Asymmetric Total Synthesis of Cyclocitrinol

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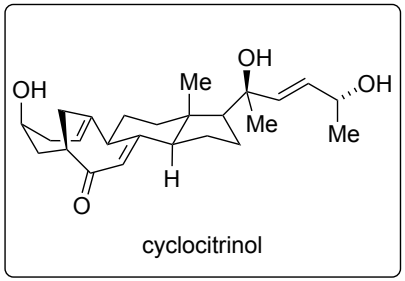
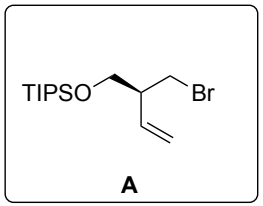
J. Am. Chem. Soc. **2018**, *140*, 5365–5369



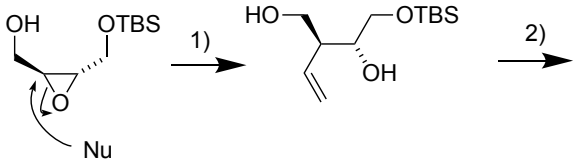
cyclocitrinol

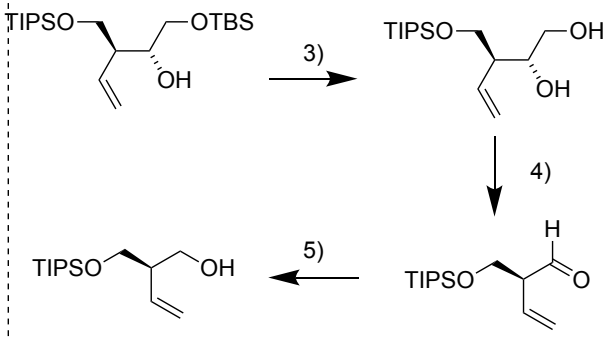
1 - 6



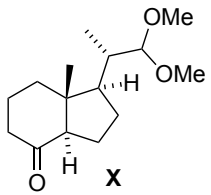
A

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





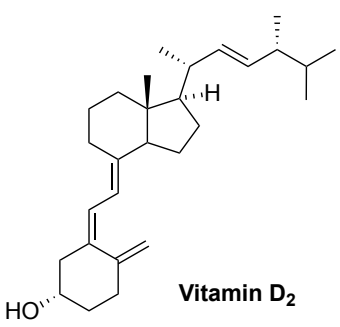
A



X

7 - 9

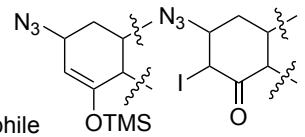
7) LDA, TMSCl
8) IBX, DMSO
9) $TMSN_3$, Py, I_2



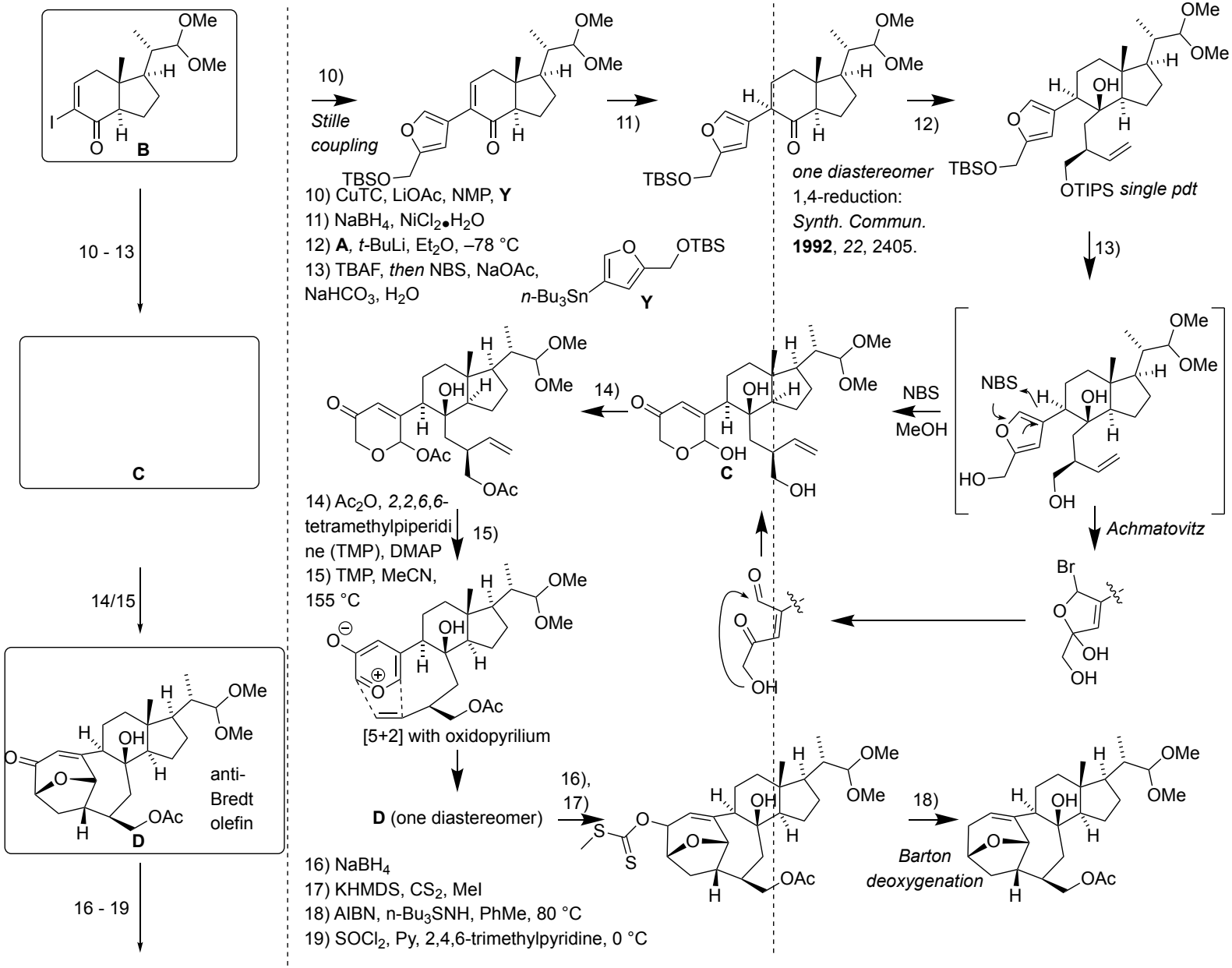
Vitamin D_2

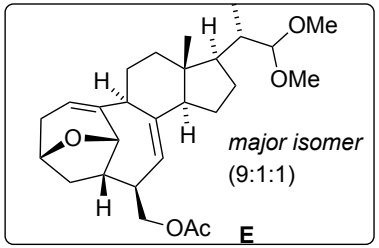
step 7: X is commercially available. How is it prepared from Vitamin D_2? Ozone, Me_2S

step 9: role of $TMSN_3$



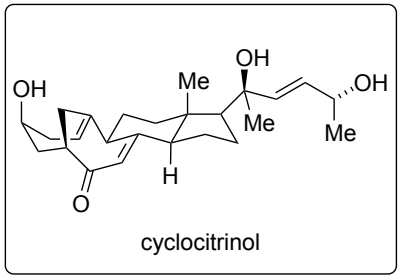
via:
azide as smaller nucleophile
for hindered substrates (usually used: DMAP, py)
Danishefsky, S. J. and coworkers
J. Am. Chem. Soc. **2008**, *130*, 13765.


B
10 - 13
C
14/15
D
anti-Bredt olefin
16 - 19
10)
Stille coupling
11)
12)
one diastereomer
1,4-reduction:
Synth. Commun.
1992, 22, 2405.
OTIPS single pdt
13)
10) CuTC, LiOAc, NMP, Y
11) NaBH4, NiCl2•H2O
12) A, t-BuLi, Et2O, –78 °C
13) TBAF, then NBS, NaOAc, NaHCO3, H2O
n-Bu3Sn
OTBS
Y
NBS
MeOH
Achmatovitz
14)
14) Ac2O, 2,2,6,6-tetramethylpiperidine (TMP), DMAP
15)
15) TMP, MeCN, 155 °C
[5+2] with oxidopyrilium
D (one diastereomer)
16),
17)
18)
Barton deoxygenation
16) NaBH4
17) KHMDS, CS2, MeI
18) AIBN, n-Bu3SNH, PhMe, 80 °C
19) SOCl2, Py, 2,4,6-trimethylpyridine, 0 °C



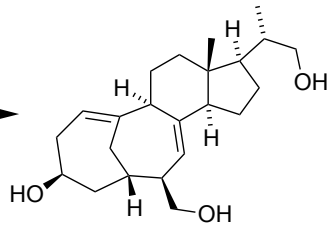
major isomer
(9:1:1)

20 - 24



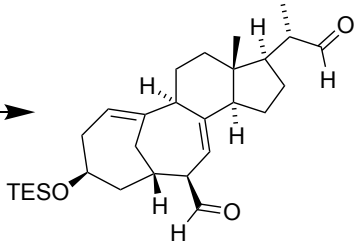
cyclocitrinol

20)

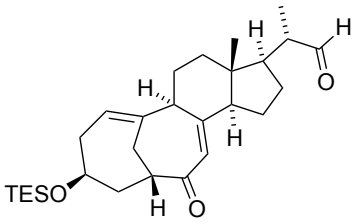


20) Li, $EtNH_2$
21) TEMPO, NCS, TBACl
22) TESOTf
23) *t*-BuOK,O_2, *t*-BuOH
24) **Y**, *n*-BuLi, THF, –78 °C, *then* TBAF

21), 22)



23)
oxidative deformylation



cyclocitrinol
single isomer