Palladium-Catalyzed Synthesis of Cyclopentane-Fused Benzocyclobutenes via Tandem Directed Carbopalladation/C-H Bond Functionalization

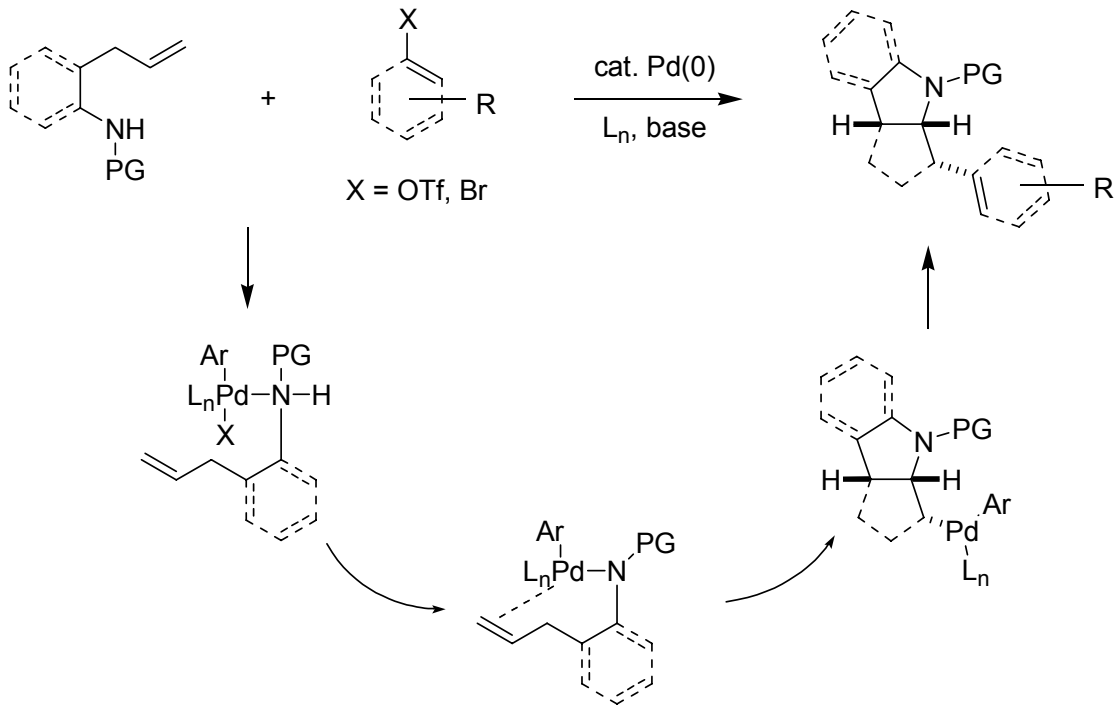
Bertrand, M. B.; Wolfe, J. P. *Org. Lett.* **2007**, *9*, 3073-3075.

Chad Hopkins

Wipf Group Literature Presentation

9-15-07

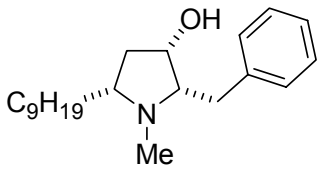
Carboamination Research in the Wolfe Group: General Mechanism



Bertrand, M. B.; Wolfe, J. P. *Org. Lett.* **2007**, *9*, 457 and references therein.

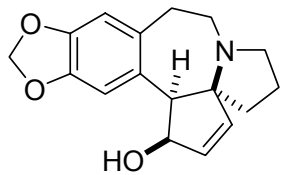
http://www.umich.edu/~wolfelab/Research.html

Significance of Pyrrolidines as Synthetic Targets



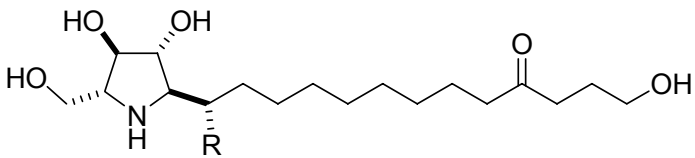
Preussin
(Antifungal, Antitumor Activity)

Schwartz, R. E. *et. al. J. Antibiot.* **1988**, *41*, 1774.



Cephalotaxine
(*O*-Acylated Derivatives Antileukemia activity)

Paulder, W. W. *et. al*. *J. Org. Chem.* **1963**, *28*, 2194.

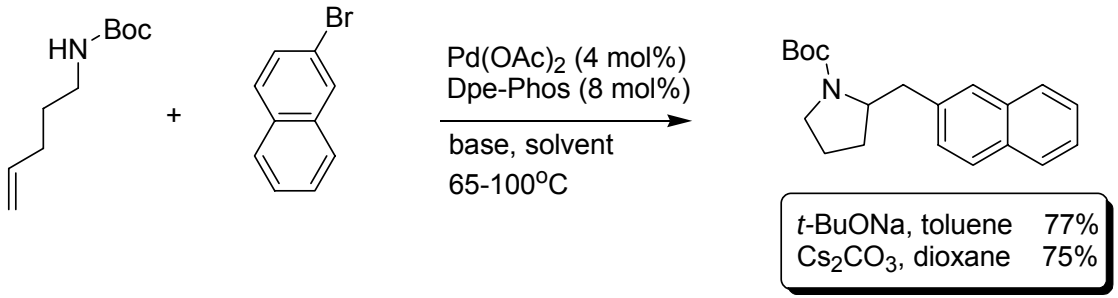


Broussonetine C (R = H)
Broussonetine E (R = OMe)
(Glycosidase Inhibitors)

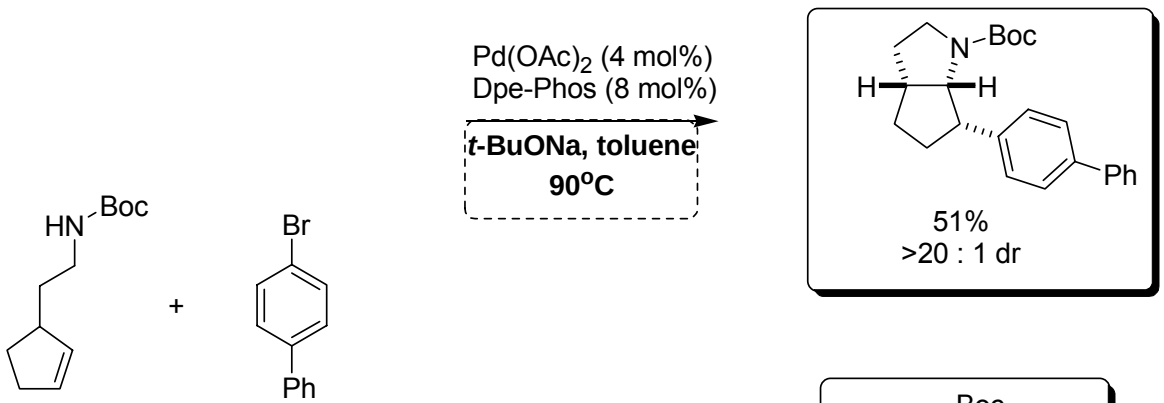
Kusano, G. *et. al. Chem. Pharm. Bull.* **1997,** *45*, 505.

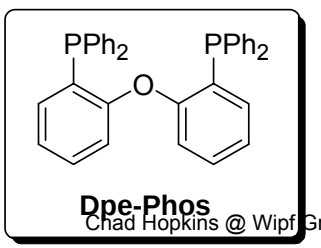
For a review on methods for the synthesis of substituted pyrrolidines see: Pichon, M.; Figadere, B. *Tetrahedron: Asymmetry* **1996**, *7*, 927-964.

Surprising Effect of Base



Bertrand, M. B.; Wolfe, J. P. *Org. Lett.* **2007**, *9*, 457.

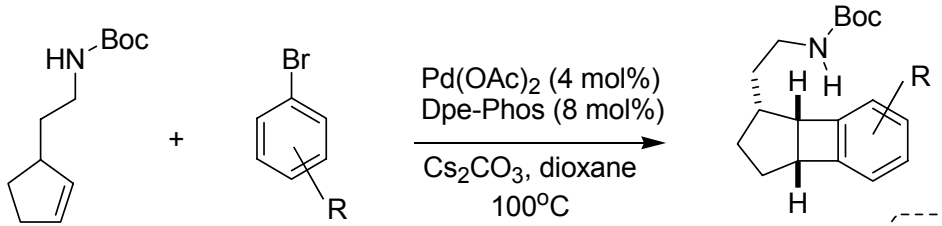


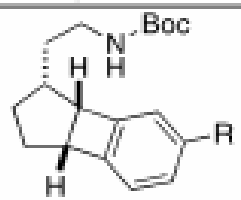
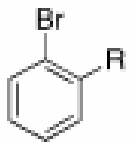
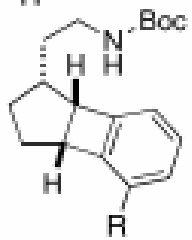
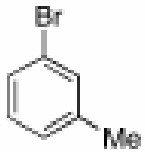
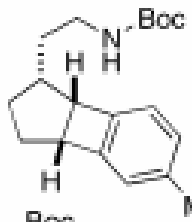
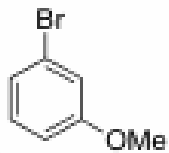
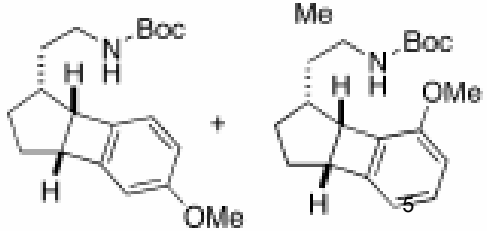


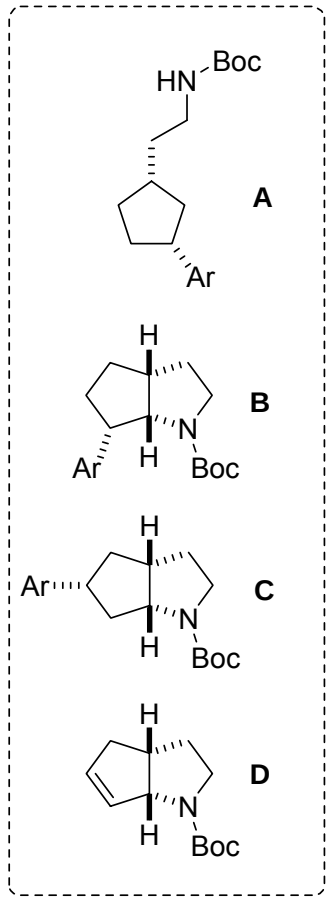
Bertrand, M. B.; Wolfe, J. P. *Tetrahedron* **2005**, *61*, 6447.

For a review on the synthesis and reactions of benzocyclobutenes see: *Chem. Rev.* **2003**, *103*, 1539.

Synthesis of Benzocylobutenes

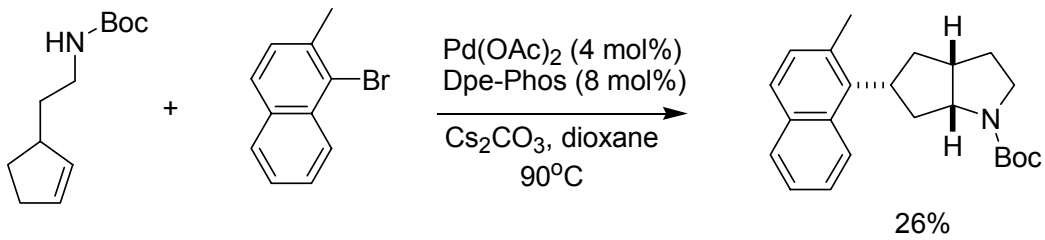


entry	ArBr	product	yield (%)[b,c]
1			R = CH_2OAc: 74
2			R = Ph: 72
3			R = Cl: 70
4			R = OMe: 58
5			R = Me: 85
6			R = Ph: 80
7			68
8			66 (2:1)

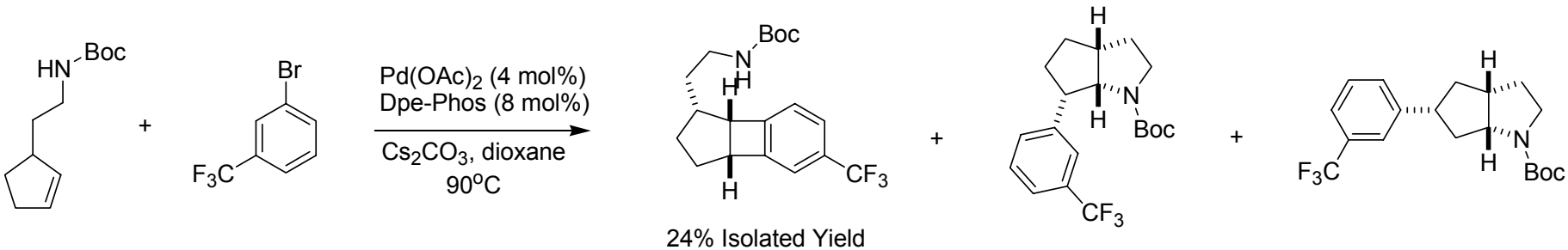


Side Products

Low Conversion Reactions



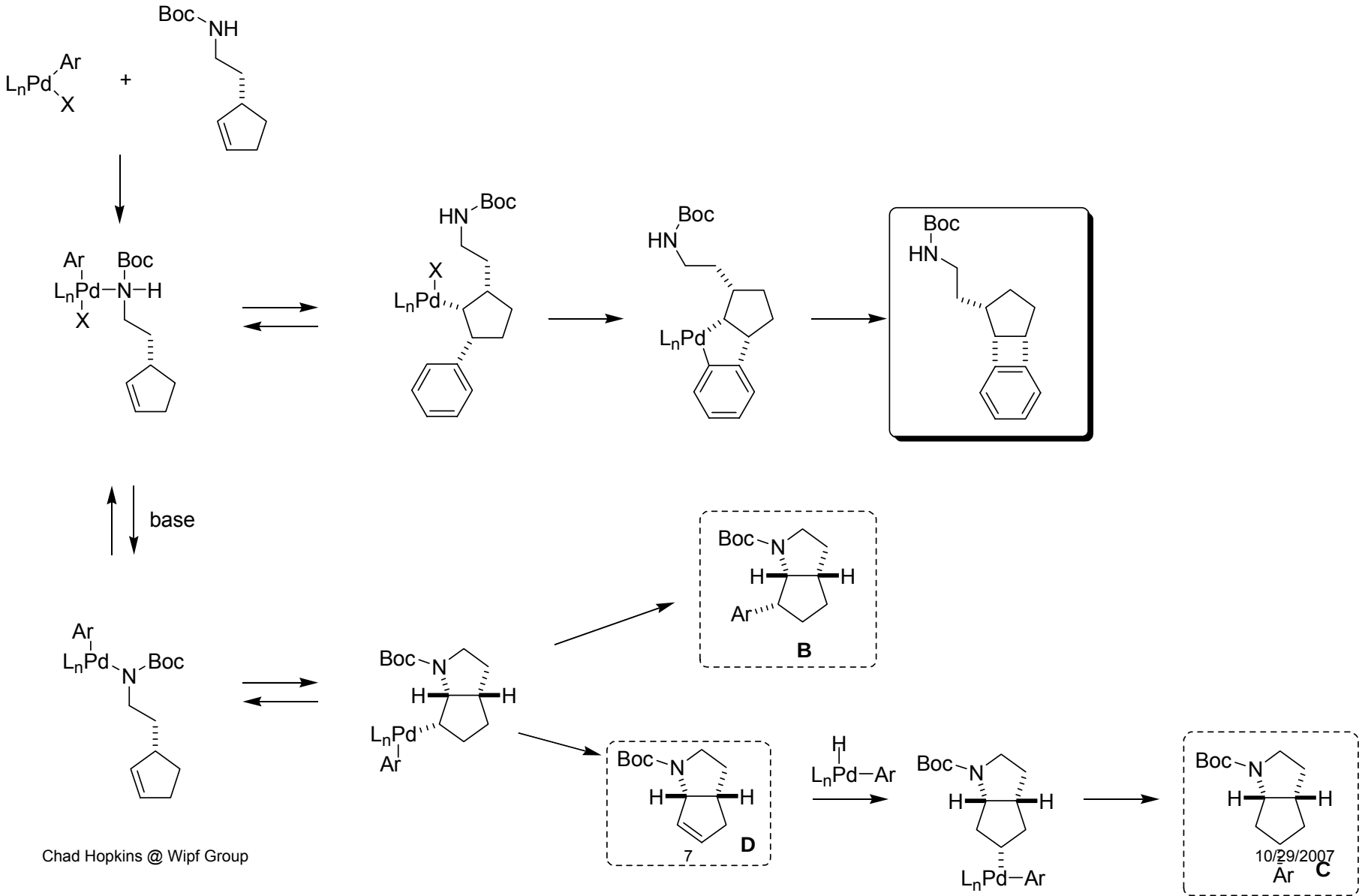
26%



24% Isolated Yield

26 : 39 : 23 (NMR)

Proposed Mechanism



Summary

- Developed a method for conversion of γ-aminoalkenes into cyclopentane-fused benzocyclobutenes.
- First examples of directed carbopalladation for the generation and functionalization of alkylpalladium intermediates lacking *syn*-β-hydrogen atoms.
- Illustrates differences in reactivity of Pd-*amino* and Pd-*amido* complexes.