Organic LETTERS

Letter

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Stereoselective Total Synthesis of Bioactive Marine Natural Product Biselyngbyolide B

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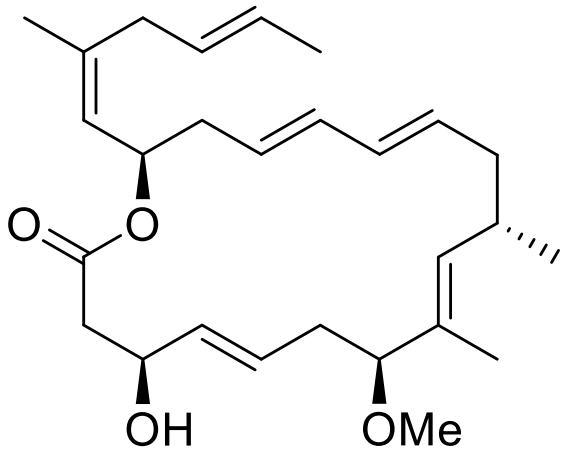
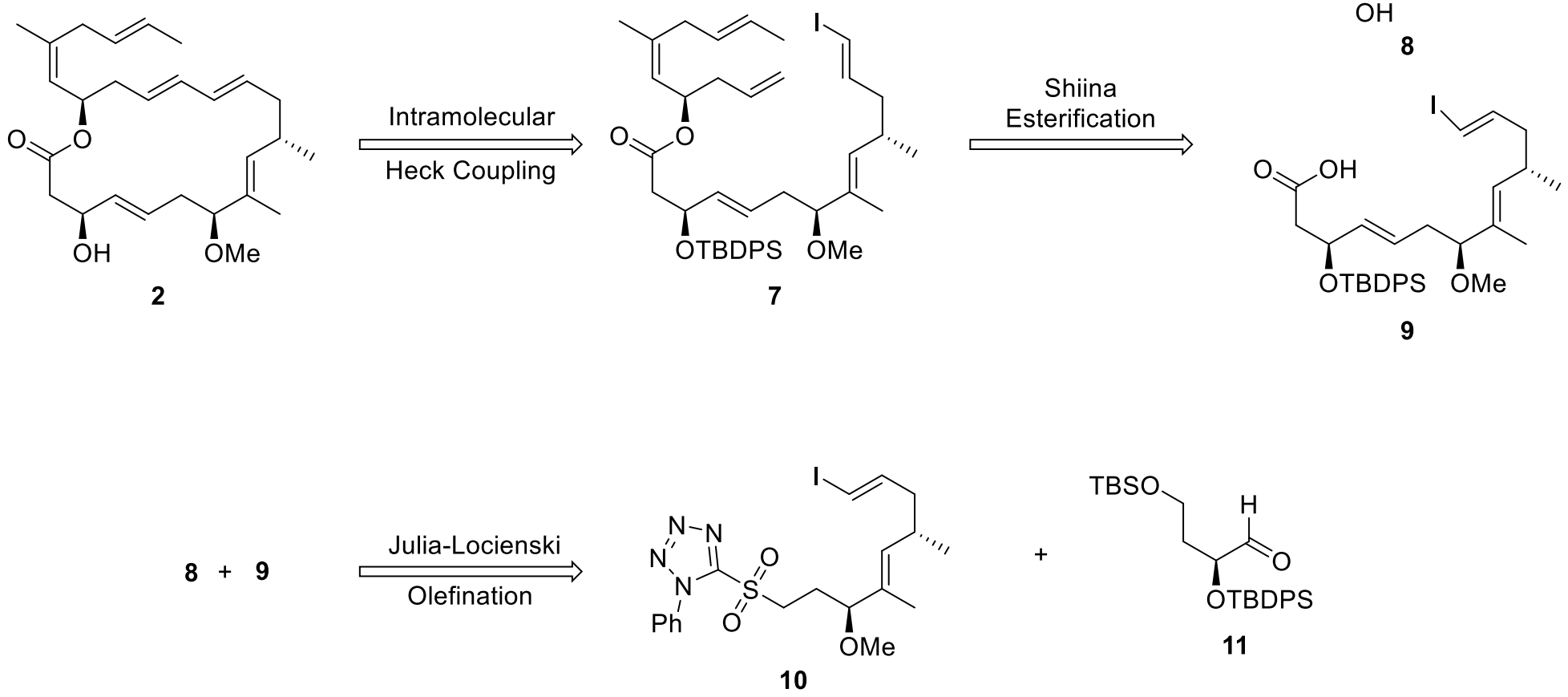
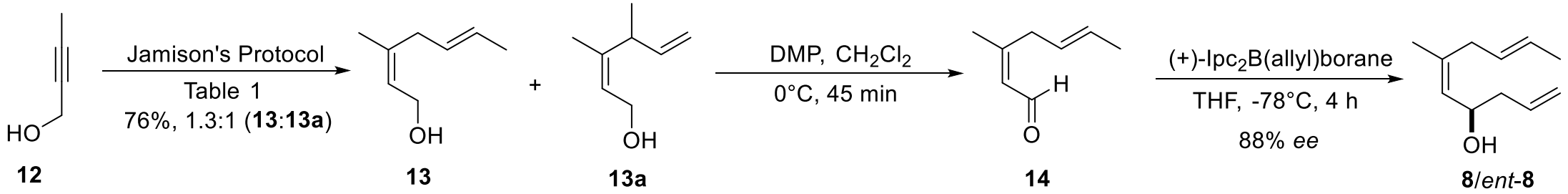


- 18-membered macrolide with four stereogenic centers;
- Exhibits inhibitory growth of human cervical cancer and leukemia cells;
- Cytotoxic against various human tumor cell lines in submicromolar concentrations;
- Biselyngbyolide B possesses 30- to 100- fold apoptosis-induction compared to congener, Biselyngbyaside

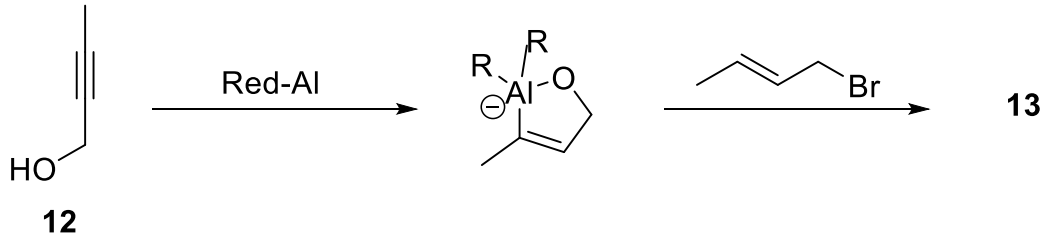
Retrosynthesis:



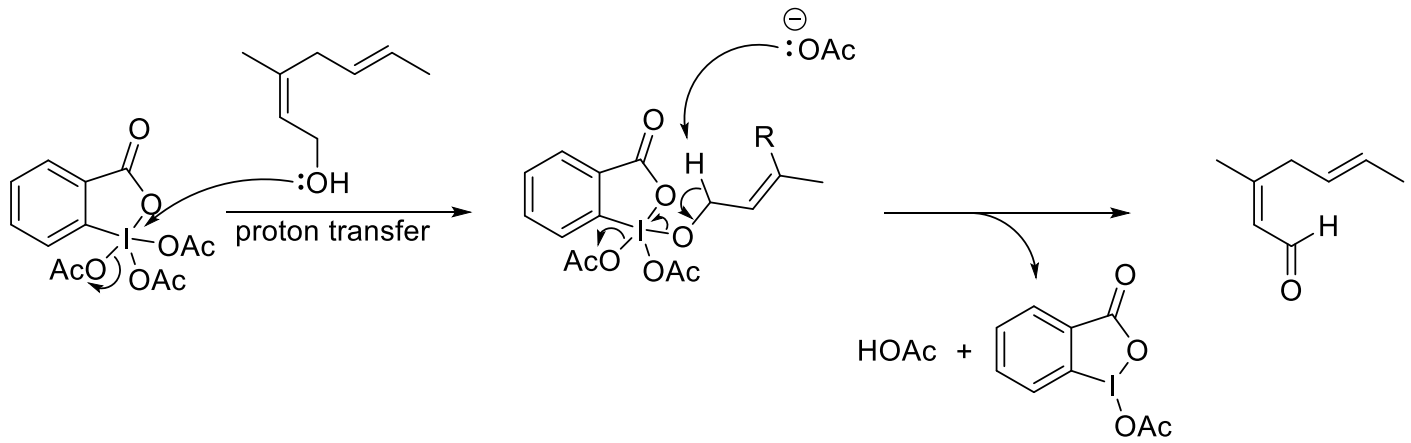
Synthesis of Intermediate 8:



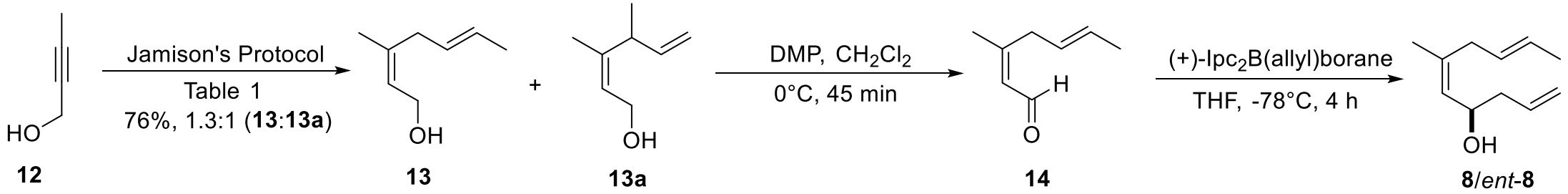
"Jamison's Protocol":



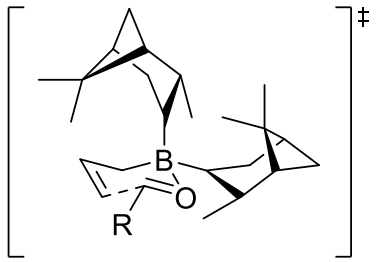
DMP Oxidation:



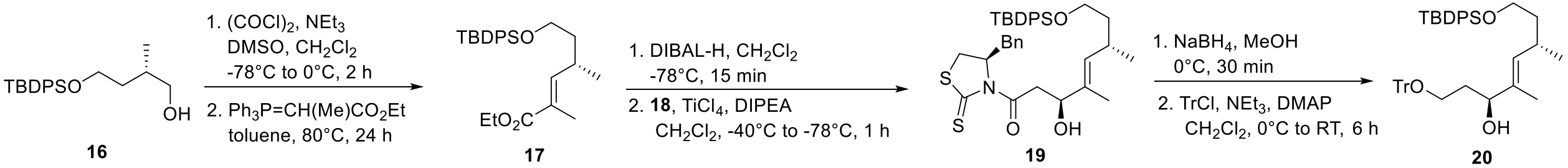
Synthesis of Intermediate 8:



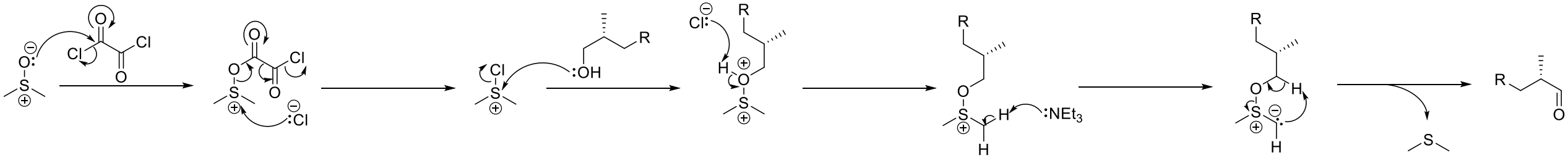
Brown Allylation:



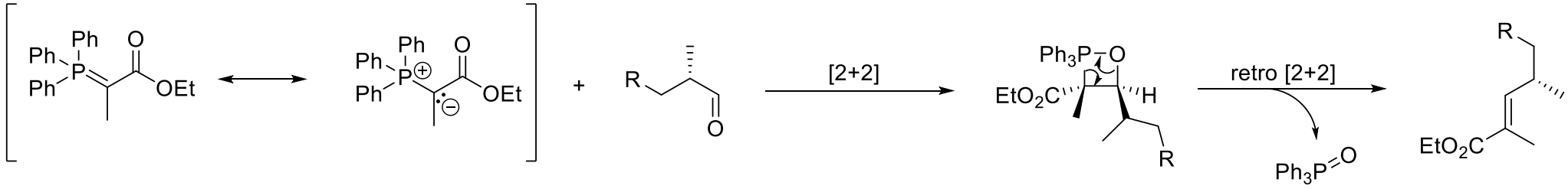
Synthesis of Sulfone 10 and Aldehyde 11:



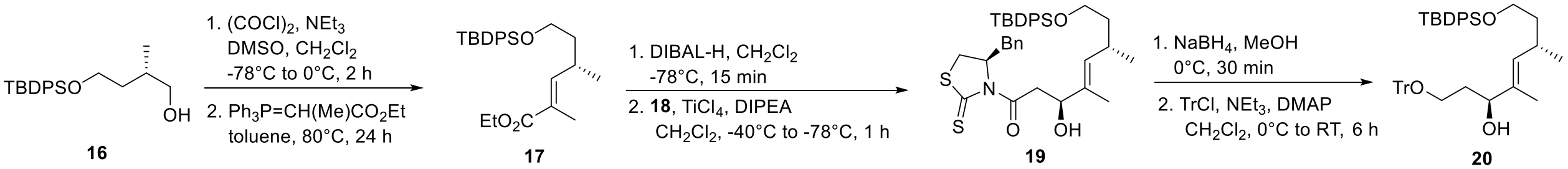
Swern Oxidation:



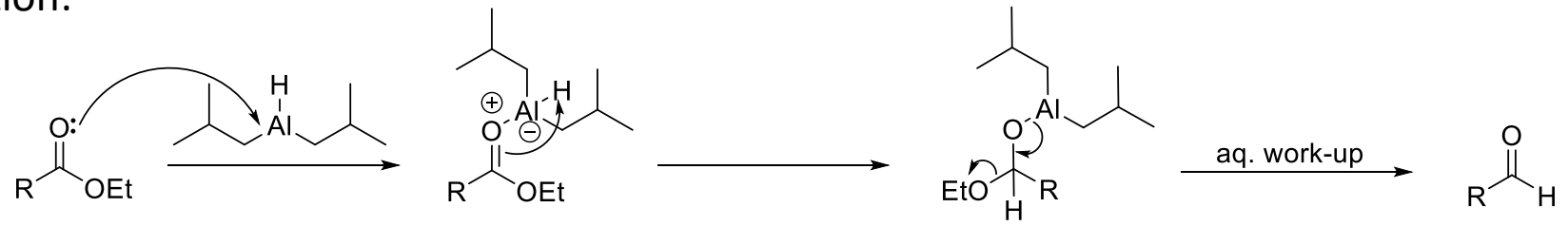
Witting Olefination:



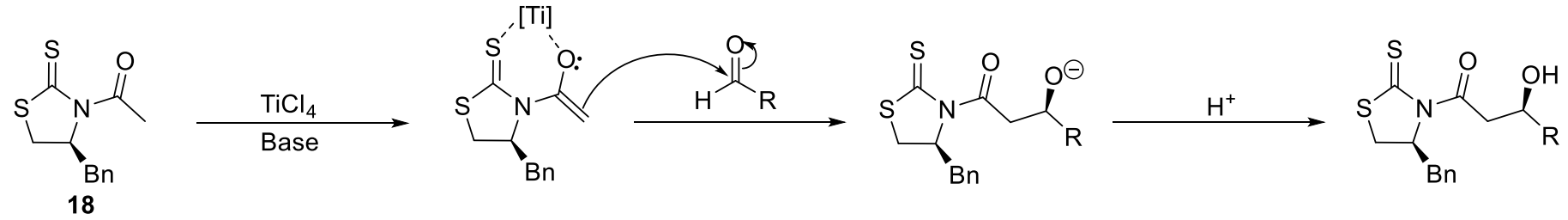
Synthesis of Sulfone 10 and Aldehyde 11:



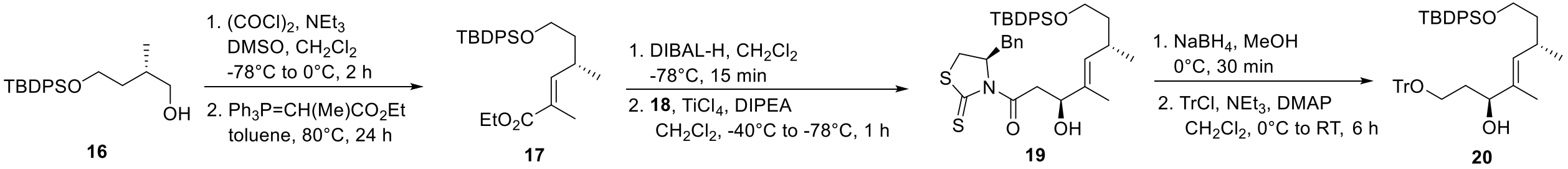
DIBAL-H Reduction:



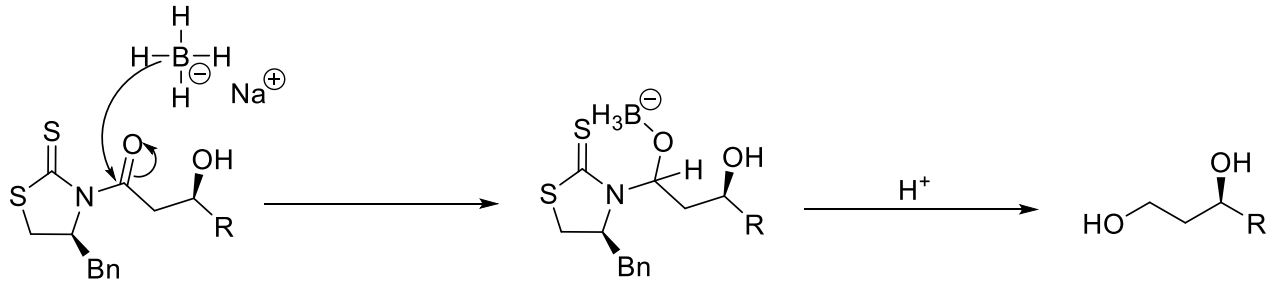
Crimmins Acetate Aldol:



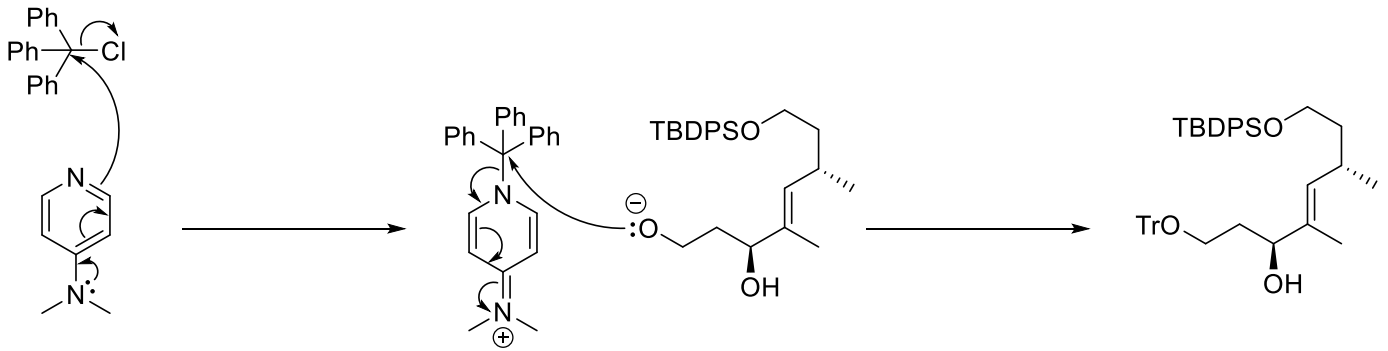
Synthesis of Sulfone 10 and Aldehyde 11:



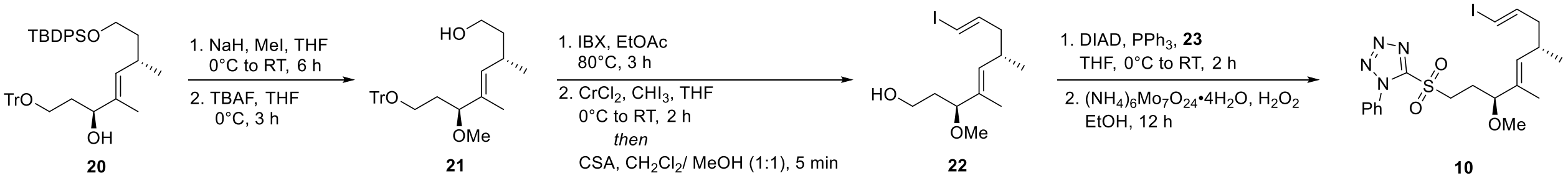
Sodium Borohydride Reduction:



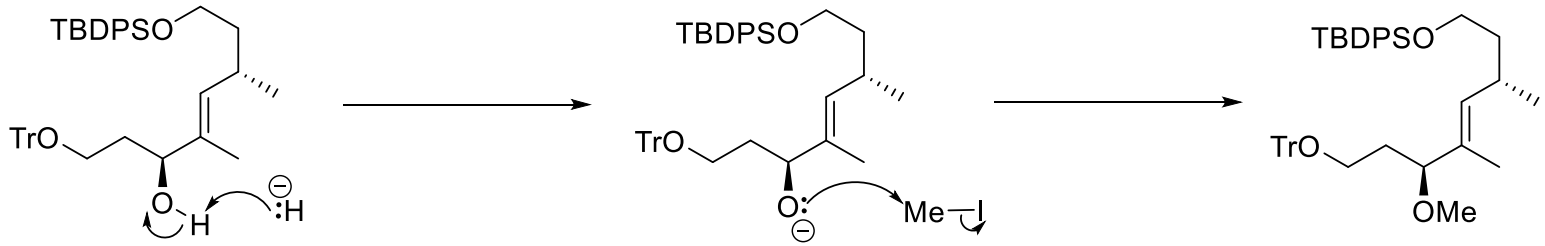
Hydroxyl Protection:



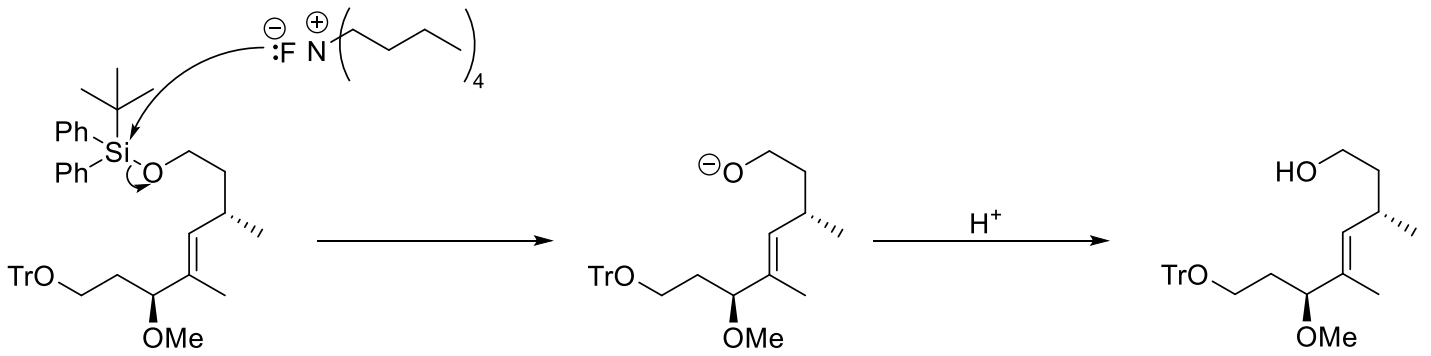
Synthesis of Sulfone 10 and Aldehyde 11:



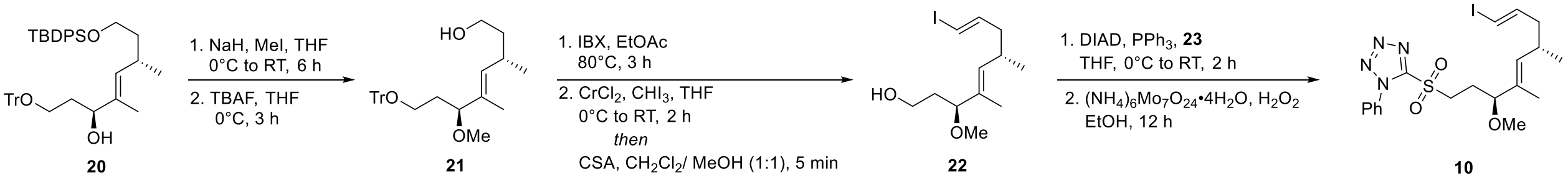
Methylation:



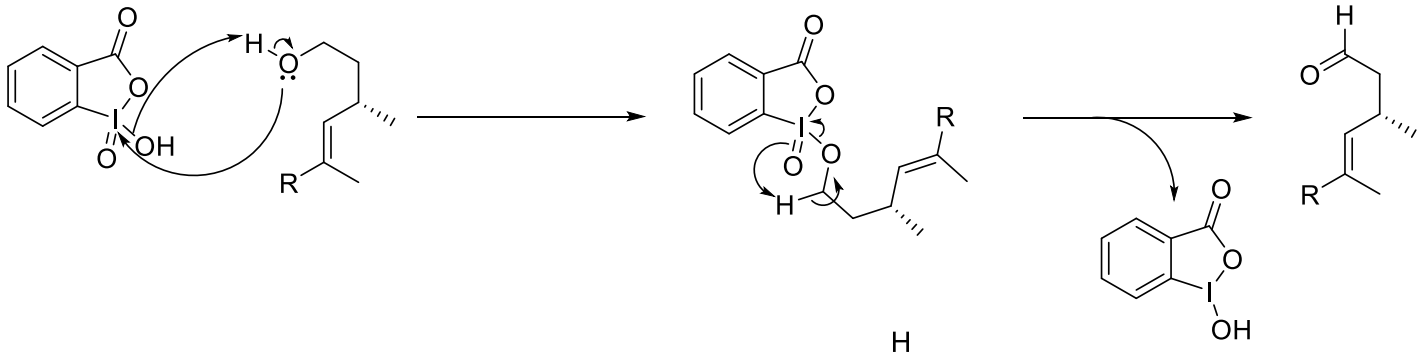
Desilylation:



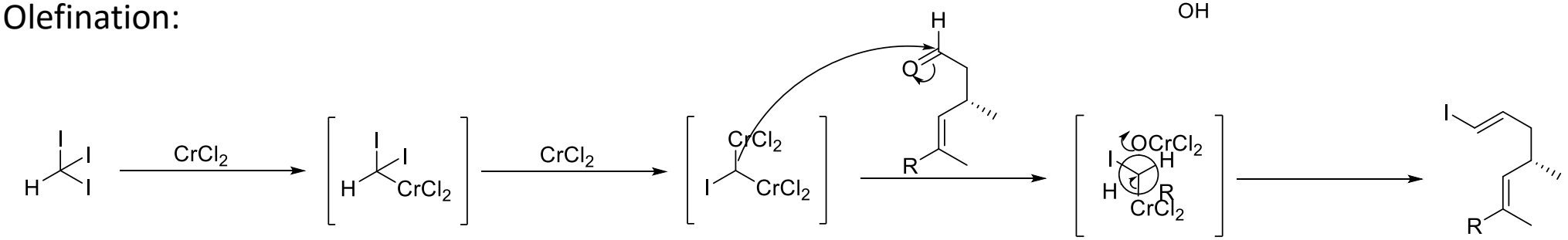
Synthesis of Sulfone 10 and Aldehyde 11:



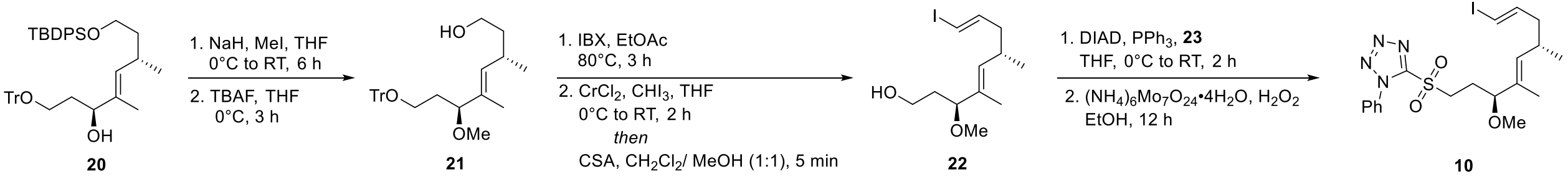
IBX Oxidation:



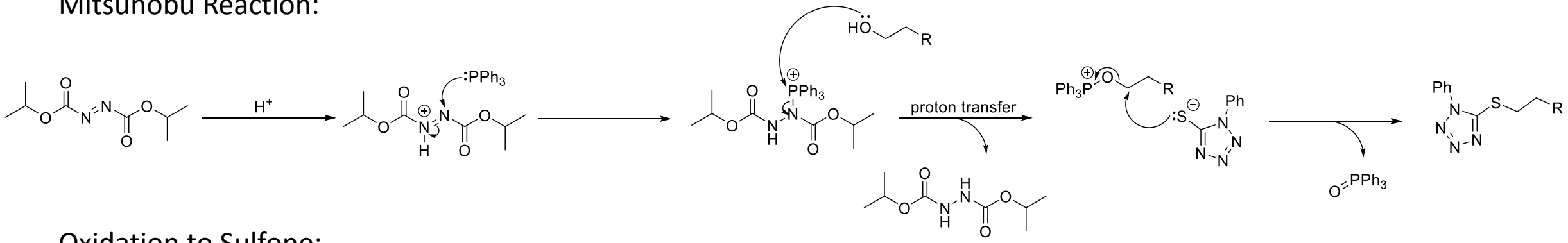
Takai Olefination:



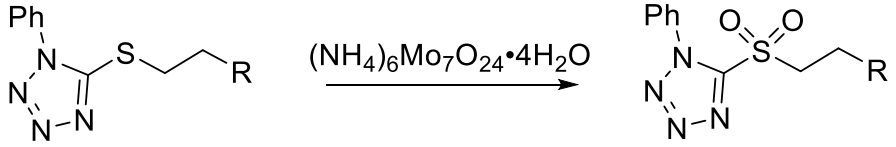
Synthesis of Sulfone 10 and Aldehyde 11:



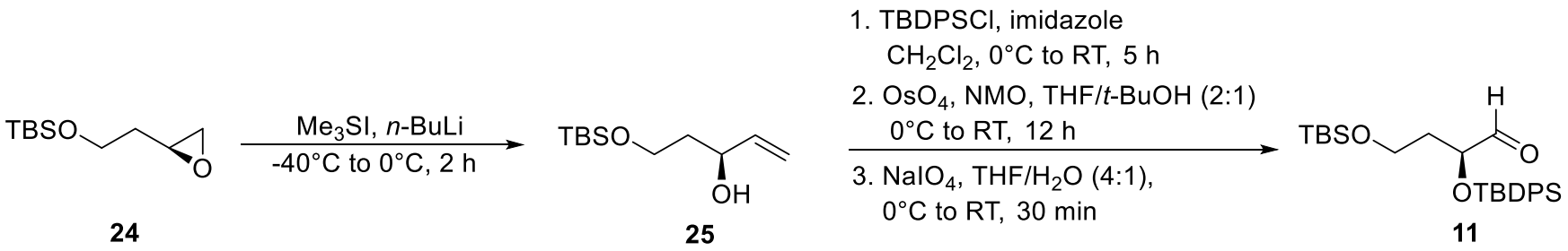
Mitsunobu Reaction:



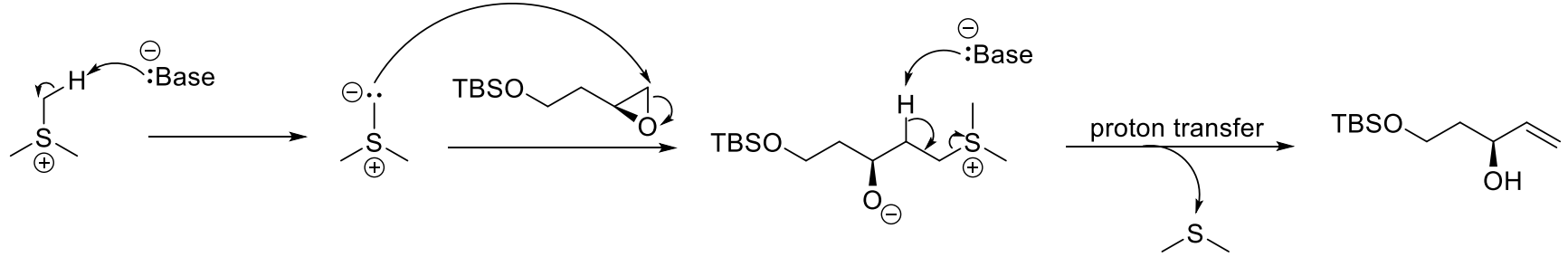
Oxidation to Sulfone:



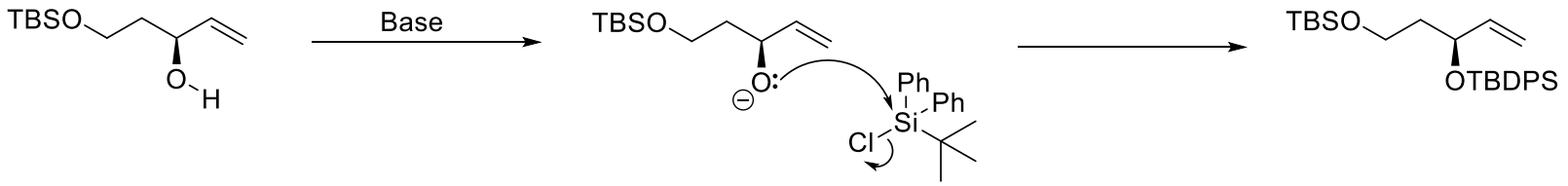
Synthesis of Sulfone 10 and Aldehyde 11:



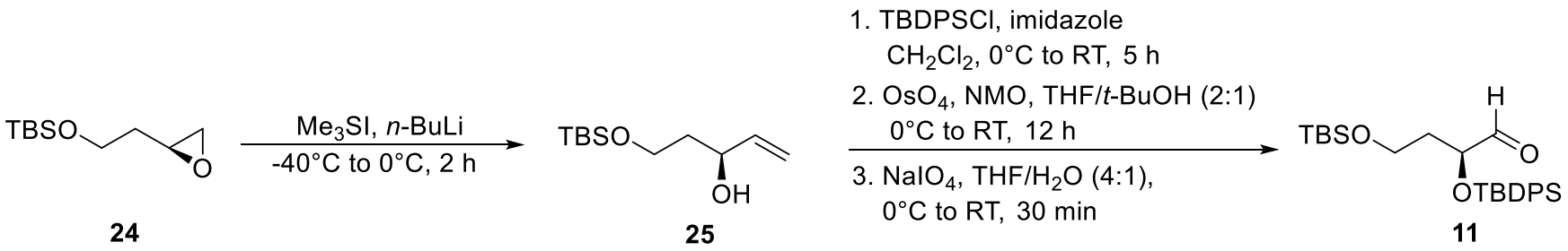
Epoxide Opening:



Silyl Protection:

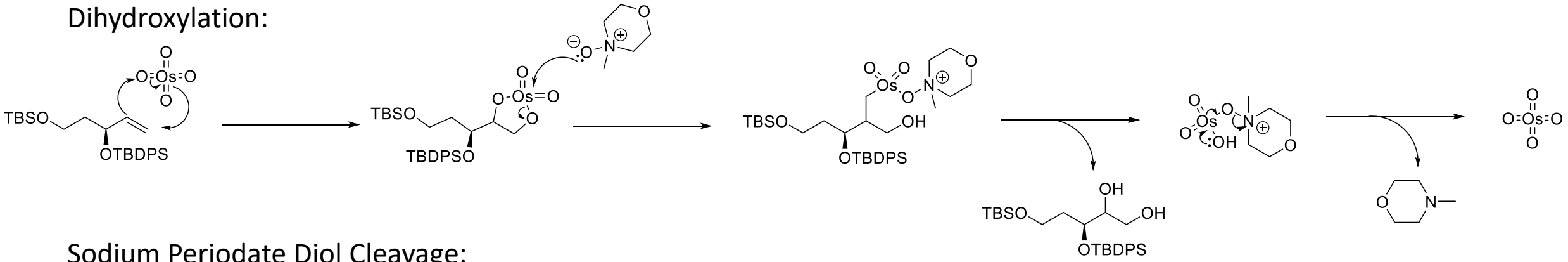


Synthesis of Sulfone 10 and Aldehyde 11:

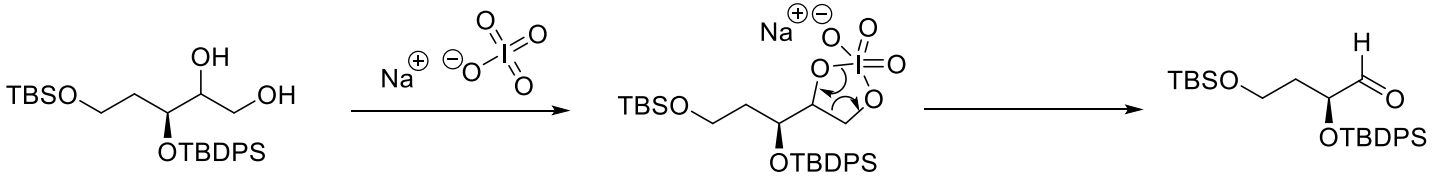


24 **25** **11**

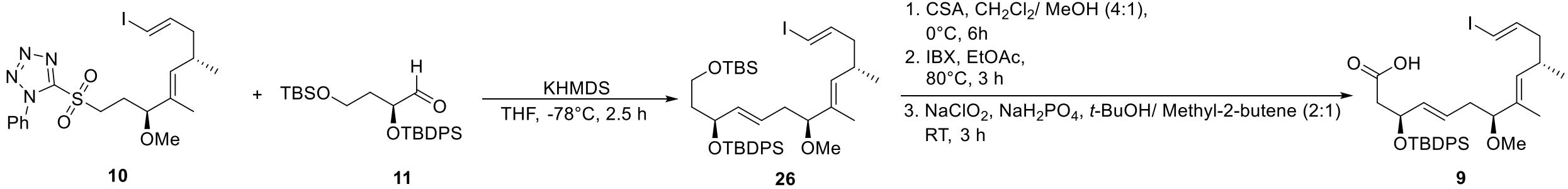
Dihydroxylation:



Sodium Periodate Diol Cleavage:

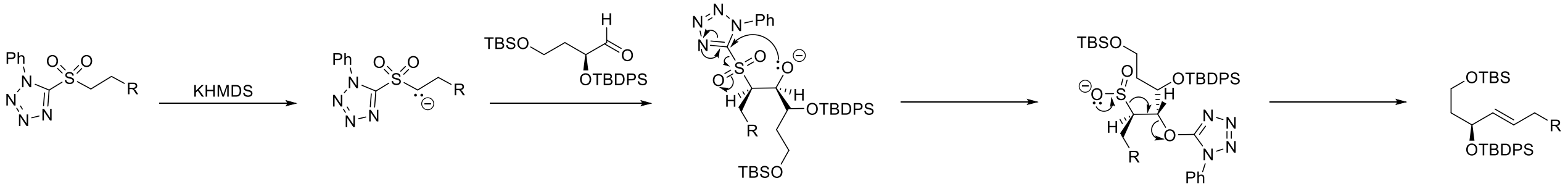


Synthesis of Acid Fragment 9:

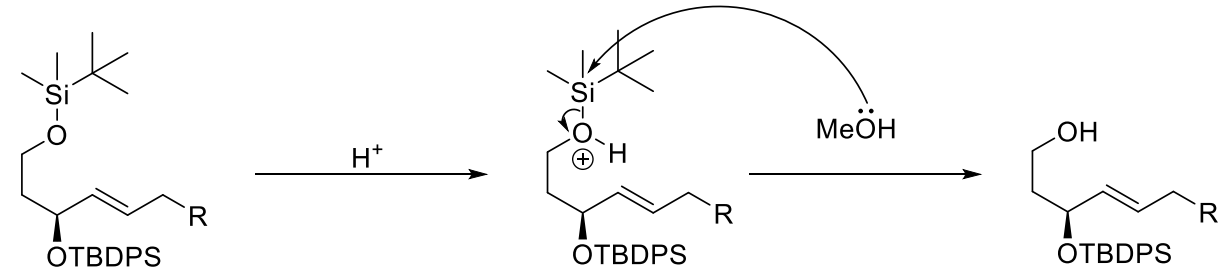


10 **11** **26** **9**

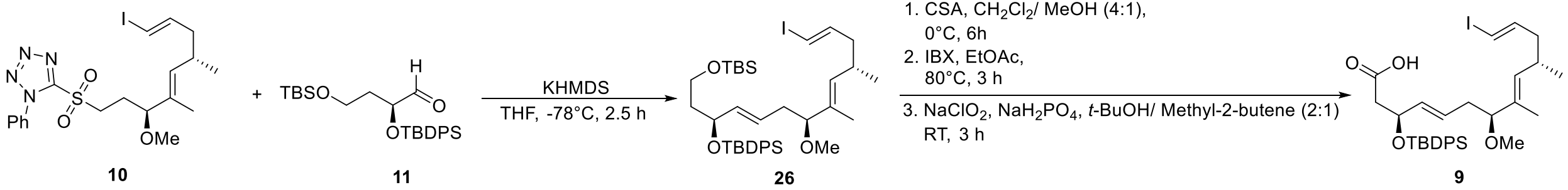
Julia-Kocienski Olefination:



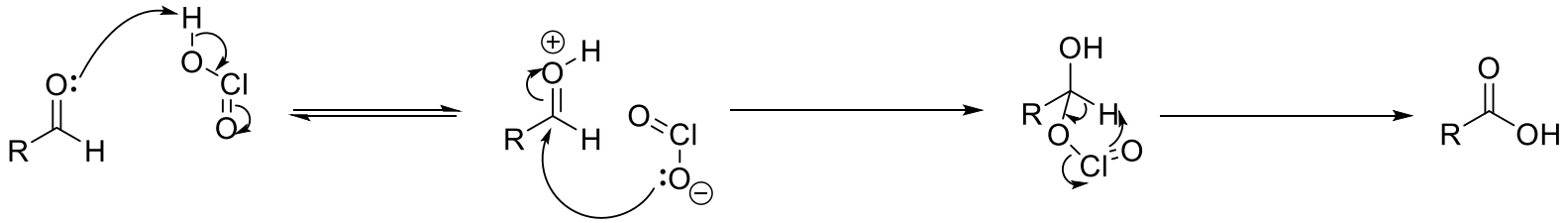
Desilylation with CSA:



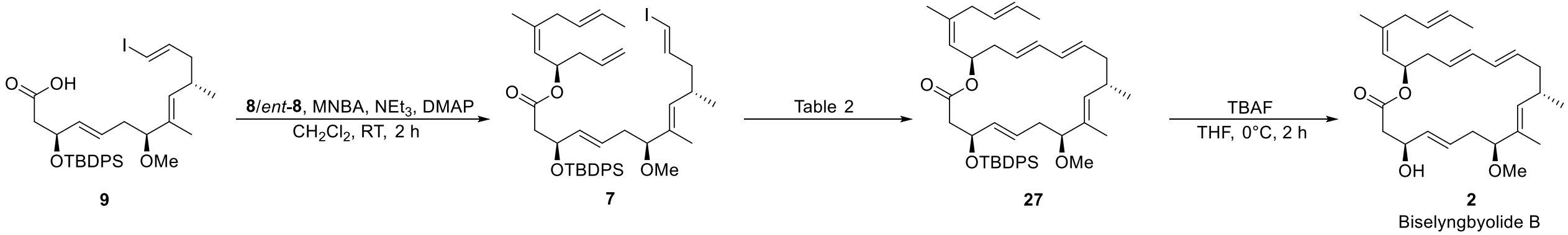
Synthesis of Acid Fragment 9:



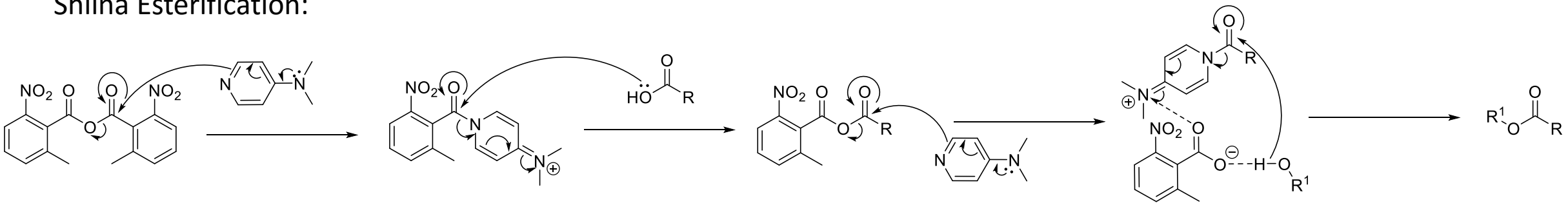
Pinnick Oxidation:



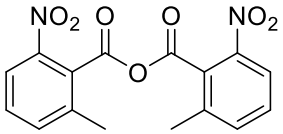
Completion of Biselyngbyolide B:



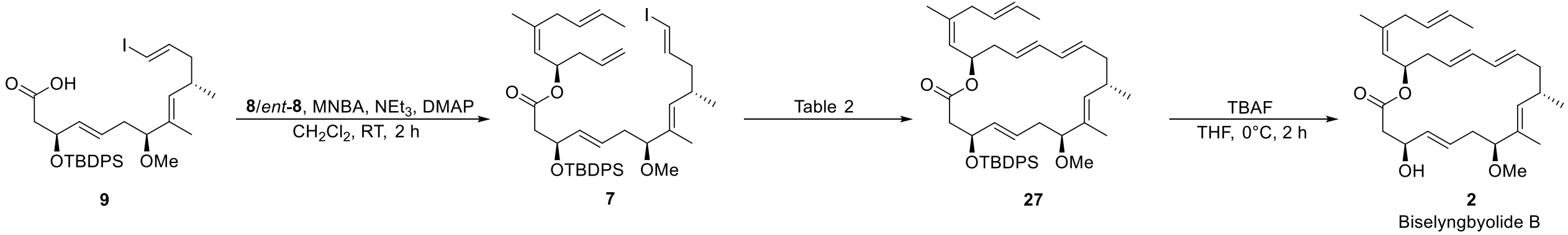
Shiina Esterification:



MNBA:



Completion of Biselyngbyolide B:



Heck Reaction:

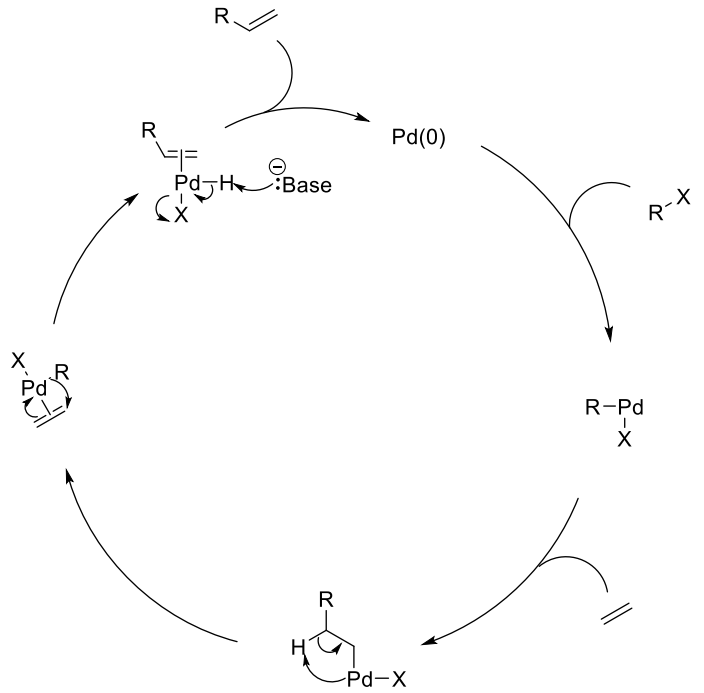


Table 2. Optimization of Intramolecular Heck Cross-Coupling

Entry	Reagents	Temperature (°C)	Time (h)	Yield (%)
1	$Pd(PPh_3)_4$, NEt_3, MeCN	60	3	decomposition
2	$PdCl_2(MeCN)_2$, NEt_3, CO_2H_2, MeCN	25	3	decomposition
3	$PdCl_2(PPh_3)_2$, K_2CO_3, Bu_4NCl, DMF	60	3	trace
4	$Pd(OAc)_2$, K_2CO_3, Bu_4NCl, DMF	60	1	58