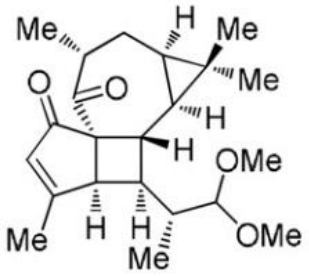
Natural Products

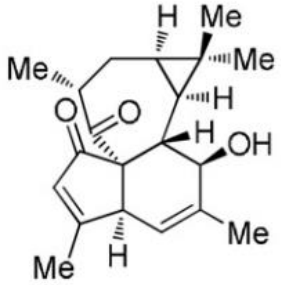
International Edition: DOI: 10.1002/anie.201915876
German Edition: DOI: 10.1002/ange.201915876

Total Synthesis of (−)-Pepluanol B: Conformational Control of the Eight-Membered-Ring System

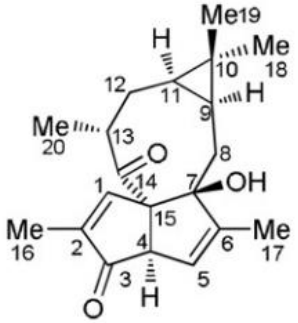
Jing Zhang, Meng Liu, Chuanhua Wu, Gaoyuan Zhao, Peiqi Chen, Lin Zhou, Xingang Xie, Ran Fang, Huilin Li, and Xuegong She**



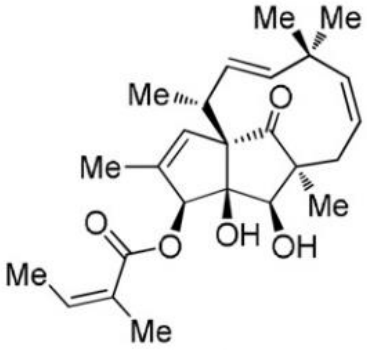
Pepluacetal (**1**)



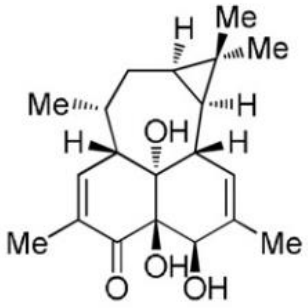
Pepluanol A (**2**)
total synthesis: Ding (2017)



Pepluanol B (**3**)
this work

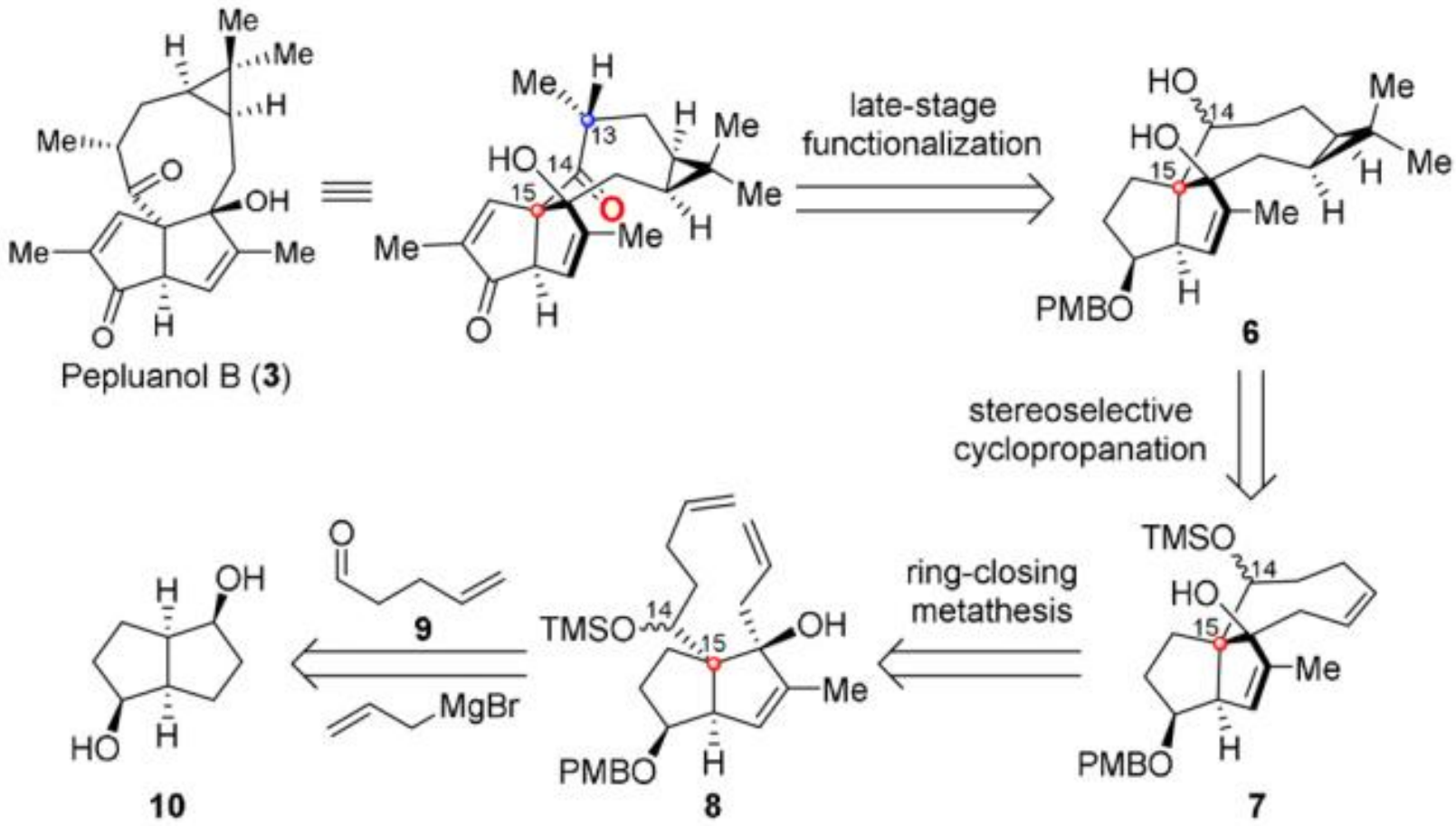


Pepluanol C (**4**)

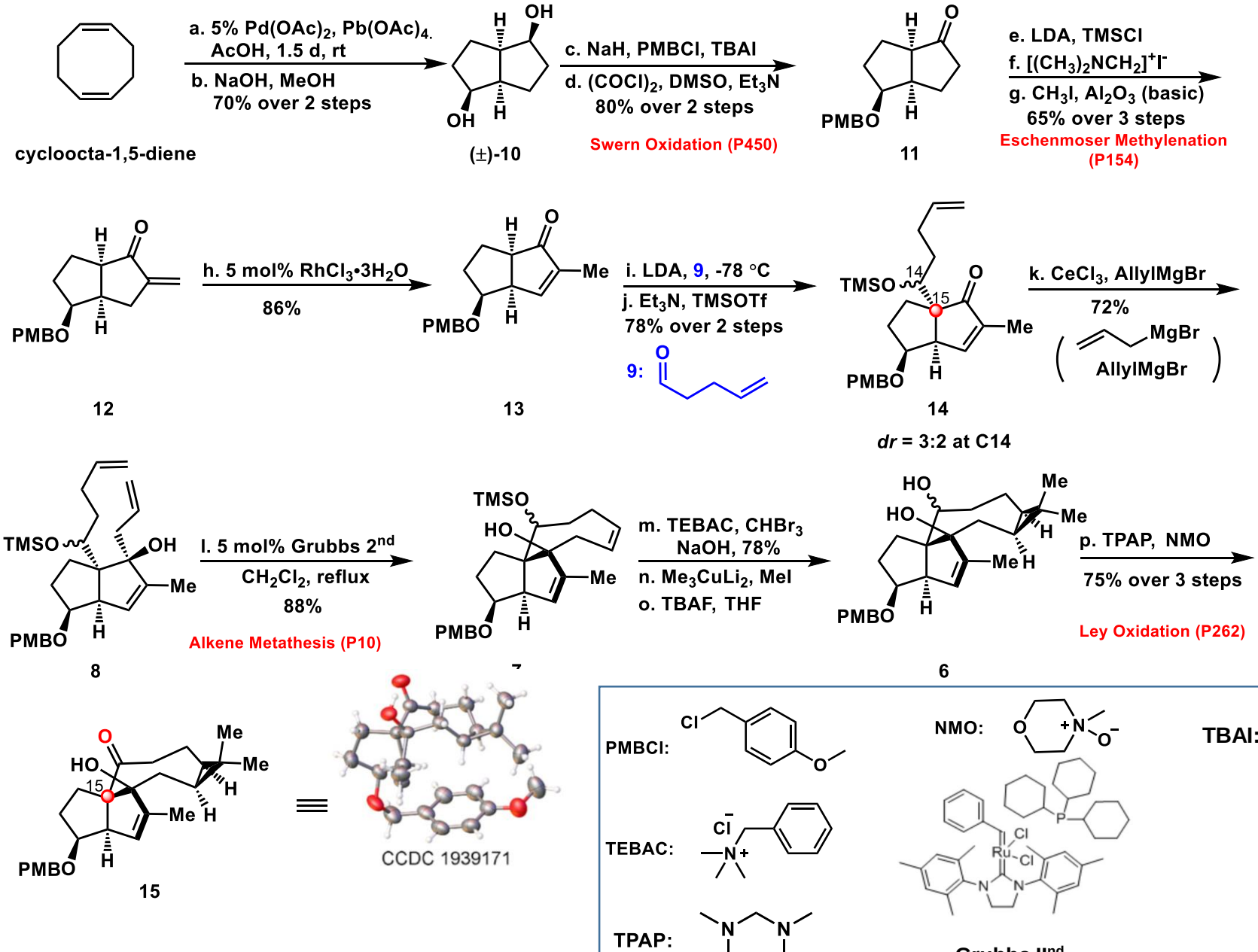


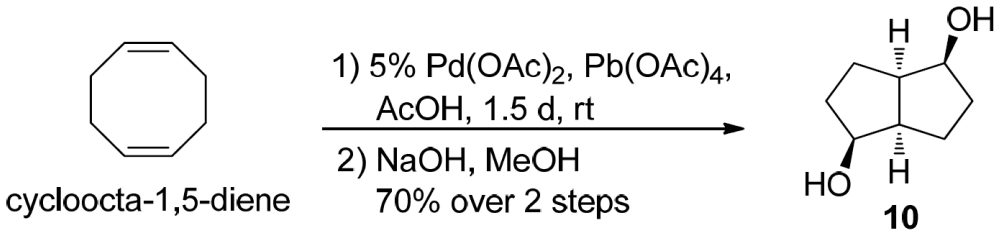
Pepluanol D (**5**)

Scheme 1. Retrosynthetic analysis of pepluanol B.



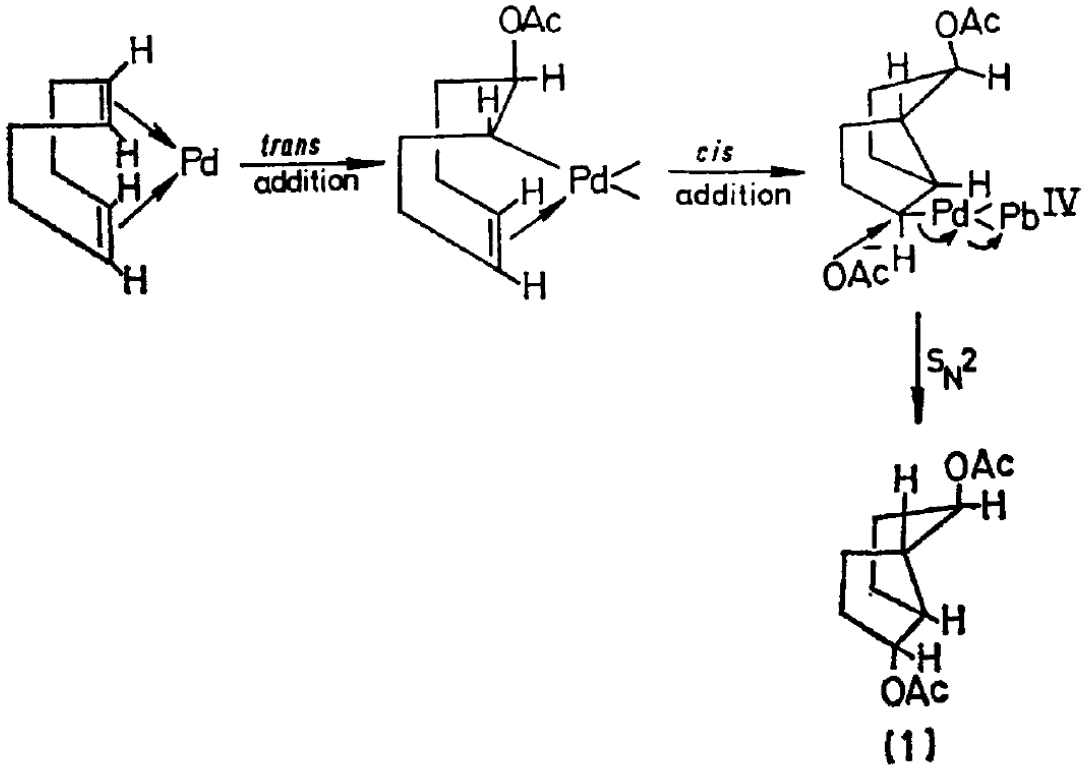
Scheme 2. Construction of tetracyclic scaffold **15**.





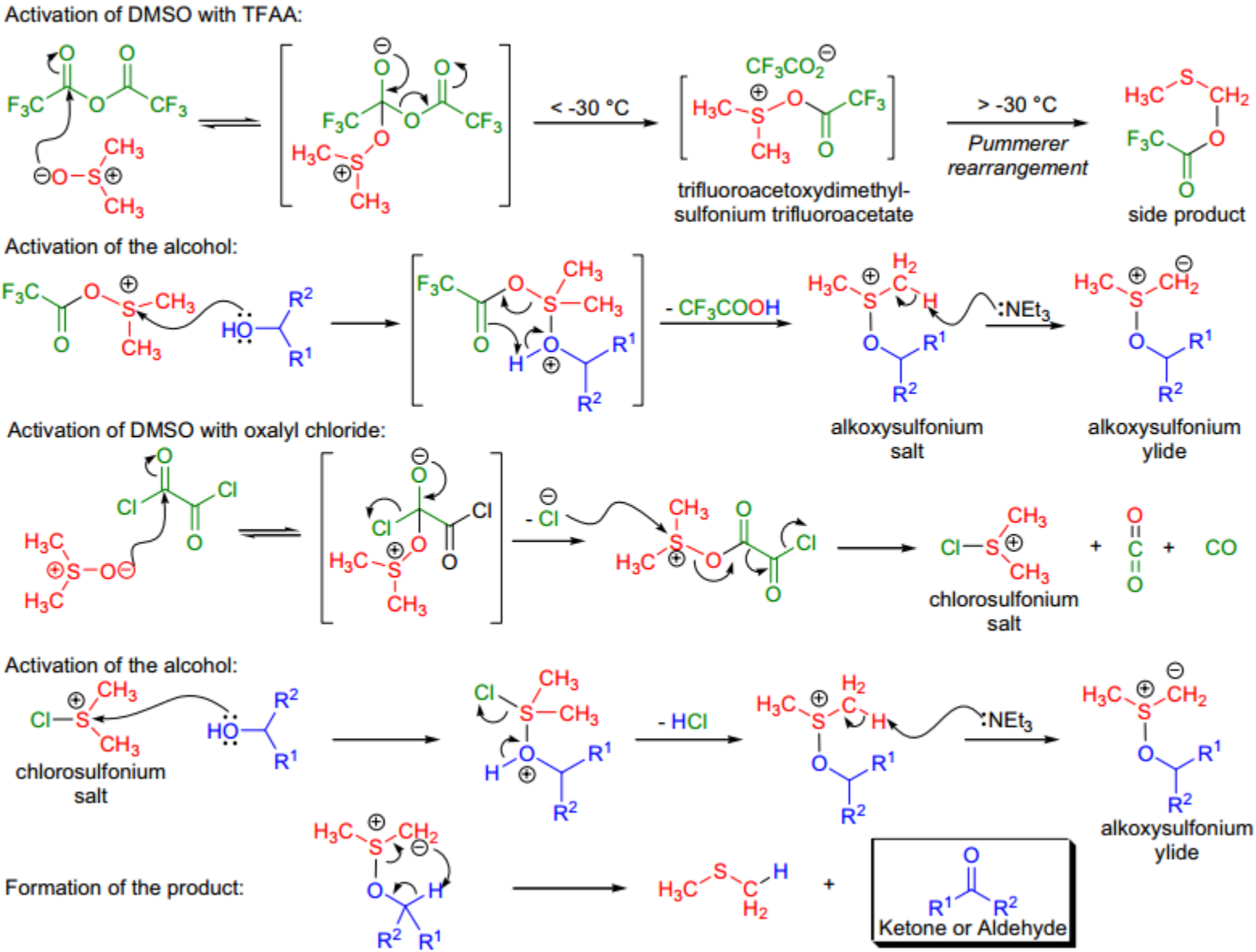
cycloocta-1,5-diene

10

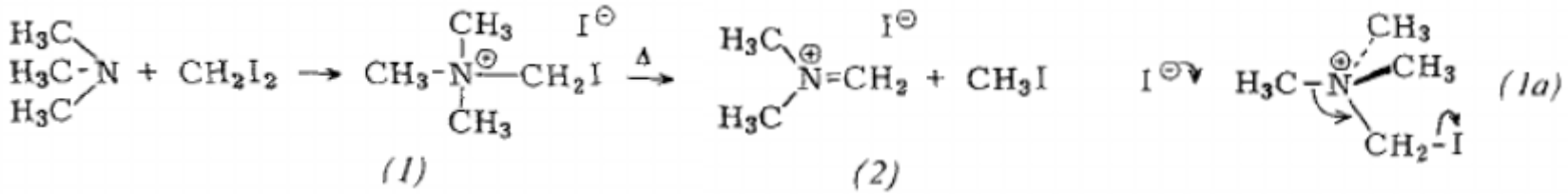


(1)

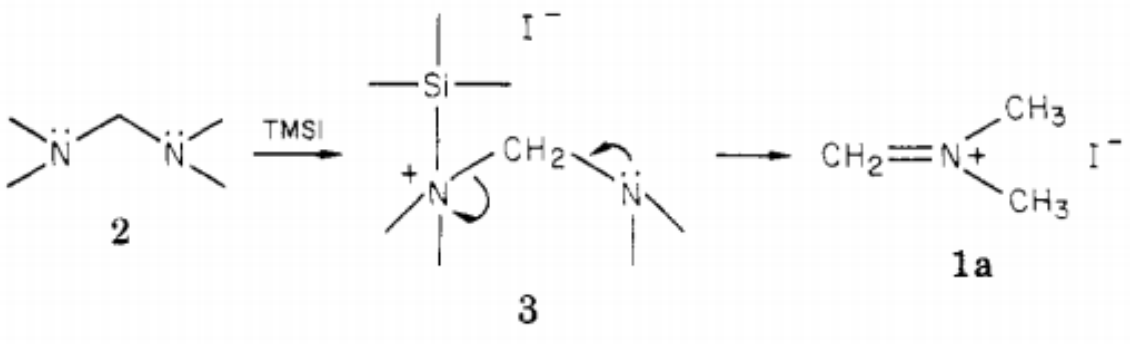
SWERN OXIDATION



Eschenmoser Salt

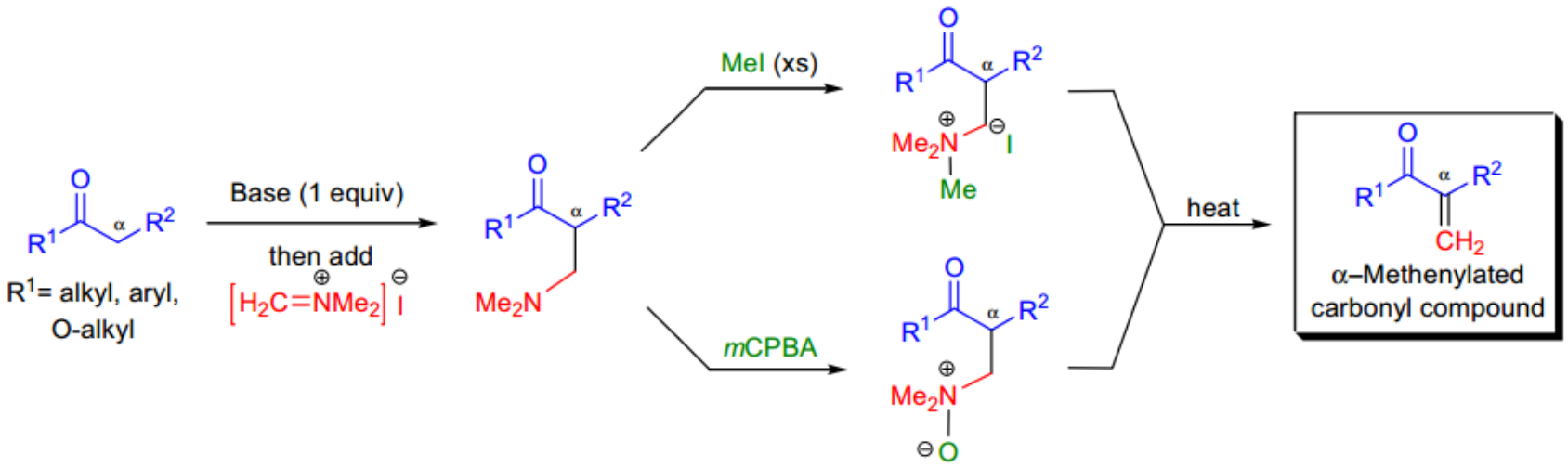


Angew. Chem. Int. Ed. Engl. **1971**, *10*, 330–331.

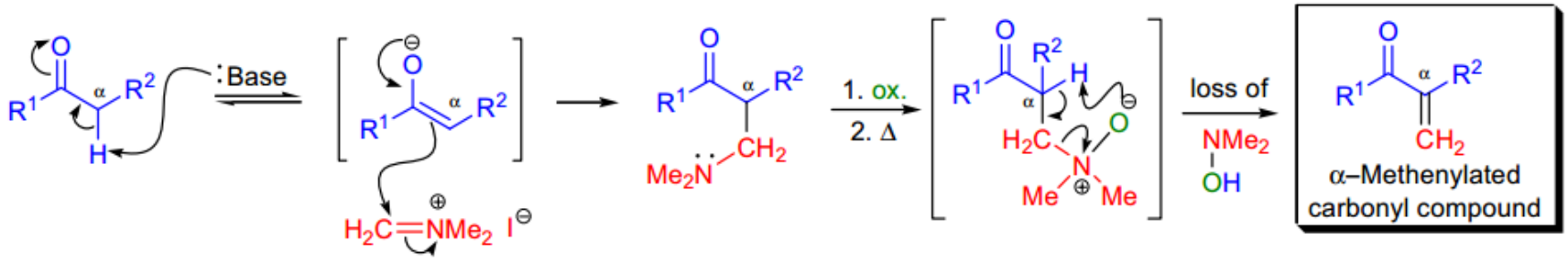


J. Org. Chem. **1980**, *45*, 524-525.

ESCHENMOSER METHENYLATION



Mechanism:



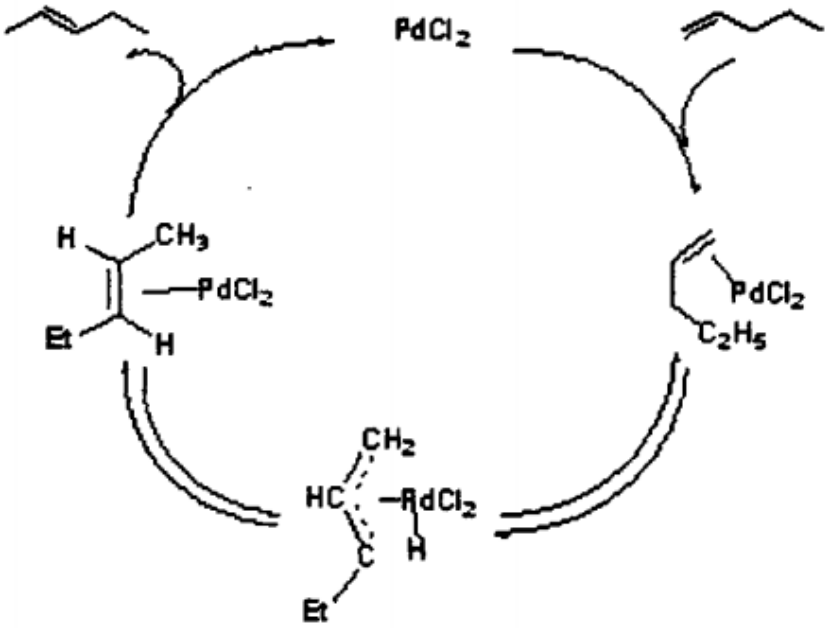
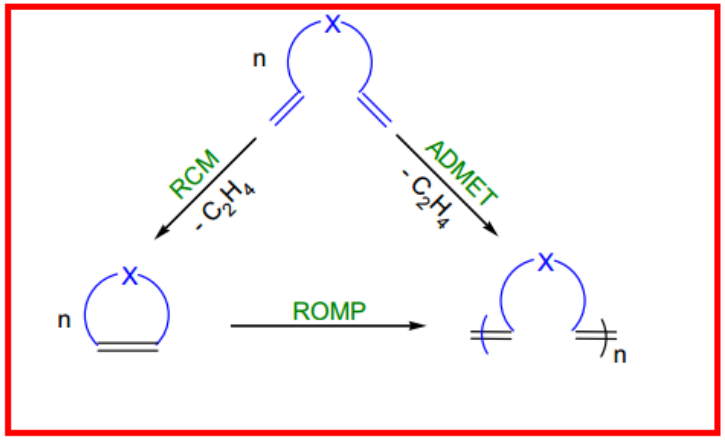


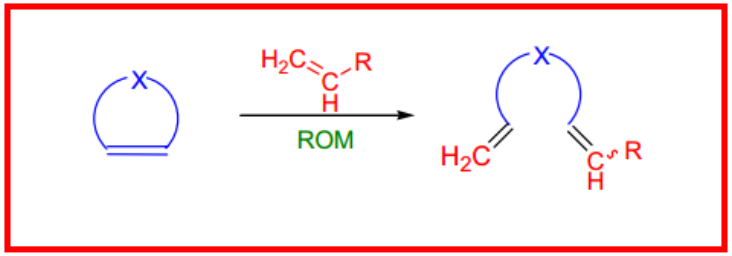
图 1-3　$PdCl_2$ 催化异构反应机理

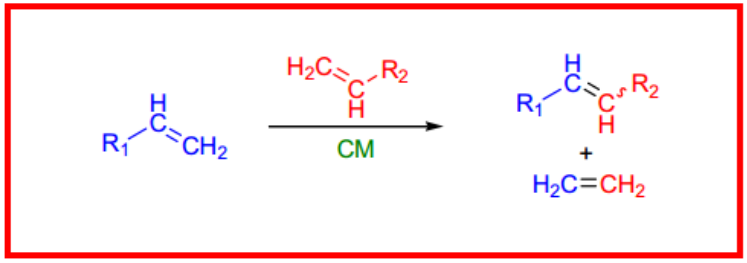
Fig. 1-3　the mechanism of olefin isomerization reaction used $PdCl_2$

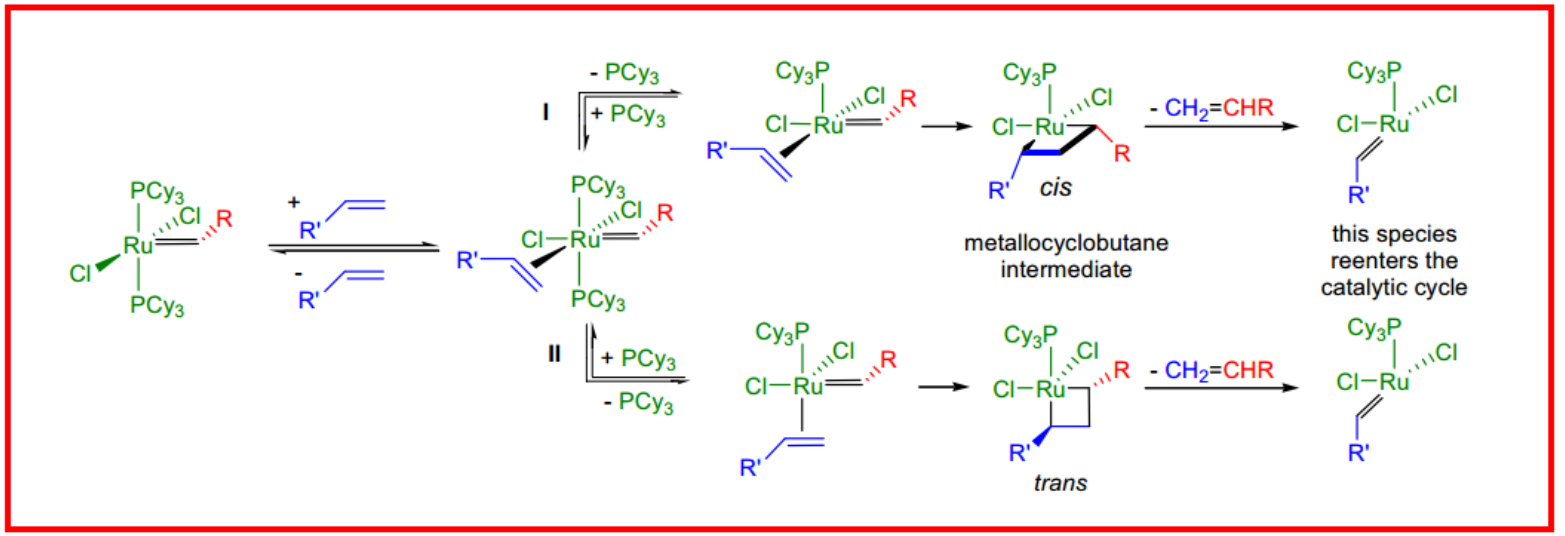
DOI: 10.7666/d.y1676999.

ALKENE (OLEFIN) METATHESIS

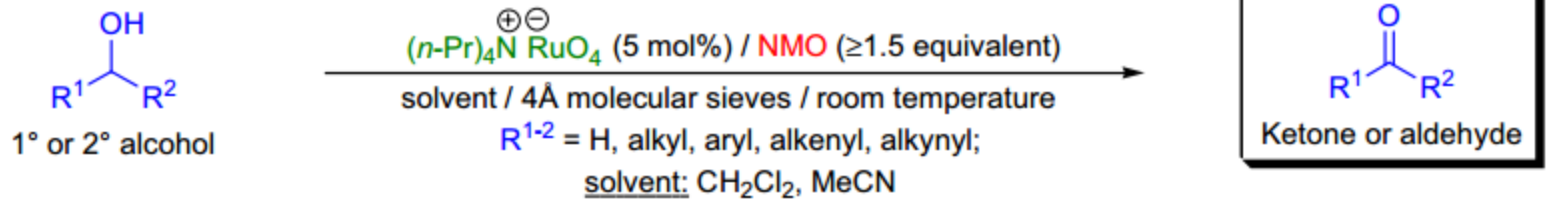






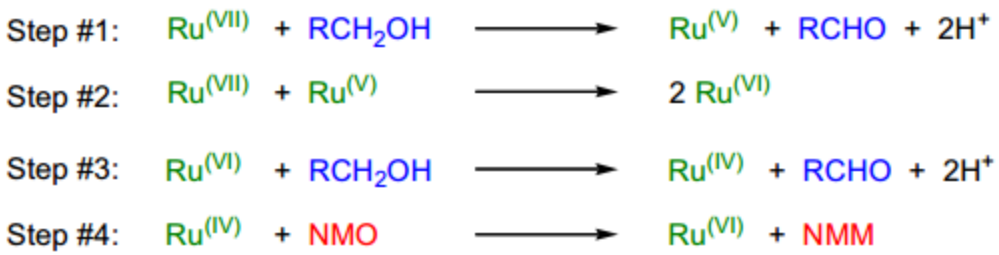


LEY OXIDATION

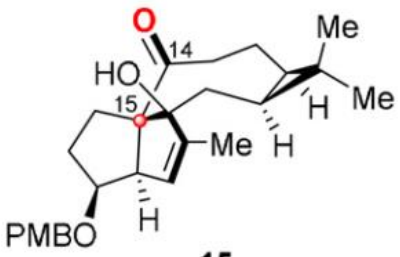


Mechanism: [19,6,20-25]

The mechanism of the *Ley oxidation* is complex and the exact nature of the species involved in the catalytic cycle is unknown. The difficulty in establishing an exact mechanism arises from the fact that the complexes of $Ru^{(VIII)}$, $Ru^{(VII)}$, $Ru^{(VI)}$, $Ru^{(V)}$ and $Ru^{(IV)}$ are all capable of stoichiometrically oxidizing alcohols to carbonyl compounds.[6] The TPAP reagent can oxidize alcohols stoichiometrically as a three-electron oxidant and can also be used as a catalyst when a co-oxidant is present (e.g., NMO, TMAO, or hydroperoxides). Data suggests that the oxidation proceeds *via* the formation of a complex between the alcohol and TPAP (ruthenate ester).[21] It was also found that the stoichiometric oxidation of isopropyl alcohol with TPAP is autocatalytic and the catalyst is suspected to be colloidal RuO_2. Small amounts of water decrease the degree of autocatalysis. This observation is supported by the finding that the addition of molecular sieves improves the efficiency of the reaction.



Scheme 3. Synthesis of compound **19**.



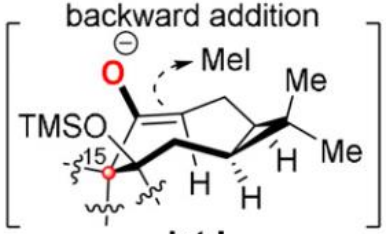
15

a. pyridine,TMSOTf

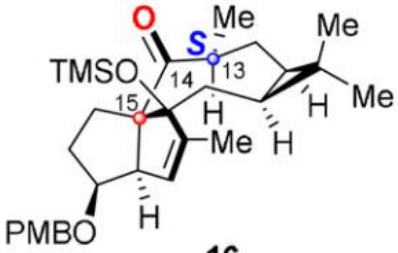
b. LDA, MeI, -78 °C

78% over 2 steps

backward addition

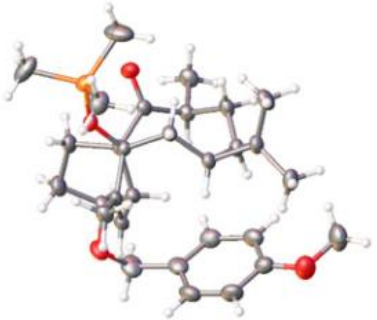


Int-I



16

≡

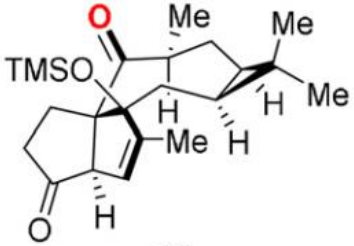


CCDC 1939170

c. DDQ, CH_2Cl_2

d. TPAP, NMO

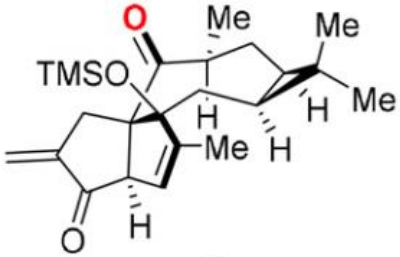
68% over 2 steps



17

e. TMMN, Ac_2O, DMF

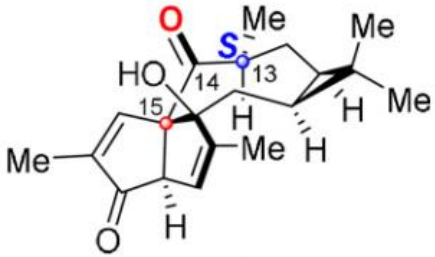
96 °C, 75%



18

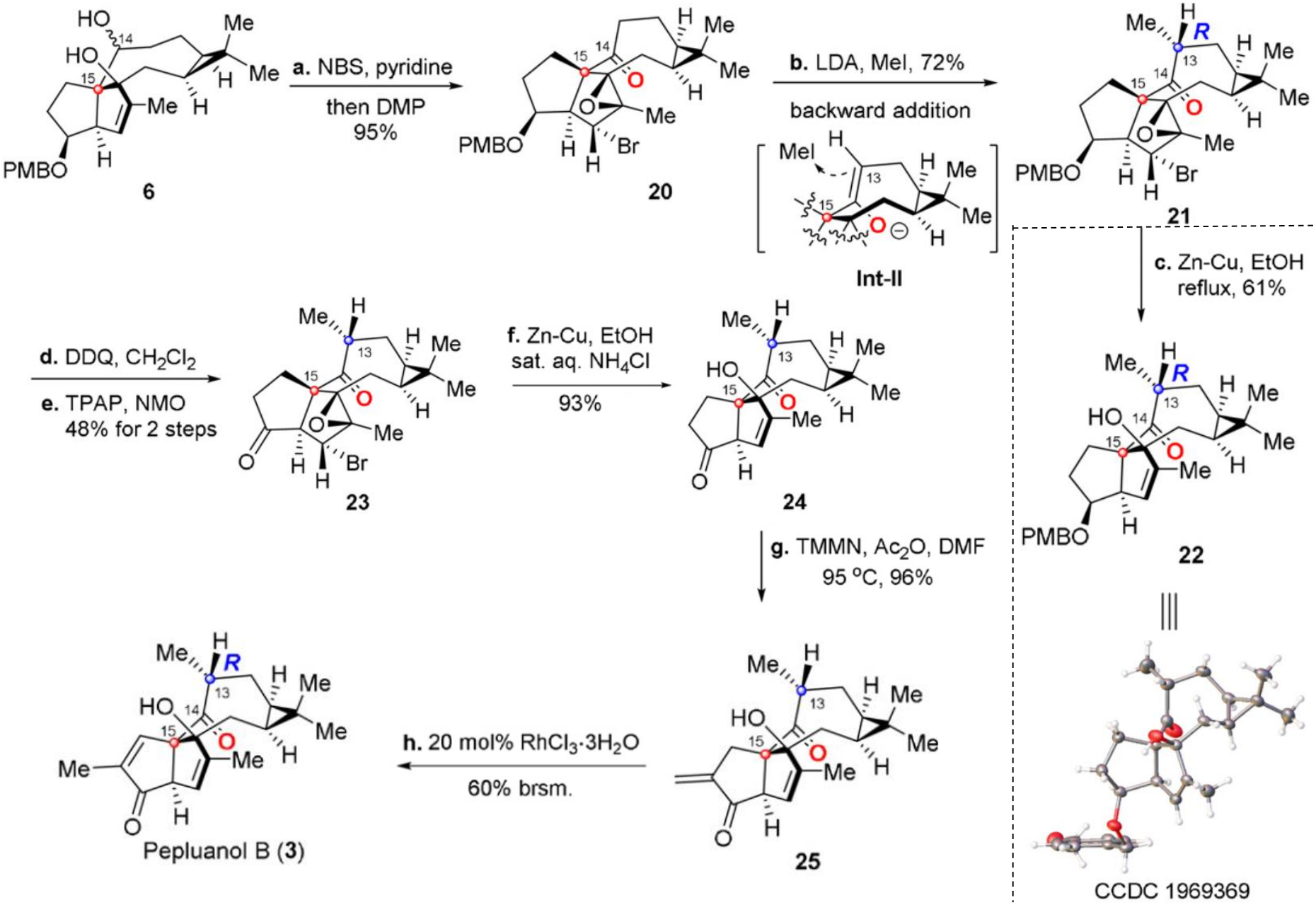
f. 20 mol% $RhCl_3 \cdot 3H_2O$

52%

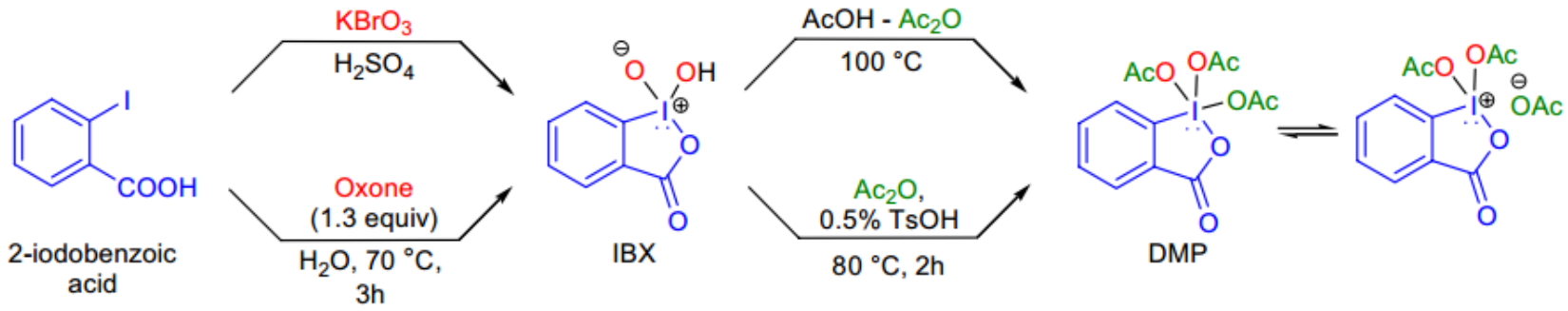


19

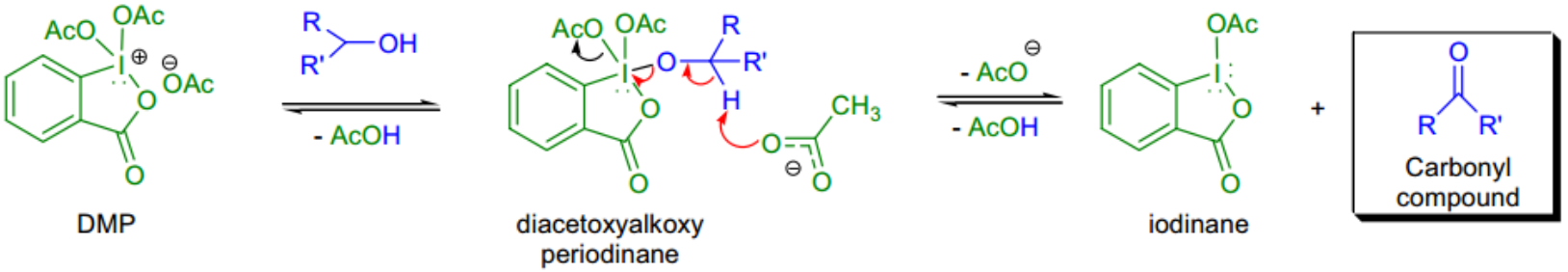
Scheme 4. Total synthesis of (±)-pepluanol B.



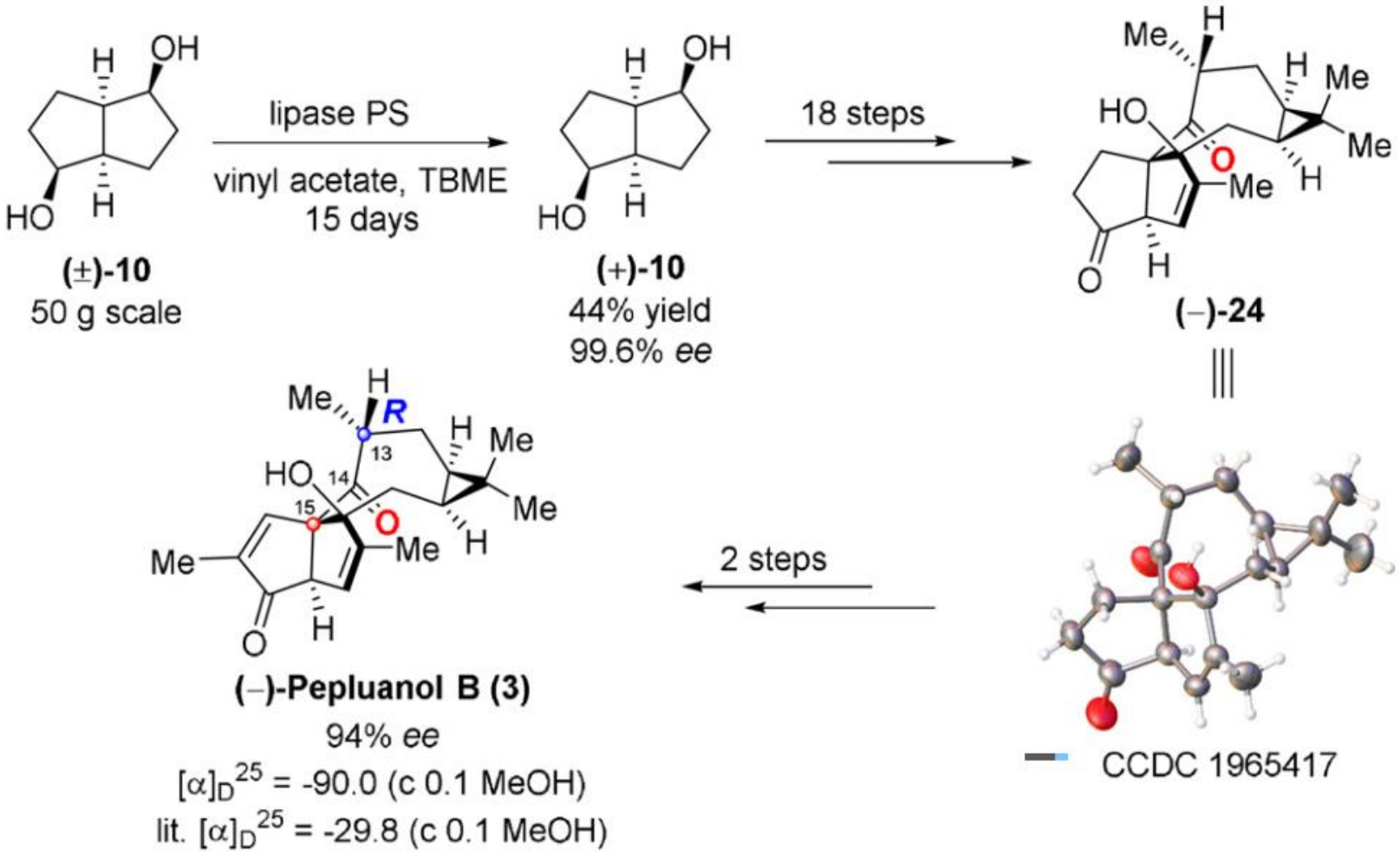
DESS-MARTIN OXIDATION

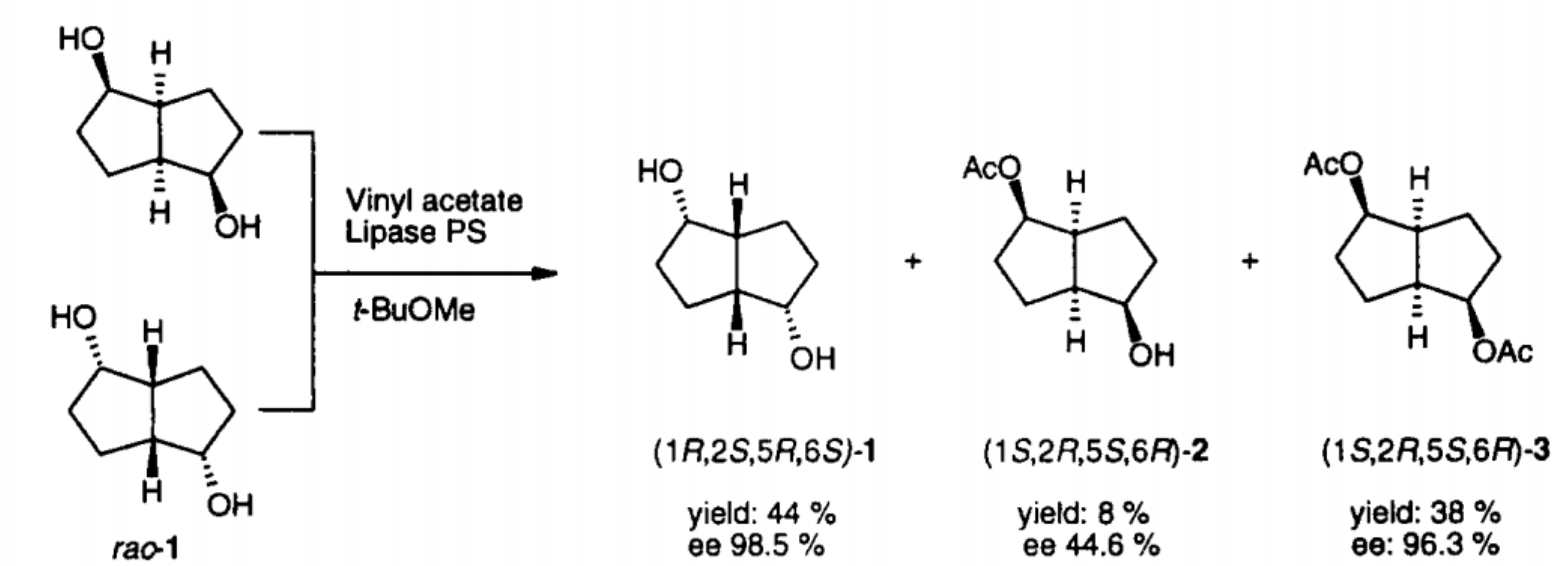


Mechanism:



Scheme 5. Enantioselective synthesis of (−)-pepluanol B.





Tetrahedron: Asymmetry **1997**, *8*, 2051–2055.