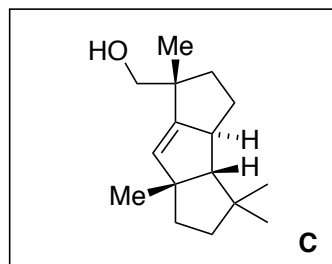
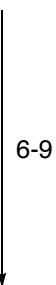
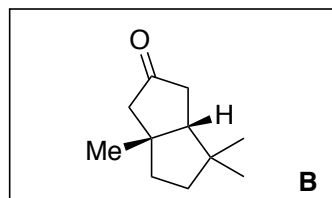
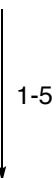
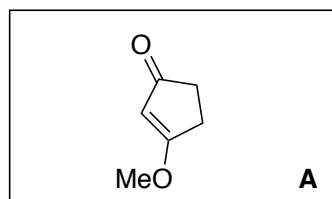


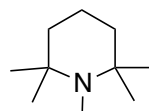
Quaternary-Center-Guided Synthesis of Complex Polycyclic Terpenes

Hu, P.; Chi, H.; DeBacker, K. C.; Gong, X.; Keim, J. H.; Hsu, I. T.; Snyder, S. A.

Nature, 2019, 569, 703.

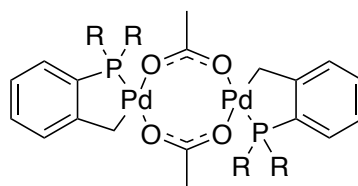


- 1) 4-bromo-2-methyl-1-butene, Mg, THF *then* 1N HCl
- 2) Cu(OTf)₂ (7.5 mol%), Hoveyda's NHC•Ag (3.75 mol%), AlMe₃, -78 °C, THF
- 3) TMSOTf, PMP, CH₂Cl₂, -78 °C
- 4) IBX•MPO, DMSO, rt
- 5) Fe(acac)₃ (30 mol%), Ph₃SiH, EtOH, (CH₂OH)₂



1,2,2,6,6-pentamethylpiperidine (PMP)

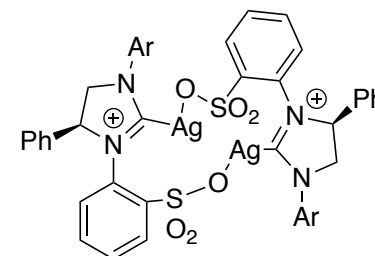
- 6) NH₂NMe₂ (3 equiv.)
- 7) LDA, HMPA, 4-iodo-2-methyl-1-butene *then* 1N HCl
- 8) KHMDS, Comins' reagent, THF, -78 to 0 °C
- 9) Pd(OAc)₂ (10 mol%), t-BuMephos (15 mol%), n-Bu₄NOAc (3 equiv.), toluene, 100 °C *then* K₂CO₃, MeOH



R = 2-MeC₆H₄
Herrmann's Catalyst

Step 4: What is the structure of IBX•MPO?
Propose a mechanism. **See page 3**

Step 5: Who first reported these conditions?
Baran - JACS - 2014 - 1304

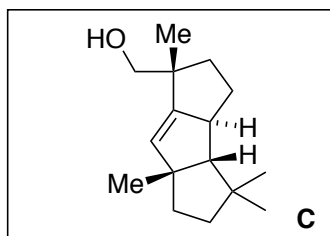


Ar = 2,6-(Et)₂C₆H₃
Hoveyda's NHC•Ag

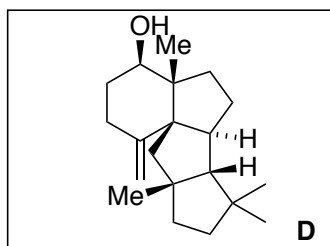
Step 6: Who first reported these conditions?
Corey - Tet Let - 1976 - 3

Step 8: What is the structure of Comins' reagent?
See page 3

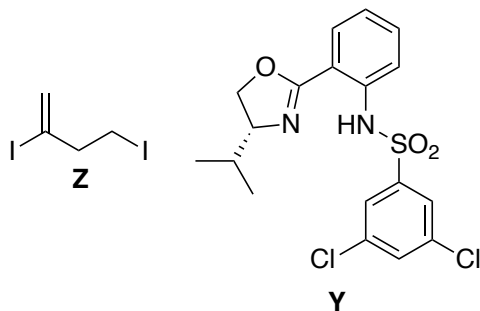
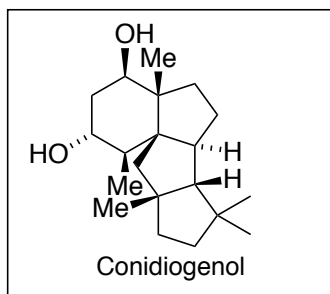
Step 9: Propose a mechanism



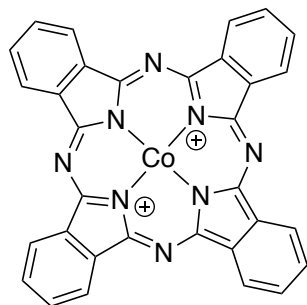
10-12



13-16



- 10) DMP, NaHCO₃, CH₂Cl₂, 0 °C
- 11) CrCl₂, Y, Z, CoPc, Mn, LiCl, TMSCl
- 12) Herrmann's Catalyst, HCO₂Na, TBAB, DMF *then* TBAF, THF



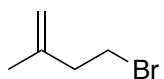
Cobalt(II) Phthalocyanine (CoPc)

- 13) Pd/C (10 mol%), H₂, EtOAc, *then* IBX, DMSO 80 °C
- 14) Triton B, t-BuOOH, THF
- 15) PhSeSePh (4.0 equiv.), NaBH₄ (8.0 equiv.) EtOH
- 16) L-Selectride, THF, -50 °C

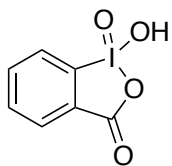
Step 11: What is the name of this type of reaction?
Radical NHTK - Kishi - JACS - 2009 - 15387

Step 14: What is the structure of Triton B?
See page 3

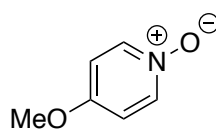
Structures:



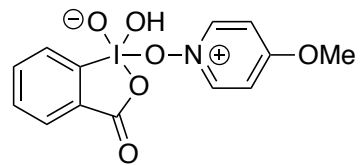
4-bromo-2-methyl-1-butene



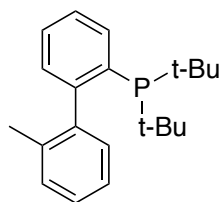
2-Iodoxybenzoic acid (IBX)



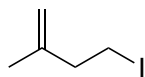
4-methoxypyridine-N-oxide (MPO)



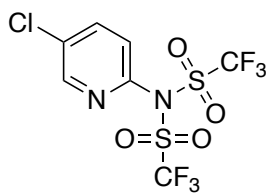
IBX·MPO



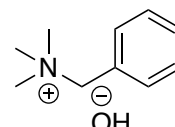
t-BuMephos



4-iodo-2-methyl-1-butene

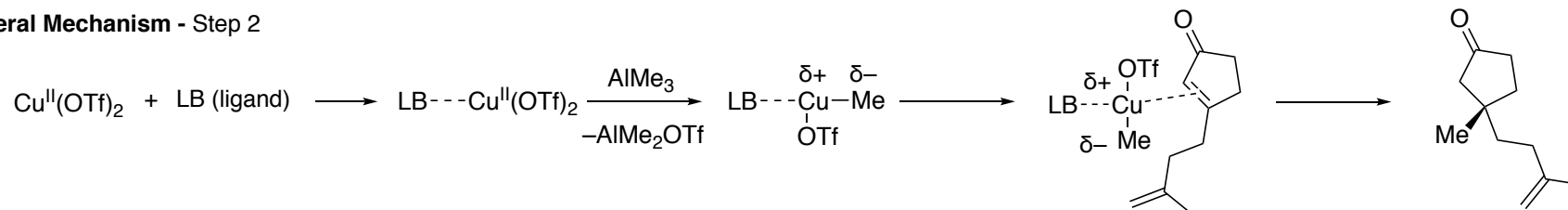


Comins' Reagent



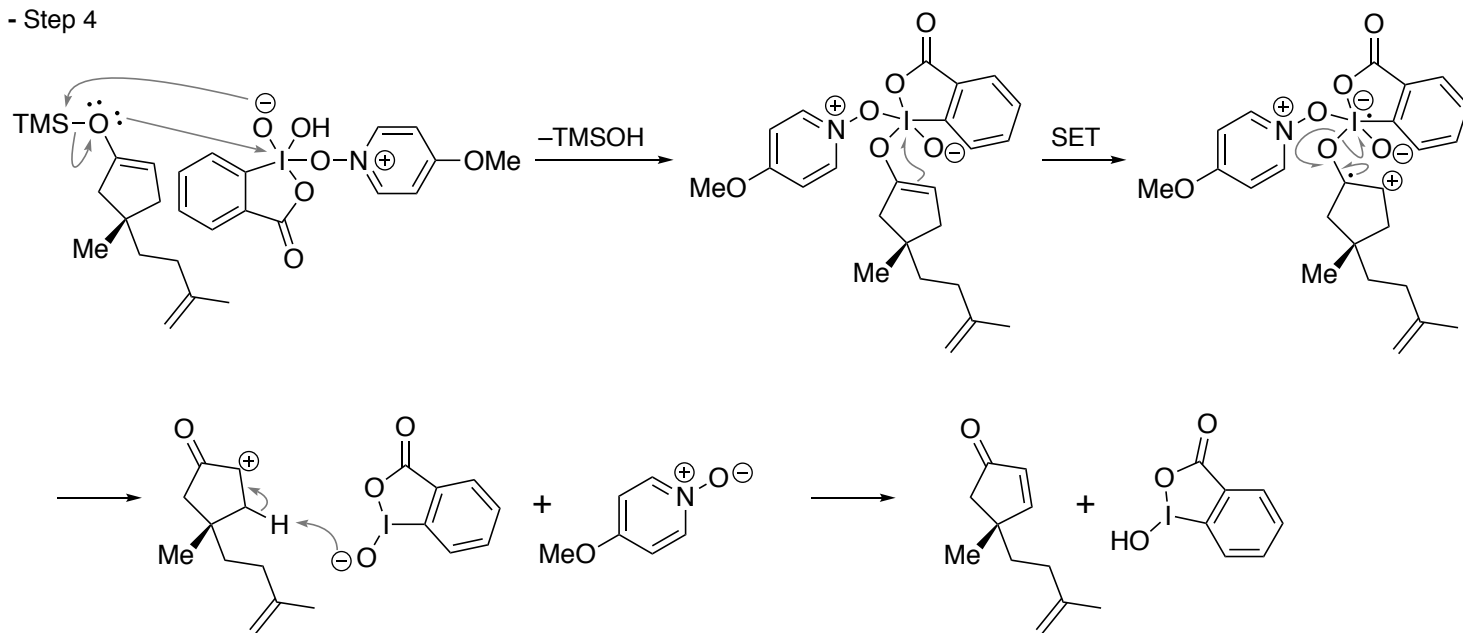
trimethylbenzylammonium hydroxide
(Triton B)

General Mechanism - Step 2



Lewis basic ligand will coordinate with the Cu-based salt. This species then transmetalates with AlMe_3 and affords a more nucleophilic Cu-bound carbon in addition to a more π -Lewis acidic Cu species. The enantioselectivity of this reaction is also controlled by the Lewis basic ligand

Mechanism - Step 4



Mechanism - Step 9

