Light-enabled Scalable Synthesis of Bicyclo[1.1.1]pentane halides and their functionalizations

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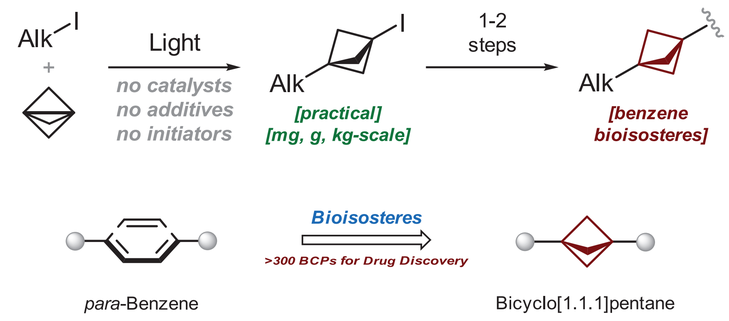
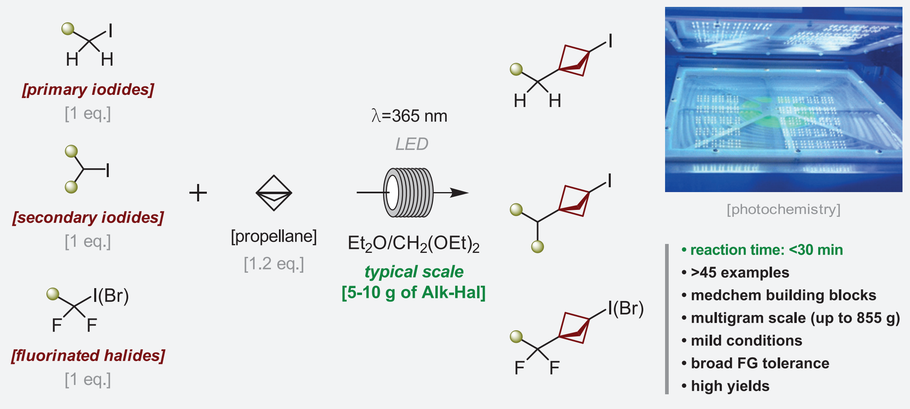
Introduction and Aim

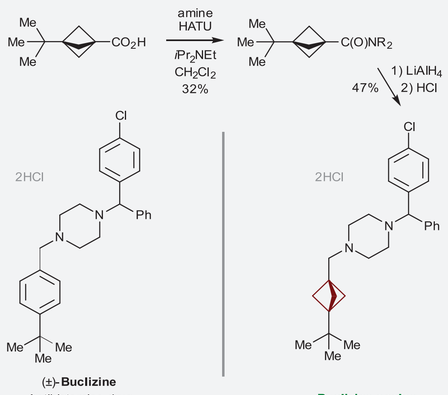
In 2012, Stepan and co-workers at Pfizer showed that a replacement of the central phenyl ring in a γ-secretase inhibitor with the bicyclo[1.1.1]pentane (BCP) retained bioactivity and improved physicochemical properties.[1,2] Scientists understood that bicyclo[1.1.1]pentanes could be used as bioisosteres of the phenyl ring in various aspects of chemistry: from medicinal chemistry to supramolecular chemistry. This understanding has led to the unprecedented popularity of bicyclo[1.1.1]pentanes.[3,4] Details of the synthesis and application of the obtained compounds will be discussed.[5]



Synthesis

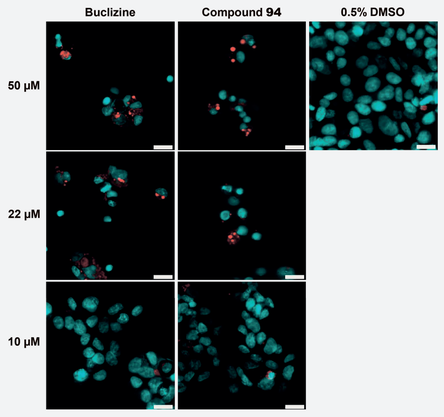


a) Buclizine analog



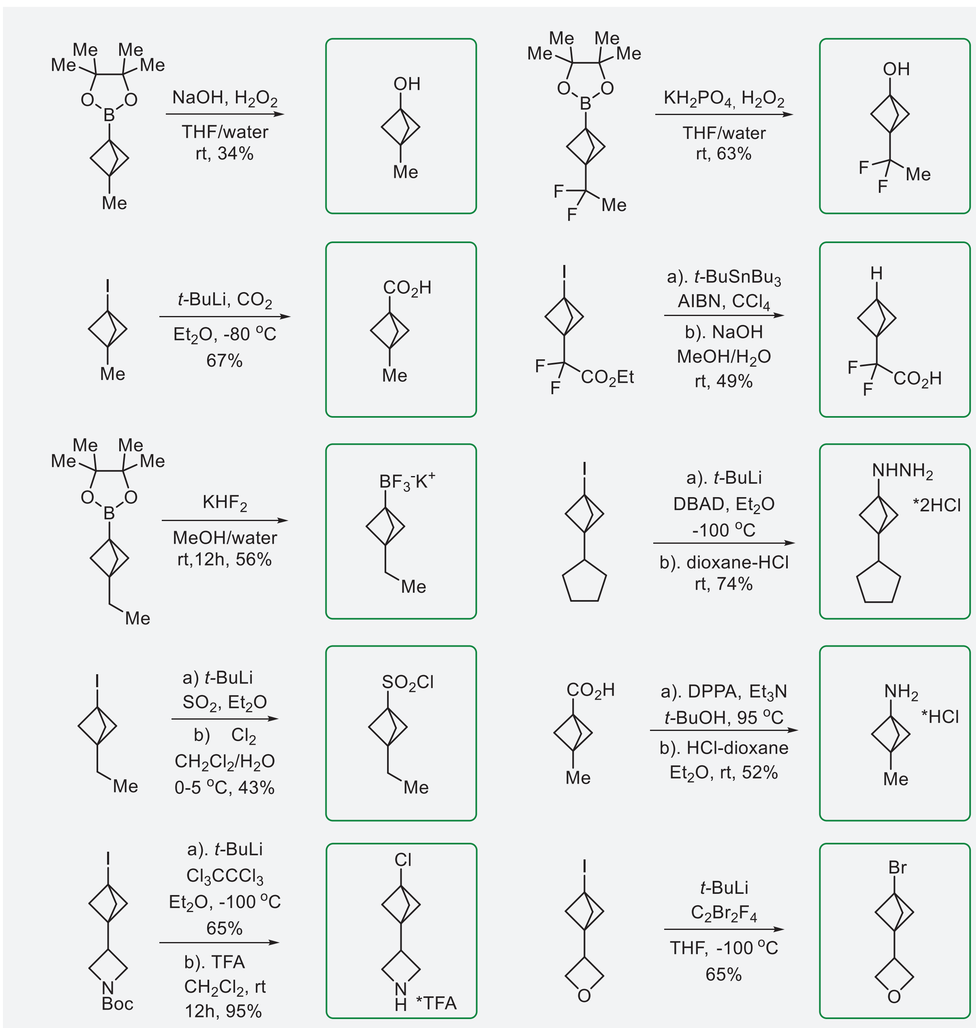
Compound	Sol.	clogP	logD	CL_{int}	$t_{1/2}$
(±)-Buclizine	>1	7.42	4.5	6*	284*
(±)-Buclizine analog	>1	6.46	3.3	9*	195*

b) Lipid droplets fluorescent imaging assay

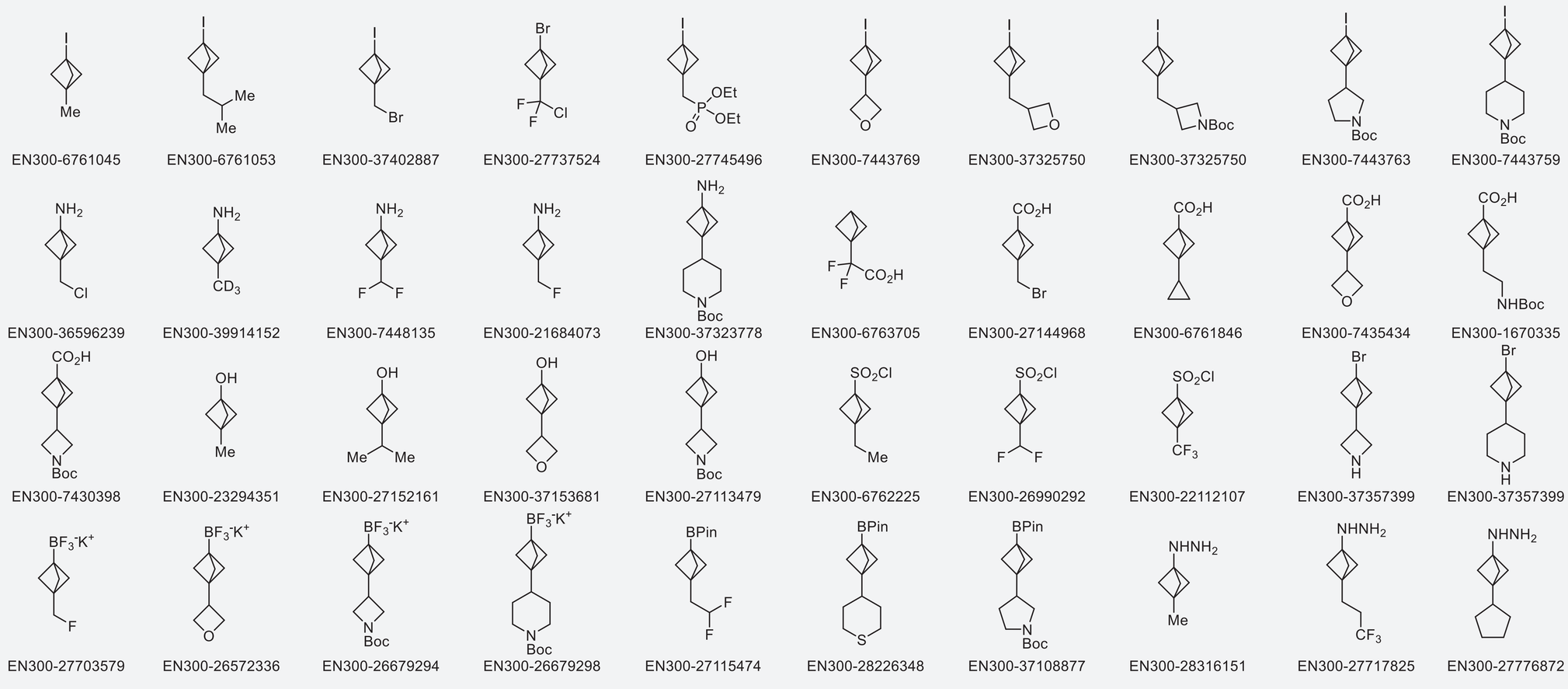


Compound	IC_{50}	EC_{50}
(±)-Buclizine	31.3 ± 7.8 μM	19.11 ± 1.45 μM
(±)-Buclizine analog	24.5 ± 1.5 μM	16.49 ± 0.56 μM

Modifications



Results



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References

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