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# Synthesis of amidines and its application to pyrimidouracil synthesis

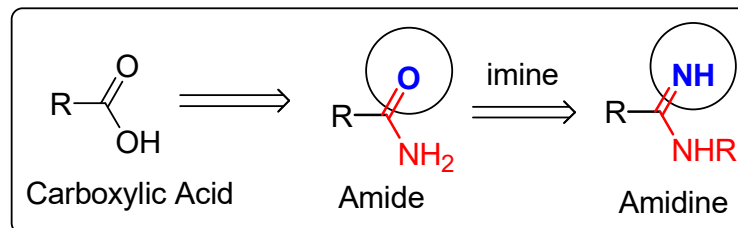
By

Dr. PRADIP DEBNATH

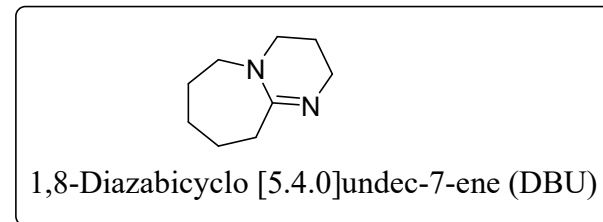
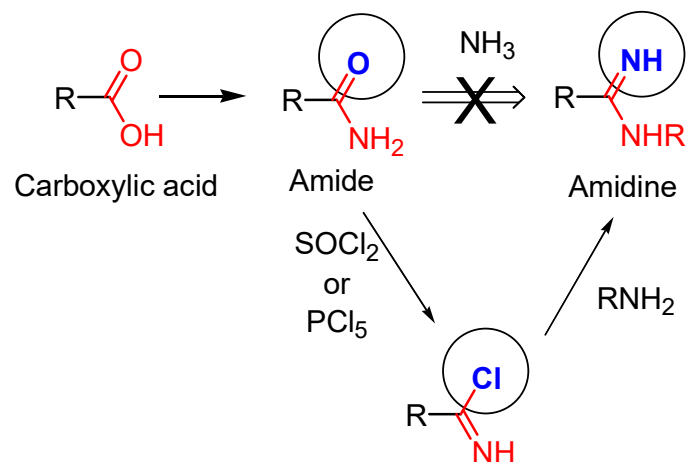
M. B. B. College

Agartala, Tripura

# What are Amidines?



- Amidines are a class of oxoacids [(RC(=O)OH)].
- The -OH group is replaced by an -NH<sub>2</sub> group and the =O group is replaced by =NR, giving amidines the general structure RC(=NR)NR<sub>2</sub>. i.e they are the imine derivatives of amides (RCONH<sub>2</sub>)
- When the parent oxoacid is a carboxylic acid, the resulting amidine is a carboxamidine or carboximidamide (IUPAC name).
- Carboxamidines are frequently referred to simply as amidines



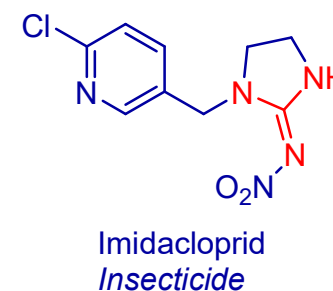
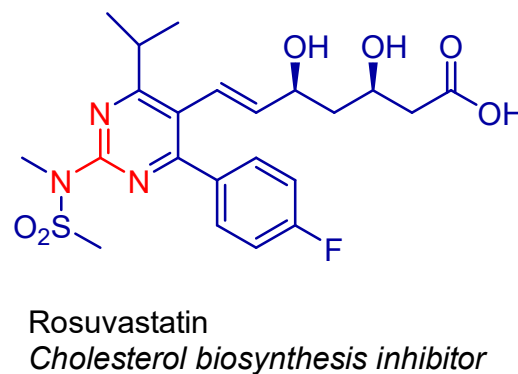
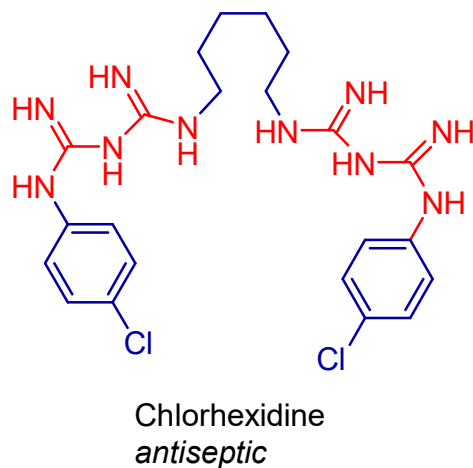
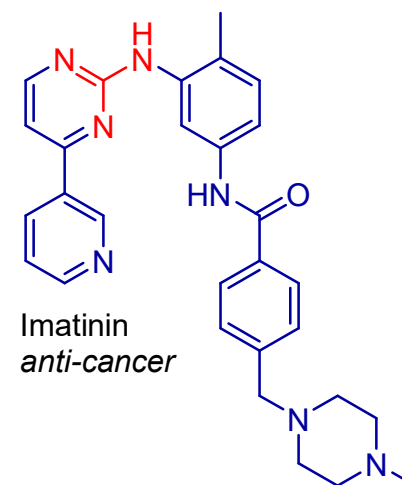
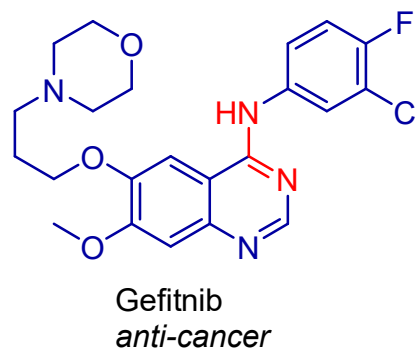
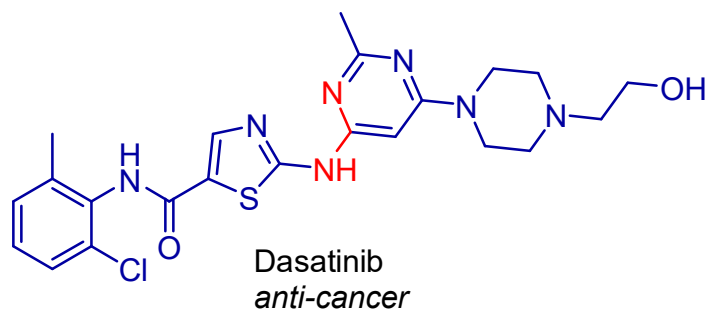
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## The importance of Amidines

- Antibiotics
- Diuretics
- Anti-inflammatory agents
- Antithrombotic agents
- Anthelmintics
- Used as muscarinic agonists for the treatment of Alzheimer's disease
- Used as a valuable precursor for the preparation of **azacyclic** compounds of biological interest

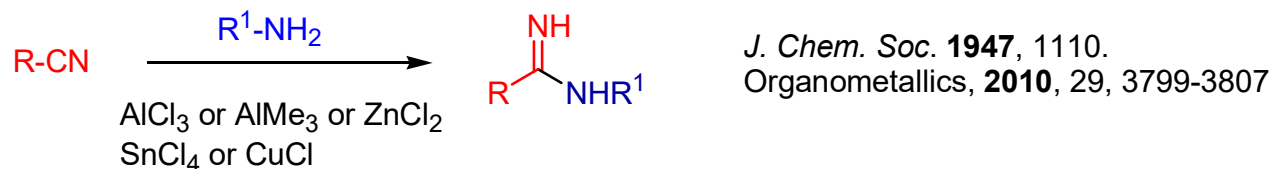
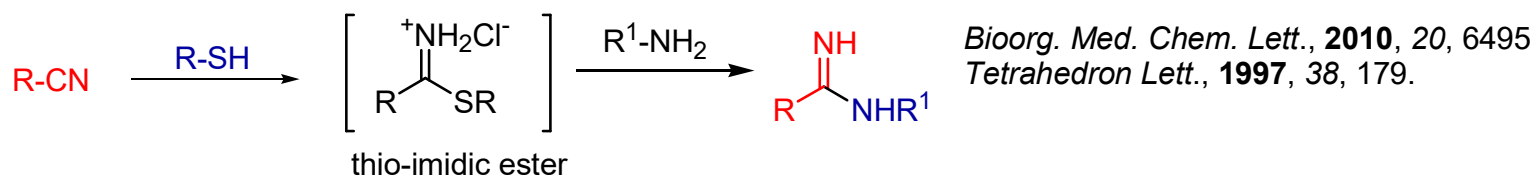
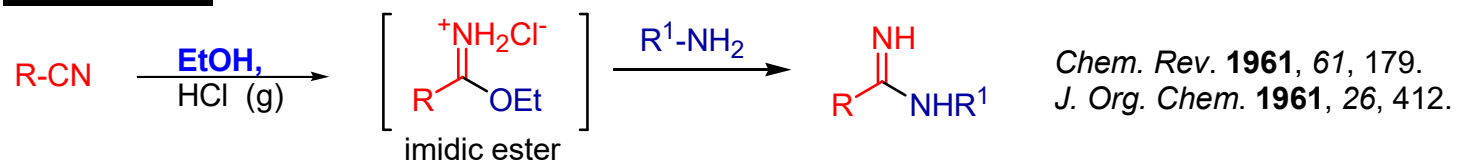


# Few examples of biologically important Molecules:



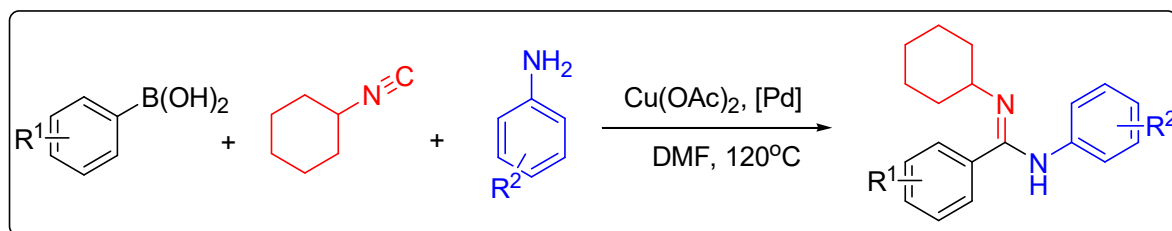
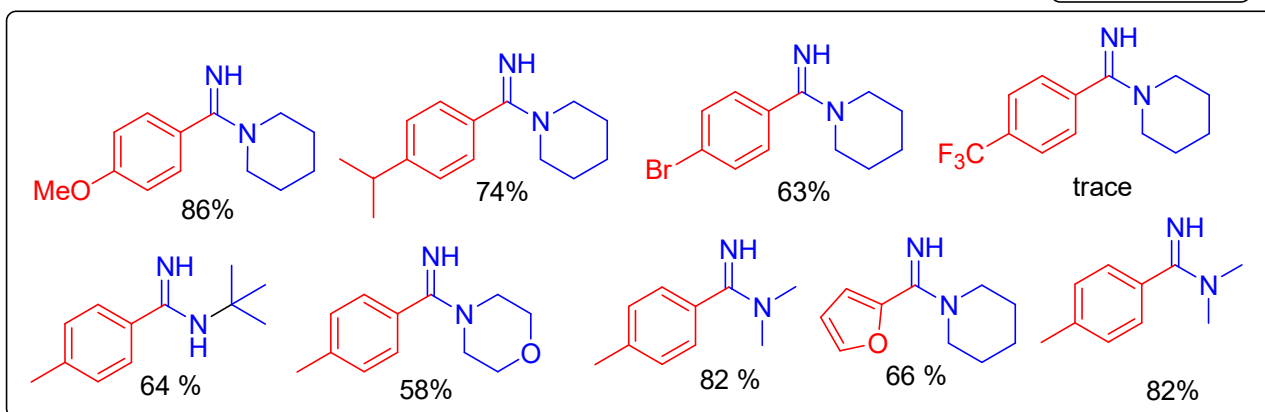
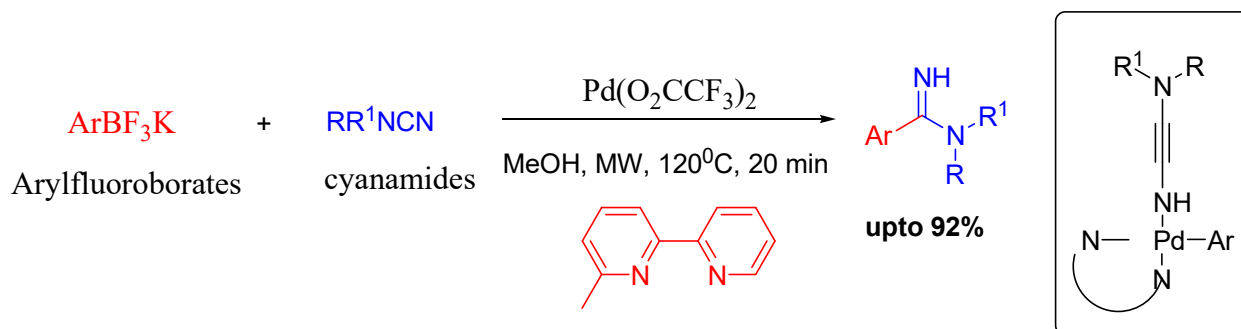
## Preparation of Amidines:

### Pinner reaction



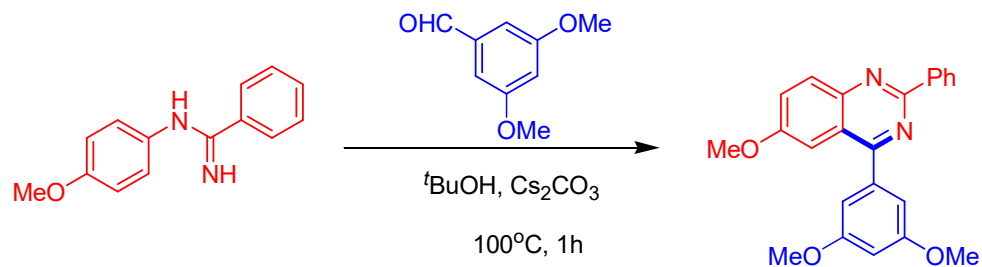
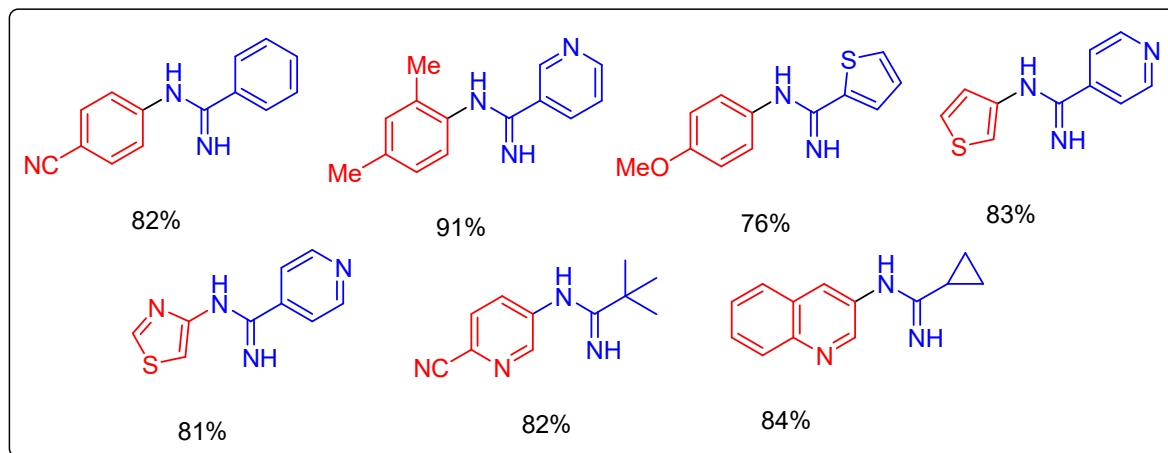
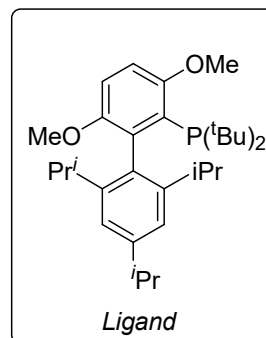
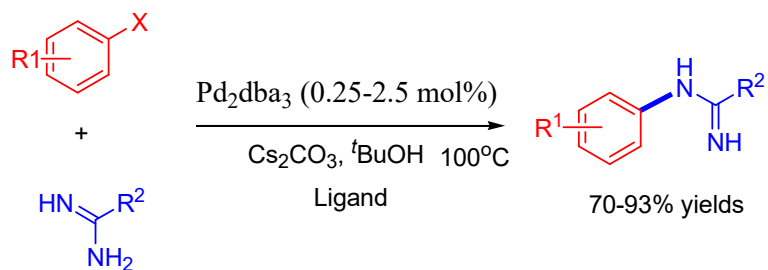
### **Synthesis of amidine from unactivated nitrile**

# Synthesis of Arylamidines from Aryltrifluoroborates



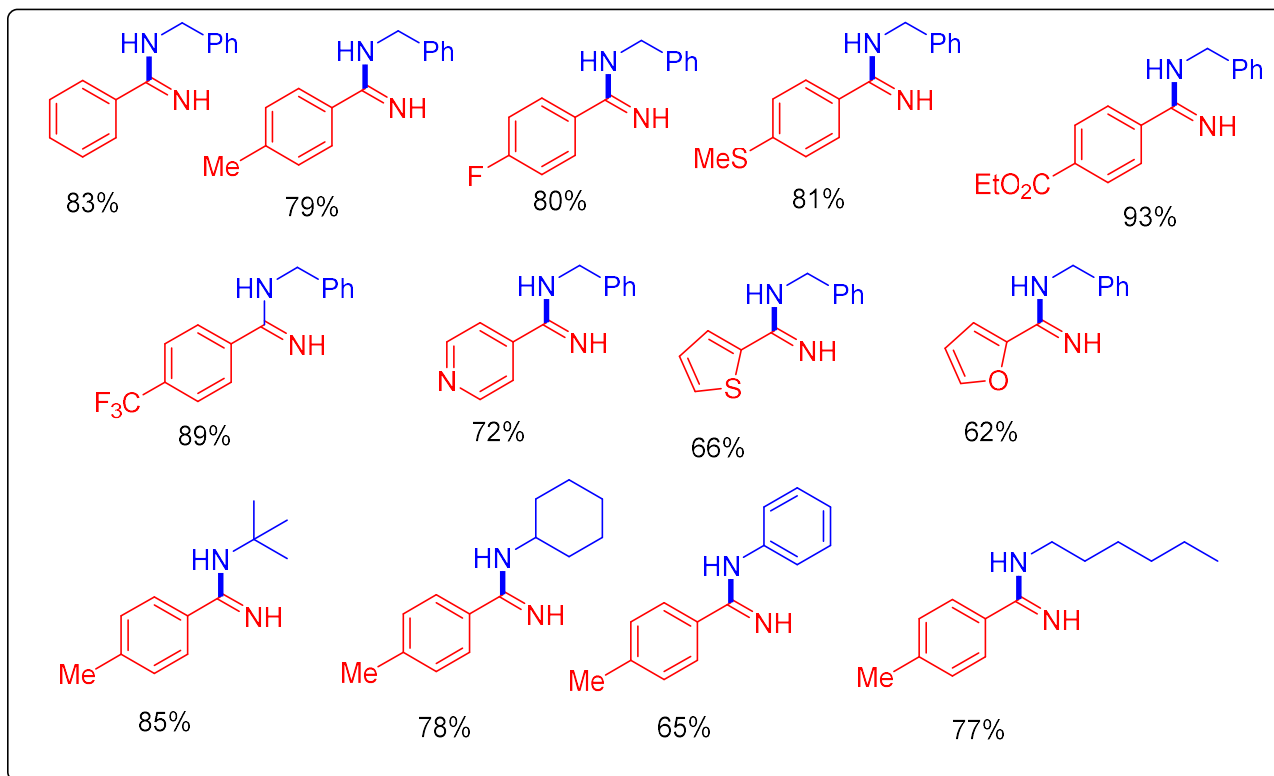
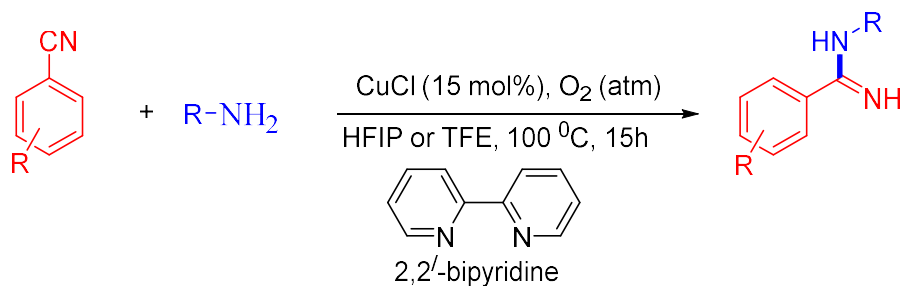
Larhed *et al.* *Org. Lett.* **2012**, *14*, 2394-2397; Bert *et al.* *Chem. Euro. J.* **2016**, *22*, 7743-7746

# N-Monoarylation of Amidines

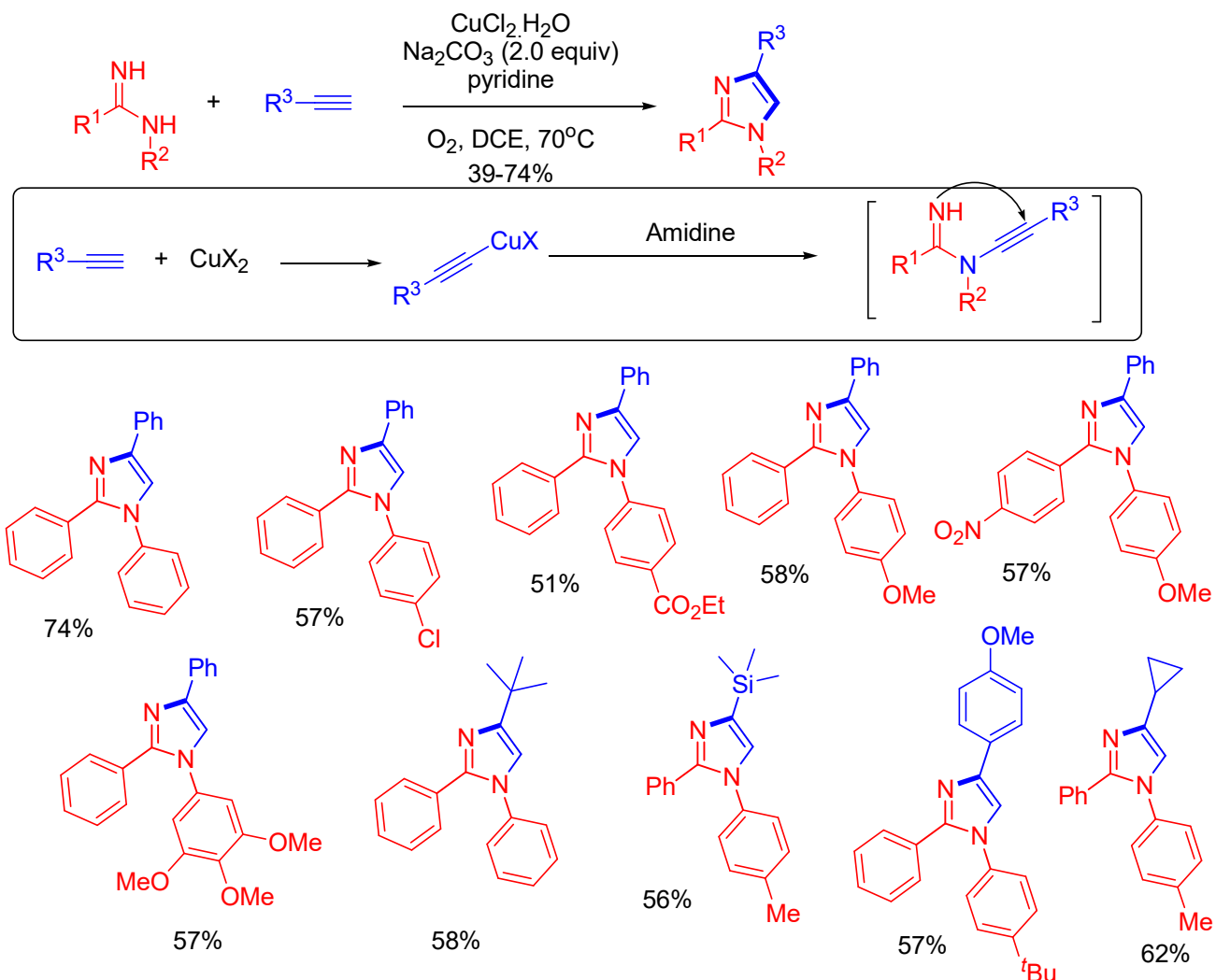




## Synthesis of Amidines (Our work):



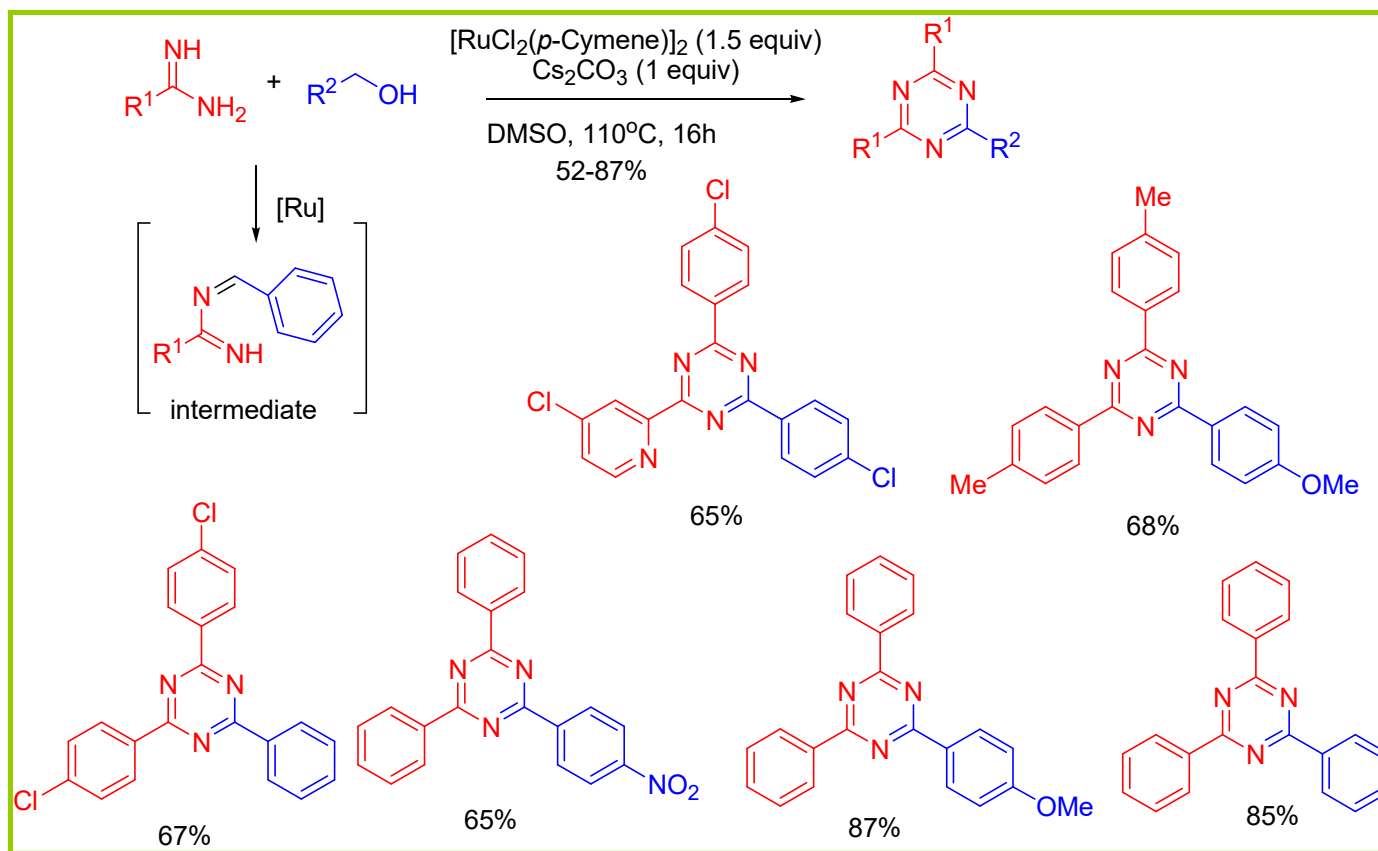
## Synthesis of Imidazoles from Amidines



J. Li and L. Neuville, *Org. Lett.*, **2013**, 15, 1752-1755.

S. Sanjaya, and S. Chiba, *Org. Lett.* **2012**, 14, 5342-5345.

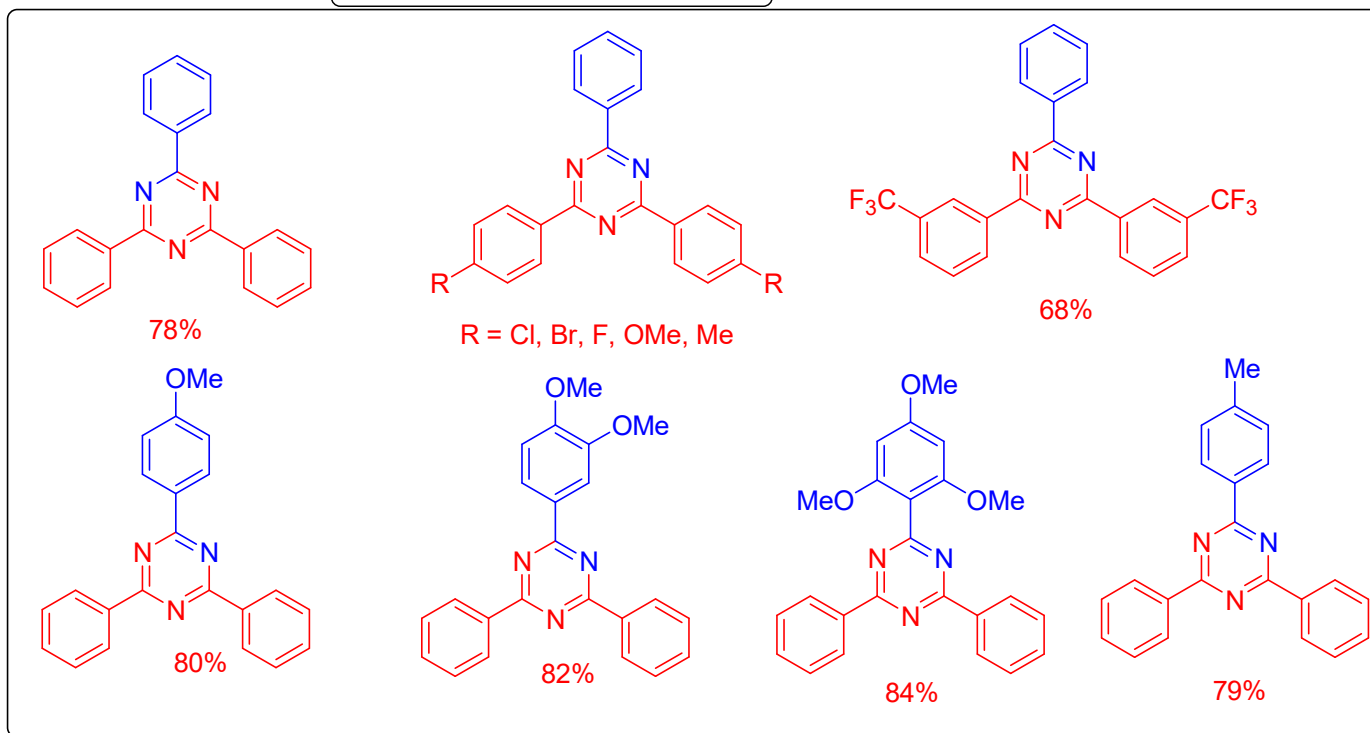
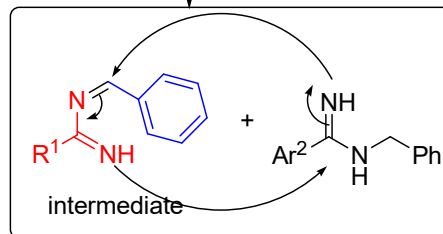
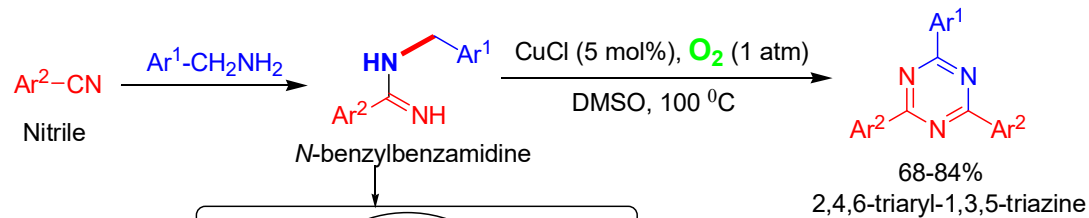
## Preparation triazines from Amidines and Aryl methanol



Zhang et al. *Org. Biomol.Chem.* **2014**, 12, 2761-2768.

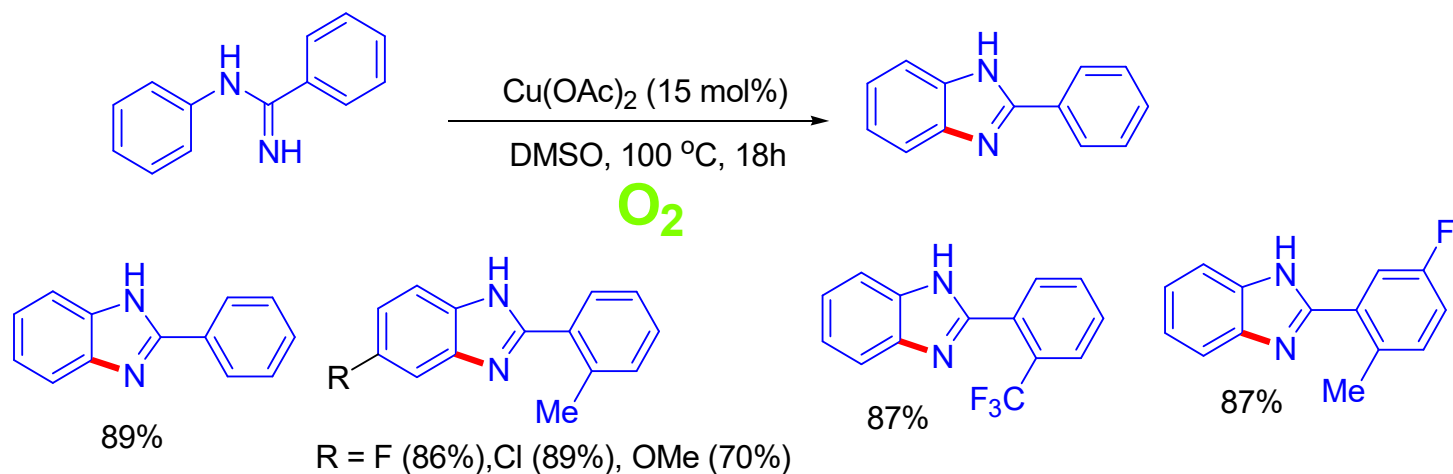
Review on triazines for anticancer activity *Euro.J. Med. Chem.* **2017**, 142, 523-549

# Synthesis of triazines from *N*-benzylbenzamides

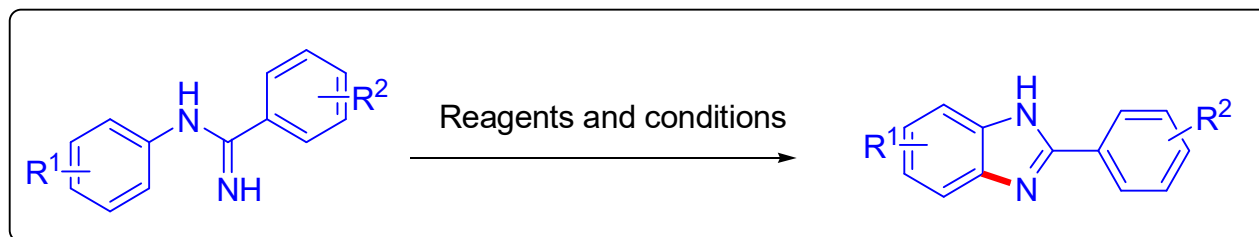


Debnath and Majumdar *Tetrahedron Lett.* **2014**, *48*, 6976-6978

## Synthesis of Benzimidazole from *N*-aryl amidines



Brasche and Buchwald, *Angew. Chem. Int. Ed.* **2008**, *47*, 1932-1934



PdCl<sub>2</sub>(PhCN)<sub>2</sub>, Cu(OAc)<sub>2</sub>, TMTU, DMSO, 100 °C, 24h.

Shi et al. *Chem. Eur. J.* **2009**, *15*, 7292.

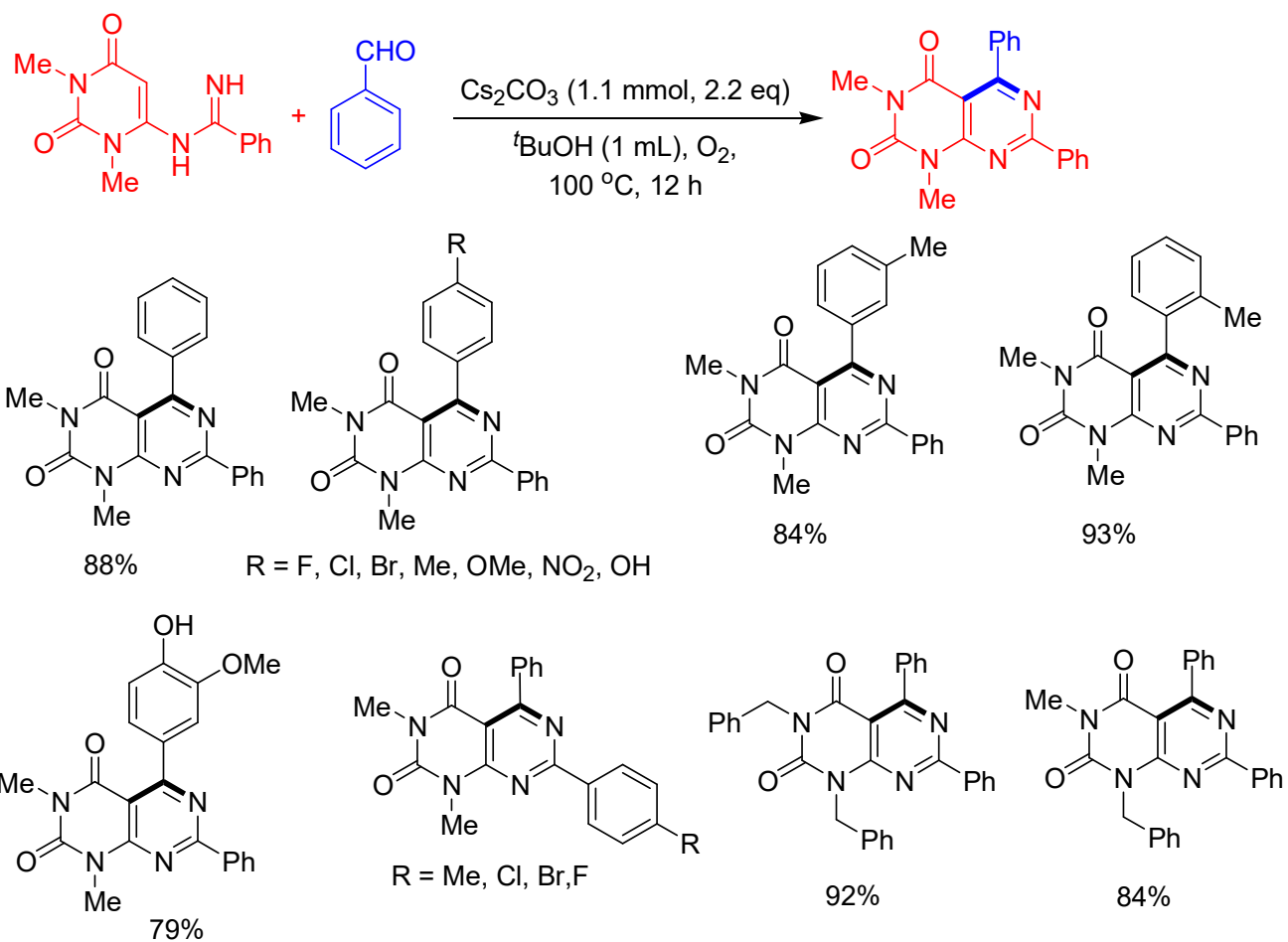
PIDA (1.1 equiv), Cs<sub>2</sub>CO<sub>3</sub>, TFE, 0 °C, 1.5 h.

Zhu et al. *Chem. Eur. J.* **2012**, *118*, 13964.

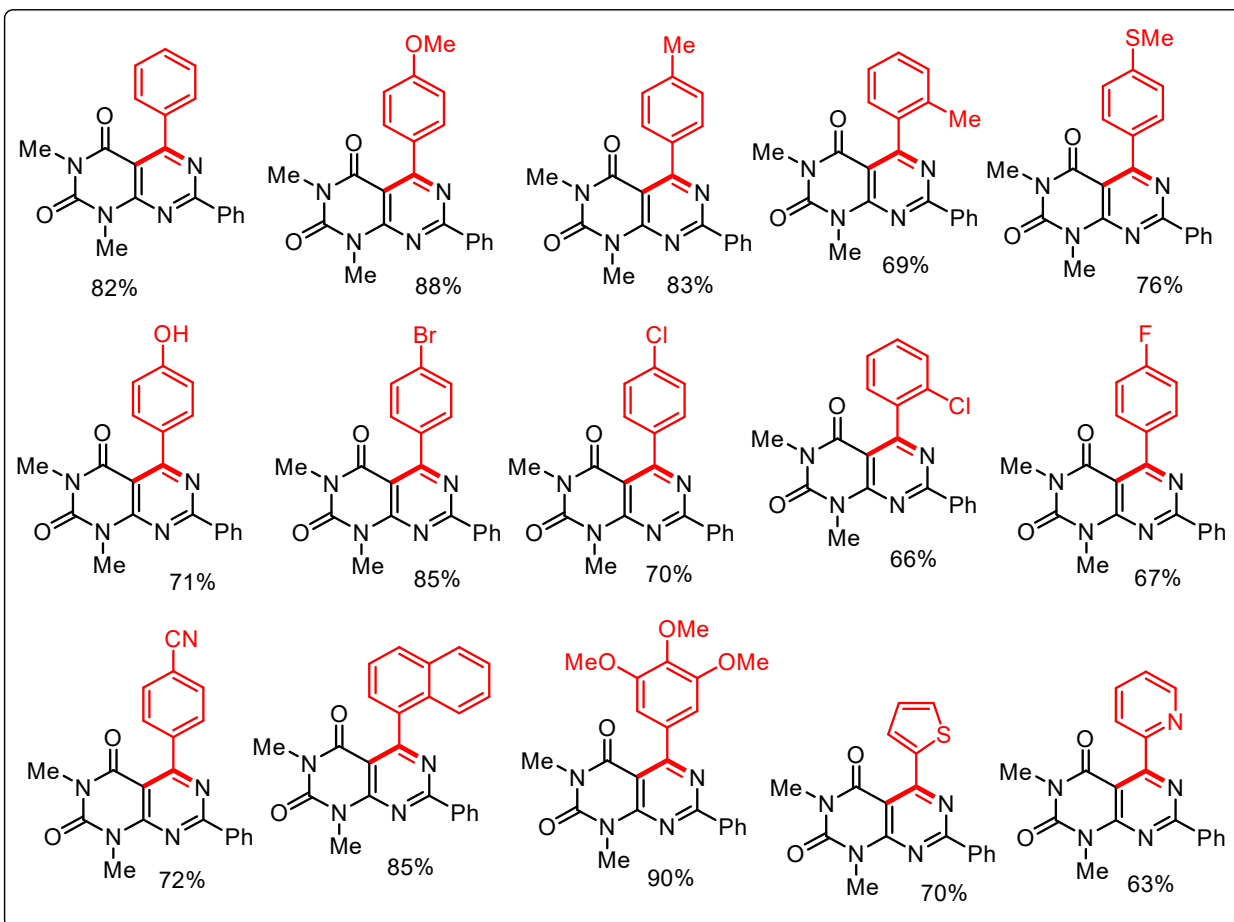
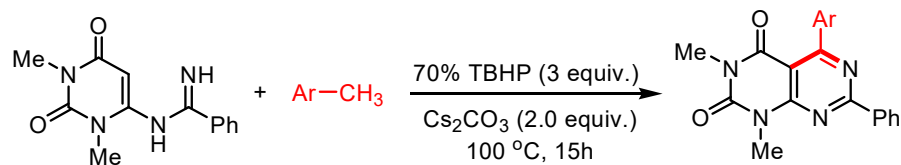
20 mol% PhI, *m*CPBA (1.5 equiv), HFIP, rt, 2-12h.

Punniyamurthy et al. *Chem. Eur. J.* **2013**, *15*, 1334-1337

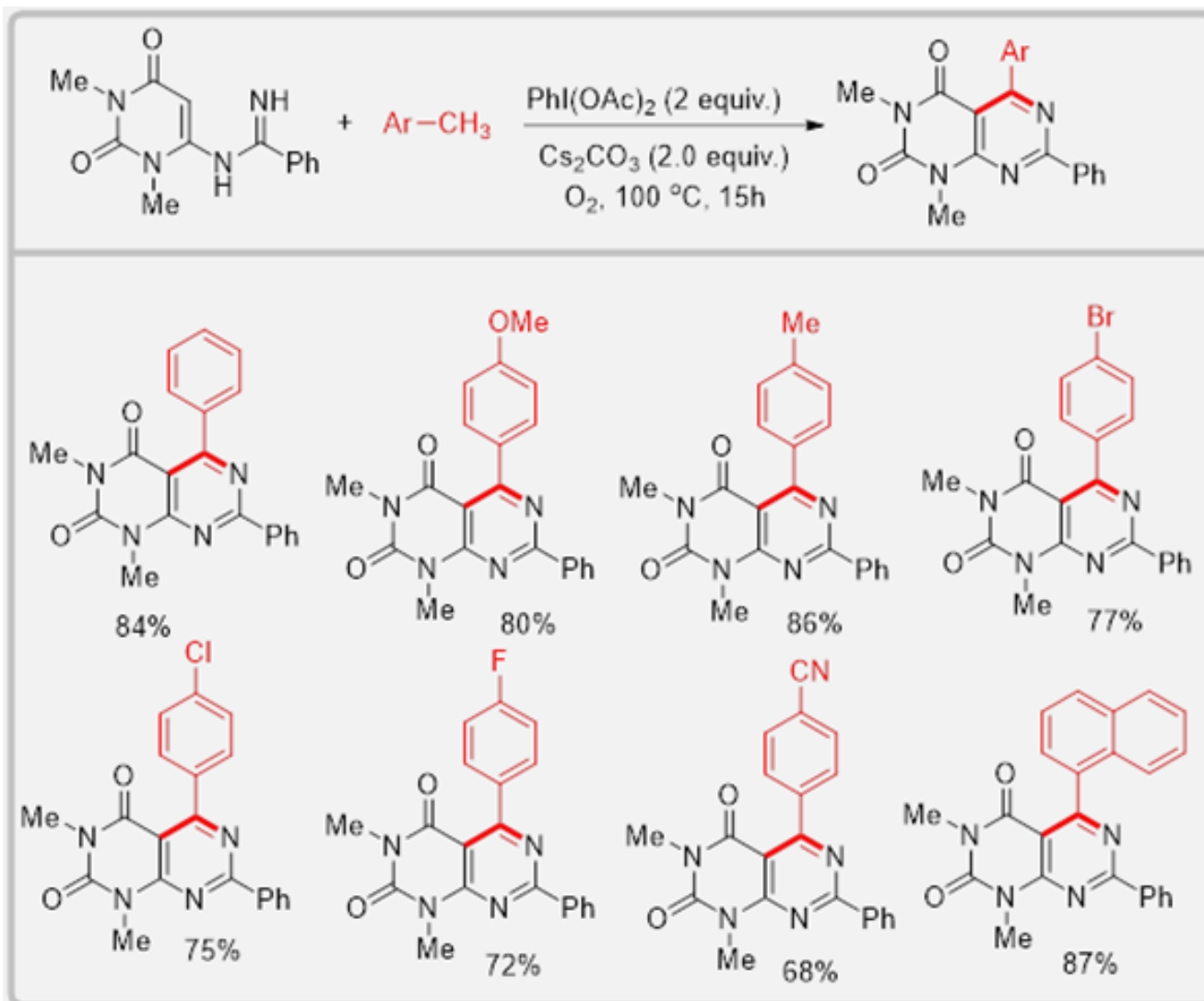
## Synthesis of Pyrimidopyrimidines from *N*-uracil amidines



## Synthesis of Pyrimidopyrimidines using methylarenes

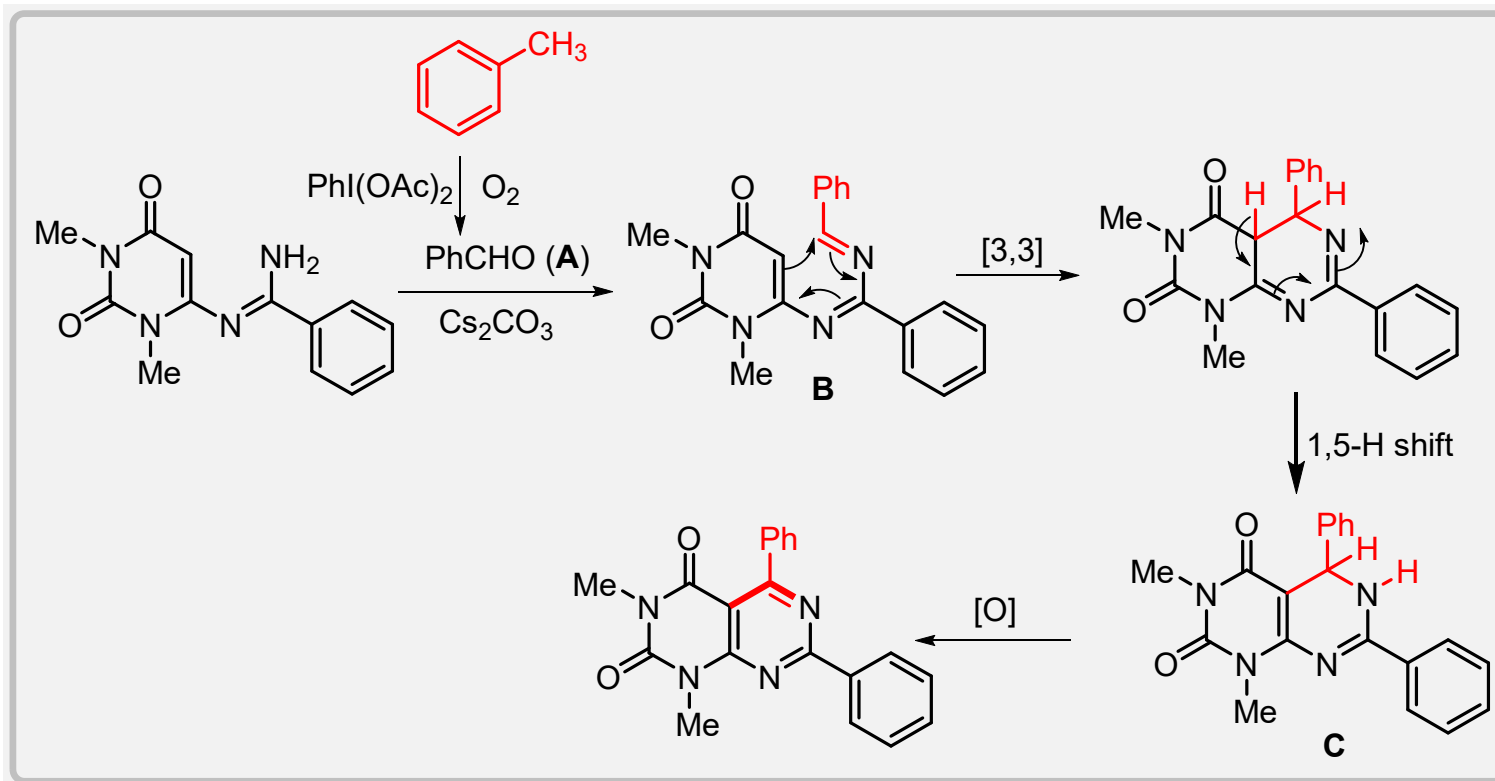


## PhI(OAc)<sub>2</sub> Mediated synthesis of pyrimidouracils (Our work)





# Mechanism for the synthesis of Pyrimidouracils



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# Thank you