Green synthesis of Tetra-substituted Imidazoles *via* a MCR Catalyzed by Nanoparticles

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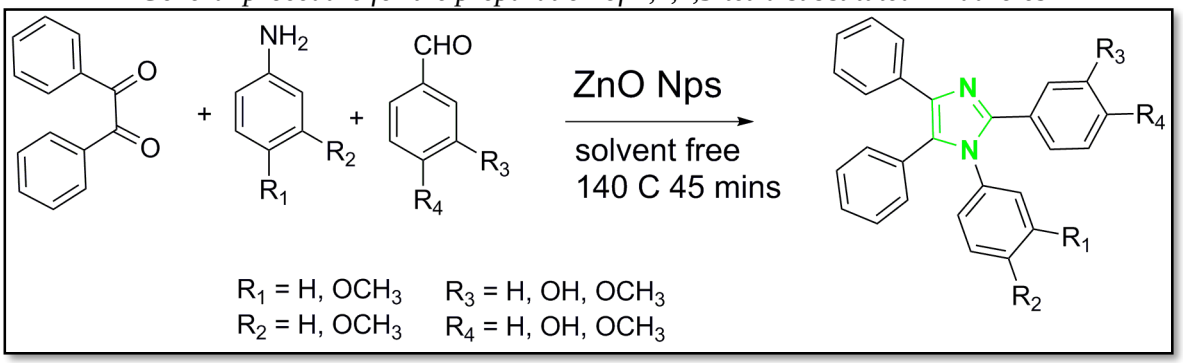
ABSTRACT

Poly substituted Imidazoles are basic units of a number of significant natural products like purine, histamine and nucleic acids. Imidazole and its derivatives improve the pharmacutical role of anti microbial and biologically importance compounds. Synthesis of substituted Imidazoles describes eco-friendly and green procedures were followed to developed derivatives of imidazole. The green catalysts were used in the synthesis have given excellent yields. Spectroscopic technique like HR-MS, ^{1}HNMR, ^{13}CNMR, and FT-IR were used to characterization of synthesized tetra substituted Imidazoles products.

1. INTRODUCTION

Multicomponent reactions (MCRs) forming heterocyclic compounds are powerful tools in the drug-discovery process as they can offer expedient synthesis of libraries of drug like compounds in a single operation. The imidazole ring represents one of the most ubiquitous heterocyclic motifs found in naturally occurring molecules[1-4]. Whereas the unsubstituted parent compound serves as a nucleophilic catalyst or corrosion inhibitor, its derivatives exhibit variable biological activities such as anti-microbial activity. The biological importance of the imidazole moiety has made it a common structure in many drug candidates[5-6]. It stands to reason that simple methods for the formation of imidazoles from readily available materials would be most welcomed by the synthetic community[7-8]. The properties of Nanoparticles depend sensitively on their shape and size. Therefore, the challenges in nanoparticles synthesis are to control not only the crystal size but also the shape and morphology. In order to produce the desired structural materials various method have been developed many methods to developed nanocalalyst of all the methodologies developed organic reactions, the green synthesis method offers an alternative simple one spot in organic solvent free reactions[9-12].

General procedure for the preparation of 1,2,4,5-tetra substituted imidazoles



2. EXPERIMENTAL SECTION

The ^{1}H NMR and ^{13}C NMR spectra were recorded with Bruker 400 MHz spectrometer instruments in $CDCl_3$ solvent. The chemical shifts (δ) were measured in ppm and with the solvents as references (For $CDCl_3$, ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.0 ppm). The multiplicities of the signals are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets. All solvents were obtained from commercial sources and were purified according to standard procedures. Column chromatography was performed on silica gel (100-200 or 200-300 mesh) using petroleum ether and ethyl acetate as eluent. Thin layer chromatography (TLC) was performed on Merck silica gel plates and visualized by UV-light (254 nm). Melting points were uncorrected.

2.2 General procedure for the synthesis of 1, 2, 4, 5-tetrasubstituted imidazoles

Diketone (Benzil-0.50 mmol), aldehydes (vallin-0.50 mmol), amines (Anisole-0.50 mmol), catalyst (100 mg) and ammonium acetate (0.75 mmol), were dissolved in ethanol (5 mL) and the mixture was heated to 120-140 °C for 45 mins. The progress of the reaction was followed by TLC. After completion of the reaction, the mixture was cooled to room temperature, dissolved in ethanol and filtered to separation of the catalyst. By addition of water to the concentrated filtrate, the solid product appeared. The product was re-crystallized in hot ethanol. All products are known and were identified by comparison of their physical and spectral data with those of authentic samples.

Table 1. Effect of catalyst on the one-spot four component synthesis of tetra substituted imidazole with the usual reactants and NH_4OAc.

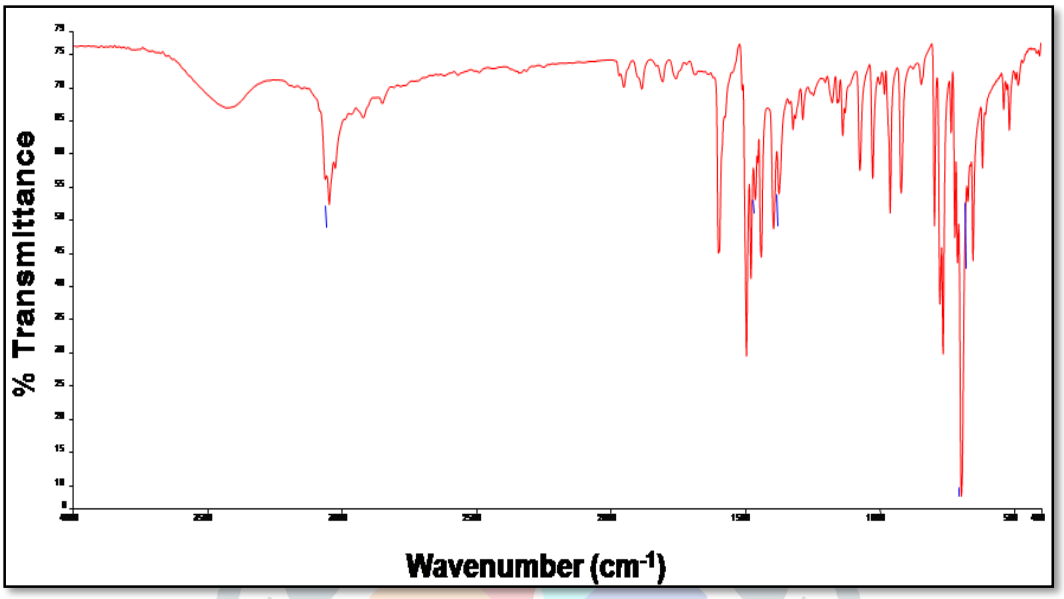
S.No	Catalyst	Temp	Time (mins)	Yield
1	$MgAl_2O_4$	140	90	70-75
2	TiO_2 Nps	140	45	75-85
3	Iodine	140	120	60-75
4	SnO_2 Nps	140	60	70-80
5	ZnO Nps	140	30	80-95
6	No catalyst	140	180	10-15

3. RESULTS AND DISCUSSION

Nano Zinc oxide (nano-ZnO), as an efficient catalyst, was prepared via pecepitapation decompostation method a reaction of nano ZnO. The dimensions of nanoparticles were observed with SEM. The particle sizes of the commercial and synthesized nano-ZnO were about 45 and 80 nm, respectively reported [8-9]. Careful literature analyses revealed that a variety of Nanoparticles catalyst have been used for this multicomponent reaction (table 1). It has been reported that many nano particles acts as a mild, useful, non-toxic and inexpensive catalyst which makes the process convenient, more economic and environmentally benign. The mild reaction conditions, operational simplicity and the excellent yields make the catalyst more versatile. The reaction is rapid, facile, and efficient and is devoid of unnecessary derivatization and generation of hazardous substance. Knowing the importance of Nanoparticles we used it as a catalyst for these multicomponent reactions. We were please to know that high yield product was obtained on using only 5 mol% of Nanoparticles. A wide range of substituted aromatic aldehydes underwent multicomponent condensation with benzil and ammonium acetate to give high yield poly-substituted Imidazole[10-11]. We also tried aqueous ethanol and some other catalysts as solvent but the results were not satisfactory. All the utilized functionalities were found to be compatible under the reaction conditions (table 1and table 2).

Table 2. One-spot four component synthesis of tetra substituted imidazole with the usual reactants substituted aldehyde and substituted amines

S.No	R_1	R_2	R_3	R_4	Yield
1	*H*	*H*	*H*	*H*	90
2	OCH_3	*H*	OCH_3	*OH*	87
3	*H*	OCH_3	OCH_3	*OH*	89
4	OCH_3	*H*	*OH*	OCH_3	84
5	*H*	OCH_3	*OH*	OCH_3	87



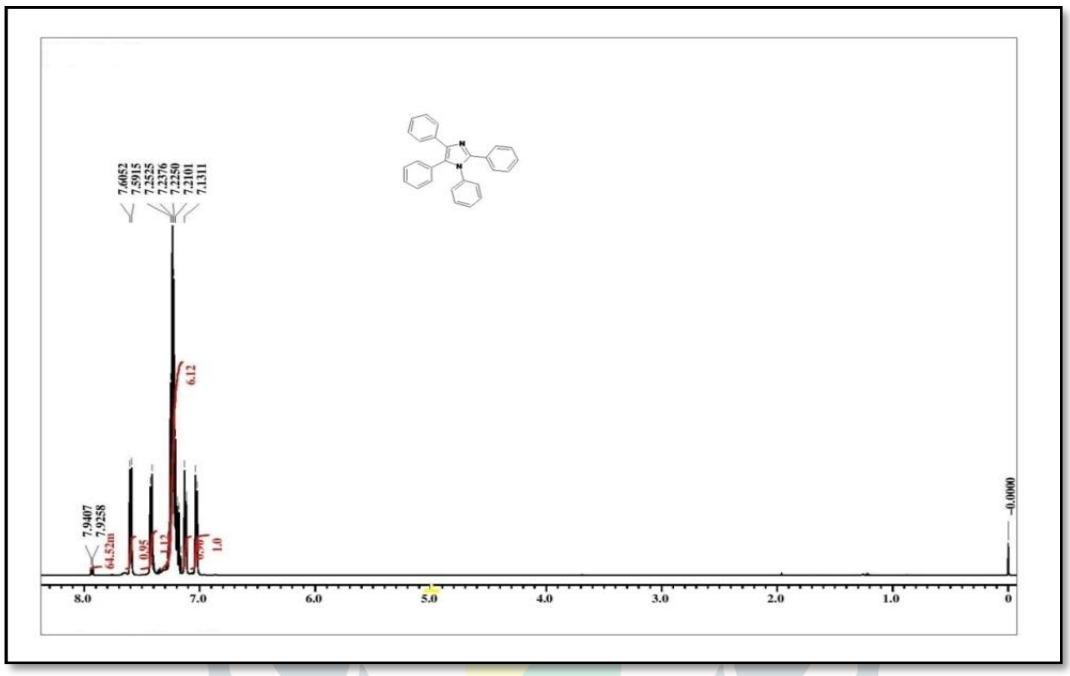
FTIR spectra of 1,2,4,5-Tetraphenylimidazole

Spectroscopic Data of the Synthesized Compounds:

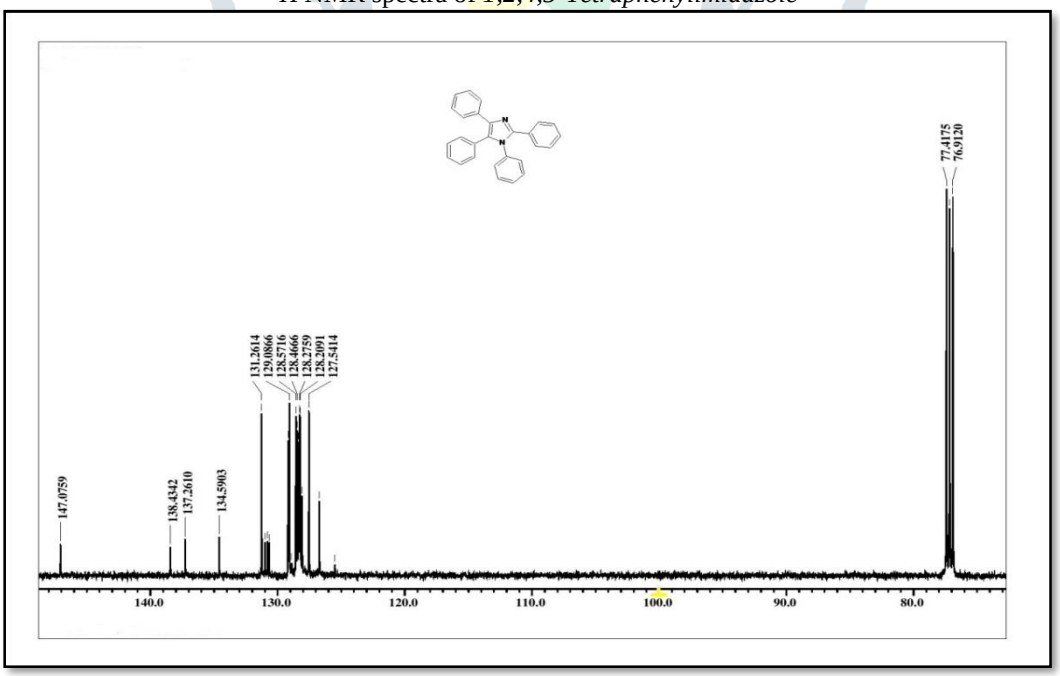
Compound 1:*1,2,4,5-Tetraphenylimidazole*: M.P: 117°C; IR (cm^{-1}, KBr): 3008, 1621, 1521, 1421; ^1H NMR ($CDCl_3$) δ = 7.10–8.45 (m, 20H) ppm; ^{13}C NMR ($CDCl_3$) δ = 123.2, 124.5, 125.1, 126.0, 127.4, 128.7,128.8, 129.2, 129.5, 129.9, 136.9 ppm; HR-MS Calcd. (Found) for 372.46 (372.16).

Compound 2:1-(3-Methoxyphenyl)- 2-(3-Methoxy-4-hydroxyphenyl)-4,5-triphenyl-1H-imidazole colourless crystal; IR (KBr) : 3058,1613, 1512,1069 cm^{-1} ^1H NMR (400 MHz, DMSO-d_6): δH 3.24 (s, 3H, CH_3), 3.42 (s, 3H, CH_3), 6.83 (d, 2H, H-Ar), 7.23–7.41 (m, 13H, H-Ar), 7.47 (d 2H, H-Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δC 55.57, 56.06, 114.07, 123.30,126.83, 128.60, 128.77, 128.89, 129.12, 129.16, 129.24, 130.12, 131.10, 131.29, 131.59, 135.0, 137.07, 137.27, 146.49, 160.0 ppm; HR-MS M/z Calcd. (Found) for 448.522 (448.182).

Compound 3:1-(4-Methoxyphenyl)- 2-(3-Methoxy-4-hydroxyphenyl) 1,4,5-triphenyl-1H-imidazole colourless crystal; IR (KBr) mmax: 3054,1621, 1508,1069, cm^{-1} ^{1}H NMR (400 MHz, DMSO-d6): dH 3.24 (s, 3H, CH3), 3.41 (s, 3H, CH_3), 6.83 (d, J = 2H, H-Ar), 7.23–7.41 (m, 13H, H-Ar), 7.47 (d, 2H, H-Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δC 55.57, 56.13, 114.17, 123.30, 126.85, 128.60, 128.79, 128.89, 129.15, 129.16, 129.26, 130.12, 131.17, 131.29, 131.56, 135.07, 137.07, 137.24, 146.49, 160.4 ppm; HR-MS M/z Calcd. (Found) for 448.522 (448.182).

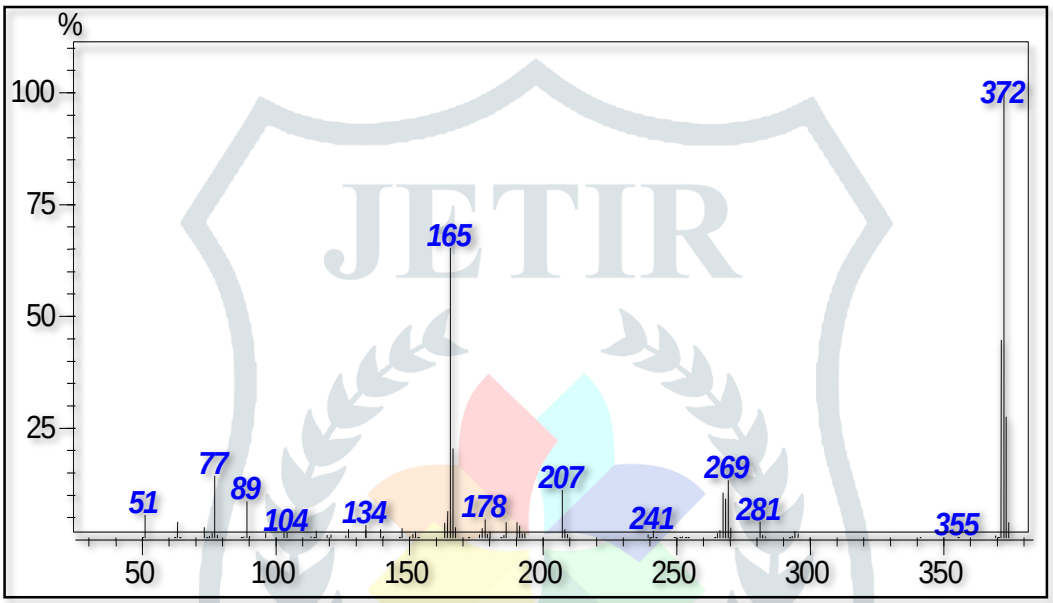


^{1}H NMR spectra of *1,2,4,5-Tetraphenylimidazole*



^{13}C NMR spectra of *1,2,4,5-Tetraphenylimidazole*

Compound 4:1-(3-Methoxyphenyl)-2-(3-hydroxy-4-Methoxy-phenyl) 1,4,5-triphenyl-1H-imidazole colourless crystal; IR (KBr) max: 3059,1611, 1516,1062 cm^{-1} ^{1}H NMR (400 MHz, DMSO-d6): δH 3.84 (s, 3H, CH_3), dH 3.87 (s, 3H, CH_3), 6.83 (d, 2H, H-Ar), 7.23–7.41 (m, 13H, H-Ar), 7.47 (d, 2H, H-Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δC 55.57, 56.13, 114.07, 123.30, 126.83, 128.60, 128.77, 128.89, 129.12, 29.16, 129.24, 130.12, 131.10, 131.29, 131.59, 135.0, 137.07, 147.24, 146.49, 160.0 ppm; HR-MS M/z Calcd. (Found) for 448.522 (448.182).



HR-MS of *1,2,4,5-Tetraphenylimidazole*

Compound 5:1-(4-Methoxyphenyl)-2-(3-hydroxy-4-Methoxy-phenyl) 1,4,5-triphenyl-1H-imidazole colourless crystal; IR (KBr) mmax: 3051,1604, 1512,1061, cm^{-1} ^{1}H NMR (400 MHz, DMSO-d6): dH 3.84 (s, 3H, CH_3), dH 3.87 (s, 3H, CH_3), 6.83 (d, 2H, H-Ar), 7.23–7.41 (m, 13H, H-Ar), 7.47 (d, 2H, H-Ar) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δC 55.54, 56.13, 114.02, 123.33, 126.83, 128.66, 128.77, 128.86, 129.12, 129.18, 129.24, 130.13, 131.10, 131.28, 131.59, 135.10, 137.09, 147.25, 146.47, 160.10 ppm; HR-MS M/z Calcd. (Found) for 448.522 (448.182).

4. CONCLUSION

Imidazoles enjoy an outstanding status due to their biological importance. nanoparticles, a non toxic and inexpensive catalyst is optimized for the synthesis of tetra- substituted imidazoles. Existing synthetic approaches are currently somewhat limited by issues of poor yields, harsh reaction conditions, expensive

catalysts etc. we have demonstrated one-spot, four-component synthesis of 1,2,4,5-tetra substituted imidazoles. Present ZnO Nps efficient solid catalyst in good to excellent yields under solvent free conditions. Environmentally friendly conditions, very good yields, and simple workup procedure. This catalyst was found to be reusable.

5. REFERENCES:

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