



**One Step Three Component Synthesis of Highly Substituted
Pyridine using Barium Oxide Nanoparticles as a Catalyst**

Report of a project carried out as a part of curriculum for the Degree of
Master of Science in Organic Chemistry

CHO-453

Submitted by

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2021-2022

DECLARATION BY THE CANDIDATE

I hereby declare that this project entitled "**One Step Three Component Synthesis of Highly Substituted Pyridine using Barium Oxide Nanoparticles as a Catalyst**" is a confide and genuine project work carried out by us under supervision of **Dr. Amol Haridas Kategaonkar**, Assistant Professor, P.G. Department of Organic Chemistry, M.V.P. Samaj's K.S.K.W. Arts, Commerce and Science College CIDCO Uttamnagar, Nashik, Maharashtra.

Date- 22.06.2022

Place- Nashik



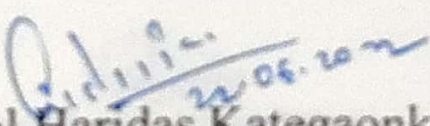
MISS. DEORE NEHA HIMMAT

CERTIFICATE BY THE SUPERVISOR

This is to certify that entitled "One Step Three Component Synthesis of Highly Substituted Pyridine using Barium Oxide Nanoparticles as a Catalyst" is a bonafide and genuine project work done by MISS DEORE NEHA HIMMAT fulfilment of the requirement for degree of Master of Science (Organic Chemistry).

Date: - 22.06.2022

Place: - Nashik


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CERTIFICATE

This is to certify that projected entitled "**One Step Three Component Synthesis of Highly Substituted Pyridine using Barium Oxide Nanoparticles as a Catalyst**" is a bonafide projected work done by Miss. DEORE NEHA HIMMAT supervision of Dr. Amol Haridas Kategaonkar.

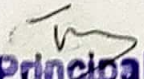

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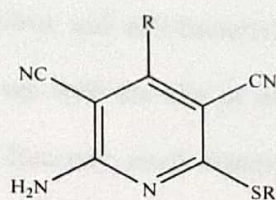
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One Step Three Component Synthesis of Highly Substituted Pyridine Using Barium Oxide Nanoparticles as a Catalyst

1. Introduction

One pot multicomponent coupling reaction (MCR) where several organic fractions are coupled in and step for carbon-carbon and carbon heteroatom bond formation is an attractive synthetic strategy for the synthesis of small molecule achieve with several degrees of structural diversities¹. The pyridine is fractions has been found in wide variety of both naturally occurring and synthetic bioactive compounds and are often with considerable Complexity²



Substituted Pyridine

The synthesis of privileged medicinal scaffolds and highly important as these compounds often acts as ligands for a number of functionally and structurally diverse biological receptors consequent serves as a platform for developing pharmaceutical agents for diverse applications is an example of privileged scaffold is a Substituted pyridine of general structure³

One-pot multicomponent coupling reaction where several organic moieties are coupled in one step, for carbon-carbon, carbon-heteroatom bond formation is an attractive synthetic strategy for the synthesis of small molecule libraries with several degree of structural diversities⁴

Multicomponent reactions are powerful devices in novel drug discovery procedure and allow the fast automated and high their production generations of organic compound the formation of C-N, C-O and C-S bond by MCRS by usual in countless Compound with pharmaceutical biological and material properties Because of significant biological and

derivatives.¹³

The last decade has witnessed enormous development in the field of nanoscience and nanotechnology. Several reports show the amazing level of the performance of nanoparticles as catalysts in terms of selectivity¹⁴, reactivity and improved yields of products. In addition, the high surface-to-volume ratio of nanoparticles provides a larger number of active sites per unit area, in comparison with their heterogeneous counter sites¹⁵

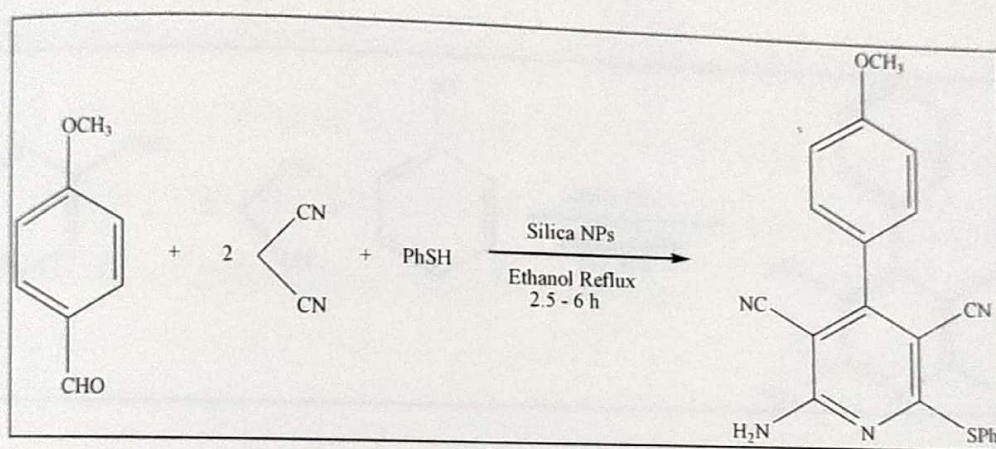
Among various nanoparticles, Barium oxide nanoparticles have been received considerable attention because of their unusual properties and in diverse fields Barium oxide in particular, has high basicity and its non-corrosive, economically benign and easy to handle compared to homogeneous catalysts is more reactive than Calcium oxide & Magnesium oxide. They require mild condition to produce high yields of product in short time¹⁶

In accordance with the above mention significance of nanoparticles in catalysis, and the importance of highly substituted pyridines as privileged medicinal scaffolds, here in, we wish to report a novel, green and mild method for the synthesis of 2-amino-3,5-dicyano-6-sulfanyl pyridines 4 via multicomponent coupling of aldehydes 1, malononitrile 2 and thiols 3, using BaO nanoparticles (BaO NPS) in aqueous ethanol (1:1) media. Barium oxide nanoparticles, as an efficient, non-explosive, eco-friendly, non-volatile, recyclable and easy to handle catalyst, can be used in the catalysis of many organic transformations

2. Literature Review

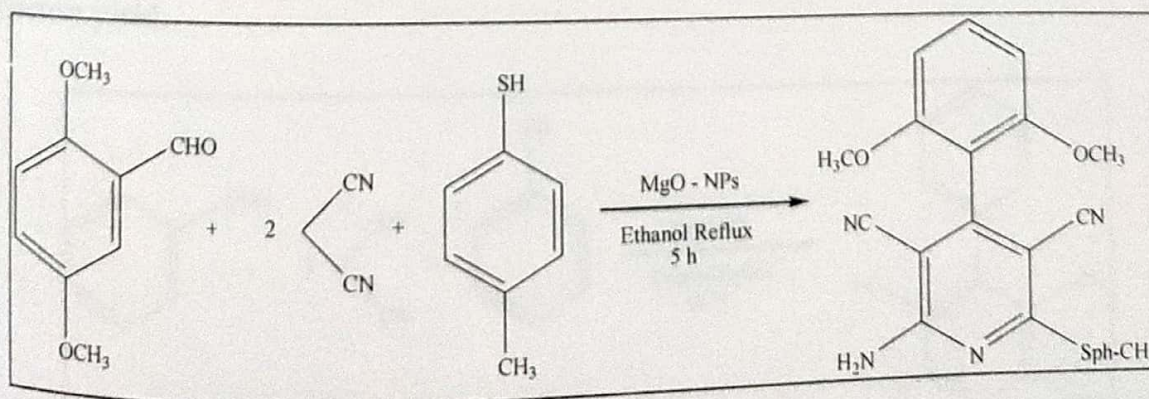
Subhash Banerjee, Grigoriy Sereda⁽¹⁾

Synthesized 2-amino-5-cyano-4-(4-methoxy-phenyl)-6-phenylsufanylnicotinic acid, aldehyde, malononitrile and thiols with silica NPs as catalyst at reflux condition with Ethanol media (Scheme 1)



Scheme 1

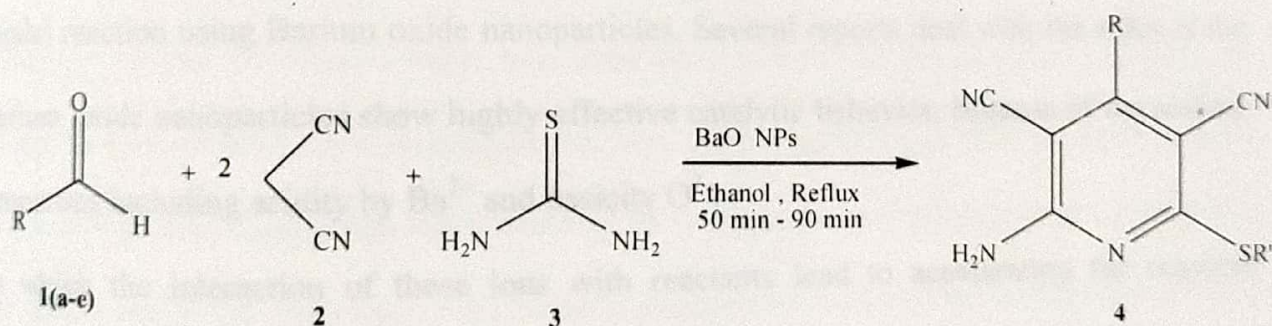
M Lakshmi Kantam, Koosam Mahendar and Suresh Bhargava⁽⁴⁾ Synthesized pyridine with 2,6-dimethoxy benzaldehyde gave the substituted pyridine instead of the predicate 1,4 dihydropyridine using aldehyde, malononitrile and thiols with MgO NPs as catalyst at reflux condition with ethanol media (Scheme 2).



Scheme 2

3. Present Work

We have performed the synthesis of 2-amino-3,5-dicyano,4-aryl 6-sulfanylpyridine derivative by three component efficient reaction between aromatic para-chlorobenzaldehyde, malononitrile and Thiourea by using Ethanol and Water mixture as a solvent in proportion (1:1). Using Barium oxide is heterogeneous base catalyst as an efficient catalyst at 50°C temperature was refluxed and stirred for 50 to 90 min. Progress of the reaction was continuously checked by TLC. When the reaction was complete, the mixture was cooled at room temperature. The method provided efficient and improved pathway for the synthesis of highly substituted pyridine in terms of short reaction time, very good yield and reusable and green catalyst (Scheme 6)



Scheme 6

Synthesis of highly substituted pyridines derivatives catalyzed by BaO nanoparticle

4. Results and Discussion

Initially in order to investigate the morphology and particles size of prepare Barium oxide nanoparticles using Thermal chemical method.

The reaction conditions were optimized on the basis of the catalyst, solvent and reactant for carbon – carbon and carbon – heteroatom bond formation. To test the efficiency of the catalytic activity, we chose to focus our initial studies on the cyclization reaction of aldehyde, thiols and malononitriles in the presence of different Nano catalyst such as BaO. We run the first reaction with using para-chlorobenzaldehyde, thiols and malononitriles. As result this experiment, we found that BaO NPs is the most reactive effective catalyst, in comparison with other catalyst, in this multicomponent reaction. the increased catalytic activity of nanoparticles is attributed to the higher surface area of nanoparticles. we run the model reaction using Barium oxide nanoparticles. Several reports deal with the roles of the barium oxide nanoparticles show highly effective catalytic behavior, because of the surface properties including acidity by Ba^{2+} and basicity O^{2-} .

In which the interaction of these ions with reactants lead to accelerating the reaction conditions.

During the optimization of reaction condition, we run the model reaction using Barium oxide nanoparticles in water, ethanol as solvent. That is the most effective solvents for this multicomponent reaction. In view of the fact that hydrogen bonding between water/ ethanol and substrate can promote the nucleophilic attack of the reactants.

In order to establish the optimum ratio of reactant, the model reaction was carried out several time in the presence of Barium oxide nanoparticles. the best result we are obtained when benzaldehyde, malononitriles and thiols were employed as substrates in a 1:2:2:1 ratio. To study the scopes of this procedure, we next used a diversity of aldehyde and thiols to investigate three components reaction under the optimized conditions.

5. Conclusion

In summary, an efficient and economical method for preparation of highly substituted pyridine derivatives been developed using BaO NPs is heterogeneous base catalyst in green media. The product we are obtained in good yield and reaction time is significantly low and remarkable method is three - component in pot of aldehyde, malononitriles and thiols in order to Synthesis 2-amino-3,5-dicyano,4-aryl6-sulfanylpyridinederivatives

8. References:

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Subhash Banerjee; Grigoriy Sereda

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J. Safaei-Ghomi; M. A. Chasemzadeh; M. Mehrabib

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M LAKSHMI KANTAM, KOOSAM MAHENDAR and SURESH BHARGAVA

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Javad Safaei-Ghomi; Marzieh Kiani; Abolfazl Ziarati^a & Hossein

Journal of sulfur chemistry (35) **2014** 450-457

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Kiran Patil; Deepak Kumbhar; Amol Patil; Shrikrishna Karhale; Vasant Helavi'