Stereochemistry of Cyclopropane Formation Involving Group IV Organometallic Complexes

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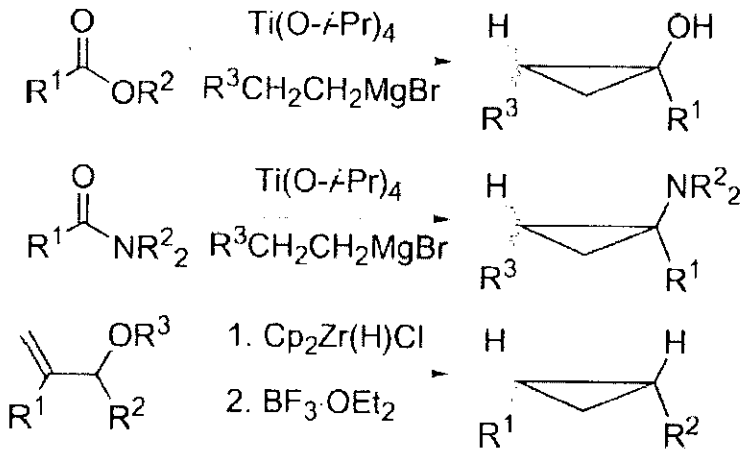


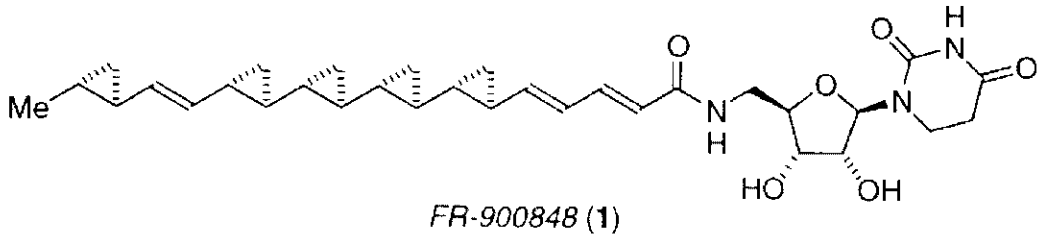
Apr. 21, 2004

Jaehyeon Park

J. AM. CHEM. SOC. 2004, *126*, 1699−1704

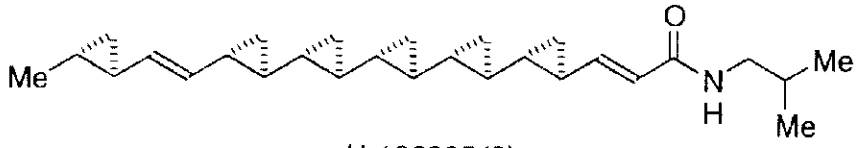
Background

- Isolation of the novel natural compounds bearing cyclopropane rings accelerated the progress of cyclopropane chemistry



FR-900848 (**1**)

J. Antibiotic. **1990**, *43*, 748

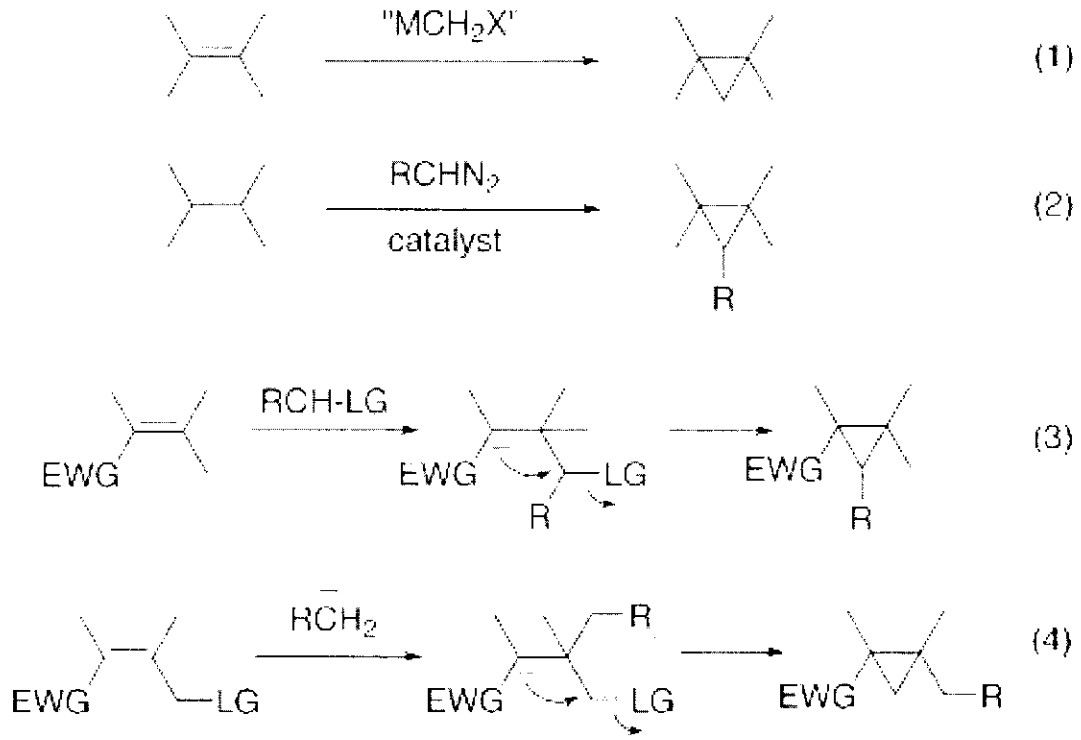


U-106305 (**2**)

J. Am. Chem. Soc. **1995**, *117*, 10629–10634

Background

- 4 basic ways to install a cyclopropane ring.

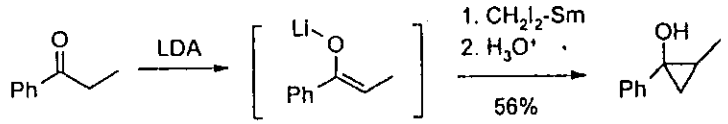


Chem. Rev. **2003,** *103,* 977–1050

Background

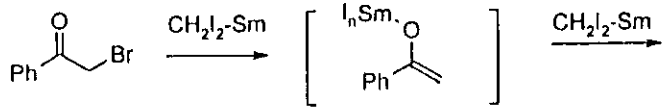
- Representative ways to prepare cyclopropanol

Scheme 1

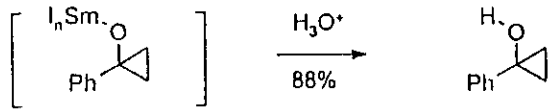


1

Scheme 2[a]



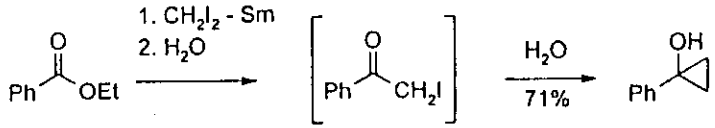
2 4



3

[a] $n = 1$ or 2.

Scheme 5

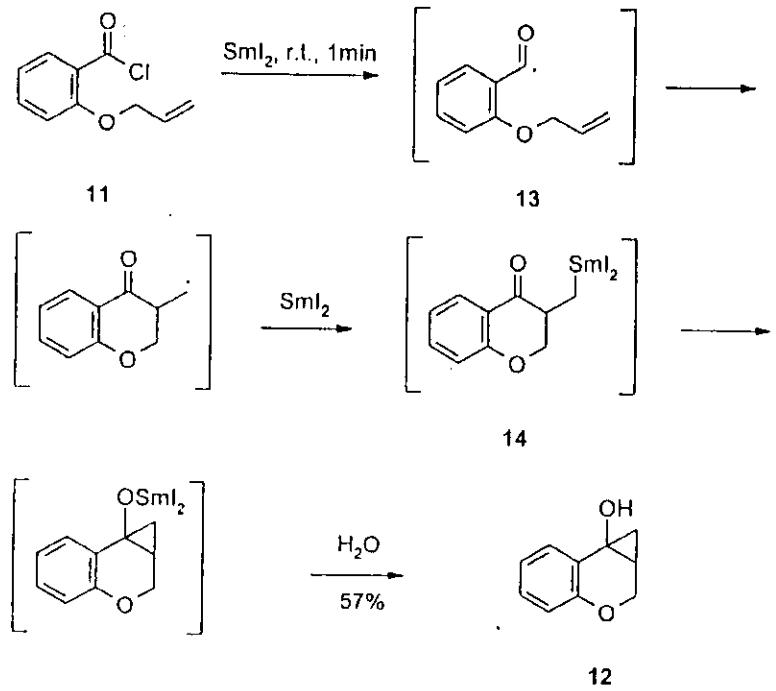


10 9

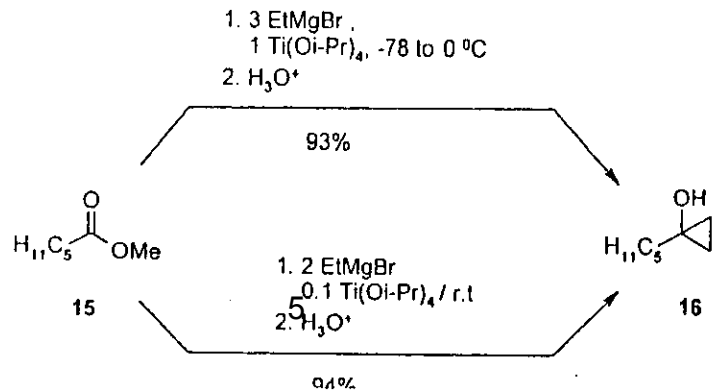
Background

- Representative ways to prepare cyclopropanol (continued)

Scheme 6

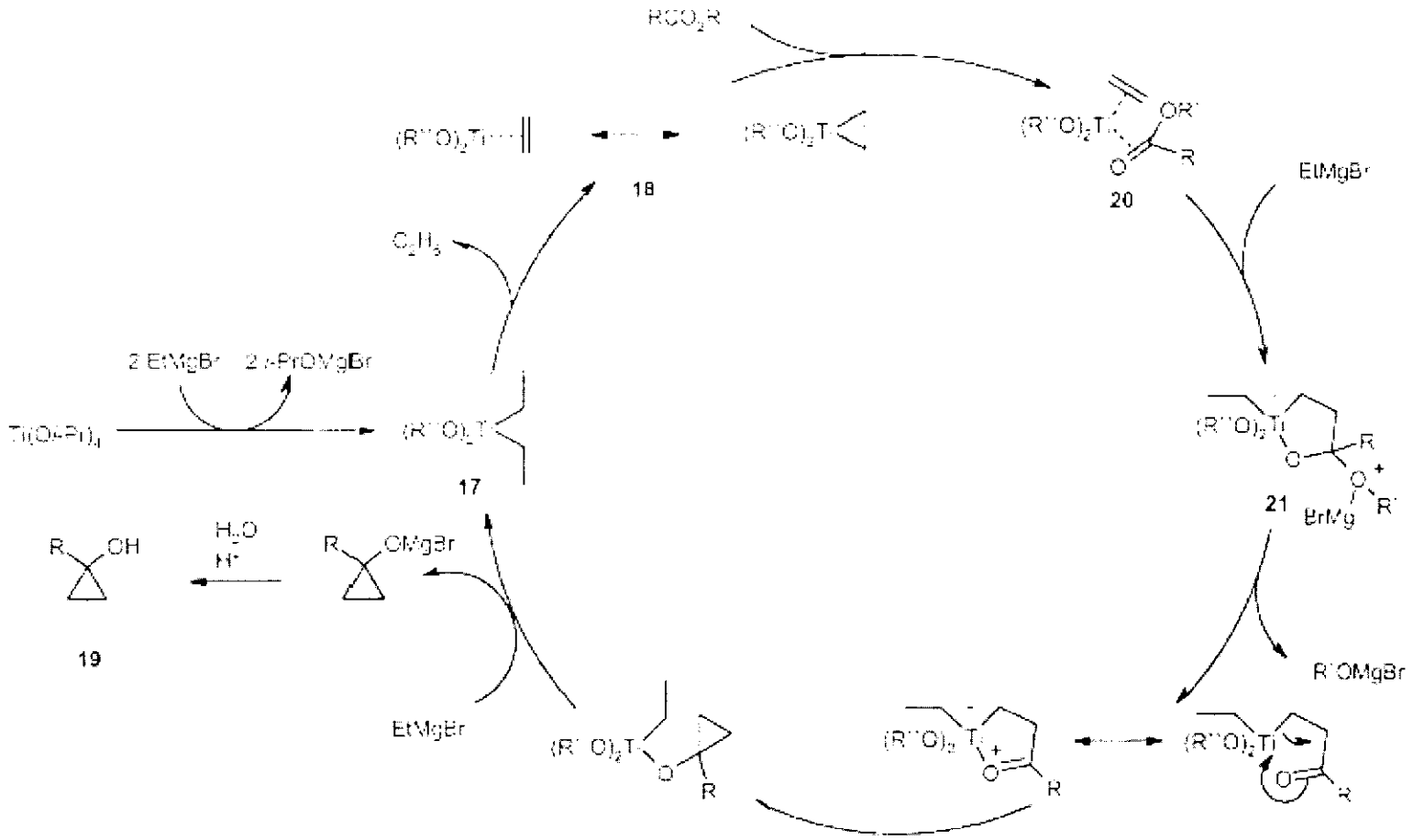


Scheme 7



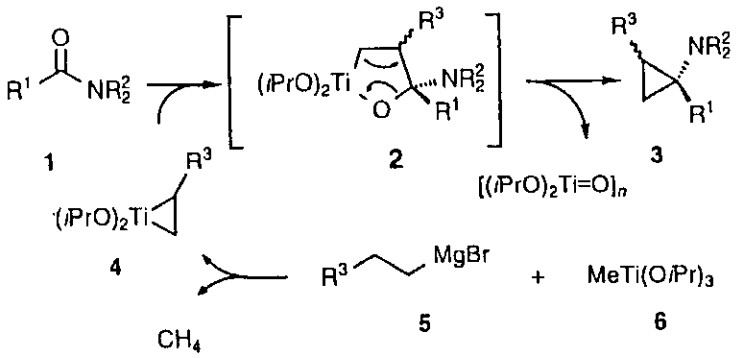
Background

- Kulinkovich reaction



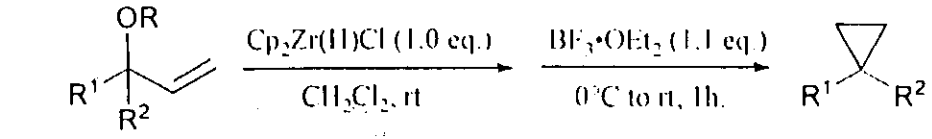
Background

- Cyclopropylamine

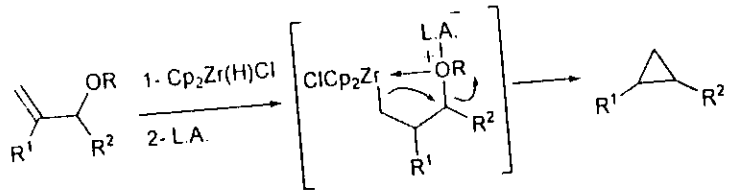


Background

- A one-pot cyclopropane synthesis from allylic ethers



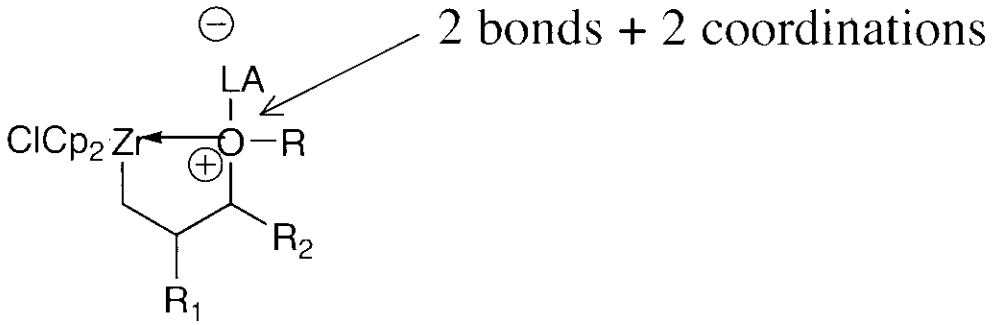
- Proposed mechanism



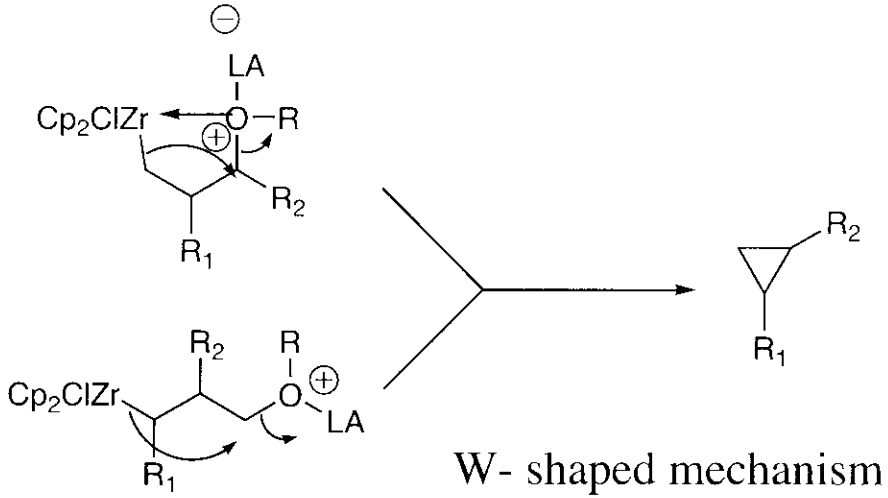
Scheme 2

Chem. Commun. **2002**, 1308-1309

- But is it a reasonable mechanism?



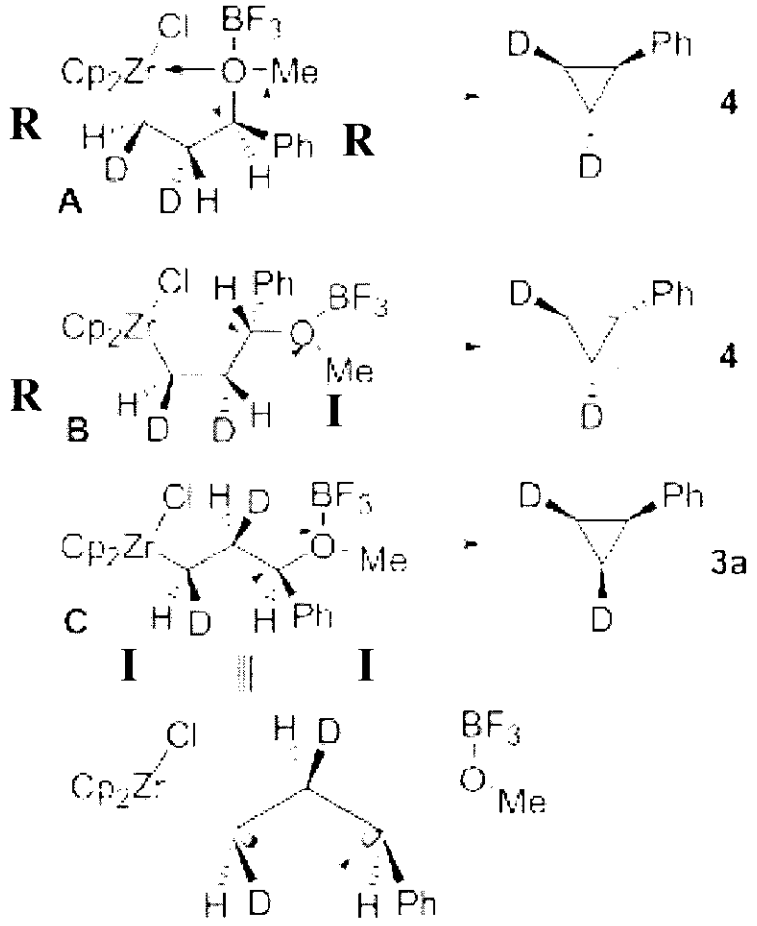
- And another mechanism is possible.



- Which one is correct? And how can it be found?

Cyclopropane

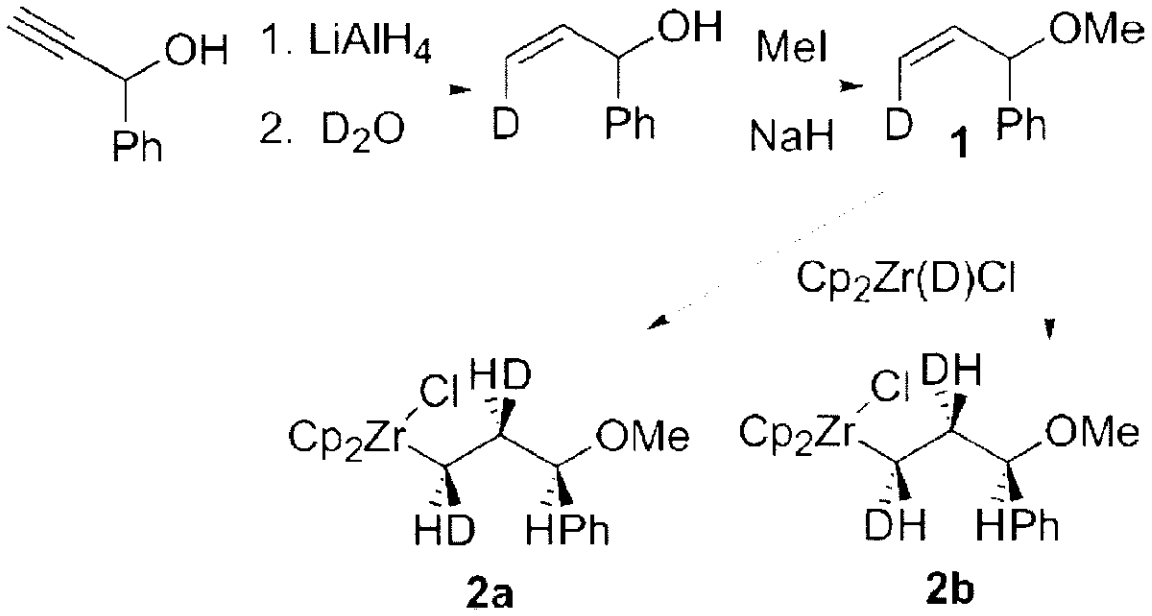
- The answer was found by installing stereocenter!



R: retention **I:** inversion of stereochemistry

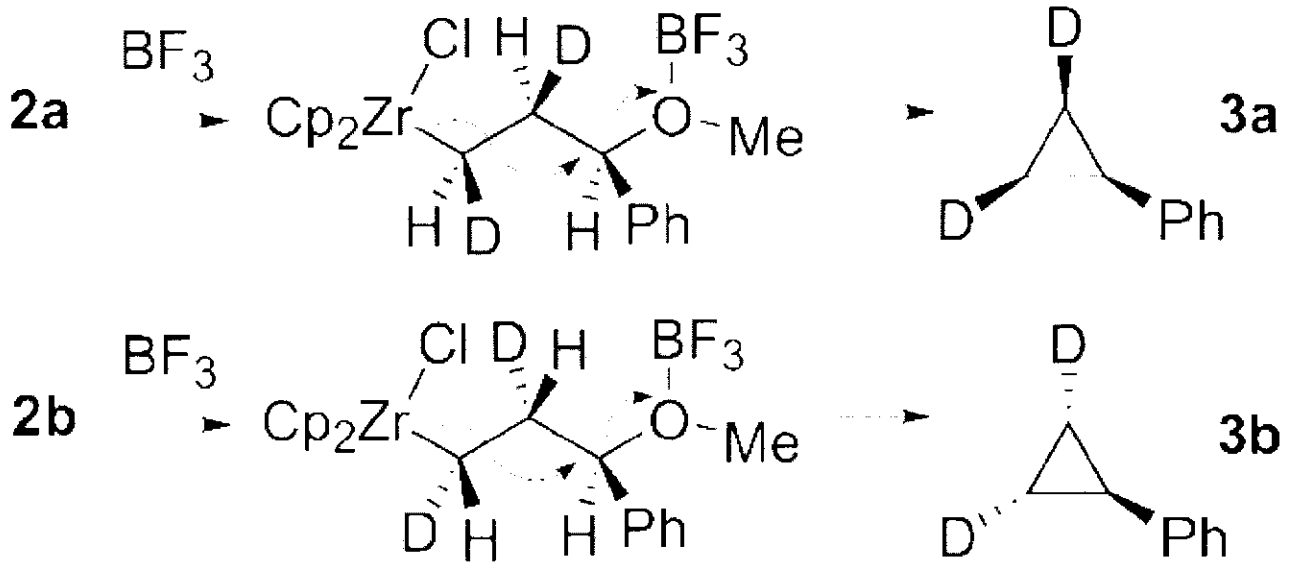
Cyclopropane

- Preparation of intermediate **2**



Cyclopropane

- Reaction with Lewis acid



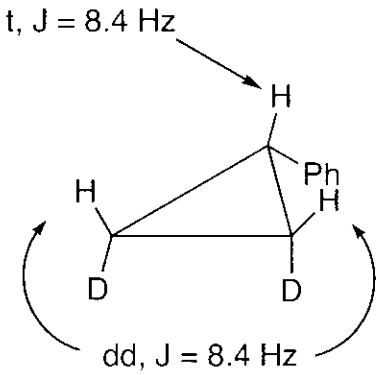
Only *cis*!

No *trans* isomer was found!

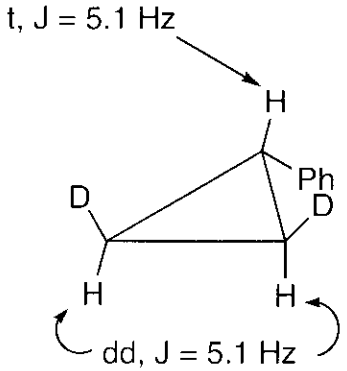
3a : **3b** = 5 : 1

Cyclopropane

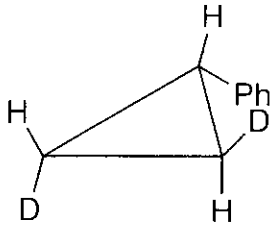
- Assignment of stereochemistry



3a



3b



Not found

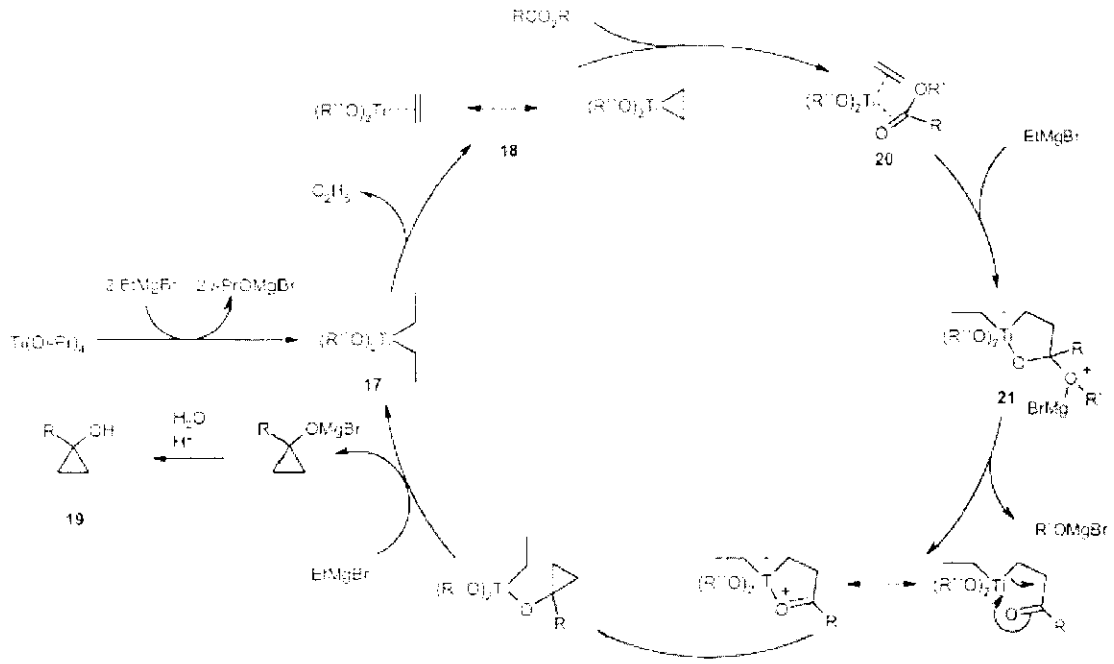
Conclusion: W - shaped mechanism was right!

Cyclopropanol

- In the case of cyclopropanol

  Before we start…..

  Revisit to the mechanism of Kulinkovich reaction

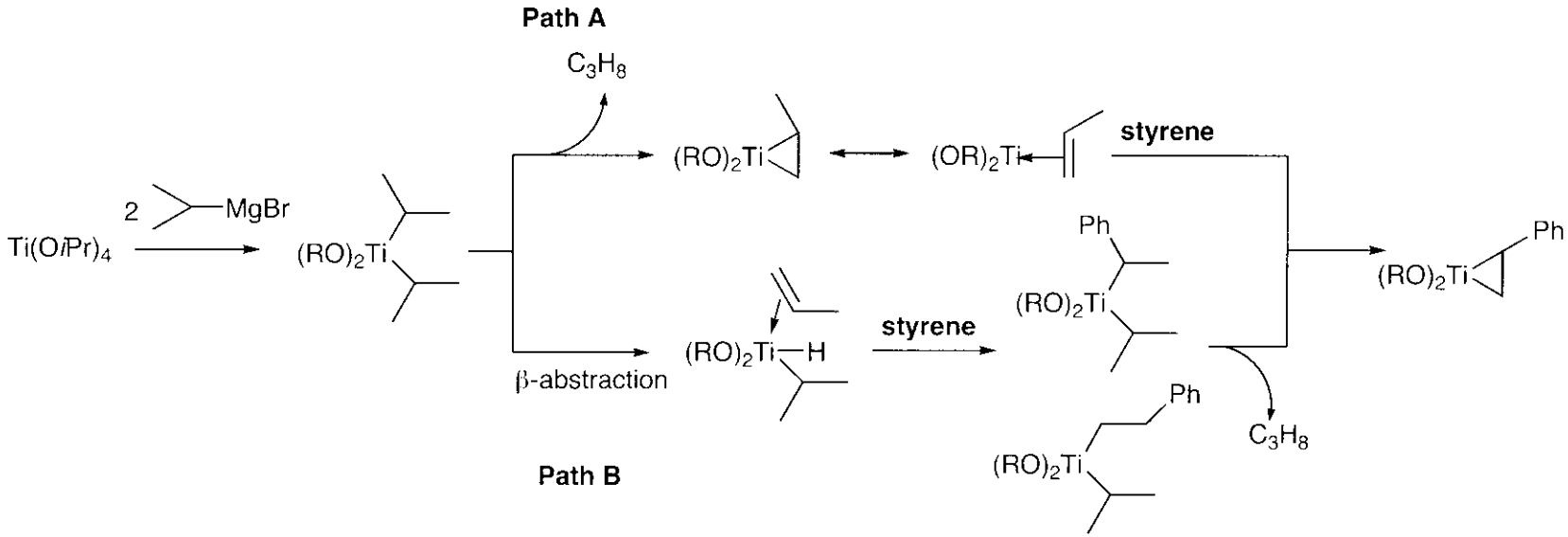


If the olefin is not a simple ethene…..

Cyclopropanol

- Modified Kulinkovich reaction

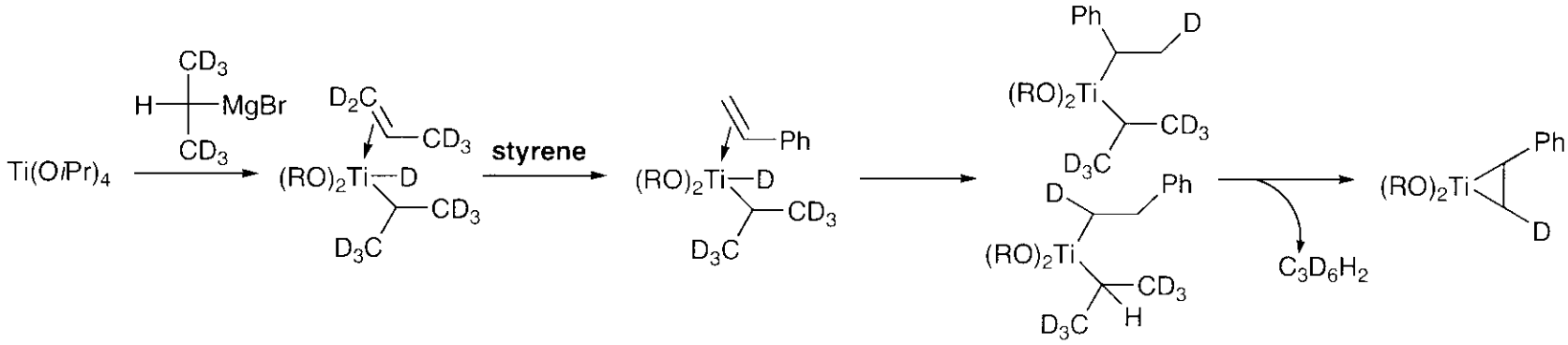
  Olefin exchange step :



Which path way is correct?

Cyclopropanol

- If the pathway 2 is correct, when a deutrated Grignard rgt was used, deutrated cyclopropane is expected to be formed



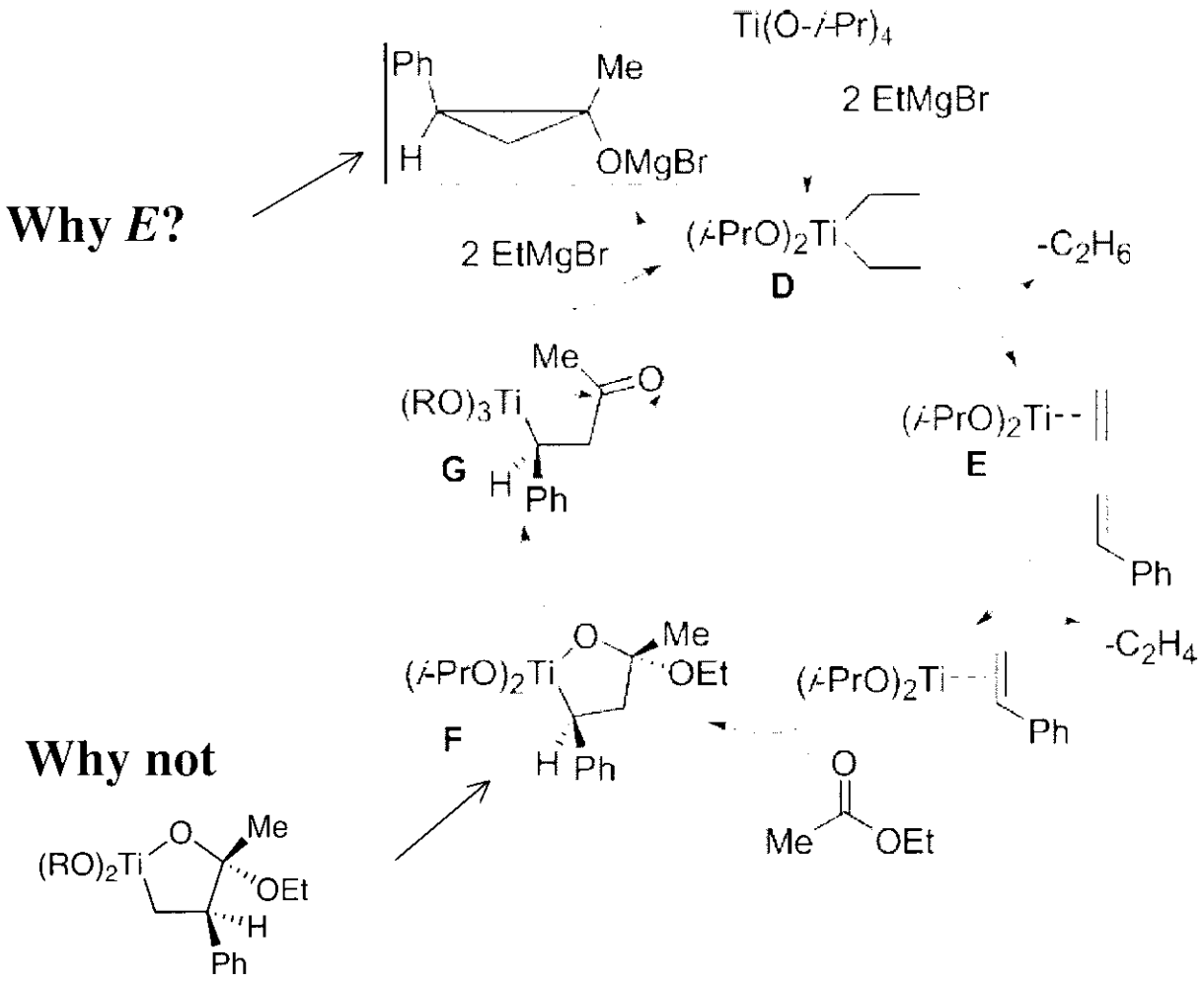
But in real, deutrated cyclopropane was not found

Conclusion: the olefin exchange step follows pathway 1 exclusively.

Tet. Lett. **1999**, *40*, 5935-5938

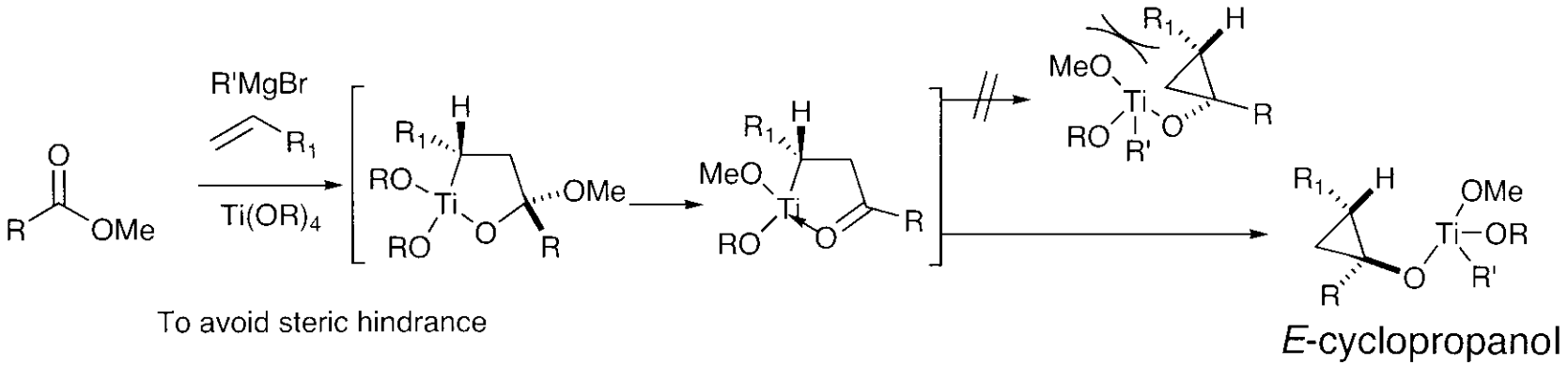
Cyclopropanol

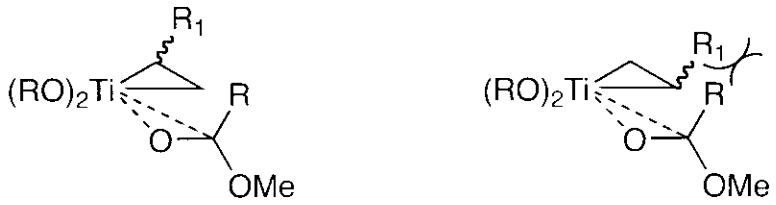
- Regioselectivity and stereoselectivity issue of Kulinkovich reaction



Cyclopropanol

- It was because of the steric hindrance





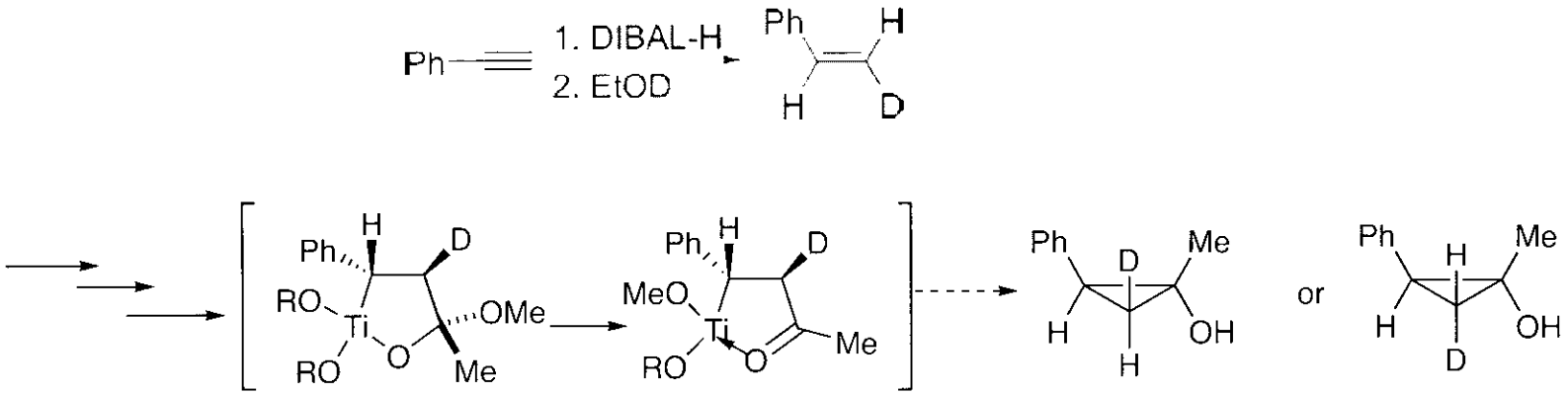
Favored **Disfavored**

OK… But what is the exact transition state?

J. Am. Chem. Soc. **2001**, *123*, 5777-5786

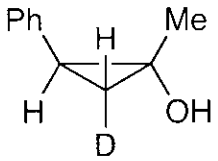
Cyclopropanol

- Introduction of deuterium in the olefin

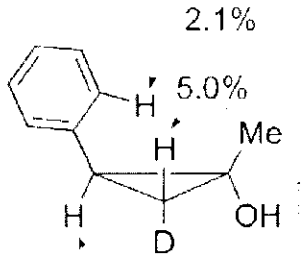


The result was:

Exculsively



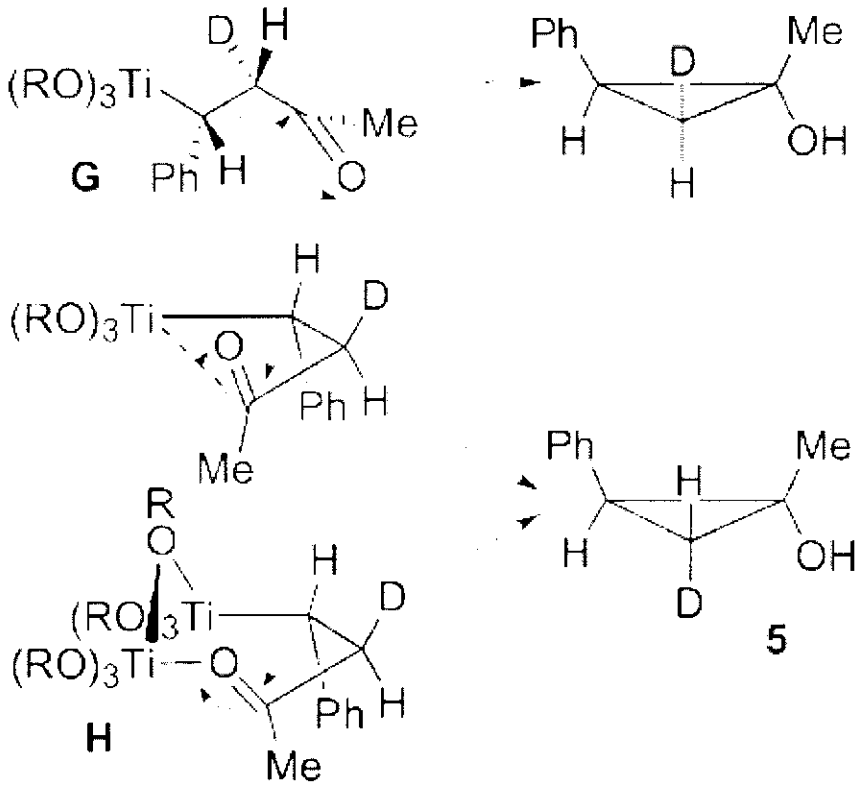
Confirmed by NOE



5

Cyclopropanol

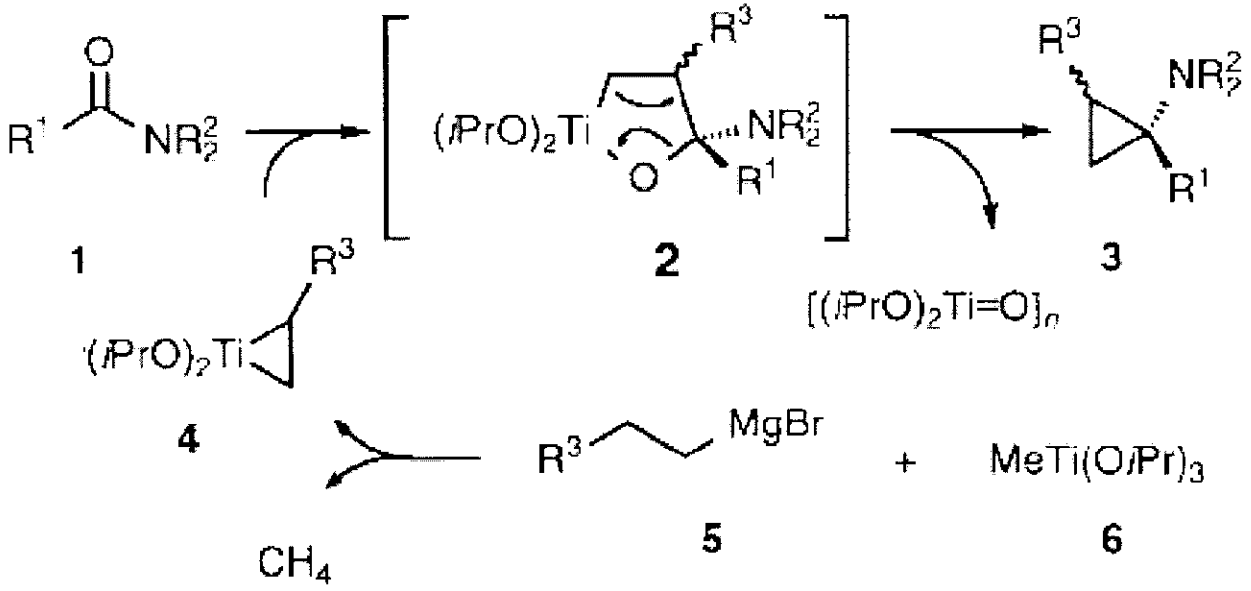
- W-shaped mechanism does not work in this case.



Reaction proceeds through front attack of titanium-carbon bond.
Titanium-oxygen coordination plays an important role.

Cyclopropanylamine

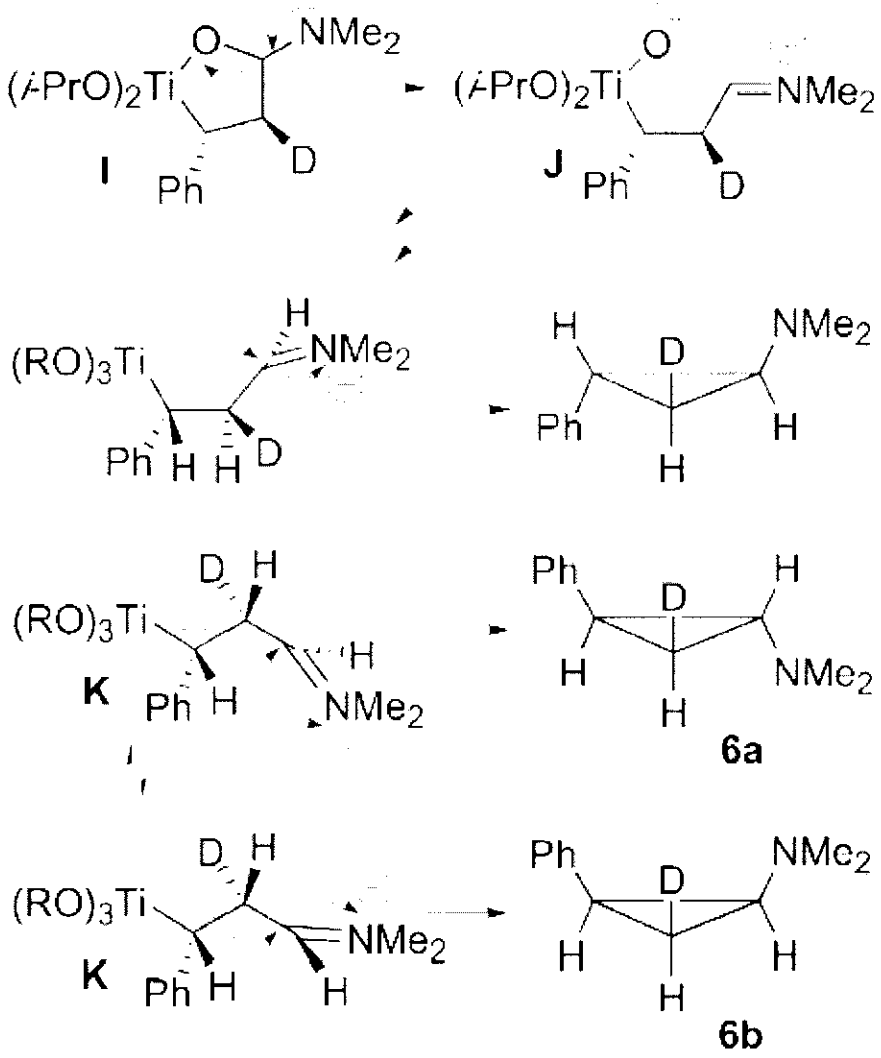
- In the case of cyclopropylamine



Would W-shaped mechanism work?

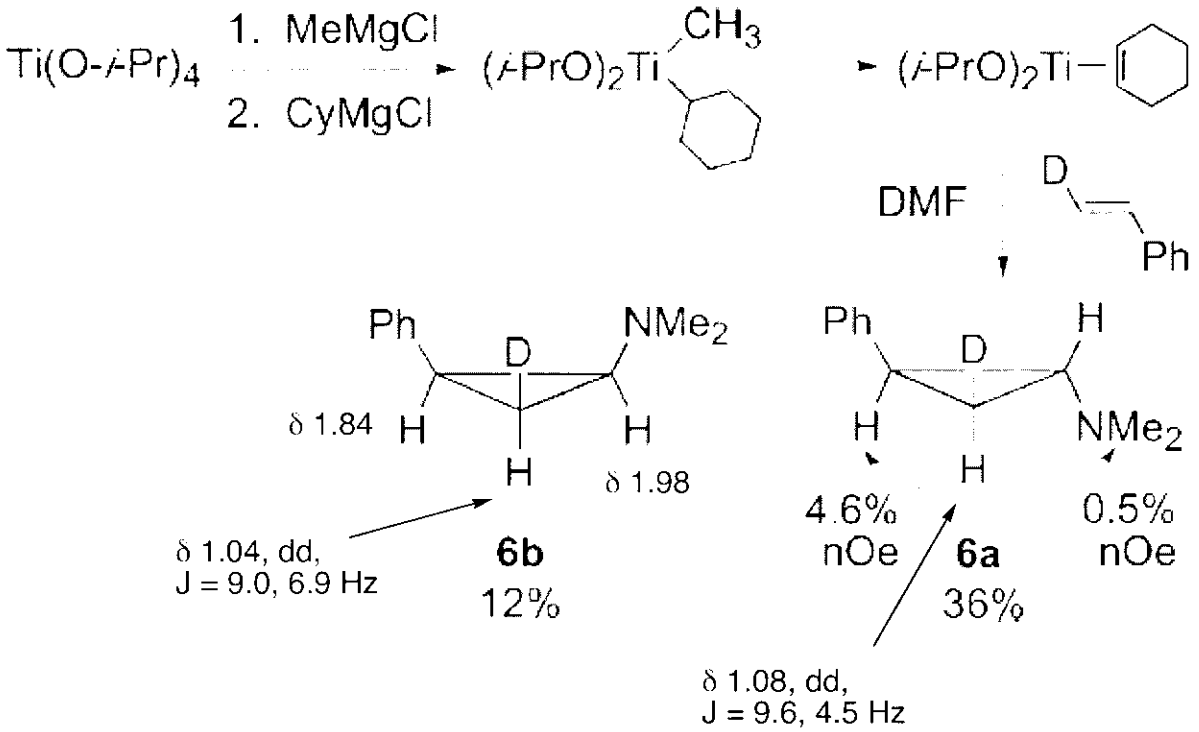
Cyclopropanylamine

- Possible mechanisms:



Cyclopropanylamine

- The result.



W-shaped mechanism works!

Conclusion

- The mechanisms of cyclopropane formation steps were confirmed to be:

  - W-shaped mechanism for cyclopropane formation from allylic ethers, Cp2Zr(H)Cl, and Lewis acid and for cyclopropylamine formation.

  - W-shaped mechanism does not work for Kulinkovich reaction presumably because of titanium-oxygen coordination.

through a very simple way (only introducing deuterium)!