Difluoro-substituted bicyclo[1.1.1]pentanes (BCPs) for medicinal chemistry

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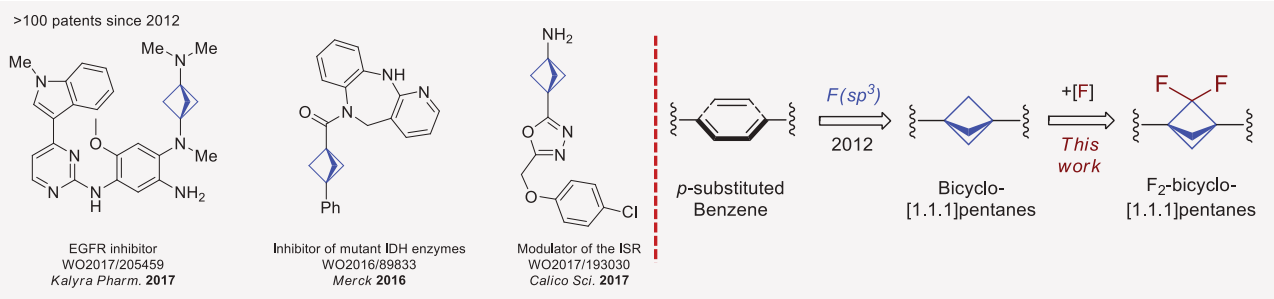
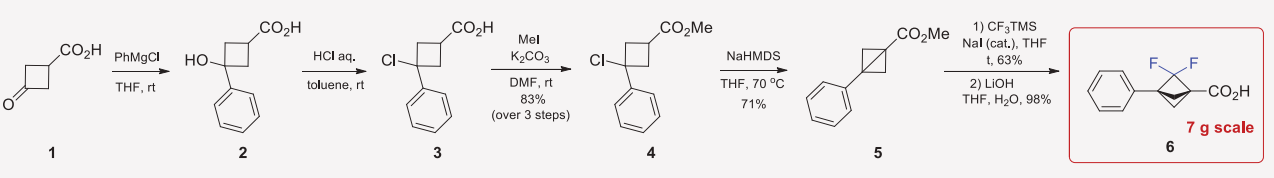
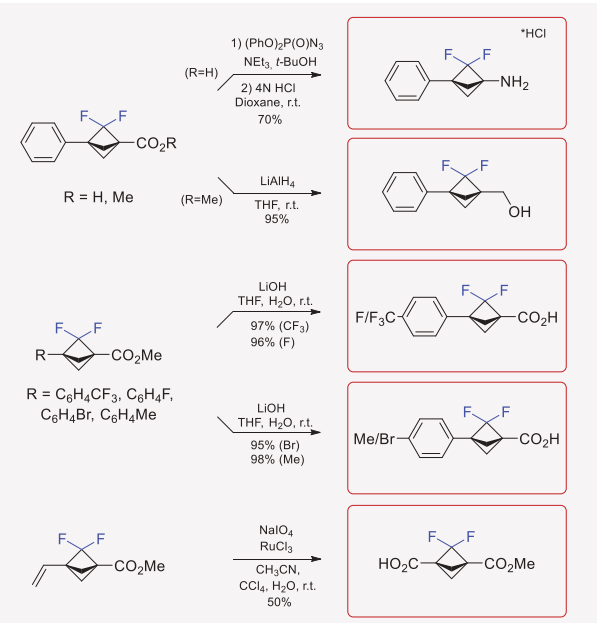
Introduction and Aim

Benzene ring is the most popular fragment in drugs and natural compounds. In the context of a concept named "*Escape from Flatland*", replacing benzene rings with saturated bioisosteres is an important strategy to obtain novel patent-free molecules with improved biological activity and physico-chemical profile. Bicyclo[1.1.1]pentyl (BCP) skeleton currently plays an important role as a bioisoster of *para*-substituted phenyl ring. Herein, we developed a strategy to synthesize the first generation of BCPs substituted at the side chain - difluoro-substituted bicyclo[1.1.1]pentanes. The key synthesis step was an addition of difluorocarbene (:CF_2) to bicyclo[1.1.0]butanes.[1,2]



Synthesis





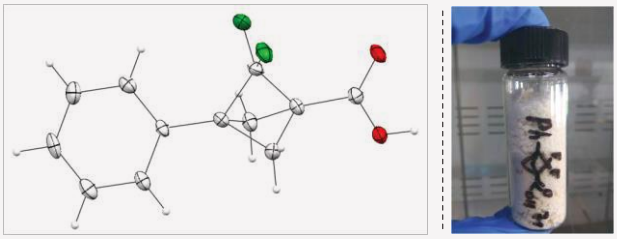
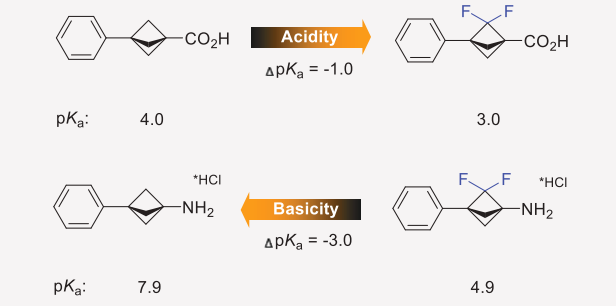
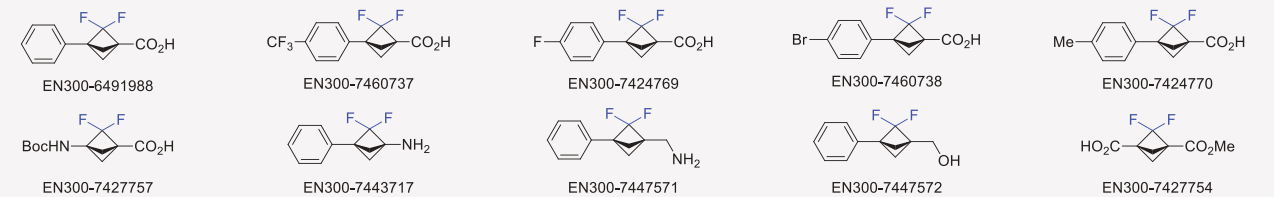


Figure 1. *X*-Ray crystal structure of acid **6**. Atoms of fluorine – green, oxygen – red.



Results



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References

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