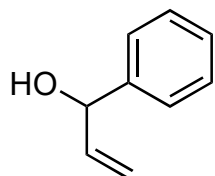


Enantioselective Total Synthesis of (–)-Daphenylline

Wu, B.-L.; Yao, J.-N.; Long, X.-X.; Tan, Z.-Q.; Liang, X. *J. Am. Chem. Soc.* **2024**, *146*, 1262–1268.



- 1) propanal, 3 mol% [Ir(cod)Cl]₂, 12 mol% **1**, 10 mol% **2**, HCO₂H
- 2) BocNH₂, Et₃SiH, TfOH
- 3) CsCHO₂, **3** 420 nm LED
- 4) PPA, heat
- 5) CuBr₂ (10 mol%), O₂, heat
- 6) Ph₃PCH₃Br, KO^tBu, heat

1) What kind of catalysis is found in this reaction?

Dual Catalysis (source: 10.1126/science.1237068)

Hint: This is a reaction between a nucleophile and an electrophile

Hint: Looking for the electrophile? Acid and alcohol

Hint: Looking for the nucleophile? Amine and Aldehyde

2) Classify the reaction

Reductive Amination

3) Provide a mechanism

(<https://doi.org/10.1021/jacs.3c03671>)

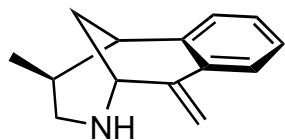
4) *Hint: Make it ring. Leave the amine alone!*

5) Provide a mechanism

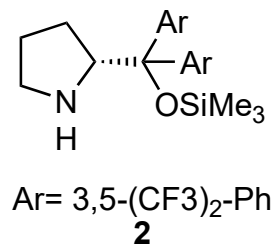
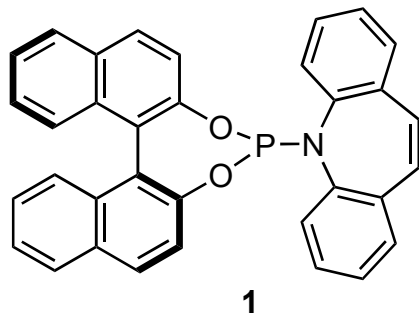
(<https://doi.org/10.1021/ja4096472>)

Hint: Use it or lose it!

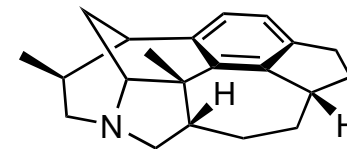
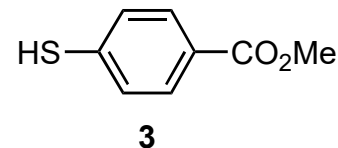
6) Provide a mechanism



A

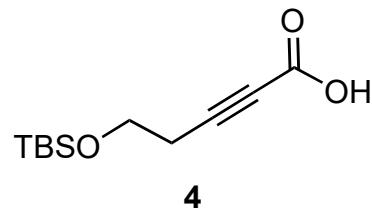


Ar = 3,5-(CF₃)₂-Ph



daphenylline

A



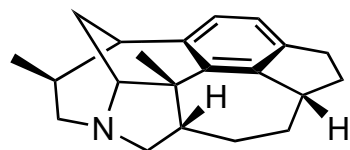
- 7) **4**, EDCI, HOBt, DIPEA
8) Rh(cod)₂OTf, BINAP, H₂
9) CSA, Pd(OH)₂/C, H₂
 then pH 6.8 buffer, TEMPO, NaClO₂, NaClO
10) (COCl)₂, cat. DMF then AlCl₃ heat
11) Ph₃PCH₃Br, KOtBu, heat
12) CsCHO₂, **3**, 420 nm LED
13) (COCl)₂, cat. DMF then AlCl₃ heat
14) Pd/C, H₂ *then* RhH(CO)(PPh₃), PhSiH₃

8) Provide a mechanism

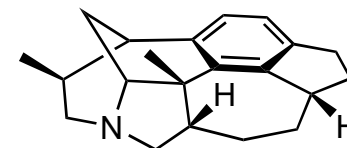
(<https://doi.org/10.1021/ja042645v>)

9) Structure of CSA, how do you make it?

10) Provide a mechanism involving DMF

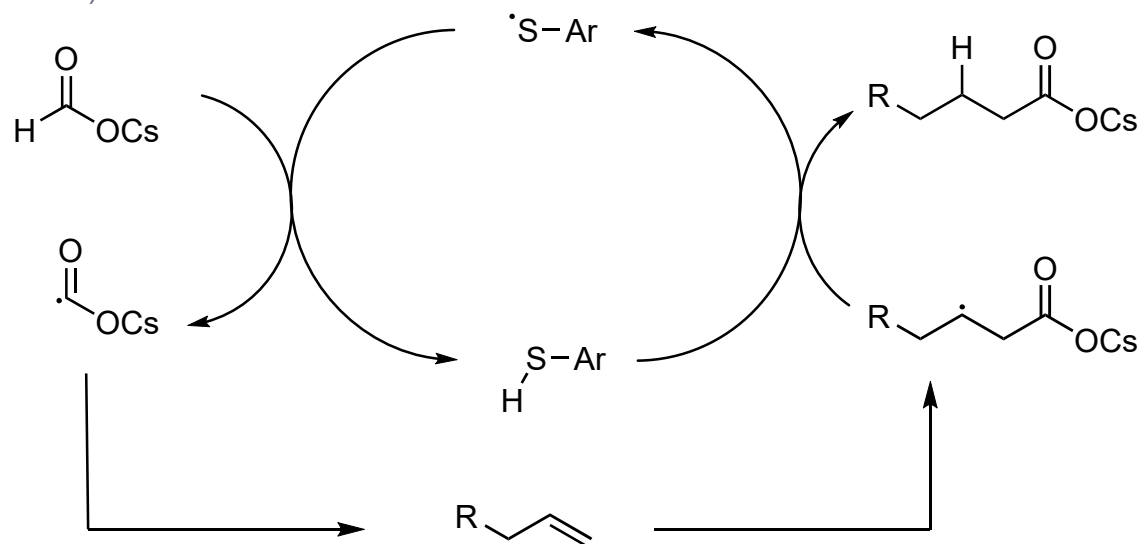


daphenylline

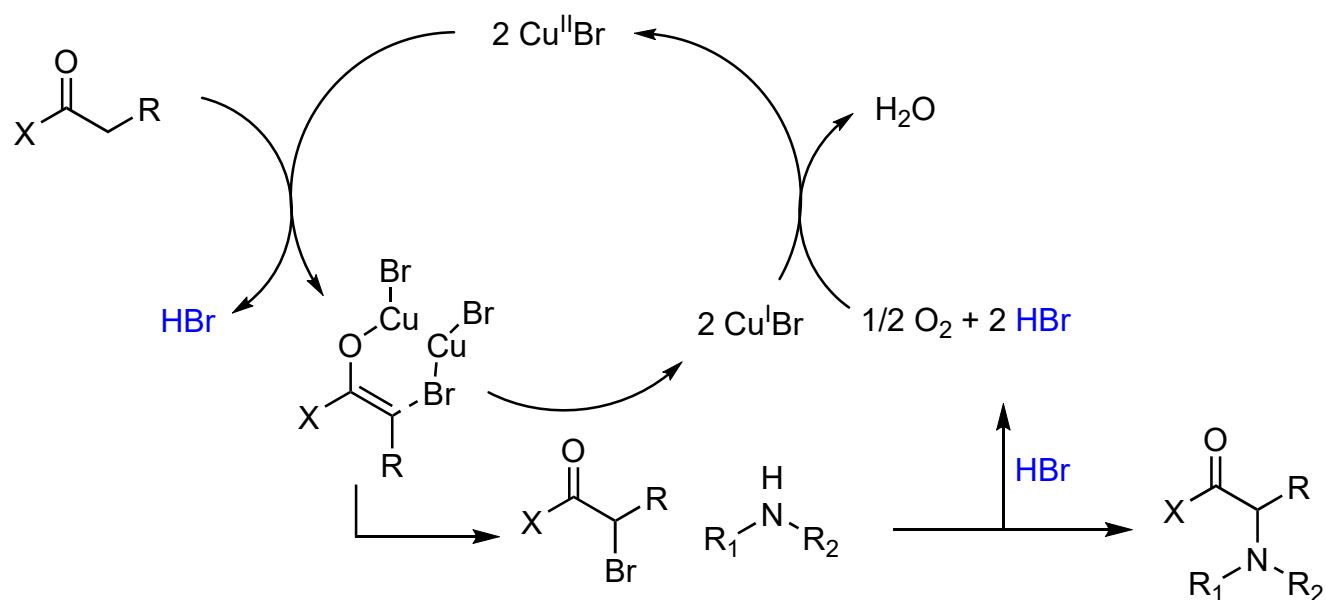


daphenylline

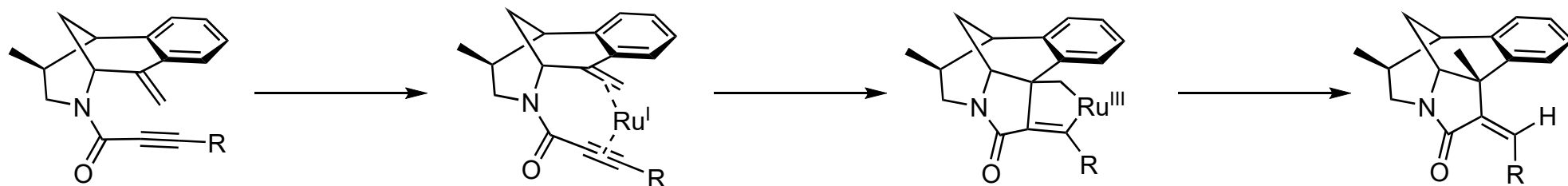
mechanism 3):
<https://doi.org/10.1021/jacs.3c03671>



mechanism 5):
<https://doi.org/10.1021/ja4096472>



mechanism 8):
(<https://doi.org/10.1021/ja042645v>)



Camphorsulfonic acid:

