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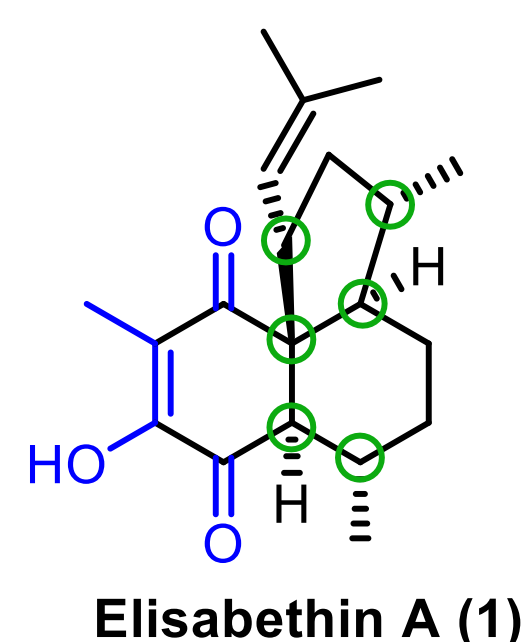
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Isolation:

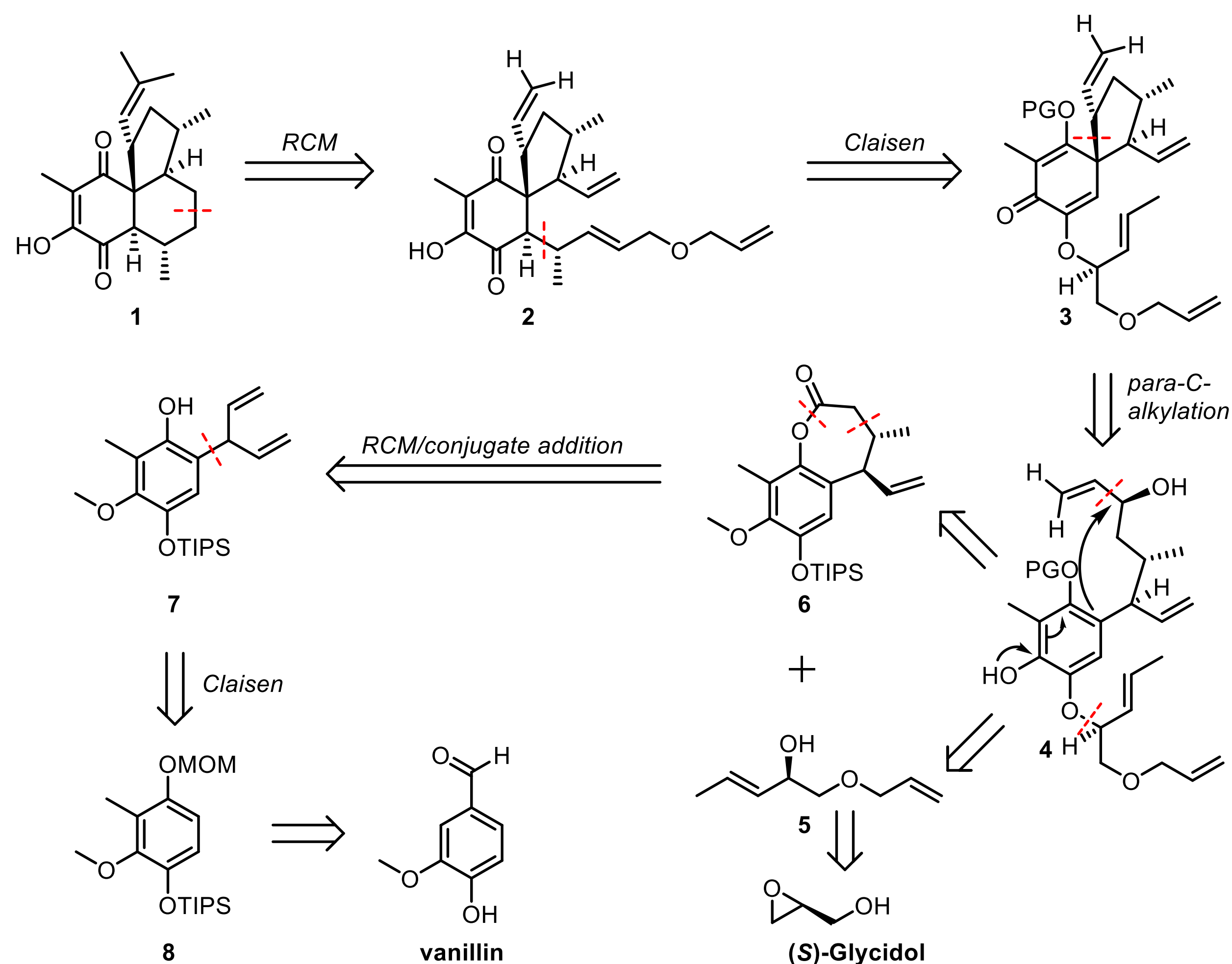
- 1988 Rodriguez *et al.*¹
- From Caribbean Sea whip *Pseudopterogorgia elisabethae*

Structure:

- Tricyclic *cis-trans*-fused 5,6,6-ring system
- Fully substituted ene dione functionality
- Six contiguous stereocenters



Retrosynthetic analysis

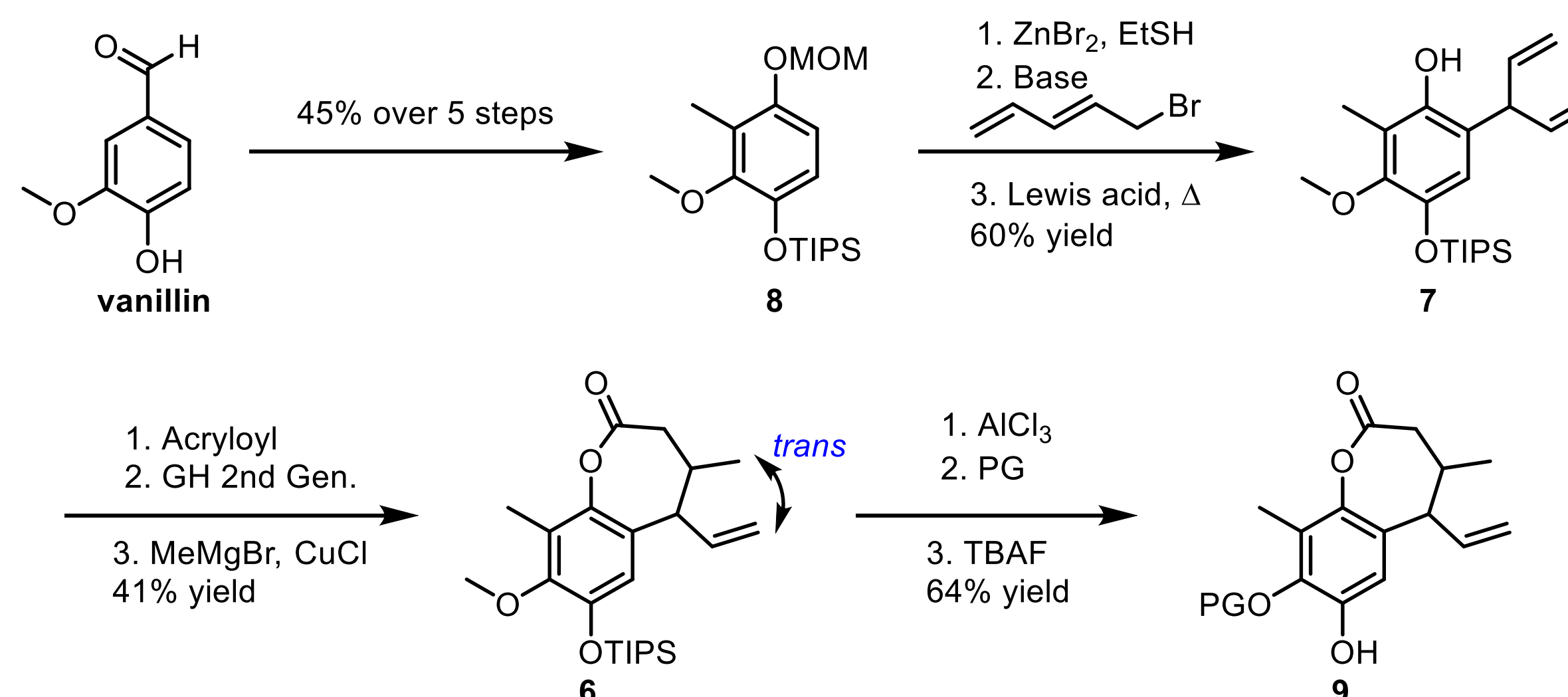


It was envisioned to construct target molecule **1** via late-stage ring closing metathesis (RCM) of ene dione **2**. Lewis acid catalyzed Claisen rearrangement would lead to ether **3**, which in turn, should be derived from *para*-C-alkylation of alcohol **4**. Further simplification leads to two building blocks: chiral allylic alcohol **5**, which could be derived from commercially available (*S*)-Glycidol and lactone **6**². This then could be prepared by an RCM/ conjugate addition sequence from prochiral phenol **7**. Exploitation of a Lewis acid mediated Claisen rearrangement developed in our laboratories should lead to orthogonally protected aromat **8**, which would arise from commercially available vanillin.

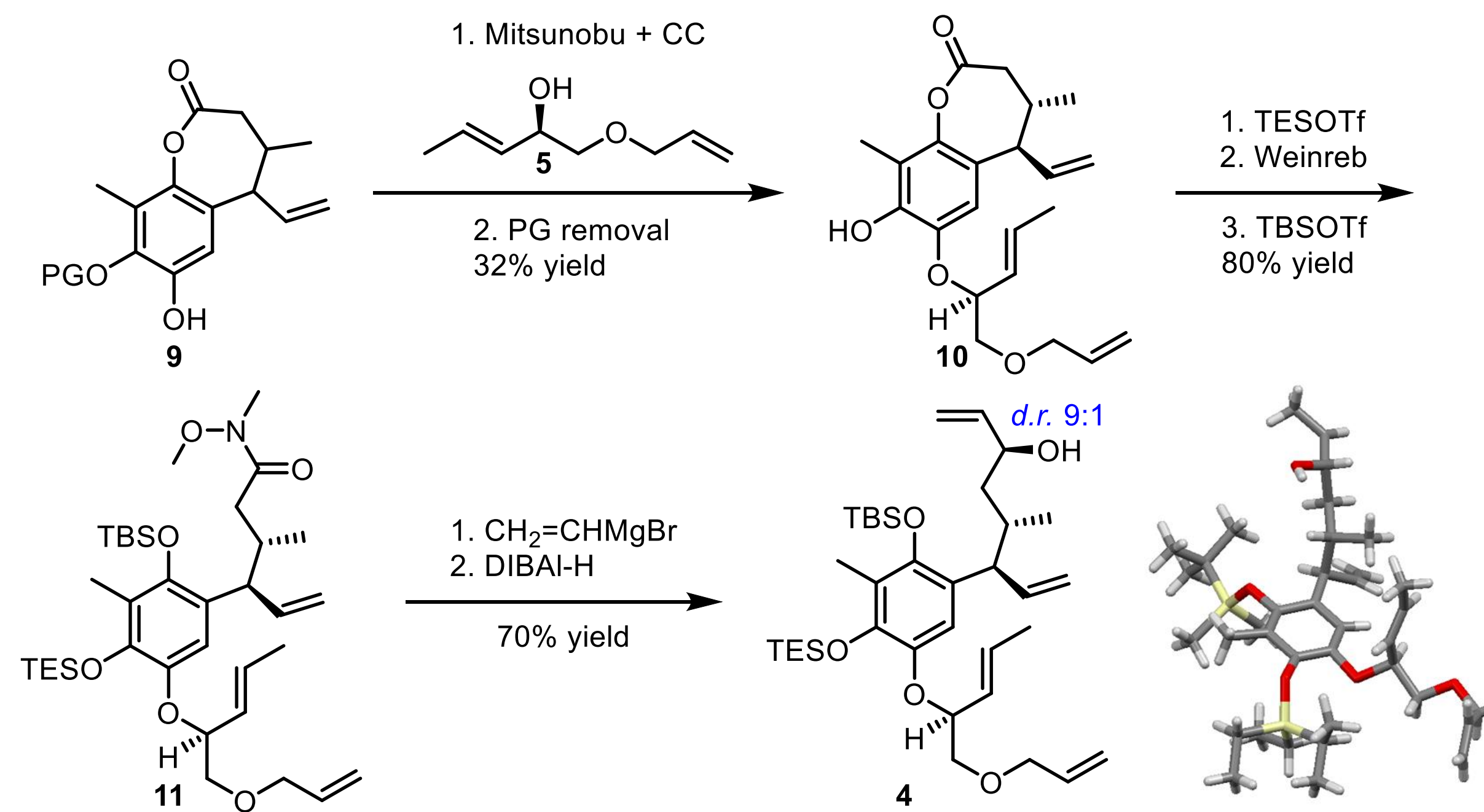
References:

- Rodríguez, A. D. *J. Am. Chem. Soc.* **1998**, *120*, 7083.
- Oliver D. Montagnat, *J. Org. Chem.* **2010**, *75*, 390–398

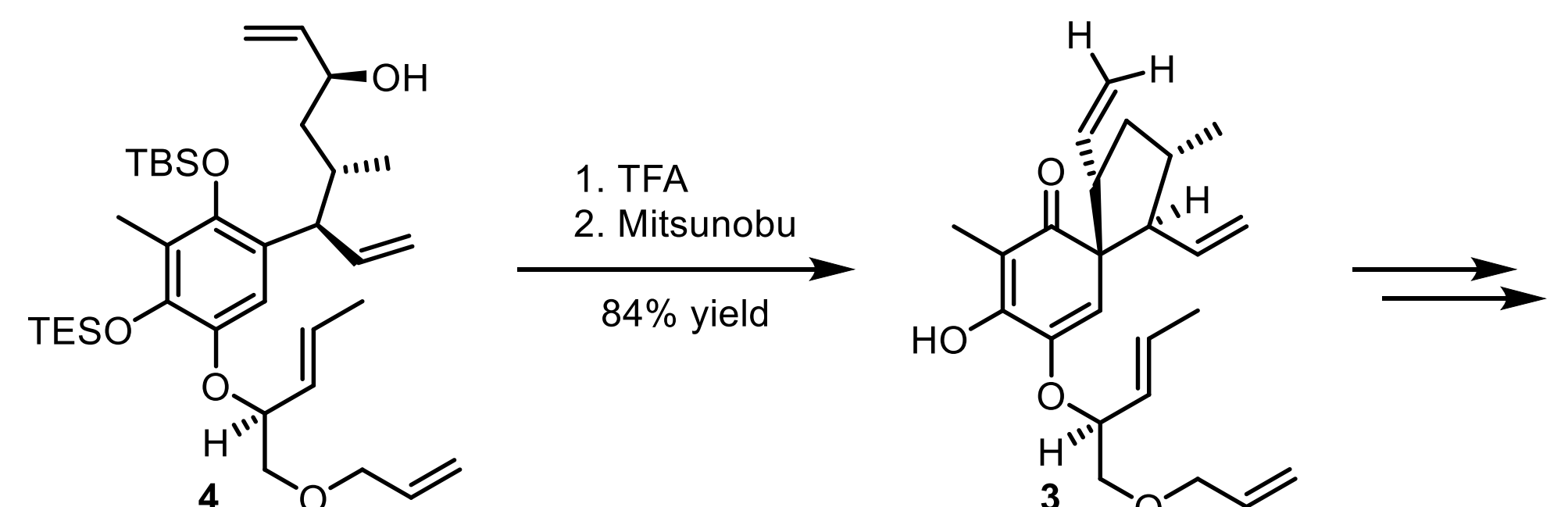
Forward synthesis



The synthesis commenced with a modified literature procedure, converting vanillin into MOM ether **8** in five steps in 45% yield. Removal of MOM protection, following etherification and subsequent Claisen rearrangement furnished phenol **7** in 60% yield. Acryl ester formation and following RCM/conjugate addition gave rise to lactone **6** in 41% yield. A three step sequence of protecting group adjustment allowed formation of phenol **9** in 64% yield over three steps.



Mitsunobu reaction of phenol **9** with chiral alcohol **5** and following removal of PG liberated phenol **10**. TES installation, Weinreb formation and final treatment with TBSOTf furnished Amide **11** in 80% yield. Vinyl Grignard addition and diastereoselective ketone reduction gave alcohol **4** in good yield and good selectivity.



Acidic TES deprotection and final cyclization under Mitsunobu conditions gave rise to spiro compound **3**, which is only a few steps away from **1**.