

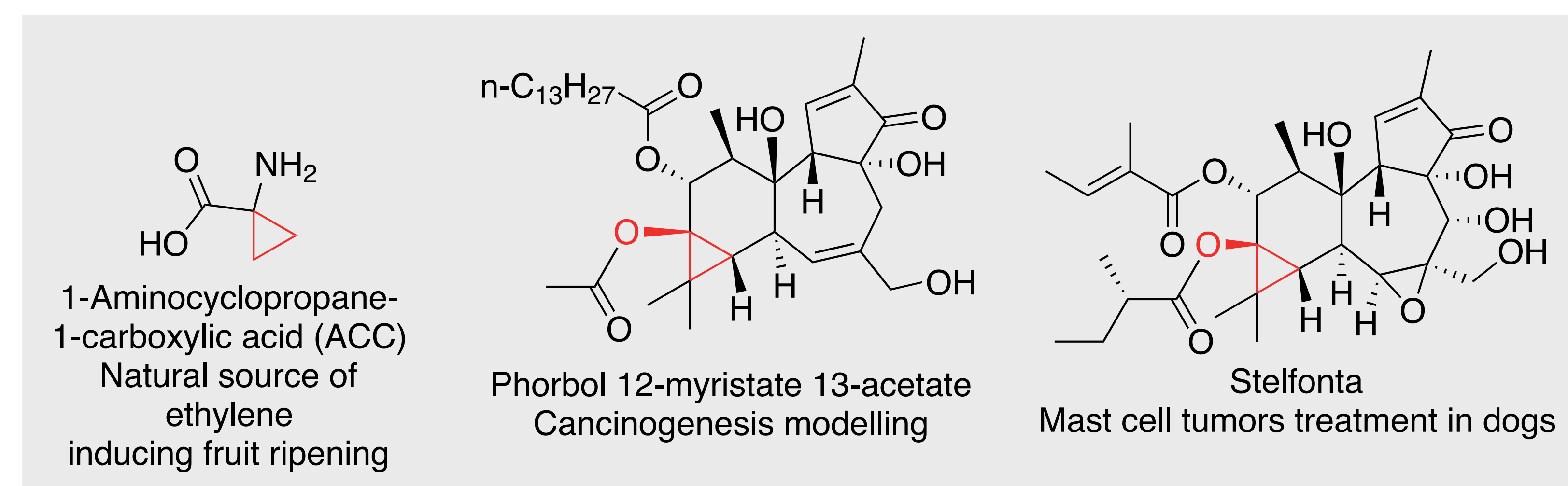
# Handy access to diverse cyclopropanols via cyclopropanation/oxidation sequence of vinyl boronates



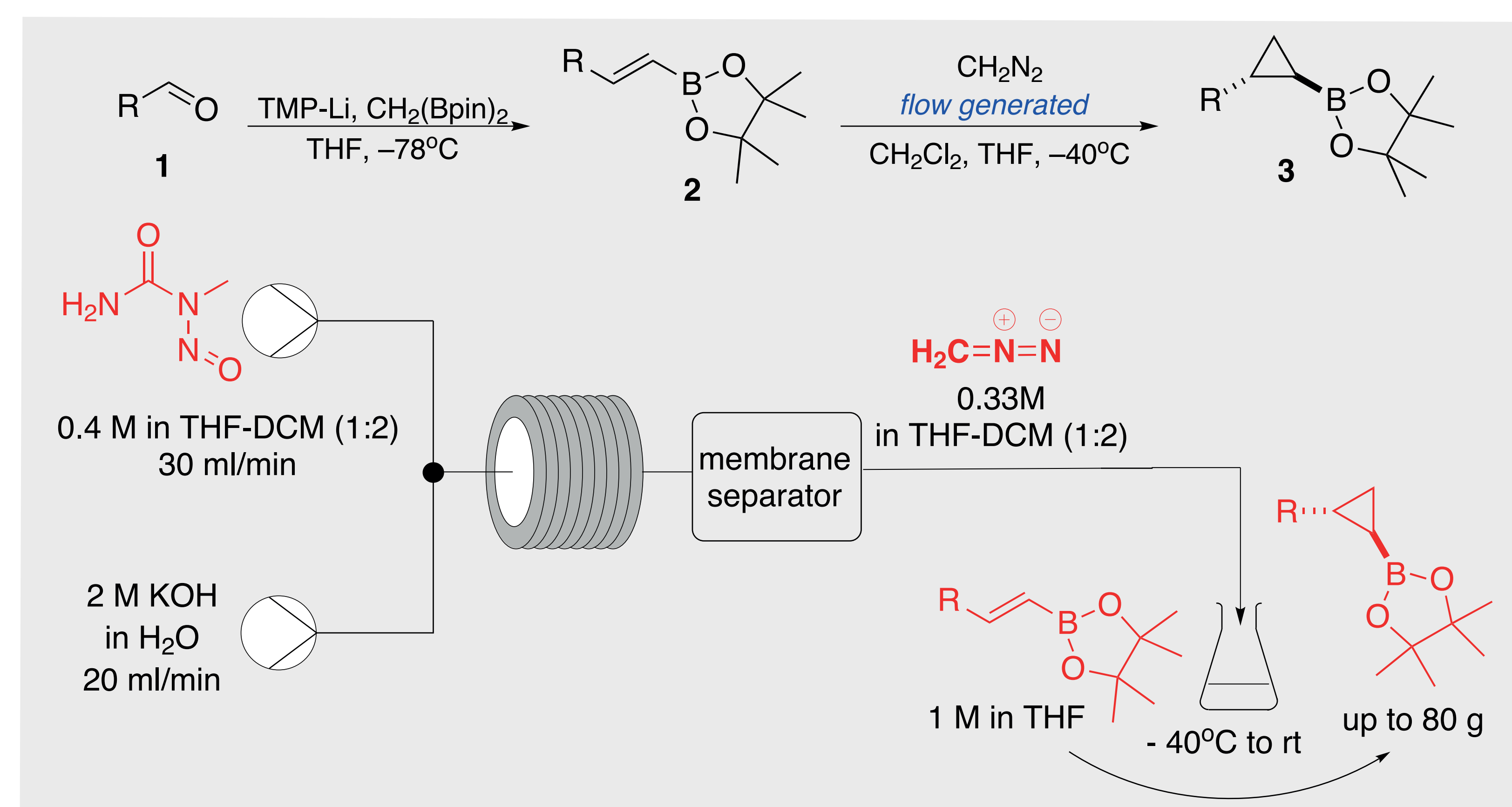
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## Background of the project

- Cyclopropane ring occurs in natural products inducing important biochemical processes (e. g., fruit ripening).
- Cyclopropanol-based natural and semi-synthetic molecules demonstrate a wide spectrum of bioactivity.
- Phorbol esters are used for carcinogenesis modeling, and tigilanol tiglate (Stelfonta) is a veterinary drug for mast cell tumors treatment.



- Diverse commercially available aldehydes **1** were introduced to Boron-Wittig olefination<sup>1</sup> with bis[(pinacolato)boryl]methane to get unsaturated boronates **2**.
- Boronates **2** were cyclopropanated with in-flow generated diazomethane<sup>2</sup> to yield the *trans*-diastereomer **3** selectively. The synthesis was scaled up to 80 g per run.

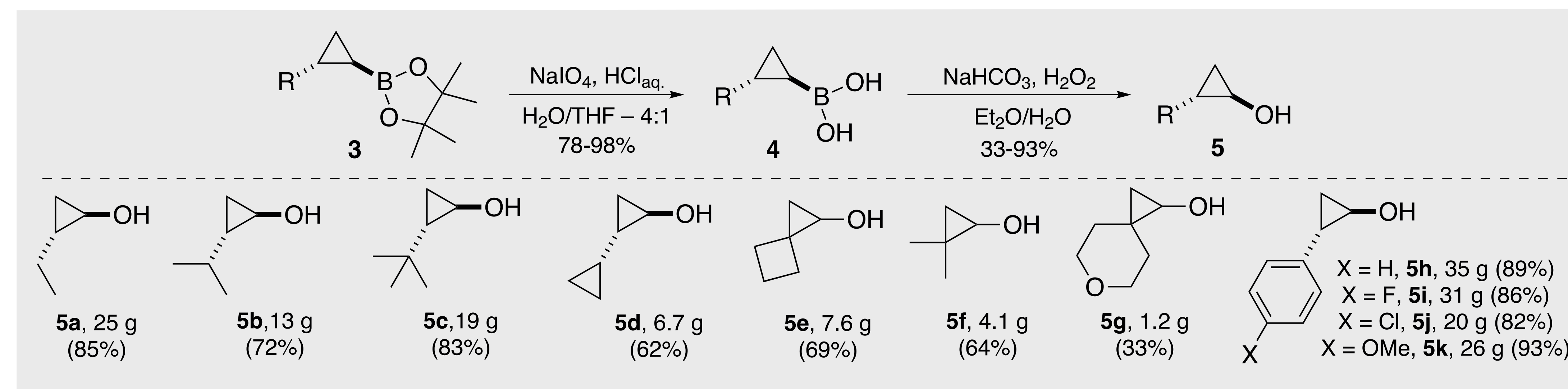


## Contact

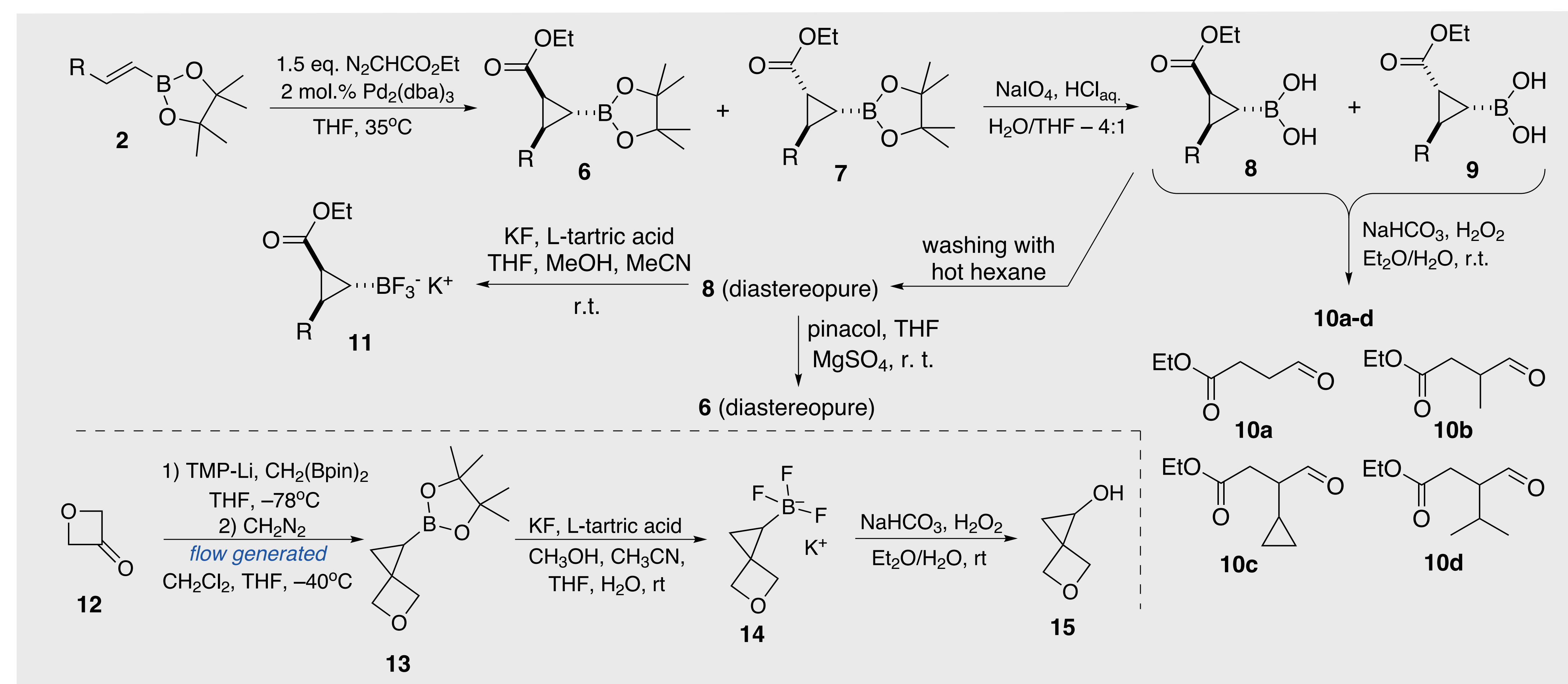
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## Exploring the reaction scope and expanding variety of the products

- Cyclopropylboronates **3** were hydrolyzed in presence of sodium periodate to yield boronic acids **4** with 78-98% yields.
- The obtained boronic acids **4** were cleaved with hydrogen peroxide under basic conditions to give the desired cyclopropanols **5a-k** in 33-93% yields.
- Tolerance towards diverse alkyl and small cycloalkyl substituents as well as ether groups was shown.



- Palladium-catalyzed cyclopropanation of boronates **2** with ethyl diazomethane yielded a mixture of diastereomers **6** and **7**.
- Pinacol ester hydrolysis lead to the mixture of boronic acids **8** and **9** that can be cleaved to  $\gamma$ -oxoesters **10a-d**.
- Less soluble diastereomer **8** was purified by washing with hot hexane and turned into diastereopure compounds **6** and **11**.



## References

- Kovalenko, M. *et al. Eur. J. Org. Chem.* **2019**, 2019(33), 5624. DOI: 10.1002/ejoc.201900648
- Kleban, I. *et al. Eur. J. Org. Chem.* **2021**, 2021(47), 6551. DOI: 10.1002/ejoc.202000977