Total Synthesis of (−)-Sinulariadiolide. A Transannular Approach


1) Name of the starting material?
2) Propose a mechanism.
3) Explain the stereoselectivity based on the Felkin-Anh model.

1) Me₂SO₄, DIPEA, then O₃, then PPh₃
2) 1, CuCl₂, TEMPO, air
3) 2
4) TBSCl, imH
5) B₂(pin)₂, t-BuONa, CuCl, 3
6) NaBO₃·6H₂O

7) H₂O₂, NaOH
8) TsNHNH₂, HOAc
9) NaClO₂, NaH₂PO₄, amylene, H₂O

Name of the starting material?
Name of the reaction?
Name of the reaction?

(-)-Sinulariadiolide
10) DCC, DMAP, NEt$_3$, 4
11) A, 60 °C
12) Ac$_2$O, DMAP, NEt$_3$
13) aq. HF
14) 5, 6
15) Zn, HOAc

10 - 15

11) Propose a mechanism.
14) Hint: Step 12 caps a functionality, which would disturb the reaction in step 14. Step 13 reduces the sterical hindrance to enable the transformation in step 14.

16) Bu$_3$SnH, [Cp*RuCl]$_4$
17) CO, Pd(OAc)$_2$, AsPh$_3$, 1,4-benzoquinone, CF$_3$COOH, MeOH
18) triphosgene, py
19) Cs$_2$CO$_3$, MeOH
20) BBr$_3$

16) Hint: *trans*-addition; The regioselectivity is controlled through coordination of the propargylic alcohol to the Ru-catalyst.
17) Hint: 1,4-benzoquinone serves as a stoichiometric oxidant. Trifluoroacetic acid is a cocatalyst. The acid lowers the LUMO of the quinone and likely promotes assembly of the substrates. (see also: H. Sommer, A. Fürstner, *Org. Lett.* 2016, 18, 3210–3213.)
18) Structure of triphosgene?
19) Hint: Several bond breaking/formation events take place with the final one being an oxa-Michael addition.