

Kinase Hinge Binders

Kinase inhibitors are a clinically important family of prescription drugs that belong to the class of so called targeted therapy, for the treatment of cancer and more recently in the immunology area for the treatment of arthritis. The ATP-binding pocket is located inside the deep cleft between the two lobes of the kinase domains. The “hinge” is a single string of the amino acid segment that connects the two lobes. The adenine ring of ATP binds to the hinge via two hydrogen bonds, one with the N-hydrogen and one with the carbonyl group of the two amino acid residues located on the hinge. Of the 23 kinase inhibitors that have reached the market so far (see **Figure 1** below), all but two are kinase ATP-binding pocket inhibitors—they form one to three hydrogen bonds to the amino acids of the hinge, thereby mimicking the hydrogen bonds that are normally formed by the adenine ring of ATP.

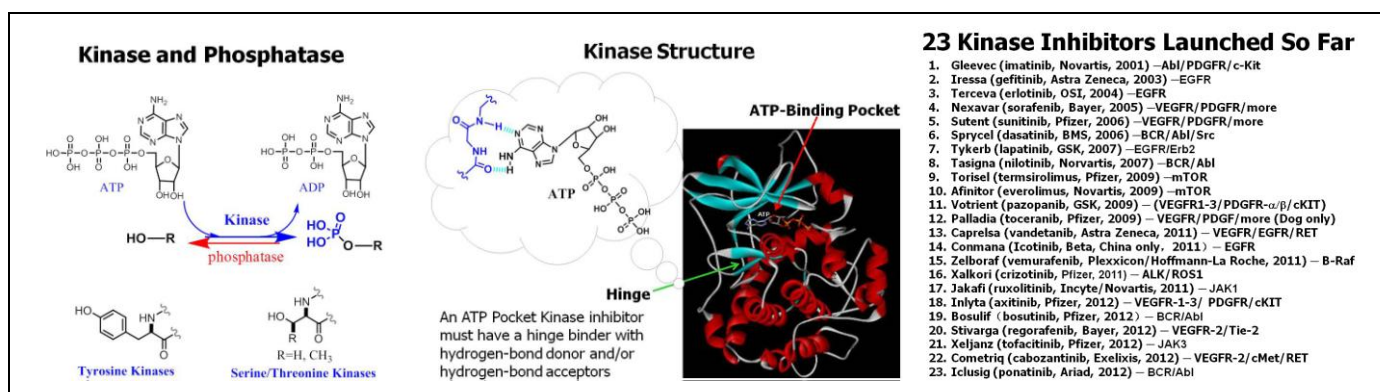


Figure 1

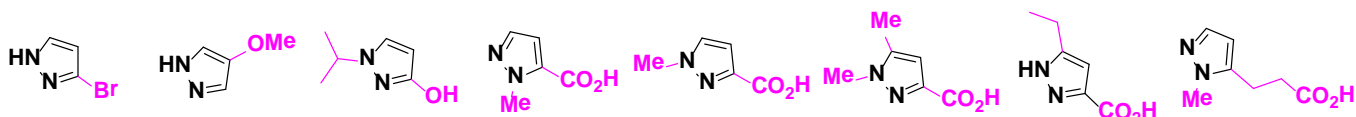
In this issue of Bellen newsletter, we highlight some of Bellen’s novel building blocks that can be used as hinge binders required for kinase ATP-pocket inhibitors. These hinge binders were designed carefully so that they can form one to three hydrogen bonds to the hinge. They contain one to multiple functional groups at various positions that can be derivatized sequentially. Additionally, the compounds with substituents such as methyl, trifluoromethyl, methoxyl, or trifluoromethoxyl groups adjacent to the functional groups for the purpose of conformation alteration are also available. We hope these compounds could spark some useful ideas for your drug design.

In addition to the building blocks, we also provide a useful collection of library set consisting of thousands of small heterocyclic compounds that can be used for fragment-based screening. Please contact us for details.

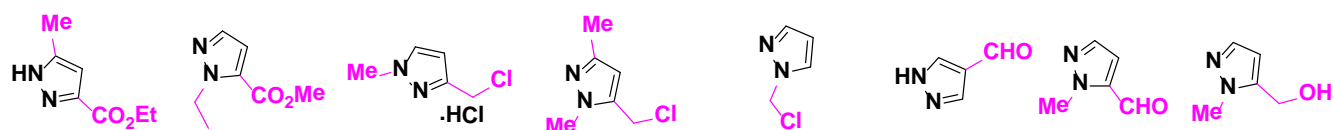
For a complete list of our catalog compounds, please visit Bellen’s website where you can do a structure search. If you do not see the compound you need, please contact us at sales_us@bellenchem.com. We also provide custom synthesis for scales ranging from milligrams to tons.



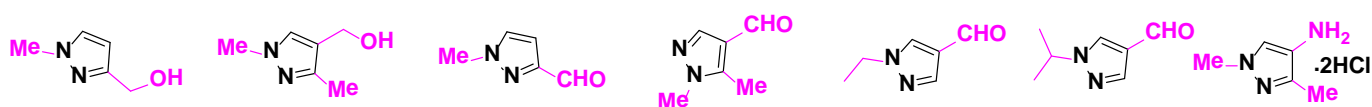
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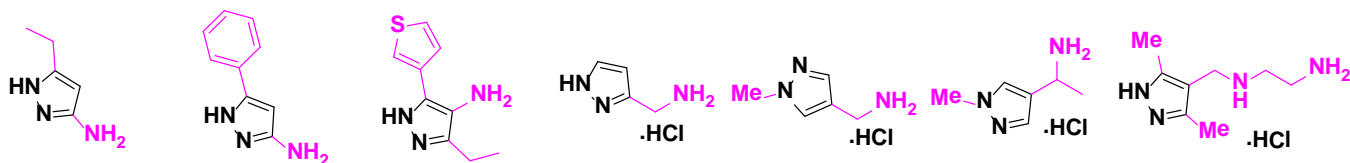
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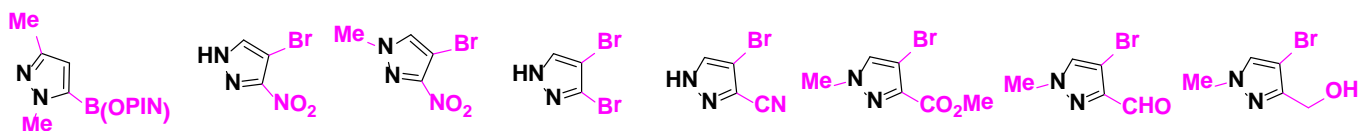
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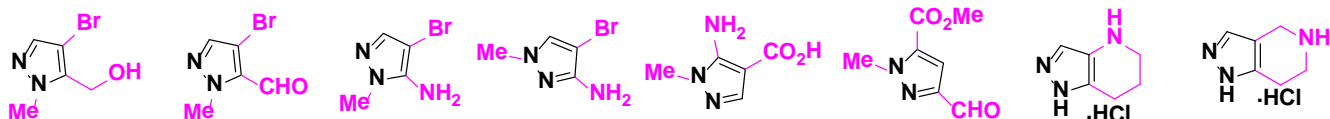
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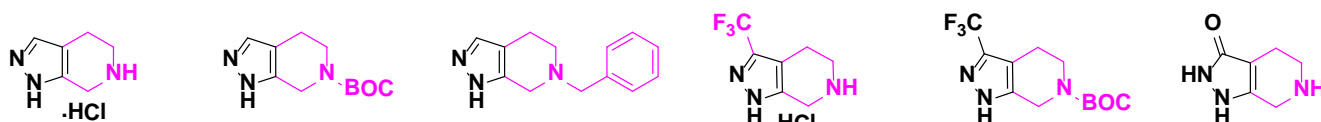
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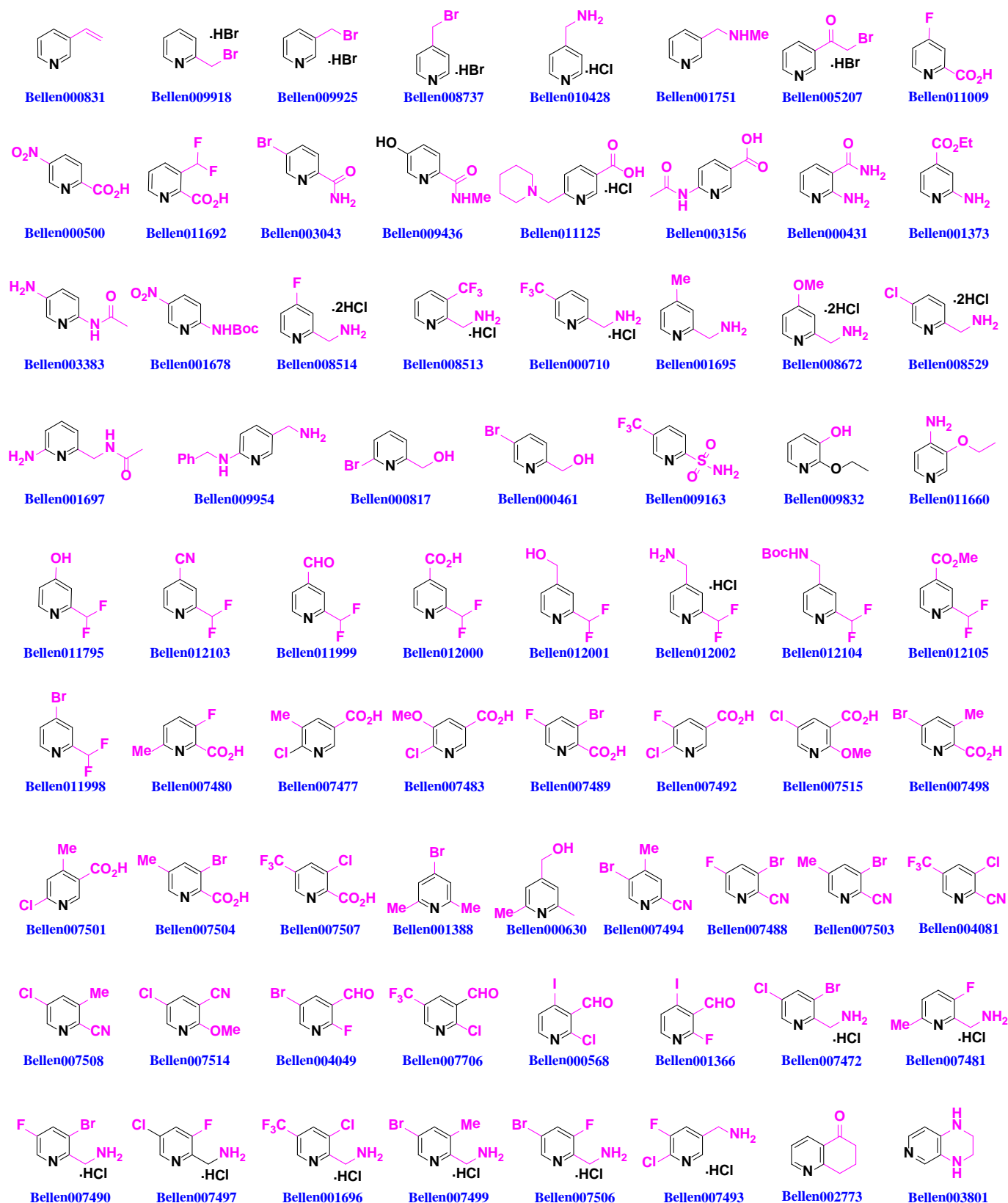
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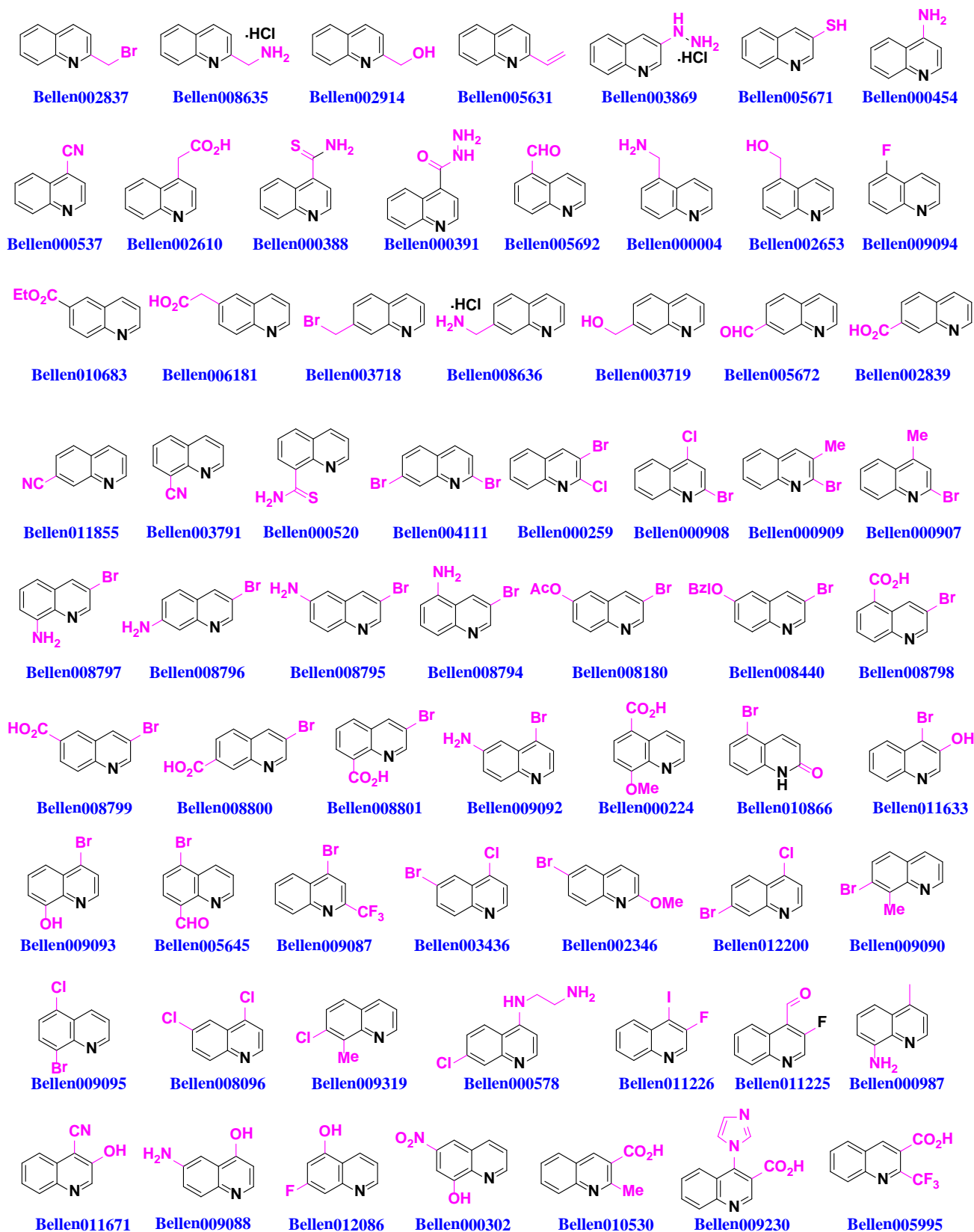
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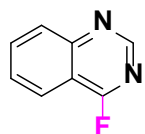
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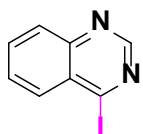
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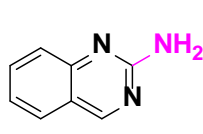
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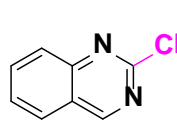
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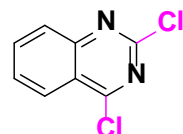
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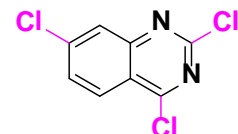
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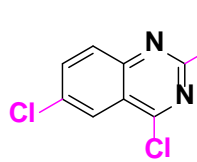
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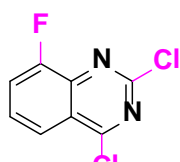
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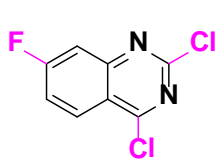
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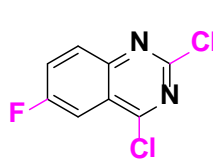
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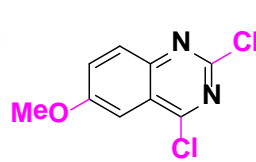
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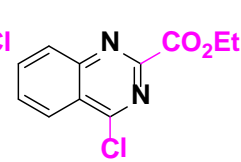
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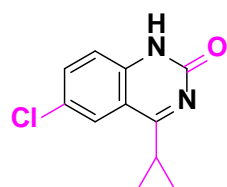
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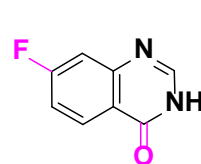
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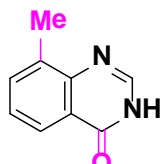
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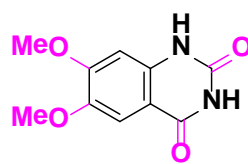
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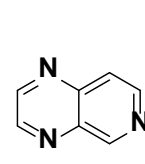
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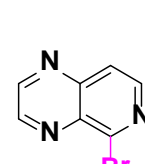
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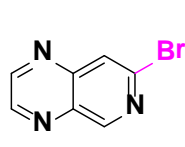
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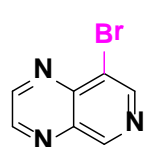
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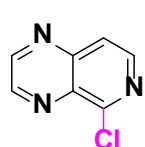
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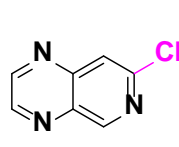
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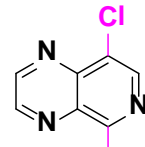
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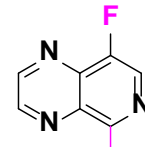
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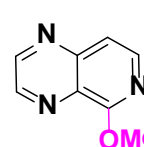
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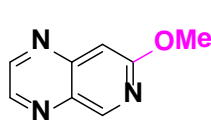
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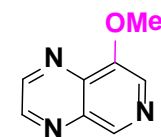
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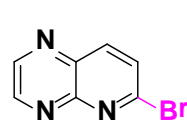
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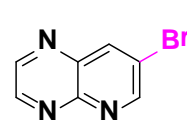
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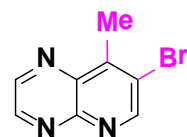
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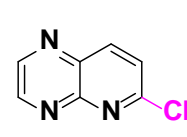
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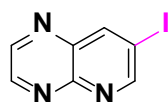
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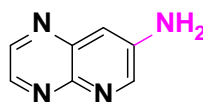
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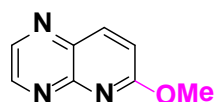
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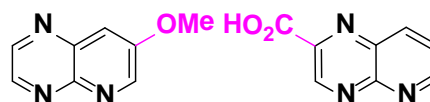
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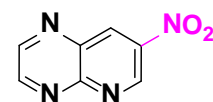
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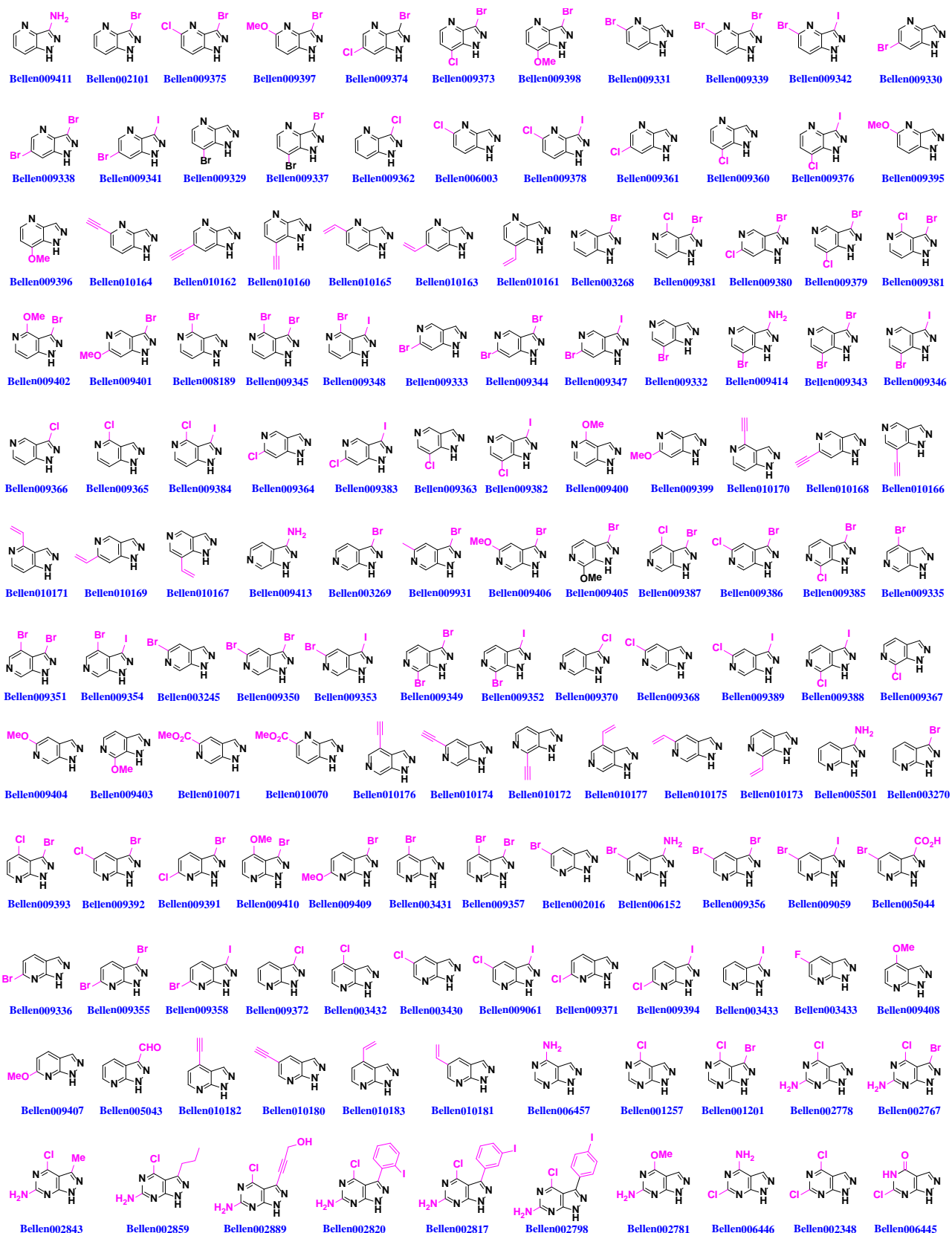
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6. Indazoles



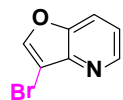
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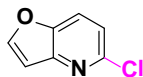
8. Azaindoles, Azabenzimidazoles and Other Heterocycles



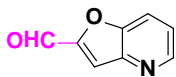
9. Isosteres of Quinolines and Quinazolines



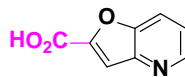
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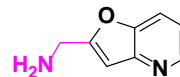
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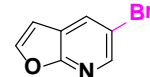
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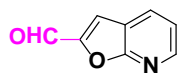
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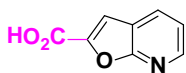
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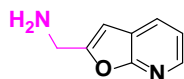
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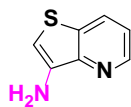
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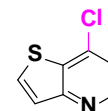
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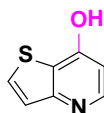
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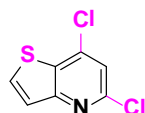
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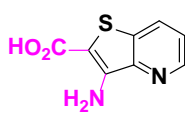
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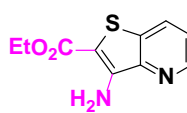
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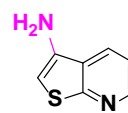
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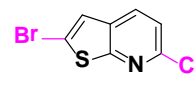
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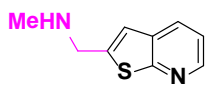
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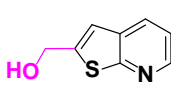
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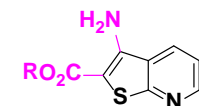
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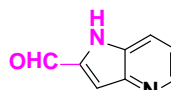
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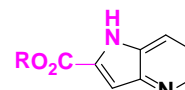
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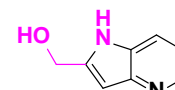
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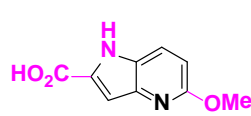
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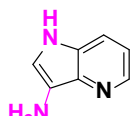
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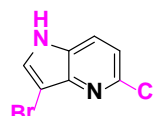
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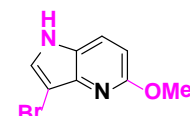
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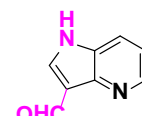
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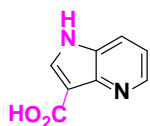
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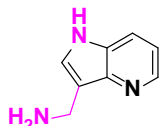
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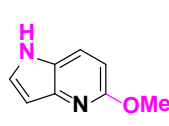
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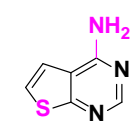
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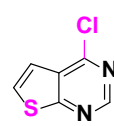
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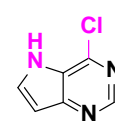
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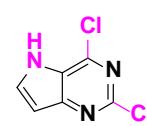
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Bellen004482



Bellen009145



Bellen009241



10. Isosteres of Isoquinolines



11. Imidazopyridines, Imidazopyrazines, Triazolopyridines and Triazolopyrazines

