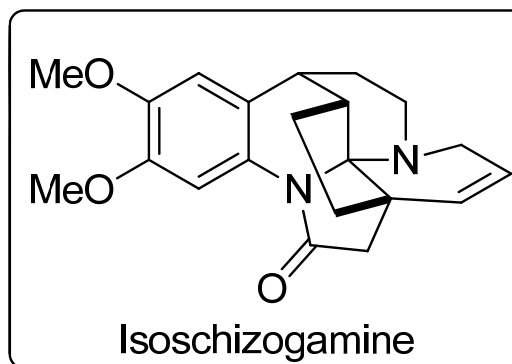


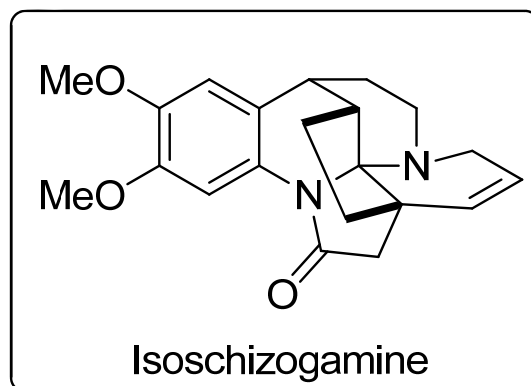
# Total Synthesis of (-)-Isoschizogamine

Yusuke Miura, Noriyuki Hayashi, Satoshi Yokoshima,  
and **Tohru Fukuyama** *J. Am. Chem. Soc.* **2012**, *134*, 11995.

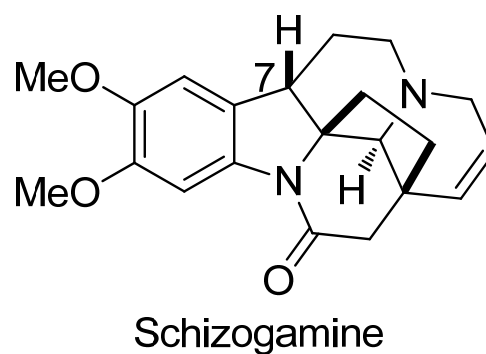


*Current literature*  
**Gong Xu**  
**2013-03-21**

## About Isoschizogamine



1

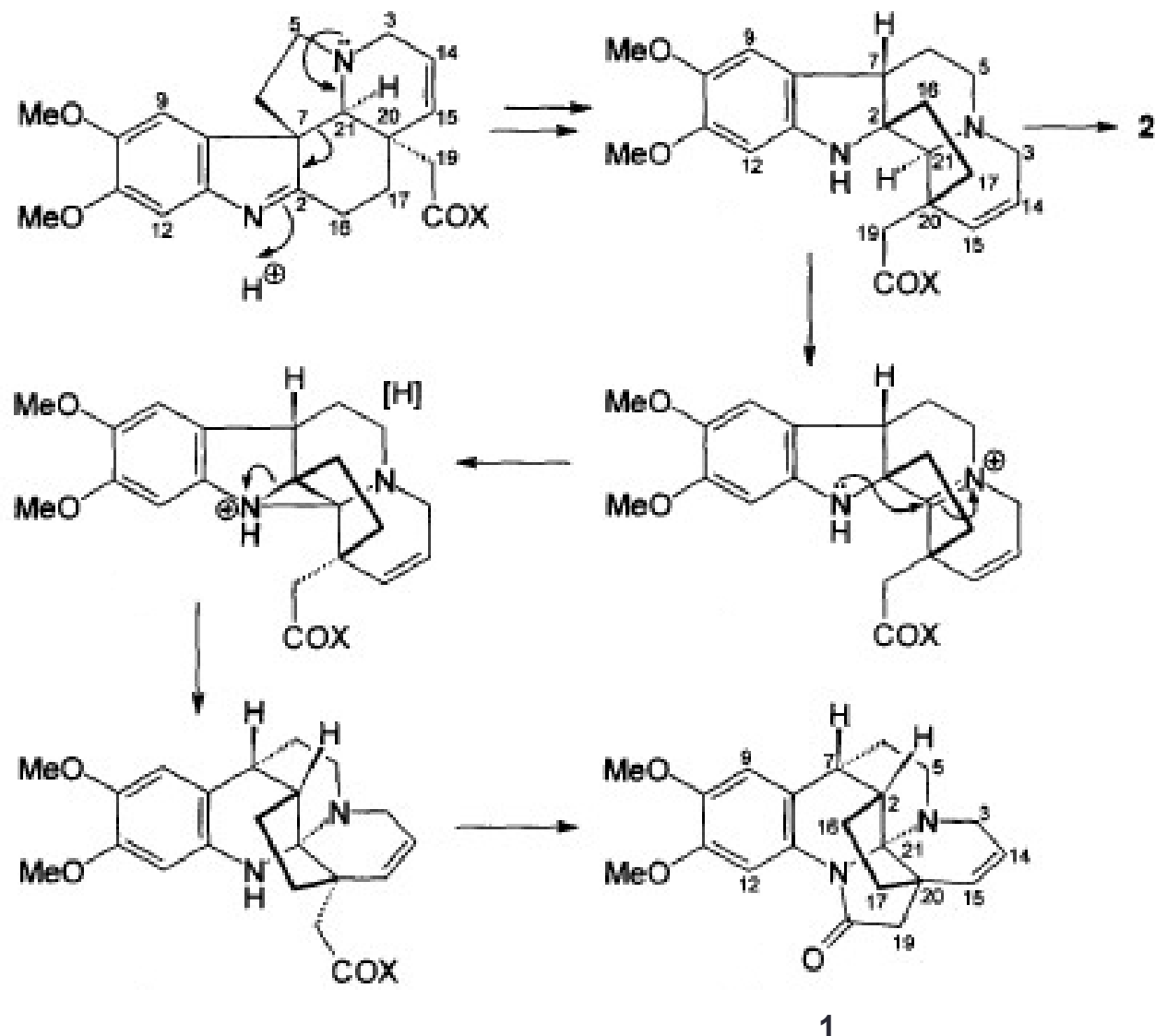


2



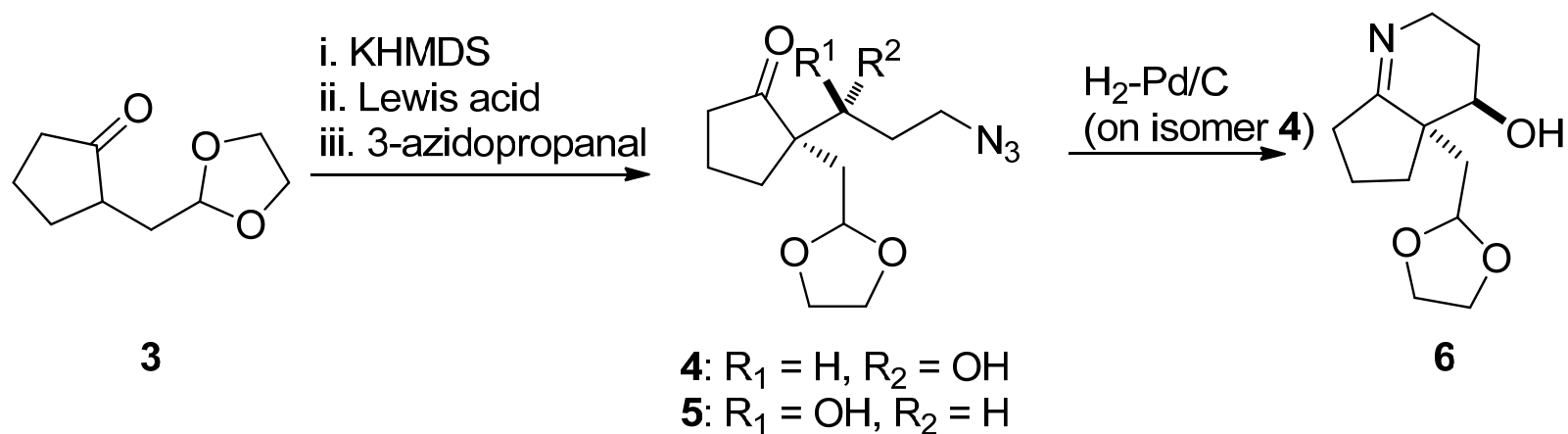
- Isolated in 1963 from **Schizogygia coffaeoides**.
- A highly fused hexacyclic compound containing **tetrahydroquinoline**, **hexahydroquinolizine**, and **pyrrolidinone** moieties.
- An **aminal** adjacent to a **quaternary carbon**.

# Biosynthetic proposal for isoschizogamine 1



# First total synthesis of the (+-)-Isoschizogamine

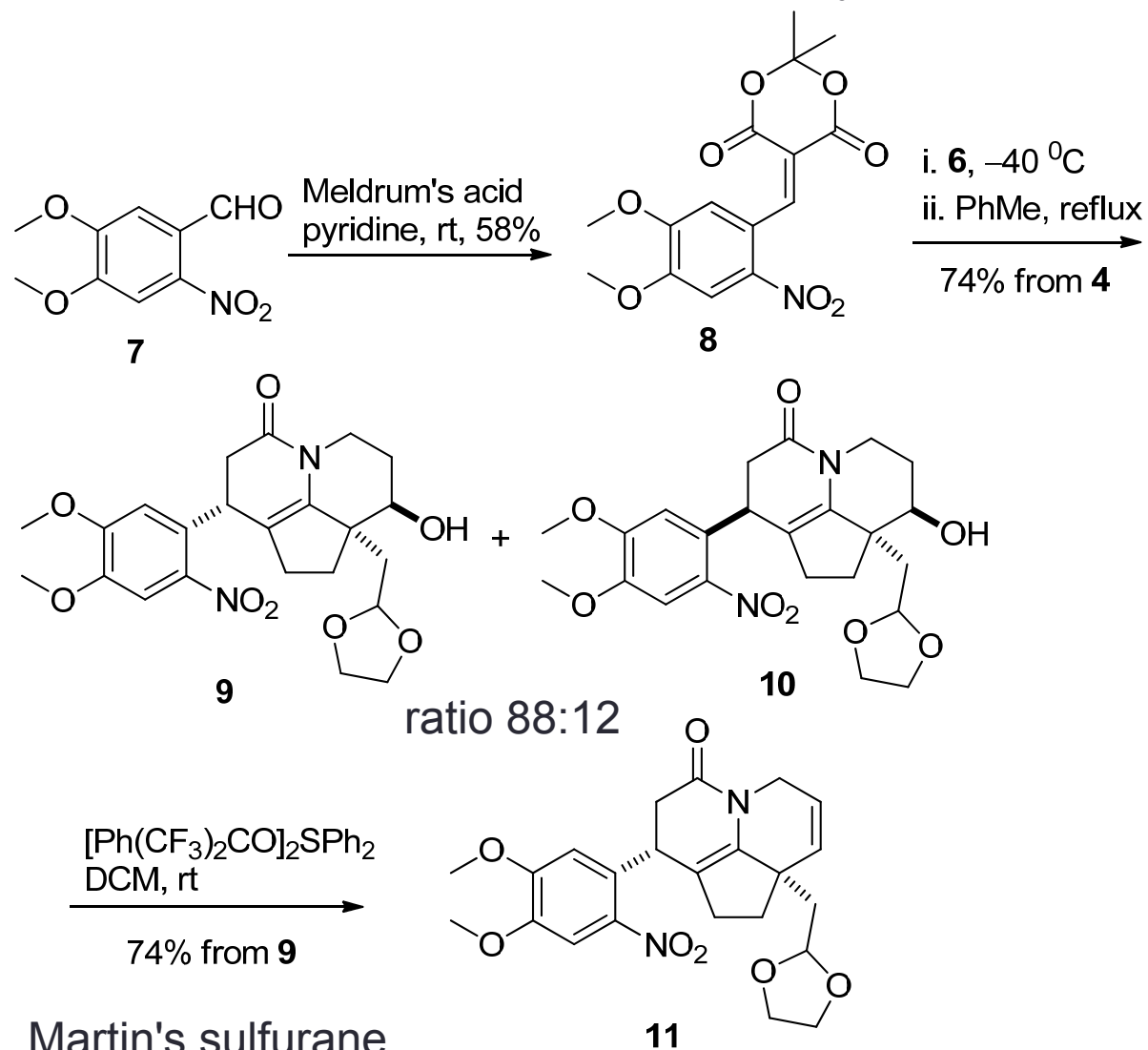
Synthesis of imine **6** via **Aldol reaction** and hydrogenation of the azide group



Lewis Acid	Yield	Ratio <b>4:5</b>
LiBr	67%	62:38
<b>Bu<sub>2</sub>BOTf</b>	<b>49%</b>	<b>&gt;95:5</b>
i-Bu <sub>2</sub> AlCl	71%	77:23

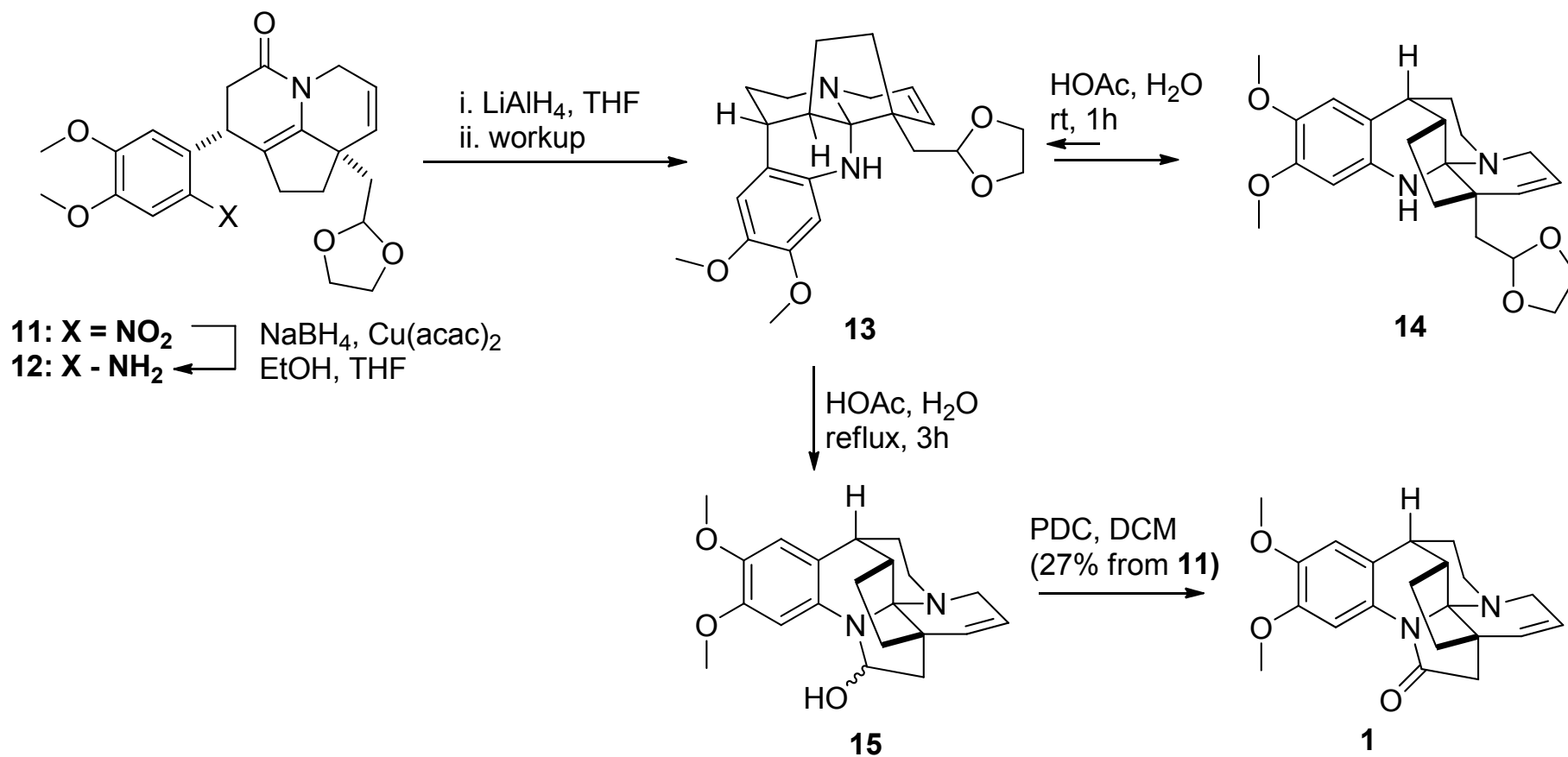
# First total synthesis of the (+-)-Isoschizogamine

Synthesis of alkene **11** via **Michael addition** and dehydration



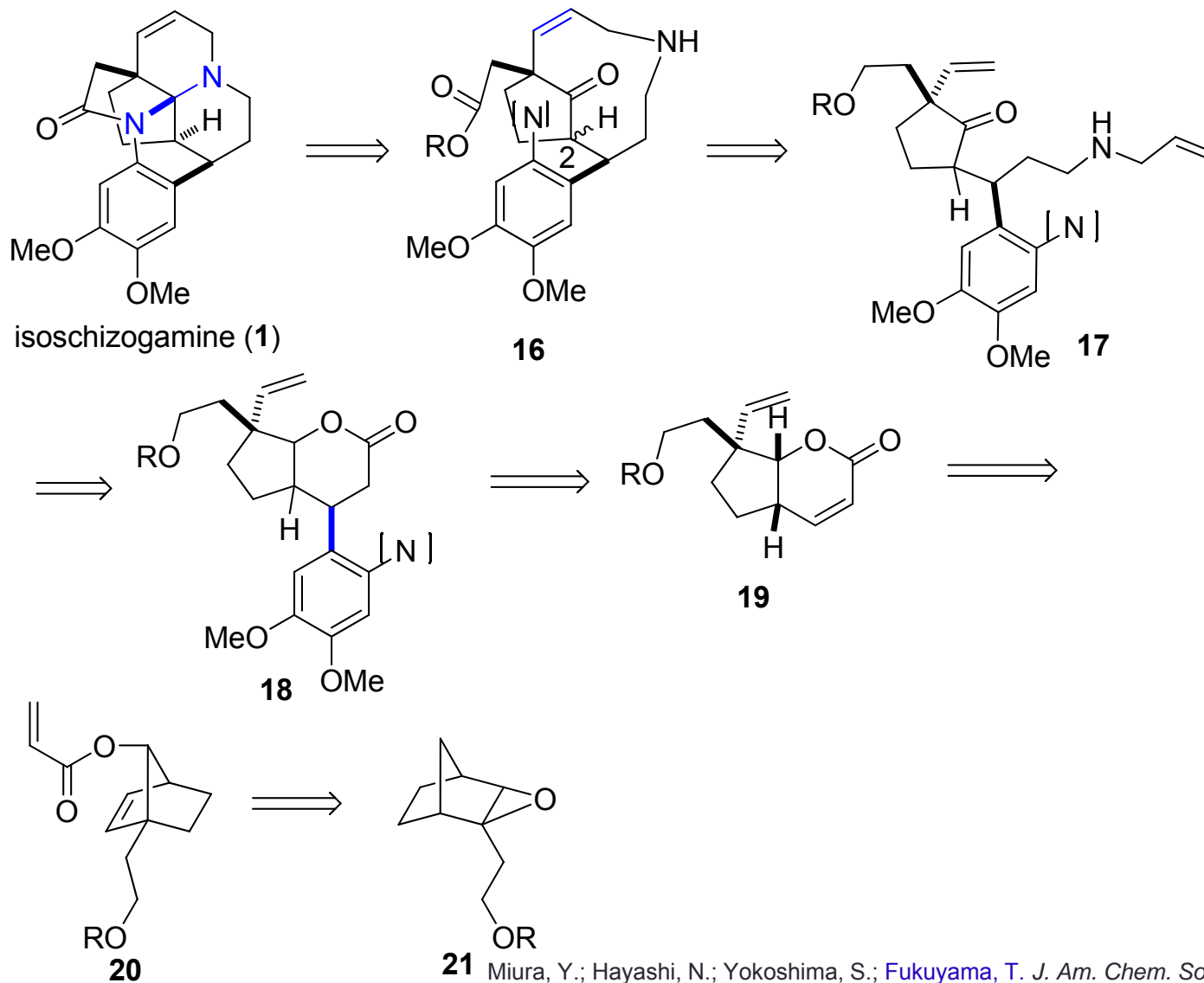
# First total synthesis of the (+-)-Isoschizogamine

## ➤ Completion of the total syntheses

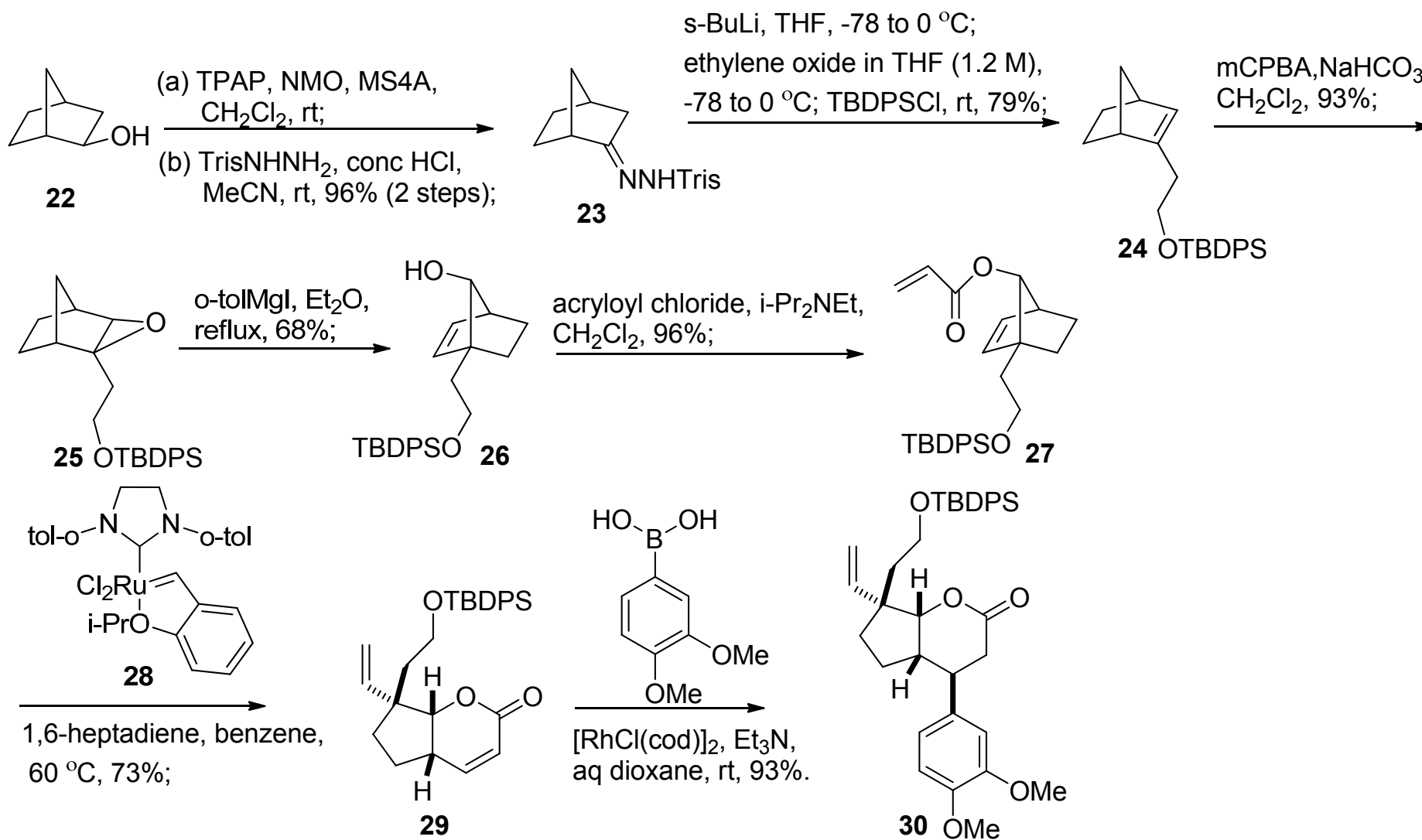


# Total synthesis of (-)-Isoschizogamine

## ➤ Retrosynthesis analysis for (-)-Isoschizogamine

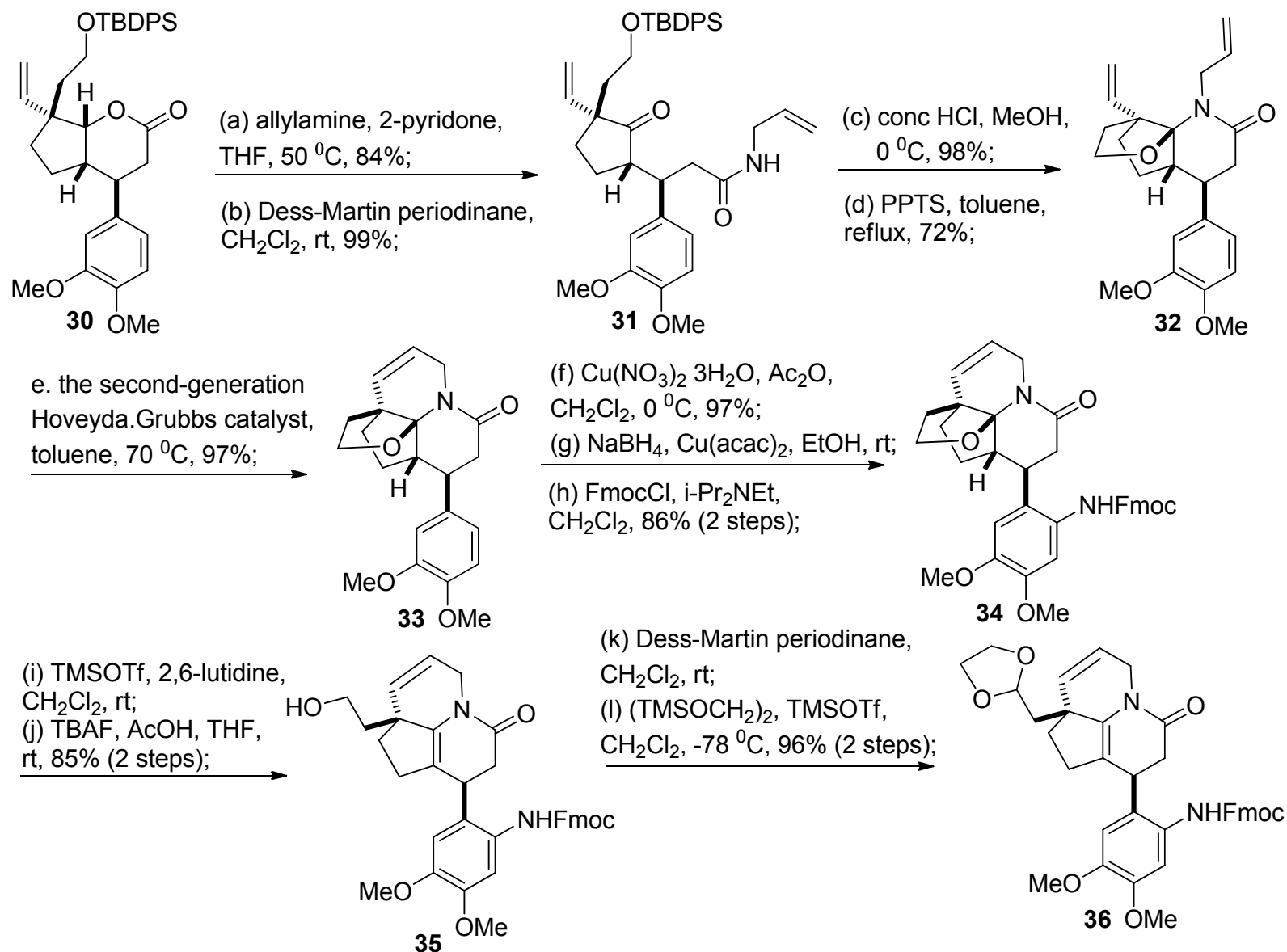


# Total synthesis of (-)-Isoschizogamine

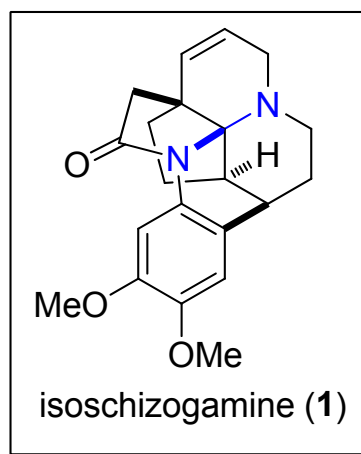
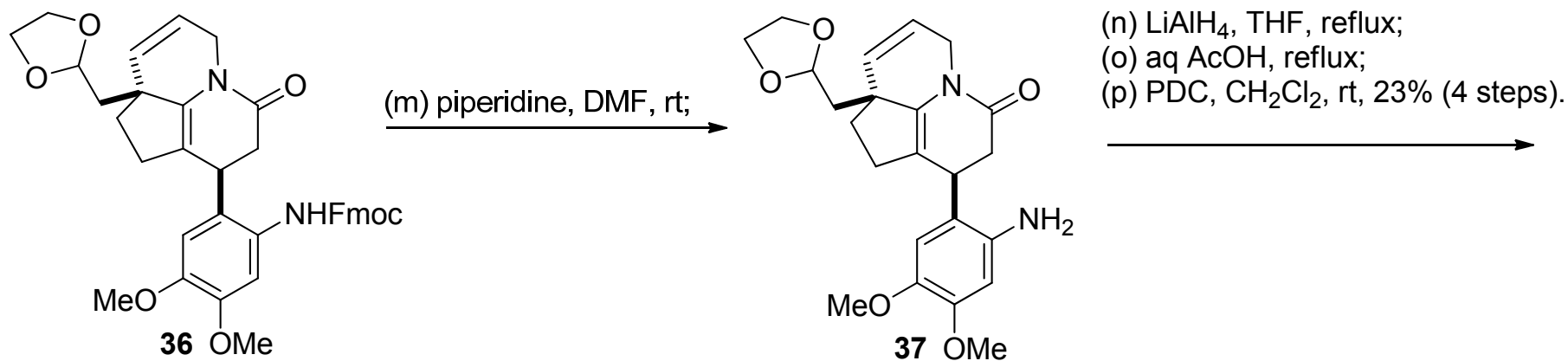




# Total synthesis of (-)-Isoschizogamine



# Total synthesis of (-)-Isoschizogamine

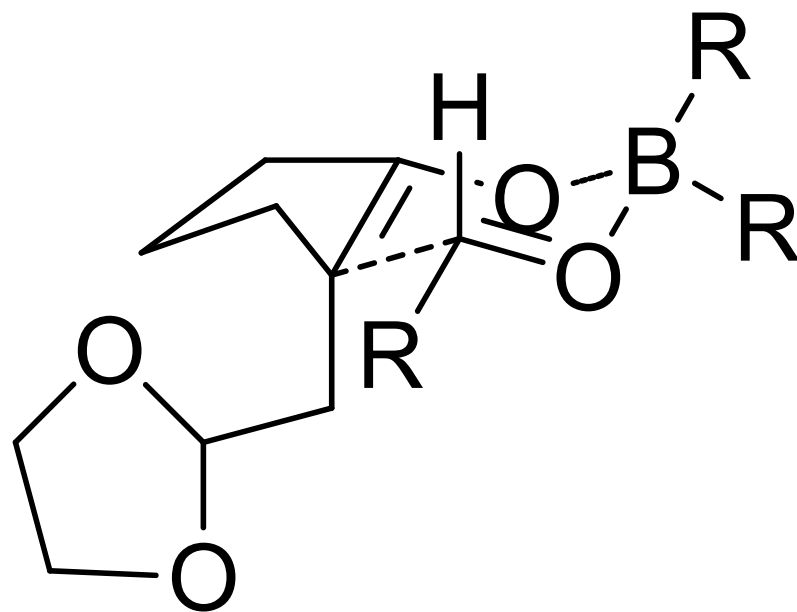


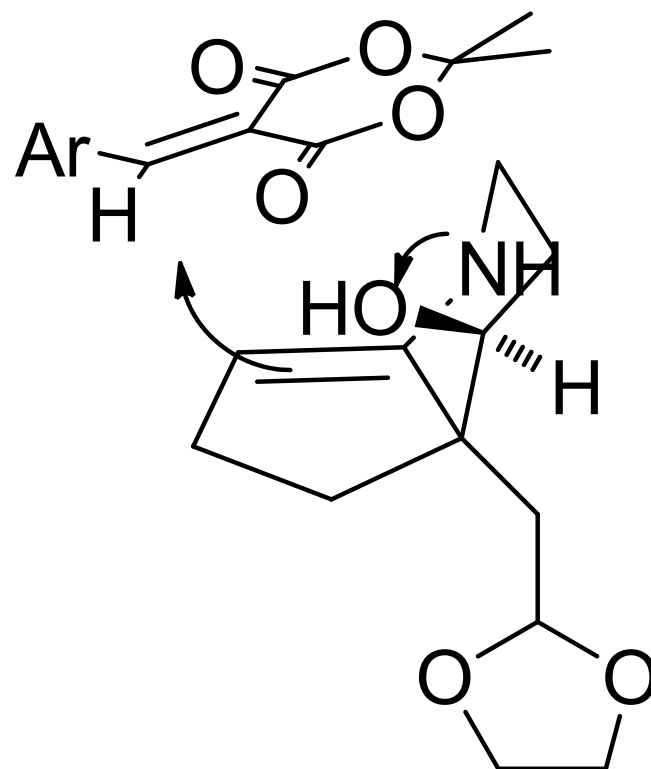
## Conclusion

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- The **first asymmetric** total synthesis of (–)-isoschizogamine;
- Key features: a facile construction of the carbon framework of the natural product using a **Wagner–Meerwein rearrangement**, a **tandem metathesis**, a stereoselective rhodium-mediated 1,4-addition of an arylboronic acid, and a ring-closing metathesis via hemiaminal ether **34**.

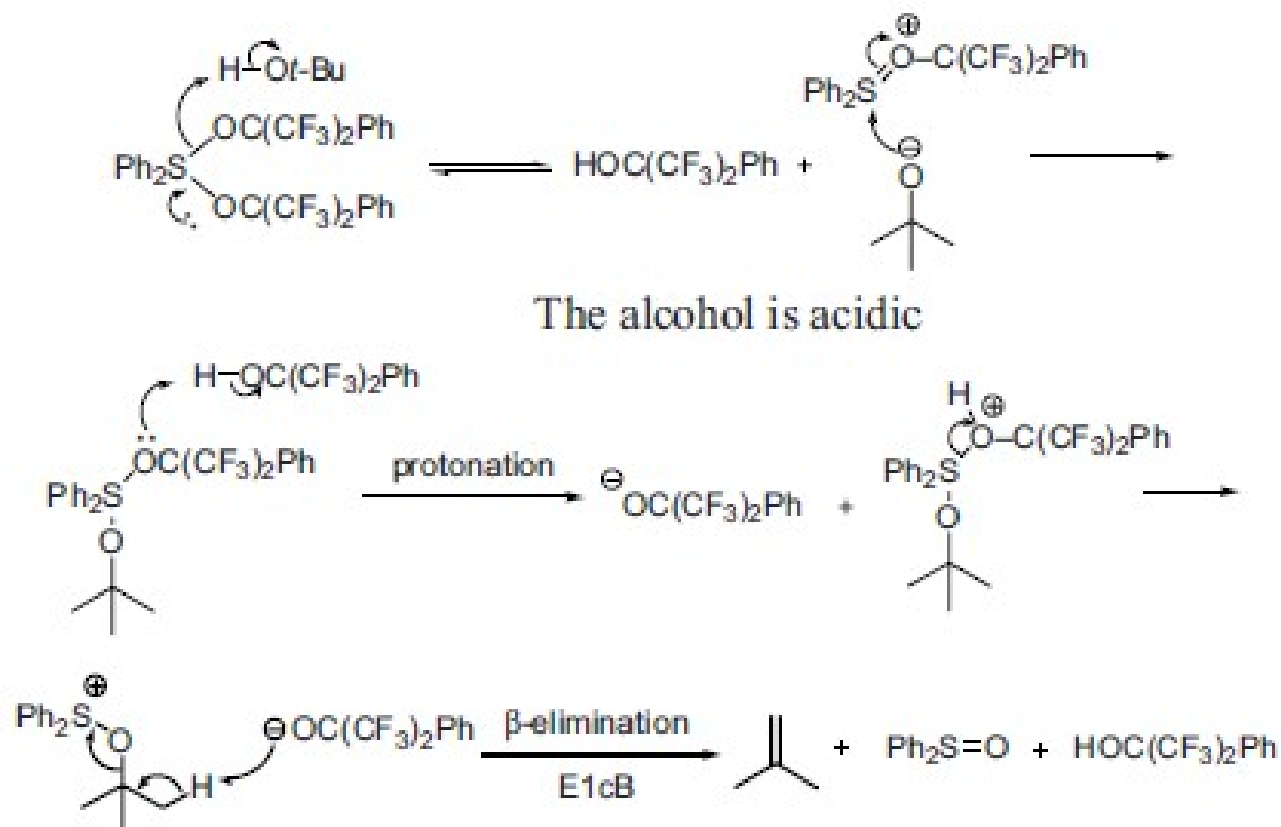
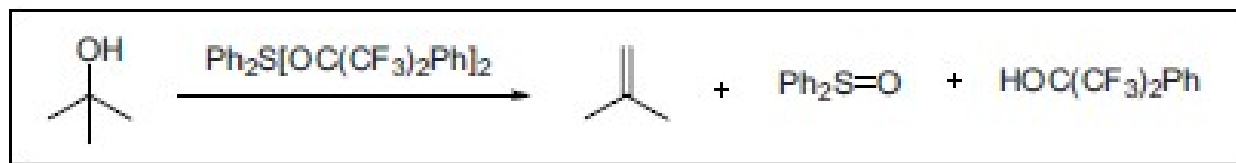
*Thank you!*

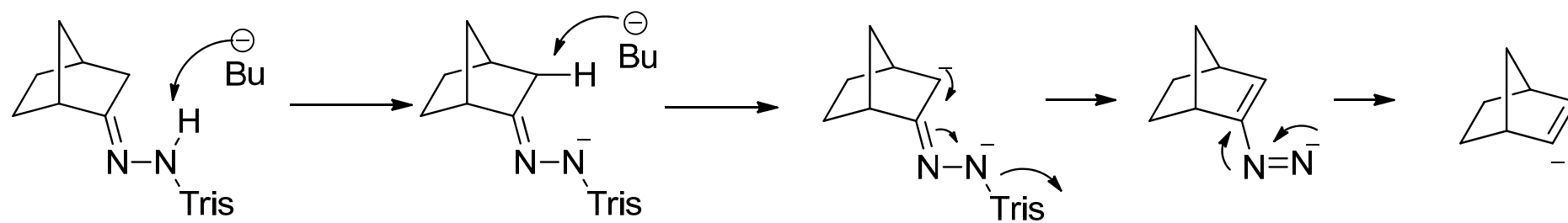




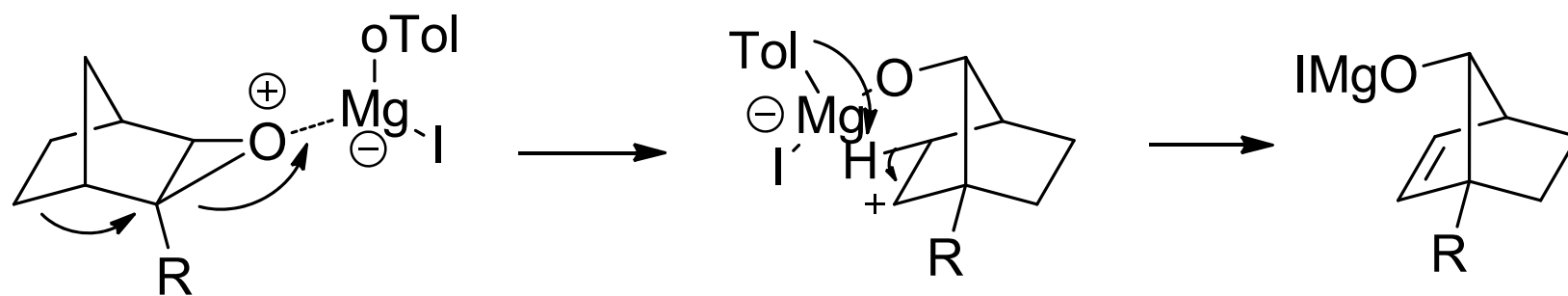
## Martin's sulfurane dehydrating reagent

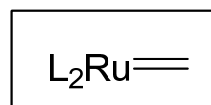
Dehydrates secondary and tertiary alcohols to give olefins, but forms ethers with primary alcohols.











the active catalyst

