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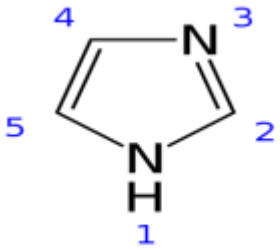
Synthesis of 2, 4, 5- Triarylimidazol by using catalysts under mild conditions

Elaf Hadi Mahdi

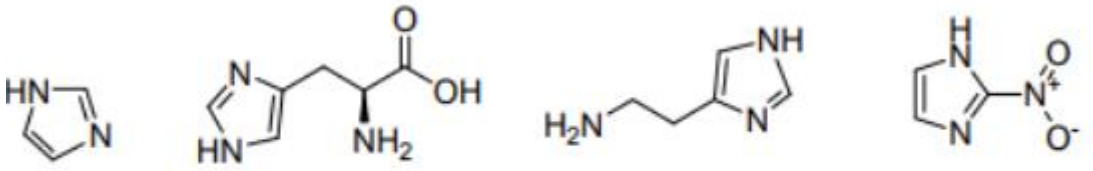
Abstract: This research involves the synthesis of compounds (1-7) of 2,4,5-triarylimidazol by using catalysts under mild conditions. Benzil was reacted with various aromatic aldehyde and ammonium acetate in ethanol in the presence of concentrated sulfuric acid and 8-hydroxy-7-iodoquinoline-5-sulfonic acid (HISA) as catalysts to yield 2,4,5-triarylimidazole derivatives. Among the two catalysts, HISA is an excellent catalyst in the reaction. The reaction conditions are mild and work-up method is simple as well as high yields. The prepared compounds were verified by melting points and were uncorrected and FT-IR spectra.

Introduction

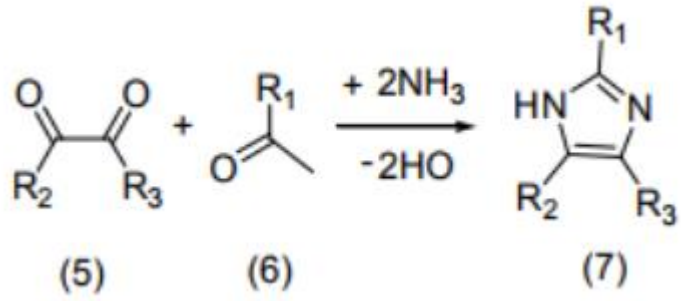
Imidazol is an organic compound with the formula C3H4N2



This aromatic heterocyclic 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) [1-5].



Imidazol was first synthesized by Heinrich Debus in 1858, but various imidazole derivatives (7) had been discovered as early as the 1840s, as shown below, used glyoxal (5) and formaldehyde (6) in ammonia to form imidazole [6]. This synthesis, while producing relatively low yields, is still used for creating C-substituted imidazoles.



Synthesis various types of 2-imidazolines are biologically and pharmaceutically very important, since many imidazoline derivatives possess antidiabetic, antihypertensive, and anti-inflammatory activity. Apart of its use for pharmaceutical purpose it also has variety of applications in industries. One of the applications of imidazole is in the purification of His tagged proteins in immobilized metal affinity chromatography (IMAC). Moreover 2-substituted imidazolines are synthetically important due to their use as a synthetic intermediates [7], catalysts [8], chiral auxiliaries [9], chiral catalysts [10] and ligands for asymmetric catalysis [11] in various synthetic reactions. To date, there are several synthetic methods for 2-imidazolines starting mainly from aldehydes and ethylenediamine with NBS [12] Some methods includes synthesis from nitriles [13], carboxylic acids [14], esters [15], ortho-esters [16], hydroxy-amides [17] and mono or disubstituted chlorodicyanovinyl benzene [18]. It is also called an important synthon for the preparation of biologically active compounds [19]

Material and methods

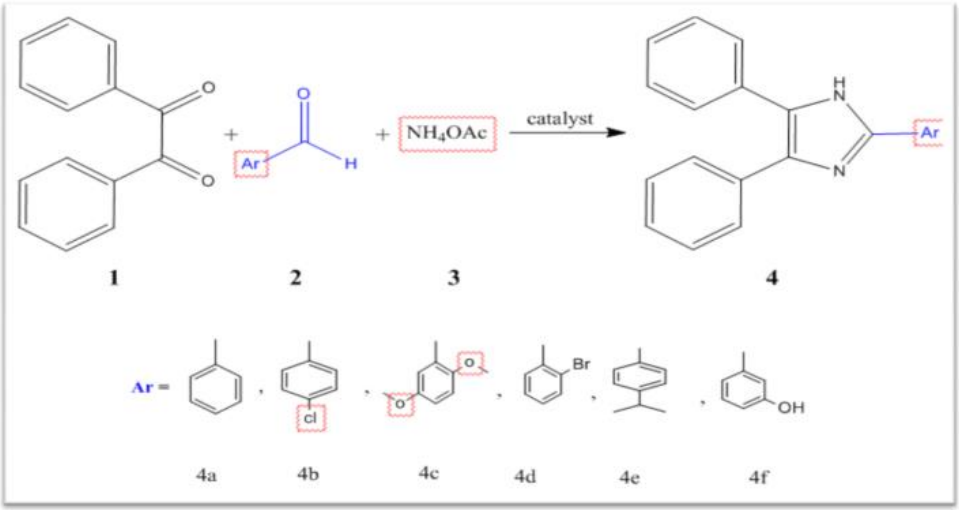
Chemicals

All the chemicals used for this work were purchased from commercial sources and the Merck or Fluka Chemical Companies and were used without further purification.

Techniques

- Melting points were recorded with an electro thermal Stuart SMP 30 capillary melting point apparatus, UK.
- Fourier transform infrared spectroscopy (SHIMADZU FTIR-8400S) was used to determine the quality and composition of the materials in Karbala University.
- Microwave reactions were performed on Domestic microwave oven in crucible

Synthesis of 2,4,5-triarylimidazole derivatives



1- By using the H2SO4 as catalyst A mixture of benzil (1 mmol), aromatic aldehyde (1 mmol) and ammonium acetate (4 mmol) in ethanol (2 mL) was taken, and H2SO4 as the catalyst (three drops),

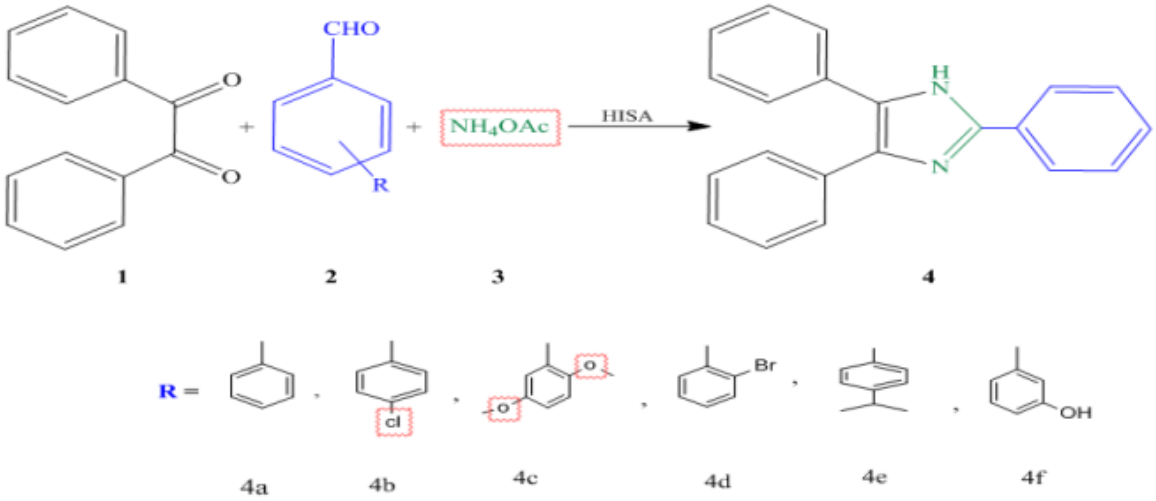
was added at room temperature. The resulting mixture was stirred and heated in microwave oven at 280W for 5 min. After completion of the reaction mixture was washed with excess cold water. The solid product was filtered, dried and recrystallization from ethanol to get 2,4,5-triarylimidazole derivatives. The same procedure was used for all other compounds.

2-By using the new catalyst A mixture of benzil (1 mmol), aromatic aldehyde (1 mmol) and ammonium acetate (4 mmol) in ethanol (2 mL) was taken, and 8-hydroxy-7-iodoquinoline-5-sulfonic acid (HISA) as the catalyst (0.05 g), was added at room temperature. The resulting mixture was stirred and heated in microwave oven at 280W for 5 min. Upon completion of the reaction mixture was washed with excess cold water. The solid product was filtered, dried and recrystallization from ethanol to get 2,4,5-triarylimidazole derivatives. The same procedure was used for all other compounds.

Result and discussion

Synthesis of 2,4,5-triarylimidazole derivatives by using the catalyst (HISA)

Reaction of benzil with aromatic aldehydes by using HISA as the catalyst to synthesis some useful 2,4,5-triarylimidazole derivatives when equivalent amounts were used:



Scheme 1 Synthesis of some useful 2,4,5-triarylimidazole derivatives using HISA

Optimization of reaction conditions The reaction between benzil (1 mmol), benzaldehyde (1 mmol) and ammonium acetate (4 mmol) was selected as a model reaction (4a) to identify the optimum reaction conditions (Scheme 1). To determine the optimum condition for this reaction, different times were used and the results are represented in Table 1. The best times when 5 min. was used. Various solvents and catalysts were utilized, and the results are represented in Tables 1 and 2. Ethanol with catalytic amounts of sulphuric acid was clearly the best choice for this reaction (Table 2, Entry 1). Catalytic efficiency was investigated between the different catalysts. The best yield was obtained with HISA (Table 3, Entry 2). In the absence of a catalyst, the formation of product was not observed (Table 3, Entry 1). Amount of HISA was also evaluated for the model reaction. The maximum yield was obtained with 0.05 g of HISA (Table 4, Entry 2)

Table 1 Effect of times on the synthesis of 2,4,5-triarylimidazole derivatives

Entry	Time (min)	Yield (%)[b]
1	1	52.43
2	3	79.39
3	5	**90.64**
4	7	86.83
5	10	88.58

Table 2 Effect of solvents on the synthesis of 2,4,5-triarylimidazole derivatives

Entry	Solvent	Time (min)	Yield (%)[b]
1	Ethanol	5	**90.64**
2	Water	5	52.26
3	Ethanol + Water	5	28.074
4	Acetone	5	88.75
5	Chloroform	5	72.56
6	Acetonitrile	5	69.45
7	Toluene	5	61.58

Table 3 Synthesis of 2,4,5-triarylimidazole derivatives catalyzed by various catalysts

Entry	Catalyst	Yield (%)[b]
1	-	N.R.
2	HISA	**95.21**
3	H_2SO_4	90.64

Table 4 Effect of the amount of catalyst on the synthesis of 2,4,5-triarylimidazole derivatives

Entry	Catalyst, g	Yield (%)[b]
1	0.01	77.70
2	0.05	**91.22**
3	0.1	70.95
4	0.15	43.92
5	0.2	74.32

After successful optimization of the reaction conditions, the series of 2,4,5- triarylimidazole derivatives from 4a-f were synthesized (Table 5). Under these conditions, the reaction between a variety of aromatic aldehydes and benzil (Scheme 1) was carried out in the presence of HISA as the catalyst to synthesis 2,4,5-triaryl- imidazole derivatives. Excellent yield of products was observed and reaction work up was simple. The obtained results are summarized in Table 5.

Table 5 Synthesis of 2,4,5-triarylimidazole derivatives using catalysts in EtOHa

Entry	Aldehyde		Yield (%)[b]		m.p. (°C)
			HISA	H_2SO_4	
1	Benzaldehyde	**4a**	95.21	90.64	271-273
2	4-chlorobenzaldehyde	**4b**	91.31	82.22	231-234
3	2,5-dimethoxybenzaldehyde	**4c**	91.08	86.36	316-319
4	2-bromobenzaldehyde	**4d**	89.89	80.12	237-240
5	4-isopropylbenzaldehyde	**4e**	80.88	78.02	221-224
6	m-hydroxybenzaldehyde	**4f**	86.55	70.61	235-238

Characterization of 2,4,5-triarylimidazole derivatives

The structures of all the products obtained were characterized well with spectral analyses FTIR (see Appendix). Moreover, the melting points were recorded and compared with that reported in previous literatures as given in Table 6. FTIR spectra of the compounds (4a-f) demonstrated peaks at 1666- 1670 and 3315-3417 cm -1 for (C=N) and (N-H) groups, respectively [20]. Table 6 includes the important FTIR absorption bands of these compounds (4a-f) (see Appendix).

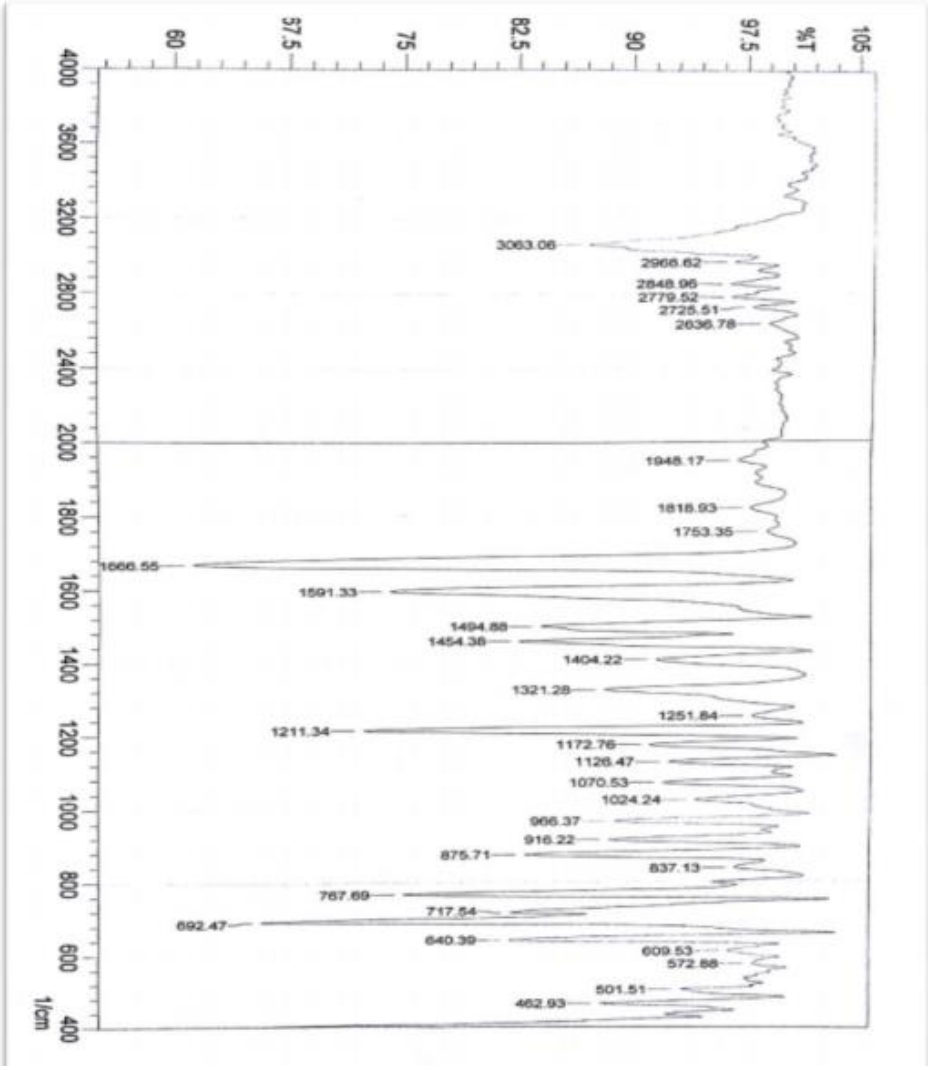


Fig. 1: IR spectrum of benzaldehyde 4a

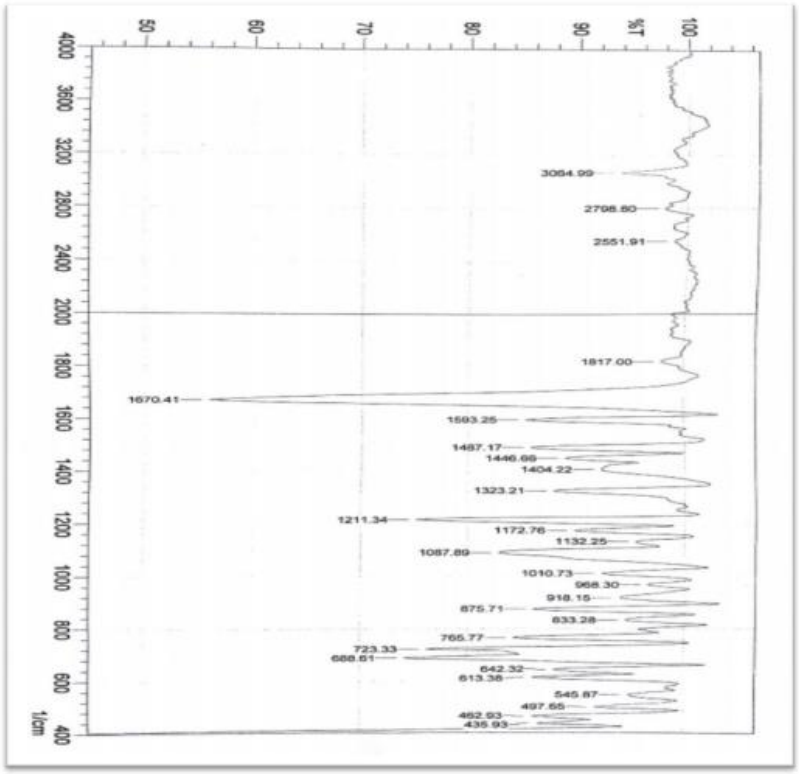


Fig. 2:IR spectrum of 4-chlorobenzaldehyde 4b

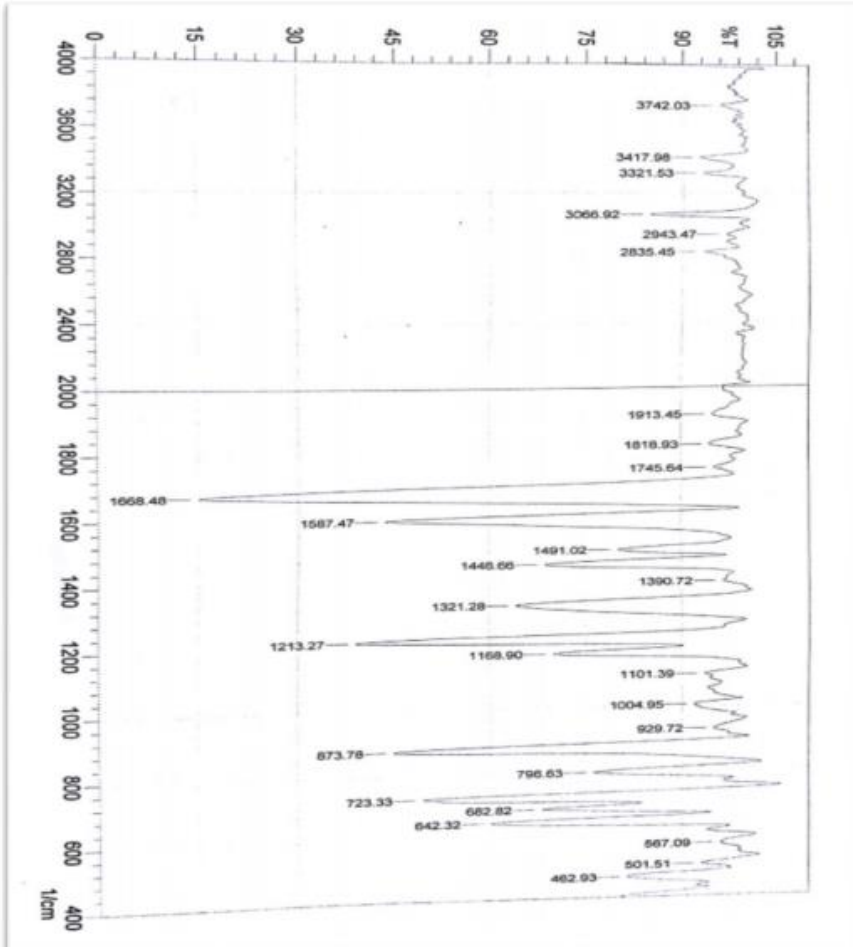


Fig. 3: IR spectrum of 2,5 –dimethoxybenzaldehyde 4c

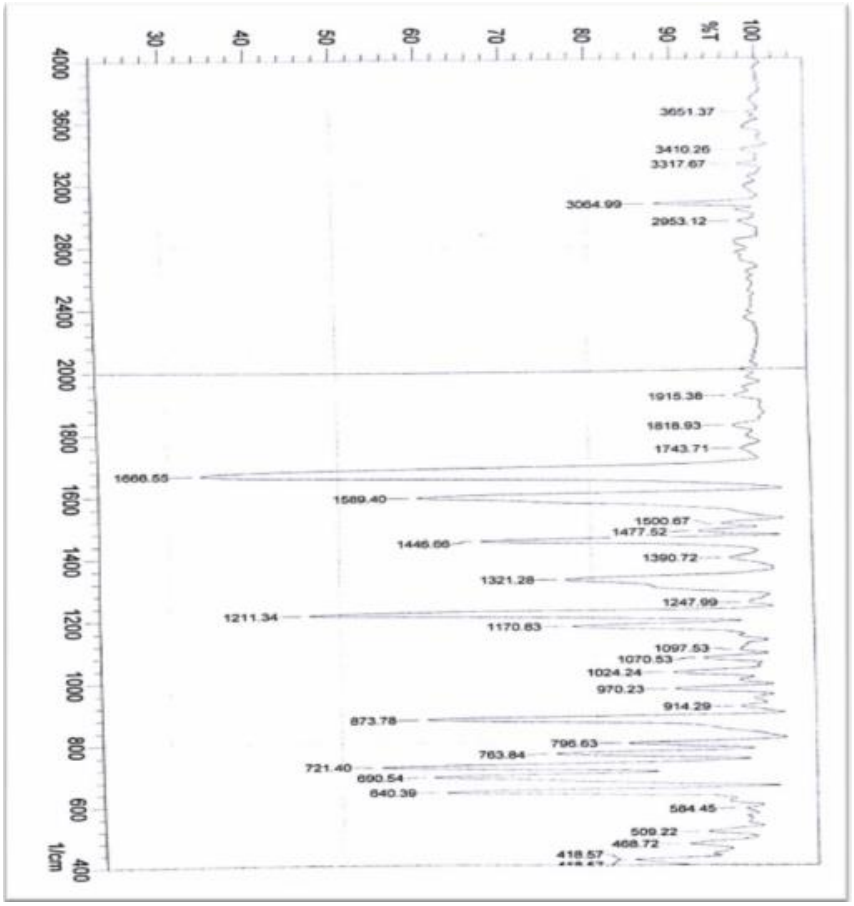


Fig.4: IR spectrum of 2-bromobenzaldehyde 4d

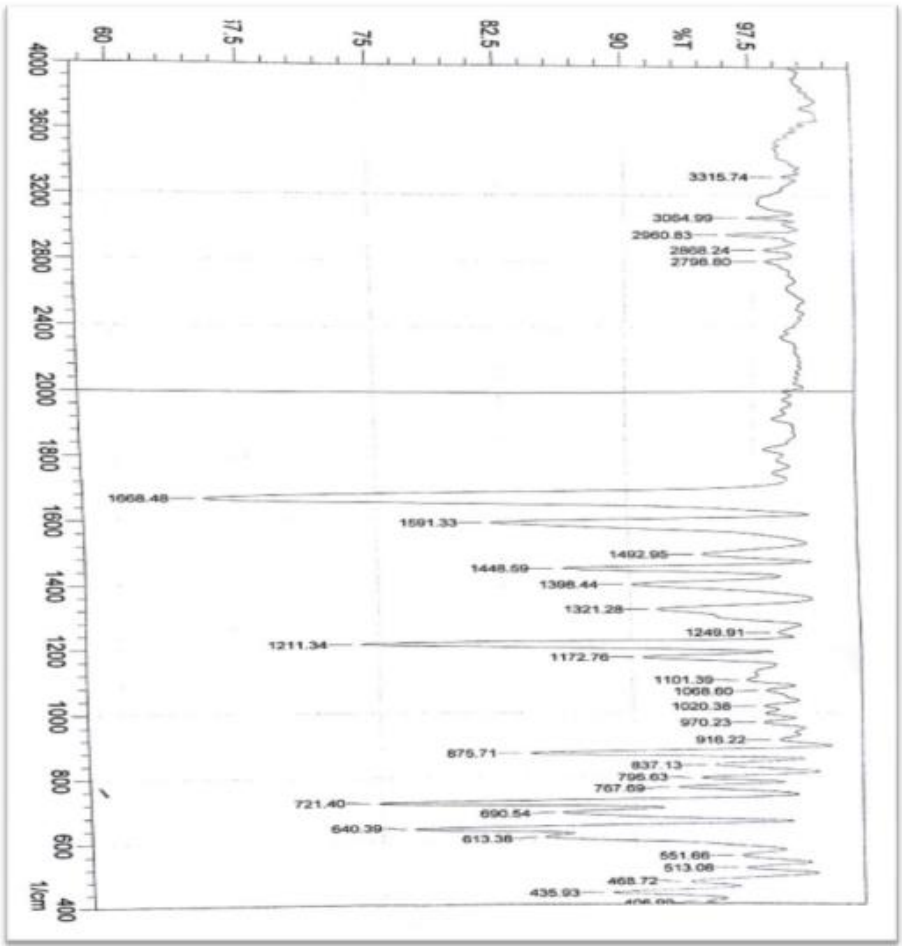


Fig. 5: IR spectrum of 4-isoproylbenzaldehyde 4e

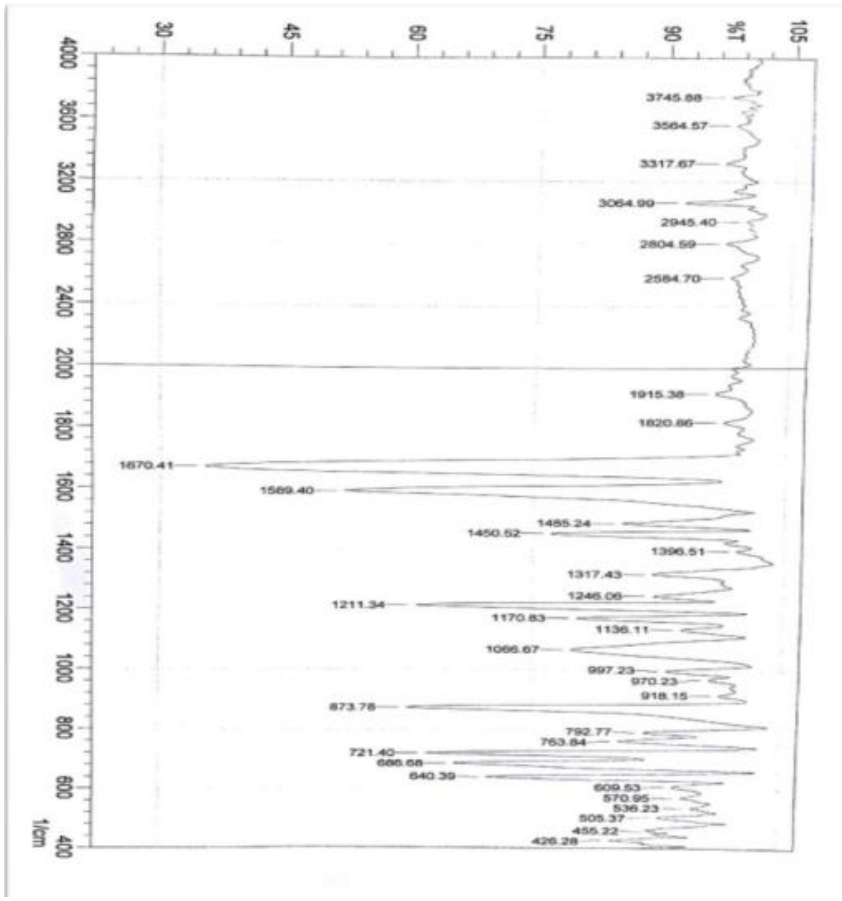


Fig. 6: IR spectrum of M-hydroxybenzaldehyde 4f

Table 6 Characteristic absorption bands of FT-IR and 1H NMR spectra for 2,4,5-triarylimidazole derivatives

Comp. No.	FT-IR (cm^{-1})			
	υ C=N	υ NH	υ C-H (aromatic)	others
4a	1666	3346	3063	-
4b	1670	3327	3064	C-Cl 765
4c	1668	3417	3066	C-O-CH_3 1213
4d	1666	3410	3064	C-Br 640
4e	1668	3315	3064	C-H (aliphatic) 2960
4f	1670	3317	3064	O-H 3564

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