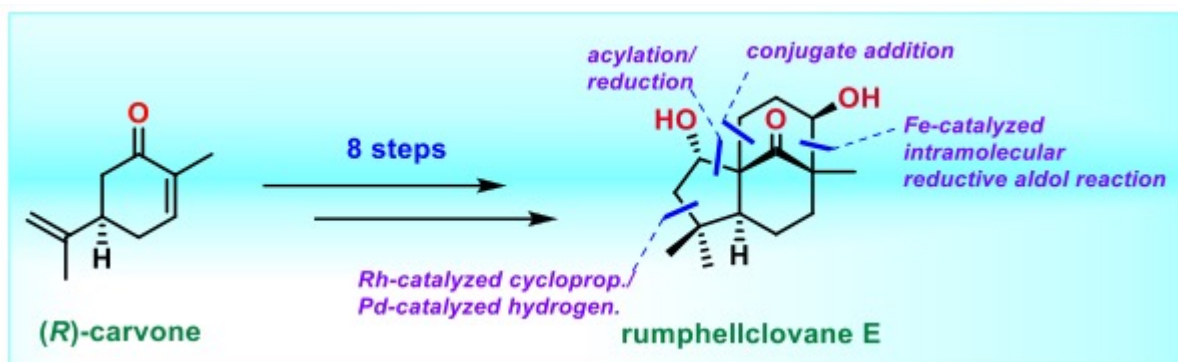


Asymmetric Total Synthesis of Rumphellclovane E

Guanggen Liu,[†] Zhijiang Zhang,[†] Shaomin Fu,^{*} and Bo Liu^{*}



- isolated from the gorgonian coral *Rumphella antipathies*
- tricyclo[6.3.1.0]dodecane ring system
- 3 stereocenters
- 8 steps synthesis in B–AB–ABC construction sequence
- this synthesis serves as a general platform to concisely access the clovane-type sesquiterpenoids.

Danylo Hatych
Liu Research Group
Total Synthesis Presentation
02/10/2021

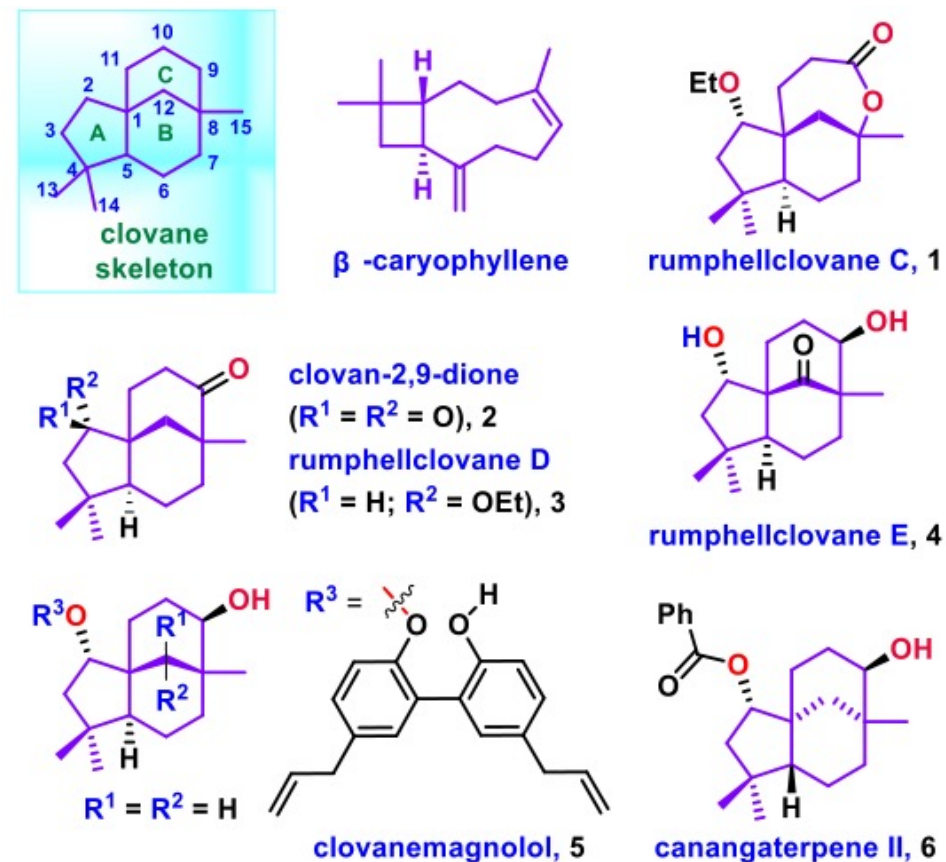
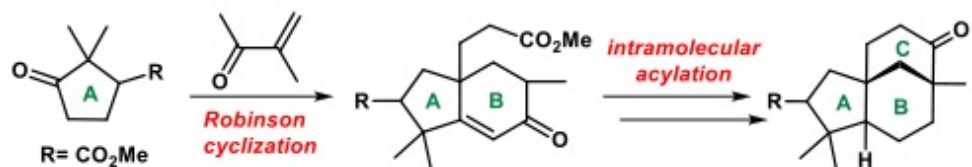


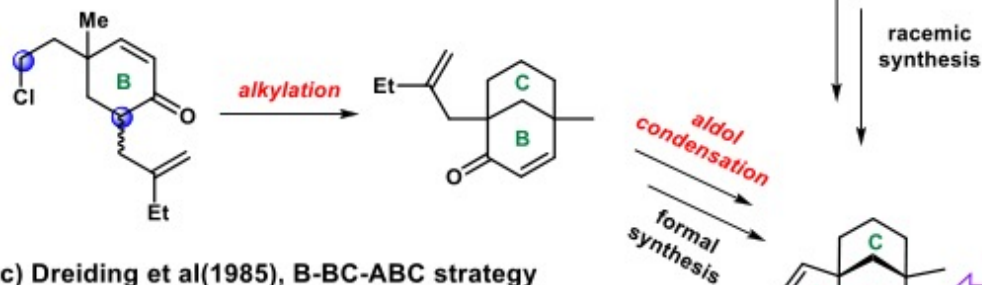
Figure 1. Representative examples of clovane-type sesquiterpenoids.

Scheme 1. Progress in Syntheses of Clovane-type Natural Products

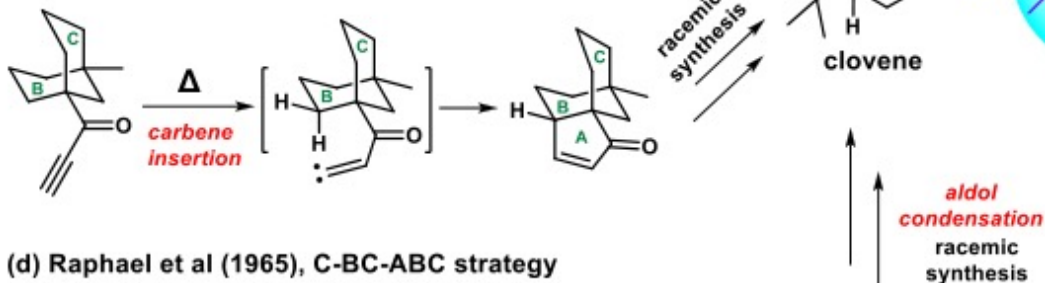
(a) Becker et al(1965), A-AB-ABC strategy



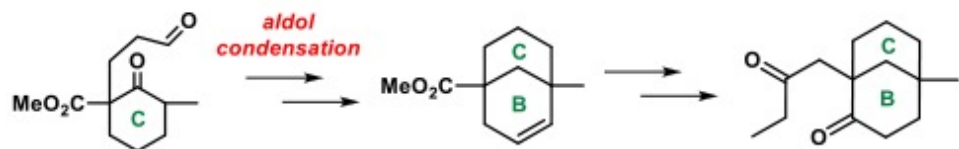
(b) Schultz et al(1983), B-BC-ABC strategy



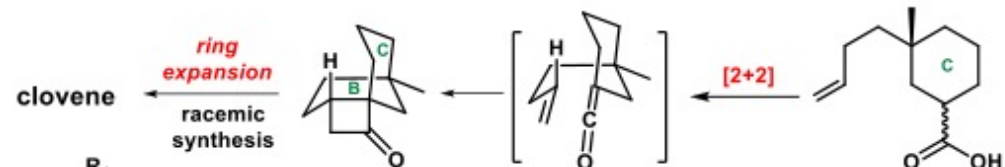
(c) Dreiding et al(1985), B-BC-ABC strategy



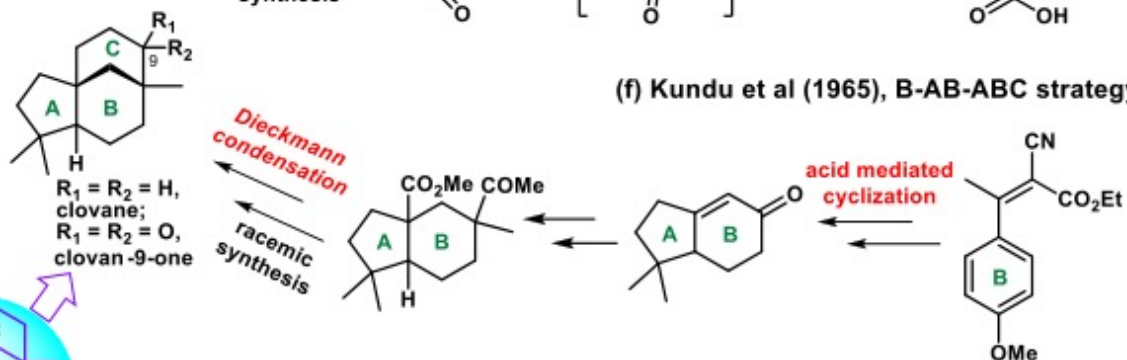
(d) Raphael et al (1965), C-BC-ABC strategy



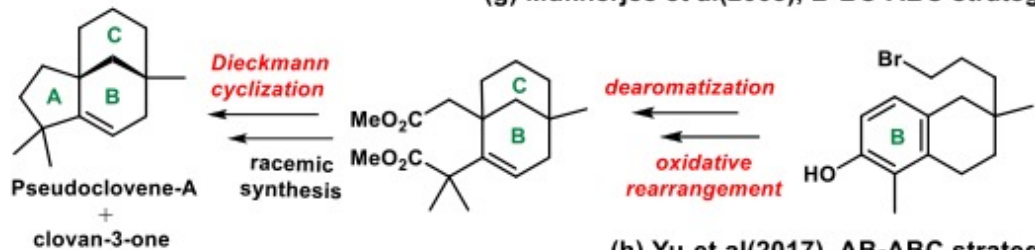
(e) Funk et al (1988), C-BC-ABC strategy



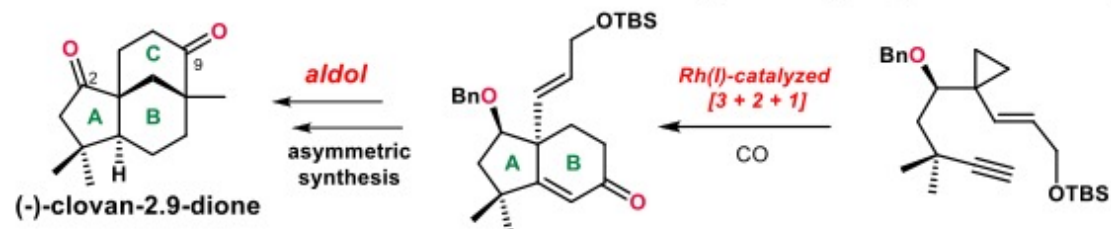
(f) Kundu et al (1965), B-AB-ABC strategy



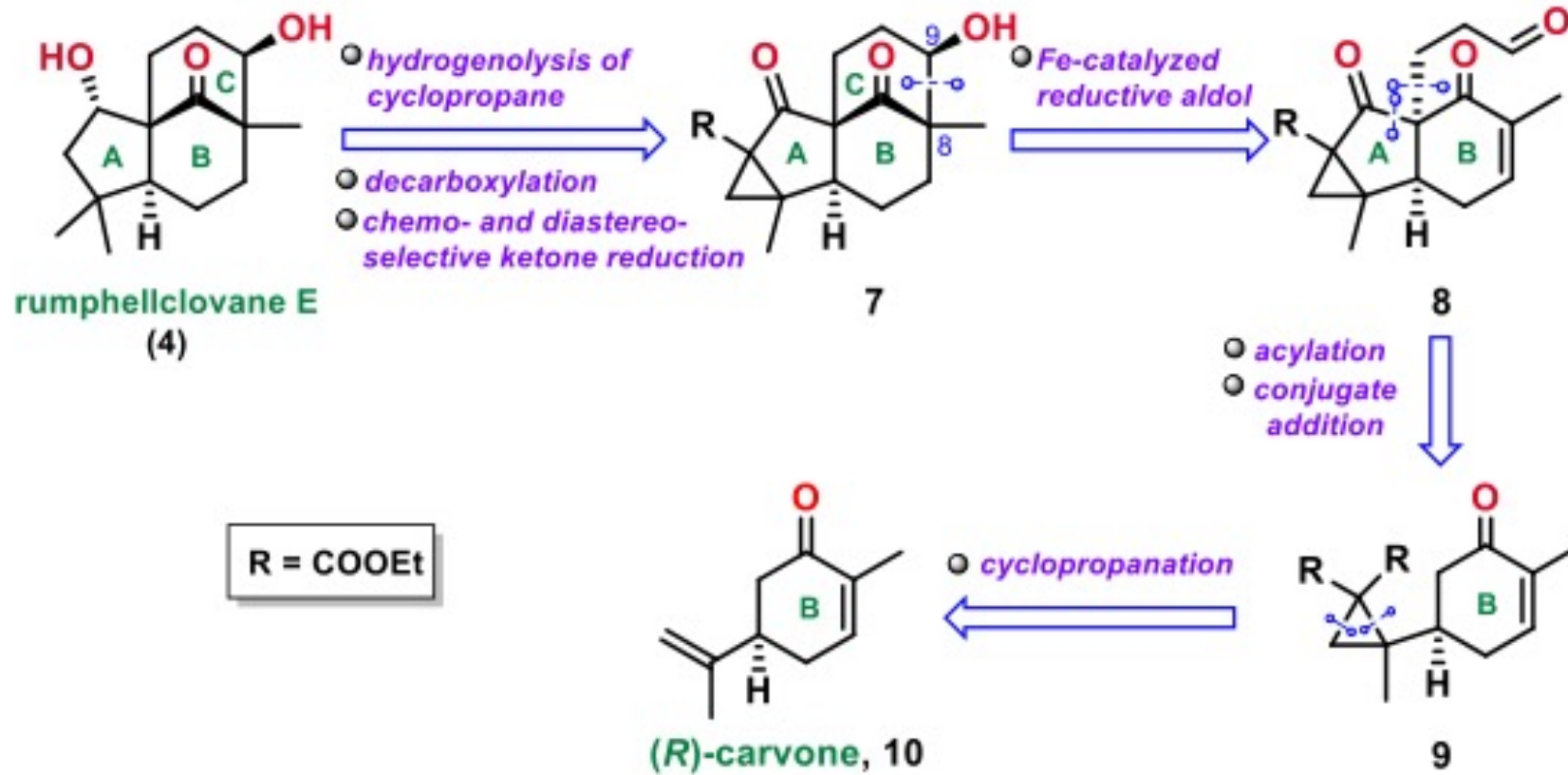
(g) Mukherjee et al(2003), B-BC-ABC strategy

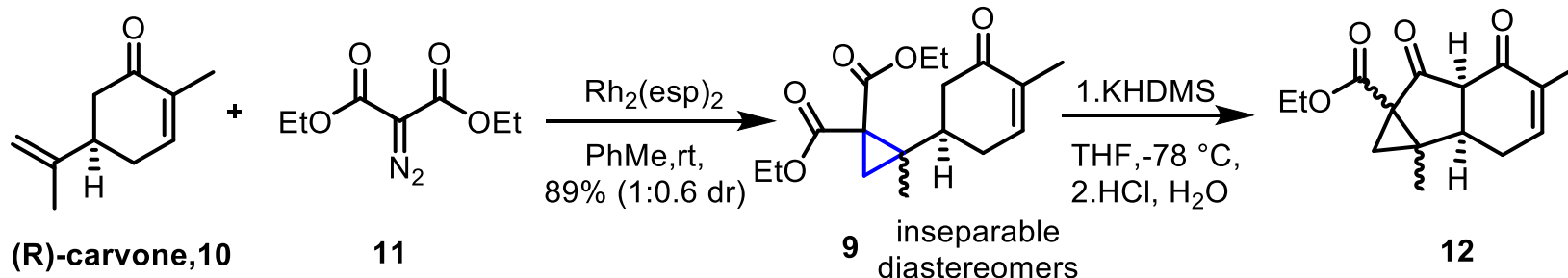


(h) Yu et al(2017), AB-ABC strategy

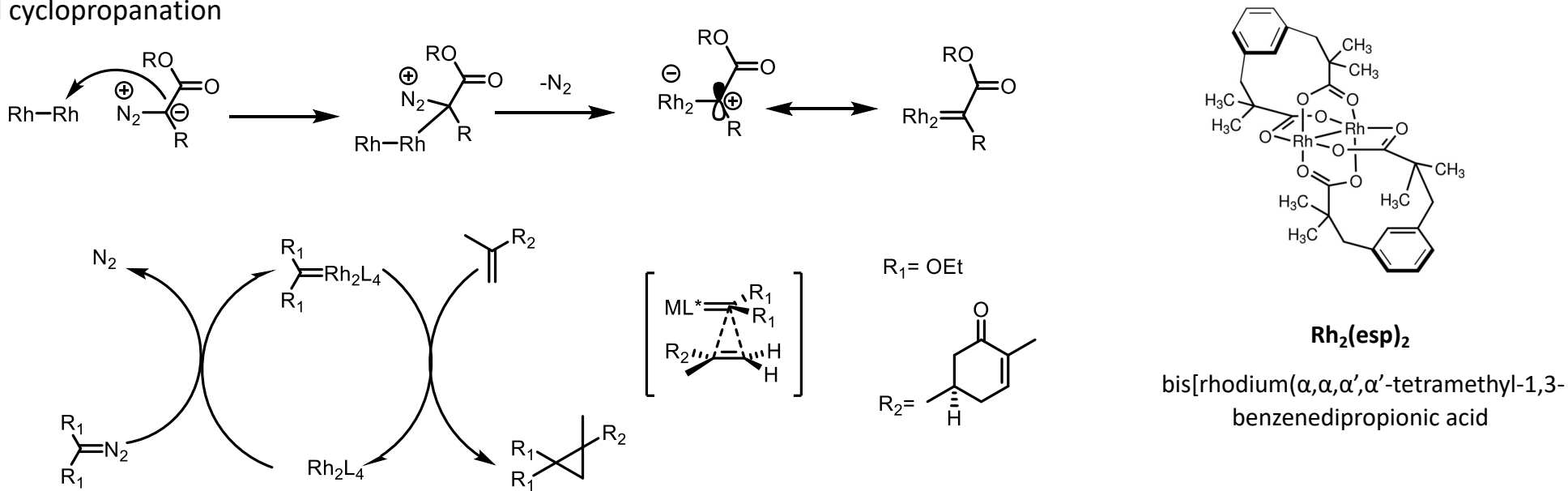


Retrosynthetic analysis of Rumphellclovane E

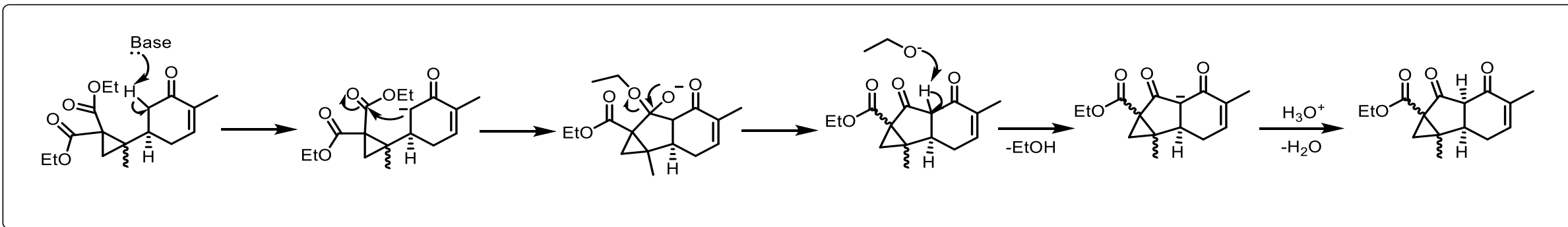


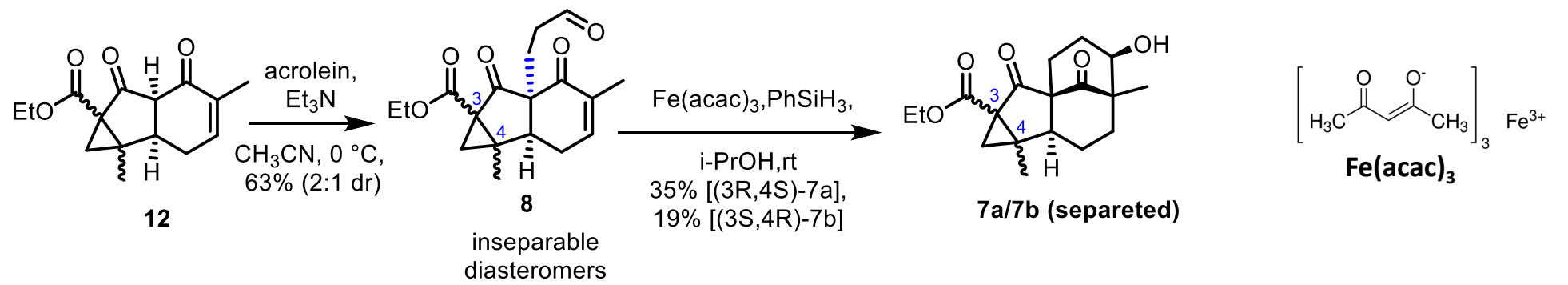


From **10** to **11**: Rh-catalyzed cyclopropanation

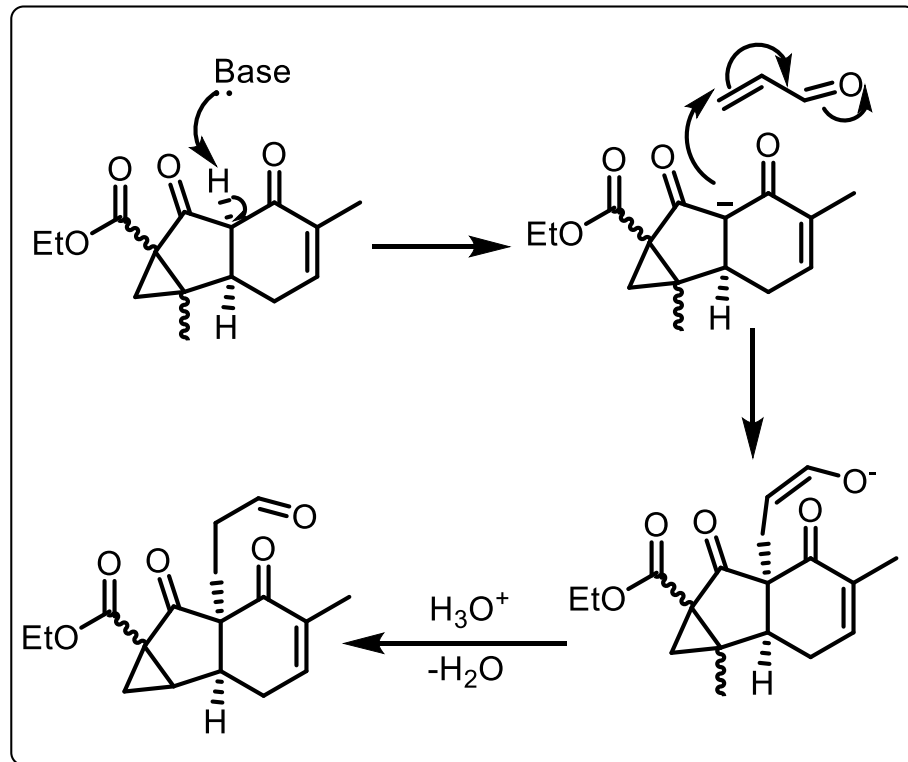


From **9** to **12**: Intramolecular acylation

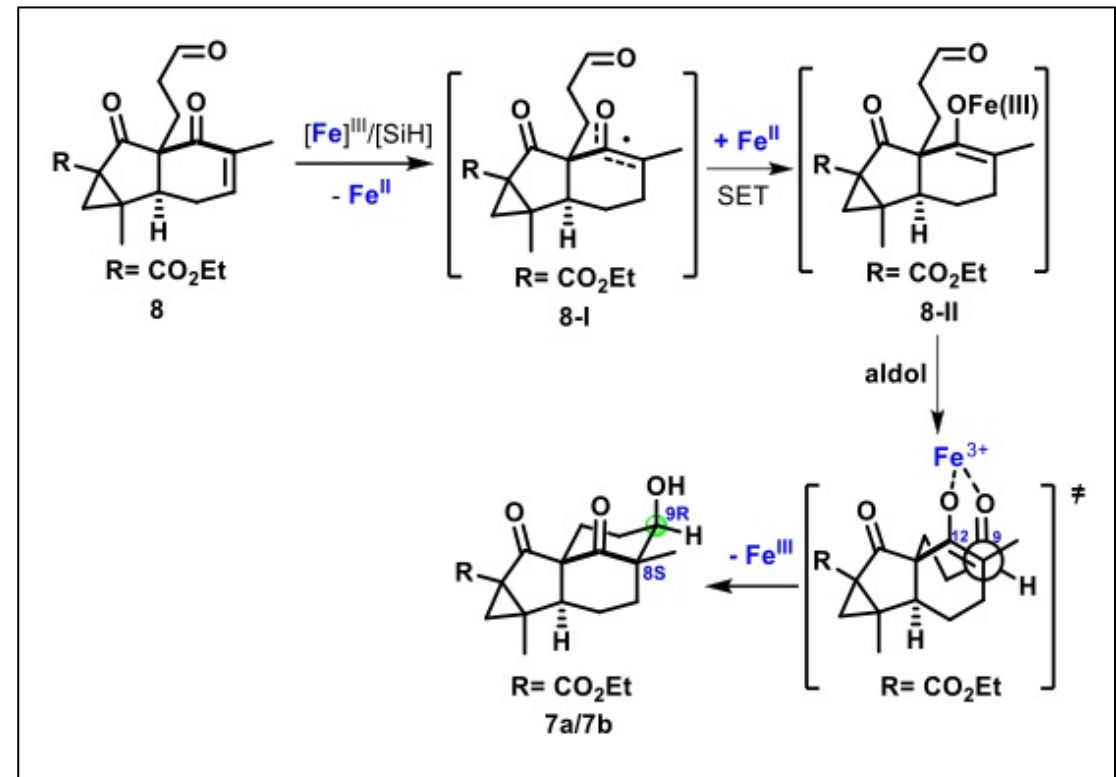


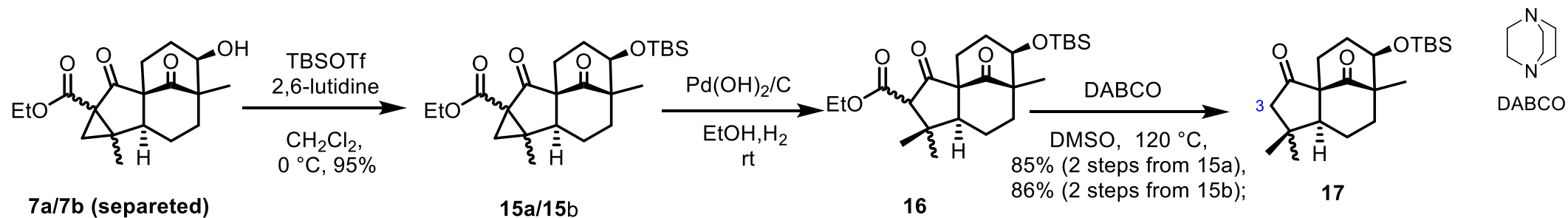


From **12** to **8**: Michael addition

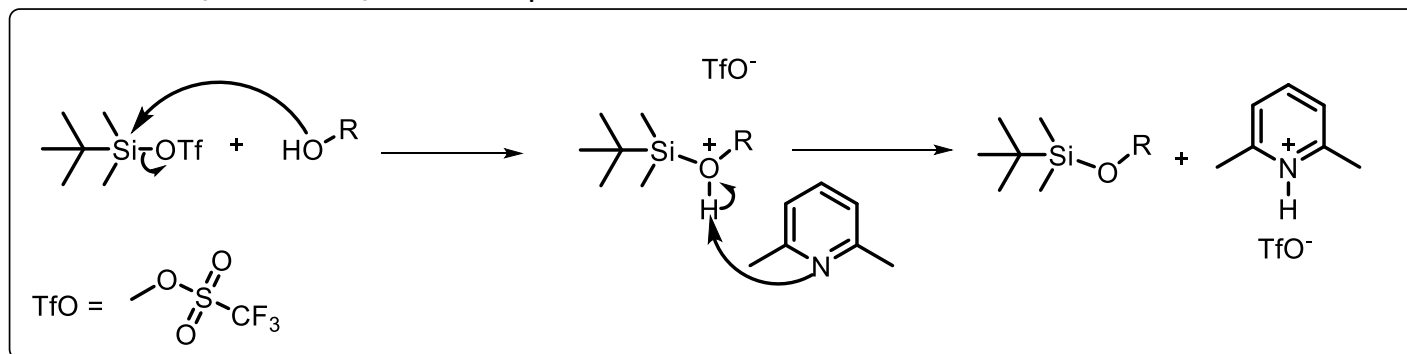


From **8** to **7a/7b**: Metal-catalyzed reductive aldol reaction

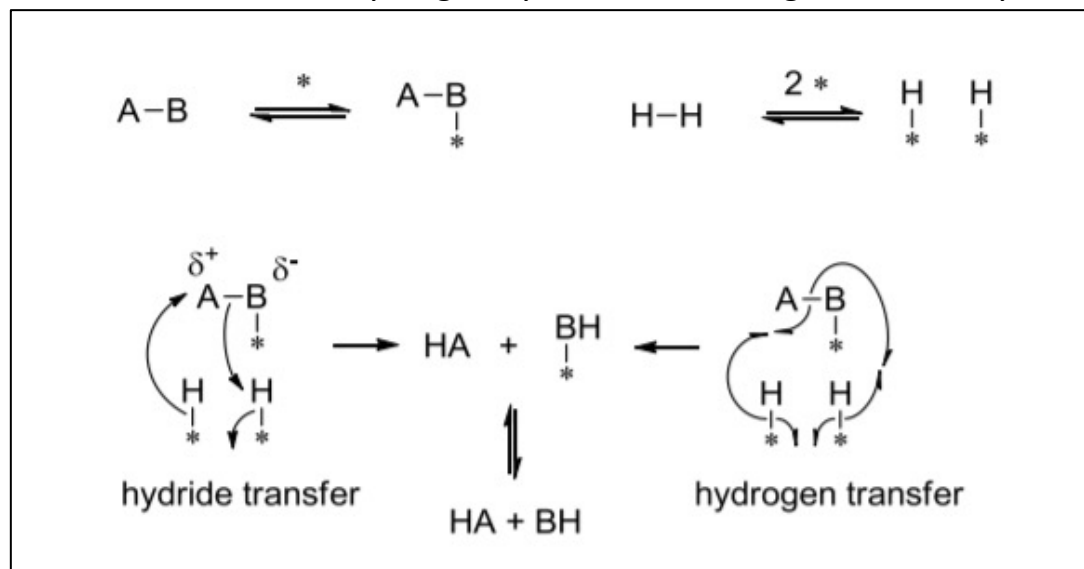




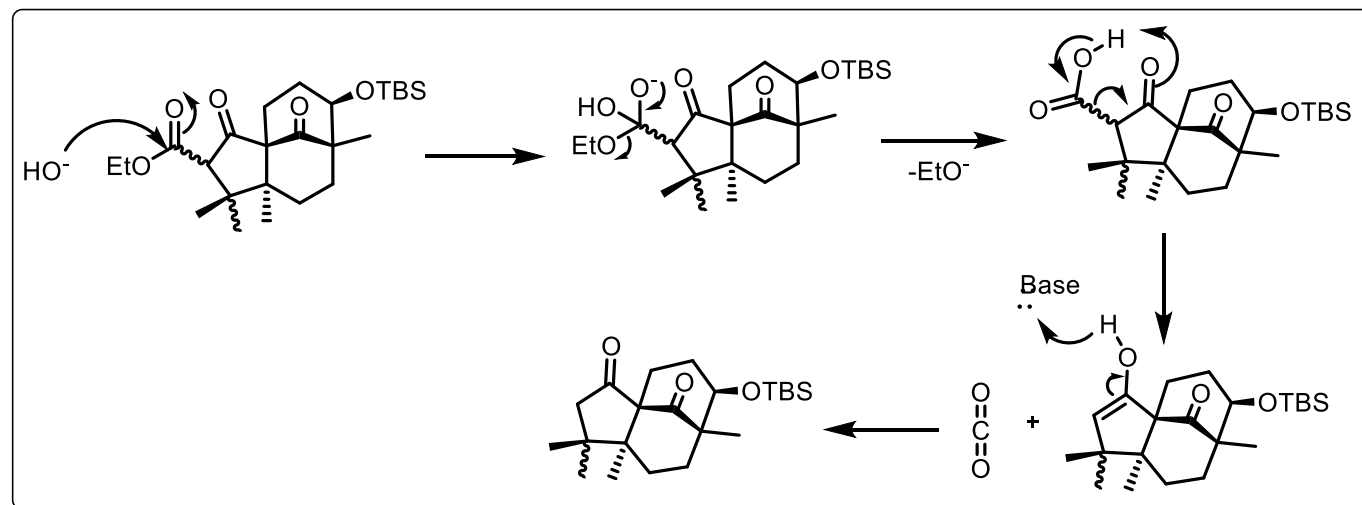
From **7a/7b** to **15a/15b** : TBS protection of alcohol

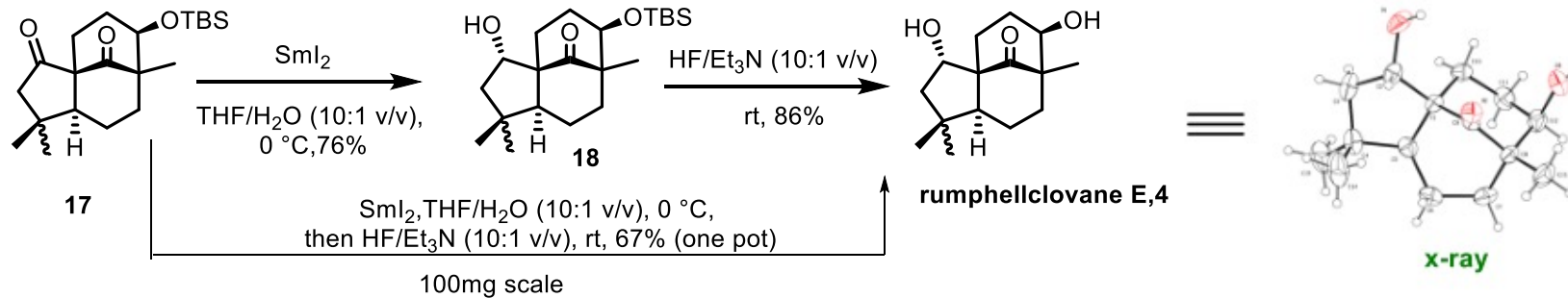


From **15a/15b** to **16**: Hydrogenolysis under heterogeneous Catalysis

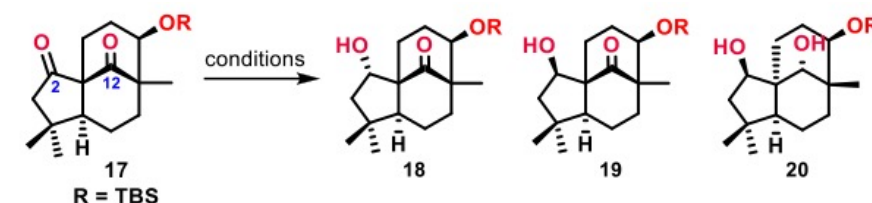
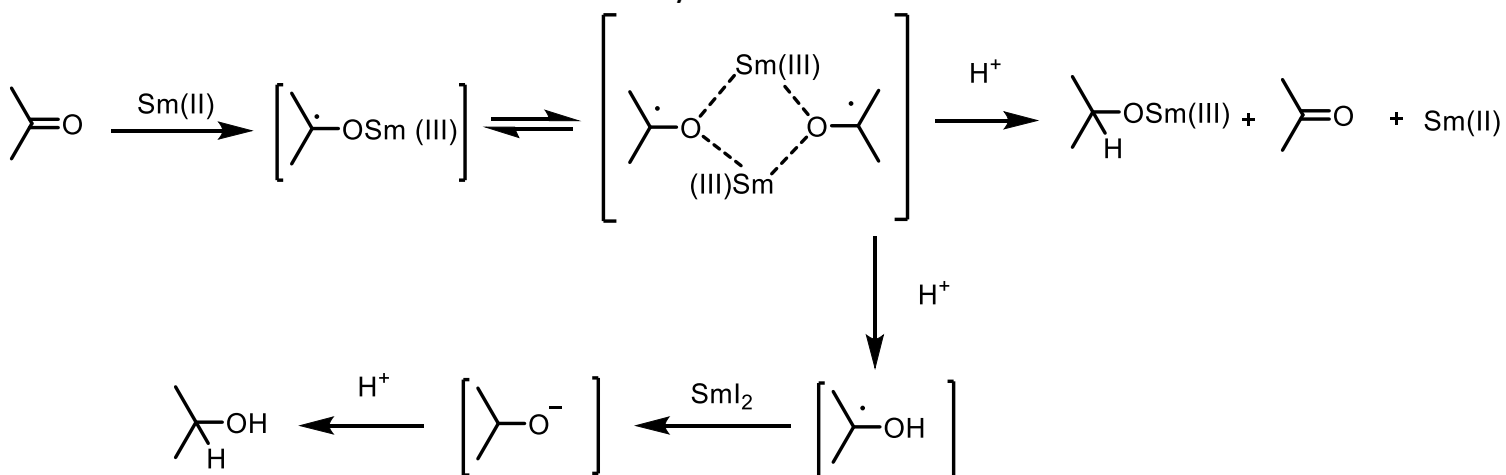


From **16** to **17**: Hydrolysis and decarboxylation



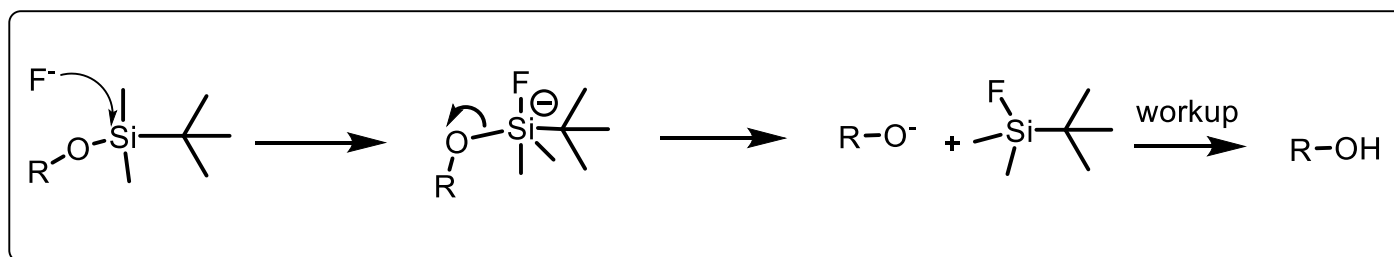


From **17** to **18**: Selective reduction of carbonyl

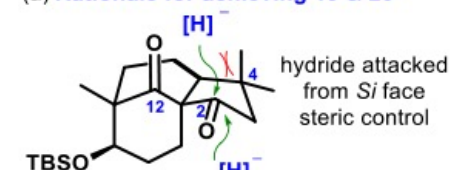


entry	conditions	yield ^a (%)
1	1 equiv of NaBH ₄ , MeOH, -78 °C	19 , 73
2	1 equiv of LiAlH ₄ , THF, -78 °C	19 , 69
3	1 equiv of (<i>R</i>)-CBS, ^c 1.5 equiv of BH ₃ , THF, -78 °C	20 , 65
4	1 equiv of (<i>S</i>)-CBS, ^d 1.5 equiv of BH ₃ , THF, -78 °C	20 , 51 (72% brsm)
5	0.1 mol/L of SmI₂, THF/H₂O(10:1 v/v), 0 °C	18 , 76
6	0.1 mol/L of SmI ₂ , THF/MeOH (10:1 v/v), 0 °C	nr ^b

From **18** to **4**: TBS deprotection



(a) Rationale for achieving **19** & **20**



(b) Rationale for achieving **18**

