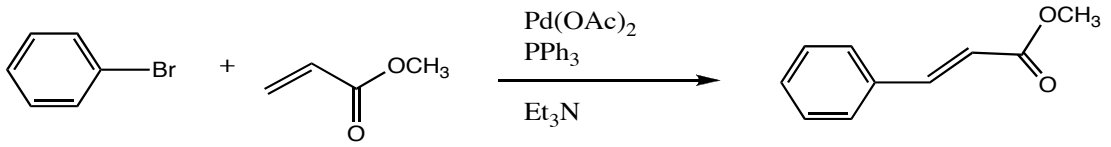
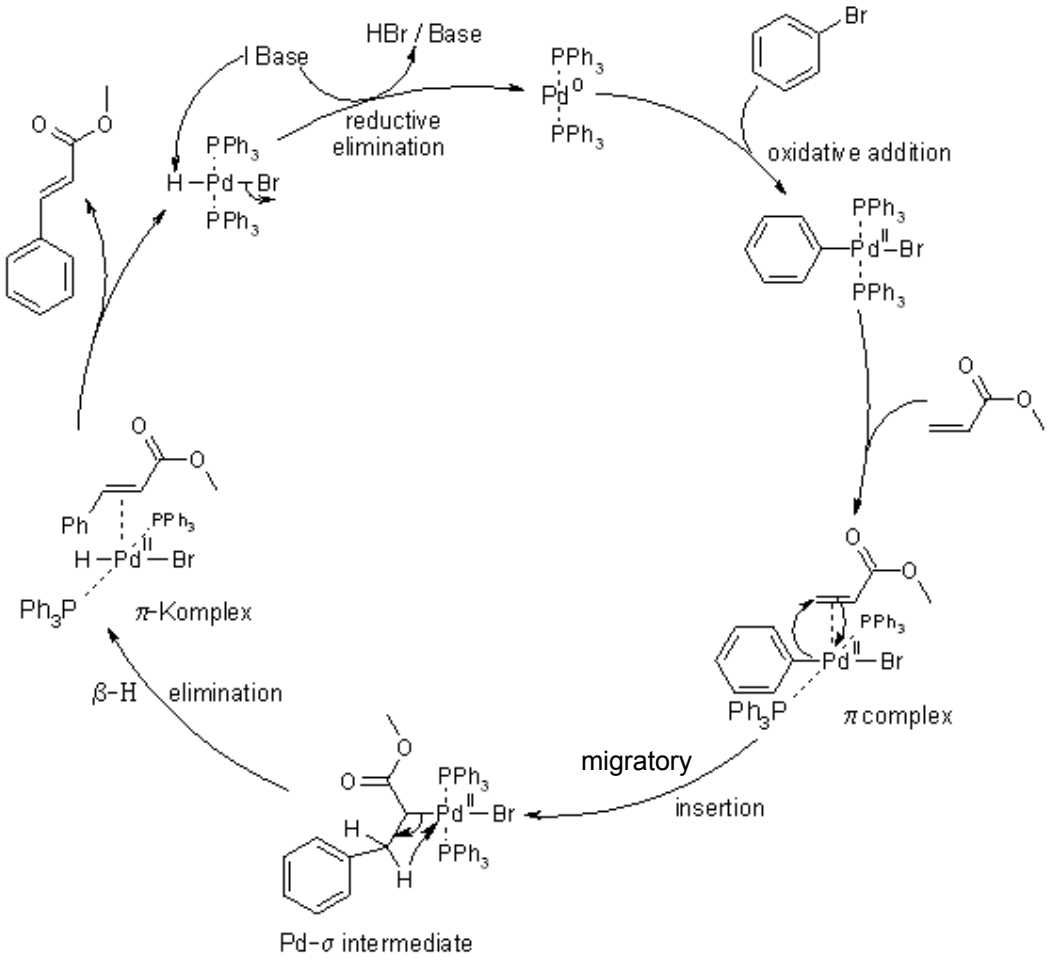
The Heck Reaction

The Heck reaction is a palladium-catalyzed C-C coupling between aryl halides or vinyl halides (or triflates) and Activated alkenes in the presence of base.

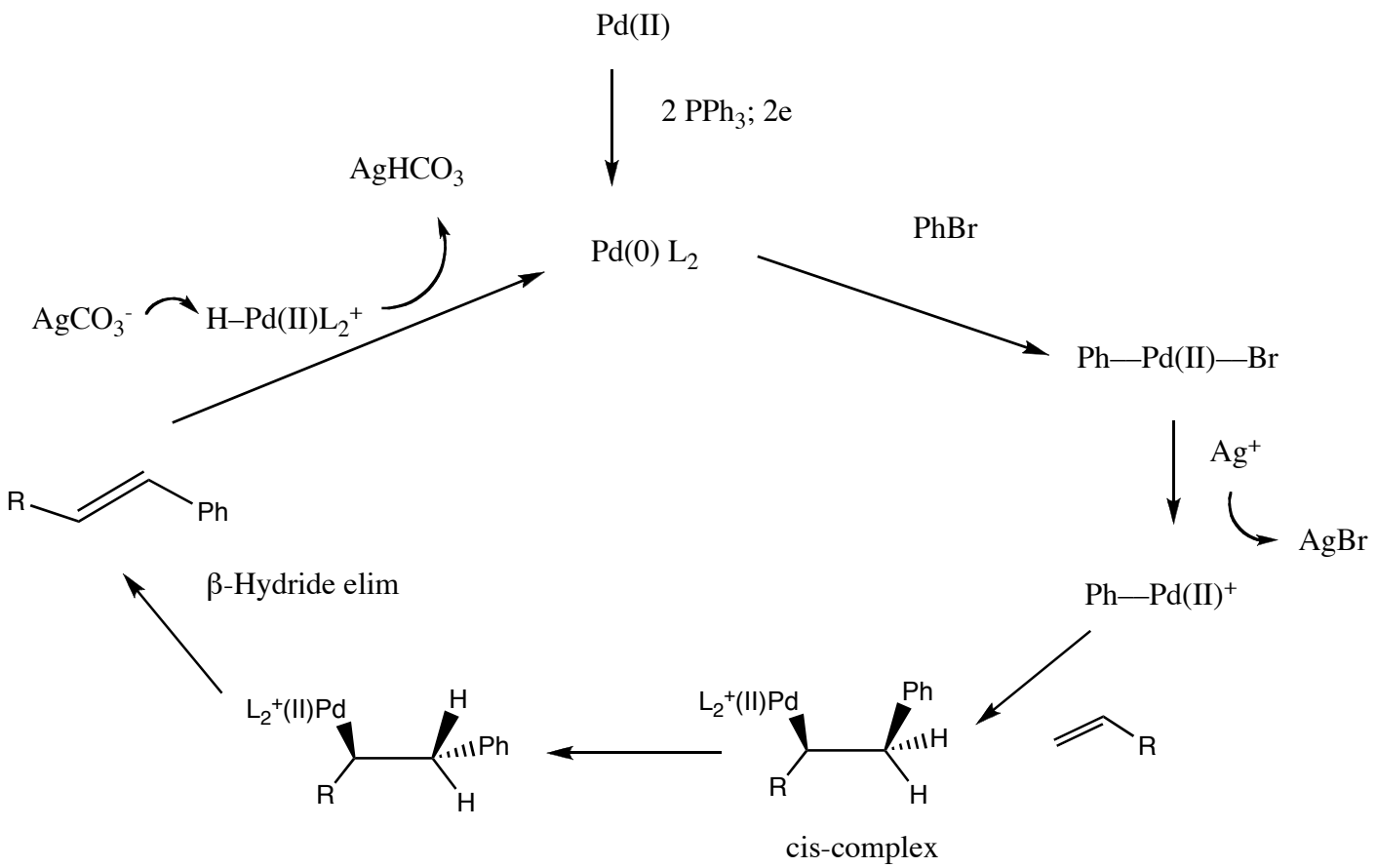
Example:



Mechanism:

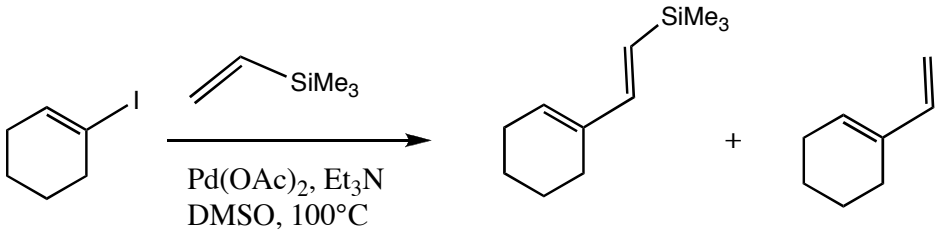


The Cationic Heck Reaction: Use of Silver Salts



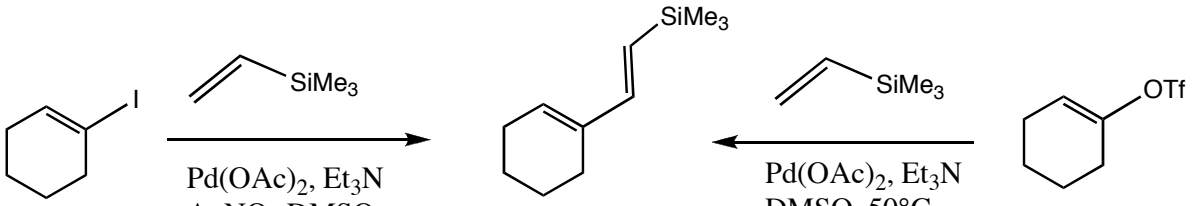
cationic palladium complex is more reactive toward pi-complexation of alkenes!

Examples



12% 57%

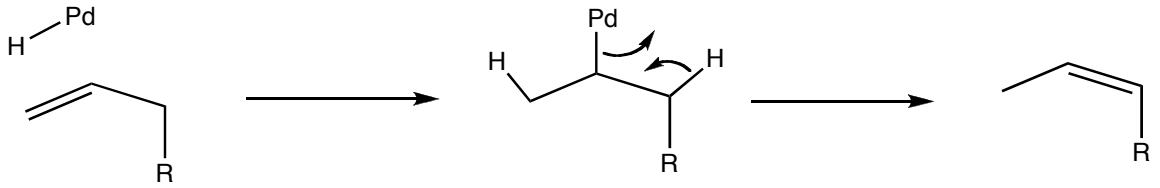
desilylation at elevated temperatures!



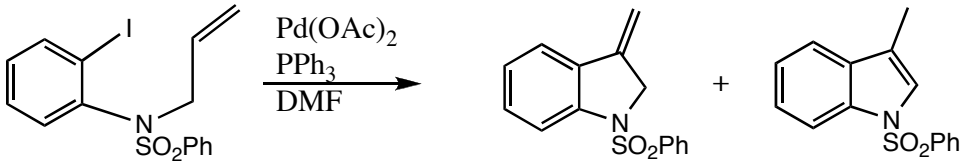
64%

JOC **1988**, 4909

Reversible β-hydride elimination leads to alkene isomerization:



The use of silver slats minimizes alkene isomerization:



A: desired **B**: by-product

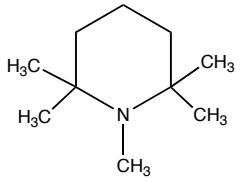
JOC **1987**, 4133

Ag_2CO_3 eq.	Yield **A**
1	35
2	80

Lifetime of $HPd(II)L_2^+$ is short in presence of base

Details of Heck Reaction

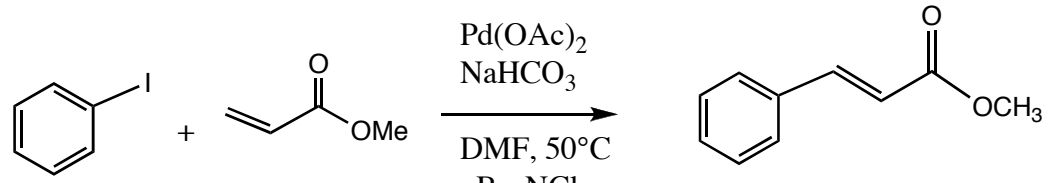
Catalysts: $Pd_2(dba)_3$, $Pd(OAc)_a$
Solvents: toluene, THF, DMF

Soluble bases: Et_3N, 

PMP

Insoluble bases: K_2CO_3, Ag_2CO_3

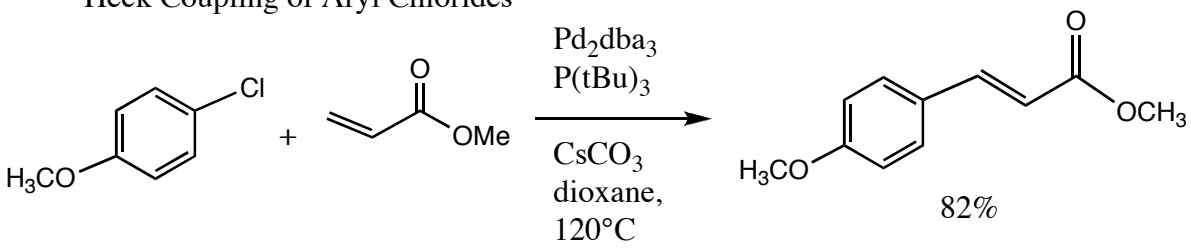
Phase Transfer Catalysis: stabilization of Pd complexes by halide ions; allows lower reaction temperatures



99% with nBu_4NCl
2% without nBu_4NCl

Tet. **1996**, 10113

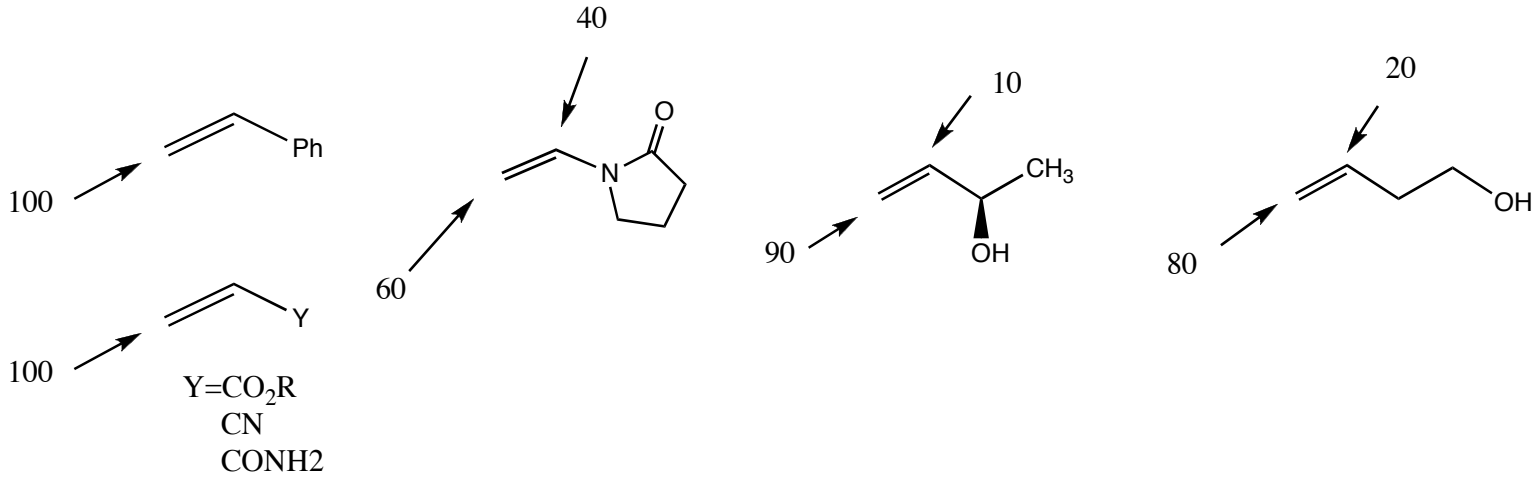
Heck Coupling of Aryl Chlorides



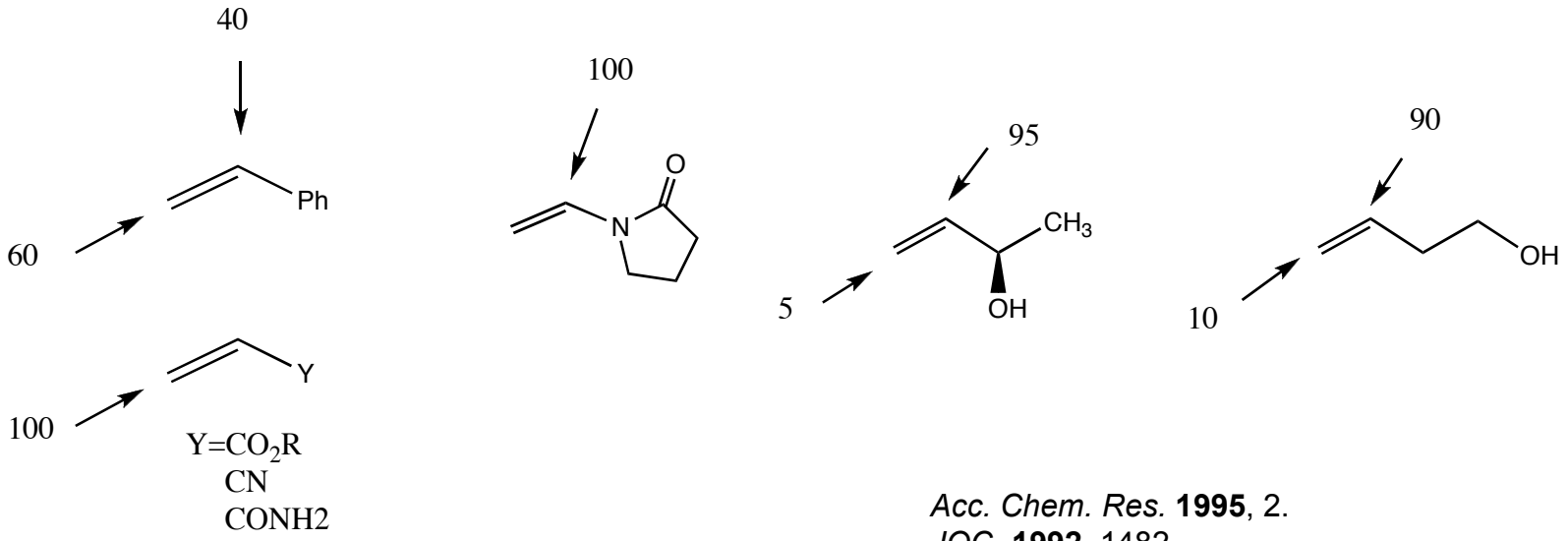
JOC, **1999**, 10

Regiochemistry of Heck Reactions

Neutral Pd complexes: regiochemistry governed by sterics

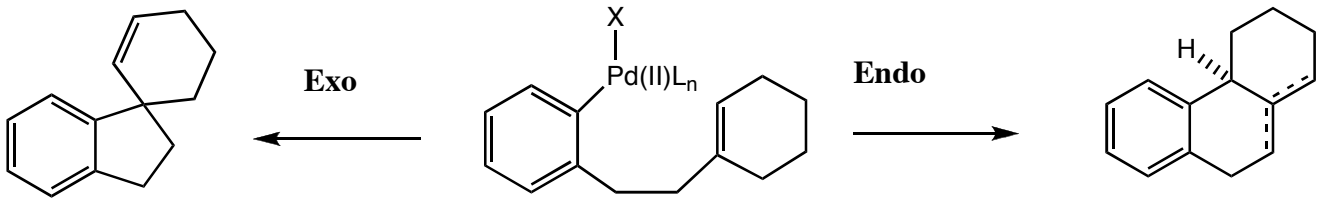


Cationic Pd complexes: regiochemistry governed by electronics; addition to the site of least electron density

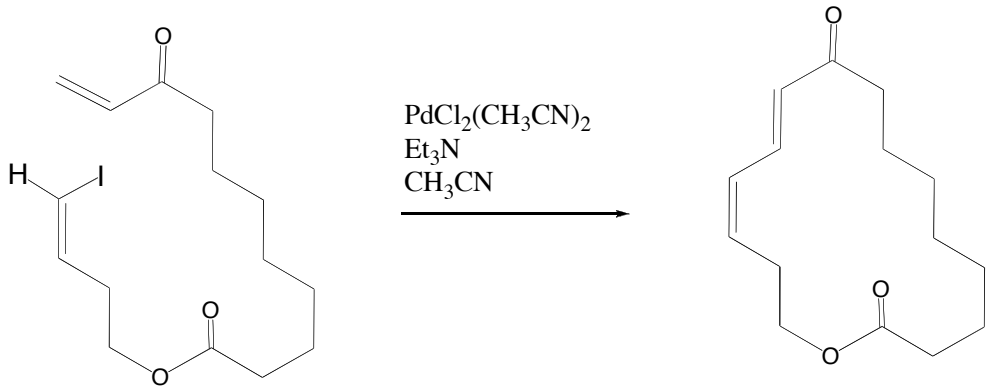


Acc. Chem. Res. **1995**, 2.
JOC, **1992**, 1482.

Ring Closure Using the Heck : Endo vs. Exo

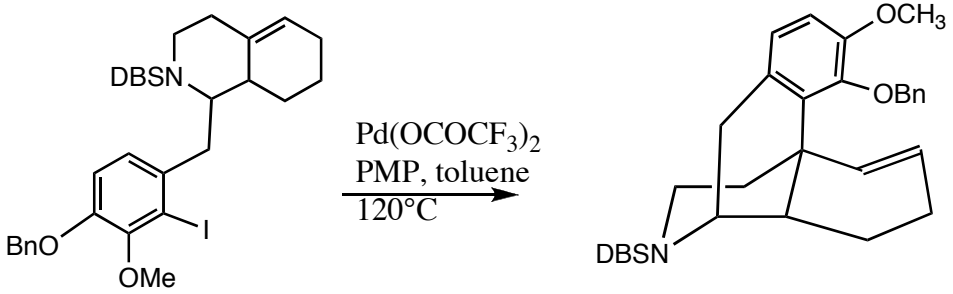


Useful for macrocyclizations:



Tet, **1981**. 4035.

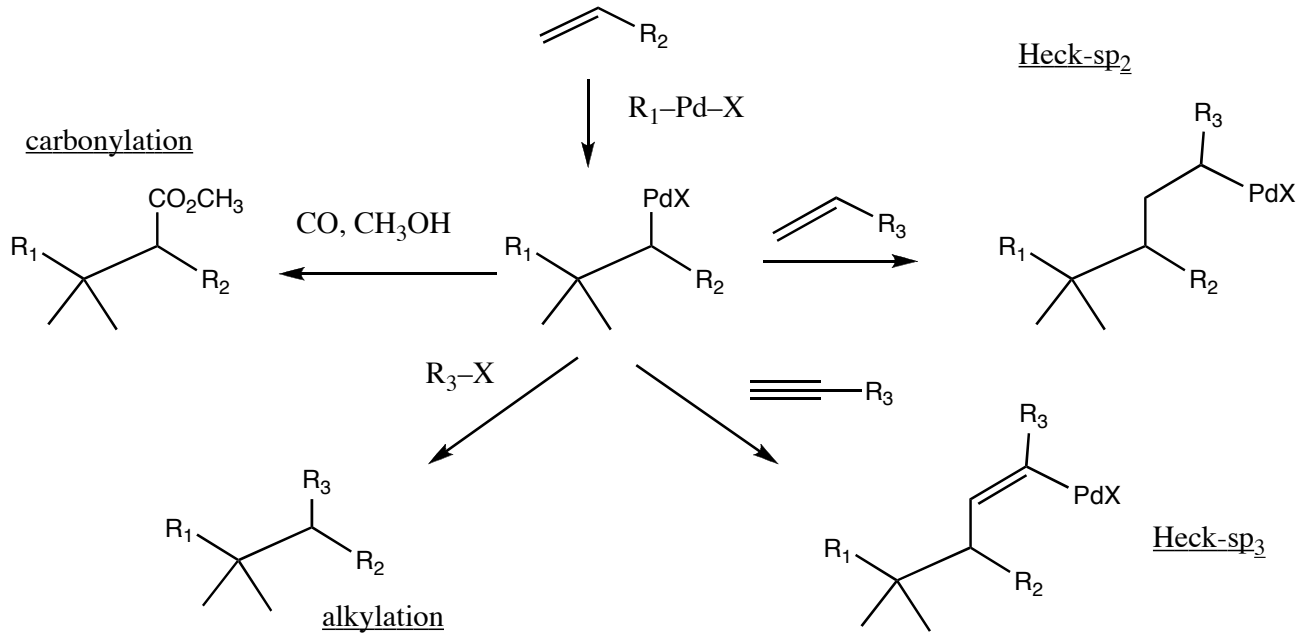
Five, Six, and Seven-membered ring closure gives predominantly exo products:



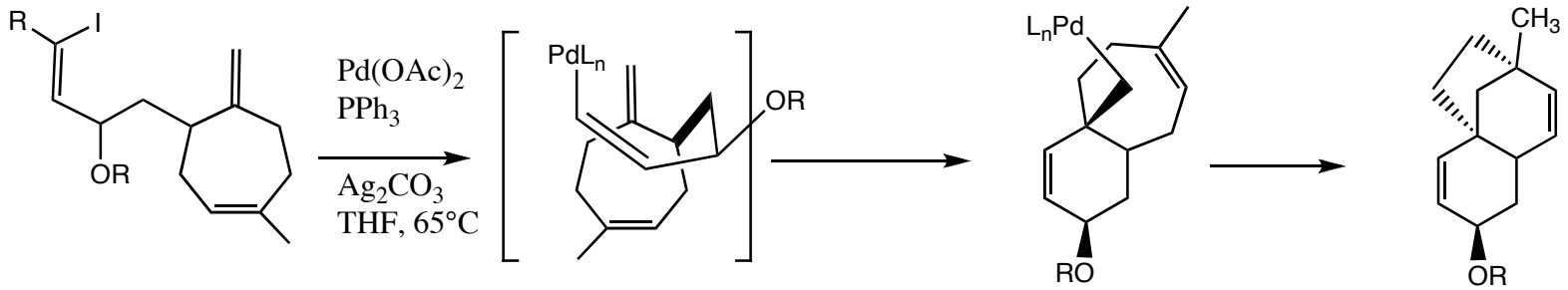
JACS, **1993**, 11028.

Tandem Reactions

When β-hydride elimination is not possible, additional reaction pathways may ensue:

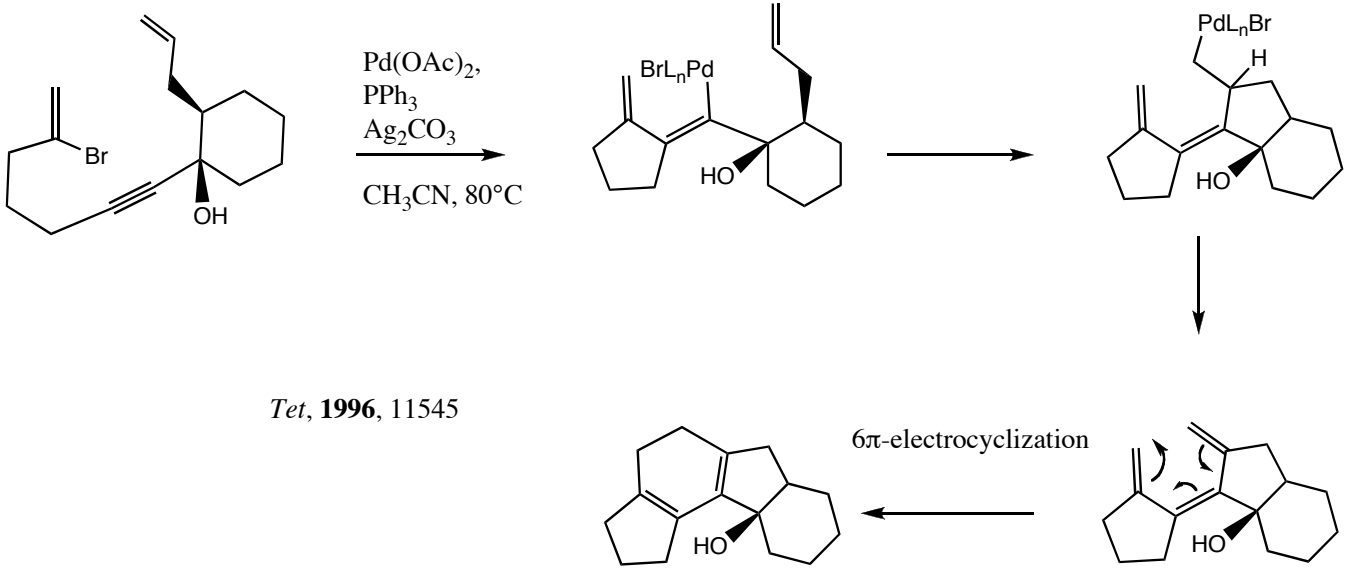


Tandem Heck Reactions:



JOC, **1993**, 5304
JACS, **1999**, 5467.

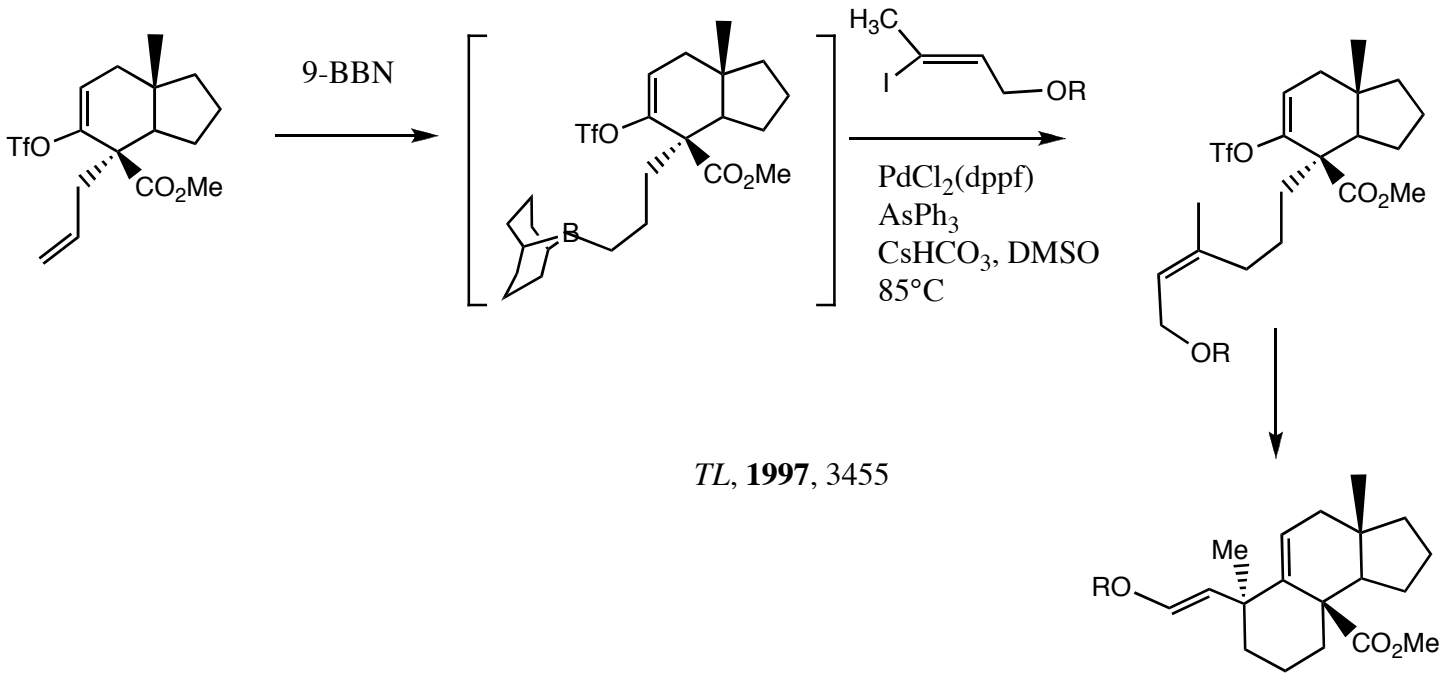
Tandem Heck Reactions, continued:



Tet, **1996**, 11545

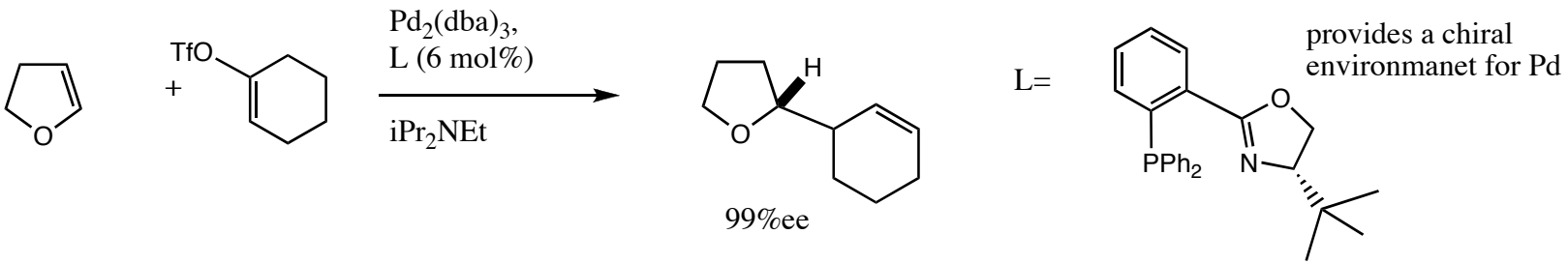
85%

Tandem Suzuki-Heck:

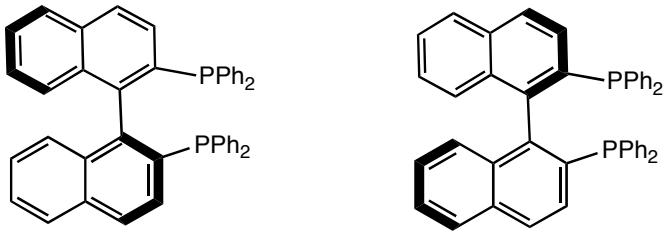


TL, **1997**, 3455

Asymmetric Heck Reactions

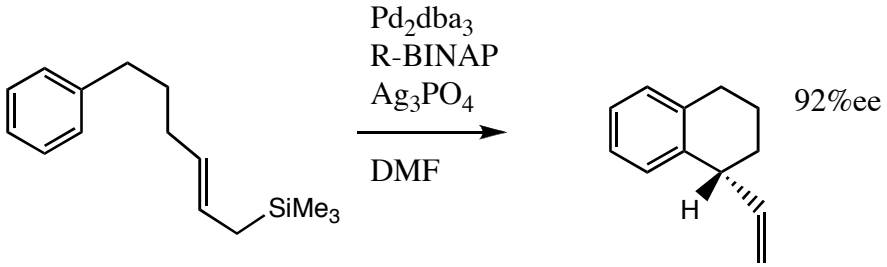


Chiral BINAP ligands for Pd:

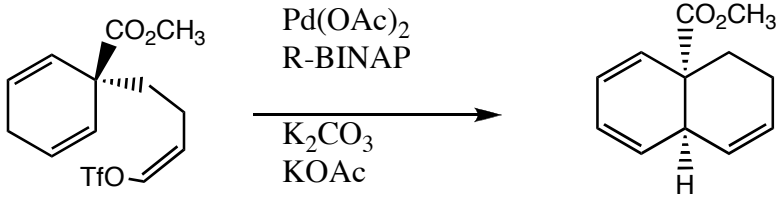


S-BINAP

R-BINAP



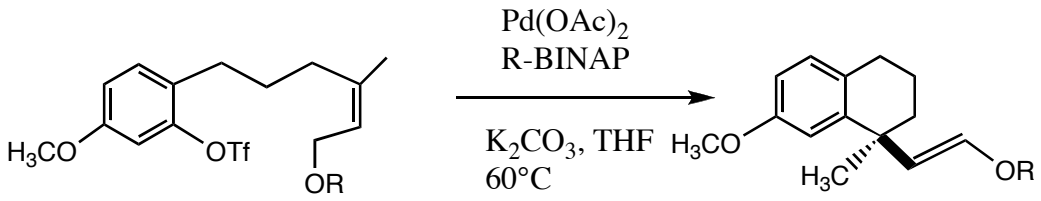
Synlett, **1995**, 597



86%ee

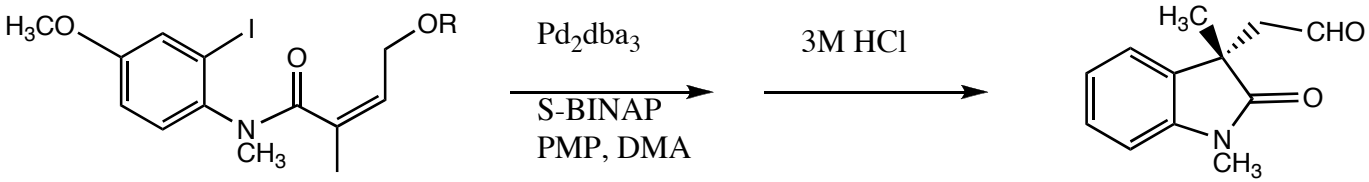
JACS, **1994**, 11737

Asymmetric Heck Reactions, Continued



JACS, **1993**, 8477

90%ee



95% ee

JACS, **1998**, 6500