

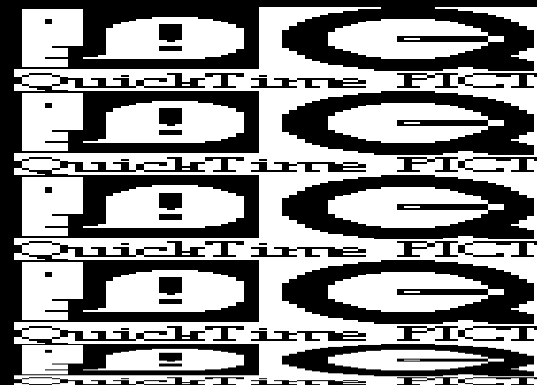
Strategies for Selective Olefin Metathesis in Complex Molecular Settings

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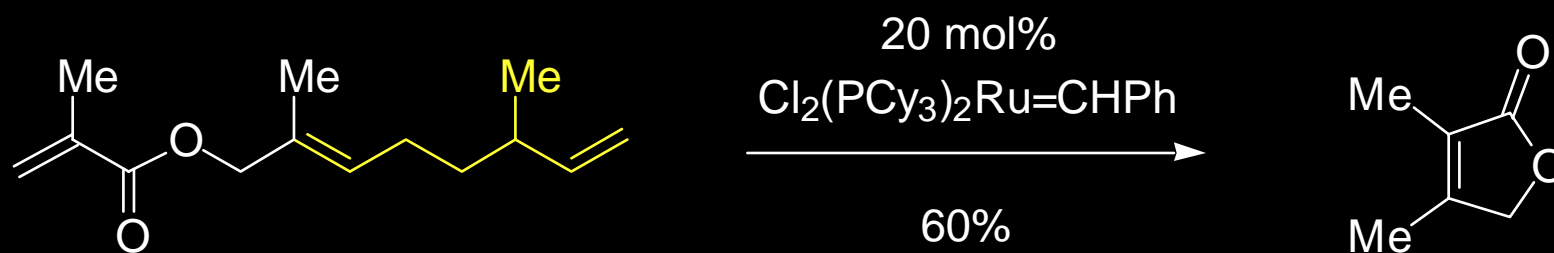


Strategies for Selective Olefin Metathesis in Complex Molecular Settings

- ❖ Callipeltoside A Relay-RCM (RRCM)
- ❖ Oocydin A RRCM
- ❖ Peloruside A Silicon-Tethered RRCM
- ❖ Gigantecin Silicon-Tethered Cross Metathesis
- ❖ Lyngbyaloside B 'Outer Sphere' Steric Effects
- ❖ Petromyzosterol Disulfate Degenerate Exchange Test
- ❖ Gigantecin Relay Cross Metathesis (Relay-CM)

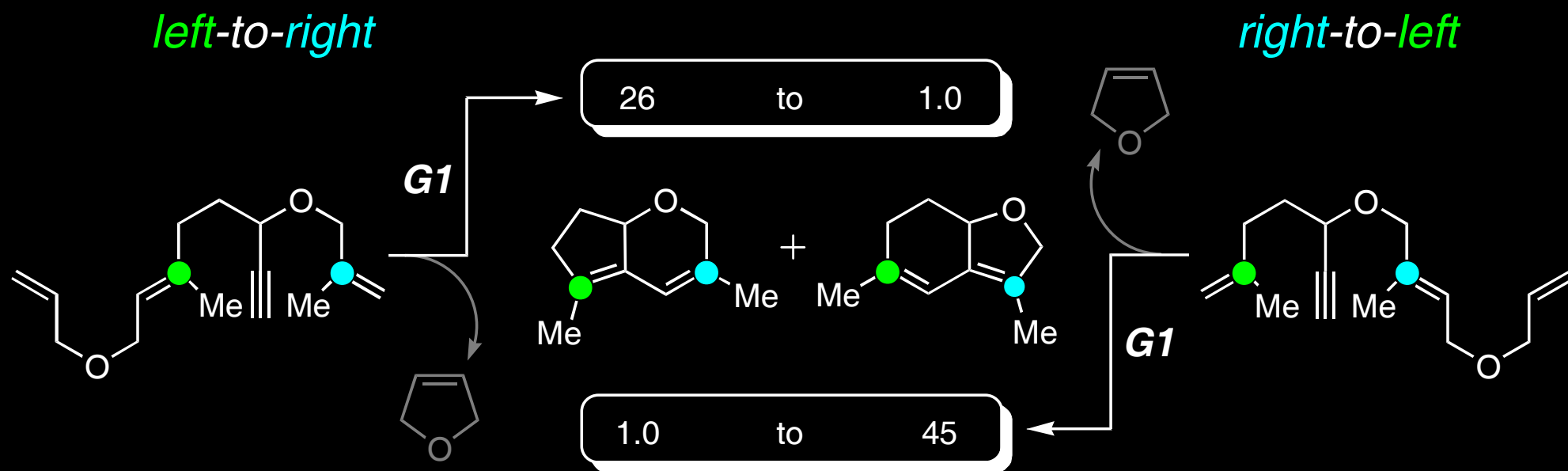
Can Ruthenium Be Loaded to Otherwise Unreactive Alkenes via a **Relay Event**?

Relay RCM: Hindered Electron Deficient Butenolide



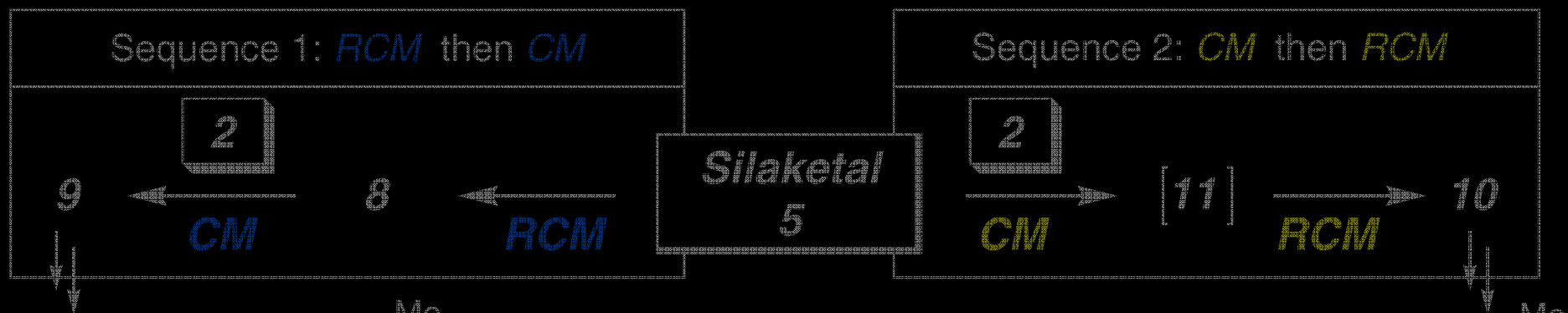
Hongyu Zhao, Ph.D. Thesis, University of Minnesota, 2000

Relay Ring Closing Metathesis (RRCM)



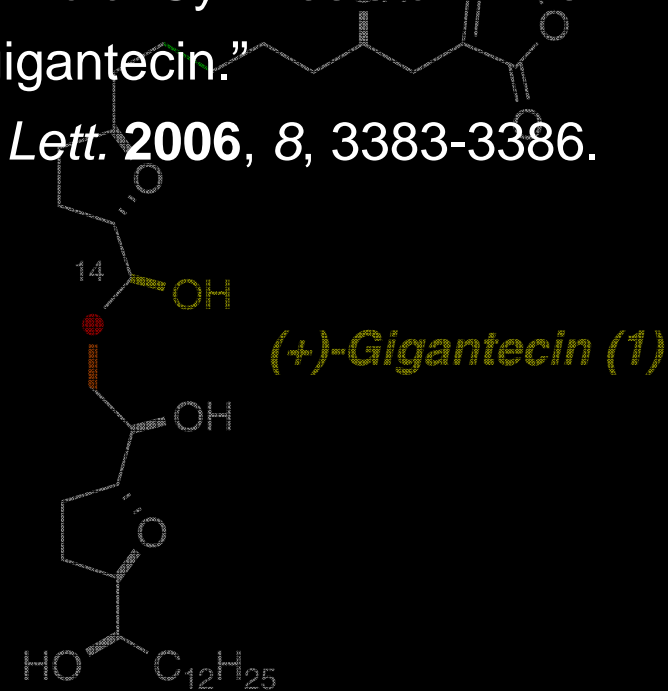
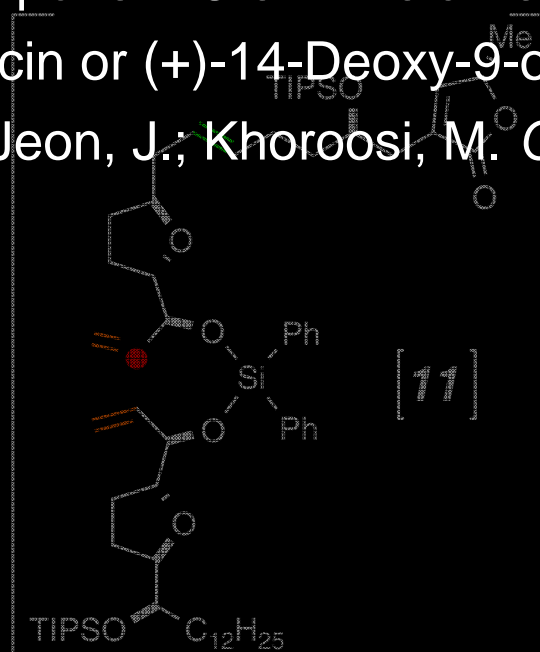
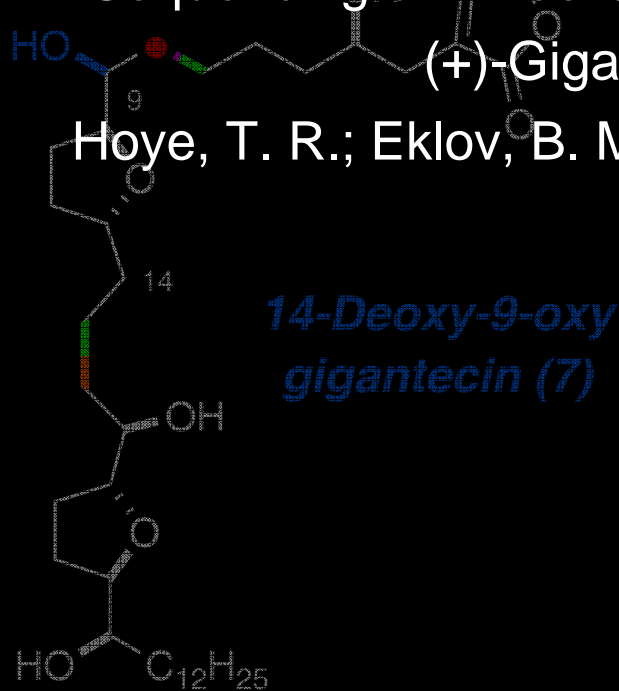
“Relay Ring Closing Metathesis (RRCM): A Strategy for Directing Metal Movement Throughout Olefin Metathesis Sequences,” Hoyer, T. R.; Jeffrey, C. S.; Tennakoon, M. A.; Wang, J.; Zhao, H. *J. Am. Chem. Soc.* **2004**, *126*, 10210-10211.

Sequencing Multi-Stage Metathesis Processes

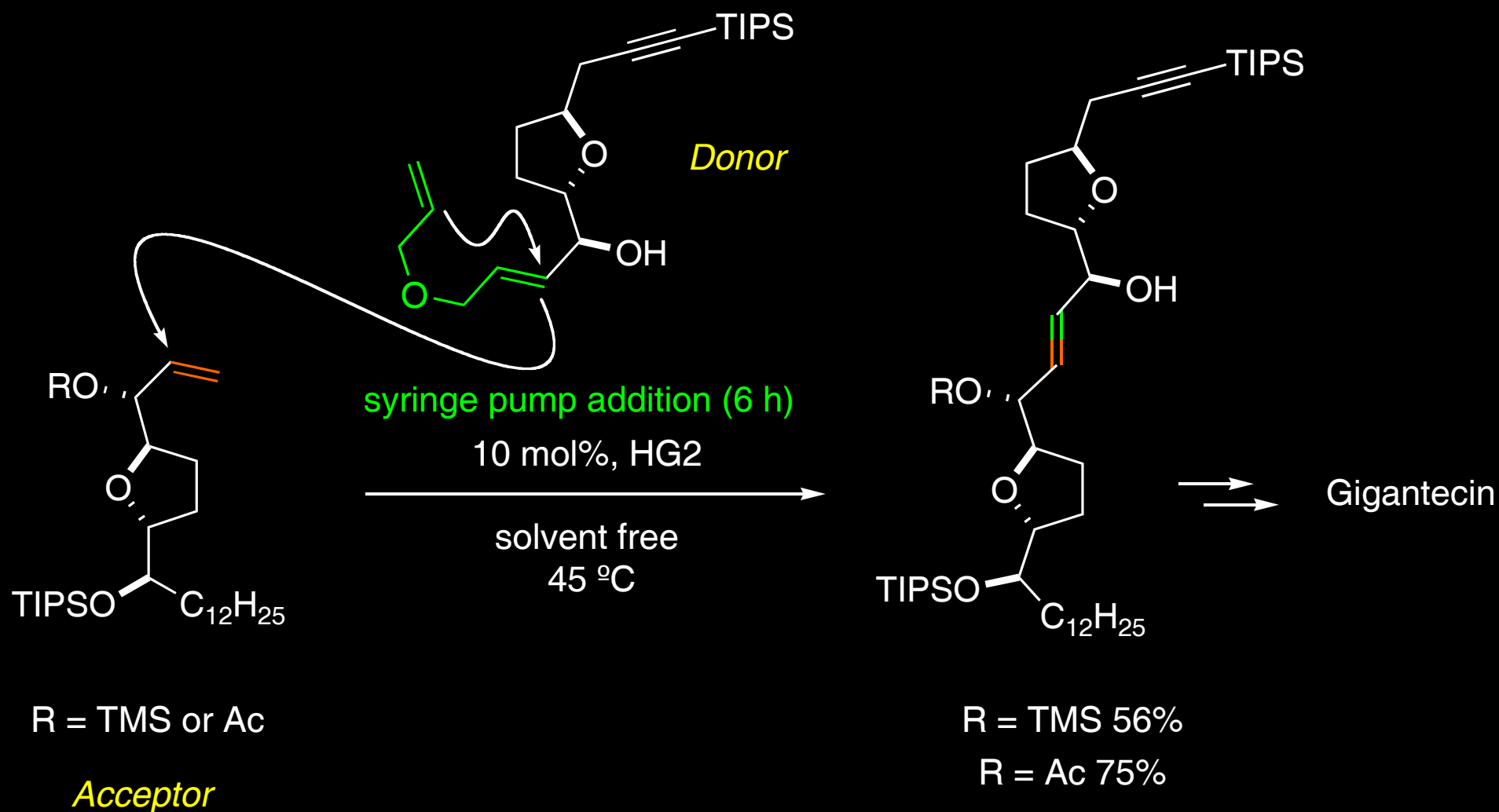


“Sequencing of Three-Component Olefin Metatheses: Total Synthesis of Either (+)-Gigantecin or (+)-14-Deoxy-9-oxygigantecin.”

Hoye, T. R.; Eklov, B. M.; Jeon, J.; Khorroosi, M. *Org. Lett.* **2006**, 8, 3383-3386.



The Relay-CM Way to Gigantecin: 1 to 1 *Donor* to *Acceptor*



Conclusions

- ❖ Substrate modification (including the size of remote substituents) offers another dimension for control of metathesis reactions.
- ❖ Relay priming allows one to dictate the site of metal loading.
 - in ring closing metathesis this determines the "endedness" of the reaction.
 - in cross metathesis this permits either alkene to serve as the donor.
- ❖ Benzylidenation by the precatalyst or degenerate $\text{CD}_2=\text{CD}_2$ exchange is diagnostic of the potential for a hindered alkene to serve as an acceptor.
- ❖ Proper staging of the addition rate of the donor alkene vis-à-vis the rates of the other primary events is likely to prove both crucial and valuable.
- ❖ Efficient cross metathesis (i.e., good yields at 1:1 stoichiometric loading) of two different complex fragments is viable.

Strategies for Selective Olefin Metathesis in Complex Molecular Settings

Callipeltoside A	Relay-RCM (RRCM)	Hongyu Zhao Mike Danielson
Oocydin A	RRCM	Jizhou Wang
Peloruside A	RRCM	Manomi Tennakoon Junha Jeon, Troy Ryba
Unequivocal Enyne Metathesis		Chris Jeffrey
Gigantecin	Silicon-Tethered Cross Metathesis	Brian Eklov Junha Jeon, Mila Khorroosi
Lyngbyaloside B	'Outer Sphere' Steric Effects	Aaron May
Petromyzosterol Disulfate	Degenerate Exchange	Aaron Burns
Gigantecin	Relay Cross Metathesis (Relay-CM)	Junha Jeon