2.1: Introduction

Imidazole is a“1, 3-diazole” and is classified as an alkaloid. Imidazole (1) refers to the parent compound, whereas imidazoles are a class of heterocycles with similar ring structure, but varying substituents. This ring system is present in important biological building blocks, such as histidine (2), and the related hormone histamine (3). Imidazole can serve as a base and as a weak acid. Many drugs contain an imidazole ring, such as antifungal drugs and nitroimidazole (4) (Brown 2012;Grimmett *et al.* 1984;Grimmett 1997;Pozharskii *et al.* 1997).

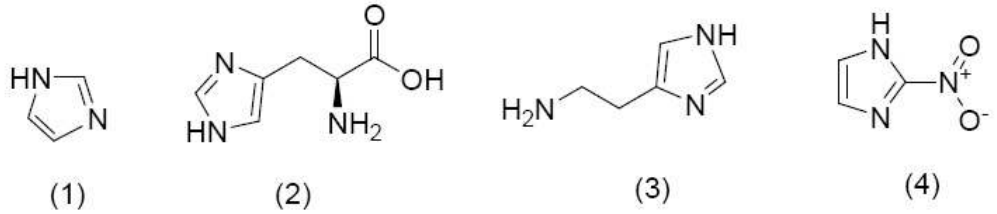


Figure: 2.1.1: Imidazole and their bio-active derivatives

Substituted imidazole derivatives are widely used as organic materials (Gostev *et al.* 2003;Park *et al.* 2005). Meanwhile, it was found that these compounds play roles in many kinds of biological activities (Bunnage and Owen 2008;Jin 2006;Kruse *et al.* 1989;Laufer *et al.* 2003;Lee *et al.* 1994;Weinreb 2007). This versatile applicability highlights the importance of access to efficient synthetic routes to well-designed and highly substituted imidazole derivatives.

Due to their great importance, many synthetic strategies have been developed. Substituted imidazoles are generally synthesized by three-component reaction of a 1, 2-diketone, α- hydroxyketone or α- ketomonoxime with an aldehyde and ammonium acetate, which comprise the use of microwaves (Oskooie *et al.* 2006;Sparks and Combs 2004;Usyatinsky and Khmelnitsky 2000;Wolkenberg *et al.* 2004), ionic liquids (Siddiqui *et al.* 2005;Xia and Lu 2007), refluxing in acetic acid (Chary *et al.* 2008), silica sulfuric acid (Shaabani and Rahmati 2006;Shaabani *et al.* 2007), $NiCl_2{\cdot}6H_2O/Al_2O_3$ (Heravi *et al.* 2007), $Yb(OTf)_3$ (Wang *et al.* 2006), $Yb(OPf)_3$(Shen *et al.* 2008), iodine (Kidwai *et al.* 2007), $Zr(acac)_4$ (Khosropour 2008), $InCl_3{\cdot}3H_2O$ (Sharma *et al.* 2008), heteropolyacid (Heravi *et al.* 2008), sodium bisulfate (Sangshetti *et al.* 2008), potassium aluminum sulfate (alum)

(Mohammadi *et al.* 2008), ceric ammonium nitrate (CAN) (Mohammadi *et al.* 2008;Shaabani *et al.* 2008), $(NH_4)_6$ $Mo_7O_{24}\cdot 4H_2O$ (Safari *et al.* 2010), zeolite HY/silica gel (Balalaie *et al.* 2000), $ZrCl_4$ (Sharma *et al.* 2006), polymer-supported $ZnCl_2$ (Wang and Cai 2009) and L-proline (Samai *et al.* 2009). Moreover, they have also been prepared by the addition of a substituted amino alcohol to a thioamide and subsequent oxidation with PDC (Paone and Shaw 2008) or by the reaction of aryl nitriles and α, α-dilithioarylnitromethanes (Hayes *et al.* 1994) or by multistep synthesis (Revesz *et al.* 1998). Khodaei and co-workers in 2007 described the synthesis of 2,4,5-trisubstituted imidazoles from 1, 2- diketone or α-hydroxyketone, aldehyde and ammonium heptamolybdate tetrahydrate in tetrabutylammonium iodide using catalytic amounts of *p*-TSA (Khodaei *et al.* 2007).

Despite their potential utility, most of these synthetic methods suffer from one or more serious drawbacks, such as laborious and complex work-up and purification, significant amounts of waste materials, strongly acidic conditions, occurrence of side reactions, low yields, high temperature, long reaction time and the use of expensive reagents. Hence, a highly efficient protocol with mild reaction conditions to construct substituted imidazoles was in great demand.

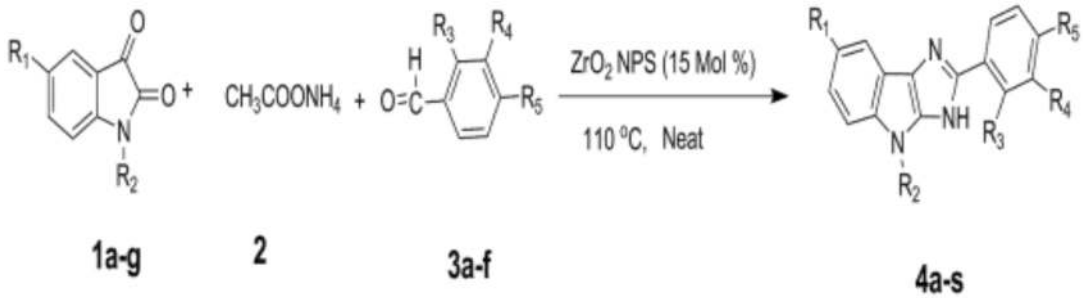
Recently, nanostructured materials are attractive candidates as heterogeneous catalysts for various organic transformations, particularly because they meet the goals of green and sustainable chemistry. Scientists have made significant advances in the synthesis of well defined nanostructured materials in recent years. Among these are novel approaches that have permitted the rational design and synthesis of highly active and selective nanostructured catalysts by controlling the structure and composition of the active nanoparticles. The ease of separation, recovery and reuse of these NPs further enhance their attractiveness as green and sustainable catalysts (Cox *et al.* 1988;Gladysz 2002;2001;Grunes *et al.* 2003;Pacchioni 2000;Polshettiwar *et al.* 2009;Polshettiwar *et al.* 2008;Polshettiwar and Varma 2010;Ramarao *et al.* 2002;Reetz and Westermann 2000;Shimizu *et al.* 2009).

Nano zirconia (ZrO_2)have been widely investigated in the past decades due to their multiple potential applications (Liu and Lin 2005;Liu and Han 2010;Lu *et al.* 2008;Luo *et al.* 2006;Sholklapper *et al.* 2007;Steiner III *et al.* 2009).The crystal phase of ZrO_2 (monoclinic and tetragonal) strongly influences the catalyst activities and selectivities (He *et al.* 2004;Rhodes and Bell 2005;Stichert *et al.* 2001;Yamaguchi 1994). ZrO_2 nanoparticle catalyst as an inexpensive, non-toxic, moisture stable, reusable, commercially available white powder is of great interest to many researchers in the recent years. In general, several similar applications of this nanoscale method, as an effective catalyst in green synthetic chemistry, have already been highlighted in the literature (Asakura *et al.* 1988;Damyanova *et al.* 1997;Khodakov *et al.* 1999;Li *et al.* 2006;Mercera *et al.* 1991;1990;Tsipouriari *et al.* 1994;Xie *et al.* 2000).

In view of the above it was thought worthwhile to synthesize some novel imidazoles fused with indole nucleus of biocidal interest, and guided by the observation that the presence of two or more different heterocyclic moieties in a single molecule often enhances the biocidal profile remarkably, in order to get targeted products, a greener "NOSE" (nanoparticles-catalyzed organic synthesis enhancement) approach under solvent free conditions has been developed.

2.2: Results and discussion

Multicomponent reaction of isatin derivatives **1a-g** with ammonium acetate **2** and substituted benzaldehydes **3a-f** in the presence of catalytic amount of ZrO_2 NPs under solvent- free conditions at 110 ^{0}C, afforded imidazole derivatives **4a-s** in good to excellent yields (**Scheme 2.2.1**). The chemical structures of the respective synthesized imidazole derivatives were established by their spectral data.



Scheme 2.2.1

In order to find optimum reaction conditions, several parameters were investigated. Expectedly, efficiency of the ZrO_2 NPs was affected by their amount (mol %). Therefore, a set of experiments using different amounts of ZrO_2 NPs were taken into account for the multicomponent reaction of isatin with ammonium acetate and benzaldehyde (**Table 2.2.1**). The synthetic route was drastically dependent on the presence of catalyst and only poor yield was observed in the absence of catalyst after 120 min (**Entry 1, Table 2.2.1**). It was found that product yield is increased with enhancing catalyst concentration. Only 5 mol % of ZrO_2 NPs was sufficient to attain 60% of product yield after 60 min (**Entry 2, Table 2.2.1**). The best yield of 88% was obtained with 15 mol % of ZrO_2 NPs (**Entry 5, Table 2.2.1**).

However, further addition of catalyst concentration (> 15 mol%) did not improve the reaction rate and product yield (**Entry 6**, **Table 2.2.1**).

The multicomponent reaction of isatin with ammoniumacetate and benzaldehyde was investigated in detail using different molar proportions of reactants (**Table 2.2.2**). A perusal of the table clearly indicates that the best result was obtained using isatin, ammonium acetate, benzaldehyde in the molar proportion 1.0:5.0:1.0 at 110 °C under solvent free conditions (**Entry 5, Table 2.2.2**).

The multicomponent reaction of isatin with ammonium acetate and benzaldehyde was examined under different temperatures. Obviously, reaction rate and product yield both were increased with enhancing temperature from 50 to 110°C. On the basis of this observation, it would be concluded that the 110°C was favorable temperature for the multicomponent reaction of isatin with ammonium acetate and benzaldehyde (**Table 2.2.3**).

To investigate the effect of solvents, the multicomponent reaction of isatin with ammonium acetate and benzaldehyde in various organic solvents at refluxing temperature using 15 mol % ZrO_2 NPs as the catalyst was carried out (**Table 2.2.4**). About 68% of the expected product **4a** was obtained when the solvent was ethanol (**Entry 1, Table 2.2.4**). Obviously, the polar solvents such as ethanol and acetonitrile were much better than non polar solvents (**Entry 1&2, Table 2.2.4**). It

was observed that reaction takes more time to give only satisfactory yield of product in the presence of solvent, under similar ratio of the reactants (**Entry 1, 2, 3&4 Table 2.2.4**). This may be due to the competitive adsorption of the solvent with the substrate molecule on the catalyst surface; hence reaction under solvent-free conditions gives excellent yield in short reaction time (**Entry 5, Table 2.2.4**). A possible explanation for higher yield in solvent free conditions is that the eutectic mixture having uniform distribution of the reactants brings the reacting species in close proximity to react than in the presence of solvent.

Table 2.2.1: Effect of catalyst amount (mol %) on yield of the product **4a**

Entry	ZrO_2 mol%	Time(min.)	%Yield
1	0	120	23
2	5	60	60
3	10	45	75
4	12	35	82
5	**15**	**30**	**88**
6	20	30	88

Table 2.2.2: Effect of molar ratio of substrates on the yield of the product **4a**

Entry	Molar ratio of reactants	%Yield
	Isatin:Ammoniumacetate: Benzaldehyde	
1	1.0 : 1.0 : 1.0	Trace amount
2	1.0 : 2.0 : 1.0	35
3	1.0 : 3.0 : 1.0	52
4	1.0 : 4.0 : 1.0	78
5	**1.0 : 5.0 : 1.0**	**88**
6	1.0 : 6.0 : 1.0	87
7	1.0 : 5.0 : 1.2	87
8	1.2 : 5.0 : 1.0	86

Table 2.2.3: Effect of temperature on the yield of the product **4a**

Entry	Temp (^{0}C)	Time	% Yield
1	rt	-	No reaction
2	50	10h	Trace amount
3	60	6h	65
4	70	4h	70
5	80	1.5h	78
6	90	55min	84
7	100	45min	86
8	**110**	**30min**	**88**
9	120	30min	88

Table 2.2.4: Effect of solvents on the yield of the product **4a**

Entry	Solvents	Time	%Yield
1	Ethanol	10h	68
2	Acetonitrile	10h	59
3	Xylene	13h	55
4	Tolune	18h	52
5	**Solvent free**	**30min**	**88**

A comparison of the efficiency of catalytic activity of the ZrO_2NPs with several other catalysts is presented in **table 2.2.5**. The result showed that ZrO_2 NPs was the best catalyst in terms of mol %, reaction time and percentage yield (**Table 2.2.5**).

Table 2.2.5: Effect of different catalysts on the yield of the product **4a**

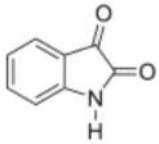
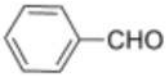
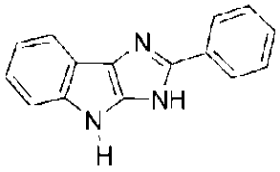
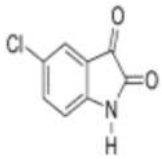
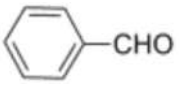
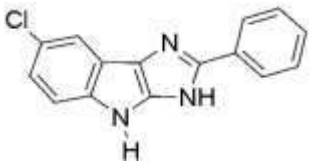
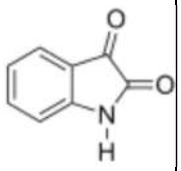
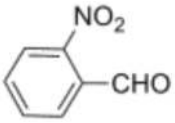
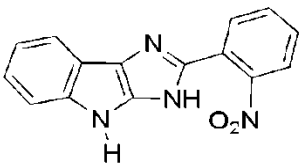
Type of catalyst	Mol %	Time (min.)	% Yield
Bentonite clay	20	60	55
K-10 clay	20	60	58
PTSA	40	75	45
NH_4Cl	30	75	44
EDTA	40	75	40
Iodine	30	60	53
$Yb(OTf)_3$	25	60	51
TiO_2 (Nano)	20	30	80
ZrO_2 (Nano)	**15**	**30**	**88**

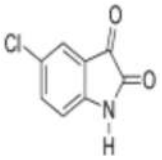
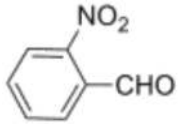
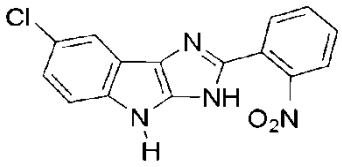
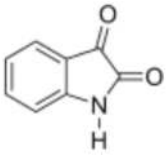
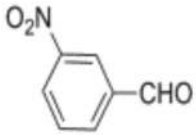
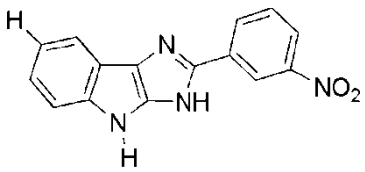
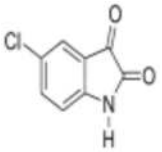
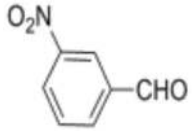
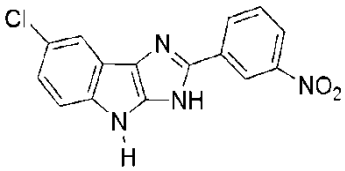
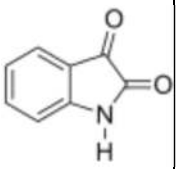
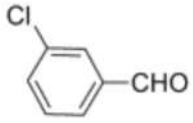
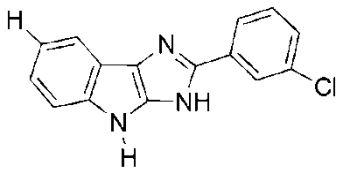
In order to investigate whether R_1 can be replaced by some electron donating groups, a reaction using 5-methyl isatin (R_1= CH_3) with benzaldehyde and ammonium acetate was attempted. The reaction was found successful and the product was isolated with 87% yield. This confirms that the proposed methodology is equally applicable for the presence of both electron donating as well as electron withdrawing groups at the 5-position of isatin moiety.

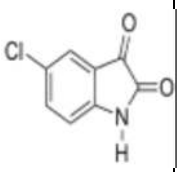
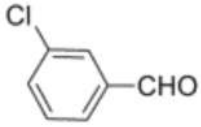
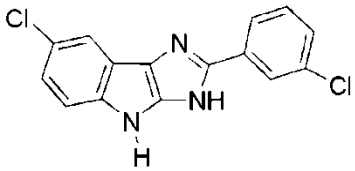
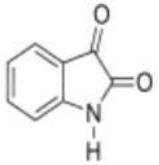
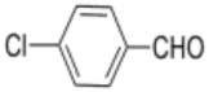
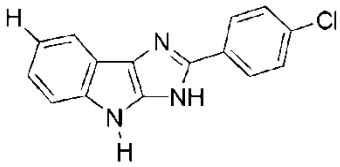
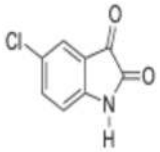
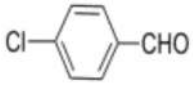
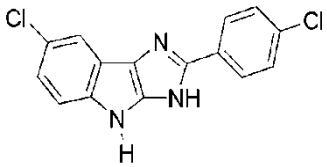
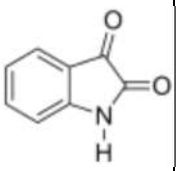
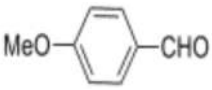
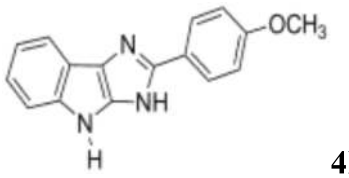
Under the optimized set of conditions, a number of isatin derivatives **1**, *viz.* isatin (**1a**), 5- choloroisatin (**1b**), *N*-acylisatin (**1c**), *N*-ethylisatin (**1d**), *N*-propylisatin (**1e**), *N*-ethylacetateisatin (**1f**) and 5-methylisatin (**1g**) were allowed to undergo multicomponent reaction with ammoniumacetate **2** and various aromatic aldehydes **3**, *viz.* benzaldehyde (**3a**), *o*-nitrobenzaldehyde (**3b**), *m*-nitobenzaldehyde (**3c**), *m*-chlorobenzaldehyde (**3d**), *p*-chlorobenzaldehyde (**3e**) and *p*-methoxybenzaldehyde (**3f**) in a molar ratio 1:5:1 with 15 mol% of ZrO_2 NPs at 110 ^{0}C for 30 min. The progress of the reaction was monitored by thin layer chromatography. After completion, 20 ml acetone was added to the reaction mixture; the catalyst was removed and washed with xylene and acetone. Then, 50 ml of double distilled water is added to the liquid portion. This resulted in the formation of precipitate which was filtered and recrystallized with ethanol to yield pure substituted imidazole derivatives **4**, *viz.* 2-phenyl-3,4-dihydroimidazo[4,5-b]indole **(4a)**, 7-chloro-2-phenyl-3,4-dihydroimidazo[4,5-b]indole (**4b**), 2-(2-nitrophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4c**), 7-chloro-2-(2-nitrophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4d**), 2-(3-nitrophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4e**), 7-chloro-2-(3-nitrophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4f**) 2-(3-chlorophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4g**), 7-chloro-2-(3-chlorophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4h**), 2-(4-chlorophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4i**), 7-chloro-2-(4-chlorophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4j**), 2-(4-methoxyphenyl)-3,4-dihydroimidazo[4,5-b]indole (**4k**), 7-chloro-2-(4-methoxyphenyl)-3,4-dihydroimidazo[4,5-b]indole (**4l**), 1-(2-(3-nitrophenyl)imidazo[4,5-b]indol-4(3*H*)-yl)ethanone (**4m**), 1-(2-(3-chlorophenyl)imidazo[4,5-b]indol-4(3*H*)-yl)ethanone (**4n**), 1-(2-(4-chlorophenyl)imidazo[4,5-b]indol-4(3*H*)-yl)ethanone (**4o**), 4-ethyl-2-(2-

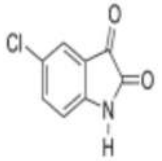
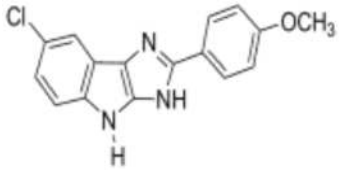
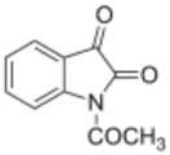
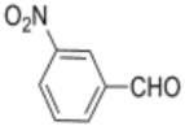
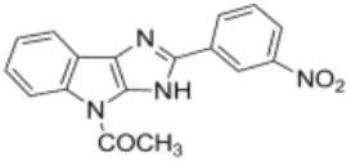
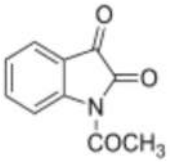
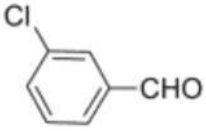
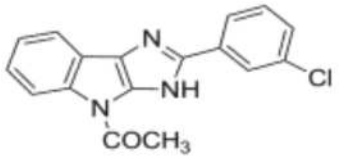
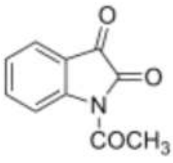
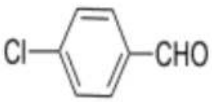
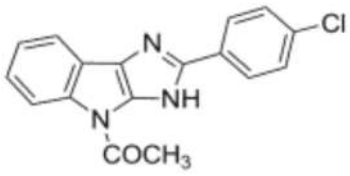
nitrophenyl)-3,4-dihydroimidazo[4,5-b]indole (**4p**), 2-(3-nitrophenyl)-4-propyl-3,4-dihydroimidazo[4,5-b]indole (**4q**), Ethyl 2-(2-(2-nitrophenyl)imidazo[4,5-b]indol-4(3*H*)-yl)acetate (**4r**), 7-methyl-2-phenyl-3,4-dihydroimidazo[4,5-b]indole (**4s**). The results are given in the **table 2.2.5**.

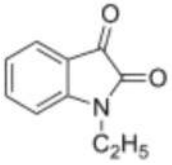
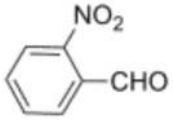
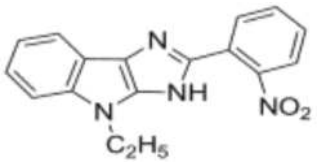
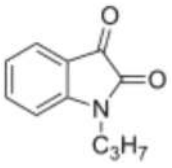
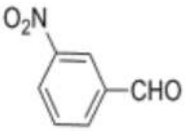
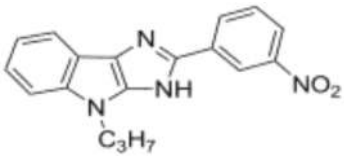
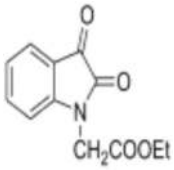
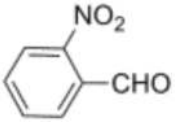
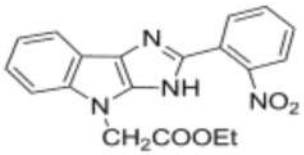
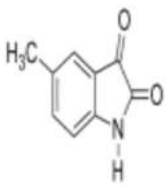
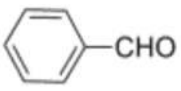
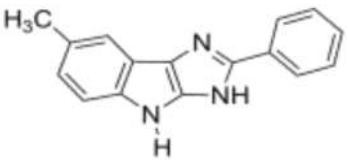
Table 2.2.5: Synthesis of substituted imidazoles (**4a-s**)

Entry	Isatins	Aldehydes	Products	%Yield	Mp (^{0}C)
1	 **1a**	 **3a**	 **4a**	88	>300
2	 **1b**	 **3a**	 **4b**	87	>300
3	 **1a**	 **3b**	 **4c**	93	240

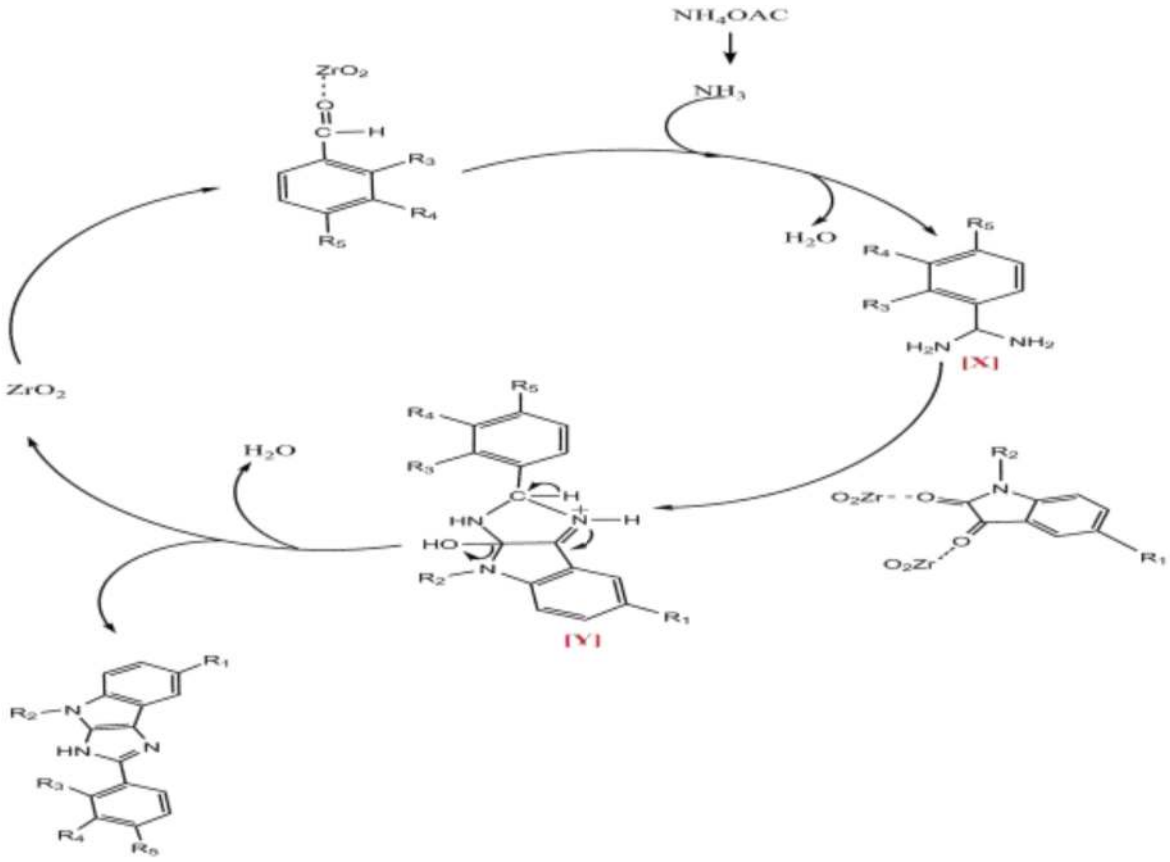
4	 **1b**	 **3b**	 **4d**	90	290
5	 **1a**	 **3c**	 **4e**	88	168
6	 **1b**	 **3c**	 **4f**	90	192
7	 **1a**	 **3d**	 **4g**	82	158

8	 **1b**	 **3d**	 **4h**	80	152
9	 **1a**	 **3e**	 **4i**	89	220
10	 **1b**	 **3e**	 **4j**	90	165
11	 **1a**	 **3f**	 **4k**	78	147

12	 **1b**	 **3f**	 **4l**	85	130
13	 **1c**	 **3c**	 **4m**	88	170
14	 **1c**	 **3d**	 **4n**	82	132
15	 **1c**	 **3e**	 **4o**	86	135

16	 **1d**	 **3b**	 **4p**	88	158
17	 **1e**	 **3c**	 **4q**	84	180
18	 **1f**	 **3b**	 **4r**	91	172
19	 **1g**	 **3a**	 **4s**	87	212

The proposed mechanism of formation of substituted imidazoles catalysed by the ZrO_2 NPs is given in **Scheme 2.2.2**. The reaction proceeds via the diamine intermediate [X], which is formed by the activation of an aldehyde carbonyl group by ZrO_2NPs. Condensation of diamine with isatin derivatives followed by dehydration, and then rearrangement through the imino intermediate [Y] yielded the desired product.



Scheme 2.2.2: Proposed mechanism for the formation of substituted imidazole **4a-s**

ZrO_2 NPs were synthesized and characterized by FTIR, XRD, SEM and TEM analysis. The specific surface area of synthesized ZrO_2 NPs was calculated by BET surface area analyzer.

In order to ascertain the molecular nature of the synthesized material, the FT-IR spectrum of the ZrO_2 sample was taken**.** The FT-IR spectrum of ZrO_2 NPs depends on the nature of the material, preparative procedures used, solid-state structure, and so forth. The observed strong FT-IR absorption peak at about 500 cm^{-1} region is due to the Zr–O vibration, which confirm the formation of ZrO_2

structure while the peak at 751 cm^{-1}, represents stretching vibrations of Zr-O-Zr, prominent peak at1340 cm^{-1} corresponds to O–H bonding, peak in the region of 1622 cm^{-1} may be due to the adsorbed moisture and in the 2855-2922 cm^{-1} region is attributed to stretching of O–H groups.

It has been observed that the sample of ZrO_2 NPs was highly crystalline as evident from XRD pattern in which broad peaks with high intensity extended over the 2θ scale. The peaks observed at 2θ= 24.2 (011), 28.2 (-111), 31.4 (111), 35.0 (020), 40.5 (-112), 45.0 (211), and 55.4 (-311) are corresponding to monoclinic zirconia (JCPDS card no. 37-1484) while diffraction peak observed at 2θ= 30.3 (101), 50.3 (212) and 60.2 (211) are corresponding to tetragonal zirconia ((JCPDS card no.79-1769). The broadening of peaks indicates the smaller particle size of ZrO_2 NPs **(Figure 2.2.1).**

Morphological investigations of 600 ^{0}C calcinated ZrO_2 NPs sample were carried out using SEM and TEM analysis that are shown in **Figure 2.2.2** and **Figure 2.2.3** respectively. The morphological characterization highlighted the importance of nanocrystalline ZrO_2 preparation in maintaining the nanostructured phase. It is clear from **Figure 2.2.2** that NPs are agglomerated and non-homogenous. **Figure 2.2.2** also indicates that ZrO_2 particles are spherical in nature and size of the particles is in the nm regime, but size could not be finely resolved from SEM. For the purpose, TEM of sample has been shown in **Figure 2.2.3**.

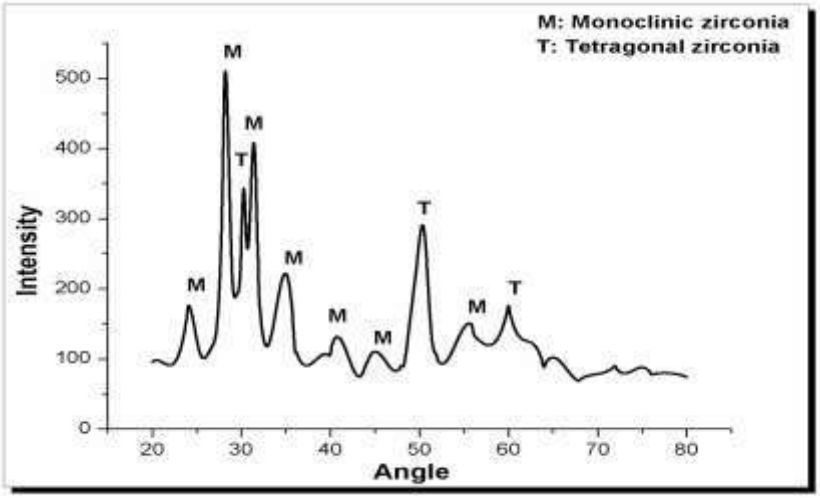


Figure 2.2.1: XRD spectra of ZrO_2 NPs

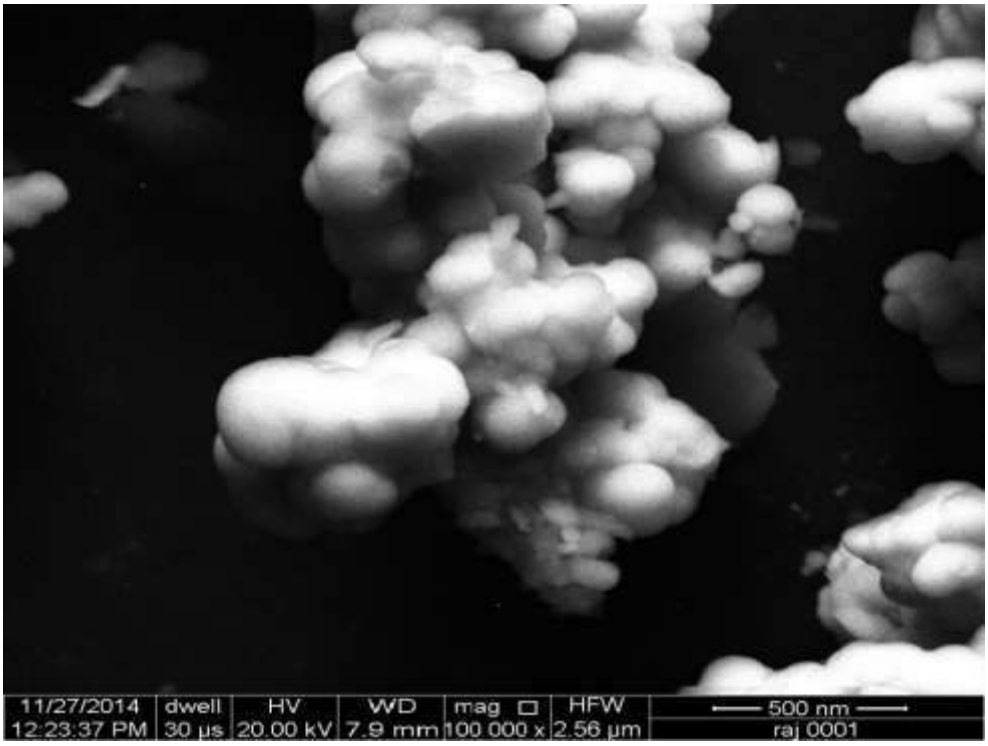


Figure 2.2.2: SEM image of ZrO_2 NPs

As can be seen from TEM micrograph of sample, some agglomeration has been observed due to different m- and t- phases present in the sample. In spite of agglomeration of the NPs, it can be observed that the sizes of the particles are of the order 20 nm.

Surface area analysis of ZrO_2 NPs was done by nitrogen absorption using BET surface area analyzer and the surface area of synthesized ZrO_2 NPs was found to be 44. 70 m^2/g.

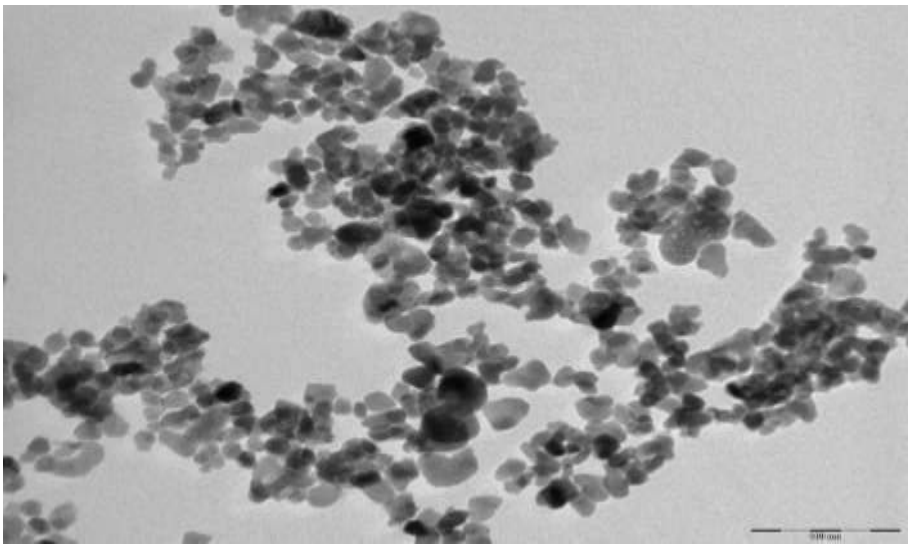


Figure 2.2.3: TEM image of ZrO_2 NPs

2.3: Experimental

2.3.1: Typical procedure for the synthesis of ZrO_2 NPs (Gusain *et al.* 2014)

0.075 M solution of $ZrOCl_2.8H_2O$ was prepared and then precipitated with NH_4OH (25%) with continuous stirring on a magnetic stirrer till the p^H raises in the range of 10 to 10.5. This resulted in the formation of precipitate of zirconium hydroxide. The precipitate was filtered and washed with double distilled water until traces of chloride ion were completely removed from the filtrate. Complete removal of chloride ion from filtrate was checked by titrating it with $AgNO_3$ solution using potassium chromate as indicator. Now, the precipitate was dried in oven at 80 – 90^0C for 24 h and calcinated at 600 ^{0}C for 3 h in order to formation of white nano zirconia powder.

2.3.2: General procedure for the synthesis of substituted imidazoles 4a-s

To a mixture of isatin derivatives **1a-g** (1 mmol), ammonium acetate **2** (5 mmol), substitutedaromatic aldehydes **3a-f** (1 mmol), 15 mol% of ZrO_2 NPs was added [**Scheme 2.2.1**]. The mixture was heated and stirred at 110 ^{0}C for 30 min. The progress of the reaction was monitored by thin layer chromatography (n-hexane: ethyl acetate, 1:1). After completion, 20 ml acetone was added to the reaction mixture; the catalyst was removed by filtration and washed with xylene and

acetone. Then, 50 ml of double distilled water is added to the liquid portion. This resulted in the formation of precipitate of products **4a-s**. The precipitate was filtered, dried and recrystallized with ethanol.

2-Phenyl-3, 4-dihydroimidazo[4,5-b]indole (4a)

Brownsolid, **IR (KBr) υ:** 3400, 3209, 3019, 2964, 1660, 1614, 1567, 1484, 1316, 1210, 1171, 1010, 877, 742, 653, 580 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 7.80-8.86 (m, 9H, aromatic protons), 9.15 (s, 1H, NH), 9.66 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 124.0, 126.7, 127.5, 130.2, 130.7, 132.0, 133.7, 135.5, 139.1, 148.2, 160.9 ppm. Anal. Calcd for $C_{15}H_{11}N_3$: C, 77.24; H, 4.74; N, 18.01 Found C, 77.20; H, 4.76; N, 18.03.

7-Chloro-2-phenyl-3, 4-dihydroimidazo[4,5-b]indole (4b)

Brownsolid, **IR (KBr) υ:** 3364, 3190, 2981, 2964, 1648, 1609, 1559, 1447, 1311, 1199, 1143, 1019, 872, 744, 651, 566 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.51-8.59 (m, 8H, aromatic protons), 9.14 (s, 1H, NH), 9.45 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 123.9, 125.7, 128.5, 128.6, 130.3, 130.8, 132.7, 135.0, 137.5, 149.2, 159.4 ppm. Anal. Calcd for $C_{15}H_{10}ClN_3$: C, 67.28; H, 3.78; N, 15.72. Found C, 67.32; H, 3.76; N, 15.70

2-(2-Nitrophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4c)

Brownsolid, **IR (KBr) υ:** 3332, 3201, 2995, 2917, 1658, 1623, 1549, 1485, 1348, 1280, 1176, 1068, 864, 708, 667, 544 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 7.61-8.69 (m, 8H, aromatic protons), 9.67 (s, 1H, NH), 9.94 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 123.8, 126.7, 128.8, 129.8, 130.1, 131.8, 135.4, 135.8, 135.9, 148.3, 160.7 ppm. Anal. Calcd for $C_{15}H_{10}N_4O_2$: C, 64.74; H, 3.62; N, 20.13 Found C, 64.69; H, 3.65; N, 20.14.

7-Chloro-2-(2-nitrophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4d)

Brownsolid, **IR (KBr) υ:** 3399, 3229, 2916, 2885, 1645, 1600, 1539, 1457, 1329, 1253, 1162, 1027, 885, 703, 647, 553 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.66-8.36 (m, 7H, aromatic protons), 8.96 (s, 1H, NH), 9.50 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 123.4, 123.8, 124.8, 127.1, 128.0, 128.6, 129.4,

133.9, 134.1, 134.4, 139.7, 148.7, 150.4, 160.6 ppm. Anal. Calcd for $C_{15}H_9ClN_4O_2$: C, 57.60; H, 2.91; N, 17.91 Found C, 57.51; H, 3.0; N, 17.94.

2-(3-Nitrophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4e)

Brownsolid, **IR (KBr) υ:** 3315, 3194, 3066, 2978, 1662, 1623, 1572, 1482, 1353, 1286, 1135, 1025, 832, 797, 661, 542 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 7.58-8.55 (m, 8H, aromatic protons), 8.97 (s, 1H, NH), 9.67 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 122.3, 123.6, 125.2, 127.9, 128.4, 129.7, 130.4, 134.4, 134.5, 135.2, 139.0, 147.6, 161.7 ppm. Anal. Calcd for $C_{15}H_{10}N_4O_2$: C, 64.70; H, 3.63; N, 20.16 Found C, 64.51; H, 3.72; N, 20.23.

7-Chloro-2-(3-nitrophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4f)

Brownsolid, **IR (KBr) υ:** 3385, 3211, 3003, 2959, 1646, 1603, 1538, 1458, 1367, 1248, 1122, 1022, 831, 741, 635, 564 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 7.77-8.83 (m, 7H, aromatic protons), 9.13 (s, 1H, NH), 9.62 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 124.0, 126.6, 127.5, 127.6, 130.2, 130.7, 132.0, 133.6, 135.4, 139.1, 148.2, 160.8, 160.9 ppm. Anal. Calcd for $C_{15}H_9ClN_4O_2$: C, 57.61; H, 2.90; N, 17.92 Found C, 57.67; H, 2.90; N, 17.90.

2-(3-Chlorophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4g)

Brownsolid, **IR (KBr) υ:** 3405, 3217, 2948, 2909, 1671, 1617, 1568, 1454, 1371, 1283, 1134, 1018, 892, 754, 641, 577 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 7.60-8.56 (m, 9H, aromatic protons and 1H, NH), 9.69 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 123.8, 126.6, 128.8, 128.7, 130.1, 131.0, 131.6, 135.2, 137.0, 148.4, 160.6 ppm. Anal. Calcd for $C_{15}H_{10}ClN_3$: C, 67.30; H, 3.77; N, 15.70 Found C, 67.29; H, 3.75; N, 15.70.

7-Chloro-2-(3-chlorophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4h)

Brownsolid, **IR (KBr) υ:** 3398, 3227, 2977, 2893, 1664, 1605, 1551, 1477, 1358, 1242, 1163, 1011, 844, 743, 650, 567 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.62-8.31 (m, 7H, aromatic protons), 8.90 (s, 1H, NH), 9.42 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 124.1, 125.8, 126.6, 128.6, 129.8, 130.3, 130.7,

133.2, 134.8, 135.2, 139.3, 149.0, 160.5 ppm. Anal. Calcd for $C_{15}H_9C_{l2}N_3$: C, 59.62; H, 3.00; N, 13.91 Found C, 59.52; H, 3.05; N, 13.89.

2-(4-Chlorophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4i)

Brownsolid, **IR (KBr) υ:** 3362, 3255, 3015, 2882, 1669, 1620, 1565, 1482, 1375, 1235, 1140, 1026, 890, 777, 663, 526 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.48-8.58 (m, 8H, aromatic protons), 9.45 (s, 1H, NH), 10.16 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 123.3, 127.8, 127.9, 128.7, 129.7, 134.9, 135.6, 136.2, 149.7, 161.3 ppm. Anal. Calcd for $C_{15}H_{10}ClN_3$: C, 67.30; H, 3.77; N, 15.70 Found C, 67.31; H, 3.75; N, 15.73.

7-Chloro-2-(4-chlorophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4j)

Brownsolid, **IR (KBr) υ:** 3386, 3233, 3047, 2960, 1657, 1612, 1558, 1435, 1348, 1282, 1153, 1019, 871, 742, 654, 552 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 7.46-8.54 (m, 7H, aromatic protons), 8.99 (s, 1H, NH), 9.35 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ**: 123.9, 125.8, 128.8, 129.8, 130.3, 133.0, 135.2, 136.0, 137.1, 149.1, 159.5 ppm. Anal. Calcd for $C_{15}H_9Cl_2N_3$: C, 59.62; H, 3.00; N, 13.91 Found C, 59.55; H, 3.10; N, 13.90.

2-(4-Methoxyphenyl)-3, 4-dihydroimidazo[4,5-b]indole (4k)

Brownsolid, **IR (KBr) υ:** 3351, 3138, 3001, 2944, 2881, 1667, 1619, 1575, 1450, 1371, 1284, 1157, 1021, 863, 743, 654, 534 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 4.00 (s, 3H, CH_3), 7.26- 8.69 (m, 9H, aromatic protons and 1H, NH), 9.72 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 56.9, 122.2, 123.2, 125.9, 127.7, 127.4, 127.9, 128.7, 129.0, 129.6, 130.7, 131.2, 131.4, 131.5, 138.5, 139.7, 140.1, 143.9, 145.8, 154.6 ppm. Anal. Calcd for $C_{16}H_{13}N_3O$: C, 72.99; H, 4.98; N, 15.96 Found C, 72.91; H, 5.04; N, 15.95.

7-Chloro-2-(4-methoxyphenyl)-3, 4-dihydroimidazo[4,5-b]indole (4l)

Brownsolid, **IR (KBr) υ:** 3370, 3259, 2991, 2911, 1675, 1614, 1558, 1480, 1436 1377, 1291, 1186, 1049, 869, 745, 651, 522 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 3.61 (s, 3H, CH_3), 7.44- 8.47 (m, 8H, aromatic protons), 8.58 (s, 1H, NH), 9.36 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 61.8, 122.16, 122.29, 124.0,

125.3, 126.6, 130.1, 130.4, 132.3, 133.9, 135.5, 138.5, 148.1, 148.2, 157.8 ppm. Anal. Calcd for $C_{16}H_{12}ClN_3O$: C, 64.54; H, 4.06; N, 14.11 Found C, 64.70; H, 4.00; N, 14.10.

1-(2-(3-Nitrophenyl)imidazo[4,5-b]indol-4(3H)-yl)ethanone (4m)

Brownsolid, **IR (KBr) υ:** 3389, 3266, 2978, 2935, 1694, 1645, 1616, 1571, 1467, 1346, 1224, 1133, 1021, 823, 744, 641, 572 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 1.91 (s, 3H, CH_3), 7.22- 8.51 (m, 8H, aromatic protons), 9.40 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 23.7, 122.1, 122.4, 123.2, 123.5, 124.8, 127.2, 127.4, 127.6, 128.2, 129.7, 130.1, 130.9, 133.0, 134.1, 134.4, 135.6, 138.0, 141.0, 148.7, 150.4, 160.3, 172.2 ppm. Anal. Calcd for $C_{17}H_{12}N_4O_3$: C, 63.75; H, 3.78; N, 17.49 Found C, 63.68; H, 3.88; N, 17.52.

1-(2-(3-Chlorophenyl)imidazo[4,5-b]indol-4(3H)-yl)ethanone (4n)

Brownsolid, **IR (KBr) υ:** 3367, 3215, 2947, 2923, 1692, 1662 1607, 1580, 1477, 1359, 1272, 1144, 1042, 807, 735, 653, 546 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 1.25 (s, 3H, CH_3), 7.34- 8.11 (m, 8H, aromatic protons), 9.36 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 23.6, 122.5, 124.1, 125.3, 126.6, 130.1, 130.4, 130.7, 132.3, 133.9, 134.6, 135.5, 138.5, 148.1, 148.2, 157.8, 160.9, 166.2 ppm. Anal. Calcd for $C_{17}H_{12}ClN_3O$: C, 65.92; H, 3.90; N, 13.57 Found C, 66.01; H, 3.95; N, 13.47.

1-(2-(4-Chlorophenyl)imidazo[4,5-b]indol-4(3H)-yl)ethanone (4o)

Brownsolid, **IR (KBr) υ:** 3350, 3285, 3011, 2935, 1685, 1654 1611, 1572, 1485, 1455, 1343, 1284, 1132, 1062, 899, 783, 659, 531 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 1.66 (s, 3H, CH_3), 7.35- 8.12 (m, 8H, aromatic protons), 9.37 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 23.5, 123.3, 125.6, 127.2, 128.1, 128.4, 128.7, 129.0, 129.2, 129.5, 133.1, 134.3, 134.6, 134.7, 136.4, 137.0, 142.0, 150.5, 160.2, 160.9 ppm. Anal. Calcd for $C_{17}H_{12}ClN_3O$: C, 65.92; H, 3.90; N, 13.57 Found C, 65.99; H, 3.93; N, 13.54.

4-Ethyl-2-(2-nitrophenyl)-3, 4-dihydroimidazo[4,5-b]indole (4p)

Brownsolid, **IR (KBr) υ:** 3416, 3199, 3012, 2999, 2942, 2872, 1654, 1607, 1561, 1441, 1453 1351, 1283, 1192, 1021, 861, 741, 657, 526 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 1.41-1.45 (t, *J*= 6.6 Hz, 3H, CH_3), 4.38-4.45 (q, *J*=6.9 Hz, 2H, CH_2), 7.53- 8.63 (m, 8H, aromatic protons), 9.63 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 12.5, 24.9, 122.1, 122.8, 123.1, 124.6, 127.5, 127.8, 130.2, 130.4, 130.7, 133.5, 134.4, 137.7, 135.4, 136.4, 137.5, 140.7, 148.3, 149.7, 159.9. ppm. Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29 Found C, 66.74; H, 4.65; N, 18.20.

2-(3-Nitrophenyl)-4-propyl-3, 4-dihydroimidazo[4,5-b]indole (4q)

Brownsolid, **IR (KBr) υ:** 3400, 3301, 3221, 3135, 3009, 2951, 2912, 2865, 1664, 1616, 1571, 1478, 1422, 1371, 1271, 1181, 1037, 873, 739, 649, 536 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$) δ:** 1.05-1.10 (t, *J*= 6.9 Hz, 3H, CH_3), 1.70-1.82 (m, 2H, CH_2), 3.19-3.24 (t, *J*=6.6 Hz, 2H, CH_2), 7.47- 8.41 (m, 8H, aromatic protons), 8.94 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, $CDCl_3$) δ:** 10.1, 21.3, 44.0, 121.5, 124.2, 125.2, 125.5, 125.6, 129.3, 136.1, 136.7, 140.5, 150.9, 159.3 ppm. Anal. Calcd for $C_{18}H_{16}N_4O_2$ C, 67.49; H, 5.03; N, 17.49 Found C, 67.44; H, 5.10; N, 17.52.

Ethyl 2-(2-(2-nitrophenyl)imidazo[4,5-b]indol-4(3H)-yl)acetate (4r)

Brownsolid, **IR (KBr) υ:** 3389, 3255, 3129, 3116, 3027, 2969, 2913, 2847, 1735, 1657, 1618, 1569, 1435, 1353, 1264, 1158, 1049, 854, 751, 651, 546 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 1.22- 1.27 (t, *J*= 7.2 Hz, 3H, CH_3), 4.19- 4.26 (q, *J*=6.9 Hz, 2H, CH_2), 5.32 (s, 2H, CH_2), 7.37- 8.28 (m, 8H, aromatic protons), 9.63 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 15.0, 52.6, 65.1, 122.3, 123.6, 125.2, 127.9, 128.4, 130.5, 134.0, 135.2, 139.0, 148.3, 149.6, 161.7, 171.0 ppm. Anal. Calcd for $C_{19}H_{16}N_4O_4$: C, 62.63; H, 4.43; N, 15.38 Found C, 62.71; H, 4.51; N, 15.30.

7-Methyl-2-phenyl-3,4-dihydroimidazo[4,5-b]indole (4s)

Brownish whitesolid, **IR (KBr) υ:** 3398, 3242, 2963, 2931, 1648, 1607, 1559, 1451, 1311, 1232, 1142, 1027, 813, 741, 655, 534 cm^{-1}. **^{1}H NMR (300 MHz, DMSO) δ:** 2.22 (s, 3H, CH_3), 7.55- 8.57 (m, 8H, aromatic protons), 9.69 (s, 1H, NH), 10.10 (s, 1H, NH) ppm. **^{13}C NMR (75.45 MHz, DMSO) δ:** 23.9, 122.9, 123.1, 127.7, 128.5, 129.6, 130.2, 130.7, 131.3, 133.3, 136.8, 146.3, 154.1, 161.2, ppm. Anal. Calcd for $C_{16}H_{13}N_3$: C, 77.71; H, 5.30; N, 16.99 Found C, 77.64; H, 5.34; N, 17.02.

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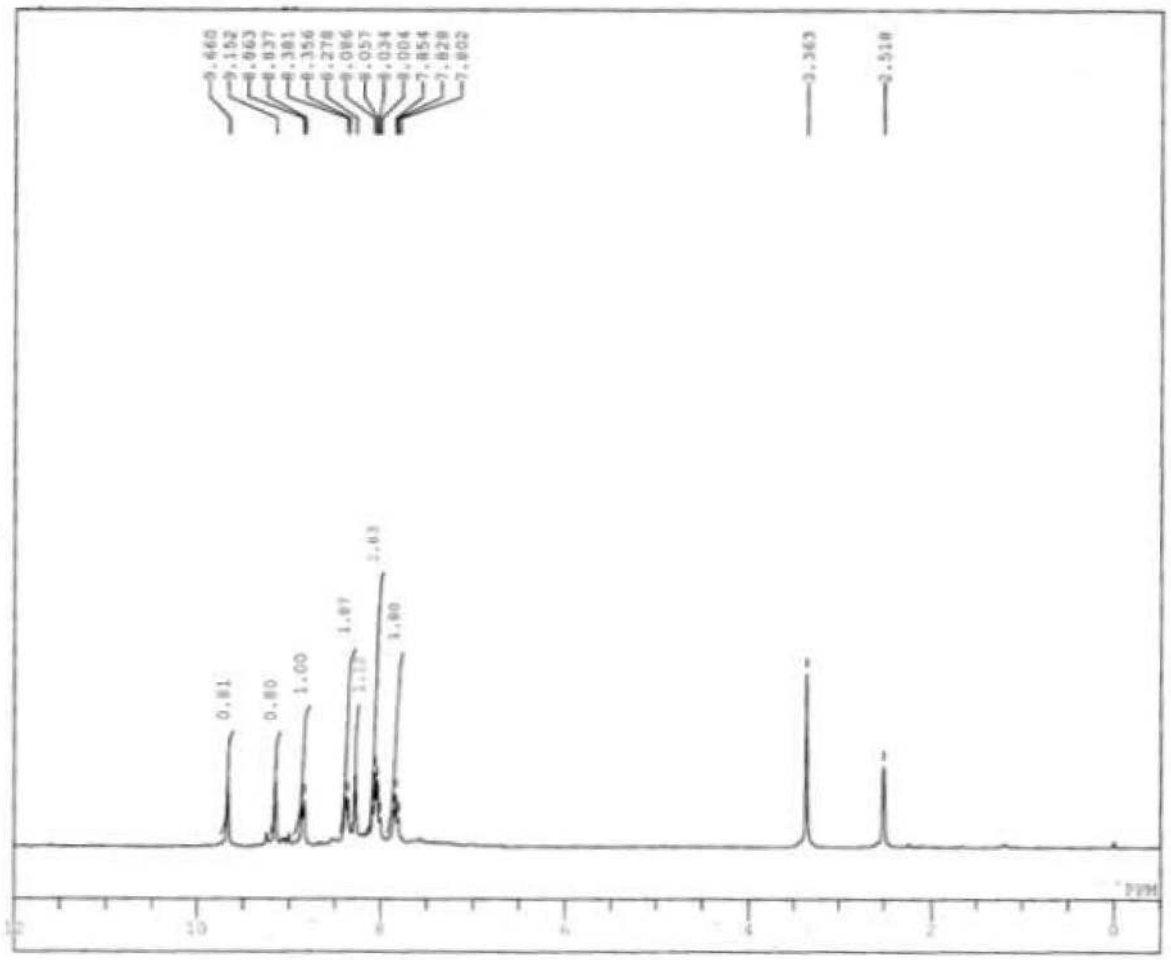
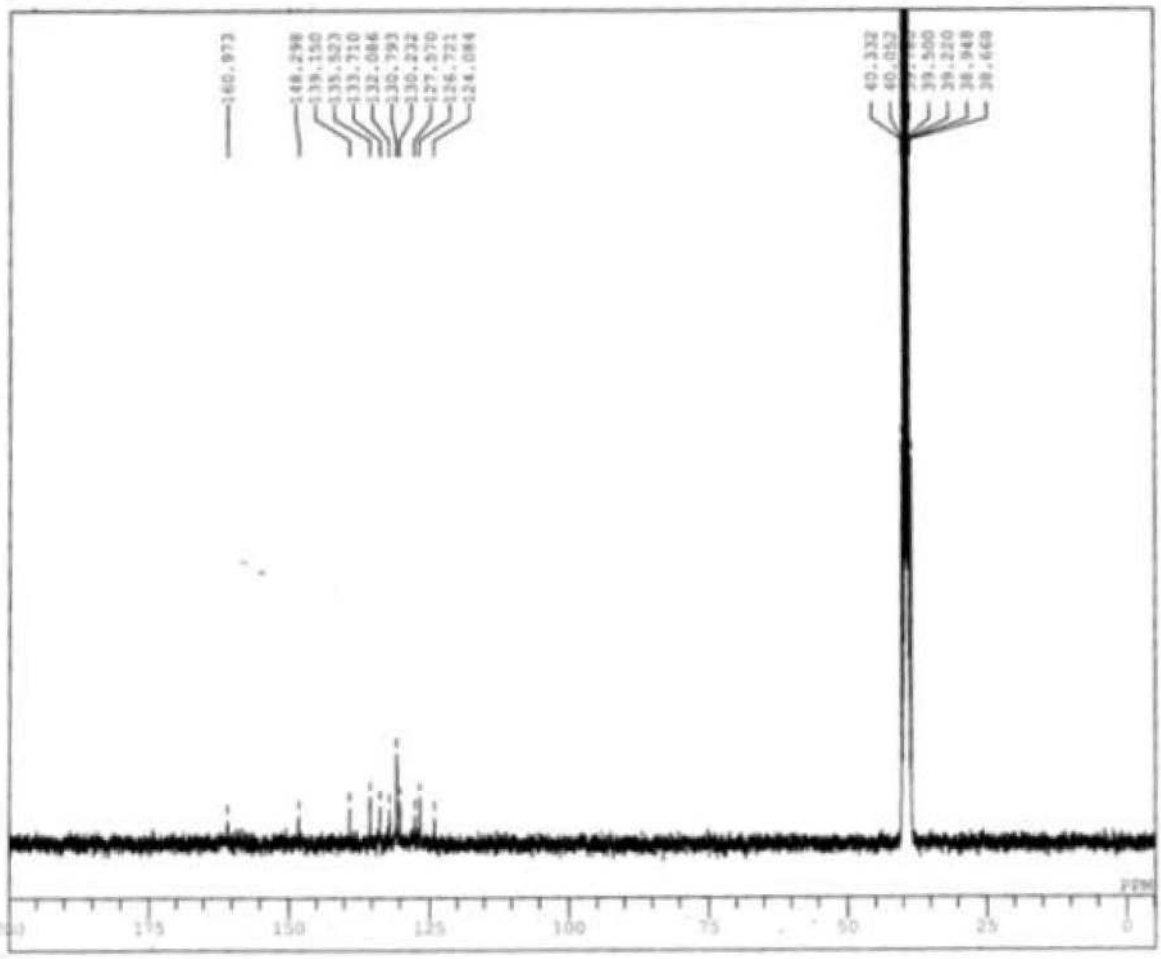
Illustration

NMR spectra of compound **4a**

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135.503
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132.086
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130.232
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124.084
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40.052
39.500
39.220
38.948
38.668
PPM
200
175
150
125
100
75
50
25
0