Asymmetric Total Synthesis of Cyclocitrinol

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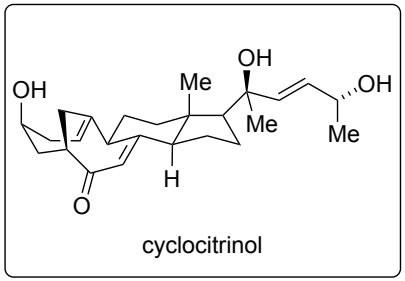
J. Am. Chem. Soc. **2018**, *140*, 5365–5369

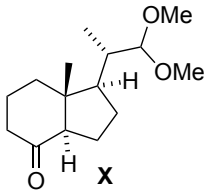


cyclocitrinol

1 - 6

1) CuI, vinylMgBr,THF, –78 °C
2) TIPSCl (1.1 equiv.), imidazole
3) PTSA, MeOH
4) $NaIO_4$
5) $NaBH_4$
6) CBr_4, PPh_3

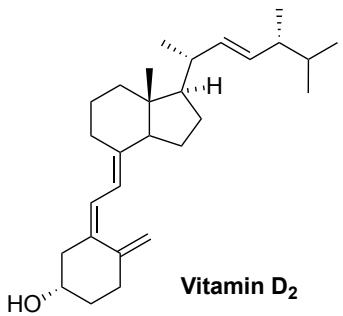
A



X

7 - 9

7) LDA, TMSCl
8) IBX, DMSO
9) $TMSN_3$, Py, I_2



Vitamin D_2

step 7: X is commercially available. How is it prepared from Vitamin D_2?

step 9: role of $TMSN_3$?

B

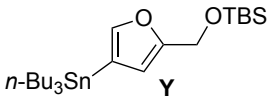
10 - 13

C

14/15

D

16 - 19



Y

10) CuTC, LiOAc, NMP, $Pd(PPh_3)_3$, **Y**
11) $NaBH_4$, $NiCl_2 \bullet H_2O$
12) **A**, *t*-BuLi, Et_2O, –78 °C
13) TBAF, *then* NBS, NaOAc, $NaHCO_3$, H_2O

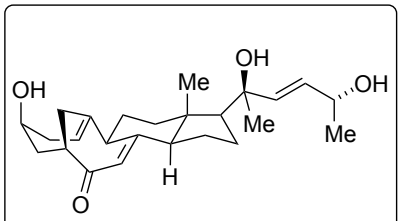
step 10: name reaction?

step 13: name reaction?

14) Ac_2O, *2,2,6,6*-tetramethylpiperidine (TMP), DMAP
15) TMP, MeCN, 155 °C

step 14: hint reaction occurs 2x
step 15: mechanism? which unusual functionality is introduced?

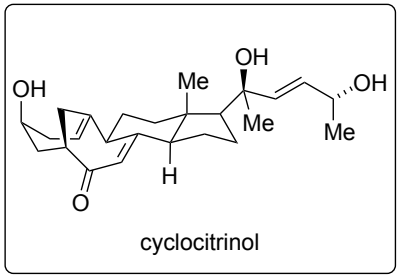
16) $NaBH_4$
17) KHMDS (1.1 equiv.), CS_2, MeI
18) AIBN, n-Bu_3SNH, PhMe, 80 °C
19) $SOCl_2$, Py, 2,4,6-trimethylpyridine, 0 °C



cyclocitrinol

E

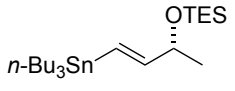
20 - 24



cyclocitrinol

20) Li, $EtNH_2$
21) TEMPO, NCS (4 equiv.), TBACI
22) TESOTf
23) *t*-BuOK,O_2, *t*-BuOH
24) **Y**, *n*-BuLi, THF, –78 °C, *then* TBAF

step 20: hint 2 deprotections occur



Y