

Synthesis of tri and four substituted imidazoles derivatives using zinc oxid nanotubes modified by SiO₂ as a powerful and reusable catalyst

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In recent years, zinc oxid nanotubes have attracted much attention. The direct use of , zinc oxid nanotubes modified by SiO₂ as recoverable catalysts for organic reactions is very rare. The catalysts were characterized by XRD. The average particle size of ZnO catalysts is 57 nm and there are high-density defects on nanotubes surfaces. A simple and efficient method for the imidazol derivatives synthesis from the condensation benzil and ammonium acetate with substituted aromatic aldehydes in the presence of a catalytic amount zinc oxid nanotubes modified by SiO₂ is described. The reason proposed for higher catalytic activity of zinc oxid nanotubes modified by SiO₂ is a combination effect of the small particle size and high-density surface defects. The practical and simple method led to excellent yields of the tri and four substituted imidazoles derivatives under mild conditions and within short times.

Keywords: Reusable catalyst; Tri and foursubstituted imidazoles derivatives; zinc oxid nanotubes

1. INTRODUCTION

Recently, lot of attention has been paid to synthesis of heterocyclic compounds. Among the various classes of heterocyclic compounds imidazol derivatives are the subject of considerable interest from both academic and industrial perspective [1, 2].

They have shown a broad spectrum of biological activities such as antibacterial [3-6], antidepressant [7] and antitumor [8] which has made them privileged structures in combinatorial drug discovery libraries [9]. Besides this, they have been used in dyes [10], building blocks for the synthesis of organic semiconductors [11], chemically controllable switches [12], cavitands [13], DNA cleaving agents [14], dehydroannulenes [15] and electroluminescent materials [16-18]. Due to their wide range of applications, a variety of improved methods have been developed for the synthesis of imidazol derivatives [19-23]. By far, the most common method is the condensation of aromatic aldehyde with benzyl and ammonium acetate under solvent free condition.

However, many of reported methods suffer from one or more limitations such as harsh conditions, unsatisfactory product yields, long reaction times, and critical product isolation procedures, use of volatile organic solvents and co-occurrence of several side products. Tri and four substituted imidazoles derivatives Obtained by the condensation of benzyl and ammonium acetate with various substituted aromatic aldehydes in solvent free.

In recent years zinc oxid nanotubes have received increasing attention since such materials exhibit a great many fascinating chemical and physical characteristics and potential technological

applications [24]; these are distinct both from those of the bulk phase and those from isolated atoms or molecules. Several papers have been published on the preparation [25, 26] and applications [27–28] of nano- sized zinc oxid nanotubes catalysts.

The zinc oxid nanotubes could be recycled by separating them from the reaction mixture. They could be used as a catalyst for the same reaction again and the change in their catalytic activity was checked. The relation between the number of cycles of the reaction and the catalytic activity in terms of yield is presented in Fig. 1.

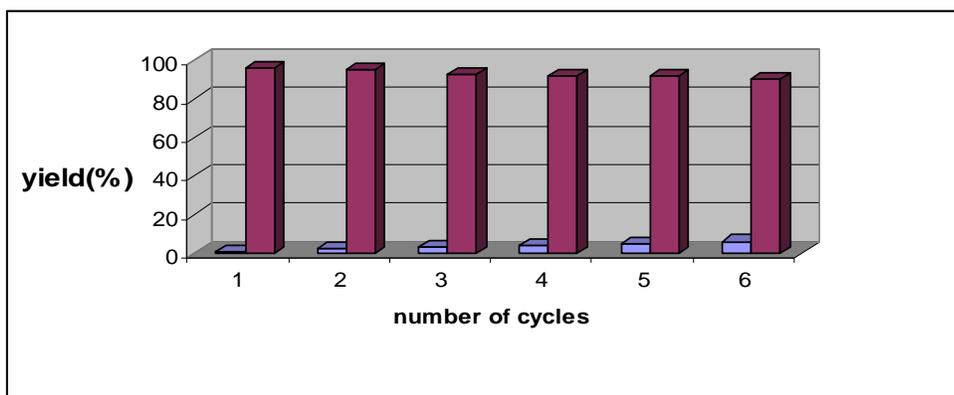


Fig. 1. Recyclability of zinc oxid nanotubes modified by SiO₂ for the formation of tri and four substituted imidazoles derivatives.

2. EXPERIMENTAL

The commercial starting materials were purchased from Merck, Fluka and Aldrich. The reactions were monitored by TLC (silica-gel 60 F₂₅₄, n-hexane: ethyl acetate). IR spectra were recorded on a FT-IR Shimadzu- 470 Spectrometer and the ¹HNMR Spectra were obtained with a Bruker-Instrument DPX- 400 MHz Avance 2 model. All products were characterized by comparison of their spectra and physical data.

2.1. General procedure for the synthesis of tri substituted imidazoles derivatives

A mixture of benzil (1 mmol), ammonium acetate (3 mmol) and substituted benzaldehydes (1 mmol), zinc oxid nanotubes modified by SiO₂ (1% mmol) in solvent free condition at 120 °C for the appropriate time. Completion of the reaction was monitored by TLC (thin layer chromatography). After completion the reaction mixture was cooled to room temperature and washed with water (2 × 10 mL) and the solid material was filtered to furnish almost pure product. The products were further purified by recrystallization from ethyl acetate there upon the catalyst was isolated from the pure product. Yield and melting point of the product(s) were determined.

2.2. General procedure for the synthesis of four substituted imidazoles derivatives

A mixture of benzil (1mmol), ammonium acetate (1mmol), aniline (1mmol), zinc oxid nanotubes (1% mmol) and aromatic aldehyde (1mmol) in solvent free condition at 120°C for the appropriate time. Completion of the reaction was monitored by TLC (thin layer chromatography). After completion the reaction mixture was cooled to room temperature and washed with water (2 × 10 mL) and the solid material was filtered to furnish almost pure product. The products were further purified by recrystallization from ethyl acetate there upon the catalyst was isolated from the pure product. Yield and melting point of the product(s) were determined.

2.3. Spectral data

2-(3-indolyl-4, 5-di(4-florophenyl) imidazole:

m.p= 303-305 °C lit.

IR (KBr) cm^{-1} : 3425, 3055, 1614, 1591, 1515, 1503, 1409, 1334, 1225, 1157, 1093, 936, 835, 750, 741, 725, 657, 608.

^1H NMR (400MHZ, CDCl_3) ;6.93-7.01 (m, 4H), 7.10-7.14 (m, 2H), 7.26 (d, 1H, J= 7.8 Hz) , 7.34-7.43 (m, 4H), 7.78 (d, 1H, J=2.5 Hz), 8.27 (d, 1H, J= 7.3 Hz) , 11.19 (s, 1H), 12.12 (brs, 1H).

^{13}C NMR (100MHZ) δ (PPM): 106.7, 115.2, 119.7, 121.4, 121.8, 123.7, 125.0, 128.6, 130.3, 135. 6, 143.7, 163.6, 165.3.

Elemental analysis: C, 74.38; H, 4.07; F, 10.23; N, 11.31.

Found: C, 74.19; H, 4.15; N, 11.10.

2-(2-methylphenyl)-4, 5-diphenyl-1H-imidazole:

m.p= 204-206 °C lit.

IR (KBr) cm^{-1} : 3020, 2985, 1597, 1485, 1440, 1395, 1138, 1065, 965, 610, 835, 765, 730, 698.

^1H NMR (400MHZ, CDCl_3) ;2.61 (s, 3H), 7.20-7.24 (m, 5H), 7.25-7.30 (m, 5H), 7.56 (m, 3H), 7.63 (d, 1H, J=7.6 Hz), 11.40 (brs, 1H).

^{13}C NMR (100MHZ) δ (PPM): 21.5, 126.0, 127.3, 128.4, 128.7, 128.8, 129.6, 130.9, 131.3, 137.3, 147.0.

1-benzil-2-(4-clorophenyl)-4, 5-diphenyl-1H-imidazol:

m.p=168-170 °C

IR (KBr) cm^{-1} : 3090, 3015, 2985, 1590, 1450, 1340, 1080, 835, 730, 690.

^1H NMR (400MHZ, CDCl_3) ;(5.13 (s, 2H), 6.85 (d, 2H, J= 6.0 Hz), 7.18-7.41 (m, 11H), 7.63 (t, 4H, J= 7.3 Hz).

^{13}C NMR (100MHZ) δ (PPM): 48.7, 126.3, 126.9, 127.2, 128.0, 128.5, 129.1, 129.2, 129.3, 129.9, 130.7, 130.9, 131.3, 134.8, 135.4, 137.8, 147.3.

1-benzil-2-(4-methylphenyl)-4, 5-diphenyl-1H-imidazol:

m.p=163-170 oC lit

IR (KBr) cm^{-1} : 3085, 3025, 2994, 1590, 1475, 1440, 1320, 820, 760.

^1H NMR (400MHZ, CDCl_3) 7.61 (4H, t, J=12Hz), 7.35 (3H, m), 7.28 (10H, m), 7.22 (2H, S), 5.82 (2H, S), 2.41 (3H, S).

^{13}C NMR (100MHZ) δ (PPM): 148.09, 139.15, 137.45, 131.40, 130.85, 130.58, 129.92, 129.37, 129.06, 128.83, 128.72, 128.51, 128.13, 127.52, 127.41, 126.93, 126.53, 126.03, 48.36, 21.40.

1-phenyl-2-(4-chlorophenyl)-4, 5-diphenyl-1H-imidazol:

m.p=134-138 oC lit

IR (KBr) cm^{-1} : 3010, 2920, 2850, 1610, 1510, 1485, 1240, 840, 700.

^1H NMR (400MHZ, CDCl_3): 0.97 (s, 12H), 1.07 (s, 12H,) 2.18 (s, 8H, J= 16.2 Hz), 2.37 (d, 4H, J= 17.6 Hz), 2.50 (d, 4H, J=17.6 Hz), 4.71 (s, 2H), 7.08 (s, 4H); **^{13}C NMR** (100MHZ) δ (PPM): 27.66, 28.98, 30.74, 32.24, 40.85, 50.69, 115.70, 128.88, 141.74, 162.42, 196.36.

1-benzil-2-(3-hydroxyphenyl)-4, 5-diphenyl-1H-imidazol:

m.p=232-235 °C

IR (KBr) cm^{-1} : 3075, 3015, 1593, 1445, 1360, 1340, 760, 695.

^1H NMR (400MHZ, CDCl_3) ;(5.00 (s, 2H), 6.63 (t, 2H, J= 7.1 Hz), 6.75 (dd, 1H, J1= 8.1 Hz, J2= 1.7 Hz), 6.93 (d, 1H, J= 7.5 Hz), 6.98-7.29 (m, 13H), 7.41 (d, 2H, J= 7.8 Hz), 9.20 (s, 1H).

^{13}C NMR (100MHZ) δ (PPM): 48.6, 116.9, 120.2, 126.5, 126.7, 127.0, 127.6, 128.3, 128.8, 129.0, 129.1, 129.9, 130.2, 131.2, 131.3, 131.9, 134.6, 137.6, 137.8.

3. RESULTS AND DISCUSSION

The catalyst was characterized by XRD. The average particle size of ZnO catalysts is 57 nm and there are high-density defects on nanotubes surfaces (Fig. 2).

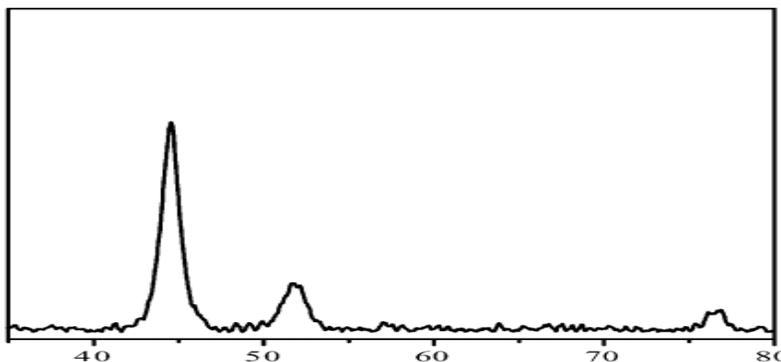


Fig. 2. XRD pattern zinc oxid nanotubes catalyst

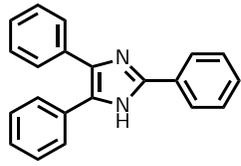
To establish the reaction conditions for the synthesis of tri- and four substituted imidazoles derivatives, using ZnO-np/SiO₂ as catalyst, the condensation reaction of benzil, benzaldehyde and ammonium acetate (1b) was taken as a model reaction.

An attempt was made to optimize the reaction conditions by taking various amounts of ZnO-np/SiO₂ in the range of 1-20 mol% at 120 °C (Table 1). It was observed that the condensation reaction could be efficiently carried out using 1 mol% of the catalyst under solvent free condition and thermal conditions. In another study, the effect of different thermal conditions upon the reaction was investigated (Table 2). The results indicate that in the thermal conditions which examined, the reaction was completed at 120 °C, successfully.

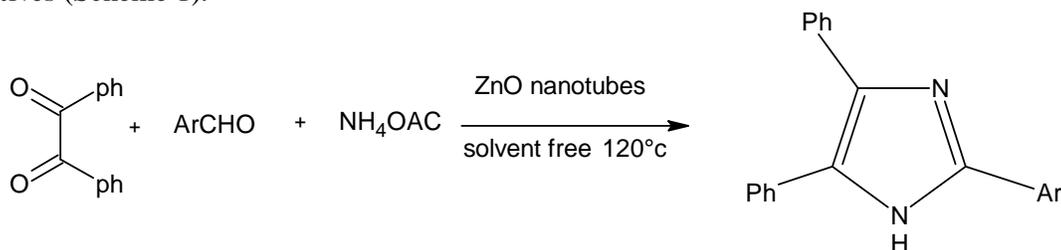
Table 1. Optimization of the amount ZnO-np/SiO₂ for synthesis of tri- substituted in the imidazoles 2a.

product	Yield (%)	Time(min)	Mole %
	96	18	1
	92	19	5
	89	20	10
	90	20	20

Table 2. Optimization of thermal reaction.

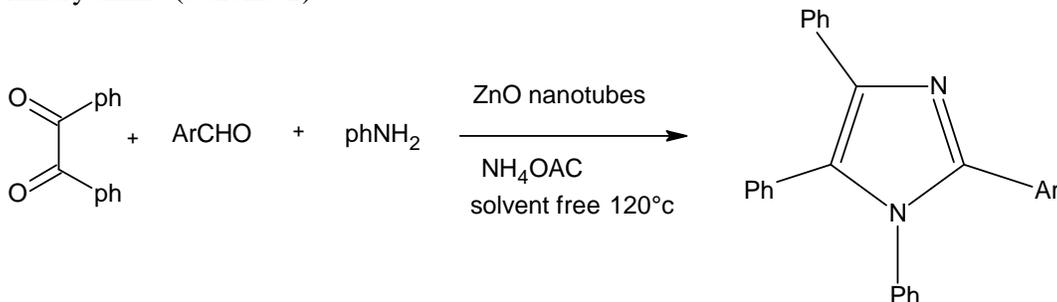
product	Yield (%)	Time(min)	Temperature (°C)
	–	–	rt
	60	60	60
	85	30	80
	96	18	120

With the optimized conditions in hand, to explore the generality of the reaction, we extended our study with various aromatic aldehydes to prepare a series of trisubstituted imidazoles derivatives (Scheme 1).



Scheme 1. synthesis of tri substituted imidazoles derivatives using zinc oxid nanotubes as a catalyst.

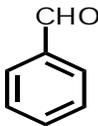
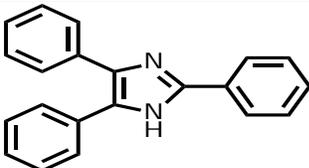
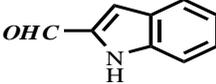
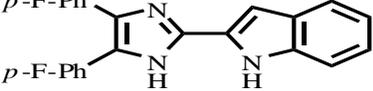
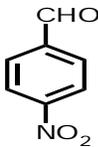
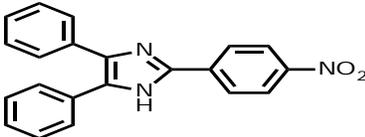
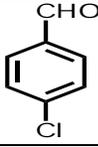
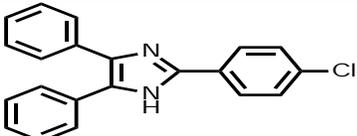
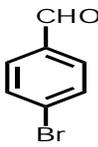
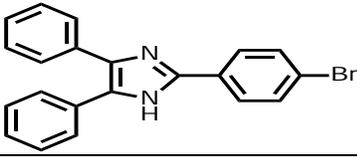
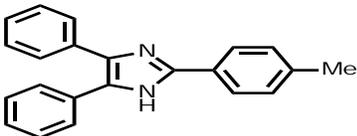
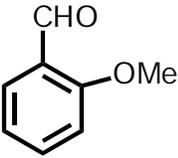
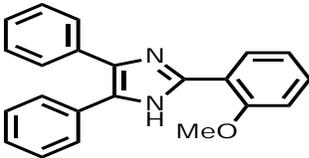
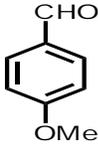
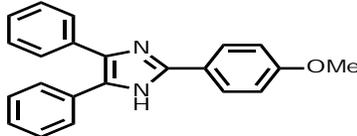
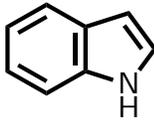
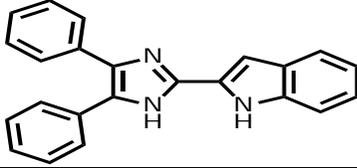
We have carried out aldehydes consisting electron withdrawing or electron donating groups at different positions but it did not show any remarkable difference in the yield of product and time of the reactions. Similarly, we have studied the condensation of benzyl, aldehyde, ammonium acetate with primary amine (Scheme 2).

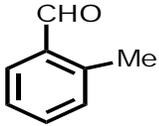
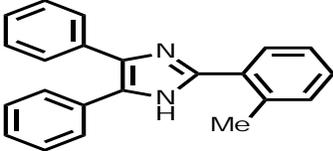
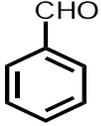
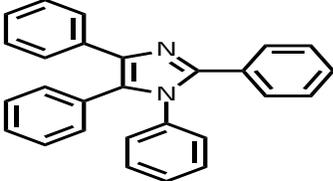
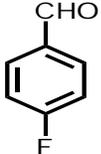
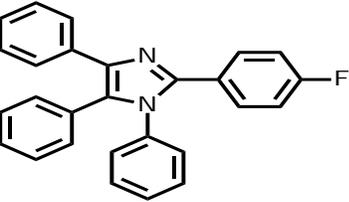
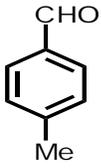
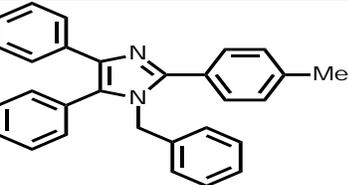
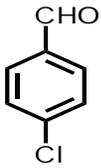
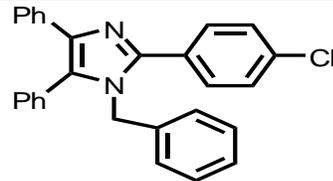
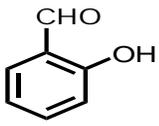
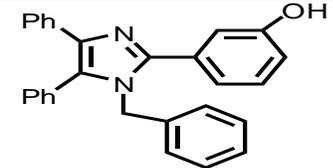
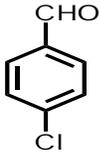
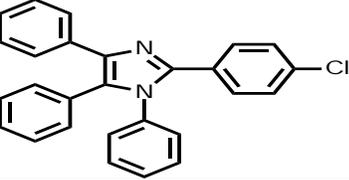
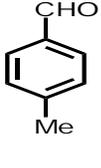
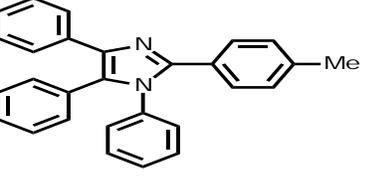


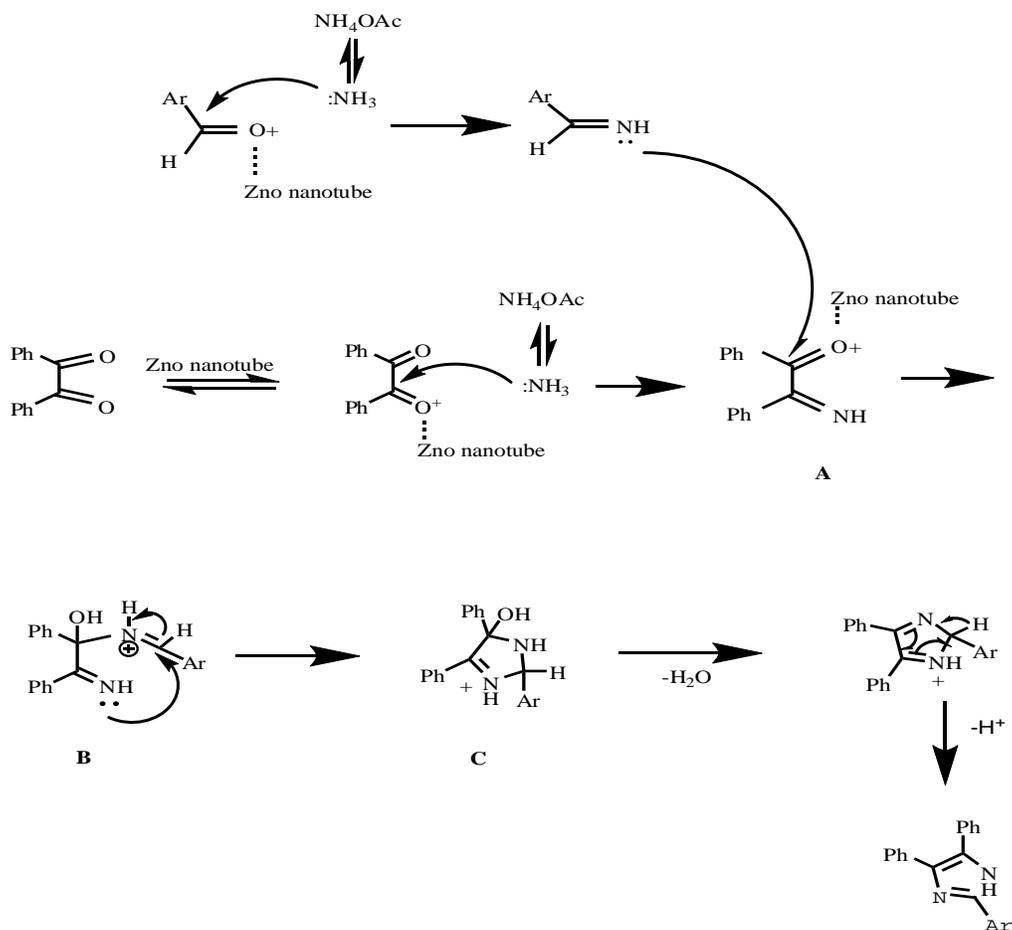
Scheme 2. synthesis of four substituted imidazoles derivatives using zinc oxid nanotubes as a catalyst

All the reaction very efficiently and the results are summarized in (Table 3).

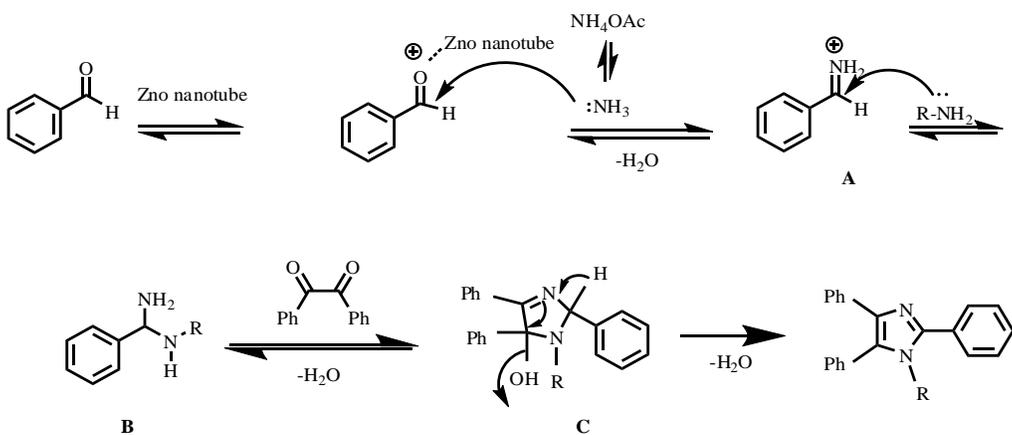
Table 3. synthesis of tri and four substituted imidazoles using zno nanotubes.

Entry	Aldehydes	Product	Time (min)	Yield (%)	M.P (⁰ C)
2a			18	96	270-272 (268-274) [9]
2b			28	90	303-305
3b			10	95	248-250 (243-247) [10]
4b			45	90	240-243 [11]
5b			52	88	219-222 [13]
6b			63	88	235-237 (235-238) [16]
7b			23	92	236-238 (235-239) [15]
8b			21	93	238-240 [18]
9b			67	89	305-307 (305-310) [19]

10b			68	86	205-207 [20]
11b			30	94	209-211 (205-210) [21]
12b			30	90	187-189 (185-187) [22]
13b			20	94	163-166 [23]
14b			20	94	168-170 (165-162) [24]
15b			16	96	232-235
16b			25	92	132-134 (130-133) [24]
17b			26	93	172-173 [25]



Scheme 3. Mechanism of reaction synthesis of tri substituted imidazoles.



Scheme 4. Mechanism of reaction synthesis of four substituted imidazoles.

4. CONCLUSION

In summary, we have presented a new application of ZnO nanotubes as an effective and reusable reagent for the synthesis of a variety of tri and four substituted imidazoles. This method relies on the condensation of dicarbonyl compounds, ammonium acetate, and different aromatic aldehydes, offering potential green chemistry advantages. This method is important from an environmental point of view and economic considerations, because it produces little waste. Simple preparation and

stability of catalyst, uncomplicated handling, simple work-up procedure and the high yields of products, short reaction times and avoid from using toxic organic solvents as media make this method a valid contribution to the existing methodologies.

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