Total Synthesis of Putative Chagosensine

Heinrich, M.; Murphy, J. J.; Ilg, M. K.; Letort, A.; Frasz, J.; Philipps, P.; Fürstner, A.

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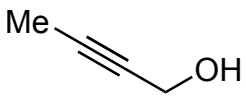
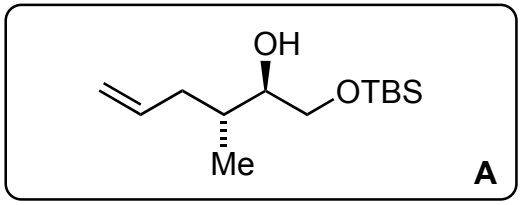


1-4

1) H_2, $Pd/BaSO_4$, quinoline
2) *t*-BuOOH, $Ti(O\textit{i}\text{-}Pr)_4$, (+)-DET
3) TBSCl, imidazole, DMAP
4) allylmagnesium chloride, CuI

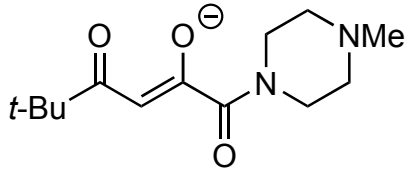
2) Please name the reaction

Sharpless-Epoxidation



A

L1



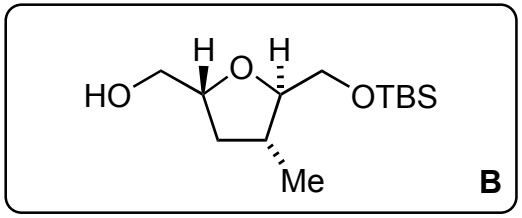
5

5) Co(**L1**)$_2$, *t*-BuOOH, O_2, *i*-PrOH

5) Please name the reaction and provide a mechanism

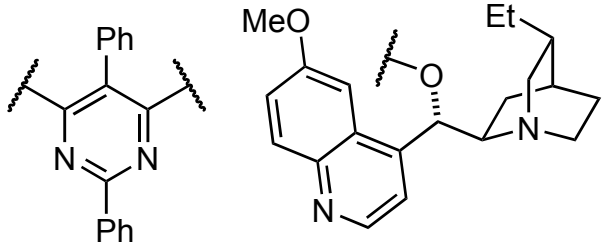
Mukaiyama-Oxidative Cyclization

see page 5



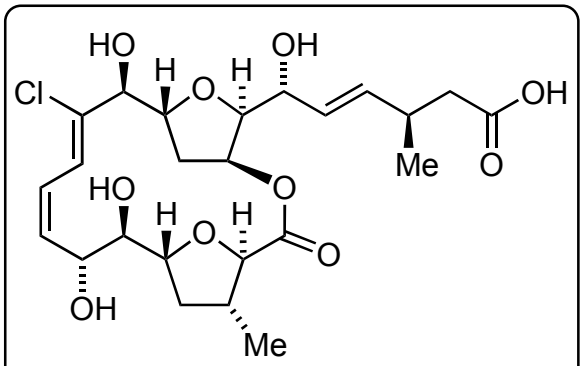
B

L2

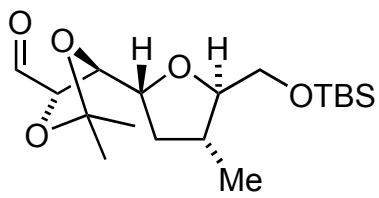


6) SO_3•Py, *i*-Pr_2NEt, DMSO
7) $(CF_3CH_2O)_2P(=O)CH_2CO_2Me$
KHMDS, 18-crown-6
8) K_2OsO_4•(H_2O), $K_3Fe(CN)_6$,
K_2CO_3, **L2**, $MeSO_2NH_2$
9) $Me_2C(OMe)_2$, *p*-TsOH
10) $LiAlH_4$
11) SO_3•Py, *i*-Pr_2NEt, DMSO

6-11

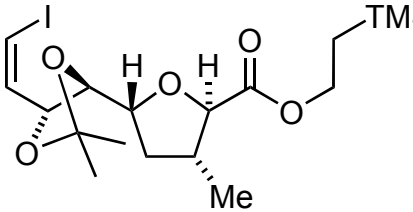


Putative Chagosensine

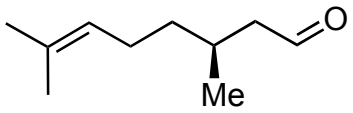


C

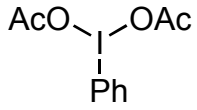
12-15



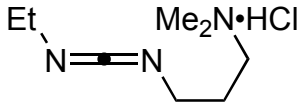
D



16-20



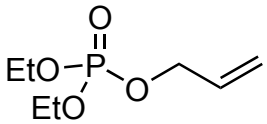
1



2

12) $[Ph_3PCH_2I]I$, NaHMDS, HMPA
13) HF•Py, pyridine
14) TEMPO, **1**, MeCN(aq)
15) $TMSCH_2CH_2OH$, **2**, DMAP

14) Provide a mechanism
see page 5



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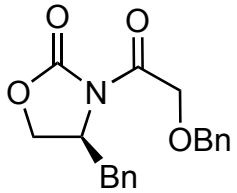
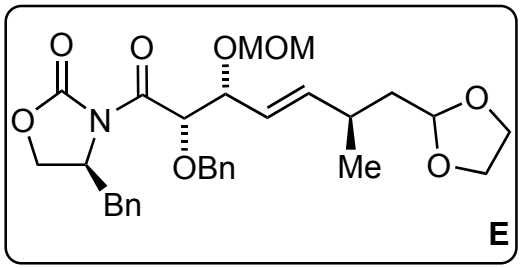


5

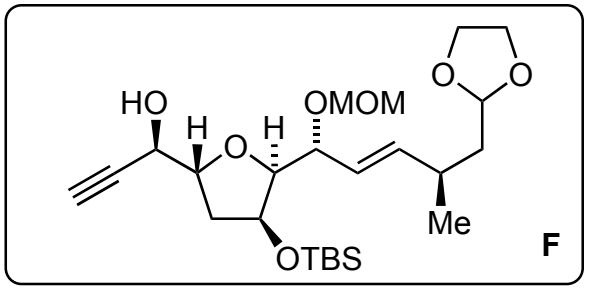
16) $(CH_2OH)_2$, $CH(OEt)_3$, CSA
17) O_3, Sudan red, *then* Me_2S
18) $Pd(OAc)_2$, **3**, $NaHCO_3$
19) **4**, Bu_2BOTf, Et_3N
20) MOMCl, TBAI

18) Please name the reaction
Hint: **2** is the terminal oxidant
Saegusa Oxidation



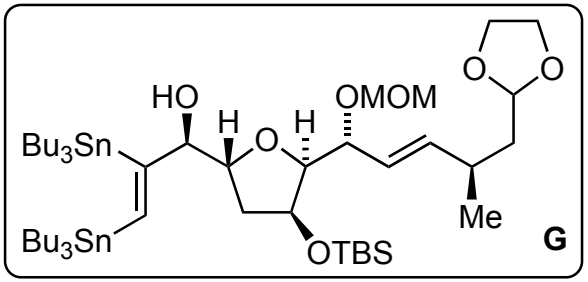
E

21-28

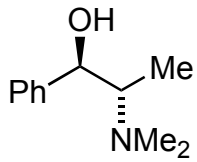


F

29



G



4

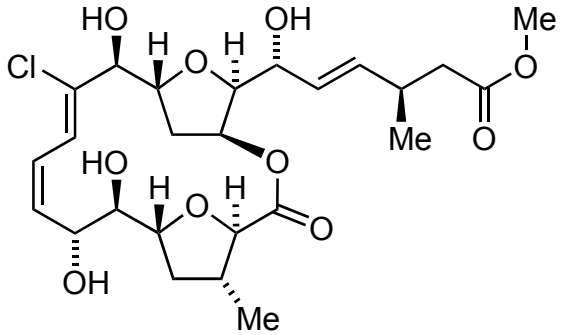
21) $LiBH_3(OH)$
22) SO_3•Py, *i*-Pr_2NEt, DMSO
23) $MgBr_2$•OEt_2, Allyl-TMS
24) TBSOTf, 2,6-lutidine,
25) DDQ, buffer Ph = 7.4
26) Co(**L1**)$_2$, *t*-BuOOH, O_2, *i*-PrOH
27) SO_3•Py, *i*-Pr_2NEt, DMSO
28) $Zn(OTf)_2$, **5**, TMS-acetylene,
i-Pr_2NEt, *then* K_2CO_3, MeOH

29) $(Bu_3Sn)_2$, $[PdCl_2(t\text{-}BuCN)_2]$

23) Provide a stereochemical model
see page 5

28) Please name the reaction
Carreira Alkynylation

30-37



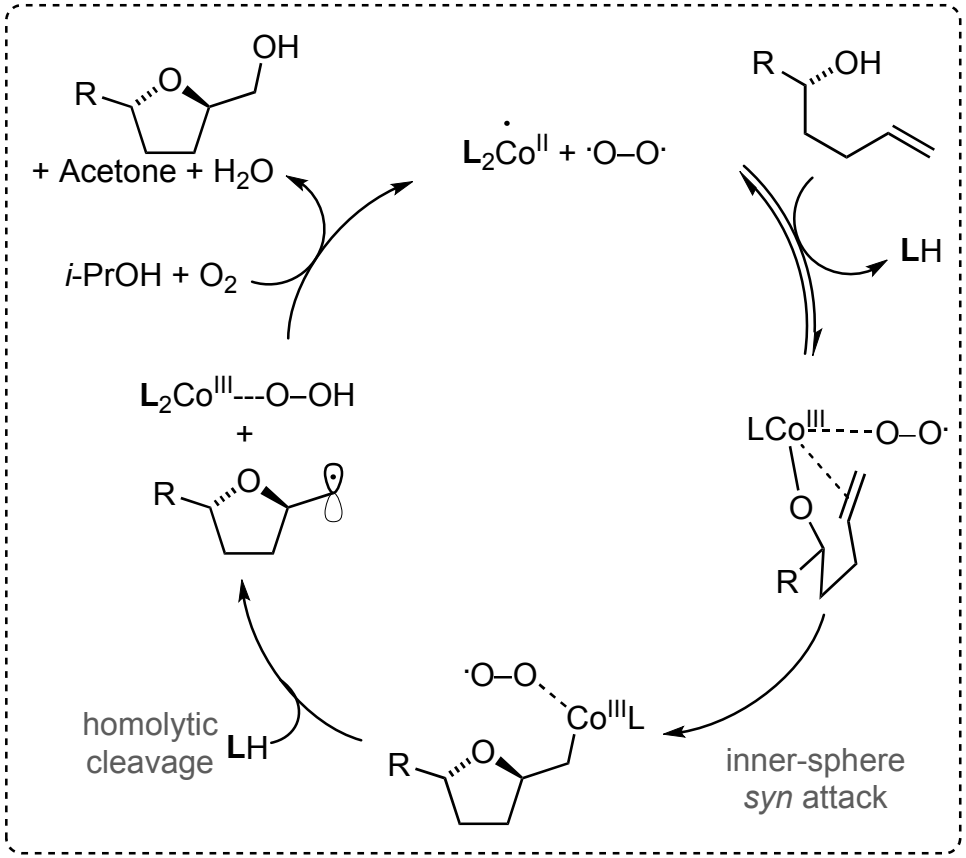
Putative Chagosensine Methyl Ester

Eleven stereogenic centers
Two 2,5-*trans*-trisubstituted THF's
Very strained 16-membered macrolatone
Unprecedented *Z*,*Z*-chloro-1,3-diene

30) [(*t*-$Bu_3P)_2Pd$], [Ph_2PO_2][NBu_4], LiCl, **D**
31) $CuCl_2$, 2,6-Lutidine
32) MOMCl, TBAI, *i*-Pr_2NEt
33) TBAF
34) 2,4,6-trichlorobenzoyl chloride, *i*-Pr_2NEt
then DMAP, Δ
35) Me_2BBr
36) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene
37) CH_2N_2

36) Please name the reaction
Pinnick Oxidation

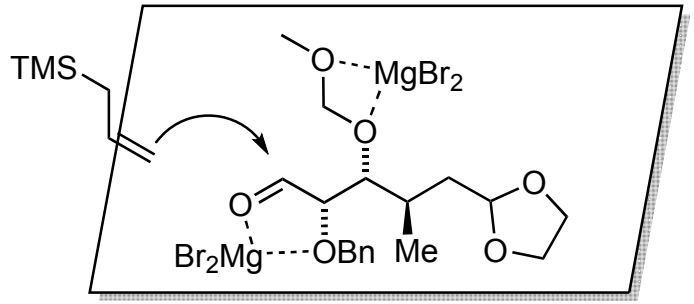
solution to step 5:



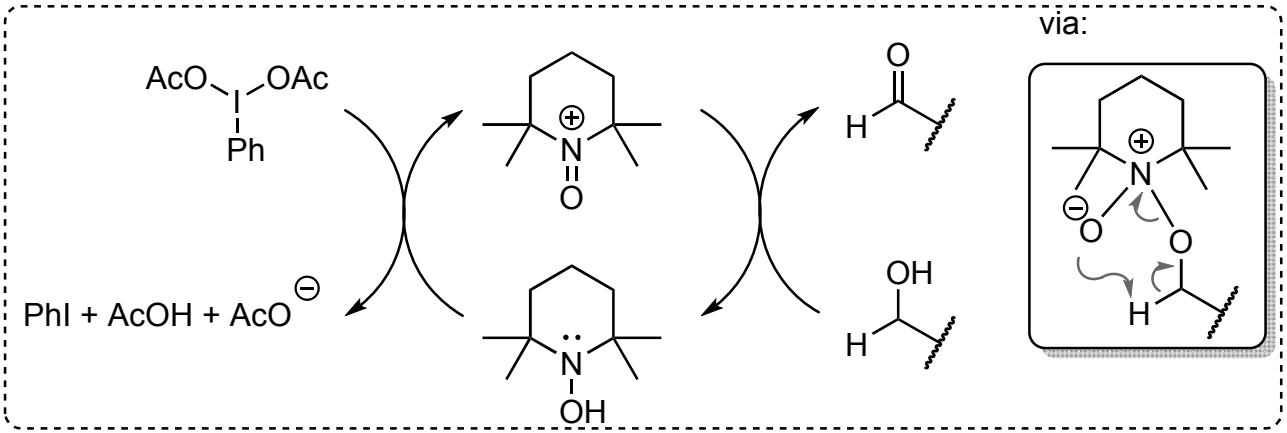
Ali, S.; Milanezi, H.; Alves, T. M. F.; Tormena, C. F.; Ferreira, M. A. B. *J. Org. Chem*. **2018**, *83*, 7694.

solution to step 23:

Cram-Chelate Model



solution to step 14:



De Mico, A.; Margarita, R.; Parlanti, L.; Vescovi, A.; Piancatelli, G. *J. Org. Chem.* **1997**, *62*, 6974.