

## *Chapter-5*

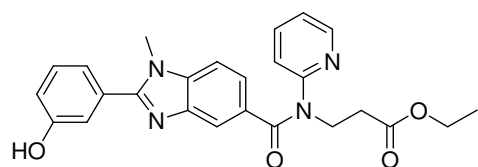
### *Summary and conclusion*

Recent medicinal chemistry applications of benzimidazole analogs include antibacterial and antifungal agents, anthelmintic agents, HIV-1-induced cytopathic inhibitor, anti-inflammatory and antiulcer agents, cytotoxic and antitumor agents, anticancer, DNA binding agents, enzyme and receptor agonists or antagonists.

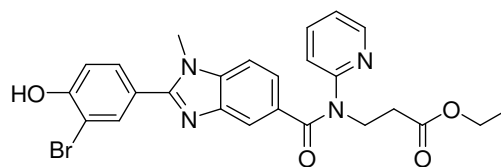
Other applications of benzimidazoles include their use as organic ligands, fluorescent whitening agent dyes and functional materials. Therefore, the construction of these heterocycles has always been of great interest to organic and medicinal chemists and has consequently received much attention.

In order to develop eco-friendly green chemistry we have decided to use air as oxidant and alcoholic solvents as the solvent media at ambient temperature to obtain novel benzimidazoles.

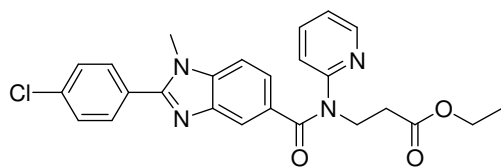
In the chapter-2 the following compounds have been synthesized:



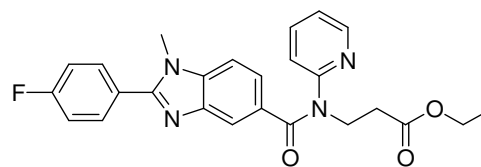
MPD-1



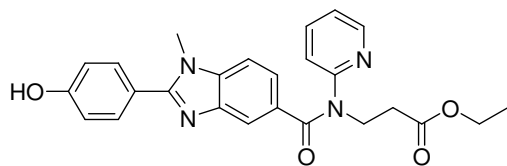
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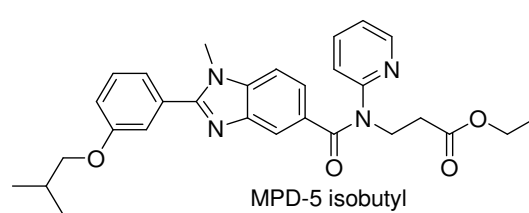
MPD-3



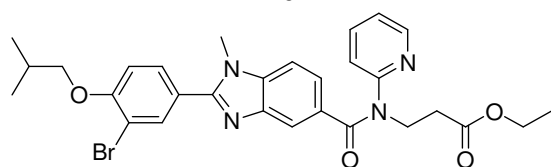
MPD-4



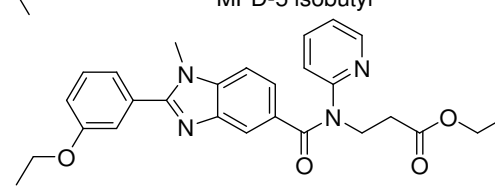
MPD-5



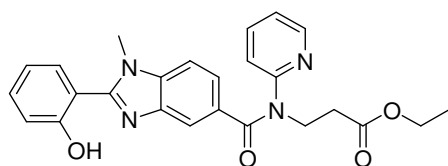
MPD-5 isobutyl



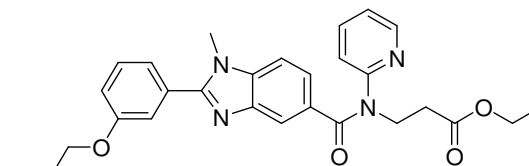
MPD-6



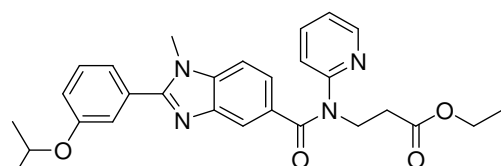
MPD-7



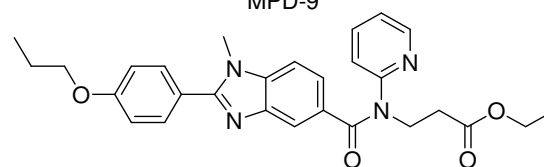
MPD-8



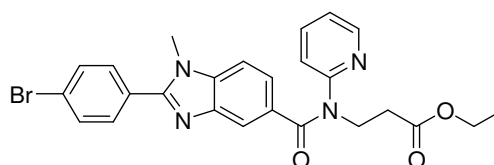
MPD-9



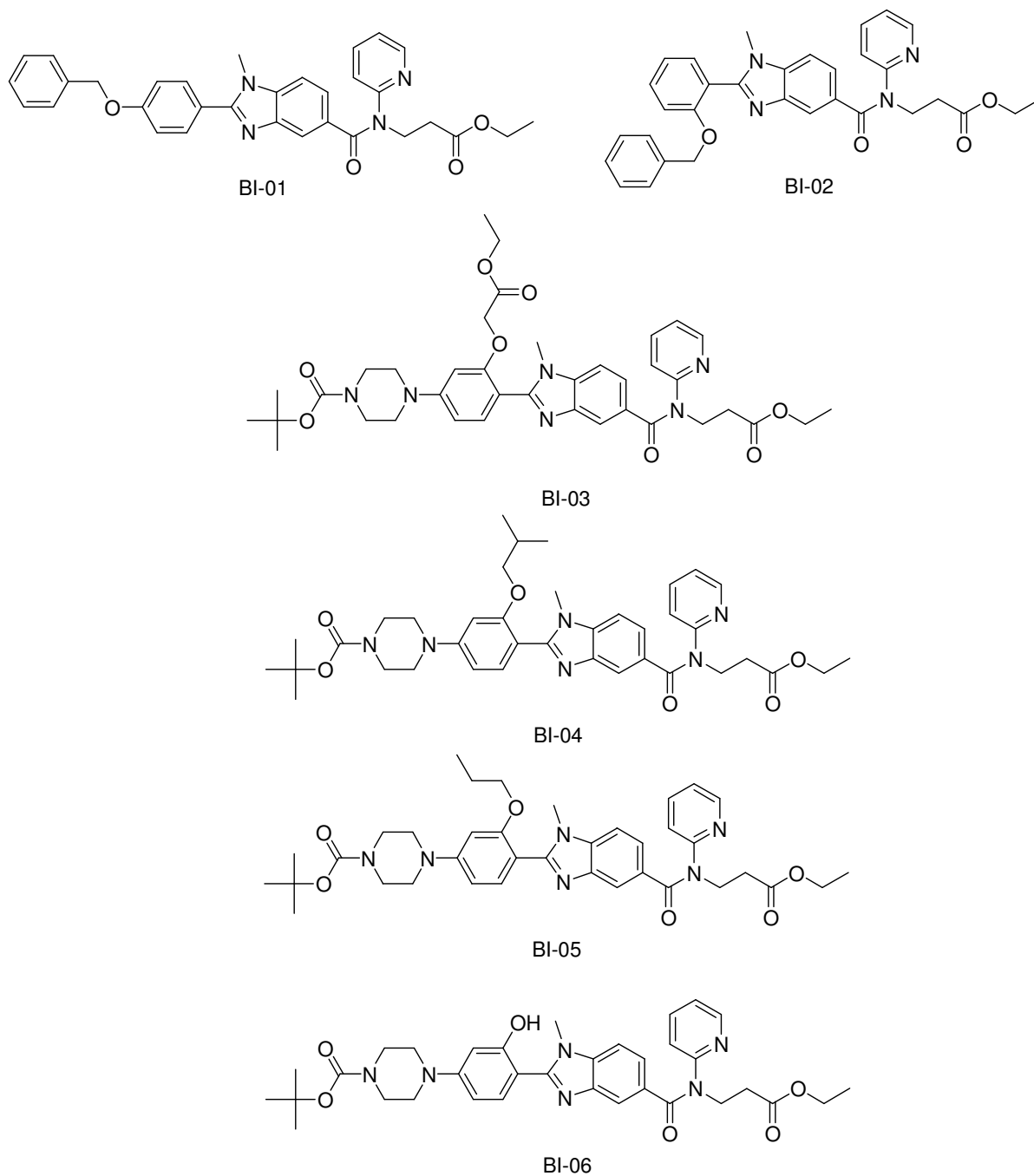
MPD-10



MPD-11



MPD-12



Biological activity of the synthesized compounds has been determined. The compound MPD5, MPD9 and MPD7 have good activity on MDA-MB-231 cell line. While, MPD2, MPD5-Isobutyl were less active or almost not effective against tested cell line.

So, further the activity of all effective compounds series were tested against normal cell line [VERO cell line] and it was concluded that compounds MPD-7, MPD5-isobutyl and BI-02 were found to be toxic for normal cell. On other side excepting MPD-7, others were not effective to inhibit tested cells.

### Conclusion

From the results, it can be concluded that compounds MPD6, MPD1 and MPD-3 gives good cytotoxic activity on MDA-MB-231 cell line. Compounds MPD5, MPD9 and MPD7 have good activity but less than std. drug. While compound MPD2, MPD5-isobutyl and BI-02 were found to be not effective.

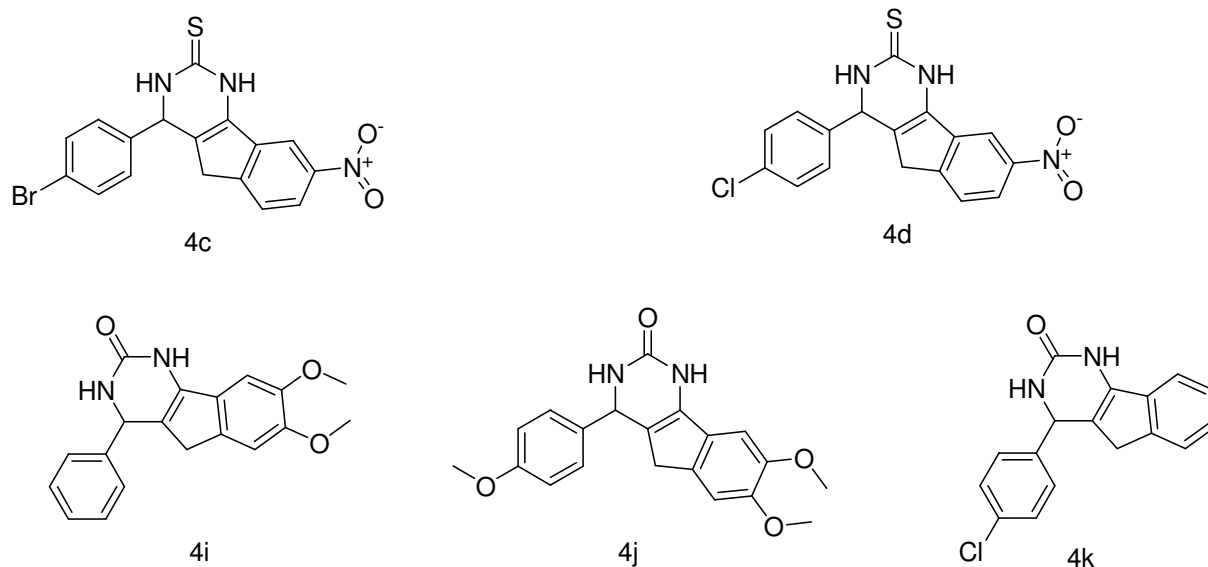
In the chapter 3 part-A compounds 4a-l has been synthesized by Biginelli reaction. Pyrimidine-2-thione and pyrimidin-2-one have been synthesized by using indanone derivatives. Substituted indanone derivatives are used to synthesize pyrimidine derivatives. Multicomponent condensation reactions (MCRs) have been discovered to be a powerful method for the synthesis of organic compounds, since the products are formed in a single step and diversity can be achieved by simply varying each component. The original Biginelli protocol for the preparation of the DHMPs consisted of heating a mixture of the three components (aldehyde,  $\beta$ -keto-ester, and urea ) in ethanol containing a catalytic amount of HCl. This procedure leads in one step-one pot to the desired DHPM. The major drawback associated with this protocol is the low yields, particularly for substituted aromatic and aliphatic aldehydes.

We have used antimony(III)chloride ( $\text{SbCl}_3$ ) in the synthesis of pyrimidine-2-thione and pyrimidin-2-one derivatives to provide better results with more sterically hindered substrates with high yield.  $\text{SbCl}_3$  is inexpensive, easy to handle on large scale. In view of the above observation, we wish to report herein biologically active heterocyclic systems containing pyrimidine-2-thione and pyrimidin-2-one derivatives. Herein antimony (III) chloride ( $\text{SbCl}_3$ ) catalyst was significantly more effective than other acid catalyst in the Biginelli reaction of cyclic ketones and it provides better results with more sterically hindered substrates with high yields.

The biological activity of the synthesized compound has been determined. It can be concluded that compound **4c** is active against Gram positive bacteria *Staphylococcus aureus* (*S.aureus*).

Compounds **4d**, **4i**, **4j** and **4k** are found to be active against Gram negative bacteria *Escherichia coli* as compared to standard antibiotic ampicillin.

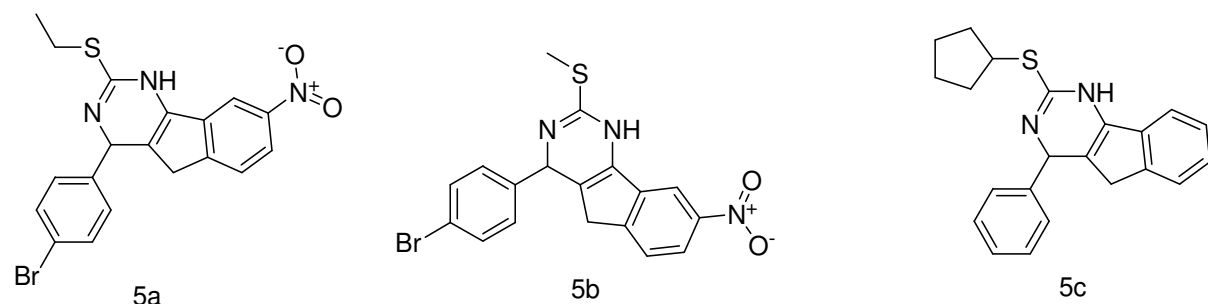
Antifungal study revealed that compounds **4c**, **4h**, **4j** and **4k** are more potent as compared to standard fungicidal griseofulvin against *Candida albicans* (*C.albicans*).



In the chapter-3 part-B alkylated derivatives of the synthesized compounds from 4a-l has been prepared. The compounds 5a-j has been prepared and biological activity has been determined.

It can be concluded that compounds 5a, 5b and 5c are found to be highly active against Gram negative bacteria *Escherichia coli* as compared to standard antibiotic ampicillin.

Antifungal study revealed that compounds 5b and 5c are more potent as compared to standard fungicidal griseofulvin against *Candida albicans* (*C.albicans*).



In the chapter-4 different compounds 2a-j and 3a-j have been synthesized. The compounds are studied for their biological activity.

A series of some derivatives (**3a-j**) have been synthesized with high yield via *insitu* approach from compounds (**2a-h**). Also, compounds (**2a-h**) can be prepared by multicomponent reaction between 1,3-cyclohexanedione, urea/thiourea and aldehydes with high yield using antimony(III)chloride as a catalyst.

It can be concluded that compound **3a** and **3c** is highly active against Gram positive bacteria *Staphylococcus aureus* (*S.aureus*), compounds **2a** and **3a** exhibited excellent activity against Gram negative bacteria *Escherichia coli* (*E.coli*) as compared to standard antibiotic ampicillin.

Antifungal study revealed that compounds **2a**, **2b** and **3a** are more potent as compared to standard fungicidal griseofulvin against *Candida albicans* (*C.albicans*).

