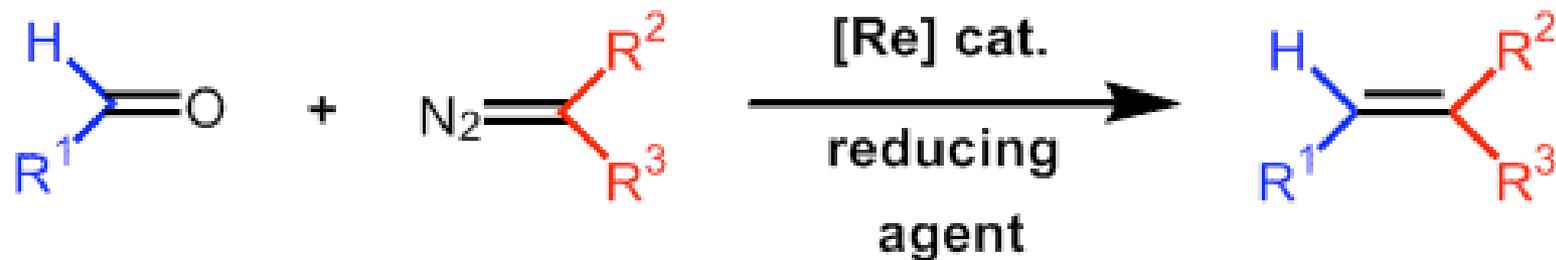


# The Mechanism of Rhenium Catalyzed Olefination of Aldehydes



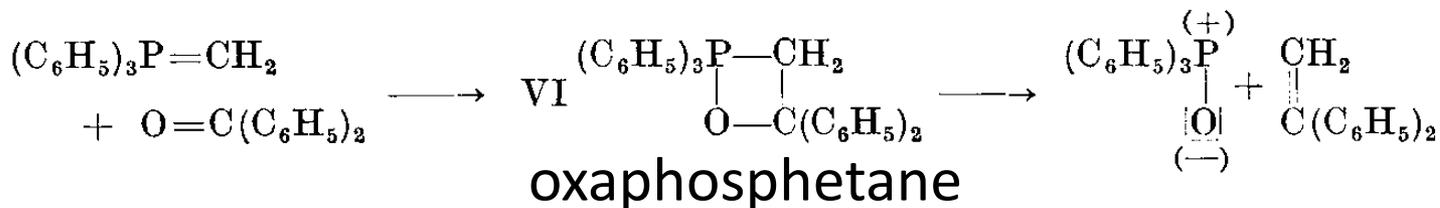
Nathan Werner  
Denmark Group Meeting  
July 22<sup>nd</sup>, 2008

# Introduction

First Use of Phosphanes to Olefinate Carbonyls:

Zur Reaktionsweise des Pentaphenyl-phosphors  
und einiger Derivate

Von Georg Wittig und Georg Geissler



Georg Wittig

## Advantages:

- Highly effective
- Broad scope
- Well-known chemoselectivity



## Disadvantages:

- Multiple step synthesis of ylides
- Ylides are water and oxygen sensitive
- Strong base needed to form phosphane
- Stoichiometric  $\text{R}_3\text{P}=\text{O}$  formation

Catalytic methods that provide mild conditions, less by-product formation are desirable

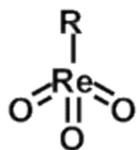
# Background

## Rhenium (General):

- was the last naturally occurring element discovered (1925)
- used for high-octane gasoline production and high-temperature super-alloys in jet engines
- the U.S. is the 3<sup>rd</sup> largest producer preceded by Chile (1<sup>st</sup>) and Kazakhstan (2<sup>nd</sup>)

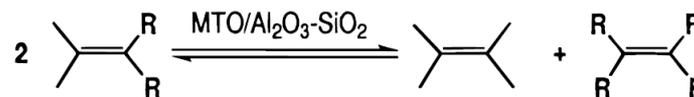


## Organorhenium Oxides as Catalysts:

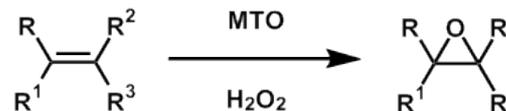


Organo-  
rhenium-  
(VII) oxide

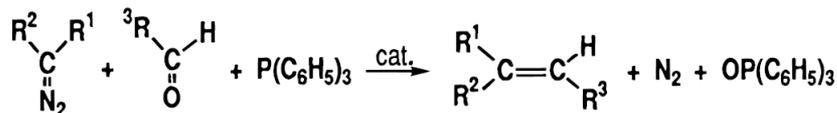
Olefin metathesis:



Olefin oxidation:



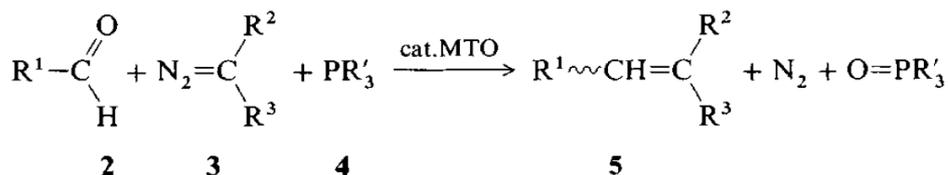
Carbonyl olefination:



US Geological Survey: <http://minerals.usgs.gov/minerals/pubs/commodity/rhenium/>  
<http://periodictable.com/Elements/075/index.html>

Herrmann, W. A.; et al. *Acc. Chem. Res.* **1997**, 169-180

# Original Discovery



**2a**, R<sup>1</sup> = (CH<sub>3</sub>)<sub>2</sub>CH

**2b**, R<sup>1</sup> = C<sub>6</sub>H<sub>5</sub>CH=CH (*trans*)

**2c**, R<sup>1</sup> = (CH<sub>3</sub>)<sub>2</sub>C=CH(CH<sub>2</sub>)<sub>2</sub>CH(CH<sub>3</sub>)CH<sub>2</sub> ←

**2d**, R<sup>1</sup> = (CH<sub>3</sub>)<sub>2</sub>C=CH(CH<sub>2</sub>)<sub>2</sub>C(CH<sub>3</sub>)=CH ←

**2e**, R<sup>1</sup> = C<sub>6</sub>H<sub>5</sub> ←

**2f**, R<sup>1</sup> = 4-BrC<sub>6</sub>H<sub>4</sub> ←

**2g**, R<sup>1</sup> = 4-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub> ←

**3a**, R<sup>2</sup> = H, R<sup>3</sup> = CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>

**3b**, R<sup>2</sup> = CO<sub>2</sub>CH<sub>3</sub>, R<sup>3</sup> = CO<sub>2</sub>CH<sub>3</sub>

**4a**, R' = (C<sub>6</sub>H<sub>5</sub>)

**4b**, R' = (*m*-C<sub>6</sub>H<sub>4</sub>SO<sub>3</sub><sup>-</sup>Na<sup>+</sup>)<sub>3</sub>

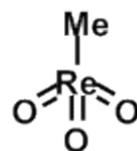
**4c**, R' = (*n*-C<sub>4</sub>H<sub>9</sub>)

no.	R <sup>1</sup> CHO	N <sub>2</sub> =CR <sup>2</sup> R <sup>3</sup>	phosphane	R <sup>1</sup> ~CH=CR <sup>2</sup> R <sup>3</sup> ( <b>5</b> ) yield [%] (E):(Z)
1	<b>2a</b>	<b>3a</b>	<b>4a</b>	82 85:15
2	<b>2a</b>	<b>3b</b>	<b>4a</b>	79 -
3	<b>2b</b>	<b>3a</b>	<b>4a</b>	97 ← 60:40
4	<b>2c</b> [b]	<b>3a</b>	<b>4a</b>	89 45:55
5	<b>2d</b> [c]	<b>3a</b>	<b>4a</b>	91 ← 43:57
6	<b>2d</b> [c]	<b>3b</b>	<b>4a</b>	75 -
7	<b>2e</b>	<b>3a</b>	<b>4a</b>	80 ← 89:11
8	<b>2e</b>	<b>3b</b>	<b>4a</b>	90 -
9	<b>2f</b>	<b>3a</b>	<b>4a</b>	96 ← 42:58
10	<b>2g</b>	<b>3b</b>	<b>4a</b>	87 -
11	<b>2g</b>	<b>3a</b>	<b>4a</b>	93 ← 92:8
12	<b>2g</b>	<b>3a</b>	<b>4a</b>	78 [d] 92:8
13	<b>2g</b>	<b>3a</b>	<b>4b</b>	76 [e] 60:40
14	<b>2g</b>	<b>3a</b>	<b>4c</b>	98 97:3
15	<b>2g</b>	<b>3a</b>	<b>4c</b>	16 91:9

[a] Reaction conditions: 20 °C, 20 min, benzene, 10 mol% CH<sub>3</sub>ReO<sub>3</sub>; see [4].

[b] (*R*)-(+)-citronellal. [c] Citral. [d] 3 mol% CH<sub>3</sub>ReO<sub>3</sub>, 120 min. [e] Two-phase system C<sub>6</sub>H<sub>6</sub>/H<sub>2</sub>O.

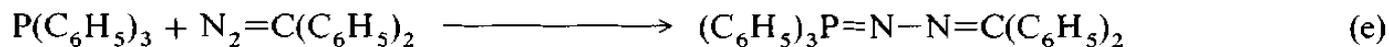
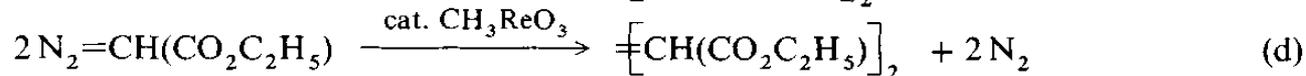
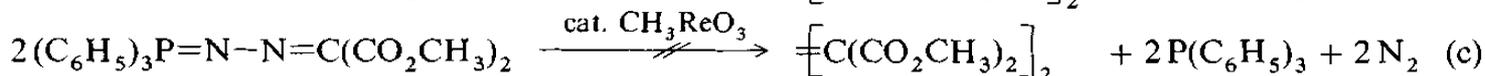
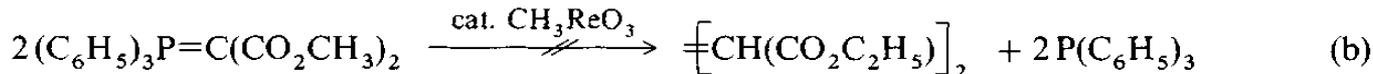
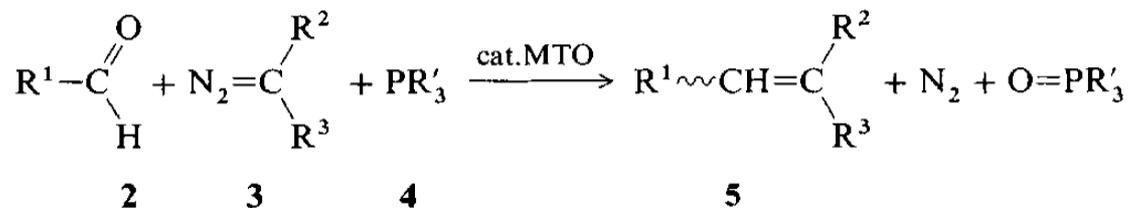
- α,β-unsaturated, alkyl, aromatic aldehydes are compatible
- Electron-poor aldehydes favor olefination



methyltrioxorhenium (MTO)

1.0 equiv of **2**, **3**, and **4** used

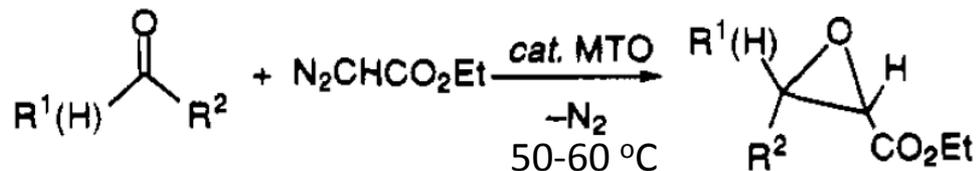
# Mechanistic Studies



- MTO does not catalyze ylides or phosphazines to olefins (b) or (c)
- Diazoacetate dimerization occurs in the presence of MTO (d)
- Phosphazines can be formed (e), and produces olefins in the presence of MTO and aldehyde
- MTO catalyzes reaction of malonate derived ylides (inert using Wittig chemistry) (f)



# MTO Catalyzed Epoxidation

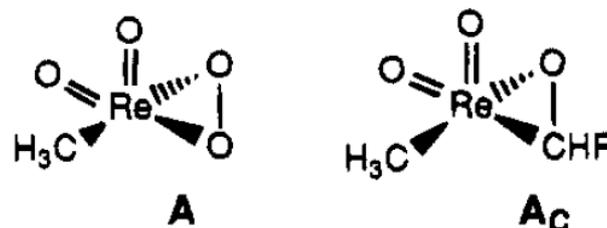


R <sup>1</sup>	R <sup>2</sup>	yield <sup>a</sup> (%)
H	C <sub>6</sub> H <sub>5</sub>	79 (52) <sup>b</sup>
H	n-Pr	75
Me	s-Bu	64
Me	C <sub>6</sub> H <sub>5</sub>	57
Me	i-Pr	49

<sup>a</sup> Isolated yields, after vacuum distillation, based on EDA, taken in small deficiency relative to the imine. <sup>b</sup> The lower yield was obtained when the EDA was added all at once rather than dropwise.

• Intermediate **A** was established for MTO/H<sub>2</sub>O<sub>2</sub> oxidation of olefins

Does the proposed carbenoid **A<sub>c</sub>** have relevance in aldehyde olefination?

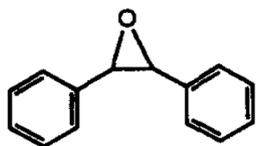


# MTO Catalyzed Deoxygenation of Epoxides

Catalytic:



Substrate	Olefin product	Yield (%)
styrene epoxide	styrene	83
cyclohexene epoxide	cyclohexene	71 <sup>b</sup>

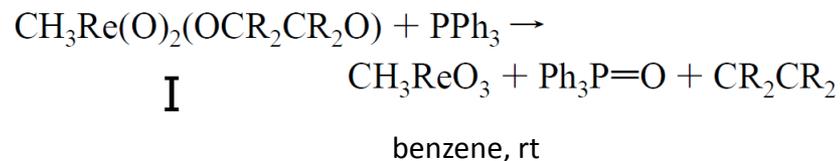
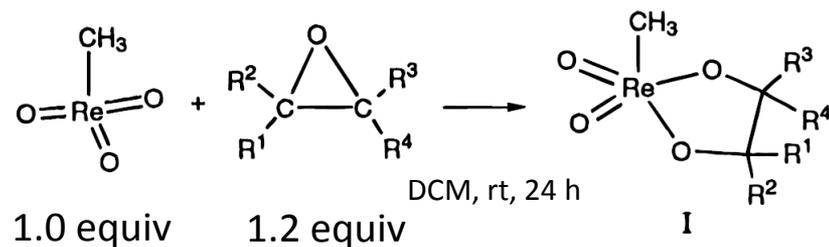


87

<sup>a</sup> In benzene at room temperature with epoxide: MTO  $\approx$  10:1.

<sup>b</sup> Product yields were calculated from <sup>1</sup>H-NMR.

Stoichiometric:

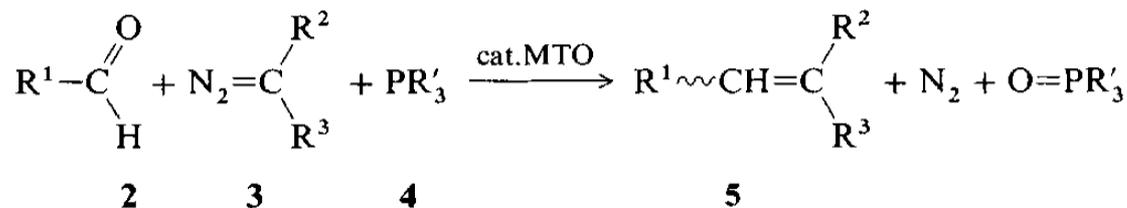


Is a bis(alkoxy)rhenium(VI) species an intermediate for olefination of aldehydes?

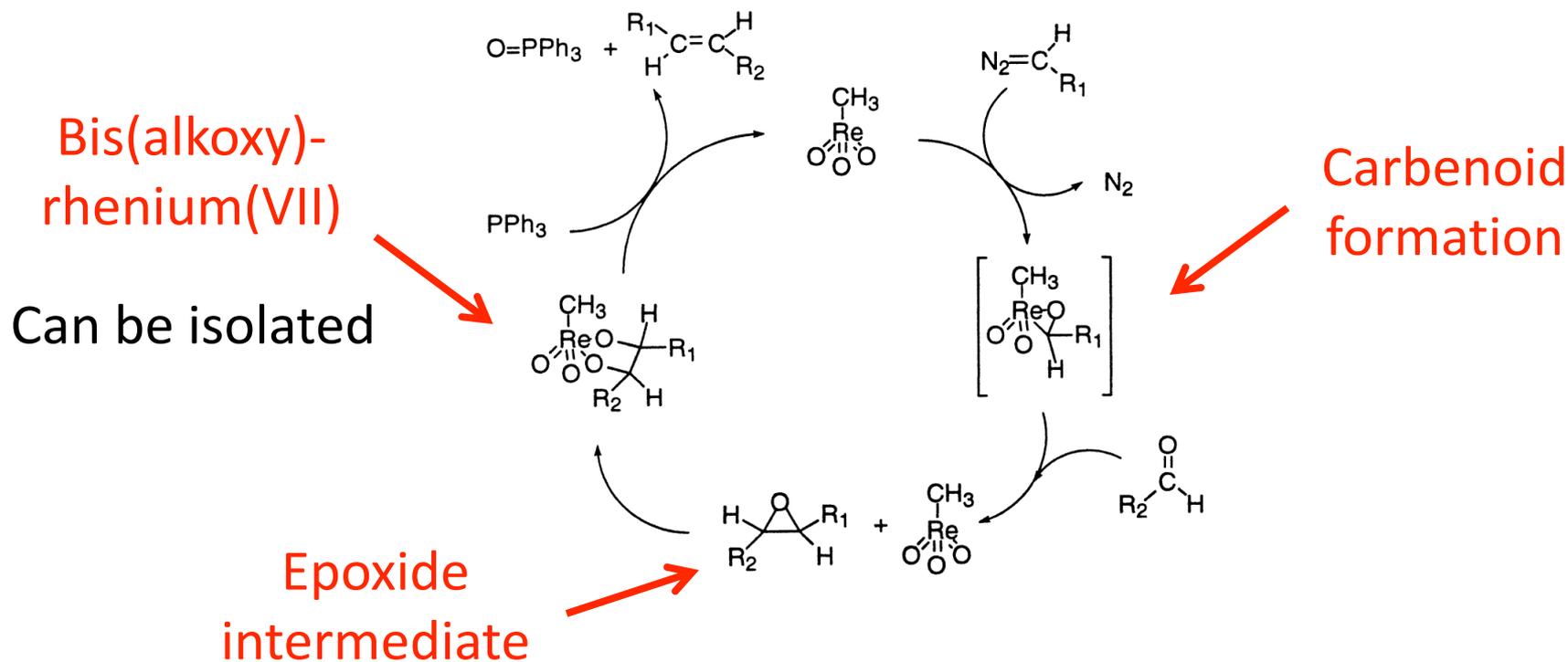
Espenson, J. H.; et al. *J. Mol. Cat.* **1995**, 87-94.

Espenson, J. H.; et al. *Inorg. Chem.* **1996**, 1408-1409.

# Abu-Omar's Proposed Mechanism

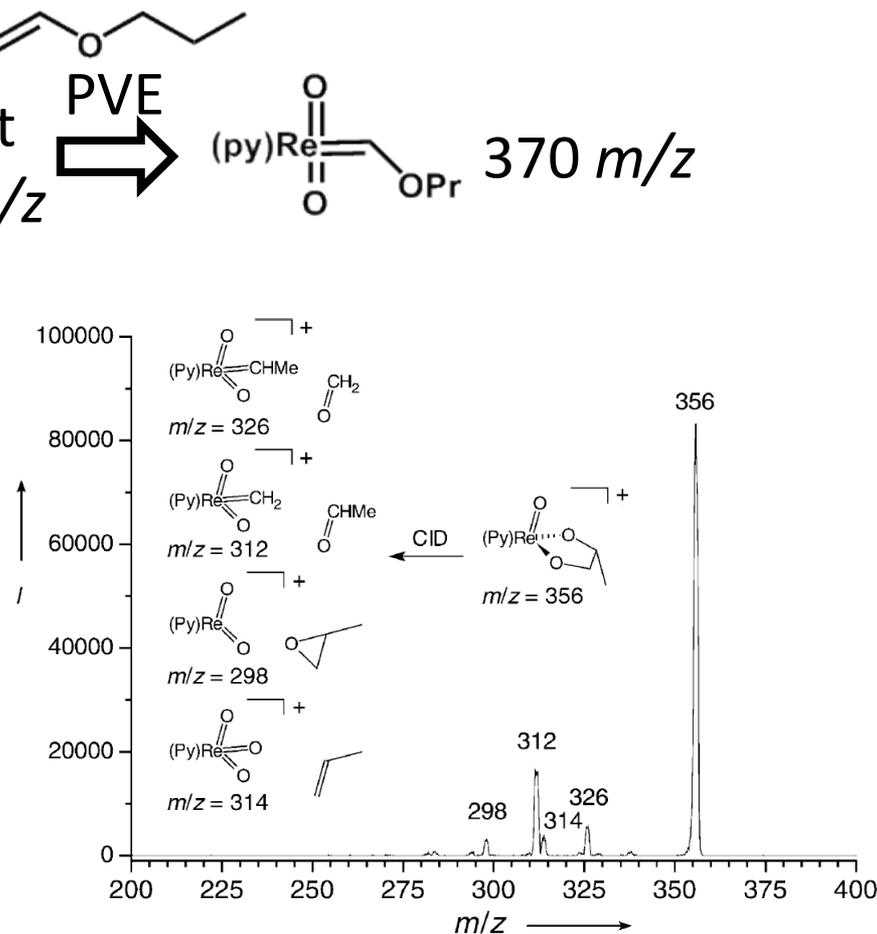
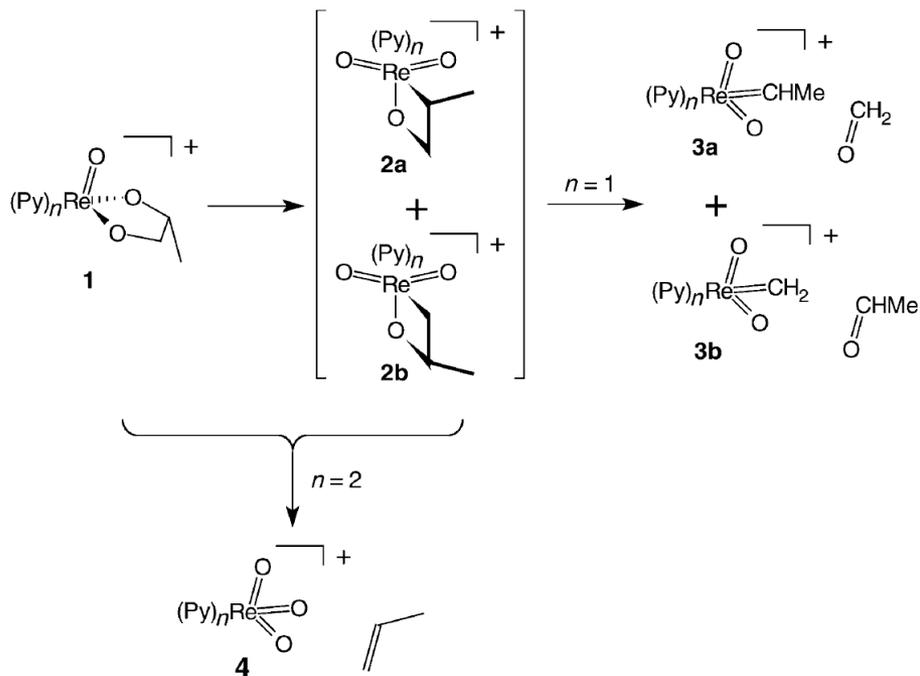
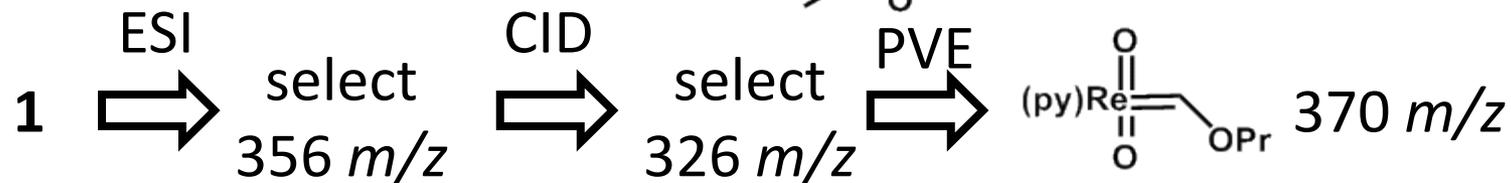


Based on the work of Espensen:



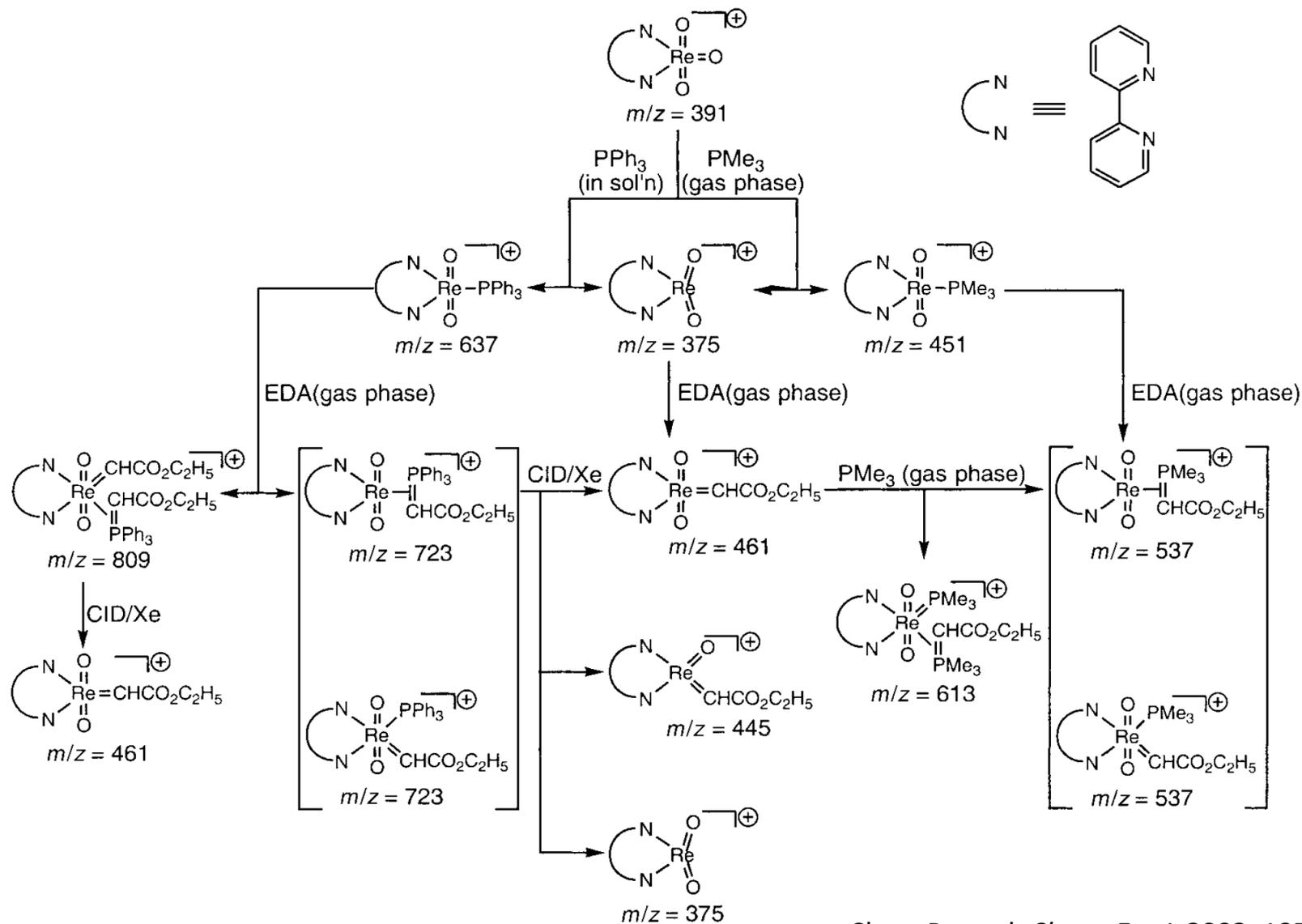
# Rhenium(VII) Carbene

## Tandem Mass Spectrometry

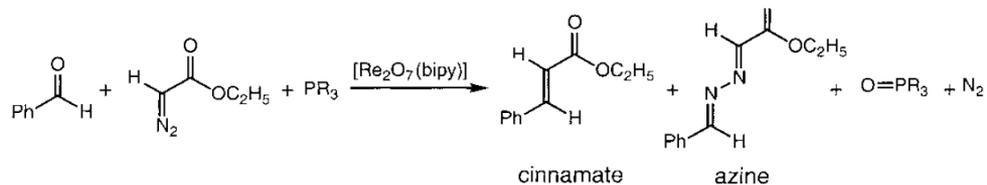


Observation of carbenes supports metallooxetane intermediacy

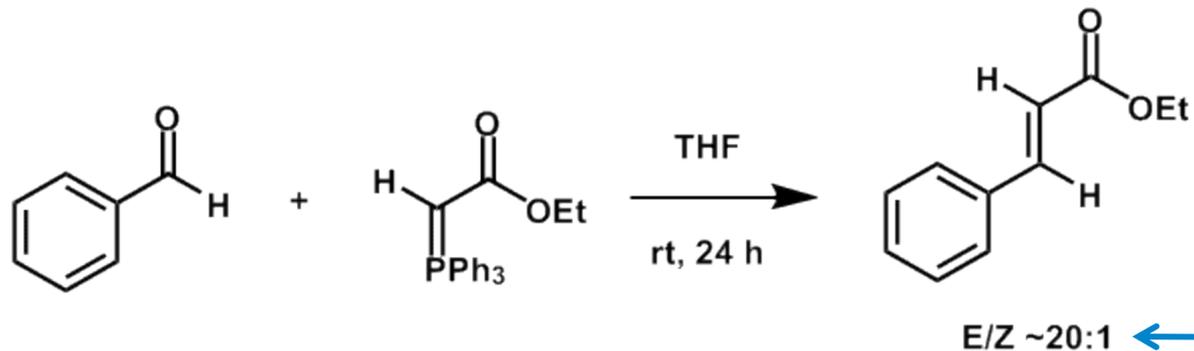
# Rhenium-Phosphane Observed



# Phosphine Effects



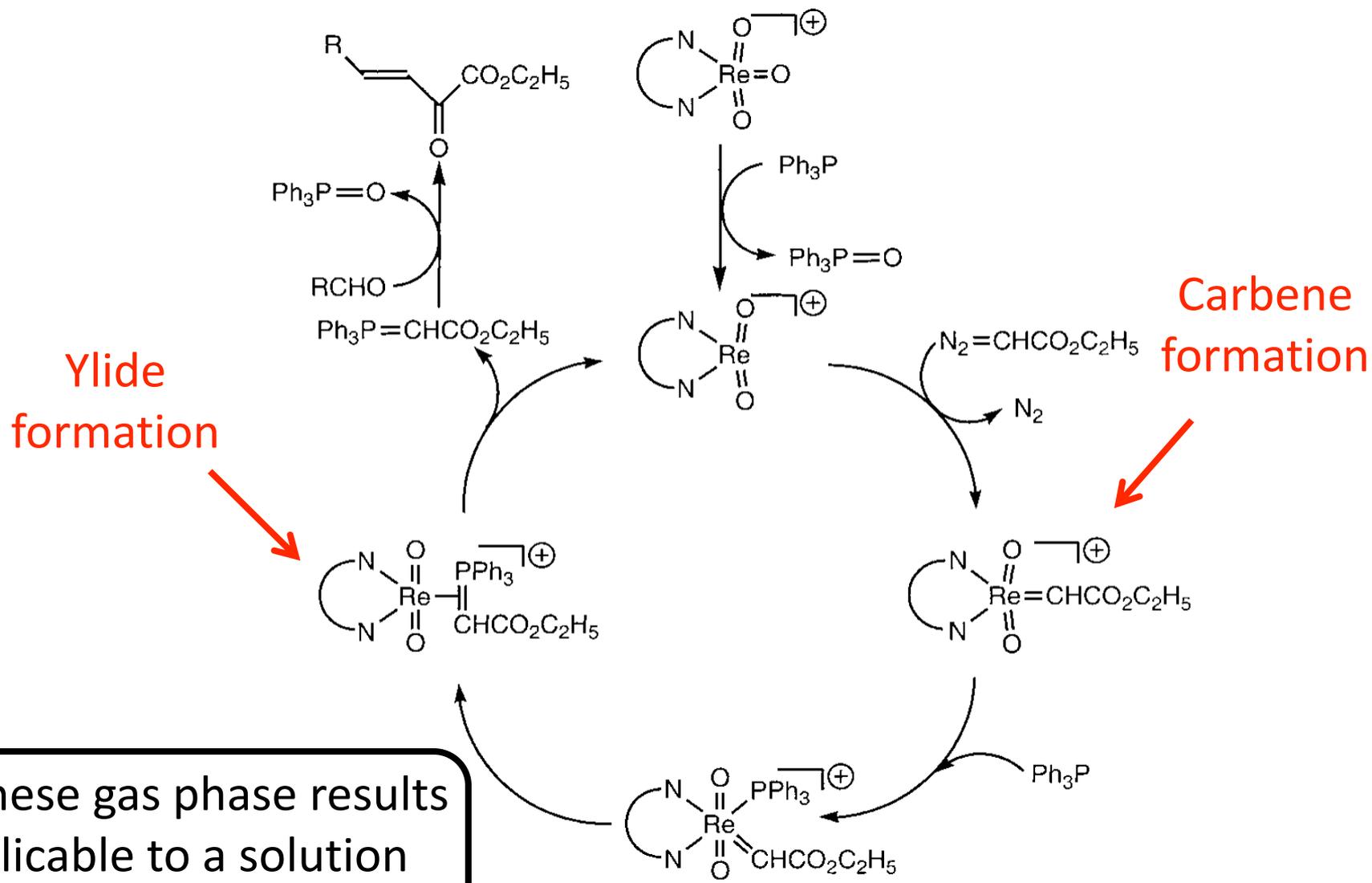
solvent	phosphine	mol% catalyst	reaction time [h]	$T$ [ $^{\circ}\text{C}$ ]	% cinnamate	$E/Z$ ratio	% azine	% recovered aldehyde
THF	$\text{PPh}_3$	3	44	25	86	38	2	12
THF	$\text{PPh}_3$	3	8	60	91	20	–	9
THF	$\text{PPh}_3$	0.7	22	60	75	31	6	19
THF	$\text{P}(\text{OMe})_3$	3.6	94	25	14	3	–	54
$\text{CH}_3\text{CN}$	$\text{PPh}_3$ ←	3	50	25	36	22 ←	16	16
$\text{CH}_3\text{CN}$	$\text{P}(\text{OMe})_3$ ←	3.6	94	25	36	3 ←	–	28
$\text{CH}_2\text{Cl}_2$	$\text{PPh}_3$	3	48	25	37	27	21	20



Phosphine effects olefin geometry

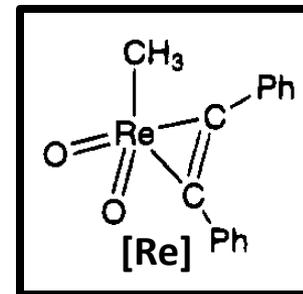
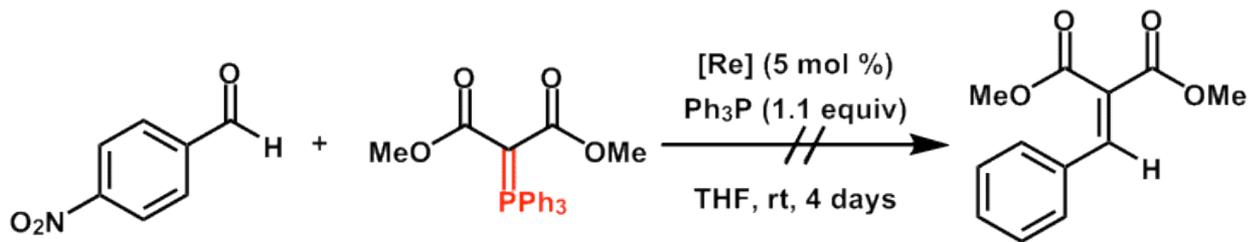
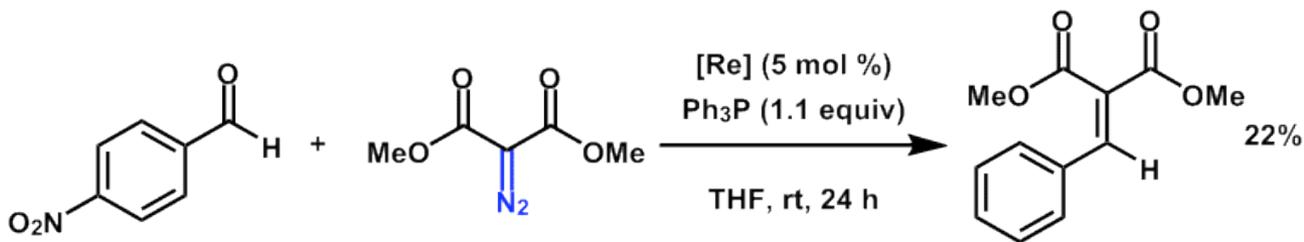
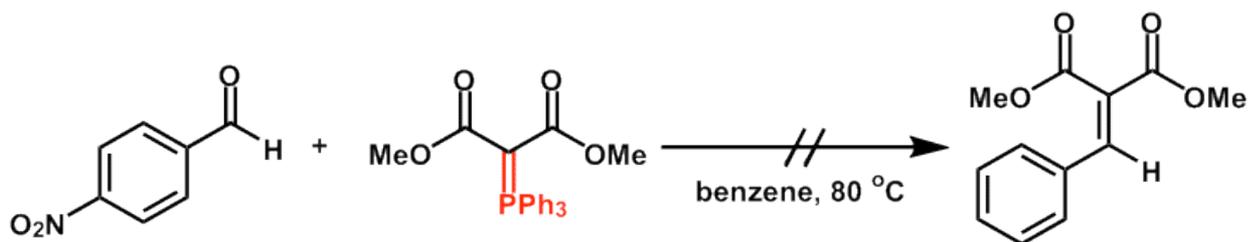
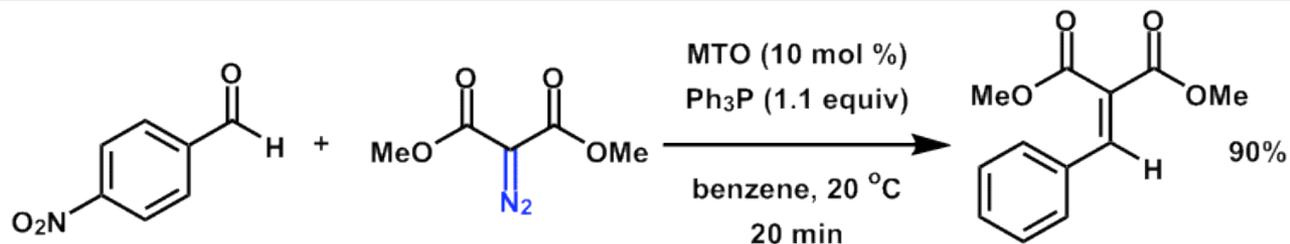
Is a classical ylide an intermediate?

# Chen's Proposed Mechanism



Are these gas phase results applicable to a solution phase reaction?

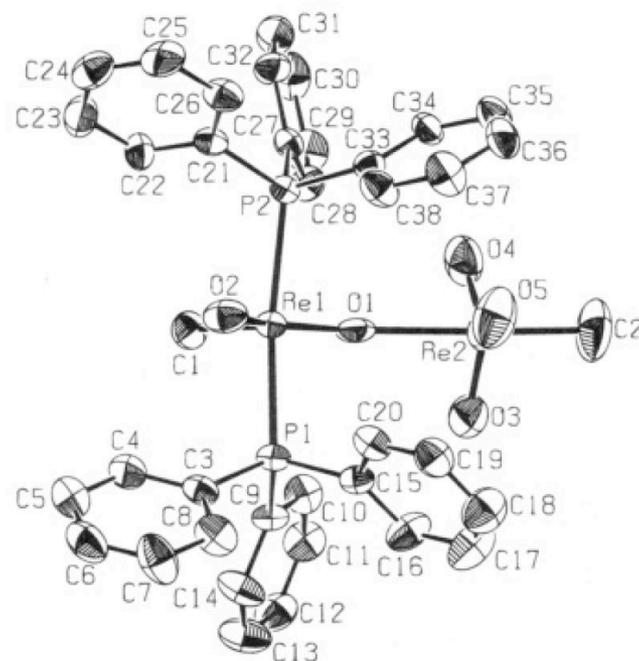
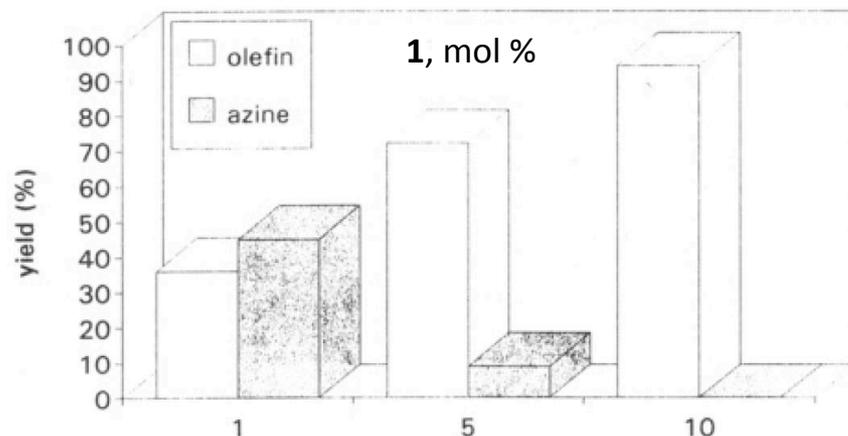
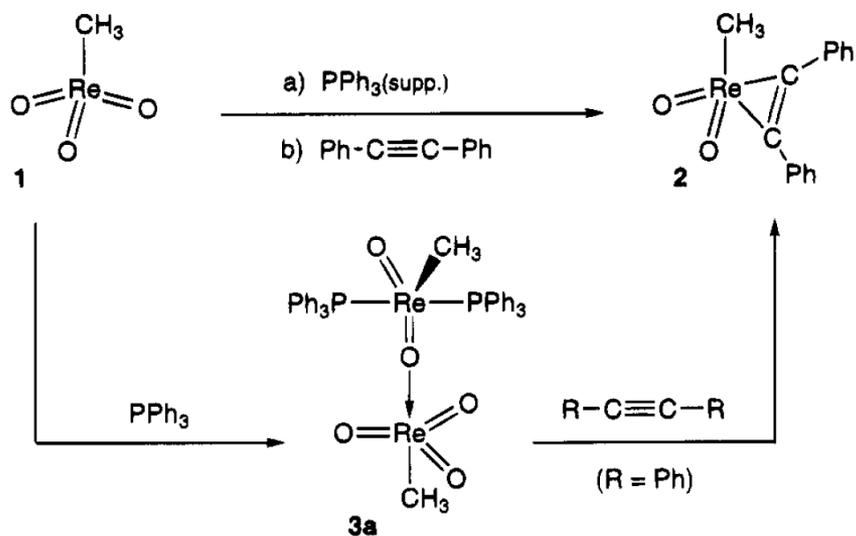
# Methyl Diazomalonate



Rhenium is involved with more than ylide formation

Herrmann, W. A.; et al. *Angew. Chem. Int. Ed.* **1991**, 1641-1642.  
Kuhn, F. E.; et al. *Chem. Eur. J.* **2004**, 6313-6321.

# Rhenium(VII) or Rhenium(V)?

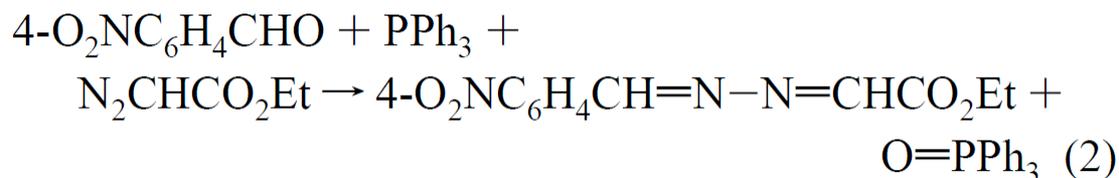
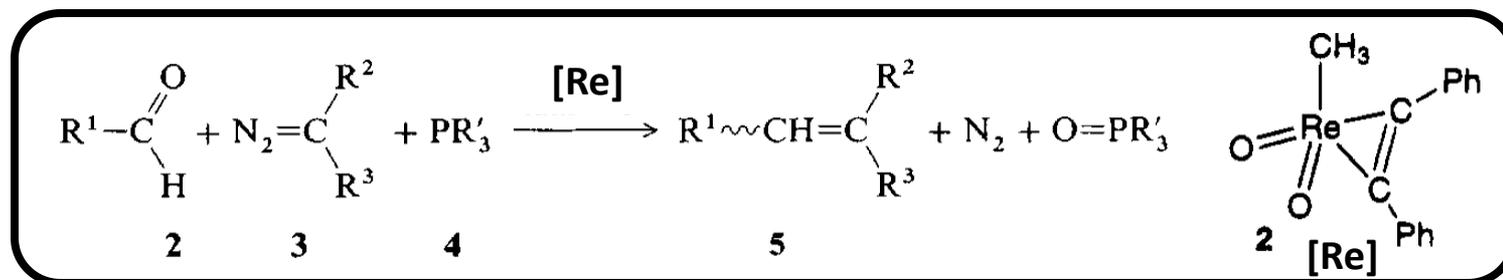


aldehyde	1 (10 mol %)		3a (5 mol %)	
	olefin (yield) (%)	<i>E/Z</i>	olefin (yield) (%)	<i>E/Z</i>
4- $\text{O}_2\text{NC}_6\text{H}_4\text{CHO}^b$	93	92/8	89	78/22
4- $\text{CH}_3\text{C}_6\text{H}_4\text{CHO}^b$	79	76/24	71	70/30
4- $\text{FC}_6\text{H}_4\text{CHO}^b$	94	66/34	89	67/33

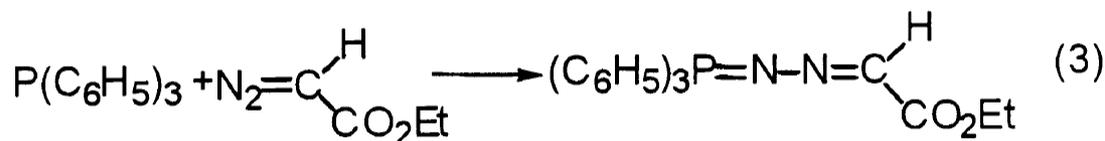
<sup>a</sup> Diazo compound,  $\text{N}_2=\text{CHCOOEt}$ ; phosphine,  $\text{PPh}_3$ ; THF. <sup>b</sup> 25 °C;

Re(V) is likely the catalytically active species

# NMR Experiments



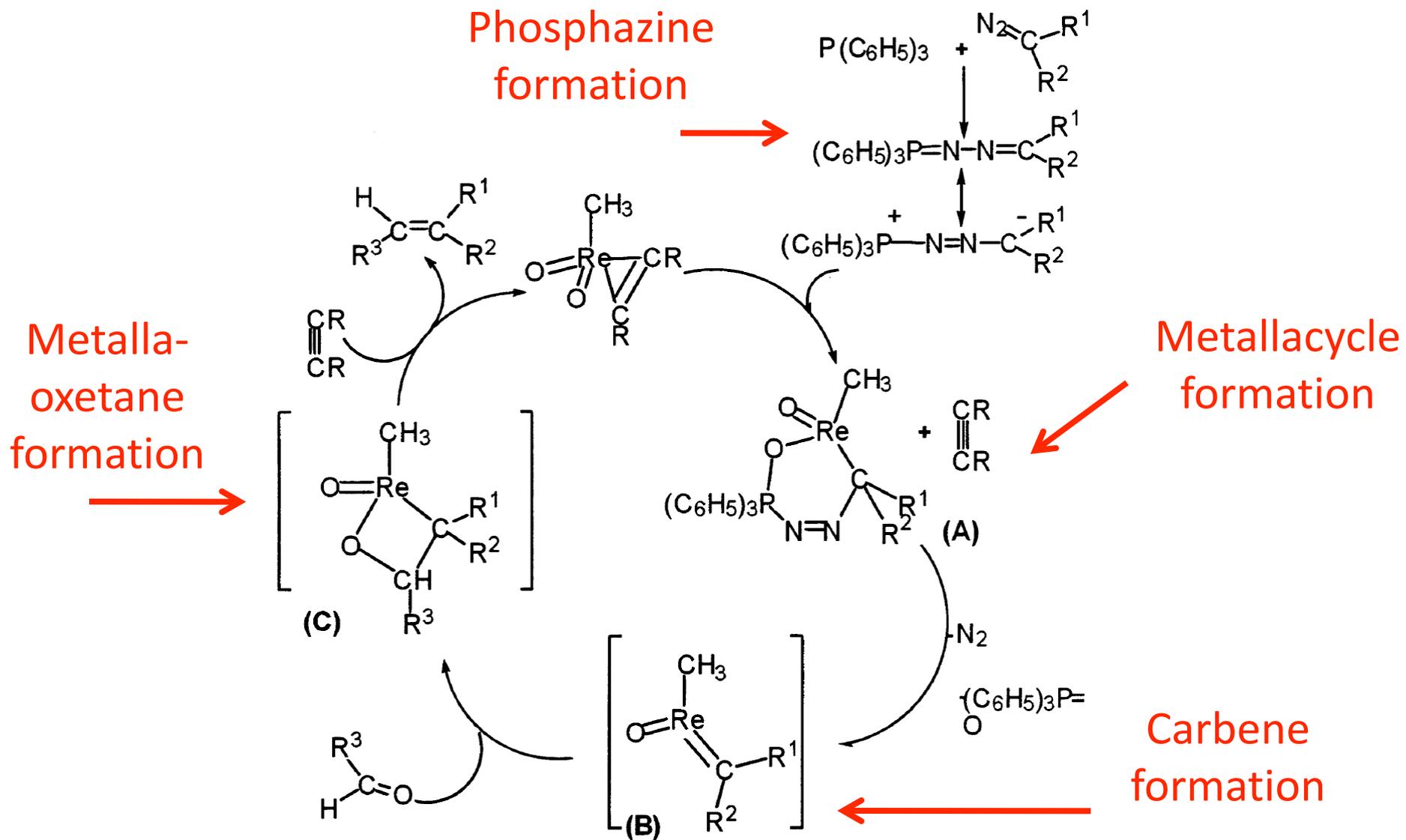
Azine - Slow



Phosphazine - Fast

- Phosphazine (1.2 equiv) reacts immediately with [Re] (<sup>17</sup>O labeled, 1 equiv) to produce N<sub>2</sub> and <sup>17</sup>OPPh<sub>3</sub>
- [Re]<sup>17</sup>O is completely consumed and forms an intermediate with a terminal oxygen ligand (<sup>17</sup>O NMR, δ 713 → 676 ppm)
- Re=C observed (δ (<sup>13</sup>C, -30 °C) 323 ppm)

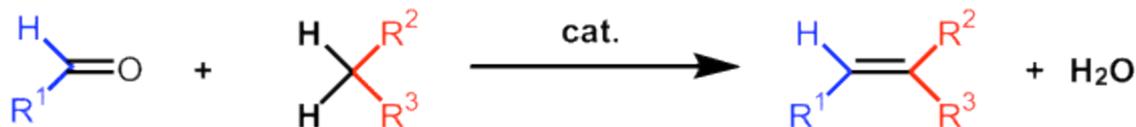
# Kuhn's Proposed Mechanism



# Conclusions

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- Compelling evidence for a Re-carbene intermediate has been reported
- Re-catalyzed ylide formation is debated, even though some stabilized ylides do not undergo Re-catalyzed olefination of aldehydes
- Re-catalyzed aldehyde olefinations provide mild conditions and access to products not available from classic Wittig chemistry
- The use of stoichiometric quantities of  $\text{Ph}_3\text{P}$  as a reducing agent is cumbersome



For additional catalytic aldehyde olefinations see:  
Kuhn, F. E.; et al. *Mini-Rev. Org. Chem.* **2004**, 55-64.