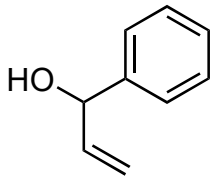
Enantioselective Total Synthesis of (–)-Daphenylline



1) propanal, 3 mol% $[Ir(cod)Cl]_2$,
   12 mol% **1**, 10 mol% **2**, HCO_2H
2) $BocNH_2$, Et_3SiH, TfOH
3) $CsCHO_2$, **3** 420 nm LED
4) PPA, heat
5) $CuBr_2$ (10 mol%),O_2, heat
6) Ph_3PCH_3Br, KO*t*Bu, heat

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

   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

3) Provide a mechanism

4) *Hint: Make it ring. Leave the amine alone!*
5) Provide a mechanism

   Hint: Use it or lose it!

6) Provide a mechanism

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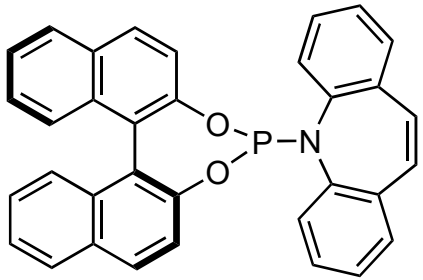

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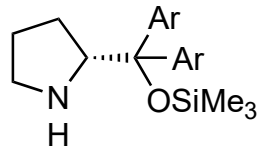
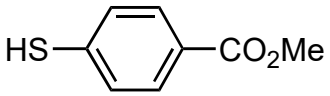


Ar= 3,5-$(CF3)_2$-Ph

2



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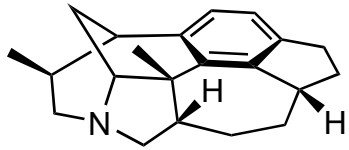

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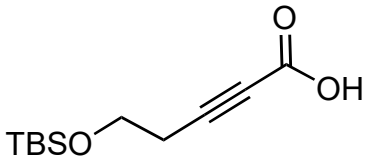

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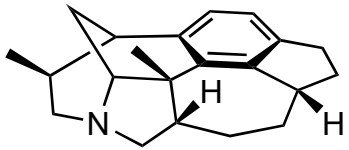
7) **4**, EDCI, HOBt, DIPEA
8) $Rh(cod)_2OTf$, BINAP, H_2
9) CSA, $Pd(OH)_2/C$, H_2
then pH 6.8 buffer, TEMPO, $NaClO_2$, NaClO
10) $(COCl)_2$, cat. DMF then $AlCl_3$ heat
11) Ph_3PCH_3Br, KO*t*Bu, heat
12) $CsCHO_2$, **3**, 420 nm LED
13) $(COCl)_2$, cat. DMF then $AlCl_3$ heat
14) Pd/C, H_2 *then* $RhH(CO)(PPh_3)$, $PhSiH_3$

8) Provide a mechanism

9) Structure of CSA, how do you make it?
10) Provide a mechanism involving DMF



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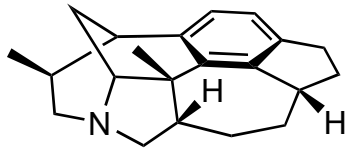

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