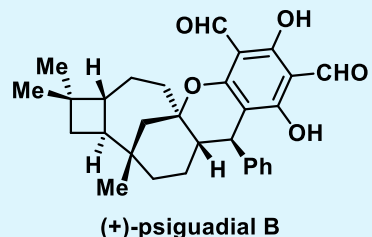


Synthesis of the Week: (+)-Psiguadial B

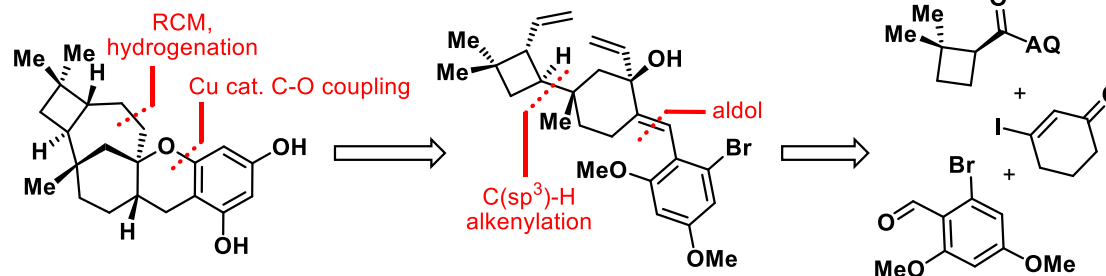


Psidium guajava flowers
Image via wikimedia commons

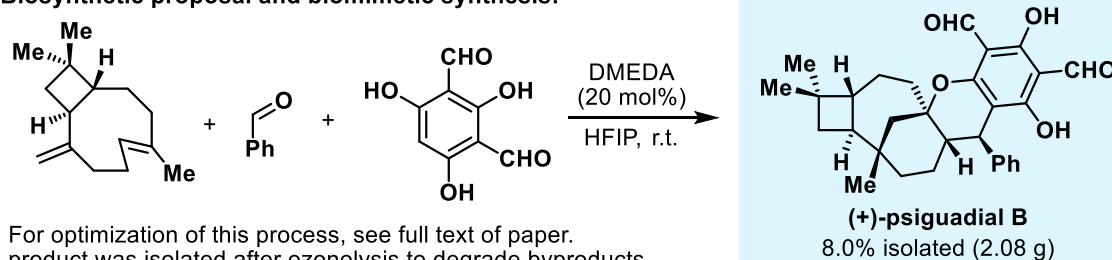
- Isolated from the common guava with related caryophyllene-derived natural products
- Plant leaves used in traditional medicine for diarrhea and hyperglycemia
- HepG2 cell inhibitor ($IC_{50} = 45.62 \pm 1.41$ nM)

Org. Lett. **2010**, *12*, 5040.

Retrosynthetic analysis for construction of (+)-psiguadial B ring system:

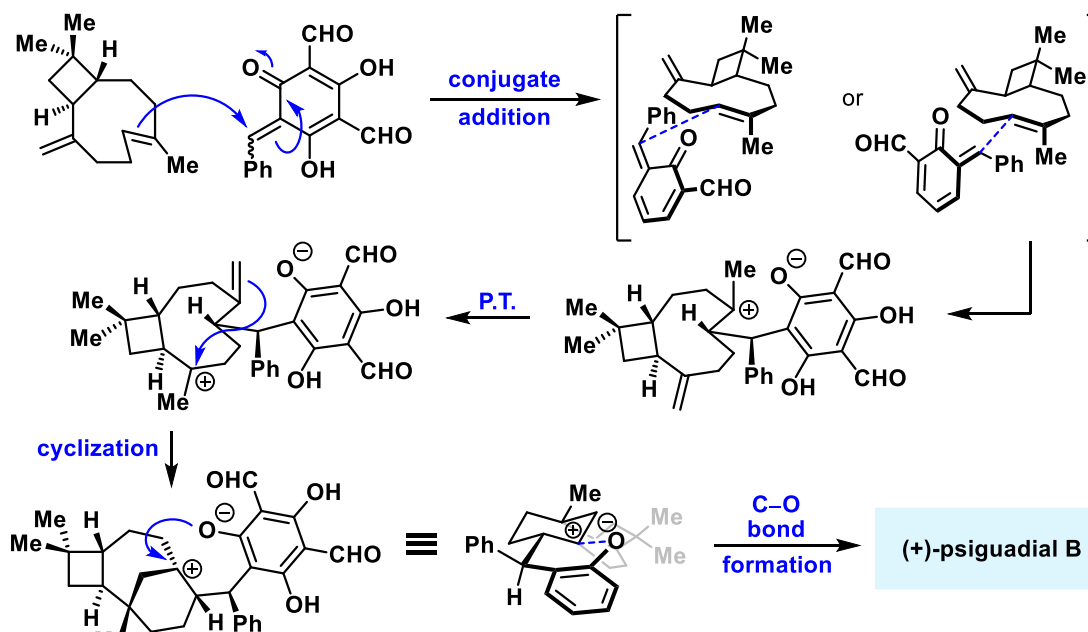


Biosynthetic proposal and biomimetic synthesis:



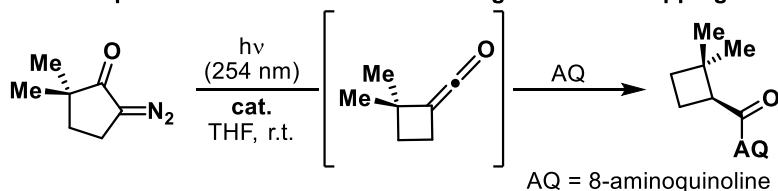
For optimization of this process, see full text of paper.
product was isolated after ozonolysis to degrade byproducts.

Proposed biosynthetic mechanism (for computation and experimental support, see full text):

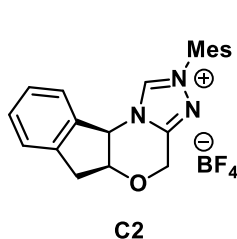
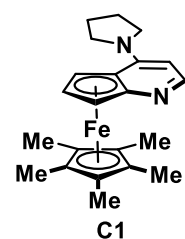


Newton, C. G.; Tran, D. N.; Wodrich, M. D.; Cramer, N. *Angew. Chem. Int. Ed.* **2017**, *56*, 13776.

Selected optimization data for Wolff rearrangement and trapping:

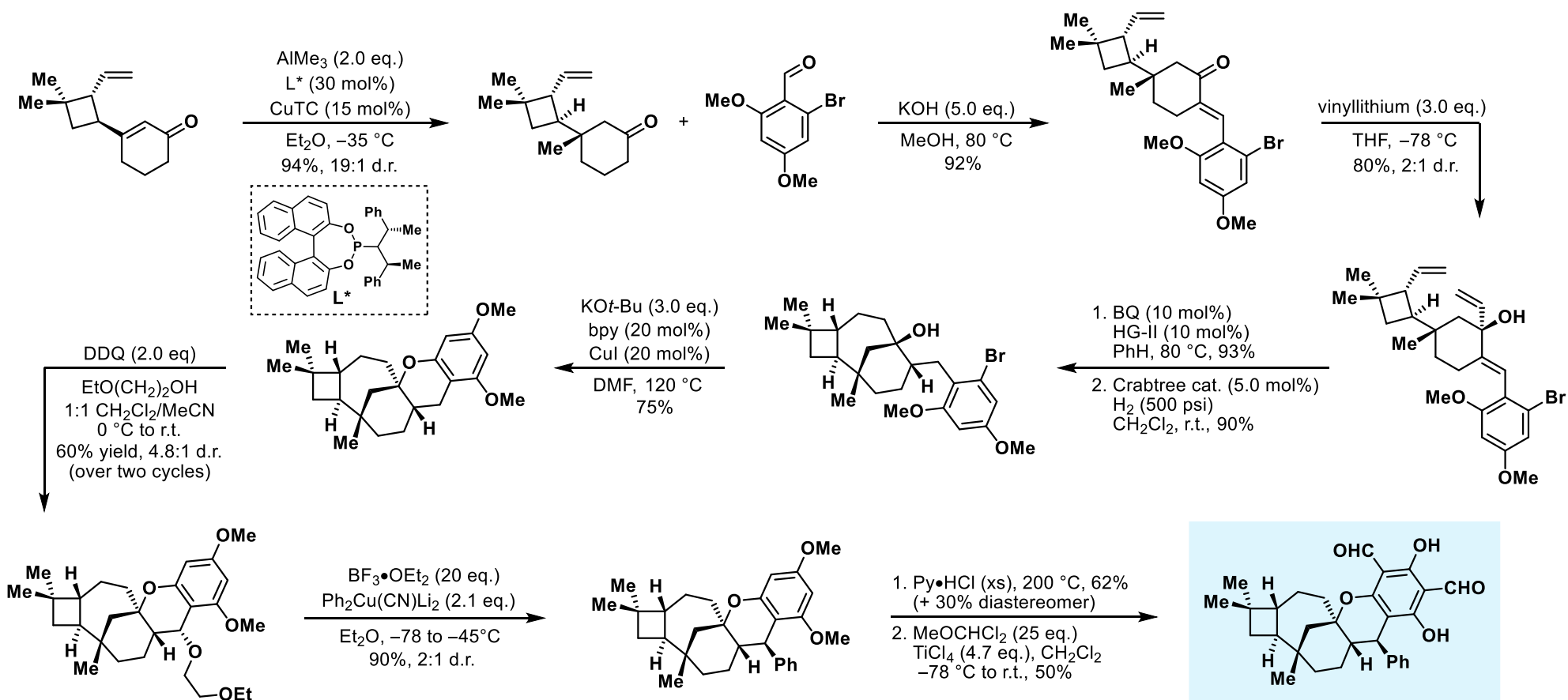
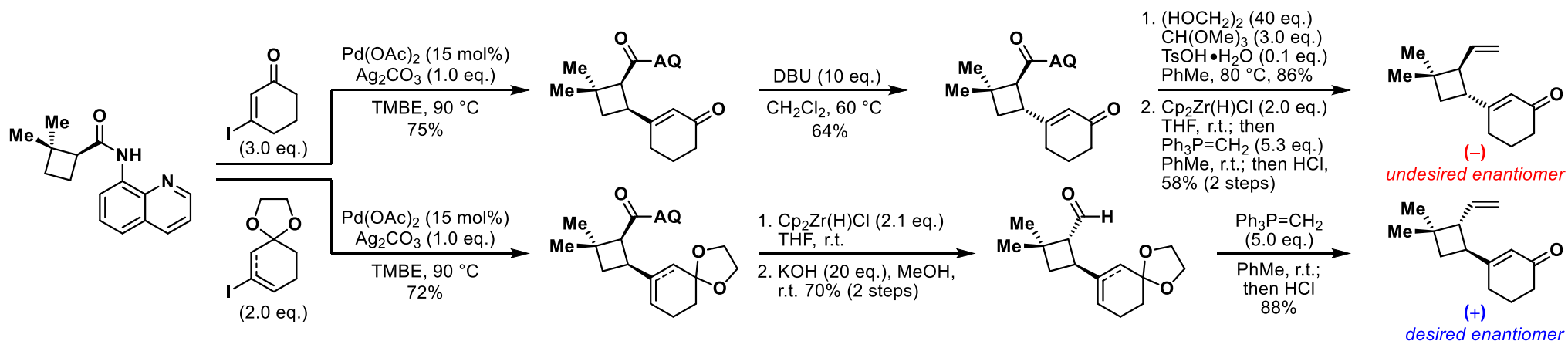


mmol	cat. (mol%)	AQ (eq.)	NMR yield (%)	ee (%)
0.10	N/A	1.0	55	0
0.10	C1 (50)	1.0	39	46
0.10	C2 (50)	1.0	32	-66
0.10	C3 (50)	1.0	58	-59
0.10	C4 (50)	1.0	72	77
0.10	C4 (20)	1.0	66 (isol.)	81
11	C4 (20)	1.0	37 (isol.)	79
15	C4 (20)	3.0	62 (isol.)	80
30	C4 (10)	3.0	62 (isol.)	79



both — : (-)-cinchonidine (**C3**)
both — : (+)-cinchonine (**C4**)

Synthesis of the Week: (+)-*Psiguadial B*

Chapman, L. M.; Beck, J. C.; Wu, L.; Reisman, S. E. *J. Am. Chem. Soc.* **2016**, *138*, 9803.For full article describing alternative routes: Chapman, L. M.; Beck, J. C.; Lacker, C. R.; Wu, L.; Reisman, S. E. *J. Org. Chem.* **2018**, *83*, 6066.