Total Synthesis of Icumazole A Using a Modified Cadiot−Chodkiewicz Coupling

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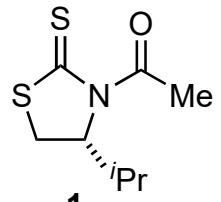
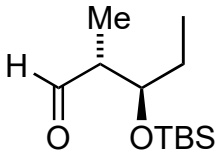
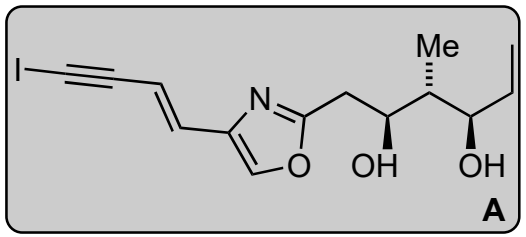


1



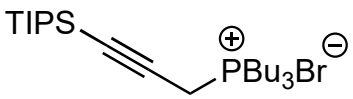
2

1–10



A

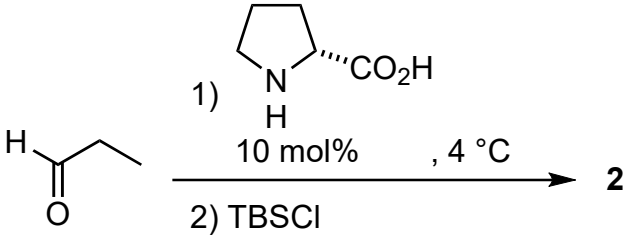
1) **1**, $TiCl_4$, *i*-Pr_2NEt, *then* **2**
2) TBSOTf, 2,6-lutidine
3) LiOH, H_2O_2
4) L-serine methyl ester, TBTU, HOBt, *i*-Pr_2NEt
5) Et_2NSF_3, K_2CO_3
6) $CuBr_2$, DBU
7) DIBAL-H
8) **3**, *n*-BuLi
9) TBAF
10) $PhI(OAc)_2$, TBAI

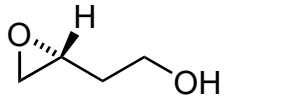


3

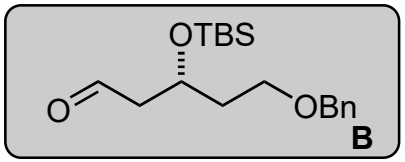
1) Hint: 4:1 anti / syn mixture

2 was prepared as follows. Draw the Zimmerman-Traxler chair-Like transition state to rationalize diastereoselectivity and enantioselectivity



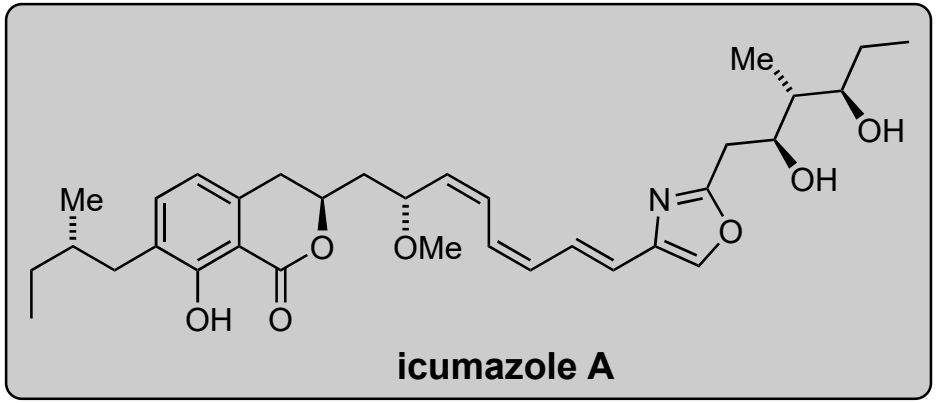


7–9

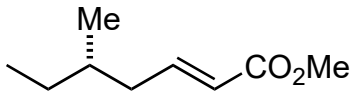


B

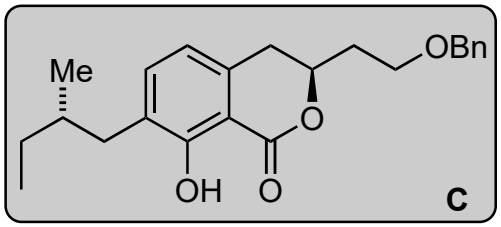
11) BnBr, NaH
12) vinyl magnesiumbromide, CuI
13) TBSCl, imidazole
14) O_3, pyridine, *then* Me_2S



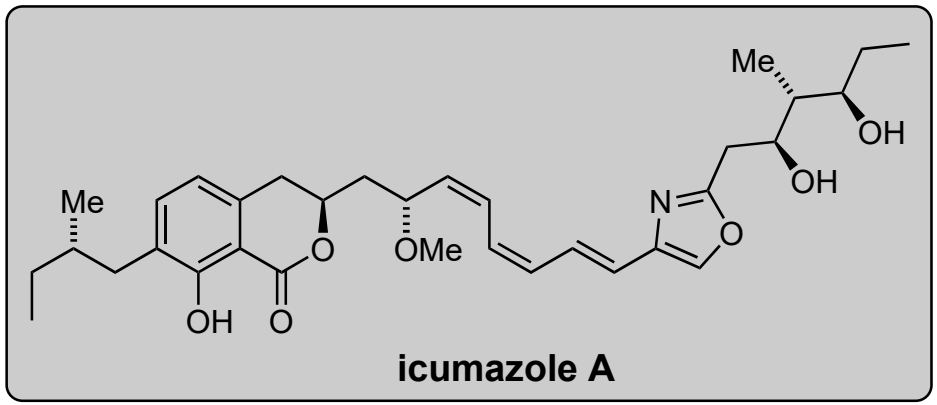
icumazole A



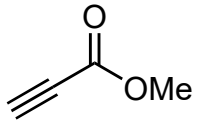
15–22



23–30



15) DIBAL-H
16) Ph_3P•HBr
17) NaHMDS, *then* **B**
18) TBAF
19) **4**, Otera's catalyst
20) NBS, $AgNO_3$
21) toluene, sealed tube, 180 °C, *then* DDQ
22) Pinacolborane, $Pd(MeCN)_2Cl_2$, SPhos, *then* NaOH, H_2O_2



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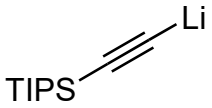
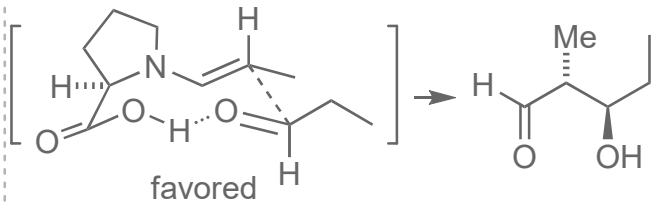


5

23) H_2, Pd/C
24) DMP
25) **5**, $CeCl_3$, LiCl
26) *p*-nitrobenzoic acid, Ph_3P, DMEAD, *then* MeONa
27) Me_3OBF_4, proton sponge
28) TBAF
29) **A**, CuI, $Pd(Ph_3P)_2Cl_2$, Et_3N
30) Zn(Cu/Ag)

1)



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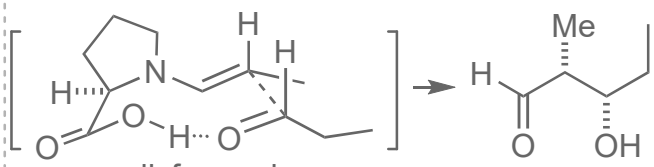

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26) Name of the reaction?
Mitsunobu reaction
29) Name of the reaction?
Cadiot−Chodkiewicz Coupling