Research Seminar 2014.1.20

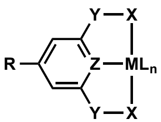
Takaya Ukai (B4)

"Pincer"
-A New Paradigm of Ligand Design-
Overview of Dehydrogenation Chemistry

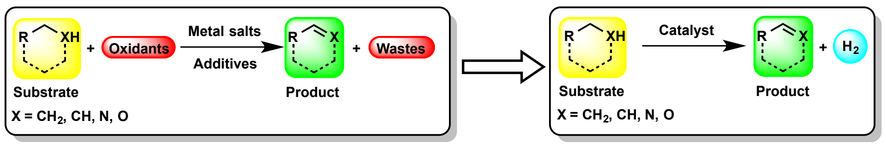
0. Introduction

Goals of This Seminar

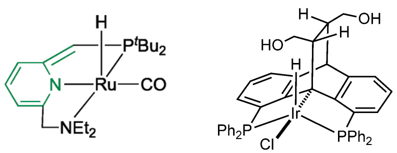
1. Understand the characteristic properties of pincer complexes



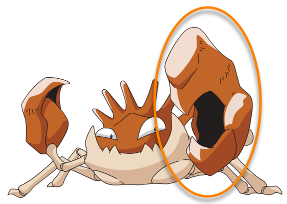
2. Understand the development of dehydrogenative bond activation



3. Understand the new concept of ligand design



What is "Pincer"?



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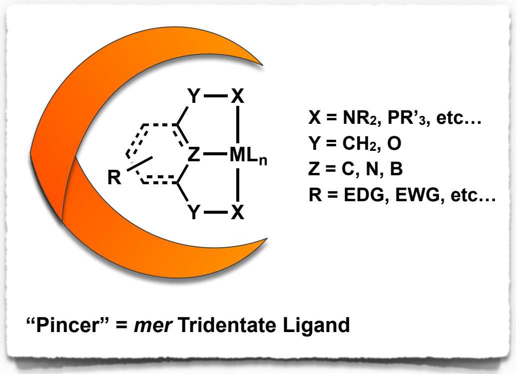
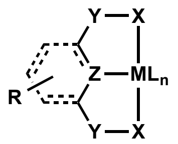


Goldman, A. S., *et al. Chem. Rev.* **2011**, 111, 1761

Pincer's Diversity

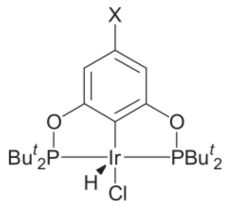


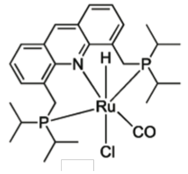
X = NR_2, PR'_3, OR, SR
Y = CH_2, O, NH
Z = C, N, B
R = EDG, EWG

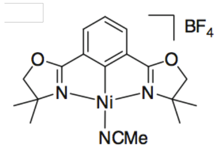
Group	Major Effects
X (Arm)	Steric control, Electron density
Y (Joint)	Indirect steric control, Ligand's Cooperativity
Z (Core)	Trans effect
R (Tail)	Remote control of electron density
Backbone (Body)	Flexibility, Other functional groups
M (Center)	Selectivity in activation of molecules (C-H, O-H, etc)

Goldman, A. S., *et al. Chem. Rev.* **2011**, 111, 1761

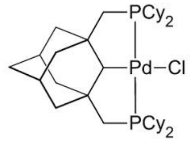
Pincer Complexes

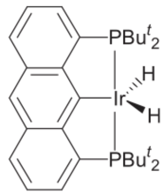


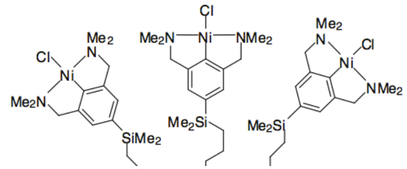


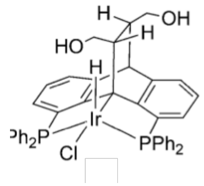


Common features:
- Stable to moisture and air (high valent)
- Stable to high temperature
- Controllable electronic and steric properties
- Ligand's Non-innocence of bond activation









Contents

1. Dehydrogenation of Alkanes and Goldman's Basic Studies on Pincer

Main Character of This Chapter

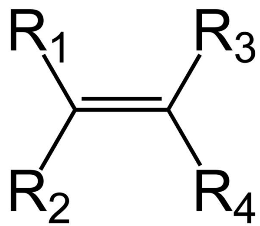
1980 B.A at Columbia University
1985 Ph.D at Caltech under the guidance of David R. Tyler then; postdoc in Jack Halpern's lab
1987 Assistant professor at Rutgers
1993 Associate professor at Rutgers
2000 Professor at Rutgers
2005 Professor (II) at Rutgers

Alan Goldman

Professor at Rutgers, State University of New Jersey
Department of Chemistry and Chemical Biology

Keywords:
- Organometallics
- Alkane dehydrogenation
- Alkane metathesis
- Sustainable Fuel Chemistry

Dehydrogenation of Alkanes

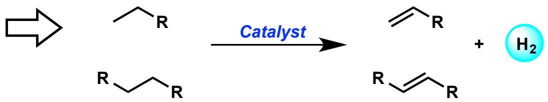


Alkene: versatile feedstock for…
- Fine chemicals
- Transportation fuels

Alkene: versatile functional group for…
- Electrophilic attack
- Pericyclic reaction
- Metathesis

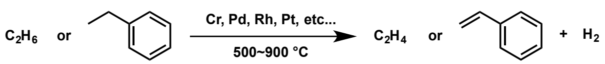
Dehydrogenation of Alkanes

What is an "ideal" synthesis?



Dehydrogenation of Alkanes

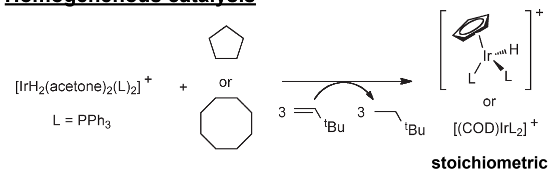
Heterogeneous catalysis



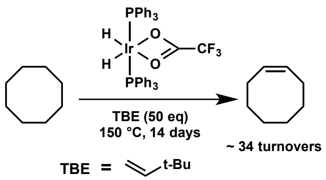
Limited scope
&
Severe Condition

Goldman, A. S., *et al. Chem. Rev.* **2011**, 111, 1761

Homogenenous catalysis



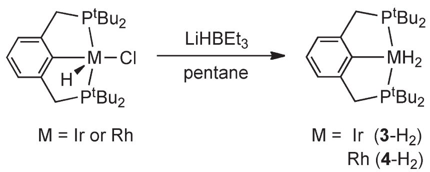
Crabtree, R. H., *et al. JACS*, **1979**, 101, 7738



Crabtree, R. H., *et al. JACS*, **1987**, 109, 8025

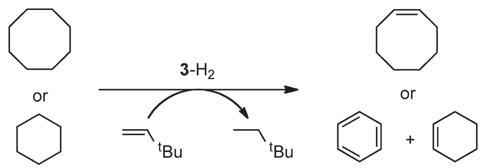
Low turnover is due to instability of catalysts at high temperature

First Reports on An Ir-Pincer Complex



PCP-Metal-H_2 complexes

First transfer dehydrogenation by the Ir-pincer complex(3)



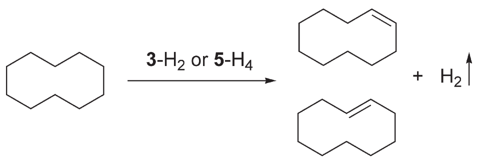
Catalyst	Turnovers / h (150 °C)
3-H_2	82
4-H_2	<1

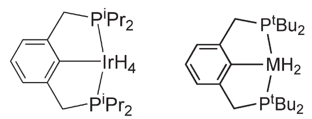
No decomposition over 1 week at 200 °C, highTBE and N_2 inhibit the reaction

Jensen, C. M., Kaska, W. C., *et al. Chem. Commun.* **1996**, 2083

First Acceptorless dehydrogenation

Acceptorless Dehydrogenation of Cyclic Alkane





5-H_4 M = Ir (3-H_2)
Rh (4-H_2)

Steric hindrance: ^{i}Pr < ^{t}Bu

Goldman, A. S., *et al. Chem. Commun.* **1997**, 2273

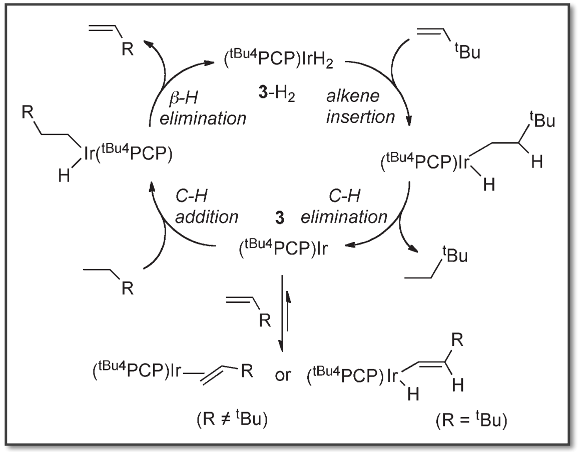
Catalyst	Turnovers/20h (200 °C)
3-H_2	163
5-H_2	700

5-H_4 also catalyzed acceptorless dehydrogenation of *n*-alkane (*n*-undecane: 70 turnovers/h)

Inhibition by *n*-Alkene is bigger than that by Cycloalkene

Goldman, A. S., *et al. Chem. Commun.* **1997**, 2273

Demystify The Mechanism



- **Transfer Dehydrogenation**

TBE	Rate Determining Step
Low	alkene insertion
High	C-H addition

Resting state differs according to the concentration of olefin.

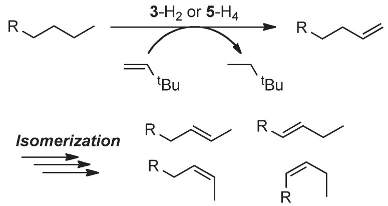
Goldman, A. S., *et al. JACS*, **2003**, 125, 7770

- **Acceptorless Dehydrogenation**

Rate Determining Step is H_2 liberation (dissociative)
Resulted olefin also inhibits the reaction

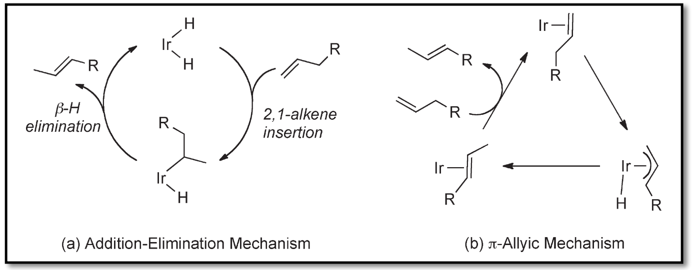
Goldman, A. S., *et al. JACS*, **2002**, 124, 11404

Demystify The Mechanism



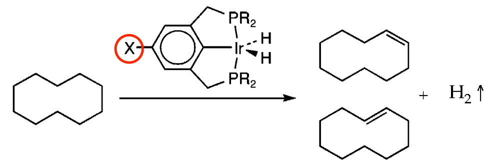
Isomerization to internal olefin was observed in Dehydrogenation of acyclic alkane

Allylic C-H activation by low-valent Ir complex is responsible for the isomerization



Goldman, A. S., *et al. Abstracts of Papers, 239th ACS National Meeting*, **2010**

Modification of Pincer -Tail-



***p*-MeO group makes Ir center more electron rich and enhances Oxidative Addition step**

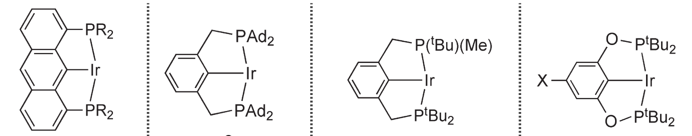
Table 1. Acceptorless Dehydrogenation of CDA (bp 201 °C)[a] Catalyzed by (X−^{R}PCP)IrH_n[a]

	catalyst; total turnovers (= mM)		
time/h	X = H; R = *t*-Bu	X = MeO; R = *t*-Bu	X = MeO; R = *i*-Pr
1	60	158	357
2	110	275	450
4	170	430	714
6	220	575	868
24	360	820	2120
48	360	820	2970
78	–	–	3050

[a] Conditions: catalyst, 1.0 mM; 1.5 mL of CDA; 250 °C oil bath; concentrations determined by GC.

Goldman, A. S., *et al. JACS*, **2004**, 126, 13044

Modification of Pincer -Arm and Joint-



R = ^{t}Bu (7a)
^{i}Pr (7b)

8
Ad = 1-adamantyl

13

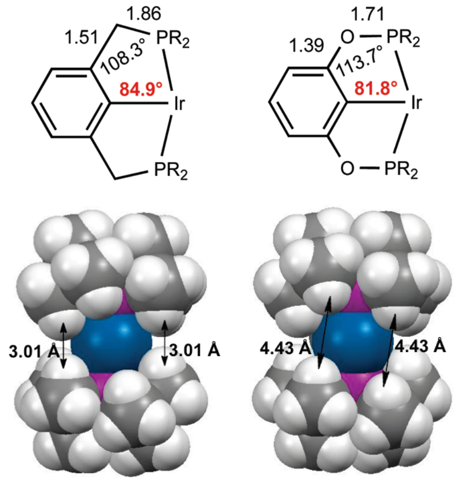
X = H (9a)

What factor determines the reactivity?

^{t}Bu / ^{i}Pr PCP (7a, 7b)	8	13	9a
Lower reactivity (low flexibility of arms)	High stability at 250 °C and exceeds ^{tBu}PCP and ^{iPr}PCP (Acceptorless Dehydrogena-tion)	980 turnovers in transfer dehydrogenation of *n*-Octane after 5h at 150 °C (96 for ^{tBu4}PCP and 208 for ^{iPr4}PCP)	(^{tBu4}POCOP)Ir Greater reactivity in transfer dehydrogenation of Cyclooctane than (^{tBu4}PCP)Ir but no improvement for *n*-Alkane's reaction

Goldman, A. S., *et al. Chem. Rev.* **2011**, 111, 1761

The Structure of POCOP-Ir Complex



(^{tBu4}PCP)Ir (^{tBu4}POCOP)Ir

P-Ir-P angle is more acute than PCP
POCOP-Ir ⇒ metal center is more open

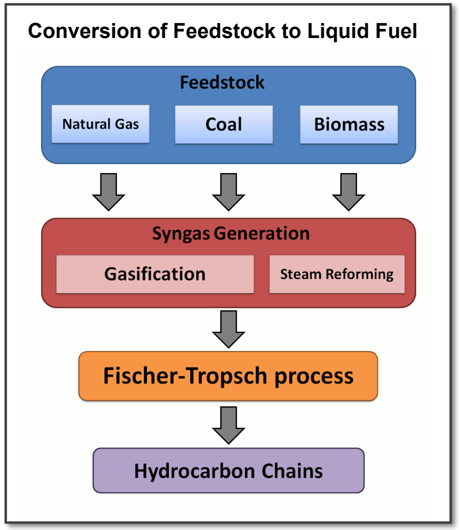
Steric Crowdedness:
(^{iPr4}PCP)Ir < (^{tBu4}POCOP)Ir < (^{tBu4}PCP)Ir

⇩

Steric environment around the metal center determines the rate determining step

Goldman, A. S., *et al. Acc. Chem. Res.* **2012**, 45, 947

Alkane Metathesis



Fischer-Tropsch Process:

$(2n + 1)H_2 + nCO \rightarrow C_nH_{(2n+2)} + nH_2O$
(Fe, Co or Ru as a catalyst)

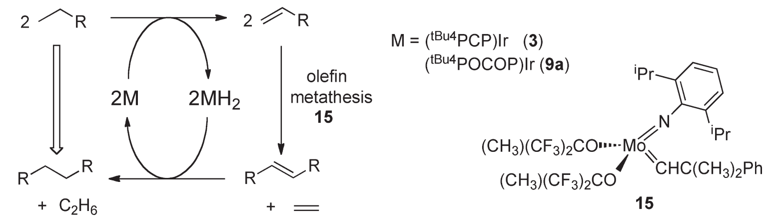
Sources of CO and H_2:
$C + H_2O \rightarrow H_2 + CO$ (Gasification of coal)
$-CH_2- + H_2O \rightarrow CO + 2H_2$ (Gasification of
$-CH_2- + 1/2O_2 \rightarrow CO + H_2$ natural gases)

⇩

Alkane Metathesis can convert a surplus of alkanes to those of more desirable numbers (e.g. C_9 - C_{19} is valuable as a clean-burning diesel component)

Goldman, A. S., *et al. Acc. Chem. Res.* **2012**, 45, 947

Alkane Metathesis



Hydrogen Autotransfer

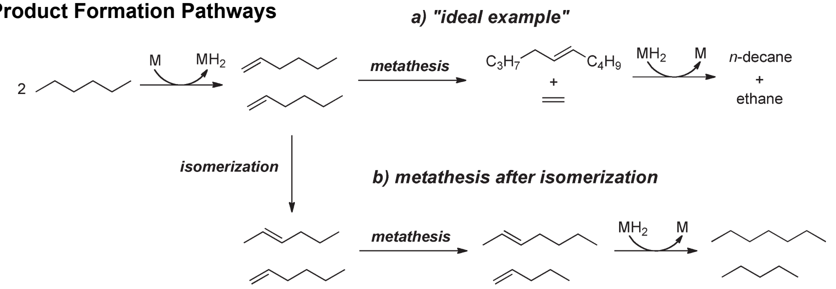
Ir catalyst	time (h)	Product Concn (mM)				total (M)	$C_{10}/(C_7 - C_{10})$
		$C_2 - C_5$	$C_7 - C_9$	C_{10}	$> C_{11}$		
(^{tBu4}PCP)IrH_2	23	740	241	232	38	1.25	49.0
(^{tBu4}POCOP)IrH_2	24	1350	548	95	53	2.05	14.8

Reaction conditions: Ir catalyst (10 mM), 15 (16 mM), TBE (20 mM) in 7.6M n-hexane at 125 °C

Goldman, A. S., Brookhart. M., *et al. Science* **2006**, 312, 257

Product Distribution: Selectivity Crisis

Product Formation Pathways



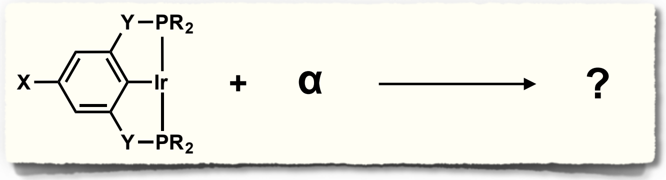
(^{tBu4}POCOP)Ir's poor selectivity in Alkane Metathesis

2 conceivable reasons

- Isomerization to internal olefin → Rate of isomerization doesn't differ from (^{tBu4}PCP)Ir complex
- Internal C-H activation to give internal olefin

Goldman, A. S., Brookhart. M., *et al. Science* **2006**, 312, 257

Future Outlook



Problems of Dehydrogenation, Alkane Metathesis chemistry

- Poor selectivity in Alkane Metathesis products
- Poor reactivity at lower temperature
  (Metathesis catalysts decomposes at high temperature)

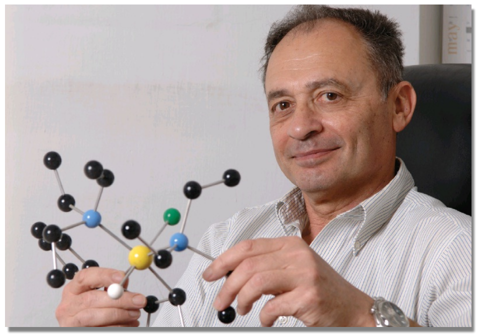
⇒ Modification of pincer catalysts has more potential to overcome these problems

Tasks of Other Chemists

- Utilization of Pincer-Ir for other reactions
- Utilization of C-H activation chemistry
- Utilization of wisdom about pincer for other catalysts

2. Dehydrogenation of Alcohols and Milstein's Advanced Studies on Pincer

Main Character of This Chapter



David Milstein

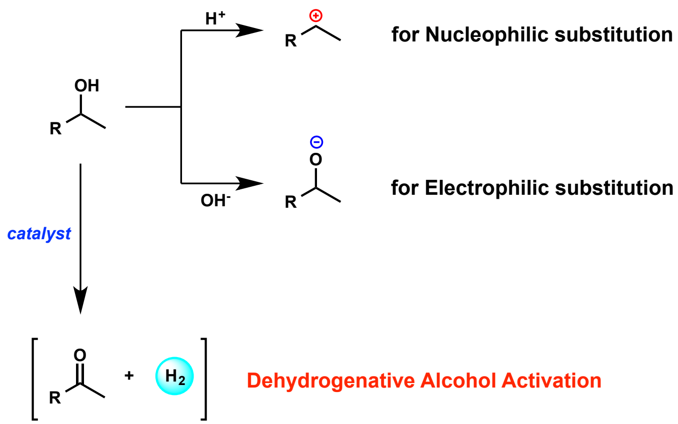
Weizmann Institute of Science
Israel Matz Professor of Organic Chemistry

1976 Ph.D at Hebrew University of Jerusalem under the guidance of Prof. Blum
then; postdoc in Stille's lab
1979 Group leader in Dupont Company
1987 Professional appointment at the Weizmann Institute of Science
1996 Israel Matz Professor at Weizmann Institute of Science

Keywords:
- Organometallics
- Metal-ligand cooperation
- Green catalysis
- Water splitting

Dehydrogenation of Alcohols

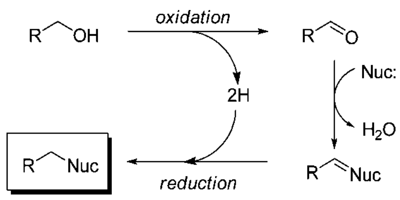
Alcohol's activation is usually limited;



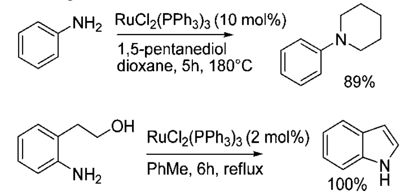
Williams, J. M., *et al. Adv. Synth. Catal.* **2007**, 349, 1555

Dehydrogenation of Alcohols

"Hydrogen Autotransfer" strategy

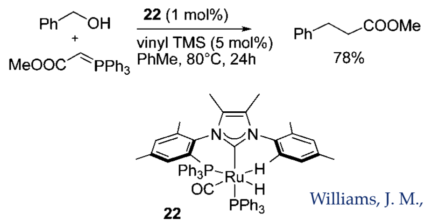


Ru-catalyzed amination



Murahashi, S. I., *et al. Chem. Rev.* **1998**, 98, 2599

Ru-catalyzed Wittig-type process

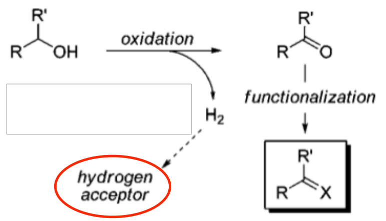


Hydrogen Autotransfer type reactions have been well developed

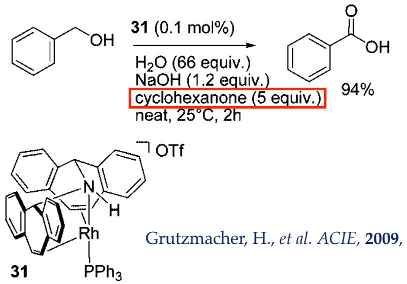
Williams, J. M., *et al. Chem. Commun.* **2004**, 1072

Dehydrogenation of Alcohols

"Net Oxidation" strategy

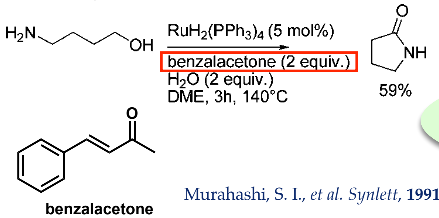


Rh-catalyzed carboxylic acid synthesis



Grutzmacher, H., *et al. ACIE*, **2009**, 48, 559

Ru-catalyzed lactam formation

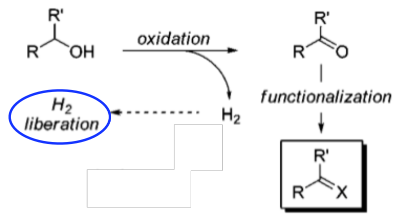


Murahashi, S. I., *et al. Synlett*, **1991**, 693

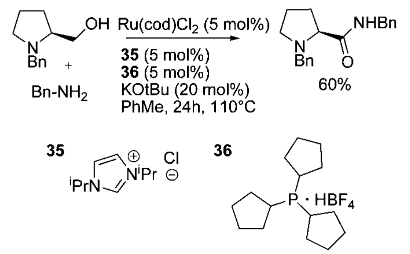
In many cases, Net Oxidation type reactions need hydrogen acceptor to reactivate catalysts

Dehydrogenation of Alcohols

Acceptorless Dehydrogenation

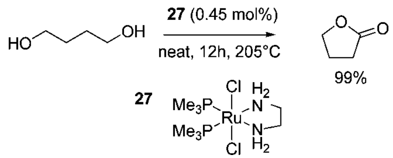


Ru-catalyzed acceptorless amidation



Madsen, R., *et al. JACS*, **2008**, 130, 17672

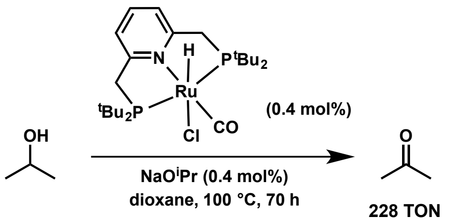
Ru-catalyzed acceptorless lactonization



Acceptorless Dehydrogenation has few examples and suffers from harsh condition or poor reactivity

Hartwig, J. F., *et al. Organometallics*, **2005**, 24, 2441

First Report on A Ru-Pincer Complexe

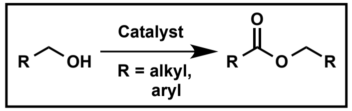


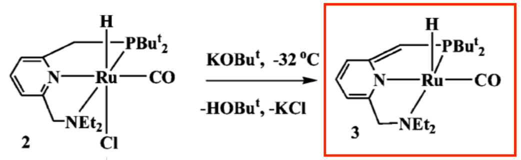
Milstein's **PNP-Ru** complex
(stable under air)
No H_2 acceptor, High turnover

David Milstein, *et al. Organometallics*, **2004**, 23, 4026

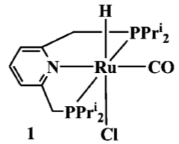
⇨ Dr. Milstein started to investigate Ru-Pincer complexes for acceptorless dehydrogenation reactions

"Serendipity" Strikes without Warning





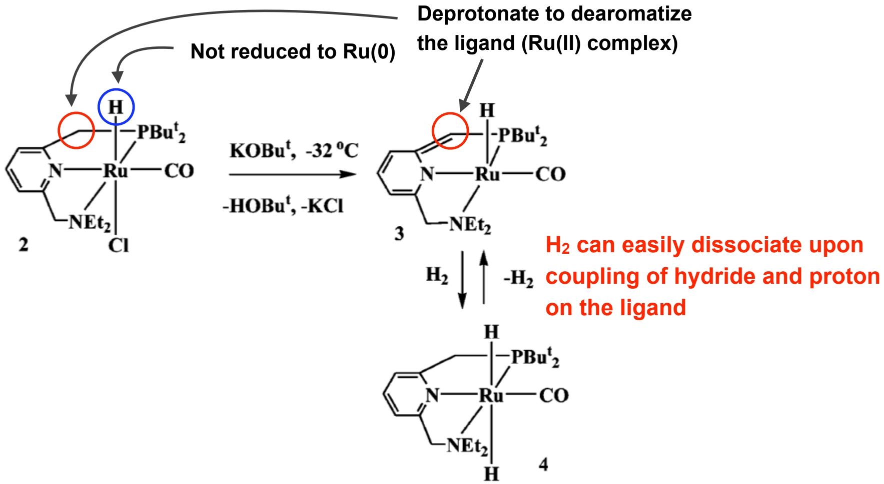
entry	cat.	KOH (equiv)	alcohol	temp. (°C)	time (h)	conv. (%)	yield (%) (ester)	yield (%) (aldehyde)
1	**1**	1	1-hexanol	157	24	70.6	67.2	2.8
2	**1**	0	1-hexanol	157	24	0	0	0
3	**2**	1	1-hexanol	157	24	90.4	90	0.3
4	**2**	0	1-hexanol	157	24	0	0	0
5	**2**	1	1-hexanol	115^b	24	95	94.5	0.1
6	**2**	1	1-butanol	117	72	92.5	91.5	1
7	**2**	1	benzyl alcohol	115^b	72	100	99.5	0
8	**3**	0	1-butanol	117	5	91	90	0.5
9	**3**	0	1-hexanol	157	2.5	91.5	91.4	0.1
10	**3**	0	1-hexanol	115^b	6	99	99	0
11	**3**	0	benzyl alcohol	115^b	4	93.2	92.1	1



No base, No H_2 acceptor, and Highly reactive

David Milstein, *et al. JACS*, **2005**, 127, 10840

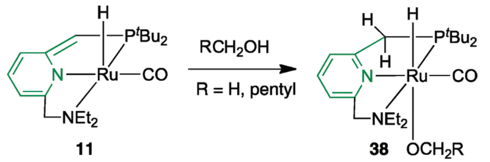
"Serendipity" Strikes without Warning



David Milstein, *et al. JACS*, **2005**, 127, 10840

Metal-Ligand Cooperation

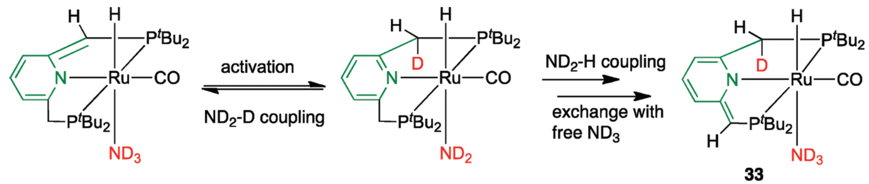
- **Alcohol Activation**



O-H bond is cleaved by Ru and Ligand cooperatively, as well as N-H bond

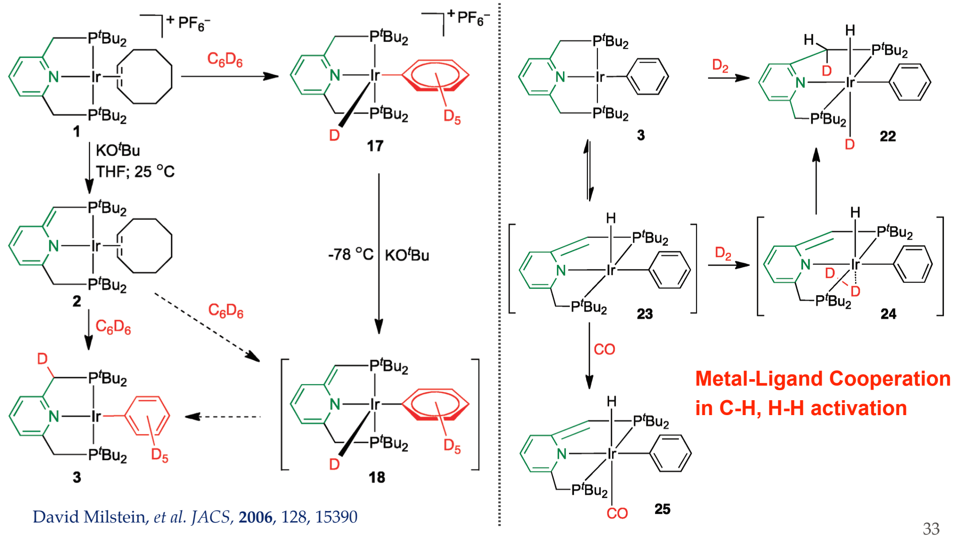
⇨ New mode of bond activation
Metal-Ligand Cooperation

- **Ammonia Activation**



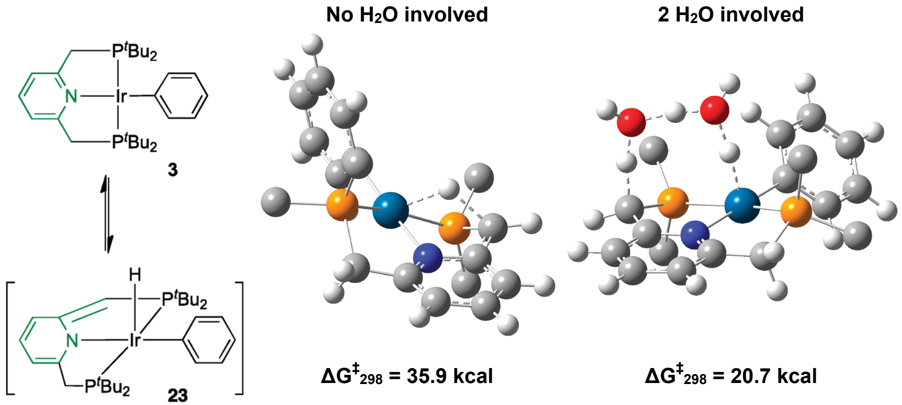
David Milstein, *et al. ACC. Chem. Res.* **2011**, 44, 588

C-H and H-H Activation by PNP-Ir



David Milstein, *et al.* *JACS*, **2006**, 128, 15390

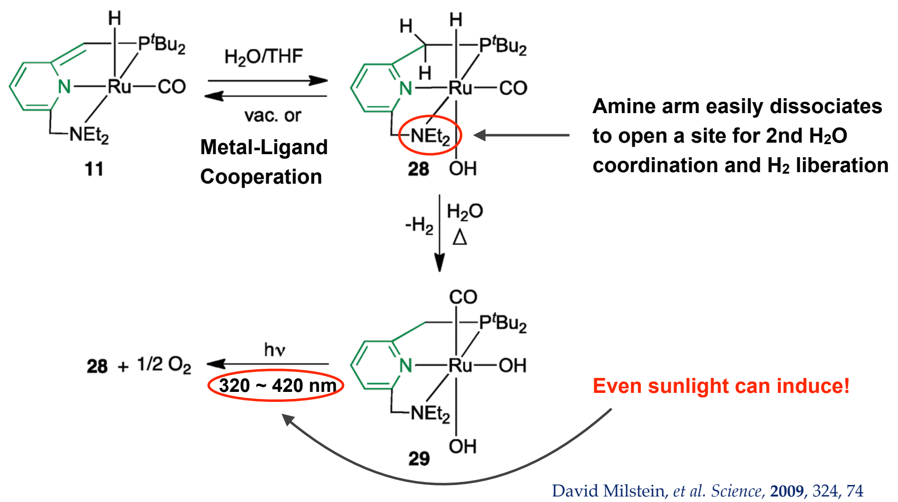
Ir(I)-Ir(III) Equilibrium: Aqua Bridge



Involvement of 2 molecules of water in deprotonation is more likely (deciphered by DFT calculation)

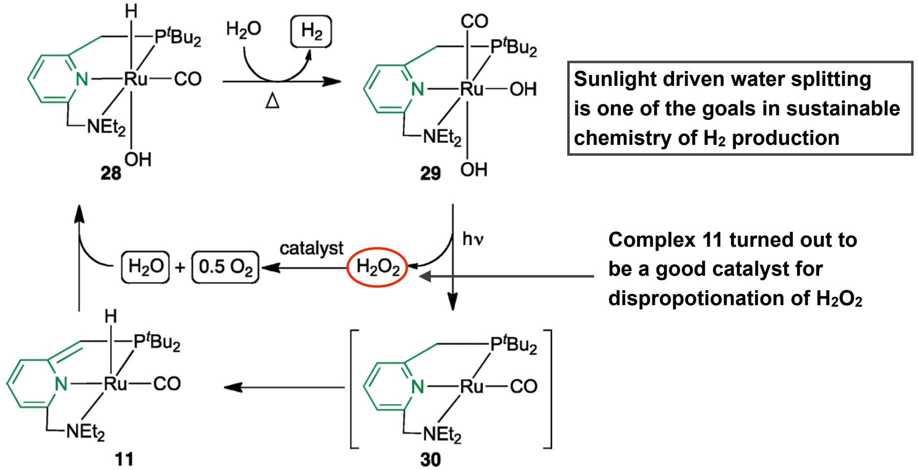
David Milstein, *et al.* *Dalton. Trans.* **2009**, 9433

H_2O Activation by PNN-Ru



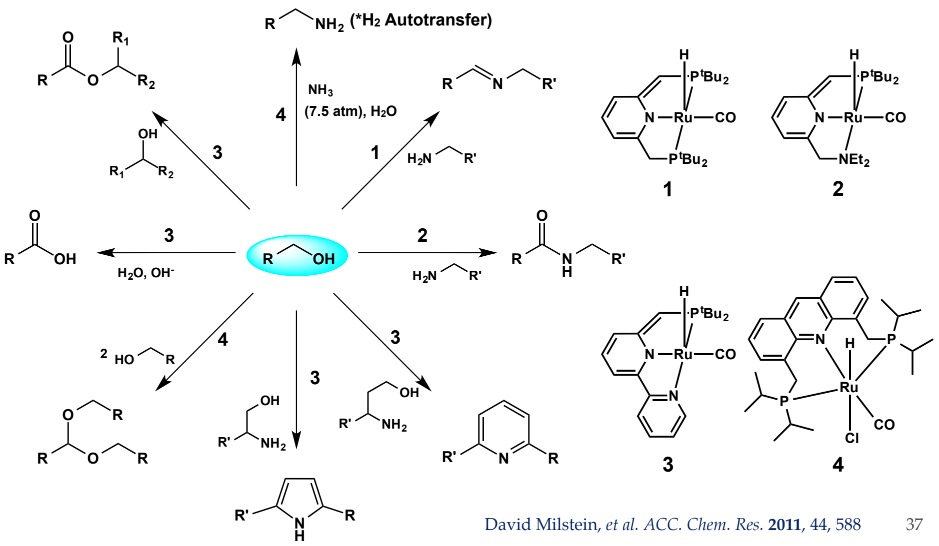
David Milstein, *et al.* *Science*, **2009**, 324, 74

Water Splitting



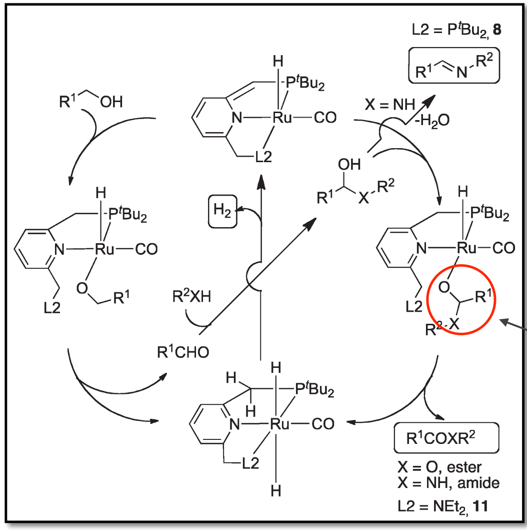
David Milstein, *et al.* *Science*, **2009**, 324, 74

Applications of Acceptorless Dehydrogenation



David Milstein, *et al. ACC. Chem. Res.* **2011**, 44, 588

Magic Arm



- **Ester, Amide and Imine Synthesis**

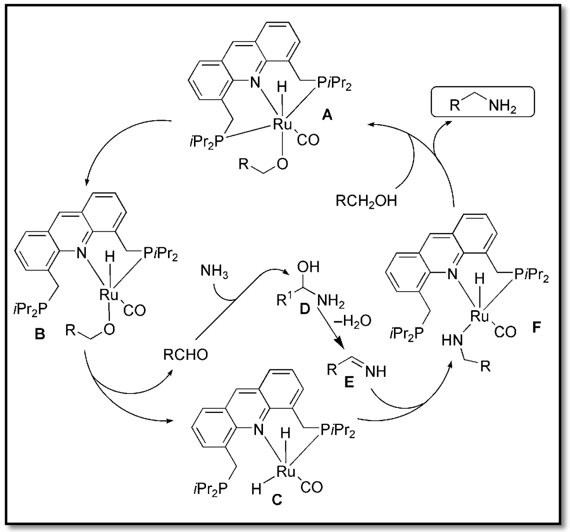
Coordination Strength:
Pyridine ≤ NEt_2 < P^tBu_2

Steric Hindrance:
Pyridine < NEt_2 < P^tBu_2

Dehydrogenation of this intermediate needs sterically less hindered coordination site

David Milstein, *et al. Science*, **2007**, 317, 790

Magic Arm



- **Amine Synthesis (*H_2 Autotransfer)**

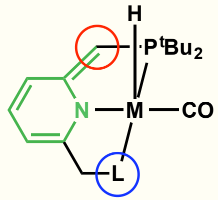
Acridine-based PNP ligand
⇒ Flexible 6-membered ring

⇩

Nucleophilic attack by Alcohol and Alcohol-Amine exchange becomes facile

David Milstein, *et al. ACIE*, **2008**, 47, 8661

Short Summary



- **Dearomatized ligand can cooperatively activate various X-H bonds (X = O, NH, CH_n)**
- **Certain metal can preferably activate certain bonds**
- **Variable arm can adjust the openness of metal center**

<u>Tasks of other chemists</u>

- **Utilization of new concepts of ligand design**
- **Investigation of new ligand-metal combinations and their reactivity**
- **Establishment of new catalytic reactions inspired by the studies above**

3. Gelman's Cooperative Catalysts for Acceptorless Dehydrogenation

Main Character of This Chapter

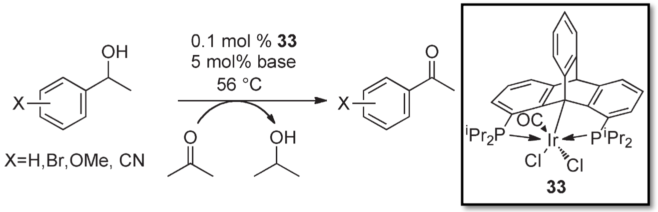
1996 B.Sc at Hebrew University
1997 M.Sc under the guidance of Prof. Aizenshtat and Prof. Blum
2002 Ph.D under the guidance of Prof. Blum then; postdoc in Buchwald's lab
2004 Senior lecturer at Hebrew University
2009 Associate professor

Dimitri Gelman

Associate Professor at Hebrew University of Jerusalem, Department of Organic Chemistry

Keywords:
- Organometallics
- C(sp^3) metalated catalyst
- Metal-ligand cooperation
- Acceptorless Dehydrogenation

1st Generation

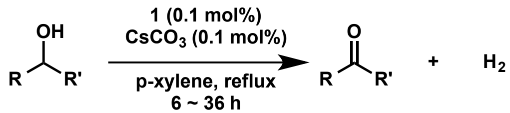


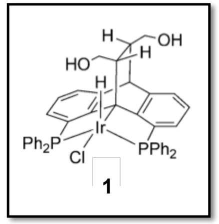
PC(sp^3)P-Ir complex
- Easy to be synthesized
- Stable under air
- Not planar

Advantages	Disadvantages
Carried out under air	Requires Hydrogen acceptor (acetone)
High FG tolerance (-Br, -CN, -OMe)	Limited to secondary benzyl alcohol

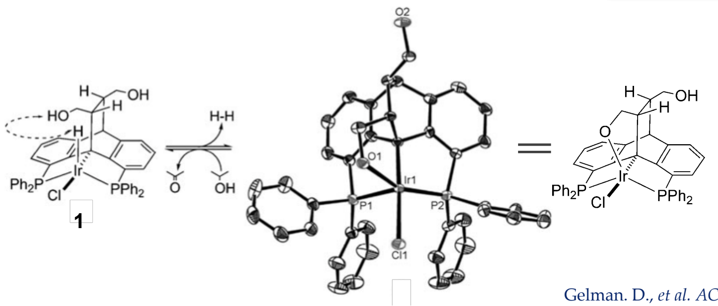
Gelman. D., *et al. Catal. Commun*, **2009**, 11, 298

2nd Generation





- No H2 acceptor (Acceptorless Dehydrogenation)
- 1° and 2° alcohols can be dehydrogenated
- Aliphatic alcohol can be dehydrogenated

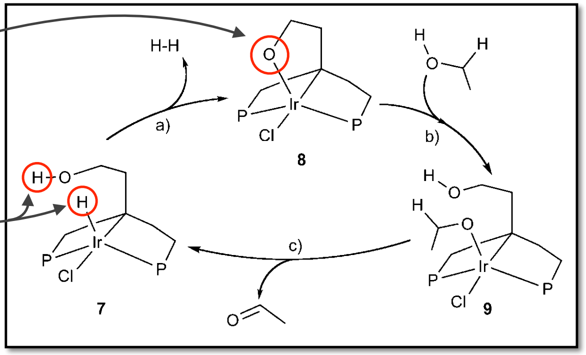


Gelman. D., *et al. ACIE*, **2011**, 50, 3533

Dual Metal-Ligand Cooperation

Metal-ligated alkoxide becomes strong base by d-π repulsion (Metal-Ligand Cooperation)

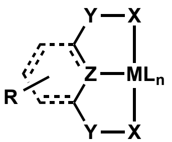
Hydride and proton can be easily coupled to get free as H_2 (Metal-Ligand Cooperation)



Gelman. D., *et al.* *ACIE*, **2011**, 50, 3533

4. Summary

Summary



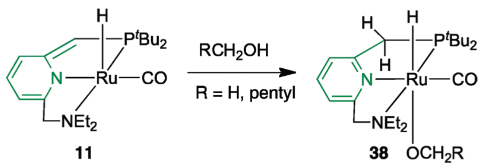
X = NR_2, PR'_3, OR, SR
Y = CH_2, O, NH
Z = C, N, B
R = EDG, EWG

Group	Major Effects	
X (Arm)	Steric control, Electron density ⇨	Adjust the accessibility to metal center
Y (Joint)	Indirect steric control, Ligand's Cooperativity ⇨	Allows Metal-Ligand Cooperation
Z (Core)	Trans effect ⇨	Allows Metal-Ligand Cooperation
R (Tail)	Remote control of electron density ⇨	Finely Adjust the electron density of the complex
Backbone (Body)	Flexibility, Other functional groups ⇨	Allows Metal-Ligand Cooperation
M (Center)	Selectivity in activation of molecules (C-H, O-H, etc) ⇨	Various functional groups can be targeted

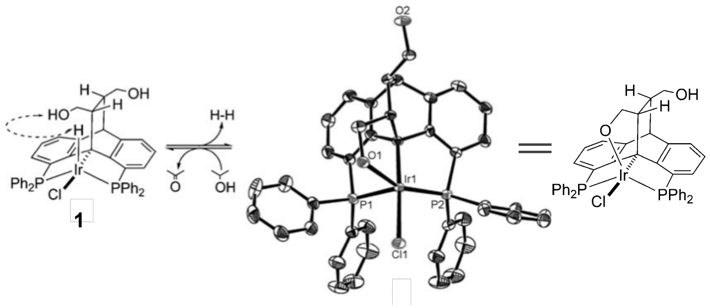
Pincer complexes have big potential as completely new catalysts!

Summary

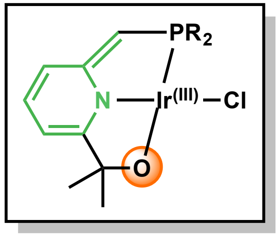
<u>Various Metal-Ligand Cooperation</u>



Metal-Ligand Cooperation provides new mechanistic insight into catalyst design



Exercise



PNO-Ir(III) complex

Bifunctional cooperative ligand

- Core: Activate C-H bond by Metal-Ligand Cooperation
- O-Arm: Strongly basic for deprotonation
- Gem-Me Joint: Stabilize the complex
- Ir-Center: Electron rich for C-H activation

*solvent or olefin ligand should be incorporated because this is still an unstable 14 e⁻ species

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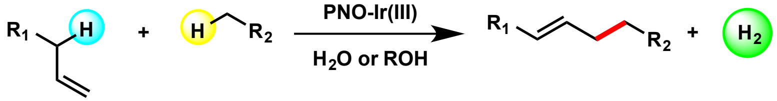
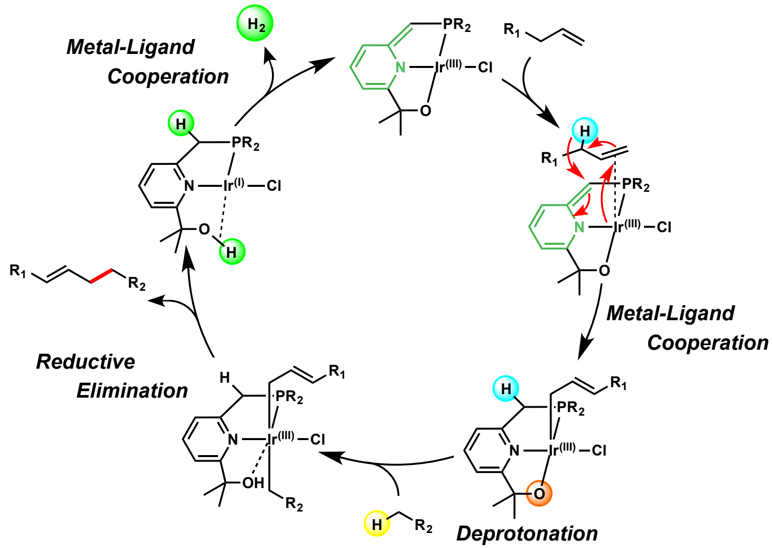
Target reaction: *Dehydrogenative C-C Coupling*

Target bonds: *Allylic C-H and Acidic C-H*



Exercise



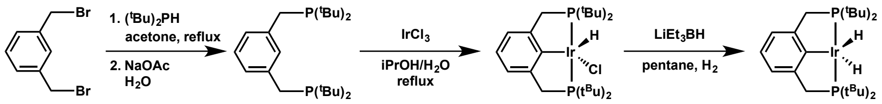
Thank You Very Much!!

りゅか @ りゅかのブログ *powered by ameba*

Appendix

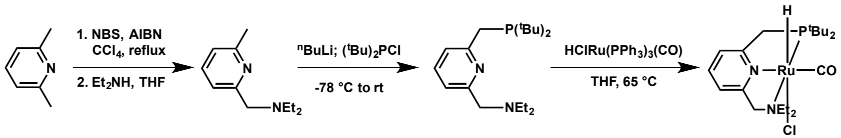
Syntheses of Pincer Complexes

- $(^{tBu4}PCP)IrH_2$ complex



Jensen, C. M., Kaska, W. C., *et al. Chem. Commun.* **1996**, 2083

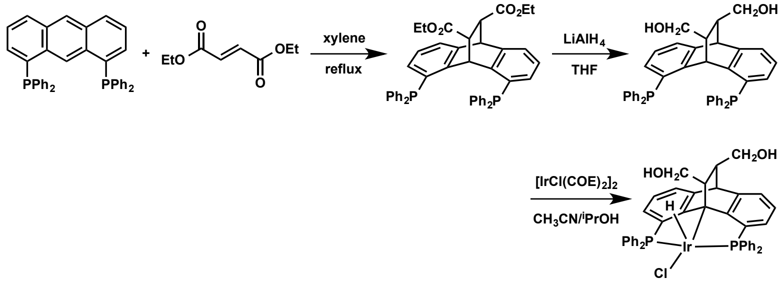
- Milstein's PNN-Ru complex



David Milstein, *et al. JACS*, **2005**, 127, 10840

Syntheses of Pincer Complexes

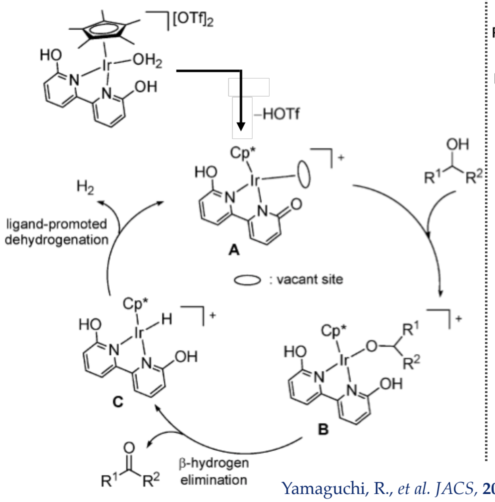
- Gelman's PC(sp3)P-Ir complex



Gelman. D., *et al. ACIE*, **2011**, 50, 3533

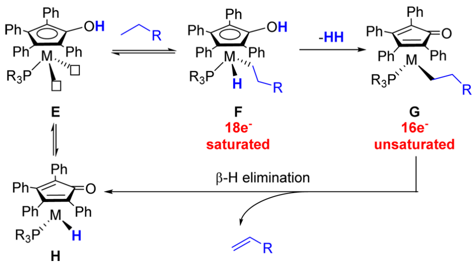
Other Cooperative Catalysts

- Yamaguchi's Cp*Ir catalyst



Yamaguchi, R., *et al. JACS*, **2012**, 134, 3643

- Nozaki's CpOH-Rh/Ir catalyst



Nozaki, K., *et al. JACS*, **2013**, 135, 18726