Enantioselective Total Synthesis of (+)-Flavisiamine F via Late-Stage Visible-Light-Induced Photochemical Cyclization

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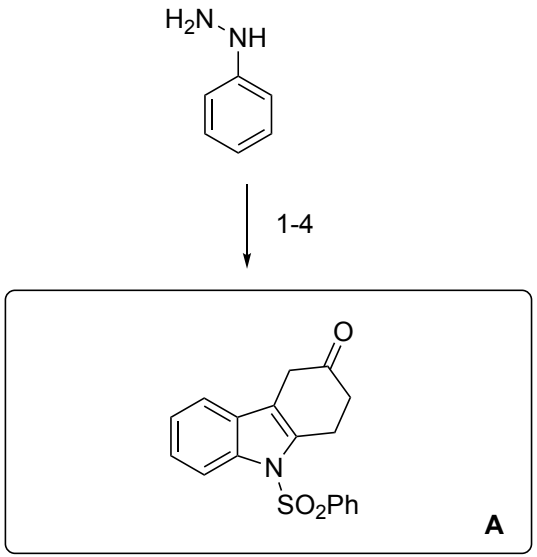
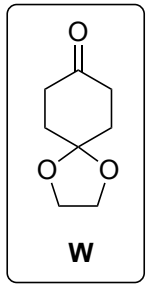
Angew. Chem. Int. Ed. **2019**, *58*, 5443–5446.



1) **W**
2) ethylene glycol 190°C
3) NaOH, *n*-Bu_4N^+ SO_4^- $PhSO_2Cl$
4) *p*-TsOH•H_2O



W

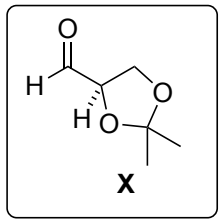
Name of step 1 and 2? Mechanism?

Fischer indole synthesis

Name three different general ways to access this class of compounds. What are the starting materials/conditions?

see below

5) LHMDS, $PhNTf_2$, HMPA:THF (1:10)
6) $CrCl_2$, $NiCl_2$ (5 mol%), **X**, 1:1 d.r.
7) IBX
8) $LiBHEt_3$, 35:1 d.r.
9) NaH, Cl_3CCN, 25 °C
10) TMSOTf, DIPEA
11) K_2CO_3, PhCl, reflux, then 1 $molL^{-1}$ HCl



X

Name of step 6? Mechanism?

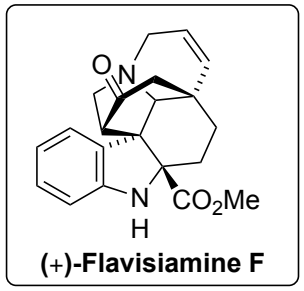
Nozaki-Hiyama-Kishi reaction

Name of step 9?

Overman rearrangement

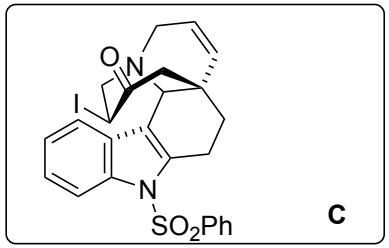
Name of step 11?

Claisen rearrangement



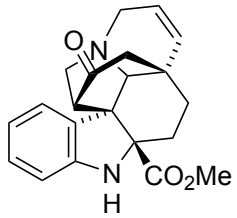
(+)-Flavisiamine F

9-13



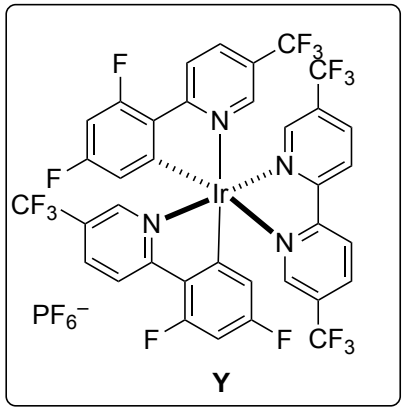
C

14-17



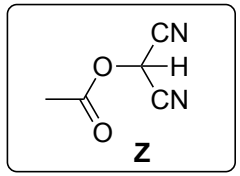
(+)-Flavisiamine F

12) Ag_2O, MeI
13) KHMDS, TBSCl
14) DIBAL
15) K_2CO_3, allyl bromide
16) aq. HCHO/EtOH, *then* 1N HCl
17) *p*-TsOH, Grubbs^{2nd} generation catalyst
18) LiHMDS, I_2



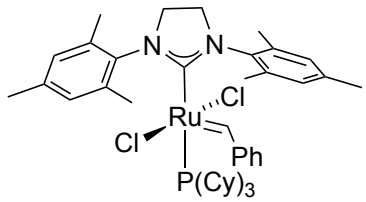
Y

19) Et_3N, **Y** (5 mol%), air, blue LED, DMF, 77% yield
20) imidazole, **Z**
21) K_2CO_3, H_2O_2
22) HCl, MeOH, reflux



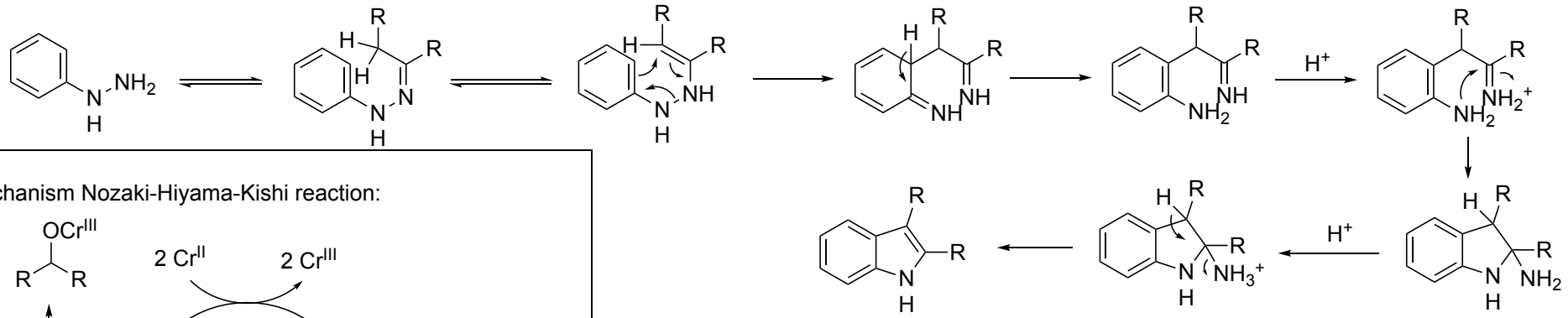
Z

Name of step 16) Mannich reaction
Structure of Grubbs 2nd generation catalyst?

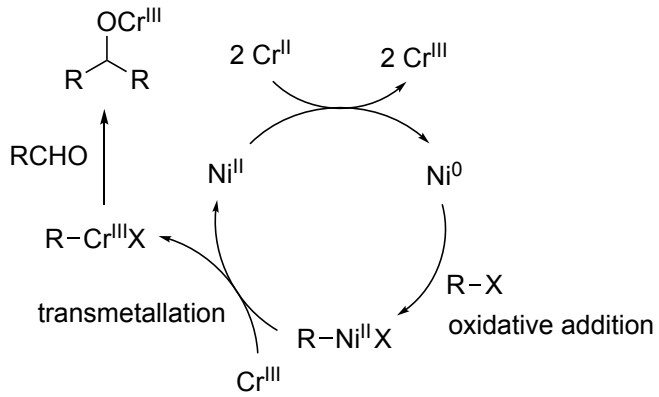


20) hint: Instead of directly introducing the methoxy carbonyl, a nitrile was isolated

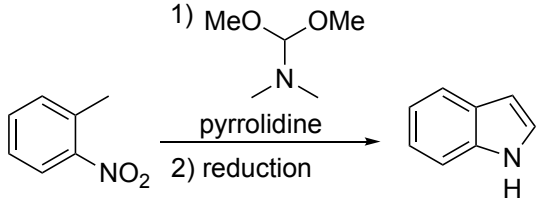
Mechanism Fischer-indole-synthesis:



Mechanism Nozaki-Hiyama-Kishi reaction:



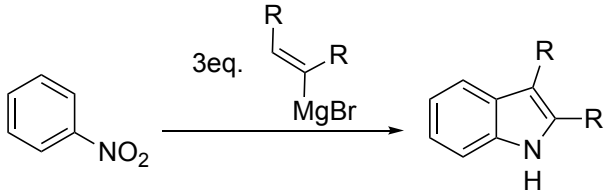
Leimgruber-Batcho:



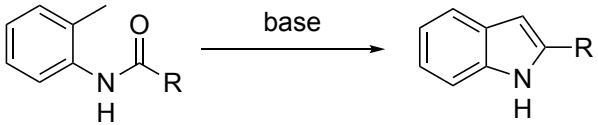
Alternative ways to make indoles:

e.g.

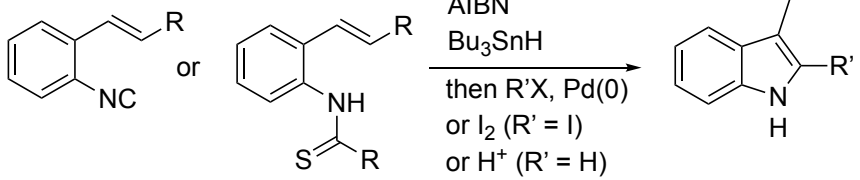
Bartoli:



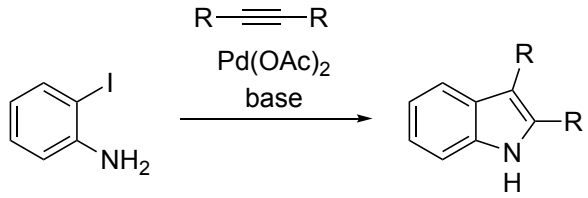
Madelung:



Fukuyama:



Larock:



Reissert: