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A facile and greener way of glycine catalyzed novel synthesis of triaryl imidazoles: Synthesis and characterization

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ABSTRACT

The facile and greener way to synthesis triaryl imidazole was discussed. The glycine has been selected as a catalyst. The chemical structures of these compounds were identified by UV, FT-IR, ^{1}H NMR and Mass spectral techniques. The progress of the reaction time, purity was checked by TLC and separated by column chromatography. All spectral techniques are well supported the formation of the compound.

Key words: Imidazole, spectral studies, TLC, Column chromatography, green synthesis.

INTRODUCTION

Developing cleaner, safer and environmentally friendly chemical processes are an important goal for chemists in both academia and industry [1]. It is no longer acceptable to make products without being concerned about environmental pollution. Several strategies have been developed based on the idea to produce the compound. To remove organic solvents from chemical processes, many old reactions have been revised and carried out in water [2], under solvent less conditions [3], in supercritical fluids [4], in ionic liquids [5], in micro emulsions [6], under high pressure [7], and by ultrasound [8] and microwaves [9]. One-pot multicomponent processes and one-pot consecutive processes have been discovered that allow compounds to be prepared without having to isolate and purify the intermediates. Imidazoles play an important role in life process and many imidazole derivatives are known to form part of vitamins, enzymes and many pharmacologically important drugs. Imidazole derivatives are probably the most well-known heterocycle, which is common and important feature of a variety of natural products and medicinal agents. Derivatives of imidazole were reported for anti-inflammatory [10-14], analgesic [15], anticonvulsant [16,17] tuberculostatic [18], antimicrobial [19] and anticancer [20] activities. Many triaryl imidazole(s) have been tested as effective inhibitors of P38 MAP kinase and B-Raf kinase plant growth regulators, glucagon receptor antagonists [21]. In addition, triarly imidazole is also used in photography as photo sensitive compounds [22]. The classical synthesis of triaryl imidazole involves multi component condensation of 1,2-di ketone, α-hydroxy ketone or ketoxime with and aldehyde and ammonia (or its salt)under pressure [23]. Review of literature has revealed a variety of catalyst used in these reactions, ex. ionic liquids [24], silica supported sulphuric acid [25], acetic acid[26], iodine [27], p-toluene sulfonic acid [28] etc., However, there was not much report observed in amino acid catalyzed reactions [24,25]. Based on the careful analysis of literature, the scope of the present investigation involves the glycine catalyzed reaction for the synthesis of triaryl substituted imidazole as starting material for the development of water soluble imidazole containing the antimicrobial polymers. On the outset the first stage have been synthesized and characterized.

MATERIALS AND METHODS

The chemicals benzil **(1),** ammonium acetate **(2),** Salicylaldehyde**(3)**, para-Chlorobenzaldehyde **(4)**, para-Methoxybenzaldehyde **(5)**, and glycine were commercially available from Merck and Avra chemicals, Hyderabad and were used as such. Siliga gel (TLC and Column grade) were purchased from Merck. The solvents were purified as per the standard procedure reported elsewhere. ^{1}H NMR (300 MHz) spectra were recorded on a Bruker Advance III 300 MHz multi nuclei solution NMR. FTIR spectra (KBr pellets) were measured on the Alpha Bruker FTIR instrument scanning the entire region of 4000 - 400 cm^{-1} with typical resolution of 1.0 cm^{-1}. UV spectra were also recorder using Alpha Bruker UV spectrophotometer. Melting point was determined using an X-5A melting point measurement instrument. Mass spectroscopy was recorded on ES-FIGIEAN ionization mass spectrometer.

Preparation of 2-(2-Hydroxyphenyl)-4,5-diphenyl-1H-imidazole (6)
A mixture of benzil (0.525g; 2.5mmol), Salicylaldehyde (0.3053g;2.5mmol), ammonium acetate (0.5g;6mmol) and amino acid (0.05g) was stirred in ethanol (10ml) for 48 hours at room temperature. The completion of the reaction was monitored by TLC. Ensuring the completion of reaction, the reaction mixture was poured into crush ice: cold ethanol mixture (1:1) and filtered to afford 2-(2-Hydroxyphenyl)-4,5-diphenyl-1H-imidazole. (Pale yellow precipitate).

Preparation of 2-(4-Chlorophenyl)-4,5-diphenyl-1H-imidazole (7)
A mixture of benzil (0.525g; 2.5 mmol), para-Chlorobenzaldehyde (0.35g; 2.5 mmol), ammonium acetate (0.5g;6mmol) and amino acid (0.05g) was stirred in ethanol (10ml) for 48 hours at room temperature. The completion of the reaction was monitored by TLC. Ensuring the completion of reaction, the reaction mixture was poured into crush ice: cold ethanol mixture (1:1) and filtered to afford 2-(4-Chlorophenyl) -4,5-diphenyl -1H – imidazole (pale yellow precipitate).

Preparation of 2-(4-methoxyphenyl) 4,5-diphenyl-1H-imidazole (8)
A mixture of benzil (0.525g; 2.5mmol), para methoxybenzaldehyde (0.340g; 2.5 mmol), ammonium acetate (0.5g;6 mmol) and amino acid (0.05g) was stirred in ethanol (10ml) for 48 hours at room temperature. The completion of the reaction was monitored by TLC. Ensuring the completion of reaction, the reaction mixture was poured into crush ice: cold ethanol mixture (1:1) and filtered to get 2-(4-methoxyphenyl) 4,5-diphenyl-1H-imidazole (pale yellow precipitate).

RESULTS AND DISCUSSION

The condensation of equimolar mixture of benzil and substituted benzaldehyde along with ammonium acetate were carried out at 80^0C in the presence of glycine as catalyst for ten minutes to get triaryl substituted imidazole(s). Based on the careful analysis of the literature and comparison of the results for the synthesis of triaryl substituted imidazole(s) as a model reaction with other catalyst **(29 – 48)** have been listed in the Table .1 One of the major advantages of using amino acid as catalyst for the isolation and ease of purification of the desired product. The amino acids are usually soluble in water and are eliminated during work-up and purification. The reactions were also carried out without the catalyst at solvent free conditions and room temperature for 48 hours, which lead to very poor yield (10-12 %) of the product. The reactions were also carried out at higher temperature in the absence of catalyst to enhance yield of the product perhaps no appreciable increments in the yield. Hence, the present investigation was very much clear enough that the presence of the catalytic amount of glycine under solvent free condition resulted excellent yield.

Preparation of 2-(2-Hydroxyphenyl)-4,5-diphenyl-1H-imidazole(6)
UV (λmax: nm) : 249, 360
FTIR (cm^{-1}) : Aromatic (3061),N-H(3316)
^{1}H NMR (ppm) : NH-proton(13.0),) Aromatic 6.7-8.3 (m,15H),
Mass (m/z) : Calculated M.W 312.75, Observed M.W 313.0

Preparation of 2-(4-Chlorophenyl)-4,5-diphenyl-1H-imidazole(7)
UV (λmax: nm) : 257.0
FTIR (cm^{-1}) : Aromatic (3060, 3028),N-H (3318).
^{1}H NMR (ppm) : NH-proton-(s,14.4),Aromatic 6.6-7.9 (m,15H).

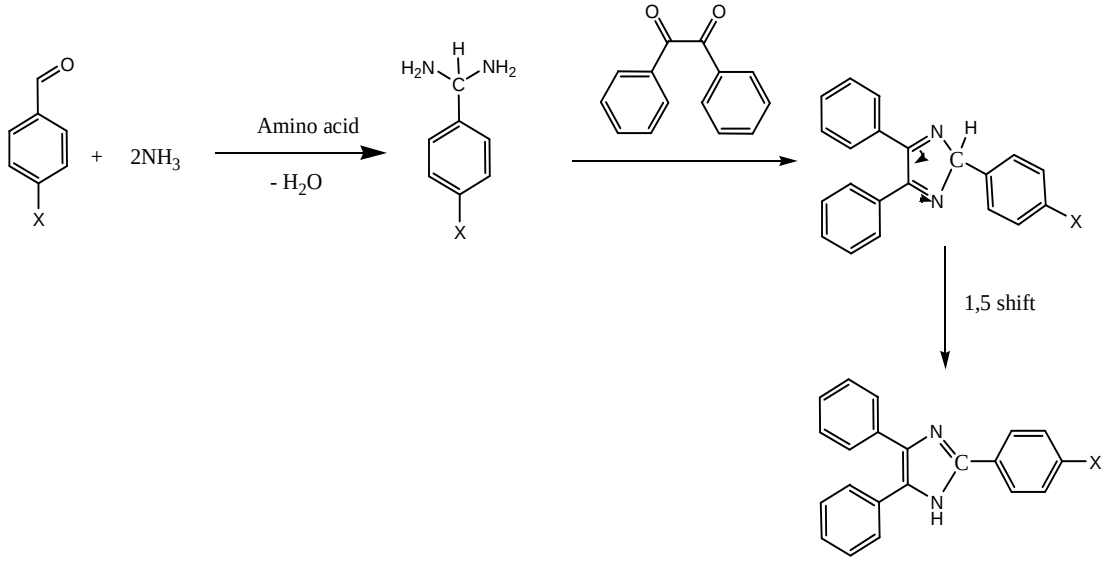
Mass (m/z) : Calculated M.W 330.827, Observed M.W 330.9

Preparation of 2-(4-methoxyphenyl) 4,5-diphenyl-1H-imidazole (8)
UV (λmax: nm) : 257
FTIR (cm^{-1}) : Aromatic (3060, 3002, 2956) , N-H (3316)
^{1}H NMR (ppm) : NH-proton(s,13.9), Aromatic Proton (m,15H)
Mass (m/z) : Calculated M.W 326.402, Observed M.W 327.0

Figure (1-3) reveals the UV absorption spectra of 2,4,5 tirphenyl-1-H-imidazole using compound **3, 4** and **5** with compound **1** in the presence of neutral amino acids viz., glycine catalyst cyclization reaction shown in the scheme 1. FTIR provides a preliminary idea in confirmation the formation of product. According to the FTIR, represented in Figure (4-6), absence of peak at 1730 cm^{-1} clearly generates the utilization of starting materials transforms into the product. Further the corresponding peaks at 3314, 3318 and 3316 cm^{-1} for N-H stretching in respect of compound **6,7** and **8** respectively. All such stretching and bending peaks have also been supported for the formation of the product. The concern mass of compound **6, 7, 8** are in good agreement with the observed (313, 330.9, 327.0 m/z) and calculated values (312.75, 330.75, 326.42 m/z) respectively were shown in Figure (7-9). Similarly, proton NMR strongly empowered for the formation of the product by its δ value at 13.0, 14.4 and 13.9 ppm corresponding to the N-H protons of compound 6, 7 and 8 respectively were mentioned in Figure (10-12).

Table 1 Comparison of the results for the synthesis of 2,4,5-triphenyl imidazoles as model reaction with other catalysts

Catalyst	Mol(%)	Solvent/Tem. (°C)	Time(min)/ Yield(%)	[Refs]
Without Glycine	-	Ethanol/RT	48/20	Our work
Glycine	3.5.5	Ethanol/80	10/98	Our work
$SbCl_3$	5	Solvent free/120	30/96	[29]
$SnCl_2\,2H_2O$	20	Solvent free/140	50/96	[29]
I_2	10	Solvent free/100	60/85	[30]
$[(CH_2)_4SO_3HMIM][HSO_4]$	15	Solvent free/140	120/90	[31]
TFA	20	Solvent free, MW(150W)	4/92	[32]
$K_5CoW_{12}O_{40}.3H_2O$	10	Solvent free/140	120/90	[33]
SiO_2	2	Solvent free, MW	8/87	[34]
SiO_2	0.1	CH_2Cl_2,Solar heat	120/80	[35]
$AlPO_4$	1	Solvent free/140	120/85	[36]
$BF_3.SiO_2$	21	Solvent free/140	120/80	[37]
L- Proline	15	MeOH/60	510/86	[38]
$InCl_3.3H_2O$	10	MeOH/RT	444/79	[39]
$ZrCl_4$	20	CH_3CN/RT	60/86	[40]



Scheme 1. Glycine catalysed synthesis of 2,4,5-triphenyl-1H-imidazole (General mechanism)

General Mechanism:

Substituted benzaldehyde on treatment with two moles of ammonia (obtained from heating of ammonium acetate) in the presence of glycine as a green catalyst to get sp^3 hybridized diamine. Which on further treatment with benzil on continuous refluxing undergoes 1,5 shift followed by cyclization resulted triaryl substituted imidazole(s).

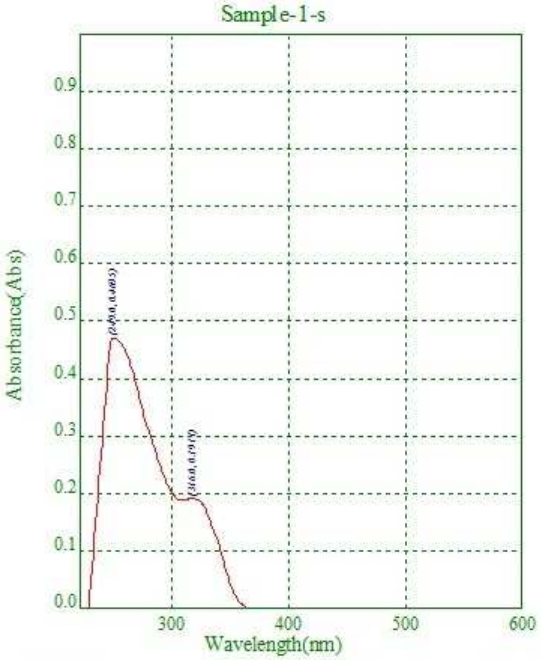


Fig.1 uv spectrum of 2-(2-hydroxyphenyl) -4,5-diphenyl-1H-imidazole

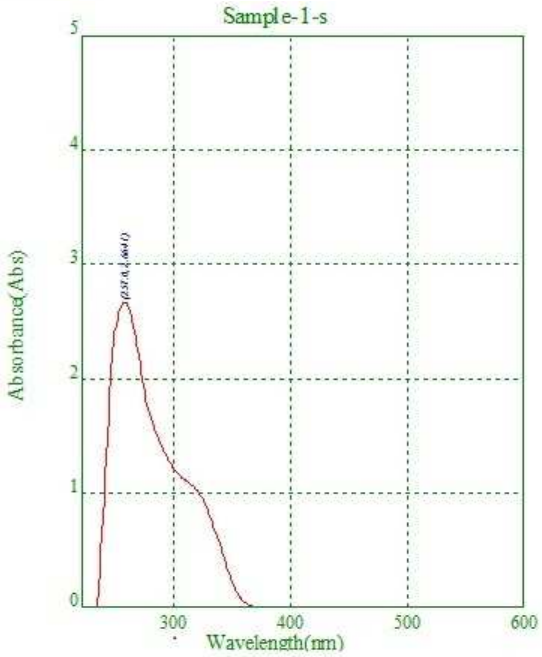


Fig.2 UV of spectrum of 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole

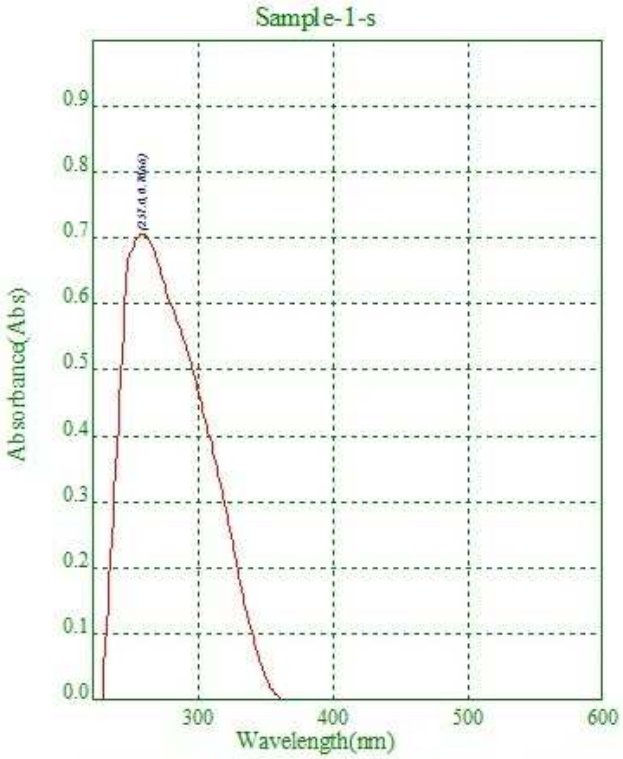


Fig.3 UV spectrum of 2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole

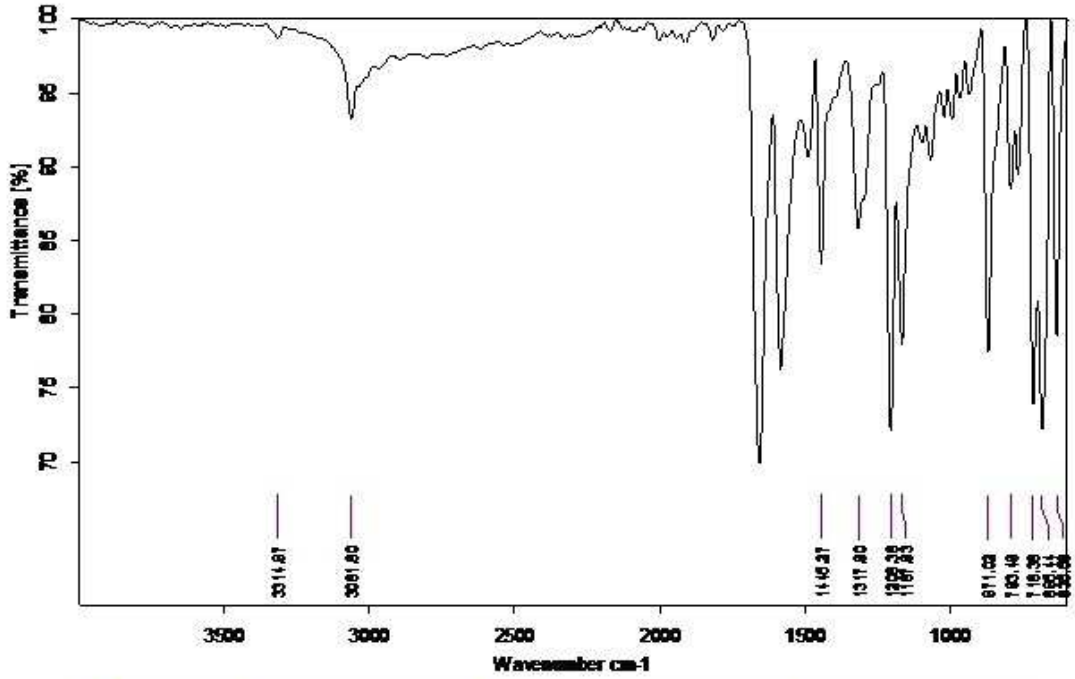


Fig.4 FTIR spectrum of 2-(2-hydroxyphenyl)-4,5-diphenyl-1H-imidazole

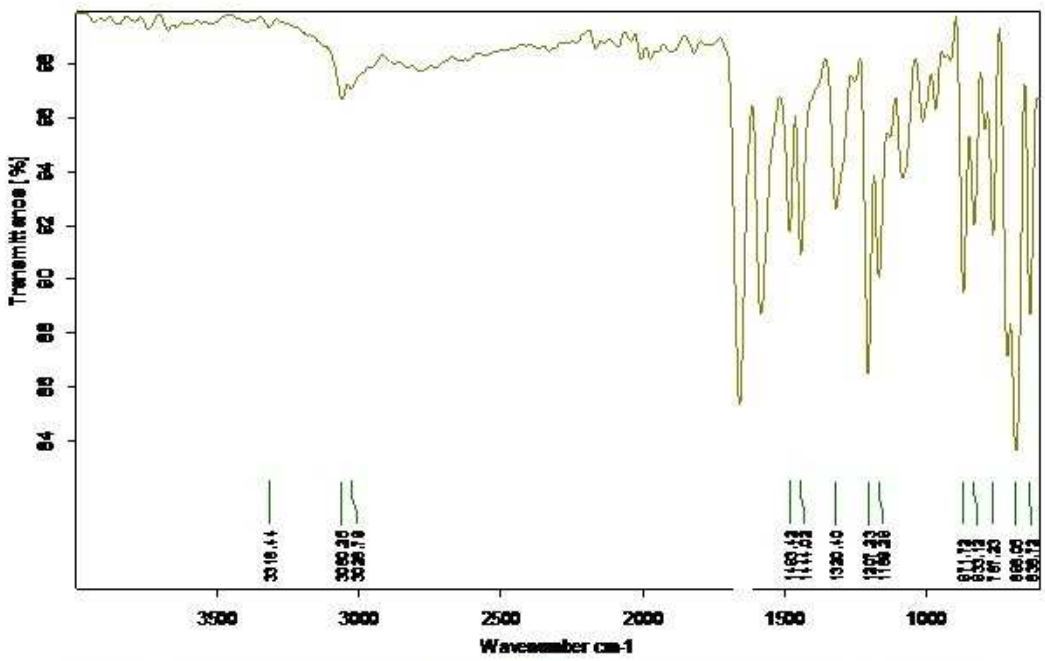


Fig.5 FTIR spectrum of 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole

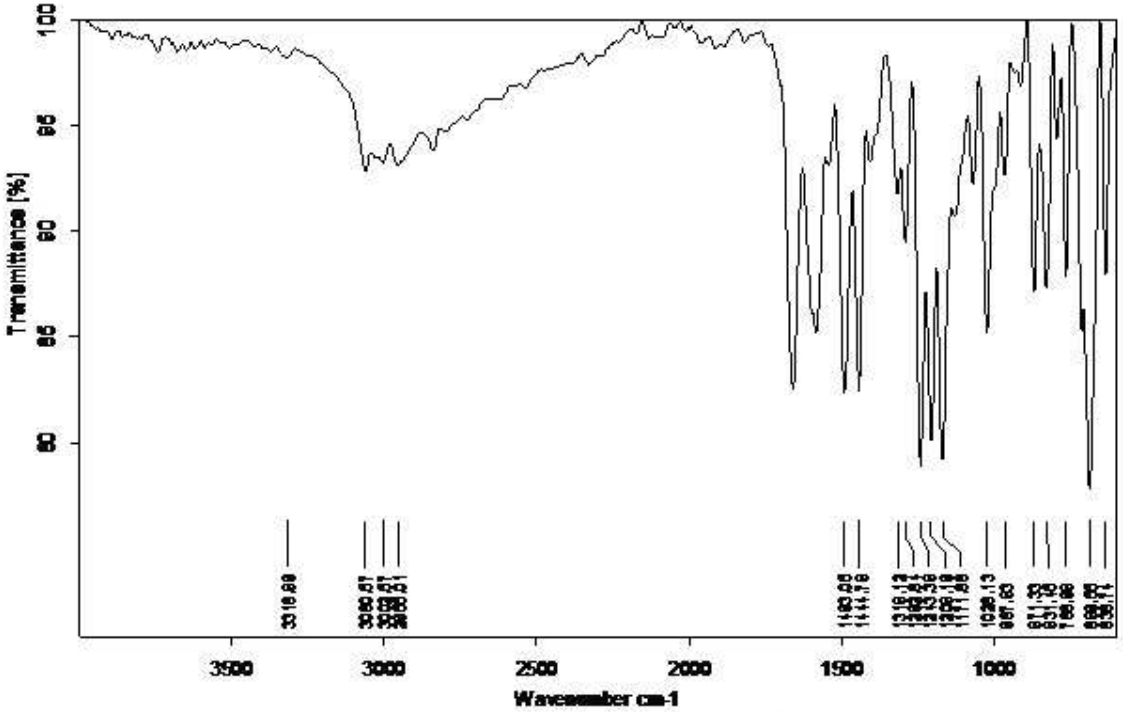


Fig.6 FTIR spectrum of 2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole

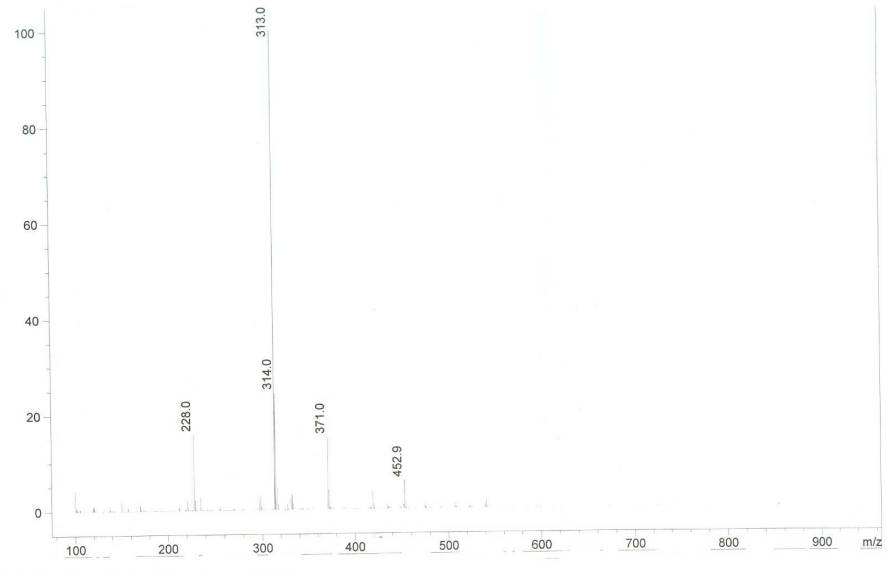


Fig.7 MASS spectrum of 2-(2-hydroxyphenyl) -4,5-diphenyl-1H-imidazole

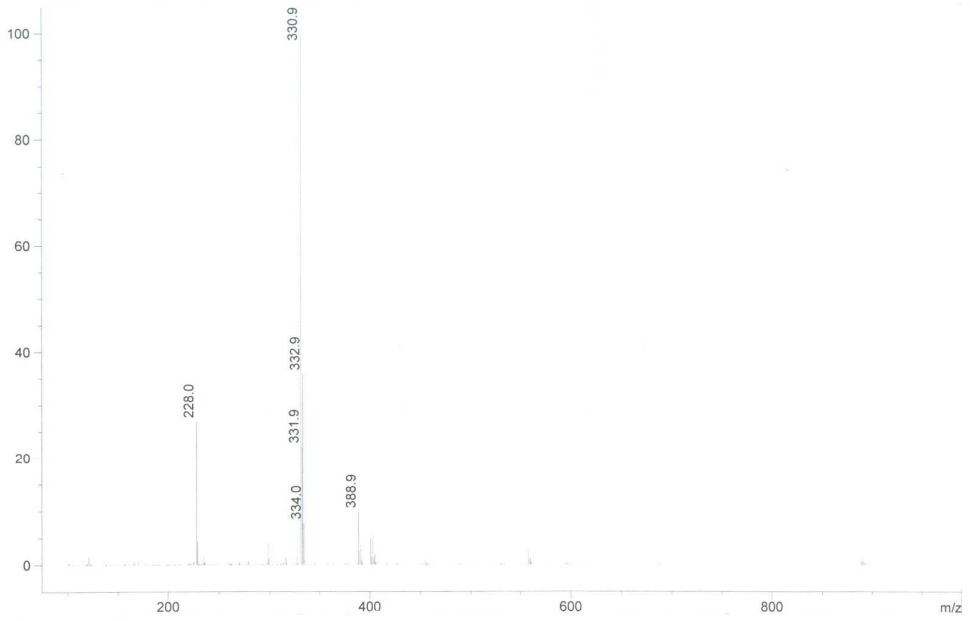


Fig.8 MASS spectrum of 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole

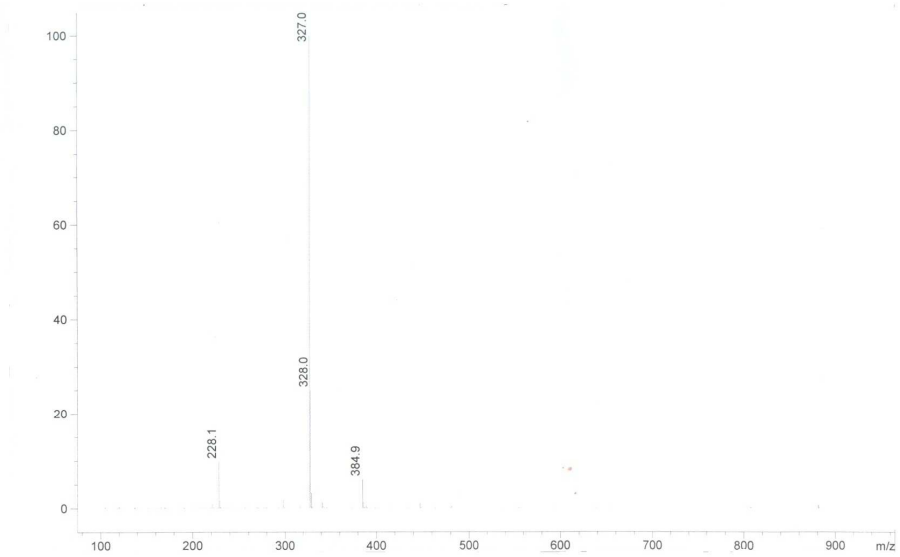


Fig.9 MASS spectrum of 2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole

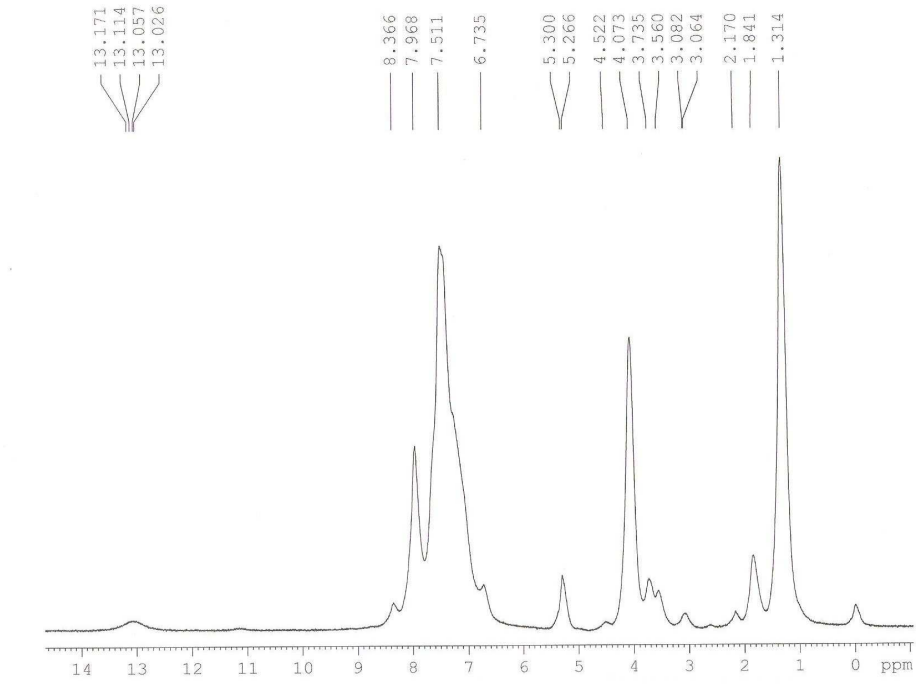


Fig. 10 [1]HNMR spectrum of 2-(2-hydroxyphenyl)-4,5-diphenyl-imidazole

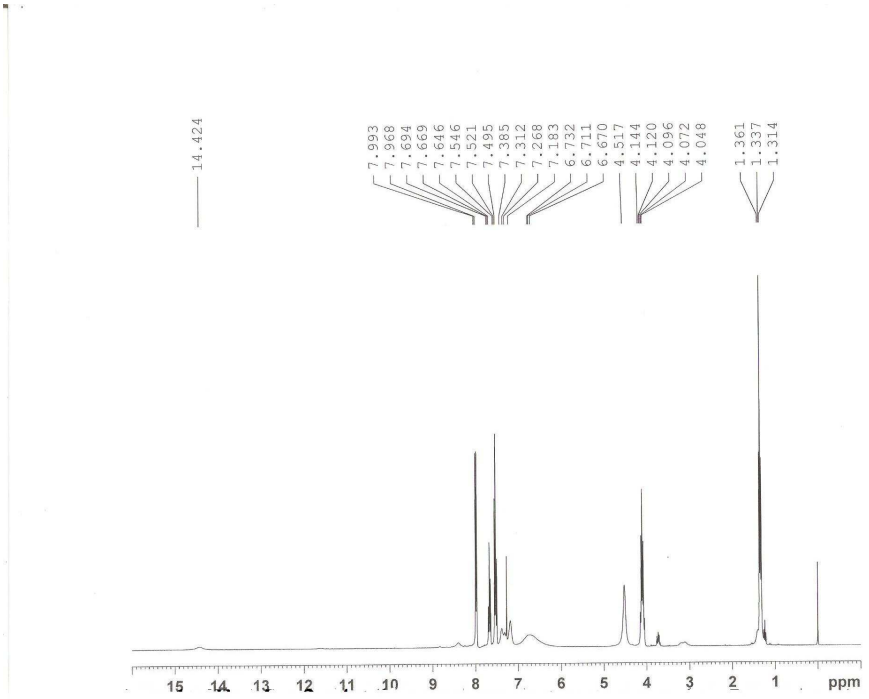


Fig. 11 [1]HNMR spectrum of 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole

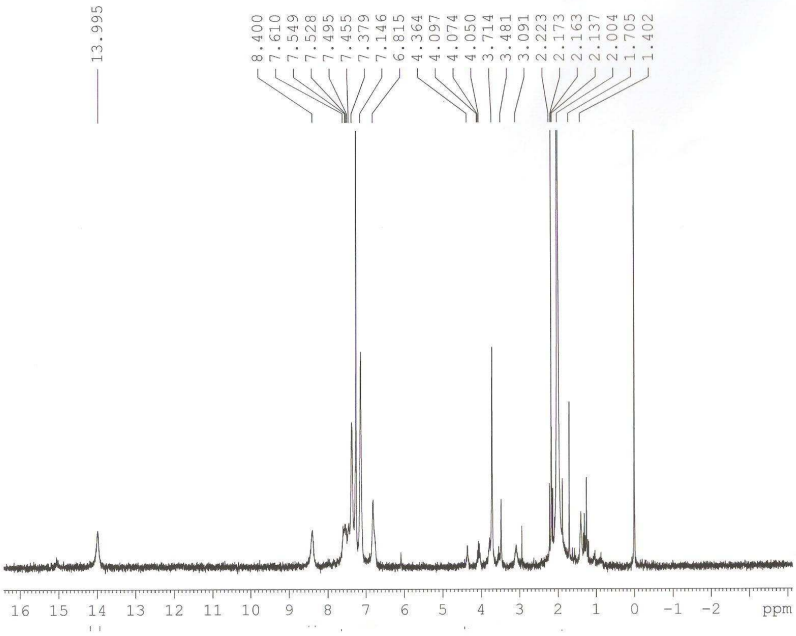


Fig. 12 [1]HNMR spectrum of 2-(4-methoxylphenyl)-4,5-diphenyl-1H-imidazole

CONCLUSION

In the present work, three aromatic aldehyde were used to check the practicability of amino acid catalysis especially neutral amino acid glycine in the reaction and characterized preliminary using FTIR. The required stretching and bending peaks have been suggested for the formation of the products. All other spectral techniques viz., UV, ^{1}H NMR and Mass are well supported the formation of the target compound. The general mechanism for the formation of the product has also been recommended. The yields in many cases were comparable and these catalysts may be extended for using various other di ketones and aldehydes in mere future. Further, the work may be recommended for the water soluble functional polymers.

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