

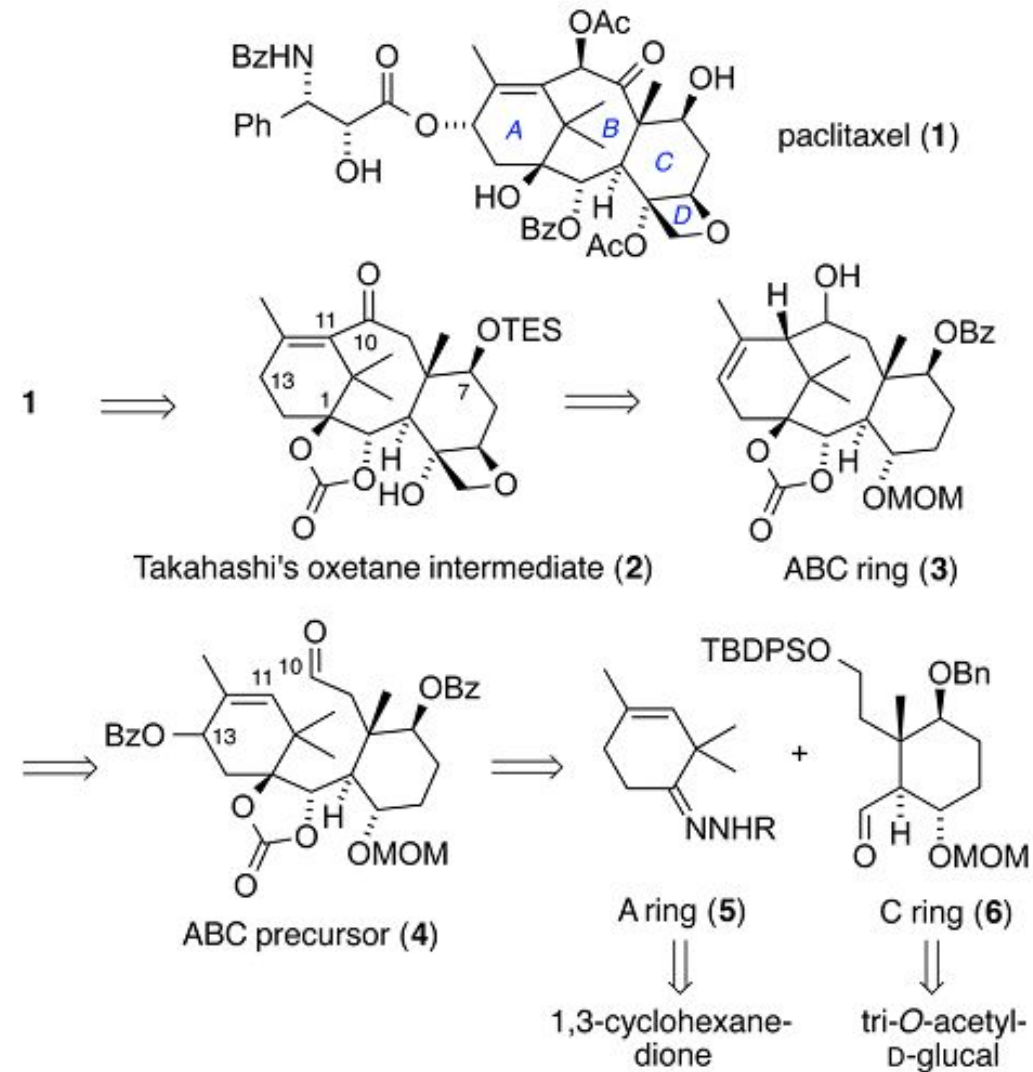
Synthesis of Paclitaxel.

1. Synthesis of the ABC Ring of Paclitaxel by SmI_2 -Mediated Cyclization
2. Construction of the ABCD Ring and Formal Synthesis

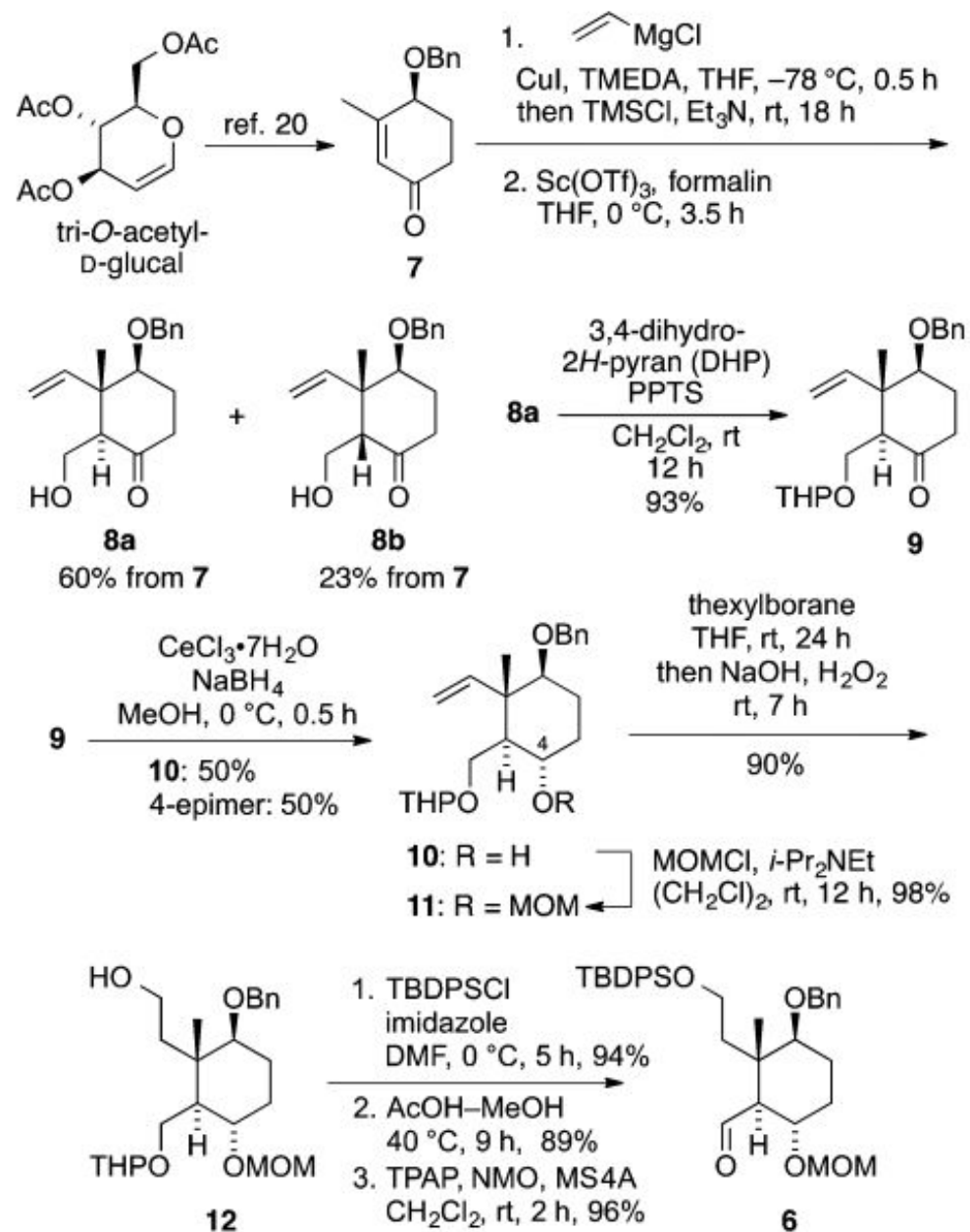
08.12.2015



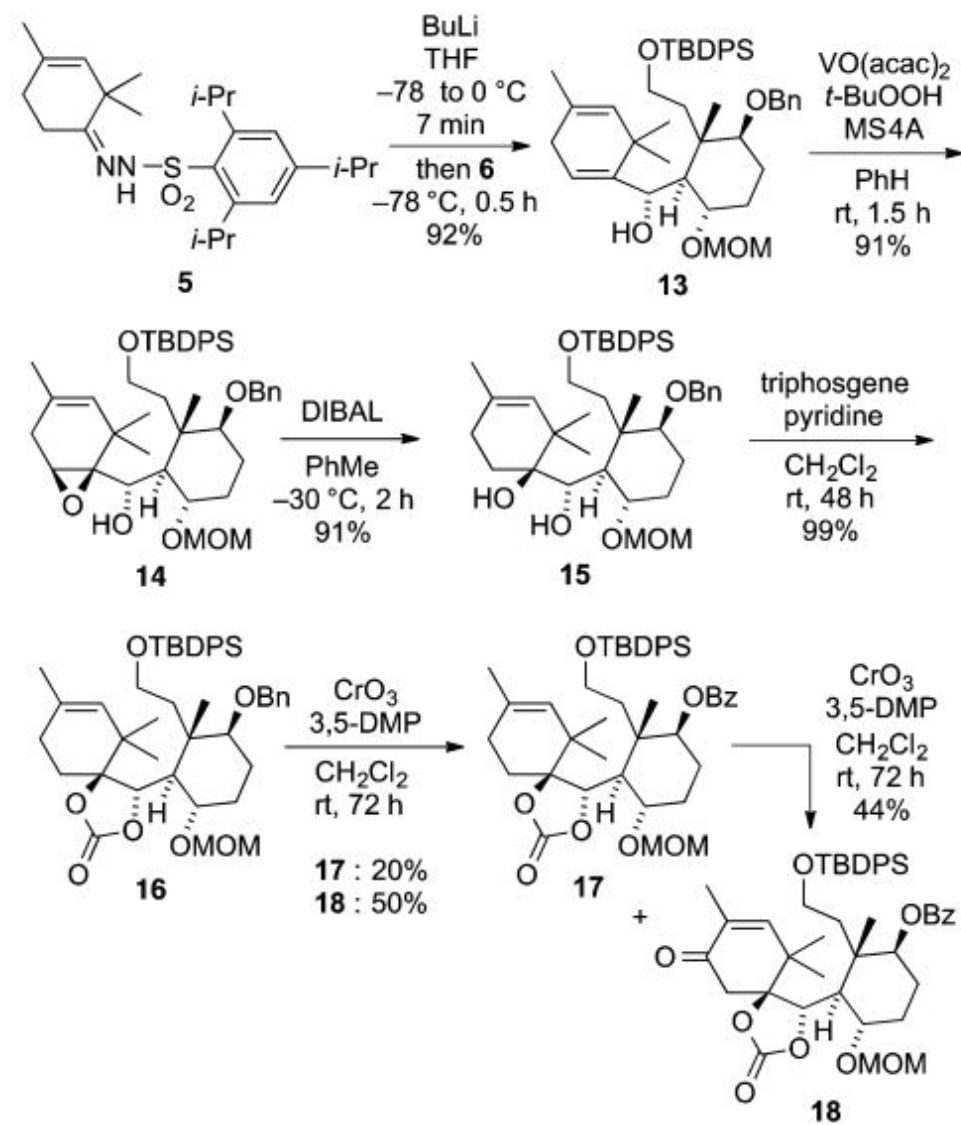
Retrosynthetic analysis of paclitaxel (1)



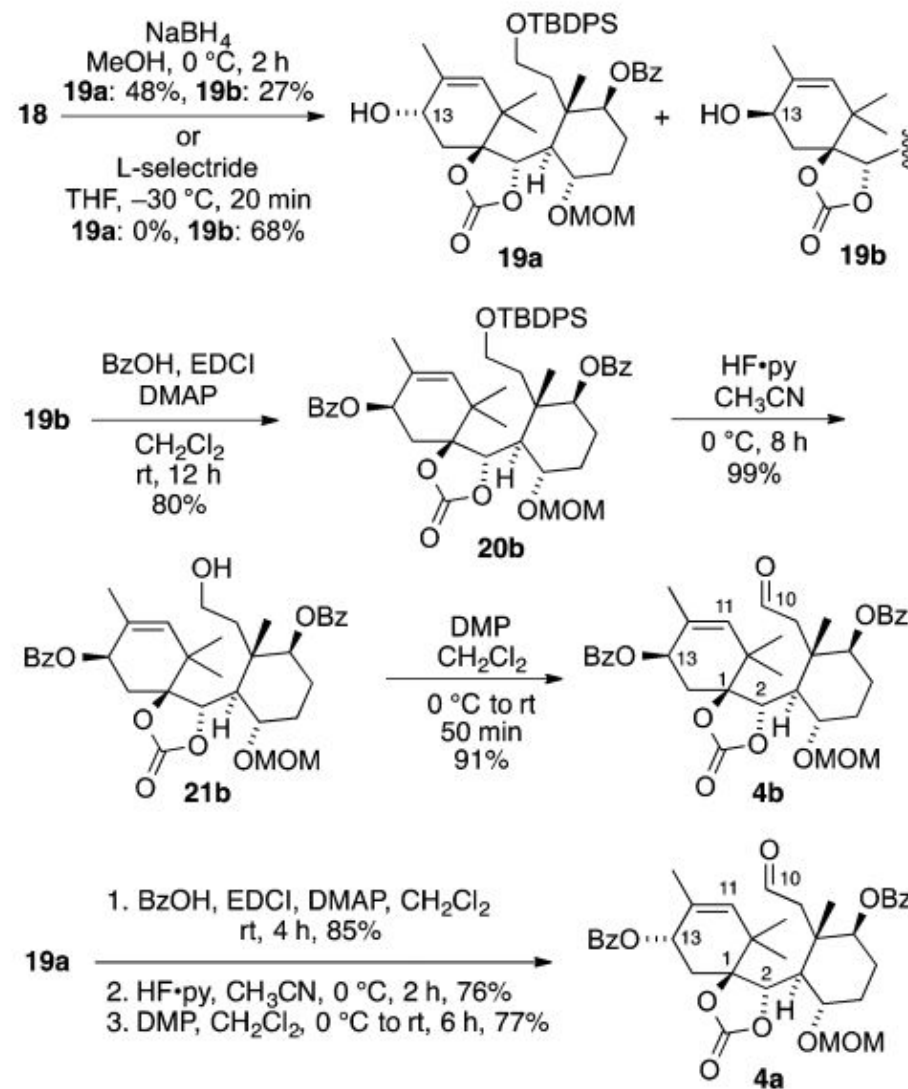
Synthesis of the C Ring of Paclitaxel



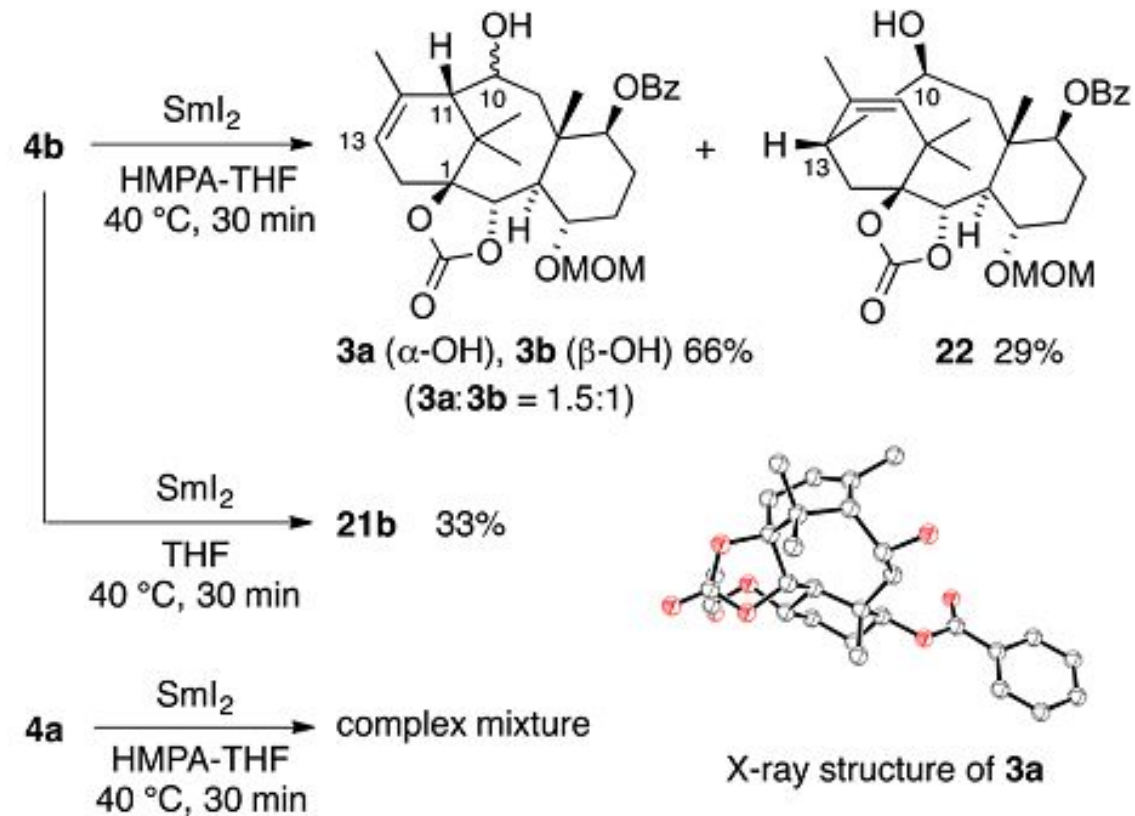
Preparation of the A–C Rings of Paclitaxel



Preparation of the ABC Precursor 4



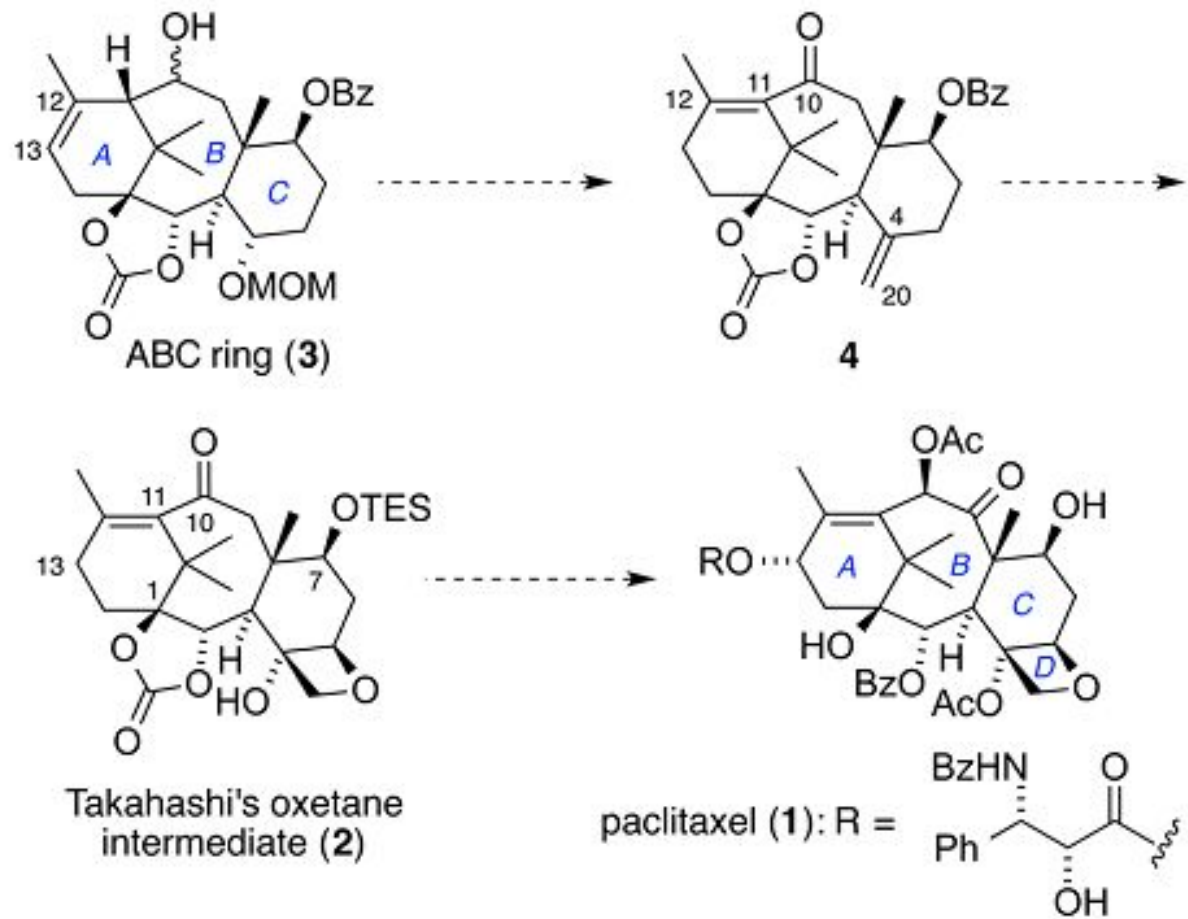
Construction of ABC Ring of Paclitaxel 3



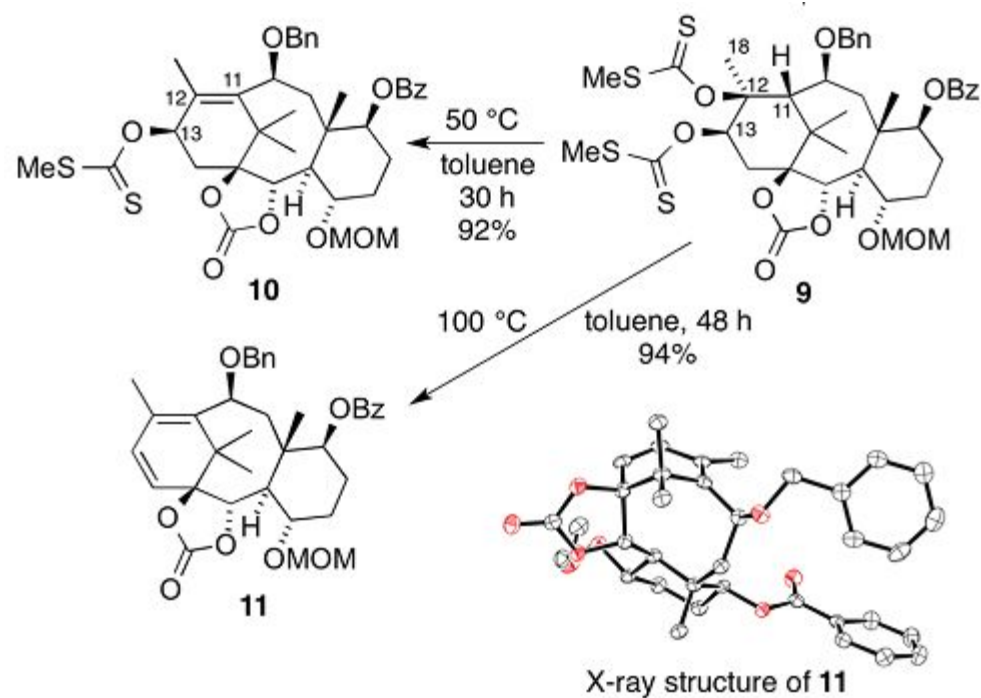
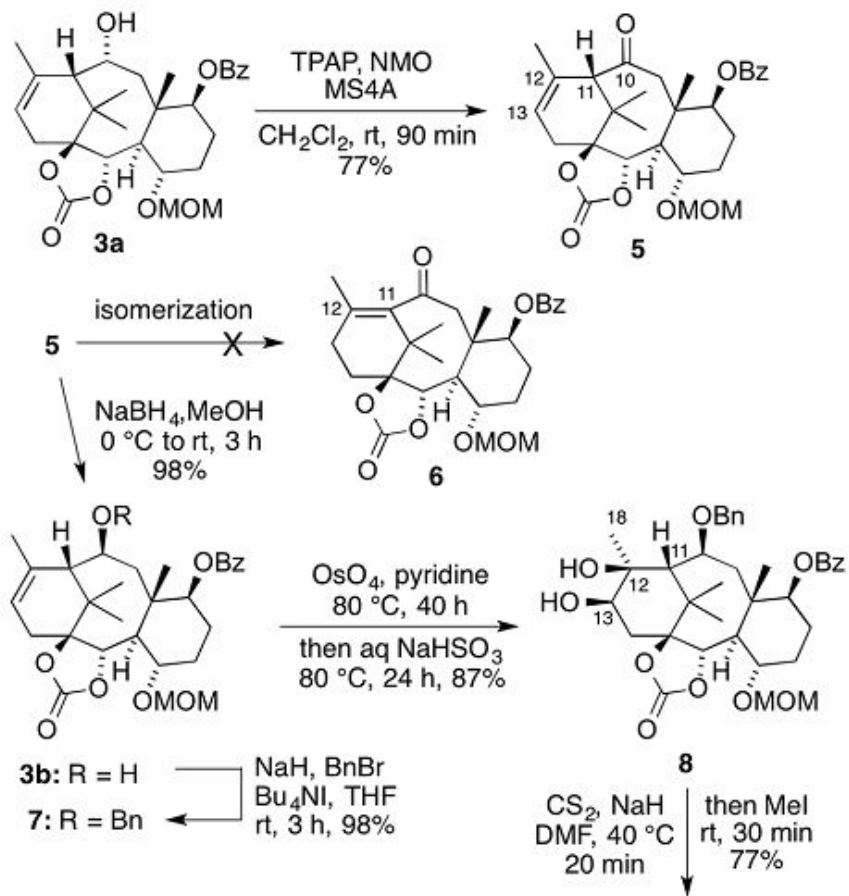
2. Construction of the ABCD Ring and Formal Synthesis



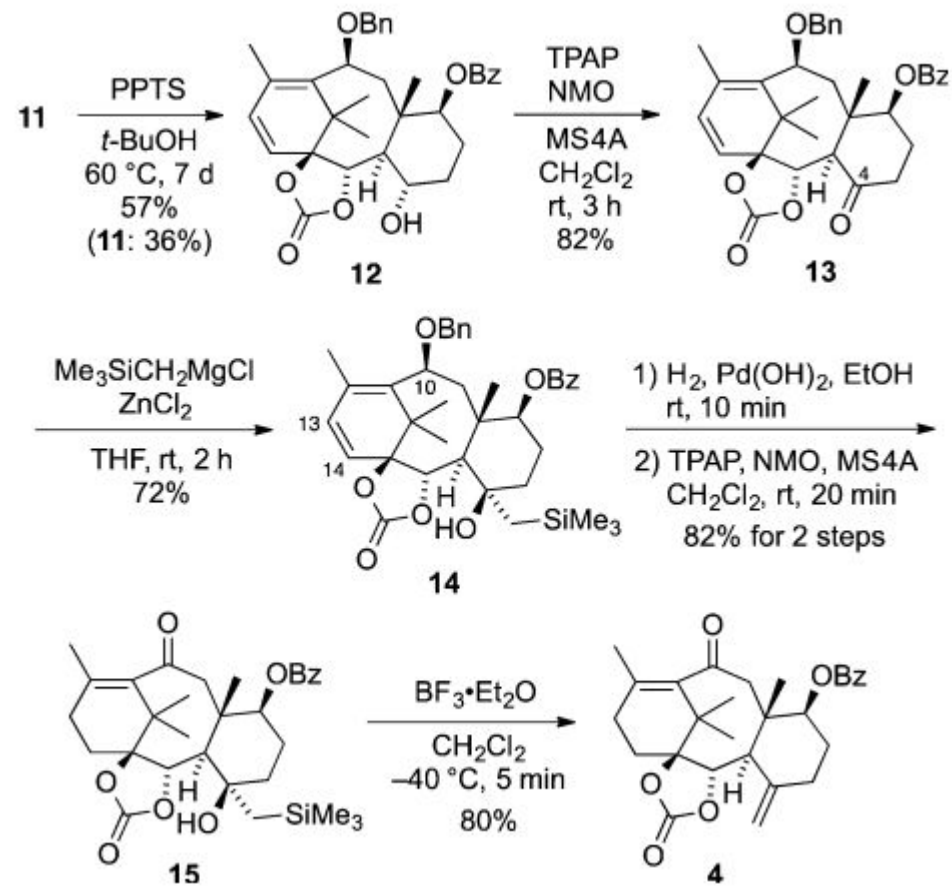
Synthetic plan for paclitaxel (1) from ABC ring (3)



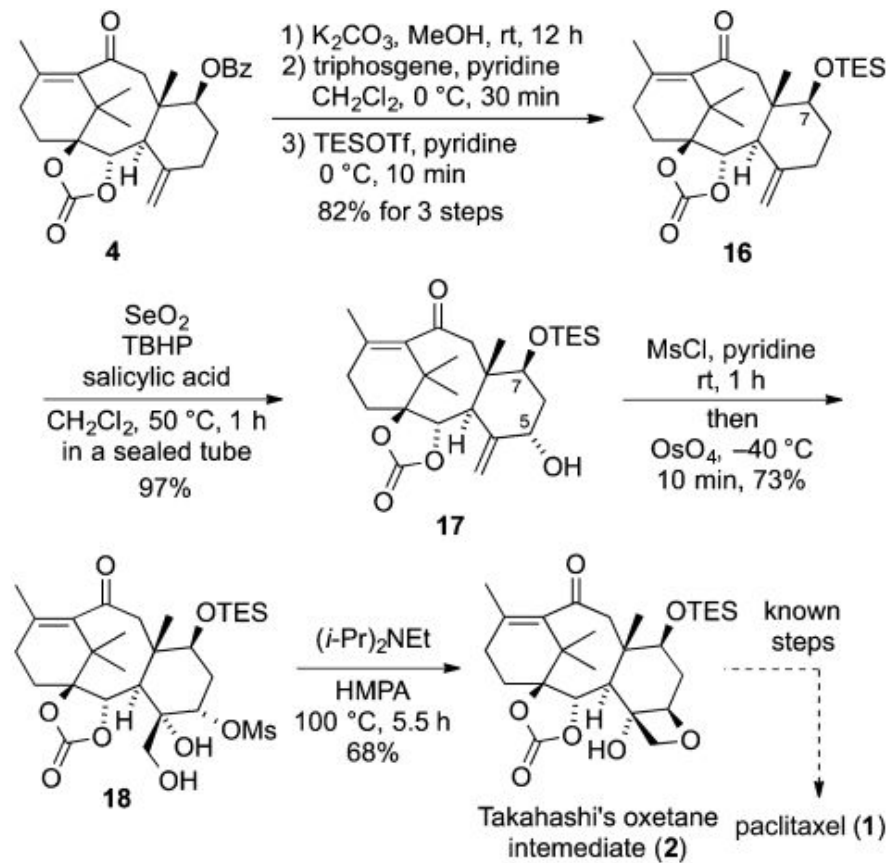
Construction of a Bridgehead Olefin by Chugaev Reaction



Synthesis of Taxoid 4

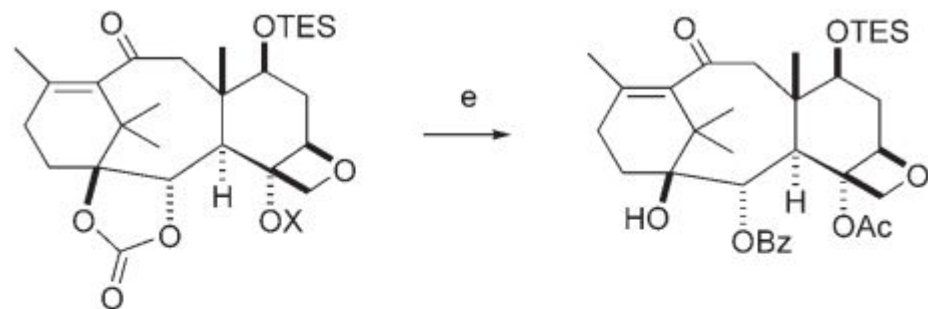


Synthesis of Takahashi's Oxetane Intermediate



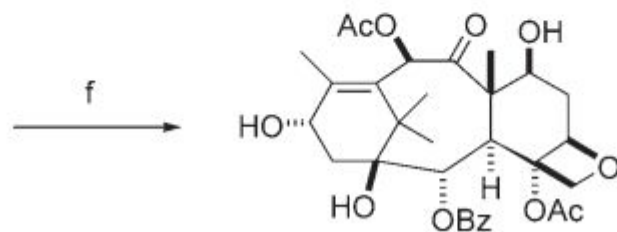
3. Total synthesis of Taxol (baccatinIII) by Takashi

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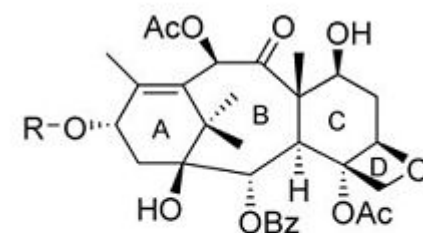
d $\left\{ \begin{array}{l} \rightarrow 43 \text{ (X = H)} \\ \rightarrow 44 \text{ (X = Ac)} \end{array} \right.$

45



(±)-baccatin III (2)

d) Ac_2O , DMAP, CH_2Cl_2 (70%); e) PhLi, THF, -78°C (70%); f)^[10] 1) $t\text{BuOK}$, $(\text{PhSeO})_2\text{O}$, THF, $-78 \rightarrow 0^\circ\text{C}$; 2) $t\text{BuOK}$, THF, -78°C (90%), 3) Ac_2O , DMAP, pyridine (50%), 4) PCC, celite, NaOAc, benzene, 85°C ; 5) NaBH_4 , MeOH (80%); 6) HF-pyridine, THF (80%). TES = triethylsilyl, HMPA = hexamethylphosphoric triamide, PCC = pyridinium chlorochromate. Bz = benzoyl.

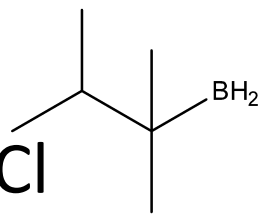


taxol (1): $(\text{R} = \text{Ph}-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}_2-\text{OH})$

baccatin III (2): $(\text{R} = \text{H})$

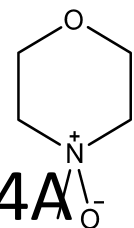
Abbreviation

• Thexylborane



• TBDPSCI $t\text{BuPh}_2\text{SiCl}$

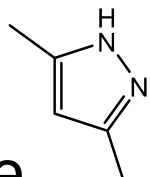
• TPAP Pr_4NRuO_4



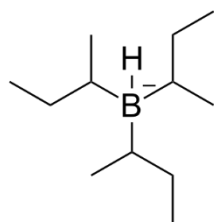
• NMO

• MS4A мол.сита 4A

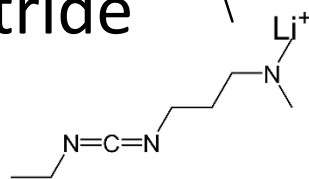
• 3,5-DMP



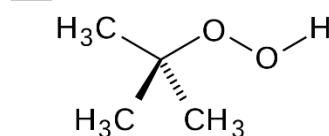
• L-selectride



• EDCI



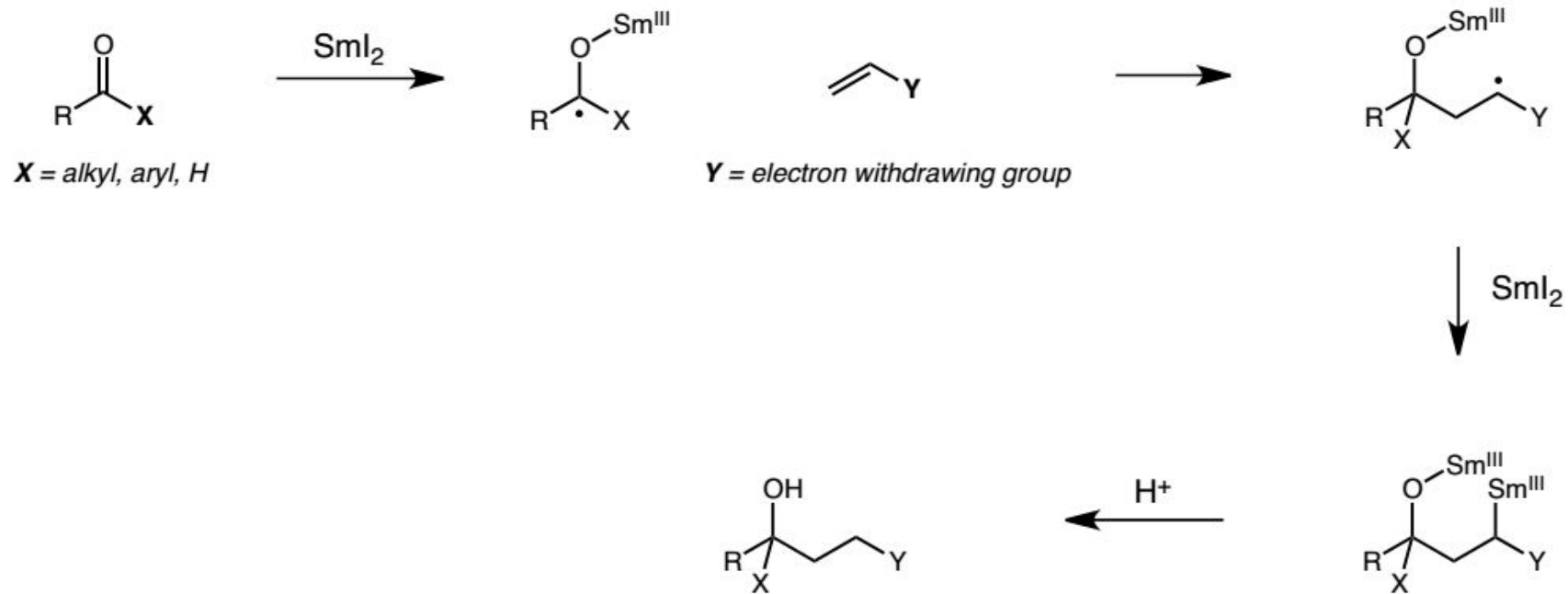
• TBHP



Carbon-Carbon Bond-forming Reactions Using SmI_2

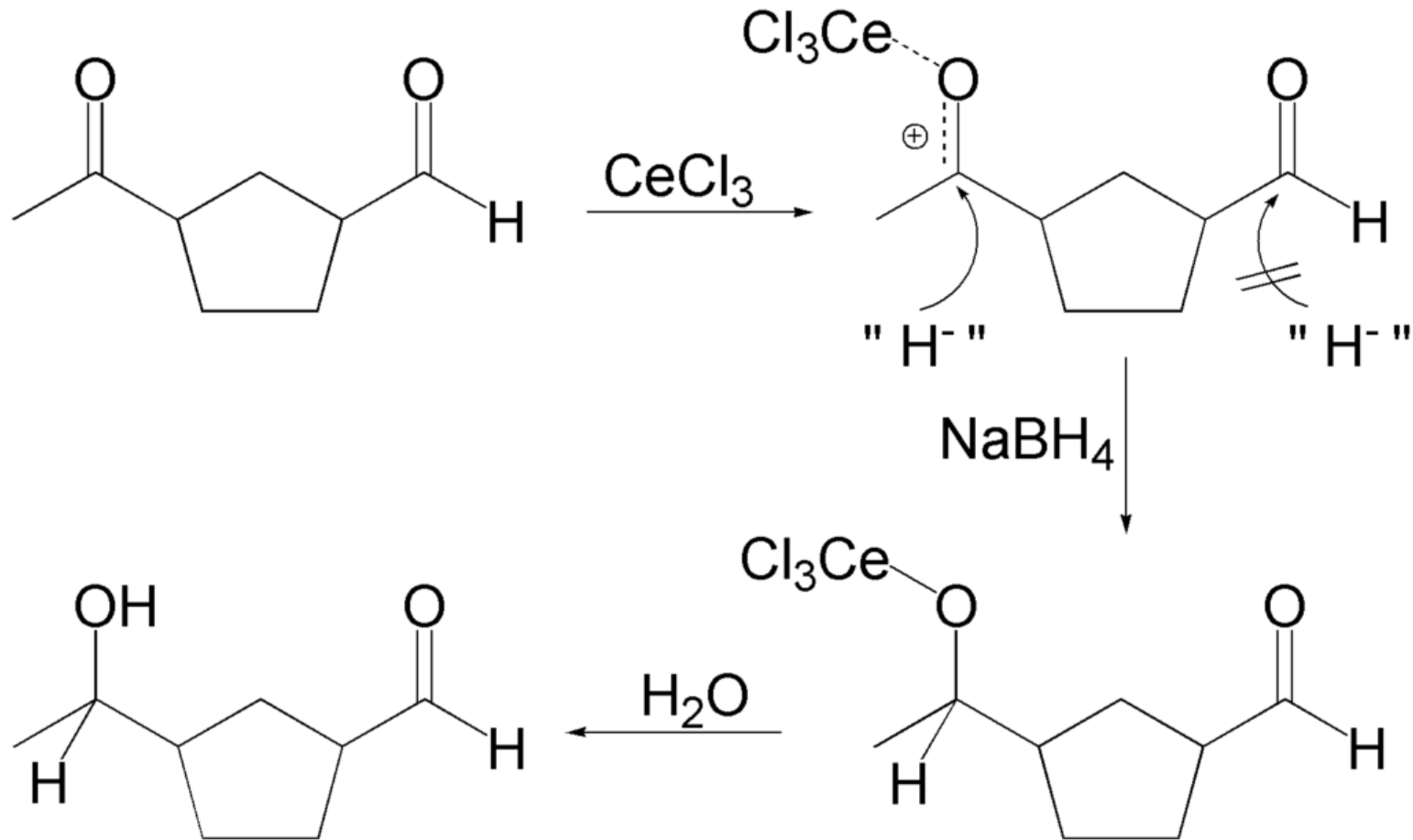
■ Carbonyl-alkene coupling

Traditional mechanism

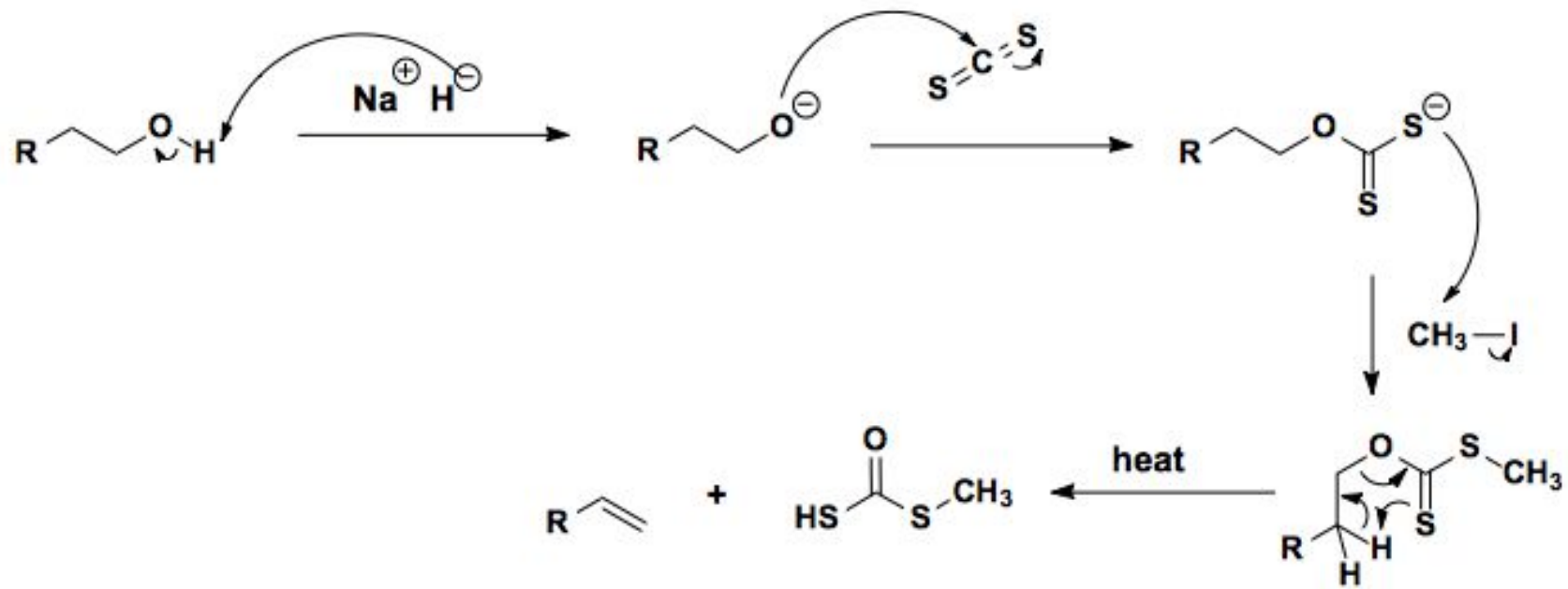


■ Intramolecular carbonyl-alkene couplings display a greater degree of tolerance in alkene components

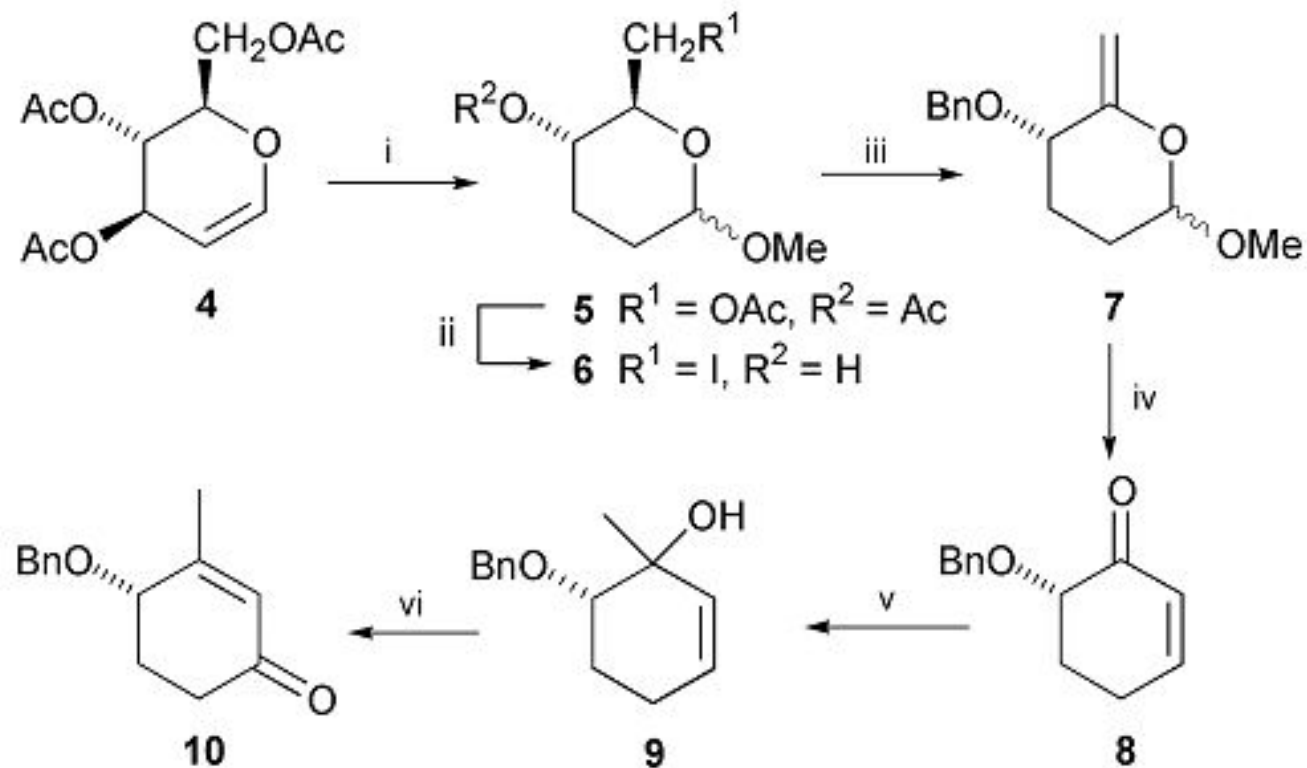
Lucho reduction mechanism



Chugaev reaction mechanism



Preparation of 7 from tri-O-acetyl-D-glucal



Scheme 1 Bn = $-\text{CH}_2\text{Ph}$. *Reagents and conditions:* i, MeOH, $\text{BF}_3 \cdot \text{OEt}_2$, PhH, 0 °C, then H_2 , 10% Pd-C, EtOAc, rt; ii, MeONa, MeOH, 0 °C, then I_2 , Ph_3P , imidazole, THF, rt; iii, NaH, DMF, 0 °C, then BnBr, $n\text{-Bu}_4\text{NI}$, DMF, 0 °C; iv, $\text{Hg}(\text{OCOCF}_3)_2$ (5 mol%), acetone– H_2O (2:1), 0 °C, then MsCl, Et_3N , CH_2Cl_2 , 0 °C; v, MeLi, Et_2O , -78 °C; vi, PCC, molecular sieves 4 Å (powder), CH_2Cl_2 , rt.