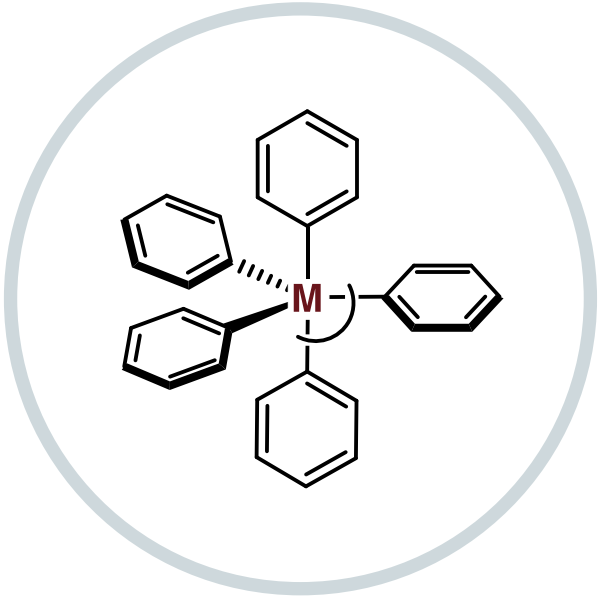
Ligand-coupling on hypervalent species: Transition metal chemistry without the metal



Literature Presentation

05 April 2023

Benjamin T. Boyle

MacMillan Group

Princeton University

Transition metal cross-couplings have transformed chemical synthesis

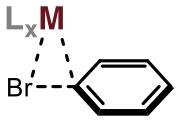
Transition metals have enabled elusive bond formations

25	26	28	29
Mn	**Fe**	**Ni**	**Cu**
Manganese	Iron	Nickel	Copper

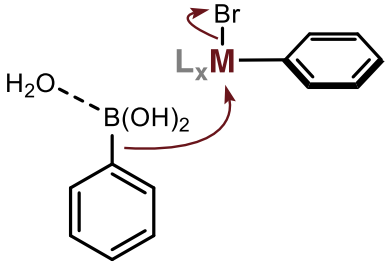
45	46	47
Rh	**Pd**	**Ag**
Rhodium	Palladium	Silver

2010 Nobel prize in chemistry

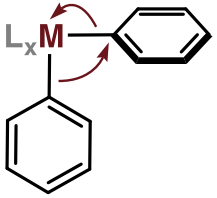
Fundamental processes:



Oxidative addition



Transmetalation



Reductive elimination

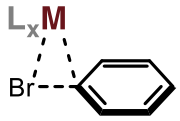
Transition metal cross-couplings have transformed chemical synthesis

Transition metals have enabled elusive bond formations

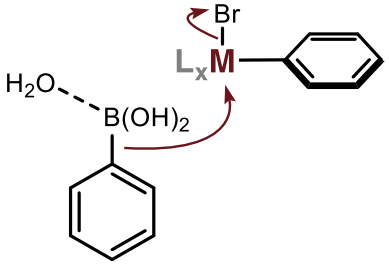
… but can we mimic this reactivity with main group elements

25 54 **Mn** Manganese	26 55 **Fe** Iron	28 58 **Ni** Nickel	29 63 **Cu** Copper			15 30 **P** Phosphorus	18 32 **S** Sulfur
	45 102 **Rh** Rhodium	46 106 **Pd** Palladium	47 107 **Ag** Silver			83 208 **Bi** Bismuth	53 126 **I** Iodine

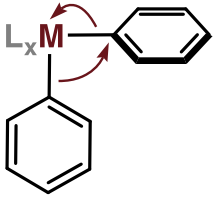
Fundamental processes:



Oxidative addition

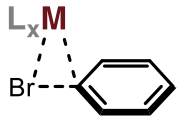


Transmetalation



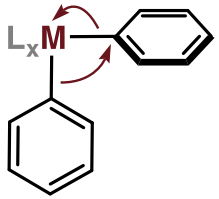
Reductive elimination

Transition metal chemistry relies on d-orbital participation



Oxidative addition

- **Oxidation state increase of +2**
- **Increase in valence electrons**
  Decrease in d-electrons



Reductive elimination

- **Oxidation state decrease of –2**
- **Decrease in valence electrons**
  Increase in d-electrons

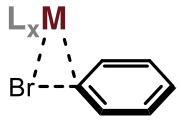
"The difference between the **common occurrence of oxidative addition in transition metal chemistry and the rare occurrence of this process in organic chemistry** contributes to the distinction between the reactivity of transition metal complexes and (organic) molecules."

"**Reductive elimination is the reverse of oxidative addition.**"

Organotransition Metal Chemistry – From Bonding to Catalysis
John F. Hartwig

Hartwig, J. F. Organotransition Metal Chemistry - From Bonding to Catalysis, 1st ed.; University Science Books, 2010.

Transition metal chemistry relies on d-orbital participation



Oxidative addition

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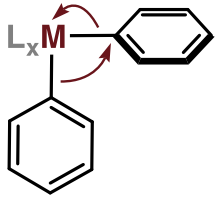


Reductive elimination

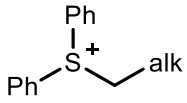
- **Oxidation state decrease of –2**
- **Decrease in valence electrons**
  Increase in d-electrons

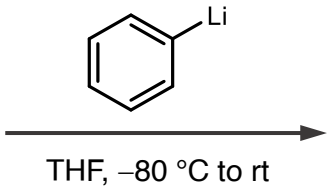
18 32

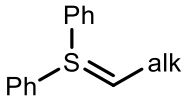
S

Sulfur

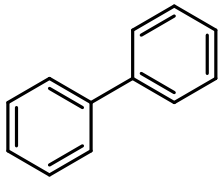
Various groups: 1960s







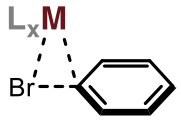
ylide product



aryl dimerization

LaRochelle, R. W.; Trost, B. M. J. Am. Chem. Soc. **1971**, 93, 6077.

Transition metal chemistry relies on d-orbital participation



Oxidative addition

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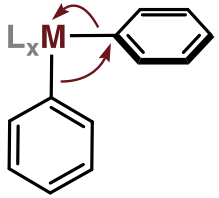
- **Increase in valence electrons**
  Decrease in d-electrons



Reductive elimination

- **Oxidation state decrease of –2**
- **Decrease in valence electrons**
  Increase in d-electrons

18 32

S

Sulfur

Various groups: 1960s

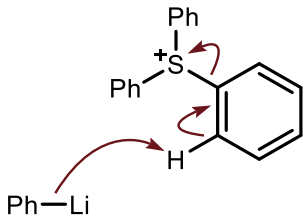
protonation

aryl dimerization
>99% yield

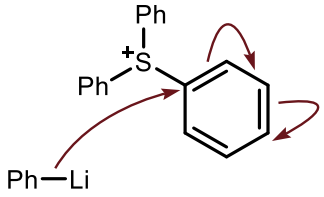
LaRochelle, R. W.; Trost, B. M. J. Am. Chem. Soc. **1971**, 93, 6077.

The curious case of triaryl sulfonium salts

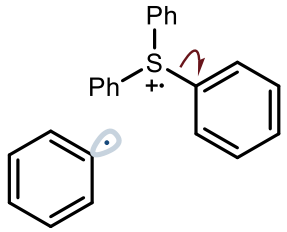
Benzyne



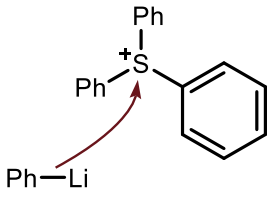
S_NAr



Radical



Sulfurane



Why are we observing aryl dimerization and what is the mechanism for its formation?

Trost: 1971

Single isomers obtained when using substituted aryls

↓

Evidence against benzyne

Retention of stereochemistry

↓

Evidence against radical

18 32

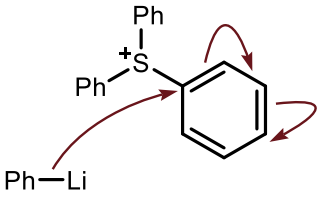
S

Sulfur

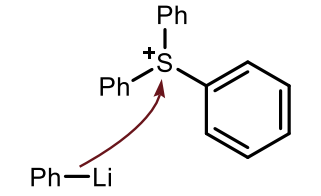
LaRochelle, R. W.; Trost, B. M. J. Am. Chem. Soc. **1971**, 93, 6077.

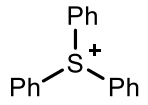
The curious case of triaryl sulfonium salts

S_NAr



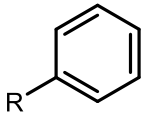
Sulfurane

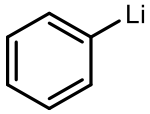




Organolithium

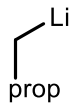
THF, –80 °C to rt



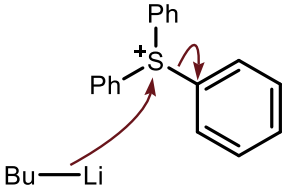


100% Ph-Ph

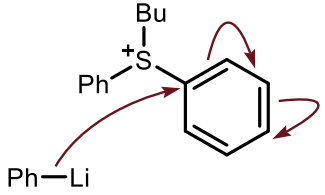
100% vinyl-Ph



50% Ph-Ph
0% Butyl-Ph



Ligand exchange

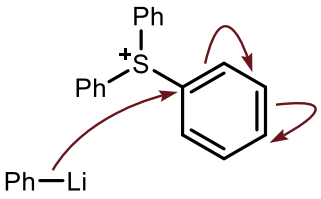


Potential for ligand exchange means we can't rule out S_NAr pathway

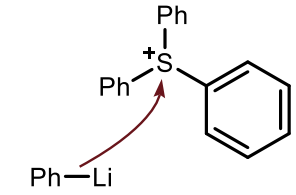
LaRochelle, R. W.; Trost, B. M. J. Am. Chem. Soc. **1971**, 93, 6077.

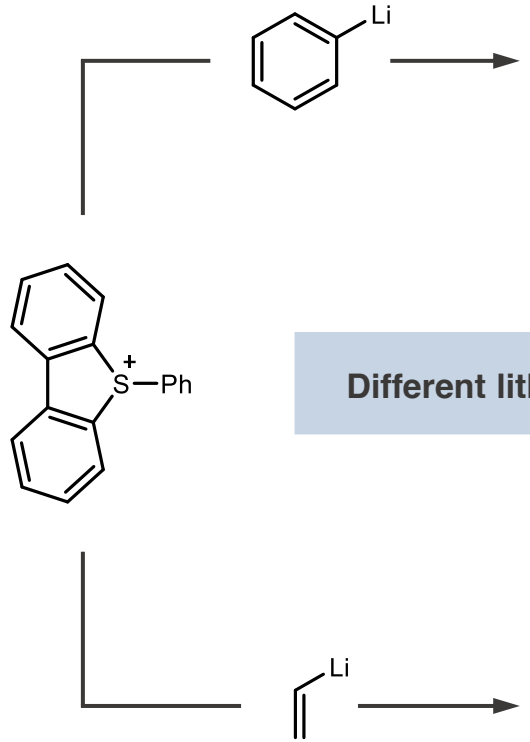
The curious case of triaryl sulfonium salts

S_NAr



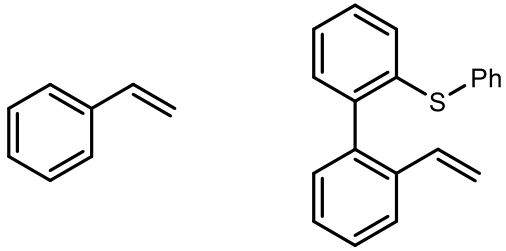
Sulfurane





Exclusive product

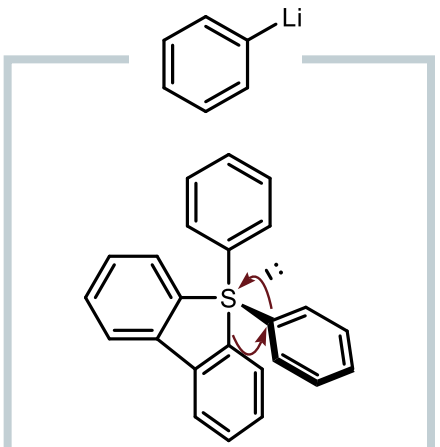
Different lithiums provide different selectivities



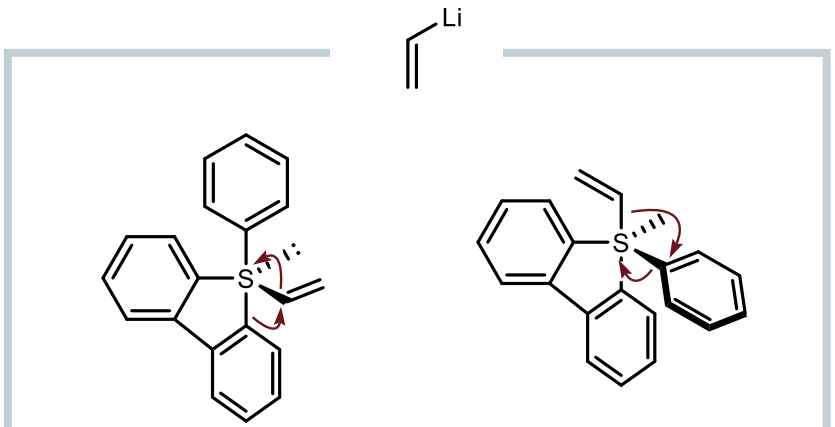
8:1 selectivity

LaRochelle, R. W.; Trost, B. M. J. Am. Chem. Soc. **1971**, 93, 6077.

Direct evidence for reductive coupling at sulfur

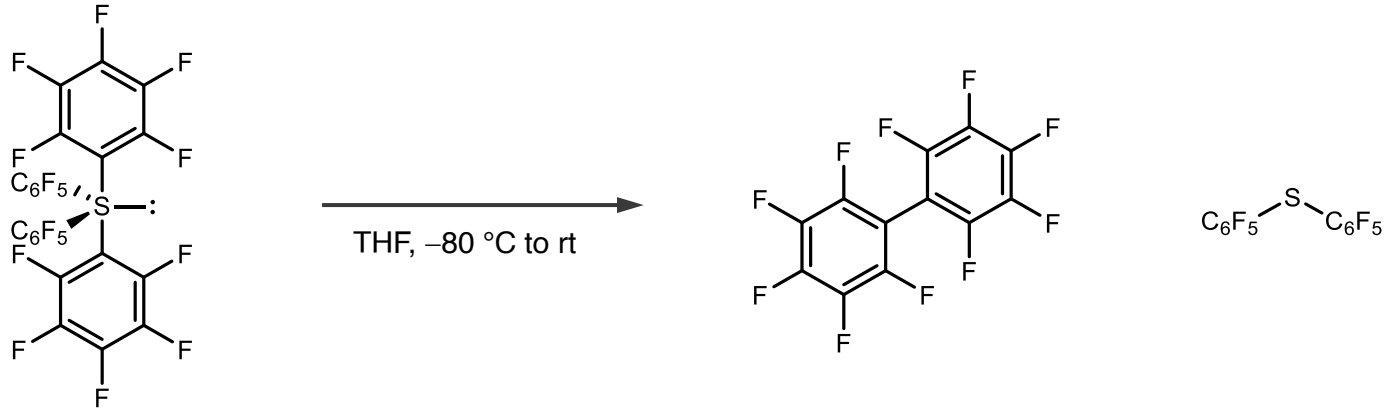


Single stereoisomer
apical-basal coupling



Two stereoisomers after addition
apical-basal coupling

Sheppard: 1971 Direct evidence for reductive coupling at sulfur



σ-sulfurane

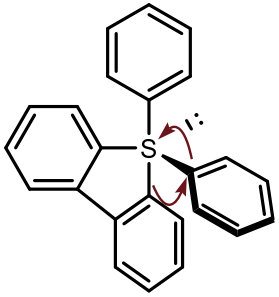
70% yield

71% yield

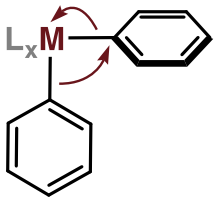
Sheppard, W. A.. J. Am. Chem. Soc. **1971**, 93, 5597

LaRochelle, R. W.; Trost, B. M. J. Am. Chem. Soc. **1971**, 93, 6077.

Ligand-coupling and reductive elimination



Sulfurane coupling



Reductive elimination

Sulfurane coupling and reductive elimination show remarkable mechanistic similarities

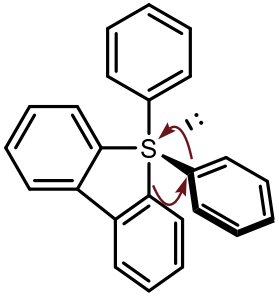
Coupling mechanism was expanded beyond sulfur and termed "ligand-coupling" around 1985 by Shigeru Oae

"In organometallic chemistry, the terms "reductive elimination" and "oxidative addition" have been used to describe many chemical phenomena… **most of these reactions can be understood in terms of ligand coupling**."

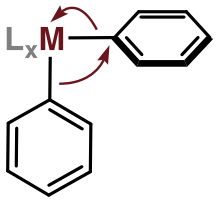
Ligand-coupling Reactions of Hypervalent Species
Shigeru Oae

Oae, S.; Uchida, Y. Acc. Chem. Res. **1991**, 24, 202.

Ligand-coupling and reductive elimination



Sulfurane coupling



Reductive elimination

Sulfurane coupling and reductive elimination show remarkable mechanistic similarities

Coupling mechanism was expanded beyond sulfur and termed "ligand-coupling" around 1985 by Shigeru Oae

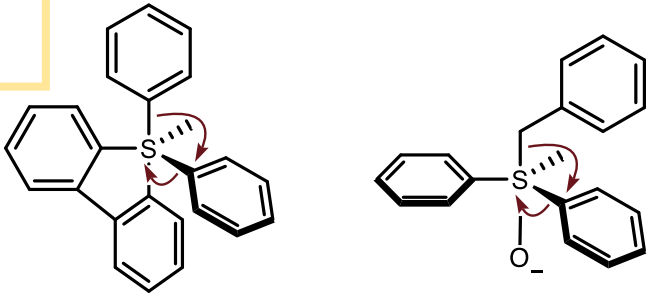
"**(Ligand-coupling reaction) is a new type of reaction and is different from widely used reductive elimination**, and is unique and specific for hypervalent compounds in general"

Organo Main Group Chemistry
Kin-Ya Akiba

Akiba, K.-Y. Organo Main Group Chemistry; John Wiley & Sons, Inc., 2011.

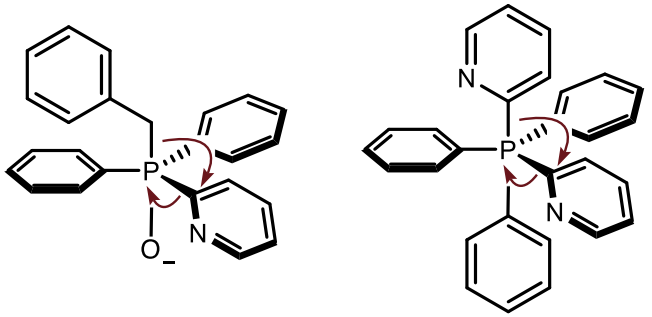
Ligand-coupling and reductive elimination

18 32
S
Sulfur



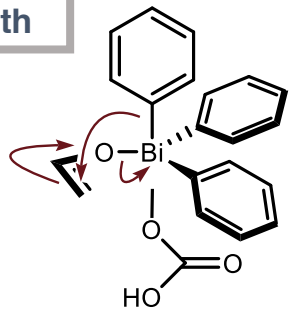
Sulfurane coupling

15 30
P
Phosphorus



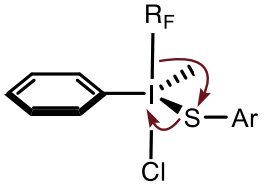
Phosphorane coupling

83 208
Bi
Bismuth



Bismuthorane coupling

53 126
I
Iodine



Iodane coupling

14 28
Si
Silicon

52 127
Te
Tellurium

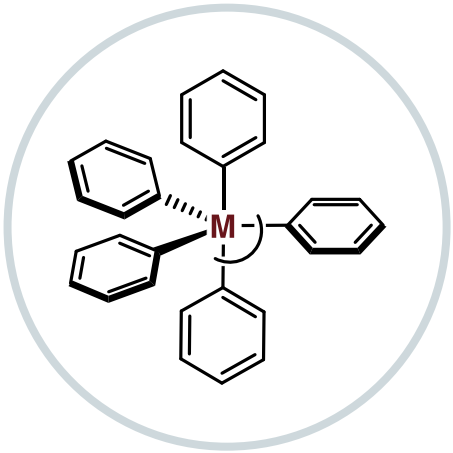
33 74
As
Arsenic

50 118
Sn
Tin

Additional Elements demonstrated to undergo ligand-coupling

Oae, S.; Uchida, Y. Acc. Chem. Res. **1991**, 24, 202.

Ligand-coupling is distinct from reductive elimination



- **Limited to main-group elements**
- **Requires hypervalency of central atom**
- **Concerted coupling process**
- **Allowed couplings are element and geometry dependent**

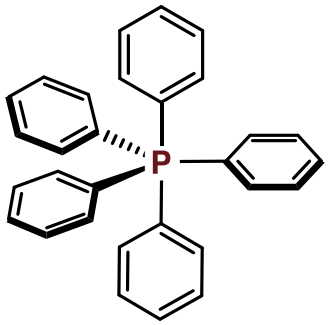
Finet, J.-P. Ligand Coupling Reactions with Heteroatomic Compounds, 1st ed.; Tetrahedron Organic Chemistry; Elsevier, 1998; Vol. 18.

Oae, S.; Uchida, Y. Acc. Chem. Res. **1991**, 24, 202.

Accessing hypervalent scaffolds

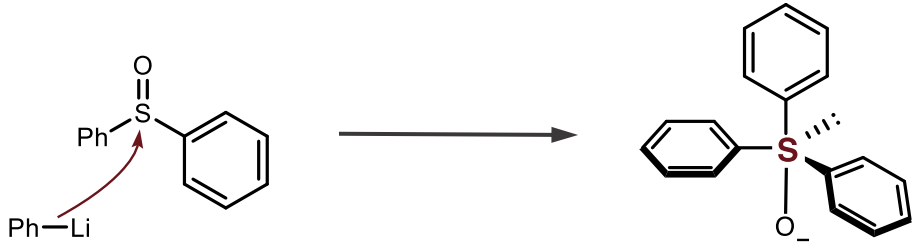
Hypervalent structures for ligand-coupling are accessed three ways

Stable compound



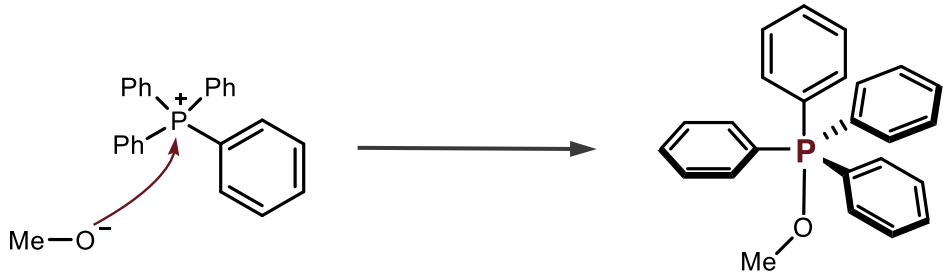
- Easy to handle
- Harsh conditions to trigger ligand-coupling

In situ addition to π bond



- Precursors typically bench stable
- Organometallic reagents often required

In situ addition to charged species or σ bond



- Established synthesis of precursors
- Alkoxide addition leads to complications in coupling

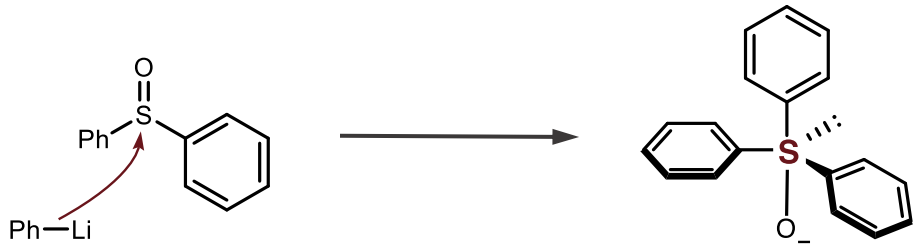
Akiba, K.-Y. Ligand Coupling Reaction. In Organo Main Group Chemistry; John Wiley & Sons, Inc., 2011.

Accessing hypervalent scaffolds

Hypervalent structures for ligand-coupling are accessed three ways

Two synthetically useful strategies

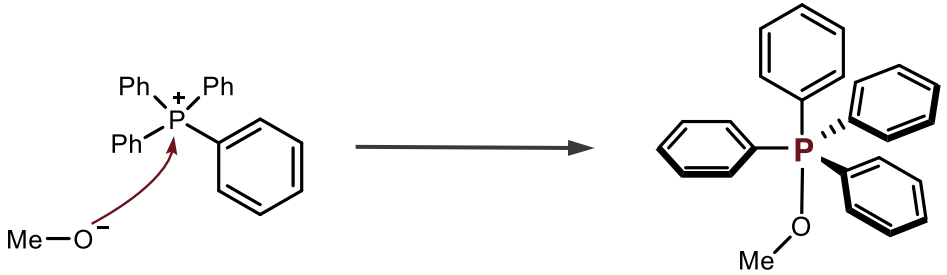
In situ addition to π bond



Precursors typically bench stable

Organometallic reagents often required

In situ addition to charged species or σ bond



Established synthesis of precursors

Alkoxide addition leads to complications in coupling

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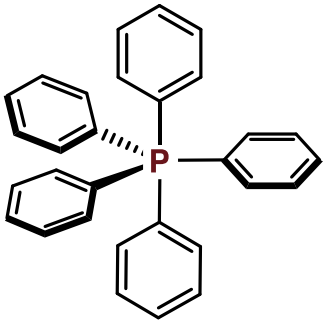
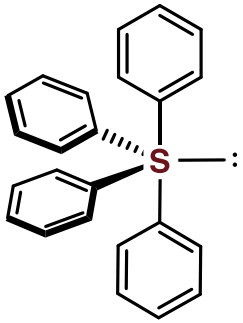
Hypervalency is the key to ligand-coupling

Hypervalent molecules: formal violation of the octet rule for bonding

3d orbitals are not involved in valence expansion



PPh_5
Pentaphenylphosphorane
"10 valence electrons"



SPh_4
Tetraphenylsulfurane
"10 valence electrons"

"Far too often have **3d orbitals been invoked as a kind of theoretical *deus ex machina*** to account for facts apparently otherwise inexplicable"

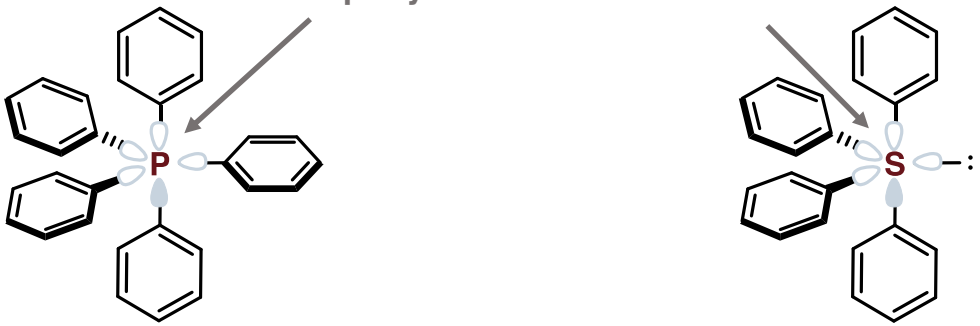
Molecular Orbital Theory of Pentacoordinate Phosphorus
Roald Hoffmann

Hoffmann, R.; Howell, J. M.; Muetterties, E. L..J. Am. Chem. Soc. 1972, 94, 3047.

Hypervalency is the key to ligand-coupling

Hypervalent molecules: formal violation of the octet rule for bonding

sp^2 hybridized central atom



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Oae, S. Pure and Applied Chemistry **1996**, 68, 805.

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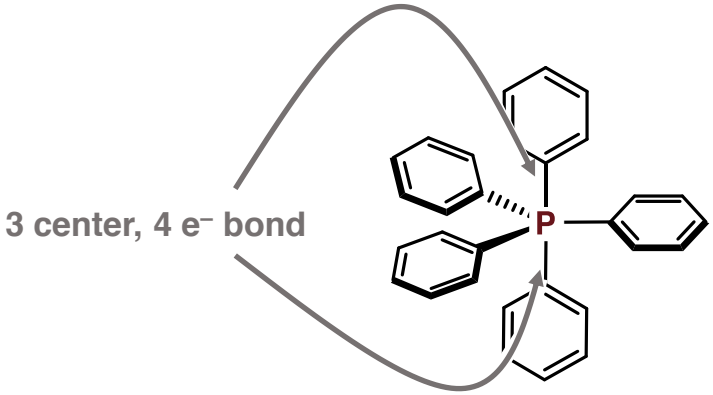

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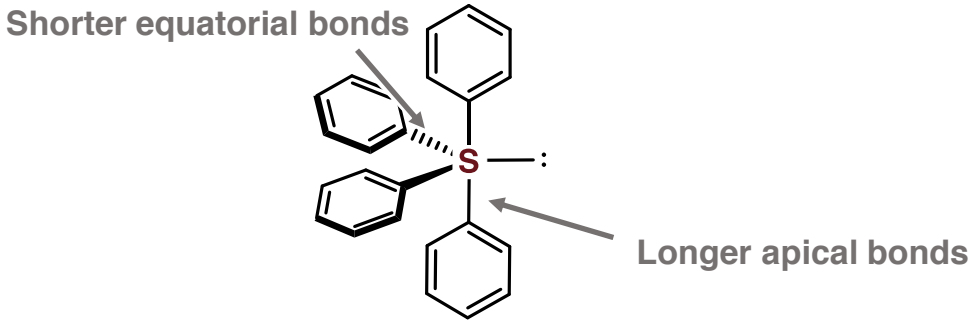

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Tetraphenylsulfurane

Apical bond described as distinct from equatorial bonds

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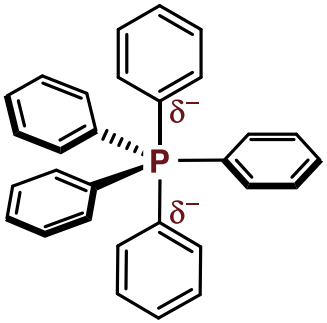

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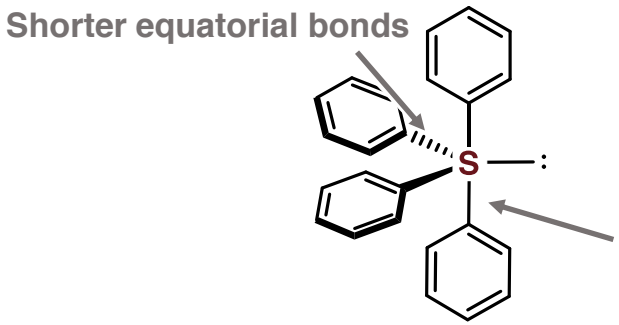
Pentaphenylphosphorane



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Apical bond described as distinct from equatorial bonds… and polarized in comparison

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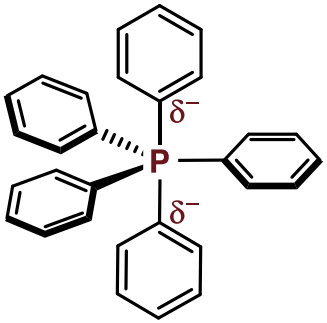

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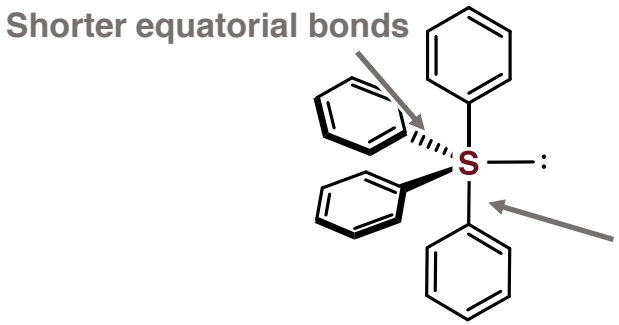


SPh_4
Tetraphenylsulfurane

Apical bond described as distinct from equatorial bonds… and polarized in comparison

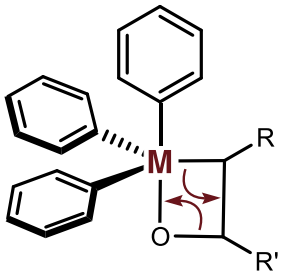
Return to normal valency through extrusion of one pair of electrons provides ligand-coupling driving force in the forward direction

Oae, S. Pure and Applied Chemistry **1996**, 68, 805.

Hypervalent molecules have three reactivity pathways

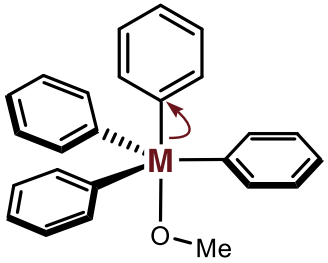
Three pathways can occur to return to normal valency

Self-decomposition



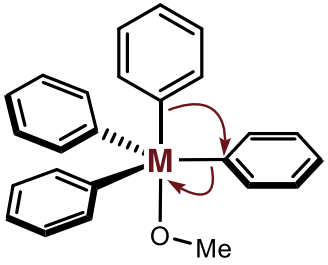
Wittig reaction pathway

Ligand-exchange



S_N2-like outcome

Ligand-coupling



Reductive coupling

Akiba, K.-Y. Organo Main Group Chemistry; John Wiley & Sons, Inc., 2011.

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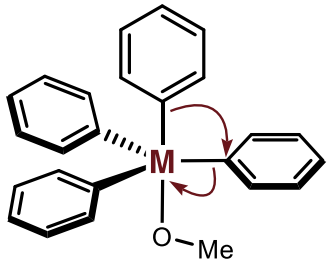

Reductive coupling

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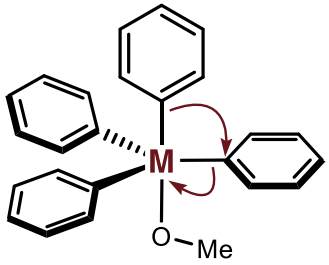
Hypervalent molecules have three reactivity pathways

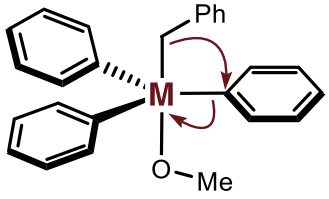
Ligand-coupling can occur through four mechanistic pathways

Ipso-ipso couplings



Homocoupling/Similar polarity: LC_H

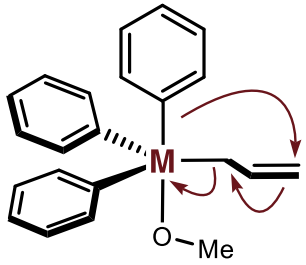
- **Synchronous pathway**



Heterocoupling/Different polarity: LC_N

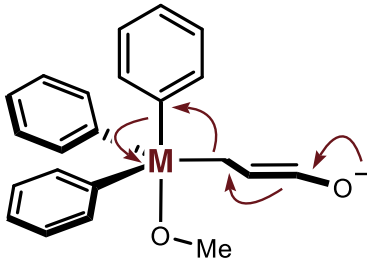
- **Asynchronous pathway**

Ipso-allyl couplings



S_N2' type process: LC_N

- **Standard polarity**



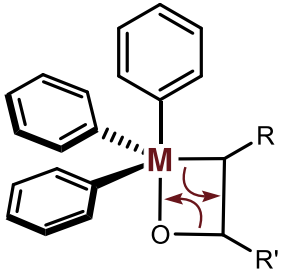
Apical electrophile: LC_E

- **Unusual equatorial nucleophile**

Akiba, K.-Y. Organo Main Group Chemistry; John Wiley & Sons, Inc., 2011.

Hypervalent molecules have three reactivity pathways

Self-decomposition



Wittig reaction pathway

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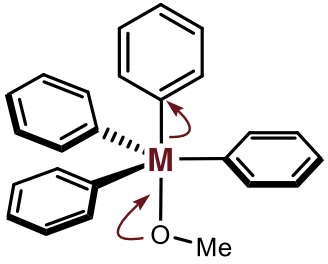
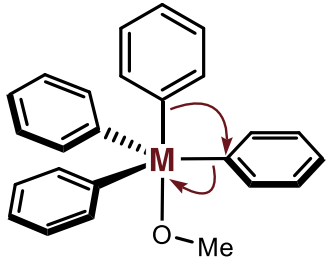


S_N2-like outcome

Ligand-coupling



Reductive coupling

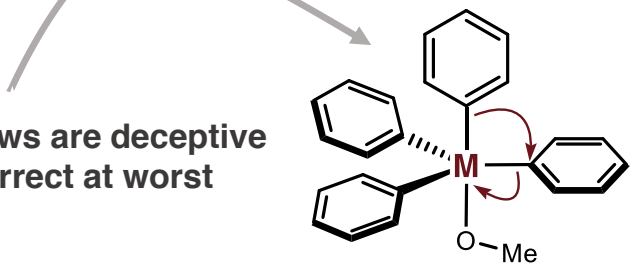
Two pathways compete directly with each other

How can we tune this reactivity?

Akiba, K.-Y. Organo Main Group Chemistry; John Wiley & Sons, Inc., 2011.

Geometry impacts the couplings available

Ligand-coupling



These RE type arrows are deceptive at best and incorrect at worst

Reductive coupling

Hoffmann, R.; Howell, J. M.; Muetterties, E. L..J. Am. Chem. Soc. **1972**, 94, 3047.

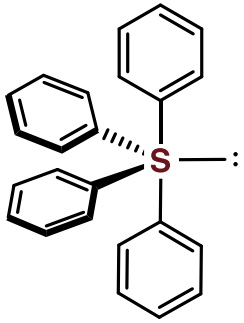
Geometry impacts the couplings available

Like transition metals, ligands position around the central atom plays a role in couplings

18 32

S

Sulfur

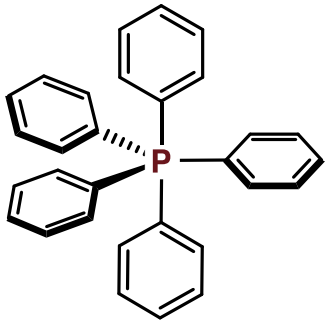


D3h

15 30

P

Phosphorus



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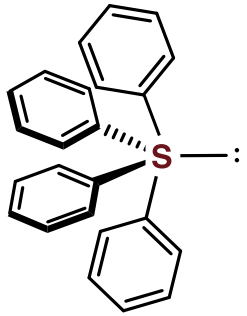
S

Sulfur

distorted trigonal bipyramidal:



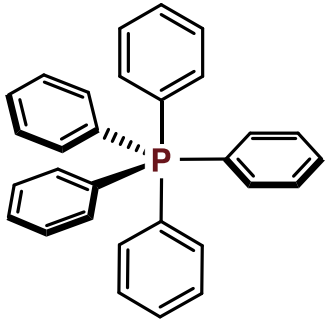
C4v

15 30

P

Phosphorus

trigonal bipyramidal:



D3h

Trost, B. M.; Arndt, H. C. J. Am. Chem. Soc. **1973**, 95, 5288.

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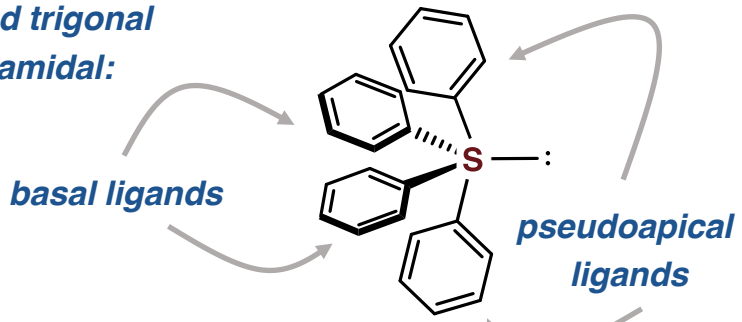

C4v

15 30

P

Phosphorus

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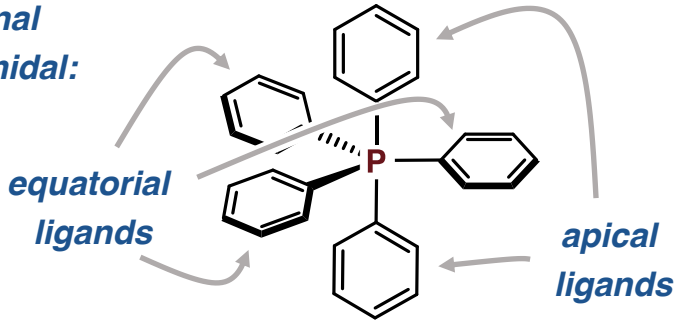

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18 32
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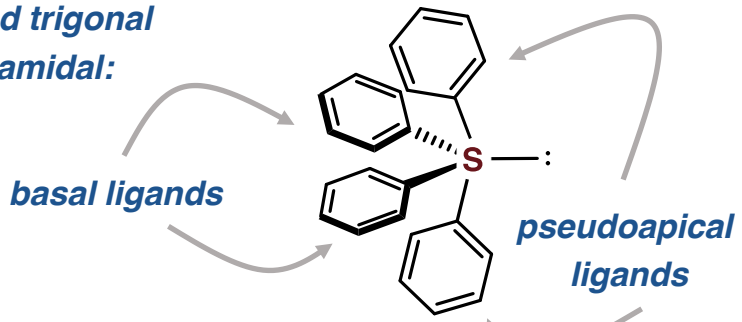
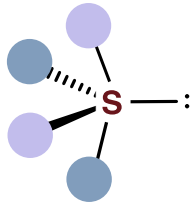
Sulfur

distorted trigonal bipyramidal:



C4v

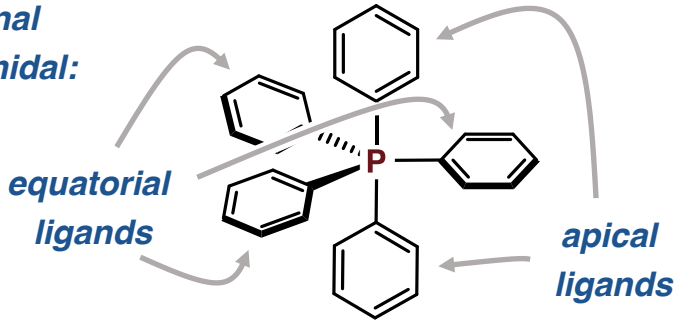
Orbital overlap



WH Allowed coupling: Apical-basal

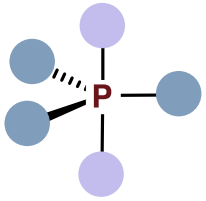
15 30
P
Phosphorus

trigonal bipyramidal:



D3h

Orbital overlap



WH Allowed coupling: Apical-apical Equatorial-equatorial

Trost, B. M.; Arndt, H. C. J. Am. Chem. Soc. **1973**, 95, 5288.

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Presence of π orbitals allows for "forbidden" ligand-couplings to occur

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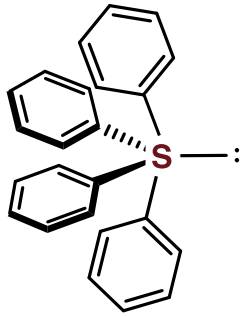
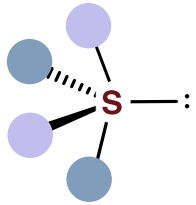
S
Sulfur



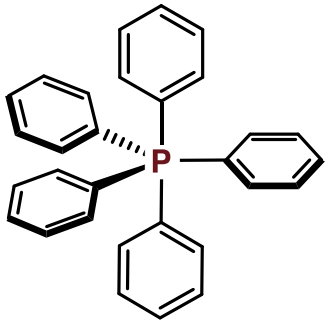
C4v

Orbital overlap



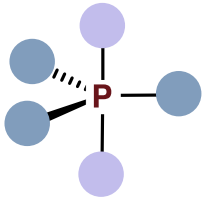
WH Allowed coupling:
Apical-basal

15 30
P
Phosphorus



D3h

Orbital overlap



WH Allowed coupling:
Apical-apical
Equatorial-equatorial

Oae, S.; Uchida, Y. Acc. Chem. Res. 1991, 24, 202. .

Hilton, M. C.; Zhang, X.; Boyle, B. T.; Alegre-Requena, J. V.; Paton, R. S.; McNally, A. Science **2018**, 362, 799.

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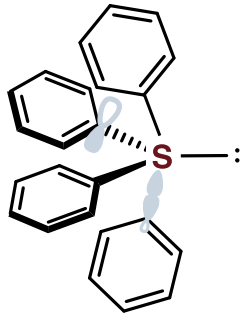
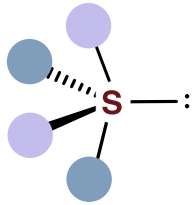


C4v

Orbital overlap

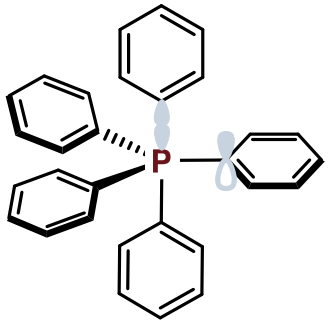


WH Allowed coupling:
Apical-basal

15 30

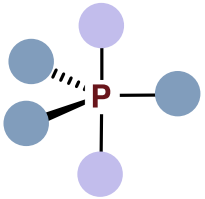
P

Phosphorus



D3h

Orbital overlap



WH Allowed coupling:
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Equatorial-equatorial

Oae, S.; Uchida, Y. Acc. Chem. Res. 1991, 24, 202. .

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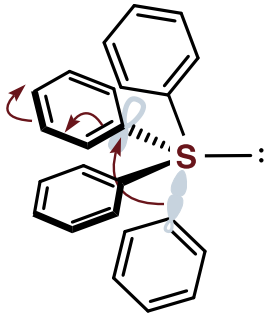
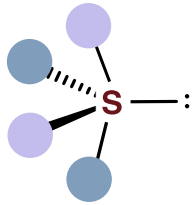
18 32
S
Sulfur



C4v

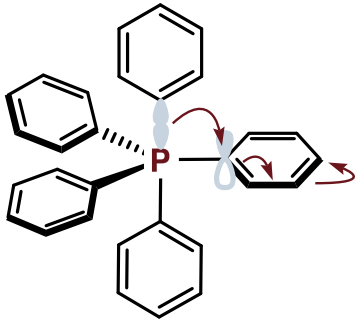
Asynchronous coupling via Meisenheimer-like intermediate

Orbital overlap



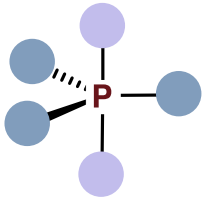
WH Allowed coupling: Apical-basal

15 30
P
Phosphorus



D3h

Orbital overlap



WH Allowed coupling: Apical-apical Equatorial-equatorial

Oae, S.; Uchida, Y. Acc. Chem. Res. 1991, 24, 202. .

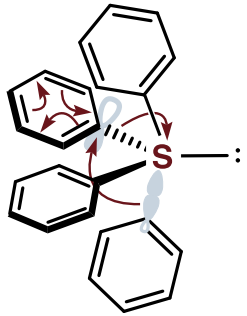
Hilton, M. C.; Zhang, X.; Boyle, B. T.; Alegre-Requena, J. V.; Paton, R. S.; McNally, A. Science **2018**, 362, 799.

The rules are more like guidelines anyways…

Presence of π orbitals allows for "forbidden" ligand-couplings to occur

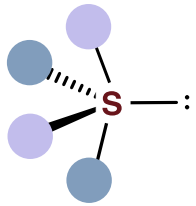
18 32
S
Sulfur

WH forbidden coupling: Trans Apical-basal



C4v

Orbital overlap

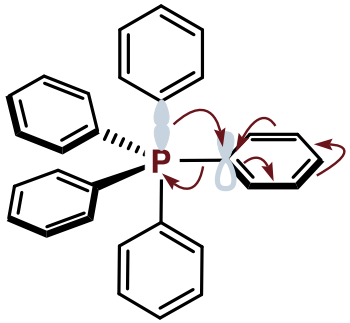


WH Allowed coupling: Apical-basal

Asynchronous coupling via Meisenheimer-like intermediate

15 30
P
Phosphorus

WH forbidden coupling: Apical-equatorial



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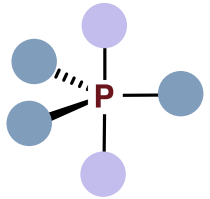

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Geometry impacts the couplings available

Like transition metals, ligands orientation around the central atom plays a role in couplings

18	32
S	
Sulfur	

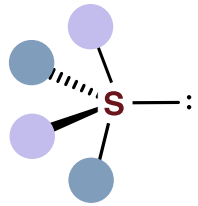
53	126
I	
Iodine	

14	28
Si	
Silicon	

52	127
Te	
Tellurium	

Lone pair containing (distorted C4v)

Orbital overlap



Allowed coupling:
Apical-basal

Non-lone pair containing (D3h)

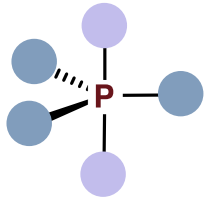
15	30
P	
Phosphorus	

83	208
Bi	
Bismuth	

33	74
As	
Arsenic	

51	121
Sb	
Antimony	

Orbital overlap



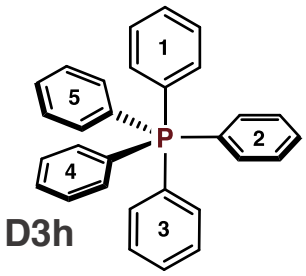
Allowed coupling:
Apical-apical
Equatorial-equatorial

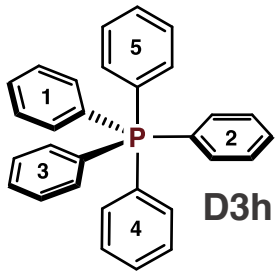
Trost, B. M.; Arndt, H. C. J. Am. Chem. Soc. **1973**, 95, 5288.

Hoffmann, R.; Howell, J. M.; Muetterties, E. L..J. Am. Chem. Soc. **1972**, 94, 3047.

Ligands on hypervalent species are not frozen in a single position

Ligands can "migrate" between positions on hypervalent species





Orientation for ligands can be manipulated through two rotation processes:

Berry pseudorotation and turnstile processes

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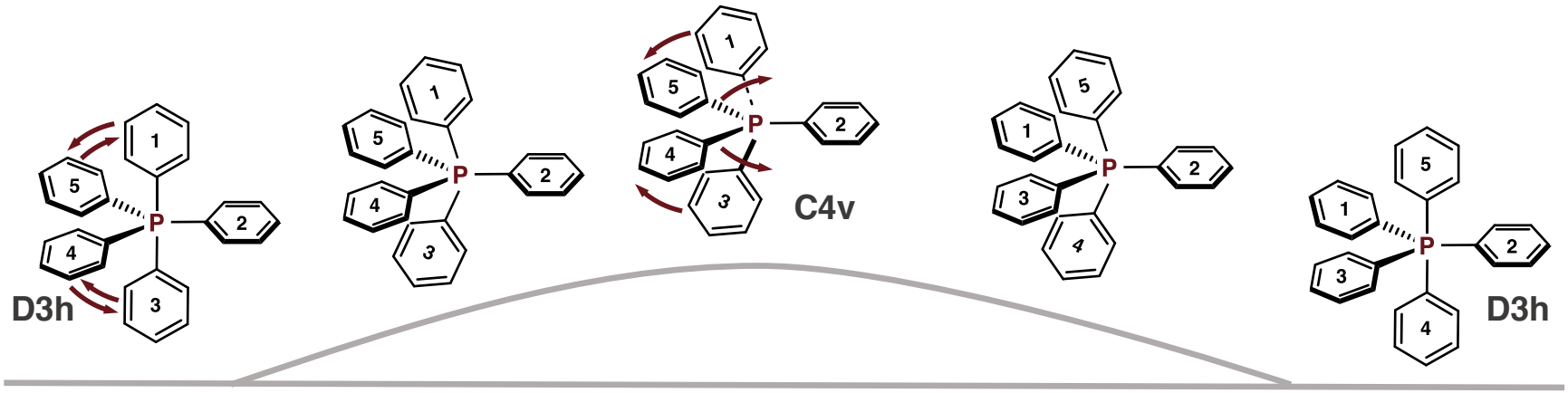
Berry pseudorotation ψ:

allows for apical and equatorial ligands to interconvert

Low barriers of <3 kcal/mol but goes through molecular geometry rearrangement

Does not actually involve rotational motion



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Ligands on hypervalent species are not frozen in a single position

Turnstile rotation:

allows for apical and equatorial ligands to interconvert

Higher barriers (5-10 kcal/mol) and viewed as less likely to occur

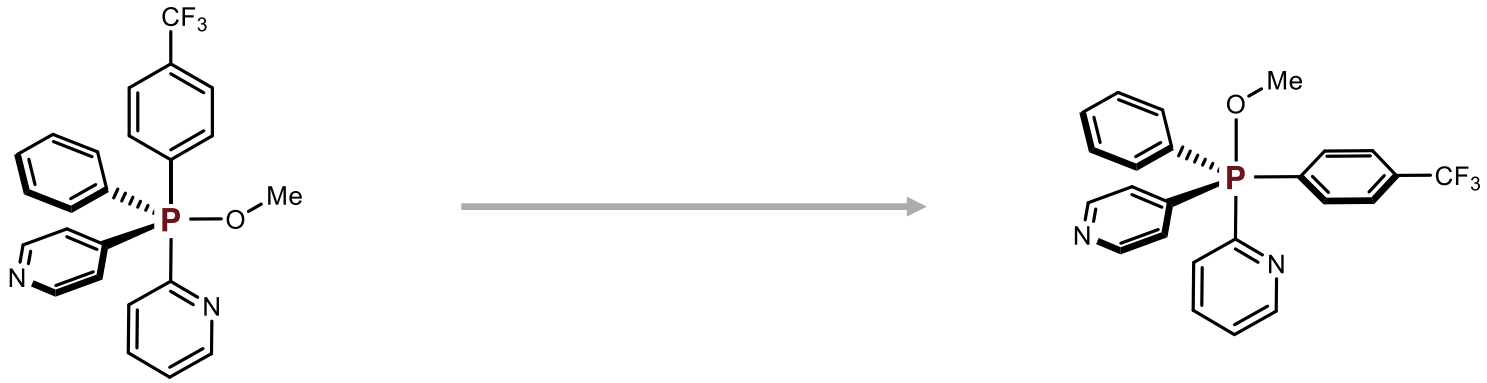
Occurs through physical rotation of pentacoordinated molecule

Orientation for ligands can be manipulated through two rotation processes:

Berry pseudorotation and turnstile processes

Ugi, I.; Marquarding, D.; Klusacek, H.; Gillespie, P.; Ramirez, F. Acc. Chem. Res. **1971**, 4, 288.

Rotation has important considerations for coupling selectivity



What is the most stable form of this phosphorane?

Equatophilicity: more electron rich and π ligands favor equatorial positions

Apicophilicity: more electron-withdrawing groups favor apical positions

Schmutzler, R. Ange. Chem. Int. Ed. **1965**, 4, 496.

Ugi, I.; Marquarding, D.; Klusacek, H.; Gillespie, P.; Ramirez, F. Acc. Chem. Res. **1971**, 4, 288.

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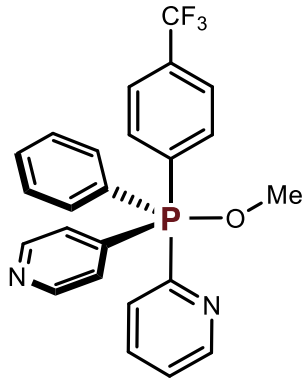

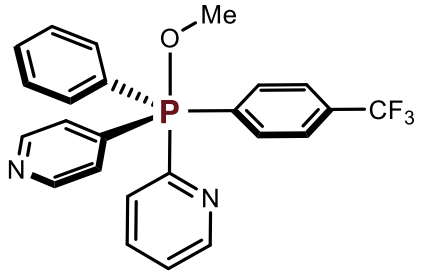

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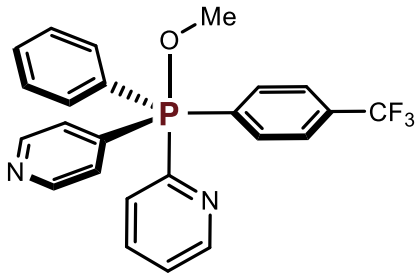

What would we expect to be the ligand-coupling products?

Boyle, B. T.; Hilton, M. C.; McNally, A J. Am. Chem. Soc. **2019**, 141, 15441.

Hilton, M. C.; Zhang, X.; Boyle, B. T.; Alegre-Requena, J. V.; Paton, R. S.; McNally, A. Science **2018**, 362, 799.

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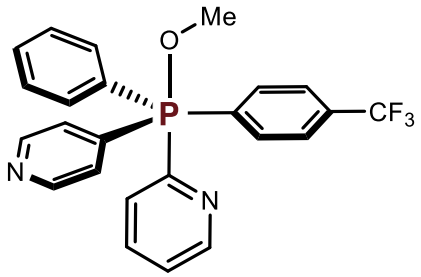
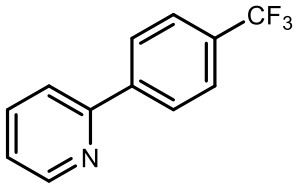
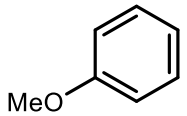


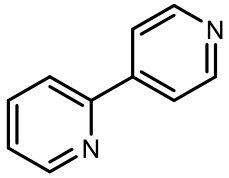
What would we expect to be the ligand-coupling products?

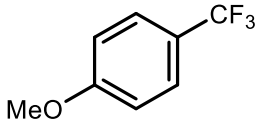
Equatorial selectivity can be rationalized by ability to stabilize charge buildup over transition state

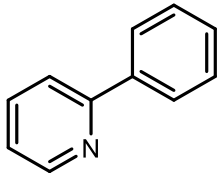
Possible coupling outcomes:

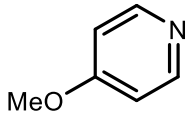












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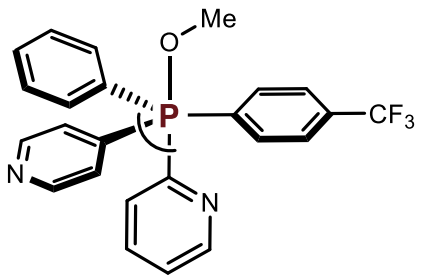
Hilton, M. C.; Zhang, X.; Boyle, B. T.; Alegre-Requena, J. V.; Paton, R. S.; McNally, A. Science **2018**, 362, 799.

Coupling selectivity is governed by electronic effects



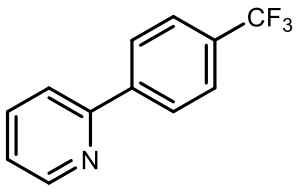
What would we expect to be the ligand-coupling products?

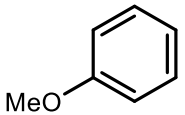
Equatorial selectivity can be rationalized by ability to stabilize charge buildup over transition state

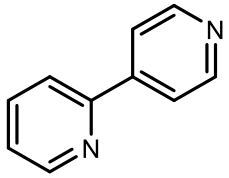
Why do we not observe C-O coupling products?

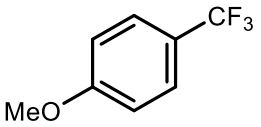
Exclusive product

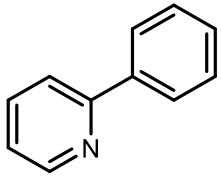
Possible coupling outcomes:

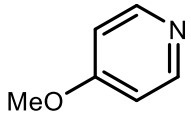












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Coupling selectivity is governed by stereoelectronic effects

In symmetrical hypervalent structures, apical ligands share bond lengths and polarization

Appleton, T. G.; Clark, H. C.; Manzer, L. E. Coordination Chemistry Reviews **1973**, 10, 335–422..

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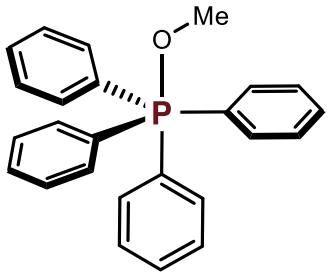

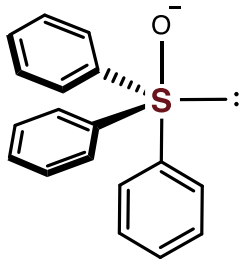

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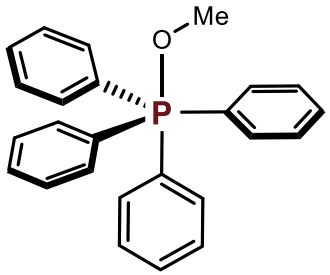
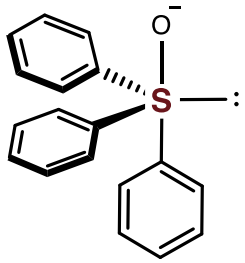
Need to consider influence of apical ligands on each other (trans influence)





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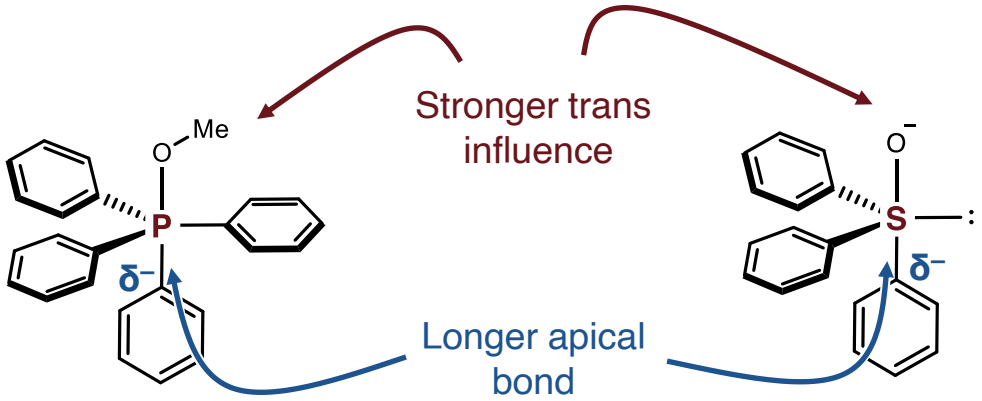

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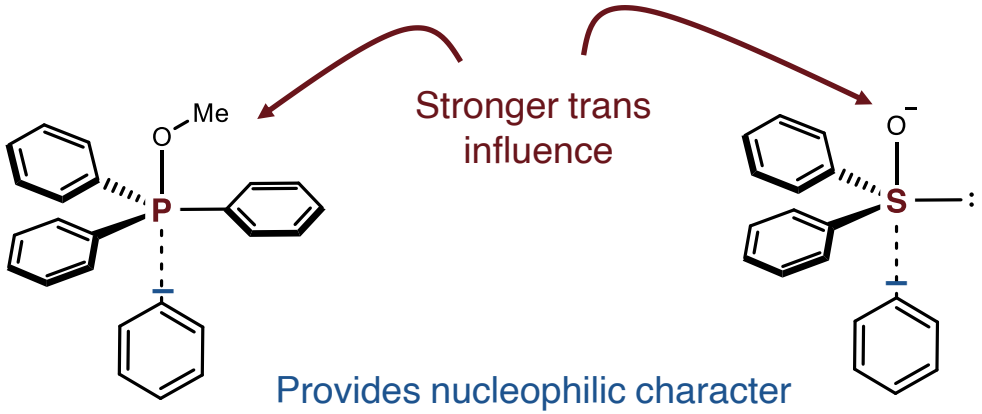

In symmetrical hypervalent structures, apical ligands share bond lengths and polarization

How does reactivity change when one apical ligand is differed?

Trans affect leads to undesired ligand exchange if dissociation outcompetes ligand coupling

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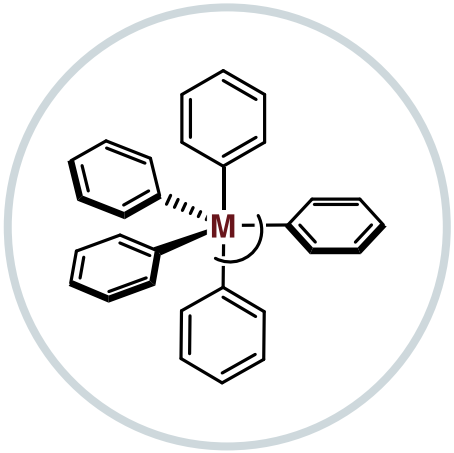
Hilton, M. C.; Zhang, X.; Boyle, B. T.; Alegre-Requena, J. V.; Paton, R. S.; McNally, A. Science **2018**, 362, 799.

Ligand-coupling reactivity summary



- **Limited to main-group elements**
- **Requires hypervalency of central atom**
- **Concerted coupling process**
- **Allowed couplings are element and geometry dependent**

- **Driving force = return to normal valency**
- **“Concerted” process can be asynchronous, enabling WH forbidden couplings**
- **(Pseudo)rotation processes play a role in orientation of ligands**
- **Kinetic and thermodynamic trans affects lead to selective coupling of single apical ligand**
- **Both apical and equatorial partners need to be able to accept electron density over the reaction**

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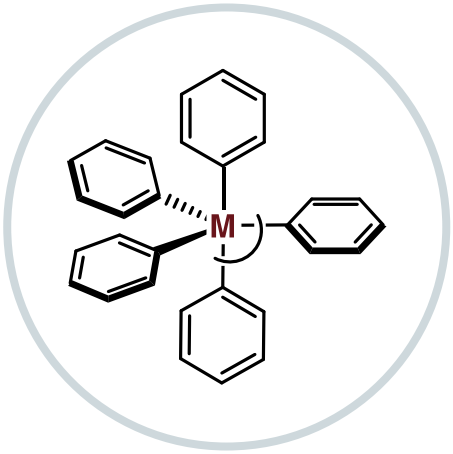
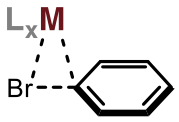
Hilton, M. C.; Zhang, X.; Boyle, B. T.; Alegre-Requena, J. V.; Paton, R. S.; McNally, A. Science **2018**, 362, 799.

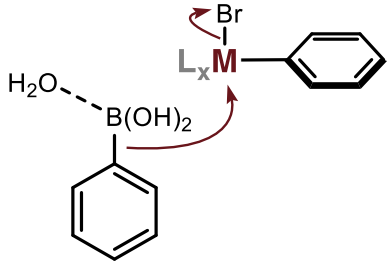
Where does ligand-coupling find use?



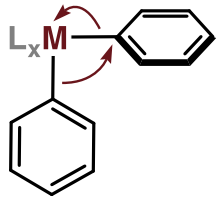
Fundamental processes:



Oxidative addition



Transmetalation

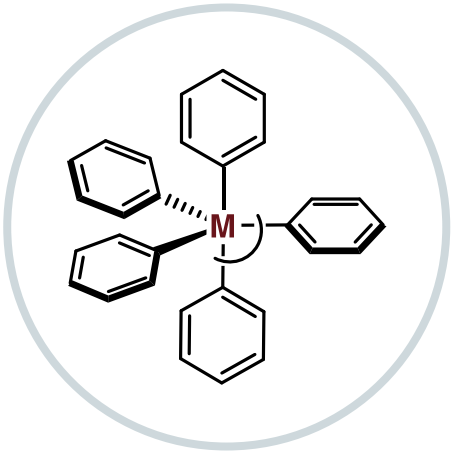


Reductive elimination

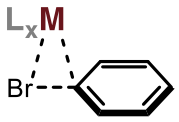
To understand the applications of ligand-coupling, we need to look at oxidative addition/transmetalation

Hartwig, J. F. Organotransition Metal Chemistry - From Bonding to Catalysis, 1st ed.; University Science Books, 2010.

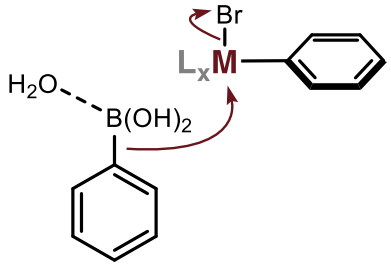
Where does ligand-coupling find use?



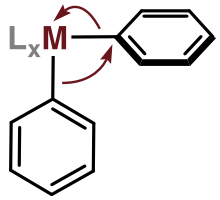
Fundamental processes:



Oxidative addition



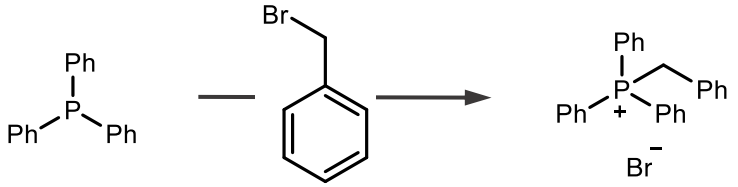
Transmetalation



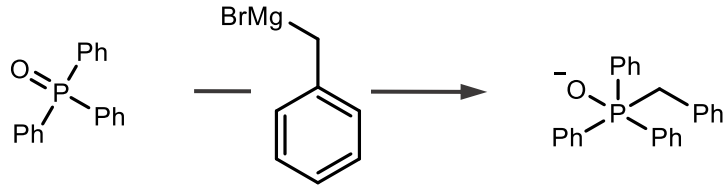
Reductive elimination

To understand the applications of ligand-coupling, we need to look at oxidative addition/transmetalation

Oxidative ligation aka S_N2 or S_NAr



"Transmetalation"



Hartwig, J. F. Organotransition Metal Chemistry - From Bonding to Catalysis, 1st ed.; University Science Books, 2010.

Commentary on ligand coupling elements

Ligand coupling advantages

- Coupling selectivity easy to understand
- Lewis basic groups tolerated
- Tunable process
- Metal-free

Ligand coupling Challenges

- Limited coupling scopes
- Starting material synthesis
- Stochiometric coupling
- Metal-free

---

18 32
S
Sulfur

- High product yields
- Challenging unactivated sp^2 systems amenable
- Typically uses organometallics
- Starting material synthesis

15 30
P
Phosphorus

- Starting material synthesis
- Ease of phosphorane formation
- Ligand exchange problematic
- Product formation can be low yielding

83 208
Bi
Bismuth

- Unique reactivity
- Most “metal” like
- Starting material synthesis

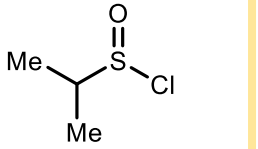
53 126
I
Iodine

- Expanded coupling possibilities
- Underexplored
- Side reactivies

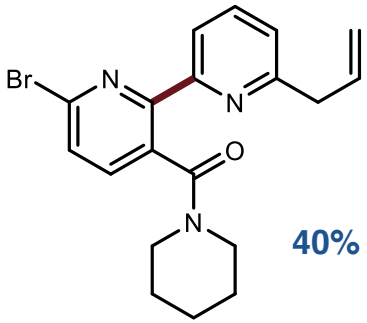
Oae, S.; Uchida, Y. Acc. Chem. Res. **1991**, 24, 202.

Ligand-coupling in recent literature

Heterobiaryl synthesis: Qin – ACIE 2020

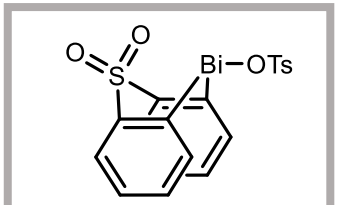


S(III) precursor

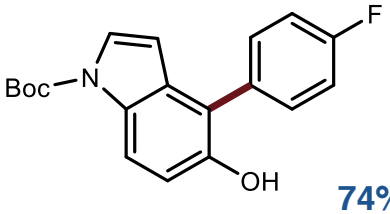


40%

Phenol arylation: Bell – Nat. Chem. 2020

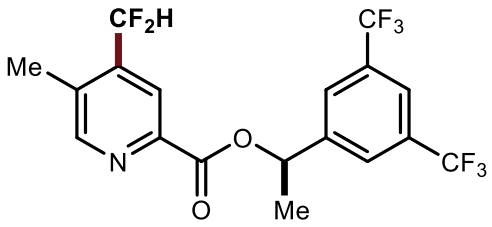


Bi(III) precursor

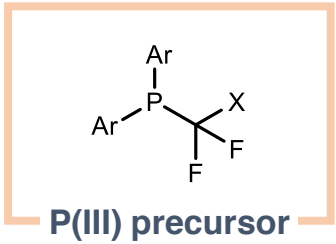


74%

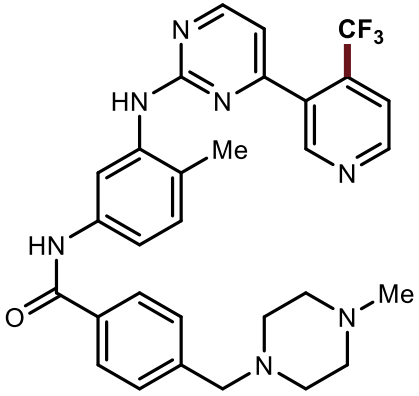
Di/Trifluoromethylation: McNally – Nature 2020



40%



P(III) precursor



44%

Jurrat, M.; Maggi, L.; Lewis, W.; Ball, L. T. Nat. Chem. **2020**, 12, 260.

Zhou, M.; Tsien, J.; Qin, T. Ange. Chem. Int. Ed. **2020**, 59, 7372.

Zhang, X.; Nottingham, K. G.; Patel, C.; Alegre-Requena, J. V.; Levy, J. N.; Paton, R. S.; McNally, A. Nature **2021**, 594, 217.

Ligand-coupling catalysis

Is catalysis possible through a ligand-coupling process?

Planas, O.; Wang, F.; Leutzsch, M.; Cornella, J. Science **2020**, 367, 313.

Oae, S.; Uchida, Y. Acc. Chem. Res. **1991**, 24, 202.

Ligand-coupling catalysis

83	208
Bi	
Bismuth	

15	30
P	
Phosphorus	

Josep Cornella: Max-Planck
Bismuth catalysis research area

Alex Radosevich: MIT
Phosphorus catalysis research area

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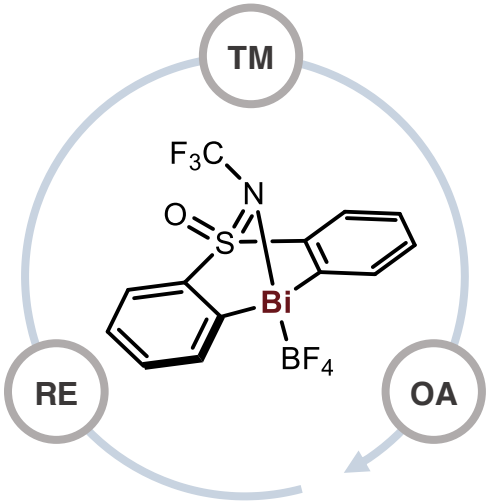
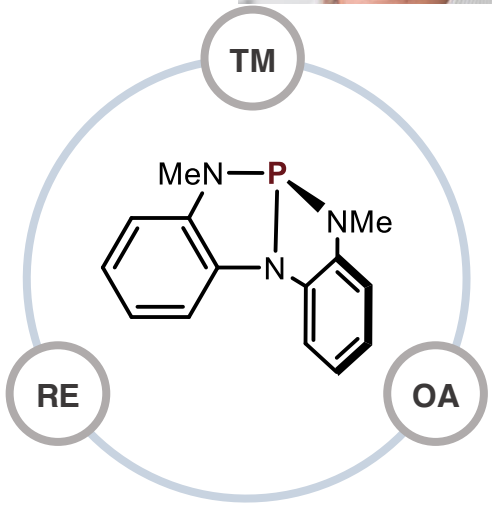
Ligand-coupling catalysis

83	208
Bi	
Bismuth	

15	30
P	
Phosphorus	





Planas, O.; Wang, F.; Leutzsch, M.; Cornella, J. Science **2020**, 367, 313.

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Ligand-coupling catalysis

83 208

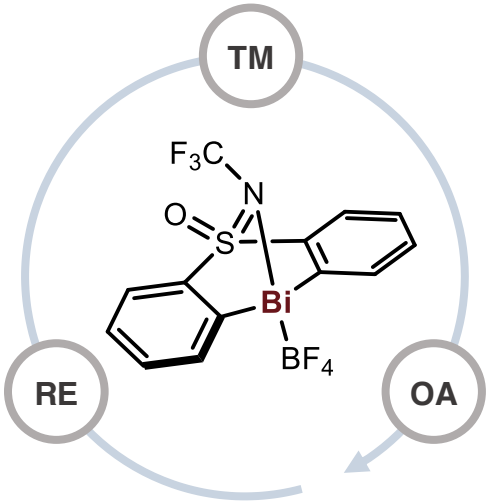
Bi

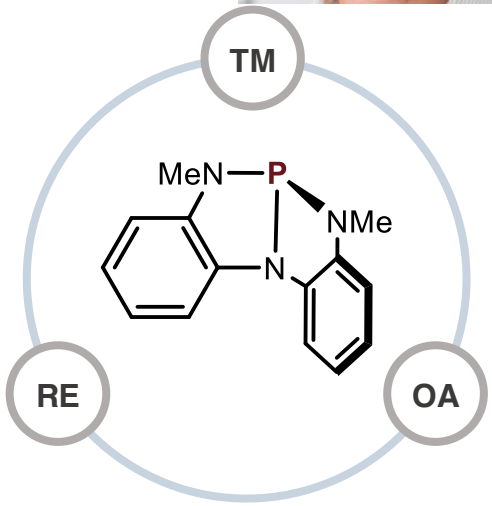
Bismuth

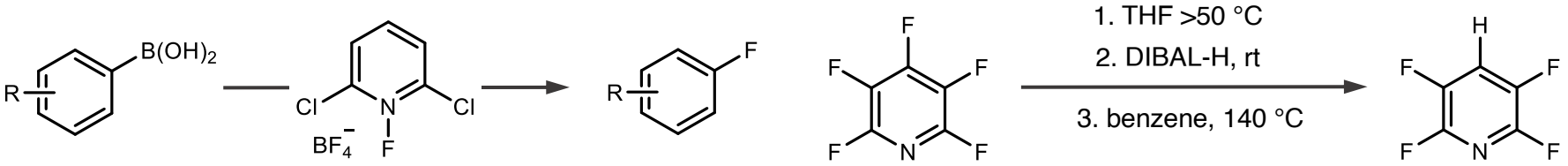
15 30

P

Phosphorus







Planas, O.; Wang, F.; Leutzsch, M.; Cornella, J. Science **2020**, 367, 313.

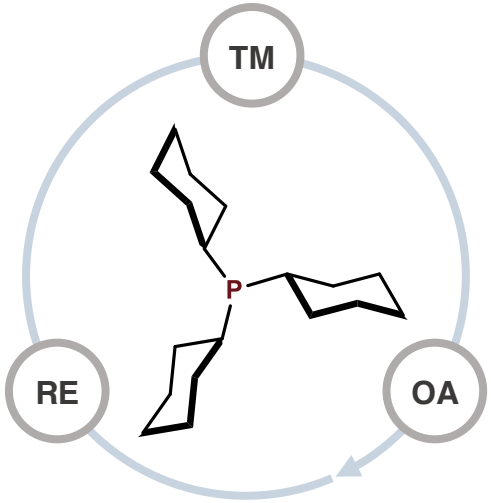
Lim, S.; Radosevich, A. T. J. Am. Chem. Soc. **2020**, 142, 16188.

Ligand-coupling catalysis…

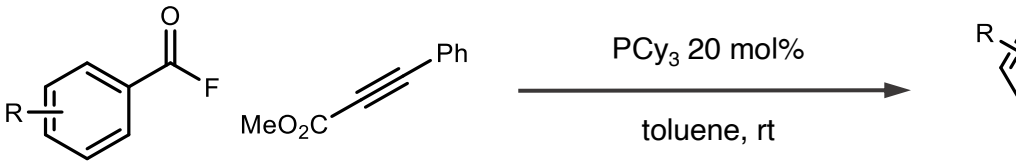
15 30

P

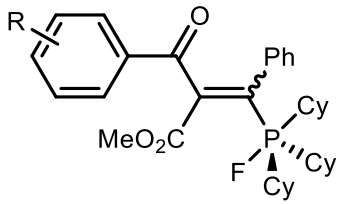
Phosphorus



Mamoru Tobisu: Rikkyo University
Phosphorus catalysis research area



Phosphorane intermediate



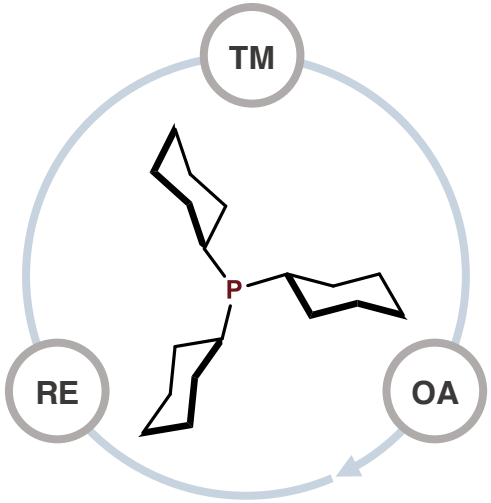
Fujimoto, H.; Kodama, T.; Yamanaka, M.; Tobisu, M. J. Am. Chem. Soc. **2020**, 142, 17323.

Ligand-coupling catalysis… or is it?

15 30

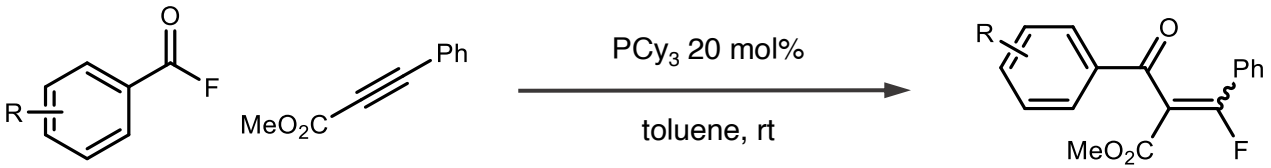
P

Phosphorus

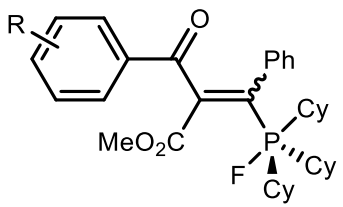


Mamoru Tobisu: Rikkyo University
Phosphorus catalysis research area

Ligand-coupling catalysis is complicated by alternate reaction pathways



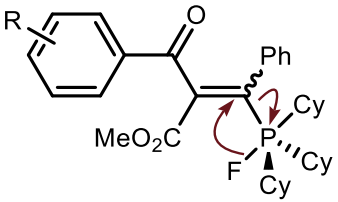
Phosphorane intermediate



Fujimoto, H.; Kodama, T.; Yamanaka, M.; Tobisu, M. J. Am. Chem. Soc. **2020**, 142, 17323.

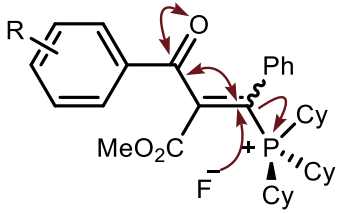
Ligand-coupling catalysis… or is it?

Phosphorane intermediate



Phosphorane ionization

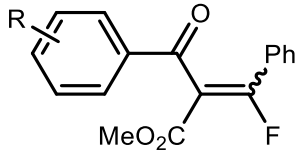
Phosphonium intermediate



Ligand Coupling

Two reaction pathways to provide same coupling product

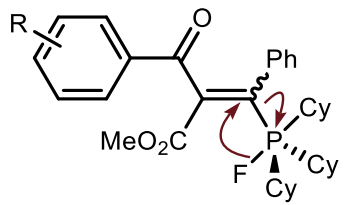
$E1_{CB}$



Fujimoto, H.; Kodama, T.; Yamanaka, M.; Tobisu, M. J. Am. Chem. Soc. **2020**, 142, 17323.

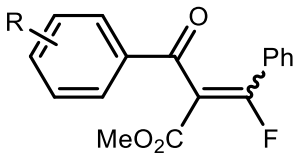
Ligand-coupling catalysis… or is it?

Phosphorane intermediate



DFT calculations: 6.9 kcal/mol barrier

Ligand Coupling

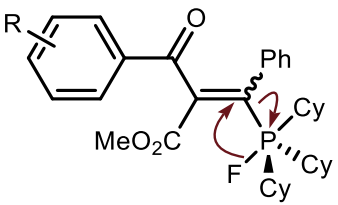


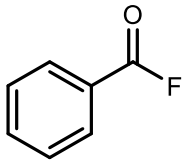
$\Delta G_{\omega B97XD/6\text{-}31+G(d,p)}$ with PCM(toluene)

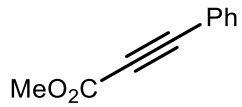
Fujimoto, H.; Kodama, T.; Yamanaka, M.; Tobisu, M. J. Am. Chem. Soc. **2020**, 142, 17323.

Ligand-coupling catalysis… or is it?

Phosphorane intermediate

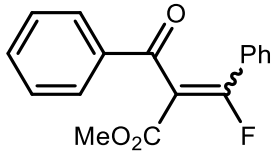






PCy_3 20 mol%

Solv., rt

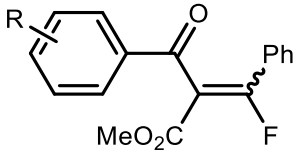


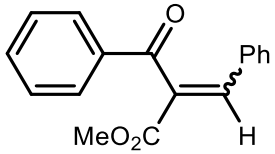
Toluene: **61% yield**

MeCN: **trace**

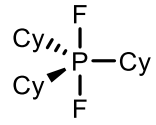
DFT calculations: 6.9 kcal/mol barrier

Ligand Coupling





34% yield



28% yield

Is this proof for ligand-coupling?

$\Delta G_{\omega B97XD/6\text{-}31+G(d,p)}$ with PCM(toluene)

Fujimoto, H.; Kodama, T.; Yamanaka, M.; Tobisu, M. J. Am. Chem. Soc. **2020**, 142, 17323.

Ligand-coupling catalysis

83 208
Bi
Bismuth

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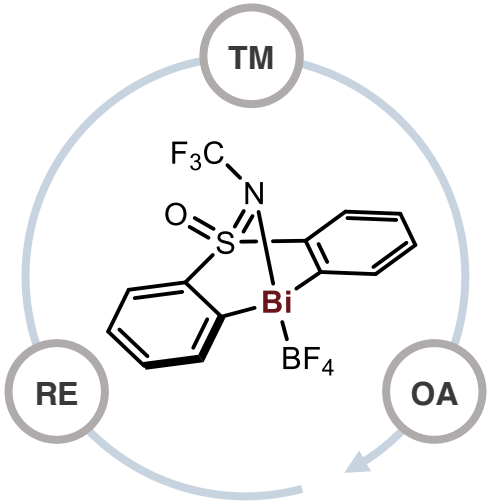
Bismuth catalysis research area

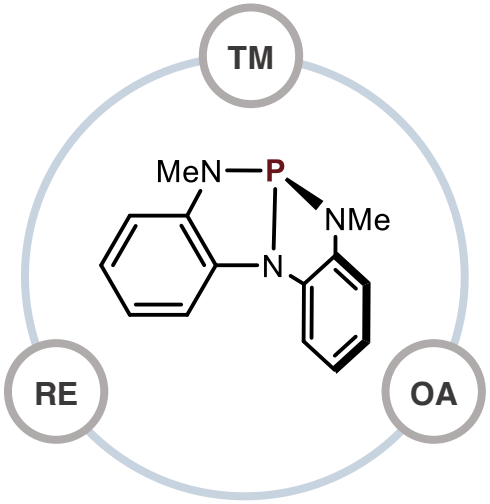
15 30
P
Phosphorus

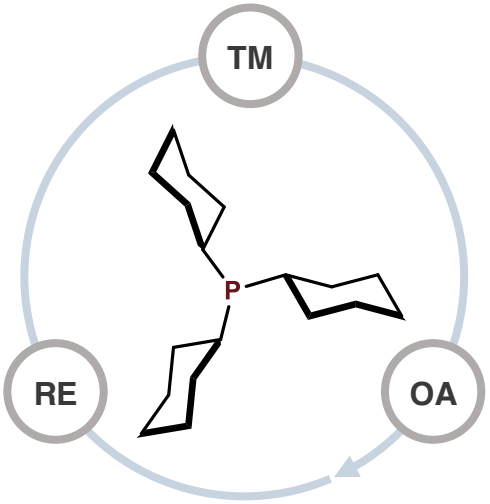
Alex Radosevich: MIT
Phosphorus catalysis research area

15 30
P
Phosphorus

Mamoru Tobisu: Rikkyo University
Phosphorus catalysis research area

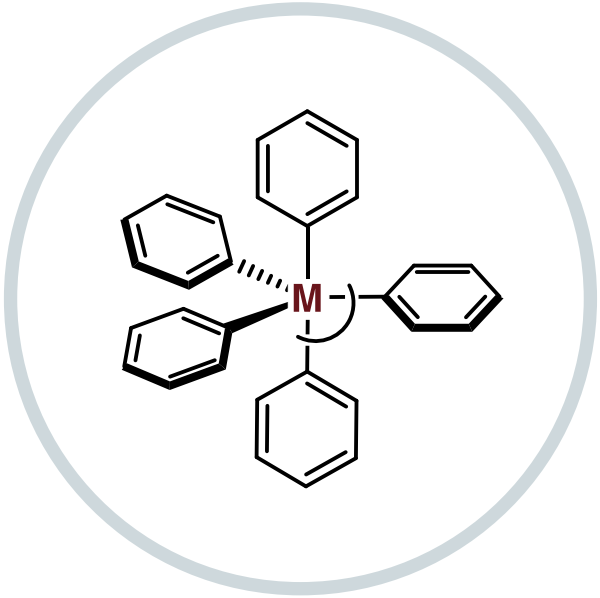






Fujimoto, H.; Kodama, T.; Yamanaka, M.; Tobisu, M. J. Am. Chem. Soc. **2020**, 142, 17323.

Ligand-coupling on hypervalent species:
Transition metal chemistry without the metal



Questions?