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Research Article

An Efficient Method for The Synthesis of Dihydropyridine by Hantzsch Reaction with Fe/SiO_2 Nano Heterogeneous Catalysts

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Abstract

An efficient method for the synthesis of dihydropyridines (DHPs) by Hantzsch reaction with Fe/SiO_2 heterogeneous catalysts was developed. The Fe/SiO_2 catalysts was prepared by impregnation method. The catalysts were characterized by IR and SEM instruments. The SEM results indicated that Fe/SiO_2 nano spheres were formed. The reaction procedure involved reaction of aldehyde, ethyl acetoacetate (EAA), ammonium acetate (NH_4OAc) and ethanol under reflux. The study was focused on optimizing reactions conditions: Standardization of catalyst, substrate of study and solvent study. In order to identify the best active catalysts, five different ratios of catalyst were synthesized and evaluated for the title reaction under similar conditions. To standardize the active catalysts, different temperature conditions (i.e. room temperature, 60 °C and 80 °C) as well as catalysts amounts were evaluated. Under these established conditions, 2.5% Fe/SiO_2 was the best active catalysts that resulted. Benzaldehyde and *p*-anisaldehyde were used to study the effect of having various substrates on the conversion and reaction time, especially the substituted aldehydes. The best results were obtained by reacting *p*-anisaldehyde with EAA, NH_4OAc, and ethanol at 60 °C with 0.3 grams of 2.5% Fe/SiO_2 heterogeneous catalysts. Thin Layer Chromatography (TLC) monitoring of the reaction mixture showed no selectivity at high temperatures (80 °C) with 15% Fe/SiO_2. Standardization of solvent study was executed with two solvents, ethanol and acetonitrile. The product dihydropyridines were analyzed using gas chromatography-mass spectrometry (GC-MS). The melting points of the products were compared with authentic samples reported in the literature. Hence, the Fe/SiO_2 catalysts is eco-friendly and economically developed for the title reaction.

Keywords: Hantzsch reaction; dihydropyridines; impregnated; Fe/SiO_2 nano; heterogeneous catalyst

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1. Introduction

Hantszch reaction is a synthetic method of synthesizing dihydropyridines (DHPs) in a one-pot multicomponent reaction system consisting of an aryl aldehyde, acetoacetic ester, and ammonia heated in refluxing methanol for a few hours [1-2]. DHPs and their derivatives are common features found in vasodilator, anti-atherosclerotic, anti-cancer, anti-diabetic and antihypertensive agents [3-4]. There are several methods are reported in literature for the syn-

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thesis of DHPs, of which most of them are limited to the modification and optimization of the Hantzsch multicomponent synthesis between an aldehyde, a 1,3-dicabonyl compound, and a source of ammonia [3,5]. Preparation of nifedipine, a dihydropyridine calcium channel blocker, acetoacetic acid methyl ester, methanol, and ammonia is used [1]. Some of the efficient methods reported for the synthesis of DHPs made use of metal triflates, I_2, CAN-Cerium ammonium nitrate, PPh_3Triphenyl phosphine, L-proline, PoylPhosphoric acid supported silica-PPA-SiO_2, Lanthanum oxide -La_2O_3 and nickel nanoparticles [3,5]. Numerous catalysts have so far been evaluated for the title reaction with Fe_3O_4/silica sulfonic acid nanocomposite [6], Fe_2O_3, CuO, ZnO [1], and Fe_3O_4/SiO_2-NH_2 nanocomposite [7]. The classical method used to synthesize DHPs has disadvantages such as long reaction times, harsh refluxing condition, excessive use of volatile solvents and low yields which precludes the wide use of these reagents [3]. For example, Fe_3O_4/SiO_2-NH_2 takes four hours to yield 94% 1,4-DHP [7], TiO_2 NPs and Fe-TDU-1 [8]. Mvumvu [9] also indicated that due to the formation of side products, after several attempts to synthesize 1,4-DHP ester analogues from ethyl acetoacetate, the experiment was considered unsuccessful. The field of Nanocatalysis provides an alternative to homogeneous catalysts by using highly porous catalysts with a large surface area for reagents to interact with catalysts [3]. Hence, metal oxide-catalyzed organic reactions are efficient catalysts for the synthesis of valuable commodities in organic synthesis that are more desirable in green chemistry point of view. Authors have developed a newer Green chemistry route for Hantzsch reaction of various aldehydes with ethyl acetoacetate and ammonium acetate in a Fe/SiO_2 at 80 °C. Fe/SiO_2 acts as an efficient catalyst. Preparation of Fe/SiO_2 nano catalysts is easier than other nano metal oxides and due to the effect of optimum conditions such as temperature, kind of surfactant, medium, and the solvent on the crystallinity and catalytic properties of nano Fe/SiO_2 [7-12]. The call for environmentally benign procedure with heterogeneous catalysts prompted authors to develop a safe alternate, economic, green method for the synthesis of 1,4-dihydropyridines in the presence of Fe/SiO_2 (NPs) in shorter duration of time (Scheme 1).

2. Materials and Methods

2.1 Materials

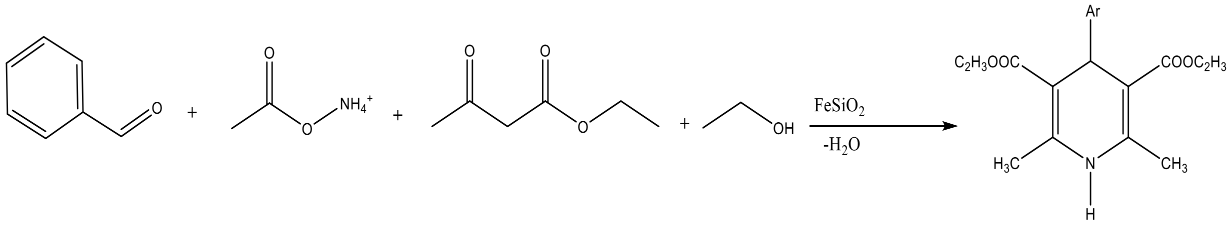
Benzaldehyde 99.0%, p-Anisaldehyde 99.0%, p-Toulaldehyde 98.0%, Silica gel 60 (SiO_2, 70-230 mesh ASTM), absolute ethanol (99.5%), and reagent grade iron(III) nitrate 99.0% were purchased from Merck.

2.2 Preparation of Fe/SiO_2 Catalyst

All chemicals were procured from Merck. For 2.5% Fe/SiO_2, ferric nitrate $Fe(NO_3)_3$ solution was prepared by dissolving 0.625 g of $Fe(NO_3)_3.9H_20$ in 25 mL distilled water. The solution obtained was then transferred to a round bottom flask equipped with a refluxing device. Solid SiO_2 (2.0344 g) was rapidly added to the solution. The mixture was then stirred for 3 hours at room temperature/25 °C. Water was evaporated off from the catalyst and dried in an oven at 100 °C for overnight. The other ratios of catalysts such as 5.0, 7.5, 10, and 15% were prepared using the same procedure used for 2.5% Fe/SiO_2 [24]. A JEOL JSM-6100 Scanning Electron Microscope (SEM) was used to study the morphology and surface topography of the Fe/SiO_2-NPs. Fourier Transform Infrared (FTIR) analysis was carried out using a FT-IR Perkin Elmar Spectrum 2 Spectrometer to study the functional group OH present in SiO_2.

2.3 Typical Procedure for Synthesis of DHPs

A solution of aldehyde (1 mmol), ethyl acetoacetate (2 mmol), ammonium acetate (2 mmol) and ethanol (10 mL) at reflux conditions was reacted in the presence of Fe/SiO_2 catalyst (0.3022 g). The resulting mixture was stirred until the TLC-Thin Layer Chromatography



Scheme 1. Various substrate evaluated with 2.5% Fe/SiO_2 catalysts.

monitoring showed completion of the starting material. The reaction mixtures were cooled to room temperature and extracted with diethyl ether. Organic layer was dried over anhydrous Na_2SO_4. After evaporation of the solvent, the obtained yellow products were purified by crystallization from ethanol. After crystallization the solvent was concentrated at reduced before subjecting to GC-Mass analysis. And the final yield of product were obtained Table 1.

3.4 GC-MS Instrument Specifications

The GC–MS analyses were performed on a Thermo Scientific Focus GC coupled to an ITQ 700 MS using helium as carrier gas at a flow rate of 1.0 mL/min (constant flow) and a split ratio of 10. A SGE BP5MS capillary GC column (30 m × 0.25 mm i.d) with volume of 5% diphenyl, 95% dimethyl polysiloxane stationary phase (0.25 µm film thickness) was used for the separations. FID (Flame Ionization Detec-

Table 1. Summary of standardization of Fe/SiO_2 catalysts.

S. No	Sub-strate	Catalyst (%Fe/SiO_2)	Grams of Fe/SiO_2 catalysts (g)	Ethanol Solvent (mL)	Reflux Temp. (^{o}C)	Time taken (min)	Yield %^{a}	Selectivity %
1.	Benzaldehyde + EAA + NH_4OAc	2.5	0.3022	10	60	122	89	90
		5.0	0.3056	10	60	125	83	0
		7.5	0.3058	10	60	110	70	0
		10	0.3078	10	60	65	77	0
		15	0.5050	10	RT^b	168	68	0
			0.5058	10	60	258	78	0
			0.5058	10	80	120	66	0
			0.3022	10	60	108	79	0

^{a}Isolated yield; ^{b}Room temperature (25 ^{o}C)

Table 2. Comparison of Fe/SiO_2 catalyst (Table 1) with various catalysts reported in literature.

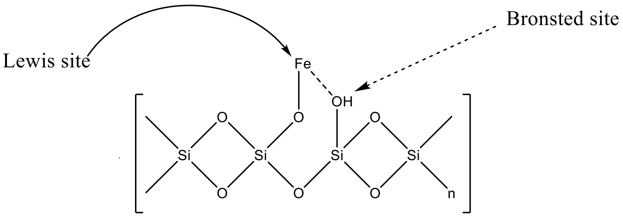
S. No	Catalysts	Solvent	Temp (^{o}C)	Time	Conversion (%)	Reference
1.	P_2O_5-SiO_2	$CHCl_3$	110	4 h	85	[13]
2.	ZnO Nano	H_2O	60	2-4 h	90	[1]
3.	Chitosan Nano	Solvent free	80	4 h	55	[15]
4.	$FeCl_3$ NPS	Ethanol	Reflux	2 h 30 min	41	[1]
5.	V_2O_5/SiO_2	Acetic acid	40	13 min	100	[14]
6.	La_2O_3/TFE	THF	RT^a	1-1.5 h	90	[3,17]
7.	Polymer	Solvent free	120	20 min	72	[16]
8.	Cyclodextrin	N,N dimethyl formamide	80	3 h	10-90	[20]
9.	TiO_2 NPs	Ethanol	80	135 mins	65	[8]
10.	Fe-TDU-1	Ethanol	80	300 mins	60	[8]
11.	Yb(OTf)3 (5 mol%)	EtOH	RT^a	2–8 h	85-95	[18]
12.	Sc(OTf)(5 mol%)	EtOH	RT^a	2–6 h	85–95	[19]
13.	(PTSA) 4-Toluene sulphonic acid	Solvent free	RT^a	36 min	50	[21]

^{a}Room temperature (25 ^{o}C)

tor) is used. The 10 mg of the intermediate 1a sample was dissolved in 1.5 mL of ethyl acetate and 1.5 of dichloromethane for analysis.

3. Results and Discussion

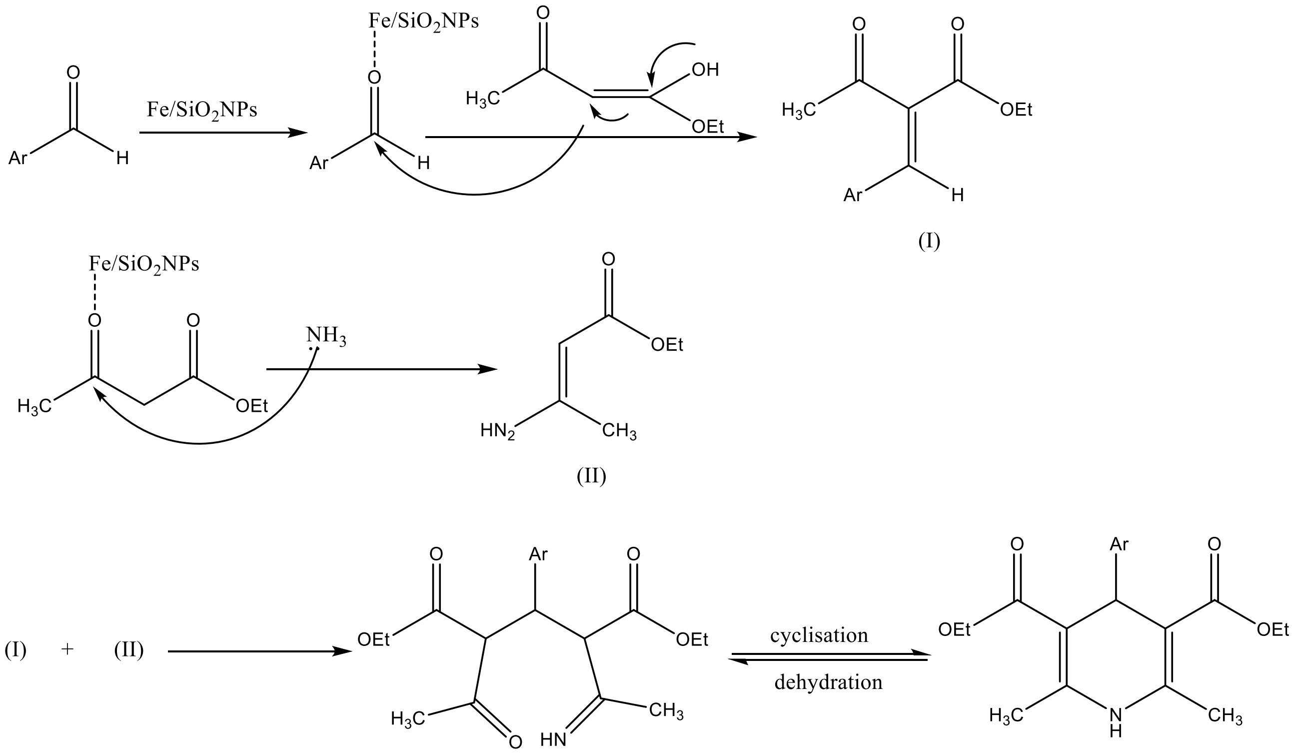
The search for new readily available and green methods is still ongoing [5], thus in this study, a new catalyst Fe/SiO$_2$ was prepared by simple impregnation method was developed and evaluated for its catalytic activity for the title reaction. The Hantzsch condensation for three substrate's of different functionality were studied namely benzaldehyde, *p*-anisaldehyde and toulaldehyde at reflux in ethanol solvent (Scheme 1). Saini *et al.* [3] reported with the chemistry of 1,4-DHPs with ethanol solvent which is proven to be better than other alcohols such as isopropanol, methanol. It has some advantages over the other methods such as the amount of water formed in the reaction, which is a fundamental aspect of Hantzsch 1,4-DHP synthesis employing sterically demanding benzaldehydes [25]. The reactions were monitored by TLC (9:1 CH_2Cl_2/AcOEt as eluent) until the disappearance of the starting benzaldehyde, anisaldehyde and taulaldehyde. With anisaldehyde the reactions were completed after 1 h 36 mins and for benzaldehyde in 2 h which is short time period reported in literature (Table 2) which is 5, 6 and 8 h duration of time [8,18,19]. With 2.5% Fe/SiO$_2$ catalysts, the reaction was fast took place.



Scheme 2. Bronsted acidity arising from inductive effect of Lewis acid center coordinated to nanosilica support.

3.1 Standardization of Catalyst

Various experiments were conducted using six different ratios of Fe/SiO$_2$ 2.5, 5, 7, 10, and 15% for each reaction with benzaldehyde. The main aim of this methodology was to evaluate the most suitable Fe/SiO$_2$ catalysts among these ratios under standards conditions. Optimization of reaction parameters, *i.e.* the temperature, time and amount of catalyst were also studied Table 1. Table 1 shows the results obtained for the reaction of benzaldehyde at different temperatures. It was observed that at high catalyst ratios there was less conversion



Scheme 3. The proposed mechanism of the synthesis of 1,4-dihydropyridines in the presence of silica (NPs) supported Fe(III).

for example (15% Fe/SiO_2 lowest yield 66% of hours at high temperature of 80 °C and 68% yield over of period of 2 hours 48 minutes at room temperature (Table 1). This could be due to uneven distribution of Fe on Silica [24]. Another study reported a selectivity of zero observed for Ni/SiO_2 catalysts reported [24]. The 10% Fe/SiO_2 catalyst gave the best results of 77% yield in 65 minutes which is a short time Table 1. 2.5% Fe/SiO_2 resulted into 89% conversion in 1 h 36 minutes (122 minutes) was obtained Table 1. The 2.5% Fe/SiO_2 catalysts gave 90% yield. Hence, with 5, 7.5, 10, and 15% Fe/SiO_2 selectivity was 0%. The blank reactions were also evaluated where $Fe(NO_3)_3$, and SiO_2 NPs involving substrates and solvent were used and these gave 0% yield after 3 h, $Fe(NO_3)_3$ 1 h 30 minutes yield 35 %, SiO_2 NPs 1 h 30 minutes yield 20% in standardized conditions.

Table 2 represents various catalysts that have been reported for Hanzsch reactions and the yields are varying between 10-95%. Almost all the catalysts took longer duration of time from 2-8 h to complete the reactions. This confirms less activity of P_2O_5-SiO_2 entry1, $Yb(OTf)_3$ (5 mol%) entry 11, Sc(OTf) (5 mol%) entry 12 and these catalysts took 8 h of duration to complete the reaction Table 2. This is ascribed due to the active sites of the catalysts which are inactive. From this data, it can be deduced that Fe/SiO_2 Nano catalyst is more active giving 89% conversion in 2 h entry 1 (Table 1) compared to the catalysts listed in Table 2 [24].

As illustrated in Scheme 2, the silica supported Fe(III) can act as Bronsted and Lewis acid catalysts [23]. Mechanism of Fe/SiO_2 NPs within reaction: In this mechanism, the author's propose that an acid–base interaction between silica supported Fe(III) and loan pair of oxygen polarizes C=O bond of aldehyde. Hence the Knoevenagel product (I) and ester enamine (II) were prepared by this interaction. While the condensation of these two fragments gives intermediate (III) which subsequently cyclizes to the 1,4-dihydropyridine Scheme 3 [1].

3.2 Characterization of Catalyst

Characterization of the catalyst was done using scanning electron microscopy (SEM), electron dispersive x-ray (EDX), and infrared spectroscopy (IR). The 2.5% and 7.5% Fe/SiO_2 ratios were analyzed with SEM and EDX. IR was used for characterization of 2.5% and 5% Fe/SiO_2 (Figure 4) SEM, EDX, EDX layered images analysis results for 2.5% are shown in Figures 1-3.

3.2.1 X-Ray diffraction XRD

The XRD of all samples showed diffuse pattern 2 theta value was 25 for Si-O-Si bond showed crystalline pattern of silica similar to the one reported by Jonnalagadda *et al.* [24].

3.2.2 Scanning electron microscopy (SEM)

SEM analysis of Fe/SiO_2 catalysts shows the morphology and size of the particles of the syn-

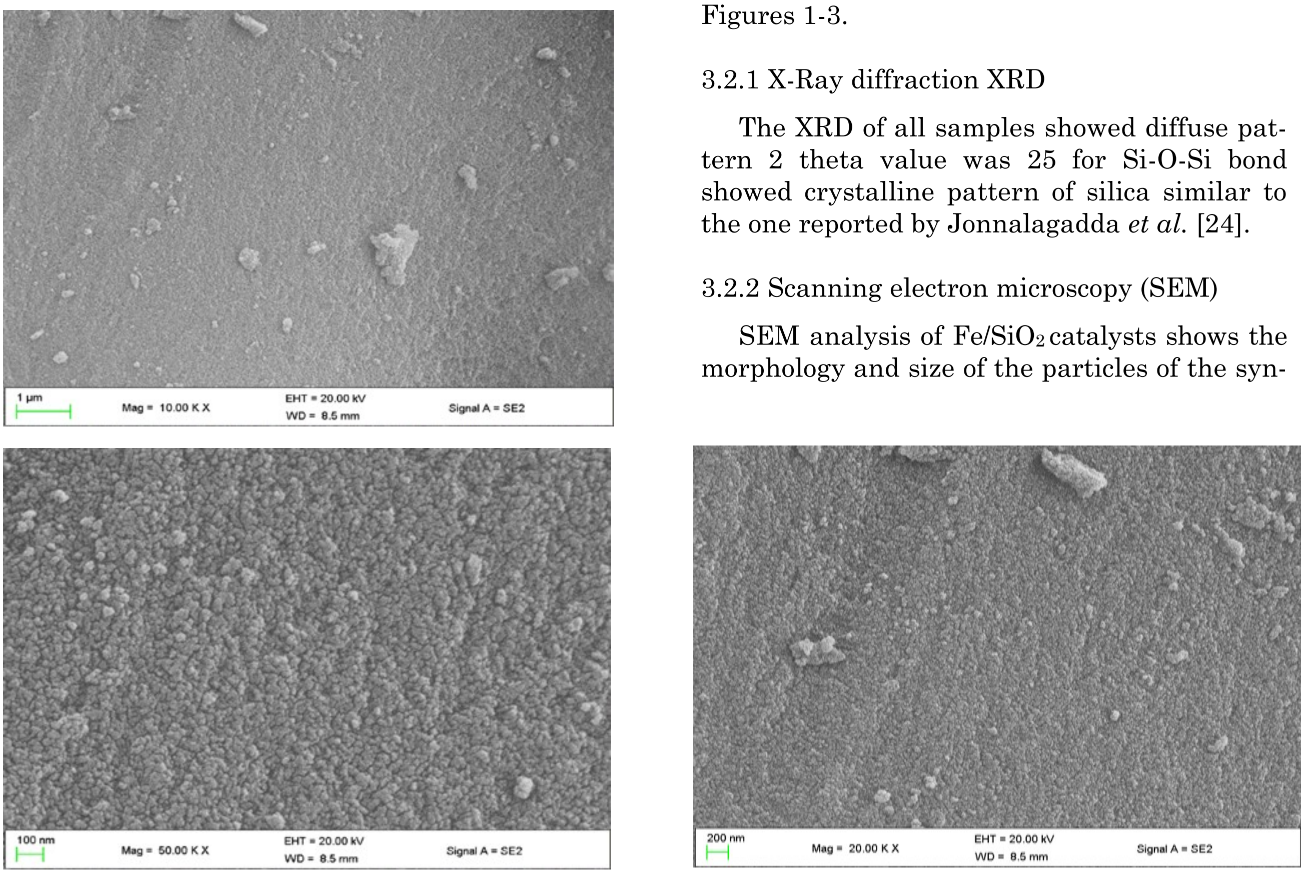
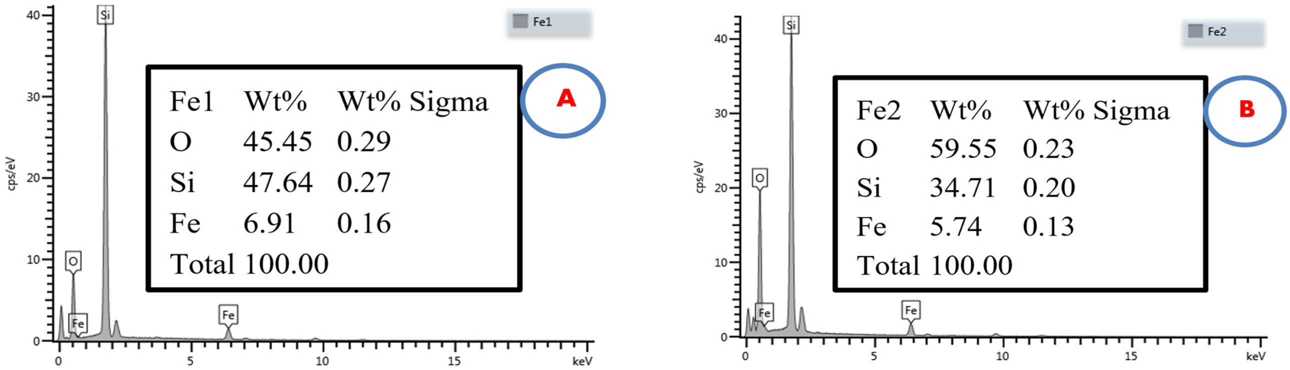


Figure 1. SEM images for 2.5% Fe/SiO_2 catalyst.

thesized. The catalyst was synthesized in nano and micrometer ranges as shown in the SEM image Figure 1 where particles are widely spread [24]. From the Figures 1 and 2 it can be seen that with 2.5% Fe/SiO_2 it is confirmed that the Fe is dispersed homogenously on the SiO_2 surface. Fe loading with 7.5% one has 6.91, which is very close to the anticipated loading. But, the 2.5% sample got 5.74% of Fe, which is way above the anticipated loading. It is also evident from the EDX images that the 2.5% Fe, has some aggregation results that are identical reported by Anabi *et al.* [26]. Hence, the gray particles is nano silica which are supported by Fe oxidized white particles [26]. From these finding its evident that 2.5% Fe/SiO_2 Fe particles are uniformly distributed on silica and this is consistent with the results reported by Jonnalagadda *et al.* [24].

3.2.3 Electron Dispersive X-ray

Figure 2 shows elemental analysis of the samples by EDX. Comparing the two samples, Iron weight percent in 2.5% Fe/SiO_2 is at 5.74%, which is lower than that of 7.5%



Fe1	Wt%	Wt% Sigma
O	45.45	0.29
Si	47.64	0.27
Fe	6.91	0.16
Total	100.00	

Fe2	Wt%	Wt% Sigma
O	59.55	0.23
Si	34.71	0.20
Fe	5.74	0.13
Total	100.00	

Figure 2. EDX analysis of 7.5% Fe/SiO_2 (A) and 2.5% Fe/SiO_2 (B).

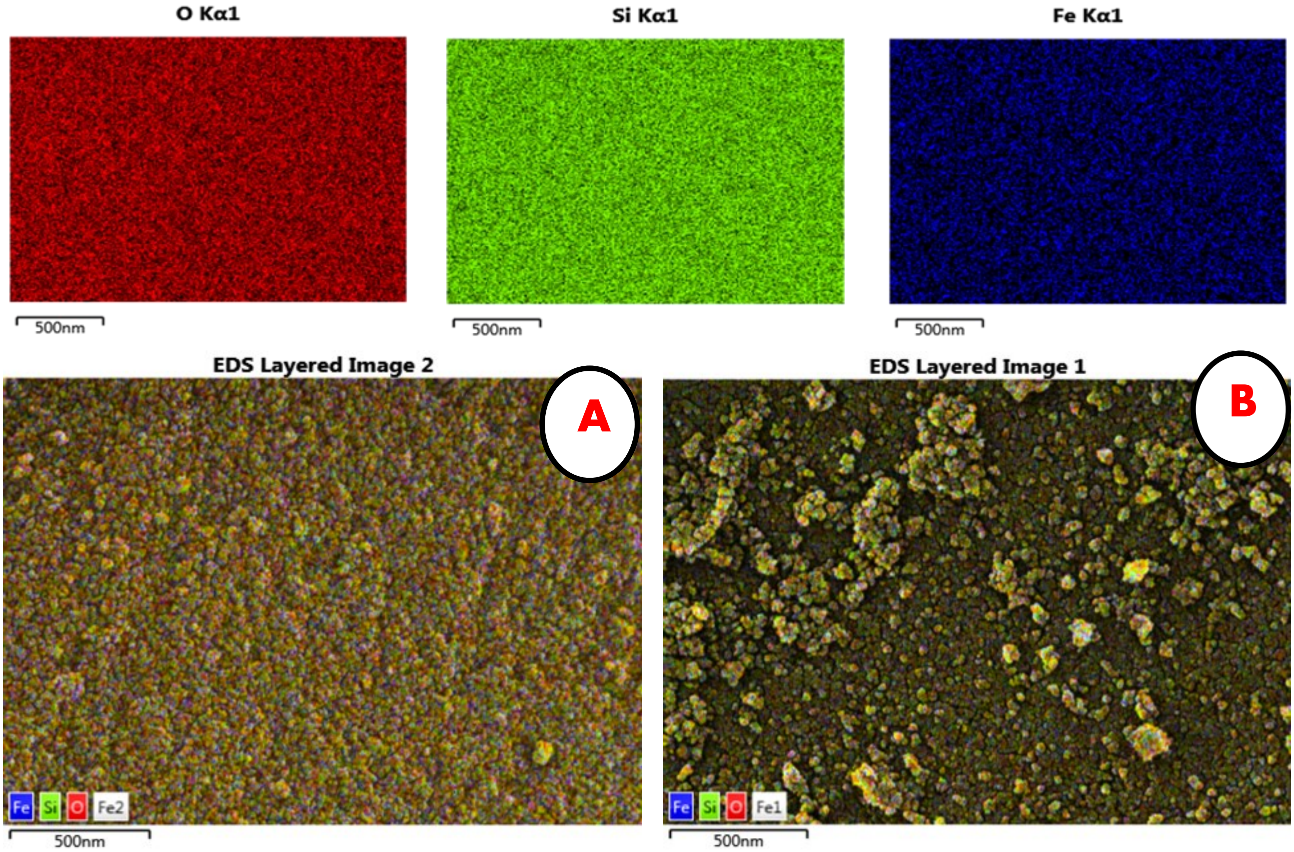


Figure 3. EDS layered images of 2.5% Fe/SiO_2 (A) and 7.5% Fe/SiO_2 (B) showing even distribution of Fe in A (best catalyst ratio) than in BB.

Fe/SiO_2 at 6.91%. This is ascribed due to the 2.5 % and 7.5 % loading of Fe samples observed for both samples [24]. The ratio of each element in each sample is indicated in the respective spectra and Tables 2.

Figure 3 is an illustration of EDS layered images of 2.5% and 7.5% Fe/SiO_2 catalysts. Figures 1a and 1b shows the results of SEM and Figures 2a-b results of EDX. From the image of SEM it can be said that the silica is small and spherical in shape. For impregnation method the image looks agglomerated and the reaction parameters, i.e. stirring the reaction at room temperature for preparing Fe/SiO_2. From the Figure 3, we confirm that there are only three components that exist in the catalyst which are iron (Fe), silica (Si) and oxygen (O). The graph shows that this catalyst has a very large amount of silica and very less amount of iron incorporated on SiO_2. The composition and weight of all three particles as shown in Figures 2a-b [23]. From these findings its evident that less amount of 2.5% Fe impregnated SiO_2 is active catalysts for Hanzsch reaction. With 7.5 wt.% Fe-loaded SiO_2 catalyst in Figure 2(b). Although with 7.5% loading of Fe on silica higher the metal loading the more concentrated the metal-representing dots appears (as seen in the EDX generated elemental mapping images Figure 3) [23].

3.2.4 IR analysis of 2.5 & 5% Fe/SiO_2 catalyst

Figures 4(i) and (ii) indicate the FTIR spectra of 2.5% Fe/SiO_2 and 5% Fe/SiO_2 catalysts, respectively. The spectra in Figure 4(iii) were obtained on a similar study but with Mo-Fe/SiO_2 catalyst [10]. The spectra in Figures 4(i) and (ii) are similar and hence are expected to have the same absorption bands. There ap-

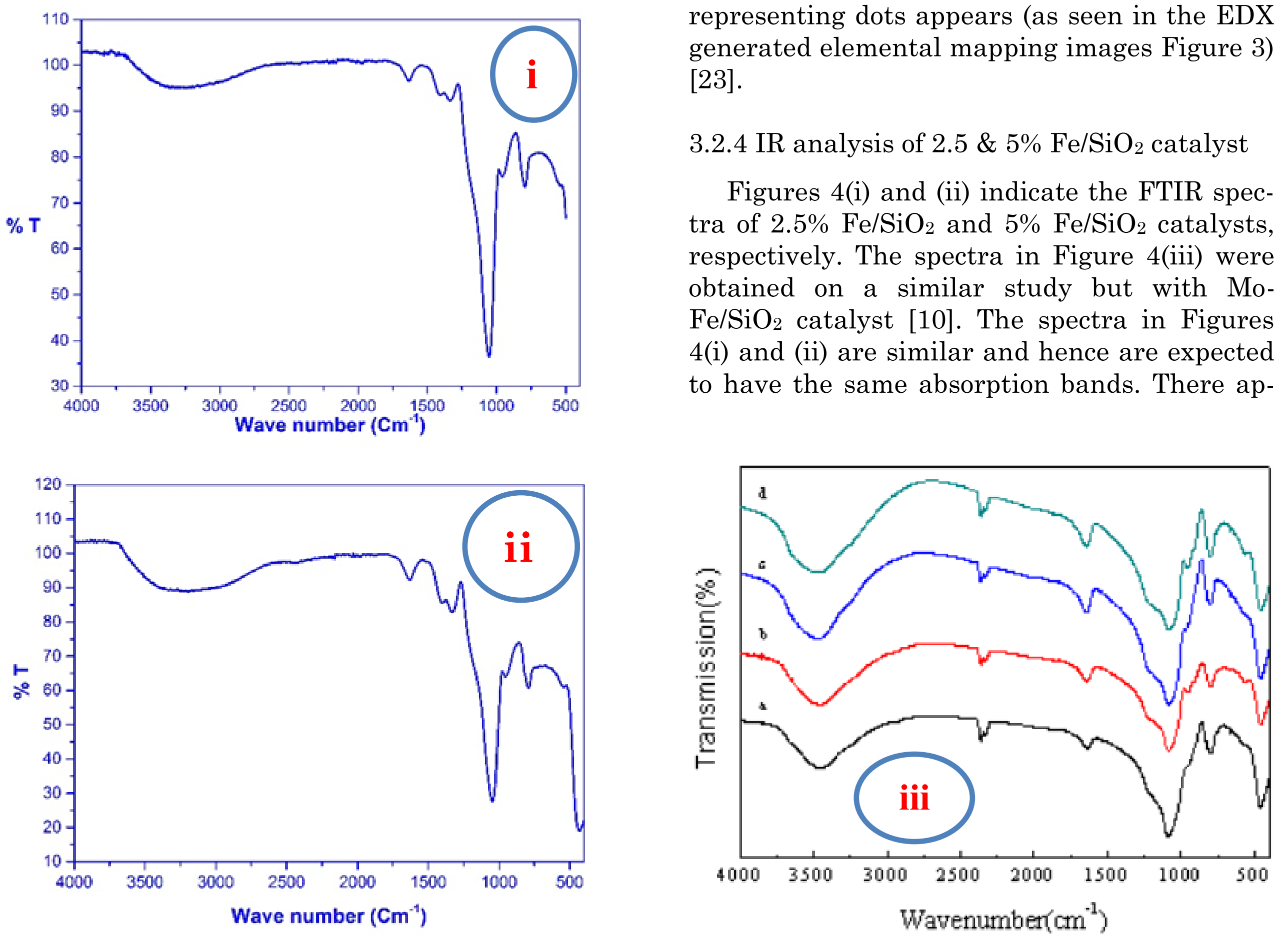


Figure 4. IR spectra of (i) 2.5% Fe/SiO_2, (ii) 5% Fe/SiO_2 as synthesized (iii) IR spectra of (a) SiO_2, (b) 15% Mo/SiO_2, (c) 10% Fe/SiO_2, and (d) 15% Mo-Fe/SiO_2 catalyst [10].

Table 3. 2.5% Fe/SiO_2 reaction with various substrates.

S. No	Substrate	Catalyst	Wt. of Fe/SiO_2	Temp	Solvent	Time (min)	Yield (%)	Melting point for product's Measured	Reported	
1.	*p*-anisaldehyde	2.5% Fe/SiO_2	0.30 g	60 °C	10 mL ethanol	102	89	260-262	260-261	[25]
2.	Benzaldehyde		0.30 g	60 °C	10 mL ethanol	122	74	202-204	203-204	[25]

pears a curve between approximately 1625-3317 cm^{-1}, which is attributed to the H-O-H stretching and bending vibration of the free or absorbed water, respectively [10,11]. Figure 4(iii) supports the findings as it also reported the presence of a strong band absorption at 3540 cm^{-1}, which was assigned to the stretching vibration of the the O-H bond. A weak band absorption was also reported at 1639 cm^{-1} and was assigned to flexural vibration of the O–H bond [10]. The strong absorption band at approximately 1060 cm^{-1} (1089 cm^{-1} in literature) is attributed to the vibration of the chemical bond of Si–O–Si. The peak at approximately 570 cm^{-1} can be assigned to Si-O-Fe, which according to literature was reported at 578 cm^{-1} [10]. These evidences proves that Fe was impregnated on the silica.

3.3 Substrate Study

Benzaldehyde and *p*-anisaldehyde were used to study the effect of various functional groups on the yield and reaction time, especially the substituted aldehydes. The best results were obtained with *p*-anisaldehyde, which resulted in 89% yield in over a shorter duration of time with 2.5% Fe/SiO_2 Table 1. With Benzaldehyde when reaction was conducted with 2.5% Fe/SiO_2 the yield was less than 74%. This confirms that electron donating groups play crucial role for Hanzsch reaction which is completed in 1.5 and 1.2 hours, duration of time respectively. The melting points were observed for both products which corresponded to the values reported in literature [25]. The results are presented in Table 3.

3.4 Solvent Study

p-Anisaldehyde substrate was chosen for solvent study with acetonitrile and ethanol, and carbon tetrachloride. Hence, acetonitrile couldn't work maybe due to nonpolar behavior and carbon tetrachloride as more polar solvent. Ethanol gave the best yield and hence, it was used as the standard solvent for all the reactions. With *p*-anisaldehyde and 2.5% Fe/SiO_2 at 60 °C the yield was 89% (Table 4).

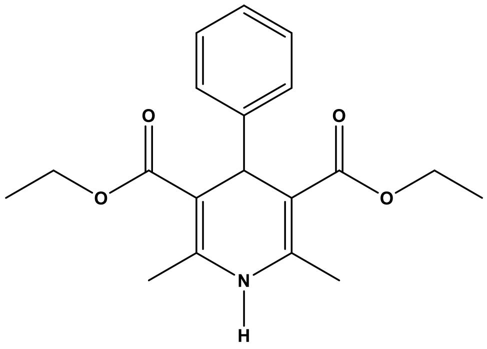
3.5 Gas Chromatography-Mass Spectroscopy (GCMS) Analysis

Gas chromatography mass spectroscopy (GCMS) was used to analyze the product. For S.No. 1 Table 3, the analysis showed the presence of the most abundant fragment which corresponds to m/z 252, which according to literature is formed directly from the loss of the substrate at 4-position [12]. The peaks at m/z 224 and m/z corresponds to consecutive loss of ethylene [12].

The graph in Figure 5 shows the fragmentations. More graphs of the same nature are found in Appendix II. Graph of electron ionization mass spectrum of the compound that elutes at Rt 22.24 mins. After comparing the obtained the fragments to those of literature, the product structure was proposed as presented in Scheme 3.

4. Conclusion

In summary, a simple and easy method for the synthesis of dihydropyridines was developed by a one pot multicomponent reaction of an aldehyde; ethyl acetoacetate, ammonium acetate and ethanol under reflux condition at 60 ˚C in the presence of Fe/SiO_2 nano heterogeneous catalyst. The catalytic activity of 2.5% Fe/SiO_2 was found to be more efficient with a high yield of 89%, in shorter duration of time with high selectivity. *p*-Anisaldehyde is the best substrate of choice due to its electron withdrawing character as it resulted in 80-89%



diethyl 2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarboxylate

Scheme 3. The proposed product structure

Table 4. Summary of solvent study with *p*-anisaldehyde.

Substrate	Solvent	Catalyst	Catalyst wt., g	Temp (°C)	Time (min)	Yield %
p-anisaldehyde	Ethanol 10 mL	2.5% Fe/SiO_2	0.3022 g Fe/SiO_2	60	102	89
	Acetonitrile 10 mL		0.3035 g Fe/SiO_2	60	122	74

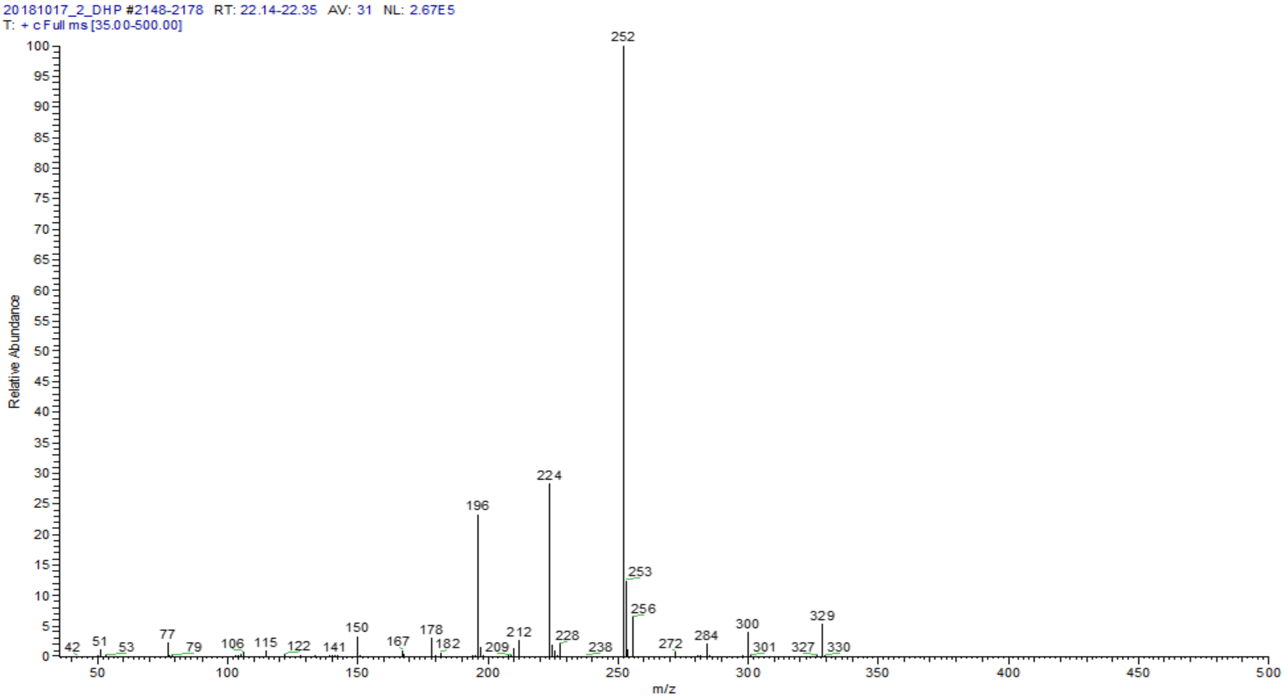


Figure 5. Electron ionization mass spectrum of the compound that elutes at Rt 22.24 min.

yield. Yield was high with the use of *p*-Anisaldehyde as compared to benzaldehyde (with conversion in the region of 60-89). GC-MS analysis shows the basis peaks at 252 and 298 for the DHPs that were analyzed. These basis peaks are major components in DHP structures. The best conversion was obtained when 2.5% Fe/SiO_2 with *p*-Anisaldehyde and ethanol at 60 °C. The catalysts were characterized by IR, and SEM. From SEM analysis it confirms that spheres of Fe/SiO_2 were formed and Fe is well adhered onto the surface of SiO_2, hence lead to the formation of Fe/SiO_2 catalysts. The IR results exhibited well formed OH groups at 35400 cm^{-1}, and Si-O-Si bond at 578 cm^{-1} assigned to Si-O-Fe. Hence finally it can be concluded that the melting points and GC-MS results for the products obtained were confirmed with the reported melting points and GC-MS in literature. Hence in comparison with other presented procedures, our method is very quick, avoids the use of expensive reagents or high temperature and leads to improved product yields by easy procedures at reflux temperature, involves shorter reaction time, and easy to workup. Thus, an ecofriendly, and economical method is developed, with the use of a reusable, and reproducible nano Fe/SiO_2 catalysts and is applicable at large scale up reactions.

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Summary statement

No conflict of interest for each contributing author.

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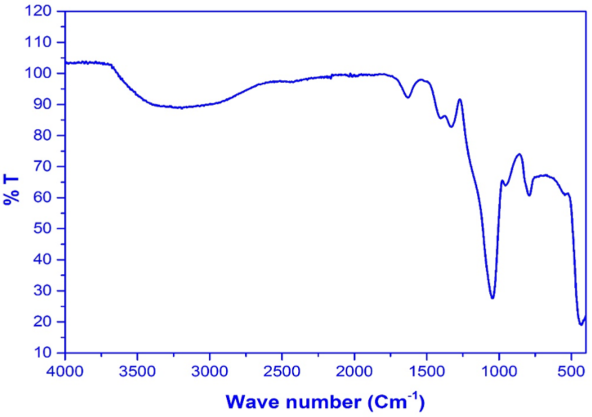
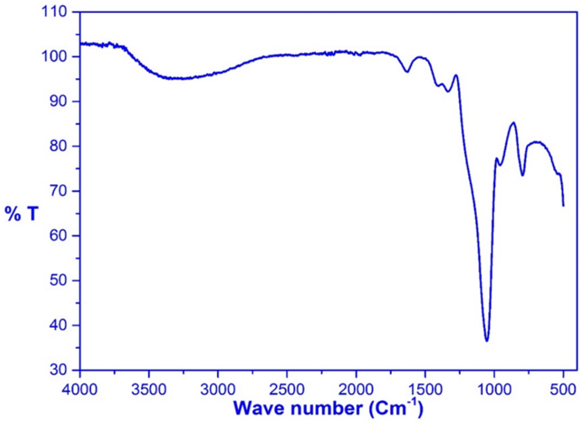
Appendices

Appendix I (IR)

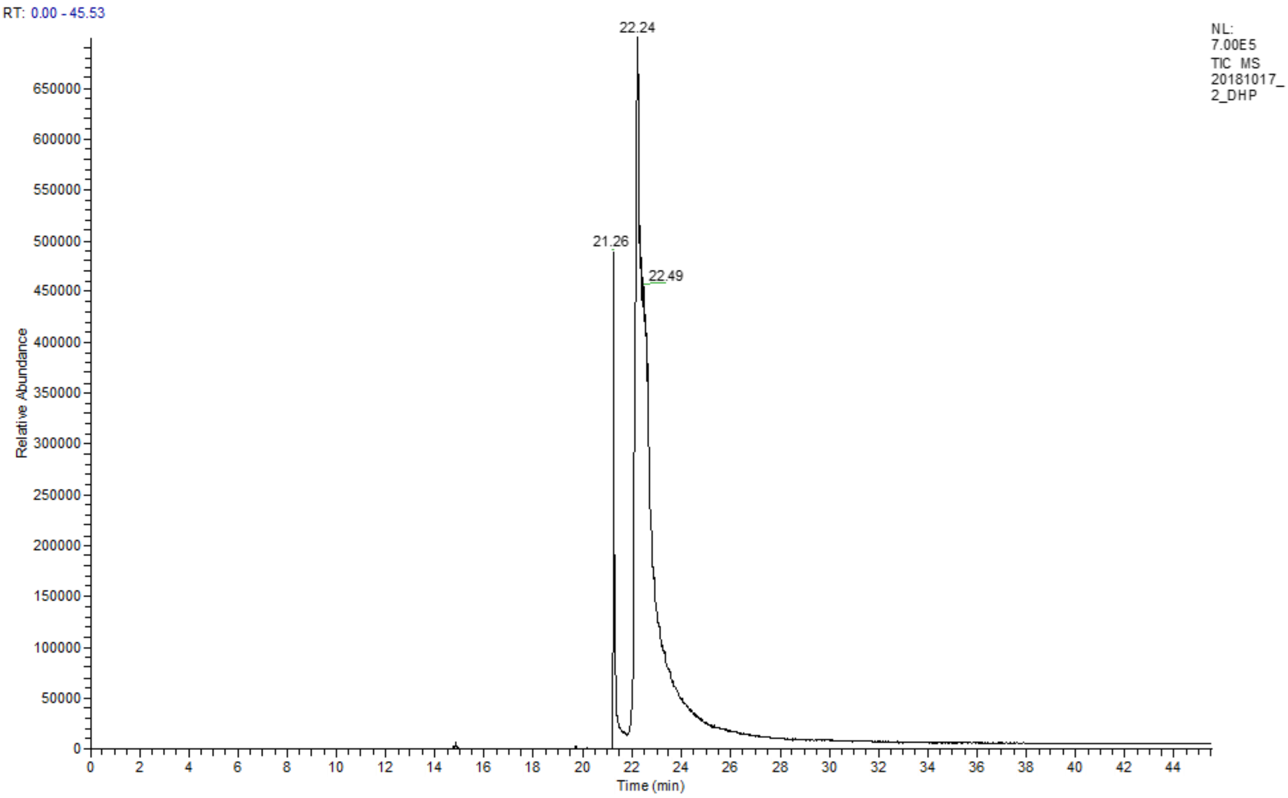


IR: 2.5 Fe/SiO_2

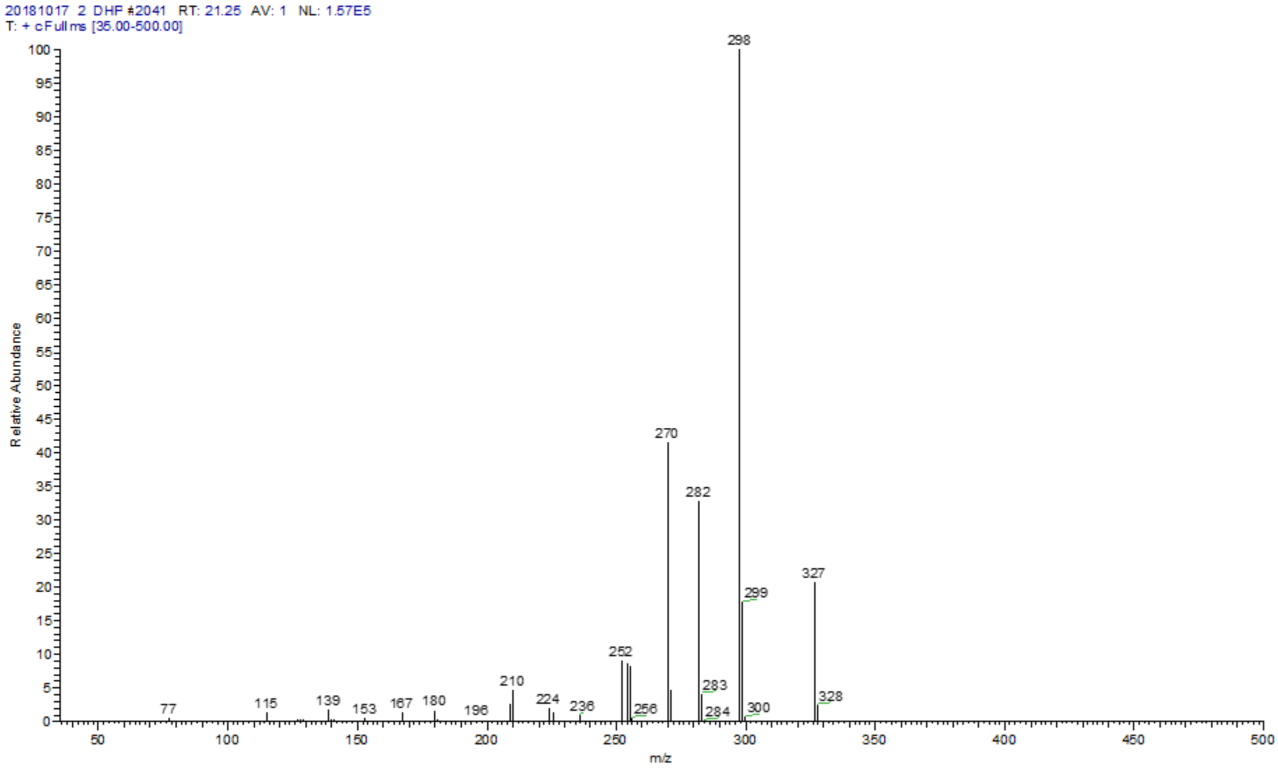


IR: 5% Fe/SiO_2

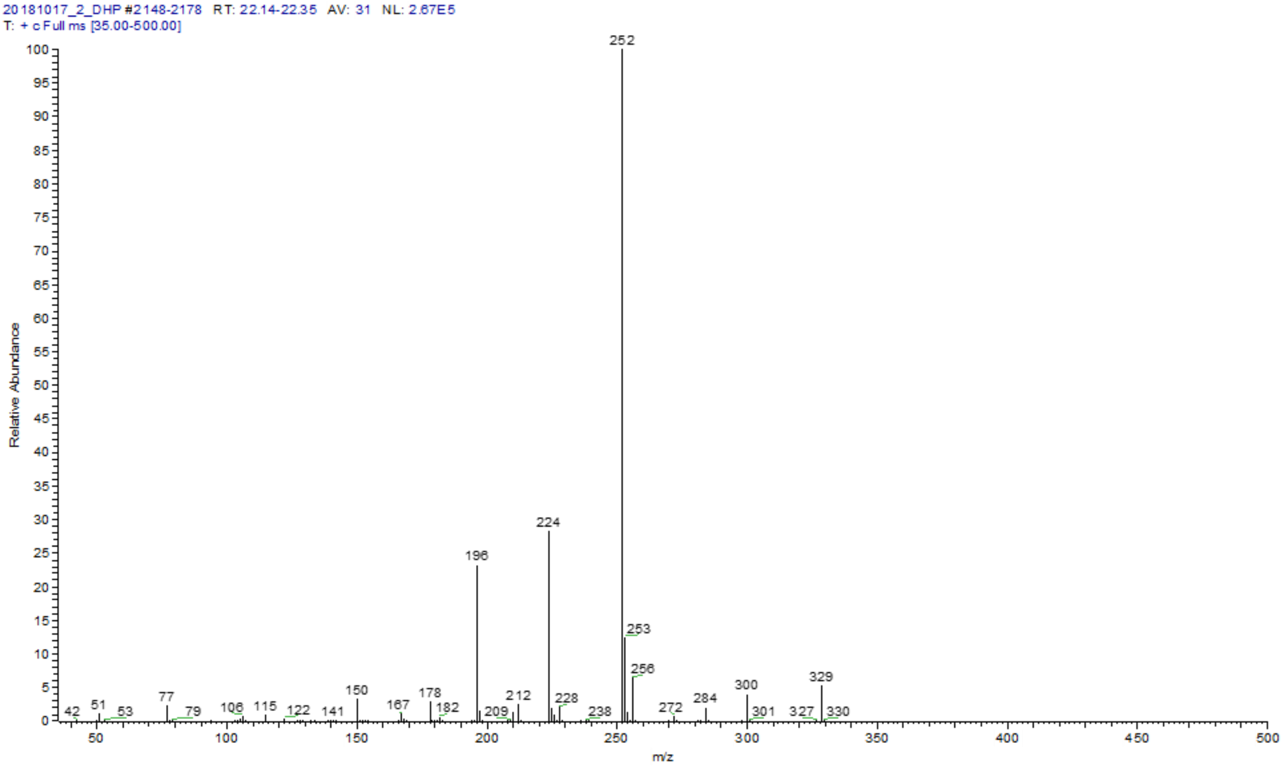
Appendix II (GC-MS)



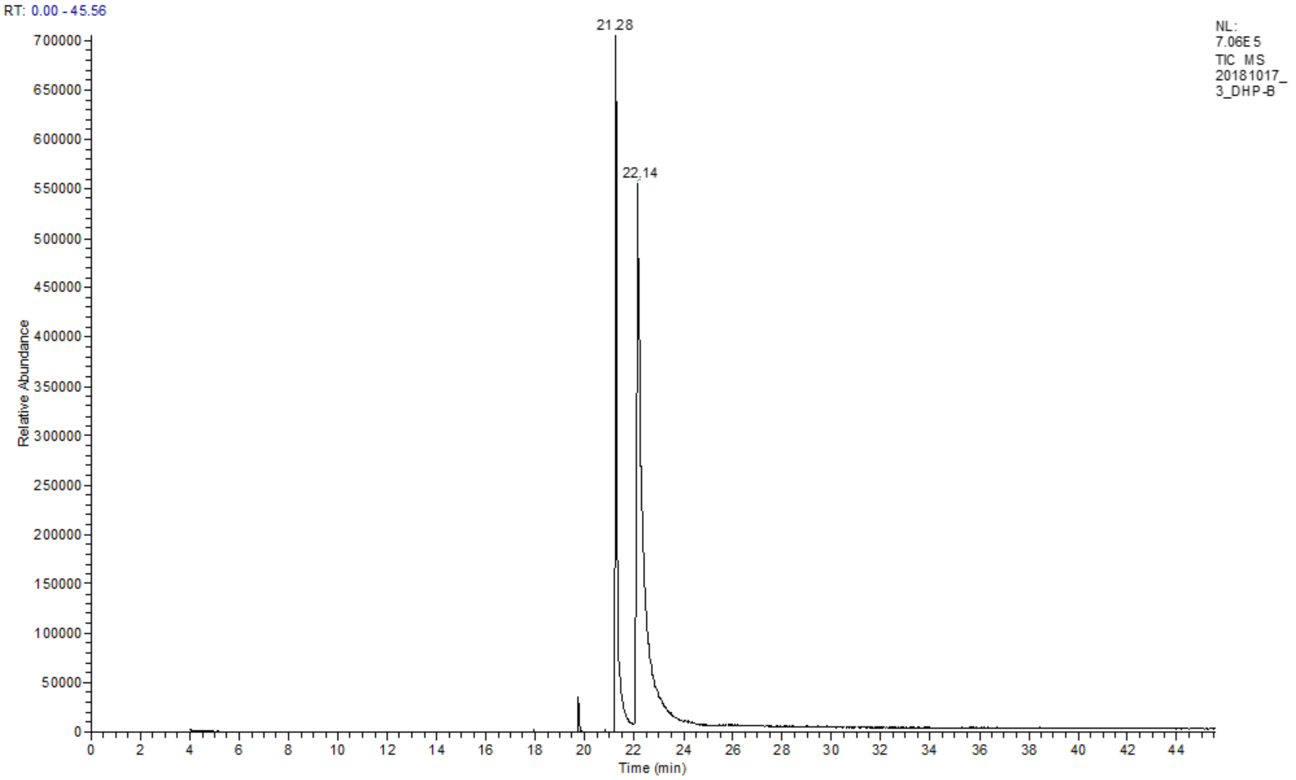
Total ion chromatogram of sample DHP.



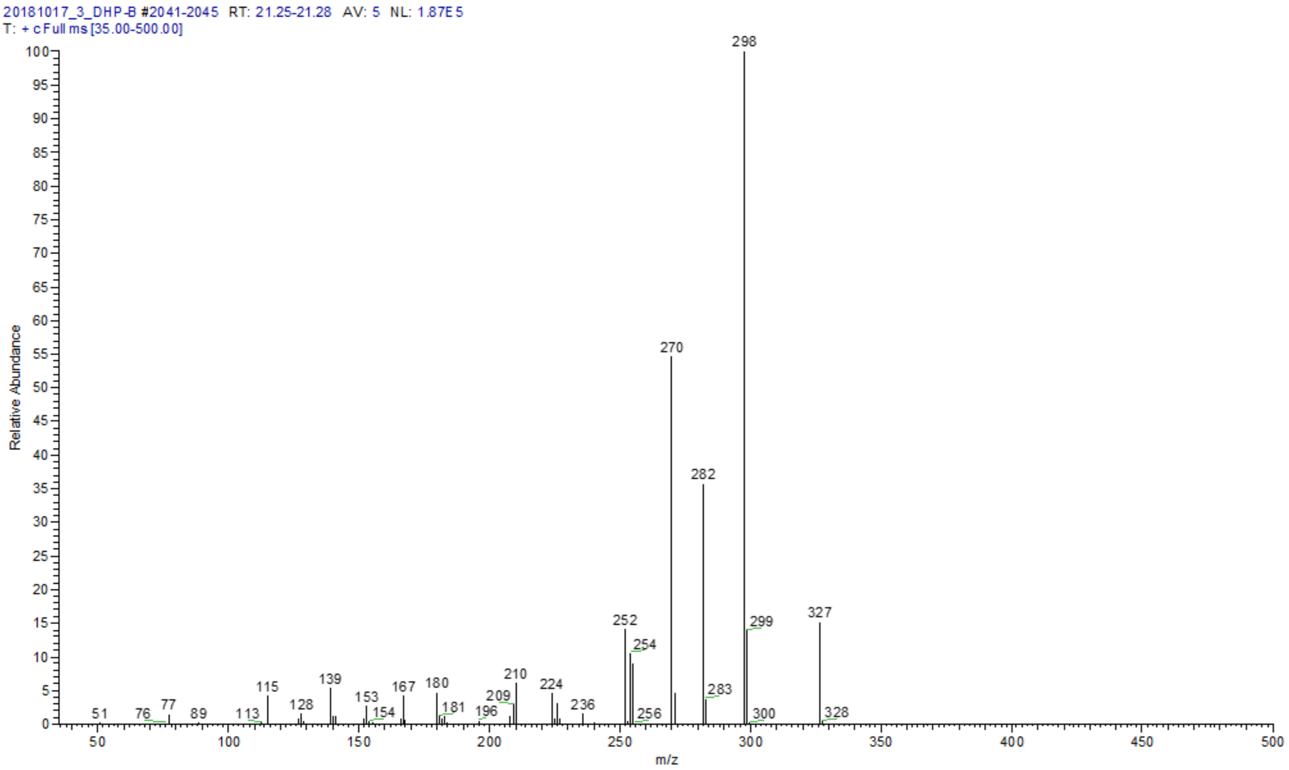
Electron ionization mass spectrum of the compound that elutes at Rt 21.26 min.



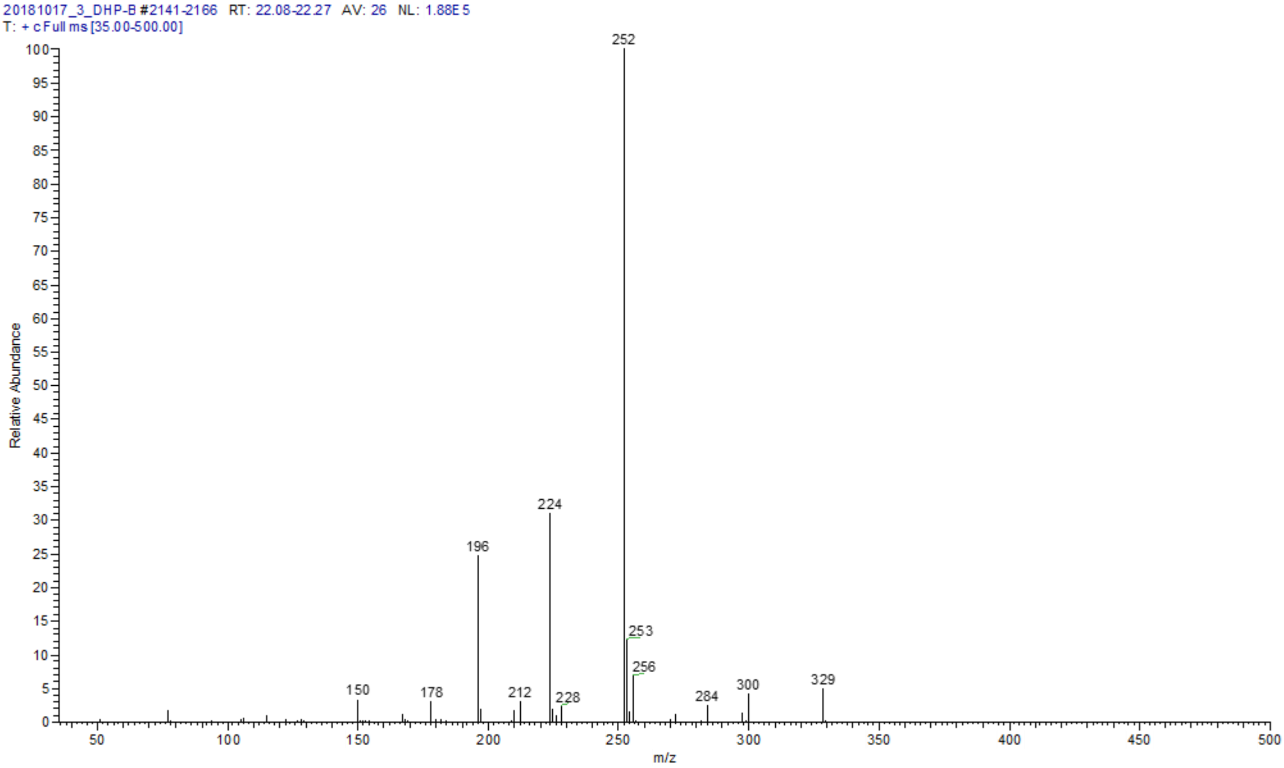
Electron ionization mass spectrum of the compound that elutes at Rt 22.24 min.



Total ion chromatogram of DHP sample B.



Electron ionization mass spectrum of the compound that elutes at Rt 21.28 min.



Electron ionization mass spectrum of the compound that elutes at Rt 22.14.