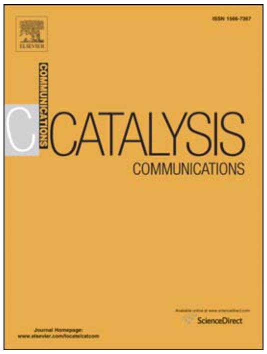

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Environmentally benign synthesis of polyhydroquinolines by Co_3O_4-CNT as an efficient heterogeneous catalyst

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Abstract

A novel and eco-friendly synthesis of polyhydroquinolines is efficiently catalyzed by Co_3O_4-CNTs nanocomposites. This recyclable catalytic system provides a simple strategy to generate a variety of polyhydroquinolines under mild conditions. Utilization of easy reaction condition, recyclable nanocatalyst, reduced environmental impacts and simple work-up make this methodology as an interesting option for the eco-friendly synthesis of polyhydroquinolines.

Keywords: Co_3O_4-CNTs, Polyhydroquinoline, Carbon nanotubes, Supported catalyst, Heterogeneous catalyst.

1. Introduction

Polyhydroquinolines have attracted considerable interest because they possess various important pharmacological properties [1]. Polyhydroquinolines have found commercial utility as an important class of Ca^{+2} channel blockers as exemplified by therapeutic agents such as Nifedine, Nitrendipine and Nimodipine [2]. These examples clearly demonstrate the remarkable potential of polyhydroquinolines as a source of valuable drugs. In view of the importance of polyhydroquinoline compounds, many classical methods reported in literature for the synthesis of polyhydroquinolines such as conventional heating [3] microwave technology [4], ultrasound irradiation [5] light induced procedure [6], various types of catalysts [7-12], grinding [13] and by refluxing in water [14]. Each of the above methods has its own merits, while some of the methods are plagued by limitations of poor yields, toxicity of solvents, critical product isolation procedures, restrictions for large scale applications, expensive catalysts, difficulty in recovery of high boiling solvents, excessive amounts of catalysts and generation of large amounts of toxic wastes in scaling up for industrial applications leading to environmental issues. Therefore, the discovery of novel and efficient catalysts is of prime importance to synthesize of polyhydroquinoline compounds for further improvement toward milder reaction conditions and higher yields.

It is important to develop metal oxides nanoparticles as heterogeneous catalysts in organic reactions, because of their interesting structure, high catalytic activities and improved selectivity [15, 16]. In general, heterogeneous nanocatalysts offer higher surface area and lower coordinating sites, which are responsible for the higher catalytic activity. On the other hand, among all metal oxides, the tricobalt tetraoxide (Co_3O_4) can be considered as a one of the best example to understand the catalytic activity based on the variable particle size [17-19]. However, the specific surface area of the pure Co_3O_4 is not high enough for the practical applications. In addition, Co_3O_4 cannot be recycled easily, and the leaching cobalt cations in the reacting liquid-phase can lead to secondary pollution [20].

Stability of the nanoparticles is an important issue and supported metal nanoparticles as catalytic systems have potential to show greater efficiency. Recently, interest in carbon nanotubes (CNTs) as nanocatalyst supports has been increasing because of their unique morphologies and various potential applications [21-23]. CNTs as excellent supports possess a high surface area for high dispersion of nanocatalysts, well-defined porosity of structure for maximum reactant contact, excellent crystallinity or low electrical resistance to facilitate electron transport during chemical transformations and good interaction between the nanosized catalysts and the carbon support [23]. Co_3O_4 supported on CNTs are attracting significant attention owing to their wide applications as Schottky-junction diode [24], electrochemical capacitors [25], Li-ion battery anode applications [26], and nanocatalyst [27]. Combination of Co_3O_4 and CNTs with excellent electron transfer rate and large specific surface area is expected to provide a chance for improvement of the durability and performance of pure Co_3O_4 particles. We devised an effective and novel Co_3O_4-CNTs catalyzed synthesis of polyhydroquinolines in an efficient reaction (Scheme 1). However, there are no reports on the use of Co_3O_4-CNTs nanocomposites for the synthesis of polyhydroquinolines under mild condition.

<scheme 1>

2. Experimental

2.1. Materials and apparatus

Chemical reagents were obtained from the Merck Chemical Company. MWNTs with surface area of 136 m^2/g and 10–20 nm in diameter were supplied from Neutrino Company, Iran. Melting points ($^{\circ}C$) were determined on an Electro thermal MK3 apparatus using an open-glass capillary and are uncorrected. FTIR spectra were recorded as KBr pellets on a Perkin–Elmer 781 spectrophotometer and on an Impact 400 Nicolet FTIR spectrophotometer. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were measured on a Bruker DPX-400 spectrometer. X-ray diffraction analysis was carried out on a Holland Philips Xpert X-ray diffraction (XRD) diffractometer (CuK, radiation, λ = 1.5406A˚), at a scanning speed of 2˚ min^{-1} from 10˚ to 100˚ (*2θ*). The TEM images were recorded using a Philips CM10 transmission electron microscope operated at a 100 kV accelerating voltage.

2.2. Preparation of Co_3O_4-CNT nanocomposites

Oxidized CNTs were prepared by purification in a ratio of 3:1 70% nitric acid and 98 sulfuric acid at 50 ºC under ultrasonication for 6 h. Composite material of Co_3O_4-CNT was prepared according to reported procedures in the literature [25]. In short, 0.5 g $Co(NO_3)_2·6H_2O$ was dissolved into 40 mL n-hexanol to form a red solution. 70 mg of oxidized CNTs were dispersed in the red solution by sonication for 2 h. Then, this solution was refluxed at 140 ˚C for 10 h. After cooled to ambient temperature, the products were washed with cyclohexane repeatedly to remove any impurities and dried. The black powder was filtered and washed with ethanol and dried at 100 °C to obtain the Co_3O_4-CNT nanocomposite.

2.3. General procedure for the Synthesis of 2-Ketomethylquinolines

Benzaldehyde (1 mmol), dimedone (1 mmol), ethyl acetoacetate (1 mmol), ammonium acetate (1.5 mmol) and Co_3O_4-CNT (0.03 g) were successively charged into a 50 mL round-bottomed flask and the contents were refluxed in EtOH (5 mL) for an appropriate period while the product formation was monitored by TLC (petroleum ether–EtOAc; v/v = 7 : 3). Upon completion, the nanocatalyst was recovered by simple filtration. Then, the ethanol was evaporated under reduced pressure to yield the crude product, which was then purified by recrystallization from hot ethanol and water to afford pure polyhydroquinolines.

3. Results and discussion

In this research, Co_3O_4-CNTs were prepared according to the schematic 2. The positive cobalt ions in the hydrophobic *n*-hexanol solution are adsorbed to the surface of the acid treated CNTs through electrostatic attraction and then in situ decomposes into Co_3O_4 according to the following process [25]:

$$3\mathbf{Co(NO_3)_2} \xrightarrow[\textbf{140-180 °C}]{\textbf{air, } \boldsymbol{n}\textbf{-hexanol}} \mathbf{Co_3O_4}\downarrow + \mathbf{6NO_2}\uparrow + \mathbf{O_2}\uparrow$$

<scheme 2>

The XRD patterns of CNTs and Co_3O_4-CNTs composites are presented in Fig. 1. The diffraction peaks at 18.63, 35.17, 43.55, 54.22, 60.08 and 65.19 correspond to (1 1 1), (3 1 1), (4 0 0), (3 3 1), (4 2 2)and (5 1 1) reflections, respectively, which they are correlated with Co_3O_4 in spinel structure (JCPDS card No. 74-1656). This confirms the crystalline nature and phase purity of Co_3O_4 nanoparticles. Also, a peak is clearly observed near 26.22, which is typical for CNTs [28]. The XRD result clearly indicates that Co_3O_4 nanoparticles were decorated on the surface of CNTs. The average crystal size of the Co_3O_4-CNTs was calculated by the Debye–Scherrer formula to be 20 nm.

<fig 1>

The physical morphologies of the acid-treated CNTs and Co_3O_4-supported CNTs were examined using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Fig. 2 shows SEM results about the interaction of CNTs and the deposited Co_3O_4nanoparticles. From the TEM micrograph, the Co_3O_4 nanoparticles were dispersed completely homogeneous on the outer wall of CNTs.

<fig 2>

After the characterization of the catalyst, the reaction conditions were optimized with the model substrates of benzaldehyde (**1)**, dimedone (**2)**, ethyl acetoacetate (**3)** and ammonium acetate **(4)** in the presence of Co_3O_4-CNTs nanocomposites in EtOH. At first, we examined the reaction parameters such as amount and type of catalyst, effect of temperature, various solvents, and also reusability of supported catalyst. Initially, the various catalysts were studied for their activities in the model reaction. As shown in Table 1, Co_3O_4-CNTs were found to be highly active in term of reaction yield under refluxing EtOH. The studies reported that CNTs not only provided a large surface area support for the nanosized metal oxide catalyst, but also stabilized the charge separation by trapping the electrons transferred from the metal to hinder charge recombination [29].

< Table 1>

Next, we performed the model reaction with different amounts of Co_3O_4-CNTs to evaluate the effect of the catalyst in the synthesis of polyhydroquinolines. As shown in Table 2, it was found that the highest yield was obtained using 0.03 g catalyst in the model reaction. Moreover, in the absence of nanocatalyst, the product was afforded only in trace amounts even after extended time (720 min). In the presence of Co_3O_4-CNTs, the reaction yield improves gradually in a shorter time (40 min) with an increase in the amount of nanocatalyst (0.03 g). A higher amount of catalyst (0.04 g) leads to decreasing the yield to 92% in the same period. With increasing the amount of nanocatalyst, an increase in the number of acidic active sites occurs, which causes a decrease in the concentration of reactants at the active sites and finally a decline in yield. Therefore, optimum amount of catalyst was found to be 0.03 g to prepare polyhydroquinolines [23].

< Table 2>

To select the appropriate solvent, the reaction with test substrates was carried out in several solvents and the solvent-free system (Table 3). The polar solvents such as EtOH and MeOH were found to be better solvents than the non-polar solvents like toluene and cyclohexane. The non-occurrence of reaction in non-polar solvents may be due to the poor solubility of the products in these solvents. Moreover, the results could be explained with the much better solubility of the reagents and the much better dispersion of the catalyst in the polar solvents. Therefore, EtOH was used as the solvent of choice, with its fast conversion, high yield and low toxicity. The effect of temperature was also studied by carrying out the model reaction at different temperatures (Table 3, entries 8-10). It was observed that the product **5a** was obtained in excellent yield if the reaction was carried out in EtOH under refluxing (Table 3, entry 8).

< **Table 3**>

After establishing the optimal conditions, in order to prove the generality of this method, we evaluated a variety of aromatic and heterocyclic aldehydes. As shown in Table 4, aromatic aldehydes bearing electron- deficient or electron-rich substituent on the aromatic ring as well as heterocyclic aldehydes afforded the corresponding products in excellent yields. Thus, the use of Co_3O_4-CNTs as an efficient catalyst is an environmentally clean technique for this condensation. All products were identified by comparing their physical (M.P.) and spectral data (^{1}H NMR, ^{13}C NMR and IR) with authentic samples.

< **Table 4**>

We propose a mechanism for the Co_3O_4-CNTs catalyzed synthesis of polyhydroquinolines (Scheme 3). In this process, the presence of CNTs leads to good dispersion and small size of Co_3O_4 nanoparticles. Co_3O_4-CNTs is supposed as a Lewis acid catalyst to facilitate the condensation between aldehyde **1** and 1,3-diketone **2** for the formation of the corresponding

Knoevenagel product **6a**, and the Michael addition between this intermediate and enamines **7a** obtained from the reaction of ethyl acetoacetate **3** and ammonium acetate **4**, for the formation of an open chain intermediates **8a** which undergo cyclohydration to furnish the desired polyhydroquinolines **5** products [3].

<Scheme 3>

Moreover, the recyclability of the supported nanocatalyst is also important for the large scale operation. It was found from Fig.3 that there was no significant decrease in activity after seven runs using the Co_3O_4-CNTs nanocomposites. It is clear from the TEM micrograph in Fig. 2(e) that the nanoparticles are stable on the surface of the nanotube after reaction.

<fig. 3>

Conclusions

In summary, this investigation deals with a novel and clean approach to synthesize polyhydroquinolines in the presence of Co_3O_4-CNTs. This method has several advantages such as simple experimental procedure, utilization of heterogeneous catalyst, short reaction times, milder conditions, excellent yields and reusability of the catalyst.

Acknowledgments

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References

[1] T. Godfraind, R. Miller, M. Wibo, Pharmacol. Rev. 38 (1986) 321-416.

[2] S.S. Mansoor, K. Aswin, K. Logaiya, S.P.N. Sudhan, Arab. J. Chem. (2012) DOI: org/10.1016/j.arabjc.2012.10.017.

[3] M. Nasr-Esfahani, S.J. Hoseini, M. Montazerozohori, R. Mehrabi, H. Nasrabadi, J. Mol. Catal. A: Chem. 382 (2014) 99-105.

[4] M. Li, Z. Zuo, L. Wen, S. Wang, J. Comb. Chem. 10 (2008) 436-441.

[5] S.J. Tu, J.F. Zhou, X. Deng, P.J. Cai, H. Wang, J.C. Feng, Chin. J. Org. Chem. 21 (2001) 313-316.

[6] P. Pratim Ghosh, S. Paul, A.R. Das, Tetrahedron Lett. 54 (2013) 138–142.

[7] L.M. Wang, J. Sheng, J.W. Zhang, J.W. Han, Z.Y. Fan, H. Tian, C.T. Qian, Tetrahedron. 61 (2005) 1539-1543.

[8] S. Ko, M.N. V.Sastry, C. Lin, C.F. Yao, Tetrahedron Lett. 46 (2005) 5771-5774.

[9] H. Adibi, H. A. Samimi, M. Beygzadeh, Catal. Commun. 8 (2007) 2119-2124.

[10] M.M. Heravi, K.N. Bakhtiri, M. Javadi, F.F. Bamoharram, M. Saeedi, H.A. Oskooi, J. Mol. Catal. A: Chem. 264 (2007) 50-52.

[11] J.L. Donelson, A. Gibbs, S.K. De, J. Mol. Catal. A: Chem. 256 (2006) 309-311.

[12] A. Kumar, R.A. Maurya, Tetrahedron Lett. 48 (2007) 3887-3890.

[13] S. Kumar, P. Sharma, K.K. Kapoor, M.S. Hundal, Tetrahedron. 64 (2008) 536-542.

[14] B.P. Bandgar, P.E. More, V.T. Kamble, J.V. Totre, ARKIVOC. 15 (2008) 1-8.

[15] N. Rakmak, W. Wiyaratn, C. Bunyakan, J. Chungsiriporn, Chem. Eng. J. 162 (2010) 84-90.

[16] G. Yuan, J. Zheng, C. Lin, X. Chang, H. Jiang, Mater. Chem. Phys. 130 (2011) 387-391.

[17] A. Tavasoli, A. Khodadadi, Y.Mortazavi, K. Sadaghiani, M.G. Ahangari, Fuel. Process. Technol. 87 (2006) 641–647.

[18] J.S. Kang, S.V. Awate, Y.J. Lee, S.J. Kim, M.J. Park, S.D. Lee, S.I. Hong, D.J. Moon, J. Nanosci. Nanotechnol. 10 (2010) 3700–3704.

[19] K.D. Bhatte, D.N. Sawant, K.M. Deshmukh, B.M. Bhanage, Catal. Commun. 16 (2011) 114–119.

[20] Z. Chen, S. Chen, Y. Li, X. Si, J. Huang, S. Massey, G. Chen, Mate. Res. Bull. 57 (2014) 170–176.

[21] C.H. Liang, Z.L. Li, J.S. Qiu, C. Li, J. Catal. 211 (2002) 278-282.

[22] H. Tang, J.H. Chen, Z.P. Huang, D.Z. Wang, Z.F. Ren, L.H. Nie, Y.F. Kuang, S.Z. Yao, Carbon. 42 (2004) 191-197.

[23] J. Safari, S. Gandomi Ravandi, New J. Chem. 38 (2014) 3514-3521.

[24] L. Fu, Z. Liu, Y. Liu, B. Han, P. Hu, L. Cao, D. Zhu, Adv. Mater. 17 (2005) 217-221.

[25] Y. Shan, L. Gao, Mater. Chem. Phys. 103 (2007) 206-210.

[26] S.M. Abbas, S.T. Hussain, S. Ali, N. Ahmad, N. Ali, K.S. Munawar, Electrochim. Acta. 105 (2013) 481-488.

[27] S. Jiang, S. Song, Appl. Catal. B: Environ. 140–141 (2013) 1-8.

[28] H.J. Kim, K.K. Jeon, J.G. Heo, J.Y. Lee, C. Kim, K.H. An, S.C. Lim, D.J. Bae, Y.H. Lee, Adv. Mater. 15 (2003) 1754-1757.

[29] D. Zhao, X. Yang, C. Chen, X. Wang, J. Colloid. Interface. Sci. 398 (2013) 234-239.

[30] C.S. Reddy, M. Raghu, Chin. Chem. Lett. 19 (2008) 775–779.

[31] N.N. Karade, V.H. Budhewar, S.V. Shinde, W.N. Jadhav, Lett Org Chem. 4 (2007) 16-19.

[32]. M. Nasr-Esfahani, T. Abdizadeh, Orient J Chem. 28 (2012) 1249-1258.

Table 1: Synthesis of product Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-phenyl-5(6H)-oxoquinolin-3-carboxylate using different catalysts under reflux conditions in EtOH.[a]

Entry	**Catalyst**	**Time (min)**	**Yield (%)**
1	CNTs	40	35
2	CNTs-COOH	40	45
3	$Co(NO_3)_2$	40	65
4	Co_3O_4	40	70
5	Co_3O_4 NP	40	80
6	Co_3O_4-CNTs	40	95

[a] Benzaldehyde (1 mmol), dimedone (1 mmol), ethyl acetoacetate (1 mmol), ammonium acetate (1.5 mmol) and catalyst (0.03 g) were refluxed in EtOH (5 mL).

Table 2. Effect of amount of Co_3O_4-CNTs on the synthesis of compound Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-phenyl-5(6H)-oxoquinolin-3-carboxylate under refluxing EtOH.[a]

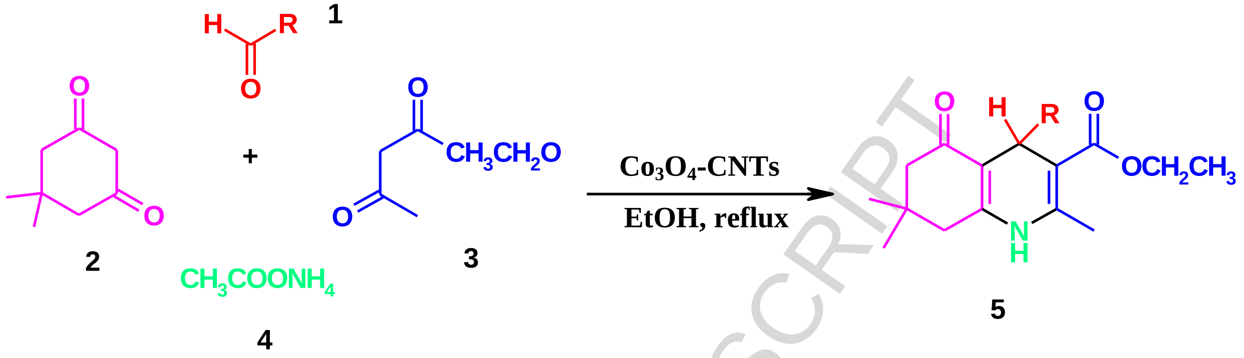
Entry	**Catalyst (g)**	**Time (min)**	**Yield (%)**
1	-	720	trace
2	0.01	60	75
3	0.02	60	85
4	0.03	40	95
5	0.035	40	94
6	0.04	40	92

[a] Benzaldehyde (1 mmol), dimedone (1 mmol), ethyl acetoacetate (1 mmol), and ammonium acetate (1.5 mmol) in the presence of Co_3O_4-CNTs in EtOH (5 mL).

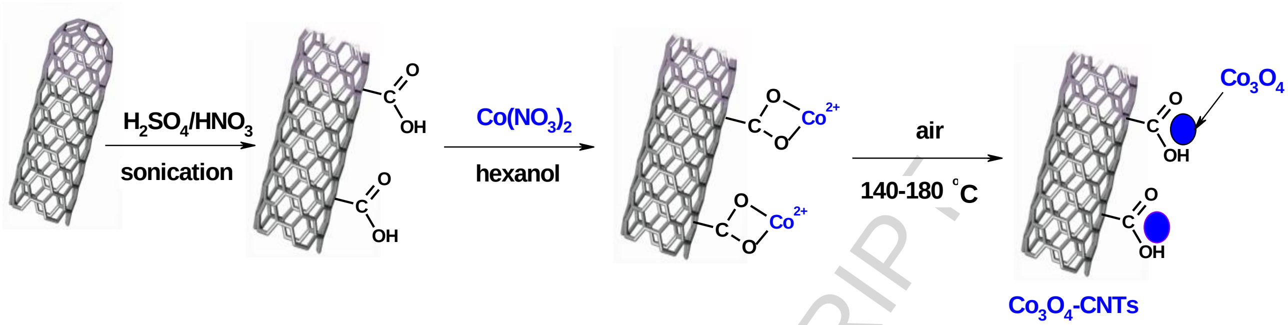
Table 3. Influence of the solvent on the synthesis of Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-phenyl-5(6H)-oxoquinolin-3-carboxylate.[a]

Entry	**Solvent**	**Temperature (°C)**	**Time (min)**	**Yield (%)**
1	-	40	100	75
2	-	80	100	90
3	CH_2Cl_2	reflux	100	40
4	MeCN	reflux	100	45
5	PhMe	reflux	100	55
6	cyclohexane	reflux	100	30
7	MeOH	reflux	40	90
8	EtOH	reflux	40	95
9	EtOH	50	90	80
10	EtOH	40	100	75

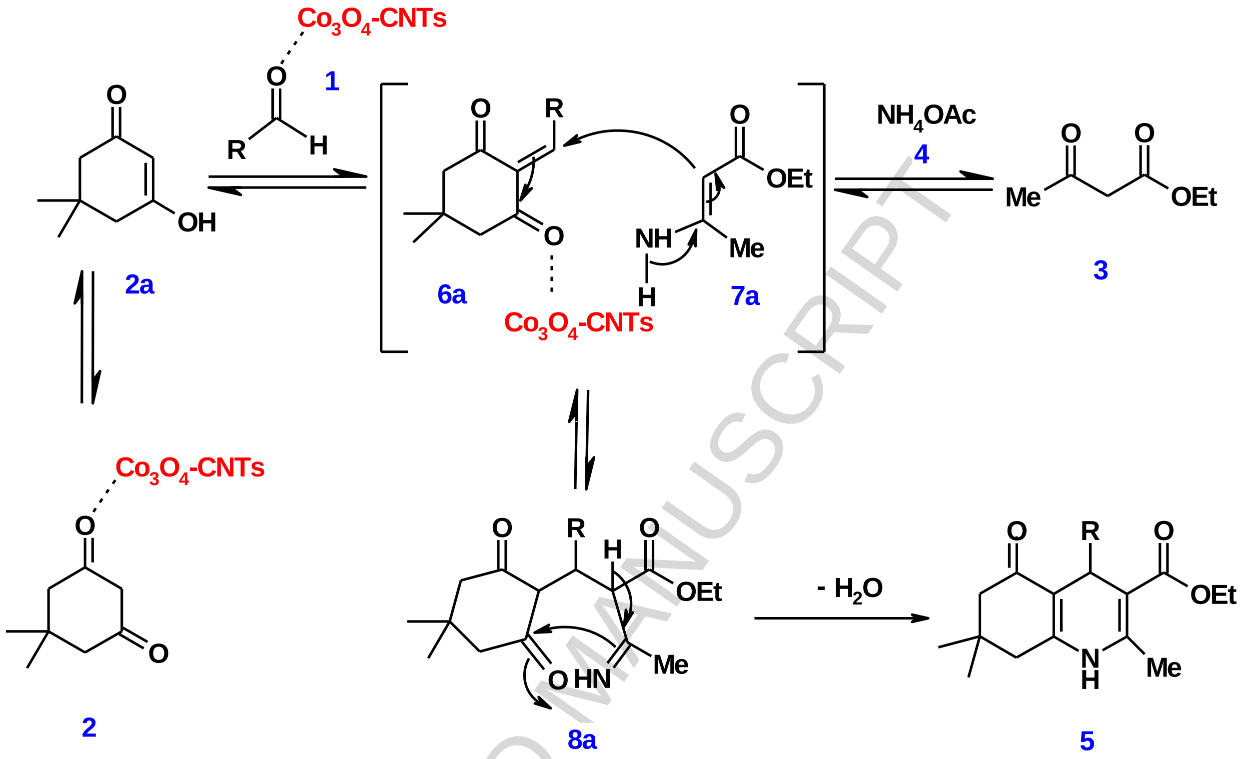
[a] Benzaldehyde (1 mmol), dimedone (1 mmol), ethyl acetoacetate (1 mmol), ammonium acetate (1.5 mmol) and Co_3O_4-CNTs (0.03 g) in various of solvent (5 mL).



Scheme 1. One-step synthesis of polyhydroquinolines using Co_3O_4-CNTs.



Scheme 2. Schematic illustration of decoration of the CNTs with Co_3O_4 nanoparticles.



Scheme 3: Proposed mechanism for the Co_3O_4-CNTs catalyzed synthesis of polyhydroquinolines.

Table 4. Co_3O_4-CNTs catalyzed synthesis of polyhydroquinolines.

Entry	**R**	**Time (min)**	**Yield (%)**	**M.P. (°C)**	
				Obs.	**Lit.**
1	C_6H_5	40	95	203-204	202-204 [7]
2	4-Cl-C_6H_4	35	97	244-246	244-246 [30]
3	2-Cl-C_6H_4	45	93	210-211	209-211 [13]
4	4-$(CH_3)_2N$-C_6H_4	45	88	229-232	229-231 [7]
5	4-MeO-C_6H_4	40	95	258-259	257-259 [7]
6	4-O_2N-C_6H_4	30	98	245-247	245-246 [13]
7	2-O_2N-C_6H_4	40	94	209-210	208-211 [31]
8	3-O_2N-C_6H_4	30	98	179-181	179-181 [32]
9	C_6H_5-CH=CH	50	93	204-206	204-206 [30]
10	2-Furyl	35	94	247-248	246-248 [7]
11	2-Thienyl	35	95	242-243	241-244 [13]
12	3-Pyridyl	40	92	148-149	147-148 [7]

Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-phenyl-5(6H)-oxoquinolin-3-carboxylate

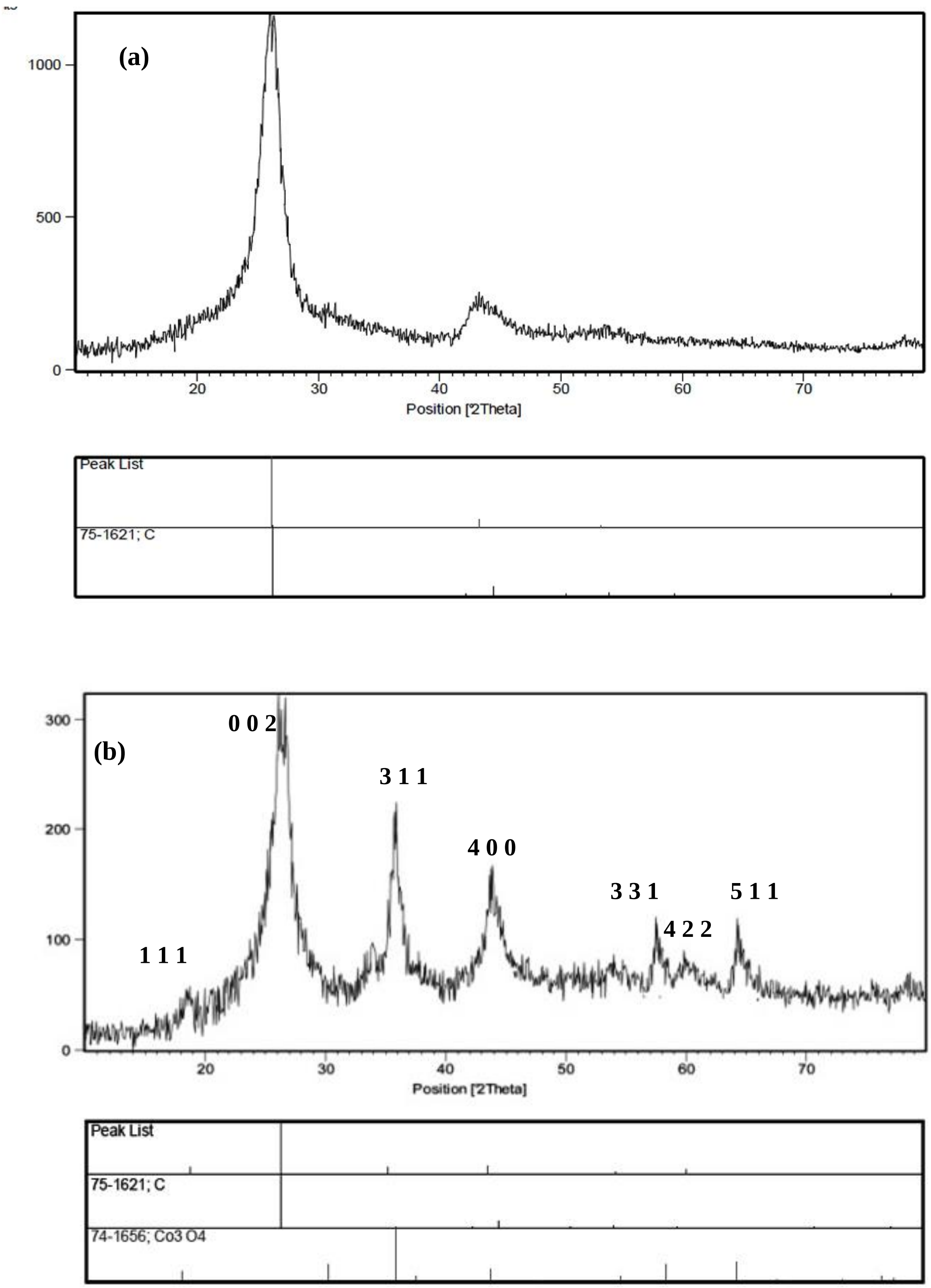


Fig. 1. XRD patterns of (a) CNT and (b) Co_3O_4-CNT nanocomposite.

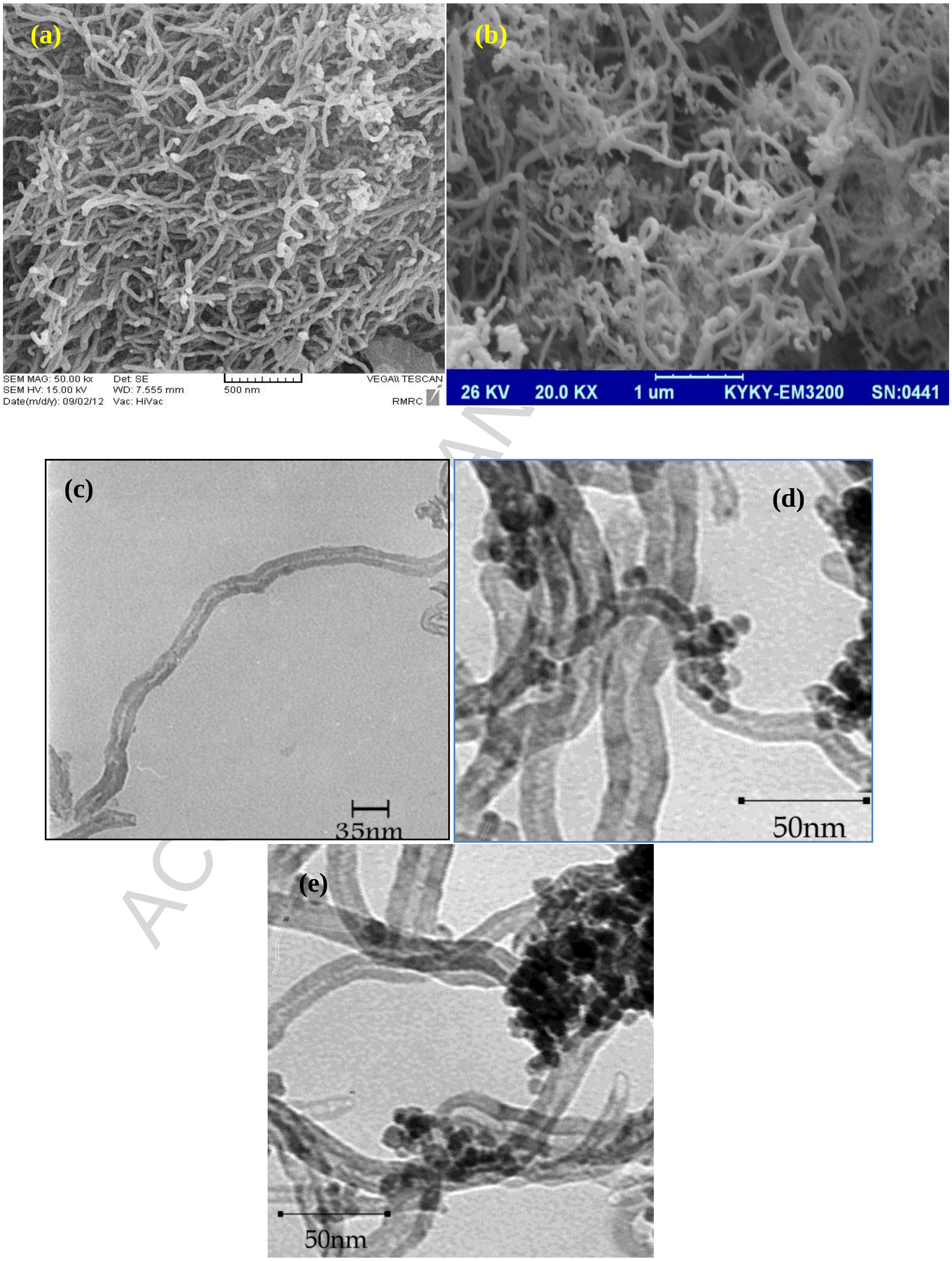


Fig. 2. SEM images of (a) CNTs, (b) Co_3O_4-CNT and TEM images of (c) CNTs, (d) Co_3O_4-CNT before the reaction, (e) Co_3O_4-CNT after the reaction.

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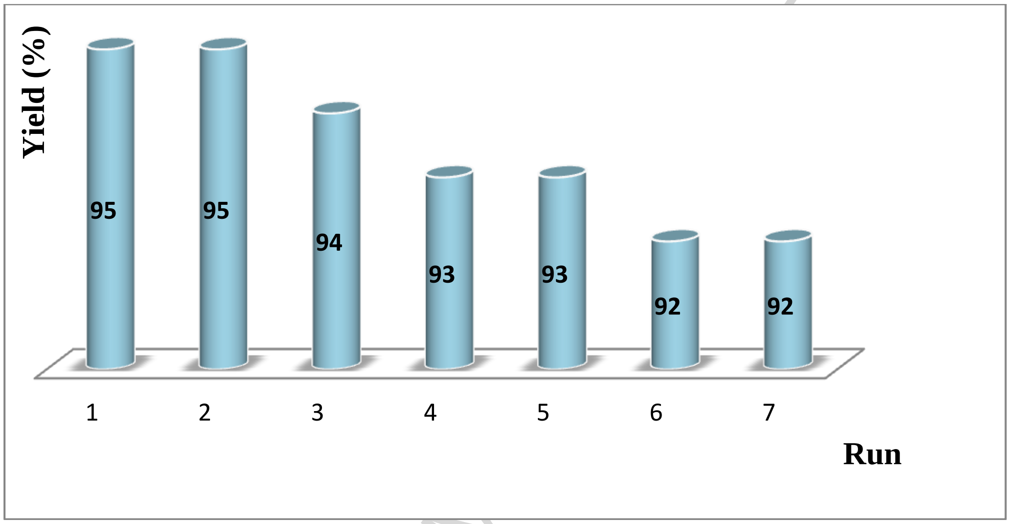
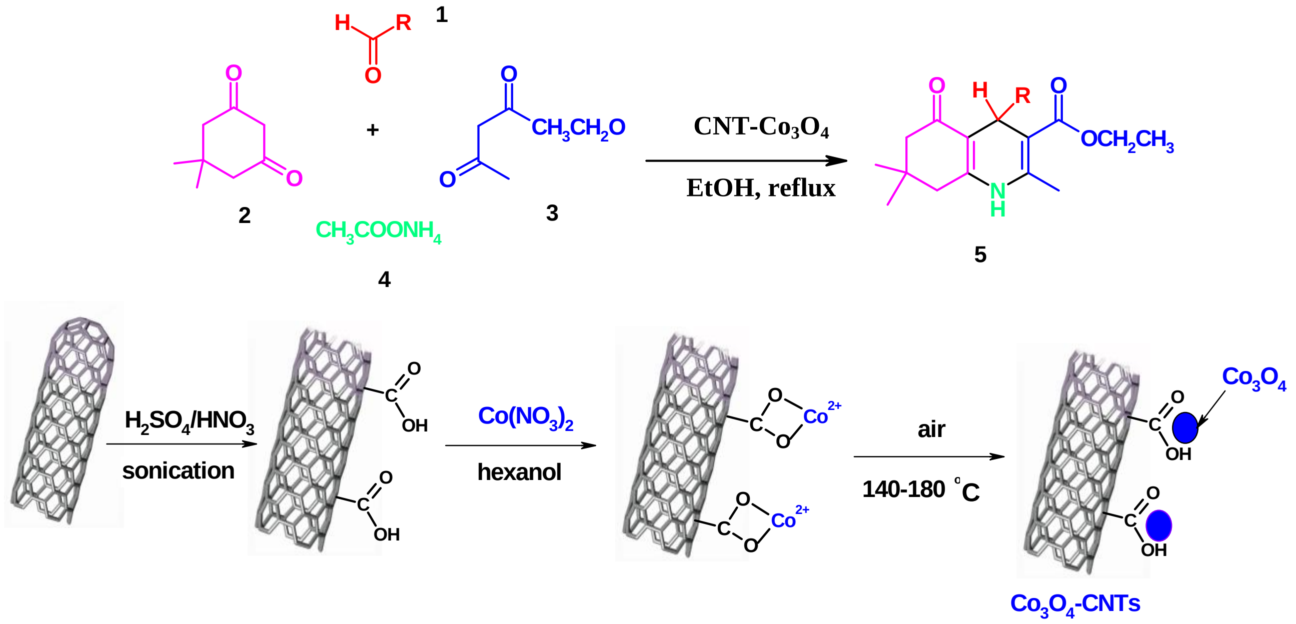


Fig. 3. Recyclability of catalyst in one-pot synthesis of Ethyl-1,4,7,8-tetrahydro-2,7,7-trimethyl-4-phenyl-5(6H)-oxoquinolin-3-carboxylate.

Graphical Abstract

Environmentally benign synthesis of polyhydroquinolines by Co_3O_4-CNT nanocomtposites as a novel heterogeneous catalys



Highlights

- CNTs as an excellent support for the metal oxide in catalytic systems.
- Introducing Co_3O_4-CNTs for the synthesis of polyhydroquinolines.
- Generality of the catalyst, easiness of separation, and recycled several times.