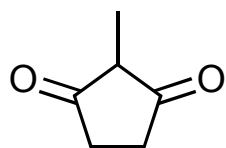


Synthesis Challenge # 49

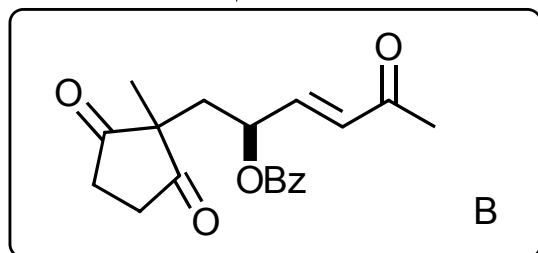
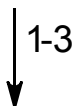
Concise Enantioselective Total Synthesis of Cardiotonic Steroids 19-Hydroxysarmentogenin and Trewianin Aglycone

W. Kaplan, H. R. Khatri, P. Nagorny, *J. Am Chem. Soc.*, **2016**, ASAP, DOI: 10.1021/jacs.6b04029

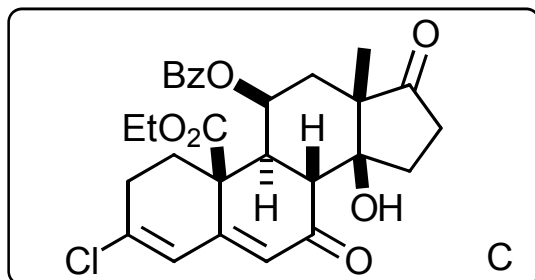
02.06.2016



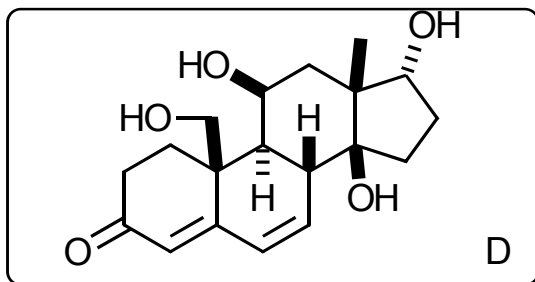
A



B



C

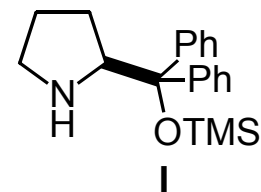


D

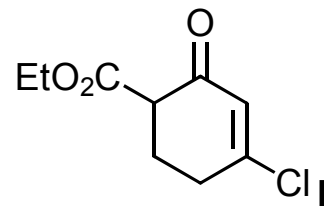
1) acrolein, H₂O, 12 h
 2) **I** (10 mol %), (BzO)₂, hydroquinone, THF, H₂O,
 c) 1-(triphenylphosphoranylidene)-2-propanone, toluene

4) **II**, Cu(OT)₂ (50 mol %), CH₂Cl₂
 5) *p*-TSA, CH₃CN, 55 °C
 6) NaHMDS, toluene, -78 to 42 °C

7) DIBALH, THF, -78 to 60 °C, 12 h
 then HCOOH, H₂O, 85 °C

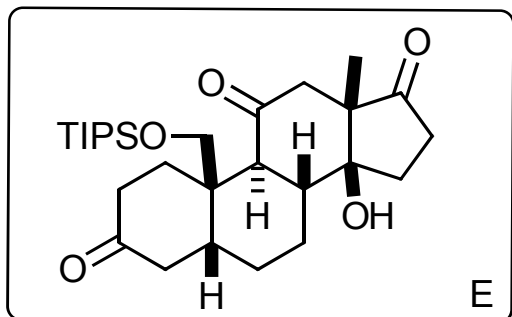


I

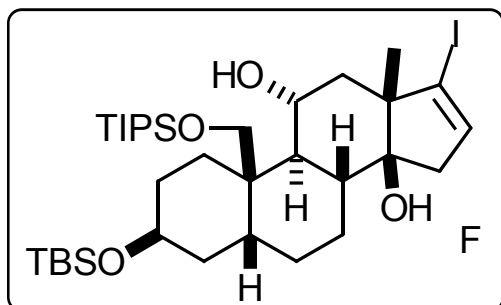


II

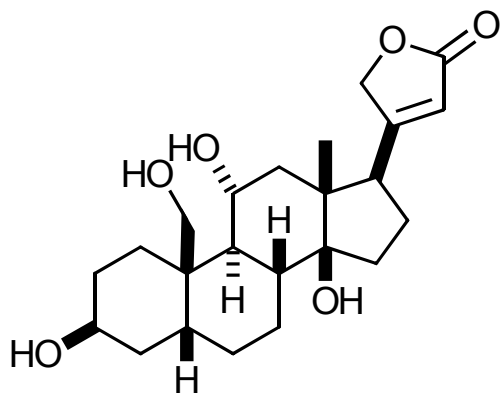
8-10



11-15



16-19

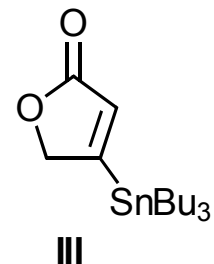


- 8) H_2 , Pd/C, KOH, quinoline, MeOH
- 9) TIPSCl, ImH, DMF, rt, 6 h
- 10) DMP, Py, CH_2Cl_2 , 2 h

- 11) $\text{LiAlH}(\text{OtBu})_3$, THF, -78 to -40 °C
- 12) TBSOTf, Et_3N , CH_2Cl_2 , -78 to -30 °C
- 13) Li, NH_3 , THF, -78 °C
- 14) TBAF, THF, -78 °C,
- 15) $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$, Et_3N , EtOH, 50 °C then I_2 , Et_3N , THF, rt

- 16) III, $\text{Pd}(\text{PPh}_3)_4$, CuCl, LiCl, DMSO, 50 °C
- 17) TMSOTf, 2,6-lutidine, CH_2Cl_2 , -78 °C to rt, 2h, then SiO_2 (dry)
- 18) H_2 , Pd/C, EtOAc, 30 min
- 19) HF in $\text{CH}_3\text{CN}/\text{H}_2\text{O}/\text{CH}_2\text{Cl}_2$

E was obtained as a mixture of diastereomers. Suggest methods for separation.



Step 18 delivers 2 diastereomers

Please provide a beautiful 3D drawing of the final product!

