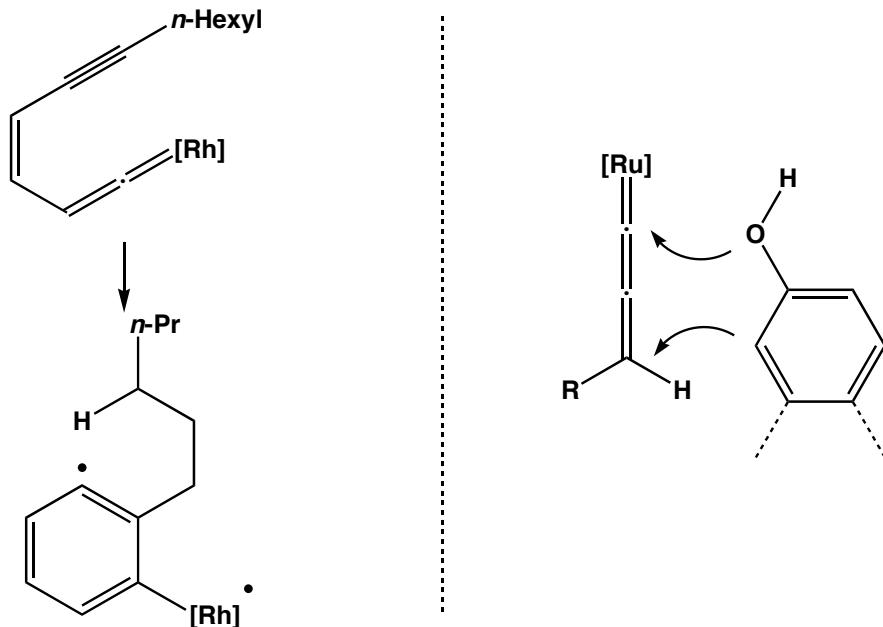


Metal Vinylidenes and Allenylenes as Intermediates in Catalytic Transformations

Literature Group Meeting
Eric Ferreira
April 26, 2004



Outline and References

Outline:

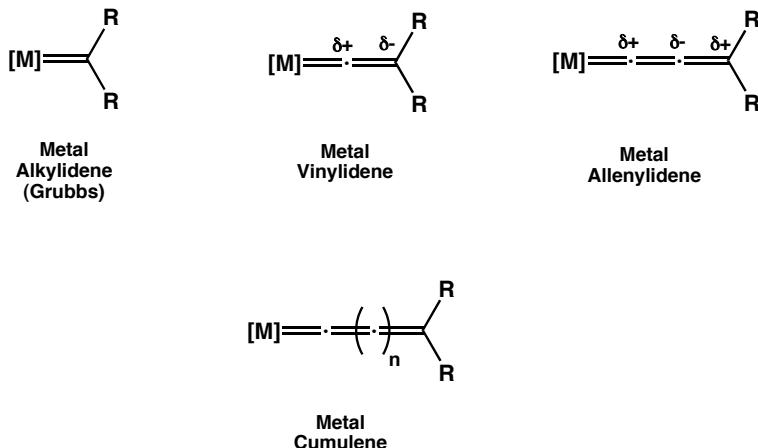
- Definitions
- Metal vinylidene generation
- Reaction types
- Vinylidenes as intermediates in catalytic reactions (anti-Markovnikov additions, reconstitutive additions)
- Allenylenes as intermediates in catalytic reactions (propargylic substitution reactions)

Key references:

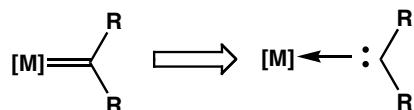
- Metal Vinylidenes in Catalysis. Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* 1999, 32, 311-323.
- Molecular Gymnastics of Alkynes Orchestrated by Ruthenium Complexes. Trost, B. M. *Chem. Ber.* 1996, 129, 1313-1322.
- Non-Metathesis Ruthenium-Catalyzed C-C Bond Formation. Trost, B. M.; Toste, F. D.; Pinkerton, A. B. *Chem. Rev.* 2001, 101, 2067-2096.

Nomenclature

What are vinylidenes and allenylidenes?

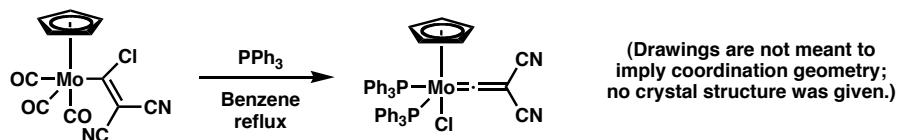


Can think of all of these species as carbenes attached to metals:



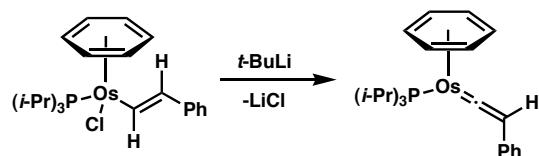
Generation of Metal Vinylidenes

First isolation of a metal vinylidene species: King, R. B.; Saran, M. S. *J. Chem. Soc. Chem. Commun.* 1972, 1053.

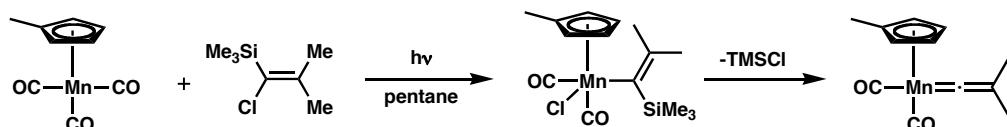


Other methods of generating metal vinylidene complexes (See Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* 1999, 32, 311):

Deprotonation of vinylmetal halide by strong base:

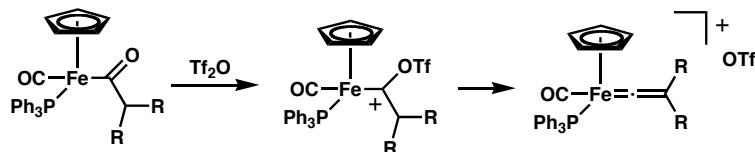


Photochemical mediated oxidative addition to vinyl chlorides followed by elimination:

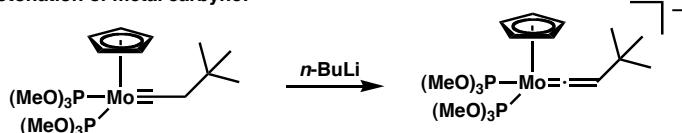


Generation of Metal Vinylidenes

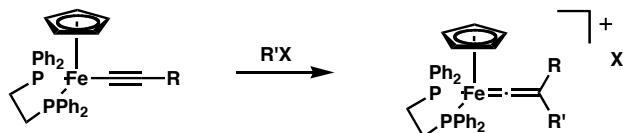
Deoxygenation of acyl metal:



Deprotonation of metal carbyne:



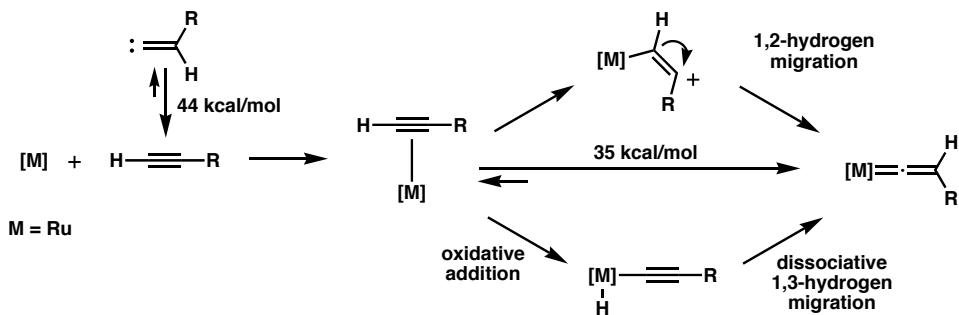
Reactions of metal alkynes with electrophiles:



- The above stoichiometric methods of vinylidene generation do not seem amenable to catalysis.

Generation of Metal Vinylidenes and Allenylenes

- One way of generating metal vinylidene is ideal for extending to catalysis:

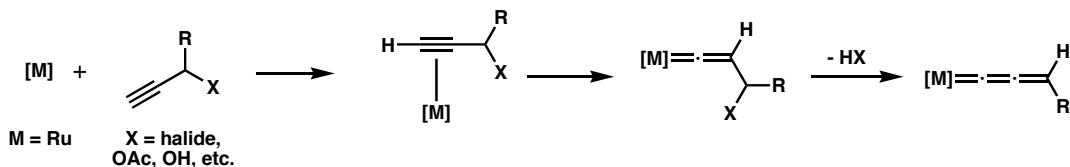


- Different catalyst complexes will proceed through different pathways.

- Top path: Wakatsuki, Y.; Koga, N.; Yamasaki, H.; Morokuma, K. *J. Am. Chem. Soc.* 1994, 116, 8105. (calculations)
- Bottom path: Rios, I.; Tenorio, M. J.; Puerta, M. C.; Valerga, P. *J. Am. Chem. Soc.* 1997, 119, 6529. (calculations)

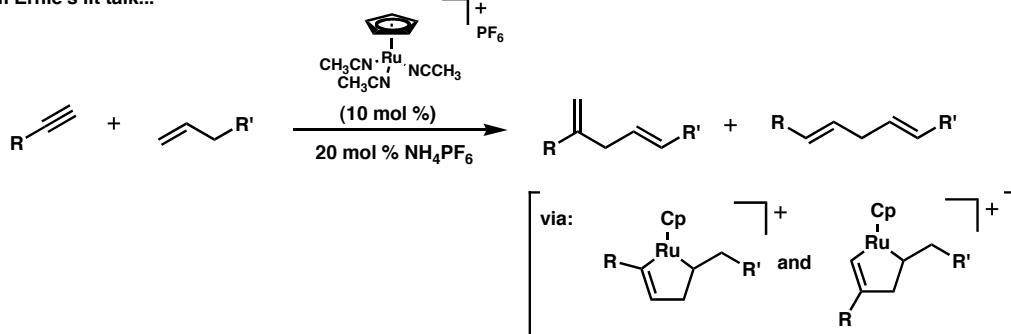
- Limited reports of vinylidene generation from other alkynes (iodo-, trialkylsilyl-, and alkythio-); terminal alkynes are typical.

- Placement of leaving group in propargylic position of the terminal alkyne will convert a vinylidene to an allenylidene.

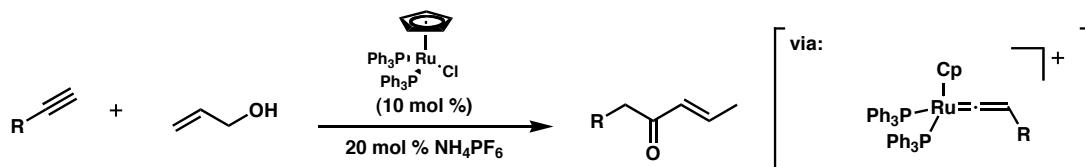


Metallacyclopentene Formation vs. Metal Vinylidene Formation

Recall from Ernie's lit talk...



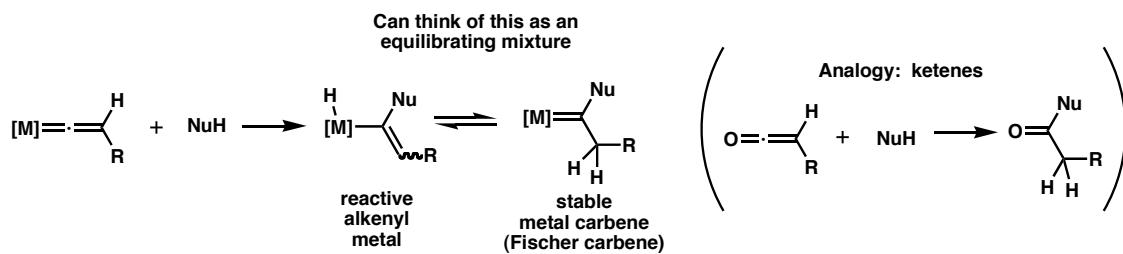
But ruthenium catalysts can also make vinylidenes with terminal alkynes...



- Precatalysts are the key! In general, precatalysts with phosphines will generate metal vinylidenes, while precatalysts with less coordinating ligands will undergo metal cycloaddition reactions.
- This is simply because phosphine precatalysts will have fewer open coordination sites to bind π -systems.

Three Fundamental Reaction Types with Metal Vinylidenes

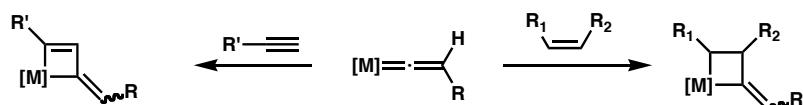
Type 1: Nucleophilic addition to C(α)



Type 2: Insertion of vinylidene into metal-alkynyl bond



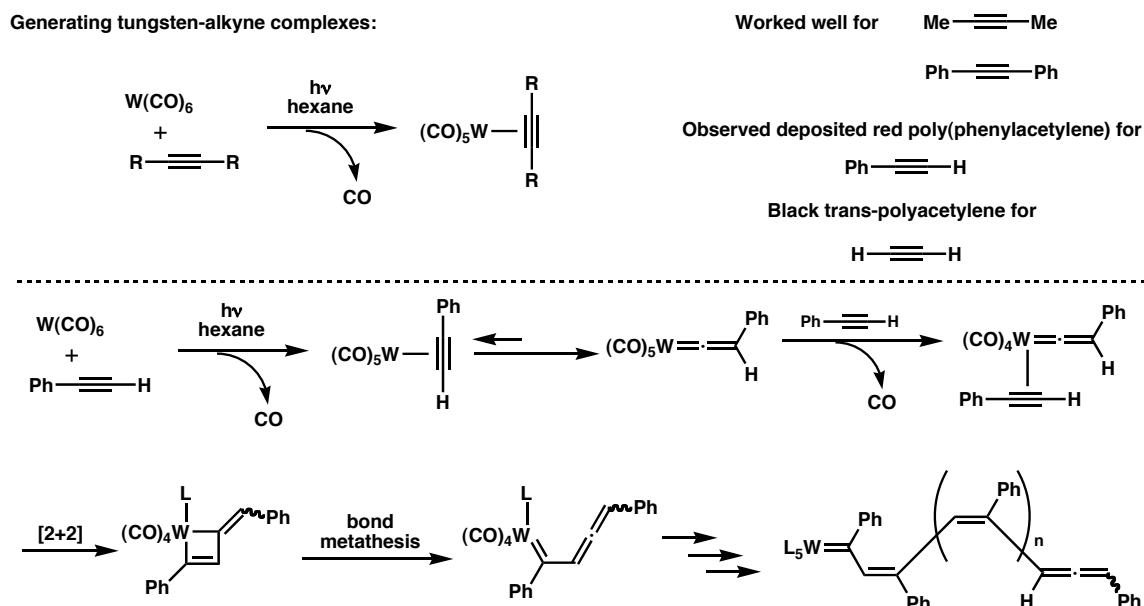
Type 3: [2+2] addition reactions



Type 3 Vinylidene Reactions: Polymerization of Terminal Alkynes

Landon, S. J.; Shulman, P. M.; Geoffroy, G. L. *J. Am. Chem. Soc.* 1985, 107, 6739.

Generating tungsten-alkyne complexes:

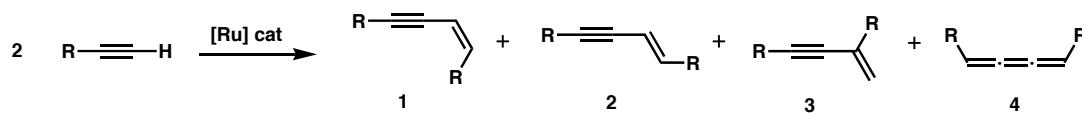


- First report of a metal vinylidene being involved in a catalytic reaction.
- Unsurprisingly, these vinylidenes have been exploited as polymerization catalysts and metathesis catalysts. (See Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* 1999, 32, 311.)

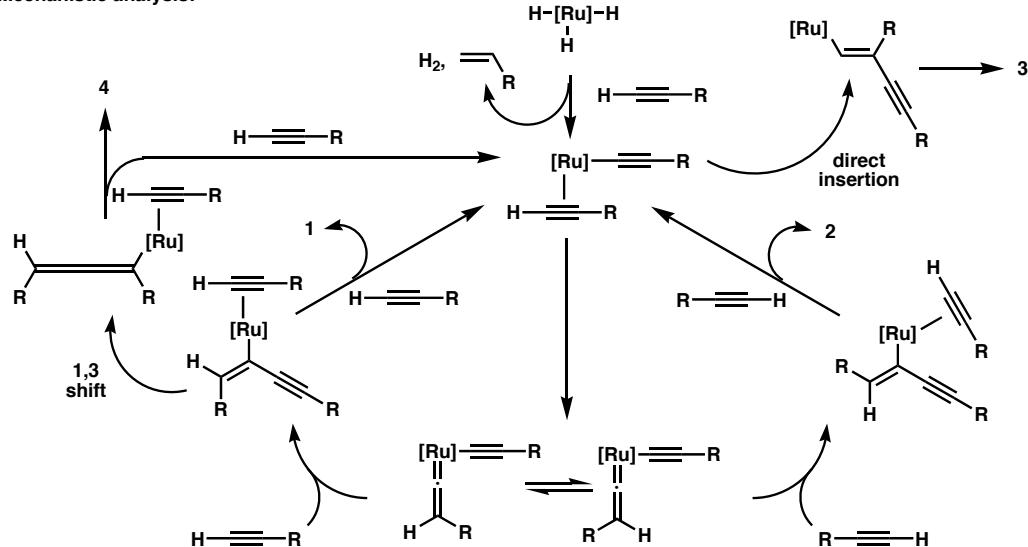
Type 2 Initiated Reactions: Dimerization of Terminal Alkynes

Review: Yi, C. S.; Liu, N. *Synlett* 1999, 281.

Can achieve selectivity with catalyst, R variations, etc.

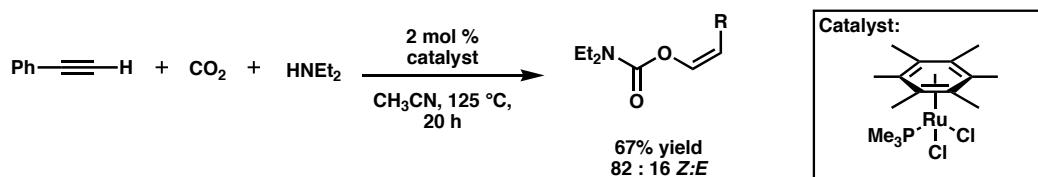


Mechanistic analysis:

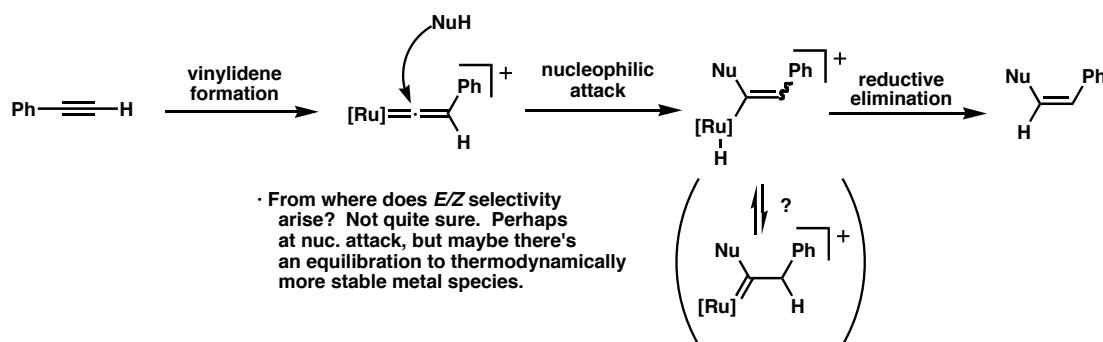
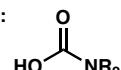


Anti-Markovnikov Addition to Terminal Alkynes: Carbamates

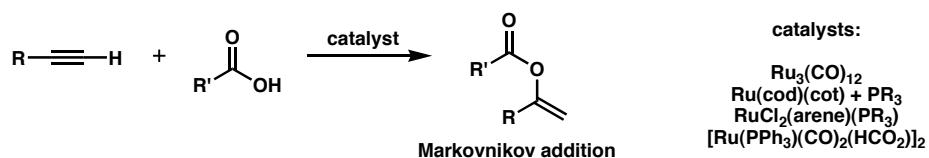
Mahe, R.; Dixneuf, P. H. *Tetrahedron Lett.* 1986, 27, 6333.
Mahe, R.; Sasaki, Y.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* 1989, 54, 1518.



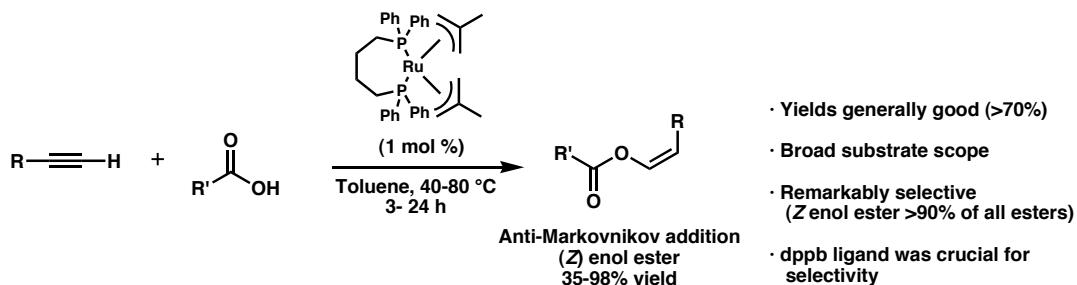
- Works for phenylacetylene, 1-hexyne
- Dialyklamine can be cyclic or acyclic aliphatic substituents
- Regioselectivity very high, geometrical purity consistently ~4:1
- Avoids the use of phosgene derivatives to make carbamates



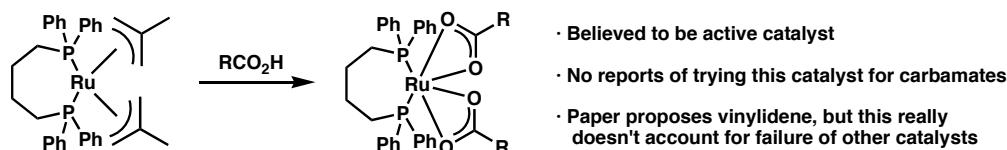
Anti-Markovnikov Addition to Terminal Alkynes: Enol Esters



Doucet, H.; Martin-Vaca, B.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* 1995, 60, 7247.

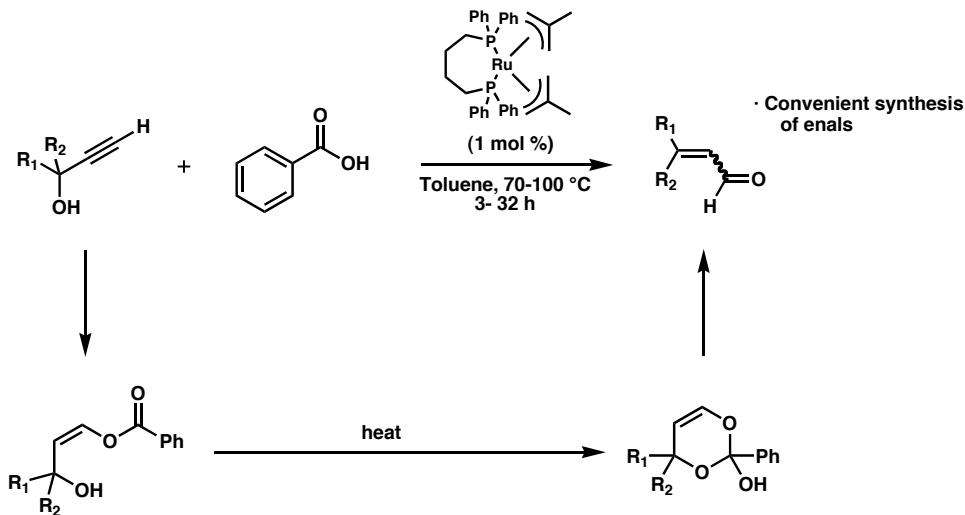


Why does this work where all others fail??

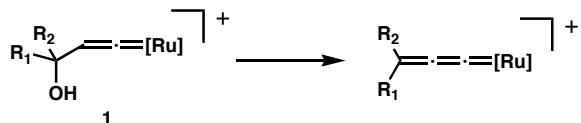


Anti-Markovnikov Addition to Terminal Alkynes: Enol Esters

Picquet, M.; Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* 1997, 1201.

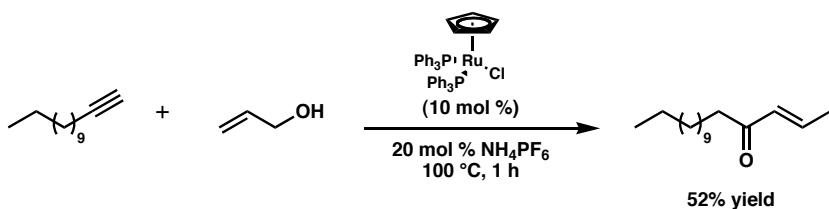


If 1 is an intermediate in the anti-Markovnikov addition, then one would expect allenylidene generation pretty quickly.

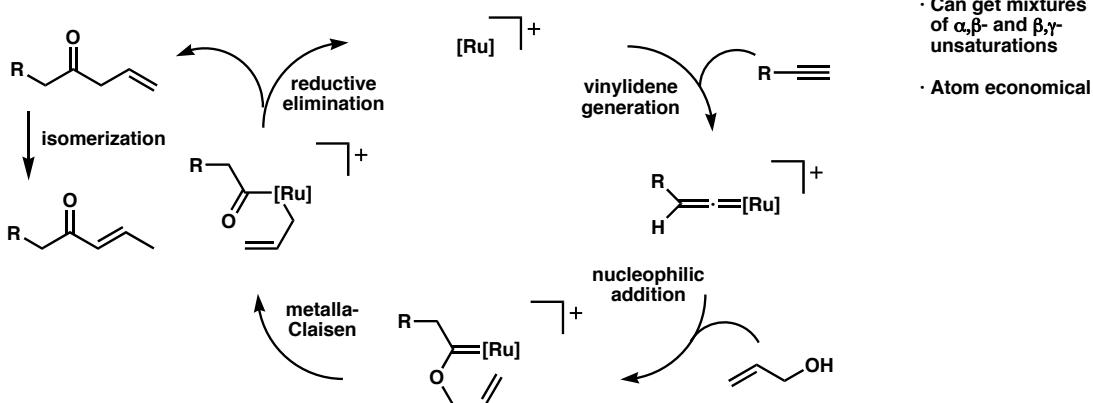


Ruthenium-Catalyzed Reconstitutive Condensation of Allylic Alcohols and Terminal Alkynes

Initial report: Trost, B. M.; Dyker, G.; Kulawiec, R. J. *J. Am. Chem. Soc.* 1990, 112, 7809.



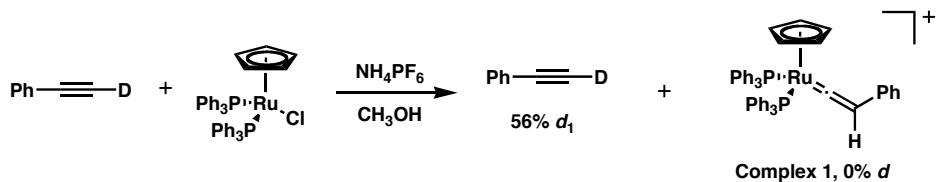
Original Mechanistic Proposal:



Ruthenium-Catalyzed Reconstitutive Condensation of Allylic Alcohols and Terminal Alkynes

Mechanistic Studies: Trost, B. M.; Kulawiec, R. J. *J. Am. Chem. Soc.* 1992, 114, 5579.

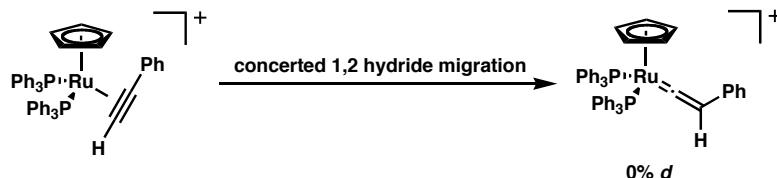
Vinylidene generation:



· Absence of deuterium in vinylidene is consistent with direct rearrangement followed by rapid proton exchange (agrees with calculations: Silvestre, J.; Hoffmann, R. *Helv. Chim. Acta* 1985, 68, 1461).

· Acetylide complex via direct deprotonation of alkyne cannot be ruled out.

· Main point: vinylidene formation is slow compared to reaction with allylic alcohol.

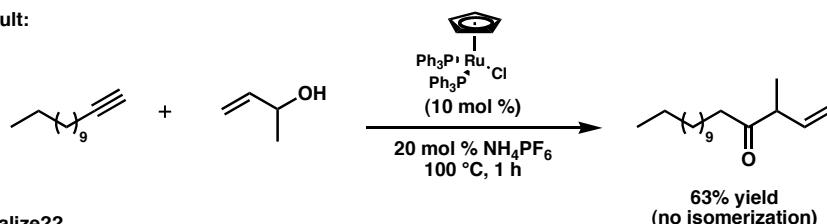


· Addition of excess PPh₃ slows reaction rate.
 · Bidentate phosphines (dppe, dppb) shut down reaction.
 · MeOH adds slowly to Complex 1; EtOH or i-PrOH don't add at all.

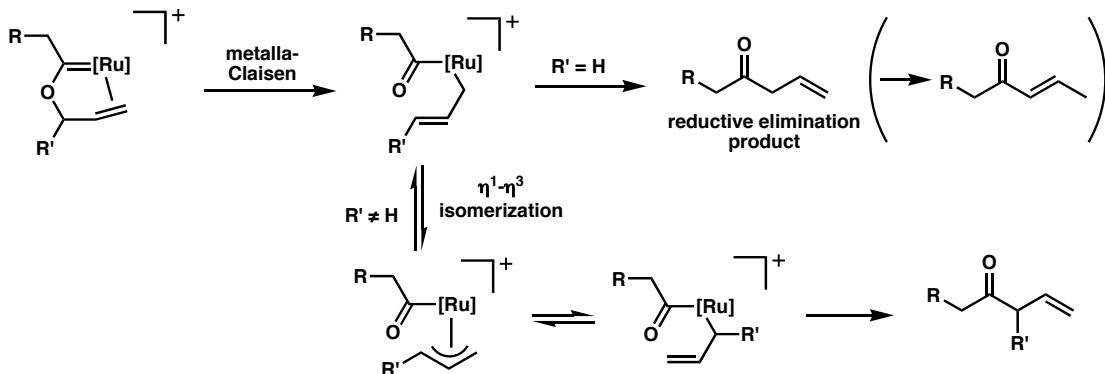
Addition of allyl alcohol requires phosphine dissociation, followed by olefin coordination and nucleophilic attack.

Ruthenium-Catalyzed Reconstitutive Condensation of Allylic Alcohols and Terminal Alkynes

A puzzling result:



How to rationalize???



· Crotyl alcohol unreactive, so could not completely verify this idea.

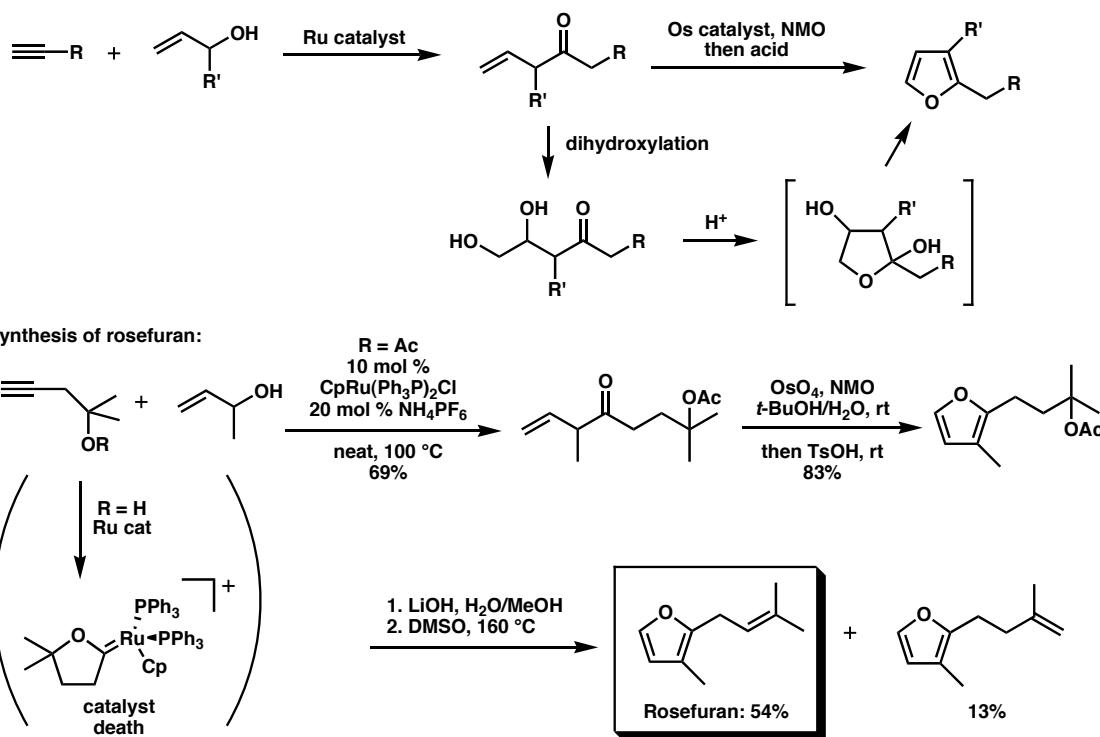
· Agreed with all deuteration studies.

· π-allyl species not surprising, considering electron counting.

$$\left\{ \begin{array}{l} 8(\text{Ru}) + 5(\text{Cp}) + 2x1(\text{Ru-C}) + 2(\text{PPh}_3) + -1(\text{charge}) \\ = 16 e^- \text{ species} \end{array} \right.$$

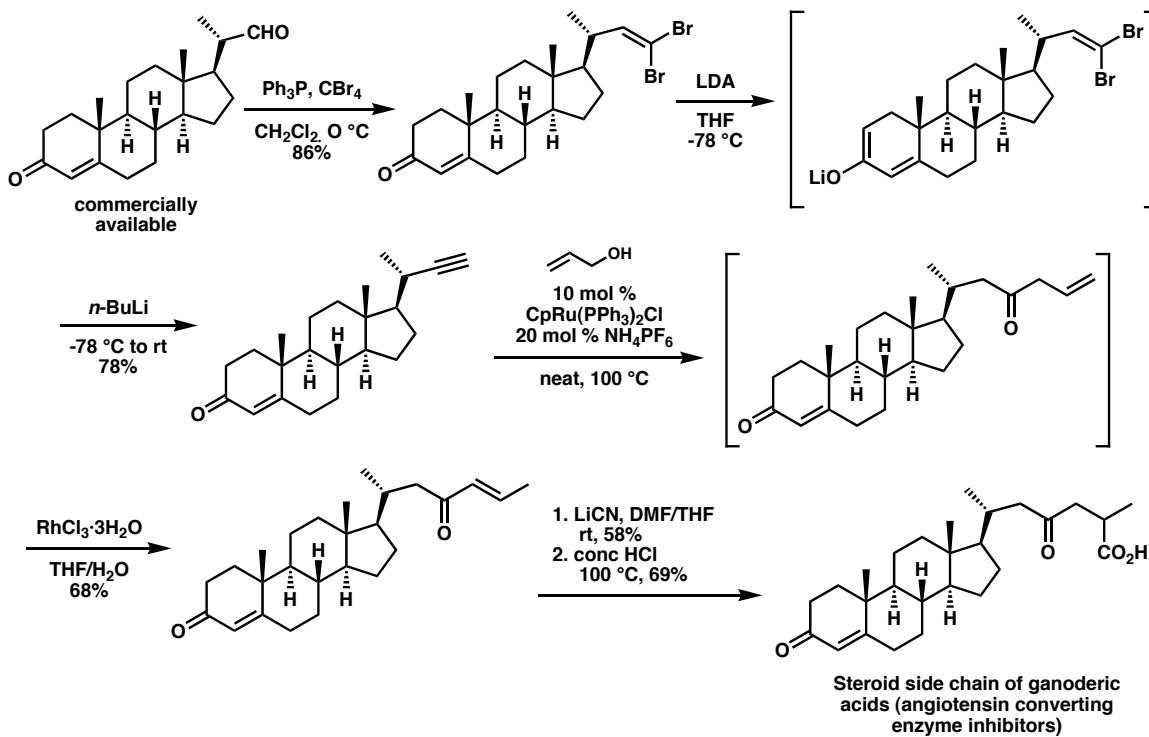
Applications of the Ruthenium-Catalyzed Reconstitutive Condensation

Synthesis of furans: Trost, B. M.; Flygare, J. A. *J. Org. Chem.* 1994, 59, 1078.



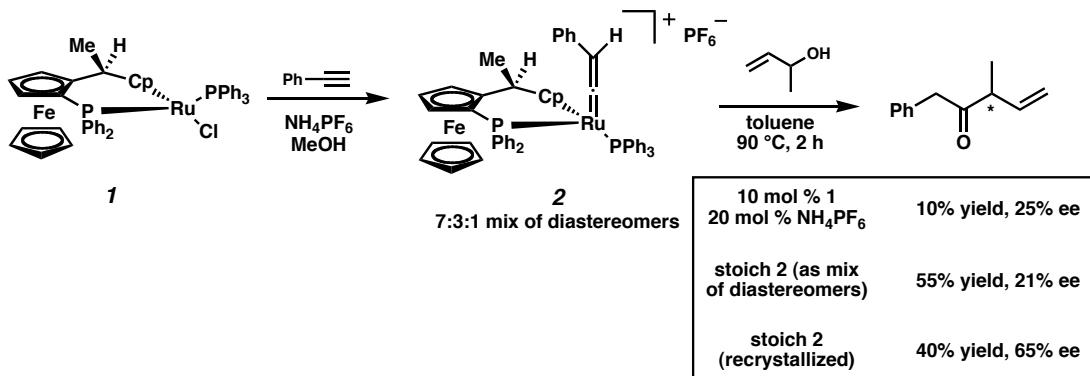
Applications of the Ruthenium-Catalyzed Reconstitutive Condensation

Steroid side chain functionalization: Trost, B. M.; Kulawiec, R. J.; Hammes, A. *Tetrahedron Lett.* 1993, 34, 587.

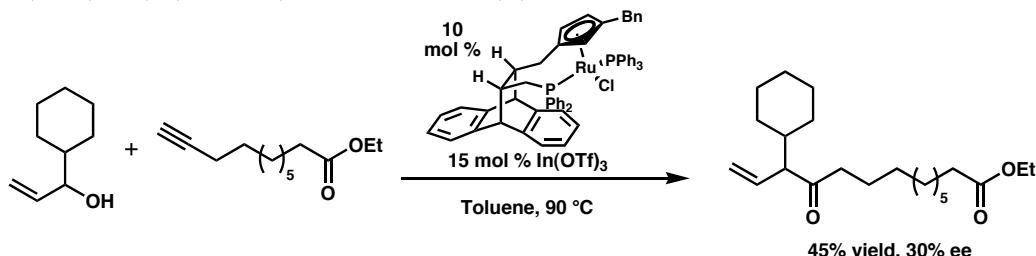


Attempts at Asymmetric Ruthenium-Catalyzed Reconstitutive Addition

Nishibayashi, Y.; Takei, I.; Hidai, M. *Organometallics* 1997, 16, 3091.



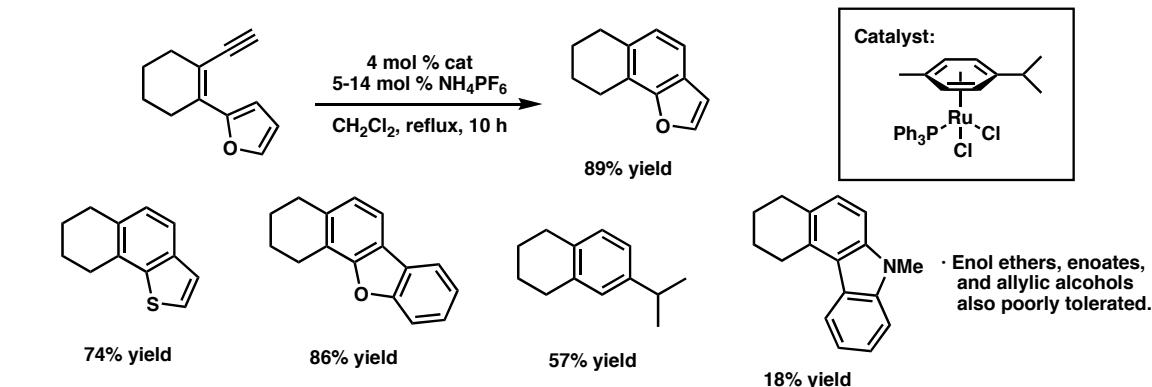
Trost, B. M.; Vidal, B.; Thommen, M. *Chem. Eur. J.* 1999, 5, 1055.



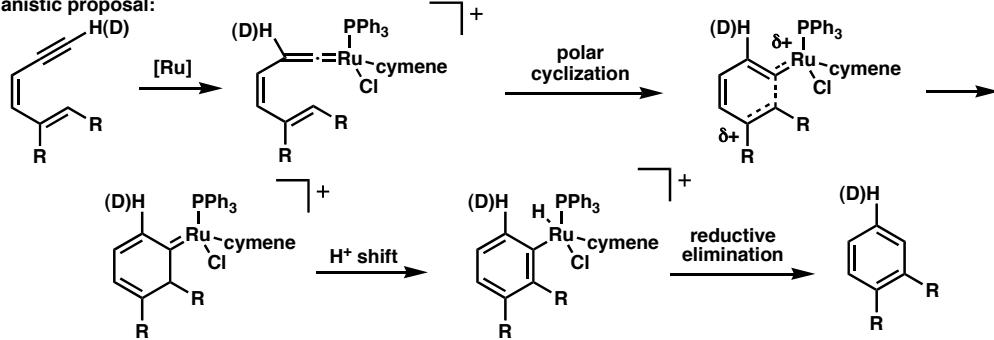
· Matched/mismatched situation observed by testing enantiopure allylic alcohol.

Cyclization of Dienylalkynes via Vinylidene Intermediates

Merlic, C. A.; Pauly, M. E. *J. Am. Chem. Soc.* 1996, 118, 11319.

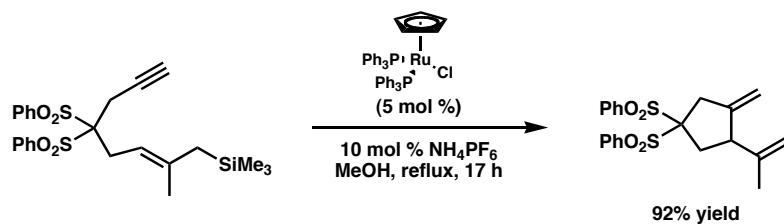


Mechanistic proposal:



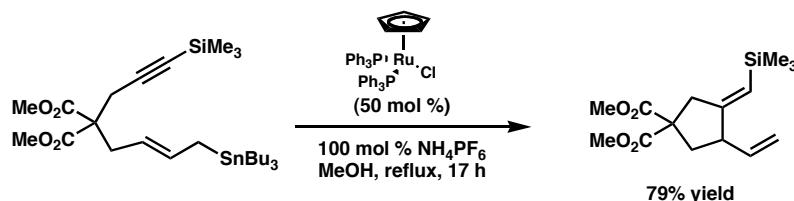
Allylsilane and Allylstannane Additions to Alkynes: Potential Vinylidene Intermediates

Fernandez-Rivas, C.; Mendez, M.; Echavarren, A. M. *J. Am. Chem. Soc.* 2000, 122, 1221.

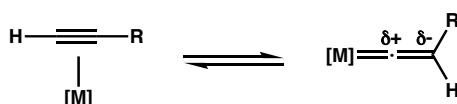


- Reaction also proceeds in 94% yield using 5 mol % PtCl₂

Is a vinylidene involved? A peculiar result...



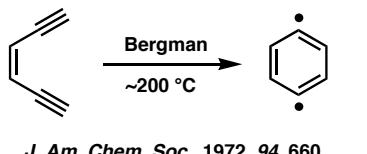
Recall polarity of carbons on a metal vinylidene:



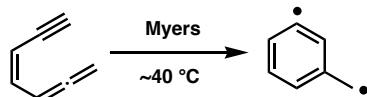
- If vinylidene was reactive intermediate, then allylsilane would attack against polarization.
 - Therefore, electrophilic activation of alkyne is much more likely to be productive intermediate.
 - This is still an unanswered question, however.

Vinylidene Intermediates as Applications to Enediyne Chemistry

- Enedyne motif present in several natural products that have anticancer properties.
(Calicheamicins, esperamicin, dynemicin A, etc.)
 - Enedyne subunit proposed to be source of the activity via cycloaromatization to generate diradicals that induce DNA cleavage
 - Acyclic enynes, however, require elevated temperatures to cyclize (Bergman reaction)
 - Allene-enyne cyclizes at a much lower temperatures (Myers reaction)

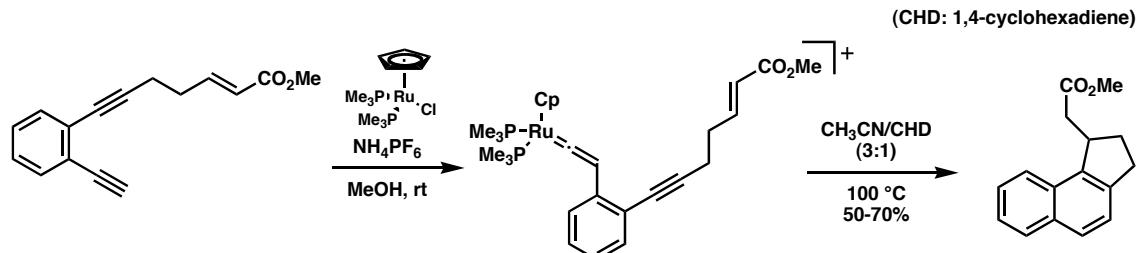


J. Am. Chem. Soc. 1972, 94, 660.



J. Am. Chem. Soc. 1989, 111, 8057.

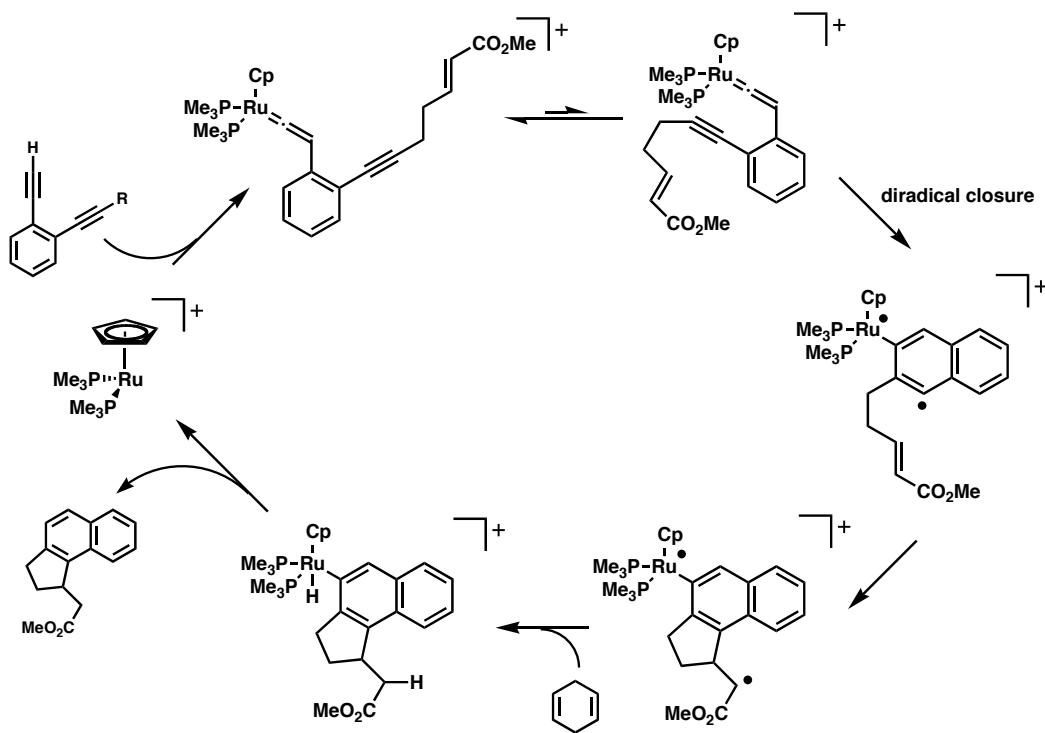
Wang, Y.; Finn, M. G. *J. Am. Chem. Soc.* 1995, 117, 8045.



- Vinylidene can be generated *in situ* as well.

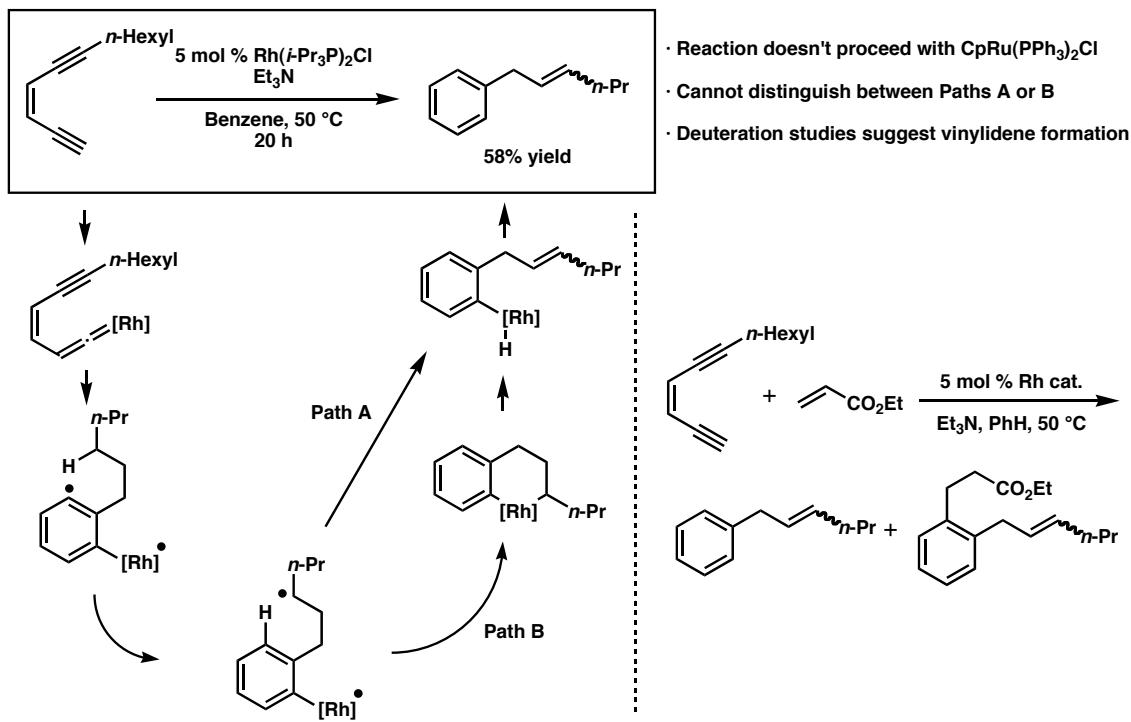
Vinylidene Intermediates as Applications to Enediye Chemistry

Wang, Y.; Finn, M. G. *J. Am. Chem. Soc.* 1995, 117, 8045.



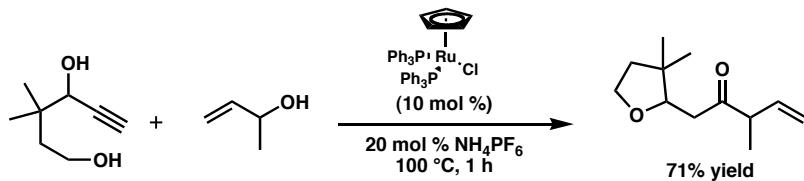
Vinylidene Intermediates as Applications to Enediye Chemistry

Catalytic example: Ohe, K.; Kojima, M.; Yonehara, K.; Uemura, S. *Angew. Chem., Int. Ed. Engl.* 1996, 35, 1823.

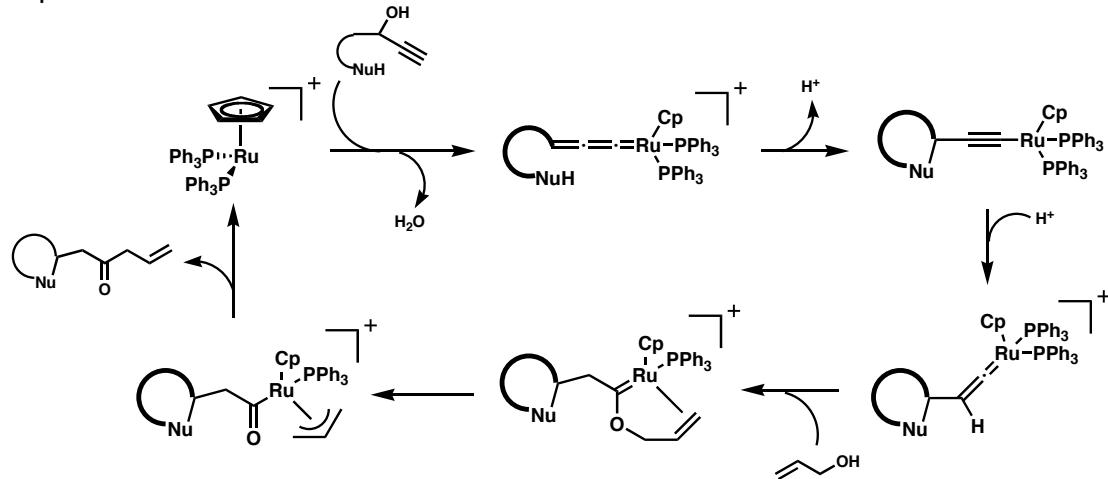


Ruthenium-Catalyzed Cyclization-Reconstitutive Addition of Propargylic Alcohols with Allylic Alcohols

Trost, B. M.; Flygare, J. A. *J. Am. Chem. Soc.* 1992, 114, 5476.

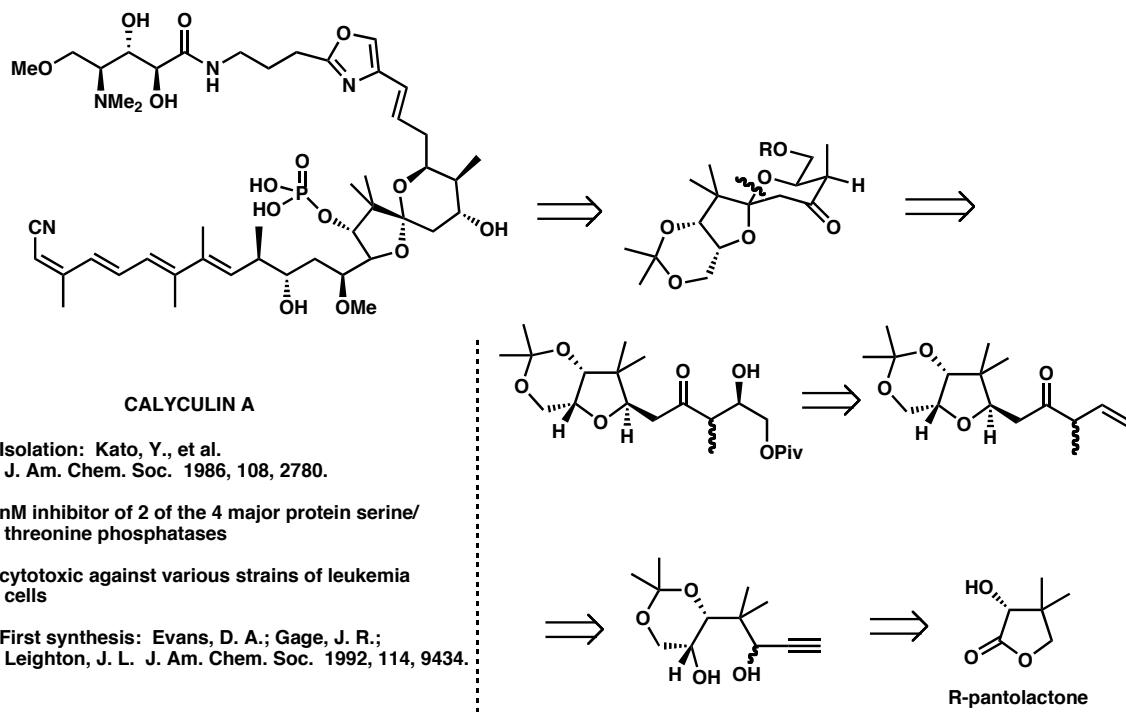


Proposed Mechanism:



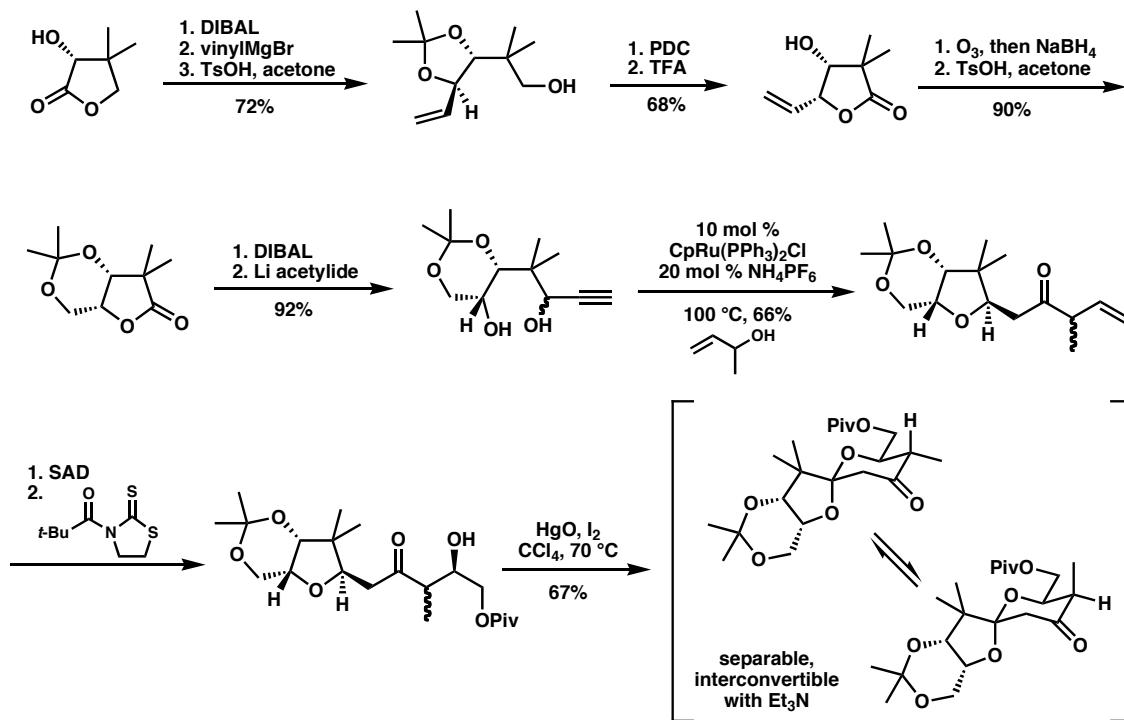
Application of the Ru-Catalyzed Tandem Cyclization-Reconstitutive Addition

Synthesis of the spiroketal subunit of calyculin: Trost, B. M.; Flygare, J. A. *Tetrahedron Lett.* 1994, 35, 4059.



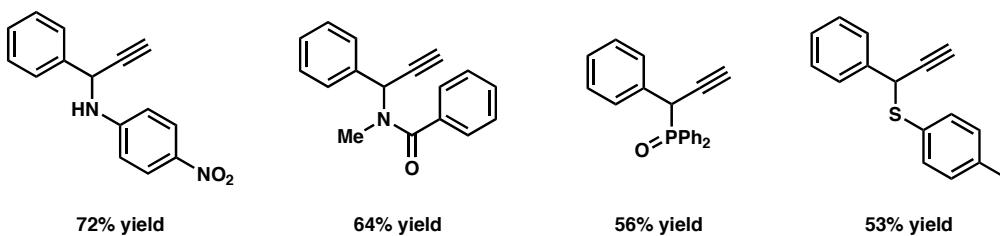
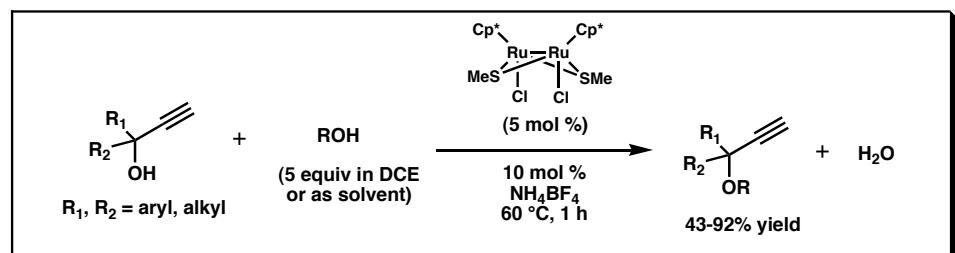
Application of the Ru-Catalyzed Tandem Cyclization-Reconstitutive Addition

Forward synthesis:

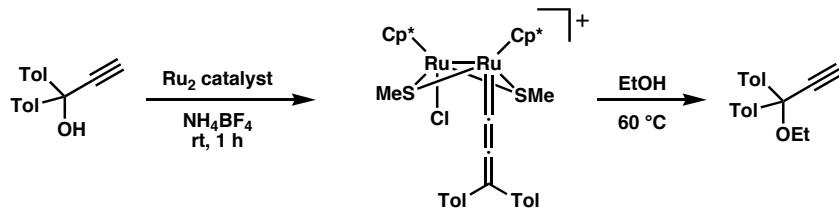


Propargylic Substitution Reactions via Ruthenium Allenylidenes

Nishibayashi, Y.; Wakiji, I.; Hidai, M. *J. Am. Chem. Soc.* 2000, 122, 11019.

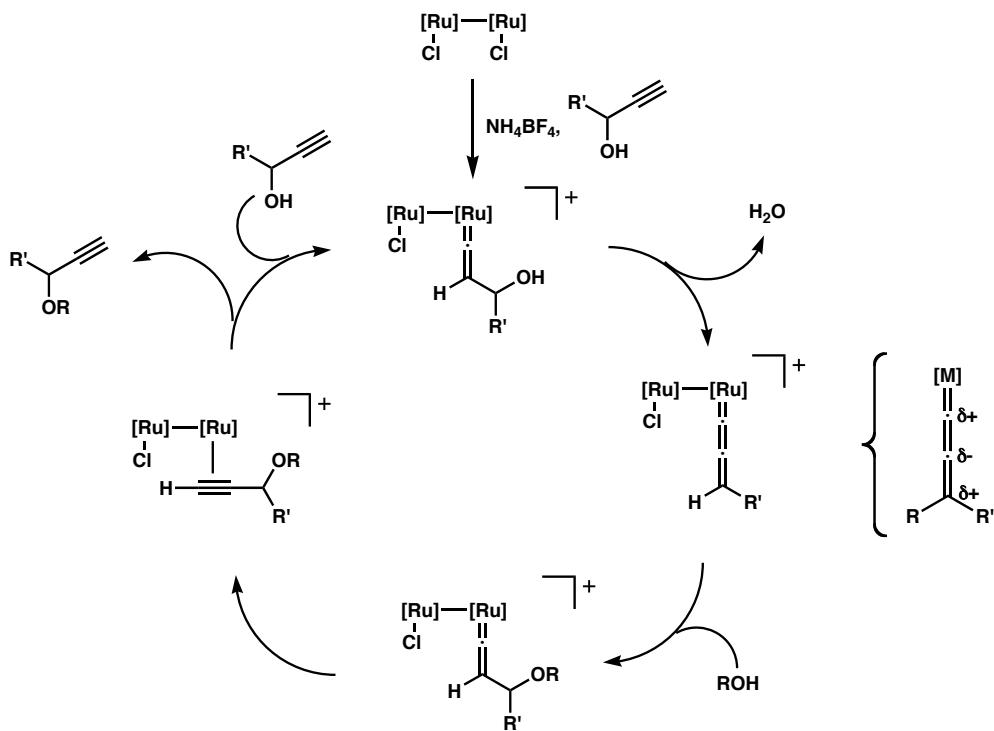


• Stoichiometric generation of allenylidene suggests involvement as reaction intermediate:



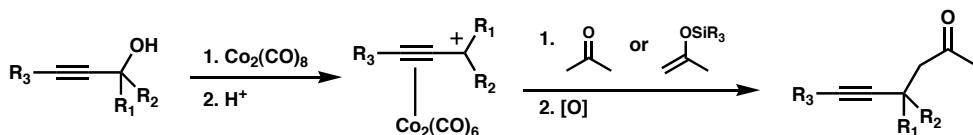
Propargylic Substitution Reactions via Ruthenium Allenylidenes

Proposed mechanism for propargylic substitution:



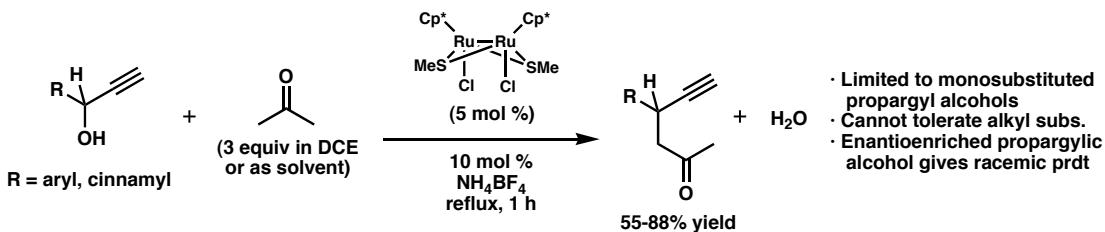
Propargylic Substitution Reactions via Ruthenium Allenylidenes

The Nicholas reaction (Nicholas, K. M. *Acc. Chem. Res.* 1987, 20, 207):

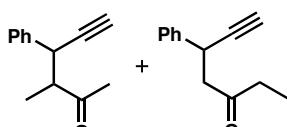


Drawbacks: multistep, stoichiometric in cobalt

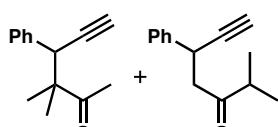
Nishibayashi, Y.; Wakiji, I.; Ishii, Y.; Uemura, S.; Hidai, M. *J. Am. Chem. Soc.* 2001, 123, 3393.



Highly regioselective with unsymmetrical nucleophiles:

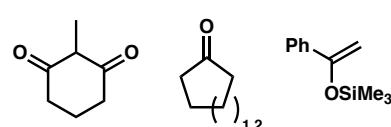


$60^\circ\text{C}, 4\text{ h}: 93:7$
 $\text{rt}, 12\text{ h}: 99:1$



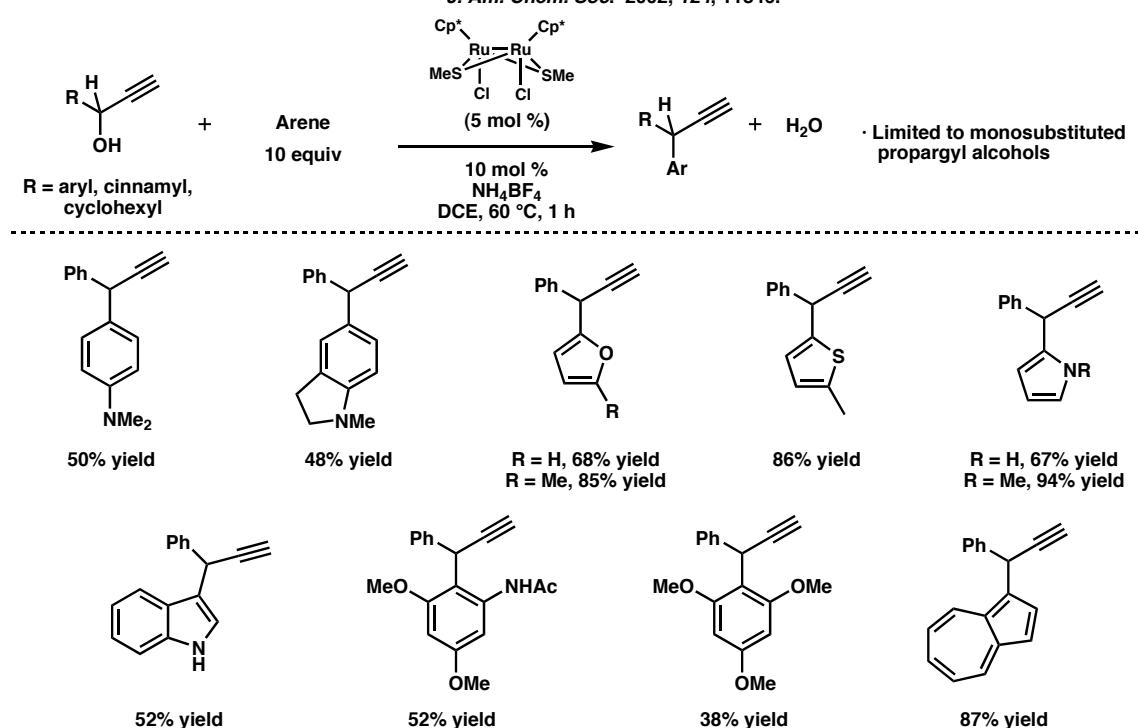
$60^\circ\text{C}, 4\text{ h}: 97:3$

Other nucleophiles:



Propargylic Substitution Reactions via Ruthenium Allenylidenes

Extension of reaction to electron-rich arenes: Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Hidai, M.; Uemura, S. *J. Am. Chem. Soc.* 2002, 124, 11846.

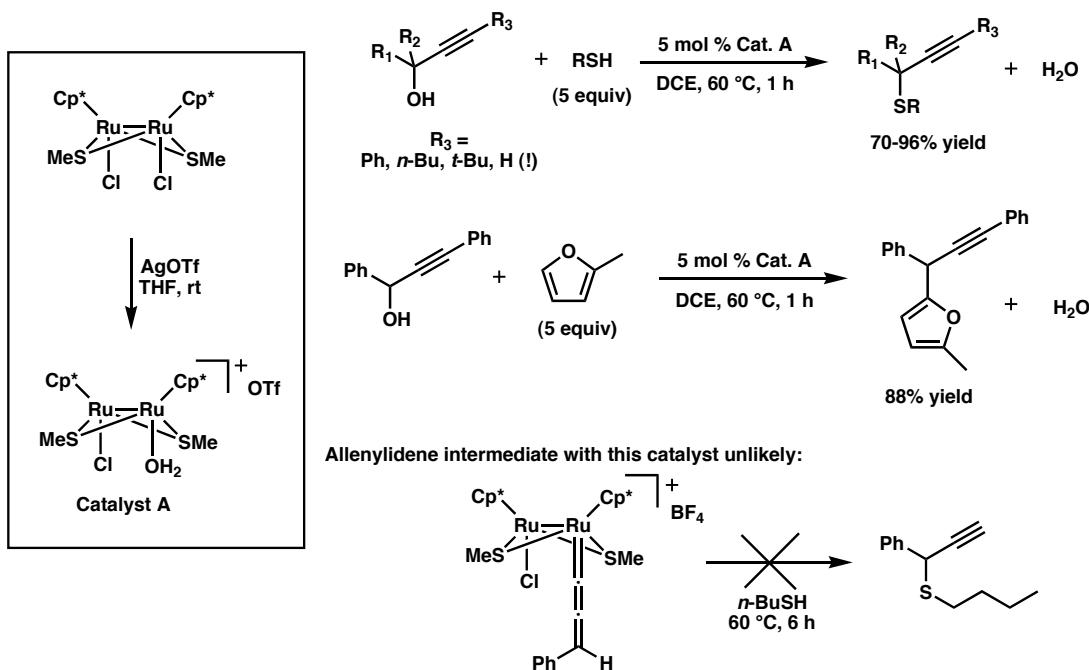


Propargylic Substitution Reactions via Ruthenium Allenylidenes

Propargylation with non-terminal alkynes catalyzed by ruthenium complexes:

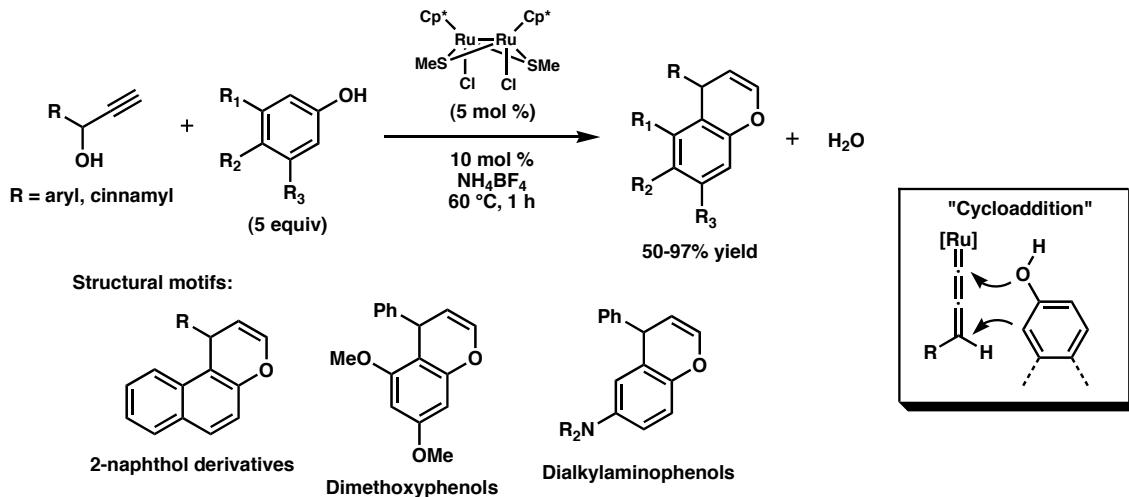
Sulfides: Inada, Y.; Nishibayashi, Y.; Hidai, M.; Uemura, S. *J. Am. Chem. Soc.* 2002, 124, 15172.

Arenes: Nishibayashi, Y.; Inada, Y.; Yoshikawa, M.; Hidai, M.; Uemura, S. *Angew. Chem. Int. Ed.* 2003, 42, 1495.

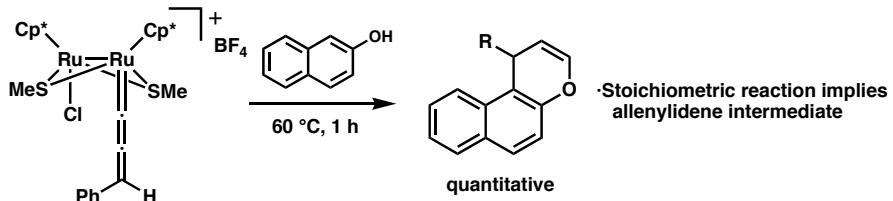


Ruthenium-Catalyzed Cycloadditions via Ruthenium Allenylidenes

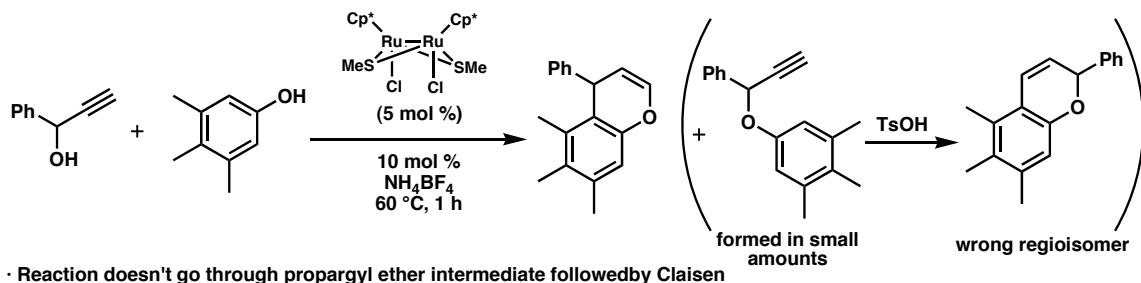
Naphthopyrans/benzopyrans: Nishibayashi, Y.; Inada, Y.; Hidai, M.; Uemura, S. *J. Am. Chem. Soc.* 2002, 124, 7900.



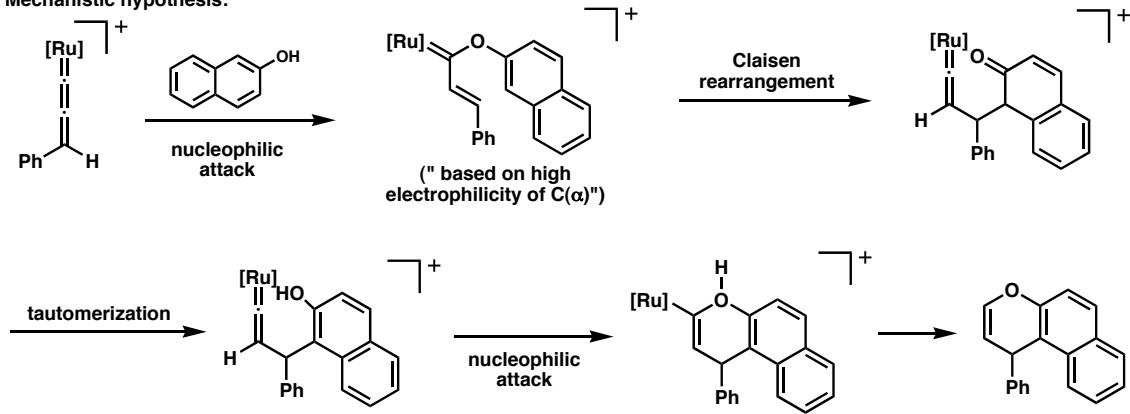
What's going on here?



Ruthenium-Catalyzed Cycloadditions via Ruthenium Allenylidenes



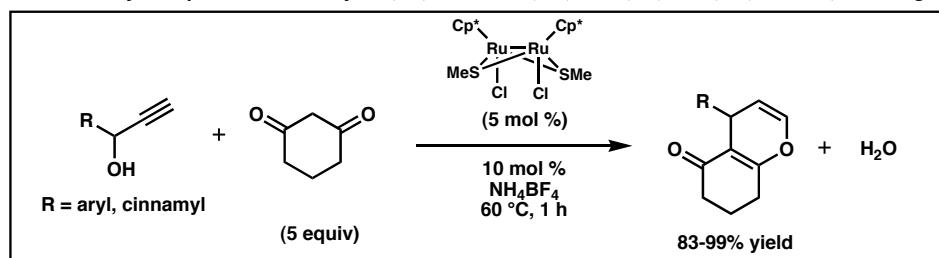
Mechanistic hypothesis:



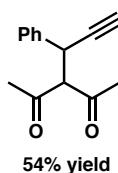
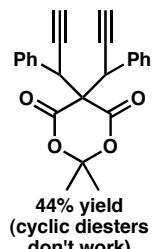
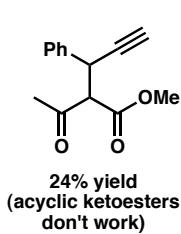
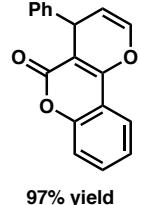
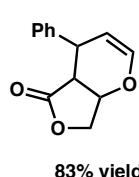
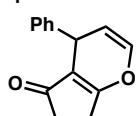
• C(1) of naphthol might attack C(γ) directly

Ruthenium-Catalyzed Cycloadditions via Ruthenium Allenylidenes

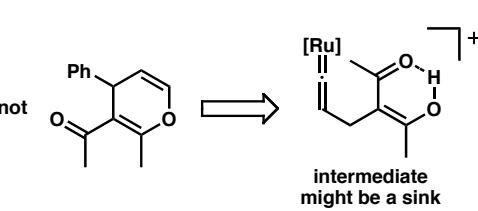
Extension to dicarbonyl compounds: Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Hidai, M.; Uemura, S. *J. Org. Chem. ASAP*



• Limited in scope wrt nucleophile.

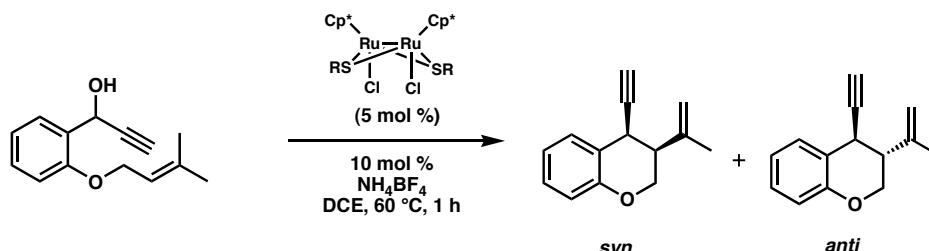
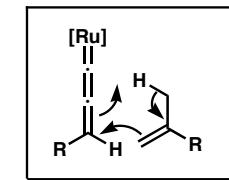
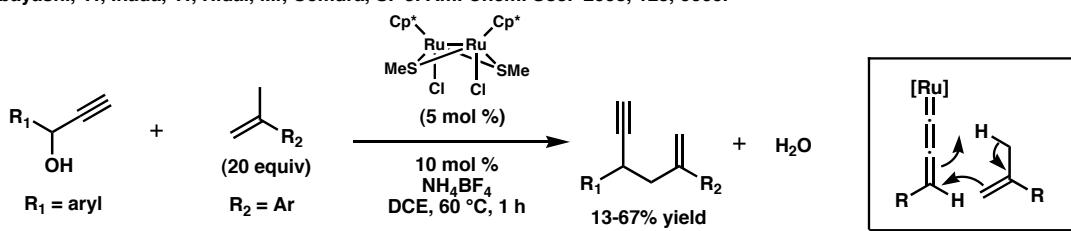


not

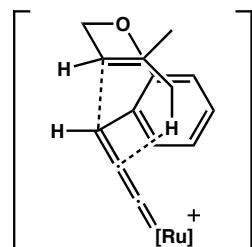


Ruthenium-Catalyzed Carbon-Carbon Bond Formation via an Allenylidene-Ene Reaction

Nishibayashi, Y.; Inada, Y.; Hidai, M.; Uemura, S. *J. Am. Chem. Soc.* 2003, 125, 6060.

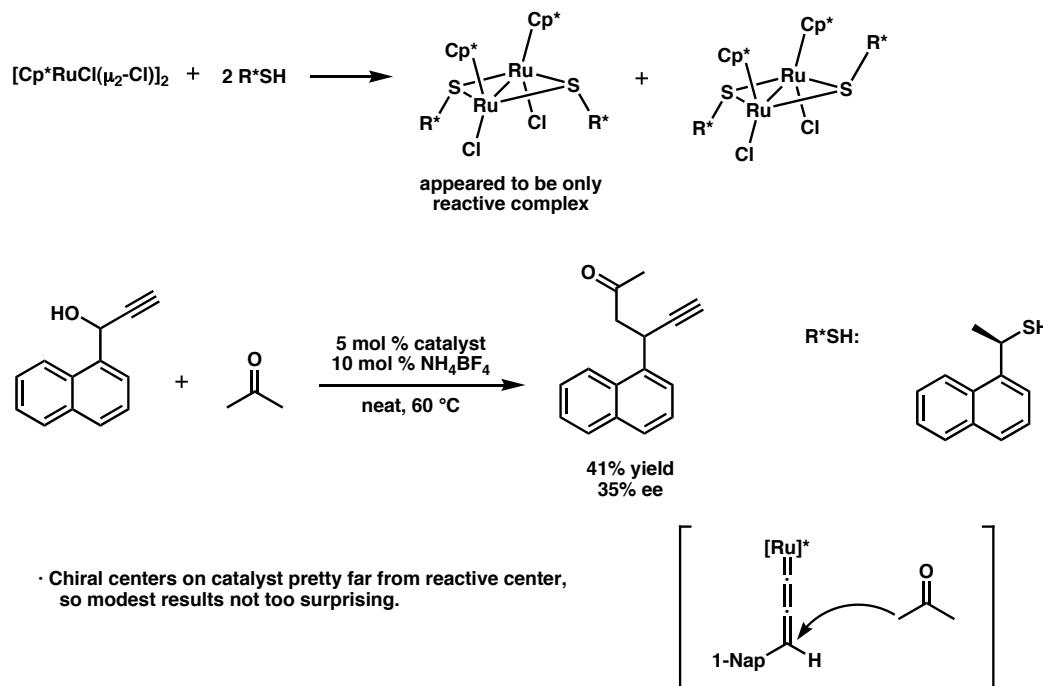


R	time	yield	<i>syn : anti</i>
Me	4 h	74%	3.7 : 1
<i>n</i> -Pr	5 h	84%	7.1 : 1
<i>i</i> -Pr	20 h	74%	19 : 1



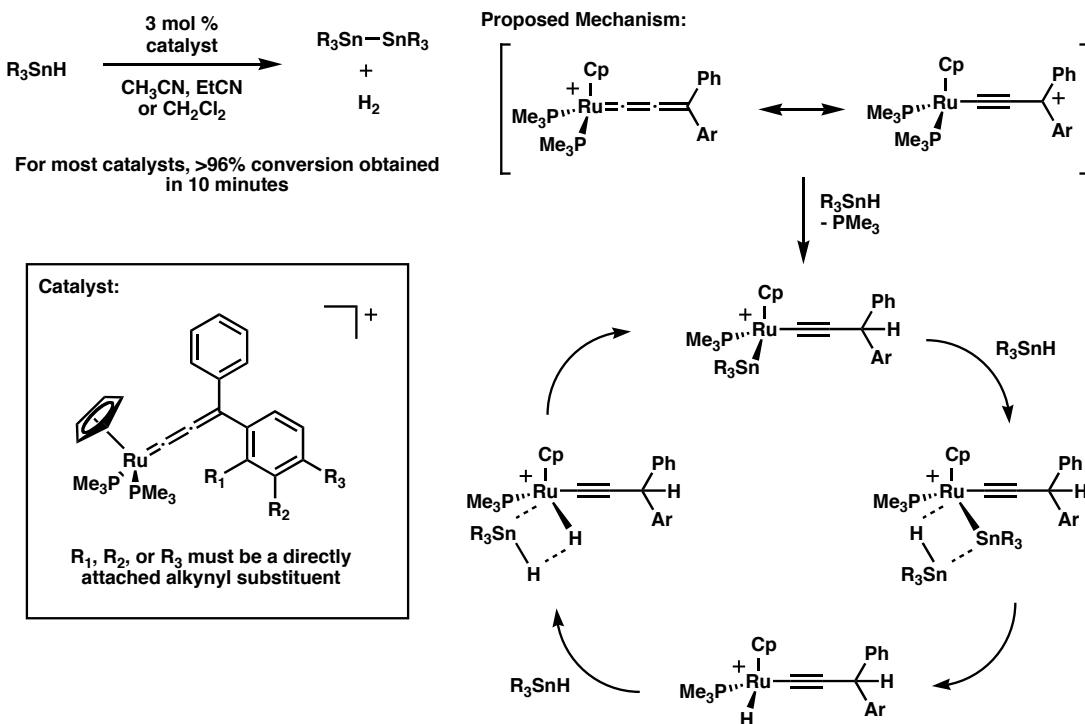
An Attempt at Chiral Propargylic Substitution Reactions

Nishibayashi, Y.; Onodera, G.; Inada, Y.; Hidai, M.; Uemura, S. *Organometallics* 2003, 22, 873.



Dimerization of Tin Hydrides By Ruthenium-Alkenylidene Catalysts

Maddock, S. M.; Finn, M. G. *Angew. Chem. Int. Ed.* 2001, 40, 2138.



Conclusions

- Generation of metal vinylidenes and allenylidenes via terminal alkynes is rather facile.
- However, reactions involving these species are quite limited.
 - Field is simply relatively unexplored.
 - Most systems could just be unreactive or limited in versatility.
 - Catalyst complexes need to be generated prior to reactions, which might discourage/slow investigations
 - Doesn't seem particularly amenable to asymmetric catalysis.
- Most likely scenario is that the area is just very young. General allenylidene synthesis was first reported in 1982, not really implicated as a catalytic intermediate for another 10 years.
- Consequently, vinylidenes and allenylidenes remain an open area of catalytic research.