10.1002/anie.202007247

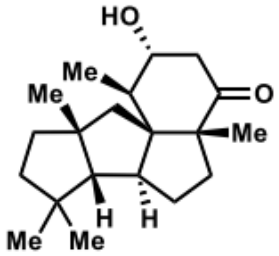
COMMUNICATION

WILEY-VCH

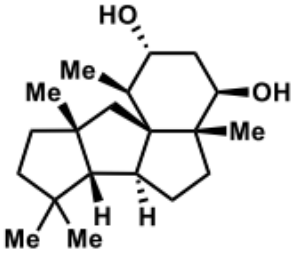
Total Syntheses of (–)-Conidiogenone B, (–)-Conidiogenone and (–)-Conidiogenol

Bo Xu,[+ [a]] Wen Xun,[+ [a]] Shaobin Su,[[a]] and Hongbin Zhai*[[a-c]]

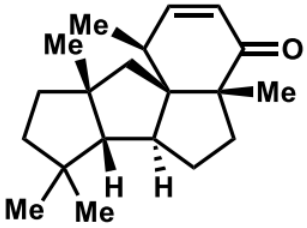
In memory of Prof. Jack E. Baldwin



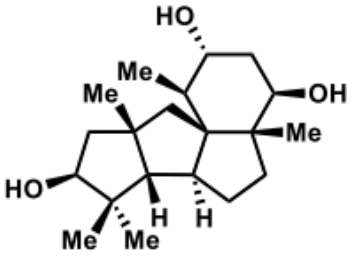
Conidiogenone



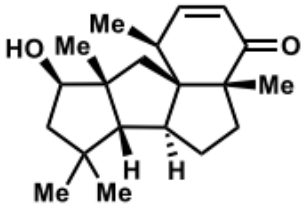
Conidiogenol



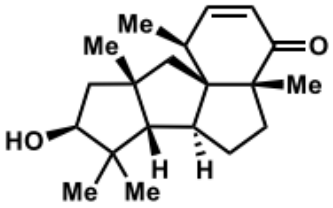
(-)-conidiogenone B (3)



Conidiogenol C



Conidiogenone E



Conidiogenone F

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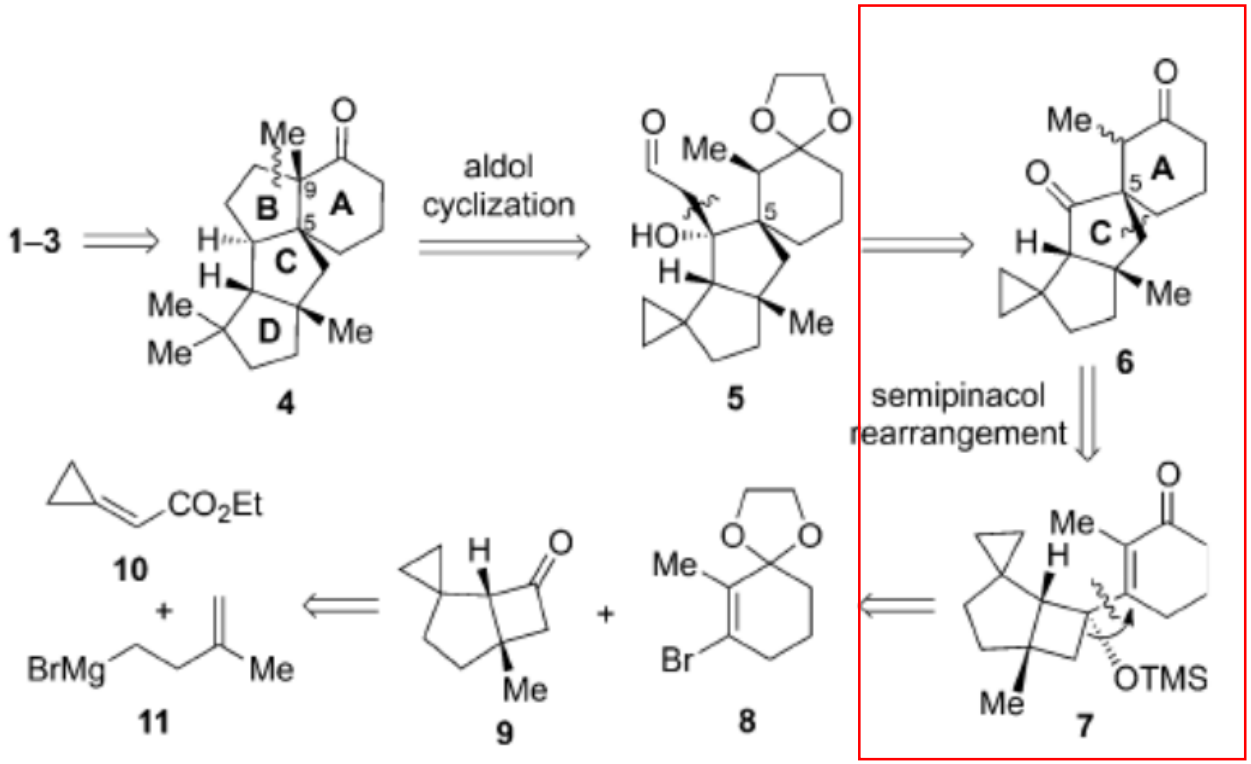
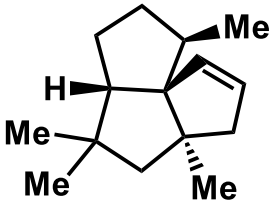


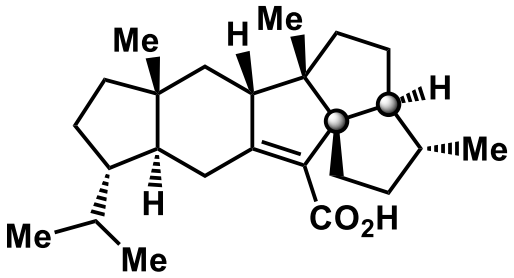
Scheme 2. Retrosynthetic analysis of **1–3**. TMS = trimethylsilyl.

Angew.Chem.Int. Ed. **2016**, *55*,4456 –4460

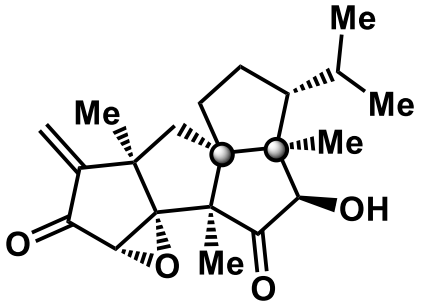
Danheiser annulation to access angular triquinane



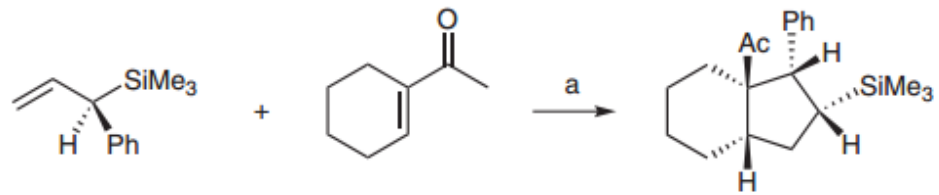
silphinene (7)



retigeranic acid A (8)

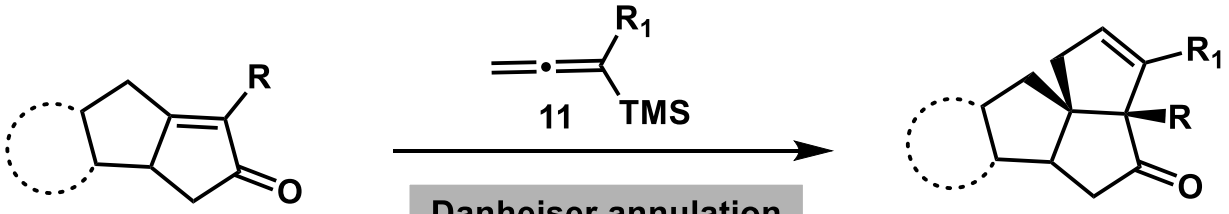


crinipellin A (9)



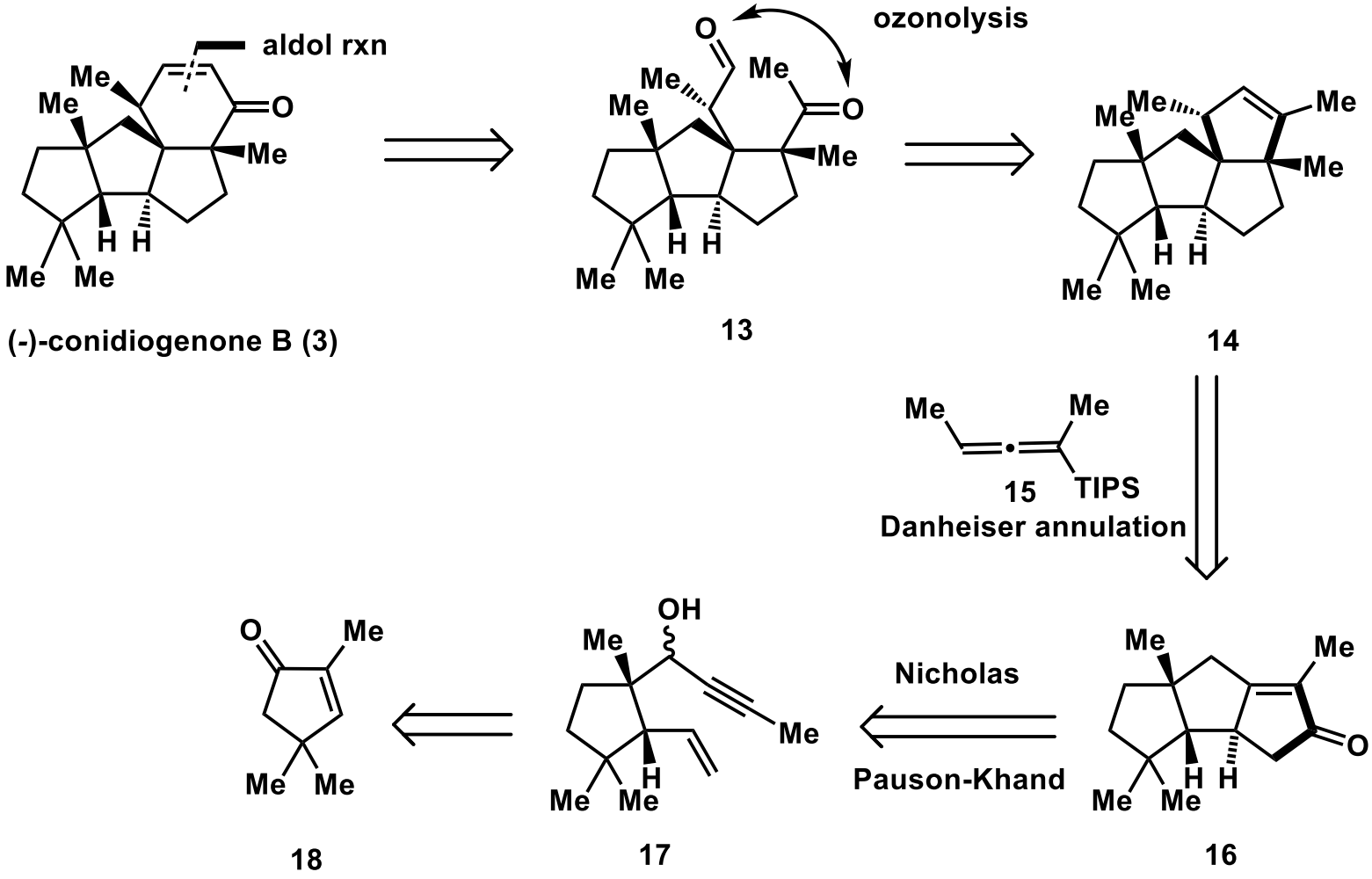
(*R*)-**24** (82% ee) **2b** (+)-**25** (82% ee)

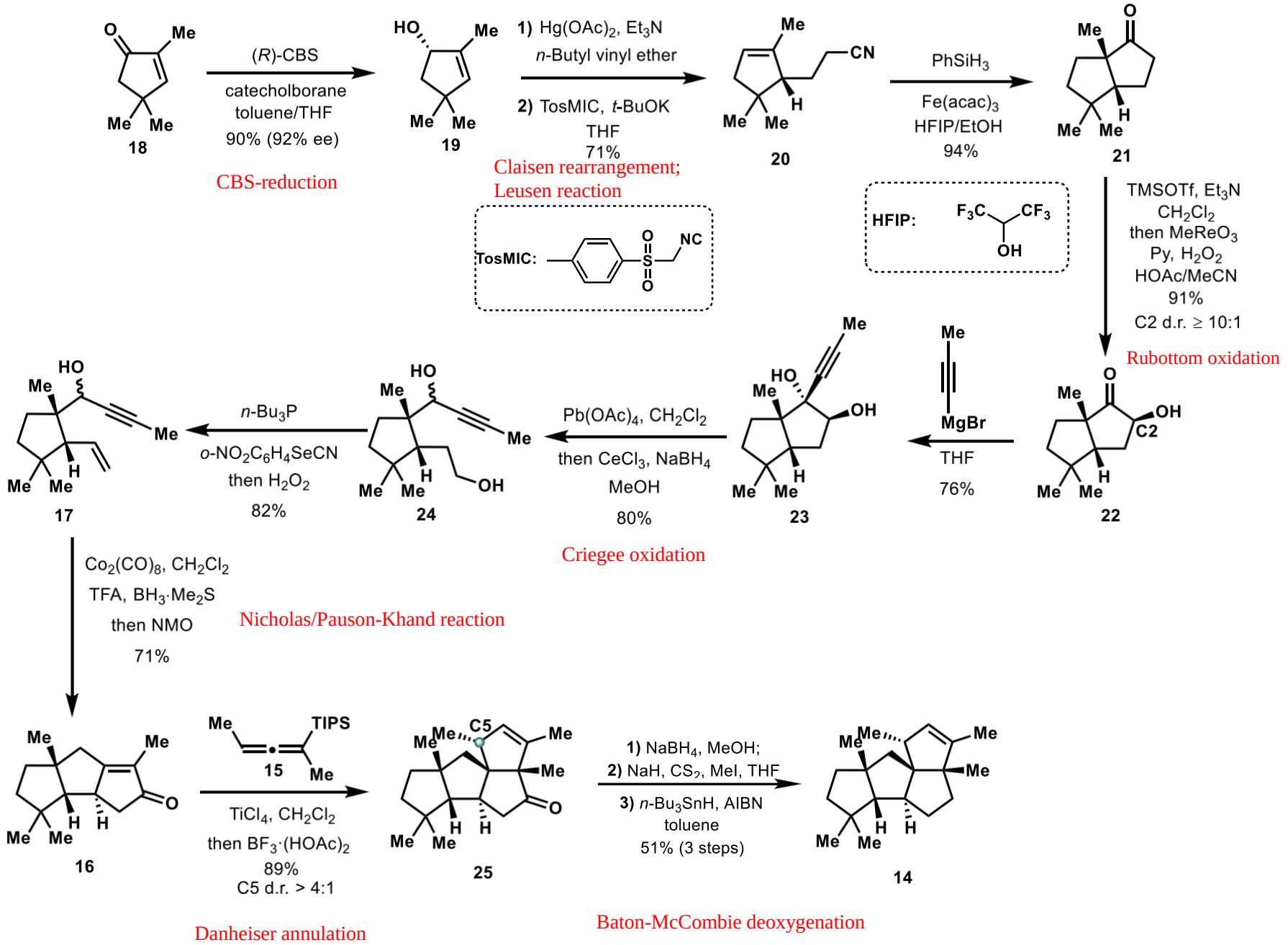
Synlett, **2010**, *15*, 2207–2239



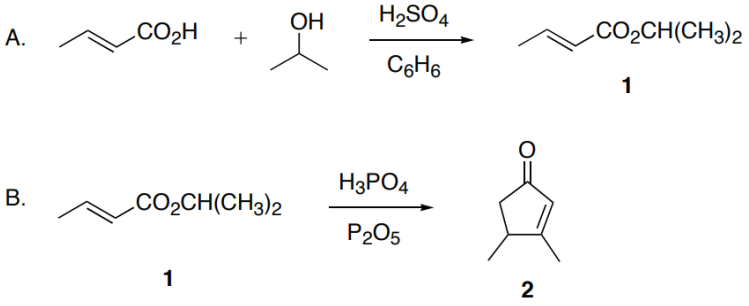
10 **angular triquinane (12)**

Retrosynthetic analysis of (-)-conidiogenone B (3)




18
(R)-CBS
catecholborane
toluene/THF
90% (92% ee)
CBS-reduction
19
1) Hg(OAc)2, Et3N
n-Butyl vinyl ether
2) TosMIC, t-BuOK
THF
71%
Claisen rearrangement;
Leusen reaction
TosMIC:
20
PhSiH3
Fe(acac)3
HFIP/EtOH
94%
HFIP:
21
TMSOTf, Et3N
CH2Cl2
then MeReO3
Py, H2O2
HOAc/MeCN
91%
C2 d.r. ≥ 10:1
Rubottom oxidation
22
MeMgBr
THF
76%
23
Pb(OAc)4, CH2Cl2
then CeCl3, NaBH4
MeOH
80%
Criegee oxidation
24
n-Bu3P
o-NO2C6H4SeCN
then H2O2
82%
17
Co2(CO)8, CH2Cl2
TFA, BH3·Me2S
then NMO
71%
Nicholas/Pauson-Khand reaction
16
15
TiCl4, CH2Cl2
then BF3·(HOAc)2
89%
C5 d.r. > 4:1
Danheiser annulation
25
1) NaBH4, MeOH;
2) NaH, CS2, MeI, THF
3) n-Bu3SnH, AIBN
toluene
51% (3 steps)
Baton-McCombie deoxygenation
14

Synthesis of Compound 18



Scheme 1

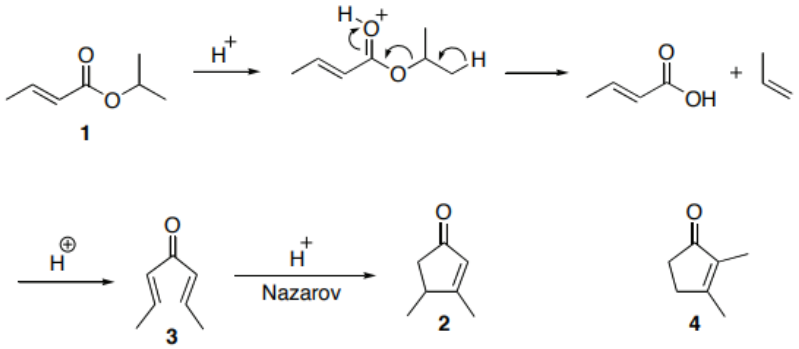
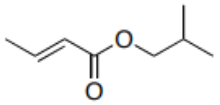
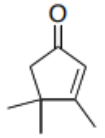
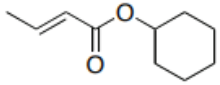
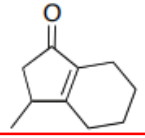
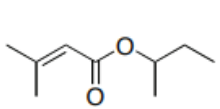
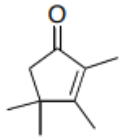
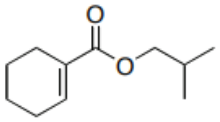
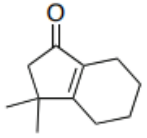
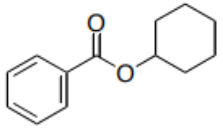
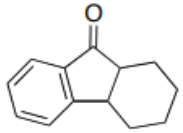


Table 1

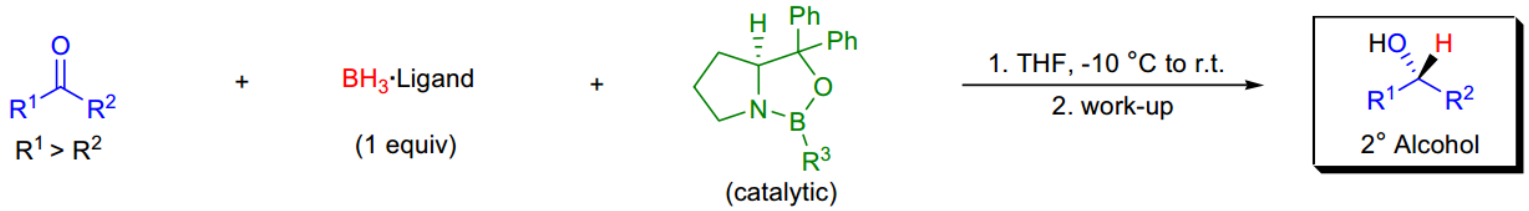
Conversion of α,β-Unsaturated Esters to Cyclopent-2-en-1-ones under Nazarov Conditions[a]

Ester	Product	Yield (%)
		60
		60
		60
		59
		40

a) H_3PO_4, P_2O_5

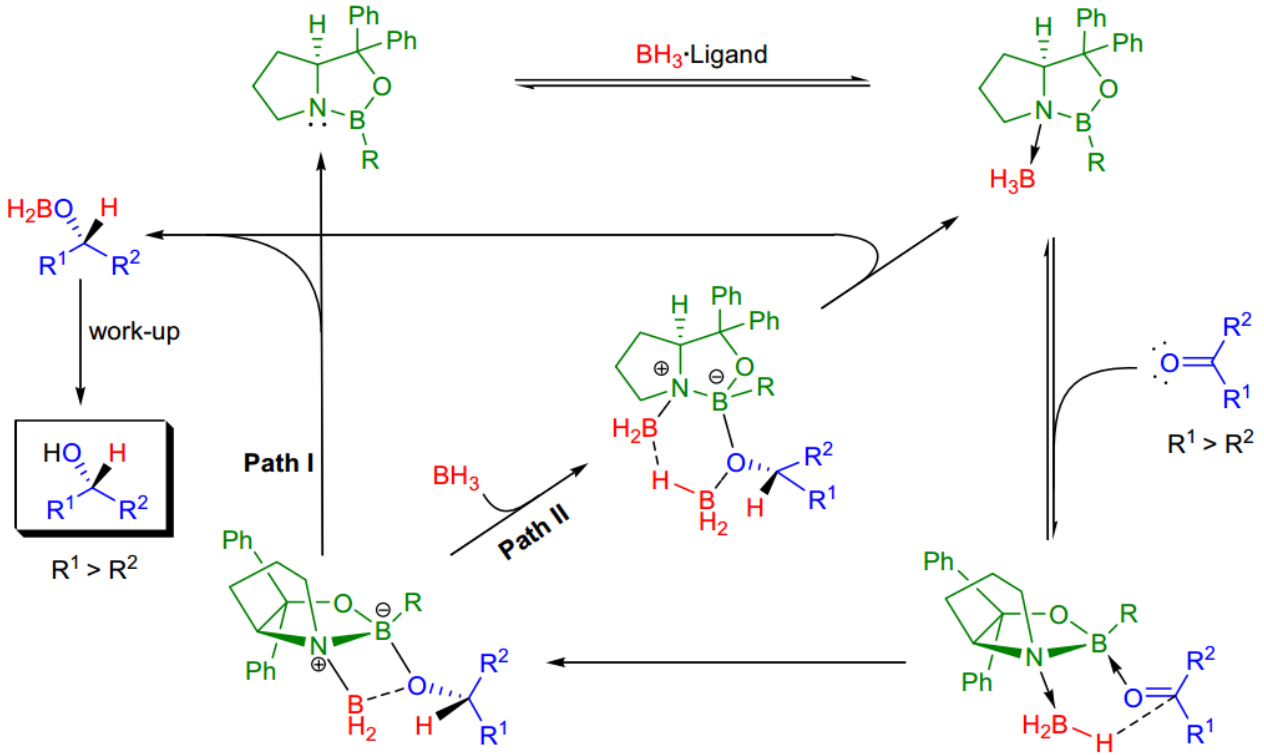
Org. Synth. **2006**, *83*, 49-54

COREY-BAKSHI-SHIBATA REDUCTION (CBS REDUCTION)

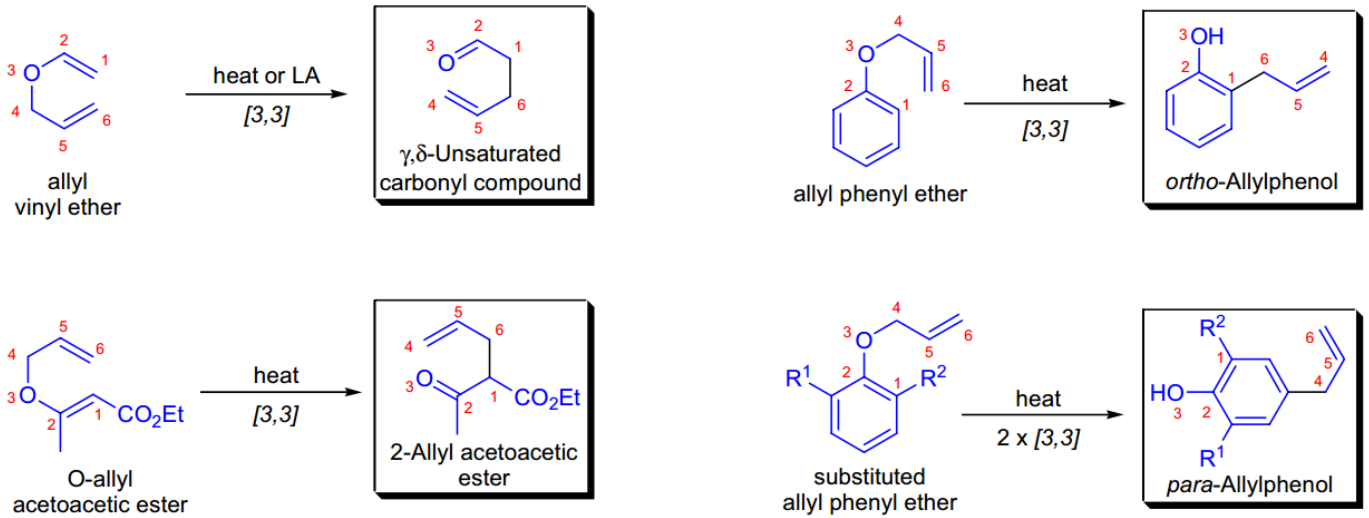


$R^{1\text{-}2}$ = alkyl, aryl; Ligand: THF, Me_2S, 1,4-thioxane, diethylaniline; R^3 = H, alkyl

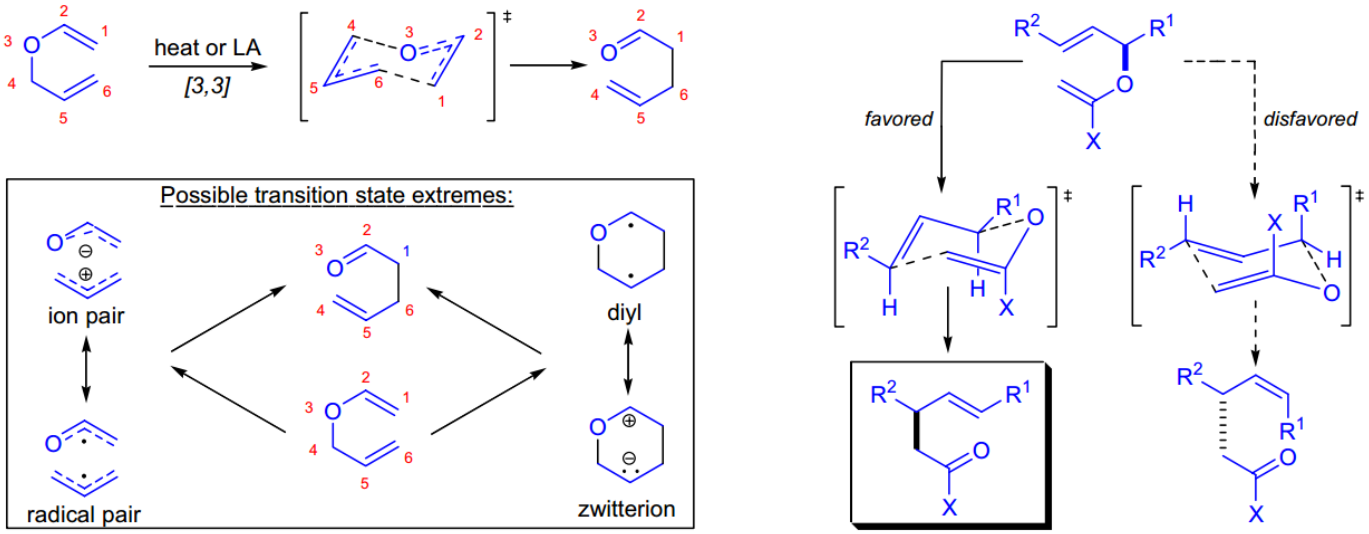
Mechanism:



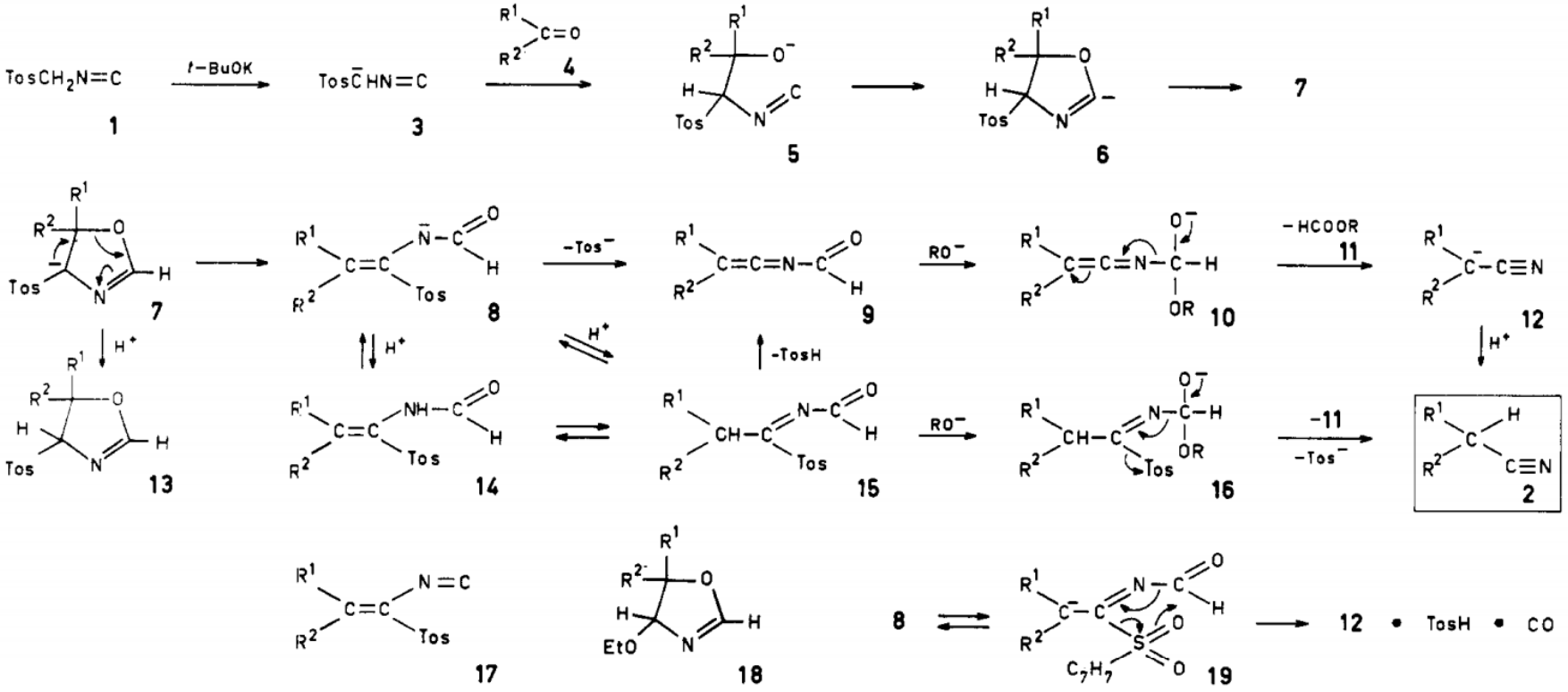
CLAISEN REARRANGEMENT



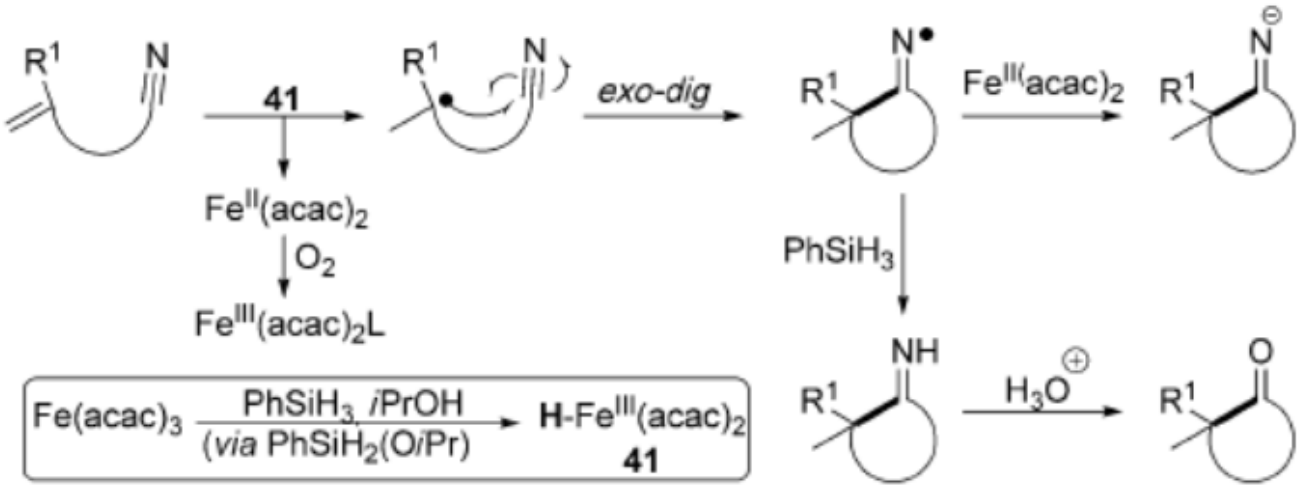
Mechanism:



Van Leusen reaction



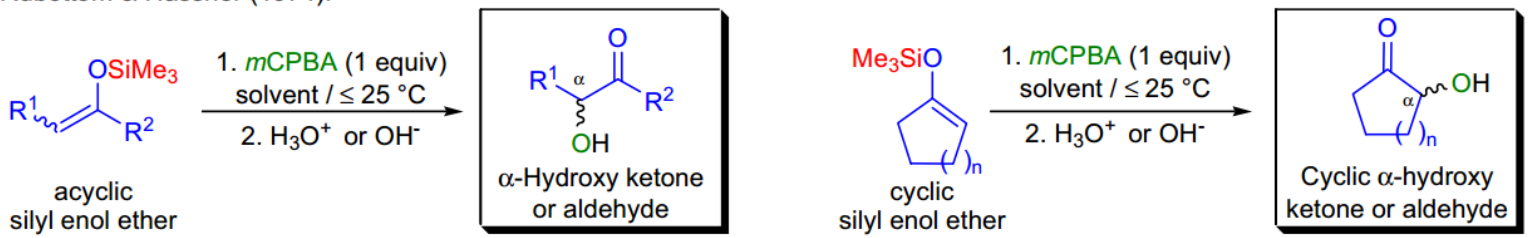
J.Org. Chem. **1977**, *42*, 3114-3118



Scheme 5. Proposed mechanism for HAT-mediated alkene-nitrile cyclisation.

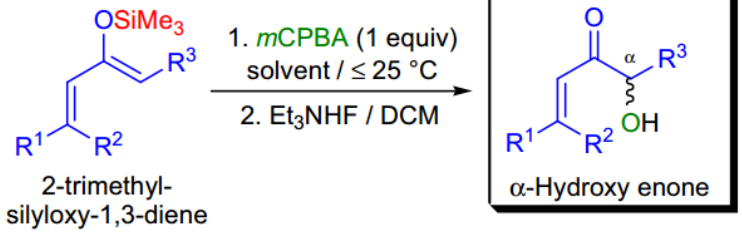
RUBOTTOM OXIDATION

Rubottom & Hassner (1974):



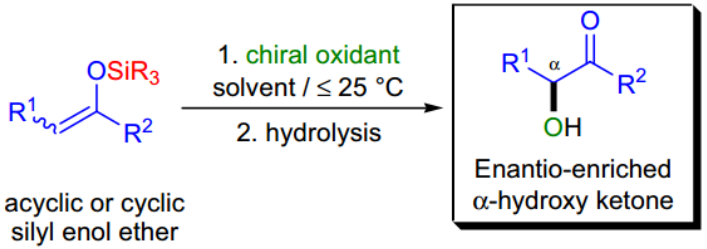
acyclic silyl enol ether

Oxidation of 2-trimethylsilyloxy-1,3-dienes:



2-trimethyl-silyloxy-1,3-diene

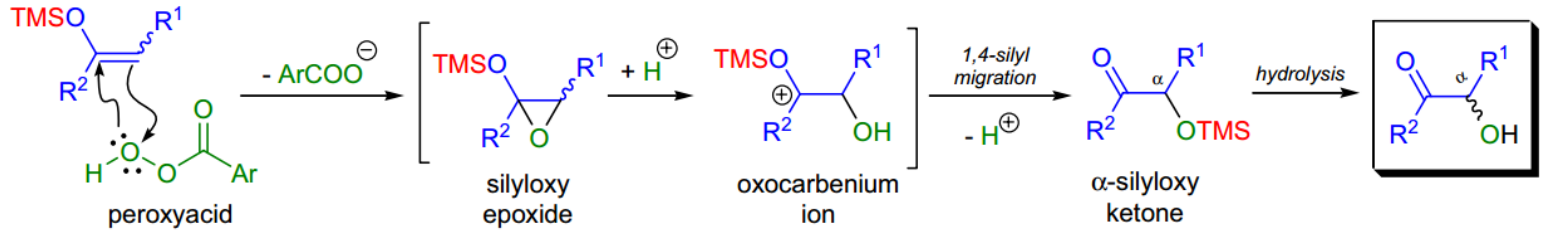
Asymmetric modification:



acyclic or cyclic silyl enol ether

R^{1-3} = H, alkyl, aryl, substituted alkyl and aryl; SiR_3 = $SiMe_3$, $SiMe_2$(t-Bu), $SiEt_3$; solvent: CH_2Cl_2, pentane, toluene; n = 1-3;
chiral oxidant: Davis' chiral oxaziridine, Shi's D-fructose derived ketone/Oxone, (Salen)manganese(III)-complexes/NaOCl or PhIO

Mechanism:

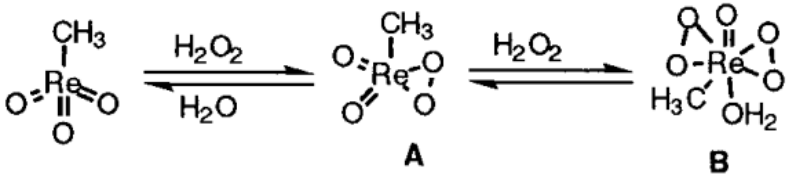


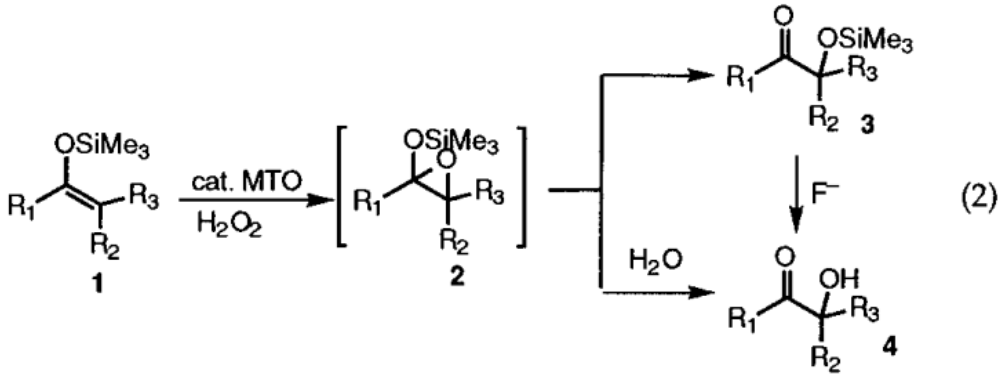
peroxyacid

silyloxy epoxide

oxocarbenium ion

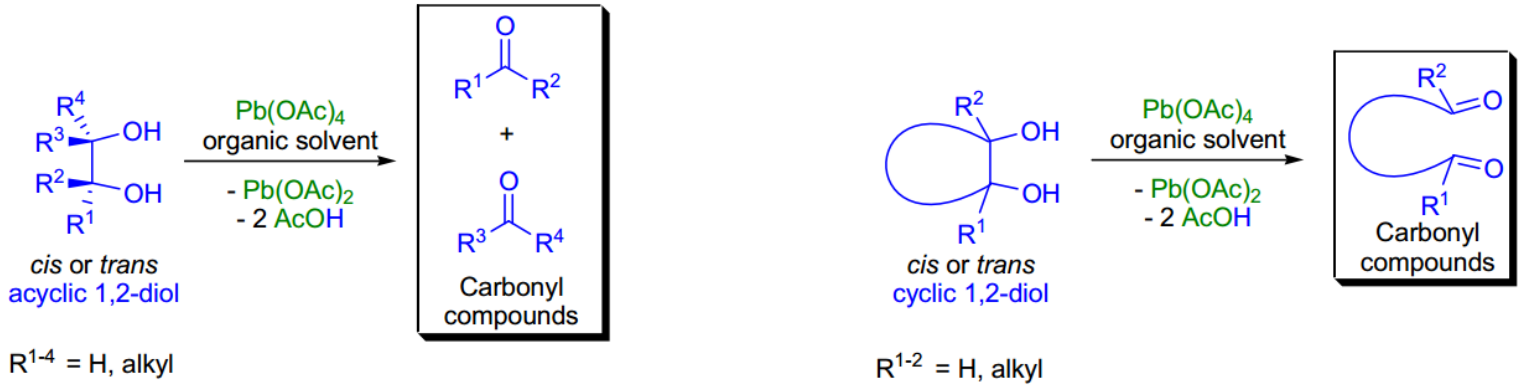
α-silyloxy ketone



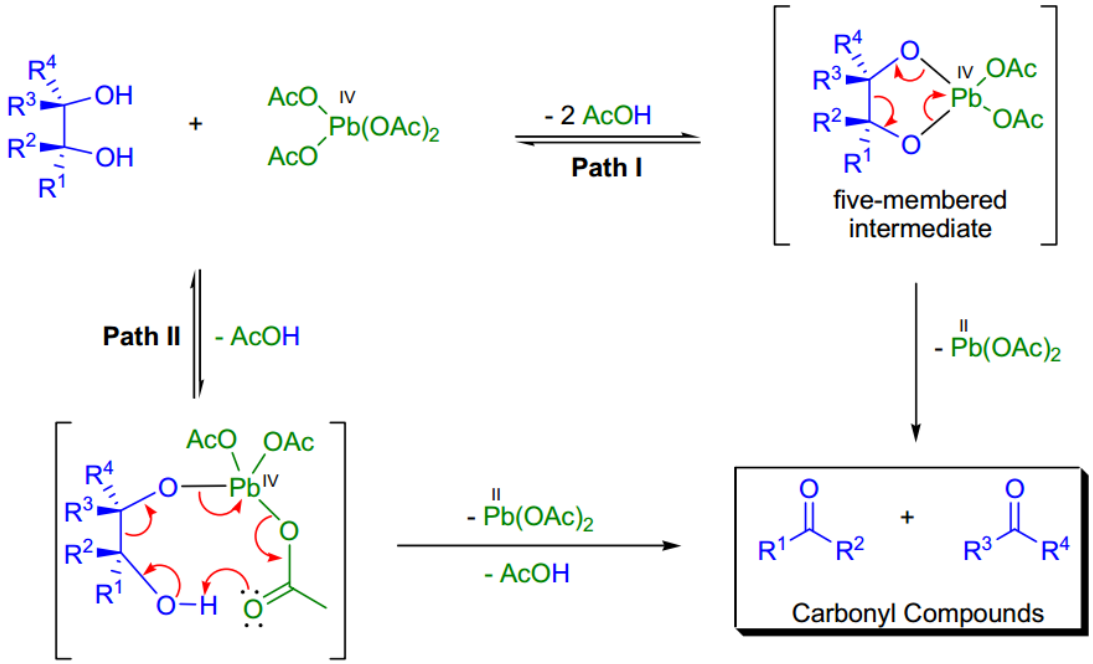


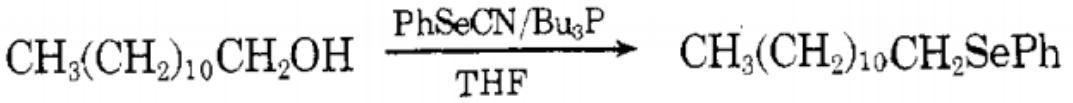
J. Org. Chem. **1998**, *63*, 4129-4130

CRIEGEE OXIDATION



Mechanism:





$$ArSeCN + Bu_3P \rightarrow ArSe\overset{+}{P}Bu_3\ CN^- \quad (6)$$

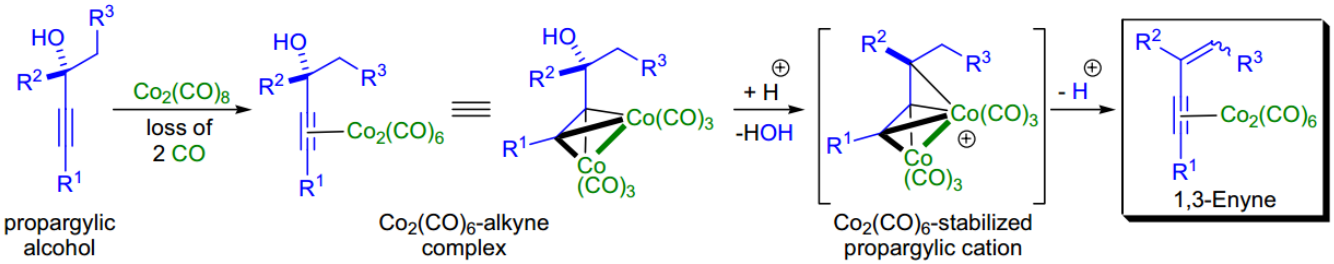
$$ArSe\overset{+}{P}Bu_3\ CN^- + RCH_2OH \rightarrow RCH_2O\overset{+}{P}Bu_3 + HCN + ArSe^- \quad (7)$$

$$RCH_2O\overset{+}{P}Bu_3 + ArSe^- \rightarrow RCH_2SeAr + Bu_3P{=}O \quad (8)$$

J. Org. Chem. **1976**, *41*, 1485-1486.

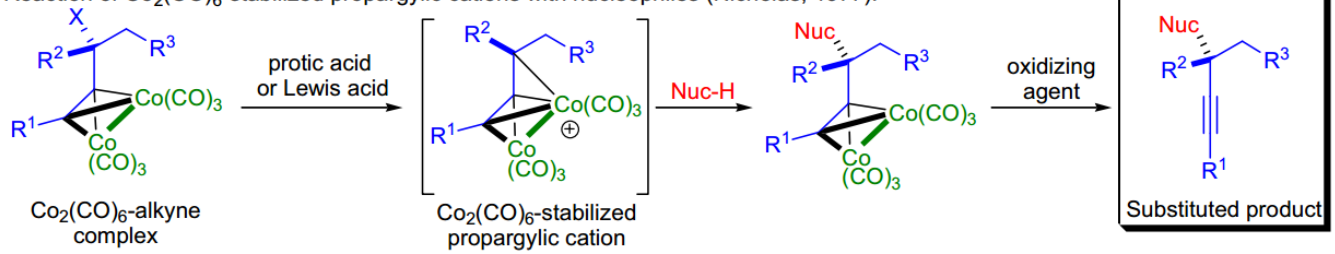
NICHOLAS REACTION

Nicholas & Pettit (1972):



propargylic alcohol — $Co_2(CO)_6$-alkyne complex — $Co_2(CO)_6$-stabilized propargylic cation

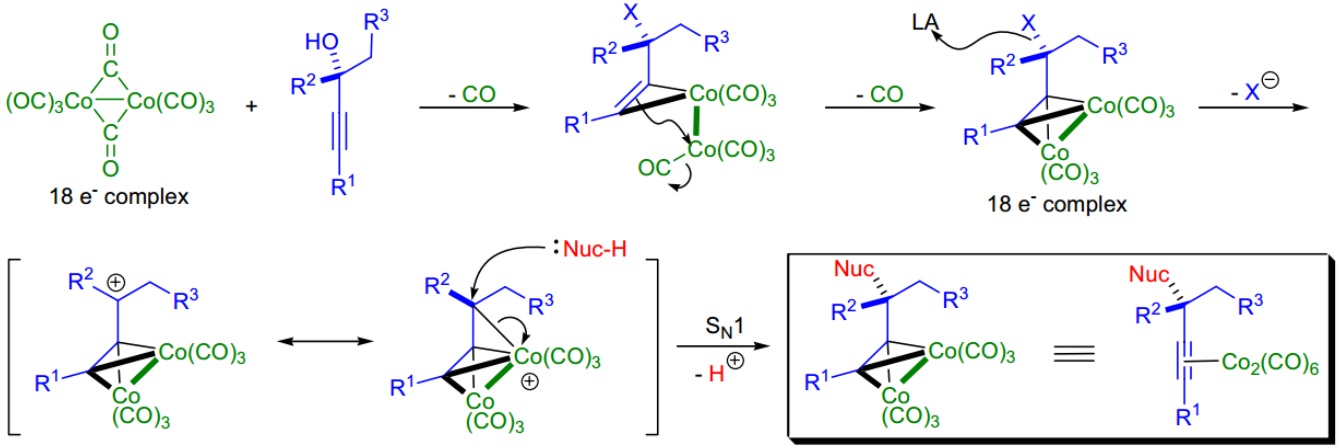
Reaction of $Co_2(CO)_6$-stabilized propargylic cations with nucleophiles (Nicholas, 1977):



$Co_2(CO)_6$-alkyne complex — $Co_2(CO)_6$-stabilized propargylic cation

R^{1-3} = H, alkyl, aryl; X = OH, O-alkyl, O-benzyl, O-silyl, acetal, OAc, OCOAr, OCO*t*-Bu, OMs, OTf, Cl; Nuc-H = e-rich aromatics, simple alkenes, allylsilanes, allylstannanes, enol ethers, silylketene acetals, ROH, N_3^-, RNH_2, RR'NH, RSH, HS(R)SH, F^-; oxidizing agent: CAN, $Fe(NO_3)_3$, NMO, TMANO, TBAF, C_5H_5N/air/ether, DMSO/H_2

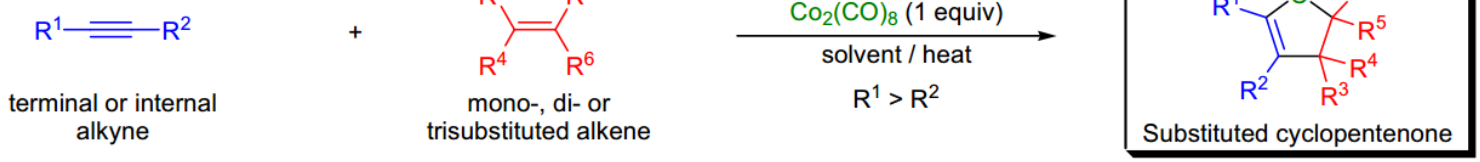
Mechanism: [2,22,20,23]



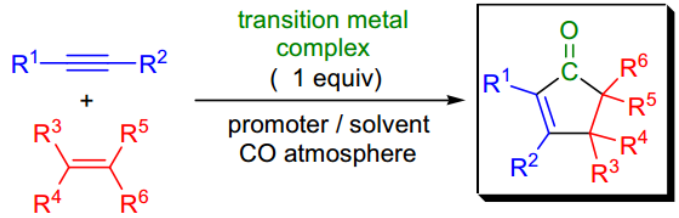
18 e⁻ complex

PAUSON-KHAND REACTION

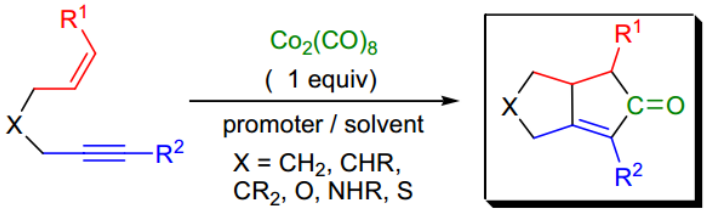
Pauson & Khand (1973):



Modified P-K reaction:

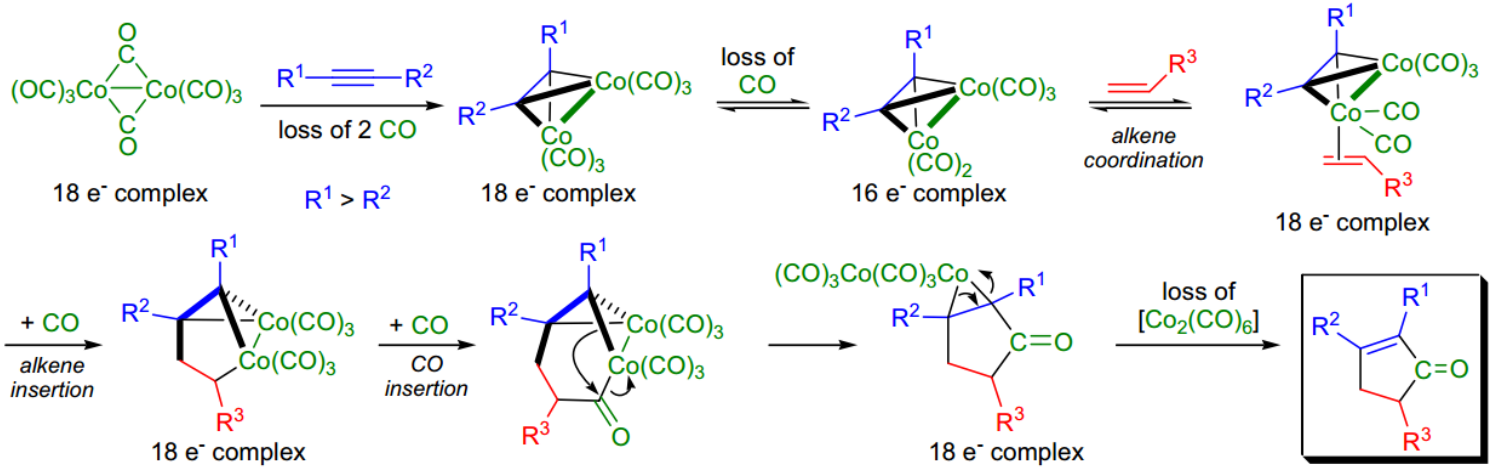


Intramolecular variant:

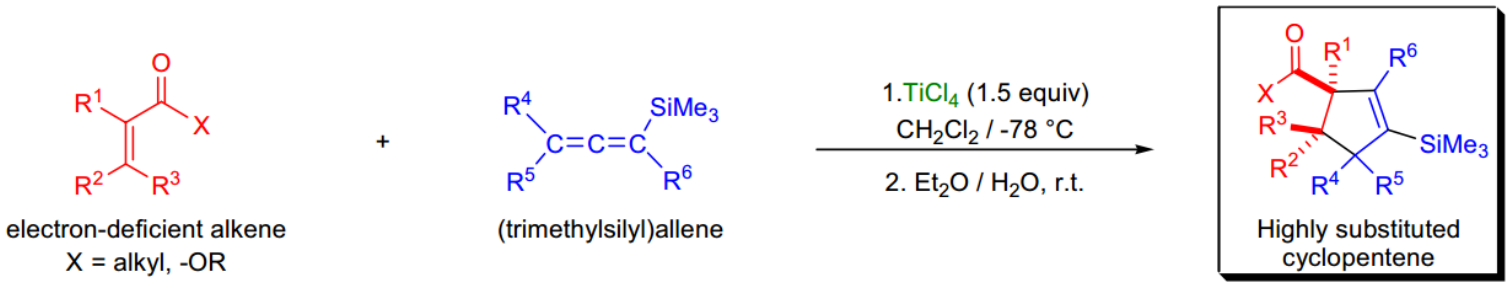


R^{1-6} = H, alkyl, aryl, substituted alkyl and aryl; transition metal complex: $Co_2(CO)_8$, $Fe(CO)_5$, $Ru_2(CO)_{12}$, Cp_2TiR_2, $Ni(COD)_2$, $W(CO)_6$, $Mo(CO)_6$, $[RhCl(CO)_2]_2$; promoter: NMO, TMAO, $RSCH_3$, high-intensity light/photolysis, "hard" Lewis base

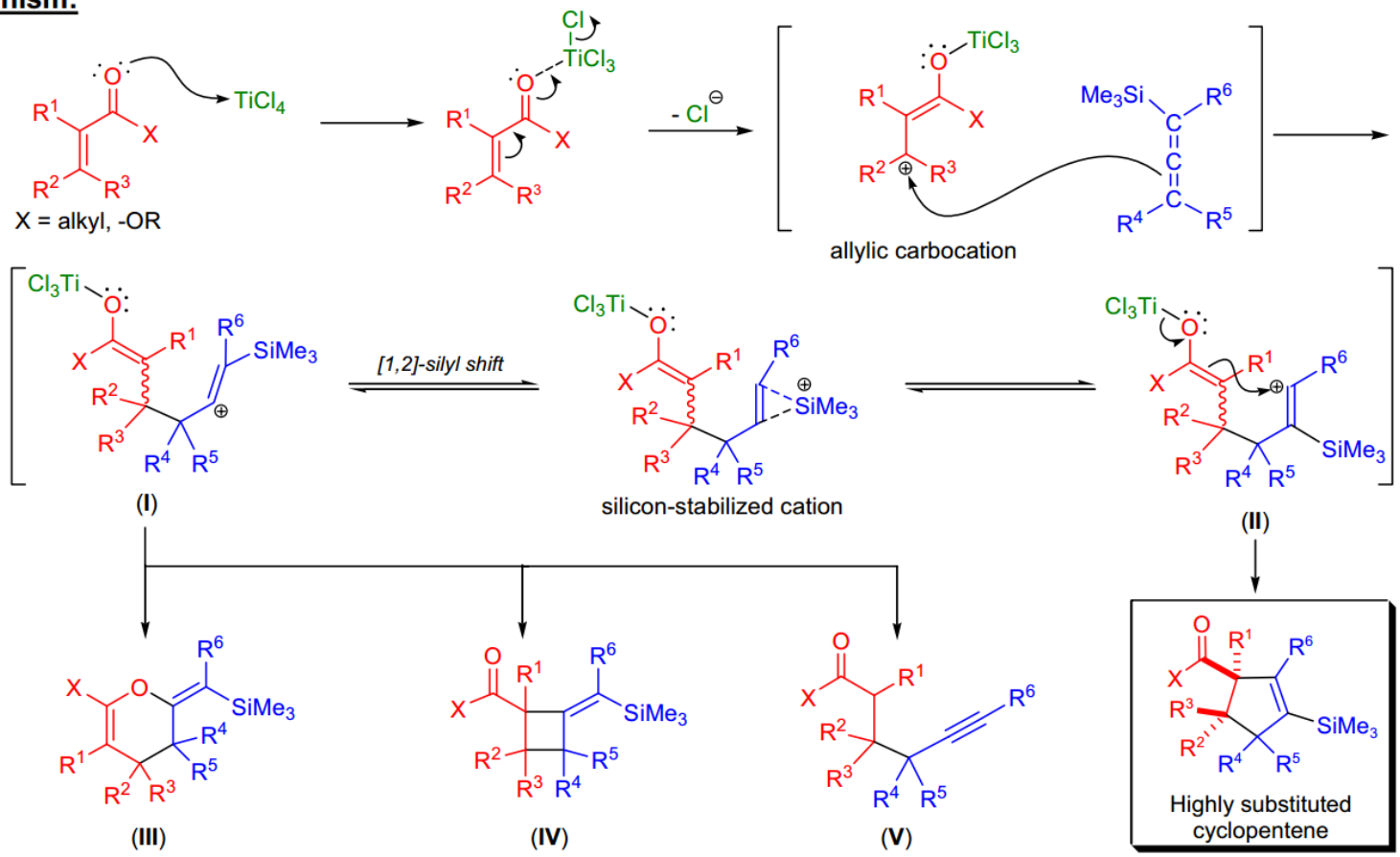
Mechanism:



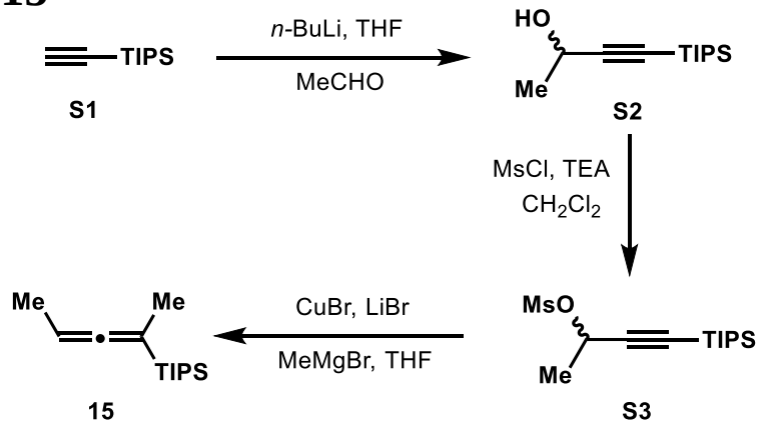
DANHEISER CYCLOPENTENE ANNULATION

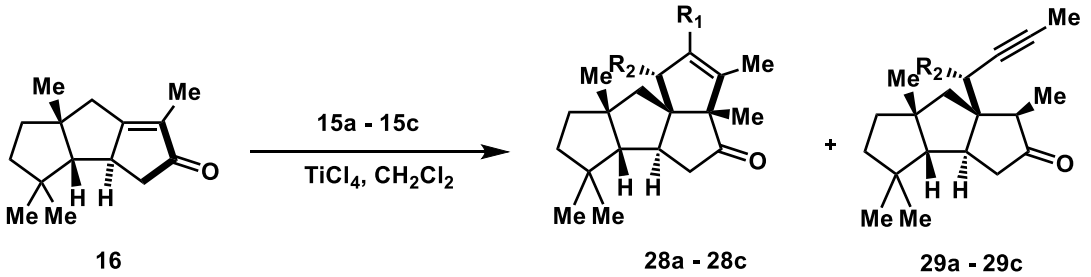


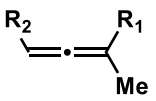
Mechanism:



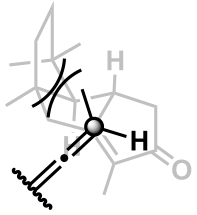
Synthesis of compound 15



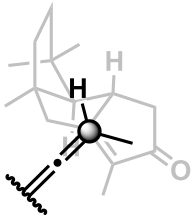




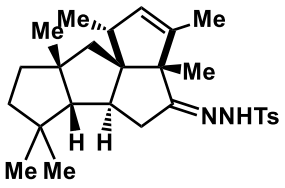
15a: R_1 = TMS, R_2 = H
28a (91%), 29a (0%)
15b: R_1 = TMS, R_2 = Me
28b (33%), 29b (46%)
15c: R_1 = TIPS, R_2 = Me
28c (89%), 29c (< 5%)



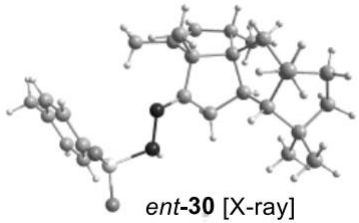
unfavored *TS*-A



favored *TS*-B

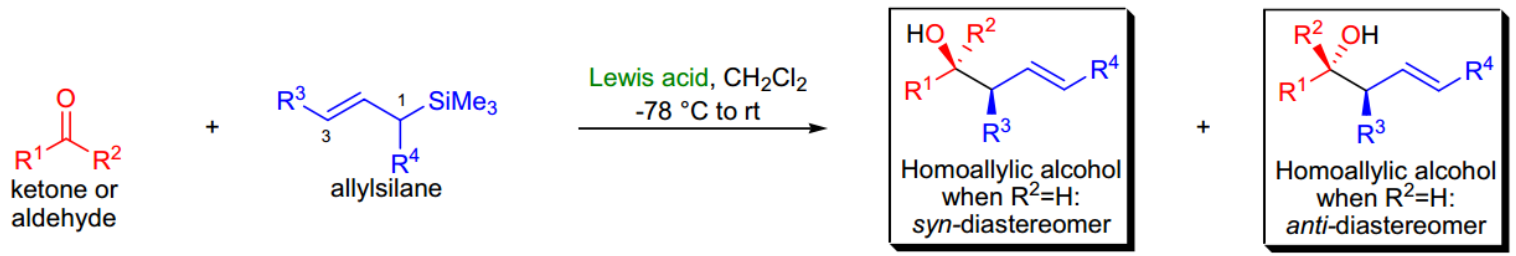


30



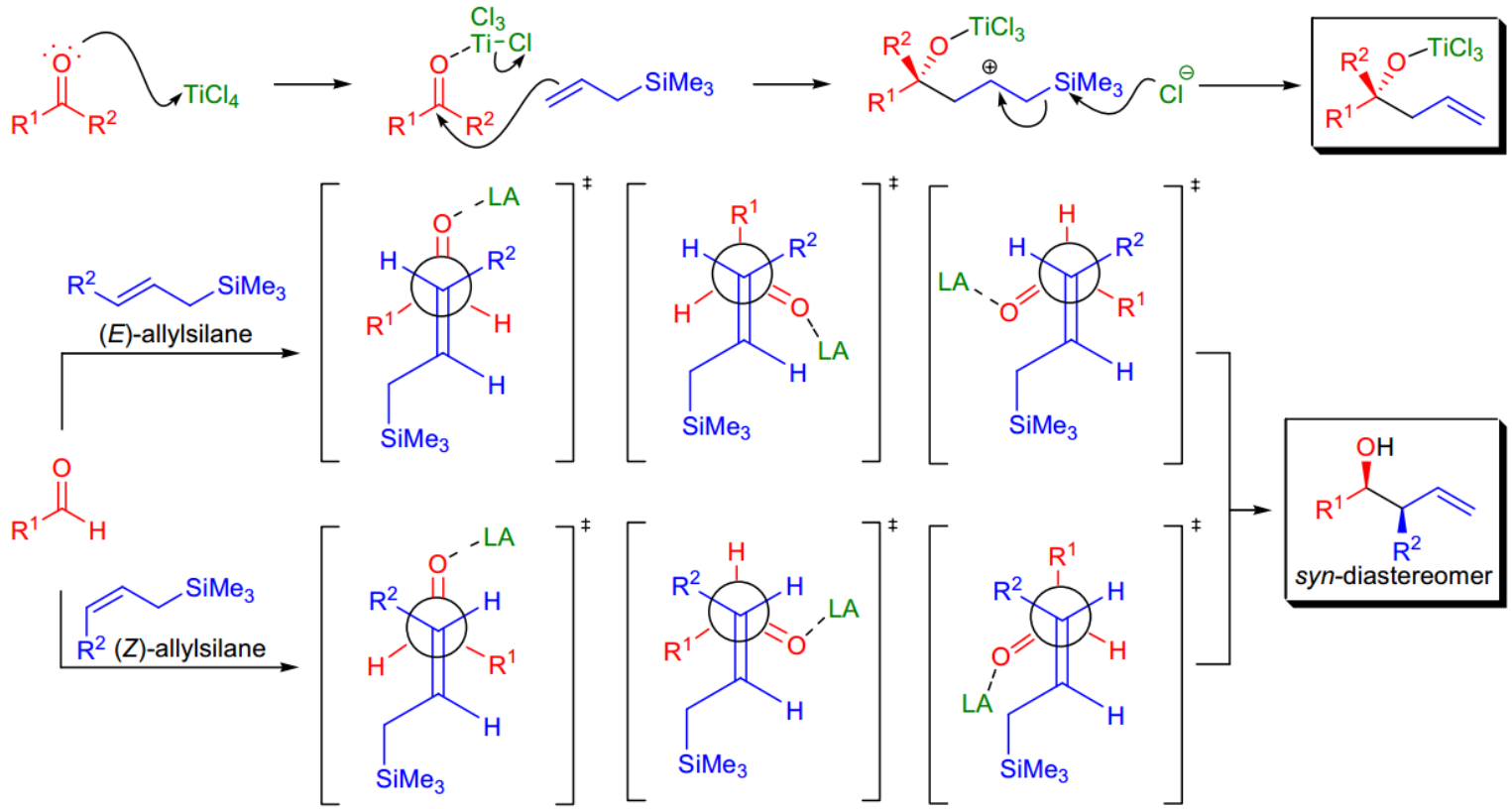
ent-**30** [X-ray]

SAKURAI ALLYLATION

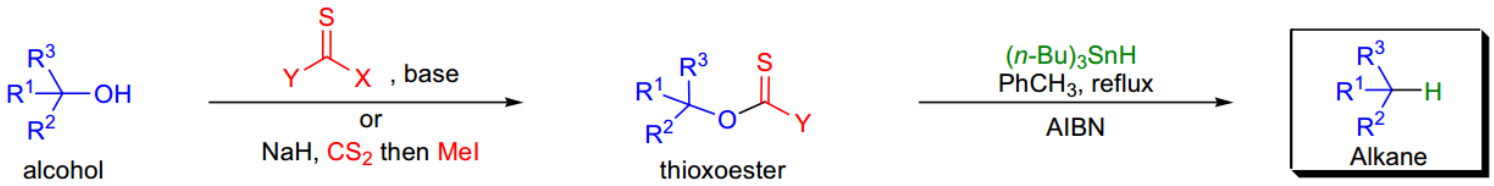


R^1 = alkyl, aryl; R^2 = H, alkyl, aryl; R^3 and R^4 = H, alkyl, aryl; Lewis acid = $TiCl_4$, $BF_3{\cdot}OEt_2$, $SnCl_4$, $EtAlCl_2$

Mechanism:



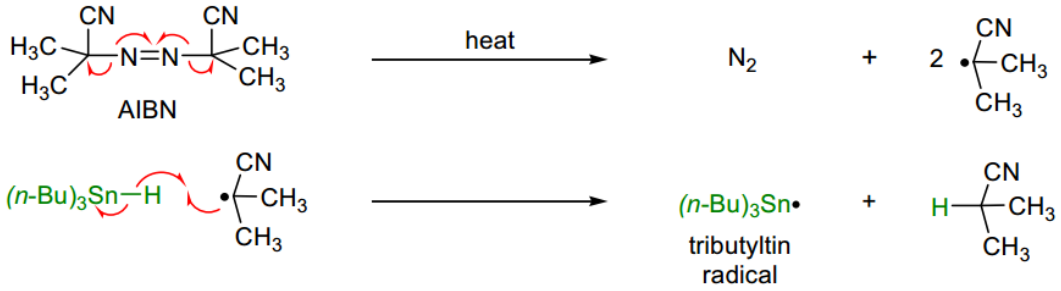
BARTON-McCOMBIE RADICAL DEOXYGENATION REACTION



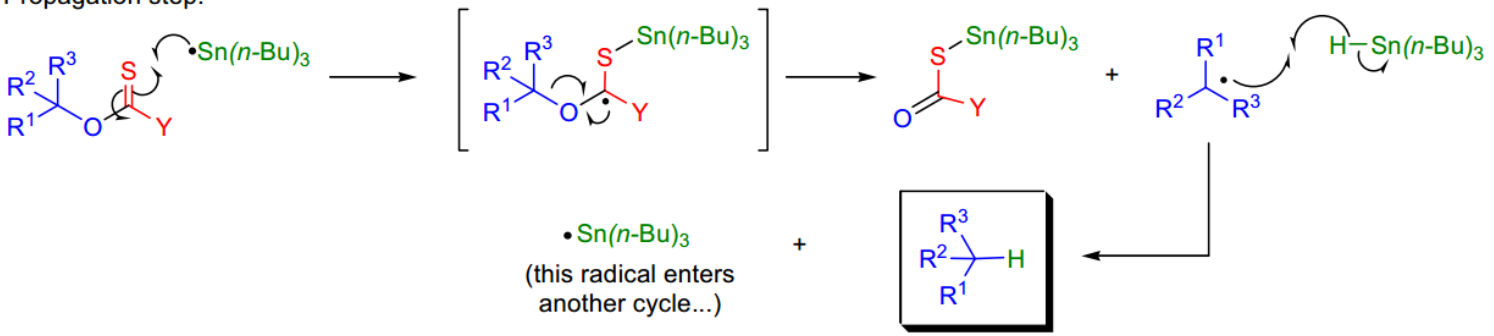
Y = SMe, imidazolyl, OPh, OMe; X = Cl, imidazolyl; base: NaH

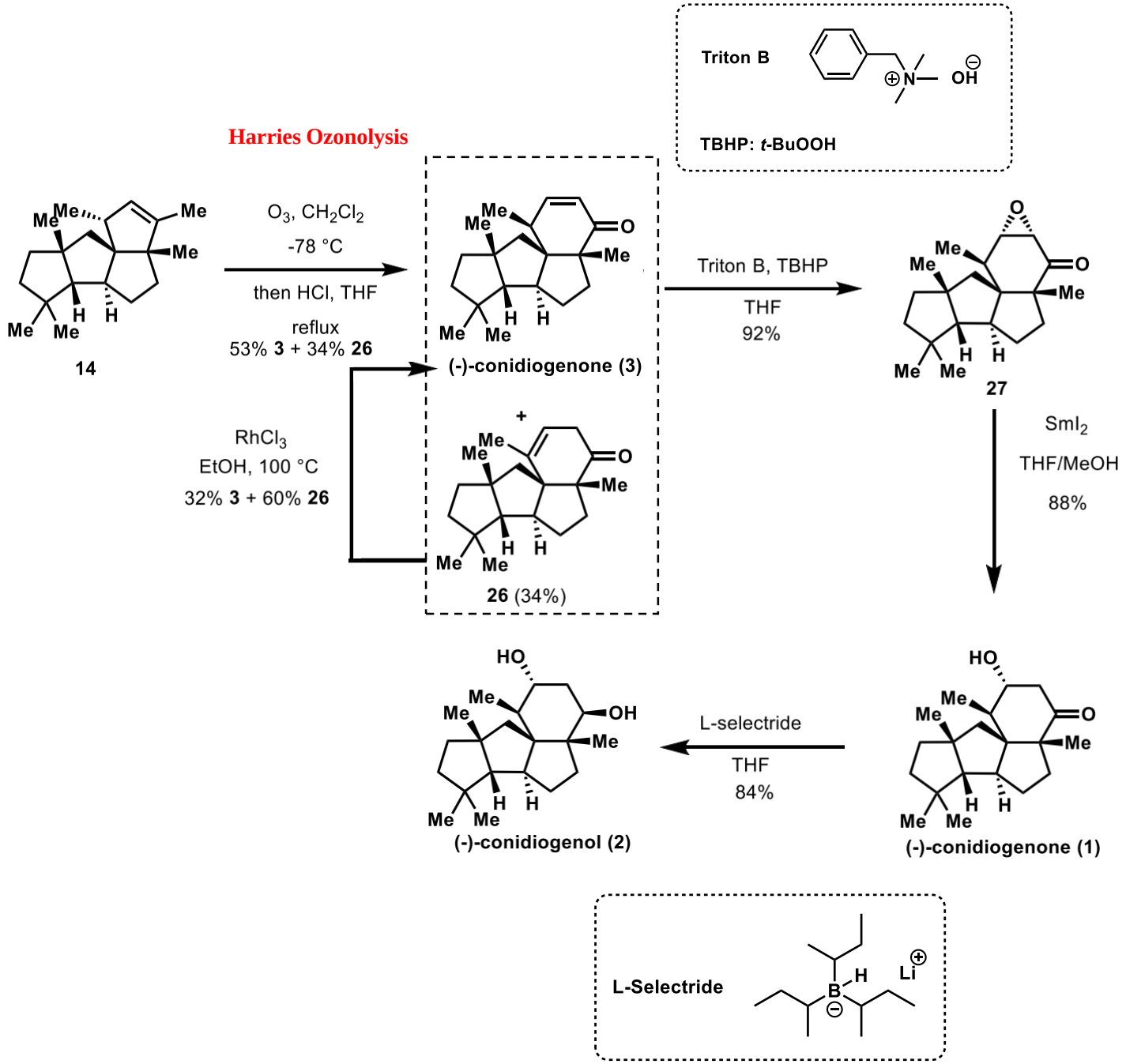
Mechanism: [25,13,26]

Initiation step:

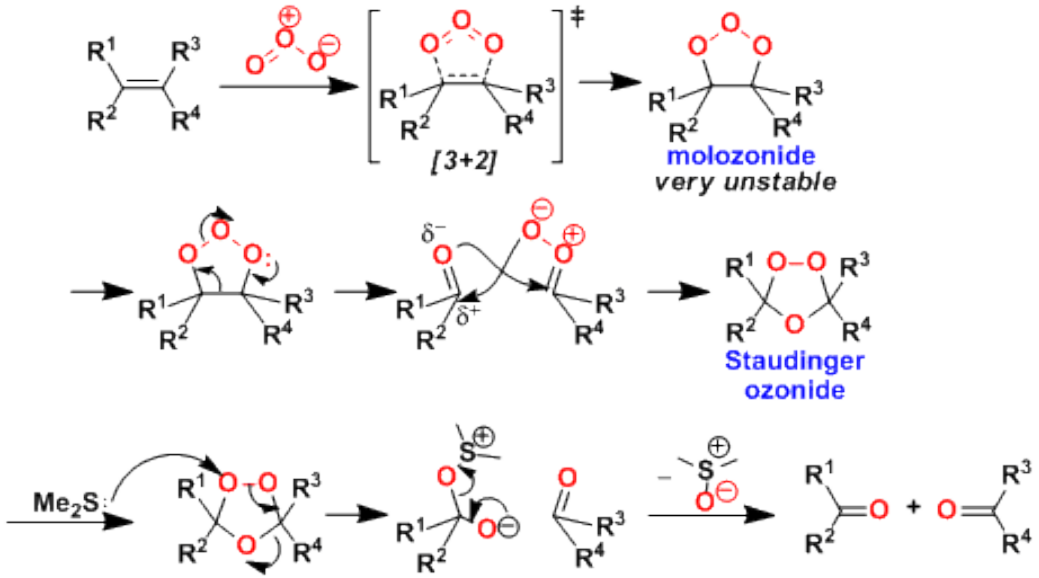


Propagation step:




Triton B
TBHP: t-BuOOH
Harries Ozonolysis
14
O3, CH2Cl2
-78 °C
then HCl, THF
reflux
53% 3 + 34% 26
(-)-conidiogenone (3)
RhCl3
EtOH, 100 °C
32% 3 + 60% 26
26 (34%)
Triton B, TBHP
THF
92%
27
SmI2
THF/MeOH
88%
(-)-conidiogenone (1)
L-selectride
THF
84%
(-)-conidiogenol (2)
L-Selectride

Harries Ozonolysis



Angew. Chem. Int. Ed,. **1975**, *87*, 745.
Eur. J. Org. Chem., **1998**, *7*,1625

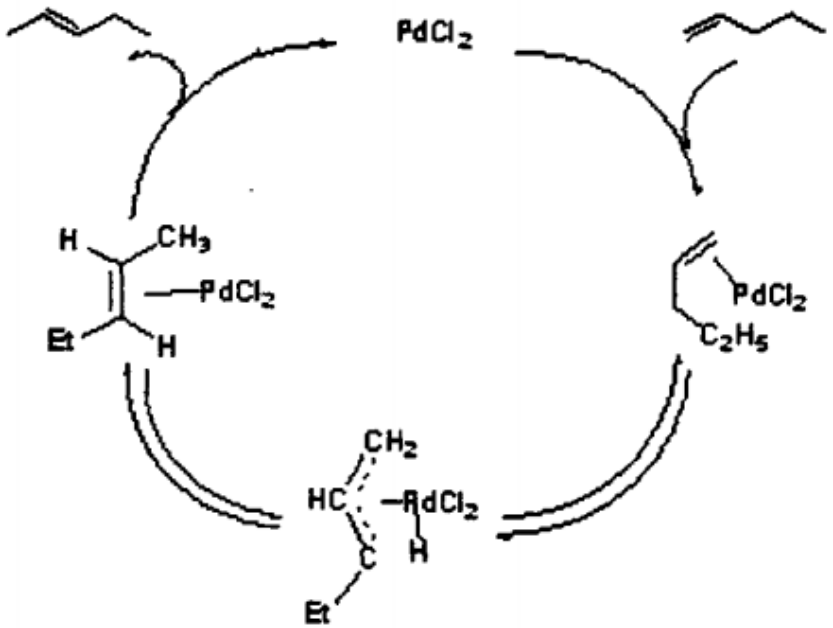
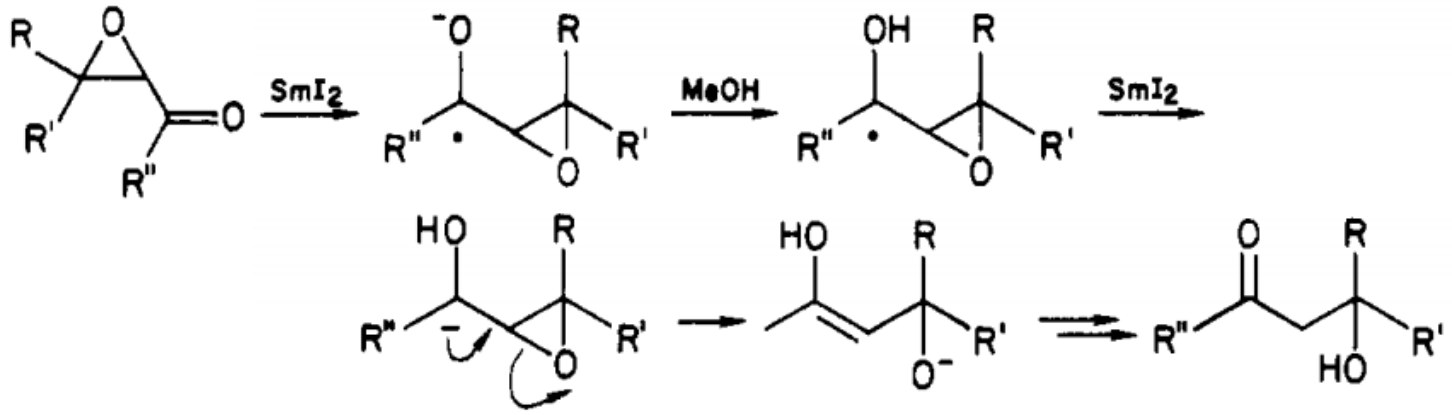


图 1-3　$PdCl_2$ 催化异构反应机理

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

DOI: 10.7666/d.y1676999.


R
O
R'
O
R''
SmI2
-O
R
R''
R'
O
MeOH
OH
R
R''
R'
O
SmI2
HO
R
R''
R'
O
HO
R
R'
O-
O
R
R''
HO
R'