

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

185,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



# Introductory Chapter: Short Insight in Synthesis and Applications of Benzimidazole and Its Derivatives

*Maria Marinescu*

## 1. Introduction

Benzimidazole is well known as an important pharmacophore among heterocyclic compounds due to the remarkable medicinal and pharmacological properties of its derivatives [1–3]. Among these currently marketed benzimidazole drugs to treat several diseases, we can mention bendamustine, selumetinib, galeterone, and pracinostat as antitumor agents; pantoprazole, lansoprazole, esomeprazole, and ilaprazole as proton pump inhibitors; bezitramide as an analgesic; mebendazole, albendazole, thiabendazole, and flubendazole as antihelminthics; ridinilazole as antibacterial; astemizole and bilastine as antihistamines; envirodin, samatasvir, and maribavir as antivirals; and candesartan and mibefradil as antihypertensive [1, 4–7]. Recent research recommends benzimidazole derivatives as potential EGFR and erbB2 inhibitors [8, 9], DNA/RNA binding ligands [10, 11], antitumor agents [12–14], anti-Alzheimer agents [15, 16], antidiabetic agents [17, 18], antiparasitic agents [10, 19], antimicrobial agents [20, 21], antiquorum-sensing agents [12], and antimalarial agents [19]. Intensive studies have demonstrated the use of the benzimidazole scaffold as key pharmacophore in clinically approved analgesic and anti-inflammatory agents [22]. Chiral benzimidazole derivatives were found to be Na<sub>v</sub>1.8 (voltage-gated sodium channels) blockers, which play a key role in the transmission of pain signals, with excellent preclinical in vitro ADME and safety profile [23]. Other benzimidazole derivatives have been shown to be anti-HIV-1 agents through the protection of APOBEC3G protein [24]. Benzimidazoles grafted with aromatic nuclei have been noted as antioxidant agents [25]. A correlation of the grafted organic functions on the benzimidazole scaffold has been found with their therapeutic potential [26]. Thus, carboxylic acids, carbamates, and amidines have been shown to be effective anticancer drugs [26–28], benzimidazole esters were reported as antifungal agents [29], and 2-aminobenzimidazole derivatives possess very good antimicrobial activity [30].

Structure-activity relationship (SAR) studies have shown that 1,2,5,6-substituted benzimidazoles with various substituents are analgesic and anti-inflammatory agents [22]. Also, SAR studies were accomplished for antiviral, anticancer, antihelminthic, antimicrobial, antimycobacterial, antidiabetic, antiprotozoal, antipsychotic, antidepressant, and antioxidant benzimidazole derivatives [1, 31–33].

## 2. Synthesis of the benzimidazole derivatives

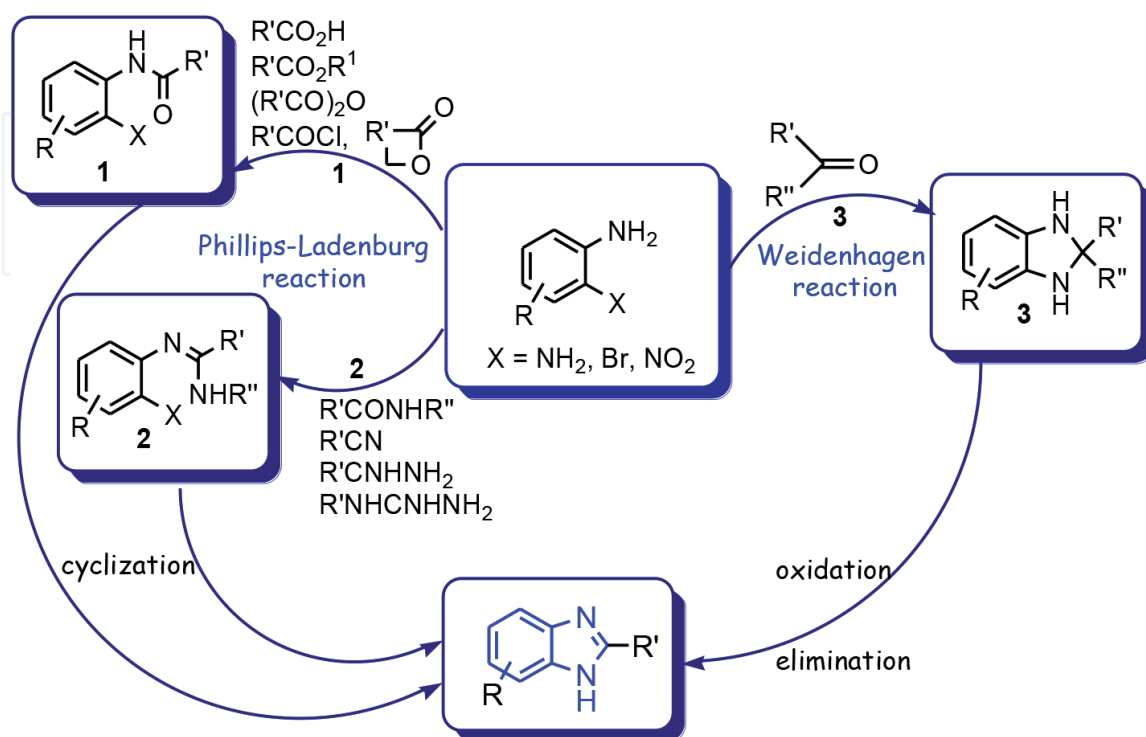
Benzimidazole synthesis reported by Hoebrecker in 1872 has greatly improved and diversified over last decades precisely because of its very diverse applications which will be discussed in the third part of this chapter. Classical synthesis was improved in terms of reaction conditions: catalysts, solvents or solvent-free, heating source, microwaves or ultrasound, and of course, nonpollutant or 'green' conditions. In the following, we will make (1) a very short presentation of classical syntheses and (2) an introduction to benzimidazole syntheses by rearrangement reactions.

### 2.1 Classical syntheses of benzimidazoles

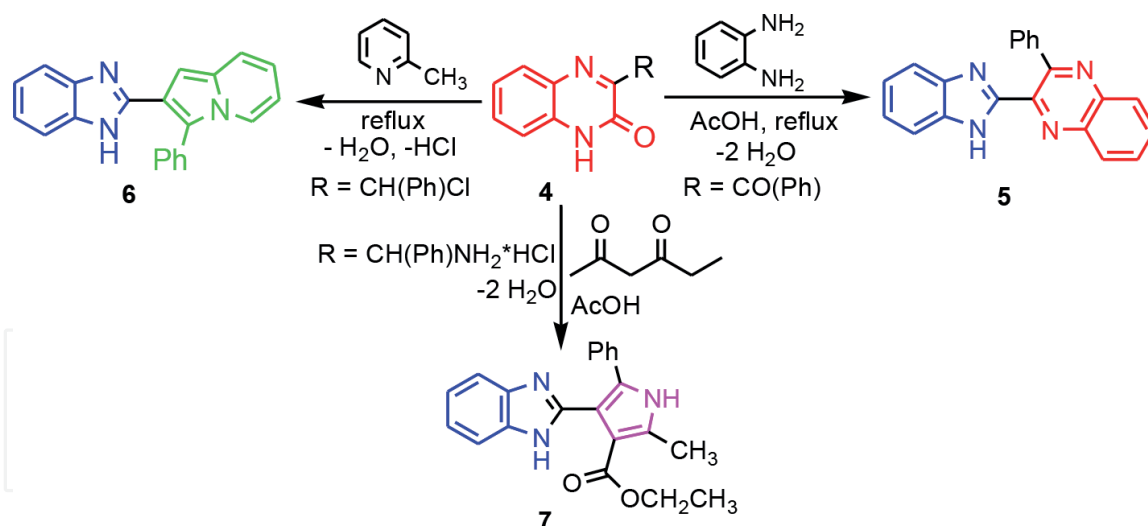
Synthesis methods of the benzimidazoles have been extensively summarized in previous studies, published by Wright [34] and Preston [35]. Actually, all classical syntheses of benzimidazoles represent modifications to two of the classic reactions [26]: (i) the Phillips-Ladenburg reaction, coupling 1,2-diaminobenzenes with carboxylic acids (see **Figure 1**) and (ii) Weitenhagen reaction, coupling of 1,2-diaminobenzenes with aldehydes and ketones (pathway 3) *via* benzimidazoline 3. In the case of the Phillips-Ladenburg reaction, esters, acid anhydrides, acid chlorides, and lactones (pathway 1) can be used instead of the acids, and benzimidazoles were generated *via* amide 1 cyclization or amides, nitriles, amidines, guanidines and benzimidazoles were resulted *via* cyclization of amidine 2 (pathway 2). The Phillips synthesis of benzimidazoles uses 4 N hydrochloric acid or glacial acetic acid, but various methods applied today use sulfuric acid or polyphosphoric acid. Reaction temperatures are high, reaching 250–300°C.

### 2.2 Synthesis of benzimidazoles *via* rearrangement of quinoxalinones

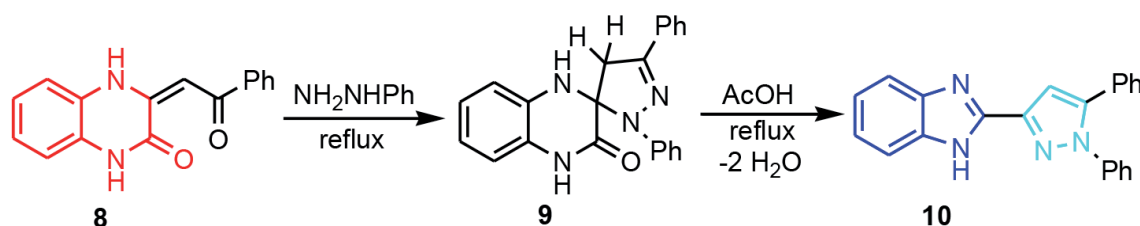
The limitations of classical synthesis, especially with respect to the synthesis of heterocyclic substituted benzimidazoles, have led to other methods [36].



**Figure 1.**  
Classical methods for synthesis of benzimidazoles.



**Figure 2.**  
Synthesis of 2-heteroaryl benzimidazoles by rearranging the quinoxalinones.



**Figure 3.**  
Synthesis of 2-(1,5-diphenyl-1H-pyrazol-3-yl)-1H-benzo[d]imidazole 10.

Rearrangements of quinoxalinones represent the most advantageous methods of synthesis currently reported [26, 36]. Hereinafter, some newer syntheses of benzimidazole derivatives are presented by quinoxalinone rearrangements. These new syntheses represent a combination of rearrangements, multicomponent reactions, and tandem sequences [26].

Thus, synthesis of benzimidazoles by the Hinsberg reaction implies condensation between 1,2-diaminobenzene and quinoxalin-2-one 4 to afford 2-benzimidazolylquinoxaline 5 in a 97% yield (see Figure 2). 2-(Indoliziny)benzimidazoles 6 were obtained in high yields using a Chichibabin reaction, by refluxing quinoxalin-2-one 4 with α-picoline [37].

2-(Pyrrol-3-yl)benzimidazole 7 was synthesized by a Knorr reaction between α-aminoketone of quinoxalinone 4 and ethyl acetoacetate [37].

Reaction of phenylhydrazine with 3-arylacylidene-3,4-dihydroquinoxalin-2(1H)-one 8 in boiling acetic acid implies the formation of spiro-compound 9, which rearranges into pyrazolylbenzimidazole 10 (see Figure 3) [26].

### 3. Applications of benzimidazole derivatives in other fields than medicinal and pharmaceutical chemistry

There are a large number of published scientific papers that refer to the synthesis, properties, and applications of benzimidazoles. Thus, if we search the keyword “benzimidazole” on Science Direct, we get 26,386 results, of which 915 are published in the last 4 months.

Particular attention has been paid to improving the synthesis of chiral benzimidazoles, a relatively young branch of chiral chemistry, due to their importance in the field of therapeutic agents [38]. Also, chiral benzimidazoles were

used as organocatalysts in Diels-Alder reaction, asymmetric aldol type reactions, asymmetric Michael addition, or enantioselective  $\alpha$ -chlorination reactions as well as in palladium and rhodium benzimidazole complexes used as catalysts in Mizoroki-Heck [39] and Suzuki-Miyaura coupling reactions or in reduction reactions [40].

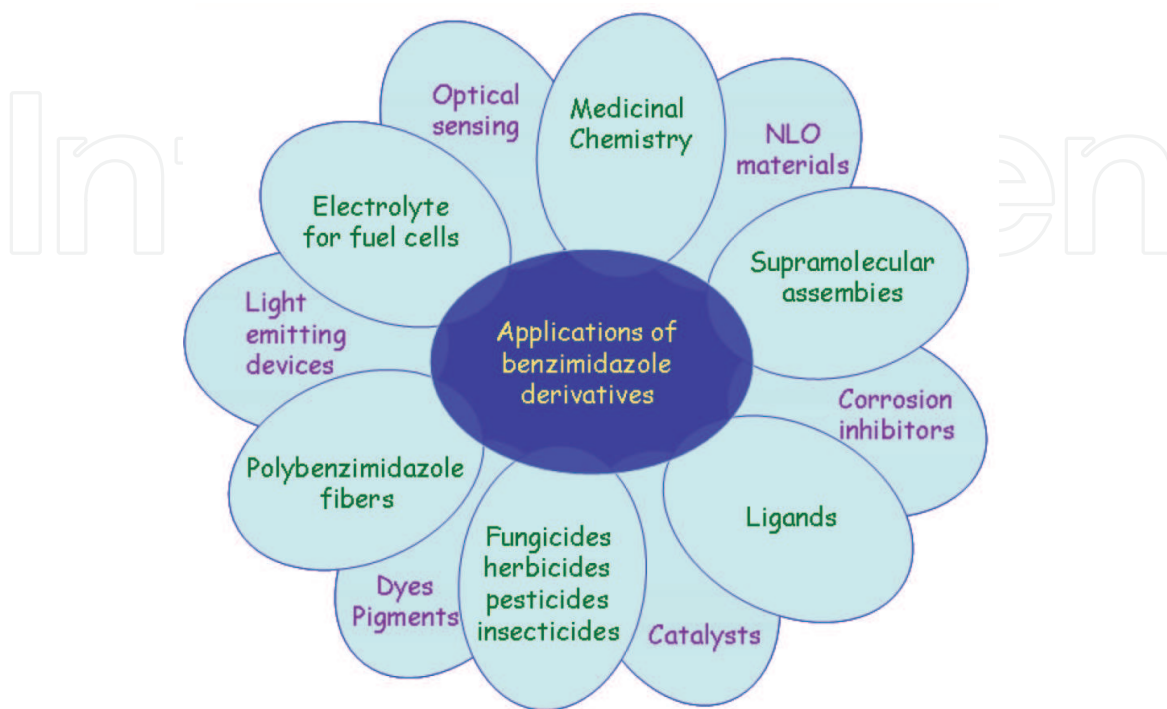
But recent research shows that benzimidazole scaffold is important not only for its therapeutic applications but also for its different uses in (nano) materials chemistry as optical chemical sensors [41], with special applications in medicine, environmental science, and chemical technology and has obvious advantage over other sensing devices, such as ease of operation and low cost (see **Figure 4**).

Supramolecular assemblies with interesting properties and with a wide range of applications like adsorbent materials, thermostable polymers, nanocontainers for small molecules, or liquid crystals for electronic conduction make up another use of benzimidazole and its derivatives [42–45].

Polybenzimidazole (PBI) derivatives: solid electrolyte for fuel cells [46], fibers [47], thin coatings [48], protective coatings for aerospace applications [49], or for the removal of uranium, thorium, and palladium from aqueous medium [50] are intensively studied in recent years. With an experience of 32 years, PBI Performance Products from Charlotte, North Carolina, is the leader in firefighter safety in Europe, USA, and the Middle East. PBI fabrics protect firefighters in a number of fire services, being renowned for their proven protection from heat and flame [51]. Another use of polybenzimidazoles is as PBI-based mixed matrix membranes with exceptional high water vapor permeability and selectivity [52].

In addition, the organic compounds are the most preferred for future photonic technology. Thus, several benzimidazoles with very good non-linear optic (NLO) properties, from very small molecules, such as 2-mercaptobenzimidazole, 2-phenyl benzimidazole, and 2-hydroxybenzimidazole [53], till molecules with more complicated structures [54], were studied.

Benomyl and carbendazim are recommended as benzimidazole fungicides having low toxicities in low doses and also are not carcinogenic, mutagenic, or teratogenic [55].



**Figure 4.**  
*Applications of benzimidazole derivatives.*



The literature shows the conditions of using common benzimidazole pesticides and reported the use of benzimidazoles as herbicides and insecticides [56].

More and more research is being reported on the use of benzimidazoles as corrosion inhibitors for various metals (Cu, Fe, and Zn) under acidic conditions [57–58].

Other authors have shown that benzimidazole is a versatile and essential chromophore for organic dyes with photophysical, electrochemical, and photovoltaic properties due to the position of donors, acceptors, and  $\pi$ -linkers in the benzene ring [59]. A broad range of nuances in watercolor painting and electrophotographic developer toner has been made over three decades using benzimidazol-2-one derivatives, highly appreciated for their durability and light resistance [36]. Benzimidazole proved to be an essential core for organic light emitting devices (OLEDs) with superior phosphorescence, thermal properties, and morphological stabilities [60].

## 4. Conclusion

Benzimidazole occupies a central place in the class of heterocyclic compounds used in pharmaceutical and medicinal chemistry. The chemistry and applications of benzimidazole and its derivatives are in continuous development, especially in the last decades. In the coming years, we expect new synthesis strategies and more exciting applications to meet world market requirements.

## Conflict of interest

There is no 'conflict of interest' in writing this chapter.

## Author details

Maria Marinescu

Faculty of Chemistry, University of Bucharest, Bucharest, Romania

\*Address all correspondence to: [maria.marinescu@chimie.unibuc.ro](mailto:maria.marinescu@chimie.unibuc.ro)

## IntechOpen

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

## References

- [1] Bansal Y, Silakari O. The therapeutic journey of benzimidazoles: A review. *European Journal of Medicinal Chemistry*. 2012;**20**(21):6208-6236. DOI: 10.1016/j.bmc.2012.09.013
- [2] Akhtar W, Khan MF, Verma G, Shaquiquzzaman M, Rizvi MA, Mehdi SH, et al. Therapeutic evolution of benzimidazole derivatives in the last quinquennial period. *European Journal of Medicinal Chemistry*. 2017;**126**:705-753. DOI: 10.1016/j.ejmech.2016.12.010
- [3] Rajesakhar S, Maiti B, Balamurali MM, Chanda K. Synthesis and medicinal applications of benzimidazoles: An overview. *Current Organic Synthesis*. 2017;**14**(1):40-60. DOI: 10.2174/1570179413666160818151932
- [4] Njar VC, Brodie AM. Discovery and development of galeterone (TOK-001 or VN/124-1) for the treatment of all stages of prostate cancer. *Journal of Medicinal Chemistry*. 2015;**58**(5):2077-2087. DOI: 10.1021/jm501239f
- [5] Moniruzzaman RS, Mahmud T. Quantum chemical and pharmacokinetic studies of some proton pump inhibitor drugs. *American Journal of Biomedical Sciences & Research*. 2019;**2**(1):3-8. DOI: 10.34297/AJBSR.2019.02.000562
- [6] Scholten WK, Christensen AE, Olesen AE, Drewes AM. Quantifying the adequacy of opioid analgesic consumption globally: An updated method and early findings. *American Journal of Public Health (AJPH)*. 2019;**109**(1):52-57. DOI: 10.2105/AJPH.2018.304753
- [7] Tahlan S, Kumar S, Ramasamy K, Lim SM, Shah SAA, Mani V, et al. Design, synthesis and biological profile of heterocyclic benzimidazole analogues as prospective antimicrobial and antiproliferative agents. *BMC Chemistry*. 2019;**13**(50):1-15. DOI: 10.1186/s13065-019-0567-x
- [8] Celik I, Ayhan-Kilcigil G, Guven B, Kara Z, Gurkan AAS, Karayel A, et al. Design, synthesis and docking studies of benzimidazole derivatives as potential EGFR inhibitors. *European Journal of Medicinal Chemistry*. 2019;**173**:240-249. DOI: 10.1016/j.ejmech.2019.04.012
- [9] Akhtar MJ, Siddiqui AA, Khan AA, Ali Z, Dewangan RP, Pasha S, et al. Design, synthesis, docking and QSAR study of substituted benzimidazole linked oxadiazole as cytotoxic agents, EGFR and erbB2 receptor inhibitors. *European Journal of Medicinal Chemistry*. 2017;**126**:853-869. DOI: 10.1016/j.ejmech.2016.12.014
- [10] Popov AB, Stolic I, Krstulovic L, Taylor MC, Kelly JM, Tomic S, et al. Novel symmetric bis-benzimidazoles: Synthesis, DNA/RNA binding and antitrypanosomal activity. *European Journal of Medicinal Chemistry*. 2019;**173**:63-75. DOI: 10.1016/j.ejmech.2019.04.007
- [11] Ding Y, Chai J, Centrella PA, Gondo C, DeLorey JL, Clark MA. Development and synthesis of DNA-encoded benzimidazole library. *ACS Combinatorial Science*. 2018;**20**:251-255. DOI: 10.1021/acscombsci.8b00009
- [12] El-Gohary NS, Shaaban MI. Synthesis, antimicrobial, antiquorum-sensing and antitumor activities of new benzimidazole analogs. *European Journal of Medicinal Chemistry*. 2017;**137**:439-449. DOI: 10.1016/j.ejmech.2017.05.064
- [13] Kanwal A, Saddique FA, Aslam S, Ahmad M, Zahoor AF, Moshin NA. Benzimidazole ring system as a

privileged template for anticancer agents. *Pharmaceutical Chemistry Journal*. 2018;**51**(12):1068-1077. DOI: 10.1007/s11094-018-1742-4

[14] Yadav S, Narasimhan B, Kaur H. Perspectives of benzimidazole derivatives as anticancer agents in the new era. *Anti-Cancer Agents in Medicinal Chemistry*. 2016;**16**(11):1403-1425. DOI: 10.2174/1871520616666151103113412

[15] Chaves S, Hiremathad A, Tomas D, Keri RS, Piemontese L, Santos MA. Exploring the chelating capacity of 2-hydroxyphenyl-benzimidazole based hybrids with multi-target ability as anti-Alzheimer's agent. *New Journal of Chemistry*. 2018;**42**(20):16503-16515. DOI: 10.1039/c8nj00117k

[16] Fang Y, Zhou H, Xu J. Synthesis and evaluation of tetrahydroisoquinoline-benzimidazole hybrids as multifunctional agents for the treatment of Alzheimer's disease. *European Journal of Medicinal Chemistry*. 2019;**167**:133-145. DOI: 10.1016/j.ejmech.2019.02.008

[17] Aboul-Enein HY, Rashedy AAE. Benzimidazole derivatives as antidiabetic agents. *Medicinal Chemistry*. 2015;**5**(7):318-325. DOI: 10.4172/2161-0444.1000280

[18] Adegboye AA, Khan KM, Salar U, Aboaba SA, Kanwal CS, Fatima I, et al. 2-Aryl benzimidazoles: Synthesis, in vitro  $\alpha$ -amylase inhibitory activity, and molecular docking study. *European Journal of Medicinal Chemistry*. 2018;**150**:248-260. DOI: 10.1016/j.ejmech. 2018.03.011

[19] Farahat AA, Ismail MA, Kumar A, Wenzler T, Brun R, Paul A, et al. Indole and benzimidazole bichalcophenes: Synthesis, DNA binding and antiparasitic activity. *European Journal of Medicinal Chemistry*.

2018;**143**:1590-1596. DOI: 10.1016/j.ejmech.2017.10.056

[20] Marinescu M, Tudorache GD, Marton GI, Zalaru CM, Popa M, Chifiriuc MC, et al. Density functional theory molecular modeling, chemical synthesis, and antimicrobial behaviour of selected benzimidazole derivatives. *Journal of Molecular Structure*. 2017;**1130**:463-471. DOI: 10.1016/j.molstruc.2016. 10.066

[21] Bansal Y, Kaur M, Bansal G. Antimicrobial potential of benzimidazole derived molecules. *Mini-Reviews in Medicinal Chemistry*. 2019;**19**(8):624-646. DOI: 10.2174/1389557517666171101104024

[22] Gaba M, Singh S, Mohan C. Benzimidazole: An emerging scaffold for analgesic and anti-inflammatory agents. *European Journal of Medicinal Chemistry*. 2014;**76**:494-505. DOI: 10.1016/j.ejmech.2014.01.030

[23] Brown AD, Bagal SK, Blackwell P, Blakemore DC, Brown B, Bungay PJ, et al. The discovery and optimization of benzimidazoles as selective  $\text{Na}_v1.8$  blockers for the treatment of pain. *European Journal of Medicinal Chemistry*. 2019;**27**:230-239. DOI: 10.1016/j.bmc. 2018.12.002

[24] Pan T, He X, Chen B, Chen H, Gheng G, Luo H, et al. Development of benzimidazole derivatives to inhibit HIV-1 replication through protecting APOBEC3G protein. *European Journal of Medicinal Chemistry*. 2015;**95**:500-513. DOI: 10.1016/j.ejmech.2015.03.050

[25] Hameed A, Hameed A, Farooq T, Noreen R, Javed S, Batool S, et al. Evaluation of structurally different benzimidazoles as priming agents, plant defence activators and growth enhancers in wheat. *BMC Chemistry*. 2019;**13**(29):1-11. DOI: 10.1186/s13065-019-0546-2



- [26] Mamedov VA. Recent advances in the synthesis of benzimidazol(on)es *via* rearrangements of quinoxalin(on)es. RSC Advances. 2016;**6**:42132-42172. DOI: 10.1039/C6RA03907C
- [27] Cheong JE, Zaffagni M, Chung I, Xu Y, Wang Y, Jernigan FE, et al. Synthesis and anticancer activity of novel water soluble benzimidazole carbamates. European Journal of Medicinal Chemistry. 2018;**144**:372-385. DOI: 10.1016/j.ejmech.2017.11.037
- [28] Bistrovic A, Krstulovic L, Harej A, Grbcic P, Sedic M, Kostrun S, et al. Design, synthesis and biological evaluation of novel benzimidazole amidines as potent multi-target inhibitors for the treatment of non-small cell lung cancer. European Journal of Medicinal Chemistry. 2018;**143**:1616-1634. DOI: 10.1016/j.ejmech.2017.10.061
- [29] Si W, Zhang T, Li Y, She D, Pan W, Gao Z, et al. Synthesis and biological activity of novel benzimidazole derivatives as potential antifungal agents. Journal of Pesticide Science. 2016;**41**(1):15-19. DOI: 10.1584/jpestics.D15-037
- [30] Nguyen TV, Peszko MT, Melander RJ, Melander C. Using 2-amino-benzimidazole derivatives to inhibit *Mycobacterium smegmatis* biofilm formation. MedChemComm. 2019;**10**(3):456-459. DOI: 10.1039/C9MD00025A
- [31] Siddiqui M, Alam MS, Sahu M, Yar MS, Alam O, Siddiqui MJA. Antidepressant, analgesic activity and SAR studies of substituted benzimidazoles. Asian Journal of Pharmaceutical Research. 2016;**6**(3):170-174. DOI: 10.5958/2231-5691.2016. 00024.1
- [32] Tahlan S, Ramasamy K, Lim SM, Shah SAA, Mani V, Narasimhan B. Design, synthesis and therapeutic potential of 3-(2-(1H-benzo[d]imidazol-2-ylthio) acetamido)-N-(substituted phenyl)benzamide analogues. Chemistry Central Journal. 2018;**12**(139):1-12. DOI: 10.1186/s13065-018-0513-3
- [33] Xu M, Wang SL, Zhu L, Wu PY, Dai WB, Rakesh KP. Structure-activity relationship (SAR) studies of synthetic glycogen synthase kinase-3 $\beta$  inhibitors: A critical review. European Journal of Medicinal Chemistry. 2019;**164**:448-470. DOI: 10.1016/j.ejmech.2018.12.073
- [34] Wright JB. The chemistry of the benzimidazoles. Chemical Reviews. 1951;**43**(3):397-541. DOI: 10.1021/cr60151a002
- [35] Preston PN. Synthesis, reactions, and spectroscopic properties of benzimidazoles. Chemical Reviews. 1974;**74**(3):279-314. DOI: 10.1021/cr60289a001
- [36] Mamedov VA, Khavizova EA, Syakaev VV, Gubaidullin AT, Samigullina AI, Algaeva NE, et al. The rearrangement of 1H, 1'H-spiro[quinoline-4,2'-quinoxaline]-2,3'(3H,4'H)-diones: A new and efficient method for the synthesis of 4-(benzimidazol-2-yl)quinolin-2(1H)-ones. Tetrahedron. 2018;**74**(45):6544-6557. DOI: 10.1016/j.tet.2018.09.035
- [37] Mamedov VA, Zhukova NA, Sinyashin OG. Advances in the synthesis of benzimidazolones *via* rearrangements of benzodiazepinones and quinoxalin(on)es. Mendelev Communications. 2017;**27**(1):1-11. DOI: 10.1016/j.mencom.2017.01.001
- [38] Khose VN, John ME, Pandey AD, Karnik AV. Chiral benzimidazoles and their applications in stereodiscrimination processes. Tetrahedron: Asymmetry. 2017;**28**(10):1233-1289. DOI: 10.1016/j.tetasy.2017.09.001

- [39] Said NR, Mustakim MA, Sani MMM, Baharin SNA. Heck reaction using palladium-benzimidazole catalyst: Synthesis, characterisation and catalytic activity. IOP Conference Series: Materials Science and Engineering. 2018;**458**(012019):1-7. DOI: 10.1088/1757-899X/458/1/012019
- [40] Gunnaz S, Gokce AG, Turkmen H. Synthesis of bimetallic complexes bridged by 2,6-bis(benzimidazol-2-yl) pyridine derivatives and their catalytic properties in transfer hydrogenation. Dalton Transactions. 2018;**47**:17317-17328. DOI: 10.1039/c8dt03178a
- [41] Horak E, Kassal P, Steinberg M. Benzimidazole as a structural unit in fluorescent chemical sensors: The hidden properties of a multifunctional heterocyclic scaffold. Supramolecular Chemistry. 2017;**30**(10):838-857
- [42] Jiang JJ, Pan M, Liu JM, Wang W, Su CY. Assembly of robust and porous hydrogen-bonded coordination frameworks: Isomorphism, polymorphism, and selective adsorption. Inorganic Chemistry. 2010;**49**(21):10166-10173. DOI: 10.1021/ic1014384
- [43] Agarwal RA, Aijaz A, Ahmad M, Sañudo EC, Xu Q, Bharadwaj PK. Two new coordination polymers with Co(II) and Mn(II): Selective gas adsorption and magnetic studies. Crystal Growth & Design. 2012;**12**(6):2999-3005. DOI: 10.1021/cg300217v
- [44] Nath I, Chakraborty J, Verpoort F. Metal organic frameworks mimicking natural enzymes: A structural and functional analogy. Chemical Society Reviews. 2016;**45**(15):4127-4170. DOI: 10.1039/C6CS00047A
- [45] Tan S, Wei B, Liang T, Yang X, Wu Y. Anhydrous proton conduction in liquid crystals containing benzimidazole moieties. RSC Advances. 2016;**6**(40):34038-34042. DOI: 10.1039/C6RA03375J
- [46] Yuan S, Guo X, Aili D, Pan C, Li Q, Fang J. Poly(imidebenzimidazole)s for high temperature polymer electrolyte membrane fuel cells. Journal of Membrane Science. 2014;**454**(12):351-358. DOI: 10.1016/j.memsci.2013.12.007
- [47] Yin C, Dong J, Zhang Z, Zhang Q, Lin J. Structure and properties of polyimide fibers containing benzimidazole and amide units. Journal of Polymer Science. 2015;**53**:183-191. DOI: 10.1002/polb.23606
- [48] Nabavian S, Naderi R, Asadi N. Determination of optimum concentration of benzimidazole improving the cathodic disbonding resistance of epoxy coating. Coatings. 2018;**8**(12):471. DOI: 10.3390/coatings8120471
- [49] HMS I, Bhowmik S, Benedictus R. Performance evaluation of polybenzimidazole coating for aerospace application. Progress in Organic Coatings. 2017;**105**:190-199. DOI: 10.1016/j.porgcoat.2017.01.005
- [50] Kumar VV, Kumar CR, Suresh A, Jayalakshmi S, Mudali UK, Sivaraman N. Evaluation of polybenzimidazole-based polymers for the removal of uranium, thorium and palladium from aqueous medium. Royal Society Open Science. 2018;**5**(171701):1-16. DOI: 10.1098/rsos.171701
- [51] Mandal S, Gwoen S. Characterizing thermal protective fabrics of firefighters' clothing in hot surface contact. Journal of Industrial Textiles. 2016;**47**(5):1-18. DOI: 10.1177/1528083716667258
- [52] Akhtar FH, Kumar M, Villalobos LF, Vovusha H, Shevate R, Schwingenschlögl U, et al. Polybenzimidazole-based mixed

membranes with exceptional high water vapor permeability and selectivity. *Journal of Materials Chemistry A*. 2017;5(41):21807-21819. DOI: 10.1039/C7TA05081J

[53] Muthuraja A, Kalainathan S. A study on growth, optical, mechanical, and NLO properties of 2-mercaptobenzimidazole, 2-phenylbenzimidazole and 2-hydroxy benzimidazole single crystals: A comparative investigation. *Materials Technology*. 2017;32(6):335-348. DOI: 10.1080/10667857.2016.1235080

[54] Tayade RP, Sekar N. Benzimidazole-thiazole based NLOphoric styryl dyes with solid state emission – Synthesis, photophysical, hyperpolarizability and TD-DFT studies. *Dyes and Pigments*. 2016;128:111-123. DOI: 10.1016/j.dyepig.2016.01.012

[55] Gupta PK. Toxicity of fungicides. In: Gupta RC, editor. *Veterinary Toxicology. Basic and Clinical Principles*. Hopkinsville, KY: Academic Press; 2018. pp. 569-580. DOI: 10.1016/B978-0-12-811410-0.00045-3

[56] Emler S, Scholze M, Kortenkamp A. Seven benzimidazole pesticides combined at sub-threshold levels induce micronuclei in vitro. *Mutagenesis*. 2013;28(4):417-426. DOI: 10.1093/mutage/get019

[57] Eldebss TMA, Farag AM, Shamy AYM. Synthesis of some benzimidazole-based heterocycles and their application as copper corrosion inhibitors. *Journal of Heterocyclic Chemistry*. 2019;56(2):371-390. DOI: 10.1002/jhet.3407

[58] Wang X, Yang H, Wang F. An investigation of benzimidazole derivative as corrosion inhibitor for mild steel in different concentration HCl solutions. *Corrosion Science*. 2011;53:113-121. DOI: 10.1016/j.corsci.2010.09.029

[59] Saltan GM, Dincalp H, Kiran M, Zafer C, Erbaş SC. Novel organic dyes based on phenyl-substituted benzimidazole for dye sensitized solar cells. *Materials Chemistry and Physics*. 2015;163:387-393. DOI: 10.1016/j.matchemphys.2015.07.055

[60] Zhao Y, Chao W, Qiu P, Li X, Wang Q, Chen J, et al. New benzimidazole-based bipolar hosts: Highly efficient phosphorescent and thermally activated delayed fluorescent OLEDs employing the same device structure. *ACS Applied Materials & Interfaces*. 2016;8(4):2635-2643. DOI: 10.1021/acsami.5b10464