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.

1) Me\textsubscript{2}SO\textsubscript{4}, DIPEA, \textit{then} O\textsubscript{3}, \textit{then} PPh\textsubscript{3}
2) 1, CuCl\textsubscript{2}, TEMPO, air
3) 2
4) TBSCI, imH
5) B\textsubscript{2}(pin)\textsubscript{2}, t-BuONa, CuCl, 3
6) NaBO\textsubscript{3}•6H\textsubscript{2}O
7) H\textsubscript{2}O\textsubscript{2}, NaOH
8) TsNHNH\textsubscript{2}, HOAc
9) NaClO\textsubscript{2}, NaH\textsubscript{2}PO\textsubscript{4}, amylene, H\textsubscript{2}O

1) Name of the starting material? (R)-carvone
2) Name of the reaction? Eschenmoser-Tanabe fragmentation
3) Name of the reaction? Pinnick-Lindgren-Kraus oxidation

(-)-Sinulariadiolide
10) DCC, DMAP, NEt₃, 4
11) A, 60 °C
12) Ac₂O, DMAP, NEt₃
13) aq. HF
14) 5, 6
15) Zn, HOAc

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16) Bu₃SnH, [Cp*RuCl]₄
17) CO, Pd(OAc)₂, AsPh₃, 1,4-benzoquinone, CF₃COOH, MeOH
18) triphosgene, py
19) Cs₂CO₃, MeOH
20) BBr₃

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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) 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.

![Chemical structures and reactions](image)