Total Synthesis of Rameswaralide Utilizing a Pharmacophore-Directed Retrosynthetic Strategy

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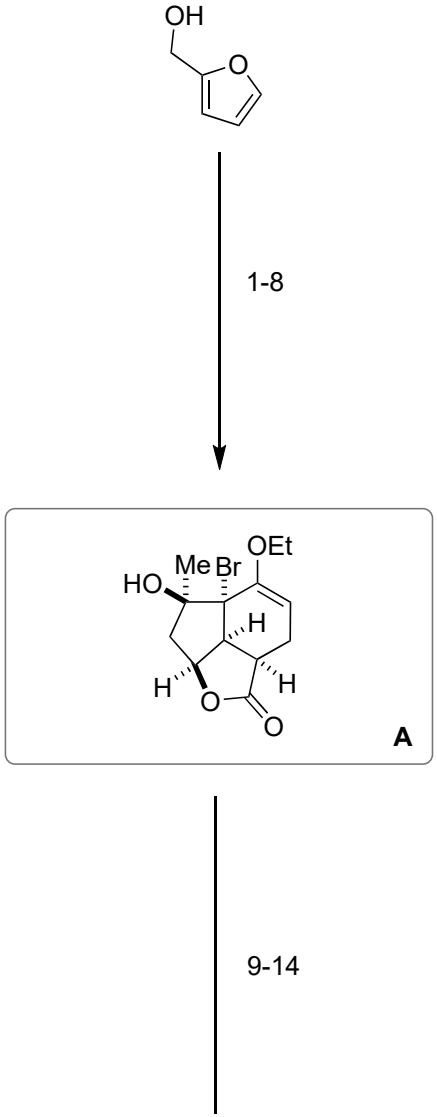
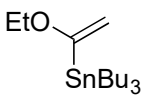


1) μW, H_2O, 200 °C
2) TBSCl
3) I_2, DMAP
4) **1**, CuTC, $AsPh_3$, $Pd_2(dba)_3$
5) MeLi
6) TBAF
7) acryloyl chloride, **2**, DIPEA
8) NBS

1



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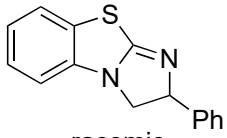


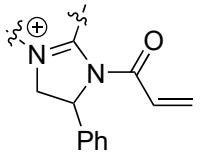
racemic

9) TESOTf, 2,6-lut.
10) AIBN, Bu_3SnH
11) TBAF
12) $ZnEt_2$ *then* $CHBr_3$, O_2
13) LiBr, CAN, NBS
14) DBU

1) Name of the reaction? Mechanism?
Piancatelli Rearrangement
Mechanism see below

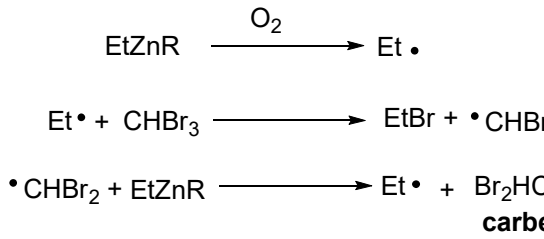
4) Name of the reaction?
Stille coupling

7) What is reactive intermediate in this reaction?



8) How would you call this transformation?
Alkene Transposition

12) Name of the reaction? Role of O_2?
Simmons-Smith cyclopropanation
Initiator



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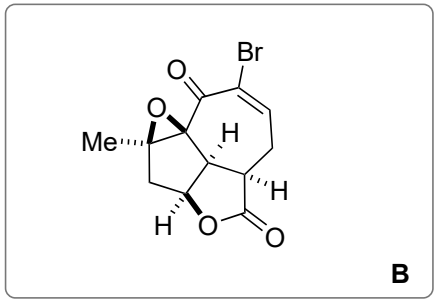
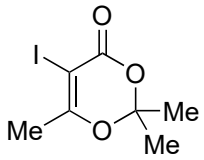
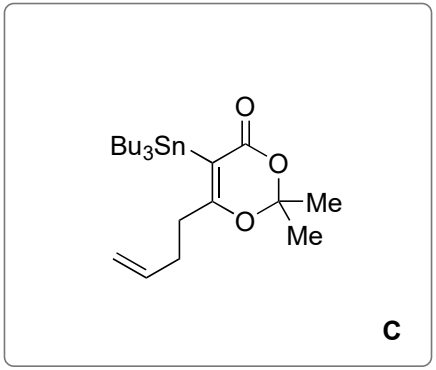




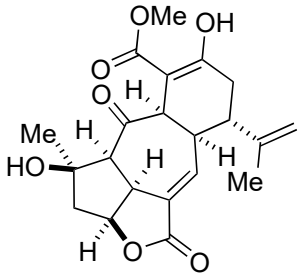
15-16

15) KHMDS, 0 °C
then allyliodide, -78 °C
16) *n*BuLi, Bu_3SnCl



B + C

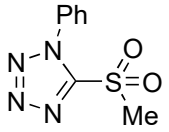
17-23



Rameswaralide

17) CuTC, $AsPh_3$, $Pd_2(dba)_3$
18) Et_3N, TESOTf (2.0 equiv)
19) TBAF, AcOH
20) air, CuCl, $Pd(OAc)_2$
21) pyrrolidine, pyrrolidine•HCl, 23 °C
22) **3**, LiHMDS
23) MeOH, mesitylene, 120 °C

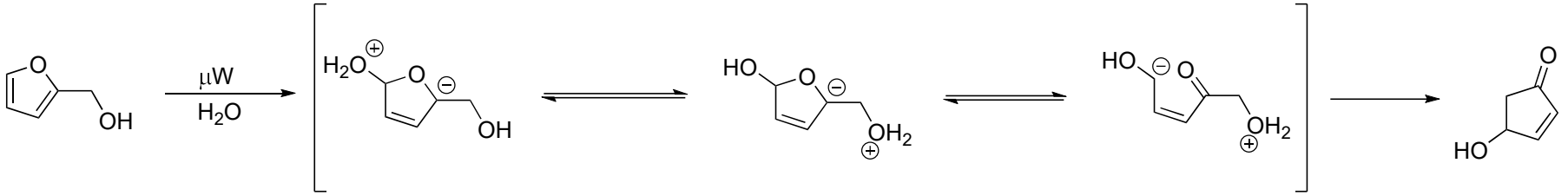
3



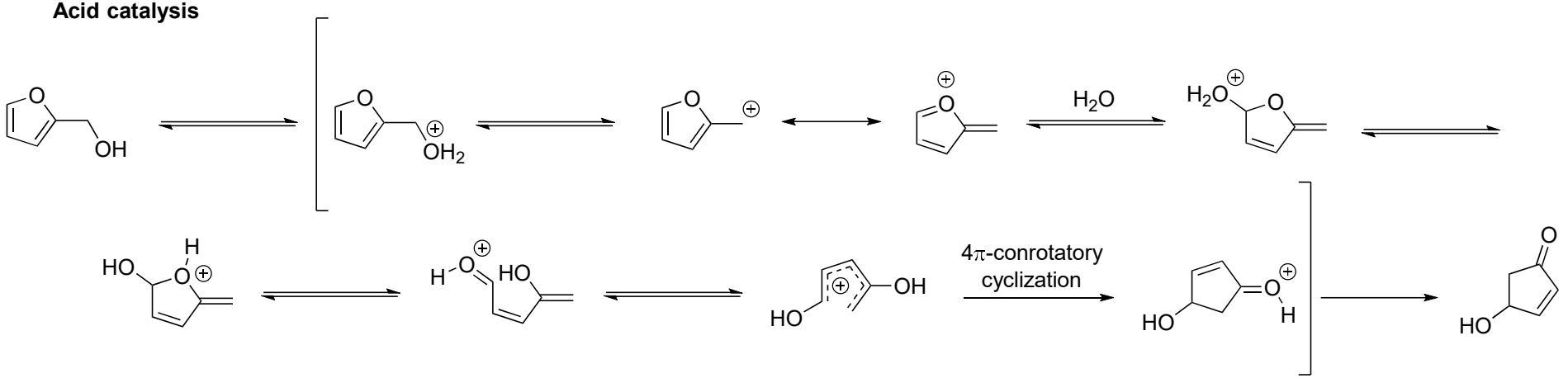
20) Name of the reaction?
Wacker oxidation

22) Name of the reaction? Alternatives for this transformation?
Julia-Kocienski olefination
Wittig, Peterson, Takai-Lombardo, Tebbe, Nysted, etc....

Step 1 - Water and high temperature



Acid catalysis



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