Modern Age of Rhodium Porphyrins:

Review of Prof. Kin Shing Chan

John Thompson

Dong Group Literature Seminar

September 26th, 2013

The Chinese University of Hong Kong

B.S. Chemistry
University of Hong Kong
1981

Post Doc- UofChicago
Prof. Jack Halpern
1989

Lecturer
1990

First Paper
1992

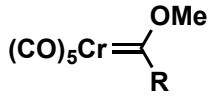
Professor
2002

9/29/1958
Born

1986
Ph.D.- UofChicago
Prof. William Wulff

1989-1990
Ass. Prof.
National Taiwan U

1996
Senior Lecturer/
Ass. Professor

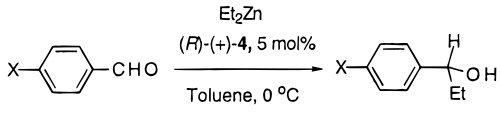


- 138 Papers Published
- Over 25 Graduate Students Trained
- Current leader in Rhodium porphyrin chemistry

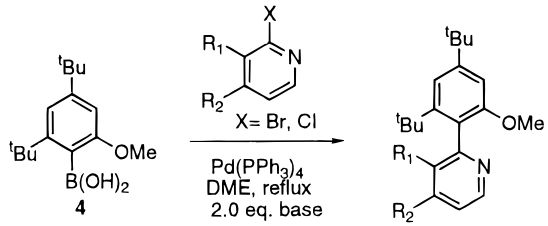
The Chinese University of Hong Kong

Chan Group Chemistry

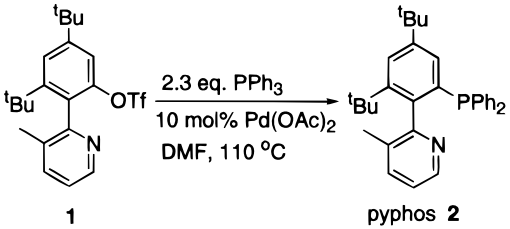
- Pre Metalloporphyrin Expansion-



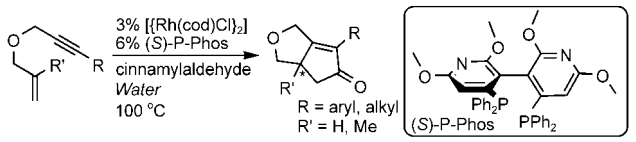
J. Org. Chem. **1996,** *61*, 8002−8003



J. Org. Chem. **1998,** *63*, 6886−6890



Organometallics **2000,** *19*, 2058−2060



Chem. Eur. J. **2005**, *11*, 3872 – 3880

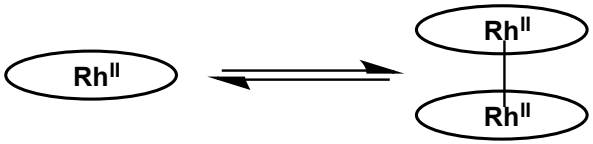
Overview

- K.S. Chan's start with rhodium porphyrins
- Research Focus:
  - 1,2-Rearrangements
  - C-C Activation
  - Base Promoted C-H Activation
  - Misc.

- Future of his chemistry

Metalloporphyrins

- Review:
  - Rhodium and Iridium coordinate strongly to porphyrins
  - The metals can exist in oxidation states of +1, +2, and +3 with porphyrin coordination
  - Ir^{II}/Rh^{II} = 7 electrons, paramagnetic metalloporphyrins
    - Unsterically hindered, exist as dimers
    - Sterically hindered, exist as stable monomers

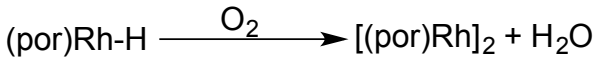


Rich history in Electrophilic Aromatic Substitution and C-H activation of alkanes.

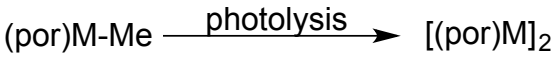
Solving Metalloporphyrin Dimer Formation

- Issue: Synthesis of the reactive Rh^{II}/Ir^{II} dimers is non trivial

Problems:



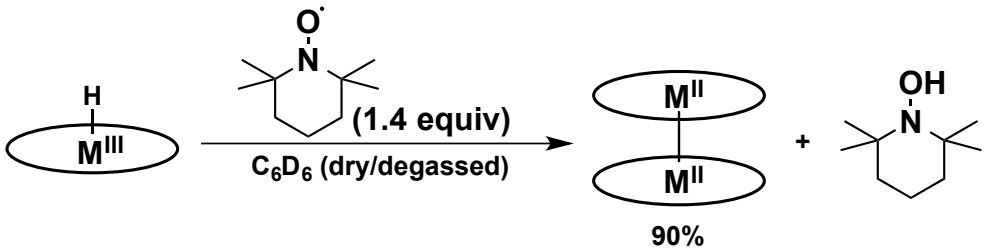
Overoxidation



Low Yielding

M= Rh, Ir

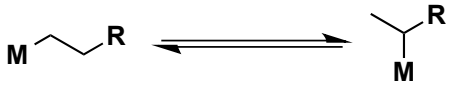
- Novel, high-yielding convenient synthesis that works for Ir and Rh



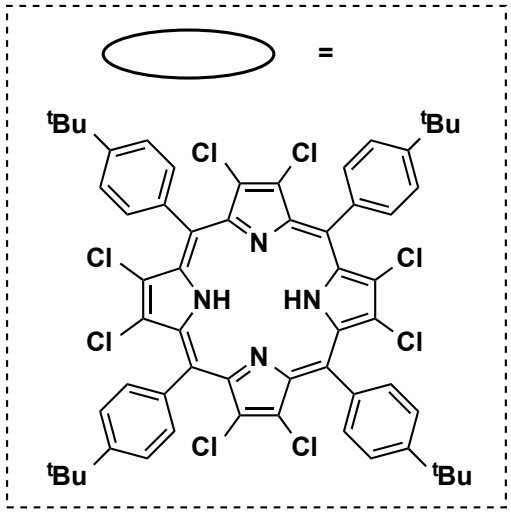
- Stoichiometric in TEMPO, quantitative in yield of dimer

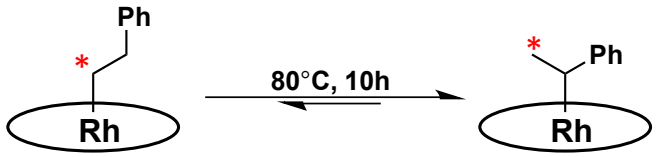
Inorg. Chem. **1994**, *33*, 3187.

1,2-Alkyl Rearrangement



- Rare occurrence in metals with macrocyclic ligands due to lack of cis-coordination





87%

- Reversible: but 2° is favored by 10.5 kcal/mol
- Driving Force: Even though more sterically bulky, electron-withdrawing phenyl group stabilizes 2° Rh-C through bond polarization

Mechanism? Cis-coordination is absent with rhodium porphryins, leaving β-H elimination hindered

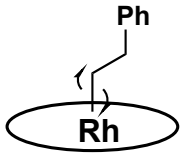
- 1st order in (por)Rh
- ^{13}C label showed Rh migration

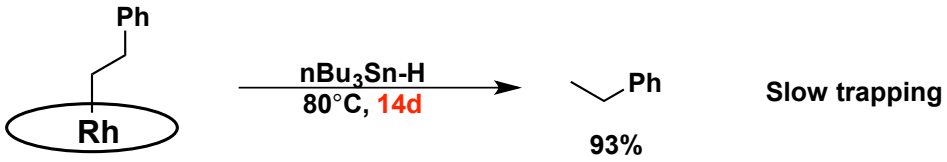
JACS **1998**, *20*, 9686.

1,2-Rearrangement Mecanism

Mechanism: Cis-coordination is absent.

1. Radical process
2. β-H elimination and M-H insertion





Erying plot studied over temperature ranges showed organized transition state

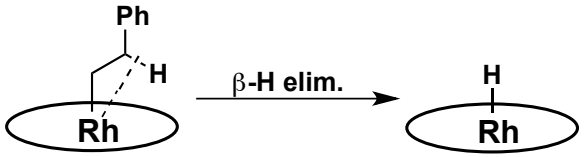
Radical involvement unlikely

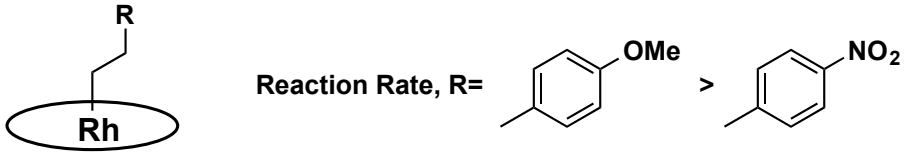
JACS **1998**, *20*, 9686.

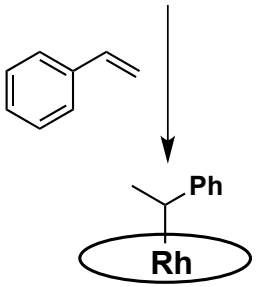
1,2-Rearrangement Mecanism

Mechanism: Cis-coordination is absent.

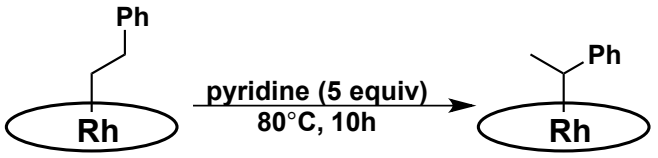
1. Radical process
2. β-H elimination and M-H insertion







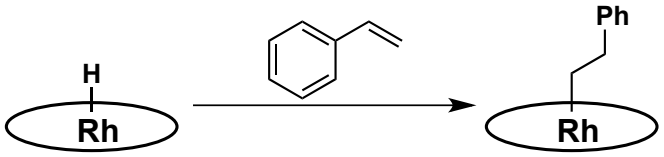
⊕ positive charge develops on benzylic carbon
- Benzylic hydrogen migrates as hydride



20%

-rate decreased to 1/8th

-pyridine caused coordination saturation



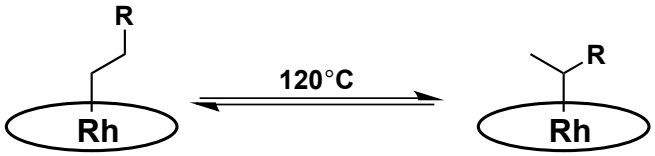
88%

plausible Rh-H intermediate

JACS **1998**, *20*, 9686.

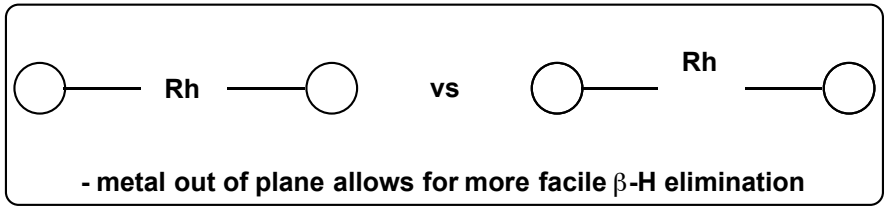
Electronic Effects of Rearrangement

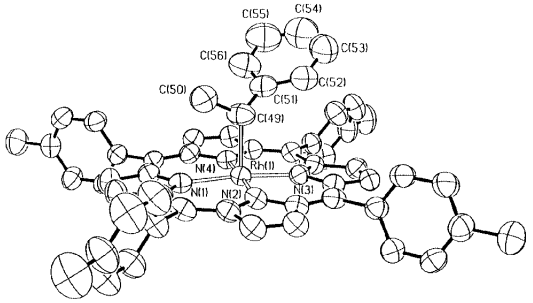
- New study with planar porphyrins



R	Time (h)	2°/1° Ratio
Ph	246	0.70
CH_3	144	7.5
OMe	18	15

 = $(TTP)H_2$ (para methyls)

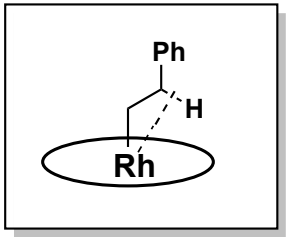




- Planar porporphyrins required higher temperature
  (Xray shows rhodium in plane of porphyrin)

- Electronic Effect:
  EWG: favors rearrangement
  EDG: favors starting material

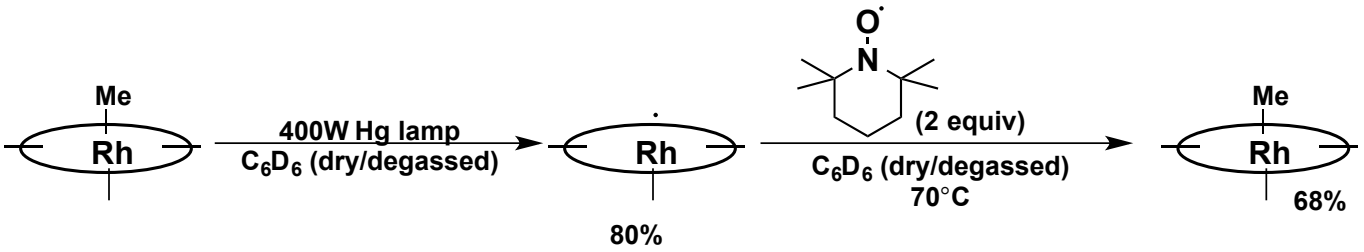
***Promotes stabilization of carbocation



J. Chem. Soc., Dalton Trans., **1999**, 3333.

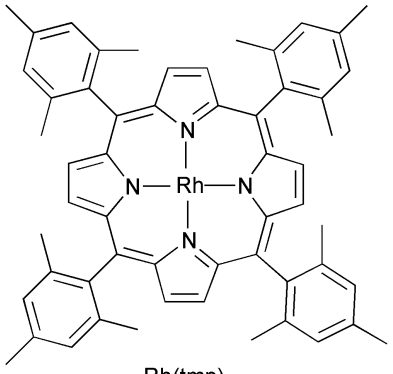
Back to TEMPO – What else could happen?

- Activation of C_{alkyl}-C_{alkyl} bonds of nitroxide radicals

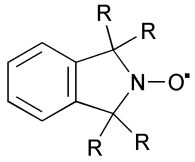


More reactive rhodium porphyrin

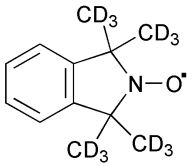
Wayland's Wo



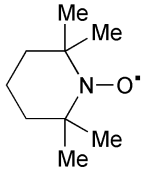
Rh(tmp)



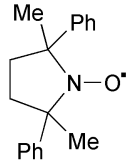
– R = Me, TMINO
R = Et, TEINO



TMINO-CD$_3$



TEMPO



DMPNO

lea

CH_4
C_6D_6, 120°C

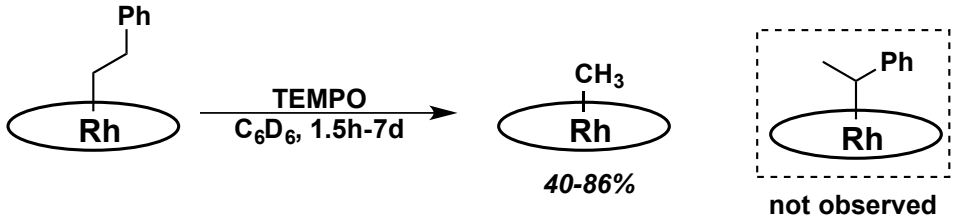
t can activate C-H Bonds

Entry	Nitroxide	Temperature/ °C	Time/h	Yield of Rh(tmp)R (%)
1	**TMINO**	70	4	73
2	**TMINO-CD$_3$**	70	4	68
3	**TEMPO**	70	4	68
4	**DMPNO**	110	46	86
5	**TEINO**	110	40	40

J. Chem. Soc., Dalton Trans., **2011**, 510.

TEMPO: Reagent, not Radical Trap

- During investigation of 1,2-rearangment of alkyl rhodium porphyrins, TEMPO underwent CCA.
  - Reactivity was depended on β-C-H bond strength



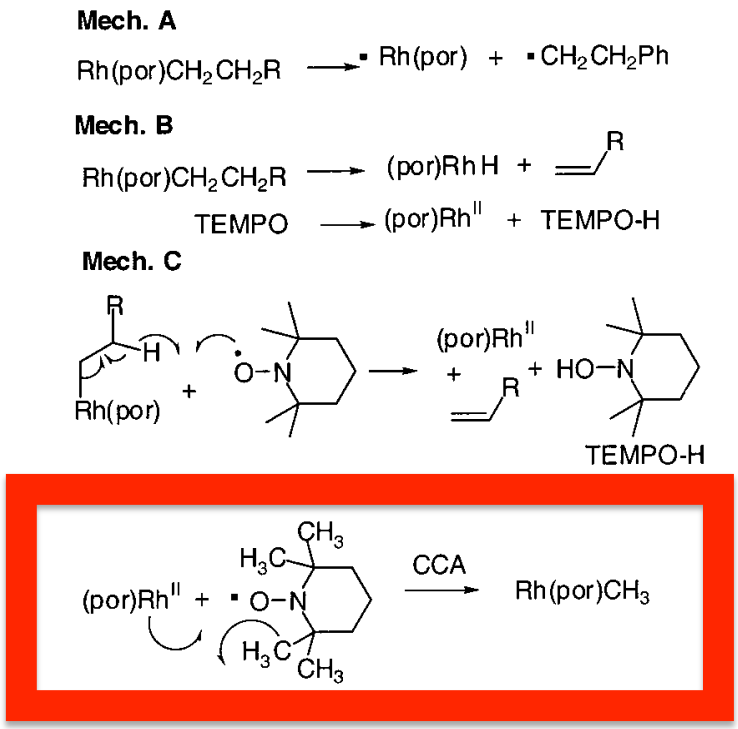
  - [TEMPO] increase → increase in reaction rate
  - Alkyl porphyrins, like propyl or ethyl, required 7 and 14 days respectively

  - Rhodium-Carbon bond was cleaved in reaction

Organometallics, **2002**, *21*, 2362.

TEMPO: Reagent, not Radical Trap

- Mechanism occurs in 2 steps:
  A) Generation of Rh^{II}
  B) CCA of TEMPO



Mech. A:
- Requires homolysis of strong Rh-C bond
- Absence of trapped product

Mech. B:
- Supported by Rh-H intermediate
- Disappearance of starting material was directly related to [TEMPO]
- Without TEMPO, 1,2-rearrangement took 10 to 144 h, no Rh-H intermediate

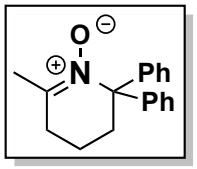
Mech. C:
- Synchronous H-abstraction with homolysis of Rh-C bond.
- Explains trend in TEMPO concentration

CCA Mechanism is still unexplored

Organometallics, **2002**, *21*, 2362.

TEMPO C-C Activation Mechanism

- Competes with CHA at lower temperatures



Isolated in Previous Work

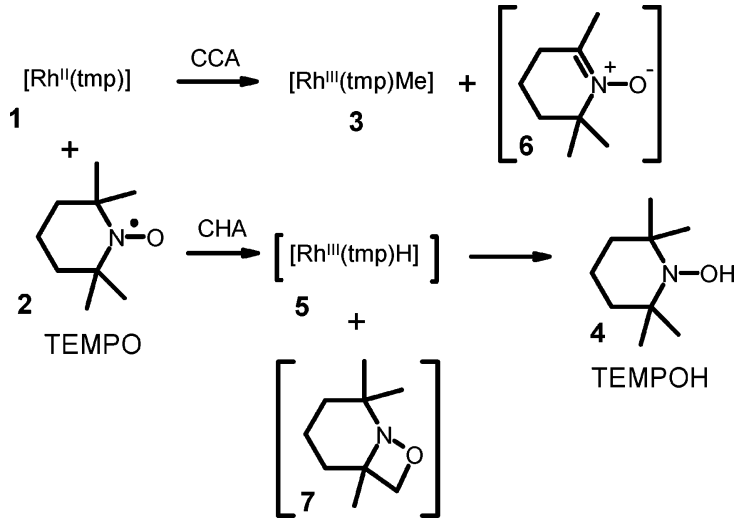
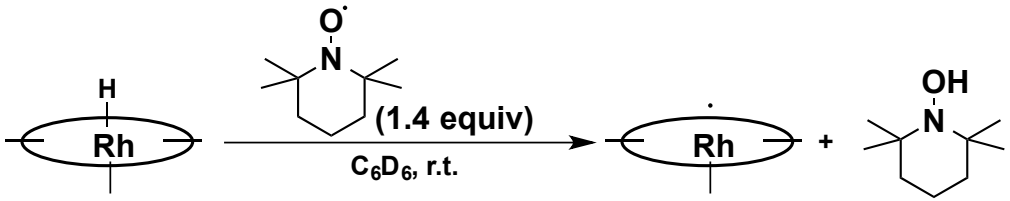


Table 1. Yields of Rh(tmp)Me and TEMPOH

entry	temp °C	TEMPO equiv	% Rh(tmp)Me	% TEMPOH	% total yield	Rh(tmp)Me: TEMPOH
1	70	1	60	5.7	65.7	10.5:1
2	70	2	76	8.0	83.0	9.5:1
3	70	5	80	9.0	89.0	8.9:1
4	70	20	82	9.3	91.3	8.8:1
5	50	20	73	16.8	89.8	4.4:1
6	60	20	76	12.3	88.3	6.1:1
7	80	20	85	3.9	88.9	21.8:1

- TEMPO-**H** believed to come from a Rh-H intermediate



>96%

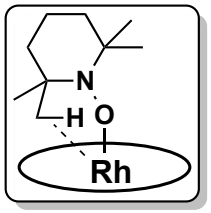
JACS, **2008**, *130*, 2051.

TEMPO-H Hydrogen Source

- If Rh-H is indeed the intermediate, then where did “H” atom originate?
  - Solvent (Benzene)
  - TEMPO
  - Starting Material [(TMP)Rh^{II}]
  - Product [(TMP)Rh^{III}-Me]

Extremely difficult
Stable in benzene at 70°C for 24h
Stable in benzene at 130°C for 2d
No reaction at 70°C

- Formed from chelation assisted CHA

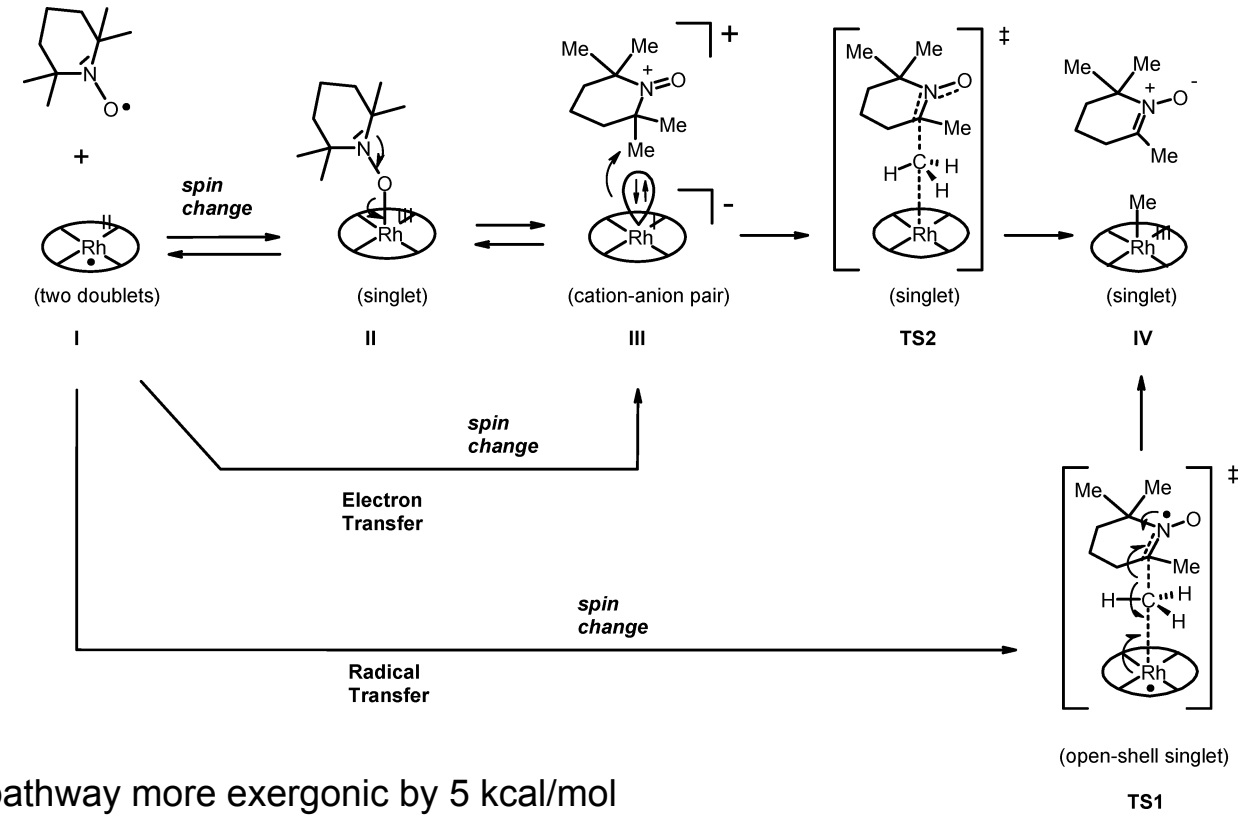


» Driven by fast TEMPO H-atom abstraction
» TEMPO-H yields do increase with higher [TEMPO]
» Binding studies showed a 1:1 adduct
» Secondary H’s unlikely due to unstable products

JACS, **2008**, *130*, 2051.

DFT Analysis of CCA

- Propose methyl transfer occurs through radical or S_N2-like transition states.

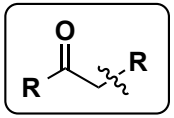


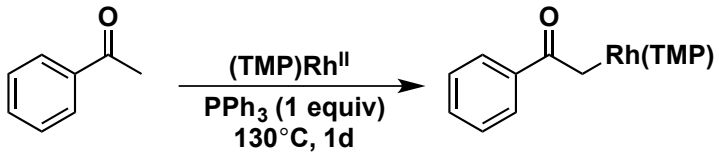
- Radical pathway more exergonic by 5 kcal/mol
  - Both are plausible

JACS, **2008**, *130*, 2051.

Activation of Ketones

- Activation of C_{CO}-C_{alkyl} has been established, while $C_{\alpha\text{-}CO}$-C_{alkyl} was unexplored



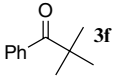
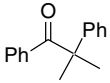
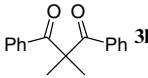
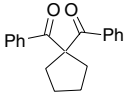
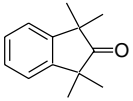
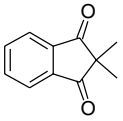
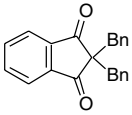


-only CHA product due to enolizable protons

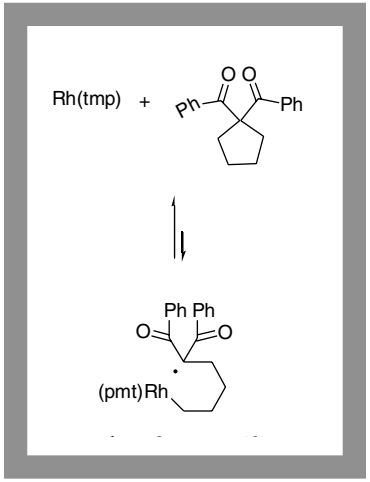
J. Organomet. Chem., **2006**, *691*, 3782.

Activation of Non-Enolizable Ketones

CCA results between Rh(tmp) and ketones

Entry	Ketone[a]	Ligand	Time (d)	Product (Yield [%][d])
1	 **3d**	None		Rh(tmp)CH_3 **1** (20)
2		Ph_3P[b]	1	Rh(tmp)CH_3 **1** (31)
3		py[c]		Rh(tmp)CH_3 **1** (22)
4	 **3e**	Ph_3P[b]	3	Rh(tmp)CH_3 **1**(trace)
5	 **3f**	Ph_3P[b]	1	Rh(tmp)CH_3 **1** (18, 16[e])
6	 **3g** [26]	Ph_3P[b]	1	Rh(tmp)CH_3 **1** (24)
7	 **3h** [27]	Ph_3P[b]	1	Rh(tmp)CH_3 **1** (14)
8	 **3i** [28]	Ph_3P[b]	3	No reaction
9	 **3j** [29]	Ph_3P[b]	1	Rh(tmp)CH_3 **1** (25)
10	 **3k** [30]	Ph_3P[b]	1	Rh(tmp)CH_3 **1** (30)
11	 **3l** [30]	Ph_3P[b]	3	Rh(tmp)Bn **10** (6)

- PPh_3 = More e^- rich/ reactive (por)Rh^{II}
- Pyridine= induces disproportionation



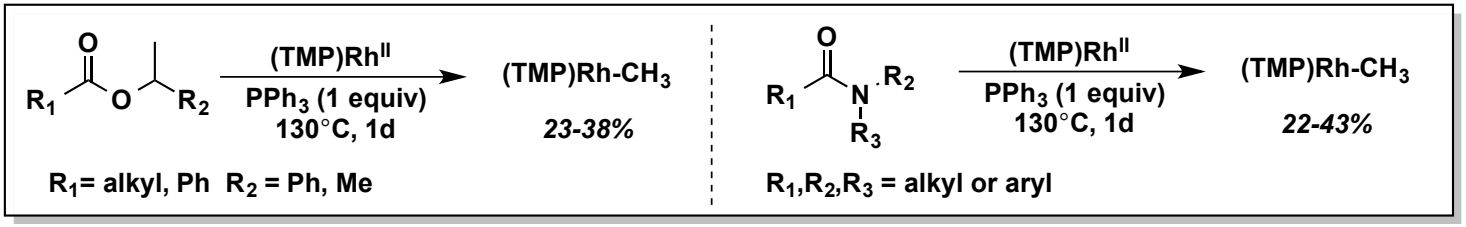
- Cyclic ketones unreactive

$$(TMP)Rh^{II} \xrightarrow{py} py(TMP)Rh^{III} + py(TMP)Rh^{I}$$

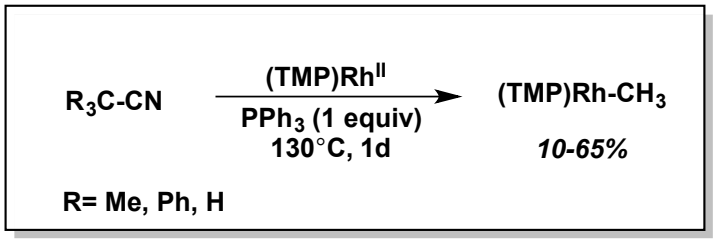
J. Organomet. Chem., **2006**, *691*, 3782.

Aliphatic Carbon-Carbon Bond Activation

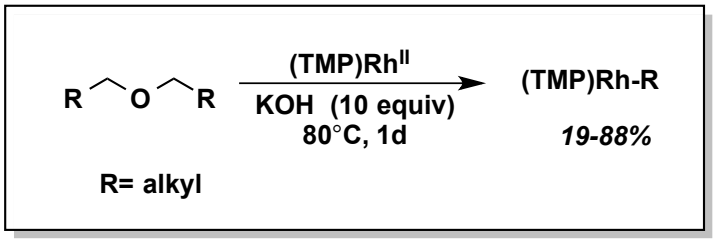
- Reactions for the $C_{\alpha\text{-}CO}$-C_{alkyl} activation were low yielding with strict substrate compatibility
- Other applications:



J. Organomet. Chem. **2007**, *692*, 2021.



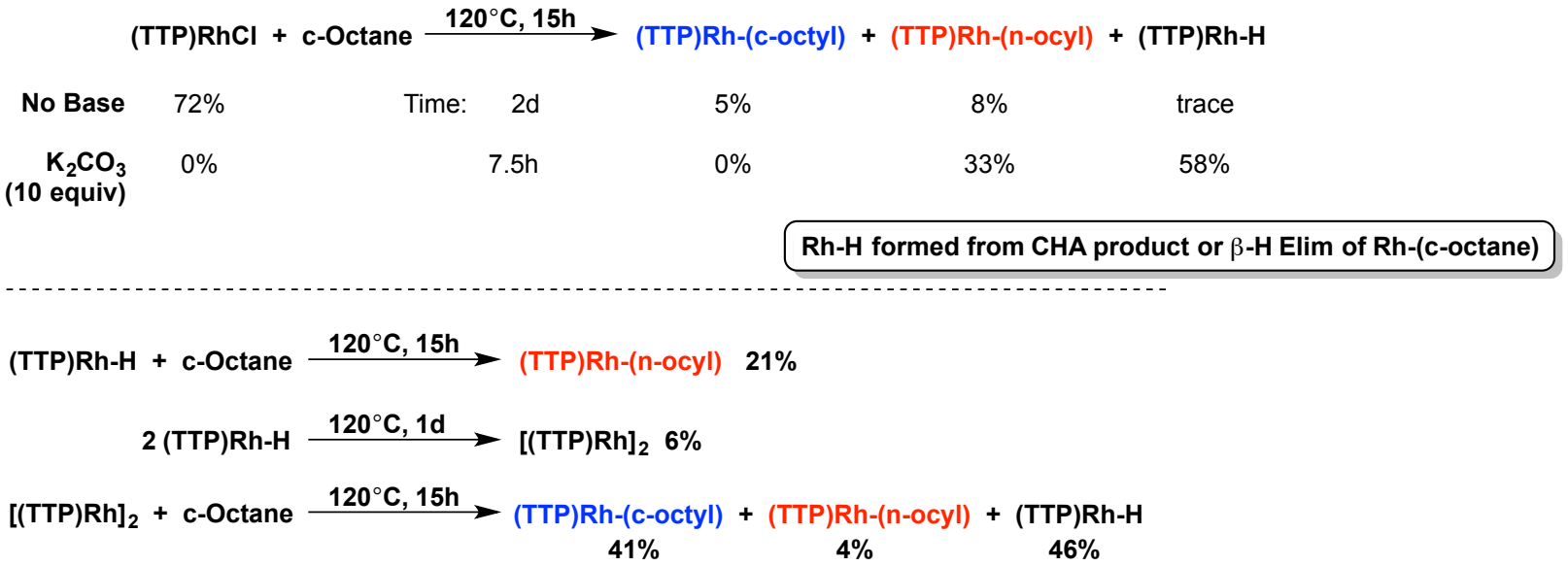
Organometallics **2007**, *26*, 2679.



Organometallics **2009**, *28*, 6845.

C-C Ring Opening of Cyclooctane

- Cyclooctane is relatively unstrained, common target for C-H activation.
- C-C activation is rare; heterogeneous conditions requiring 530°C or oxidative conditions with Co (II)/Mn(II)/N-hydroxyphthalides yielding the diacid in 2% yield.



- Both (TPP)Rh-H and $[(TPP)Rh]_2$ gave low yields
  - Only minor intermediates by themselves

JACS **2010**, *132*, 6920.

C-C Ring Opening of Cyclooctane

CCA catalyzed by [Rh^{II}]

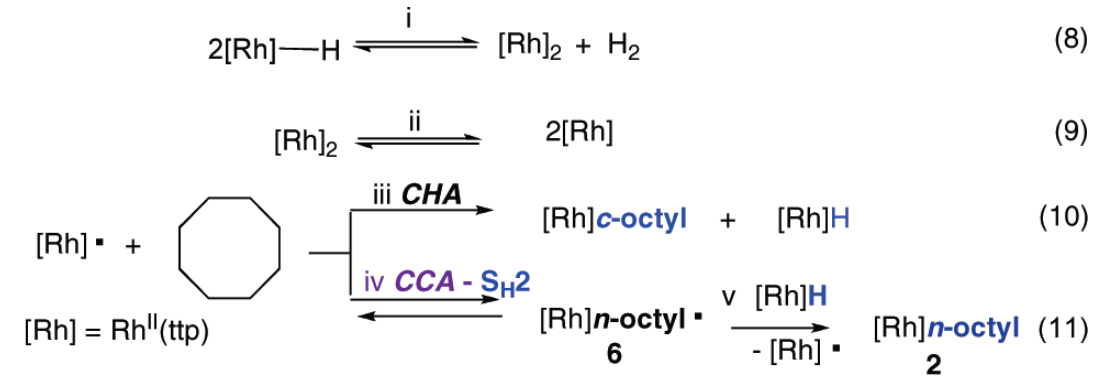
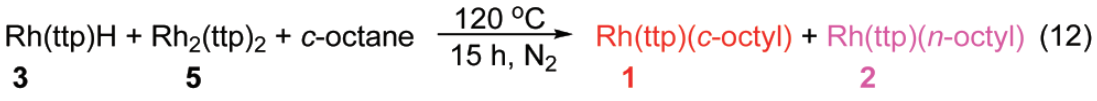


Table 1. Rh^{II}(ttp)-Catalyzed CCA of *c*-Octane wih Rh(ttp)H



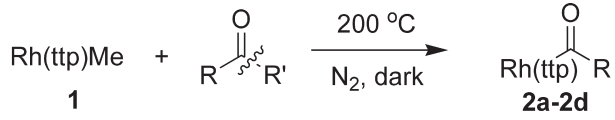
Entry[a]	3:5	Yield **1** (%)	Yield **2** (%)	Total yield (%)
1[b]	1:0	0	21	21
2	2:1	60	18	78
3	5:1	53	26	79
4	10:1	0	73	73

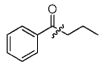
[a] The results are the average of at least duplicate. [b] 73% Rh(ttp)H recovered.

JACS **2010**, *132*, 6920.

Selective C_{co}-C_{α} Bond Cleavage of Ketones

Table 1. CCA of Ketones by Rh(ttp)Me

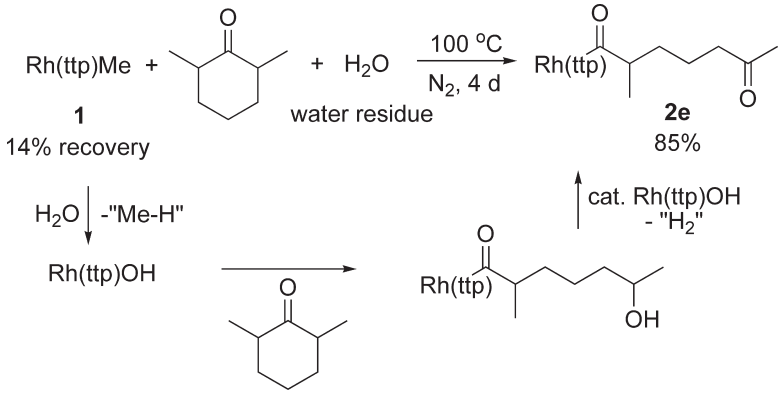


entry	ketones	C(CO)-C(α) BDE[7]/ kcal mol^{-1}	time	% yield
1		85.0	15d	**2a** 93
2		82.2	15d	**2a** 44
3		---	19d	**2a** 43
4		---	1d	**2a** 97
5		84.1	17d	**2b** 20
6		82.3	16d	**2c** 45
7		81.3	1d	**2b** 95
8		~81.3	30 min	**2d** 86[a]

[a] Acetone was observed after the reaction.

- Side reaction from original C-C activation of ketones

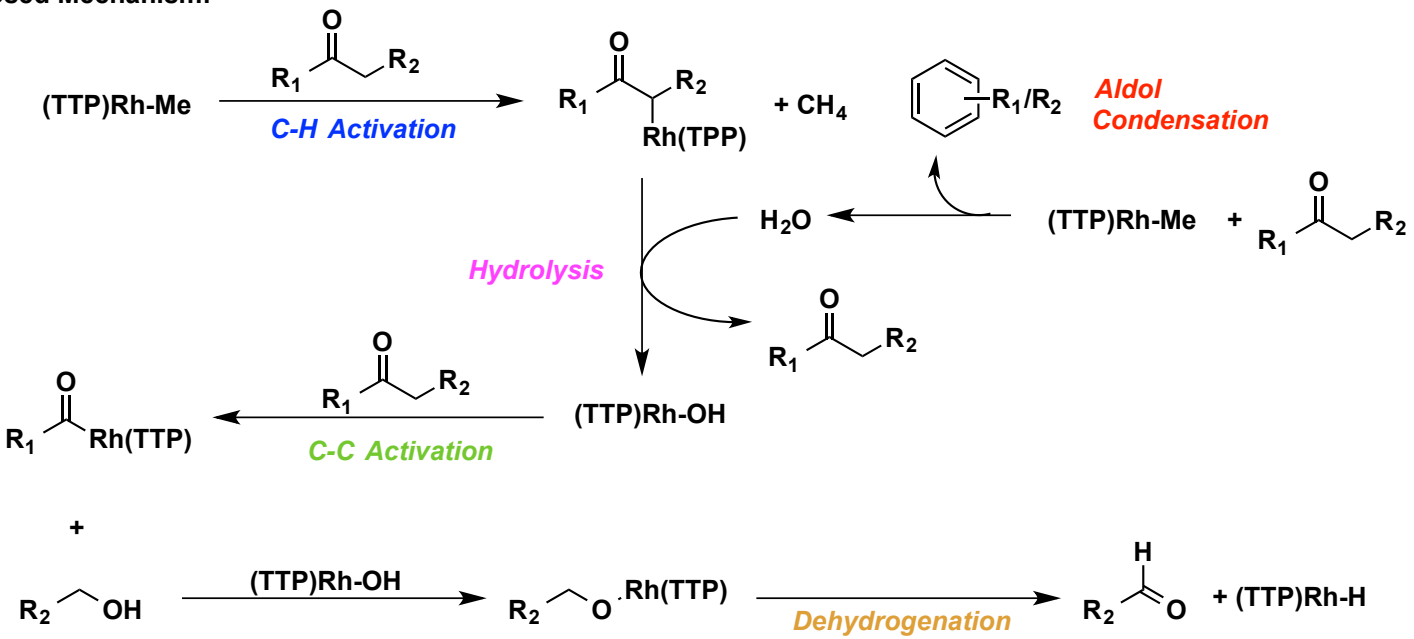
Scheme 2. Reaction of Rh(ttp)Me with 2,6-Dimethylcyclohexanone



Organometallics **2010**, *29*, 4421.

C_{CO}-C_{α} Bond Cleavage Mechanism

Proposed Mechanism:



C-H Activation

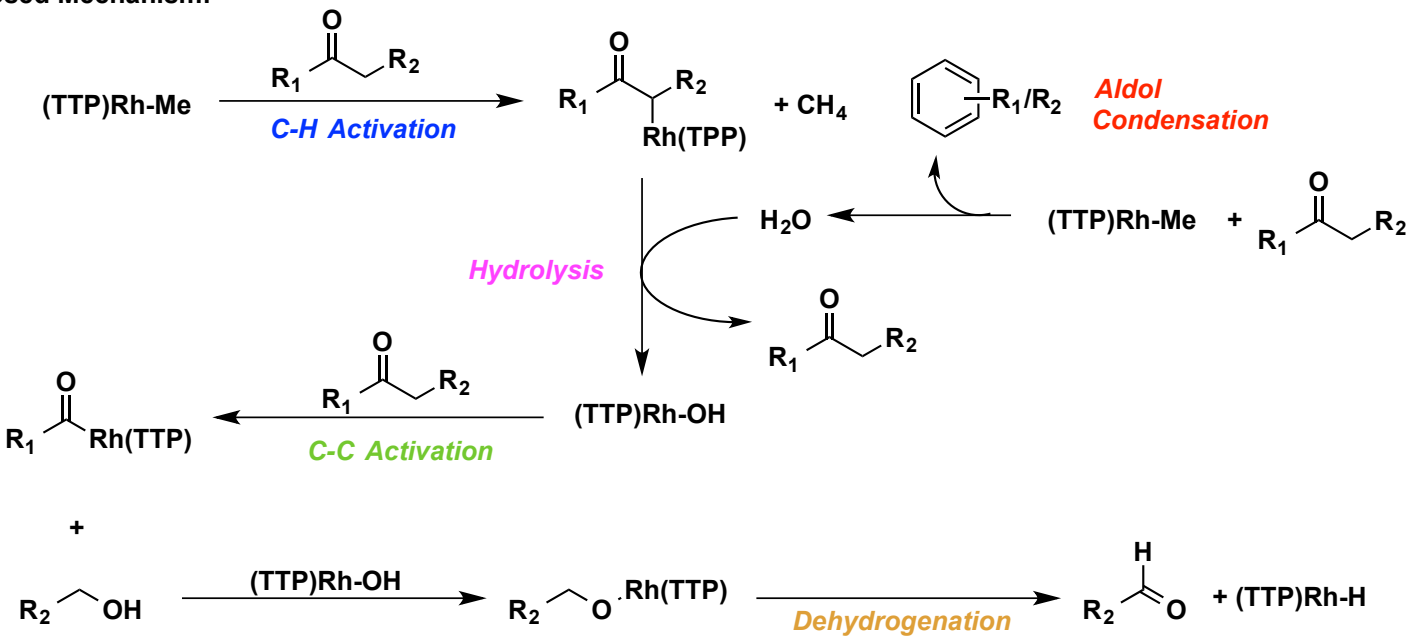
$$\mathrm{Rh(ttp)Me} + \mathrm{PhCOMe} \xrightarrow[\mathrm{C_6D_6,\ 30\ min}]{200\ ^{\circ}\mathrm{C}} \mathrm{Rh(ttp)CH_2COPh} + \mathrm{Rh(ttp)H} + \mathrm{Me\text{-}H} \quad (4)$$

1 100 equiv **4** 66% **3b** 33% 87%

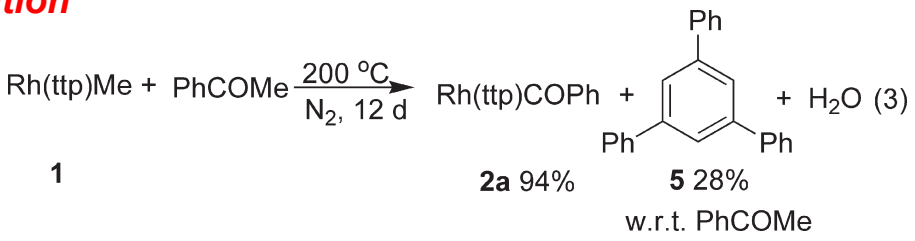
Organometallics **2010**, *29*, 4421.

C_{CO}-C_{α} Bond Cleavage Mechanism

Proposed Mechanism:



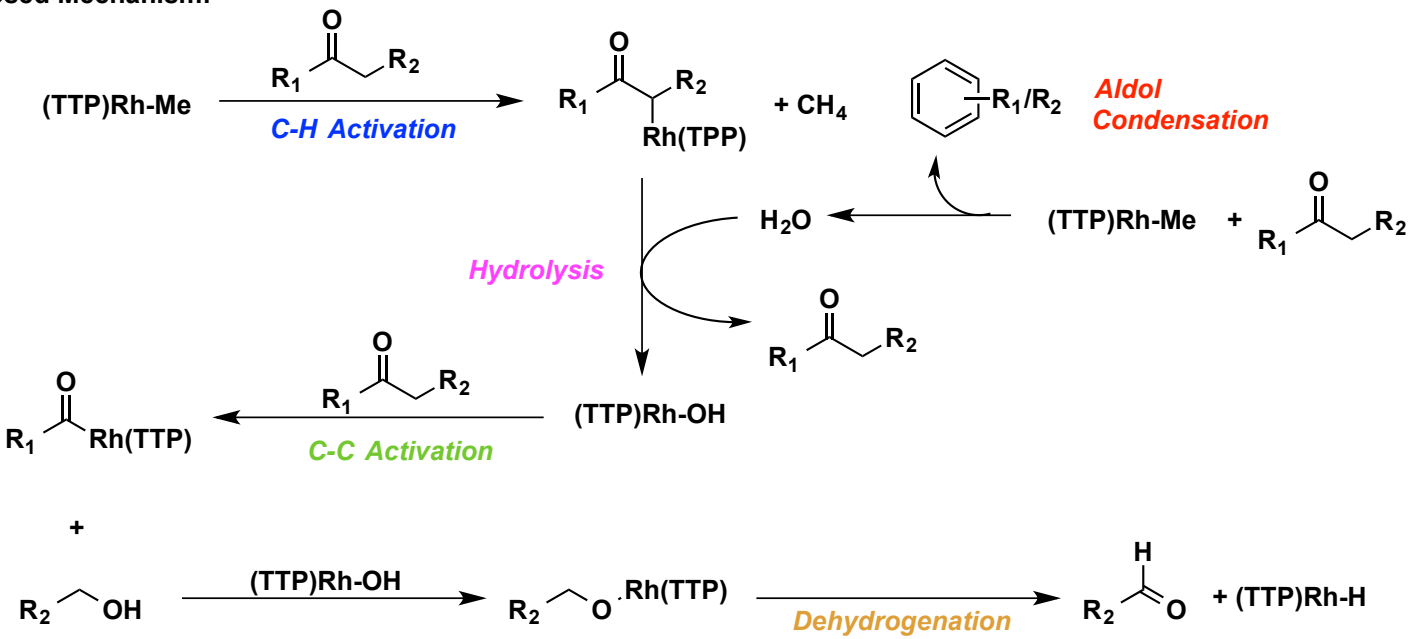
Aldol Condensation



Organometallics **2010**, *29*, 4421.

C_{CO}-C_{α} Bond Cleavage Mechanism

Proposed Mechanism:



Hydrolysis

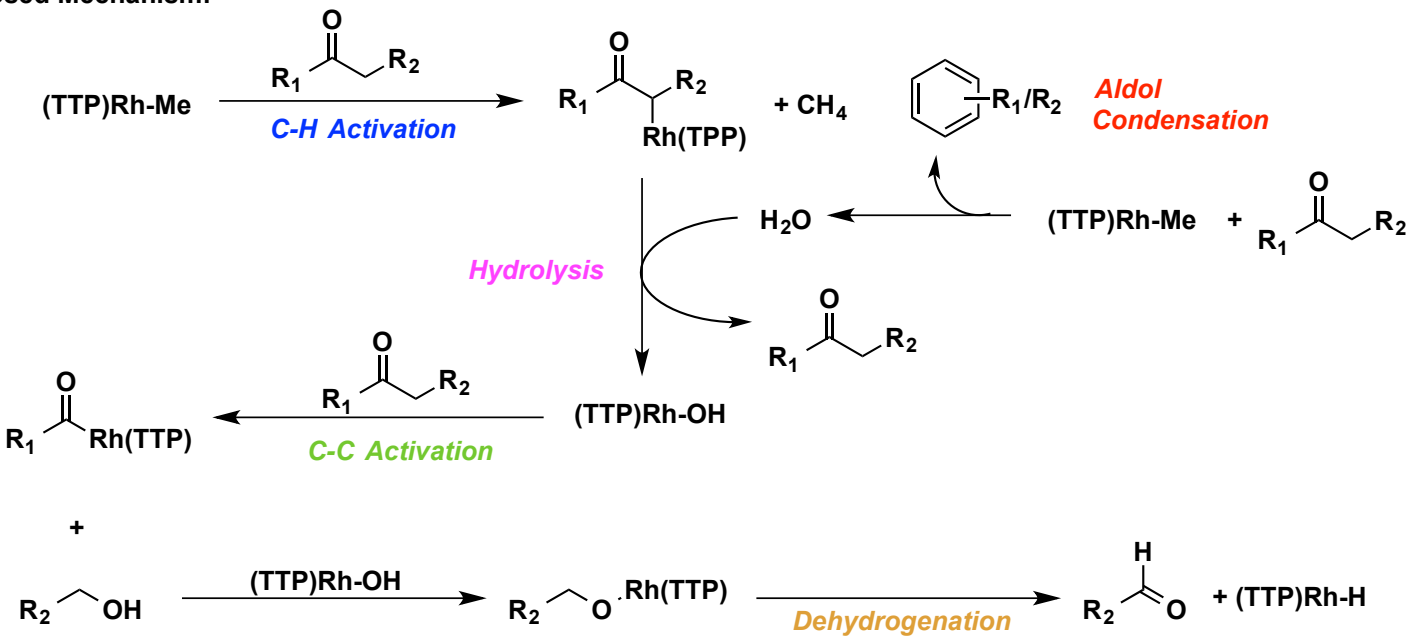
$$Rh(ttp)CH_2COPh + H_2O \xrightarrow[C_6D_6,\ 5\ min]{200\ ^{o}C} Rh(ttp)H + Rh_2(ttp)_2 + PhCOMe \quad (5)$$

4b ~42% recovery; 100 equiv; **3b** ~42%; **3c** ~13%; 57%; NMR yield w.r.t. Rh

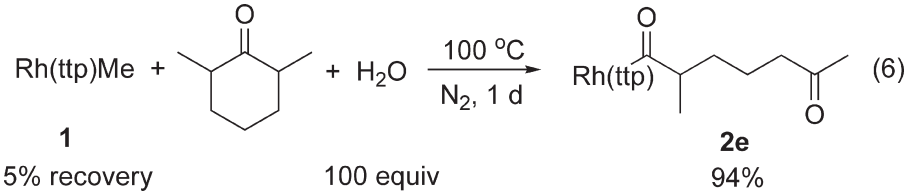
Organometallics **2010**, *29*, 4421.

C_{CO}-C_{α} Bond Cleavage Mechanism

Proposed Mechanism:



C-C Activation (σ-bond metathesis)
Dehydrogenation

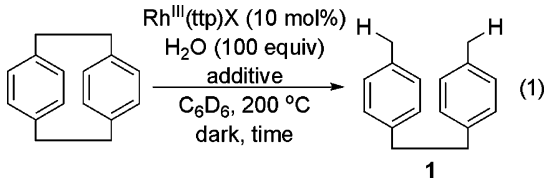


Organometallics **2010**, *29*, 4421.

Catalytic C-C σ-Bond Hydrogenation

- Replaces H_2 with H_2O as hydrogen donor in hydrogenation in tandem CCA

Table 1. Catalytic Carbon–Carbon Bond Hydrogenation of PCP with Water

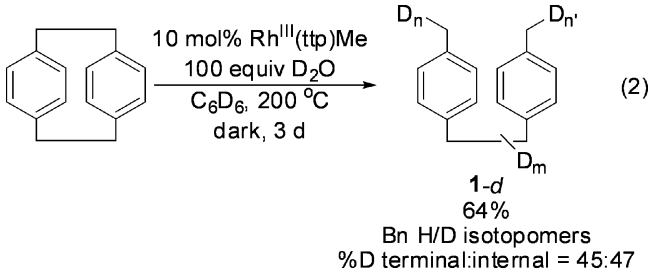


(1)

1

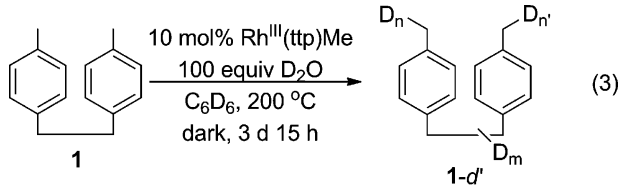
entry	X	additive	time/h	yield of **1** (%)
1	I	KOH (1 equiv)	25	83
2[a]	Me	–	54	78

[a] A 79% yield of CH_4 with respect to Rh^{III}(ttp)Me was formed.



(2)

1-*d*
64%
Bn H/D isotopomers
%D terminal:internal = 45:47



(3)

1

1-*d'*
quantitative
Bn H/D isotopomers
%D terminal:internal = 8:71

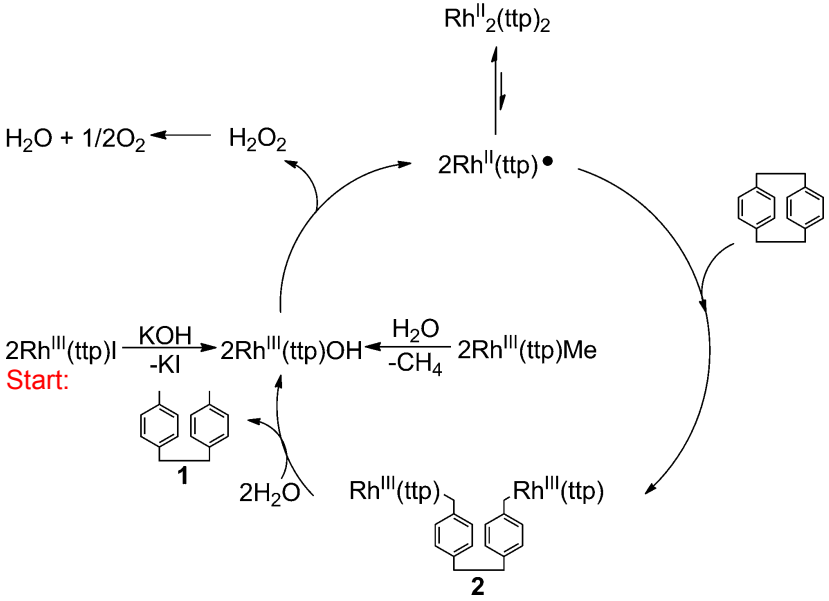
- No CHA was occurring
- Reaction was 2nd order with (TMP)Rh
- Mechanism of Rh-Me exchange is through σ-bond metathesis

- Deuterium experiments confirmed H_2O was source of hydrogen

JACS, **2012**, *134*, 11388.

Catalytic C-C σ-Bond Hydrogenation

Scheme 2. Proposed Catalytic Cycle



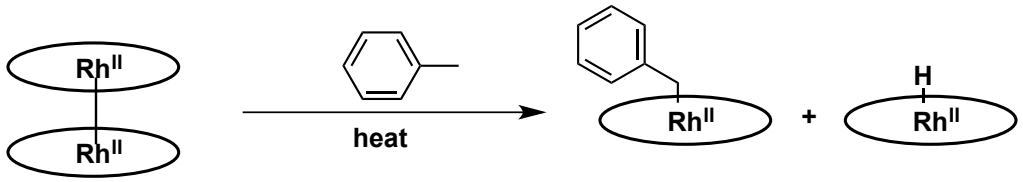
- Replaces H_2 with H_2O as hydrogen donor in hydrogenation in tandem CCA

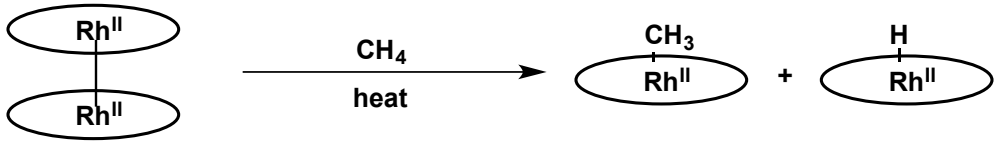
$$\underset{2\%}{Rh^{III}(ttp)Bn} \xrightarrow[200\ ^{o}C,\ dark,\ 3.5\ d]{1000\ equiv\ H_2O,\ benzene\text{-}d_6} \underset{66\%}{PhCH_3} + \underset{15\%}{Rh^{III}(ttp)H} + \underset{41\%}{\text{Rh porphyrin unknowns}} \quad (5)$$

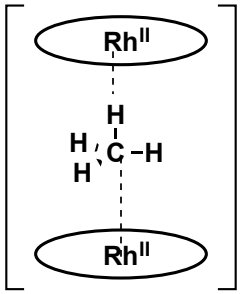
JACS, **2012**, *134*, 11388.

Switch Gears: C-H Activation

- Before Chan, this field was dominated by Bradford Wayland







JACS, **1991**, *113*, 5305.

Switch Gears: C-H Activation

- Went into C-H Activation field going back to Wayland's work, but found an interesting discovery

120°C, 3days:	**26%**	**26%**	**13%**
200°C, 1day:	**65%**	**0**	**0**

- High temperature favored less stable rhodium-alkyl bond
- Coordinating ligands were not effective, only forming complexes with rhodium

- 10equiv base
- 30min-1hr rxn

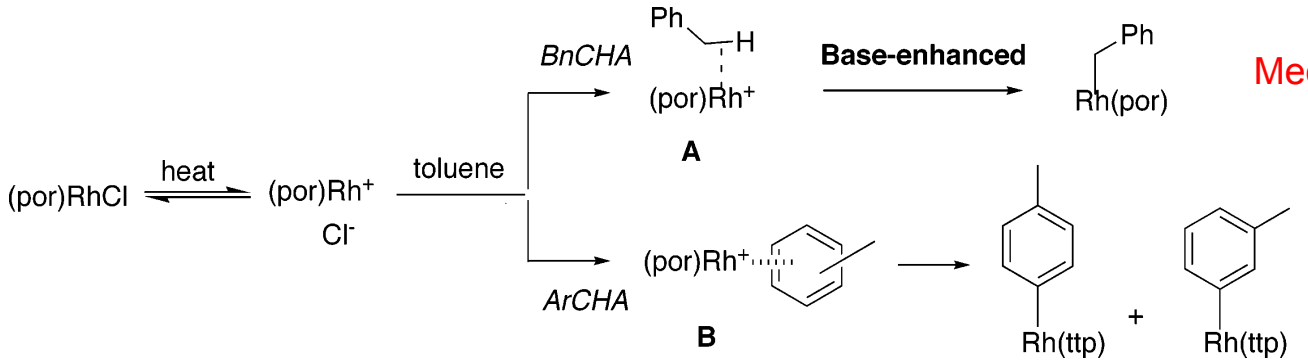
Table 2. Base Effect in CHA

entry	base	time/min	yield/%
1	NaOH	45	94
2	KOH	60	94
3	K_2CO_3	30	97
4	$KHCO_3$	600	94

Organometallics, **2007**, *26*, 1117.

C-H Activation of Toluenes

Scheme 1. Mechanism of CHA



Mech discussed later

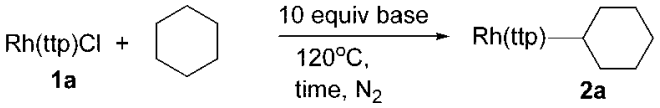
Table 3. Benzylic CHA of Toluenes

		entry A (K_2CO_3)		entry B (no K_2CO_3)	
entry	FG	time/min	product (yield/%)	time/days	product (yield/%)
1	OMe	30	**2a** (92)	2	**2a** (78)
2	^{t}Bu	45	**2b** (98)	2	**2b** (84)
3	Me	45	**2c** (90)		
4	*3,5*-Me_2	45	**2d** (45)	3	**2d** (35)
5	H	30	**2** (97)	3	**2** (26)
6	F	240	**2e** (64)	3	**2e** (72)
7	CN	60	**2f** (83)	3	no reacn
8	NO_2	30	**2**g (98)	1	no pdt

Organometallics, **2007**, *26*, 1117.

C-H Activation of Alkanes

Table 2. Base Effect in CHA

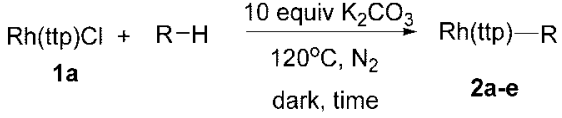


(2)

entry	base	time (h)	yield (%)
1	none	24	31
2	PPh_3	24	0[a]
3	2,2′-bpy[b]	48	50
4	2,6-dbpy[c]	24	50
5	2,6-dppy[d]	24	58
6	2,6-dppy[d]	6	23
7	NaOH	6	47
8	NaOAc	6	51
9	K_2CO_3	6	59
10	K_2CO_3	24	40

[a] Rh(ttp)Cl(PPh_3) (**2f**) was obtained in 83% yield. [b] 2,2′-bpy = 2,2′-bipyridine. [c] 2,6-dbpy = 2,6-di-*tert*-butylpyridine. [d] 2,6-dppy = 2,6-diphenylpyridine.

Table 5. Activation of Alkanes with Rh(ttp)Cl



(5)

entry	substrate	time (h)	product (yield (%))
1	cyclopentane	6	**2b** (76)
2	cyclohexane	6	**2a** (59)
3	*n*-pentane	24	**2c** (29)
4	*n*-hexane	24	**2d** (40)
5	*n*-heptane	24	**2e** (58)

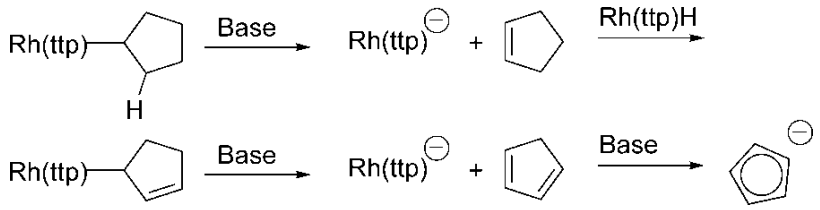
- Inorganic bases promoted both yields and rates of reaction (at 10 equiv)
- More electron deficient porphyrins reacted faster
- Linear alkanes required longer time but yields increased for longer chains due to solubility

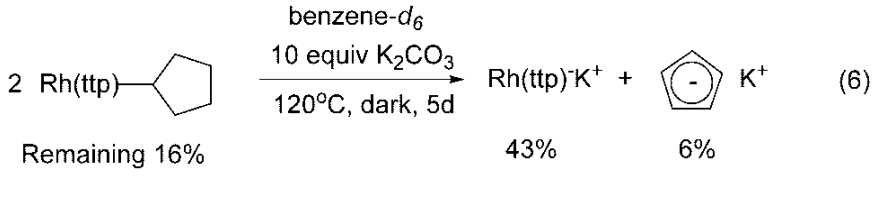
Organometallics, **2008**, *27*, 4625.

C-H Activation of Alkanes

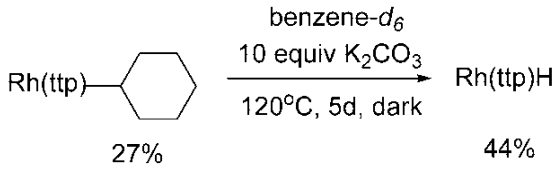
- What happens to the rhodium alkyls over time with base to cause lower yields?

Scheme 1. Proposed Decomposition Pathway of Rh(ttp)(cyclopentyl)





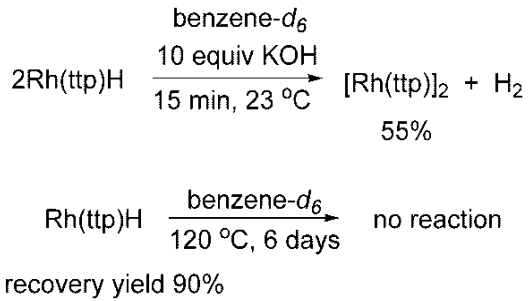
- E2 elimination of (TTP)Rh (Rh-H is moderately strong acid, pka~11)
- C-H activation at allylic position occurs → E2 again → polymer or forms cyclopentadienyl anion



- Cyclohexyl was more stable due to smaller dihedral angle, disfavoring E2 elimination

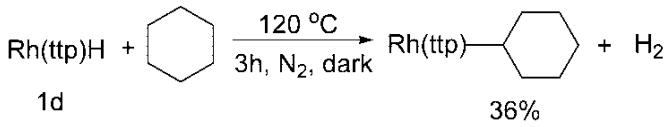
Organometallics, **2008**, *27*, 4625.

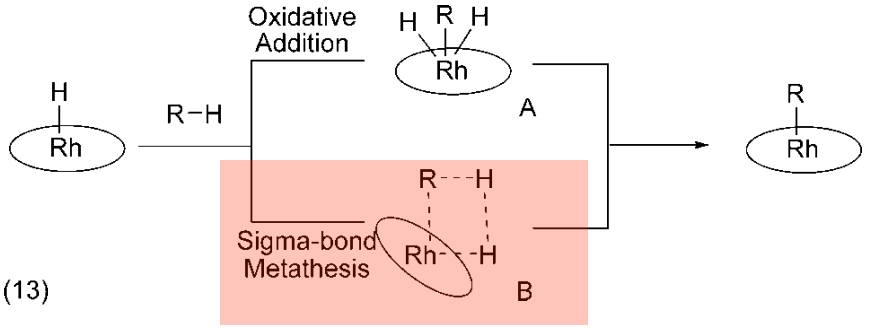
C-H Activation Mechanism

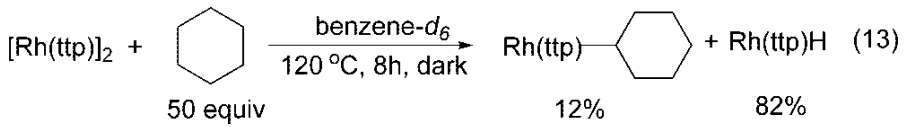


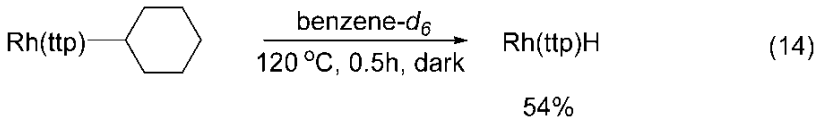
- Possible intermediates: Rh-H or Rh^{II}
  - Conditions form Rh^{II} but Rh-H is stable
  - Both were found to undergo CHA
    - Lower yields due to β-H elim.

- Proposed Mechanism





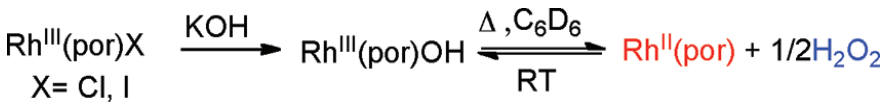




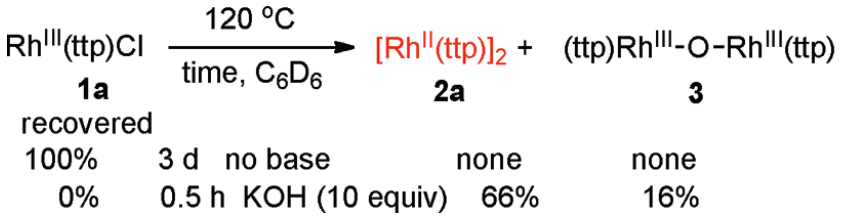
Organometallics, **2008**, *27*, 4625.

Role of $^-$OH: The Reductant

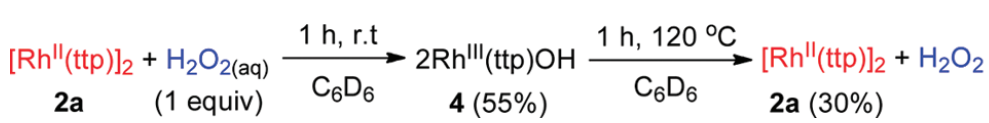
- In these base catalyzed reactions, the role of hydroxide has only hypothetically been examined

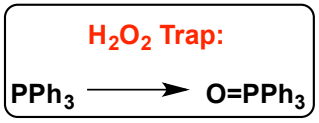


- Rh-OH bond is weak



- Ligand substitution of Rh-Cl to Rh-OH
  - Hydroxide ion is a reducing agent
  - Donates 1 e^- to Rh^{III} to make Rh^{II} and hydroxide radical (reported for Mn/Fe/Co porphyrins)

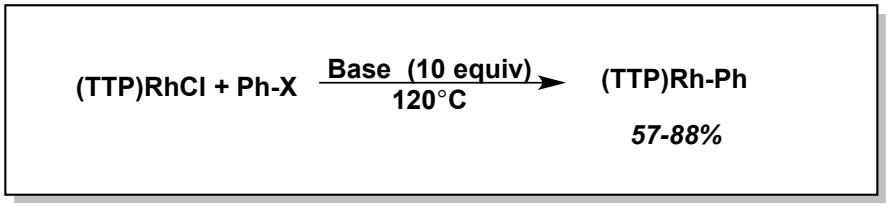




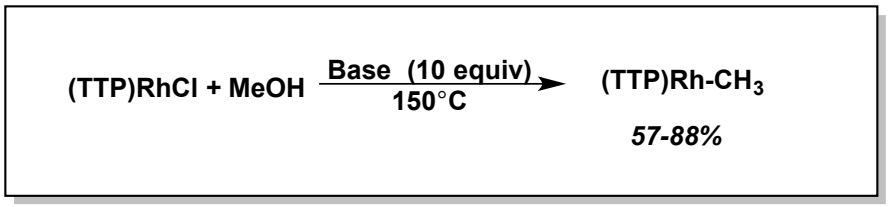
Organometallics **2011**, *30*, 2633.

Uses of the Base Reduction

- This discovery helps explain past results and produce new chemical reactions

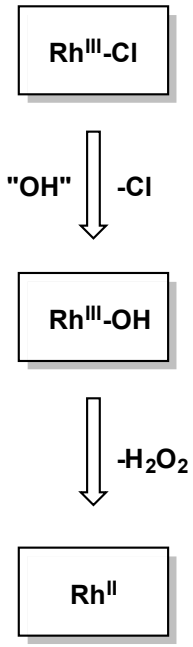


Organometallics **2012**, *31*, 5452.



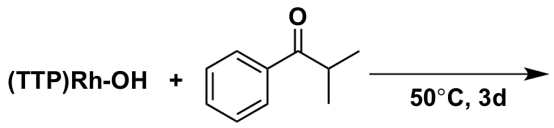
Organometallics **2009**, *28*, 3981.

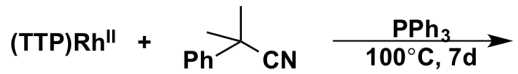
Base Reduction used commonly in Chan's Iridium Chemistry

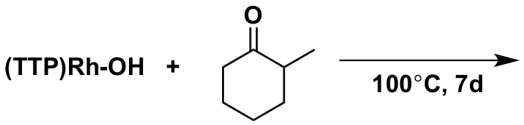



THANK YOU!
Questions?

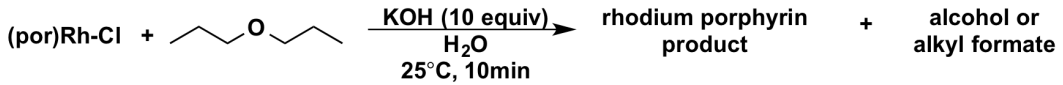
1. Predict the product.



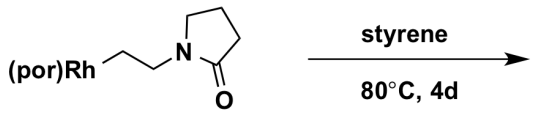




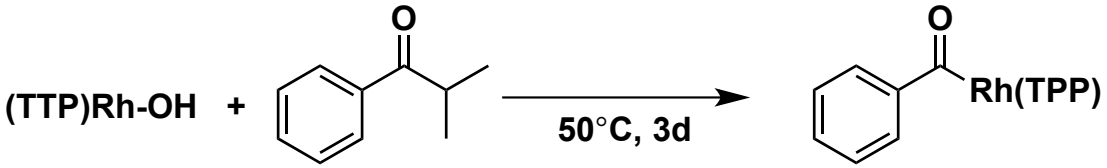
2. Propose a mechanism for the reaction below. Provide the rhodium porphyrin product and one of the ether by-products.

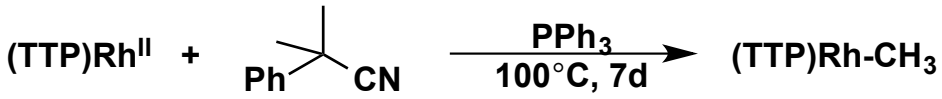


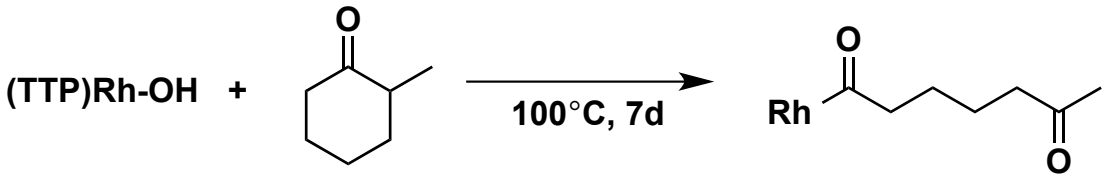
3. Propose a mechanism and predict the inorganic and organic product.

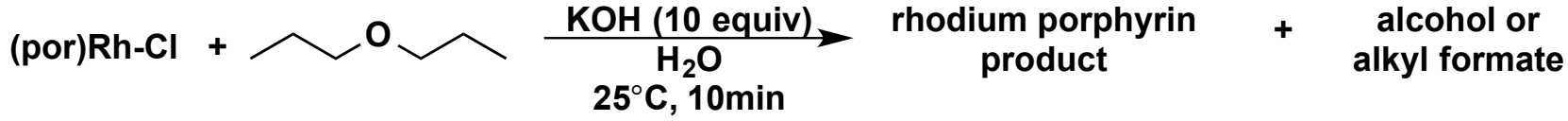


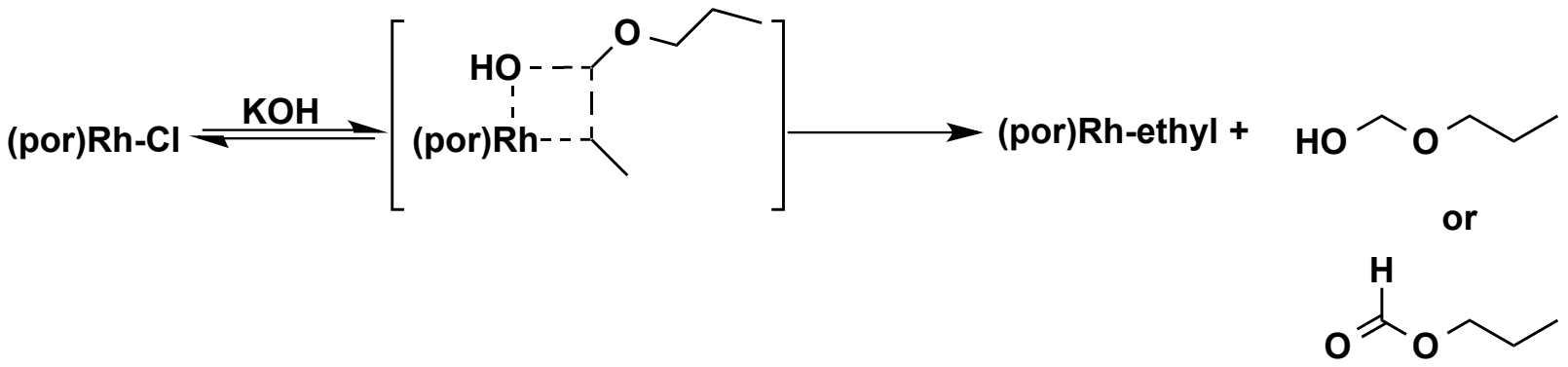
Problem #1

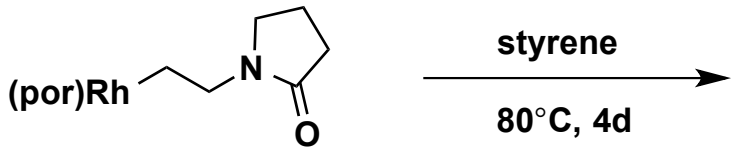

(TTP)Rh-OH +
O
50°C, 3d
O
Rh(TPP)

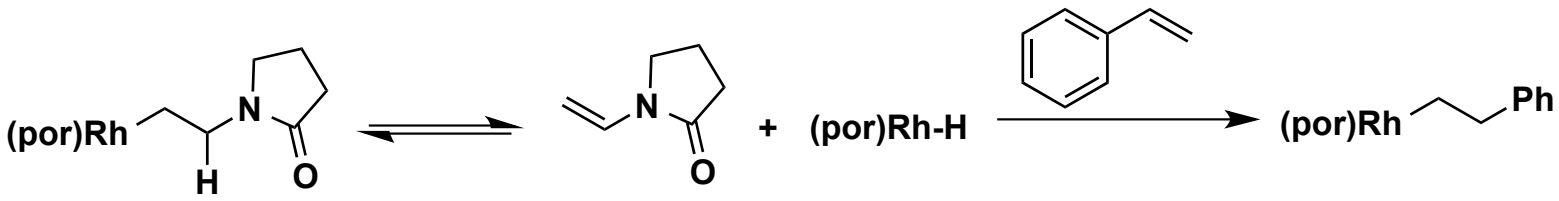

(TTP)Rh^II +
Ph
CN
PPh3
100°C, 7d
(TTP)Rh-CH3

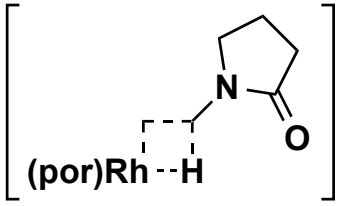

(TTP)Rh-OH +
O
100°C, 7d
O
Rh
O

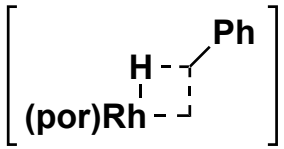

(por)Rh-Cl
+
O
KOH (10 equiv)
H2O
25°C, 10min
rhodium porphyrin
product
+
alcohol or
alkyl formate


(por)Rh-Cl
KOH
HO
O
(por)Rh
(por)Rh-ethyl +
HO
O
or
H
O
O


(por)Rh
N
O
styrene
80°C, 4d


(por)Rh
N
H
O
N
O
+
(por)Rh-H
(por)Rh
Ph


N
O
(por)Rh
H


Ph
H
(por)Rh