WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 5, 1460-1466. Research Article ISSN 2277– 7105

SYNTHESIS AND CHARACTERISATION OF 2-(4-THIAZOLYL) BENZIMIDAZOLE DERIVATIVE

Amit Aher* and Dr. Shobha Borhade

S.M.B.S.T.College, Sangamner, Ahmednagar, Maharashtra, India 422605.

Article Received on
16 March 2016,
Revised on 08 April 2016,
Accepted on 30 April 2016
DOI: 10.20959/wjpr20165-6183

***Corresponding Author**
Amit Aher
S.M.B.S.T.College,
Sangamner, Ahmednagar,
Maharashtra, India

ABSTRACT

Benzimidazole is heterocyclic compound. we synthesized the derivative of 2-(4-Thiazolyl) Benzimidazole derivative. The synthesis of novel Benzimidazole derivatives and investigation of their chemical and biological behavior have gained more importance in recent decades. During the recent years there has been intense investigation of different classes of Benzimidazole nucleus are known to exhibit unique anti bacterial, anti oxidant, anti fungal, anti histaminic, anti psychotic ,narcotic analgesic, proton pump inhibitor-anti ulcer, anti dopamenergic, anti coagulant activities respectively. The structure of synthesized compound was confirmed by ^{1}H-NMR and Mass spectroscopy.

KEYWORDS: Benzimidazole, Thiabendazole derivative, Pharmacological Activities**.**

INTRODUCTION

Heterocyclic are present in a wide variety of drugs, most vitamins, many natural products, biomolecules, and biologically active compounds, including antitumor, antibiotic, anti-inflammatory, antidepressant, antimalarial, anti-HIV, antimicrobial, antibacterial, antifungal, antiviral, antidiabetic, herbicidal, fungicidal, and insecticidal agents [1-7] .Also, they have been frequently found as a key structural unit in synthetic pharmaceuticals and agrochemicals.[8,9]

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 and imidazole. Benzimidazole drugs are widely used for presentation and treatment of parasitic infection [10]. Nowadays is a moiety of choice which possesses many pharmacological properties. Benzimidazole and its derivatives have a long history as antimicrobial agents. The benzimidazole derivatives have different

pharmacological activities like antimicrobial, antifungal, neuroleptic, anti-HIV, anthelmintic, antihistaminic, antiulcer, cardio tonic & antihypertensives1 **[11,12]** **.** .In order to obtain more effective chemotherapeutic agents, a variety of reports have been presented on the synthesis and biological evaluation of novel benzimidazole derivatives. The literature survey revealed the importance of the substitutions at 1, 2 and 5 positions of the benzimidazole ring for their pharmacological activities. 2-(phenyl substituted) benzimidazoles with different biological activities like antimicrobial, antibacterial, antitumor, antiviral, and anti-inflammatory have been reported.[13,14]

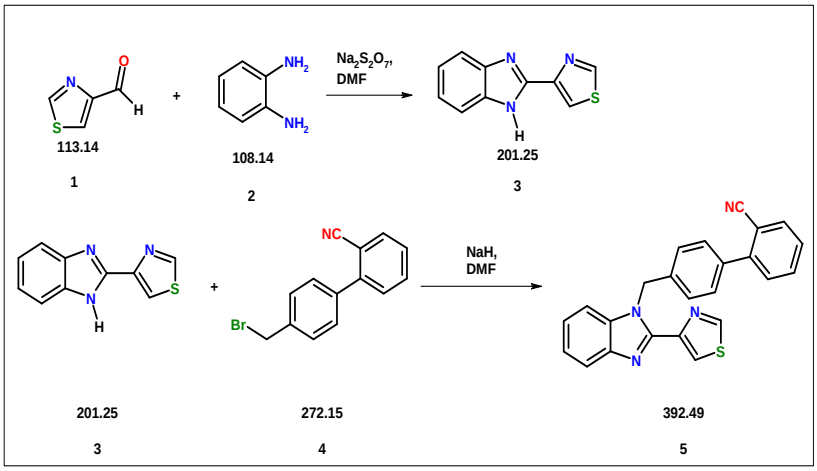
The benzimidazole compounds have been proved to be the most important group of fungicides with systemic activity and are well known for their pronounced ability to control a large number of fungal disease. Because of their systematic activity, they can help to control some diseases after infection. Benzimidazole fungicides are also used to prevent post-harvest rots and in soil-drench treatments.[15] The derivative of benzimidazole, 2-(4-thiazolyl)-1H-benzimidazoles are structurally analogous to benzimidazoles, well known as an anthelminitic agent and systemic fungicide. Its fungicidal properties and systemic properties in plants have already been reported as a fungicide with protective and curative action. It is used to control of Aspergillus, Botrytis, Ceratocystis, Cercospora, Colletotrichum, Corticium, Diaporthe, Diplodia, Fusarium, Gibberella, Gloeosporium, Oospora, Penicillium, Phoma, Rhizoctonia, Sclerotinia, Septoria, Thielaviopsis, Verticillium spp., etc**.**[16] It is commonly used as an anthelminitic in human and veterinary medicine too.[17] Benzimidazole and thiazole analogues have found applications in medicine and agriculture.[18] Thiabendazole is systemic fungicides which were found to be effective in controlling leaf spot of sugarbeet, caused by Cercospora beticola Sacc.[19-22], The metal complexes of thiabendazole structure, antimicrobial activity and photodynamic effects has been done.[23] Synthesis, X-ray crystal structures and biomimetic and anticancer activities of novel copper thiabendazole is done.**[24]** Thiabendazole was the first benzimidazole marketed. It is used primarily to control mold, blight, and other fungal diseases in fruits e.g. oranges and vegetables; it is also used as a prophylactic treatment for Dut chelm disease. Thiabendazole works by inhibition of the mitochondrial, helminth-specific enzyme, fumarate reductase, with possible interaction with endogenous quinone.

MATERIALS AND METHODS

Synthesis of 2-(4-Thiazolyl) benzimidazole (3): 10.0 g (80.38 mmol) of Thiazole 4-Aldeyde, 9.55 g (80.38 mmol) 1,2-phenylenediamine, 100 ml DMF and Sodium pyrosulphate were added in round bottom flask. Reaction mass was stirred at 130°C for 6 hr. Solvent was evaporated and residue was purified by Column Chromatography DCM/ MeOH system. Crude Thiabendazole recrystallized in DMF.

Synthesis of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole (5)

6.0 g (29.81 mmol) of Thiabendazole and 60.0 ml DMF were added in round bottom flask. 1.43 g (59.62 mmol) NaH was added slowly in reaction mass at 5-10°C. Added slowly 8.11 g (29.81 mmol) 4-bromomethyl 2-Cyano biphenyl. Stirred the reaction mass till starting nil. Reaction was monitored by TLC. Solvent was evaporated and residue was poured into water and extracted with DCM. Solvent was evaporated and crude compound was purified by Column Chromatography.



CHARACTERISATION

NMR spectra: NMR spectra of synthesized compound has been taken . Instrument used BRUKER AC 400F NMR spectrophotometer 33 HZ with DMSO solvent. The NMR spectra of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole (5) as shown in Fig 1.

Mass chromatogram Mass chromatogram of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole (5) as shown Fig 2.

RESULTS AND DISCUSSION

Weight of 2-(4-Thiazolyl) benzimidazole (3)is 6.9 gm. and weight of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d] imidazol-2-yl) thiazole (5) is 6.5 gm. Yield of 2-(4-Thiazolyl) Benzimidazole 65 % is about 6.9 gm. and yield of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole gives 56 % is about 6.5 gm.

For 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole (5)) ^{1}H NMR: 6.21(s, 2H), 7.26 (d, 5H), 7.53(d, 5H), 7.74(t, 2H), 7.92(d, 1H), 8.60(s, 1H), 9.36(s,1H). Mass of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole (5) is m/z is 392 (M+).

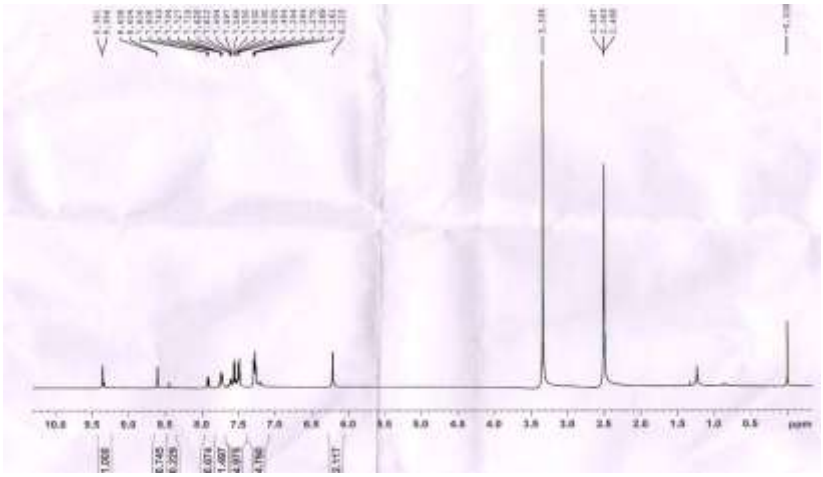


Fig 1: 1H NMR of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole (5) in DMSO

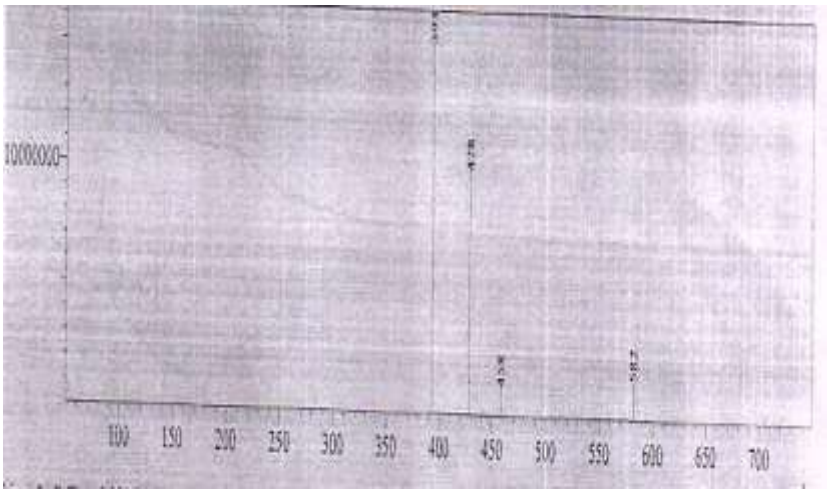


Fig 2. Mass Chromatogram of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole (5)

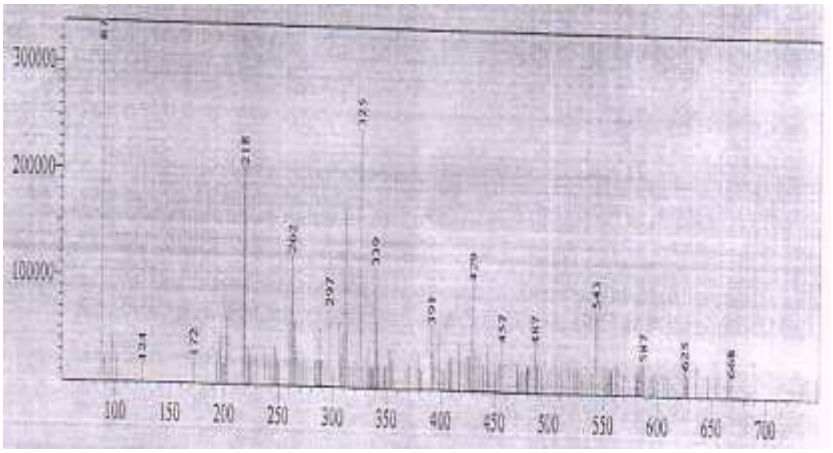


Fig 3.

CONCLUSION

In summary, this work is a rapid and efficient for the synthesis of 4-(1-(2-Cyano methyl biphenyl)-1H benzo[d]imidazol-2-yl) thiazole and results obtained confirmed by NMR spectra and Mass chromatogram.

ACKNOWLEDGMENTS

The authors are grateful to the Head, Department of Chemistry, S.M.B.S.T.College, Sangamner, Ahmednagar.

REFERENCE

1. Zhang C, Zhong B, Yang, Simin Pan, Liangkun YU, Siwang Li, Zhongiun, Su Bin, Meng Xiangbao, Bioorganic and Medicinal Chemistry, 2015; 23(13): 3774-3780.
2. Macpherson LS, Kirubakaran SG, Suresh Kumar Riera, Thomas VD, Aquino, J Alejandro, Journal of the American Chemical Society, 2010; 132: 1230-1231.
3. Kirubakaran S, Gorla S, Sharling L, Zhang M, Liu Xiaoping, Ray Soumya S, Macpherson lain S, Striepen Boris, Hedstrom Lizbeth, Cuny Gregory D, Bioorganic and Medicinal Chemistry Letter, 2012; 22(5): 1985-1988.
4. Lim Chae Jo, Kim Jeong, Lee Byung HO, Kwang-Seok, Hi Kyu Yang, Bulletin of the Korean Chemical Society, 2013; 34(8): 2305-2310.
5. Pissinate K , Rostrirolla DC , Pinheiro LM , Suryadevara P , Yogeeswari P , Sriram, DB , Headstrom L ,Cuny GD, Journal of the Brazilian Chemical Society, 2015; 26(7): 1357-1366.
6. Yale University, JORENSEN William, BUCALA Richard, J. Patent, 2010; WO2010/21693 A2.

7. Usha V, Hobrath JV, Gurcha SS, Reynolds RC, Besra GS,. PLoS One 2012, 7, e33886.
8. Umejiego NN, Gollapall DS, Sharling L, Volftsun A, Lu J, Benjamin NN, Stroupe AH, Riera TV, Striepen B, Hedstrom, L, Chem. Biol. 2008; 15: 70.
9. Hedstrom L, Chem. Rev. 2009; 109: 2903.
10. Makowska-Grzyska M, Kim Y, Wu R, Wilton R., Gollapalli DR, Wang XK, Zhang R, Jedrzejczak R, Mack JC, Maltseva N, Mulligan R, Binkowski TA, Gornicki P, Kuhn ML, Anderson W F, Hedstrom L, Joachimiak A, Biochemistry 2012; 51: 6148.
11. Ansari KF, Lal C, Synthesis, physicochemical properties and antimicrobial activity of somenew Benzimidazole derivatives, European Journal of Medicinal Chemistry. 2009; 44: 4028–4033.
12. Patil A, Ganguly S ,Surana SA, Systematic review of benzimidazole derivatives as anantiulcer agent, Rasayan J Chem. 2008; 1(3): 447-460.
13. Metwally KA, Abdel-Aziz LM, Lashine el SM, Husseiny MI , Badawy RH, Hydrazones of 2-aryl- -4- carboxylic acid hydrazides : synthesis and preliminary evaluation as antimicrobial agents. Bioorg Med Chem. 2006; 14(24): 8675-82.
14. Spasov A, Yozhitsa L, Bugaeva I ,Anisimova VA, Benzimidazole derivatives: Spectrum of pharmacological activity and toxicological properties. Pharmaceutical Chemistry Journal. 33; 5: 232-243.
15. Kadam SS, Mahadik KR,Bothara KG, Principles of Medicinal Chemistry, 1997; (1&2).
16. Rostirolla DC, Assunçao TM, Bizarro CV, Basso LA, Santos DS, RSC Adv. 2014; 4: 26271.
17. Tomlin CE, The Pesticide Manual, Crop Protection Publications, The Royal Society of Chemistry Publication, 1994; 10: 972-973.
18. Mothilal KK, Karunakaran C, Rajendran A , Murugesan R, Synthesis, X-ray crystal structure, antimicrobial activity and photodynamic effects of some thiabendazole complexes. Journal of Inorganic Biochemistry, 2004; 98(2): 322-332.
19. Darppoux HT, Staron A, Lebrun B, Dela Tullaye, Action curative remarquable d u thiabendazole sur la cercosporiose de la betterave. Phytiat Phytopharm., 1966; 15: 110-120.
20. Delp CJ, Klopping HL, Performance attributes of a new fungicide and mite ovicide candidate. PI. Dis. Deptr. 1968; 52: 95-99.
21. Froyd JD, Johnson HG, Fungicide nemotocide Tests .Amer. PhytopathoI. Soc. 1967; 22: 98.

22. Solel Z, The systemic fungicidal effect of benzimidazole derivatives and thiophanate against Cercospora leaf spot of sugarbeet, Phytopathology , 1970; 60: 1186-U90.
23. Devereux M , Shea DO, Kellett A, McCann M, Walsh M , Egan D, Deegan C, Dziora KK, Rosair G, Muller-Bunz H, Synthesis X-ray crystal structures and biomimetic and anticancer activities of novel copper (II) benzoate complexes incorporating 2-(4′-thiazolyl) benzimidazole (thiabendazole), 2-(2-pyridyl) benzimidazoleand 1, 10-phenanthroline as chelating nitrogen donor ligands. Journal of Inorganic Biochemistry, 2007; 101(6): 881-892.
24. Habib NS, Rida SM, Badawey EAM, Fahmy HTY , Ghozlan HA, Synthesis and biological investigations of some novel thiazolylbenzimidazoles and benzimidazolylthiazolo[4,5-d]pyrimidines Pharmazie , 1997; 52(5): 346-350.
25. Laskowski RA, McArthur MW, Moss DS, Thornton JM, J. Appl. Cryst. 1993; 26: 283.