BENZIMIDAZOLE COMPOUND GREEN SYNTHESIS AND SUMMARIZE OF BULK DRUG SYNTHESIS.

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ABSTRACT

Green chemistry is the new and rapidly emerging field of chemistry. It involves the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products. In recent decades, a large number of reports related to synthesis of Nitrogen, Oxygen and Sulphur containing heterocyclic have appeared owing to a wide variety of their biological activity. In recent years, numerous reports concerning the synthesis of heterocyclic compounds under various conditions like solvent-free, reactants immobilized on solid support, microwave irradiation condition, green catalyst and green solvent have appeared. Benzimidazole is a heterocyclic aromatic organic compound. It is an important pharmacophore and privileged structure in medicinal chemistry.

Keywords: *Green Synthesis, Drug Synthesis, Aromatic organic compound.*

INTRODUCTION

Benzimidazole is a heterocyclic aromatic organic compound. It is an important pharmacophore and a privileged structure in medicinal chemistry. This compound is bicyclic in nature which consists of the fusion of benzene (1) and imidazole (2). The use of benzimidazole dates many years back. It plays a very important role with plenty of useful therapeutic activities such as: Antiulcer, antihypertensive, analgesic, anti-inflammatory, anti-viral antifungals, anticance, antibacterial and anthelmintic [1-5]

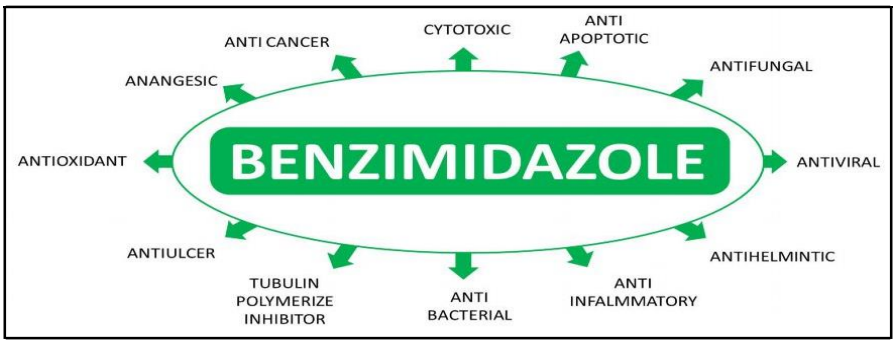

Figure: 1 showing various pharmacological activities of Benzimidazole.

1 : Synthesis of Benzimidazole from 2-nitro-4-methyl acetanilide by Hoebrecker

Preparation of benzimidazoles practically starts with benzene derivatives possessing nitrogen-containing functions ortho to each other i.e. the starting material o –Phenylenediamines (4) (OPD) react readily with most carboxylic acids (5) to give 2-substituted benzimidazoles (6), usually in very good yield. The reaction is carried out usually by heating the reactants together on a steam bath, by heating together under reflux or at an elevated temperature, or by heating in a sealed tube.[6,7]

In the last two decades it has become increasingly clear that the chemical and allied industries, such as pharmaceuticals, are faced with serious environmental problems. Many of the classical synthetic methodologies have broad scope but generate copious amounts of waste, and the chemical industry has been subjected to increasing pressure to minimize or, preferably, eliminate this waste. For every kg of phloroglucinol produced 40 kg of solid waste, containing chromium sulphate Cr2(SO4)3, ammonium chloride NH4Cl, ferrous chloride FeCl2 and potassium hydrogen sulphate KHSO4 were generated. This led to the introduction of the E (environmental) factor (kilograms of waste per kilogram of product) as a measure of the environmental footprint of manufacturing processes [8-11] in various segments of the chemical industry.

The E factor represents the actual amount of waste produced in the process, defined as everything but the desired product. It takes the chemical yield into account and includes reagents, solvent losses, process aids, and, in principle, even fuel. Water was generally excluded from the E factor as the inclusion of all process water could lead to exceptionally high E factors in many cases and make meaningful comparisons of processes difficult. A higher E factor means more waste and, consequently, a larger environmental footprint. The ideal E factor is zero. Put quite simply, it is the total mass of raw materials minus the total mass of product, all divided by the

total mass of product. The factor of any chemical process can be reduced or minimized by applying the greener chemical methods.[12-16]

In 1990, Paul Anastas and John Warner defined Green Chemistry: "The design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances". Human society is constantly facing such environmental issues and problems as ozone depletion, air pollution, global climate change, soil and water pollution, acid rain, the depletion of natural resources, and the accumulation of hazardous waste. There are twelve principles of Green Chemistry[17-21] Paul T. Anastas and John C. Warner first published their 12 principles of Green Chemistry in their book, Green Chemistry: Theory and Practice, in 1998. Both serve as members of the California Green Chemistry Science Advisory Panel. In summary, the 12 principles are:

1. Prevent waste rather than treating it or cleaning it up.
2. Incorporate all materials used in the manufacturing process in the final product.
3. Use synthetic methods that generate substances with little or no toxicity to people or the environment.
4. Design chemical products to be effective, but reduce toxicity.
5. Phase-out solvents and auxiliary substances when possible.
6. Use energy efficient processes, at ambient temperature to reduce costs and environmental impacts.
7. Use renewable raw materials for feed stocks.
8. Reuse chemical intermediates and blocking agents to reduce or eliminate waste.
9. Select catalysts that carry out a single reaction many times instead of less efficient reagents.
10. Use chemicals that readily break down into innocuous substances in the environment.
11. Develop better analytical techniques for real-time monitoring to reduce hazardous substances.
12. Use chemicals with low risk for accidents, explosions, and fires.

Green Synthesis of Benzimidazole:

Davood Azarifar et al., in 2010 Synthesised benzimidazoles by condensation of o-phyneline diamine promoted by acetic acid under microwave. They concluded that a mild, manipulatable procedure, eco-friendly and green aspects avoiding hazardous solvents, shorter reaction times and high yields of the products are the advantages of this method [22-24]

Kabeer A. Shaikh et al., 2012 have been efficiently synthesized Benzimidazoles in high yields by treatment of 1, 2- diamine with aldehydes using the metal coordinate complex K4[Fe(CN)6] as a catalysis. The method was carried out under solvent free condition via oxidation of carbon-nitrogen bond which is green, mild and inexpensive process.

B.N.B.vaidehi et al., had synthesised set of 2-substituted benzimidazoles successfully by condensation of o- phenylenediamine with substituted acids in presence of ring closing agents like Polyphosphoric acid / HCl. The present work has demonstrated the use of a simple Cyclocondensation method, Ring closing agents for synthesis of 2-substituted benzimidazoles.

Chunxia chen et al., has been developed A straightforward method for the synthesis of the benzimidazole ring system through a carbon-nitrogen cross-coupling reaction in the presence of K2CO3 in water at 100 °C for 30 h, the intermolecular cyclization of N-(2-iodoaryl) benzamidine provides benzimidazole derivatives in moderate to high yields. Remarkably, the procedure occurs exclusively in water and doesn't require the use of any additional reagent/catalyst, rendering the methodology highly valuable from both environmental and economic points.

D Kathirvelan et al ., synthesized various 2 substituted benzimidazole in moderate to good yields in a one pot reaction by condensation of o – phynelyene diamine and an aldehyde in the presence of ammonium chloride as a catalyst at 80 to 90 0C and concluded that this method was green and economical30.

M. Rekha et al., studied catalytic activity of alumina, zirconia, manganese oxide/alumina, and manganese oxide/zirconia in the condensation reaction between o-phenylenediamine and an aldehyde or a ketone to synthesise 2-substituted benzimidazoles and 1, 5-disubstituted benzodiazepines respectively and found to be simple and economical.

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Mita D. Khunt et al., has synthesised the benzimidazole by reacting o-phynelinediamine with several aldehydes using a green solvent PEG400 and got good yield [26-28].

CONCLUSION

Benzimidazoles are been used in many fields and are very essential for human kind and it is most important nuclei in many drugs. In conventional method of synthesis the yield was less and the chances of environmental pollution were more, but in greener methods the yields are higher which reduces byproducts. Even though green methods are available for the synthesis of benzimidazoles there is a necessity for the development of further more effective methods as the utilization of benzimidazole derivatives is high not only in the field of pharmacy but also in other viz polymer industry.

REFERENCES

1. Madan Mohan & Munesh Kumar, Polyhedron 4 (1985) 1929.
2. B. Egneus, Talanta 19 (1972) 387.
3. N. Andersen, J.W. Gallagher, I.V. Hertel, Phys. Rep. 165, 1 (1988).
4. N. Andersen, K. Bartschat, J.T. Broad, I.V. Hertel, Phys. Rep. 279, 251 (1997).
5. N. Andersen, K. Bartschat, J. Phys. B 35, 4507 (2002)
6. L. Vuskovic, L. Maleki, S.Trajmar, J. Phys. B 17, 2519 (1984).
7. S.T. Chen, A.C. Gallagher, Phys. Rev. A 17, 551 (1978).
8. I.P. Zapesochnyi, E.N. Postoi, I.S. Aleksakhin, Sov. Phys .-JETP 41,865(1976).
9. B.V. Hall, A.J. Murray, W.R. MacGillivray, M.C. Standage, I. Bray, Proc. Abstr. XXI

ICPEAC (1999) p.190-SA050.

10. G.W.H. Cheeseman, J. Chem. Soc. (1964) 1387.
11. Pradeep, Ishwar and Deepak, IJCRT 9(8) 684 (2021)
12. N. Shashikala, E.G. Leelamani and G.K.N. Reddy, Ind. J. Chem. 21A (1982) 743; J. Ind. Chem. Soc. 62 (1985) 928.
13. P.K. Nath, N.C. Mishra, V.Chakravorty & K.C. Dash, Polyhedron 6 (1987) 455.
14. L.D. Prabhakar, K.M.M.S. Prakash & M.C. Chowdhary, Ind. J. Chem. 26A (1987) 142.
15. C. Keshavolu, R.S. Naidu & R.R. Naidu, Polyhedron 4 (1985) 761.
16. Madan Mohan & Munesh Kumar, Polyhedron 4 (1985) 1929.
17. B. Egneus, Talanta 19 (1972) 387.
18. G.W.H. Cheeseman, J. Chem. Soc. (1964) 1387.
19. A. Bistrzycki & G. Przeworski, Berft. Chem. Ges. 45 (1912) 3492.
20. Pradeep, Ishwar , Jyotsna and Deepak, IJERT ENCADEMS-2020 Conference Proceedings.
21. Dr. Pradeep kumar, Deepak Dubey, Indian Journal of Applied Research, Vol 10(1) 2020
22. Dr. Pradeep Kumar, Dr. Ishwar Singh, Dr. Deepak Dubey,International Journal of Creative Research
23. Thoughts,Volume 9, Issue 8 August 2021
24. Dr. Pradeep Kumar, Prashant Kumar, Ishwar Singh, Ritika Saini, International Journal of Recent