Synthesis of N-Mannich bases from 3, 4-dihydropyrimidin-2(1H)-ones by using nanostructured Cobalt Chloride Doped Polyaniline Composite as Catalyst (PANI-Co)

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Abstract: The Mannich reaction is the type proton assisted of carbon-carbon bond formation reaction that involves the addition of resonance-stabilized carbon nucleophiles to iminium salts and imines. The product of the Mannich reaction is β-amino carbonyl compounds of biological interest synthesized from the aldehyde, amine, and carbonyl compounds. This reaction is very limited to the only highly reactive aldehydes such as formaldehyde and acetaldehyde, a secondary amine. The direct Mannich-type reaction expanded with the development of the scope of Mannich reaction, and very much efficient method for highly stereo selective type Mannich reactions were extensively well studied and reported in the literature. This study aimed at investigating the synthesis of N-Mannich Bases from the 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co). The Synthesis of N-Mannich Bases from 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co) was carried out. The effective method for the synthesis of the Mannich bases of synthetically important compounds has been coined. We synthesized the different Mannich Bases from 3, 4-Dihydropyrimidin-2(1H)-ones which give up to 94 % yield.

1. Introduction
The end product of the Mannich reaction is beta amino compound [1-2]. The Mannich reaction is a type of nucleophilic addition reaction in the condensation of a compound with active hydrogen(s) with primary or secondary amine and formaldehyde [3]. The general schematic representation of Mannich reaction is given in fig. 1. The Mannich bases has found to be the great synthetic important and it acts as a biologically active compound and it is a potential agents for the synthesis of various medically valuable compounds which composes the amino alkyl chain in it. The amino alkyl chain containing mannich bases are clinically important for example, biperiden cocaine, ethacrynic acid, atropine, ranitidine, trihexyphenidyl, fluoxe- tine procyclidine, etc. [4–6]. The Mannich bases are reactive compound and can be converted in to the other compound easily for example active amino alcohols physiologically [7].

The Mannich bases also possesses the number of potent activities such as anti-HIV [8], antimalarial [9], antifungal [10, 11], anticonvulsant [12], antiviral [13], antifilarial [14], anticancer [15, 16], anthelmintic[17], antibacterial [18,19], antipsychotic [20], antitubercular [21, 22], analgesic [23], anti-inflammatory [24, 25], along with the biological activity the Mannich bases are found to their extensive use in the detergent synthesis and commonly used as a additive in it. Such as the polymers surface active reagents[26]. The Mannich bases and the derivatives of these bases are extensively used as the intermediates for the synthesis of the biologically active compounds [27,28]. Also the extensive use of this reaction is to prepare or synthesized the compound containing Nitrogens [29].
The Mannich bases have the great importance in antibacterial activity [30], and also found to have the extensive use in the field of the agrochemicals as growth regulators in the plants.

In this present research work we have synthesized the N-Mannich Bases from 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co). The 3, 4-Dihydropyrimidin-2(1H)-ones were synthesized by the well known reaction called as the Bijinelli reaction by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co). The Bijinelli reaction is a multicomponent reactions (MCR) are defined as the reaction in which three or more different reactant molecules that react to form a product, where most, if not all of the atoms are incorporated in the final product. This reaction tool allows compounds to be synthesized in a few steps and usually in one-pot operation. The multicomponent reactions (MCRs) define the new horizons towards the development of organic synthesis. Obviously, due to this reason MCRs are underlined as important routes and protocols in organic synthesis and medicinal chemistry [31].

The general schematic representation of synthesis of 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co), is given in Fig.2. The synthesis of the N-Mannich Bases from 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co), was found to be the convenient method for the synthesis of the number of the Mannich bases which was characterized and found to have the extensive use in the synthetic chemistry. The general schematic representation of the synthesis of N-Mannich Bases from 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co) is given in the fig.3.

There are seven Mannich bases have been synthesized from the 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co) and they were found to have the excellent result with the good yield of the Mannich product.

| Sr. | Product | Time | Isolate | Melting Point | Mannich Base |
|-----|---------|------|---------|--------------|--------------|
|     |         |      |         |              |              |
| No. |   | Yield % | Obs.  | Reported   |
|-----|---|---------|-------|------------|
| 1   | 25| 70      | 251   | 255-257[32]|
| 2   | 30| 88      | 203   | 206[33]    |
| 3   | 30| 71      | 229   | 259-260[34]|
| 4   | 30| 85      | 217   | 209-212[34]|
| 5   | 30| 92      | 211   | 213-214[34]|
| 6   | 20| 94      | 229   | 230-231[34]|
Table. a. Reaction conditions: aldehyde = 20 mmol, urea/thiourea=25 mmol, β-keto-ester =15 mmol, catalyst = 25 wt. % with respect to aldehyde, solvent free, temp. = 35°C. All compounds are well characterized by spectroscopic techniques.

The 3, 4-Dihydropyrimidin-2(1H)-ones by Cobalt Chloride Doped Polyaniline nanostructure (PANI-Co) catalyst [35-39], green organic chemistry [40, 41]. Previously, we have reported Cobalt Chloride Doped Polyaniline (PANI-Co) composite as a heterogeneous Catalyst basic and synthesis of beta- amino carbonyl compounds [41]. From the above 3, 4-Dihydropyrimidin-2(1H)-ones we have synthesize the Mannich base and got the good result.

1.1 The Representative Data of Few Compounds

5- Ethoxycarbonyl-4-(2-methoxyphenly)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (Table;a Entry 1)

Yellowish solid, obtained in 68 % yield, Mp: 257 °C. IR (KBr) νmax: 3240, 3174, 2960, 1693, 1643, 1514, 1462 cm⁻¹. ¹H NMR (DMSO-d₆): δ = 9.14 (s,1H,NH), 7.31(s,1H,NH),7.24 (m,1H,CH ), 7.05(d,1H, J= 6.2 Hz,CH), 6.99 (d,1H,J=8.2 Hz,CH), 6.88(m,1H, CH), 5.49 (d,1H, 3=2.9 Hz, CH), 3.92 (q, 2H, J=7.1 HzOCH₂), 3.94 (s,3H,OCH₃), 2.28(s,3H,CH₃), 1.03 (t, 3H, J = 7.1Hz, CH₃). Mass (ES/MS): M/Z 290 (M-H).

5-Ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one (Table ;a, Entry 02)

Yellowish solid, obtained in 93 % yield, Mp: 205°C, IR (KBr) νmax : 3242, 3117, 2980, 1721, 1637, 1522, 1462, 1288, 1092, 770 cm⁻¹. ¹H NMR (DMSO-d₆): δ=9.18 (s, 1H, NH), 7.74 (s, 1H, NH), 7.22 (m, 5H arom), 5.14(d, 1H, J=3.6 Hz, H-4), 3.40 (q, 2H, J=6.9 Hz, OCH₂), 2.24 (s, 3H, CH₃), 1.09 (t, 3H, J=6.9 Hz, CH₃). Mass (ES/MS): m/z 259 (M-H).

2. Experimental Details
2.1 Material

All chemicals supplied by the Merck (Extra pure) Chemical Companies and used were without further purification. IR spectra were recorded on a Perkin-Elmer 1640 FT-IR instrument. The ¹H- and ¹³C-NMR spectra were recorded on a Bruker DPX-300 NMR machine. Unless otherwise specified,
CDCl$_3$ was used as solvent. Mass spectra were recorded with a Bruker Daltonic Data Analysis 2.0 spectrometer.

**2.2 Preparation PANI-Co composite as a catalyst**

The nanostructure Cobalt Chloride Doped Polyaniline (PANI-Co) composite as Catalyst was prepared by the chemical doping method. The polyaniline was synthesized by the chemical oxidization method at low temperature (0 to 5$^\circ$C). Ammonium Persulphate and Hydrochloric acid used as a oxidizing agent as received without further purification. 15 ml Aniline was first dissolve in 2 M 100 ml Hydrochloric Acid (HCl) (Merck). Then this solution is kept in the ice bath below 5$^\circ$C temperature. Ammonium Persulphate solution (Usually 10%) was added to the above solution with constant stirring. This polymerization process were completed within the three to four hours and the finally the green color polyaniline was formed. It is washed with the hot dilute HCl and dried it in the oven for 24 Hours.

An appropriate amount of the Cobalt Chloride 0.1 M was dissolve in polyaniline (PANI) solution. Doping of cobalt was done by the chemical doping method. For uniform distribution of cobalt to form the Cobalt Chloride Doped Polyaniline (PANI-Co) composite stirring was continued for 2 hours. PANI-Co composite was formed and confirmed by the instrumental technique and used as the effective catalyst.

**2.3 General procedure of synthetic 3,4-dihydropyrimidin-2(1H)-one**

A mixture of aromatic aldehyde (1 mmol), 1,3-dicarbonyl compounds (1 mmol), urea or thiourea (1.5 mmol) was prepared. After that we added nanostructured Cobalt Chloride Doped Polyaniline (PANI-Co) composite (3 mol %) as catalyst. The mixture was dissolved in 2mL of absolute ethanol. The mixture was refluxed for suitable time and the progress of the reaction was monitored by TLC. After completion of the reaction the catalyst was recovered by filtration, the filtrate was evaporated and the solid was then washed with cold water. Recrystalize the product with ethanol we got the pure 3,4-dihydropyrimidin-2(1H)-one.

**2.4 General procedure of synthesis of the Mannich Base**

The solution of the DHPMs (0.2 Mole) (I), Formaldehyde (0.4 Mole) (II) will be added under stirring. The reaction Mixture will be stir at room temperature for some time to complete the reaction of formaldehyde and to yield the methylol derivative of DHPM. To this solution the solution of Secondary amine (0.2 Mole) (III) will be added dropwise and reflux for half an hour. The workout the reaction by pouring the reaction mixture in the ice cold water. Then recrystalized the product by Chloroform to give the Mannich Base.

**3. Results and Discussion**

The synthesis of N-Mannich Bases from 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co), was carried out according to the reaction as shown in the Fig.3 and found to be the most effective method for the synthesis of the Mannich bases of synthetically important compounds.

**4. Conclusion**

In this above reported work we investigated the methodology for the synthesis of Synthesis of N-Mannich Bases from 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co). We synthesize the nine different Mannich Bases from 3, 4-Dihydropyrimidin-2(1H)-ones which give 94 % yield by using the these 3, 4-Dihydropyrimidin-2(1H)-ones by using nanostructure Cobalt Chloride Doped Polyaniline composite as Catalyst (PANI-Co).

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