Some Hartwig Chemistry – Experimental Approaches and Detailed Mechanistic Analysis

b. 1964

1986 A.B. Princeton U, Maitland Jones

1990 Ph.D. UC Berkeley, Robert Bergman and Richard Anderson

1990-92 Post-doc, MIT, Stephen Lippard

1992 Yale Faculty

Stoltz Group Meeting
15 March 2004, 8:00pm
147 Noyes
Raissa Trend

Experimental Approaches to and Detailed Mechanistic Analysis of Fundamental Organometallic Reactions

1) Reductive elimination of Ar–X from Palladium(II)

2) β-Hydrogen elimination from Ir(I)

NMR
IR
Organometallic Synthesis
Kinetic analysis
Equilibrium analysis
X-ray crystallography
Computational analysis
Microscopic reverse
GC

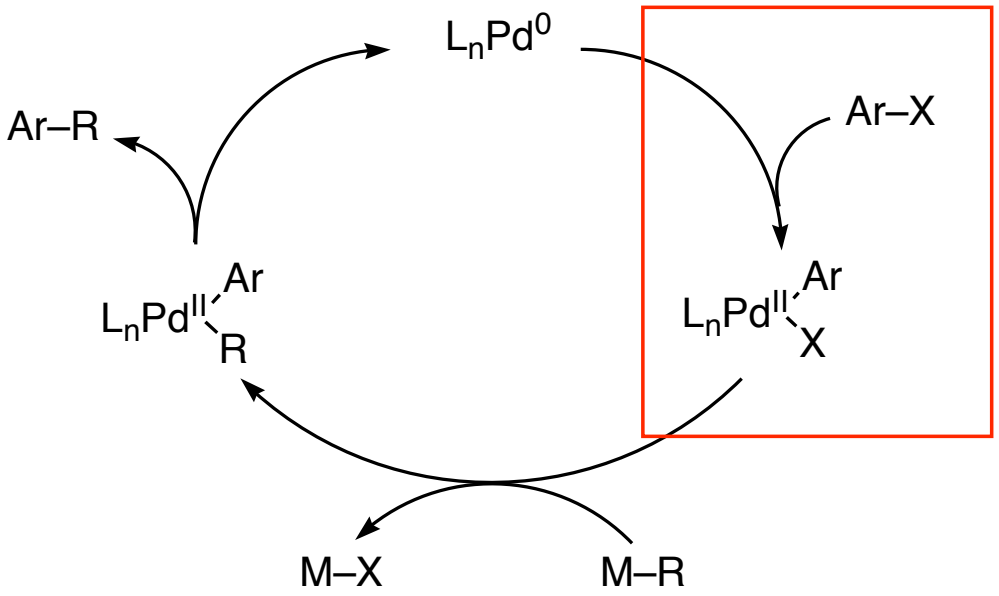
$\Longrightarrow$ Simple, observable systems

Other topics:

Amination of aryl halides and sulfonates
a-arylation of carbonyl compounds
Regiospecific funcionalization of alkanes with Rh and B
Olefin hydroamination
Enantioselective allylic amination and etherification

Fundamental Reactions and Common Steps in Catalysis

From reductive elimination to unsaturated arylpalladium(II) halide intermediates:

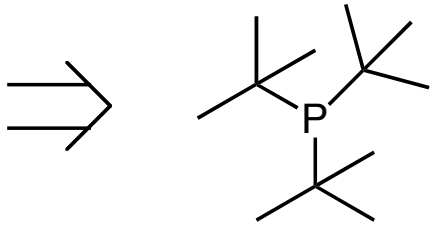


What can we learn about oxidative addn. by studying reductive elimination of aryl halides?

Reductive elimination of aryl halides: Roy; Hartwig. *JACS*, **2001**, 1232.
Monomeric Pd complexes with one dative ligands: Stambuli; Bühl, Hartwig. *JACS*, **2002**, 9346
Directly observed Reductive elimination: Roy; Hartwig. *JACS*, **2003**, *125*, 13944.
Monomeric Pd complexes full paper: Stambuli; Incarvito, Bühl, Hartwig. *JACS*, **2004**, 1184.

Reductive Elimination of Aryl Halides from Pd(II)

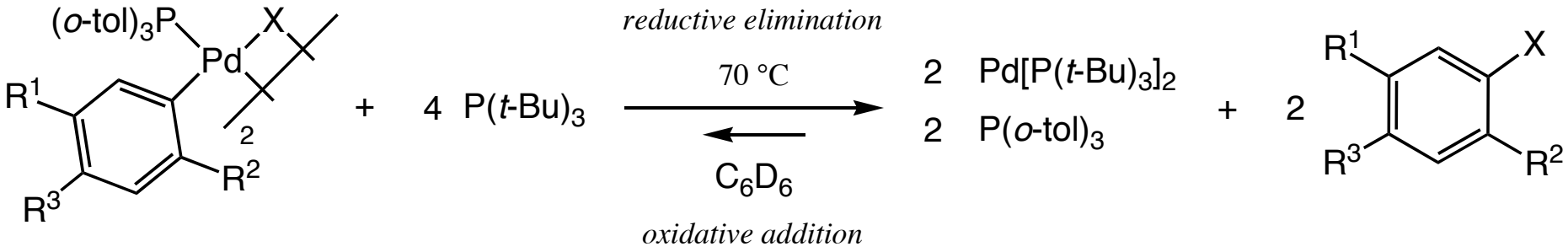
More electron-donating ligands undergo faster oxidative addition – greater driving force for oxidation of a more electron-rich metal

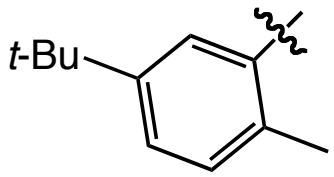


SURPRISING RESULT:

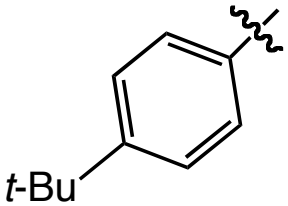
Reductive elimination is induced by addition of $(t\text{Bu})_3\text{P}$ and is thermodynamically favored over oxidative addition

Reaction studied:





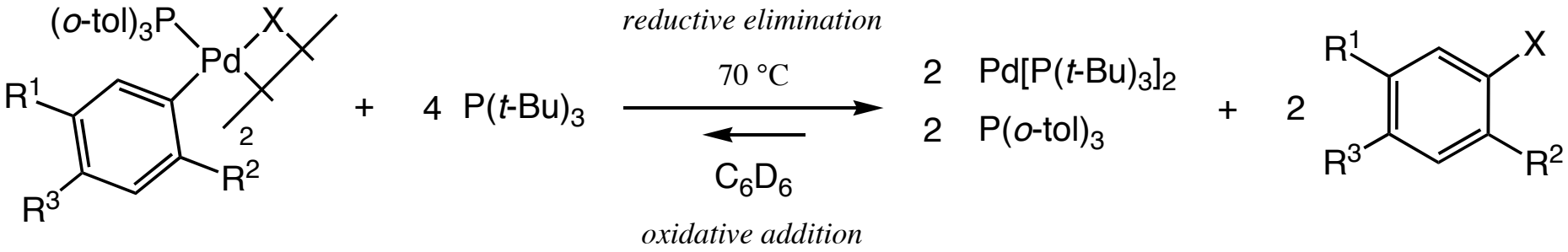
X = Cl
X = Br
X = I



X = Cl
X = Br

Qualitative rates observed
Reactions initiated from both sides of the reaction
K_{eq} values, yields obtained

Reductive Elimination of Aryl Halides from Pd(II)



	Dimer	yield	K_{eq}	rate
a.	R^1 = *t*-Bu, R^2 = Me, X = Cl	70	9(3) x 10^{-2}	Slower
b.	R^1 = *t*-Bu, R^2 = Me, X = Br	70	2.3(3) x 10^{-3}	Faster
c.	R^1 = *t*-Bu, R^2 = Me, X = I	39	3.7(2) x 10^{-5}	
d.	R^3 = *t*-Bu, X = Cl	30	n.d.	
e.	R^3 = *t*-Bu, X = Br	75	3.3(6) x 10^{-4}	

Yields for for the red. elim. paralled thermodynamic driving force, but rates did not.

Amt of added P(*t*-Bu)$_3$ was crucial for high yields of Ar–X.

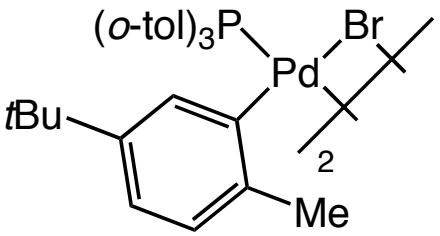
o-Substitution increases K_{eq} by factor of 10 (compare b and e).

K_{eq} for each halide is different by factor of 100 (compare a–c).

Ox. Addn. of Ar–X to Pd-dimer does not occur for c and e in the absence of P(*o*-tol)$_3$.

⟹ Red. Elim occurs from a monomer? What is the monomer and how does it form? Is formation or reaction of the monomer rate determinig?

Reductive Elimination of Aryl Halides from Pd(II)



\+ $P(t\text{-Bu})_3$

reductive elimination

55 °C

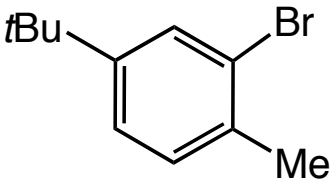
C_6D_6

oxidative addition

$Pd[P(t\text{-Bu})_3]_2$

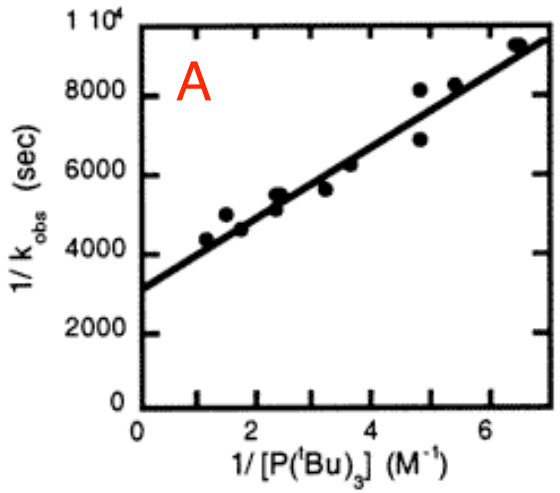
$P(o\text{-tol})_3$

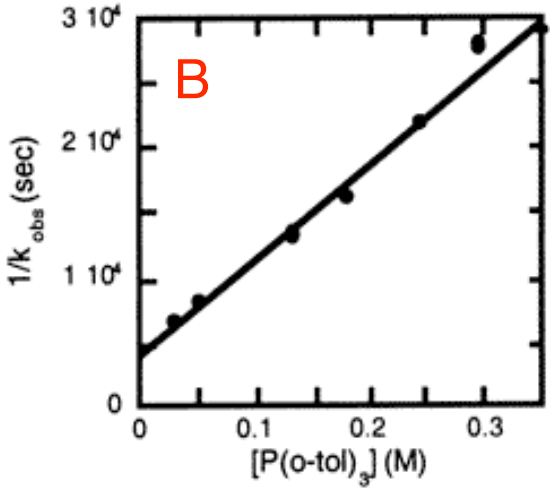
\+



Varied [P(*t*-Bu$_3$)], [P(*o*-tol)$_3$], and [Pd-dimer] – first-order appearance of each product was observed.

Rxns monitored by ^{1}HNMR





Plot A:

k_{obs} faster at higher [P(*t*Bu)$_3$] – reaction induced by P(*t*Bu)$_3$ (Lineweaver-Burk)

Non-zero *y*-intercept for Plot A = $1/V_{max}$, where V_{max} is the limiting rate at high [P(*t*Bu)$_3$].

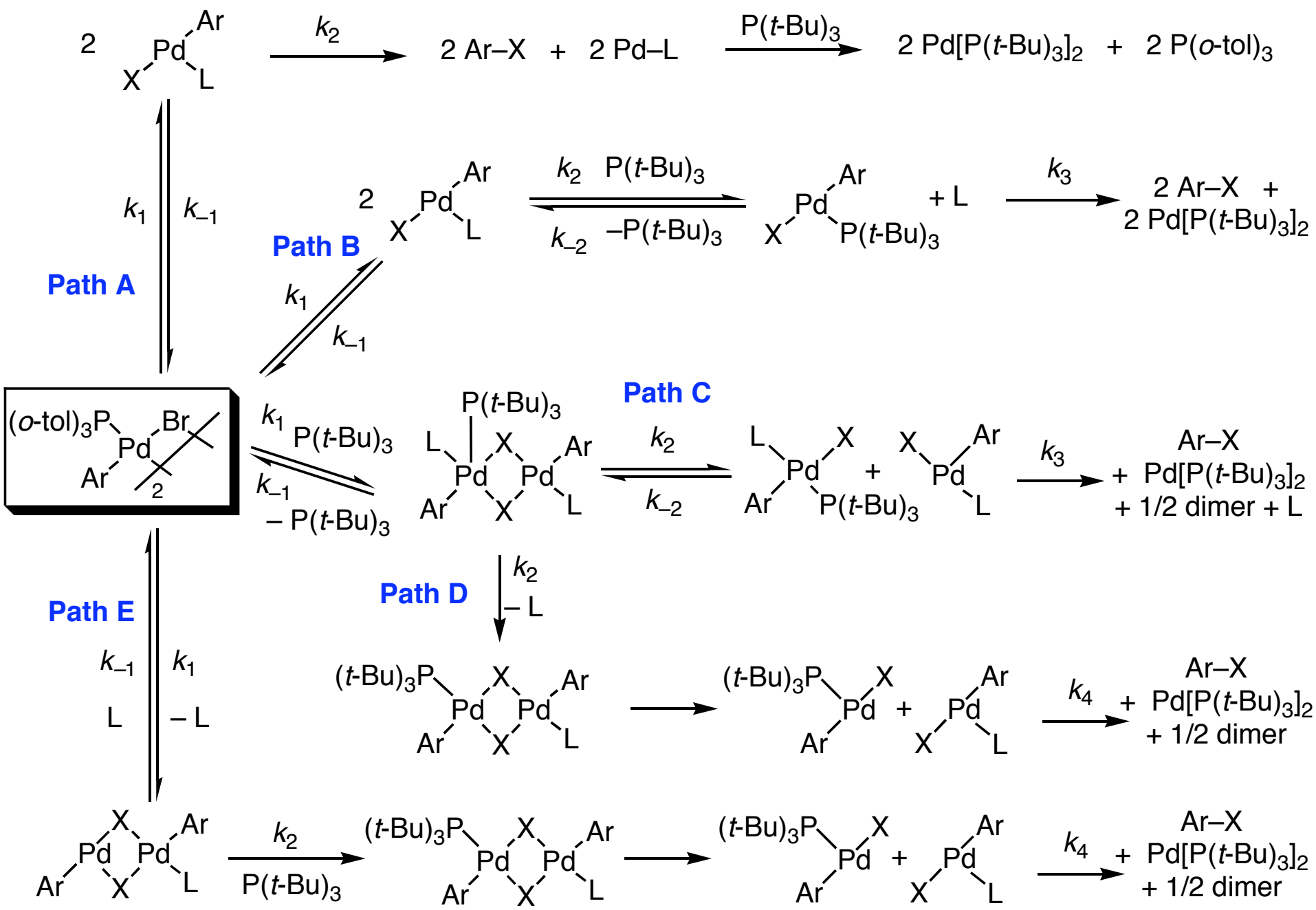
Plot B:

Inverse dependence of $1/k_{obs}$ on [P(*o*-tol)$_3$] – k_{obs} slowed by P(*o*-tol)$_3$

Non-zero *y*-intercept for Plot B: V_{max} is the limiting rate with no [P(*o*-tol)$_3$].

$$v = \frac{V_{max}[S]}{K_m + [S]} \qquad \frac{1}{v_i} = \frac{1}{V_{max}} + \frac{K_m}{V_{max}}\frac{1}{[S]_0}$$

Reductive Elimination of Aryl Halides from Pd(II) – Possible Paths



Reductive Elimination of Aryl Halides from Pd(II) – Path E

All data are consistent with Path E

Features: Irreversible dissociative ligand substitution – unusual for square-planar geometry.
Cleavage of the dinuclear species before reductive elimination.

Rate law:

Irreversible association of P(*t*-Bu)$_3$:

$$\text{rate} = k_{obs}[\text{dimer}]$$

$$k_{obs} = \frac{k_1 k_2[P(t\text{-Bu})_3]}{k_{-1}[P(o\text{-tol})_3] + k_2[P(t\text{-Bu})_3]}$$

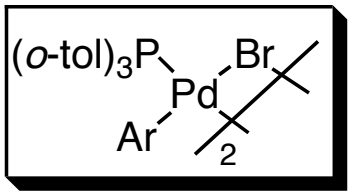
$$\frac{1}{k_{obs}} = \frac{k_{-1}[P(o\text{-tol})_3]}{k_1 k_2[P(t\text{-Bu})_3]} + \frac{1}{k_1}$$

Reversible association of P(*t*-Bu)$_3$, irreversible dimer cleavage:

$$\text{rate} = k_{obs}[\text{dimer}]$$

$$k_{obs} = \frac{K_1 K_2 k_3[P(t\text{-Bu})_3]}{[P(o\text{-tol})_3]}$$

y-intercept = 0

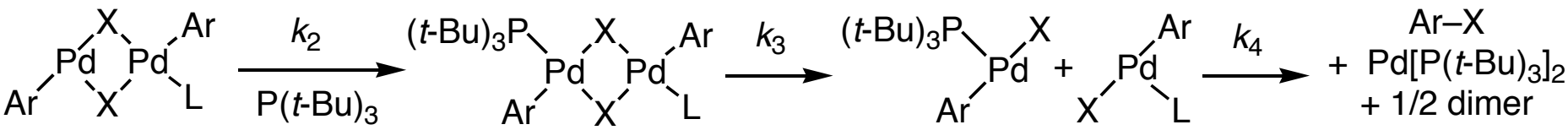


Predicts positive slopes and non-zero *y*-intecepts for Plots A and B.
First-order behavior in [dimer] = irreversible monomer formation.
If *y*-intercept is non-zero, k_2 step must be irreversible.
Every substitution event leads to reductive elimination
---> formation of monomers and reductive elimination is faster than dissociation of P(*t*-Bu)$_3$.

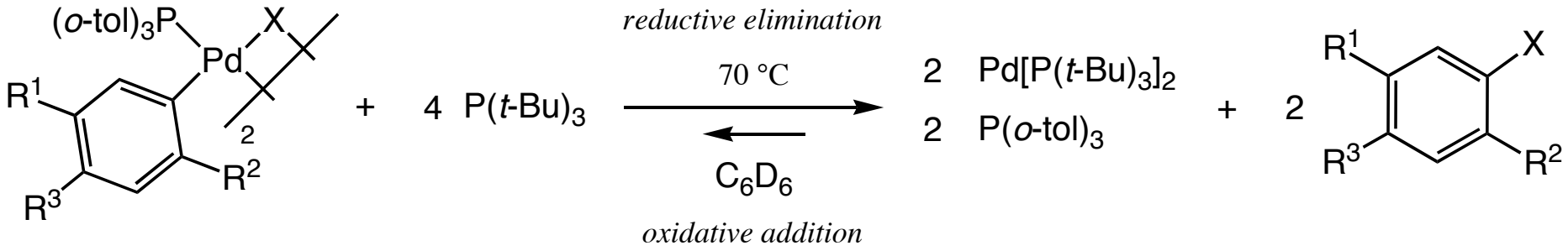
Path E

k_{-1} L

k_1 – L



Reductive Elimination of Aryl Halides from Pd(II) – Conclusions



Some "fundamental principles" uncovered:

Reductive elimination is induced by coordination of a strongly electron-donating ligand, P(*t*-Bu)$_3$; coupled with steric crowding, the thermodynamics can be altered so mcuh that reductive elimination of Ar–X becomes favord thermodynamically.

Despite the weak driving force, oxidative addition of Ar–X occurs rapidy to P(*t*-Bu)$_3$ ligated Pd(0) in catalysis.

Ligand subsitituion is the square-planar system is dissociative, probably due to steric situtation.

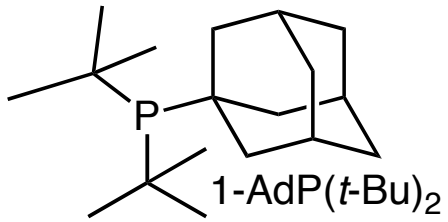
Implies aromatic halide exchange is feasible.

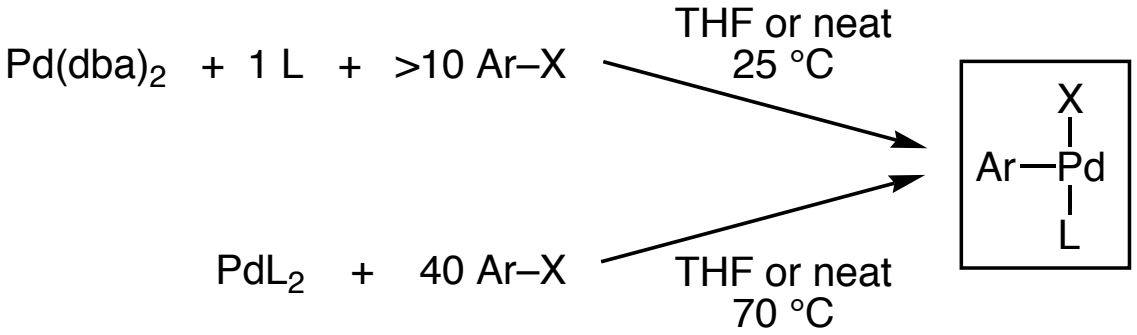
Equilibrium measurements
Kinetic evaluation
Forward and reverse reactions

But: Species undergoing reductive elimination was never directly observed.

The Next Step – Synthesis of a Monomeric Arylpalladium Halide

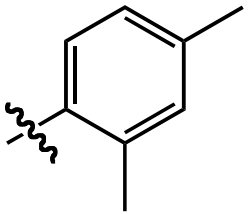
Can the unsaturated species that are often intermediates in organometallic reactions be observed directy?

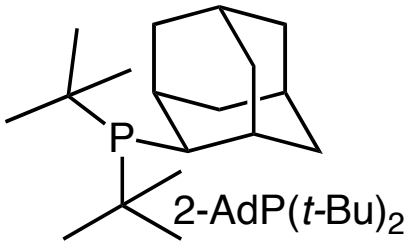


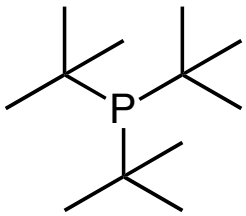


X = Br or I

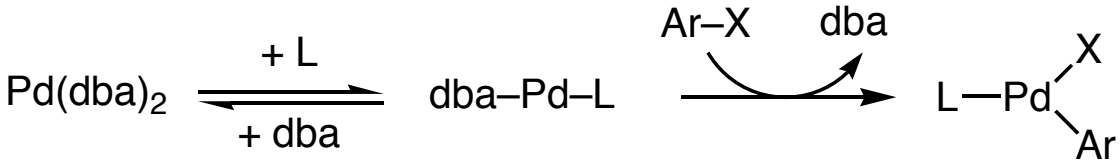
Ar = Ph or







Proposed Mechanism:



Addition to $Pd(dba)_2$ formed side products at > 0.1 M

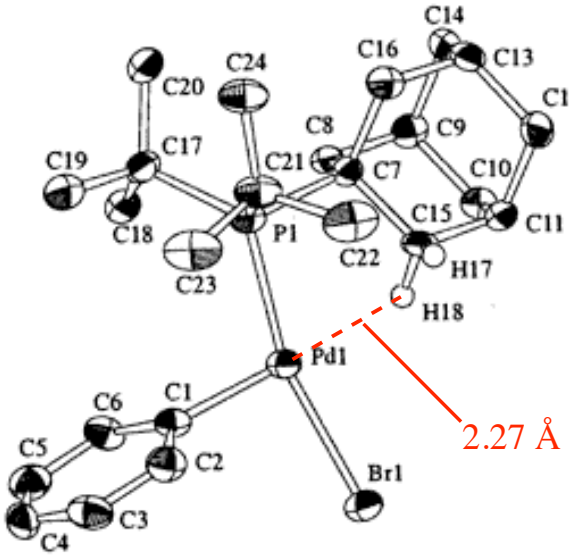
Oxidative additions to PdL_2 were slower than those to 1:1 mixture of $Pd(dba)_2$ and ligand.

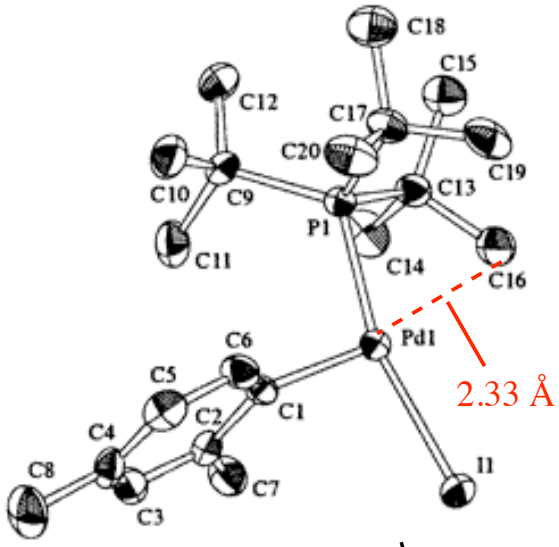
Reactions cannot occur through $L_2Pd(0)$.

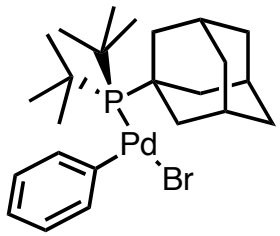
Parallels reactivity in catalytic reactions

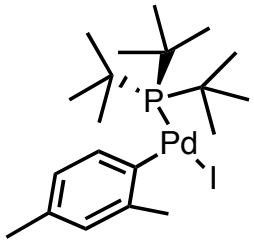
JACS **2002**, *124*, 9346

A Monomeric Arylpalladium Halide – Characterization and Agostic Interaction









– Monomeric

– T-shaped

Ligand with greatest steric demand binds to the least hindered position.

Covalent ligand with the largest trans effect binds trans to the open site.

Similar structures present in solution:

^{31}P and ^{13}C NMR:

^{31}P NMR chemical shifts of arypalladium halide complexes usually downfield from the Pd(0) complex – upfield shift observed.

Cis disposition of Ar and L indicated by small J_{P-C} for C1.

No definitive ^{1}H NMR evidence (upfield signal).

IR:

Ar = Ph, X = Br, L = 2-AdP(*t*-Bu)$_2$ showed medium-strong band at 2710 cm^{-1}, reduced relative to free ligand, which indicates a strong agostic interaction.

The Trans Effect

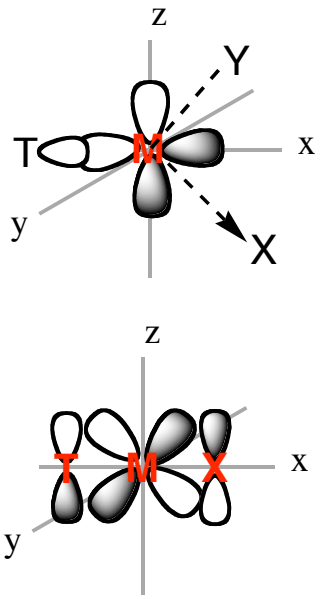
Kinetic effect of the *trans* substituents on the lability of a leaving group, and on location of substitution
Associative substitution pathway
σ and π component

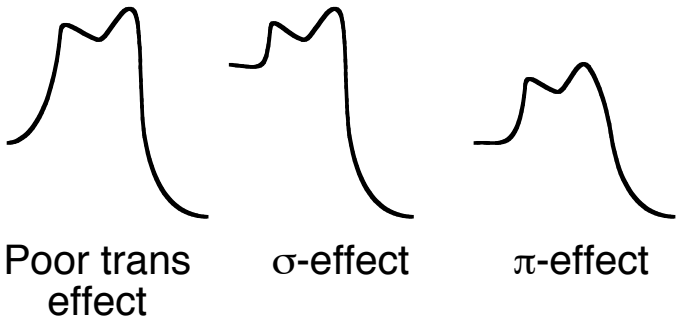
$CO \sim CN^- \sim C_2H_4 > PR_3 \sim H^- > {}^-CH_3 > SC(NH_2)_2 > {}^-C_6H_5 > NO_2^- > \sim SCN^- \sim I^- > Br^- > Cl^- > py, NH_3 \sim {}^-OH \sim H_2O$

very large effect — small effect

σ Effect:
Provide more p orbital to the *trans* group by moving the LG out of the region of strong overlap when the new group comes in to empty p_z orbital.
---> weakening of M–X bond

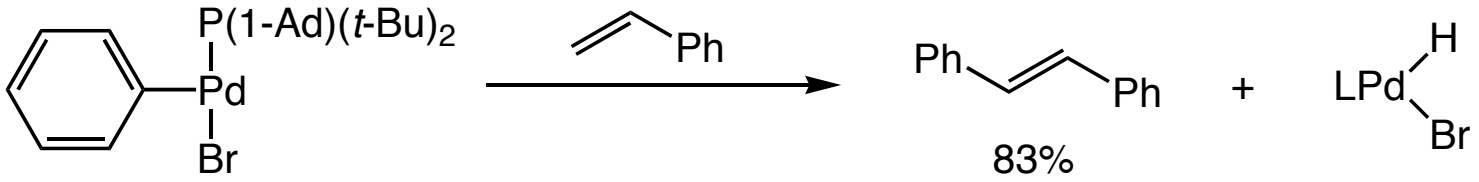
π Effect:
Trans ligand accomodates excess charge from entering ligand with empty π-symmetry orbitals – it lowers the overall activation energy.
---> TS energy lowered.





Also called trans infulence

Monomeric Arylpalladium Halides – Reactivity and Potential

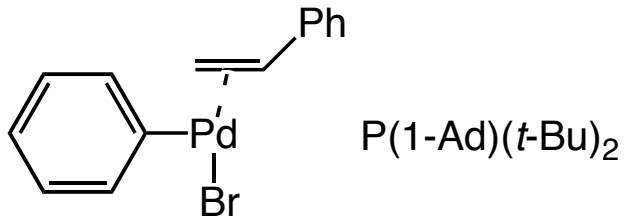


– Reaction inhibited by added phosphine – clean inverse first-order behavior.
– No adduct with added ligand was detected.

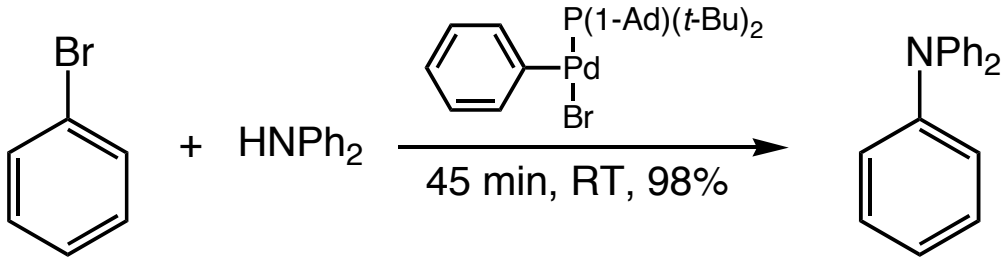
→ Transition state of the rate-determining step lacks any coordinated phosphine.

+ a number of other reactions...

Dissociation of large phosphine may be necessary to allow olefin binding, or cis disposition of the olefin and the aryl group.



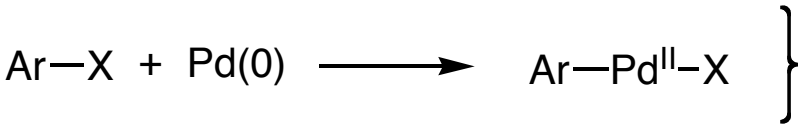
Kinetically competent as an intermediate in amination of aryl halides:



Unique complexes, viable intermediates

---> Mechanistic studies of a variety of Pd-catalyzed processes

Monomeric Complexes in Action – Directly Observed Reductive Elimination



First step in almost all Pd cross-coupling reactions.

Empirical observation of rates for ox. addn.: Ar–I > Ar–Br > Ar–Cl

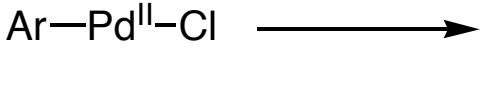
faster ← slower

Attributed to strengths of Ar–X bonds.

But:

– No thermodynamic data on oxidative addition.
– Rates for elimination from Ar–Pd–X directly have not been measured.

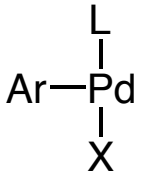
→ **Fundamental issues**



Faster than from Br or I if bond strength control relative reaction rates.

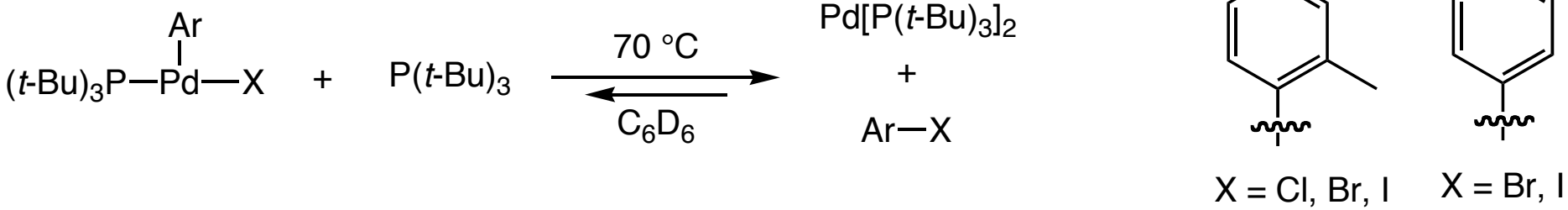
Slower than from Br or I if properties of the transition state control rates.

Address fundamental issues by studying reductive elimination from:



JACS, **2003**, *125*, 13944.

Directly Observed Reductive Elimination – Kinetics vs. Thermodynamics



	Complex	yield Ar–X	K_{eq}	rate
a.	X = Cl, Ar = *o*-tol	76	10.9×10^{2}	slowest
b.	X = Br, Ar = *o*-tol	98	32.7×10^{-1}	fastest
c.	X = I, Ar = *o*-tol	79	1.79×10^{-1}	faster
d.	X = Br, Ar = Ph	68	13.4×10^{-1}	
e.	X = I, Ar = Ph	60	0.51×10^{-1}	

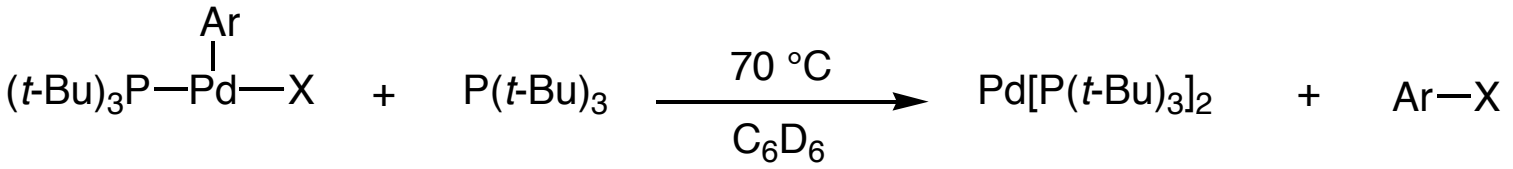
Values of K_{eq} determined by initiating reactions in both directions and establishing equilbrium.

Red. Elim. from a more favorable than from b by a factor of 3000, b more favorable than c by a factor of 20.

Values of K_{eq} parallel strength of Ph–X bonds.

Kinetics do not correlate with thermodynamics.

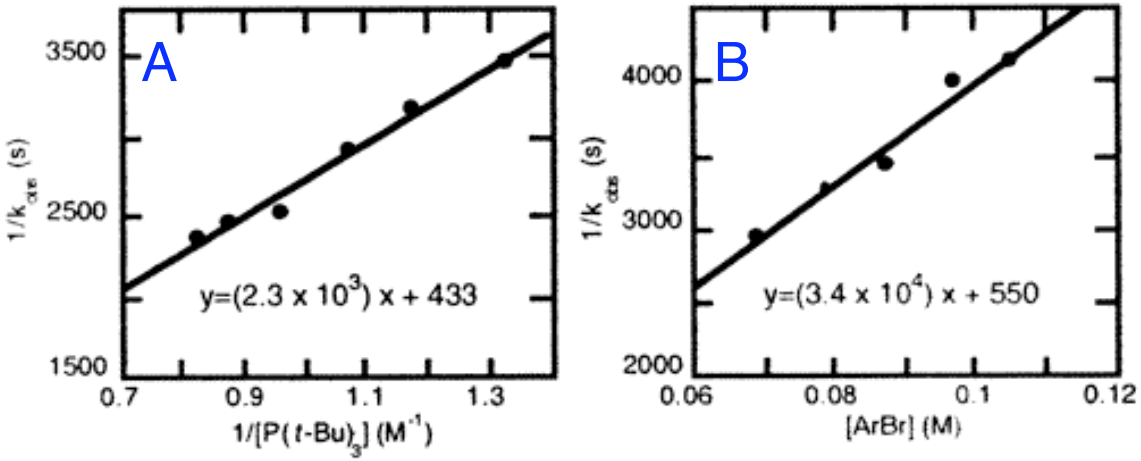
Directly Observed Reductive Elimination – Kinetic Data



First order appearance of product.

Dependence of rate on ArBr and on P(t-Bu)$_3$.

Measured by ^{1}H NMR.



Plot A:

k_{obs} faster at higher [P(tBu)$_3$] – reaction induced by P(tBu)$_3$ (Lineweaver-Burk)

Non-zero y-intercept for Plot A = $1/V_{max}$, where V_{max} is the limiting rate at high [P(tBu)$_3$].

Plot B:

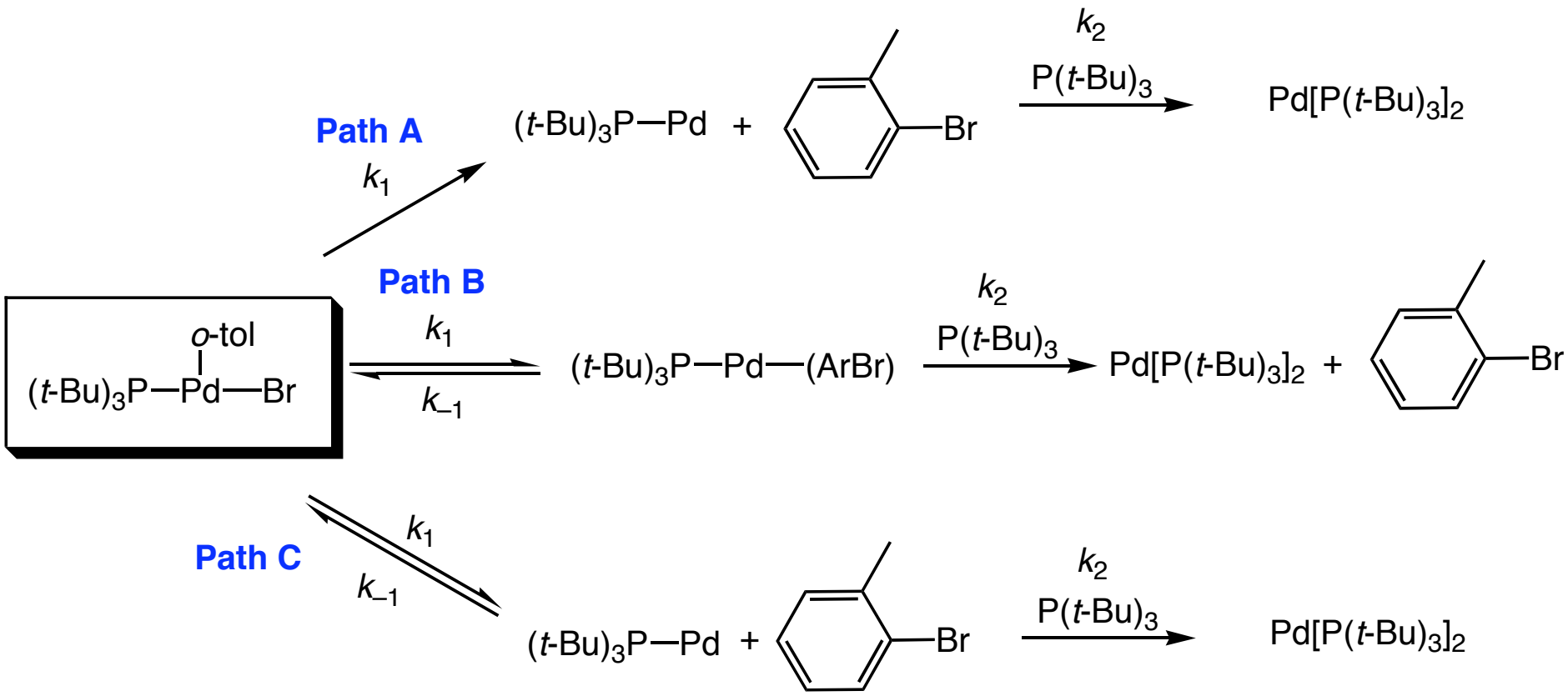
Inverse dependence of $1/k_{obs}$ on ArBr – k_{obs} slowed by ArBr

Non-zero y-intercept for Plot B: V_{max} is the limiting rate with no ArBr

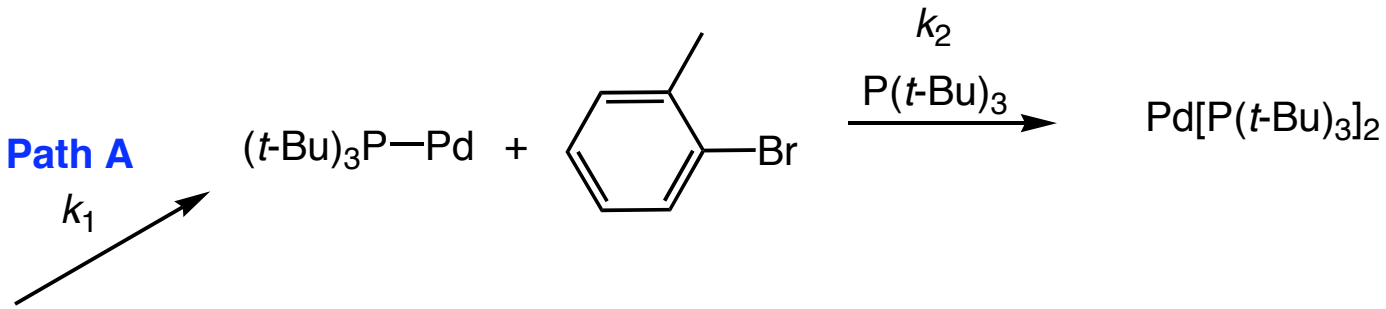
$$v = \frac{V_{max}[S]}{K_m + [S]} \qquad \frac{1}{v_i} = \frac{1}{V_{max}} + \frac{K_m}{V_{max}}\frac{1}{[S]_0}$$

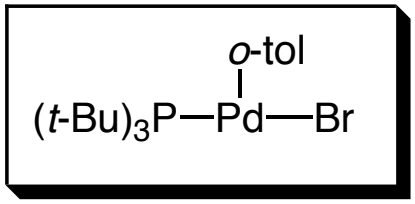
Directly Observed Reductive Elimination – Possible Pathways

Reductive elimination faster from 3-coordinate
than from 4-coordinate complexes:



Directly Observed Reductive Elimination – Path A





Features: Reductive elimination from starting arylpalladium bromide.

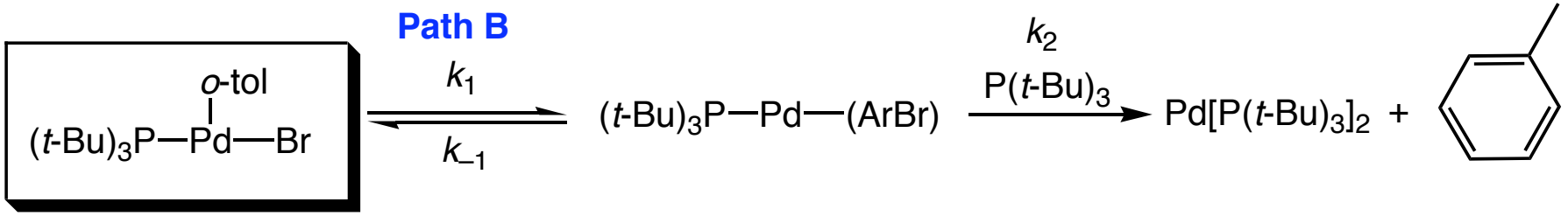
In the case where the equilibrium is heavily to the side of reductive elimination:

zero-order in [ArBr]
zero-order in [$\text{P}(t\text{-Bu})_3$]

↓

Not consistent with data

Directly Observed Reductive Elimination – Path B



Features: Reversible reductive elimination of Ar–Br to P(t-Bu)$_3$ ligated complex with coordinated ArBr.

Associative ligand substitution of phosphine for ArBr.

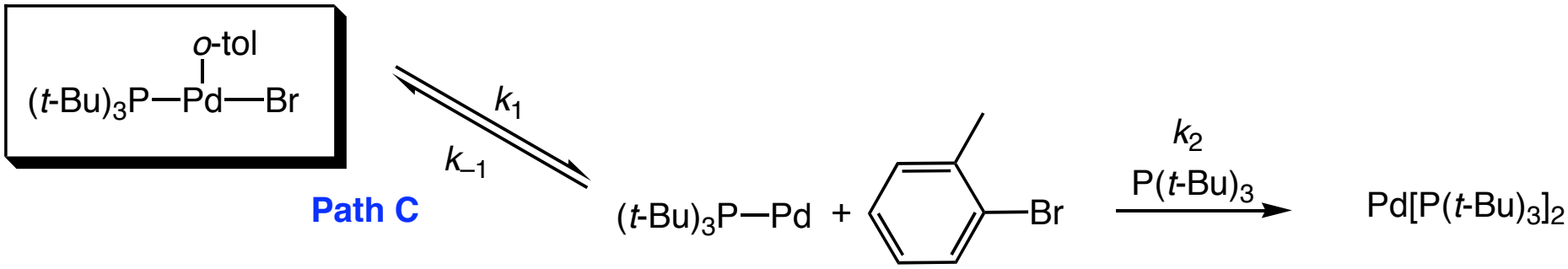
Rate law: rate = k_{obs}[Pd]

$$k_{obs} = \frac{k_1 k_2[P(t\text{-Bu})_3]}{k_{-1} + k_2[P(t\text{-Bu})_3]}$$

⟹ √ first-order in Pd
X zero-order in ArBr
√ first-order in P(t-Bu)$_3$ at low [P(t-Bu)$_3$]
zero-order in P(t-Bu)$_3$ at high [P(t-Bu)$_3$]

⟶ Not consistent with data

Directly Observed Reductive Elimination – Path C



Features: Reversible reductive elimination of ArBr, with or without inermediate ArBr complex.

Trapping by P(*t*-Bu)$_3$

Rate law:

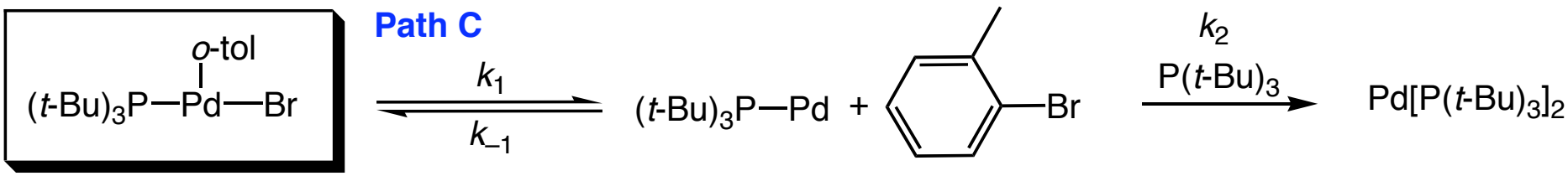
$$\text{rate} = k_{obs}[Pd] \qquad k_{obs} = \frac{k_1 k_2[P(t\text{-Bu})_3]}{k_{-1}[ArBr] + k_2[P(t\text{-Bu})_3]}$$

⟹ √ first-order in Pd
√ inverse first-order in ArBr *when* k_2 *competes with* k_{-1}
√ first-order in P(*t*-Bu)$_3$ at low [P(*t*-Bu)$_3$]
zero-order in P(*t*-Bu)$_3$ at high [P(*t*-Bu)$_3$]

→ Consistent with data

Reaction most likely occurs by Path C

Directly Observed Reductive Elimination – Conclusions



Rate law: rate = k_{obs}[Pd]

$$k_{obs} = \frac{k_1 k_2[P(t\text{-Bu})_3]}{k_{-1}[ArBr] + k_2[P(t\text{-Bu})_3]}$$

From Plots A & B: When [ArBr] = 0, *y*-intercept of $1/k_{obs}$ vs. [ArBr] corresponds to $1/k_1$, so $k_{obs} = k_1$, and is the rate constant for reductive elimination.

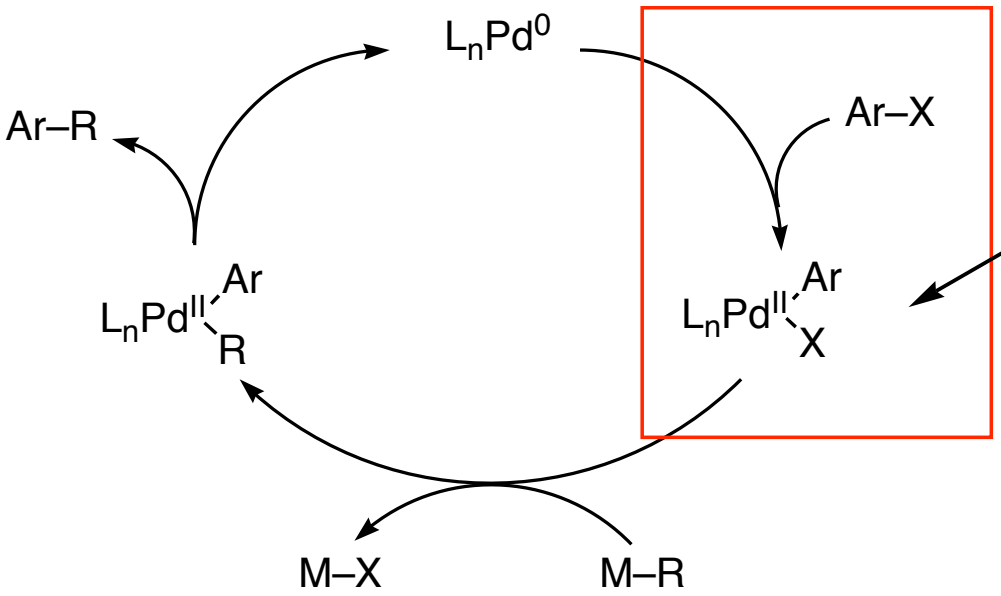
k_{-1}/k_2 = ratio of relative rate constants for oxidative addition and coordination of phosphine to Pd[P(*t*-Bu)$_3$]. $k_{-1}/k_2 \approx 65$.

Oxidative addition to Pd[P(*t*-Bu)$_3$] is faster than coordination of ligand.

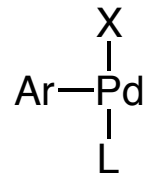
Conclusions:
- Reductive Elimination of Ar–X was directly observed.
- Thermodynamic parameters for Ox. Addn. and Red. Elim determined.
- High kinetic barrier for Ox Addn and Red. Elim of Ar–Cl.
- Evidence for reversible Ar–X cleavage on the path to Red. Elim.

$\Longrightarrow$ Slow activation of Ar–Cl is due to more than relative strength of ArCl bond.
Oxidative addition > ligand coordination for Pd[P(t*B*u)$_3$].

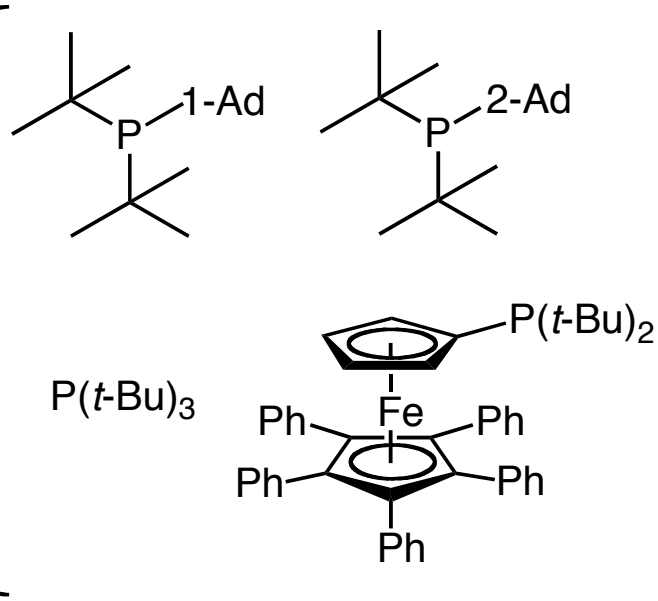
Ongoing Investigation of Unsaturated Arylpalladium(II) Halide Complexes



Improved synthetic methods needed



L =



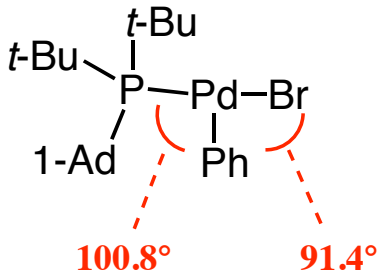
Ar = Ph, 2,4-xylyl

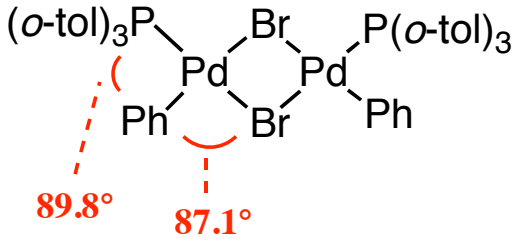
X = Cl, Br, I, OTf

Weak agostic interaction confirmed by computational studies, and in once case, spectroscopically.

Geometric distortions accomidate the bulky ligands.

A bulky R_3P cannot adopy a conformation that avoids steric interactions in a planar 4-coordinate geometry.



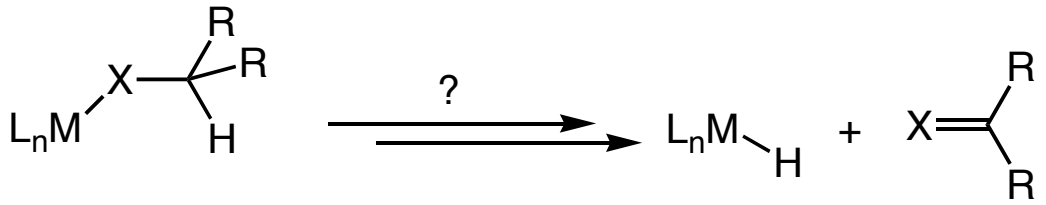


Factors that dictate nuclearity
Factors that control reactivity

JACS **2004**, *126*, 1184.

Fundamental Reactions and Common Steps in Catalysis

β-hydrogen elimination and migratory insertion:

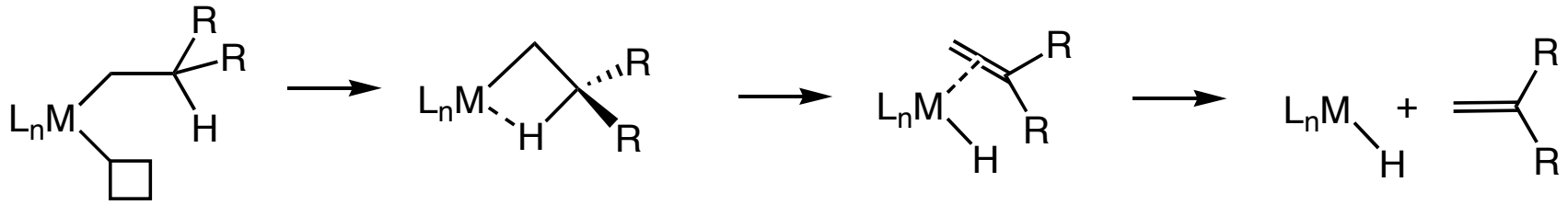


X = O, NH, NR

Direct observations from alkoxo and amido complexes uncommon.

β-Hydrogen elimination from M–alkoxo is not mechanistically well-defined.

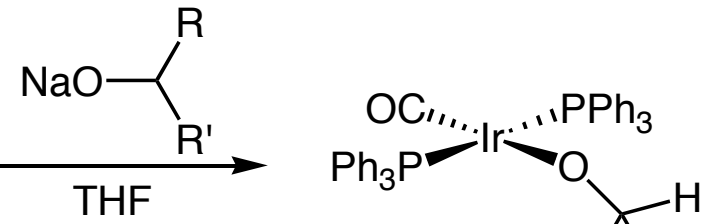
Is it similar to the conventional mechanism for metal-alkyls?



Pt, Ir, Re, and Rh alkoxide examples show evidence for mechanisms distinct from that for metal-alkyls.

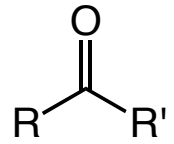
Ir-alkoxide β-hydrogen elimination: Zhao, Hesslink, Hartwig. *JACS*, **2001**, *123*, 7220.
Pd-alkoxides as intermediates: Mann, Hartwig. *JACS*, **1996**, *118*, 13109.
Ir-amido β-hydrogen elimination: Hartwig. *JACS*, **1996**, *118*, 7010.
Pd-hydroxides and N–H activation: Driver, Hartwig. *Organometallics*, **1997**, *16*, 5706.

Vaska-type Alkoxo Complexes – Clean Thermolysis



R = R' = H
R = R' = Me
R = Me, R' = *t*Bu
R = H, R' = *i*Pr
R = H, R' = Cy

PPh_3
70 °C
tol-d_8



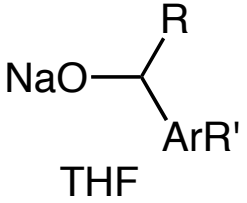
\+ $(PPh_3)_3(CO)Ir–H$

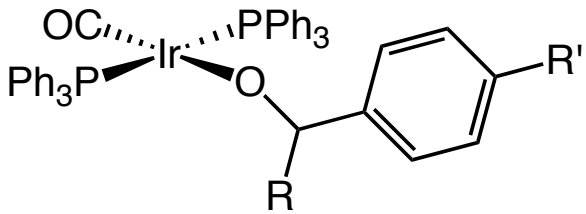
81–92%

Overall β-elimination is irreversible

First-order in [Ir]–OR
Zero-order in PPh_3 at low [PPh_3]
Small inhibition at high [PPh_3]

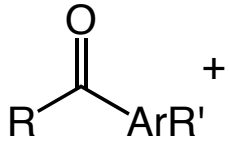
Similar rates in toluene, THF, Ph-Cl





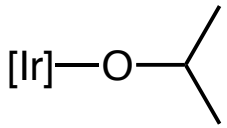
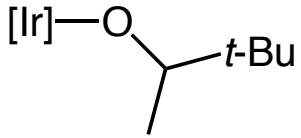
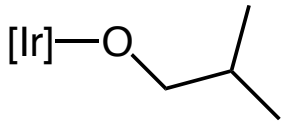
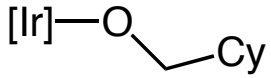
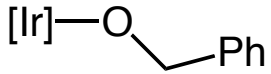
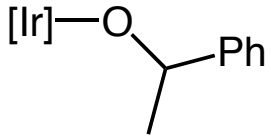
R = R' = H
R = Me, R' = H
R = Me, R' = OMe
R = Me, R' = Cl
R = Me, R' = CF_3

PPh_3
95-108 °C
tol-d_8



\+ $(PPh_3)_3(CO)Ir–H$

β-Hydrogen Elimination – Kinetic Data

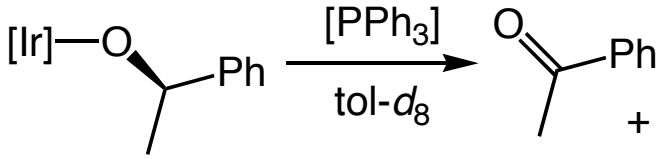
	k_{obs} x 10^4 s^{-1}
[Ir]—OMe	2.1
[Ir]—O 	1.9
[Ir]—O(*t*-Bu) 	3.0
[Ir]—O 	2.2
[Ir]—O—Cy 	3.5
[Ir]—O—Ph 	2.6
[Ir]—O(Ph) 	1.5

Rate does not depend on steric and electronic properties at the β-hydrogen

Hammett correlation:

electron-withdrawing substituents decrease the reaction rate

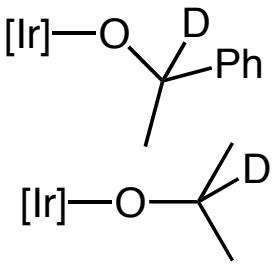
- Stability of ketone + TS stabilization — X
- Reduced stability of alkoxide — ?
- Migration of H atom with hydridic character



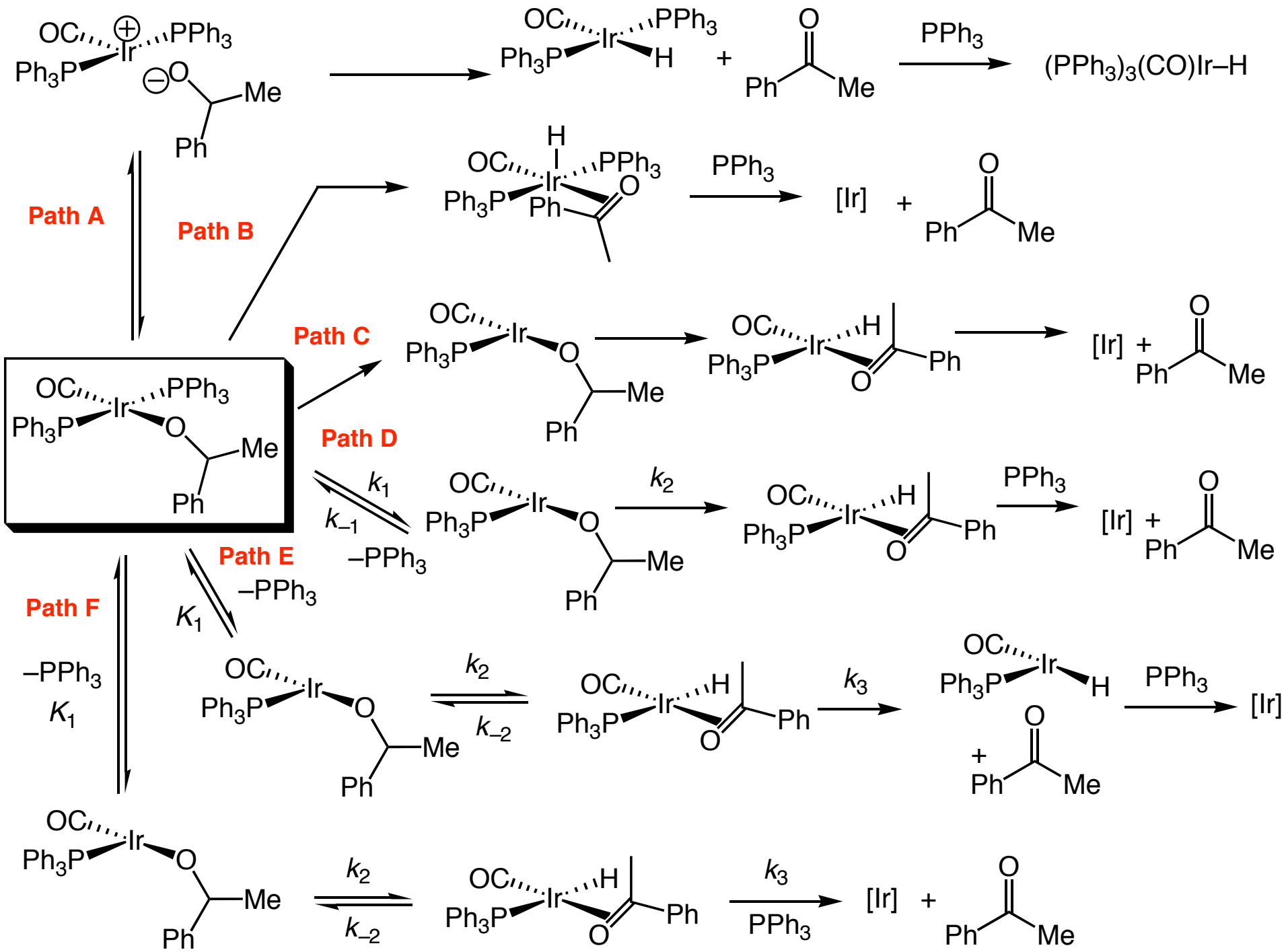
+ racemization

starting %ee	$[PPh_3]$ (M)	conv (%)	%ee after conv
84	0.3	40	84
84	0.3	75	81
>95	0.02	20	64
>95	0.02	40	18
>95	0.02	80	17

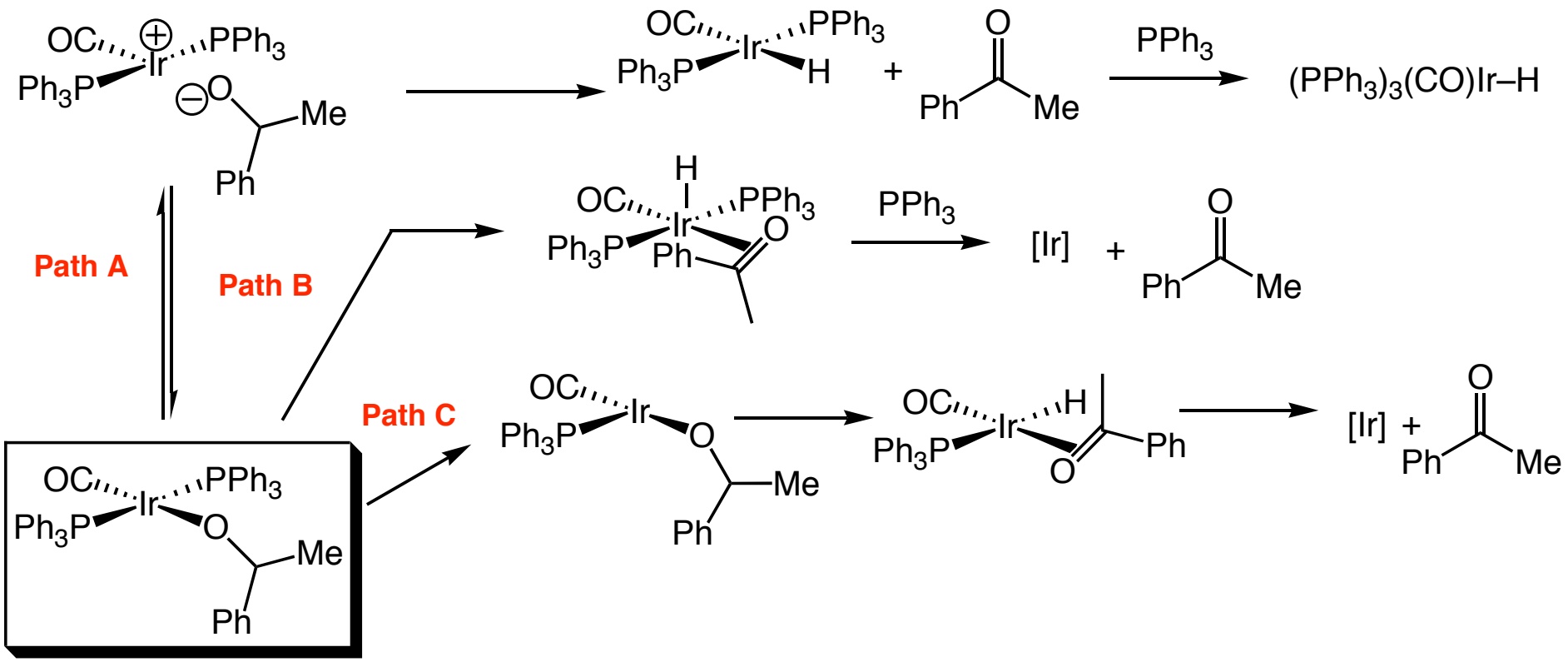
racemization at low $[PPh_3]$



Effect of $[PPh_3]$ on KIE determined – kinetic importance of C–H bond cleavage depends on whether PPh_3 dissociation and β-H elim. are reversible.


Path A
Path B
Path C
Path D
Path E
Path F
PPh3
[Ir]
(PPh3)3(CO)Ir–H
k1
k–1
–PPh3
k2
k–2
k3
K1

β-Hydrogen Elimination – Possible Mechanistic Paths



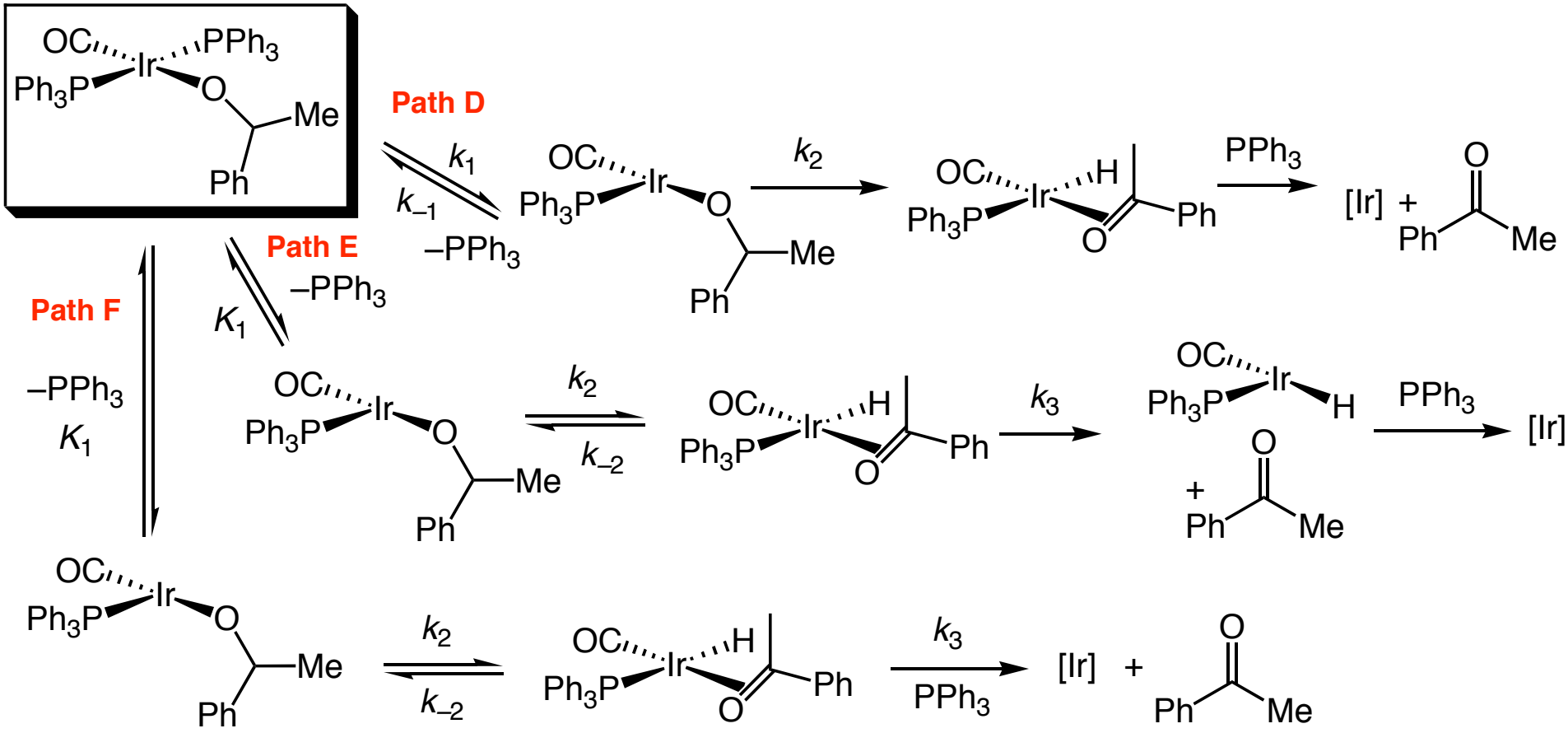
Path A: – Alkoxide dissociation
– Dependent on solvent polarity
– Zero-order in [PPh_3]
– Stereochemistry independent of [PPh_3]

Path B: – Direct elimination
– Independent of solvent polarity
– Zero-order in [PPh_3]
– Stereochemistry independent of [PPh_3]

Path C: – Irreversible PPh_3dissociation
– Zero-order in [PPh_3]
– Stereochemistry independent of [PPh_3]

None is consistent with data

β-Hydrogen Elimination – Possible Mechanistic Paths



Path D, E, F:

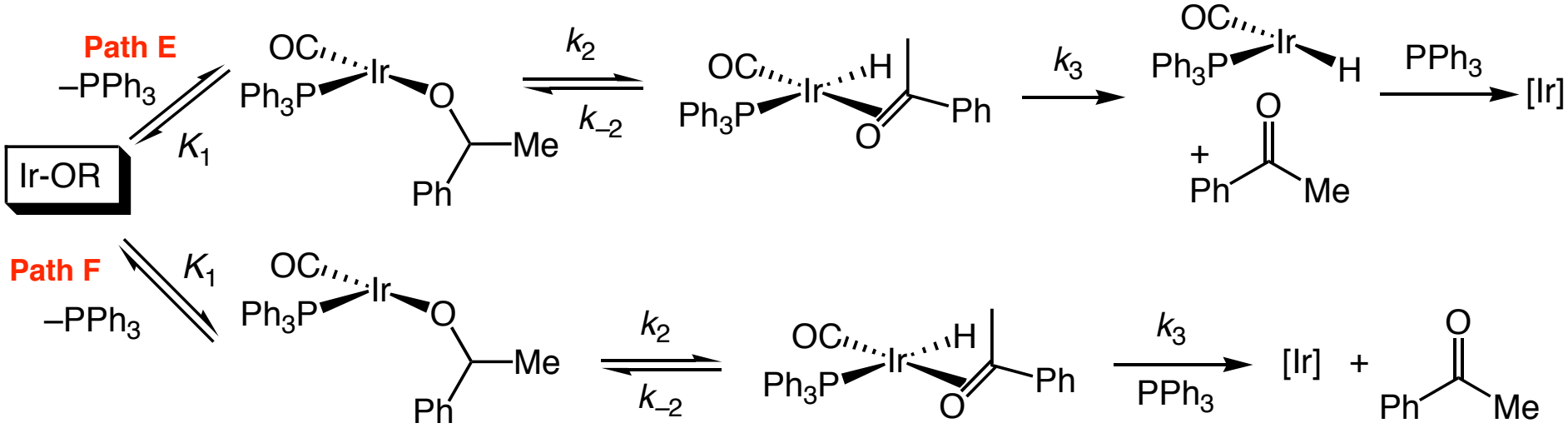
rate = k_{obs}[Ir-OR]

Path D: – Reversible PPh_3 dissociation
– Irreversible β-hydrogen elimination
– Inverse first-order in PPh_3 at high [PPh_3]
– Racemization not accounted for

$$\frac{1}{k_{obs}} = -\frac{1}{k_1} - \frac{k_{-1}[PPh_3]}{k_1 k_2}$$

predictions not consistent with observed data

β-Hydrogen Elimination – Possible Mechanistic Paths



Path E: – Reversible PPh_3 dissociation
– Reversible β-hydrogen elimination
– Dissociation of ketone in the last step

$$\frac{1}{k_{obs}} = -\frac{1}{K_1 k_2} - \frac{k_{-2}[PPh_3]}{K_1 k_2 k_3}$$

rate = k_{obs}[Ir-OR]

Path F: – Reversible PPh_3 dissociation
– Reversible β-hydrogen elimination
– Associative substitution of PPh_3 for ketone

$$\frac{1}{k_{obs}} = -\frac{k_{-2}}{K_1 k_2 k_3} - \frac{[PPh_3]}{K_1 k_2}$$

At low [PPh_3], Path E zero-order in PPh_3
β-H elim >> PPh_3 recoordination

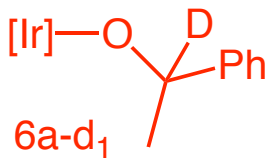
At high [PPh_3] dependent on [PPh_3]
recoordination PPh_3 >> β-H elim.
PPh_3 dissociation is reversible.

At low [PPh_3], reversible PPh_3 dissociation, β-H elim., associative displacement all occur.
Nearly zero-order in PPh_3 (cancellation).

At high [PPh_3], inhibition by [PPh_3]:
Assoc. displacement >> ketone reinsertinon;
β-H elim. is irreversible, PPh_3 only involved in dissociative preequilibrium.

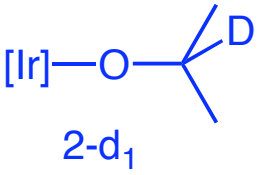
β-Hydrogen Elimination – Ligand affect on KIE

Effect of [PPh_3] on KIE determined – kinetic importance of C–H bond cleavage depends on whether PPh_3 dissociation and β-H elim. are reversible.



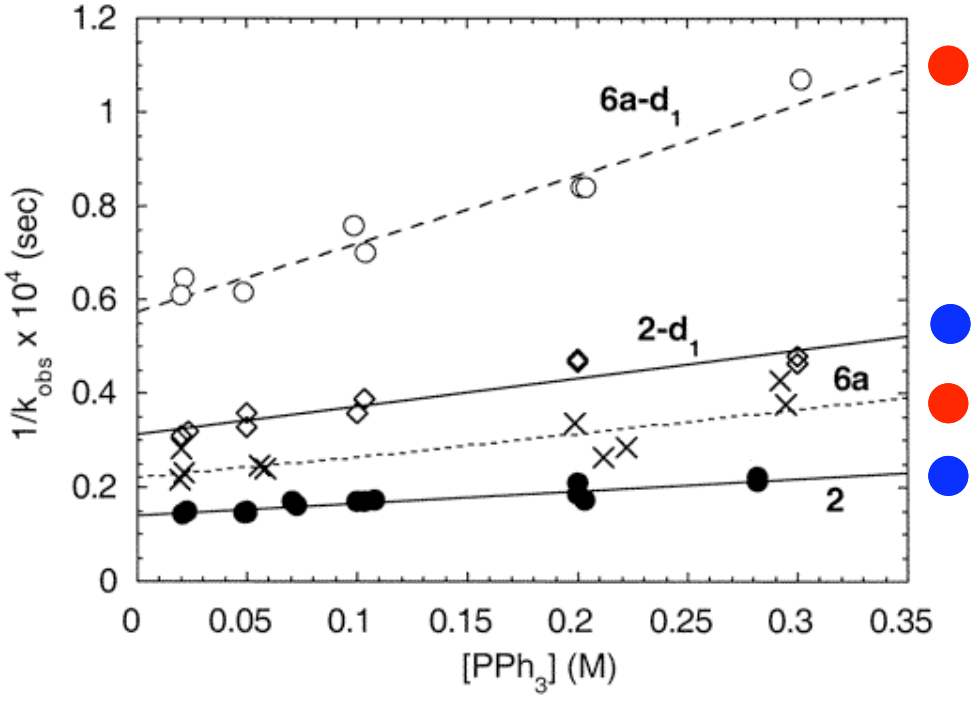
6a-d_1

y-intercept
KIE = 2.6



2-d_1

y-intercept
KIE = 2.3



Path E

$$\frac{1}{k_{obs}} = -\frac{1}{K_1 k_2} - \frac{k_{-2}[PPh_3]}{K_1 k_2 k_3}$$

Path F

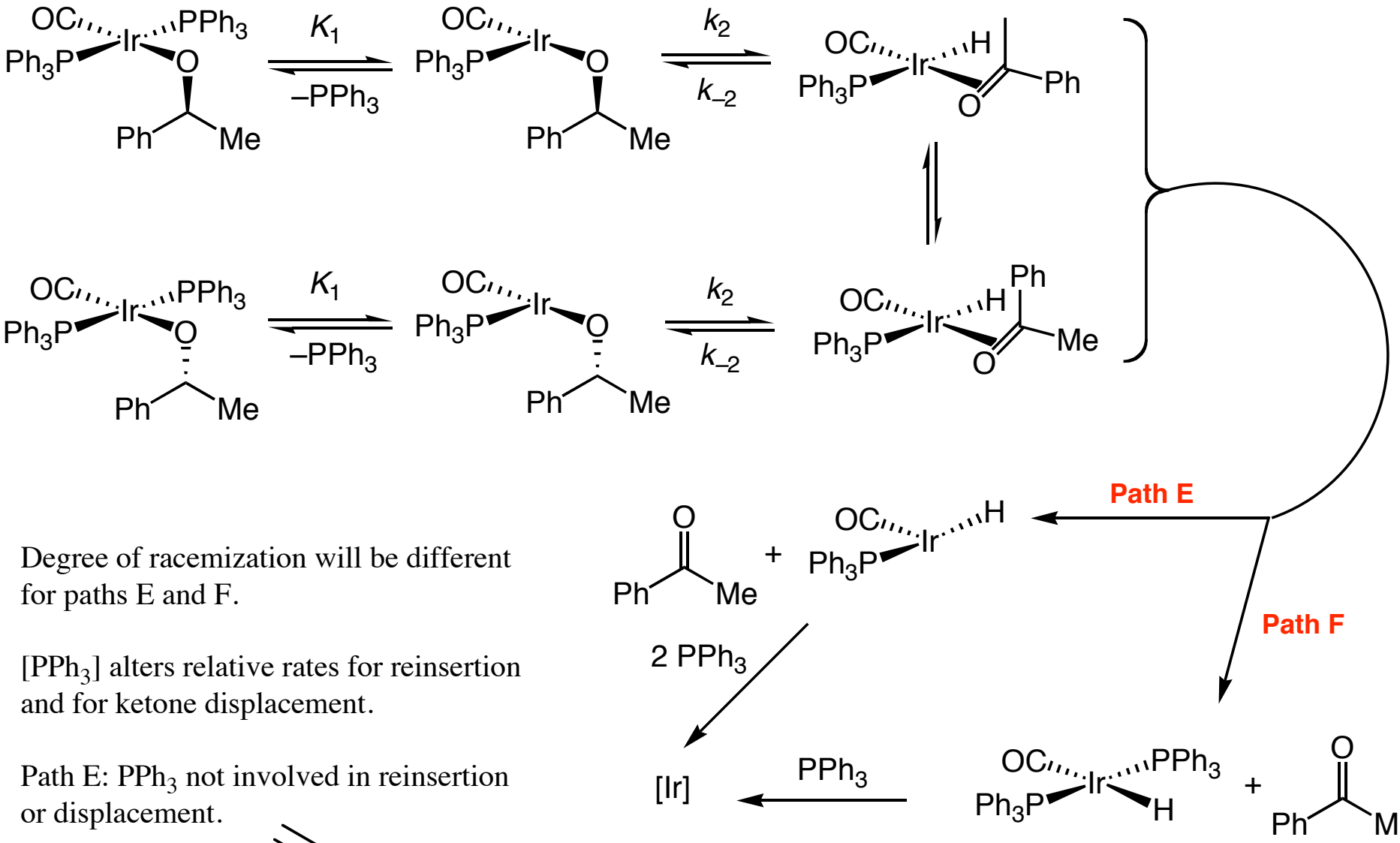
$$\frac{1}{k_{obs}} = -\frac{k_{-2}}{K_1 k_2 k_3} - \frac{[PPh_3]}{K_1 k_2}$$

y-intercept contains rate constant for β-H elimination, k_2

β-H elimination, C–H bond cleavage, must be reversible.

Path D would not have a significant KIE, because *y*-intecercept would only contain rate constant for ligand dissociation.

β-Hydrogen Elimination – Distinguishing Paths E and F



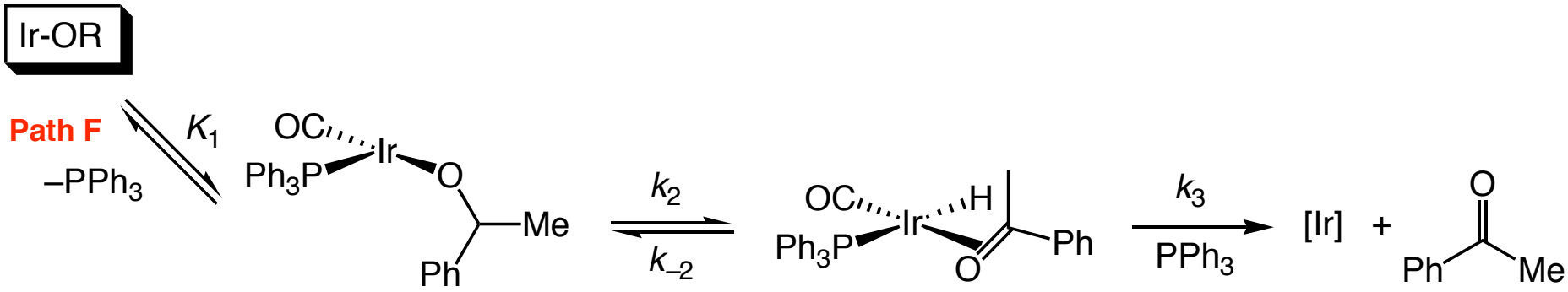
Degree of racemization will be different for paths E and F.

[PPh_3] alters relative rates for reinsertion and for ketone displacement.

Path E: PPh_3 not involved in reinsertion or displacement.

Path F

β-Hydrogen Elimination – Conclusions

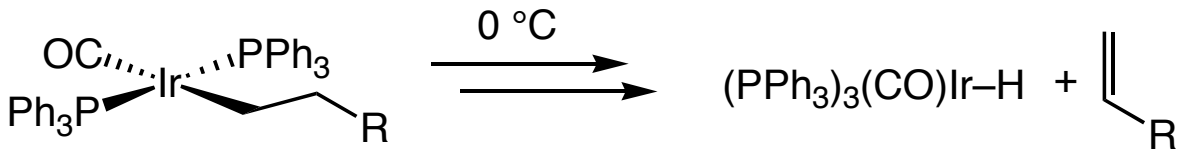


Mechanism for β-hydrogen elimination from Ir–OR similar to that for alkyl analogues and does not involve:

solvent-assisted ligand dissociation
direct elimination
bimolecular hydride abstraction

Ir–alkoxides are far more stable than alkyl analogues, despite open coordination site and labile monodentate phosphines.

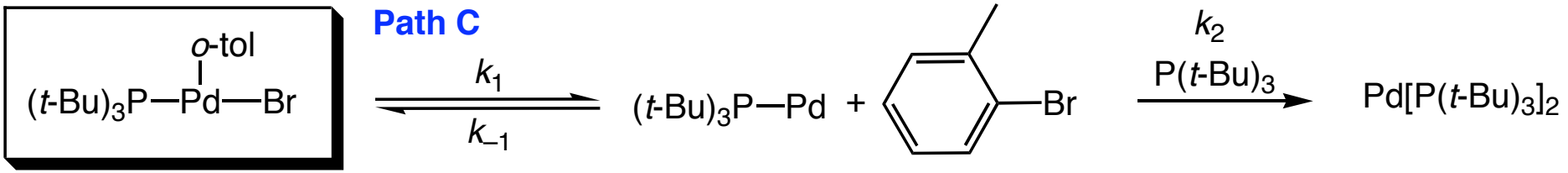
Vaska alkyl analogues undergo β-hydrogen elimination near 0 °C.



Alkoxo and amido complexes have simlar elimination rates.
Red. Elim. for C–O << C–N.
--> coupling of aryl halide + alcohol w/ α-hydrogen difficult

Imines should be as reactive as ketones towards insertion, but olefins are the fastest.

Experimental Approaches to and Detailed Mechanistic Analysis of Fundamental Organometallic Reactions



Reactivity of Ar–X bonds is not just due to ground-state effects

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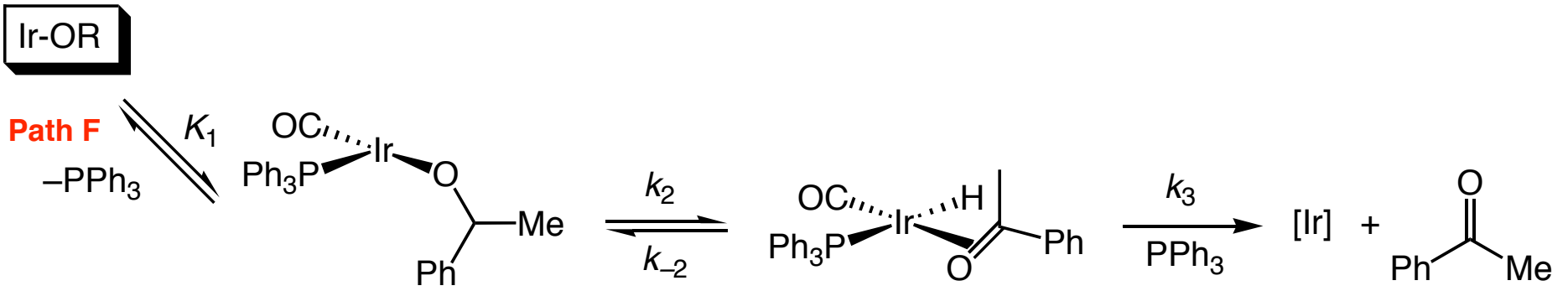

Ir-alkoxides react like their alkyl analogues, and are actually more stable.
Late transition-metal b-hydrogen elimination can occur by several mechanisms.

If you have a system you can study, detailed mechanistic studies can provide insight into basic organometallic transformations that are nevertheless not well understood.