Piperazine Bioisosteres for Drug Design

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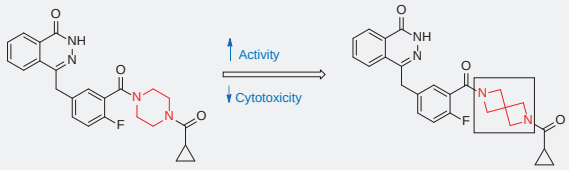
Introduction and Aim

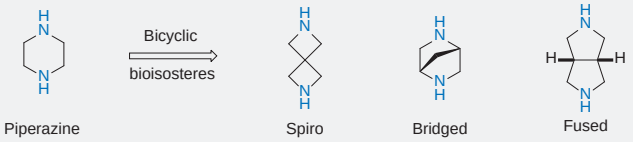
More than 100 FDA-approved drugs contain the piperazine moiety.[1] Piperazine-based analogues may advantageously alter important pharmacokinetic properties when grafted onto molecular scaffolds.[2-5] In 2018, chemists showed that replacing a piperazine ring in the drug Olaparib with the spirodiamine analogue beneficially affected activity and reduced cytotoxicity of the parent compound.[6] Herein we have designed and synthesized a library of piperazine analogues for drug design.



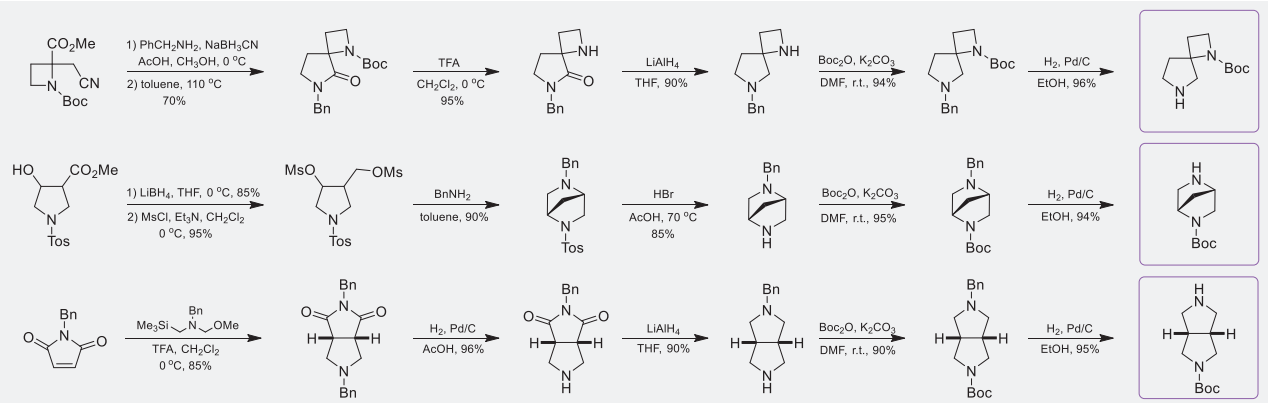
Olaparib (anti-cancer drug)
AstraZeneca and Merck & Co.

SpiroOlaparib

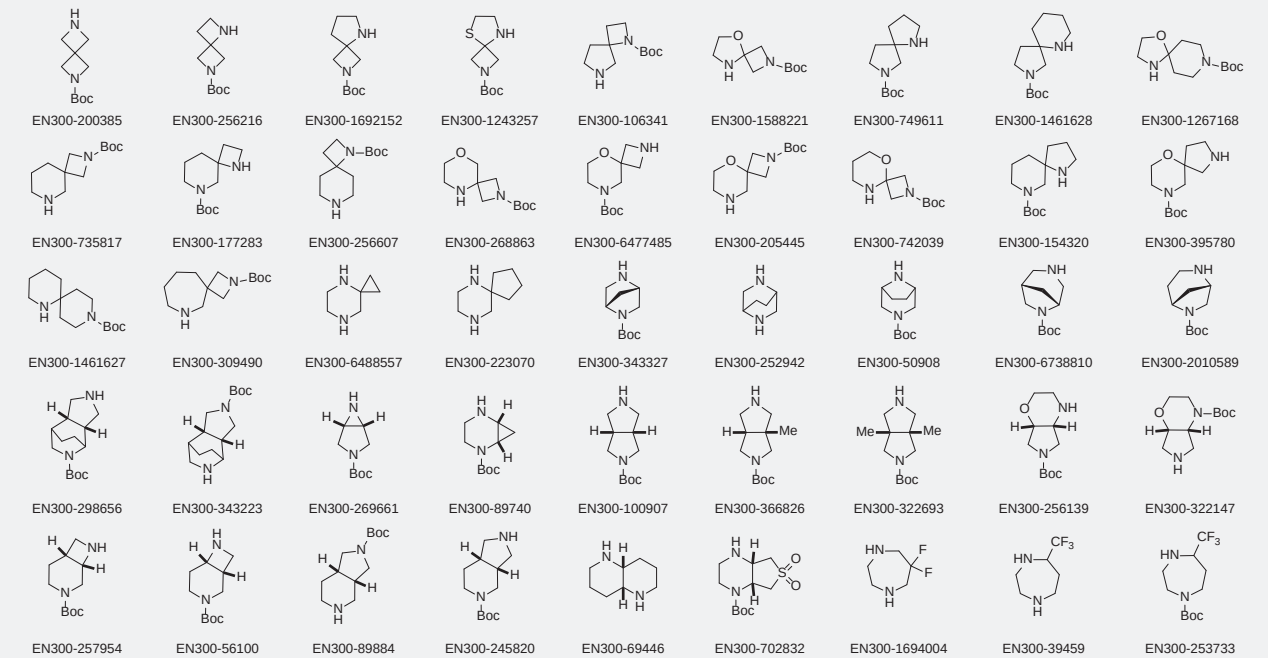
Design



Synthesis



Results



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