Total Synthesis of (±)-Cristaxenicin A

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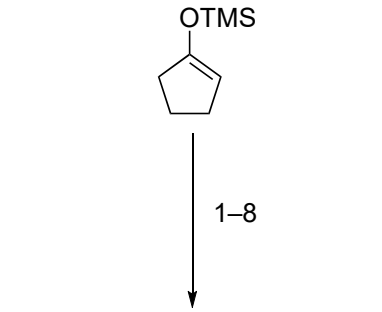
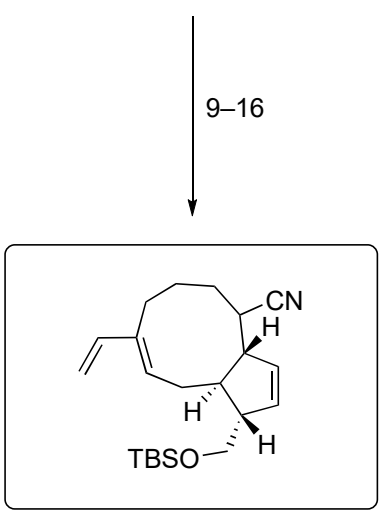
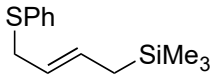


A



B

1) $CH_2(OBn)_2$, TMSOTf, 2,6-DTBP, MeCN
2) **1**, Cp_2TiCl_2, *n*-BuLi, THF, 0 °C
3) MsOH, CH_2Cl_2, 0 °C
4) Li, $NH_{3(liq.)}$, THF, –78 °C
5) ABNO, CH_2Cl_2, 23 °C
6) H_2NOSO_3H, AcOH, H_2O, 50 °C
7) $LiNEt_2$, **2**, HMPA, –30 °C
8) **3**, PhMe, 160 °C



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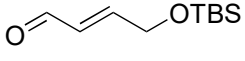

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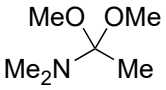
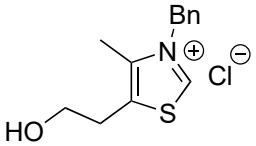


3

9) Cp_2ZrCl_2, $LiAl(O\text{-}t\text{-}Bu)_3H$, 0 °C
10) **4**, NEt_3, EtOH, 50 °C
11) $MeReO_3$, pyridine, H_2O_2, CH_2Cl_2 0 °C
12) O_3, MeOH, CH_2Cl_2, –78 °C *then* Me_2S
13) Zn, AcOH, THF, 23 °C
14) **5**, $Bi(OTf)_3$, PhMe, 23 °C
15) LHMDS, Tf_2O, Et_2O, –78 °C
16) $Pd(PPh_3)_4$, HCO_2NH_4, DMF, 50 °C



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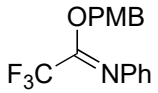


5

2) Hint: SPh is not present in the product; branched product.

3) Hint: Strong acid, vinyl shifts

6) Hint: Does not stop at imine formation.

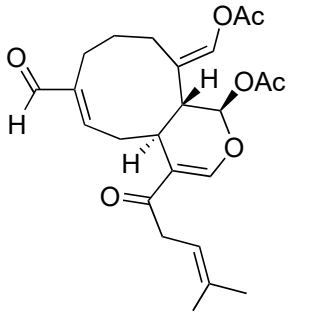
8) Draw the mechanism and name the reactions.
Hint: Two transformations.
see, below Eschenmoser–Claisen Rearrangement
Cope Rearrangement

10) Draw the mechanism, name reaction
see below, Stetter
11) Hint: Epoxidation of a diene; the double bond inside the ring gets oxidized.

13) Hint: An allylic alcohol is formed.

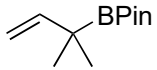
B

17–28



(±)-Cristaxenicin A

17) DIBAL-H, PhMe, 0 °C
18) *t*-BuOK, Ac_2O, THF, –78 °C
19) TBAF, AcOH, THF 50 °C
20) OsO_4 TMEDA, CH_2Cl_2, –78 °C
21) $PhB(OH)_2$, THF, –78 °C
22) DMP, pyridine, CH_2Cl_2, 23 °C
23) **6**, PhMe, 50 °C
24) DMP, pyridine, CH_2Cl_2, 23 °C
25) pinacol, AcOH, 23 °C
26) $NaIO_4/SiO_2$, CH_2Cl_2, 23 °C
27) AcOH, EDCI•HCl, DMAP, DCE, 35 °C
28) DDQ, buffer pH = 7, CH_2Cl_2 23 °C



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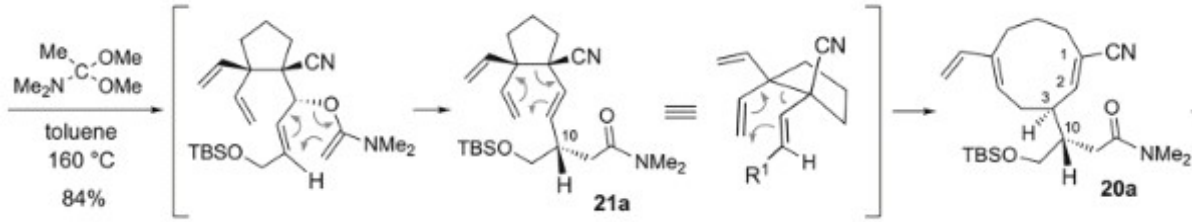

Stetter Catalytic Cycle