The Balance Between Steric Effect and London Dispersion: A Design Principle in Catalysis

Seminar talk presented by
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March 17th, 2017

Institute of Organic Chemistry
Justus-Liebig-University Giessen

Outline

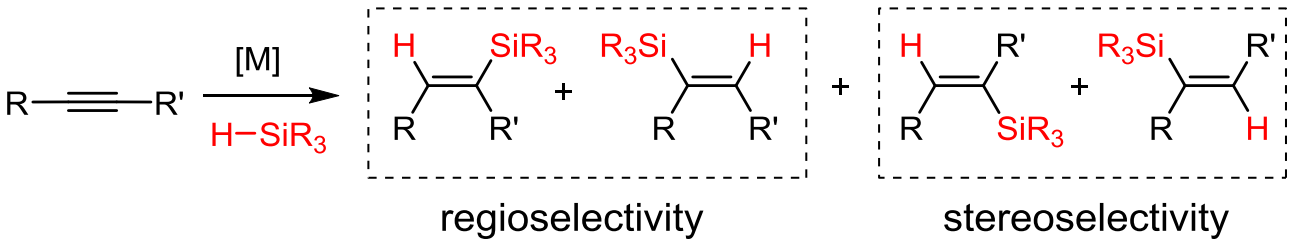
PhD work on theoretical studies on alkyne reduction

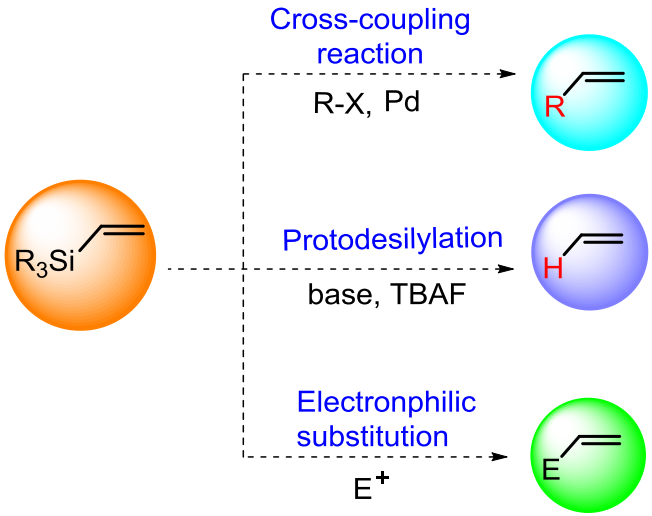
- Introduction
- Ligand-controlled selectivity
- Hydrofunctionalization
- Summary

Future study on dispersion in catalysis

- Introduction
- Quantification of DEDs
- Dispersion in catalysis

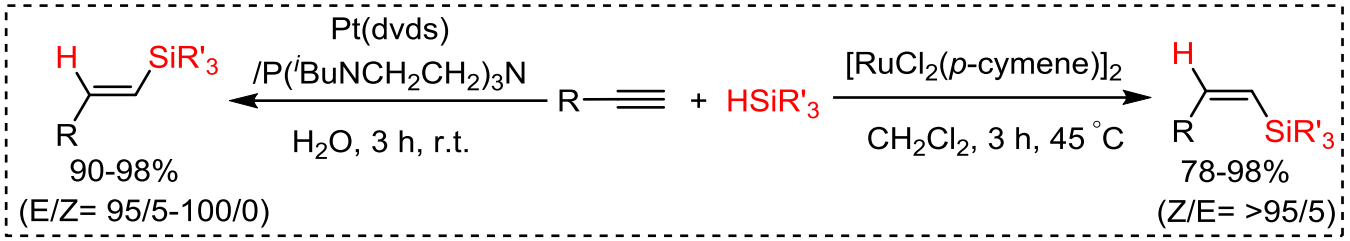
Introduction





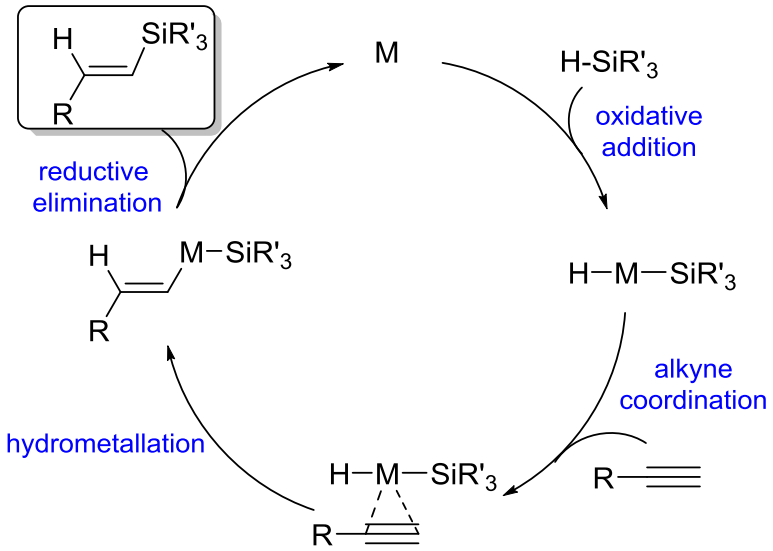
Denmark, S. E. and coworkers. *Acc. Chem. Res.* **2008,** *41*, 1486; Trost, B. M. and coworkers. *J. Am. Chem. Soc.* ***2002****, 124,* 7922; Fleming, I. and coworkers. John Wiley & Sons, Inc. **2004**.

Proposed Reaction Mechanism

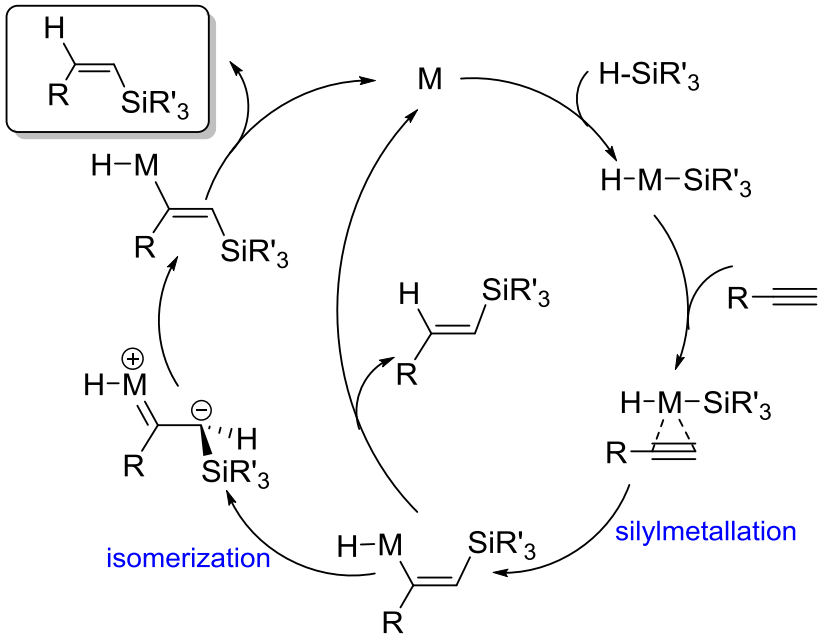


Aneetha, H.; Wu, W.; Verkade, J. G. *Organometallics* **2005,** *24*, 2590
Na, Y.; Chang, S. *Org. Lett.* **2000,** *2*, 1887

Chalk-Harrod Mechanism

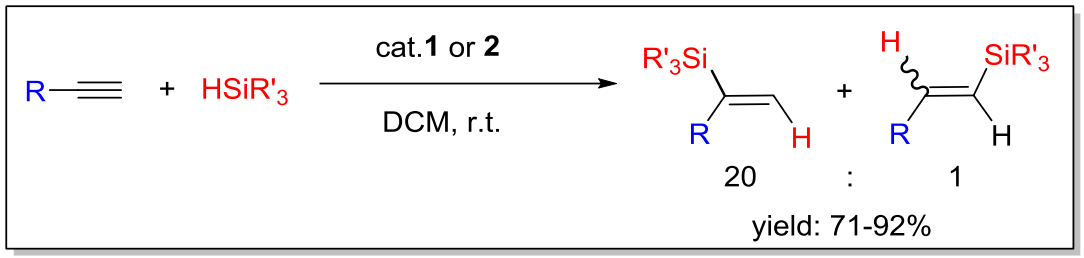


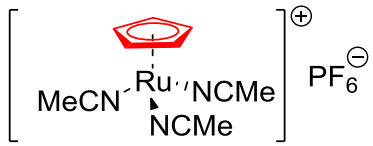
Modified Chalk-Harrod Mechanism



Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc*. **2001**, 123, 12726; Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 16; Tanke, R. S.; Crabtree, R. H. *J. Am. Chem. Soc.* **1990,** *112*, 7984. Ojima, I.; Clos, N.; Donovan, R. J.; Ingallina, P. *Organometallics* **1990**, *9*, 3127.

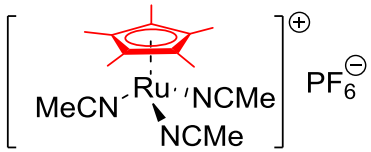
Unusual Regioselectivity





[**Cp**Ru(MeCN)$_3$]PF$_6$

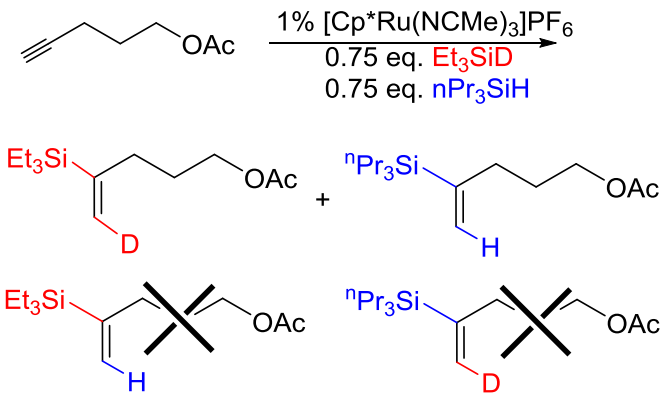
1

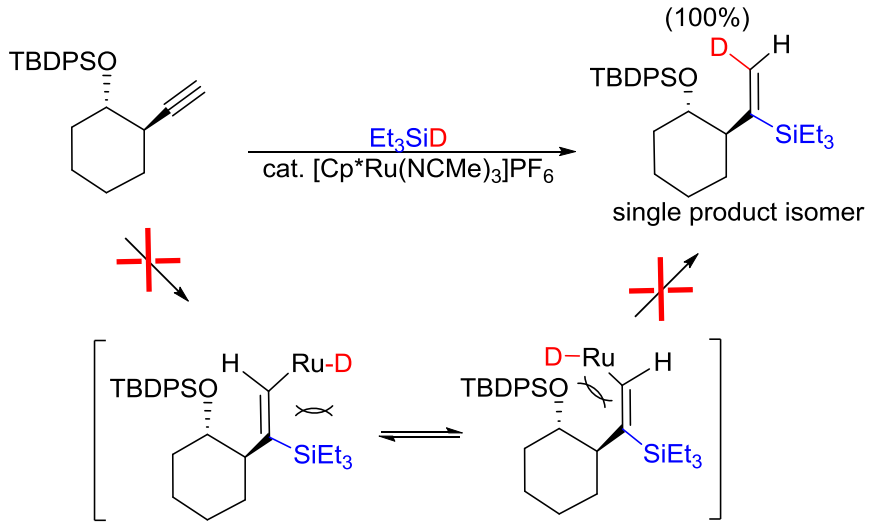


[**Cp***Ru(MeCN)$_3$]PF$_6$

2

Mechanistic studies

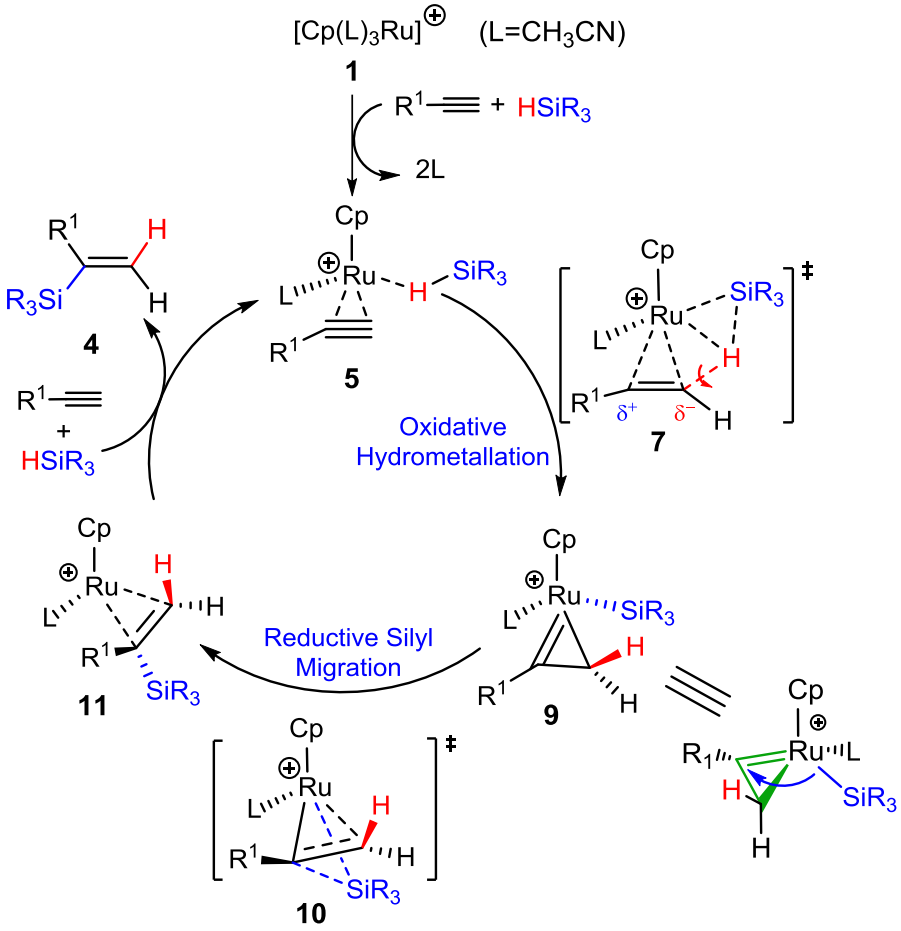


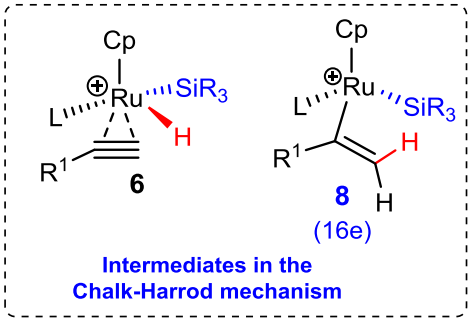


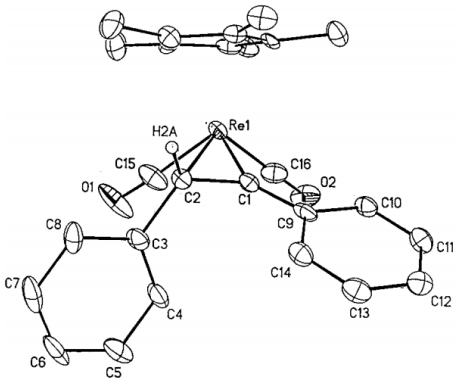
B. M. Trost, Z. T. Ball, *J. Am. Chem. Soc*. **2001**, 123, 12726

Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc* . **2003**, 125,31

Wu-Trost Mechanism



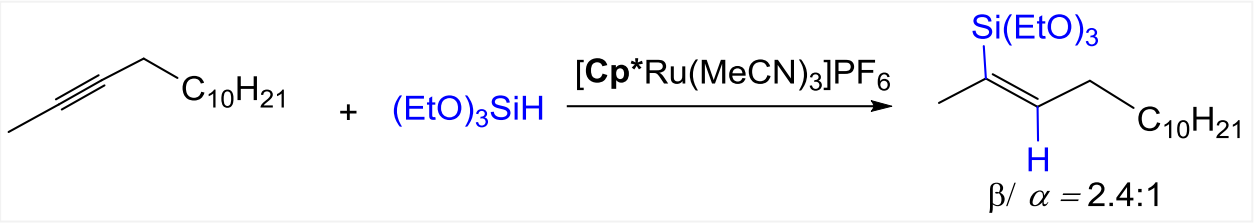




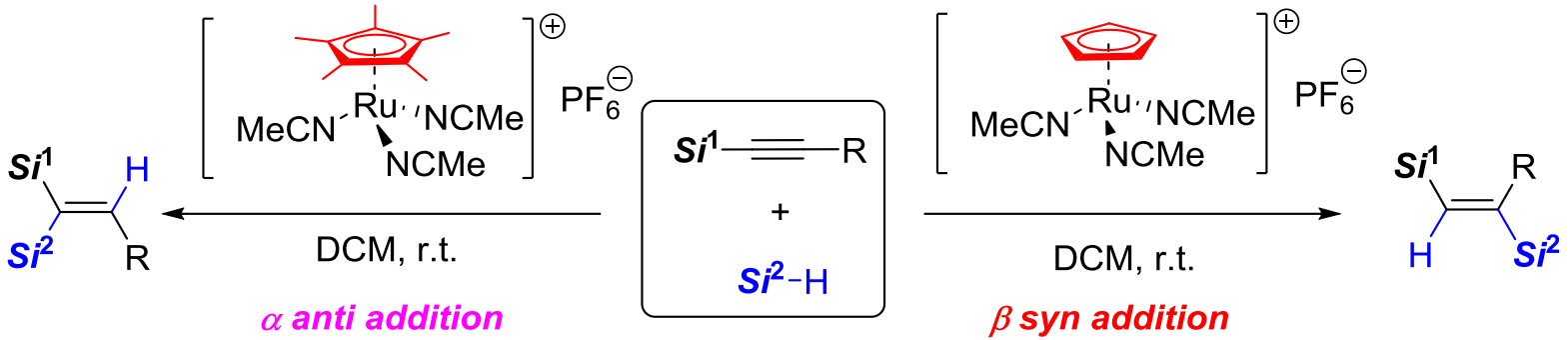
$Cp^*(CO)_2Re(\eta^2\text{-}CPhCHPh)^+\text{-}BF_4^-$

Chung, L. W.; Wu, Y.-D.; Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc* . **2003**, 125,11578.
Casey, C. P.; Brady, J. T.; Boller, T. M.; Weinhold, F.; Hayashi, R. *J. Am. Chem. Soc.* **1998**, *120*, 12500.

Ligand-Controlled Selectivity



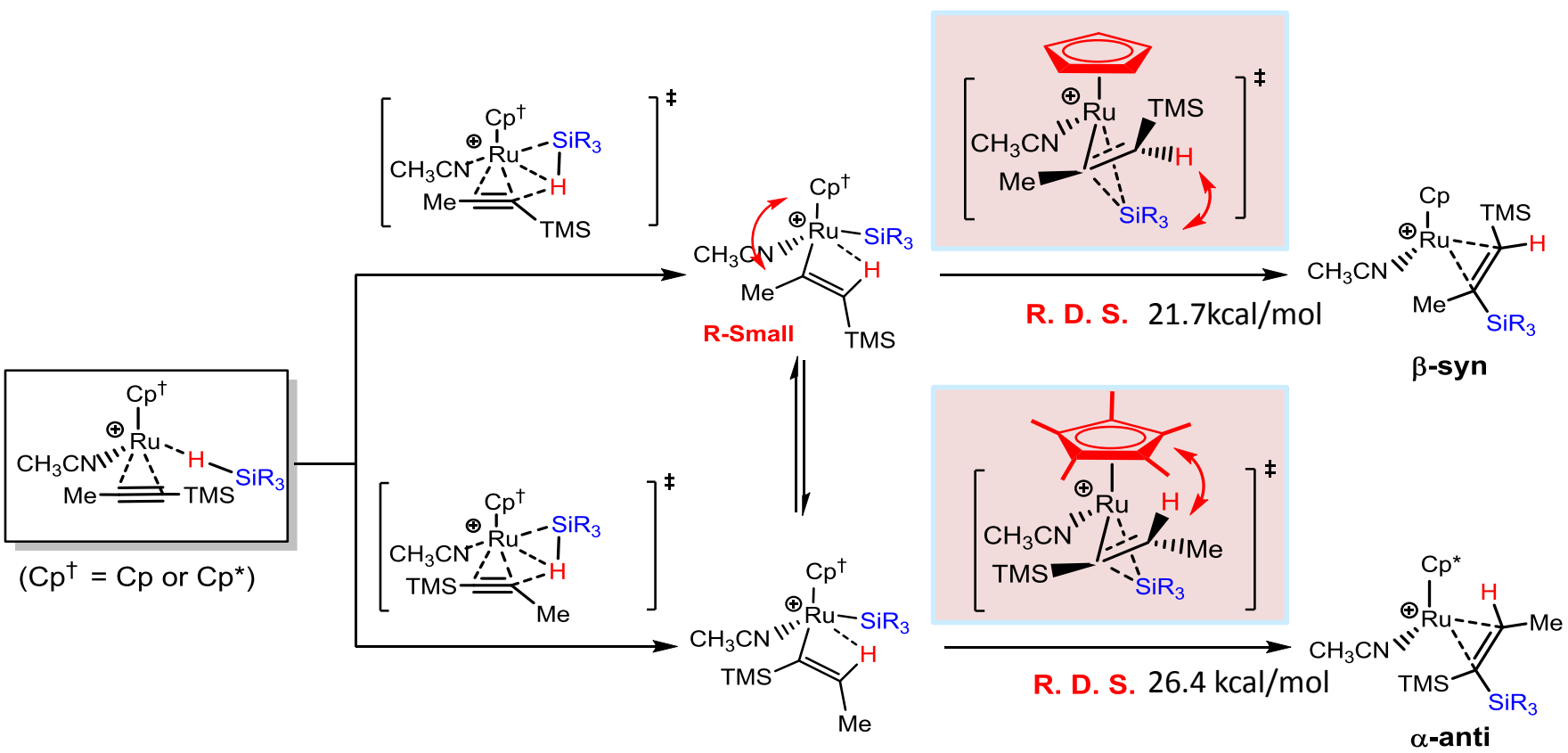
poor regioselectivity



- ✓ Different ligands lead to different regio- & stereo-selectivity
- ✓ Mild reaction conditions, tolerance of functional groups

Ding, S.; Song, L.-J.; Chung, L. W.; Zhang, X.; Sun, J.; Wu, Y.-D. *J. Am. Chem. Soc*. **2013**, 135, 13835.

Origin of the Selectivity

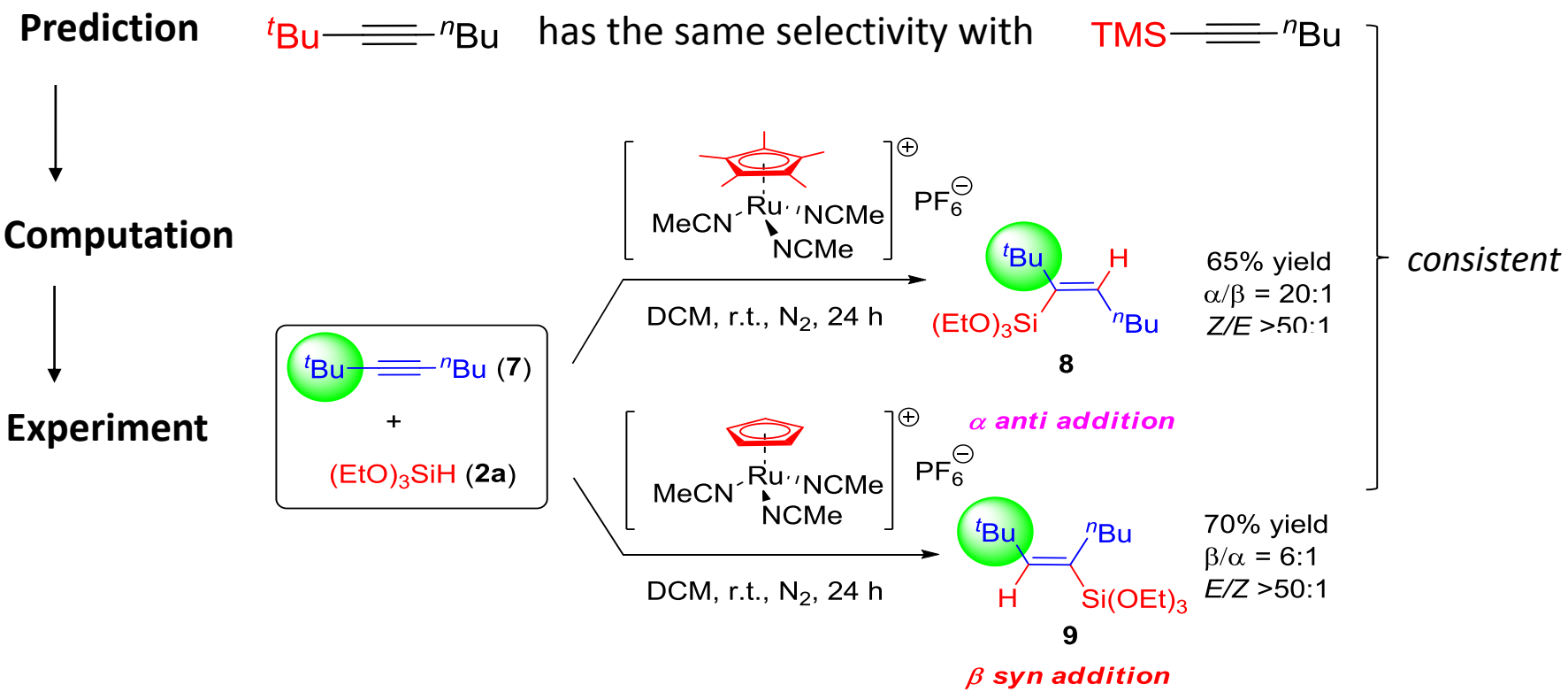


Steric repulsion of bulky substrate and ligand determines

B3lyp/6-31g*/ Lanl2dz

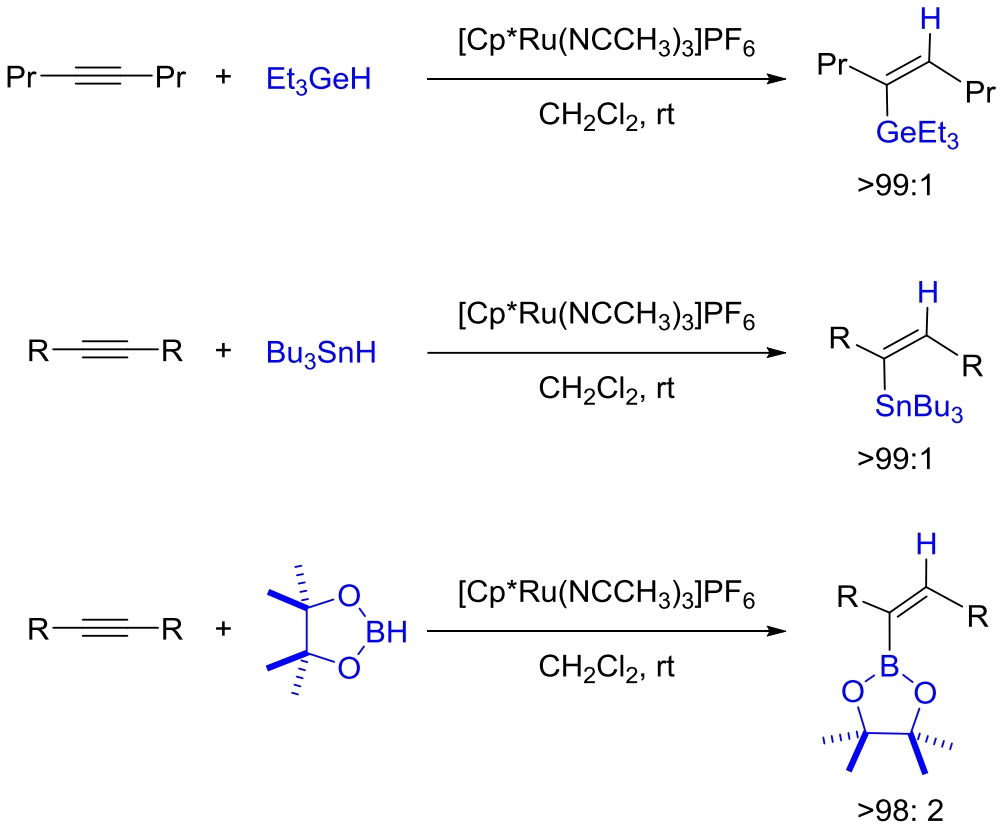
Ding, S.; Song, L.-J.; Chung, L. W.; Zhang, X.; Sun, J.; Wu, Y.-D. *J. Am. Chem. Soc*. **2013**, 135, 13835.

Computational Evaluation and Verification



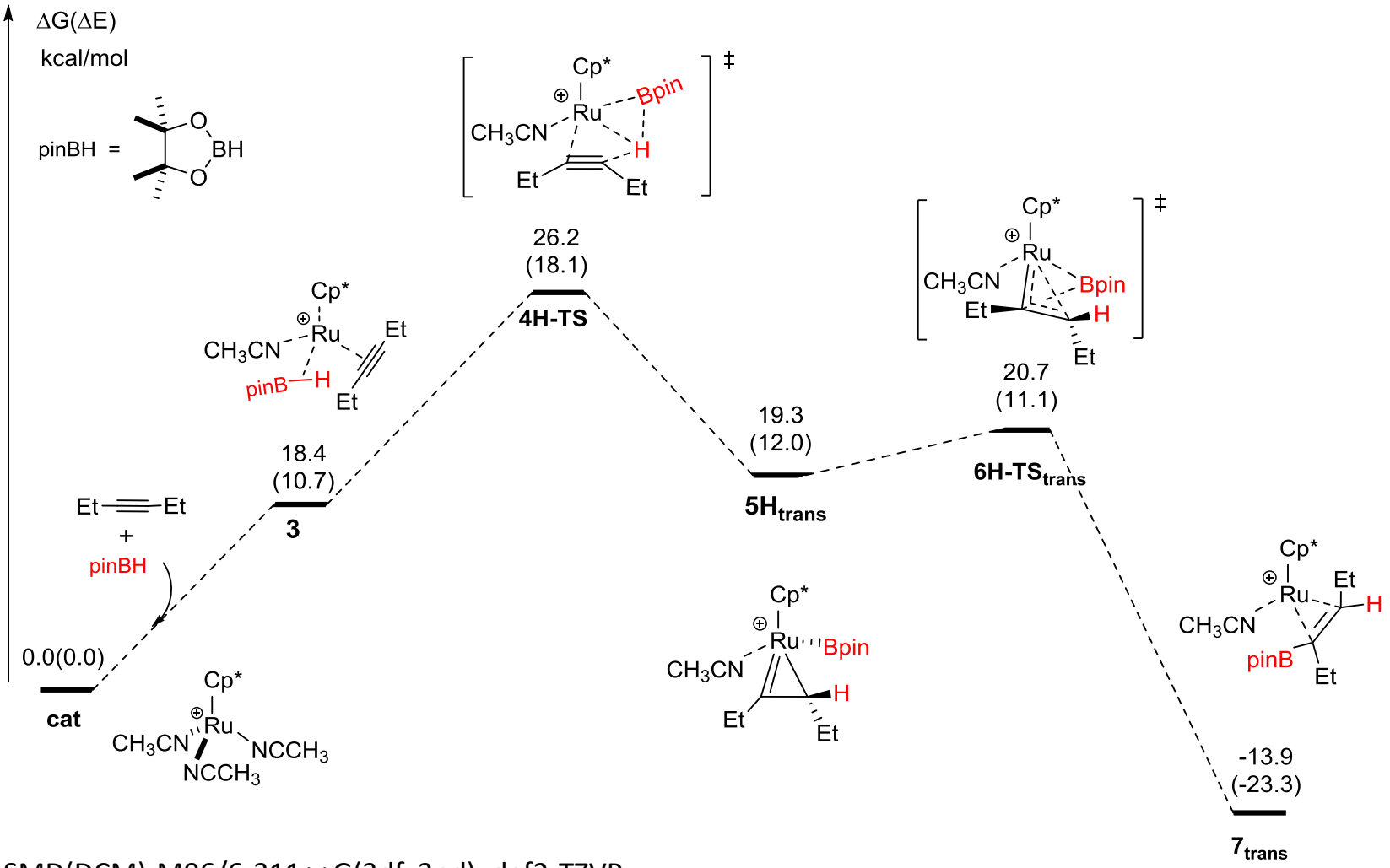
Ding, S.; Song, L.-J.; Chung, L. W.; Zhang, X.; Sun, J.; Wu, Y.-D. *J. Am. Chem. Soc*. **2013**, 135, 13835.

Other Hydrofunctionalization



Matsuda, T.; Kadowaki, S.; Yamaguchi, Y.; Murakami, M. *Org. Lett.* **2010**, *12*, 1056; Radkowski, K.; Sundararaju, B.; Fürstner, A. *Angew. Chem. Int. Ed.* **2013**, 52, 355; Sundararaju, B.; Fürstner, A. *Angew. Chem. Int. Ed*. **2013**, 52, 14050;

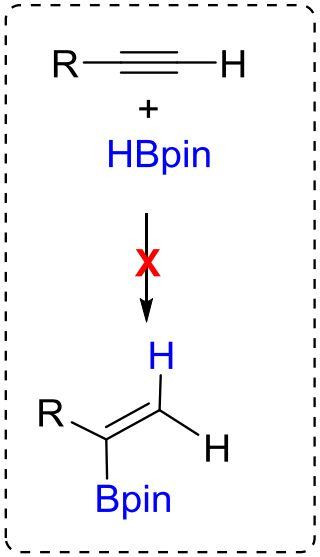
Mechanism of RuCp* Catalyzed Hydrofunctionalization

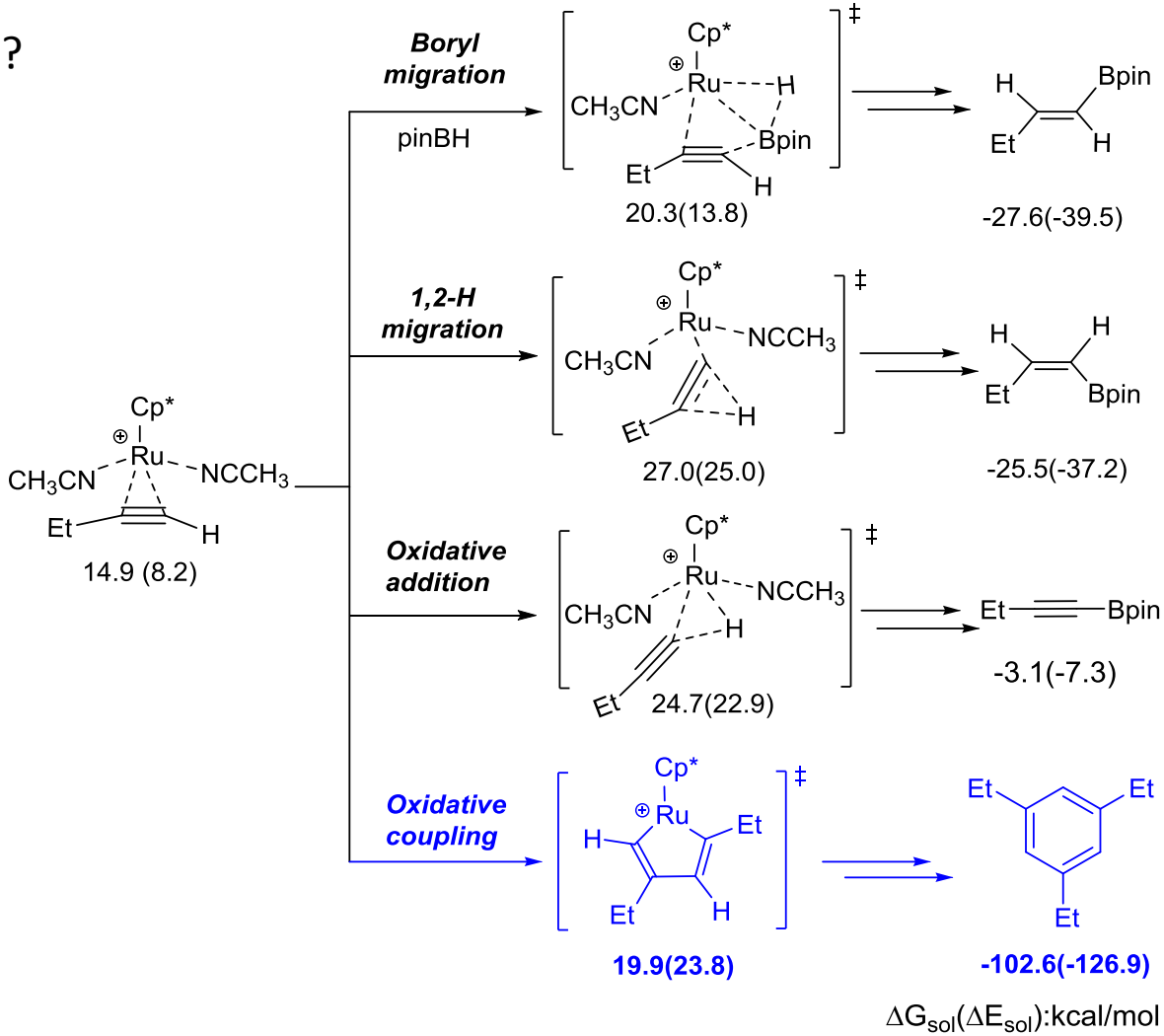


SMD(DCM)-M06/6-311++G(3df, 3pd), def2-TZVP
//B3LYP/6-31G(d), Lanl2dz

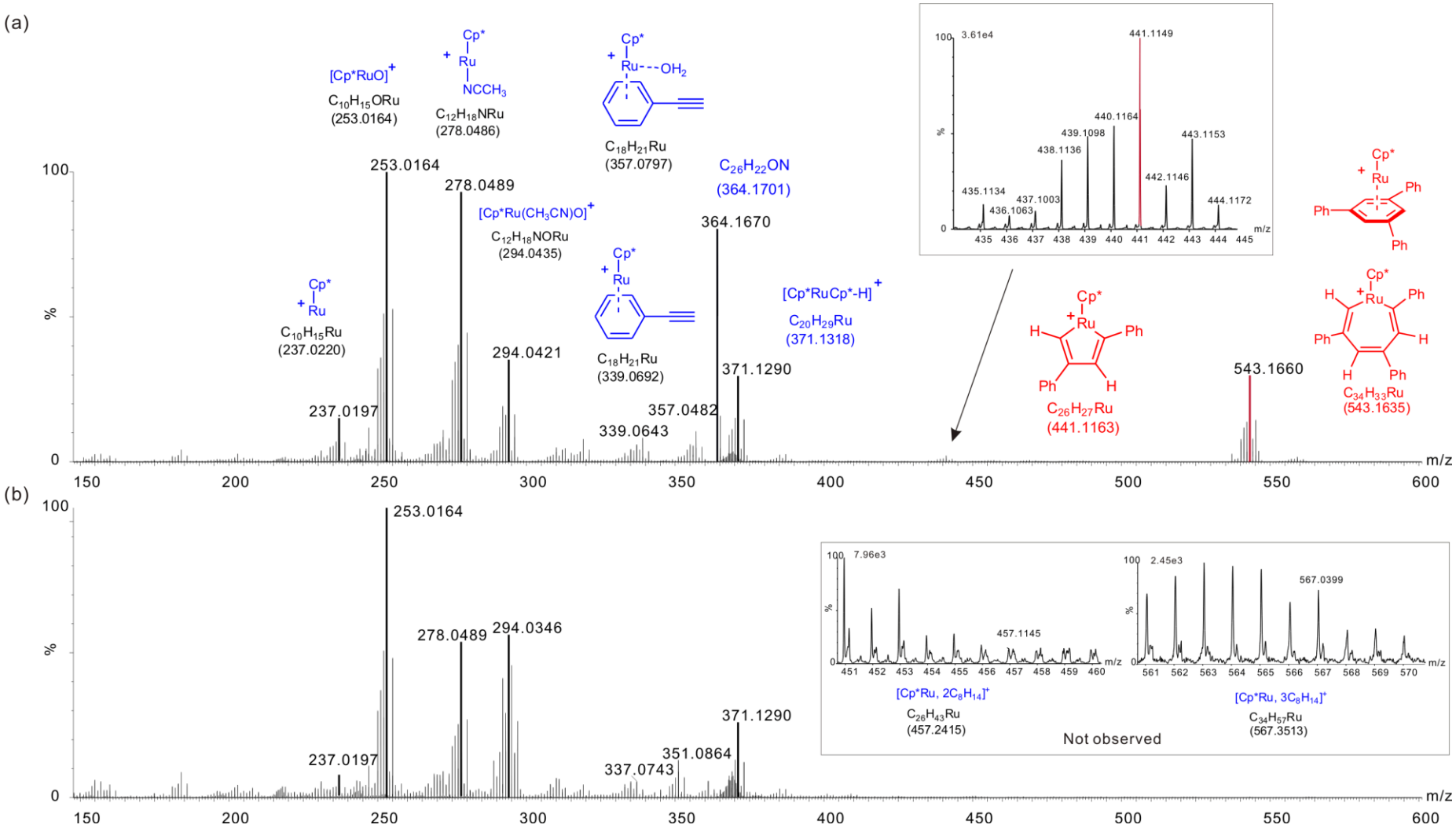
Song, L.-J.; Wang, T.; Zhang, X.; Chung, L. W.; Wu, Y.-D. *ACS catal*. **2017**, *7*, 1361.

Terminal alkynes failed ?



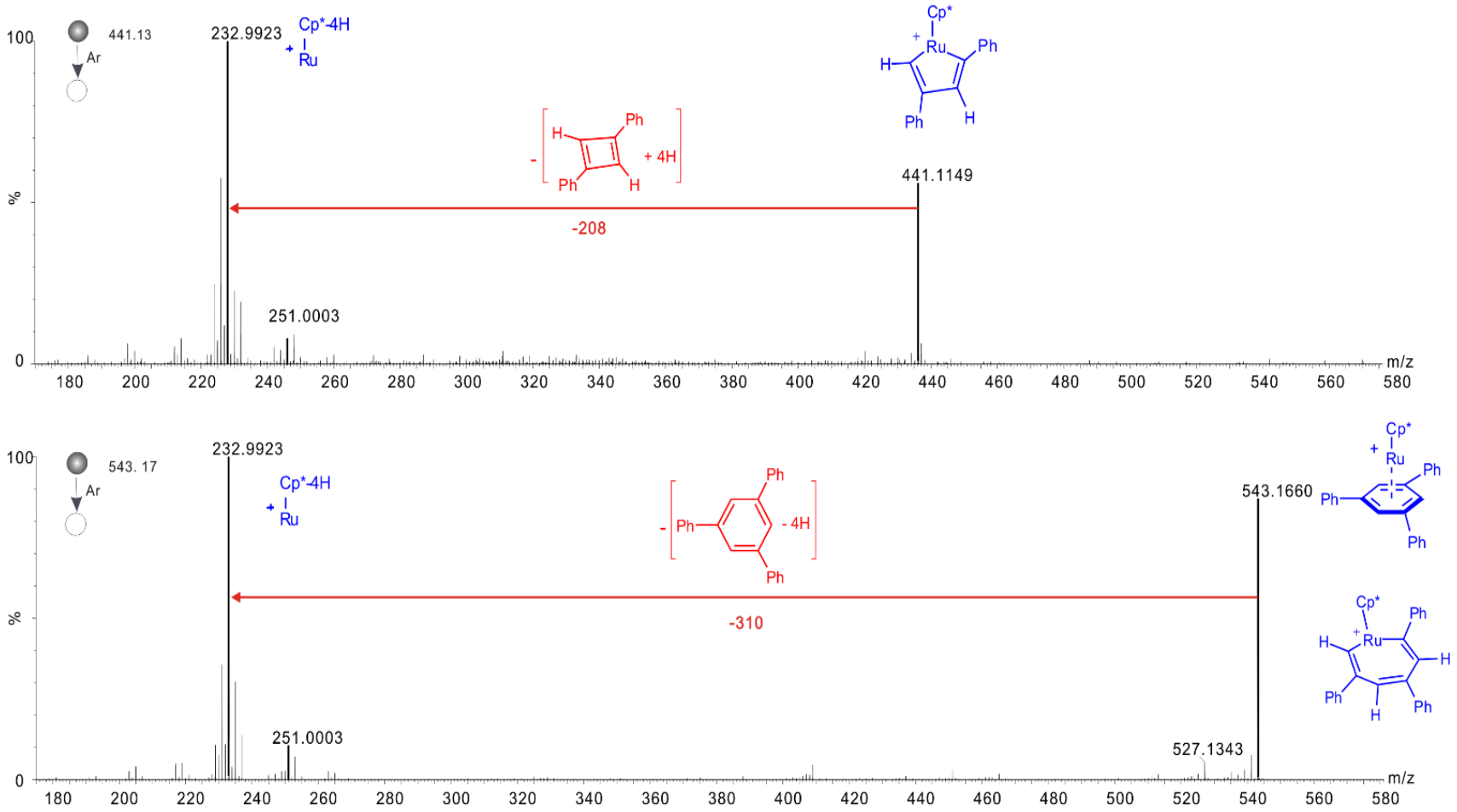


[catalyst + terminal alkyne] vs. [catalyst + internal alkyne]



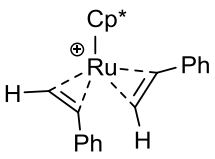
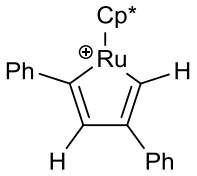
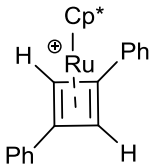
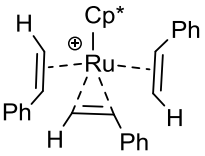
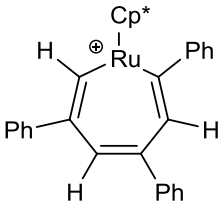
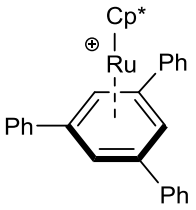
Song, L.-J.; Wang, T.; Zhang, X.; Chung, L. W.; Wu, Y.-D. *ACS catal*. **2017**, *7*, 1361.

CID (collision induced dissociation)



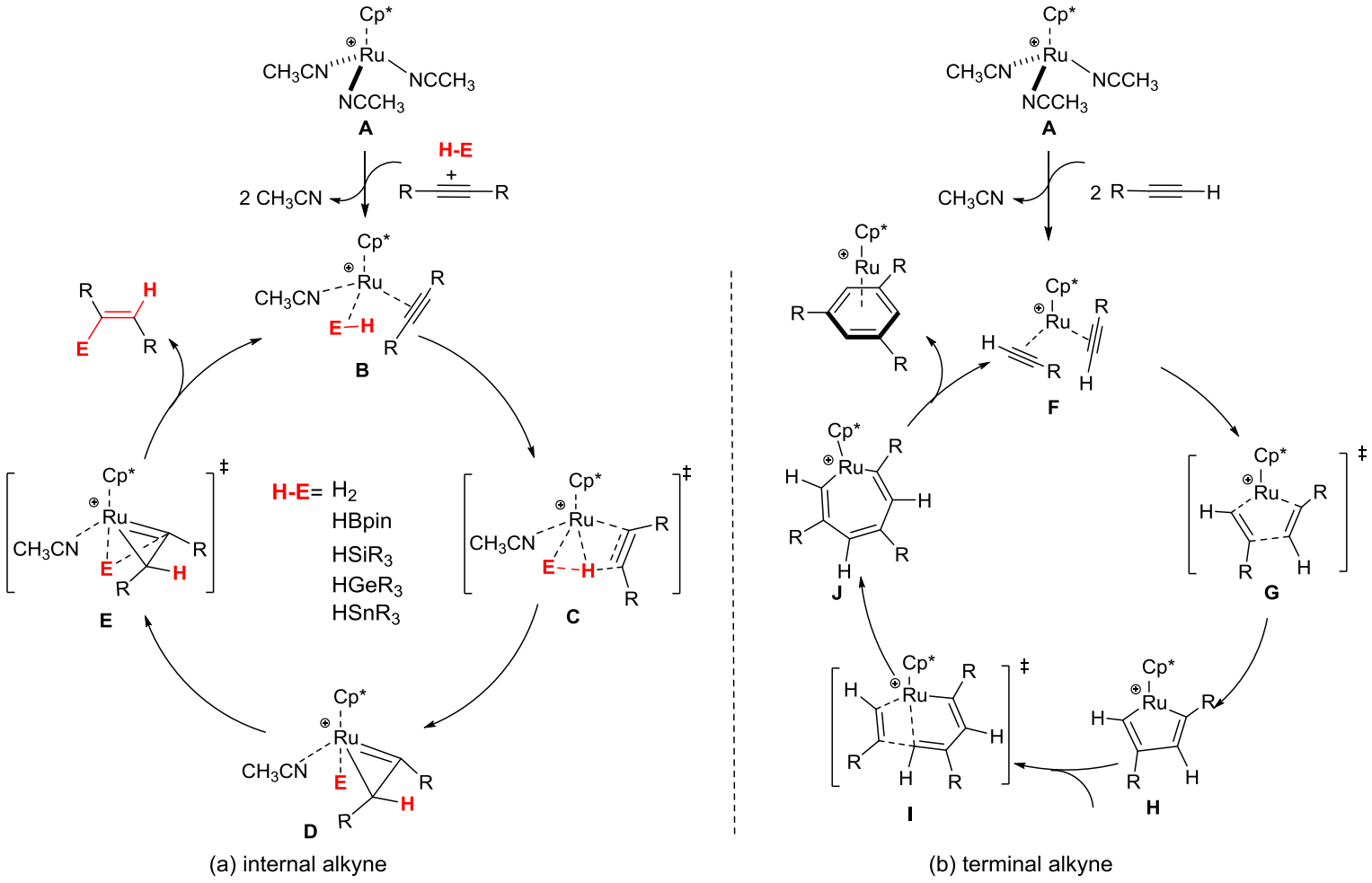
Song, L.-J.; Wang, T.; Zhang, X.; Chung, L. W.; Wu, Y.-D. *ACS catal*. **2017**, *7*, 1361.

CCS (collision-cross section)

m/z	CID	IMS		
		CCS_{Exp} (Å^2)	CCS_{Cal} (Å^2)	
441	-$C_{16}H_{16}$ (208 Da)	131	 **d1** 131	 **d2** 132	 **d3** 125
543	-$C_{24}H_{22}$ (310 Da)	154	 **t1** 157	 **t2** 155	 **t3** 153

Song, L.-J.; Wang, T.; Zhang, X.; Chung, L. W.; Wu, Y.-D. *ACS catal*. **2017**, *7*, 1361.

Mechanisms for Internal and Terminal alkyne



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Understanding and Utilizing the Role of London Dispersion Interactions in Catalysis

- No systematic study on identifying effective dispersion energy donors (DEDs)
- Accurate determinations of attractive dispersion interactions in transition metal complexes are challenging
- London Dispersion (LD) interactions are attenuated in solution

Aims of Our Study

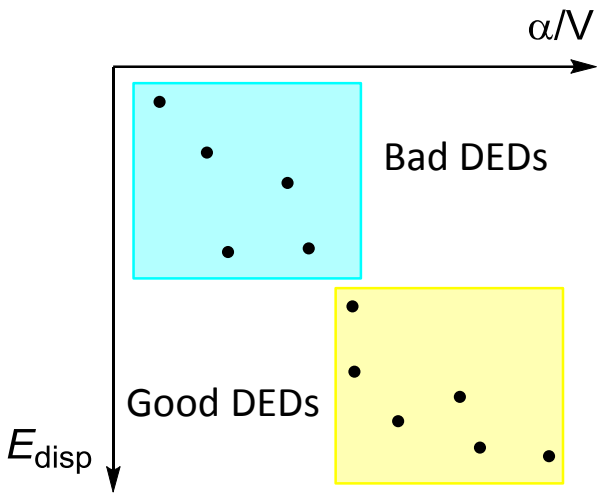
Quantifying DEDs according to their size and polarizability

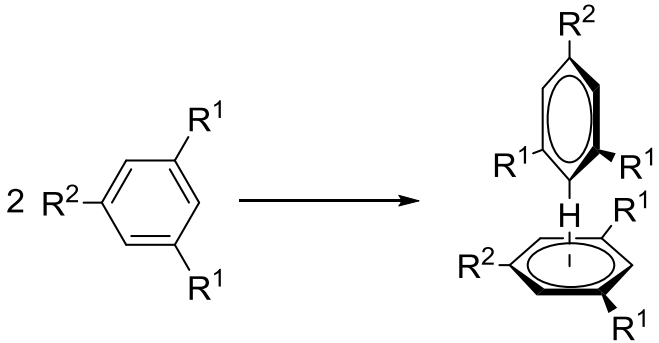
Identifying a model to rank DEDs

Utilizing LD in the design of catalyzed chemical reactions

$$E_{\text{disp}} \propto C\frac{\alpha}{V}$$

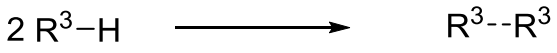
(α: polarizability V: volume)





R_1=R_2=H, Me, F, Cl, Br...

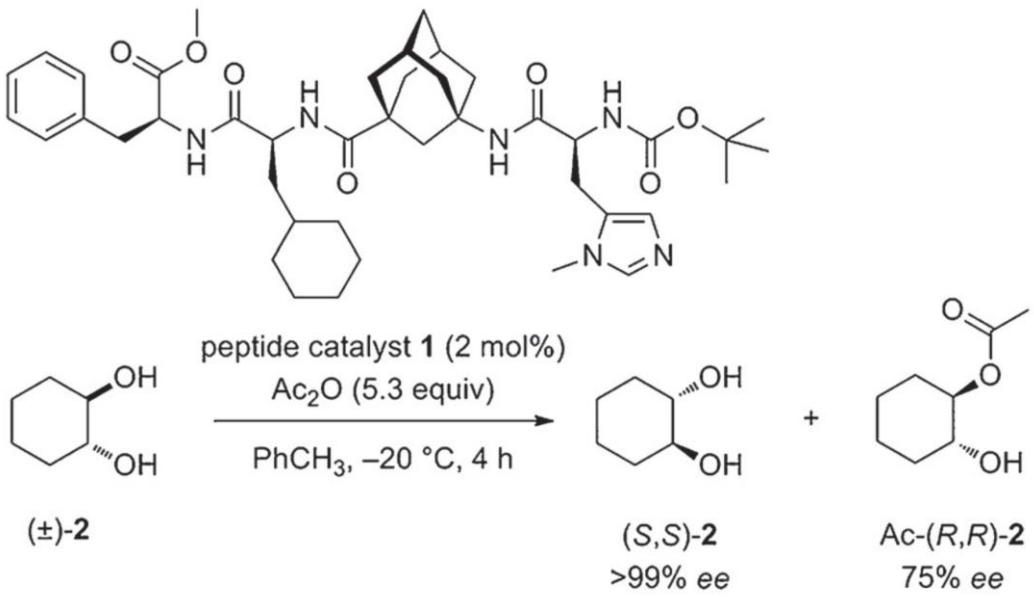
R_2=H, R_1=Et, ^{i}Pr, ^{t}Bu, $SiMe_3$....



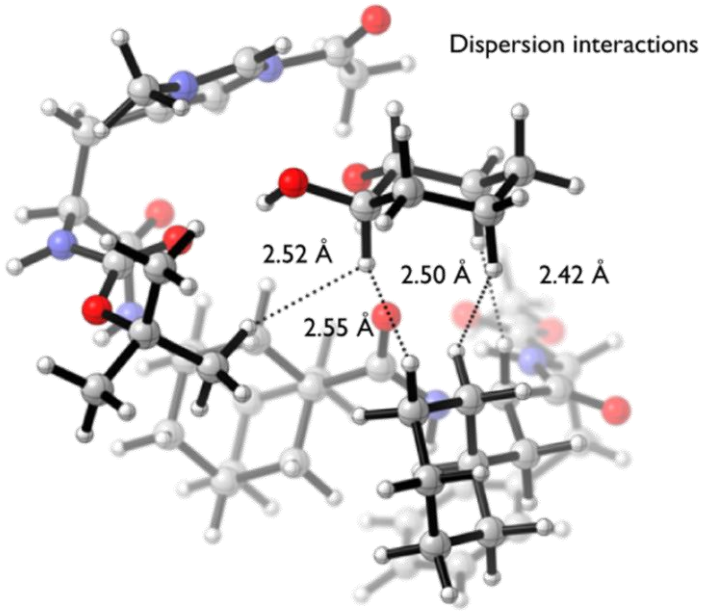
R_3=Et, ^{i}Pr, ^{t}Bu, Cy, Ad...

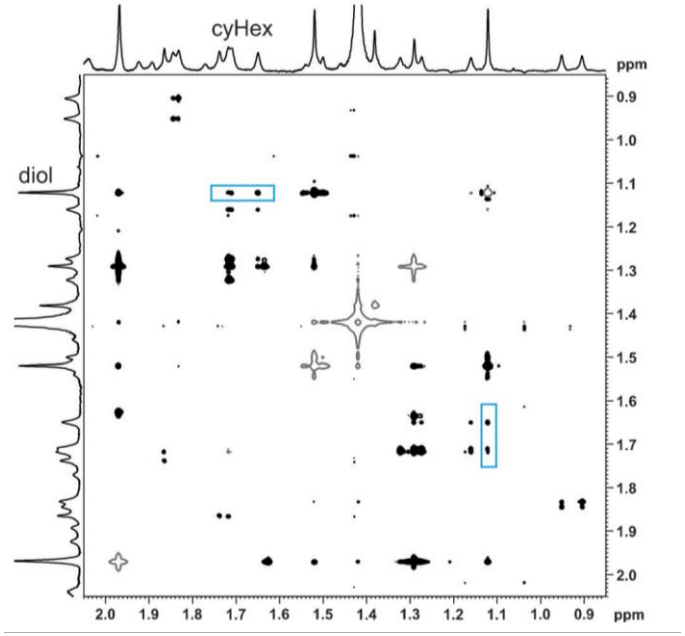
$\Delta\Delta E_{disp} = \Delta H(D3) - \Delta H$

Enantioselective peptide-catalyzed acylation



Dispersion in Catalysis – Organocatalysis

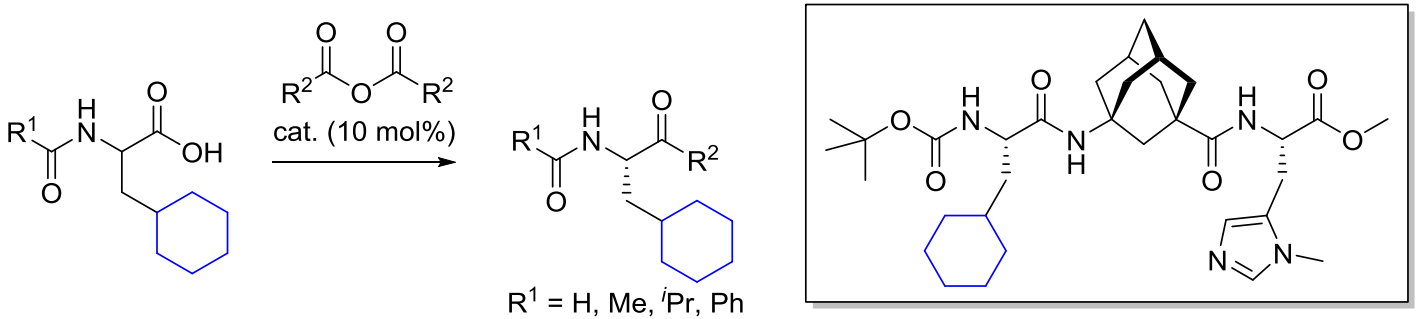


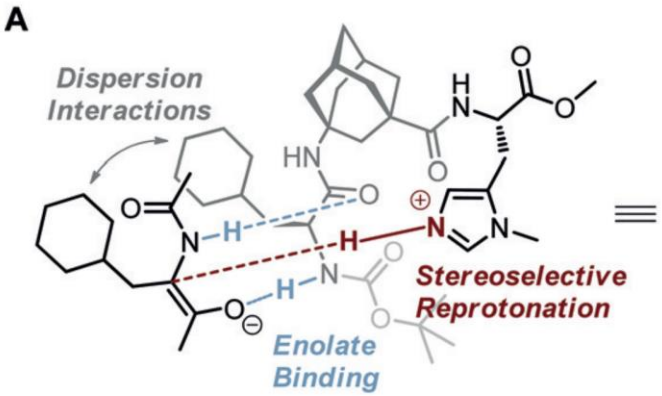


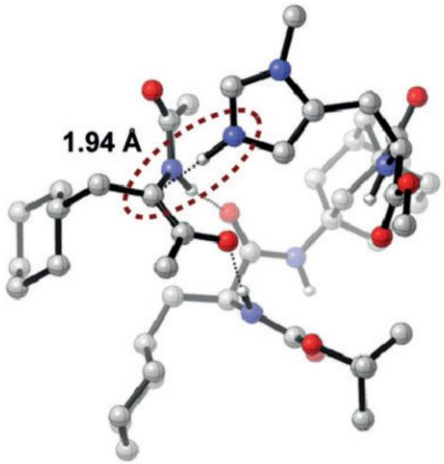
M06-2X/6-31+G(d,p)

Müller, C. E.; Zell, D.; Hrdina, R.; Wende, R. C.; Wanka, L.; Schuler, S. M.; Schreiner, P. R. *J. Org. Chem*. **2013**, *78*, 8465; Procházková, E.; Kolmer, A.; Ilgen, J.; Schwab, M.; Kaltschnee, L.; Fredersdorf, M.; Schmidts, V.; Wende, R. C.; Schreiner, P. R.; Thiele, C. M. *Angew. Chem. Int. Ed.* **2016**, *55,* 15754.

Enantioselective Dakin–West reaction





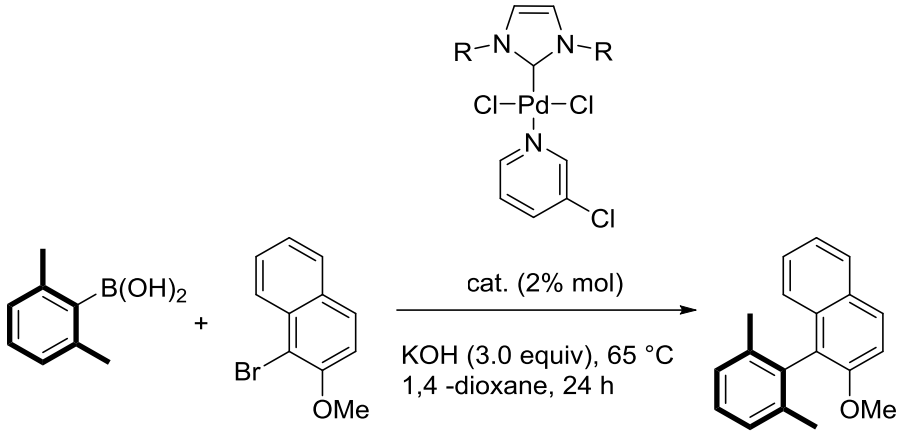


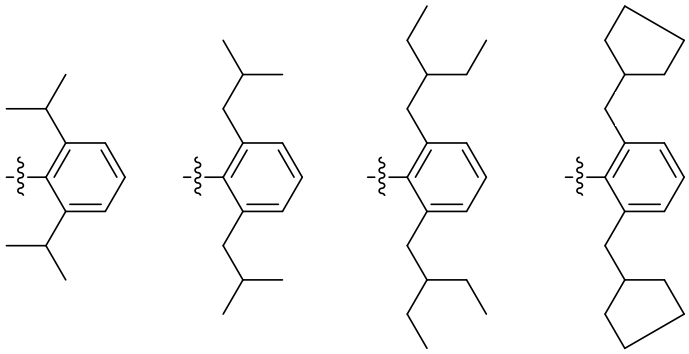
Dispersion controls the enantioselectivity?

B3LYP-D3(BJ)/6-31+G(d,p)

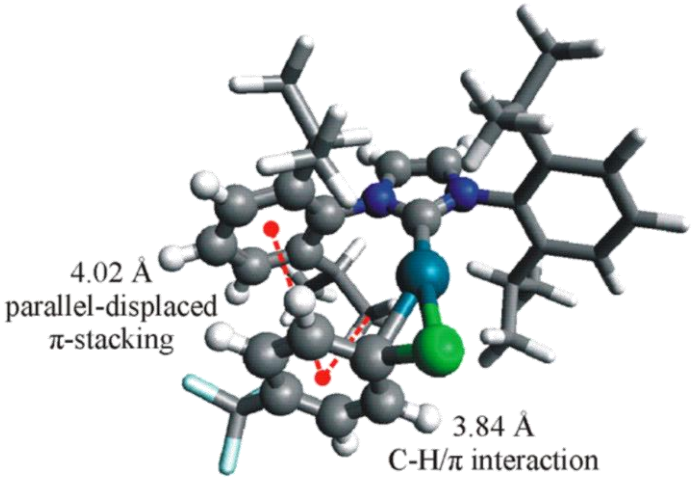
Wende, R. C.; Seitz, A.; Niedek, D.; Schuler, S. M. M.; Hofmann, C.; Becker, J.; Schreiner, P. R. *Angew. Chem. Int. Ed.* **2016**, *55*, 2719–2723.

Suzuki–Miyaura cross-coupling





R	G8	G12	G14	G15
Conversion [%]	41	4	91	9



RI-B97-D/cc-pVTZ //RI-B97-D/6-31G*

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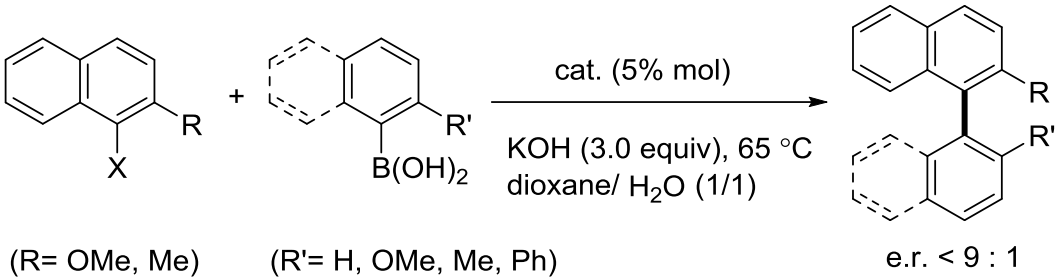
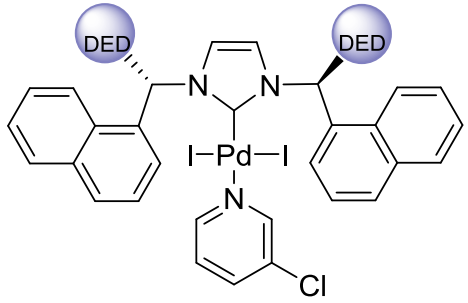
Asymmetric Suzuki–Miyaura cross-coupling



(R= OMe, Me) (R'= H, OMe, Me, Ph) e.r. < 9 : 1



$$E_{\text{disp}} \propto C\frac{\alpha}{V}$$

⇩

Identifying good DEDs

⇩

Selectivity-determining step

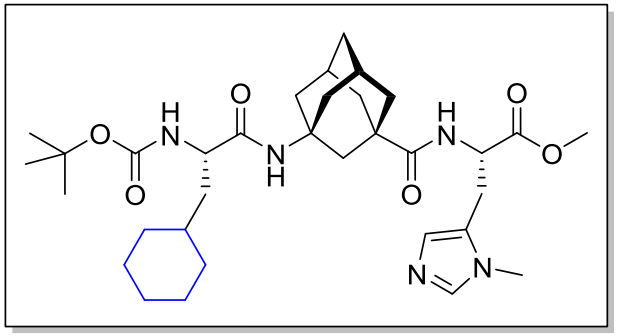
Improving enatioselectivity ?

Broaden substrate scope ?

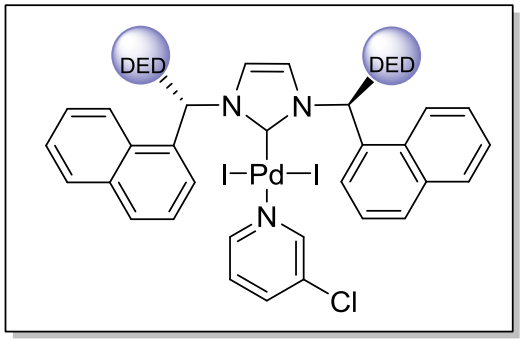
Benhamou, L.; Besnard, C.; Kündig, E. P. *Organometallics* **2014**, *33*, 260; Zhang, D.; Wang, Q. *Coord. Chem. Rev*. **2015** *286*, 1.

$$E_{\text{disp}} \propto \mathrm{C}\frac{\alpha}{V}$$

Identifying DEDs



Organocatalysis



Organometallic catalysis

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Thank you for your attention !