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

1) Name of the starting material? Geranic acid
2) Propose a mechanism. see below
3) Explain the stereoselectivity based on the Felkin–Anh model. see below
4) Name of the reaction? Eschenmooser–Tanabe fragmentation
5) Name of the reaction? Pinnick–Lindgren–Kraus oxidation
6) Name of the starting material? (R)-carvone
7) Name of the reaction? Eschenmooser–Tanabe fragmentation
8) Name of the reaction? Pinnick–Lindgren–Kraus oxidation
10) DCC, DMAP, NEt₃, 4
11) A, 60 °C
12) Ac₂O, DMAP, NEt₃
13) aq. HF
14) 5, 6
15) Zn, HOAc

10 - 15

11) Propose a mechanism. see below
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) Bu₃SnH, [Cp*RuCl]₄
17) CO, Pd(OAc)₂, AsPh₃, 1,4-benzoquinone, CF₃COOH, MeOH
18) triphosgene, py
19) Cs₂CO₃, MeOH
20) BBr₃

16 - 20

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.

\[ \text{RCO} + \text{R}^2\text{N} \rightarrow \text{RNCOR}^2 \]

3) \[ \text{R}^1\text{O} \rightarrow \text{R}^2\text{Nu} \]

11) \[ \text{PhCO} \rightarrow \text{R}^1\text{CO} \]