Synthesis Challenge # 48

Isolation and Asymmetric Total Synthesis of Perforanoid A

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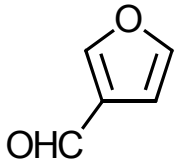
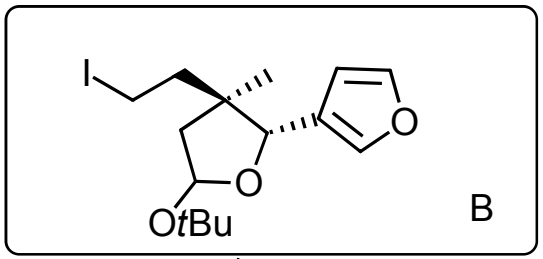


A

1-3

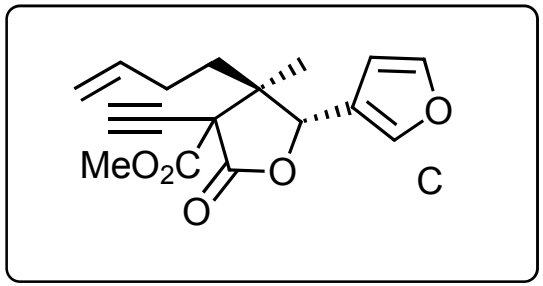
1) ligand **I** (15 mol%), 2-butyne, Cy_2BH, Me_2Zn , toluene,
2) 2-methyl-2-(vinyloxy)- propane, $Pd(OAc)_2$ (0.1 equiv), benzoquinone, AcOH, CH_3CN,
3) $ZrCp_2Cl_2$ (1.5 equiv), $LiAlH(OtBu)_3$, THF, I_2 (2.0 equiv)



B

4-6

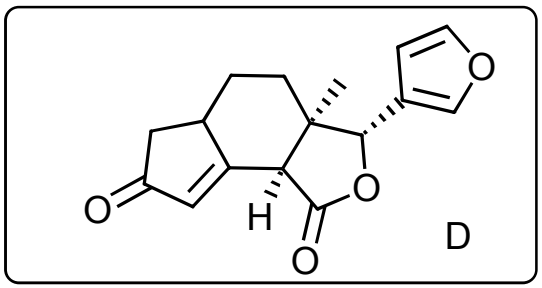
4) $NiBr_2$ glyme (10 mol%), potassium vinyltrifluoroborate, bathophenanthroline, NaHMDS, *t*-BuOH/CPME (1:1),
5) Jones oxidation
6) LiHMDS, $ClCO_2Me$, then **II**, TBAF



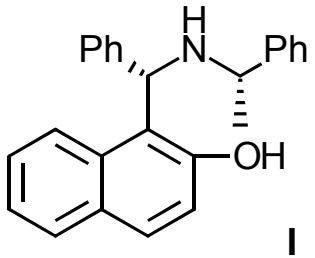
C

7-8 17-18

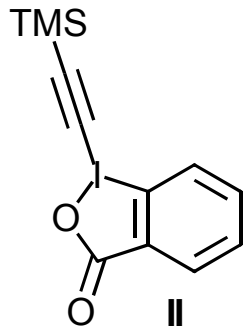
7) LiCl, H_2O (5.0 equiv), DMF, 130 ºC
8) $[Rh(CO)_2Cl]_2$ (7%), CO (balloon pressure), toluene



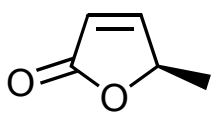
D



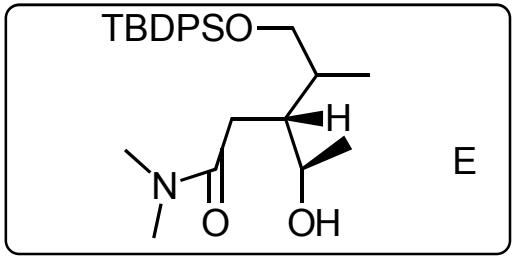
I



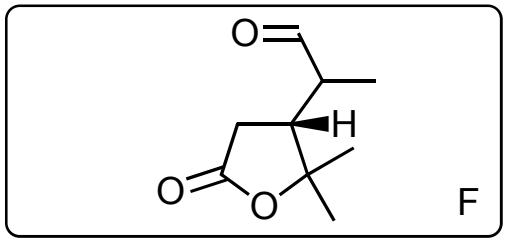
II



9-12

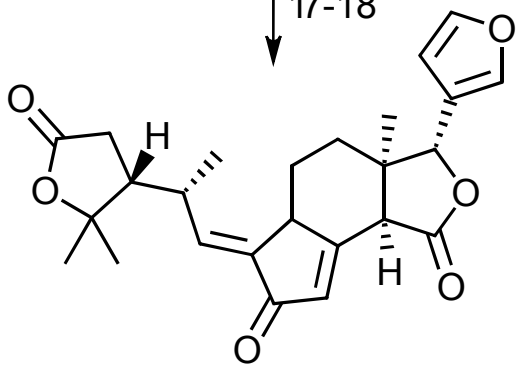


13-16



D + F

17-18



9) PhSCu, then but-3-en-2-ylmagnesium chloride (
10) O_3, CH_2Cl_2-MeOH (1:1), −78ºC, then $NaBH_4$
11) imidazole, TBDPSCl, CH_2Cl_2,
12) Me_3Al, dimethylamine hydrochloride

13) DMP, $NaHCO_3$, CH_2Cl_2, RT
14) MeMgCl, −20ºC then 1 M HCl
15) TBAF, 50C
16) DMP, $NaHCO_3$, CH_2Cl_2, RT

17) LDA, THF, −78ºC
18) Burgess reagent

E was obtained as a mixture of diastereomers. Suggest methods for separation.

Esterfication with Moshers ester afetr step 15