Low Valent Group 4 Metal Complexes of Alkenes and Alkynes in Synthesis

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Denmark Group Meeting

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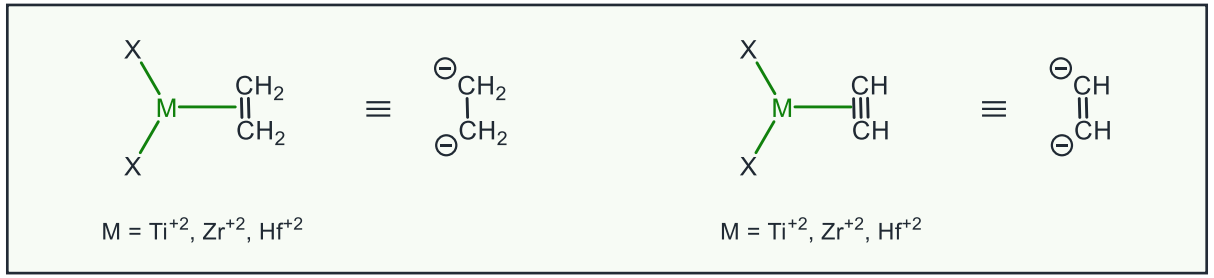
Purpose of This Presentation

- Get acquainted with low oxidation state **Ti** and **Zr** olefin complexes:
  - Electronic structure and properties
  - Methods for generating said compounds
  - Fundamental reactivity principles

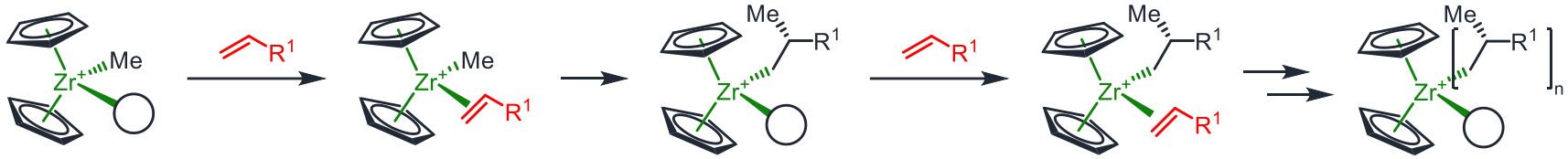
- Understand the consequences of “reducing” alkene/alkyne activation
  - Metal-olefin vs metallacyclopropane
  - Generating reactive organometallics
  - Stoichiometric and catalytic processes

- See a few examples ranging from total syntheses to industrial scale applications.

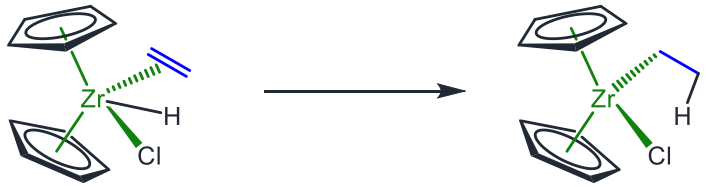


Related Topics not Covered Herein

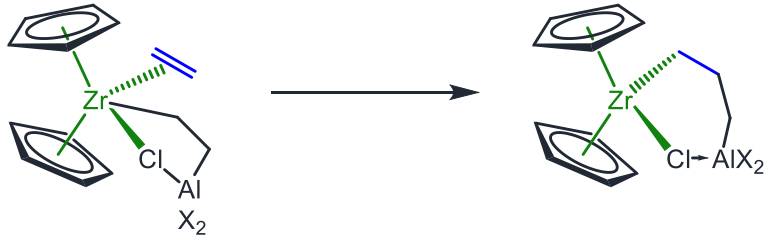
1. Alkene polymerization (Ziegler-Natta)



2. Alkene/alkyne hydrozirconation (Schwartz) / hydrotitanation



3. Alkene/alkyne hydroalumination, ZACA (Negishi)



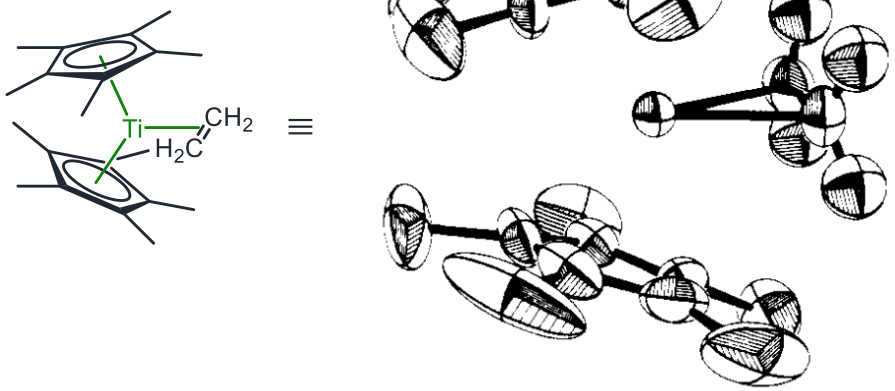
4. Hafnium metal

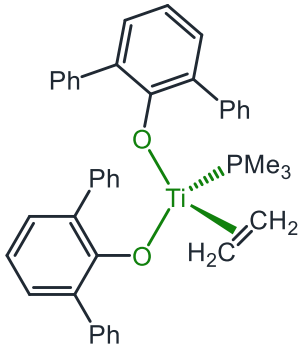
Part 1.
Structure and Bonding.

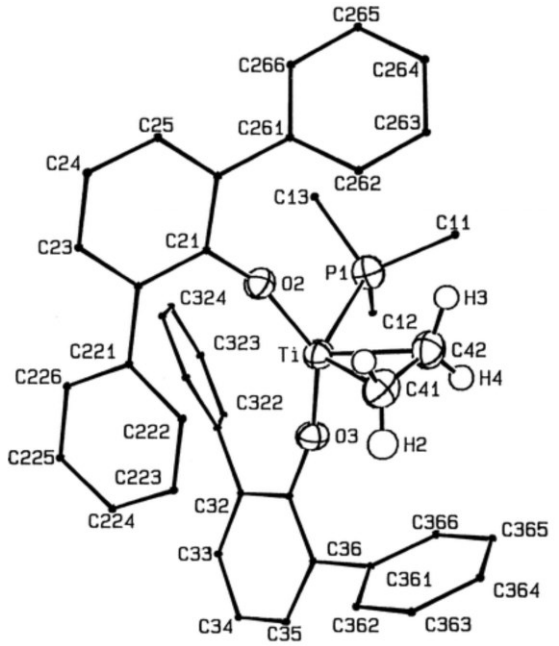
- Orbital and electronic picture of ethylene bonding
- Chemical consequences
- Olefin exchange

Experimental SCXRD Structure of M-ethylene complex

- Crystal structure of $Cp^*_2Ti(C_2H_4)$ was the first Ti-olefin complex isolated and characterized.



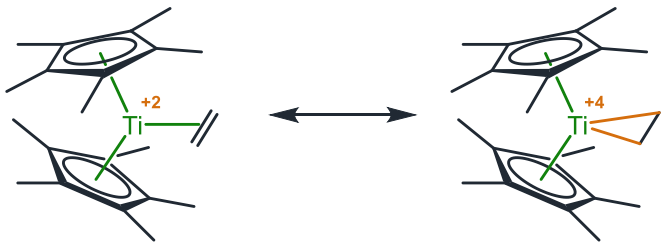




Both complexes exhibit structural features that indicate low π-bond character

Cohen SA, Auburn PR, Bercaw JE. *J. Am. Chem. Soc.* **1983**, *105* (5), 1136–1143.
Thorn MG, Hill JE, Waratuke SA, Johnson ES, Fanwick PE, Rothwell IP. *J. Am. Chem. Soc.* **1997**, *119* (37), 8630–8641.

Experimental SCXRD Structure of M-ethylene complex



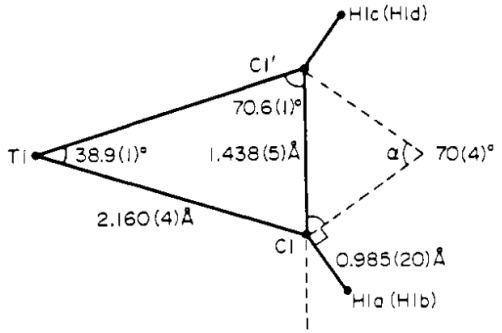


Table VI. Structural Data for Selected Ethylene and Heterocyclopropane Compounds

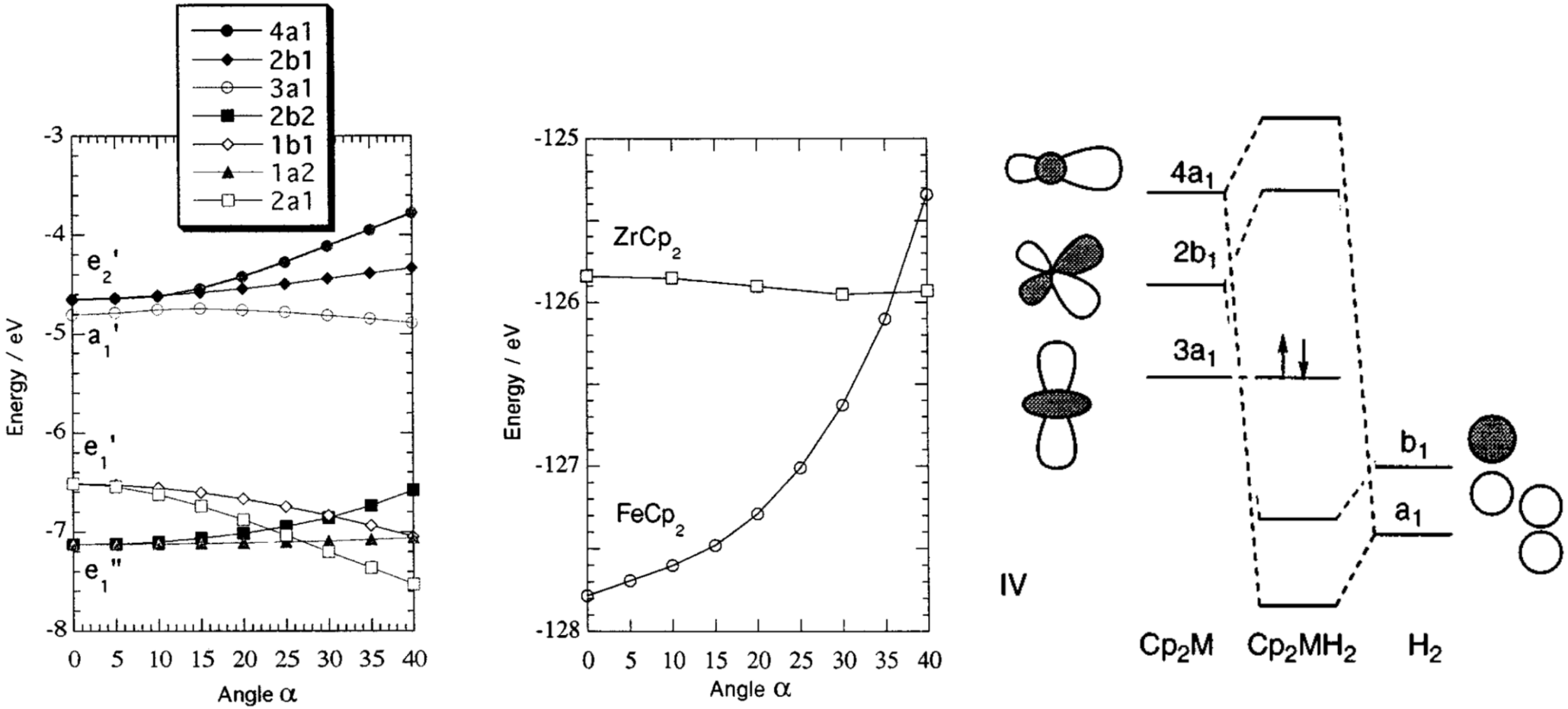
compound	C–C, Å	C–H, Å
C_2H_4	1.337 (2)	1.103 (2)
$(\eta\text{-}C_5H_5)Rh(\eta\text{-}C_2F_4)(\eta\text{-}C_2H_4)$	1.358 (9)	0.956 (40)
$(\eta\text{-}C_5H_5)Rh(SO_2)(\eta\text{-}C_2H_4)$	1.366 (5)	0.95 (10)
$KCl_3Pt(\eta\text{-}C_2H_4)\cdot H_2O$	1.375 (4)	1.087 (7)
$(PMe_2Ph)_2RuCl_2(CO)(\eta\text{-}C_2H_4)$	1.376 (10)	0.92 (18)
$(\eta\text{-}C_5H_5)_2Nb(C_2H_5)(\eta\text{-}C_2H_4)$	1.406 (13)	0.98 (14)
$(\eta\text{-}C_5Me_5)Rh(PPh_3)(\eta\text{-}C_2H_4)$	1.408 (16)	0.90 (5)
$(PPh_3)_2Ni(\eta\text{-}C_2H_4)$	1.431 (15)	
$(PPh_3)_2Pt(\eta\text{-}C_2H_4)$	1.434 (13)	
$(\eta\text{-}C_5Me_5)_2Ti(\eta\text{-}C_2H_4)$	1.438 (5)	0.985 (20)
$[(o\text{-}CH_3C_6H_4O)_3P]_2Ni(\eta\text{-}C_2H_4)$	1.46 (2)	
$(\eta\text{-}C_5Me_5)Ta(CHCMe_3)(PMe_3)(\eta\text{-}C_2H_4)$	1.477 (4)	1.090 (8)
$\overline{CH_2CH_2S}$	1.484 (3)	1.083 (2)
$\overline{CH_2CH_2PH}$	1.502 (5)	1.093 (5)

Bond distance indicates that the structure is 70% of the way between ethylene and thiirane

Hence, ***Titanacyclopropane***

Cohen SA, Auburn PR, Bercaw JE. *J. Am. Chem. Soc.* **1983**, *105* (5), 1136–1143.

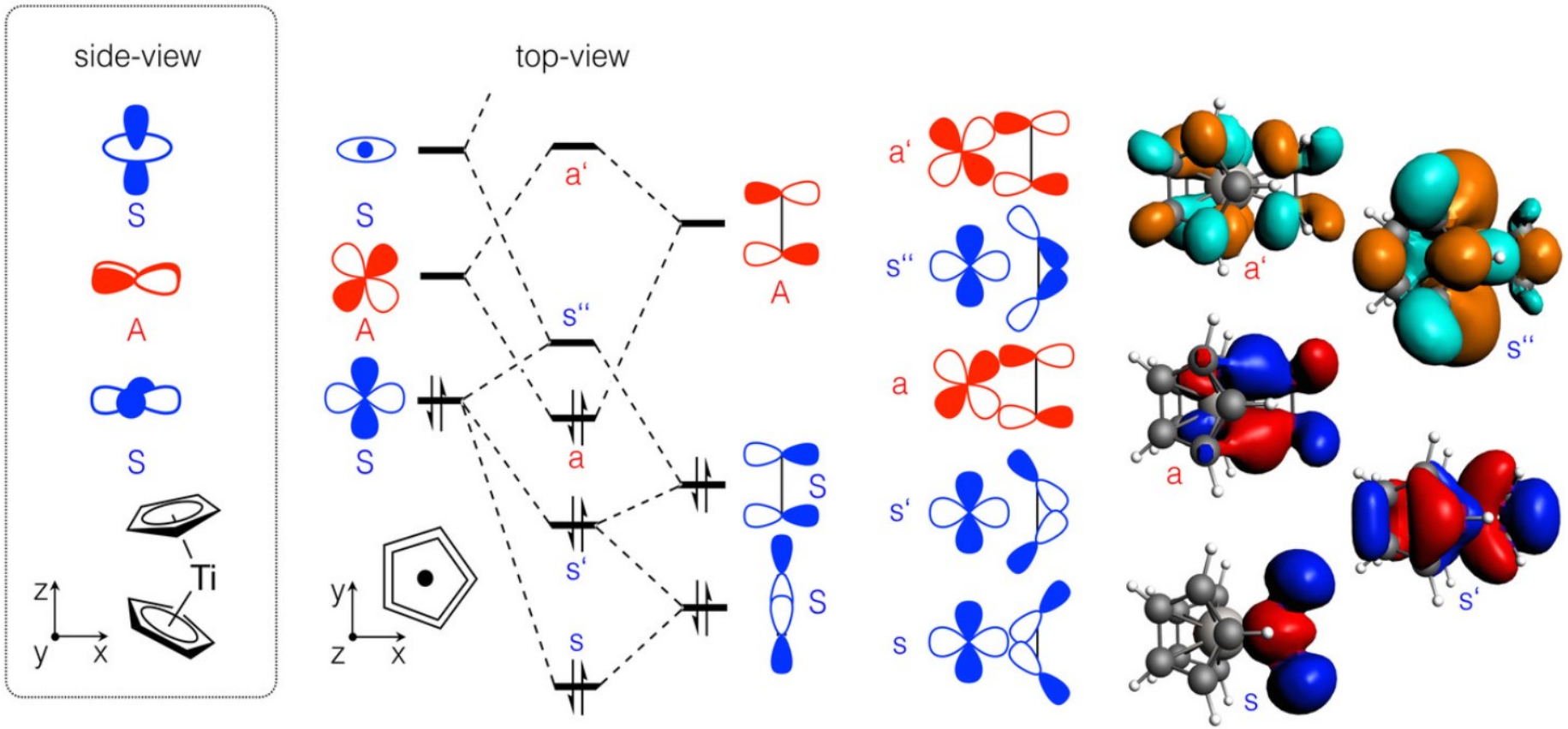
Electronic Structure of Bent Metallocenes



$4a_1$ and $2b_1$ orbitals are primary contributors to bonding.

Green JC. *Chem. Soc. Rev.* **1998**, *27* (4), 263–272.

Electronic Structure of Bent Metallocenes



a *and* ***s*** *molecular orbitals are both filled. Their antibonding couterparts are not.*

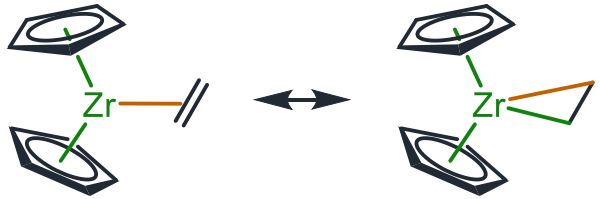
Total bond order is then close to 2.

Gordon CP, Andersen RA, Copéret C. *Helvetica Chimica Acta* **2019**, *102* (9), e1900151.

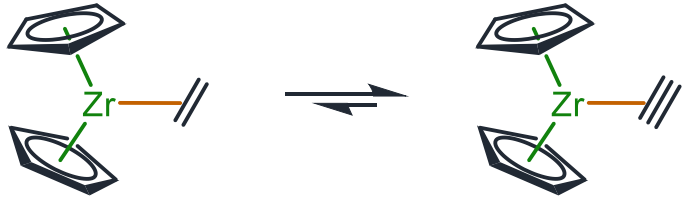
Summary of the Electronic Structure

1. Group 4 metallocenes have 2 empty orbitals and one nonbonding d orbital available for bonding
    1. Coordination number of 1 – 3 are known and realizable.

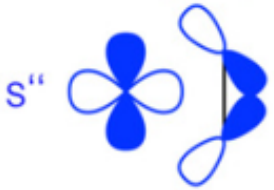
2. Very strong backbonding disrupts the pi bonding in alkenes to a significant extent
    1. Very strong evidence for dominant metallacyclopropane behavior
    2. Yet there is still “normal” olefin behavior



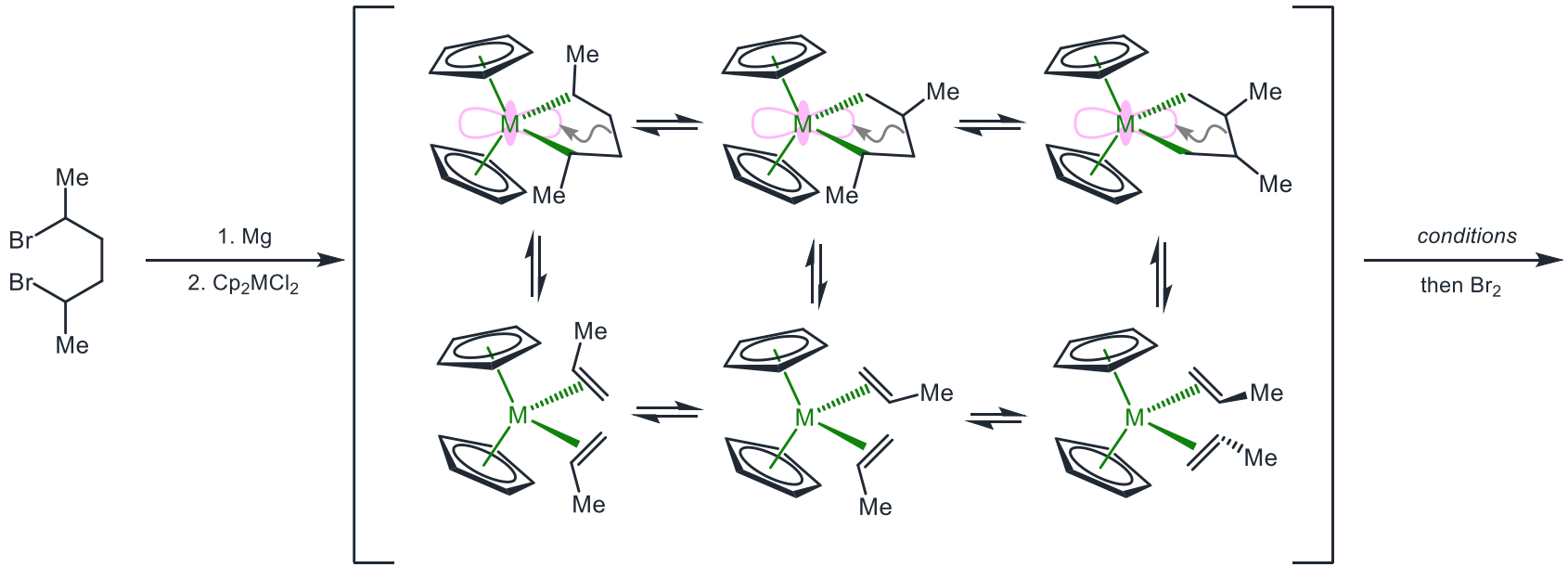
3. Alkynes bind stronger than alkenes (but not irreversibly)
    (higher s-character in the M-C bonds, higher electronegativity)



4. Nonbonding vacant orbital is very important for the reactivity.
    Later it will be shown how it likely participates in hydride elimination and



Group 4 Metallacyclopentanes: Dynamic Structures

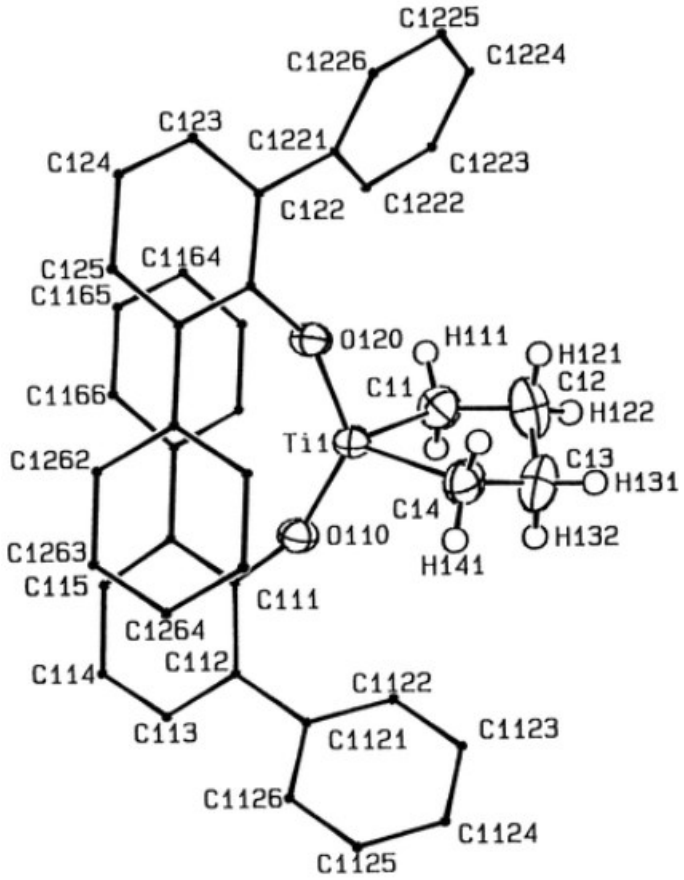


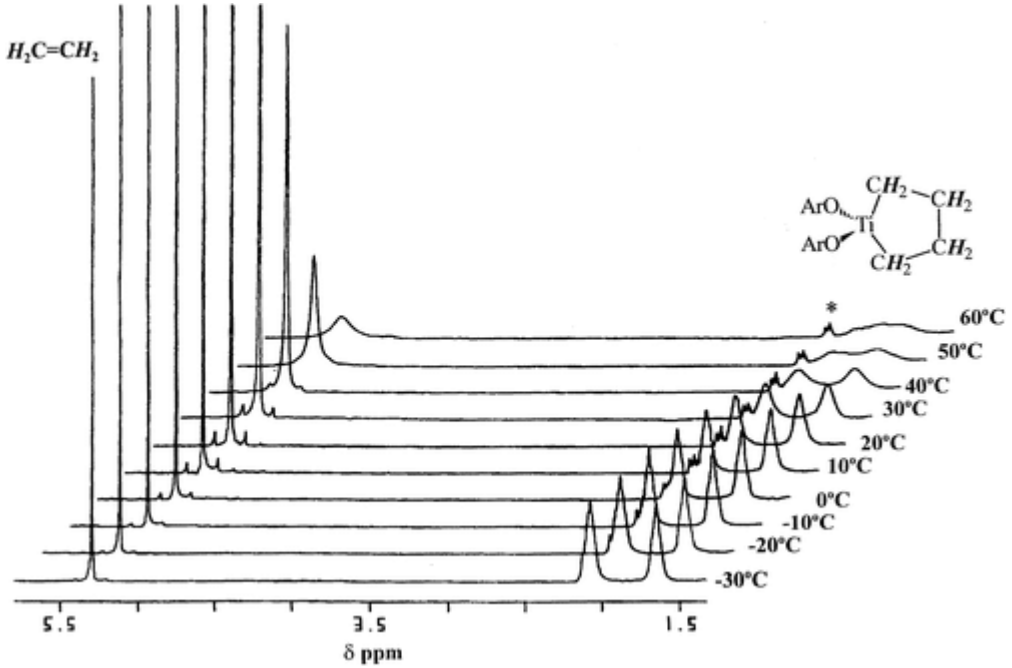
The equilibrium is heavily shifted because of steric repulsions between Cp ligands and the methyl groups.

Zircona and hafnacyclopentanes are dynamic structures due to facile rupture of β,γ-C—C bond that is positioned next to the vacant orbital

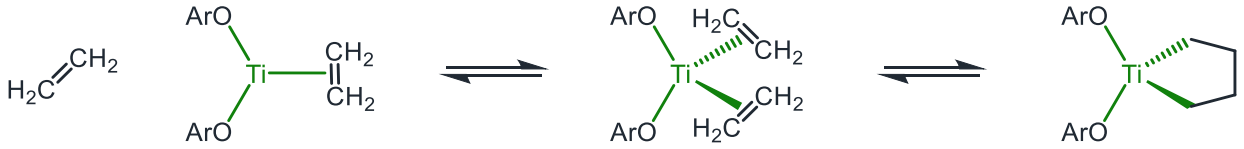
Takahashi T, Fujimori T, Seki T, Saburi M, Uchida Y, Rousset CJ, Negishi E. *J. Chem. Soc., Chem. Commun.* **1990**, No. 2, 182–183.

DNMR Picture of Equilibrium





$$\Delta G^{\neq} = 15.9 \text{ kcal mol}^{-1}$$

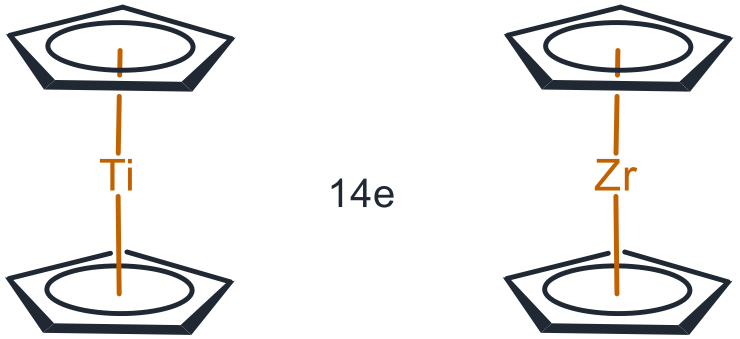


Titanacyclopentanes also exhibit dynamic behavior.

Note phenoxide ligands (not Cp or Cp)*

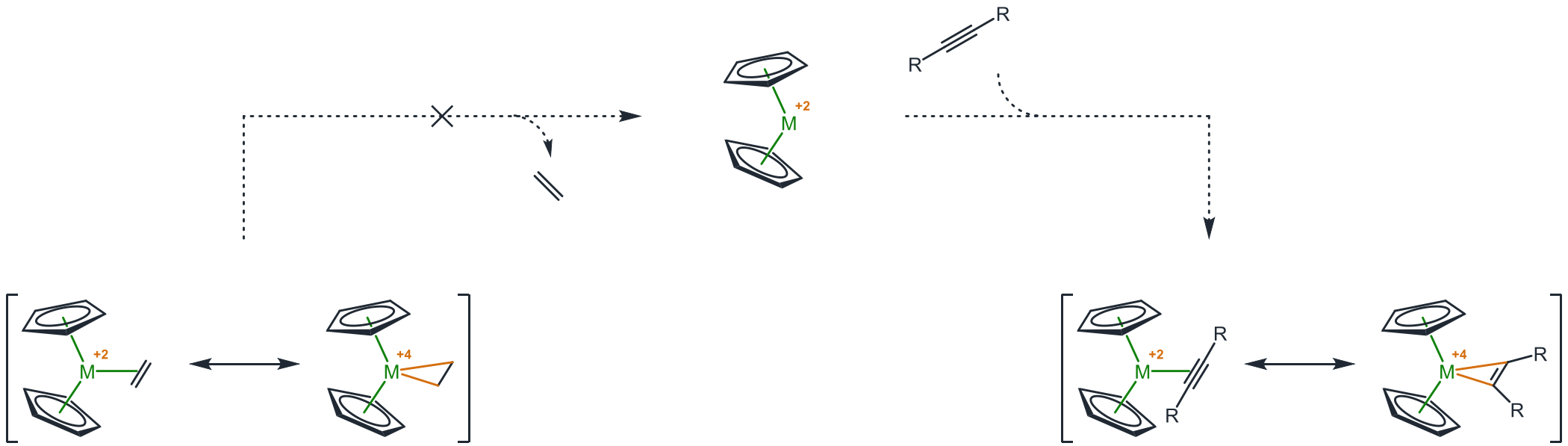
Thorn MG, Hill JE, Waratuke SA, Johnson ES, Fanwick PE, Rothwell IP. *J. Am. Chem. Soc.* **1997**, *119* (37), 8630–8641.

Existence of “Naked” Group 4 Metallocenes



- **There is no experimental proof that “naked” Group 4 metallocenes exist.**
- Calculations suggest that zirconocene has a triplet ground state.
- Cp_2Ti and Cp_2Zr are predicted to be bent in the ground state.

Associative Olefin Substitution Mechanism



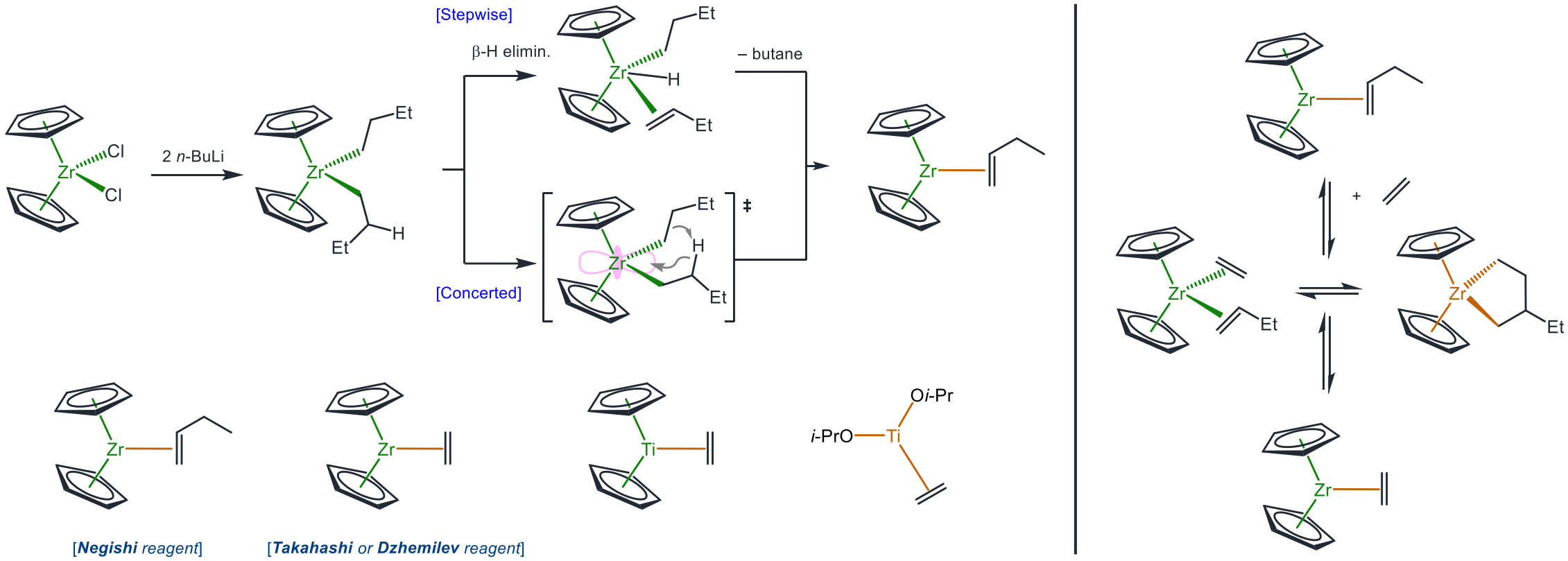
Group 4 metals undergo olefin ligand metathesis with associative mechanism.

This avoids invoking “naked” metallocene intermediates.

Part 2.
Reactivity of *Complexes* with Alkenes and Alkynes

- Preparation of the complexes
- Allylic functionalization
- Diene, enyne and diyne cyclizations
- Carbometalations

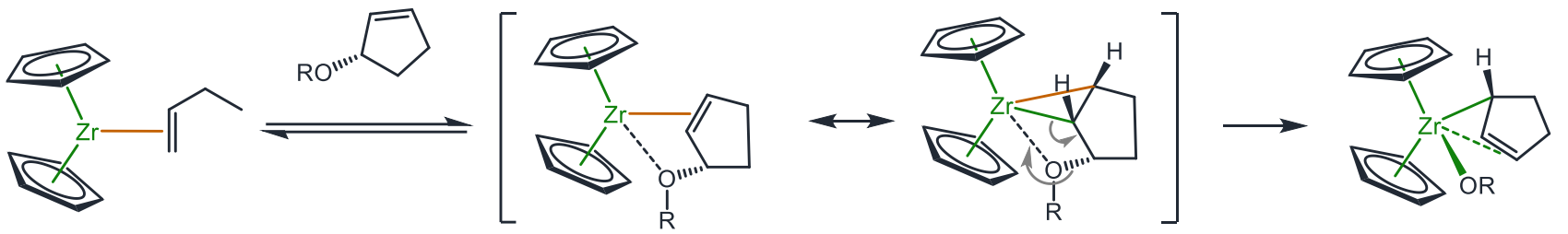
Preparation of Metal-Olefin Complexes

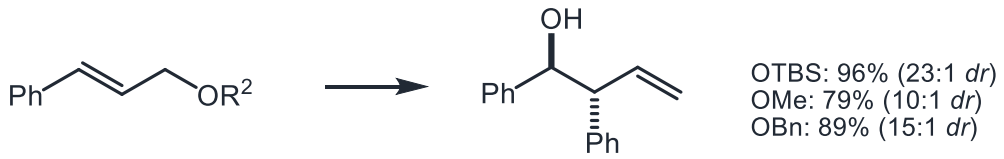


Due to reactivity and instability, these reagents are generated in situ from readily available metallocene dichlorides or isopropoxide. Alkene or alkyne ligands can then be exchanged via an associative pathway. ***Q: How to escape metallacyclobutane?***

Negishi E, Cederbaum FE, Takahashi T. *Tetrahedron Letters* **1986**, *27* (25), 2829–2832.

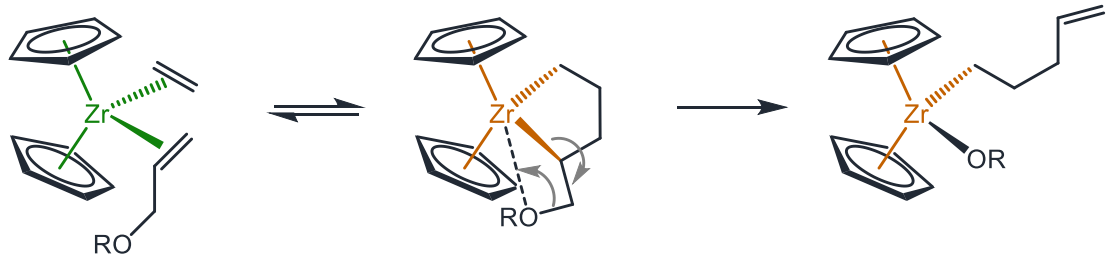
Escaping Metallacyclopentane: β-Elimination as the Driving Force





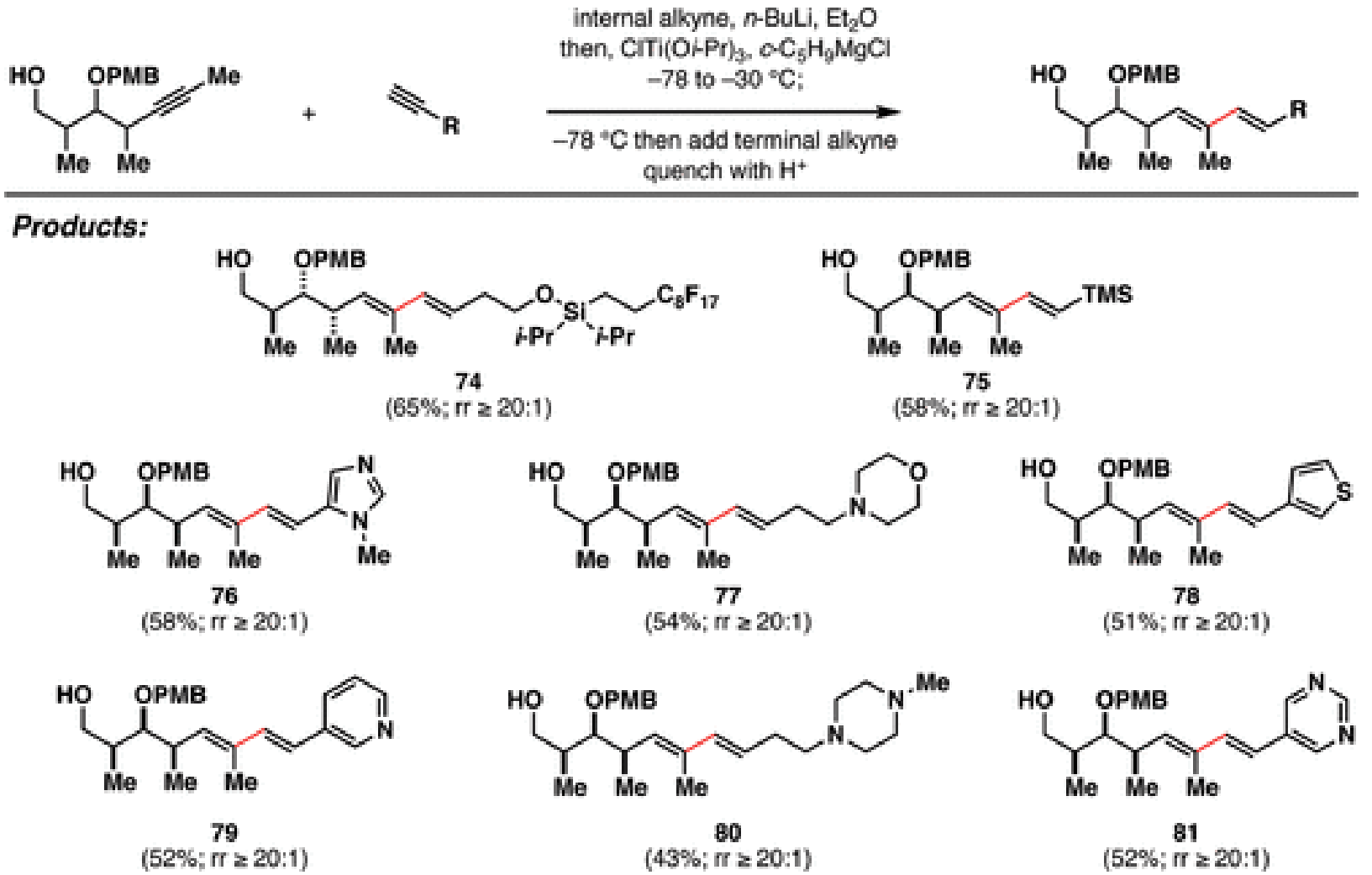
OTBS: 96% (23:1 *dr*)
OMe: 79% (10:1 *dr*)
OBn: 89% (15:1 *dr*)

- *Syn* oxidative addition allows to activate simple allyl ethers (OMe, OAlkyl, OTBS, etc)
- Predominantly σ-bound, but can undergo facile metallotropic shifts (η^1–η^3–η^1)
- The latter intermediate is quite similar to allylzinc



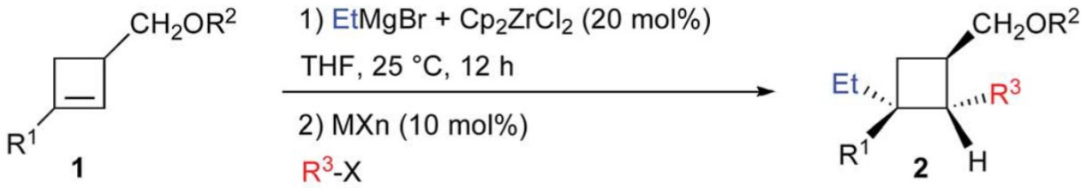
Adjacent alkoxide moiety stabilizes proximal isomer of metallacyclopentene and allows subsequent β-elimination

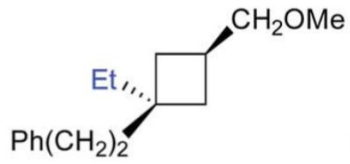
Alkyne Reductive Coupling



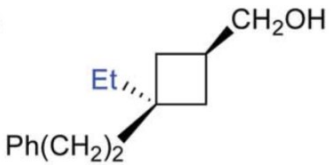
Perez LJ, Shimp HL, Micalizio GC. *J. Org. Chem.* **2009**, *74* (19), 7211–7219.

Mg–Zr Exchange: Carbomagnesiation

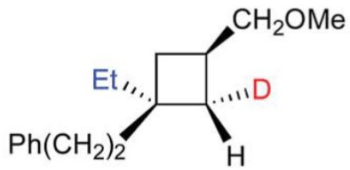




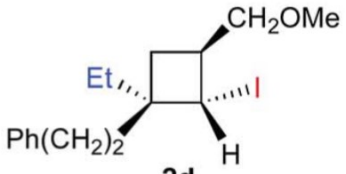
2a
82%
dr >98:2



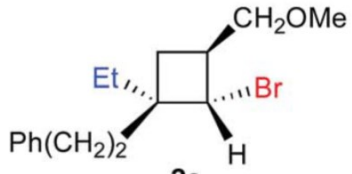
2b
64%
dr >98:2



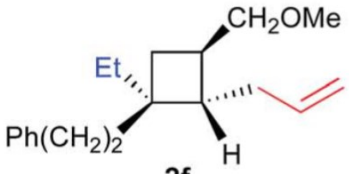
2c
80%
dr >98:2:0:0



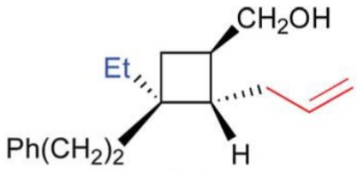
2d
67%
dr 92:8:0:0



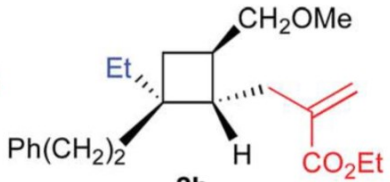
2e
58%
dr 93:7:0:0



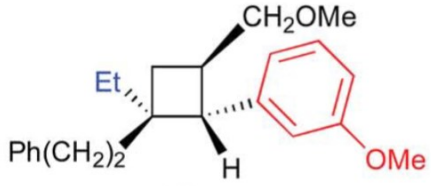
2f
72%
dr >98:2:0:0
(after transmetalation to Cu)



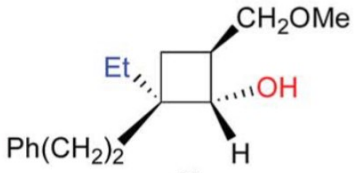
2g
66%
dr 90:10:0:0
(after transmetalation to Cu)



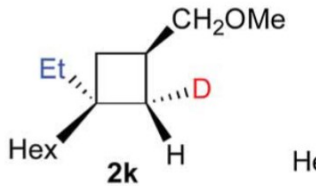
2h
71%
dr >98:2:0:0
(after transmetalation to Cu)



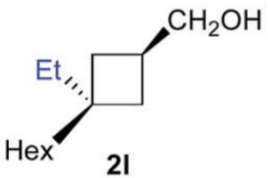
2i
58%
dr 93:7:0:0
(after transmetalation to Cu and Pd)



2j
67%
dr >98:2:0:0
(after transmetalation to Zn)



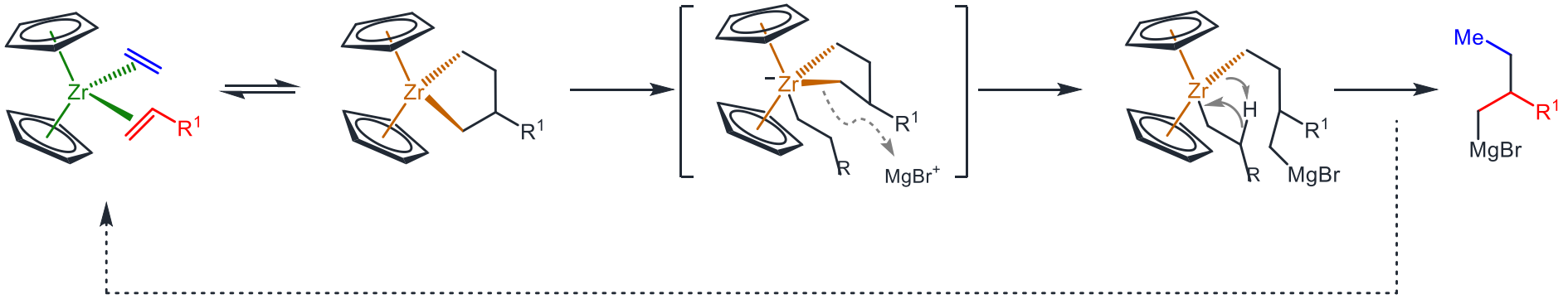
2k
80%
dr >98:2:0:0

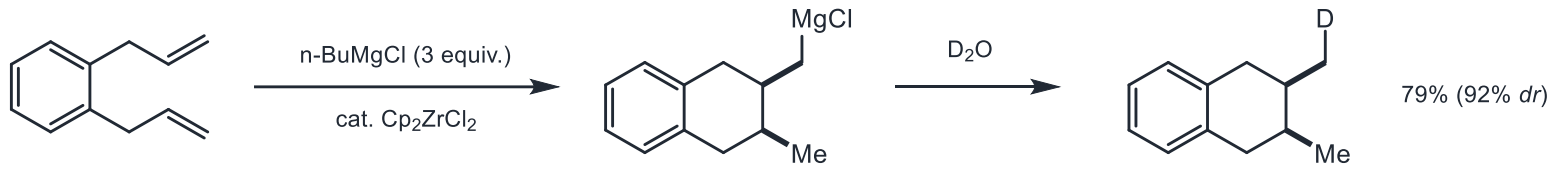


2l
69%
dr 94:6:0:0

Roy SR, Eijsberg H, Bruffaerts J, Marek I. *Chem. Sci.* **2016**, *8* (1), 334–339.

Escaping Metallacyclopentane: Transmetalation

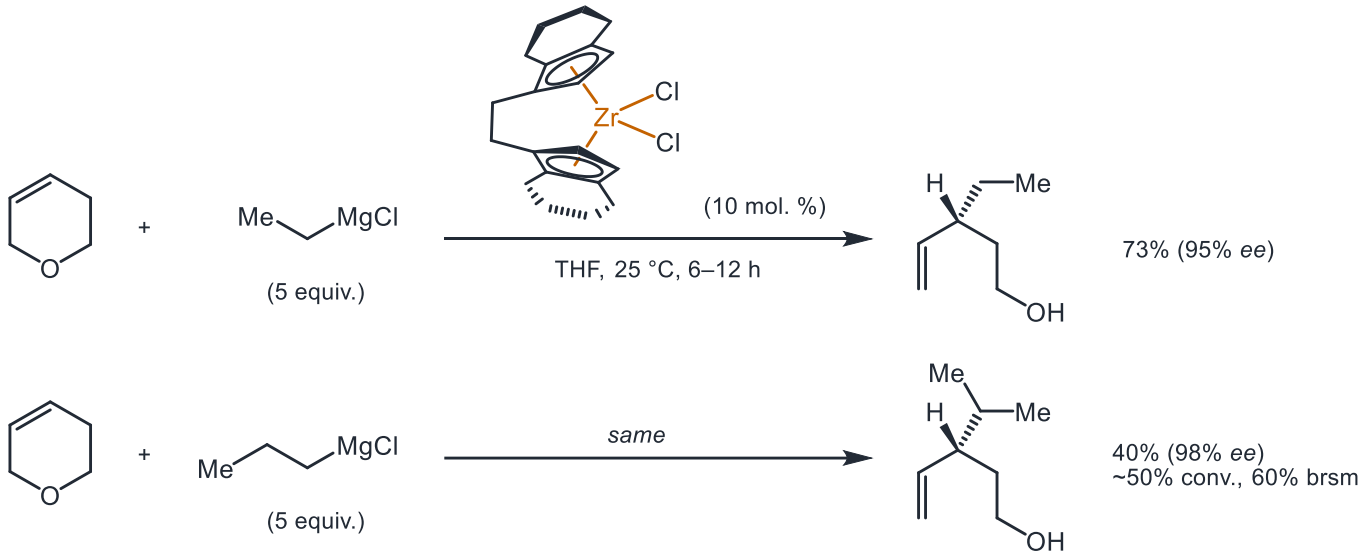




While the transmetalation seems to go in an unfavorable direction, subsequent hydride elimination makes the reaction irreversible.

Group Problem 1

1. Propose a mechanism for the following transformation.
2. Identify the mechanistic reason and the driving force for the propyl group isomerization.
3. Propose a stereochemical model to explain observed selectivity.
4. Identify the stereodetermining step.

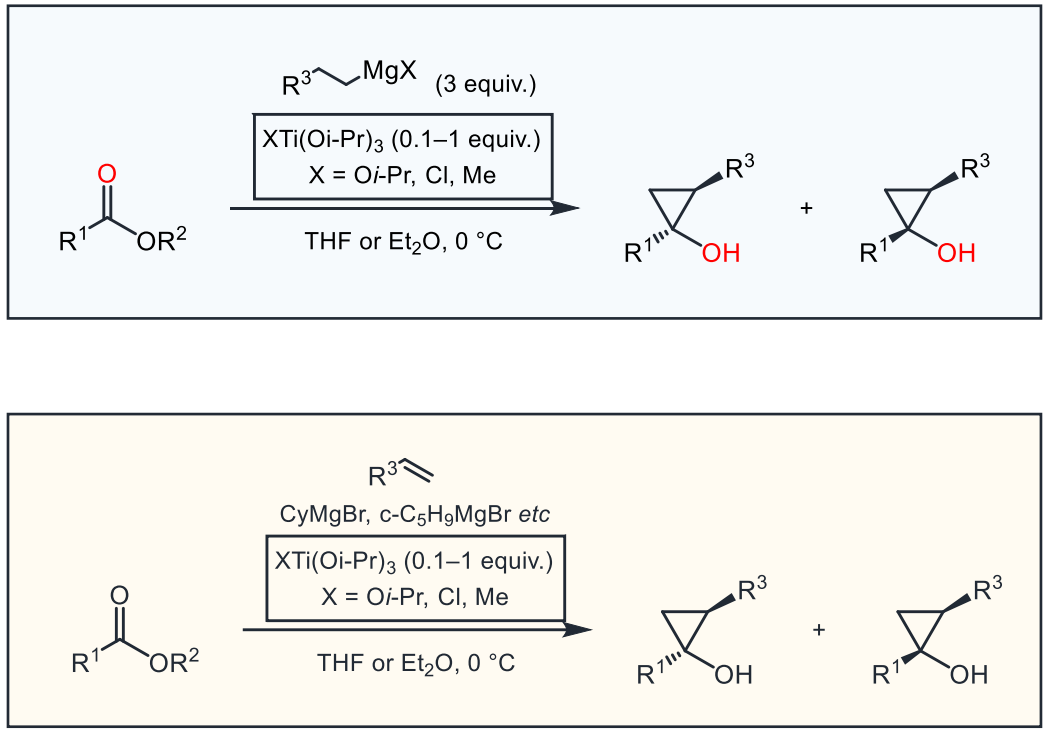


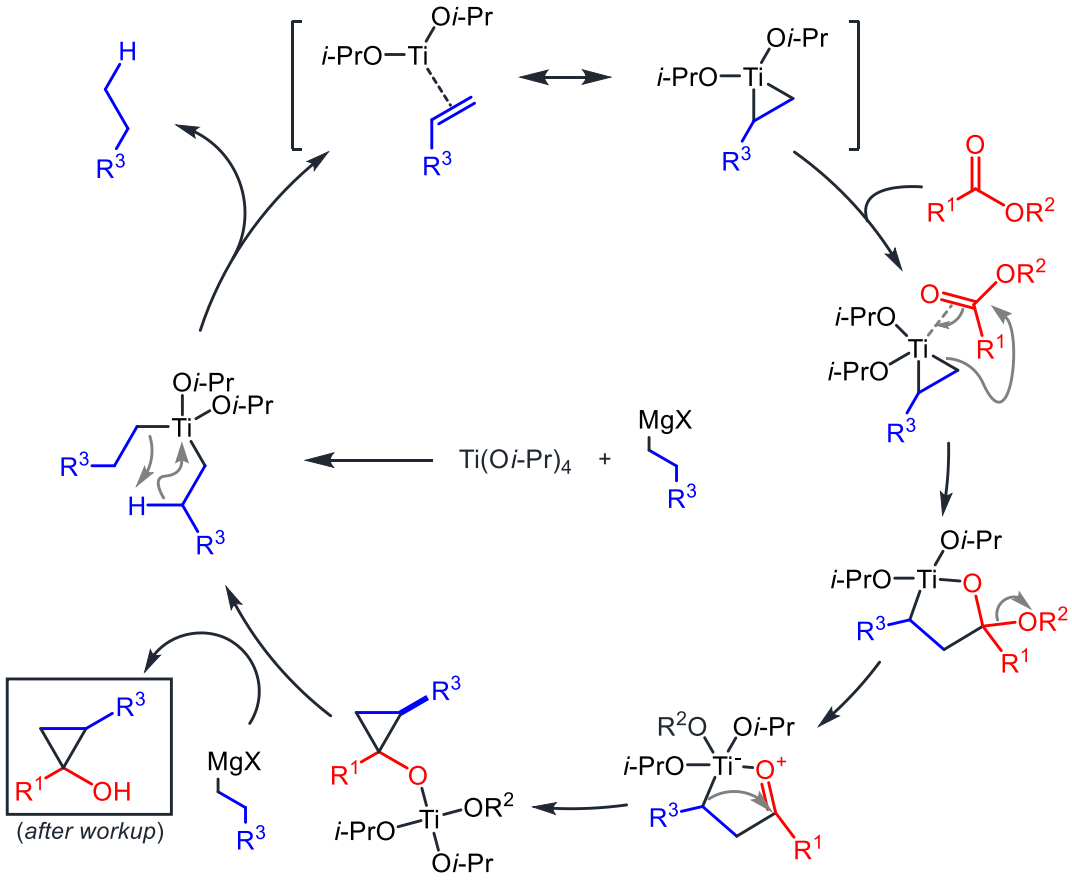
[Group Problem 1: Answer Key]

Part 3.
Reactivity of *Complexes* with Carboxylic Acid Derivatives

- Kulinkovich reaction (+ de Meijere, Szymoniak)
- Intramolecular Nucleophilic Acyl Substitution

Kulinkovich Cyclopropanation + Mechanism



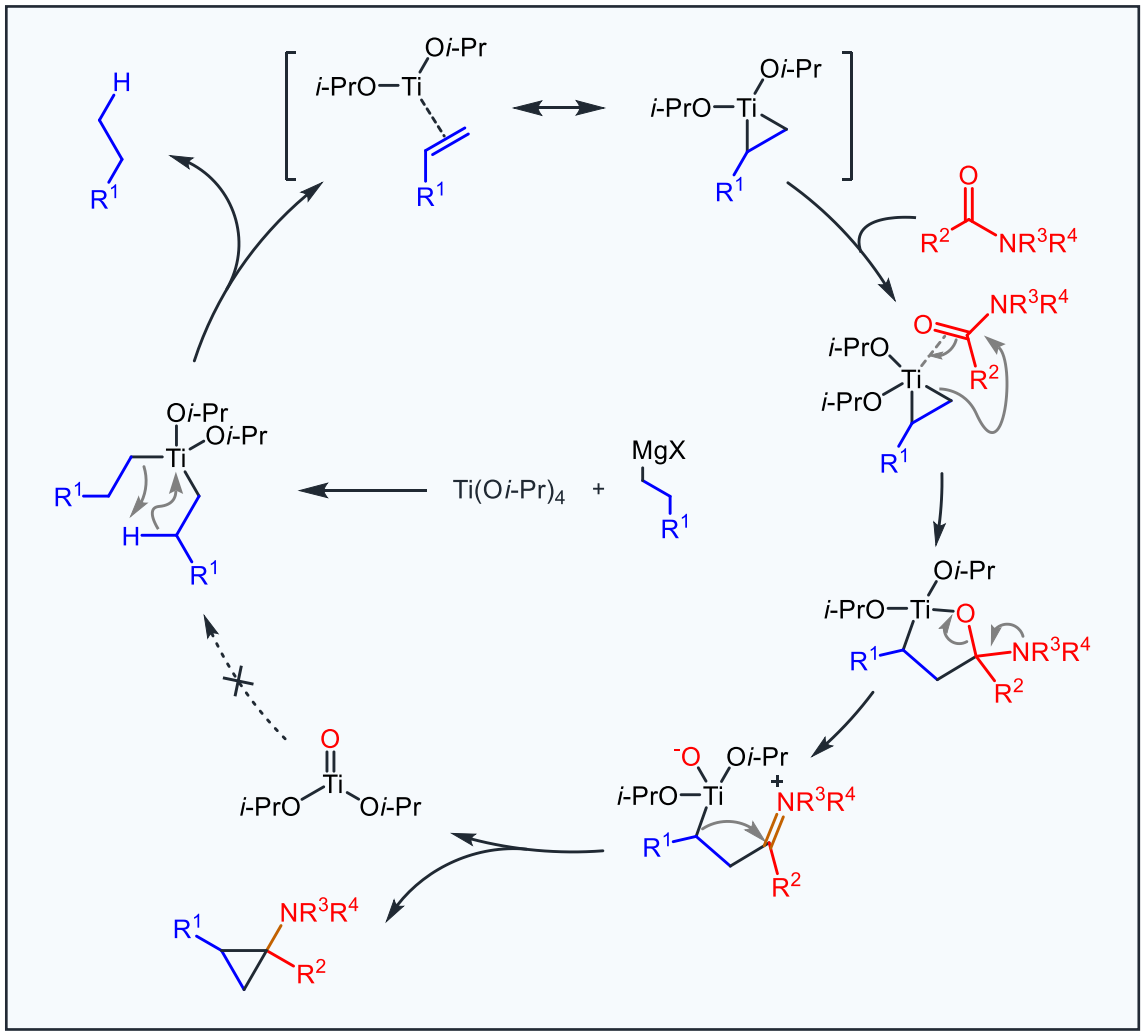


The reaction is catalyzed by titanium. Substoichiometric quantities may be employed.

When incorporation of exogenous alkenes is desired, sacrificial Grignard rgt must be employed.

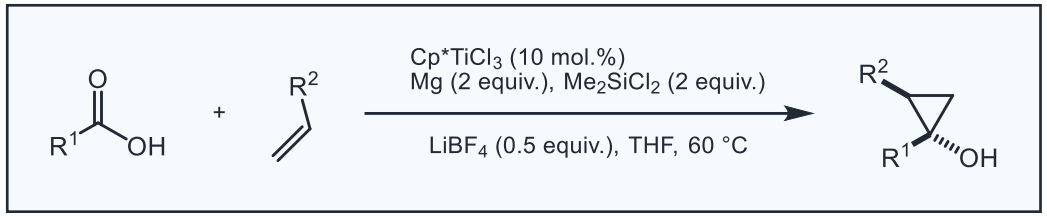
Wu Y-D, Yu Z-X. *J. Am. Chem. Soc.* **2001**, *123* (24), 5777–5786.

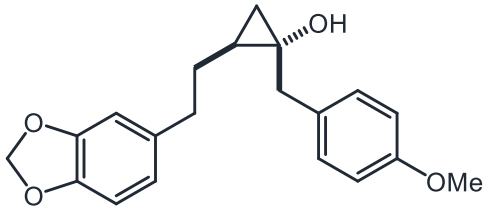
de Meijere and Szymoniak Modifications



The reaction requires stoichiometric Ti loadings. Byproduct oxo complex is not recyclable.

Cp^*TiCl_3 Catalyzed Coupling





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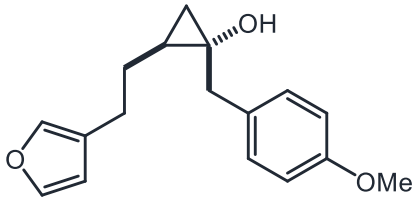
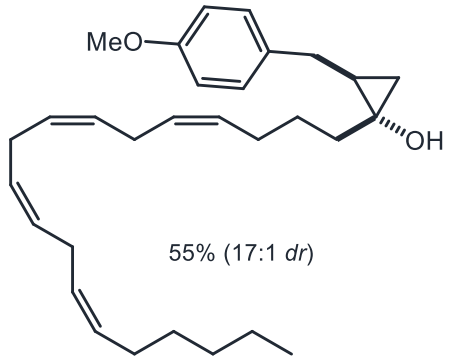
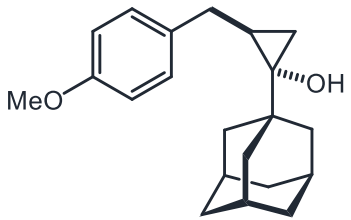


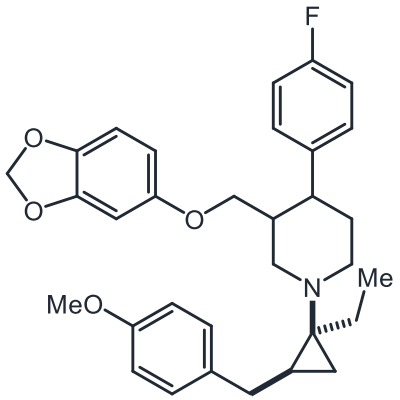
72% (19:1 *dr*)



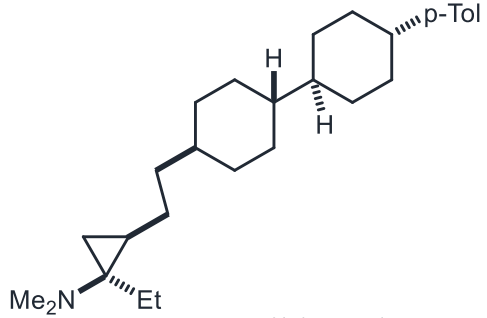
55% (17:1 *dr*)



35% (4:1 *dr*)



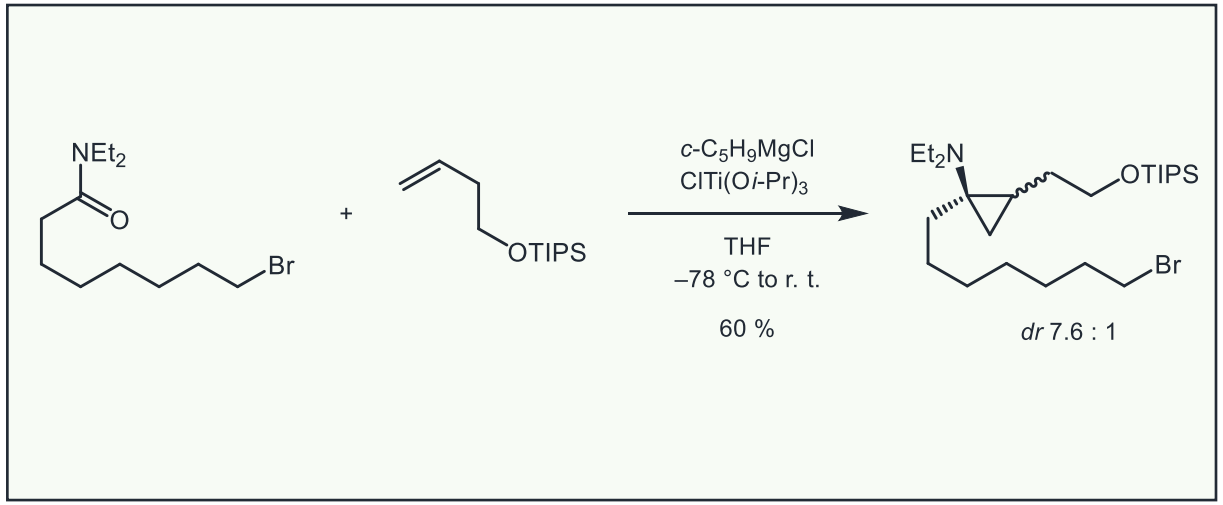
69% (8:1 *dr*)

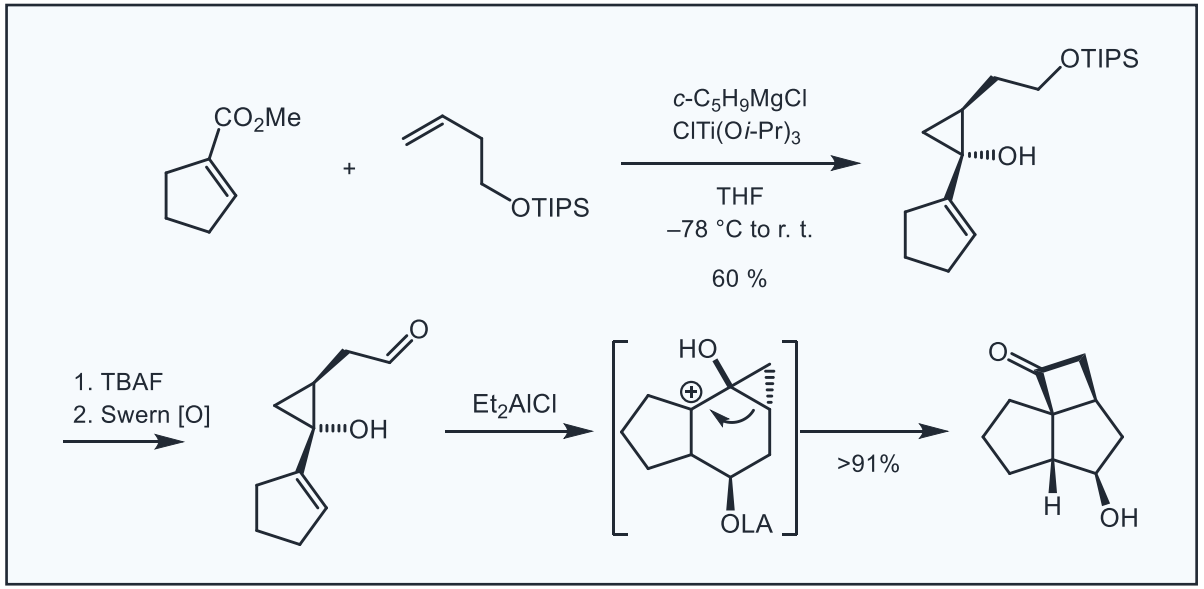


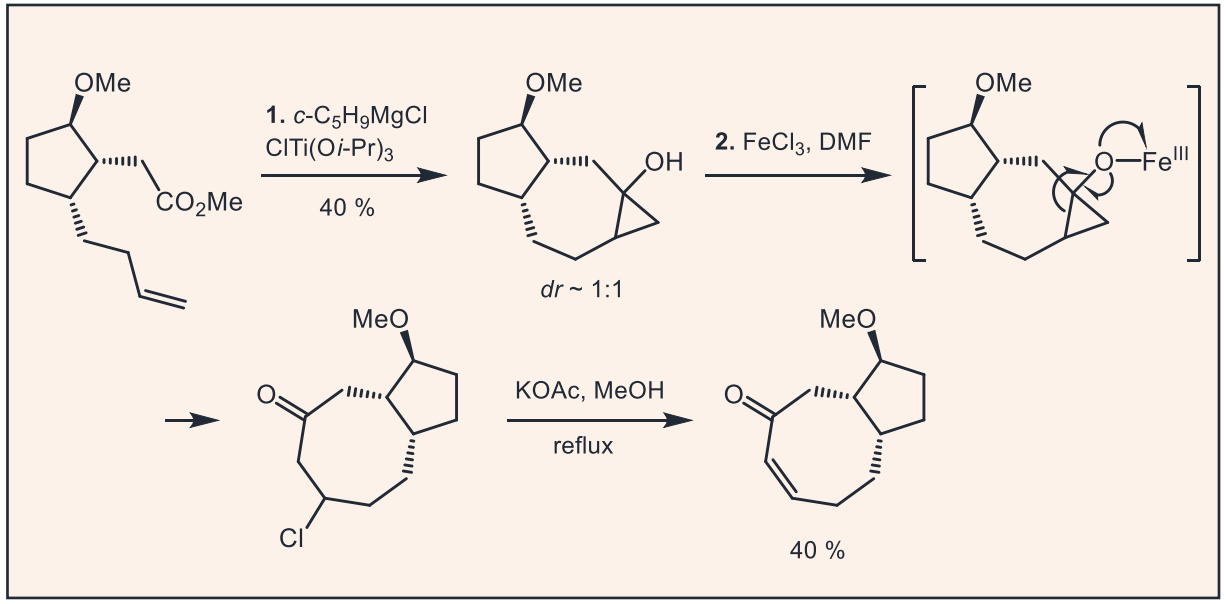
53% (15:1 *dr*)

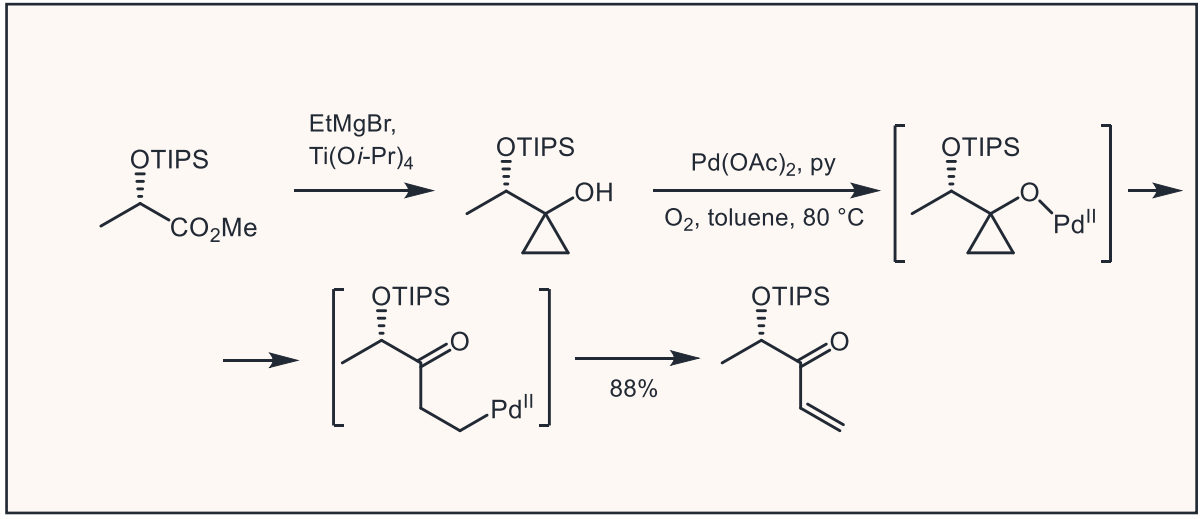
Ni J, Xia X, Zheng W-F, Wang Z. *J. Am. Chem. Soc.* **2022**, *144* (17), 7889–7900.

Applications of the Kulinkovich and related Reactions



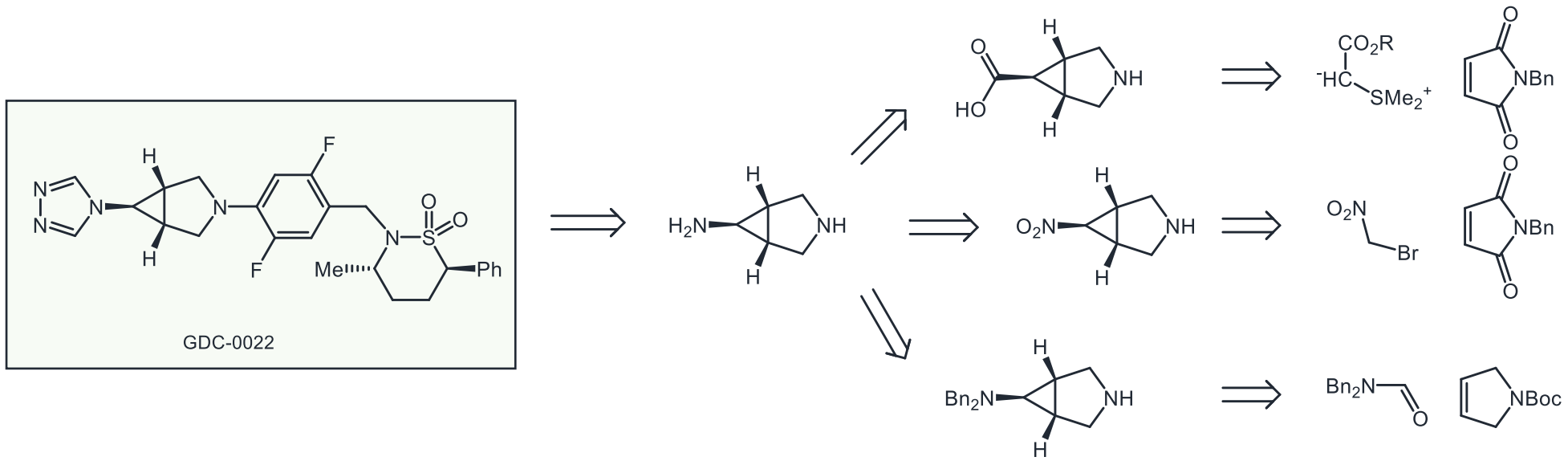


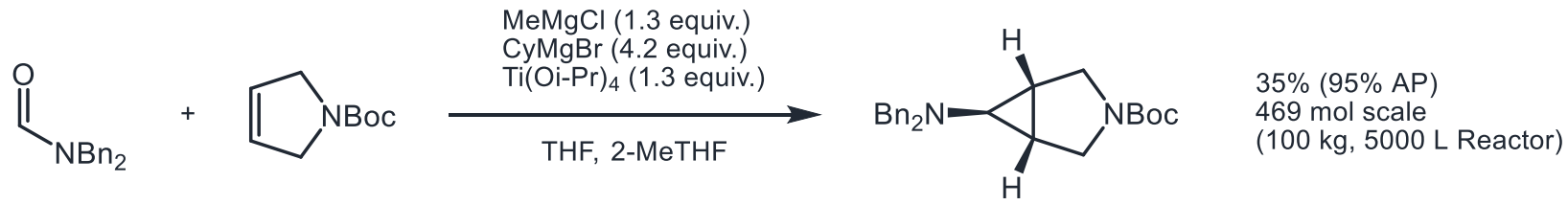




Cha JK, Kulinkovich OG. The Kulinkovich Cyclopropanation of Carboxylic Acid Derivatives. In *Organic Reactions*; John Wiley & Sons, Ltd, 2012; pp 1–160. de Meijere A, Kozhushkov SI, Savchenko AI. Titanium-Mediated Syntheses of Cyclopropanols and Cyclopropylamines. In *Titanium and Zirconium in Organic Synthesis*; John Wiley & Sons, Ltd, 2002; pp 390–434.

Industrial Scale Cyclopropanation

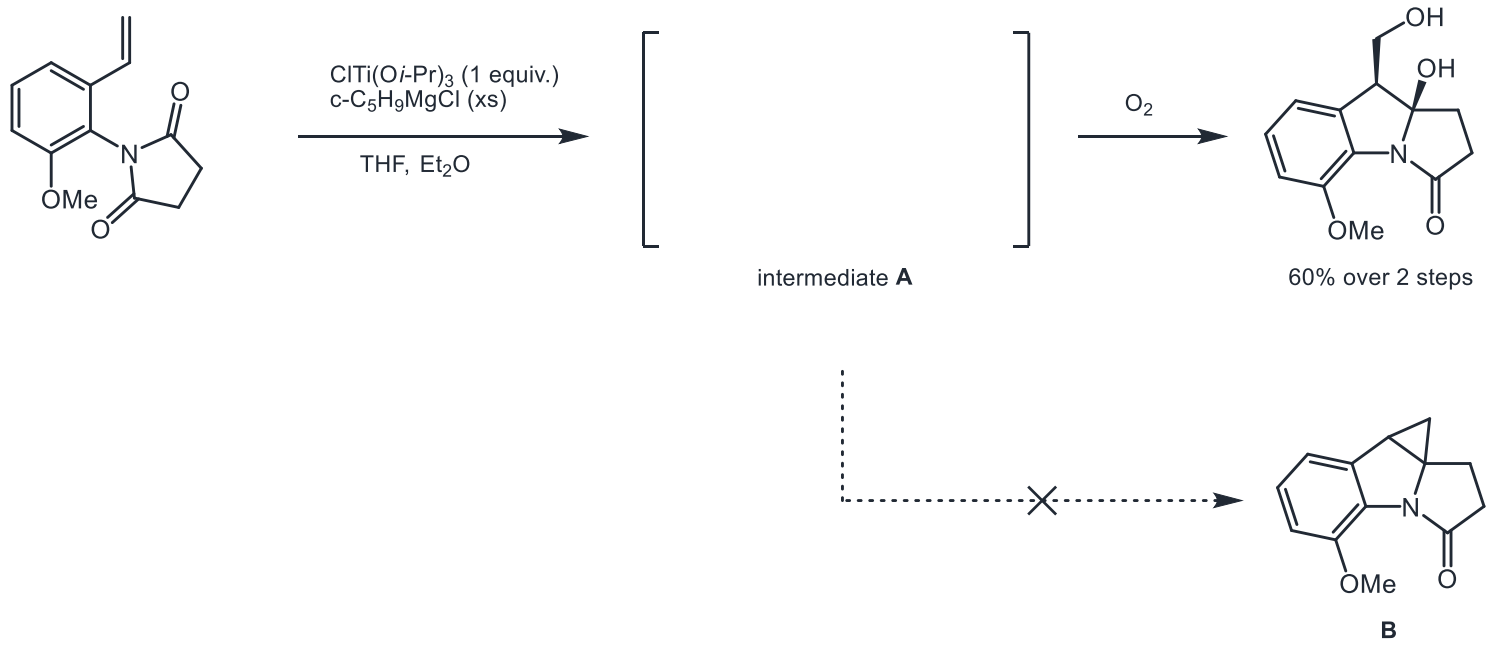




The reaction does not pose a safety risk on scale, avoids toxic reagents.

Group Problem 2: Interrupted Cyclopropanation

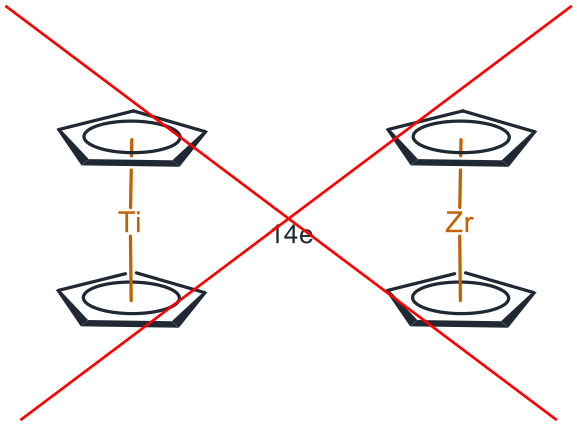
- Deduce the structure of intermediate **A**.
- Provide a mechanistic rationale for the transformation that leads to the intermediate **A**.
- What is the reason for the reaction to diverge from a normal Kulinkovich pathway (**A** → **B**)?
  - How would you attempt to restore this reactivity?

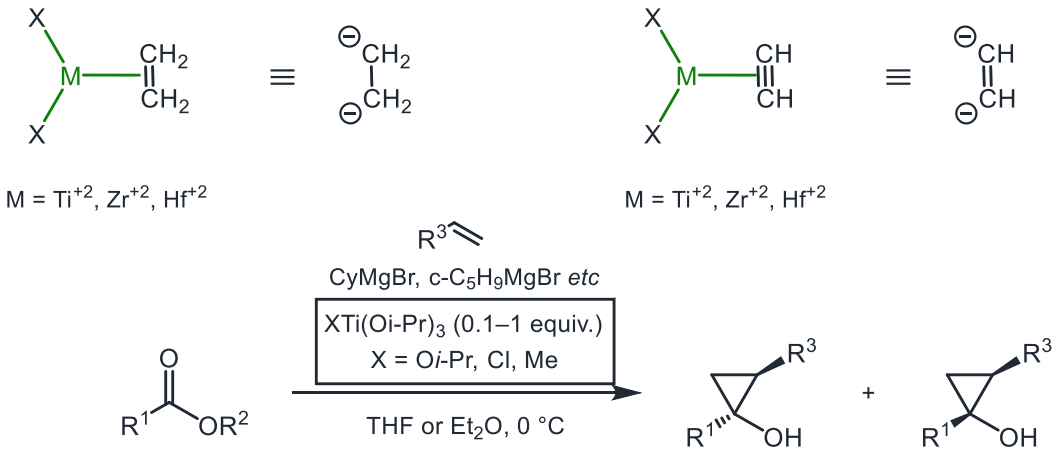


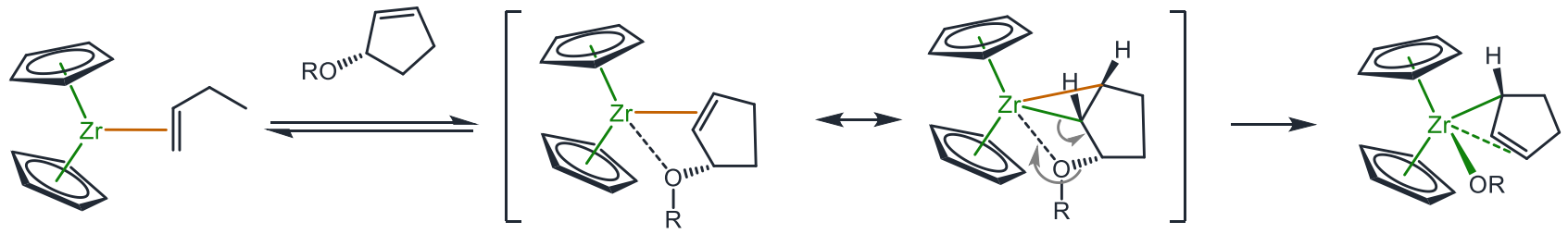
[Group Problem 2: Answer Key]

Conclusions

Summary of the Take-Home Messages







Further Reading

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2. Takahashi T, Li Y. Zirconacyclopentadienes in Organic Synthesis. In *Titanium and Zirconium in Organic Synthesis*; John Wiley & Sons, Ltd, 2002; pp 50–85.
3. de Meijere A, Kozhushkov SI, Savchenko AI. Titanium-Mediated Syntheses of Cyclopropanols and Cyclopropylamines. In *Titanium and Zirconium in Organic Synthesis*; John Wiley & Sons, Ltd, 2002; pp 390–434.
4. Negishi E. A quarter of a century of explorations in organozirconium chemistry. *Dalton Trans.* **2005**, No. 5, 827–848.
5. Cha JK, Kulinkovich OG. The Kulinkovich Cyclopropanation of Carboxylic Acid Derivatives. In *Organic Reactions*; John Wiley & Sons, Ltd, 2012; pp 1–160.

Thanks for your attention!

Questions?