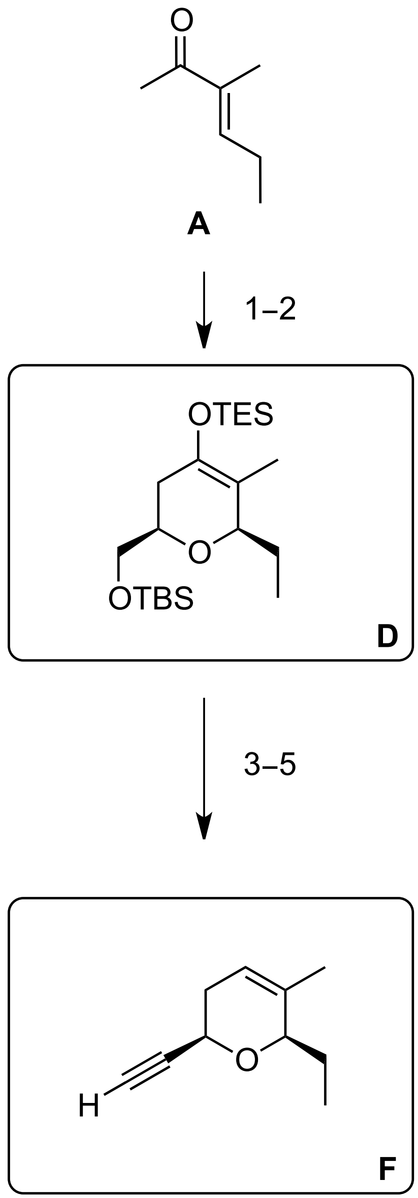
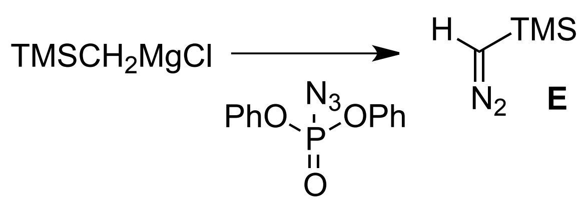
Total Synthesis of (+)-Ambruticin

P. Liu, E. N. Jacobsen, *J. Am. Chem. Soc.* **2001**, *123*, 10772–10773.

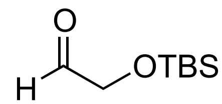


1) TESOTf, NEt_3
2) **B**, 5 mol-% **C**, rt

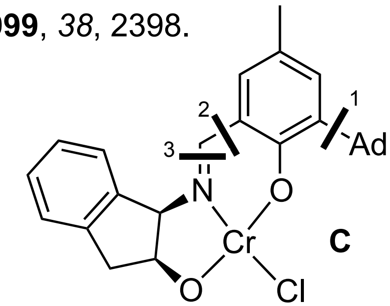
3) BH_3 • THF; 10% aq. HCl, reflux
4) $(COCl)_2$, DMSO, NEt_3
5) **E**, LDA



What is the name of reaction 2 and how would you synthesize **C**?
Jacobsen asymmetric hetero-Diels-Alder reaction; *ACIE* **1999**, *38*, 2398.



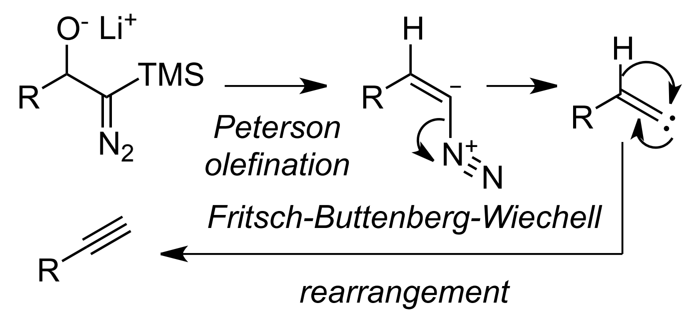
B



C

1) Friedel-Crafts alkylation; 2) formylation; 3) condensation with aminoindanol (c.a.)
Synthesis of aminoindanol: *Org. Synth.* **1999**, *10*, 29;

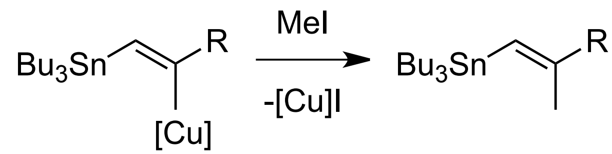
Name of reaction 5? Names of reactions involved in the mechanism of reaction 5?
Shioiri alkyne synthesis by Colvin rearrangement, *Synlett* **1994**, 107–108.



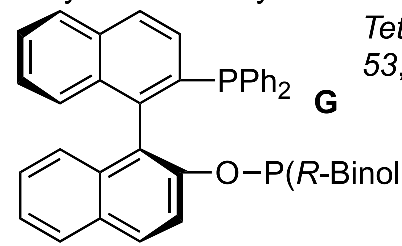
6–9

6) $Bu_3SnCu(Bu)CNLi_2$, MeI
7) I_2
8) $H_2C{=}CHMgBr$, 5 mol-% $Pd(PPh_3)_4$
9) 0.5 mol-% $Rh(acac)(CO)_2$,
2 mol-% **G**, 20 atm H_2/CO
30–35 °C

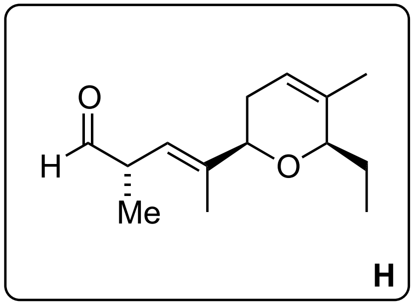
Mechanism of reaction 6?



Name of reaction 8 and 9?
Kumada coupling
Takaya–Nozaki asymmetric hydroformylation



Tetrahedron **1997**, *53*, 7795–7804.

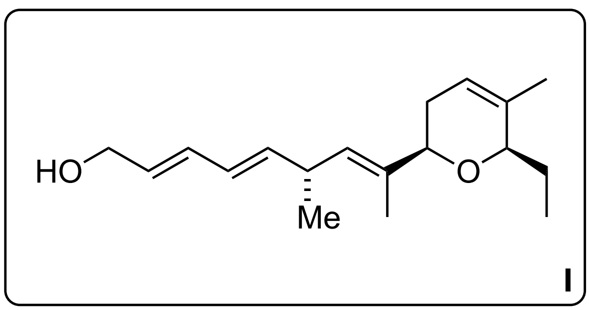


phosphite ligands accelerate migratory CO insertion since their LUMO lies lower than the LUMO of usual phosphine ligands. This reduces the π-backbonding of Rh to CO ligand and thus weakens the Rh–CO bond

10–12

10) $CrCl_2$, CHI_3
11) ethyl acrylate, 10 mol-% $Pd(OAc)_2$, Ag_2CO_3
12) DIBAL

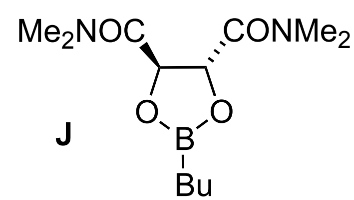
Names of reactions 10 and 11?
Takai olefination; Heck reaction
Role of Ag(I) in reaction 11?
Ag(I) binds strongly as a π-lewis acid to olefins and prevents reversible hydropalladation/ β-H elimination which would lead to olefin isomerization to the thermodynamic minimum (all conjugated)

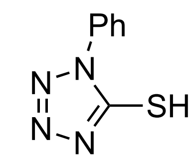


13–14

13) $Zn(CH_3CHI)_2$•DME, **J**, −10 °C
14) PPh_3, PTSH, DEAD; Mo(VI)/H_2O_2

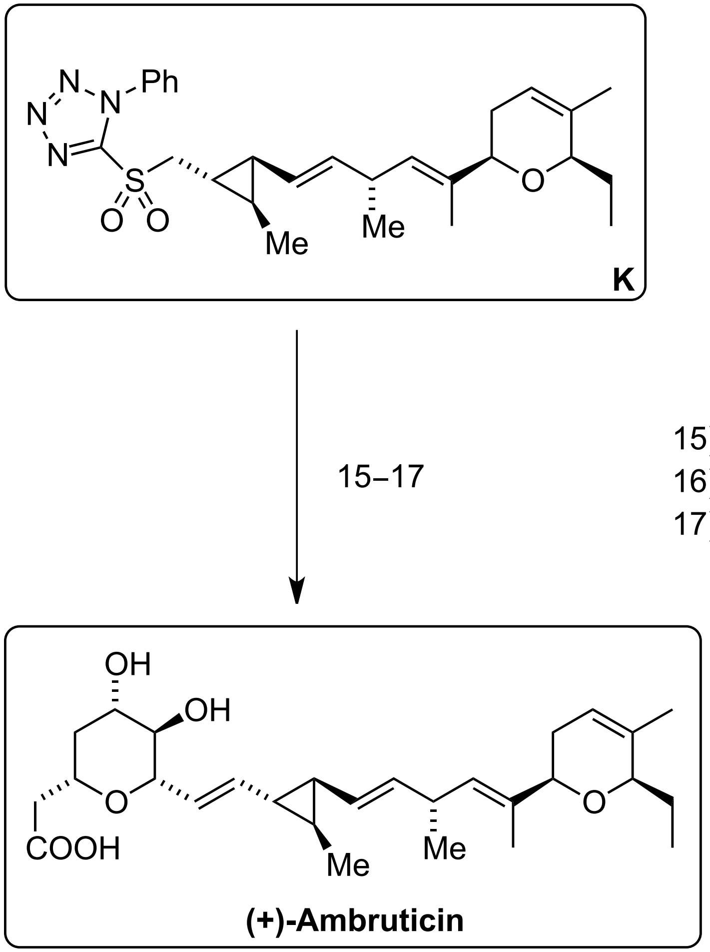
J





PTSH

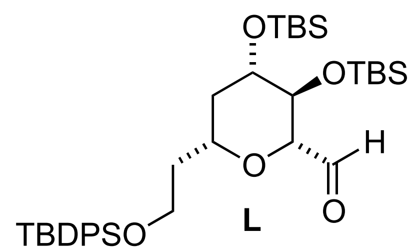
Name and mechanism of reactions 13 and 14?



15) LiHMDS, DMF/DMPU, –35 °C, **L**
16) TBAF
17) Pt, O_2, H_2O/acetone, 50 °C

Charette asymmetric cyclopropanation
(asymmetric Simmons-Smith cyclopropanation)
JACS **1994**, *116*, 2651–2652.
Mitsunobu reaction

Name and mechanism of reactions 15 and 17?
Julia-Kocienski olefination
Synlett **1997**, 26–28.
Heyns oxidation; *Basic Reactions in Organic Synthesis* **2006**, 43–60.
Please suggest a possible synthesis of building block **L**. (see original paper, same hetero-Diels-Alder reaction involved)



L

In polar solvents, the Julia-Kocienski olefination procedes via an open transition state in the crucial first aldol-type reaction (apolar solvent: Zimmermann-Traxler like TS). The formed *anti*-product leads to an *E*-configured olefin.
one step in the mechanism: Smiles-rearrangement