



# Review on Synthesis and Biological Study on Benzimidazolo[2,3-*b*] and Benzothiazolo Quinazolinone Derivatives

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## Abstract

In Heterocyclic chemistry Fused heterocyclic compounds such as benzothiazolo, imidazolo and 1,3,4-thiadiazolo quinazolinone are played crucial role in biological activity such as anticancer, antioxidant, anti analgesic, antibacterial, antitumor, antiviral and antifungal. In this review article we discuss the various benzothiazole, benzimidazole and thiadiazole derivatives of quinazoline and we focus their synthetic methodology and biological application with different synthetic routes.

**Keywords:** Benzothiazole, benzimidazole, 1,3,4-thiadiazole and quinazolinone, antimicrobial activity, biological study.

## Introduction:

Generally Heterocyclic compounds are very popular in drugs discovery, such as N,S-contain fused heterocyclic compounds play unique role in pharmaceutical due to their potent physiological properties, Interestingly benzothiazole [4,5] quinazolines and 1,3,4-thiadiazole derivatives are involved in biological application due to presence of heteroatom (N&S). Benzothiazole are more reliable and relevant towards in biological and pharmacological activity such as anticancer<sup>1</sup>, anti-inflammatory<sup>2</sup>, antibacterial<sup>3</sup>, antiviral<sup>4</sup> and antifungal<sup>5</sup>.

1,3,4-Thiadiazole was first reports in 1882 by Fischer and further described by Busch and co-workers, 1,3,4 thiadiazole looking a planar system which is more feasible in protein conjugation further which helps to make antibodies. Stelling *et al.*<sup>6</sup> was reported the more convient sulfur drug and the later discovered the mesoionic compounds which is greatly accelerated the rate of progress in this field. The literature survey revealed that various thiadiazoles having many potential drugs and are known to exhibit a broad scope in pharmacological properties and biological properties such as antimicrobial<sup>7</sup>, antituberculosis<sup>8</sup> , anti-

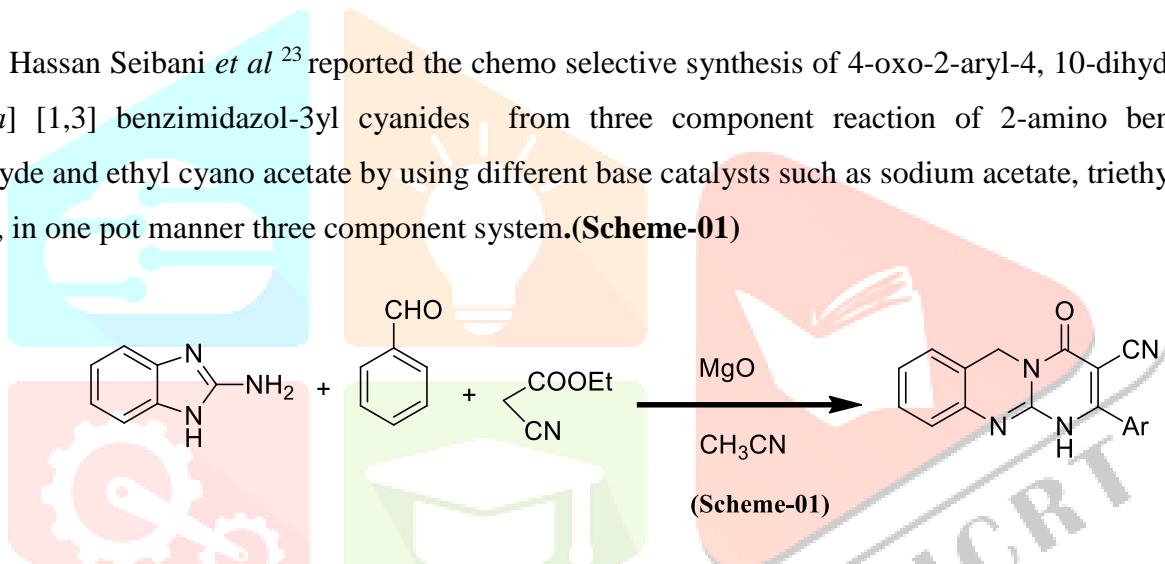
inflammatory<sup>9</sup>, anticonvulsant<sup>10</sup>, antihypertensive<sup>11</sup>, antioxidant<sup>12</sup>, antifungal<sup>13</sup>, and anticancer activity<sup>14</sup>, anti tumor<sup>15</sup>, amoebicidal, antipyretic, CNS depressant, antischistosomal<sup>16</sup>.

Quinazolines had nice results, extraordinary scope in biological activity such as propyl hydroxylate inhibitor<sup>17</sup>, antidiabetics<sup>18</sup>, antiantineoplastic<sup>19</sup> and potent immune suppressive agent<sup>20</sup>. They also emerged as integral back bones of calcium channel blockers<sup>21</sup> and antitumor activity<sup>22</sup>.

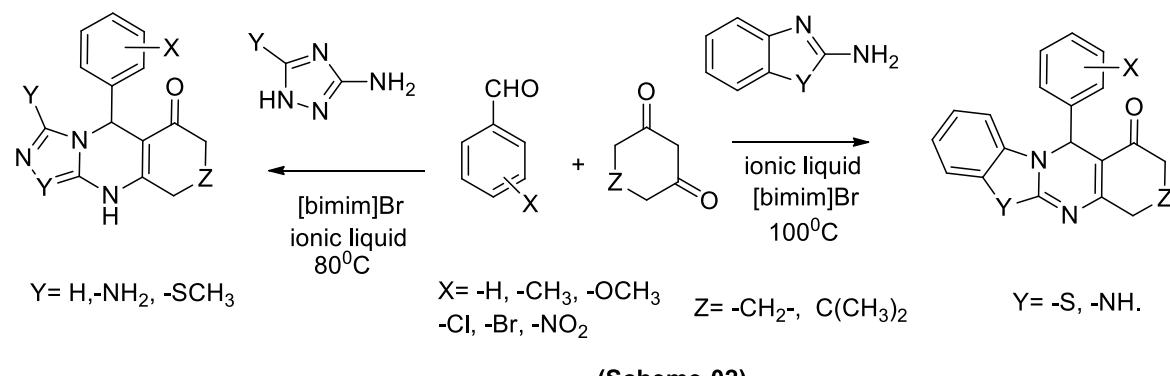
### Review of literature:

In this review article we discuss about the importance of 1, 3, 4-thiadiazole, benzothiazole and 2-amino benzimidazole derivatives it is glad to play pharmacological activities and it is used in agro chemistry, medicinal chemistry, herein, we showed, the reported synthesis with different routes, which involved three component system.

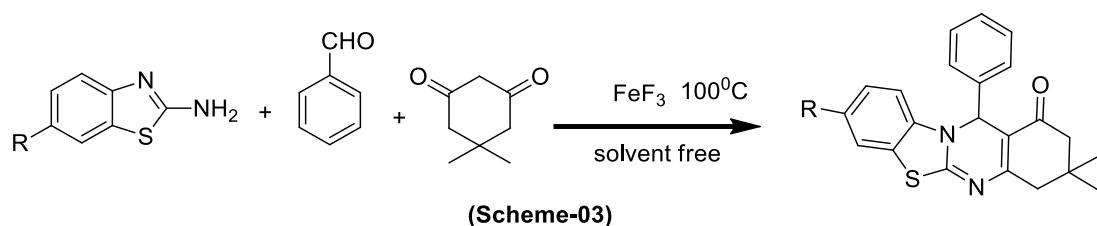
Hassan Seibani *et al*<sup>23</sup> reported the chemo selective synthesis of 4-oxo-2-aryl-4, 10-dihydro pyrimido [1,2-a] [1,3] benzimidazol-3yl cyanides from three component reaction of 2-amino benzimidazole, aldehyde and ethyl cyano acetate by using different base catalysts such as sodium acetate, triethyl amine and MgO, in one pot manner three component system. (**Scheme-01**)



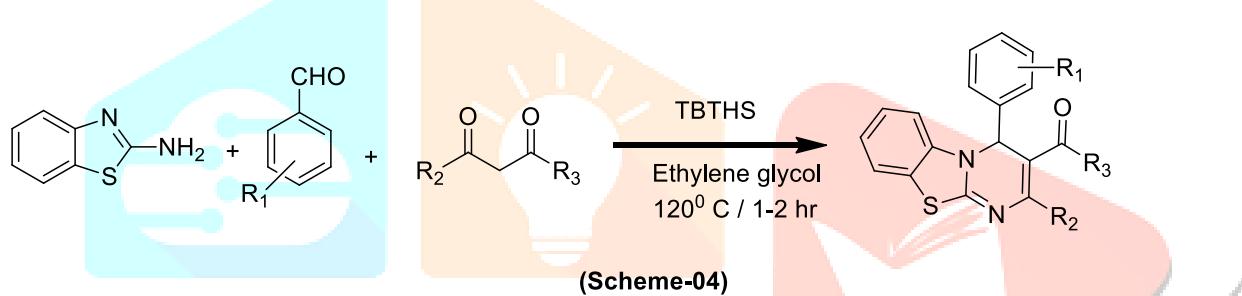
Shaabani *et al*<sup>24</sup> showed the synthesis of benzothiazolo [2,1-b] quinazolinones and triazolo[2,1-b] quinazolinones followed by the condensation reaction of an aldehyde and a cyclic  $\beta$ -diketone with, 2-amino benzimidazole, 2-amino benzothiazole or 1,2,4-triazole derivatives in 1-butyl-3-methylimidazolium bromide (**Scheme-02**).



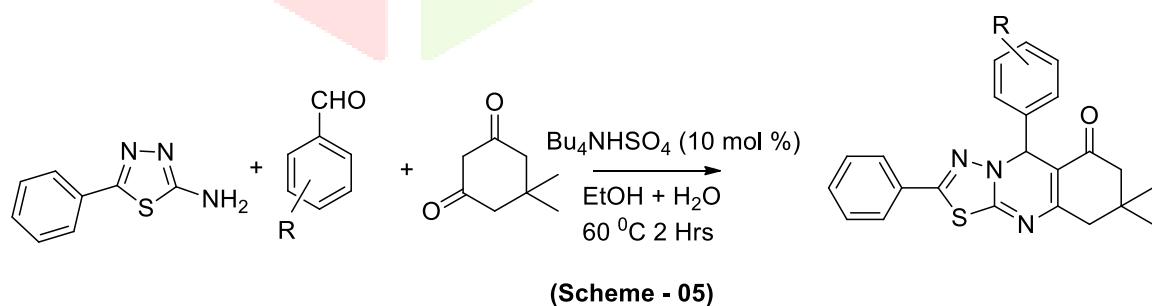
A. B. Atar *et al.*<sup>25</sup> reported the one pot synthesis of 4H-pyrimido [2, 3-b] benzothiazole by using iron fluoride as a catalyst solvent free condition from 2-amino benzothiazole, aromatic aldehyde and dimedone, disulfide bond and having moderate activity against the antimicrobial properties. (**Scheme-03**).



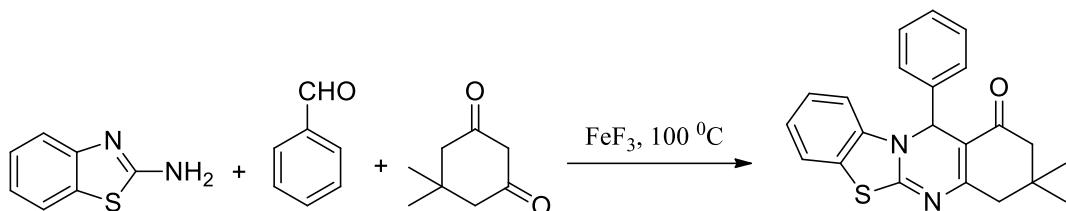
Lingaiah Nagarapu *et al.*<sup>26</sup> discuss the one pot three component synthesis of 4H-pyrimido [2,3-b] benzothiazole derivatives from 2-amino benzothiazole, substituted benzaldehyde and  $\beta$ -dicarbonyl derivatives in the presence of tetrabutylammonium hydrogen sulfate (TBAHS) in ethylene glycol and compound having moderate antimicrobial activity. (**Scheme-04**)



Gopinath S. Khansole *et al.*<sup>27</sup> reported the synthesis of thiadiazolo [2,3-b] quinazolin-6-(7H)-one derivatives from 2-amino-5-phenyl 1,3,4-thiadiazole, dimedone and tetra butyl ammonium hydrogen sulphate (TBAHS) in water-ethanol reaction performs with different substituted aromatic aldehyde and obtained compounds screened for their potent antioxidant activity. (**Scheme-05**)

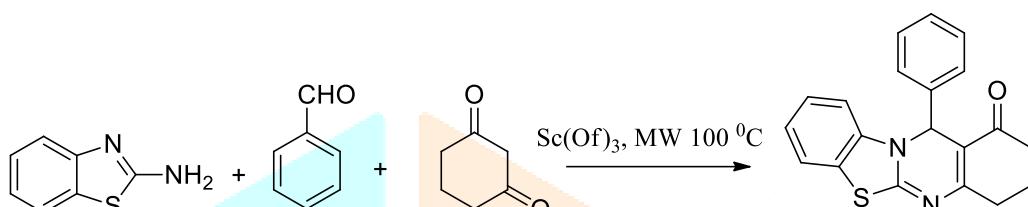


Amol B. Atar *et al.*<sup>28</sup> described the iron fluoride assisted synthesis which is made with convenient strategy for the synthesis of 4H-pyrimido [2, 1-b] benzothiazole derivatives in solvent-free media from benzothiazole, substituted aromatic aldehyde and dimedone. (**Scheme-06**)



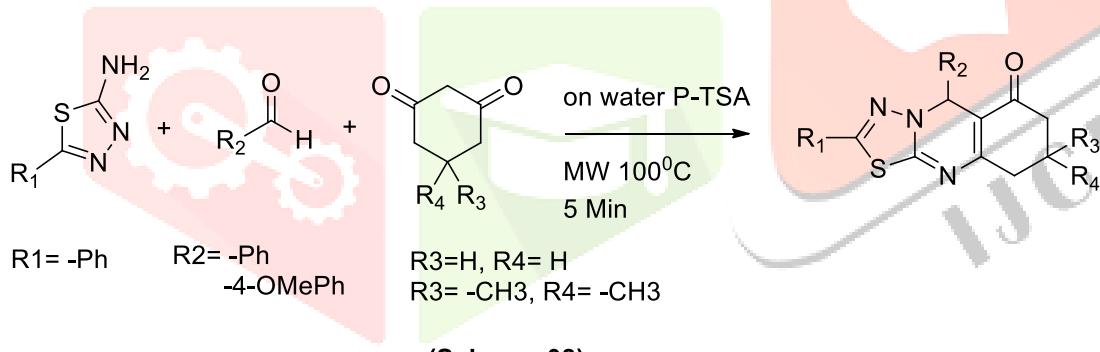
(Scheme-06)

Somaiah Gajaganti *et al.*<sup>29</sup> reported the synthesis of benzimidazolo/benzothiazolo quinazolinone derivative have been developed under solvent free condition and microwave irradiation from 2-aminobenzimidazole/2-aminobenzthiazole, aromatic aldehyde and 1,3-diketone. (**Scheme-07**)



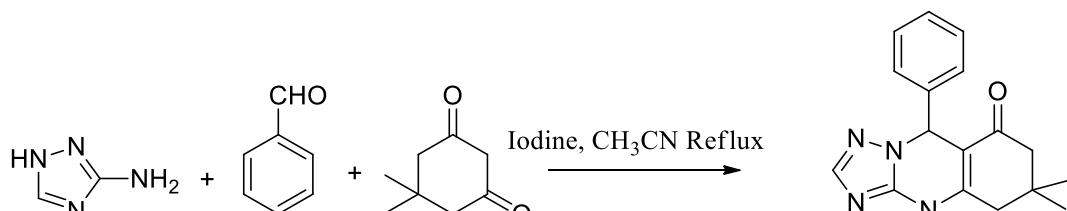
(Scheme-07)

Preeti Wadhwa *et al.*<sup>30</sup> described the synthesis of novel thiadiazolo [2,3-b] quinazolinones from 5-aryl-1,3,4-thiadiazol-2-amine, cyclic1,3-dicarbonyls and aldehydes with microwave irradiation by using p-toluenesulfonic acid in aqueous medium. (**Scheme-08**)



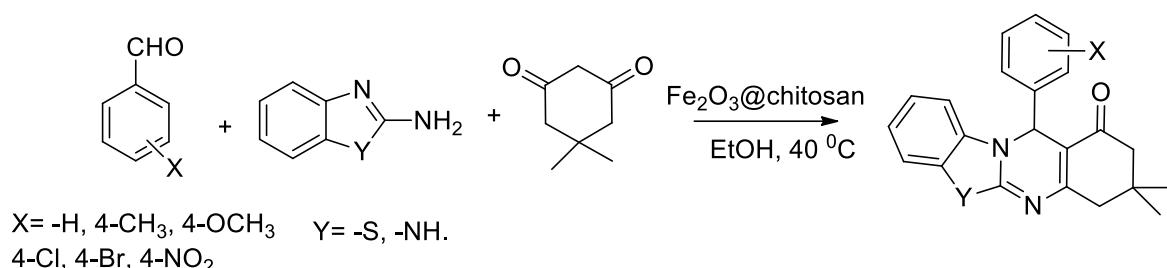
(Scheme-08)

Ravinder G. Puligoundla *et al.*<sup>31</sup> showed synthesis of quinazolinone derivatives by condensation of 3-amino-1,2,4-triazole and 2-aminobenzimidazole, aromatic aldehyde and dimedone in the presence of iodine in acetonitrile as shown in scheme-09.



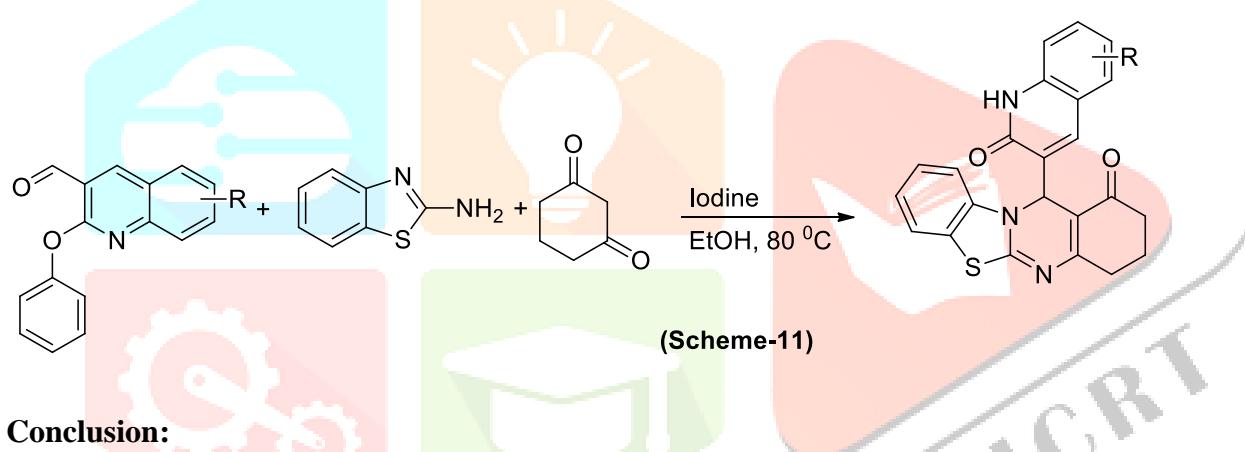
(Scheme-09)

Ali Maleki *et al.*<sup>32</sup> reported the one-pot multicomponent synthesis of tetraheterocyclic benzimidazolo[2,3-b] quinazolines derivatives from 2-aminobenzimidazole or 2-aminobenzothiazole, dimedone and substituted aldehyde using Fe<sub>2</sub>O<sub>3</sub> chitosan which is nanocomposite catalyst. (**Scheme-10**)



(Scheme-10)

Madhava Reddy Manne *et al.*<sup>33</sup> reported 12-(2-Oxo-1,2-dihydroquinolin-3yl)-2,3,4,12-tetrahydro-1h-benzo[4,5]-thiazolo[2,3-b] quinazolin-1-one from substituted-2-phenylthioquinoline-3-carbaldehyde, 2-amino benzothiazole and 1,3-cyclohexanedione in ethanol as shown in **Scheme-11**.



### Conclusion:

In this review article, we discuss the efficient synthesis and convenient route of thiadiazole, benzothiazole and benzimidazole quinazolinone derivatives. On the bases on their structural arrangement, it is more reliable to bind with proteins and increase the immense response. Substituted thidiazolo quinazoline, benzothiazolo quinazoline and benzimidazolo quinazoline are played vital role in biological and pharmacological properties.

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### Conflict of Interest:

The authors declared that they do not have any conflict of interest regarding this research article.

**References:**

1. M. B. El-Ashmawy, M. A. El-Shebeny, N. S. El-Sayed, Mansoura, J. Pharm. Sci., 26 (2010) 60.
2. A. Shafiee, Kalezari, J. Heterocycl. Chem. 12(1975) 675
3. V. K. pandey, N. Raj, Curr. Sci. 55 (1986)785.
4. Shigeta, S.; Mori, S.; Baba, M.; Hosoya, M.; Mochizuki, N.; Chiba, T.; De Clercq, E. *Antiviral Chem. Chemother*, **1992**, 3, 171.
5. S. K. Modi, V. Kumar, K. S. Narang, Indian J. Chem, 8(1970) 716.
6. Stelling, M. R.; Welbourn, A. P.; Walter, D. S. *J. Med. Chem.* **1986**, 29, 2280-2284.
7. K. Zamani.; K. Faghli.; M. S. Mehranjani. *Polish J. Pharm.* **2003**, 55, 1111.
8. O. Pintilie.; L. Profire.; V. Sunel.; M. Popa.; A. Pui. *Molecule*, **2007**, 12, 103.
9. A. Faroumadi.; M. Mirzaei.; A. Shafiee. *Pharmazie*. **2001**, 56, 610.
10. P.Srinivas Rao.; Sudeendra.; R. H. Udupi. *Indian J. Heterocyclic Chem.* **2006**, 15, 65.
11. A. Sayyed .; Tabatabai. *Bioorg. Med. Chem. Lett.* **2004**, 14, 6057.
12. J. J. Baldwin.; E. L. Engelhardt.; R. Hirschmann.; G. S. Ponticella. *J. Med. Chem.* **1980**, 23, 65.
13. D. Kumar.; N. Maruthi Kumar.; Kuei-Hua Chang.; S. Kavita. *European J. Med. Chem.* **2010**, 45, 4664.
14. G. Sorba.; A. Stilo.; A. M. Gasco.; M. Gill. *Farmaco* **1992**, 47, 1992.
15. Zhang, Y.; Wang, H.; Wang, X.; Xlao-kui W.; Zhi-qiang Z.; X. Song-qiang. *Guoqiang Huaxue Shi ji.*; **2009**, 31(9) 682-684.
16. Jain, A. K.; Sharma, S.; Vaidya, A.; Ravichandran, V.; Agrawal, R. K. *Chemical biology & Drug design*, **2013**, 81(5), 557-576.
17. Chai, D.; Fitch, D.M. Propyl Hydroxylase Inhibitors. WO Patent 09039322 A1. **2009** (March).
18. Kato, F.; Kimura, H.; Omatsu, M.; Yamamoto, K.; Miyamoto, R. WO Patent 02040485, **2002**, May 23.
19. Hafez, A.; Monem, A. A. *Arch. Pharm. Res.* **2007**, 30, 678.

20. Lunn, W. H. W.; Harper, R. W.; Stone, R. L. *J. Med. Chem.* **1971**, 14, 1069.
21. Alajarín, R.; Vaquero, J. J.; Alvarez-Builla, J.; Faude Casa-Juana, M.; Sunkel, C.; Priego, J.; Gómez-Sal, P.; Torres, R. *Bioorg. Med. Chem.* **1994**, 2, 323.
22. Ishida, J.; Wang, H. K.; Bastow, K. F.; Hu, C. Q.; Lee, K. H. *Bioorg. Med. Chem. Lett.* **1999**, 9, 3319.
23. Hassan Sheibani.; Fahimeh Hassni. *J. Hetero. Chem.* **2011**, 48, 915.
24. Shaabani Ahmad.; Farhangi Elham.; Shaabani Shabnam. *Iran. J. Chem. Eng.* **2013**, 32, 1, page no. 3-10
25. Amol, B. Atar.; Yong Seok Jeong.; Yeon Tae Jeong. *Tetrahedron*, **2014**, 70, 5207
26. Lingaiah Nagarapu.; Hanmant K. Gaikwad.; Jyothsna Devi, Palem.; Ramineni Venkatesh.; Rajashaker Bantu.; B. Sridhar. *Synth. Commun.* **2013**, 43, 104.
27. G. S. Khansole.; Diya Prasad.; J. A. Angulwar.; A. B. Atar.; B. M. Nagaraja.; A. H. Jadhav.; V. N. Bhosale.; *Materiaaltodays: Proceedings*, **2019**, 9, 653-660.
28. Atar A. B.; Jeong Y. S.; Jeong Y. T. *Tetrahedron* **2014**, 70, 5207-5213. Doi.: 10.1016/j.tet.2014.05.094
29. Gajaganti S.; Kumari s.; Kumar, D.; Allan, B. K.; Srivastava, V.; Singh, S. *J. Heterocyclic Chem.* **2018**, 55, 2578-2584. doi: 10.1002/jhet.3314 .
30. P. Wadhawa.; T. Kaur.; N. Singh.; V. P. Singh.; A. Sharma. *Asian J. Org. Chem.* **2016**, 5, 120-126. doi:10.1002/ajoc.201500397.
31. Puligoundla, R. G.; Karnakanti, S.; Bantu, R.; Nagaiah, K.; Kondra, S. B.; Nagarapu, L. *Tetrahedron Lett.* **2013**, 54, 2480-2483. Doi:10.1016/j.tetlet.2013.02.099.
32. Ali Maleki, Morteza Aghaei nad Nakisa Ghamari *Chem Lett.* **2015**, 44, 259-261 doi: 1.1246/cl.141074.
33. M. R. Manne.; R. R. Panicker.; A. Sivaramkrishana.; *Syn. Commu.* **2020**, 1-11. Doi: 10.1080/003979.2020.1821221.