

Design and Synthesis of a Heterocyclic Compound Collection for Probing the Spatial Characteristics of ATP Binding Sites

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CSIR Biosciences

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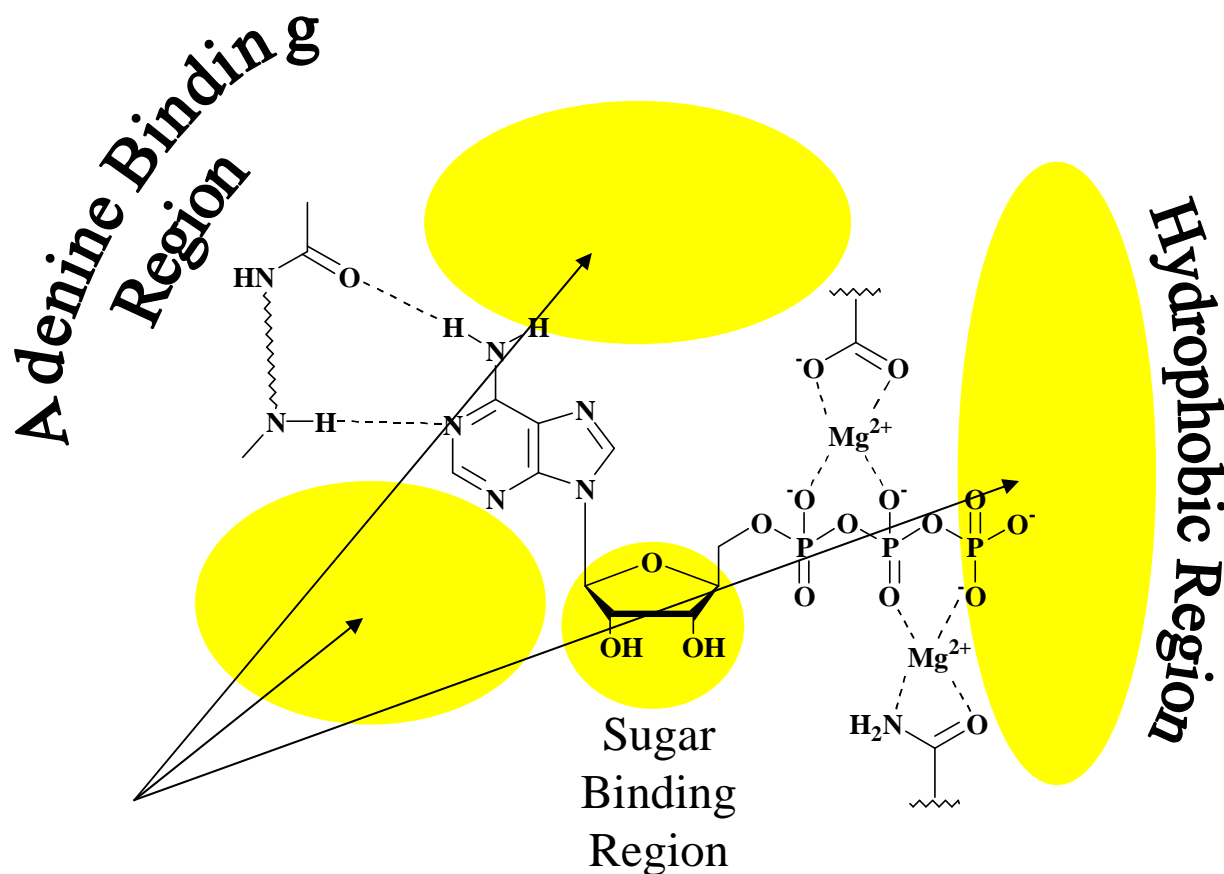
- The kinases
- The nature of the ATP site
- A basis for selectivity
- Types of potential guest molecules
- Methodology for preparation

The Kinases

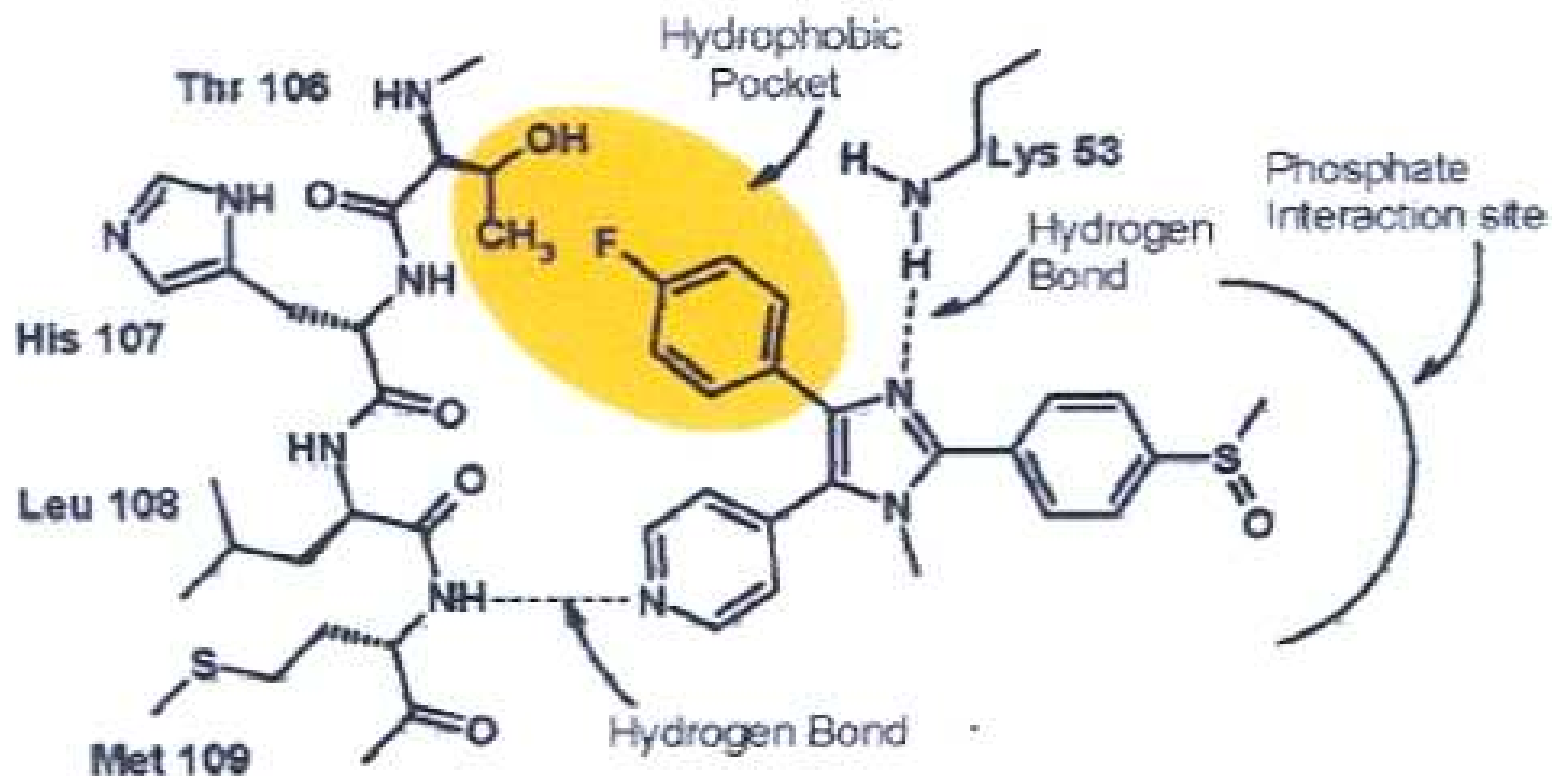
- Proteins which transfer phosphoryl residues
- Utilise ATP as phosphate source
- All have an ATP site
- Why are kinases attractive targets?

Basic Structural Characteristics of the ATP Site

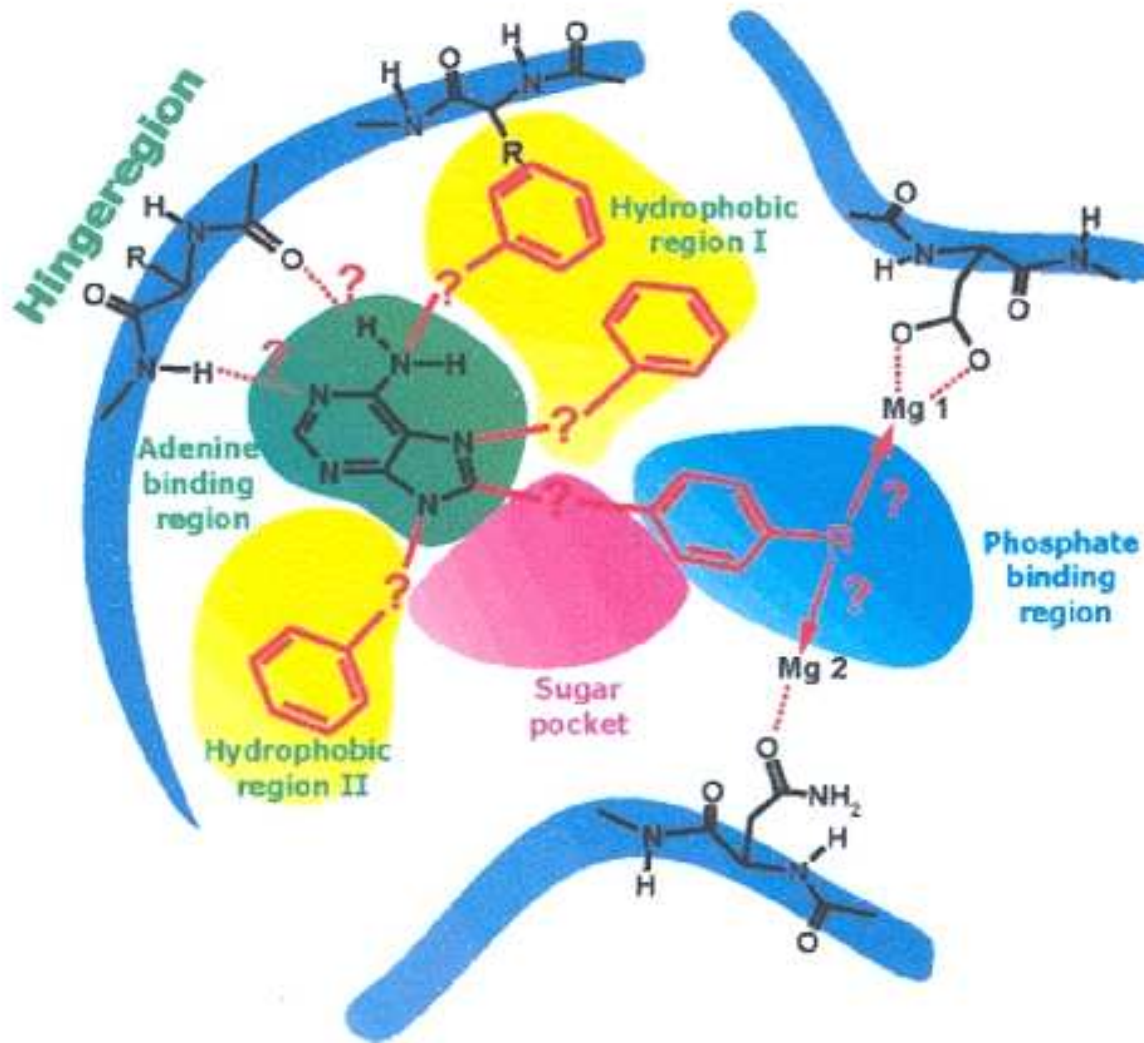
Typical ATP binding site



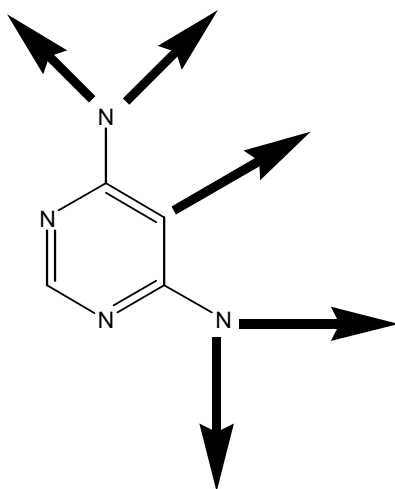
Pharmaceutical example: Interactions of SB203580 in the p38 MAP Kinase



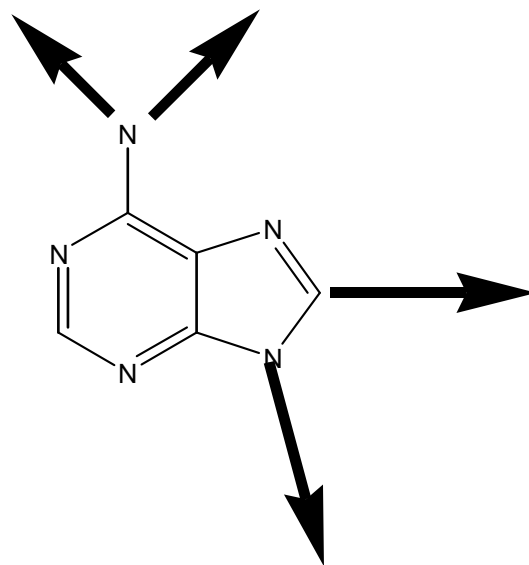
Rational Basis of Design



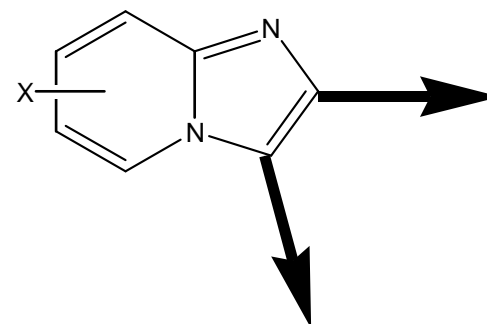
Scaffold Selection



Pyrimidines

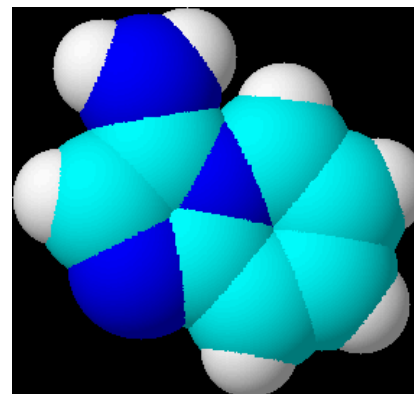
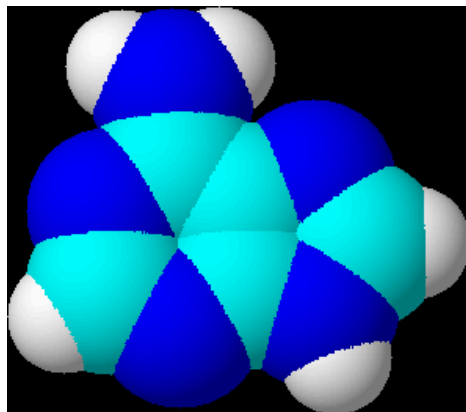
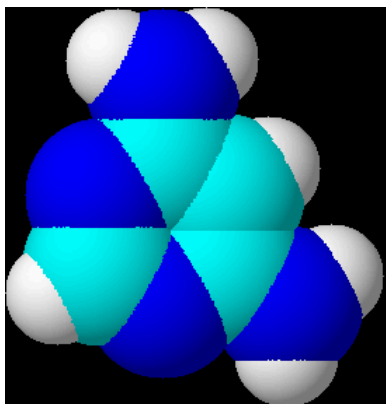
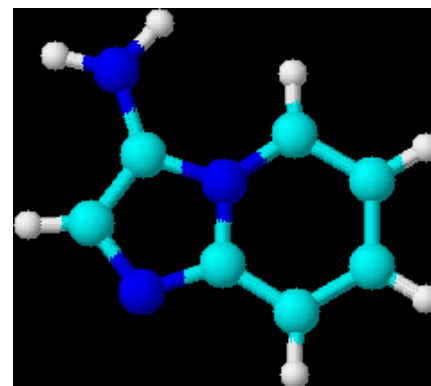
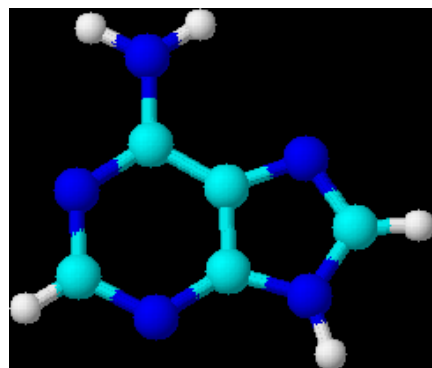
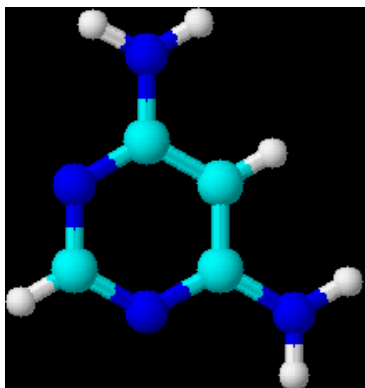


Purines

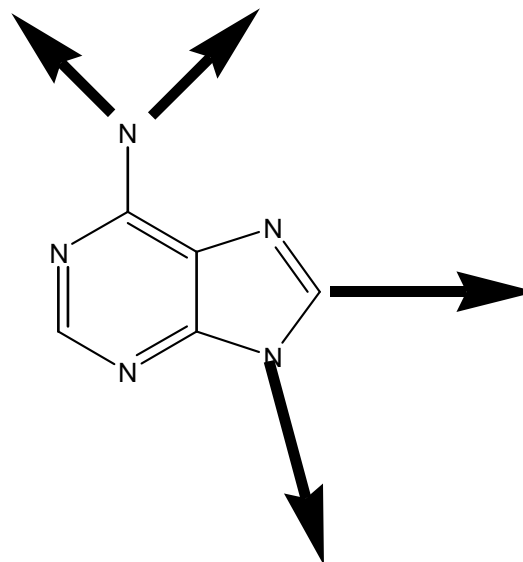
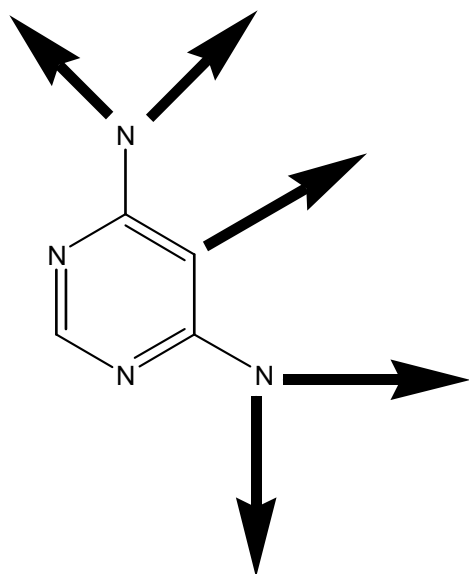


Imidazopyridines

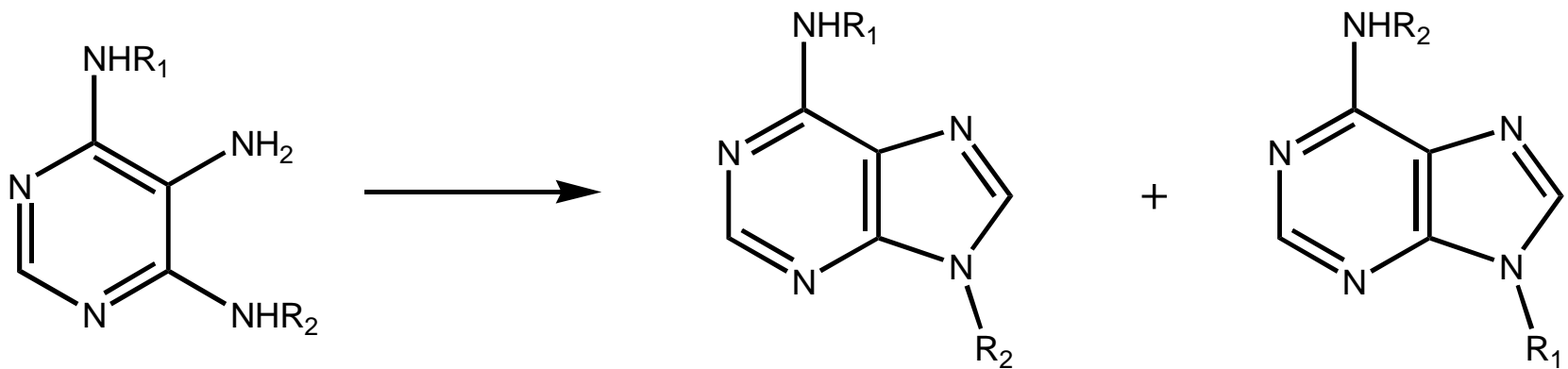
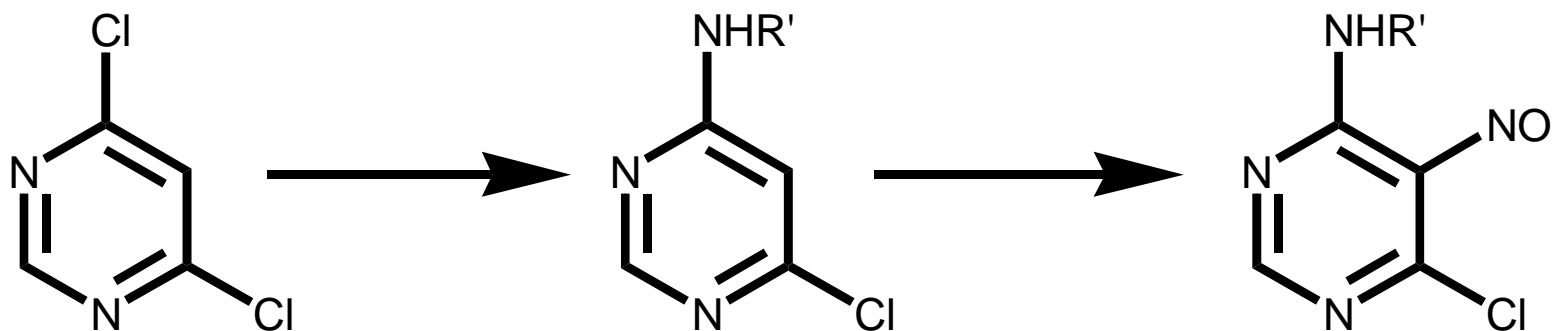
Spatial Comparison of Scaffolds



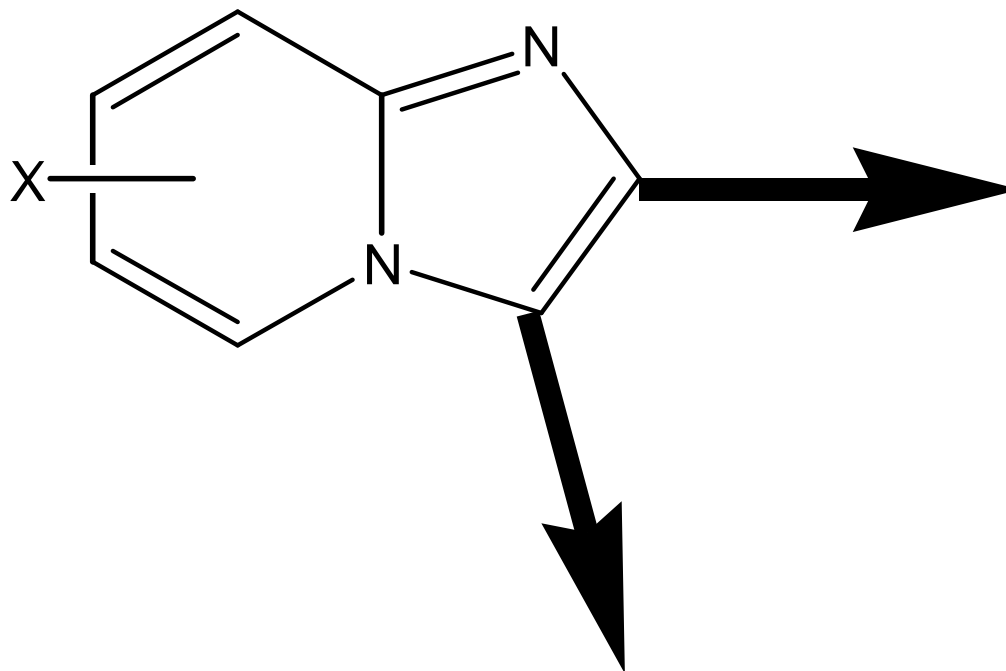
Pyrimidines and Purines



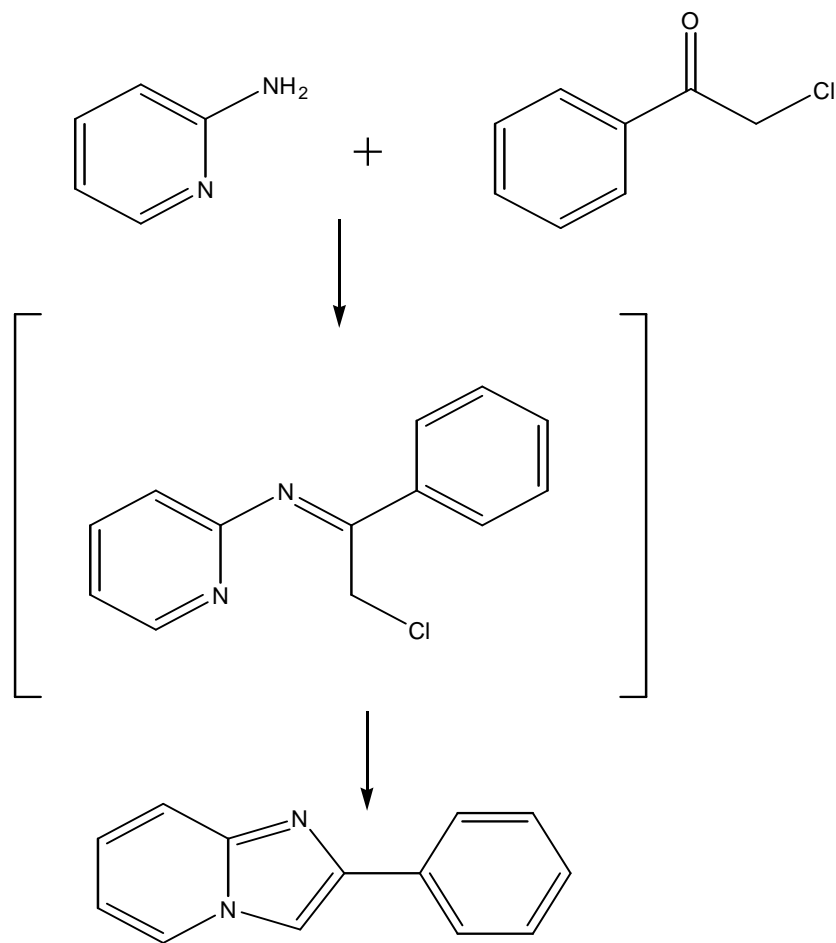
Synthesis of Pyrimidines and Purines



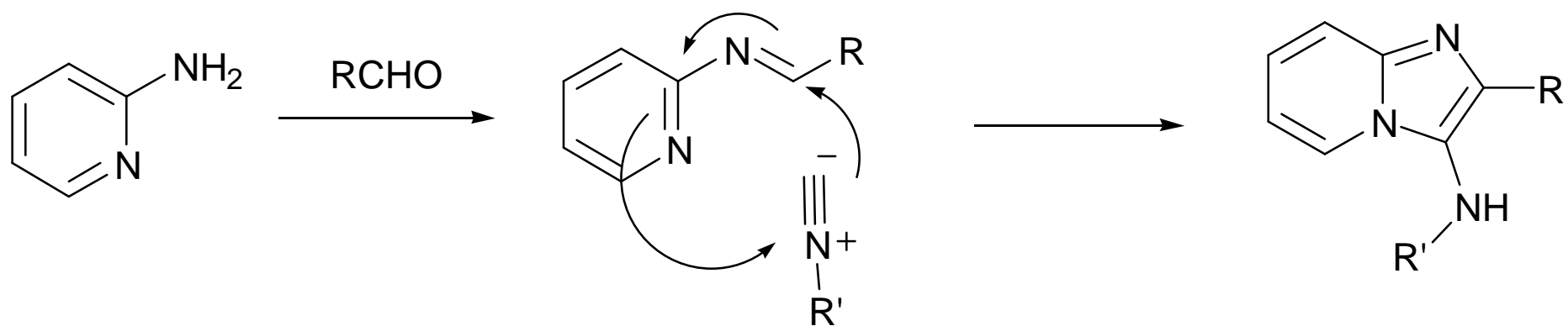
Imidazopyridines

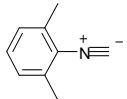
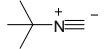
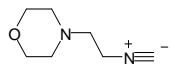
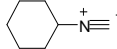
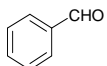
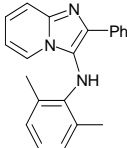
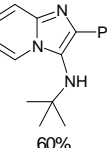
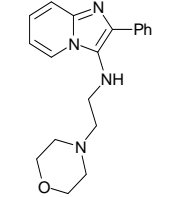
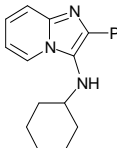
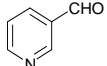
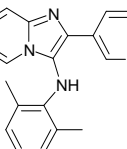
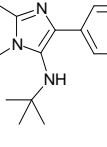
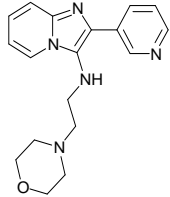
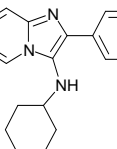
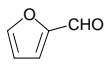
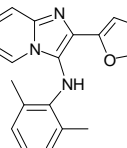
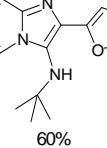
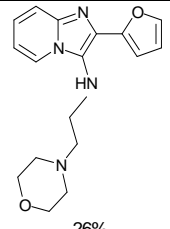
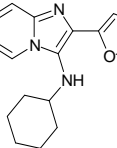
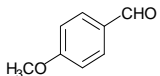
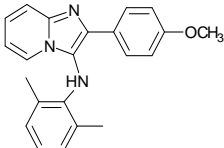
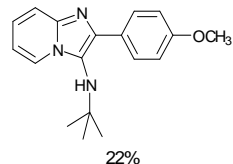
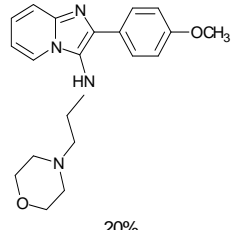
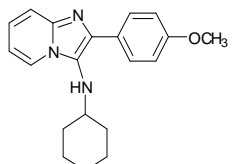


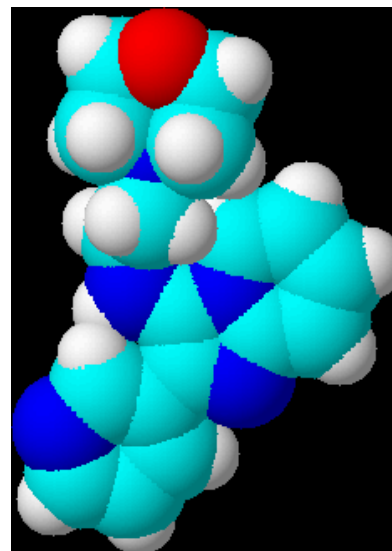
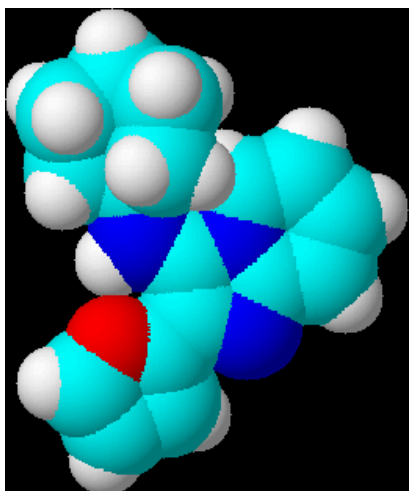
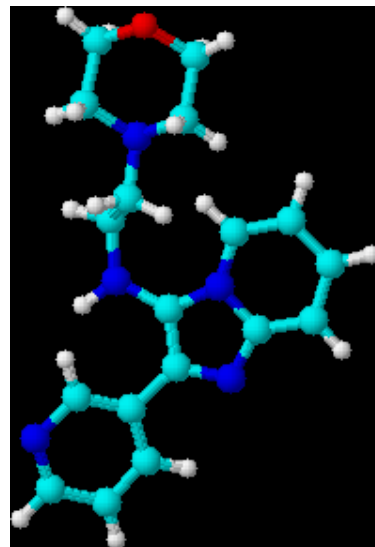
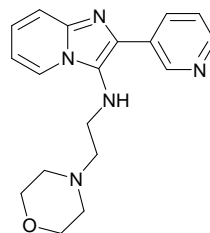
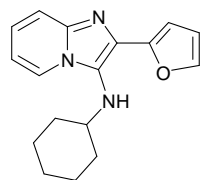
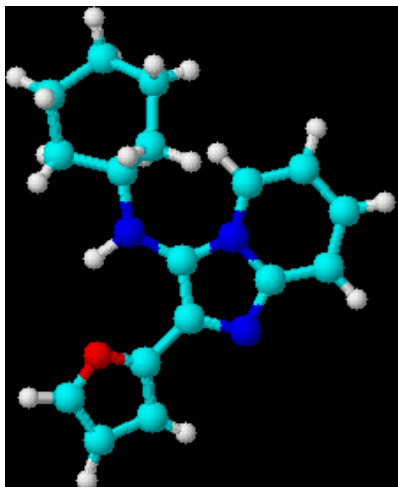
The Classical Approach



Diversity Orientated Approach

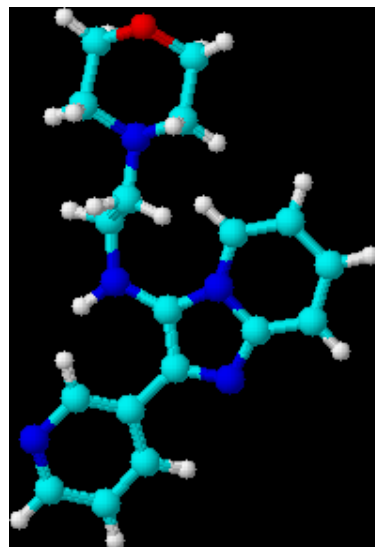
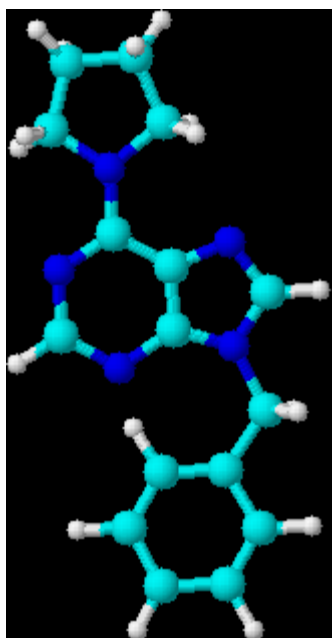


Aldehyde	Isocyanide			
				
	 72%	 60%	 14%	 78%
	 54%	 57%	 20%	 59%
	 25%	 60%	 26%	 73%
	 48%	 22%	 20%	 42%



The Way Ahead

Explore the untapped dimension
Kinase and ATP –ase studies



Thanks To.....

CSIR Thematic Programmes

Department of Science and Technology

