

## Green Synthesis of 2, 4, 5-triphenyl-1H-imidazole Derivatives by using Cellulose based Cerium (IV) Catalyst

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### Abstract

*We report simple, efficient and one pot multicomponent protocol for the synthesis of 2,4,5-triphenyl-1H-imidazole derivatives via reaction of various aromatic aldehyde and benzil in the presence of catalytic amount of cellulose based cerium (IV) catalyst. CMC-Ce<sup>IV</sup> was prepared by metathesis strategy and characterized by FT-IR techniques. The catalyst was recovered and reused for five several cycles without considerable loss of activity. The advantages of the protocol include rapid reactions with good yields and simple workup. The synthesized compounds were characterized by FT-IR technique.*

**Keywords:** Imidazole derivatives, Multi-component reaction, Metathesis Reaction.

### Introduction

Imidazole is an important core organic molecule. It is found in many naturally occurring compounds like vitamin B<sub>12</sub>, histidine, histamine, pilocarpine alkaloids, and biotin.<sup>1-3</sup> It is also showing good activity as herbicide, plant growth regulator, anti-epileptic, anticonvulsant, anti-inflammatory, analgesic, anticancer, etc.<sup>4-8</sup> Also, imidazoles are found as the main core molecule in drugs like Omeprazole, Pimobendan, Losartan, Olmesartan, Eprosartan, and Trifenagrel.<sup>9</sup>

Owing to their wide range of biological advancement, synthesis of title compounds are still of intrigue. The available reported method for the synthesis of substituted imidazoles suffers from drawbacks such as the catalysts used for synthesis are either toxic or expensive and requires harsh reaction condition. Therefore, a need still exists for further development of an efficient, reusable, inexpensive and eco-friendly catalyst for the synthesis of substituted imidazoles. In organic synthesis, the product yield and reaction time are extremely important. The increase in reaction

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steps results in a decrease in final product yield and increase in total reaction time. Multicomponent reactions help to solve this problem. By novel developing multicomponent reaction strategies, synthesis of the desired product in the one-pot method is possible thereby increases the product yield and reducing reaction time required for the reaction.

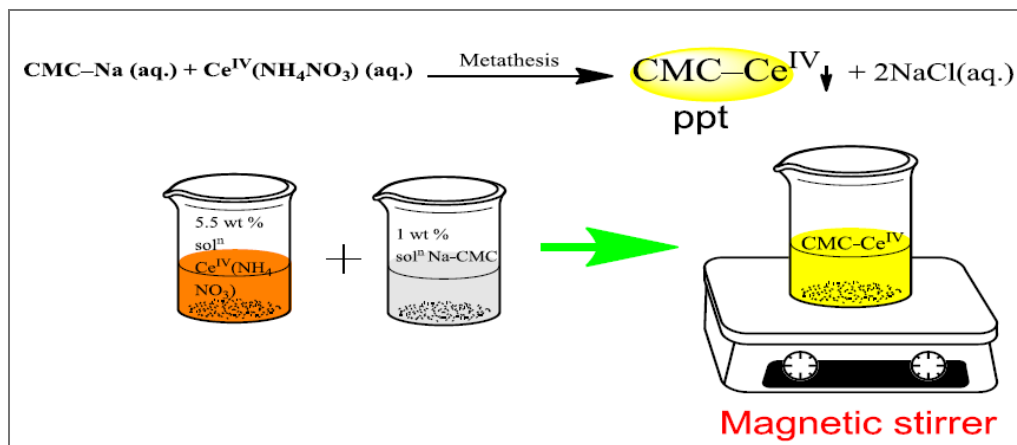
The interest in metal NPs, attributable to their high surface area, incredible availability, high biocompatibility and low toxicity. In addition, the high catalytic activity of metallic NPs can be accounted due to its Lewis acid site.<sup>10</sup> Considering these facts, we have decided to synthesize 2,4,5 triaryl-imidazole derivatives of various substituted benzaldehydes and benzil efficiently using CMC-Ce<sup>IV</sup> as a recoverable and reusable catalyst. For this transformation we used ethanol as green solvent and considering green chemistry approach.

## **Materials and Methods**

All reagents used were of laboratory grade. Melting points were determined in open capillaries. Progress of reaction was monitored by silica gel-G coated TLC plates in n-hexane: ethyl acetate system (9:1). The spot was visualized by exposing dry plate in UV chamber. IR spectra were recorded on Shimadzu FT-IR (Affinity Model) using KBr.

### **Preparation of Ce(IV) carboxymethylcellulose (CMC– Ce<sup>IV</sup>) Catalyst<sup>11</sup>**

The Ce(IV) carboxymethylcellulose (CMC– Ce<sup>IV</sup>) catalyst was prepared by metathesis reaction of ceric ammonium nitrate and Na-CMC. The yellow solid was precipitated which was left to equilibrate in a solution for overnight. The resulting yellow solid was separated from the solution and washed thoroughly with distilled water. The wet CMC– Ce<sup>IV</sup> was dried at 60°C in the oven till constant weight. (**scheme 1**)



### Scheme 1- Preparation of Ce(IV)carboxymethylcellulose (CMC– Ce<sup>IV</sup>) Catalyst<sup>11</sup>

General procedure for synthesis of 2,4,5-triphenyl-1H-imidazole derivatives by using CMC– Ce<sup>IV</sup> as catalyst:

In 150 ml round bottom flask, a mixture of benzaldehyde (10 mmol), benzil (10 mmol) and ammonium acetate (10mmol), as ammonia source, and CMC-Ce<sup>IV</sup>(20mg) were stirred and refluxed in ethanol for appropriate time (Table 1). The progress of the reaction was monitored by TLC. After completion of the reaction, the precipitate thus obtained was wash with ethanol and then purified by recrystallization by ethanol to get corresponding pure product (Scheme 2).

## Results and Discussions

### Optimized Reaction Conditions:

#### b) Effect of catalyst:

To optimize the reaction condition, we performed the model reaction of p-anisaldehyde with different amount of CMC– Ce<sup>IV</sup> catalyst loaded as shown in Table 1.

**Table 1: Optimized amount of catalyst loaded**

Entry	Catalyst (mg)	Time (min)	Yield (%)
1	5	80	60
2	10	50	82
3	15	35	90
4	<b>20</b>	<b>15</b>	<b>96</b>
5	25	15	93

It was found that, the 20 mg catalyst is sufficient to push the reaction forward.

#### b) Effect of the Solvent

To investigate the role of solvent in model reaction of p-anisaldehyde was performed in different

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solvent like ethanol, water and another organic solvent, as shown in **Table 2**.

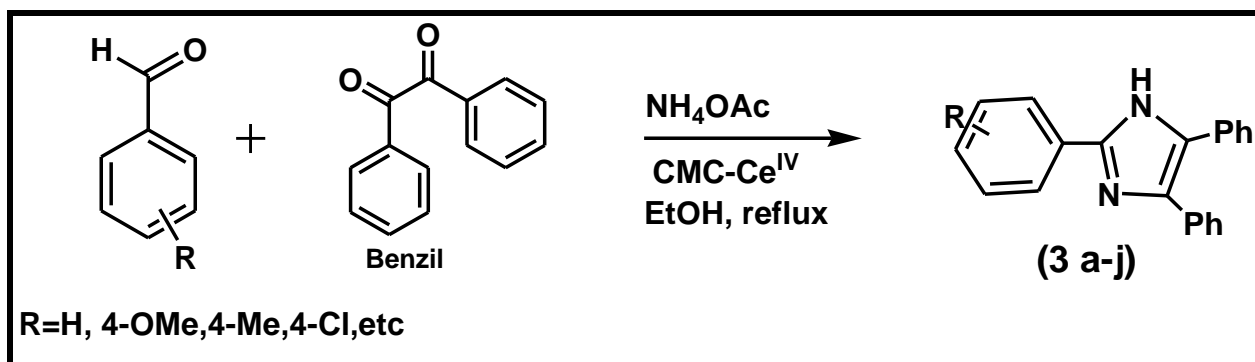
**Table 2: Effect of solvent**

Entry No.	Solvent	Time(Min)	Yield (%)
1.	Solvent Free	60	71
<b>2.</b>	<b>Ethanol</b>	<b>10</b>	<b>96</b>
3.	Water	20	40
4.	CH <sub>2</sub> Cl <sub>2</sub>	30	53
5.	n-Hexane	30	62
6.	Toluene	45	55

From the above table it clear in pure ethanol get high yield of product & minimum time required for the completion of reaction.

It was observed that, when we used pure ethanol as a solvent the yield of product increases up to 96% and time also reduced about 10 min. Imidazole formation was increases in ethanol, while the same reaction occurred slowly in water and another organic solvent.

After the study of above optimized reaction conditions were explored for the synthesis of series of 2,4,5-triphenyl-1H-imidazole derivatives(3 a-j) from various substituted benzaldehydes and benzil efficiently using CMC-Ce<sup>IV</sup> catalyst as shown in **Scheme 1** and the results of (3a-d) derivatives are summarized in **Table 3**.



**Scheme 1: Synthesis of 2,4,5-triphenyl-1H-imidazole derivatives**

**Table 3: Synthesis of 2,4,5-triphenyl-1H-imidazole derivatives (3a-d)**

Sr. No.	Substituted benzaldehyde s	Product	Time (min )	Yield (%)	Meltin g Point (°C)

3a.			15	90	210
3b.			15	92	250
3c.			20	90	252
3d			10	96	212

### Data

3a) Cream White solid, IR (cm<sup>-1</sup>): 3340(NH); 1668(C=N), 1587(CN), 1320 (CN), 1510 (C=C aromatic), 3061(C=CH).

3b) Yellow solid, IR (cm<sup>-1</sup>): 3319(NH); 1670(C=N), 1583(CN), 1311 (CN), 1520 (C=C aromatic), 3064(C=CH).

3c) Lemon Yellow solid, IR (cm<sup>-1</sup>): 3322(NH); 1648(C=N), 1590(CN), 1313 (CN), 1534(C=C aromatic), 3066(C=CH).

3d) Brown solid, IR (cm<sup>-1</sup>): 3340(NH); 1668(C=N), 1579(CN), 1315 (CN), 1519 (C=C aromatic), 3067(C=CH).

## **Applications**

These investigations involve use of green solvent method. The procedure offers advantages in terms of better yields, short reaction times, mild reaction conditions, and reusability of the catalyst. The low cost, and ready availability of catalyst, an environmentally benign procedure makes this methodology, a useful contribution to the existing procedures available for the synthesis of 2,4,5-triphenyl-1H-imidazole derivatives as a biologically and pharmaceutically relevant materials.

## **Conflict of Interest**

There is no conflict of interest for given article

## **Conclusion**

The CMC-Ce<sup>IV</sup> NPs were prepared by the ion exchange reaction. The inclusion phenomenon of sodium carboxymethyl cellulose with ceric ammonium nitrate was successfully characterized by FT-IR techniques. We have developed a simple and efficient protocol for one-pot synthesis of 2,4,5-triphenyl-1H-imidazole derivatives from various substituted benzaldehydes and benzil efficiently using CMC-Ce<sup>IV</sup> as a catalyst. The high catalytic activity of CMC-Ce<sup>IV</sup> was accounted due its Lewis acid sites. The advantages of procedure include simplicity of operation, good yields, wide substrate scope, no chromatographic separation technique, an easy recovery of the catalyst and recyclability of catalyst.

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## One-pot multicomponent synthesis of 2-amino-5,6,7,8-tetrahydro-4-phenylquinoline-3-Carbonitrile Derivatives

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### Abstract

*We report simple, efficient and one pot multicomponent protocol for the synthesis of the highly substituted 2-amino-5,6,7,8-tetrahydro-4-phenylquinoline-3-carbonitrile derivatives via the reaction of various aromatic aldehydes, malanonitrile, cyclic ketones and ammonium acetate in the presence of catalytic amount of cellulose based cerium (IV) as reusable catalyst at room temperature. For this transformation we used ethanol as green solvent and considering green chemistry approach. The synthesized compounds were characterized by FT-IR technique. The advantages of procedure include simplicity of operation, wide substrate scope, good yields, no chromatographic separation technique, and easy recovery & recyclability of the catalyst.*

**Keywords:** Multicomponent reactions, Green chemistry, aromatic aldehydes, Ce(IV)CMC, Pyridines.

### Introduction

In the recent years, all the chemist being focused on green chemistry by using environmentally benign reagent, prevent waste, design safer chemicals, no toxicity to human and environment. Particularly those reactions are performed by using green solvent, eco-friendly catalyst; maximize atom economy as well as reaction performs at room temperature, to increase energy efficiency<sup>1</sup>. Multicomponent reactions (MCRs) have becomes an important tool for the efficient synthesis of wide variety of organic molecule<sup>2-3</sup>.

Nitrogen contains heterocyclic compounds and their derivatives have attracted the attention of chemist mainly because of broad spectrum biological and pharmacological<sup>4</sup>.

A lot of pyridine derivatives possess a wide range of biological and pharmacological activities and are already used as dopamine transporter inhibitors, anti-inflammatory agent<sup>5</sup>, and antimicrobial agent<sup>6</sup>. The 2-amino-3-cyano-pyridine derivatives have medicinal



applications as such as analgesic and anti-pyretic properties<sup>7</sup>. Pyridine containing compounds have medicinal applications as anti-viral, anti-malarial and anti-cancer<sup>8</sup>.

Due to their wide range of biological advancement, synthesis of title compounds are still of intrigue. The preparation of 2-amino-5,6,7,8-tetrahydro-4-phenylquinoline-3-carbonitrile derivatives has been reported in the literature via a reaction of four components under reflux condition<sup>9</sup>. However many of these methods suffer from drawbacks such as expensive catalyst, long reaction time, low ordinary yield and environment pollution.

There is no attention has been paid to using biopolymer and its derivatives as a carrier in the preparation of support catalyst for this synthesis. The biopolymer carboxymethylcellulose (CMC) supported Ce<sup>IV</sup> metal particles provided good surface area, by cationic absorption of CMC makes it active catalyst<sup>10</sup>. Smaller particles are dispersed onto a high surface area refractory support. Nano-particles (NPs) of catalyst are dispersed on surface and make it more active<sup>11</sup>.

Considering these facts, we report simple, efficient and one pot multicomponent protocol for the synthesis of the highly substituted 2-amino-5,6,7,8-tetrahydro-4-phenylquinoline-3-carbonitrile derivatives, via the reaction of various aldehydes, malanonitrile, cyclic ketones and ammonium acetate in the presence of catalytic amount of cellulose based cerium (IV) as biodegradable catalyst at room temperature. For this transformation we used ethanol as green solvent and considering green chemistry approach.

### Materials and Methods

All reagents used were of laboratory grade. Melting points were determined in open capillaries. Progress of reaction was monitored by silica gel-G coated TLC plates in n-hexane: ethyl acetate system (9:1). The spot was visualized by exposing dry plate in UV chamber. IR spectra were recorded on Shimadzu FT-IR (Affinity Model) using KBr.

### Preparation of Cu(II)carboxymethylcellulose (CMC–Ce<sup>IV</sup>) Catalyst<sup>12</sup>

The Ce(IV)carboxymethylcellulose (CMC–Ce<sup>IV</sup>) catalyst was prepared by metathesis reaction of ceric ammonium nitrate and Na-CMC. The yellow solid was precipitated which was left to equilibrate in a solution for overnight. The resulting yellow solid was separated from the solution and washed thoroughly with distilled water. The wet CMC–Ce<sup>IV</sup> was dried at 60°C in the oven till constant weight.

### Synthesis of Polysubstituted pyridine by using CMC-Ce(IV) Catalyst

In 150 ml round bottom flask, a mixture of ketone (10 mmol), malononitrile(10 mmol) and

ammonium acetate (15 mmol), as ammonia source, and CMC-Ce<sup>IV</sup>(20mg) were added to 30ml ethanol solution of aromatic aldehyde (10 mmol) and stirred for appropriate times at room temperature (Table 3). The progress of the reaction was monitored by TLC. After completion of the reaction, catalyst was recovered simply by recrystallization of crude product in hot ethanol. Catalyst is insoluble in ethanol and by using this method catalyst was easily recovered and to get corresponding pure product.

### Result and discussion:-

#### Optimized reaction conditions:

##### a) Effect of the Solvent

It is well known that the reaction medium plays an important role on the reaction rate. To optimize the reaction condition; we performed the model reaction of p-nitro bezaldehyde and cyclohexanone using various solvent and without solvent as shown in **table (1)**.

**Table 1: Effect of solvent**

Entry No.	Solvent	Time(Min)	Yield (%)
1.	Solvent Free	150	71
<b>2.</b>	<b>Ethanol</b>	<b>120</b>	<b>93</b>
3.	Water	180	40
4.	CH <sub>2</sub> Cl <sub>2</sub>	180	53
5.	CH <sub>3</sub> CN	180	68
6.	n-Hexane	180	62
7.	Toluene	180	55

From the above table it clear in pure ethanol get high yield of product & minimum time required for the completion of reaction.

##### b) Effect of catalyst:

Initially we performed reaction without catalyst the yield of product only about 60% and time required was also more to complete the reaction. To optimize the reaction condition; we performed the model reaction of p-nitro bezaldehyde and cyclohexanone with different amount of CMC– Ce<sup>IV</sup> catalyst loaded as shown in **table-2**.

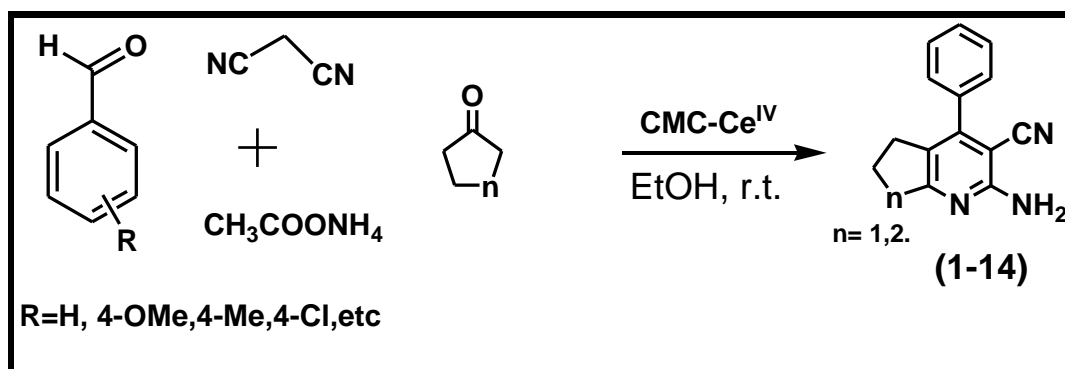
**Table 2: Optimized amount of catalyst loaded**

Entry	Catalyst (mg)	Time(Min)	Yield (%)
1.	0	150	60

2.	5	80	71
3.	10	60	93
4.	15	60	93

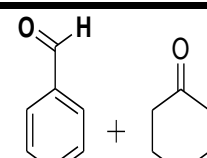
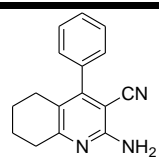
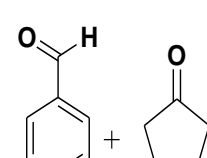
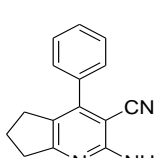
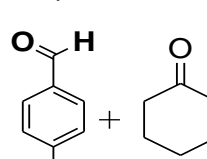
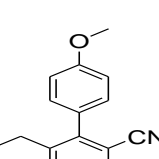
It was found that, the 10 mg catalyst is sufficient to push the reaction forward. Hence the reaction was performed with 10 mg catalyst by optimized the reaction condition.

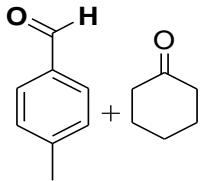
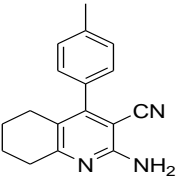
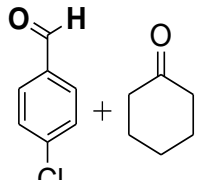
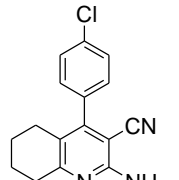
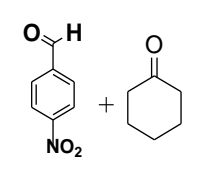
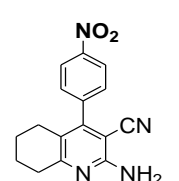
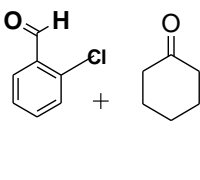
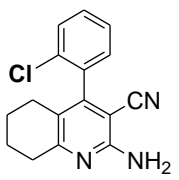
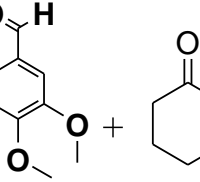
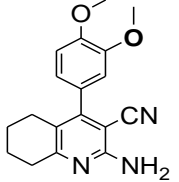
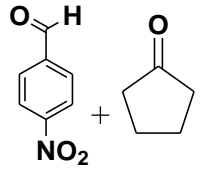
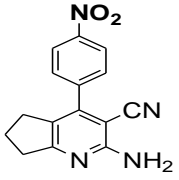
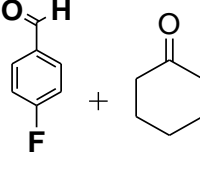
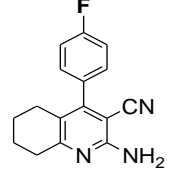
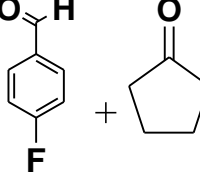
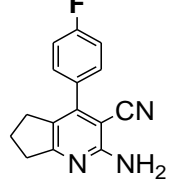
After the study of above optimized reaction condition were explored for the synthesis of series of 2-amino-5,6,7,8-tetrahydro-4-phenylquinoline-3-carbonitrile derivatives polysubstituted pyridines derivatives(1-14) from various substituted benzaldehyde, ketone, malononitrile and ammonium acetate using CMC-Ce<sup>IV</sup> as catalyst as shown in **scheme-1** and the results are summarized in **Table-3**.

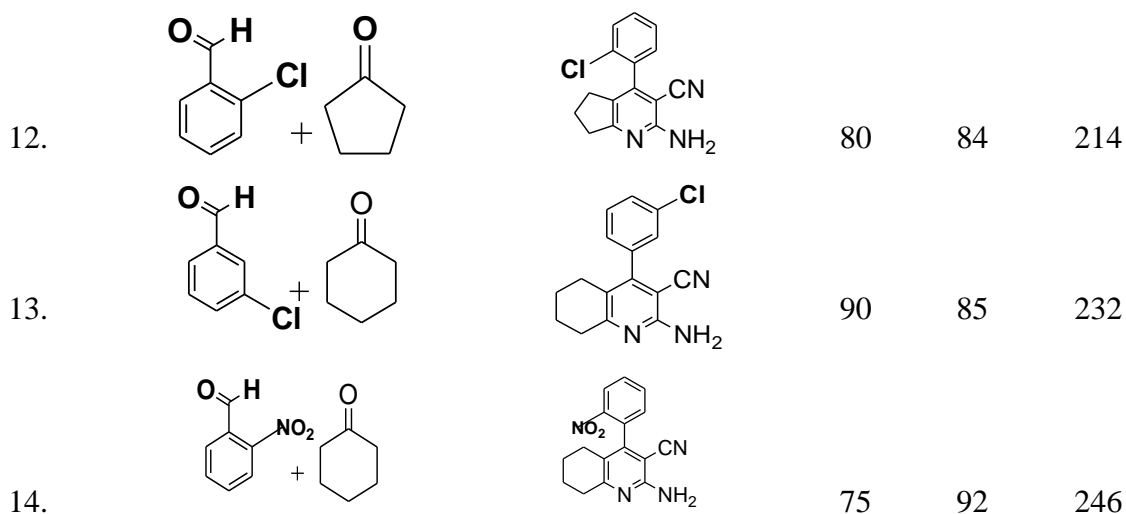


**Scheme 1:** Synthesis of polysubstituted pyridines by using CMC-Ce<sup>IV</sup> as catalyst

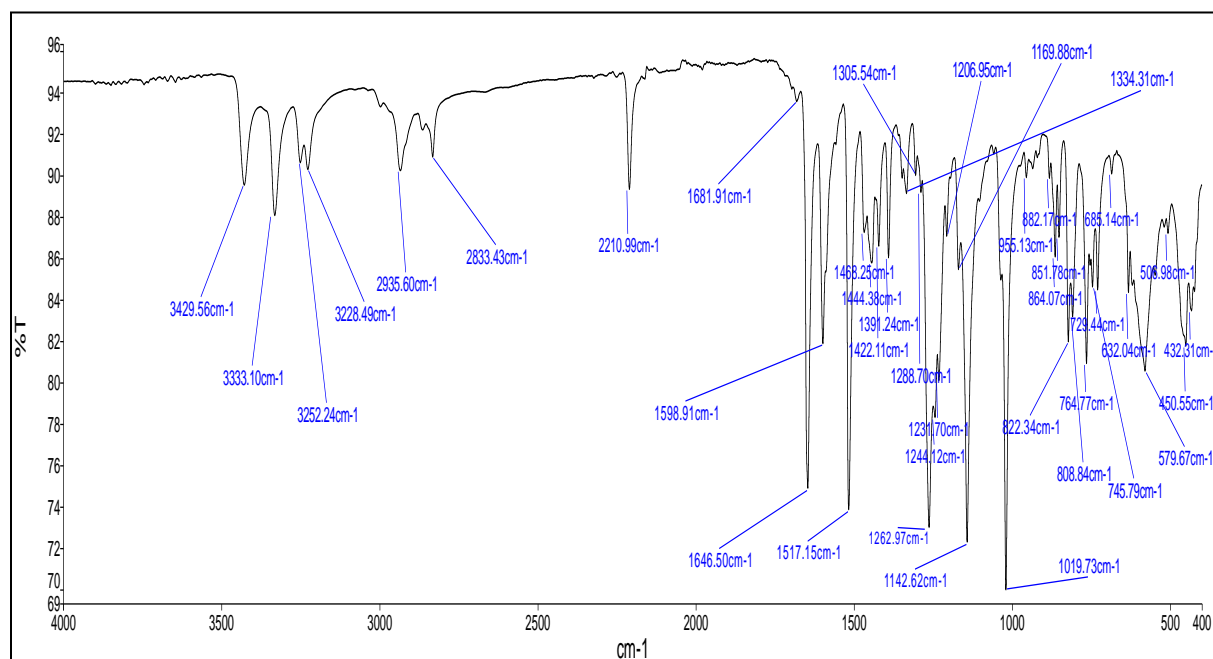
**Table-3:** Synthesis of polysubstituted pyridines derivatives(1-14)

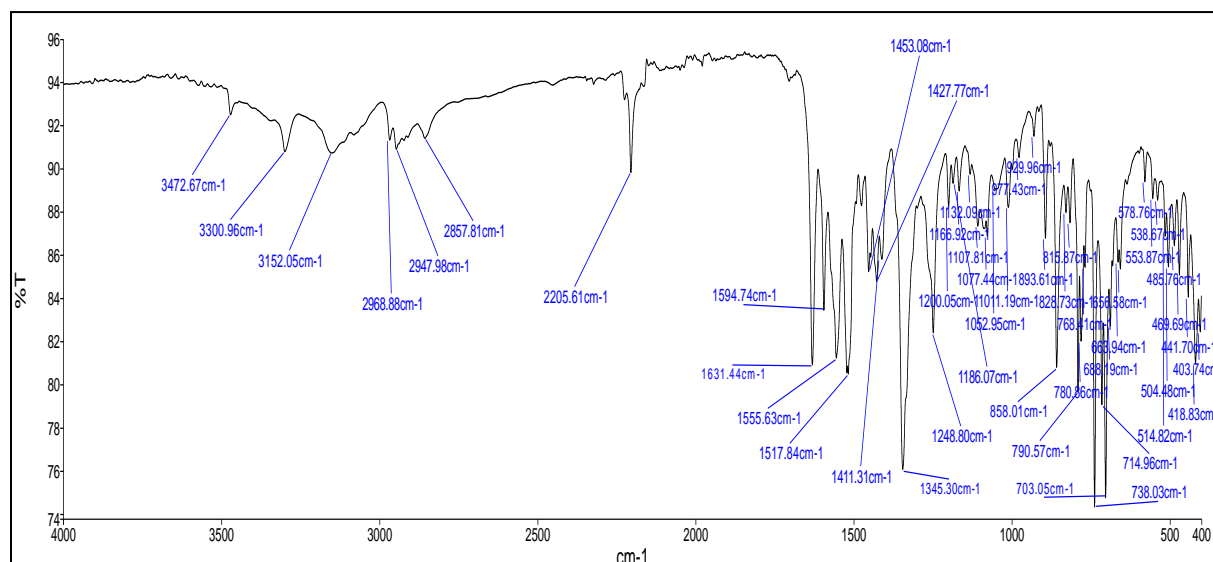
Entry NO.	Starting compounds	Product	Time (min)	Yield (%)	Melting point(°c)
1.			90	93	234
2.			80	88	218
3.			120	90	234

4.			80	92	246
5.			50	90	224
6.			60	93	232
7.			75	86	218
8.			80	92	214
9.			60	83	228
10.			80	88	256
11.			80	87	224



### IR Spectra of compounds (1&2)





### Data

- 1) Cream white IR ( $\text{cm}^{-1}$ ): 3333.1(-N-H); 2210.9 (-CN), 1646.5(C=N), 1589.2(C=C), 1330 (C-N),
- 2) White solid, IR ( $\text{cm}^{-1}$ ): 3300.9(-N-H); 2205.6(-CN), 1631(C=N), 1594.74(C=C), 1311 (C-N), 790.57(C-Cal)
- 3) White solid, IR ( $\text{cm}^{-1}$ ): 3339.9(-N-H); 2235.99 (-CN), 1603.3(C=N), 1598.74(C=C), 1344 (C-N),
- 4) Brown solid, IR ( $\text{cm}^{-1}$ ): 3349.0(-N-H); 2211.3(-CN), 1638(C=N), 1589.2(C=C), 1311 (C-N), 1346.86( $\text{NO}_2$ )
- 5) Pale Yellow solid, IR ( $\text{cm}^{-1}$ ): 3338.0(-N-H); 2227.(-CN), 1661(C=N), 1589.2(C=C), 1311 (C-N),
- 6) White solid, IR ( $\text{cm}^{-1}$ ): 32909.9(-N-H); 2205.99 (-CN), 1623.3(C=N), 1578.74(C=C), 1304 (C-N),

### Conflict of Interest

There is no conflict of interest for given article

### Conclusion

The CMC-Ce<sup>IV</sup> NPs were prepared by the ion exchange reaction. The inclusion phenomenon of sodium carboxymethyl cellulose with ceric ammonium nitrate was successfully characterized by FT-IR techniques. We have developed a simple and efficient protocol for one-pot synthesis of the highly substituted 2-amino-5, 6, 7, 8-tetrahydro-4-phenylquinoline-3-carbonitrile derivatives via the reaction of various

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aldehydes, malanonitrile, cyclic ketones and ammonium acetate in the presence of catalytic amount of cellulose based cerium(IV) as reusable catalyst at room temperature. For this transformation we used ethanol as green solvent and considering green chemistry approach. The high catalytic activity of CMC-Ce<sup>IV</sup> was accounted due its Lewis acid sites. The advantages of procedure include simplicity of operation, wide substrate scope, good yields, no chromatographic separation technique and an easy recovery of the catalyst and recyclability of catalyst.

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