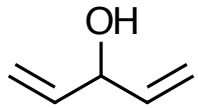
Synthesis Challange # 30

AG Wegner

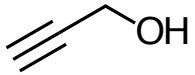
02.04.2015



A

1-3

B



C

4-5

D

1) $Ti(OiPr)_4$ (cat), (+)-diisopropyl tartrate (cat), cumene hydroperoxide, CH_2Cl_2, MS 4 Å
2) TBSCl, imidazole, DMF
3) H_2 (1atm),Pd/C(cat),EtOAc

4) ethylvinyl ether, $pTsOH \cdot H_2O$ (cat),
5) a) EtMgBr, THF, 45 ºC ; b) CuCl (5 mol %), propargyl bromide, 60 ºC

Please give a transition state for step 1).

B + D

6-9

E

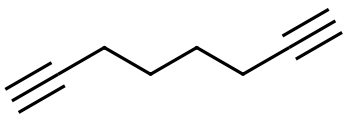
10-12

F

6) a) D, nBuLi, THF, –78 ºC
b)) BF3·Et2O, then B, –78 ºC
7) PPTS, MeOH, 30 ºC
8) H_2 (1 atm), Ni (25 mol %), EtOH
9) CBr_4, PPh_3, CH_2Cl_2, 0 ºC

10) propynylmagnesium bromide,
CuI (50 mol %), THF, –15 ºC - –10 ºC
11) CBr_4, PPh_3, toluene, 65ºC
12) HF·pyridine, THF, 0ºC

Please, provide a detailed mechanism for step 9).



G

13-15

H

16-18

I

13) LiHMDS, THF, –78 ºC, then TMSCl, –78 –C to RT
14) nBuLi, THF, –78 ºC, then MeI, –78ºC to RT
15) MeLi, THF, –78 ºC,then ClC(O)OMe, –78 to 0 ºC

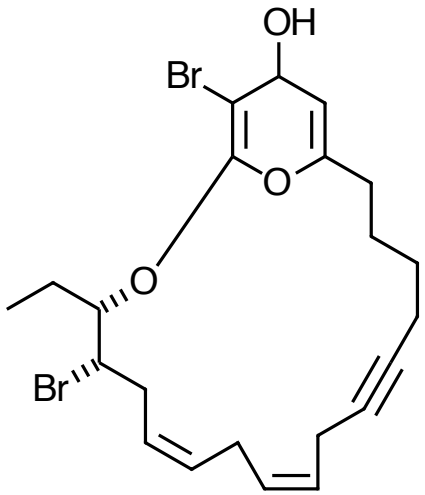
16) tBuOAc, LDA, –78 ºC, then H
17) TFA, CH_2Cl_2
18) F, DCC, DMAP (cat), CH_2Cl_2, 0ºC

Please, provide a detailed mechanism for sequence 18).

19

J

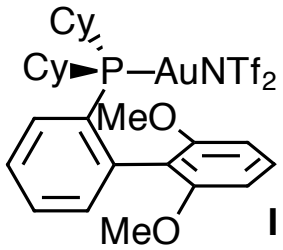
20-21



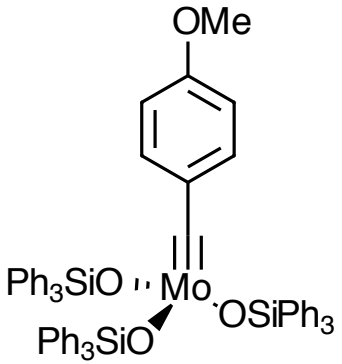
19) **I** (3 mol%), MeCN/HOAc (4:1)

20) **II** (5 mol%), MS 5 Å, toluene
21) NBS, THF

Please provide a mechanism for step 19.



I



II

Please provide a mechanism for step 20