

Club Phosphorus

No “Guys” Allowed

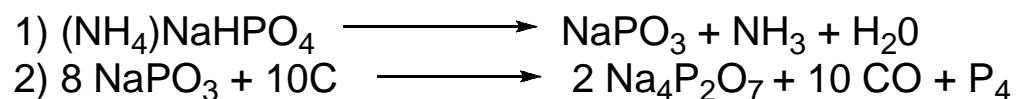
Mark Mans

Group Meeting

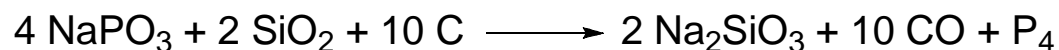
December 5, 2007

Isolation

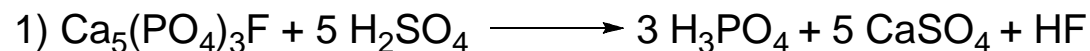
-Herring Brand discovered phosphorus in 1669 - allowed urine to putrify, boiled it down to a paste, finally heated to high temps and collected the vapors. The white waxy substance that resulted would glow in the dark. Thus phosphorus = "light bearer"



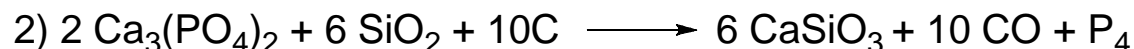
-Robert Boyle later improved upon this synthesis by adding sand to the urine



-Today it's a little more fun to isolate



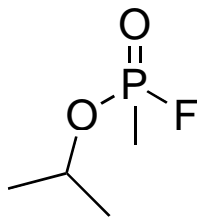
or



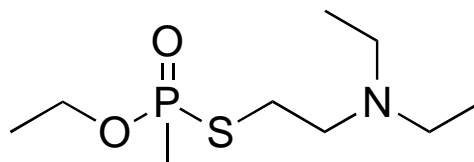
Applications

- Most useful as phosphoric acid for fertilizer
- White phosphorus was a main ingredient in matches from 1840s to 1910. However, its use led to “phossy jaw” where the jawbone rots away and can actually glow green
- Calcium phosphate used in production of fine china
- Red phosphorus used for matchbook strikers, flares, cap gun caps, street methamphetamine
- Dopant for N-type semiconductors
- ^{32}P and ^{33}P used as radioactive tracers

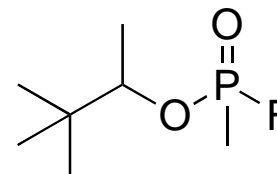
-Nerve Gases



Sarin



VX

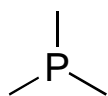


Soman

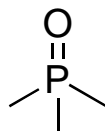
- And of course.....organic chemistry!

Fun Facts about Phosphorus

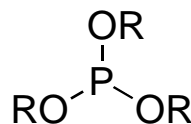
- Several allotropes : white (aka yellow), red, and black. White most reactive
- Common oxidation states: -3, -1, 1, 3, 5
- Fun with names:



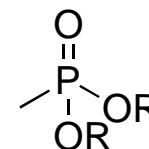
Phosphine



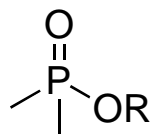
Phosphine Oxide



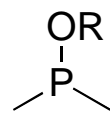
Phosphite



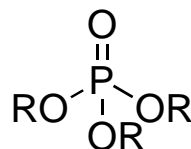
Phosphonate



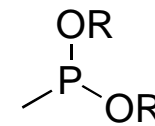
Phosphinate



Phosphinite



Phosphate



Phosphonite

- Phosphines have a higher barrier to inversion (~30 kcal/mol) than amines (~5 kcal/mol) = phosphines can display optical isomerism

Phosphine Organocatalysis

- In the 1960s, 70, and 80s, phosphines behaving as nucleophilic catalysts reported sporadically but field grown significantly in the last ten years
- Ph₃P used traditionally (low cost, air stable), but outperformed by the more air-sensitive trialkylphosphines when greater nucleophilicity is required (at least partially due to cone angle) .
- Due to high barrier of inversion, can have chiral phosphine catalysts
- Phosphines are less basic, more nucleophilic, and softer than amines
- Typical reactions include

Rauhut-Currier and Morita-Bayless-Hillman reactions

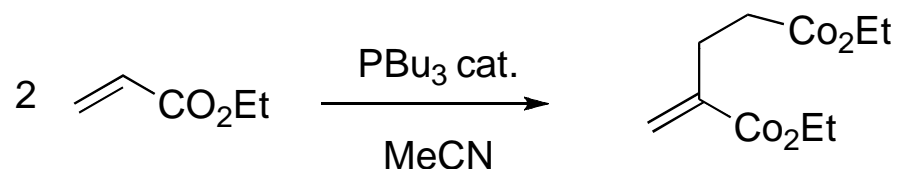
Michael additions to activated alkenes and alkynes

Cycloadditions

Alcohol acylation and kinetic resolution

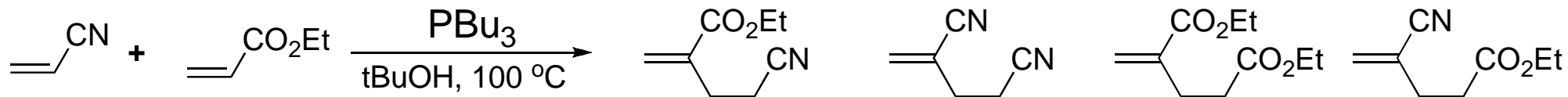
Rauhut-Currier Reaction

- Dimerization of activated alkenes reported in 1963
- Intermolecular version gave yields ~50%



M. Rauhut, H. Currier, *U.S. Patent 3074999*, **1963**

- 1970, McClure reports first cross-coupling reaction between ethyl acrylate and acrylonitrile



1:1 ratio of reactants

yields calculated based on 21% conversion
of both reactants

48%

25%

22%

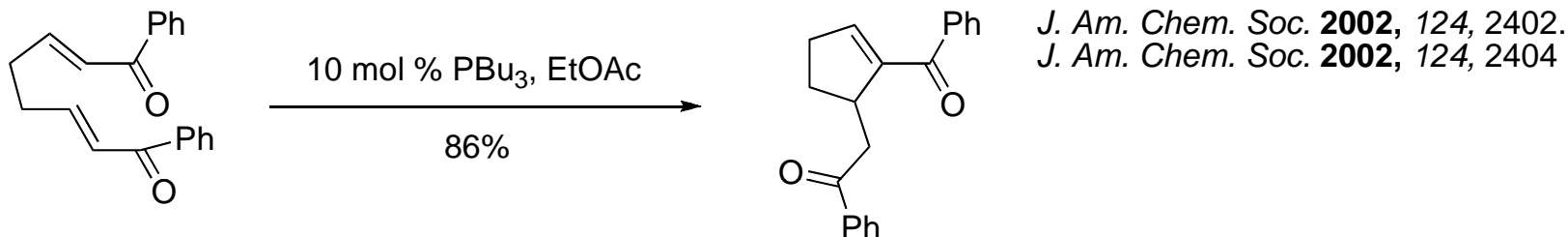
0%

J. Org. Chem. **1970**, 35, 3045.

- Lack of ability to control cross-coupling remained a problem

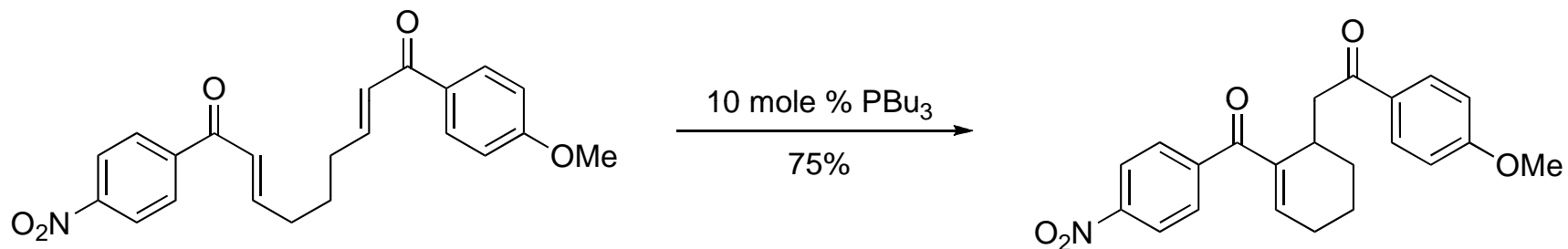
Intramolecular Version

- Roush and Krische revisited the reaction using an intramolecular version that gave good results

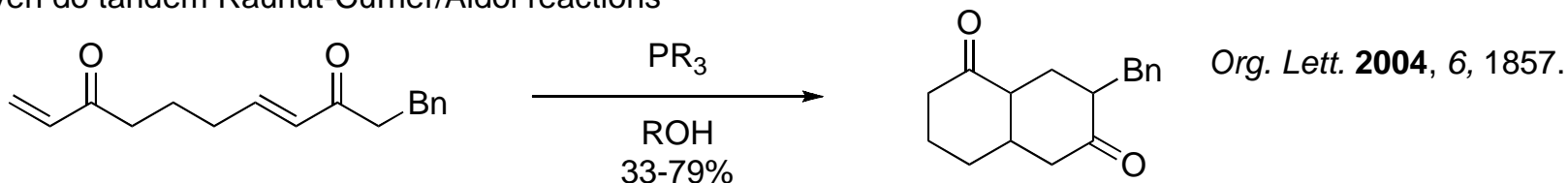


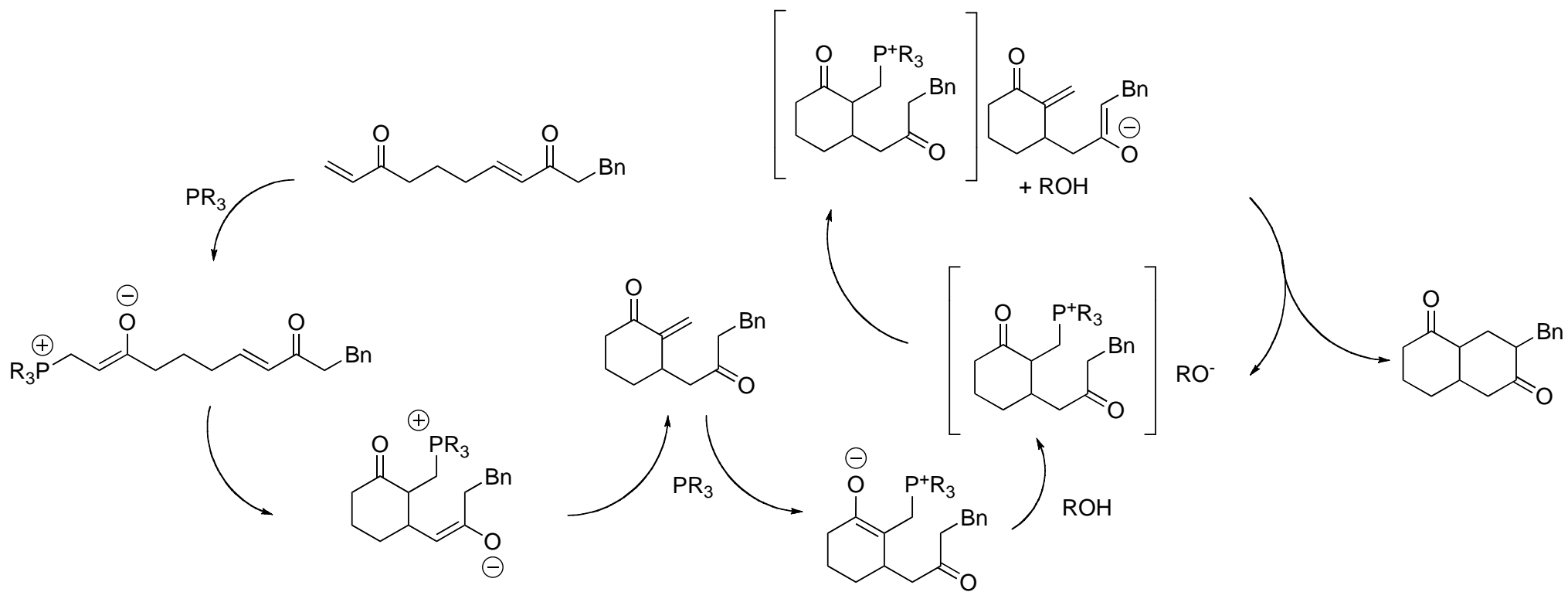
-phosphines behaved better than DABCO, DBU, and DMAP b/c activated alkenes = soft electrophile and phosphine = softer nuc than amines

-unsymmetric / electronically differentiated bis(enones) undergo chemoselective addition of the more electrophilic alkene onto the less electrophilic alkene as shown below



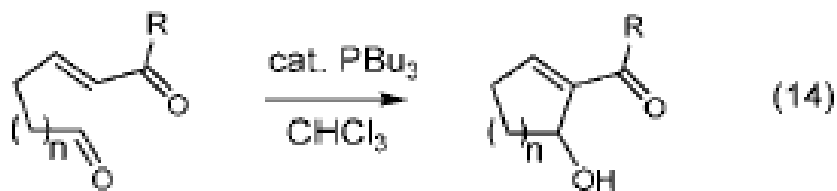
- Can even do tandem Rauhut-Currier/Aldol reactions



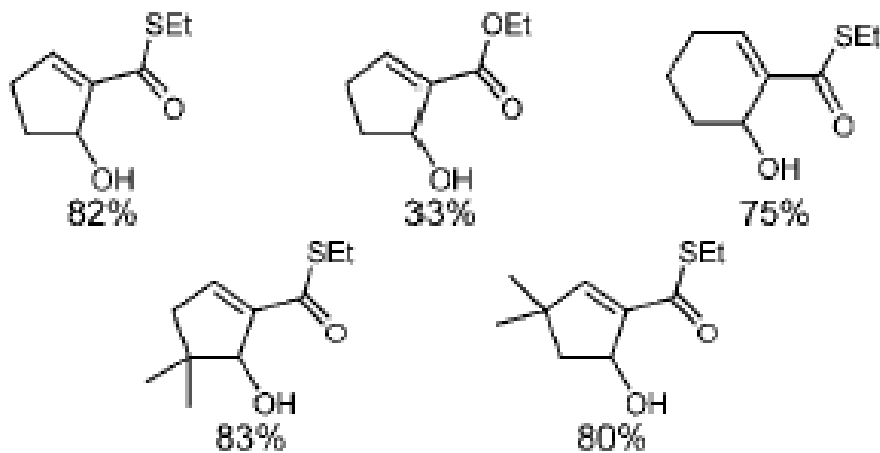
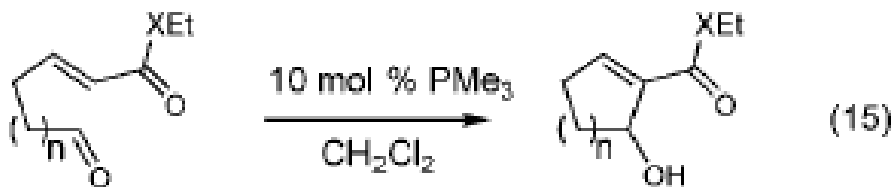


Morita-Baylis-Hillman Reactions

- Initially Morita used phosphines to couple an activated alkene with an aldehyde while Baylis and Hillman used tertiary amines (DABCO)
- Phosphines have come back to life and in some cases perform better than amines



n	R	mol % PBu ₃	time	yield (%)
1	Ph	20	17 h	20
	OEt	40	28 d	40
2	Ph	20	2 h	75
	OEt	20	24 h	50



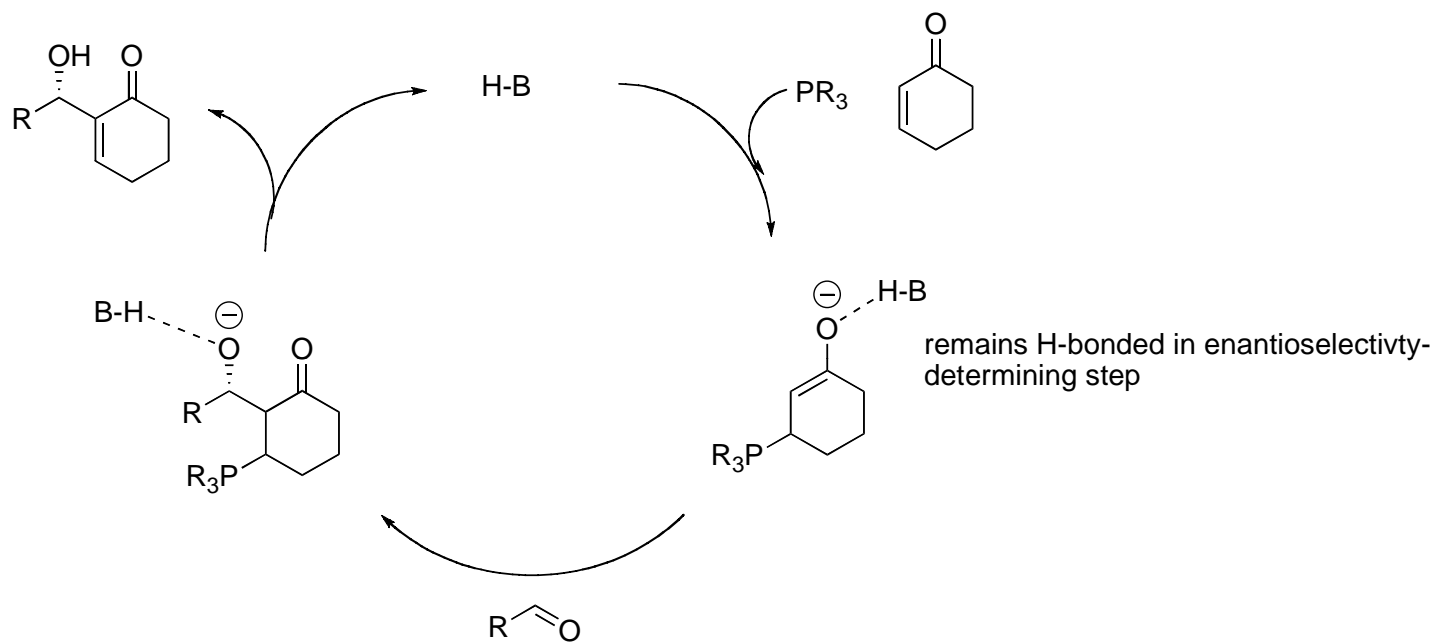
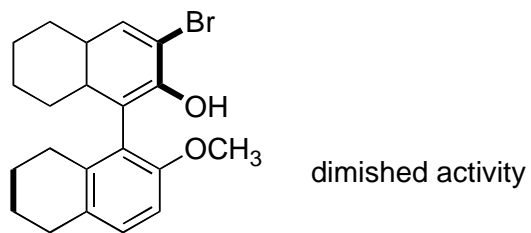
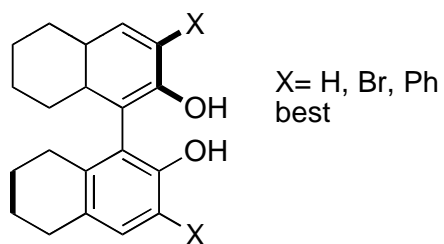
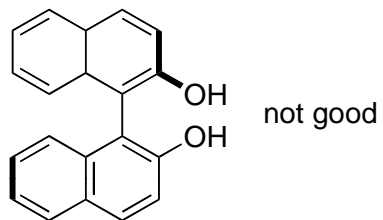
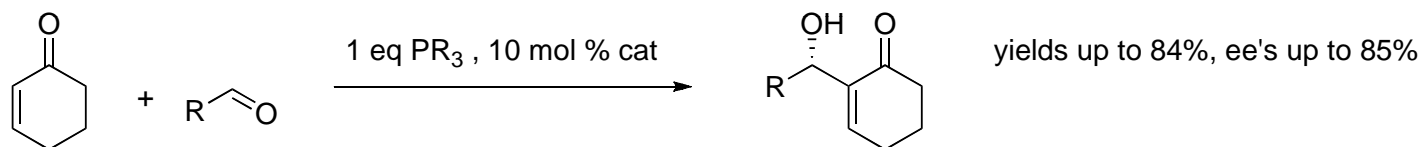
Slow cyclization of unsaturated esters, but thiol esters cyclize nicely

Tet. Lett. **1999**, 40, 3279

Catalytic Asymmetric M-B-H Reactions

- Most of the focus to date has been on coupling aldehydes and acrylates using sultam auxiliaries, quinidine-derived chiral nucleophilic amines, or chiral lanthanide lewis acids
- Schaus found that mild acids (phenol, BINOL) speed up M-B-H reactions of cyclic enones

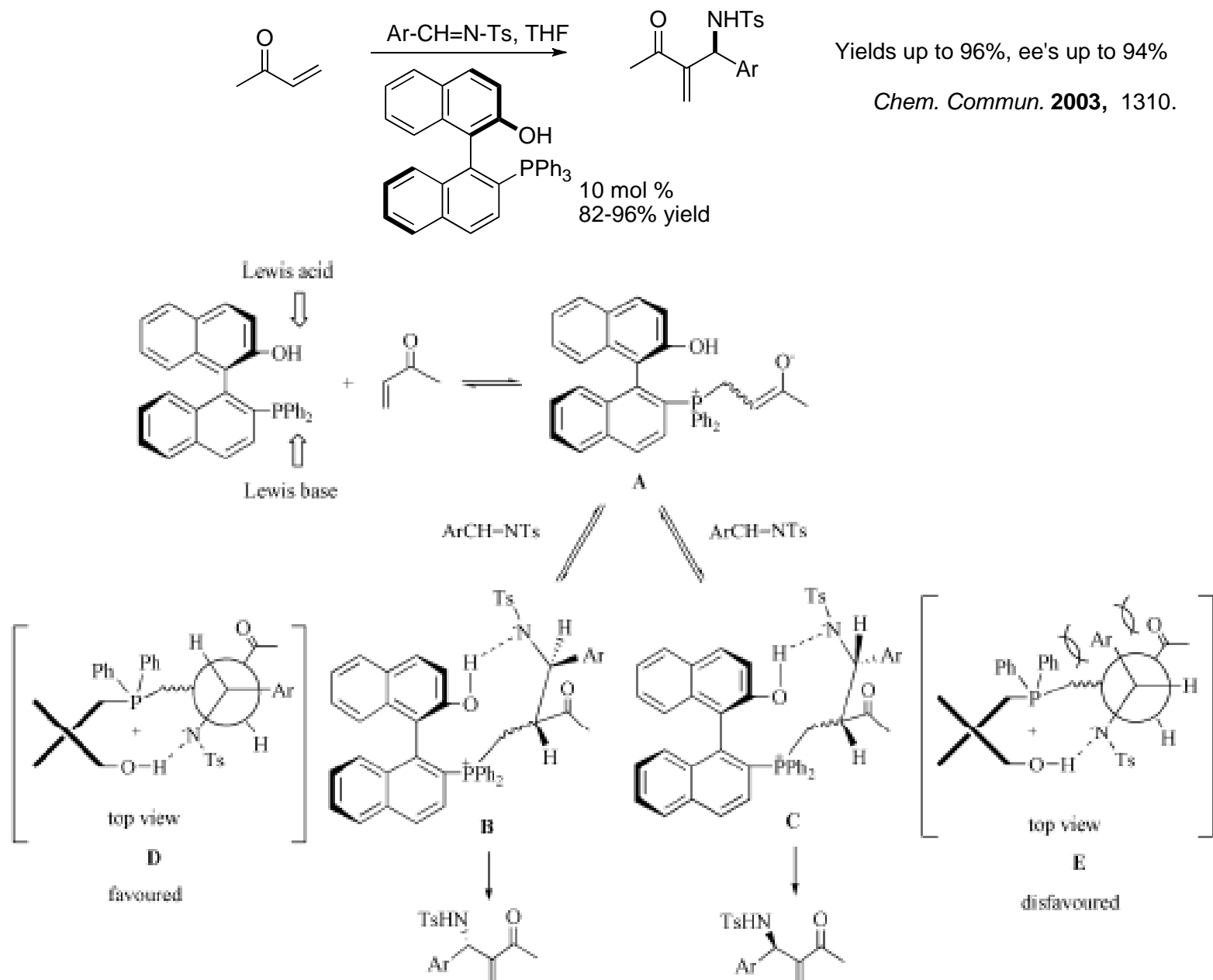
Catalysts:



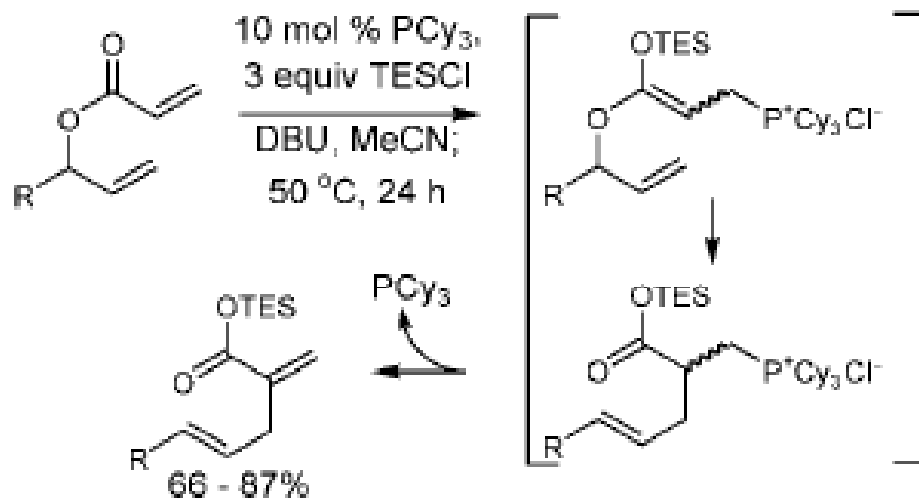
J. Am. Chem. Soc. **2003**, *125*, 12094.

Catalytic Asymmetric M-B-H Part II

- Shi and co-workers replaced aldehydes with the more reactive N-arylidine-4-methylbenzenesulfonamides with good results



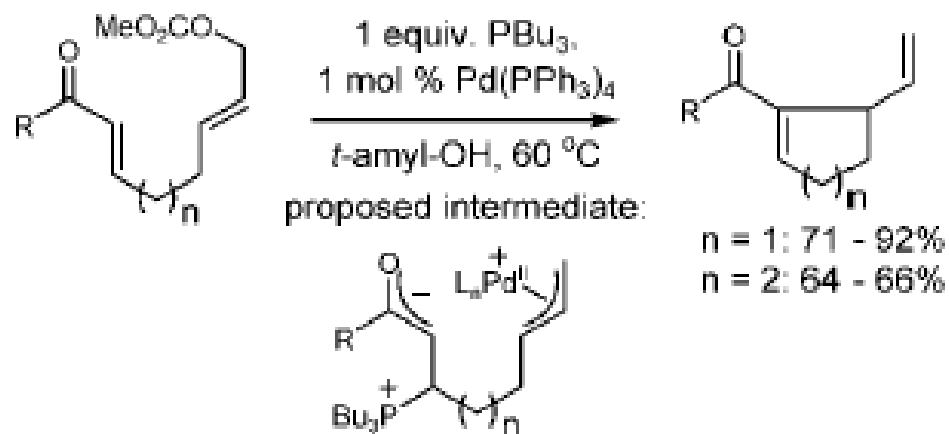
Related Reactions



phosphonium silyl ketene acetal undergoes Ireland-Claisen rearrangement
J. Org. Chem. **1993**, *58*, 299.

Combination of the M-B-H reaction and a Tsuji-Trost for intramolecular allylation

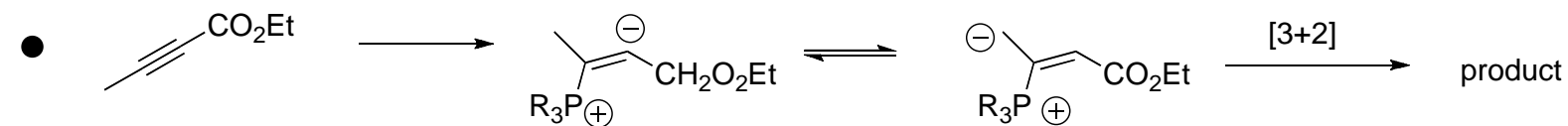
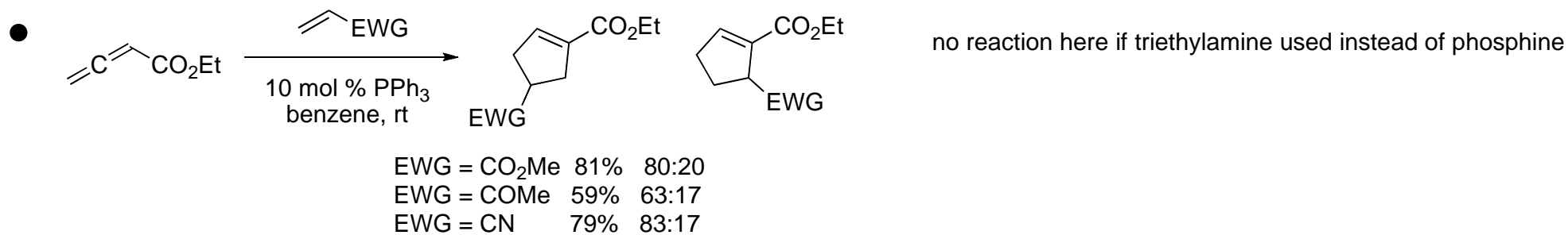
J. Am. Chem. Soc. **2003**, *125*, 7758.



Cycloadditions

- Phosphines used as nucleophilic catalysts in lots of [3+2] cycloadditions.

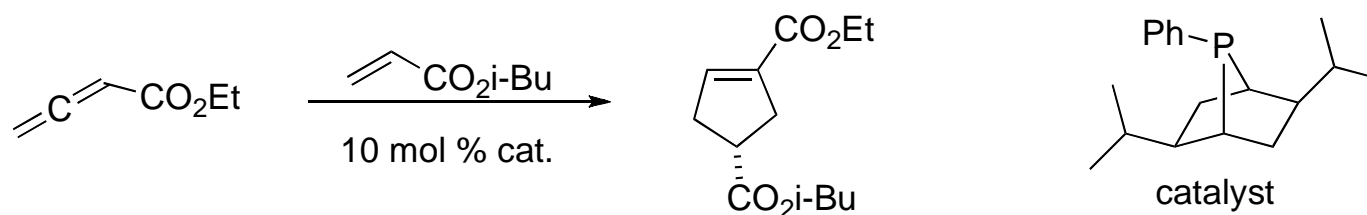
- Allows for facile construction of cyclopentenes using 2-butynoates or 2,3-butadienoates (commercially available) as simple 3 carbon moiety in the [3+2] reaction



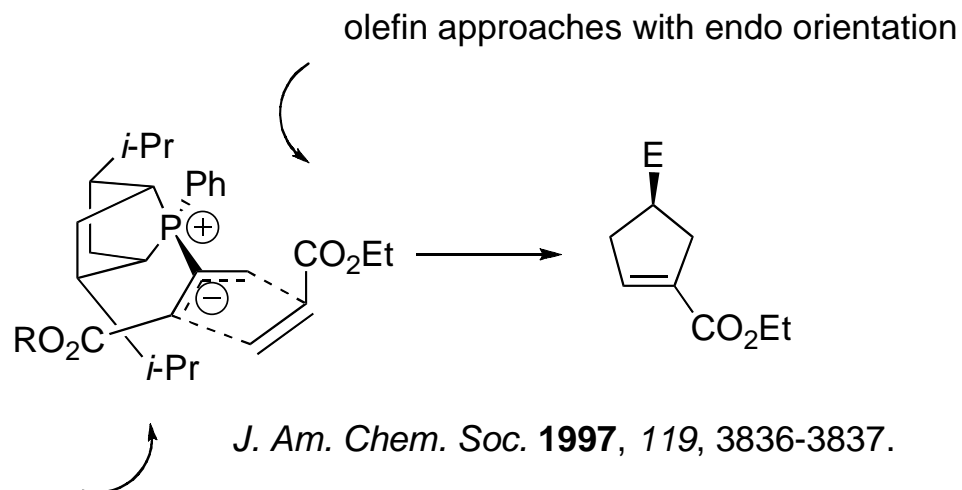
J. Org. Chem. **1995**, *60*, 2906.

Asymmetric [3+2] Variants

- Asymmetric variants developed based on chiral phosphines

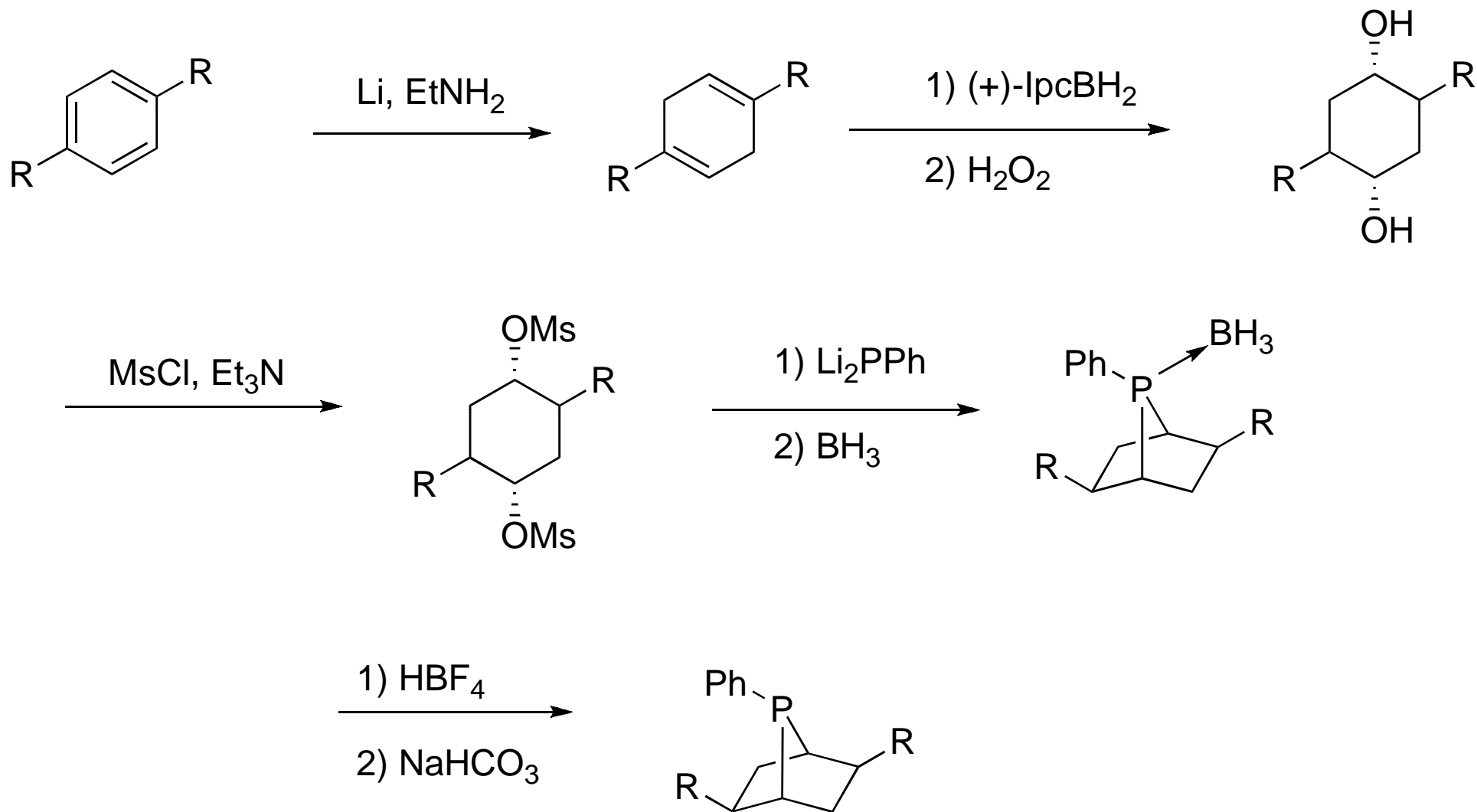


- Stereochem of starting E or Z olefin preserved in the product.....authors conclude a concerted mechanism.



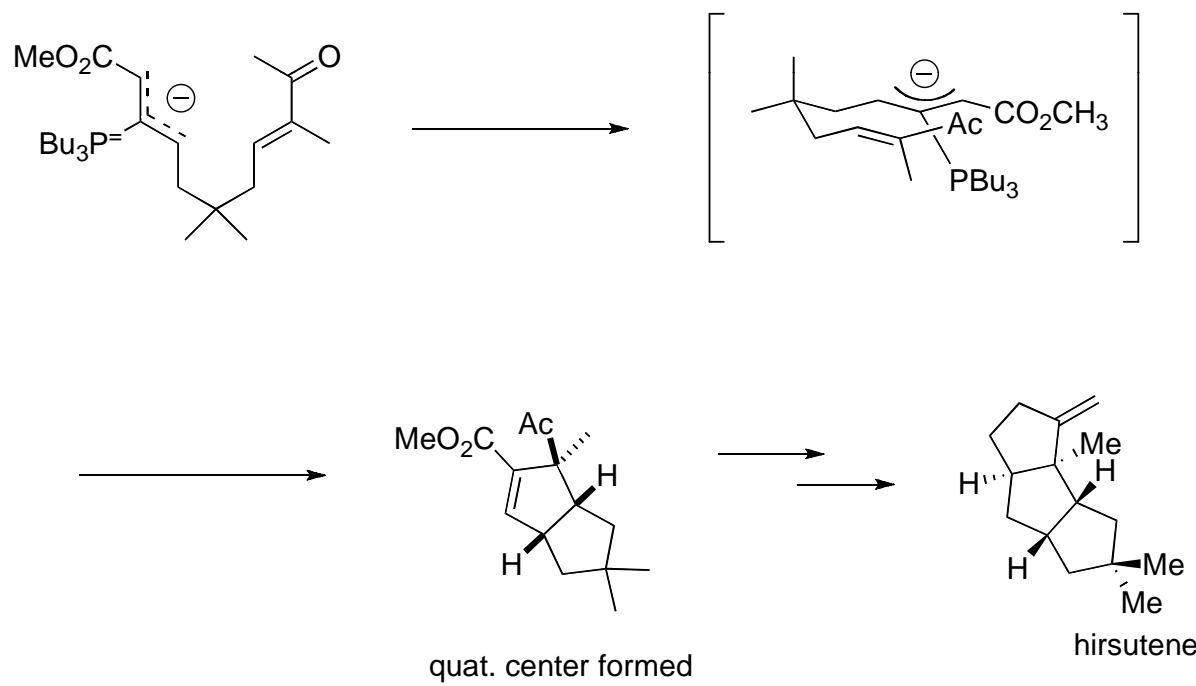
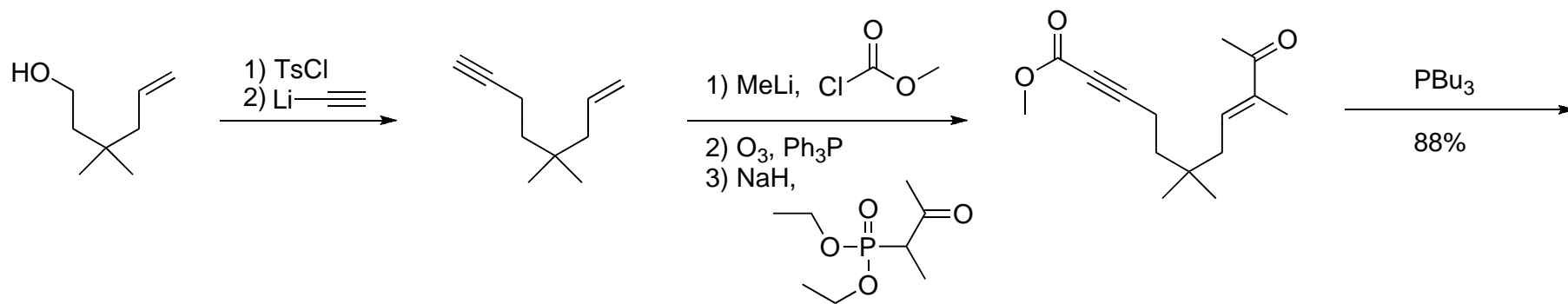
R group (isopropyl) blocks bottom face

Catalyst Synthesis

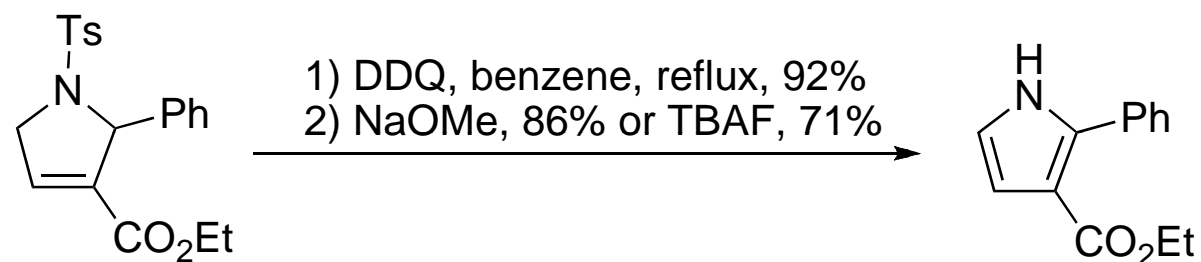
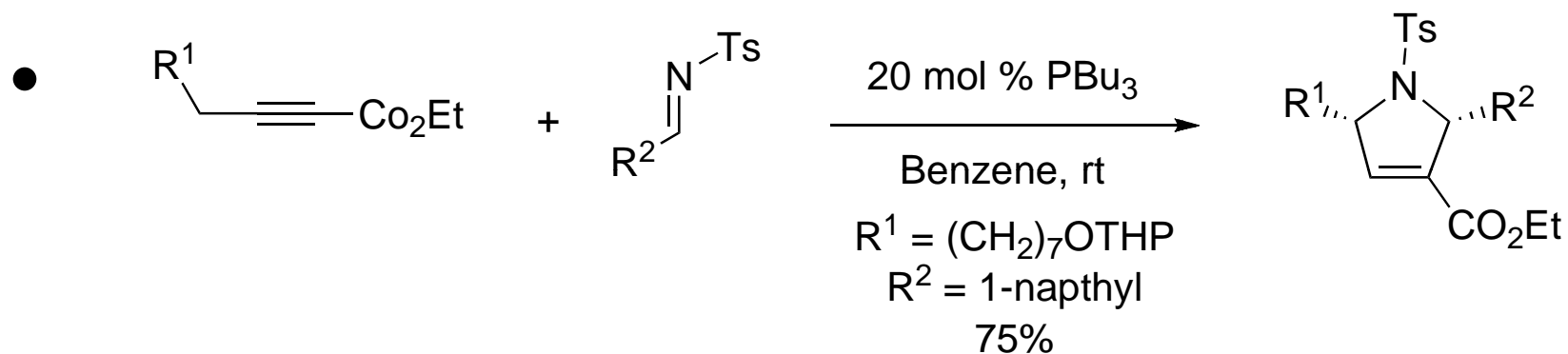


J. Am. Chem. Soc. **1997**, *119*, 3836.

Methodology in the Synthesis of Hirsutene

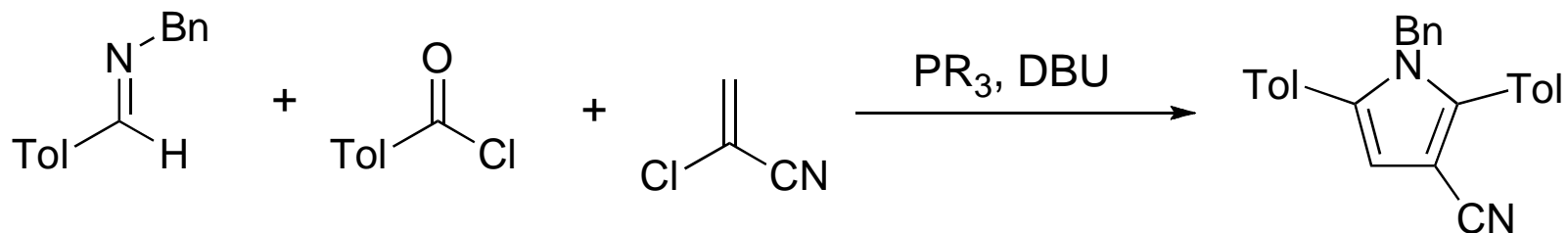


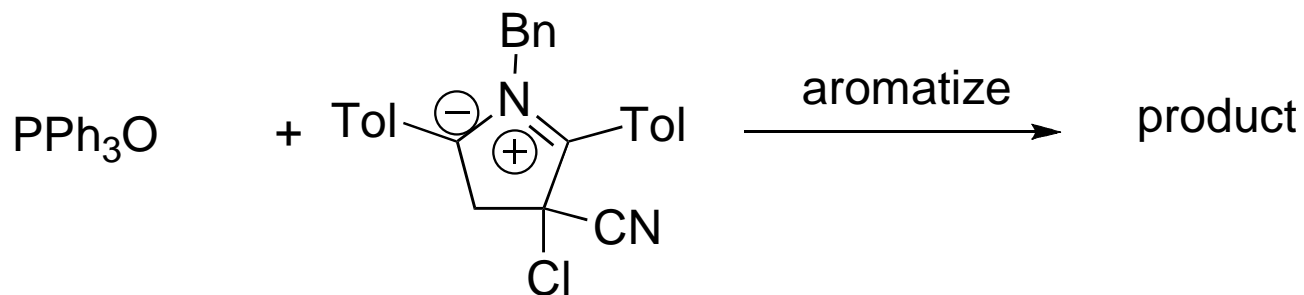
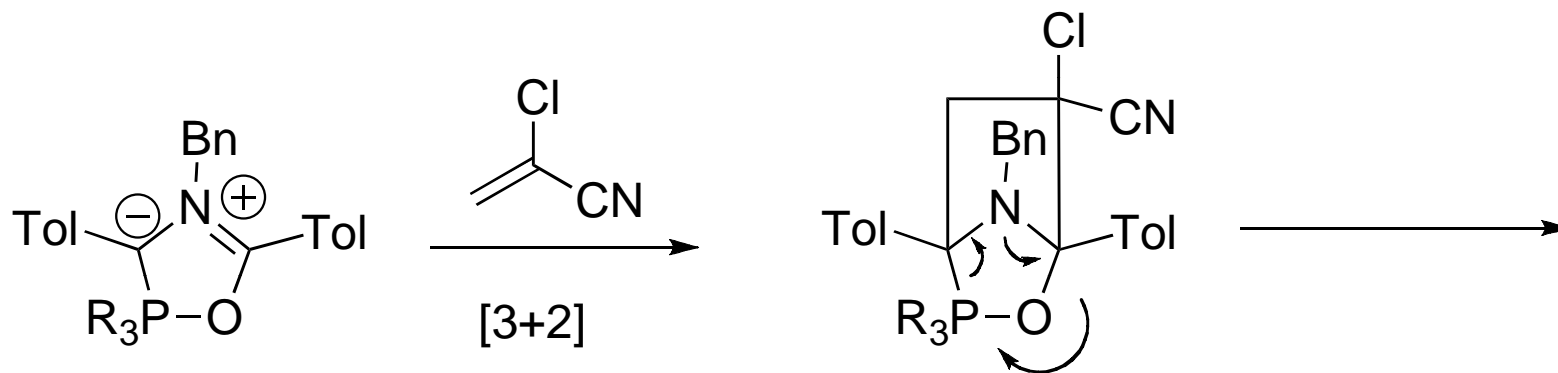
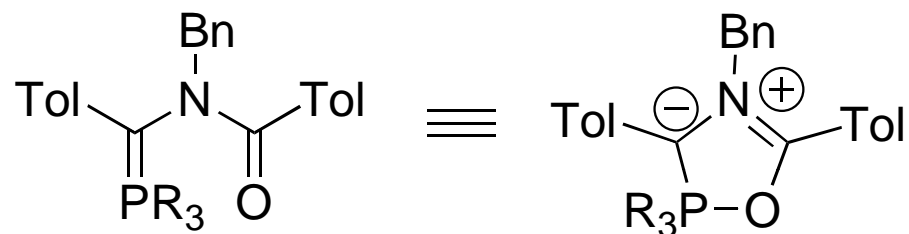
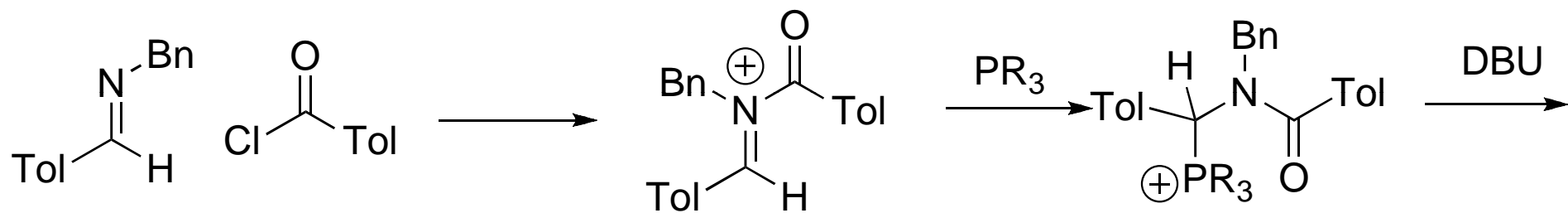
Pyrrole Synthesis via Cycloaddition



Tet. Lett. **1999**, 40, 549.

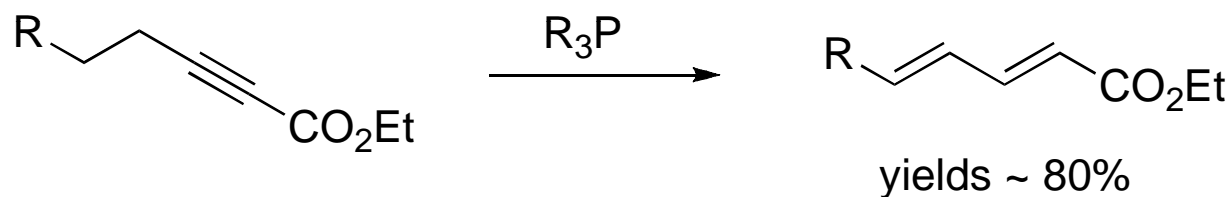
- Recent Literature *J. Am. Chem. Soc.* **2007**, 129, 12366-12367.



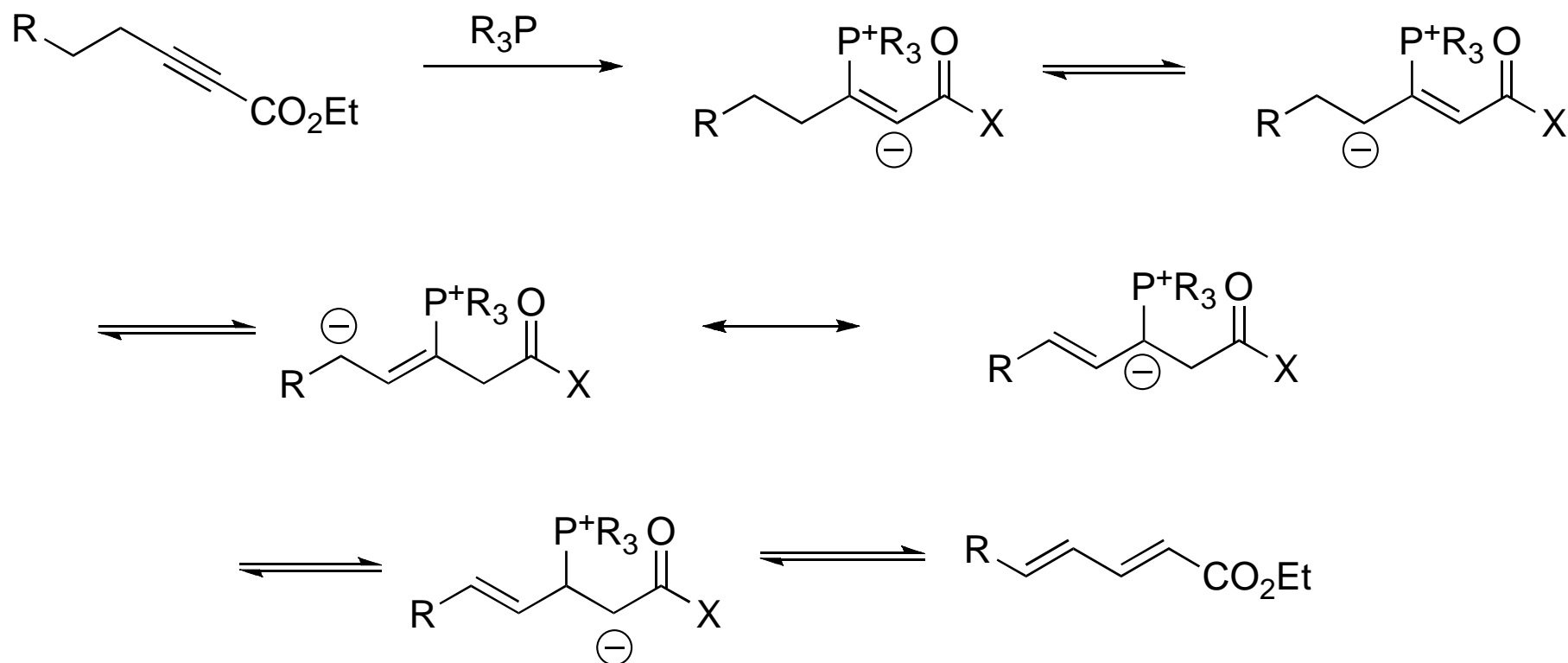


Additions to Alkynes

- Triaryl Phosphines isomerize ynones to dienones. Originally performed with $\text{RuH}_2(\text{PPh}_3)_4$, later realized that only the phosphines doing any of the work.



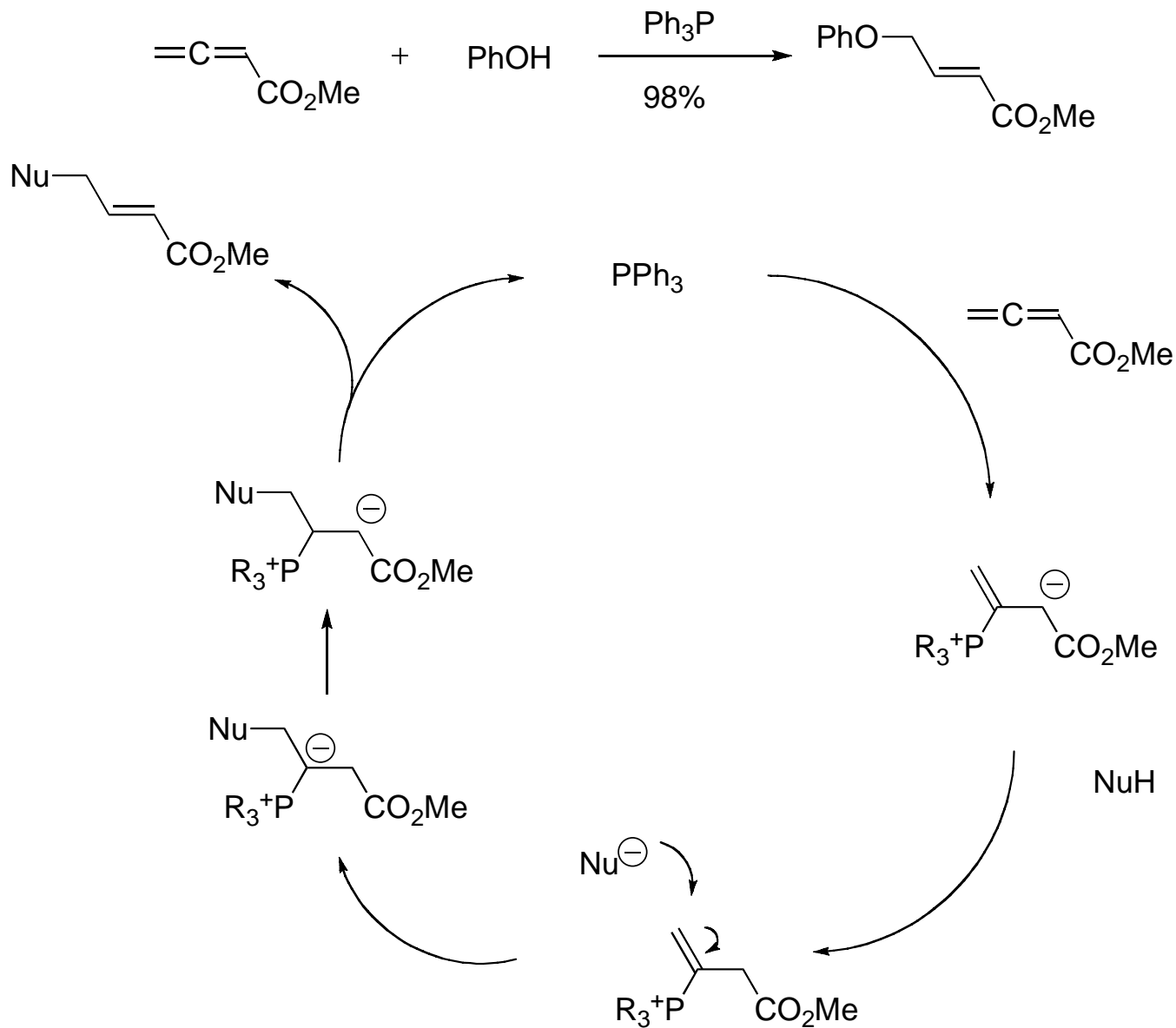
J. Am. Chem. Soc. **1988**, 110, 2301.



Additions to Allenes

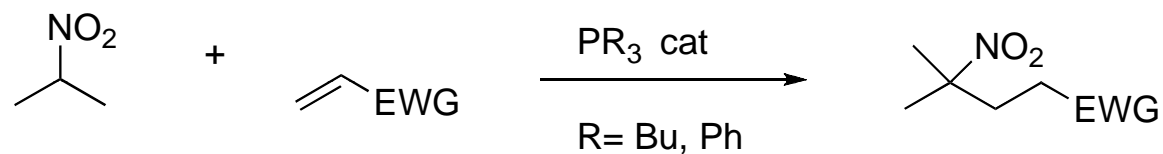
- Normally, addition of nucleophiles to electron-deficient allenes occurs at the alpha-beta double bond...but with triphenylphosphine the addition takes place at the beta-gamma double bond (effectively umpolung addition)

Bull. Soc. Chem. Fr. **1985**, 980.



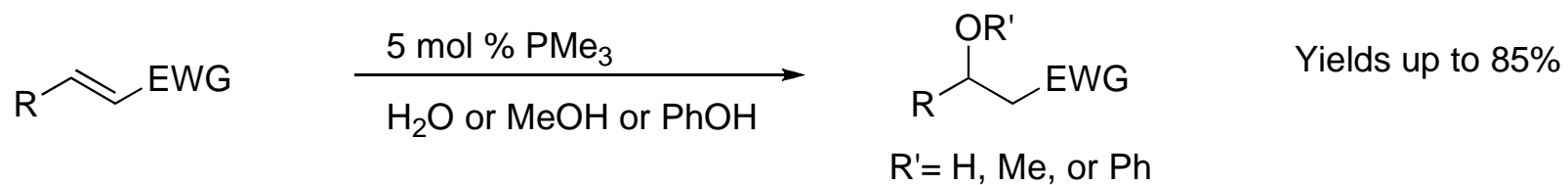
More Michael Additions

- Michael addition of carbon acids usually done with strong base, but phosphines can catalyze some additions

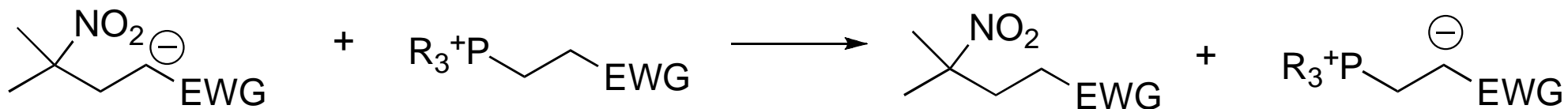
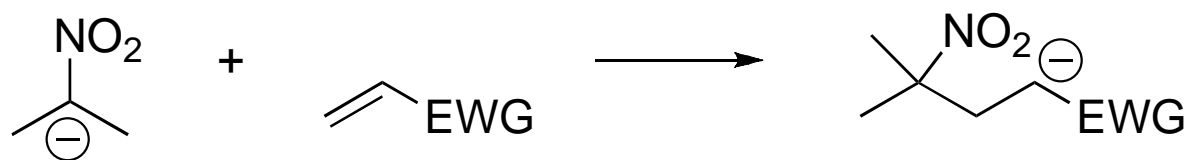
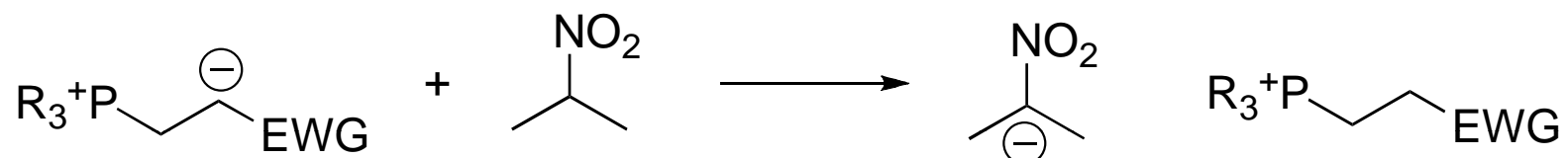
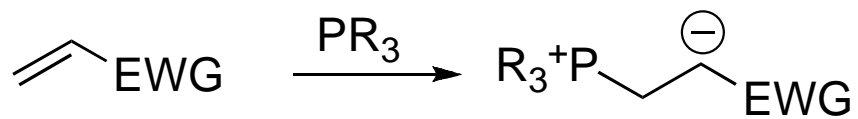


Tet. Lett. **1973**, 14, 3597.

- Toste showed alcohols and water could add to activated alkenes

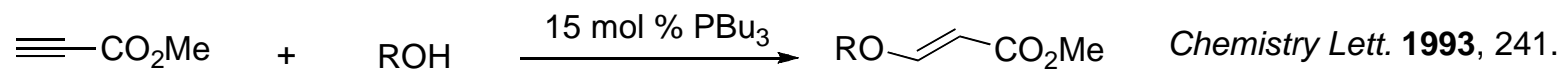


J. Am. Chem. Soc. **2003**, 125, 8696.

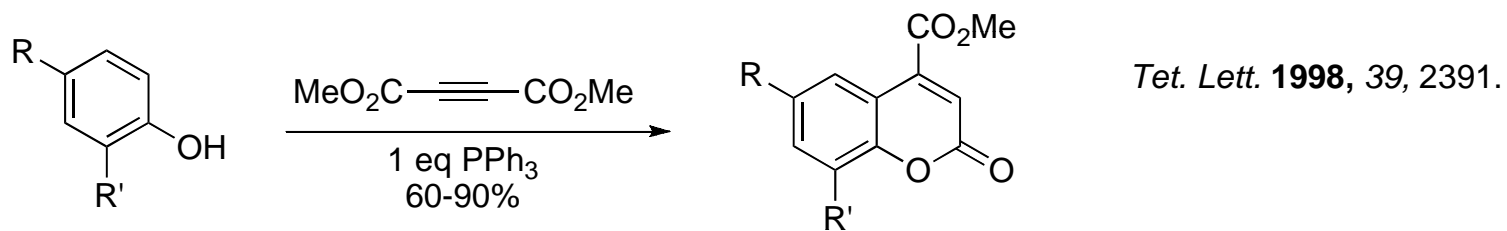


Additions to Alkynes

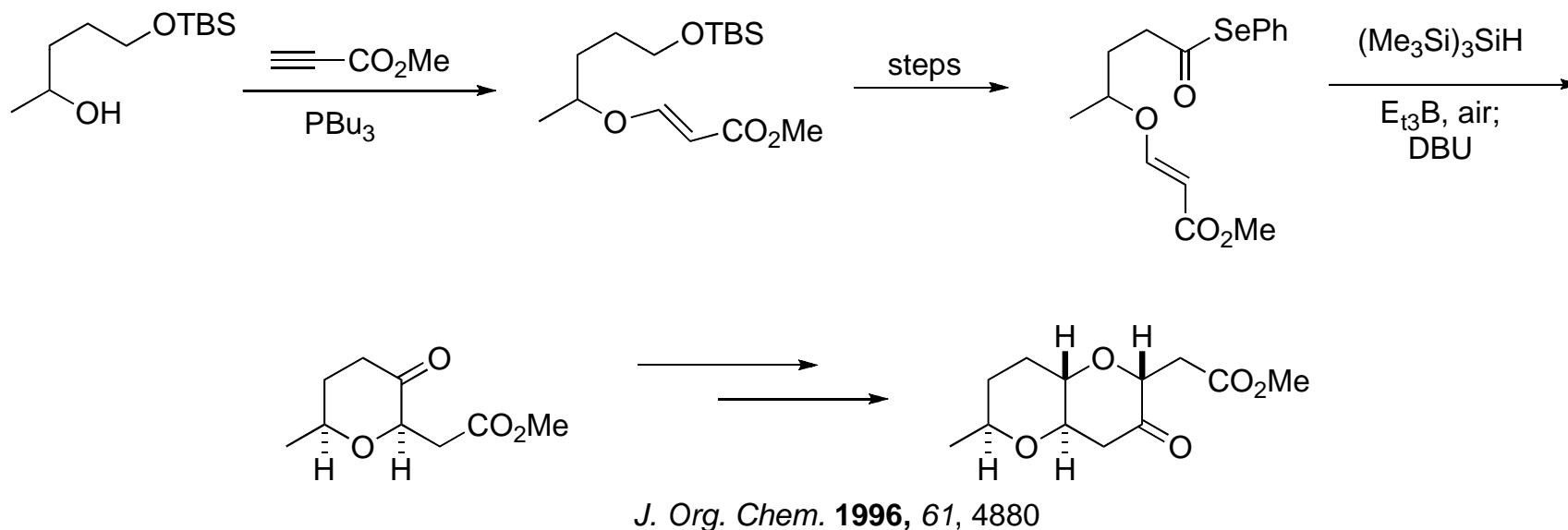
- Phosphines catalyze Michael addition of alcohols to activated alkynes as well

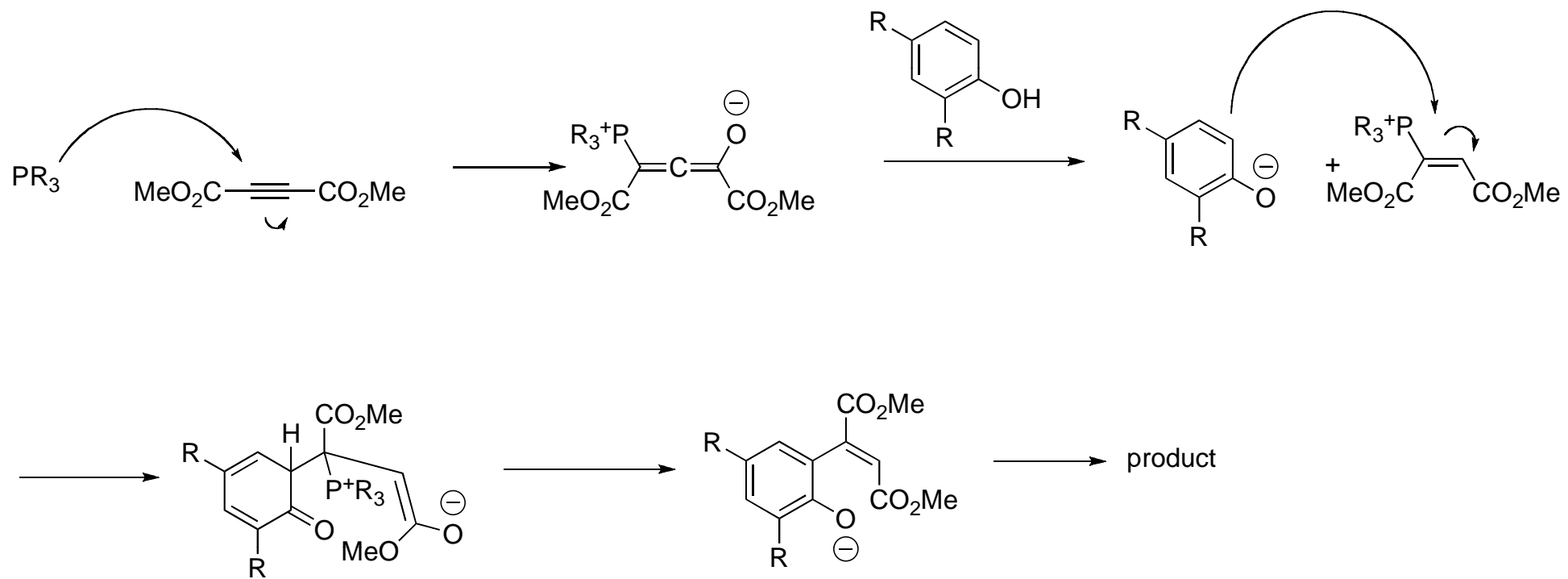


- Used in the synthesis of coumarins (Yavari)



- Used by Evans to make fused pyran structures





Conclusions

- Phosphines are good for more than just ligands, Wittig, and Mitsunobu
- Phosphines are more nucleophilic and less basic than amines
- Phosphines are excellent for Michael additions
- Can be used in asymmetric organocatalysis