2-Cl	$-CH_3$	4c	72	208-210 (213-215)[20]
4	4- CH_3	$-CH_3$	4d	86	222-224 (224-225) [13]
5	4-O CH_3	$-CH_3$	4e	89	184-186 (183-185) [20]
6	4-NO_2	$-CH_3$	4f	91	236-238 (237-238) [13]
7	3-NO_2	$-CH_3$	4g	90	244-246 (256-258) [13]
8	H	$-C_6H_5$	4h	89	238-240 (238-240) [13]
9	4-Cl	$-C_6H_5$	4i	82	168-170 (168-170) [13]
10	4- CH_3	$-C_6H_5$	4j	91	214-216 (214-215) [13]
11	4-O CH_3	$-C_6H_5$	4k	84	204-206 (206-208) [13]
12	4-NO_2	$-C_6H_5$	4l	86	230-232 (228-229) [13]
13	3-NO_2	$-C_6H_5$	4m	82	242-244 (242-243) [13]

[a] Reaction condition: β-naphthol (1 mmol), aldehyde (1 mmol),amide (1.1 mmol) catalyst (40 mg) and DCE (3 ml), Microwave Irradiation.

[b] Isolated yield.



Scheme. 2: Recycle studies of [MC-Cu(acac)$_2$] catalysts.

MATERIALS AND METHODS

All the chemicals were used without any additional purification. Cu(acac)$_2$ and polystyrene were purchased from Sigma-Aldrich chemical company. Polystyrene CAS No. 9003-53-6 having average molecular weight ~280,000 by GPC. Some selected products were characterized using ^{1}H-NMR on 300MHz spectrophotometer and ^{13}C-NMR on 75MHz spectrophotometer in DMSO-d_6 as solvent and recorded in ppm relative to the TMS as an internal standard. IR spectra were recorded on a Perkin-Elmer spectrum on FTIR spectrophotometer using KBr pellets. TLC was performed on 0.25mm. E. Merck precoated silica gel plates (60 F254). Melting points were determined in open capillary tubes and are uncorrected. For the microwave irradiation experiment described below a conventional domestic microwave oven (Kenstar, Microwave output 800W ±10%; microwave frequency 2450MHz, Videocon Industries Pvt. Ltd. India) was used.

General Procedure

Preparation of catalyst: Microencapsulated-Cu(acac)$_2$ catalyst was prepared by using a reported procedure;Polystyrene (1.0 gm) was dissolved in cyclohexane (20 mL) at 40˚C and to this solution was added Cu(acac)$_2$ (0.12 gm), this mixture was stirred for 1 hr at 40˚C and then slowly cooled to 0˚C with vigorous stirring. The polystyrene solidified around the Cu(acac)$_2$ dispersed in the solution. Hexane (30 ml) was added to harden the capsule walls and the mixture was stirred at room temperature for 1hr and then the capsules were washed with acetonitrile several times and dried under vacuum.

General reaction procedure: A mixture of aromatics aldehyde (1 mmol), β-napthol (1 mmol), amide (1.1 mmol) and MC-Cu(acac)$_2$ (40 mg) in 1,2-dichloroethane (3 ml)were taken in a sealed tube, it was set in domestic microwave (Kenstar, Microwave output 800W±10%; microwave frequency 2450MHz) irradiation for a 5 min. The progress of the reaction was monitored by TLC. On completion of the reaction was cooled to room temperature and diluted with ethyl acetate (20 ml), then catalyst was filtered and the filtrate concentrated and poured on chilled water, purified by recrystallisation from EtOH-H_2O (1:1) and the pure products were obtained.

The NMR spectral data of some selected compounds of the amidoalkyl naphthol are summarized below.

1)*N*-[(2-hydroxynaphthalen-1-yl)(phenyl)methyl]acetamide; (4a)

M. P. 240-242 (241-243)[19]; ^{1}H-NMR (300 MHz, DMSO-d$_6$) :- δ; 10.06 (s, 1H), 8.46 (d, *J*=8.4 Hz, 2H), 7.81 (s, 1H), 7.77 (d, *J*=9.3 Hz, 2H), 7.36-7.22 (m, 4H), 7.19-7.11 (m, 4H), 1.98 (s, 1H). ^{13}C-NMR (75 MHz, DMSO-d$_6$):- δ 169.84, 153.58, 143.00, 132.76, 129.72, 129.01, 128.90, 128.46, 126.80, 126.57, 126.47, 123.70, 122.88, 119.25, 118.89, 48.26, 23.09.

2)*N*-[(2-chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl]acetamide; (4c)

M. P. 208-210 (213-215)[20];^{1}H-NMR (300 MHz, DMSO-d$_6$) :- δ; 9.91 (s, 1H), 8.62 (d, *J*=8.4 Hz, 1H), 7.99 (t, 1H), 7.81-7.74 (m, 1H), 7.57, (d, *J*=5.4 Hz, 1H), 7.43-7.26 (m, 6H), 7.16-7.07 (m, 2H), 1.93 (s, 3H). ^{13}C-NMR (75 MHz, DMSO-d$_6$):- δ 169.24, 154.10, 140.19, 133.23, 132.72, 130.31, 129.89, 129.69, 129.06, 128.73, 128.65, 126.79, 123.25, 122.76, 119.03, 117.46, 48.06, 22.82.

3)*N*-[(4-nitrophenyl)(2-hydroxynaphthalen-1-yl)methyl]acetamide; (4f)

M. P. 236-238 (237-238)[13]; ^{1}H-NMR (300 MHz, DMSO-d$_6$) :- δ; 10.19 (s, 1H), 8.59 (d, *J*= 7.8 Hz, 1H), 8.13 (d, *J*= 8.7 Hz, 2H), 7.84-7.79 (m, 4H), 7.39 (d, *J* = 8.7 Hz, 3H), 7.31-7.16 (m, 2H), 2.02 (s, 3H). ^{13}C-NMR (75 MHz, DMSO-d$_6$):- δ; 170.29, 153.76, 151.62, 146.36, 132.61, 130.36, 129.14, 128.88, 128.57, 127.20, 123.69, 123.32, 123.08, 118.81, 118.25, 48.32, 22.96.

1)*N*-[(2-hydroxynaphthalen-1-yl)(phenyl)methyl]benzamide; (4h)

M. P. 238-240 (238-240)[13]; ^{1}H-NMR (300 MHz, DMSO-d$_6$) :- δ; 10.39 (s, 1H), 9.04 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.88-7.79 m, 4H), 7.57-7.44 (m, 5H), 7.34-7.21 (m, 7H). ^{13}C-NMR (75 MHz, DMSO-d$_6$):- δ; 166.24, 153.64, 142.45, 134.77, 132.77, 131.92, 129.85, 129.09, 128.99, 128.84, 128.67, 127.59, 127.25, 127.03, 126.89, 123.17, 119.13, 118.78, 49.69.

5) *N*-[(4-chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl]benzamide; (4i)

M. P. 168-170 (168-170)[13]; ^{1}H-NMR (300 MHz, DMSO-d$_6$) :- δ; 10.35 (s, 1H), 9.03 (d, J= 7.8 Hz, 1H), 8.06 (d, J= 8.1 Hz, 1H), 7.88-7.79 (m, 4H0, 7.58-7.46 (m, 4H), 7.36-7.22 (m, 7H). ^{13}C-NMR (75 MHz, DMSO-d$_6$):- δ; 166.38, 153.71, 141.53, 134.64, 132.68, 131.96, 131.56, 130.06, 129.13, 128.94, 128.80, 128.58, 127.69, 127.32, 123.18, 119.09, 118.34, 49.20.

CONCLUSION

We have developed an effective and eco-friendly procedure for one pot multicomponent synthesis of amidoalkyl naphthol via three component condensation reaction of 2-naphthol, aryl aldehyde and amide using a MC-Cu(acac)$_2$ as a catalyst in a DCE with microwave irradiation for 5min.. MC-Cu (acac)$_2$ is acted as a heterogeneous and recyclable catalyst. This extraordinary characteristic made this new procedure which is economically, eco-friendly, attractive and inexpensive.

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