# Green Protocol For Synthesis of 7 (1Hbenzimidazol-2-Yl)-5-(Substituted Phenyl) Pyrido [2, 3-D] Pyrimidin-4-Amine

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**Abstract**

*Sequence of 7-(1H-benzimidazol-2-yl)-5-(substituted phenyl) pyrido [2, 3-d] pyrimidin-4-amine were synthesized by reacting substituted cyanopyridine derivatives with formamide, formic acid and dimethyl formamide using green approach. The synthesized compounds are studied for their spectral analysis. These compounds are studied for in vitro antioxidant activity by agar diffusion and DPPH methods, respectively. These compounds show better activity.*

**Key words**: Benzimidazole, Spectral Chacterisation, antioxidant activity.

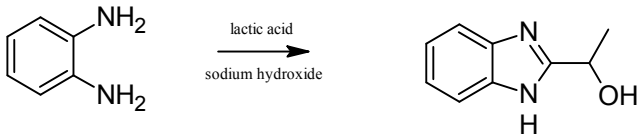
## Introduction

Most of the hetocyclic compounds having the pyridopyrimidine as basic nucleus having very intrusted pharmacological activities interesting pharmacological properties. One of them pyridopyrimidine derivatives has versatile biological activities like antiinflammatory[1], antifungal[2] anti-tumor[3] and antimicrobial[4] etc. Most of the Benzimidazole derivatives represent one of the most active of biological compounds. Many of them have very good biological activity such as antifungal[5], antibacterial [6] anticancer [7], Anthelmintic[8,-14] other vast biological activities. Selected of these compounds activities include , antioxidant. Due to this immense importance we have planned for synthesis of these compounds. The synthesis of 7-(1H-benzimidazol-2-yl)-5-(substituted phenyl) pyrido [2, 3-d] pyrimidin-4-amine. The antioxidant activity was performed by DPPH· method using ascorbic acid as standard.

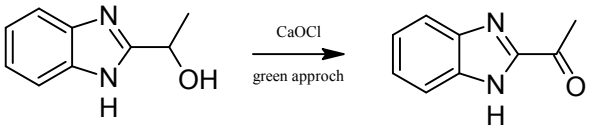
Green route used for the synthesis of these benzimidazole derivatives compounds **were** synthesized by reacting 2-amino-6-(1*H*-benzimidazol-2-yl)-4-(substituted phenyl) pyridine-3-carbonitrile with formamide, formic acid and dimethyl formamide in sonication method . 2-amino-6-(1*H*-benzimidazol-2-yl)-4-(substituted phenyl) pyridine-3- carbonitrile **(**was prepared by reaction between benzimidazole chalcone in malanonitrile and ammonium acetate in ethanol medium under sonication method. Benzimidazole chalcone was prepared by reaction between 2-acetyl benzimidazole **in** potassium hydroxide in aromatic aldehydes in microwave method . 2-acetyl benzimidazole was prepared by reaction between 2-(α-hydroxyethyl) benzimidazole in potassium dichromate in sulphuric acid medium in Sonication . 2-(α-hydroxyethyl) benzimidazole was prepared by reaction between o-phenylenediamine (**1**) and lactic acid in sodium hydroxide medium[11-12.]

**Reaction Scheme**

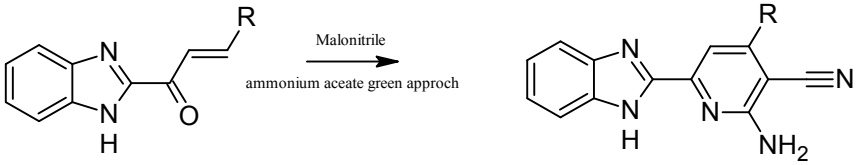
**Step I**



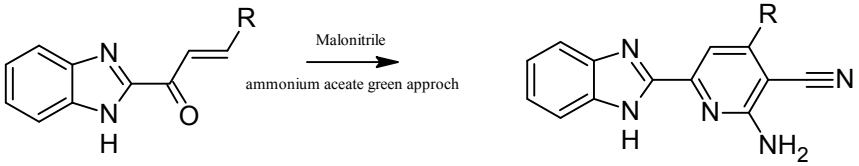

**Step II**



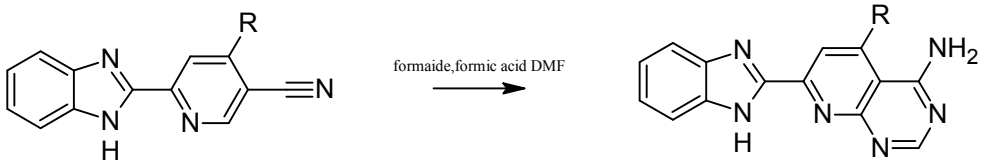

Step III




Step IV




Step V




## Experimental

Melting points of the synthesized compounds were determined using Thiele's method were found uncorrected. The IR spectra of the synthesized using Automated IR spectra and frequencies were recorded in wave numbers (cm-1). The 1H NMR spectra were recorded on Punjab university Chandigarh Chemical shifts (δ) are reported in parts per million (ppm) down field from internal reference tetramethylsilane (TMS). Purity of the compounds was studied by thin layer chromatography.

***Step I: Synthesis of 2-(α-hydroxyethyl) benzimdiazole:***

A mixture of 10 mmol of o-phenylene diamine, lactic acid 30 mmol and ferrous sulphate 2 gm. were taken in conical flask and kept in microwave oven for specified time. Check progress of reaction using thin layer chromatography .after completion of reaction, Cool at room temperature. The completion of this reaction was monitored by TLC. The resulting solution was filtered and washed with water dried into vacuum and recrystallized from ethanol.

***Step II: Synthesis of 2 – acetyl Benzimidazole:***

To a solution of **(** 10 mole) in Dioxane (20 ml), was added solid CaOCl2 (1.42gm, 10 mole) and the solution was sonicated at 40 $^0$c for 2 - 4 hrs. During this period, the progress of the reaction was monitored on TLC for the disappearance of the starting material. No product formation was observed on TLC and starting material was recovered on processing the reaction mixture by filtration and evaporation of the filtrate.

***Step III: Synthesis of Arylidene acetophenones***

Derivatives: Sodium hydroxide pellets (0.02mmole) and compound from (10mmoles) were ground in a mortar to a fine powder at room temperature. To this 10mmoles of aromatic aldehyde is added and the mixture was at for sonication a few more minutes till the condensation was complete as shown by TLC. After completion of reaction pour product in crushed ice neutralized by dilute hydrochloric acid. The crude compound was recrystallized from a suitable organic solvent (acetic acid) to get the pure product. A single spot on the TLC plate confirmed the purity.

***Step IV: Aldol condensation reaction***

10 mmole of compound from step III in dry conical flask to this add 10 mmole of the malanonitrile and 20 mmole of the ammonium acetate sonicate this mixture at 40 0c for 2 hours, check progress of reaction using thin layer chromatography, after completion of reaction pour reaction mixture over crushed ice to obtain the product. Purify the product using acetone as solvent.

***Step V: 7-(1hbenzimidazol-2-yl)-5-(substituted phenyl) pyrido [2, 3-d] pyrimidin-4-amine***

A mixture (10 mmol) from step IV , formamide (10 MMOLE ), formic acid (10m mol) and dimethyl formamide (10 mol) were taken in 100 mL round bottom flask, sonicate for 6 h at 40$^o$C.The reaction completion was monitored through TLC and reaction medium was cooled, the product obtained was filtered and recrystallized with ethanol. The formation of 7-(1hbenzimidazol-2-yl)-5-(substituted phenyl) pyrido [2, 3-d] pyrimidin-4-amine is
Confirmed by the difference in M.P. and Rf value.

## Result

**Table 1 7-(1hbenzimidazol-2-yl)-5-(substituted phenyl) pyrido [2, 3-d] pyrimidin-4-amine derivatives**

| Sr.No. | Compound with aldehyde | Molecular weight | Melting point(0c) | % yield |
|---|---|---|---|---|
| 1 | C6H5 | 339 | 195 | 67 |
| 2 | FC6H4 | 356 | 186 | 71 |
| 3 | ClC6H5 | 372 | 170 | 70 |
| 4 | OHC6H4 | 355 | 178 | 74 |
| 5 | OCH3C6H4 | 369 | 170 | 75 |
| 6 | N(CH3)2C6H4 | 381 | 165 | 76 |

## Spectral Analysis

**Compound 1**

**7-(1*H*-benzimidazol-2-yl)-5-phenylpyrido [2, 3-*d*] pyrimidin-4-amine (6a)**

**IR (υ, cm-1)** 2460 ($NH_2$), 1869 (ArC-H), 1231 (C=N), 1209 (ArC=C).

**$^1$H NMR** ($CDCl_3$, 400 MHz) δ (ppm), 5.2 (s, 2H, -$NH_2$), 4.82 (s, 1H, -NH), 7.32-7.428 (s, 5H, Ar-H), 7.26 -6.45 (s, 4H, Ar-H), 7.7 (m, 1H, -CH), 8.0 (s, 1H, Ar-H),

**Spectral Analysis**

**Compound 4**

**IR (υ, cm-1),** 3310 ($NH_2$), 2747 (ArC-H), 1611 (C=C), 1647 (-OH) .

**$^1$H NMR** ($CDCl_3$, 400 MHz) δ (ppm), 3.74 (s, 2H, -$NH_2$), 4.70 (s, 1H, -NH), 5.72 (s, 1H, Ar-OH),6.81-7.97 (s ,4H, Ar-H), 7.77-8.05 (s, 4H, Ar-H), 7.57 (s, 1H, Ar-CH ),

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