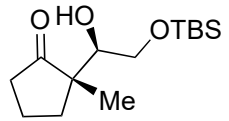
Total Synthesis of Gukulenin B via Sequential Tropolone Functionalizations

K. C. Nicolaou, Ruocheng Yu, Zhaoyong Lu, and Fernando G. Alvarez *J. Am. Chem. Soc*. **2022**, *144*, 5190-5196.



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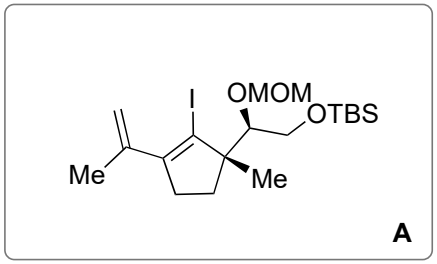

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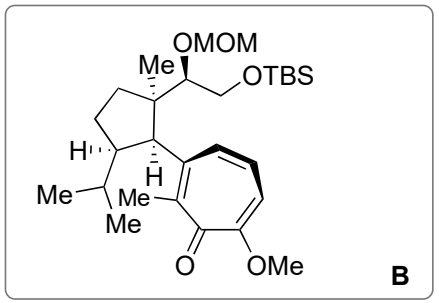
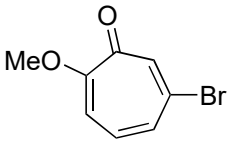


1) MOMCl
2) $TsNHNH_2$, $MgSO_4$
3) *n*-BuLi *then* acetone *then* *n*-BuLi *then* I_2
4) Martin sulfurane

5) *t*-Buli, $ZnCl_2$ *then* **1**, $Pd_2(dba)_3$, RuPhos, LiCl
6) OsO_4, $NaIO_4$, 2,6-lutidine
7) H_2, $Pd(OH)_2/C$
8) Nysted reagent,
9) H_2, Crabtree´s catalyst BAr_F analogue
10) Palau´chlor, 2,4,6-trimethylaniline (cat.)
11) **2**, SPhos-Pd-G4



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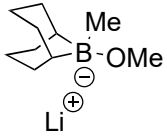
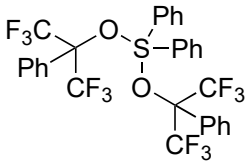
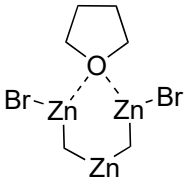


2

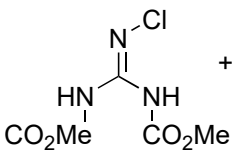
2) + 3) Name of the reaction?
Shapiro reaction
4) Martin sulfurane structure?



5) Name of the reaction?
Negishi coupling
7) Name of the catalyst?
Pearlman's catalyst
8) Structure of Nysted reagent?
9) Structure of Crabtree´s catalyst $[Ir(PCy_3)(py)(cod)]PF_6$
10) Structure of Palau´chlor?
Role of the 2,4,6-trimethylaniline?

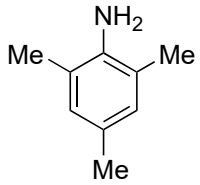


Nysted reagent

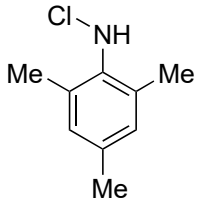


Palau´chlor

+



in-situ

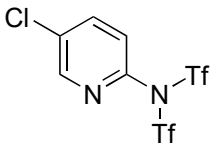


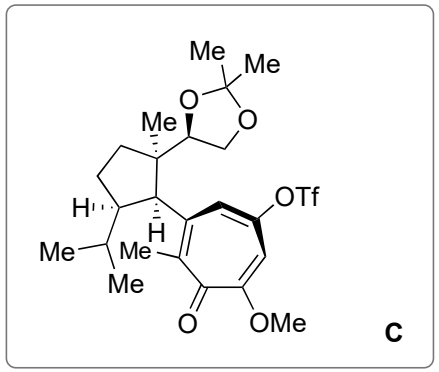
actual chlorination agent, more selective

12-16

12) HCl, MeOH
13) TsOH, $Me_2C(OMe)_2$
14) $[Ir(cod)(OMe)]_2$, dtbpy, B_2pin_2
15) $NaBO_3$
16) Comins´ reagent, Et_3N

16) Strucuture of Comins´ reagent?



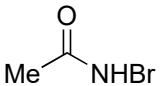


C

B

17-20

17) HCl, MeOH
18) DMP
19) $MgBr_2$, THF, reflux
20) **3**



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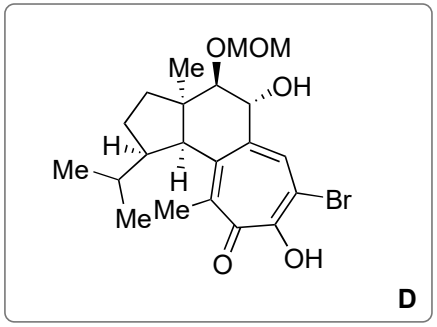
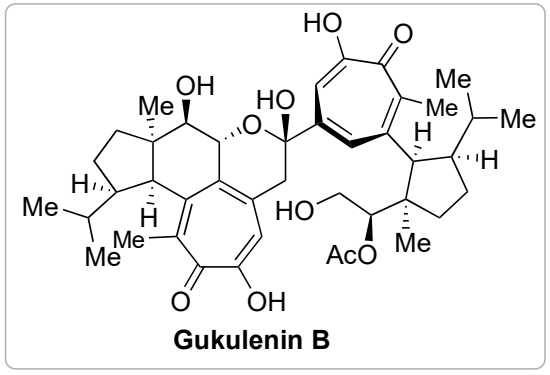
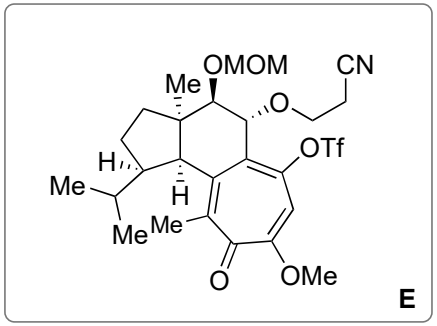


D



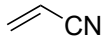
Gukulenin B

21-25



E

21) NaOBn (excess)
22) MeI
23) **4**, Cs_2CO_3
24) 1,4-cyclohexadiene, Pd/C
25) Et_3N, Comins´ reagent



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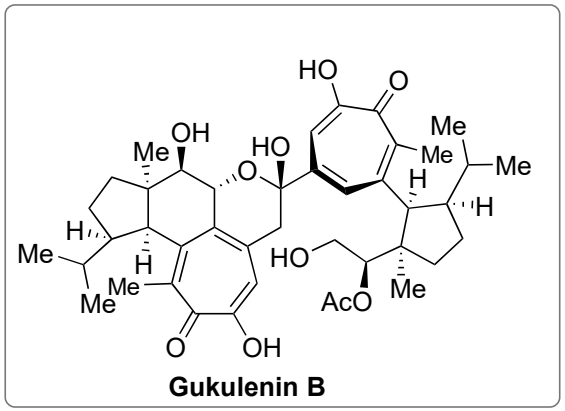
21) *hint* - 4 things happen
2x deprotonation - Br elimination - OBn addition
22) *hint* - selective mono-methylation

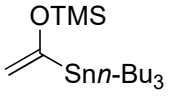
C

26-31



Gukulenin B

26) **5**, $Pd(PPh_3)_4$, CuDPP
27) **E**, $Pd(P\textit{t}\text{-}Bu_3)$, $\textit{n}\text{-}Bu_3SnF$
28) KHMDS
29) Me_2BBr, DIPEA
30) $Yb(OTf)_3$, $MeC(OMe)_3$ *then* H_2O
31) MgI_2



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