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Benzimidazole in medicinal chemistry: An overview

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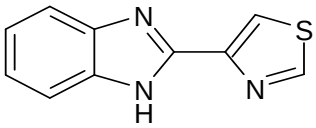
Abstract

Benzimidazole is a bicyclic heterocycle system consisting of two nitrogen atoms and fused phenyl ring shows wide range of biological activities. Benzimidazole can be synthesized using o-phenylenediamine and carboxylic acid. Benzimidazole posses wide spectrum of biological activities like including antibacterial, antifungal, antiviral, anti-inflammatory, anticonvulsant, antidepressant, antihypertensive, analgesic, and hypoglycemic properties. The present reviews attempted to gather the various developments in synthesis and biological activities of Benzimidazole derivatives.

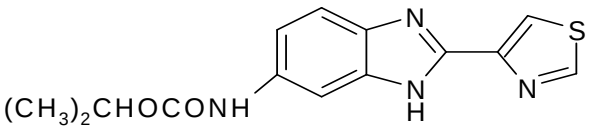
Key-words: Benzimidazole, Biological activities, SAR, Total synthesis.

INTRODUCTION

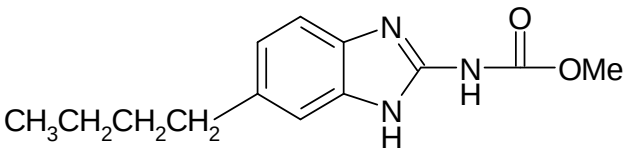
Benzimidazoles are readily formed by heating o-Phenylenediamine with carboxylic acid. Following drugs containing Benzimidazole moiety possessing anthelmentic activity. [1]



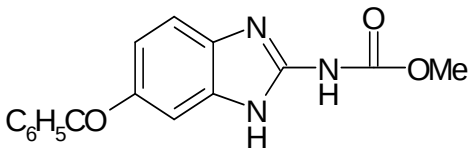
Thiabendazole



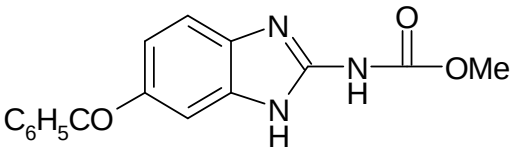
Cambendazole



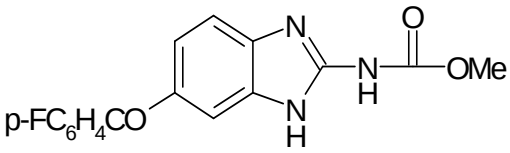
Parbendazole



Mebendazole



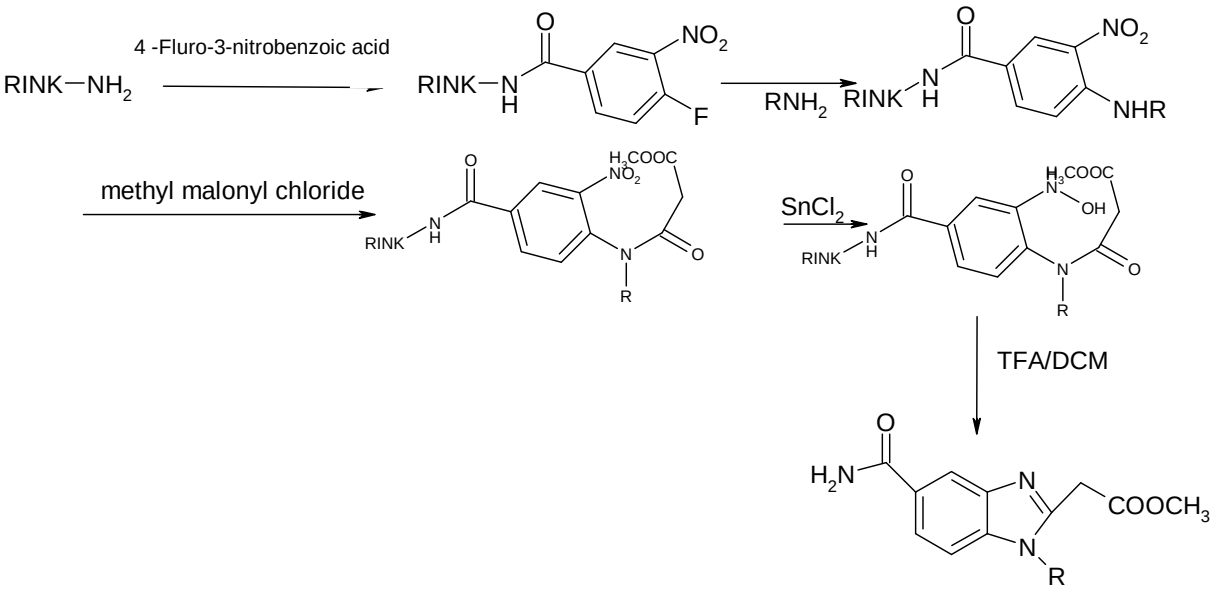
Albendazole



Flubendazole

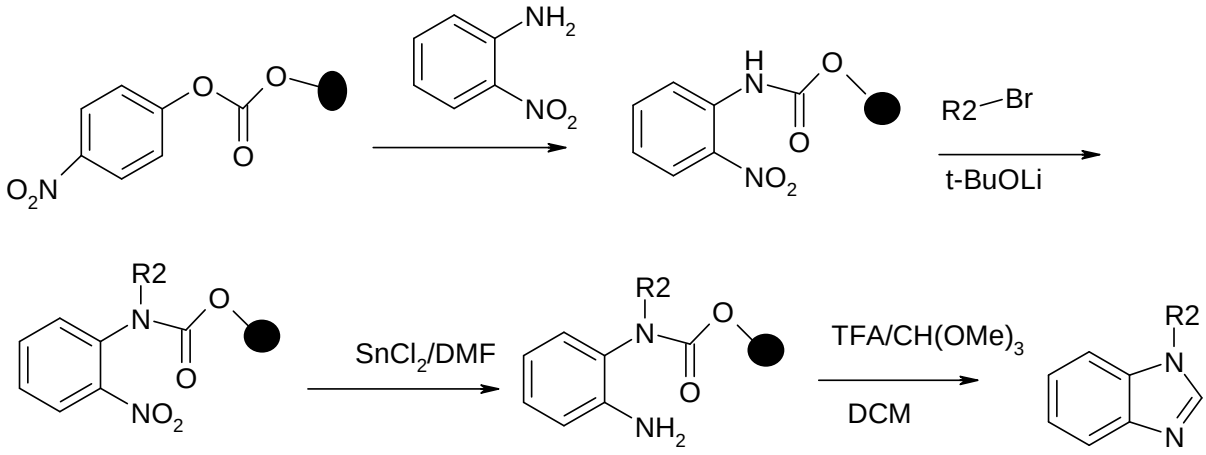
Solid-phase synthesis of benzimidazole *N*-oxides on SynPhase™ Lanterns

A solid-phase synthesis of benzimidazole *N*-oxides was developed while attempting to synthesize 1,5-benzodiazepine- 2,4-diones. The key step of the synthesis involves the reduction of an arylnitro to a hydroxyamino intermediate which subsequently condenses with an internal carbonyl group to give a benzimidazole *N*-oxide. A library of nine benzimidazole *N*-oxides was prepared on SynPhase™ Lanterns using this reduction–cyclization methodology.[2]



A New "Traceless" Solid-phase Synthesis Strategy: Synthesis of a Benzimidazole Library

A new strategy to achieve "traceless" solid-phase synthesis has been developed. Using this strategy, a "traceless" benzimidazole library with diversity on the benzene, moiety was synthesized efficiently in high yield with high purity. During the final step of this new synthetic sequence, cleavage and cyclic nucleus elaboration take place by a series of substitution and elimination reactions on the solid phase followed by release to the solution phase.[3]



Ytterbium perfluorooctanesulfonates catalyzed synthesis of benzimidazole derivatives in fluorous solvents

Catalytic condensation of o-Phenylenediamine and aldehydes was accomplished using rare earth(III)perfluorooctane sulfonates (RE(OPf)3), RE = Sc, Y, La _ Lu) as catalysts in fluorous solvents. Ytterbium perfluorooctanesulfonates (Yb(OPf)3) catalyzes the high-efficient synthesis of benzimidazole derivatives in fluorous solvents. By simple separation, fluorous phase containing only catalyst can be reused several times.[4]

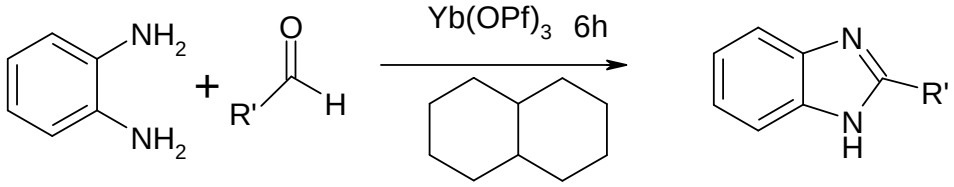
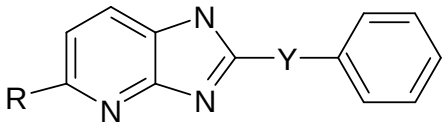
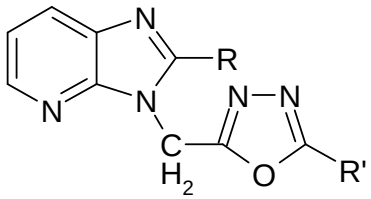
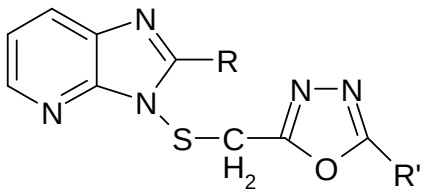
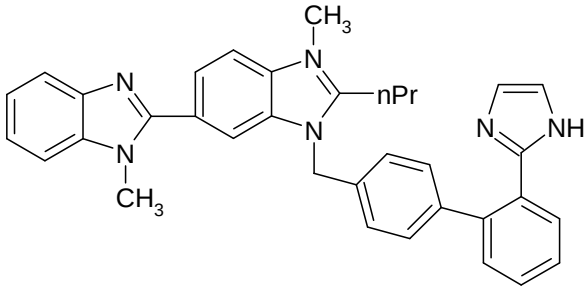
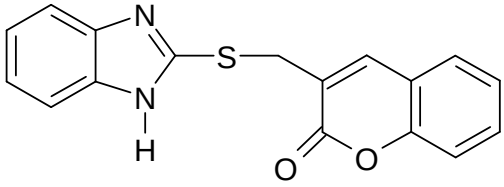
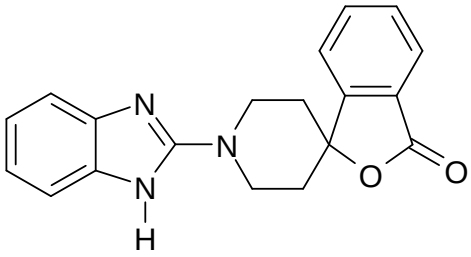
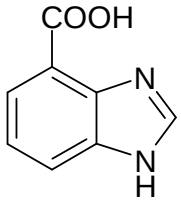
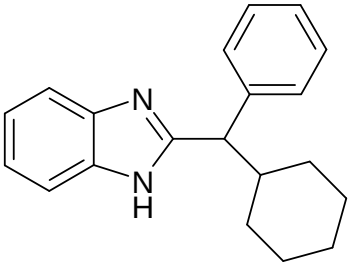
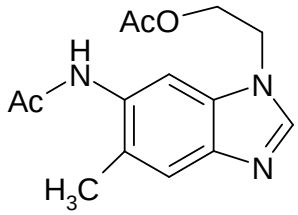
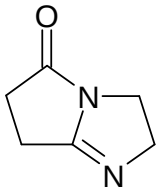
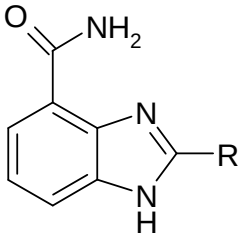
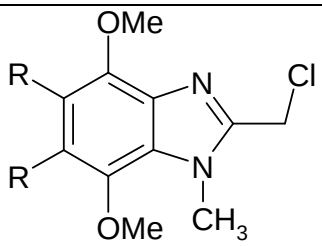
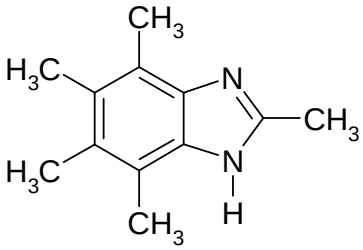
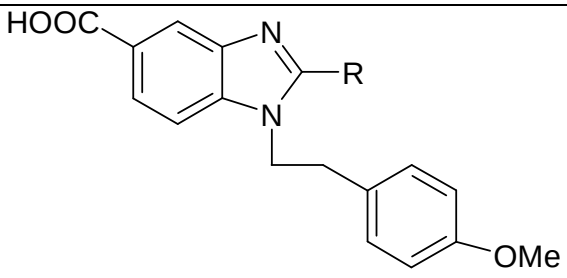
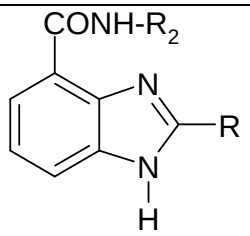
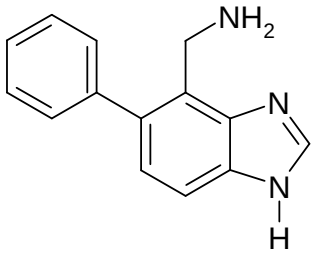
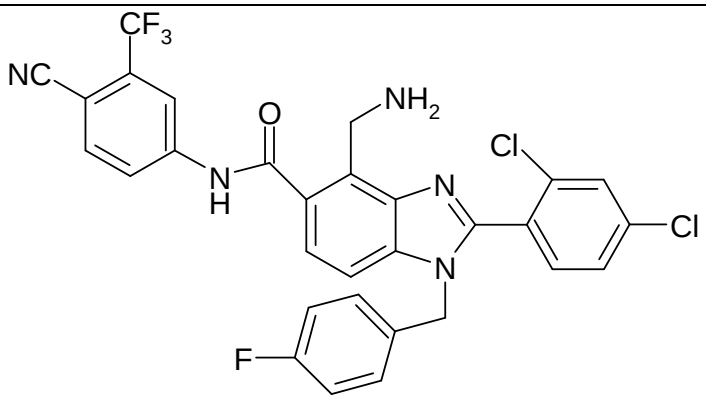
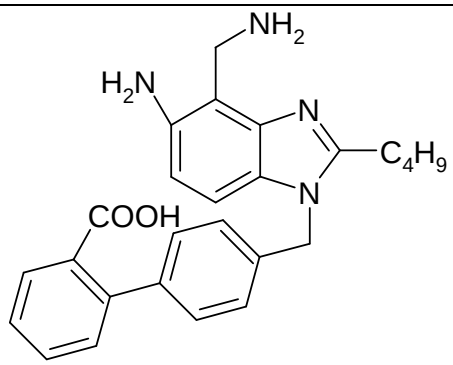
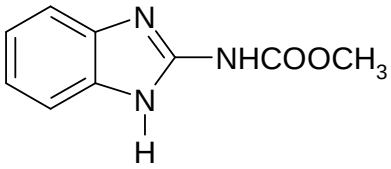
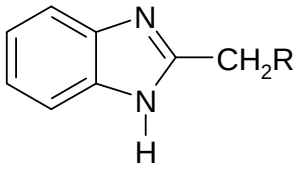


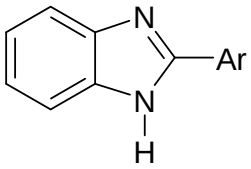
Table 1: Various pharmacological activities of Benzimidazole

Sr. No.	Authors	Structure	Pharmacological activity
1	Ismail Yalc *et al*;1998.		Antimicrobial activity [5]
2	C. Lal *et al:* 2009		Antimicrobial activity [6]

3	Kallappa M. Hosamani *et al*;2010		anticonvulsant, antidiabetic and DNA cleavage studies [7]
4	Xiao-Xia Lu *et al;*2008		angiotensin II receptor antagonists [8]
5	Jih Ru Hwu *et al;*2008		anti-hepatitis C virus agents [9]
6	Norikazu Ohtake *et al;*2008		NPY Y5 receptor antagonists [10]
7	Bellinda Benhamu *et al*;1999		Selective 5-HT4 Receptor Antagonists [11]
8	Julie Charton,*et al* ;2006		AMP-activated protein kinase activators [12]

9	Edward B. Skibo *et al*; 2006		Anticancer activity [13]
10	S.K. Agrawal *et al*;2010		anti-inflammatory [14]
11	Gui-Dong Zhu *et al*;2008		Anticancer activity [15]
12	Patrice Vanelle *et al*;2008		Anticancer activity [16]
13	Maria Bretner *et al*;2004		Antiamoebic activity [17]
14	Kanchugarakoppal S. *Rangappa et al*;2009		antileukemic activity [18]

15	Xianjin Luo *et al*;2005		antiviral activity [19]
16	Michael B. Wallace *et al*;2008		Antidiabetic activity [20]
17	K. S. Rangappa *et al*;2008		In treatment of Breast cancer [21]
18	Gulshan Bansal, *et al*;2005		Antihypertensive activity [22]
19	Francisco Herna´ndez-Luis *et al*;2009		cysticidal activity [23]
20	Paola Vicini *et al*;2005		Analgesic, antipyretic activity [24]

21	Gabriel Navarrete-Va´zquez, *et al*;2006		spasmolytic activity [25]

CONCLUSION

The plethora of research subscribed in this review indicates a wide spectrum of pharmacological activities exhibited by Benzimidazole derivatives. The biological profiles of these new generations of Benzimidazole would represent a fruitful matrix for further development of better medicinal agents. An attempt is made to focus on some synthetic methods of Benzimidazole including Solid phase synthesis and Traceless synthesis. It can act as an important tool for medicinal chemists to develop newer compounds possessing Benzimidazole moiety that could be better agents in terms of efficacy and safety.

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