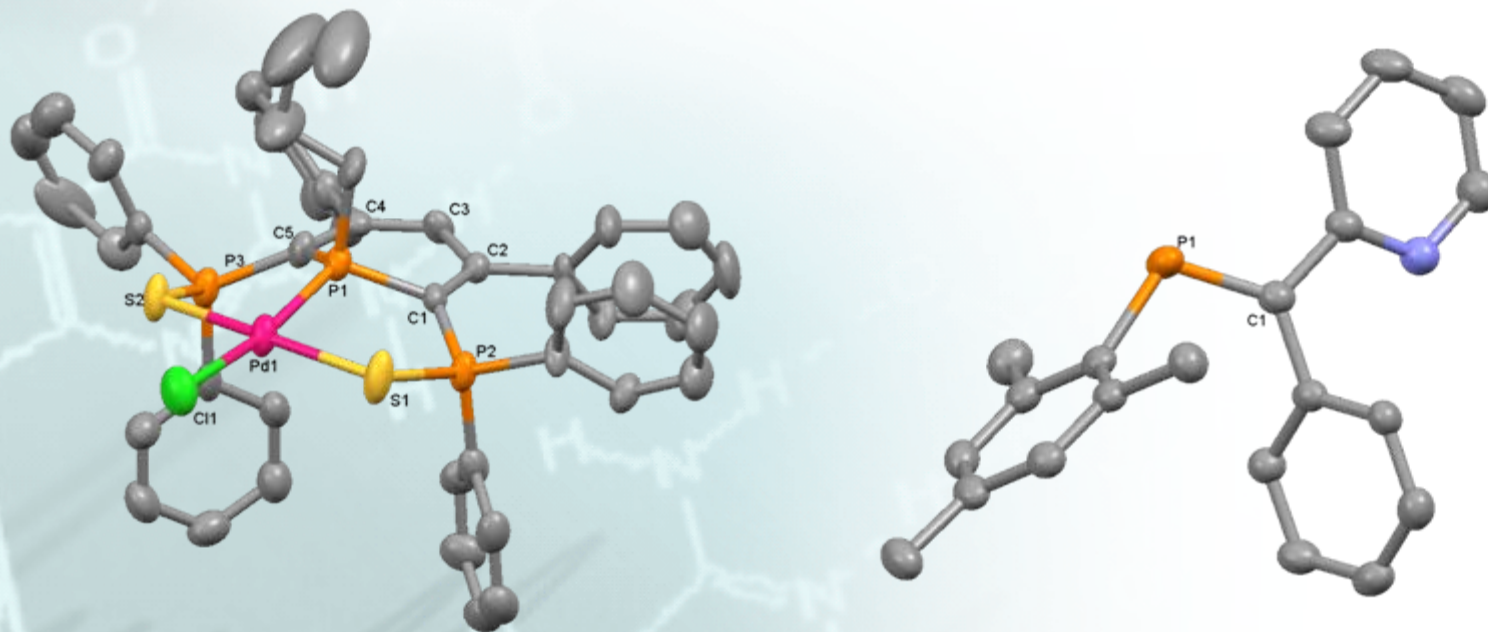


# Organic Chemistry of Low-Coordinate Phosphorus Compounds



Tom Hsieh

University of Toronto

Organic and Biological Seminar

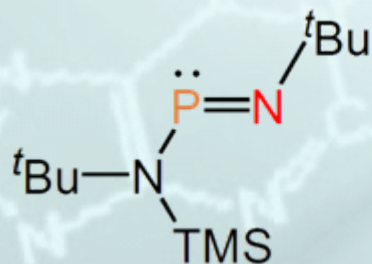
November 12, 2007

# I. Background: Making Bonds Analogous to C-C Double Bonds

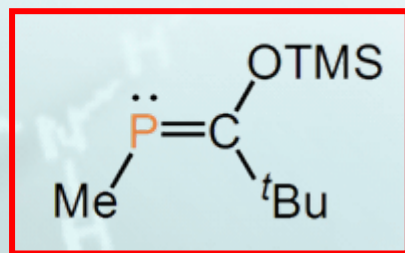
The background of the slide features several faint, light blue chemical structures. These include a nucleotide-like structure with a five-membered ring, a nitrogen atom, and a phosphate group, as well as other organic molecules with various functional groups and bonds. The structures are semi-transparent and serve as a decorative backdrop for the text.

# Breaking the "Double Bond Rule"

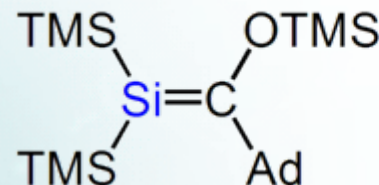
**Generally held belief:** *elements outside the first row do not form multiple bonds*



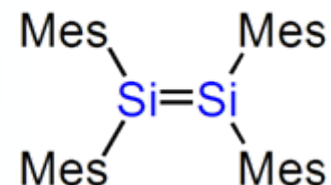
Niecke, 1973



Becker, 1976



Brook, 1981

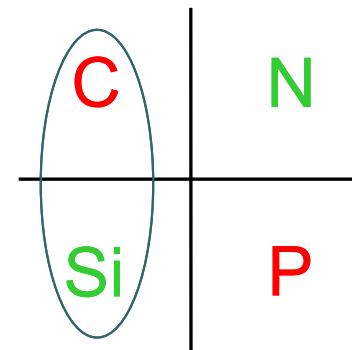
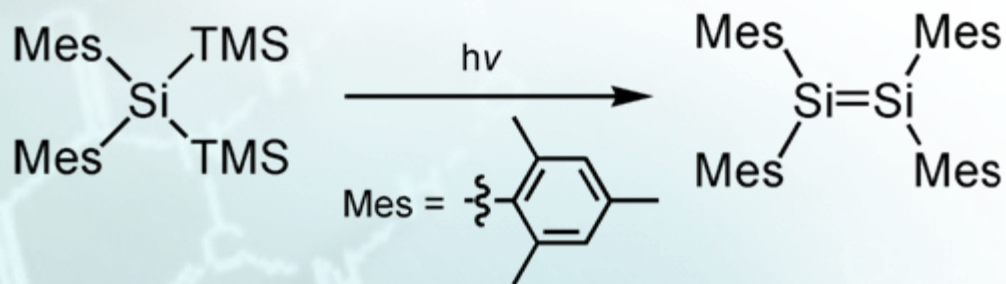


West, 1981

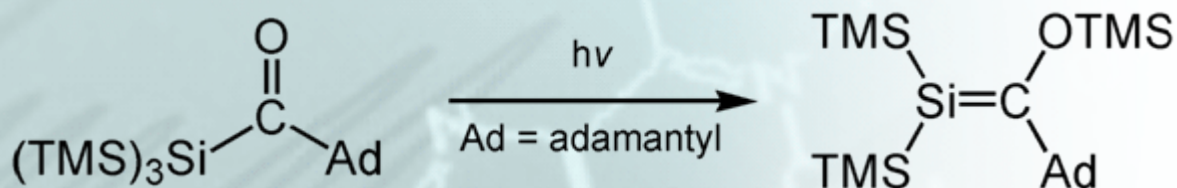
Phosphaalkene chemistry deals with **3p-2p** (P=C)  $\pi$ -bonds!!

# Carbon-Silicon Multiple Bonds

- 1981: West discovered Si=Si double bond



- 1981: Brook discovered Si=C double bond

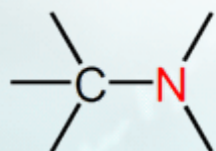


West, Fink, Michl. *Science*. **1981**, 214, 4527.

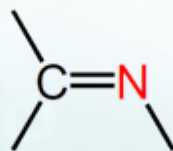
Brook, Abdesaken, Gutekunst, Gutekunst, Kallury. *J. Chem. Soc., Chem. Commun.* **1981**, 191.

# Carbon-Nitrogen Multiple Bonds

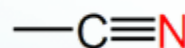
- C-N bonds are ubiquitous



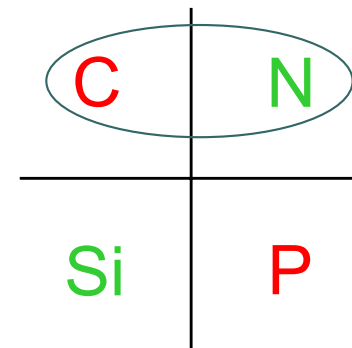
Single



Double



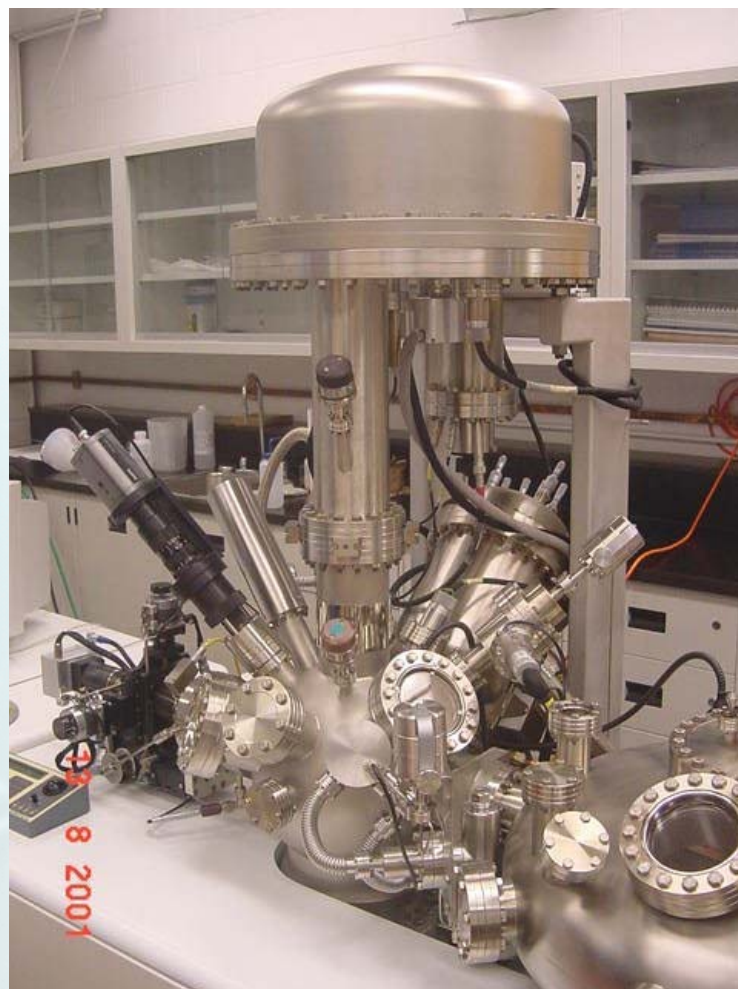
Triple



- C=N and C=C double bonds are stable
- Reactivity requires either:
  - high-lying HOMOs
  - accessible, low-lying LUMOs
- $\pi$ -bonds, strained rings, electron deficient species, etc.

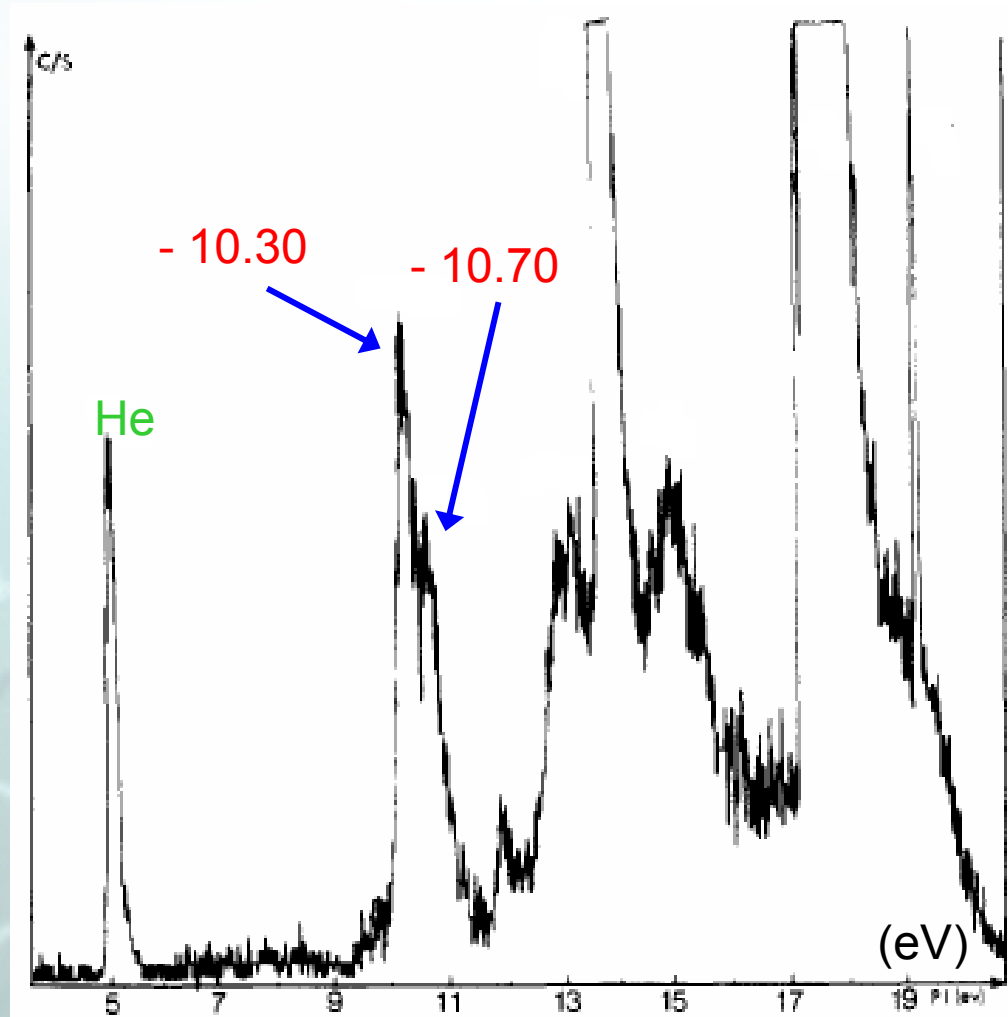
# Ultraviolet Photoelectron Spectroscopy (UPS)

- UPS determines molecular energy levels in the valence region
- Helium discharge lamp is used as the photon source
- Measures the kinetic energy spectra of electrons emitted by UV photons



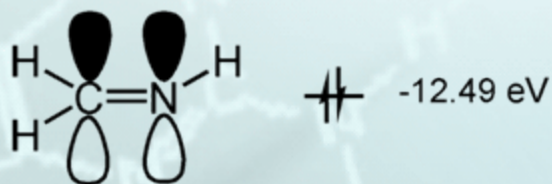
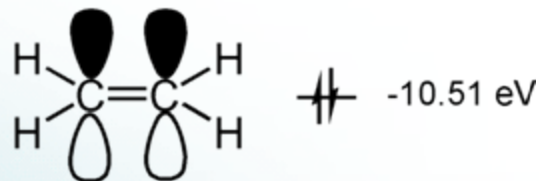
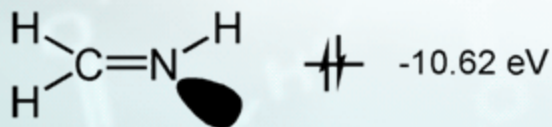
# Ultraviolet Photoelectron Spectroscopy (UPS)

- Each of the peaks in the spectrum corresponds to the MO energy level (in eV) of one valence-region



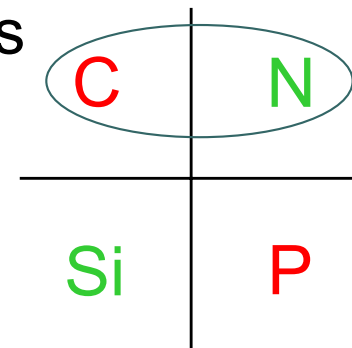
# Methanimine vs. Ethylene

- UV photoelectron spectroscopic measurements



$D(\text{C}=\text{N}): 73 \text{ kcal/mol}$

$D(\text{C}=\text{C}): 65 \text{ kcal/mol}$



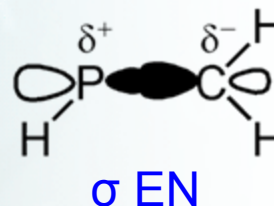
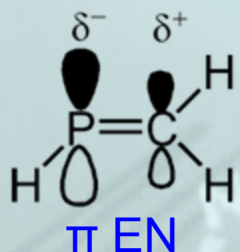
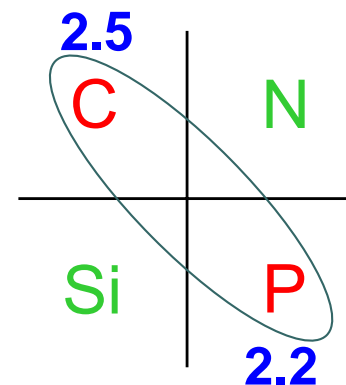
- HOMO** of methanimine is the **lone pair**
- $\pi$ -bond lies much lower in energy
- Consequently, methanimine usually **reacts through its lone pair** before through its  $\pi$ -bond

Lacombe, Gonbeau, Cabioch, Pellerin, Denis, Pfister-Guillouzo. *J. Am. Chem. Soc.* **1988**, 110, 6064

Schmidt, Truong, Gordon. *J. Am. Chem. Soc.* **1987**, 109, 5217.

# Carbon and Phosphorus

- The P=C double bond is *relatively apolar*
- Electronegativity (EN) governs an element's ability to release or accept electrons
  - i.e. reactivity is strongly influenced by EN
- $\sigma$  EN of phosphorus is **lower** than carbon
- $\pi$  EN of phosphorus is **higher** than carbon



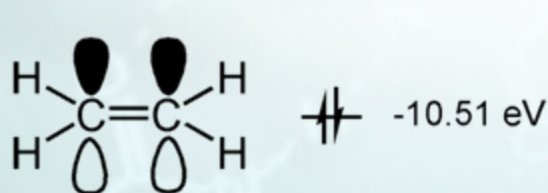
- Phosphorus is a  **$\sigma$ -electron donor** & a  **$\pi$ -electron acceptor**

Waluk, Klein, Ashe III, Michl. *Organometallics*. **1989**. 8. 2804.

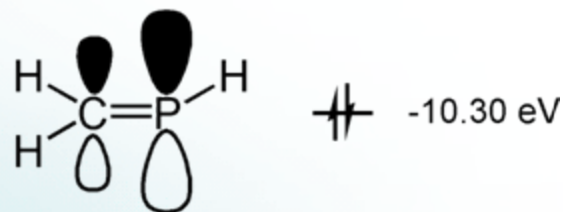
Le Floch. *Coord. Chem. Rev.* **2006**. 250. 627.

# Ethylene vs. Phosphaethylene

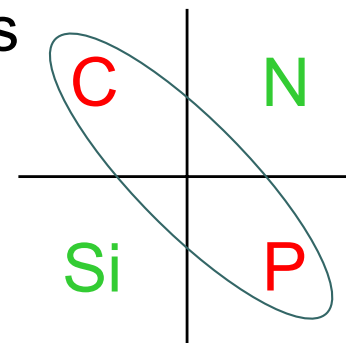
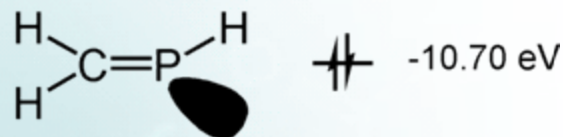
- UV photoelectron spectroscopic measurements



$D(\text{C}=\text{C}): 65 \text{ kcal/mol}$



$D(\text{C}=\text{P}): 44 \text{ kcal/mol}$

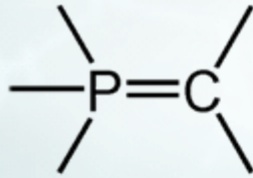


- HOMO of phosphoethylene is the  $\pi$ -bond
- The lone pair lies slightly lower in energy
- Consequently, phosphoethylene tends to **react through its  $\pi$ -bond** before through its lone pair

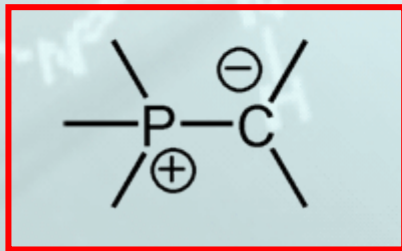
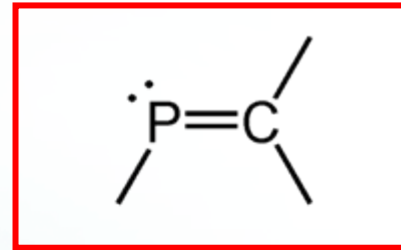
Lacombe, Gonbeau, Cabioch, Pellerin, Denis, Pfister-Guillouzo. *J. Am. Chem. Soc.* **1988**, 110, 6064

Schmidt, Truong, Gordon. *J. Am. Chem. Soc.* **1987**, 109, 5217.

# Phosphaylide vs. Phosphaalkene



vs.



phosphaylide

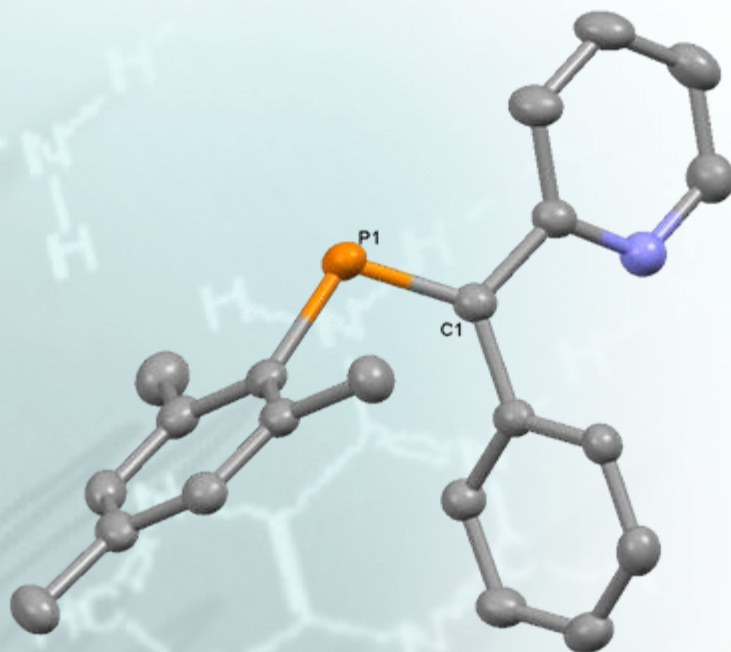


phosphaalkene

- Coordination number = **4**

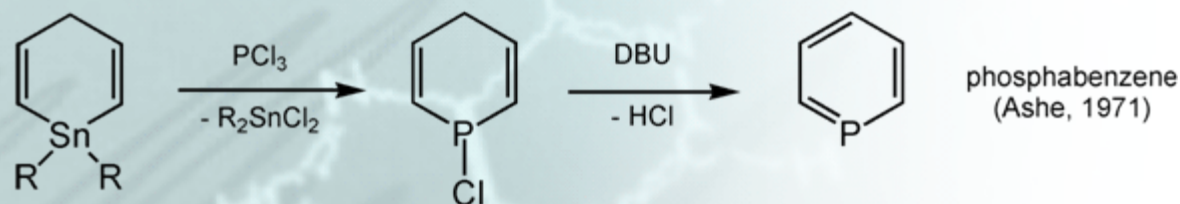
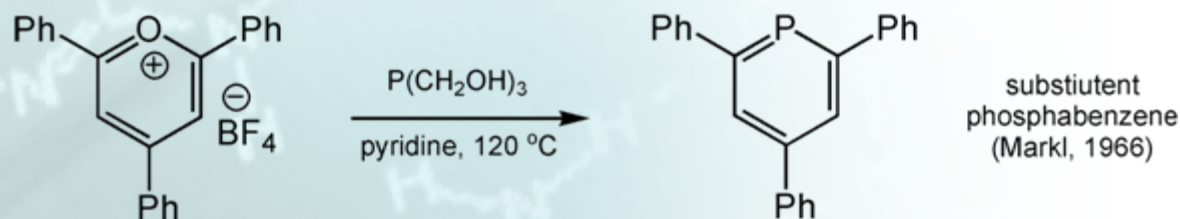
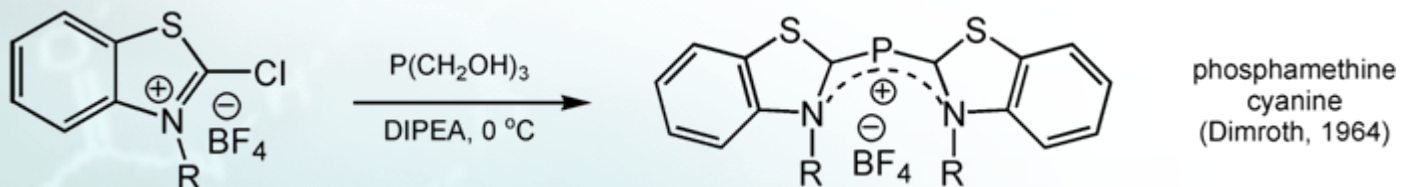
- Coordination number = **2**

## II. Synthesis of Phosphaalkenes



# First Isolable P-C Multiple Bond

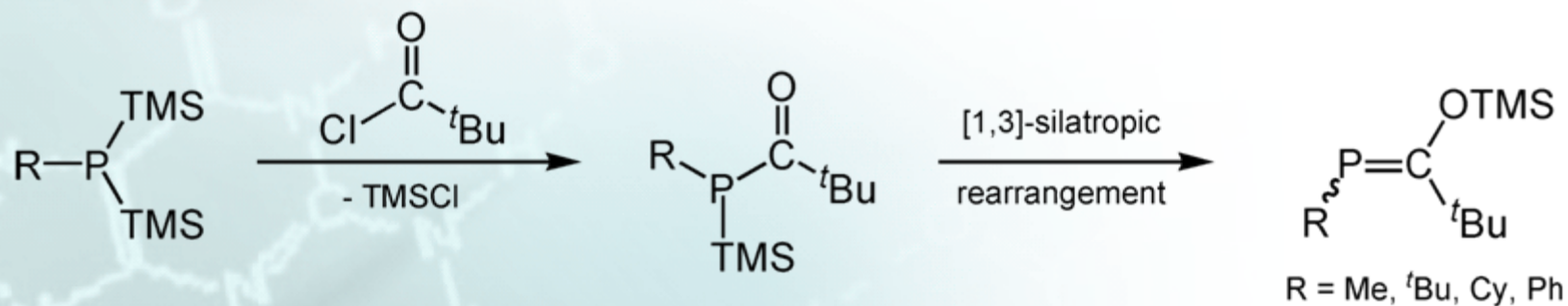
- First stable, isolable (3p-2p)  $\pi$ -bonded compounds



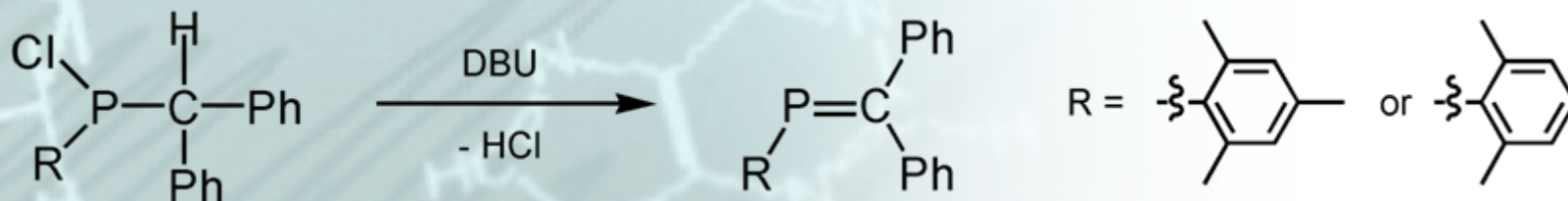
- Stabilized by the delocalization of electrons

# First Localized P=C Double Bond

- 1976: Becker reports first isolable P=C compound with a localized  $\pi$ -bond



- 1978: Bickelhaupt reports first isolable P=C compound with all-carbon substituents

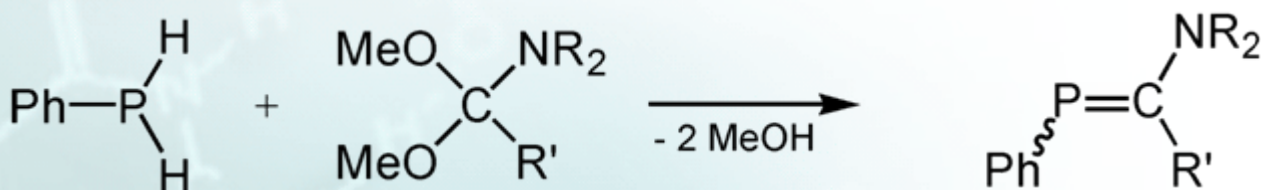


Becker. *Z. Anorg. Allg. Chem.* **1976**, 423, 242.

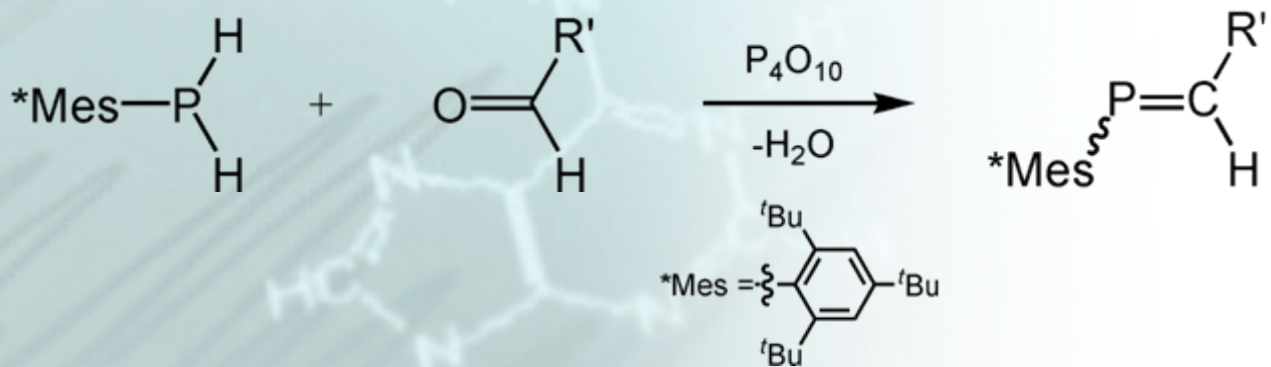
Klebach, Lourens, Bickelhaupt. *J. Am. Chem. Soc.* **1978**, 100, 4886.

# Condensation Strategies to Phosphaalkenes

- Condensation of primary phosphines
  - Reaction with acetals



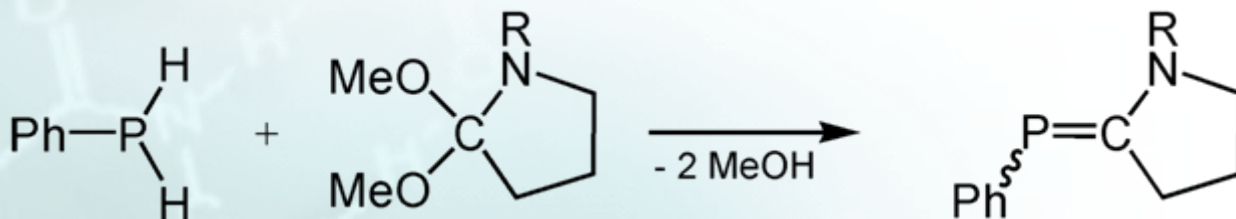
- Reaction with aldehydes



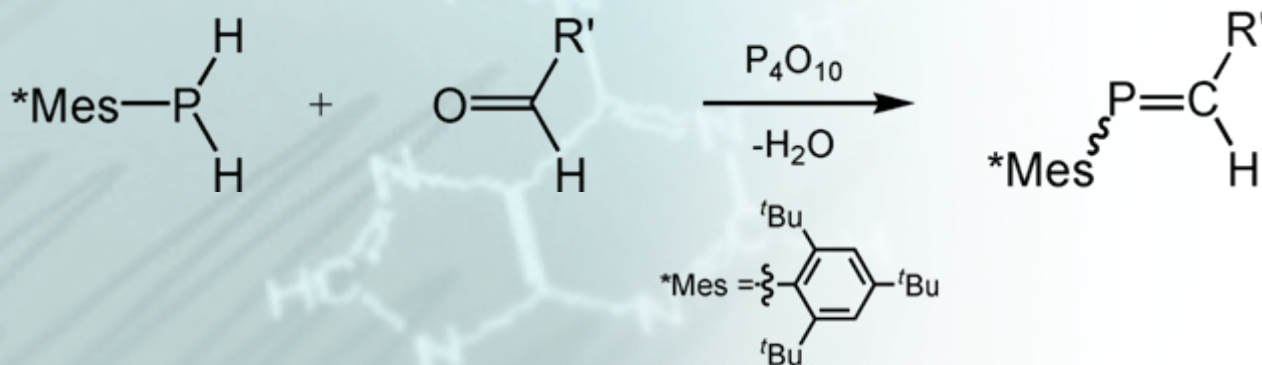
# Condensation Strategies to Phosphaalkenes

- Condensation of primary phosphines

- Reaction with acetals

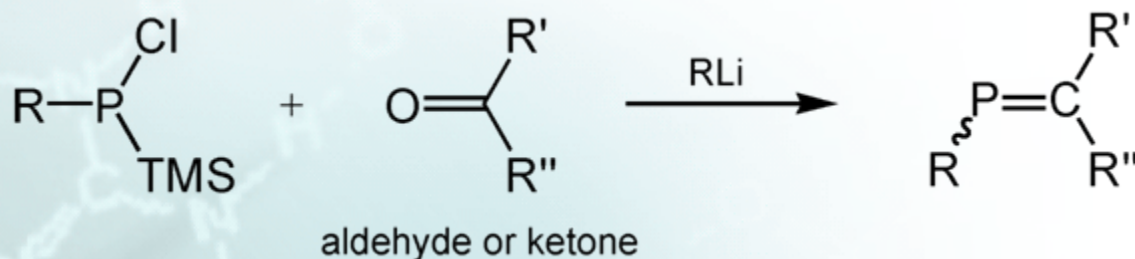


- Reaction with aldehydes

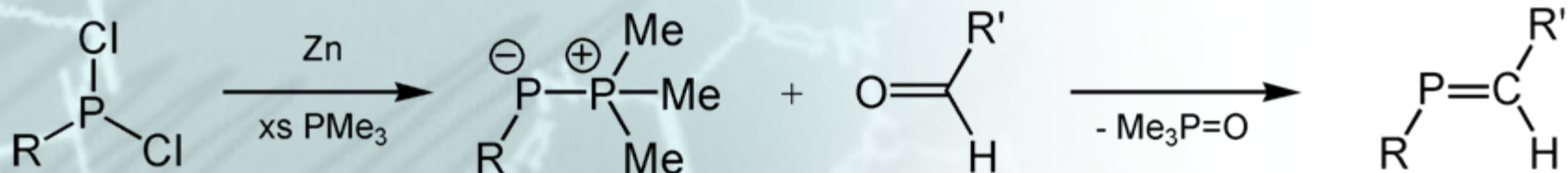


# Phospha-Olefination of Carbonyl Compounds

- Phospha-Peterson olefination
  - Lithium activated phosphides



- Phospha-Wittig olefination

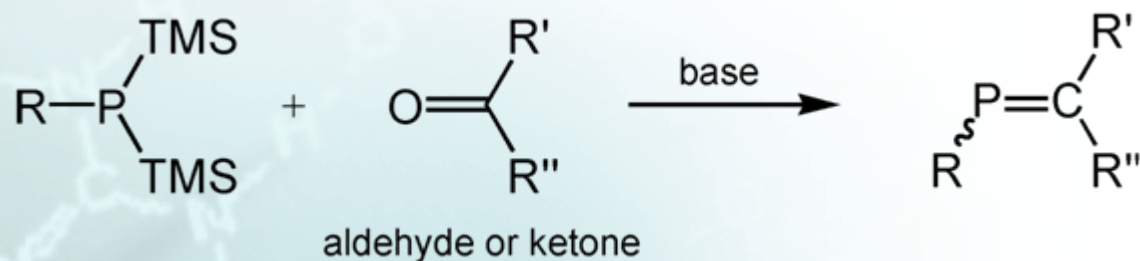


Gates. *Top. Curr. Chem.* **2005**, 250, 107.

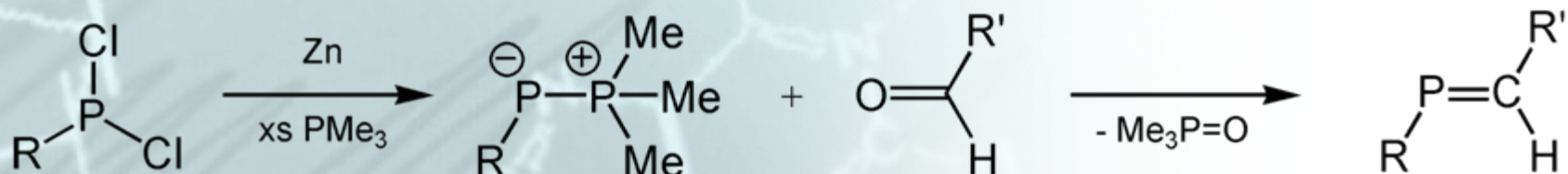
Mathey. *Angew. Chem. Int. Ed.* **2003**, 42, 1578.

# Phospha-Olefination of Carbonyl Compounds

- Phospha-Peterson olefination
  - Base-catalyzed



- Phospha-Wittig olefination

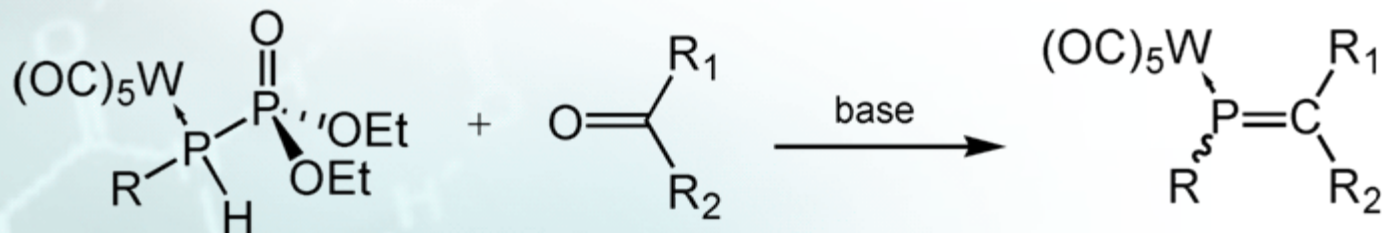


Gates. *Top. Curr. Chem.* **2005**, 250, 107.

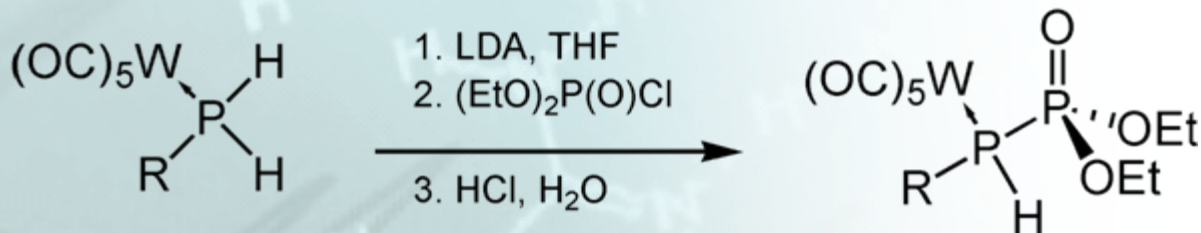
Mathey. *Angew. Chem. Int. Ed.* **2003**, 42, 1578.

# Phospha-Olefination of Carbonyl Compounds

- Phospha-Horner-Wadsworth-Emmons olefination



- Phosphorylphosphine complex/reagent



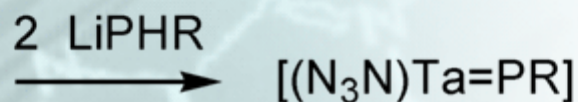
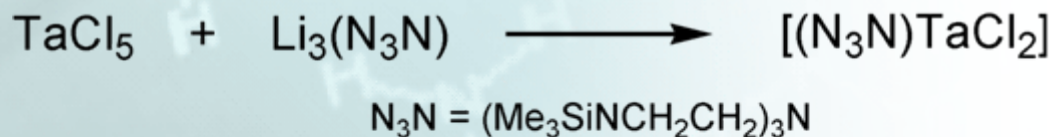
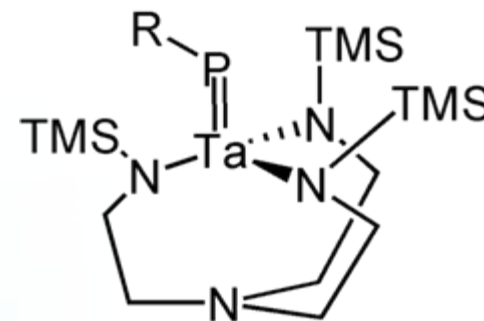
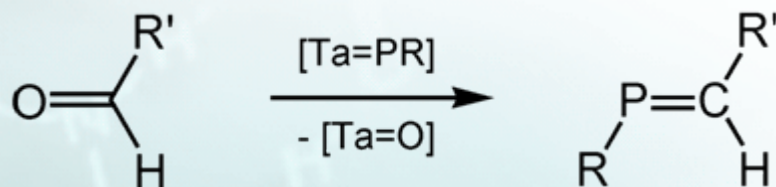
- Works for **both** aldehydes and ketone

Marinetti, Bauer, Ricard, Mathey. *Organometallics*. **1990**, 9, 793.

Mathey. *Angew. Chem. Int. Ed.* **2003**, 42, 1578.

# Phosphaalkenes Via Metal Phosphinidenes

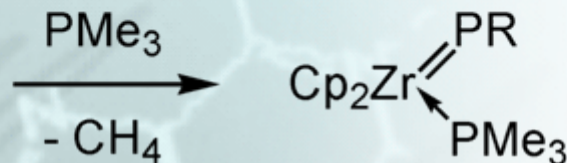
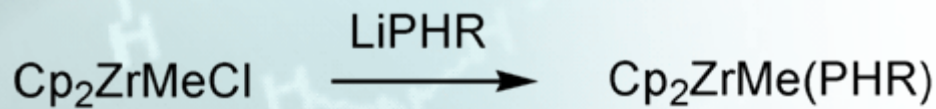
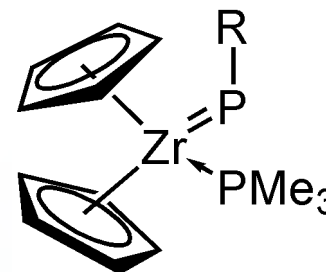
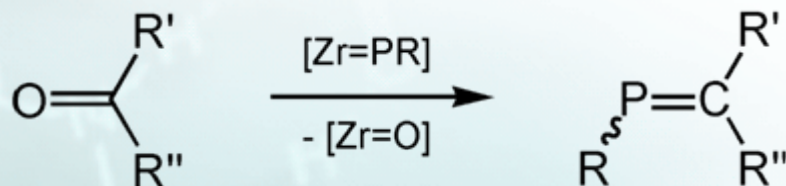
- Schrock's Tantalum (V) phosphinidene complex



- Limited to **only** aldehydes

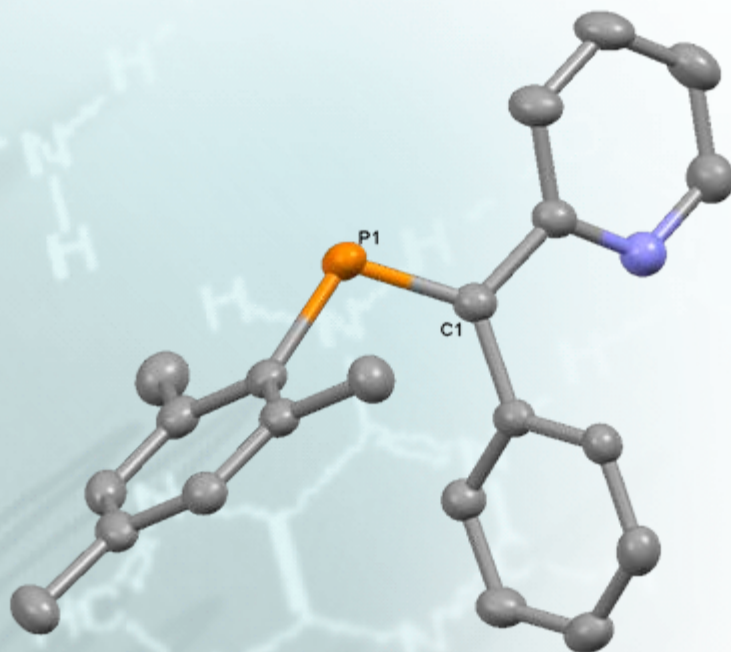
# Phosphaalkenes Via Metal Phosphinidenes

- Stephan's Zirconium (IV) phosphinidene complex



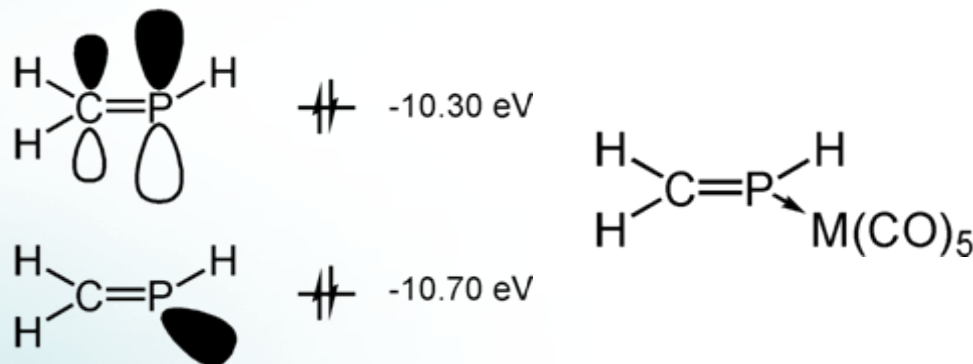
- Reacts with **both** aldehydes and ketones

# III. Reactivity of Phosphaalkenes

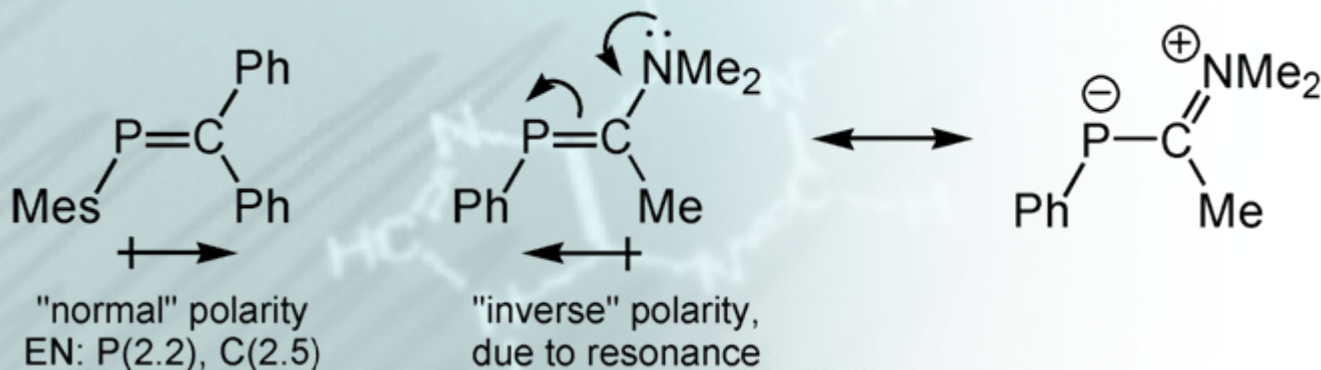


# Considerations for P=C Reactivity

- Small  $\Delta E$  between the P=C  $\pi$  and  $n_P$  orbitals
  - Interference of lone pair
  - Metal-coordination

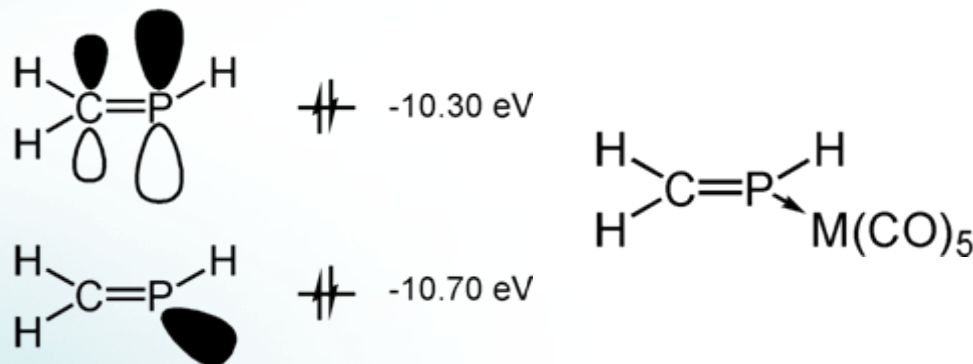


- Quaternization at phosphorus centers is slow and difficult
- Polarity of the P=C bond can be reversed
  - Alters the reactivity of P=C

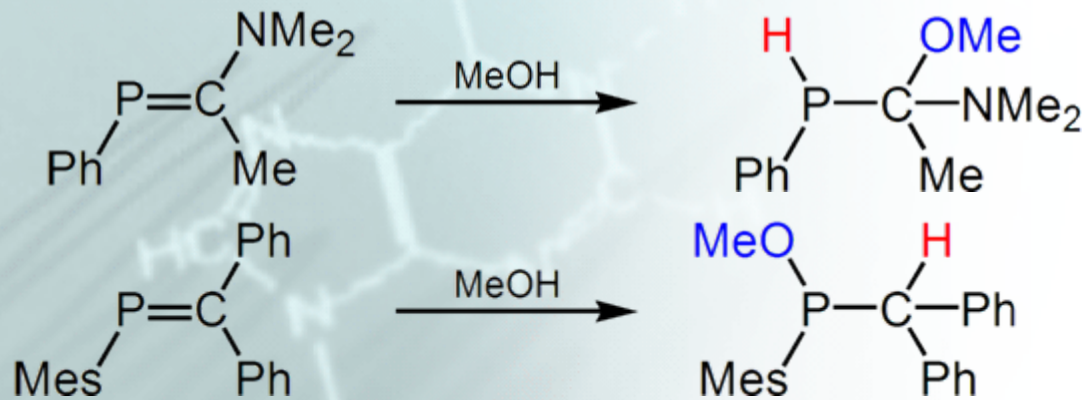


# Considerations for P=C Reactivity

- Small  $\Delta E$  between the P=C  $\pi$  and  $n_P$  orbitals
  - Interference of lone pair
  - Metal-coordination



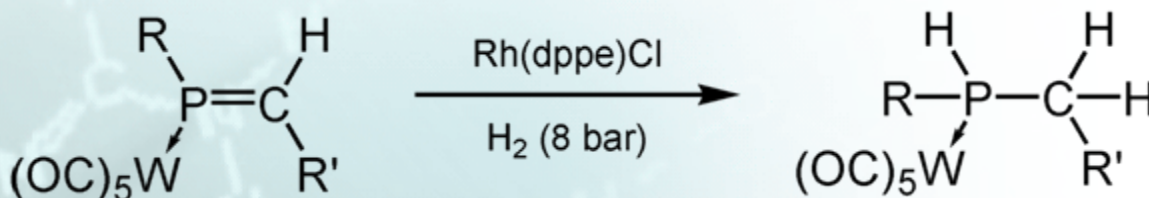
- Quaternization at phosphorus centers is slow and difficult
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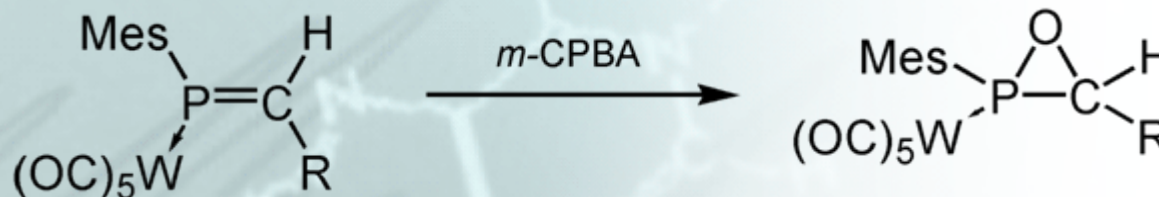
Mathey. *Angew. Chem. Int. Ed.* **2003**, *42*, 1578.

# Hydrogenation and Epoxidation of P=C

- Lone pair interferes with these reactions so coordination with  $W(CO)_5$  is necessary otherwise **no** reaction
  - Catalytic **hydrogenation** with metal-complexes



- **Epoxidation** with *m*-CPBA



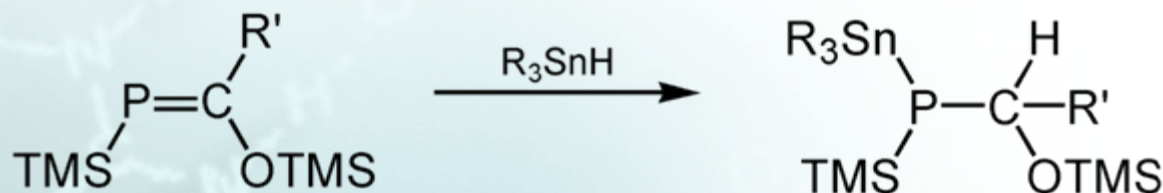
Vaumas, Marinetti, Mathey. *J. Organomet. Chem.* **1991**, 413, 41.

Bauer, Marinetti, Ricard, Mathey. *Angew. Chem. Int. Ed. Engl.* **1990**, 29, 1166.

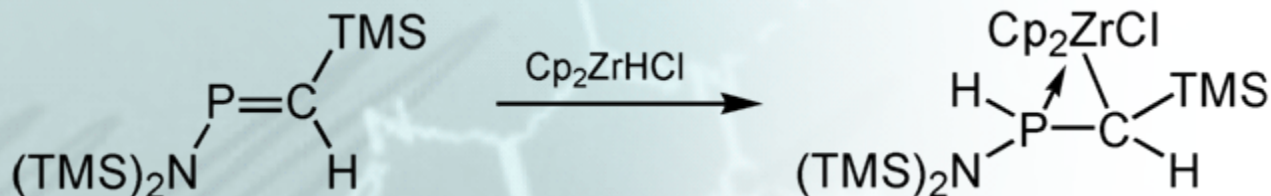
# Regioselective Hydrometalation of P=C

- Lone pair does **not** interfere with these reactions

- **Hydrostannation**



- **Hydrozirconation**

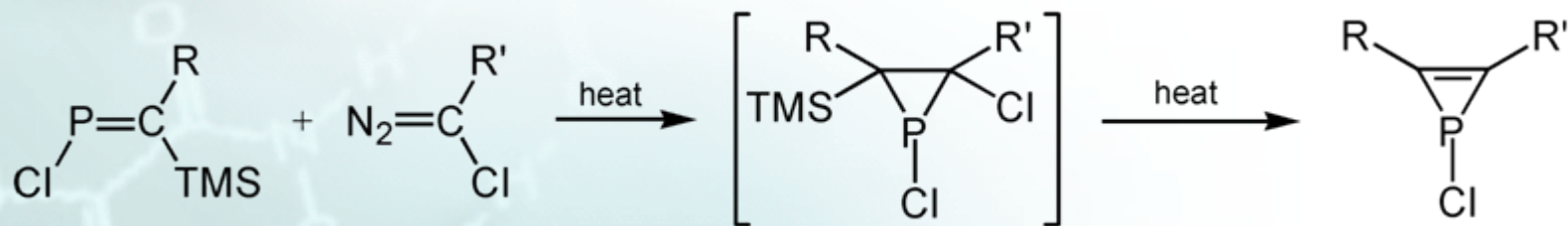


Schmitz, Leininger, Bergstrasser, Regitz.. *Heteroat. Chem.* **1998**, 9, 453.

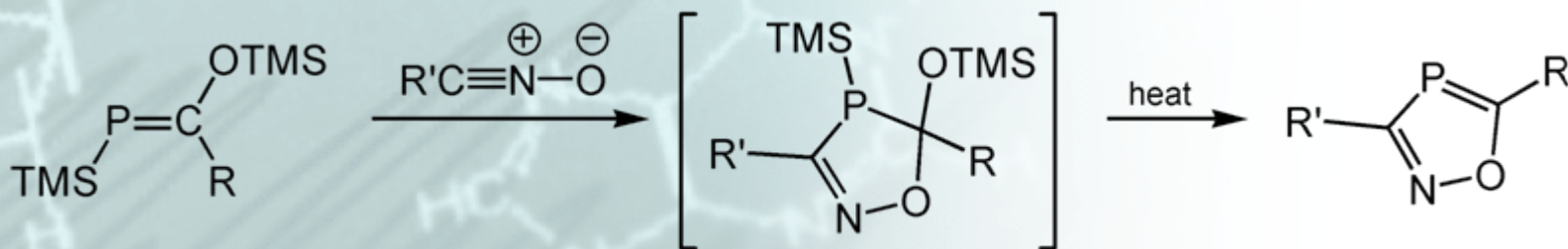
Dufour, Caminade, Basso-Bert, Igau, Majoral. *Organometallics.* **1992**, 11, 1131.

# P-Heterocycles via Cycloadditions

- [2+1] – P=C to chlorocarbenes



- [2+3] – P=C to 1,3-dipole compounds
  - results in aromatic P-heterocycles

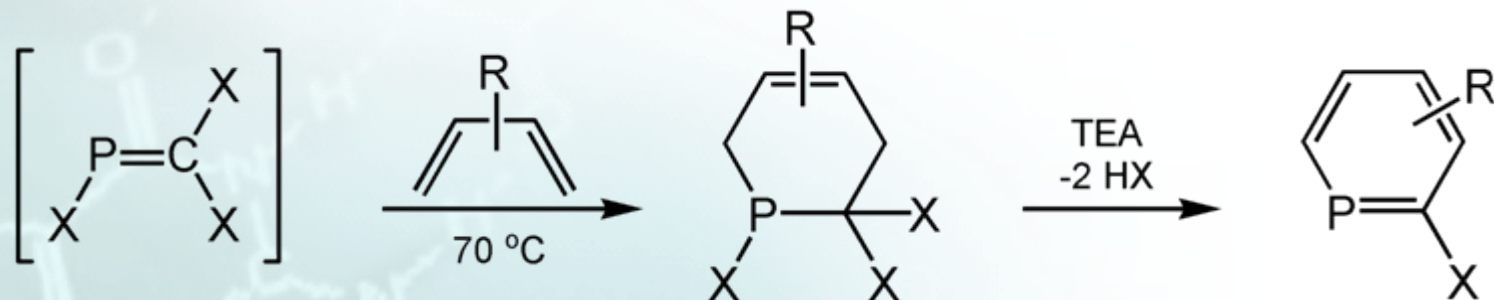


Schnurr, Regitz. *Tetrahedron Lett.* **1989**, 30, 3951.

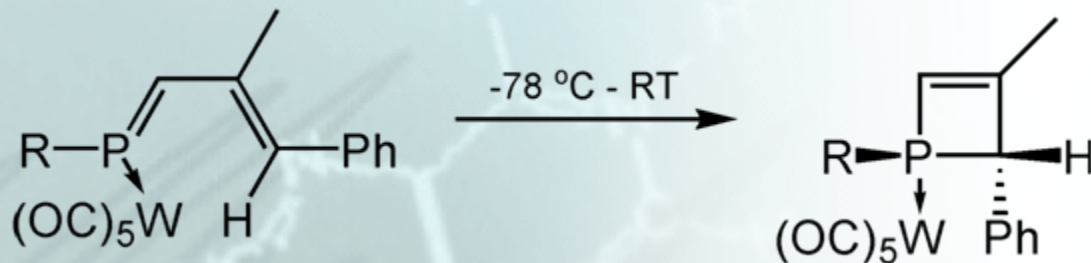
Allspach, Regitz, Becker. *Synthesis.* **1986**, 31.

# Diels-Alder and Electrocyclization of P=C

- **Diels-Alder** – synthesis of 2-halophosphabenzenes



- $4\pi$  conrotatory **electrocyclization**

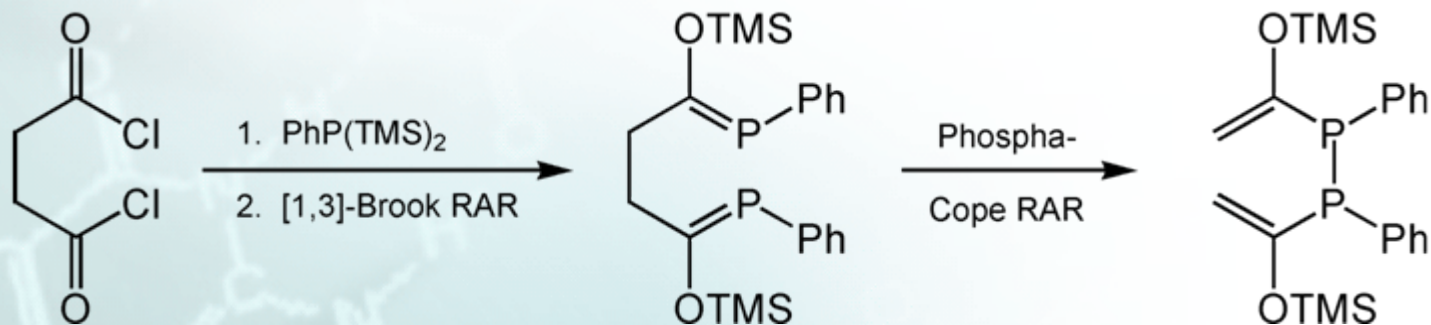


Mathey. *Angew. Chem. Int. Ed.* **2003**, 42, 1578.

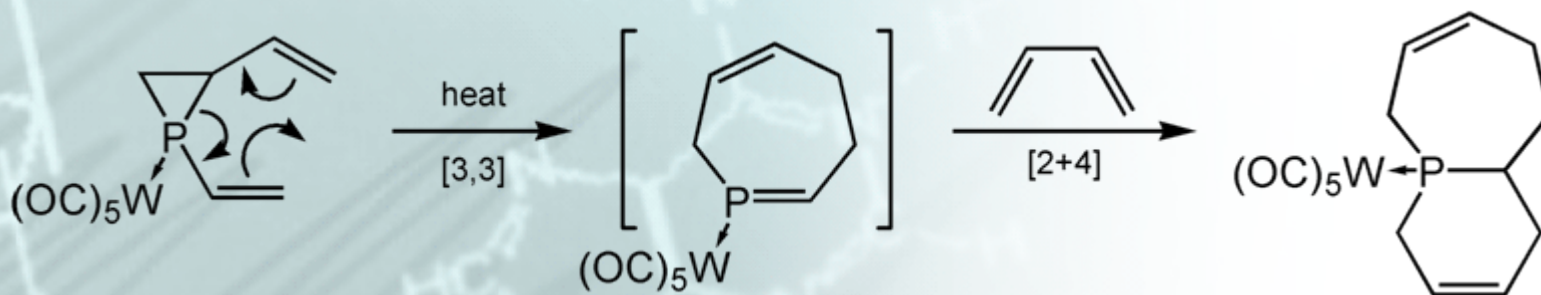
Marinetti, Ricard, Mathey. *Organometallics.* **1990**, 9, 788.

# [3,3] Sigmatropic Rearrangement

- Phospha-Cope rearrangement



- [3,3] Ring-expansion

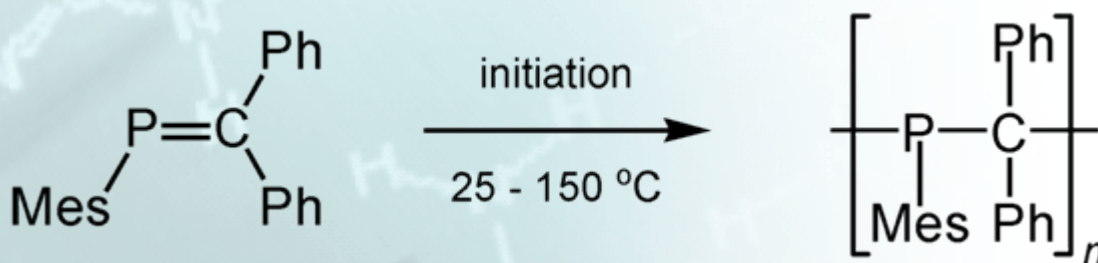


Appel, Barth, Halstenberg. *Chem. Ber.* **1982**, 115, 1617.

Huy, Marinetti, Ricard, Mathey. *Organometallics.* **1992**, 11, 1438.

# Addition Polymerization of P=C

- Thermal, radical and anionic initiation are known
  - Cationic initiation has yet to be reported
  - Thermal and anionic initiation gives a regioregular polymer
  - Radical initiation gives a regioirregular polymer

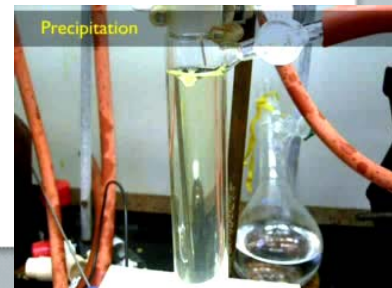


- Laser-light scattering methods detect  $M \approx 30,000$  g/mol

Tsang, Yam, Gates. *J. Am. Chem. Soc.* **2003**, 125, 1480.

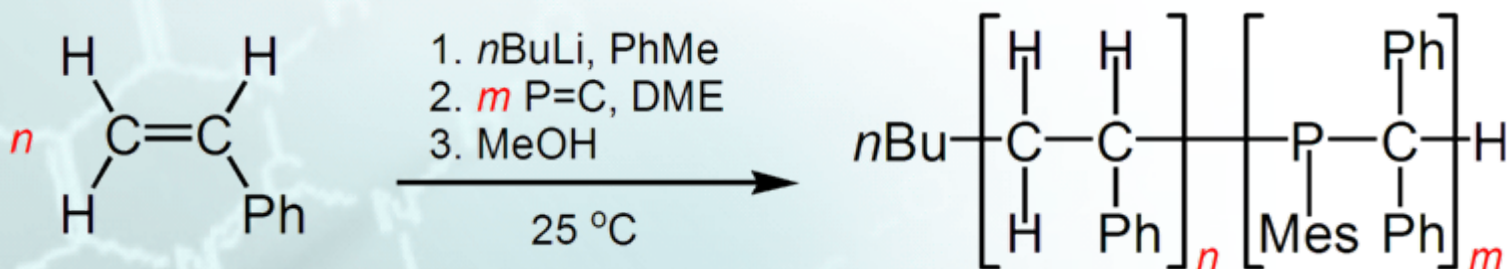
Tsang, Baharloo, Riendl, Yam, Gates. *Angew. Chem. Int. Ed.* **2004**, 43, 5682.

Noonan, Gates. *Angew. Chem. Int. Ed.* **2006**, 45, 7271.



# Addition Copolymerization of P=C

- Block copolymers have also been synthesized via **radical** and **anionic** living polymerization



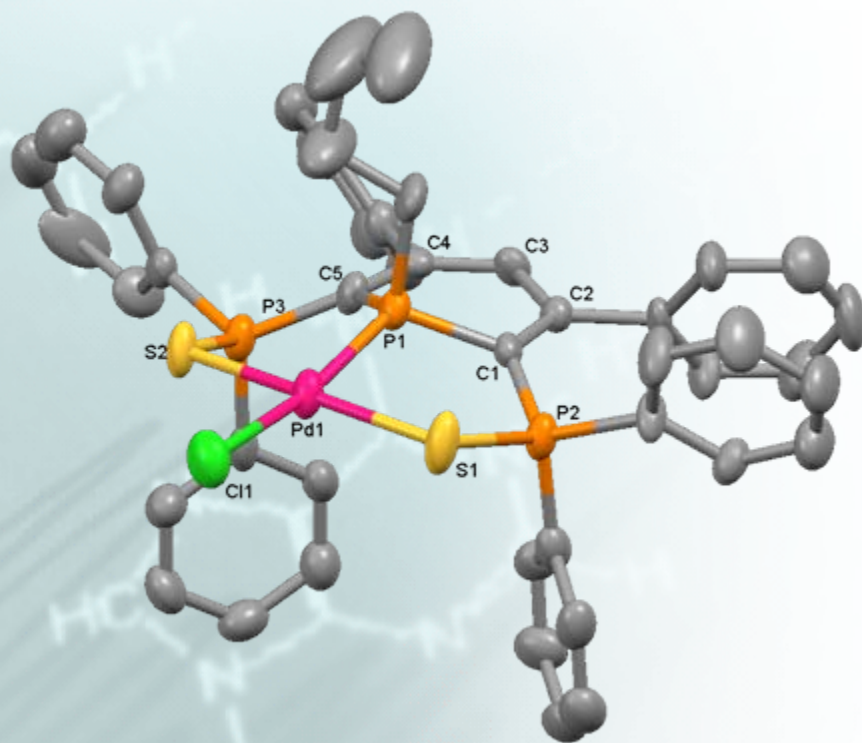
- Used in **Suzuki** coupling reactions as phosphine ligands
  - Isolated yields of biphenyl up to 90%
  - Polymer/catalyst precipitates in hexanes
  - Chromatography is **not** needed

Tsang, Yam, Gates. *J. Am. Chem. Soc.* **2003**, 125, 1480.

Tsang, Baharloo, Riendl, Yam, Gates. *Angew. Chem. Int. Ed.* **2004**, 43, 5682.

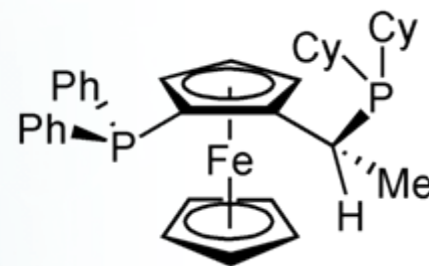
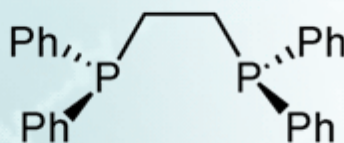
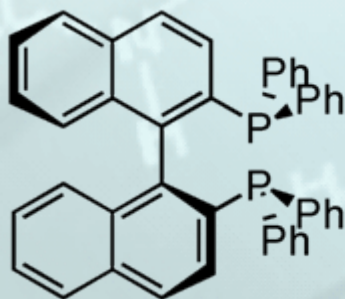
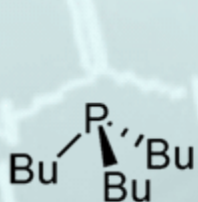
Noonan, Gates. *Angew. Chem. Int. Ed.* **2006**, 45, 7271.

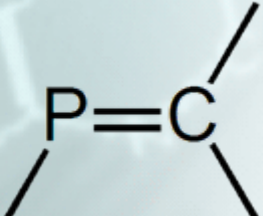
# IV. Low-Coordinate Phosphorus in Homogeneous Catalysis



# Homogeneous Catalysis

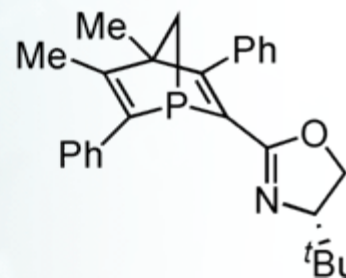
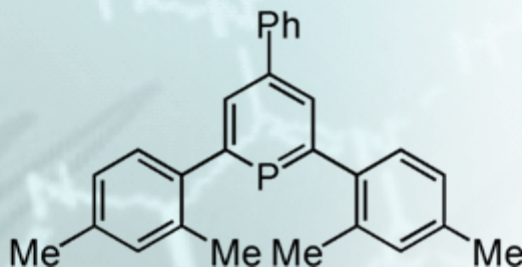
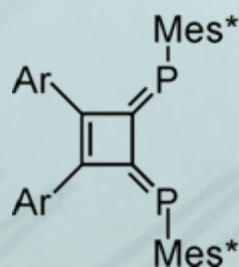
- Phosphorus is very prominent in modern catalysis
  - Particularly as privileged ligands
  - Majority are  $sp^3$ -hybridized at phosphorus



What about  in catalysis?

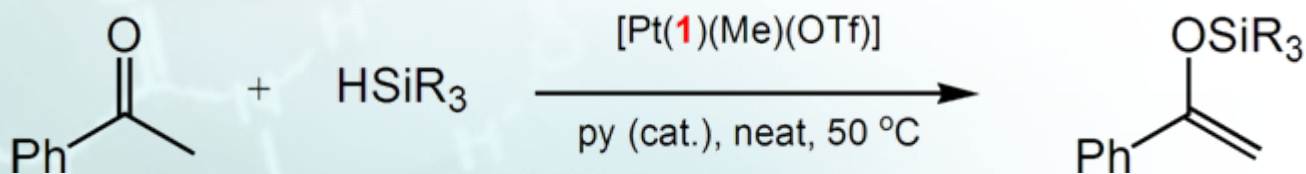
# P=C in Homogeneous Catalysis

- Low-coordinate-phosphorus chemistry contributes to homogeneous catalysis in two ways
  - Low-coordinate organophosphorus species can be ligands
  - Reactivity of low-coordinate P species can be used to prepare  $sp^3$ -hybridized P ligands that are otherwise inaccessible

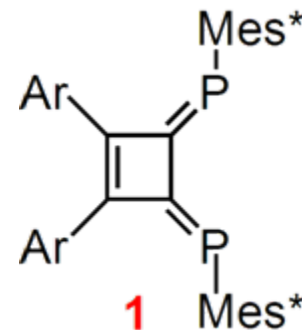
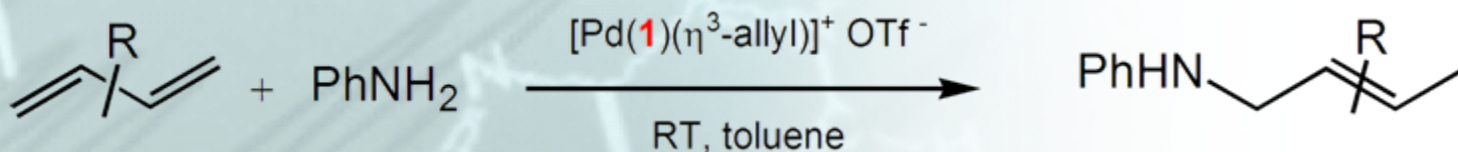


# Diphosphinidene-cyclobutenes

- Pt-catalyzed **dehydrogenative silylation** of ketones



- Pd-catalyzed **hydroamination** of 1,3-dienes

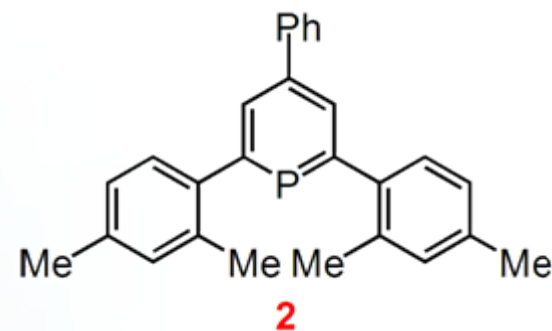
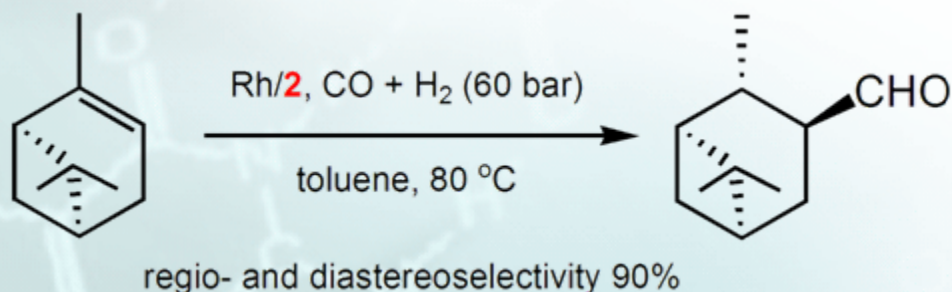


Ozawa, Yamamoto, Kawagishi, Hiraoka, Ikeda, Minami, Ito, Yoshifuji. *Chem. Lett.* **2001**, 972.

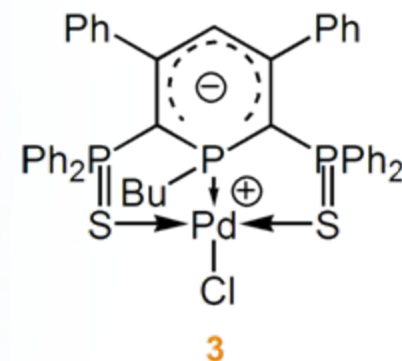
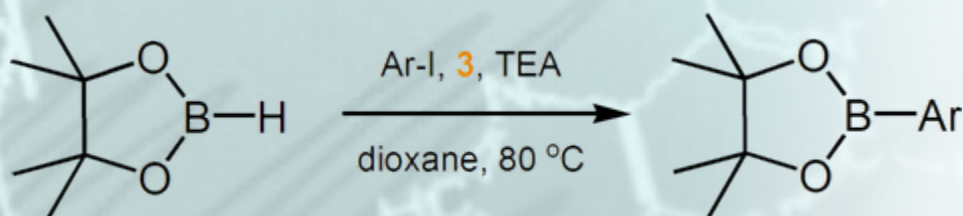
Minami, Okamoto, Ikeda, Tanaka, Ozawa, Yoshifuji. *Angew. Chem. Int. Ed.* **2001**, 40, 4501.

# Phosphabenzenes

- Rh-catalyzed **hydroformylation** of alkenes



- Pd-catalyzed **coupling** of pinacolborane



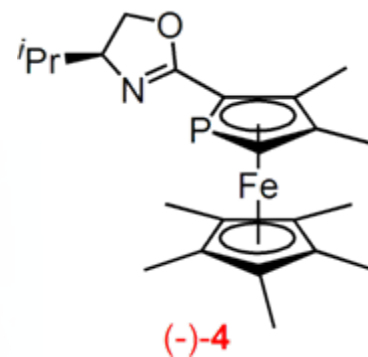
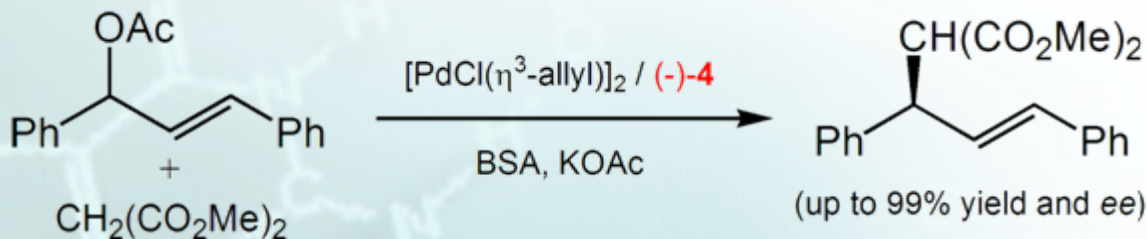
Breit, Winde, Mackewitz, Paciello, Harms. *Chem. Eur. J.* **2001**, 7, 3106.

Doux, Mezailles, Melaimi, Ricard, Le Floch. *Chem. Commun.* **2002**, 1566.

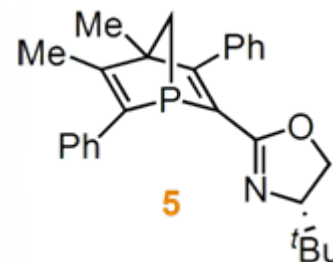
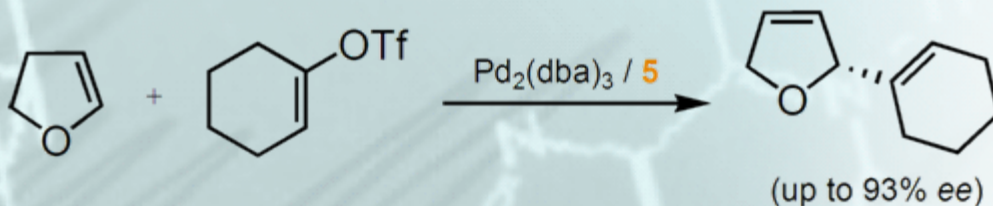
# Asymmetric Catalysis: Novel P-Ligands

- Pd-catalyzed asymmetric allylic alkylations

- BSA = *N,O*-bis(trimethylsilyl)acetamide



- Pd-catalyzed asymmetric Heck reaction



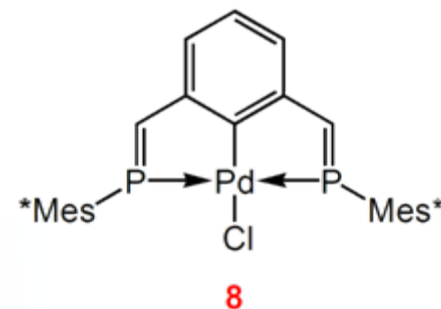
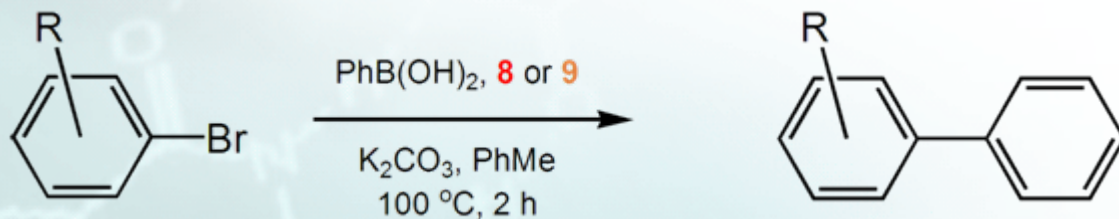
Shintani, Lo, Fu. *Org. Lett.* **2000**, 2, 3695.

Ogasawara, Yoshida, Hayashi. *Organometallics.* **2001**, 20, 3913.

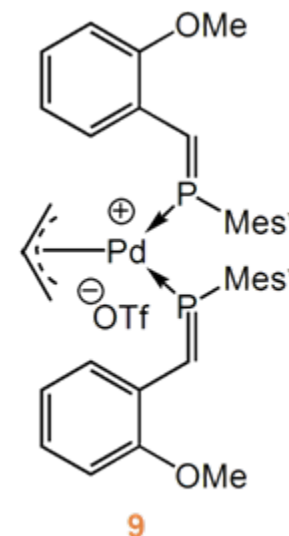
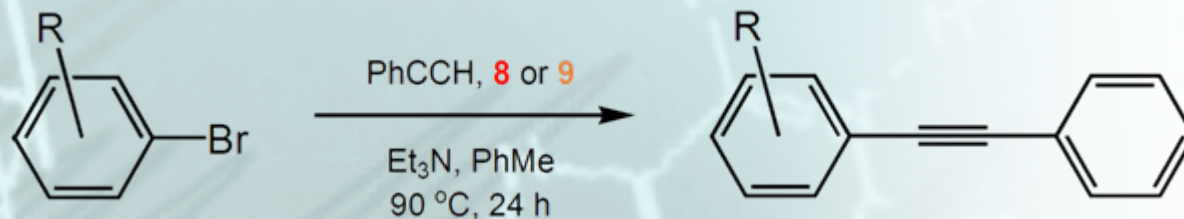
Gilbertson, Genov, Rheingold. *Org. Lett.* **2000**, 2, 2885.

# Cross-Coupling with P=C Ligands

- Suzuki cross-coupling



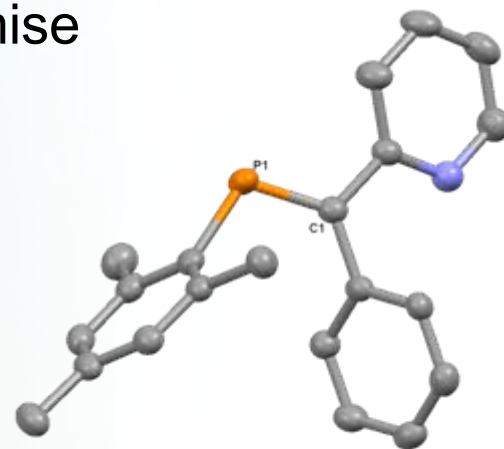
- Sonogashira cross-coupling reactions



# Conclusions

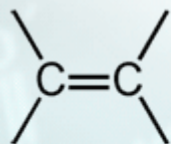
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- P=C and C=C are quite **similar** with regards to
  - Bonding, polarity
  - Methods of preparation
  - Reactivity
- P=C proves to be **efficient ligands** in catalysis
  - Early stages of development shows promise



# Phosphorus: The Carbon Copy

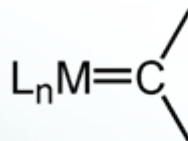
- Consider replacing a CR fragment with a P moiety



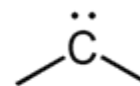
alkenes



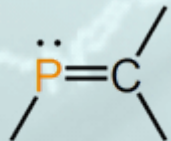
alkynes



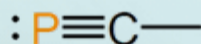
metal carbenes



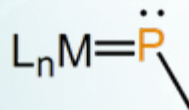
carbenes



phosphaalkenes



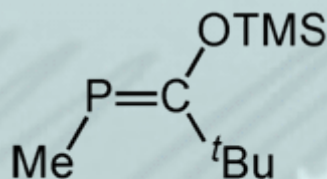
phosphaalkynes



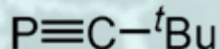
metal phosphinidenes



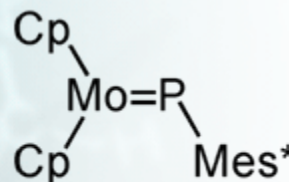
phosphinidenes



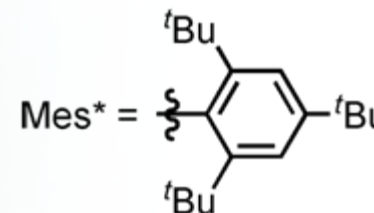
Becker, 1976



Becker, 1981



Lappert, 1987



# Phosphorus: The Carbon Copy

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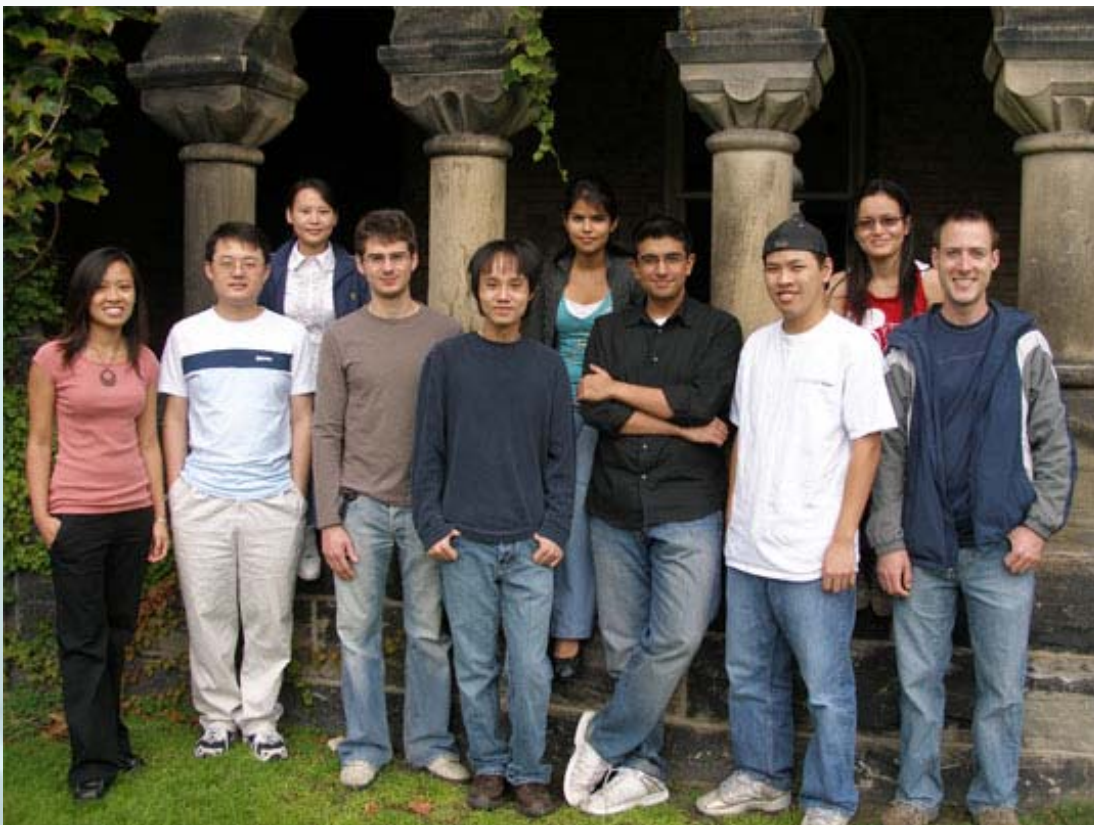
*“To fully realize what (**phospha-organic**) chemistry means, it is only necessary to imagine what would be left of **organic** chemistry if alkenes, alkynes and carbenes **did not** exist.”*



- Francois Mathey -

# Acknowledgements

- Prof. Vy M. Dong
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  - Thi Phan
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*Photo Credit: Wilmer Alkhas*