Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(17):137-141
(http://derpharmachemica.com/archive.html)

Heterogeneous Microencapsulated Copper (II) Acetylacetonate as Green Catalyst for Synthesis of Amidoalkyl Naphthol

[a]Bhikan J. Khairnar, [a]Pravinsing S. Girase, [b]Dhananjay V. Mane and [a]Bhata R. Chaudhari*

[a]Dept. of Chemistry, JET's Z. B. Patil College, Dhule (MS), India
[b]Dept. of Chemistry, Shri Chhatrapati Shivaji College, Omerga Dist. Osmanabad.(MS), India

---

ABSTRACT

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

Key words: MC-Cu(acac)$_2$, Multicomponent reaction, β-Naphthol, Aldehyde, Heterogeneous catalysis.

INTRODUCTION

One-pot multicomponent reactions have attracted considerable attention in recent years. MCRs are furnished the desired product in a single operation without need to isolate any intermediates during the processes. This reaction reduces the reaction time considerably increase the yield of the products than normal multistep methods, save an energy input [1-3]. They have merits over two components reaction in several aspects including the simplicity of a one pot procedures, good yield, possible structural variation and building up complex molecules. Biginelli [4,5], Ugi [6], Passerini [7,8] and Mannich [9,10] are some examples of MCRs. In addition the implementation of several transformations in a single manipulation 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 [11,12]. It is noteworthy that 1-amidoalkyl-2-naphthol can be easily hydrolyzed to important biologically actives 1-aminoalkyl-2-naphthol derivatives, which compounds show biological activities like hypotensive and bradycardic effects [13-15].

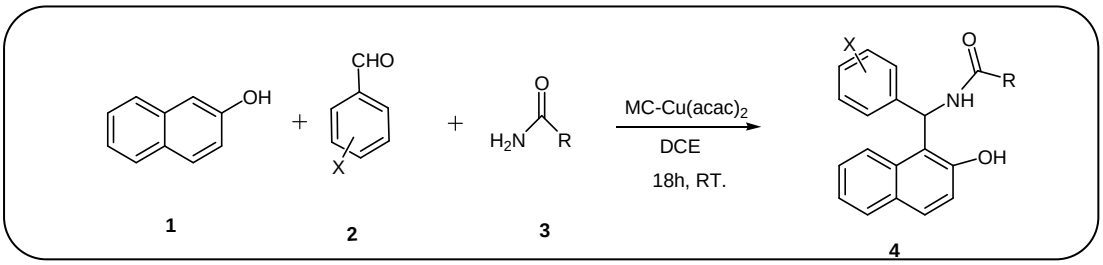
Traditionally, these compounds have been synthesized by one-pot multicomponent condensation reaction of β-naphthol, aryl-aldehyde and amide in presence of different acid catalysts such as *p*-TSA [16], $Ce(SO_4)_2$ [17], Iodine [18,19], $Yb(OTf)_3$ [20], $Fe(HSO_4)_3$ [21], $ZrOCl_2.8H_2O$ [22], Montmorillonite K-10 [23], P_2O_5 [24], $Sr(OTf)_2$ [25], $InCl_3$ [26], TMSCl/NaI [27], 2,4,6,-trichloro-1,3,5-triazine [28], polyphosphate ester [29], $Bi(NO_3)_3.5H_2O$ [30], $Bi(OTf)_3$ [31]. However these procedures have suffers from the some drawbacks of green chemistry such as high reaction temperature, prolonged reaction time, low yield, recovery and 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 necessitated us to develop an alternative method for the synthesis of amidoalkyl naphthol.

Heterogeneous catalysts have gained much importance in recent years due to economic and environmental considerations [32,33]. These catalysts are generally less expensive, highly reactive, environmentally benign, easy to handle, reduce reaction times, 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, isolation and reuse of the catalyst [34,35]. Recently Kobayashi et. al. [36-39] and Kantam et. al. [40] has reported the use of microencapsulation as a technique for immobilizing metal complexes. Microencapsulation is a moderately new method for immobilizing transition metal catalysts into polymers accomplished envelopment by the 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 various reactions [36,41,42]. [MC-Pd(PPh_3)] for allylic substitution, Suzuki coupling and Mizoroki Heck reactions [38]. 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 [40].

Considering the advantages of the microencapsulation technique, we have developed a MC-Cu$(acac)_2$ catalysts used for the one-pot multicomponent synthesis of 2-amidoalkyl naphthol.

In our continuous work on the development of C-C and C-N bond forming reactions [43,44] by using an efficient and environmental benign catalyst herein, we are reporting the multicomponent reaction of β-naphthol, aromatic aldehyde and amide using MC-Cu$(acac)_2$ as catalyst at room temperature for the preparation of amidoalkyl naphthol in good to excellent yield (**Scheme 1**).



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

Therefore no reports on the use of MC-Cu$(acac)_2$ as catalyst in the synthesis of amidoalkyl naphthol. It has various advantages due to low toxicity, low price, ease of handling and experimental simplicity.

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 tetramethylsilane 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). All compounds are already well known in the literature; melting points were determined in open capillary tubes and are uncorrected.

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$(acac)_2$ (0.040 gm) in 1,2-dichloroethane (3 ml) at rt was stirred for the 18h. The progress of the reaction was monitored by TLC. On completion of the reaction was 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 (67- 93% yields).

The NMR spectral data of some selected compounds are summarized below.
1) [(2-Hydroxy naphthalene-1-yl)-phenyl-methyl]acetamide; (Table 2, entry 1) : ^{1}H-NMR (300 MHz, DMSO-d_6) :- δ 10.06 (s, 1H), 8.62 (d, 2H), 7.82 (s, 1H), 7.77 (d, 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) [(2-Hydroxy naphthalene-1-yl)-phenyl-methyl]benzamide; (Table 2, entry 8) : ^{1}H-NMR (300 MHz, DMSO-d_6) :- δ 10.39 (s, 1H), 9.04 (d, *J* = 8.4 Hz, 2H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.885- 7.793 (m, 4H), 7.577-7.446 (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.

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 [36]. 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 [45]. Peak at 1446 cm^{-1} shows ν(C=C) and the peak at 451cm^{-1} for ν(Cu-O) stretching.

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

Entry	Catalyst	Catalyst loading (mg)	Solvent	Temp. (˚C)	Time (h)	Yield (%)
1	None	--	DCE	Reflux	24	--
2	Polystyrene	50	DCE	Reflux	24	--
3.	Cu(acac)$_2$	25	DCE	rt	24	68
4	Cu(acac)$_2$	25	DCE	Reflux	24	76
5	MC-Cu(acac)$_2$	30	DCE	rt	24	72
6	MC-Cu(acac)$_2$	40	DCE	rt	24	92
7	MC-Cu(acac)$_2$	50	DCE	rt	24	90
8	MC-Cu(acac)$_2$	40	DCE	rt	18	91
9	MC-Cu(acac)$_2$	40	CH_3CN	rt	18	78
10	MC-Cu(acac)$_2$	40	CH_3OH	rt	18	64
11	MC-Cu(acac)$_2$	40	$CHCl_3$	rt	18	74
12	MC-Cu(acac)$_2$	40	DCE	rt	16	84

[a]Reaction conditions: β-naphthol (1 mmol), Benzaldehyde (1 mmol), acetamide (1.1 mmol). [b]Isolated yield.

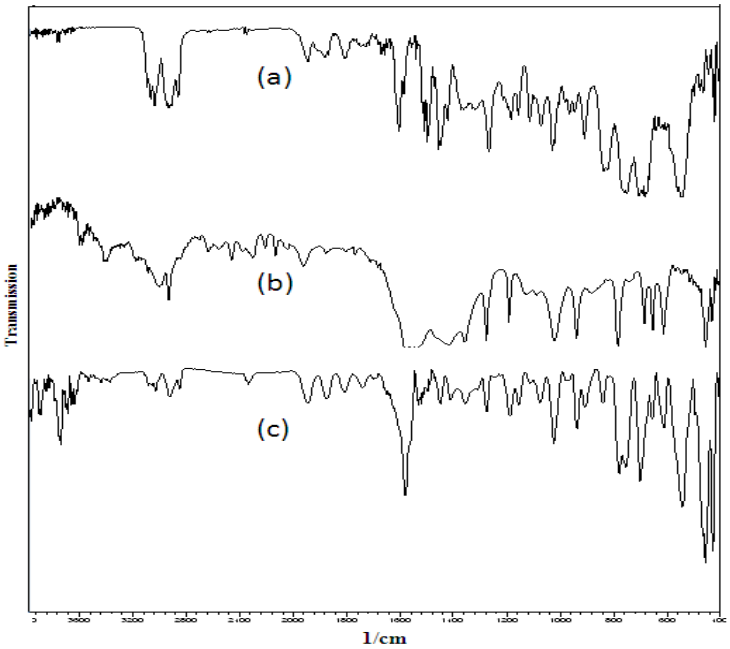


Figure 1: FT-IR spectra comparison of (a) polystyrene, (b) Cu(acac)$_2$, (c) MC- Cu(acac)$_2$

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)$_2$ at room temperature in various solvent to afford amidoalkyl naphthols. A series of experiments were performed to optimize various reaction parameters, such as the nature of the catalyst and effect of catalyst loading, solvent, temperature and time. Initially we screened various catalysts, such as polystyrene, Cu(acac)$_2$, and MC-Cu(acac)$_2$ for the present multicomponant reaction. The MC-Cu(acac)$_2$ was the best catalyst as compaired with polystyrene and Cu(acac)$_2$ giving good yield of the desired product **4a** (Table 1, entries 1-5). We further studied catalyst loding from 0 mg to 50 mg. Only trace product was detected in absence of MC-Cu(acac)$_2$ catalyst. The yield improved as the amount of MC-Cu(acac)$_2$ catalyst increased from 0 to 40 mg and became almost steady when the amount of catalyst was further increased beyond this. (Table 1, entry-1, 5-7). We have studied the effect of various solvents on the model reaction and found that 1,2-dichloroethane (DCE) was the best solvent for the reaction stirred at room temperature for 18 hr to give good yield of desired products (Table 1 entries 8-12).

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, possibly due to steric hindrance. The results of these reactions are summarized in **Table 2**. Additionally we also investigated the reusability of the catalytic system and the results are described in the **Table 3**. After completion of the reaction according to TLC, the reaction mixture was diluted with ethyl acetate and catalyst was filter by simple filtration. The catalyst was washed with acetonitrile (3×10 ml), then the catalyst was used directly in the reusability studies.

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

Entry	X	R	Product	Yield (%)[b]	M. P. (˚C), (Reported)[(ref.)]
1	H	-CH_3	**4a**	91	238-240 (241-243)[17]
2	2-Cl	-CH_3	**4b**	68	210-212 (213-215)[21]
3	4-Cl	-CH_3	**4c**	90	232-234 (237-238)[24]
4	4-O CH_3	-CH_3	**4d**	86	182-184 (183-185)[21]
5	4- CH_3	-CH_3	**4e**	89	222-224 (224-225)[24]
6	3-NO_2	-CH_3	**4f**	88	240-242 (256-258)[24]
7	4-NO_2	-CH_3	**4g**	90	242-244 (237-238)[24]
8	H	-C_6H_5	**4h**	89	234-236 (238-240)[24]
9	4-Cl	-C_6H_5	**4i**	84	168-170 (168-170)[24]
10	4-O CH_3	-C_6H_5	**4j**	86	202-204 (206-208)[24]
11	4- CH_3	-C_6H_5	**4k**	88	214-216 (214-215)[24]
12	3-NO_2	-C_6H_5	**4l**	78	240-242 (242-243)[24]
13	4-NO_2	-C_6H_5	**4m**	82	228-230 (228-229)[24]

[a]Reaction condition: β-naphthol (1 mmol), aldehyde (1 mmol), amide (1.1 mmol) catalyst (40 mg) and DCE (3 ml) at rt for 18 hr.
[b]Isolated yield.

Table 3 : Recycle studies of Mc-Cu(acac)$_2$ catalysts[a]

Entry	Recycle no	Yield (%)[b]
1	Fresh	91
2	1st recycle	86
3	2nd recycle	80
4	3rd recycle	76

[a]Reaction condition: benzaldehyde (1 mmol), β-napthol (1 mmol), acetamide (1.1 mmol) catalyst (40 mg) and DCE (3 ml) at rt for 18 hr.
[b]Isolated yield.

CONCLUSION

We have developed an efficient 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 at rt for 18h. MC-Cu (acac)$_2$ is acted as a heterogeneous and recyclable catalyst. The mild reaction conditions, operational simplicity, recyclable catalytic system and high yields are the notable advantages of this method. These remarkable characteristics made this new protocol which is economically, eco-friendly, attractive and inexpensive.

Acknowledgements
The authors are thankful to Hon'ble Principal and Head of Department of Chemistry, JET's Z. B. Patil College, Dhule for providing the laboratory facilities. One of the author BJK is greatly thankful to CSIR, New Delhi, India for providing the senior research fellowship.

REFERENCES

[1] J. Zhu, H. Bienayme; Multicomponent reactions; Wiley-VCH: Weinheim, **2005**.
[2] A. Domling, I. Ugi, *Angew. Chem. Int. Ed.* **2000**, 39, 3168.
[3] A. Domling, *Chem. Rev.* **2006**, 106, 17.
[4] D. Prajapati, J. S. Sandhu, *Synlett*, **2003**, 1241.
[5] A. K. Bose, S. Pednekar, S. H. Ganguly, G. Chakrabarty, M. S. Manhas, *Tetrahedron Lett.* **2004,** 45, 8351.
[6] G. F. Ross, E. Herdtweck, I. Ugi, *Tetrahedron*, **2002**, 58, 6127.
[7] K. Kobayashi, T. Matoba, I. Susumu, M. Takashi, O. Morikawa, H. Konishi, *Chem. Lett.* **1998**, 551.
[8] R. Bossio, C. F. Marcos, S. Marcaccini, R. Pepino, *Tetrahedron Lett.* **1997**, 38, 2519.
[9] T. Akiyama, K. Matsuda, K. Fuchibe, *Synlett*, **2005**, 322.
[10] G. Zhao, T. Jiang, H. Gao, B. Han, J. Huang, D. Sun, *Green Chem.* **2004**, 6, 75.
[11] S. Knapp, *Chem. Rev*. **1995**, 95, 1859.
[12] D. Seebach, J. L. Matthews; *J. Chem. Soc. Chem. Commun.* **1997**, 2015.
[13] T. Dingermann, D. Steinhilber, G. Folkers; In molecular Biology in Medicinal Chemistry; Wiley-VCH, **2004**.
[14] A. Y. Shen, C. T. Tsai, C. L. Chen, *Eur. J. Med. Chem.* **1999**, 34, 877.
[15] A. Y. Shen, C. L. Chen, C. I. Lin, *Chin. J. Physiol.* **1992**, 35, 45.
[16] M. M. Khodaei, A. R. Khosropour, H. Moghanian, *Synlett*, **2006**, 916.
[17] N. P. Selvam, P. T. Perumal, *Tetrahedron Lett.* **2006**, 47, 7481.
[18] B. Das, K. Laxminarayana, B. Ravikanth, B. R. Rao, *J. Mol. Cat. A: Chem.* **2007**, 261, 180.
[19] R. R. Nagawade, D. B. Shinde, *Mendeleev Commun.* **2007**, 17, 299.
[20] A. Kumar, M. S. Rao, I. Ahmad, B. Khungar, *Can. J. Chem.* **2009**, 87, 714.
[21] H. R. Shaterian, H. Yarahmadi, M. Ghashang, *Bioorg. Med. Chem. Lett.* **2008**, 18, 788.
[22] R. R. Nagawade, D. B. Shinde, *Acta. Chim. Slov.* **2007**, 54, 642.
[23] S. Kantevari, S. V. N. Vuppalapati, L. Nagarapu, *Catal. Commun.* **2007**, 8, 1857.
[24] G. C. Nandi, S. Samai, R. Kumar, M. S. Singh, *Tetrahedron Lett.* **2009**, 50, 7220.
[25] W. K. Su, W. Y. Tang, J. J. Li, *J. Chem. Res.* **2008**, 3, 123.
[26] N. L. Chavan, P. N. Naik, S. K. Nayak, R. S. Kusurkar, *Synth. Commun*. **2010**, 40, 2941.
[27] G. Sabitha, K. Arundhathi, K. Sudhakar, B. S. Shastry, J. S. Yadav, *J. Heterocycl. Chem.* **2010**, 47, 272.
[28] P. Zang, Z. H. Zhang, *Monatsh Chem.* **2009**, 140, 199.
[29] H. Moghanian, S. Ebrahimi, *Journal of Saudi Chemical Society*, **2014**, 18, 165.
[30] M. Wang, Y. Liang, T. T. Zhang, J. J. Gao, *Chin. Chem. Lett.*, **2012**, 23, 65.
[31] A. E. Schneider, G. Manolikakes, *J. Org. Chem.* **2015**, 80, 6193.
[32] P. T. Anastas, J. C. Warner, Green Chemistry theory and practice; Oxford University: Oxford, **1998**.
[33] M. Benaglia; Recoverable and Recyclable catalysts: John Wiley & Sons: Chichester, **2009**.
[34] R. Akiyama, S. Kobayashi, *Chem. Rev.* **2009**, 109, 594.
[35] A. Akelah, D. C. Sherrington, *Chem. Rev.* **1981**, 81, 557.
[36] S. Kobayashi, S. Nagayama, *J. Am. Chem. Soc*. **1998**, 120, 2985.
[37] S. Nagayama, M. Endo, S. Kobayashi, *J. Org. Chem.* **1998**, 63, 6094.
[38] R. Akiyama, S. Kobayashi, *Angew. Chem. Int. Ed*. **2001**, 40, 3469.
[39] S. Kobayashi, T. Ishida, R. Akiyama, *Org. Lett.* **2001**, 3, 2649.
[40] M. Laxmi Kantam, B. Kavita, V. Neeraja, Y. Haritha, M. K. Chaudhari, S. K. Dehury, *Tetrahedron Lett.* **2003**, 44, 9029.
[41] S. Kobayashi, R. Akiyama, *J. Chem. Soc. Chem. Commun.* **2003**, 449.
[42] T. Suzuki, T. Watahiki, T. Oriyama, *Tetrahedron Lett.* **2000**, 41, 8903.
[43] B. J. Khairnar, B. R. Chaudhari, *J. Chem. Pharm. Res*. **2015**, 7, 241.
[44] P. S. Girase, B. J. Khairnar, D. V. Nagarale, B. R. Chaudhari, *Der Pharma Chemica*, **2015**, 7, 241.
[45] Y. Moreno, R. Arrue, R Saavedra, J. Y. Pivan, O. Pena, T. Roisnell, *J. Chil. Chem. Soc.* **2013**, 58, 2122.