ARTICLE

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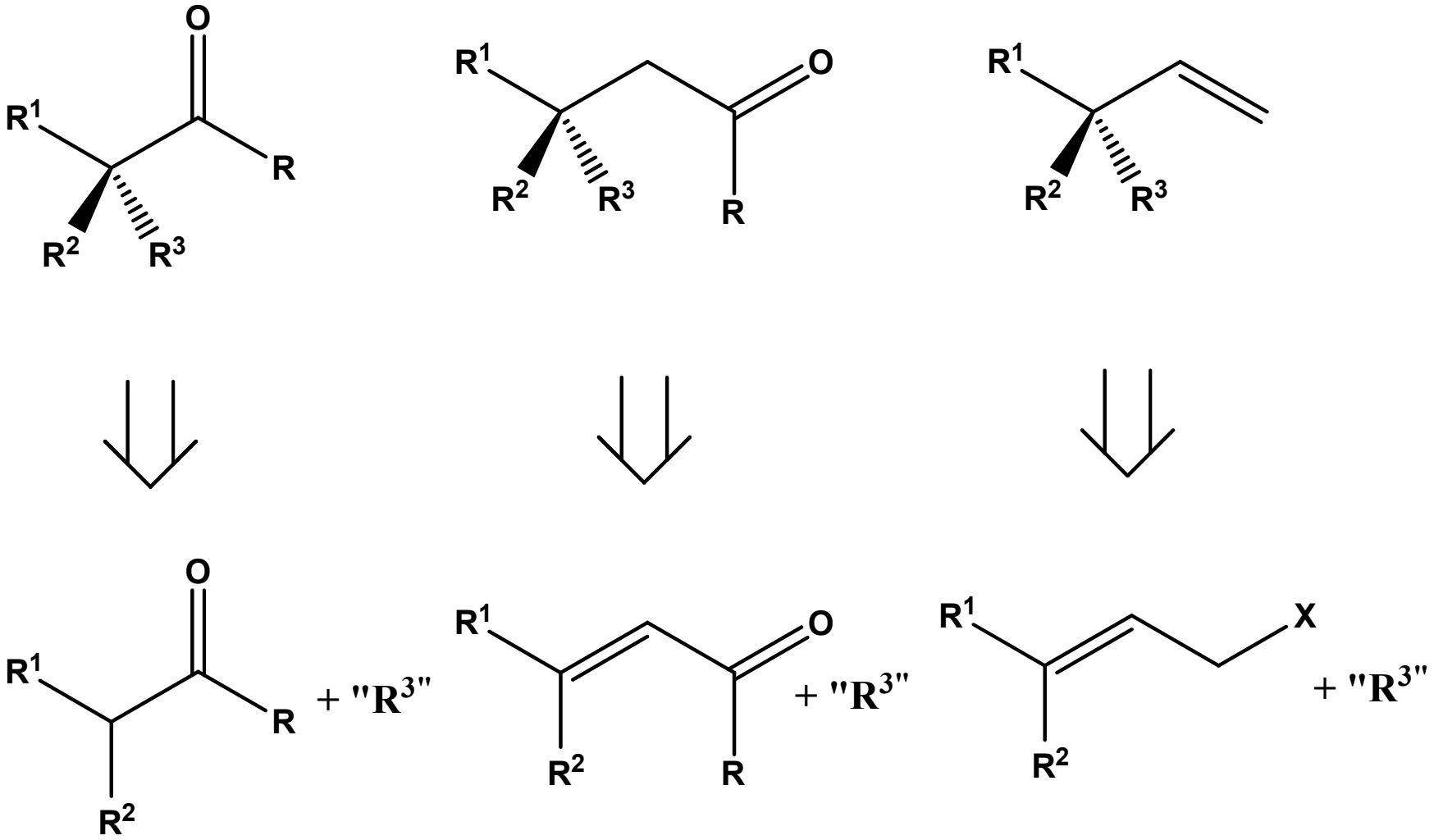
Enantioselective construction of remote quaternary stereocentres

Tian-Sheng Mei[1], Harshkumar H. Patel[1] & Matthew S. Sigman[1]

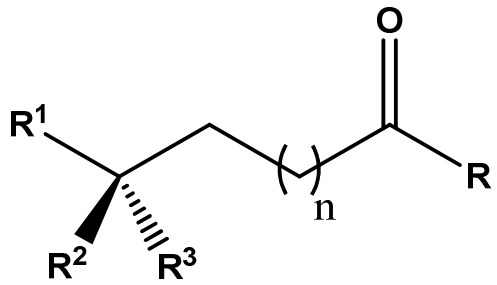
Sigman et al., *Nature* **2014**, 508, 340-344

Synthesis of a quaternary center in an acyclic system



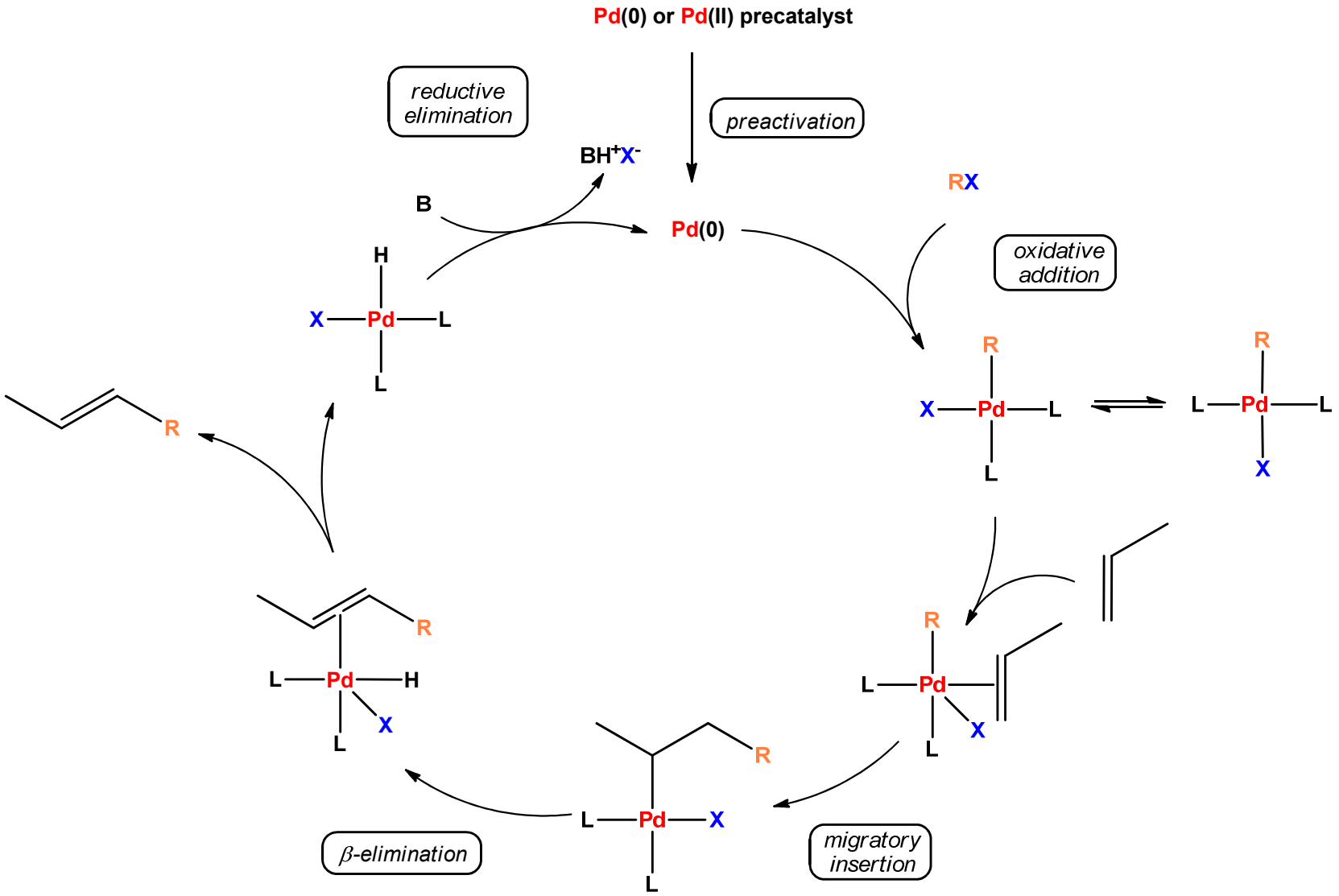
C. J. Douglas, L. O. Overman, *Proc. Natl. Acad. Sci.* **2004**, 101, 5363-5367

Challenge: Synthesis of a remote quaternary center



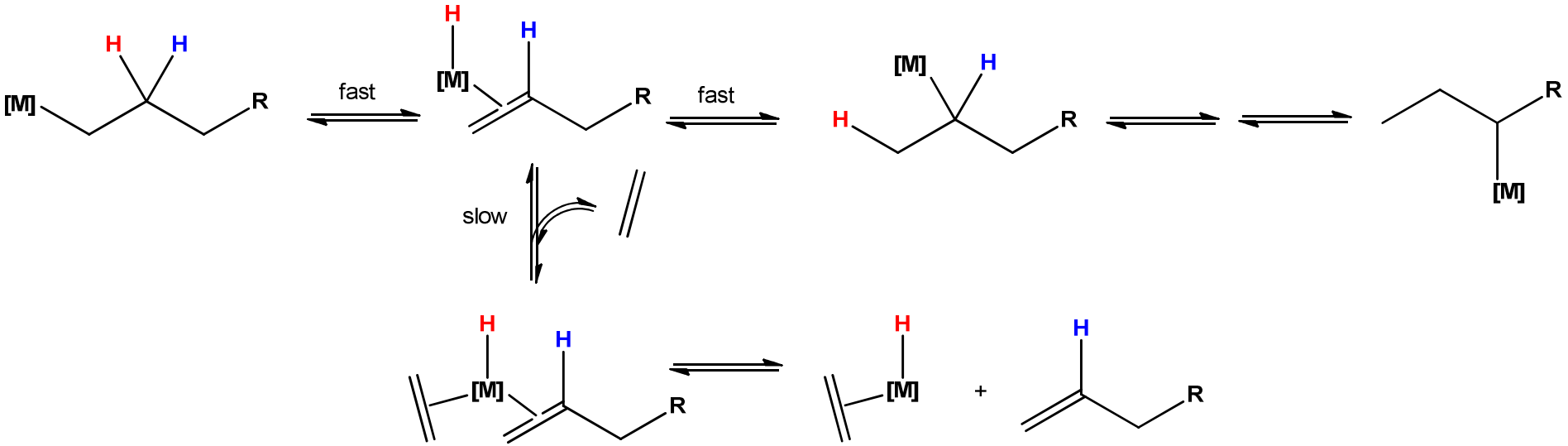
?

Heck reaction



Beletskaya et al., *Chem. Rev.* **2000**, 100, 3009-3066

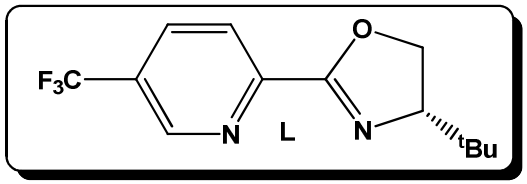
Chain-walking isomerisation

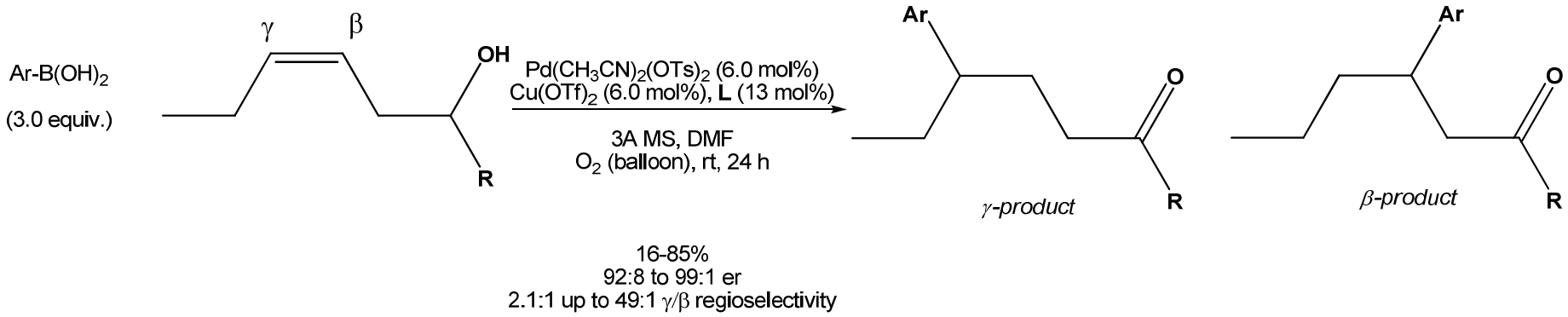


Chain walking is a mechanism in which an alkylmetal species undergoes rapid β-hydride elimination and reinsertion to change the position of the metal on the alkyl chain without dissociation of the olefin during the process

T. Kochi et al., *J. Am. Chem. Soc.* **2012**, 134, 16544-16547

Previously in the Sigman group



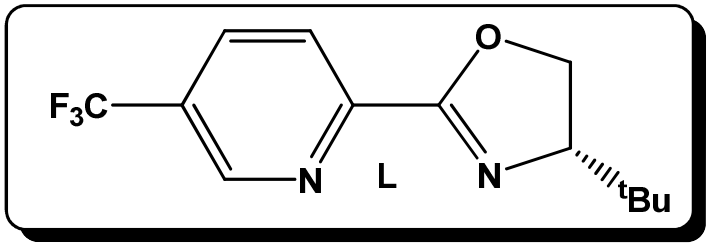


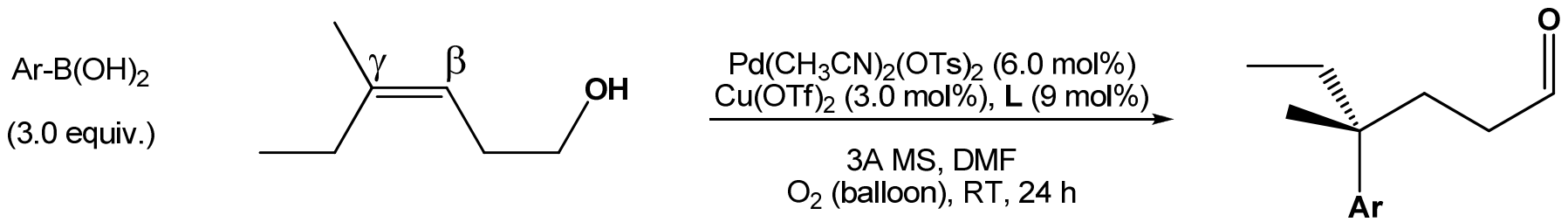
16-85%
92:8 to 99:1 er
2.1:1 up to 49:1 γ/β regioselectivity

Best yields with electron-rich arylboronic acids
Best regioselectivity with electron-poor arylboronic acid

Sigman et al., *J. Am. Chem. Soc.* **2013**, 135, 6830-6833

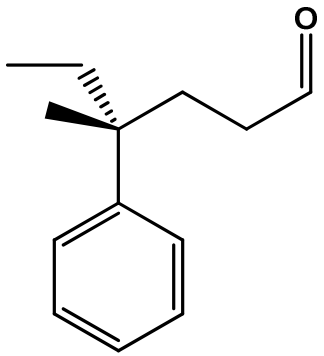
This work



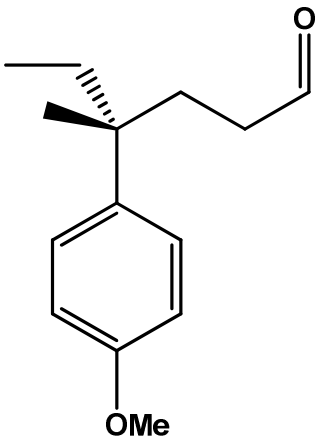


Sigman et al., *Nature* **2014**, 508, 340-344

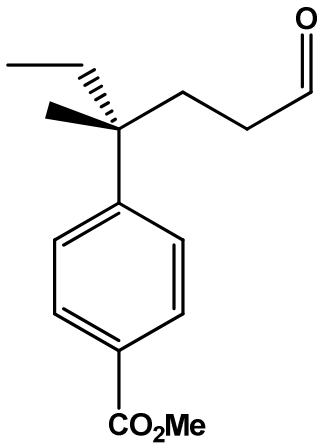
Selected examples



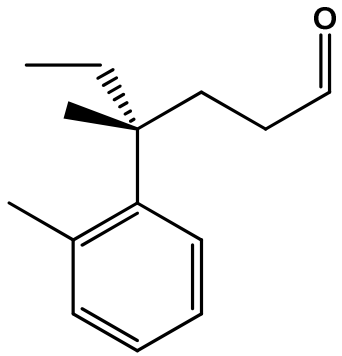
81%
98:2 e.r.



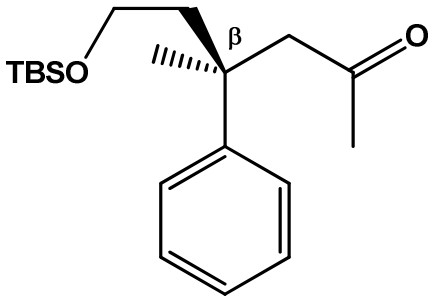
77%
97:3 e.r.



55%
99:1 e.r.

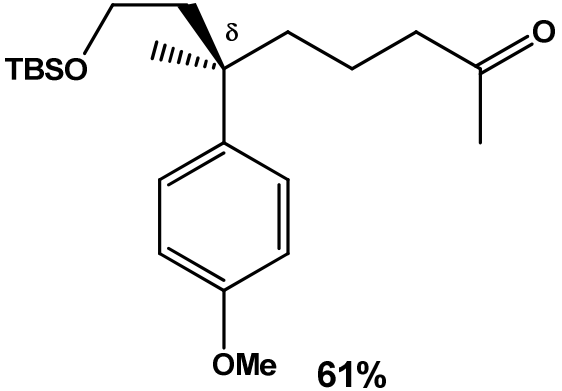


70%
99:1 e.r.



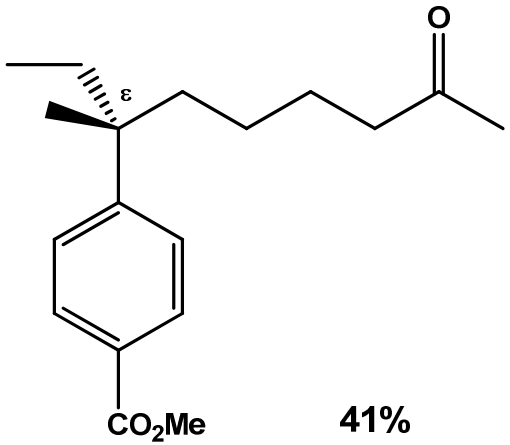
75%
96:4 e.r.

(from (E)-alkene)



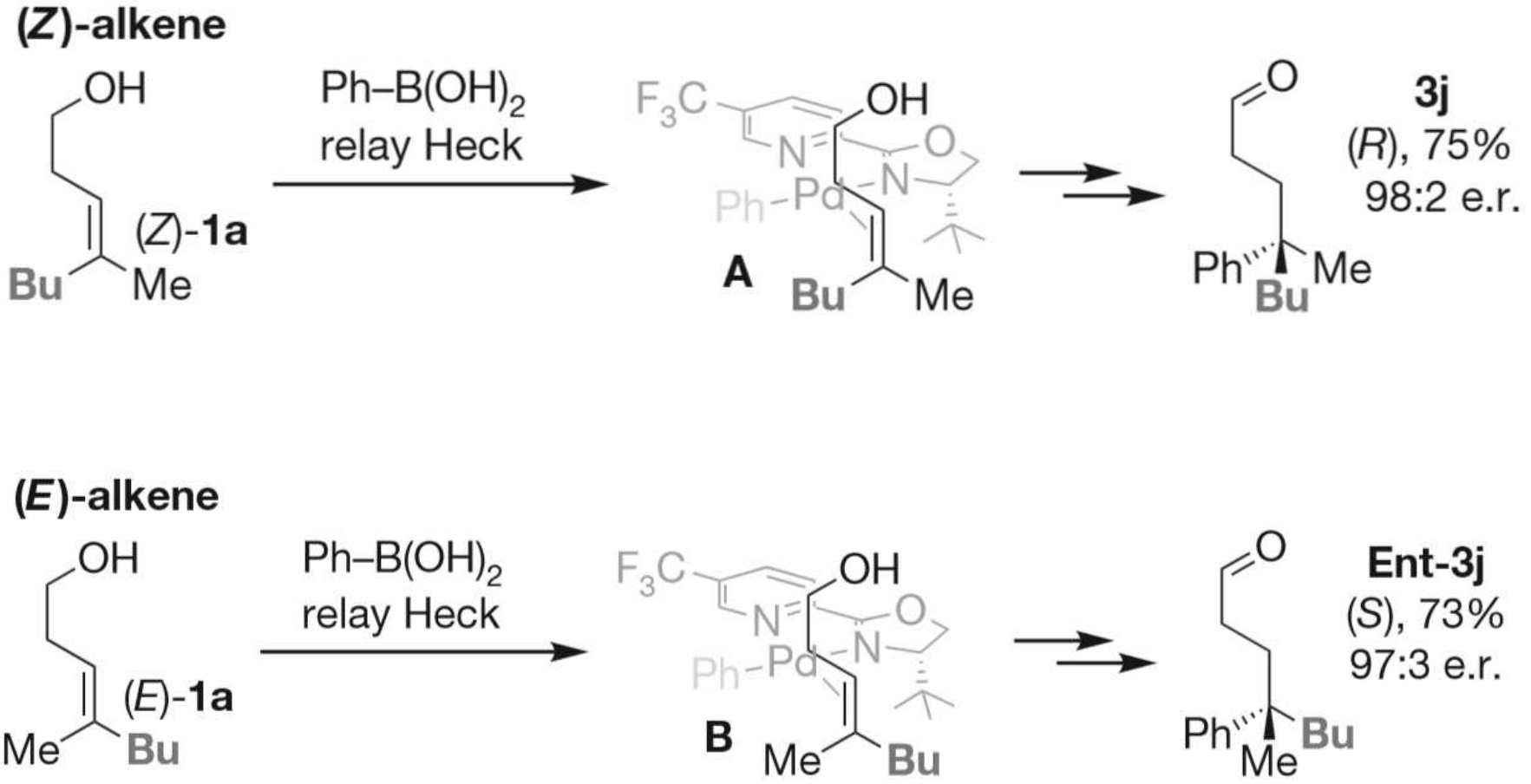
61%
93:7 e.r.

(from (E)-alkene)

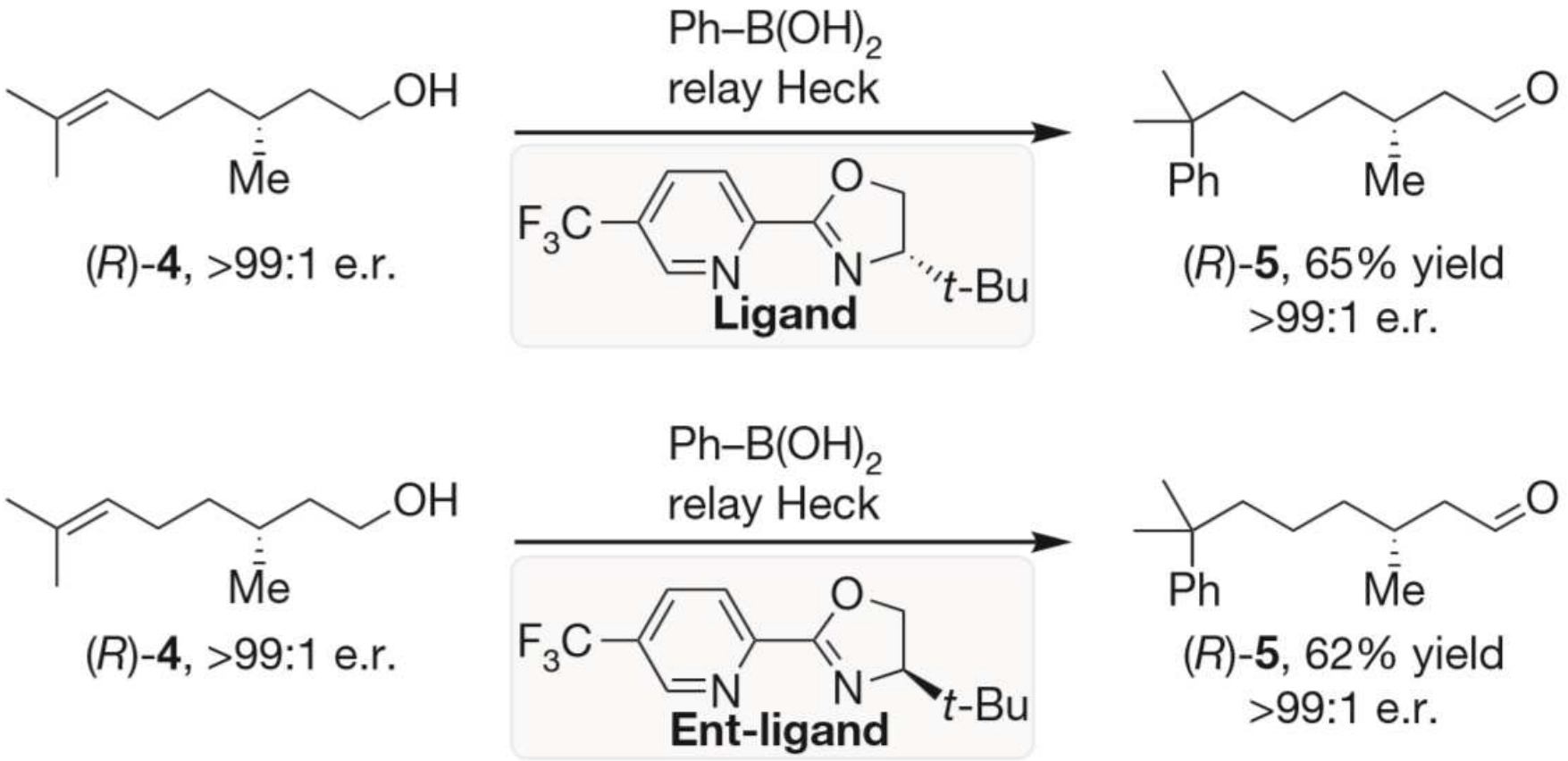


41%
99:1 e.r.

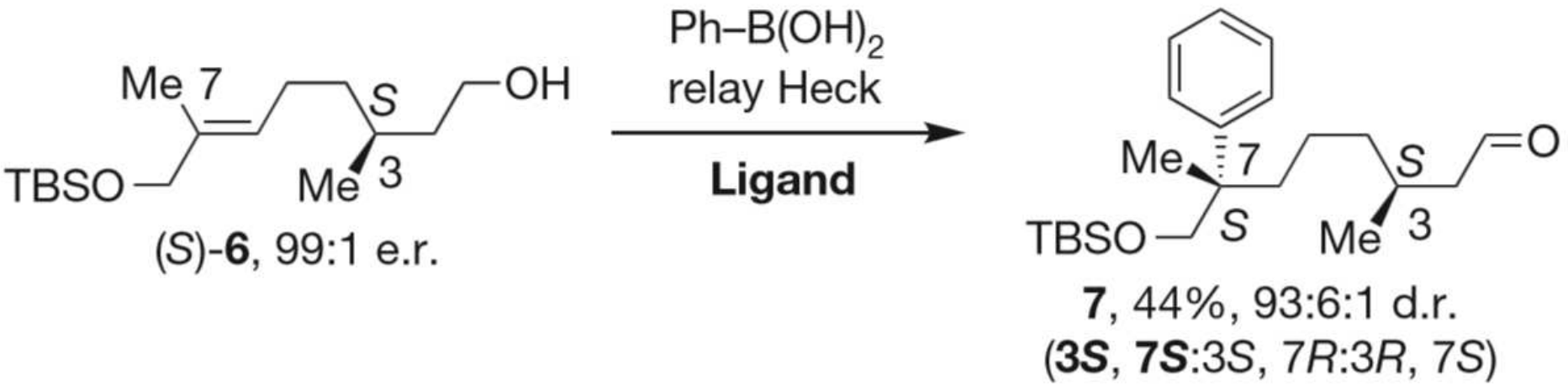
Stereospecificity



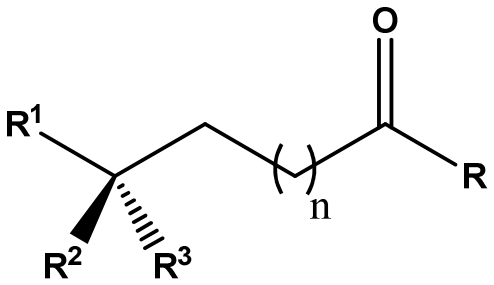
Preservation of a preinstalled stereocentre



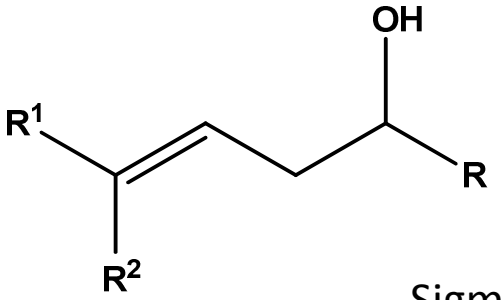
Control of two remote chiral centres



Conclusion



- Highly regio/stereoselective addition
- Stereospecific reaction
- High modularity (intermolecular on acyclic substrates)
- Readily available arylboronic acids and alkenes



- Compatibility with other functionnalities
- Scope limited to aryles

Sigman et al., *Nature* **2014**, 508, 340-344