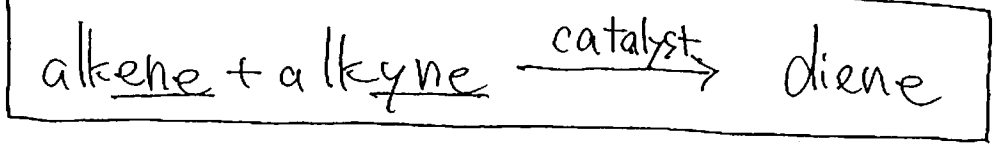
A New Entry to Diene Synthesis: Ring-Closing Enyne Metathesis Catalyzed by Ruthenium Carbene Complex

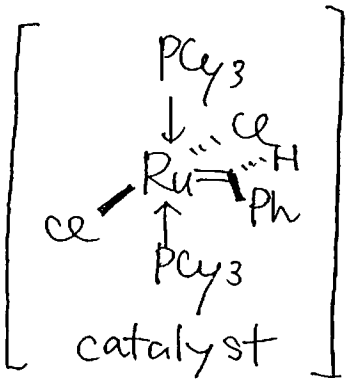
H. Mori, 2005

Contents

1. Introduction

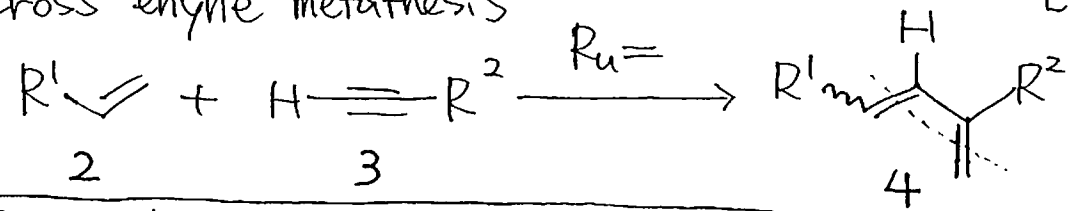
1.1. What is enyne metathesis?



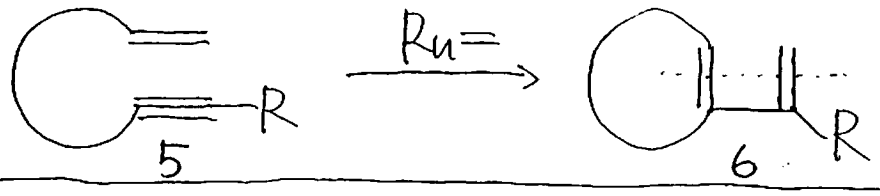


catalyst 1a

- Cross enyne metathesis



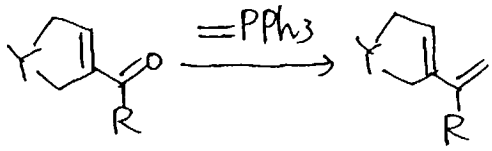
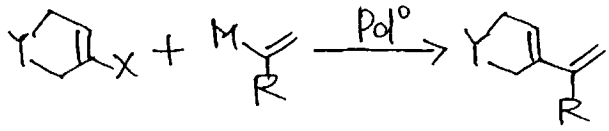
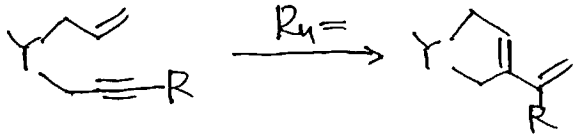
- Ring-closing enyne metathesis



⇨ today's topic

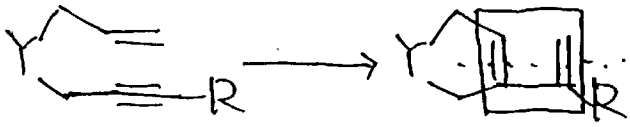
2 Advantages of enyne metathesis

Comparison of enyne metathesis with conventional methods

Method	general scheme	reaction	waste
Wittig		Stoichio-metric	$Ph_3P=O$
Cross-coupling		catalytic	MX
enyne metathesis		catalytic	none

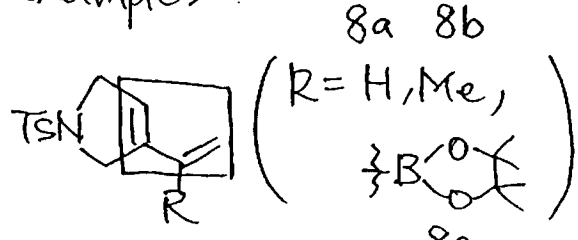
1.3 Reaction patterns of ring-closing enyne metathesis

① Monocyclization



7 8

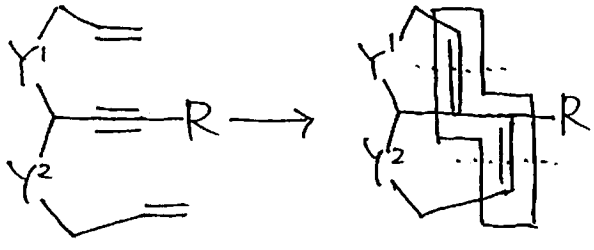
examples



8a 8b (R = H, Me,)

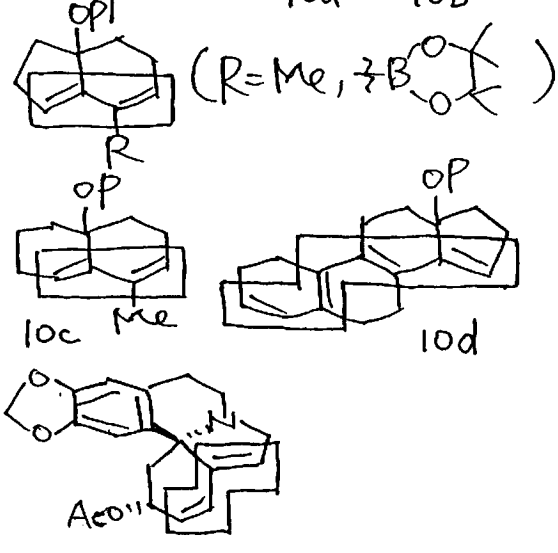
8c

② Polycyclization



9 10

examples



10a 10b 10c 10d

10e

2. Mechanism of Ring-Closing Enyne Metathesis.

2.1. Difference between olefin metathesis and enyne metathesis

2.2. Difference between internal alkyne and terminal alkyne

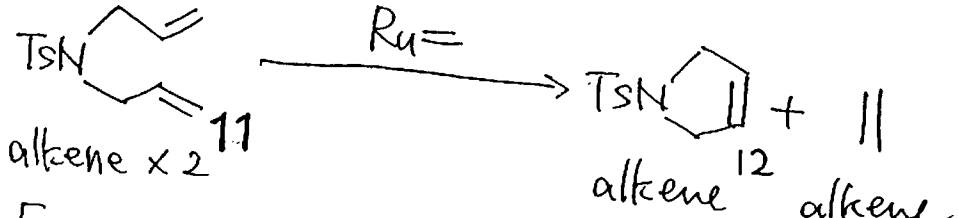
2.3. Role of ethylene gas

2.4. Summary

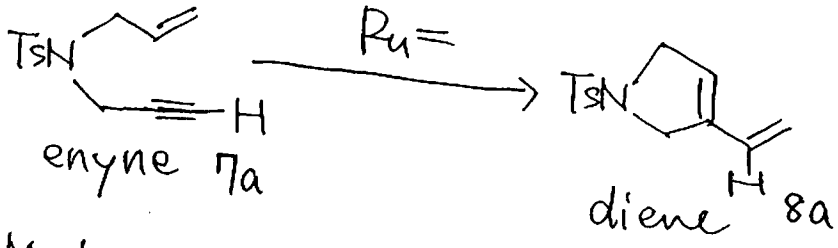
2.1. Difference between olefin metathesis and enyne metathesis

① Formal difference

- Olefin metathesis



- Enyne metathesis



② Mechanistic difference

Mechanism and Activity of Ruthenium Olefin Metathesis Catalysts: The Role of Ligands and Substrates from a Theoretical Perspective

Christian Adlhart and Peter Chen*

Contribution from the Laboratorium für Organische Chemie, Swiss Federal Institute of Technology, ETH Zürich, CH-8093 Zürich, Switzerland

Received October 6, 2003; E-mail: chen@org.chem.ethz.ch

J. AM. CHEM. SOC. 2004, *126*, 3496–3510

Mechanism of Enyne Metathesis Catalyzed by Grubbs Ruthenium–Carbene Complexes: A DFT Study

Jörg J. Lippstreu and Bernd F. Straub*

Contribution from the Department Chemie und Biochemie der Ludwig-Maximilians-Universität München, Butenandtstr. 5-13 (Haus F), D-81377 München, Germany

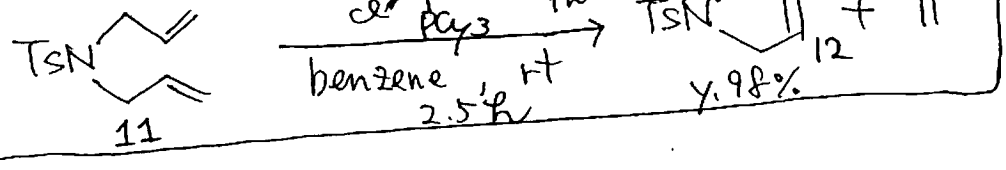
Received December 8, 2004; E-mail: Bernd.F.Straub@cup.uni-muenchen.de

J. AM. CHEM. SOC. 2005, *127*, 7444–7457

3/14

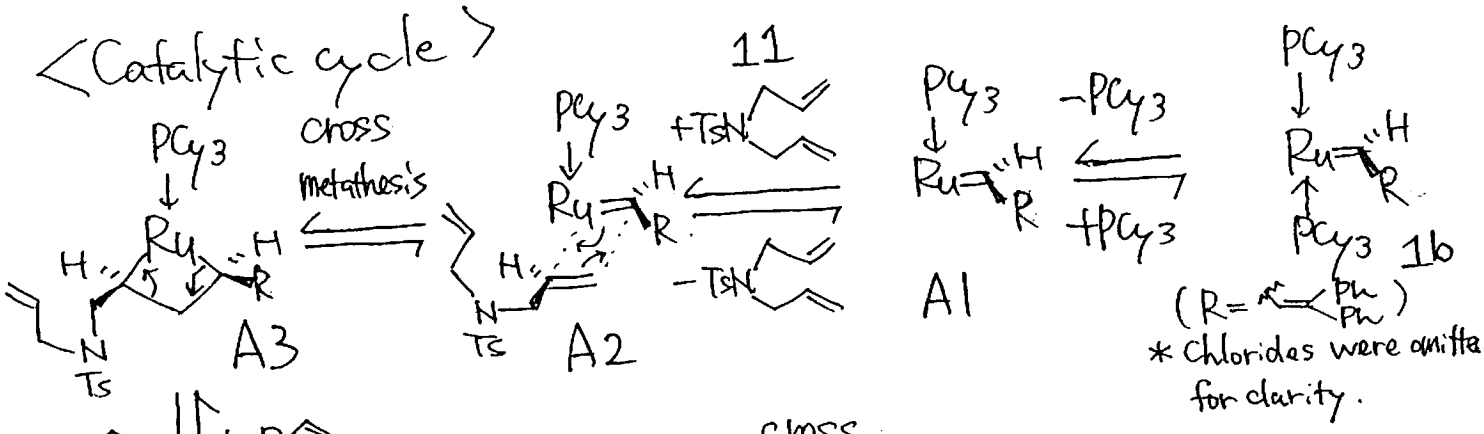
◦ Ring-closing olefin metathesis

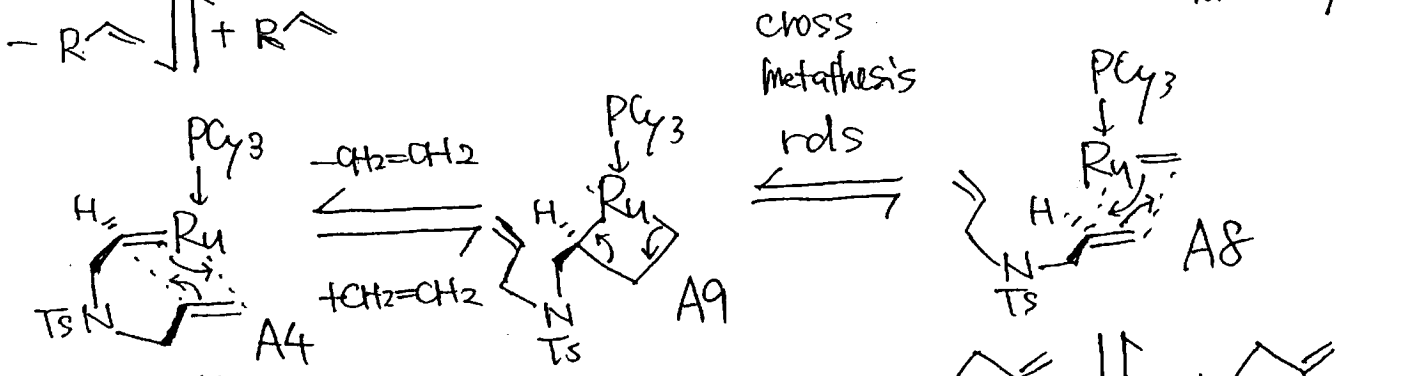
- model reaction —

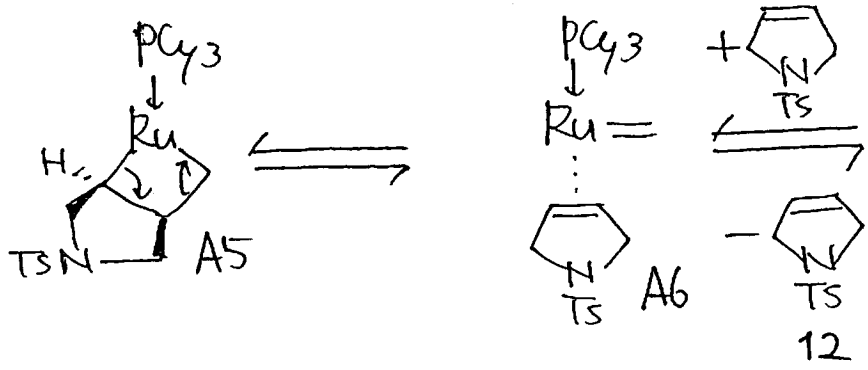


Mori, M. et al Synlett 1994, 1020.

<Catalytic cycle>





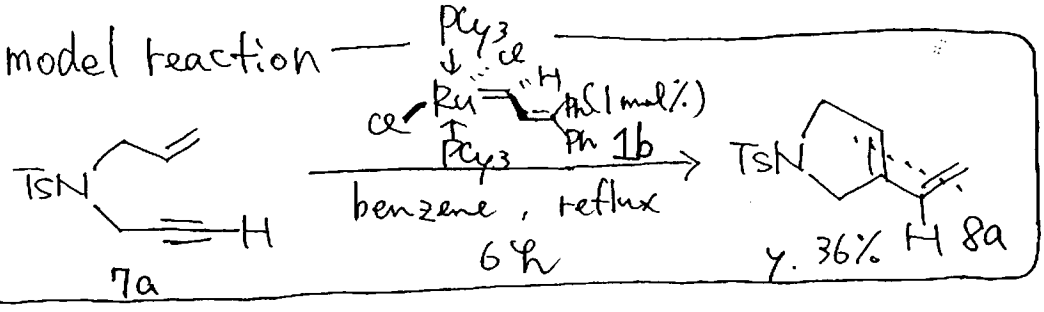


<Mechanistic features>

1. Reversible process
2. One molecule/cycle required.
3. Cross metathesis seems rds.

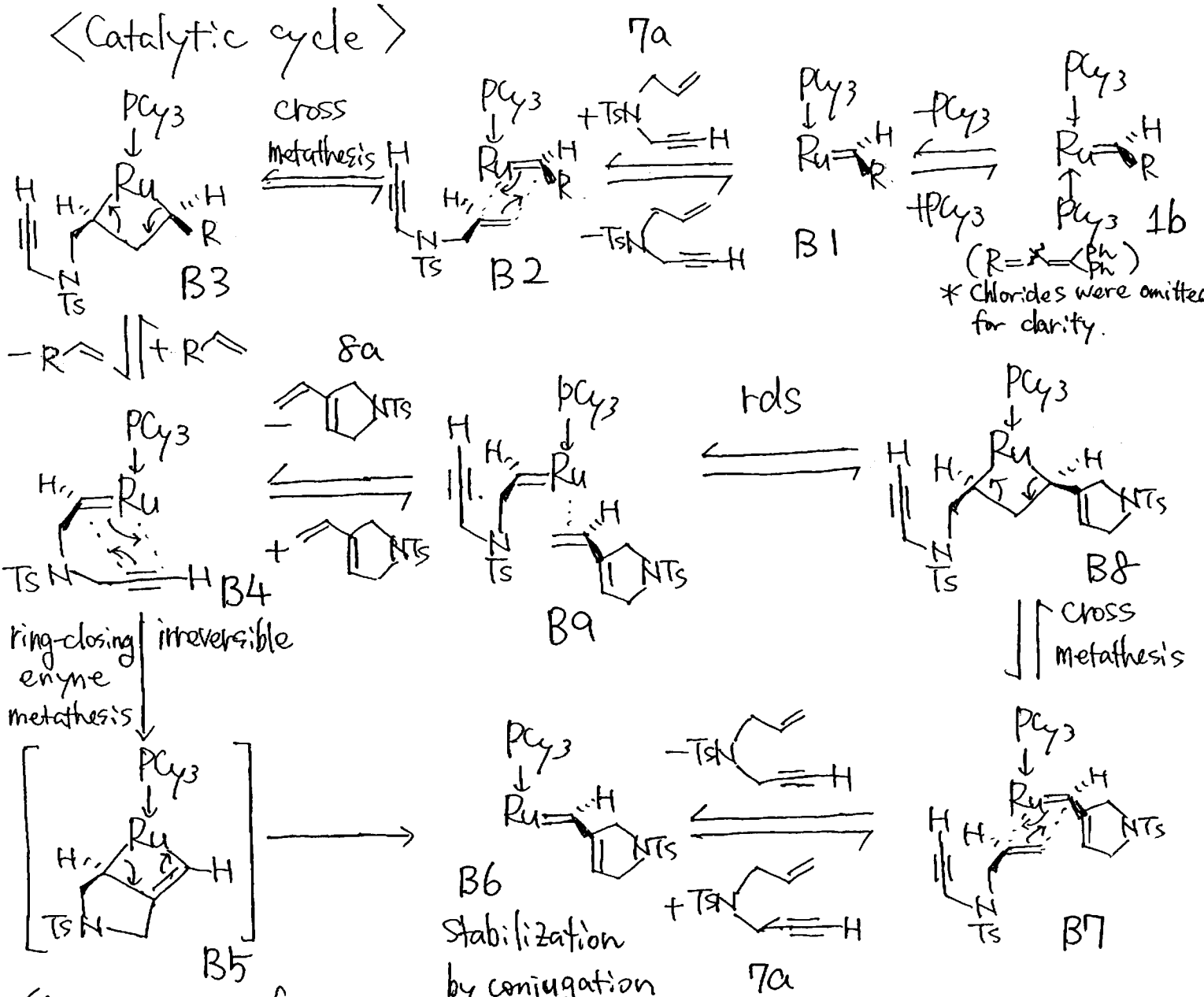
○ Ring-closing enyne metathesis

model reaction



Mori, M. et al
Synlett 1994, 1020.

<Catalytic cycle>



<Mechanistic features>

1. Irreversible process
2. Two molecules/cycle required.
3. Cross metathesis is rds.

* For experimental supports of alkene initiation, see Appendix 3 (p. 14).

③ Summary

reaction	SM	TM	catalytic cycle	number of molecule/cycle	rds
olefin metathesis	alkene ×2	alkene ×2	reversible	1	cross metathesis faster than enyne metathesis
enyne metathesis	enyne	diene	irreversible	2	cross metathesis slower than olefin metathesis

④ Examples of enyne metathesis reaction

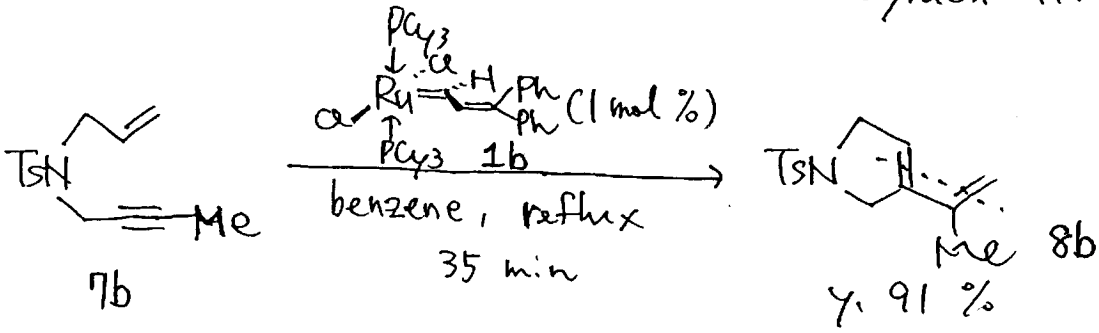
Ruthenium Catalyzed Enyne Metathesis

Atsushi Kinoshita and Miwako Mori*

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060

Received 30 August 1994

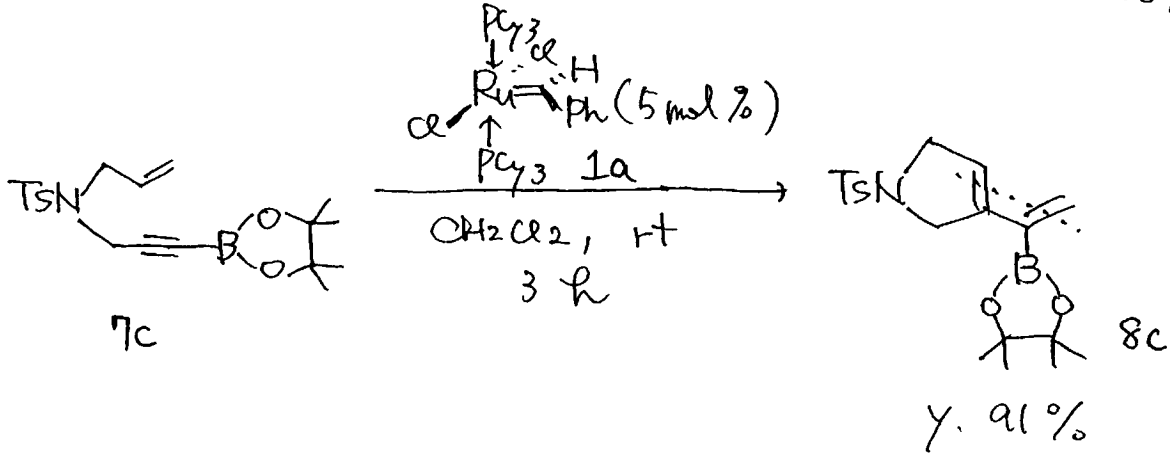
Synlett 1994, 1020.



Ruthenium-Catalyzed Enyne Metathesis of Acetylenic Boronates: A Concise Route for the Construction of Cyclic 1,3-Dienylboronic Esters

Johanne Renaud,* Claus-Dieter Graf, and Lukas Oberer

Angew. Chem. Int. Ed. 2000, 39, 3101.



For other interesting examples, see Appendix 1 (p. 12).

2.2. Difference between internal alkyne and terminal alkyne

< Substituent effect on alkyne >

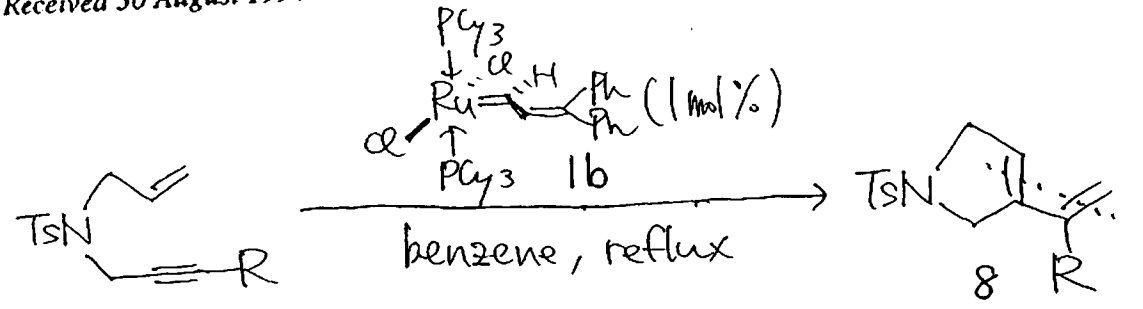
Ruthenium Catalyzed Enyne Metathesis

Atsushi Kinoshita and Miwako Mori*

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060

Received 30 August 1994

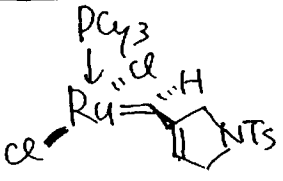
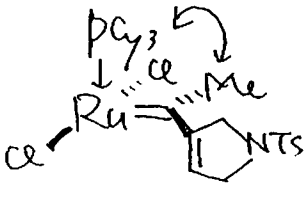
Synlett 1994, 1020.



R=H : y. 36% (6h)

R=Me : y. 91% (35min)

< Reasonable explanation >

R	intermediate	stability	activation energy	regeneration of catalyst
H (7a)		stable	high	slow
Me (7b)		unstable	low	fast

2.3. Role of ethylene gas

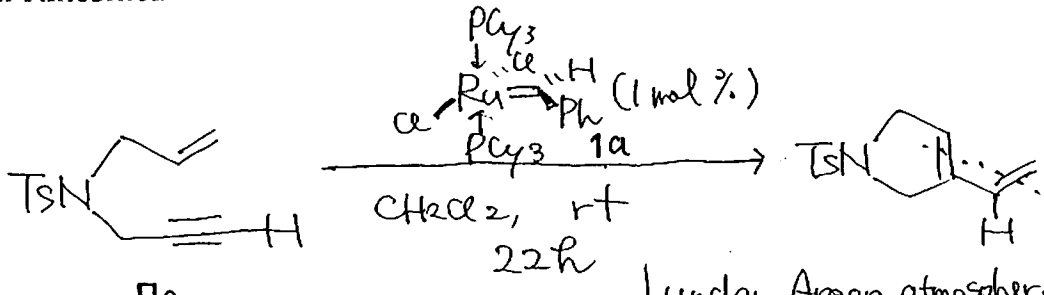
Remarkable Effect of Ethylene Gas in the Intramolecular Enyne Metathesis of Terminal Alkynes

Miwako Mori,* Norikazu Sakakibara, and Atsushi Kinoshita

Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan

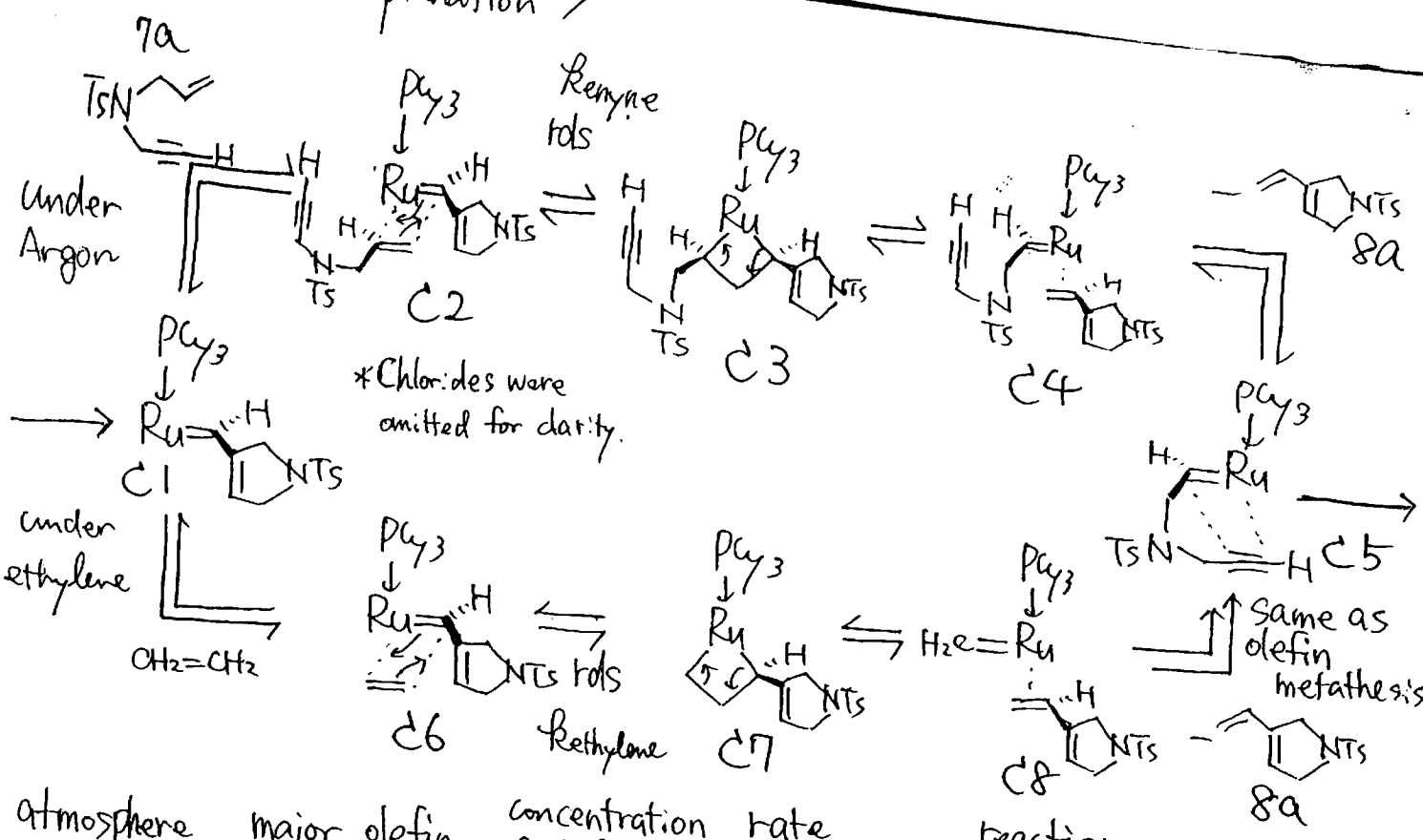
Received May 13, 1998

J. Org. Chem. **1998**, *63*, 6082–6083



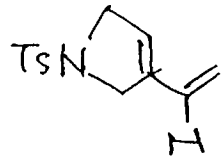
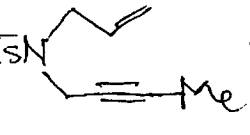
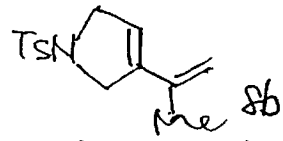
under Argon atmosphere : y. 21%

under ethylene atmosphere : y. 90%



atmosphere	major olefin	concentration of olefin	rate constant (k)	reaction rate
Argon	enyne	low (~0.05 M)	small	slow
ethylene	ethylene	high (~0.3 M)	large	fast

2.4. Summary

enyne (SM)	alkene	alkyne	conditions: atmosphere	conditions: others	diene (TM)
 7a	terminal	terminal	ethylene	CH_2Cl_2 rt 22 h	 8a y. 90%
 7b	terminal	internal	Argon	benzene reflux 35 min or benzene rt 27 h	 8b y. 91 or 89 %

3. Tandem Ring-Closing Enyne Metathesis – Ring-Closing Metathesis — One-pot synthesis of polycyclic polyenes —

3.1. Symmetrical case

3.2. Unsymmetrical case

Catalytic Ring Closing Metathesis of Dienynes: Construction of Fused Bicyclic Rings

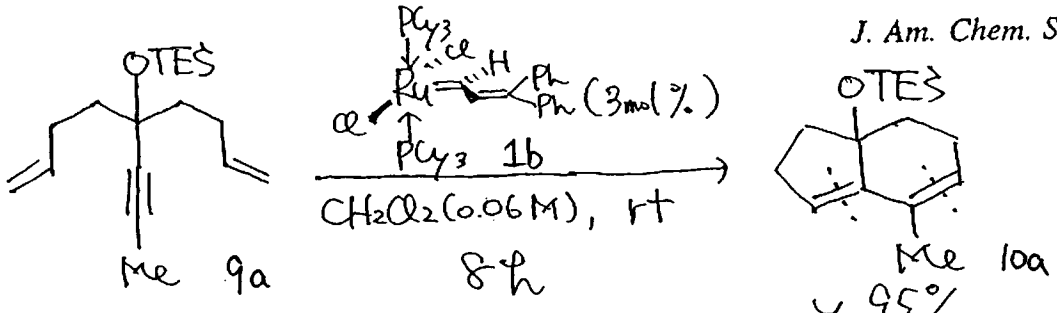
Soong-Hoon Kim, Ned Bowden, and Robert H. Grubbs*

Contribution No. 8988
The Arnold and Mabel Beckman Laboratory of Chemical Synthesis
Division of Chemistry and Chemical Engineering
California Institute of Technology
Pasadena, California 91125

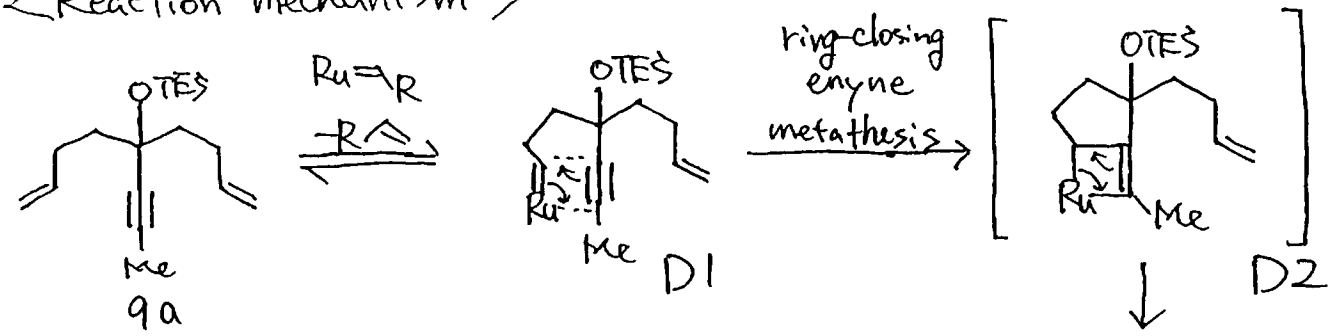
Received July 29, 1994

J. Am. Chem. Soc. **1994,** *116,* 10801–10802

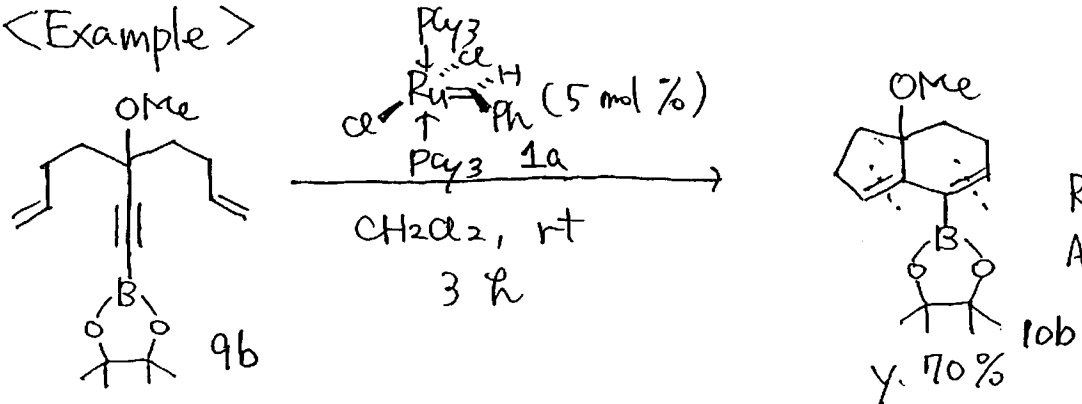
3.1. Symmetrical case



<Reaction mechanism>



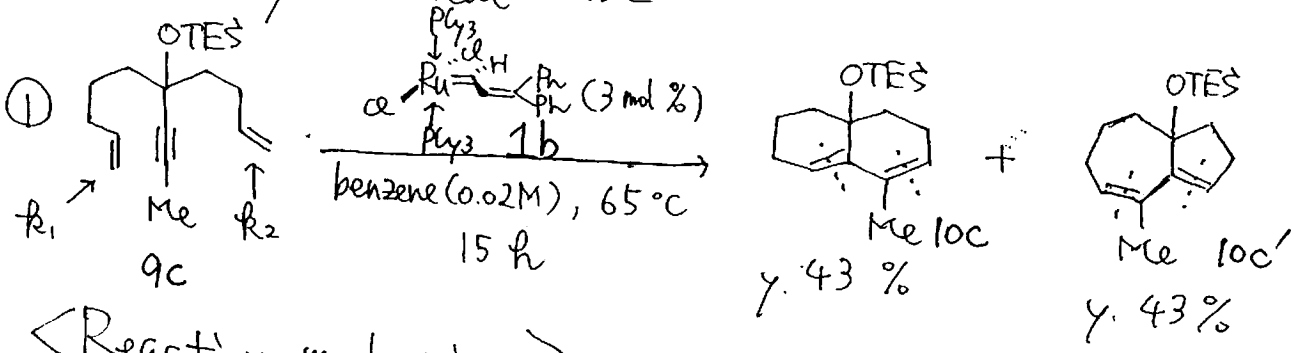
<Example>



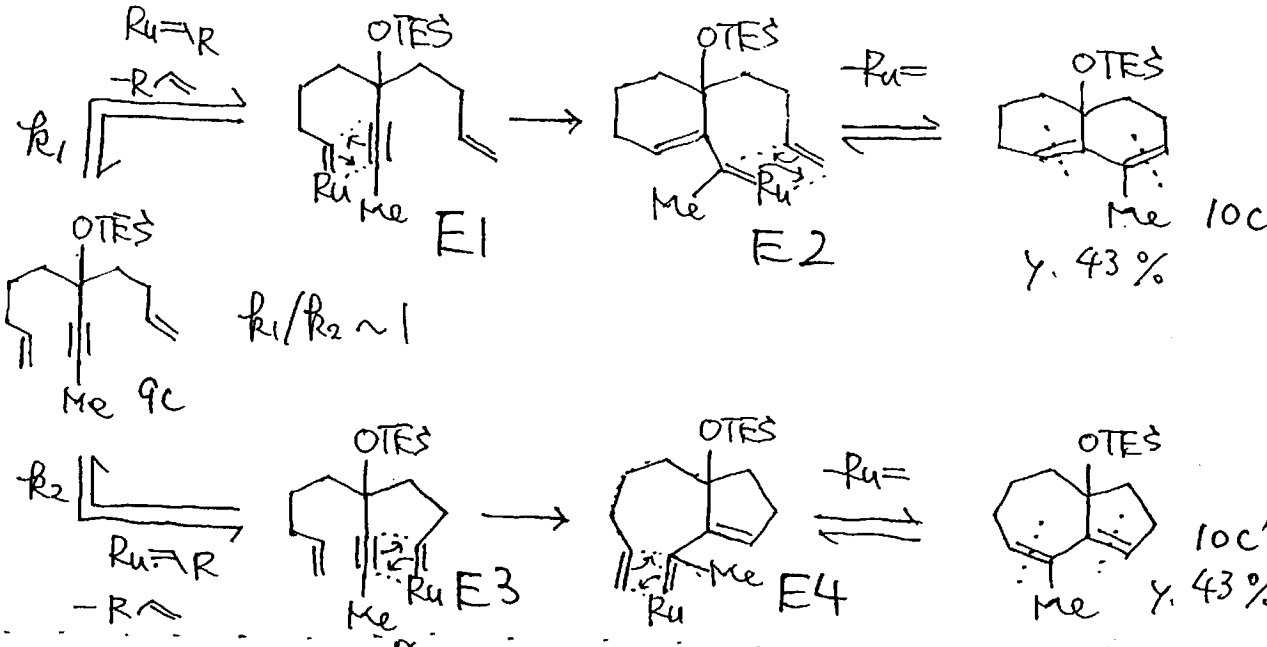
Renaud, J. et al
Angew. Chem. Int. Ed.
2000, 39, 3101.

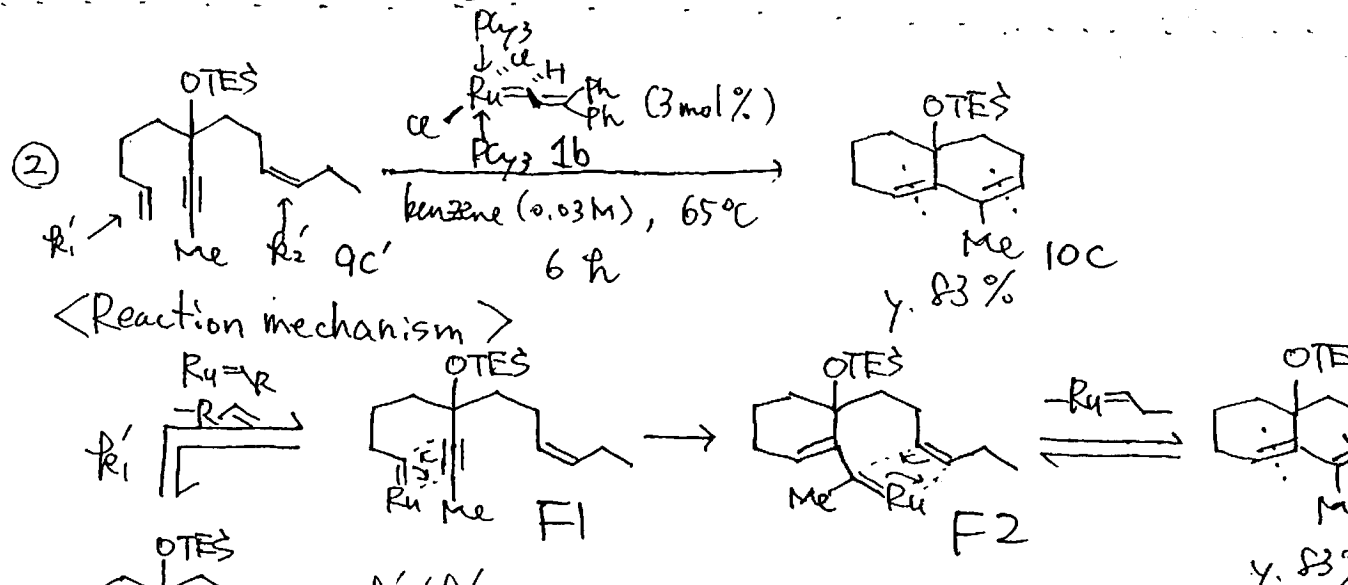
(See p. 6)

3-2. Unsymmetrical case

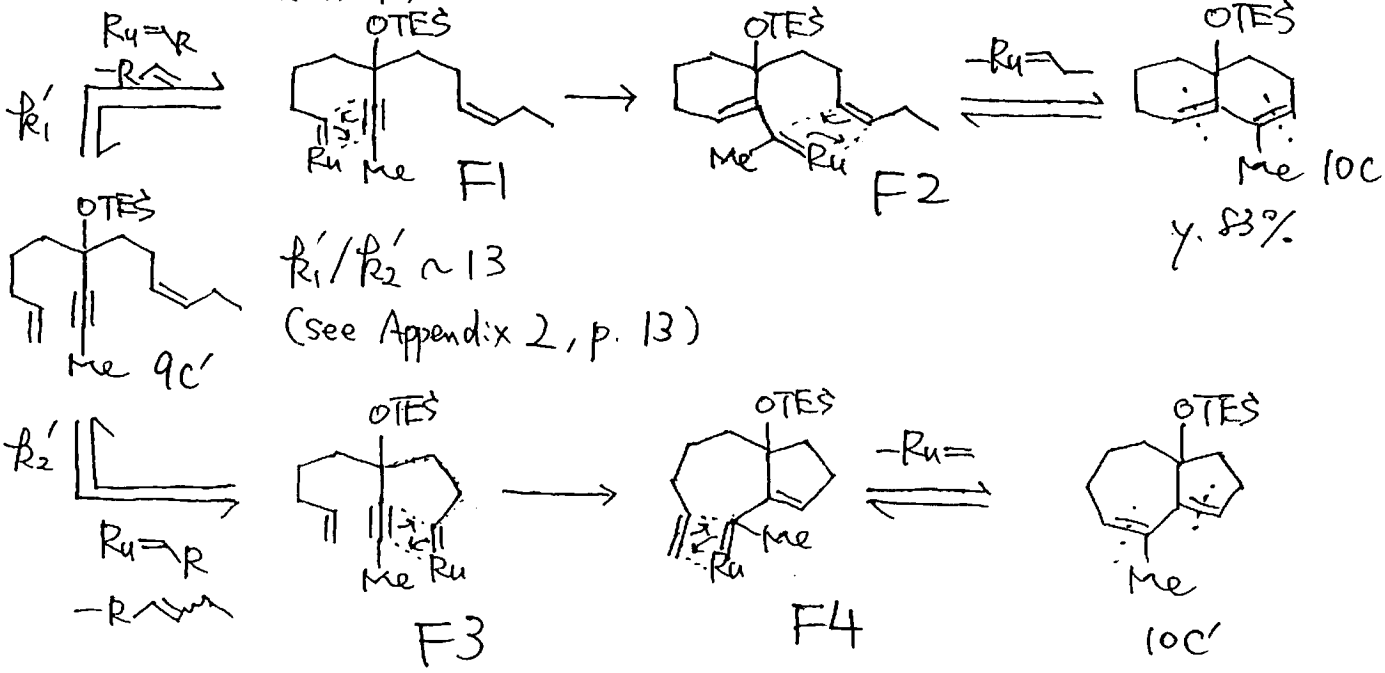


<Reaction mechanism>





<Reaction mechanism>



<Examples>

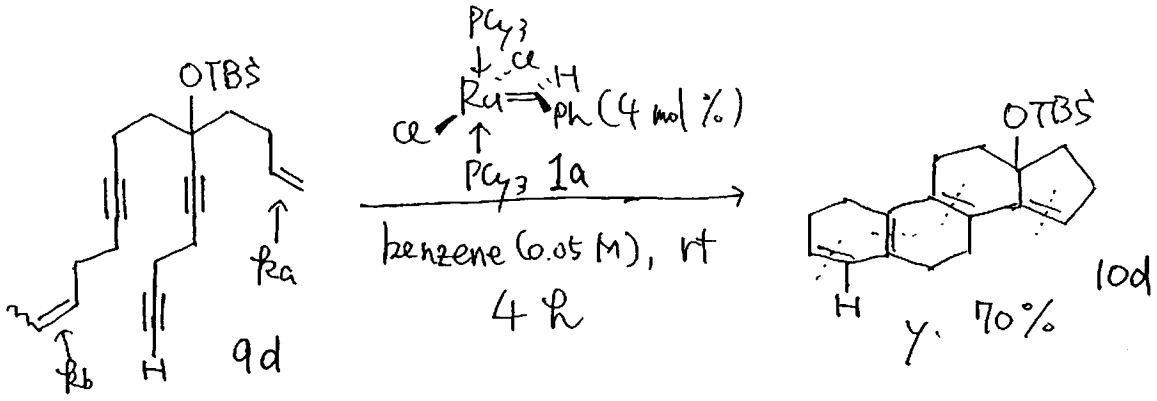
Ruthenium-Catalyzed Polycyclization Reactions

William J. Zuercher, Matthias Scholl, and Robert H. Grubbs*

The Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125

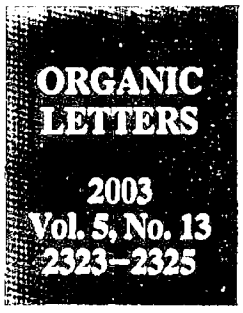
J. Org. Chem. 1998, *63*, 4291−4298

Received December 18, 1997



Ra/Rb ~19 (see Appendix 2, p. 13)

Novel Synthesis of Heterocycles Having a Functionalized Carbon Center via Nickel-Mediated Carboxylation: Total Synthesis of Erythrocarine

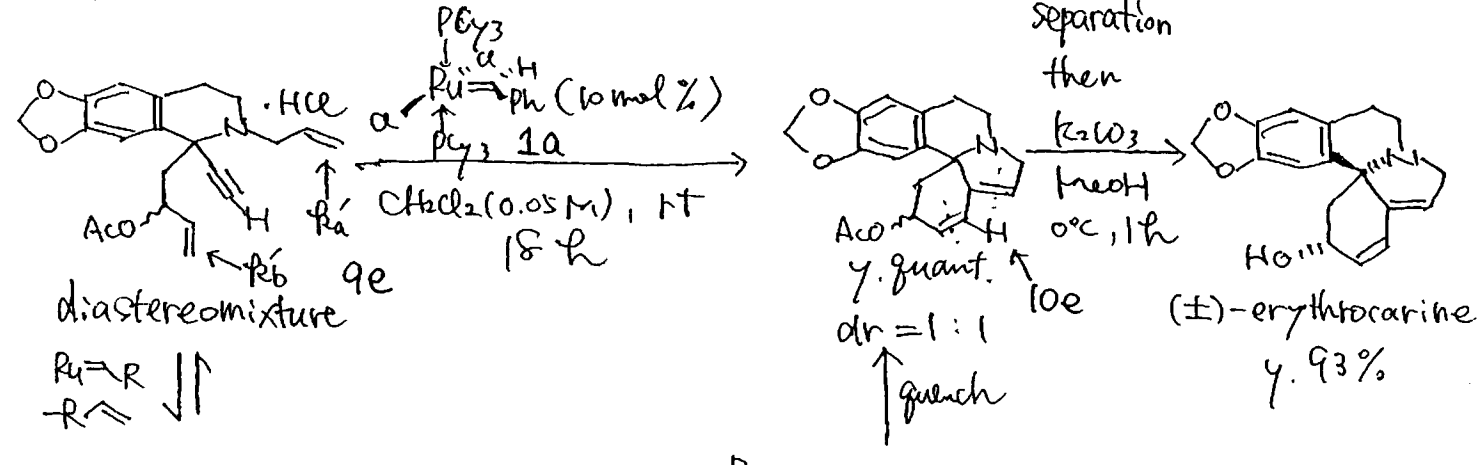


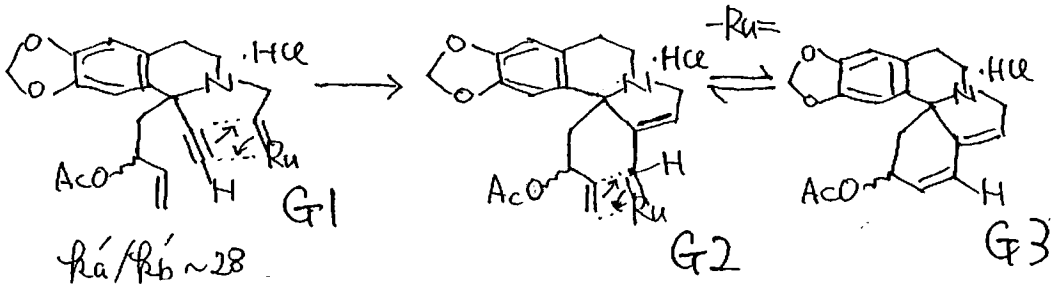
Kazuya Shimizu, Masanori Takimoto, and Miwako Mori*

Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo 060-0812, Japan

mori@pharm.hokudai.ac.jp

Received April 21, 2003



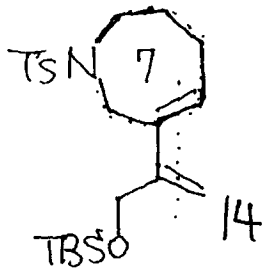


Ra'/Rb' ~28

(See Appendix 2, p. 13)

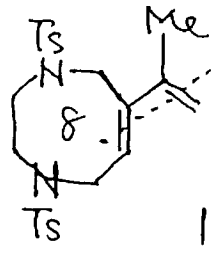
Appendix 1. Generality of ring-closing metathesis.

① Size of ring



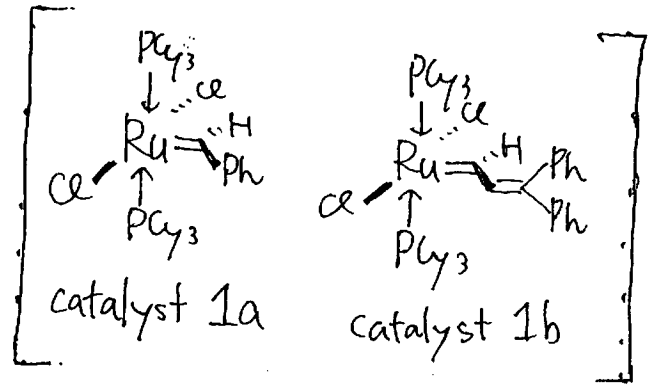
14

cat. 1b (1 mol %)
benzene, Argon
reflux, 2.5 h, y. 77%
Mori, M. et al
Synlett. 1994, 1020.



15

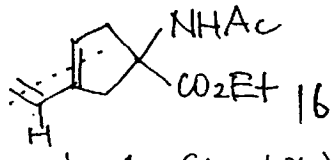
cat. 1a (10 mol %)
CH_2Cl_2, Argon
rt, 14.5 h, y. 95%
Mori, M. et al
Org. Lett. 2000, 2, 543.



catalyst 1a　　catalyst 1b

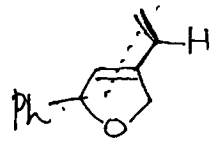
- For 9- or larger-membered ring synthesis, see: Lee, D. et al J. Am. Chem. Soc. 2003, 125, 9582; 2004, 126, 15074.

② Carba/oxa/sila/bora cycles



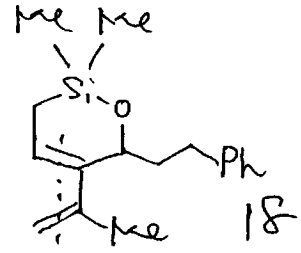
16

cat. 1a (10 mol %)
CH_2Cl_2, Argon
rt, 24 h, y. 75%
Kotha, S. et al
Eur. J. Org. Chem. 2001, 787.



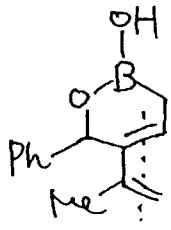
17

Cat. 1a (1 mol %)
CH_2Cl_2, ethylene
rt, 22 h, y. 96%
Mori, M. et al
J. Org. Chem. 1998, 63, 6082.



18

cat. 1a (3 mol %)
CH_2Cl_2, Argon
45°C, 3 h, y. >88%
Yao, Q.
Org. Lett. 2001, 3, 2069.



19

cat. 1a (9 mol %)
CH_2Cl_2, N_2
reflux, 38 h, y. 92%
Schreiber, S. L. et al
Angew. Chem. Int. Ed. 2002, 41, 152.

Reviews of enyne metathesis

(a) Mori, M. Top. Organomet. Chem. 1998, 1, 133.
(b) Mori, M. J. Synth. Org. Chem. Jpn. 1998, 56, 433.
(c) Madsen, R. et al Synthesis 2003, 1.
(d) Diver, S. T. et al Chem. Rev. 2004, 104, 1317.
(e) Mori, M. J. Synth. Org. Chem. Jpn. 2005, 63, 5.

dix 2. substituent effect of olefin on reaction rate.

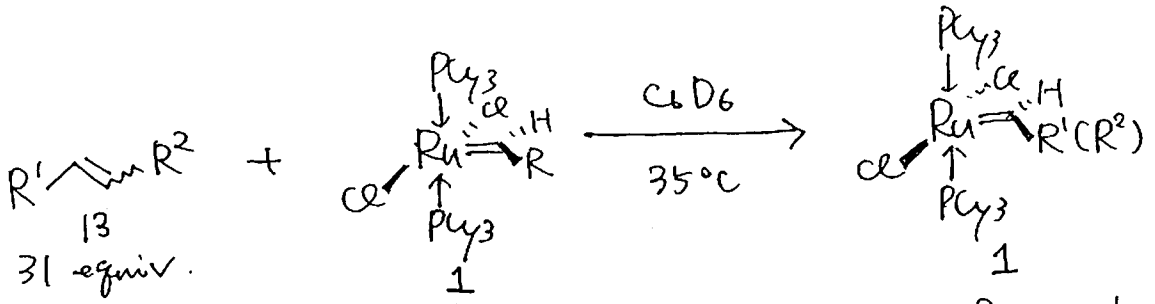
tive Reaction Rates of Olefin Substrates with athenium(II) Carbene Metathesis Initiators[1]

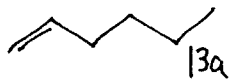
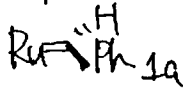
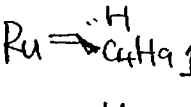
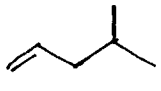
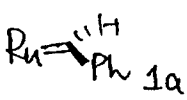
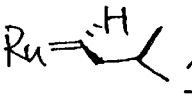
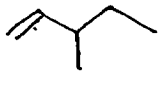
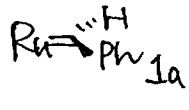
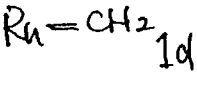
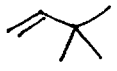
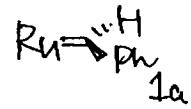
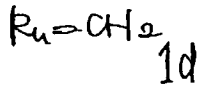
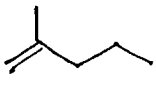
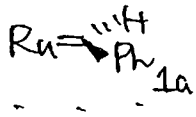
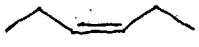
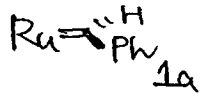
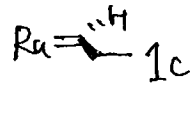
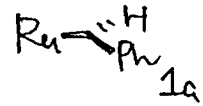
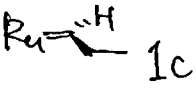
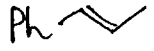
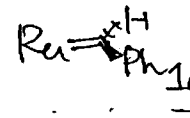
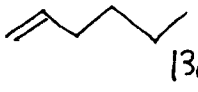
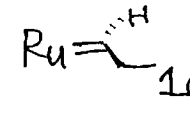
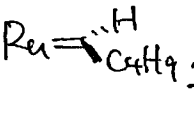
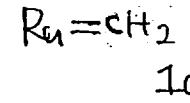
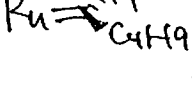
Michael Ulman and Robert H. Grubbs*

The Arnold and Mabel Beckman Laboratory of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125

Organometallics **1998**, *17*, 2484–2489

Received November 19, 1997



entry	olefin	carbene complex	product	k_p ($M^{-1} \cdot s^{-1}$)
1	 13a	 1a	 1e	$\sim 10^{-2}$
2	 13b	 1a	 1f	6.9×10^{-3}
3	 13c	 1a	 1d	2.5×10^{-4}
4	 13d	 1a	 1d	slow
5	 13e	 1a	No reaction	———
6	 13f	 1a	 1c	7.6×10^{-4}
7	 13g	 1a	 1c	3.0×10^{-4}
8	 13h	 1a	No reaction	———
9	 13a	 1c	 1e	$\sim 4.7 \times 10^{-2}$
10	 13a	 1d	 1e	6.1×10^{-4}

Appendix 3 Experimental supports of alkene initiation p

An Enyne Metathesis/(4 + 2)-Dimerization Route to (±)-Differolide

Thomas R. Hoye,* Scott M. Donaldson, and Tricia J. Vos

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

hoye@chem.umn.edu

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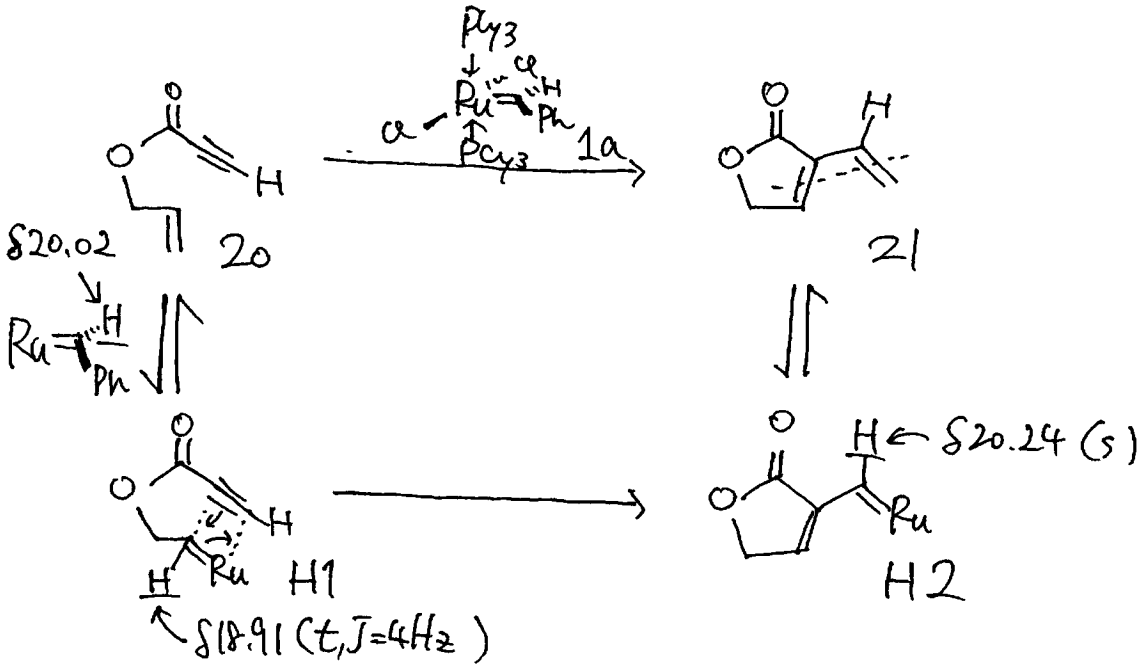


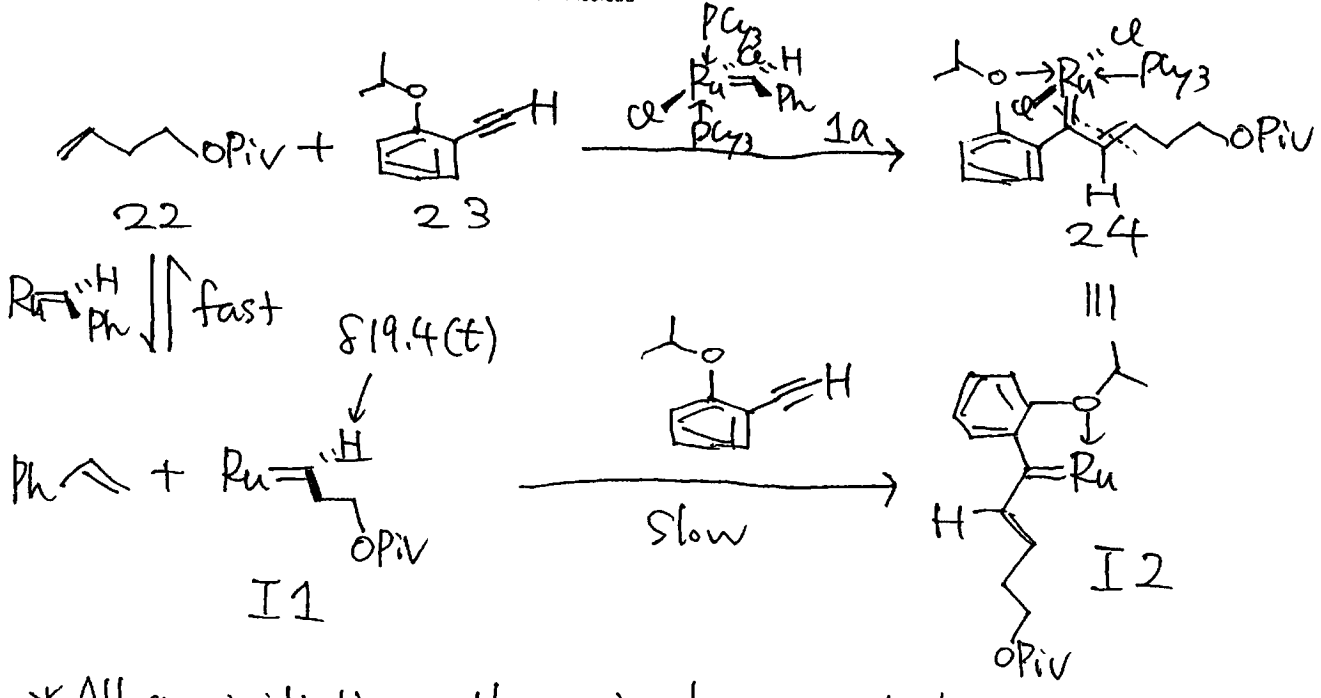
Ring Closing Enyne Metathesis: Control over Mode Selectivity and Stereoselectivity

Eric C. Hansen and Daesung Lee*

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

Received July 29, 2004; E-mail: dlee@chem.wisc.edu

J. Am. Chem. Soc. 2004, 126, 15074.



* Alkene initiation pathway is also supported by theoretical calculation (see p. 3).