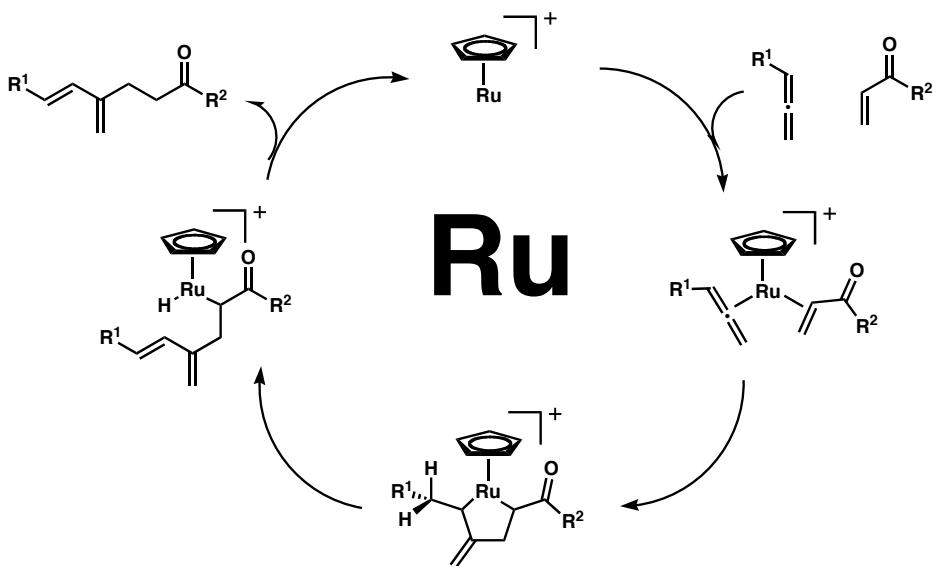


Ruthenium in Organic Synthesis



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Literature Presentation
02 February 2004
147 Noyes

Ruthenium in Organic Synthesis: Outline

- I. Regioselective Reductions
- II. Oxidations
- III. C-C bonds
 - A. Ruthenacycle Intermediates
 - B. Heteroatom Additions to Alkynes
 - C. C-H Activation
 - D. Diazo Compounds
- IV. Appendix: Preparation of Ruthenium Catalysts

RUTHENIUM AT A GLANCE

Name: From the Latin *Ruthenia*, Russia.
Atomic mass: 101.07.
History: Ruthenium was discovered by Karl Karlovich Klaus, a Russian chemist, in 1844.
Occurrence: Found in platinum and other ores.
Appearance: Silvery white, solid metal.
Behavior: RuO₄ is toxic and explosive.
Uses: Used as a catalyst in many industrial processes and to increase the corrosion resistance of titanium.



Trost



Noyori



Ley



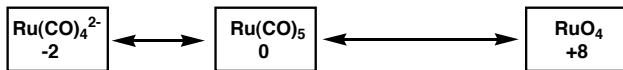
Murahashi

Reviews

Murahashi *Chem. Rev.* 1998, 98, 2599.
Trost and Toste *Chem. Rev.* 2001, 101, 2067.

Properties of Ruthenium

- Ruthenium has the widest range of oxidation states of any element



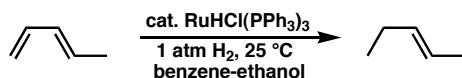
- Ruthenium complexes can adopt several coordination geometries

Oxidation State	Coordination number	Geometry	Example
Ru(0)	5	trig. bipy.	$\text{Ru}(\text{CO})_5$
Ru(II)	5	trig. bipy.	$\text{RuHCl}(\text{PPh}_3)_3$
	6	octahedral	$\text{RuCl}_2\text{CO}(\text{PR}_3)_3$
Ru(III)	6	octahedral	$[\text{Ru}(\text{NH}_3)_5\text{Cl}]^{2+}$
Ru(VI)	4	tetrahedral	RuO_4^{2-}
Ru(VII)	4	tetrahedral	RuO_4^-
Ru(VIII)	4	tetrahedral	RuO_4

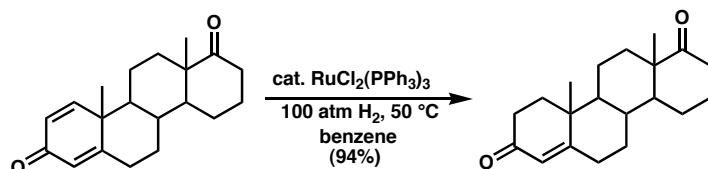
- Range of reactivity due to properties of Ru complexes:

- High electron transfer ability
- High Lewis acidity
- Low redox potentials
- Stabilities of reactive metallic species such as oxometals, metallacycles, and metal carbene complexes

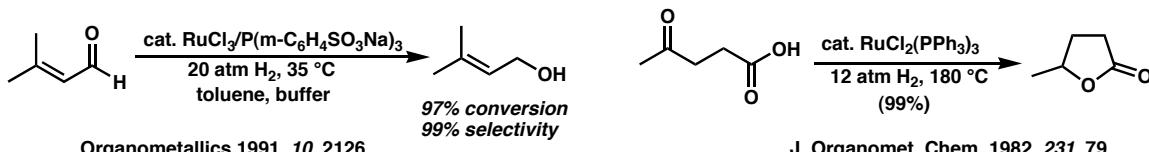
Regioselective Reductions



J. Chem. Soc. Chem. Comm. 1967, 305.

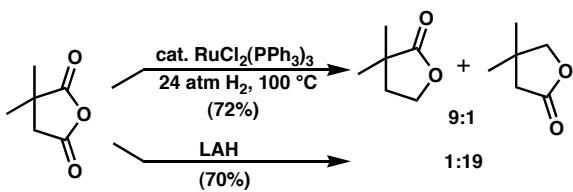


Bull. Chem. Soc. Jpn. 1975, 48, 2852.



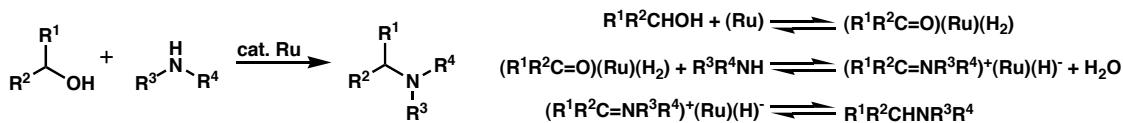
Organometallics 1991, 10, 2126.

J. Organomet. Chem. 1982, 231, 79.



J. Chem. Soc. Chem. Comm. 1976, 314.

Alcohol Oxidation-Reductive Amination

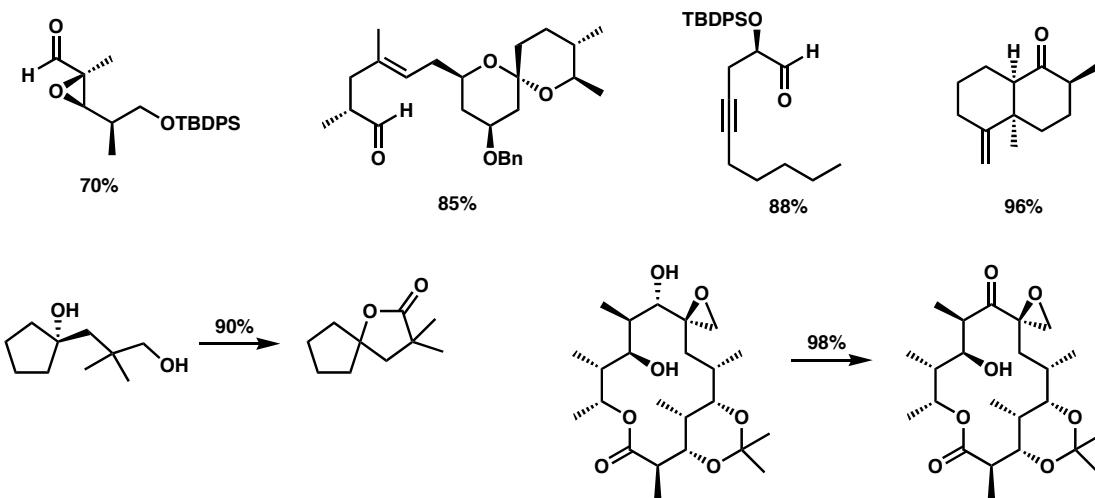


catalyst	amine	alcohol	product	% yield
$\text{RuH}_2(\text{PPh}_3)_4$	$\text{C}_8\text{H}_{17}\text{NH}_2$	$\text{C}_7\text{H}_{15}\text{OH}$	$\text{C}_7\text{H}_{15}\text{NHC}_8\text{H}_{17}$	92
$\text{RuCl}_2(\text{PPh}_3)_3$	PhNH_2	$\text{C}_3\text{H}_7\text{OH}$	$\text{PhN}(\text{C}_3\text{H}_7)_2$	88
$\text{RuCl}_3\cdot\text{nH}_2\text{O}\cdot\text{P(OBu)}_3$		CH_3OH		99
$\text{Ru}(\text{cod})(\text{cot})$		$\text{C}_2\text{H}_5\text{OH}$		85
$\text{RuCl}_2(\text{PPh}_3)_3$				100

Murahashi TL 1982, 229.

Tetrapropylammonium Perruthenate (TPAP) Oxidations

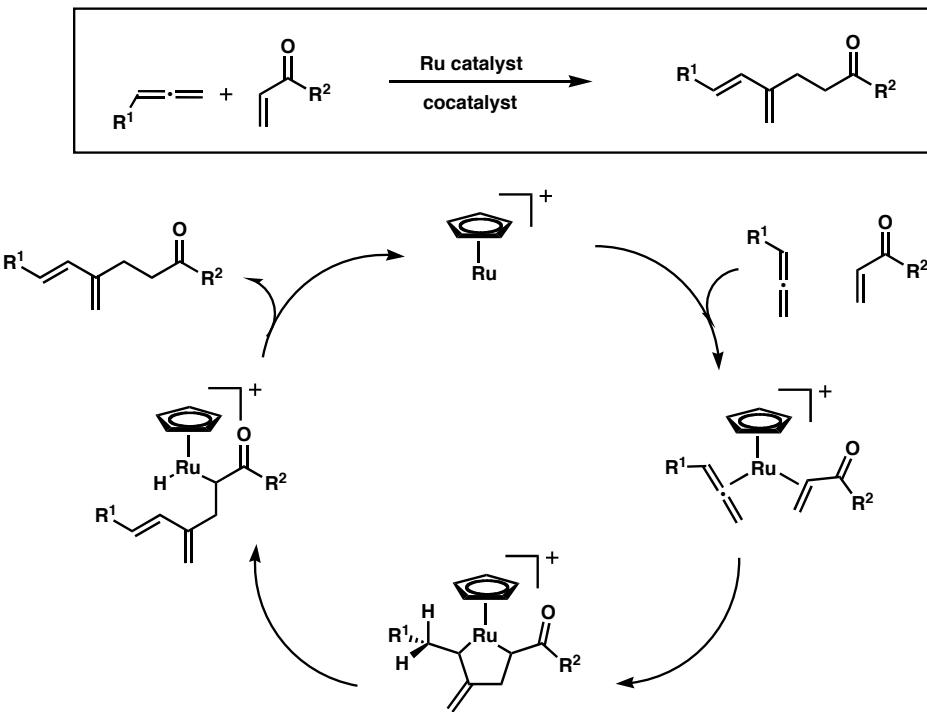
- $[\text{RuO}_4]^-$ is a milder oxidant than RuO_4 ; can cleave some C=C bonds
- $[\text{RuO}_4]^-$ salts with large organic cations are soluble in organic solvents
- Water inhibits catalyst turnover; use molecular sieves
- TPAP catalytic (5 mol %) with suitable co-oxidants; NMO most effective
- Wide tolerance of functional groups
 1. Double bonds, polyenes, enones, halides, cyclopropanes, epoxides, and acetals
 2. Esters, amides, lactones, amines, peroxides, and catechols
 3. Protecting groups: SEM, MOM, BOM, MEM, trityl, silyl, benzyl, PMB, THP, acetate, and benzoate
 4. Piperidines, pyrroles, indoles, furans, thiophenes, and pyridines are unreactive



Ley Synthesis 1994, 7, 639 and ref. therein.

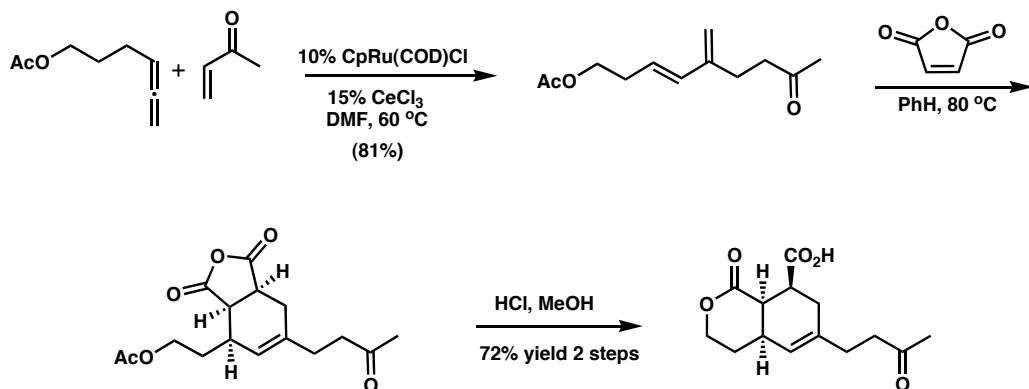
Panek JACS 2002, 124, 12806.

Ruthenacyclopentane: Allene and Vinyl Ketone Coupling



JACS 1999, 121, 4068.

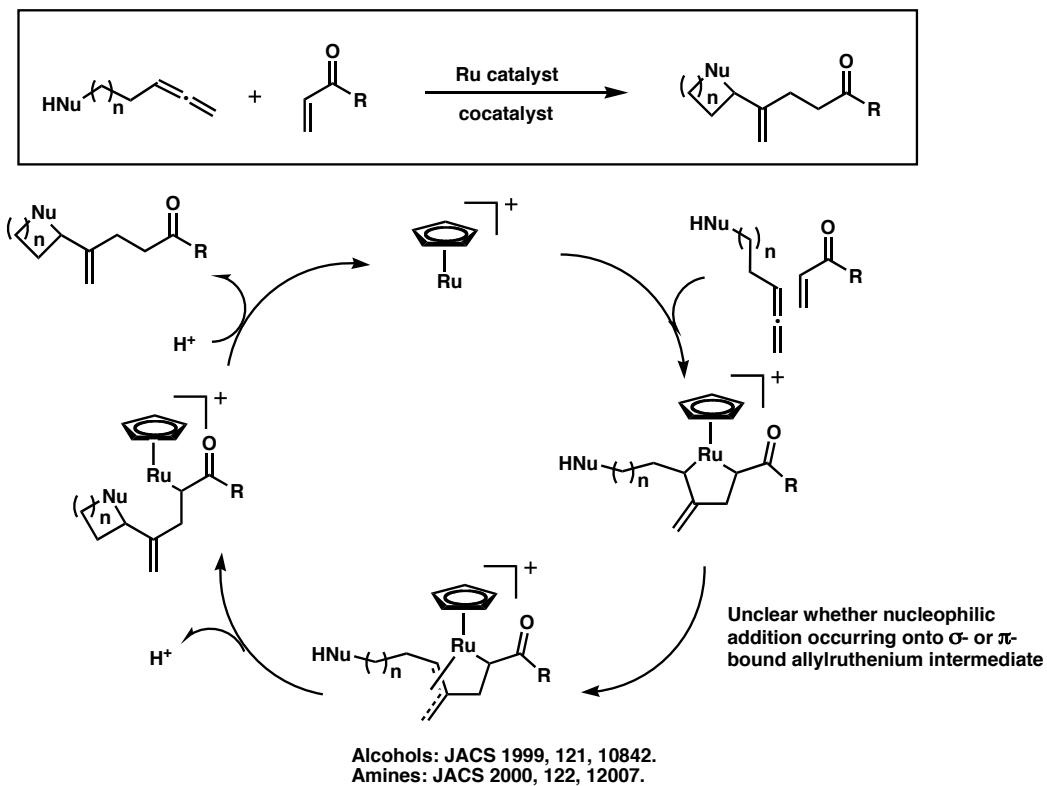
Ruthenacyclopentane: Allene and Vinyl Ketone Coupling



- Role of CeCl_3 cocatalyst unknown; may activate enone
- Variety of allenes coupled to methyl or phenyl vinyl ketone in good yields (53-81%)

JACS 1999, 121, 4068.

Ruthenacyclopentane: Allene and Vinyl Ketone Coupling

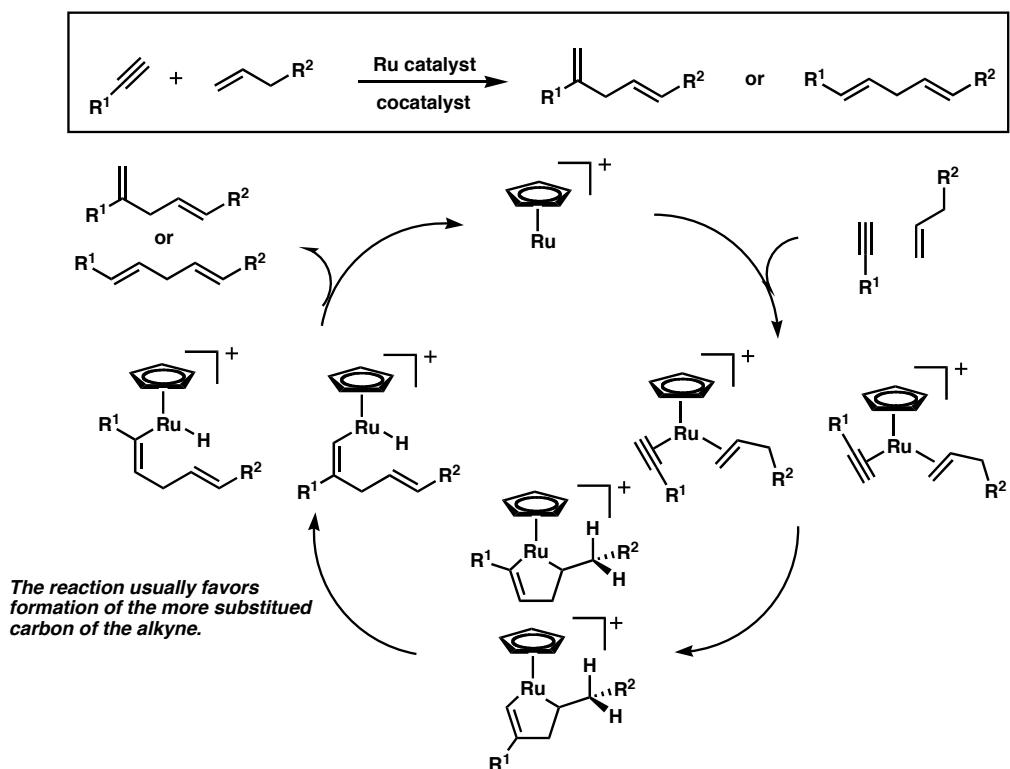


Ruthenacyclopentane: Allene and Vinyl Ketone Coupling

allene	Product	Yield
		X = O 82% X = NBn 73%
		X = O 74% X = NBn 67%
		X = O 70% X = NBn 62%
		X = O 68% X = NBn 90%
		X = O 67% X = NBn 71%

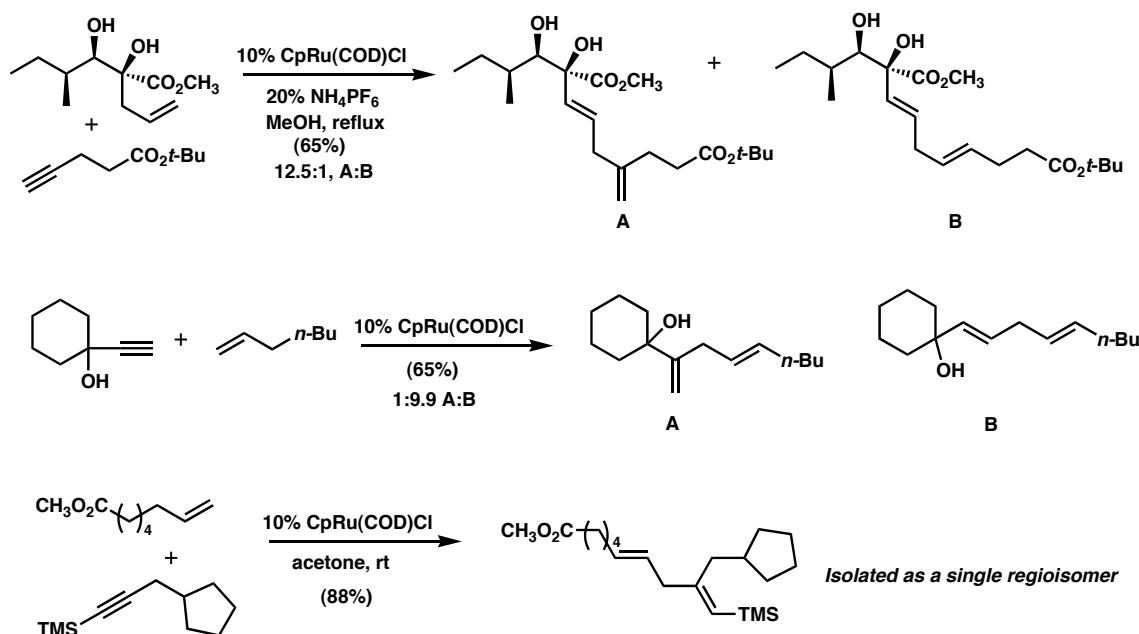
- Ru catalyst: 10% $\text{CpRu}(\text{CH}_3\text{CN})_3\text{PF}_6$
- Cocatalyst:
 - Alcohols require 15% CeCl_3
 - Amines use 15% TiCl_4 or MeAlCl_2

Ruthenacyclopentene: Alkyne and Alkene Coupling--An Alder-Ene Reaction



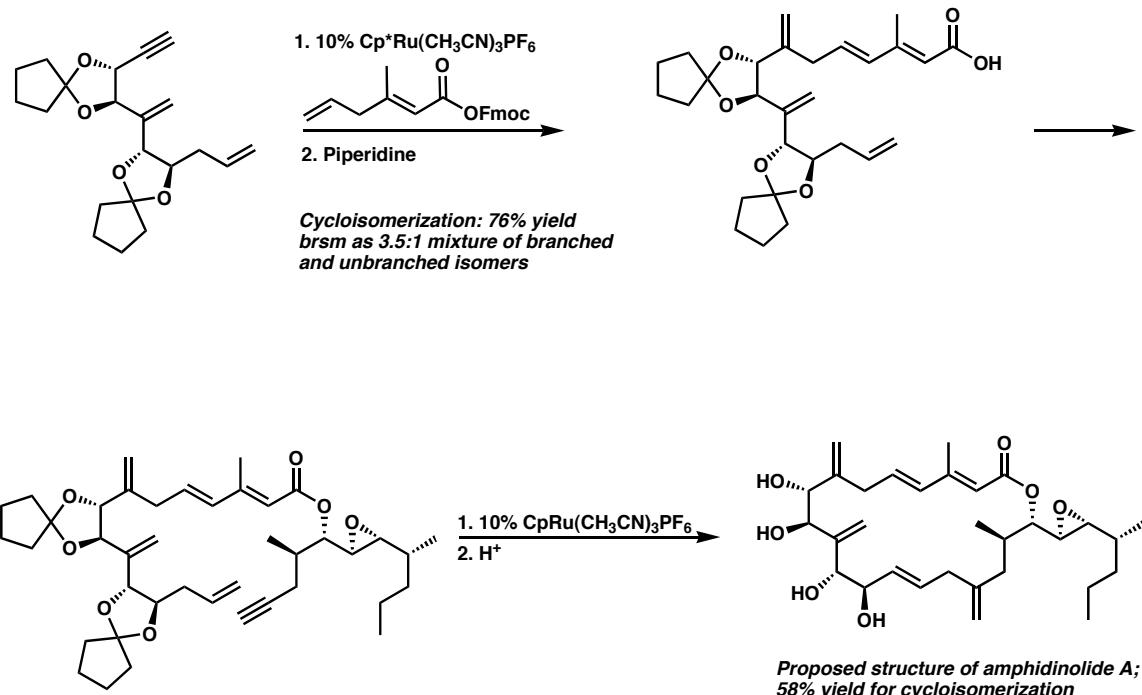
JACS 1993, 115, 4361; JACS 1995, 117, 615.

Ruthenacyclopentene: Alkyne and Alkene Coupling--An Alder-Ene Reaction



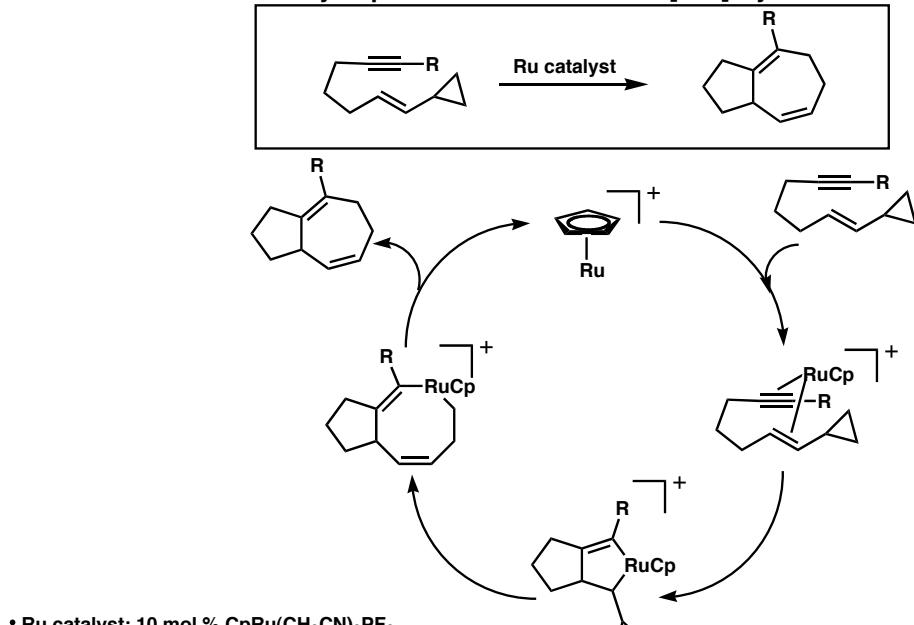
JACS 1993, 115, 4361; JACS 1995, 117, 615.

Application in Total Synthesis: The Proposed Structure of Amphidinolide A



Trost JACS 2002, 124, 12420.

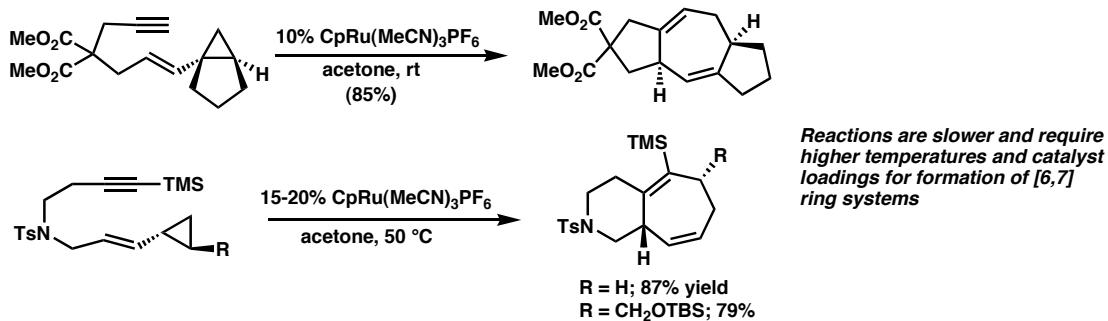
Ruthenacyclopentene: Intramolecular [5+2] Cycloaddition



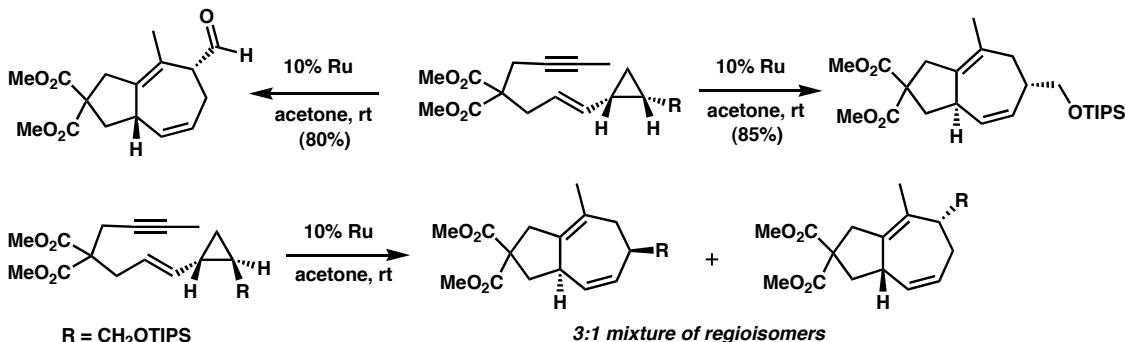
Trost JACS 2000, 122, 2379.

Ruthenacyclopentene: Intramolecular [5+2] Cycloaddition Examples

• "Complete diastereoselectivity is always observed" (Diastereomers are observed for substitution at other allylic position)

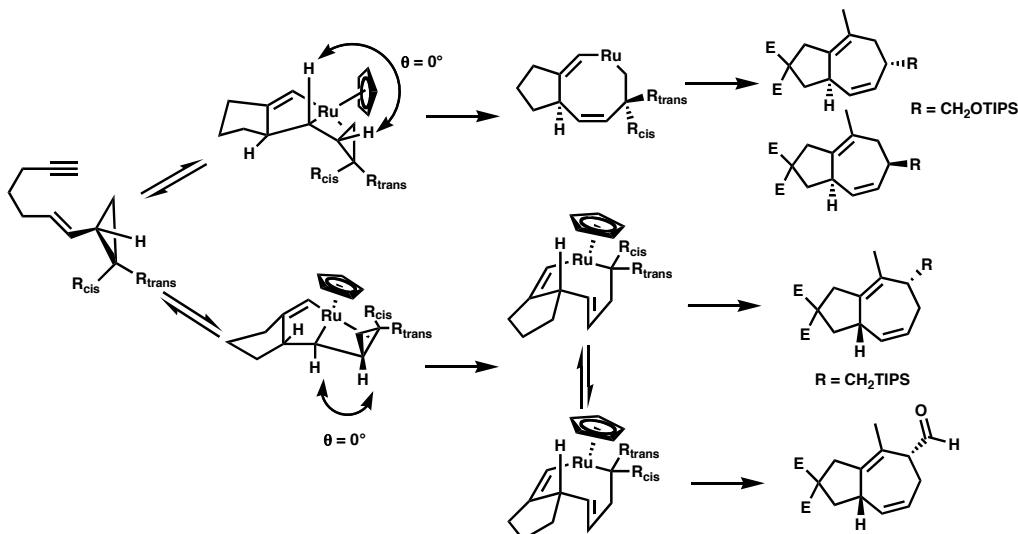
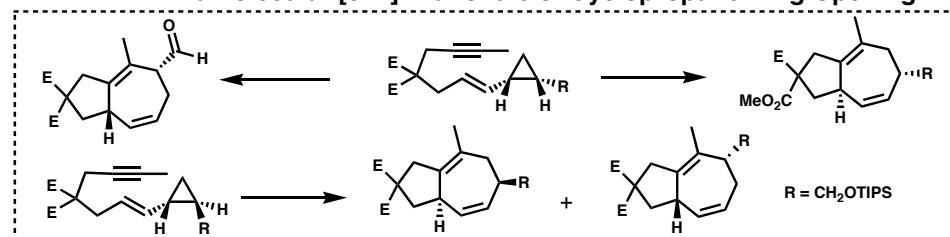


• Regioselectivity controlled by choice of substituents



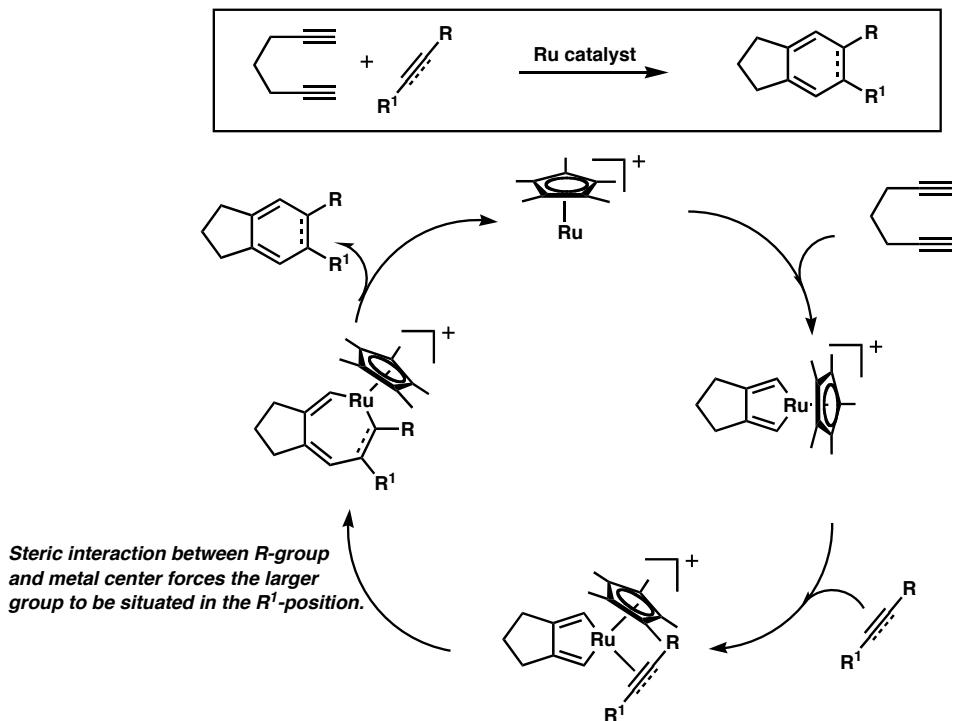
Trost JACS 2000, 122, 2379.

Intramolecular [5+2]: Rationale of Cyclopropane Ring Opening



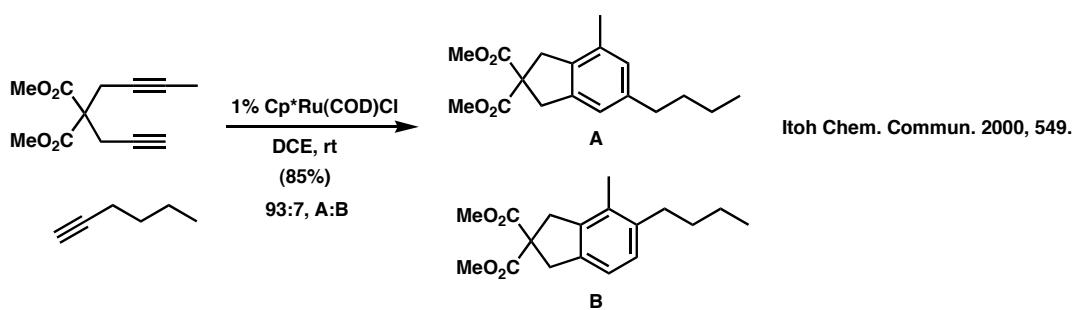
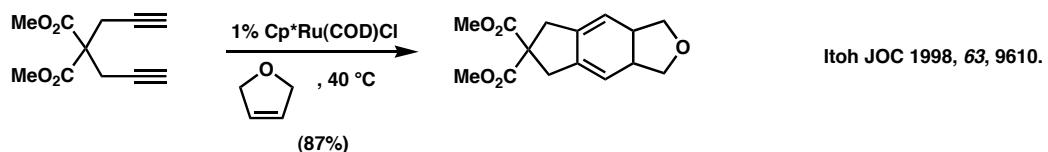
Trost JACS 2000, 122, 2379.

Ruthenacyclopentadiene: [2+2+2] cycloaddition

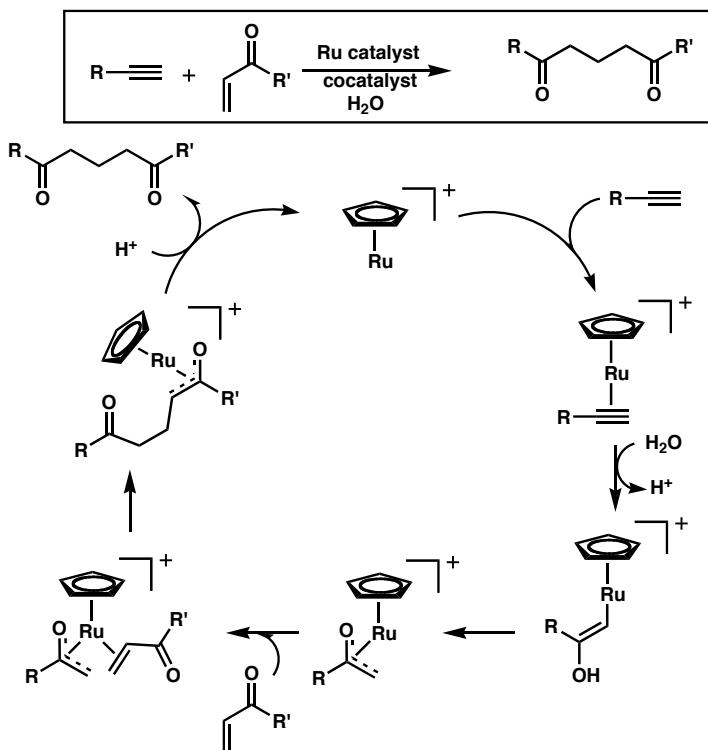


Itoh JOC 1998, 63, 9610; Chem. Commun. 2000, 549.

Ruthenacyclopentadiene: [2+2+2] cycloaddition

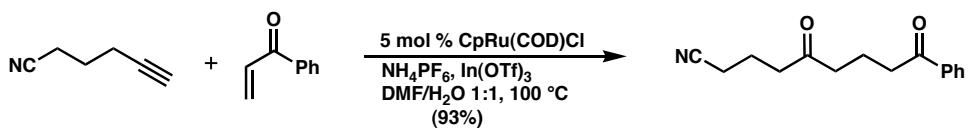


Heteroatom Additions to Alkynes: Addition of Water



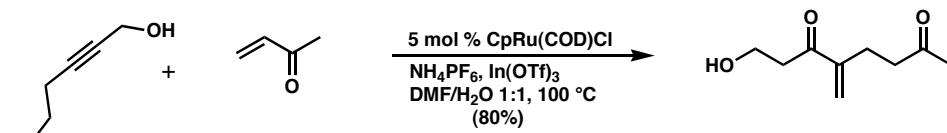
Trost JACS 1997, 119, 836.

Heteroatom Additions to Alkynes: Addition of Water



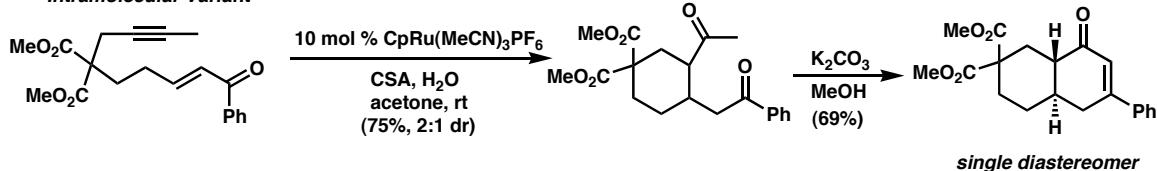
*Role of indium unclear;
Cl scavenger?*

Trost JACS 1997, 119, 836.



Trost JACS 1997, 119, 11319.

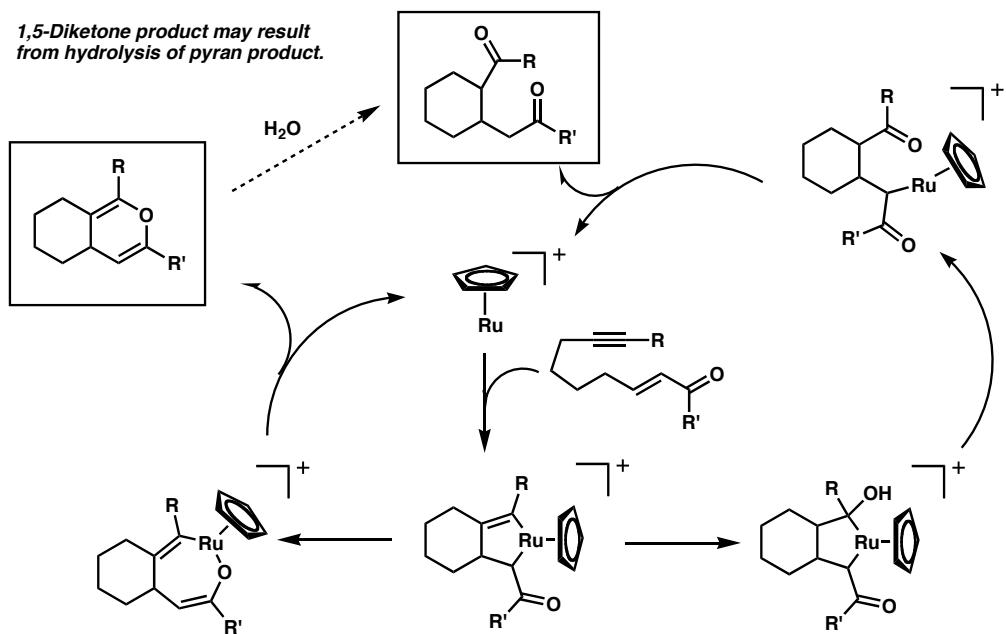
• Intramolecular Variant



Trost JACS 2000, 122, 5877.

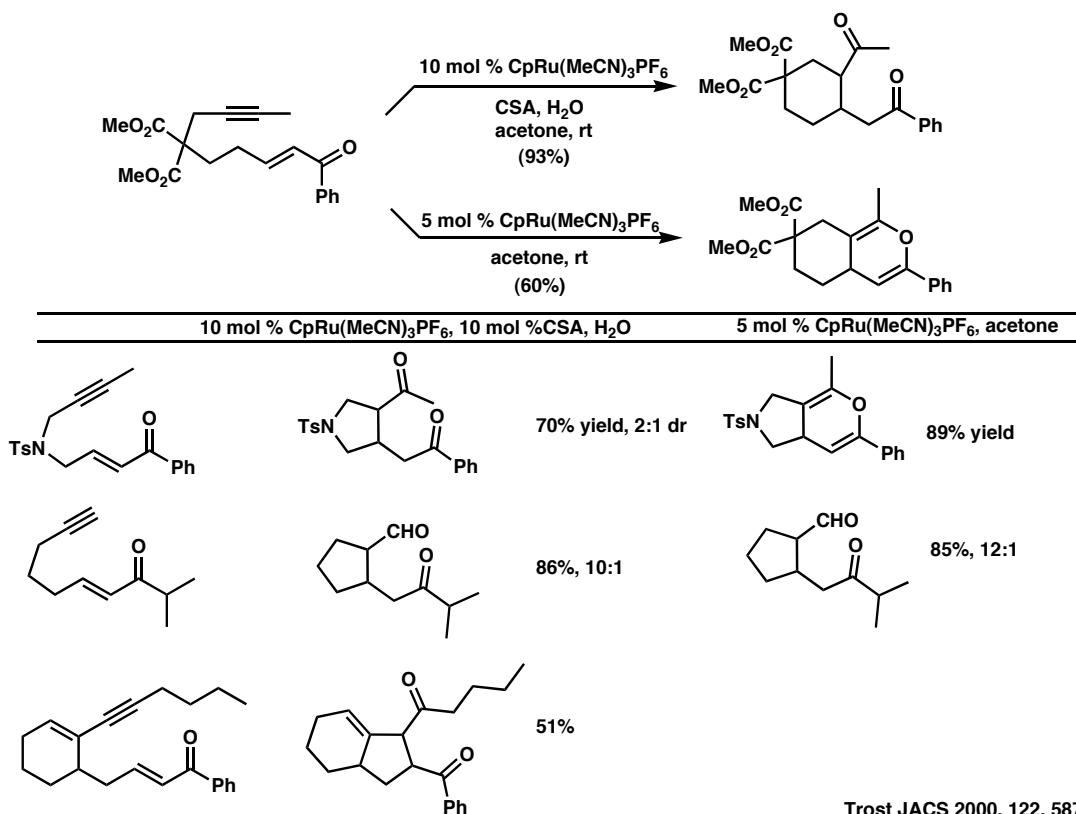
An alternative mechanism at work?

Heteroatom Additions to Alkynes: Addition of Water (Alternative Mechanism)



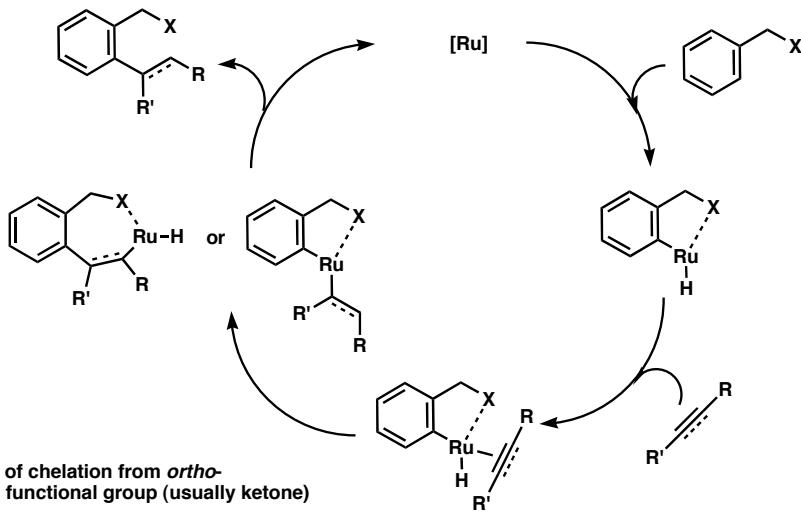
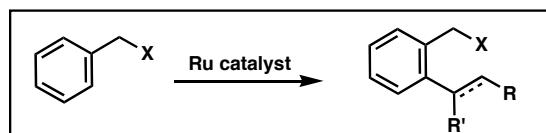
Trost JACS 2000, 122, 5877.

Heteroatom Additions to Alkynes: Addition of Water (Alternative Mechanism)



Trost JACS 2000, 122, 5877.

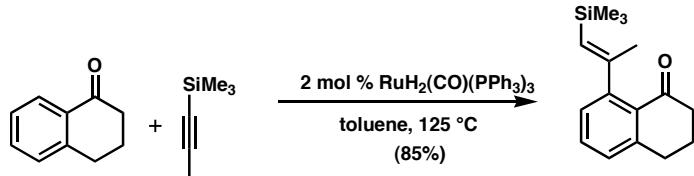
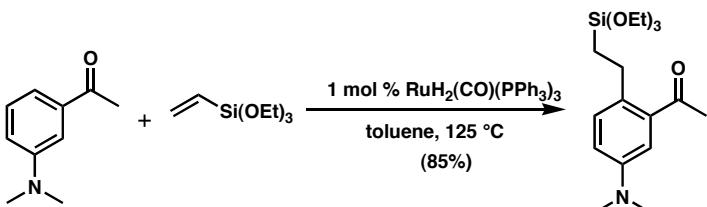
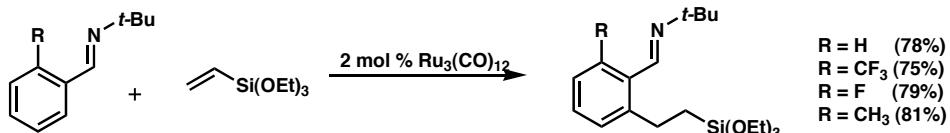
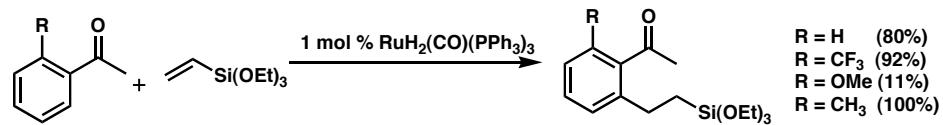
Aromatic C-H Bond Activation



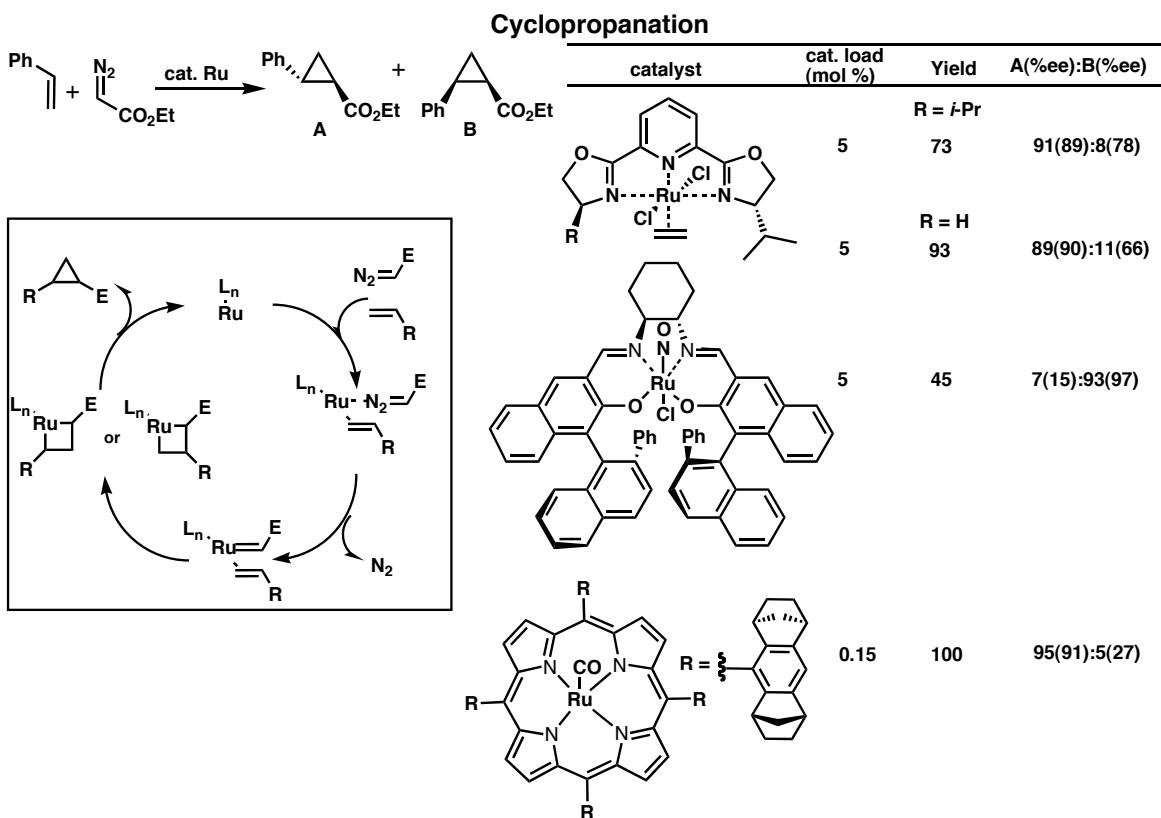
- Requires aid of chelation from *ortho*-coordinating functional group (usually ketone)
- Excellent control of regioselectivity for activation of aromatic C-H at the less hindered *ortho*-position

Reviewed in Murai Pure Appl. Chem. 1997, 589.

Aromatic C-H Bond Activation

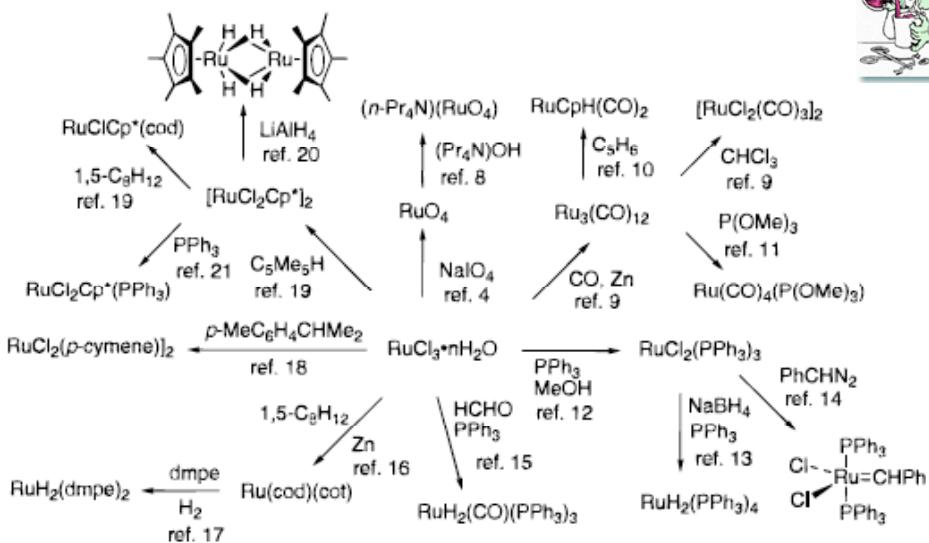


Reviewed in Murai Pure Appl. Chem. 1997, 589.



Trost Chem. Rev. 2001, 2067 and ref. therein.

Preparation of Ruthenium Catalysts



4. Encyclopedia Reagents Org. Syn. 1996, Vol. 6, 4415.
8. Synthesis 1994, 639; Aldrichimica Acta 1990, 23, 13.
9. J. Organomet. Chem. 1981, 214, 391.
10. J.C.S., Dalton Trans. 1975, 1710.
11. J. Organomet. Chem. 1980, 195, 77.
12. Inorg. Synth. 1970, 12, 237.
13. JACS 1968, 90, 1089.
14. ACIEE 1995, 4, 2039; JACS 1996, 118, 100.

15. Inorg. Synth. 1974, 15, 45.
16. JCS Dalton Trans. 1980, 1961.
17. JCS Chem. Comm. 1982, 1388.
18. JCS Dalton Trans. 1974, 233.
19. Chem. Lett. 1984, 1161.
20. Organometallics 1988, 7, 2243.
21. J. Organomet. Chem. 1986, 314, C46.

Conclusion

- Wide scope of reactions catalyzed or mediated by Ruthenium complexes
- Relatively new area in C-C bond formation;
50% literature cited in Trost's review was published in 1997 or later
- "Prospects are clearly bright for more reactions to be discovered." --Trost