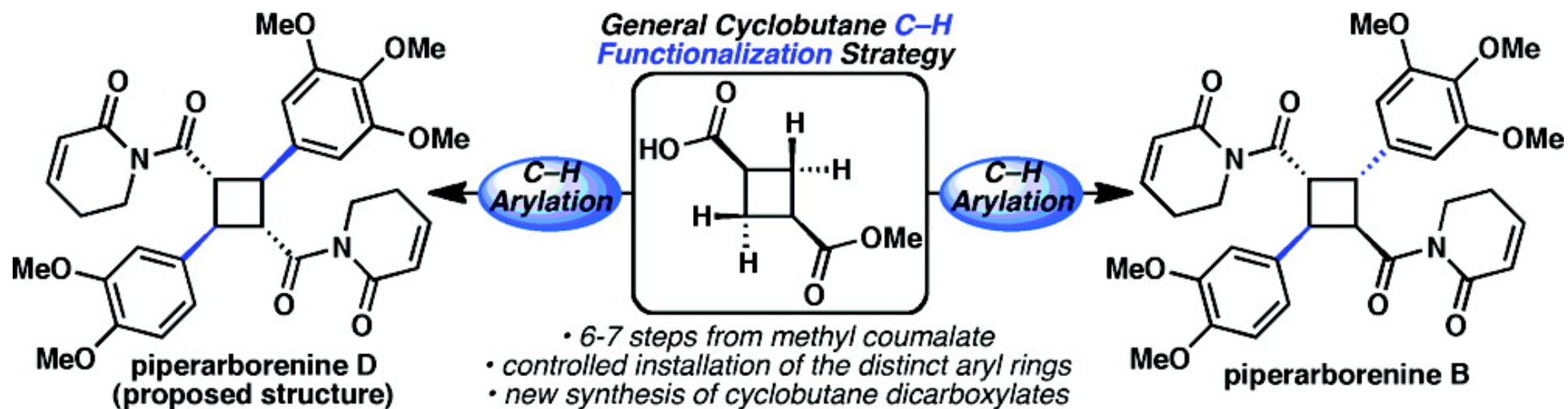


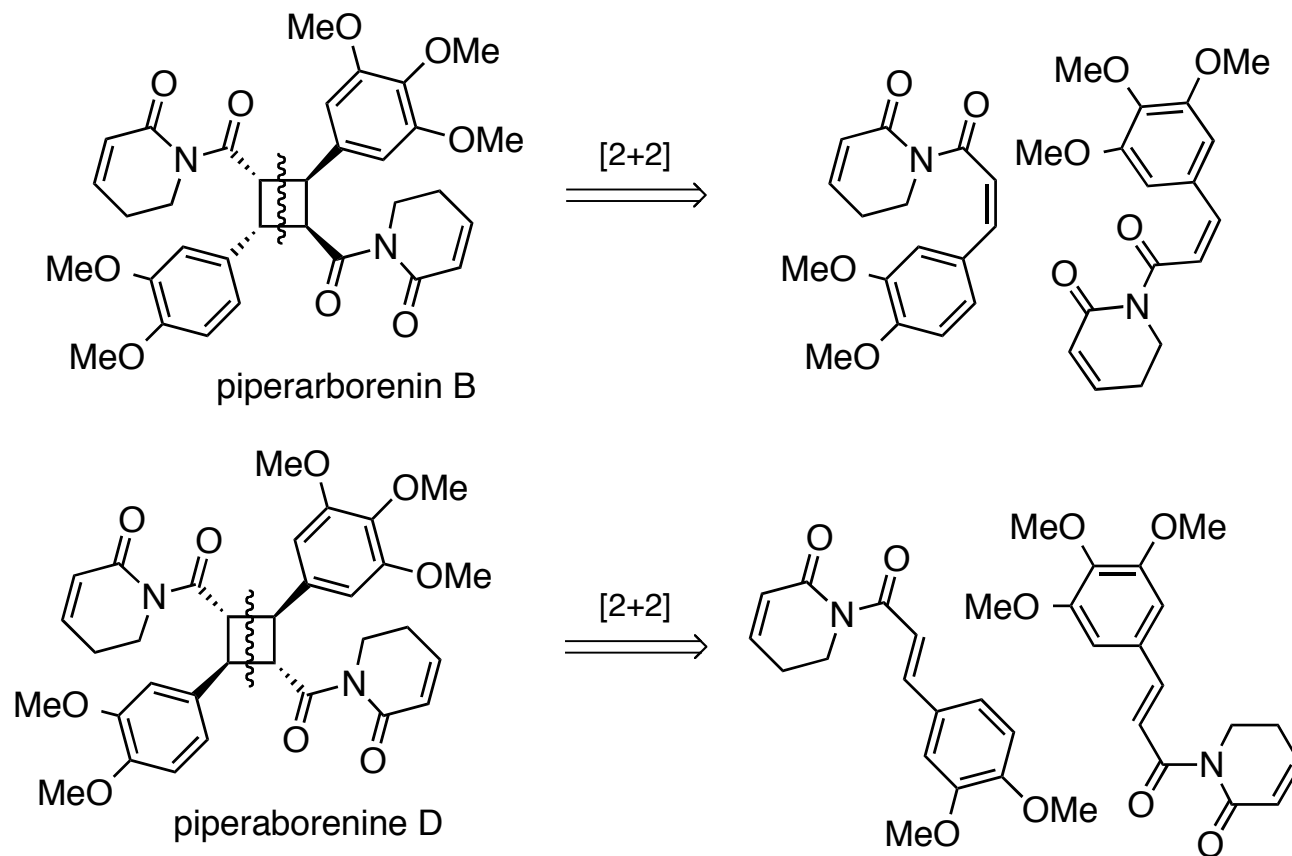
Total Synthesis and Structural Revision of the Piperarborenines via Sequential Cyclobutane C-H Arylation



Will R. Gutekunst and Phil S. Baran
Presented by: Jared Hammill

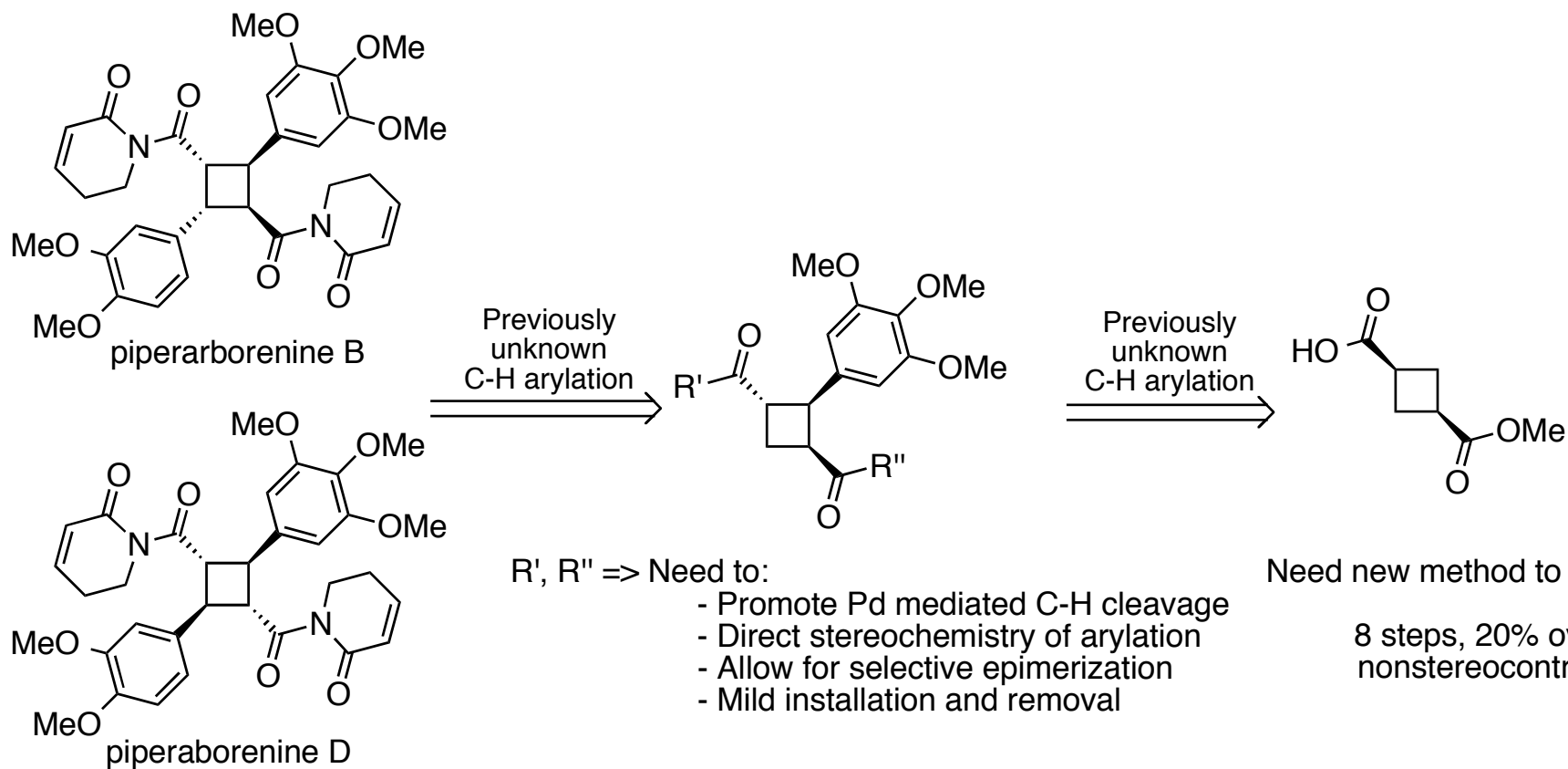
J. Am. Chem. Soc., 2011, 133 (47), pp 19076–19079

Potential for [2+2]



Unfortunately in the flask homodimerization, orientation (head to head vs. head to tail), and E/Z isomerization, lead to a variety of structural and stereochemical outcomes

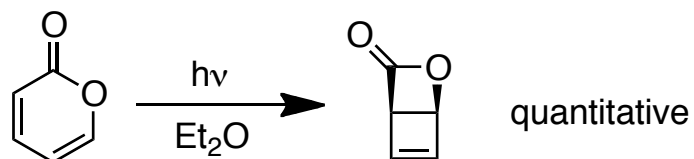
The Plan



“If I have seen further it is by
standing on the shoulders of giants”

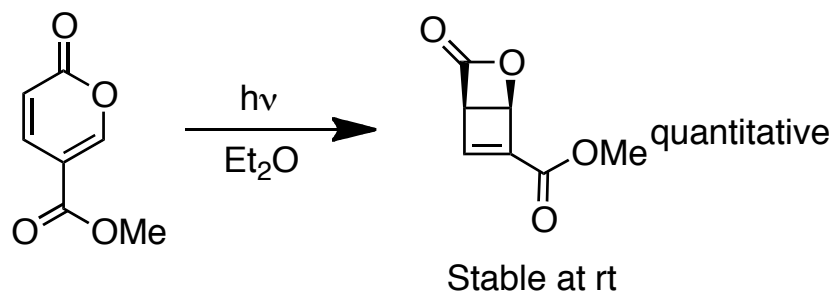
Isaac Newton in a letter to Robert Hooke (1676)

The Precedence A New Synthesis



hygroscopic
pyrophoric, and explosive
in air with mild Δ

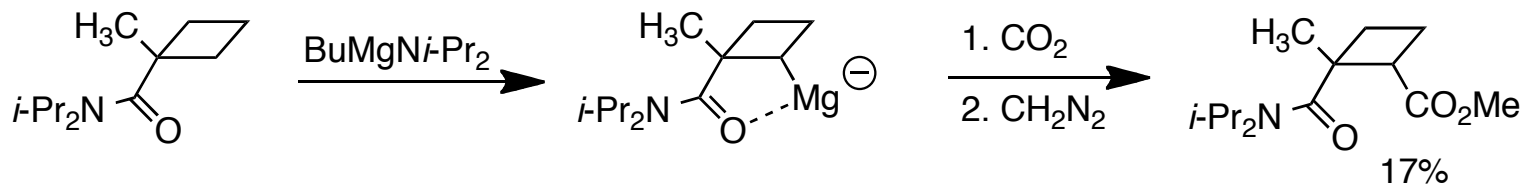
Corey, E. J.; Streith, J. J. *Am. Chem. Soc.* 1964, 86, 950–951.



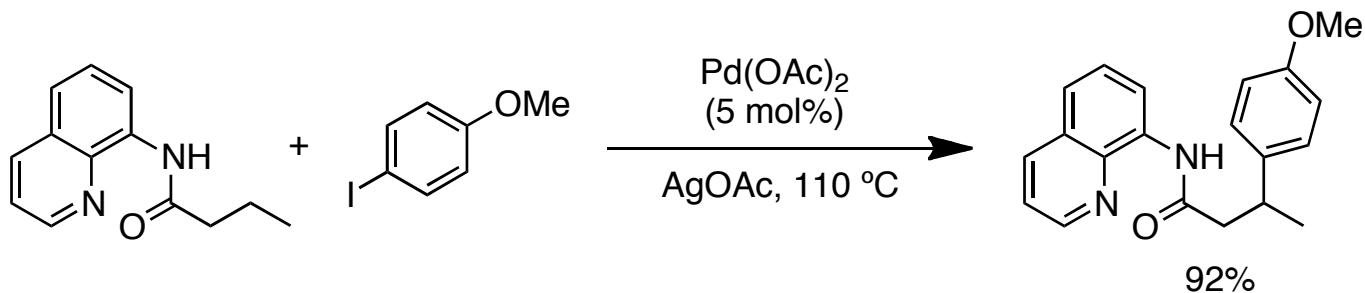
Only a C-O and a C=C
reduction away
from our desired SM

Frebault, F.; Luparia, M.; Oliveira, M. T.; Goddard, R.;
Maulide, N. *Angew. Chem., Int. Ed.* 2010, 49, 5672–5676.

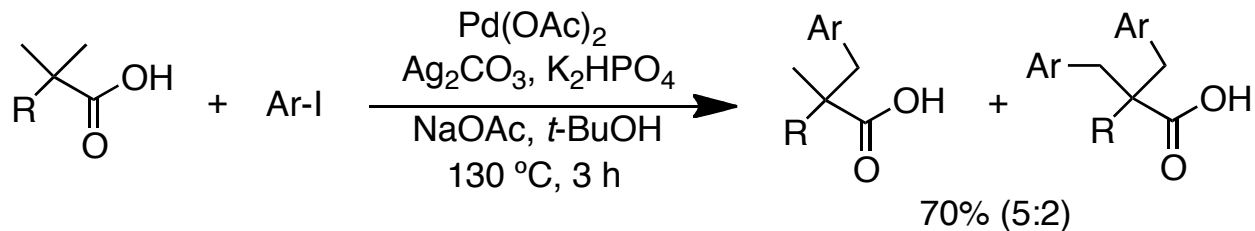
The Precedence C-H Arylation



Zhang, M.-X.; Eaton, P. E. *Angew. Chem., Int. Ed.* 2002, 41, 2169–2171.

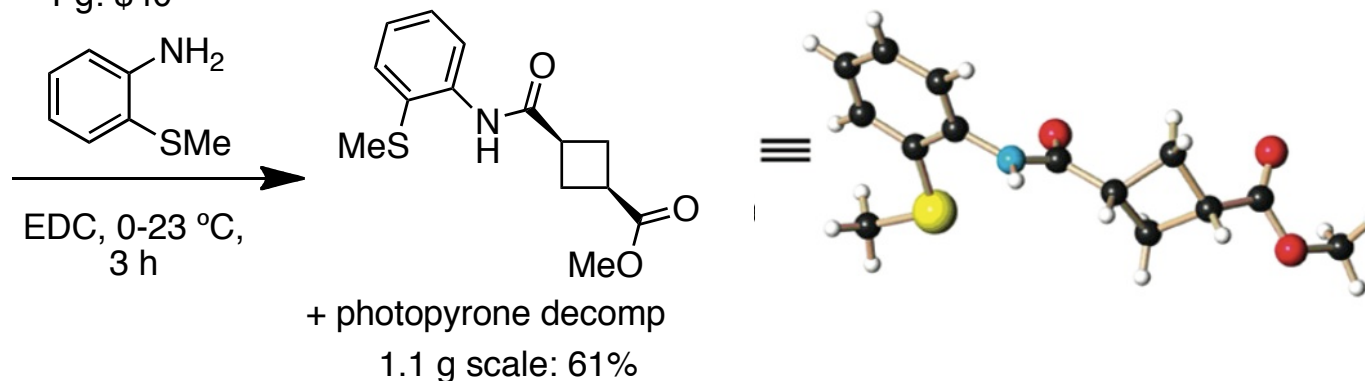
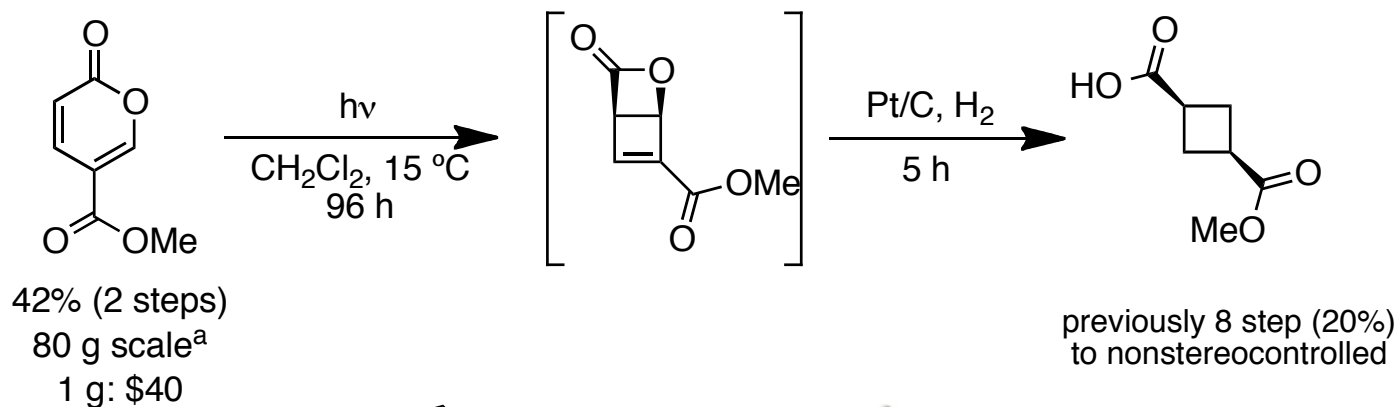
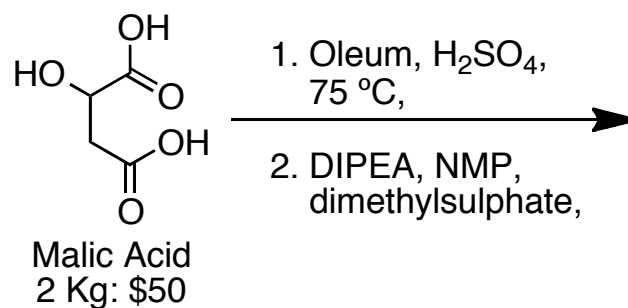


Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* 2005, 127, 13154.



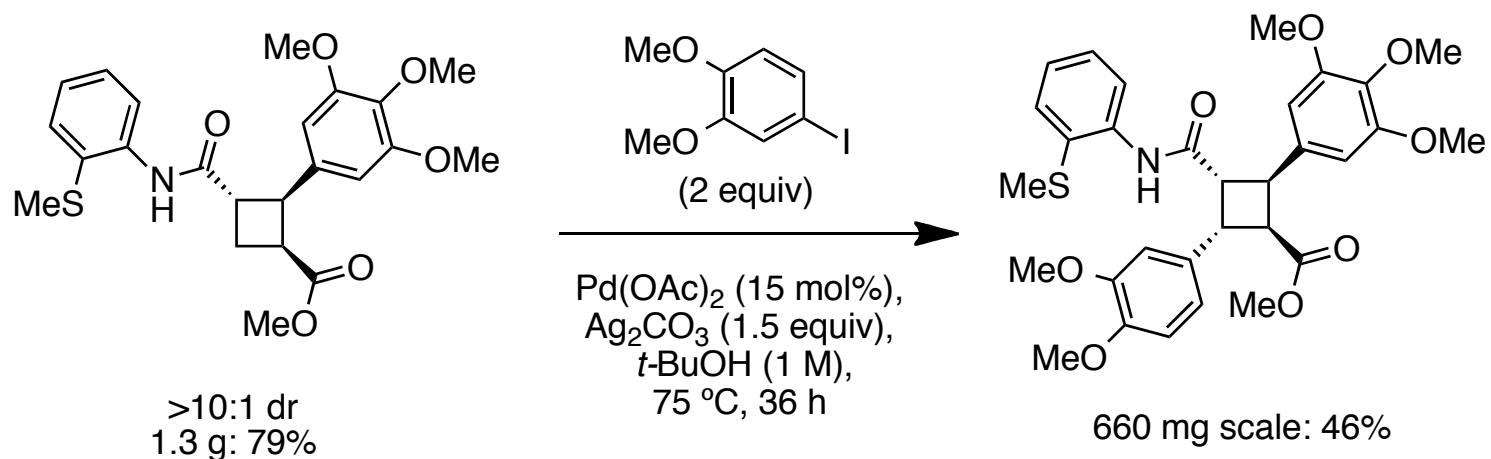
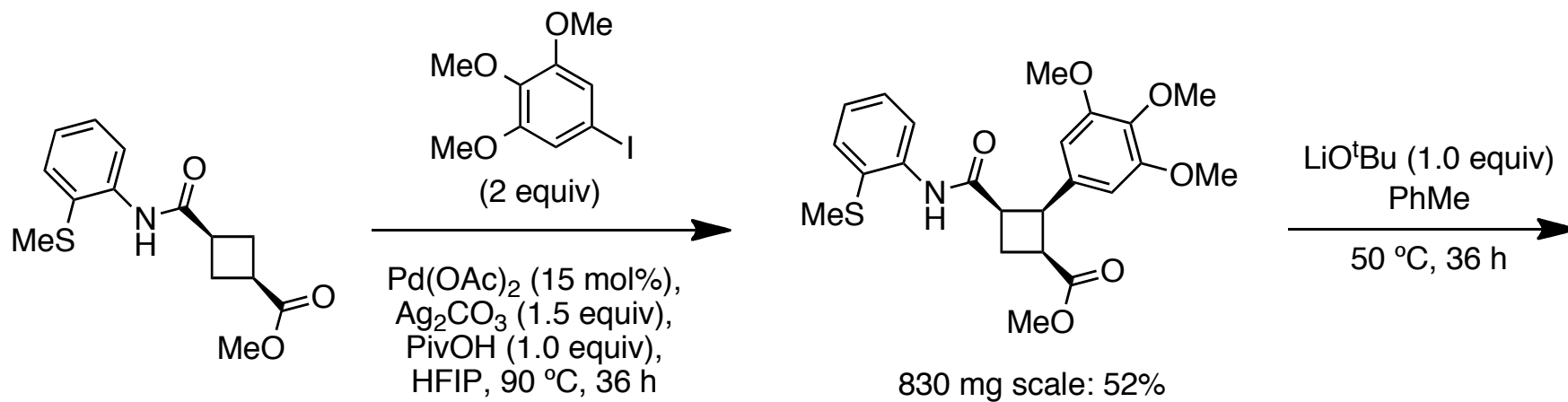
Giri, R.; Maugel, N.; Li, J.-J.; Wang, D.-H.; Breazzano, S. P.; Saunders, L. B.; Yu, J.-Q. *J. Am. Chem. Soc.* 2007, 129, 3510–3511.

[2+2] Photocycloaddition

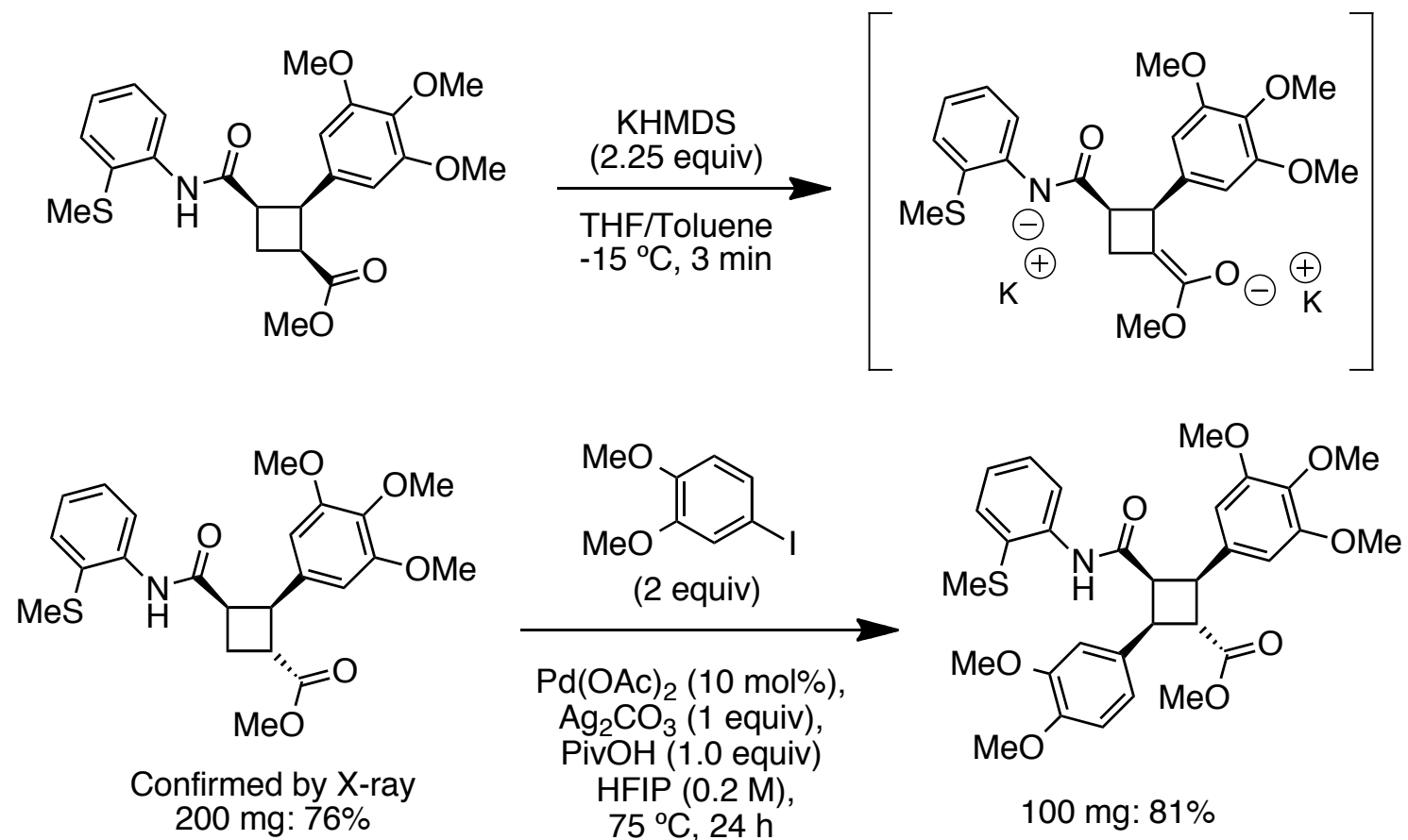


^aJ. Org. Process Res. Dev. 2003, 7, 74–81

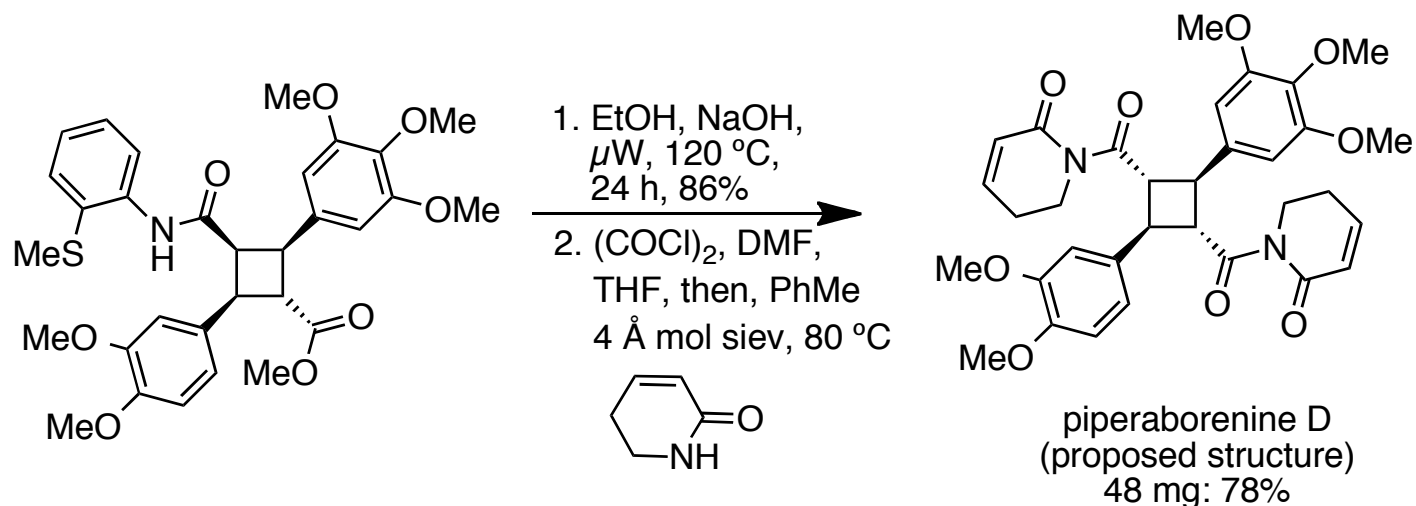
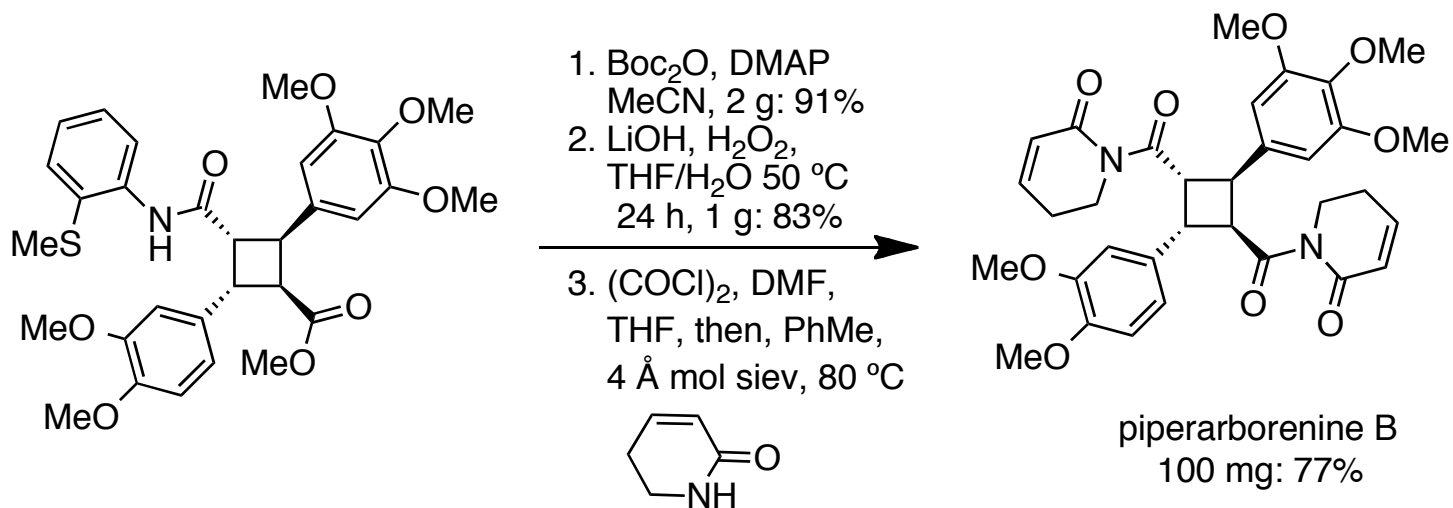
Cyclobutane C-H Arylation



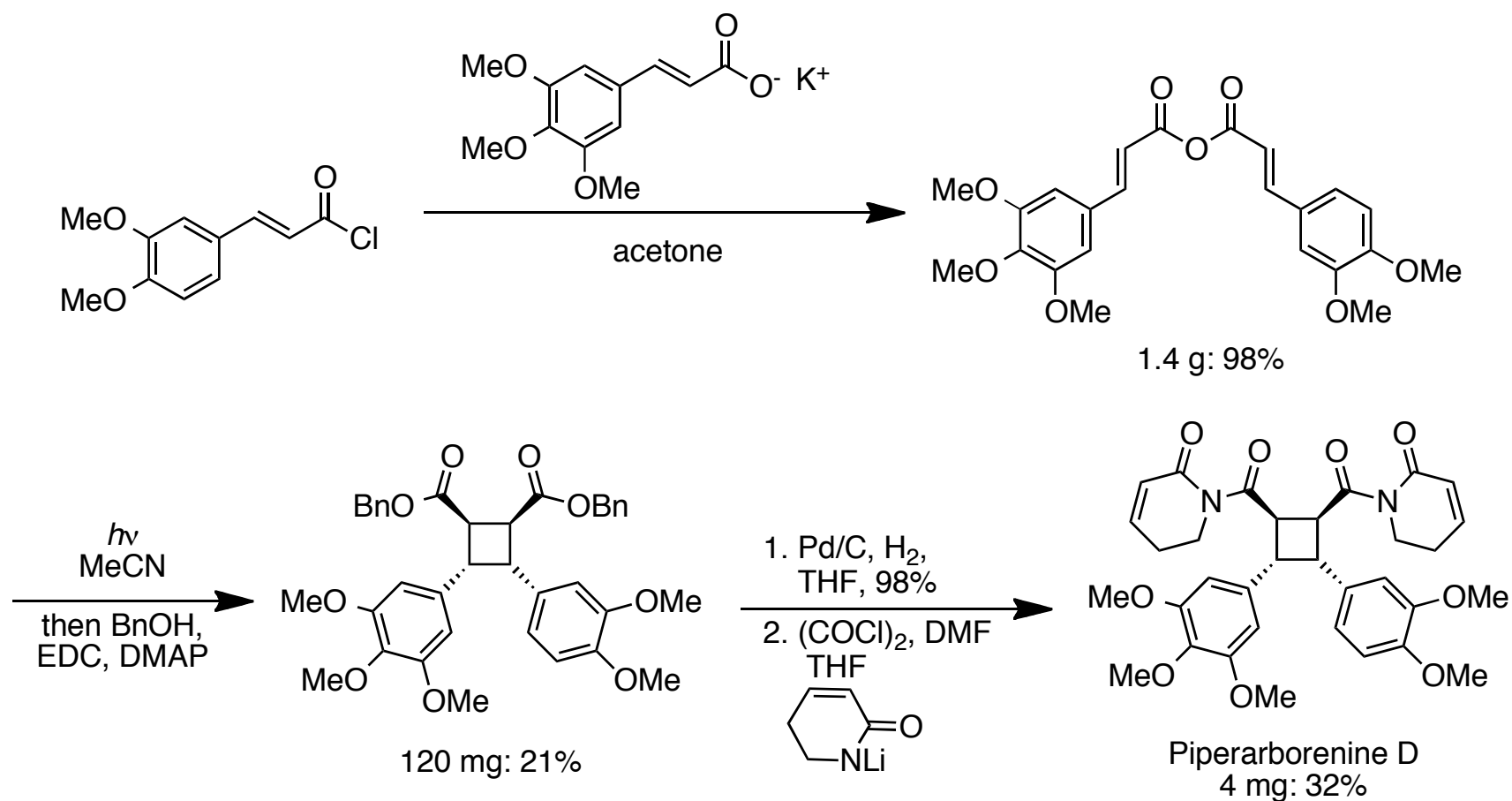
Cyclobutane C-H Arylation



Completion of Piperarborenine B & Proposed Structure of Piperarborenine D



Structural Revision and Synthesis of Piperarborenine D



Conclusions

- Piperarborenine B was synthesized in 7 steps, 7% overall yield
- Proposed structure for piperarborenine D was synthesized in 6 steps, 12% overall yield
- 1st catalytic transition metal mediated C-H activation of cyclobutane ring
- Use of divergent epimerization and sequential Sp³ arylation strategy to arrive at two NP from a common SM
- Expedient synthesis of desired cyclobutane SM in a stereocontrolled fashion
- Structural revision and synthesis of piperarborenine D

Questions?