IOSR Journal of Applied Chemistry (IOSR-JAC)
e-ISSN: 2278-5736.Volume 16, Issue 12 Ser. I (December 2023), PP 01-04
www.iosrjournals.org

One Pot Environmental Benign Protocol For Synthesis Of Quinoline-3-Carbonitrile Derivatives

Bansode Shivaji Ishwar[*A],
[A]*medesse Laboratories Pvt. Ltd. Hyderabad 500072*

Abstract:
Bleaching earth clay catalyzed multicomponent reaction of Heterocyclic aldehyde, 2-cyanoacetohydrazide and substituted Anilines, In PEG-400 is carried out. This method has been applied for the synthesis of quinoline-3-carbonitrile with good to excellet yield. In this study a comparison is made on triethylamine, piperidine, morpholine with Bleaching earth clay and with no catalyst. The studies revealed that bleaching earth clay and PEG-400 are more effective than other catalyst and solvents. It increasing the yield of product with less time consumption. All the synthesized compounds were characterized for their spectral analysis.
Keyword*: Bleaching earth clay (BEC), PEG-400, Heterocyclic aldehyde, recyclability.*

Date of Submission: 26-11-2023 Date of Acceptance: 06-12-2023

I. Introduction:

The predominant occurrence of thequinoline-3-carbonitrile derivative in various natural products and established medicinal compounds[1-3] had proven to be a versatile scaffold in organic and medicinal chemistry. quinoline-3-carbonitrile have recognized to acquire varied biological activities such as antibacterial[4], antiviral[5], anticancer[6], antifungal[7], antimalarial[8], anti H.I.V[9], anti-inflammatory[10]. Quinoline-3-carbonitrile derivativeare acknowledged medicinal compounds known to be present in the bioactive natural products[11].Heterocyclic aldehydes are proven to contain varied biological activities[12]. By interpretating these points we combine the heterocyclic aldehydes with anilines and 2-cyanoacetohydrazide assuming that the present combination may lead to formation of improved biological hybrid.

There is always been quest for advancementof the synthetic rout for the conversion of readily available reagent in to widely used organic compounds. For accomplishing this multicomponent reaction (MCR) are recognized as an important tool from economic as well as environmental point of view[13]. Along with the MCR method, use of green solvent is also considered to be an environmental benign access. Amongst the green solvents used for MCR strategy PEG-400 is considered to be well known green solvent[14].

In the previous literature there are abundant synthetic strategies for the synthesis of quinoline-3-carbonitrile derivatives[15]. Development of an heterogenous catalyst for the synthesis of numerous important organic motifs was always been a center of interest for organic chemistry students[16-17].Ease of handling, reusability, easy extraction are some peculiar advantages of heterogenous catalysts. Amongst those heterogeneous catalysts Bleaching earth clay (BEC) is considered as a remarkable heterogenous catalyst for various organic transformations[18].Taking in account these facts we represent an MCR protocol for synthesis of by Consolidation of heterocyclic aldehydes with anilines and 2-cyanoacetohydrazide Manipulating Bleaching earth clay as catalyst and PEG-400 as green solvent.

II. Result and discussion

A facile one pot three componentprotocol for the synthesis of new quinoline-3-carbonitrile derivative**4a-j**is reported by utilizing equimolar heterocyclic aldehydes**2a-j**, anilines**3a-c** and 2-cyanoacetohydrazide**1 Scheme 1**. The synthetic protocol commences with sequential addition of 2-cyanoacetohydrazide and heterocyclic aldehydes in round bottom flask previously filled with catalytic amount of BEC and PEG-400 as green solvent, after completion of reaction as indicated by TLC the anilineswas added in the same pot and the reaction mixture was further stirred at 80°C for the formation of product. the first attempt was made using the Triethylamine as a catalyst which results in formation of the product with 50% yield and time required for completion of reaction was 65 minutes Entry1 Table1. Observing these results, we moved for other catalysts piperidine and morpholine Entry 2and 3 Table 1 respectively which the outcomes of 40 and 30% yield with the time of 70 and 60 minutes. When we moved for using BEC as a catalyst 1 Wt%resulting in production of improved 60% yield Entry 4 table1. Enthused with these results we further investigate different wt% compositions of BEC (pH 12.5). We came to investigation that satisfactory yield was obtained when we

utilized 15wt% of BEC. The yield was found to hampered when 10 wt% and 20wt% BEC were used Entry 5 and 7 Table 1. However, there was no formation of product when reaction was carried out in absence of catalyst when stirred at RT Entry 8. Even though when reaction mixture was stirred at 80°C without catalyst the formation of product was not observed Entry 9 Table 1. The optimized reaction conditions were found when 15wt% of BEC was used.

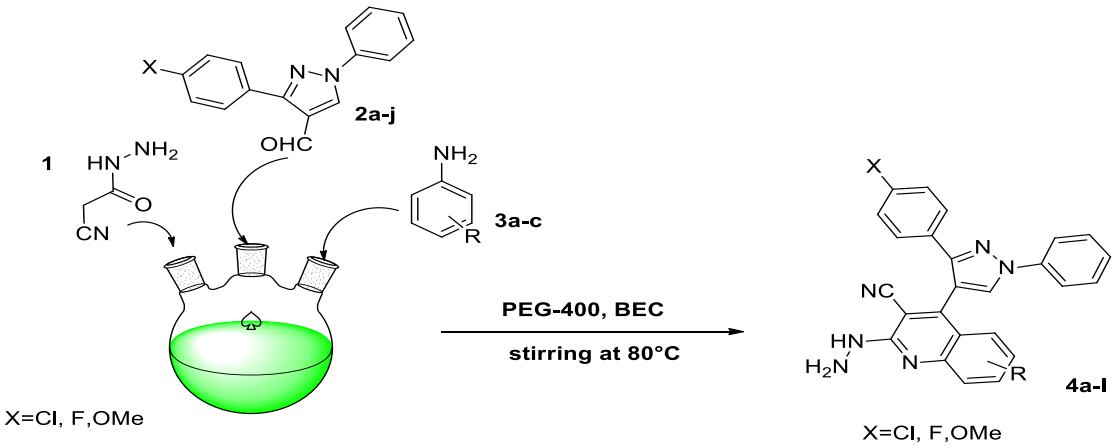
Table1: Optimized reaction conditions

Entry	Catalyst (Mol/wt%)	Temp (°C)	Time (Min)	Yield of 4a (%)
1	Triethylamine (Mol%)	70	65	50
2	Piperidine (Mol%)	80	70	40
3	Morpholine (Mol%)	80	60	30
4	Bleaching earth Clay 1 wt%	80	50	60
5	Bleaching earth Clay 10 wt%	80	40	70
6	Bleaching earth Clay 15 wt%	80	35	90
7	Bleaching earth Clay 20 wt%	80	20	70
8	No catalyst	**RT**	70	0
9	No catalyst	80	80	0

[a]Reaction progress was monitored by thin layer chromatography (TLC)
[b]Yield refers to isolated yield

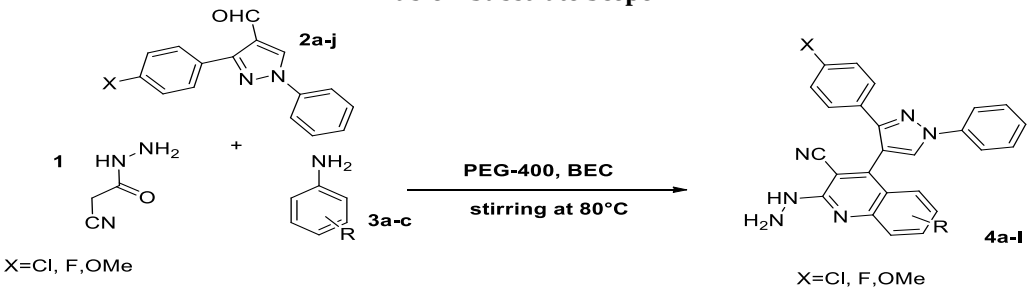
With these optimized conditions we initiated to find the substrate scope the reaction condition was found to operate for varied substrate scope Table 2.

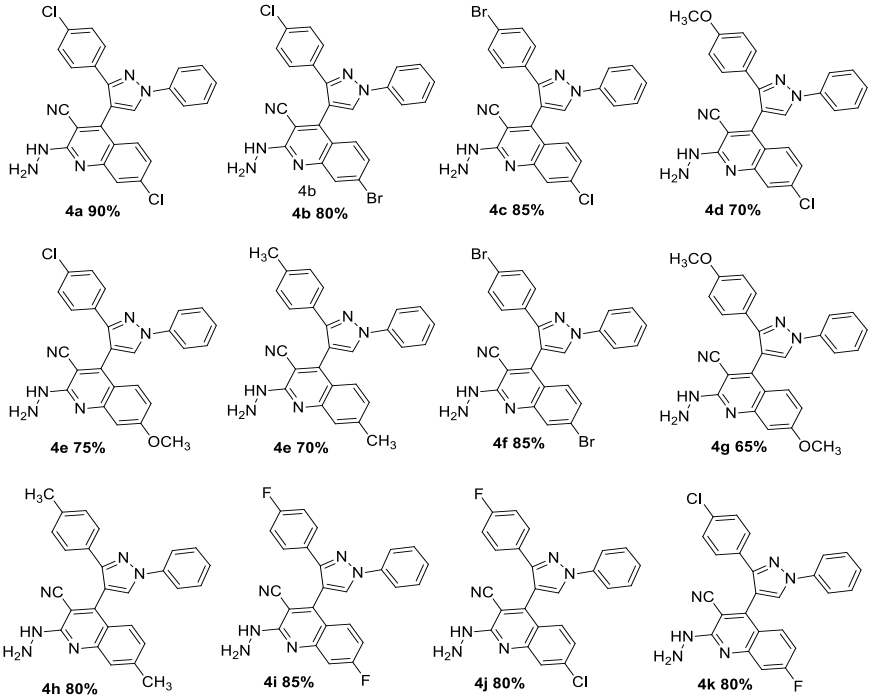
Scheme 1



The finding of the substrate scope indicates that the MCR strategy allows variety of substrate to undergo smoothly with formation of product with satisfactory yield. Interpretation of the yield of the substrate scope indicate that the reactant with electron donating group either on aldehyde 2a-j or on the anilines 3a-c renders the productyield. The substrates with electron withdrawing groups on the aldehydes or on the anilines are providing the products with good yield.

Table 2 Substrate Scope

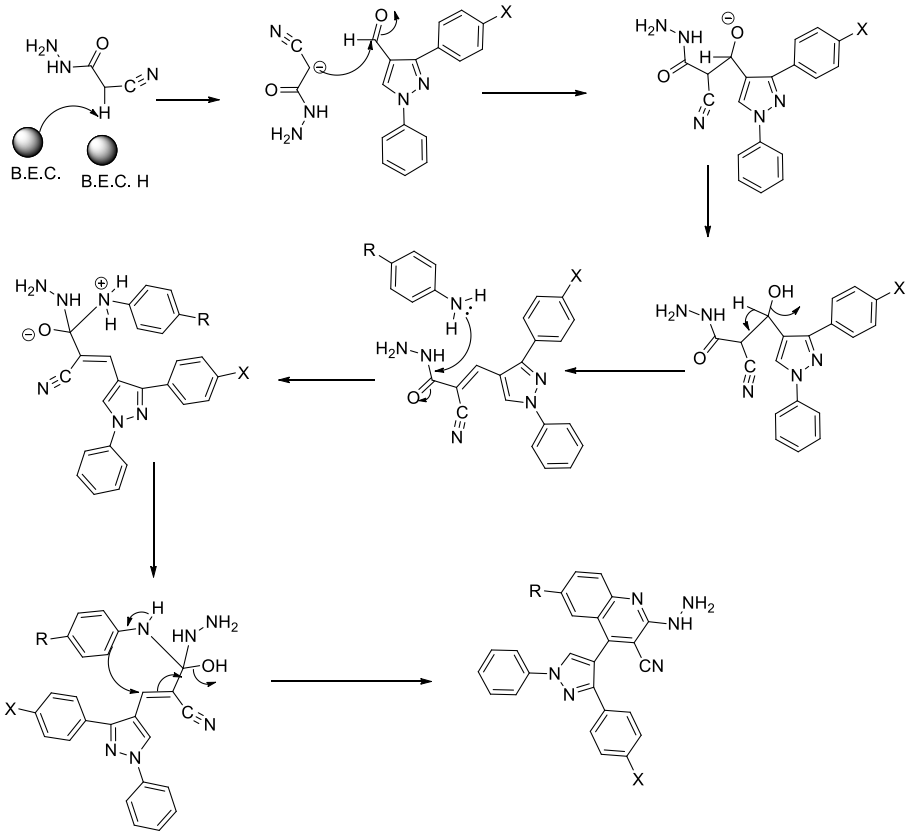




[a] Yield refers to isolated product after column chromatography

The plausible mechanistic path was proposed in Scheme 2. The mechanism indicate reaction was proceeds through abstraction of proton from 2-cyanoacetohydrazide by BEC then the anion attack on the carbonyl of heterocyclic aldehyde. Furthermore, addition of substituted anilines leads to formation of final product.

Scheme 2 Plausible mechanism



III. Conclusion:

The proposed protocol provides an easy access for the synthesis of quinoline-3-carbonitrile derivatives. the MCR strategy for the synthesis is woven with the environmental benign approach through the use of BEC as a catalyst and PEG-400 as a solvent. The protocol delivers an efficient access for the formation of new hybrid product with coupling of easily available reactants which may lead to improved biological activities.

References:

[1]. Nainwal, L. M., Tasneem, S., Akhtar, W., Verma, G., Khan, M. F., Parvez, S., Shaquiquzzaman, M., Akhter, M., Alam M. Eur. J. Med. Chem.2019, 164, 121-170.
[2]. Mukherjee, S., Pal, M. Drug Discov. Today, 2013, 18, 389-398.
[3]. Chung, P. Y., Bian, Z. X., Pun, H. Y., Chan, D., Chan, A.S.C., Chui, C. H., Tang, J.C.O., Lam, K. H. Future Med. Chem. 2015, 7, 947-967.
[4]. Khan, S. A., Asiri, A. M., Basisi, H. M., Asad, M., Zayed, M. E., Sharma, K., Wani, M. Y., Bioorg. Chem. 2019, 88, 102968.
[5]. Ibrahim, M. A., Badran, A. S. Syn. Commun. 2020, 50, 1871-1882.
[6]. Liu, B., You, Q. D., Li, Z. Y. Chin. Chem. Lett. 2010, 21, 554-557.
[7]. Gholap, A. R., Toti, K. S., Shirazi, F., Kumari, R., Bhat, M. K., Deshpande, M. V., Srinivasan, K. V. Biorg. Med. Chem. 2007, 15, 6705-6715.
[8]. Shah, N. M., Patel, M. P., Patel, R. G. Eur. J. Med. Chem. 2012, 54, 239-247.
[9]. Jentsch, N. G., Hart, A. P., Hume, J. D., Sun, J., Mcneely, K. A., Lama, C., Julia, A., Pigza, M. G., Donahue G., Kessl, J. J., Acs Med. Chem. Lett. 2018, 9, 1007-1012.
[10]. Tu. S. J., Jiang, B., Jia, R. H., Zhang, J. Y., Zhang, Y., Yao, C. S., Shi, F.Org. Biomol. Chem. 2006, 4, 3664-3668.
[11]. Kawanishi, N., Sugimoto, T., Shibata, J., Nakamura, K., Masutani, K., Ikuta, M., Hirai, H. Biorg. Med. Chem. 2006, 16, 5122-5126.
[12]. Vo, C. V. T., Luescherf, M. U., Bode, J. W., Nature Chemistry, 2014, 6, 310-314.
[13]. Eydokimov, N. M., Kireev, A. S., Yakovenko, A. A., Antipin, M. Y., Magedov, I. V., Kornienko, A., J. Org. Chem.2007, 72, 3443-3453.
[14]. Shitole, N. V., Shelke. K. F., Sadaphal, S. A., Shingate, B. B., Shingare, M. S., Green Chem. Lett. Rev. 2010, 3, 83-87.
[15]. Aly, R. M., Serya, R. A., El-Motwally, A. M., Esmat, A., Abbas, S., Abou El Ella, D. A., Bioorg. Chem. 2017, 75, 368-392.
[16]. Argyle, M. D., Bartholomew, C. H., Catalysts, 2015, 5, 145-269.
[17]. Boey, P. L., Maniam, G. P., Abd Hamid, S., Chem. Eng. J., 2011, 168, 15-22.
[18]. Gaikwad, M. V., Kamble, R. D., Hese, S. V., Acharya, A. P., Mogle, P. P., Kadam, S. N., Dawane B. S., Res. Chem, Intermed. 2015, 41, 4673-4678.