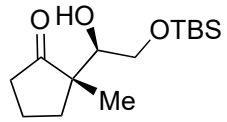
Total Synthesis of Gukulenin B via Sequential Tropolone Functionalizations

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



1 - 4

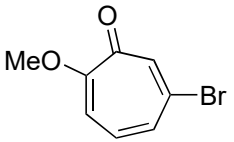
A

5 - 11

B

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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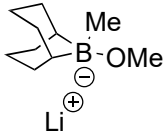


2

3) Name of the reaction?

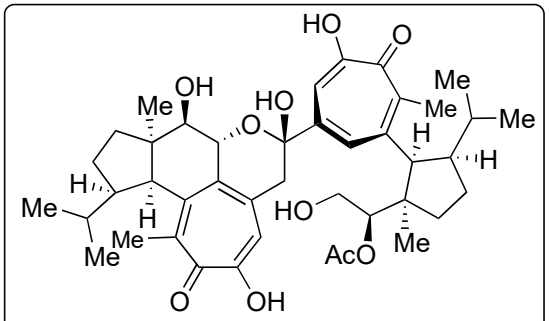
4) Martin sulfurane structure?

5) Name of the reaction?

7) Name of the catalyst?

8) Structure of Nysted reagent?
9) Structure of Crabtree´s catalyst

10) Structure of Palau´chlor?
Role of the 2,4,6-trimethylaniline?



Gukulenin B

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

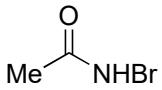
16) Strucuture of Comins´ reagent?

C

B

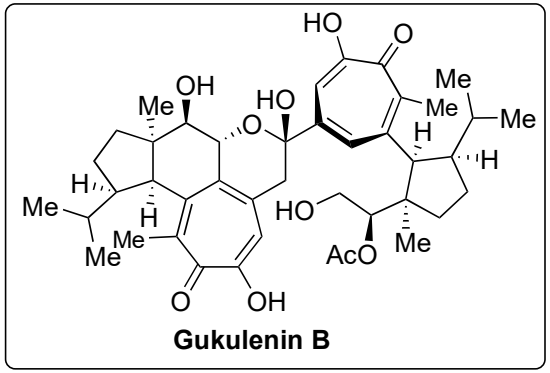
17-20

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



3

D



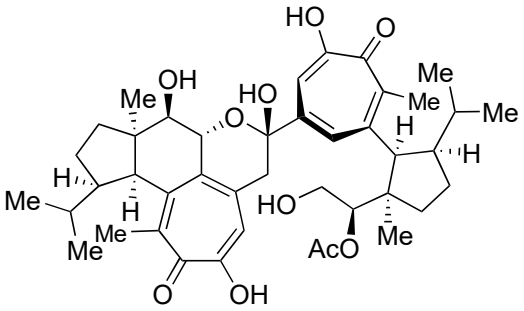
Gukulenin B

21-25

E

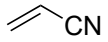
C

26-31



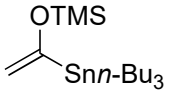
Gukulenin B

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



4

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



5

21) *hint* - 4 things happen
22) *hint* - selective mono-methylation