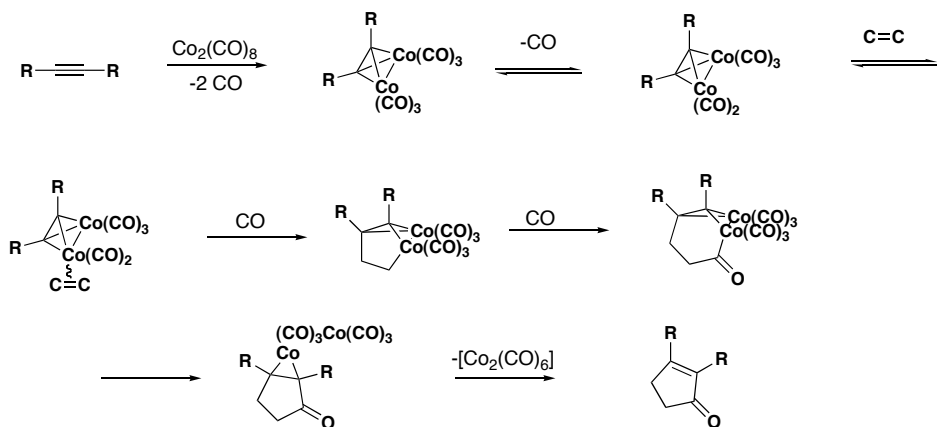


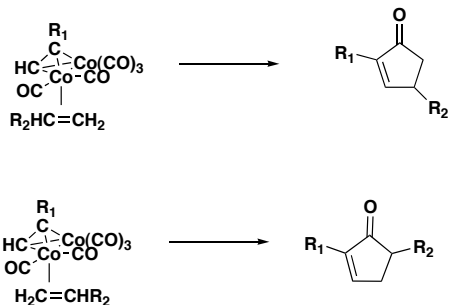
Review: Organic Reactions 1991, 40, 1

- Formal [2+2+1] cyclization of an alkene, an alkyne, and CO to give a cyclopentenone
- Catalyzed by a metal, usually $\text{Co}_2(\text{CO})_8$
- Initially reported by Pauson and Khand in 1973

Proposed Mechanism

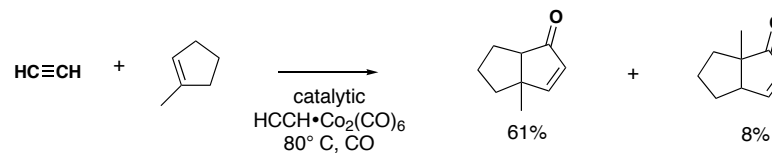


Regioselectivity for Monosubstituted Alkenes and Alkynes

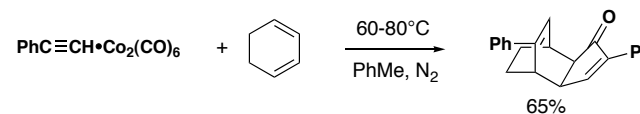


preferred on steric grounds, but only for very large R_1 and R_2

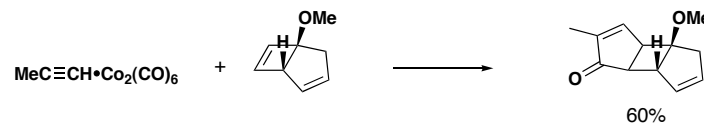
Examples of the Pauson-Khand Reaction



Cyclohexadiene Diels-Alder/Pauson-Khand Cascade



Bicyclo[3.2.0]hept-6-enes react exclusively on *exo* face of the cyclobutene olefin

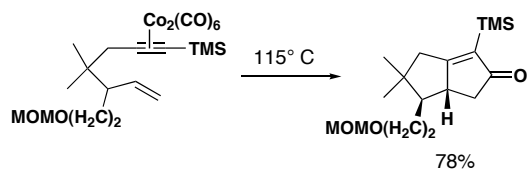


complete regioselectivity observed on steric grounds

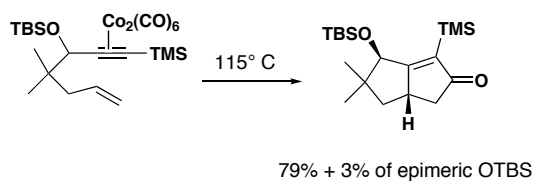
Intramolecular Pauson-Khand

- Intramolecular reactions often generate good yields of [3.3.0] and [4.3.0] systems

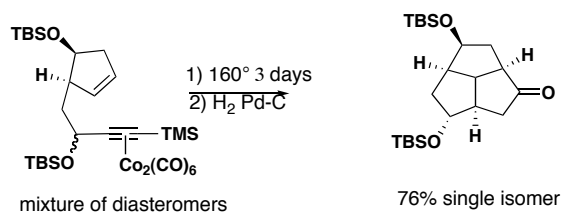
In hept-1-en-6-yne, C-3 and C-5 substituents exhibit a strong preference for the exo face of the product



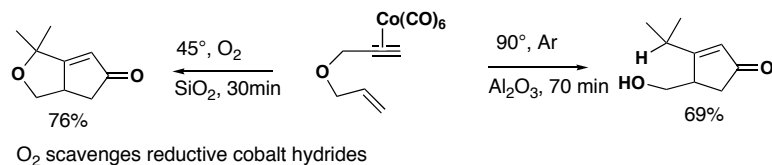
pseudo-1,3-diaxial interaction forces anti-Felkin addition and cis product



- Equilibration of propargylic leaving groups can occur



- Allyl propargyl ethers give good yields in solid phase



Recent Developments

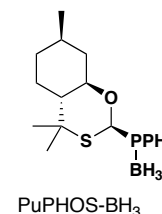
- Catalytic reaction using Co nanoparticles on charcoal (Org. Lett. 4(22), 2002, 3983-3986)

Good yields for intramolecular reaction, intermolecular reaction using norbornadiene

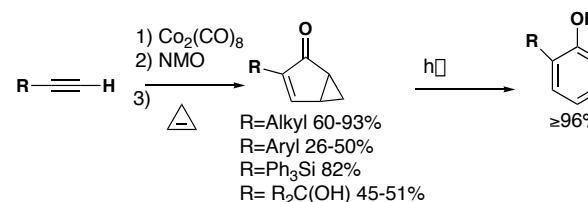
- Asymmetric variant using stoichiometric chiral ligand (JACS, 122(41), 10243)

Initial complexation with Co and alkyne gives 1:1-4.5:1 dr

Reaction with Alkene after separation of diastereomers gives 70-99% ee and $\geq 90\%$ yield with norbornadiene

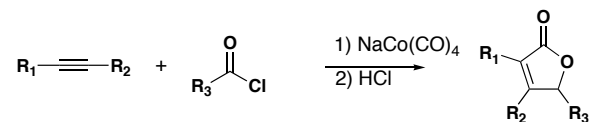


- Synthesis of Phenols (OL, 3(22), 2001, 3193-3196, 3197-3200)

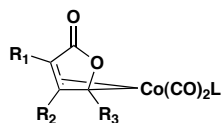
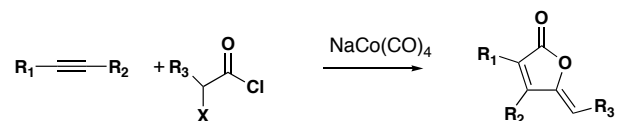


Co Mediated Butenolide Synthesis

TL, 31, 5139-5142, 1990; Synlett, 865-866, 1991.



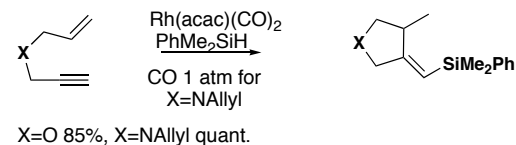
For $R_1=R_2=Et$, yields ranged from 56% ($R_3=neopentyl$) to 92% ($R_3=Pr$)
 For $R_1=Pr$, $R_2=Me$, a 1:1 mixture of regioisomers was obtained
 $R_2=Me$, $R_1=Ph$ or TBS gave >30:1 regioselectivity, but ,50% yield
 $R_1=t-Bu$, $R_2=Me$, $R_3=Et$ gave 91% yield, 20:1 regioselectivity

Reaction proceeds via η^3 -allyl lactonyl complexUse of η^3 -chloro acyl chlorides gives butadienolides

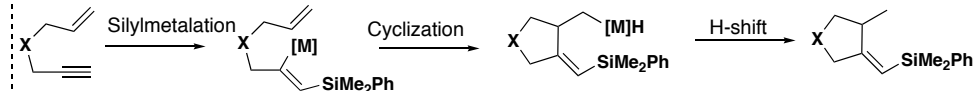
For $R_1=R_2=Et$, yields ranged from 49% ($R_3=Ph$, $X=AcO$) to 85% ($R_3=H$, $X=PhO$)
 For $R_1 \neq R_2$, regioselectivity ranged from 7:1 to 15:1

Rh Catalyzed Silylcarbocyclization

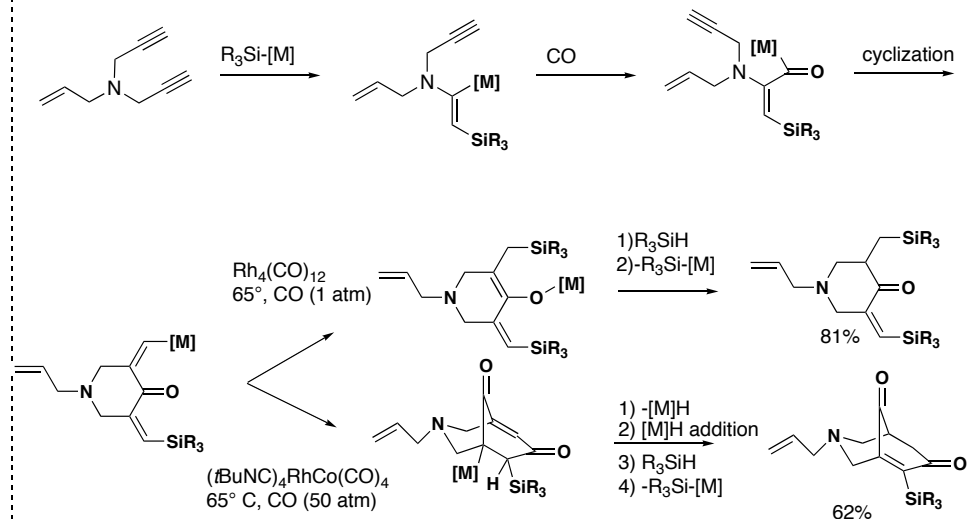
JACS. 1992, 114, 6580-6582



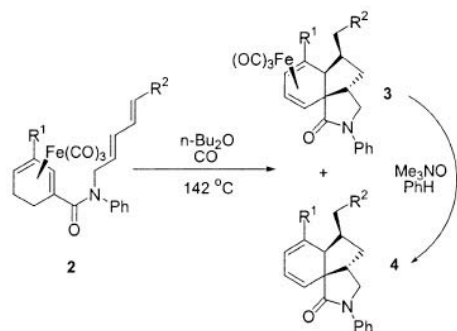
Proposed Mechanism



Silylation-Double Cyclization



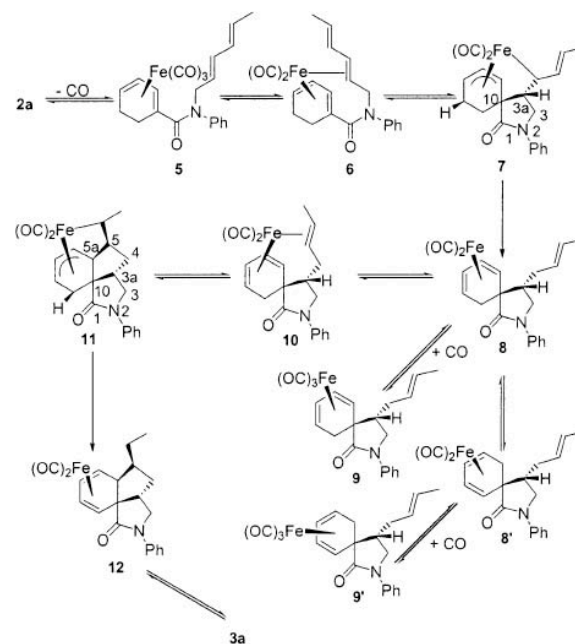
Reaction of polyene- Iron Carbonyl complexes under a CO atmosphere gives tricyclic systems



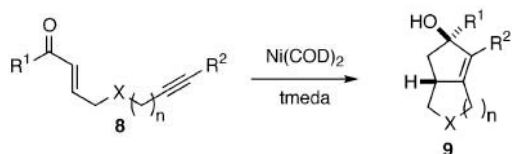
reactant	R ¹ , R ²	time ^a (h)	product	concentration (mol/L) ^b	yield 4 ^c (%)
2a	H, Me	10	4a	0.02	75
2b	OMe, Me	24	4b	0.004	54
2c	H, CO ₂ Me	12	4c	0.004	51
2d	OCH ₃ , CO ₂ Me	24	4d	0.004	34

Reaction tolerates a wide variety of functional groups

Proposed Mechanism

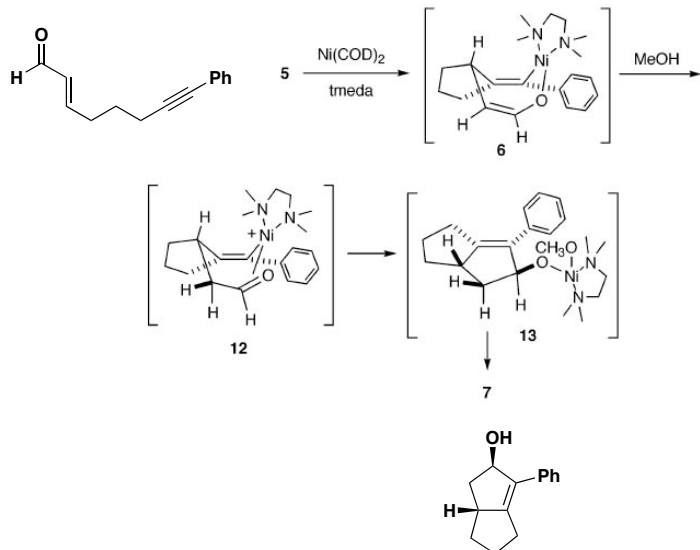


Fe coordinates initial alkene, which causes cyclization and elimination to reform Iron carbonyl-diene complex. This process is repeated with the second alkene to yield the tricyclic system as a single diastereomer.

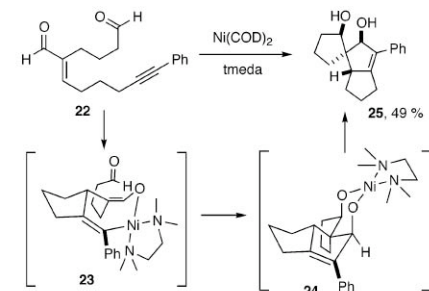
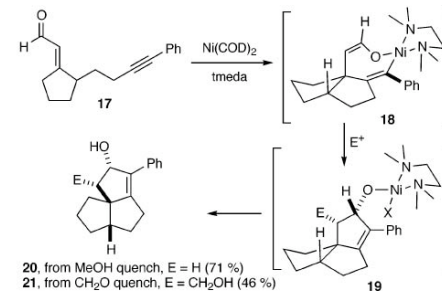


- Reaction gives good (50-80%) yields for X=CH₂ or O, R₁=H or Ph and R₂= Alkyl, Aryl, SiR₃
- Reaction gives poor yields when R₂=H or COCH₃
- Mechanistic experiments, including isolation of initial Nickel enolate, were carried out

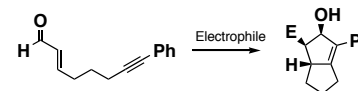
Proposed Mechanism



Multiple Cyclizations

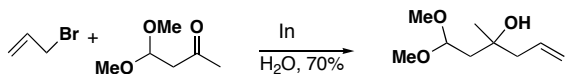


Trapping with Electrophiles



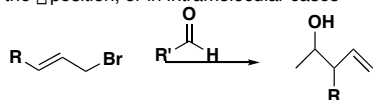
Yields of 68-82% for Alkyl, Allyl, and Benzyl Iodides, Aldehydes, and Acyl Chlorides

Reaction of allyl halides with indium metal yields allylindium reagents, which can react with electrophiles. These reagents are often generated in the presence of the electrophile.

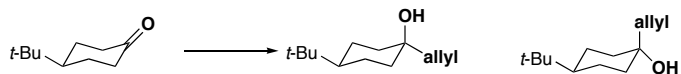


Indium-mediated allylations can be carried out in water and do not require that acidic groups such as hydroxyl be protected.

Attack of allylindium reagent occurs from the β -carbon unless a very bulky (R_3Si , or tBu) substituent is in the α -position, or in intramolecular cases.

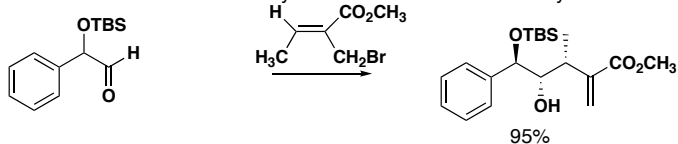


Diastereoselectivity in addition to cyclic substrates is far superior to that of Grignard reagents.



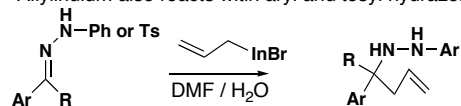
Synthesis, 2003, 633-655

Excellent diastereoselectivity has also been observed in acyclic cases.

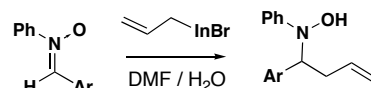


Synthesis, 2003, 765-774.

Allylindium also reacts with aryl and tosyl hydrazones and aldonitrone



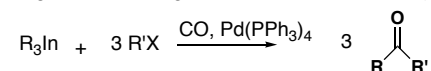
75-90% for R=H, Me, or Ph, fails for aliphatic hydrazones



75-90%

Tet. Lett. 41, 2000, 9311-9314

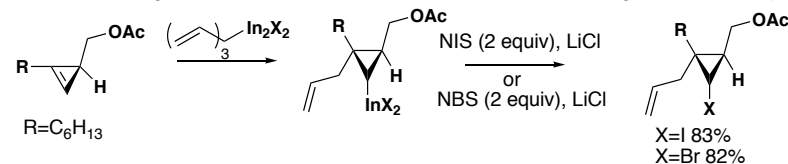
Organoindium reagents can be used in carbonylative couplings with aryl and vinyl halides and triflates.



70-94% for R= Ph, PhCC, Me, or Bu, R'=Aryl or Vinyl, X=Br, I, or OTf

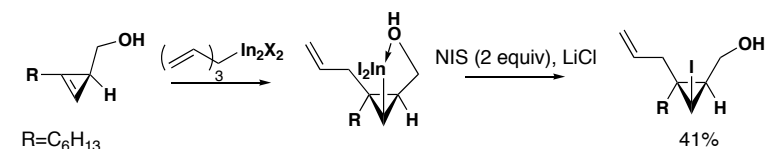
Synthesis, 2003, 780-784.

Allylindium reagents can be also be used for the *syn* allylation / halogenation of cyclopropenes.



Halogen is transferred from Indium, use of 1 equiv. NIS gave X=H (86%)

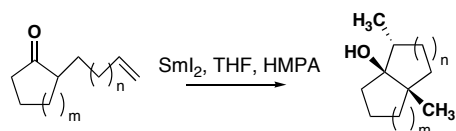
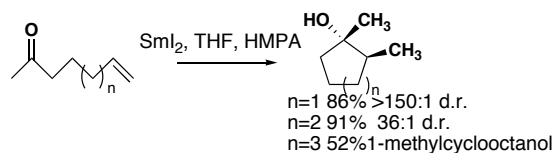
If OAc replaced by a directing group, addition is *syn*



Tet. Lett. 43, 2002, 8033-8035.

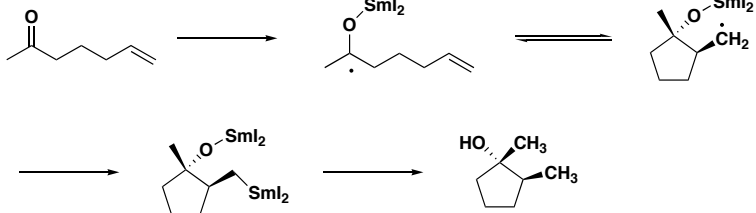
Radical Cyclizations

Samarium(II) easily loses an electron to form a stable Samarium (III) species. It is therefore a good stoichiometric radical initiator.

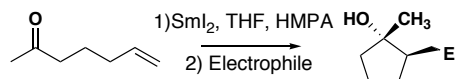


yields 85-92% for n and $m = 1$ or 2
 good d.r. except for $m=n=2$ (2:1:1)
 reaction fails when $n=0$

Mechanism



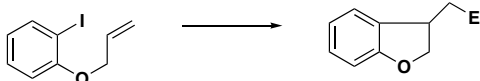
Resulting samarium grignard can also be trapped by electrophiles



Yields 65-83% for a wide range of electrophiles, including ketones, aldehydes, anhydrides, CO_2 , O_2 , and $\text{CH}_2\text{NMe}_2^+\text{I}^-$

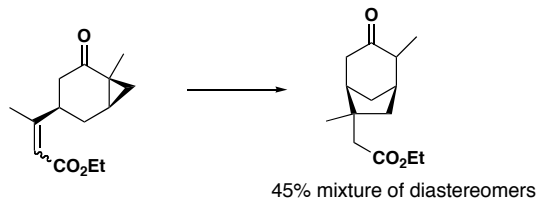
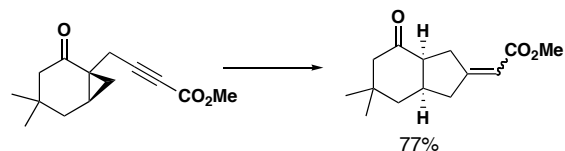
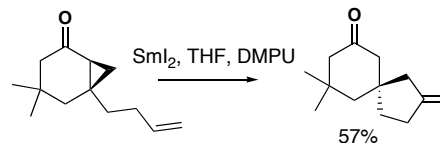
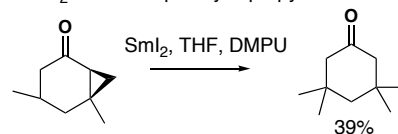
JOC. **1992**, *57*, 3132-3139

Other combinations of substrates and electrophiles are possible

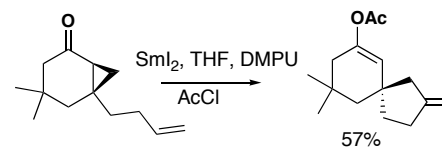


Yields of 55-96% for ketones, I_2 , Bu_3SnI , PhNCO , $(t\text{PrO})_2\text{O}$, $(\text{PhS})_2$, $(\text{PhSe})_2$
JACS, **1992**, *114*, 6050-6058

Sml_2 can also open cyclopropyl ketones



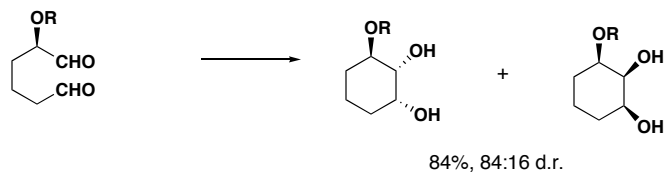
The resulting samarium enolate can be trapped with electrophiles



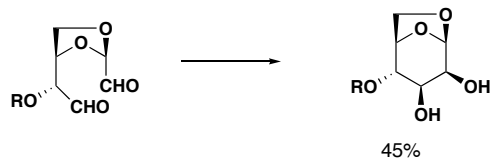
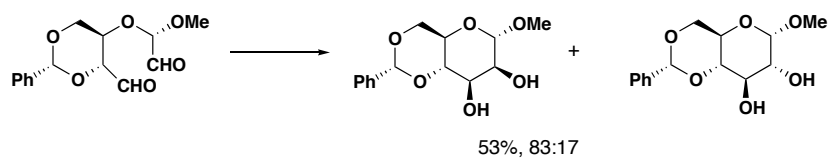
Tet. Lett., **32**, 6649-6652, **1991**.

SmI₂ Initiated Pinacol Couplings

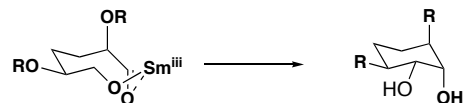
Ketyl radicals generated by SmI₂ can undergo intramolecular pinacol coupling



This reaction can be used to synthesize carbohydrate-like structures

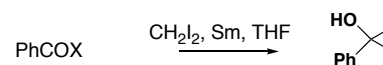


Preferred orientation of resulting diol groups is *syn* and *anti* to neighboring alkoxy substituents. This implies a 9 membered ring controls diol stereochemistry.



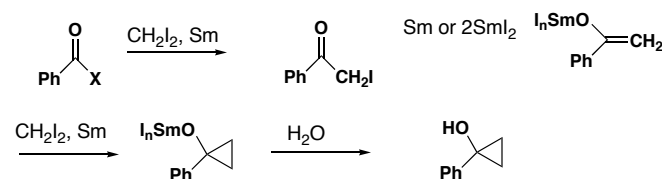
Tet. Lett. 32, 1125-1128, 1991.

One-Carbon Homologation of Esters to Cyclopropanols

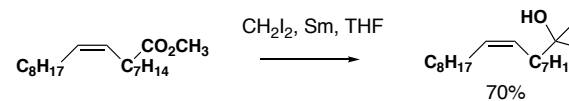
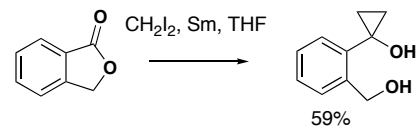


76% optimized yield for X=OEt, low unoptimized yields for X=O*i*Pr, Cl, S*Bu*, NMe₂, and OH acid chlorides undergo competitive coupling to diketones and acylins

Proposed Mechanism:

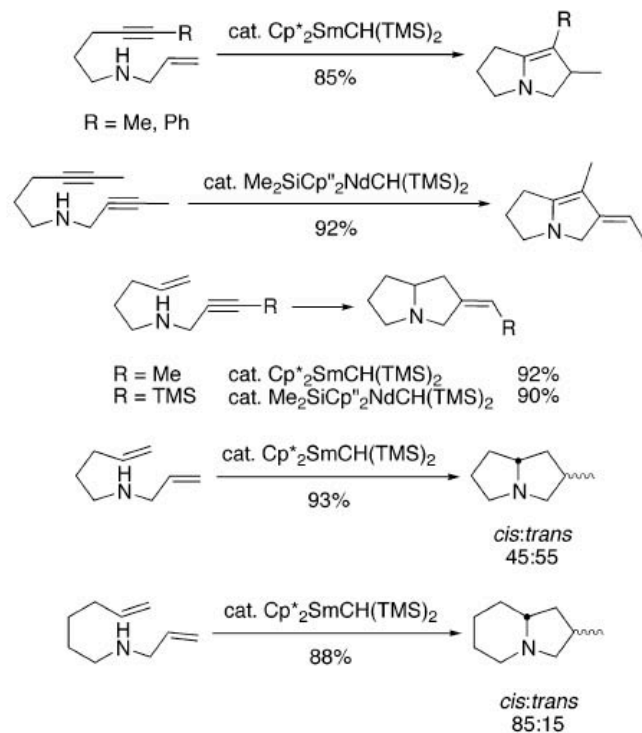


Other Substrates:

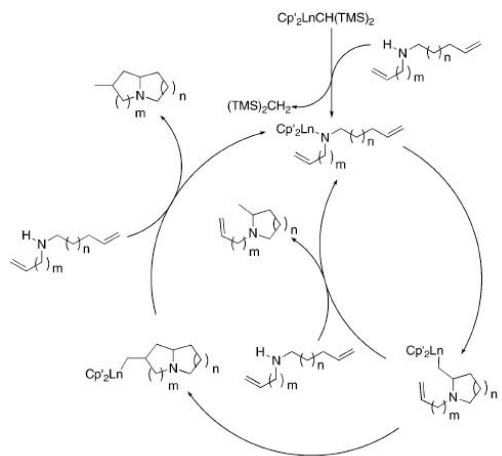


Tet. Lett. 30, 5149-5152, 1989.

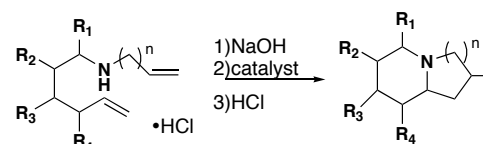
Samarium complexes catalyze the cyclization of dienes and enynes to bicyclic structures



Proposed Mechanism



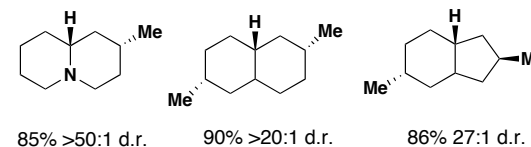
Formation of Quinolizidines and Indolizidines



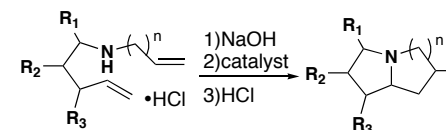
catalyst = $\text{Cp}_2\text{NdCH}(\text{TMS})_2$, $\text{Cp}_2\text{SmCH}(\text{TMS})_2$,
 $\text{Me}_2\text{SiCp}_2\text{NdCH}(\text{TMS})_2$, or $[\text{Cp}^{\text{TMS}}_2\text{NdCH}_3]_2$

Yields were 80-90% for monomethyl compounds, $n=1$ or 2
 d.r. was high for Me at R_1 or R_2 , low for Me at R_3 or R_4

Stereochemistry of Various Products



Formation of Indolizidines and Pyrrolizidines

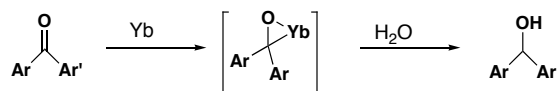


Yields were 83-91% for monomethyl compounds, $n=1$ or 2
 d.r. was high for $\text{R}_1=\text{Me}$, $n=2$, moderate for $\text{R}_3=\text{methyl}$, $n=2$,
 low for others

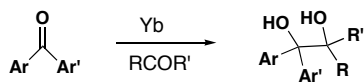
J. Org. Chem. **2003**, *68*, 9214-9220.

Ytterbium mediated umpoled addition of ketones to electrophiles

Yb metal is known to reduce ketones to alcohols

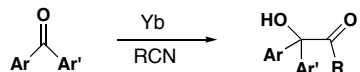


The ytterbo-oxocyclopropane intermediate can be trapped by electrophiles



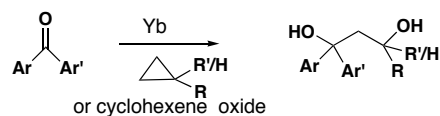
Yields are generally >80%, except with acetone
small amounts of diaryl alcohol are also formed

Trapping with nitriles gives acyloins after aqueous workup



Yields are generally >75%, except with acetonitrile
small to moderate amounts of diaryl alcohol is formed

Trapping with epoxides yields 1,3-diols

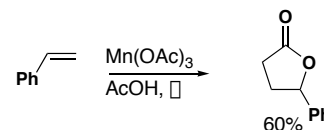


Yields were 40-75%, propylene oxide and styrene oxide
gave attack at more substituted carbon, isobutylene oxide
wa attacked at less substituted position

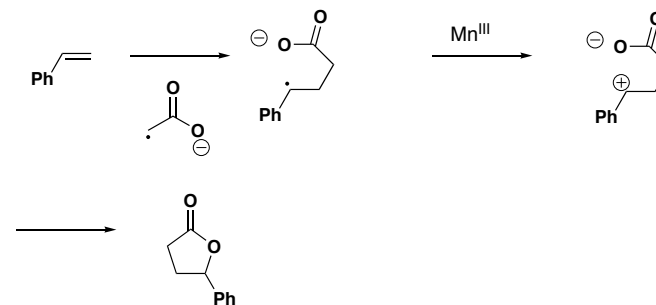
Diphenylacetylene and Acetaldehyde were attacked in good yield
Phenyl isocyanide and Dimethylformamide gave moderate yields
of the hydroxy amide and hydroxy aldehyde, respectively

JOC. **1988**, *53*, 6077-6084.

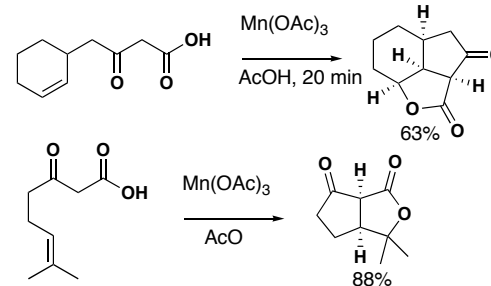
Mn^{III} Promoted Lactonization of Olefins



Reaction Proposedly Proceeds the Generation of an acetate radical anion



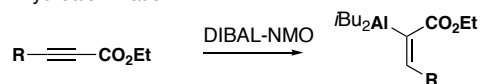
This method allows for the generation of complex bi- and tri-cyclic lactones



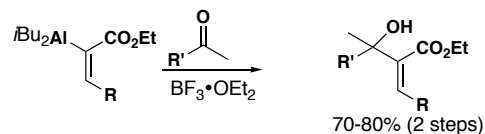
JACS. **1984**, *106*, 5384-5385

Aluminum promoted Baylis-Hillman Alternative

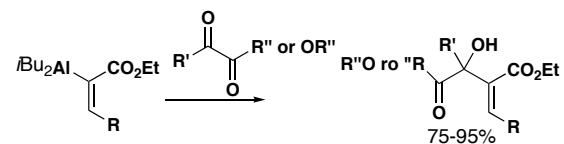
Complexation of DIBAL with NMO prevents reduction of esters and allows hydroalumination



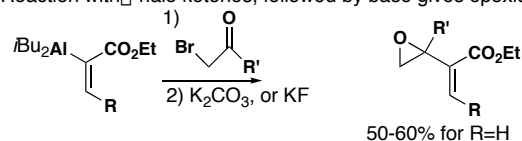
These reagents can be trapped with ketones, α -keto esters, and α -halo ketones



Succeeds with 2-butanone, which fails under Baylis-Hillman Conditions



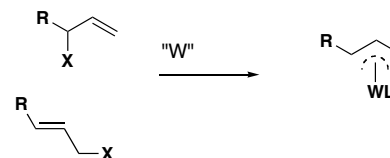
Reaction with α -halo ketones, followed by base gives epoxides



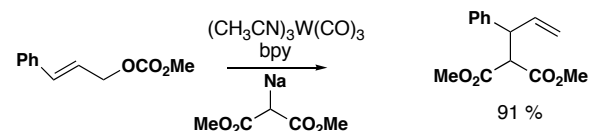
J. Org. Chem. **2003**, *68*, 9310-9316

Tungsten-Catalyzed Allylic Alkylations

Tungsten carbonyl compounds are known to form π -allyl complexes with allyl halides



These complexes undergo attack by nucleophiles in a manner similar to Pd complexes. Regioselectivity is reversed however; attack occurs at the most substituted carbon

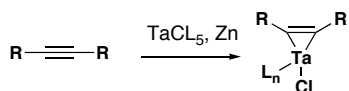


A large variety of aryl substituted allyl halides were tested, yields were mainly >80% in most cases >95% regioselectivity was observed

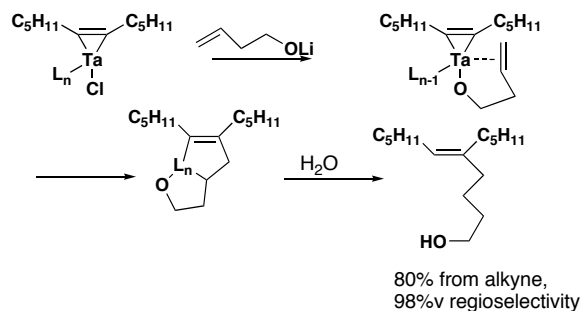
JACS, **115**, **1983**, 7757-7759.

Insertion of Homoallylic Alkoxides Into Tantalum-Alkyne Complexes

Tantalum-alkyne complexes can be generated from TaCl_5 and alkynes

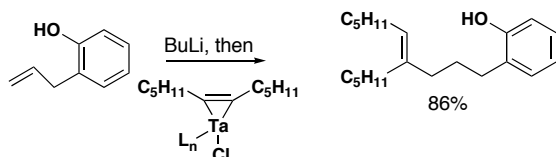


Normal alkenes fail to insert into these complexes, but do when a directing group is present to coordinate to the Tantalum



Multiple olefins were tested: substitution on the double bond lowered yields dramatically, but substitution elsewhere gave yields 70-80%. Addition of a third methylene between the alkene and alkoxide had little or no effect on yields

A phenol was also tested

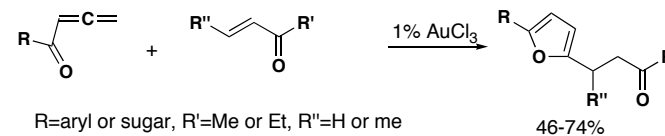


JOC, 59, 1994, 5852-5853

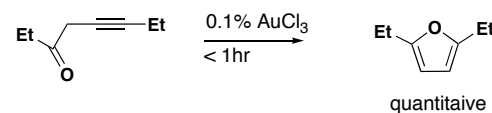
Gold Catalyzed Furan Formation

Although some stoichiometric gold reactions are known, there are surprisingly few Gold-catalyzed reactions

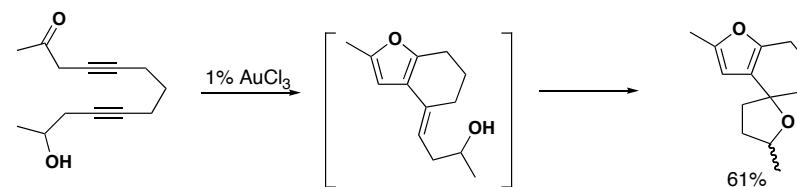
AuCl_3 catalyzes the formation of furans from keto allenes or keto alkynes



R=aryl or sugar, R'=Me or Et, R''=H or me



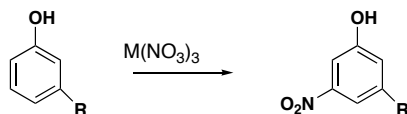
Multiple Cyclizations are possible



Angew. Chem. Int. Ed. 2002, 39, 2285-2288

Lanthanide Nitrate Nitration of Phenols

Lanthanide Nitrates are known to nitrate phenols



M=La, Ce, Sm, Dy, Ho

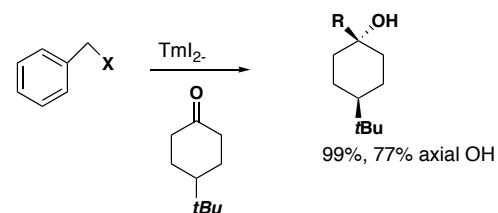
Yields ranged from 60-85%

R groups included NO₂, Me, Cl, OH, NHCOCH₃, CO₂H, OMe

Syn. Comm. 27, 2793-2797, 1997

Thulium Coupling of Alkyl Halides

Thulium Diiodide acts in a similar manner to SmI₂, but is more powerful



Yields were > 97% for RX where R= Me, Bu and X=Cl, Br, or I

JACS. 2002, 122, 2118-2119.

