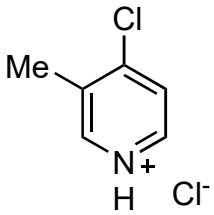
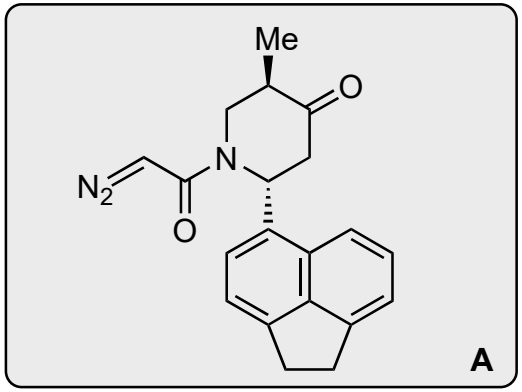
Navigating Excess Complexity: Total Synthesis of Daphenylline

Brandon A. Wright, Alessio Regni, Nattawadee Chaisan, Richmond Sarpong*

J. Am. Chem. Soc. **2024**, *146,* 1813.

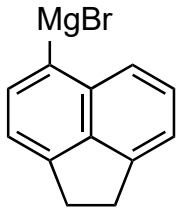


1-4

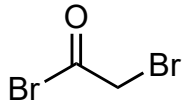


5-6

1) NaOMe, MeOH, 80 °C
2) **1**, CBz-Cl, THF, −5 °C
then 2 M HCl
3) Zn, AcOH, 40 °C
then Pd/C, H_2
4) **2**, K_3PO_4, CH_2Cl_2
then TsHNNHTs, TMG



1



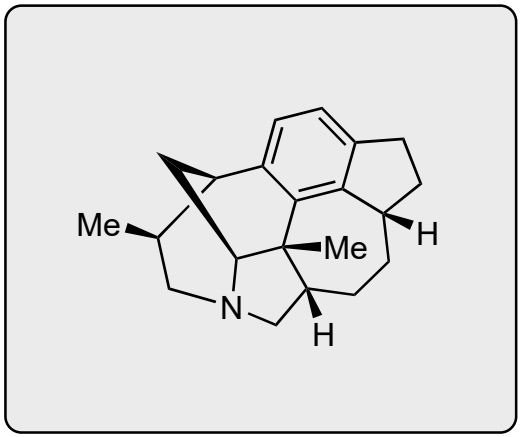
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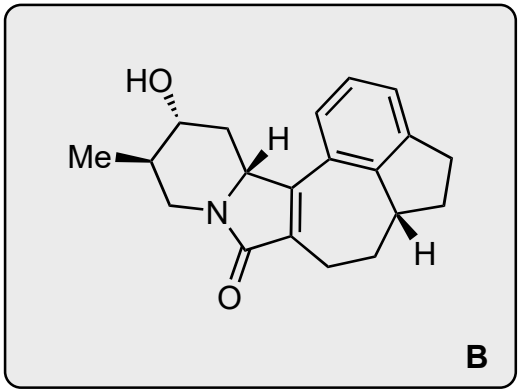
5) $Rh_2(OAc)_4$, 4 Å MS, CH_2Cl_2, 0 °C
6) 1,2-DCB, 250 °C, μW
then H_2, Pd/C, EtOAc
then Bu_4NBH_4

1) Reaction type? Draw a mechanism
S_NAr

4) Draw a mechanism for the second half-reaction. What's TMG? Give an estimate for its pK_a *(~13 in H_2O)*

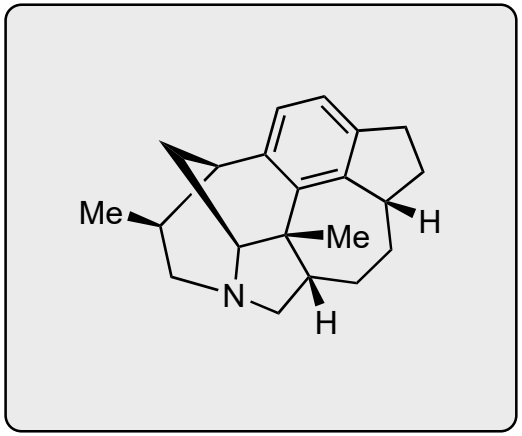
5&6) Name? (*Buchner ring expansion*)
6) Propose a mechanism. *Hint:* two-step dearomatisation-rearomatisation (*disrotatory 6π-electrocyclic ring opening, then 1,5-H-shift*)

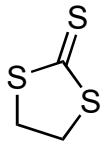




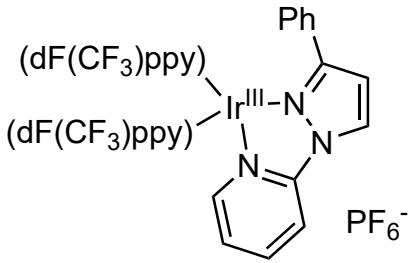
B

7-12



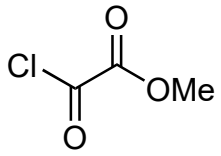


3



4

7) **3**, cat **4**, CH_2Cl_2, 400 nm LED
8) $LiAlH_4$, THF, 0 → 70 °C
then Ra-Ni, H_2O, 0 → 70 °C
9) CrO_3, H_2SO_4, H_2O/acetone
10) 48% HBr, 100 °C
11) **5**, DMAP, Et_3N, CH_2Cl_2
12) Bu_3SnH, AIBN, PhH, 80 °C



5

7) Name? (*thia-Paterno-Büchi*)
Hint: A four-membered heterocycle is formed.
8) Propose a mechanism.